ПРОПЕДЕВТИКА ВНУТРЕННИХ БОЛЕЗНЕЙ

Под редакцией
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Издательство «Медицина»
Москва

INTERNAL DISEASES

An Introductory Course

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Translated from the Russian by
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Mir Publishers
Moscow

First published 1987
Second edition 1990
Revised from the 1989 Russian edition

Printed in the Union of Soviet Socialist Republics

На английском языке

ISBN 5-03-001686-4

PREFACE

Internal medicine is the major branch of medical practice and research because internal diseases are the most common and run a grave and protracted course involving many complications and impairing the patient's objective condition and his working capacity. Internal diseases have the highest mortality rates as well. Therefore prophylaxis of internal diseases is the main concern in the health care system of all countries, and the study of internal diseases is the leading subject of medical training.

The term "internal diseases" came into use in the 19th century to stand alongside with the then-popular term "therapy". The development of new, complicated methods of diagnosis and treatment, requiring specialized skills and training on the part of the physician, has led to the formation of separate branches of medicine such as cardiology, gastroenterology, endocrinology, and haematology. This by no means indicates the division of the concept of "internal medicine" into "daughter subjects". Clinical medicine of the second half of this century is characterized by parallelism of differentiation and integration. Therefore, despite a further separation of special branches, general medical training and education, and the integrating research into internal diseases and related subjects are now even more important.

It should also be noted that the new offshoots of medicine develop at the "interface" of several clinical subjects. Thus cardiology, which was formerly only a branch of internal medicine, gave rise to heart surgery and anaesthesiology.

At the present time the knowledge of internal diseases has improved greatly: many new diseases have been described, the aetiology and pathogenesis of the known diseases and their clinical course studied, and new methods of diagnosis and treatment have been developed and improved. Therefore, despite the branching of internal medicine into special subjects, the amount of knowledge that is necessary today for a practitioner is much greater than say 20 or even 10 years ago. The requirements for adequate medical training have thus increased accordingly.

The course in internal diseases is given differently in various countries: the student may be educated at one clinic during his entire course of studies, or he may take classes in different departments consecutively. But in all cases there exists a certain optimum sequence in the studies. During their first years (usually the third year) the students study the main methods of examination, symptoms of internal diseases, and the main principles of

their management. This book is a course in diagnostic principles and special pathology. In other words, this is an introduction to therapy, or *propaedeutics* to internal diseases. This course is given to students after they have studied the fundamentals of medicine, such as anatomy, physiology, biochemistry, etc.

During their further studies the students broaden and improve their knowledge of all major internal diseases, their differential diagnoses, and their treatment. The students start managing patients independently. Future physicians are thus trained in stages.

This particular manual is intended for third-year medical students. It describes symptoms and syndromes, the main methods of examination used by internists and methodology of diagnosis. It helps students master the practical diagnosis of internal diseases and their management. The authors hope that this manual will help the student in his further detailed study of internal diseases and that it may also be useful to those who master other special medical subjects. The authors believe also that this book may be helpful to a practitioner.

The contributors to this manual are members of the staff of the Moscow First Medical Institute named after I. Sechenov.

The authors would gladly accept any criticisms or comments which would improve this manual.

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GENERAL PART

Chapter 1

INTERNAL MEDICINE: SUBJECT MATTER, PURPOSE AND OBJECTIVES

General Concepts

Internal medicine encompasses the majority of human diseases and is the most important area of practical medicine. This is the science of diseases of the internal organs and the entire body.

S. P. Botkin, the great Russian physician and scientist, defined the objectives of practical medicine as follows: "The most important and essential objectives of practical medicine are the prevention and treatment of disease, and the alleviation of the patient's suffering". Once we assume that the first objective of a physician is to reveal disease, we must then define what a disease is. What causes a disease, and what is actually a disease? What must we investigate and learn? We all know in general terms what a disease is, but this does not mean that the disease has been understood. The general concept of disease, its essence and genesis, have undergone significant changes during the progress of medicine; and the purpose and objectives of diagnosis have changed accordingly.

Health and disease are opposite yet interdependent forms of the organism's functioning in the physical and social environment. Health is defined by (a) the integrity of the organism (in the broad sense this word implies anatomical and functional integrity, and the absence of injury), (b) sufficient adaptability by the body to the environment; quantitative objective characteristics are very important in this respect. Just as disease may have various degrees of severity, so health can also be weak or strong, and it is determined by the reserves in the body's organs and systems, accurate functional regulation, homeostasis, etc. (interdependence of the body and the environment is the basis of their integrity); and (c) good disposition (this is a subjective criterion, since e.g. euphoria does not rule out pathology).

What then is a disease? Disease is not only an anatomical or functional disorder caused by a pathogenic or an extraordinary stimulus; neither is it their total; it is rather a whole set of changes which arise from affections. Changes in the body in response to stimuli or damage are considered as a

response or reaction. This is manifested by functional and morphological processes. But a disease in its pure form, where one can easily differentiate between a damage and the response to it, occurs infrequently, e.g. an injury, an acute infection, etc. A clinicist who treats patients, especially those with chronic diseases, observes a complex of secondary, tertiary and other phases and stages of the damage and the response of the body to this damage.

The first essential sign of a disease is damage caused to the organism (damage to its integrity, its "breakdown", structural damage, functional disorder, the absence of enzymes or other biologically active substances, insufficient homeostasis, etc.).

Another important sign of a disease is the body's response to various affections; response to a stimuli is one of the fundamental properties of a living body (irritation function). A dead body does not respond to damage. Damage and a response to it are the requisite and sufficient signs for the basic definition of a disease. *Disease is a response of the body to its damage.* It is understood that the entire body responds to damage: a local affection causes a response in the entire body, since the response is the complicated result of activity of many systems of the living body. Our definition "a disease is a response of the body to its damage" expresses the *dialectical contradiction* of the development of pathology: two incompatible and mutually interconditioned opposite processes (i.e. damage and response) occur simultaneously. It should be noted that the response (or a chain of reactions) in a living organism is mediated. The body does not act directly against the external aetiological factor (physical, chemical, etc.) but it develops a reaction to the damage, to the changes in the structure and the functions of the body itself that are caused by the pathological factor. This response depends both on the perceptive apparatus (receptors) and on the entire regulatory system. This corresponds to the biological law which states: environmental conditions are altered by the body and converted into its internal conditions. In a physiological sense, a stimulus causes changes in tissues (receptors) to induce or inhibit various functions; the quality of the function depends on the basic properties of the tissue or organ (muscle, glandular or nervous tissue, etc.), their functional state at the moment of stimulation, and on the intensity of the stimulus rather than on the character of the stimulus.

In pathology an injury (depending on its character and localization) accounts for the response by the tissue, the system, and the entire body. A very complicated chain reaction occurs, including activity of the first, second and third order, involving several systems. Pain, for example, develops in an injured tissue as a result of the action of bradykinins that are formed in the injured tissue, on the corresponding receptors; an inflam-

matory reaction of tissues is connected with the action of mediators produced in the damaged cells. It is well known that body response to damage often eliminates the defect for the survival of the entire body, i.e. the body response is an adaptive reaction. This special property is the result of "experience" of many millions of generations of living organisms. Patients often recover before any therapy. If a person has a history of a certain disease (e.g. measles, smallpox, etc.) his body is protected from repeated infection: it acquires increased specific and non-specific resistance to the pathogenic factor.

But the response to damage cannot always be regarded as an adaptive reaction. These responses can even sometimes be dangerous to the body, e.g. in autoallergy; carcinoma cannot be regarded as an adaptive reaction to the irritating factor that damages the complicated apparatus of the cell.

Our definition of disease explains the initial purpose of diagnosis: identification (and differentiation) of diseases, what is the damage and what is the response to this damage, and what form of adaptation has occurred in each case. Of course, this is only the initial stage of diagnosis; the correct character of the response and the damage must always be determined in order to give appropriate treatment.

Definition of disease is based on the initial and most general signs; these signs are of major importance for us. Needless to say that disease in man is not only a biological but also a social phenomenon; there is not only a somatic but also a psychic suffering.

Our traditional requirements for complete identification of disease (revealing symptomatology, morphological and functional changes in the body, the causes and pathogenesis of the disease) can be defined as generalized concepts of individual diseases or nosological entities. Although there is no unified classification of diseases, one must consider the qualitative differences between them. The existing classification of internal diseases is characterized by the following two signs: aetiology of the disease and the site of affection.

Diseases of definite aetiology are classified by the aetiological principle, e.g. acute and chronic infectious diseases, injuries, etc; in some cases it is necessary to specify the main site of affection, like the syphilis of the liver. Other diseases are differentiated by the affected organs (localization). This is especially so if the aetiology is unclear or not very important from the practical standpoint, e.g. ulcer of the stomach, cirrhosis of the liver, colitis, or pancreatitis. Pathogenesis rather than the cause is important in certain other diseases since the cause may be unknown, e.g. allergic sensitization. Finally, there are diseases that are classified by their special anatomical and functional characteristics. These are tumours.

It should be remembered that disease is a general response by the body

which is regulated by the nervous and humoral systems; an affection of an organ is a most pronounced local manifestation of the response of the entire body; the special localization of the process depends on the causative factor and on the condition of the body before the affection. In every disease the entire body is involved. For example, the main site of affection in pneumonia is the lungs, but the cardiovascular system and many other organs of the body are involved simultaneously.

Causes of disease. "Our concept of disease is closely connected with its cause, which always depends on the environmental factors affecting the body either directly or through the agency of its close or remote relatives" (Botkin).

The following causes of disease are distinguished: (1) mechanical (closed and open injuries, concussion, etc.); (2) physical (high or low temperature, electric current, light, radiation); (3) chemical (spoiled foods, poisons); (4) biological (microorganisms); (5) psychogenic; (6) genetic (hereditary).

Strong emotions, fear, and frustration disrupt equilibrium of the normal nervous processes (inhibition and excitation) in the cerebral cortex. They change the activity of the subjugated subcortical vegetative centres regulating the function of the internal organs and upset hormone regulation. The environmental factors (the word included) can strongly affect the activity of various organs through the agency of the nervous system. In some cases they may cause disease (by disturbing function of the heart, stomach and other organs or causing essential hypertension).

Most diseases develop as a result of the combined action of many factors, such as unfavourable living conditions (inadequate nutrition, fatigue, overstrain, excitation, etc.). They upset the regulatory and protective function of the nervous system to impair the adaptability of the body to the changing environmental conditions. The resistance of the body to harmful factors (infection, poison, etc.) is decreased allowing a disease to develop. Congenital and acquired specific features and properties of the body are important in aetiology of diseases. They weaken body resistance to harmful environmental factors. A person with congenital heart disease may develop a grave circulatory insufficiency when physically overstrained. Asthenic persons when weakened by a grave disease or malnutrition are more susceptible to infectious diseases.

A thorough study of causes of weakening of the body in persons affected by disease, and especially the causes of spreading of diseases among population, shows that good health largely depends on the environment and the conditions of work and home life, i.e. social factors. Russian medical workers always emphasized the importance of the environment in the development of pathology. According to a prominent Russian clinicist

A. Ostroumov (1844-1908), "the task of a clinical examination is the study of living conditions of man in the environment, his adaptability to the environment, and disorders". Soviet scientists also emphasize that social environment and relations between people are decisive for their health. Due to favourable social conditions in the Soviet Union morbidity among population decreases significantly and medico-prophylactic activities widely develop. A medical worker must therefore have a profound knowledge of the biological and social principles of medicine.

Sometimes a disease develops suddenly and lasts a comparatively short time. Such diseases are called acute. Chronic diseases are characterized by prolonged course and may exacerbate periodically. The main disease may provoke another, sometimes grave disease to develop. For example ulcerous perforation of the stomach causes an acute inflammation of the peritoneum. Such a new affection is called a *complication* of the disease. Sometimes, a disease may recur after a patient recovers. This is a *relapse. A* patient may have more than one disease at a time. A person with a gastric ulcer may have bronchitis. The more severe disease is called the *main* disease, while the other disease is the *concurrent*, or *concomitant*. A person may recover completely or the disease may become chronic; a possible outcome of disease is death of the patient.

Successful treatment of disease becomes only possible with a correct diagnosis (a good diagnostician is a good doctor), and with identification of the cause of the disease, the specific properties of the patient, the course of the disease, and the knowledge of various medical means.

Diagnostics (Gk *dia* through, *gnosis* knowledge) is the science of methods by which diseases are identified. It is the branch of medicine dealing with methods for the examination of patients in order to identify a disease, determine the patient's condition and prescribe the appropriate treatment and prophylaxis. The term diagnostics also implies examination and observation of the patient by the doctor who makes a conclusion about the disease and the patient's condition. Diagnostics as a science studies anatomical and physiological features of man and his relationships with the environment.

Diagnosis is a concise conclusion by a doctor of the essence of the disease and the patient's condition, expressed in terms of modern medical science. *Diagnosis morbi* (definition of the disease according to the accepted classification) and *diagnosis aegroti* (determination of individual characteristics of a given patient) are distinguished. The disease is identified on the basis of the examination of the patient and the study of symptoms of the disease. The result of a diagnostic examination is the diagnosis of the disease.

Diagnostics includes: (1) the study of methods of observation and ex-

amination of the patient (physical and laboratory-instrumental methods); this is the medical *diagnostic technique;* (2) the study of the diagnostic value of the symptoms of the disease; this is known as *semeiology* (Gk *semeion* sign) or symptomatology; and (3) the study of special ways of pondering aimed at identification of the disease— *diagnostic methods.*

In compliance with the main tenets of the Soviet clinic the following general trends should be followed as precursors of treatment during each diagnostic examination:

1. Disease is a response of the body to damage. Clinical analysis should therefore include the study of both damage and the response. The adaptive tendencies of the response should also be determined.

2. The principle of integrity or unity of an organism requires a complete diagnosis of the disease and the study of the condition of all physiological systems of the body, and also of the patient's personality.

3. The principle of unity of the organism and the environment is the basis for aetiological analysis of the relationships between the patient and the environment, including social factors.

4. The principle of nervism requires the concrete study of the role of the nervous system (higher nervous activity included) in the development of the disease.

The main object of a physician is to cure his patient. Recovery in most diseases is either impossible or takes much time unless timely and effective medical aid is given to the patient. Some patients will inevitably die unless urgent treatment is given. Some diseases can be cured by the inner forces of the body, and any recovery is impossible without their active involvement. Hippocrates would say that "Nature will cure most ailments if she is given a chance". A physician only helps Nature. The main object of treatment is therefore *to maintain and increase the forces of the patient* in his struggle against the disease. Another important principle is to "do no harm" to the patient by inappropriate action, since the patient's health is already impaired by the disease.

Best results may be attained where the cause of the disease can be removed. For example, a poisoned patient may be given an antidote or the poison may be removed from his body, or the causative agent may be killed by antibiotics or sulpha drugs. This treatment is called casual or aetiological. But the cause is not always known and cannot therefore be removed. The purpose of treatment then is to act on the mechanism of the disease development (pathogenesis), to provide good conditions for the patient's struggle against the harmful effects, to facilitate and improve the function of the affected organs, to strengthen the patient, for example, by improving his diet, leisure, climatic conditions (tuberculosis patients), or by giving digitalis to patients with cardiac insufficiency. This treatment is known as pathogenetic treatment.

Treatment may also be symptomatic by which only some symptoms of the disease are removed. For example, strong pain may be abated by morphine, while the cause of the pain or the mechanism of the pathological process in not affected by this treatment. Symptomatic treatment is often given along with aetiological or pathogenetic therapy.

The doctor must treat the patient rather than the disease (M. Mudrov). For example, a tuberculosis patient may need an envigorating therapy and climatic treatment, while another requires surgical intervention. Treatment should therefore always agree with the character and the course of the disease, individual properties of the patient, and the condition of his nervous system. Psychotherapeutic action on the patient is also requisite. Outstanding Russian clinicists, such as Mudrov, Botkin, Ostroumov, and Zakharyin, always took into account the psychic factor. They emphasized that the psychic influence of the doctor on the patient is of great therapeutic importance. The task of medical personnel is first to calm the patient, and to remove his fears and anxiety for the outcome of the disease, then to persuade the patient that the outcome will be favourable, and to strengthen his will-power which is necessary for a successful fight against the disease.

From the very start of the treatment, the physician should work out his tactics thoughtfully and do his best to implement his planned therapy. The planned treatment includes out-patient (home) and hospital treatment, adequate care, accurate fulfilment of the doctor's prescriptions, regular examination of the patient's condition and assessment of the effect of the therapy given. The socialist system provides not only free medical aid, but also a paid sick-leave in loss of working capacity. Patients with long-standing and grave diseases are given special pensions, depending on the degree of disability. On recovery, the patient is given recommendations concerning his future employment, work environment, and life. If recovery is incomplete, health resort therapy is prescribed.

Admitting Medical Students to the Clinic and Fundamentals of Medical Deontology

Students are admitted to the clinic for direct contact with patients in the second year of their studies. From their first day in the hospital, the students should learn the complicated and important science of association with the patient, the final purpose of which is the complete recovery of the patient. This is not only a science but also a medical talant and intuition. There are no strictly defined rules because each patient requires a special approach due to his special personality traits, pathology, mental development, education, and other special conditions (fatigue, frustration, enjoyment, excitation, etc.).

The science of the duties and rights of the doctor in relation to his patient is called deontology (Gk *deon* obligation, *logos* science). Deontology may also be defined as the set of rules and principles of medical ethics which govern a member of the medical profession in the exercise of his professional duties.

The concepts of morals and professional duties of practitioners have changed during the centuries, depending on the social, economic and class relationships, the political structure of the state, the level of civilization, national culture, religious traditions, and many other factors. There are many examples of selflessness in the history of the Russian medicine. The great Russian author Anton Chekhov, who was also a physician, wrote: "Being a doctor is a feat. The profession requires higher selflessness, purity of thought and aspiration. Not everybody is capable of being a doctor". The profession of the doctor is hard labour, sleepless nights, doubts, tormenting experiences, patience, and self-control. At any time the doctor must be ready to render aid to the patient. A real doctor will stay with his patient after his official time is over if the situation requires. He will not spare his leisure time to help the patient without shifting his duties to someone else.

From literature, newspapers, radio, and TV we know that in order to save his patient a doctor may travel long distances at any time of the day or season, despite the danger to his own health and sometimes even life. Many physicians do experiments on themselves to study a disease or the mechanism of its spreading, volunteer to fight epidemics of severe infectious diseases. The Russian physician S. Andrievsky proved the infectious nature of anthrax by experimenting on himself. D. Samoilovich infected himsefl with plague in an attempt to find a way of fighting this disease. Soviet medical workers showed their uttermost selflessness during the Civil War and World War Two.

The profession of a physician is heroic. The student must understand this from the very start to prepare himself for a life of hard labour and anxiety. But this life gives moral satisfaction that can hardly be given by any other profession.

Successful therapy greatly depends on the authority of the doctor. This authority is won not only by selfless labour but also by profound knowledge, because an authoritative physician is always a competent physician. Hippocrates would emphasize that only serious study can bring success to the doctor and that only industriousness combined with knowledge may give ripe fruits. N. Chistovich emphasized that a good physician must work constantly and incessantly; only those who do everything to meet the demands of modern medicine may consider themselves to conscientiously fulfil their duties. The main deontological re-

quirement is high medical skill and a constant drive to improve one's knowledge and skill. A good physician should know all recent advances in medicine, follow all periodicals and other publications in his profession, attend meetings of medical societies, conferences, take active part in them, and should also be acquainted properly with the problems of the neighbouring medical specialities.

The authority of a physician largely depends on his attitude toward the patient, his compassion and sympathy for the patient. An indifferent physician decreases the patient's confidence in him and may drastically impair the condition of the patient. If the patient trusts his doctor and sees he has a desire to relieve his sufferings, the treatment will often be much more effective with the same prescriptions. The Russian author and physician V. Veresaev wrote that the doctor may be a good diagnostician and be quite exacting in his prescriptions, but all his talents are useless if he is unable to conquer the patient's soul. Compassion for the patient is not a formal duty but a genuine sympathy for the patient and the desire to help him. And the patient should feel this compassion whenever he is in contact with medical personnel, beginning with the nurse and secondary personnel and ending with his 'saviour', the physician. Hastiness, indifference by the physician during his examinations and conversation sometimes inflict a heavy blow to a patient that may be decisive to the result of treatment.

When examining the patient, the physician should show his compassion and interest, ask the patient about his complaints, about the beginning and development of the disease, show his sympathy for the patient, so that he might feel confidence in his doctor and sometimes tell him not only his main complaints but intimate details of his life that might be helpful for the diagnosis and treatment. These requirements should be fulfilled by the medical students as well when they come for practical training at hospitals. If a student is not serious, the patient will not feel confidence in him, nor in other medical students that might come next.

As soon as the physician has gained as much information as possible about the disease from clinical findings and results of examination, he must do his best to quiet the patient, raise his spirits, and convince him that there are good signs of his recovery (fall of body temperature, better pulse, improved appetite, etc.), without dwelling on the unfavourable symptoms of the disease. It is recommended that in some cases the disease be compared with other more serious diseases helping the patient believe that his disease is not so grave. The patient's attention may be directed to a symptom absent in his case. This makes the patient forget for a time his upsetting thoughts. For example, if a patient with cardiac decompensation is told that his dyspnoea still persists but the cough is already absent, the patient's mood may improve. If the physician is successful in suggestion, the

patient will not concentrate on the main symptoms of the disease and this in turn may remove depression and increase the patient's tone. The Russian physician G. Zakharyin indicated that, for rare exceptions, the patient's spirits are depressed. In order to successfully treat him the physician should first improve the patient's mood by giving him hope for recovery. A motivating hope can give good results immediately, e.g. patient's insomnia will be removed, which is a good remedy not only for the patient's nerves but for the entire body. At the same time, the physician's task should not be understood as reassuring his patient that the disease is not so grave but rather to convince the patient of his possible recovery (even in malignant cases).

While prescribing medicines and giving advice the physician should explain the treatment schedule, its mode of administration. Improper administration of medicines will give no desirable results. For example, astringent bismuth nitrate should be taken before meals so that the preparation might act on the gastric mucosa. Improper administration of preparations may harm the patient, as in the case with acetylsalicylic acid, amidopyrine or some other medicines that should be given after meals and in powdered form, rather than in tablets which might cause gastric ulcer. If the patient believes his doctor and the power of his prescriptions, the efficacy of the prescription increases. In other words, the belief in the power and skill of the doctor and his prescriptions points the way to recovery. An outstanding Russian physician V. Bekhterev wrote that a patient feels better after a talk with a true doctor. If a patient feels that his doctor is doubting, this is detrimental to his health. This is especially important in acute cases, such as myocardial infarction, cardiac asthma, or unforeseen complications during a surgical operation. The medical student should learn how to be confident without being self-conceited.

While discussing the case with his colleagues at the patient's bedside, the physician should avoid words and terms that might be unknown to the patient or might be misunderstood by him. An occasional thoughtless word from the physician may impair the mood of the patient, impair his sleep, appetite, and general condition. The student should remember that a patient might ask him a question which he dares not ask the physician. The question will always concern his disease, and the student should therefore always be aware of the damage he may do to the patient by an inappropriate answer. If the student is not sure, he must consult the doctor before answering the patient. It should be remembered that even in hopeless cases (cancer with multiple metastases, fatal heart disease, irreversible affections of the liver, or kidneys) the patient believes that he may recover, and the truth should therefore always be concealed from him. The

duty of the physician is to persuade the patient by all possible means that his disease may be cured.

The practical work of the physician is tightly connected with research. Diagnosis itself is research. The prescription of medicines and observation of their effects, change of preparations and selection of more efficacious means in each particular case implies an individual approach and element of research. The Russian physician V. Manassein wrote that a good doctor is always a researcher, either in the laboratory or at bedside. The student should therefore take part in scientific medical societies, where he may acquire the habits of a researcher. These habits will help him in his future independent work, although he may only work as a practitioner.

When a student begins his practical work at clinic, he must remember that his appearance is very important for the first impression on the patient. Inappropriate dress or appearance may impair the belief of the patient in his power as a doctor. During breaks in studies students should not talk loudly. They should behave like real physicians and not students, avoiding loud discussions, all the more so since noise annoys the patients. Quiet and calm strengthen the nervous system of the patient and improve his condition.

It should be remembered that personal conduct of the physician is very important to the patient. For example, if the doctor insists that the patient stops smoking but smokes himself, his recommendation will not be taken seriously.

Medical deontology implies keeping medical secrets. All the physician knows about his patient should be kept secret, otherwise the patient will suffer moral and sometimes material loss. This however does not hold for cases where keeping a secret may do harm to other people. For example, if the disease is infectious, the patient should be hospitalized because his isolation arrests the spreading of the disease and provides better conditions for treatment. People close to the patient should sometimes be informed of the disease so that they might strictly follow sanitary rules and that any new cases, if any, might be treated in due time.

The problems of medical deontology are closely connected with professional ethics. Some physicians try to hide their inadequate knowledge and skill behind aplomb and undue self-assurance. In order to improve their authority, some physicians may criticize their predecessors in the presence of the patient and give "new" prescriptions that actually do not differ substantially from the previous ones. Such physicians may criticize others in a way that will undermine their own authority and the patient's belief in medicine in general. The patient may speculate: "If the previous doctor gave me wrong prescriptions, why should I believe this new doctor?"

If a physician discovers an error in the prescriptions and methods of his predecessor, he must correct it tactfully so that the patient does not lose his belief in medicine and in his recovery. Medical ethics should be learned by the students from the very start of their education, because the medical students of today are physicians of tomorrow.

Once a person decides to become a physician he must obey the medical laws and fulfil his duties properly in accordance with this oath: "Having received the high calling of being a doctor and upon entering the medical profession, I solemnly swear that I shall commit all my knowledge and strength to the protection and improvement of man's health, to the treatment and prevention of his diseases. I swear to be ready to render medical assistance at any time of my life and carefully, attentively help my patients, and keep their confidence. I swear that I shall always continue to improve my medical knowledge and skill so that my work might advance medical science and practical medicine. I swear that I shall consult colleagues if I may require medical advice, and shall give such advice to my colleagues whenever they need it. I swear that I shall keep sacred, and further develop the noble traditions of the Fatherland's medicine and always remember my duties to mankind. Being aware of the danger of nuclear weapons for mankind, I shall fight indefatiguably for prevention of nuclear war. I swear that I shall be true to this oath for the whole of my life".

Chapter 2

HISTORY OF DIAGNOSIS

A Short Historical Survey

Modern knowledge in medicine, methods of diagnosis of human diseases, and their treatment have been built on the experience accumulated by man over his long history, a history measured by thousands of years. Our concept of disease and diagnosis developed together with biology and other sciences. The history of diagnosis is therefore part of the general history of medicine. The current state and development of the science of disease and diagnosis are closely connected with the level of philosophy in each epoch and a concrete knowledge of nature.

During the age of primitive medicine, simple symptoms, such as vomiting and diarrhoea, fever and pain, or obvious fractures and wounds were used for primitive diagnosis. Diagnosis was based on the simplest examination techniques, such as palpation and inspection, which were not planned and were carried out without a detailed study of symptoms of the disease.

Physicians of ancient Egypt and India paid attention to the body temperature; they used auscultation and palpation. Chinese physicians developed the science of the pulse. The Cos and Cnidus medical schools in Greece (Hippocrates) greatly contributed to the development of the science of diagnosis; the Cos school is considered the precursor of modern clinical medicine.

The diagnostic studies of Hippocrates were based on thorough observation of the patient at his bedside and by comparing his condition before and during the disease. Some tests were used to determine the response of the patient. "If the symptoms of the disease are not sufficiently obvious, man must help nature to show these symptoms". The patient was thus asked to move about or his chest was shaken (Hippocratic succussion). Some tools were also used for diagnostic purposes (a probe to examine the uterus, vaginal and rectal specula). Hippocrates auscultated the lungs, palpated the liver and the spleen. He paid great attention to the general condition of the patient rather than to a search for an affected site or the naming of the disease, because he believed that the condition of a part depends on the condition of the whole. Diagnosis of the disease was based on understanding of the unity of the human body: "Everything is in-

terdependent in a living body". Disease is a suffering of the entire body. Diagnosis included the determination of the stage or a period of the disease, and also its origin: "The main object is to determine the cause of the disease, and the source of the original defect".

Hippocrates is the founder of diagnostics. Some of the general principles used at his time are still valuable for modern medicine. Hippocrates created a method of diagnostic examination and thinking which includes the study of all symptoms of the disease in their succession. He developed rich clinical casuistics and symptomatology. They were not an occasional combination of signs or certain diseases, but a connection of the symptoms with periods of the diseases, steps in the course of the diseases depending on the combination of various conditions. Hippocrates dismissed the existence of "sacred" causes for diseases and considered them to be a natural phenomenon and the result of various external effects.

Hippocrates was aware of the difficulties that the physician meets, and believed that the cooperation of society in carrying out practical medical measures was necessary. "Nothing could be further from the aloof oracular physician-priest. Here, the doctor enlists the patient's help, and that of the 'externals'—the forces of Nature". Following Hippocrates, the science of diagnosis developed for centuries according to his postulates, mainly in special cases enriching medicine with new methods of examination and the symptomatology of new diseases.

Important contributions to the development of medicine and diagnostics were made by Galen ("Corpus medicorum") and especially by Avicenna ("Canon"). The influence of Avicenna continued until the 16th century, both in the Arabian East and in Europe.

New diagnostic methods were developed during the Renaissance. Paracelsus' attempts to diagnose by chemical and physical methods were significant. He was followed by van Helmont and Sylvius, who discovered fermentation and importance of acid-base equilibrium. Santorio used a balance and a hygrometer in his attempts to determine the metabolic indices, while Borelly applied the laws of mechanics and mathematics to explain the work of the heart and the skeletal muscles.

The revival of Hippocrates' methods of medical diagnosis (bedside observation) was an important event (Padua and Leiden Universities, and also England).

New valuable methods of examination were introduced into clinical practice in the 18- 19th centuries. Thermometry was suggested by de Haen in 1758. Percussion discovered by Auenbrugger in 1761 was another important event of that time. A still more important innovation was the stethoscope invented by Laennec in 1819. The Russian physicians M. Mudrov, G. Zakharyin, and A. Ostroumov introduced systematic in-

quiry (anamnesis) into diagnostic methods. V. Obraztsov proposed a planned palpation of the abdominal organs and L. Traube proposed a method of clinical assessment of thermometry.

Clinical observation of the patient and physical examination by auscultation, palpation, measuring temperature, weighing, etc., remained the main and most important diagnostic procedures until almost the 20th century. Practical medicine was then enriched with new additional diagnostic methods, such as laboratory and instrumental techniques. A sphygmograph (Marey, 1860), a sphygmomanometer, Riva-Rocci apparatus (1891) were invented.

A method for determining arterial pressure was proposed by a Russian physician Korotkov (1905), oesophagoscopy and a gastric tube (sound) were proposed by Kussmaul (1867- 1868), gastroscopy by Mikulicz (1881), cystoscopy and rectoscopy by Nitze (1879), bronchoscopy by Killian (1897-1898), spirometry by Hutchinson (1894), ophthalmoscopy by Helmholtz (1851), laryngoscopy by Garcia (1855); a method for determining basal metabolism was proposed by Pettenkofer (1861—1862), a method for estimating protein in urine was proposed by Esbach (1874). Biochemical studies were also introduced into clinical practice. The discovery of X-ray by Roentgen was a valuable contribution to diagnostics (1895). Einthoven invented a string galvanometer and was a pioneer in electro- and phonocardiography. Pirquet (1907) proposed an allergic skin test for the diagnosis of tuberculosis. Rieder (1904) worked out a method for X-ray examination of the gastrointestinal tract. Widal proposed the agglutination test for diagnosis of typhoid fever (1896) and a method of cytological diagnosis (1900). Schilling used differentiated counts of leucocytes (1912), Bernatsky substantiated a diagnostic value of the erythrocyte sedimentation rate (1894), Arinkin proposed sternal puncture (1927) for intravital study of the bone marrow. Zimnitsky (1923) proposed a method for functional diagnosis of renal diseases; Sahli (1907) introduced sphygmometry and Pachon (1909) oscillometry. Frank (1914) recorded the heart sounds and Castelianos (1937) introduced angiocardiography. Next were introduced ballistocardiography, laparoscopy, and other methods. Methods of biopsy, puncture of the lymph nodes, liver, spleen and other organs have become popular now.

Our concepts of the essence of pathological processes occurring in the body have changed with the development and introduction into clinical practice of new diagnostic methods and with the description of earlier unknown symptoms of diseases and the study of their pathogenesis. In ancient times, the physician would establish diagnosis by the outward symptoms of the disease, and would interpret the disease quite subjectively and speculatively. A more accurate diagnosis of diseases have become possible

with development of biology and other related sciences. In the 18th- 19th centuries the physicians did not limit themselves by mere speculations but observed their patients from scientific standpoints and discovered many new diseases that had been unknown before. Sydenham, for example, described scarlet fever (1675), Vieussens mitral stenosis (1715), and Boerhaave mediastinal tumours (1718). Heberden described the clinic of angina pectoris (1768), etc. Each decade enriched the list of known diseases. Botkin (1883) gave an account of acute infectious hepatitis, Obraztsov and Strazhesko (1909) described the clinic of thrombosis of coronary arteries. The number of discovered nosological entities continues increasing, especially during the past decades. The list of known diseases probably doubles each next decade. Diseases that are known to medicine now count to 10000. The number of nosological terms is 8000, and the number of syndromes is about 1600.

The rapid growth of the list of symptoms, syndromes, and diseases can be explained by the development of more accurate diagnostic techniques. Biochemical studies of the blood, urine, and other bodily fluids and excretions, methods of functional diagnosis of the respiratory organs, the circulatory system, alimentary tract, urinary tract, metabolic system, etc., have become very important for diagnosis during the past decades. X-rays are also widely used for diagnostic purposes (angiocardiography, encephaloroentgenography, etc.). Electrophysiology is also used to diagnose diseases of the heart and brain (electroencephalography, vectorcardiography, etc.). Traced elements help the diagnosis of many diseases. Immunological methods (radio-immunological determination of gastrin of the blood serum included), echographic studies of the heart, gall bladder and pancreas, pH metering (pH-metry) of the gastric contents are now widely used for diagnostic purposes. A thermographic method was developed in 1970 in the Soviet Union (Ivanova and other scientists) and it is now employed for clinical diagnosis. Endoscopic instruments are being continually improved: flexible endoscopes are now quite safe and the diagnostic procedure is easily tolerated by the patient. Biopsy of various organs becomes more important from the diagnostic standpoint. The methods by which the bioptic specimens are studied are improved as well. In addition to histological examination of the specimen, modern diagnosis is now facilitated by histochemical, electron-microscopic, immunomorphological and other studies. Samsonov (1970) proposed a morphometric method. (The ratio of the cell elements of the gastric glands is, for example, determined by this method.) Various functional "load" tests are now widely used in clinical practice. They provide an accurate information on the functional state of various internal organs (bicycle ergometry, glucose load test, histamine, pentagastrin, and other tests).

The choice of diagnostic means continues increasing. New techniques are developed and old improved. Special tests are proposed. The identification of diseases becomes more accurate and early, while the diagnostic procedures require many new laboratory and instrumental methods and tools. New diagnostic methods help discover new properties of the human body and enrich our knowledge of the patient and the disease to provide grounds for successful treatment.

The Role of Russian and Soviet Scientists in Development of Diagnosis and the General Therapy of Internal Diseases

The Russian and Soviet clinicists Mudrov, Zakharyin, Botkin, Ostroumov, Obraztsov, Strazhesko, Konchalovsky, Lang and many others made an important contribution to the development of the diagnosis and general therapy of internal diseases.

The founder of the Russian therapeutic school, Matvey Mudrov (1776-1831), assumed that disease is a result of exposure of man to unfavourable effects of the environment. Accordingly he was the first to interrogate the patient in order to substantiate the anamnestic method. He developed a planned clinical examination, and recording case histories. Mudrov was the first in Russia to organize practical clinical studies for students, he organized special laboratories and a museum. In the field of general therapy he followed the principle of individual approach and claimed that the patient should be treated rather than his disease. He also emphasized the great importance of hygiene.

Grigory Zakharyin (1829-1897) worked out in detail the anamnestic method of diagnosis which helped establish individual diagnosis (in addition to the physical examination of the patient) in the presence of not only morphological but also functional changes in various organs. An outstanding French clinicist Huchard wrote: "Zakharyin's school used observation, accurate anamnesis, and knowledge of aetiology, which where raised to the level of an art". Zakharyin worked at the diagnosis of tuberculosis and its classification, he described zones of hypersensitivity of the skin in diseases of internal organs. According to Zakharyin, the therapy of disease should include hygienic procedures, climate therapy, dietary treatment, and medicamentous treatment. His contribution to symptomatic therapy is very great; he proposed treatment with koumiss (fermented mare's milk) and mineral water.

Sergei Botkin (1832-1889) founded the physiological school in medicine and pioneered in experimental pharmacology, therapy, and pathology in Russia. Botkin considered that a clinical experiment is a tool

for opening the mechanism of disease development. He widely introduced the physiological and instrumental study in clinical practice. Guided by Sechenov's ideas, Botkin worked out the theory of disease development, in which the first role was given to the nervous system. This enabled him and his pupils to show the role of the nerve centres in regulation of haemopoiesis and body temperature. In the field of diagnosis, Botkin established the difference between hypertrophy and dilatation of the heart, discovered the postsystolic murmur in stenosis of the left venous orifice (which was later described as a protodiastolic murmur), described the listening points for diastolic murmur in aortic valve incompetence, was the first to diagnose thrombosis of the portal vein. Botkin pointed out for the first time the infectious aetiology of catarrhal jaundice (which was later given his name); he gave a detailed description of the disease known as Wolhynian (five-day) fever, and discovered the role of tissue destruction in the pathogenesis of fever.

Botkin believed that the main task of practical medicine is disease prevention. He was a social worker and was the first to organize out-patient and then hospital treatment free of charge. He is justly considered to be the founder of military field therapy.

Aleksey Ostroumov (1844-1906) actively fought for the connection of theory with practical medicine. He emphasized the importance of physics, chemistry and biology for the development of clinical medicine. Physiological studies by Ostroumov proved the important role the central nervous system plays in man. They were aimed at solving problems of clinical medicine. He worked out the main principles of the theory of reflex disorders in various organs due to affection of the nervous system. Ostroumov believed that variations in the course of one disease depend on the special properties of an individual macroorganism and its nervous system. He emphasized the importance of the relationships between man and the environment, and the role of hereditary factors in the pathogenesis of diseases. Ostroumov worked out in detail the clinic of early tuberculosis, balneo- and physiotherapy, indications and contraindications to sanatorium and health resort therapy in tuberculosis and nervous diseases. In Ostroumov's opinion, individual therapy, envigorating and symptomatic treatment should be combined with specific treatment of patients.

Vasily Obraztsov (1849-1920) was among the founders of the Soviet therapeutic school. He developed and improved methods for clinical study of patients. He devised and substantiated the method of deep sliding palpation of the stomach and the intestine, and palpation of other organs. He was the first to propose direct percussion of the thoracic and abdominal organs, direct auscultation of the heart to differentiate between the gallop rhythm and the third heart sound. Together with Strazhesko, Obraztsov

gave a complete account of the clinic of thrombosis of the coronary arteries and proved the possibility of intravital diagnosis of thrombosis. He also classified enteritis as an independent clinical form.

Nikolai Strazhesko (1876-1952) was the disciple and successor of Obraztsov. He continued developing methods to study internal organs. He substantiated the principles of examination of the alimentary organs, which he described in his book "Fundamentals of Physical Diagnosis of Diseases of the Abdominal Cavity", which has remained a valuable manual for the therapist of today. His studies of the cardiovascular system enabled him to work out the teaching of functional circulatory insufficiency, to classify (together with Vasilenko) circulatory insufficiency, to describe various symptoms in diseases of cardiovascular system (e.g. a pistol-shot sound in complete heart block). Strazhesko described rheumatism as an infectious-allergic disease of the streptococcal aetiology, revealed special features of rheumatism and connections between rheumatism, sepsis, and endocarditis; he described the relation between cardiac asthma and angina pectoris.

Maksim Konchalovsky (1875-1942) demonstrated the importance of the syndrome approach to diagnosis of diseases and worked out the infectious-allergic theory of rheumatism; he described its clinical forms and course, and also determined indications and contraindications to blood transfusion in the clinic of internal diseases. Konchalovsky described the clinic of late chlorosis, the "tourniquet" sign in thrombocytopenia, and developed the teaching of the haemopoietic function of the stomach. Konchalovsky struggled for the union between therapy and broad prophylactic measures, for therapy of premorbid conditions; he developed methods for functional diagnosis, and worked at problems of employment prognostication.

Georgy Lang (1875-1948) was the first to define essential hypertension as an independent disease caused by disordered cortical and subcortical regulation; he classified diseases of the circulatory system and was the first to propose the term "myocardial dystrophy".

Lang founded a new "functional" trend in haematology which treats some diseases of the blood system in connection with disorders in the circulatory and haemolytic systems. He proposed a classification of liver diseases. Lang and his pupils developed methods for functional diagnosis of cardiovascular diseases and diseases of the liver. He was the first to propose treatment of fibrillation with quinidine.

The Soviet clinicists Zimnitsky, Pletnev, Zelenin, Yanovsky, Kurlov, Shklyar, Chernorutsky, Vovsi, Myasnikov, Molchanov and many others made an important contribution to the development of internal medicine, diagnosis of diseases in particular. Many other outstanding Soviet scien-

tists and clinicists, talented teachers continue the traditions of the Russian and Soviet medicine and work to solve many important problems of internal pathology.

Soviet Public Health System: A New Stage in Medicine

Soviet medicine is based on the progressive theory of dialectical materialism. The object of Soviet medicine is to improve the health of the entire population. The work of the public health system is aimed at broad prophylactic and health-improving measures, and at rendering skilled medical aid free of charge.

The prophylactic trend is an important feature of the Soviet medicine in compliance with the tradition of the Russian clinical school. The founder of the first clinic in Moscow, Mudrov, wrote more that 150 years ago: "To take into our hands healthy people, to protect them from diseases, either inherited or threatening, and to prescribe an appropriate way of life for them—this is the most honest and trouble-free duty of the physician, since it is easier to prevent a disease than to cure it. This is the first duty of the physician". Zakharyin emphasized that "only hygiene can successfully fight diseases".

This was the challenge of the past. Now prevention of diseases, both infectious and non-infectious, has become the main object of Soviet medicine, which is successfully fulfilled by the Soviet public health system. The socialist public health system fights diseases according to a thoughtful plan and the results of this planned struggle are wonderful: health standards of the population of the Soviet Union are among the best in the world. Improvement of the well-being of the population and the high cultural standards facilitate further development of the Soviet public health to decrease morbidity and mortality among population.

Social prophylaxis (prevention of diseases) is accomplished in the Soviet Union by the continuous growth of the well-being and the cultural level of the Soviet people. The living and working conditions are constantly improved. The quality of food is controlled by special authorities. The living conditions in large regions are improved by irrigation and other measures. The health of people is protected and diseases are prevented by a wide range of measures including the improvement of the well-being and cultural level of the population, by development of all links in the public health system, by giving medical assistance free of charge, by health education of the population, mother and child care, by development of sports, by building rest homes, sanatoria, and health resorts, and by the Soviet social security system. There are many dispensaries and special (car-

diological, gastroenterological, etc.) centres and hospitals, special departments at policlinics, and sanatoria in the Soviet Union. Dispensaries are specialized centres that are responsible for the early detection of disease and give regular medical assistance to patients with chronic diseases, hospitalize patients, organize prophylactic aid at home and in industry. The number of hospitals and beds for stationary treatment of patients is continuously growing.

The Constitution of the Soviet Union guarantees protection of its citizens health. The Communist Party and the Government of the Soviet Union do their best to further improve the system of health protection and prevention of diseases among the population of the Soviet Union.

Chapter 3

METHODS OF CLINICAL EXAMINATION OF PATIENTS AND GENERAL SYMPTOMATOLOGY OF DISEASES OF THE INTERNAL ORGANS

In order to arrive at a correct diagnosis it is necessary to be able to identify the signs of the disease, and to reveal the appropriate changes in the patient. Various methods are used to reveal and study the numerous symptoms of the disease. These methods include questioning the patient, measuring his body temperature, and complicated techniques of examination (microscopy of the formed elements of the blood, chemical studies of the bodily fluids, X-ray examination of the patient, etc.).

A healthy person does not feel any unpleasant sensations. Pain, nausea, vomiting, elevated body temperature, enlargement of certain internal organs, e.g. of the spleen, occur only in the sick, and are considered as signs or symptoms (Gk *symptoma* that which happens) of diseases. Some symptoms indicate changes that occur in the entire body (e.g. elevated temperature), while others (e.g. diarrhoea) may only indicate dysfunction of a particular organ or a system, or changes in the structure of an organ (e.g. an enlarged and firm spleen).

Pain or nausea are *subjective symptoms* experienced by the patient. These sensations reflect objective changes that occur in the patient's body. Signs of the disease that are revealed by the physician during his examination of the patient, e.g. jaundice or enlarged liver, are *objective symptoms* of the disease.

It is almost impossible to diagnose a disease by only one symptom. A correct diagnosis can only be established by investigating several symptoms. Most incorrect diagnoses are the result of an insufficient examination. The main requirement is therefore a thorough and systematic examination of the patient. A correct diagnosis can be established if the physician follows a definite plan in his examinations.

The examination begins with an *interview.* The patient tells his complaints which often are of no less importance than a thorough objective examination of the patient. Some diseases are diagnosed almost exclusively by the patient's complaints. Angina pectoris, for example, is frequently diagnosed almost entirely from the character of pain in the region of the heart. Cholelithiasis is diagnosed by attacks of pain in the right upper abdominal quadrant. A detailed questioning of the patient concerning the

time of the onset of the disease, its early symptoms (until the time of medical examination) is even more important in establishing a correct diagnosis. All this information is usually called anamnesis morbi, i.e. remembering the present disease by the patient, as distinct from anamnesis vitae which is the history of previous diseases of the patient. Stages of development of the present disease are traced back while collecting an anamnesis from the history of the disease as given by the patient himself and also from the information supplied by his relatives.

Another stage of examination is *objective examination* of the patient's condition at the present time (status praesens). This examination includes various diagnostic procedures (inspection, measuring temperature, percussion, auscultation, palpation, laboratory tests, X-ray examination, etc.) and reveals changes in the patient's body and deviations from normal structure and function of various organs that could not be sensed by the patient himself.

As a rule, a patient undergoes repeated examinations during his observation by medical personnel. These examinations reveal subjective and objective changes in the state of the patient, the disease progression, and the efficacy of the therapy given. This is information on the course of the disease (decursus morbi).

All information obtained by questioning the patient and by objective examinations, information on the course of the disease and the prescribed treatment are recorded to make a history of the case. A complete diagnosis (i.e. the main disease and the accompanying diseases and complications, if any) are given on the first page.

At the end of the history record, when observation of the patient is over, a conclusion or epicrisis should be given, where the special character of the disease and the result of the treatment should be described.

Inquiry

The art of collecting a correct anamnesis is not easy. The reliability of complaints related by patients vary. Some patients forget to mention the most important symptoms while others dwell on unimportant and irrelevant details. The history will therefore be incomplete if the patient is allowed to tell the history of his illness by himself (unguided by the physician). It should be remembered that some patients may be shy and do not readily talk about some diseases (e.g. venereal) or harmful habits (alcoholism).

In order to collect information that might be actually important for a correct diagnosis, the physician should know the symptoms of the disease and the character of its progress. These are the subject matter of special pathology and therapy of internal diseases. The physician must learn the

art of correct inquiring. The science of diagnostics concerns the art of the correct and systematic collecting of anamnestic data. The physician first collects general information about the patient: his name, age, place of birth, and occupation. Age is important in the development of some diseases, e.g. essential hypertension, atherosclerosis, and malignant tumours which commonly develop in the aged. Occupation and social status of the patient are often responsible for the onset of the disease (e.g. poisoning, chills, etc.).

The next step is a systematic and thorough functional inquiry of the patient according to a predetermined scheme.

The Present Complaints

The main complaints of the patient should first be determined. If the patient complains of retrosternal pain, the character and exact location of this pain, its focus and intensity should be determined; the time of the onset, and possible causes that provoked the pain (strain, cough, taking food, etc.) should be established. The patient should be asked which remedies remove this pain. Other complaints should also be analysed. In pneumonia, for example, the patient would normally complain of weakness, high temperature, side pain (pleurodynia), and cough; he would note that the onset of the disease was marked a few days ago by a sudden chill and pricking in the side when coughing and breathing deeply.

The study of the main complaints can often lead the examiner to a conclusion concerning the general character of the disease, e.g. high body temperature would normally indicate an infectious process, cough and expectorated sputum indicate possible disease of the lungs. Knowledge of the exact time of the onset of the disease is informative of the character of the disease (acute or chronic).

The inquiry should not be limited to these main points. So as not to omit any symptoms and determine the functional condition of all the organs (status functionalis) the patient should be questioned according to a specially outlined scheme. Changes in the patient's general state should be established (loss of weight, fever, weakness, oedema, headache). The condition of the respiratory system (cough, expectoration of sputum and blood, pain in the throat) should also be established. Next is the cardiovascular system (tachycardia, dyspnoea, heart pain, swelling of feet). Then follows the gastro-intestinal system (appetite, swallowing, vomiting, epigastric pain, etc.).

The condition of the nervous system is established by asking the patient about his subjective condition, his sleep, irritability or indifferent attitude to the surroundings, weakness, excitement, headache, state of con-

sciousness and the main senses. The patient should be asked about his conduct, responses to external stimuli, his attitude to work and his associates. This is necessary to establish the special properties of his higher nervous activity at the present time and in the past, and the type of his nervous system according to Pavlov's classification. The inquiry at this stage gives the physician information concerning the condition of various organs and systems of the patient (respiration, blood circulation, digestion, urinary function, motor function, nervous system, etc.).

History of the Present Disease

Exact answers should be obtained from the patient concerning the following aspects of his present disease (anamnesis morbi): (1) the time of the onset of the disease; (2) the character of the first symptoms; (3) the course of the disease; (4) examinations and their results, if any; (5) treatment, if any, and its efficacy. The answers to these questions may give the physician the necessary information on the present disease.

The history of the disease should include information concerning the onset of the disease and its development until the present. The patient's general condition before the disease should first be determined and the causes that might have provoked the disease established wherever possible. The patient should be questioned in detail about the first signs of the disease and the chronology of their development (dynamics), about relapses or exacerbations, remissions and their duration. If the patient was examined during an exacerbation of the disease by some other physician, the results should be studied. Excess verbosity of the patient should be prevented, because the results of the examinations and treatment only are important (therapy with cardiac glycosides, vasodilators, diuretics, antibiotics, hormones, etc.). Motives for hospitalization should also be determined (exacerbation of the disease, verification of the diagnosis, etc.).

Anamnesis Vitae

The past history is often very important for establishing the character, the cause, and conditions for the onset of the disease. Anamnesis vitae is a history or a medical biography of the patient in every period of his life (infancy, childhood, adolescence, and maturity).

Collecting the anamnesis begins with the *general biographical information.* Birth place is important, because some diseases (e.g. endemic goitre) usually predominate in one locality and are not met in others. The age of the parents is also important. The patient should be asked if he was born at term, if there were other children in the family, if he was breast fed or ar-

tificially; the age at which the patient began walking and talking is important, and the patient should inform the physician if he had marked signs of rickets during his childhood. This information is important to evaluate the patient's health at birth and during childhood. Conditions of life in childhood and adolescence and health during these periods of life are important information. It is necessary to find out if the patient's physical and mental development was not retarded and what was his progress at school. The time of sex maturity should be determined. Women should report the number of pregnancies and parturitions, and the course of labour.

Social conditions are important for the health of people. The patient should inform the physician on the conditions of his housing (separate apartment, hostel, country house, illumination, the presence of dampness, if any, hygienic conditions, etc.). The composition of the family is important: large or small family, their health, well-being, income, etc. Malnutrition is an important factor for the onset of some diseases. The patient should be asked if his diet is sufficiently rich in vegetables, fruits, etc. The way in which the patient spends his leisure time is also important. The patient should report on the time he sleeps, rests, walks in the fresh air, and what sports and exercises he goes in for.

Unfavourable *labour conditions* and *industrial hazards* (some harmful dusts) are important, for they may cause bronchial asthma and chronic diseases of the bronchi and lungs. Strong noise, vibration, high ambient temperature, drafts, and cold (work in the open) can cause pathology. Industrial poisoning by mercury, lead, carbon monoxide and other harmful agents, and also exposure to radiation (improper safety measures) may also cause disease. The working schedule is also important. Establishing whether there are unfavourable industrial factors helps the physician give recommendations for organization of the patient's work.

Past illnesses are also important. Some infectious diseases, such as measles or scarlet fever, do not recur because of acquired immunity, while other diseases, such as rheumatism or erysipelas, tend to recur. Rheumatism or diphtheria often provoke heart diseases. Nephropathy often develops after scarlet fever, and incompetence of heart valves often results from the previous endocarditis.

It should be remembered that the patient may not know about his past diseases. Therefore in dubious cases the physician should ask the patient whether he had certain symptoms by which a suspected past disease might manifest itself (e.g. prolonged fevers, swelling of and pain in the joints are characteristic of rheumatism, general oedema indicates kidney disease, attacks of right hypochondriac pain may be the cause of the gall bladder disease, etc.). Contacts with infectious patients are important, especially in the presence of epidemics (e.g. influenza).

Family history. Health of the parents, sisters or brothers is often informative. If some of the family have had tuberculosis, the other members of the family may also develop tuberculosis. Syphilis may be transmitted by an intrauterine route. By comparing the pathology of the patient with diseases of his relatives, the physician can make a conclusion on the role of hereditary factors in the development or origin of the disease.

Life of man is tightly connected with the environment, and pathology always depends on external effects. Harmful environmental factors may affect the patient's offspring: his children may be predisposed to some diseases. But this predisposition does not obligatory provoke the disease. Special conditions are usually required for the disease to develop, and if these special factors are absent the person will not develop the disease. Moreover, if conditions favour, the person may strengthen his health and eradicate the hereditary predisposition to an illness.

Hereditary or familial (genotypical) and non-hereditary (paratypical) diseases are distinguished. But this classification is only conventional. As genetics progresses it becomes more obvious that some diseases that would be considered to be resistant to the hereditary factors, are actually genotypical diseases. Internists mainly deal with diseases that are not usually transmitted to the offspring but merely predispose them to these diseases (e.g. essential hypertension, atherosclerosis, cholelithiasis, etc.). Under certain environmental conditions this predisposition may enable the person to develop the disease. It should be remembered that the inherited character may have varying expressivity, or hereditary disease may develop in one member of the family only, or it may be inherited by an offspring after several generations, or it may develop only in family members of one sex (e.g. only males develop haemophilia which is transmitted from a grandfather to a grandson through a healthy daughter). The onset of certain hereditary diseases is sometimes erroneously attributed to an external factor, which was actually only the stimulus that provoked the disease.

In order to establish the hereditary character of a disease, the familial factors should be first given a thorough clinico-genealogical analysis. For the sake of convenience, genealogical schemes should be made out, using the special conventional symbols.

According to the adopted terminology, the patient is called a proband. His brothers and sisters are given in the order of their birth, from left to right. The Roman numerals are used to designate (at the left) successive generations. Each member of the generation is designated by an Arabic numeral. Symbols designating the proband's relatives, who were affected by the same disease, are shaded. The diagram must include data concerning the disease occurring in both parental lines of the proband.

Three main types of inheritance have been established. The first,

autosomal-dominant type, is the most prevalent. It is characterized by full penetrance of the mutant gene. In this type of inheritance the disease is directly transmitted from both parents to their offspring with 50 per cent of both sexes being affected (Fig. 1). Those who do not inherit the mutant gene have normal offspring. If penetrance of the mutant gene is incomplete, the direct order of inheritance is more difficult to detect. Suspicion that an inherited disease is dominantly transmitted can be verified by analysis of the offspring from repeated marriages (affected children from each marriage). The direct order of inheritance occurs, for example, in subjects with anatomical abnormalities (of the internal organs included).

Heterozygotic carriage of the recessive gene in autosomal-recessive inheritance does not cause the disease, which only develops in homozygotic carriers (Fig. 2). A blood relationship between parents is often revealed in recessive inheritance (otherwise difficult to reveal). Many enzymopathies, certain diseases of the nervous system, etc. are often inherited by the autosome-recessive type.

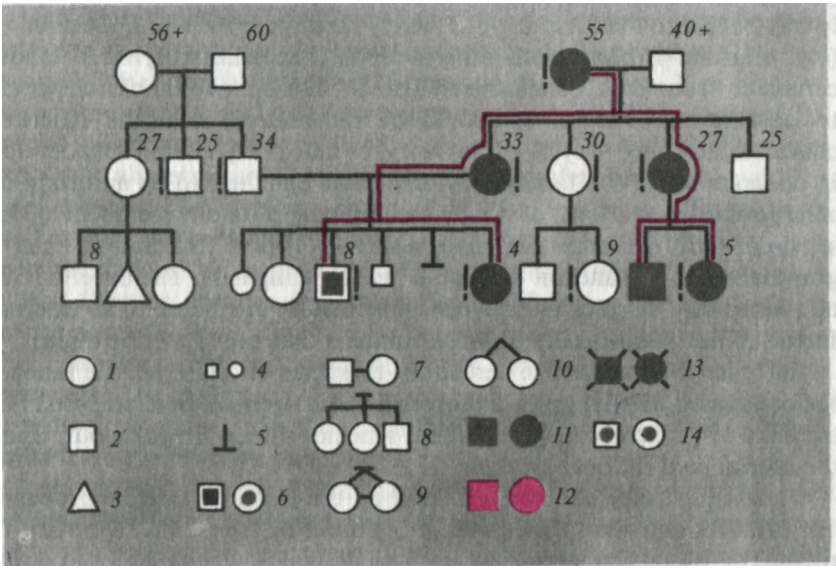


Fig. 1. Familial genealogy with dominant inheritance.

1—female; *2*—male; *3*—sex unknown; *4*—stillborn; *5*—miscarriage; 6—proband; 7—wife and husband; *8*—children; 9—monozygotic twins; *10*—dizygotic twins; *11*—sick; *12*—suspected carriers of recessive character; 13—children with malformations; *14*—phenotypically healthy carrier of recessive character. The exclamation mark is used to designate subjects observed by the physician.

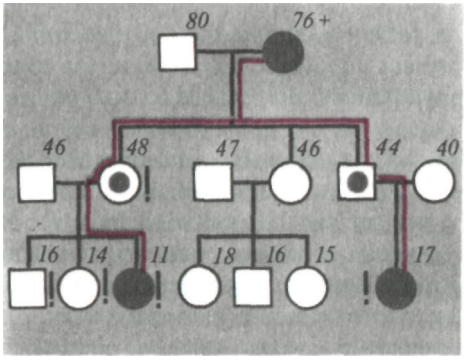


Fig. 2. Familial genealogy in recessive inheritance (designations are the same as in Fig. 1).

In sex-linked inheritance the mutant genes are linked with the X chromosome. The disease transmitted by dominant inheritance develops equally in both sexes. In cases of recessive inheritance the disease develops only in males (the males have one X chromosome and one Y chromosome), and not in females (they have two X chromosomes and the characteristics of the mutant chromosome are suppressed by the healthy X chromosome). Inheritance of the disease linked with the X chromosome is transmitted to phenotypically healthy females, while only males are affected by the disease. Typical examples of such diseases are haemophilia and agammaglobulinaemia (congenital defect of the protein metabolism).

Methods of cytogenetic genetics of somatic cells and certain other methods that are more complicated than the genealogical one are now widely used in medicine. Genetic analysis ensures early diagnosis of inherited diseases, their rational prophylaxis, assessment of the risk of bearing a child with a genetic disease, and in some cases possible pathogenic therapy for inherited human disease (this trend in genetics is probably very promising).

Allergological anamnesis is very important. Some patients (and even healthy subjects) often develop a pathologically heightened (or an inverted) response of the immune system (allergy), and this factor is essential in the pathogenesis of certain diseases of internal organs. It is necessary therefore to collect an allergological anamnesis, that is determine whether the patient or his relatives had allergic reactions to various foods, because strawberry, eggs, canned crabs, and other foods may frequently act as allergen. Some medicinal preparations, perfumes, pollen also do. Allergic reactions in man are quite varied: from vasomotor rhinitis, nettle rash or Quincke's oedema to anaphylactic shock.

Physical Examination

After listening to the patient's complaints and becoming acquainted with the history of the present disease, social and housing conditions, and the family history, the physician should proceed to do a physical examination of the patient.

Objective study of the patient (status praesens) gives information on the condition of the entire body and the state of the internal organs. The general condition of the patient can be evaluated from the information given by the patient (psychic condition, asthenia, wasting, elevated temperature). The condition of separate organs can also be evaluated from the patient's complaints. More accurate information on the patient's general condition and separate organs can be obtained by special diagnostic procedures. It is necessary to remember that dysfunction of an organ always produces disorders in the whole body. In order to obtain full and systematic information on the patient's condition, physical examination should be carried out according to a predetermined plan. The patient is first given a general inspection, next the physician should use palpation, auscultation, percussion, and other diagnostic procedures by which the condition of the respiratory organs, the cardiovascular, gastro-intestinal and the urinary system, locomotion, lymph nodes, endocrine glands, and the nervous system may be examined. Laboratory tests, X-raying, and endoscopy are objective methods of clinical examination.

Diagnostic methods can be divided into main and auxiliary. The main clinical methods include systematic inquiry, inspection, palpation, percussion, auscultation, and measuring. Each patient should be examined repeatedly. These methods are called main because only after having applied them, the physician can decide what auxiliary methods (laboratory and instrumental tests) should be used to establish or verify the diagnosis.

Auxiliary investigation is often carried out by other specialists, rather than the physician. Auxiliary methods are no less important than the main ones and in some cases their results are decisive in establishing a correct diagnosis or locating the pathological focus (e.g. biopsy, endoscopy, X-ray examination, etc.).

Practical value of the main diagnostic methods can be assessed tentatively by statistics. According to some authors, anamnesis alone can be used for a correct diagnosis in 70 per cent cases with gastroduodenal pathology and ischaemic heart disease. According to other data, a physician can arrive at a correct diagnosis in 55 per cent cases from an anamnesis and inspection of the patient. A successful start of diagnostic examination encourages the physician and in more than 50 per cent cases it stimulates the diagnostic search in correct direction to help the physician correctly evaluate the personality of the patient (for whom this procedure becomes a kind of catharsis). Anamnesis restores retrospectively the course of the disease (errors however are likely to occur), whereas objective examination (status praesens) reflects the

present condition of the patient. Despite the great value of anamnesis, it is never sufficient for establishing a diagnosis: the conjectured diagnosis is confirmed by the main and auxiliary clinical examinations.

General Inspection

Despite the many instrumental and laboratory tests available at the present time, general inspection of the patient (inspectio) has remained an important diagnostic procedure for any medical specialist. The patient's condition on the whole can be assessed and a correct diagnosis can sometimes be made at "first sight" (acromegaly, toxic goitre, etc.). Pathological signs revealed during inspection of the patient are of great help in collecting an anamnesis and in further studies. In order to make the best possible inspection, the following special rules should be followed, which concern illumination during inspection, its technique and plan.

Illumination. The patient should be examined in the daytime, because electric light will mask any yellow colouring of the skin and the sclera. In addition to direct light, which outlines the entire body and its separate parts, side light will also be useful to reveal pulsation on the surface of the body (the apex beat), respiratory movements of the chest, peristalsis of the stomach and the intestine.

Inspection technique. The body should be inspected by successively uncovering the patient and examining him in direct and side light. The trunk and the chest are better examined when the patient is in a vertical posture. When the abdomen is examined, the patient may be either in the errect (upright) or supine (dorsal) position. The examination should be carried out according to a special plan, since the physician can miss important signs that otherwise could give a clue for the diagnosis (e.g. liver palm or spider angiomata which are characteristic of cirrhosis of the liver).

The entire body is first inspected in order to reveal general symptoms.. Next, separate parts of the body should be examined: the head, face, neck, trunk, limbs, skin, bones, joints, mucosa, and the hair cover. The general condition of the patient is characterized by the following signs: consciousness and the psyche, posture and body-built.

Consciousness. It can be clear or deranged. Depending on the degree of disorder, the following psychic states are differentiated.

1. Stupor. The patient cannot orient himself to the surroundings, he gives delayed answers. The state is characteristic of contusion and in some cases poisoning.

2. Sopor. This is an unusually deep sleep from which the patient recovers only for short periods of time when called loudly, or roused by an external stimulus. The reflexes are preserved. The state can be observed in some infectious diseases and at the initial stage of acute uraemia.

3. Coma. The comatose state is the full loss of consciousness with complete absence of response to external stimuli, with the absence of reflexes, and deranged vital functions. The causes of coma are quite varied but the loss of consciousness in a coma of any aetiology is connected with the cerebral cortex dysfunction caused by some factors, among which the most important are disordered cerebral circulation and anoxia. Oedema of the brain and its membranes, increased intracranial pressure, effect of toxic substances on the brain tissue, metabolic and hormone disorders, and also upset acid-base equilibrium are also very important for the onset of coma. Coma may occur suddenly or develop gradually, through various stages of consciousness disorders. The period that precedes the onset of a complete coma is called the precomatose state. The following forms of coma are most common.

Alcoholic coma. The face is cyanotic, the pupils are dilated, the respiration shallow, the pulse low and accelerated, the arterial pressure is low; the patient has alcohol on his breath.

Apoplexic coma (due to cerebral haemorrhage). The face is red, breathing is slow, deep, noisy, the pulse is full and rare.

Hypoglycaemic coma can develop during insulin therapy for diabetes.

Diabetic (hyperglycaemic) coma occurs in non-treated diabetes mellitus.

Hepatic coma develops in acute and subacute dystrophy and necrosis of the liver parenchyma, and at the final stage of liver cirrhosis.

Uraemic coma develops in acute toxic and terminal stages of various chronic diseases of the kidneys.

Epileptic coma. The face is cyanotic, there are clonic and tonic convulsions, the tongue is bitten. Uncontrolled urination and defaecation. The pulse is frequent, the eye-balls are moved aside, the pupils are dilated, breathing is hoarse.

4. Irritative disorders of consciousness may also develop. These are characterized by excitation of the central nervous system in the form of hallucinations, delirium (delirium furibundum due to alcoholism; in pneumonia, especially in alcoholics; quiet delirium in typhus, etc.).

General inspection can also give information on other psychic disorders that may occur in the patient (depression, apathy).

Posture of the patient. It can be active, passive, or forced.

The patient is *active* if the disease is relatively mild or at the initial stage of a grave disease. The patient readily changes his posture depending on circumstances. But it should be remembered that excessively sensitive or alert patients would often lie in bed without prescription of the physician.

Passive posture is observed with unconscious patients or, in rare cases, with extreme asthenia. The patient is motionless, his head and the limbs

hang down by gravity, the body slips down from the pillows to the foot end of the bed.

Forced posture is often assumed by the patient to relieve or remove pain, cough, dyspnoea. For example, the sitting position relieves orthopnoea: dyspnoea becomes less aggravating in cases with circulatory insufficiency. The relief that the patient feels is associated with the decreased volume of circulating blood in the sitting position (some blood remains in the lower limbs and the cerebral circulation is thus improved). Patients with dry pleurisy, lung abscess, or bronchiectasis prefer to lie on the affected side. Pain relief in dry pleurisy can be explained by the limited movement of the pleural layers when the patient lies on the affected side. If a patient with lung abscess or bronchiectasis lies on the healthy side, coughing intensifies because the intracavitary contents penetrate the bronchial tree. And quite the reverse, the patient cannot lie on the affected side if the ribs are fractured because pain intensifies if the affected side is pressed against the bed. The patient with cerebrospinal meningitis would usually lie on his side with his head thrown back and the thighs and legs flexed on the abdomen. Patients with angina pectoris and intermittent claudication prefer to stand upright. The patient is also erect (standing or sitting) during attacks of bronchial asthma. He would lean against the edge of the table or the chair back, with the upper part of the body slightly inclined forward. Auxiliary respiratory muscles are more active in this posture. The supine posture is characteristic of strong pain in the abdomen (acute appendicitis, perforated ulcer of the stomach or duodenum). The prone position (lying with the face down) is characteristic of patients with tumours of the pancreas and gastric ulcer (if the posterior wall of the stomach is affected). Pressure of the pancreas on the solar plexus is lessened in this posture.

Habitus. The concept of habitus includes the body-build, i.e. constitution, height, and body weight.

Constitution (L *constituero* to set up) is the combination of functional and morphological bodily features that are based on the inherited and acquired properties, and that account for the body response to endo- and exogenic factors. The classification adopted in the Soviet Union (M. Chernorutsky) differentiates between the following three main constitutional types: asthenic, hypersthenic, and normosthenic.

The *asthenic* constitution is characterized by a considerable predominance of the longitudinal over the transverse dimensions of the body by the dominance of the limbs over the trunk, of the chest over the abdomen. The heart and the parenchymatous organs are relatively small, the lungs are elongated, the intestine is short, the mesenterium long, and the diaphragm is low. Arterial pressure is lower than in hypersthenics; the vital capacity of the lungs is greater, the secretion and peristalsis of the

stomach, and also the absorptive power of the stomach and intestine are decreased; the haemoglobin and red blood cells counts, the level of cholesterol, calcium, uric acid, and sugar in the blood are also decreased. Adrenal and sexual functions are often decreased along with thyroid and pituitary hyperfunction.

The *hypersthenic constitution* is characterized by the relative predominance of the transverse over the longitudinal dimensions of the body (compared with the normosthenic constitution). The trunk is relatively long, the limbs are short, the abdomen is large, the diaphragm stands high. All internal organs except the lungs are larger than those in asthenics. The intestine is longer, the walls are thicker, and the capacity of the intestine is larger. The arterial pressure is higher; haemoglobin and red blood cell count and the content of cholesterol are also higher; hypermobility and hypersecretion of the stomach are more normal. The secretory and the absorptive function of the intestine are high. Thyroid hypofunction is common, while the function of the sex and adrenal glands is slightly increased.

Normosthenic constitution is characterized by a well proportioned make-up of the body and is intermediate between the asthenic and hypersthenic constitutions.

The *posture* or attitude of the patient is often indicative of his general tone, the degree of muscle development, and sometimes of his occupation and habits. Most patients with grave diseases or with psychic depression are often stooped. Erect posture, easy gait, and free and unconstrained movements indicate the normal condition of the body. Some gaits are specific for certain diseases of the nervous system (hemiplegia, sciatica, etc.). Surgical diseases of the bones and joints, rheumatism, or deranged blood circulation in the lower extremities change the gait and make walking difficult. The so-called waddling gait is characteristic of osteomalacia or congenital dislocation of the femur.

During the general inspection, the physician should pay attention to the open parts of the patient's body, the head, the face and the neck.

Changes in the size and shape of the *head* can give diagnostic clues. Excessive growth of the skull occurs in hydrocephalus. An abnormally small head is typical of microcephalus, which is also marked by mental underdevelopment. A square head, flattened on top, with prominent frontal tubers, can indicate congenital syphilis or rickets in past history. The position of the head is also important in diagnosing cervical myositis or spondylarthritis. Involuntary movements of the head (tremor) are characteristic of parkinsonism. Rhythmical movements of the head in synchronism with the cardiac pulse are characteristic of aortic incompetence (Musset's sign). The presence of scars on the head may suggest the cause of persistent headache. It is necessary to find out whether the patient has ver-

tigo which is typical particularly for Meniere's syndrome, or epileptiform attacks.

Countenance. The facial expression can indicate the mental composure and various psychic and somatic conditions. It also depends on age and sex and can therefore give diagnostic clues when diagnosing some endocrine disorders (woman-like expression in men and masculine features in women). The following changes in the face are diagnostically essential:

1. A puffy face is observed in (a) general oedema characteristic of renal diseases; (b) local venous congestion in frequent fits of suffocation and cough; (c) compression of lymph ducts in extensive effusion into the pleural and pericardial cavity, in tumours of mediastinum, enlarged mediastinal lymph nodes, adhesive mediastinopericarditis, compressed superior vena cava (Stokes' collar).

2. Corvisart's facies is characteristic of cardiac insufficiency. The face is oedematous, pale yellowish, with a cyanotic hue. The mouth is always half open, the lips are cyanotic, the eyes are dull and the eyelids sticky.

3. Facies febrilis is characterized by hyperaemic skin, sparkling eyes and excited expression. There are special features of facies febrilis characteristic of some infectious diseases: feverish redness in acute lobar pneumonia (more pronounced on the side of the affected lung); general hyperaemia of the puffy face is characteristic of louse-borne typhus, the sclera is injected ("rabbit eye" according to F. Yankovsky); slightly icteric yellow colour is characteristic of typhoid fever. Tuberculosis patients with fever have "burning" eyes on an exhausted and pale face with blush localized on the cheeks. An immobile face is characteristic of septic fever; the face is pale, sometimes slightly yellowish.

4. Face and its expression are altered in various endocrine disorders; (a) a face (Fig. 3) with enlarged promient parts (such as nose, chin, and cheek bones) and enlarged hands are characteristic of acromegalia (hands become enlarged in some pregnancies); (b) myxoedematous face indicates thyroid hypofunction; the face may be uniformly puffy with oedematous mucosa, narrowed eye slits, the face features smoothed down, the hair is absent on the outward portions of the eyebrow; the presence of a blush on a pale face resembles the appearance of a doll; (c) facies basedovica (see Fig. 112): this is the face of a patient with thyroid hyperfunction; the face is lively with widened eye slits and abnormally sparkling eyes; the eyes are protruded and the face looks as if frightened; (d) an intense red, moon-like glittering face with a beard and mustaches in women is characteristic of the Itsenko-Cushing disease.

5. Facies leontina with nodular thickening of the skin under the eyes and over the brows, with flattened nose is observed in leprosy.

6. Parkinson's mask (or facies) is an amimic face characteristic of encephalitis patients.

Fig. 3. The face of a patient with acromegaly.

7. A slightly puffy wax-doll, very pale face with a yellowish tint, and seemingly tranlucent skin, is characteristic of Addison-Biermer anaemia.

8. Risus sardonicus with a semblance of a grin occurs in tetanus patients: the mouth widens as in laughter, while the skin folds on the forehead express grief.

9. Facies hippocratica (first described by Hippocrates) is associated with collapse in grave diseases of the abdominal organs (diffuse peritonitis, perforated ulcer of the stomach or duodenum, rupture of the gall bladder). The face is characterized by sunken eyes, pinched nose, deadly livid and cyanotic skin, which is sometimes covered with large drops of cold sweat.

10. Asymmetric movements of facial muscles indicate a history of cerebral haemorrhage or facial neuritis.

Inspection of the *eyes* and eyelids can reveal some essential diagnostic signs. Oedema of the eyelids, especially of the lower eyelids, is the first indication of acute nephritis; it is also observed in anaemia, frequent attacks of cough, and deranged sleep; oedema of the eyelids can also occur in the morning in healthy persons as well.

The colour of the eyelids is important. The eyelids are dark in diffuse toxic goitre and Addison disease. Xanthomas indicate deranged cholesterol metabolism. A dilated eye slit with the eyelids that do not close is characteristic of paralysis of the facial nerve; persistent drooping of the upper eyelid (ptosis) is an important sign of some affections of the nervous system. Narrowing of the eye slit occurs in myxoedema and general oedema of the face. Exophthalmos (protrusion of the eyeball) is observed

in thyrotoxicosis, retrobulbar tumours, and also in strong myopia. Recession of the eyeball in the orbit (enophthalmos) is typical of myxoedema and is an important sign of "peritoneal face". Unilateral recession of the eye into the orbit attended by narrowing of the eye slit, drooping of the upper eyelid and narrowing of the pupil, is the Horner's (Bernard-Homer) sydrome caused by the affection of the pupil sympathetic innervation of the same side (due to various causes).

The shape of the pupils, their symmetry, response to light, accommodation and convergence, and also their "pulsation" are of great diagnostic significance in certain diseases. Abnormally contracted pupil (miosis) is observed in uraemia, tumours and intracranial haemorrhages, and in morphine poisoning. Enlargement of the pupil (mydriasis) occurs in comatose states (except uraemic coma) and cerebral haemorrhages, and also in atropine poisoning. Anisocoria (unequal size of the pupils) occurs in some affections of the nervous system. Squinting results from paralysis of the ocular muscles due to lead poisoning, botulism, diphtheria, affections of the brain and its membranes (syphilis, tuberculosis, meningitis, cerebral haemorrhage).

The size of the *nose* may attract attention providing some diagnostic signs, e.g. it has an abnormal size in acromegaly, or its shape deviates from the normal in rhinoscleroma. The nose may be sunken as a result of syphilis in the past history (saddle nose). Soft tissues of the nose are disfigured in lupus.

When inspecting the *mouth* attention should be paid to its shape (symmetry of the angles, permanently open mouth), the colour of the lips, eruption on the lips (cold sores, herpes labialis), and the presence of fissures. The oral mucosa should also be inspected (for the presence of aphthae, pigmentation, Filatov-Koplik spots, thrush, contagious aphthae of the foot and mouth disease, haemorrhage). Marked changes in the gums can be observed in some diseases (such as pyorrhoea, acute leukaemia, diabetes mellitus, and scurvy) and poisoning (with lead or mercury). The teeth should be examined for the absence of defective shape, size, or position. The absence of many teeth is very important in the aetiology of some alimentary diseases. Caries is the source of infection and can affect some other organs.

Disordered movement of the tongue may indicate nervous affections, grave infections and poisoning. Marked enlargement of the tongue is characteristic of myxoedema and acromegaly; less frequently it occurs in glossitis. Some diseases are characterized by the following abnormalities of the tongue: (1) the tongue is clear, red, and moist in ulcer; (2) crimson-red in scarlet fever; (3) dry, with a brown coat and grooves in grave poisoning and infections; (4) coated in the centre and at the root, but clear at the tip

and margins in typhoid fever; (5) smooth tongue without papillae (as if polished) is characteristic of Addison-Biermer disease. The glassy tongue is characteristic of gastric cancer, pellagra, sprue, and ariboflavinosis; (6) local thickening of the epithelium is characteristic of smokers (leucoplakia). Local pathological processes, such as ulcers of various aetiology, scars, traces left from tongue biting during epileptic fits, etc., are also suggestive of certain diseases.

During inspection of the *neck* attention should be paid to pulsation of the carotid artery (aortic incompetence, thyrotoxicosis), swelling and pulsation of the external jugular veins (tricuspid valve insufficiency), enlarged lymph nodes (tuberculosis, lympholeukaemia, lymphogranulomatosis, cancer metastases), diffuse or local enlargement of the thyroid gland (thyrotoxicosis, simple goitre, malignant tumour).

The colour, elasticity, and moisture of *the skin,* eruptions and scars are important. The *colour of the skin* depends on the blood filling of cutaneous vessels, the amount and quality of pigment, and on the thickness and translucency of the skin. Pallid skin is connected with insufficiency of blood circulation in the skin vessels due to their spasms of various aetiology or acute bleeding, accumulation of blood in dilated vessels of the abdominal cavity in collapse, and in anaemia. In certain forms of anaemia, the skin is specifically pallid: with a characteristic yellowish tint in Addison-Biermer anaemia, with a greenish tint in chlorosis, earth-like in malignant anaemia, brown or ash-coloured in malaria, cafe au lait in subacute septic endocarditis. Pallid skin can also be due to its low translucency and considerable thickness; this is only apparent anaemia, and can be observed in healthy subjects.

Red colour of the skin can be transient in fever or excess exposure to heat; persistent redness of the skin can occur in subjects who are permanently exposed to high temperatures, and also in erythraemia. Cyanotic skin can be due to hypoxia in circulatory insufficiency (Plate 1), in chronic pulmonary diseases, etc. Yellowish colour of the skin and mucosa can be due to upset secretion of bilirubin by the liver or due to increased haemolysis. Dark red or brown skin is characteristic of adrenal insufficiency. Hyperpigmentation of the breast nipples and the areola in women, pigmented patches on the face and the white line on the abdomen are signs of pregnancy. When silver preparations are taken for a long time, the skiri becomes grey on the open parts of the body (argyria). Foci of depigmentation of the skin (vitiligo) also occur.

The skin can be wrinkled due to the loss of elasticity in old age, in prolonged debilitating diseases and in excessive loss of water.

Elasticity and turgor of the skin can be determined by pressing a fold of skin (usually on the abdomen or the extensor surface of the arm) between

the thumb and the forefinger. The fold disappears quickly on normal skin when the pressure is released while in cases with decreased turgor, the fold persists for a long period of time.

Moist skin and excess perspiration are observed in drop of temperature in patients recovering from fever and also in some diseases such as tuberculosis, diffuse toxic goitre, malaria, suppuration, etc. Dry skin can be due to a great loss of water, e.g. in diarrhoea or persistent vomiting (toxicosis of pregnancy, organic pylorostenosis).

Eruptions on the skin vary in shape, size, colour, persistence, and spread. The diagnostic value of eruptions is great in some infections such as measles, German measles, chicken- and smallpox, typhus, etc. *Roseola* is a rash-like eruption of 2—3 mm patches which disappears when pressed. This is due to local dilatation of the vessels. Roseola is a characteristic symptom of typhoid fever, para-typhus, louse-borne typhus, and syphilis.

Erythema (Plate 2) is a slightly elevated hyperaemic portion of the skin with distinctly outlined margins. Erythema develops in some persons hypersensitive to strawberries, eggs, and canned crabs. Erythema can develop after taking quinine, nicotinic acid, after exposure to a quartz lamp, and also in some infectious diseases, such as erysipelas and septic diseases.

Weals (urticaria, nettle rash) appear on the skin as round or oval itching lesions resembling those which appear on the skin bitten by stinging nettle. These eruptions develop as an allergic reaction.

Herpetic lesions are small vesicles 0.5 to 1 cm in size. They are filled with transparent fluid which later becomes cloudy. Drying crusts appear in several days at the point of the collapsed vesicles. Herpes would normally affect the lips (herpes labialis, or cold sore) and the ala nasi (herpes nasalis). Less frequently herpetic lesions appear on the chin, forehead, cheeks, and ears. Herpetic lesions occur in acute lobar pneumonia, malaria, and influenza.

Purpura is a haemorrhage into the skin (Plate 3) occurring in Werlhoff's disease, haemophilia, scurvy, capillarotoxicosis, and long-standing mechanical jaundice. The lesions vary in size from small pointed haemorrhages (petechiae) to large black and blue spots (ecchymoses).

Lesions of the skin are quite varied in character when they appear as allergic manifestations.

Desquamation of the skin is of great diagnostic value. It occurs in debilitating diseases and many skin diseases. Scars on the skin, e.g. on the abdomen and the hips, remain after pregnancy (striae gravidarum), in Itsenko-Cushing disease, and in extensive oedema. Indented stellar scars, tightly connected with underlying tissues, are characteristic of syphilitic affections. Postoperative scars indicate surgical operations in past history.

Cirrhosis of the liver is often manifested by development of specific vascular stellae (telangiectasia). This is a positive sign of this disease.

Abnormal growth of hair is usually due to endocrine diseases. Abnormally excessive growth of hair (hirsutism, hypertrichosis) can be congenital, but more frequently it occurs in adrenal tumours (Itsenko-Cushing sydrome) and tumours of the sex glands. Deficient hair growth is characteristic of myxoedema, liver cirrhosis, eunuchoidism, and infantilism. Hair is also affected in some skin diseases.

Nails become excessively brittle in myxoedema, anaemia and hypovitaminosis, and can also be found in some fungal diseases of the skin. Flattened and thickened nails are a symptom of acromegaly. Nails become rounded and look like watch glass in bronchiectasis, congenital heart diseases and some other affections.

Subcutaneous fat can be normal or to various degrees excessive or deficient. The fat can be distributed uniformly or deposited in only certain parts of the body. Its thickness is assessed by palpation. Excessive accumulation of subcutaneous fat (adiposis) can be due to either exogenic (overfeeding, hypodynamia, alcoholism, etc.) or endogenic factors (dysfunction of sex glands, the thyroid, or pituitary gland) (Plate 4). Insufficient accumulation of subcutaneous fat may result from constitutional factors (asthenic type), malnutrition, or alimentary dysfunction. Excessive wasting is referred to as cachexia, and may occur in prolonged intoxication, chronic infections (tuberculosis), malignant newgrowths, diseases of the pituitary, thyroid and pancreas, and in some psychological disorders as well. Weighing the patient gives additional information about his diet and is an objective means in following up on the patient's weight changes during the treatment of obesity or cachexia.

Oedema can be caused by penetration of fluid through the capillary walls and its accumulation in tissues. Accumulated fluid may be congestive (transudation) or inflammatory (exudation). Local oedema is a result of some local disorders in the blood or lymph circulation; it is usually associated with thrombosis of the veins, that is, compression of the veins by tumours or enlarged lymph nodes. General oedema associated with diseases of the heart, kidneys or other organs is characterized by general distribution of oedema throughout the entire body (anasarca) or by symmetrical localization in limited regions of the body. These phenomena can be due to the patient lying on one side. If oedema is generalized and considerable, transudate may accumulate in the body's cavities: in the abdomen (ascites), pleural cavity (hydrothorax) and in the pericardium (hydropericardium). Examination reveals swollen glossy skin. The specific relief features of the oedema-affected parts of the body disappear due to the levelling of all irregularities on the body surface. Stretched and tense skin appears transparent in oedema, and is especially apparent on loose

subcutaneous tissues (the eyelids, the scrotum, etc.). In addition to observation, oedema can also be revealed by palpation. When pressed by the finger, the oedematous skin overlying bones (external surface of the leg, malleolus, loin, etc.) remains depressed for 1-2 minutes after the pressure is released. The mechanism of the development of oedema and methods to reveal this condition will be discussed in detail in the special section of this textbook.

Normal *lymph nodes* cannot be detected visually or by palpation. Depending on the character of the process, their size varies from that of a pea to that of an apple. In addition to simple inspection, the physician should resort to palpation in order to make a conclusion on the condition of the lymphatic system. Attention should be paid to the size of the lymph nodes, their tenderness, mobility, consistency and adherence to the skin. Submandibular, axillary, cervical, supraclavicular, and inguinal lymph nodes are commonly enlarged. Submandibular nodes swell in the presence of inflammation in the mouth. Chronic enlargement of the cervical lymph nodes is associated with development of tuberculosis in them, which is characterized by purulent foci with subsequent formation of fistulae and immobile cicatrices.

Cancer of the stomach and, less frequently, cancer of the intestine can metastasize into the lymph nodes of the neck (on the left). The axillary lymph nodes are sometimes enlarged in mammary cancer. In the presence of metastases the lymph nodes are firm, their surface is rough, palpation is painless. Tenderness of a lymph node in palpation and reddening of the overlying skin indicates inflammation in the node. Systemic enlargement of the lymph nodes is observed in lympholeukaemia, lymphogranulomatosis, and lymphosarcomatosis. In lymphatic leukaemia and lymphogranuloma the nodes fuse together but do not suppurate. Puncture or biopsy of the lymph nodes is required to diagnose complicated cases.

During examination of the *muscular system* the physician should assess its development, which depends on the patient's occupation, his sporting habits, etc. Local atrophy of muscles, especially muscles of the extremities, is diagnostically important. Atrophy can be determined by measuring the girth of the symmetrical muscles of both extremities. Determination of muscular strength and detection of functional muscular disturbances (cramps) are also important for diagnosis. Muscular dysfunction may occur in renal insufficiency (eclampsia), disorders of the liver (hepatic insufficiency), affections of the central nervous system (meningitis), tetanus, cholera, etc.

Defects (deformities or bulging) of the *bones* of the skull, chest, spine, and the extremities, may be revealed by external inspection. But in many cases palpation is necessary. Peripheral bones of the extremities (of the fingers, toes), cheek bones or the mandible grow abnormally in acromega-

ly. Rachitic changes occur in the form of the so-called pigeon breast, rachitic rosary (beading at the junction of the ribs with the cartilages), deformities of the lower extremities, etc. Tuberculotic lesions (the so-called haematogenic osteomyelitis) are localized mainly in the epiphyses of the bones, with formation of fistulae through which pus is regularly discharged. Multiple affections of the flat bones of the skeleton (the skull included) that can be seen radiographically as round light spots (bone tissue defects) are typical of myeloma. Diseases of the spine cause deformation of the spinal column and the chest. Considerable deformities of the spine (kyphosis, scoliosis) can cause dysfunction of the thoracic organs.

When examining *the joints,* attention should be paid to their shapes, articulation, tenderness in active or passive movements, oedema, and hyperaemia of the adjacent tissues. Multiple affections of large joints are characteristic of exacerbated rheumatism. Rheumatoid arthritis affects primarily small joints of the hands with their subsequent deformation. Metabolic polyarthritides, e.g. in gout, are characterized by thickening of the terminal phalanges of the fingers and toes (so-called Heberden's nodes). Monarthritis (affection of one joint) would be usually observed in tuberculosis and gonorrhoea.

Examination of the *extremities* can reveal varicosity of the veins, oedema, changes in the skin, muscles, tremor of the extremities, deformities, swelling and hyperaemia of the joints, ulcers, and scars. Diseases of the central nervous system (tumous, cerebral haemorrhage) and also of the peripheral nervous system can cause atrophy and paralysis of the muscles.

Hippocratic fingers (Fig. 4) or clubbing of the terminal phalanges of the fingers and toes are important diagnostically. The changed shape of the

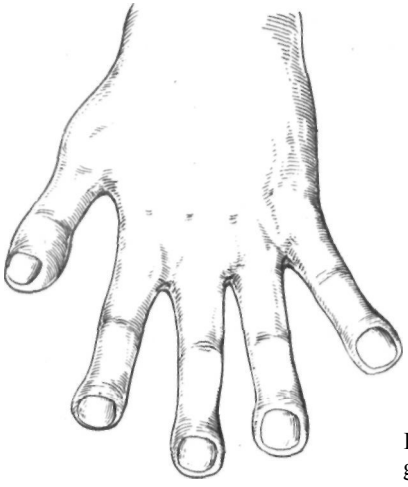


Fig. 4. Hippocratic fingers.

nails resembles hour glass. This symptom is characteristic of prolonged diseases of the lung (chronic purulent processes), heart (subacute septic endocarditis, congenital heart defects) and liver (cirrhosis). Periodically occurring vascular spasms in the extremities cause the development of the symptom known as the dead finger, transient pallor of the fingers and toes, which is characteristic of Raynaud's disease. Prolonged spasms of blood vessels can cause gangrene of the fingers.

When examining the legs, attention should be paid to possible flat foot. Saber shins occur in rickets and sometimes in syphilis. Uneven thickening of the leg bones indicates periostitis which can sometimes be of syphilitic aetiology.

Palpation

Palpation (L *palpare* to touch gently) is the clinical method by which the physical properties, topographic correlation, tenderness and functional characteristic of tissues and organs can be studied by the sense of touch.

Palpation has been known since the ancient times. Hippocrates mentioned palpation in his works. But this method was formerly used mainly to study the physical properties of superficially located organs, e.g. the skin, joints, bones, or pathological growths (tumours), and also for feeling the pulse. It was only recently that physicians began using palpation to detect physiological phenomena. For example, physicians began studying vocal fremitus and the apex beat by palpation only in the middle of the last century (Laennec, Skoda), while systematic use of palpation of the abdominal cavity was begun late in the 19th century, mainly after publication of works by Botkin, Glenard, Obraztsov, and Strazhesko.

The history of development of palpation technique emphasizes the importance of experience and exercise and also of a thoroughly developed methodology for palpation of various parts of the body. The physiological base of palpation is the sense of touch of the examining fingers, and also feeling of temperature. When an organ or growth is palpated through a separating medium (e.g. through the abdominal wall), the examiner obtains useful information only if the density of the palpated organ is higher than that of the separating medium. A relatively soft object, e.g. the intestine, can be felt by pressing the intestine against the hard underlying tissues (pelvic bones, the palm of the examiner pressed against the loin).

Palpation is widely used as an important method for diagnosis of diseases of the internal organs, muscles and bones, lymphatic system, and the skin. Depending on the object of examination, palpation technique differs for examining various organs and systems, but the physician should always follow a certain plan in his manipulations. Neglect of this rule gives

obscure and sometimes erroneous results. For example, the skin or muscles are felt in a fold; this gives information on the thickness, elasticity, and other properties of the material felt. In order to feel temperature of separate parts of the body, the physician should place his palms flat on the body or the extremities, on symmetrical joints (the skin overlying the affected joint is warmer), etc. The pulse is determined by feeling the skin over the artery by the fingers; the properties of the arterial wall and the character of the pulse can thus be determined. Palpation is used to reveal vocal fremitus; this method is useful for the diagnosis of diseases of the lungs and the pleura. Palpation is also very important for the diagnosis of diseases of the abdominal organs. Special techniques used for this purpose will be described in detail in relevant sections. Special palpation techniques are used in obstetrics, gynaecology, and urology.

Deep and *surface palpation* are differentiated. (A variant of deep palpation is penetrating palpation during which the finger tip is impressed into the body to determine the painful area.) Among other palpation techniques are bimanual palpation (with both hands) and ballotment of firm organs (liver, spleen, tumours) in the abdomen containing much fluid, kneepan (exudate in the knee joint), etc. Obraztsov and Strazhesko developed a palpating technique known as sliding palpation, which is used for studying organs located deep in the abdomen.

Despite the wide use of radiography for the diagnosis of diseases of bones, and especially of joints, palpation still remains an important diagnostic technique and is the first and indispensable method for examining the lymph nodes. Palpation is especially important in the study of clinical anatomy and the physiology of the internal organs (along with other direct methods of diagnostic examination).

Percussion

Percussion (L *percutere* to strike through) was first proposed by an Austrian physician Auenbrugger in 1761. Tapping various parts of the human body produces sounds by which one can learn about the condition of the underlying organs. The organs or tissues lying beneath the percussed area begin vibrating and these vibrations are transmitted to the surrounding air whose vibration is perceived by our ears as sounds. Liquids and airless tissues give dull sounds which can be heard with difficulty, such as the sound of a percussed femur (femoral sound). Airless organs and also liquids cannot therefore be differentiated by percussion. The properties of each particular sound obtained by percussion of the chest or the abdomen, and differing from the femoral sound, depend on the amount of air or gas enclosed within the chest or abdomen. The difference in the sounds of percussed lungs, liver, spleen, heart, stomach and other organs depends on (a)

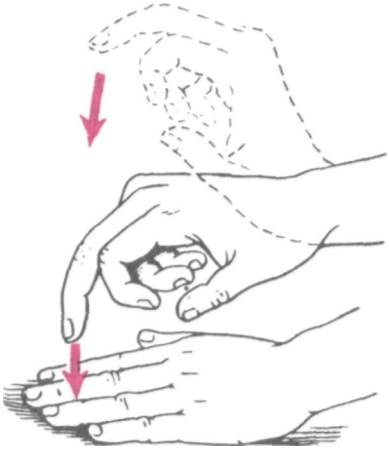


Fig. 5. Correct position of the hands during finger-to-finger percussion.

the different amount of gas or air inside or round the percussed organ; (b) tension of the tissue; and (c) different strength of the percussion stroke transmitted to this gas or air.

Percussion is done by tapping with a plexor (hammer) on a pleximeter placed on the body, or by a finger on another finger (Fig. 5). This is *mediate* percussion. In *immediate* percussion the examined part of the body is struck directly by the soft tip of the index finger. To make tapping stronger, the index finger may be first held by the side of the middle finger and then released. This method was proposed by Obraztsov. Its advantage is that the striking finger feels the resistance of the examined part of the body.

Percussion is done with a slightly flexed middle finger on the dorsal side of the second phalanx of the middle finger of the opposite hand, which is pressed tightly against the examined part of the body. Percussion should be done by the movement of the wrist alone without involving the forearm into the movement. Striking intensity should be uniform, blows must be quick and short, directed perpendicularly to the intervening finger. Tapping should not be strong.

Sounds obtained by percussion differ in strength (clearness), pitch, and tone. Sounds may be strong and clear (resonant) or soft and dull; they may be high or low, and either tympanic or non-tympanic (and with metallic tinkling).

Resonance (clearness) of the percussion sound largely depends on the vibration amplitude: the stronger the tapping the louder is the sound; uniform strength of tapping is therefore required. A louder sound will be heard during percussion of an organ containing greater amount of air. In healthy persons resonant and clear sounds are heard in percussion of

thoracic and abdominal organs filled with gas or air (lungs, stomach, intestine).

Soft or dull sound is heard during percussion of the chest and the abdominal wall overlying airless organs (liver, heart, spleen), and also during percussion of muscles (femoral sound). Resonant and clear sound will become soft if the amount of air decreases inside the lung or if liquid is accumulated between the lungs and the chest wall (in the pleural cavity).

The *pitch* of the sound depends on the vibration frequency: the smaller the volume of the examined organ, the higher the vibration frequency, hence the higher the pitch. Percussion of healthy lungs in children gives higher sounds than in adults. The sound of a lung containing excess air (emphysema) is lower than that of a healthy lung. This sound is called bandbox. Normal vibration frequency of a healthy lung during percussion is 109-130 per second, while in emphysema the frequency decreases to 70-80 c/s. Quite the opposite, if the pulmonary tissue becomes more consolidated, the frequency increases to 400 c/s and more.

The *tympanic* sound resembles the sound of a drum (hence its name: Gk *tympanon* drum). Tympany differs from a non-tympanic sound by higher regularity of vibrations and therefore it approaches a musical tone, while a non-tympanic sound includes many aperiodic vibrations and sounds like noise. A tympanic sound appears when the tension in the wall of an air-containing organ decreases. Tympany can be heard during percussion of the stomach and the intestine of healthy people. Tympany is absent during percussion of healthy lungs, but if the tension in the pulmonary tissue decreases, tympanic sounds can be heard. This occurs in incomplete compression of the lung by the pleural effusion, in inflammation or oedema of the lung (the percussion sound then becomes dull tympanic). A tympanic sound can also be heard if air cavities are formed in the lungs or when air penetrates the pleural cavity. Tympany is heard over large caverns and in open pneumothorax (the sound is resonant). Since air-filled organs produce resonant percussion sounds and airless organs give dull sounds, the difference between these sounds helps locate the borders between these organs (e.g. between the lungs and the liver, the lungs and the heart, etc.).

Topographic percussion is used to determine the borders, size and shape of organs. Comparison of sounds on symmetrical points of the chest is called *comparative percussion.*

Tapping strength can vary depending on the purpose of the examination. Loud percussion (with a normal force of tapping), light, and lightest (threshold) percussion are differentiated. The heavier the percussion stroke, the greater is the area and depth to which the tissues are set vibrating, and hence the more resonant is the sound. In heavy or deep percussion, tissues lying at a distance of 4- 7 cm from the pleximeter are involved. In light or surface percussion the examined zone has the radius of

2—4 cm. Heavy percussion should therefore be used to examine deeply located organs, and light percussion for examining superficial organs. Light percussion is used to determine the size and borders of various organs (liver, lungs and heart). The lightest percussion is used to determine absolute cardiac dullness. The force of the percussion stroke should be the slightest (at the threshold of sound perception). The Goldscheider method is often used for this purpose, the middle finger (flexor) of the right hand is used to tap the middle finger of the left hand flexed at the second phalanx and placed at a right angle touching the surface only with the soft tip of the terminal phalanx (pleximeter).

Main rules of percussion. 1. The patient should be in a comfortable posture and relaxed. The best position is standing or sitting. Patients with grave diseases should be percussed in the lying position. When the patient is percussed from his back, he should be sitting on a chair, his face turned to the chair back. The head should be slightly bent forward, his arms should rest against his lap. In this position muscle relaxation is the greatest and percussion thus becomes more easy.

2. The room should be warm and protected from external noise.

3. The physician should be in a comfortable position as well.

4. A pleximeter or the middle finger of the left hand, which is normally used in the finger-to-finger percussion, should be pressed tightly to the examined surface. The neighbouring fingers should be somewhat set apart and tightly pressed to the patient's body. This is necessary to delimit propagation of vibrations arising during percussion. The physician's hands should be warm.

5. The percussion sound should be produced by the tapping movement of the hand alone. The sound should be short and distinct. Tapping should be uniform, the force of percussion strokes depending on the object being examined (see above).

6. In topographic percussion, the finger or the pleximeter should be placed parallel to the anticipated border of the organ. Organs giving resonant note should be examined first: the ear will better detect changes in sound intensity. The border is marked by the edge of the pleximeter directed toward the zone of the more resonant sounds.

7. Comparative percussion should be carried out on exactly symmetrical parts of the body.

Auscultation

Auscultation (L *auscultare* to listen) means listening to sounds inside the body. Auscultation is *immediate (direct)* when the examiner presses his ear to the patient's body, or *mediate (indirect,* or instrumental). Auscultation was first developed by the French physician Laennec in 1816. In 1819

it was described and introduced into medical practice. Laennec also invented the first stethoscope. He substantiated the clinical value of auscultation by checking its results during section. He described and named almost all the auscultative sounds (vesicular, bronchial respiration, crepitation, murmurs). Thanks to Laennec, auscultation soon became an important method for diagnostication of lung and heart disease and was acknowledged throughout the world, Russia included. The first papers devoted to auscultation methods were published in Russia in 1824.

The development of auscultation technique is connected with improvement of the stethoscope (Piorri, Yanovsky, and others), invention of the binaural stethoscope (Filatov and others), invention of the phonendoscope, and the study of the physical principles of auscultation (Skoda, Ostroumov, Obraztsov, and others). Elaboration of methods for recording sounds (phonography) that arise in various organs has become a further development of auscultation. The graphic record of heart sounds was first made in 1894 by Einthoven. Improved phonographic technique made it possible to solve many important auscultation problems and showed the importance of this diagnostic method.

Respiratory act, cardiac contractions, movements in the stomach and the intestine produce vibrations in the surrounding tissues. Some of these vibrations reach the surface of the body and can thus be heard directly by the physician's ear or by using a phonendoscope. Both direct and indirect auscultation is used in practical medicine. Immediate or direct auscultation is more effective (heart sounds and slight bronchial respiration are better heard by direct auscultation) because the sounds are not distorted and are taken from over a larger surface (the area covered by the physician's ear is larger than that of the stethoscope chest piece, or bell). Immediate auscultation is impractical for auscultation of the supraclavicular fossa and armpits and sometimes for hygienic considerations. Mediate (instrumental) auscultation ensures better localization and differentiation of the sounds of various aetiology on a small area (e.g. in auscultation of the heart), although the sounds themselves are slightly distorted by resonance. Sounds are usually more distinct with mediate auscultation.

During mediate auscultation with a solid stethoscope, vibrations are transmitted not only by the air inside the instrument but also through the solid part of the stethoscope and the temporal bone of the examiner (bone conduction). A simple stethoscope manufactured from wood, metal or plastics consists of a tube with a bell which is pressed against the chest wall, the other end of the stethoscope bearing a concave plate for the examiner's ear. Binaural stethoscopes are now widely used. These consist of two rubber tubes ending with self-retaining ear pieces connected to a single chest piece. The binaural stethoscope is more convenient, especially for auscultation of children and seriously-ill patients. Phonendoscopes differ from

simple stethoscopes in that they have a membrane covering the bell. Stethoscopes with electrical sound amplification were designed. They, however, were declined by most physicians because of difficulties in differentiation and interpretation of sounds which can be achieved by experience. Amplifiers that are now available do not ensure uniform amplification of all frequencies and this distorts the sounds.

A stethoscope is a closed acoustic system where air serves as a transmitting medium for sounds. Therefore, if the tube is clogged, or communicates with ambient air, auscultation becomes impossible. The skin against which the bell of the stethoscope is pressed acts as a membrane whose acoustic properties change under pressure: if the pressure on the skin increases higher frequencies are better transmitted, and vice versa. Excess pressure on the bell damps vibration of the underlying tissues. A large bell better transmits lower frequencies.

In order to decrease resonance (i.e. to lessen intensification of one tone in the combination of various tones) it is necessary that the ear and the chest piece were not very deep, while the internal cavity of the phonendoscope bell had a parabollic section; the length of a solid (one-piece) stethoscope should not exceed 12 cm. It is also desirable that the tubes of inelastic phonendoscope be as short as possible while the amount of air inside the system as small as possible.

The human ear perceives vibrations in the range from 16-20 to 20000 per second, i.e. from 16 to 20000 Hz; variations in frequency are differentiated better than in the sound intensity. The highest sensitivity of the ear is to sounds of 2000 Hz. The sensitivity decreases sharply with decreasing frequency. For example, it decreases to 50 per cent at 1000 Hz and to 0.9 per cent at 100 Hz. It should also be remembered that a weak sound is perceived with difficulty after a loud sound.

All auscultation sounds are noise, i.e. a mixture of sounds of various frequencies. Noise percepted during auscultation of the heart and lungs are mostly vibrations in the range from 20 to 600 Hz. Bronchial respiration produces sounds in the range of frequencies from 240 to 1000 Hz, friction sounds and cardiac murmurs from 75 to 500 Hz, the first heart sound from 28 to 150 Hz, of the gallop sound from 28 to 150 (commonly from 30 to 60 Hz) and of the third heart sound from 25 to 35 Hz (at the threshold of audibility). Phonocardiographic studies show that the lower limit of sound frequencies produced by the heart is to 5-10 Hz, i.e. beyond audibility threshold of the human ear. Low frequency vibrations can be felt by palpation, e.g. vibration of tissues in the precardial region which is known as cat's purr in mitral and aortal stenosis, vibrations produced by pleural friction and friction of the pericardium in dry pleurisy and pericarditis, etc.

Auscultation has remained an indispensable diagnostic technique for examining the heart, lungs and vessels, determining arterial pressure by Korotkoff's method, for diagnosing arteriovenous and intracranial aneurysms, and also in obstetrical practice. Auscultation is important for the study of the alimentary organs (intestinal murmurs, peritoneal friction) and also of joints (friction of intra-articular surfaces of the epiphysis).

Auscultation techniques. Special rules should be followed during

auscultation paying particular attention to conditions in which it is carried out. The first requirement is silence in the room and the absence of any extraneous sounds that might mask the sounds heard by the physician. The ambient temperature should provide comfort for the undressed patient. During auscultation the patient is either sitted or stands upright. If the patient is in grave condition he may remain lying in bed. During auscultation of the lungs of a lying patient, his chest is first auscultated on one side and then the patient is turned to the other side and auscultation is continued.

The skin to which the bell of the phonendoscope is pressed should be hairless because hair produces additional friction which interferes with differentiation and interpretation of the sounds. When using a stethoscope its bell should be pressed firmly and uniformly to the patient's skin but the pressure should be moderate since excess pressure damps vibration of the skin to diminish the intensity of the sounds. The bell of the stethoscope should be held by the thumb and the forefinger. The posture of the patient should be varied in order to ensure better conditions for auscultation of each particular organ. For example, the diastolic sound in aortic incompetence is better heard with the patient in the sitting or standing position, while the diastolic sound in mitral stenosis, with a patient lying on his side (especially on his left side). The respiration of the patient should be regulated by the physician and in some cases the patient is asked to cough (e.g. rales in the lungs may disappear or change their properties after expectoration).

Many various stethoscopes and phonendoscopes are now produced by the medical industry but they differ mostly in design. It is important that the physician should use an instrument to which he got accustomed. An experienced physician will always feel it difficult to differentiate and interpret sounds if a new stethoscope is used for some reasons. This explains the necessity of sufficient theoretical knowledge on the part of the physician so that he might correctly interpret the heard sounds. Hence the necessity of constant training in auscultation. Only permanent use of this diagnostic technique will make it a useful tool of diagnosis.

Laboratory and Instrumental Methods of Examination

Laboratory and instrumental methods of examination are quite varied and their number constantly increases. As distinct from the main methods, such as inquiry, inspection, palpation, percussion and auscultation, the instrumental and laboratory methods depend on the advances in modern physics, chemistry, biology and related sciences; these methods require more sophisticated instruments and equipment (thermometers, electrocardiographs, X-ray units, laboratory equipment, etc.) and a specially trained

medical personnel (laboratory technicians, physicians, roentgenologists and others).

Wide use of laboratory and instrumental techniques in the clinical and experimental practice for examination of patients facilitates the study of the disease, helps discover new, earlier unknown diseases and, what is more important, it ensures earlier diagnosis of the disease and hence its timely treatment. The laboratory and instrumental methods were formerly known as additional techniques since they are used not in all cases and only after examination of the patient by the main diagnostic methods. But they are now widely used in medicine and sometimes the results of instrumental and laboratory examination become so important that the physician cannot establish a correct diagnosis without using them first. This section describes only general principles of the laboratory and instrumental methods of examination. They will be given in more detail during discussion of diseases of separate organs and systems.

Anthropometry

Anthropometry (Gk *anthropos* human being and *metron* measure) is the method of examination based on the comparative measurements of morphological and functional signs of man. Measurement of comparatively small number of signs is sufficient for practical medicine (clinical anthropometry). The main anthropometric sings are the man's height and weight.

The man's *height* depends on the dimensions of the skeleton and is determined by the height meter. The normal height of males varies from 165 to 180 cm and of females from 155 to 170 cm. Deviations on either side are connected with endocrine dysfunction. Dwarfism may be due to hypofunction of the anterior lobe of the pituitary (nanism) or of the thyroid gland (cretinism). Gigantism can be due to dysfunction of the anterior lobe of the pituitary or hypofunction of the sex glands.

The height of man is measured by a wooden or metal graduated plank fixed in a floor-mounted base. A horizontal plank slides freely along the vertical plank to read the height. A special collapsible seat is provided to measure the sitting height (the length of the trunk). Another graduated scale begins reading at the level of the seat. In order to measure the height of a man, he is asked to stand barefoot on the floor plate and to assume an erect attitude so that his back is pressed against the vertical plank; the head should be in a position where the upper edge of the external auditory meatus is level with the outer angle of the eye. The sliding horizontal plank is then lowered to come in contact with the patient's head and fixed in this Position. The patient is asked to step out from the height meter. The lower edge of the sliding Plank reads the height. The sitting height is measured in the same way except that the patient is asked to sit.

Patient's height and the length of his trunk are important for the assessment of both his physical growth and proportions of his separate parts

which can be upset in some congenital diseases (e.g. chondrodystrophy) and diseases acquired in childhood.

In addition to measurement of the patient's height (and sitting height), measured also are the girth of his chest, abdomen, neck, head, lower extremities, pelvis, and some internal organs (by percussion). The technique and importance of measurements will be discussed in relevant chapters.

Weight is measured on a special medical balance. Weighing should be done in the morning, on a fasting stomach, after defaecation and urination. Whenever possible, the patient should be with no clothing or he should wear a light garment. In order to follow changes in the patient's weight during treatment (e.g. in treatment of asthenia or obesity, treatment of oedema, etc.) repeated weighings should be done in the same conditions (with the patient either undressed or with the same clothes on) in order to rule out the error.

The weight of the human body depends mainly on the height and the girth of the chest. The correlation between these two factors determines proportionate constitution of man. Normal weight can be calculated approximately by measuring the man's height and subtracting 100. For example the normal weight of a 180 cm high man should be 80 kg (180 - 100).

The following factors are practically important:

1. The statural-weight value. It reflects proportionality of height to weight and is determined by the formula

$$\frac{P \times 100}{a}$$

where P is the weight of the body in kg and a is the height in cm. The normal height to weight ratio is expressed by the index 37 - 40. Lower index indicates malnutrition and higher overfeeding of the patient.

2. The index of proportionality between height (a) and the girth of the chest *(T)* is determined by the formula

$$\frac{T \times 100}{a}$$

Normal index is from 50 to 55; lower figures indicate narrow chest (stenothorax), and higher broad chest.

3. The normal proportional ratio between the three parameters a — $(T + P)$ is about 20 and it deviates significantly if this proportion is abnormal.

Muscular force is measured by *dynamometry.* The patient is asked to compress an elliptic steel spring provided with a scale and a reading arrow. Other devices are also available by which power of various muscles can be measured.

Thermometry

Body temperature is measured in each patient. It helps reveal fever and is very important diagnostically. Fever is usually caused by infection and products of tissue decomposition. Fever is a normal reaction of the body to infection. Sometimes an infectious disease can develop without fever or it can temporarily proceed without elevation of temperature (tuberculosis, syphilis). The degree to which the body temperature rises depends on the patient's condition: the same infection can cause different fever in various persons. For example, in the young the temperature in pneumonia rises to 40 °C and over, while in old or asthenic patients with the same disease the temperature rises insignificantly or it may remain at normal level.

Elevation of temperature unconnected with infection is sometimes observed in malignant tumours or tissues necrosis (e.g. in myocardial infarction), tissue haemorrhages, rapid decomposition of red blood cells in the blood, etc. Fever occurs less frequently in diseases of the central nervous system and also in diseases of reflex aetiology. Non-infectious fever does not strongly affect the patient's condition and is usually transient.

The temperature is measured by a thermometer graded in 0.1 ° (C or F). Electric thermometers are also used in medical research. The sensitive element in such thermometers is a thermocouple. An electric thermometer quickly responds to variations in temperature. It can be used to measure and compare temperature of various areas of the skin. Some electric thermometers (including multi-channel) are provided with a device that automatically records variations in temperature on a graph paper (electrothermographs).

When temperature is measured, the thermometer is kept in the armpit for about ten minutes. The thermometer should come in tight contact with the patient's skin; the forearm should be tightly pressed against the chest to close the armpit. When temperature is measured in asthenic patients or in children, assistance is required to keep their forearm pressed to the chest. Sometimes temperature is measured in the rectum for which purpose the thermometer coated with oil is inserted in the rectum; the patient should lie on his side. Rectal temperature is 0.5-1° higher than in the armpit.

As a rule temperature is taken twice a day (at 7 or 8 a.m. and 5 or 7 p.m.). Thermometer readings should be registered on a special chart for several days where the morning and the evening temperature is designated by dots. The dots are then interconnected to give a curve which is characteristic for many specific diseases.

Normal temperature of the body (as measured in the armpit) is 36.4- 36.8 °C. The temperature undergoes circadian variations. The lowest temperature is between 3 and 6 a.m. and the maximum between 5 and 9 p.m. The difference between the morning and evening temperature

does not exceed 0.6 °C in normal persons. The temperature of the body slightly rises after meals and physical strain, and also at high ambient temperatures.

Fever is characterized not only by elevated temperature but also by the upset function of the entire body. The rise in temperature is a very important (but not always decisive) sign for assessing severity of fever. It is accompanied by accelerated pulse and respiration rate; arterial pressure often drops; the patient complains of being hot, exhausted, of headache, dryness and the unpleasant feeling in the mouth, thirst, and the absence of appetite; the tongue is coated and often dry; the amount of excreted urine decreases. Fever intensifies metabolic processes. And since the patient would often refuse food, his weight often decreases significantly.

A quick and intense rise in temperature (e.g. in malaria or pheumonia) is often attended by chills, which can last from a few minutes to an hour, and in rare cases for longer periods. The skin blood vessels strongly contract in chills, the skin becomes pallid, goose-flesh (cutis anserina) appears, the nailbeds become cyanotic; the patient feels intense cold, he shivers, the teeth begin chattering. If the temperature rises gradually, the chills are only slight. At high temperature the skin reddens and becomes warm; the patient feels hot. A sudden drop in temperature is accompanied by heavy perspiration. The temperature of the patient with fever is higher in the evening than in the morning. Its rise over 37 °C suggests a disease.

Elevated temperatures are characterized as follows (Fig. 6): temperatures from 37° to 38 °C are called subfebrile, from 38° to 39 °C moderately high, from 39° to 40 °C high, and over 40 °C very high. Temperatures over 41° and 42 °C are called hyperpyretic and are dangerous to the patient's life.

Not only elevated temperature itself but also its circadian variations are very important for diagnosing the diseases. Variations of temperature during the day determine the *type of fever* (Fig. 7). The following main six types of fever are differentiated.

1. *Continued fever (febris continua).* The circadian variation does not exceed 1 °C. It is observed in patients with acute lobar pheumonia or II stage typhoid fever.

2. *Remittent fever (febris remittens).* The circadian variations exceed 1 °C, the morning lowest temperature being over 37 °C; it often occurs in tuberculosis, III stage typhoid fever, purulent diseases, and lobular pneumonia.

3. *Intermittent fever (febris intermittens).* The daily variations exceed 1 °C, with complete apyrexia in remissions.

4. *Hectic fever (febris hectica).* The temperature rises sharply (by 2°-4 °C) and drops to normal and subnormal level. The fever is often ac-

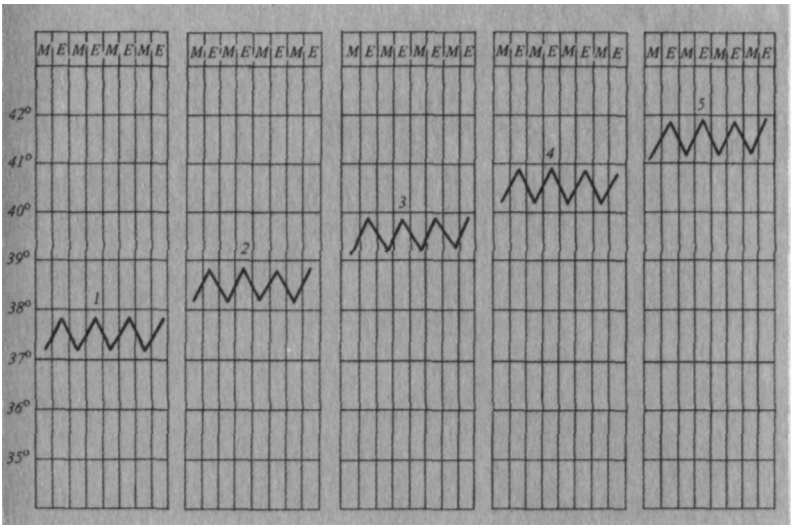


Fig. 6. Types of fever.
/—subfebrile (37-38 °C); *2*—moderate (38-39 °C); *3*—high (39-40 °C); *4*—very high (over 40 °C); *5*—hyperpyretic (over 41-42 °C).

companied by excessive sweating. It usually occurs in grave pulmonary tuberculosis, suppuration, and sepsis.

5. *Inverse fever (typhus inversus).* The morning temperature is higher than in the evening; it sometimes occurs is sepsis, tuberculosis, and brucellosis.

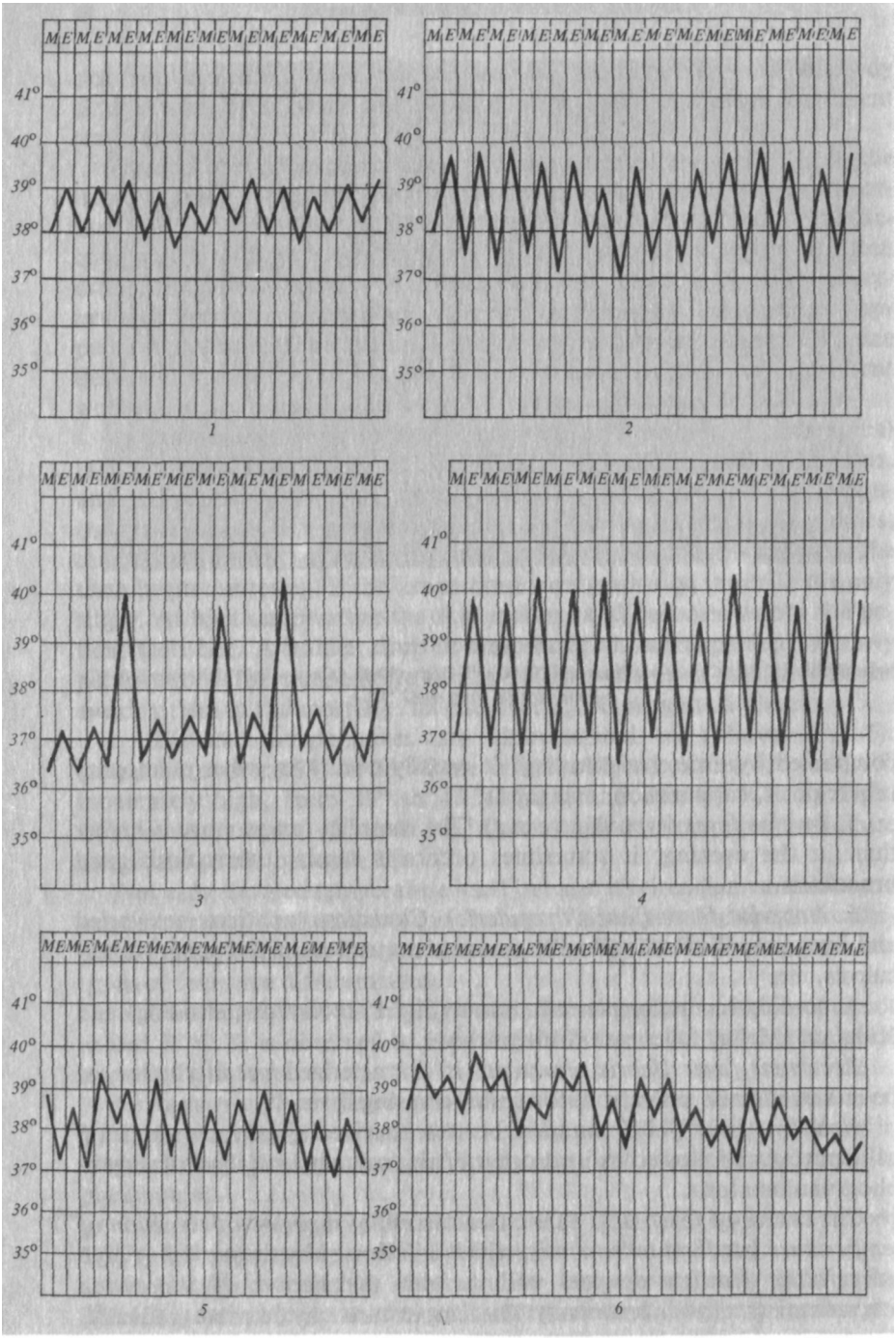
6. *Irregular fever (febris irregularis).* Orcadian variations are varied and irregular. It often occurs in rheumatism, endocarditis, sepsis, tuberculosis, etc.

According to the *temperature curve* (Fig. 8) recurrent (relapsing) and undulant (Malta) fevers are distinguished.

Recurrent fever (febris recurrens) is characterized by alternation of fever and afebrile periods; it occurs in relapsing fever.

Undulant fever (febris undulans) is characterized by periodic elevation of temperature followed by its drop; it often occurs in brucellosis and lymphogranulomatosis .

The *course of fever* (Fig. 9) is characterized by a *period of elevation of temperature (stadium incrementi),* which is followed by *the period of high temperature (fastigium),* and ending with the *period of decreasing temperature (stadium decrementi).* The temperature may decrease gradually,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2
3
4
5
6

Fig. 7. Circadian temperature variations.
1-continuous fever; 2—remittent fever; 3—intermittent fever; *4*—hectic fever; *5*—inverted fever; *6*—irregular fever.

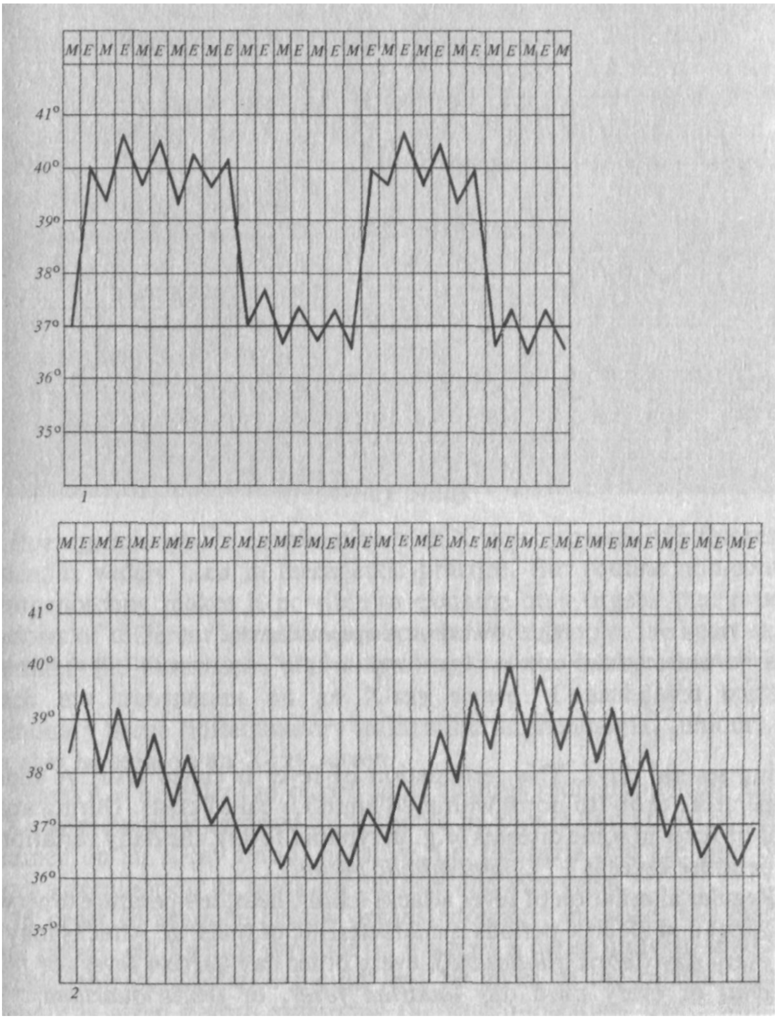


Fig. 8. Special forms of temperature curves,
1—recurrent fever; 2—undulant fever.

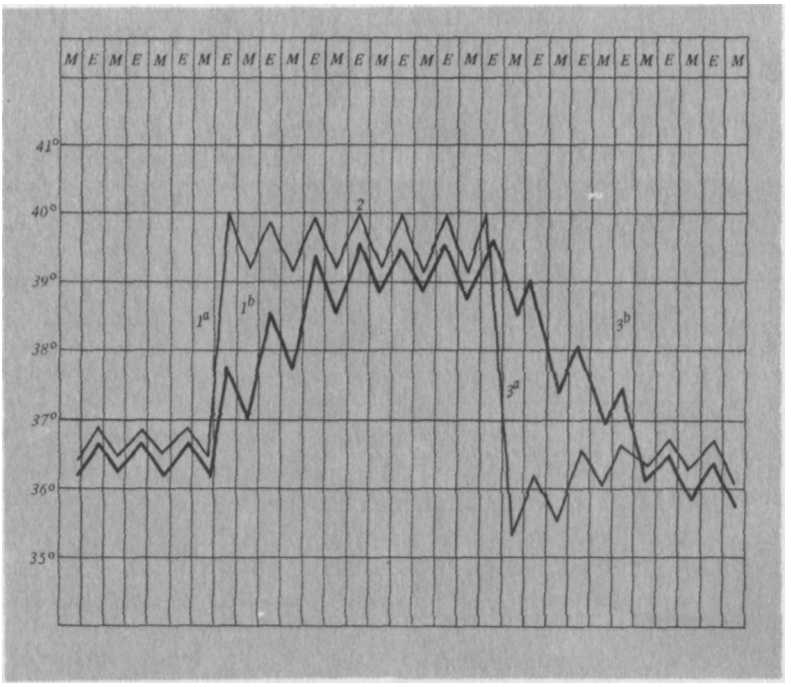


Fig. 9. Periods of temperature curves.
1^a, 1^b —two variants of stadium incrementi; 2—stadium fastigii; 3^a, 3^b—two variants of stadium decrementi.

during several days. This termination *of* fever is called lysis. A sudden temperature drop (to norm within 24 hours) is called crisis. During abatement of fever in some diseases (e.g. in typhoid fever), the daily variation of temperature exceeds 1 °C *(amphibolic period).*

Regular alternation of fever attacks (chills, heat, temperature drop with sweating) and afebrile periods is characteristic of malaria. Attacks may occur every day *(febris quotidiana),* every other day *(tertian fever,* or *febris tertiana)* or every third day *(quartan fever,* or *febris quartana).* The temperature rise may be only transient, for few hours (one-day fever, or febris ephemera, febriculara.) It occurs in mild infection, excess exposure *to* the sun, after blood transfusion, sometimes after intravenous injections of medicinal preparations.

Fever lasting up to 15 days is called acute, and over 45 days—chronic.

Hypothermia (subnormal temperature) often occurs in the critical fall of temperature; it persists for 1-2 days at about 35 °C; the pulse is full, slow, the patient's condition satisfactory. Subnormal temperature may be observed in grave circulatory collapse; the pulse becomes weak and frequent, respiration superficial, the skin pallid and covered with sweat. Hypothermia occurs after profuse bleeding, in starvation and asthenia, during convalescence after infectious diseases, and in overcooling.

In addition to measuring the body temperature with a thermometer, the temperature of various parts of the body should be felt by hand. Elevated temperature of the skin overlying a joint indicates its inflammation; cold extremities of patients with fever suggest peripheral circulatory failure (collapse, cardiac insufficiency).

Since 1970, thermography—thermovision—has been introduced in practical medicine in the Soviet Union. The method is based on detection of zones with increased infra-red radiation emanating from the organs affected by acute inflammatory, cancerous, and other diseases by using special apparatus—thermovision system.

Measuring temperature inside some hollow organs (stomach, large intestine, etc.) by special radio devices is of great diagnostic significance.

X-Ray Study

Roentgenoscopy, or examination with X-rays by means of a fluorescent screen, is widely used in therapeutic practice. But routine non-contrast roentgenoscopy makes it possible to examine only organs that produce shadows of different intensity on a screen. For example, the heart can be examined (its dimensions and shapes) against the background of lungs which are transparent on an X-ray screen. Consolidated parts of pulmonary tissue (inflammatory infiltration in pneumonia, tumour, etc.) can also be seen on an X-ray screen.

When it is necessary to record some changes radiography (the making of X-ray pictures) is resorted to. It should be kept in mind that the pattern obtained on an X-ray film is negative, i.e. the parts that are light on an X-ray screen appear as black on the film and vice versa.

In order to examine hollow organs (stomach, intestine, gall bladder, renal pelves, etc.) which produce on a screen a dense uniform shadow, a special contrast substance should first be given to the patient. Barium sulphate is given before examining the gastro-intestinal tract; when the large intestine is examined the suspension of barium sulphate is administered as an enema. Iodine preparations are given to examine the gall bladder and intrahepatic bile ducts *(cholecystography, cholegraphy).* Some

preparations (e.g. bilitrast or iopanoic acid) are given per os while others (e.g. bilignost) intravenously. These substances are carried by the blood to the liver and excreted together with bile to accumulate in the gall bladder. X-ray examination of the renal pelves *(pyelography)* is done with sergosin given intravenously as well. In X-ray examination of the bronchi *(bronchography)* they are filled with a special contrast substance (iodolipol); cardiotrast is used in *angiography* (X-ray examination of the blood vessels).

Sometimes an X-ray image of an organ becomes more distinct after the surrounding tissues or cavity are filled with air. During X-ray examination of the kidneys for suspected tumour, air is injected into the perirenal fat; the abdominal cavity is filled with air to reveal growth of the tumour into the stomach walls (artificial *pneumoperitoneum).*

A number of new improved X-ray techniques have been elaborated recently. For example, *roentgenokymography* is used to examine the moving organs such as the heart. A special lead plate is interposed in the path of X-ray emitted by the X-ray tube and passed through the examined part. The plate has horizontal slits and moves through a certain distance in the plane perpendicular to the contour of the examined organ. Since the organ (e.g. the heart) moves, the X-ray image on the film is in the form of a toothed line. The amplitude and the shape of the teeth are informative of the contractile strength of the heart and the character of its contractions.

Tomography or sectional radiography is often used as well. During an exposure, the X-ray tube is moved so that the selected structures only remain stationary on the moving film and their image is clear and sharp while structures located at other depths (in all other planes) have a relative displacement on the film and appear obliterated or blurred. Tomography is used to reveal tumours, inflammatory infiltrations and other pathological growths. Computer tomography has become popular in recent times.

The quality of images has improved significantly during the past years. X-ray machines are now equipped with special electronic optical amplifiers which give brighter and more distinct images, while the time of a patient's exposure to X-rays is diminished. This makes it possible to film the entire process of examination or its separate stages *(cineradiography).* It is especially important in functional disorders of organs (oesophagospasm, dyskinesia of the intestine, etc.). The film can be reviewed as many times as may be necessary, which is important at consultation, etc. The electronic optical devices can transmit the image to TV receivers, whose screens give a more distinct picture than an ordinary X-ray machine. The screen of a special TV set can be demonstrated remotely in places protected from excess radiation. All manipulations with the X-ray machine (its adjustment in the vertical or horizontal plane, taking pictures, etc.) can be done at a distance from a remote control panel.

Endoscopy, Biopsy, and Cytological Studies

Endoscopy (Gk *endon* within, *skopein* to watch) is the examination of the interior of hollow or tubular organs by direct observation of their internal surface by means of endoscopes. The simplest endoscope is a metal tube (or two collapsible tubes) provided with an optical system that enlarges the image, and an illuminating device. New types of endoscopes have been devised recently. The image is transmitted in them through fibrous light guides (optical fibres). The main advantage of these endoscopes is their high flexibility which facilitates examination and makes it practically safe.

Endoscopy is used for inspecting the oesophagus *(oesophagoscopy),* stomach *(gastroscopy),* duodenum *(duodenoscopy),* rectum and sigmoid colon *(rectoromanoscopy),* the entire large intestine *(colonoscopy),* trachea and bronchi *(tracheobronchoscopy),* the abdominal cavity and its organs *(laparoscopy),* urinary bladder *(cystoscopy),* and of some other organs. A special endoscope is used in each particular case, the design of the instrument being specially adapted to the anatomophysiological properties of the particular organ.

The diagnostic value of endoscopy increases because specimens of mucosa or tissues of the examined organ can be taken *(biopsy).* These samples are used for cytological, histological, and histochemical analyses. Biopsy can however be an independent procedure (without endoscopy). "Blind" biopsy is used to take specimen of mucosa of the stomach or duodenum, of the liver tissue (transcutaneous biopsy) and kidneys; sternal puncture is used for taking samples of bone marrow, etc. Photographic pictures can be taken during endoscopy using special photographic adaptors. Modern endoscopes can transmit the picture onto a TV screen so that other physicians engaged in the treatment of a given patient can also observe the changes revealed by endoscopy. Video tape-recorder makes it possible, whenever necessary, to compare the picture with the results of repeated endoscopy (e.g. to follow cicatricial changes in gastric ulcer, etc.).

Endoscopy is often used for therapeutic purposes as well. Foreign bodies and polyps can be removed by an endoscope, ulcers can be cauterized, and other manipulations can be performed under control of an endoscope. It should be remembered that endoscopy can only be carried out by a specially trained physician and for special indications because complications can arise due to anaesthesia and narcosis (which are often used to make endoscopy painless) and to endoscopy itself. *Ophthalmoscopy* (inspection of the fundus of the eye) and *capillaroscopy* (examination of the capillaries in the nailbed) resemble endoscopy in certain respects for both are used for diagnosis of internal pathology (essential hypertension, diabetes mellitus, etc.).

Instrumental-Functional Methods of Examination

Various methods are used in the clinic to study functional activity of various organs. These methods can conventionally be divided into three groups. The first group includes methods based on the recording of biopotentials arising during functioning of the organs. These are electrocardiography, electroencephalography, electrogastrography, and electromyography. The second group includes methods by which motor activity (kinetics) of organs is recorded. These are "bulb" kymography of various parts of the gastro-intestinal tract (done with a rubber tube ending with a rubber bulb; the other end of the tube is communicated with an instrument which records all variations in pressure inside the air-filled bulb resulting from contractions of the oesophagus, stomach, or the intestine); study of peristalsis and pressure inside the alimentary organs by means of a radio-capsule; apical cardiography (recording the apex beat); oesophagoatriography (recording of pressure variations inside the oesophagus which are transmitted from the adjoining left atrium); ballistocardiography (recording vibrations of the human body caused by heart contractions and the reactive forces); rheography (registration of changes in the tissue resistance in connection with the circulatory dynamics during heart contractions); spirography and pneumotachymetry (registration of the outer respiration function). The third group includes the methods by which various sounds generated during contraction and movement of various organs are recorded. The most important of them is phonocardiography (recording heart sounds). Phonopneumography and phonointestinography (recording sounds arising in the lungs and the intestine) are less popular.

Radioisotope Methods

Radioisotope methods of study are now coming into wide use. *Scanning* is among them. The patient is given a radioactive preparation that can concentrate in the desired organ: ^{131}I and ^{132}I are used to examine the thyroid; iodine-labelled rose bengal or a colloidal solution of gold (^{198}Au) are used to study the liver; neohydrin labelled with mercury isotopes ^{197}Hg or ^{203}Hg are given to study the liver, etc. The patient is placed on a bed beneath a detector of the scanning apparatus (gamma-topograph or a scanner). The detector (scintillation counter of gamma-radiation) moves along a predetermined line over the object of study and receives the radioactive impulses emitted from the examined organ. Signals of the counter are modified by a collimator into various forms of records (scin-

tiscans or scans). The results of scanning can be recorded either graphically as a black-and-white or colour shaded pictures, photographically, or digitally (after processing of the information on a computer). Since the radiation intensity over the organ where the radioisotope is accumulated is much higher than over the surrounding tissues or organs, the density of lines or points are higher on the portion of the scan corresponding to this organ. Thus a "shadow" picture of the organ under examination is obtained on a scan. In focal affections of the parenchyma of an organ (tumour, cyst, abscess, etc.) rarefied foci can be distinguished on the scan.

Scanning can be used to determine displacement of the organ and changes in its size and functional activity (by diffuse lessening of density on the scan). It is used to study the thyroid, liver, kidneys and (less frequently) some other organs.

Radioisotopes are widely used to study the function of some organs. The rate of entrance and accumulation of a radioactive isotope in a given organ, and also removal of the isotope from the body are studied. The function of the thyroid gland is assessed by the dynamics of the absorption of sodium iodide (^{131}I) in the thyroid, and concentration of protein-bound ^{131}I in the patient's blood plasma. Renal function is studied by the rate of discharge of ^{131}I-labelled hippuran. Radioactive isotopes are used to study absorption in the small intestine and also for some other investigation.

Ultrasound Echography

Ultrasound echography (syn. echolocation, ultrasound scanning, sonography) is a diagnostic method based on different reflection of ultrasound waves that pass at various velocities through tissues and media of various density. Ultrasound is acoustic frequency from 2×10^4 to 10^8 Hz, which are not perceived by the human ear. Ultrasound well propagates in body tissues even at low energies (0.005-0.008 W/cm^2), which is hundreds or thousands times lower than the doses used for therapeutic purposes (ultrasound therapy). Ultrasound travels in the human body at a velocity of about 1 500 m/s. Using ultrasound for diagnostic purposes is based on its ability to propagate in media in a given direction in the form of a fine concentrated beam of waves. Ultrasound waves are differently absorbed (damped) in various tissues and differently reflected from them. Sensitive instruments differentiate reflection of ultrasound pulses from tissues if their density differs as slightly as by only 1 per cent. This makes ultrasound a useful diagnostic aid. Modern apparatus produce ultrasound pulses lasting for 2-5 μs at a frequency of 1000 Hz at short intervals of time. The

reflected ultrasound pulses are detected, transformed, and transmitted to an oscilloscope from which the pulses are read off.

First attempts to use ultrasound for diagnostic purposes were undertaken more than 35 years ago, but satisfactory technical apparatuses have been devised and introduced into clinical practice only during recent time. The advantage of ultrasound is that it can be used to determine the structure of various organs without producing any harmful effect on the patient; moreover the procedure is not in the least annoying to the patient. The examination can be repeated (for example in order to assess the dynamics of the process) without any detriment to the patient. Great diagnostic reliability and the value of data obtained with ultrasound make this method very important. It has advantages in comparison with other methods since it needs no contrast, radioactive, or other substances to be given to the patient before the procedure.

Ultrasound is obtained by conversion of energy of electromagnetic oscillations (the inner piezoelectric effect). The phenomenon is based on the property of some crystals to change their electric charge under the compressing or stretching effect. The value of the charge is directly proportional to the mechanical pressure applied. This phenomenon is used in ultrasound diagnostic apparatus for recording the sound oscillations. The reverse piezoelectric effect, by which electric energy is converted into acoustic energy, is utilized for the generation of ultrasound energy.

Transmission and *location* (echography) ultrasound methods are used for examination of patients. The transmission method is seldom used. The source of ultrasound oscillations is applied to one side of the patient while the receiver of the ultrasound beam is positioned on the other side. The location method is however more popular. The piezocrystal is used as both the source of ultrasound and as the receiver. Ultrasound is converted into electric energy and the structure of the studied organ can be visualized on the screen of an oscilloscope.

One- and *two-dimensional* methods of visualization are used. In the one-dimensional (A-method) echography, ultrasonic waves reflected from the studied object are converted into electric pulses and delivered onto the vertically deviating plates of an X-ray tube. Whenever several anatomical media, located at different distances from the receiver, arise in the pathway of the ultrasonic beam, the vertical spikes are fixed on the horizontal scanning in succession, in accordance with the time of arrival of the ultrasonic pulse reflected from this or that object. Since this process is repeated at high frequency, the scanning line with spikes on it appears as a stationary pattern on the oscilloscope screen.

The A-method can be used to measure accurately the distance to the object under examination, to determine its anteroposterior dimensions, and sometimes to obtain information concerning special properties of the structure. The method fails to give complete information on the configuration and the size of the object studied, especially so if the object has irregular form.

The two-dimensional method (B-method) gives information about shapes, dimensions, and the structure of the object under study. The information is recorded on a polaroid film, on a videotape, or common photographic film. Modern instruments give direct information during the examination, which accelerates processing and interpretation of the data.

Systems with sectoral scanning are now also widely used. Electronic amplifiers and converters of the echo-signals make it possible to record on the echogram 8-10 shades of grey colour: from black to white.

Soviet-made apparatus "Echo-11" and "Echo-12" are widely used in echographic examinations though more improved models are being developed. The image is recorded from the oscilloscope of the echograph on a photographic film with the help of a camera.

Ultrasound is now widely used in the diagnosis of internal diseases, such as the diseases of the heart, liver, gall bladder, pancreas, kidneys, the thyroid, etc. The use of echography in cardiology makes it possible to determine the presence and character of heart defects, calcification of the cusps in rheumatism, tumour of the heart, and other changes in this organ. Ultrasonic echography is used in neurology (for the study of the brain, cerebral ventricles), in ophthalmology (to determine the optic axis of the eye, the degree of retinal detachment, to locate and assess the size of foreign bodies, to diagnose tumours of the eye and the orbit, etc.), in otorhinolaryngology (for differential diagnosis of loss of hearing), in obstetrics and gynaecology (to determine terms of pregnancy, multifoetation, extrauterine pregnancy, to diagnose new growths of the female genitalia, pyo- and hydrosalpinx, to study the mammary glands, etc.), and in urology (to study the bladder, the prostate, etc.).

The Doppler effect is used for determining moving objects. Sound or light waves are reflected from the moving objects and return to their source with the changed wave frequency. This change is recorded by a receiving element and converted into an audible signal. Instruments utilizing the Doppler effect as their operating principle work with a continuous single frequency.

The ultrasonic Doppler system is used for assessment of the blood circulation parameters. The formed elements of blood (and other moving objects) reflect ultrasonic waves whose frequency is modulated. The modulation frequency is proportional to the velocity of motion of the studied object. Velocity is calculated as the difference between the emitted and received frequencies (Doppler formula). The Soviet-made echocardiograph (ultrasonic Doppler heart locator) is used for the study of kinetics of the heart valves and muscles and to measure the time of movements of the left and right chambers of the heart, which is especially important for the assessment of the myocardial function.

This brief analysis of the methods shows the importance of echography. In the opinion of experts, ultrasound will soon be used on a greater scale than X rays. According to some authors, a revolution is expected in medical diagnosis in the nearest future, because a branch of medicine can hardly be found where ultrasound could not be used successfully.

Laboratory Methods of Examination

Laboratory methods are widely used in clinical practice. Excretions and secretions, excrements, the blood, exudates and transudates are analysed in the laboratory.

The laboratory investigations can be grossly classified as follows: (1) the study of the general properties of the examined material, the physical properties included (quantity, colour, appearance, odour, the presence of impurities, density, etc.); (2) microscopic studies;. (3) chemical studies for the determination of the presence of certain substances (substances that are normally contained in various bodily fluids and excrements such as metabolites, microelements, hormones and products of their conversion, and substances appearing in disease); (4) bacteriological, proctological and virological studies; (5) serological diagnosis.

Chapter 4

GENERAL METHODOLOGY OF DIAGNOSIS

The Importance of Medical Theory for Development of Diagnostics

The importance of medical theory for the general development of diagnostics, for elaboration of examination methods, and for assessment of the disease and the patient's condition is a commonplace. It is important that a diagnosis should be worded in the generally accepted terms and that the meaning of these concepts should correspond to the modern status of the medical science, i.e. diagnosis should be correct not only in form but in content as well.

History of medicine shows that, depending on the general concept of disease and its forms, physicians devise and use the corresponding diagnostic methods and give the various assessment of the observed phenomena. Beginning with Hippocrates and almost until the 19th century, diseases were regarded as a combination of symptoms, and simple observation was sufficient to arrive at a diagnosis. This empirical period of the *descriptive clinical and symptomatological trend,* which existed from the times of Morgagni's clinico-anatomical studies (1761), was then replaced by a deeper approach to the study of the disease. Physicians began comparing the phenomena observed during the life time of the patient with the changes in his organs observed after his death. They noted that almost each disease was connected with visible changes in certain organs and believed that the cause of the disease should be looked for in the anatomical changes in organs. Diagnostic methods of examinations now included the study of anatomical changes in the patient's organs. These were the methods of physical diagnosis (percussion, auscultation, palpation). A microscope was invented and histological studies improved accordingly. Physicians could now detect very fine changes in tissues and cells of organs of dead patients. A new science, pathological anatomy, was thus initiated. It became the foundation for the study of diseases.

Diseases were now considered as being dependent on affections of various organs, and organolocalistic classification of diseases thus emerged. Most diseases were given definite names depending on the site (localization) of major changes: the inflammation of the pleura was given the name of pleurisy, of the lung pneumonia, of the kidneys nephritis, etc.

Pathological anatomy discovered many new facts and explained many

symptoms of diseases. But the creators of this science, Rudolf Virchow and his disciples, concentrated their attention on the finest changes occurring in the cells and forgot about man as a whole, about the integrity of the organism; in their opinion, the life of a body is a simple sum of the lives of cells; they understood disease as a simple sum of changes in the structure of cells, i.e. as a local affection of the body. This *anatomical* localistic medical thinking was not widely accepted in the Russian clinical medicine.

Since the time of discovery of blood circulation by William Harvey (1578-1657) scientists began to be interested not only in the structure but also the function of various organs. Physiology was thus started. This was the science of life and function of various organs and systems of the body (Claude Bernard and others). Works of an outstanding scientist, the father of Russian physiology I. M. Sechenov (1829-1905), a prominent internist of the middle of the 19th century S. P. Botkin (1832-1889), the great Soviet physiologist, materialist, the creator of the teaching of higher nervous activity I.P. Pavlov (1849-1936), and of many others greatly contributed to the development of medical science. It was established that the function of organs (the heart, lungs, brain, etc.) is decisive for the life of man and animal, and that anatomical changes in an organ or cell is only partial manifestation of the disease. The living body was now understood as an integral system, and the activity of the nervous system was admitted to play a decisive role in regulation of the functions of the human body.

"Physiology and medicine are fundamentally inseparable. If the physician is in his actual practice, and even more important, in his ideals, a mechanic of the human organism, then inevitably every fresh discovery in physiology will sooner or later increase his power over this extraordinary machine, his power to conserve and repair this organism." *(Lectures on Conditioned Reflexes* by Ivan Petrovich Pavlov. New York, 1928, pp. 95-96.)

Scientists began studying human diseases by modelling them in animals. Experimental study of diseases has given a start to a new science, pathological physiology, which treats of the changes in the function of an affected body and the developmental mechanisms of diseases. Pavlov wrote that "only through experiment shall medicine become what it should actually be: conscious and hence fully purposeful active science".

The function of organs in the sick became an important object of studies in practical medicine. New diagnostic methods for the study of the blood and urine, digestion, methods for measuring blood pressure, etc. were devised. Functional methods of studies became very important in diagnostics. *The functional trend* in medical science thus developed in its struggle against the one-sided anatomical (localistic) medical thinking.

The invention of the microscope has enriched medicine not only with

the information on the structure of the human body. The discovery of multitude of microbes in the human environment and also inside man himself (microbes were found in the organs and the blood of patients with various diseases) was an outstanding event. Microbes were found in the lungs of patients with pneumonia (pneumococci) and tuberculosis (tuberculosis bacillus*), in the throat of diphtheria patients, and in the blood in sepsis, etc. It was then proved that many infectious diseases develop because of pathogenic microbes which get inside the body of healthy people. Bacteriology owes its birth to the wonderful discoveries of Luois Pasteur ("Fermentasions et generasions dites pontanees", 1858), Robert Koch ("Die Aetiologie der Tuberculose", 1882), I. I. Mechnikov ("Inflammation", 1892), and others. Later D. I. Ivanovsky opened the epoch of virology. Diagnostics was thus enriched with new methods of investigation: bacteriological, virological, and immunological. The discovery of the cause of infectious diseases opened wide prospects for their control: prevention of infection (prophylaxis) and treatment. It became evident that an important condition for correct treatment is the discovery of the cause of the disease (aetiology). Microbes, poisons, and other factors were regarded as the cause of human diseases.

The discovery of causes of diseases, and of the role that microbes and other factors play in development of diseases of internal organs provided the basis for a new, *aetiological* trend in medical thinking. Classification of diseases, together with organopathological principle, became enriched with the determination of their aetiology.

But further study of the causes and aetiology of various diseases showed that penetration of microbes into a healthy body is not enough for the disease to develop. Not all persons who were in contact with patients during epidemics got affected with the disease. Tuberculosis mycobacterium is present inside many healthy persons but only some of them get affected with the disease. Some persons carry pathogenic microbes but do not develop the disease (bacteria carriers). It was found that the condition of the body is the decisive factor for the development of a disease; this factor is decisive in the attitude of man to bacteria: the body of a particular person should be sensitive to harmful effects and his resistance to this harmful effects should be weakened in order to develop a particular disease.

It was shown that various symptoms and the course of a given disease depend mainly on the patient's response to the harmful factors. For example, pneumonia in a young person is accompanied with high temperature and soon ends in complete recovery, while elevation of temperature is in-

* Today these microbes are called mycobacteria.

significant in the old in whom the disease has a protracted course and complications develop. It was discovered that infection with a certain microbe, e.g. a streptococcus, can be manifested by various functional and morphological changes in the body, i.e. one disease may have different forms, from catarrh of the mucosa to suppuration and even sepsis.

Development of immunology (Mechnikov, Pirquet, and others) explained many aspects of the clinical course of diseases up to autoaggression and auto-immune processes in non-infectious diseases. Louis Pasteur, the founder of microbiology, was the author of a paradoxical saying that microbe is nothing but soil is everything for the development of a disease.

The discovery of various aetiological factors did not thus contradict the valuable clinical observations which showed that one and the same factor can cause a disease in one person and cannot in the another, and that the course of the disease of the same aetiology differs in various persons. The condition and reactivity of the body are the decisive factors in the onset of the disease. Under exposure to a conventionally pathogenic factor (most infections, physical or psychic factors), the development and course of the disease largely depend on the features of the body, hereditary factors and acquired traits. Study of this aspect of the clinic, the forms and stages of the development of pathological processes are the subject matter of the science treating of the mechanism of development of the disease, which is called *pathogenesis.* The term can be given a simplified interpretation: "how the disease attacks man". But along with pathogenesis, one can always find phenomena which can be interpreted as protective or adaptational response of the body, i.e. sanogenesis.

It was easier to discover the specific cause of the disease (e.g. tuberculosis mycobacterium, streptococcus, injury) than to reveal the entire sequence of functional and morphological changes occurring in the development of pathology. Pathogenesis proper, which is prerequisite for understanding disease, stood therefore next to aetiology in importance. The primitive notion of the mechanism of the development of a disease as "microbe—disease" as a direct causal link was replaced with time by the understanding of the role of the predisposing conditions, predisposition or resistance of the body to the pathogenic factor. But this came with the clinical experience. Aetiological trend implies the search of causative factors in each case, which should then be followed by evaluation of the inner factors of the patient. On the whole it had lead to the understanding of the relations between the cause and the body response. It should be remembered that disease is not only a somatic but also psychic suffering, not only a biological but also a social phenomenon. The appropriate

medical and social studies widen the field of investigations from an individual patient to social conditions which can favour the development of the disease. Study of the pathogenesis of a disease resulted in description of new groups of diseases (allergic diseases, collagenoses, etc.) and in the development of new methods for determination of reactivity of the body (allergic and biological tests, immunological, genetic, hormonal studies, etc.).

A powerful impetus to the development of medicine, diagnostics included, was given by the development and acceptance of the theory of nervism by S. P. Botkin and I.P. Pavlov. The theory substantiates the hypothesis that the nervous system accomplishes the most perfect connection between separate parts of the body to account for its integrity, and also connection between the body and the environment, i.e. the nervous system is the leading and decisive system in the vital activity of the sick and a healthy person. The vigorous development of endocrinology from the time of its foundation by Brown-Sequard (1818-1894) stimulated the development of the theory of general pathology in which the decisive role in the development of disease is given to the organs of internal secretion (Selye theory, 1950), which rivalled the theory of nervism. Of course, the role of the humoral factors in the pathogenesis of diseases cannot be disregarded, but this does not diminish the role of the nervous system. The study of the nervous and the humoral regulation of the functions of a human body in health and pathology is a valuable source of facts for a practitioner.

The twentieth century was marked by the event of the greatest historical importance, the Great October Socialist Revolution in Russia in 1917. The revolution gave birth to a new health care system. The Soviet science was enriched by the *method of social analysis of problems in medicine and medical sociology*. The importance of governmental support of practical medicine was vividly demonstrated to all other countries.

At each stage of its development medicine was enriched with new data and deeper understanding of human diseases. From simple description of disease medicine came to the study of anatomical changes occurring in the affected body, and further to the study of the functional condition of a sick organism and discovery of the causes of the disease, and still further to the study of susceptibility of the subject to a disease, the importance of the environment and the leading role of the nervous system in the life of man in health and pathology. At the same time, each new stage of development of clinical thinking originated from the previous stage (anatomical, aetiological, etc.) and included it as an indispensible part for a wider understanding of pathology.

Planning Diagnostic Examination

Two types of diagnostic examination of the patient are distinguished. One of them consists in the following. As suggested by the main or a more vivid symptom, e.g. cardiac pain, jaundice, cough, vomiting, etc., the physician examines the corresponding organs or functions. He arrives at a diagnosis from the symptom through a concise additional examination. For example, if a patient complains of right iliac pain, and palpation in this region is painful a diagnosis of appendicitis may be established (provided other signs are revealed). This method is often used for a quick diagnosis in emergency cases. But this method is effective only in simple cases and is fraught with danger of erroneous diagnosis, because the patient's general condition and all the systems of his body are not examined thoroughly. Moreover, the examination is carried out without any plan and method and the diagnosis is thus incomplete and abstract.

The other approach can be called methodical and is more complicated. All the organs and systems of the patient are examined following a certain plan. Clinical anatomy (pathological anatomy included), physiology, constitution (including the body make-up, functional performance, type of the nervous system, reactivity, which is important for individual diagnosis), separate signs of the disease are studied, i.e. a physician carries out an analysis the purpose of which is to assess the condition of the body as a whole. This can be done by the synthesis of the findings. The study of the patient is not, however, completed at this stage. Additional laboratory and instrumental studies should be carried out on the basis of the discovered symptom or syndrome in order to verify the lesion or the affected organ and to reveal the essence of the pathology, the symptoms are compared to establish connections that may exist between them, and finally all findings are put together to arrive at a final diagnosis.

Even if a diagnosis can be established at first sight (e.g. exophthalmic goitre, a wound, erysipelas, heart defect, etc.), a methodical study of the patient is also necessary. This complicated examination should end by establishing a diagnosis, not only a correct but also detailed enough in order to suggest the proper choice of therapy.

It should be noted that the diagnosis of the disease and of the patient cannot be regarded as a constant formula since it changes with the development of the disease. Under the effect of treatment or during development of complications, the condition of the patient can change markedly, and the diagnosis and prognosis will change accordingly. The diagnostic study of the patient's condition is thus continued during the entire period of

clinical observation and treatment. This is the diagnosis of the course of the disease and also verification of the initial diagnosis.

The diagnostication process can be divided schematically into identification of the disease and the study of the patient during the course of the treatment. The diagnostic conclusion covering the entire period of observation and treatment is summarized in epicrisis.

Special Features of Diagnostic Examination

The first and prerequisite condition to identify a disease and assess the condition of the patient is the knowledge of medical subjects and special pathology, i.e. nosological forms of the diseases. But clinical pictures of various diseases are described in textbooks only schematically. Clinical experience shows that actual cases would usually differ from these schematic descriptions since the origin, course and clinical manifestations of the disease strongly depend on the condition of the patient and the environment.

An important diagnostic factor is that the human body responds to various stimuli or aetiological factors by a limited number of general reactions, e.g. the normal response to most infections is fever, to local irritation it responds by inflammation, etc. Moreover, the general reaction of the body to various uncommon stimuli is often the same, especially at the onset of the disease. Clinical signs themselves are not therefore sufficient for the determination of the concrete aetiological factor or for the discovery of specific changes.

Several groups of diseases are distinguished according to various responses of the body to the pathogenic cause or injury. When establishing a diagnosis, the physician first of all decides to what group of the diseases can this particular affection be attributed. In other words, the physician first decides if a particular case is an infectious disease, upset metabolism, inflammatory process, newgrowth, allergic disease, autoallergy, upset neurohumoral regulation, etc.

Another difficulty is that various combinations of pathological processes are encountered in various patients. And finally, even in seemingly typical cases, there are always special features that do not occur in other patients.

The necessary condition to identify a disease is the professional skill of the physician to apply his knowledge in the varied and changeable conditions of life. The professional skill is acquired with experience in solving diagnostic problems. An independent practitioner is formed through mastering the method by which the acquired knowledge can be applied to practical cases. Correctness of the diagnosis largely depends on this skill.

Selection of a particular scientific method depends mainly on the object of study, its purpose, and the working conditions. This explains the difference between diagnostic methods and the methods that are used in other sciences. The diagnostic study is aimed at understanding of the patient's condition in order to change it, i.e. at determining the disease as a phenomenon that should be removed. The study should not be limited to finding the general and typical features (which is common for all theoretical sciences); the physician should direct his studies and thinking to understand any particular case which differs from all similar cases. This is the necessary condition for carrying out his objectives: prophylaxis and treatment.

An important feature of the object of study, i.e. of man, is its complexity with respect to structure and function and also with respect to connections and interactions with the environment (morphological, physiological, psychic, social features). This explains the necessity of using many methods. The number of methods that a physician uses to examine the patient is

greater than the number of methods used by representatives of other sciences. The physician uses not only medical methods but those employed in other branches of science, from inquiry by questioning, chemical, physiological, biological and other methods, to very complicated and precise techniques such as electrocardiography, X-ray examination, and others.

This great variety of methods depends not only on the extreme complexity of the object of studies. It is also explained by insufficiency of the methods for complete medical understanding and by the fact that one method cannot be applied to all cases. Moreover, in some cases a certain method cannot be applied without injuring the patient. Medical examination should by no means do any harm to the patient. The physician therefore has to obtain the necessary information by indirect methods and speculations (e.g. incompetence of the heart valves can be determined by percussion, auscultation, type of the pulse, etc.). These difficulties account for diagnostic errors.

Finally, it should be remembered that a physician may have little time to establish a full diagnosis in urgent cases when he has to act immediately to save the patient.

These are the working conditions in which the physician should do his best to apply efficiently scientific methods.

Diagnostic Observation and Examination

Scientific studies (diagnostic studies included) begin with observation and are based on experience. Observation is actually an active perception of phenomena substantiated by a purpose which directs the attention of the observer to this or that aspect of the phenomenon. In an exact meaning of this word, observation is a direct perception of natural phenomena (as distinct from experiment where the observed phenomena are modified or induced by the observer).

Observation principles. The diagnostic study begins with decomposition of a whole into component parts, i.e. from the study of simpler parts (analysis). The physician observes the patient by studying his systems and organs in a certain sequence. Observation is thus the first step in the study of the patient (analysis) so that the findings could be synthesized at the next stage of diagnostication. It other words, a whole will be composed from parts that were preliminarily examined separately. It follows that observation provides the elements for construction of diagnosis. Since disease is a combination of affections and certain reactions of the body, it is evident that the visible signs of the disease, the symptoms, are not the disease itself. There are other symptoms that are hidden from the observer and should be revealed. On the other hand, it should be remembered that the symptom of the disease is its external sign which cannot be regarded as a separate phenomenon, existing apart from the pathological process.

The first rules of scientific observation are reliability and accuracy, in both quantitative and qualitative aspects; the second requirement is completeness and comprehensiveness of observations in all their details, and finally, the requisite condition is orderly, systematic and methodic observation along with classification and comparison of the observed phenomena.

Comparison of the data obtained consists in consideration of common and different features of two facts, one of which is the reference against which the other is compared.

Medical examination *is not limited by observation alone; it also includes some elements of experiment.* By experiment we understand artificially induced changes occurring in the patient's body by giving him, for example, tuberculin (Pirquet test), or special "loads" by which functional disorders can be revealed. Experiment requires a special predetermined idea and reveals the existence of certain connections between the observed phenomena. A limiting factor of the experiment is damage that might be inflicted to the patient. Experiments are therefore rarely used in clinic. But it should be remembered that only experiment can give a complete picture of the functional state and pathogenic connections between processes occurring in the patient. It should also be remembered that all phenomena occurring in the body are very complicated and interdependent and the results of the experiment should therefore be interpreted very thoughtfully.

The following conditions are requisite for a successful diagnostic observation. 1. Sufficient skill of clinical observation which is decisive for reliability and accuracy of the data obtained. 2. Accurate knowledge of all symptoms. 3. Comparison of the corresponding indices in norm and pathology. This requires adequate knowledge of anatomy, physiology, and the human body on the whole. This enables the physician to decide definitely whether a given phenomenon is a pathological symptom or a sign of a disease. Comparison can be made on the patient himself, e.g. comparison of the structure and function of symmetrical joints. 4. Determining the degree of probability of this or that disease. First considered should be the probability of a more dangerous or common, or an epidemic disease (e.g. influenza); the probability of endemic disease should also be considered in certain geographical zones; the season is essential for the incidence of some infectious diseases, for relapses of gastric ulcer; patient's age is another important factor (diseases of childhood, diseases occurring mostly in old patients, etc.). Sex, occupation, modus vivendi, constitution, and heredity are important in the sense of the predisposition of the patient to this or that disease. 5. Conditions and organization of medical examinations and confidence of the patient in his doctor are other important factors.

Accuracy and reliability of medical observation depend on (a) use of special tools and apparatus and also accurate recording of the changes occurring during the course of observation. The knowledge of the degree of accuracy and of the error limits for each method are very important; (b) the rule of double and triple verification of the symptom observed; the rule consists in that a given symptom, sign, or any finding are repeatedly check-

ed by various methods (e.g. the lower border of the stomach can be determined by percussion, palpation, and percussive palpation; the gallop rhythm is determined by auscultation, palpation, and phonocardiography, etc.). Coincidence of data obtained by various methods ensures accuracy and reliability in assessment of a given symptom; (c) relationships between the discovered symptom and other related (casually dependent) phenomena which strengthen the probability of accurate observations (like detalization of the symptom). Abstractly stated symptom (e.g. pain in the abdomen) is not important diagnostically in itself. The picture is quite different if the intensity, localization and character of this pain, and the accompanying signs can be determined as well. Concretization of the symptom gives sufficient material for a correct diagnosis.

Completeness of observation cannot always be ensured because the clinical forms and picture of a disease vary with time (under the influence of the therapy in particular). Medical observation is thus a continuous process that lasts for the entire time of contact between the physician and the patient. It is especially difficult to apply the "necessary and sufficient" principle to emergency cases where the grave condition of the patient imposes limitations to examination procedures, but requires an urgent decision. Profound knowledge and vast experience can only help in such cases.

In grave cases, and in conditions of limited possibilities, the first rule that should be followed by the physician in his observations is the examination of vitally important organs. This is necessary to assess the degree of danger to the patient's life. Prognostic evaluation is first of all required. Next the disease should be diagnosed, because the first task of the physician is to save the patient (which is sometimes possible without a detailed diagnosis, for example in shock, coma, acute abdomen, uraemia, etc.). Here the purpose of medical examination is to assess the gravity of the patient's condition and to give the appropriate treatment. This is the first and preliminary measure that should be followed by treatment based on a more detailed diagnosis.

A complete observation is only possible with a follow-up observation of symptoms and determination of the direction in which a given pathology develops since otherwise clinical observation is useless for the diagnostic and therapeutic purposes. Despite the great multitude of methods available observation is never complete. The cause of possible error is the absence of system in observations and erroneous interpretation of findings or unawareness of their clinical importance. Absence of adequate knowledge and experience can be the cause of underestimation of some important observation methods and overestimation of others. Moreover, accumulation of facts and symptoms without proper synthesis of the collected data is another factor that can give a diagnostic error.

Recording Form

When formulating the diagnosis the following should be stated: (1) the main disease for which the patient is treated (or which is the cause of death). Stated also should be the nosological unit, degree of compensation or the stage of the disease, the character of pathoanatomical process, main localization of pathological changes, the character and the degree of functional disorders, the aetiology and pathogenesis of the disease. Depending on a particular case, the wording may be short or detailed, but the mentioned aspects should always be described in formulation of the main disease; (2) complications of the main disease; (3) attendant diseases. In all cases the diagnosis should contain sufficient data for the assessment of the patient's working ability (work capacity).

Types of Diagnosis

By the *method of its establishment,* diagnosis may be (1) direct or by analogy; (2) differential (diagnosis differentialis) and by exclusion (diagnosis per exclusionem) (a variety of differential diagnosis); (3) synthetic or complete diagnosis (diagnosis morbi et aegroti); (4) diagnosis by observation (diagnosis ex observatione); (5) diagnosis by therapeutic effect (diagnosis ex juvantibus), formerly this diagnosis was differentiated from the diagnosis established by the harmful effect of treatment (diagnosis ex nocentibus).

By the *time of establishment* there may be (1) early diagnosis; (2) late diagnosis; (3) retrospective diagnosis; (4) post-mortem (pathological) diagnosis.

By the *degree of certainty* diagnoses are differentiated as (1) provisional or hypothetic diagnosis; (2) final diagnosis; and (3) questionable diagnosis (in the absence of certainty).

Methods and Theory of Diagnosis

Observation, as the first stage in diagnosis, is the period of analysis, while the next stage is synthesis of the data obtained. It should be understood that both analysis and synthesis occur simultaneously during examination of the patient because the physician not only observes and listens but also thinks. The main methodological problem of diagnosis is to identify disease by its signs and to proceed from a symptom to diagnosis.

In practice, the physician often passes from the symptom directly to diagnosis by a logical jump which is based on a conjecture, memory, and medical experience. This process often occurs subconsciously and the

method is not reliable. Thus established diagnosis cannot be complete, the diagnostician himself is not sure in his conjecture, and besides, this method, which depends mainly on memory, is partly automatic.

The simplest and elementary method is *diagnosis by similarity.* It consists in comparison of symptoms observed in the patient with the symptoms of known diseases. If the symptoms are similar to signs of a definite nosological unit, the condition of the patient is classified to be identical to it. Unreliability of this method is evident from the fact that the absence of some symptoms makes the diagnosis by similarity difficult, it does not prevent mistaking of symptoms, nor does it prove the absence of concurrent diseases. Moreover, this simple method can only suggest the name of the disease without giving a comprehensive picture of the patient himself.

The *inductive method* is quite rapid and simple. It is based on the primary hypothetic generalization and subsequent verification of the conclusion by the facts observed. This method of identification occurs simultaneously with observation, and both end simultaneously. A physician observes one or several symptoms and makes a conjecture. Then he suggests that his conjecture is correct provided some other symptoms of the supposed disease are present. Once these other symptoms are found, the diagnosis is considered proved; if the anticipated symptoms are not found, the conjecture is considered to be wrong and another is produced instead, and so on. This method is, however, useful for an abstract diagnosis rather than for a concrete one. Since completeness of diagnosis and orderliness of examinations are not requisite, this method cannot give a comprehensive impression of the patient on the whole, and can only be used to diagnose one disease without revealing many possible pathological changes and various complications of the disease. This diagnostic method based on coincidence and similarity of several symptoms observed in the patient with the symptoms of the conjectured disease can give a diagnosis of a complication instead of the disease itself. Finally, this method is based not on the revealing of the relationship between the symptoms, but mainly on mechanical collection and comparison of the symptoms.

The specific feature of the inductive method is a conjecture or a hypothesis. S.P. Botkin emphasized the hypothetic character of diagnosis and wrote that once a diagnosis is established, we produce a more or less probable hypothesis which is either confirmed or disproved by further course of the disease. The physician must undertake actions proceeding from his hypothesis. When the hypothesis is verified and confirmed, it is no longer a hypothesis but a theory or fact; if the hypothesis is disproved, it is declined altogether.

The first and foremost condition for using a hypothesis (in diagnosis included) is a critical attitude to it and accurate knowledge of what is a con-

jecture and what is fact in a particular case. The main danger consists in mistaking a hypothesis for a fact. It is necessary that a hypothesis (a) would be based on actual facts; (b) would not contradict them; (c) could be checked directly or by conclusions that might be derived from it. When the physician has to choose between equally probable conjectures, most frequently occurring version should be preferred.

A diagnostic hypothesis can be substantiated by analogy. In this case several symptoms observed coincide with the symptoms of a particular disease, and a conjecture is produced that the patient develops this particular disease and that some other signs of the disease will more or less coincide. Of course, the lesser the number of symptoms, the greater the number of conjectured diagnoses.

Differential diagnosis. The diagnosis established by analogy has only one proof: greater or smaller similarity of the observed signs with the described symptoms of a certain disease. The diagnosis becomes more reliable if the presence of other diseases is excluded. In other words, differential diagnosis based on the search of differences between a given case and all other possible cases, with exclusion of hypotheses that have not been proved correct, is more positive.

Checking correctness of the diagnosis is the principle of clinical identification not only in dubious and complicated cases but also in diseases whose symptoms suggest a definite conclusion. Nevertheless it is necessary to take into consideration all other possible affections. Consideration of possible cases helps the physician reveal accurately and timely the symptoms that he might anticipate in the patient with a particular disease.

The starting point in differential diagnosis is, as a rule, the leading symptom. The physician then recollects all diseases for which this symptom is common and the course of the disease is now compared with the description of those diseases. A particular case may have common features with diseases for which this symptom is common. These differences are used to exclude all other diseases which might first be suspected as having this symptom. Finally in the presence of the greatest similarity and the least number of differences with the disease to which the present case is compared (while all other possible diseases are excluded) the physician may conclude that a given patient has this particular disease.

Phases of differential diagnosis. The first phase. The leading symptom, which should be used as the starting point in conjectures, should not be too common (say, fever) because too many diseases will be involved in differentiation. The more specific the symptom, the smaller is the number of diseases to be differentiated. The procedure becomes the least labour-consuming and more rapid if a combination of symptoms, i.e. symptom complex, rather than a single symptom, is considered as the starting point.

The second phase. An important condition is consideration of all possible symptoms characteristic for a particular case because if any symptom is disregarded, the reliability of the diagnosis diminishes. Most probable and most frequently occurring disease should be considered first.

The *third phase.* The studied case is compared with several possible diseases. First, similarity with respect to the number and character of coinciding symptoms should be considered. Second, established should be the differences with respect to the absence of symptoms characteristic of the disease with which this particular case is compared, and with respect to the presence of symptoms that are not characteristic of the supposed disease.

The fourth phase. The disease that was first conjectured is excluded if the differences are found which contradict one of the main three principles of differentiation. The first principle is *substantial difference.* The observed case does not belong to the disease with which it is compared because its permanent symptom is absent. For example, the absence of albuminuria excludes glomerulonephritis, or the absence of intensified basal metabolism rules out exophthalmic goitre. But since there are transient symptoms in most diseases, the physician should be more careful. The absence of a symptom does not exclude a disease. The signs of the early period of some diseases are often so insignificant, transient and nonspecific that any of them may be absent during examination. Moreover, in complicated cases these symptoms may either disappear or be masked by complications or other diseases. For example, in rare cases of diffuse affections of the kidneys, albuminuria, which is otherwise a very significant symptom, may be absent, or pneumonia may proceed without elevated temperature, etc.

Another formulation of the first differentiation principle reads: the observed case does not belong to the type with which we compare it because we find a symptom which never occurs in the disease with which we compare it. This formulation is even more conventional because it cannot be applied to complicated cases and therefore does not always rule out the supposed disease.

The second differentiation principle is *exclusion through the opposite.* It can be put as this: the observed case is not the disease with which we compare it because in the disease with which we compare there is a constant, quite opposite symptom. For example, achylia can hardly concur with duodenal ulcer because an opposite symptom, gastric hypersecretion, is observed in this disease. What has been said of the first differentiation principle, holds true for the second as well. It should also be added that some symptoms are transformed into their opposites during the course of the disease. For example, excitation is replaced by inhibition, etc. The importance of the antagonism of symptoms is therefore no less relative than their absence.

The third principle is the *non-coincidence of signs.* As we compare quality, intensity, and special features of an observed symptom with a similar symptom of another disease with which we compare a given case, we can find the non-coincidence and the presence of various properties and different origin, which makes us doubt and rule out the supposed disease. This principle is used for making tables of differential diagnosis.

It should be remembered that comparison of a given case with the picture of a supposed disease is more useful than establishing similarity or difference by one or several symptoms. Differential diagnosis requires further study of the patient in directions that are suggested by the possible presence of this or that disease in order to look for symptoms corresponding to the supposed disease. The advantage of this method is repeated examination of the patient which ensures a more complete observation and discovery of new symptoms.

The *fifth phase.* The diagnostic conclusion is derived from the established similarity of a given case with the disease to which it is compared and from the difference of the case from all other possible diseases.

Thus, differential diagnosis by exclusion not so much establishes the diagnosis directly; it rather gives evidence that the disease, that has greater similarity to it, is more probable than the others; in other words, it proves correctness of the diagnosis by exclusion of all other possible diseases. *Diagnosis that is established by direct exclusion of all other diagnoses is called diagnosis per exclusionem.*

Differential diagnosis may be a more or less important aspect in physician's speculations. The main feature of this method is a thorough revision of all possibilities which is the final stage in the most common pathway of all investigations. Verification of the diagnosis occurs simultaneously with the continuing observation of those effects which are derived from the conjectured diagnosis. It should be noted that differential diagnosis is used to verify the diagnosis but it does not explain the features of the patient's condition.

Diagnosis does not end by identification of the disease because the changing condition of the patient causes the corresponding changes in the process of differentiation. Diagnosis is thus a dynamic process and it must develop and be completed by the analysis of the continuing variations in the patient's condition. The study of these changes is another test for correctness of the primary diagnosis.

The diagnosis (mostly its anatomical part) is confirmed or disproved during a surgical operation, or on postmortem section. It should be noted that the anatomical changes do not always prove correctness of the diagnosis; these changes can explain the patient's condition to the extent to which the results can be used to conclude on the chain of the preceding events, and the structural changes can be used to judge on functional

disorders. A systematic checking of diagnosis by comparing clinical and pathoanatomical diagnosis has been adopted in the Soviet Union since 1935 (clinico-anatomical conferences).

The described diagnostic methods are used to identify the disease to establish the *diagnosis of the disease* (diagnosis morbi). Establishing this diagnosis helps the physician systematize the observed phenomena. This diagnosis defines the essence of the disorder, but does not explain all special properties of a given patient, nor does it explain his concrete condition. The nosological diagnosis gives much but not everything that is necessary to a physician to prevent possible complications and to treat the disease. The described methods cannot give a concrete *individual diagnosis* (diagnosis aergroti). The diagnosis cannot be detailed, the degree of anatomical changes, functional disorders, the character and importance of the aetiological factors cannot be established by these methods. A nosological diagnosis is not thus a synthetic diagnosis.

An additional diagnosis (diagnosis ex juvantibus) should be mentioned. The results of the treatment given are used to make a conclusion on the disease. This method can therefore be regarded as a kind of retrospective diagnosis. Reliability of this method is quite disputable (except in rare cases).

Sometimes the physician has to limit himself to a *provisional diagnosis*. In the broad sense of the word any diagnosis is provisional because no diagnosis can be complete and it undergoes continuous changes (at least insignificant) with the condition of the patient. In a narrower meaning of this term provisional diagnosis is one which is dubious for the physician himself, mainly due to insufficiency of the data available.

Finally, an *early diagnosis* should be mentioned as a very important kind of diagnosis and which is a difficult problem of modern clinical medicine. This problem is being solved by two ways. One of them is the search for diagnostic methods suitable for the period of the disease at which a successful therapy can be given (e.g. radical cure of gastric or lung cancer). This diagnosis is only comparatively early as distinct from hopelessly *late diagnosis* when the physician cannot help the patient. When examining a patient, it is reasonable to suspect in the first instance the most dangerous malignant diseases, because late diagnosis makes cure impossible. A more difficult but necessary way is the search for methods to reveal a disease when the very first signs only appear or even before these signs become detectable. It implies also the problem of the threshold of clinical manifestations of pathological processes, and possible assessment of the quality of the process at its early development. The problem of early diagnosis is also directly connected with the problem of predisposition or susceptibility.

A way to solve the problem of early diagnosis is regular surveillance of practically healthy population. Vivid disorders in the condition of a person may be absent not only during the unitial period of the disease but also in the presence of marked anatomical changes, i.e. when the disease is latent and the sick person does not apply for medical aid. Heart diseases, tuberculosis infiltration or a cancer node in the lung can be revealed by X rays; chronic nephritis can be detected by urinalysis, etc.

Synthetic diagnosis. Synthetic or pathogenetic method is used to establish a concrete diagnosis of a given disease or condition. The method is based on successive synthesis and establishment of the pathogenetic connections between the observed phenomena.

The first problem in the synthetic method is grouping symptoms in compliance with the medical objectives. If a patient is given a systematic and planned examination, the revealed symptoms are naturally grouped according to the bodily systems. The physician obtains the first preliminary information on the functional condition and the degree of affection of this or that system. Then the physician studies the functional relations between the systems. The obtained material is only "crude" and requires further processing, in the first instance by establishing connections between the revealed symptoms, establishing their origin, and arranging the symptoms in pathogenic groups. The physician proceeds from the symptom to phenomena associated anatomically, functionally, or aetiologically with this symptom.

The groups of symptoms should then be evaluated diagnostically, prognostically, and therapeutically. Correct estimation of the symptom from the prognostic and therapeutic aspects requires adequate knowledge of its pathogenesis, which is the subject matter of semeiotics.

Synthesis of the collected data (observed symptoms) begins with grouping the symptoms by various signs, such as time of appearance, relation to a particular organ, function, origin, and causality.

A group of pathogenetically connected symptoms is called a *syndrome.* A syndrome is thus the first result of synthesis and the second step in establishing a diagnosis. Two types of syndromes are distinguished, e.g. anatomical and functional. Combination of physical symptoms or signs which correspond to the structural changes in the organs are called anatomical syndrome. For example, dullness in the region of the lungs, bronchial respiration and intensified fremitus make an anatomical syndrome of consolidation or infiltration of pulmonary tissue.

Combination of functional symptoms gives a physiological or functional syndrome. For example, diminished alkaline reserve of the blood, increased ammonia of the urine, and decreased CO_2 tension in the alveolar air make the functional syndrome of non-gaseous acidosis. When the

physician reveals syndromes he proceeds from the statement of symptoms in a given patient to establishing deeper connections and interdependence between them. Separate symptoms and their combinations (syndromes) make it possible to conclude on the anatomical and functional condition of organs. During the transition from symptoms to a syndrome, the physician selects certain diagnostic conjectures by excluding others.

Simple and complicated syndromes are distinguished. In other words, a patient can combine not only anatomical or functional disorders of a particular organ, but have changes in his systems and the entire body. Complicated syndromes are called large. They are aggregates of symptoms interconnected pathogenetically and involving the entire body in pathology. For example, diffuse affections of the kidneys may be classified as large syndromes: azotaemic, chloruraemic, and hypertensive syndromes. The specific feature of syndromes is their changeability; a syndrome is not a fixed condition. Syndromes develop, modify, disappear, combine with one another, or separate from one another. Renal syndromes, for example, are only a moment in the development of nephritis in a given patient; this holds also for many other diseases.

A specific feature of a syndrome is that it can be a result of various pathogenic effects on the body, i.e. a body often responds similarly to various harmful effects by a limited group of similar reactions (e.g. by inflammation). One and the same syndrome can be observed in various diseases and the same disease (at various stages and clinical forms) can be manifested by various syndromes. Syndromes arise and change depending on the progress and stage of the disease; they may develop due to various causes, and reflect, in the first instance, the special properties of the body's reactions. After establishment of a syndrome, the physician should determine the causes, background, and conditions of the development of the given functional and organic disorders in the patient. He thus determines the sites of therapeutic application.

Correctness of determination of the cause of a particular syndrome depends firstly on the experience and knowledge by the physician of special pathology; secondly on the knowledge of the patient's condition at the present moment by the clinical picture and by special examination (e.g. microscopy, serological and other tests); and thirdly, on the detailed study of circumstances under which the disease developed, heredity, and also the progress and character of the pathological process, and the patient's condition.

In connection with the study of aetiology of a disease it is necessary to remember the following three circumstances. There are diseases which are essentially polyaetiological but monopathogenic, e.g. certain neuroses, allergic conditions. Accurate determination of pathogenesis is therefore of

decisive importance in such cases. Results of aetiological factors are observed in some diseases, e.g. results of a mechanical, radiation, or psychic injury. Finally, there are diseases whose specific cause is not yet clear.

A no less important stage of diagnosis is the study of circumstances under which a disease develops. Social, home and working conditions, and constitutional properties are important for a correct diagnosis, because the character and clinical manifestations of the disease mainly depend on the patient's condition before the onset of the disease, which in turn depends on constitutional factors and the mode of previous life. Knowledge of all these factors provides conditions for passing from a diagnosis to the study of the patient. This helps explain the patient's individual properties and the course of the disease which is observed exactly in this concrete case and which distinguish him from other cases. This is especially important for prescription of the appropriate therapy and for prognosis of the disease.

The synthetic method begins with grouping the collected data (symptoms) and continues by identifying the syndromes occurring in the patient. It leads to substantiation of the observed phenomena by aetiological basis (in the broad sense of the word) with due consideration of the patient's traits and the environmental factors. The physician thus definitely and accurately identifies the disease and studies the patient. He keeps in mind that individualization of each particular case based on the factual scientific data is the object of clinical medicine and is at the same time the most solid ground for therapy (S.P. Botkin). This method consists in revealing symptoms of the disease, explaining their causes, and proceeding from one form of connection to another, deeper and more general. The synthetic method includes successive and repeated phases of analysis and synthesis to give finally a concrete understanding of the patient. The study passes from a symptom to a syndrome (which gives a new understanding of the patient's condition) in which each particular symptom becomes part and moment in the development of the whole syndrome. A similar transition from a syndrome to a symptom complex (large syndrome) is a new step in which the syndrome is only a component element. The transition from a syndrome to a disease as a nosological unit through knowledge of causes and interaction between the body and the environment gives a new, more perfect notion of the disease. The most essential factor in this method is the successive character in the synthesis of a diagnosis, in the transition from a lower stage to a higher one (i.e. orderliness), and also in the search for and establishment of connections between phenomena in a given patient by their causal dependence and interaction. Compared with the other methods, the synthetic method is more rational and reliable.

Comparison, conjectures, and tests are characteristic of each step in

establishing a diagnosis. The object of a concrete diagnosis is to reveal all individual properties, causes and conditions of the development of pathology in a given patient. This diagnosis brings the physician closer to a better understanding of the pathogenesis of the disease.

Attributing a case to a certain nosological unit, i.e. abstract diagnosis, reveals to some extent the essence and also possible aetiology of a pathological process. A concrete diagnosis of the patient's condition discloses the specific reaction of the body and the degree of disorder in the patient, as well as the constitutional and social background of the disease. The most complete diagnosis is a combination of the symptomatic, anatomical, functional, aetiological and social investigation. In other words, this is a synthesis: establishing the unity of various aspects of the patient's condition and specific properties. Understanding the cause and essence of a phenomenon is the necessary condition for a successful action, i.e. modification or eradication of this phenomenon.

It follows that two stages of understanding a disease can be distinguished. The first one is the simplest. In each particular case the physician tries to find out or remember what he already knows about the observed phenomenon. Here is simple recognition rather than a cognition process. By recognition, the physician, first, determines the elements of the disease and its symptoms as revealed by observation and experiment; second, the recognition process extends to the determination of the nosological unit corresponding to this particular symptom. This type of cognition in investigating the case is the simplest; it does not reveal any newness but only establishes the known in a new object. The second process is diagnosis. The physician faces the problem of cognition of the new and unknown. This happens when the physician proceeds from an abstract to a concrete diagnosis, to determination of all specific properties of the patient and the role of his working and living conditions. Novelty here is the disclosure of connections, casual relationship between the symptoms, and finally, the determination in each case of combination of all specific properties of the patient's reactions and the conditions (endo- and exogenic) for the origin of the given disease. The diagnostic cognition follows the general rule: "From living perception to abstract thought, *and from this to practice*—such is the dialectical path of the cognition of *truth,* of the cognition of objective reality".*

Unfortunately, incomplete investigation and incorrect diagnosis of a disease occur rather often. Comparison of clinical and pathoanatomical diagnoses shows that, according to different statistical data, almost 10 per

* V. I. Lenin. *Collected Works.* Moscow, Progress Publishers, 1976, vol. 38, p. 171.

cent of intravital diagnoses are incorrect. Pathoanatomical diagnosis is impossible in almost 3 per cent of cases.

Causes of incorrect diagnosis. The causes of erroneous diagnoses can be divided conventionally into three groups. First, a disease may remain without being diagnosed if this particular disease has not yet been studied by the present time. New diseases are being discovered and described every year and the number of unstudied diseases is considerable. Second, the disease might have been described but its clinical picture and diagnosis are not studied sufficiently well, which is an obstacle to correct diagnosis. Finally, the disease is known and studied well, but the physician may be unaware of it, or be acquainted with it only theoretically (without practical acquaintance).

The second group of diagnostic errors is determined by the incomplete or incorrect examination of the patient. This may be due to insufficient skill of the physician in techniques of clinical examination, the lack of knowledge of laboratory and instrumental methods that should be used in a particular case to identify the disease, or due to the absence of the appropriate laboratories (remote rural areas, etc.). The patient himself may be responsible for incomplete examination. For example, it is very difficult to obtain an anamnesis of a deaf and dumb patient or a foreigner. A patient in coma cannot be given a complete examination either (even by the main methods such as auscultation, percussion, or palpation): in emergency cases the physician has no time for a detailed examination.

The third cause of erroneous diagnosis is incorrect conclusion due to inadequate knowledge of symptomatology and methodology of diagnosis or due to conceptions forced on the physician by an authoritative conclusion of a more experienced physician. Unfortunately some cowardly physicians choose to abstein from speaking out their conjectured diagnosis in the face of high-rank or more experienced physicians even in very important cases. Incorrect diagnosis may also be due to overestimation by the physician of his own experience and due to his vanity, or when he is guided by his own intuition and experience and disregards the opinion of his colleagues or declines the necessity of carrying out some examination procedures.

An incorrect diagnosis due to an honest delusion of a physician should be differentiated from a deliberately incorrect diagnosis, which is crime.

It should be remembered that today diagnosis is not the responsibility of only one physician but of many medical specialists such as specialists in internal diseases, surgeons, highly skilled consultant physicians and diagnosticians, roentgenologists, endoscopists, laboratory technicians, etc.

The following *two groups of difficulties* can be distinguished *in diagnostics:* (1) quantitative difficulties, due to avalanching scientific information; (2) the necessity of as early and accurate diagnosis as possible

(which facilitates effective treatment of the disease) and even of revealing predisposition to the disease in practically healthy persons.

The first-group difficulties are due to an ever increasing amount of scientific information which should be collected in each particular case. For example, for diagnosis of liver affections it is necessary to carry out up to 30 biochemical tests (more that 100 tests are used for the purpose). This vast information is an additional obstacle to correct thinking (perception, storage and analysis of information, selection of the necessary conclusions from an increasing amount of facts such as diseases, syndromes, symptoms, tests, etc.).

But there is room for optimism however, because medicine borrows methods of investigation from more precise related sciences. Human thinking is now aided by computers which have flawless memory, a strictly definite order of comparison and selection of information (algorithm) and which solve various problems at a surprisingly short time. In 1960 A. A. Vishnevsky introduced cybernetics into clinical practice. B. V. Petrovsky wrote that "computers and mathematical methods will acquire higher importance in the development of medical science and practical health care". The progress in medicine is now backed by many new accurate methods of examination and by computers which accelerate the thinking process. Using special charts, which are filled in by patients, and also diagnostic machines will be indispensable in mass-scale prophylactic examination of the population.

But it should be understood that no computer or a diagnostic machine will rival the physician at the patient's bedside. Computers will only help the physician and never take his place. The physician has to collect an anamnesis, detect haemorrhage, hear the systolic sounds, discover (in a microscope) tuberculosis mycobacterium, in other words, the physician "feeds" the computer which "digests" the information using its electron "memory" and yields conclusion. Furthermore, at the present time the computer cannot reveal or describe new diseases or syndromes.

Computers help solve the problem of early and accurate diagnosis. There are other ways by which diagnostic difficulties may be overcome. These are broad-scale research, special training of physicians, improving their medical education, improvement of diagnostic apparatus, etc. The USSR public health system and the prophylactic trend in the Soviet medicine open further prospects for improving diagnostics. Larger part of the population undergoes regular prophylactic observations. Medical aid in the USSR is not only free of charge but is readily available. The purpose of diagnostics is broadened in the direction of revealing premorbid conditions and latent forms of diseases. New methods and plans for examination of various groups of the population are being created, the number of

laboratories increases, new diagnostic and therapeutic centres open, and many new diagnostic tools and instruments are supplied to the medico-prophylactic institutions.

Prognosis

Prognosis (Gk *pro* before, *gnosis* knowledge) is foreseeing the onset, the character of development, and the outcome of a disease. Prognosis is based on the knowledge of regularities of the course of pathological processes. Prognosis is also defined as diagnosis of the future.

The power of forecasting was highly esteemed in ancient Greece. Hippocrates would repeatedly stress that foreseeing would be the best what a physician might do, and that the physician might be of better use to those patients who could control the development of the disease in themselves provided the physician could forecast a possible disease as much before the actual onset of the disease as possible. Prognosis is necessary for successful treatment, but a correct prognosis also improves the patient's confidence in the physician. In Hippocrates' opinion timely prognosis of incurable cases saves medical art from accusation.

General problems of prognosis are the necessary and also difficult aspects of clinical medicine. Nevertheless prognosis has been given much less attention than diagnosis until recent times. The importance of prognosis in the clinic depends on the main purposes of practical medicine, namely prevention of diseases and treatment of patients. In this respect the work of a physician is like that of an investigator: "studying laws in order to be able to predict phenomena, and to predict phenomena in order to be able to master them" (Loeb). Knowledge of the aetiology of diseases, and of harmful working and living conditions which might impair health enables the physician to foretell under which conditions a given person or a group of people are likely to develop a particular disease. This is a prerequisite condition for successful personal and social hygiene.

Extensive prophylactic measures against epidemic diseases are based on the faculty to foresee possible ways of spreading of the contagious disease. For example, if a case of diphtheria or typhus is revealed, hygienic-prophylactic measures are undertaken on a broad scale, while the threat of an outbreak of seasonal influenza should involve mass-scale vaccination of the population, etc. In cases where a complication or a relapse is possible, prophylactic therapy is prescribed to prevent, for example, relapses of rheumatic fever, peptic ulcer, etc. Work of the public health services is based on the prognosis of changes in the incidence and localization of general illness among the population and of individual diseases in particular.

Analysis of medical work, like that of any other practical activity, shows that it is always connected with the prognosis of a given disease and with the forecasting of the results of medical and prophylactic measures. In his work, the physician must envisage the results (respice finem). The prognostic evaluation determines the selection of therapeutic means; for example, the discovery of even a small cancer tumour dictates a radical operation. Prescription of any medicinal preparation should be supported by a consideration of possible various side-effects and consequences of this therapy. For example, when giving a purgative, the physician must consider a possible negative effect of this measure, as in acute appendicitis. Development of a disease in accordance with the prognosis can indirectly confirm the correctness of the diagnosis. Prognosis is thus an indispensable part of practical medicine.

Forms of prognosis. The most important problem that concerns both the patient and the physician is whether the illness is fatal (prognosis quoad vitam). The other problem is the question of complete recovery (prognosis quoad valitudinem), how long the patient can live (prognosis quoad longitudinem vitae), what will be the progress of the disease in the immediate and far-off future (prognosis quoad decursum morbi), and whether the patient's functions will be restored (prognosis quoad functionem).

The physician must foresee the results of his therapy, the dangers of operative intervention and decide whether the patient will recover completely with time or whether he will be unable to continue with his normal life and occupation. If not, then he must decide what form of labour will be safe for the patient in his new condition (prognosis quoad laborem). Prognosis can be favourable, doubtful, bad, or unfavourable (prognosis bona, dubia, mala, pessima). Prognosis can also be lethal (prognosis lethalis).

Prognosis of a disease. Prognosis of a disease depends in the first instance on accurate and complete diagnosis. "When foretelling, the physician takes into consideration the main disease, the condition of the patient, his sex, age, social position, hereditary traits, the changes that have occurred in his condition as the result of previous diseases, his adaptability and the psychic and physical conditions under which the patient has been living. The physician cannot know the degree of stability of the patient's vital organs" (Botkin). The physician first considers the danger of a given disease (mortality rate, incidence of complete recovery, and residual effects following recovery). Prognosis is based mainly on statistical data concerning the disease.

The general prognosis of a disease is determined by the following two factors, namely the essence of the disease and advances made in modern therapy. Prognostic study of diseases has revealed with sufficient accuracy

that there exist (a) diseases that are completely incurable, e.g. leucoses; (b) diseases that are essentially very dangerous but which are curable at their early stages (e.g. sepsis, malignant tumours) and undoubtedly lethal in their late stages (e.g. profuse metastases of cancer or sarcoma). The other group includes diseases that resolve either spontaneously, or with the appropriate treatment (acute rhinitis, acute alimentary gastritis, minor injuries); these diseases result in complete recovery (restitutio ad integrum), although any disease causes changes in the body (residual effects due to the disease itself or its treatment, e.g. operative).

However, most diseases occupy an intermediate position between these two extremes (from the point of view of their prognostic assessment). These diseases vary greatly in terms of the degree of danger that they constitute to life. Many incurable diseases present no immediate danger to the patient's life and may last for years, only imparing the working capacity of the sufferer. Mortality in various diseases varies with time depending on advances in medicine and practical health care; the general prognosis of diseases improves with time as well. For example, many infectious diseases can now be successfully treated following the discovery of antibiotics; the use of vitamin B_{12} has moved Biermer disease (pernicious anaemia) to the category of curable diseases; certain congenital heart defects can now be corrected due to advances in heart surgery, etc.

The gravity of a disease is determined by certain signs, such as localization and extent of affliction, the body's reaction, the degree of functional disorder of the vital organs and the reversibility of functional and morphological changes of the body. Functional diagnosis gives valuable information for the prognosis of diseases.

Prognosis of the course of a disease foretells the length and possible complications of the disease. All diseases are classified as chronic and acute by their duration. Acute infectious diseases usually continue for a definite time depending on the nature of the pathology and immunobiological reaction of the patient's organism. Knowledge of the length of the disease is important for orientation in a particular case, sometimes for checking correctness of the diagnosis, or for the search of a developing complication (e.g. post-influenzal pneumonia). Statistical data on the incidence of complications in a given disease are no less important (e.g. small intestine perforation in typhoid fever, gastro-intestinal haemorrhage in cirrhosis of the liver, post-operative thrombosis of the veins). If the physician is aware of complications that may arise in a given disease, they can be timely revealed and better precluded. By foreseeing possible complications, the physician can take timely measures to prevent their development, e.g. by giving anticoagulants to prevent thrombosis, CO_2 respiration to prevent post-operative atelectasis of the lungs, etc.

The course of the disease and its complications depend on the

pathogenesis of the disease and individual properties of the patient's organism. Prognosis is always more favourable in the young: youth is the best friend of the patient. The course of the disease is influenced by constitution, hereditary factors, past diseases, living conditions, and also the health of the patient before the onset of the disease. Social conditions are often decisive for the prognosis of the disease, especially in capitalist countries, where medical aid is sometimes very expensive.

Evaluation of each symptom is very important for prognosis. The main diagnosis of the disease, knowledge of the aetiology and essence of the pathology give a clue to the physician in his forecast concerning possible curability or incurability and the duration of the disease. Symptoms of the disease give a concrete picture of its gravity and the degree of danger for life, and can be used to foresee the nearest course of the disease in a given patient, i.e. to establish an individual prognosis. The appearance of the eyes, voice, or strength of a handshake are informative of the patient's condition. The posture of the patient in his bed (active, passive, forced) is also prognostically important. Inspection of the tongue is necessary: a dry tongue is almost always an alarming sign; the loss of appetite is regarded as the "despair of nature in overcoming the disease", while good appetite is a "flag of health" (Obraztsov). The prognostic assessment of any symptom depends on the knowledge of its pathogenesis and the role in the main process. Dyspnoea, for example, in mitral stenosis and left ventricular failure due to hypertension has different prognostic significance. Diagnostic and prognostic importance of this or that symptom often coincide. For example, pulsus alternans or the gallop rhythm indicate a serious heart insufficiency. Observation of changes in separate symptoms has different prognostic importance. For example, growing tachycardia or change in the arterial pressure can be used as a guide to understanding the direction in which the disease develops. It should be remembered that a symptom (e.g. leucocytosis or fever) cannot always be indicative of disease gravity. It can only be a manifestation of the protective response of the body. The absence or weakening of such a reaction (i.e. the absence of pronounced symptoms) sometimes indicates gravity of prognosis, e.g. leucopenia in appendicitis or insignificant rise in temperature in a cachectic patient with pneumonia.

Individual reactivity of the patient's body requires a thorough clinical analysis. For example, neurotic patients can severely suffer from a mild disease, while some patients with grave diseases may abstain from any complaints. Each separate symptom can acquire a prognostic importance only when it can be used to judge on the function of the organ and the general condition of the body. A symptom becomes prognostically important only when it is considered in connection with the essence of the disease. For example, a sudden death can occur during the first pain attack in coronary failure.

Hereditary factors are important because the patient may be predisposed to some diseases, e.g. hypertension, obesity, etc. Knowledge of family diseases and the cause of death of parents is sometimes of great importance in assessing the probable development and the course of this or that disease in a particular patient. Age of parents is, for example, important for prognosis of a disease in offspring.

The appearance of a patient, the make-up of the body, and the constitution are prognostically important. It should be remembered however that subtility by no means excludes longevity even of a sickly looking person. Quite the contrary, a blooming person may more readily become a victim of an acute infection or cerebral apoplexy than an asthenic person. Excess weight, and especially predisposition to obesity, are aggravating factors.

Past diseases often change the body substantially. Stable immunity develops after acute infections attended by skin eruptions (measles, scarlet fever, smallpox, etc.). Other diseases, e.g. acute lobar pneumonia, rheumatic fever or peptic ulcer often recur.

Study of a healthy person for prognostic purpose should be as complete as the study of patients because prophylaxis of diseases is the main principle of the Soviet public health system. In this connection the dispensary system is being constantly broadened in this country. Dispensary observation of practically healthy population help reveal by X-ray studies cancer of the lung in persons who never complained of any malaise, or diagnose chronic nephritis or diabetes mellitus by the urinalysis. More common, however, is the discovery in practically healthy people of a tendency to develop certain chronic diseases or pre-clinical stage of diseases, e.g. hypercholesterolaemia which is a sign of disturbed lipid metabolism that often precedes the development of atherosclerosis, or moderate alimentary hyperglycaemia which is a sign of a prediabetic disorder in carbohydrate metabolism. No less important is the tendency to elevation of arterial pressure during emotional stress since it may indicate (not obligatory) the development of essential hypertension in future. Revealing signs of allergic reaction of the body (e.g. nettle rash) enables the physician to predict possible similar reactions and partially foresee the course of other diseases and the response to their treatment.

Determination of the type of higher nervous activity is very important for assessing the character of emotional reactions, which can (under special conditions) give rise to the development of neuroses or diseases of the central nervous system, vessels, etc. Furthermore, it should be remembered that certain people can be neglectful with respect to the prevention or treatment of a disease, as distinct from other people who, on the contrary, may be overanxious about their health or disease (which can sometimes be only imaginary).

Occupation or working conditions can sometimes be decisive for the health of a person, especially so if the character of work does not correspond to constitution of the person. The positive role of work in preservation of health of man is revealed, for example, in certain cases of depression or low somatic tone, or decreased resistance to some diseases in middle-aged healthy persons who retire to pension. Inadequate living conditions (housing, nutrition, climate, etc.) and unhygienic habits predispose to the development of various diseases. Overeating, smoking, alcohol, etc., should be regarded as pathogenic factors which often cause grave diseases in the near or remote future. Foreseeing the conditions under which diseases can develop is requisite for their prevention.

General prognosis is closely connected with advances in therapy; mortality from most diseases drops from year to year thanks to new discoveries in medicine and improved organization of the public health system. Mortality in pneumonia was as high as 25-40 per cent before chemotherapeutic preparations came into use. After the discovery of antibiotics this figure dropped to 8-10 per cent and even lower. The specific causative agent is very important for the prognosis in pneumonia. Prognosis is worse with type III pneumococcus than with types I and II. The percentage of fatal outcomes in epidemics of one and the same disease differs. This was earlier designated by the term "genius epidemicus". This depends on changeability in the pathogenic properties of the causative agent and resistance of the body. The latter factor was decisive for the character of pandemic influenza after World War I. Prophylactic vaccinations are also important for a milder course of infections.

Depending on aetiology and pathogenesis of each infectious or other disease, a specific organ is mostly affected, e.g. myocardium is affected in diphtheria, vessels in louse-borne fever. Maximum attention should therefore be paid to observation of the function of the corresponding systems or organs so that the degree of their affection might be assessed and possible outcome predicted. In all cases, the physician must observe and study vitally important organs and systems (blood circulation, respiration, etc.). This observation is very important for the prognosis of the near and.remote outcome of the disease. All possible complications (e.g. pneumonia in influenza, intestinal haemorrhage in louse-borne fever, etc.) should be considered by the physician in order to prognose the course of the disease and to control timely a sudden worsening of the patient's condition. No less important is it to know during what period of the disease this or that complication may develop. Any impairment of the patient's condition will not then be unexpected. Daily observation of patients with grave infectious diseases helps determine the tendency or direction of the pathological process. The physician should take pulse and temperature, determine leucocytosis, the character of urination, etc.

It is more difficult to foresee the outcome of a chronic than of an acute disease. Prognosis of some incurable diseases almost entirely depends on the therapy with preparations that compensate for the pathological changes (e.g. diabetes mellitus, myxoedema, etc.). The course of many chronic diseases associated with incurable defects in the structure and function of some organs can only be assessed after observation of the patient and assessment of the progress of the pathology (e.g. in lung emphysema, atherosclerosis, heart valve defects, etc.). The compensation of the affection or defect is very important for the prognosis of the disease. An example of almost unlimited compensation ability of the body is good subjective condition and working capacity of patients with fully closed coronary artery provided there is sufficient time for a vascular collateral to develop. When one of paired organs is lost (e.g. one kidney) the remaining organ ensures normal function for an indefinitely long time. It is known that preservation of a small portion of any organ, e.g. of the liver, the lung, etc., is compatible with life, which may sometimes be quite active. Consideration of adaptability of the body to the changed environmental conditions is the main basis for a prognosis in chronic diseases. Adaptability, which is the main property of any living organism, differs, however, in various subjects. Adaptability of healthy people to hard environmental conditions depends not only on the congenital factors but also on training in direct sense of this word (e.g. in physical strain) and also in a figurative sense; for example, people who had successful operations in their past history, better tolerate a new one. "Hot-house" conditions impair resistance of the body. A disease itself is one of the forms of more or less adequate adaptation of the body. For example, a local inflammation prevents generalization of infection and often removes the causative agent or unjury leading to complete recovery. At the same time, a chronic disease or an injury has its effect on the future life of man.

Individual traits of the patient's temperament are important to predict the outcome of a disease and working capacity of the patient after his recovery. Some patients become disabled by insignificant affections, while others bravely challenge grave diseases, such as chronic arthritis or heart diseases, and continue living an active life. Some patients are passive in their attitude to the prescribed therapy while others actively fight the disease and recover their working capacity.

Almost any chronic disease is characterized by certain periodicity, in which relapses alternate with remissions. Remissions and relapses depend on both special features of pathology and on the environmental conditions, which sometimes are difficult to control. Concomitance of several pathological processes markedly aggravates the prognosis. According to certain authors, signs of coronary atherosclerosis were observed in 10 out of 1000 practically healthy aged male patients during four years. In cases

with concurrent hypercholesterolaemia, obesity, and hypertension (or any two of these three diseases), the incidence of coronary affections was as high as 143 per 1000 patients (i.e. more than ten times higher). Development of an acute disease in a patient with a chronic one (e.g. infection in a diabetes patient) is especially dangerous.

Prognostic errors. The difficulty of prognosis is that it is based on the diagnosis. "Diagnosis is only a more or less probable hypothesis. Foreseeing based on this hypothesis is, of course, less probable than the first main hypothesis, the more so that many unknown factors continue their effect on the patient during the time when this medical problem is being solved" (Botkin). Difficulties in foreseeing the course of a disease are emphasized by all clinicians. "Despite advances in modern medicine, the most difficult problem is to foresee the course of the disease and its outcome" (Konchalovsky). Incorrect or incomplete diagnosis is the main source of the erroneous prognosis, because a correct prognosis is only possible with a correct diagnosis.

A physician's forecast consists in determining the conditions under which this or that phenomenon is likely to occur, and prognostic error depends on the incomplete knowledge of these conditions. Diagnosis is incomplete if only the disease is diagnosed while the condition of the patient has not been studied. It is difficult then to predict the course of the disease in the nearest or remote future.

Prognostic errors often arise from the inaccurate determination of the compensatory properties and reserve forces of the organism. Psychological and subjective features of a physician may become the source of prognostic errors. For example, in his desire to see the patient recovered from the disease, the physician may misinterpret new and sometimes dangerous symptoms, which might be taken as some extraneous factors rather than the signs of the main disease. Prognosis of the remote future is still more difficult than the foreseeing of the immediate events because new conditions may occur which would affect the main course of the disease.

Prognosis and the patient. The patient is usually mostly interested in prognosis rather than diagnosis, which is his second interest. But the diagnosis has a prognostic importance to the patient as well, since it may tell him whether or not his disease is curable. The physician should always be ready to answer this question about the diagnosis. The relations between the physician and the patient should obey the main purpose of medicine, namely, prevention and treatment of disease. The prognosis that the physician gives to his patient should not therefore contradict this main medical law. The prognosis of cancer should always be excluded from conversation with the patient and even with his relatives if there is the danger that the patient might know the truth from them. Botkin wrote, "I think that the

physician has no right to tell his patient his doubts concerning possible unfavourable outcome of his disease". Possible diagnostic errors should also be taken into consideration. That physician is the best who can persuade the patient that the disease is curable. Sometimes this persuasion is the best medicine.

Any disease evokes the feeling of fear, anxiety, and other unfavourable emotions, and the prognosis should not therefore aggravate the condition of the patient. The responsibility of the physician for the prognosis is thus very high. The physician takes also high responsibility when he recommends that the patient should change his occupation or place of residence, or else the mode of life for a long time. The physician should abstain from careless words or gestures that might reveal the gravity of the prognosis. The physician should put his prognosis in words that might be clearly understood by the patient without undue details. Uncertain prognosis may aggravate the patient's anxiety by arousing doubts in him; neither should the physician outline definite terms for a complete recovery. The predicted term may prove incorrect and this may strengthen the patient's anxiety and decrease his confidence in the physician. The prognostic evaluation should be worded in conventional terms such as, for example, "You will recover if you follow my prescriptions", and the like. In some cases it is reasonable to give the patient a wrong diagnosis, e.g. of tuberculosis, if the patient has cancer. This will encourage the patient. The foretelling should be worded neither too seriously nor too carelessly. In all cases it should be close to the real one but supplemented with optimism in severe cases.

A favourable prognosis should be spoken out without waiting for the patient's question, because some patients choose not to know the truth from the fear of losing any hope. It is not infrequent that some patients (physicians included) choose to deceive themselves despite the vivid signs of incurability of their disease (e.g. cancer). This should be regarded as a peculiar protective reaction. If there is no other way to persuade a patient to give consent to an operation in cancer of the stomach, for example, it is reasonable to tell him half-truth by saying that the operation is necessary to remove a tumour which may otherwise become malignant. In other words, the prognosis depends on the necessity of treatment. The prognosis should therefore be not only definite and encouraging, but it will also show possible danger if the patient does not follow medical recommendations. This will strengthen the patient's confidence in the physician. The physician has to conceal grave truth from his patient but his condition should be assessed properly and the relatives should be informed of this condition, provided the physician is sure that the relatives will keep the truth from the patient.

Possible diagnostic error should always be considered. But prognosis depends on diagnosis, and indubious cases it is better to abstain from the

forecast rather than to show undue optimism. The patient and his relatives should be prepared for a possible worsening in the patient's condition. Such a prediction prevents possible depression which can develop from a sudden and unexpected exacerbation of symptoms. It is necessary to inform the patient of the approximate duration of the disease and treatment, in order to prepare him for a possible protracted course of treatment and slow recovery.

Prognostic methods. Methods of medical prognostication have changed with the development of medicine. Prognosis at the early stage of medical science was only empirical; it is still important now. It consists in comparison of the general condition and functions of the patient's organs with those of a healthy person, the degree of deviation being the measure of the condition gravity. Comparison of the vital functions and the anatomical changes in the patient with those of a healthy person is the first step in the diagnostic and prognostic study. But the conclusion will be only very general. Marked deviation of the bodily functions from normal indicate danger but cannot be used for a definite prognosis of the outcome of the disease because functional disorders often depend not only on the affection but are often a protective and useful response of the body, e.g. vomiting in poisoning, cough in the presence of foreign bodies in the respiratory ducts, etc. During repeated examinations in the modern clinic, the present condition of the patient and the individual symptoms are compared with those observed during earlier examinations. This comparison is very important for judgement on the direction of the pathological process, and for assessment of worsening or improvement of the patient's condition.

Another empirical method is based on a suggestion of possible occurrence or a relapse of an event provided a phenomenon preceding this event was noted. This kind of prognostic signs can be regarded as a necessity only if the events follow one another as cause and effect. But two events that follow one another may have no causal dependence, or they may be effects of one and the same cause. Hence only relative value of such signs.

Still another prognostic method is based on conclusions derived from many separate events, e.g. on statistical regularity. Statistical data on the outcomes of diseases are of general importance and hold for mass-scale phenomena, but they can give only tentative information for the prognosis in individual cases (higher or lower probability of the expected event). Speculations are based on diagnosis, but the patient's condition may vary with one and the same diagnosis (e.g. tuberculosis, myocardial infarction, etc.) depending on many conditions.

Personal experience is an important factor in prognosis. It is equally important for correct prognosis and correct diagnosis. Experience of a

physician depends on his memory, i.e. the power to recollect information on more or less significant number of similar cases. In contrast to scientific investigation, medical experience of a physician cannot be substantiated statistically while generalizations based on personal experience are not sufficiently accurate. Lengthy observation of patients from the onset of the disease to its end is valuable for aquisition of experience in foretelling. Therefore formerly prognostic conclusions of a family doctor were often more correct than conclusions of scientific consultants. Once the physician knows individual properties of a given patient, it is easier for him to predict the response of his patient to this or that aetiological factor.

Scientific knowledge of the course and outcome of a disease is as important as a personal experience of a physician. These data are used to predict the patient's condition in future. Personal experience of a physician is always based on achievements in medicine. Scientific investigations give information on the possible course of a disease depending on its form, stage, the patient's constitution, and the like, and also explain the causes of such a course, the mechanisms of body affection, the character and signs of convalescence, i.e. they establish regularities of patho- and sanogenesis of a disease. Scientific prediction is based on the knowledge of regularities of a given pathological process, e.g. malignant newgrowth, inflammation, acute infection, etc. Once effects of particular causes are known, one can foretell future developments.

Modern medical prognosis requires a thorough clinical analysis and evaluation of the symptoms of a disease, consideration of the progress of pathology and protective processes or sanogenesis, and also vital reserves of the important body organs. A single examination can be used to assess the gravity of the present condition of the patient, while the direction of the pathology can be determined from anamnesis and from lengthy observation of the patient. But various signs of a disease, e.g. temperature, pulse, respiration, leucocytosis, can vary sharply with the course of the process. The curve of a high temperature in acute lobar pneumonia always drops at the end which can be either due to the high antibody level (crisis) and beginning convalescence, or due to a grave toxicosis and a circulatory collapse. Observation also gives information on the effects of the therapy. The number of factors involved in prognostication of the disease is thus greater than for its diagnosis. They are supplemented by the results of the prescribed treatment, and speculations of a physician in prognosis are more complicated than during statement of the patient's condition. Prognosis is based on regularities of the pathological processes and knowledge of the action of aetiological factors.

The logical fundamentals of prognosis are more complicated and differ substantially from diagnostic knowledge. In order to diagnose the present

condition of a person, the physician examines him, finds and evaluates the symptoms. By examining the combination and sequence of the symptoms, the physician concludes on the character of the pathology (i.e. he proceeds from phenomena to the essence). Finally, he investigates the aetiology and conditions under which the disease developed. The physician can reconstruct the picture of the development of the disease (i.e. the past history) from the present conditions and anamnesis. Diagnostic knowledge proceeds from the present facts to the cause of the disease and to the past condition of the patient. Prognosis is the forecast of the patient's future condition, knowledge of what may or must happen because of the present condition. In diagnosis the physician follows from the effect to its cause, while in prognosis he foretells effects from the present cause. This corresponds to the deductive way of arriving to a conclusion. Once the cause is revealed (e.g. an infection or an injury is discovered) the physician should know what particular effects may follow, i.e. he must know the regular reaction of the body to any particular affection. Determining effects of aetiological factors is complicated by the fact that various subjects react differently to one and the same stimulus.

The first logical process in prognosis is the ability to derive a conclusion from the examined pathology. The vital processes are very complicated and it is therefore difficult to consider all possible tendencies and regularities. Prognosis should in such cases be based on the main tendencies and regularities.

The next stage of predicting future changes in the patient's condition is dialectical understanding of development as a contradictory process producing qualitative changes. Any pathological process causes an antagonistic process and both interact to enter a new stage of the disease which can end either in cure or death. The body's response to an injury is not an instantaneous response but a process occurring in time through certain phases. Prognosis is based on the regularities of the development of this process. But conditions that may change these regularities are also taken into consideration. In practice the situation is even more complicated because the physician interferes with the "normal" course of the disease. Treatment should therefore also be taken into account during prognostication.

The number of papers devoted to the prognosis of individual forms of diseases constantly increases and broader generalizations will probably soon appear. Advances in medicine and health care show that prognosis of diseases will be more accurate and favourable because the high reliability of diagnostic studies and observations help reveal diseases at their earlier stages and ensure greater success in their treatment. Improvement of the medical and prophylactic aid and a steady rise in the well-being of the population in the Soviet Union give grounds for this optimistic prognosis.

SPECIAL PART

Chapter 5

RESPIRATORY SYSTEM

Methods of Examination

Inquiry

Complaints. The main complaints typical for the respiratory system are dyspnoea, cough, bloody expectorations, and pain in the chest. Fever, asthenia, indisposition and loss of appetite are not infrequent.

Dyspnoea in its manifestation can be subjective, objective, or subjective and objective simultaneously. By subjective dyspnoea is understood the subjective feeling of difficult or laboured breathing. Objective dyspnoea is determined by objective examination and is characterized by changes in the respiration rate, depth, or rhythm, and also the duration of the inspiration or expiration. Diseases of the respiratory system are often accompanied by mixed (i.e. subjective and objective) dyspnoea. It is often associated with rapid breathing (tachypnoea). These symptoms occur in pneumonia, bronchogenic cancer, and in tuberculosis. Cases with purely subjective dyspnoea (in hysteria, thoracic radiculitis) or purely objective dyspnoea (in pulmonary emphysema or pleural obliteration) occur less frequently. Dyspnoea is possible with both normal and slow rate of breathing (bradypnoea). Three types of dyspnoea are differentiated by the prevalent breathing phase: inspiratory dyspnoea, expiratory dyspnoea and mixed dyspnoea when both expiration and inspiration become difficult.

Dyspnoea may be physiological (caused by heavy exercise) and pathological (associated with pathology of the respiratory organs, diseases of the cardiovascular and haemopoietic systems, and poisoning).

Dyspnoea associated with respiratory pathology may be of various aetiology. It can be caused by obstruction of the respiratory ducts, contraction of the respiratory surface of the lungs due to their compression by liquid or air accumulated in the pleural cavity, decreased pneumatization of the lung in pneumonia, atelectasis, infarction or decreased elasticity of the lungs. These conditions are associated with decreased total (vital) lung capacity and ventilation, which causes increased carbon dioxide content of blood, and acidosis of tissues due to accumulation in them of incompletely oxidized metabolites (lactic acid, etc.). The so-called alveolar-capillary block is also possible in some cases. This is associated with exudative and

proliferative inflammation of the interstitial tissue in interstitial pneumonia or lung oedema.

A mechanical obstruction in the upper respiratory ducts (larynx, trachea) complicates and slows down passage of the air into the alveoli and causes inspiratory dyspnoea. When the trachea and a large bronchus are sharply contracted, both inspiration and expiration become difficult and noisy (stridulous respiration). Narrowed lumen in the fine bronchi and bronchioles due to inflammatory oedema and swelling of their mucosa, or else in spasms in the smooth muscles (bronchial asthma), interferes with normal air passage from the alveoli and the expiration becomes difficult. Expiratory dyspnoea thus develops. Pathological conditions caused by a significant decrease in the respiratory surface of the lungs are accompanied by mixed dyspnoea (transient or permanent). Respiration becomes superficial and painful in inflammation of the pleura. Pronounced mixed dyspnoea, often painful, with deep inspiration and expiration occurs in embolism or thrombosis of the pulmonary artery. The patient has to assume a forced, sometimes sitting posture (orthopnoea) to remove the discomfort. Heavy dyspnoea, often followed by asphyxia, is called suffocation. It occurs also in acute oedema of the lungs, bronchiolitis in children, and in fibrinous bronchitis. Asphyxia arising as a sudden attack is asthma. Bronchial asthma, in which an attack of dyspnoea occurs as a result of spasms of smaller bronchi and is accompanied by difficult, lengthy and noisy expiration, is differentiated from cardiac asthma which is secondary to left heart failure and is often accompanied by lung oedema with very difficult expiration.

Cough is a complicated reflex act which is actually a defence reaction aimed at clearing the larynx, trachea, or bronchi from mucus or foreign material. Mucus and inhaled dust particles are normally discharged from the bronchi by ciliated epithelium. But an inflamed bronchial mucosa produces a secretion which acts on the sensitive reflexogenic zones in the respiratory mucosa to stimulate the nerve endings and to activate the coughing reflex. The most sensitive reflexogenic zones are located at branching points of the bronchi, in the tracheal bifurcation points, and in the interarythenoid space of the larynx. The reflexogenic zones producing cough are found in other regions as well, e.g. in the mucosa of the nose, fauces, pleura, etc.

Various diseases of the respiratory organs are characterized by specific cough. The physician should therefore ask the patient to describe the character of his cough, length and time of coughing attacks, loudness and timbre of cough, etc.

Cough may be dry, without sputum, and moist, during which various amounts of sputum of different quality are expectorated. Some diseases

are attended only by dry cough, e.g. laryngitis, dry pleurisy or compression of the main bronchi by the bifurcation lymph nodes (tuberculosis, lymphogranulomatosis, cancer metastases, etc.). Bronchitis, pulmonary tuberculosis, pneumosclerosis, abscess, or bronchogenic cancer of the lungs can be first attended by dry cough, which will then turn into moist one with expectoration of the sputum.

If a patient complains of cough with sputum, the physician should try to determine the amount of sputum expectorated during one fit and during the entire day; it is also important to know the time of the day during which the sputum is expectorated and the position of the body at which cough is provoked; the colour, odour, and other properties of sputum are also important. Morning cough is characteristic of patients with chronic bronchitis, bronchiectasis, lung abscess, and cavernous tuberculosis of the lungs. The sputum accumulates during the night sleep in the lungs and the bronchi, but as the patient gets up, the sputum moves to the neighbouring parts of the bronchi to stimulate the reflexogenic zones of the bronchial mucosa. This causes cough and expectoration of the sputum. The amount of the sputum expectorated during the morning may amount to two thirds of the entire daily expectoration. Depending on the gravity of the inflammatory process in patients with mentioned diseases, the daily amount of the expectorated sputum may vary from 10—15 ml to as much as 2 litres. In unilateral bronchiectasis, sputum may be better expectorated in a definite posture, for example, on the right side with bronchiectasis in the left lung, and vice versa. If bronchiectasis is found in the anterior region of the lungs, expectoration is easier in the supine position, and if in the posterior parts, in the prone position.

Patients with pneumonia and bronchitis may complain of cough attacks during the entire day, but attacks may intensify by night ("evening" cough). "Night" cough is characteristic of tuberculosis, lymphogranulomatosis, or malignant newgrowths. Enlarged mediastinal lymph nodes in these diseases stimulate the reflexogenic zone of the bifurcation, especially during night when the tone of the vagus nerve increases, to produce the coughing reflex.

Cough is differentiated by its length. It may be permanent and periodic. Permanent cough is rarer and occurs in laryngitis, bronchitis, bronchogenic cancer of the lungs or metastases into the mediastinal lymph nodes, and in certain forms of pulmonary tuberculosis. Periodic cough occurs more frequently. It always occurs in influenza, acute catarrhs of the upper air ways, pneumonia, pulmonary tuberculosis, chronic bronchitis, especially during exacerbation. Periodic cough can be in the form of slight single cough bursts (during the initial stage of tuberculosis, in neurosis), succession of such bursts, and finally strong and sometimes prolonged at-

tacks of cough (in rupture of the abscess, in whooping cough, or when foreign bodies get in the upper air ways). Strong and long cough expulsions sharply increase the intrathoracic pressure and sometimes cause transient dilation of the neck veins, cyanosis, and puffiness of the face. Strong and long fits of cough in children with whooping cough stimulate the adjacent vomiting centre to cause vomiting.

Cough is also classified by its loudness and timbre. Loud barking cough is characteristic of whooping cough, compressed trachea (due to retrosternal goitre or tumour), affection of the larynx and swelling of the false vocal cords, and in hysteria; soft cough or tussiculation (hacking cough) is characteristic of the first stage of acute lobar pneumonia, dry pleurisy and the early stage of pulmonary tuberculosis. Inflammation of the vocal cords is attended by strong cough while ulceration of the cords is characterized by voiceless cough.

Haemoptysis is expectoration of blood with sputum during cough. The physician must determine the origin of haemoptysis and the amount and character of blood expectorated with sputum. Haemoptysis can develop in diseases of the lungs and air ways (bronchi, trachea or larynx), as well as in diseases of the cardiovascular system. Pulmonary tuberculosis and cancer, virus pneumonia, bronchiectasis, abscess and gangrene of the lung, actinomycosis, tracheitis and laryngitis associated with virus influenza are often attended by haemoptysis. This symptom is also characteristic of some heart defects, such as stenosis of the left venous (mitral) orifice which causes congestion of blood in the lesser circulation, thrombosis or embolism of the pulmonary arteries and subsequent pulmonary infarction.

The amount of blood expectorated with sputum is mostly scant. Blood appears in the form of thin streaks, or it may give diffuse colouration to the sputum, which can be jelly-like or foamy. Cavernous tuberculosis, bronchiectases, degrading tumour and pulmonary infarction may be attended by lung haemorrhage, which is usually accompanied with strong cough.

Blood expectorated with sputum can be fresh and scarlet, or altered. Scarlet blood in the sputum is characteristic of pulmonary tuberculosis, bronchogenic cancer, bronchiectasis, and actinomycosis of the lungs. Blood expectorated with sputum in acute lobar pneumonia (second stage) has the colour of rust (rusty sputum) due to decomposition of the red blood cells and formation of the pigment haemosiderin. Blood in the sputum is fresh and scarlet during the first 2-3 days in lung infarction while in subsequent 7-10 days it becomes altered.

Pain in the chest is classified by its location, origin, character, intensity, duration, and irradiation, by its connection with the respiratory movements, cough, and the posture. Pain may arise during the develop-

ment of a pathological condition in the thoracic wall, the pleura, heart, and the aorta, and in diseases of the abdominal organs (by irradiation). Special clinical signs are characteristic of pain of any particular origin, and in this respect pain may have diagnostic value.

Pain in the chest wall ("surface" pain) is usually localized, boring or piercing, often intense and prolonged; it intensifies during deep breathing, coughing, lying on the affected side, and in brisk movements. Pain may develop in injury to the skin (trauma, erysipelas, herpes zoster, etc.), muscles (trauma, myositis), intervertebral nerves (thoracic radiculitis in spondylarthrosis), ribs and costal pleura (metastases of the tumour, fractured bones, periostitis).

Pain in the chest in diseases of the respiratory organs depends on irritation of the pleura, especially of the costal and diaphragmal parts where sensitive nerve endings are found. (They are absent in the pulmonary tissue.) Pleura may be injured during its inflammation (dry pleurisy), in subpleural pneumonia (acute lobar pneumonia, lung abscess, pulmonary tuberculosis), in lung infarction, tumour metastasis into the pleura or development in it of the primary tumour, in injury (spontaneous pneumothorax, wound, rib fracture), in subdiaphragmal abscess, and in acute pancreatitis.

Localization of pain depends on the pathological focus. Pain in the left or right inferior part of the chest (pain in the side) is characteristic of dry pleurisy. Inflammation of the diaphragmal pleura may be manifested by pain in the abdomen to simulate acute cholecystitis, pancreatitis, or appendicitis.

Pleural pain is often piercing, while in diaphragmal pleurisy and spontaneous pneumothorax it is acute and intense. Pain is intensified in deep breathing, coughing, or when the patient lies on the healthy side. The respiration movements in this position become more intense in the affected side of the chest to strengthen friction of the inflamed pleura (rough from deposited fibrin). Pain lessens when the patient lies on the affected side. Pleural pain is also lessened when the chest is compressed to decrease the respiratory excursions.

Pain in cardiovascular diseases is localized in the region of the heart or the retrosternal region. It arises in physical strain, excitement, and unfavourable emotions. The attack often develops suddenly and may continue from a few seconds to several hours. Pressing pain of various intensity often occurs as the feeling of discomfort in the chest. Neurosis of the heart is manifested by intermittent cutting pain at the apex of the heart. Pain intensity does not change during cough, deep breathing or movements of the body. Tumour of the mediastinum may be attended by permanent intense retrosternal pain which is sometimes attended by signs of compres-

sion of large mediastinal vessels. Retrosternal pain may arise in hiatus hernia or by reflectory routes in case of ulcer, tumour of the cardiac part of the stomach, and in cholelithiasis.

Anamnesis. When questioning the patient the physician should determine the time the disease began. Acute onset is characteristic of acute pneumonia, especially acute lobar pneumonia. Pleurisy begins more gradually. A non-manifest onset and a prolonged course are characteristic of pulmonary tuberculosis and cancer. The onset of many diseases may be provoked by chills (bronchitis, pleurisy, pneumonia).

Determining epidemiological conditions is very important for establishing the cause of the disease. Thus influenzal pneumonia often occurs during epidemic outbreaks of influenza. Establishing contacts with tuberculosis patients is also very important. Specific features of the course of the disease and the therapy given (and its efficacy) should then be established.

When collecting the life anamnesis, the physician should pay attention to conditions under which the patient lives and works. Damp premises with inadequate ventilation or work in the open (builders, truck drivers, agricultural workers, etc.) can become the cause of acute inflammation of the lungs with more frequent conversion into chronic diseases. Some dusts are harmful and cause bronchial asthma. Coal dust causes a chronic disease of the lungs called anthracosis. Regular exposure to silica dust (cements, pottery, etc.) causes silicosis, the occupational fibrosis of the lungs.

The patient should give a detailed report of his past diseases of the lungs or pleura, which helps the physician establish connections between the present disease and diseases of the past history.

Physical Examination

INSPECTION

Examination of the chest should be done according to a definite plan. The general configuration of the chest should first be estimated (position of the clavicles, supra- and subclavicular fossae, shoulder blades); the next step is to define the type, rhythm and frequency of breathing, respiratory movements of the left and right shoulder blades, and of the shoulder girdle, and involvement of the accessory respiratory muscles in the breathing act. The patient should be better examined in the upright (standing or sitting) position with the chest being naked. Illumination of the body should be uniform.

The shape of the chest may be normal or pathological. A normal chest is characteristic of healthy persons with regular body built. Its right and

left sides are symmetrical, the clavicles and the shoulder blades should be at one level and the supraclavicular fossae equally pronounced on both sides. Since all people with normal constitution are conventionally divided into three types, the chest has different shape in accordance with its constitutional type. Pathological shape of the chest may be the result of congenital bone defects and of various chronic diseases (emphysema of the lungs, rickets, tuberculosis).

Normal form of the chest. 1. *Normosthenic (conical) chest* in subjects with normosthenic constitution resembles a truncated cone whose bottom is formed by well-developed muscles of the shoulder girdle and is directed upward. The anteroposterior (sternovertebral) diameter of the chest is smaller than the lateral (transverse) one, and the supraclavicular fossae are slightly pronounced. There is a distinct angle between the sternum and the manubrium (angulus Ludowici); the epigastric angle nears 90°. The ribs are moderately inclined as viewed from the side; the shoulder blades closely fit to the chest and are at the same level; the chest is about the same height as the abdominal part of the trunk.

2. *Hypersthenic chest* in persons with hypersthenic constitution has the shape of a cylinder. The anteroposterior diameter is about the same as the transverse one; the supraclavicular fossae are absent (level with the chest). The manubriosternal angle is indistinct; the epigastric angle exceeds 90°; the ribs in the lateral parts of the chest are nearly horizontal, the intercostal space is narrow, the shoulder blades closely fit to the chest, the thoracic part of the trunk is smaller than the abdominal one.

3. *Asthenic chest* in persons with asthenic constitution is elongated, narrow (both the anteroposterior and transverse diameters are smaller than normal); the chest is flat. The supra- and subclavicular fossae are distinctly pronounced. There is no angle between the sternum and the manubrium: the sternal bone and the manubrium make a straight "plate". The epigastric angle is less than 90°. The ribs are more vertical at the sides, the tenth ribs are not attached to the costal arch (costa decima fluctuens); the intercostal spaces are wide, the shoulder blades are winged (separated from the chest), the muscles of the shoulder girdle are underdeveloped, the shoulders are sloping, the chest is longer than the abdominal part of the trunk.

Pathological chest. 1. *Emphysematous (parrel-like) chest* resembles a hypersthenic chest in its shape, but differs from it by a barrel-like configuration, prominence of the chest wall, especially in the posterolateral regions, the intercostal spaces are enlarged. This type of chest is found in chronic emphysema of the lungs, during which elasticity of the lungs decreases while the volume of the lungs increases; the lungs seem to be as if at the inspiration phase. Natural expiration is therefore difficult not only

during movements but also at rest (expiratory dyspnoea is found). Active participation of accessory respiratory muscles in the respiratory act (especially m. sternocleidomastoideus and m. trapezius), depression of the intercostal space, elevation of the entire chest during inspiration and relaxation of the respiratory muscles and lowering of the chest to the initial position during expiration become evident during examination of emphysema patients.

2. Paralytic chest resembles the asthenic chest. It is found in emaciated patients, in general asthenia and constitutional underdevelopment; it often occurs in grave chronic diseases, more commonly in pulmonary tuberculosis and pneumosclerosis, in which fibrous tissue contracts the lungs and diminishes their weight due to the progressive chronic inflammation. During examination of patients with paralytic chest, marked atrophy of the chest muscles and asymmetry of the clavicles and dissimilar depression of the supraclavicular fossae can be observed along with typical signs of asthenic chest. The shoulder blades are not at one level either, and their movements during breathing are asynchronous.

3. *Rachitic chest (keeled or pigeon chest).* It is characterized by a markedly greater anteroposterior diameter (compared with the transverse diameter) due to the prominence of the sternum (which resembles the keel of a boat.) The anterolateral surfaces of the chest are as if pressed on both sides and therefore the ribs meet at an acute angle at the sternal bone, while the costal cartilages thicken like beads at points of their transition to bones (rachitic beads). As a rule, these beads can be palpated after rickets only in children and youths.

4. *Funnel chest* can occur in normosthenic, hypersthenic or asthenic subjects; it has a funnel-shaped depression in the lower part of the sternum. This deformity can be regarded as a result of abnormal development of the sternum or prolonged compressing effect. In older times this chest would be found in shoemaker adolescents. The mechanism of formation of the funnel chest was explained by the permanent pressure of the chest against the shoe; the funnel chest was therefore formerly called cobbler chest.

5. *Foveated chest* is almost the same as the funnel chest except that the depression is found mostly in the upper and the middle parts of the anterior surface of the chest. This abnormality occurs in syringomyelia, a rare disease of the spinal cord.

The chest may be abnormal in subjects with various deformities of the spine which arise as a result of injuries, tuberculosis of the spine, rheumatoid arthritis (Bekhterev's disease), etc. Four types of spine deformities are distinguished: (1) lateral curvature of the spine, called scoliosis; (2) excessive forward and backward curvature of the spine (gibbus and

kyphosis, respectively); (3) forward curvature of the spine, generally in the lumbar region (lordosis); (4) combination of the lateral and forward curvature of the spine (kyphoscoliosis).

Scoliosis is the most frequently occurring deformity of the spine. It mostly develops in schoolchildren due to bad habitual posture. Kyphoscoliosis occurs less frequently. Lordosis only occurs in rare cases. Curvature of the spine, especially kyphosis, lordosis, and kyphoscoliosis cause marked deformation of the chest to change the physiological position of the lungs and the heart and thus interfere with their normal functioning.

The shape of the chest can readily change due to enlargement or diminution of one half of the chest (asymmetry of the chest). These changes can be transient or permanent.

The enlargement of the volume of one half of the chest can be due to escape of considerable amounts of fluid as the result of inflammation (exudate) or non-inflammatory fluid (transudate) into the pleural cavity, or due to penetration of air inside the chest in injuries (pneumothorax). Levelling or protrusion of the intercostal spaces, asymmetry of the clavicles and the shoulder blades and also unilateral thoracic lagging can be observed during examination of the enlarged part of the chest. The chest assumes normal shape after the air or fluid is removed from the pleural cavity.

One part of the chest may diminish due to (1) pleural adhesion or complete closure of the pleural slit after resorption of effusion (after prolonged presence of the fluid in the pleural cavity); (2) contraction of a considerable portion of the lung due to growth of connective tissue (pneumosclerosis) after acute or chronic inflammatory processes, such as acute lobar pneumonia (with subsequent carnification of the lung), lung infarction, pulmonary abscess, tuberculosis, etc.; (3) resection of a part or the entire lung; (4) atelectasis (collapse of the lung or its portion) that may occur due to closure of the lumen in a large bronchus by a foreign body or a tumour growing into the lumen of the bronchus and causing its obturation. The closure of the air passage into the lung with subsequent resorption of air from the alveoli and a decrease in the volume of the lung diminish the corresponding half of the chest. The chest thus becomes asymmetrical, the shoulder of the affected side lowers, the clavicle and the scapula lower as well, and their movements during deep respiration become slower and limited; the supra- and subclavicular fossae become more depressed, the intercostal spaces decrease in size or become invisible. The marked depression of the supraclavicular fossa on one side often depends on the diminution of the apex of a fibrosis-affected lung.

Respiratory movements of the chest should be examined during inspection of the patient. In physiological conditions they are performed by the

contraction of the main respiratory muscles: intercostal muscles, muscles of the diaphragm, and partly the abdominal wall muscles. The so-called accessory respiratory muscles (mm. sternocleidomastoideus, trapezius, pectoralis major et minor, etc.) are actively involved in the respiratory movements in pathological conditions associated with difficult breathing.

The type, frequency, depth and rhythm of respiration can be determined by carefully observing the chest and the abdomen. Respiration can be costal (thoracic), abdominal, or mixed type.

Thoracic (costal) respiration (Fig. 10a). Respiratory movements are carried out mainly by the contraction of the intercostal muscles. The chest markedly broadens and slightly rises during inspiration, while during expiration it narrows and slightly lowers. This type of breathing is known as costal and is mostly characteristic of women.

Abdominal respiration. Breathing is mainly accomplished by the diaphragmatic muscles; during the inspiration phase the diaphragm contracts and lowers to increase rarefaction in the chest and to suck in air into the lungs. The intra-abdominal pressure increases accordingly to displace anteriorly the abdominal wall. During expiration the muscles are relaxed, the diaphragm rises, and the abdominal wall returns to the initial position. This type of respiration is also called diaphragmatic (Fig. 106) and is mostly characteristic of men.

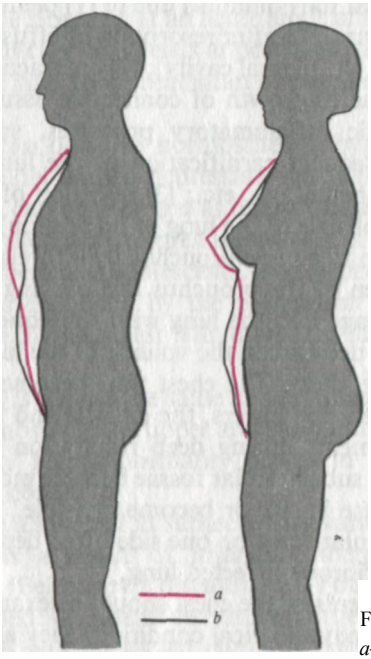


Fig. 10. Types of respiration. *a*—thoracic; *b*—abdominal.

Mixed respiration. The respiratory movements are carried out simultaneously by the diaphragm and the intercostal muscles. In physiological conditions this respiration sometimes occurs in aged persons and in some pathological conditions of the respiratory apparatus and the abdominal viscera. For example, in women with dry pleurisy, pleural adhesion, myositis, and thoracic radiculitis, the contractile activity of the intercostal muscles decreases and the respiratory movements are carried out by the accessory movements of the diaphragm. In extensive pleural adhesion, lung emphysema, and in strong pain in the chest due to acute inflammation of the intercostal muscles or nerves, respiration is temporarily carried out by the diaphragmatic muscles exclusively. Mixed respiration occurs in men with underdeveloped diaphragmatic muscles, in diaphragmatitis, acute cholecystitis, perforating ulcer of the stomach or the duodenum. Respiration in such cases is sometimes carried out only by the intercostal muscles.

Respiration rate. Respiration rate can be determined by counting the movements of the chest or the abdominal wall, with the patient being unaware of the procedure. The pulse rate should first be taken and then the respiration rate. The number of respiratory movements in a healthy adult at rest should be 16 to 20 per minute, in the newborn 40-45, this rate gradually decreasing with age. The respiration rate decreases during sleep to 12-14 per minute, while under physical load, emotional excitement, or after heavy meals the respiration rate increases.

The respiration rate alters markedly in some pathological conditions. The causes of accelerated respiration may be (1) narrowing of the lumen of small bronchi due to spasms or diffuse inflammation of their mucosa (bronchiolitis occurring mostly in children), which interfere with normal passage of air into the alveoli; (2) decreased respiratory surface of the lungs due to their inflammation and tuberculosis, in collapse or atelectasis of the lung due to its compression (pleurisy with effusion, hydrothorax, pneumothorax, tumour of mediastinum), in obturation or compression of the main bronchus by a tumour, in thrombosis or embolism of the pulmonary artery, in pronounced emphysema, when the lung is overfilled with blood or in a case of lung oedema in certain cardiovascular diseases; (3) insufficient depth of breathing (superficial respiration) which can be due to difficult contractions of the intercostal muscles or the diaphragm in acute pain (dry pleurisy, acute myositis, intercostal neuralgia, rib fracture, or tumour metastasis into the ribs), in a sharp increase in the intra-abdominal pressure and high diaphragm (ascites, meteorism, late pregnancy), and finally in hysteria.

Pathological deceleration of respiration occurs in functional inhibition of the respiratory centre and its decreased excitability. It can be due to increased intracranial pressure in patients with cerebral tumour, meningitis,

cerebral haemorrhage, or oedema of the brain, and also due to the toxic effect on the respiratory centre when toxic substances are accumulated in the blood, e.g. in uraemia, hepatic or diabetic coma, and in certain acute infectious diseases.

Respiration depth. The depth of breathing is determined by the volume of the inhaled and exhaled air at rest. This volume varies in an adult from 300 to 900 ml (500 ml on the average). Depending on depth, breathing can be either deep or superficial. Superficial (shallow) breathing often occurs in pathologically accelerated respiration when the length of the inspiration and the expiration phases becomes short. Deep breathing is, on the contrary, associated in most cases with pathological deceleration of the respiration rate. Deep and slow respiration, with marked respiratory movements, is sometimes attended by noisy sounds. This is *Kussmaul's respiration* (Fig. 11) occurring in deep coma. In some pathological conditions, however, rare respiration can be shallow, while accelerated breathing deep. Rare superficial respiration can occur in sharp inhibition of the respiratory centre, pronounced lung emphysema, and sharp narrowing of the vocal slit or the trachea. Respiration becomes accelerated and deep in high fever and marked anaemia.

Respiration rhythm. Respiration of a healthy person is rhythmic, of uniform depth and equal length of the inspiration and expiration phases. Rhythm of the respiratory centre can be inhibited in some types of oedema. Derangement of the respiratory function can cause oedema in which a series of respiratory movements alternates with a pronounced (readily detectable) elongation of the respiratory pause (lasting from a few seconds to a minute) or a temporary arrest of respiration (apnoea). This respiration is known as periodic.

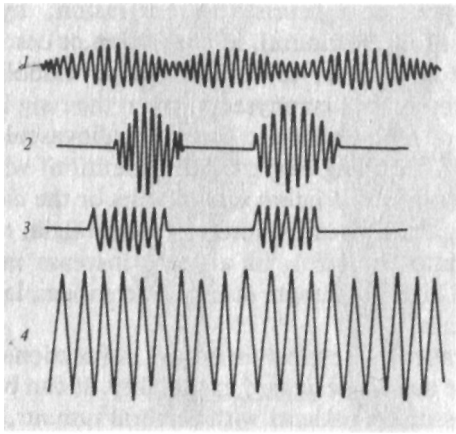


Fig. 11. Spirograms in pathological respiration. *a*—Grocco's respiration; *b*—Cheyne-Stokes' respiration; *3*—Biot's respiration; *4*—Kussmaul's respiration.

Biot's respiration is characterized by rhythmic but deep respiratory movements which alternate (at approximately regular intervals) with long respiratory pauses (from few seconds to half a minute). Biot's respiration occurs in meningitis patients and in agony with disorders of cerebral circulation.

Cheyne-Stokes' respiration is characterized by periods (from few seconds to a minute) of cessation of respiration, followed by noiseless shallow respiration, which quickly deepens, becomes noisy to attain its maximum at the 5-7th inhalation, and then gradually slows down to end with a new short respiratory pause. During such pauses, the patient often loses his sense of orientation in the surroundings or even faints, to recover from the unconscious condition after respiratory movements are restored. This respiratory disorder occurs in diseases causing acute or chronic insufficiency of cerebral circulation and brain hypoxia, and also in heavy poisoning. More frequently this condition develops during sleep and is more characteristic of aged persons with marked atherosclerosis of the cerebral arteries.

Undulant (wave-like) Grocco's respiration somewhat resembles Cheyne-Stokes' respiration except that a weak shallow respiration occurs instead of the respiratory pause with subsequent deepening of the respiratory movement, followed by slowing down. This type of arrhythmic dyspnoea can probably be regarded as the early stages of the same pathological processes which are responsible for Cheyne-Stokes respiration.

PALPATION

Palpation is used as an additional means of examination to verify findings of observation (the shape of the chest, its dimensions, respiratory movements), for determining local or profuse tenderness of the chest, its elasticity (resilience), vocal fremitus, pleural friction and sounds of fluid in the pleural cavity.

Palpation should be done by placing the palms on the symmetrical (left and right) parts of the chest. This examination helps follow the respiratory excursions and deviation of the chest movements from their normal course. The epigastric angle is determined by palpation as well. The thumbs should be pressed tightly against the costal arch, their tips resting against the xiphoid process (ensiform cartilage).

Palpation is used to locate pain in the chest and its irradiation. For example, in rib fracture, pain is localized over a limited site, namely at the point of the fracture. Displacement (careful!) of bone fractures will be attended in this case by a specific sound (crunch). Inflammation of the inter-

costal nerves and muscles also causes pain, but it can be felt during palpation over the entire intercostal space. Such pain is called superficial. It is intensified during deep breathing, when the patient bends to the affected side, or lies on this side.

Resilience or elasticity of the chest is determined by exerting pressure of the examining hands from the front to the sides of the chest or on the back and the sternum, and also by palpation of the intercostal spaces. The chest of a healthy person is elastic, plaint and yields under the pressure. In the presence of pleurisy with effusion, or pleural tumour, the intercostal space over the affected site becomes rigid. Rigidity of the chest increases in general in the aged due to ossification of the costal cartilages, development of the lung emphysema, and also with filling of both pleural cavities with fluid. Increased resistance of the chest can then be felt during examining the chest by compression in both the anteroposterior and lateral directions.

Palpation is used for determining the strength of voice conduction to the chest surface *(fremitus vocalis s. pectoralis)*. The palms of the hands are placed on the symmetrical parts of the chest and the patient is asked to utter loudly a few words (with the letter 'r' in them to intensify vibration). The voice should be as low as possible since voice vibrations are better transmitted by the air column in the trachea and the bronchi to the chest wall in this case. Fremitus vocalis can also be determined by one hand as well: the palm of the examining hand should be placed alternately on the symmetrical parts of the chest.

Vocal fremitus is of about the same intensity in the symmetrical parts of the chest of a healthy person. Vocal vibrations are louder in the upper parts of the chest and softer in its lower parts. Moreover, voice conduction is better in men with low voice and thin chest; the vibrations are weaker in women and children with higher voice (and also in persons with the well developed subcutaneous fat tissues). Vocal fremitus can be stronger or weaker (or in some cases it can even be impalpable) in pathological conditions of the respiratory organs. In focal affections, vocal fremitus becomes unequal over symmetrical parts of the chest.

Vocal fremitus is intensified when a part of the lung or its whole lobe becomes airless and more uniform (dense) because of a pathological process. According to the laws of physics, dense and uniform bodies conduct sound better than loose and non-uniform. Induration (consolidation) can be due to various causes, such as acute lobar pneumonia, pulmonary infarction, tuberculosis, accumulation of air or fluid in the pleural cavity, etc. Vocal fremitus is also intensified in the presence in the pulmonary tissue of an air cavity communicated with the bronchus.

Vocal fremitus becomes weaker (1) when liquid or gas are accumulated in the pleural cavity; they separate the lung from the chest wall to absorb

voice vibrations propagating from the vocal slit along the bronchial tree; (2) in complete obstruction of the bronchial lumen by a tumour which interferes with normal conduction of sound waves to the chest wall; (3) in asthenic emaciated patients (with weak voice); (4) in significant thickening of the chest wall in obesity.

Low-frequency vibrations due to pleural friction (friction fremitus) in dry pleurisy, crepitation sounds characteristic of subcutaneous emphysema of the lungs, vibration of the chest in dry, low (low-pitch buzzing) rales can also be determined by palpation.

PERCUSSION

Depending on the object of examination, various methods of percussion are used to examine the lungs. The examination begins with comparative percussion.

Comparative percussion. A certain sequence is followed in comparative percussion. Percussion sounds over the lung apices (in the front) on the symmetrical points of the chest are first compared; the pleximeter finger is placed parallel to the clavicle. The plexor finger is then used to strike the clavicle which is used as a pleximeter in this case. During percussion of the lungs below the clavicle, the pleximeter finger is placed in the interspace at the strictly symmetrical points of the left and right sides of the chest. The percussion sounds are compared only to the level of the 4th rib along the medioclavicular line (and medially). The heart lying below this level changes the percussion sound. For comparative percussion of the axillary region, the patient should raise his arms and clamp the hands at the back of the head. Comparative percussion of the lungs on the back begins with suprascapular areas. The pleximeter finger is placed horizontally, while during percussion of the regions between the scapulae, the pleximeter should be vertical. The patient should cross his arms on the chest to displace the scapulae anteriorly (away from the backbone). During percussion of the points lying below the scapulae, the pleximeter should again be horizontal; in the interspace it should be placed parallel to the ribs (Fig. 12a and *b)*.

Percussion sounds of the lungs of a healthy person cannot be of equal strength, length or pitch even if the percussion blows are uniform at symmetrical points. This depends on the mass and thickness of the pulmonary layer and also on the influence of the adjacent organs on the percussion sound. It is softer and shorter (1) over the right upper lobe because it is located somewhat below the left (due to the shorter right upper bronchus) and also because of the better development of the muscles of the apt side of the shoulder girdle; (2) in the second and third interspace on the left,

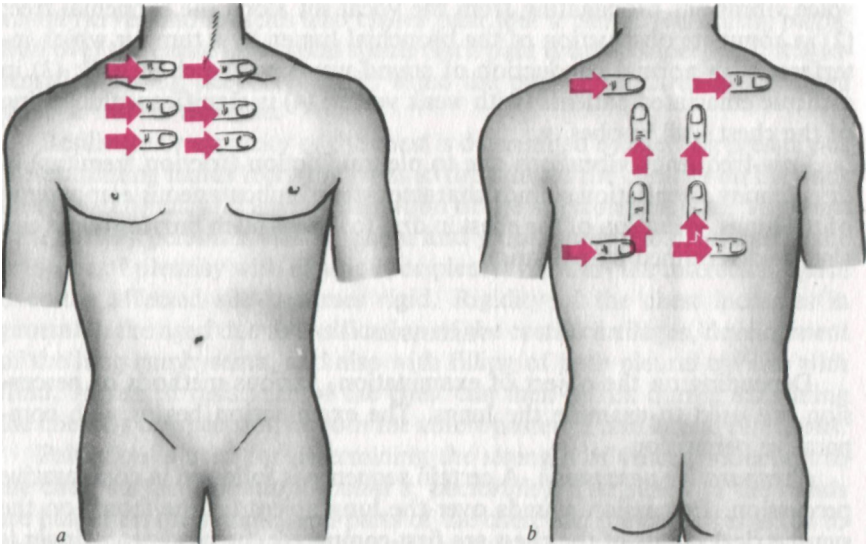


Fig. 12. Comparative percussion on the anterior (a) and posterior *(b)* surfaces of the chest.

because of the closer location of the heart; (3) over the upper lobes of the lung (compared with the lower lobes) because of the varying thickness of pneumatic pulmonary tissue; (4) in the right axillary region (compared with the left one) because of the closer location of the liver. The difference in percussion sounds here depends on the fact that the diaphragm and the lung border on the left with the stomach whose bottom is filled with air and gives a loud tympanic sound during percussion (Traube's semilunar space). The percussion sound in the left axillary region is therefore louder and higher (with tympanic character) because of the resonant effect ('air bladder') of the stomach.

The percussion sound can change in pathological processes because of the decreased content or full absence of air in a part of the lung, and because of the pleural fluid (transudate, effusion, blood), increased airiness of the lung tissue, and the presence of air in the pleural cavity (pneumothorax).

The amount of air in the lungs decreases in (1) pneumosclerosis, fibrous-focal tuberculosis, (2) pleural adhesion or obliteration of the pleural cavity which interferes with normal distention of the lung during inspiration; the difference in the percussion sound will be more pronounced at the inspiration level and weaker during the expiration; (3) lobular and especially confluent pneumonia, in which pulmonary tissue alternates with consolidations; (4) considerable oedema of the lungs, especially in the in-

feriolateral regions due to insufficient contractility of the left ventricle; (5) compression of the pulmonary tissue by the pleural fluid (compression atelectasis) above the fluid level; (6) complete obstruction of the large bronchus with a tumour and gradual resorption of air from the lungs below the closure of the lumen (obstructive atelectasis). Clear pulmonary sounds become shorter and higher (i.e. duller) in the mentioned pathological conditions. If these conditions are attended by decreased tension in the elastic elements of the pulmonary tissue, e.g. in the presence of compression or obstructive atelectasis, the sound over the atelectatic zone becomes dull with a tympanic tone. This sound can also be heard during percussion of a patient with acute lobar pneumonia at its first stage, when the alveoli of the affected lobe, in addition to air, contain also a small amount of fluid.

A complete absence of air in the entire lobe of the lung or its part (segment) is observed in the following cases: (a) acute lobar pneumonia at the consolidation stage, when the alveoli are filled with the inflammatory exudate containing fibrin; (b) formation in the lung of a large cavity, which is filled with the inflammatory fluid (sputum, pus, echinococcous acid, etc.), or heterogeneous airless tissue (tumour); (c) accumulation of fluid in the pleural cavity (transudate, exudate, blood). Percussion over airless parts of the lung or over fluid accumulated in the pleural cavity gives a soft short and high sound which is called dull or, by analogy with the percussion sounds of airless organs and tissues (liver, muscles), liver dullness. But the absolute dullness identical to the percussion sound of the liver can only be heard in the presence of a large amount of fluid in the pleural cavity.

The amount of air in the lung increases in emphysema. The percussion sound in lung emphysema is louder than the dull tympanic sound because of the increased airiness of the pulmonary tissue and decreased elasticity of the tense pulmonary tissues; but the tympanic character is preserved. The percussion sound resembles the one produced by a stroke on a box; hence the name bandbox sound.

The amount of air held inside the lung increases with formation in it of a smooth-wall cavity filled with air and communicated with the bronchus (abscess, tuberculotic cavern). The percussion sound over this area will be tympanic. If the cavity is small and situated deeply in the chest, vibrations of the pulmonary tissue will not reach this cavity and no tympanic sound will be heard. Such a cavity will only be revealed by roentgenoscopy. The sound over a very large smooth-wall cavity in the lung (6-8 cm in diameter) will be tympanic, resembling a stroke on a metal (metallic percussion sound). If this cavity is located superficially and is communicated with the bronchus through a narrow slit, the percussion sound will be soft and will resemble that of a cracked pot (hence the name—cracked-pot sound).

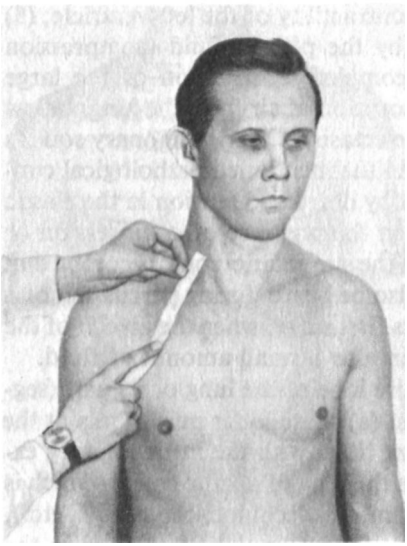


Fig. 13. Determining the superior border of the lung on the anterior surface of the chest.

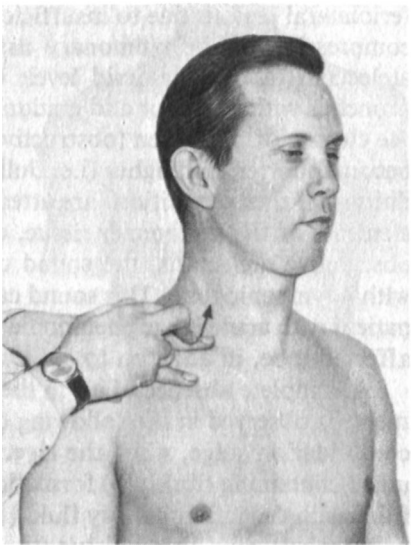


Fig. 14. Determining the position of the lung apex over the clavicle.

Topographic percussion. Topographic percussion is used for determining (1) the upper borders of the lungs or the upper level of their apices and their width (Kroenig's area); (2) the lower borders of the lungs, and (3) variation mobility of the lower border of the lung.

The position of the *upper borders* (apices) of the lungs is determined both anteriorly and posteriorly. In order to locate the apex of the lung, the plexímeter finger is placed parallel to the clavicle (Fig. 13) and percussion is effected from the middle upwards and slightly medially, to dullness. The upper level of the apices in healthy persons is 3—4 cm above the clavicles (Fig. 14). The upper posterior border of the lungs is always determined by their position with respect to the spinous process of the 7th cervical vertebra. The plexímeter finger is placed over the supraspinous fossa, parallel to the scapular spine and stroked from the middle. The plexímeter finger is moved gradually upward to the point located 3-4 cm laterally to the spinous process of the 7th cervical vertebra, at its level, and percussion is then continued until dullness. Normal height of the lung apices (posterior) is about at the level of the spinous process of the 7th cervical vertebra.

The so-called *Kroenig's area* is a band of clear resonance over the lung apices. The width of these areas is determined by the low anterior border of the trapezius muscle and is (on an average) 5—6 cm wide, but its width can vary from 3 to 8 cm. The anterior border of the trapezius muscle divides

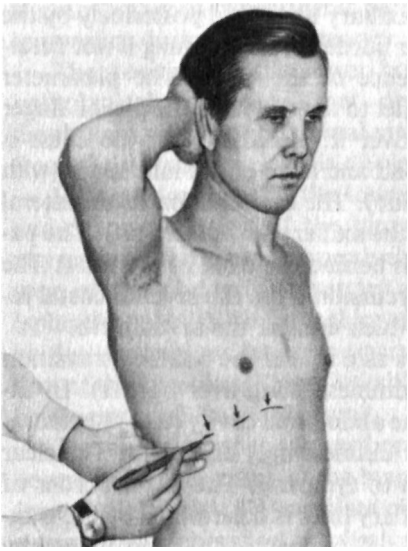


Fig. 15. Determining the inferior border of the lung in the right parasternal, midclavicular, and anterior axillary line.

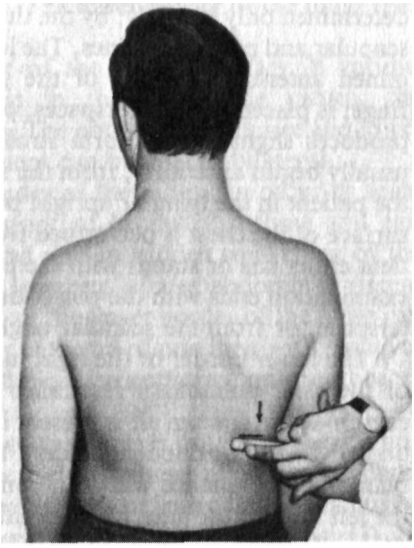


Fig. 16. Determining the inferior border of the lung in the scapular line.

the Kroenig area into its anterior field which extends to the clavicle, and the posterior one that widens toward the supraspinous fossa. Light or subliminal percussion is used to determine the width of the lung apex. The pleximeter finger is held over the middle portion of m. trapezius, perpendicular to its anterior margin, and percussion is first carried out medially, and then laterally, to dullness. The distance between the points of transition of the clear pulmonary resonance to dullness is measured in centimetres.

The upper border of the lungs and the width of the Kroenig area can vary depending on the amount of air in the apices. If the amount of air is high (which may be due to emphysema) the apices increase in size and move upwards. The Kroenig area widens accordingly. The presence of connective tissue in the lung apex (which usually develops during inflammation as in tuberculosis or pneumonia or inflammatory infiltration) decreases the airiness of the pulmonary tissue. The upper border of the lung thus lowers and the width of the Kroenig area decreases.

To outline the *lower borders* of the lungs their percussion is carried out in the downward direction along conventional vertical topographical lines. The lower border of the right lung is first determined anteriorly along the parasternal and the medioclavicular lines, then laterally along the anterior, medial and posterior axillary lines (Fig. 15), and posteriorly along the scapular and paraspinal lines (Fig. 16). The lower border of the left lung is

determined only laterally, by the three axillary lines, and posteriorly by the scapular and paraspinal lines. The lower border of the left lung is not determined anteriorly because of the presence of the heart. The pleximeter finger is placed in the interspaces, parallel to the ribs, and the plexor finger produces slight and uniform strokes over it. Percussion of the chest is usually begun anteriorly, from the second and third costal interspace (with the patient in the lying or upright position). The examination of the lateral surface of the chest is performed from the axillary fossa (arm pit). The patient either sits or stands with the hands behind the back of the head. The examination ends with the posterior percussion from the seventh costal interspace, or from the scapular angle, which ends at the seventh rib.

The lower border of the right lung is as a rule at the point of transition of the clear pulmonary resonance to dullness (lung-liver border). In exceptional cases, when air is present in the abdominal cavity (e.g. in perforation of gastric or duodenal ulcer), liver dullness may disappear. The clear pulmonary resonance will then convert to tympany. The lower border of the left lung by the anterior and midaxillary lines is determined by the transition of clear pulmonary resonance to dull tympany. This is explained by the contact between the lower surface of the lung (through the diaphragm) and a small airless organ, such as the spleen and the fundus of the stomach, which give tympany (Traube's space).

Table 1

Normal Lower Border of the Lungs

Percussion point	Right lung	Left lung
Parasternal line	5th costal interspace	
Midclavicular line	6th rib	—
Anterior axillary line	7th rib	7th rib
Midaxillary line	8th rib	8th rib
Posterior axillary line	9th rib	9th rib
Scapular line	10th rib	10th rib
Paraspinal line	Spinous process of 11th thoracic vertebra	Spinous process of 11th thoracic vertebra

The lower borders of the lungs in normosthenic persons usually occur as given in Table 1. The position of the border varies depending on the constitutional properties of the body. The lower border of the lungs in asthenic persons is slightly lower than in normosthenics and is found at the interspace (rather than on the rib as in normosthenics) whereas this border is

slightly higher in hypersthenic persons. The lower border of the lungs rises temporary during late pregnancy.

The position of the lower border of the lungs can vary in various pathological conditions that develop in the lungs, the pleura, the diaphragm, and the abdominal viscera. The border can both rise and lower from the normal level. This displacement can be uni- or bilateral.

Bilateral lowering of the lower border of the lungs can occur in acute and chronic dilation of the lungs (attack of bronchial asthma and emphysema of the lungs, respectively) and also in sudden weakening of the tone of the abdominal muscles and lowering of the abdominal viscera (splanchnoptosis). Unilateral lowering of the lower border of the lungs can be due to vicarious (compensatory) emphysema of one lung with inactivation of the other lung (pleurisy with effusion, hydrothorax, pneumothorax, hemiparesis of the diaphragm).

The elevation of the lower border of the lungs is usually unilateral and occurs in (1) shrivelling of the lung due to development of connective tissue (pneumosclerosis); (2) complete obstruction of the lower-lobe bronchus by a tumour which causes gradual collapse of the lung, atelectasis; (3) accumulation of fluid or air in the pleural cavity which displace the lung upwards and medially toward the root; (4) marked enlargement of the liver (cancer, echinococcosis), or of the spleen (chronic myeloleukaemia). Bilateral elevation of the lower borders of the lungs occurs in the presence of large amounts of fluid (ascites) or air in the abdomen due to an acute perforation of gastric or duodenal ulcer, and also in acute meteorism.

After determining the lower border of the lungs at rest, *respiratory mobility of pulmonary borders* should be determined by percussion during forced inspiration and expiration. This mobility is called active, and is usually measured by the difference in the position of the lower border of the lungs between the two extremes. Measurements are done by three lines on the right side (midclavicular, axillary, and scapular lines) and two lines on the left side (midaxillary and scapular lines). The normal variation of the lower border of the lungs is described by the figures given in Table 2. Mobility of the lower border of the left lung by the midclavicular line cannot be determined because of the interference of the heart.

The respiratory mobility of the lungs is determined as follows. The lower border of the lungs in normal respiration is first determined and marked by a dermograph. The patient is then asked to make a forced inspiration and to keep breath at the height. The pleximeter finger should at this moment be held at the lower border of the lung (determined earlier). Percussion is now continued by moving the pleximeter downwards to complete dullness, where the second mark should be made by a dermograph at the upper edge of the pleximeter finger. The patient is then asked to exhale

Table 2

Respiratory Mobility of the Lower Border of Normal Lungs

Topographic line	Mobility of the lower border of the lung, in cm					
	right lung			left lung		
	inhalation	exhalation	total	inhalation	exhalation	total
Midclavicular line	2-3	2-3	4-6			
Midaxillary line	3-4	3-4	6-8	3-4	3-4	6-8
Scapular line	2-3	2-3	4-6	2-3	2-3	**4-6**

maximum air from the lungs and to keep breath again. The percussion is now continued in the upward direction until the clear vesicular resonance appears. The third dermographic mark should be made at the point where relative dullness is heard. The distance between the extreme marks is measured (Fig. 17). It corresponds to the maximum respiratory mobility.

The patient in a grave condition is unable to keep breath and another method is recommended to determine the respiratory mobility of the lungs.

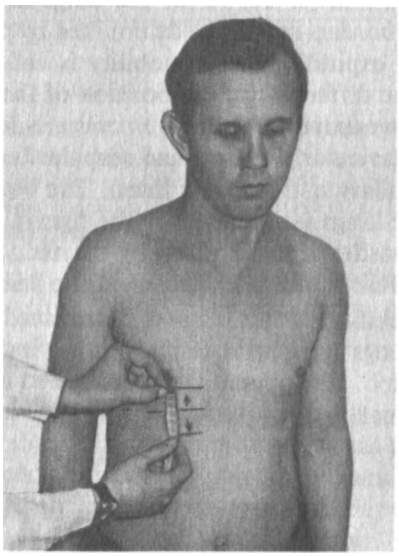


Fig. 17. Determining the mobility of the lower lung border in the midclavicular line.

After marking the lower border of the lung in quiet breathing, the patient is asked to make deep inhalations and exhalations without keeping breath. Percussion should be continuous during deep breathing and the pleximeter finger should gradually move downwards. First the percussion sound is loud and low during inhalation and soft and high during exhalation. Soon a point is attained where the sounds become of the same pitch and strength during both inhalation and exhalation. This point is the lower border of the lung at forced inspiration. The lower border at forced exhalation is determined in the same way.

Respiratory mobility of the lower border of the lungs is diminished in inflammatory infiltration or congestive plethora of the lungs, decreased elasticity of the pulmonary tissue (emphysema), profuse pleural effusion, and in pleural adhesion or obliteration.

The so-called passive respiratory mobility is determined in some diseases. This is the mobility of the lung borders during changes in the posture. When the patient changes his posture from the upright to horizontal one, the lower border of the lungs descends some 2 cm, while the lower border of the right lung of a patient lying on his left side may lower 3-4 cm. In pathological conditions, e.g. in pleural adhesion, the variation of the lower border of the lungs is markedly limited.

AUSCULTATION

Like percussion, auscultation of the lungs should be carried out according to a plan. Stethoscope or phonendoscope should be placed in strictly symmetrical points of the right and left sides of the chest (Fig. 18). Auscultation begins with the anterior wall of the chest, from its upper part, in the supra- and subclavicular regions, and then the stethoscope should be moved downward and laterally. The lungs are then auscultated in the same order from the posterior wall of the chest and in the axillary regions. In order to increase the area of auscultation between the scapulae, the patient should be asked to cross his arms on the chest and in this way to displace his shoulder-blades laterally from the spine, while for convenience of auscultation of the axillary regions he should place his hands on the back of the head.

The posture does not matter, but the patient should better sit up on a stool with his hands on the laps. The patient may stand, but the physician should remember that deep breathing (hyperventilation of the lungs) may cause vertigo and the patient may faint. Bearing this in mind, and also to ensure a tight contact between the stethoscope and the skin (especially if a one-piece stethoscope is used) the physician should always use his free hand to support the patient on the side opposite to the point of application of the stethoscope bell.

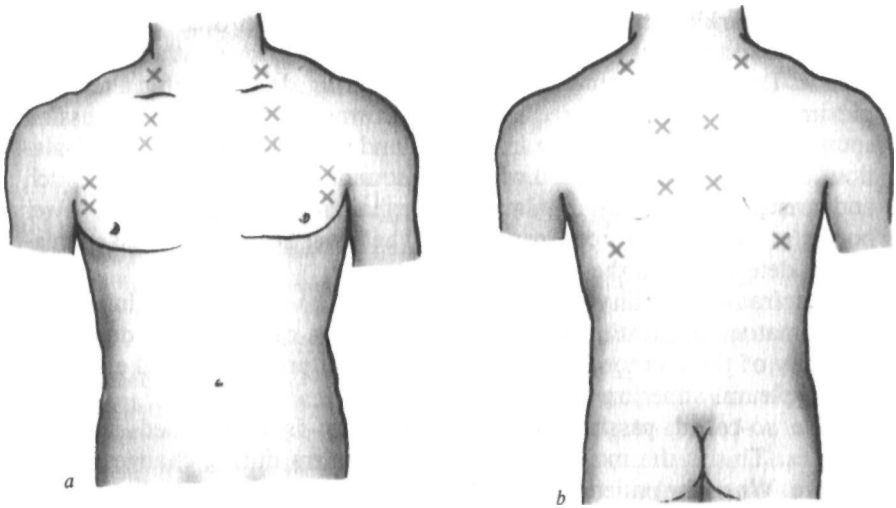


Fig. 18. Lung listening points,
anterior (a) and posterior *(b)* surface of the chest.

Respiratory murmurs (breath sounds) during various phases of respiration are first compared during auscultation of the lungs as well as their character, length, and intensity (loudness). Then these sounds are compared with the respiratory murmurs at the symmetrical points of the other half of the chest (comparative auscultation). Attention should be paid to the *main respiratory sounds,* such as vesicular (alveolar) breathing which is heard over the pulmonary tissues, and bronchial (laryngotracheal) breathing which is heard over the larynx, trachea, and large bronchi.

In the presence of pathology in the air ways, in the alveolar tissue or in the pleura, adventitious sounds such as rales, crepitation, and pleural friction, are heard in addition to the main breath sounds during inspiration and expiration. These adventitious sounds should be examined only after the character of the main sounds has been established. Normal breathing sounds should be better auscultated with the nasal breathing (with the patient's mouth closed) while adventitious sounds are better heard with deep respiration through the open mouth.

Vesicular breathing. Respiratory sounds known as vesicular breathing arise due to vibration of the elastic elements of the alveolar walls during their filling with air in inspiration. The alveoli are filled with air in sequence. Therefore, the summation of the great number of sounds produced during vibration of the alveolar walls gives a long soft (blowing) noise that can be heard during the entire inspiration phase, its intensity

gradually increasing. This sound can be simulated by pronouncing the sound T during inspiration, or by drawing tea from a saucer. Alveolar walls still vibrate at the initial expiration phase to give a shorter second phase of the vesicular breathing, which is heard only during the first third of the expiration phase (Fig. 19a), because vibrations of elastic alveolar walls are quickly dampened by the decreasing tension of the alveolar walls.

Normal vesicular breathing is better heard over the anterior surface of the chest, below the 2nd rib, laterally of the parasternal line, and also in the axillary regions and below the scapular angle, i.e. at points where the largest masses of the pulmonary tissue are located. Vesicular breathing is heard worse at the apices of the lungs and their lowermost parts, where the masses of the pulmonary tissue are less abundant. While carrying out comparative auscultation, it should be remembered that the expiration sounds are louder and longer in the right lung due to a better conduction of the laryngeal sounds by the right main bronchus, which is shorter and wider. The respiratory sound sometimes becomes bronchovesicular over the right apex; or it may be mixed due to more superficial and horizontal position of the right apical bronchus.

Alterations in vesicular breathing. Vesicular breathing can vary, i.e. it may be louder or softer for both physiological and pathological reasons.

Physiological weakening of vesicular breathing (Fig. *19b)* occurs in patients with thicker chest wall due to excessively developed muscles or subcutaneous fat. *Physiological intensification* of vesicular breathing (Fig. 19c) may be observed in patients with underdeveloped muscles or subcutaneous fat. Intensified vesicular breathing is characteristic of children with a thin chest wall, good elasticity of the alveoli and the in-

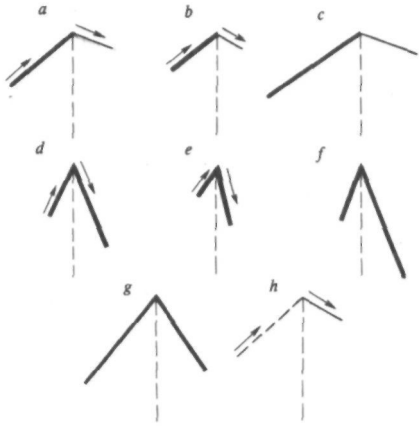


Fig. 19. Types of respiration.

a—vesicular; *b*—decreased vesicular; *c*—increased vesicular; *d*—bronchial; *e*—decreased bronchial; /—increased bronchial; *g*—bronchovesicular; *h*—cogwheel.

teralveolar septa. This respiration is called 'puerile respiration' (L *puer* child). Vesicular respiration is intensified during exercise; respiratory movements become deeper and more frequent. Physiological changes in vesicular respiration always involve both parts of the chest, and respiratory sounds are equally intensified or weakened at the symmetrical points of the chest.

In pathology, alterations in vesicular breathing may be both uni- and bilateral, or else only over one lobe of the lung. Respiratory sounds become weaker or inaudible at all; or they may be intensified. Alterations in vesicular respiration in such cases depend on the amount of intact alveoli and the properties of their walls, the amount of air contained in them, on the length and strength of the expiration and inspiration phases, and finally on the conditions of sound conduction from the vibrating elastic elements of the pulmonary tissue to the surface of the chest.

Pathologically decreased vesicular respiration can be due to a significantly diminished number of the alveoli because of atrophy and gradual degradation of the interalveolar septa and formation of larger vesicles incapable of collapsing during expiration. This pathological condition is observed in pulmonary emphysema, at which the remaining alveoli are no longer elastic; their walls become incapable of quick distention and do not give sufficiently strong vibrations.

Decreased vesicular breathing can be due to inflammation and swelling of the walls in a part of the lung and decreased amplitude of their vibration during inspiration, which is characteristic of early acute lobar pneumonia. During the second stage of this disease, the alveoli of the affected part of the lung become filled with effusion and vesicular breathing becomes inaudible over this region. Vesicular breathing can be decreased also in insufficient delivery of air to the alveoli through the air ways because of their mechanical obstruction (e.g. by a tumour). Air admission to the alveoli can be decreased in patients with a markedly weakened inspiration phase (as a result of inflammation of the respiratory muscles, intercostal nerves, rib fracture, extreme asthenia of the patient and adynamia).

Vesicular respiration decreases also due to obstructed conduction of sound waves from the source of vibration (alveolar walls) to the chest surface, as, for example, in thickening of the pleural layers or accumulation of air or fluid in the pleural cavity. If the amount of fluid or air in the pleural cavity is great, respiratory sounds are not heard. Conduction of sound to the surface of the chest may be absent in atelectasis of the lung due to complete obstruction of the lumen in the large bronchus.

Abnormally increased vesicular breathing (Fig. 19c) can be heard during expiration or during both respiratory phases. Increased expiration depends on obstruction to the air passage through small bronchi or their

contracted lumen (inflammatory oedema of the mucosa, bronchospasm). Expiration becomes louder and longer.

Deeper vesicular breathing during which the inspiration and expiration phases are intensified, is called *harsh.* It occurs in marked and non-uniform narrowing of the lumen in small bronchi and bronchioles due to inflammatory oedema of their mucosa (bronchitis).

Another type of pathological respiration is interrupted or *cogwheel respiration.* This vesicular respiration is characterized by short jerky inspiration efforts interrupted by short pauses between them; the expiration is usually normal. Interrupted breathing also occurs in non-uniform contraction of the respiratory muscles, e.g. when a patient is auscultated in a cold room, or when he has nervous trembling, or diseases of the respiratory muscles, etc. Interrupted breathing over a limited part of the lung indicates difficult passage of air from small bronchi to the alveoli in this region and uneven unfolding of the alveoli. Interrupted breathing indicates pathology in fine bronchi and is more frequently heard at the apices of the lungs during their tuberculous infiltration.

Bronchial breathing. Respiratory sounds known as bronchial or tubular breathing (Fig. *I9d)* arise in the larynx and the trachea as air passes through the vocal slit. As air is inhaled, it passes through the vocal slit to enter wider trachea where it is set in vortex-type motion. Sound waves thus generated propagate along the air column throughout the entire bronchial tree. Sounds generated by the vibration of these waves are harsh. During expiration, air also passes through the vocal slit to enter a wider space of the larynx where it is set in a vortex motion. But since the vocal slit is narrower during expiration, the respiratory sound becomes louder, harsher and longer. This type of breathing is called laryngotracheal (by the site of its generation).

Bronchial breathing is well heard in physiological cases over the larynx, the trachea, and at points of projection of the tracheal bifurcation (anteriorly, over the manubrium sterni, at the point of its junction with the sternum, and posteriorly in the interscapular space, at the level of the 3rd and 4th thoracic vertebrae). Bronchial breathing is not heard over the other parts of the chest because of large masses of the pulmonary tissue found between the bronchi and the chest wall.

Bronchial breathing can be heard instead of vesicular (or in addition to the vesicular breathing) over the chest in pulmonary pathology. This breathing is called *pathological bronchial respiration.* It is conducted to the surface of the chest wall only under certain conditions, the main one being induration of the pulmonary tissue when the alveoli are filled with effusion (acute lobar pneumonia, tuberculosis, etc.), with blood (lung infarction), or due to compression of the alveoli by air or fluids accumulated in the

pleural cavity, and compression of the lung against its root (compression atelectasis). In such cases the alveolar walls do not vibrate, while consolidated airless pulmonary tissue becomes a good conductor of sound waves in laryngotracheal respiration to the surface of the chest wall. Lungs may be consolidated due to replacement of the inflated pulmonary tissue by connective tissue (pneumosclerosis, carnification of the lung lobe, which sometimes occurs in acute lobar pneumonia due to growth of connective tissue into the inflamed lobe of the lung, etc.).

Depending on degree of induration, its size and location in the lung, pathological bronchial breathing may have different intensity and pitch. If the induration is large and superficial, loud bronchial breathing is heard. It is heard as if near the ear; the pitch of the sound is higher in this case (Fig. 19f). Bronchial breathing can be heard in acute lobar pneumonia at its second stage (affection of the entire lobe of the lung). If a segment of a lung is indurated, and the affection is deep seated, breathing will be weaker and the pitch lower (Fig. 19e). This sound can be heard in lobular pneumonia if several foci are close to one another or fuse together to form a large focus of induration (confluent pneumonia). Especially soft and low sounds are heard in patients with compression atelectasis. The sound resembles an echo, as if entering the physician's ear from a far off source.

Pathological bronchial respiration can be heard if an empty cavity is formed in the lung (abscess, cavern) and it is communicated with the bronchus. Consolidation of pulmonary tissue round the focus facilitates conduction of sound waves of laryngotracheal breathing to the surface of the chest wall, the more so that the sound is intensified in the resonant cavity and that at the moment of air passage from the narrow bronchus the air is set in a vortex motion.

Amphoric respiration arises in the presence of a smooth-wall cavity (not less than 5-6 cm in diameter) communicated with a large bronchus. Because of a strong resonance, additional high overtones appear along with the main low-pitch laryngotracheal breathing. These overtones alter the main tone of the bronchial respiratory sound. Sounds of this kind can be produced by blowing over the mouth of an empty glass or clay jar. This altered bronchial breathing is therefore called amphoric (Gk *amphoreus* jar).

Metallic respiration differs from both bronchial and amphoric. It is loud and high, and resembles the sound produced when a piece of metal is struck. Metallic respiration is heard in open pneumothorax when the air of the pleural cavity communicates with the external air.

Stenotic respiration is exaggerated laryngotracheal breathing, which is heard in cases with narrowed trachea or a large bronchus (due to a tumour); it is heard mainly at points where physiological bronchial breathing is normally heard.

Bronchovesicular or *mixed respiration* is heard in lobular pneumonia or infiltrative tuberculosis, and also in pneumosclerosis, with foci of consolidated tissue being seated deeply in the pulmonary tissue and far from one another. Mixed breathing, when the inspiration phase is characteristic of vesicular breathing and the expiration phase of bronchial breathing, is often heard in such cases instead of weak bronchial breathing.

Adventitious sounds are rales, crepitation, and pleural friction.

Rales arise in pathology of the trachea, bronchi, or if a cavern is formed in the affected lung. Rales are classified as dry (rhonchi) and moist rales.

Dry rales, or rhonchi, may be due to various causes. The main one is constriction of the lumen in the bronchi. Constriction may be total (in bronchial asthma), non-uniform (in bronchitis), or focal (in tuberculosis or tumour of the bronchus). Dry rales can be due to (1) spasms of smooth muscles of the bronchi during fits of bronchial asthma; (2) swelling of the bronchial mucosa during its inflammation; (3) accumulation of viscous sputum in the bronchi which adheres to the wall of the bronchus and narrows its lumen; (4) formation of fibrous tissue in the walls of separate bronchi and in the pulmonary tissue with subsequent alteration of their architectonics (bronchiectasis, pneumosclerosis); (5) vibration of viscous sputum in the lumen of large and medium size bronchi during inspiration and expiration: being viscous, the sputum can be drawn (by the air stream) into threads which adhere to the opposite walls of the bronchi and vibrate like strings.

Dry rales are heard during inspiration and expiration and vary greatly in their loudness, tone and pitch. According to the quality and pitch of the sounds produced, dry rales are divided into sibilant (high-pitched and whistling sounds) and sonorous rales (low-pitched and sonoring sounds). High-pitched rales are produced when the lumen of the small bronchi is narrowed, while low-pitched sonorous rales are generated in stenosis of medium calibre and large calibre bronchi or when viscous sputum is accumulated in their lumen.

Propagation and loudness of dry rales depend on the size of the affected area in the bronchial tree, on the depth of location of the affected bronchi, and the force of the respiratory movements. When the walls of a medium size and large bronchi are affected to a limited extent, rhonchi are insignificant and soft. Diffuse inflammation of the bronchi or bronchospasm arising during attacks of bronchial asthma is attended by both high-pitched sibilant and low-pitched sonorous rales which vary in tone and loudness. These rhonchi can be heard at a distance during expiration. If rhonchi are due to accumulation of viscous sputum in the bronchi, during deep breathing (or immediately after coughing) they can be either intensified or weakened, or else disappear altogether for a short time.

Moist rales are generated because of accumulation of liquid secretion (sputum, oedematous fluid, blood) in the bronchi through which air passes. Air bubbles pass through the liquid secretion of the bronchial lumen and collapse to produce the specific cracking sound. This sound can be simulated by bubbling air through water using a fine tube. Moist rales are heard during both the inspiration and expiration, but since the air velocity is higher during inspiration, moist rales will be better heard at this respiratory phase.

Depending on the calibre of bronchi where rales are generated, they are classified *as fine, medium* and *coarse bubbling* rales. Fine bubbling rales are generated in fine bronchi and are percepted by the ear as short multiple sounds. Rales originating in the finest bronchi and bronchioles are similar to crepitation from which they should be differentiated (see below). Medium bubbling rales are produced in bronchi of a medium size and coarse bubbling rales in large calibre bronchi, in large bronchiectases, and in pulmonary cavities (abscess, cavern) containing liquid secretions and communicating with the large bronchus. Large bubbling rales are characterized by a lower and louder sound.

Moist rales originating in superficially located large cavities (5-6 cm and over in diameter) may acquire a metallic character. If segmentary bronchiectases or cavities are formed in the lung, rales can usually be heard over a limited area of the chest. Chronic bronchitis or marked congestion in the lungs associated with failure of the left chambers of the heart is as a rule attended by bilateral moist rales of various calibre, which occur at the symmetrical points of the lungs.

Depending on the character of the pathology in the lungs, moist rales are subdivided into *consonating* or *crackling,* and *non-consonating* or *bubbling* rales. Consonating moist rales are heard in the presence of liquid secretions in the bronchi surrounded by airless (consolidated) pulmonary tissue or in lung cavities with smooth walls surrounded by consolidated pulmonary tissue. The cavity itself acts as a resonator to intensify moist rales. Moist consonating rales are heard as if just outside the ear. Consonating rales in the lower portions of the lungs suggest inflammation of the pulmonary tissue surrounding the bronchi. Consonating rales heard in the subclavicular or subscapular regions indicate tuberculous infiltration or cavern in the lung.

Non-consonating rales are heard in inflammation of bronchial mucosa (bronchitis) or acute oedema of the lung due to the failure of the left chambers of the heart. The sounds produced by collapsing air bubbles in the bronchi are dampened by the "air cushion" of the lungs as they are conducted to the chest surface.

The so-called falling-drop sound (gutta cadens) can be heard by auscultation. It can occur in large cavities of the lungs or at the base of the pleural cavity which contain liquid pus or air as the patient changes his posture from recumbent to upright position or vice versa. Tenacious liquid containing pus sticks to the surface of the cavity and as the patient changes his position it gathers in drops which fall one after another into the liquid (sputum or pus) accumulated at the bottom.

Crepitation. As distinct from rales, crepitation originates in the alveoli. Some authors erroneously classify these sounds as crepitant and subcrepitant rales. Crepitation is a slight crackling sound that can be imitated by rubbing a lock of hair. The main condition for generation of crepitation is accumulation of a small amount of liquid secretion in the alveoli. During expiration, the alveoli stick together, while during inspiration the alveolar walls are separated with difficulty and only at the end of the inspiratory movement. Crepitation is therefore only heard during the height of inspiration. In other words, crepitation is the sound produced by many alveoli during their simultaneous reinflation.

Crepitation is mainly heard in inflammation of the pulmonary tissue, e.g. at the first (initial) and third (final) stages of acute lobar pneumonia, when the alveoli contain small amounts of inflammatory exudate, in infiltrative pulmonary tuberculosis, lung infarction, and finally in congestions that develop due to insufficient contractile function of the left-ventricular myocardium or in marked stenosis of the left venous orifice of the heart. Crepitation can be heard in the inferolateral portions of the lungs of aged persons during first deep inspirations, especially so if the patient was in the recumbent position before auscultation. The same temporary crepitation can be heard in compressive atelectasis. During pneumonia, crepitation is heard over longer periods and disappears when a large amount of inflammatory secretion is accumulated in the alveoli or after its complete resolution.

By its acoustic properties, crepitation can often resemble moist fine rales that are produced in fine bronchi or bronchioles filled with liquid secretion. Differentiation of moist rales from crepitation is of great diagnostic importance. Persistent crepitation may indicate pneumonia while fine non-consonating rales suggest bronchitis. Differential-diagnostic signs of these rales and crepitation are as follows: moist fine rales are heard during both inspiration and expiration; they can be intensified or disappear after coughing, while crepitation can only be heard at the height of inspiration; nor does it change after coughing.

Pleural friction sound. In physiological conditions visceral and parietal layers of the pleura are constantly "lubricated" by a capillary layer of pleural fluid and are therefore smooth. Their friction during breathing is

noiseless. Various pathological conditions alter the physical properties of the pleural surfaces and their friction against one another becomes more intense to generate a peculiar adventitious noise, known as the pleural friction sound. Fibrin is deposited in inflamed pleura to make its surface rough; moreover, cicatrices, commissures, and bands are formed between pleural layers at the focus of inflammation. Tuberculosis or cancer are also responsible for the friction sounds.

Pleural friction sounds are heard during both inspiration and expiration. The sounds are differentiated by intensity, or loudness, length, and site over which they are heard. During early dry pleurisy the sounds are soft and can be imitated by rubbing silk or fingers in the close vicinity of the ear. The character of pleural friction sound is altered during the active course of dry pleurisy. It can resemble crepitation or fine bubbling rales (sometimes crackling of snow). In pleurisy with effusion, during the period of rapid resorption of exudate, the friction sound becomes coarser due to massive deposits on the pleural surfaces. This friction (to be more exact, vibrations of the chest) can be even identified by palpation of the chest.

The time during which pleural friction sound can be heard varies with diseases. For example, in rheumatic pleurisy pleural friction is only heard during a few hours; after a period of quiescence it reappears. Pleural friction persists for a week and over in dry pleurisy of tuberculous aetiology and pleurisy with effusion at the stage of resorption. Pleural friction sounds can be heard in some patients for years after pleurisy because of large cicatrices and roughness of the pleural surfaces.

The point over which pleural friction can be heard depends on the focus of inflammation. Most frequently it is heard in the inferolateral parts of the chest, where the lungs are most mobile during respiration. In rare cases this sound can be heard over the lung apices, when they are affected by tuberculosis with involvement of the pleural membranes.

If the inflammatory focus is localized in the pleura adjacent to the heart, *pleuropericardial friction* sound may be heard during both inspiration and expiration, and also during cardiac systole and diastole. As distinct from cardiac murmurs, this noise is best heard at the height of a deep inspiration because at that time the pleural surfaces come in closer contact with the pericardium.

Pleural friction sounds can be differentiated from fine bubbling rales and crepitation by the following signs: (1) the character of rales is altered or rales can disappear for a short time after coughing, while pleural friction sound does not change in these conditions; (2) when a stethoscope is pressed tighter against the chest, the pleural friction sound is intensified, while rales do not change; (3) crepitation is only heard at the height of inspiration, while pleural friction sound is heard during both inspiration and ex-

piration; (4) if a patient moves his diaphragm in and out while his mouth and nose are closed, the sound produced by the friction of the pleura due to the movement of the diaphragm can be heard, while rales and crepitation cannot because there is no air movement in the bronchi.

Succusion (Hippocratic) sound. This is the splashing sound heard in the chest of a patient with hydropneumothorax, i.e. when serous fluid and air are accumulated in the pleural cavity. The sound was first described by Hippocrates, hence the name. The sound can be identified by auscultation: the physician presses his ear against the chest of the patient and then shakes the patient suddenly. The splashing sounds are sometimes heard by the patient himself during abrupt movements.

Bronchophony. This is the voice conduction by the larynx to the chest, as determined by auscultation. But as distinct from vocal fremitus, the words containing sounds 'r' or 'ch' are whispered during auscultation. In physiological conditions, voice conducted to the outer surface of the chest is hardly audible on either side of the chest in symmetrical points. Exaggerated bronchophony (like exaggerated vocal fremitus) suggests consolidation of the pulmonary tissue (which better conducts sound waves) and also cavities in the lungs which act as resonators to intensify the sounds. Bronchophony is more useful than vocal fremitus in revealing consolidation foci in the lungs of a patient with soft and high voice.

Instrumental and Laboratory Methods

X-RAY EXAMINATION

Roentgenological methods used to examine the respiratory organs include roentgenoscopy, roentgenography, tomography, bronchography, and fluorography of the chest.

The most popular method of examination is *roentgenoscopy* of the lungs by which translucency of the lung fields may be determined. It is used to determine consolidation foci (indurations, pneumosclerosis, newgrowths) and cavities in the pulmonary tissue, foreign bodies of the trachea and bronchi, the presence of fluid or air in the pleural cavity, and also coarse pleural adhesions.

Roentgenography (radiography) is used for diagnostic purposes and for film recording of pathological changes in the respiratory organs discovered by roentgenoscopy. Some changes (indistinct focal consolidations, bronchovascular pattern, etc.) can be better examined on a roentgenogram (radiograph) rather than during roentgenoscopy.

Tomography gives layer-by-layer X-ray pictures of the lung. It is used for more accurate diagnosis of the tumours and also small indurations, cavities and caverns in the lungs.

Bronchography is used to study bronchi. After preliminary anaesthesia, the radiopaque substance (iodolipol) is administered into the lumen of the bronchi. Roentgenograms (radiographs) of the lungs are then taken which give a distinct pattern of the bronchial tree. This method is used to reveal bronchiectasis, abscesses, and caverns in the lungs and contraction of the lumen in the bronchi by a tumour.

Fluorography is a variant of the X-ray examination method by which the image is made on a roll film of a small size. This is a convenient means for screening the population.

ENDOSCOPY

This includes bronchoscopy and thoracoscopy. *Bronchoscopy* is used to inspect the tracheal and bronchial mucosa of the second and third order. It is performed by means of a special apparatus known as a bronchofibroscope (Fig. 20). Special forceps are used with a bronchoscope to take samples for biopsy, extract foreign bodies, or polyps. A photographic device is also used with the bronchoscope.

Mucosa of the upper airway is first anaesthetized by a 1-3 per cent dicaine solution. Next a bronchoscope is introduced via the mouth into the vocal slit and farther into the trachea. The physician examines the mucosa

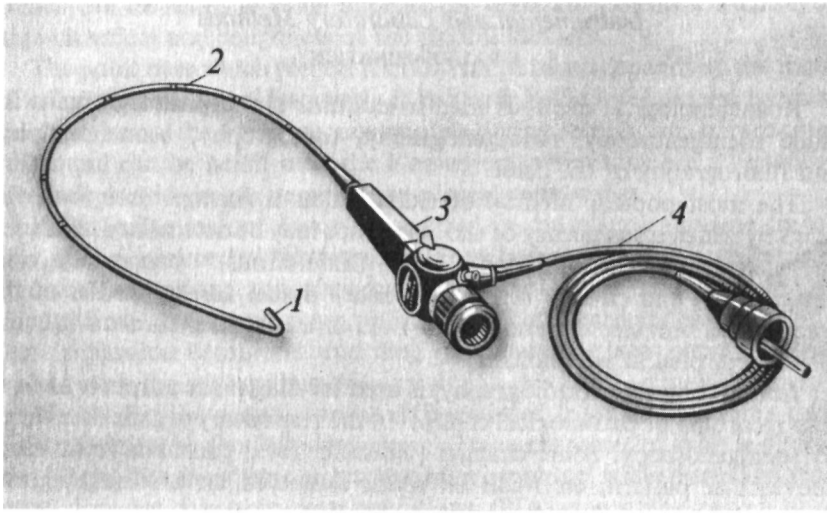


Fig. 20. Bronchofibroscope.
1—controllable distal end; *2*—flexible rod; *3*—instrument body with an eye-piece and control handle; *4*—fibre-optic cable.

of the bronchi and the trachea. Using special forceps, tissue samples can be taken from a suspected area (biopsy) for histological and cytological analysis (Plate 5). Photography can also be made whenever necessary.

Bronchoscopy is used for diagnosing erosions and ulcers of the bronchial mucosa and tumours of the bronchial wall, removing foreign bodies, extracting polyps, and treating bronchiectasis and centrally located abscesses of the lungs. Sputum containing pus is first aspirated through the bronchoscope, and then antibiotics are administered into the bronchial lumen or cavity.

Thoracoscopy is carried out with a special electrically lighted instrument known as a thoracoscope that consists of a hollow metal tube and a special optic device. Thoracoscopy is used for examination of the visceral and parietal pleura and for severance of pleural adhesion bands that may interfere with placing artificial pneumothorax (in cavernous pulmonary tuberculosis).

METHODS FOR FUNCTIONAL DIAGNOSIS

Functional studies of the external respiratory system are very important for an integrated examination of patients with diseases of the lungs and bronchi. A functional study cannot diagnose the disease which caused the respiratory insufficiency, but often reveals it long before its clinical symptoms are apparent, establishes its type, character and degree, and can be used to follow up functional changes in the external respiratory apparatus in the course of the disease and under the effect of treatment.

Lung ventilation. The indices of lung ventilation are not constant and depend not only on the pathological conditions of the lungs or bronchi, but also on the patient's constitution, physical fitness, height, weight, sex, and age. The data obtained during examination of the patient are therefore assessed by comparing them with the data that might be expected from a person with the given physical properties. These data are calculated by special nomograms and formulas that have been compiled from basal metabolism indices.

Measuring respiratory capacity. Various indices are used to characterize lung ventilation. The so-called volumes of the lungs are most popular but they are not accurate enough.

1. The *respiratory volume* (RV) is the volume of air inspired and expired during normal breathing. It is 500 ml on the average varying from 300 to 900 ml. Of this volume, about 150 ml is the physiological dead-space volume of air (PDSV) which is present in the larynx, trachea, and bronchi, but which does not participate in respiratory exchange. It should however be remembered that the air of the PDSV is mixed with the inspired

air to warm and moisten it, which makes residual air physiologically important.

2. The *expiratory reserve volume* (ERV) (1500-2000 ml). This is the volume of air which can be expired by maximum effort after completion of a normal expiration.

3. The *inspiratory reserve volume* (IRV) (1500-2000 ml). This is the volume of air that can be inspired after a normal inspiration.

4. The *vital capacity* (VC) is found by summation of the IRV and ERV and the respiratory volume (3700 ml on the average). This is the greatest volume of air that can be expired from the lungs after a maximum inspiration. The vital capacity of the lungs can be calculated by multiplying the tabulated (optimal) volume of basal metabolism by an empirically found factor 2.3. The deviation from the expected (optimum) vital capacity calculated by this method should not exceed ±15 per cent.

5. The *residual air volume* (RAV) (1000-1500 ml) is the air that remains in the lungs after maximum expiration.

6. The *total lung capacity* (TLC) is the sum of the RV, ERV and IRV, and RAV. It is about 5000-6000 ml.

Respiratory volumes can be used to assess possible compensation of respiratory insufficiency by increasing respiratory depth at the expense of expiration and inhalation and residual volume.

Normal respiratory volume is about 15 per cent of the vital lung capacity; expiratory and inspiratory air volumes are 42-43 per cent (inspiratory air usually slightly exceeds expiratory air volume); residual air is about 33 per cent of the vital capacity of the lungs. The VC slightly decreases in patients with obstructive hypoventilation, while expiratory and residual air volumes increase at the expense of decreased inspiratory air. RAV (especially the RAV: TLC ratio) increases in some cases to 50 per cent of the TLC (in lung emphysema, bronchial asthma, to a lesser degree in aged persons). VC in patients with hypoventilation also decreases because of the decreased IRV, while the RAV changes only insignificantly.

Spirography gives more reliable information on respiratory volumes (Fig. 21). A spirograph can be used not only to measure various respiratory volumes but also some additional ventilation characteristics such as the respiratory volume, minute volume, maximum ventilation of the lungs, and the volume of forced expiration. A spirograph can also be used with a bronchoscope to determine all indices separately for each lung (bronchospirography). Using an absorber of carbon dioxide, it is possible to determine oxygen absorption per minute.

The RAV can also be determined by spirography. A spirograph with a closed system and a carbon dioxide absorber is used for the purpose. The apparatus is filled with pure oxygen and the patient breathes into the ap-

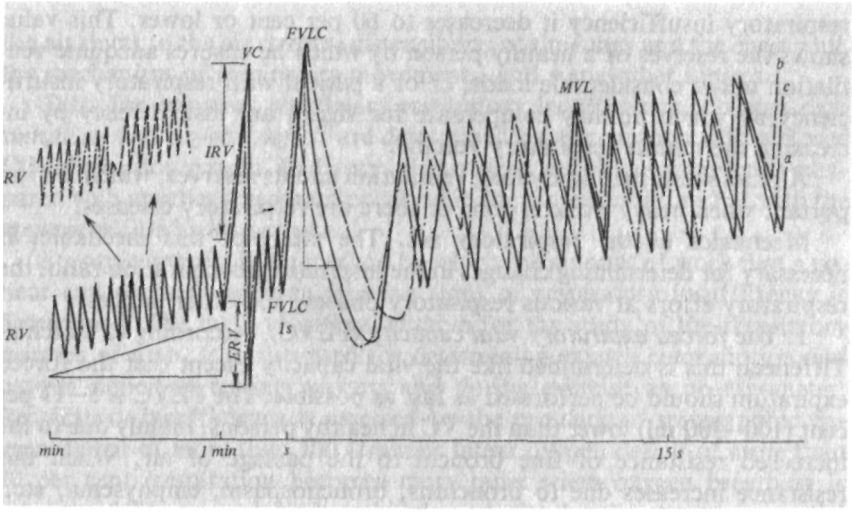


Fig. 21. Spirograms of a healthy individual (a) and of patients with obstructive *(b)* and restrictive (c) respiratory insufficiency.

paratus for ten minutes, after which the RAV is determined by calculating the amount and concentration of nitrogen captured by the spirograph from the patient's lungs.

It is difficult to determine the PDSV. It can only be assessed by calculating the ratio of partial pressure of CO_2 in the expired air and the arterial blood. PDSV increases in patients with large caverns and in the presence of ventilated pulmonary areas that are not sufficiently supplied with blood.

Intensity of lung ventilation. 1. The *minute volume* (MV) is calculated by multiplying the respiratory volume by respiratory rate; it is about 5000 ml on the average. More accurately the MV can be determined by a Douglas bag or using a spirograph.

2. The *maximum lung ventilation* (MLV) is the amount of air that can be handled by the lungs by maximum effort of the respiratory system. It is determined by spirometry during deepest breathing at a rate of 50 r/min; normal ventilation is 80-200 l/min. According to Dembo, the predicted value of the maximum ventilation is the vital capacity of the lungs multiplied by 35 (MLV = VC × 35).

3. The *respiratory reserve* (RR) is determined by the formula RR = = MLV - MV. In norm the RR exceeds the MV by at least 15-20 times. In healthy persons the RR is 85 per cent of the MLV, while in patients with

respiratory insufficiency it decreases to 60 per cent or lower. This value shows the reserves of a healthy person by which he ensures adequate ventilation under considerable loads, or of a patient with respiratory insufficiency by which he may compensate for significant insufficiency by increasing the minute respiratory volume.

All these tests help study lung ventilation and its reserves, which are important when heavy work is done or there are respiratory diseases.

Mechanics of the respiratory act. The study of this mechanics is necessary for determining changes in the inspiration to expiration ratio, the respiratory effors at various respiratory phases, and other indices.

1. The *forced expiratory vital capacity* (FEVC). According to Votchal-Tiffeneau this is determined like the vital capacity except that the forced expiration should be performed as fast as possible. The FEVC is 8-11 per cent (100-300 ml) lower than the VC in healthy persons, mainly due to the increased resistance of fine bronchi to the passage of air. When this resistance increases due to bronchitis, bronchospasm, emphysema, etc., the difference may be as great as 1500 ml and more. The volume of forced expiration per minute is also determined. In healthy persons it is 82.7 per cent of the VC. The length of the forced expiration until the moment it slows abruptly is also determined. These investigations can only be done with a spirograph. Broncholytics (e.g. using theophedrine) to determine the FEVC or the various modifications of this test enable us to assess the role of bronchospasm in the aetiology of the respiratory insufficiency and decreased values of the above indices. If, after giving theophedrine, the findings remain markedly subnormal bronchospasm is not the cause of their reduction.

2. The *forced inspiratory vital capacity* (FIVC) is determined during forced inspiration at a maximum speed. It does not change in emphysema non-aggravated by bronchitis but decreases in obstructed patency of the airways.

3. *Pneumotachymetry* is the technique used for measuring peak velocities of air streams in forced inspiration and expiration and is intended to determine the condition of bronchial patency.

4. *Pneumotachygraphy* is measuring the volumetric rate and pressure arising at various phases of respiration (both normal and forced). The instrument used for the purpose is known as a pneumotachygraph. The technique is based on recording pressures of air streams at various points and during different phases of the respiratory cycle. Pneumotachygraphy is used to determine the volumetric rate of air streams during both inspiration and expiration (in normal breathing it is about 300-500 ml/s, and in forced respiration 5000-8000 ml/s), the length of the inspiration and expiration phases, the minute volume, intra-alveolar pressure, resistance of

the air ducts to the air stream, distensibility of the lungs and the chest wall, the mechanism of respiratory movements, and some other indices.

Tests for apparent and latent respiratory insufficiency. *Oxygen consumption* and *oxygen deficit* are determined by spirography with a closed CO_2 absorption system. In determining oxygen deficit, a spirogram is compared with another spirogram obtained in the same conditions but with the apparatus filled with oxygen.

Ergospirography is the method by which the amount of work that a patient can perform without showing signs of respiratory insufficiency is determined. The method is thus suitable for the study of the respiratory reserves of man. It is also used for determining oxygen consumption and oxygen deficit in resting patients and during exercise on an ergometer. Respiratory insufficiency is assessed by the presence of spirographic oxygen deficit of more than 100 l/min or latent oxygen deficit of more than 20 per cent (respiration becomes more quiet when oxygen breathing is substituted for normal air breathing), and also by the change in partial pressure of oxygen and carbon dioxide of the blood.

Study of blood gases. Blood samples are obtained from the skin of a warmed up finger which is pierced through with a needle. It has been proved that the gas composition of the blood taken from the finger tip is similar to that of the arterial blood. The blood sample is transferred into a measuring cylinder where it is kept under a layer of warm vaseline oil (to prevent oxidation by atmospheric oxygen). A Van-Slike apparatus is used for the study of the gas composition of blood. The technique is based on displacement of gases from their combination with haemoglobin into vacuum (by chemical means). The following is determined: (1) oxygen content, in units of volume; (2) oxygen capacity of blood (i.e. the amount of oxygen that can be bound by a given blood unit); (3) percentage of oxygen saturation of the blood (normal, 95); (4) partial pressure of oxygen (normal, 90-100 mm Hg); (5) carbon dioxide content in arterial blood (normal, about 48% v/v); (6) partial pressure of carbon dioxide (normal, about 40 mm Hg). Partial tension of gases (O_2 and CO_2) in arterial blood can now be determined by a special apparatus, or by some other techniques.

The oxygen saturation of the blood can also be determined by oxyhaemometry. A photoelectric device is attached to the patient's ear lobe and the scale of the instrument reads oxygen saturation during breathing with air and oxygen. A great difference in the readings indicates oxygen deficit in the blood.

Determining separately the flow rate in the greater and the lesser circulation gives important diagnostic and prognostic information in patients with dysfunction of the external respiration.

PLEUROCENTESIS

Pleurocentesis is used: (1) to take samples of the pleural fluid for diagnostic studies, (2) to remove fluids from the pleural cavity, and, whenever necessary, to administer medicinal preparations. During the operation the patient sits on a chair, facing the chair back, with his arms crossed on the chest. The site of puncture is treated with an alcohol iodine solution and then with an anaesthetic. The chest is punctured in the posterior axillary line at the point of maximum dullness, which is preliminarily determined by percussion (this is usually the 7th or 8th intercostal space); the puncture is made at the upper edge of the underlying rib, because intercostal vessels are invested at the lower margin of the rib (Fig. 22). An exploratory puncture is done by a syringe (10 ml) with a thick and long needle. Large amounts of fluids are aspired from the pleura by the Patain apparatus or by an electric pump. As the needle enters the pleural cavity the physician "feels" a free space. The needle sometimes meets resistance which is usually thickened pleura. The amount of fluid taken for diagnostic purposes is 50-150 ml. The fluid undergoes physicochemical, cytological, and bacteriological analyses. If much fluid is present in the pleural cavity, 800-1200 ml is first taken. If larger amounts of the liquid are removed, the mediastinal organs may be quickly shifted toward the affected side and collapse may occur. After the needle has been removed, the punctured site should be treated with a 5 per cent iodine solution.

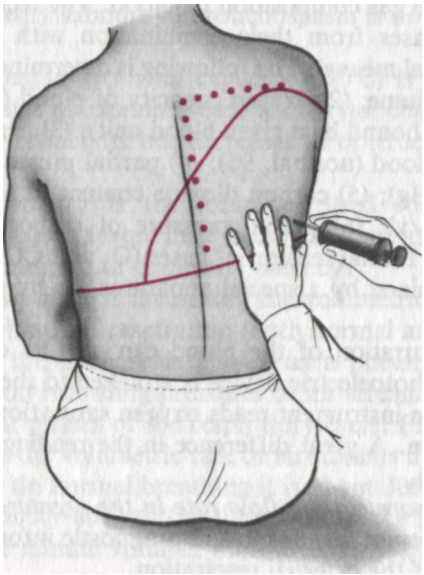


Fig. 22. Pleurocentesis.

LABORATORY STUDIES

Study of the sputum. Sputum is a pathological material that is expelled from the respiratory organs during the coughing act. Sputum may contain mucoid secretions, serous fluid, blood cells, desquamated respiratory epithelium, protozoa, and, in rare cases, helminths and their ova. The study of the sputum gives information concerning the pathology of the respiratory organs and in some cases helps establish its aetiology.

The morning sputum taken before breakfast (after mouth rinsing) is the best material for examination. If the sputum is scarce, it should be collected during one or two days for examination for the presence of tuberculosis mycobacteria. Saprophytic flora rapidly multiplies in sputum to destroy the formed blood elements. Special calibrated bottles provided with screw caps should be used for gathering sputum.

The study begins with observation of the sputum first in a transparent bottle and then in a Petri dish which is placed alternately on the black and white surface. *General properties, colour,* and *consistency* of the sputum are noted. Mucoid sputum is usually colourless; it occurs in acute bronchitis. Serous sputum is also colourless, liquid, and foamy; it occurs in pulmonary oedema. Mucopurulent sputum is yellow or greenish and tenacious; it is characteristic of chronic bronchitis, tuberculosis, etc. Purulent uniform semiliquid sputum with a greenish-yellow tint is typical of the ruptured lung abscess. Sputum may contain blood. It occurs in pulmonary haemorrhage (tuberculosis, cancer, bronchiectasis). Sputum may also be mucopurulent with streaks of blood (in bronchiectasis), serous blood-stained foamy (in lung oedema), mucous bloody (in lung infarction or in congestion in the lesser circulation), or bloody purulent (in gangrene and abscess of the lung). If blood is not expectorated from the respiratory tract immediately but stays there for some time, the haemoglobin converts into haemosiderin to give a rusty hue to the sputum, which is characteristic of acute lobar pneumonia.

Sputum may form layers on standing. Three-layer sputum is characteristic of chronic purulent processes. The upper layer is mucopurulent, the middle one serous, and the lower layer is pus. Purulent sputum is sometimes separated into two layers, i.e. serous and purulent.

Sputum is usually *odourless.* Foul odour of freshly expectorated sputum depends on the putrefactive decompositon of tissues (gangrene, degrading cancer tumour) or on the decomposed protein of the sputum retained in various cavities (abscess, bronchiectases).

The following elements can be seen in the sputum by an unaided eye: *Curschmann spirals* (in the form of small dense twisted threads); fibrin clots (whitish and reddish branching elastic formations, occurring in

fibrinous bronchitis and sometimes in pneumonia); compact lenticular greenish-yellow formations consisting of calcified elastic fibres, cholesterol crystals and soaps containing tuberculosis mycobacteria; *Dittrich's plugs*, that resemble the lenticular formations in appearance and composition but free of tuberculosis mycobacteria and having offensive odour on pressing (occur in gangrene, chronic abscess, and fetid bronchitis); *lime grains*, that are found during decompositon of old tuberculosis foci; *actinomycete drusen* in the form of yellow formations resembling coarse flour; necrotized pieces of lung tissues and tumours; food remains.

The *medium of the sputum* is alkaline as a rule; it becomes acid in the presence of gastric juice and during decomposition; this helps differentiate between haemoptysis and haematemesis.

Microscopic study of the sputum can be done with native and stained preparations. In the first case, small clots or white threads of the purulent and blood stained material are taken from a sputum sample and transferred onto an object to make a thin semitransparent preparation which is covered by another glass. Examination begins with general observation at a small magnification in order to identify Curschmann spirals. Formed elements are then differentiated at a greater magnification. Curschmann spirals are mucous threads consisting of a dense central filament and a spiral mantle containing leucocytes (often eosinophils) and Charcot-Leyden crystals (Fig. 23). Curschmann spirals are found in the sputum during bronchial spasms, mostly in bronchial asthma, less frequently in pneumonia and lung cancer.

Leucocytes can be found in native preparations at large magnification. A small quantity of leucocytes can be found in any sputum, while their

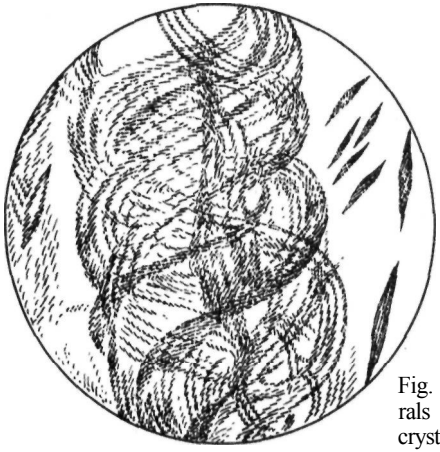


Fig. 23. Curschmann's spirals and Charcot-Leyden crystals in sputum.

large amounts are characteristic of inflammatory and especially purulent processes. *Eosinophils* (Plate 6) can be identified in the native preparation by their uniform large lustrous grains, but they are better identified by staining. *Erythrocytes* (red blood cells) appear during decomposition of lung tissue, in pneumonia, congestion in the lesser circulation, lung infarction, etc.

Squamous epithelium gets into the sputum mostly from the mouth and is diagnostically unimportant. *Columnar ciliated epithelium* is contained in small quantity in any sputum, but its large amounts are found in bronchitis, bronchial asthma, and other affections of the respiratory ducts. *Alveolar macrophages* are large cells (twice or thrice as great as leucocytes) of reticulohistiocyte aetiology. Their cytoplasm contains many inclusions. They can be colourless (meylin grains), black from coal particles (dust cells) (Plate 7), or brown-yellow from haemosiderin (heart-disease cells or siderophages). Small quantities of alveolar macrophages are contained in any sputum but their large amounts are found in inflammatory diseases. Heart-disease cells (Plate 8) occur where erythrocytes get into the alveolar cavities (in congestion of the lesser circulation, especially in mitral stenosis, lung infarction, and also in acute lobar pneumonia). Berlin blue is used for their reliable identification. A small quantity of sputum is placed on an object glass, 1-2 drops of a 5 per cent potassium ferrocyanide solution are added, and the same amount of a 2 per cent hydrochloric acid added in 2—3 minutes; the material is mixed and is covered with another glass. Haemosiderin grains become stained blue in a few minutes.

Malignant tumour cells are often present in the sputum, especially so if the tumour degrades or grows endobronchially. These cells can easily be identified by their atypical view: they are mostly large and disfigured, their nuclei are large; several nuclei are sometimes found in one cell. Lining epithelium of the bronchi becomes metaplastic in chronic inflammation; it acquires atypical features and may resemble tumour cells. Cells can therefore be identified as tumour cells only in the presence of the whole complex of atypical and polymorphous cells, especially if they are found on fibres or together with elastic fibres.

Elastic fibres (Plate 9) are found in the sputum during decomposition of the lung tissue in tuberculosis, cancer and abscess. Elastic fibres are fine formations of two dichotomically branching filaments of the uniform thickness. They often occur as coils in alveoli. Since these fibres do not occur in every drop of the sputum, they should be concentrated to make their search easier. To that end, a few millilitres of sputum are mixed with an equal (or double) quantity of a 10 per cent potassium hydroxide solution and heated to dissolve the mucus. All formed elements of the sputum, except elastic fibres, are dissolved; the mixture is then cooled, centrifuged,

3-5 drops of a 1 per cent alcohol eosin solution are added, and the precipitate examined in a microscope. Elastic fibres preserve their character and are clearly seen as bright red formations.

Actinomycetes are separated from small yellow compact grains (drusen) of sputum. When a druse is compressed in a drop of glycerol between two object glasses, its central part consisting of interlaced mycelium and radiant flask-shaped formations can be seen in a microscope. When the crushed druse is stained after Gram, the mycelium acquires violet and the flask crimson colouration. Another important fungus occurring in the sputum is *Candida albicans,* which affects the lungs during prolonged antibiotic therapy of asthenic patients. Budding yeast-like cells and branching mycelium (on which the spores are arranged in churns) are found in the native preparation.

Sputum can contain *Charcot-Leyden* crystals. These are colourless octahedra of various size, resembling the pointer of a compass. They consist of protein released during decomposition of eosinophils and are therefore found in the sputum containing much eosinophils. Old sputum contains greater amount of these crystals. *Haematoidin* can be found in the sputum after pulmonary haemorrhage (provided blood is not liberated with the sputum immediately). Crystals of haematoidin are rhombic or needle-shaped brown-yellow formations.

Microscopy of stained preparations is carried out to study microbial flora of the sputum and of some of its cells. Determination of malignant tumour cells is the most important object of microscopy. A smear of suspected material found in the native preparation is carefully fixed (not to crush cells) in methyl alcohol or Nikiforov mixture and stained after Romanovsky-Giemsa (or by some other differentiating staining). Tumour cells are characterized by polymorphism and variable size, the presence of very large cells, large (often hyperchromic and also hypochromic) nuclei, sometimes multiple irregular nuclei with large nucleoli; homogeneous, sometimes vacuolized cytoplasm, markedly basophilic in some cells; and also mytotic figures (in some cases). Complexes of polymorphic cells of the described character are more important diagnostically.

Romanovsky-Giemsa stained smears are suitable for identification of eosinophilic leucocytes. Another staining is also useful: the material is first treated with a 1 per cent eosin solution (2-3 minutes) and then with a 0.2 per cent methylene blue solution (0.5— 1 minute). Single eosinophils can occur in any sputum; large amounts of eosinophils (up to 50—90 per cent of all leucocytes) are found in bronchial asthma, eosinophilic infiltrations, helminthic invasions of the lungs, etc.

Smears for bacterioscopic studies are prepared by crushing a clot of sputum between two object glasses. The dried smear is fixed by passing it

three times through a flame of a gas burner, and then stained; Ziehl-Neelsen staining is used to detect tuberculosis mycobacteria, and Gram staining in other cases.

Ziehl-Neelsen staining. A piece of blotting paper, the size of the smear, is placed over a smear fixed on a glass, Ziehl carbol fuchsine solution is then used to wet the paper and the preparation is held in a low flame of a burner until vapour appears. The paper is then removed, the preparation is washed with water and decoloured in a 3 per cent hydrochloric acid solution and 96 per cent alcohol (or in a 5-10 per cent sulphuric acid solution). The preparation is then washed in water thoroughly, and stained again for 0.5-1 minute in a 0.5 per cent methylene blue solution. A final washing is then given. Acid-fast bacteria are thus reliably stained. They are not discoloured and remain red against the blue background of the other sputum elements that are discoloured in the acid and become stained in other colours.

If bacterioscopy fails to reveal tuberculosis mycobacteria (Plate 10) in the sputum because of their scarce quantity, other techniques should be used. In *luminescent microscopy* a common fixed smear is coloured with a luminescing dye (rhodamine, acridine orange) and then with another stain (acid fuchsine, methylene blue), that masks the background luminescence. Luminescence of mycobacteria in the ultraviolet rays of a luminescent microscope is so bright, that mycobacteria can be seen in a dry lens (40 ×). It covers a larger field of vision than the immersion lens. There exist various techniques to concentrate mycobacteria. *Flotation* is the most popular one. The sputum is homogenized with alkali, shaken with toluene, xylene or benzine, and mycobacteria entrapped in the droplets of the solvents float to the surface. Cream-like layer which separates on standing, is transferred by a pipette onto a warm glass, drop by drop (on one site). The preparation is allowed to dry and then fixed and stained after Ziehl-Neelsen. Another concentration method is *electrophoresis.* As direct current passes through the liquefied sputum, tuberculosis mycobacteria move toward the cathode. Smears are taken from the cathode and stained after Ziehl-Neelsen.

Gram staining. Fire-fixed smear is covered with a strip of blotting paper, and carbolic solution of methyl violet is placed on top. The paper is removed in 1.5-2 minutes and the smear is covered with Lugol's solution for 2 minutes. The solution is then removed and the preparation is placed in 96 per cent alcohol for 30-60 seconds (until the stain stops dissolving). The preparation is then rinsed in water and given another staining by carbon fuchsine solution (1:10 dilution) for a minute.

Several microbes can be differentiated by Gram staining. These are Gram-positive capsulated pneumococcus, streptococcus, staphylococcus, klebsiella (gram-negative capsulated Friedlaender's diplobacillus, Plate 11), Pfeiffer's bacillus, etc. All these microorganisms occur in small quantities in the sputum of the respiratory ducts of healthy persons and only become pathogenic under certain unfavourable conditions when they cause

pneumonia, lung abscess, bronchitis, etc. Their amount in the sputum then increases markedly. But the quantitative factor is however not decisive for their pathogenicity.

If bacterioscopy does not reveal the expected causative agent, the sputum is used to inoculate the nutrient medium. Bacteriological studies help identify the microbe and determine its virulence and drug-resistance. This is necessary to prescribe a correct medicamentous therapy. Finally, if the described simple procedures fail to identify the causative agent, the sputum is used to infect an experimental animal.

Study of the pleural fluid. The amount of fluid contained in the pleural cavity of a healthy person is insignificant. Its composition is close to that of lymph. The fluid serves as a lubricant to decrease friction between the pleural membranes during respiration. The volume of pleural fluid may increase in disordered circulation of the blood and lymph in the lungs. This can be either transudate (of non-inflammatory origin) or effusion (occurring in inflammatory affections in the pleura). Effusion can also be due to clinical causes such as primary infection of the pleura or it can be a symptom attending some general infections and some diseases of the lungs or mediastinum (rheumatism, infarction, cancer and tuberculosis of the lungs, lymphogranulomatosis, etc.). The pleural fluid is studied in order (1) to determine its character (transudate, effusion, pus, blood, chylous fluid); (2) to study the cell composition of the fluid in order to obtain information concerning the character of the pathology and sometimes its diagnosis (when cancer cells are detected); (3) to reveal the causative agent of an infectious disease and to determine its sensitivity to antibiotics. Analysis of the pleural fluid includes macroscopic, physicochemical, microscopic and sometimes microbiological and biological analysis.

The *appearance* of the pleural fluid depends mostly on its cell composition and partly on the chemical composition. Fluids of the following character are differentiated: serous, serofibrinous, fibrinous, seropurulent, purulent, putrefactive, haemorrhagic, chylous, and chylous-like.

Transudate and serous effusion are clear and slightly opalescent. Turbidity of the fluid may be due to abundance of leucocytes (seropurulent and purulent effusion), erythrocytes (haemorrhagic effusion), fat drops (chylous effusion) or cell detritus (chylous-like effusion). The character of the cells can be determined by microscopy. The chylous character of the effusion is determined by an ether test (opacity disappears in the presence of ether). This fluid can be due to congestion of lymph or destruction of the thoracic duct by a tumour or an injury. The chylous character is given to the pleural fluid by fatty degeneration of cells contained in ample quantity. Fat is stained with Sudan III in both cases.

The *colour* of transudate may be pale yellow, serous effusion from pale

yellow to golden, and in jaundice it may be deep yellow. Purulent effusion is greyish or greenish-yellow; in the presence of blood it becomes reddish or, more frequently, greyish-brown. The putrefactive effusion is of the same colour. Depending on the amount of the haemorrhage and also on the time of blood retention in the pleura, the haemorrhagic fluid can be pink to dark red or even brown. In haemolysis it may have the appearance of lacquer. Chylous effusion looks like thin milk.

The *consistency* of pleural effusion is usually liquid. Purulent fluid can be thick, cream-like, and sometimes it enters the puncture needle with difficulty. Pus of the old encapsulated empyema can be of puree consistency, with grains, and fibrin flakes.

Only putrefactive effusion has offensive smell (gangrene of the lung). The smell depends on protein which is decomposed by anaerobic enzymes.

Physicochemical studies of the pleural fluid include determination of relative density of the fluid and protein; these are the main criteria for differentiation between the effusion and transudate. Relative density of the pleural fluid is determined by a hydrometer; a urometer is normally used for the purpose (see "Analysis of Urine"). Relative density of the transudate is about 1.015 g/cm^3 (1.006-1.012), and of the effusion is slightly higher, i.e. 1.018-1.022.

Protein content is lower in transudate than in the pleural fluid, i.e. not higher than 3 per cent (usually 0.5-2.5 per cent). The pleural effusion contains from 3 to 8 per cent of protein. A refractometric method is more suitable for determining protein in the pleural fluid, but some other methods can also be used, such as biuretic, gravimetric, Roberts-Stolnikov method (see "Analysis of Urine") and others. The composition of protein fractions of the pleural fluid is about the same as of blood serum. Albumins prevail in transudate while fibrinogen is absent or almost absent for which reason transudate does not clot. The fibrinogen content of pleural effusion is lower than that of blood (0.05-0.1 per cent) but its quantity is sufficient to clot spontaneously most of them. The total protein content of transudate rarely reaches 4-5 per cent and additional tests are therefore used to differentiate it from the pleural effusion. *Rivalta's reaction:* a cylinder is filled with water acidified with a few drops of acetic acid; 1 or 2 drops of the punctate are added; as effusion sinks to the bottom it leaves a cloudy trace (like cigarette smoke), while in case of transudate the reaction is negative. *Lucaerini test: 2* ml of hydrogen peroxide (3 per cent solution) are placed on a watch glass (against a black background) and a drop of the punctate is added: opalescence appears in case of the positive reaction. Both reactions are used to detect the presence of seromucin in effusion. This is a mucopolysaccharide complex which is absent from transudates.

Microscopy is used to study the precipitate of the pleural fluid obtained by centrifuging. The fluid may clot before or during centrifuging, and the precipitate becomes unsuitable for examination because most of its cells will be captured in clots. To preclude clotting, sodium citrate or heparin is added to the test fluid. Precipitate cells are studied by several techniques. Studied are native preparations, dry smears stained after Romanovsky-Giemsa or Papanicolaou. Fluorescence microscopy, histological studies of the precipitate in paraffin, or cell culture are used to detect tumour cells.

In order to prepare a native preparation, a drop of the precipitate is placed on an object glass and is covered by a glass. The preparation is examined with a dry system in a simple or a phase-contrast microscope. The quantity of formed elements is then assessed (many, moderate number, few). An accurate calculation of leucocytes and erythrocytes is unimportant because their quantity in the preparation depends largely on the duration and speed of centrifugation. A small quantity of erythrocytes can be contained in any punctate because of puncturing of the tissues. Their number is high in haemorrhagic effusion in patients with tumours, injuries, and hemorrhagic diathesis. The leucocyte count is high in bacterial infections of the pleura. Leucocytes are scarce in transudates, which contain many mesothelium cells. Exudates sometimes contain cells suspected for tumour, but it is difficult to determine their nature in native preparation. The precipitate containing minimum supernatant liquid is used to make a smear. The elements of the precipitate, i.e. neutrophils, lymphocytes, eosinophils, monocytes, macrophages, mesothelial cells and tumour cells, can be differentiated by colour.

Leucocytes of pleural fluids look like those of blood. Mesothelial cells are large, round, spheric or polygonal, rarely with 2 or 3 nuclei. The round nucleus, with a rather gentle chromatin network, sometimes contains a nucleolus. The cytoplasm is blue and often vacuolized. Macrophages differ from monocytes by the presence in the cytoplasm of products of phagocytosis. The properties of tumour cells are the same as described in the section "Study of Sputum". It is very difficult to determine tumour cells in the pleural fluid, because in long-standing and sometimes acute pleural affections (and also in transudates) mesothelial cells acquire many properties that are inherent in blastoma cells. Luminescent microscopy helps in this situation: when stained with rhodamine, acridine orange or some other fluorochromes, tumour cells luminesce differently than the normal cells.

Neutrophils are found during the first 5-7 days in effusions of any aetiology. In tuberculous and rheumatic pleurisy, neutrophils are replaced by lymphocytes. Effusions rich in neutrophils are characteristic of pleural affections with pyogenic flora. Effusions containing considerable (sometimes prevailing) quantities of eosinophils also occur.

Transudates used for *microbiological studies* are as a rule sterile but they can be infected during repeated paracenteses. Effusion may be sterile (e.g. in rheumatic pneumonia or lung cancer). Mycobacteria are usually not found bacterioscopically in serous effusion of tuberculous aetiology, but inoculation of the nutrient medium of guinea pigs with the effusion gives sometimes positive results. The bacteria can often be detected by bacterioscopy of Gram-stained smears in pleurisy caused by pyogenic flora. Otherwise inoculation of media is required. In addition to pneumococci, streptococci, staphylococci, and enterococci, effusions contain *also Klebsiella* organisms, Pfeiffer's bacilli, colibacilli, etc. In order to prescribe a correct therapy, the revealed microbes are tested for antibiotic sensitivity.

Study of pleural washings. This is necessary to reveal tuberculosis mycobacteria in them (e.g. in patients who do not expectorate sputum), or to detect malignant tumour cells. The patient should lie on the affected side. His pharynx and larynx should be anaesthetized with a dicaine solution, and then 10—12 ml of warm isotonic sodium chloride solution are slowly injected into the larynx and the trachea using a laryngeal syringe. The solution irritates the bronchial mucosa to cause cough and expectoration of mucus. The expectorated washings are collected in a sterile vessel. Mycobacteria are detected in them by the flotation method or by inoculation of a nutrient medium. To prepare material for cytological studies, the washings are centrifuged and native preparations and smears are prepared from the precipitate. Native preparations are inspected in a common phase-contrast microscope, or in a fluorescence microscope (after fluorochrome treatment). Smears are stained after Romanovsky-Giemsa (or by fluorochromes) for fluorescence microscopy.

Main Clinical Syndromes

Syndrome of focal consolidation of pulmonary tissue. The syndrome of focal consolidation of lung tissue is caused by filling of the alveoli with the inflammatory fluid and fibrin (in pneumonia), blood (in lung infarction), growing connective tissue in the lung (pneumosclerosis, carnification) in long-standing pneumonia, or developing tumour. The common complaint of the patient is dyspnoea. Examination of the patient reveals thoracic lagging of the affected side during respiration; vocal fremitus is intensified in the consolidated area; the percussion sound over the consolidation site is slightly or absolutely dull; auscultation reveals bronchial respiration, exaggerated bronchophony and (in the presence of liquid secretion in fine bronchi) resonant (consonating) rales. X-ray examination shows the focus of consolidation as an area of increased density in the lung tissue, its size and contours depending on the character and stage of the disease, and some other factors.

Cavity in the lung. Cavity in the lung is formed in abscess or tuberculosis (cavern) or during degradation of the lung tumour. An empty large cavity is communicated with the bronchus and surrounded by a ring of inflamed tissue. Examination of the chest reveals unilateral thoracic lagging and intensified vocal fremitus. Percussion reveals dulled tympany or (if the cavity is large and peripheral) tympany with a metallic tinkling. Auscultation reveals amphoric breathing, intensified bronchophony, and often medium and large resonant vesicle rales. X-ray examination proves the presence of the cavity in the lung.

Fluid in the pleural cavity. The syndrome of accumulation of pleural fluid occurs in hydrothorax (accumulation of non-inflammatory effusion, i.e. transudate, for example in cardiac failure), or in pleurisy with effusion (inflammation of the pleura). The syndrome is characterized by dyspnoea due to respiratory insufficiency caused by lung compression and decreased respiratory surface, asymmetry of the chest (enlargement of the side where pleural effusion is accumulated) and unilateral thoracic lagging during respiration. Vocal fremitus is markedly weakened over the area of the pleural effusion, or it may be undeterminable; percussion reveals a dulled sound or absolute dullness; in auscultation respiration and bronchophony are markedly weakened or absent. X-ray examination reveals an area of increased density in the area of accumulation of the pleural fluid, which is usually at the bottom of the chest (often bilateral in hydrothorax). Its upper border is quite distinct. If transudate is accumulated in the pleural cavity its border is more horizontal, while in the presence of pleural effusion, the border is scant, to coincide with the Damoiseau's curve as determined by percussion (see "Pleurisy with Effusion").

Air accumulation in the pleural cavity. Air is accumulated in the pleural cavity when the bronchi are communicated with the pleural cavity (in subpleural tuberculosis cavern or abscess), in injury to the chest, or in artificial pneumothorax (injection of air into the pleural cavity for medical purposes in the presence of large caverns in the lungs). Asymmetry of the chest found in this syndrome is due to the enlarged side where air is accumulated; the affected side of the chest cannot take part in the respiratory act. Vocal fremitus is markedly weaker or absent altogether over the site of air accumulation; percussion reveals tympany. Breathing sounds and bronchophony are either weak or absent and are not conducted to the chest surface to be detected by auscultation. X-ray examination reveals a light pulmonary field without pulmonary pattern; a shadow of the collapsed lung can be seen toward the root.

External respiratory dysfunction. The function of the external respiratory apparatus is to supply the body with oxygen and to remove carbon dioxide formed by exchange reactions. This function is realized firstly

by ventilation, i.e. gas exchange between the outer and alveolar air. This ensures the required oxygen and carbon dioxide pressure in the alveoli (an important factor is intrapulmonary distribution of the inspired air). Secondly, this function is realized by diffusion of carbon dioxide and oxygen through the walls of the alveoli and lung capillaries (oxygen is supplied from the alveoli to the blood and carbon dioxide is diffused from the blood to the alveoli). Many acute and chronic diseases of the bronchi and the lungs cause respiratory insufficiency (Wintrich, 1854). The degree of morphological changes in the lungs does not always correspond to the degree of their dysfunction.

Respiratory insufficiency is now defined as the condition with abnormal gas composition of the blood, or this abnormality is compensated for by intense work of the external respiratory apparatus and higher load on the heart. This decreases functional abilities of the body. It should be noted that the external respiratory function is closely connected with the blood circulatory function: the heart work is intensified during external respiratory insufficiency, which is an important compensatory element of the heart function.

Respiratory insufficiency is manifested clinically by dyspnoea and cyanosis; at later stages, when cardiac failure joins the process, oedema occurs.

The patient with respiratory insufficiency employs the same compensatory reserves as a healthy person does during heavy exercise. But the compensatory mechanisms of a sick person are actuated much earlier and at loads under which a healthy person would feel no discomfort (e.g. dyspnoea and tachypnoea can develop in a patient with lung emphysema even during slow walking).

Among the first signs of respiratory insufficiency are inadequate changes in ventilation (rapid and deep breathing) at comparatively light loads for a healthy individual; the minute volume increases. In certain cases (bronchial asthma, lung emphysema, etc.) respiratory insufficiency is compensated by intensified work of the respiratory muscles, i.e. by the altered respiratory mechanics. In other words, in patients with pathology of the respiratory system, the external respiratory function is maintained at the required level by mobilizing compensatory mechanisms (i.e. by efforts greater than required for healthy persons), and by minimizing the respiratory reserves: the maximum lung ventilation decreases, the coefficient of oxygen consumption drops, etc.

Various mechanisms are involved gradually to compensate for progressive respiratory insufficiency depending on its degree. At the early stages of respiratory insufficiency the external respiratory function at rest is realized in normal way. The compensatory mechanisms are only actuated

during exercise in a sick person. In other words, only reserves of the external respiratory apparatus are decreased at this stage. As insufficiency further progresses, tachypnoea, tachycardia, and signs of intensified work of the respiratory muscles (during both inspiration and expiration), with involvement of accessory muscles, develop during light exercise and even at rest. At the later stages of respiratory insufficiency, when the body compensatory reserves are exhausted, arterial hypoxaemia and hypercapnia develop. In addition to the growing vivid arterial hypoxaemia, signs of latent oxygen deficit also develop; underoxidized products (lactic acid, etc.) are accumulated in the blood and tissues.

Still at later stages, right ventricular incompetence joins pulmonary insufficiency because of the developing hypertension in the lesser circulation, which is attended by increased load on the right ventricle, and also because of dystrophic changes in the myocardium occurring as a result of its constant overload and insufficient oxygen supply. Hypertension in the vessels of the lesser circulation in diffuse affections of the lungs arises by reflex mechanisms in response to insufficient lung ventilation and alveolar hypoxia— the Euler-Liliestrand reflex (this reflex mechanism is an important adaptation means in focal lung affections; it limits blood supply to insufficiently ventilated alveoli). Further, in chronic inflammatory diseases of the lungs due to cicatricial and sclerotic changes in the lungs (and due to affections in the lung vessels) blood passage through the lesser circulation becomes even more difficult. Increased load on the myocardium of the right ventricle stimulates gradual development of its insufficiency to cause congestion in the greater circulation (pulmonary heart).

Depending on the cause and mechanism of developing respiratory insufficiency, three types of disordered lung ventilation are distinguished: obstructive, restrictive and mixed (combined).

The obstructive type is characterized by difficult passage of air through the bronchi (because of bronchitis, bronchospasm, contraction or compression of the trachea or large bronchi, e.g. by a tumour, etc.). Spirography shows marked decrease in the MLV and PVC, the VC being decreased insignificantly. Obstruction of the air passage increases the load on the respiratory muscles. The ability of the respiratory apparatus to perform additional functional load decreases (fast inspiration, and especially expiration, and also rapid breathing become impossible).

The restrictive type of ventilation disorder occurs in limited ability of the lungs to expand and to collapse, i.e. in pneumosclerosis, hydro- and pneumothorax, massive pleural adhesions, kyphoscoliosis, ossification of the costal cartilages, limited mobility of the ribs, etc. These conditions are in the first instance attended by a limited depth of the maximum possible inspiration. In other words, the vital capacity of the lungs decreases

(together with the maximum lung ventilation), but the dynamics of the respiratory act is not affected: no obstacles to the rate of normal breathing (and whenever necessary, to significant acceleration of respiration) are imposed.

The mixed, or combined type includes the signs of the two previous disorders, often with prevalence of one of them; this type of disorder occurs in long-standing diseases of the lungs and the heart.

External respiratory dysfunction occurs also when the anatomical dead space increases (in the presence of large cavities inside the lung, caverns, abscesses, and also in multiple large bronchiectases). Similar to this type is the respiratory insufficiency due to circulatory disorders (e.g. in thromboembolism, etc.) during which part of the lung is excluded from gas exchange, while its ventilation is to a certain degree maintained. Finally, respiratory insufficiency arises during uneven distribution of air in the lungs (distribution disorders), when a part of the lung is not ventilated (in pneumonia, atelectasis), with preservation of blood circulation. Part of venous blood is not oxygenated before it enters pulmonary veins and the left chambers of the heart. Similar to this type of respiratory insufficiency (with regard to pathogenesis) is the so-called vascular bypass or shunting (from right to left), during which part of the venous blood from the pulmonary artery system enters directly the pulmonary vein (bypassing the capillaries) to mix with oxygenated arterial blood. Oxygenation of blood in the lungs is thus upset but hypercapnia may be absent due to compensatory intensification of ventilation in the intact parts of the lung. This is partial respiratory insufficiency (as distinct from total insufficiency where hypoxaemia and hypercapnia are present).

Respiratory insufficiency is characterized by upset gas exchange through the alveolar-capillary membrane of the lungs. It occurs when this membrane is thickened to interfere with normal gas diffusion through it (the so-called pneumonoses, alveolar-capillary block). It is not accompanied by hypercapnia either since the rate of CO_2 diffusion is 20 times higher than that of oxygen. This form of respiratory insufficiency is, in the first instance, characterized by arterial hypoxaemia and cyanosis. Lung ventilation is intensified.

Respiratory insufficiency associated with toxic inhibition of the respiratory centre, anaemia, or oxygen deficit in the inhaled air, is not connected directly with the pathology of the lungs.

Acute and chronic respiratory insufficiency are differentiated. The former occurs in attacks of bronchial asthma.

Three degrees and three stages of respiratory insufficiency are also distinguished. The degrees of respiratory insufficiency reflect the gravity of the disease at a given moment. The first degree of respiratory insufficiency

(dyspnoea, in the first instance) becomes evident only at moderate or significant physical load. Dyspnoea develops during light exercise in the second degree of insufficiency; the compensatory mechanisms are involved when the patient is at rest and functional diagnosis can reveal some deviations from the normal indices. The third degree is characterized by dyspnoea at rest and cyanosis as a manifestation of arterial hypoxaemia; deviations from the normal indices during functional pulmonary tests are significant.

Stages of respiratory insufficiency in chronic diseases of the lungs reflect the changes occurring during the progress of the disease. Stages of latent pulmonary, pronounced pulmonary, and cardiopulmonary insufficiency are normally differentiated.

Treatment. The treatment of respiratory insufficiency includes (1) treatment of the main disease upon which the insufficiency depends (pneumonia, pleurisy with effusion, chronic inflammations in the bronchi and the pulmonary tissue, etc.); (2) removal of bronchospasm and improvement of lung ventilation (giving broncholytics, remedial exercises, etc.); (3) oxygen therapy; (4) pulmonary heart is treated by cardiac glycosides and diuretics; (5) phlebotomy is indicated in the presence of reflex erythrocytosis and congestion in the greater circulation.

Special Pathology

Among the very great number of various diseases of the respiratory organs, most common are inflammatory affections of the bronchi (acute and chronic bronchitis, bronchiectasis), of pulmonary tissue (acute and chronic pneumonia, less frequently destructive affections such as abscess or gangrene of the lungs), and of the pleura (pleurisy, empyema). The lungs are affected selectively only in tuberculosis. The incidence of tuberculosis was high in old times. Certain occupational hazards (silicons and the like) can cause special forms of inflammatory diseases of the lungs provided safety measures are not taken and the exposure becomes chronic. Diseases with a protracted course, and also inadequately treated inflammatory diseases (or in decreased reactivity of the body) can terminate in focal or diffuse pneumosclerosis. Frequent are tumours of the lungs (bronchogenic cancer, metastases into the lungs of cancer tumours of other organs). Pulmonary vessels are also often affected (embolism, lung infarction); these affections may also include affections due to foreign bodies of the bronchi, injuries to the lung (contusion, compression, etc.), congenital abnormalities (cysts, etc.), and genetically determined systemic diseases with lung affections (mucoviscidosis, deficit of alpha-1-antitrypsin, etc.); comparatively often occur allergic diseases (bronchial asthma), and many other pulmonary pathologies.

Bronchitis

Bronchitis is inflammation of the bronchi. The disease stands first in the list of respiratory pathologies and occurs mostly in children and the aged.

Primary and secondary bronchitis are distinguished. In primary bronchitis, inflammation develops as the primary process in the bronchi. Secondary bronchitis attends other diseases, such as influenza, whooping cough, measles, tuberculosis, chronic diseases of the lungs and the heart. According to the type of the inflammatory reaction bronchitis is subdivided into catarrhal, mucopurulent, purulent, fibrinous, and haemorrhagic. Bronchitis can also be focal or diffuse, depending on the localization of inflammation. Inflammatory process can reside only in the trachea and large bronchi (tracheobronchitis), the bronchi of the fine and medium calibre (bronchitis), or in the bronchioles (bronchiolitis, occurring mostly in infants). According to the course of the disease, acute and chronic bronchitis are differentiated.

ACUTE BRONCHITIS

Aetiology and pathogenesis. Acute bronchitis can arise (1) in acute infectious diseases, such as influenza, whooping cough, measles, and the like; (2) in chills which decrease the body's resistance to microbes (saprophytes) that are present in the upper air ways, i.e. pneumococci, pneumobacilli (Klebsiellae), streptococci, etc. Mechanical and chemical factors, such as coal, cement or lime dusts, formaldehyde, acids, or acetone may promote the onset of the disease. Asthenia (especially after grave diseases) and chronic sinusitis and rhinitis are also predisposing factors to the development of acute bronchitis.

Pathological anatomy. The disease begins with hyperaemia and swelling of the bronchial mucosa, hypersecretion of mucus and diapedesis of leucocytes; then follows desquamation of epithelium and formation of erosions; in grave bronchitis, inflammation may involve the submucous and muscular layers of the bronchial walls and peribronchial interstitial tissues.

Clinical picture. The patient feels discomfort in the throat and retrosternal smarting. The voice becomes hoarse, the patient feels weakness, and excess perspiration develops. Cough is first dry or with expectoration of scant tenacious sputum; cough may be coarse, resonant, sometimes barking; it may come in excruciating attacks. Sputum is expectorated on the second or the third day of the disease. First it is mucopurulent, sometimes with streaks of scarlet blood; then it becomes purulent; coughing gradually subsides and softens.

The body temperature in focal bronchitis is normal or subfebrile; in grave diffuse bronchitis it may rise to 38-39 °C. The respiration rate in-

creases insignificantly; it can only accelerate to 30-40 per minute in diffuse affections of fine bronchi and bronchioles. Dyspnoea and tachycardia develop.

Percussion sounds over the lungs are usually unchanged. Auscultation reveals harsh breathing and dry buzzing and whistling rales, which often change their character and amount after cough. During resolution of inflammation in the bronchi, tenacious sputum is thinned by the action of proteolytic enzymes contained in it, and moist dulled rales may be heard together with dry rales. X-ray examination in acute bronchitis does not reveal any changes. The leucocyte count of the blood may rise to 9000-11 000 in one microlitre. ESR slightly increases. The sputum is mucous or mucopurulent, sometimes with streaks of blood; it contains columnar epithelium and other cell elements. Fibrin clots (bronchial casts) are expectorated in acute fibrous bronchitis.

Course. The patient usually recovers in two or three weeks. Under the effect of some aggravating factors, such as smoking or chilling, or in the absence of timely treatment, the disease may run a protracted course or become complicated with bronchopneumonia.

Treatment. Antibiotics and sulphonamides, broncholytics (ephedrine or isoprenaline) in combination with expectorants, e.g. thermopsis infusion (1:200), a tablespoonful three times a day, alkaline inhalations and other remedies are prescribed. Antibiotics and broncholytics should better be taken as aerosols. Also recommended are cups, mustard plasters and compresses on the chest, foot baths.

Prophylaxis. Hardening of the body (cool showers, bathing); removal of irritants of the upper air ways (smoking, occupational hazards) and treatment and prevention of chronic diseases of the nose and throat.

CHRONIC BRONCHITIS

Chronic bronchitis is chronic inflammation of the bronchi and bronchioles.

Aetiology and pathogenesis. Infection is an important factor in development and further course of the disease. Chronic bronchitis may develop after acute bronchitis or pneumonia. Chronic occupational inhalation of dusts or chemicals, and also residence in cities with moist climate and frequent fluctuations of the weather conditions, are also predisposing factors. No less important factor for the development of chronic bronchitis is smoking: bronchitis occurs in 50—80 per cent of habitual smokers while its incidence among non-smoking population is only 7-19 per cent. Autoimmune allergic reactions occurring due to absorption of products of protein decomposition (that are formed in the lungs in inflammatory foci) are important factors for persistent chronic bronchitis.

Pathological anatomy. At the early stage of the disease, the mucosa is plethoric, cyanotic, and hypertrophic at some points. Mucous glands are hyperplastic. Inflammation eventually involves the submucous and muscle layers, where cicatricial tissue develops. The mucosa and cartilaginous lamina become atrophied. Bronchial walls become thin to increase the lumen and to cause bronchiectasis. The peribronchial tissue can also be involved in the process with subsequent development of interstitial pneumonia. Interalveolar septa become gradually atrophied and lung emphysema develops; the number of capillaries of the pulmonary artery decreases. Muscular hypertrophy of the right ventricle and also right-ventricular incompetence may join the pulmonary insufficiency.

Clinical picture. The picture of chronic bronchitis depends on the degree of bronchial involvement and on the depth of affection of the bronchial wall. The main symptoms of chronic bronchitis are cough and dyspnoea. Cough may differ in character and change depending on the season and weather. In dry weather, especially in summer, cough is mild and dry, or it may be absent. At increased air humidity and in rain, cough intensifies, while in the cold season it becomes persistent and intense, with expectoration of tenacious mucopurulent or purulent sputum. Sputum is sometimes so thick that it is expectorated in the form of fibrinous bands that look like casts of the bronchial lumen (fibrinous bronchitis).

Dyspnoea in chronic bronchitis is not only due to the lung hypoventilation but also due to lung emphysema that develops as a secondary process. The character of dyspnoea is mostly mixed. First difficult breathing occurs only during exercise such as ascending a hill or upstairs. Further dyspnoea becomes more pronounced. In diffuse inflammation of fine bronchi, dyspnoea becomes expiratory. The disease may be attended by the general symptoms such as weakness, rapid fatigue, excess perspiration; temperature rises in exacerbation of bronchitis.

Inspection, palpation and percussion of the chest, and also X-ray examination do not reveal any changes in non-complicated chronic bronchitis. In grave chronic bronchitis, when pneumosclerosis, pulmonary emphysema, and cardiopulmonary insufficiency attend the main process, accessory muscles become actively involved in the respiratory act, the neck veins become swollen, and cyanosis develops. In this case percussion of the lungs gives a bandbox sound; mobility of the lower border of the lung is limited. Breathing can be vesicular, harsh, or (when emphysema develops) weakened vesicular. Buzzing and whistling dry (less frequently moist) rales are also heard on auscultation.

The blood picture only changes in exacerbation of bronchitis. The changes include increased leucocyte counts and accelerated ESR.

Sputum of a patient with chronic bronchitis is mucopurulent or purulent. In putrefactive bronchitis, sputum is greenish-brown or brown because of decomposed blood; the smell is offensive. Microscopy reveals a great number of leucocytes, degrading erythrocytes, and ample coccal flora.

X-ray examinations in chronic bronchitis, complicated by developing pneumosclerosis or lung emphysema, reveal signs of these diseases. Deformation of the bronchi may be revealed on bronchography. Bronchoscopy gives a picture of atrophic (less frequently hypertrophic) bronchitis (with thinning or swelling of the bronchial mucosa).

Course. The course of chronic bronchitis varies. It may persist for many years, but the signs of the anatomical and functional changes are mildly pronounced. In other patients chronic bronchitis progresses slowly to give exacerbations on chills and during epidemic outbreaks of influenza, or under the effect of some occupational hazards. Recurrent bronchitis and peribronchitis give bronchiectases and often pneumonia. Obstruction of bronchial patency provokes the development of emphysema and cardiopulmonary insufficiency.

Treatment. In chronic bronchitis treatment is aimed at eradication and subsequent prevention of exacerbations (the patient should be kept under regular medical observation). The inflammatory process in the bronchi should be removed. In aggravation of chronic bronchitis sulpha drugs (sulphadimethoxin, 1— 1.5 g a day and ethasol syn. sulphaethidole) and antibiotics are prescribed. If the disease is protracted and aggravated by asthma, broncholytics are given in addition. Corticosteroids, which have anti-allergic and anti-inflammatory action, are given in some cases. To lessen cough, antitussives (codeine and libexin) and expectorants (thermopsis infusion, 1.0:200.0, a tablespoonful 3-4 times a day) are prescribed. Harmful occupational and domestic factors (smoking in particular) should be removed.

Climate therapy favours recovery. Warm marine climate is especially helpful.

Prophylaxis consists in removal of harmful factors provoking the onset of inflammation of the bronchi (e.g. smoking), improvement of working conditions (especially in industry where air may be contaminated with dusts, etc.), treatment of chronic diseases of the upper airways, and strengthening the organism's defence forces (hardening by cool showers, swimming, exercises, walks, etc.).

Bronchial Asthma

Bronchial asthma is an allergic disease which is manifested by paroxysmal attacks (Gk *asthma* panting).

Aetiology and pathogenesis. Bronchial asthma is a polyaetiological disease. It can be provoked by external agents (exogenic allergens) and internal causes (endogenic allergens that usually depend on the infections of the airways). Non-infectious allergic (atopic) and infectious-allergic asthma are distinguished accordingly.

Attacks of asthma can be provoked by various odours, such as those of flowers, hay, perfumes, petrol, carpet or pillow dusts, moulds (in damp rooms), the smell of ursol dyes, asbestos dust; by some foods such as eggs, crabs, strawberries (food asthma), and medicinal preparations. An attack of asthma can sometimes be provoked not by the allergen itself but by memory of it or by remembrance of the conditions under which the allergen acted in the past. The patient can develop an asthmatic attack when he reappears in a certain room or a house or street, where he once had an attack, or even by remembrance of this particular room, house, street, etc.

Endogenic allergens causing attacks of asthma include microbial antigens that are formed during various inflammatory processes, such as sinusitis, chronic bronchitis, chronic pneumonia, etc. Products of decomposition of microbes and tissue proteins forming due to proteolytic process at the inflammatory focus can act as allergens.

Asthma is an allergic disease in which the body is sensitized mainly by the substances of protein nature; other substances and effects can also provoke the disease.

The allergen becomes active in the body only under certain conditions. Bronchial asthma and its attacks develop when the body's reactivity is changed. An important factor promoting sensitization of the body and pathological reactivity is the hereditary-constitutional factor. Climate is also important in this respect. For example, attacks of asthma more often occur during spring or autumn; they can be removed in certain climatic zones, e.g. in highland conditions, or, on the contrary, they may be intensified. Attacks are more likely to occur in cold and damp weather. Pathological response of the parasympathetic nervous system to stimuli received from various exteroceptors and interoceptors, hyperexcitation of the vagus nerve centres, development of pathological reactions in the afferent receptors of the bronchial walls and their hypersensitivity to local irritants are also important factors in the development of asthma attacks. There is evidence of the importance of partial β-adrenergic blockade in the pathogenesis of bronchial asthma and reduced activity of cyclic adenosine monophosphate (intracellular mediator) during attacks of the disease. Finally, certain hormonal shifts are also important, which in the first instance is connected with the adrenal glands. This is confirmed, in particular, by the favourable effect of corticosteroid therapy on the course of the disease.

It has recently been established that attacks of asthma are provoked by an allergic reaction occurring in the bronchial tissue. Three stages in the course of an attack of atopic bronchial asthma, which proceeds as an allergic reaction of the immediate type, are distinguished. In the first (immunological) stage the antigen combines with the specific antibodies

reagins (the IgE class compounds fixed mainly on mast, plasma, and lymph cells); in the second (pathochemical) stage histamine, serotonin, a slow-acting substance anaphylactin, and other biologically active substances are released from these cells as a result of degranulation and alteration; in the third (pathophysiological) stage, spasms develop in the bronchi along with the exudative reaction and oedema of the bronchial mucosa, as the result of the action of the above mentioned substances. An attack of an infectious-allergic asthma develops in the same way, but a delayed (cellular) allergic reaction may be involved in its origination.

Pathological anatomy. Macroscopic study of the lungs of patients who died from an attack of asthma reveals diffuse or irregular focal emphysema. Bronchi contain thick tenacious secretion that clogs the lumen of separate small bronchi and causes atelectasis. The bronchial mucosa is markedly hyperaemic and swollen. Microscopy shows desquamation of the epithelium, thickening of the basal membrane, hypertrophy of the muscular layer and eosinophilic infiltration of the bronchial wall.

Clinical picture. The classical description of bronchial asthma was given in 1838 by G. I. Sokolsky. An attack of allergic asthma begins abruptly and acutely and usually quickly subsides. Attacks of dyspnoea developing against the background of chronic infectious diseases of the respiratory ducts (infectious-allergic asthma) are often not severe but protracted. Signs of chronic bronchitis, pneumosclerosis, and lung emphysema can be revealed in such patients in periods clear of paroxysms.

Attacks of dyspnoea in bronchial asthma are quite similar; they arise suddenly, gradually increase in strength, and last from a few minutes to several hours and even several days. A prolonged attack of asthma is called status asthmaticus. During such an attack, the patient has to assume a forced attitude; he usually sits in bed, leans against his laps, his breath is loud, often whistling and noisy, the mouth is open, the nostrils flare out. The veins of the neck become swollen during expiration and return to norm during inspiration. At the peak of an attack, the patient begins coughing with poorly expectorated thick and tenacious sputum. The chest expands during an attack (to the size of the chest during inspiration). Accessory respiratory muscles are actively involved in the respiratory act. Percussion of the lungs gives the bandbox sound, the lower margins of the lungs are below normal, the mobility of the lower borders is sharply limited during both inspiration and expiration. Auscultation reveals many whistling rales against the background of weakened vesicular respiration with a markedly prolonged expiration. The whistling rales are sometimes heard even at a distance. Tachycardia is usually observed. The borders of complete dullness of the heart cannot be determined because of the acute inflation of the lungs. By the moment the attack abates the sputum thins and expec-

toration becomes easier: high and dry rales in the lungs determined by auscultation decrease to give ways to low buzzing and often moist non-consonant rales of various calibres; the attack of dyspnoea gradually abates.

Blood test during attacks shows moderate lymphocytosis and eosinophilia. The sputum contains 40 to 60 per cent of eosinophils and often Curschmann spirals and Charcot-Leyden crystals.

X-ray examination of the thoracic organs during an attack of asthma shows high translucency of the lung fields and limited mobility of the diaphragm.

Patients with uncomplicated bronchial asthma have no complaints in the periods clear of attacks. Physical, X-ray, and laboratory examinations reveal no changes except eosinophilia of the blood.

Course. Attacks of asthma sometimes occur very rarely (once a year or even several years). Some patients develop a more severe course with frequent and grave attacks. Concurrent chronic bronchitis, pneumosclerosis, and emphysema of the lungs cause the corresponding changes detectable by routine examinations; cardiopulmonary insufficiency gradually develops. In rare cases the patient may die during an attack.

Treatment. The provoking factor should be first identified and eliminated whenever possible. The removal of the causative stimulus will prevent the development of the disease. The allergen can be identified by sensitivity skin tests using suspected substances in special allergological laboratories. Once the allergen is known, desensitization should be attempted. Foci of infection should be treated in infectious-allergic asthma (bronchitis, bronchiectasis, sinusitis, etc.). Unfortunately it is not always easy to remove the cause of bronchial asthma or to carry out effective pathogenic therapy. Symptomatic therapy should then be given to remove or prevent attacks of asthma.

An attack of asthma can be removed by subcutaneous injections of 0.2-1 ml of a 0.1 per cent adrenaline hydrochloride solution or 1 ml of a 5 per cent ephedrine solution. Euphylline (aminophylline) is given intravenously. Broncholytics are also prescribed (inhalations included). A protracted status asthmaticus is an indication to corticosteroid therapy. To prevent attacks of bronchial asthma, broncholytics are given in courses. Remedial exercises and health-resort therapy are also indicated.

Acute Pneumonia

Pneumonia is an acute inflammation of the lungs developing either independently or as a complication in other diseases. Pneumonia is prominent among other diseases of the internal organs. It prevails in epidemic in-

fluenza. Men are more susceptible to the disease than women; it is especially severe in children and elderly patients.

An aetiological classification of pneumonia has been adopted. Differentiated are bacterial pneumonia (pneumococcal, staphylococcal, streptococcal, etc.), virus (caused by the influenza virus, viruses or ornithosis, psittacosis), mycotic (candidiasis, etc.) and pneumonia caused by irritating gases, vapours, dusts, etc. It has long been established that the clinical aspects of bacterial pneumonia somewhat vary depending on the initial body's reactivity. This mainly refers to pneumonia caused by pneumococcus, especially of types I and II. Sometimes the disease is hyperergic, which accounts for its special acuity, cyclic character of its course, frequent affection of the whole lobe of the lung (with involvement of the pleura) and a special character of effusion due to a markedly impaired permeability of the vessel wall (the presence of fibrin and erythrocytes in the effusion). As distinct from more frequently occurring bronchopneumonia (syn.: focal, catarrhal, lobular pneumonia), this pneumonia is called croupous (syn.: acute lobar, fibrinous pneumonia, pleuropneumonia). Pleuropneumonia was formerly diagnosed very frequently but now it rarely occurs in its typical form.

BRONCHOPNEUMONIA (FOCAL PNEUMONIA)

Separate lobules of the lungs are affected in bronchopneumonia, hence another name, lobular pneumonia. Inflammatory foci may be multiple, or they may fuse (confluent pneumonia); the foci may be located in various parts of both lungs simultaneously (mostly in the lower parts of the lungs).

Aetiology and pathogenesis. Quite varied bacterial flora would be normally found in bronchopneumonia. The wide use of antibiotics has changed the proportion of microbes that are found in pneumonia. The importance of pneumococci has significantly decreased while the role of other microorganisms, especially of streptococci and staphylococci, has increased. Acute pneumonia is caused in many cases by viruses (in influenza, ornithosis, and psittacosis).

In addition to the infectious factor, predisposing conditions are also very important. They decrease the immunological properties of the body (overcooling, acute respiratory diseases, etc.). Bronchopneumonia can develop against the background of chronic diseases of the lungs (bronchiectasis, chronic bronchitis) due to haematogenic infection in purulent inflammatory diseases (sepsis, after operations, etc.). Aged patients with long-standing and severe diseases or subjects with plethoric congestion of the lungs can develop hypostatic pneumonia. Aspiration of foreign bodies (food, vomitus, etc.) causes aspiration pneumonia. Inhalation of suf-

focating or irritating gases or vapours (benzene, toluene, benzine, etc.) or other toxic substances can also provoke the onset to bronchopneumonia. The aetiological factor is often decisive for the clinic and course of pneumonia, but irrespective of aetiology, there are always some general signs of the disease.

Development of bronchopneumonia is associated with the extension of the inflammatory process from the bronchi and bronchioles to the pulmonary tissue (hence another name of bronchopneumonia—catarrhal pneumonia, which reflects the transition of inflammation and infection with the mucous secretion from the inflamed bronchi into the alveoli). Infection gets inside the pulmonary tissue via the bronchi, and more frequently peribronchially, i.e. by lymph ducts and interalveolar septa. Local atelectasis that occurs in obstruction of the bronchus by a "mucopurulent plug" (N. Filatov) is important in the pathogenesis of bronchopneumonia. Obstruction of bronchial patency can be caused by a sudden bronchospasm and oedema of the bronchial mucosa, inflammation (bronchitis), etc. Recently bronchopneumonia occurs mostly in children and the aged, usually during cold seasons (spring, autumn, winter).

Pathological anatomy. The microscopic picture of inflammatory foci in bronchopneumonia is quite varied because of the different persistence of the foci. The alveoli at the site of inflammation are filled with serous or mucous effusion containing large amounts of leucocytes. If bronchopneumonia is associated with influenza, microscopy shows the rupture of fine vessels. In confluent pneumonia, the inflammatory foci fuse together to involve several segments or even the whole lobe of the lung.

Clinical picture. The onset of the disease is usually overlooked because it often develops against the background of bronchitis or catarrh of the upper airways. The findings of physical examination of the patient at the onset of bronchopneumonia are the same as in acute bronchitis. Sites of consolidated tissue are often small and difficult to reveal by X-ray examination. But if a patient with clinical signs of acute bronchitis develops high temperature and has symptoms of a more severe disease, he should be considered to have bronchopneumonia (M. Konchalovsky).

The most typical signs of bronchopneumonia are cough, fever, and dyspnoea. If the inflammatory focus is at the periphery of the lung and the inflammation involves the pleura, pain in the chest during coughing and deep breathing may occur. Fever may persist for various terms in bronchopneumonia. Usually fever is remittent and irregular. The temperature is often subfebrile or it may even be normal in the middle-aged or old patients.

Objective examination can sometimes reveal moderate hyperaemia of the face and cyanosis of the lips. Respiration accelerates to 25—30 per min;

respiratory lagging of the affected side of the chest may be observed. Percussion and auscultation may prove ineffective if the inflammatory foci are small and deeply located. In the presence of a large focus, especially if it is located at the periphery of the lung tissue, and also in confluent pneumonia, the percussion sounds lose resonance (or become completely dull), and auscultation reveals vesiculobronchial or bronchial breathing. Vocal fremitus and bronchophony are characteristic of such cases. Dry and moist rales are frequent, but consonating moist rales and crepitation that are heard over a limited part of the chest are especially informative. X-ray examination reveals indistinct densities; in confluent pneumonia densities are spotted (mostly in the lower portions of the lungs). The shadows of the lung roots may be expanded due to enlarged lymph nodes. X-ray examination of the lungs reveals focal inflammations at least 1—2 cm in diameter; very small and separated foci of consolidated lung tissue are undeterminable; therefore in the absence of the X-ray signs of pneumonia the diagnosis of bronchopneumonia cannot be rejected in the presence of clinical symptoms.

Sputum is mucopurulent, first tenacious but later more thin, sometimes there are traces of blood, but it is not rusty. It contains a great number of leucocytes, macrophages and columnar epithelium. Bacterial flora is varied and ample. But it is scant in virus pneumonia. The blood count shows mild neutrophilic leucocytosis, a certain shift to the left, and a moderately increased ESR.

Course. Bronchopneumonia is usually more protracted and flaccid than pleuropneumonia. Prognosis is favourable with appropriate treatment. But the disease can transform into its chronic form. Bronchopneumonia can be aggravated by abscess of the lung and bronchiectasis.

ACUTE LOBAR PNEUMONIA

Aetiology and pathogenesis. All authors who studied the aetiology of acute lobar pneumonia (pleuropneumonia, crupous pneumonia), discovered Frenkel pneumococci (mostly types I and II, less frequently types III and IV) in about 95 per cent of cases. Fridlaender diplobacillus, Pfeiffer's bacillus, streptococcus, staphylococcus, etc. are found less frequently.

Acute lobar pneumonia occurs mostly after severe overcooling. The main portal of infection is bronchogenic, less frequently lymphogenic and haematogenic. Congestion in the lungs in cardiac failure, chronic and acute diseases of the upper airways, avitaminosis, overstrain and other factors promote the onset of pneumonia. Acute lobar pneumonia is relatively fre-

quent in patients who had pneumonia in their past history (it recurs in 30-40 per cent of cases which is another evidence of the hyperergic character of the disease).

Pathological anatomy. Four stages are distinguished in the course of acute lobar pneumonia. The stage of *congestion* is characterized by acute hyperaemia of the lung tissue, exudation, obstruction of capillary patency, and stasis of the blood. It lasts from 12 hours to 3 days. The stage of *red hepatization* continues from 1 to 3 days. The alveoli are filled with plasma rich in fibrinogen and erythrocytes: The stage of *grey hepatization* is characterized by cessation of erythrocyte diapedesis; the erythrocytes contained in the exudate decompose and their haemoglobin converts into haemosiderin. The alveoli (containing fibrin) become filled with leucocytes. The lungs become grey. The stage lasts from 2 to 6 days. The last stage is *resolution.* Fibrin is liquefied by proteolytic enzymes and exudate is gradually resorbed.

Clinical picture. *The onset of the disease.* Typical acute lobar pneumonia begins abruptly with shaking chills, severe headache, and fever (to 39-40 °C). The chills usually persist for 1-3 hours, then pain appears in the affected side; sometimes it may arise below the costal arch in the abdomen to simulate acute appendicitis, hepatic colics, etc. (this usually occurs in inflammation of the lower lobe of the lung, when the diaphragmal pleura becomes involved in the process). Cough is first dry and in 1-2 days rusty sputum is expectorated. The patient's general condition is grave.

General examination shows hyperaemia of the cheeks, more pronounced on the affected side, dyspnoea, cyanosis, often herpes on the lips and nose; the affected side of the chest lags behind in the respiratory act. Vocal fremitus is slightly exaggerated over the affected lobe. Sounds over the lungs are quite varied and depend on the distribution of the process, the stage of the disease, and other factors. At the onset of the disease, shortened percussion sound can be heard over the affected lobe, often with tympanic effect because liquid and air are simultaneously contained in the alveoli; the vesicular breathing is decreased while bronchophony is increased; the so-called initial crepitation (crepitus indux) is present.

The *height of the disease* (classified by pathologists as the red and grey hepatization stages) is characterized by the grave general condition. It can be explained not only by the size of the affected area of the lung which thus does not take part in respiration but also by general toxicosis. Respiration is accelerated and superficial (30-40 per min) and tachycardia (100-200 beats per min) is characteristic. Dullness is heard over the affected lobe of the lung; bronchial respiration is revealed by auscultation; vocal fremitus and bronchophony are exaggerated. Vocal fremitus is in some cases either absent or enfeebled (in combination with pleurisy with effusion, and also in massive acute lobar pneumonia, in which the inflammatory exudate fills large bronchi); bronchial breathing is inaudible. Before the antibiotic era, the patient with acute lobar pneumonia would often develop vascular

failure with a marked drop in the arterial pressure due to toxicosis. Vascular collapse is attended by general asthenia, drop of temperature, increased dyspnoea, cyanosis, and accelerated and small pulse. The nervous system is also affected (sleep is deranged, hallucinations and delirium are possible, especially in alcoholic patients). The heart, liver, kidneys and some other organs are also affected. Fever persists for 9-11 days if antibiotics or sulpha drugs are not given. The temperature then drops either abruptly during 12-24 hours or lytically, during more than 2-3 days.

Resolution stage. The exudate thins, air again fills the alveoli to decrease dullness of the percussion sound, tympany increases, and bronchial breathing lessens. Crepitation is heard again (crepitus redux) because the alveolar walls separate as air fills them. Moist rales are heard. Exaggerated vocal fremitus, then bronchophony, and finally brorlchial breathing disappear. The leucocyte count in the blood increases to $15 \times \times 10^9$-25×10^9 per litre (15 000-25 000 per microlitre); neutrophils account for 80-90 per cent of the leucocytes; a shift to the left with the appearance of juvenile forms is sometimes observed. The number of eosinophils decreases and they can disappear completely in grave cases. Relative lymphopenia and monocytosis are observed. The ESR increases. The red blood does not change.

Sputum is tenacious during the congestion period; it is slightly crimson and contains much protein, a small number of leucocytes, erythrocytes, alveolar cells, and macrophages. In the stage of red hepatization sputum is scant and rusty; it contains fibrin and a higher number of formed elements. In the stage of grey hepatization leucocyte count in the sputum increases significantly; the sputum becomes mucopurulent. In the resolution stage, leucocytes are converted into detritus, which is found in the sputum; many macrophages are also found. Pneumococci, staphylococci, Friedlaender diplobacilli can be detected in the sputum.

X-Ray changes in the lungs depend on the stage of the disease. The lung pattern is first intensified, then dense foci develop, which later fuse. The shadow usually corresponds to the lung lobe (Fig. 24). The lungs become normally clear in two or three weeks. Dynamics of the X-ray changes depends on the time when the therapy is begun.

Course and complications. Fatal outcomes in acute lobar pneumonia were formerly 20-25 per cent. Before antibiotics and sulpha drugs came into wide use, complications (purulent processes in the lungs and pleurisy, usually purulent) were frequent; their incidence has now decreased significantly. If pleurisy develops before resolution of pneumonia, it is called parapneumonic. If it occurs after resolution, it is referred to as metapneumonic pleurisy. Other complications occur as well:

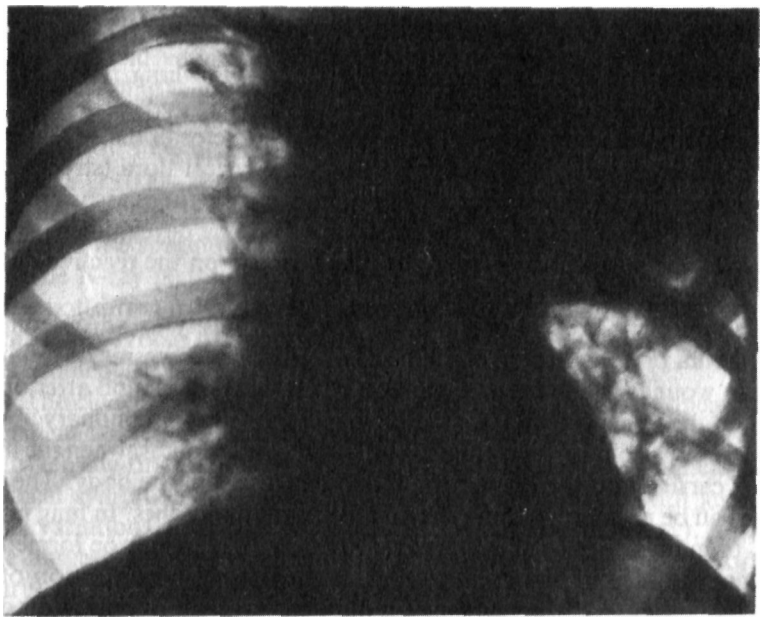


Fig. 24. X-ray of the upper lobe of the left lung in acute lobar pneumonia.

myocarditis, meningitis, and focal nephritis. If resolution of the exudate is delayed, and connective tissue grows into it, cirrhosis of the affected lobe of the lung develops (carnification). Mortality from acute lobar pneumonia has recently decreased significantly.

Treatment of pneumonia. The patient should be hospitalized and kept in bed. Food should be rich in vitamins and easily assimilable. Antibiotics (penicillin, 300000-500 000 units, 4 to 6 times a day intramuscularly, streptomycin, tetracycline, and other antibiotics) and sulpha drugs (sulphadimezine, sulphaethidole, sulphadimethoxine, etc.) are the main preparations for treating pneumonia. Oxygen therapy (an oxygen mask or a tent) is also helpful. It improves metabolism and has a favourable effect on the cardiovascular system. Vascular insufficiency is treated by coffein and camphor; in the presence of heart failure, digitalis and strophanthine preparations are given. Expectorants (thermopsis, etc.) should be given, especially during the resolution of pneumonia; cups, mustard plaster, and physiotherapy accelerate elimination of residual effects of pneumonia. Respiratory exercises are important to improve lung ventilation.

Prophylaxis mainly consists in strengthening and hardening of the body.

Pulmonary Abscess

Pulmonary abscess is a purulent melting of the lung tissue circumscribed by an inflammatory swelling.

Aetiology and pathogenesis. The aetiological factor in the development of a purulent process in the lungs is mostly the coccal flora (streptococci, staphylococci, and pneumococci). The disease is sometimes associated with saprophytic autoinfection of the upper airways. The development and intensity of the purulent process in the lungs depend on the reactivity of the lung tissue and of the entire body.

The purulent process in the lungs develops mostly as an outcome of pneumonia or complicated bronchiectasis. Primary abscesses of the lungs arise in wounds to the chest, aspiration of foreign bodies, and after operations on the upper airways (tonsillectomy and the like). Pulmonary abscess can develop also by a haematogenic or lymphogenic routes, when the infection is carried into the lungs from a purulent focus in the body. The lung tissue can be resorbed without the involvement of microbes. In lung infarction, or in the presence of a degrading tumour, a cavity may be formed due to local disorder in blood circulation. In such cases necrotization of the lung tissue can be the precursor of a purulent process. Suppuration of an echinococcal cyst in the lung can be another cause.

Pathological anatomy. Pulmonary abscesses are characterized by the presence of a single or multiple purulent foci that may be found in one or both lungs. After the abscess opens, a cavity is formed which is surrounded by inflammatory infiltration. Acute abscesses are surrounded by a thin ridge of the inflamed tissue. Chronic abscesses are encapsulated in fibrous tissue.

Clinical picture. Two periods are distinguished: before and after opening of an abscess. *The first period* is formation of the abscess. It continues for 10-12 days, on the average. At the onset of the disease patients complain of general indisposition, weakness, chills, cough with meagre sputum, and pain in the chest. Fever is first moderate but gradually becomes remittent, and then hectic. Dyspnoea develops even in the presence of a small abscess.

Palpation of the chest can in some cases detect painfulness in the intercostal spaces of the affected side. This symptom is associated with involvement in the process of the costal pleura. Unilateral thoracic lagging corresponding to inflammation may be observed. Vocal fremitus depends on the location of the inflammatory focus. It is often exaggerated in peripheral location and remains unchanged in deep location of the inflammatory focus.

Percussion can determine loss of resonance (or dull sound) on the affected side. Auscultation in small deep abscesses does not reveal any abnor-

malities. If the abscess is superficial, respiration over the affected side is decreased and vesicular, sometimes with a bronchial character. In some cases breathing is harsh, and dry rales can be heard.

The blood picture is an important and objective criterion in the diagnosis of lung abscess. Neutrophilic leucocytosis, 15×10^9—25×10^9 per litre (15000-20000 per microlitre), is observed; a shift to the left, to the myelocytes, is also characteristic. The ESR increases significantly. Study of the sputum is not specific before the abscess opens.

The X-ray picture of the abscess during the first period of the disease does not differ from that in common pneumonia or tuberculous infiltration: a large focus of increased density with rough and indistinct margins is determined.

The clinical picture of the *second period* begins with the opening of the purulent abscess into the bronchus. There may be a transitory condition between the first and second periods of the disease during which the main clinical symptoms are intensified (elevated temperature with great circadian variations, heavy cough, dyspnoea, pain in the chest, etc.). Rupture of the abscess into the bronchus is attended by a sudden release of ample purulent sputum ("full mouth"), sometimes with offensive odour, which on standing separates into two or three layers: mucous, serous, and purulent. Further expectorations will depend on the volume of the cavity and vary from 200 ml to 1—2 l a day. Objectively the patient looks feverish. If the pleura is involved, unilateral thoracic lagging is observed on the affected side. After the cavity is free from pus, and depending on its location and size, physical findings may be different. Tympany is determined in the presence of large and superficial abscesses by percussion. Respiration can be either bronchovesicular or bronchial; if a large cavity containing air communicates with the bronchial lumen, respiration can be amphorical. Resonant moist moderate and large bubbling rales are usually heard over a limited area. In the presence of concurrent diffuse bronchitis, intense rales interfere with location of the abscess.

Neutrophilic leucocytosis with a shift to the left and increased ESR are observed. In grave and protracted cases, iron-deficiency (hypoferric) anaemia develops.

On standing, sputum separates into three layers: the upper (foamy and mucous), the middle (liquid, serous) and the bottom layer (pus). Microscopy of the sputum reveals the presence of elastic fibres (in addition to many leucocytes and erythrocytes). The absence of elastic fibres in the sputum indicates termination of degradation of the lung tissue. Bacteriological flora is ample, mostly containing cocci; in the presence of antibiotic therapy the flora is meagre.

X-raying of the emptied abscess shows a specifically increased

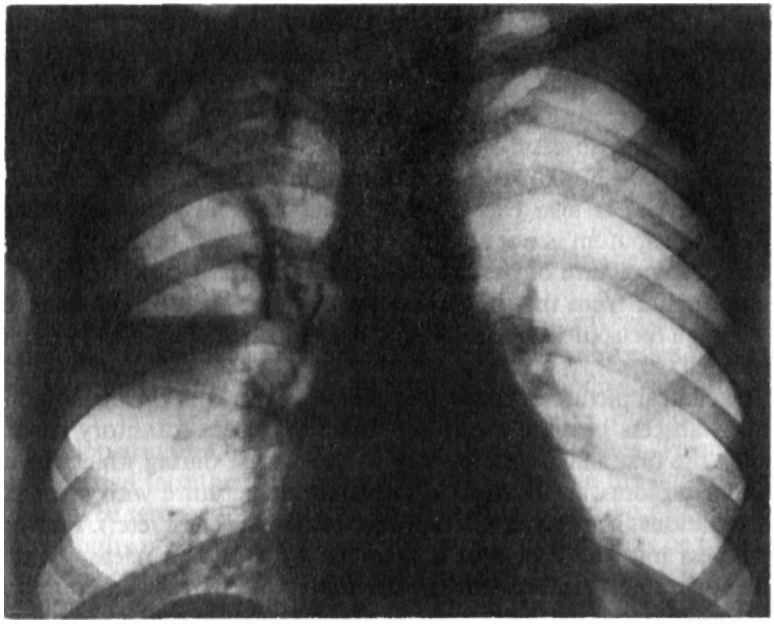


Fig. 25. X-ray of abscess in the right lung.

translucency. Variation of the liquid level (Fig. 25) can be observed with variation of the patient's posture. If the draining bronchus is at the bottom of the cavity (which is common with abscesses of the lung apices), the liquid level is undeterminable (the fluid flows down and is withdrawn through the outlet bronchus). The abscess cavity is surrounded on all sides by a border of inflamed tissue with a diffuse outer contour.

Course. Development of the lung abscess and its healing depend on location of the cavity, conditions for its emptying, and concurrent complications. In most cases abscesses heal with formation of focal pulmonary fibrosis at the site of the common cavity, but in 30-40 per cent of patients recovery is incomplete and the disease becomes chronic. Chronic diseases of the lungs (bronchiectasis, pulmonary fibrosis, etc.) promote a protracted course of pulmonary suppuration. The following complications of the lung abscess are distinguished: (1) rupture of the abscess into the pleural cavity with development of pyopneumothorax; (2) pulmonary haemorrhage; (3) development of new pulmonary abscesses; (4) metastases of the abscesses into the brain, liver and other organs. Complications aggravate the prognosis of the disease.

Treatment. Bed-rest regimen in hospital is necessary. Antibiotics and sulpha drugs should be given as early as possible. Penicillin and strep-

tomycin should be given along with broad-spectrum antibiotics such as tetracycline (0.2-0.3 g 4-6 times a day after meals, oletetrin, etc.). Sulpha drugs (sulphadimidine, sulphadimethoxine, etc.) should be given in sufficiently large doses and for a long period. In addition to peroral or intramuscular administration, antibiotics should be given intratracheally or as aerosols (1-2 times a day for 2-4 weeks). Therapeutic bronchoscopy is widely used to remove pus from the cavity and to administer antibiotics directly into it. Symptomatic treatment consists in prescribing expectorants and broncholytics (ephedrine, drotaverine, and others) which liquefy sputum. Adequate draining is very important for a better emptying of the cavity: the patient should find a posture at which sputum withdrawal is the best and to assume this posture for 30 minutes two or three times a day.

If conservative therapy proves ineffective, surgical treatment should be given in a month or two (earlier, in grave cases). The operation consists in removal of the lobe (or the whole lung if abscesses are multiple).

Pleurisy

Pleurisy is inflammation of the pleura. Dry pleurisy (pleuritis sicca) and pleurisy with effusion (pleuritis exudativa) are distinguished. The character of the inflammatory effusion may be different: serous, serofibrinous, purulent, and haemorrhagic.

Aetiology and pathogenesis. Serous and serofibrinous pleurisy attend tuberculosis (in 70-90 per cent of cases), and pneumonia, certain infections, and also rheumatism in 10-30 per cent of cases. The purulent process in the pleura may be caused by pneumococci, streptococci, staphylococci, and other microbes. Haemorrhagic pleurisy arises in tuberculosis of the pleura, bronchogenic cancer of the lung with involvement of the pleura, and also in injuries to the chest.

Most diseases of the pleura (pleurisy included) are secondary to disease of the lung. Pleurisy usually develops as a reaction of the pleura to pathological changes in the adjacent organs, in the lungs in the first instance, and less frequently as a symptom of a systemic disease (polyserosites of various aetiology). Serous pleurisy often arises as an allergic reaction. Purulent pleurisy is often a complication of bronchopneumonia: inflammation may extend onto the pleura, or an inflammatory focus may turn into an abscess which opens into the pleural cavity. Inflammation of the pleura is always attended by markedly increased permeability of the wall of the affected capillaries of the pulmonary pleura.

Reactivity of the body is a very important factor in the pathogenesis of pleurisy. In fibrinous or dry pleurisy fibrin precipitates from the exudate (which is produced in a small amount) and gradually deposits on the

pleura. Serous pleurisy may become infected to convert into purulent; exudate becomes turbid and contains many leucocytes. In the presence of purulent processes in the lungs or adjacent organs (pericarditis, perioesophagitis, etc.), purulent pleurisy often develops abruptly. The affection of the pleura in tumours, which in most cases are metastatic (less frequently primary), decreases its absorptive function to promote accumulation of pleural effusion (haemorrhagic effusion in most cases).

Pathological anatomy. Dry pleurisy is characterized by thickening of the pleura and deposition of fibrin in it. Pleural membranes become dull and hyperaemic; commissures and sometimes more significant adhesions develop. Pleurisy with effusion is characterized by the presence of exudate in the pleural cavity, mostly in the outer costal-diaphragmatic sinus. Parietal, supradiaphragmatic and interlobar pleurisy also occur. After abatement of inflammation, effusion (serous, serofibrinous, haemorrhagic, purulent) usually resolves but the pleura remains thickened, its membranes adhere to one another, and the pleural cavity is completely obliterated in some cases. Effusion sometimes remains between adhesions to stimulate encapsulated pleurisy.

DRY PLEURISY

Clinical picture. A characteristic symptom of dry pleurisy is pain in the chest which becomes stronger during breathing and coughing. Cough is usually dry, the patient complains of general indisposition; the temperature is subfebrile. Respiration is superficial (deep breathing intensifies friction of the pleural membranes to cause pain). Lying on the affected side lessens the pain. Inspection of the patient can reveal unilateral thoracic lagging during respiration. Percussion fails to detect any changes except decreased mobility of the lung border on the affected side. Auscultation determines pleural friction sound over the inflamed site. X-ray picture shows limited mobility of the diaphragm because the patient spares the affected side of his chest.

The blood picture remains unchanged but moderate leucocytosis is observed in some cases.

Course. Dry pleurisy has a favourable course and the patient recovers completely in one or three weeks.

PLEURISY WITH EFFUSION

Clinical picture. Patients suffering from pleurisy with effusion usually complain of fever, pain or the feeling of heaviness in the side, and dyspnoea (which develops due to respiratory insufficiency caused by compression of the lung). Cough is usually mild (or absent in some cases). The patient's general condition is grave, especially in purulent pleurisy, which is attended by high temperature with pronounced circadian fluctuations,

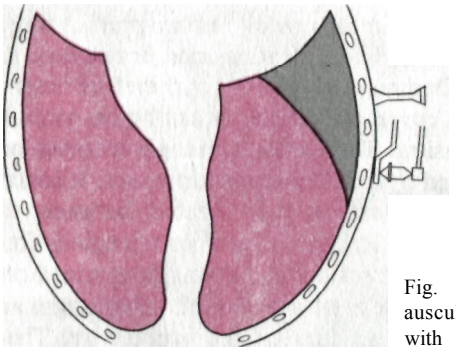


Fig. 26. Percussion and auscultation in pleurisy with effusion.

chills, and signs of general toxicosis. Inspection of the patient reveals asymmetry of the chest due to enlargement of the side where the effusion is accumulated; the affected side of the chest usually lags behind in respiratory movements. Vocal fremitus is not transmitted at the area of fluid accumulation.

Percussion over the area of fluid accumulation produces dullness (Fig. 26). The upper limit of dullness is usually the S-shaped curve (Damoiseau's curve) whose upper point is in the posterior axillary line. The effusion thus occupies the area, which is a triangle both anteriorly and posteriorly. The Damoiseau curve (Fig. 27) is formed because exudate in pleurisy with effusion more freely accumulates in the lateral portions of the

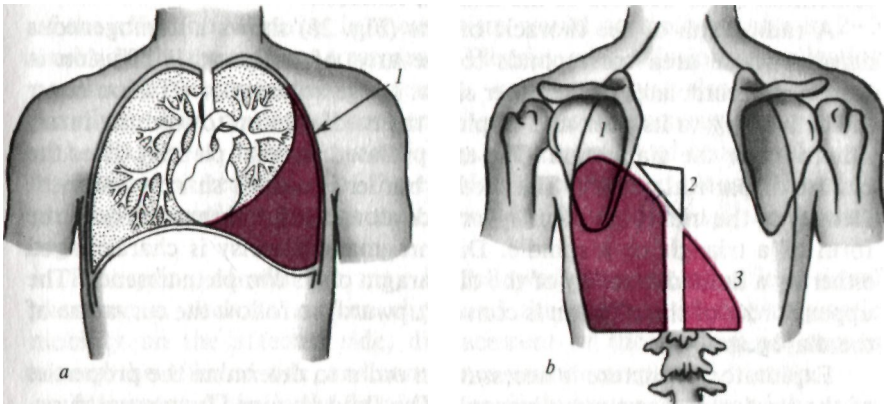


Fig. 27. Pleurisy with effusion.
a—anterior view; *b*—posterior view; 1—Damoiseau's curve; *2*—Garland's triangle; *3*—Rauchfuss-Grocco triangle.

pleural cavity, mostly in the costal-diaphragmatic sinus. As distinct from effusion, which is restricted by adhesions, transudate more freely presses the lung and the Damoiseau curve is not therefore determined. In addition to the Damoiseau curve, two triangles can be determined by percussion in pleurisy with effusion. The Garland triangle is found on the affected side and is characterized by a dulled tympanic sound. It corresponds to the lung pressed by the effusion, and is located between the spine and the Damoiseau curve. The Rauchfuss-Grocco triangle is found on the healthy side and is a kind of extension of dullness determined on the affected side. The sides of the triangle are formed by the diaphragm and the spine, while the continued Damoiseau curve is the hypotenuse. The triangle is mainly due to displacement of the mediastinum to the healthy side. Mobility of the lower border of the lung on the affected side is not usually determined in pleurisy with effusion. Left-sided pleurisy with effusion is characterized by the absence of the Traube space (the left pleural sinus is filled with effusion and a dulled percussion sound is heard over the gastric air bubble instead of the tympany).

Respiration in the region of accumulated effusion is not auscultated, or it can be very weak. Respiration auscultated slightly above the effusion level is usually bronchial which is due to compression of the lung and displacement of air from it. Vocal fremitus and bronchophony over the effusion are not determined because the vibrating walls of the bronchi that conduct voice are separated from the chest wall by the fluid. The heart is usually displaced by the effusion toward the healthy side. Tachycardia is observed. Arterial pressure may be decreased. Dizziness, faints, etc., sometimes occur because of the marked toxicosis.

A radiograph of the thoracic organs (Fig. 28) shows a homogeneous density whose area corresponds to the area of dullness. If effusion is scarce, it accumulates in the outer sinus. Large volumes of effusion cover the entire lung to its apex and displace the mediastinum toward the intact side to lower the diaphragm. The encapsulated parietal pleurisy gives the picture of parietal density. The medial border is usually sharply outlined. Density of the interlobar pleurisy extends along the interlobar sulcus in the form of a triangle or a spindle. Diaphragmatic pleurisy is characterized either by a limited mobility of the diaphragm or its complete absence. The upper border of the effusion is convex (upward) to follow the curvature of the diaphragm.

Exploratory puncture is necessary in order to determine the properties of the exudate for accurate diagnosis. The fluid obtained by pleural puncture is studied at the laboratory.

During the initial stage of the disease the blood picture may show mild leucocytosis (marked leucocytosis is characteristic of purulent pleurisy) and

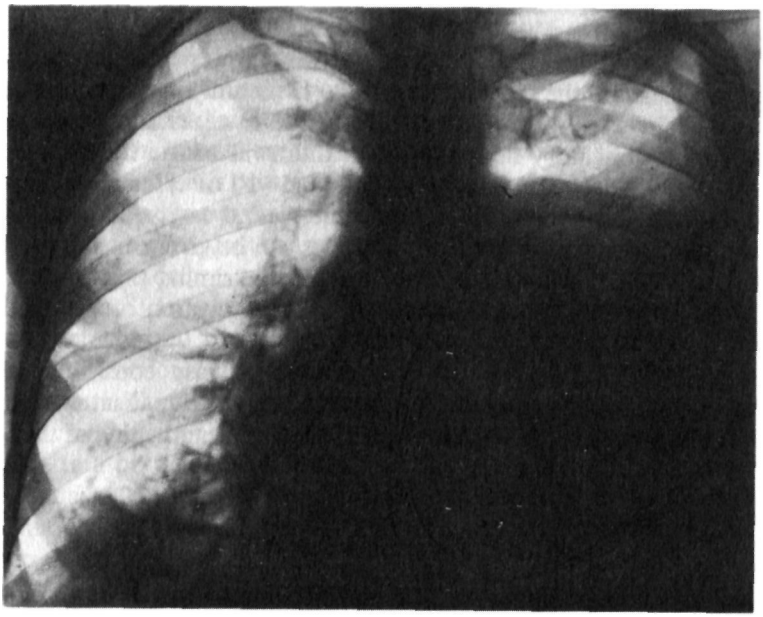


Fig. 28. X-ray of the left lung in pleurisy with effusion.

sometimes eosinophilia. The ESR is increased. Tuberculosis pleurisy is characterized by lymphocytosis, while rheumatic pleurisy by neutrophilosis.

Course. The course of pleurisy with effusion depends on the aetiology of the affection. Pleurisy in rheumatism would normally resolve in 2-3 weeks (with appropriate treatment). Pleurisy with effusion complicating pneumonia (metapneumonic pleurisy, usually serous) also has a comparatively mild course. A protracted course is characteristic of pleurisy with effusion of tuberculous aetiology. Development of coarse adhesions interferes with resorption of the effusion (encapsulated pleurisy), while a prolonged purulent process may result in amyloidosis of the internal organs.

Resorption of effusion may be followed by some specific residual phenomena, such as sunken chest and the absence of diaphragmatic mobility on the affected side, displacement of the mediastinal organs toward the affected side, and sometimes permanent pleural friction.

Treatment. This, in the first instance, includes the therapy of the main disease, such as rheumatism (salicylates, amidopyrine, corticosteroids), pneumonia (sulpha drugs, and antibiotics), tuberculosis (PASA, phthivazide, streptomycin, canamycin, and others). Symptomatic therapy

includes general strengthening (vitamins, etc.), desensitizing preparations, and high-calorie diet. Thermal procedures (compresses, diathermy) are useful to accelerate the resolution process. If pleural fluid is not resorbed during 2—3 weeks, evacuation of the effusion is necessary. Purulent exudate should obligatory be removed. Withdrawal of the fluid should be slow to avoid collapse or faint. As a rule, 0.5-1 1 of effusion is removed and antibiotics are injected instead into the pleural cavity. In order to accelerate resorption of the effusion, diuretics can be given. In the presence of cardiac failure, cordiamine, strophanthine and similar preparations are indicated. To prevent pleural adhesion during resorption of the exudate, remedial exercises should be prescribed.

Prophylaxis. Prevention of serofibrinous pleurisy consists in early diagnosis and active treatment of tuberculosis, rheumatism and other diseases which may provoke pleurisy, and also in strengthening of the body (exercises, cool shower, etc.).

Chronic Pneumonia

Aetiology and pathogenesis. Chronic pneumonia often develops as a result of protracted bronchopneumonia. Its development is facilitated by frequent recurrent inflammations in the bronchi and the lungs, influenza epidemics, inhalation of harmful chemicals, smoking, etc. Involvement of auto-immune processes helps conversion of acute and subacute diseases of the lungs into the chronic form. In most cases no specific causative agents are found in chronic pneumonia; streptococci, staphylococci, and pneumococci would be usually revealed by inoculation tests. If pneumonia is cured incompletely, the inflammatory process becomes slow (interstitial pneumonia) to give finally focal or diffuse pneumosclerosis. Bronchiectasis is formed in such patients, or they may develop emphysema and respiratory insufficiency.

Pathological anatomy. Areas of chronic inflammation in the lungs are observed along with the growth of connective tissue (focal or diffuse). Inflammatory changes may involve the bronchial walls and pleura; pulmonary vessels become stenosed and even obliterated.

Clinical picture. Many patients with chronic pneumonia (especially the aged) may have normal temperature, the amount of expectorated sputum may be small, and there may be no changes in the blood. Dyspnoea, subfebrile temperature, permanent cough with expectoration of purulent or mucopurulent sputum, mild leucocytosis are found in some patients. Percussion may fail to reveal loss of resonance over the affected side due to a concurrent emphysema. Auscultation of the affected side reveals fine and moderate moist rales, sometimes againts the background of dry diffuse

rales. X-ray examination is important: the interlobar septa are thickened, the lung pattern in the region of the inflammation is intensified, and the lung root is changed (enlarged lymph nodes).

The **course** of the disease is usually protracted and slowly progressing. Three stages of the disease are distinguished in this country. The first stage of chronic pneumonia is protracted pneumonia (lasting over 6 weeks) and chronic bronchitis concurrent with relapsing pneumonia. The second stage is characterized by frequent exacerbations of the inflammation in the lungs alternating with more or less prolonged remissions in the presence of symptoms of pneumosclerosis, lung emphysema and bronchiectasis. The third stage is characterized by marked symptoms, frequent exacerbations and pronounced functional disorders of external respiration and circulation.

Treatment. Combined treatment is necessary. Broad-spectrum antibiotics should be used with their frequent alternation to prevent microbial resistance to a particular antibiotic. For example, oletetrin is given per os for 5-10 days (250 mg 4-6 times a day), then it is replaced by the sodium salt of ampicillin (250—500 mg 4-6 times a day intramuscularly). Combination of antibiotics with sulpha drugs is effective. Bronchial draining is necessary in addition to the antibiotic therapy. It can be stimulated by giving expectorants, such as thermopsis preparations or ammonium chloride. In certain cases, corticosteroids are prescribed together with antibiotics to suppress auto-immune processes.

Bronchiectasis

This is a condition characterized by dilatation of the bronchi. Bronchiectatic conditions are divided into primary (congenital, which are very rare) and secondary (secondary to various diseases of the bronchi, lungs and pleura).

As an independent (and frequently occurring) disease bronchiectasis has a specific clinical picture. It develops as a result of infection of bronchiectases and in the presence of chronic inflammation in them. Bronchiectasis may also be regarded as a form of chronic non-specific pneumonia. The disease occurs at any age, but more commonly between the ages of 20 and 40. The incidence among men is 6-7 times higher than it is in women.

Aetiology and pathogenesis. Inflammation of bronchi and development of bronchiectasis in children can be the result of repeated acute bronchitis, whooping cough, measles, diphtheria, and sometimes tuberculous bronchoadenitis. Bronchiectases in youths and adults are formed due to acute diffuse bronchitis that develops against the background of chronic relapsing bronchitis, non-resolved pneumonia, and also lung abscess, in recurrent pneumonia, and pulmonary tuberculosis. Bronchiectases develop

in bronchitis only when the inflammatory process extends onto the muscular layer of the bronchial wall or onto all its layers. Muscle fibres are destroyed, the bronchus tone is lost at this area and its walls become thin. The absence of ciliated epithelium at the inflamed portions of the bronchus promotes accumulation of sputum in its lumen, upsets its draining function, and thus stimulates chronic inflammation. The inflamed site is first granulated but later connective tissue develops which disfigures the bronchus. Severely affected portions of the bronchi dilate during intense coughing.

Pathological anatomy. Cylindrical, saccular, and fusiform bronchiectases are differentiated. They are mostly located in the lower lobes of the lungs. Severely affected bronchial walls are markedly destroyed. Inflammatory infiltration, granulation, and mature cicatricial tissues are found in these portions of the bronchi. Capillaries, arterioles, and smaller arteries of the bronchi are affected and blood flow in them is disturbed. Nerve endings and branches of the vagus that innervate the bronchus are also affected. Inflammation spreads onto the interstitial peribronchial tissue of the lung, as a rule.

Clinical picture. This depends on the size of bronchiectases, their location, the degree of affection, and activity of the inflammatory process, the presence of emphysema of the lungs, and the degree of functional disturbances of external respiration. If bronchiectasis affects the upper lobes of the lungs, the draining function of the bronchi remains intact, or is mildly affected. If bronchiectases are located in the lower lobes of the lung, sputum is expectorated with difficulty to account for persistence of the inflammatory process.

The main symptom is cough with expectoration of seromucopurulent (three layers) or purulent sputum (sometimes foul-smelling). The daily amount of expectorated sputum varies from 50 to 500 ml and more. Blood streaks may be seen. Cough is paroxysmal in character and occurs mainly in the morning. The sputum accumulated during the night sleep irritates the sensitive nerve endings of the bronchial mucosa (due to alterations in posture). The sputum expectorated in the morning makes two thirds of the daily amount. Cough during the daytime is infrequent, and depends on accumulation of the sputum in the bronchiectases. Cough and expectoration of the sputum may also occur when the patient assumes the posture that stimulates the draining function of the ectatic bronchi. Haemoptysis, dyspnoea, excess sweating, weakness, headache, dyspepsia, deranged sleep and appetite, and wasting can also be observed. Bronchiectatic condition is exacerbated mostly in wet and cold weather: the body temperature rises, leucocytosis develops, and ESR increases. General inspection of the patient reveals acrocyanosis (at later stages of the disease) and oedematous face; in some cases the terminal phalanges of the fingers become clubbed (Hippocratic fingers), and the nails resemble the watch glass. The chest is of

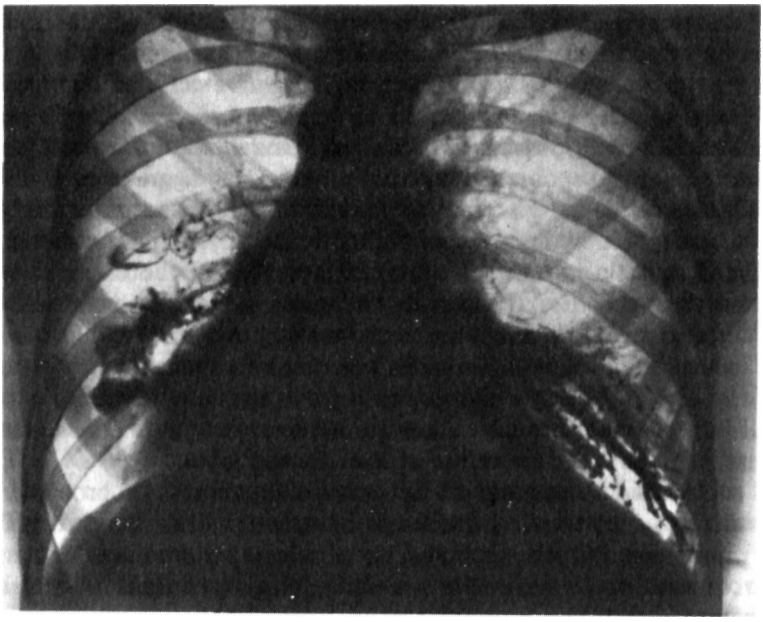


Fig. 29. Bilateral bronchiectasis.

normal shape or emphysematous. Unilateral thoracic lagging occurs in the presence of unilateral bronchiectasis. Percussion sound is usually pulmonary, with a bandbox tone (due to a concurrent emphysema), less frequently with a tympanic tone (over the bronchiectatic area). The mobility of the lower border of the lung can be limited. Respiration is usually harsh or decreased vesicular (due to emphysema). Dry and sometimes fine and moderate bubbling non-consonant rales are heard over the bronchiectatic area. Pleural friction can be heard if inflammation extends onto the pleura and in the presence of pleural adhesions.

X-ray examination shows increased translucency of the lungs, deformation of the lung pattern, and the presence of bands in the lower lobes. Bronchography and tomography reveal the presence of bronchiectases and show their size and shape (Fig.29).

Spirometry shows decreased vital lung capacity. In grave cases it decreases 2 or 3 times. The blood picture shows compensatory erythrocytosis and neutrophilic leucocytosis; the ESR may be increased, while at high erythrocytosis it may be decreased to 1—2 mm/h.

Course. The disease progresses if untreated. Anti-inflammatory therapy can cause a prolonged remission but the process may be exacerbated in a lapse of time (e.g. after overcooling).

Three stages of the disease are distinguished: the initial, moderately pronounced, and terminal. The final stage is characterized by marked changes in the internal organs; chronic right-ventricular heart failure (pulmonary heart), and amyloidosis of the liver, kidneys, and of other internal organs develop. Lung abscess, empyema of the pleura, pulmonary haemorrhage, and spontaneous pneumothorax may aggravate the disease.

Treatment. Broad-spectrum antibiotics are given intramuscularly, intratracheally, and by inhalation. Antibiotic therapy can be combined with sulpha drugs. To imporve the draining function of the bronchi, expectorants, broncholytics (ephedrine, theophedrine, euphylline), and also anti-allergic preparations (in concurrent bronchospasms) should be given. The concomitant right-ventricular heart failure requires active cardiac therapy. Oxygen therapy and respiratory exercises are helpful.

If large saccular bronchiectases are localized only in one lobe, surgical treatment is indicated (resection of the affected lobe).

Prophylaxis. Prevention of the onset and progress of bronchiectasis consists in regular medical check-ups of patients with chronic bronchitis and pulmonary fibrosis, their regular treatment, and control of harmful environmental and other effects (smoking, industrial hazards). Strengthening of the body is also important.

Emphysema of the Lungs

Lung emphysema is characterized by increased airiness of the lungs due to overdistended or destroyed alveoli.

Aetiology and pathogenesis. The most common causes of emphysema of the lungs are obstructive bronchitis, chronic pneumonia, long-standing bronchial asthma, occupational lung diseases, etc. Lung emphysema occurs in mechanical overdistension of the lungs (in musicians playing woodwind and brass instruments) or in heavy physical exertions associated with retention of breath. Advanced age is another predisposing factor.

Pathological anatomy. The pathological changes in lung emphysema are characterized by destruction of interalveolar septa. The alveoli fuse to form bullae (bullous emphysema). The destroyed alveoli are not restored. The lungs are distended and lose elasticity.

Clinical picture. The patient mainly complains of dyspnoea, which at the onset of the disease may only develop during exercise but later it occurs at rest. Dyspnoea increases in cold seasons, in chills, and exacerbations of bronchitis; it is especially pronounced during attacks of cough. Dyspnoea is usually expiratory: a healthy person expires air whereas the patient with emphysema pressess it out from the chest with an effort. The intrathoracic pressure increases during expiration and the neck veins therefore become

swollen. If heart failure concurs, the veins remain swollen during inspiration as well. Inspection reveals oedematous face, cyanotic mucosa, cheeks, nose and the ear lobes; the skin is greyish. The terminal phalanges are often clubbed, and the nails look like watch glass. In long-standing disease, the chest becomes barrel-shaped. Supraclavicular fossa are usually levelled or protrude over the clavicles. The tissues under the clavicles may protrude as well. Accessory muscles are actively involved in the respiratory act. During inspiration the rigid chest seems to rise due to contraction of the accessory muscles. A bandbox sound can be heard on percussion. Descending of the lower borders of the lungs and a limited mobility of the lower borders and the respiratory excursions of the lungs are characteristic of emphysema. Diminished vesicular respiration is heard on auscultation (the sounds are especially weakened in grave cases). In the presence of concurrent bronchitis, diffuse dry rales are heard.

The X-ray picture of the lungs is especially translucent. The lung borders are lowered, the mobility of the diaphragm is markedly limited.

The residual volume increases significantly in emphysema while the maximum lung ventilation and the vital capacity decrease accordingly. The vital capacity may decrease 2.5-3 times and this intensifies the work of the respiratory apparatus (especially the respiratory muscles) and increases the oxygen demand. In order to decrease tissue hypoxia, compensatory mechanisms become actuated: cardiac rhythm is accelerated, the minute blood volume and erythrocyte counts are increased as well (compensatory erythrocytosis). Permanent intense cardiac activity in lung emphysema with insufficient oxygen supply to the heart muscle is a cause of gradually progressing myocardial dystrophy which results finally in the right-ventricular failure. The respiratory insufficiency is then supplemented by heart failure with the specific clinical symptoms. The course of bronchitis and pneumonia in such patients is grave.

Course. Emphysema of the lungs usually progresses slowly. The patient may die from cardiopulmonary insufficiency.

Treatment and prophylaxis. These include treatment of bronchitis and pneumonia (see above). Remedial exercises are especially important. Digoxin, ATP and other drugs stimulating the myocardium should be given in the presence of cardiac failure. Smoking control is also important in prophylaxis of emphysema.

Chapter 6

BLOOD CIRCULATORY SYSTEM

Methods of Examination

Inquiry

Patients with diseases of the heart usually complain of dyspnoea, i.e. distressing feeling of air deficit. Dyspnoea is a sign of the developing circulatory insufficiency, the degree of dyspnoea being a measure of this insufficiency. When questioning the patient, it is therefore necessary to find out the conditions under which dyspnoea develops. At the initial stages of heart failure, dyspnoea develops only during exercise, such as ascending the stairs or a hill, or during fast walk. Further, it arises at mildly increased physical activity, during talking, after meals, or during normal walk. In advanced heart failure, dyspnoea is observed even at rest. Cardiac dyspnoea is caused by some factors which stimulate the respiratory centre.

Attacks of asphyxia, which are known as cardiac asthma, should be differentiated from dyspnoea. An attack of cardiac asthma usually arises suddenly, at rest, or soon after a physical or emotional stress, sometimes during night sleep. It may develop in the presence of dyspnoea. In paroxysmal attacks of cardiac asthma, the patient would usually complain of acute lack of air; respiration becomes stertorous, the sputum is foamy with traces of blood.

Patients often complain of palpitation. They feel accelerated and intensified heart contractions. Palpitation is determined by the increased excitability of the patient's nerve apparatus that controls heart activity. Palpitation is a sign of affection of the heart muscle in cardiac diseases such as myocarditis, myocardial infarction, congenital heart diseases, etc., it may arise as a reflex in diseases of some other organs, in fever, anaemia, neurosis, hyperthyroidism, and after administration of some medicinal preparations (atropin sulphate, etc.). Palpitation may also occur in healthy persons under heavy physical load, during running, emotional stress, smoking or coffee abuse. Patients with serious heart diseases may feel palpitation constantly, or it may arise in attacks of paroxysmal tachycardia.

Some patients complain of intermissions (escaped beats) which are due to disorders in the cardiac rhythm. Intermissions are described by the patient as the feeling of sinking, stoppage of the heart. Questioning the patient is aimed at determining the circumstances under which intermissions

develop. They may arise at rest or during exercise, they may be intensified in special postures of the patient, etc.

Pain in the heart region is an important and informative sign. The character of pain is different in various diseases of the heart. The physician should determine (by questioning) the location of the pain, the cause or condition under which it develops (exercise, emotional stress, walking, attack of pain at rest, during night sleep), the character of pain (acute, boring, piercing, a feeling of heaviness or retrosternal pressure, small boring pain in the region of the apex), duration and radiation of pain, conditions under which the pain abates. Pain often develops due to acute insufficiency of the coronary circulation, which results in myocardial ischaemia. This pain syndrome is called stenocardia or angina pectoris. In angina pectoris pain is retrosternal or slightly to the left of the sternum; it most commonly radiates to the region under the left scapula, the neck, and the left arm. The pain is usually associated with exercise, emotional stress, and is abated by nitroglycerin. Angina pectoris pain occurs mostly in patients with coronary atherosclerosis but it may arise in inflammatory diseases of the vessels, e.g. rheumatic vasculitis, syphilitic mesaortitis, periarteritis nodosa, and also in aortal heart diseases and grave anaemia.

Pain is especially intense in myocardial infarction and, unlike in angina pectoris, it persists for a few hours, and sometimes for several days. It does not abate after vasodilatory preparations are given. Pain in dissecting aneurysm of the aorta is piercing (like in myocardial infarction). Unlike in myocardial infarction, pain radiates usually to the spinal column, and moves gradually along the course of the aorta. Myocarditis is characterized by intermittent and pressing pain; it is dull, mild, and is intensified during exercise. Pain in pericarditis is located at the middle of the sternum or throughout the entire cardiac region; the pain is stabbing or shooting, and is intensified during movements, cough, even under the pressure of a stethoscope; the pain may persist for several days or arise in attacks. Permanent pain behind the manubrium sterni that does not depend on exercise or emotional stress (the so-called aortalgia) occurs in aortitis. Stabbing pain at the heart apex that arises in emotional stress or fatigue is characteristic of cardioneurosis. It should be remembered that pain in the cardiac region may arise due to affections of intercostal muscles, nerves, pleura, or the adjacent organs (diaphragmatic hernia, cholecystitis, ulcer, gastric cancer).

Patients with heart diseases often complain of cough which is due to congestion in the lesser circulation. The cough is usually dry; sometimes a small amount of sputum is coughed up. Dry cough is also observed in aortal aneurysm because of the stimulation of the vagus nerve. Haemoptysis in grave heart diseases is mostly due to congestion in the lesser circulation and

rupture of fine bronchial vessels (e.g. during coughing). Haemoptysis mostly occurs in patients with mitral heart disease. It may occur in embolism of the pulmonary artery. When the aneurysm opens into the respiratory ducts, profuse beeding occurs.

Venous congestion in the greater circulation occurs in severe heart diseases (see "Circulatory Insufficienty"). The patients would complain of oedema, which first develops only in the evening and resolves during the night sleep. Oedema occurs mostly in the malleolus region and on the dorsal side of the foot; shins are then affected. In graver cases when fluid is accumulated in the abdominal cavity (ascites) the patient would complain of heaviness in the abdomen and its enlargement. Heaviness most commonly develops in the right hypochondrium due to congestion and enlargement of the liver. In rapidly developing congestion, pain is felt in this region due to distention of the liver capsule. Patients may complain also of poor appetite, nausea, vomiting, and swelling of the abdomen. These symptoms are associated with disordered blood circulation in the abdominal organs. The renal function is upset for the same reason and diuresis decreases.

Patients with cardiovascular pathology often have dysfunction of the central nervous system, which is manifested by weakness, rapid fatigue, decreased work capacity, increased excitability, and deranged sleep. Complaints of headache, nausea, noise in the ears or the head are not infrequent in essential hypertension patients.

Some heart diseases (myocarditis, endocarditis, etc.) are attended by elevated (usually subfebrile) temperature; sometimes high fever may occur. The patient should be asked about the time of the day when the temperature usually rises, how long it persists and if this rise is accompanied by chills, profuse sweating, etc.

History of present disease. The time of the onset of the disease and its first symptoms should be determined such as pain, palpitation, dyspnoea, elevation of the arterial pressure, the character and intensity of these symptoms, connection with infections and other diseases of the past, cooling, and physical overloads. The character of development of the primary symptoms is important. It is also necessary to find out if any treatment was given and its effect, if any. If there were exacerbations of the disease, their course and causes should be established.

Anamnesis. Special attention should be paid to various possible causes of the present heart disease. Information should be carefully collected concerning diseases of the past, especially such diseases as rheumatism, frequent tonsillitis, diphtheria, syphilis, which would normally provoke cardiovascular pathology. It is important to know the unfavourable living and working conditions, chronic exposure to cold and high humidity, nervous

and psychic overstrain, hypodynamia, overeating, occupational hazards, smoking and alcohol abuse and other harmful habits. It is also important to ask the patient about cardiovascular diseases that occurred in his relatives, because familial predisposition to some heart diseases is possible. It is necessary to inquire women about past pregnancies and labour, the onset of menopause because sometimes symptoms of cardiovascular pathology develop in them during this period.

Physical Examination

INSPECTION

The general appearance of the patient, his posture in bed, colour of the skin and visible mucosa, the presence or absence of oedema, the shapes of the terminal finger phalanges (drum-stick fingers) and of the belly should be assessed. Patients with a marked dyspnoea usually assume a half-sitting position; if dyspnoea is grave, the patient assumes a forced position; he sits in bed with the legs on the floor (orthopnoea). Greater portion of blood is retained in the vessels of the lower extremities in this position to decrease the volume of the circulating blood and congestion in the lesser circulation. Lung ventilation is thus improved. Furthermore, the diaphragm descends in the orthopnoeic position; if ascites is present, the pressure of the ascitic fluid on the diaphragm is lessened to facilitate respiratory excursions of the lungs and to improve gas exchange.

Patients with exudative pericarditis choose to sit in bed slightly leaning forward. Patients with enlargement of the heart lie on the right side because they feel discomfort when lying on the left side (the dilated heart more tightly presses the anterior wall of the chest).

Cyanotic skin is a common sign of heart diseases. In patients with circulatory disorders, cyanosis is more pronounced in parts of the body that are farther remoted from the heart, i.e. the fingers and toes, the tip of the nose, the lips, and the ear lobes. This phenomenon is known as acrocyanosis. It depends on the increased content of reduced haemoglobin in the venous blood because of excessive oxygen absorption by tissues in slow circulation of the blood (see "Circulatory Insufficiency"). In other cases, cyanosis becomes central in conditions of oxygen hunger of blood due to its insufficient arterialization in the pulmonary bed. The degree of cyanosis varies from a slightly detectable blue tinge to the dark blue colour. Cyanosis is especially pronounced in patients with congenital heart diseases and arteriovenous shunting. It should be remembered that cyanosis can arise in poisoning by chemicals or drugs that form methaemoglobin and sulphmethaemoglobin.

The colour of the skin is important for diagnosis of some heart diseases. Mitral stenosis can be diagnosed by the violet-red colour of the patient's cheeks, mildly cyanotic colour of the lips, nose, and extremities. The skin and visible mucosa of patients with aortal heart diseases are usually pale. Cyanosis in combination with pallor (pallid cyanosis) is characteristic of stenosis of the orifice of the pulmonary trunk or thrombosis of the pulmonary artery. Icteric colour of the sclera and skin is characteristic of grave circulatory insufficiency. The skin of patients with persisting septic endocarditis has a peculiar colour resembling that of coffee with milk.

Oedema frequently attends heart diseases. If the patient stays out of bed, oedema is localized mainly in the malleolus, the dorsal side of the feet, and the shins, where a pressure of fingers leaves slowly levelling impressions. If the patient lies in bed, oedema is localized in the sacrolumbar region. If oedema is significant, it may extend onto the entire body while the ascitic fluid accumulates in various cavities of the body, such as the pleural cavity (hydrothorax), abdominal cavity (ascites), or in the pericardium (hydropericardium). Generalized oedema is called anasarca. The oedematous skin, especially the skin of the extremities, is pallid, smooth, and tense. In persistent oedema, the skin becomes rigid, its elasticity is lost, and the skin acquires a brown tinge due to diapedesis of erythrocytes from the congested vessels. Linear rhexes may develop in the subcutaneous fat of the abdomen in pronounced oedema, which resemble the scars of pregnancy. In order to assess objectively the degree of oedema, the patient should be weighed regularly and the amount of liquid taken and excreted should be strictly recorded.

Local oedema sometimes develops in cardiovascular pathology. When the superior vena cava is compressed, for example in exudative pericarditis or aneurysm of the aortal arch, the face, neck, and the shoulder girdle can be affected by oedema (the collar of Stokes). In thrombophlebitis of the shin or thigh oedema of the affected extremity forms; ascites develops during thrombosis of the portal vein or the hepatic veins.

The shape of the nails and terminal phalanges of the fingers is informative. Drum-stick (Hippocratic) fingers are characteristic of subacute septic endocarditis and some congenital heart diseases.

Inspection of the heart region and peripheral vessels. Cardiac "humpback" can be seen during inspection of the precordium. This is bulging of the area over the heart, the degree of protrusion depending on the enlargement and hypertrophy of the heart (provided these defects develop in childhood when the chest is liable to changes). General protrusion of the cardiac region and levelling of the costal interspaces are observed in massive effusive pericarditis. The cardiac humpback should be differen-

tiated from deformation of the chest caused by changes in the bones, e.g. in rickets.

In patients with underdeveloped subcutaneous fat and asthenic body build, a limited rhythmic pulsation (the apex beat) can be seen in the fifth interspace, medially of the midclavicular line. This is caused by the thrust of the heart apex against the chest wall. In cardiac pathology, the apex beat may produce a stronger pulsation (see "Palpation of the Heart"). If precordial depression is found instead of prominence, the apex beat is said to be negative. It occurs in adhesive pericarditis because of adhesion of the parietal and visceral layers of the pericardium.

Pulsation is sometimes observed to the left of the sternal line over a vast area extending to the epigastric region. This is the so-called cardiac beat. It is due to contractions of the enlarged right ventricle; a synchronous pulsation can also be seen in the upper epigastric region (below the xiphoid process).

Pulsation in the region of the heart base is sometimes observed. Pulsation of the aorta can be felt in the second costal interspace to the right of the sternum; it appears either during its strong dilation (aneurysm of the ascending part and of the arch of the aorta; aortic valve incompetence), or in sclerotic affection of the overlying right lung. In rare cases, the aneurysm of the ascending aorta can destroy the ribs and the sternum. Elastic throbbing tumour is then seen. Pulsation in the second and third costal interspace, that can be seen by an unaided eye, is caused by dilatation of the pulmonary trunk. It occurs in patients with mitral stenosis, marked hypertension in the lesser circulation, patent ductus arteriosus with massive discharge of the blood from the aorta to the pulmonary trunk, and in primary pulmonary hypertension. Pulsation occurring lower, in the third and fourth interspace to the left of the sternum, can be due to the aneurysm of the heart in post-infarction patients.

Inspection of the vessels is very important for assessing the cardiovascular system. Swollen and tortuous arteries, especially temporal arteries, are found in patients with essential hypertension and atherosclerosis; this is the result of their elongation and sclerotic changes. Pulsation of the carotids can only be observed in healthy persons; this pulsation is synchronous with the apex beat. In pathological conditions, mainly in aortic valve incompetence, pronounced pulsation of the carotid arteries can be observed (carotid shudder). Synchronously with pulsation of the carotid arteries, the head of the patient may rhythmically move. This is de Musset's sign. Pulsation of arteries, e.g. subclavian, brachial, radial and other arteries can also be observed. Even arterioles may pulsate (the so-called capillary pulse). In order to reveal the capillary pulse, the finger nail should be slightly pressed in order to form a small white spot: the

margin between the red and blanched part will be seen to ebb and flow with each pulse beat. Similar pulsation can be seen on hyperaemic skin, e.g. of the forehead, after rubbing it. The name "capillary pulse" is not quite correct because it mostly depends on pulse variations in the arterioles. Capillary pulse can be found in patients with aortic valve failure and sometimes in thyrotoxic goitre.

During inspection of the veins the physician can observe their overfilling and dilation. This picture is found in general venous congestion and also in local disorders of blood outflow from the veins. The general venous congestion is caused by affection of the right heart and also by diseases that increase intrathoracic pressure and interfere with the outflow of venous blood through the venae cavae. The neck veins are dilated and become swollen. Local congestion is caused by compression of the vein from the outside (tumour, scars, etc.), or by its thrombosis. Local venous stasis is characterized by dilation of collaterals, while oedema is formed at the site where blood outflows through the corresponding vein. In conditions of difficult outflow of blood through the superior vena cava, dilated are the veins of the head, neck, upper extremities, and the anterior surface of the trunk. Via the collaterals the blood is delivered to the system of the inferior vena cava, i.e. the blood flow in the dilated veins (the subcutaneous veins of the chest included) is directed downward. In conditions of difficult blood outflow through the inferior vena cava, the veins of the lower extremities and lateral surfaces of the abdominal wall are dilated. The blood flow in this case is directed into the system of the superior vena cava, i.e. upwards. If the blood outflow through the portal vein is difficult, the collaterals, connecting the system of the portal vein with the vena cava, become arranged round the umbilicus to form the caput Medusae and the blood is directed through the dilated superficial veins to the system of the superior and inferior vena cava. In order to determine the direction of the blood flow in dilated veins, a length of a thick vein is pressed by the finger (after the blood is displaced from it). As the vein becomes filled, the direction of the blood flow can easily be determined: when it is directed downward, the vein portion lying above the compressed site is filled, it is directed upward when the part below this point is filled.

Jugular veins can be seen pulsating on the neck. Blood flow in the jugular vein is slowed down during atrial systole and accelerated during ventricular systole. The neck veins somewhat swell when the blood flow slows down, and collapse when the blood flow is accelerated. It follows that the veins collapse during systolic dilation of the arteries. This is the so-called negative venous pulse. It is hardly noticeable in healthy persons and becomes more evident when the veins are filled with blood due to congestion. Pulsation of the jugular veins caused by pulsation of the carotid

arteries can be mistaken for the venous pulse. It should therefore be remembered that pulsation of the carotid artery can be seen medially of the sternocleidomastoid muscle, while pulsation of the vein laterally of this muscle. Moreover, if the vein is pressed by a finger along its course, the transmitted vibrations of the peripheral portion of the vein become more visible, whereas pulsation of this portion discontinues in genuine venous pulse. Distinct pulsation of the neck vessels in the presence of a slow pulse on the radial artery is caused by venous and not by arterial pulsation.

PALPATION

Palpation of the heart helps reveal more accurately the apex beat, the presence of the cardiac beat, the visible pulsation, or detect cat's purr symptom. In order to determine the apex beat, the palm of the right hand is placed on the patient's chest. (The left mammary gland in women is first moved upward and to the right.) The base of the hand should be rested on the sternum, while the fingers should be directed toward the axillary region, between the 3rd and 4th ribs. The terminal phalanges of three fingers should be flexed to form a right angle to the surface of the chest, and moved slowly along the interspaces toward the sternum until the moderately pressing fingers feel the movement of the heart apex. If the apex beat is felt over a considerable area, its borders are outlined by locating the extreme left and lower points of the protruding area, which is considered to be the point of the apex beat. The apex beat can be better detected if the patient slightly leans forward, or by palpation during a deep expiration: in this position the heart is pressed closer to the chest wall.

A normal apex beat is found in the fifth interspace, 1-1.5 cm toward the sternum from the left midclavicular line. When the patient lies on his left side, the beat is displaced 3-4 cm to the left, and 1-1.5 cm to the right when the patient lies on the right side. Stable displacement of the apex beat may depend on the changes in the heart itself or the adjacent organs. For example, if the left ventricle is enlarged, the apex beat is displaced to the left to the axillary line, and downwards to the 6th and 7th interspace. If the right ventricle is dilated, the apex beat may be displaced to the left as well because the left ventricle is moved to the left by the distended right ventricle. In cases with abnormal congenital heart position, e.g. in dextrocardia, the apex beat is felt in the fifth costal interspace, 1-1.5 cm toward the sternum from the right midclavicular line.

The position of the apex beat depends also on the diaphragm. Increased pressure in the abdominal cavity (in pregnancy, ascites, meteorism, tumours) displaces the apex beat upward and to the left because the heart is not only lifted but also turned to the left to assume a horizontal position. If

the diaphragm is low (after childbirth, wasting, visceroptosis), the apex beat is displaced downward and slightly to the right to assume the more vertical position.

In the presence of effusion or gas in the right pleural cavity, the apex beat is displaced to the left accordingly. Pleuropericardial adhesions and sclerotic affection of the lungs due to growth of connective tissue in them displace the heart to the involved side. In patients with left-sided pleurisy with effusion and in accumulation of the fluid in the pericardial region, the apex beat disappears. In about one third of cases the apex is impalpable (covered by the rib).

If the apex beat is palpable, its properties are determined: width (or area), height, strength, and resistance. If the area exceeds 2 cm in diameter, apex beat is considered diffused; if the area is smaller, the apex beat is restricted. Most frequent and important diagnostic cause of diffuse apex beat is enlargement of the heart, especially of the left ventricle. The width of the apex beat may increase also due to a closer contact of the heart apex to the chest wall, in patients with thin thoracic wall, wide interspaces, sclerotic affection of the lower border of the left lung, displacement of the heart anteriorly by a growing tumour of the mediastinum, etc. The area of the apex beat decreases in patients with developed or oedematous subcutaneous fat tissue, narrow interspaces, emphysema of the lungs, and low diaphragm.

The height of the apex beat is the amplitude of vibration of the chest wall at the apex beat area. High and low apex beats are thus differentiated. This property of the apex beat usually varies with the width. Moreover, the height of the apex beat depends on the contractile strength of the heart. When a person is excited, performs exercises, or has fever, or thyrotoxicosis, the height of the apex beat increases due to the increased contractions of the heart.

The strength of the apex beat is estimated by the pressure that the heart apex thrusts against the palpating fingers. Like the former two properties, the strength of the thrust depends on thickness of the chest wall and the distance from the heart apex to the examining fingers; but it depends mostly on the strength of contractions of the left ventricle. Forced apex beat occurs in hypertrophy of the left ventricle; if hypertrophy is concentric, the beat strength may increase, the width of the beat remaining the same.

Resistance, i.e. density of the heart muscle, is another property of the apex beat that can be determined in addition to its height, width, and strength. Density of the left ventricular muscle considerably increases with its hypertrophy to cause resistant apex beat. Hypertrophy of the left ventricle is characterized by diffuse, high, forced, and resistant apex beat. In pronounced hypertrophy of the left ventricle attended by its dilation, the

apex of the heart becomes tapered and can be felt by the palpating fingers as a dense and firm dome.

Extra-apical pulsations. Aortic pulsation is not palpable in healthy subjects (except in asthenic persons with wide costal interspaces). Palpation can be used to detect pulsation of the aorta during its distension. If the ascending part of the aorta is dilated, pulsation can be felt to the right of the sternum, and if the aortic arch is dilated, the pulsation can be felt in the region of the sternal manubrium. Aneurysm or pronounced dilation of the aortic arch is characterized by pulsation in the jugular fossa (retrosternal pulsation). Thinning and usure of the ribs or the sternum can be caused by the pressure of the dilated aorta.

Epigastric pulsation, i.e. visible protrusion and retraction of the epigastric area, is synchronous with the heart work, and may depend not only on hypertrophy of the right ventricle, but on the pulsation of the abdominal aorta and the liver. Epigastric pulsation due to hypertrophy of the right ventricle is usually felt under the xiphoid process and becomes especially vivid during deep inspiration, whereas pulsation caused by the abdominal aorta is slightly lower and becomes less marked during deep inspiration. Intact abdominal aorta can pulsate in asthenic patients with a flaccid abdominal wall.

Pulsation of the liver can be detected by palpation. True and transmitted pulsations of the liver are distinguished. The true liver pulsation is the so-called positive venous pulsation; it may be seen in patients with tricuspid valve incompetence. During systole, the blood flows back from the right atrium to the inferior vena cava and hepatic veins. The liver therefore swells rhythmically with each heart contraction. The transmitted pulsation depends on the impulses transmitted by the contracting heart. Each systolic contraction displaces the entire mass of the liver in one direction.

The symptom of a cat's purr, i.e. low vibrating murmur, resembles purring of a cat. It is of great value in the diagnosis of heart diseases. This sign depends on the same causes that are responsible for the murmur arising in stenosed valve orifices. In order to determine the thrill, the palpating hand should be placed flat on the points where the heart is normally auscultated. Cat's purr palpated over the heart apex during diastolic contraction is characteristic of mitral stenosis, and thrills felt over the aorta during systole indicate stenosed aortic orifice.

PERCUSSION

Percussion is used to determine the size, position and shape of the heart and the vascular bundle. The right contour of dullness of the heart and the vascular bundle is formed (from top to bottom) by the superior vena cava

to the upper edge of the 3rd rib and by the right atrium at the bottom. The left contour is formed by the left part of the aortic arch at the top, then by the pulmonary trunk, by the auricle of the left atrium at the level of the 3rd rib and downward by a narrow strip of the left ventricle. The anterior surface of the heart is formed by the right ventricle. Being an airless organ, the heart gives a dull percussion sound. But since it is partly covered on its sides by the lungs, dullness is dual in its character, i.e. it is relative (deep) and absolute (superficial). The relative cardiac dullness is the projection of its anterior surface onto the chest. It corresponds to the true borders of the heart, while the absolute dullness corresponds to the anterior surface of the heart that is not covered by the lungs. Percussion can be done with the patient in both erect and lying position. It should, however, be remembered that the area of cardiac dullness in the vertical position is smaller than in the horizontal. This is due to mobility of the heart and the displacement of the diaphragm as the patient changes his posture.

Determining relative cardiac dullness. When determining the borders of relative cardiac dullness, interspaces should be percussed in order to avoid lateral distribution of vibrations along the ribs. The percussion stroke should be of medium strength. The pleximeter-finger should be tightly pressed against the chest so that the percussion vibration might penetrate deeper regions.

When determining the border of relative dullness, the remotest points of the cardiac contour are first found on the right, then on the left, and finally at the top (Fig. 30). Since the border of cardiac dullness depends on the position of the diaphragm, the lower border of the right lung is first determined in the midclavicular line; its normal position is at the level of the 6th rib. The position of the lower border of the lung indicates the level

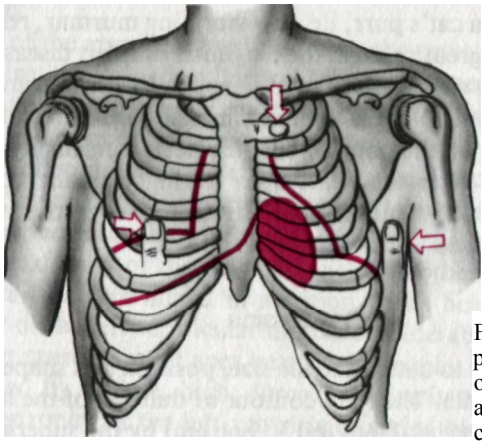


Fig. 30. Position of the pleximeter-finger during outlining the upper, right, and left borders of relative cardiac dullness.

of the diaphragm. The pleximeter-finger is then moved one interspace above the lower border of the right lung and placed parallel to the right border of the heart being determined (normally, in the 4th costal interspace). Percussion is continued by moving the pleximeter-finger gradually along the interspace toward the heart until the percussion sound dulls. The right border of the heart is marked by the outer edge of the finger directed toward a clear resonant sound. Its normal position is 1 cm laterally of the right edge of the sternum.

The left border of the relative cardiac dullness is determined in the interspace, where the apex beat is present. The apex beat is therefore first determined by palpation, and the pleximeter-finger is then placed laterally of this point, parallel to the sought border, and the interspace is percussed toward the sternum. If the apex beat cannot be determined, the heart should be percussed in the 5th interspace from the anterior axillary line toward the sternum. The left border of relative cardiac dullness is located 1-2 cm medially of left midclavicular line; it coincides with the apex beat.

The upper border of the relative cardiac dullness is determined 1 cm to the left of the left sternal line. To that end, the pleximeter-finger is placed perpendicularly to the sternum, near its left margin, and then moved downward until dullness appears. The normal upper border of the relative cardiac dullness is in the 3rd interspace.

Once the area of relative cardiac dullness of the heart has been established, its transverse length is measured by a measuring tape, from the extreme points of the relative dullness to the anterior median line. The normal distance from the right border of relative cardiac dullness (usually in the 4th interspace) to the anterior median line is 3 or 4 cm, while the distance from the left border of relative cardiac dullness (usually in the 5th interspace) to the same line is 8 or 9 cm. The sum of these lengths is the transverse length of relative cardiac dullness (normally 11-13 cm).

The shape of the heart can be determined by percussion of the borders of the vascular bundle in the 2nd intercostal space on the right and left, and of relative cardiac dullness in the 4th or 3rd interspace on the right, and in the 5th, 4th, or 3rd interspace on the left. The pleximeter-finger is moved parallel to the borders of expected dullness and the elicited points of dullness are marked on the patient's skin. The points are then connected by a line to mark the contours of the relative cardiac dullness. Normally, an obtuse angle is formed by the lines of the left heart contour between the vascular bundle and the left ventricle. The heart is of normal configuration in such cases. In pathological conditions, when the chambers of the heart are dilated, mitral and aortal configurations are distinguished.

Determining absolute (superficial) cardiac dullness. The anterior wall of the heart is not covered by the lungs and the area of absolute cardiac

dullness corresponds to the area of the heart. Percussion of this area gives dullness. To determine absolute dullness of the heart, light percussion strokes are needed. The right border of absolute cardiac dullness is first elicited. The plexímeter-finger is placed on the right border of relative (deep) cardiac dullness, parallel to the sternum, and then moved medially, to the left, to dullness. The border is marked by the outer edge of the finger directed toward resonance. In normal subjects this border passes along the left edge of the sternum.

To outline the left border of absolute cardiac dullness, the plexímeter-finger is placed slightly outside the border of relative cardiac dullness, and then moved medially to dullness. The left border of absolute cardiac dullness is normally 1—2 cm medially of the border of relative cardiac dullness. To elicit the upper border of absolute cardiac dullness, the plexímeter-finger is placed on the upper border of relative cardiac dullness and then moved downward to dullness. The superior border of absolute cardiac dullness is normally at the level of the 4th rib. It is sometimes difficult to differentiate between absolute and relative cardiac dullness, if percussion is done from the lungs to the heart. The plexímeter-finger should in such cases be placed at the centre of absolute dullness and then moved to its borders (from dullness to diminished dullness). The first sign of the admixed pulmonary resonance indicates the transition from the area of absolute dullness to the area of relative dullness.

The *borders of the vascular bundle* are determined by light percussion in the second intercostal space, to the right and left from the midclavicular line, toward the sternum. When the percussion sound dulls, a mark should be made by the outer edge of the finger. The right and left borders of vascular dullness are normally found along the edges of the sternum; the transverse length of dullness is 5—6 cm.

The *area of cardiac dullness* can be modified by extracardiac factors. At high position of the diaphragm, the heart assumes a horizontal position and its transverse dimensions thus increase. When the diaphragm is low, the heart assumes the vertical position and its transverse diameter is thus diminished. Accumulation of liquid or air in one pleural cavity displaces cardiac dullness toward the healthy side; in atelectasis and pneumosclerosis, or in the presence of pleuropericardial adhesion the borders of cardiac dullness are displaced to the affected side. The area of absolute cardiac dullness markedly diminishes or disappears in pulmonary emphysema, while it increases in pneumosclerosis. The area of absolute dullness is also enlarged in the anterior displacement of the heart (e.g. by a mediastinal tumour, due to accumulation of fluid in the pericardium, or in dilatation of the right ventricle). The borders of relative dullness are displaced in the presence of enlarged heart chambers. Displacement to the

right is due to dilatation of the right atrium and the right ventricle. If the left atrium or the conus of the pulmonary trunk is enlarged, the area of relative dullness is displaced upwards. Dilatation of the left ventricle displaces the area of relative dullness to the left. It should be remembered that a markedly enlarged and hypertrophied right ventricle displaces the left ventricle and can also displace the border of relative dullness to the left. Aortic dilatation increases the dullness area in the second interspace.

AUSCULTATION

Heart sounds. The sounds produced by a working heart are called heart sounds. Two sounds can be well heard in a healthy subject; the first sound, which is produced during systole and the second sound, which occurs during diastole.

In order to understand better the mechanism by which the heart sounds are produced, the phases of the cardiac cycle should be remembered. The heart contraction begins with the systole of the atria, which is followed by contraction of the ventricles. During the early systole the following phases are distinguished: (1) *asynchronous contraction;* the myocardium is involved only partly and the intraventricular pressure does not increase; (2) *isometric contraction;* it begins when the main mass of the myocardium is involved; atrioventricular valves are closed during this phase and the intraventricular pressure markedly increases; (3) *ejection phase;* the intraventricular pressure increases to level with that in the main vessels; the semilunar valves open. As soon as the blood has been ejected, the ventricles relax (diastole) and the semilunar valves close. The ventricles continue relaxing after the closure of the atrioventricular and semilunar valves until the pressure in them is lower than in the atria *(isometric relaxation phase).* The atrioventricular valves then open to admit blood into the ventricles. Since the difference between pressures in the atria and the ventricles is great during the early diastole, the ventricles are quickly filled *(ventricle rapid filling phase).* The blood flow then slows down *(slow filling phase).* Atrial systole begins, and the cardiac cycle is repeated.

The first sound is produced by several factors. One of them is the valve component, i.e. vibrations of the cusps of the atrioventricular valves during the isometric contraction phase, when the valves are closed. The second component is muscular, and is due to the myocardial isometric contraction. The intensity of myocardial and valvular vibrations depends on the rate of ventricular contractions: the higher the rate of their contractions and the faster the intraventricular pressure grows, the greater is the intensity of these vibrations. The first heart sound will thus be more resonant. The third component of the first heart sound is the vascular one. This is due to vibrations of the nearest portions of the aorta and the pulmonary trunk caused by their distention with the blood during the ejection phase. The fourth component is atrial; it is generated by vibrations caused by atrial contractions. This fourth component gives rise to the first sound since the atrial systole precedes the ventricular systole. Vibrations caused

by the atrial systole are normally blended with vibrations caused by the ventricular systole, and are heard as one sound.

The *second sound* is generated by vibrations arising at the early diastole when the semilunar cusps of the aortic valve and the pulmonary trunk are shut (the valve component) and by vibration of the walls at the point of origination of these vessels (the vascular component).

Both sounds can be heard over the entire precordium but their strength changes depending on the proximity of the valves involved in the formation of the first or second sound. Therefore, in order to assess correctly the findings of auscultation, it is necessary to know the sites where the valves project on the chest wall (the auscultatory valve areas) and also areas where the sounds produced by a valve can be better heard.

The sites of projections of the valves on the anterior chest wall are very close to one another (Fig. 31). The mitral valve projects to the left of the sternum, at the 3rd costosternal articutation, and the tricuspid valve, on the sternum midway between the 3rd left and 5th right costosternal articulations. The valve of the pulmonary trunk is projected in the 2nd intercostal space, to the left of the sternum; the aortic valve is projected in the middle of the sternum, at the level of the 3rd costosternal articulation. Since all heart valves are projected on a small area of the chest, it is difficult to decide which of them is damaged if the valves are auscultated at sites of their actual projections. Perception of sounds generated in the heart depends on the distance from the valve to its projection on the chest wall and on sound conduction by the course of the blood flow. It is

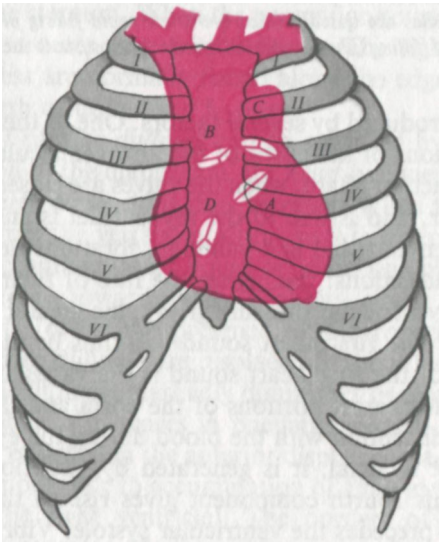


Fig. 31. Projection of the heart valves on the chest wall and listening points of the heart.

A—mitral valve; *B*—aortic valve; C—pulmonary trunk valve; *D*—tricuspid valve.

therefore possible to find certain sites on the chest where sounds of each valve can be better heard.

These auscultatory areas are as follows: (1) the area of the apex beat for the mitral valve because the vibrations are well transmitted by the firm muscle of the left ventricle and the cardiac apex is at the nearest distance to the anterior chest wall during systole; (2) the lower part of the sternum near its junction with the xiphoid process (the right-ventricular area); for the tricuspid valve; (3) the valve of the pulmonary trunk is best heard at its anatomical projection onto the chest, i.e. in the second intercostal space, to the left of the sternum; (4) the aortal valve is best heard in the second intercostal space, to the right of the sternum where the aorta is the nearest to the anterior chest wall. Moreover, the heart sounds which are associated with the contractions of the aortic valve or which develop during its affection, can be heard to the left of the sternum at the 3rd and 4th costosternal articulation (the so-called fifth listening post at the Botkin-Erb point).

Rules for auscultation of the heart. The heart is usually auscultated by a stethoscope or a phonendoscope, but direct (immediate) auscultation is also used. The condition of the patient permitting, the heart sounds should be heard in various postures of the patient: erect, recumbent, after exercise (e.g. after repeated squatting). Sounds associated with the mitral valve pathology are well heard when the patient lies on his left side, since the heart apex is at its nearest position to the chest wall; aortic valve defects are best heard when the patient is in the upright posture or when he lies on his right side. The heart sounds are better heard if the patient is asked to inhale deeply and then exhale deeply and keep breath for short periods of time so that the respiratory sounds should not interfere with auscultation of the heart. The valve sounds should be heard in the order of decreasing frequency of their affection. The mitral valve should be heard first (at the heart apex); next follows the aortic valve (in the second intercostal space to the right of the sternum), the pulmonary valve (in the second intercostal space, to the left of the sternum), tricuspid valve (at the base of the xiphoid process), and finally the aortic valve again at the Botkin-Erb point. If any deviations from normal sounds have been revealed at these points, the entire heart area should be auscultated thoroughly.

Normal heart sounds. The *first sound* is produced during systole, after a long pause. It is best heard at the heart apex since the systolic tension of the left ventricle is more pronounced than that of the right ventricle. The first sound is longer and louder than the second heart sound. The *second sound* is generated during diastole, after a short pause, and is best heard at the heart base because it is produced by the closure of the semilunar cusps of the aortic and pulmonary trunk valves. As distinct from the first sound, the second sound is shorter and higher. The tone of the heart sounds may

Table 3

Differentition between the First and Second Heart Sounds

Main sign	First sound	Second sound
The best listening post	Heart apex	Heart base
Relation to cardiac pause	Follows the long pause	Follows the short pause
Duration	0.09-012 s	0.05-0.07 s
Relation to apex beat	Synchronous	Follows the apex beat
Relation to carotid pulse	Synchronous	Asynchronous

change in pathology, and in order to differentiate between the first and second sounds it should be remembered that the first sound coincides in time with the apex beat (if the latter can be palpated) or with the pulse of the aorta and the carotid artery. Table 3 gives signs that help differentiate between the first and second heart sounds.

Sometimes the third and the fourth sounds can be heard, especially in children and in thin youths.

The *third sound* is caused by vibrations generated during quick passive filling of the ventricles with the blood from the atria during diastole of the heart; it arises in 0.15-1.12 s from the beginning of the second sound (Fig. 32).

The *fourth sound* is heard at the end of ventricular diastole and is produced by atrial contractions during quick filling of the ventricles with blood.

The third and fourth sounds are low-pitch and soft and are therefore hardly heard in normal subjects. But they are clearly seen on a phonocardiogram. These sounds are better heard in immediate (direct) auscultation. The presence of the third and fourth sounds in the middle-aged usually indicates severe affection of the heart muscle.

Changes in the heart sounds. The heart sounds may increase or decrease their intensity, the tone, or length; they may be split or reduplicated, or adventitious sound may appear.

Intensity of the heart sounds may depend on conditions of the sound wave transmission, i.e. on the extracardiac causes. If subcutaneous fat or muscles of the chest are overdeveloped, or there are lung emphysema, liquid in the left pleural cavity, and some other affections that separate the heart from the anterior chest wall, the intensity of the heart sounds decreases. If conditions for sound transmission are improved (thin chest wall, the lung edges are sclerosed, the heart is pressed against the anterior chest wall by a growing tumour in the posterior mediastinum, etc.), the in-

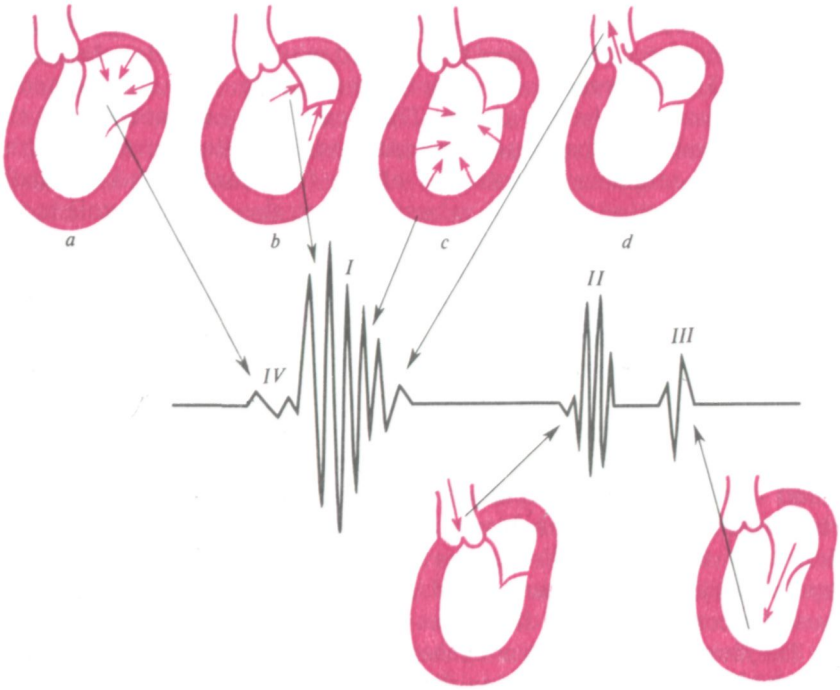


Fig. 32. Formation of heart sounds.

a—atrial component (heard sometimes as an independent fourth sound); *b*—valvular component of the first sound; c—muscular component of the first sound; *d*—vascular component of the first sound; *e*—formation of the second sound; f—formation of the third sound.

tensity of the heart sounds increases. The sounds can also be increased by the resonance in large empty cavities filled with air (a large cavern in the lung, large gastric air-bubble). The intensity of the heart sounds also depends on the composition of the blood flowing through the heart: if the blood viscosity decreases (in anaemia) the intensity increases.

Variations in the heart sounds associated with affections of the heart proper are of great diagnostic importance.

The *intensity of the heart sounds can decrease* in decreased myocardial contractility in patients with myocarditis, myocardial dystrophy, cardiosclerosis, collapse, and accumulation of fluid in the pericardial cavity.

Both heart sounds can be increased due to the effect of the sympathetic nervous system on the heart. It occurs in physical and emotional strain, during exercise, and in patients with exophthalmic goitre.

Changes in only one heart sound is very important diagnostically.

The *intensity of the first heart sound diminishes* in the mitral and aortic valve insufficiency. The cusps of the affected mitral valve fail to close completely the left atrioventricular orifice during systole. Part of the blood is thus regurgitated to the left atrium. The pressure of the blood against the ventricular walls and the cusps of the mitral valve is below normal, and the valvular and muscular components of the first heart sound markedly diminish. The period of closed valves is absent also during systole in the aortic valve insufficiency. It means that the valvular and muscle components of the first heart sound will also diminish significantly.

In tricuspid and pulmonary valve failure, the diminution of the first heart sound will be better heard at the base of the xiphoid process due to the diminution of the muscular and valvular components of the right ventricle.

The first sound can be diminished at the heart apex in stenotic aortal orifice because systolic tension of the myocardium grows slowly when the blood flow from the left ventricle is obstructed and it is overfilled with blood; the amplitude of the sound vibrations decreases. In diffuse affections of the myocardium (due to dystrophy, cardiosclerosis or myocarditis), the first heart sound only may be diminished because its muscular component also diminishes in these cases.

The first sound increases at the heart apex if the left ventricle is not adequately filled with blood during diastole. The first sound often becomes louder in stenosis of the left atrioventricular orifice, when less than normal amount of blood is discharged from atrium to the ventricle during diastole. The muscle of the left ventricle is therefore less distended by the blood by the start of systole; it is more relaxed and therefore contracts more rapidly and energetically to intensify the first sound. The first sound increases in stenosed right atrioventricular orifice at the base of the xiphoid process. This sound is also intensified during extrasystole (premature contraction of the heart) due to inadequate diastolic filling of the ventricles.

The variation of the first sound at the heart base is not important because this sound is transmitted here from its best auscultative area, i.e. from the cardiac apex area. The second heart sound is heard over the base. In normal cases the intensity of this sound over the aorta is the same as over the pulmonary trunk. Although the blood pressure in the aorta is higher and the cusps of its valve are closed with a greater force than those of the pulmonary valve, the sound produced by the closing aortic valve is perceived by the examiner as being of the same intensity as the sound of the pulmonary valve, because of the deeper location of the aortic valve.

The *second sound* over the aorta *is diminished* in aortic valve affections because either the cusps of the valve are destroyed or their vibrating power decreases due to developing cicatrices. Moreover, the thrust of the blood

discharged at early diastole from the aorta to the cusps of the aortic valve is weaker than in normal persons because part of the blood is regurgitated to the ventricle through an incompletely closed aortic orifice. The second sound can be inaudible over the aorta if the aortic valve is much destroyed. The second sound diminishes over the aorta in cases with marked hypotension; the second sound diminishes over the pulmonary trunk in cases with aortic valve incompetence (in very rare cases) and in decreased pressure in the lesser circulation.

The *second sound may increase* either over the aorta or over the pulmonary trunk. If the sound is more intense over the aorta, it is said to be accentuated over the aorta, and if it is stronger over the pulmonary trunk, accentuation of the second sound over pulmonary artery is meant.

The aortic second sound is accentuated when the blood pressure in aorta increases (in essential hypertension, during heavy exercise, in psychic excitation), because during early diastole, the aortic valve cusps are closed with a greater force due to increased blood pressure in the aorta. The tone of the second heart sound over the aorta often varies. For example, in patients with sclerotic aortic valve, the second sound over the aorta acquires a metallic character which, however, can be heard in normal arterial pressure as well.

The accentuated second sound over the pulmonary artery occurs when pressure in the lesser circulation is elevated or when the vessels of the lesser circulation are overfilled with blood (e.g. in mitral heart diseases), deranged circulation in the lungs and stenosed pulmonary artery (in lung emphysema or pneumosclerosis).

Reduplication of the heart sounds may be revealed by auscultation. Two short sounds which quickly follow one another are heard instead of one. Reduplication of the sounds occurs in asynchronous work of the left and right chambers of the heart. Asynchronous closure of the atrioventricular valves splits the first sound while asynchronous closure of the semilunar valves causes reduplication of the second heart sound. If the two short sounds follow one another at a short interval, they are not perceived as two separate sounds, the sound is said to be split. Both physiological and pathological splitting of the heart sounds are possible. Physiological *reduplication* or *splitting of the first sound* is due to asynchronous closure of the atrioventricular valves, e.g. during very deep expiration, when the blood is ejected into the left atrium with a greater force to prevent the closure of the mitral valve; the valvular component of the left ventricle is therefore split and is perceived as a separate sound.

Pathological reduplication of the first sound can occur in impaired intraventricular conduction (through the His bundle) as a result of delayed systole of one of the ventricles.

The *second sound is reduplicated* more frequently than the first heart sound. Reduplication occurs due to asynchronous closure of the valve of the aorta and pulmonary trunk because of the different length of contractions of the left and the right ventricles. The length of the ventricular systole depends on the volume of the ejected blood and the pressure in that vessel (aorta or the pulmonary artery) into which the blood is expelled. When the amount of blood in the left ventricle decreases and the pressure in the aorta is low, systole of the left ventricle ends sooner and the aortic valve cusps will close earlier than the cusps of the valve of the pulmonary trunk. The second heart sound can therefore be duplicated in cases with diminished or increased filling of one of the ventricles or when pressure in the aorta or the pulmonary artery changes. Physiological reduplication of the second sound is mostly connected with various respiratory phases: the filling of the right and left ventricles differs during inspiration and expiration and the length of their systole changes accordingly, as well as the time of closure of the valve of the aorta and pulmonary trunk. The amount of blood flowing to the left ventricle decreases during inspiration because part of blood is retained in the distended vessels of the lungs. The left-ventricular systolic blood volume decreases during inspiration, its systole ends earlier, and the aortic valve therefore closes earlier as well. At the same time, the stroke volume of the right ventricle increases, its systole prolongs, the pulmonary valve closure is delayed and the second sound is thus doubled.

Pathological reduplication of the second sound can be due to delayed closure of the aortic valve in persons suffering from essential hypertension, or if the closure of the pulmonary valve is delayed at increased pressure in the lesser circulation (e.g. in mitral stenosis or emphysema of the lungs), delayed contraction of one of the ventricles in patients with bundle-branch block.

True reduplication of the heart sounds should be differentiated from apparent doubling which is connected with the appearance of adventitious sounds. The *mitral valve opening sound* is an example. This sound is heard at the heart apex of patients with mitral stenosis. The sound is heard 0.07-0.13 s following the second sound, during diastole. In normal conditions, the cusps of the atrioventricular valve open noiselessly, they are freely forced back by the blood flow ejected from the atria to the ventricles. In mitral stenosis, the cusps of the sclerosed valve adhere to each other by their edges and cannot freely move to the walls of the ventricle. Therefore, blood thrusts against the valve as it passes from the atrium to generate sound vibrations that are responsible for the appearance of adventitious sounds.

The mitral valve opening sound follows soon after the second heart

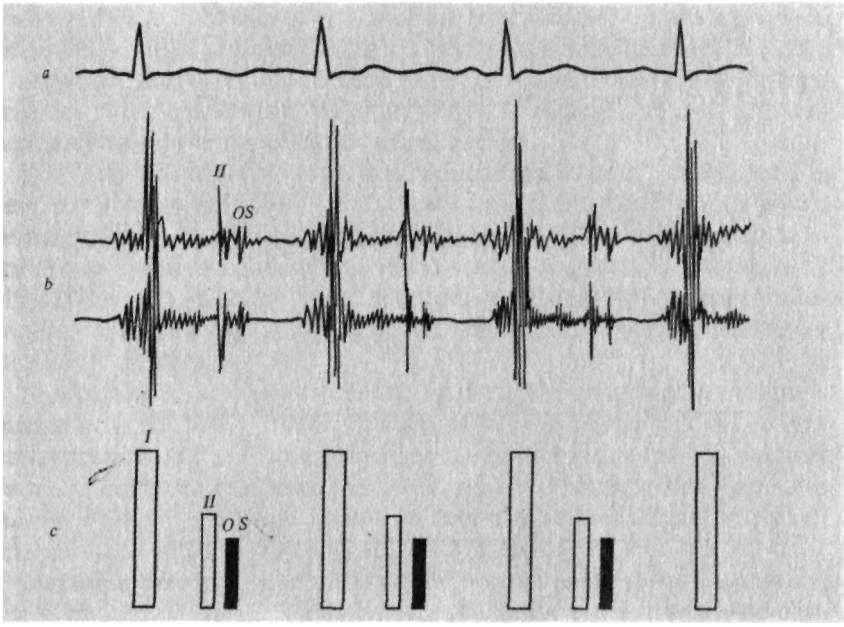


Fig. 33. Heart sounds in mitral stenosis.
a—ECG; *b*—PCG; c—changes in the heart sounds: OS—sound of the mitral valve opening

sound to give it the character of reduplication. This sound is best heard at the heart apex rather than at the heart base; it is characterized by stability and is combined with other auscultative signs of mitral stenosis. The mitral valve opening sound is heard together with a loud (snapping) first sound characteristic of mitral stenosis, and the second sound, to form a specific *triple rhythm* (Fig. 33).

An *extra-pericardial-sound* can occur in pericardial adhesion. It originates during diastole, 0.08-0.14 s after the second sound, and is generated by the vibrating pericardium during the rapid dilatation of the ventricles at the beginning of diastole. The extra sound in adhesions in the pericardium can also arise during systole, between the first and the second heart sounds. This short and loud sound is also known as the systolic click.

Changes in heart sounds in heart diseases can be due to intensified physiological third or fourth sound. In normal subjects these sounds are better revealed in graphic recording (phonocardiography). But if the ventricular myocardium is much weakened, these sounds can be revealed by auscultation. Intensification of one of these sounds gives a three-sound rhythm, known as the *gallop rhythm* (because it resembles the galloping of a horse). The sounds of the gallop rhythm are usually soft and low, always

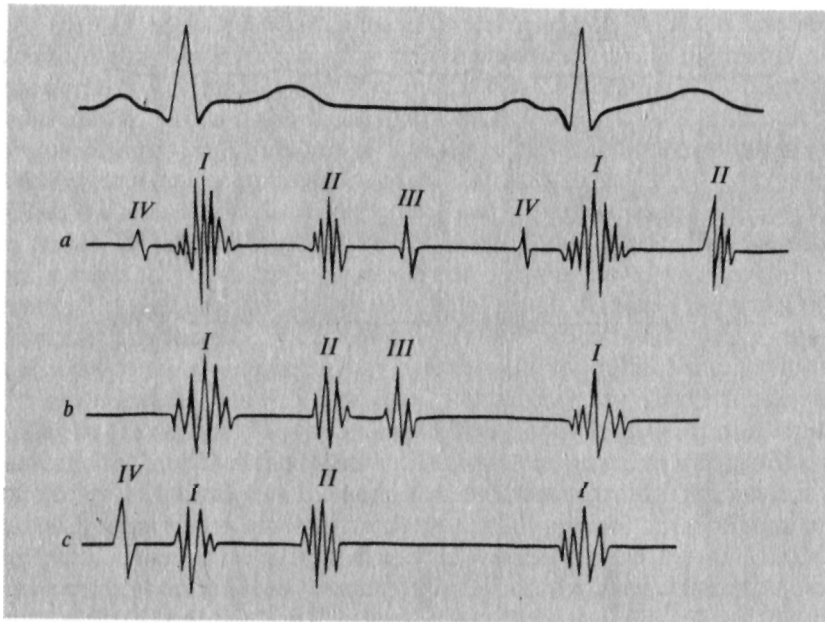


Fig. **34.** Gallop rhythm.
a—four normal heart sounds; *b*—protodiastolic gallop rhythm formed due to intensification of the physiological third sound; *c*—presystolic gallop rhythm formed at the expense of the fourth sound.

attended by a thrust, for which reason they are best heard on direct auscultation; the gallop rhythm can also be heard in auscultation with a phonendoscope, but the patient should lie on the left side after a mild exercise. Protodiastolic (at the beginning of diastole), mesodiastolic (in the middle of diastole), and presystolic (at the end of diastole) gallop rhythms are distinguished by the time of appearance of the extra sound in diastole. Gallop rhythm is also classified as ventricular or atrial, according to its origin.

Protodiastolic gallop rhythm arises in considerably diminished tone of the ventricular myocardium. The ventricles distend quickly during their filling with blood at the beginning of diastole and the vibrations thus generated are audible as an extra sound. The sound appears 0.12-0.2 s after the second heart sound and is an increased physiological third sound (Fig. 34).

Presystolic gallop rhythm arises in intensification of the physiological fourth sound, which is due to the diminished tone of the ventricular myocardium and a stronger atrial contraction. Intensified contraction of

the overfilled atrium increases blood ejection into the ventricle, while a diminished tone of the ventricular myocardium causes quicker distention of its walls. The presystolic gallop rhythm is better detected in delayed atrioventricular conduction, when atrial systole is separated from the ventricular systole by a longer than normal period.

Both the third and the fourth heart sounds can intensify significantly in grave myocardial affection, but in tachycardia they sum up to give a *mesodiastolic ox summation gallop rhythm.* Gallop rhythm is an important sign of myocardial weakness, and it has a great diagnostic and prognostic value. It develops in severe heart affections in patients with myocardial infarction, essential hypertension, myocarditis, chronic nephritis, decompensated heart diseases.

A pronounced acceleration of the cardiac rhythm makes the diastolic pause shorter so that it becomes almost as short as the systolic one. If the heart sounds heard at the cardiac apex are similar in intensity, a peculiar auscultative picture resembles the tic-tac or foetal rhythm, known also as *embryocardial ox pendulum rhythm.* It occurs in severe cardiac failure, attacks of paroxysmal tachycardia, high fever, etc.

Cardiac murmurs. In addition to the normal heart sounds, abnormal sounds known as murmurs may be heard. Cardiac murmurs may be both endo- and exocardiac. *Endocardiac murmurs* occur most frequently. These may occur in anatomical changes in the structure of the heart valves (organic murmurs) or in dysfunction of the intact valves (functional murmurs). Functional murmurs may be heard with increased rate of blood flow or decreased blood viscosity. The mechanism of endocardiac murmurs can be easier understood if one remembers the laws of physics concerning the flow of liquids in tubes. If a tube has a point where its otherwise even lumen is narrowed, the passing liquid produces noise. This noise is associated with turbulent flow of liquid above the narrowed portion of the tube, which causes vibration of the tube. The intensity of noise depends on two factors, viz., the liquid velocity and the extent of narrowing. The higher the velocity of the liquid, the more intense is the noise; when the liquid velocity decreases, the noise lessens or disappears. As to the extent of tube narrowing, its influence on noise intensity is directly proportional only within a certain range. If the lumen is narrowed to a very high degree, noise may weaken or even disappear. Liquid is also set in vortex movement when it passes a narrow portion of the tube and enters its wider part again. The same reasons account for the murmurs that arise in the heart. If the passage is narrowed or on the contrary widened, blood is set in turbulent flow which generates murmurs. If the vascular lumen remains unchanged, murmurs may be produced by the changes in the blood flow rate, as is the case with thyrotoxicosis, fever, or nervous excitation. Decreased blood

viscosity (e.g. in anaemia) increases the flow rate of blood and can also be the cause of murmurs. The most frequent cause of endocardiac murmur are various heart defects.

According to the time of appearance, murmurs are classified as systolic and diastolic. *Systolic murmur* occurs in cases when, during systole, blood moves from one chamber of the heart to another, or from the heart to the main vessels and meets an obstacle. Systolic murmur is heard in stenotic orifice of the aorta or the pulmonary trunk because blood ejected from the ventricles meets a narrowed vessel. Systolic murmur is also heard in cases with mitral and tricuspid incompetence. Generation of systolic murmur is explained by regurgitation of blood which is not completely expelled into the aorta and pulmonary trunk during the ventricular systole, but is partly returned to the atrium through an incompletely closed mitral or tricuspid orifice. Since this partly closed orifice is actually a narrow slit, murmur is generated as blood passes through it.

Diastolic murmur occurs if blood meets a narrowed passage during diastole. This murmur is heard in stenosed left or right atrioventricular orifice, since blood meets a narrow passage in its flow from the atria into the ventricles. Diastolic murmur also occurs in aortic or pulmonary valve incompetence. Murmur is generated when blood flows back from the vessels into the ventricles through a slit formed by incomplete closure of the cusps of the affected valve.

The following should be determined during auscultation: (1) the relation of the murmur to the phase of the heart activity (to systole or diastole); (2) the features, character, strength, and length of murmur; (3) localization of the murmur, i.e. the area where this murmur is heard best; (4) direction of transmission (radiation).

The relation of murmurs to systole or diastole is determined by the same signs that are used to differentiate between the first and the second heart sounds. Systolic murmur appears with the first heart sound, during a short pause of the heart; it is synchronous with the apex beat and the carotid pulse. Diastolic murmur follows the second sound, during the long pause of the heart. Three types of diastolic murmurs are distinguished: (1) *protodiastolic murmur* which arises at the very beginning of diastole, immediately after the second heart sound; (2) *mesodiastolic murmur* which is heard soon after the second heart sound; and (3) *presystolic murmur* which appears at the end of diastole (Fig. 35).

Properties of murmurs. By their character, murmurs may be soft, blowing, or on the contrary rough, grating or grazing sounds; musical murmurs can also be heard. By duration, heart murmurs are classified as short and long, and by their intensity as soft and loud. The intensity of the noise may change with the phase of the heart activity. Murmur may become

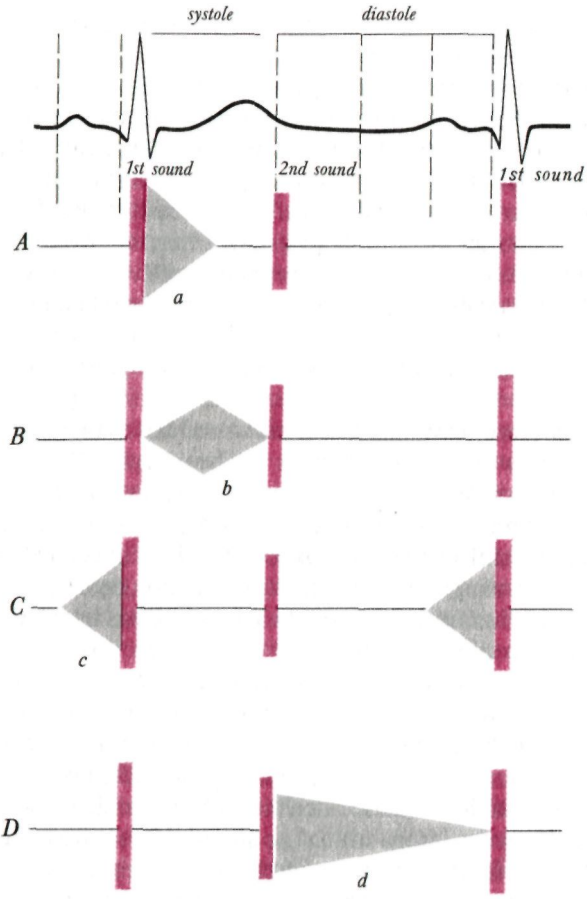


Fig. 35. Relations between the heart sounds and murmurs.
A, B—systolic murmur: a—decrescendo; *b*—crescendo-decrescendo (diamond-shaped); *C, D*—diastolic murmur: c—presystolic; *d*— protodiastolic.

weaker (decrescendo) or louder (crescendo). Decrescendo murmurs occur more frequently. This can be explained as follows: as blood begins flowing from one heart chamber to another, or from the heart to the main vessel, the difference in pressures in two chambers is high and the blood flow rate is therefore high as well. But as the blood is expelled, the pressure inside the chamber from which the blood is ejected gradually decreases, the blood flow rate slows down, and the noise intensity decreases. Presystolic murmur has an increasing character and occurs mostly in stenosis of the anterior left atrioventricular orifice, at the very end of ventricular diastole,

when atrial systole begins to increase the blood outflow from the left atrium to the left ventricle.

The location of murmur corresponds to the best listening post of that particular valve where this murmur is generated. In certain cases, however, murmurs are better heard at a distance from the point where they are generated, provided their transmission is good. Murmurs are well transmitted in the direction of the blood flow. They are better heard in areas where the heart is close to the chest wall and where it is not covered by the lungs. Systolic murmur due to mitral valve incompetence is best heard at the heart apex. It can be transmitted by the firm muscle of the left ventricle to the axillary area or by the course of the backward blood flow from the left ventricle to the left atrium, i.e. into the second and third interspace, to the left of the sternum.

Diastolic murmur generated in a narrowed left atrioventricular orifice is usually heard over a limited area at the heart apex.

Systolic murmur due to stenosed aortic orifice is heard in the second interspace, to the right of the sternum. As a rule, it is well transmitted by the course of the blood flow onto the carotid arteries. Since this heart defect is characterized by a rough and loud (grating, grazing) sound, it can be determined in auscultation over the entire heart region and be transmitted to the interscapular space.

Diastolic murmur due to aortic valve incompetence is better heard not over the aortic valve but rather at the Botkin-Erb point, where it is transmitted by the back flow of blood from the aorta to the left ventricle.

Systolic murmur associated with tricuspid insufficiency is best heard at the base of the xiphoid process, since the right ventricle is the closest to the chest wall at this point, from which the sound can be transmitted upwards and to the right, in the direction of the right atrium. In the rare heart disease associated with stenosis of the right atrioventricular orifice, the diastolic murmur is heard over a limited area at the base of the xiphoid process.

It should be remembered that murmurs are best heard in certain postures of the patient. Systolic murmurs associated with incompetence of atrioventricular valves or with stenosis of the aortic or pulmonic orifice, are best heard with the patient in the recumbent posture because the blood flow from the ventricles is facilitated and the blood-flow rate increases. Diastolic murmurs arising due to stenosis of the atrioventricular orifice or incompetence of the aortic valve and the valve of pulmonary trunk are better heard in the upright position, since the blood flow to the ventricles from the atria or from the vessels (in insufficiency of the corresponding valves) is thus facilitated and the blood-flow rate increases.

Differentiation of murmurs. If several murmurs are heard

simultaneously over different valves, it is necessary to determine the affected valves and the character of their affections. Systolic and diastolic murmurs over one valve indicate its composite affection, i.e. incompetence of the valve and stenosis of the orifice. If systolic murmur is heard over one valve and diastolic murmur over the other, a combined affection of two valves can be diagnosed.

It is more difficult to decide whether one or two valves are affected if murmurs can be heard at various listening points during one and the same phase of heart activity. The character of the murmur should then be analysed. If a soft and blowing murmur is heard over one valve, and rough and grating over the other, the murmurs are generated by two different affected valves. By moving the stethoscope bell along the line connecting the two valves, the changes in the murmur intensity should be followed. If at some point of the line the murmur disappears or weakens markedly, and then again becomes louder, it will in most cases indicate affection of two valves. If the murmur decreases or increases as the stethoscope bell moves in the direction of the second valve, it usually indicates affection of only one valve. But this is not an indisputable sign because the degree of valve affection may differ too, and an independent, though less loud, murmur will then be heard over milder stenotic affection. The character of murmur transmission helps differentiation. For example, systolic murmur occurring in mitral valve incompetence is transmitted into the axillary region. It may be heard also over the aortic valve but it will not be transmitted onto the carotid arteries (as distinct from systolic murmur associated with stenosis of the aortic orifice).

During auscultation of the heart, it is necessary to differentiate between functional and organic, and between endocardial and exocardial murmurs. The following properties of *functional murmurs* help differentiate them from *organic murmurs:* (1) in most cases functional murmurs are systolic; (2) functional murmurs are not permanent and may arise and disappear when the person changes his posture, after exercise and during various respiratory phases; (3) they are mostly heard over the pulmonary trunk and less frequently over the heart apex; (4) functional murmurs are transient and are rarely heard during the entire systole; these are soft and blowing sounds; (5) the murmurs are normally heard over a limited area and are not transmitted to long distances from their source; (6) functional murmurs are not accompanied by other signs of valve affections (e.g. enlargement of the heart chambers or changes in the heart sounds).

Exocardial murmurs. Although synchronous with the heart work, they arise outside the heart. These are pericardial and pleuropericardial friction sounds.

Pericardial friction murmurs are connected with the changes in the

visceral and parietal pericardial layers in which fibrin is deposited (in pericarditis), cancer nodes develop, etc. The mechanism by which pericardial friction sounds are generated is similar to that of the pleural friction sounds, except that they depend not on the respiratory movements but on the movements of the heart during systole and diastole. Pericardial friction murmurs vary. Sometimes they resemble pleural friction or the crisping sounds of snow, and sometimes they are very soft, as if produced by rattling of paper or scratching. The following signs can be used to differentiate pericardial friction sounds from intracardiac sounds: (1) there is no complete synchronism of pericardial friction sounds with systole and diastole; friction sounds are often continuous, their intensity increasing during systole or diastole; (2) friction sounds can be heard for short periods during various phases of the heart work, either during systole or during diastole; (3) pericardial friction sounds are not permanent and can reappear at intervals; (4) friction sounds are heard at sites other than the best auscultative points; they are best heard in the areas of absolute cardiac dullness, at the heart base, at the left edge of the sternum in the 3rd and 4th intercostal spaces; their localization is inconstant and migrates even during the course of one day; (5) friction sounds are very poorly transmitted from the site of their generation; (6) the sounds are heard nearer the examiner's ear than endocardial murmurs; (7) friction sounds are intensified if the stethoscope is pressed tighter to the chest and when the patient leans forward, because the pericardium layers come in closer contact with one another.

Pleuropericardial friction murmurs arise in inflammation of the pleura adjacent to the heart and are the result of friction of the pleural layers (synchronous with the heart work). As distinct from pericardial friction sounds, pleuropericardial friction is always heard at the left side of relative cardiac dullness. It usually combines with pleural friction sound and changes its intensity during the respiratory phases: the sound increases during deep inspiration when the lung edge comes in a closer contact with the heart and decreases markedly during expiration, when the lung edge collapses.

Physical and Instrumental Studies of the Vessels

The vessels are studied by inspection, by palpation of arteries and veins, by auscultation of large vessels, and by instrumental examination of the vascular system.

STUDY OF ARTERIAL PULSE

Pulse is the rhythmical vibration of the arterial walls caused by contractions of the heart, blood discharge into the arterial system, and changes in pressure in this system during systole and diastole. Pulse wave is transmit-

ted due to the ability of arterial walls to distend and collapse. The velocity of the pulse wave varies from 4 to 13 m/s, i.e. exceeds significantly the linear velocity of the blood flow, which does not exceed 0.5 m/s even in large arteries.

Palpation of the pulse is the main method of examination of pulse. As a rule, pulse is studied first on the radial artery, since it is superficial and runs immediately under the skin and can thus be readily felt between the styloid process of the radial bone and the tendon of the internal radial muscle. The patient's hand is grasped by the examiner so that the thumb of the right hand is placed on the dorsal side of the arm (near the radiocarpal joint) while the other fingers remain on the frontal side of the arm. As soon as the artery is found, it is pressed against the underlying bone. The pulse wave is felt by the examining fingers as a dilation of the artery. The pulse may be different on different arms, and therefore it should first be palpated simultaneously on both radial arteries. The condition of the vascular wall should be assessed simultaneously. To that end, the artery is pressed by the index and middle fingers of the left hand slightly above the point where the pulse is examined by the right hand. When the vessel stops pulsating under the fingers of the right hand, the arterial wall is felt. A normal artery is a thin elastic tube. In some diseases, for example, in atherosclerosis, the arteries change, their walls become firm, and the course more tortuous. If calcification is considerable, the artery walls are rough, tortuous tubes, sometimes with bead-like thickenings.

Various properties of pulse can be better understood if sphygmograms (pulse curves) are first studied. The diagnostic importance of the pulse will be described later.

Sphygmography. Pulsation of the vascular wall is recorded as a curve (sphygmogram) by an apparatus called sphygmograph. Special pick-ups convert mechanical oscillations of the vascular wall into electric pulses, which are amplified and recorded by an electrocardiograph.

Direct and volumetric sphygmography are distinguished. Direct sphygmography is used to record oscillations of the wall of any superficial artery, for which purpose a funnel is placed on the examined vessel. Volumetric sphygmography records total vibrations of the vascular wall that are converted into vibrations of a portion of the body (usually an extremity). Volumetric sphygmogram is taken by placing a special cuff on the extremity. Curves obtained by direct and volumetric sphygmography do not differ substantially. The distance of the artery from the heart is important for the shape of the pulse curve. Central and peripheral sphygmograms are distinguished accordingly. Central sphygmograms are taken from the carotid and subclavian arteries. Sphygmograms of the radial and femoral arteries, and also volumetric sphygmograms of the extremities are peripheral.

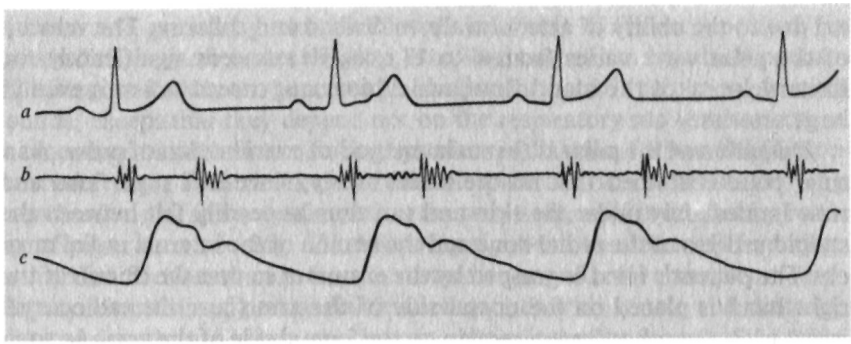


Fig. 36. Normal sphygmogram of the carotid (c) recorded simultaneously with ECG *(a)* and PCG *(b)*.

Normal sphygmogram. Both the central and peripheral sphygmograms (Fig. 36) of a healthy individual have a sharp upstroke (the anacrotic wave), a peak of the curve, and a gradually declining downstroke (the catacrotic wave). The catacrotic limb of a peripheral sphygmogram has smaller waves one of which is more pronounced and is known as a dicrotic wave, which is due to repulsion of the blood from the closed aortic valve during early diastole. A central sphygmogram differs from a peripheral one by a pre-anacrotic vibration, a steeper anacrotic wave, a pronounced catacrotic incisura (corresponding to closure of the aortic valve), and a small dicrotic wave. In interpreting a sphygmogram, special attention should be paid to the shape of the pulse waves, the rate of ascent of the anacrotic wave and of descent of the catacrotic wave, the amplitude of the pulse wave, the height of the dicrotic wave, etc.

Properties of arterial pulse. The study of the arterial pulse gives information on the work of the heart and the condition of the circulatory system. The pulse should be taken in the following order. First the examiner must determine if the pulse can be equally felt on both arms. To that end both radial arteries should be palpated simultaneously and the magnitude of pulse waves on both hands compared (normally it is the same). The pulse wave on one arm may happen to be lower. It occurs in unilateral structural abnormalities in peripheral course of the artery, its constriction, compression by a tumour, or a scar, etc. Pulse may also be different when similar changes occur in the brachial or subclavian artery, or due to compression of large arterial trunks by the aortic aneurysm, mediastinal tumour, retrosternal goitre, or markedly enlarged left atrium. The smaller pulse wave may lag in time. If the pulse on the two arms is different, its further study should be carried out on that arm where the pulse

wave is more pronounced. The following properties of pulse are examined: rhythm, rate, tension, filling, size, and form.

Rhythm. In healthy subjects, cardiac contractions and pulse waves follow one another at regular intervals: the pulse is said to be rhythmic or regular. When the cardiac rhythm is upset, pulse waves follow at irregular intervals: the pulse becomes arrhythmic, or irregular. Some pulse waves may be missing or they may appear prematurely, which is characteristic of extrasystole and also complete arrhythmia (fibrillation), in which pulse waves follow one another at irregular intervals.

Pulse rate in normal conditions corresponds to the rate of cardiac contractions and is 60—80 per minute. If the heart rhythm is accelerated (tachycardia), the number of pulse waves increases and the pulse rate increases accordingly (pulsus frequens); slowed cardiac rhythm (bradycardia) is characterized by a respective slowing of the pulse (pulsus rarus). The pulse rate is counted for one minute. If the pulse is arrhythmic, the heart beats should also be counted and compared with the pulse rate. During frequent and irregular contractions of the heart, some systoles of the left ventricle can be so weak that the blood is not ejected into the aorta or the amount of the discharged blood is very small and the pulse wave does not reach the peripheral arteries. The difference between the heart rate and the pulse is called the pulse deficit while the pulse itself is called pulsus deficiens. The greater the deficiency, the worse is the effect it produces on the circulation of blood.

Pulse pressure is determined by the force that should be applied to the pulsating artery to compress it completely. This property of pulse depends on the magnitude of the systolic arterial pressure. If arterial pressure is normal, the artery can be compressed by a moderate pressure. A normal pulse is therefore of moderate tension. The higher the pressure, the more difficult it is to compress the artery; such a pulse is called pulsus durus (hard or high-tension pulse). If the arterial pressure is small, the artery is easy to compress and the pulse is soft (pulsus mollis).

Volume of pulse. Pulse volume shows the artery filling with blood, which in turn depends on the amount of blood that is ejected during systole into the arterial system and which produces variations in the artery volume. Pulse volume depends on the stroke volume, on the total amount of circulating blood, and its distribution in the body. If the stroke volume is normal and the artery is sufficiently filled with blood, the pulse is said to be full (pulsus plenus). In abnormal circulation and blood loss, the pulse volume decreases (pulsus vacuus).

Pulse size. The pulse size implies its filling and tension. It depends on the expansion of the artery during systole and on its collapse during diastole. These in turn depend on the pulse volume, fluctuation of the

arterial pressure during both systole and diastole, and distensibility of the arterial wall. Pulse wave increases with increasing stroke volume, great fluctuations in the arterial pressure, and also with decreasing tone of the arterial wall. This pulse is called large-volume pulse or pulsus magnus. A large-volume pulse is characterized by a high amplitude of pulse fluctuations on a sphygmogram, and it is therefore also called high pulse (pulsus altus). Large-volume or high pulse is characteristic of aortic valve incompetence in thyrotoxicosis, when the pulse wave increases due to the high difference between systolic and diastolic arterial pressure. Such a pulse may develop in fever in connection with decreased tone of the arterial wall.

Pulse wave decreases with decreasing stroke volume and amplitude of pressure fluctuations during systole and diastole and with increasing tone of the arterial wall. The pulse wave and the pulse become small (pulsus parvus). Pulse is small when the amount of blood discharged into the arterial system is small, and the rate of its discharge is low. This is observed in stenosis of the aortic orifice or of the left venous orifice, and also in tachycardia and acute cardiac failure. The pulse wave may be quite insignificant (barely perceptible) in shock, acute cardiac failure and massive loss of blood. This pulse is called thready (pulsus filiformis).

In normal conditions, pulse is rhythmic and the pulse wave uniform. Such a pulse is called uniform (pulsus aequalis). In cardiac rhythm disorders, when the heart contracts at irregular intervals, the pulse wave becomes non-uniform, and this pulse is called unequal (pulsus inaequalis). In rare cases (in rhythmic pulse), high and low pulse waves alternate. This is alternating pulse (pulsus alternans). It is believed that this pulse is due to alternation of heart contractions that vary in force. It usually occurs in severe myocardial affection.

Pulse character (Fig. 37a). This depends on the rate of change in the arterial pressure during systole and diastole. If much blood is discharged into the aorta during systole and the pressure in the aorta increases rapidly, while during a diastole this pressure quickly falls, the arterial wall will expand and collapse quickly as well. This pulse is called quick pulse (pulsus celer or pulsus saliens). On a sphygmogram this pulse gives a steeper anacrotic rise and sharp catacrotic fall (Fig. *31b).* Quick pulse is characteristic of aortic incompetence, since in this condition the stroke volume and systolic pressure increase, while during diastole the pressure falls rapidly due to blood regurgitation into the left ventricle. Pulse in such cases is not only quick but also high (pulsus celer et altus). Quick pulse is less characteristic of thyrotoxicosis or nervous strain.

Slow pulse (pulsus tardus) is, on the contrary, connected with slow rise and fall of pressure in the arterial system and its small fluctuation during

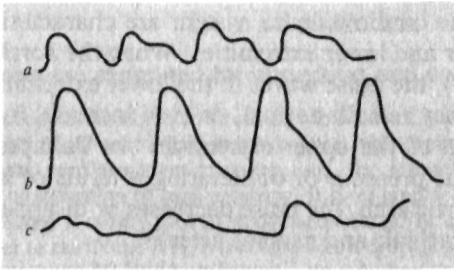


Fig. 37. Sphygmograms. *a*—normal pulse; *b*—quick and high pulse; c—small and low pulse.

the cardiac cycle (Fig. 37c). This condition is characteristic of aortic stenosis: blood ejection from the left ventricle is difficult and the pressure in the aorta therefore increases slowly. The pulse wave decreases and the pulse is therefore not only slow but also small (pulsus tardus et parvus).

Other changes in the arterial pulse. Sometimes, when the pulse wave decreases, another wave can be detected which is connected with increasing dicrotic wave; this wave normally is not detectable and can only be seen on a sphygmogram. If the tone of the peripheral arteries decreases (e.g. in fever or infectious diseases), the dicrotic wave can be detected by palpation as well. This pulse is called dicrotic (pulsus dicroticus). Paradoxical pulse (pulsus paradoxus) is also distinguished. It is characterized by smaller pulse waves during inspiration. It develops in cases with adherent pericardium due to compression of large veins and decreased blood filling of the heart during inspiration.

After the examination of pulse on the radial artery has been finished, it is studied on other vessels, e.g. on the temporal, carotid, femoral, popliteal arteries, dorsalis pedis and other arteries. Examination of pulse on other arteries is especially important in suspected affections of these arteries (obliterating endocarditis, atherosclerosis, thrombosis of the vessels).

The femoral artery is readily palpable in the groin, better with the straightened and slightly outwardly turned thigh. The pulse of the popliteal artery is well palpated in the popliteal fossa with the patient in the prone position. The posterior tibial artery is palpated in the region of the condyle of the internal malleolus. The dorsalis pedis artery is felt on the dorsal surface of the foot in the proximal part of the first intermetatarsal space. The pulse taken on the latter two arteries is very important for diagnosis of obliterating endarteritis.

The pulse of the carotid arteries should be examined carefully, one after the other, beginning with a slight pressure on the arterial wall, because of the danger of the carotid reflex: the heart may slow down markedly (or even stop) and the arterial pressure drop significantly. The clinical signs of this reflex are vertigo, faint, and convulsions.

Some diseases of the cardiovascular system are characterized by different pulse in the upper and lower extremities. When the aortic isthmus is constricted (coarctation), the pulse waves in the lower extremities decrease significantly, whereas they remain normal, or even increase, in the carotid arteries and the arteries of the upper extremities. In Takayasu's disease (pulseless disease), in the presence of obliterating arteritis of large vessels originating from the aortic arch, the pulse decreases or disappears at all in the carotid, axillary, brachial, and radiant arteries.

Velocity of the pulse wave. An additional method of examination of the arterial system is determining velocity at which the pulse wave is propagated; this is used to assess the elasticity of the vascular walls. The firmer the wall, the higher the velocity at which the pulse wave is propagated.

In order to determine velocity of pulse wave propagation (V), it is necessary to know the length of the vessel (L), and the pulse wave lag time (0 on the periphery at instantaneous sphygmography at two points of the vascular system. The pulse wave velocity can then be calculated from the formula:

$$V = \frac{L}{t}.$$

In order to determine the velocity of pulse wave, two sphygmograms are usually taken synchronously from the carotid and femoral arteries (see "Sphygmography"). One pickup is placed at the bifurcation of the carotid artery (at the level of the upper thyroid cartilage) and the other, on the femoral artery, in the region of the inguinal ligament. A measuring tape is then used to measure the distance from the jugular fossa to the first pickup (l_1) and to the second one (l_2). The true length of the vessel (L) can be found by subtracting two lengths from the jugular fossa to the pickup on the carotid artery ($2l_1$) from the sum of the lengths l_1 and l_2, because the direction in which the pulse wave propagates in the carotid artery is opposite to that in the aorta. It follows that $L = (l_1 + l_2) - 2 \times l_1 = l_2 - l_1$. Once the length of the vessel is known, the lag time is now determined for the pulse wave at the periphery, i.e. the period lasting from the anacrotic ascent on the sphygmogram of the femoral artery to the anactrotic ascent on the carotid sphygmogram (in hundredth fractions of a second). The higher the velocity of pulse wave, the less the time lag.

Once the length and lag time of the pulse wave have been determined, one can find the velocity of the pulse wave mainly in the descending aorta. In normal cases it varies from 4.5 to 8 m/s. This velocity increases with age. It also increases in atherosclerosis and essential hypertension. The pulse wave velocity decreases in hypotension, anaemia, heart diseases, and thrombosis of the abdominal artery.

STUDY OF CAPILLARIES

Capillaries are examined by inspection and capillaroscopy.

Capillaroscopy is the method of studying capillaries of intact surface epithelial coats (e.g. skin or mucosa). Slight-magnification microscopes with common diffuse day-light illumination, or special capiUaroscopes may be used for the purpose. Capillarography is a photographic modification of capillaroscopy. It gives graphic patterns.

Capillaroscopy is mostly used to study capillaries at the edge of the nail bed of the ring finger. In order to clarify the skin, it is coated with a drop of peach-kern or cedar oil. In normal conditions, the capillaries can be seen as elongated pale red loops against the yellowish pink background. The arterial bend of the capillary is normally narrower and shorter than the venous one; the transition part of the loop is usually rounded. Figure-eight-shaped loops sometimes occur. The number of capillaries is 16-20 in the field of vision. The blood flow is almost indiscernible in them; it is continuous and faster in the arterial bend than in the venous one. The capillaroscopic picture changes during vascular spasms, congestions, and in diabetes mellitus.

STUDY OF VENOUS PULSE

Venous pulse is studied by inspection and phlebography.

Phlebography is the recording of the venous pulse. Vibrations of the venous walls connected with the change in filling of the large veins located close to the heart are recorded in the form of a curve (phlebogram). The principle underlying phlebography is similar to that used in sphygmography. Phlebograms of the jugular veins, where the pulsation is more pronounced, are usually taken. A phlebogram of the cardiac cycle in healthy subjects includes a number of waves (Fig. 38). These are positive *(a, c,* v) and negative *(x, y)* pulse waves. Their origination is explained as follows.

1. The positive wave *a* appears during contraction of the right atrium. At this moment, emptying of the venae cavae from the inflowing peripheral venous blood is delayed; the veins become overfilled and swollen.

2. Wave *c* follows wave *a* after an insignificant descent of the curve. It

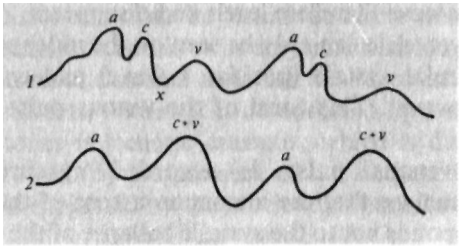


Fig. 38. Phlebograms. 1—normal; *2*—positive venous pulse.

is associated with ventricular systole and arises due to transmission of pulsation of the carotid artery that runs in the vicinity of the jugular vein.

3. Next follows the negative wave x, which is caused by a systolic collapse and is explained by filling of the right atrium with venous blood during ventricular systole; the veins are emptied and collapse. Fast emptying of the veins is facilitated by the falling intrathoracic pressure due to heart contraction and discharge of the systolic blood to the peripheral vessels.

4. Positive wave v comes at the end of the ventricular systole with the closed tricuspid valve. It is connected with accumulation of blood in the atria which holds back the delivery of new portions of blood from the venae cavae.

5. Wave v is followed by a new collapse of the vein (the diastolic collapse *y)* which begins with opening of the tricuspid valve and delivery of blood into the right ventricle. This promotes the inflow of blood from the venae cavae into the right atrium and collapse of the vein.

In the analysis of a phlebogram, it is useful to pay attention to the shape and width of separate waves and their relation to the sphygmographic findings. A phlebogram shows the activity of the right heart chambers and pressure fluctuation in the right atrium. A normal phlebogram has a sharp wave a; this form of the venous pulse curve is called *atrial.* If sphygmogram and phlebogram are taken simultaneously, the maximum ascent of the normal sphygmographic curve corresponds to the negative deviation *(x)* of the phlebogram, because atrial diastole and blood flow into the atria from the veins begin during ventricular systole and blood ejection into the arterial system. Hence another name of a normal venous pulse, *negative venous pulse.*

The size of separate waves on phlebograms changes in pathology. The waves may increase, decrease, or disappear. For example, with difficult blood outflow from the right atrium (in stenotic right atrioventricular orifice, or increased pressure in the right ventricle), the contractile force of the atrium and the *a* wave increase. The *a* wave broadens and becomes lower, or it can even disappear altogether in progressive weakness of the right atrium, and blood congestion in it. Since the blood pressure does not fall significanlty during diastole either, emptying of the veins becomes difficult. The negative *x* wave therefore levels and disappears. As a result, the activity of the right ventricle can only be seen on the phlebogram: the vein swells during ventricular systole (positive v wave) and collapses during diastole (negative *y* wave). This form of the venous pulse is called ventricular.

If ventricular venous pulse is recorded synchronously with sphygmogram, one can see that the maximum ascent of the curve on the sphygmogram corresponds not to the systolic collapse of the vein but to the

positive deviation, the v wave. This explains another name of the pulse, *positive venous pulse* (see Fig. 38).

Positive ventricular venous pulse is observed in tricuspid incompetence, pronounced venous congestion in the greater circulation, in fibrillation and complete transverse heart block.

AUSCULTATION OF VESSELS

Auscultation of arteries. Arteries of medium calibre, such as the carotid, subclavian, or femoral artery, are usually auscultated. The artery is first palpated, then heard by a phonendoscope without applying pressure, since stenotic murmurs may otherwise appear. Sounds and murmurs can be heard over arteries. These can be generated either in the arteries themselves or be transmitted from the heart and aortic valves. The transmitted sounds and murmurs can only be heard on the arteries that are located close to the heart, such as the carotid and the subclavian arteries.

Two sounds can be heard on the carotid and subclavian arteries in healthy persons. The first sound is due to the tension of the arterial wall distended by the running pulse wave, and the second sound is transmitted onto these arteries from the aortic semilunar valve. One systolic sound can sometimes be heard on the femoral artery. Like the first sound of the carotid and subclavian arteries, the second sound is generated by the vibration of the tensed arterial wall when the pulse wave passes it. In aortic incompetence, the first sound over the arteries becomes louder because of the higher pulse wave, and it can be heard at greater distances from the heart, e.g. on the brachial and radial arteries. Two sounds can sometimes be heard on the femoral artery in aortic incompetence. This doubled tone *(Traube's doubled tone)* is generated by intense vibration of the vascular wall during both systole and diastole.

Sounds heard over the arteries are mostly systolic. Systolic sound produced by the stenosed aortal orifice is usually well transmitted onto the carotid and subclavian arteries. Systolic sound associated with decreased viscosity of blood and increased flow rate (e.g. in anaemia, fever, exophthalmic goitre) can also be heard on these vessels. Systolic sound sometimes appears in stenosis or aneurysmal dilation of large vessels. The *Vinogradov-Duroziez doubled tone* can be heard in aortic incompetence over the femoral artery when it is compressed by a stethoscope bell. The first of these tones is stenotic murmur, which is due to the blood flow through a narrowed (by the pressure of the stethoscope) vessel, while the second sound is explained by the accelerated backflow to the heart during diastole.

Auscultation of veins. Neither sounds nor murmurs are normally heard over veins. Auscultation of the jugular veins, over which the so-called *nun's murmur* may be heard, is diagnostically important. This is a permanent blowing or humming sound, which is produced by accelerated flow of blood with decreased viscosity in anaemic patients. It is better heard on the right jugular vein and becomes more intense when the patient turns the head in the opposite side.

MEASURING ARTERIAL PRESSURE

The pressure of the blood in the arterial system varies rhythmically, attaining its maximum during systole and lowering during diastole. This is explained as follows: when blood is ejected during systole it meets resistance of the arterial walls and of the blood contained in the arterial system; the pressure in the arteries thus increases to cause distention of the arterial walls. During diastole the arterial pressure falls and remains at a certain level due to the elastic contraction of the arterial walls and resistance of the arterioles, owing to which the blood flow into the arterioles, capillaries, and veins continues. It follows therefore that arterial pressure is proportional to the amount of blood ejected by the heart into the aorta (i.e. the stroke volume) and the peripheral resistance.

Arterial pressure is expressed in millimetres of mercury column. The normal *systolic (maximal) pressure* varies from 100 to 140 mm Hg and *diastolic (minimal)* from 60 to 90 mm Hg. The difference between systolic and diastolic pressure is called the *pulse pressure* (normally it is 40—50 mm Hg). Arterial pressure can be measured by a direct or indirect method. In the direct method, the needle or a cannula is introduced directly into the artery and connected to a pressure gauge. This method is mostly used in heart surgery.

Three techniques exist to take blood pressure indirectly. These are auscultatory, palpatory, and oscillographic. The auscultatory method is commonly used in medical practice. The method was proposed by N. Kbrotkoff in 1905 and is used to measure systolic and diastolic blood pressure. A sphygmomanometer is used to read pressure. It consists of a mercury or a spring manometer which is connected to a cuff and rubber bulb used to inflate the cuff through a connecting tube. A valve on the bulb is used to admit air into the cuff and the manometer, and to hold pressure at the needed level. A more accurate instrument is a Riva-Rocci mercury manometer. This is a mercury container communicated with a thin vertical glass tube attached to a scale graduated in millimetres from 0 to 300.

The pressure in the brachial artery is usually measured. To that end, the

arm of the patient is freed from tight clothes and a cuff is attached snugly and evenly onto the arm (a finger-breadth between the cuff and the skin). The inlet socket of the cuff should be directed downward, 2-3 cm above the antecubital fossa. The arm should be placed comfortably on a level surface, the palm up; the muscles of the arm should be relaxed. The phonendoscope bell is placed over the brachial artery in the antecubital space, the valve on the bulb is closed, the air is pumped into the cuff and the manometer. The pressure of the air in the cuff that compresses the artery corresponds to the mercury level as read off the instrument scale. Air is pumped into the cuff until pressure inside it is 30 mm above the level at which the brachial or radial artery stops pulsating. The valve is then opened slowly to release air from the cuff. Using the phonendoscope, the brachial artery is auscultated and the readings of the manometer followed. When the pressure in the cuff drops slightly below systolic, tones synchronous with the heart beats are heard. The manometer readings at the moment when the tones are first heard are taken as the systolic pressure. This value is usually recorded to an accuracy of 5 mm Hg (e.g. 135, 130, 125 mm Hg, etc.).

N. S. Korotkoff described four phases of sounds that are heard during measurement of arterial pressure. The *first phase* is the appearance of the tone over the artery. The tones arise at the moment when the pressure in the artery during systole becomes slightly above the pressure in the cuff and the first portions of blood pass into the vessel below the point of constriction to cause pulsation of the relaxed wall of the emptied vessel. Although the tones appear at a pressure slightly below the systolic one, this difference is insignificant and is disregarded. As air pressure in the cuff continues decreasing, greater amount of blood passes the compressed portion of the vessel and the pulsation of the arterial wall below the point of constriction intensifies. The tones become louder, and murmurs caused by the blood turbulation below the constricted point join the tones *(second phase)*. A further reduction of the air pressure inside the cuff decreases pressure on the artery and the sounds disappear. The tone loudness increases during this time because the pressure in the cuff still remains above diastolic. The artery below the point of compression remains relaxed, and since greater amounts of blood pass into the vessel during each systole, pulsation of the vessel is intensified and the tones become louder. The moment when loud tones become audible is designated as the *third phase*. When pressure inside the cuff equals diastolic one, and the blood flow is no longer obstructed, the pulsation of the vessel suddenly decreases. This moment is characterized by a marked weakening and disappearance of the tones *(fourth phase)*.

The palpatory method is only used to take systolic pressure. As the air is released from the cuff slowly, the radial artery is palpated. When the pressure in the cuff drops slightly below the systolic one, the first weak pulse tones appear.

The oscillographic method is used to record systolic, mean, and diastolic pressure in the form of an oscillogram, and also to assess the tones of the arteries, elasticity of their wall and patency. When blood passes the compressed portion of the artery during systole, the pressure in the cuff in-

creases, and pressure fluctuations are recorded as a curve on a paper chart by an oscillograph. A simple oscillograph consists of a cuff, a manometer, and recording device. Pulsation of large arteries (e.g. brachial or femoral artery) is studied by oscillography. To that end, the artery in question is compressed by air which is pumped into the cuff. When the artery is compressed completely, the oscillograph only records insignificant vibrations due to the pulse thrust against the blind end of the compressed artery. The release valve is then opened and the pressure in the cuff begins decreasing. As soon as it equals the systolic pressure (to be more exact, as soon as the pressure becomes slightly lower than the systolic one), pulsations appear in the vessel wall, they are recorded as waves of small amplitude. As the pressure continues falling in the cuff, the amplitude of the waves increases. The maximum oscillations correspond to the so-called *mean* or *dynamic blood pressure.* The concept of the mean arterial pressure was formulated by I. Sechenov in 1861. According to Sechenov, this is constant pressure that might (without pulsation) ensure movement of the blood in the system at the same rate. Normal mean pressure is from 80 to 100 mm Hg. Mean pressure can only be determined from an oscillogram. It can approximately be calculated by the following formula: $P_{mean} = P_{diastolic} + \frac{1}{3}P_{pulse}$. As the pressure in the cuff further drops, the amplitude of oscillations decreases. The moment when the oscillations disappear (the last wave on the oscillogram) corresponds to the level of diastolic pressure.

Oscillograms taken at symmetrical points of the upper and lower extremities of healthy persons have a similar pattern. If patency of vessels decreases, oscillations of the affected artery decrease markedly or disappear altogether. Any indirect method of measuring systolic pressure may give somewhat exaggerated results because artificial compression of the vessel imposes additional resistance to the blood flow not only by the vascular wall itself but also the tissues surrounding the vessel. Systolic pressure may also be influenced by the hydraulic impact arising at the blind end of the artery compressed by the cuff as it meets the thrust of the pulse wave. Arterial pressure of healthy subjects varies physiologically within a certain limit depending on physical exertion or emotional strain, the posture, time of meals, and other factors. The lowest pressure is normally observed at rest, before breakfast, in the morning, i.e. in conditions under which basal metabolism occurs. This pressure is therefore called *basal.* When pressure is taken for the first time, it may appear slightly higher than actual which is explained by the patient's response to the procedure. It is therefore recommended that pressure be taken several times at a run without taking off the cuff but only deflating it completely. The last and the least value should be considered the closest to the true pressure. A transient increase in the arterial pressure may occur during heavy exercise

(especially in persons who are unaccustomed to it), in excitation after taking alcohol, strong tea or coffee, in heavy smoking or during attacks of intense pain.

Many diseases are attended by changes in arterial pressure. Elevation of systolic pressure over 140 mm and of diastolic over 90 mm Hg is called *arterial hypertension.* A drop in the systolic pressure below 100 mm and of diastolic below 60 mm Hg is known as *arterial hypotension.* Long-standing elevation of arterial pressure occurs in essential hypertension, many renal diseases (glomerulonephritis, vascular nephrosclerosis), in certain endocrinological diseases, and heart diseases, etc. Systolic pressure alone is sometimes elevated, whereas diastolic pressure remains normal or decreased. This causes a marked increase in the pulse pressure. This condition occurs in aortic incompetence, thyrotoxicosis, less markedly in anaemia of any aetiology and atherosclerotic affections of the vessels.

Arterial pressure may be decreased due to constitutional properties in asthenic persons, especially in the upright position (orthostatic hypotension). As a pathological symptom, hypotension occurs in many acute and chronic infectious diseases, Addison's disease, etc. A sudden drop in the arterial pressure occurs in profuse blood loss, shock, collapse, or myocardial infarction. Systolic pressure alone sometimes decreases while diastolic pressure does not change or even increases. This causes a decrease in the pulse pressure. The phenomenon is observed in myocarditis or exudative and adhesive pericarditis when cardiac output decreases to cause the corresponding fall in the systolic pressure. Pulse pressure decreases also in the presence of stenotic aortal orifice.

Pressure changes in the brachial and certain other arteries (of the lower extremities in particular) are diagnostically important. Aortic coarctation (congenital stenosis of the aorta) is characterized by considerably lower pressure in the femoral arteries compared with the brachial arteries. In order to measure pressure in the femoral artery, the cuff is placed on the thigh of the patient who is in the prone position. The pulse is auscultated in the popliteal fossa. Pressure on both arms and both legs is sometimes measured.

MEASURING VENOUS PRESSURE

Venous pressure is measured in millimetres of water column. In healthy subjects it varies from 60 to 100 mm H_2O. Direct and indirect phlebotonometry are used to measure venous pressure. The direct method is more accurate. The phlebotonometer is a manometer comprising a glass tube (inner diameter of 1.5 mm) fixed in a stand with a scale graduated from 0 to 350. The lower end of the glass tube is connected by rubber tub-

ing to a needle. Before measuring venous pressure, the tubes are sterilized and filled with isotonic sodium chloride solution. The level in the glass tube is adjusted to zero and the rubber tube is then stoppered by a clamp. Venous pressure is measured with the patient at complete rest in lying position. The instrument is adjusted so that the zero reading of the scale be at the level of the right atrium (at the lower edge of the pectoralis major muscle). Venous pressure in the ulnar vein is usually measured. The vein is punctured by the needle and connected to the apparatus through the rubber tube. The clothes should not compress the arm; the tourniquet on the vein should not be kept for a long time because venous congestion may influence the result of measurement. The needle is then connected to the apparatus, the pressure in the vein levelled (for 1-2 minutes), and the clamp is removed from the rubber tubing to admit the blood into the system: the column of isotonic sodium chloride solution in the glass tube reads venous pressure.

Venous pressure can be determined tentatively by raising the arm until the vein is emptied and the limb becomes pallid. The height (in millimetres) to which the arm is raised from the level of the right atrium corresponds tentatively to the venous pressure. It is pretty constant in healthy subjects at rest. Physical exertion and nervous strain can elevate the pressure. The respiratory phases have a substantial effect on venous pressure. During inspiration the intrathoracic pressure decreases to intensify the venous outflow to the heart and thus to reduce the venous pressure. During deep inspiration the pressure increases. Measuring venous pressure is important for diagnosing diseases and assessing functional condition of the cardiovascular system, especially so if this examination is carried out repeatedly.

Instrumental Study of the Heart

ELECTROCARDIOGRAPHY

Electrocardiography is a method of graphic recording of electric currents generated in the working heart. Contractions of the heart are preceded by its excitation during which physicochemical properties of cell membranes change along with changes in the ionic composition of the intercellular and intracellular fluid, which is accompanied by generation of electric current.

The heart can be regarded as a source of action current located inside a conductive body, i.e. in the human body, round which an electric field is generated. Each muscular fibre is an elementary system known as a dipole. Countless microdipoles of separate myocardial fibres make (during excitation) a summary dipole (e.m.f.) bearing a positive charge in the head and a negative in the tail. As excitation fades, the poles change places. Since excitation begins at the

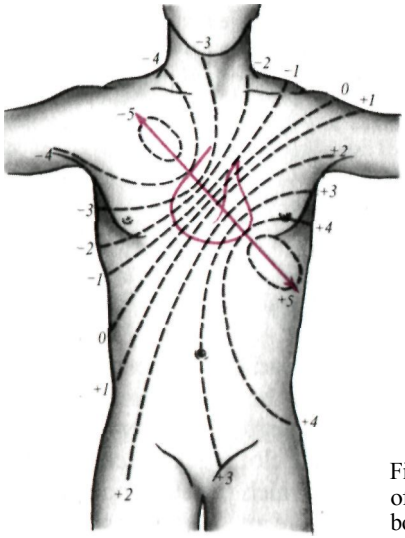


Fig. 39. Isopotential lines of the heart's e.m.f. on the body surface.

heart base, this region is the negative pole, while the region of the apex—the positive pole. The electromotive force has a certain magnitude and direction, i.e. it is a vector. The direction of the electromotive force is known as the electrical axis of the heart, which is normally parallel to its anatomical axis (Fig. 39). The zero potential line is perpendicular to the electrical axis.

Biocurrents of the heart can be recorded by special instruments, electrocardiographs. Development of electrocardiography is connected with the name of a Dutch physiologist Einthoven, who was the first in 1903 to record biocurrents of the heart by a string galvanometer. He developed some theoretical and practical principles of electrocardiography. The Russian investigator A. Samoilov, working independently and at the same time as Einthoven, developed the main principles of electrophysiology of the heart.

Construction. A modern electrocardiograph is actually a voltage measuring instrument. It includes the following parts: (1) the sensitive elements, electrodes, which are attached to the body of the patient to pick up the potential differences that arise during excitation of the heart muscle, and lead wires; (2) amplifiers, which amplify the minutest voltage of e.m.f. (1-2 mV) to the level that can be recorded; (3) a galvanometer to measure the voltage; (4) a recording instrument, including a traction mechanism and a time marker; and (5) a power unit (the instrument is supplied either from the AC mains or a battery).

Operating principle. Fluctuations in the potential difference that arise during excitation of the heart muscle are sensed by the electrodes attached to the patient's body and transmitted to the apparatus. The input voltage is extremely low, and it is therefore amplified 600—700 times. Since the magnitude and direction of the electromotive force incessantly change during the cardiac cycle, the galvanometer pointer shows variations in the voltage while a recording device draws a curve on a moving paper to show graphically these fluctuations.

The recording principle differs with various instruments. Electrocardiographs are popular in which the fluctuations are recorded on a moving tape during the measurement. These are ink-writing instruments which draw curves on paper. There are electrocardiographs in which special heat-sensitive paper is used. Dark paper is coated with a heat-sensitive layer of paraffin and chalk; the record is done by a hot stylus which removes paraffin from the col-

oured supporting paper. The tape may move at various speeds, from 25 to 100 mm/s, but the speed of 50 mm/s is usually preferred. Once the speed of the tape is known, it is easy to calculate the duration of separate elements of the ECG. If an electrocardiogram is recorded at a speed of 50 mm/s, each millimetre of the curve corresponds to 0.02 second. For the sake of convenience, paper graduated in millimetres is used. If a photosensitive material is used, a special time marker makes exposures on the tape at 0.05-second intervals.

Whichever instrument is used, the sensitivity of the galvanometer is so selected that the voltage of 1 mV causes 1-cm deviation of the recording device (a beam of light, or a stylus). The sensitivity and amplification of the apparatus should be checked before recording electrocardiograms. To that end, a standardization voltage of 1 mV should be used, and this causes a 1-cm deviation of the beam or stylus. A normal one-millivolt curve looks like a square wave. The height of the vertical lines is 1 cm.

Recording ECG. Twelve-lead ECG recording has gained wide use: three standard leads (classical), six chest, and three unipolar limb leads. Special leads are also used in some cases.

Bipolar limb leads. Moist cloths are placed on the lower third of both arms and the left leg, upon which the electrode plates are then placed. The electrodes are connected to the apparatus by special wires (different in colours). The red wire with one ring is connected to the electrode on the right arm and yellow wire with two rings to the left arm electrode, and a green wire with three rings to the left leg. Three bipolar limb leads are distinguished: I, II, and III. Lead I ECG is recorded with the electrodes placed on the arms, in lead II the ECG is taken from the right arm and left leg and in lead III from the left arm and the left leg. These leads are called bipolar because two electrodes are used to record the potentials of the corresponding parts of the body. ECG taken with bipolar limb leads is the resultant of the potential difference between two points of the body. The limbs themselves act as conductors and have but little effect on the ECG.

Chest leads. For a more accurate diagnosis of various myocardial affections, ECG is recorded with leads placed on the anterior surface of the chest. The electrode is placed successively at 6 positions: (1) right sternal border, the 4th intercostal space; (2) left sternal border, the 4th interspace; (3) left parasternal line, between the 4th and 5th interspace; (4) left midclavicular line, the 5th interspace; (5) left anterior axillary line, the 5th interspace; (6) left midaxillary line, the 5th interspace (Fig. 40).

Chest leads can be uni- and bipolar. One unipolar electrode is placed on the chest, and the other on the right arm or left leg. If the second electrode is placed on the right arm, the lead is designated CR (chest, right). Depending on the position of the chest electrode, the leads are given the respective subscripts: CR_1, CR_2, etc. If the second electrode is placed on the left leg, the leads are designated CF (foot): CF_1, CF_2, etc.

Unipolar chest leads proposed by Wilson are more popular now. The chest electrode which is attached to the positive pole of the electrocar-

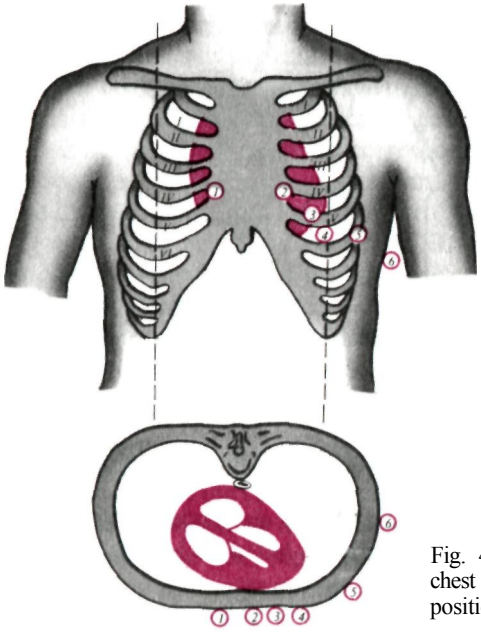


Fig. 40. Taking ECO in chest leads; six electrode positions.

diograph is only active; the electrodes leading from the limbs are united and connected to the negative terminal of the apparatus. With this connection, the total potential difference recorded from the limbs is practically zero. Unipolar chest leads are designated by the letter V and the position of the chest electrode is subscribed to give V_1, V_2, etc.

Unipolar limb leads differ from bipolar limb leads in that the potential difference in them is recorded mostly by one electrode, i.e. the active electrode, which is placed successively on the right arm, left leg, and left arm. The other electrode (as that for recording chest leads) is formed by connecting together three limb electrodes; it is indifferent. Voltage of thus recorded ECG is very small and electrocardiograms are difficult to interpret. Goldberger (1942) proposed that the active exploring limb electrode should not be connected with the other electrodes, thereby increasing the ECG voltage by 50 per cent. These leads are called *augmented unipolar limb leads.*

The following leads are distinguished. Right arm lead, aVR: the active electrode is located on the right arm; electrodes of the left arm and left leg are connected together to form the central terminal of apparatus, while the wire of the right arm is not connected (Fig. 41).

Left arm lead (aVL) is recorded by placing the active exploring elec-

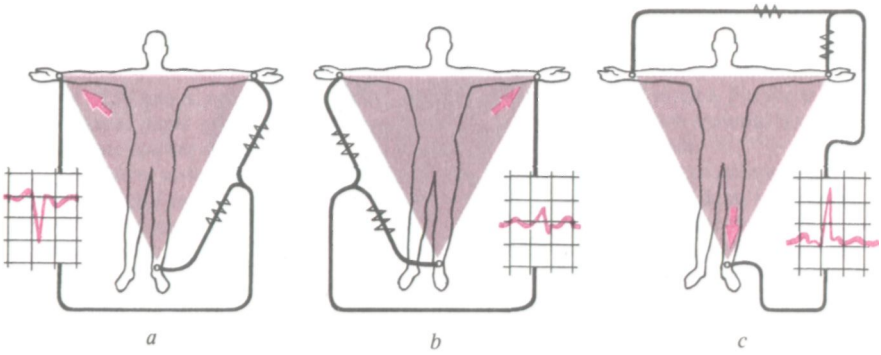


Fig. 41. Unipolar augmented limb leads.
a—lead aVR; b—lead aVL; c—lead aVF.

trode on the left arm; the central electrode is formed by the electrodes of the right arm and left leg; the left arm lead is not used for the central electrode (Fig. 41).

Unipolar left leg lead (aVF) is recorded by placing the active electrode on the left leg and connecting the electrodes from the right and left arms together (see Fig. 41).

Normal ECG. During diastole the heart does not generate current and an electrocardiograph records a straight line which is called isoelectrical. Action current is represented by a specific curve. An ECG of a healthy subject has the following elements: (1) positive waves *P, R,* and *T,* negative waves *Q* and *S;* the positive wave *U* is accidental; (2) *P-Q, S-T, T-P,* and *R-R* intervals; (3) *QRS* and *QRST* complexes. Each of these elements characterizes the time and sequence of excitation of various parts of the myocardium.

In normal conditions, the cardiac cycle begins with excitation of the atria (*P* wave on an ECG). The ascending portion of the *P* wave is mainly due to excitation of the right atrium, while the descending one of the left atrium. The wave is small, and its normal amplitude does not exceed 1-2 mm; the length is 0.08-0.1 s. The *P* wave is followed by a straight line lasting to *Q* wave; if this wave is small, the line extends to the *R* wave. This is the *P-Q* interval. It extends from the beginning of the *P* wave to the beginning of the *Q* (or *R)* wave and corresponds to the time from the beginning of atrial excitation to the beginning of ventricular excitation, i.e. includes the time of pulse propagation in the atria and its physiological delay in the atrioventricular node. The normal length of the *P-Q* interval is 0.12-0.18 s (to 0.20 s).

Excitation of the ventricles corresponds to the *QRS* complex. Its waves vary in size and are different in various leads. The length of the *QRS* complex (measured from the beginning of the *Q* wave to the end of the *S* wave) is 0.06—0.1 s. This is the time of intraventricular conduction. The first wave of this complex is the negative *Q* wave. It corresponds to excitation of the interventricular septum. Its amplitude is small and does not normally exceed *V** amplitude of the *R* wave; the lenght of the *Q* wave does not exceed 0.03 s. The *Q* wave may be absent on an ECG. The *R* wave corresponds to almost complete excitation of both ventricles. It is the highest wave of the ventricular complex; its amplitude varies from 5 to 15 mm. The negative *S* wave is recorded in full excitation of the ventricles; usually it is not high, actually not exceeding 6 mm (2.5 mm on the average). Sometimes the *S* wave is very small. At the moment of complete depolarization of the myocardium, the potential difference is absent and the ECG is therefore a straight line (the *S-T* interval.) The length of this interval varies greatly depending on the cardiac rhythm; the S-T interval may be displaced from the isoelectric line to not more than 1 mm.

The *T* wave corresponds to the repolarization of the ventricular myocardium. The *T* wave is normally asymmetrical: the gradual ascent converts into a rounded summit, which is followed by an abrupt descent. Its amplitude varies from 2.5 to 6 mm, the length from 0.12 to 0.16 s. A small positive *U* wave sometimes follows the *T* wave in 0.02-0.04 s. Its amplitude exceeds 1 mm in rare cases: the length is 0.09-0.16 s. The origin of the *U* wave is disputed.

The *Q-T* interval *(QRST* complex) shows the time of excitation and recovery of the ventricular myocardium i.e. it corresponds to their electrical system. It extends from the beginning of the *Q* wave (or the *R* wave, if the *Q* wave is absent) to the end of the *T* wave. Its length depends on the rate of cardiac contractions: in accelerated heart rhythm the *Q-T* interval shortens. The *Q-T* interval in women is longer than in men (at the same heart rate). For example, at the rate of 60—80 beats per minute, the length of the *Q-T* interval in men is 0.32-0.37 s and in women—0.35-0.40 s.

The *T-P* interval (from the end of the *T* to the beginning of the *P* wave) corresponds to the electrical diastole of the heart. It is located on the isoelectric line because all action currents are absent at this moment. Its length depends on the cardiac rhythm: the faster the heart rate the shorter the *T-P* interval.

The *R-R* interval is a distance between the summits of two neighbouring *R* waves. It corresponds to the time of one cardiac cycle, whose length depends on the cardiac rhythm as well.

The *electrocardiogram is interpreted* as follows.

1. Regularity of the cardiac rhythm is first determined. Since the

sinoatrial node is the pacemaker of a normal heart, and the excitation of the ventricles is preceded by excitation of the atria, the *P* wave should come before the ventricular complex. The/?-/? intervals should be equal. Its fluctuations normally do not exceed 0.1 s. Greater variations in the length of the *R-R* intervals indicate disordered cardiac rhythm.

2. The heart rate is calculated. To that end, duration of one cardiac cycle (the *R-R* interval) and the number of such cycles in one minute length should be determined. For example, if one cycle lasts 0.8 s, there will be 75 such cycles in a minute (60 : 0.8 = 75). If the cardiac rhythm is irregular, the length of five or ten *R-R* intervals is determined, the mean *R-R* interval found, and the cardiac rate is finally determined as for regular cardiac rhythm. Lengths of the maximum and minimum *R-R* intervals are given in parentheses.

3. Voltage of the ECG is determined. To that end, the amplitude of *R* waves is measured in standard leads. Normal amplitude is 5—l5 mm. If the amplitude of the highest *R* wave does not exceed 5 mm in standard leads, or the sum of amplitudes of these waves in all three leads is less than 15 mm, the ECG voltage is considered decreased.

4. The electrical axis of the heart is determined by the shape of ventricular complexes in standard leads. The relation between the electrical axis and the magnitude of the *QRS* complexes in standard leads is described by the so-called Einthoven triangle. Since ECG in standard leads shows the direction of the e.m.f. of the heart in the frontal plane, this plane can be shown as an equilateral triangle whose base is at the top (Fig. 42). The apices of the triangle correspond to the limb leads, i.e. *R* for the right arm, *L* for the left arm and *F* for the left leg (foot). The sides of the triangle correspond to the leads I *(R-L),* II *(R-F),* and III *(L-F).* The magnitude and direction of the e.m.f. are designated by the A-B arrow. If vertical lines are drawn from the ends of this arrow to the sides of the triangle, the difference of potentials recorded in each lead can be obtained. With normal position of the axis, the maximum potential difference will be recorded in the second lead because this lead is parallel to the electrical axis. It follows therefore that the maximum voltage of the ventricular complex, especially of the *R* wave, will be in the same lead. A lower difference of potentials is recorded in the first lead and still lower in lead III. Using the Einthoven formula, it can be calculated that the magnitude of the *R* wave in lead II is equal to the algebraic sum of *R* in leads I and III, i.e. $R_2 = R_1 + R_3$. Values of/? waves with normal position of the electrical axis can be shown as this: $R_2 > R_1 > R_3$ (Fig. 43).

The position of the electrical axis changes with changes of the position of the heart in the chest. If the diaphragm is low (in asthenic persons), the electrical axis is more vertical (Fig. 44). As can be seen from the Einthoven triangle, the maximum potential difference in this position will be in lead

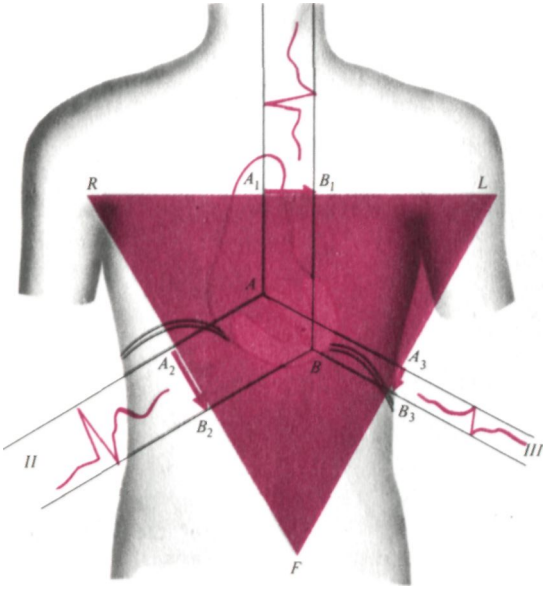


Fig. **42.** Normal position of the electrical axis of the heart.

III (because this lead is now parallel to the electrical axis). It follows that the highest *R* wave will be recorded in lead III (Fig. 45). If the diaphragm is high (in hypersthenics), the electrical axis is more horizontal, i.e. parallel to lead I (Fig. 46), and the highest *R* wave is therefore recorded in lead I (Fig. 47).

5. The length and size of ECG elements *(P* wave, *R-Q* interval and *QRST* complexes) are then determined in those leads where the waves are the largest (usually in lead II). Moreover, the direction of the *P* and *T* waves is determined (they can be positive and negative). Smaller and split waves can be present as well. Additional waves can appear. The shape of

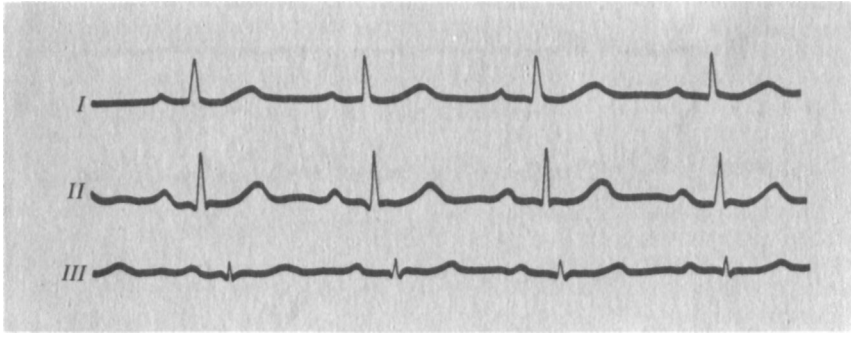


Fig. 43. ECG in standard leads with normal position of the heart's electrical axis.

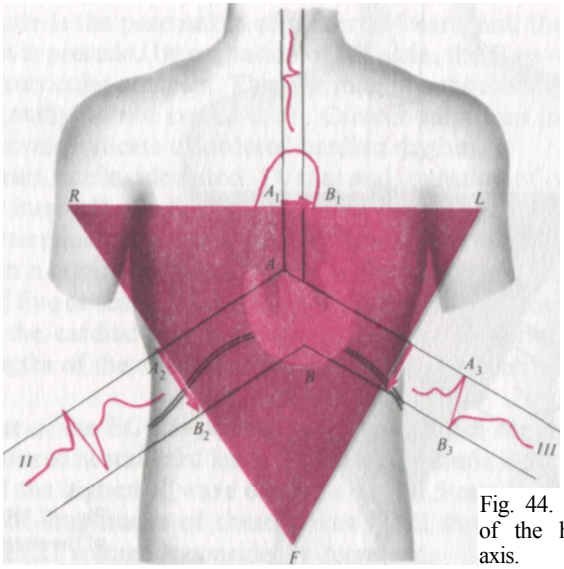


Fig. 44. Vertical position of the heart's electrical axis.

the ventricular complex in all leads is thoroughly examined. The isoelectrical character of the *S-T* interval is noted.

6. The length of the *QRST* complex (*Q-T* interval) depends on the heart rate: the higher the rate, the shorter the interval. Each particular heart rate is characterized by a certain normal lenght of the Q-T interval and the *Q-T* interval of a given ECG should be compared with this standard. The normal value is calculated by the formula $Q\text{-}T = K\sqrt{P}$, where K is constant (0.37 for men and 0.39 for women); and P is the length of one cardiac cycle *(R-R* interval) expressed in seconds. Normal *Q-T* lengths for any heart rate can be found in special tables.

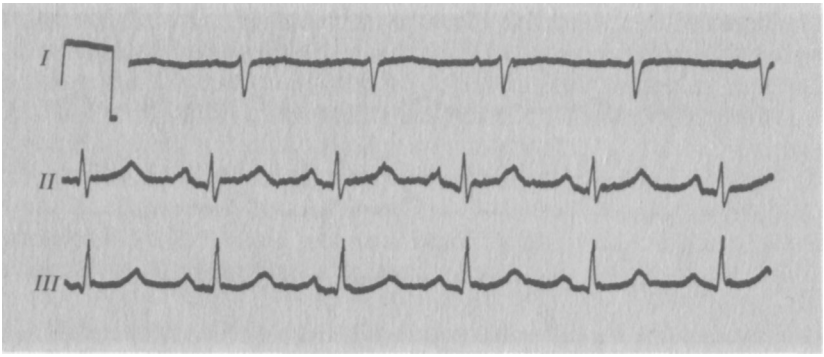


Fig. 45. ECG in standard leads with the vertical position of the heart's electrical axis.

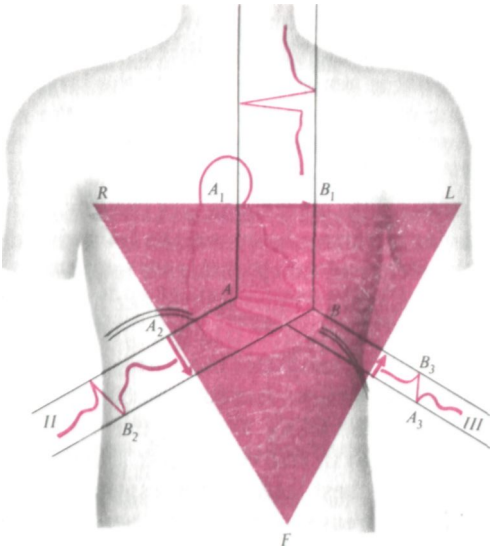


Fig. 46. Horizontal position of the heart's electrical axis.

The ECG of healthy persons depend on their age and constitution, on the posture at the moment of taking an ECG (sitting, lying), on the preceding exercise, etc. ECG may change during deep breathing (the position of the heart in the chest is changed during deep inspiration and expiration), in increased tone of the sympathetic and parasympathetic nervous systems and in some other conditions.

It is difficult to overestimate the *clinical importance of electrocardiography*. It is used to reveal disorders of heart activity, and to diagnose coronary circulatory disorders. ECG can reveal enlargement of heart chambers. If the atrium is enlarged and its myocardium is hypertrophied,

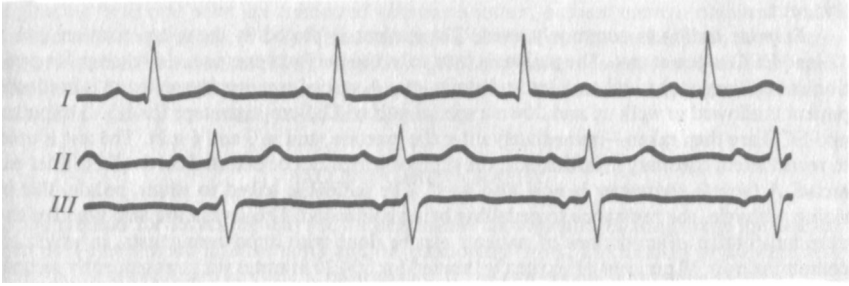


Fig. 47. ECG with the horizontal position of the heart's electrical axis.

the *P* wave changes. Since an enlarged atrium is slower excited, the length of the *P* wave becomes longer than 0.1 s. The amplitude of the *P* wave increases because a higher potential is generated to excite the large mass of the myocardium. If dystrophic or sclerotic changes occur in the myocardium, the shape of the *P* wave changes: it becomes serrated and split (with two phases). Enlargement of the left atrium changes the *P* wave in standard leads I and II. Enlargement of the right atrium changes the *P* wave in standard leads II and III. Ventricular hypertrophy causes the following changes in ECG: (1) the position of the electrical axis is changed: in left-ventricular hypertrophy it deviates to the left, and in right-ventricular hypertrophy to the right; (2) the amplitude of the ventricular complex and its length increase, i.e. the time of excitation of the ventricles increases; (3) the recovery of the myocardium is upset and this shows itself in the changed terminal part of the ventricular complex of the ECG, namely, the *S-T* segment is displaced and the *T* wave changes; (4) in left-ventricular hypertrophy, the amplitude of the *S* wave in the right chest leads increases: the amplitude of the *R* wave in the left chest leads increases too. In right-ventricular hypertrophy the changes in the *S* and *R* waves are the reverse, i.e. a high *R* wave appears in the right chest leads, and a deeper *S* wave in the left leads.

Electrocardiography helps reveal dystrophic and sclerotic changes in the myocardium. ECG changes also in abnormalities of electrolyte metabolism, due to various toxic substances or certain medicines (e.g. quinidine, digitalis, etc).

However informative the ECG findings may be, they are only useful when correlated with the clinical data, since various pathologies can give similar ECG. Underestimation of the clinical data and overestimation of electrocardiography may cause serious diagnostic errors.

Electrocardiography is used for functional examination of the cardiovascular system. Combination of electrocardiographic studies with functional tests helps reveal latent coronary insufficiency and differentiate between functional organic disorders. Differential diagnosis is now widely used not only in clinical practice but also in sports medicine, occupational orientation, etc.

Exercise testing is commonly used. The patient is placed in the lying position and a 12-lead ECG taken at rest. The patient is then asked to perform exercise, e.g. change his position (sit up), squat, ascend and descend stairs, etc. A special two-step exercise test is used: the patient is allowed to walk up and down a special pair of 22.5-cm-high steps for 15—3 minutes, and ECG are then taken—immediately after the exercise, and in 3 and 6 min. The test is used to reveal latent coronary insufficiency, the signs of which can be detected on the ECG after exercise. A *bicycle ergometer* is now also used. The patient is asked to rotate pedals, like in riding a bicycle, the resistance to pedalling being controlled. Treadmills are also used for the purpose. Similar examinations of patients can be done with hypoxaemic tests, in which air containing only 10 per cent of oxygen is inhaled for 10—20 minutes with subsequently recorded ECG, which also reveals latent coronary insufficiency.

Telecardiography (radioelectrocardiography) is now also used to study the effects of

physiological stress imposed on the heart. The electric currents of the heart are transmitted by a radio device attached to the examinee and the ECG is thus recorded at a distance from the patient. This method is very useful for taking ECG during exercise, (sportsmen, astronauts, pilots).

Pharmacological tests are used to differentiate between functional and organic disorders in coronary circulation. Amyl nitrite and nitroglycerin are used for the purpose. The original ECG is compared with ECG taken after amyl nitrite or nitroglycerin intake. Disappearance of signs of myocardial ischaemia after taking vasodilatory preparations indicates the functional character of coronary disorders. Inderal and potassium chloride are used to differentiate between neuroendocrine and metabolic disorders and coronary insufficiency in cases with changed terminal part of the ventricular complex *(S-T* interval and *T* wave). These preparations remove mainly metabolic and functional changes.

Tests by which the tone of the vagus nerve is modified are used to assess some disorders of the cardiac rhythm.

Aschner's test. Pressure on the eyeball for 6-10 s increases the tone of the vagus to increase its effect on the heart: the heart slows down and the time of the atrioventricular transmission increases. If an attack of paroxysmal tachycardia occurs during the Aschner test, the sinus rhythm can be restored.

Atropine test. The subject is given 1 ml of a 0.1 per cent atropine solution by a subcutaneous injection, and ECG are then taken in 5, 15, and 30 minutes. Atropine blocks the vagus and thus provides conditions for a better interpretation of disorders in the cardiac rhythm and transmission. If, for example, the *P-Q* interval on the pre-injection ECG was elongated but normalized after administration of atropine, the disorder in the atrioventricular transmission was due to the increased vagus tone and not due to an organic myocardial affection.

VECTORCARDIOGRAPHY

Electrocardiography cannot completely show the entire complexity of electrical phenomena occurring in the myocardium because it only shows changes in the electrical field in one plane. Since the heart is a three-dimensional organ, its electrical field in three-dimensional space should be examined. The method of study of the heart's electric field in three planes is called vectorcardiography. It has already been said that the e.m.f. of the heart has a certain magnitude and direction. In other words it is a vector, and is therefore indicated by an arrow whose length corresponds to the magnitude of the e.m.f. At any given moment of the cardiac cycle, a specific resultant potential difference arises. It has its own magnitude, direction, which is called instantaneous vector. If the.ends of instantaneous vectors originating from one point are connected with one another, a closed curve is obtained, which is called vectorcardiogram (VCG). These curves can be obtained for excited atria (loop *P* corresponds to the *P* wave on an ECG), ventricles *(QRS* loop), and recovered ventricular myocardium (loop *T).* A special apparatus, vectorcardiograph, is used to take vectorcardiograms. A cathode-ray tube is the main part in this apparatus.

BALLISTOCARDIOGRAPHY

A method for recording the body's mechanical movements resulting from the beating heart as it ejects blood into the aorta and the pulmonary trunk. The amount of displacement of the body in each cardiac cycle is informative of the myocardial contractile function.

Three main forces are generated by the working heart: (1) ejection of the blood from the ventricles to the vessels is attended by a thrust (like a recoil force in firing a gun) which is transmitted to the body; (2) movement of blood in the vessels displaces the body in the direc-

tion of the blood flow; (3) when the blood stream meets an obstacle to its flow (a bend or bifurcation of the vessel), the body moves in the opposite direction. These mechanical movements of the body can be recorded by a ballistocardiograph in the form of a curve known as a *ballistocardiogram* (BCG). Depending on the design, ballistocardiographs can record one of the three parameters characterizing any mechanical movement; these are (1) the amount of displacement, i.e. the distance to which the body travels from its initial position to the final one; (2) the speed of displacement (the velocity in centimetres per second); and (3) acceleration (the change in the velocity per unit time).

Ballistocardiographs of various designs are available but all of them utilize one operating principle, that is they perceive mechanical vibrations of the human body caused by the beating heart, convert them into electrical pulses, amplify and transmit them to the recording apparatus. Any electrocardiograph can be used to record ballistocardiograms.

A *normal BCG* is a record of successive waves that are generated during each cardiac cycle. These waves are designated by the Latin letters from *F* to *O.* BCG waves are related to one another in certain order with respect to their magnitude and length. Differentiated are the systolic complex (waves *H, /, J,* and *K)* and the diastolic complex (waves *L,M,N,* and *O).* The *H* wave arises 0.04-0.06 s after the *R* wave on an ECG. It is due to the thrust of the heart from the rising atrioventricular septum at the beginning of the isometric phase of the ventricular systole. The *I* wave follows the *R* wave in 0.12—0.15 s. It is associated with the recoil force generated during ejection of blood from the ventricles into the vessels. The *J* wave appears 0.2 s after the *R* wave on an ECG and shows the thrust of the blood stream against the aortic arch and the bifurcation of the pulmonary trunk artery. This is the highest wave of the systolic complex. Wave *K* corresponds to the blood flow along the descending part of the aorta. Diastolic waves *L, M, N,* and *O* are connected with flow of blood to the heart and its filling. Normally they are small and inconstant; the highest of them is the *L* wave. The systolic wave *H* is sometimes preceded by the *G* wave, which is due to the atrial systole. The amplitude of BCG waves varies within wide limits depending on the respiratory phases: during inspiration the amplitude increases and during expiration decreases.

In pathological conditions the shape, length and amplitude of BCG waves change, and the respiratory fluctuations of the waves are altered too. BCG is especially helpful in follow-up studies. Changes associated with coronary insufficiency, for example, can be earlier revealed on ballistocardiograms than on electrocardiograms (exercise test).

ECHOCARDIOGRAPHY

Echocardiography is used to study the heart by detecting ultrasound echoes from its various structures, such as the valves, ventricular myocardium, interventricular septum, etc. The instrument used for the purpose is known as the echocardiograph. It emits ultrasound impulses which are returned from the organ under examination and received as echoes to be represented graphically on a moving paper chart, the echocardiograms.

The device emitting ultrasound impulses (the probe) is placed in the region of absolute dullness where the heart is not covered by the lungs, i.e. to the left of the sternum at the 2nd or 3rd intercostal space in hypersthenics and 4th or 5th interspace in asthenics.

Echocardiography is very useful for the diagnosis of various heart diseases since it determines the condition of the heart valves and reveals

hypertrophy and dilatation of the heart chambers. Echocardiography can be used to diagnose prolapse of the mitral valve, to evaluate the condition of the myocardium in various disease, e.g. in ischaemic heart disease, myocarditis, or congestive cardiomyopathies, to diagnose subaortic stenosis, to reveal the presence of fluid in the pericardium, etc.

If the anterioposterior dimensions of the left ventricle during systole and diastole are known, it is possible to determine the stroke volume and other indices characterizing contractility of the left ventricular myocardium.

PHONOCARDIOGRAPHY

This is the method for recording sounds generated in the beating heart. Phonocardiography is an essential supplement to heart auscultation because it can record sounds otherwise inaudible to the human ear, such as the third and fourth heart sounds, low-frequency components of the first and the second heart sounds, and low-frequency murmurs.

Sounds generated in the heart are recorded on a phonogram as a curve (PCG) by an apparatus known as a phonocardiograph. It consists of a microphone, an amplifier, a system of sound filters, and a recording device. The microphone picks up sounds and converts them into electrical signals. These are amplified and transmitted into the system of sound filters where the sounds are separated by their frequencies (low, medium- and high-frequency sounds) for their separate recording. Oscillations of a certain frequency are transmitted to the recording device which draws a curve. A phonogram can be recorded by ink on a chart paper, or by a beam of light (on a photosensitive paper). Phonocardiograms are taken in complete silence with the patient in the lying position; the breath should be kept at the expiration phase. The microphone is placed successively on those sites of the chest where heart sounds are audible during auscultation, and also on those areas where the sounds can be heard best. Phonocardiograms should be analysed and diagnosis established only by interpreting the phonocardiogram together with the auscultation findings. For a better interpretation of phonocardiograms, an electrocardiogram should be taken synchronously.

A *normal phonocardiogram* gives a graphic picture of vibrations caused by the first and second heart sounds, with a straight line in between, corresponding to the systolic and diastolic pauses (Fig. 48a and *b)*. The first sound is represented as several vibrations arising after the *Q* wave synchronously with the ECG (70-150 Hz). The initial vibrations of the first sound have a low amplitude; these are connected with atrial systole. The main or central part of the first sound is shown in the form of 2-3 vibrations of high amplitude, which are found at the level of the *S* wave and cor-

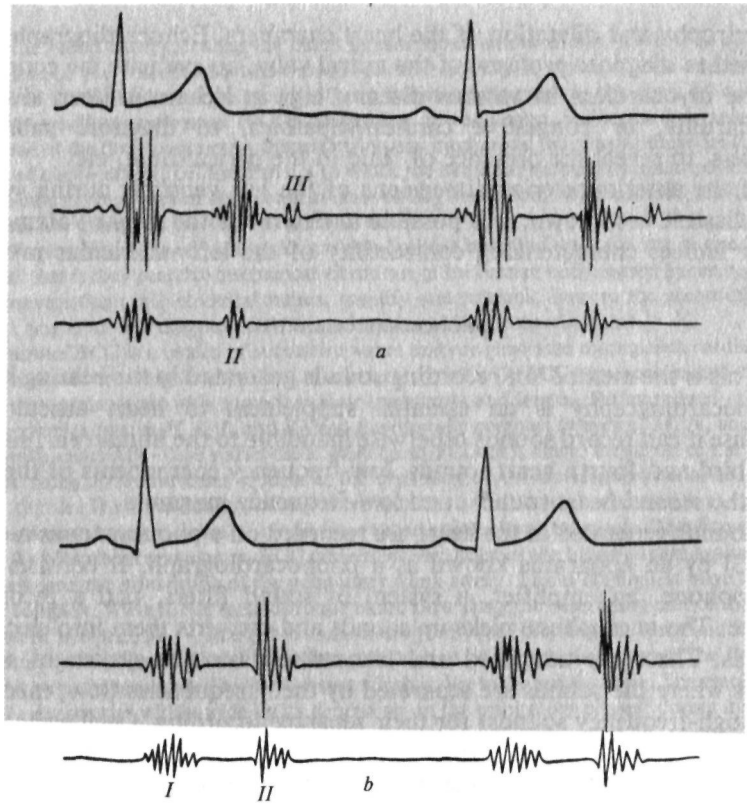


Fig. 48. Normal PCG.
a—at the heart apex; *b*—at the heart base.

respond to vibrations of closed atrioventricular valves. The main portion of the first sound is followed by additional vibrations of lower amplitude which are caused by vibrations of the myocardium and by the vascular component.

The amplitude of sound waves on a PCG depends not only on the work of the heart but also on the conditions of sound conduction (for example, the amplitude decreases in patients with obesity or lung emphysema).

The amplitude of the first sound is the highest at the heart apex, where it exceeds 1.5-2 times the amplitude of the second sound. The amplitude of the first sound at the heart base can be very small. While interpreting this sound at the heart apex, it is necessary to determine the lag of its central portion from the *Q* wave on a synchronously recorded ECG. The normal *Q*-I sound interval does not exceed 0.04-0.06 s. It corresponds to the time lasting from the beginning of ventricular excitation to the closure of

the mitral valve. If pressure in the left atrium increases (e.g. in mitral stenosis), the mitral valve closes with a delay and the *Q-I* sound interval increases.

The second sound is composed of several vibrations which appear at the end of the *T* wave synchronous with ECG. Its frequency varies from 70 to 150 Hz. Higher amplitude corresponds to the closure of the aortic valve, while subsequent lower amplitude corresponds to the closure of the valve of the pulmonary trunk. The amplitude of the second sound is the highest at the base of the heart, where it exceeds the amplitude of the first sound.

In addition to the first and second sounds, a phonocardiogram often has the third heart sound which is recorded as two or three low-frequency waves of small amplitude. They follow the second sound in 0.12-0.18 s and appear before the *P* wave of a synchronous ECG. The fourth heart sound is recorded less frequently. It has the form of one or two low-frequency low-amplitude waves appearing after the *P* wave.

Phonocardiography helps diagnose many cardiovascular diseases, heart defects in the first instance. It verifies and supplements auscultative findings. This is especially important in tachycardia or arrhythmias, i.e. in cases where it is difficult to establish by auscultation alone during which phase of the cardiac cycle the sounds appeared. PCG helps reveal changes in the heart sounds, their duplication, splitting, and ensures a more correct interpretation of additional sounds, such as physiological third and fourth heart sounds, the sound of the opening of the mitral valve, and the gallop rhythm. Phonocardiograms show graphically the changes in the heart sounds that were first revealed by auscultation. For example, in stenosis of the left venous orifice the amplitude of the first sound at the apex markedly increases, and in mitral valve incompetence it decreases. The amplitude of the second sound over the aorta in patients with essential hypertension is higher than over the pulmonary trunk.

The sound of the opening of the mitral valve, usually designated *OS* (opening snap), is very important in diagnosis of mitral stenosis. As distinct from the third heart sound, it is recorded in the high-frequency channel, 0.04-0.12 s after the second heart sound. This II sound-OS interval (like the *Q-I* sound interval) depends on the pressure in the left atrium: the higher the pressure, the earlier opens the mitral valve during diastole, and the shorter the II sound-OS interval will be.

Phonocardiography is very helpful in interpreting the character of heart murmurs; PCG determines the time of appearance of murmur, site of its maximum intensity, length, and frequency (which is determined mainly by the sound intensity as recorded in the high- or low-frequency channel). The frequency of systolic sound usually varies from 50 to 600 Hz and of

diastolic from 120 to 800 Hz. Murmurs are shown on a PCG as a group of oscillations of various amplitude (depending on the murmur intensity) which appear during the systolic or diastolic pause.

The systolic murmur may last during the entire systole or only during its part, or it may be between the first and the second heart sound, or else it may combine with them. Attention is paid to the wave form of systolic murmur, which may be rhomboid, spindle- or band-shaped. This is important for diagnosing heart defects. Rhomboid or spindle-shaped waves of the systolic murmur (not combined with the second heart sound) are characteristic of stenosed aortic orifice.

When evaluating diastolic murmur, it is important to determine the moment of diastole at which it appears (i.e. to establish whether the murmur is protodiastolic, mesodiastolic or presystolic). The change in the murmur intensity is then determined (decreasing or increasing murmur); next the frequency characteristics of the murmur are determined. Diastolic murmur in aortic insufficiency is better recorded in the high-frequency channel, while in mitral stenosis in the low-frequency one.

The various frequency characteristics of murmurs, different time of their appearance during the course of a given phase of the cardiac cycle help diagnosing combined affections of the heart valves. Phonocardiograms in heart diseases will be discussed later in the section "Heart Diseases".

FUNCTIONAL TESTING OF THE CIRCULATORY SYSTEM

Blood flow rate is determined by the time during which blood passes a certain length of the cardiovascular system and mainly depends on myocardial contractile power and the condition of the peripheral vessels. The amount of the circulating blood and its viscosity are also important. When blood flow rate is determined, substances are used which cause a biological response (e.g. dilatation of the vessels or alteration of respiration), or can easily be determined in the blood (radioactive isotopes or stains). These substances should not be toxic, nor should they affect the flow rate. The action of such a substance on man should only be transient.

Magnesium sulphate test. Magnesium sulphate (1 ml of a 50 per cent or 2 ml of 25 per cent solution) is injected into the cubital vein of the patient. The injection should be quick, and the time of injection should be marked by a stop-watch. As magnesium sulphate solution passes the vessels of the lesser circulation, it enters the greater circulation to dilate capillaries. The subject feels warmth, first in the mouth and then in the entire body and the limbs. The moment when the patient feels the warmth in the mouth is noted by the stop-watch (Fig. 49). The normal time, as determined by this

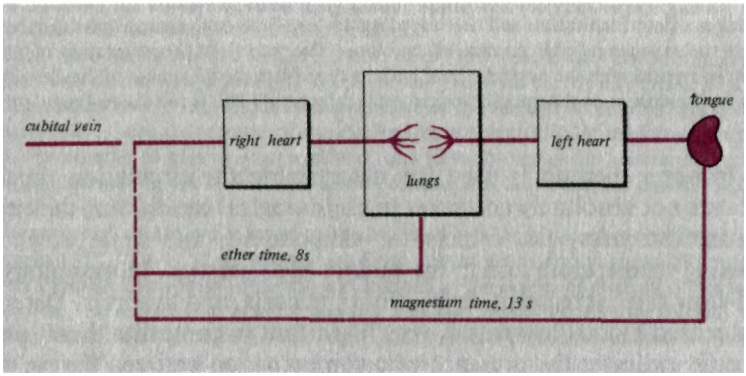


Fig. 49. Determining circulation time.

method, is 10—15 s. The same method can be carried out with calcium chloride. Decholin or saccharine is sometimes injected into the vein. The time of appearance of bitter or sweet taste in the mouth is determined by a stop-watch.

Ether test. This is used to assess the state of the circulatory system over a shorter length (from the cubital vein to the pulmonary alveoli). A dose of 0.3 ml of sterile ether is injected into the cubital vein and the time when an ether breath appears is noted (arm-to-lung time). The normal time is 4-8 s.

Lobeline test. This is a more objective test. Intravenous administration of a 1 per cent lobeline solution (0.1 mg/kg body weight) causes a transient dry cough or dyspnoea the time of appearance of which is determined by a stop-watch. The changes in respiration are due to irritation of the pulmonary branches of the vagus. Respiratory movements can synchronously be recorded by a kymograph. Normal "lobeline time" is 8-10 s.

A number of other methods for assessing blood-flow rate are based on *determining the degree of dilution of stains* added to the blood. For example, 2 ml of a 20 per cent fluoresceine is injected into the cubital vein and the time when the lip mucosa becomes greenish-yellow is determined by a stop-watch. The normal time is 12-16 s. Time of blood circulation over longer paths, using fluoresceine (to the cubital vein of the other arm), can be determined by taking blood samples from the vein of the other hand at 5-second intervals. Normal arm-to-arm time is **15-30** s.

Radioisotope method. Circulation time can be determined by injecting isotopes (^{24}Na, ^{131}I, ^{85}Kr) intravenously and detecting them by a special counter at any given point of the vascular system.

Oxyhaemography. This method can also be used for determining blood circulation time. The sensitive unit of an oxyhaemograph includes a photocell which detects changes in the colour of the blood depending on its oxygen content. The pick-up is attached to the lobe of the ear, where it records blood oxygen saturation. The respiratory movements are recorded synchronously. After the initial blood oxygen content has been determined, the patient is asked to keep breath for 10-15 s, which reduces the oxygen concentration in the blood. The patient

then makes a deep inspiration and the recording device of the oxyhaemograph records the increase in the oxyhaemoglobin content of the blood. The records of the respiratory movements are then compared with the oxygen curve, and the time from the beginning of the deep inspiration to the increase in oxyhaemoglobin content is calculated. This is the ear-to-lung circulation time.

Whichever method is used for determining the circulation time, the results are not absolutely accurate. In physiological conditions, the circulation time increases with exercise or temperature, and slows down with decreasing temperature and in the middle-aged persons. In pathology, the blood-flow rate increases in fever, thyrotoxicosis, and anaemia. Determining increased blood-flow rate is very important in congenital heart defects because it indicates the presence of communication between the right and left chambers of the heart (in defects of interatrial or interventricular septum). The flow rate slows down in decreased contractile power of the heart and disordered circulation, especially in congestion in the lesser circulation (decompensated heart defects, myocardial infarction, etc.).

Systolic **and minute volumes of blood.** Systolic (stroke) volume of blood is the amount of blood that is ejected by the heart per each contraction. The normal systolic volume varies from 50 to 75 ml. The minute volume is the amount of blood pumped by the heart during one minute. Normally it is 3.5-8 1 (at rest).

In clinical practice, only the minute volume of blood is determined, while the stroke volume is calculated by dividing the minute volume by the number of heart beats per minute. The most accurate method is based on Fick's principle. According to this method, the amount of substance delivered to the blood during one minute and the increase of its concentration in the blood are determined. The oxygen (O) concentration in the blood passed through the pulmonary vessels increases by the value which is determined as the arterio-venous oxygen difference *(A - B)*. Once the total oxygen consumption during one minute is known (determined by the oxygen deficit in the expired air) and the arterio-venous oxygen difference is determined, the minute volume *(MV)* can be found from the formula: $MV = \frac{O}{A - B}$. The method is complicated, because in order to determine the oxygen concentration in the blood it is necessary to puncture the artery, and for obtaining specimens of the arterio-venous blood, the heart's right chambers should be catheterized. This method is therefore only used in patients in whom the heart is catheterized for diagnostic purposes.

Indirect methods (radioisotopic and stain dilution) for determining minute volumes are more popular. The patient is given stain intravenously (Evans blue) or substances labelled by radioactive isotopes; their concentrations in the arterial blood are then measured. Once the amount of the injected substance, its concentration in the blood, and the time of passage through a given length of the circulatory system are known, the minute volume can be calculated by special formulas.

The minute volume depends on sex, age, ambient temperature, and some other factors. The minute volume increases markedly during heavy exercise. Well-trained athletes may have minute volumes as high as 40 1 which is mainly due to the increased stroke volume (to 150-200 ml).

The minute volume increases in lung emphysema, anaemia, and thyrotoxicosis. It decreases in cardiac insufficiency (sometimes to 2—1.5 1), decompensated heart diseases, myocardial infarction, myocarditis, and some other diseases.

Determining the volume of circulating blood. Stains and radioactive isotopes are mostly used to determine the volume of circulating blood.

When the *staining method* is used, 20 ml of a 1 per cent Evans blue are injected intravenously to colour the plasma (the dye does not penetrate the erythrocytes). The blood specimen is taken in 3-6 min and the concentration of the azo dye in the blood is determined colorimetrically. Once the amount of the dye and its concentration in the blood plasma are known, the volume of plasma is determined, and then, by using the haematocrit (the apparatus for determining the ratio of the blood corpuscles to the volume of plasma) the entire volume of blood is calculated.

The *radioisotope method* is based on the injection into the blood of erythrocytes labelled by isotopes (^{32}P, ^{51}Cr, ^{131}I). Erythrocytes of the patient or of donor blood (0 group, Rh-negative) are used. The volume of blood is calculated by the degree of dilution of the labelled erythrocytes. The volume of circulating blood in a healthy person depends on his body weight and varies from 3 to 5 l (75 ml/kg body weight, on the average). Blood volumes are increased in cardiac insufficiency and erythraemia. Decreased blood volumes are observed in cases associated with loss of blood, in shock, and severe dehydration.

CARDIAC CATHETERIZATION

This method is used to measure blood pressure and study the gas composition of the blood in various chambers of the heart and the main vessels, to reveal abnormal communications between them in congenital heart defects, to record ECG and PCG directly in the heart chambers, and to carry out angiography.

Cardiac catheterization is carried out in specially equipped operating rooms. Right chambers of the heart and the pulmonary trunk are usually catheterized. To that end one of the peripheral veins (usually the basilic vein of the left arm) is opened and a catheter introduced. The progress of the catheter is controlled by X-rays. The catheter is introduced into the right atrium, right ventricle, the pulmonary artery and further into one of its branches. Pressure of blood is measured and its specimens are taken from all heart chambers.

Left chambers of the heart are usually catheterized by a septal puncture of the left atrium, i.e. the catheter is passed from the right atrium to the left one through the interatrial septum. The left chambers of the heart can also be examined by passing the catheter through a peripheral artery (e.g. femoral artery) and further through the aorta and the aortic valve, into the left ventricle; the left atrium is inaccessible through the mitral orifice.

Pressure in the heart chambers and the great vessels can vary in cardiovascular diseases. In stenosis of the left venous orifice, for example, the blood flow from the left atrium to the left ventricle during diastole becomes difficult and diastolic pressure therefore increases in the left atrium and decreases in the ventricle. This difference in diastolic pressure increases with the degree of stenosis. In stenosis of the pulmonary artery, systolic pressure in the right ventricle increases, while systolic pressure in the pulmonary artery remains normal.

The gas composition of blood taken from various chambers of the heart is of great importance for diagnosis of congenital heart diseases and for detection of pathological communications between the heart chambers and the great vessels. In the presence of interventricular communication, blood passes from the left ventricle to the right one, and oxygen saturation of blood in the right ventricle will be higher than in the right atrium. If there is no difference between oxygen saturation of blood in the right atrium and right ventricle, while the oxygen content of blood taken from the pulmonary artery is increased, it suggests an open arterial communication through which arterial blood passes from the aorta into the pulmonary trunk.

X-RAY STUDY

Roentgenoscopy is a very important instrumental method for the study of the cardiovascular system. Routine X-ray studies include roentgenoscopy and roentgenography. In direct projection, the patient faces the screen with the X-ray tube being behind the patient's back. In oblique projections, the patient is positioned at an angle of 45° to the screen: first with the right and then with the left shoulder forward. Direct projection outlines the silhouettes of the heart and the great vessels: they appear as convex (anteriorly) arches (Fig. 50). The upper flattened arch is formed by the aorta and the superior vena cava, while the lower arch by the right atrium. The upper arch is formed on the left by the aorta; the next arch is the pulmonary trunk and the left pulmonary artery; the lower part of the contour is formed by the auricle of the left atrium and still inferiorly by the left ventricle. The silhouette of the heart with the vessels depends on the body build of the patient and position of his heart in the chest. In hypersthenic individuals and in subjects with hight diaphragm, the heart assumes a more horizontal position than it does in normosthenic subjects. The position of the heart in asthenic individuals and in subjects with low diaphragm is more central and vertical, and its silhouette is therefore smaller since the heart has a contact with the diaphragm over a small area. It looks as if hanging from the vascular bundle (drop heart). The heart position in the chest may change in pleurisy, pleuropericardial adhesion, in the presence of mediastinal tumours, etc.

When examining the silhouette of the heart and the great vessels in direct projection, it is necessary to pay attention to the magnitude of the angle formed by the bundle of the great vessels and the heart silhouette on the left. The angle becomes more significant when the left ventricle is

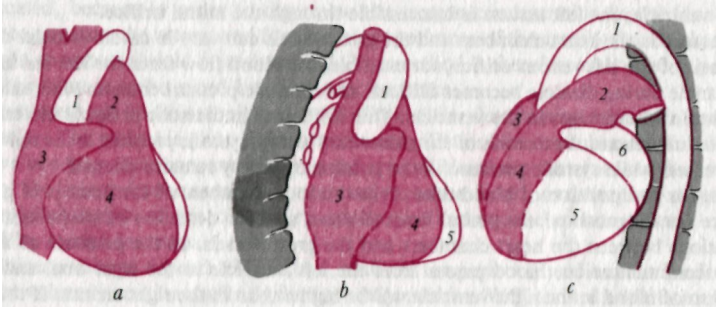


Fig. 50. Position of the heart's chambers in *(a)* direct projection; *(b)* first oblique and (c) second oblique projection.
1—aorta; *2*—pulmonic artery; *3*—right atrium; *4*—right ventricle; *5*—left ventricle; *6*—left atrium.

enlarged. Since it is more pronounced in aortic incompetence, this configuration of the heart is known as *"aortic"*. The left atrium is enlarged and the pressure in the pulmonary artery increases in mitral incompetence. In this connection the second and third arches of the left contour formed by the pulmonary trunk, the left pulmonary artery, and the auricle of the left atrium, become protruded. This configuration of the heart is known as *"mitral"*.

In the first oblique position (Fig. 50b) (or in the right anterior position), the anterior contour is formed by the ascending aorta, the pulmonary cone, and the right and left ventricles. The posterior contour of the heart silhouette is formed by the aorta, and the left and right atria. A 2—3 cm wide translucent area can be seen in healthy individuals in this position between the shadow of the spinal column and the silhouette of the heart and the great vessels (retrocardiac or H space). The width of the translucent area changes if the atria are enlarged: it narrows in the upper portion if the left atrium is enlarged, and in the lower part if the right atrium is enlarged. A contrast study of the oesophagus is very important for a more correct evaluation of the enlargement of the left atrium, which is necessary for diagnosis of mitral incompetence. The patient is given a barium sulphate suspension that fills the oesophagus. If the atrium is enlarged, the oesophagus deviates posteriorly at the level of this chamber. The condition of the pulmonary cone should be established in this position: it protrudes if pressure increases in the lesser circulation. Distention of the ascending portion of the aorta should also be evaluated.

The silhouette of the heart and the great vessels in the second oblique (or in the left anterior) position is formed by the superior vena cava, ascending aorta, the right atrium and right ventricle. The posterior contour is formed by the descending portion of the aorta, the left atrium and left ventricle. Normally the posterior contour of the cardiac silhouette does not superimpose onto the spine silhouette. If the left ventricle is enlarged, the posterior contour of the heart can be seen against the background of the spine silhouette or even posteriorly of it. If the right chambers of the heart are enlarged, the anterior contour of the heart is seen anteriorly of the vascular silhouette. In the second oblique position, the aortic silhouette can be seen, i.e. its ascending portion, the arch, and the descending portion, which is projected on the spinal silhouette. Changes in the aorta (its elongation, dilatation, or calcification) can therefore be revealed in this projection.

X-ray examination should be used to study the character and depth of contractions of various heart chambers. The depth of contractions shows the contractile power of the myocardium. Displacement of the heart silhouette should be correlated with the phases of the heart work. If the

heart silhouette is displaced in the lateral rather than in the medial direction during systole, pulsation is assessed as paradoxical, which is characteristic of cardiac aneurysm.

Electrokymograph)/. This is the method for studying contractile activity of the myocardium by recording the pulsating movements of the X-ray silhouette of the heart and the great vessels by a photocell which converts vibrations in screen luminescence into electric pulses which are then amplified and recorded as a curve (electrokymogram). Pulsation of both atria, ventricles, the aorta, the pulmonary trunk and the pulmonary vessels are recorded successively. ECG and PCO are taken synchronously so that they could be compared with the electrokymogram.

A normal electrokymogram (EKG) of each heart chamber has a specific configuration, while lengths of separate parts of the curve correspond to the cardiac phases. On a normal EKG of the left ventricle, the *A -B* line corresponds to systole and the *B-C* interval corresponds to diastole. The shape and length of its separate portions change in cardiovascular diseases. The value of electrokymography is that it shows the function of each heart chamber. It is very helpful in diagnosing acquired and congenital heart defects, in revealing large sclerotic foci in the myocardium, and heart aneurysms; it gives information about the condition of the lesser circulation.

Angiocardiography is the method of X-ray examination by which pictures of various heart chambers or the great vessels can be taken after administration of special contrast substances into them. Venous angiocardiography and selective angiocardiography are distinguished. In the former case a contrast substance (cardiotrast, diotrast, etc.) is injected into a peripheral vein and X-ray pictures are taken to record the entry of the substance into the right chambers of the heart and the vessels of the lesser circulation. The left chambers are poorly contrasted because the contrast substance is highly diluted in the blood flowing in the left chambers and the vessels of the lesser circulation. In selective angiography contrast substance is administered through a catheter directly into the right or left chambers of the heart (see "Cardiac Catheterization"). A better contrast is thus obtained in the studied part of the heart or vessel with a small amount of the administered substance.

Angiocardiography is very useful in diagnosing congenital heart defects. It reveals pathological communications between the heart chambers and the great vessels, determines the direction and amount of blood ejected from one chamber of the heart to another, locates stenosed portions of the vessels, and determines the degree of stenosis. Moreover, angiocardiography helps diagnose complicated acquired heart defects and evaluate indications for surgical treatment in cases where clinical findings are insufficiently informative. Selective angiography of the aorta and its branches (aortography) is used to study the condition of the vessels. This method is widely used to determine the condition of the coronary arteries (coronography).

Major Clinical Syndromes

Cardiac Rhythm Disorders (Arrhythmias)

Any deviations from the normal rhythm of the heart are called arrhythmias. These imply alterations in the heart rate, in succession or force of heart contractions, and also changes in the sequence of excitation and contraction of the atria and ventricles. Most arrhythmias are connected with functional changes or anatomical affections of the heart's conduction system.

Under normal conditions, the sino-atrial node has the highest automaticity and is therefore the pacemaker of the cardiac rhythm. Impulses are generated in the sino-atrial node at regular intervals (from 60 to 70 beats per min). The impulses are transmitted from the sino-atrial node (Wenckebach, Bachman, Thorel bundles) to the atrioventricular node at a rate of 0.8— 1 m/s. This rate sharply decreases in the region of the atrioventricular node (to 0.05 m/s) and the atrial systole therefore ends earlier than the excitation spreads over onto the myocardium of the ventricles to cause their contraction. Impulses are trasmitted from the atrioventricular node through the His bundle at a higher rate (1-1.5 m/s), while the rate of impulse propagation in Purkinje's fibres is as high as 3-4 m/s. Excitation is the triggering mechanism for the heart contraction. During the heart contraction, and immediately after systole, the cardiac muscle is absolutely refractory; then its excitability gradually restores.

Automaticity is characteristic of the entire conduction system of the heart, but in normal conditions it is inhibited by the high activity of the sino-atrial node, which is the automaticity centre of the first order. If the sino-atrial node is affected, or the transmission of excitation to the atrioventricular node is impaired, the atrioventricular node becomes the pacemaker (the second-order automaticity centre). Impulses are generated here at a rate of 40 to 50 per min. If the His bundle is affected, the impulses causing contraction of the heart may be generated in the Purkinje fibres (automaticity centre of the third order), but the rate of the cardiac rhythm then slows down to 20-30 beats per min.

The normal cardiac rhythm may change (1) in affected automaticity of the sino-atrial node, when the rate or sequence of impulses is altered; (2) in development of a focus of increased activity in the myocardium, that can generate impulses to initiate heart contractions apart from their generation in the sino-atrial node (ectopic arrhythmia); (3) in disordered conduction of the impulses from the atria to the ventricles or inside the ventricles themselves. Abnormal rhythm can also be due to impaired contractility of the myocardium. Arrhythmia can sometimes depend on changes in several functions of the heart such as automaticity, excitability, conduction or contractility.

Arrhythmias associated with altered automaticity of the sino-atrial node (sinus arrhythmia). When automaticity of the sino-atrial node is upset, the rate of impulse generation may either accelerate (sinus tachycardia) or slow down (sinus bradycardia), or the sequence of impulses may be changed with their generation at irregular intervals (sinus arrhythmia).

Sinus tachycardia is directly connected with effects of biologically active substances which increase excitability of the sino-atrial node. This phenomenon may also depend on the change in the tone of the vegetative nervous system. It develops with intensified effect of the sympathetic nervous system. The rate of cardiac contractions in sinus tachycardia usually varies from 90 to 120 and sometimes to 150-160 per min. Sinus tachycardia develops during meals, physical exertion and emotional stress. At elevated body temperature, the heart rate increases by 8-10 per min per each degree over 37 °C. Sinus tachycardia is a frequent symptom of myocarditis, heart defects, and other diseases. It develops by reflex

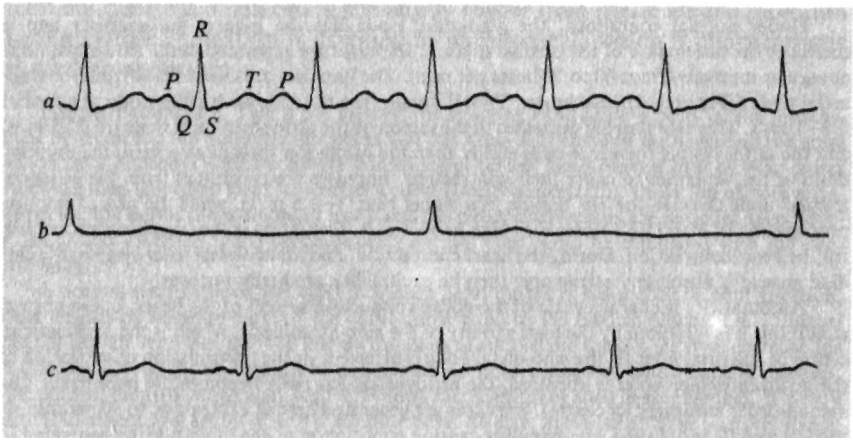


Fig. 51. Sinus arrhythmia.
-sinus tachycardia (110 b.p.m.); b—pronounced sinus bradycardia (34 b.p.m.); *c*—sinus arrhythmia. Cardiac complexes last for 0.70, 0.94, 0.82, and 0.86 s.

mechanism in heart failure and in response to the increased pressure in the orifices of venae cavae. Tachycardia often develops in neurosis, anaemia, hypotension, and in many infectious diseases and toxicosis; it can be provoked by some pharmacological preparations (adrenaline, caffeine, atropine sulphate, etc.), and in thyrotoxicosis.

The clinical signs of sinus tachycardia are heart palpitation and accelerated pulse. The *T-P* interval on ECG shortens and the *P* wave may interpose on the *T* wave (Fig. 51a).

Sinus bradycardia is connected with slowed excitation of the sino-atrial node, which in turn depends mostly on the increased influence of the parasympathetic nervous system on the heart (or decreased influence of the sympathetic nervous system). Automaticity of the sino-atrial node decreases in sclerotic affections of the myocardium and in the cold. The cardiac rate in sinus bradycardia decreases to 50—40 (in rare cases to 30) beats per min. Bradycardia may occur in well-trained athletes. It is not permanent and the heart rhythm is accelerated during exercise as distinct from pathological bradycardia in atrioventricular block when bradycardia persists during and after exercise. If automaticity of the sino-atrial node sharply decreases (sick-sinus syndrome), the second- or third-order centres may function as the pacemaker, i.e. ectopic arrhythmias develop (see below).

Sinus bradycardia occurs in increased intracranial pressure (tumour and oedema of the brain, meningitis, cerebral haemorrhage), in myx-

oedema, typhoid fever, jaundice, starvation, lead and nicotine poisoning, and due to effect of quinine and digitalis preparations. It may develop by reflex during stimulation of baroreceptors of the carotid sinus and the aortic arch in essential hypertension, and can be provoked by pressure on the eye-ball (Dagnini-Aschner reflex), or by irritation of receptors of the peritoneum and the internal organs.

Mild bradycardia is not attended by any subjective disorders, nor does it produce any effect on the circulation. Marked bradycardia (under 40 beats per min) may cause nausea and loss of consciousness due to cerebral anaemia. Objective examination reveals slow pulse. The ECG in sinus bradycardia (Fig. *5lb)* reveals the unchanged atrial or ventricular complexes; the *T-P* interval only increases to show protraction of electrical diastole of the heart; the *P-Q* interval sometimes increases insignificantly (to 0.20-0.21 s).

Sinus arrhythmia. Sinus arrhythmia characterized by irregular generation of impulses is due to variations in the tone of the vagus. It would commonly be associated with respiratory phases *(respiratory arrhythmia):* the cardiac rhythm accelerates during inspiration and slows down during expiration. Sinus arrhythmia is observed in children and adolescents (juvenile arrhythmia), in patients convalescing from infectious diseases, and in certain diseases of the central nervous system. It can be a sign of pathology in rare cases when arrhythmia is not connected with respiration or when it develops in the aged during normal respiration.

Clinically sinus arrhythmia is not attended by any subjective disorders. The cardiac rhythm and pulse rate only change with respiratory phases, and the intervals between the heart complexes *(R-R* intervals) vary in length on the ECG (Fig. 51c).

Ectopic arrhythmias. Additional (heterotopic or ectopic) foci of excitation can arise at any site of the conduction system (in the atria, ventricles, atrioventricular region). They can cause premature contraction of the heart before termination of the normal diastolic pause. This premature contraction is called extrasystole, and the disorder of the cardiac rhythm is called extrasystolic arrhythmia. If the activity of the ectopic focus is very high, it can become a temporary pacemaker, and all impulses governing the heart will during this time be emitted from this focus. The cardiac rhythm is then markedly accelerated. The condition is known as paroxysmal tachycardia.- Ectopic arrhythmias are often due to increased excitability of the myocardium.

The phenomenon known as re-entry can be another mechanism of ectopic arrhythmia. If an impulse meets an obstacle in the pathway of its conduction (local conduction disorder), the excitation wave can return from this obstacle to excite the myocardium.

Extrasystolic arrhythmia. Extrasystole usually develops during normal contractions of the heart governed by the sino-atrial node (nomotopic contractions). Ectopic foci of excitation can arise at any site of the conduction system. Usually excitations arise in the ventricles, less frequently in the atria, the atrioventricular node, and in the sino-atrial node (sinus extrasystole). A nomotopic contraction of the heart that follows extrasystole occurs in a longer (than normal) lapse of time. This can be explained as follows. During the atrial extrasystole, excitation from the ectopic focus is transmitted to the sino-atrial node to "discharge" it, as it were. The next impulse arises in the sino-atrial node only in a lapse of time that is required to "discharge" the node and to form a new impulse.

In ventricular extrasystole, the time between the extrasystolic contraction and subsequent nomotopic contraction is even longer. The impulse from the heterotopic focus, located in the ventricles, propagates only over the ventricular myocardium; it would not be usually propagated to the atria via Aschoff-Tawara node. The impulse occurs in normal time in the sino-atrial node but it is not transmitted to the ventricles because they are refractory after the extrasystolic excitation. The next impulse from the sino-atrial node will only excite and contract the atria and the ventricles. A long "compensatory" pause therefore follows the ventricular extrasystole which lasts till the next nomotopic contraction.

Extrasystolic arrhythmia is quite common. It may occur in practically healthy individuals as a result of overexcitation of certain sites of the conduction system due to the action of the extracardiac nervous system in heavy smokers and in persons abusing strong tea or coffee; it can occur by reflex in diseases of the abdominal organs. Extrasystole often attends various cardiovascular pathological conditions due to inflammatory or dystrophic affections of the myocardium or its deficient blood supply; or it may be due to hormonal disorders (thyrotoxicosis, menopause), various intoxications, disorders of electrolyte metabolism, etc.

Patients with extrasystole can feel their heart missing a beat (escape beat) and a subsequent strong stroke. Auscultation of the heart reveals its premature contraction with a specific loud first sound (due to a small diastolic filling of the ventricles). Extrasystole can be easily revealed by feeling the pulse: a premature weaker pulse wave and a subsequent long pause are characteristic. If extrasystole follows immediately a regular contraction, the left ventricle may be filled with blood very poorly and the pressure inside it may be so small that the aortic valve would not open during the extrasystolic contraction and the blood will not be ejected into the aorta. The pulse wave on the radial artery will not be then detectable (missing pulse). The ECG of all extrasystoles are characterized by: (1) premature appearance of the cardiac complex; (2) elongated pause between the ex-

trasystolic and subsequent normal contraction. According to the site of origin, extrasystoles are classified as atrial and atrioventricular (nodal), which are given a common name of supraventricular, and also ventricular (left- and right-ventricular) extrasystoles.

Excitation of the atria only changes in *atrial extrasystole* because the impulse is generated not in the sino-atrial node, and the ventricles are excited by the usual way. The ECG of atrial extrasystole is characterized by the following signs (Fig. 52a): (1) premature appearance of the cardiac complex; (2) preservation of the atrial *P* wave which may be slightly disfigured and superimposed on the preceding *T* wave; this depends on the abnormal atrial excitation from a heterotopic focus; (3) normal shape of the ventricular complex; (4) slight elongation of the diastolic pause *(T-P* interval) following the extrasystolic contraction.

In *atrioventricular (nodal) extrasystole* the excitation of the atria differs from normal more substantially than in atrial extrasystole. The Aschoff-Tawara node impulse is transmitted to the atria retrogradely, from bottom to top. The ventricles are excited in nodal extrasystole in the usual way. The following signs are characteristic of the ECG in nodal extrasystole: (1) premature appearance of the cardiac complex; (2) changes in the *P* wave which becomes negative to show the retrograde atrial excitation (in some cases the *P* wave is absent on the ECG); (3) the position of the *P* wave with respect to the ventricular complex changes, which depends on the rate of

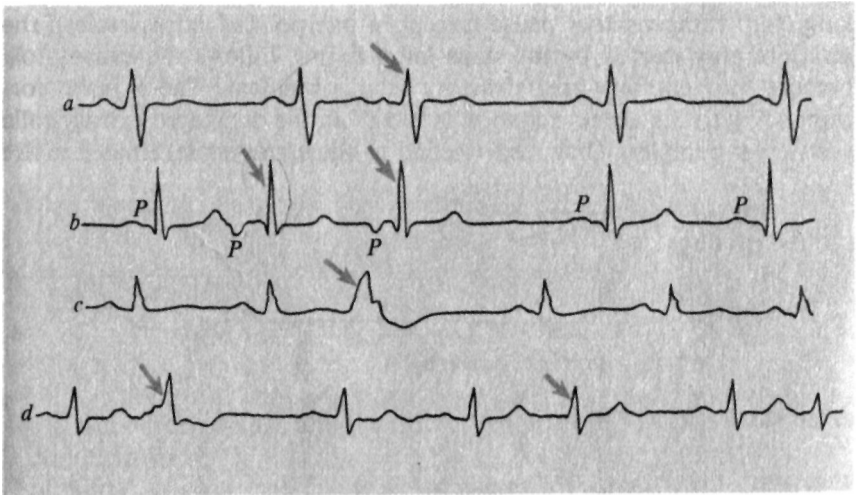


Fig. 52. Extrasystole.
a—atrial; *b*—nodal; *c*—ventricular; *d*—polytopic. Extrasystoles are marked by the arrows (for details see the text).

propagation of the excitation wave onto the atria and the ventricles. If excitation of the atria is followed by excitation of the ventricles, the negative *P* wave is recorded before the *QRS* complex; if the ventricles are excited first, the negative *P* wave follows the *QRS* complex. If the atria and ventricles are excited synchronously, the *P* wave is not recorded separately but superimposes the *QRS* complex to alter somewhat its configuration (see Fig. 53). In other cases, the configuration of the ventricular complex in nodal extrasystole usually does not change; the diastolic pause becomes longer.

Heart excitation order changes sharply in *ventricular extrasystole.* First, the ventricular impulse is not usually transmitted retrogradely through the Aschoff-Tawara node and the atria are not therefore excited. Second, the ventricles are not excited synchronously (as in normal cases), but one after another, i.e. that ventricle is excited first where the ectopic focus is located. The time of excitation of the ventricles is therefore longer and the *QRS* complex wider. The ECG is characterized by the following signs: (1) premature appearance of the ventricular complex; (2) absence of the atrial *P* wave; (3) deformation of the *QRS* complex due to its increased voltage and length; (4) since the sequence of relaxation in the ventricles changes, the shape and the height of the *T* wave changes as well. As a rule, the *T* wave is enlarged and its direction is opposite to that of the maximum wave of the *QRS* complex (the *T* wave is negative if the *R* wave is high, and positive if the *S* wave is deep). The ventricular extrasystole is followed by a long (full) compensatory pause (except in interpolated extrasystoles): the atria are only excited by the sinus impulse that follows the extrasystole because the ventricles are refractory at this moment. The *P* wave corresponding to the atrial excitation is "lost" in the disfigured extrasystolic ventricular complex. Only next (second to the extrasystole) sinus impulse

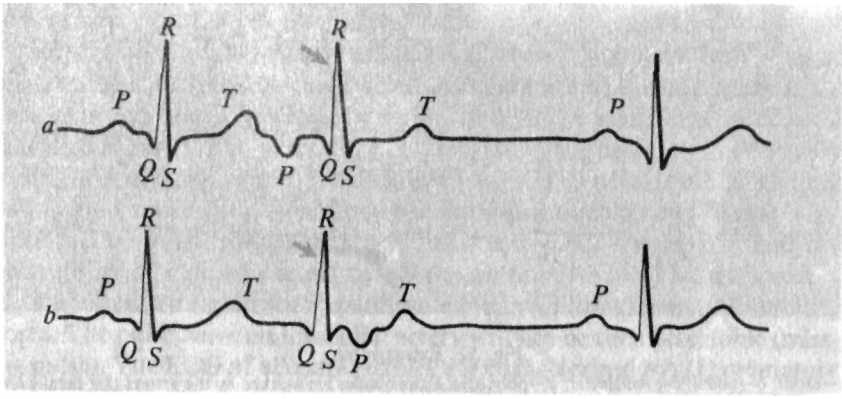


Fig. 53. Nodal extrasystoles.
a—from the upper part of the sino-atrial node; *b*—from the lower part of the node.

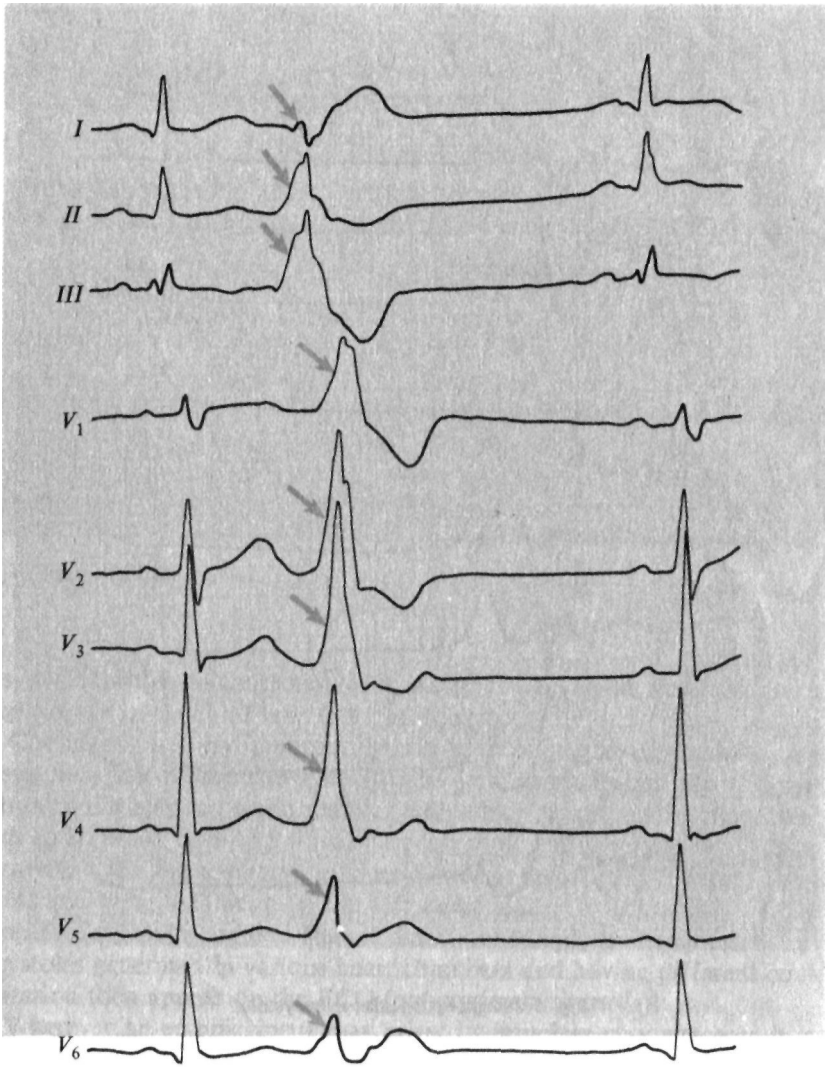


Fig. 54. Left-ventricular extrasystole.

excites both the atria and the ventricles, while the ECG shows a normal cardiac complex.

Sometimes it is possible to determine in which particular ventricle the ectopic focus is located. This can be done from the configuration of the ventricular complex in various ECG leads. Left-ventricular extrasystole is characterized by a high *R* wave in the third standard lead and the deep *S* wave in the first lead (Fig. 54). In right-ventricular extrasystole, the ex-

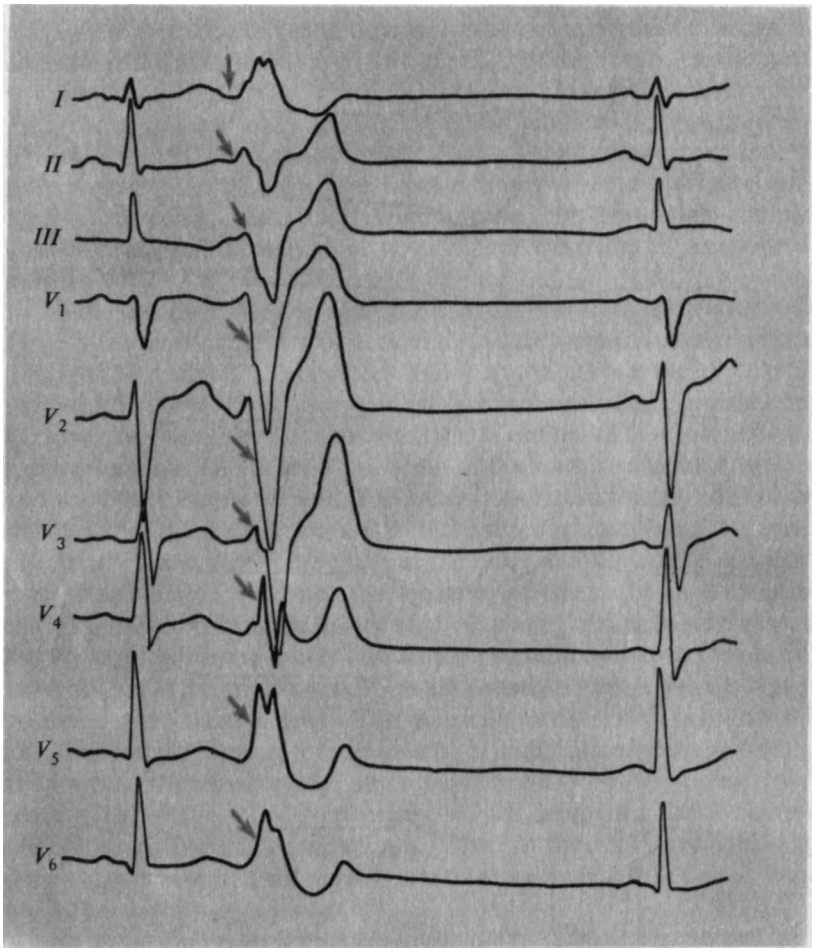


Fig. 55. Right-ventricular extrasystole.

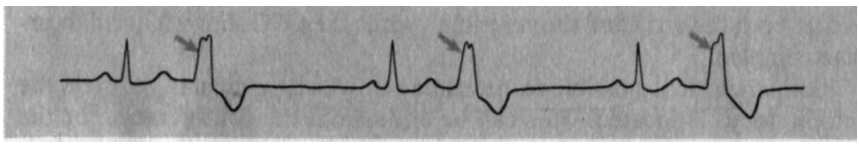


Fig. 56. Ventricular bigeminy.

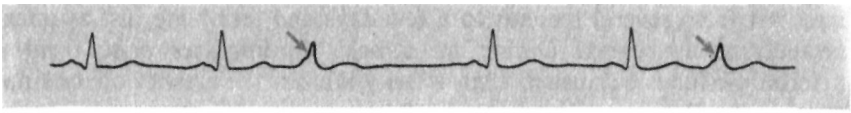


Fig. 57. Ventricular trigeminy.

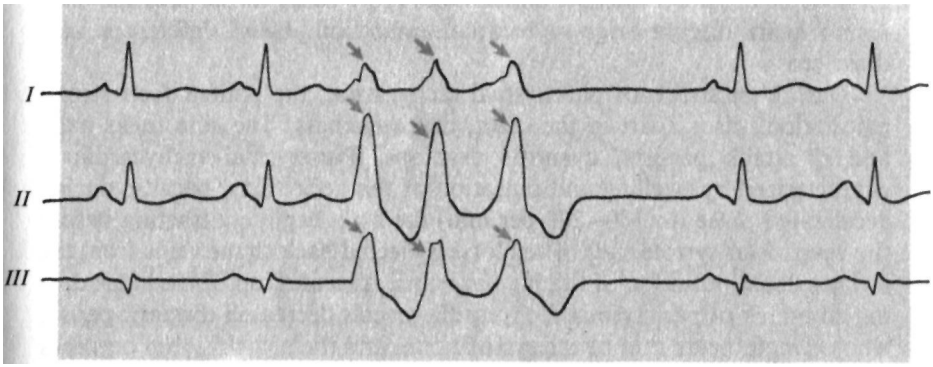


Fig. 58. Group extrasystole. Two normal cardiac complexes are followed by three ventricular extrasystoles.

trasystolic complex is characterized by a high *R* wave in the first lead, and a deep *S* wave in the third lead (see Fig. 55).

Chest leads are very important for the topic diagnosis of ventricular extrasystole. Left-ventricular extrasystoles are characterized by the appearance of the extrasystolic complex with a high *R* wave in the right chest leads and a broad or deep S wave in the left chest leads. In right-ventricular extrasystole, on the contrary, the deep S wave is recorded in the right chest leads, and a high *S* wave in the left chest leads. If excitability of the myocardium is high, several (rather than one) ectopic foci may exist. Extrasystoles generated in various heart chambers and having different configuration then appear on the ECG *(polytopic extrasystole)*.

Wherever an ectopic focus may arise, its impulses may alternate in a certain order with the normal impulses of the sino-atrial node. This phenomenon is known as *allorhythmia.* Extrasystole may alternate with each sinus impulse (bigeminy; see Fig. 56), or it may follow two normal impulses (trigeminy; see Fig. 57), or three normal impulses (quadrigeminy), etc. If the heterotopic focus is even more active, a normal contraction may be followed by several extrasystoles at a run (group extrasystole; Fig. 58), which sometimes precedes an attack of paroxysmal tachycardia.

Paroxysmal tachycardia. This is a sudden acceleration of the cardiac rhythm (to 180-240 beats per min). At attack of paroxysmal tachycardia

may last from several seconds to a few days and terminate just as unexpectedly as it begins. During an attack, all impulses arise from a heterotopic focus because its high activity inhibits the activity of the sino-atrial node. Paroxysmal tachycardia (like extrasystole) may occur in subjects with increased nervous excitability, in the absence of pronounced affections of the heart muscle, but it arises more likely in the presence of a severe heart disease (e.g. myocardial infarction, heart defects or cardiosclerosis).

During an attack of paroxysmal tachycardia, the patient feels strong palpitation, discomfort in the chest, and weakness. The skin turns pale, and if attack persists, cyanosis develops. Paroxysmal tachycardia is characterized by swelling and pulsation of the neck veins, because during accelerated pulse (to 180—200 per min) the atria begin contracting before the ventricular systole ends. The blood is ejected back to the veins from the atria to cause pulsation of the jugular veins. Auscultation of the heart during an attack of paroxysmal tachycardia reveals decreased diastolic pause, whose length nears that of the systolic one, and the heart rhythm becomes foetal (pendulum). The first sound increases due to insufficient ventricular diastolic filling. The pulse is rhythmic, very fast, and small. Arterial pressure may fall. If an attack persists (especially if it develops in the presence of a heart disease) symptoms of cardiac insufficiency develop.

Like in extrasystole, the heterotopic focus in paroxysmal tachycardia may be located in the atria, the atrioventricular node, and the ventricles. It is possible to locate the focus only by electrocardiography: a series of extrasystoles follow on an ECG at regular intervals and at a very fast rate. Figure 59a shows the ECG taken during an attack of supraventricular paroxysmal tachycardia (the *P* wave cannot be seen because of accelerated cardiac rhythm and the shape of the ventricular complex is not changed); an ECG which follows next is taken in a patient with ventricular tachycardia; it shows a series of altered and broadened ventricular complexes (similar to those in ventricular extrasystoles).

Arrhythmias due to disordered myocardial conduction. Transmission of the impulse may be blocked at any part of the heart's conduction system. The following types of heart blocks are distinguished: (1) sino-atrial block, in which beats are sometimes missing in the sino-atrial node and the impulse is not transmitted to the atria; (2) intra-atrial block, in which transmission of excitation through the atrial myocardium is impaired; (3) atrioventricular block, in which conduction of impulses from the atria to the ventricles is impaired; (4) intraventricular block, in which conduction of impulses through the His bundle and its branches is impaired.

Block may develop in inflammatory, dystrophic, and sclerotic affec-

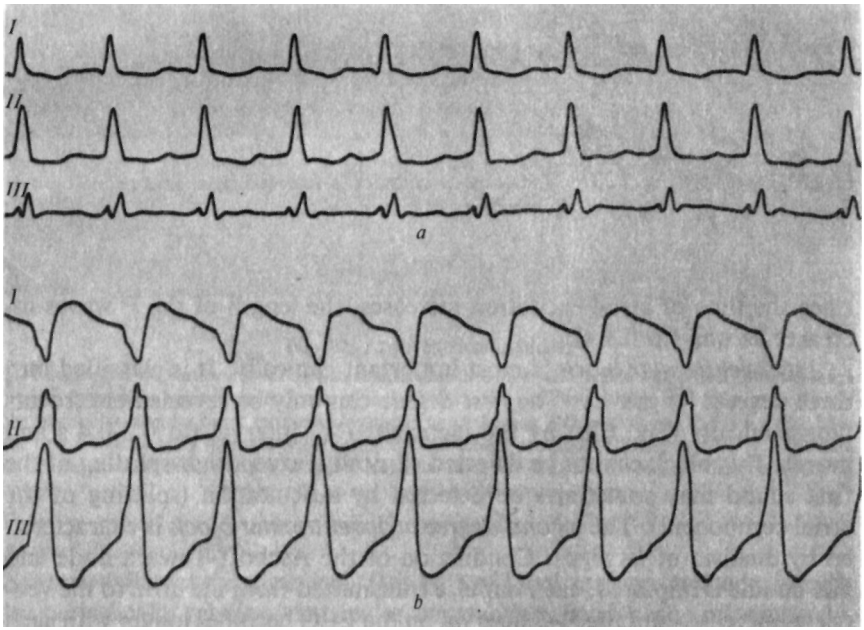


Fig. 59. Paroxysmal tachycardia.
a—supraventricular paroxysmal tachycardia (170 b.p.m.); *b*—ventricular paroxysmal tachycardia (170 b.p.m.).

tions of the myocardium (e.g. rheumatic and diphtheritic myocarditis or cardiosclerosis). The conduction system may be affected by granulomas, cicatrices, toxins, etc. Conduction is often impaired in disordered coronary circulation, especially in myocardial infarction (the interventricular septum is involved). Block may be persistent and intermittent. Persistent block is usually connected with anatomic changes in the conduction system, whereas intermittent block depends largely on the functional condition of the atrioventricular node and the His bundle and is often connected with increased influence of the parasympathetic nervous system; atropine sulphate is an effective means that restores conduction.

Clinical signs of block depend on its location. *Sino-atrial block* is characterized by periodic missing of the heart beat and pulse beat. The ECG (Fig. 60) shows periodic missing of the heart complex in the presence of a regular sinus rhythm (neither *P* wave nor the *QRST* complex are recorded); the length of diastole doubles.

Intra-atrial block can only be detected electrocardiographically because clinical signs are absent. Figure 61 shows the ECG with altered *P* waves;

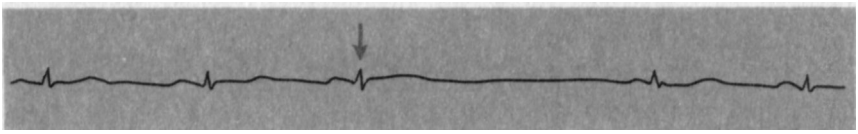


Fig. 60. Sino-atrial block. The third cardiac complex is followed by a pause equal to two preceding *R-R* intervals.

since the time of atrial excitation increases, the length of the *P* waves increases as well (to 0.1 s).

Atrioventricular block is most important clinically. It is classified into three degrees by gravity. *The first degree* can only be revealed electrocardiographically (Fig. 62c) by the increased *P-Q* interval (to 0.3-0.4 s and more). This block cannot be detected clinically, except that splitting of the first sound may sometimes be detected by auscultation (splitting of the atrial component). The *second-degree atrioventricular block* is characterized by dualism of its signs. Conduction of the Aschoff-Tawara node and His bundle is impaired: each impulse transmitted from the atria to the ventricles increases and the *P-Q* interval on the ECG becomes longer with each successive beat. A moment arrives at which one impulse does not reach the ventricles and they do not contract, hence the missing *QRS* complex on an ECG (Fig. *62b).* During a long diastole, which now follows, the conduction power of the atrioventricular system is restored, and next impulses will again be transmitted, but their gradual slowing down will be noted again; the length of the *P-Q* interval will again increase in each successive complex (Fig. 626). The length of diastole which follows the *P* wave is called the

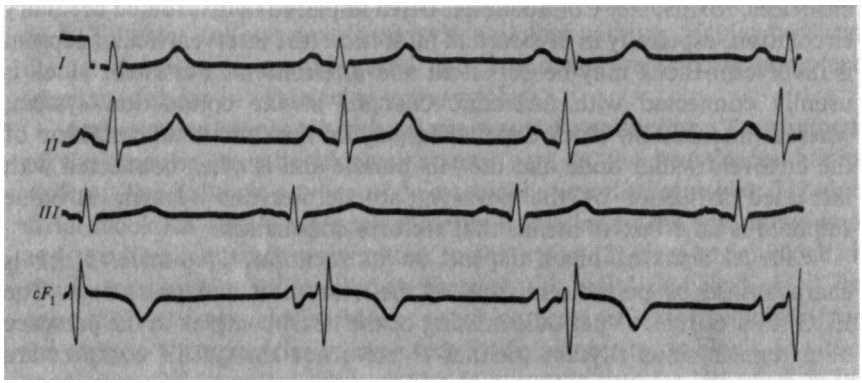


Fig. 61. Intra-atrial block. *P* waves are broadened (P = 0.14 s) and serrated; the *P* wave in the first chest lead has two phases.

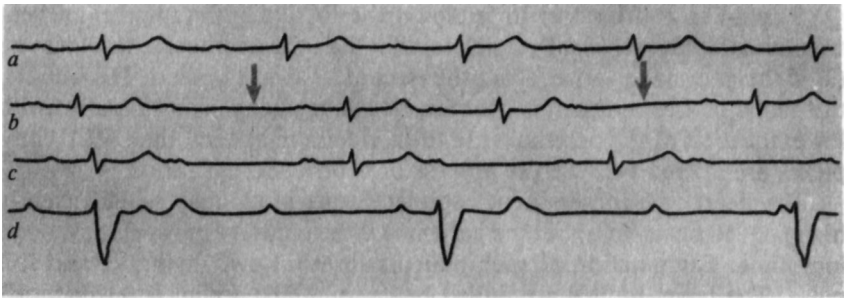


Fig. 62. Atrioventricular block.
a—I degree (the *PQ* interval in all cardiac complexes is 0.40 s); *b*—IIa degree with Samoilov-Wenckebach periods (marked by arrows); the *PQ* interval in the first cardiac complex is 0.36 s, then follows the *P* wave; the ventricular complex is not recorded after the *P* wave; the next *PQ* interval is 0.28 s and then 0.38 s; the next *P* wave is again followed by the Samoilov-Wenckebach period; *c*—IIb degree block with the ratio of 2:1; the atrial rhythm is 84 c.p.m., and the ventricular rhythm is 42 c.p.m.; *d*—complete heart block; atrial rhythm is 85 cp.m.; the ventricular rhythm 20 c.p.m.

Samoilov- Wenckebach period. This type of block is characterized clinically by periodically missing ventricular contractions, and hence missing pulse beats, which correspond to the Samoilov-Wenckebach period. On the other hand, the second-degree atrioventricular block can be characterized by a worse conduction. The *P-Q* interval remains constant, but only each second, third, or (less frequently) fourth impulse is transmitted to the ventricles. The number of *P* waves on the ECG is therefore larger than of ventricular complexes (see Fig. 62c). This is known as incomplete heart block with a 2:1, 3:1, etc. ratio. Considerable deceleration of the ventricular rhythm and slow pulse are characteristic, especially in 2:1 block. If each third or fourth beat is missing, the pulse is irregular and resembles trigeminy or quadrigeminy with early extrasystoles and pulse deficit. If the heart rhythm slows down significantly, the patient may complain of giddiness, everything going black before his eyes, and transient loss of consciousness due to anaemia of the brain. The *third-degree atrioventricular block* is called complete heart block. Atrial impulses do not reach the ventricles and the sino-atrial node becomes the only pacemaker for the atria. The ventricles contract by their own automaticity in the centres of the second or third order. The number of their contractions in complete heart block is about 30—40 per min, and ventricular rhythm slows down with the lower position of the pacemaker in the conduction system.

The ECG in complete heart block is characterized by the following signs: (1) atrial *P* waves and ventricular complexes are recorded independently of each other, and part of the *P* waves may superimpose the

QRS complex and become invisible on the ECG; (2) the number of ventricular complexes is usually much smaller than the number of atrial waves; (3) if the pacemaker arises from the Aschoff-Tawara node or His bundle, the shape of the ventricular complex does not change substantially; with lower location of the pacemaker in the conduction system, the *QRST* complexes are altered because the process of ventricular excitation is upset.

The heart rate in persistent complete heart block may be sufficiently high (40-50 beats/min) but the patient may be unaware of the disease for a long time. Examination of such patients reveals slow, rhythmic, and full pulse. The heart sounds are dulled but a loud first sound ("pistol-shot" sound according to Strazhesko) may be heard periodically. It occurs due to coincidence of the atrial and ventricular contractions. If the ventricular rhythm slows down significantly (to 20 beats/min and less), or the heart misses a beat when incomplete heart block converts into a complete one, i.e. when the impulses from the atria are not conducted to the ventricles, while their automaticity has not yet developed, attacks (the Morgagni-Adams-Stokes syndrome) may occur due to disordered blood supply, mainly to the central nervous system. During an attack the patient loses consciousness, falls, general epileptiform convulsions develop, the respiration becomes deep, the skin pallid, the pulse very slow or even impalpable.

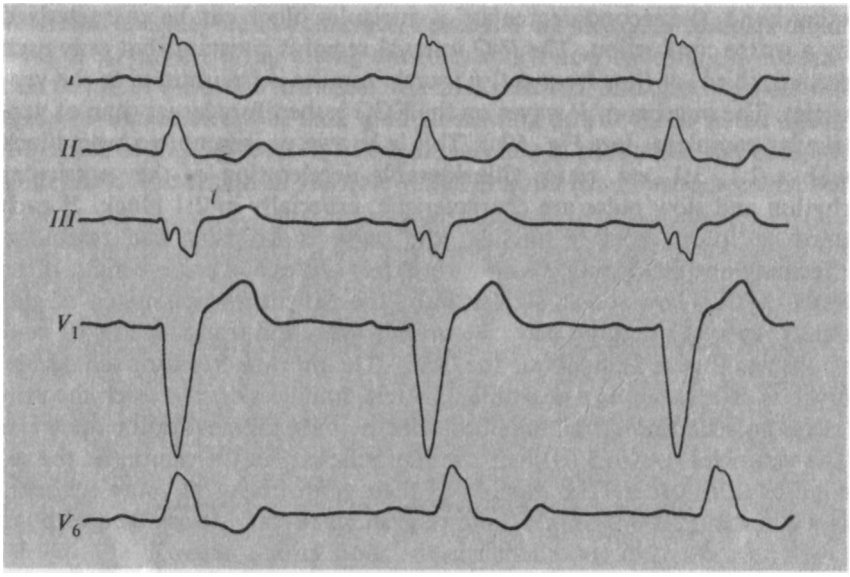


Fig. 63. Block of the left branch of the His bundle (time of intraventricular conduction is 0.17 s).

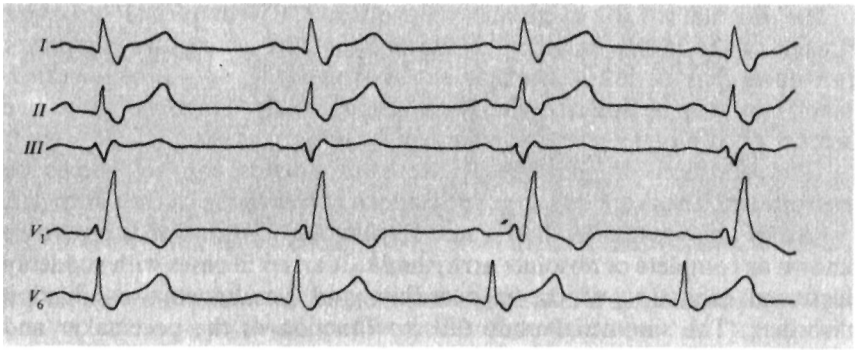


Fig. 64. Block of the right branch of the His bundle (time of intraventricular conduction is 0.15 s).

When the ventricular automaticity restores, the patient regains his consciousness and all other signs of the syndrome disappear. If automaticity is not restored for a time, fatal outcome is possible.

Intraventricular block usually develops as the right or left bundle-branch block. The left limb of the His bundle ramifies almost immediately to give left anterior and left posterior branches. Only one branch can therefore be blocked. Block of the right limb may be combined with block of the branches of the left limb. In complete block of either of the limbs, the impulse from the sino-atrial node is normally conducted through the Aschoff-Tawara node and the main part of the His bundle to meet an obstacle to its conduction in that ventricle whose branch is affected. The ventricle with the intact branch is therefore first excited and excitation is transmitted to the ventricle with the affected branch. The ventricles are thus excited slowly and in an unusual way.

The bundle-branch block is characterized electrocardiographically as follows (Figs. 63 and 64): (1) the *P* wave does not change; (2) the ventricles contract rhythmically by the impulse from the sino-atrial node, but since the order of the ventricular excitation is upset, markedly altered and broadened *QRS* complexes (which resemble complexes in ventricular extrasystole) are recorded; (3) the time of intraventricular conduction increases to 0.12-0.18 s and more. The shape of the ventricular complexes depends on the particular bundle branch which is blocked. If the left branch is blocked, its excitation is delayed and the ventricular complexes acquire the shape of the right-ventricular extrasystolic complexes (Fig. 63), i.e. the *QRS* complex broadens and changes in its shape, the *S-T* interval shifts, and the direction of the *T* waves changes to the opposite with respect

to the direction of the maximum wave of the *QRS* complex. If the right branch of the bundle is affected, the shape of the ventricular complexes resembles that of left-ventricular extrasystoles (Fig. 64). Bundle-branch block can only be detected electrocardiographically. It has no subjective signs.

Reduplication or splitting of the heart sounds can sometimes be auscultated. These are due to asynchronous contractions of the ventricles.

Atrial and ventricular flutter and fibrillation. *Fibrillation* is otherwise known as complete or absolute arrhythmia. It arises in cases with suddenly increased excitation of the myocardium and simultaneous conduction disorders. The sino-atrial node fails to function as the pacemaker and many ectopic excitation foci (to 600-800 per min) arise in the atrial myocardium, which becomes only possible with a marked shortening of the refractory period. Since conduction of these impulses is difficult, each of them only excites and causes contraction of separate muscular fibres rather than the entire atrium. As a result, minor contractions develop in the atrium (atrial fibrillation) instead of adequate atrial systole. The mechanism of fibrillation is not fully understood. It is believed that permanent circulation of the circular excitation wave in the atria can account for the development of this disorder. Only part of the impulses are transmitted to the ventricles through the Aschoff-Tawara node. Since conduction of atrial impulses is irregular, the ventricles contract at irregular intervals to cause complete arrhythmia of the pulse. Depending on the conductability of the Aschoff-Tawara node, three forms of atrial fibrillation are distinguished: tachyarrhythmic, in which ventricles contract at a rate from 120 to 160 per min, bradyarrhythmic, in which the heart rate does not exceed 60 per min, and normosystolic, in which the ventricles contract at a rate of 60-80 per min.

Fibrillation is characteristic of mitral heart diseases (especially of mitral stenosis), coronary atherosclerosis, thyrotoxicosis, etc. Fibrillation may occur as a permanent symptom or in attacks of tachyarrhythmia. Clinically fibrillation (bradyarrhythmia) may cause no subjective symptoms. Tachyarrhythmia is usually characterized by palpitation. Examination of the heart reveals complete irregularity of the heart contractions. Variations in the length of diastole account for variations in ventricular filling and hence in the intensity of the heart sounds. The pulse is also arrhythmic, pulse waves vary in height (irregular pulse), and pulse deficit often develops in frequent heart contractions. The ECG of a patient with fibrillation (Fig. 65) shows the following changes: (1) the P wave disappears; (2) multiple small waves appear which are designated by the letter 'f'; (3) ventricular complexes follow at irregular intervals, their shape does not change substantially.

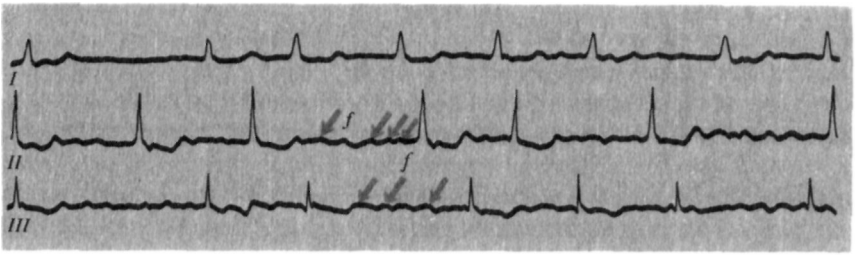


Fig. 65. Fibrillation. Ventricular complexes follow on the ECG at irregular intervals; *P* waves are absent; small waves (f) are recorded instead.

Atrial flutter is the upset cardiac rhythm, which nears in its pathogenesis to fibrillation. As distinct from fibrillation, the number of impulses arising in fluttering atria does not usually exceed 250—300 per min, and their conduction through the Aschoff-Tawara node is usually rhythmic. As a rule, not all atrial impulses are conducted to the ventricles. Each other, third or fourth impulse, is only conducted to the ventricles since partial (incomplete) atrioventricular block develops simultaneously. Conduction of the Aschoff-Tawara node sometimes constantly changes: each other impulse is now conducted; then the rhythm changes to conduction of each third impulse, and the ventricles contract arrhythmically. Like fibrillation, atrial flutter occurs in mitral defects, coronary atherosclerosis, and thyrotoxicosis; flutter sometimes develops in poisoning with quinine or digitalis.

Patients with accelerated heart rate (high conduction of the Aschoff-Tawara node) complain of palpitation. Examination reveals tachycardia that does not depend on the posture of the patient, exercise or psychic strain, since the sino-atrial node does not function as the pacemaker in atrial flutter (being governed by extracardial nerves). Heart contractions are arrhythmic in patients with varying conduction of the Aschoff-Tawara node. The ECG shows high waves (Fig. 66) instead of the normal atrial *P* waves. The number of high waves preceding each ventricular complex depends on the conduction of the Aschoff-Tawara node.

Ventricular fibrillation and flutter are gross disorders of the heart rhythm. The absence of adequate ventricular systole and contraction of separate ventricular muscles cause pronounced disorders in the haemodynamics and rapidly lead to death. Ventricular fibrillation and flutter occur in grave affections of the myocardium (diffuse myocardial infarction, etc.). The patient loses consciousness, becomes pallid, the pulse and arterial pressure become indeterminable. The ECG shows abnormal complexes on which separate waves are distinguished with difficulty (Fig. 67).

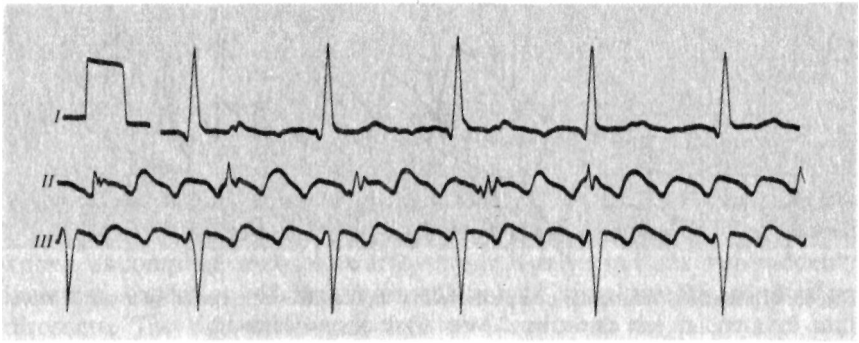


Fig. 66. Atrial flutter. High atrial waves are seen on the ECG.

Treatment of cardiac arrhythmia includes the following measures: (1) management of the diseases which caused arrhythmia (myocarditis, ischaemic heart disease, neurosis, hyperthyroidism, etc.); (2) using means to restore ionic equilibrium in the myocardium and improve metabolism (potassium salts, vitamins, ATP, etc.); (3) in cases with increased excitability of the myocardium and in ectopic arrhythmias the following preparations are recommended: quinidine, novocainamide, aimaline, beta-adrenergic blocking agents β-blockers), etc.; (4) progressive ventricular fibrillation is managed by electric defibrillation, i.e. short (0.01 s) single electric discharge of 5000-7000 V, which causes instantaneous excitation of all parts of the myocardium and restores the normal cardiac rhythm. Defibrillation is managed by an apparatus known as a defibrillator. Its two electrodes are attached to the chest (one below the left scapula and the other on the heart, or one below the right clavicle and the other over the heart apex). Electric impulses are also given to treat permanent fibrillation or paroxysmal tachycardia if medicamentous therapy proves inefficient; (5) electric stimulation of the heart (artificial pacemaker) is also indicated in stoppage of the heart, in pronounced bradycardia, in complete atrioventricular block.

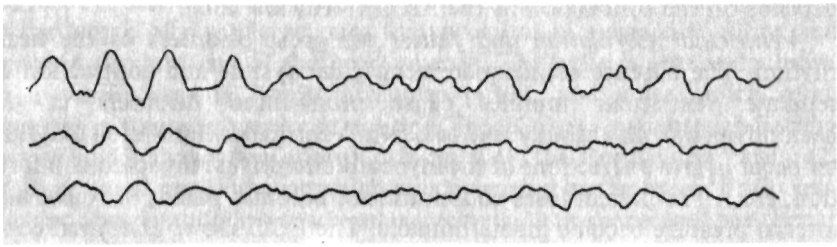


Fig. 67. Ventricular flutter and fibrillation.

Circulatory Insufficiency

This is a pathological condition in which the cardiovascular system fails to supply the necessary amount of blood to the organs and tissues for their adequate function. This condition arises due to affection of the heart or of the vessels alone, or it may be secondary to general disorders of the cardiovascular system. The clinic of circulatory insufficiency is usually associated with heart failure in which the function of the entire circulatory apparatus soon becomes affected.

Heart failure is associated with decreased contractility of the myocardium. The amount of venous blood flowing to the heart and the resistance, which the myocardium has to overcome in order to eject blood into the vessels, exceeds the power of the heart to handle the blood flowing from the veins into the arteries. The numerous causes of heart failure can be classified into the following two major groups.

1. Heart failure caused by diseases which affect primarily the myocardium and its metabolism. This condition arises in (a) infectious, inflammatory, and toxic affections of the myocardium (myocarditis of various aetiology, intoxication of the myocardium with alcohol, narcotic drugs, and other poisons); (b) insufficient blood supply to the myocardium (disordered coronary circulation, anaemia); (c) metabolic disorders, avitaminosis, and endocrine dysfunction.

2. Heart failure due to overloading or overstrain of the myocardium which arises in pathological changes in the heart proper or in the blood vessels (heart defects, hypertension in the greater or lesser circulation). The left or right ventricle, or the entire heart are overloaded due to various causes.

The left ventricle is overloaded (1) in the presence of obstacles to blood ejection from the ventricle; this may be due to the narrowing of the aortic isthmus or orifice, or a sharp and persistent increase in the arterial pressure; (2) in diastolic overfilling of the left ventricle in patients with aortic incompetence or mitral insufficiency.

The right ventricle may be overloaded (1) in difficult blood outflow from this ventricle due to the narrowing of the pulmonary trunk orifice, or increased pressure in the lesser circulation; (2) in diastolic overfilling of the right ventricle associated with tricuspid or pulmonary valve incompetence.

Both ventricles are overloaded in combined or concurrent heart diseases, in some congenital heart diseases, in adhesive pericarditis, etc. Primary affections of the myocardium and its overloading sometimes contribute to the development of heart failure. Rheumatic myocarditis or rheumatic heart disease can, for example, become the cause of circulatory insufficiency in a rheumatic patient. Heart failure may be aggravated by various infections and intoxications, physical strain, pregnancy, injuries,

and surgical operations. The same factors can become a direct cause of heart failure in patients with heart diseases, cardiosclerosis, etc.

Abnormal activity of the heart can for a long time be compensated by its intensified work and also by some extracardiac factors that ensure adaptation of the entire circulatory system to the increased demands of the body: (1) the force of heart contractions is increased by the action of the vagus nerve; (2) heart rate increases because elevated pressure in the orifice of the vena cava accelerates the cardiac rhythm (Bainbridge reflex); (3) diastolic pressure decreases due to dilatation of arterioles and capillaries; this ensures a more effective systolic emptying of the heart; (4) utilization of oxygen by tissues increases.

But prolonged overloading on the myocardium decreases the cardiac output and increases the residual systolic blood volume. This causes ventricular overfilling during diastole since the ventricle has to accept also its normal portion of blood. Diastolic pressure in the ventricle increases, the ventricle becomes distended, and the so-called *tonogenic dilatation* of the myocardium occurs. This dilatation, and the accompanying distention of the muscle fibres, intensify, according to Starling, contractility of the myocardium, cause its hyperfunction, and lead to its hypertrophy. Compensatory hypertrophy of the myocardium increases the heart activity to maintain circulation for a long period of time.

Long-standing hypertrophy of the myocardium becomes the cause of its wear out, dystrophic, and sclerotic processes. These processes are also promoted by impaired blood supply to the myocardium, because hypertrophy of the heart is attended only by the increase in the weight of the myocardium, while the coronary vessels remain unchanged. The contractile power of the myocardium thus decreases and even its marked distention during diastole does not intensify contractility. Decrease in contractility and the tone of the myocardium are attended by a significant dilatation of the heart chambers, which is called *myogenic dilatation* (as distinct from the compensatory tonogenic dilatation). Myogenic dilatation can arise without preceding hypertrophy of the myocardium, in primary affections of the heart muscle (in myocarditis or myocardial infarction).

Tachycardia, which first develops as a compensatory mechanism to maintain the normal minute blood volume at decreased stroke volume, later becomes the cause of myocardial weakening, because diastole shortens in tachycardia and the time of restoration of the biochemical processes in the myocardium decreases.

Thus, dilatation and hypertrophy of the heart and tachycardia can only partially compensate for disorders in the cardiovascular system. As heart failure progresses, these compensatory mechanisms themselves become the source of harmful effects. Further decrease in myocardial contractility causes marked disorders in haemodynamics.

Haemodynamic changes. As myocardial contractility decreases and myogenic dilatation of the ventricle develops, diastolic ventricular pressure increases while systolic pressure falls because the ability of the ventricle to strain during diastole sharply diminishes. This decreases the cardiac output and the *minute blood volume.* The mass of the circulating blood usually increases proportionally to the degree of circulatory insufficiency. This is favoured by retention of sodium chloride and water in decreased renal filtration and increased reabsorption of sodium, and the increasing number of red blood cells (hypoxia is attended by intensified haemopoiesis to compensate for the developing insufficiency). The *rate of blood flow* decreases. *Blood pressure* changes as well: venous and capillary pressure increases in the greater circulation; arterial pressure remains normal or diastolic pressure slightly increases and the pulse pressure decreases.

Haemodynamic disorders are attended by abnormal *gas exchange.* Slowing of the blood flow rate increases oxygen absorption by the tissues; to 60—70 per cent of oxygen (instead of the normal 30 per cent) is consumed in capillaries. The arteriovenous difference in the oxygen content of the peripheral blood increases. Developing disorders in gas exchange associated with heart failure upset the carbohydrate metabolism. Lactic acid that is formed in skeletal muscles is decomposed only partly in insufficient oxygen supply to tissues; the blood content of lactic and pyruvic acids therefore increases. The increased content of lactic acid upsets acid-base equilibrium and decreases alkaline reserve. At the beginning of heart failure acidosis is compensated for because lactic acid displaces carbon dioxide which is removed from the body through the lungs. If pulmonary ventilation is upset and carbon dioxide is not expired in sufficient amount, decompensated acidosis develops.

Accumulation of underoxidized metabolites in the blood and intensified work of respiratory muscles intensify basal metabolism to complete a vicious circle: the body's demands in oxygen increase, whereas the circulatory system fails to meet them. Oxygen debt thus increases.

Haemodynamic and metabolic disorders account for various clinical signs of heart failure.

Clinical manifestations of heart failure. An early and specific symptom of circulatory insufficiency is *dyspnoea.* It is manifested by unreasonably accelerated and intensified respiration; dyspnoea develops at rest or during mild exercise. Dyspnoea arises in upset gas exchange and accumulation of underoxidized metabolites in the blood. It has already been said that lactic acid accumulated in the blood combines with bicarbonate alkalis to displace carbon dioxide which stimulates the respiratory centre to accelerate and deepen respiration. Especially pronounced disorders in gas exchange arise in blood congestion in the lesser circulation when the respiratory surface and the respiratory excursions of the lungs decrease.

Development of dyspnoea is also provoked by accumulation of liquid in the pleural and the abdominal cavities which interferes with the respiratory excursions of the lungs. During exercise dyspnoea markedly increases; it also becomes more pronounced after meals, and in the recumbent position of the patient. Grave dyspnoea sometimes occurs in attacks, which are called *cardiac asthma.*

Heart failure is often attended by *cyanosis.* The skin and the mucosa turn blue with increasing content of the reduced haemoglobin in capillary blood (over 50 g/l, or 5 g/100 ml), which, in contrast to oxyhaemoglobin, is dark. The dark blood is seen through the skin to colour it bluish; the colour is especially intense at sites where the skin is thinner (lips, cheeks, ear auricles). Cyanosis in circulatory insufficiency may be due to overfilling of vessels of the lesser circulation with blood and impaired arterialization of blood (the so-called central cyanosis). Peripheral cyanosis, however, occurs more frequently. It is connected with the slowing down of the blood flow and increased oxygen utilization by the tissues. Since the slowing down of the blood flow is more pronounced in parts of the body remote from the heart, the blue colour appears in the limbs, the ears, and the tip of the nose (acrocyanosis). Cyanosis is favoured by the widening of the venous network in the skin, increased volume of the circulating blood, and its increased haemoglobin content.

Oedema is an important sign of circulatory insufficiency. Its development in individuals with heart diseases depends on the following factors: (1) increased hydrostatic pressure in the capillaries and slowed blood flow which promote transudation of fluids into tissues; (2) abnormal hormonal regulation of the water-salt metabolism. Insufficient supply of arterial blood to the kidneys intensifies excretion of renin which increases secretion of adrenal cortex hormone, aldosterone. Aldosterone in turn increases the reabsorption of sodium in convoluted renal tubules to promote retention of fluid in the tissues. Furthermore, secretion of antidiuretic pituitary hormone increases to intensify re-absorption of water. These disorders in water-salt metabolism increase the volume of blood plasma, venous and capillary pressure, and intensify transudation of fluid in tissues; (3) during long-standing venous congestion in the great circulation, liver function decreases and the production of albumins becomes disordered to decrease oncotic pressure of blood plasma. Moreover, liver dysfunction inhibits the decomposition of the antidiuretic hormone and aldosterone in the liver.

Cardiac oedema can first be latent. Retention of fluid in the body (sometimes to 5 1 and more) does not immediately cause visible oedema but provokes a rapid gain in the patient's weight and his decreased urination. Oedema becomes visible in the first instance in the lower part of the body: in the lower limbs (if the patient sits or stands) and in the sacral region (if

the patient keeps bed). If circulatory insufficiency is progressive, oedema increases and dropsy of the body cavities develops. Fluid can be accumulated in the abdominal cavity (ascites), in the pleural cavity (hydrothorax), and in the pericardial cavity (hydropericardium). Ascites may be provoked by a prolonged venous congestion in the liver attended by its fibrosis and portal hypertension. Ascites then prevails over dropsy of other cavities.

Practically all other organs are changed in patients with heart failure. Changes in the lungs are connected with prolonged congestion of blood in the lesser circulation. Congested lungs become rigid to decrease respiratory excursions of the chest and limit mobility of the lower border of the lungs. The so-called congestive bronchitis thus develops. Patients develop cough; it may be dry or with expectoration of small amounts of mucous sputum; harsh respiration is heard over the lungs during auscultation; dry rales (intense in the postero-inferior parts of the chest) are heard; later they become moist. Long-standing venous congestion in the lesser circulation stimulates development of connective tissue in the lungs, which in turn impaires gas exchange. The overfilling of smaller vessels with blood may be accompanied by their rupture and the appearance of blood in the sputum. Insignificant haemorrhage, and also insinuation of erythrocytes through the blood vessels, promote deposition of the blood pigment in the lungs and development of brown induration; heart-failure cells can be detected in the sputum.

There are also some cardiovascular signs indicating inadequate contractility of the myocardium. Considerable myogenic dilatation of the heart chambers can cause relative insufficiency of atrioventricular valves. The heart borders broaden, the sounds of the heart (especially the first sound) weaken, tachycardia develops, and gallop rhythm sometimes occurs to suggest a grave affection of the myocardium and lowering of its tone. Organic murmurs usually weaken, because the blood-flow rate slows down; functional murmurs associated with relative atrioventricular incompetence may develop.

The liver quickly responds to venous congestion in the greater circulation. It becomes enlarged, Glisson's capsule distended, and the patient complains of the right hypochondrium pain. If congestion develops gradually, the patient feels heaviness in the epigastric and right hypochondrium. Prolonged venous congestion in the liver stimulates development of connective tissue (cardiac fibrosis of the liver) with subsequent hepatic dysfunction and portal hypertension.

The gastro-intestinal function is also impaired. Congestion in the greater circulation provokes congestive gastritis and intestinal dysfunction. Patients complain of poor appetite, nausea, and vomiting; they develop

meteorism and constipation. Dyspeptic and metabolic disorders cause disturbances in nutrition; as circulatory insufficiency further progresses, grave asthenia (cardiac cachexia) develops.

Venous congestion in the kidneys decreases the daily amount of the urine, and its specific gravity increases. A small amount of protein, red blood cells, and casts can be found in the urine.

Circulatory insufficiency soon becomes attended by dysfunction of the central nervous system. Rapid fatigue, decreased work capacity and mental power, high irritability, deranged sleep, and sometimes, depression are characteristic.

The clinical signs and changes in various organs of the body depend on the degree and duration of heart failure, and on the particular side of the heart that is affected (right or left).

Bearing these factors in mind, Strazhesko and Vasilenko provided their *classification of circulatory insufficiency,* which was adopted at the 12th Ail-Union Congress of Therapeutists in 1935. According to this classification, the following forms of circulatory insufficiency are distinguished.

1. Acute circulatory insufficiency. It can depend on acute heart failure (either side) or failure of any of its chambers, (left or right ventricle, left atrium), or else it may be caused by acute vascular insufficiency (collapse or shock).

2. Chronic circulatory insufficiency. This can be divided into three stages.

The first stage (initial) is latent circulatory insufficiency, which is only manifested during physical exercise, while at rest the haemodynamics and functions of the organs are normal; the work capacity is decreased.

The second stage is characterized by a pronounced prolonged circulatory insufficiency, haemodynamic disorders (congestion in the lesser or greater circulation) and dysfunction of organs at rest; the work capacity of patients is markedly decreased. Two periods are distinguished at this stage: (1) the initial period, with mild haemodynamic disorders; and (2) the final period characterized by grave haemodynamic disorders.

The third stage is the terminal or dystrophic stage of circulatory insufficiency. In addition to grave haemodynamic disorders, irreversible morphological changes develop in the organs along with persistent metabolic disorders and disability.

Clinical forms of heart failure. *Acute heart failure* may develop in grave disorders in the cardiac rhythm (paroxysmal tachycardia, ventricular fibrillation, myocardial infarction, acute myocarditis, and the like). Acute heart failure is attended by a marked drop in the minute volume and filling of the arterial system; clinically it is very much like circulatory insufficiency of the vascular genesis (it is sometimes termed as acute cardiac collapse). Clinically it is manifested by sudden and pronounced asthenia, sometimes

by syncopes due to brain ischaemia, pallidness and cyanosis of the skin, cold limbs, small or thready pulse, and decreased arterial pressure.

The cardiac aetiology of circulatory insufficiency is confirmed by changes in the heart proper (valve incompetence or arrhythmia, broadening of the heart borders, changes in the heart sounds and gallop rhythm). The attending venous congestion is manifested by dyspnoea, swelling of the neck veins, rales in the lungs, and enlargement of the liver. Acute heart failure may depend not on the weakening of the entire myocardium but on a pronounced decrease in contractile capacity of the myocardium of one of the heart chambers: left ventricle, left atrium, or right ventricle.

The *syndrome of acute left-ventricular heart failure* arises in patients in whom the left ventricle is mostly affected (essential hypertension, aortic incompetence, myocardial infarction). A typical symptom of acute left-ventricular heart failure is cardiac asthma (attacks of severe dyspnoea due to acute congestion in the lungs and upset gas exchange). Attacks can be provoked by physical exercise and nervous strain. Attacks usually occur during night sleep. This can be explained by an increased vagus tone during sleep, which causes narrowing of the coronary arteries and thus impairs nutrition of the myocardium. Moreover, blood supply to the respiratory centre decreases during sleep and its excitability diminishes. The lesser circulation becomes overfilled with blood because during a sharply decreased contractility of the left-ventricular myocardium, the right ventricle continues working intensely to pump the blood from the greater circulation to the lesser one.

During an attack of cardiac asthma, the patient develops asphyxia and marked weakness; cold sweat appears. He has to assume a forced position—sitting with his legs hanging down from the bed (or he stands up). The patient begins coughing and expectorates tenacious sputum. The skin becomes pallid and cyanotic. Moist and dry rales are heard over the lungs. The heart sounds are weakened at the apex and over the pulmonary artery intensified (the second sound). Tachycardia and small frequent pulse are characteristic. If congestion in the lesser circulation progresses, the blood plasma and blood corpuscles pass from the overfilled pulmonary capillaries to the alveoli and accumulate in the respiratory ducts; oedema of the lungs develops to intensify still more the feeling of suffocation and cough; respiration becomes rattling; ample foaming sputum with traces of blood (pink or red) is expectorated. Many moist rales of various calibres are heard over the lungs (over their entire surface). Auscultation of the heart often reveals gallop rhythm. Pulse is markedly accelerated and thready. Oedema of the lungs requires prompt and energetic measures to be taken to prevent possible death.

The *syndrome of acute left-atrial failure* develops in patients with mitral stenosis in markedly weakened contractility of the left atrium and

normal function of the right ventricle, which continues pumping blood into the lesser circulation. This causes overfilling of its vessels with venous blood and development of the same clinical symptoms as those in acute left-ventricular failure.

The *syndrome of acute right-ventricular failure* is especially pronounced in embolism of the trunk of the pulmonary artery or its branches into which the thrombus is carried from veins of the greater circulation or from the right chambers of the heart. Patients breathe rapidly, cyanosis and cold sweat appear; they feel pressure and pain in the heart. The pulse becomes small and frequent, the arterial pressure drops. Acute right-ventricular failure causes a pronounced venous congestion in the greater circulation. The venous pressure increases; the neck veins become swollen and the liver enlarges; oedema later develops.

Like acute heart failure, *chronic heart failure* may first depend mostly on failure of one of the heart chambers. The syndrome of *chronic left-ventricular failure* develops in many diseases attended by affections of the left ventricle (aortic incompetence, mitral failure, arterial hypertension, coronary insufficiency due to dystrophy of the left-ventricular muscle, etc.). The syndrome is characterized by a persistent blood congestion in the lesser circulation. The vital lung capacity decreases, the rate of the blood flow through the vessels of the lesser circulation is slowed, the gas exchange is upset, and dyspnoea, cyanosis, and congestive bronchitis develop. Blood congestion in the lesser circulation is even more pronounced in *chronic left-atrial failure* in patients with mitral stenosis. It is manifested by dyspnoea, cyanosis, cough, and haemoptysis. Prolonged venous congestion in the lesser circulation stimulates growth of connective tissue in the lungs and sclerosis of the vessels. Another, pulmonary barrier is thus produced to become an obstacle to normal passage of blood through the vessels of the lesser circulation. Pressure in the pulmonary artery elevates to increase the load on the right ventricle, which later becomes the cause of its failure.

The *syndrome of chronic right-ventricular failure* arises in mitral heart diseases, lung emphysema, pneumosclerosis, tricuspid incompetence, and in certain congenital heart defects. It is characterized by a marked venous congestion in the greater circulation. The patient is cyanotic, the skin sometimes becomes icterocyanotic. The peripheral veins, especially the neck veins, become swollen, the venous pressure increases, oedema and ascites develop, and the liver is enlarged.

Primary dysfunction of one of the heart chambers may eventually cause total heart failure, which is characterized by venous congestion in both the greater and lesser circulation. Moreover, chronic heart failure attended by dysfunction of the entire circulatory system arises in diseases affecting the myocardium (myocarditis, intoxication, ischaemic heart disease, etc.).

The severity of clinical signs in heart failure depends on the stage of circulatory disorders (see classification of circulatory insufficiency).

In the *initial,* latent *stage* of circulatory insufficiency, the patient's work capacity decreases, physical exertion provokes dyspnoea, palpitation, and oxygen debt increases to a greater degree than that in healthy subjects. These symptoms subside at rest.

The *second stage* of circulatory insufficiency is characterized by haemodynamic disorders. In the initial period (stage A), the patient develops dyspnoea during normal exercise (e.g. in walking), and his work capacity decreases markedly. Examination reveals moderate cyanosis and pastous shins. Congestion in the lungs is not pronounced: the respiratory movements of the chest and excursions of the lower lung borders are decreased; the vital capacity of the lungs is diminished. The liver is mildly enlarged. The venous pressure increases. Stage B is characterized by marked congestion in the greater and lesser circulation. Dyspnoea develops even at rest which is intensified during slight physical exertion. Patients are fully disabled. Typical signs of heart failure (pronounced cyanosis, oedema, ascites, dysfunction of various organs) are revealed.

The *third stage* is characterized by pronounced metabolic disorders caused by a prolonged circulatory insufficiency. The patient would be extremely asthenic, with irreversible morphological changes in the lungs, liver, and kidneys. The combination of metabolic disorders in circulatory insufficiency was called by Vasilenko "circulatory dystrophy".

In addition to. circulatory insufficiency, which is manifested by haemodynamic disorders, some authors distinguish also energodynamic insufficiency (according to Hegglin). This depends on metabolic disorders in the myocardium and occurs in pronounced hypokaliaemia, diabetic coma, severe diarrhoea, toxicosis and infections, and is characterized by a considerable shortening of the mechanical systole of the heart. This can be revealed by the second sound which appears on a PCG (at the end of the *T* wave) earlier than in normal cases. The *Q-T* interval on the ECG (representing the electric systole of the ventricles) is on the contrary prolonged.

Vascular insufficiency. Circulatory insufficiency of the vascular aetiology arises in cases where the equilibrium between the capacity of the vessels and the volume of the circulating blood is upset. It develops when the volume of blood is diminished (loss of blood, dehydration of the body), or when the vascular tone drops. Diminished vascular tone depends mostly on (1) reflex disorders in the vasomotor innervation of the injured vessels, irritation of serous membranes, myocardial infarction, embolism of the pulmonary artery, etc.; (2) disordered vasomotor innervation of cerebral aetiology (hypercapnia, acute hypoxia of the diencephalon, psychogenic reactions); (3) vascular paresis of toxic origin which occurs in many infections and toxicosis. Diminished vascular tone disturbs normal distribution

of blood in the body: the amount of deposited blood increases, especially in the vessels of the abdominal organs, whereas the volume of circulating blood decreases; the decreased volume of circulating blood weakens venous blood flow to the heart; the stroke volume of blood decreases and arterial and venous pressure diminish as well. Circulatory insufficiency of vascular genesis is usually acute and is then called circulatory *collapse.* Decreased volume of circulating blood and reduced arterial pressure cause ischaemia of the brain; acute vascular insufficiency is therefore characterized by giddiness, darkening in the eyes, noise in the ears, and often by loss of consciousness (syncope). Objective examination of the patient reveals pallid skin, cold sweat, cold limbs, accelerated and superficial respiration, small and sometimes thready pulse, and decreased arterial pressure.

A *syncope* is a symptom of acute vascular insufficiency. This is an abrupt and transient loss of consciousness due to insufficient blood supply to the brain. A syncope may occur in fatigue, excitation, fright or stay in a non-ventilated room, etc. This phenomenon is connected with upset central nervous regulation of the vascular tone, as a result of which blood is accumulated in the vessels of the abdominal cavity. A patient in a syncope is covered with cold sweat, has a pallid skin, cold limbs, and small or thready pulse. Some patients lose consciousness when they suddenly change from lying to the upright position. It is especially characteristic of young asthenic subjects, mostly women. Fatigue, anaemia, and infectious diseases also predispose to a syncope. Such a syncope is called orthostatic collapse. It is explained by a delayed response of the vasomotor apparatus, owing to which blood flows from the upper portion of the body to the vessels of the lower limbs and the abdomen when an individual changes his posture.

Chronic vascular insufficiency does not as a rule cause severe circulatory disorders. Us main symptom is persistent arterial hypotension. Endocrine and constitutional factors (which often occur in asthenic persons) are essential for the pathogenesis of chronic vascular insufficiency. Such patients develop rapid fatigue and are susceptible to a syncope. Their skin is pallid, the limbs are cold to the touch, and cyanotic; the heart is small; a tendency to tachycardia is observed. Chronic vascular insufficiency can be secondary in its character, and be a manifestation of general asthenia which develops in fatigue, exhaustion, chronic infections, in Addison's disease, and some other diseases.

Treatment of patients with circulatory insufficiency. Causes of cardiovascular insufficiency should first be removed. These may be rheumatism, essential hypertension, myocarditis, coronary insufficiency, or other diseases. If a heart disease, adhesive pericarditis, or heart aneurysm are the cause of circulatory insufficiency, possibility of surgical treatment should first of all be considered in order to remove or lessen the mechanical obstacles to normal work of the heart.

The patient should be given physical and mental rest. If heart failure is severe, the patient must keep bed. As the condition improves, dosed exercises are recommended, and remedial exercises are prescribed. The intake of liquid should be limited to 500-600 ml a day. The amount of salt should also be limited to 1-2 g a day. The diet should be sufficiently rich in vitamins; it should not provoke flatulence.

The initial stages of circulatory disorders should be treated by rest and sedative preparations, which will restore normal function of the cardiovascular system. If circulatory insuffciency is significant, cardiac glycosides should be given: digitalis preparations (e.g. digoxin, 0.00025 g twice a day, in tablets, per os); strophanthin (0.5 ml of a 0.05 per cent solution, intravenously, slowly, in 20 ml of a 20 per cent glucose solution), and other preparations by the influence of which cardiac activity will be improved to increase the minute volume, to slow down the cardiac rhythm, and to decrease venous pressure. Diuretics are very important in the therapy of circulatory insufficiency. Most modern diuretics are saluretic, i.e. substances that decrease re-absorption of sodium and water in the renal tubules. Furocemide is often given (0.04 g, one tablet per os, or a solution containing 0.02 mg of the active principle in 2 ml of a 1 per cent ampouled solution, intramuscularly). Other diuretics are also given. If venous congestion is significant, phlebotomy is indicated (200-400 ml). If fluid is accumulated in the pleural and abdominal cavities, it should be removed by puncture. Oxygen therapy is indicated to patients with circulatory disorders to decrease tissue hypoxia. In order to improve metabolism in the myocardium, vitamins of group B, ascorbic acid, ATP, inosine, and potassium preparations are prescribed.

A patient with an acute vascular insufficiency should be placed in the horizontal position with the legs slightly elevated on a special collapsible bed. The cause of acute vascular insufficiency should be removed: haemorrhage should be arrested, anaesthetics given in shock, and the patient should be warmed. An isotonic sodium chloride solution, antishock fluid, blood substitutes (polyglucin, blood plasma, etc.) should be given intravenously. Blood transfusion is indicated in cases with loss of blood. The vascular tone is raised by caffeine, cordiamine, mesaton, and corticosteroid hormones.

Special Pathology

Diseases of the cardiovascular system stand among the first in the list of diseases of internal organs. They are a frequent cause of early disability and untimely death of patients. Most common are ischaemic heart disease, rheumatism and rheumatic heart diseases, endocarditis, myocarditis of various genesis, and essential hypertension.

Rheumatism

Rheumatism is a general infectious and allergic disease in which connective tissues, mainly of the cardiovascular system, are affected by inflammation; joints, serous membranes, internal organs, and the central nervous system are often involved. Rheumatism is a collagenous disease, i.e. a disease characterized by a systemic and progressive derangement of connective tissue.

Rheumatism was classified as an independent disease with typical affections not only of the joints but mainly of the heart in 1835 by a French clinicist Bouillaud and in 1836 by the Russian physician Sokolsky. Until that time rheumatism had been considered a disease of joints.

Aetiology and pathogenesis. Beta-haemolytic streptococcus of group A is believed to be the causative agent of rheumatism. This conjecture is confirmed by (1) frequent incidence of rheumatism following streptococcal infection; (2) increased antibody titres to various antigens and enzymes of the streptococcus in the blood of rheumatic patients; (3) successful prophylaxis of rheumatism by antibacterial preparations.

The pathogenesis of rheumatism is complicated and not well studied. At the present time, the development of the disease is described as follows. Most persons affected by streptococcus develop stable immunity. This immunity does not develop in 2-3 per cent of the affected subjects due to weakness of their defence mechanisms and they become sensitized by the streptococcus antigen. In these conditions the infection re-enters the body to cause a hyperergic response in connective tissues; clinical signs of the disease thus develop. Autoimmune processes are very important in the onset of rheumatism. The affected connective tissue acquires antigenic properties; auto-antigens (secondary antigens) cause formation of aggressive auto-antibodies. They affect not only the connective tissue that has already been affected by the primary antigen but also intact tissue to aggravate the pathology. Re-infection, cooling, and overstrain promote formation of new auto-antigens and auto-antibodies to strengthen the pathological reaction of the upset immunity and to provide conditions for the recurring progressive course of the disease.

Pathological anatomy. Four phases of derangement of connective tissue are differentiated in rheumatism: (1) mucoid swelling; (2) fibrinoid changes; (3) granulomatosis; and (4) sclerosis.

Mucoid swelling is characterized by superficial derangement of connective tissue which involves mainly the interstitial substances and only insignificantly the collagenous complex. The processes occurring at this stage are reversible. Derangement of connective tissue occurring at the fibrinoid stage is deep and irreversible. Histiocytes form granulomas (Aschoff-Talalaev granulomas, rheumatic nodules) which contain lymphoid cells, leucocytes, and cardiohistiocytes. Rheumatic granulomas would be usually located in perivascular connective tissue of the myocardium, in the endocardium, and (in slightly modified form) in synovial

membrane of the articular bursa, periarticular and peritonsillar tissue, vascular adventitia, etc. At the phase of sclerosis, a cicatrix is gradually formed, which may develop at the site of fibrinoid changes and also as a result of cicatrization of rheumatic granulomas. Each phase of rheumatism lasts on the average one or two months, and the entire cycle continues for at least six months.

Tissues in the zone of old cicatrices may be affected in relapses of rheumatism and sclerosis may develop. Affection of connective tissue of the valvular endocardium which causes sclerosis and deformation of the valve cusps (their adhesion to one another) is the most common cause of heart diseases, while relapses of rheumatism (recurring attacks) aggravate affections of the valves. Non-specific exudative reactions may develop, mostly in the pericardium and the joints, and less frequently in the pleura, peritoneum, and the myocardium. Vasculitis (capillaritis, arteritis, phlebitis) are also non-specific rheumatic affections.

Clinical picture. The clinical picture of rheumatism is quite varied and depends mostly on the localization of the inflammatory changes in connective tissues of various organs and on acuity of the rheumatic process. As a rule, the disease develops in 1-2 weeks after a streptococcal infection (e.g. tonsillitis, pharyngitis or scarlet fever). Most patients develop subfebrile temperature, weakness, and hidrosis. Later (in 1-3 weeks), new symptoms develop to indicate affection of the heart. The patient complains of palpitation and intermissions in the work of the heart, the feeling of heaviness or pain in the heart, and dyspnoea.

Less frequently the onset of the disease is acute. Remitting temperature develops (38-39 °C), which is accompanied by general asthenia, fatigue, and perspiration. Simultaneously (or several days later) the patient feels pain in the joints (mostly in large joints, such as the ankle, knee, shoulder, elbow joints, and in hands and feet). Affections of the joints are usually multiple and symmetric. The migrating character of pain is also characteristic: pain disappears in one joint and develops in others. Rheumatic polyarthritis is usually benign. Acute inflammation subsides in a few days, although dull pain in the joints may persist for a long time. Abatement of inflammation in the joints does not mean recovery because other organs become involved in the pathological process. The cardiovascular system is mostly involved, but the skin, serous membranes, lungs, liver, kidneys, and the nervous system may also be affected.

Examination of the patient with active rheumatism reveals pallid skin (even at elevated temperature) and increased perspiration. In some patients, the skin of the chest, neck, abdomen, and the face is affected by annular erythema (pale-pink painless rings not elevating over the surrounding skin). In other cases nodular erythema develops: circumscribed indurated dark red foci on the skin varying in size from a pea to a plum; they are usually found on the lower limbs. If permeability of capillaries is increased, small haemorrhages into the skin sometimes occur. In rare cases, rheumatic subcutaneous nodules (firm, painless formations varying in size

from a millet grain to a bean) can be palpated, mostly on the extensor surfaces of the joints, along the course of tendons, and in the occipital region. The involved joints are swollen and oedematous, the overlying skin reddens and becomes hot to the touch. Articulation becomes very limited.

Lungs are affected in very rare cases. This is specific rheumatic pneumonia. Dry pleurisy or pleurisy with effusion are more common. Heart affections may be the only clinical manifestation of rheumatism. On the other hand, practically all rheumatic patients have their heart muscle affected (rheumatic myocarditis). Rheumatic myocarditis is characterized by dyspnoea, the feeling of heaviness and pain in the heart, palpitation, and intermissions in the heart work. In addition, certain objective signs are found: enlargement of the heart, decreased heart sounds (especially the first sound); gallop rhythms develop in severe affection of the myocardium. A soft systolic murmur can be heard at the heart apex. It is associated with relative incompetence of the valve or affection of the papillary muscles. The pulse is small and soft; tachycardia and arrhythmia are frequent. Arterial pressure is usually decreased. Circulatory insufficiency rapidly develops in grave diffuse myocarditis. Myocardial cardiosclerosis develops in benign outcome of the disease.

Rheumatic myocarditis usually concurs with rheumatic endocarditis (rheumocarditis). Early endocarditis signs are not pronounced (symptoms of myocarditis prevail). Further development of the heart disease proves the presence of endocarditis. At earlier stages of endocarditis systolic murmurs are coarser than in myocarditis; the murmur becomes louder after exercise; in some cases it becomes "musical". Diastolic murmur may be heard as well. It is probably explained by deposition of thrombotic mass on the valve cusps which produces turbulence in the blood flow as it passes from the atrium to the ventricle. These thrombotic deposits on the valves can leave their seat and become the cause of embolism or infarctions in various organs (e.g. the kidneys or the spleen). The mitral valve is mostly affected in endocarditis. Next in incidence follows the aortic valve; the tricuspid valve is affected still less frequently. If early attacks of rheumatic endocarditis are treated timely, development of the valvular heart disease may be prevented.

In a grave course of rheumatism the affection of the myocardium and endocardium may combine with rheumatic pericarditis, i.e. all membranes of the heart may be involved (pancarditis). Pericarditis may be dry or exudative.

The alimentary system is rarely affected. Acute pain in the abdomen (the abdominal syndrome) associated with rheumatic peritonitis (mostly in children) sometimes occurs. The liver is affected in certain cases (rheumatic hepatitis).

Affections of the kidneys are also common. Protein or red blood cells can be found in the urine due to affections of the renal vessels and (less frequently) developing nephritis.

The nervous system is often involved in rheumatism. This is due to either rheumatic vasculitis (attended by small haemorrhages or thrombosis of cerebral vessels) or inflammation of the brain and the spinal cord. Children would develop encephalitis with predominant localization in the subcortical nodes (chorea minor). It is manifested by emotional lability and hyperkinesia (abnormal movements of the extremities, the trunk, and the facial muscles).

Special laboratory tests help diagnose rheumatism. Moderate leucocytosis (with a shift to the left) is characteristic of acute rheumatism; eosinophilia, mono- and lymphocytosis may further develop. The erythrocyte sedimentation rate is always increased (to 50—70 mm/h in grave cases). Dysproteinaemia is characteristic: the albumin content drops below 50 per cent, the globulin content increases, and the albumin-globulin factor decreases below unity. A proteinogram shows increased α_2-globulin and γ-globulin fractions; fibrinogen content increases to 0.6-1 per cent (normally it does not exceed 0.4 per cent). The blood contains C-reactive protein which is absent in healthy individuals. The level of mucoproteins increases and it can be revealed by a diphenylamine test. The titres of antistreptolysine O, antistreptohyaluronidase, and antistreptokinase increase significantly.

ECG often shows deranged conduction, especially atrioventricular block of the first and second degree, extrasystole or other rhythm disorders, and decreased voltage of the ECG waves. Defective nutrition of the myocardium due to its inflammation can change the *T* wave and lower the *S-T* segment. Phonocardiograms show specific rheumocarditic changes in heart sounds, the appearance of murmurs, etc.

Course. An active rheumatic process continues for three to six months; in some cases it may be longer. Depending on the strength of the clinical symptoms and the character of the disease course, three degrees of rheumatic activity are distinguished: (1) maximum active (acute) process with continuous relapses; (2) moderately active or subacute; and (3) rheumatism with minimal activity (flaccid or latent). If the clinical symptoms of the disease are absent and no signs of active rheumatism are revealed by laboratory testing, rheumatism is considered inactive.

Rheumatism is characterized by relapses (recurring attacks) which are provoked by infection, overcooling, and physical overstrain. The clinical symptoms of relapses resemble the primary attack of the disease, but the signs of affection of the joints or serous membranes are less pronounced. Symptoms of heart affection prevail.

Treatment. Active rheumatism is treated at hospital. The patient should stay in bed and be given desensitizing and anti-inflammatory preparations, corticosteroid hormones, acetylsalicylic acid, amidopyrin, butadion, and chloroquine. Antibiotics are given as well, especially in the presence of infectious foci (e.g. carious teeth, tonsillitis or sinusitis). These foci should be eliminated by appropriate means.

Prophylactic measures against rheumatism include hardening of the body, improvement of housing and working conditions, and control of streptococcus infection (treatment of chronic tonsillitis, otitis, sinusitis, etc.). Rheumatic patients should be kept under regular medical observation. To prevent relapses of rheumatism in spring and autumn, medicamentous prophylaxis should be given (bicillin in combination with salicylates or amidopyrine and chloroquine).

Bacterial (Septic) Endocarditis

Bacterial endocarditis is a severe general disease characterized by inflammation of the endocardium and ulceration of the heart valves in the presence of sepsis.

Acute bacterial endocarditis (a manifestation of acute sepsis) and subacute bacterial endocarditis are distinguished according to the course of the disease.

SUBACUTE BACTERIAL ENDOCARDITIS

Aetiology and pathogenesis. Subacute bacterial endocarditis (endocarditis septica lenta) is usually caused by *Streptococcus viridans,* less frequently by enterococcus and *Staphylococcus albus* or *St. aureus.* In most cases, protracted bacterial endocarditis affects the valves that are changed by the rheumatic process, or develops in congenital heart diseases. It is believed that upset haemodynamics in heart diseases inflicts microinjuries to the valves which provoke changes in the endocardium, especially along the contact line of valve cusps. Factors weakening immunological reactions facilitate the development of the disease.

Pathological anatomy. This is characterized by the presence of ulcerous endocarditis. Ulcerated surfaces become covered with polyp-like thrombotic mass which sometimes looks like cauliflower. The valves become sclerosed and disfigured. The aortic valve is especially frequently involved. Endothelium of fine vessels is affected to cause vasculitis or thrombovasculitis: vascular permeability increases and small haemorrhages develop in the skin and mucosa.

Clinical picture. The symptoms of the disease mainly depend on toxaemia and bacteriaemia. The patients complain of weakness, rapid fatigue,

and dyspnoea. As a rule, subfebrile fever first develops, which is followed by irregular elevation of temperature to 39 °C and more. Chills and excess sweating are characteristic. The skin and visible mucosa are pallid due to anaemia and aortic incompetence, which is characteristic of this disease. The skin sometimes becomes yellowish-grey (coffee with milk). Small haemorrhages in the skin, mucosa of the mouth (especially the soft and hard palate), on conjunctiva, and the eyelid folds (the Libman-Lukin symptom) indicate affection of the joints. Positive Konchalovsky-Rumpel-Leede sign is another indication of this process: if the arm of the patient is compressed by a tourniquet or by a cuff of a Riva-Rocci sphygmomanometer, multiple petechiae appear on the flexor surface of the elbow, and also distally of it (Fig. 68). Brittleness of capillaries can also be established by pinching the skin. In most cases the patient's fingers become clubbed (Hippocratic fingers), while the nails are flat like a watch glass.

Auscultation of the heart reveals signs of acquired or congenital diseases in most patients. Development of endocarditis is attended by the appearance of functional murmurs due to anaemia and murmurs that are caused by changes in the affected valve. Aortic valve cusps are usually involved, and signs of aortic incompetence therefore develop, while symptoms of mitral insufficiency develop in affections of the mitral valve.

Subacute bacterial endocarditis is characterized by embolisms (caused by decomposing thrombotic deposits on the valves) in the vessels of the spleen, kidneys or brain, followed by infarction of the involved organ. The spleen is enlarged due to the response of the mesenchyma to sepsis. The disease is characterized by involvement of the kidneys which gives the picture of diffuse glomerulonephritis and much less frequently focal glomerulonephritis without pronounced symptoms (slight proteinuria and haematuria, and insignificant cylindruria). Hypochromic anaemia (caused by increased haemolysis and inhibited erythropoiesis) and a markedly increased ESR are also characteristic. Leukocyte count varies. Eosinophil count decreases and there is a tendency to monocytosis and histiocytosis. If the number of histiocytes in blood taken from the ear lobe after its massage increases compared with their amount in the blood taken before the

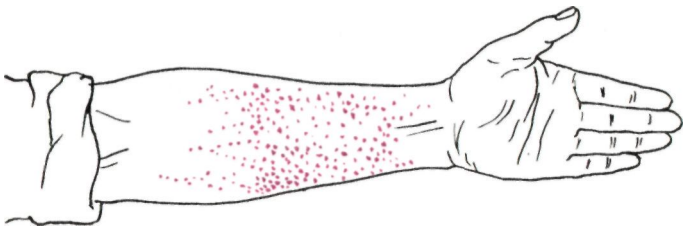


Fig. 68. Konchalovsky-Rumpel-Leede symptom.

massage (Bittorf-Tushinsky test), it indicates affection of the vascular endothelium. Biochemical study of the blood reveals dysproteinaemia (hypoalbuminaemia, increased content of gamma-globulins); thymol and formol tests are positive. The causative agent of the disease can be revealed in blood cultures.

Echocardiography can be used to reveal vegetation on the cusps of the aortic valve, and less frequently on the mitral valve.

Treatment. The patient should be hospitalized and given antibiotics in large doses.

Heart Valvular Diseases

Stable pathological changes in the structure of the heart that interfere with its normal function are called heart disease. Congenital and acquired diseases of the heart are distinguished. The incidence of acquired heart diseases is much higher.

Congenital diseases of the heart arise due to abnormal development of the heart and the great vessels during the intrauterine growth of the foetus with preservation of the intrauterine character of circulation after birth. In defective division of the primary single-chamber arterial trunk into the pulmonary trunk and the aorta, and during formation of the heart chambers, defects in the interatrial and interventricular septa may be formed along with various abnormalities in the arrangement of the great vessels and their narrowing. Preservation of the intrauterine character of circulation after birth is the cause of patent ductus arteriosus (Botallo's duct) and patent foramen ovale. Congenital heart defects may often combine with communicated greater and lesser circulation systems and stenosis of the great vessels. Moreover, the valves (bicuspid, tricuspid, aortic, and pulmonary valves) may also have congenital defects.

Endocarditis, and especially rheumatic endocarditis, is the main cause of acquired heart defects. Less frequently heart disease is the result of sepsis, atherosclerosis, syphilis, injuries, etc. Inflammatory processes occurring in the valve cusps often end in their sclerosis: deformation and shortening. An affected valve does not close completely to cause valvular incompetence. The cusps of the valves may adhere to one another because of inflammation to narrow the orifice they close. This narrowing is called stenosis.

MITRAL INCOMPETENCE

Incompetence of the mitral (bicuspid) valve (mitral insufficiency) is incomplete closure of the atrioventricular orifice during left-ventricular systole. As a result, the blood is regurgitated from the ventricle back to the atrium. Mitral incompetence may be organic and functional.

Organic insufficiency arises as a result of rheumatic endocarditis. Connective tissue develops in the cusps of the mitral valve which then contracts

to shorten the cusps and the tendons. The edges of the affected valve do not meet during systole and part of the blood is regurgitated through the slit into the left atrium from the ventricle during its contraction.

In functional (relative) incompetence the mitral valve is not altered but the orifice, which it has to close, is enlarged and the cusps fail to close it completely. Functional incompetence of the mitral valve may develop because of dilatation of the left ventricle (in myocarditis, myocardial dystrophy, or cardiosclerosis) and weakening of the circular muscle fibres that form the ring round the atrioventricular orifice. Affection of papillary muscles may also cause functional mitral incompetence. Functional insufficiency thus depends on dysfunction of the muscles responsible for the closure of the valve.

Haemodynamics. If the mitral valve fails to close completely during systole of the left ventricle, part of the blood is regurgitated into the left atrium. Blood filling of the atrium thus increases (because of the blood from the pulmonary veins which is added to the normal blood volume). Pressure in the left atrium increases, the atrium is dilated and becomes hypertrophied.

The amount of blood that is delivered into the left ventricle from the overfilled left atrium during diastole exceeds normal and the atrium is thus overfilled and distended. The left ventricle has to perform excess work and becomes hypertrophied. Intensified work of the left ventricle compensates for the mitral incompetence during a long time (Fig. 69). When the contractile power of the left ventricular myocardium weakens, diastolic pressure in it increases and this in turn increases pressure in the left atrium.

Increased pressure in the left atrium increases pressure in the pulmonary veins and this in turn causes reflex contraction of the arterioles

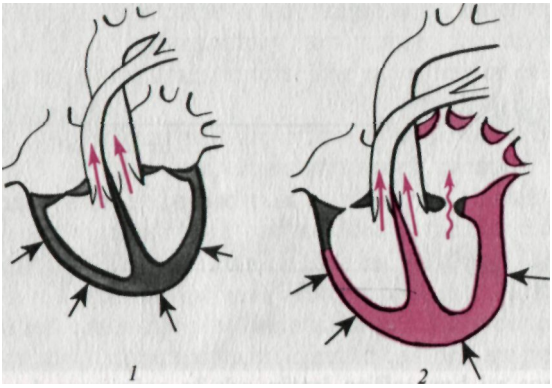


Fig. 69. Changes in the intracardiac haemodynamics in mitral incompetence.
/—normal heart; *2*—heart with mitral incompetence (the hypertrophied chambers are printed in red; normal blood flow is shown by straight arrows, and the regurgitated flow is shown by the wavy arrow).

in the lesser circulation (Kitaev's reflex) due to stimulation of baroreceptors. Spasm in the arterioles increases significantly pressure in the pulmonary artery to intensify the load on the right ventricle which has to contract with a greater force in order to eject blood into the pulmonary trunk. The right ventricle can therefore also be hypertrophied during long-standing pronounced mitral incompetence.

Clinical picture. Most patients with mild or moderate mitral incompetence have no complaints for a long time and look very much like healthy subjects. As congestion in the lesser circulation develops, dyspnoea, palpitation of the heart, cyanosis, and other symptoms appear.

Palpation of the heart area reveals displacement of the apex beat to the left and sometimes inferiorly. The beat becomes diffuse, intensified, and resistant, which indicates hypertrophy of the left ventricle. Percussion reveals displacement of the heart's borders to the left and superiorly because of the enlarged left atrium and left ventricle. The configuration of the heart becomes mitral with an indistinct heart waist. The border of the heart shifts to the right in hypertrophy of the right ventricle. Auscultation of the heart reveals decreased first sound at the heart apex because the valves never close completely in this disease. Systolic murmur can be heard at the same point, which is the main sign of mitral incompetence. It arises during systole when the stream of blood passes a narrow slit leading from

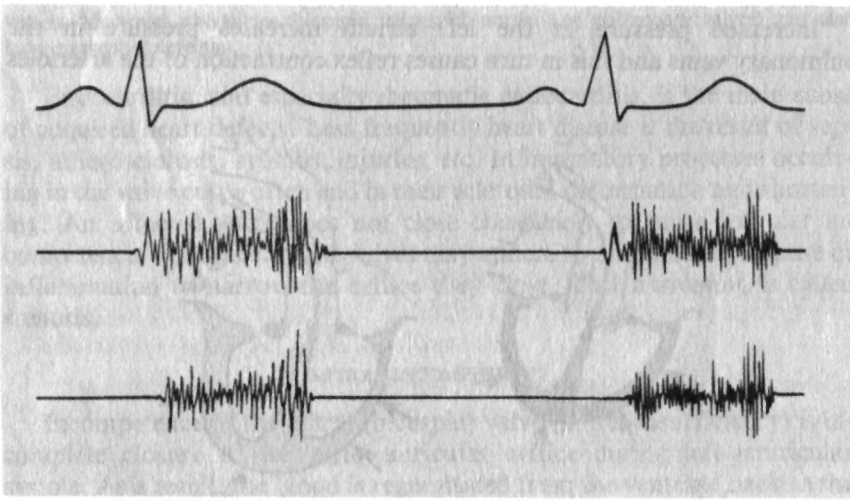


Fig. 70. PCG in mitral incompetence. The amplitude of the first sound is decreased on a PCG taken at the heart apex; systolic murmur occupies the entire pause between the first and second heart sounds.

the left ventricle to the left atrium. The systolic murmur is synchronous with the first sound. When the blood pressure rises in the lesser circulation, an accent of the second sound can be heard over the pulmonary trunk.

Auscultation findings are confirmed and verified by phonocardiography (Fig. 70). The pulse and arterial pressure do not change in compensated mitral incompetence. X-ray studies show a specific enlargement of the left atrium and the left ventricle detectable by enlargement (to the left, superiorly and posteriorly) of the heart silhouette. When blood pressure increases in the lesser circulation, the pulmoanry arch dilates. Signs of hypertrophy of the left atrium and the left ventricle can also be found on the ECG: it becomes the left type and the *P* waves become higher.

Echocardiography reveals distention of the left heart chambers (atrium and ventricle), movement of the mitral valve cusps in the opposite direction, their thickening and the absence of full closure during systole.

Mitral incompetence may remain compensated for a long time. But a long-standing pronounced mitral incompetence and decreased myocardial contractility of the left atrium and the left ventricle cause venous congestion in the lesser circulation. Contractility of the right ventricle can later be affected with subsequent development of congestion in the greater circulation.

STENOSIS OF THE LEFT ATRIOVENTRICULAR ORIFICE

The left atrioventricular orifice usually narrows in a long-standing rheumatic endocarditis (stenosis ostii venosi sinistri). In very rare cases mitral stenosis may be congenital or secondary to septic endocarditis. The atrioventricular orifice narrows due to adhesion of the mitral cusps, their consolidation and thickening, and also shortening and thickening of the tendons. The valve thus becomes a diaphragm or a funnel with a slit in the middle. Cicatricial and inflammatory narrowing of the valvular ring is less important in genesis of mitral stenosis. The valve may be calcified in long-standing stenosis.

If stenosis is significant and the orifice is narrowed from the normal 4-6 cm^2 to 1.5 cm^2 and less, *haemodynamics* becomes affected considerably. During diastole, blood fails to pass from the left atrium to the left ventricle and the remaining blood is added to the blood delivered from the pulmonary veins. The left atrium thus becomes overfilled with blood, the pressure in the ventricle increases. Excess pressure is first compensated for by intensified contraction of the atrium and its hypertrophy, but the force of the left atrial muscle is insufficient to compensate permanently for the pronounced narrowing of the mitral orifice and its contractile force soon weakens; the atrium becomes dilated, and the pressure inside it rises. This in turn increases pressure in the pulmonary veins, produces a reflex

spasm in the arterioles of the lesser circulation and increases pressure in the pulmonary artery. All this requires intensified work of the right ventricle, which later also becomes hypertrophied. The left ventricle in mitral stenosis receives smaller volumes of blood and is therefore less active; its size slightly decreases (Fig. 71).

Clinical picture. When congestive changes occur in the lesser circulation, the patient develops dyspnoea and palpitation on physical exertion; he complains of pain in the heart, cough, and haemoptysis. Inspection reveals acrocyanosis and cyanotic blush on the face. If the disease develops in childhood, the patient's physical growth often slows down and infantilism may develop ("mitral nanism"). Visual examination of the heart region often reveals a cardiac beat consequent upon dilatation and hypertrophy of the right ventricle. The apex beat is not intensified; its palpation can reveal diastolic cat's purr (presystolic thrill). The broadening of cardiac dullness to the right and superiorly due to hypertrophy of the left atrium and right ventricle can be determined by percussion. The heart becomes "mitral" in configuration.

In auscultation of the heart the first sound at the apex becomes loud and snapping because the left ventricle receives little blood and its contraction is fast. An adventitious sound due to the opening of the mitral valve can be heard at the apex beat. It follows the second sound of the heart. The loud first sound, second sound, and the sound of mitral valve opening give a specific murmur which is characteristic of mitral stenosis. The second sound becomes accentuated over the pulmonary trunk when pressure in the lesser circulation increases. Diastolic murmur is characteristic of mitral stenosis because the passage from the left atrium to the ventricle during diastole is narrowed. This murmur can be heard to follow the mitral valve

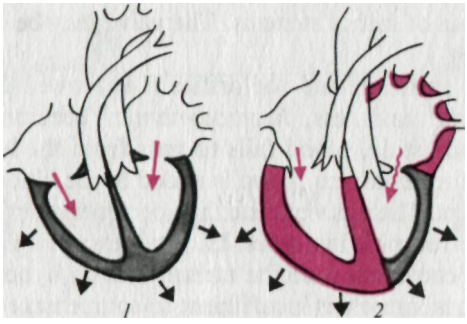


Fig. 71. Changes in the intracardiac haemodynamics in mitral stenosis. The wavy arrow indicates an obstructed passage of blood from the atrium to the ventricle (for designations see Fig. 69).

opening sound (protodiastolic murmur) because the velocity of the blood flow in early diastole is higher due to the pressure difference in the atrium and the ventricle. The murmur disappears when the pressures equalize. If stenosis is not pronounced, the murmur can be heard only at the end of diastole, immediately before systole proper (presystolic murmur); it arises during acceleration of the blood flow at the end of ventricular diastole because of the early atrial systole. Diastolic murmur can be heard in mitral stenosis during the entire diastole. It increases before systole and joins the first snapping sound.

The pulse in mitral stenosis may be different on the left and right arms. In considerable hypertrophy of the left atrium, the left subclavian artery is compressed and the pulse on the left arm becomes smaller (pulsus differens). If the left ventricle is not filled completely and the stroke volume is decreased, the pulse becomes small (pulsus parvus). Mitral stenosis is often complicated by atrial fibrillation, and the pulse becomes arrhythmic. Arterial pressure usually remains normal; the systolic pressure sometimes slightly decreases and diastolic pressure increases. X-ray patterns of the heart show the specific enlargement of the left atrium, which leads to disappearance of the heart waist and "mitral" configuration appears (Fig. 72c). Enlargement of the left atrium is determined in the first oblique position by the degree of displacement of the oesophagus which becomes especially vivid with barium sulphate suspension (Fig. 726). If pressure in the lesser circulation increases, X-rays show swelling of the pulmonary arch and hypertrophy of the right ventricle. X-ray pictures sometimes show calcification of the mitral valve. Pneumosclerosis develops during long-standing hypertension of the lesser circulation; it may also be revealed during X-ray examination.

The ECG of the heart with mitral stenosis shows hypertrophy of the left atrium and the right ventricle: the amplitude and duration of the *P* wave increase, especially in the first and second standard leads; the electrical axis of the heart deviates to the right, a high *R* wave appears in the right chest leads and a pronounced *S* wave in the left chest leads.

A phonocardiogram taken at the apex shows the high amplitude of the first sound; the second sound is followed by the mitral valve opening sound and diastolic murmur; the amplitude of the second sound over the pulmonary artery increases compared with that over the aorta (Fig. 73). If PCG and ECG are taken synchronously, attention should be paid to the length of the interval *Q*-I sound (from the beginning of the *Q* wave on the ECG to the first sound on the PCG) and the second sound—*OS* interval. Echocardiograms in mitral stenosis are characterized by the following:

1. The *A* wave, describing the maximum opening of the valve during atrial systole either decreases or disappears altogether.

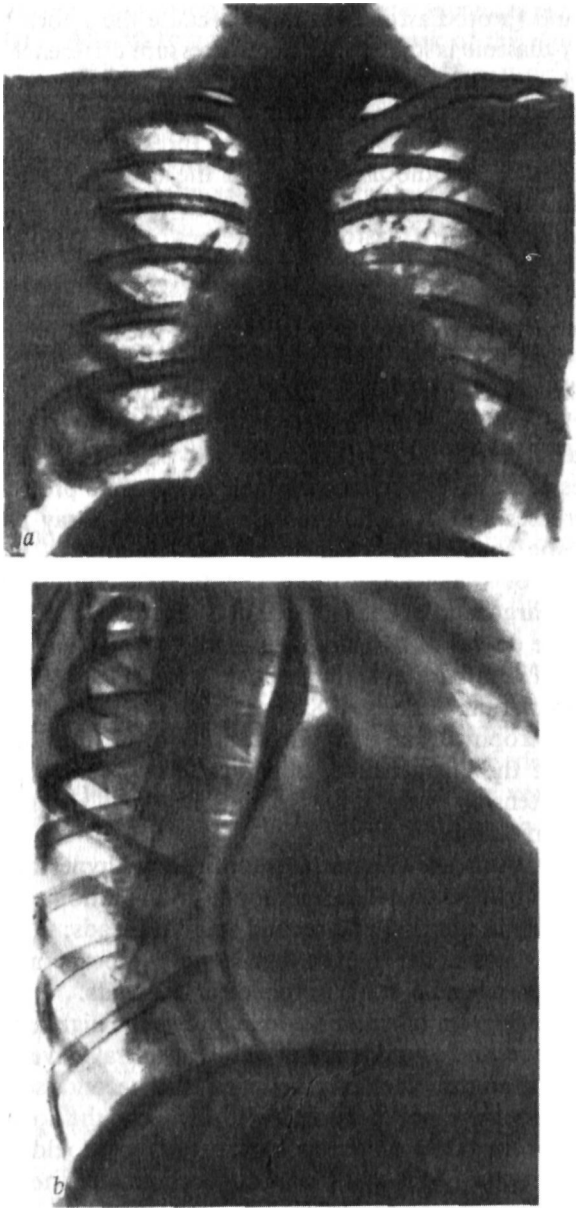


Fig. 72. X-ray of a heart with mitral stenosis.
a—mitral heart; *b*—deviation of the contrasted oesophagus by the small radius arc in the right anterior oblique position.

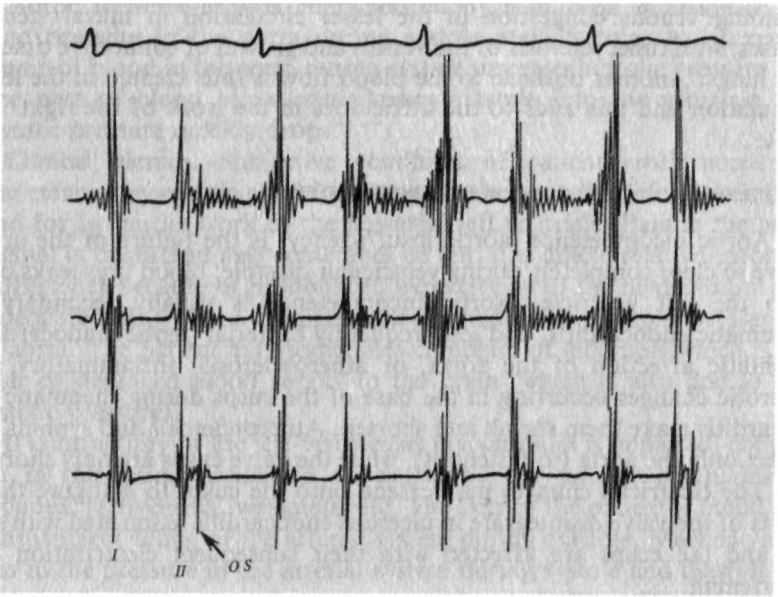


Fig. 73. PCG in mitral stenosis. The PCG taken at the heart apex shows increased amplitude of the first sound, diastolic (presystolic) murmur, and the sound of the mitral valve opening (OS).

2. The speed of diastolic closure of the anterior mitral cusps decreases to decrease the *E-F* slope.

3. Movements of the cusps change. The cusps of a normal mitral valve move in the opposite direction to set apart during diastole: the anterior cusp moves toward the anterior wall while the posterior cusp to the posterior wall. In stenosis, these movements become unidirectional because the more massive anterior wall pulls the posterior one by adhesion. The movement of the valve is represented on the echocardiogram in the form of a square wave. Enlargement of the left atrium and changes in the cusps (fibrosis, calcinosis) can also be detected by echocardiography.

Mitral stenosis soon becomes attended by congestion in the lesser circulation which requires greater work of the right ventricle. Decreased contractility of the right ventricle and venous congestion in the greater circulation develop therefore in mitral stenosis earlier and more often than in mitral incompetence.

Dilatation of the right ventricle and weakening of its myocardium are sometimes attended by relative tricuspid insufficiency. Moreover, long-

standing venous congestion in the lesser circulation in mitral stenosis causes, with time, sclerosis of the vessels and growth of connective tissue in the lungs. Another obstacle to the blood flow is thus created in the lesser circulation and this adds to the difficulties in the work of the right ventricle.

AORTIC INCOMPETENCE

Aortic incompetence (aortic insufficiency) is the failure of the aortic valve to close completely during ventricular diastole; blood thus leaks back into the left ventricle. Aortic incompetence is usually secondary to rheumatic endocarditis, and less frequently bacterial (septic) endocarditis, syphilitic affection of the aorta, or atherosclerosis. Inflammatory and sclerotic changes occurring in the base of the cusps during rheumatic endocarditis make them shrink and shorten. Atherosclerosis and syphilis can affect only the aorta (to distend it), while the valve cusps are only shortened. The cicatricial changes may extend onto the cusps to disfigure them. Parts of the valve disintegrate in ulcerous endocarditis associated with sepsis and the cusps are affected with their subsequent cicatrization and shortening.

Haemodynamics. During diastole, blood is delivered into the left ventricle not only from the left atrium but also from the aorta due to regurgitation, which overfills and distends the left ventricle during diastole. During systole, the left ventricle has to contract with a greater force in order to expell the larger blood volume into the aorta. Intensified work of the left ventricle causes its hypertrophy, while the increased systolic volume in the aorta causes its dilatation (Fig. 74).

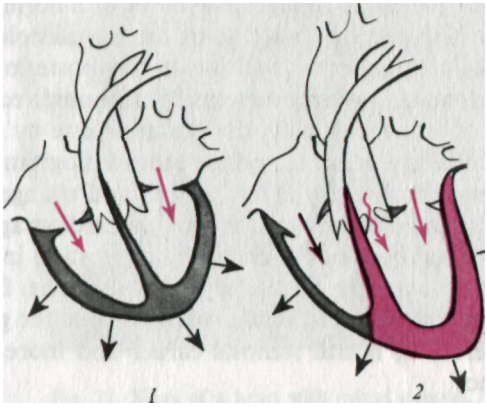


Fig. 74. Changes in the intracardiac haemodynamics in aortic incompetence. The hypertrophied chambers are printed in red (for designations see Fig. 69).

Aortic incompetence is characterized by a marked variation in the blood pressure in the aorta during systole and diastole. An increased volume of blood in the aorta during systole increases systolic pressure and since part of blood is returned during diastole into the ventricle, the diastolic pressure quickly drops.

Clinical picture. Subjective condition of patients with aortic incompetence may remain good for a long time because the defect is compensated for by harder work of the powerful left ventricle. Pain in the heart (anginal in character) may sometimes be felt; it is due to relative coronary insufficiency because of pronounced hypertrophy of the myocardium and inadequate filling of the coronary arteries under low diastolic pressure in the aorta. The patient may sometimes complain of giddiness which is the result of deranged blood supply to the brain (which is also due to low diastolic pressure).

If contractility of the left-ventricular myocardium is impaired, congestion in the lesser circulation develops and the patient complains of dyspnoea, tachycardia, weakness, etc. The skin of the patient is pallid due to insufficient filling of the arterial system during diastole. Marked variations in the pressure in the arterial system during systole and diastole account for the appearance of some signs, such as pulsation of the peripheral arteries, the carotids (carotid shudder), subclavian, brachial, temporal, and other arteries; rhythmical movements of the head synchronous with the pulse (Musset's sign), rhythmical change in the colour of the nail bed under a slight pressure on the nail end, the so-called capillary pulse (Quincke's pulse), rhythmical reddening of the skin after rubbing, etc.

The apex beat is almost always enlarged and shifted to the left and inferiorly. Sometimes, along with the elevation of the apex beat, a slight depression in the neighbouring intercostal spaces can be observed. The apex beat is palpable in the sixth and sometimes seventh hypochondrium, anteriorly of the midclavicular line. The apex beat is diffuse, intense, and rising like a dome. This indicates significant enlargement of the left ventricle. The border of cardiac dullness can be found (by percussion) to shift to the left; the heart becomes "aortic" (with pronounced waist of the heart).

Auscultation reveals decreased first sound at the apex, since during left-ventricular systole the period when the valves are closed is absent. The second sound on the aorta is also weak, and if the valve is damaged significantly, it can be inaudible. The second sound can be quite loud in atherosclerotic affection of the aorta. Diastolic murmur heard over the aorta and at the Botkin-Erb listening point is characteristic. This is a low blowing protodiastolic murmur which weakens by the end of diastole as the blood pressure in the aorta drops and the blood-flow rate decreases. The described changes in the sounds and murmurs are clearly visible on

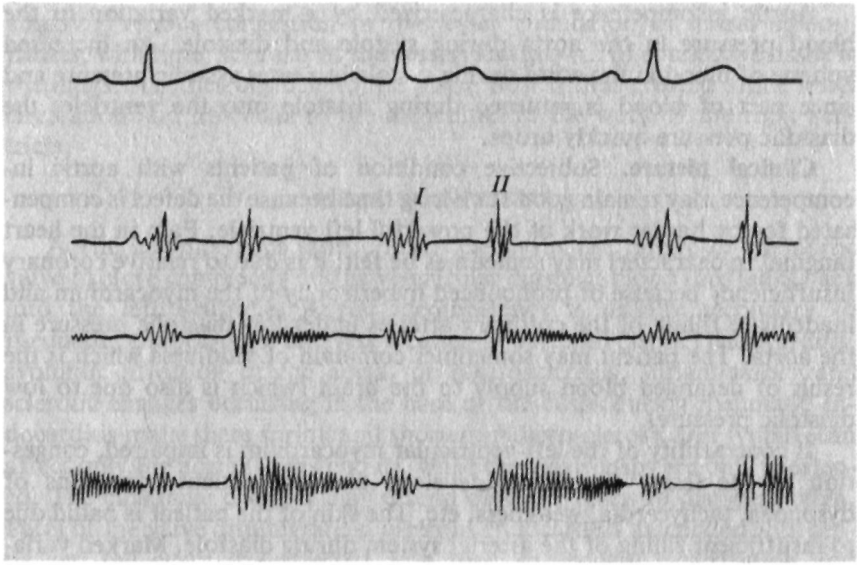


Fig. 75. PCO in aortic incompetence. The amplitude of the heart sounds and diastolic murmur are decreased on the PCG taken over the aorta.

phonocardiograms (Fig. 75). Murmurs of functional aetiology can also be heard in aortic incompetence at the heart apex. If the left ventricle is markedly dilated, relative mitral incompetence develops and systolic murmur can be heard at the heart apex. Diastolic murmur (presystolic or Austin Flint murmur) can sometimes be heard. It arises due to an intense regurgitation of the blood that moves aside the mitral valve cusp to account for functional mitral stenosis. Doubled sound (Traube double sound) and doubled Vinogradov-Duroziez murmur can sometimes be heard over the femoral artery in this disease.

The pulse in aortic incompetence is fast, full, and high, which is due to high pulse pressure and increased volume of blood delivered into the aorta during systole. Arterial pressure constantly varies: the systolic pressure rises and diastolic falls, and the pulse pressure is therefore high.

X-ray studies show an enlarged left ventricle with a distinct waist of the heart (Fig. 76) and dilatation of the aorta; pulsation of the aorta is intense.

The ECG also reveals various signs of hypertrophy of the left ventricle (Fig. 77): the electrical axis is deviated to the left, the S waves in the right chest leads are deep and the amplitude of the *R* wave is higher in the left chest leads; these signs often combine with signs of overstrain in the left ventricle and relative coronary insufficiency (changes in the terminal part

of the ventricular complex, displacement of the *S-T* interval, and the negative *T* wave).

Echocardiograms taken from patients with aortic failure show flutter of the anterior mitral cusp during diastole caused by the thrust of the blood regurgitated from the aorta into the ventricle.

Aortic incompetence can for a long time be compensated for by intensified work of the hypertrophied left ventricle. When its contractile force decreases, congestion in the lesser circulation develops. Acute weakness of the left ventricle sometimes develops and is manifested by an attack of cardiac asthma. Dilatation of the weakened left ventricle can cause relative mitral incompetence. This increases venous congestion in the lesser circulation associated with decompensated aortic incompetence and adds to the load on the right ventricle. This is mitralization of aortic incompetence, which may become the cause of venous congestion in the greater circulation.

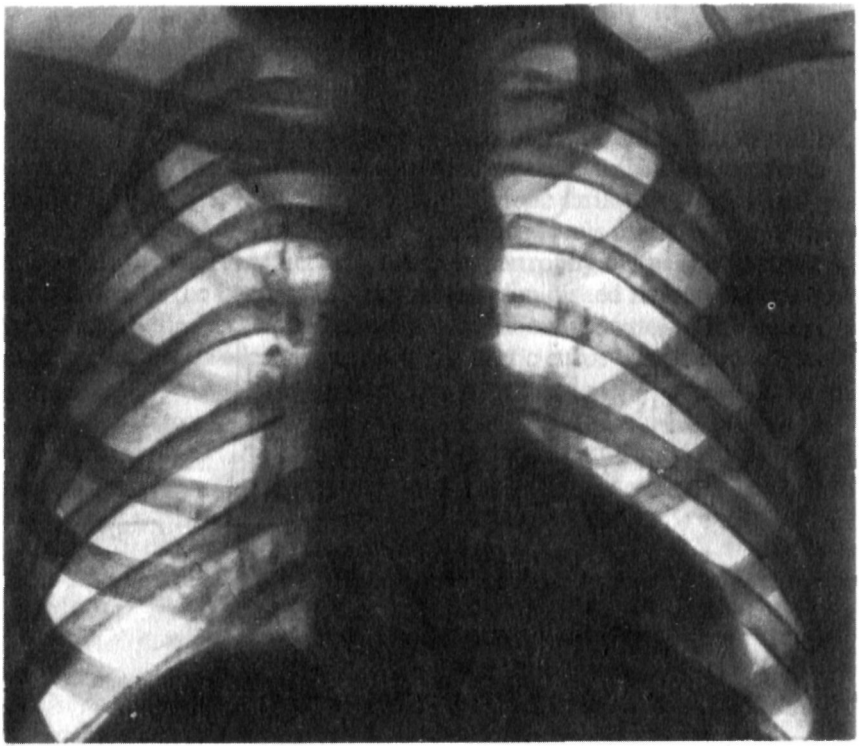


Fig. 76. X-ray in aortic incompetence. The heart's configuration is aortic; the left ventricle is dilated and hypertrophied, the ascending aorta is dilated.

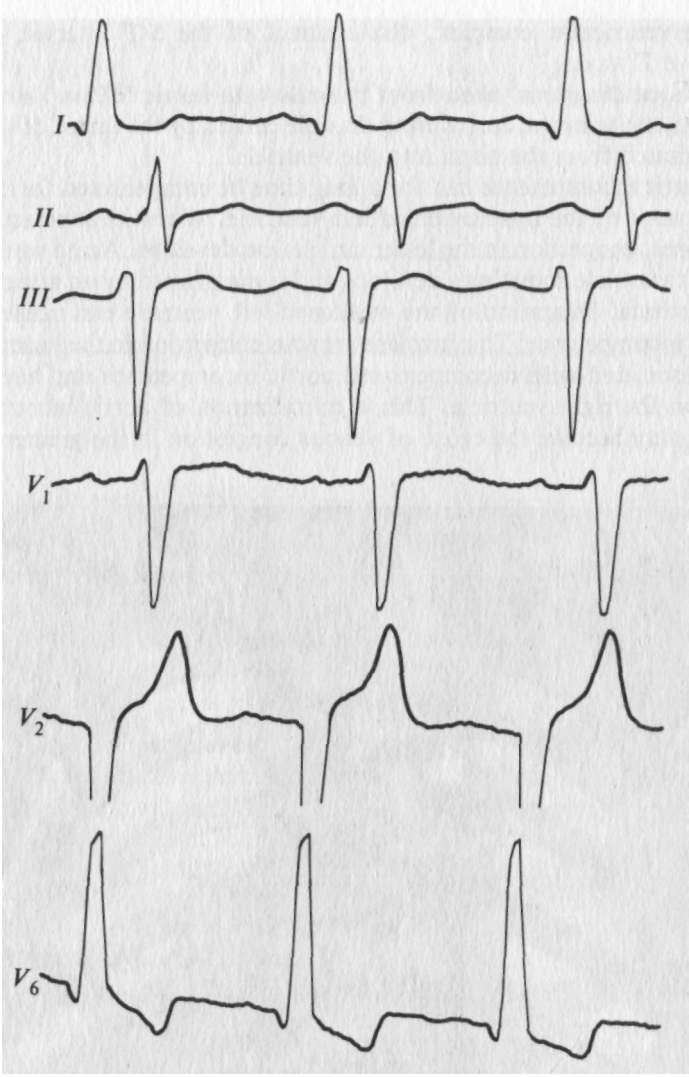


Fig. 77. ECG in aortic incompetence.

AORTIC STENOSIS

The narrowing of the aortic orifice (aortic stenosis) interferes with expulsion of blood into the aorta during contraction of the left ventricle. Aortic stenosis is usually caused by rheumatic endocarditis; less frequently

it develops due to bacterial endocarditis, atherosclerosis, or it may be congenital. Stenosis results from adhered aortic valve cusps or develops due to cicatricial narrowing of the aortic orifice.

Haemodynamics. During systole, the left ventricle is not emptied completely because part of blood fails to pass the narrowed orifice into the aorta. A new normal portion of blood delivered during diastole from the left atrium is mixed with the residual volume and the ventricle becomes overfilled. The pressure inside it thus rises. This disorder is compensated for by an intensified activity of the left ventricle to cause its hypertrophy (Fig. 78).

Clinical picture. Aortic stenosis can remain compensated for years and would not cause any unpleasant subjective sensations (even during intense physical exertion). If obstruction of the aortic orifice is considerable, insufficient blood ejection into the arterial system upsets normal blood supply to the hypertrophied myocardium and the patient feels pain in the heart (angina pectoris-type pain). Disordered blood supply to the brain is manifested by giddiness, headache, and tendency to fainting. These symptoms like pain in the heart would more likely occur during physical exercise and emotional stress.

The skin of the patient is pallid due to insufficient blood supply to the arterial system. The apex beat is displaced to the left, less frequently inferiorly; it is diffuse, high, and resistant. Systolic thrill (cat's purr) can be palpated in the region of the heart. Percussion reveals displacement of the left border; the heart is "aortic" due to hypertrophy of the left ventricle. Auscultation of the heart at its apex reveals diminished first sound due to overfilling of the left ventricle and prolongation of systole. The second sound is diminished over the aorta. If the aortic cusps adhere and are im-

Fig. 78. Upset intracardiac haemodynamics in stenosed aortic orifice (for designations see Fig. 69).

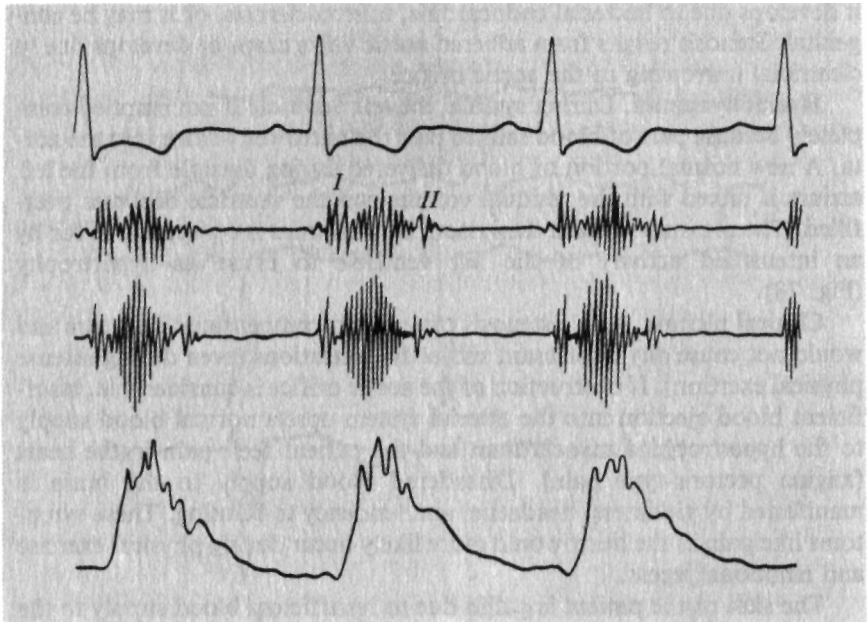


Fig. 79. PCG and sphygmogram in aortic stenosis. The PCG taken over the aorta shows crescendo-decrescendo (diamond-shaped) systolic murmur; the peak of the sphygmogram is serrated like a cock's comb.

mobile, the second sound can be inaudible. Rough systolic murmur over the aorta is characteristic. This murmur is generated by the blood flow through the narrowed orifice. It is conducted by the blood onto the carotids and can sometimes be heard in the interscapular space. The pulse is small, slow, and rare, since the blood slowly passes into the aorta and its volume is decreased. Systolic arterial pressure is usually diminished, while diastolic remains normal or increases. The pulse pressure is therefore decreased.

X-ray examination shows hypertrophied left ventricle, "aortic" configuration of the heart, and dilatation of the ascending aorta (poststenotic); the cusps of the aortic valve are often calcified.

The ECG usually shows signs of hypertrophy of the left ventricle and sometimes of coronary insufficiency. The phonocardiogram shows the specific changes in the heart sounds: diminished amplitudes of the first sound at the heart apex and of the second sound over the aorta. Systolic murmur over the aorta is typical; its oscillations are recorded in the form of specific diamond-shaped figures (Fig. 79).

Sphygmograms of the carotids reveal slowed ascent and descent of the pulse wave (slow pulse), small amplitude of the pulse waves, and specific serrated pattern of their peaks (sphygmograms in the form of a cock's comb) showing oscillations associated with conduction of systolic murmur onto the neck vessels.

Echocardiograms show decreased opening of the aortic valve during systole. Echoes from the cusps become more intense and signs of hypertrophy of the left ventricle appear.

Aortic stenosis remains compensated for a long time. Circulatory insufficiency develops in diminished contractility of the left ventricle and it is manifested as in aortic incompetence.

TRICUSPID INCOMPETENCE

Insufficiency of the tricuspid valve can be functional (relative) and organic (permanent). Organic tricuspid incompetence occurs in rare cases, mainly due to rheumatic endocarditis. Tricuspid incompetence usually combines with affections of other heart valves; as an independent disease, it occurs in exceptionally rare cases.

Relative (functional) insufficiency of the tricuspid valve occurs more often. It is due to dilatation of the right ventricle and distention of the right-atrioventricular orifice. Tricuspid incompetence often combines with mitral diseases because the right ventricle has to perform greater work due to the high pressure in the lesser circulation. This causes overstrain and distention of the right ventricle.

Haemodynamics. Due to incomplete closure of the tricuspid valve during right-ventricular systole, part of blood is regurgitated into the right atrium, where it is mixed with the normal volume of blood delivered from the venae cavae. The atrium thus becomes distended and hypertrophied. During diastole, a larger volume of blood is delivered into the right ventricle from the right atrium because the portion of blood that was regurgitated into the atrium during systole is added to the normal volume of blood delivered. This causes dilatation and hypertrophy of the right ventricle (Fig. 80). Compensation in this disease is attained by intensified work of the right atrium and the right ventricle whose compensatory power is not great and congestion in the greater circulation therefore soon develops.

Clinical picture. Pronounced venous congestion in the greater circulation in the presence of tricuspid incompetence causes oedema, ascites, feeling of heaviness and right hypochondriac pain (due to enlargement of the liver). The skin becomes cyanotic, sometimes with a yellowish tint. The neck veins swell and pulsate; the positive venous pulse and pulsation of the liver are also observed. These pulsations are explained by the regurgitation

of blood from the ventricle to the atrium through an incompletely closed atrioventricular orifice, owing to which pressure increases in the atrium and emptying of the neck and liver veins is made difficult. Tricuspid incompetence is characterized by extensive hepatic pulsation: the liver is displaced anteriorly and swells. This can be felt by trying to hold the liver by both hands: the pulsating liver sets the hands apart during the pulse wave.

Inspection of the patient reveals pronounced pulsation in the region of the right ventricle. As distinct from the heart beat in mitral stenosis, this pulsation is characterized by systolic retraction and diastolic protrusion of the chest.

Systolic retraction of the chest in the region of the right ventricle is explained by pronounced diminution of its volume because much blood is delivered at that moment to the hepatic veins. Systolic retraction of the chest corresponds to the systolic swelling of the liver, and vice versa, diastolic overfilling of the right ventricle and protrusion of the chest in the ventricular region combine with diastolic diminution of the liver volume. Therefore, if the examiner places one hand on the region of the right ventricle and the other hand over the liver, he can feel specific rolling movements of the hands. The apex beat is as a rule not pronounced because the left ventricle is displaced posteriorly by the hypertrophied right ventricle. Percussion reveals marked displacement of the heart border to the right due to hypertrophy of the right atrium and right ventricle.

Auscultation at the base of the xiphoid process reveals diminished first sound; systolic murmur can be heard at the same listening point and also at the 3rd and 4th interspaces, to the right of the sternum; this murmur in-

Fig. 80. Changes in intracardiac haemodynamics in tricuspid incompetence (for designations see Fig. 69).

creases when the patient keeps his breath at the height of inspiration. Since pressure in the lesser circulation decreases in tricuspid incompetence, the second sound over the pulmonary trunk decreases in its clearness.

Pulse does not change significantly or it becomes small and fast, because serious heart failure often occurs in tricuspid incompetence. Arterial pressure usually decreases. The venous pressure increases markedly.

Signs of hypertrophy of the right heart's chambers can be detected roentgenographically. Electrocardiography also shows hypertrophy. Phonocardiography records systolic murmur at the base of the xiphoid process and at the 3rd and 4th intercostal spaces, to the right of the sternum; the systolic murmur has a decreasing character. When a phonocardiogram is taken at the height of inspiration, the vibration amplitude increases.

A phlebogram of the jugular vein reveals a high positive *a* wave which is connected with the intensified activity of the hypertrophied right atrium, or the wave has the form characteristic of the positive venous pulse.

Echocardiography of the tricuspid valve is more difficult than that of the mitral or the aortic valve. Echocardiograms can reveal paradoxical movements of the interventricular septum in overloading of the right ventricle associated with tricuspid insufficiency.

Tricuspid incompetence usually combines with grave circulatory insufficiency. Long-standing congestion in the greater circulation upsets the function of many organs, such as the liver, kidneys, or the gastro-intestinal tract. The liver is especially affected: prolonged congestion in the liver is attended by growth of connective tissue to provoke the development of the so-called cardiac fibrosis of the liver. This, in turn, even more interferes with the normal function of the organ and causes severe metabolic disorders.

COMBINED AND CONCOMITANT HEART DISEASES

Acquired diseases of the heart, rheumatic in particular, often occur as combined affections of the valves, i.e. valve incompetence and stenosis of the orifice occur simultaneously. Moreover, concomitant affection of two, and sometimes three valves (mitral, aortic, and tricuspid) may occur simultaneously.

Mitral incompetence is most common. It usually concurs with stenosis of the left venous orifice. Signs of both heart diseases are then found but one sign dominates as a rule; less frequently, signs of valvular incompetence and stenosis are equally pronounced.

Dyspnoea and cyanosis are early symptoms of the mitral disease. The

heart expands to the left, superiorly, and to the right, because both ventricles and the left atrium are hypertrophied. Intensity of the first sound at the apex depends on the prevalent disease: if mitral incompetence is the leading syndrome, the first heart sound diminishes; if mitral stenosis dominates, the first sound increases and becomes squelching. Two sounds are heard at the apex: systolic due to valvular insufficiency, and diastolic due to stenosed orifice.

Pulse and arterial pressure do not change in prevalence of mitral incompetence, while if mitral stenosis dominates, systolic arterial pressure may decrease and diastolic pressure increase; the pulse becomes small.

Combined aortic incompetence is usually secondary to rheumatic endocarditis. Both systolic and diastolic murmurs are characteristic; these sounds can be heard over the aorta. Vascular pulsation and high pulse pressure are typical of aortic incompetence; they are not so pronounced in combined aortic affection. At the same time, slow and small pulse, and low pulse pressure that are typical of aortic stenosis, are also less pronounced in combined aortic incompetence.

Detailed clinico-instrumental examination of patients with concomitant affections of several valves reveals signs typical of each particular disease. It is necessary in such cases to conclude on the gravity of each disease and the prevalence of one of them. This is especially important for prognostic conclusions and for prospective surgical treatment.

Prognosis and treatment of heart diseases. The course of heart diseases and their prognosis depend on many factors. Mild changes in the heart valves, in the absence of marked affections of the myocardium, can remain non-manifest for a long time without impairing the work capacity of the patient. Aortic insufficiency is compensated for a long time but when decompensation develops, the patient soon dies. Mitral stenosis has a worse prognosis because the disease is compensated by a weaker left atrium. Congestion soon develops in the lesser circulation, which is followed by incompetence of the right heart chambers, and the greater circulation soon becomes affected by congestion. Repeated rheumatic attacks have an adverse effect on the course of the disease: the valvular apparatus of the heart is progressively impaired and the myocardium is affected. These disorders provoke circulatory insufficiency. Moreover, any infection, poisoning, physical or nervous overstrain, pregnancy and labour may give an impetus to the development of heart failure.

Restitution prognosis depends on the general condition and physical fitness of the patient. In the absence of symptoms of circulatory insufficiency, the patient may return to his usual occupation; in the presence of signs of decompensation, the patient should be recommended to change his occupation. Work capacity can be preserved in a patient with heart disease

provided he fulfills special recommendations for his work and rest, if he abstains from overeating, smoking, or drinking. Remedial exercises can be prescribed to strengthen the myocardium in the absence of cardiac insufficiency.

Prophylaxis of heart diseases consists mainly in prevention of rheumatism, sepsis and syphilis. Prophylaxis also implies sanation of infectious foci, strengthening of the body, and exercises.

Conservative treatment of patients with heart diseases consists in prophylaxis and treatment of heart failure. Mitral stenosis is often corrected surgically (mitral comissurotomy). The adhered cusps are disjoined and the atrioventricular orifice is widened. This operation removes severe haemodynamic disorders. Aortic comissurotomy is performed in stenosed aortic orifice, but this operation is much more complicated. Surgical treatment of mitral and aortic incompetence consists in replacement of the destroyed valve by an artificial one.

Patients with rheumatic heart disease should be regularly observed in out-patient conditions.

Myocarditis

Myocarditis is inflammation of the myocardium. The disease affects both men and women at any age. Acute, subacute, and chronic myocarditis are differentiated. The disease may be local or diffuse.

Aetiology and pathogenesis. Aetiological factors responsible for the development of myocarditis are various bacterial and virus infections. The most common cause of myocarditis is rheumatism, next come sepsis, diphtheria, rickettsiosis, scarlet fever, and virus infections. Myocarditis may develop in sensitization to some medicinal preparations (allergic myocarditis). Inflammatory changes in the myocardium caused by various infections are the result of allergic reaction of the body sensitized by certain microbes. The microbe antigen or its toxin act on the myocardium to cause formation of tissue antigens (auto-antigens) in it. As a result, auto-antibodies are formed which account for the vast changes in the myocardium.

Pathological anatomy. Dystrophic processes in the muscle fibres are characteristic. Predominant exudative or proliferative processes are also observed in the interstitial tissue (interstitial myocarditis). The outcome of the inflammatory changes is cardiosclerosis.

Clinical picture. This includes signs of decreased contractility of the myocardium and upset cardiac rhythm. The patient complains of dyspnoea in physical exertion, extreme weakness, palpitation, intermissions, dull and boring pain, or attacks of pain in the heart (like in angina pectoris).

The skin is pallid, sometimes with a slight cyanotic shade. In pronounced heart failure the neck veins become swollen. The pulse is small, soft, sometimes arrhythmical and accelerated: it may however be slowed down too. Extrasystole and, less frequently, paroxysmal fibrillation develop in deranged excitation function and automaticity.

Decreased diffuse apex beat, which is displaced anteriorly, is revealed on examination of the heart. Percussion can detect displacement of the heart to the left. Auscultation reveals a markedly decreased first sound at the early systole (due to decreased rate of rise in the intraventricular pressure). The second sound is either unchanged or diminished due to hypotension. Gallop rhythm can be heard in significantly decreased myocardial contractility. Systolic murmur can often be heard over the heart apex. It arises due to relative mitral incompetence. Arterial pressure, especially systolic, decreases and the pulse pressure falls accordingly.

ECG changes in myocarditis are quite varied and transient. Sinus tachycardia, sinus arrhythmia, and extrasystole (in the form of separate or group atrial or ventricular extrasystoles) can most frequently be found on electrocardiograms. Conduction is deranged according to incomplete or complete atrioventricular block. Diffuse affections of the myocardium are shown on ECG as diminished and split *P* wave, changed *QRS* complex (decreased voltage of the waves and their splitting), decreased *S-T* interval, the presence of two phases and inversion of the decreased *T* wave.

The blood counts show moderate neutrophilic leucocytosis with shift to the left, increased ESR, and hyperglobulinaemia (mainly due to α_2- and γ-globulins).

Course. The course of myocarditis is usually favourable and ends with recovery. Sclerosis of the myocardium develops in some patients (myocardial cardiosclerosis).

Treatment. Myocarditis patients are prescribed strict bed-rest. The main cause that provokes the disease is treated by antibiotics, desensitizing preparations, and hormones. Cardiac glycosides and diuretics are given in the presence of heart failure. In order to improve metabolism in the myocardium, carboxylase, ATP, vitamins, and potassium preparations are prescribed. Deranged cardiac rhythm can be restored by appropriate preparations.

Cardiomyopathy

Cardiomyopathy includes diseases of unknown aetiology characterized by affections of the heart muscle attended by enlargement of the heart and its insufficiency.

The following three types of cardiomyopathy would be usually dif-

ferentiated: (1) congestive or dilatation; (2) hypertrophic; and (3) restrictive cardiomyopathy.

Congestive cardiomyopathy is characterized by dilatation of the heart chambers with pronounced heart failure. The patients develop dyspnoea during slightest physical exertion and even at rest, attacks of suffocation and cardiac pain which cannot be removed by nitroglycerin; heart palpitation and intermissions are also characteristic. As circulatory insufficiency progresses, the liver becomes enlarged and oedema and hydrops of the cavities develop. The borders of the heart are markedly displaced to the right, upwards, and to the left. The heart sounds at the apex are dulled, the second sound over the pulmonary trunk is accentuated, gallop rhythm often develops along with systolic murmur at the apex due to developing relative mitral insufficiency. The pulse is small and fast, sometimes arrhythmical. The arterial pressure is usually decreased.

ECG in congestive cardiomyopathy shows various changes in the myocardium; signs of overloading of the heart chambers and focal changes develop along with rhythm and conduction disorders.

Echocardiography reveals marked dilatation of the heart chambers and decreased contractility of the myocardium.

Hypertrophic cardiomyopathy is characterized by the primary hypertrophy of the myocardium with subsequently developing cardiac insufficiency which differs but little from congestive cardiomyopathy by its symptoms.

The special form of hypertrophic cardiomyopathy is obstructive cardiomyopathy, which is also known as idiopathic hypertrophic subaortic stenosis. This cardiomyopathy is characterized by asymmetric hypertrophy of the interventricular septum in the region of blood outflow from the left ventricle. The cavity of the left ventricle diminishes. A circular ridge of the hypertrophied myocardium is formed beneath the aortic valve. The ridge interferes with blood ejection into the aorta. This form of myocardiopathy is first manifested by symptoms characteristic for aortic stenosis: the patient develops headache, giddiness, faints, and heart pain (like in angina pectoris). Palpation and percussion of the heart reveals hypertrophy of the left ventricle; auscultation reveals coarse systolic murmur which is best heard at the 3rd or 4th intercostal space at the left edge of the sternum. The pulse is small and slow. Symptoms of circulatory insufficiency soon appear.

Echocardiography is most important among additional methods used to diagnose hypertrophic subaortic stenosis. It reveals asymmetrical hypertrophy of the interventricular septum, narrowing of the left ventricle and systolic deflection of the mitral valve cusp in the direction of the interventricular septum.

Hypertrophic cardiomyopathy can be familial, inherited by the autosome-dominant type.

Restrictive cardiomyopathy is associated with disordered distensibility of the myocardium due to endocardial and subendocardial fibrosis. The diastolic function of the myocardium becomes upset and heart failure (without marked hypertrophy of the myocardium or dilatation of the heart chambers) develops.

Pericarditis

Pericarditis is inflammation of the pericardium.

Aetiology and pathogenesis. In most cases pericarditis develops in the presence of rheumatism or tuberculosis. Rheumatic pericarditis usually concurs with affection of the myocardium and endocardium. Rheumatic, and mostly tuberculous pericarditis are manifestations of infectious allergic process. In certain cases, tuberculous pericarditis depends on the spread of infection from the foci in the lungs and tracheobronchial lymph nodes (via the lymph ducts to the pericardium). Pericarditis can develop in other infections as well (e.g. scarlet fever, measles, influenza, or sepsis). Sometimes it develops due to the transition of inflammation from the adjacent organs in pleurisy, pneumonia, myocardial infarction, and also in injuries to the heart and in uraemia.

Pathological anatomy. Dry (fibrinous) pericarditis and pericarditis with effusion are distinguished. Depending on the character of effusion, pericarditis may be serous, serofibrinous, purulent, or haemorrhagic. Serous effusion and small masses of fibrinous exudate may be fully resorbed. Fibrinous and purulent effusions undergo organization to thicken the pericardium membranes and cause commissures. Pericardium layers sometimes become adherent and the pericardial sac disappears (concretio pericardii). This condition is known as adherent (adhesive) pericarditis. Calcium is often deposited in the affected pericardium and the heart becomes enclosed in a rigid case. The dense fibrous thickening of the pericardium compresses the heart. This condition is known as constrictive pericarditis.

DRY PERICARDITIS

Clinical picture. Pain in the heart is often the only complaint of patients with dry pericarditis. The pain varies in character from discomfort and pressure to strong torturing pain with radiation to the left part of the neck and the shoulder blade.

Inspection and percussion of the heart do not reveal any changes unless myocarditis or other heart diseases concur. The most important, and sometimes the only sign of dry pericarditis is the sound of pericardial friction. Dry pericarditis ends with complete recovery in 2-3 weeks; or the disease may convert into pericarditis with effusion or adhesive pericarditis.

PERICARDITIS WITH EFFUSION

Clinical picture. Patients complain of the pressing sensation in the chest and pain in the heart. As effusion is accumulated, dyspnoea develops. Dysphagia develops in compression of the oesophagus and hiccup when the phrenic nerve is compressed. Fever is an almost obligatory symptom.

The appearance of the patient is characteristic: the face is oedematous and the skin is cyanotic and pallid. The neck veins are swollen due to an obstructed blood flow to the heart via the superior vena cava. Compression of this vein accounts for the oedematous appearance of the face, neck, and the anterior surface of the chest (Stokes' collar). The neck veins may sometimes swell only during expiration. If much exudate is collected in the pericardial sac, the patient assumes a characteristic posture: he sits in bed and inclines forward, his hands resting against the pillow lying on his knees. The feeling of heaviness in the heart is thus lessened and respiration made easier.

Inspection of the heart region reveals levelling of the interspaces. The apex beat is absent; if it is palpable, it appears to be displaced superiorly or medially of the left border. Percussion shows considerable enlargement of the cardiac dullness in all directions, absolute and relative dullness being almost undistinguishable. The area of dullness resembles a trapezium or a triangle: the right cardiohepatic angle becomes obtuse. If much exudate is accumulated, dullness extends to the left to diminish the tympany zone of Traube's space. Heart sounds are markedly decreased. The pulse is accelerated, small, and sometimes paradoxical. Arterial pressure is normal or decreased. Venous pressure is elevated. Palpation of the abdomen reveals marked enlargement of the liver due to congestion of blood in it. X-ray study shows enlarged heart silhouette in the transverse direction and superiorly; the waste of the heart is absent, the pulsation is markedly weak, which is especially vivid on the X-ray picture.

The ECG shows low voltage of all waves and also changes in the S-*T* interval and the *T* wave in all standard leads. The *S-T* interval is first located above the isoelectric line and then below it. The *T* wave is first low and then becomes negative. The ECG changes are like those observed in myocardial infarction except that they are equally pronounced in all leads (concordant), and that the *Q* wave remains unchanged.

Echocardiography is very important in the diagnosis of pericarditis with effusion. Echocardiography reveals the space between the pericardium and epicardium which is filled with fluid that does not return the probing ultrasound pulses. If effusion is small, the echo-free space can only be revealed between the pericardium and the posterior wall of the heart in a

patient in the supine position. In the presence of a large effusion, this space can be revealed in the region of the anterior wall of the heart.

Course. Purulent pericarditis is a grave danger to the patient's life unless urgent treatment is given. Serous pericarditis may end in complete recovery. Adhesive pericarditis produces persistent pathology because operative separation of the pleural layers is not sufficiently effective.

Treatment. Treatment depends on the cause of pathology. Rheumatic pericarditis is treated as rheumatism, and tuberculous pericarditis as tuberculosis. Various cardiacs and stimulants should be given in the presence of cardiac insufficiency. If effusion is large, the pericardium is punctured and the fluid withdrawn.

Essential Hypertension

Essential hypertension (morbus hypertonicus) is the condition in which elevated arterial pressure is the leading symptom. The disease is provoked by nervous and functional disorders in the regulation of the vascular tone. Men and women, mostly over 40, are equally attacked by the disease.

Essential hypertension should accurately be differentiated from *symptomatic hypertension* in which arterial pressure rises as a symptom of some other disease, this symptom being far from the leading one. Symptomatic hypertension occurs in aortic coarctation, atherosclerosis of the aorta and its large branches, in endocrine dysfunction (e.g. Itsenko-Cushing disease, phaeochromocytoma, primary aldosteronism, or the Conn syndrome), affection of the renal parenchyma, occlusive affection of the main renal arteries, and in some other diseases.

Aetiology and pathogenesis. Overstrain of the central nervous system, caused by prolonged and strong emotional stress and also mental overstrain, are believed to be the main cause of the disease. In some cases essential hypertension develops after brain concussion (concussion-commotion form). The importance of neurogenic factors was emphasized by Lang in 1922; later this hypothesis was confirmed by the Soviet physicians during World War II: the incidence of essential hypertension increased significantly in the sieged Leningrad.

Development of the disease greatly depends on occupation: it occurs mostly in subjects whose occupation is associated with nervous and mental overstrain, e.g. in scientific workers, engineers, physicians, drivers, etc. Familial predispostion is another important factor.

The early stage of essential hypertension is characterized by nervous-functional disorder in regulation of the vascular tone. Vegetative-endocrine disorders and changes in the renal regulation of the vascular tone are later steps of the pathological process. Overstrain of the higher nervous

activity causes vasopressor adrenal reaction by which arterioles, mainly the arterioles of the internal organs and especially of the kidneys, are narrowed. Ischaemia of the renal tissue develops as a result. This in turn stimulates production of renin by the juxtaglomerular cells of the kidneys. Renin stimulates formation of angiotensin-II which in turn causes a pronounced pressor effect and stimulates secretion of aldosterone (sodium-retaining hormone) by the adrenal cortex. Aldosterone promotes transition of sodium from the extracellular fluid into the intracellular fluid to increase the sodium content of the vascular wall. This causes oedematous swelling of the wall and narrowing of the vessel, which in turn promotes elevation of arterial pressure.

There is a system of depressor factors in the body whose dysfunction plays an important role in the pathogenesis of essential hypertension. Bradykinin and angiotensin, which produce a depressive effect, have been isolated. It is believed that the depressor system becomes altered by some unknown reason during essential hypertension.

Pathological anatomy. Essential hypertension gradually affects permeability of vascular walls and their protein content. At late or grave forms of the disease, this causes sclerosis or necrosis of small arteries and secondary changes in the tissues of organs. Walls of large vessels are usually affected by atherosclerotic changes. The extent of vascular affection differs in various organs and various clinicoanatomical variants of the disease therefore arise, with a prevalent affection of the vessels of the heart, brain, or kidneys (primary cirrhosis of the kidneys thus develops).

Clinical picture. During the early stage of the disease, the patient would usually complain of neurotic disorders: general weakness, impaired work capacity, inability to concentrate during work, deranged sleep, transient headache, a feeling of heaviness in the head, vertigo, noise in the ears, and sometimes palpitation. Exertional dyspnoea (ascending upstairs, running) develops later.

The main objective sign of the disease is elevated systolic pressure (over 140—160 mm Hg) and diastolic pressure (over 90 mm Hg). Arterial pressure is very liable during the early stage of the disease, but later it stabilizes. Examination of the heart reveals signs of hypertrophy of the left ventricle: expanding apex beat, and displacement of the cardiac dullness to the left. The second sound is accentuated over the aorta. The pulse becomes firm and tense.

X-rays reveal "aortic" silhouette of the heart. The aorta is elongated, consolidated, and dilated.

The ECG is of the left type with displaced *S-T* segment, low, negative, or two-phase *T* wave in the 1st and 2nd standard chest leads (V_5-V_6).

Coronary atherosclerosis concurs not infrequently. This may cause angina pectoris and myocardial infarction. In the late period of the disease,

heart failure may develop due to fatigue of the heart muscle as a result of increased arterial pressure. Heart failure is often manifested by acute attacks of cardiac asthma or oedema of the lungs; or chronic circulatory insufficiency may develop.

Vision may be deteriorated in grave cases. Examination of the fundus oculi reveals its general pallidness; the arteries are narrow and tortuous, the veins are mildly dilated; haemorrhage into the retina (angiospastic retinitis) is sometimes observed.

High arterial pressure in the affected cerebral vessels can derange cerebral circulation. This can cause paralysis, disorders in sensitivity, and sometimes death of the patient. Cerebral circulation is deranged due to spasms of the vessels, their thrombotic obstruction, haemorrhage due to rupture of the vessel, or diapedetic discharge of erythrocytes.

The affected kidneys become unable to concentrate urine (nicturia or isohyposthenuria develops). Metabolites (otherwise excreted with urine) are retained to provoke uraemia.

Essential hypertension is characterized by periodically recurring transient elevations of arterial pressure (hypertensive crisis). Development of such crises is preceded by psychic traumas, nervous overstrain, variations in atmospheric pressure, etc.

Hypertensive crisis develops with a sudden elevation of the arterial pressure that can persist from a few hours to several days. The crisis is attended by sharp headache, feeling of heat, perspiration, palpitation, giddiness, piercing pain in the heart, sometimes by deranged vision, nausea, and vomiting. In severe crisis, the patient may lose consciousness. The patient is excited, haunted by fears, or is indifferent, somnolent, and inhibited. Auscultation of the heart reveals accentuated second sound over the aorta, and also tachycardia. The pulse is accelerated but can remain unchanged or even decelerated; its tension increases. Arterial pressure increases significantly. ECG shows decreased *S-T* interval and flattening of the *T* wave. In the late stages of the disease, with organic changes in the vessels, cerebral circulation may be deranged during crisis; myocardial infarction and acute left-ventricular failure may also develop.

Classification. According to Myasnikov, three stages of the disease are classified; each stage is further divided into two phases, A and B.

The A phase of the first stage is latent; it is characterized by elevated arterial pressure during a psychic stress, while under normal conditions arterial pressure is normal. The B phase is transient (transitory hypertension); arterial pressure increases only occasionally and under certain conditions; objective changes are absent.

In the second stage, arterial pressure is elevated permanently and more significantly. Phase A is characterized by permanent but unstable

hypertension. Subjective sensations are pronounced; hypertensive crises are possible; spasms of the cerebral and coronary arteries are likely to occur as well. Signs of hypertrophy of the left ventricle develop. Phase B is characterized by a significant and stable elevation of the arterial pressure. Hypertensive crises are frequent. Paroxysms of angina pectoris and derangement of cerebral circulation of the angiospastic character occur. Changes in the fundus oculi and pronounced signs of hypertrophy of the left ventricle can be revealed.

During the third stage, sclerotic changes in the organs and tissues are observed along with stable and marked elevation of the arterial pressure. Phase A is compensated. Arteriosclerosis of the kidneys is observed, but the renal function is not upset significantly. Cardiosclerotic changes do not provoke stable heart failure; and sclerosis of cerebral vessels is not attended by pronounced disorders in the cerebral circulation. Phase B is decompensated, with grave dysfunction of various organs and with renal insufficiency; cerebral circulation is disordered and hypertensive retinopathy is observed. In this stage of the disease, the arterial pressure may normalize after infarction or apoplectic stroke.

Treatment. Complex therapy is required. Reasonable work should be alternated with rest, sufficient sleep, and remedial exercises. Sedatives should be given to improve sleep and to normalize excitation and inhibition processes. Hypotensive preparations (rauwolfia, ganglioblocking preparations, magnesium sulphate) are prescribed to inhibit the increased activity of the vasomotor centres and the synthesis of noradrenaline. Diuretics (saluretics) are given to decrease intracellular sodium; aldosterone blocking agents (spironolactone) and other preparations are also given.

Atherosclerosis

Atherosclerosis is a chronic disease characterized by systemic affection of arteries due to metabolic disorders in the vascular wall. Atherosclerosis is one of the most common diseases and the most frequent cause of disability and premature death. It usually attacks people over 40-45 but sometimes occurs in younger patients. The incidence of atherosclerosis in men is 3-4 times higher than in women.

Aetiology. The aetiology of the disease is uncertain. It has been established that atherosclerosis occurs in subjects who undergo long nervous and psychic overstrain, hypodynamia, who suffer from overeating (taking much food rich in animal fats) and obesity, and diabetes mellitus, or myxoedema. The pathogenesis of the disease is complicated and not clear. It is believed that the function of a complicated neurohumoral apparatus regulating metabolism becomes upset by some causal factors. As a

result, biochemical, physico-chemical, and morphological composition of the blood is affected along with impairment of the blood coagulation system, disorders of structure, biochemistry and function of the arteries, and of their permeability. Hereditary predisposition to atherosclerosis is important in some cases.

Pathological anatomy. The changes are localized in large elastic arteries, i.e. in the aorta, the coronary, cerebral, renal arteries and the large arteries of the limbs.

The atherosclerotic process occurs in stages. First, lipids are deposited in the arterial intima to form fat spots and strips, which do not rise above the surface of the intima. Later, connective tissue grows in the region of lipid accumulation to form a fibrous atherosclerotic plaque which rises above the intima surface to narrow the lumen of the vessel. The lipid-protein complex inside the plaque can decompose to ulcerate its surface and to form an atheromatous ulcer. The ulcerated plaques can become the cause of thrombosis of the vessel and calcification of the fibrous plaques, which causes even greater changes in the arterial walls.

Clinical picture. The disease may be asymptomatic for years (preclinical period). Study of the blood during this period shows increased cholesterol or beta-lipoprotein content. The further picture of the disease depends on the affection of particular vessels (aorta, coronary arteries of the heart, cerebral vessels, renal arteries, and the limb arteries). This is the clinical period of the disease, which is divided into three stages, namely the ischaemic stage, during which ischaemic changes occur in the organs (e.g. angina pectoris attacks occur in atherosclerosis of the coronary arteries); the second or thrombonecrotic stage, characterized by thrombosis in the changed arteries (myocardial infarction may occur at this stage); and the third, fibrous stage, characterized by the development of connective tissue in the organs (e.g. cardiosclerosis).

Atherosclerosis of the coronary arteries (see "Angina Pectoris", "Myocardial Infarction" and "Cardiosclerosis").

Aortic atherosclerosis usually occurs in individuals aged over 40, but even its grave forms can sometimes be asymptomatic. Atherosclerosis of the ascending aorta and its arch occurs more frequently. The patient feels pressing or burning pain in the retrosternal region which radiates in both arms, the neck, the back, and the upper abdomen. As distinct from pain in angina pectoris this pain is more persistent; it can continue for hours and even days, with periodic weakening and strengthening. The elastic properties of the aorta decrease and the heart has to perform greater work, which causes hypertrophy of the left-ventricular myocardium. Inspection of the heart reveals increased apex beat and its displacement to the left; on percussion, the borders of dullness of the vascular bundle are expanded. Retrosternal pulsation can be palpated in the jugular fossa because of the high standing of aortic arch (due to its elongation). The first heart sound is

as a rule dull, the second sound is heard over the aorta; systolic murmur is also found which appears or becomes intensified when the patient raises his arms (Sirotinin-Kukoverov symptom). Systolic murmur is due to both sclerotic narrowing of the aortic orifice and roughness of the inner surface of the aorta. Maximum arterial pressure increases, while minimum pressure either remains unchanged or slightly falls. X-ray study reveals straightened, dilated, and elongated aorta. Atherosclerosis of the abdominal aorta is rarely diagnosed during life.

Atherosclerosis of the mesenteric arteries impairs blood supply to the intestine and may cause attacks of angina abdominis: the patient suddenly feels (3—6 hours after meals) piercing pain in the upper abdomen or in the umbilical region, which persists from 2 or 20 minutes to 1-2 hours. The pain is attended by the swelling of the abdomen, regurgitation, constipation, palpitation, and increased arterial pressure. In thrombosis of mesenteric arteries, the intestinal loops begin necrotizing, which is manifested by haemorrhage and paralytic intestinal obstruction.

Atherosclerosis of the renal arteries causes vascular nephrosclerosis, which is manifested by hypertension and isohyposthenuria.

Atherosclerosis of the cerebral arteries is manifested by decreased work capacity (mental in particular), impaired memory, decreased active concentration, and rapid fatigue. The patient complains of insomnia and giddiness. The behaviour of the patient with pronounced atherosclerosis of the cerebral arteries changes: he becomes fussy, selfish, fidgety, and captious; his mental power decreases. Atherosclerosis of the cerebral arteries is complicated by disturbed cerebral circulation (haemorrhage, thrombosis).

Atherosclerosis of the limb arteries. Clinical signs of this disease are pain in the gastrocnemius muscles during walking. The pain is very severe and the patient has to stop for a while, but as he proceeds with walking, the pain soon develops again (intermittent claudication). The patient feels chill and cold in the legs. Examination of the legs reveals the absense of pulse (or weak pulse) on the dorsalis pedis artery and the posterior tibial artery. Dry gangrene of the lower extremities develops in grave cases due to local circulatory disorder. Angiography of the affected vessels reveals deformation, tortuosity, narrowing of the lumen, and microaneurysms.

Treatment. Combined therapy is aimed at removal of nervous effects, normalization of metabolic processes by prescribing rational diet and appropriate medicinal preparations to control the lipid content (lecithin, vitamin C, nicotinic acid, miscleron—2—3 capsules a day per os for several months, in courses, etc.).

Rational diet, correct alternation of work and rest, regular exercise, quiet at home and at work are important conditions for prophylaxis of atherosclerosis.

Ischaemic Heart Disease

The term ischaemic heart disease includes many diseases, such as angina pectoris, myocardial infarction, and coronary cardiosclerosis. The pathology is based on insufficient blood supply to the heart. The disproportion between the heart's demand for blood and the actual blood supply may arise when the heart's demands increase significantly, or when the actual blood supply diminishes for some reasons.

Angina Pectoris

Angina pectoris is a frequently occurring disease. Its main clinical symptoms are attacks of retrosternal pain due to acute but transient disorder in the coronary circulation. The disease develops mainly in people over 40, and predominantly in men. Mental workers would mostly suffer from this disease.

Aetiology and pathogenesis. The most frequent cause of angina pectoris is atherosclerosis of the coronary arteries of the heart. Much less frequently it develops in infectious and infectious-allergic vascular diseases, such as syphilitic aortitis, panarteritis, periarteritis nodosa, rheumatic vasculitis, and obliterating endarteritis. Angina pectoris often concurs with essential hypertension. Paroxysms of angina pectoris may develop due to upset nervous regulation of the coronary arteries as a reflex or in cholelithiasis, hiatus hernia, diseases of the stomach, etc. by reflex. Spasms of the coronary arteries (without their anatomical changes) can sometimes provoke angina pectoris. The spasm may develop in heavy smokers or as a result of a strong emotional stress.

Hypoxaemia (ischaemia) of the myocardium provokes the attack. Ischaemia develops in conditions when the insufficient amount of blood is delivered to the heart muscle through the coronary arteries, and the myocardium does not receive the necessary amount of oxygen. Transient oxygen hunger causes a reversible disorder in the oxidation-reduction processes in the myocardium. Stimulation of the interoceptors of the myocardium or the vascular adventitia by the products of upset metabolism produces a current of impulses via the centripetal pathways to the cerebral cortex to cause the specific symptom of the disease, retrosternal pain. High activation of the sympatheticoadrenal system is also very important for the onset of angina pectoris.

Pathological anatomy. No organic changes are sometimes found in those who died from an attack of angina pectoris. But in 85—90 per cent of cases signs of atherosclerosis of the coronary arteries pronounced to a different degree are discovered.

Clinical picture. The main clinical symptom of the disease is pain in the centre of the sternum (retrosternal pain). Less frequently the pain originates in the heart region. The character of pain varies: the patient may feel constriction, compression, heaviness, burning, and sometimes sharp or stabbing pain. Pain is usually severe and the patient develops morbid fear of death. Pain radiates into the left shoulder, left arm, left side of the neck and the head, the mandible, the interscapular space, and sometimes to the upper abdomen (Fig. 81). The characteristic radiation of pain during angina pectoris is due to hypersensitivity of the patient's skin to pain in the zones innervated by the 7th cervical and lst-5th thoracic segments of the spinal cord (Zakharyin-Head zones). Stimuli from the heart are transmitted through these segments to the centrifugal nerves of the spinal cord (by the viscerosensory reflex). Pain arises under certain conditions: during walking (especially fast walking) and other exercises (angina pectoris of effort).

During physical exertion, the heart muscle requires more nutrition from blood. Atherosclerotic vessels cannot deliver the appropriate amount of blood and the patient has to stop exercise (walking) for a few minutes until pain subsides. Specific sign of angina pectoris is development of pain when the patient leaves a warm room and walks in the open during cold seasons. The symptom is even more pronounced if atmospheric pressure changes. Under emotional stress, the patient develops an attack of angina pectoris without any exercise. Attacks of pain may occur during sleep (angina pectoris at rest), after meals, in abdominal distention, and in high diaphragm.

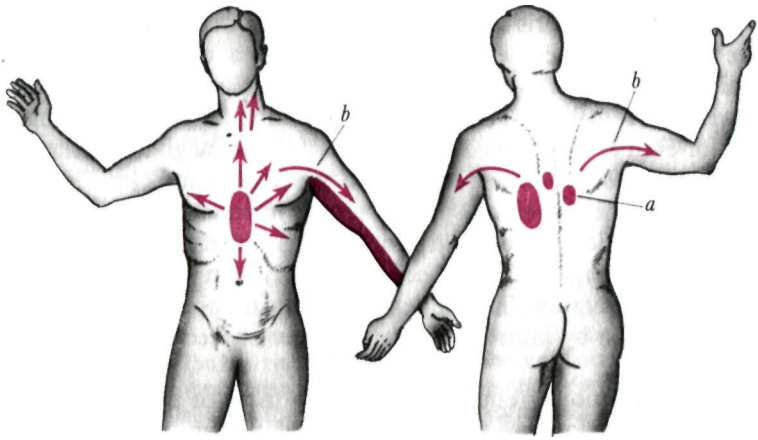


Fig. 81. Localization and radiation of pain in angina pectoris: Zakharyin-Head zone *(a);* nerve pathways of pain radiation *(b).*

Pain may last from few seconds to 20—30 min. Quick removal of pain after taking nitroglycerin suggests angina pectoris.

The strength of attacks differs. In rare cases attacks end lethally. During an attack, the pulse is usually slow and rhythmical, but tachycardia, extrasystole, and increased arterial pressure are sometimes observed. Percussion and auscultation of the heart sometimes cannot reveal any abnormality, provided pronounced atherosclerotic cardioslecrosis is absent. The body temperature remains normal. Usually there are no changes in the peripheral blood.

Electrocardiographic studies during attacks of angina pectoris sometimes reveal signs of disordered coronary circulation: the *S-T* segment is low, the two-phase or negative *T* wave is small in standard leads, and also in the corresponding chest leads, depending on the localization of affection in the coronary system. When the attack is abated, the electrocardiographic picture soon normalizes, ECG can sometimes reveal the described changes only during physical load. Coronarography with contrast substances is sometimes carried out to reveal occlusion of the coronary arteries.

Course. The disease is chronic. Attacks can be rare, once a week or even less frequently; attacks may be absent for months or even years, or their frequency may increase and they become more severe. An attack of angina pectoris lasting more than 30-60 minutes can end in myocardial infarction. Patients with long-standing angina pectoris develop cardiosclerosis; the cardiac rhythm becomes disordered and symptoms of heart failure develop.

Treatment. Depending on the gravity of the course, four functional classes of angina pectoris are distinguished. The first class is characterized by rare attacks and they occur only during physical exertion; in the second and third classes tolerance to exercise decreases progressively, while patients with the fourth class develop attacks of angina pectoris during slight exercise or even at rest. Vasodilatory preparations are given during attacks of angina pectoris and measures taken to prevent new attacks. The most effective preparation to remove pain is nitroglycerin: 1-3 drops of a 1 per cent alcohol solution placed on a lump of sugar or a tablet (both should be kept under the tongue). The effect of nitroglycerin becomes appreciable usually in 1-2 minutes. The patient with angina pectoris should always keep nitroglycerin by himself. Mustard plaster or leeches on the heart are also effective.

In order to remove frequent and severe attacks of pain and to prevent myocardial infarction, a surgical method of treatment is now used by which the coronary arteries are by-passed.

Sedatives (valerian, motherwort, trioxazin, etc.) in combination with vasodilatory preparations are regularly given to prevent attacks of angina pectoris.

Myocardial Infarction

Myocardial infarction is formation of a necrotic focus in the heart muscle due to upset coronary circulation. Myocardial infarction occurs mainly in people over 45; the incidence in men is higher than in women.

Aetiology. One of the main causes of myocardial infarction (in at least 90-95 per cent cases) is atherosclerosis of the coronary arteries. In exceptionally rare cases, myocardial infarction is secondary to embolism of the coronary vessel in endocarditis or septic thrombophlebitis, in inflammatory affections of the coronary arteries such as rheumatic coronaritis, obliterating endarteritis, and nodular periarteritis. Overstrain, both physical and nervous, overeating, alcohol and nicotin poisoning can also provoke myocardial infarction.

Pathogenesis. The pathogenesis of myocardial infarction is complicated and has not been sufficiently studied. According to current views, several factors are responsible for the onset of the disease. The main of them is believed to be coronary thrombosis and stenotic coronary sclerosis. Coronary thrombosis develops due to local changes in the vascular wall which are characteristic of atherosclerosis, and also as a result of disorders in the blood coagulating system which are manifested by the decreased blood content of heparin and decreased fibrinolytic activity. In the absence of thrombosis, intense work of the heart in conditions of decreased blood supply to the myocardium (stenotic coronary sclerosis) is very important for the development of myocardial infarction. According to other investigators, the main factor responsible for myocardial infarction are functional disorders in the coronary circulation which provoke a prolonged spasm in the coronary arteries or their paresis. In their opinion atherosclerosis of the coronary arteries promotes development of myocardial infarction. Certain researchers believe that electrolyte imbalance in the heart muscle and accumulation of catecholamines in it and some other factors are important for the development of myocardial infarction.

Pathological anatomy. When blood supply to a part of the myocardium becomes inadequate, ischaemia develops, which is followed by necrosis. Inflammatory changes then develop round the necrotized area, and granular tissue grows. Necrotized mass is resorbed and replaced by cicatricial tissue. The heart muscle may rupture at the site of necrosis with haemorrhage into the pericardial sac (heart tamponade). In gross myocardial infarction the scar tissue may be so thin that it can swell to give cardiac aneurysm. Myocardial infarction usually develops in the left ventricle. Muscle layers located beneath the endocardium are usually involved in the

necrotic process (subendocardial form), but in severe cases, the entire muscle is involved (transmural infarction). Fibrinous pericarditis usually arises in such cases. Fibrin is sometimes deposited on the inner membrane of the heart at sites corresponding to myocardial necrosis (parietal thromboendocarditis). Thrombotic masses may be torn off and carried by the blood to account for embolism of the cerebral, abdominal, lung, and other vessels. According to the size of the necrotized focus, micro- and macrofocal myocardial infarctions are differentiated.

Clinical picture. The outstanding Russian physicians Obraztsov and Strazhesko were the first to describe the clinical picture of myocardial infarction in **1909;** they differentiated between three variants of its course, namely, anginous, asthmatic, and abdominal (gastralgic) forms.

The anginous form occurs most frequently; clinically it is characterized by the pain syndrome. Pressing pain behind the sternum or in the region of the heart develops, like in angina pectoris. As a rule, pain radiates into the left shoulder and the left arm; less frequently into the right shoulder. Pain is sometimes so severe that cardiogenic shock develops which is characterized by the increasing weakness and adynamia, paleness of the skin, cold sweat, and decreased arterial pressure. As distinct from angina pectoris, pain in myocardial infarction is not removed by nitroglycerin and persists for longer time (from 30—60 minutes to several hours). Prolonged pain in myocardial infarction is termed as status anginosus.

The asthmatic form begins with an attack of cardiac asthma and lung oedema. The main syndrome is either absent or weak.

The abdominal form of myocardial infarction is characterized by pain in the abdomen, mostly in the epigastric region. The pain may be attended by nausea, vomiting, and constipation (gastralgic form of myocardial infarction). This form of the disease occurs mostly in infarction of the posterior wall of the left ventricle.

Further observations have shown that the disease has considerably greater number of clinical signs. Myocardial infarction may sometimes begin with a sudden heart failure or collapse, various disorders in the cardiac rhythm or heart block, while the pain syndrome is either absent or is weak (painless form). This course often develops in recurrent infarction. The cerebral form of the disease is characterized by disorders in the cerebral circulation of various intensity.

Examination of the cardiovascular system reveals enlargement of cardiac dullness and low percussion sounds. The gallop rhythm can sometimes be heard. Pericardial friction is audible over a limited area, in the 3rd-4th interspaces, in transmural myocardial infarction. Pericardial friction becomes audible on the second or third day of the disease and persists for a few hours or may last one or two days. Pulse in myocardial infarction is often small, accelerated, or arrhythmical (in affection of the conduction system). Arterial pressure increases during pain attacks but then it falls.

Depending on the localization of infarction, circulation may be disordered by the left-ventricular or (less frequently) right-ventricular type. In the former case, congestive moist rales can be heard in the lungs; asphyxia resembling cardiac asthma may develop, which is then followed by oedema of the lungs. In the latter case, the heart is enlarged to the right; the liver is enlarged too; the lower extremities are affected by oedema.

Fever and leucocytosis develop on the second or third day of the disease. They result from reactive processes which depend on absorption of the autolysis products from the site of infarction. The larger the necrotized area, the higher is the temperature and the longer the pyretic period and leucocytosis. Elevated temperature persists for 3—5 days, sometimes 10 days and more; ESR begins increasing and leucocytosis decreases from the second week of the disease.

Diagnosis of myocardial infarction depends substantially on the determination of activity of some blood serum enzymes which are released due to necrotic changes in the myocardium, e.g. the activity of creatine phosphokinase, the first and the fifth enzymes of lactic dehydrogenase, aminotransferase, and especially asparagine and (to a lesser degree) alanine increase by the end of the first day of the disease. The activity of creatine phosphokinase normalizes in 2-3 days, of aminotransferase in 4-5 days, and of lactic dehydrogenase in 10—14 days.

Electrocardiographic examination is especially important. It establishes the presence of myocardial infarction and also some important details of the process such as localization, depth of the process, and the size of the affected area (Fig. 82).

The *S-T* segment and *T* wave change during the first hours of the disease. The descending limb of the *R* wave transforms into the *S-T* segment without reaching the isoelectric line. The 5-7 segment rises above the isoelectric line to form a convexing arch and to coincide with the *T* wave. A monophase curve is thus formed. These changes usually persist for 3—5 days. Then the S-T segment gradually lowers to the isoelectric line while the *T* wave becomes negative and deep. A deep *Q* wave appears, the *R* wave becomes low or disappears at all. The *QS* wave is then formed, whose appearance is characteristic of transmural infarction. Depending on localization of infarction, changes in the ventricular complex are observed in the corresponding leads (Figs. 83 and 84). The initial shape of ECG can be restored during cicatrization, or the changes may remain for the rest of life.

The radionuclide method can be helpful in diagnosing myocardial infarction. The patient is given pyrophosphate labelled with "Tc which is mainly concentrated in necrotized tissue, i.e. in the zone of infarction. The extent of the affection can thus be estimated.

Retrosternal oppression and general weakness are the usual symptoms

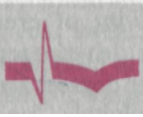
Ventricular complex	Stage	Changes	Time of appearance
	Acute	ST and T give one wave (monophase damage potential)	Hours and days from onset of infarction
	Subacute	Deep Q, low R, early differentiation of negative T	1-3 weeks from onset of infarction
	Restorative	Deep Q isoelectric S-T negative T (ischaemic)	2-6 weeks
	Cicatrization	Deep and broad Q, negative T	May remain permanently

Fig. 82. ECG signs of myocardial infarction at its various stages.

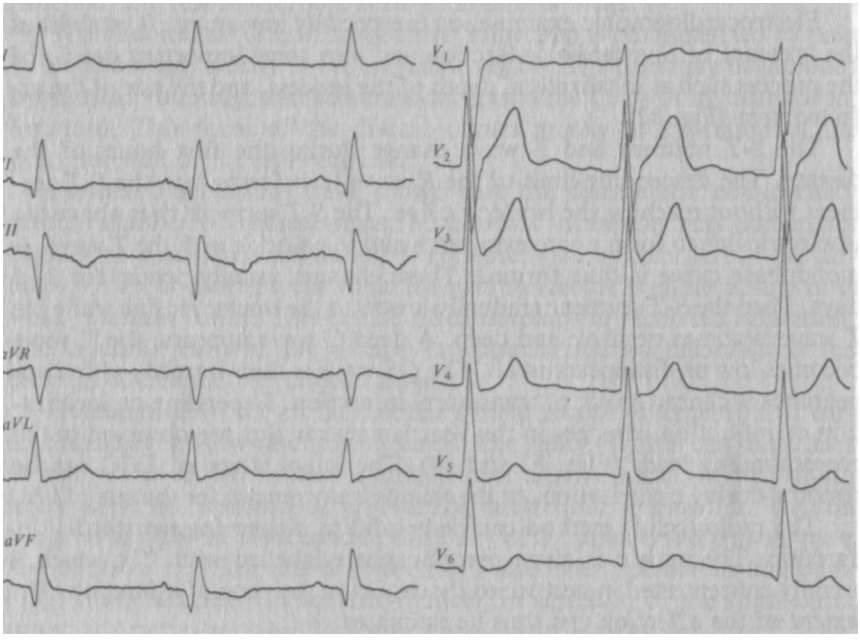


Fig. 83. ECG signs of focal myocardial infarction in the posterior wall of the hypertrophied left ventricle during cicatrization.

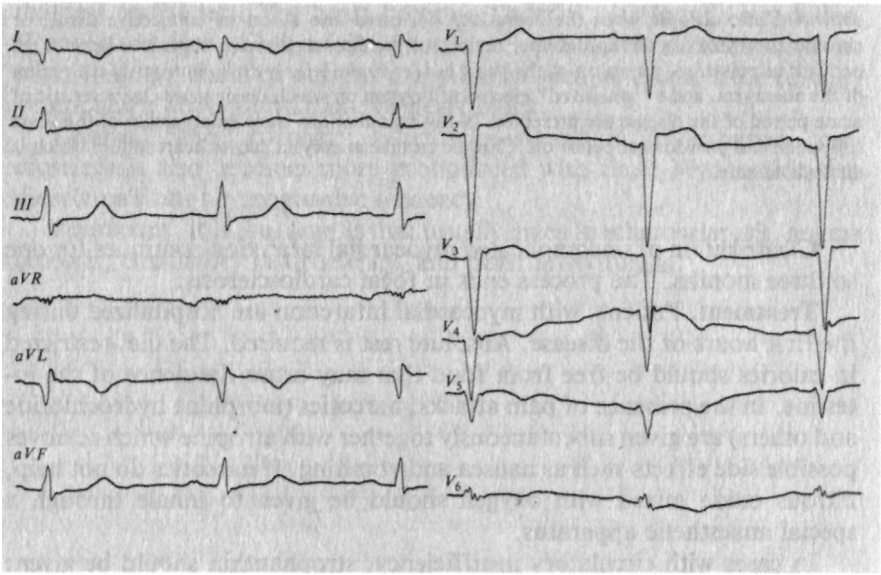


Fig. 84. Massive myocardial infarction of the entire anterior wall of the left ventricle, the apex, and the lateral wall.

in microfocal myocardial infarction. Moderately high temperature usually persists for 1-2 days. Mild leucocytosis is only transient; ESR is slightly increased and the enzymatic activity is increased. The ECG changes are as follows: the *S-T* segment is below and sometimes above the isoelectric line, and the *T* wave is either negative or two-phase. These changes disappear in a few days or in a month.

Course. This depends on the size of the affected area, the condition of other arteries of the heart and collateral circulation, on the degree of cardiac and circulatory insufficiency, and on the presence of complications. Cardiorrhexis is among them. It occurs during the first ten days of the disease, during pronounced myomalacia leading to rapid (within a few minutes) death. Fatal outcome may be caused by ventricular fibrillation. Cardiac aneurysm can develop during the disease. An acute aneurysm occurs during the first days of transmural infarction: the increased intraventricular blood pressure causes a protrusion at the site of myomalacia of intact layers of the heart wall. The aneurysm is usually formed in the wall of the left ventricle.

The *clinical picture* of acute cardiac aneurysm is characterized by pericardial pulsation in the 3rd or 4th intercostal space, to the left of the sternum. Auscultation of the heart reveals the gallop rhythm, systolic murmur, and pericardial friction. An acute cardiac aneurysm is

converted into chronic when the necrotized site turns into a scar of connective tissue, or chronic aneurysm can develop at later periods of the disease. Signs of chronic aneurysm are pericardial pulsation, extension of the heart border to the left, systolic murmur in the region of the aneurysm, and a "stabilized" electrocardiogram on which the changes characteristic of acute period of the disease are preserved. X-ray examinations show enlargement of the heart silhouette and paradoxical pulsation. Chronic cardiac aneurysm causes heart failure which is difficult to cure.

Cicatrization of uncomplicated myocardial infarction continues for one to three months. The process ends in focal cardiosclerosis.

Treatment. Patients with myocardial infarction are hospitalized during the first hours of the disease. Absolute rest is required. The diet restricted in calories should be free from food that may cause flatulence of the intestine. In the presence of pain attacks, narcotics (morphine hydrochloride and others) are given subcutaneously together with atropine which removes possible side effects such as nausea and vomiting. If narcotics do not help, nitrous oxide mixed with oxygen should be given to inhale through a special anaesthetic apparatus.

In cases with circulatory insufficiency, strophanthin should be given; noradrenaline or mesaton should be given intravenously by a drip method in collapse. Anticoagulants (of direct and then indirect action) should be given during the very first hours of the disease. The duration of hospital stay depends on the gravity of the clinical picture and the degree of the myocardial affection. Spasmolytics and sedatives should be given during the entire disease. Gross transmural, and also recurrent myocardial infarctions should be treated for 3-6 months. The patient often remains disabled.

Cardiosclerosis

Cardiosclerosis (fibroid heart) is the disease of the myocardium caused by developing fibroid elements (cicatrix) in the heart muscle. Atherosclerotic and myocarditic cardioscleroses are distinguished. The latter may result from any myocarditis. Atherosclerotic cardiosclerosis is the result of atherosclerosis of the coronary arteries (diffuse atherosclerotic cardiosclerosis). Myocardial infarction that ends in the formation of scars becomes the cause of focal post-infarction cardiosclerosis.

Clinical picture. The patient complains of decreased work capacity, dyspnoea, first only during heavy exertion, and if the heart muscle is affected considerably, these symptoms appear during usual walk or work. Objective examination of the patient reveals enlargement of the cardiac

dullness to the left. The heart becomes "aortic", its sounds are dulled. Pronounced signs of heart failure may develop later. Cardiosclerosis is the most frequent cause of various arrhythmias such as extrasystole (usually ventricular), atrial fibrillation, or heart block.

Course. Since coronary atherosclerosis tends to progress, cardiosclerosis also becomes more pronounced with time. Myocarditic cardiosclerosis has no progressive tendency.

Treatment. It is the same as that usually given in atherosclerosis, angina pectoris, circulatory insufficiency, and heart arrhythmias.

Chapter 7

DIGESTIVE SYSTEM

OESOPHAGUS

Methods of Examination

Inquiry

Complaints. *Dysphagia* (difficult passage of food via the oesophagus) is the most frequent symptom of oesophageal pathology. The patient feels difficulty in swallowing (mostly solid food); the food bolus sometimes stops in the oesophagus and the patient feels pain and oesophageal distention. Dysphagia can be due to organic or functional narrowing of the oesophagus. Organic stenosis develops gradually and progresses in cancer, and cicatricial stenosis of the oesophagus. Solid food first passes with difficulty, then the patient feels difficulty in swallowing soft, and then liquid food. When cancer tumour disintegrates, patency of the oesophagus may be restored almost completely. Dysphagia develops immediately in the presence of a foreign body or if the oesophagus is burnt. Dysphagia may also develop due to compression from outside by an aortic aneurysm or mediastinal tumour.

Functional narrowing of the oesophagus is explained by muscular spasms caused by reflex disorders in innervation of the oesophageal muscles, or by neurosis. As distinct from organic dysphagia, functional dysphagia more often occurs in paroxysms when food passes the oesophagus. Sometimes solid food passes more readily than liquid.

Pain occurs in acute inflammation of the oesophageal mucosa (oesophagitis) and in burns. The patient usually feels pain by the course of the entire oesophagus, both with and without swallowing; pain may radiate into the interscapular region.

Patients with achalasia of the cardia (cardiospasm) may have spontaneous attacks of pain, usually during night. Pain is quite severe; it radiates into the back, upwards by the oesophagus, into the neck, the jaws, and continues for minutes and even hours. In the presence of hiatus hernia and gastroesophageal reflux, pain may radiate into the left side of the chest and simulate heart diseases.

Oesophageal vomiting occurs in considerable narrowing of the oesophagus. Food is accumulated over the constricted point, in the wider portion of the oesophagus, and is expelled by antiperistaltic contractions of the muscles. Oesophageal vomiting differs from gastric vomiting in the following: it occurs without nausea and is preceded by the feeling of food

retained behind the sternum; the vomitus includes unaltered (non-digested) food which contains neither hydrochloric acid (gastric juice) nor pepsin; the vomitus containing food that has been taken long time ago has foul odour; taken food can be retained for long periods in the presence of oesophageal diverticulum or degrading cancer.

Regurgitation is the return of swallowed food into the mouth due to oesophageal obstruction. Regurgitation sometimes occurs in neuropathic patients in whom it becomes a habitual symptom or a result of cardiospasm.

Hypersaiivation occurs in oesophagitis, cicatricial narrowing of the oesophagus or in cancerous stenosis as a result of the oesophagosalivary reflex.

Afoul breath may be due to a cancer tumour of the oesophagus or congestion and decomposition of food in cardiospasm.

Heartburn (pyrosis) is a specific burning sensation behind the sternum associated with regurgitation of gastric contents into the inferior portion of the oesophagus. This is the cause of the so-called reflux oesophagitis.

Haemorrhage can be due to ulcer of the oesophagus, injury to the oesophagus by a foreign body, degradation of a tumour, bleeding of dilated oesophageal veins (which occurs in congestion of blood in the portal vein system), and also bleeding of the mucosa due to small lacerations of the vessels in the oesophagogastric junction in straining and vomiting (Mallory-Weiss syndrome).

History of present disease. In organic affections of the oesophagus, the disease has a progressive course. Functional diseases (cardiospasm) are characterized by exacerbations connected with psychogenic factors which are followed by remissions. From the anamnesis of the patient's life it can be established whether the patient had past burns of the oesophagus, since acid or alkali burns are frequent causes of cicatricial changes in the oesophagus. Syphilis is an important disease of the past history since the patient's complaints of dysphagia can sometimes be associated with syphilitic aortitis (compression of the oesophagus by a dilated aorta). Development of traction diverticula in the oesophagus may be due to broncho-adenitis in the past (tuberculous broncho-adenitis included). Pulsion diverticula arise due to oesophagospasm.

Physical Examination

The main objective examination techniques are unimportant for diagnosis of oesophageal pathology. The general inspection of the patient with dysphagia may suggest an organic affection of the oesophagus if the patient is extremely asthenic (cachexia).

Laboratory and Instrumental Methods

Laboratory methods of diagnostication include *cytological studies* of washings obtained by lavage of the oesophagus with an isotonic sodium chloride solution, or by artificial separation of cells using a bulbous bougie which has rough surface. This procedure should obligatory be done in all cases of suspected newgrowths.

X-ray studies are decisive for diagnosis of oesophageal diseases. Contraindications to X-raying are possible destructive effects of this procedure on the oesophageal wall. Barium sulphate suspensions of various consistency are used as a contrast substance for X-ray examinations. When the suspension is swallowed, the oesophagus becomes visible over its entire length. The oesophageal function can be assessed by observing the passage of the swallowed suspension during roentgenoscopy. X-rays can be used to record separate moments of the oesophagus filling, and also to assess the condition of the oesophageal mucosa. Roentgenocinematography makes it possible to assess peristaltic and contraction ability of the oesophagus. The condition of the oesophageal lumen can be fully assessed only by examining the patient in various positions, e.g. vertical, horizontal, and with the head-end of the bed being thrown back.

The motor function of the oesophagus can be assessed by *balloon kymography*. Endoscopy with an oesophagofibroscope (a fibre-optic apparatus provided with a device for taking samples of newgrowths protruding into the lumen of the oesophagus) is a valuable diagnostic method. The instrument is very flexible and convenient for endoscopic procedures. Burns of the oesophagus (the first 7-10 days of the disease), corrosive oesophagitis, aortic aneurysm, hypertension (III stage), circulatory insufficiency, and diseases of the larynx are contraindications to oesophagoscopy.

Special Pathology

Achalasia of the Cardia

Achalasia (syn. cardiospasm, megaoesophagus) is characterized by the failure of atonic muscles of the cardia to relax, disturbed peristaltic activity of the oesophagus, deranged reflex opening of the cardia on swallowing, and hence impaired passage of food into the stomach and dilatation of the oesophagus due to retention of food in it.

The aetiology and pathogenesis of this condition are not sufficiently studied.

Pathological anatomy. The disease is characterized by dystrophic changes in the intramural nerve plexus of the oesophagus and cardia, dilatation of the oesophagus, and congestive oesophagitis.

Clinical picture. Retrosternal pain, dysphagia and regurgitation are the main symptoms. The pain manifests itself by paroxysmal attacks occurring usually at night, and is often associated with the empty or, on the contrary, overdistended oesophagus. Dysphagia is first occasional. In advanced cases it occurs during each meal and is especially marked during swallowing dry or inadequately chewed food in hurried eating. Emotional stress intensifies dysphagia. In order to facilitate the passage of food into the stomach, the patient resorts to various tricks such as drinking a gulp of water or taking a deep breath, which sometimes helps. The food mass is regurgitated as a person bends down with his oesophagus overfilled or during night sleep. The regurgitated mass may be aspired causing recurrent aspiration pneumonia.

The diagnosis is confirmed by X-ray examination which demonstrates dilatation and elongation of the oesophagus (sometimes a sigmoid dilatation) of varying degree, upset peristalsis, accumulation of liquid (saliva, mucus) or food in the oesophagus while the stomach is empty. A barium meal is retained in the oesophagus and its upper level is often as high as the clavicle. (The barium swallow would then suddenly 'fall' into the stomach.) The cardial segment of the oesophagus is narrowed and has regular outlines; it does not open on swallowing and the barium meal does not pass into the stomach; the gastric air bubble is absent (the pathognomonic sign).

Course. The disease progresses rapidly with intensifying dysphagia and other symptoms; weight loss is also progressive. Recurrent pneumonia and chronic bronchitis supervene due to aspiration of regurgitated oesophageal contents.

Treatment. The efficacy of medication is low. The condition is commonly corrected by cardiodilatation using Einhorn's dilator, or by balloon dilatation which are usually performed in specialized hospitals. Cases with severe dilatation and elongation of the oesophagus require surgical treatment.

Oesophagitis

Oesophagitis is inflammation of the oesophagus. It is a common disease of the gastrointestinal tract. Acute and chronic oesophagitis are distinguished.

Aetiology and pathogenesis. Acute oesophagitis develops in response to irritation of the oesophageal mucosa by hot food or drinks, by chemicals

(iodine tincture, strong acids, or alkalies); it may be secondrary to acute infectious diseases such as scarlet fever, diphtheria, sepsis, or may attend acute pharyngitis or gastritis. Chronic oesophagitis develops due to repeated exposure of the oesophageal mucosa to hot or rough (spicy) food, alcohol, some industrial poisons that are inhaled with dust or ingested with food, etc. Congestive oesophagitis develops due to retention and decomposition of food in the oesophagus in achalasia and oesophageal stenosis patients. A more common cause of subacute and chronic oesophagitis is the reflux of the gastric juice into the oesophagus due to cardial insufficiency (reflux oesophagitis). Reflux oesophagitis usually occurs in axial hiatal hernia. Cardial insufficiency and reflux oesophagitis may also be secondary to surgical procedures (resection of or injury to the cardial sphincter). Relative, i.e. functional cardial insufficiency may be seen in peptic ulcer, cholelithiasis, and some other diseases. It is due to spastic contraction of the pylorus or gastric hypertonia and high intragastric pressure. Cardial insufficiency and reflux oesophagitis occur in pregnancy and large new-growths of the abdominal cavity (due to high intra-abdominal pressure).

Pathogenesis. The condition arises as a result of irritation which may be thermal, chemical, toxic, or peptic (in cardial insufficiency and reflux oesophagitis); bacterial toxic or toxic-allergic effects may in rare cases produce oesophagitis as well.

Clinical picture. This depends on the acuity of the process, its aetiology, and extension. Acute catarrhal oesophagitis presents with pain on swallowing, discomfort, and sometimes dysphagia. Haemorrhagic oesophagitis can be manifested by haematemesis and melaena. Pseudomembranous oesophagitis (it usually supervenes diphtheria and scarlet fever) is characterized by the presence of fibrin membranes in the vomitus. The clinical picture is especially severe in cases where abscess and phlegmon of the oesophagus are aggravated by sepsis and toxaemia (phlegmonous oesophagitis).

Chronic oesophagitis presents with heartburn and retrosternal discomfort. In rare cases there is pain and dysphagia. The main symptoms of reflux oesophagitis are heartburn and regurgitation which intensify on lying down or when the patient bends. Retrosternal pain on swallowing (sometimes resembling coronary pain) is not infrequent.

Radiography provides little evidence for the diagnosis of oesophagitis. In reflux oesophagitis it usually reveals hiatal hernia and visualizes gastro-oesophageal reflux. The patient must be examined in both the vertical and horizontal positions, and the intra-abdominal pressure must be raised by coughing, sneezing, straining the prelum, or by applying the pressure of the X-ray tubulus to the epigastrium. Oesophagoscopy is decisive in the

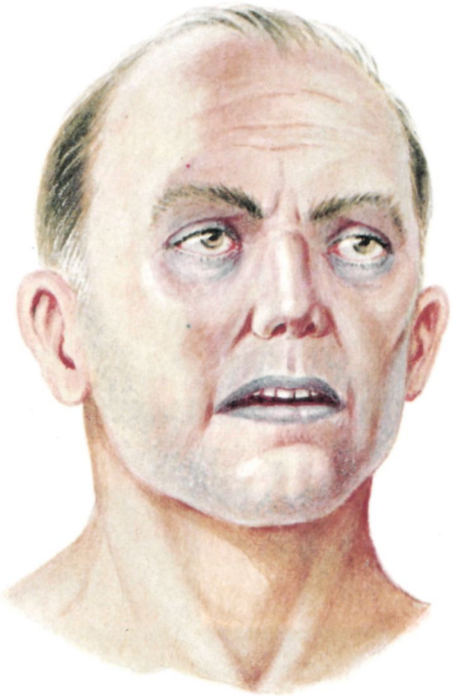


Plate 1. Cyanosis.

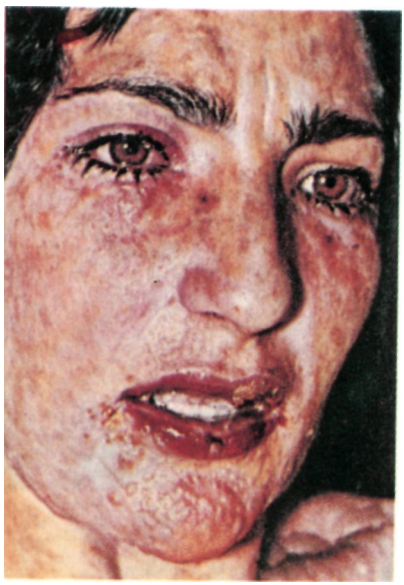


Plate 2. Erythema.

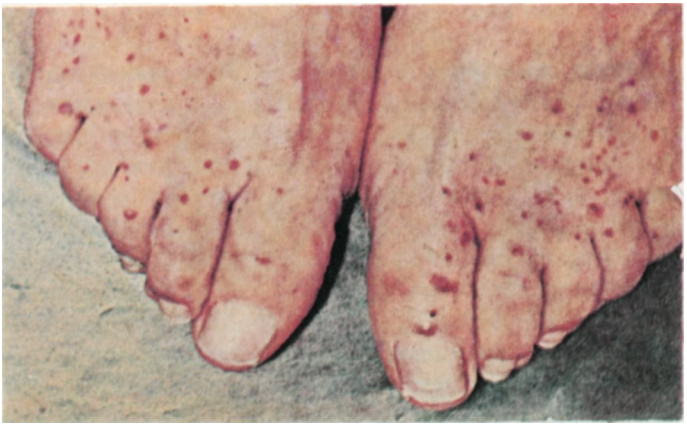


Plate 3. Purpura.

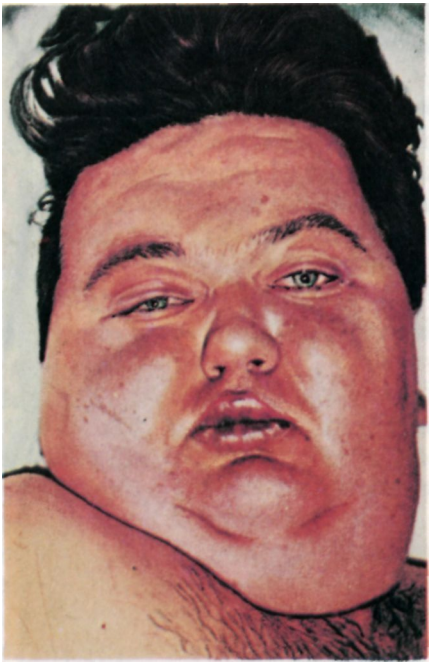
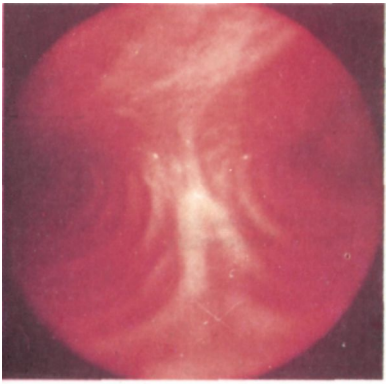
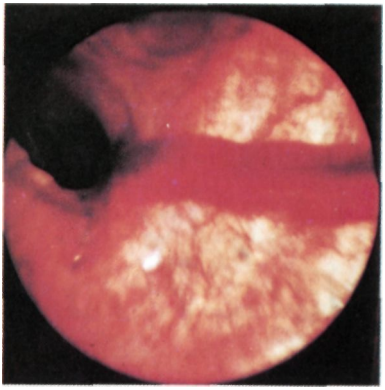
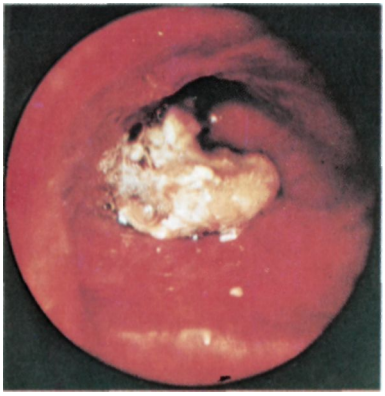


Plate 4. Obesity.







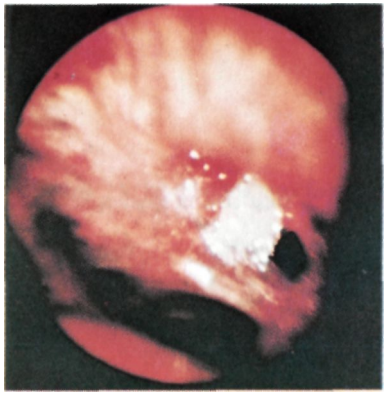


Plate 5. Bronchoscopic pictures.

a—normal bronchoscopic picture of bifurcation of the trachea and openings to the main bronchi; *b*—haemorrhage in the bronchus (a streak of blood is seen); c—bronchohth; *d*—exophytic form of central cancer of the bronchus.

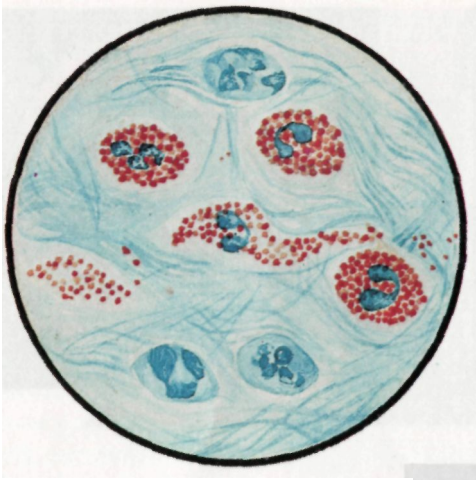


Plate 6. Eosinophils.

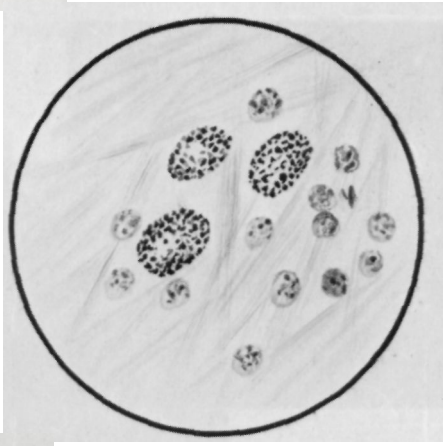


Plate 7. Dust cells in sputum.

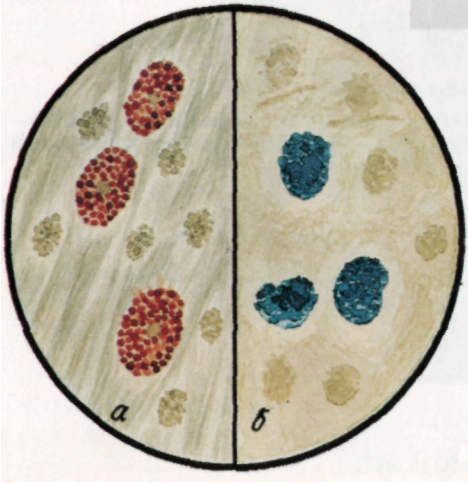


Plate 8. Heart failure cells.
a—in native preparation; *b*—stained by Berlin blue.

Plate 9. Eosin-stained elastic fibres.

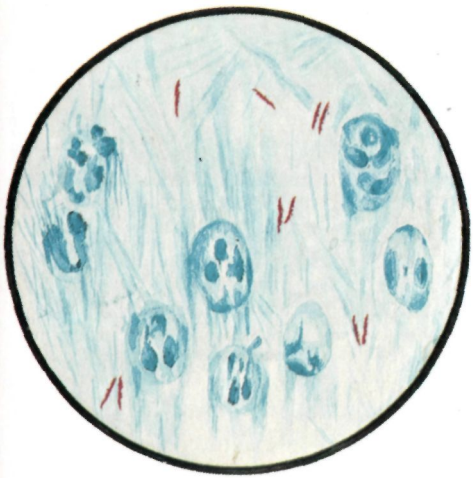


Plate 10. Tuberculosis mycobacteria.

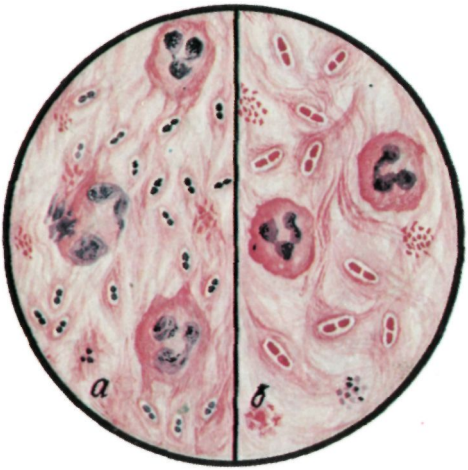
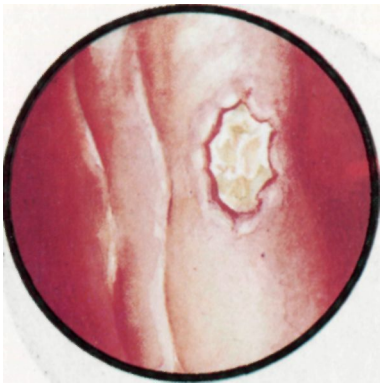
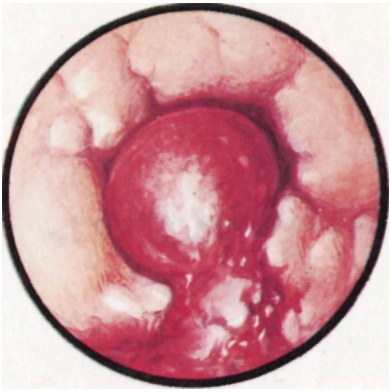


Plate 11. Pneumococcus *(a)* and Friedlander's diplobacillus *(b)*.





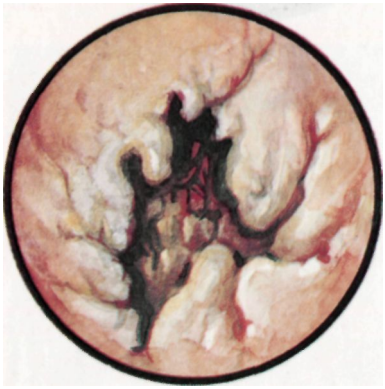


Plate 12. Gastrofibroscopic pictures. a—acute gastric ulcer; *b*—bleeding polyp of the antral part of the stomach; c—chronic gastric ulcer.

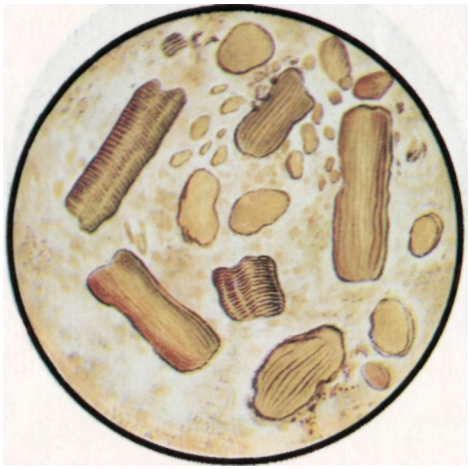
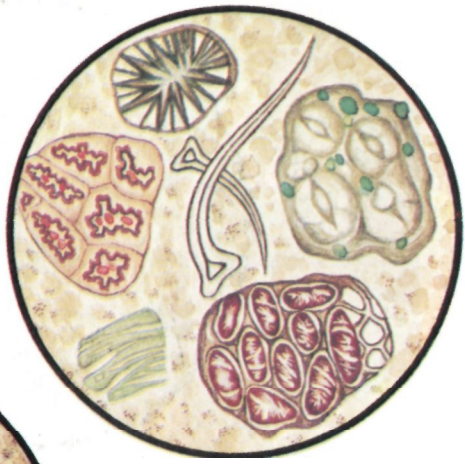


Plate 13. Coprology: undigested muscle fibres.

Plate 14. Coprology: undigested plant cellular tissue.



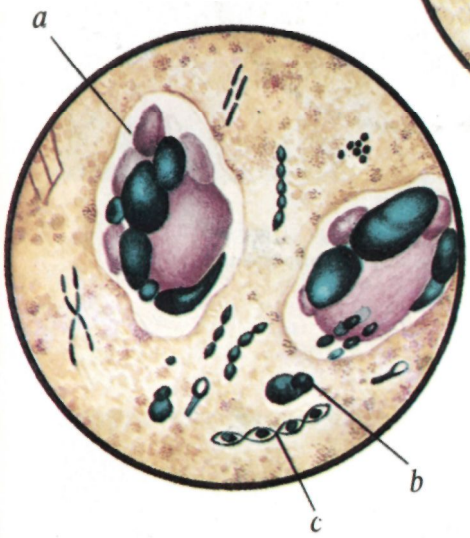
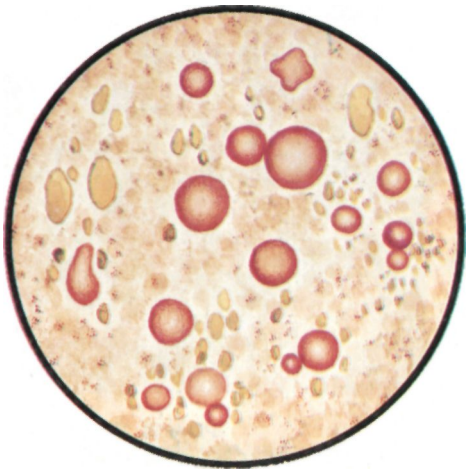


Plate 15. Coprology.

a—potato cells with grains stained by Lugol's solution; *b* and *c*—iodophilic flora.

Plate 16. Coprology: neutral fat (Sudan-stained).



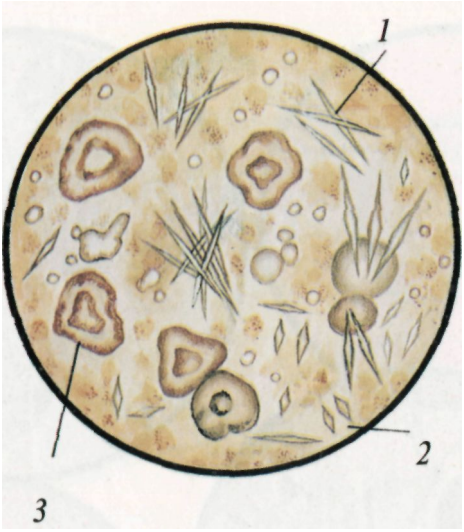


Plate 17. Coprology.
1—fatty acids; *2*—crystalline soaps; 3—soap grains.

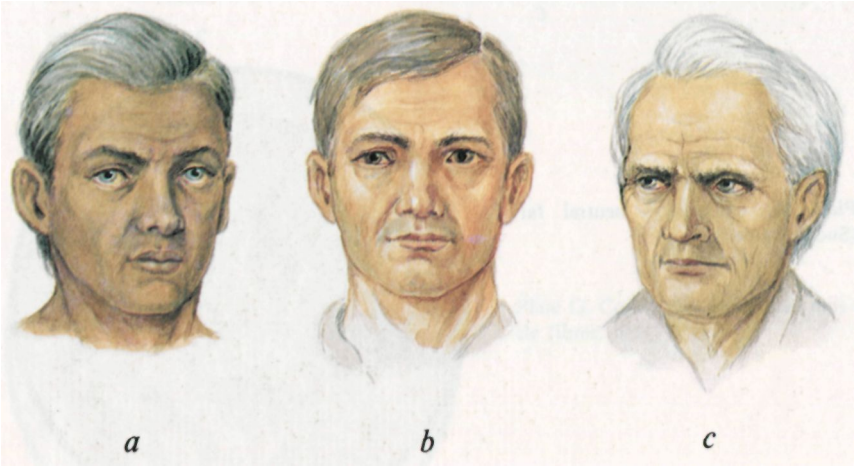


Plate 18. Various types of jaundice.
a—obstructive; *b*—parenchymatous; *c*—haemolytic.

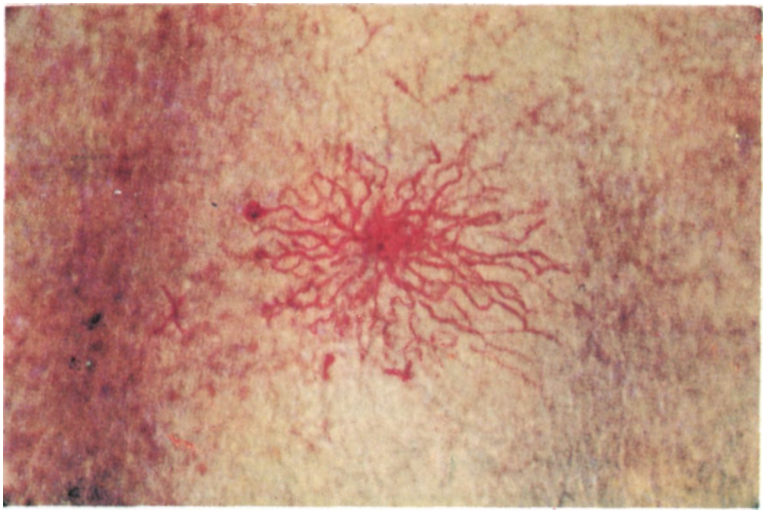


Plate 19. Spider angioma (telangiectasia).

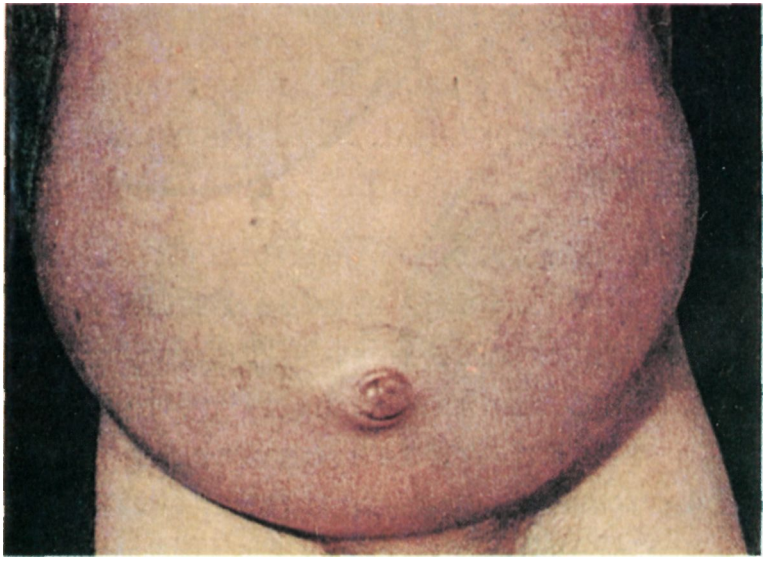


Plate 20. Abdominal distension in ascites with everted umbilicus and prominent venous pattern.

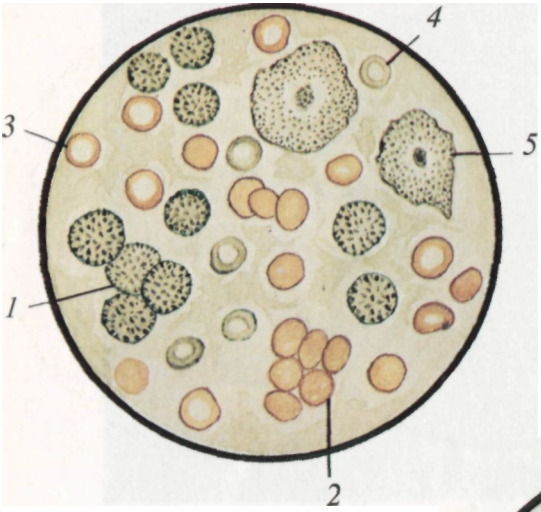


Plate 21. Microscopy of urine sediment.

1—leucocytes; *2*—unaltered red blood cells; *3*—slightly altered red blood cells; *4*—altered red blood cells (leached); *5*—squamous epithelium cells.

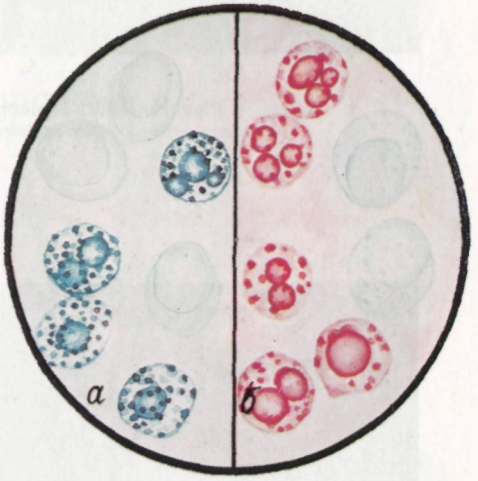


Plate 22. Motile leucocytes in urine sediment.

a—stained with methylene blue; *b*—stained with a mixture of gentian violet and safranine.

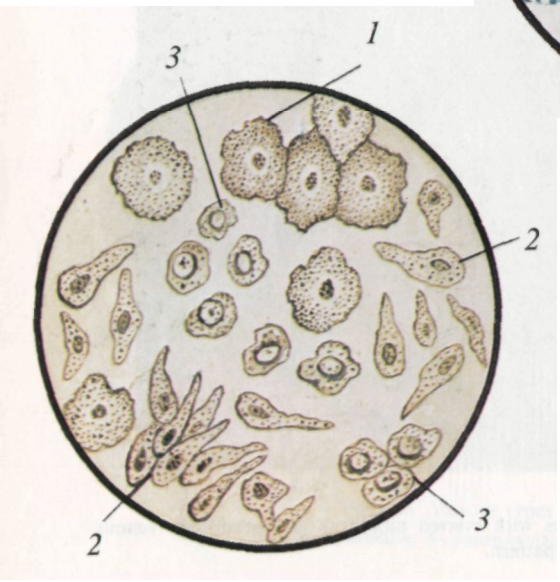


Plate 23. Epithelial cells in urine sediment.

1—squamous epithelium; *2*—transitional epithelium; *3*—glomerular epithelial cells.

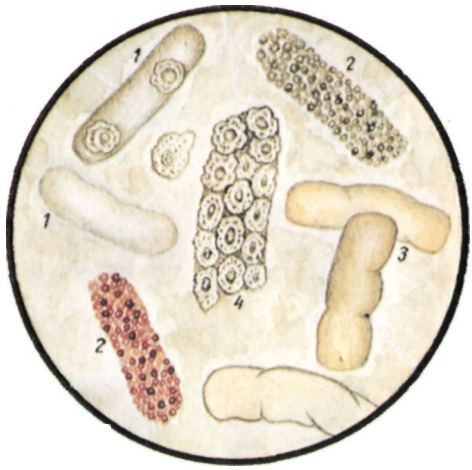


Plate 24. *Casts* in urinary sediment.
1—hyaline cast; *2*—granular casts; *3*—waxy casts; *4*—epithelial cast.

Plate 25. Salts of acid urinary sediment.
1—calcium oxalate crystals; *2*—uric acid crystals.

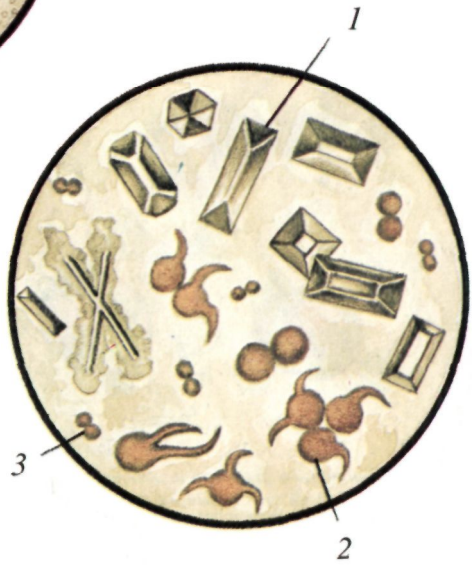


Plate 26. Salts found in alkaline urinary sediment.
1—triple phosphate; *2*—ammonium urate; *3*—lime carbonate

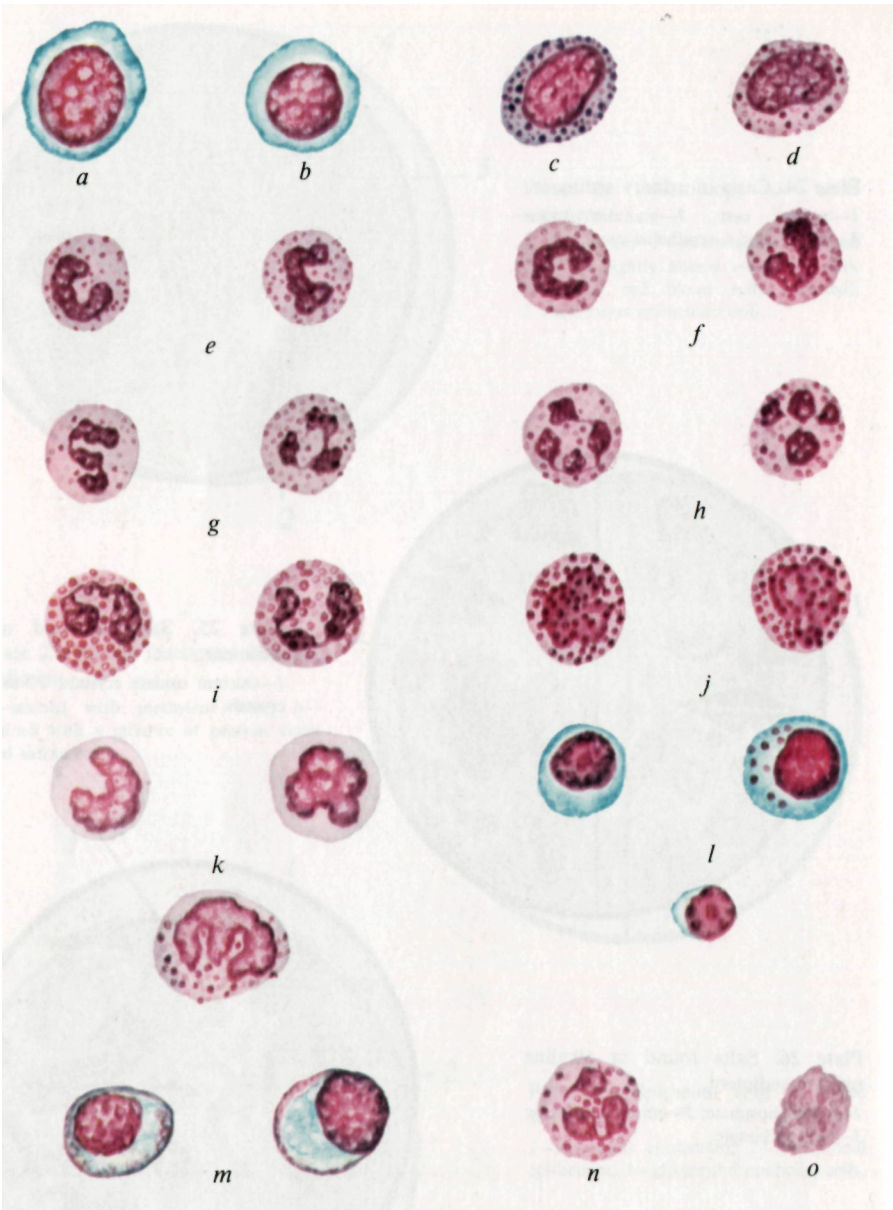


Plate 27. Leucopoietic cells.

a—stem cell; *b*—myeloblast; *c*—promyelocyte; *d*—myelocyte; *e*—metamyelocyte; /—stab neutrophil; *g, h*—segmented neutrophils; *i*—eosinophils; *j*—basophils; *k*—monocytes; *l*—lymphocytes; *m*—plasma cells; «—neutrophils with toxic grains; *o*—Botkin-Gumprecht silhouettes.

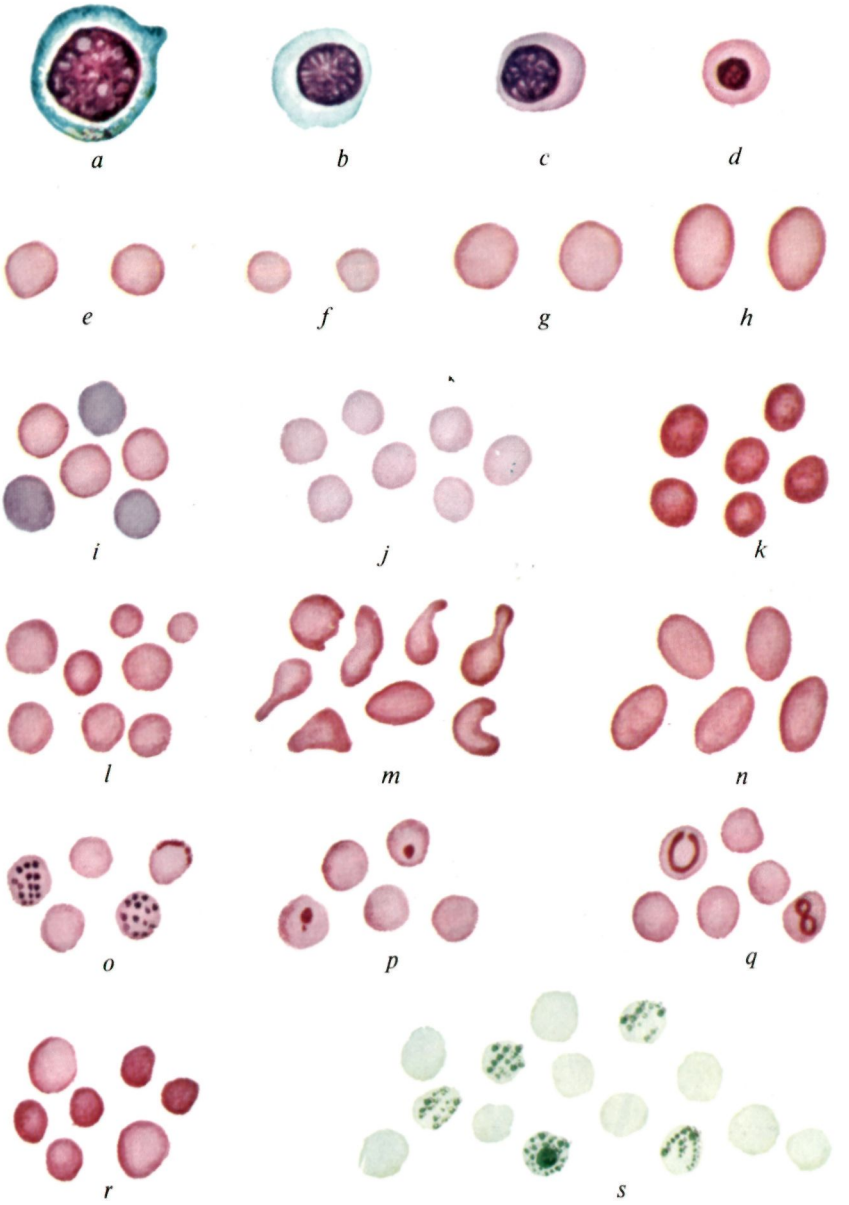


Plate 28. Erythropoietic cells.

a—erythropoietin-sensitive cell (precursor of erythropoiesis); *b*—basophilic erythroblast; *c*—polychromatic erythroblast; *d*—oxyphilic erythroblast; *e*—normocytes; *f*—microcytes; *g*—macrocytes; *h*—megalocytes; i—polychromatic erythrocytes; *j*—hypochromic erythrocytes; *k*—hyperchromic erythrocytes; *l*—anisocytes; *m*—poikilocytes; *n*—ovalocytes; *o*—erythrocytes with basal granules; *p*—Jolly's bodies; *q*—Cabot's rings; *r*—microspherocytes; *s*—reticulocytes.

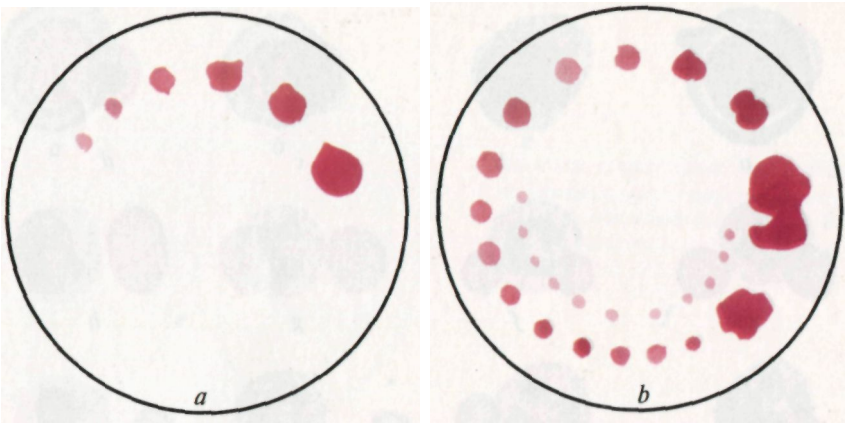


Plate 29. Determining bleeding time after Duke in norm (a) and in Werlhofs disease *(b)*.

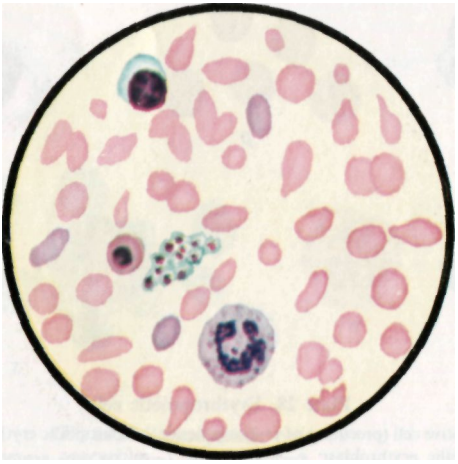


Plate 30. Blood in iron deficiency posthaemorrhagic anaemia.

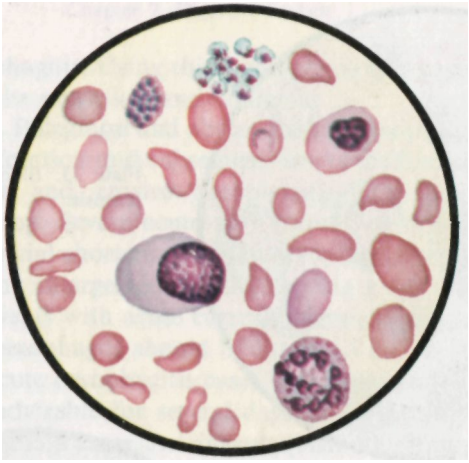


Plate 31. Blood in vitamin B_{12} (folic acid) deficiency anaemia.

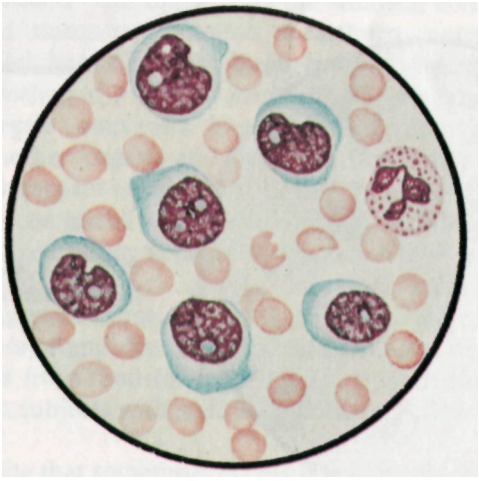


Plate 32. Blood in acute leucosis.

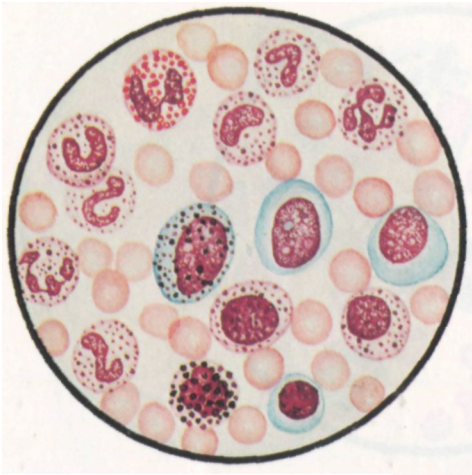


Plate 33. Blood in chronic myeloleucosis.

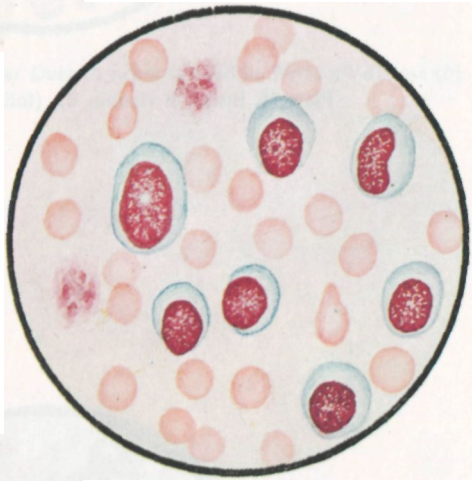


Plate 34. Blood in chronic lympholeucosis.

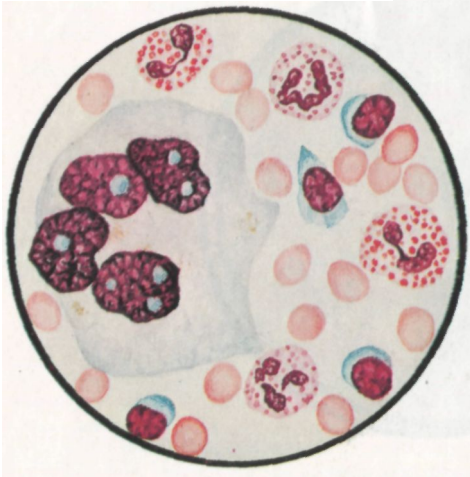


Plate 35. Lymph node punctate in lymphogranulomatosis.

diagnosis of oesophagitis. Using this technique allows to assess the degree of inflammation, its extension and character.

Complications. Phlegmon and abscess of the oesophagus may be complicated by its perforation and subsequent severe mediastinitis or peritonitis. Haemorrhagic and erosive oesophagitis may be attended with oesophageal bleeding. Severe acute and chronic oesophagitis may cause stricture and cicatricial shortening of the oesophagus which, in turn, promotes formation or enlargement of the existing axial hiatal hernia.

Treatment. Patients with acute corrosive oesophagitis and abscess and phlegmon of the oesophagus should be managed in a hospital setting. In all acute and subacute oesophagitis cases bland feeds are prescribed. Fasting is sometimes advisable for several days. Antibiotics are administered in abscess and phlegmon cases. Astringents (bismuth nitrate, 1.0 g, or 20 ml of a 0.06 per cent silver nitrate solution, 4-6 times a day before meals) are given for other acute forms of oesophagitis. Any job that might require bending down or strain of the abdominal muscles is contraindicated to patients with reflux oesophagitis. Sleeping in the semireclining position is recommended.

STOMACH

Methods of Examination

Inquiry

Complaints. Patients with diseases of the stomach complain of poor appetite, perverted taste, regurgitation, heartburn, nausea, vomiting, epigastric pain, and haematemesis. Regurgitation, heartburn, nausea, vomiting, and the feeling of overfilled stomach after meals are the group of the so-called dyspeptic complaints. These symptoms may be observed in diseases of some other organs and systems. Determining the specific character of each symptom is important during inquiry of the patient.

Deranged (poor or increased) *appetite* occurs in infectious diseases, metabolic disorders, etc. Poor appetite or its complete absence (anorexia) is usually characteristic of gastric cancer. This symptom is often an early sign of cancer. Appetite often increases in peptic ulcer, especially in duodenal ulcer. Loss of appetite should be differentiated from cases when the patient abstains from food for fear of pain (cibophobia). This condition often occurs in subjects with gastric ulcer, though their appetite is increased.

Perverted appetite that sometimes occurs in patients is characterized by the desire to eat inedible materials such as charcoal, chalk, kerosine, etc.

Appetite is perverted in pregnant women and in persons suffering from achlorhydria. Some patients with cancer of the stomach or some other organs often feel aversion to meat. The developmental mechanism of appetite is connected with excitation of the food centre (according to Pavlov). Excitation or inhibition of this centre depends on impulses arriving from the cerebral cortex, on the condition of the vegetative centres (excitation of the vomiting centre causes loss of appetite), and on reflex effects from the alimentary organs. The multitude of factors that act on the food centre account for the high variation in appetite.

Taste may be perverted due to the presence of unpleasant taste in the mouth and partial loss of taste in an individual. It can often be associated with some pathology in the mouth, e.g. caries or chronic tonsillitis. A coated tongue can be another cause of unpleasant taste in the mouth.

Regurgitation usually implies two phenomena: a sudden and sometimes loud uprise of wind from the stomach or oesophagus (eructation), and the return of swallowed food into the mouth (sometimes together with air). Regurgitation depends on contraction of the oesophageal muscles with the open cardia. Regurgitation may be due to air swallowing (aerophagy). It is heard at a distance and occurs in psychoneurosis. In the presence of motor dysfunction of the stomach, fermentation and putrefaction of food with increased formation of gas occur in the stomach (the phenomenon otherwise absent in norm). In abnormal fermentation in the stomach, the eructated air is either odourless or smells of bitter oil, which is due to the presence of butyric, lactic and other organic acids that are produced during fermentation in the stomach. In the presence of abnormal putrefaction, the belched air has the odour of rotten eggs (hydrogen sulphide). Bitter belching indicates intensive degradation of proteins. Belching is characteristic of stenosed pylorus with great distention of the stomach and significant congestion in it. Acid regurgitation is usually associated with hypersecretion of gastric juice and occurs mostly during pain attacks in ulcer. But it can also occur in normal or insufficient secretion of the stomach in the presence of insufficiency of the cardia (when the stomach contents are regurgitated into the oesophagus). Bitter regurgitation occurs in cases with belching up of bile into the stomach from the duodenum, and also in hyperchlorhydria; bitterness depends on the bitter taste of peptones.

Pyrosis is otherwise known as *heartburn,* i.e. burning pain in the epigastric and retrosternal region. Heartburn arises in gastro-oesophageal reflux, mostly in the presence of gastric hyperacidity in various diseases of the alimentary tract (e.g. peptic ulcer or cholecystitis), hiatus hernia, and sometimes in pregnancy. Heartburn in healthy subjects can be due to hypersensitivity to some foods.

Nausea, the reflectory act associated with irritation of the vagus nerve, is an indefinite feeling of sickness and sensation of compression in the epigastrium. Nausea is often attended by pallidness of the skin, general weakness, giddiness, sweating, salivation, fall in the arterial pressure, cold in the limbs, and sometimes semisyncopal state. Nausea often (but not necessarily) precedes vomiting. The mechanism of nausea is not known. Its frequent association with vomiting suggests that it might be the early sign of stimulation of the vomiting centre. The leading role in the development of nausea is given to the nervous system and also the tone of the stomach, the duodenum, and the small intestine. Nausea may develop without any connection with diseases of the stomach, e.g. in toxaemia of pregnancy, renal failure, deranged cerebral circulation, and sometimes in healthy people in the presence of foul odour (or in remembrance of something unpleasant). Some diseases of the stomach are attended by nausea, e.g. acute and chronic gastritis or cancer of the stomach. Nausea associated with gastric pathology usually occurs after meals, especially after taking some pungent food. Nausea often develops in secretory insufficiency of the stomach.

Vomiting (emesis) occurs due to stimulation of the vomiting centre. This is a complicated reflex through the oesophagus, larynx and the mouth (sometimes through the nose as well). Vomiting may be caused by ingestion of spoiled food, by seasickness, or irritation arising inside the body (diseases of the gastro-intestinal tract, liver, kidneys, etc.). In most cases vomiting is preceded by nausea and sometimes hypersalivation. Factors causing the vomiting reflex are quite varied. This can be explained by the numerous connections that exist between the vomiting centre (located in the medulla oblongata, in the inferior part of the floor of the 4th ventricle) and all bodily systems. Depending on a particular causative factor, the following can be differentiated: (1) nervous (central) vomiting; (2) vomiting of visceral aetiology (peripheral or reflex); (3) haematogenic and toxic vomiting.

Vomiting is an important symptom of many diseases of the stomach, but it can be regarded as the symptom of a particular disease only in the presence of other signs characteristic of this disease. Vomiting of gastric aetiology is caused by stimulation of receptors in the gastric mucosa by inflammatory processes (acute or chronic gastritis), in ingestion of strong acids or alkalis, or food acting on the gastric receptors by chemical (spoiled food) or physical (overeating or excessively cold food) routes. Vomiting can also be caused by difficult evacuation of the stomach due to spasms or stenosed pylorus.

If the patient complains of vomiting, the physician should inquire about the time when the vomiting occurred, possible connections with

meals, association with pain, the amount and character of the vomited material. Morning vomiting (on a fasting stomach) with expulsion of much mucus is characteristic of chronic gastritis, especially in alcoholics. Hyperacid vomiting in the morning indicates nocturnal hypersecretion of the stomach. Vomiting occurring 10-15 minutes after meals suggests ulcer or cancer of the cardial part of the stomach, or acute gastritis. If vomiting occurs 2-3 hours after meals (during intense digestion) it may indicate ulcer or cancer of the stomach body. In the presence of ulcer of the pylorus or duodenum, vomiting occurs 4—6 hours after meals. Expulsion of food taken a day or two before is characteristic of pyloric stenosis. Patients with peptic ulcer often vomit at the height of pain thus removing it, which is typical of the disease. The odour of the vomit is usually acid, but it can often be fetid (putrefactive processes in the stomach); the odour may be even faecal (in the presence of a faecal fistula between the stomach and the transverse colon).

The vomited material may have acid reaction (due to the presence of hydrochloric acid, in hyperchlorhydria), neutral (in achylia), or alkaline (in the presence of ammonia compounds, in pyloric stenosis, hypofunction of renal function, and also in regurgitation of the duodenal contents into the stomach). Vomitus may contain materials of great diagnostic importance, e.g. blood, mucus (in chronic gastritis), ample bile (narrowing of the duodenum, gastric achylia), and faecal matter. Vomiting may attend acute gastritis, exacerbation of chronic gastritis, gastric neurosis, peptic ulcer, spasm and organic stenosis of the pylorus, and cancer of the stomach.

Pain is the leading symptom in diseases of the stomach. Epigastric pain is not obligatory connected with diseases of the stomach. It should be remembered that the epigastrium is the "site of encounter" of all kinds of pain. Epigastric pain may be due to diseases of the liver, pancreas, and due to hernia of the linea alba. Epigastric pain may develop in diseases of other abdominal organs (sometimes of organs located outside the abdomen) by the viscero-visceral reflex (acute appendicitis, myocardial infarction, affection of the diaphragmatic pleura, etc). In order to locate correctly the source of pain, the physician should ask the patient (1) to show exactly the site of pain; (2) to characterize the pain which may be periodical or paroxysmal (at certain time of the day); permanent or seasonal (in spring or autumn); (3) to describe the connection (if any) between pain and meals, the quality of food and its consistency; (4) to indicate possible radiation of pain (into the back, shoulder blade, behind the sternum, left hypochondrium); (5) to describe conditions under which pain lessens (after vomiting, after taking food or baking soda, after applying hot-water bottle or taking spasmolytics); (6) to describe possible connections between pain and

physical strain (weight lifting, traffic jolting, etc.), or strong emotions. Intensity and character of pain are also important diagnostically. The pain may be dull, stabbing, cutting, etc. Pain in hollow organs with smooth muscles (e.g. stomach) is provoked by spasms (spastic pain), distension of the organ (distensional pain), and by its motor dysfuncion.

Paroxysmal, periodical epigastric pain is due to the spasm of the pyloric muscles. It arises under the influence of strong impulses arriving from the vagus nerve centre in cerebral cortex dysfunction. The spasm of the pylorus is stimulated by the hyperacidity of gastric juice due to hyperstimulation of the vagus. Depending on the time of paroxysmal pain (after meals), it may be early (occurring 30-40 min after meals), late (90-120 min after meals), nocturnal, and hunger pain (which is abated after taking food). If pain occurs after meals stimulating secretion of gastric juice (bitter, pungent, spicy or smoked foods), this indicates the leading role of hypersecretion in its aetiology. The pain then localizes in the epigastrium, radiates to the back, and is rather intense; it is abated after vomiting and taking alkali or foods that decrease acidity of gastric juice, and also after taking antispastic preparations and applying hot-water bottle (which removes spasms).

A seasonal character of pain, i.e. development of periodic pain during spring and autumn, is characteristic of peptic ulcer, especially if the process is localized in the peripyloric region. Permanent boring pain is usually caused by stimulation of the nerve elements in the mucous and submucous layer of the stomach; the pain is usually intensified after meals and is characteristic of exacerbation of chronic gastritis or cancer of the stomach.

Perigastritis (chronic inflammation of the peritoneum overlying the stomach and its adhesion to the neighbouring organs) is manifested by pain developing immediately after taking much food (irrespective of its quality). The full stomach distends to stimulate nerve fibres in the adhesions. In the presence of perigastritis and adhesions between the stomach and the adjacent organs, pain may be caused by any physical strain and when the patient changes his posture.

Gastric haemorrhage is a very important symptom. It can be manifested by vomiting of blood (haematemesis) or by black tarry stools (melaena). Gastric haemorrhage is usually manifested by the presence of blood in the vomitus. The colour of the vomitus depends on the time during which the blood is present in the stomach. If the blood was in the stomach for a long time, the blood reacts with hydrochloric acid of the gastric juice to form haematin hydrochloride. The vomitus looks like coffee grounds. If haemorrhage is profuse (damage to a large vessel) the vomitus contains much scarlet (unaltered) blood. Haematemesis occurs in peptic ulcer, cancer, and polyps, in erosive gastritis, rarely in sarcoma,

tuberculosis and syphilis of the stomach, and in varicosity of the oesophageal veins. Tarry stools are not an obligatory sign of gastric haemorrhage.

When collecting **anamnesis,** the patient should be asked about his nutrition. It is important to establish if meals are regular because taking food at random is an important factor in the aetiology of gastric diseases. Food quality is as important as its amount taken during one meal. Mastication of food matters as well. Conditions of rest and work, and possible occupational hazards should be established. Abuse of alcohol and smoking are important factors in the aetiology of gastric diseases. It is very important to find out if the patient's condition has undergone some changes during recent time (e.g. loss of weight, anaemia, blood vomiting, or tarry stools). Gastro-intestinal diseases of the past, surgical intervention on the abdominal organs, long medication with preparations irritating the stomach mucosa (acetylsalycilic acid, sodium salycilate, steroid hormones, potassium chloride, etc.) are also very important.

Physical Examination

INSPECTION

During general inspection of the patient the physician may assess poor nutrition of the patient (cachexia) which is characteristic of stomach cancer and untreated benign pyloric stenosis. Pale skin is observed after gastric haemorrhage. Patients with uncomplicated peptic ulcer look practically healthy.

Next stage is inspection of the mouth. The absence of many teeth accounts for inadequate disintegration and mastication of food in the mouth, while the presence of carious teeth favours penetration of microbial flora into the stomach. The tongue is not the "mirror of the stomach" as it was formerly believed. Nevertheless in some diseases its appearance is informative: clean and moist tongue is characteristic of uncomplicated peptic ulcer, while the tongue coated with a foul smelling white-grey material is characteristic of acute gastritis; a dry tongue indicates a severe abdominal pathology or acute pancreatitis; a tongue with atrophied papillae suggests cancer of the stomach, atrophic gastritis with pronounced gastric secretory hypofuncion, or vitamin B deficiency.

Inspection of the abdomen may give information about the contours and peristalsis of the stomach if the patient is cachectic. In pathological cases (pyloric stenosis), peristalsis can be easily seen (ridges raising the abdominal wall). If the physician rubs or taps on the epigastric region

peristalsis becomes more distinct. Sometimes, in neglected cases, the abdominal wall can be protruded (tumour).

PALPATION

The stomach should be palpated in both the vertical and horizontal position of the patient because the lesser curvature of the stomach and its high standing tumours are impalpable in the lying position. First palpation should be superficial and tentative. Its aim is to establish tenderness of the epigastrium, irritation of the peritoneum (Shchetkin-Blumberg symptom), divarication of the abdominal muscles, the presence of hernia of the linea alba, tension in the abdominal wall in the region of the stomach, and the presence of muscular defence (defense musculaire). Deep palpation of the stomach should be carried out according to Obraztsov and Strazhesko. The examiner pulls up the skin on the abdomen and presses carefully the anterior wall of the abdomen to penetrate the depth until the examining fingers reach the posterior wall. When pressed against the posterior wall of the abdomen, the stomach slips from under the examining fingers. The shape of the stomach and the size of the examined part can thus be assessed. The greater curvature and the pylorus can best of all be examined by this method.

The greater curvature can be examined by deep sliding palpation in 50-60 per cent and the pylorus in 20-25 per cent of healthy subjects; the lesser curvature can be palpated in gastroptosis. The greater curvature is found to either side of the median line, 2-3 cm above the navel. It appears to palpating fingers as a ridge on the back bone and by its sides. In cases with gastroptosis, the greater curvature can descend below the navel. Correctness of determination can be confirmed if the position of the ridge coincides with that of the lower border of the stomach as determined by other techniques (by percussion, by the splashing sound or stethacoustic palpation). The pylorus is located in the triangle formed by the lower edge of the liver to the right of the median line, by the median line of the body, and the transverse line drawn 3—4 cm above the navel, in the region of the right rectus abdominis muslce. Since the position of the pylorus is oblique (upwards to the right) the palpating movements should be perpendicular to this direction, i.e. from left downwards to the right. The pylorus is identified by palpation as a band (tense or relaxed). When the pylorus is manipulated by the fingers, a soft rumbling sound can be heard. When contracted spastically (pylorospasm) the pylorus remains firm for a long time. Sometimes the pylorus is mistaken for cancer infiltration.

Palpation of the stomach can reveal tumours of the pylorus, of the

greater curvature, and of the anterior wall. Tumours of the lesser curvature can be diagnosed with the patient in the upright position. Tumours of the cardial part of the stomach are inaccessible to palpation. Exact information on their location gives X-ray examination.

PERCUSSION

Percussion is used to determine the inferior border of the stomach. Provided professional skill is high, the inferior border of the stomach can be outlined by light percussion by differentiating between gastric and intestinal tympany.

If the patient cannot eat the full meal (the capacity of the stomach gradually decreases), it is necessary to determine the Traube's space, which can be markedly decreased. The presence of these two symptoms requires an X-ray examination to exclude cancer of the stomach (scirrhus). Short strokes of the hammer or the flexed fingers on the epigastrium (Mendel sign) are used to determine involvement of the parietal peritoneum: pain indicates affection of the peritoneum.

Splashing sound (succussion) can be heard if the patient is lying on his back, while the examiner pushes the anterior wall of the peritoneum with four flexed fingers of the apt hand. The other hand of the physician should fix the muscles of the abdominal prelum against the sternal edge. The thrust of the hand is transmitted through the stomach wall to the liquid and air contained inside it to cause a readily audible splashing sound which is inaudible outside the inferior borders of the stomach. This technique for outlining the inferior border of the stomach is effective in cases where the stomach border formed by the greater curvature is at the normal level or lowered. Succussion gives information about the evacuatory function of the stomach: the splashing sounds in healthy subjects can only be heard after meals. Splashing sounds heard 7-8 hours after meals suggest evacuatory dysfuncion of the stomach (mostly in pyloric stenosis) or its pronounced hypersecretion (gastrosuccorrhoea). Splashing sounds heard to the right of the median line of the abdomen indicate dilatation of the prepyloric part of the stomach (Vasilenko's symptom).

AUSCULTATION

Auscultation of the stomach is practically non-informative. It is only helpful when used together with palpation of the stomach to outline its inferior border. Stethacoustic palpation is performed as follows: a

stethoscope is placed beneath the left costal arch, below the Traube's space. The examiner rubs the abdominal wall overlying the stomach by the finger and gradually moves the finger away from the stethoscope bell. As long as the finger rubs the skin overlying the stomach, the physician hears the friction, but when the finger moves outside the stomach borders, the sound disappears. This method is very simple but the findings are sometimes inaccurate.

Laboratory and Instrumental Methods

EXAMINATION OF THE SECRETORY FUNCTION

Study of gastric secretion is an indispensable part of complex diagnosis of the gastric mucosa function. The most reliable data on the gastric secretion can be obtained by studying gastric juice.

A thick tube was used for many years to study gastric secretion. The main disadvantage of this method is that a mixture of gastric juice and test meal is extracted and it is thus impossible to obtain reliable qualitative and quantitative characteristics of gastric secretion. This method can therefore be considered obsolete.

Adequate probing implies obtaining pure gastric juice and studying gastric secretion for long periods of time, during various periods of the secretory cycle. Information about gastric juice must be not only qualitative but also quantitative. In other words, probing must give maximum information about the condition of gastric mucosa. Suitable agents stimulating secretion of gastric juice should be used for the purpose. In order to follow-up gastric secretion a thin tube is used.

This is an elastic rubber tube with the outer diameter of 4-5 mm and the inner diameter 2-3 mm. The blind end has two lateral openings. Since the tube is elastic and soft, it is impossible to introduce it in the oesophagus by force (as is the case with a thick tube). The patient has to swallow it gradually. If the vomiting reflex arises, the tube can be introduced through the nose. When the tube reaches the stomach it no longer provokes vomiting and may be left in the stomach for more than two hours. The stomach contents can thus be withdrawn at any suitable time and the secretory gastric function can thus be assessed not at a single moment but can be followed up for considerable length of time. A syringe attached to the free end of the tube is used to suck off the stomach contents.

The study usually begins with removal of gastric juice from a fasting stomach. This done, an agent stimulating gastric secretion can be introduced. According to other methods, from two to four 15-minute samples of the juice are taken from the fasting stomach. This is the so-called basal secretion, though the term does not exactly define the essence of the pro-

cess, because it is very difficult to decide whether the obtained juice is spontaneous secretion or secretion induced by the swallowing movements, or the tube itself.

After the last (fourth) portion of the basal secretion is obtained (in 60 min), the patient is given a stimulating agent (test meal), which may be given either through the gastric tube or parenterally (pentagastrin, histamine, insulin). Pentagastrin (synthetic) and histamine are very effective; these are physiological stimulants of gastric secretion. Histamine is contraindicated in organic cardiovascular diseases, allergic diseases, high arterial pressure, phaeochromocytoma, and after recent (2-3 weeks ago) gastro-intestinal haemorrhage. The dose of histamine is calculated according to the patient's weight (0.01 mg per kg body weight). This stimulation of gastric secretion is submaximal. There exists an optimum (maximum) dose of histamine: a further increase of the dose does not intensify secretion of the stomach (0.04 mg of histamine phosphate per kg body weight). If the maximum dose of histamine is given (Kay's test), the patient should first be given an antihistamine preparation.

After administration of histamine or pentagastrin, gastric juice is collected for an hour, at 15-minute intervals.

There exist many enteral stimulants of gastric secretion. These are beaf tea, a 5 per cent alcohol solution, caffeine (0.2 g in 300 ml of water), a 7 per cent decoction of dry cabbage, etc. They are given to patients to whom histamine is contraindicated.

If stimulants of gastric secretion are given per os, gastric juice is obtained by the Leporsky method. After extraction of four portions of the basal secretion, 300 ml of cabbage decoction (20 titration units) are given into the stomach through the tube. First a 10-ml specimen is taken in 10 minutes, and then, in 15 minutes, the entire stomach contents are aspirated. Four other 15-minute portions are then taken which contain pure gastric juice excreted by the stomach in response to the removed stimulant. Each juice specimen is collected in a separate vessel and its quantity is marked. A fasting stomach of a healthy individual contains to 50 ml of the fluid; sometimes this amount is larger. An hourly basal secretion is 30—150 ml (50 ml on the average). The evacuating function of the stomach is determined by the volume of gastric juice contained in it 25 minutes after a test meal. The normal volume is 75 ml, on the average. Summation of the last four portions gives the hourly secretion. A 15-minute portion (with intermittent aspiration) is not quite informative because part of gastric juice passes into the duodenum. A continuous aspiration of gastric juice (with separation of 15-minute portions) ensures more accurate determination of hourly secretion. Normally it is about 60 ml with intermittent aspiration, while with continuous aspiration this figure increases 1.5—2 times. If

parenteral stimulants are used, gastric juice is aspirated for 60 minutes straight after their administration.

The colour of the extracted juice, its consistency, the presence of admixtures, and odour are assessed. Normal gastric juice is almost colourless. Bile (that may be belched into the stomach from the duodenum) colours the juice green or yellow; blood admixtures give the juice a red colour, or (more frequently) brownish-black. If much unaltered scarlet blood is aspirated together with juice probing should be discontinued immediately. Normal juice is liquid; the presence of mucus makes it tenacious and it is sometimes difficult to separate a portion from the whole mass of the juice taken. Ample mucus in the juice may suggest gastritis. Supernatant mucus originates from the airways. Residues of food taken the day before the examination may also be present in gastric juice. This indicates motor dysfunction of the stomach.

After the physical properties of gastric juice have been determined, its chemical properties should be established. Free hydrochloric acid is first determined in each sample; next determined are bound hydrochloric and lactic acid; pepsin is determined in the sample with maximum acidity.

Acidity of gastric juice is determined by titrating it with a 0.1 N sodium hydroxide solution in the presence of indicators. Acidity is expressed in millilitres of NaOH which are spent to neutralize 100 ml of the juice. It has become usual now to express acidity in milligrams of HC1 or milliequivalents (MEq). Two drops of a 0.5 per cent alcoholic solution of dimethylamidoazobenzene and two drops of a 1 per cent alcoholic solution of phenolphthalein (phenol red is now very popular) are added to a 5- or 10-ml aliquot. Dimethylamidoazobenzene turns red in the presence of free HC1. Alkali is buretted, drop by drop, to the gastric juice until it turns pinky orange to indicate the point of equivalence. The amount of the alkali spent is determined and titration is continued. The liquid first turns yellow and then red again: all acid has been neutralized and phenolphthalein turns red. The new spent volume of alkali is measured again. The number of millilitres of the alkali that were spent at the first stage of titration are multiplied by 20 to give the amount of free hydrochloric acid. The amount of alkali spent for the entire titration should also be multiplied by 20 to determine total acidity. This is the sum of all acids contained in the stomach, e.g. free and bound hydrochloric acid, organic acids, and acid phosphates. Bound acid is non-dissociated hydrochloric acid of protein hydrochloride molecules of gastric juice. Normal gastric juice contains proteins (pepsin, gastromucoprotein). The protein content increases in gastritis, bleeding ulcer, or degradation of a tumour; the amount of bound hydrochloric acid increases accordingly. Bound acid is determined indirectly by titrating a small (5 ml) portion of the juice in the presence of alizarin

sodium sulphonate which is yellow in the presence of any free acid. When acid is neutralized, the solution turns violet. Bound HCl is determined by subtracting the number of millilitres of alkali spent for titration with alizarin from total acidity and multiplying the difference by the factor of 20. Indices of acidity that were considered to be normal for decades have now been revised. Thus the normal content of hydrochloric acid in the fasting stomach of a healthy subject was considered to be maximum 10—20 titrating units (t.u.), or the acid might be absent at all. Normal acidity after taking a test meal was 20—40 titrating units for free HCl and 40—60 for total acidity. Findings of many investigators who observed a great number of healthy people show that "normal" acidity is found in only 50 per cent of them, while in others acidity is either below or above this "normal" level and is their constitutional feature. Total acidity below 20 t.u. should therefore be considered hypo-acidity and over 100 t.u. hyperacidity. Complete absence of hydrochloric acid is a very important diagnostic sign. The absence of free HCl in gastric juice after giving the maximum dose of histamine is called histamine refractory achlorhydria. This symptom may suggest atrophic process in gastric mucosa.

Acidity (concentration of the acid) does not characterize completely the acid-secreting function of the stomach. A more detailed information can be obtained by determining the hourly secretion of the stomach. To that end, acid concentration in the gastric juice should be multiplied by the hourly secretion of the stomach and divided by 100 (if acid concentration is expressed in mg/100 ml) or by 1000 (if the concentration is given in mEq/1).

Acidity in titration units can be expressed as concentration of the acid in mg/100 ml by multiplying the acidity index by 3.65, because the weight equivalent of the titration unit is 3.65 mg HCl or 0.1 mEq HCl in 100 ml of gastric juice. For example, acidity of 60 t.u. can be expressed as (3.65 × 60) mg/100 ml or 60 mEq/1, or 60 mmol/1 HCl. Indices of gastric secretion for various phases and with various stimulants are given in the Appendix.

Since probing is contraindicated to some patients (with degrading tumour of the stomach, stenosis of the oesophagus, aortic aneurysm, etc.), and since some patients fail to swallow the gastric tube, many investigators search for techniques by which acidity of the gastric secretion can be determined without using any tubes. In 1905, Sahli suggested a simple method. The patient swallows a small rubber bag (tied up with catgut) containing 0.1 g of methylene blue and has a normal meal. If hydrochloric acid is present in the stomach, catgut is digested and methylene blue is absorbed in the stomach contents to colour urine later. Methods employing ion-exchange resins have been recently proposed. Ion-exchange pills contain

substances that are displaced from them by hydrochloric acid in the stomach and then excreted in the urine. Quinine, stains (azur I) and other substances are used in such pills. These methods are quite reliable but they can only determine complete absence or presence of the acid in the stomach and cannot give quantitative information. Moreover, these methods are applicable to patients with preserved renal function.

A new and promising radiotelemetric method is now used to determine acidity (to be more exact, the pH) of gastric juice. This method is known as endoradioprobing.

Another important property of gastric juice is its peptic power. It is determined mostly by the extent to which protein is digested.

The simplest method of establishing peptic activity of gastric juice was proposed in 1899 by Mett. Narrow glass tubes filled with coagulated egg white are immersed in gastric juice (which is acidified, if free HCl is absent) and then placed in a thermostat for 24 hours. The length of tubes (in mm) freed from the albumen is measured. If pepsin content is normal, the total number of millimetres (on both ends of the tube) should be 6-12.

V. Tugolukov proposed a standard method by which more accurate results can be obtained. A 2 per cent solution of dry plasma is placed in two accurately graduated centrifugal tubes and gastric juice in question (diluted 1:100) is added. A portion of boiled juice is added to one test tube and both are kept in a thermostat for 20 hours. Trichloracetic acid is then added to the test tubes, the contents are mixed thoroughly, and the solutions are centrifuged. The peptic power of gastric juice is assessed by the volume of precipitated albumin. The findings are compared with the results of similar experiments carried out with pure dry pepsin of different dilutions. The pepsin content of gastric juice can thus be expressed in milligrams.

If the pepsinogenic function of the stomach is estimated without probing, pepsinogen is determined in the urine (uropepsinogen). It has been established that pepsin is not fully secreted into the stomach, but about 1 per cent of it is mixed with blood and liberated with urine. The presence of pepsinogen in the urine therefore indicates its secretion by the gastric mucosa. Uropepsinogen is determined in the same way as pepsin in gastric juice; Tugolukov's method (or milk coagulation method) can also be used for the purpose.

Determination of lactic acid in gastric juice has a certain diagnostic importance as well. The acid is produced either by the lactobacillus, which grows in the stomach only in the absence of hydrochloric acid, or by a malignant tumour: anaerobic glycolysis occurs in its cells with formation of lactic acid. The presence of lactic acid in gastric juice is not pathognomonic for tumour, but requires a thorough examination of the patient. Uffelmann reaction is used for determining lactic acid. A 1—2 per

cent phenol solution is placed in a test tube (2/3 full capacity) and 2—3 drops of a 10 per cent ferric chloride solution added: the reagent turns dark-violet. The test tube is then inclined and 2-3 drops of gastric juice are added by the wall. In the presence of lactic acid, the drops of juice sink to the bottom and become coloured bright-yellow by the iron lactate formed.

Microscopic studies. Native preparations are made from a settled or centrifuged precipitate. Gastric juice precipitate of healthy subjects contains mostly cells of the mouth (squamous epithelium and leucocytes). The presence of food remains (muscle fibres, fat, fatty acids, subcutaneous fat) indicates evacuation dysfuncion of the stomach. Acid stagnant juice contains sarcinae. If acidity is absent, lactic bacilli are present in the juice. Erythrocytes in small quantities are diagnostically unimportant because their presence may be due to an injury caused by probing or strain during vomiting. Ample erythrocytes suggest the presence of ulcer, tumour, or erosive gastritis.

Exfoliative cytology. Early cancer of the stomach, when the tumour cannot be palpated and revealed by X-ray, is difficult to diagnose. Exfoliative cytology is a simple method by which tumour of the stomach can be established to a high degree of certainty. The method is based on the specific property of cancer cells to be easily separated from one another and shed into gastric contents. The cells are recovered from the precipitate or the gastric washings. Special gastric tubes with inflated bulbs which have rough surface to separate cancer cells are used to obtain desquamated cells. In order to prevent degradation of cancer cells, the obtained gastric juice should be immediately centrifuged and the precipitate examined either in native preparations or in a phase-contrast microscope after staining with fluorochromes, or in dry smears stained by haematoxylin-eosin, or after Romanowsky-Giemsa or Papanicolaou. Differentiation of gastric tumour cells requires great experience, because they are very much like cells of other tumours (see "Study of Sputum").

STUDY OF GASTRIC MOTOR FUNCTION

The motor function of the stomach is assessed by its peristole, peristalsis (of a fasting stomach and after meals), intragastric pressure, and the evacuatory function. Various methods exist to study these characteristics, e.g. inquiry of the patient, physical examination, balloon kymography, electrogastrography, radiotelemetry, and roentgenography. It should be noted that none of them can give exhaustive characteristic of the motor function of the stomach. At the same time, each method adds to the picture of this complicated process.

Balloon kymography. The movements of the stomach and the height of its peristalsis are recorded on a moving paper chart by a kymograph employing a float. The variables are picked up by a single- or a multichannel gastric tube ending with balloons (sensitive elements) which is swallowed by the patient. The fasting stomach is thus examined. The position of the balloon in the stomach is controlled by X-rays.

The following regularities of a fasting stomach in healthy individuals have been established: the stomach "works" from 10 to 40 minutes, and then a period of relative rest, lasting from 40 to 120 minutes, follows. The height of waves on a gastrogram varies from 3 to 6 cm, while the number of contractions per minute is 1 or 2 on the average. Pressure in the stomach body varies from 6 to 10 cm H_2O. The contraction frequency in the pyloric part of the stomach is higher (2—3 contractions per minute); the waves are higher too (to 7 cm).

Electrogastrography, This is the method of recording biopotentials characterizing the motor function of the stomach. Electrogastrography is the best method to record digestive peristalsis of the stomach. Since action currents are taken off from the surface of the human body, no tube should be swallowed. The absence of the tube inside the stomach, in turn, does not interfere with its normal secretory function. When a tube is swallowed, it may happen that food gets between the electrode and the stomach wall to break contact. This distorts intragastric records or makes recording unfeasible at all.

The active electrode is placed on the median line of the abdomen, below the xiphoid process, at the point of projection of the antral end of the stomach. The other electrode is placed on the right leg of the patient. An electrogastrogram is recorded after giving a test meal (150 g of wheat bread and a cup of sweet tea). The most distinct peristalsis of the stomach is recorded in 30-120 minutes after the test meal. When interpreting the ECG, the general character of the curve, the amplitude and frequency of waves, and the peristaltic rhythm are assessed. The amplitude of waves on an ECG of a healthy individual does not exceed 1/4 mV and only some amplitudes are 0.5 or 1 mV. The rhythm of oscillations is three per minute. Electrogastrography is of little use in differential diagnosis of affections of digestive organs, but it can help assess objectively effects of various pharmacological and other factors on gastric peristalsis during digestion, and follow up changes in the motor function of the stomach during treatment.

Endoradioprobing. The operating principle of this radiotelemetric study is recording of signals emitted from an ingested miniature transmitter (endoradioprobe) that responds to physiological, physical, and chemical changes occurring inside the digestive tract. Endoradioprobe consists of a transmitter and a sensitive element (made in the form of a cylinder) which responds to changes in the controlled variable (pressure pH, temperature) and generates high-frequency electromagnetic oscillations. The emitted signals are received and recorded. A flexible aerial transmits the signals. It is enclosed in a silk belt attached to the patient's body. A special calibrating device is provided to ensure high accuracy of measurement of physiological parameters. The transmitter is introduced into the patient's stomach together with a thin gastric tube which is usually used for taking gastric juice specimens. The probe has openings at its lower end to aspirate the contents of the stomach or the duodenum. Depending on the object of study, the tube may be introduced into a fasting stomach or after taking a test meal. The patient assumes the recumbent position.

The radio transmitter can also be used to study gastric secretion, evacuatory function of the stomach, and effect of various pharmacological preparations, and to record variations in pressure inside the stomach.

X-RAY STUDY

Roentgenoscopy and roentgenography are important methods for examination of the stomach. They are used to outline the shape, size, position, and mobility of the stomach, and to locate its ulcers or tumours.

Relief of the gastric mucosa and its functional conditions can also be determined roentgenologically.

An empty stomach is examined with a barium meal as a contrast substance (100—150 g of barium sulphate in a cup of water).

In the presence of hypersecretion or evacuatory dysfunction the stomach of the patient may contain considerable quantity of material. This should be removed through a tube before giving the barium meal. The patient is then asked to swallow one or two mouthfuls of barium sulphate suspension. By palpating the anterior wall of the abdomen, the suspension is distributed by the surface of the gastric mucosa to fill its folds: gastric mucosa becomes visible on an X-ray screen. The direction of the folds, their thickness, continuity, thickness height, and elasticity should be assessed. After the relief of the gastric mucosa has thus been examined, the patient is asked to drink the remaining meal to fill the stomach so that its shape, size, position, general outline, mobility, evacuation function, possible affections, and the condition of the gastric gas bubble might be examined. During examination, the patient is asked to turn before the screen in both horizontal and vertical planes. Whenever necessary, X-ray pictures are made. In order to study the motor function of the stomach a series of pictures are taken (roentgenocinematography).

Folds of gastric mucosa are longitudinal in the region of the lesser curvature, and oblique in the region of the greater curvature. The folds in the region of the antrum can be seen to extend in both directions. The shape of the folds is important: they may be broad and rough; or they may be absent (in atrophied mucosa). Continuity of the folds should be established: if the folds disappear, the presence of pathology may be suggested at this site (e.g. cancer, or other process destroying the gastric mucosa).

When the stomach is full, it resembles a hook located in the upper portion of the abdominal cavity, to the left of the median line. The shape of the stomach can change significantly in pathology, e.g. it can look like a bag in decreased tone, or resemble a sand glass in the presence of cicatricial adhesions.

The stomach outlines are of great diagnostic importance. Permanent protrusion of the stomach silhouette (niche) is a direct indication of gastric ulcer. If barium sulphate fails to fill any portion of the stomach a filling defect forms; it may suggest a tumour. Peristaltic movements of the stomach alter its contours, but as distinct from organic changes in the stomach wall, they are only transient.

The evacuatory function of the stomach is characterized by the time which is necessary for the stomach to discharge the barium meal. Normally, one third of the taken suspension may be present in the stomach in an hour.

The position of the stomach is also very important. The upper pole of a

normal stomach is at the level of the 11—12th thoracic vertebrae; the pylorus is at the level of the 3rd lumbar vertebra; and the lower point (sinus) at the level of the 3rd and 4th vertebrae (not below this level).

GASTROSCOPY

Gastroscopy is inspection of the stomach by a gastroscope. This instrument is similar in design to all other endoscopes. Fibroscopes have recently come in wide use. These are flexible gastroscopes in which the picture is transmitted through a bundle of glass fibres (as thin as a human hair). Another novelty in gastroscopy is taking tissue samples under visual control, and taking pictures and filming of the gastric mucosa. As distinct from common gastroscopes, gastrofibroscopes are flexible and much more convenient for use. Safety of the new instrument is another important factor.

Gastroscopy of a fasting stomach is carried out in the morning. An injection of atropine sulphate (0.001 g) is given to the patient 30 minutes before the procedure. The pharynx and the upper oesophagus are anaesthetized by a 3 per cent dicaine solution. A gastroscope is then introduced following special instructions.

As viewed through a gastroscope the mucosa of the stomach may be pale-crimson to red. The mucosa of the anterior wall is smooth and covered with a thin glassy layer of mucus (its folds are stretched by the inflating air). Big folds and interconnecting ridges can be seen on the posterior wall of the stomach. The pylorus appears as a cone-shaped structure. The antrum looks like a funnel with its narrow part being directed toward the pylorus. When opened, the pylorus looks like a dark cavity; when the stomach muscles contract, the folds are converged to make a stellar pattern.

Gastroscopy is an important procedure since the condition of the gastric mucosa can be visualized: its colour, minutest changes in the surface, growths, erosions, and ulcers (Plate 12). Gastroscopy reveals the condition of the vessels, haemorrhages, and formation of mucus. It can be used to study the relief of the inner surface of the stomach, i.e. height, width, and density of folds, which is an important supplement to the X-ray examination. Gastroscopy helps reveal tumours or ulcers that were not identified by roentgenoscopy. Gastric mucosa can be filmed through a gastroscope using a special photographic attachment (Fig. 85).

A comprehensive X-ray examination of the patient should be done before gastroscopy in order to reveal possible contraindications (narrowing of the oesophagus or cardia due to a tumour; diverticula of the oesophagus; affections of the mediastinum, which displace the

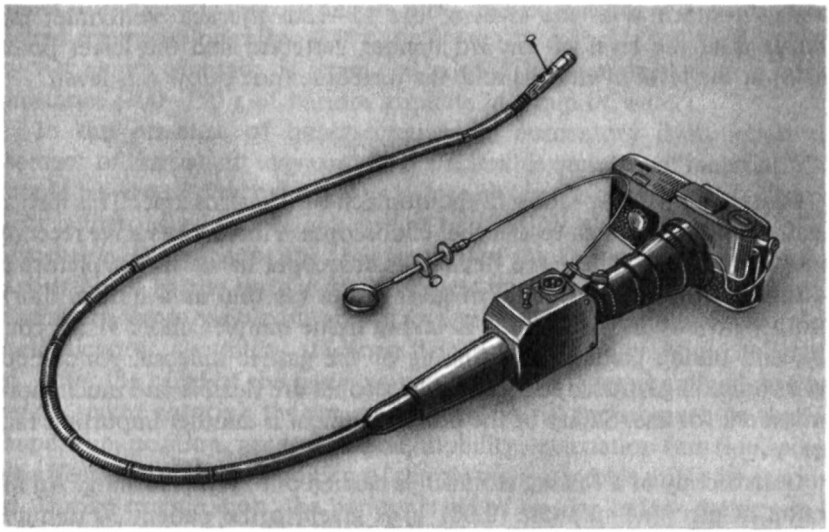


Fig. 85. Gastroscope.

oesophagus, especially aneurysm of the aorta and enlarged left atrium; kyphoscoliosis, varicosity of the oesophageal veins).

Endofibroscopes are now used for therapeutic purposes as well. Polyps of the oesophagus, stomach, duodenum, and of the large intestine can be removed through the endoscope. Endoscopes are used to arrest haemorrhage, to extract foreign bodies, or to administer medicines directly into the focus of affection, e.g. in ulceration of the gastro-intestinal tract.

Possible complications of gastroscopy are perforations of the oesophagus or stomach which rarely occur with experienced doctors.

METHODS OF MORPHOLOGICAL STUDIES

Intravital morphological studies of gastric mucosa are now widely used. The material for examination is obtained by gastrobiopsy: a piece of mucosa is pulled (by aspiration) and cut off by a special blade or forceps. Gastrobiopsy is carried out now mostly under visual control.

If visual control cannot be ensured, a 3-5 mm tube is used with a special capsule at the distal end by which the material is aspired through a lateral opening. A piece of gastric mucosa is then cut off by a special blade. The mucosa is sucked into the tube by a syringe attached to its other end. The tube is introduced into the fasting stomach to a depth of 60 cm

without anaesthetizing the throat. The aspiring vacuum is strictly maintained at 400 mm Hg for 2 seconds. A pressure gauge is provided for the purpose.

This method can only be used for biopsy in diffuse affections of the stomach (gastritis).

Visual or sighted biopsy is carried out with a gastrofibroscope provided with special forceps by which a mucosa specimen can be cut off. Biopsy is obligatory in cases suspected for cancer.

Special Pathology

Gastritis, peptic ulcer, and cancer are most common diseases of the stomach.

Gastritis

Gastritis is inflammation of the gastric mucous membrane. Acute and chronic gastritis are differentiated.

ACUTE GASTRITIS

Acute gastritis is a very common disease. Catarrhal, corrosive and acute phlegmonous gastritis are distinguished.

Aetiology and pathogenesis. The alimentary factor is the leading one among the other causes of gastritis. Ingestion of fatty, coarse, poorly assimilated or decomposed food, of very cold or hot meals or alcoholic drinks provokes gastritis. The gastric mucosa may also be irritated by prolonged taking of some medicines (salicylates, sulpha preparations, steroid hormones, butadione, iodine preparations, etc.). An allergic reaction to some foods (fish, eggs) can sometimes also cause gastritis. Various infectious diseases, such as influenza, measles, or scarlet fever can be attended by acute gastritis. It is the leading symptom in food poisoning.

Clinical picture. Symptomatology of acute gastritis is quite varied. It may proceed asymptomatically or be manifested by severe local and general symptoms. Inflammation begins 2-3 hours after the irritating agent has been ingested, while the clinical picture develops in 6-8 hours. The symptoms of acute gastritis are loss of appetite, unpleasant taste in the mouth, nausea and vomiting (first with food remains and later with bile). The patient complains of pressure, bulging, and pain in the epigastrium. The rise of temperature is often preceded by chills. The patient is pale, his pulse is accelerated, the tongue coated, and breath is foul. Palpation of the epigastric region is painful and stimulates nausea. The amount of excreted urine decreases. In persistent vomiting the haemoglobin and erythrocyte counts increase while the level of chlorides decreases.

The onset of the disease is characterized by hypersecretion and hyperchlorhydria which is followed by inhibition of gastric secretion. The motor (evacuatory) function of the stomach sharply decreases, while the absorptive power of the gastric mucosa increases. Gastroscopy reveals hyperaemic mucosa coated by a thick layer of glassy mucus; haemorrhage and erosion sometimes occur. Morphological reconstruction of the gastric mucosa complete by the end of the second week. The patient recovers clinically in 3 or 4 days. X-ray examination fails to reveal any changes in the relief of the gastric mucosa.

Course. The disease ends by recovery in most cases, but acute process can convert into a chronic one in the absence of appropriate treatment and if exposure to the harmful factors (alcohol, overeating) continues.

The special forms of acute gastritis (corrosive and phlegmonous) are called fulminant gastritis. Corrosive acute gastritis develops from irritation of the gastric mucosa by acids or alkalis, and acute phlegmonous gastritis is a rare disease characterized by purulent inflammation of a part or the entire stomach wall. The clinical course of both forms is grave. Perforation of the stomach is possible. Prognosis is unfavourable in most cases.

Treatment. During the first 2 or 3 days the patient is given only nutritive liquid, and the diet is then gradually enriched by the end of the second week. Bed rest is indicated during the first days of the disease; antacid and astringent preparations are given. The stomach should be lavaged as soon as possible in corrosive gastritis. Antibiotics should be given in phlegmonous gastritis.

CHRONIC GASTRITIS

Chronic gastritis is a frequently occurring disease; it affects mostly men.

Aetiology and pathogenesis. Chronic gastritis is closely connected aetiologically with acute gastritis. All exogenous aetiological factors responsible for acute gastritis are important for the development of chronic gastritis. Among important endogenous factors causing chronic gastritis are reflex effects on the stomach from pathologically changed organs (gall bladder, intestine, pancreas), upset hormone system (affection of the thyroid, pituitary, adrenal glands), chronic infections (tuberculosis, malaria, syphilis), chronic septic foci (tonsillitis, carious teeth). Chronic gastritis may develop from disordered metabolism (diabetes, obesity, gout, renal failure). Finally, chronic gastritis may be secondary to diseases accounting for hypoxia of tissues, the gastric mucosa included (chronic circulatory insufficiency, pulmonary heart, uraemia).

Chronic gastritis is a polypathogenic disease. The leading role in its development undoubtedly belongs to disorders in the nervous, humoral, and hormonal mechanisms regulating the digesting function. But the direct action of irritants on the gastric mucosa cannot be disregarded either. Autoallergic processes are important for maintaining the disease.

Pathological anatomy. Differentiated are superficial affections of the mucosa, affection of the glands without their atrophy, atrophy of the gastric mucosa of various degree, and combination of atrophy with hyperplasia.

Classification of chronic gastritis. There is no universally accepted classification of chronic gastritis. S. Ryss proposed a classification based on four principles: aetiological (exogenous and endogenous), morphological, functional (chronic gastritis with preserved secretion and with secretory insufficiency of various degree, up to achlorhydria), and clinical (compensated chronic gastritis or remission phase; decompensated gastritis or exacerbation phase). Moreover, gastritis can be regarded as an indepen-

dent disease and as a disease secondary to other pathologies (peptic ulcer, chronic colitis, etc.).

Clinical picture. The signs of chronic gastritis are difficult to describe because the course and symptomatology of the disease are quite variable. Some patients do not complain of anything during remissions; the disease may also develop for a long time without any manifestations and it is therefore difficult to establish the time of its onset.

The main syndrome of chronic gastritis is gastric dyspepsia. It may combine with intestinal dyspepsia characterized by meteorism, rumbling sounds in the abdomen, constipation, and diarrhoea. The patient with chronic gastritis can also feel pressure and distention in the epigastrium, and sometimes pain. These symptoms are connected with distention of the stomach by ingested food and the attending pathological sensitivity of mucosal interoceptors. Pain is dull and boring, but sometimes becomes severe. The general condition of patients with chronic gastritis varies. Some patients do not lose weight, remain active, while others lose weight, become flaccid and slow, their appetite is poor. A pronounced decrease in gastric secretion may be attended by diarrhoea which causes even greater wasting and impairs absorption of proteins, vitamins, and iron. Anaemia develops along with signs of polyhypovitaminosis and albumin deficiency.

Examination of the abdomen sometimes reveals inflation. Palpation of the epigastrium is in most cases painless. The acid secretion may remain normal or it may decrease. Free hydrochloric acid may be absent from the gastric juice (achlorhydria). In neglected cases secretion of pepsin (achylia) is upset as well.

Roentgenography is but of little use in the diagnosis of chronic gastritis. Gastroscopy can give valuable diagnostic information, especially if it is combined with sighting biopsy. Aspiration biopsy and exfoliative cytology are also important for the study of patients with chronic gastritis.

Chronic gastritis should be differentiated from peptic ulcer and gastric neurosis ("irritated stomach") in the presence of hyperchlorhydria and functional achylia.

Course. The disease usually slowly progresses but the appropriate treatment improves the patient's condition. Complete anatomical restoration of the gastric mucosa and normalization of the secretory function occur rarely. Chronic gastritis with secretory insufficiency is considered as a precancer condition.

Treatment. Therapy of chronic gastritis should be combined, differential, lengthy, and planned. Diet is especially important. When prescribing an appropriate diet, the stage of the disease, and also the secretory background of the stomach should be taken into consideration.

Substitution therapy (preparations of gastric juice) is given in anacid

gastritis. In spastic and pain syndromes, spasmolytics are given and thermotherapy applied. Health-resort and sanatorium therapy are also indicated in combined treatment.

Prophylaxis. Rational nutrition and observation of hygienic requirements are requisite in prevention of chronic gastritis. Fighting against smoking and drinking alcohol, sanation of chronic inflammatory foci (carious teeth, tonsillitis) should also be included into the list of preventive measures. Patients with chronic gastritis should be regularly observed in out-patient conditions.

Peptic Ulcer Disease (Gastric and Duodenal Ulcer)

Peptic ulcer is a general chronic and relapsing disease characterized by seasonal exacerbations with ulceration of the stomach wall or the duodenum.

Aetiology and pathogenesis. The aetiology and pathogenesis of the disease is still unknown despite the intense clinical and experimental research.

The main affection, the lesion in the wall of the stomach or duodenum, is caused by the action of gastric juice. But in normal conditions the gastric or duodenal mucosa is resistant to the digestive effect of the juice due to the presence of complex protective mechanisms. Therefore, in order to cause self-digestion, certain factors should be involved which decrease resistance of the mucosa to the digestive effect of the gastric juice or increase its digestive properties; or both these factors should be involved. Many theories have been proposed to explain these phenomena but none of them fully explains the causes of peptic ulcer disease.

From the findings available at the present time, the following main factors in the pathogenesis and aetiology of the disease have been established: (1) disordered neurohormonal mechanisms regulating digestion; (2) disorders in the local digestive mechanisms; (3) structural changes in the gastric and duodenal mucosa.

The predisposing factors are heredity and environmental factors, among which nutrition is the leading one. Irregular nutrition, with prevalence of easily assimilable carbohydrates in the diet, excess ingestion of poorly assimilated and long digested foods cause hypersecretion of the stomach. In the presence of the main factors, the predisposing factors cause ulceration with time. Alcohol and nicotine have also an adverse effect on the gastric mucosa.

The central role in the aetiology and pathogenesis of peptic ulcer belongs to disorders in the nervous system which can arise in the central

and vegetative systems under the action of various effects (negative emotions, physical and mental overstrain, viscero-visceral reflexes, etc.).

Current research shows the important role of endocrine dysfunction in the development of peptic ulcer (dysfunction of the pituitary or the adrenal glands). Disorders in local mechanisms (the acid-peptic factor, gastric hormones, mucous barrier, regeneration of mucosa, blood circulation in the stomach wall and the duodenum, morphological reconstruction of the mucosa, changes in the motor function, condition of local secretory depressor mechanisms) result from disordered neurohormonal regulation of the gastroduodenal system.

It can thus be concluded that the causes of peptic ulcer are varied, while its pathogenesis is complex and uncertain. Nervous genesis may probably prevail in some cases, while humoral or neurohumoral in others; disorders in the local mechanisms of gastric digestion may also be the leading factor in the aetiology and pathogenesis of peptic ulcer.

Pathologial anatomy. Margins of a chronic ulcer are consolidated. Ulcers with especially hard elevated edges are called callous. Inflammatory infiltrations are usually formed round the ulcer. A bleeding vessel can be found on its floor. An ulcer can destroy the wall of the stomach (perforating ulcer) or it can penetrate the adjacent organs.

The ulcer is healed by epithelization or cicatrization. These processes can change the shape of the stomach and narrow its outlet. Adhesion of the stomach and duodenum to the neighbouring organs can result from the previous inflammation of the serous membrane at the site of affection.

Classification. There is no universally accepted classification of peptic ulcer disease. Location of an ulcer determines to a certain degree the clinical course of pathology. Ulcers mostly develop on the lesser curvature. The cardia is affected less frequently. The usual site of ulcer in the duodenum is the bulb. Pyloric, postbulbar, and extrabulbar ulcers are also differentiated. Age and sex are important for the clinic of the disease. Hence juvenile ulcers, ulcers of the elderly and old patients, and also peptic ulcer disease of women are differentiated.

Clinical picture. Symptoms of peptic ulcer disease vary and depend on the age, sex, the general condition of the patient, the duration of the disease, frequency of exacerbations, location, kind of lesion, and the presence of complications.

The leading symptom of peptic ulcer is pain, which may be periodic, seasonal, increasing in severity, intensifying or lessening after vomiting or taking meals, alkalis, thermal procedures, or cholinolytic preparations.

Early pain is typical of gastric ulcer; late pain, nocturnal or hunger pain are characteristic of peripyloric and duodenal ulcer. Permanent pain is atypical and is usually due to complications (perivisceritis, penetration of the ulcer). Regular connection between pain in peptic ulcer and quantity

and quality of food is obvious. Ample, bitter, sour, salty, spicy and coarse food always cause severe pain.

The seasonal character of pain (vernal and autumnal) is very typical of peptic ulcer disease and can positively be used to differentiate it from pain in other diseases. Exacerbations of pain are alternated with remissions even in the absence of treatment. The cyclic character *of* peptic ulcer disease is probably due to seasonal changes in general reactivity of the human body. Upset vitamin balance in spring may play a certain role in the course of the disease as well. Periodicity of pain may be not quite obvious at the early stages of the disease. Except hunger pain, which lessens after meals, pain attains its maximum severity at the height of digestion.

Although a lesion cannot always be located by pain, it has, however, been noticed that gastric ulcer is manifested by pain in the epigastrium above the navel, while in duodenal ulcer pain is felt in the epigastrium to the right of the median line; ulcer of the cardia is characterized by pain in the vicinity of the xiphoid process. Pain may radiate into the left breast nipple, behind the sternum, the left shoulder blade, and into the thoracic part of the spine.

The pathogenesis of pain in peptic ulcer is uncertain. It has been established that common stimuli causing pain when applied to the skin are ineffective when applied to the wall of the stomach or the intestine. Irritating factors for these organs are muscular strain, especially spasms, and elevation of the intravisceral pressure, which are caused by disorders of nervous regulation.

The acid factor acting on the motor function of the stomach and the duodenum, and also changes in the mucosa of these organs are very important in the aetiology of pain in peptic ulcer disease.

Vomiting occurs in 70—75 per cent of patients. It arises without preliminary nausea, at the height of pain, and relieves it. The vomitus is acid to taste and smell. Secretion of the gastric juice in a fasting stomach is often attended by vomiting as well.

Heartburn is encountered in 60-85 per cent of patients. It occurs not only during exacerbations but can also precede exacerbation for several years; it can be periodic or seasonal. The mechanism of heartburn is associated with motor dysfunction of the oesophagus (in addition to the acid factor of the gastric contents, which was formerly believed to be decisive).

Eructation, regurgitation, and salivation are frequent symptoms. Appetite is often increased. Regular connection between meals and development of pain is the cause of a morbid fear of eating (cibophobia).

The intestinal symptoms of peptic ulcer disease are constipations, which are closely connected with the character of nutrition and bed-rest

during exacerbations, and are mainly connected with reflex dyskinesia of the small and large intestine.

Wasting is characteristic of exacerbations. The skin and mucosa are pallid after haemorrhage. The tongue is usually clean. The configuration of the abdomen is normal. In the presence of pyloric stenosis peristaltic and antiperistaltic movements of the epigastrium can be seen. Brown pigmentation develops on the abdomen after prolonged application of warmth. During exacerbations, the epigastric region is tender to surface palpation; if the peritoneum is involved (positive Mendel's test) the muscles are strained. Late splashing sound to the right of the median line (Vasilenko's symptom) indicates gastric evacuatory dysfunction or increased secretion between meals.

Gastric secretory function. If the ulcer is found in the stomach, hydrochloric acid, pepsin, mucoprotein and albumin fractions of the gastric juice vary within normal limits. In duodenal ulcer all these indices singificantly exceed normal values. Hypersecretion of the gastric juice is determined in this case by hypersensitivity of the vagus, intensified adrenal function, and increased quantity and hypersensitivity of the parietal cells. Study of the basal secretion of a fasting stomach is very important for the diagnosis of duodenal ulcer. In the presence of active basal secretion and specific complaints of the patient, he should be given the appropriate treatment despite negative results of X-ray examination.

The *motor function of the stomach and duodenum* is upset in peptic ulcer. This is the leading factor in the development of the main symptoms, e.g. pain, nausea, vomiting, and heartburn. Upset motor function increases the tone of the stomach and the duodenum, intensifies their peristalsis, and disturbs periodicity of their activity. The observed changes in the motor function are not specific for peptic ulcer disease and cannot therefore be regarded as its diagnostic signs. But a certain regularity of these changes can indicate the stage *of* the disease and be a criterion for the objective judgement about the efficacy of treatment.

Latent haemorrhage is almost always revealed on examination of faeces during exacerbation of peptic ulcer.

X-ray examination. A direct proof of peptic ulcer is a niche which is found in 75—80 per cent of patients. The ulcer is usually located on the lesser curvature (Fig. 86). It has the regular J shape, the barium depot extending beyond the normal contour of the stomach. In duodenal ulcer, the niche can be found inside the bulb or outside it (extrabulbar ulcer).

In the absence of direct X-ray signs (the absence of a niche), indirect symptoms become important. These are intensified peristalsis of the stomach, and the presence of a thick layer of secretion between the air and the contrast substance.

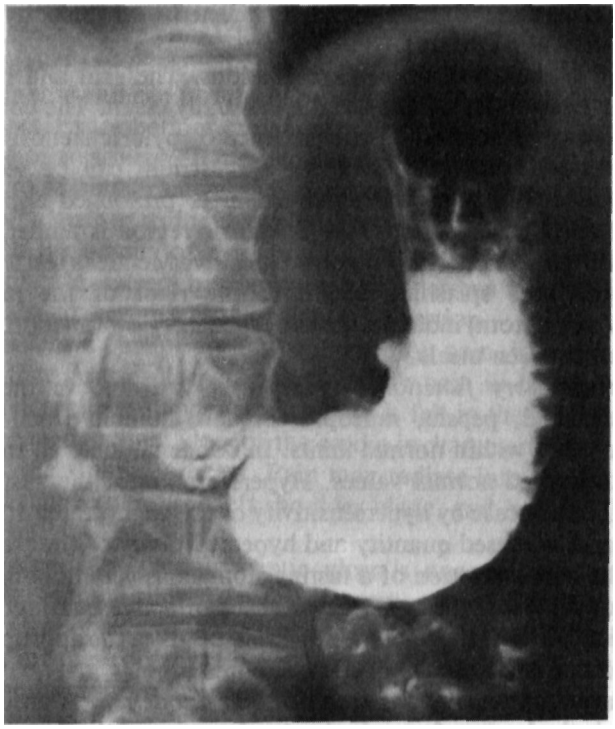


Fig. 86. X-ray of ulcer of the lesser curvature.

Gastroscopy. Gastroscopy is used to reveal gastric ulcer; if gastroscopy is repeated, it shows the cicatrization process. A fibroscope can be used not only to view the stomach, but the duodenum as well. Ulcers that fail to be detected by X-rays can be revealed by gastroscopy, which is also important for differentiation between benign and malignant changes (sighting biopsy).

Course. Four stages are distinguished in the clinic of peptic ulcer: stage I ("prelude to ulcer", according to M. Konchalovsky) is characterized by a marked disorder in the activity of the vegetative nervous system and gastroduodenal dysfunction; stage II is attended by development of organic changes (gastroduodenitis); stage III is formation of an ulcer; and stage IV is development of post-ulcerous processes.

This classification of ulcer stages is only conventional but still useful because it may help the physician to establish early diagnosis. Remission

periods last from several months to many years. Exacerbations continue for 4—6 weeks. Cicatrization of the ulcer is completed in 6—8 weeks. Remission may occur without treatment. Seasonal exacerbations are more characteristic of duodenal ulcer. Unless complicated by haemorrhage or perforation, peptic ulcer is never fatal.

Haemorrhage. This is the most frequent complication. It may be manifested by haematemesis (blood vomiting) and tarry faeces (melaena). Among other causes of gastric haemorrhage, peptic ulcer is accounted for 60-65 per cent. Gastric ulcers bleed more often than others. Vomiting may be absent in duodenal ulcer, and the first signs of haemorrhage are sudden weakness, giddiness and palpitation (before the appearance of tarry stools). The patient's general condition depends on the length and intensity of bleeding.

Perforation. Predisposition to open perforation depends mainly on anatomical factors: the probability of perforation is especially high in location of the ulcer on the anterior wall of the duodenum. Perforation may occur in the absence of patient's complaints ("silent ulcer") or the appropriate anamnesis. Signs of perforation are a sudden stabbing pain, the reflex collapse, acute abdomen, and progressive peritonitis (unless a timely surgical aid is given to the patient). The pain is felt beneath the xiphoid process or in the right hypochondrium. The abdominal wall is tense. The patient assumes a forced posture on his back; the tongue is dry and coated. The pulse is retarded, the temperature is subnormal. In most cases the diagnosis is undoubtful and a timely surgical intervention saves the patient's life.

Stenosis. Ulcers heal to leave scars. If the ulcer was in the pylorus, the cicatricial tissue may narrow the lumen and interfere with free passage of the gastric contents into the duodenum. First the narrowing is compensated for by hypertrophy of the gastric muscles, but later the stomach becomes distended, food stays inside it for a longer period, and fermentation and putrefaction occur in the stomach. Absorption of water is impaired (the impairment begins in the duodenum). This upsets the water-salt balance, causes general dehydration of the body, and decreases the chloride content in the blood and urine.

Patients complain of permanent pain (which intensifies by night), eructation with rotten egg wind, and profuse morning vomiting with food that was ingested several days ago. Constipation is alternated with diarrhoea, through irritation of the small intestine by fermented food discharged into it from the pylorus which is opened by intensified peristalsis. If stenosis is pronounced, the patient is cachectic. Examination of the epigastrium reveals peristaltic and antiperistaltic contractions of the stomach. Late splashing sound can be heard.

Treatment and prophylaxis. Anti-ulcer treatment implies combined and individual therapy. Non-complicated peptic ulcer is treated conservatively. Exacerbations should be treated in hospital where bed-rest, special diet, medicinal preparations (tranquilizers, cholinolytics, antacids) and thermal procedures are given. The diet should not stimulate the secretory function of the stomach. It should decrease the motor function of the gastroduodenal system and have buffer properties. The diet should also be sparing with respect to its chemical and mechanical effect on the stomach.

Patients in remission should be regularly observed in out-patient conditions. Smoking and alcohol are prohibited in peptic ulcer disease. Attending diseases should also be treated and sanation of the mouth carried out. Sanatorium and health-resort therapy is indicated. Employment of patients should be sparing. Persons with "irritated" stomach (functional stage of peptic ulcer) should be regularly observed in out-patient conditions.

Prophylactic measures should be aimed at prevention of the disease, its relapses or complications. Current knowledge of the developmental mechanisms of peptic ulcer suggests that population should be given information on rational nutrition, labour, and rest. The adverse effect of alcohol and smoking should be especially emphasized.

INTESTINE

Methods of Examination

Inquiry

Complaints. The main complaints with intestinal diseases are pain, meteorism (inflation of the abdomen), motor dysfunction of the intestine (constipation and diarrhoea), and intestinal haemorrhage.

Pain. If the patient complains of pain in the abdomen, the following should be established: location of pain, its radiation, intensity, character, duration, and means by which it is lessened. The general signs by which intestinal pain may be differentiated from gastric one are: (1) absence of regular dependence of pain on food taking; the only exception is inflammation in the transverse colon (transversitis): pain develops immediately after meals; the pathogenesis of this pain is connected with reflex peristaltic contractions of the transverse colon when food enters the stomach; (2) close association of pain with defaecation: pain occurs before, during, and (rarely) after defaecation; (3) pain relief after defaecation or passage of gas.

Pain may be boring and spasmodic (intestinal colic). Colicky pain is characterized by short repeated attacks which arise and disappear quite of a sudden. Pain may very quickly change its location, the main site being

round the navel. Sometimes pain may arise in other areas of the abdomen. Boring pain is sometimes permanent; it intensifies during cough, especially if the mesenterium or peritoneum are involved. Pain is characteristic of inflammatory diseases of the intestine. As inflammation extends onto the peritoneum, pain is attended by a pronounced muscular defence.

Exact location of the source of pain is very important. Pain in the right iliac region occurs in appendicitis, tuberculosis, cancer, or inflammation of the caecum (typhlitis). Acute pain in the left lower abdomen occurs in intestinal obstruction and inflammation of the sigmoid (sigmoiditis). Pain in the umbilical region occurs in inflammation of small intestine (enteritis) and inflammation or cancer of the colon. Pain in the perineal region, and especially during defaecation (with the presence of blood in faeces), is characteristic of the rectum diseases (proctitis, cancer). Pain in intestinal pathology may radiate into the chest; pain associated with affection of the spleen angle of the descending large intestine radiates into the left side of the chest (it is sometimes mistaken for pain attacks of angina pectoris); colics of appendicitic origin radiate into the right leg.

In acute affection of the left portions of the large intestine (dysentery), pain radiates into the sacral area. Thermal procedures, spasmolytics, passage of gas, and emptying of the bowels can relieve pain or remove it completely.

Intestinal pain is caused by obstruction of intestinal patency and upset motor function. Intestinal pain is mostly caused by spasms (spasmodic contraction of smooth muscles; hence spastic pain), or by distension of the intestine by gases. Both mechanisms often become involved.

Spastic pain can be due to various causes. Individual predisposition to spastic contractions in general (vegetoneurosis) may be as important as irritation originating in the intestine proper, e.g. in enteritis, colitis, intestinal tumour, poisoning with arsenic or lead, and also in diseases of the central nervous system (posterior spinal sclerosis).

Pain arising due to intestinal distension by gases, and associated with tension and irritation of the mesentery, differs from spastic pain (1) by the absence of periodicity; it is long-standing and gradually lessens in prolonged inflation; and (2) by exact localization. In intestinal obstruction (complete or partial) colicky pain is combined with almost permanent pain in the abdomen. It is characterized by exact and permanent location (the umbilical region and large intestine). The pain intensifies with intestinal peristalsis.

Appendicular colic first localizes round the navel and the epigastrium but in several hours (or even on the next day) it descends to the right iliac region where it intensifies gradually. Sometimes the pain arises straight in the right iliac region.

Rectal colic, or tenesmus, is also known. It occurs in frequent and painful tenesmus to defaecate and is associated with spasmodic contractions of the intestine and the sphincter ani. Only clots of mucus are sometimes expressed instead of actual defaecation. Tenesmus occurs in dysentery and other inflammatory or ulcerous diseases, and in cancer of the rectum. Pain associated with defaecation depends on many factors. Pain preceding defaecation is associated with the disease of the descending colon or sigmoid colon. Pain during defaecation is characteristic of haemorrhoids, anal fissures, and cancer.

Meteorism. The patient feels flatulence, inflation, and boring distension of the abdomen. The causes of meteorism are (1) excessive gas formation in the intestine due to ingestion of vegetable cellular tissue and easily fermented food (peas, beans, cabbage, etc.); (2) intestinal motor dysfunction due to decreased tone of the intestinal wall or intestinal obstruction; (3) lowered absorbability of gases by the intestinal wall, the process of gas formation being normal; (4) aerophagia, i.e. excess swallowing of air, with its subsequent propulsion to the stomach and the intestine; (5) hysterical meteorism: the abdomen is rapidly inflated to the size of the abdomen of a pregnant woman at her last weeks; this nervous mechanism is very complicated.

When inquiring the patient, the physician should ask about the character of his nutrition and the site of abdomen inflation (the entire abdomen or only its limited part may be inflated). If inflation is local, it is necessary to ask the patient whether or not inflation occurs always at one and the same area. In intestinal obstruction, the patient feels rumbling sounds inside the abdomen, feels movement of liquid in the intestine, and intense peristaltic movements above the point of obstruction.

Diarrhoea. Frequent and liquid stools is a common sign of intestinal pathology. Diarrhoea occurs in acute and chronic intestinal infections (enteritis, enterocolitis, sigmoiditis, proctitis), in various exogenous intoxications (poisoning with arsenic or mercury), endogenous intoxications (uraemia, diabetes, gout), in endocrine disorders (adrenal dysfunction, thyrotoxicosis), and in hypersensitivity to some foods (allergy).

The mechanism of diarrhoea is very complicated. Different pathogenic factors may prevail in various pathological conditions. Accelerated movement of the liquefied food in the intestine due to peristalsis is among them. Almost undigested food can thus be evacuated. Another factor is disordered absorptive function of the intestine. Affection of the intestinal wall, disordered mechanisms regulating absorption, purgatives and upset water metabolism produce a marked change in the absorption process and are the cause of diarrhoea.

The third cause of liquid stools is inflammation of the intestine. Large

quantities of inflammatory secretion stimulating the intestinal receptors are released into the lumen of the intestine to intensify its peristalsis and to impair its absorptive function.

Paradoxical diarrhoea occurs in prolonged constipation due to mechanical irritation of the intestinal wall by hard faecal masses.

Upset equilibrium between the fermentative and putrefactive flora of the intestine is another important factor in the aetiology of diarrhoea. If fermentative flora prevails, *fermentative dyspepsia* occurs which is characterized by flatulence of the abdomen and semiliquid acid faeces (2-3 stools a day); the faeces contain numerous gas bubbles, numerous starch grains, vegetable cellular tissue, and iodophilic microbes. Fermentative dyspepsia develops in connection with deranged digestion of carbohydrates, if they are ingested in excess.

Putrid dyspepsia more often occurs in secretory hypofunction of the stomach. The absence of bactericidal action of gastric juice is connected with the absence of hydrochloric acid; rapid passage of insufficiently digested food from the stomach to the intestine has a negative effect in the first instance on digestion of proteins. This in turn provokes putrid dyspepsia. It is characterized by liquid dark excrements containing clots of undigested food; the faeces react alkaline and have a foul putrid smell. Microscopy of faeces reveals much fats, muscular fibres with vivid transverse and longitudinal striation and even ends (creatorrhoea). The content of organic compounds in the faeces is increased. The iodophilic flora is absent.

Diarrhoea occurring in organic affections of the large intestine is mostly of the inflammatory character. It is not copious, nor does it produce strong negative effect on the patient's general condition (as compared with affections of the small intestine which is attended by profuse diarrhoea associated with deranged motor and absorption function of the intestine). The pronounced disorder in digestion causes some metabolic disorders in the patient (impaired absorption of proteins, iron, vitamins, and electrolytes).

Obstipation. This is obstinate constipation during which faeces are long retained in the intestine (for more than 48 hours). But the duration of constipation is only relative, because in many cases it is not the result of pathology but of the living conditions and nutrition. If vegetable food dominates in the diet, the subject may defaecate two or three times a day. Stools become rarer if the diet is rich in meat. A radical change in nutrition can remove constipation. Limited mobility of the subject, hunger, and irregular defaecations (during the day) may prolong pauses between defaecation. The main factor determining defaecation is the condition of intestinal motor function. Bowel contents are retained in the large intestine and the rectum during constipation.

Organic and functional constipation is differentiated. Organic constipation is usually associated with mechanical obstruction, such as narrowing of the intestinal lumen due to a tumour, scar, adhesion, and also abnormalities in the intestine (megacolon, dolichosigmoid, megasigmoid, diverticulosis).

Functional constipation is subdivided into: (1) alimentary constipation; it occurs due to ingestion of easily assimilable foods, which leave small residue and normally stimulate peristalsis of the intestine by irritating its nervous receptors; (2) neurogenic constipation due to dysfunction of the intramural nervous apparatus or vagus nerve; these are the so-called dyskinetic constipation, caused by the reflex action on the intestinal motor function of another affected organ (cholecystitis, adnexitis, prostatitis, etc.), or by organic affections of the central nervous system (tumours of the brain, encephalitis, posterior spinal sclerosis); (3) constipation associated with inflammatory affections, mainly of the large intestine (dysentery); (4) toxic constipation occurring in exogenous poisoning with lead, morphine, or cocaine; (5) constipation of endocrine aetiology, occurring in thyroid or pituitary hypofunction; (6) constipation caused by lack of physical exercise; (7) constipation caused by flaccidity of the prelum.

Intestinal haemorrhage often occurs in ulcerous affections of the alimentary system. It develops in the presence of tumour, protozoal and helminthic invasions, acute infections (typhoid fever, bacillary dysentery), in thrombosis of mesenteric vessels, ulcerous non-specific colitis, etc.

Anamnesis. The patient should be inquired thoroughly about his nutrition from his early childhood till the onset of the disease (especially directly before the disease), about poisonings in the past history and hypersensitivity to some foods. It is necessary to find out if the patient's meals are regular, if the food is varied, and if the patient smokes or drinks alcohol. Information on the past diseases of the intestine and also on pathology of other organs is sometimes decisive for establishing the cause of the present affection.

Some functional disorders of the intestine can be associated with occupation (lead or arsenic poisoning, constipation due to frequent suppression of tenesmus to defaecate).

Physical Examination

INSPECTION

Severe prolonged affection of the absorptive function causes grave cachexia. Oedema is possible in loss of protein with simultaneous retention in the body of water and salt. Inspection of the skin reveals its dryness and pallidness; the mucosa is pale due to insufficient absorption of iron and anaemization of the patient. Insufficient absorption of vitamins results in

development of fissures of the lips, the skin becomes rough and perleche develops.

Facies hippocratica (facies abdomihalis) is a very important diagnostic sign of peritonitis or intestinal obstruction. The tongue in intestinal diseases often becomes crimson (cardinal tongue), its papillae are smoothed down. The gums may be loose and bleeding.

Inspection of the abdomen. The general outlines of the abdomen should be inspected. The abdomen can be of a normal shape with slightly protruding suprapubic region; it can be enlarged due to excess subcutaneous fat, and inflated in the presence of meteorism or ascites. Regularity of the abdomen shape should be assessed. An enlarged liver may protrude in the upper abdomen; an enlarged uterus causes protrusion of the lower abdomen.

The patient is asked to breathe "with his abdomen" to assess the mobility of the abdominal wall. The patient is unable to take a deep breath in the presence of pain, e.g. in an attack of acute appendicitis or cholecystitis. Divarication of the rectus abdominis muscles can be revealed if the patient raises his head. Regular application of hot-water bottle leaves its traces on the abdomen; these, together with postoperative scars, often help the physician to interpret correctly the present patient's complaints. Antiperistaltic movements in the epigastrium or by the course of the intestine can give a hint on the presence of an obstacle to propulsion of food masses in the intestine.

If the abdomen is inflated, the causes should be established. These may be obesity, accumulation of liquid, or meteorism. Slight distension of the abdomen may be due to a tumour, encapsulated fluid, or meteorism associated with intestinal stenosis. The latter suggestion is confirmed by visible peristalsis over the constricted portion of the intestine where the flatulence is observed.

PALPATION

Palpation of the abdomen. Along with X-ray examination, palpation is the main method of physical examination in diagnosis of diseases of the abdominal organs. This method was first appreciated by French physicians (Glenard). Later the Russian internists (Obraztsov, Strazhesko, and others) further developed this useful method.

Glenard proposed palpation of the abdomen and believed that this method should systematically be used for clinical examination of the abdominal cavity. He maintained that palpation can be used to examine not only the abdominal organs but also various portions of the intestine. Having established that the caecum, transverse colon, sigmoid, and the colon proper can sometimes be palpated, he erroneously believed that their palpability indicated

their pathology. Independently of Glenard, Obraztsov developed methods for palpation of the gastro-intestinal tract and proved that some parts of the stomach and the intestine can be palpated in the absence of any pathology. He gave a detailed description of physical properties of each part of the abdominal organs in normal conditions. He thus substantiated usefulness of palpation in clinical practice along with other physical methods of examination; secondly he stimulated the study of the topographic relationships in the abdominal cavity of a living person before X-rays were discovered; and thirdly his teaching made it possible to compare the physical properties of organs and their topographic relations in health with those in pathology, which has become an important tool in the diagnosis of diseases of the abdominal cavity.

Later Obraztsov and his pupils developed in detail palpation techniques for examination of the abdominal cavity; they studied the organs and their separate parts that can be palpated under various conditions, and also gave a detailed description of normal palpatory signs of organs and their changes in various pathological conditions. They have proved finally the importance of palpation as an invaluable method of examination of the abdominal organs. It should however be emphasized that it is very difficult to master properly the palpation techniques for diagnostic purposes. It requires much experience and training. The palpation method described below has been proposed by Obraztsov and Strazhesko.

It is necessary that the abdominal cavity should be accessible to palpation, i.e. that its muscles (prelum) be relaxed and that the examiner should not provoke their straining by his manipulations. The patient should relax in his bed. (The bed should not be too soft.) His legs should be stretched and the arms flexed on the chest. The patient's breathing should not be deep; his head should rest against a small firm pillow. This position ensures relaxation of the abdominal muscles. The physician takes his place by the right side of the bed, facing the patient. The chair should be firm and level with the patient's bed. The ambient temperature should be comfortable for the patient, and the hands of the doctor should be warm and dry.

The examining movements should be careful and gentle so as not to hurt the patient. Touching the abdomen roughly with cold hands will cause reflex contraction of the prelum to interfere with palpation of the abdomen. The patient with distended abdomen should first be given cathartics or enema to empty the bowels. These are the conditions for palpation of the patient in the recumbent position. But some organs or their parts can only be palpated when they hang by gravity with the patient in the erect position. Thus the left lobe of the liver, the lesser curvature of the stomach, the spleen, the kidneys, the caecum, or tumours can become palpable. The epigastrium and the lateral parts of the abdominal cavity should also be palpated with the patient in the erect position.

Palpation is used to establish normal topographic relations between the abdominal organs and their normal physical condition; the other object is to detect any possible pathology that changes the morphological condition of the organs and their topographic relations responsible for their dysfunction, to locate the defect, and to determine its nature. Surface and deep

palpation are used. Deep palpation gives information on the physical and sometimes functional condition of the organs and also on their position in the abdominal cavity. In other words, deep palpation gives information on the topography of the abdominal cavity (topographic palpation).

Surface tentative palpation. The physician assumes his position by the bedside as described above and places his right hand flat on the abdomen of the patient (the fingers may be slightly flexed) to examine carefully and gradually the entire abdomen without trying to penetrate the deep parts of the abdomen. By this examination the physician should establish the strain of the prelum, its tenderness, and location of the painful site. The left inguinal area should be examined first, provided the patient does not complain of pain in this region. Palpation is then continued by examining symmetrical points of the abdomen on its left and right sides to end in the epigastric region. If the patient complains of pain in the left inguinal area, the sequence of palpation should be so changed that the least painful site on the anterior abdomen should first be examined. The physician should simultaneously assess the condition of the abdominal skin and subcutaneous connective tissue, the strain of the abdominal wall, the zones of superficial and deeper painful areas to locate them accurately. Hernial separation of muscles and protrusions, and also other anatomical changes should be revealed, if any. Resistance and marked strain of muscles of the abdominal wall are usually palpated over the organ affected by inflammation, especially so if the peritoneum is involved. In the presence of acute inflammation of the peritoneum (local inflammation included, e.g. in purulent appendicitis, cholecystitis, and the like), local pressure causes strong pain but it becomes even more severe when the pressure is released (Shchetkin-Blumberg symptom). In the presence of pronounced enlargement of the parenchymatous organs, in strained abdomen or intestinal loops, and also in the presence of large tumours, even surface palpation can give much diagnostic information. But only deep systematic palpation can give full information about the condition of the abdominal cavity and its organs, as well as their topography.

Deep sliding palpation (according to Obraztsov and Strazhesko). When starting deep palpation the examiner should always be aware of the anatomical relations in the abdominal cavity, the shape and physical properties of the organs, their supporting structures and possible deviations in topographical relations that may depend on the constitution of the patient, his special condition, nutrition, relaxation of the abdominal muscles, etc.

Obraztsov used the double-checking principle in his examinations. For example, in order to make sure that a given section of the intestine is actually ileum terminale it is necessary to locate the caecum; to determine the size of the stomach, the palpatory findings are checked by percussion and

percussive palpation of the stomach. Respiratory excursions of the organs should be taken into consideration during palpation according to a strictly predetermined plan, beginning with more readily accessible parts. The following sequence is recommended: the sigmoid, the caecum with the appendix, pars coecalis ilii, the ascending and descending colon, the stomach with its parts, the transverse colon, the liver, the spleen, the duodenum, the pancreas, and the kidneys.

Success of palpation depends on strict observation of the rules. The posture of the patient and the physician should be the same as in surface palpation. Palpation should be carried out by the apt hand. In some cases the other hand should be placed on the examining hand to increase pressure. Palpation can also be bimanual (palpation with both hands simultaneously). If only one hand is used, the other hand presses the prelum laterally to the palpated zone in order to lessen or overcome resistance of the abdominal wall and hence to promote relaxation of the prelum in the palpated zone. The other hand can be used to move the palpated organ closer to the examining hand or in order to perform bimanual palpation.

The palpation technique includes the following four steps. First: proper positioning of the physician's hands. The right hand is placed flat on the anterior abdominal wall, perpendicular to the axis of the examined part or the edge of the examined organ. Second: formation of a skin fold to facilitate further movements of the examining hand. Third: moving the hand inside the abdomen. Deep palpation is when the fingers are moved gradually, with each expiration, into the abdomen when the abdominal wall is relaxed. The examining hand thus reaches the posterior wall of the abdomen or the underlying organ. Fourth: sliding movement of the fingertips in the direction perpendicular to the transverse axis of the examined organ. The organ is pressed against the posterior wall and the examining fingers continue moving over the examined intestine or the stomach curvature. Depending on the position of the organ, the sliding movement should be either from inside, in the outward direction (the sigmoid, caecum) or in the downward direction (the stomach, transverse colon); the movements should then be more oblique in accordance with the deviation of the organ from the horizontal or vertical course. The examining hand should always move together with the skin and not over its surface.

By palpating the intestine, the physician establishes its localization, mobility, tenderness, consistency, diameter, the condition of the surface (smooth, tubercular), the absence or presence of rumbling sounds during palpation. All these signs indicate the presence or absence of pathology.

The *sigmoid* (Fig. 87) is palpated from top right to medial left, downward and laterally, perpendicularly to the axis of the intestine which

runs obliquely in the left iliac space at the border of median and the outer third of the linea umbilico-iliacae. Palpation is carried out by four fingers, placed together and slightly flexed, or by the ulnar edge of the right little finger. The fingers are immersed medially of the expected position of the intestine and as soon as the posterior wall of the abdomen is reached, the fingers slide along the intestine in the given direction, i.e. laterally and downward. The intestine is pressed against the posterior wall and first slides along it (to the extent allowed by the mesenteric length) but later it slips from under the examining fingers. The sigmoid can be palpated by the described technique in 90-95 per cent of cases. The sigmoid is only impalpable in excess inflation of the abdomen and in obese patients. If the sigmoid is not found where it belongs, it may be displaced to some other location because of long mesenterium which accounts for the high sigmoid mobility. It is then usually displaced closer to the navel and to the right. The sigmoid can usually be found by deep palpation of the infraumbilical and suprapubic areas. Normally the sigmoid can be palpated over the length of 20-25 cm as a smooth firm cylinder, its thickness being that of a thumb or an index finger; the sigmoid is painless to palpation, it does not produce rumbling sounds, its peristalsis is rather flaccid and infrequent. The sigmoid can be displaced 3-5 cm to either side.

The *caecum* is palpated by the same technique (Fig. 88), except that the direction is different. Since the caecum is situated at the border of the median and lateral third of the umbilico-iliac line (5 cm by the iliac spine), the

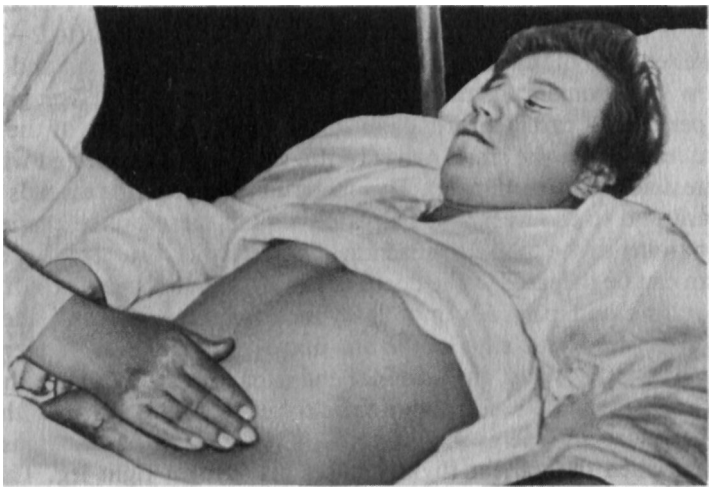


Fig. 87. Palpation of the sigmoid.

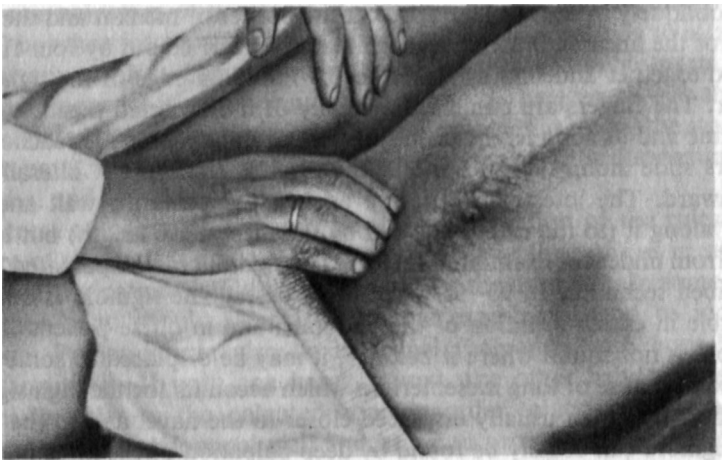


Fig. 88. Palpation of the caecum.

palpation is carried along this line or parallel to it. Palpation is used not only to locate the caecum but also a certain part of the ascending colon (10-12 cm of its length), i.e. the part of the large intestine which is known in the clinic as typhlon. A normal caecum can be palpated in 80-85 per cent of cases as a moderately strained cylinder (widening to the round bottom), 2—3 cm in diameter; when pressed upon, it rumbles. Palpation is painless. It reveals a certain passive mobility of the caecum (to 2—3 cm). The lower edge of the caecum is 0.5 cm above the bi-iliac in man and 1-1.5 cm below it in women. Further palpation of the right iliac region gives (in 80-85 per cent of cases) information on the 15-20 cm length of the *ileum* which ascends from the small pelvis to the right, to be connected with the large intestine (ileum terminale). This section of the intestine extends mostly upward and to the right and palpation should therefore be carried out almost parallel to the umbilico-iliac line (but below it). The terminal end of the ileum can be palpated in the depth of the right iliac space as a soft, easily peristalting and passively mobile cylinder, the thickness of the little finger (or a pencil); it slips out from under the examining fingers and rumbles distinctly. When the terminal end of the ileum is found, the *vermiform process* can be found above or below it. It is found easier if the belly of the psoas muscle is first found. The location of this muscle is facilitated when the patient slightly raises his straight right leg. The vermiform process then becomes more pronounced over the contracted belly of the psoas muscle. The vermiform process can be palpated in 20-25 per

cent of cases. This is a thin (goose-feather thick) painless cylinder. When palpated the process does not change its consistency; nor does it rumble. Once the cylinder has been felt above or below the ileum, the examiner cannot be quite sure that he has found the vermiform process because it can be simulated by mesenteric duplicature and a lymph bundle. It is difficult to find the vermiform process also because its position varies with respect to the caecum. It becomes impalpable at all when located behind the caecum. When the process is inflamed it becomes much easier to find it because of its thickening, fixation, and consolidation. The caecum, the terminal part of the ileum, and the vermiform process are palpated by four fingers of the right hand; the fingers should be held together and slightly flexed. If the prelum is tense, the muscles in the palpation zone can be relaxed by pressing the umbilical area with the radial edge of the left hand.

The *ascending and descending colons* are palpated by two hands (Fig. 89). The left hand is placed under the left and then the right lumbar side, while the fingers of the right hand press on the anterior wall of the abdominal cavity until the examiner feels his right and left hands meet. The examining fingers then slide laterally, perpendicularly to the axis of the intestine (Vasilenko).

The *transverse colon* is palpated by four fingers of the right hand held together and slightly flexed (Fig. 90). Bimanual palpation can also be used. Since the position of the transverse colon is unstable, it is useful first to determine by percussive palpation (after Obraztsov) the lower border of

Fig. 89. Palpation of the descending colon.

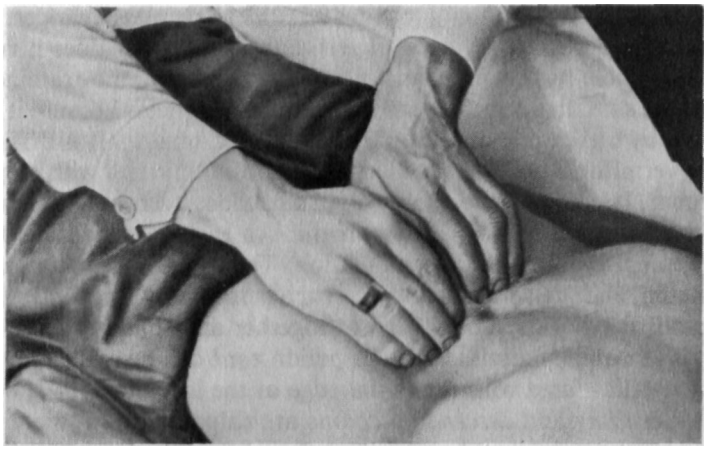


Fig. 90. Palpation of the transverse colon.

the stomach, and only then to search for the colon some 2-3 cm below this border. The right hand (or both hands) is placed on the sides of the linea alba and the skin is moved slightly upwards. The examining hand is then immersed gradually during relaxation of the prelum at expiration until the posterior wall of the abdomen is felt. Once the posterior wall is reached, the examining hand should slide down to feel the intestine: this is an arching (transverse) cylinder of moderate density (2—2.5 cm thick), easily movable up and down, painless and silent. If the intestine is impalpable in this region, the same technique should be used to examine the lower and lateral regions, the position of the palpating hands being changed accordingly. Normal transverse colon can be palpated in 60-70 per cent of cases.

In addition to the mentioned portions of the intestine, the horizontal parts of the duodenum and the curvature of the colon can in rare cases be palpated; an occasional loop of the small intestine that may happen in the iliac cavity can also be palpated. But the small intestine is usually impalpable because of its deep location, high mobility, and thin walls; it cannot be pressed against the posterior abdominal wall, which is the necessary condition for palpation of normal intestine.

The *rectum* can be probed by a finger after cleansing it with enema. The patient Should assume the knee-chest position. The examining index finger should first be coated with vaseline oil and then introduced carefully into the rectum to the maximum possible depth. If the patient is especially sensitive, or the rectum and the ampulla are affected with inflammation or

fissures, the sphincter and the ampulla should be anaesthetized before the intervention. As the examining finger passes the sphincter, it feels anteriorly the prostate in men and the vaginal part of the uterus in women. The finger should be moved upwards to pass the sacrococcygeal plica and to reach, if possible, the terminal rectal plica that closes the entrance to the sigmoid (11-13 cm above the anus). Palpation of the rectum can be facilitated if the patient squats and strains (makes evacuatory efforts). After examination of the anterior wall, the posterior wall of the rectum is felt by the finger. The finger is turned through 180° and the posterosacral and then lateral walls are examined. The examiner should get an idea of the mucosa (the presence of papilloma, polyps, varicose nodes, oedema and swelling of the mucosa, cicatricial narrowings, newgrowths, etc.) and the connective tissue surrounding the rectum, Douglass space, the prostate, the uterus and its appendages, and the pelvic bones.

Palpability of *tumours of the abdominal cavity gave* the impetus to detailed and systematic development of palpation techniques. This method is still important for the diagnosis of tumour. Palpation is used to reveal a tumour, to determine its belonging and relation to the neighbouring organs. Palpation is now sometimes carried out under roentgenoscopic control. Once a tumour has been revealed, it is necessary to establish its location: whether it is located in the abdominal wall proper, inside the abdominal cavity, or behind the peritoneum. If a tumour is present in the abdominal cavity, it is necessary to determine the organ to which it relates and also its relation to other organs; mobility of the tumour should then be determined, and also the presence of inflammatory process in the peritoneum round the tumour.

As distinct from intra- and retroperitoneal tumours, tumours of the abdominal wall are located more superficially and can easily be revealed by inspection. When the prelum is strained the tumour becomes fixed and its palpation becomes more difficult but it does not disappear from the palpation field, as is the case with intraperitoneal tumours (during respiratory excursions, intraperitoneal tumours move anteroposteriorly because the prelum protrudes during inspiration and retracts during expiration).

Tumours located behind the peritoneum are in close contact with the posterior abdominal wall; their mobility is low during respiration or palpation; moreover, they are always covered by the intestine or the stomach. Retroperitoneal tumours are characterized by high respiratory and passive mobility. The closer they are located to the diaphragm, the greater their vertical mobility during inspiration. The width and length of the overlying ligaments of the organ to which the tumour is related determine passive mobility of the tumour. But sometimes tumours of fastened parts of the gastro-intestinal tract become highly mobile due to congenital excessively long mesenterium and ligaments, or due to distension of the supporting apparatus by the growing tumour. For example, pyloric tumours or tumours of the caecum are highly mobile. Intraperitoneal tumours lose their respiratory and passive mobility if inflammation of the surrounding peritoneum develops with formation of firm adhesions between the tumour and the neighbouring organs.

Detecting a tumour and locating it inside the abdomen is the first stage in its identification. Next determined are its shape, density, elasticity, features of the surface, the presence of fluctuation, tenderness, and relation to a particular organ. This becomes only possible after preliminary topographic palpation of the entire abdominal cavity and establishment of the position and properties of each separate organ. This concrete study of topographic relations is necessary because, due to the growth of a tumour and changed intra-abdominal pressure,

these relations are often upset and perverted and knowledge of the normal position of the organs and their relation to each other is no more useful.

Every physician must be able to perform methodic palpation in order to treat patients with pathologies of the abdominal organs. This may be an internist, a surgeon, a gynaecologist, or a urologist.

None of the known methods of clinical studies rules out any other. Only combination of various methods can give a complete picture of the present disease.

PERCUSSION

Percussion of the abdomen is only relatively informative. Percussion of the anterior abdominal wall at points of projection of the intestine gives tympany of various character which depends on the uneven distribution of gaseous, liquid or solid intestinal contents.

AUSCULTATION

Auscultation gives information about the motor function of the intestine. During gastric digestion and movement of the chyme along the small intestine, long periodic rumbling can be heard. Rhythmic intestinal murmurs can be heard in the caecum 5—7 hours after meals. In mechanical obstruction of the intestine, its peristalsis is resonant (in large waves). Peristalsis disappears in paralytic obstruction of the intestine; the abdomen is absolutely "silent" in perforation of the ulcer with secondary paralysis of the intestine; peritoneal friction can be heard in patients with fibrinous peritonitis during respiratory movements.

Laboratory and Instrumental Methods

X-RAY STUDY

X-ray studies are used to determine the morphological and functional properties of the *small intestine.* Contrast substance (100 g of barium sulphate in an equal quantity of water) is used for the purpose. The patient takes the barium meal and 2.5 hours later the suspension enters the caecum. Earlier or delayed entrance of the suspension from the small intestine to the caecum indicates its upset motor function. The relief of the mucosa in the small intestine has a feather-like pattern, which becomes disfigured in its inflammatory affections. Shallow horizontal ridges between accumulations of liquid and gas in the intestinal loops can sometimes be seen in hypersecretory disorders. Small protrusions and diverticula occur sometimes along the course of the small intestine. Tumours of the small intestine have no specific X-ray signs.

X-ray study of the *large intestine is* carried out after giving the patient a barium meal by mouth or administering the suspension by enema (per rectum). If barium is given per os, it reaches the caecum in 2.5-4 hours. The ascending portion of the intestine is filled in 3—6 hours. The transverse colon is filled with barium in 12 hours. In 24 hours the large intestine can be seen along its entire course. This roentgenological study of the large intestine gives information on its motor function, length, position, shape, tone, and haustration.

Giving a contrast substance per rectum (200 g of barium sulphate suspension in 1.5 litres of water) ensures a more detailed information on possible constrictions and adhesions in the large intestine and also the relief of its mucosa.

RECTOSIGMOIDOSCOPY AND COLONOSCOPY

Rectosigmoidoscopy is a direct visualization of the mucosa in the rectum and the sigmoid colon. A sigmoidoscope is a 35 cm-long metal tube, with a diameter of 2 cm. A metal mandrin (obturator) passes the lumen of the tube. The outer end of the tube is closed by a tightly screwed disc with.a glass window through which the physician observes the intestine. The outer surface of the instrument is graduated in centimetres so that the depth of penetration of the instrument could be read off. Air is used to inflate the collapsed intestine. The lower end of the large intestine is preliminarily emptied by giving a cleansing enema 1—2 hours before rectosigmoidoscopy. The patient assumes either a knee-chest position or lies on his left side with the legs flexed on the abdomen. The instrument is first introduced at a right angle to the plane of the rectal entrance and then the direction is slightly changed posteriorly, toward the sacrum, along the course of the large intestine. When the tube is passed to the depth of 6-8 cm, the obturator is removed and an electric lamp introduced instead. The outer end of the tube is then closed tightly with the "window" disc and an air cylinder is connected. Further progress of the tube is controlled visually-

The instrument can be used to inspect the mucosa of the rectum and sigmoid colon to the depth of 35 cm. Normal mucosa is smooth, moist, and moderately red. In acute inflammation the mucosa is oedematous, opaque, and covered with mucus. Haemorrhage, erosions, ulcers, haemorrhoids, and fissures of the anus can also be seen. Rectosigmoidoscopy helps early diagnosis of cancer tumours in the rectum and the lower portion of the sigmoid colon. The instrument is provided with a special device for sighting biopsy for morphological studies. Finger examination of the rectum is only possible at depths of 6 to 8 cm.

A more complete endoscopy of the large intestine can be done with a colonoscope (endofibroscope), whose length is 86-186 cm. Because of high flexibility, it can be introduced through the anus to reach any portion of the large intestine. In addition to visual examination, the instrument can be used to take specimens of the intestinal mucosa for establishing a diagnosis.

COPROLOGICAL STUDIES

Analysis of faeces is an important item in the study of patients with diseases of the alimentary system.

Faeces of a healthy subject consist of about equal volumes of undigested food remains, secretions of the alimentary organs and microbes (mainly dead ones). Faeces are studied to detect blood, ova of helminths, etc. General clinical analysis helps assess assimilation of food, discover disorders in the biliary secretion, latent haemorrhage, inflammation, the presence of parasites, etc. Coprology includes macroscopy, microscopy, and simple chemical analysis. Microbiological studies of faeces are necessary in cases suspected for infectious diseases of the intestine.

Faeces are collected in a dry clean container and studied as soon as possible (not later than 8-12 hours after defaecation, provided the specimen is kept in the cold). Faeces should be examined for the presence of protozoa immediately after defaecation. When faeces are examined for the degree of food assimilation, the patient is given a common diet (or a special diet for more detailed studies) several days before the study.

Macroscopy of faeces includes assessment of the amount of daily excretion, the colour of faeces, their consistency, shape, odour, presence of undigested food remains, mucus, blood, pus, and parasites.

The normal daily excretion (with varied nutrition) is 100—200 g. The amount of faeces increases in ample vegetable diet, poor assimilation of food (in diseases of the pancreas), and intensified peristalsis. Faeces are meagre in proteinous diet, in constipations and hunger. Shapes of faeces depend mainly on their consistency. Normal faeces resemble sausage and are usually soft. In constipation faeces are hard, while in spastic colitis they resemble faeces of sheep (small nuts). The consistency of faeces depends largely on absorption of water in the intestine. Faeces are pasty when rich in fat.

Normal faeces are brown due to the presence of bilirubin derivatives (stercobilin and mesobilifuscin). In constipation, and also during antibiotic therapy, bilirubin is not reduced and faeces are golden-yellow. In cases with upset bile excretory function, faeces are greyish-white, clayish, or sandy (acholic faeces). In the absence of acholia, fatty faeces are grey as well

(amyloidosis of the intestine, or sprue), but they darken on exposure to light and give a positive reaction to stercobilin. Black colour of faeces can be due to haemorrhage in the upper portions of the gastro-intestinal tract (formation of sulphur compounds of iron), due to ingested black currants, coffee, carbolen, preparations of bismuth, iron, etc. Other medicinal preparations and plant pigments are also important for the colour of faeces. The odour of faeces changes with intensification of fermentation (acid odour of organic acids) or putrefaction (putrid dyspepsia), especially in degradation of tumour of the large intestine.

Remains of undigested food are easier detectable in faecal emulsion in a Petri dish placed against a dark background. Remains of vegetable foods are usually found. In the insufficiency of gastric and pancreatic digestion, or in the absence of teeth, faeces usually contain otherwise readily digested food (lientery). Connective tissue remains undigested (in the form of whitish fibrous structures) in gastric achylia. Ample fat in stools (steatorrhoea) is characterized by the appearance of a solidified fat coat on the faecal surface.

The *pathological components of stools,* such as mucus, blood, and pus can be seen by an unaided eye if they originate in the large intestine. If these components join faeces in the small intestine, mucus is mixed with faeces, while leucocytes and erythrocytes are decomposed. Clots or bands of mucus found on the surface of faeces indicate inflammatory changes in the large intestine. In membranous colitis, mucus is excreted in the form of dense bands which are sometimes mistaken by the patients for helminths. Dysentery and ulcerative colitis are characterized by secretion of blood-stained mucus. In haemorrhoidal bleeding, unaltered blood is seen on the surface of stools. Pus is liberated with faeces in ulcerative affections of the large intestine (dysentery, tuberculosis, degrading tumour), or in rupture of a paraproctal abscess. Faeces may contain stones (gallstones, coproliths, pancreatic calculus).

Ascarides, acanthocephala, and members of platyhelminths can be found in stools.

Microscopy of faeces is done to reveal remains of food cells, mucus, eggs of helminths, and protozoa. Most components of faeces can be found in a native preparation which is prepared from faecal emulsion in a small quantity of water. The preparation is then covered with a glass and viewed in the dark field with small and great magnification. Detritus is the main component of faeces. This is material whose particles (minutest particles of food, decomposed cells and microbes) are difficult to differentiate. Among food remains, only muscle fibres and connective tissue can be identified. *Muscle fibres* (Plate 13) are yellow cylinders with a transverse striated pattern which remains unchanged after cooking of meat but which disappears

under the action of digestive enzymes. Faeces of a healthy individual on a meat diet contain separate fibres which have lost their striated pattern. Many muscular fibres can be found in faeces (creatorrhoea) if the transport speed of the intestinal contents through the bowels is accelerated. The presence of fibres with preserved striated pattern indicates enzymatic insufficiency of digestive glands.

Connective tissue in faeces indicates inadequate gastric digestion. It appears as semitranslucent fibres with indistinct contours.

Starch and *vegetable cellular tissue* can be identified among remains of carbohydrate food. Plant cells are easily identifiable by thick coats, and vegetable tissue by thick intercellular partitions (Plate 14). The amount of cellular tissue depends on the character of food and the time of its passage through the large intestine, where it is partly destroyed by microbes. In order to reveal starch, a drop of Lugol's solution is added to the faecal emulsion. Starch grains are stained blue or violet (Plate 15). Starch is a readily assimilable product and normal faeces contain it in very small quantity or do not contain at all. Increased starch content of the faeces (amylorrhoea) is usually associated with diseases of the small intestine: starch remains unsplit due to accelerated peristalsis.

Neutral fat and products of its decomposition are found both in native preparations and preparations stained with Sudan III. From 90 to 98 per cent of neutral fat is assimilated by normal digestion. The remaining fat is excreted mainly as soaps. A great amount of fat is found in faeces (steatorrhoea) in the absence of sufficient lipase. If bile is present in deficient quantity, fatty acids are found in faeces. Sudan III stains neutral fat bright-orange (Plate 16). Crystals of fatty acids occur either as colourless needles with pointed ends (Plate 17) or drops and grains stained with Sudan III. Soaps form fine rhomboids and grains that are not stained with Sudan.

In addition to mucus, the intestinal wall supplies the following elements: leucocytes, erythrocytes, macrophages, cells of intestinal epithelium and of malignant tumours.

Leucocytes occur in normal faeces only as single cells, and their large accumulations (mainly with mucus and erythrocytes) are found in ulcerative affections of the large intestine (dysentery, tuberculosis, ulcerative colitis, cancer). Neutrophils prevail among leucocytes. Eosinophils are found in amoebic dysentery and some helminthiases. Erythrocytes occur in faeces of patients with ulcerative affections of the large intestine, fissures of the anus, and haemorrhoids. If the lesion stands higher in the intestine, erythrocytes decompose before they reach the rectum and the presence of blood in faeces should be determined by chemical analysis. Macrophages occur in faeces in the presence of inflammation, especially in bacterial dysentery. Macrophages are larger than leucocytes.

The cytoplasm contains many inclusions, products of phagocytosis. Single cells of intestinal columnar epithelium can occur in normal faeces. Their large accumulations, which are usually found in mucus, suggest colitis. They are often disfigured by digestion and impregnation with soaps. Cells of malignant tumours can be found only in the presence of newgrowths at the distal end of the large intestine.

Oxalates, cholesterol, triple phosphates, and Charcot-Leyden crystals occur in faeces.

An important object of microscopic studies is the detection of *protozoa* and *helminths*. If ova are numerous they are found in native preparations. If their quantity is scarce, their concentration should be increased as follows. Faeces are triturated with a heavy liquid (saturated solution of sodium chloride or sodium sulphate): lighter ova float to the surface of the emulsion and are collected together with the surface film by a metal loop and are transferred to an object glass.

Ova of helminths can be isolated by precipitation. To that end an aqueous emulsion of faeces is passed through a gauze to separate it from large particles; the liquid is allowed to stand; then it is decanted and the precipitate is used to prepare the material for microscopy. Telemann's method is more effective. The procedure is essentially the same except that hydrochloric acid and ether are used instead of water: most of the undigested food is decomposed. Ova are precipitated by centrifuging. Acanthocephala ova are detected in the material scraped from the perianal folds using a spatula or a cotton wool tampon wetted with glycerin.

Protozoa should be better revealed in freshly defaecated material. The staining techniques are difficult. Cysts of protozoa are well differentiated by staining with Lugol's solution. Amoeba, lamblia, and balantidia are important pathogenic factors.

Only several simple qualitative tests are usually carried out in normal general clinical analysis of faeces. More complicated **chemical analysis** is used to determine metabolic indices or to study functions of separate parts of the digestive system.

The *medium* of faeces is determined by litmus paper. If faeces are hard, the paper should be moistened. Normally faeces react weakly alkaline or neutral. This reaction depends on the vital activity of the intestinal flora, which is either fermentative or putrid. If carbohydrate assimilation is insufficient the fermentative flora is activated and faeces become acid (fermentative dyspepsia). If proteins are poorly assimilated (gastric or pancreatic achylia), and also in the presence of inflammation in the large intestine with exudation of protein, putrid flora becomes more active (putrid dyspepsia): faeces become markedly alkaline due to formation of ammonia.

More detailed information on the relations between fermentative and

putrefactive processes in the intestine is obtained by determining organic acids and ammonia in faeces.

If faeces are decoloured, it is important to find out whether secretion of bile into the intestine has stopped or only decreased. This can be determined by carrying out the test for *stercobilin.* A small specimen of faeces is triturated in a porcelain dish with a 7 per cent solution of mercury dichloride. The result is ready in two days: the mixture becomes crimson in the presence of stercobilin.

The presence of *blood* in faeces is of great diagnostic importance since it indicates ulcer or newgrowth of the gastro-intestinal tract. The colour of faeces changes only in profuse haemorrhage. Scant blood, or its latent presence can be determined by chemical analysis. In order to identify haemorrhage as a gastro-intestinal one, it is necessary to rule out other possible sources of bleeding, e.g. nose, gums, oesophagus, haemorroids, etc. and also foods containing blood, e.g. meat and fish which should be excluded from the diet three days before the analysis. Tests for iron are impracticable with determination of blood in faeces because iron can be taken with food or medicine. Methods used for the purpose are based on the property of haemoglobin to catalyse oxidation-reduction reactions. Pairs of oxidants and reductants are so selected that reactions between them only occur in the presence of haemoglobin (catalyst). Hydrogen peroxide is an oxidant and benzidine a reductant in the Gregersen test. Benzidine changes its colour on oxidation in the presence of blood. There exists a simple modification of this sensitive test. Undiluted faeces are applied in a thin layer to an object glass, which is then placed in a Petri dish on a sheet of white paper. The Gregersen reagent is placed in drops on the smear. (The reagent is prepared extemporarily by mixing equal quantities of a 1 per cent benzidine solution and 50 per cent acetic acid in hydrogen peroxide.) In the presence of blood, a green or blue colour develops, whose brightness and the speed of development depend on the amount of the blood present (the higher the blood content, the brighter the colour and the sooner it appears).

Weber's guaiac test is less sensitive than the benzidine one. It only becomes positive in the presence of profuse haemorrhage. The procedure is as follows: 3 to 5 g of faeces is mixed with strong acetic acid in the quantity sufficient to prepare a semiliquid paste, which is transferred into a test tube. An equal volume of ether is added, the test tube is stoppered and rolled on the table to obtain an ether extract. The mixture is allowed to stand for 30 minutes, the ether layer is decanted into another test tube, 1-2 ml of hydrogen peroxide is added, and then an extemporarily prepared alcoholic solution of guaiac resin is added drop by drop (15—20 ml): blue or violet colour appears in the presence of blood.

Food protein is almost completely split by enzymes in the absence of in-

tensified peristalsis. The presence of soluble protein in faeces therefore indicates its intense liberation by the intestinal wall during inflammation and ulceration (which are attended by cell decomposition), and haemorrhage. The Triboulet-Vishnyakov test is used to detect soluble protein. Equal portions of a 3 per cent aqueous emulsion of faeces are placed in three test tubes: 2 ml of a 20 per cent trichloroacetic acid solution (or 7 per cent hydrochloric acid) is added to one test tube, 2 ml of a 20 per cent acetic acid to the other, and 2 ml of water to the third test tube (control). The result is assessed in 24 hours: soluble protein coagulates in the presence of mercury perchloride or trichloroacetic acid and precipitates to trap microbes and detritus; the liquid is thus clarified. In the presence of excess mucus, the emulsion clarifies in the test tube containing acetic acid.

The study of activity of intestinal enzymes and absorption in the small intestine is also of diagnostic importance.

Major Clinical Syndromes

The Acute Abdomen

The term 'acute' or 'surgical' abdomen is used to designate a great number of acute conditions associated with the diseases of abdominal organs that may be regarded as a direct indication for emergency surgery. This term is however only used in preliminary (provisional) diagnosis, while deciding whether the patient should or should not be taken to hospital, when an accurate diagnosis at patient's bedside is not possible.

The diseases, that can be manifested by the clinical picture of the acute abdomen may conventionally be classed into the following four groups:

1. Perforation of hollow organs, e.g. the stomach, the intestine, the gall bladder, with discharge of their contents into the abdominal cavity. Peritoneal irritation evokes severe stabbing pain and collapse with subsequent acute peritonitis.

2. Acute inflammatory diseases: acute appendicitis, acute cholecystitis, acute pancreatitis, acute adnexitis, gastric phlegmon, etc. As the disease progresses, it is attended by extensive purulation, necrosis of the organ (pancreas), or its wall (appendix, gall bladder), escape of pus into the abdominal cavity with local or diffuse acute serous or purulent peritonitis. The clinical picture is characterized by rapidly purulent peritonitis. The clinical picture is characterized by rapidly aggravating abdominal pain, inflammatory symptoms, and toxaemia.

3. Intestinal obstruction by strangulation or obturation, strangulation of internal or external hernia, necrosis of the intestinal wall. The intestine

necrotizes in all these cases, except in obstruction; peritonitis is likely to develop. Severe abdominal pain, vomiting and meteorism are characteristic.

4. Occult bleeding into the abdominal cavity (due to rupture of the uterine tubes in ectopic pregnancy, apoplexy of the ovary, rupture of the spleen or liver due to injury, etc.). The main symptoms are severe abrupt abdominal pain that can gradually abate, and circulatory collapse.

Clinical picture. Each specific disease that presents as the acute abdomen is characterized by a variety of clinical symptoms some of which are common for all of them and may be used to establish a provisional diagnosis.

1. The main symptom is a paroxysm of severe abdominal pain. Sometimes it develops suddenly and manifests as a severest attack of stabbing pain (in perforation of the gastric or intestinal wall). In other cases pain is first relatively mild but its intensity rapidly increases to become severe (in inflammation of the abdominal organs; colics).

2. Symptoms of peritoneal irritation. The symptoms are severe and persistent in perforation of the hollow abdominal organs, acute bleeding into the peritoneal cavity, acute inflammation of the abdominal organs. Local or diffuse muscular strain in the anterior abdominal wall (muscular defense) can also be seen. Perforated peptic ulcer may be manifested by board-like rigidity of the abdomen. Respiratory excursions of the abdomen are either limited or absent. The Shchetkin-Blumberg sign is positive.

3. A group of symptoms demonstrating severely disordered peristalsis and tone of the digestive tract: nausea, vomiting, pronounced meteorism, constipation and passage of flatus. These symptoms may mostly be due to organic causes such as intestinal obstruction, or they may arise by reflex. In obturating or strangulating intestinal obstruction, the abdomen is inflated unevenly. The inflation combines with a severe abdominal pain and visible wave-like peristaltic protrusions and retractions on the abdomen (Wahl's symptom). Percussion of the abdomen over the inflated zone reveals tympany; X-ray examination reveals multiple air-fluid levels (Kloiber's symptom).

4. Circulatory collapse: pallor, syncope, cold sweat, rapid and weak pulse, low arterial pressure, pinched face (facies Hippocratica). These symptoms are either due to massive blood loss or develop by reflex due to perforation, inflammation of the abdominal organs, acute intestinal obstruction, or peritonitis.

5. General rapidly progressing signs of inflammation: fever, neutrophilic leucocytosis, and accelerated ESR combined with severe abdominal pain and symptoms of peritoneal irritation. These are characteristic of gastrointestinal perforation or obstruction with subsequent peritonitis and also acute inflammation of the abdominal organs.

In typical cases, the symptoms of the acute abdomen are so specific

that findings of the examination, palpation and percussion of the abdomen, as well as questioning of the patient are sufficient to diagnose the acute abdomen, although it is often difficult to establish the underlying cause. The condition is an emergency and requires rapid correction since irreversible changes may rapidly develop. The patient must therefore be taken to hospital in the presence of at least one sign of the acute abdomen. The necessary examinations must be urgently conducted at hospital to establish the diagnosis and to decide on surgical or therapeutic tactics.

The patient's condition permitting, the first necessary examinations at a hospital include hourly taking body temperature, total blood counts, ECG, radiographic examination of the abdomen (roentgenoscopy and roentgenography) with the patient in an upright position (in the absence of suspicion for myocardial infarction). Other examinations may also be performed depending on the specific character of each particular case.

Treatment. It is necessary to remember, that some symptoms of the acute abdomen may be quite misleading. Thus, some 'obvious' cases of the acute abdomen may not require operative intervention, while even the 'mildest' abdominal pain may sometimes require an urgent surgical correction. Before the patient is delivered to hospital, spasmolytics (baralgin) may be given parenterally to alleviate pain. Preparations correcting the cardiovascular function should be given whenever necessary. Narcotics may be given only in special cases to control shock during patient's transportation. Undue administration of narcotics may cause transient improvement of the patient's condition but mask the symptoms of peritoneal irritation thus making the diagnosis difficult. Laxatives are absolutely contraindicated. A precise record of the drugs administered before hospitalization should be made. The exact time of administration should also be indicated.

Inadequate Digestion Syndrome

This is a symptom complex characterized by digestive disorders in the gastrointestinal tract. Disorders can be associated with upset cavital digestion, i.e. in the stomach and the intestine (dyspepsia), and parietal digestion. Mixed forms also occur.

Aetiology and pathogenesis. *Dyspepsia.* This occurs due to noncompensated secretory insufficiency of the stomach, exocrine dysfunction of the pancreas, upset secretion of bile, disordered passage of chyme through the gastrointestinal tract (stasis, congestion due to stenosis and compression of the intestine, or accelerated passage due to intense peristalsis). Intestinal infection, dysbacteriosis, and alimentary disorders (overeating, diet rich in proteins, fats, or carbohydrates, intake of large amounts of fermented drinks) are also important. Dyspepsia may be functional, but commonly it is due to a digestive tract disease.

Pathogenesis: incomplete breakdown of food particles, active propagation of bacterial flora in the intestine with its invasion of the proximal parts of the small intestine, dysbacteriosis, abnormally high activity of bacteria in the enzymatic decomposition of food with formation of toxins (ammonia, indole, low-molecular fatty acids, etc.) that irritate the intestinal mucosa, intensify peristalsis, and cause symptoms of toxaemia due to their penetration into the blood.

Clinical picture. *Gastric dyspepsia.* This condition occurs in achlorhydria and achylia, long-standing decompensated pyloric stenosis, atrophic gastritis, and cancer of the stomach. The disease is characterized by the feeling of discomfort, pressure or distension in the epigastrium after meals, frequent eructation, regurgitation (often with acid or fetid odour), unpleasant taste in the mouth, nausea, and poor appetite. Achylous diarrhoea and meteorism are not infrequent. Examination of the gastric juice reveals achlorhydria or achylia (both hydrochloric acid and pepsin are absent from the gastric juice).

Intestinal dyspepsia occurs in the presence of exocrine dysfunction of the pancreas, chronic inflammatory diseases of the small intestine, and some other conditions. It presents as inflation and rumbling in the abdomen (borborygmus), intensive passage of flatus, diarrhoea with putrefactive or acid smell and (in rare cases) constipation. Coprologic findings: steatorrhoea, amylorrhoea. X-ray findings: accelerated passage of the barium meal through the small intestine. Studies of the secretory function of the pancreas, aspiration biopsy, determination of enterokinase and alkaline phosphatase in the intestinal juice, and other tests help verify the cause of intestinal dyspepsia. Tests for hyperglycaemia with an oral starch load and radionuclide studies with glycerol trioleate, sunflower-seed or olive oil are used to estimate the degree of the cavital digestion derangement. The study of intestinal microflora is also important.

Treatment. This, in the first instance, is aimed at eradication of the underlying disease. Symptomatic therapy includes special diets and medication for diarrhoea; enzyme preparations (pancreatin, abomin, festal), astringents, and carbolen are also administered.

Inadequate parietal digestion can be seen in congenital secretory insufficiency of the intestinal wall (disaccharidase deficit enteropathy) and in chronic diseases of the small intestine attended with dystrophic, inflammatory, and sclerotic changes in its mucosa, upset structure of the villi and microvilli, and their decreasing number, deranged intestinal peristalsis (enteritis, sprue, intestinal lipodystrophy, exudative enteropathy, etc.).

The symptoms, course, and clinical picture are the same as in intestinal dyspepsia and in the malabsorption syndrome (see below).

The diagnosis is established on the basis of determination of enzymes

(amylase, lipase) during their desorption in homogeneous preparations of the small-intestine mucosa specimens taken by aspiration biopsy. The glycaemic curve drawn after oral intakes of disaccharides and monosaccharides helps differentiate the syndrome of inadequate parietal digestion (flat curve after the intake of maltose, saccharose, lactose; normal curve after the glucose and galactose intake) from lesions of the small intestine that are attended with malabsorption of the products of food decomposition in the small intestine. After an intake of polysaccharides (starch) this syndrome may be differentiated from inadequate cavital digestion. Aspiration biopsy reveals atrophy of the intestinal mucosa (indirect sign).

Treatment is aimed at the main disease. For methods of management of malabsorption syndrome see below. Symptomatic therapy includes enzyme preparations (abomin, festal) and astringents (tannalbin, albin). The drugs are given per os.

Malabsorption Syndrome

This symptom complex is due to upset absorption in the small intestine. The syndrome often develops in combination with the syndrome of inadequate digestion. Primary and secondary malabsorption syndromes are distinguished.

Malabsorption is probably explained by congenital disorders in the fine structure of the intestinal mucosa and genetically determined intestinal enzymopathy. The onset of the secondary malabsorption syndrome is due to acquired structural changes in the intestinal mucosa evoked by acute and chronic enteritis, sprue, intestinal lipodystrophy, exudative enteropathy, lesions of the small intestine in amyloidosis, systemic scleroderma, and other disease conditions attended with digestive disorders. The upset intestinal digestion and accelerated passage of chyme through the intestine are decisive in acute and subacute diseases. In chronic conditions the decisive factors are dystrophy and atrophic fibrous changes in the mucosa of the small intestine, shortening and levelling of the villi and crypts, significant reduction of the microvilli number, fibrous tissue formation in the intestinal wall with impairment of blood and lymph circulation, and disordered parietal digestion. All these changes limit absorption of the products of hydrolysis of proteins, fats, and carbohydrates, and of mineral salts and vitamins in the intestinal wall (see *Alimentary dystrophy).*

Clinical picture. Course. Gradual wasting, symptoms of metabolic disorders of all types (protein, fat, vitamin, water-salt), dystrophic changes in the internal organs with their subsequent dysfunction, and also constant steatorrhoea, creatorrhoea, and amylorrhoea are characteristic. Hypoproteinaemia develops (mostly at the expense of reduction of the serum

albumin level); hypocholesterolaemia, hypocalcaemia, and moderate hypoglycaemia occur. Hypoproteinaemic oedema develops in the presence of hypoproteinaemia below 40-50 g/1. The characteristic symptoms of polyhypovitaminosis are osteoporosis, anaemia (hypochromic anaemia in predominant malabsorption of iron, and hyperchromic anaemia in upset absorption of vitamin B12), trophic changes in the skin, nails, progressive atrophy of the muscles, signs of polyglandular insufficiency, weakness, and (in severe cases) acidosis and cachexia.

Diagnosis. Laboratory examinations determine hypoproteinaemia, hypocholesterolaemia, hypoglycaemia, and other disorders due to malabsorption.

Coprologic studies reveal increased content of undigested food in the faeces and also increased excretion of the products of enzymic decomposition of food. Enterobiopsy reveals atrophic changes in the mucosa of the proximal parts of the small intestine. Since the walls of the small intestine absorb great amounts of various substances, different methods are used to study their absorption. These are tests with carotine, folic acid, galactose, D-xylose absorption test, etc. Caseine, albumin, oleic acid, methionine, glycine, vitamin B_{12}, folic acid, and other substances labelled with radioactive isotopes have recently beed used. The method is based on the determination of concentration of labelled substances and the time of their appearance in the blood, their excretion with the urine or faeces, and assessment of residual radioactivity of faecal masses that is indicative of the amount of unabsorbed substances. Determination of the absorbed nutrients is based on the study of the chemical composition of food and stools during a certain period of time.

The course of the disease depends on the underlying condition and prospects for its cure. The prognosis is unfavourable in severe cases.

Treatment. The underlying disease should be treated. Symptomatic treatment: parenteral nutrition, administration of vitamins, plasma, protein hydrolyzates, glucose, nutrient enema, correction of electrolyte metabolism.

Prophylaxis includes timely treatment of diseases that usually concur with the malabsorption syndrome.

Special Pathology

Most common diseases of the intestine are dyskinesia, inflammatory affections (enteritis, colitis, enterocolitis) and tumours (mostly cancer of the large intestine).

According to their clinical course, inflammation of the small intestine (enteritis) and of the large intestine (colitis) may be acute or chronic.

Acute Enterocolitis

Acute inflammation of the small and large intestine usually combines with affection of the gastric mucosa and arises after ingestion of spoiled food infected with microorganisms or after ingestion of a large amount of hardly digestable or incompatible foods (gastroenterocolitis).

Clinical picture. The clinic of acute enterocolitis varies from mild illness to fatal outcomes. The onset of the disease is sudden (3-4 hours following ingestion of inadequate food). Its first symptom is dyspepsia (diarrhoea). The body temperature is subfebrile or higher. The tongue is dry and the abdomen distended, tenderness is diffuse. Acute symptoms subside in 8-12 hours and the patient's condition improves in few days. Collapse may occur in severe cases due to poisoning.

Treatment. The stomach should be lavaged and purgative salts given. Sulpha drugs are given with a special diet; subcutaneous injections of sodium chloride are useful in marked dehydration.

Prophylaxis. This consists in adequate hygiene of nutrition, thorough inspection of cooking and foods storage conditions, especially during hot seasons.

Chronic Enteritis

Aetiology **and** pathogenesis. Chronic enteritis arises due to various causes. These are (1) infection: typhoid fever, dysentery, salmonellosis, etc.; (2) acute enteritis (a forerunner); (3) dysbacteriosis: upset microbial equilibrium in the intestine; (4) alimentary factor: irregular meals, ingestion of cold food, chronic overeating of poorly digestable foods; (5) radioactive exposure; (6) alcohol abuse; (7) allergic factors; (8) congenital enzymopathy; deficient quantity of enzymes responsible for absorption of foods (gluten and lactase deficiency); (9) endocrine factors (diarrhoea in thyrotoxicosis); (10) diseases of other alimentary organs (stomach, hepatobiliary system, pancreas). For example, in the presence of achlorhydria, insufficiently digested food enters the small intestine to irritate its mucosa and to provoke inflammation.

Pathological anatomy. Mucosa of the small intestine is oedematous and hyperaemic. Haemorrhage and ulceration are possible. In grave cases, inflammation may involve all layers of the intestinal wall to cause its perforation.

Clinical picture. The patient usually complains of pain in the umbilical region and distension of the abdomen. Stools are not formed; constipations are alternated with diarrhoea. Nutrition is impaired, the skin is pallid. Signs of polyhypovitaminosis are present: dry skin, brittle and laminated nails. Splashing and rumbling sounds are heard in the right iliac region. Stools contain mucus; microscopy of faeces reveals the presence of drops of neutral fat and muscle fibres. Specific X-ray signs are hypotonia, the

presence of gas and liquid in the small intestine, and level relief or feather-like pattern of its mucosa.

Course. Chronic enteritis can be complicated by involvement of the pancreas, the liver, the large intestine, by development of hypochromic anaemia, and polyhypovitaminosis.

Treatment. Complex therapy is required. It is necessary to take into account the degree of the peptic disorder, complications if any, and the general condition of the patient. In exacerbations of the disease, sulpha preparations, eubiotics, and enzyme preparations (abomin, pancreatin, pansinorm, festal, and others) are indicated.

Prophylaxis. This consists in eradication of possible causes of the disease and timely and thorough treatment of acute enterocolitis, chronic gastritis, diseases of the liver and the pancreas.

Chronic Colitis

Aetiology and pathogenesis. Causes of inflammatory affections of the large intestine are quite varied. Most frequent causes of chronic colitis are infections (dysentery, salmonellosis, tuberculosis, syphilis, etc.), parasites (helminths, protozoa, etc.), and toxic effects (poisoning with arsenic, phosphorus, mercury, etc.). Irregular nutrition, overeating, and chronic constipations can account for development of colitis as well.

In the presence of motor hyperfunction of the small intestine, the ingested food is not processed sufficiently before it enters the large intestine, and it thus irritates its mucosa. Long-standing kinetic disorders cause colitis. Persistent constipations can provoke chronic colitis. Mucosa of the large intestine has the excretory function. It releases microbes and their toxins, i.e. toxic products that circulate in the body in cases with upset metabolism. These factors can become the cause of chronic colitis, e.g. renal dysfunction causes development of colitis. And finally, auto-infection (e.g. coli bacilli which become pathogenic under certain conditions) can stimulate the onset of colitis.

Classification of colites. The following colites are distinguished: I, infectious colites: (1) specific, and (2) non-specific; II, parasitary colites: (1) protozoal (amoebic, trichomonal, lambliogenic), (2) helminthic; III, toxic colites: (1) exogenous and (2) endogenous; IV, alimentary colites; V, symptomatic or secondary colites; and VI, colites of mixed aetiology.

Pathological anatomy. The entire large intestine or its separate sections may be affected by inflammation. Catarrhal, follicular, infiltrative, purulent, ulcerative, and gangrenous colites are differentiated from the standpoints of pathological anatomy.

Clinical picture. The patient with chronic colitis complains of local and general disorders. Local complaints include pain in the lower abdomen or the iliac region, distension of the abdomen, tenesmus, constipation and diarrhoea. General complaints are irritability, deranged sleep, headache, and low moods. Appetite is decreased, nausea and sometimes vomiting occur. Objective examination shows that nutrition is adequate. The study of the abdominal cavity reveals pain by the course of the large intestine and rumbling. Protozoa or helminths can be found in faeces. Stools may also contain traces of blood and mucus; dysbacteriosis is also possible. X-ray examination may reveal spasms, atonia of separate portions of the large intestine, and changes in the relief of the intestinal mucosa. Rectosigmoidoscopy and colonoscopy are valuable diagnostic techniques.

According to the *clinical course* of the disease, mild, medium gravity and grave chronic colites are distinguished. Mild forms of colitis have no pronounced symptoms; only occasional diarrhoea or constipations are observed; the general condition of the patient is not affected substantially.

Signs of the disease are pronounced in chronic colitis of medium gravity. Grave forms of the disease are marked by fever, headache, asthenia, disability, involvement of other organs, and complications (haemorrhage, perforation).

Treatment. A correct treatment is only possible if the cause of chronic colitis has been discovered. Changes in other organs of the digestive system and the presence of complications should also be taken into account. The appropriate diet should be prescribed along with symptomatic therapy (spasmolytics, analgesics, etc.).

Prophylaxis. Prophylactic measures are quite varied; this agrees with the variety of causes that provoke development of chronic colitis. Labour hygiene, sanitary conditions at home, and adequate nutrition are of primary importance. Patients with acute intestinal disorders should be thoroughly examined and treated. Regular out-patient observation of population is also important (control of intestinal parasitosis, treatment of constipation and other diseases of the digestive system that may cause pathologies in the large intestine, e.g. peptic ulcer, chronic gastritis, etc.).

LIVER AND BILE DUCTS

Methods of Examination

Inquiry

Complaints. Patients with disorders of the hepatobiliary system usually complain of abdominal pain, dyspepsia, skin itching, jaundice, enlargement of the abdomen, and fever.

Pain is localized in the right hypochondrium and sometimes in the epigastrium and differs depending on the cause. Pain may be persistent and dull, or it may be severe and occur in attacks. Persistent pain is usually boring, or the patient feels pressure, heaviness, or distension in the right hypochondrium. Pain may radiate to the right shoulder, scapula, and in the interscapular space (in chronic cholecystitis, perihepatitis and pericholecystitis, i.e. when the process extends onto the peritoneum overlying the liver and the gall bladder, and also in rapid and considerable enlargement of the liver which causes distension of Glisson's capsule). This radiation of pain is quite characteristic of many diseases of the liver and gall bladder, because the right phrenic nerve, innervating the capsule in the region of the falciform and the coronary ligaments of the liver and the extrahepatic bile ducts, originates in the same segments of the spinal cord where the nerves of the neck and shoulder originate as well. Pain usually becomes more severe in deep breathing; in adhesion of the liver or the gall bladder to the neighbouring organs, pain is also intensified when the patient changes his posture, and sometimes during walking.

Attacks of pain (biliary or hepatic colics) develop suddenly and soon become quite severe and unbearable. The pain is first localized in the right hypochondrium but then spreads over the entire abdomen to radiate upwards, to the right, and posteriorly. An attack of pain may continue from several hours to a few days during which pain may subside and then intensify again; the attack ends as suddenly as it arises; or pain may lessen gradually. Attacks of pain occur mostly in cholelithiasis. They are provoked by jolting (as in riding) or by fatty food. Pain attacks occur also in hypermotoric dyskinesia of the gall bladder and bile ducts. Pain usually develops quite unexpectedly due to spastic contractions of muscles of the gall bladder and large bile ducts caused by irritation of their mucosa by a stone, and due to comparatively rapid distension of the gall bladder in congestion of bile (e.g. due to obstruction of the common bile duct by a stone). Warmth applied to the liver (provided the attack is not attended by considerable fever) and also administration of cholino- and myospasmolytics

(atropine sulphate, papaverin hydrochloride, etc.) remove pain characteristic of the colic. An attack of hepatic colic can be attended by subfebrility (fever develops with pain and subsides with alleviation of pain), which is followed by a slight transient subicteric colour of the sclera or pronounced jaundice in obstruction of the common bile duct by a stone.

Pain developing in dyskinesia of the bile ducts is associated with upset coordination between contractions of the gall bladder and of the Oddi sphincter under the effect of increased tone of the vagus nerve. As a result, bile congests in the ducts, and the gall bladder is no longer emptied. This causes its convulsive contraction. Dyskinetic pain is characterized by the absence of signs of inflammation (leucocytosis, ESR, etc.).

Dyspeptic complaints include decreased appetite, often bitter taste in the mouth, eructation, nausea, vomiting, distension of the abdomen and rumbling, constipations or diarrhoea. These complaints are characteristic not only of diseases of the hepatobiliary system but also of other parts of the digestive system. Causes of these symptoms in diseases of the liver and bile ducts are explained by deranged secretion of bile (and hence impaired digestion of fats in the intestine) and derangement of the detoxicating function of the liver.

Fever occurs in acute inflammatory affection of the gall bladder and bile ducts, in abscess and cancer of the liver, in hepatitis, and active cirrhosis.

Skin itching attends hepatic or obstructive jaundice. It can develop without jaundice, as an early forerunner of the liver disease. Itching is caused by accumulation in the blood of bile acids which are otherwise excreted together with bile, or by stimulation of sensitive nerve endings in the skin. Itching is usually persistent and is a great annoyance to patients during night sleep (to cause insomnia). Severe itching causes scratching of the skin with its subsequent infection.

Icteric colouration of the skin and the visible mucosa (jaundice) is due to accumulation of bile pigments in the blood and tissues. Jaundice may develop unnoticeably to the patient and only the surrounding people may pay attention to the icteric colouration of the sclera and then the skin. In other cases jaundice can occur all of a sudden, following an attack of hepatic colics (in obstruction of the common bile duct by a stone in cholelithiasis). Jaundice may persist for months or even years, only slightly changing in intensity (chronic hepatitis and cirrhosis of the liver, benign bilirubinaemia). For details of the mechanism of developing jaundice and its diagnostic importance see below.

Enlargement of the abdomen (sometimes rapid) can be due to accumulation of ascitic fluid in the abdominal cavity (in obstructed blood

outflow from the intestine via the portal vein), in considerable meteorism (due to deranged digestion in the intestine in upset bile excretory function), or in pronounced hepato- or splenomegaly. Many chronic diseases are attended by *general weakness, non-motivated fatigue, and decreased work capacity.*

History of the present disease. When collecting anamnesis, it is necessary to find out if the patient had in his past history jaundice or acute diseases of the liver or the gall bladder (Botkin's disease, acute cholecystitis, cholangitis), attacks of hepatic colics, enlargement of the liver or the spleen, which might be an early symptom of the present disease (chronic hepatitis, liver cirrhosis, chronic cholecystitis, cholangitis, cholelithiasis).

Life history of patient. When inquiring the patient it is necessary to establish factors that might be important for the aetiology of the present disease of the liver or bile ducts: liking for fat and meat foods, exposure to chemical and vegetable poisons (alcohol, carbon tetrachloride, compounds of phosphorus, copper, lead, arsenic, dichloroethane, etc.), poisoning with mushrooms containing strong hepatotropic poisons (e.g. helvellic acid, amanitotoxin, etc.), some infectious diseases (Botkin's disease, lambliosis, typhoid fever, malaria, syphilis, etc.), diseases of the gastro-intestinal tract (gastritis, colitis), and diabetes mellitus. Familial predisposition is also important in the development of some liver diseases (e.g. congenital benign hyperbilirubinaemia) and diseases of the gall bladder (cholelithiasis).

Physical Examination

INSPECTION

The general condition of the patient is first assessed. In the presence of marked functional hepatic insufficiency of various aetiology (liver cirrhosis, cancer, prolonged obstructive jaundice, etc.), the patients's condition can be grave because of pronounced poisoning (hepatic coma). The patient's condition may be grave in acute inflammatory diseases of the liver (abscess), gall blader (acute cholecystitis), or bile ducts (acute cholangitis). But in many chronic diseases of the liver and the bile ducts, the general condition of the patient may remain satisfactory for long periods of time. Patients with hepatic colics are restless, they toss in bed, try to find (without success) a position in which the pain might be relieved. A hepatic

coma is characterized by deranged consciousness in the form of pronounced euphoria or inhibition to complete loss of consciousness.

The general appearance (habitus) of the patient usually does not change. At the same time, a hypersthenic constitution with predisposition to obesity is often characteristic of patients with cholelithiasis. Quite the reverse, significant wasting (to cachexia) occurs in cirrhosis or malignant tumour of the liver or the bile ducts. If the disease of the liver begins in childhood or adolescence, the patient may look infantile.

An important diagnostic sign is *jaundice* of varying intensity. In order to assess correctly the colour of the skin, the patient should be inspected in daylight or in the light of the luminescent lamp. A subicteric symptom is jaundice of the sclera, the lower surface of the tongue, and the soft palate; next coloured are the palms, soles, and finally the entire skin. Inspection of the sclera helps differentiate between true (bilirubinogenic) and exogenic jaundice. Prolonged use of quinacrine, ethacridine lactate (rivanol), carotin (carrots), excess tangerines and oranges, exposure to trinitrotoluene and picric acid can cause slight jaundice of the skin (false jaundice) but the sclera is not coloured in such cases. Hepatic jaundice is usually attended by itching and scratching of the skin.

Icteric skin can be of various hues (Plate 18). The skin is orange-yellow (rubinicterus) due to accumulation of bilirubin in the skin; it is usually characteristic of the early stages of the disease. Lemon-yellow colour of the skin (flavinicterus) is characteristic of haemolytic jaundice. Greenish-yellow colour (verdinicterus) is due to accumulation of biliverdin (the product of gradual oxidation of bilirubin); it is mostly due to obstructive jaundice. In long-standing mechanical jaundice the skin becomes dark bronzy (melasicterus).

In certain cases the skin becomes pallid due to anaemization (haemorrhage from varicose oesophageal or haemorrhoidal veins in portal cirrhosis); the skin may be greyish ("dirty") in patients with some hepatic diseases. Greyish-brown or brown skin is characteristic of haemochromatosis (bronzed diabetes or pigmentary cirrhosis of the liver), the disease associated with primary or secondary excessive absorption of iron in the intestine and accumulation of haemosiderin in various organs and tissues (in the first instance in the liver and the pancreas). Local hyperpigmentation of the skin in the right hypochondrium can be due to frequent application of a hot-water bottle, which indicates persistent pain in this region (in chronic diseases of the gall bladder).

Inspection of the skin (especially in obstructive and less frequently in

parenchymatous jaundice) can reveal *scratches* due to severe itching. The scratches are often infected and purulent. Jaundice of this type can be attended by haemorrhagic diathesis—*petechial eruption* and haemorrhage into the skin (ecchymosis).

In patients with cirrhosis of the liver associated with disordered cholesterol metabolism, cholesterol is deposited intracutaneously in the form of yellow plaques *(xanthomatosis)* which are often located on the eyelids *(xanthelasma)* and less frequently on the hands, elbows and soles *(xanthomas)*. Xanthomatosis occurs also in other diseases attended by cholesterol metabolic defect (atherosclerosis, diabetes mellitus, essential hyperlipaemia, etc.).

An important symptom for diagnosis of chronic diseases of the liver are *spider angiomata* (Plate 19). These are slightly elevated pulsating angiomata with fine vessels radiating from the centre. Their size varies from that of a pin head to 0.5-1 cm in diameter. The angiomata are often found on the neck, face, shoulders, hands, and the back; less frequently they are practically absent from the lower part of the body. The spider angiomata may disappear with improvement of the liver function. In addition to these angiomata, patients with chronic diseases of the liver may have specifically coloured palms and soles—*liver palms*; symmetrical reddening is especially characteristic in the thenar and hypothenar region. When pressed, the reddened site becomes pale but when the pressure is removed, the redness is quickly restored. The mechanism of development of the spider angiomata and liver palms is believed to be connected with the grave hepatic dysfunction of the liver during which oestrogens are destroyed incompletely and therefore act as a vasodilatory agent on the skin vessels.

Excess oestrogens in the blood are also associated with other symptoms that may be revealed on inspection. Patients with chronic diseases of the liver have a glassy crimson tongue *(raspberry tongue)*. Uni- or bilateral enlargement of the mammary glands often occurs in men (gynaecomastia) along with defective growth of hair on the chin, chest, and the abdomen. Hair growth is decreased in the armpits and on the pubis in women. When the, hepatic condition improves, the hair growth is restored. Drum (Hippocratic) fingers, sometimes with white nails, occur in patients with chronic diseases of the liver. It is believed to depend on excess oestrogens and serotonin in the blood.

A greenish-brown Kayser-Fleischer ring round the outer edge of the cornea is characteristic of the Konovalov-Wilson disease (congenital disease characterized by decreased synthesis in the liver of ceruloplasmin, the copper transport protein, and its increased deposition in tissues).

Inspection of the mouth can reveal angular stomatitis (inflammation of the mucosa and skin in the mouth angles) characteristic of group B hypovitaminosis occurring amongst patients with chronic liver diseases.

Inspection of the abdomen should be done with the patient in erect or lying position. Important diagnostic symptoms can often be found during inspection of the abdomen. The abdomen can be enlarged significantly due to accumulation of free fluid *(ascites)*. This occurs in liver cirrhosis concurrent with portal hypertension. The abdomen may be enlarged due to pronounced hepato- or splenomegaly. When the patient with ascites stands erect, his abdomen becomes pendulous due to the downward flow of fluid; in the lying position the abdomen is flattened ("frog belly"). The navel often becomes protruded in ascites when the patient stands erect. It is due to increased intra-abdominal pressure. This sign can be used to differentiate between enlargement of the abdomen in ascites (also large intra-abdominal tumours) and pronounced obesity (the navel is retracted).

Inspection of the abdomen can reveal another important symptom of portal hypertension, the presence of *dilated venous network on the anterior abdominal wall* (Plate 20). This network is formed by anastomoses of the portal and both vena cava systems. The superior vena cava and portal vein are anastomosed above the navel, while the portal and inferior vena cava are anastomosed below the navel; cavocaval anastomoses are located on the sides of the abdomen. Anastomoses may develop in obstructed blood flow in the inferior vena cava (thrombosis, compression, etc.). Dilated, swollen and twisted venous collaterals, found round the navel and radiating from it, form the so-called Medusa head. These symptoms are characteristic of the portal hypertension syndrome occurring in cirrhosis of the liver, thrombosis and compression of the portal vein. Establishing the direction of the blood flow in the collaterals helps determine the type of anastomosis and hence locate the vessel where the blood flow is obstructed in the system of the portal vein or the inferior vena cava. To that end a small area of the dilated venous branch is pressed between two fingers (with an attempt to empty this area from the blood). In a short lapse of time the pressure of the upper finger is released. If blood fills the vessel to the level of the other finger, the blood flows from the portal vein system to the inferior vena cava (i.e. in the downward direction). If the vessel remains empty, the blood flows upwards, i.e. from the vena cava inferior-system to the superior vena cava.

In patients with cachexia and pronounced enlargement of the liver, the right hypochondrium and epigastrium are protruded. If the abdominal wall is thin, the protruded surface is uneven and tuberous (in tumours or cysts of the liver). Only significantly enlarged gall bladder can be responsi-

ble for protrusion of the abdomen, especially in cachectic patients (in hydrops of the gall bladder, cancer of the common bile duct, or cancer of the pancreas head which compresses the common bile duct). The left hypochondrium is protruded in cases with considerably enlarged spleen attending cirrhosis of the liver (hepatolienal syndrome).

PERCUSSION

Percussion is used to determine the borders, size and configuration of the liver. The superior and inferior borders of the liver are outlined. Two *superior borders of liver dullness* are distinguished: relative dullness, which is the true upper border of the liver, and the absolute dullness, i.e. the upper border of that part of the anterior surface of the liver which is directly adjacent to the chest and is not covered by the lungs. Practically, absolute dullness is only determined because the position of the superior border varies depending on the size and configuration of the chest, the height of the right diaphragm cupola, and also because the upper edge of the liver is deeply hidden behind the lungs. Finally, the liver usually becomes enlarged in the downward direction. This is determined by the position of its inferior edge.

Percussion of the liver is carried out with observation of the general rules of topographic percussion. Light percussion is used to determine the absolute liver dullness. The direction of percussion is from top to bottom, along the vertical lines, like in determining the borders of the right lung. The border is detected by contrast between the clear pulmonary resonance and liver dullness. The found border is marked on the skin by dots, by the upper edge of the pleximeter-finger, in each vertical line. Normally the superior border of absolute liver dullness is found in the right parasternal line at the superior edge of the 6th rib, in the right midclavicular line at the 6th rib, and in the right anterior axillary line at the 7th rib. In other words, the border of absolute dullness corresponds to the position of the lower edge of the right lung (Fig. 91). The upper border of the liver can likewise be determined posteriorly, but normally the determination ends by percussion in the three mentioned lines.

Determination of the lower absolute dullness is difficult because of the presence of hollow organs in the vicinity of the liver. The stomach and the intestine give high tympany that masks the liver dullness. The lightest percussion should therefore be used. Direct percussion by one finger according to Obraztsov should better be used instead.

Determination of the *lower border of absolute dullness* (according to Obraztsov and Strazhesko) should be begun from the right part of the ab-

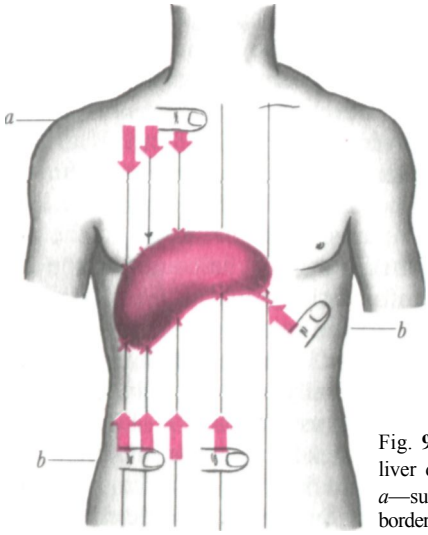


Fig. **91.** Determining absolute liver dullness.
a—superior border; *b*—inferior border.

domen along the right anterior axillary line with the patient in the horizontal position. The pleximeter-finger is placed parallel to the expected inferior border of the liver, some distance away from it, so that tympany might first be heard (at the umbilical level or slightly below the navel). As the pleximeter-finger is then moved upwards, tympany is followed by absolute dullness. The point of disappearance of tympany is marked in each vertical line (right midclavicular, right parasternal, and anterior median line). If enlargement of the liver is significant, the mark should be made also in the left parasternal line, by the lower edge of the pleximeter-finger.

When determining the left border of liver dullness, the pleximeter-finger is placed perpendicularly to the edge of the left costal arch, at the level of the 8—9th ribs, and percussion is carried out to the right, directly over the edge of the costal arch, to the point where tympany changes to dullness (in the region of Traube's space).

Normally the inferior border of absolute dullness of a lying patient with normosthenic chest passes at the 10th rib in the right anterior axillary line, at the superior edge of the right arch in the midclavicular line, 2 cm below the interior edge of the right costal arch in the right parasternal line, and 3-6 cm away from the inferior edge of the xiphoid process (at the border of the upper third of the distance from the base of the xiphoid process to the navel) in the anterior median line; on the left the border does not extend beyond the left parasternal line.

The lower margin of the liver in norm can very depending on the shape of the chest and constitution of the patient, but this only has its effect on

the position in the anterior median line. The lower margin of the liver in a hypersthenic chest is slightly above the mentioned level, while in an asthenic chest below it, approximately midway between the base of the xiphoid process and the navel. If the patient is in the upright posture, the lower margin of the liver descends 1—1.5 cm. If the liver is enlarged, its lower margin is measured in centimetres from the costal arch and the xiphoid process. The border of the left lobe of the liver is determined in centimetres in the left parasternal line, down to the margin of the costal arch and to the left in this line (by the course of the costal arch).

Percussion gives information about the vertical dimensions of the area of liver dullness. The distance between the superior and inferior borders of absolute dullness is measured in the vertical lines. This distance in the right anterior axillary line is normally 10-12 cm, in the right midclavicular line 9-11 cm, and in the left parasternal line 8-11 cm. It is difficult to determine liver dullness on the back because it is masked by dullness of the thick layer of lumbar muscles, the kidneys, and the pancreas. In some cases, a 4—6 cm wide band of liver dullness can be determined. This precludes erroneous diagnosis of liver enlargement in cases where the liver descends below the right costal arch, or where it is turned anteriorly round its axis; dullness then becomes narrower.

Outlining the liver by percussion is diagnostically important. But ascending or descending of the superior margin of the liver is usually associated with extrahepatic changes (high or low diaphragm, subdiaphragmal abscess, pneumothorax, or pleurisy with effusion). The superior margin of the liver can ascend only in echynococcosis or cancer of the liver. Elevation of the inferior margin indicates diminution of the liver; it can also occur in meteorism and ascites which displace the liver upwards. The lower border usually descends when the liver is enlarged (due to hepatitis, cirrhosis, cancer, echynococcosis, blood congestion associated with heart failure, etc.). But it can sometimes be explained by low position of the diaphragm. Systematic observation of the liver borders and changes in the liver dullness gives information on changes in its size during the disease.

The gall bladder cannot as a rule be determined by percussion. But if its enlargement is pronounced, it can be determined by very light percussion.

Percussion is used not only to determine the borders of the liver and the gall bladder (topographic percussion) but also to assess their condition: careful percussion of the area overlying an enlarged liver or the gall bladder causes painful sensations in the presence of inflammation (hepatitis, cholecystitis, pericholecystitis, etc.). Succussion on the right costal arch also causes pain in diseases of the liver and the bile ducts, especially in cholelithiasis (Ortner's symptom).

PALPATION

Surface palpation in diseases of the liver can reveal a tender zone in the right hypochondrium and epigastrium. Especially severe local pain (caused even by a slight touch on the anterior abdominal wall in the zone overlying the gall bladder) is observed in acute cholecystitis and biliary colic. In chronic cholecystitis slight or moderate tenderness is only revealed at the point of projection of the gall bladder fundus onto the anterior abdominal wall. In healthy subjects this point is found immediately below the right costal arch by the lateral edge of the right rectus abdominis muscle.

The liver is palpated by the Obraztsov and Strazhesko method. As the lower edge of the liver descends to meet the examining fingers during a deep inspiration it slides over the fingers and thus becomes detectable. It should be remembered that the respiratory mobility of the liver is the highest compared with that of the other abdominal organs because the liver is the closest to the diaphragm. It follows therefore that during palpation of the liver, the active role belongs to its respiratory mobility rather than to the palpating fingers (as is the case with palpation of the intestine).

The patient should stand or lie during palpation of the liver and the gall bladder. But in certain cases the liver can be easier palpated if the patient lies on his left side: the liver hangs by gravity from under the hypochondrium and its inferio-anterior edge can thus be better palpated. Common rules should be followed during palpation of the liver and the gall bladder. Special attention should be paid to the antero-inferior margin of the liver whose properties (outlines, form, tenderness, consistency) are indicative of the condition of the liver, its position, and configuration. In many cases (especially if the liver is enlarged or lowered) the liver can be palpated not only from the left hypochondrium to the right hypochondrium, but its superio-anterior surface becomes palpable as well.

The examiner sits by the right side, facing the patient. He places four fingers of his left hand on the right lumbar region of the patient and uses his left thumb to press on the costal arch to move the liver closer to the palpating fingers of the right hand and to prevent expansion of the chest during inspiration. This stimulates greater excursions of the right cupola of the diaphragm. The palm of the right hand is placed flat on the abdomen below the costal arch in the midclavicular line. The slightly flexed fingers press lightly on the abdominal wall (Fig. 92). The patient is asked to take a deep breath; the liver descends to touch the palpating fingers and then slides to bypass them (Fig. 93). The examiner's hand remains motionless. The procedure is repeated several times. The position of the liver margin varies depending on conditions. It is therefore necessary first to determine the lower margin of the liver by percussion before positioning the palpating fingers.

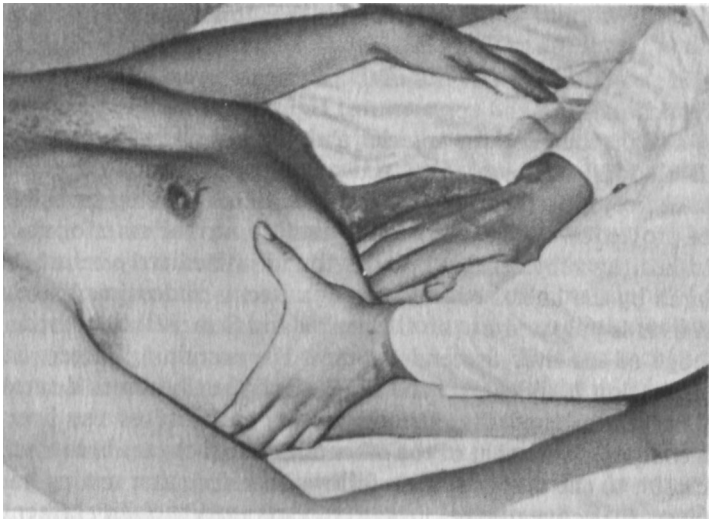


Fig. 92. Palpation of the liver.

According to Obraztsov, normal liver can be palpated in 88 per cent of cases. Physical properties of the liver can be determined by palpating its lower edge (it can be soft, firm, rough, sharp, rounded, tender, etc.). The margin of an unaffected liver palpated at the height of a deep inspiration is 1-2 cm below the costal arch. It is soft, sharp, readily bending, and insensitive.

The lower edge of a normal liver is usually palpated in the right midclavicular line; the liver is impalpable to the right of this line because it

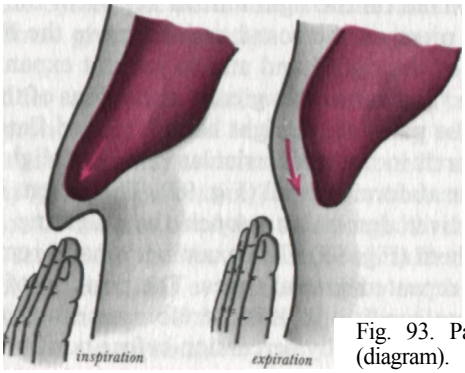


Fig. 93. Palpation of the liver (diagram).

is located behind the costal arch; the liver is hardly palpable to the left of the line because of the abdominal muscles. An enlarged or consolidated liver can be palpated in all lines. The liver of patients with pronounced distension of the abdomen should be examined with the empty stomach to facilitate palpation. In accumulation of much fluid in the abdominal cavity (ascites) the liver is not always palpable if the patient is lying. The patient should then be examined in the erect position, or he may lie on his left side. If the amount of fluid in the abdomen is very large, it should be released by paracentesis.

In accumulation of much fluid in the abdominal cavity, ballotment should be used to palpate the liver. To that end the right hand (two or four flexed fingers) should be placed on the lower right part of the abdomen, perpendicularly to the expected lower edge of the liver. The abdominal wall is given a sharp tap from the palpating fingers which move upward to meet the firm object, the liver, which is first tossed to the deeper parts of the abdominal cavity but is then returned back to strike the fingers.

Palpation is painful if the liver is inflamed and the affection extends onto the liver capsule; the liver is also tender when it is distended (e.g. in blood congestion due to heart failure). The liver of a healthy subject (if it is accessible to palpation) is soft; it becomes firmer in hepatitis, hepatosis, and cardiac congestion. The liver is especially firm in cirrhosis. Its edge becomes sharp and the surface smooth or covered with small tubercles. The liver is also firm in the presence of tumour and multiple metastases of cancer. Its surface then becomes covered with rough tubercles (surface metastases) and the lower margin is rough. The liver is firm in amyloidosis. Comparatively small tumours and echinococcosis can sometimes be palpated. Protrusion of the lower margin of an enlarged liver is assessed with respect to the costal arch in the right anterior axillary line, right midclavicular line, right parasternal line, anterior median line, and left parasternal line. Palpation verifies the findings obtained by percussion of the liver.

The gall bladder cannot be palpated in healthy subjects because of its soft consistency and the insignificant protrusion. But if the gall bladder is enlarged (hydrops, stones in the bladder, cancer, etc.) it becomes palpable. The position of the patient for palpation of the gall bladder is the same as in palpation of the liver. After the margin of the liver has been found, the gall bladder should be palpated at the lateral edge of the right rectus abdominis muscle. The palpation technique is the same as that for palpation of the liver. The gall bladder can easier be found by moving the palpating fingers in the direction perpendicular to the axis of the gall bladder. The bladder is felt like a pear of variable size, firmness and tenderness depending on the character of pathology in the gall bladder proper or the sur-

rounding organs (e.g. the gall bladder is enlarged, soft, and elastic in tumour-obstructed bile duct: Courvoisier-Terrier sign; the bladder is firm and tuberous in the presence of newgrowths in its wall, in overfilling with stones, in inflammation of the wall, etc.). An enlarged gall bladder is mobile during respiration (it performs lateral pendulum-like movements). The gall bladder loses its mobility in inflammation of the overlying peritoneum (pericholecystitis). In the presence of cholecystitis and cholelithiasis, the palpation is difficult because of sharp pain and reflectory rigidity of the muscles of the anterior abdominal wall.

The described technique of palpation of the liver and the gall bladder is simple and effective. Difficulties encountered in palpation and also the belief that only palpation can give valuable diagnostic information have stimulated the search for new palpation techniques. But most of them differ only in the position of the examining hands (Glenard, Mathieu, Chaufard, Chiray) or the position of the physician himself with respect to the patient during examination. For example, the liver and the gall bladder are examined (according to Chiray) from behind the leaning patient; the liver edge is palpated by two hands simultaneously, one hand feeling the liver from below and the other from top (according to Gilbert). But none of these techniques used for palpation of the liver and the gall bladder can boast of having significant advantages over others. Success of palpation depends not on the variety of techniques but on the experience of the examiner.

AUSCULTATION

The importance of auscultation for diagnosis of diseases of the liver and gall bladder is only relative. In only rare cases peritoneal friction can be heard over the liver and the gall bladder (in perihepatitis or pericholecystitis). This sound resembles pleural friction, and is a dangerous sign. It indicates deep extension of inflammation onto all walls of the gall bladder and possible perforation.

Laboratory and Instrumental Methods

FUNCTIONAL STUDY OF THE LIVER

Not all functions are affected in an involved liver; the dysfunctions are not simultaneous, and their degree is different. The reserves of the liver are significant: preservation of 20 per cent of the functioning parenchyma is sufficient to maintain vital activity of experimental animals. The regenerative power of the liver is great too. Therefore, certain hypofunction of the liver cannot bear substantial effect on the patient's condition: the affected liver is able to maintain the main vital processes in the new conditions.

Most functional tests impose increased loads on the studied organ. The load is usually so high that an affected organ cannot meet the new conditions. Functional tests for liver are intended to reveal the specific activity of this organ, e.g. detoxicating or protein and pigment forming function. These tests demonstrate only partially the liver function, because the liver is not involved independently in some types of metabolism, but is connected with the other organs in their complex involvement. Tests for carbohydrate, water, and fat metabolism are examples of such tests.

Pigmentary metabolism. Concentration of bilirubin and its reduction products in the blood, faeces, and urine demonstrate the pigment function of the liver. Deranged pigment metabolism indicates disordered functional condition of hepatocytes and helps differentiate between various types of jaundice.

Bilirubin is formed in the reticulo-endothelial cells of the bone marrow, lymph nodes, and mainly in the spleen and the stellar reticuloendotheliocytes of the liver (Fig. 94). Bilirubin is formed from haemoglobin which is released during the physiological break-down of erythrocytes. Haemoglobin breaks down into the globin and haem (containing iron). Unbound bilirubin is formed in the cells of the reticulohistiocytary system from the released haem. Bilirubin circulates in the blood, being loosely connected with protein. The normal blood bilirubin content is 8.55-20.52 mmol/1 (from 0.5 to 1.2 mg/100 ml). The main bulk of unbound bilirubin is supplied to the liver where it is disjoined from albumin and bound (by the agency of the liver enzymes) by glucuronic acid to form water-soluble bilirubin glucuronide (mono- and diglucuronide or "bound biliburin") which is released into the bile ducts.

The liver thus participates in bilirubin metabolism to perform the following functions: (1) formation of bilirubin in stellar reticulo-endothelial cells; (2) capture of unbound bilirubin from blood; (3) formation of bilirubin compounds with glucuronic acid; (4) secretion of bilirubin glucuronide (bound bilirubin) into bile.

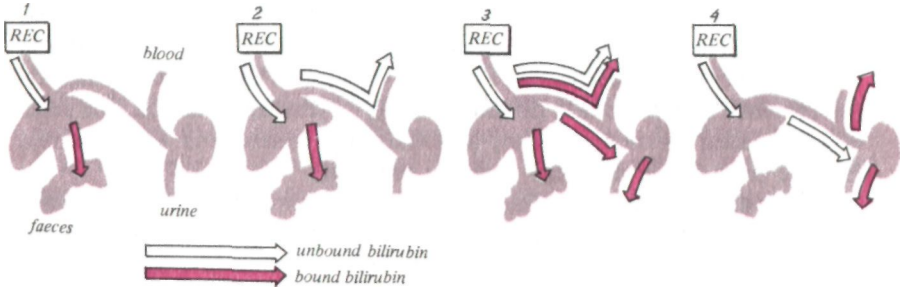


Fig. 94. Secretion of bilirubin in norm (1), in haemolytic jaundice *(2);* in parenchymatous jaundice (3), and in obstructive jaundice *(4).* *i*

Early in the 20th century, van den Bergh noted different reaction of jaundice serum with sulphodiazo reagent in jaundice of various aetiology. The serum of a patient with obstructive jaundice turned red immediately after the diazo reagent was added, while the serum of a patient with haemolytic jaundice turned red only after alcohol was added. The first reaction was called "direct" and the second "indirect". Unbound bilirubin gives indirect reaction while bilirubin glucuronide gives a direct reaction. Depending on the number of molecules (one or two) of glucuronic acid added to the bilirubin molecule, mono- or diglucuronide of bilirubin is formed.

The blood of healthy people contains only free liver pigment. In diseases attended by disordered or perverted bound-bilirubin excretion with bile, the bound bilirubin enters blood and both pigments then become involved in the circulation. (They can be determined separalety.) Van der Bergh's qualitative test gives only tentative information: if the reaction is indirect, it may be considered that unbound bilirubin alone is present in the blood; if the reaction is direct, the proportion of both pigments in the blood is unknown because the positive direct reaction masks the presence of any quantity of unbound bilirubin. The bilirubin fractions are now determined separately. The same diazo reagents (as in qualitative tests) are used in most techniques. Diazo reagent I is prepared by dissolving 5 g of sulphanylic acid and 15 ml of strong hydrochloric acid in distilled water, which is then added to make 1 litre. Diazo reagent II is a 0.5 per cent solution of sodium nitrite. (The diazo mixture consists of 10 ml of solution I and 0.25 ml of solution II.)

Qualitative test: 0.25 ml of the diazo mixture is added to 0.5 ml of serum. If the mixture turns red sooner than in 1 min, the reaction is quick direct to indicate the presence of bound bilirubin in the serum. If the colour changes slowly (within 1-10 min), the bound bilirubin content is relatively small; the reaction is considered to be slow direct. If the solution turns red in more than ten minutes, the direct reaction is considered to be negative. If it is necessary to make sure that the yellow colour of the serum depends on the presence of bilirubin, a double quantity of alcohol is added, the solution is passed through a filter, and the diazo mixture is added to the filtrate: pink colour develops (indirect reaction).

There are many methods for *quantitative determination of the bilirubin fractions*. Some of them are based on the reaction of bilirubin with the diazo reagent in the presence of caffeine (which is used in a common Jendrassik test), methyl alcohol, and some other reagents which act like a catalyst. The total amount of both fractions contained in the serum treated with the catalyst can be determined. Only bound pigment is determined in

another portion of the serum containing no catalyst. The amount of free bilirubin can be found by subtracting the bound fraction from the total bilirubin content of the blood. Other methods for separate determination of bilirubin fractions (chemical, chromatographic) are more complicated.

Unbound bilirubin is insoluble in water and cannot be excreted by the kidneys. When bound with glucuronic acid it becomes soluble and can be determined in the urine of patients with subhepatic and hepatic jaundice. Only bound bilirubin (bilirubin glucuronide) is excreted into the bile ducts. A small portion of bilirubin is reduced to urobilinogen in the large bile ducts and the gall bladder (especially if they are affected by inflammation) and farther in the intestine. Urobilinogen is resorbed in the upper portion of the small intestine and delivered to the liver with the blood of the portal vein. A healthy liver completely traps it and oxidizes, but an affected liver cannot perform this function and urobilinogen passes into blood and is excreted with urine as urobilin. Urobilinuria is an early and very sensitive sign of liver dysfunction. The greater portion of bilirubin is reduced in the intestine to stercobilinogen. Its main portion is excreted with faeces in which it is converted into stercobilin to give faeces its normal colour (upon exposure to air and light). A small portion of stercobilinogen is absorbed in the lower portions of the large intestine, bypasses the liver, and enters the general circulation through the haemorrhoidal veins to be excreted by the kidneys. Normal urine always contains traces of stercobilinogen which converts into stercobilin on exposure to air and light.

Most reactions by which products of bilirubin reduction are discovered in urine give similar results with both urobilin and stercobilin, although these two compounds differ in their chemical structure and physical properties. Methods of their separation are relatively complicated. They are therefore determined together and designated by a common name of urobilinoids.

Urobilin content of the urine increases not only in the presence of hepatic insufficiency, but also in increased haemolysis. In this case, due to release of considerable quantity of haemoglobin, greater amounts of bilirubin are produced and liberated into the intestine. Increased production of stercobilin intensifies its excretion with urine. In obstructive jaundice, when bile is not supplied to the intestine, stercobilin is absent from faeces and the urine is free from urobilin casts. Bilirubin excretion with bile and stercobilin content of faeces decrease in hepatic jaundice, while urobilin casts of urine increase. Their normal ratio is from 10:1 to 20:1, but in pathology it decreases significantly, and is as low as 1:1 in severe liver affections.

Stercobilin content of faeces in haemolytic jaundice exceeds significantly urobilin excretion in the urine. Their ratio increases to 300:1-500:1.

The ratio between the bilirubin reduction products in faeces and urine is much more informative for differentiation of various types of jaundice than the absolute content of each substance.

Carbohydrate metabolism. With participation of the enzyme systems, liver cells synthesize glycogen and deposit it; glycogenosis and glyconeogenesis also occur here. The normal sugar content of blood is maintained also by some other organs and systems, such as the pancreas, the pituitary-adrenal system, etc. In this connection, the blood sugar content with the fasting stomach changes only in very severe liver affections, and therefore functional tests can only reveal carbohydrate hypofunction of the liver. The glucose tolerance test is not effective because the blood glucose content depends not only on the above-mentioned organs but also on the condition of the vegetative nervous system, on the glycogen stores in the liver and muscles, and some other factors.

The *galactose tolerance test* is an effective method to assess the liver function. Galactose is not assimilated by the bodily tissues or organs except the liver; its blood content does not depend on hormones. The patient is given to drink a solution of 40 g of galactose in 200 ml of water, and galactose excretion in the urine is then determined. Normally maximum 3 g of galactose are excreted in 4 hours. The renal function and the absorption power of the intestine may affect galactose excretion in the urine, and the determination of galactose in the blood is therefore more reliable. The maximum rise of the blood sugar occurs in 30—60 minutes with the normal liver function. The maximum level does not exceed 150 per cent of the initial one, which is restored in two hours. If the liver function is inadequate, the sugar level is higher, while the decrease in the galactose level in the blood is slower.

The glycogenosis function is determined by the *adrenaline test.* The patient is given subcutaneously 1 ml of a 0.1 per cent adrenaline solution. In healthy subjects this injection increases the blood sugar level by at least 50 per cent. If the liver is affected, no rise is observed.

The role of the liver in the *protein metabolism* is very important: the liver synthesizes and retains proteins. Amino acids, polypeptides of food, and products of breakdown of tissue proteins are delivered into the liver with blood where they are catabolized, detoxicated, and the unused breakdown products are removed. Some amino acids are deaminated and reaminated. The released ammonia is converted by the liver into less toxic urea. Amino acids (both produced by the liver and carried from outside) are used by the liver to build proteins of its own tissue and also blood proteins: albumin, globulins, (alpha, beta, and to a certain extent gamma globulins), fibrinogen, prothrombin, heparin, and certain enzymes. The liver synthesizes also compounds of proteins with lipids (lipoproteins) and

carbohydrates (glycoproteins). The disorder in the protein-synthesizing function of the liver is revealed by studying the proteins of the blood plasma or serum. This dysfunction has its effect not only on the total protein content but also on the ratio of its different fractions, which is more important diagnostically: the upset protein ratio (dysproteinaemia) is characteristic of most liver pathologies.

Paper electrophoresis is widely used in clinic now. Depending on the size and shape of molecules, their charge, and some other factors, various proteins move at different velocities toward the positive electrode. Various protein fractions concentrate on different portions of paper during electrophoresis; proteins are then revealed by staining. The content of each separate fraction is determined by colour intensity. Proteins of the blood plasma are separated into five main fractions: albumins, alpha$_1$, alpha$_2$, beta, and also gamma globulins (see Table 4). Electrophoresis in other media *(agar,* starch gel, etc.) separates proteins into greater quantity of fractions.

Table 4

Normal Proteinogram

Fraction	Normal percentage	
	average	variation
Albumins	60.9	**56.3-68.8**
Globulins:	**39.1**	**32.0-43.0**
alpha,	4.2	**3.0- 5.8**
alpha$_2$	8.2	**6.9-10.5**
beta	**11.5**	**7.3-12.5**
gamma	**15.2**	**12.8-19.2**
A-G ratio	1.2-2	

The A-G ratio most frequently decreases in liver diseases. This occurs mainly due to the decrease in the albumin content (their upset synthesis). In patients with acute inflammation of the liver (acute hepatitis) the content of alpha$_2$ globulins in the blood plasma increases, while in chronic hepatitis the gamma globulin content increases probably due to accumulation of antibodies which move during electrophoresis with gamma globulins. The total serum protein content often increases as well. The total protein content decreases sharply (at the expense of albumins) in patients with liver cirrhosis; the content of gamma globulins, however, increases markedly.

During electrophoresis, fibrinogen migrates together with gamma globulins and cannot be detected separately. For *quantitative determination of fibrinogen,* it is precipitated from plasma by calcium chloride with

subsequent weighing of the washed and dried precipitate, or by determining protein in the precipitate after its dissolution. Fibrinogen is synthesized in the liver and its content of plasma therefore decreases significantly if the liver is seriously affected. This affects blood coagulation. The normal fibrinogen content of plasma is from 200 to 400 mg/100 ml (2-4 g/1 or 8-13 mg/ml; clot weight).

The *total plasma protein content* is determined mostly by the refractometric method; if a refractometer is not available, chemical methods can be used (Kjeldahl method, biuret test, nephelometric method, etc.).

The ratio of the protein fractions can also be determined by immunoelectrophoresis, ultracentrifuging, etc. In addition to direct determination of the ratio of the protein fractions, dysproteinaemia can also be determined by simple methods. These are the so-called *protein sedimentation (flocculation)* tests. In the presence of dysproteinaemia (especially in decreased albumin content) the equilibrium of the colloidal blood system becomes upset. This disturbance can be revealed by adding electrolyte to the blood serum in the concentration that would not alter normal serum but in dysproteinaemia would cause cloudiness or precipitation of flakes (protein flocculation). The presence of paraproteins (pathological proteins) can also be detected in the blood. These tests include reactions with corrosive sublimate (Takata-Ara test, Grinsted and Gross sublimate tests), zinc sulphate, cadmium sulphate, Lugol's iodine solutions, etc. In another group of flocculation tests the stability of a colloidal solution is upset by adding a small portion of dys- or paraproteinaemic serum (thymol, colloidal gold test, etc.).

The *thymol turbidity test* is based on determination of turbidity of a colloidal thymol reagent caused by adding 1/60 volume of serum. The test is positive mostly in the increased blood serum beta-lipoprotein content. It is always positive in virus hepatitis and diffuse affections of the liver. It is negative in obstructive jaundice.

In the presence of significant excess of globulins, and especially of fibrinogen, the *formol-gel test* becomes positive (the serum converts into a gel from the addition of formaldehyde).

Dozens of sedimentation tests have been proposed. They all are nonspecific and are positive not only in the presence of liver diseases but also in multiple myeloma, collagenosis, etc. These tests reveal dysproteinaemia more easily than electrophoresis.

Prothrombin (factor II of blood coagulation) is synthesized in the liver with participation of vitamin K. The cause of hypoprothrombinaemia is either upset synthesis of prothrombin by the hepatocytes or vitamin K deficiency (vitamin K is fat-soluble and is delivered to the liver from the intestine). In the presence of obstructive jaundice, when absorption of fats

and vitamin K is deranged due to the obstructed delivery of bile acid to the intestine, the synthesis of prothrombin in the liver decreases and the blood prothrombin content decreases as well. In order to reveal the cause of hypoprothrombinaemia, a *test with parenteral administration of vitamin K* is used. If the blood prothrombin content increases after administration of vitamin K, the prothrombin synthesizing function of the liver is normal. This test helps differentiate between obstructive and parenchymatous jaundice. Prothrombin is determined by the rate of coagulation of recalcified plasma in the presence of excess thromboplastin.

Amino acids, urea, residual nitrogen and ammonia are the products of protein decomposition which have a certain diagnostic importance. The total blood content of amino acids increases only in severe affections of the liver with impairment of its deaminating and urea-forming functions (otherwise rather stable). The condition for the increase in residual nitrogen of blood is a simultaneous renal dysfunction. Increased residual nitrogen occurring in renal insufficiency alone differs from that occurring in hepatorenal insufficiency by the main component of residual nitrogen. This is urea in renal insufficiency and amino acids in hepatorenal dysfunction. Separate determination of amino acids of the blood by chromatographic methods does not give reliable diagnostic information and the labour-consuming chromatographic procedure is not thus justified. Determination of *leucine and tyrosine crystals* that appear in the urine sediment in the presence of acute dystrophy of the liver is of certain diagnostic importance.

The blood ammonia content increases when the liver is unable to detoxicate ammonia delivered from the intestine (by synthesizing urea). Accumulation of ammonia in the blood produces a toxic effect on the central nervous system. Hyperammoniaemia is therefore a forerunner of hepatic coma.

The importance of the liver is especially great in *fat metabolism.* The liver performs the decisive role in the synthesis and splitting of fats, phospholipids, and cholesterol, in esterification and liberation of cholesterol, and in maintaining constant cholesterol content of blood. Blood lipids change their concentration in liver affections. Normal blood serum cholesterol content is 3.9-5.2 mmole/l (150-200 mg/100 ml). The cholesterol concentration decreases in patients with severe forms of acute and chronic hepatitis and cirrhosis of the liver. Cholesterol increases in most obstructive jaundices. The activity of alkaline phosphatase usually increases simultaneously. But these quantitative shifts are not always demonstrative. The degree of esterification of cholesterol (their combination with fatty acids), which occurs mostly in the liver, is more informative diagnostically. Normally 60-70 per cent of blood cholesterol is ester-

bound, but this percentage decreases in liver affections due to the decreased esterase activity. The decrease is proportional to the degree of liver dysfunction. The ratio of the ester-bound cholesterol to the total blood cholesterol (normally 0.6-0.7) is called esterification coefficient. When markedly decreased, this coefficient is a poor prognostic sign.

The blood phospholipid content in the presence of liver pathology changes mainly in the same way as the content of cholesterol. The blood content of lipoprotein fractions is also affected by liver diseases.

Certain blood **microelements** are important diagnostically. The most informative are *iron* and *copper*. Both elements are contained in the serum as metal proteids, i.e. compounds with proteins, in which they are present in microgram quantities. These metals are also present in the liver, which serves as a depot for them. Iron is deposited in the liver as ferritin, an iron-protein complex, that is a reserve of iron used for the synthesis of haemoglobin in the bone marrow. Another iron compound is haemosiderin, the product of haemoglobin decomposition, which is accumulated in the liver in increased haemolysis and also in some diseases. Transferrin (the transport protein) which carries iron from the liver to the bone marrow is also synthesized in the liver. Iron that is not bound in haemoglobin is also determined in the blood serum for diagnostic purposes: its content increases significantly (2-3 times) in acute hepatitis; in chronic hepatitis and cirrhosis the increase is less significant, while it does not change (or even decreases) in obstructive jaundice.

Copper is contained in the blood as an oxidative enzyme ceruloplasmin; it is also contained in the liver as a copper-containing protein hepatocuprein. The blood serum copper content slightly increases in hepatitis, and the increase is pronounced in obstructive jaundice. The iron to copper ratio is always decreased in obstructive jaundice and is mostly increased in parenchymatous affections of the liver.

Study of liver enzymes. The liver cells contain numerous enzymes regulating metabolic processes in the liver. Affection of hepatocytes causes an increased excretion into the blood of some enzymes, while the synthesis of other enzymes decreases. Changes in activity of enzymes in the blood serum, which are a sensitive and quick response to liver affections, are widely used for diagnostic purposes. Some of these enzymes are produced not only by the liver but also by some other organs. But changes occurring in some enzymes during liver pathology are so constant that their determination becomes of great practical value. These are transaminase, aldolase, alkaline phosphatase, cholinesterase, lactic dehydrogenase (see Table 12).

Determination of isoenzymes of certain enzymes mentioned above gives more reliable diagnostic information. Isoenzymes are group of enzymes

that have similar catalytic action but differ in the structure of their proteins. During electrophoresis in starch gel, an isolated enzyme is subdivided into isoenzymes due to their different electrophoretic mobility.

A spectrum of certain isoenzymes is typical for affection of separate organs. For example, of the five isoenzymes of lactic dehydrogenase, the fifth fraction (LDG_5) is regularly increased in chronic hepatitis and cirrhosis of the liver, while the increase in the LDG, is characteristic of myocardial infarction. Determination of isoenzymes of aldolase, aspartate aminotransferase, leucine aminopeptidase, and of some other enzymes is also important.

Changes in the activity of organospecific enzymes, i.e. the enzymes characteristic only of liver cells, are even more informative: their activity changes only in pathology of the liver. These enzymes are ornithine carbamoyl transferase and arginase taking part in the synthesis of urea, sorbitol dehydrogenase catalysing oxidation of sorbitol to fructose, guanine deaminase catalysing conversion of guanine to xanthine, quinine oxidase oxidizing quinine, etc.

Transaminases are the enzymes catalysing the transfer of the amino group from amino acids to keto acids. Among them diagnostically important are *aspartate aminotransferases* (AsAT, glutamino-oxalo-acetic acid transaminase) and *alanine aminotransferase* (A1AT, glutaminopyruvic transaminase). Although their increasing activity is a non-specific sign because it is observed in liver diseases and generally in their diffusion from injured tissues (e.g. myocardium, kidneys, pancreas), their activity may nevertheless be very high in myocardial infarction and hepatitis. A1AT dominates in hepatitis, and As AT in myocardial infarction. The main importance of the test is that activity of both transaminases increases significantly during non-icteric period of acute hepatitis (Botkin's disease). This facilitates its early diagnosis and also identification of non-icteric forms of hepatitis.

The content of *aldolase* (fructose 1,6-phosphate aldolase) increases markedly in the blood serum of patients with liver diseases. Hyperaldolasaemia regularly attends epidemic hepatitis and the test for aldolase is therefore obligatory for diagnosis of the disease.

Alkaline phosphatase is the enzyme hydrolysing esters of phosphoric acid. It is mostly formed outside the liver but is excreted by this organ. The increase in the activity of the blood alkaline phosphatase is especially pronounced in obstructive jaundice, due to malignant tumour, and also in intrahepatic cholestasis, and biliary cirrhosis. In patients with the affected liver parenchyma, the activity of this enzyme increases moderately.

Serum cholinesterase (pseudocholinesterase) splits acetylcholine and other choline esters. It is formed in the cells of the liver parenchyma. Its

determination is of great prognostic importance: the lower the activity of pseudocholinesterase in hepatitis, the more severe is the course of the disease.

Detoxicating function of the liver. Blood of the portal vein supplied from the gastro-intestinal tract contains various toxic substances for which the liver imposes a barrier. These substances are retained by the liver and almost completely detoxicated by the enzymes responsible for oxidation, reduction, deamination, hydrolysis, methylation, combination with sulphuric acid, glucuronic acid, and with glycine. These reactions give less toxic or more readily soluble substances that can be excreted in the bile or urine. Ammonia, for example, is converted into less toxic urea, free bilirubin combines with glucuronic acid to turn into a less toxic and water-soluble compound that can be excreted in the bile and urine. Phenols, indoles, ketones, alcohols, sulpha preparations, amidopyrine, camphor, and morphine are detoxicated mainly by combining with glucuronic or sulphuric acid; sodium benzoate combines with glycine; santonin oxidizes to oxysantonin; metals react with nucleoproteins. Stellar reticuloendotheliocytes retain and phagocytise microbes.

Sodium benzoate test. Sodium benzoate is given per os or intravenously. It combines with glycine in the liver to give hippuric acid which is excreted in the urine. The detoxicating function of the liver is assessed by the percentage of urine-excreted sodium benzoate in the form of hippuric acid. If the liver parenchyma is affected, synthesis of hippuric acid is disturbed and its excretion is slowed. The test has some disadvantages: it precipitates in obstructive jaundice, tumours, fevers (positive test), and requires normal renal function.

Excretory function of the liver. Among substances to be excreted from the body are water-soluble compounds that are excreted mainly by the kidneys, and water-insoluble or protein-bound compounds that are excreted by the liver. The normal hepatic excretory capacity is restricted. In significantly intensified haemolysis, a healthy liver cannot excrete all bilirubin from the blood where it thus accumulates. Parenchymal affections decrease the excretory capacity of the liver to cause, for example, bilirubinaemia, which however is not an obligatory symptom. In order to reveal the disordered excretory function of the liver, especially in non-icteric affections, tests are used with administration into the blood of substances that should be excreted with bile.

Bilirubin test is most informative: after an intravenous injection of 50 mg of bilirubin, its content in the blood is determined in 5 minutes and in 4 hours. If excretory function of the liver is normal the pigment concentration decreases in 4 hours to 15 per cent of its concentration as determined in 5 minutes after the injection. The test is not however used universally because of expensiveness of the preparation and uselessness of the test in the presence of jaundice.

The *bromsulphthalein test* is one of the most specific. Bromsulphthalein is given intravenously (5 mg/kg body weight) and the first specimen of blood is taken in 3 minutes (when the concentration of the preparation in the blood attains its maximum). Another specimen is taken in 45 minutes after the injection. Concentration of bromsulphthalein is determined colorimetrically: it turns red-violet when alkali is added. If the liver function is adequate, the preparation concentration in the blood in 45 minutes does not exceed 5 per cent of its initial concentration, which is assumed to be 100 per cent. The stain can be detected in the bile in 15 minutes after the injection. The test is very sensitive: even insignificant hepatic dysfunction that cannot be detected by other methods is revealed by the bromsulphthalein *test.*

Indocyanine green test is based on the same principle. The preparation is given intravenously in a dose of 0.5 mg/kg. Normally, not more than 4 per cent of the injected stain remains in the blood in 20 minutes. The test is more sensitive than that with bromsulphthalein.

The number of tests for the liver function is great. But clinicists are not satisfied by merely stating this or that type of metabolic disorder without relating them to the provoking changes occurring in the liver. There is therefore a tendency to unite groups of pathologically altered test results into *syndromes characteristic of various pathologies.* For example, when bile drainage is disordered, the concentration of cholesterol, bile acids, bound bilirubin, alkaline phosphatase, and copper in the blood increases. The combination of these positive tests gives the *syndrome of cholestasis.* The *syndrome of hepatocyte insufficiency* is characterized by decreased concentration in the blood of substances synthesized by hepatocytes: serum albumins, cholesterol, prothrombin, etc. Inflammatory changes in the liver are characterized by an increased content of various globulin fractions produced by reticulohistiocytary elements of the liver. This is revealed by a number of positive protein sedimentation tests (the *inflammatory syndrome).* These syndromes can bring the physician closer to understanding of prevailing pathological processes occurring in the liver.

STUDY OF DUODENAL CONTENTS

Duodenal contents are studied for determining the bile composition, which in turn is necessary to diagnose affections of the gall bladder and bile ducts, and also to estimate the function of the pancreas.

Technique. Duodenal contents are obtained by probing the duodenum by an elastic rubber tube 3-5 mm in diameter. The oval bulb at the end of the tube opens into its lumen. The overall length of the tube is about 150

cm. The tube bears a mark at a distance of 45 cm from its distal end (the distance to the stomach); next marks follow at 70 and 80 cm lengths.

The procedure is carried out on a fasting stomach. The patient sits with the mouth slightly open. The tube is placed in the mouth so that the bulb is at the root of the tongue and the patient is asked to make swallowing movements. The operator should only slightly promote the independent movement of the tube. If the patient attempts to vomit, he is recommended to breathe deeply through the nose. In rare cases the throat and the upper oesophagus are anaesthetized. When, according to the marks, the tube reaches the stomach, its position is verified by aspiring the stomach contents with a syringe which is inserted into the outer end of the tube: extraction of a slightly turbid acid fluid shows that the tube is inside the stomach. The fluid may be coloured yellow by the duodenal contents, but the reaction remains acid. The patient is now placed on his right side so that the tube bulb would be directed (by gravity) toward the pylorus. A soft pad is placed under the patient's pelvis. The patient continues swallowing the tube to the mark of 70 cm. Breathing should be through the mouth. The tube end passes the pylorus and enters the duodenum in about 60—90 minutes (sometimes even later). The outer end of the tube is lowered into a test tube in the stand placed on a low stool at the head-end of the bed. Sometimes the tube passes the pylorus in a shorter time if the patient walks slowly about for 15-20 minutes and continues the swallowing movements. When the tube is swallowed to the mark of 70 cm, the patient lies on his right side. If the bulb has reached the duodenum, yellow alkaline fluid is gathered in the test tube. If the common bile duct is obstructed (pronounced jaundice) the duodenal contents are colourless and the reaction is alkaline. In order to check the position of the tube end (if no juice is discharged from the probe) air can be forced into the tube by a syringe. If the probe is inside the stomach, the patient feels the stream of the injected air, and bubbling can be heard. If the tube is in the duodenum, the patient does not feel anything and no sounds are heard. The position of the tube can most accurately be established by X-rays. The correct position of the tube bulb is between the descending and the lower horizontal portions of the duodenum. If the tube is stopped before the pylorus, the patient is given to drink a warm solution (2-3 g) of sodium hydrocarbonate in 10 ml of water.

The normal duodenal contents discharged from the tube (the *first phase* of examination) is golden-yellow, slightly viscous, clear, and opalescing. If it contains gastric juice, it becomes turbid from precipitating bile acids and cholesterol. This portion is designated by the letter A. This is a mixture of bile, pancreatic and intestinal secretion. Their proportion in the mixture is unknown and the diagnostic value of this fluid is therefore low. Bile A is

collected for 10—20 minutes. An agent stimulating contraction of the gall bladder is then given through the tube. This is usually a warm solution of magnesium sulphate (25-50 ml of 25—33 per cent solution). Less frequently this is vegetable oil, egg yellow, 10 per cent sodium chloride solution, 30-40 ml of a 40 per cent glucose solution or 40 per cent sorbitol solution, and also hormones (cholecystokinin or pituitrin) which are given subcutaneously.

Following the administration of the stimulant into the duodenum, the Oddi sphincter contracts and excretion of bile is discontinued. This is the *second phase.* Normally it continues 4—6 minutes following the administration of magnesium sulphate and about 10 minutes after administration of olive oil. The phase is elongated if the tone of the Oddi sphincter is increased and shortened in its hypotonia. Next follows the *third phase,* the excretion of golden-yellow contents of the bile duct and the neck of the gall bladder (portion A_1). The *fourth phase* is evacuation of the gall bladder, which is attended by discharge of thicker dark-yellow, brown or olive bile. It is greenish when congested or if the gall bladder is inflamed. Portion B is the bile of the gall bladder, whose secretion is associated with positive Meltzer-Lyon reflex: contraction of the gall bladder concurrent with relaxation of the bladder sphincter and Oddi sphincter. Bladder bile (B bile) is a kind of concentrated liver bile. The wall of the gall bladder has selective absorbability: the sodium ion and water are absorbed especially actively. Ions of potassium, calcium, and chlorine are absorbed much slower. As a result, the content of bile acids and their salts increases 5-8 times, and that of bilirubin and cholesterol 10 times compared with their content in the hepatic bile (C bile). Epithelium of the gall bladder secretes mucin whose concentration in B bile is from 1 to 4 per cent. In accordance with the capacity of the gall bladder, the amount of secreted B bile is 30—60 ml during 20-30 minutes. The bladder reflex may sometimes be absent in healthy subjects after administration of magnesium sulphate, but it usually appears in repeated examinations, or after giving vegetable oil, pituitrin, or atropine (subcutaneously). The appearance of the reflex after giving procaine or atropine indicates spasm of the sphincter and the absence of organic obstacles. Persistent absence of the bladder reflex is observed in cholelithiasis, cirrhosis of the gall bladder, obstruction of the bile duct with a stone or an inflammatory process in its mucosa, in contractile dysfunction of the gall bladder, etc. Excretion of very thick dark bile or ample amounts of bile indicates its congestion in dyskinesia of the bile ducts. Intensification of colour alone indicates haemolysis (excess secretion of bilirubin).

After B bile excretion discontinues, C bile (hepatic bile) is delivered from the tube. This is the *fifth phase* of the examination. The golden-

yellow C bile is considered to be hepatic though it also contains admixtures of duodenal juice. Five-minute portions are collected separately during the entire examination. This fractional duodenal probing is used to determine the properties of the contents, volumes of separate portions of the bile system, and the tone of its sphincters. All the three portions of bile are studied by microscopic, chemical and sometimes bacteriological methods.

Microscopy of duodenal contents should be carried out immediately after collection of each portion. Leucocytes are decomposed more slowly but their breakdown is still very rapid. If the sample of bile cannot be examined immediately corrosive sublimate or a 10 per cent formaldehyde should be added (with warming up). But these reagents distort the cells and kill lamblia. Flakes of mucus are pipetted from the bile and transferred onto an object glass. The remaining liquid is centrifuged and the precipitate (as well as the flakes) is examined in native preparations.

Untill recently, the *presence of leucocytes in bile* was given great diagnostic importance. Their presence in B bile was considered as a diagnostic sign of cholecystitis, and in C bile of cholangitis. If the leucocytes were impregnated with bile (coloured by bilirubin), this was considered a proof of their genesis from the gall bladder. At present, many investigators believe that accumulations of round cells in bile are actually altered and rounded nuclei of intestinal epithelium. Their combination with bilirubin depends probably not on the place of their origin but on the thickness of mucous coat that protects them. Diagnostic importance can therefore only be given to the presence of leucocytes in bile after their identification (by peroxidase staining). *Epithelium* can be quite informative provided it is well preserved and its properties can be indicative of the site of its origin: fine prisms originate from the bile ducts, elongated columnar cells with oblong nuclei originate from bile passages; large cells with a large round nucleus and vacuolized cytoplasm are attributed to the mucosa of the gall bladder; large epithelial cells with a round nucleus, accounting for the expanded lower third of the cell, and with a thickened cuticle, belong to the duodenum. The cells can easily be identified in the native preparation by phase-contrast microscopy.

The presence of *tumour cells* in bile is of great diagnostic importance. Microscopy of native preparations only in rare cases can reveal them. Histological study of consolidated duodenal precipitate is more informative.

Discovery of *cholesterol crystals* and brown grains of *calcium bilirubinate* are of importance. They can be found in small quantities in healthy subjects but large amounts suggest cholelithiasis.

Discovery of *parasites* in bile is of great significance. *Lamblia intestinalis* occur frequently; the eggs of liver fluke or Chinese fluke, eggs of

duodenal wryhead and also larvae of intestinal *Strongyloides stercoralis* are found less frequently.

Some **chemical constituents of bile** are determined. These are bilirubin, cholesterol, bile acids, and protein. It is not the total *bilirubin* of bile that is important, but rather bilirubin proportion in C and B bile, which characterizes the concentration capacity of the gall bladder. The normal bilirubin content in B bile is 3.4-6.8 mmol/1 (200-400 mg/100 ml) and of C bile, 0.17-0.34 mmol/l (10-20 mg/100 ml). Decreasing concentration of bilirubin in the gall bladder can depend on bile dilution with inflammatory exudation. Concentration of bilirubin is determined by the icterus index: bile is diluted to match its colour with that of a standard solution of potassium dichromate. The degree of dilution indicates "units of bilirubin". *Cholesterol* is determined as in the blood. A bile contains about 0.5 mmol/1 (20 mg/100 ml), B bile about 2.6-23.4 mmol/1 (100-900 mg/100 ml), and C bile 2-2.6 mmol/1 (80-100 mg/100 ml) of cholesterol. Protein is absent from the normal bile. Its presence (proteincholia) indicates inflammation.

Bile acids are determined colorimetrically using the Pettenkofer test (and its modifications) based on the interaction between bile acids and sucrose in the presence of sulphuric acid and subsequent development of cherry-red colour. There are more accurate, though more complicated methods for determining bile acids. These are chromatographic, luminescence and other methods. Decreasing the cholate to cholesterol ratio below 10 in bile (the *cholatocholesterol coefficient)* indicates predisposition to formation of bile stones.

The ability of the liver to excrete foreign substances together with bile (stains, medicines, iodine compounds, salts of heavy metals) is used for diagnostic purposes. Patency of bile ducts is determined by the speed of excretion with bile of *bromsulphthalein* given intravenously. If the concentrating capacity of the gall bladder is impaired, it is difficult to differentiate between A, B and C biles by colour. A methylene blue test *(chromodiagnostic probing)* is then used. The reagent is reduced in the liver to a colourless leucobase, but it again oxidizes in the gall bladder and its colour reappears. The patient is given 0.15 g of methylene blue in a capsule in the evening and common probing is performed in the morning. If blue bile is discharged after giving magnesium sulphate, this indicates that it is B bile.

Bacteriological study of bile is only of relative importance because it is difficult to establish the origin of the cultured flora (it may originate in the mouth, the intestine, or the bile ducts). But if the same flora is found in repeated studies of the same portion of bile, it can be suggested that the found microbes may originate in the bile ducts.

X-RAY STUDY

Survey roentgenoscopy and roentgenography of the liver and gall bladder are not diagnostically important because the increased density due to consolidated liver tissue can hardly be differentiated from shadows of the other abdominal organs. Therefore only in rare cases (usually in thin and asthenic patients) it is possible to determine the lower border of the liver, its position, configuration, and the size of the liver and the spleen. In some cases X-ray examination can reveal inclusions in the liver tissue (calcified echinococcal cysts, tuberculous foci), in the gall bladder and bile passages (stones containing much calcium salts).

Various X-ray techniques have been proposed during the past decade to study the liver vessels with contrast substances. *Splenoportography* is most widely used now. This is the method by which the splenic vein and portal vein with its intrahepatic ramifications can be determined with contrast substances and with serial radiography. The patient is given local anaesthesia and the spleen is punctured in the 8th and 9th intercostal spaces in the left midaxillary line to administer 40—50 ml of a contrast substance (70 per cent solution of cardiotrast or triombrin). Series of X-ray pictures are then taken in 2, 5, 10, 20, 35, and 45 seconds, which are used for combined examination of the portal circulation and the condition of the bile-secretion system. A splenoportogram gives a distinct picture of branching veins. Their section and the pattern of branching can be used to judge about intra- and extrahepatic causes of portal hypertension, the development of collateral circulation, the character of extension and the degree of pathology of the liver (cirrhosis, primary and metastatic tumours, cysts). Splenoportography is especially indicated in cases of portal cirrhosis of the liver with ascites, when the patient is offered an operation for placing a portocaval anastomosis to bypass a part of blood outflow from the portal vein into the inferior vena cava and to decrease the degree of portal hypertension. The presence of portal hypertension can be established indirectly by contrast X-ray study of the oesophagus (using barium meal). It reveals varicosity of the oesophageal veins.

The arterial system of the liver is examined by *coeliacography,* the method based on the administration of a contrast substance into the coeliac artery through a catheter, which is usually passed into the coeliac artery through the femoral and then abdominal artery, and then the abdominal aorta. This method reveals foci of liver affection (primary and metastatic tumours, cysts, and abscesses).

All X-ray studies should be carried out only for special indications with proper consideration of all possible contraindications (acute diseases of the liver, haemorrhagic diathesis, hypersensitivity to iodine preparations, etc.).

Peroral cholecystography and intravenous cholangiography are widely used to study the gall bladder and bile ducts. *Cholecystography* is based on a peroral administration of iodine-containing contrast substance, e.g. bilitrast (3-3.5 g) or iopanoic acid (cholevid) in a dose of 3—6 g for one examination. The contrast substance is given after a light early supper. The substance is absorbed in the intestine, trapped by the liver, and secreted with bile to enter the gall bladder, where iodine is gradually accumulated. Next morning, the patient with a fasting stomach is given an X-ray examination of the gall bladder. A distinct shadow of the gall bladder can be seen 10—15 hours following the intake of the contrast substance; this indicates normal concentration function of the gall bladder. If this faculty of the gall bladder is impaired, or if patency of the cystic duct is obstructed, the shadow of the gall bladder is absent from the X-ray picture. In the presence of stones the shadow is non-uniform and areas of rarified density

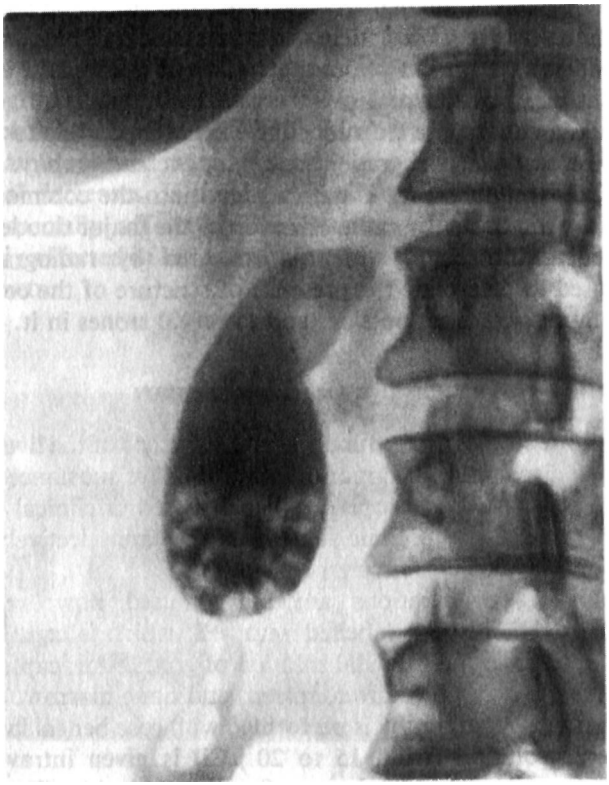


Fig. 95. Cholecystogram with gallstones.

can be seen, their number and size corresponding to the number and size of the stones (Fig. 95). If the shadow of the bladder is free from stones, the next stage of examination is begun: a cholecystokinetic (usually 10 ml of raw egg yellow) is given to the patient. The preparation provokes contraction and evacuation of the gall bladder. Series of pictures taken at regular intervals are used to assess the motor function of the gall bladder (by the time of its evacuation and the size of the maximum contracted gall bladder).

A contrast substance, bilignost, is given in *cholangiography* (30-40 ml of a 20 per cent solution, a slow intravenous injection). If the patient's condition is normal, radiographs taken 5-10 minutes after the injection show large intra- and extrahepatic bile ducts and the gall bladder (provided the bile duct is patent). Cholangiography reveals not only the shadow of the gall bladder and areas of rarified density in the presence of stones, but also gives information on the position, calibre, and patency of the intra- and extrahepatic bile ducts. Cholangiography is used to study the intra- and extrahepatic bile ducts (e.g. in patients with removed gall bladder) and also the gall bladder in patients in whom the shadow of the bladder is not determined by cholecystography.

Advances in endoscopic technique have made it possible to work out a method of endoscopic (retrograde) *cholangiopancreatography.* An iodine-containing contrast substance is administered into the common bile duct and the pancreatic ducts (by catheterization of the major duodenal papilla during duodenofibroscopy) which is followed by radiography. This method is used to determine the presence of stricture of the common bile duct, its compression from outside, and to reveal stones in it.

RADIOISOTOPE METHODS OF STUDY

Radioisotope studies of the function and structure of the liver are based on tracing the distribution and motion of radioactive substances inside the human body. Short-lived isotopes are usually used in clinical practice to label certain mineral and organic substances that are selectively absorbed by various cells of the liver tissue.

The following preparations are mostly used now: rose bengal (dichlortetraiodofluorescein) labelled with ^{131}I, which is captured by the liver hepatocytes, and the colloidal solution of gold ^{198}Au, captured by the reticulohistiocytic cells of the liver, spleen, and bone marrow.

Radioisotope hepatography is performed with rose bengal labelled with ^{131}I. Its sterile solution (from 15 to 20 μCi) is given intravenously in 0.5-0.9 ml of sterile isotonic solution of sodium chloride. The liver function is then examined by a radiometric apparatus whose scintillation

transmitters are fixed over the heart region (to determine stain withdrawal from the blood; blood clearance), over the right lobe of the liver (to determine stain accumulation and withdrawal), and the central part of the abdomen (to control stain discharge via the bile passages to the intestine). Changes in radioactivity over these areas are recorded for 60-90 minutes, and in some cases (in obstructive jaundice, various forms of liver cirrhosis) the time of examination can be prolonged to 24-72 hours. The results are presented graphically as hepatograms (Fig. 96).

In healthy subjects, the half-period clearance (the time of blood clearance from 50 per cent stain absorbed by the liver) is from 10 to 15 minutes. During the first two minutes following injection of the stain, radioactivity of the liver increases sharply to characterize the condition of its blood flow. Further absorption of the stain by the liver is slow. The time of maximum accumulation of the stain in the liver is normally 16-22 minutes. The time during which half of the stain is released from the liver to the gall bladder and the small intestine (period of half-clearance) varies between 75 and 110 minutes. Not more than 2.5 per cent of the initial amount of the preparation remains in the liver in 24 hours. Radiohepatography can thus assess blood circulation in the liver, the absorption-excretion function of the liver, and patency of the bile ducts.

In liver pathology, the rate and the degree of absorption and discharge of rose bengal decreases. If polyhedral cells are affected, the absorption process is especially affected. The secretory function of the liver is predominantly affected in inflammation and especially in impaired patency of the bile ducts.

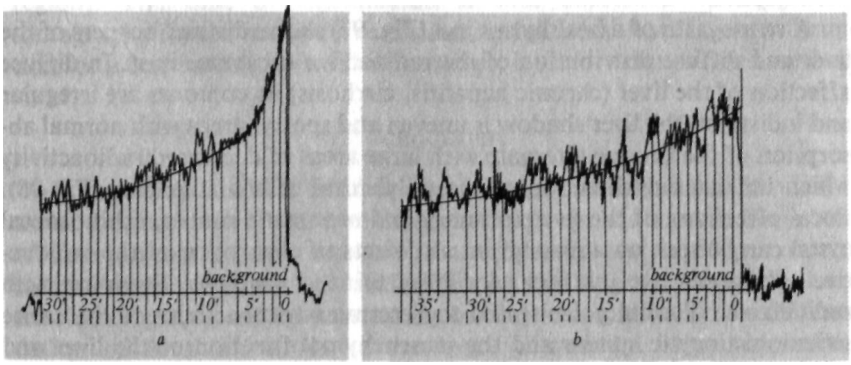


Fig. 96. Accumulation and excretion of rose bengal.
a—in norm; *b*—in hepatitis.

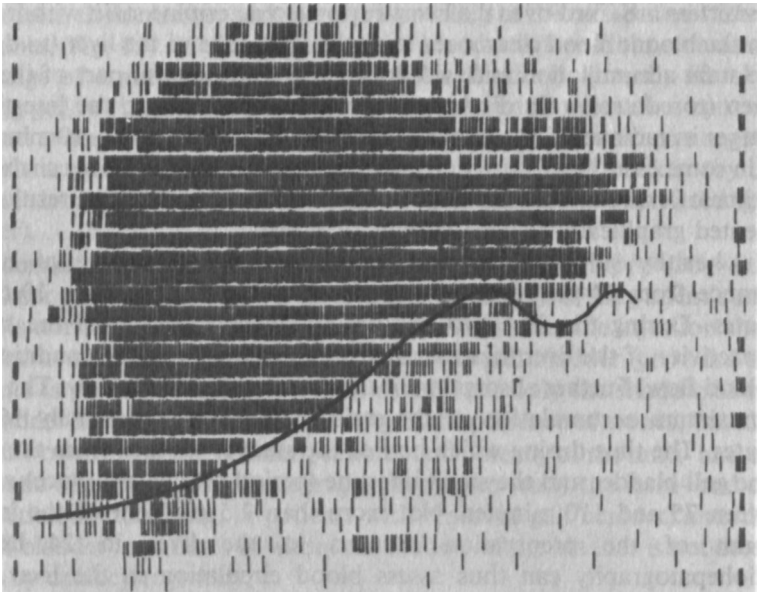


Fig. 97. Scanogram of a normal liver.

Scanning is a graphic registration of distribution of labelled compounds in the liver (hepatoscanogram). The patient is given intravenously rose bengal labelled with ^{131}I (3 μCi/kg) in 0.8-1 ml of isotonic sodium chloride solution (or labelled with ^{198}Au). Scanning is carried out in 30 minutes after the injection.

A scanogram of a healthy subject (Fig. 97) shows distinct borders of the liver and diffuse distribution of the radioactive substance in it. In diffuse affection of the liver (chronic hepatitis, cirrhosis) its contours are irregular and indistinct, the liver shadow is uneven and spotty: areas with normal absorption of the isotope alternate with large areas of decreased radioactivity which indicates dysfunction of the polyhedral cells of the liver (Fig 98). Focal affections of the liver (primary and metastatic cancer, echinococcal cysts) can be seen on a scanogram as defects of absorption of the radioactive substances, i.e. as foci of diffuse thinned shadows. Scanning with radioactive colloidal gold is used to determine total activity of the entire reticulohistiocytic system and the mesenchymal function of the liver and spleen. In healthy people ^{198}Au is accumulated mainly in the liver as compared with the spleen. Absorption of the colloidal gold in an enlarged spleen increases in cirrhosis of the liver (Fig. 98).

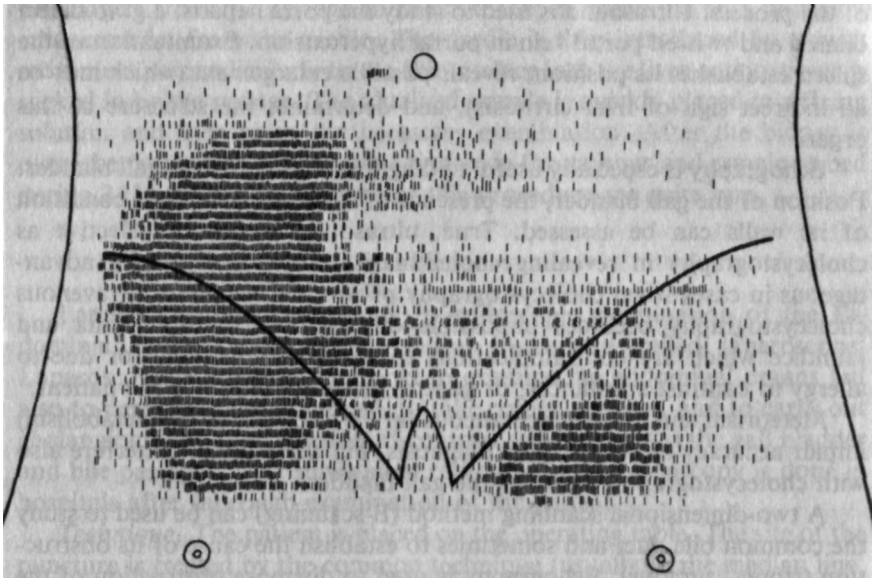


Fig. 98. Scanogram in portal liver cirrhosis.

Colour scanning has been used in recent years. Scanograms more vividly show different colouration of various zones due to different accumulation of the isotope in the organs. Scanograms are interpreted quantitatively by special gamma-chambers which record simultaneously radioactivity over the entire organ (without moving the detector over the examined region). The time of examination is thus shortened. Computerized tomography is used in cases where scanning fails to give sufficient information for a correct diagnosis. This, however, is a more complicated method.

ECHOGRAPHY

Echography is widely used in hepatology. Ultrasound can be used to assess the condition of the liver tissue, to detect cysts (almost in 90 per cent of cases), abscesses and tumours of the liver (almost in 80 per cent of cases). Successive use of radioisotope scanning of the liver and echohepatography improves accuracy of diagnosis and facilitates differentiation of focal affections of the liver. Ultrasound helps to perform sighting biopsy of the liver and to differentiate between cirrhosis, hepatitis, and fatty degeneration, and to assess the extent of liver affection. This method can be used to reveal liver affections in a comparatively early stage

of the process. Ultrasound is used to study the porta hepatis, e.g. to detect dilated and twisted portal vein in portal hypertension. Examination of the spleen establishes its position, reveals possible enlargement (which may be an indirect sign of liver cirrhosis), and determines the structure of this organ.

Echography is especially useful to diagnose diseases of the gall bladder. Position of the gall bladder, the presence of stones in it, and the condition of its walls can be assessed. True, ultrasound is not so effective as cholecystography in revealing cholelithiasis, but it is especially advantageous in cases when cholecystography proves ineffective or intravenous cholecystography becomes impossible due to hyperbilirubinaemia and jaundice which are contraindications to these examinations, or due to allergy to contrast substances, or general grave condition of the patient.

Meteorism and much subcutaneous fat (in disorders of fat metabolism) impair accuracy of echographic diagnosis, but these factors interfere also with cholecystographic study of the gall bladder.

A two-dimensional scanning method (B-scanning) can be used to study the common bile duct and sometimes to establish the cause of its obstruction (stones, tumour). Echography is used to diagnose obstruction of the gall bladder by a stone, dropsy or empyema of the gall bladder which arise in such obstructions, and also cancer of the gall bladder, which occurs not infrequently.

PUNCTURE BIOPSY OF THE LIVER

Puncture biopsy is used to take specimens of liver tissue from a patient for histochemical examinations (electron microscopy) and also to study liver enzymes. Puncture biopsy helps in cases where diagnosis of diffuse liver affections is difficult. The procedure is only carried out for special indications. Two methods of biopsy are used: "blind" and sighting (under control of laparoscope). The former method is used in diffuse affections, and the latter in focal affections, e.g. in suspected cancer.

Technique. The patient lies on his back without pillow, slightly turning to his left side with the right arm behind the head. The skin is properly treated and anaesthetized at the site of puncture. A 1 or 2 per cent procaine solution is used for anaesthesia (2-3 ml). Using a stilette, the skin is cut to the depth of 2—4 mm in the region of the 9th interspace, in the anterior axillary line. This is the broadest zone of liver dullness. A special Menghini needle (or its modification according to Bluger and Sinelnikova) with a plunger inside it is introduced into the punctured skin. The needle is connected to a syringe containing a few millilitres of isotonic sodium chloride solution. After puncturing the skin, part of the isotonic solution is

discharged from the syringe in order to expell pieces of skin and subcutaneous fat from the needle. The needle is then introduced by a swift movement perpendicularly to the skin surface into the liver and its tissue is sucked in by the syringe. The obtained sample is quickly placed in a fixing solution and then given the necessary examination. After the biopsy is over, the patient should lie on his right side for an hour and remain in bed during 24 hours. Complications of this procedure are quite rare.

LAPAROSCOPY

Laparoscopy (peritoneoscopy) is endoscopic examination of the abdominal cavity by a special optical instrument called laparoscope. Laparoscopy is now used not only to examine the abdominal organs but also to perform sighting biopsy, to take colour pictures, and to carry out cholangiography (introduction of contrast substances into the gall bladder and bile passages, with subsequent radiography). Laparoscopy is done in hospitals after thorough examination of the patient.

Technique. The patient is placed on the operating table. The site of the puncture is treated by the common technique (usually in the median line, 3-4 cm below the navel, or in the anterolateral parts of the mesogastric region, anteriorly of the abdominal rectus muscles; Fig. 99). In order to ensure higher safety and better conditions for examination of the abdominal

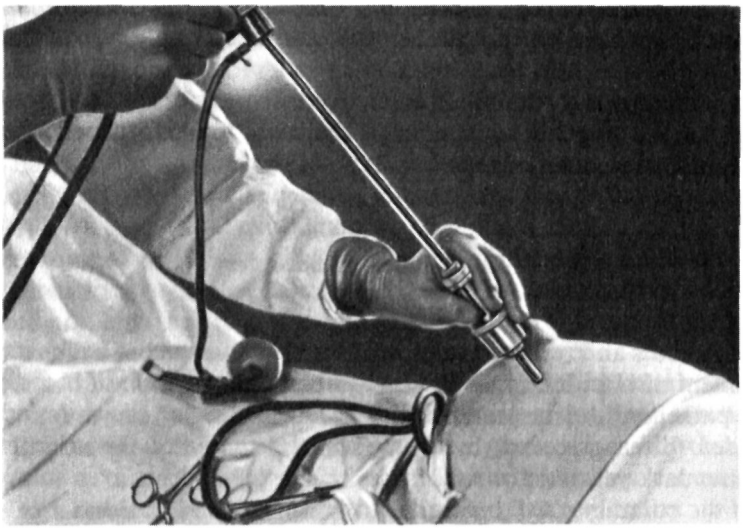


Fig. 99. Introducing a laparoscope into the abdomen.

organs, pneumoperitoneum is first placed (oxygen, carbon dioxide or nitrous oxide are injected into the abdomen through a blunt-pointed needle). In cases with ascites, the fluid is removed. After infiltrative anaesthesia with a 0.25 per cent procaine solution, a 1-cm cut is made by a scalpel at a needed site and a trocar of the laparoscope is passed into the cut. The optical part of the laparoscope is then passed inside the trocar. The abdominal organs are inspected according to a predetermined plan. Depending on the object of examination (stomach, liver, gall bladder, etc.) the patient assumes the appropriate position on the operating table. After laparoscopy is over, air (gas) is released from the abdominal cavity, the trocar is removed, and the wound is sutured. The patient should remain in bed for three days. (The air remaining in the abdomen is absorbed within several days).

Anterosuperior and inferior surfaces of the liver can be examined during laparoscopy. The size of the liver, its colour, the character of the surface, the condition of the liver edge, and its consistency, and also a considerable part of the gall bladder are determined by laparoscopy. Laparoscopy should be done strictly for special indications. It is used in cases where other techniques fail to diagnose the disease. Laparoscopy is especially valuable in diagnosis of focal affections of the liver (tumour, cyst), in establishing the cause of ascites of unknown aetiology (cirrhosis, cancer of the liver, tuberculous peritonitis, etc.), in establishing the character of jaundice (differentiation of obstructive jaundice from hepatic one, and location of possible site and character of obstruction), in cases suspected for cancer of the gall bladder, and in splenomegaly of dubious origin.

Laparoscopy is contraindicated in severe diseases of the cardiovascular system, of the lungs, in haemorrhagic diathesis, grave forms of anaemia, and some other conditions.

Main Clinical Syndromes

Jaundice

Jaundice is an icteric colouration of the skin and mucosa by the increased content of bilirubin in the tissues and blood. The serum of blood taken from patients with true jaundice also becomes intense yellow. Jaundice is attended (often preceded) by changes in the colour of the urine, which becomes dark-yellow or brown; faeces can be very light or even colourless, or on the contrary, dark-brown.

Jaundice can develop very quickly, within 1-2 days, to become very intensive, or it can develop gradually and be not pronounced (subicteric). Pa-

tients themselves (or their relatives) notice yellow colour in their skin. They consult a doctor for this reason. Jaundice can develop with severe itching of the skin, skin haemorrhages and haemorrhages of the nose and the gastro-intestinal tract.

Jaundice occurs in many diseases of the liver, bile ducts, blood, and also diseases of other organs and systems, to which bilirubin metabolic disorders are secondary. Some clinical symptoms attending jaundice are to a certain degree suggestive of its type and origin. Accurate diagnosis of various types of jaundice is possible with special laboratory studies.

True jaundice can develop due to the following three main causes: (1) excessive decomposition of erythrocytes and increased secretion of bilirubin (haemolytic jaundice); (2) impaired capture of unbound bilirubin by the liver cells and its inadequate combination with glucuronic acid (parenchymatous jaundice); (3) obstacles to excretion of bilirubin with bile into the intestine and reabsorption of bound bilirubin in the blood (obstructive jaundice).

Haemolytic (haematogenous) jaundice develops as a result of excessive destruction of erythrocytes in the cells of the reticulohistiocytic system (spleen, liver, bone marrow). The amount of unbound bilirubin formed from haemoglobin is so great that it exceeds the excretory liver capacity to account for its accumulation in the blood and development of jaundice. Haemolytic jaundice is the main symptom of haemolytic anaemia. It can also be a symptom of other diseases, such as B_{12}-(folic)-deficiency anaemia, malaria, protracted septic endocarditis, and other diseases.

The skin of a patient with haemolytic jaundice is lemon-yellow. Skin itching is absent. The amount of unbound bilirubin in the blood is moderately increased (50-200 per cent); the van den Bergh test for bilirubin is indirect. Bilirubin is absent from the urine but the urine is still coloured rather intensely by the markedly increased (5—10 times) stercobilinogen and (partly) urobilinogen. Faeces are intense dark due to the presence of considerable amount of stercobilinogen.

Parenchymatous (hepatocellular) jaundice develops due to the damage of the parenchyma cells (hepatocytes). These cells can capture bilirubin of the blood and bind it with glucuronic acid (the natural detoxicating function of the liver). The natural process of bilirubin excretion in the bile in the form of bilirubin glucuronide (bound bilirubin) is thus impaired. The content of free and bound bilirubin in the blood serum thus increases 4-10 times. In rare cases the increase may be even greater: free bilirubin increases due to hepatocyte dysfunction and bound bilirubin content increases as a result of back diffusion of bilirubin glucuronide from biliary into blood capillaires in dystrophy of the liver cells. Bound bilirubin appears in the urine (bilirubin glucuronide is water soluble and easily passes

via the capillary membranes as distinct from free bilirubin). Bile acids are also present in urine, but their content gradually increases. Excretion of stercobilinogen with faeces also decreases because the amount of bilirubin excreted by the liver into the intestine decreases, but faeces are rarely completely discoloured.

This type of jaundice is mainly determined by infection (virus hepatitis or Botkin's disease, leptospirosis) and toxic affections of the liver (poisoning with mushrooms, phosphorus, arsenic and other chemical substances, medicinal preparations included). But parenchymatous jaundice can develop also in liver cirrhosis.

The skin of patients with this jaundice is typically yellow with a reddish tint. Skin itching is less frequent than in obstructive jaundice because the synthesis of bile acids by the affected liver cells is upset. Symptoms of pronounced hepatic insufficiency may develop in severe course of the disease.

There exists a group of congenital pigmentary hepatoses in which the liver is not affected pathologically, the functional tests are negative, while the process of bilirubin conjugation with glucuronic acid is upset at some of these stages (Gilbert syndrome). This condition is attended by a permanent or intermittent jaundice, which is sometimes pronounced and develops from infancy.

Obstructive (mechanical) jaundice develops due to partial or complete obstruction of the common bile duct. This occurs mostly due to compression of the duct from the outside, by a growing tumour (usually cancer of the head of the pancreas, cancer of the major duodenal papilla, etc.), or due to obstruction by a stone. Bile congestion above the point of obstruction develops and this elevates pressure inside bile passages in continuing bile excretion. As a result, the interlobular bile capillaries become distended and bile diffuses into the liver cells (where dystrophic processes develop) and passes into the lymph and the blood. Moreover, due to increased pressure inside fine bile capillaries, communications are formed at the periphery of the lobules between the capillaries and the lymph spaces, through which bile enters the blood vessels.

Skin and mucosa of patients with obstructive jaundice are yellow. Later, as bilirubin is oxidized to biliverdin, the skin and mucosa turn green and dark-olive. The bound bilirubin content in the blood with direct van der Bergh test is as high as 250-340 mmol/l or 15-20 mg/100 ml, and more. In protracted jaundice associated with liver dysfunction, free bilirubin content increases as well. Bound bilirubin can be found in the urine (the presence of bile pigments is determined by urinalysis) to give it brown colour and bright-yellow foaming. Faeces are colourless either periodically (in incomplete obstruction, usually by a stone), or for lengthy periods of time (in compression of the bile duct by a tumour). Jaundice in-

creases progressively in such cases; the skin and mucosa gradually turn greenish-brown; cachexia of the patient increases. In complete obstruction of the bile ducts, faeces become colourless (acholic); their colour is clayish and grey-white; stercobilin is absent from faeces.

Bound bilirubin and also bile acids produced by the hepatocytes in ample quantity (cholaemia) are delivered to the blood in this type of jaundice. Some symptoms associated with toxicosis develop: pronounced skin itching, which intensifies by night, and bradycardia (bile acids increase the tone of the vagus nerve by reflex). The nervous system is also affected: the patient develops rapid fatigue, general weakness, adynamia, irritability, headache, and insomnia. If it is impossible to remove the cause of impatency of the common bile duct (stones or a tumour) the liver is gradually affected to add symptoms of hepatic insufficiency.

Portal Hypertension

Portal hypertension is characterized by a stable increase in the blood pressure in the portal vein. Portocaval anastomoses are dilated, ascites develops and the spleen increases in size.

Portal hypertension develops due to obstructed blood outflow from the portal vein as a result of its compression from the outside (by a tumour, enlarged lymph nodes of the porta hepatis in cancer metastases, etc.), or by obliteration of part of its intrahepatic branching in chronic affections of the liver parenchyma (in cirrhosis), or due to thrombosis of the portal vein or its branches. Growth and subsequent cicatrization of connective tissue at the site of degraded hepatic cells of a cirrhotic liver cause stenosis or complete obliteration of part of hepatic sinusoids and intrahepatic vessels. An obstacle is thus created to the blood flow which increases portal pressure and interferes with blood outflow from the abdominal viscera. In these conditions, transudation of fluids from the vessels into the abdominal cavity is intensified to account for the development of ascites. Decreased oncotic pressure of plasma is an important factor in the development of ascites associated with liver cirrhosis. The pressure decreases because of upset synthesis of albumins in the liver. Sodium and water retention is also important. It occurs due to hypersecretion of aldosterone by the adrenal glands (secondary aldosteronism) and its inadequate inactivation in the liver. The time of the onset of ascites depends on the degree of development of collateral circulation, i.e. on portocaval anastomoses. For a long time the disturbed portal circulation can be compensated for by delivery of blood into the superior and inferior venae cavae from the portal vein via normally existing anastomoses. But in portal hypertension these anastomoses become highly developed.

There exist three groups of natural portocaval anastomoses: (1) in the zone of haemorrhoidal venous plexus; these are anastomoses between the inferior mesenteric vein (the portal vein system) and haemorrhoidal veins emptying into the inferior vena cava; haemorrhoidal nodes develop in portal hypertension which rupture to cause rectal haemorrhage; (2) anastomoses in the zone of the oesophagogastric plexus: this is a collateral leading through the left gastric vein, the oesophageal plexus, and hemiazygos vein into the superior vena cava. In pronounced portal hypertension, marked varicose nodes are formed in the lower portion of oesophagus whose injury (e.g. by hard food) is responsible for possible haemorrhage in the form of haematemesis (blood vomiting), which is the most serious complication of diseases attended by portal hypertension and which is a frequent cause of death; (3) anastomoses in the system of paraumbilical veins communicating with the veins of the abdominal wall and the diaphragm, carrying blood to the superior and inferior venae cavae. In portal hypertension, varicose veins radiate from the umbilicus to give a peculiar pattern known as the caput medusae.

The degree of increase in the pressure in the portal vein system can be determined by a special needle and a water pressure gauge. The pressure is measured in the spleen (splenometry) or in varicose veins of the oesophagus. In the latter case the needle is introduced through the oesophagoscope. It is believed that pressure in the spleen is the same as in the portal vein trunk. Normally it is 70—150 mm H_2O, while in portal hypertension it rises to 400-600 mm H_2O. Contrast techniques are used to reveal obstruction of the portal vein: these are splenoportography and in rare cases transumbilical portohepatography.

The spleen may be somewhat enlarged in venous congestion associated with portal hypertension.

Treatment. In order to remove portal hypertension, whose first danger are oesophagogastric and haemorrhoidal haemorrhages, the patients are operated on for placing anastomoses between the portal vein system and the inferior vena cava.

Hepatolienal Syndrome

The hepatolienal syndrome is characterized by concurrent enlargement of the liver and the spleen in primary affection of either of these organs. Involvement of both organs in a pathological process (diseases of the liver, blood, certain infections, poisoning) is explained by their richly developed reticulohistiocytic tissue. In certain cases, e.g. in thrombosis of the hepatic veins, simultaneous enlargement of the liver and the spleen is determined

by venous congestion in them. In addition to palpation, scanning can be used to reveal the hepatolienal syndrome.

Considerable enlargement of the spleen is usually attended by its hyperfunction *(hypersplenism),* which is characterized by anaemia, leucopenia, and thrombocytopenia. The latter can cause haemorrhagic complications. These changes are explained by inhibition of the haemopoiesis in the bone marrow due to hyperactivity of the spleen as a result of which destruction of the blood cells in the spleen is intensified, and antierythrocytic, antileucocytic, and antithrombocytic auto-antibodies are formed in the spleen.

Hepatic Insufficiency and Coma

Despite the considerable compensatory capacity of the liver, its grave acute and chronic diseases are attended by deep disorders in its numerous and very important functions due to the marked dystrophy and destruction of the hepatocytes. Clinicists define this condition as the *hepatic insufficiency syndrome.*

Depending on the character and acuity of the affection acute and chronic hepatic insufficiency are distinguished. The following three stages of the disease are also distinguished: (1) early compensated stage; (2) pronounced decompensated; and (3) terminal dystrophic stage that ends in a hepatic coma and death.

Acute hepatic insufficiency arises in grave forms of virus hepatitis (Botkin's disease) and poisoning with hepatotropic substances (affecting the liver in the first instance). These may be chemical substances (e.g. phosphorus compounds, arsenic, large doses of alcohol) or vegetable poisons (inedible mushrooms containing amanitotoxin, helvellic acid, or muscarine extracted of male fern, etc.). Acute hepatic insufficiency develops rapidly, within several days or hours.

Chronic hepatic insufficiency develops in many chronic diseases of the liver, e.g. in cirrhosis and tumours. Its development is slow and gradual.

Development of hepatic insufficiency is underlain by marked dystrophy and necrobiosis of hepatocytes which is attended by a considerable impairment of all liver functions with formation of collaterals between the portal vein system and the venae cavae. Collaterals develop in cases when the blood flow from the portal vein into the liver is obstructed in any affection of this organ. Large amounts of blood containing toxic substances absorbable in the large intestine pass through the collaterals into the greater circulation system to bypass the liver. Hepatic insufficiency is explained by various complicated metabolic disorders in the liver, upset bile secretory and excretory function, and impaired detoxicating function of the liver.

The pathogenesis of hepatic coma is manifested by grave self-poisoning of the body due to almost complete dysfunction of the liver. The body is poisoned by the non-detoxicated products of intestinal (bacterial) protein decomposition, final products of metabolism, and especially ammonia. Normally, the major part of ammonia is captured by the hepatocytes and converted to urea (in the ornithine Kreb's cycle), which is then excreted by the kidneys. Phenols, which are normally detoxicated in the liver by their combination with glucuronic and sulphuric acids, also have a toxic effect. Other toxic substances also accumulate in the blood in the presence of hepatic insufficiency. The electrolyte metabolism becomes upset, and in severe cases, hypokaliaemia and alkalosis develop.

Hepatic insufficiency may be aggravated and coma may be provoked by alcohol, barbiturates, some analgesics (morphine, promedol), protein-rich diet (which intensifies putrefactive processes in the intestine, production of toxic substances and their absorption in the blood), by profuse haemorrhage from the digestive tract (which often aggravates portal cirrhosis of the liver), by large doses of diuretics, instantaneous withdrawal of large amounts of ascitic fluid, severe diarrhoea, and the attending grave infectious diseases.

Clinical signs of hepatic insufficiency usually combine with symptoms of the liver disease that provoked hepatic insufficiency.

The intensification of the symptoms by stages is vividly illustrated by the progressive development of hepatic insufficiency (in patients with liver cirrhosis, tumour of the liver, and other diseases of this organ).

The clinical symptoms are absent during the early stage of hepatic insufficiency, but the body's tolerance to alcohol and also to other toxic substances decreases, and the findings of laboratory load tests change.

During the second stage, clinical signs of hepatic insufficiency develop; first mild but later more pronounced non-motivated fatigue, poor appetite, increased weakness in usual physical exertion, frequent dyspepsia (poor tolerance of fat food, the presence of meteorism, rumbling and pain in the abdomen, changed stools), which are explained by disorders of bile secretion and digestive processes in the intestine. Upset assimilation of vitamins explains polyhypovitaminosis. Fever, which is not infrequent in hepatic insufficiency, can be due to both the main disease and impaired detoxication of some proteinous pyrogens by the liver. Jaundice and hyperbilirubinaemia with accumulation of free (indirect) bilirubin in the blood are frequent in hepatic insufficiency. Deranged structure of the liver and upset cholestasis can stimulate accumulation of bilirubin glucuronide ("direct" bilirubin) in the patient's blood.

Deranged albumin synthesis in the liver and also pronounced hypoalbuminaemia can cause hypoproteinaemic oedema and intensify

ascites, which often occurs in patients with chronic liver affections. Upset synthesis of some blood coagulating factors (fibrinogen, prothrombin, proconvertin) and also decreased blood platelet content (due to hypersplenism that attends many chronic diseases of the liver) provoke the onset of haemorrhagic diathesis (skin haemorrhages, nasal bleeding, haemorrhage in the intestinal tract). Inadequate inactivation of oestrogens by the chronically affected liver provokes endocrine disorders (gynaecomastia in men, menstrual disorders in women, etc.).

Changes in laboratory tests (hepatic tests) are significant in the second stage of hepatic insufficiency. Characteristic is the decreased content of substances produced by the liver: albumin, cholesterol, fibrinogen, etc. Considerable changes in the liver function are also revealed by radioisotope hepatography.

The third, final stage of hepatic insufficiency is characterized by even deeper metabolic disorders and dystrophic changes, which are pronounced not only in the liver but also in other organs. Patients with chronic liver diseases develop cachexia. They also suffer from nervous and psychic disorders which are precursors of coma: decreased mental ability, slow thinking, slight euphoria, sometimes depression, and apathy. The patient becomes easily irritable, his moods are quickly changed, attacks of melancholy and frustration occur at times, and sleep is deranged. Derangement of consciousness and loss of orientation in time and space develop along with partial loss of memory, disordered speech, hallucinations, and somnolence. Specific tremor (slow and fast) of the upper and lower limbs is characteristic.

The precoma period may last from a few hours to several days and even weeks. The patient may recover from this state, but coma develops in most cases.

The clinical picture is characterized first by excitation and then by general inhibition (stupor) and progressive derangement of consciousness (sopor), to its complete loss (coma). The EEG curve is flattened. The reflexes are decreased, but hyper-reflexia and pathological reflexes (sucking and grasping) develop. Motor anxiety, clonic convulsions due to hypokaliaemia, muscular twithching, and tremor of the extremities (arrhythmical and rhythmical twitching of the fingers and toes) are characteristic. Respiration rhythm becomes upset. Kussmaul respiration (less frequently Cheyne-Stokes respiration) develops. Incontinence of faeces and urine ensues. The patient's breath (and also urine and sweat) smells "sweety hepatic" (fetor hepaticus) because of liberation of methyl mercaptan which is formed in deranged methionine metabolism. Inspection of the patient often reveals signs of haemorrhagic diathesis (bleeding gums, nasal and skin haemorrhage). The patient's temperature in the ter-

minal period is subnormal. Jaundice is intensified. The liver may remain enlarged or its size may decrease. Laboratory tests show moderate anaemia, leucocytosis, increased ESR, low counts of platelets and fibrinogen; the prothrombin time increases, hepatic functional tests become sharply upset, and the bilirubin level increases. The content of residual nitrogen and ammonia in the blood serum increases to indicate secondary affections of the kidneys (the hepatorenal syndrome). Hyponatriaemia, hypokaliaemia, and metabolic acidosis develop. Hepatic coma usually terminates fatally. But the patient can in some cases be saved.

Treatment. Intensive therapy is required in acute hepatic insufficiency: infusion of plasma, polyglucin, glutamic acid solution (to bind ammonia), oxygen, correction of water-salt disorders; the life of the patient should be maintained during the critical period (several days) to help the strong regenerative capacity of the liver. In addition to the treatment of the main disease, chronic liver diseases should be treated by removing the aggravating factors (oesophagogastric haemorrhage, attending infections). The diet should be poor in protein in order to suppress the putrefactive processes in the intestine; antibiotics decrease absorption of decomposed proteins. The electrolyte disorders are corrected and haemorrhages are controlled.

Recently methods for transplantation of healthy liver to patients with hepatic insufficiency are being developed.

Special Pathology

The most common affection of the liver is its inflammation. Acute and chronic hepatitis, and also cirrhosis and hepatosis are distinguished. Primary cancer of the liver occurs in rare cases; as a rule malignant tumours metastasize into the liver from other organs. Echinococcus usually localizes in the liver. The liver is also affected in opisthorchiasis and some other parasitary invasions.

Affections of the bile secretion system are quite common. These are cholelithiasis, acute and chronic cholecystitis, cholangitis, dyskinesia of the bile ducts, and primary cancer of the gall bladder.

Chronic Hepatitis

Chronic hepatitis* is a chronic diffuse or focal inflammatory affection of the liver.

Aetiology. The following groups of chronic hepatitides are distinguish-

* Acute hepatitis (virus and toxic) is described in detail in special courses dealing with infectious diseases and occupational pathology.

ed: (1) infectious and parasitogenic; infectious hepatitis develops secondary to virus hepatitis, brucellosis, tuberculosis, syphilis, and some other diseases; (2) toxic hepatitis caused by industrial, medicamentous, domestic and food chronic poisoning by hepatotropic toxic substances (chloroform, trinitrotoluene, aminazine, lead compounds, etc); (3) toxico-allergic hepatitis, which develops not only in response to direct toxic effect of some medicines or hepatotropic chemicals, but also due to hypersensitivity of the liver cells of the entire body to these substances (medicamentous hepatitis, hepatitis associated with collagenosis); (4) metabolic hepatitis, which arises due to metabolic disorders in the liver, associated with protein-vitamin deficiency, and also in fat dystrophy and amyloidosis.

In 40-70 per cent of cases chronic hepatitis develops as an outcome of an acute epidemic or serum hepatitis. Hepatitides are mostly diffuse affections of the liver. Liver affections are focal in tuberculosis (tuberculous granulomas, caseous abscesses or tuberculoma), syphilis (gumma), some protozoal disease (amoebic abscesses), fungal and bacterial affections (usually abscesses), and in some other cases.

Pathogenesis. This is mostly determined by the aetiology of the disease. When exposed chronically to hepatotropic toxic substances, the hepatocytes become progressively affected (to necrobiosis); the secondary inflammatory reaction of the liver mesenchyma is equally important in the pathogenesis of chronic hepatitis. Hepatitis of virus nature is probably associated with persistence of the virus in the liver cells and with the progressive cytopathic effect of this virus, which kills the hepatocytes to cause inflammatory reaction of the connective tissue. In many cases autoimmune processes are of primary importance. They arise in response to the primary affection of the liver tissue by any aetiological factor. Obstructed bile excretion and bile congestion, cholangitis and cholangiolitis (with subsequent extension of inflammation onto the liver tissue), and also some medicamentous poisonings (phenothiazine derivatives) are decisive in the pathogenesis of the so-called cholestatic hepatitis.

Pathological anatomy. Among diffuse inflammatory affections of the liver benign (non-active, persisting), aggressive (recurrent, active), and cholestatic chronic hepatitis are distinguished.

Non-active hepatitis is characterized by inflammation in the periportal zones, preservation of the lobular structure, and sometimes by moderate dystrophic changes in the hepatocytes. The liver is enlarged, the capsule is thickened, and streaks of connective tissue are seen on its surface. The inflammatory and cicatricial processes are more distinct in the liver affected by active hepatitis. Inflammatory infiltration extends from the periportal zones inside the liver lobules whose outlines are indistinct. Hepatocytes are extensively necrotized and have dystrophic changes; fibrosis is found in the liver. The size of the liver increases, its surfaces are coarse and necrotized zones can be seen as red amorphous spots. Cholestatic hepatitis is also characterized by marked affection of bile ducts (cholangitis and cholangiolitis) and signs of cholestasis.

Hepatocellular hepatitis (epithelial and parenchymatous) and mainly mesenchymal hepatitis are also differentiated.

Clinical picture. Chronic hepatitides are characterized by (1) dyspeptic symptoms; (2) jaundice (it may be absent in some cases); (3) moderate enlargement and induration of the liver and the spleen; (4) dysfunction of the liver as determined by laboratory tests and radiohepatography. But the clinical picture and also the course of each clinico-morphological form of hepatitis have their special features.

Chronic benign hepatitis is characterized by obliterated clinical picture. The patients complain of heaviness or dull pain in the right hypochondrium, decreased appetite, bitter taste in the mouth, nausea and eructation. Jaundice is usually absent or it is moderate. Objective studies reveal a mildly enlarged liver with a smooth surface and a moderately firm edge, which is slightly tender to palpation. Enlargement of the spleen is not marked.

Laboratory studies. The blood bilirubin content is usually normal; in the presence of jaundice it increases to about 17-50 μmol/l (1-3 mg/100 ml); the blood globulin content is mildly increased, activity of the enzymes is either normal or only slightly changed; the prothrombin content is normal or slightly decreased; the bromsulphthalein test is slightly positive.

Chronic active (aggressive) hepatitis is characterized by complaints and objective symptoms: weakness, loss of weight, fever, pain in the right hypochondrium, loss of appetite, nausea, regurgitation, meteorism, skin itching, jaundice, and frequent nasal bleeding. The liver is enlarged, firm, with a sharp edge. The spleen is enlarged.

Laboratory tests often reveal anaemia, leucopenia, thrombocytopenia (a sign of hypersplenism), and increased ESR. Functional tests are changed considerably: they show hyperbilirubinaemia, hyperproteinaemia, hypergammaglobulinaemia, positive protein-sedimentation tests, increased activity of transaminase, aldolase, and alkaline phosphotase; decreased activity of cholinesterase. The serum iron content is significantly increased while the prothrombin index is sharply decreased; excretion of bromsulphthalein is delayed.

Puncture biopsy of the liver and (for special indications) laparoscopy establish the special histological and macroscopic changes in the liver characteristic of these forms. These techniques are also used for differentiation of chronic hepatitis from other diseases of the liver (cirrhosis, amyloidosis, etc). It should be noted that histological and histochemical studies of liver bioptates often reveal early morphological changes in the liver which precede the clinical and laboratory signs of chronic hepatitis.

Chronic cholestatic hepatitis is mainly characterized by the cholestatic syndrome: jaundice (subhepatic), severe skin itching, hyperbilirubinaemia,

increased activity of alkaline phosphatase in the blood, and high cholesterol of blood. Persistent subfebrile temperature and regular increase in ESR are also not infrequent.

Course. A benign persistent chronic hepatitis can last to 20 years; exacerbations are rare and arise only in the presence of strong provoking factors. Liver cirrhosis develops in rare cases. Complete clinical recovery is sometimes possible, especially so if the patient is specifically treated. The morphological structure of the liver is restored in such cases.

Aggressive hepatitis is characterized by relapses, whose frequency depends on various factors. Frequent relapses accelerate progressive dystrophic, inflammatory and cicatricial changes in the liver and stimulate development of cirrhosis. Prognosis in this form of hepatitis is bad.

The course and prognosis in cholestatic hepatitis depend on its aetiology and the possibility of removing the obstacle to bile outflow (in compression of the common bile duct by a tumour, cicatricial or inflammatory stenosis, etc.).

Treatment. The cause of chronic hepatitis should be removed in the first instance: complete discontinuation of taking alcohol or exposure to harmful substances, etc.

During exacerbations, the liver should be spared as much as possible, and regeneration of liver cells stimulated (bed rest, diet, parenteral use of vitamins, glucose, etc).

Cirrhosis of the Liver

Cirrhosis of the liver is a chronic progressive disease characterized by increasing hepatic insufficiency in connection with dystrophy of the liver cells, cicatricial cirrhosis, and structural reconstruction of the liver.

Aetiology. Cirrhosis of the liver is a polyaetiological disease. It may develop due to (1) infection (virus of epidemic hepatitis); (2) alcoholism; (3) protein- and vitamin-deficient diet; (4) toxico-allergic factor; (5) cholestasis. Of the mentioned aetiological factors, the leading role in this country belongs to the virus of epidemic hepatitis. Cirrhosis caused by the virus is probably explained by its long persistence in the liver cells.

Chronic alcoholic poisoning is also a very important aetiological factor. It affects absorption of vitamins and proteins in the intestine to provoke cirrhosis of the liver. It also acts directly and specifically on metabolism of the liver cells. The alimentary factor (malnutrition, mainly protein- and vitamin deficit) is a frequent cause of liver cirrhosis in some developing countries. In this country the alimentary factor (malnutrition) is only of endogenous origin: deranged absorption of proteins and vitamins (in grave chronic diseases of the gastro-intestinal tract, in patients with total resec-

tion of the stomach, resection of the intestine, chronic pancreatitis, and in some other cases). Toxic cirrhosis of the liver arises in repeated and chronic exposure to carbon tetrachloride, compounds of phosphorus or arsenic, in food poisoning (inedible mushrooms, seeds of heliotrope). Toxico-allergic cirrhosis of the liver includes also affections connected with hypersensitivity (autoallergy) to various drugs (aminazine, chloroform, some antibiotics, sulpha preparations, etc); hypersensitivity can cause dystrophy and necrosis of the liver parenchyma.

Obturation of intra- and extrahepatic bile ducts and their inflammation cause congestion of bile and cholestasis, and are important factors in the development of biliary cirrhosis.

The aetiological factor does not always determine the way of development of liver cirrhosis. One and the same factor can cause various morphological variants of cirrhosis (portal, postnecrotic, and biliary); at the same time various aetiological factors can cause similar morphological changes.

Pathogenesis. The pathogenesis of liver cirrhosis is closely connected with morphogenesis. The greatest importance in the developmental mechanism of liver cirrhosis belongs to recurrent necrosis of the liver cells which is provoked by aetiological factors and cause collapse of the reticulin framework of the liver, formation of cicatrices, and derangement of circulation in the adjacent portions of the preserved liver parenchyma. Intact hepatocytes or lobe fragments begin their intense regeneration under the effect of growth stimulants supplied from the necrotic focus. The formed large nodes of regenerated tissue compress the surrounding tissue with the invested vessels; the hepatic veins are compressed especially strongly. The blood outflow becomes upset to provoke portal hypertension and formation of anastomoses between the branches of the portal and hepatic veins that facilitate intrahepatic circulation. Blood now bypasses the liver parenchyma to impair drastically its blood supply, to cause new ischaemic necroses, and to stimulate the progress of cirrhosis even in the absence of the primary aetiological factor. Collagenous connective tissue grows intensively: connective tissue partitions (septa) grow into the parenchyma from the periportal fields to cause fragmentation of the liver lobules. These false lobules can later become the source of nodular regeneration. Chronic direct exposure to certain toxic hepatotropic substances, and also autoimmune and some other mechanisms are important in the pathogenesis of certain forms of cirrhosis.

Pathological anatomy. Three main morphological variants of liver cirrhosis are distinguished: portal (septal), postnecrotic, and biliary.

Portal (septal) cirrhosis of the liver is usually the result of alimentary insufficiency and alcoholism; less frequently it is secondary to Botkin's disease (virus hepatitis). Its develop-

ment is underlain by formation of connective-tissue septa interconnecting periportal fields with the central zone of the lobule and causing its fragmentation. Macroscopically the liver may be enlarged or diminished. Small nodes of regenerated tissue, circumscribed by narrow septa of connective tissue, are distributed uniformly over the entire surface of the liver. The nodes are almost equal in size. The microscopic picture: marked fatty infiltration of the liver cells is observed in alimentary or alcoholic cirrhosis; these changes may be absent in cirrhosis that develops after virus hepatitis. "False bile ductules", leucocyte infiltration, and compressed small veins are found in the stroma between the nodes of regenerated tissue.

Postnecrotic cirrhosis of the liver develops as a result of submassive and massive necrosis of the liver cells due to virus and (less frequently) toxic hepatitis. Macroscopic picture is characterized by irregular changes in the liver, which is usually diminished in size. Nodes of various form and size can be seen on the liver surface. Microscopy shows irregular nodes of regenerated tissue and intact portions of the parenchyma. Broad fields of collapsed collagenized stroma with closely running portal tracts, venules, and cell infiltrates can be found between the nodes of the regenerated tissue. Inflammatory infiltration is marked.

Biliary cirrhosis of the liver has two variants. Primary biliary cirrhosis (pericholangiolitic) arises after epidemic hepatitis or toxico-allergic action of some medicinal preparations. Its development is underlain by obstruction of fine intrahepatic bile ductules which accounts for bile congestion. Macroscopy: the liver is enlarged and consolidated and is dark-green or olive in colour; it is microgranular. Extrahepatic bile ducts are patent. Microscopy is characterized by the presence of intralobular and periportal cholestases. The periportal fields are broad, with fibrosis around proliferating cholangioles; intralobular fibrosis develops around intralobular cholangioles with dissociation of the liver cells and their groups. Secondary biliary cirrhosis arises as a result of prolonged obstruction of extrahepatic bile ducts by stones, tumour, etc. It provokes dilation of the bile ducts, development of cholangitis, and pericholangitis; cirrhosis of the liver develops if these changes progress.

In addition to the described variants of cirrhosis, they may also be mixed: morphological signs of other variants may join the main variant. Activity of cirrhosis is characterized by the presence of new dystrophic and regenerative processes in the parenchyma, intense inflammatory infiltrations in the stroma, proliferation of cholangioles, indistinct borders between nodular parenchyma and internodular stroma. A neglected cirrhotic process is characterized by replacement of liver tissue by nodes of regenerated tissue, markedly pronounced portal hypertension, large quantity of vascular connective-tissue septa growing into the parenchyma (portohepatic anastomoses). According to the morphological picture, fine- and large-nodular cirrhosis is distinguished. Mixed variants also occur.

Clinical picture. Portal cirrhosis of the liver occurs mostly between the ages of 40 and 60. The incidence in men is twice higher than in women. Postnecrotic and biliary cirrhosis of the liver develop in younger patients, mostly in women.

Clinical manifestations of liver cirrhosis depend on the degree of affection of the liver cells and the associated hepatic dysfunction and portal hypertension, on the stage of the disease (compensated or decompensated), and also on the activity of the process. The following symptoms of the disease are most characteristic of the majority of patients with various forms of liver cirrhosis.

Pain in the region of the liver, in the epigastrium, or diffuse pain in the whole abdomen is usually dull and boring, intensifying after meals,

especially after fatty food, ample drinking and physical exercise. Pain is usually associated with enlargement of the liver and distension of the capsule, or with necrotic foci located near the capsule, with perihepatic symptoms, and also concurrent inflammatory affections of the bile ducts.

Dyspepsia in the form of decreased appetite to complete anorexia, the feeling of heaviness in the epigastrium after meals, nausea, vomiting, meteorism and dyspeptic stools (especially after fatty meals) depend mainly on deranged secretion of bile and hence defective digestion. But they can also be associated with the attending dyskinesia of the bile ducts or alcoholic gastroenteritis.

Decreased work capacity, general weakness, fatigue and insomnia are often observed in cirrhosis of the liver. Fever is usually irregular and sometimes of the undulant type. It often attends postnecrotic cirrhosis of the liver and is explained by necrotic destruction of the liver cells. Marked fever is characteristic of the active period and infectious cirrhosis.

A haemorrhagic syndrome is observed in 50 per cent of patients with cirrhosis of the liver. Profuse bleeding from varicose veins of the oesophagus and the stomach can often be early signs of portal cirrhosis; they are caused by increased pressure in the veins of the oesophagus and the stomach. In other variants of cirrhosis nasal, gum, uterine and skin haemorrhages develop in marked decompensation. They depend on the decreased coagulability of blood due to liver dysfunction.

Signs of cirrhosis are as follows. Cachexia is especially characteristic of patients with portal cirrhosis of the liver. In long-standing disease the subcutaneous fat disappears along with atrophy of muscles, especially of the upper shoulder girdle. The appearance of such patients is quite specific: the face is very thin with grey or subicteric skin; the lips and the tongue are bright-red; the cheek bone region is affected by erythema; the extremities are thin and the abdomen is large (due to ascites, enlarged liver and spleen); the subcutaneous veins of the abdominal wall are dilated, the legs are oedematous. Malnutrition is usually associated with disordered digestion and assimilation of food, and impaired synthesis of proteins in the affected liver.

Jaundice (except the cases with biliary cirrhosis) is a sign of hepatocellular insufficiency associated with necrosis of the liver cells. The affected hepatocytes partly lose their capacity to capture bilirubin from blood and to bind it with glucuronic acid. Bilirubin excretion into bile is disordered as well. Free (indirect) and bound (direct) bilirubin of blood serum therefore also increases. Jaundice is usually characterized by partial decolouration of faeces and by the presence of bile in the duodenal contents. Jaundice is often attended by skin itching. Jaundice associated with biliary cirrhosis resembles obstructive jaundice; severe skin itching is

observed. The intensity of jaundice varies from light subicteric to marked jaundice (depending on the degree of obstruction of the bile ducts). In prolonged obstruction of the extrahepatic duct the skin acquires a greenish tint which depends on oxidation of bilirubin to biliverdin. Moreover, brown pigmentation of the skin may also be observed. It depends on accumulation of melanin.

"Minor" signs of cirrhosis can also be revealed during examination of the patient. These signs are as follows: (1) spider angiomata (they may develop years before marked symptoms of the disease develop); their number increases and the colour intensifies during exacerbation of the disease; (2) erythema of the palms; (3) red lustrous lips, scarlet mucosa of the mouth, scarlet (lacquered) tongue; (4) gynaecomastia (increased mammary glands) and other female sex characters developing in men (decreasing growth of hair on the face, chest, abdomen, and the head); (5) xanthomatous plaques on the skin (observed in patients with biliary cirrhosis of the liver); (6) Hippocrates fingers with hyperaemic skin at the nail beds. Inspection of the abdominal skin can reveal dilation of the veins that can be seen through the thinned skin of the abdominal wall (caput medusae). Collateral venous system can be seen on the chest as well. Haemorrhoidal veins are often dilated.

Ascites is the most characteristic sign of portal cirrhosis. Ascites may develop slowly and the abdomen grow to huge size; the patient develops dyspnoea. Oedema may develop; hydrothorax may also occur in some cases. In other variants of cirrhosis, ascites develops at later stages of the disease.

Enlarged liver can be palpated in 50-75 per cent of patients with cirrhosis. The enlargement can be insignificant, only determinable by percussion, or considerable when the liver occupies the entire left part of the abdominal cavity. The liver is firm, the surface is sometimes irregular, and the lower edge sharp. Enlargement of the spleen is often attended by its increased activity (hypersplenism).

Laboratory findings. An active cirrhotic process is characterized by anaemia, leucopenia, thrombocytopenia, and increased ESR. Anaemia can be due to hypersplenism and gastro-intestinal haemorrhage, hepatocellular insufficiency, and often increased haemolysis, which is accompanied by reticulocytosis of the peripheral blood.

The blood serum bilirubin content becomes considerable only in the final stage of the disease. At the same time, the affection of the excretory function of the cirrhotic liver can be assessed by the presence of the conjugated fraction of bilirubin (bound bilirubin). Its content increases in normal and increased total bilirubin. The free bilirubin content increases in the blood serum as a result of upset conjugation of bilirubin in the liver cell

and haemolysis. The blood serum bilirubin content varies in biliary cirrhosis of the liver from 26 to 340 μmol/l (1.5-20 mg/100 ml), mostly at the expense of bound bilirubin.

The presence of much urobilin in the urine indicates liver insufficiency. The amount of urobilin in the urine and stercobilin in the faeces decreases in the presence of pronounced jaundice when a small amount of bilirubin enters the intestine. Bilirubin is found in the urine of patients with jaundice.

The upset excretory function of the liver is manifested by retention of bromsulphthalein in the blood (during its intravenous administration) and also by radioisotopic hepatography and scanning of the liver.

Affection of liver cells is manifested by characteristic changes in the protein indices: decreased concentration of serum albumins and hypergammaglobulinaemia which in turn decreases the albumin-globulin coefficient. Activation of the inflammatory process in the liver involves an increase in the α_2-globulins, while jaundice causes an increase in β-globulins. During remissions, all these changes become less pronounced. The blood level of lipids and cholesterol also increases considerably in the presence of biliary cirrhosis. A sensitive index of liver dysfunction is the decreased activity of cholinesterase. Transaminase activity increases in exacerbation of liver cirrhosis. Activity of alkaline phosphatase also increases in biliary cirrhosis.

The decreased prothrombin content (which is synthesized by the liver cells), increased antithrombin coagulative activity and decreased total coagulative activity of plasma are important in the aetiology of haemorrhagic diathesis in liver cirrhosis.

Laparoscopy and especially biopsy of the liver help reveal intravital morphological signs of each variant of liver cirrhosis. Varicose veins of the oesophagus are revealed by X-rays.

It is not always possible to differentiate between all variants of liver cirrhosis from the data of clinical and instrumental methods of examination, nevertheless, by comparing the mentioned signs, one can notice that the symptoms of portal hypertension in *portal cirrhosis of the liver* are often revealed long before the functional insufficiency develops. Hepatic insufficiency only develops at a later stage of the disease. But in the presence of *postnecrotic cirrhosis of the liver,* the symptoms of hepatic insufficiency develop early. They largely determine the entire clinical picture of the disease. Chronic jaundice (obstructive type) prevails in the clinical picture of biliary cirrhosis along with satisfactory general condition of the patient, who suffers from skin itching, sometimes fever (associated with chills); the blood alkaline phosphatase and cholesterol content increases. Transcutaneous cholangiography is used to determine the cause of cholestasis. The procedure is done when indicated.

Complaints of patients with *compensated liver cirrhosis* are not serious. The disease is often revealed accidentally during examination (enlarged liver and spleen). Remissions may be long (measured by years). *Decompensated active cirrhosis* is characterized by marked symptoms of the disease and rapid progressive course.

Course. The course of the disease is usually progressive. The overall term of the disease is usually 3 to 5 years; in rare cases the disease may last 10 years and even longer (usually in biliary cirrhosis of the liver).

The terminal period of the disease, irrespective of the form of cirrhosis, is characterized by gastro-intestinal haemorrhage and progressive signs of functional insufficiency of the liver, with finally developing coma. These are two most frequent direct causes of death of patients with liver cirrhosis. Gastro-intestinal haemorrhage (blood vomiting and melaena) is caused by the rupture of varicose nodes in the lower third of the oesophagus or, less frequently, in the stomach. A direct cause of varicose haemorrhage is physical strain or local affection of the mucosa (e.g. by coarse food). Profuse haemorrhage (if it does not cause death) can cause anaemia with subsequent impairment of the function of the liver cells and accelerated development of hepatic coma.

Treatment. Cirrhosis of the liver in the compensation stage is treated by preventing its further affection with alcohol, toxic substances, etc., and also by rational organization of work regimen and nutrition (high-calorie diet rich in protein and vitamins). During decompensation stage, hospital treatment is required. Glucocorticosteroid hormones are given in the active process (except cases complicated by dilation of the oesophageal veins); syrepar (hydrolysate of cattle liver), essential (a complex preparation containing essential phospholipids), and vitamins are also prescribed. Patients with ascites are prescribed a diet restricted in salt and diuretics (periodically). If ascites cannot be cured by diuretics, the fluid is released by paracentesis.

In order to decrease the lipid content of the serum in primary biliary cirrhosis, lipoic acid preparations are prescribed. Skin itching is removed by cholestyramine (preparation binding fatty acids). Surgical treatment is indicated in cases with secondary biliary cirrhosis of the liver, e.g. in obstruction of the bile duct by a stone.

Cholelithiasis

Cholelithiasis is characterized by formation of stones in the gall bladder or, less frequently, in the bile ducts. The incidence of the disease is rather high. According to the data of postmortem examination, stones are found in the gall bladder of every tenth patient who dies from various causes. At

the same time, clinical signs of cholelithiasis are only found in 10 per cent of carriers of stones, mainly in women aged 30—55.

Aetiology and pathogenesis. The disease is underlain by general metabolic disorders which provoke formation of stones. Infection and bile congestion are also important. Upset cholesterol metabolism with hypercholesterolemia attended by the increased bile cholesterol content is decisive because most stones contain cholesterol. This is also confirmed by the fact that cholelithiasis often concurs with atherosclerosis, diabetes mellitus, obesity, and other conditions attended by hypercholesterolaemia. Frequent formation of pigmented stones in the presence of excess bilirubin in bile in haemolytic anaemia (haemolytic jaundice) is explained in a similar way. At the same time, blood cholesterol is not increased in all patients with cholelithiasis. There is no parallelism between cholesterol level of bile and blood.

The main components of stones are cholesterol, bilirubin, and calcium. These are contained in bile in the form of unstable colloidal solutions. Cholesterol is retained in bile mainly by bile acids. When cholate level in the bile decreases, cholesterol precipitates as crystals. The ratio between salts of bile acids (cholates) and cholesterol in normal bile is 15:1; in cholelithiasis this ratio decreases to 6:1. Disorders in the physico-chemical composition of bile are believed to be decisive for stone formation. Hepatocyte dysfunction decreases the formation of bile acids which may be the cause of dyscholia.

The importance of the infectious factor consists in that protein-rich exudate of inflamed gall bladder upsets the normal colloidal and chemical composition of bile to precipitate bilirubin, cholesterol and calcium, and to cause formation of mixed stones typical for infectious diseases of the gall bladder.

Bile congestion in the gall bladder provides conditions for stone formation because it promotes concentration of bile and stimulates an increase (10-12 times) in cholesterol concentration in the bile, while gradual absorption of bile acids decreases their content in the bile. Moreover, bile congestion can provide favourable conditions for development of infection. Disordered neurohumoral regulation of contractility of the gall bladder and bile ducts (dyskinesia), as well as the anatomical changes in the bile passages (bends, adhesions, scars), are essential factors provoking bile congestion. Factors interfering with normal emptying of the gall bladder are also important: increased intra-abdominal pressure (e.g. during pregnancy), ptosis of the internal organs, persistent constipations, hypodynamia, and rare meals are among these factors.

Hereditary predisposition is also very important. Stones often occur in several generations of one family (especially among women). Excessive

food rich in fats and calories causes hypercholesterolaemia and stimulates formation of gall stones.

Pathological anatomy. There exist three major groups of gall stones. Purely cholesterol stones are white or yellowish concretions which are found in the gall bladder. They usually develop as single round or oval concretions. The stones are light (float on the surface of water) and burn with a bright flame. The section of a stone shows its radial structure (crystals of cholesterol). Pigment stones consist of bilirubin and calcium. Their shapes vary. Usually pigment stones are small and multiple. Their colour is black with a greenish tint; the stones are dense but brittle. Stones consisting of only calcium carbonate rarely occur. Mixed stones consisting of cholesterol, calcium, and pigment occur most frequently. They are heavier than water and burn with difficulty. A section reveals laminar structure. The shape and size of mixed stones vary but they are usually small and multiple. If stones are tightly packed in the gall bladder, their surfaces become facetted (from mutual pressure).

The mucosa of the gall bladder can be affected with inflammation in the presence of stones (see "Cholecystitis"). Prolonged presence of stones in a non-inflamed gall bladder can cause atrophy and sclerosis of the bladder wall or (in very rare cases) decubitus and perforation of its walls.

Clinical picture. Pain attacks in the right hypochondrium (the so-called biliary colic) are the most characteristic symptom of cholelithiasis. Colics are usually provoked by small stones as they move in the region of the neck of the gall bladder, its isthmus, or directly in the cystic duct. Pain is caused by spastic contractions of the gall bladder and the ducts which develop as a result of a sudden distension of the gall bladder and increased pressure inside it due to a mechanical obstruction to bile outflow. The pain develops also by the reflex mechanism, as a response to irritation of the cystic duct receptors by stones. A gall-bladder colic can be provoked by physical or nervous strain, jolting motion, ingestion of much fat, etc.

A gall-stone colic develops suddenly. The pain is first diffuse and is felt in the entire right hypochondrium. Later it localizes in the region of the gall bladder or in the epigastrium. Pain is piercing and so severe that cannot be tolerated without pain-relieving preparations. The patient groans and tosses in bed vainly seeking for a convenient posture. The pain can specifically radiate upwards, to the right posteriorly, to the right shoulder, neck, the jaw, and into the right subscapular region. Pain can radiate also into the heart to provoke an attack of angina pectoris.

Pain can continue from several minutes to a few hours and even days, periodically subsiding and strengthening. Intensified contractions of the gall bladder promote further propulsion of the stone (not more than 1.5 cm in diameter) from the neck or the cystic duct into the common bile duct. Sometimes, after relaxation of the spasm the stone may return back to the "silent" zone (the fundus of the gall bladder). In both cases, the pain attack discontinues as suddenly as it begins. The patient's condition rapidly improves. The attack can often be alleviated by applying warmth or giving

spasmolytics (atropine sulphate, 16 ml of a 0.1 per cent solution, or papaverine hydrochloride, 2 ml of a 2 per cent solution subcutaneously). This is a valuable differential-diagnostic sign: these remedies fail to relieve pain in acute cholecystitis, while warmth (e.g. a hot-water bottle) is contraindicated because warmth intensifies blood inflow and the inflammatory process.

If the colic is long-standing, jaundice may develop at the end due to a spasm of the common bile duct. The jaundice usually is not intense and is only transient (2 to 3 days).

Gall-stone colic is usually attended by nausea and recurrent vomiting. The reflex mechanism explains the fever which often attends the pain attack. The fever ends with the attack. If fever persists, it indicates its connection with inflammatory complication of cholelithiasis. This is confirmed by an increase in leucocytosis, ESR, and a sharp deterioration of the patient's general condition.

The patient may sometimes be obese, with xanthomatous plaques (cholesterol deposits) on the upper eyelids (less frequently on the other parts of the skin). The abdomen is distended; surface palpation reveals tension of the anterior abdominal wall, especially in the region of the right hypochondrium, and also excessive tenderness of this region. As pain is abated, the muscular tension subsides, and the tender edge of the liver can then be palpated. The gall bladder can sometimes be palpated as an oval or pear-shaped elastic body.

Tender points and sites of hyperaesthesia can sometimes be determined on the body according to Zakharyin and Head (Fig. 100). These are as follows: (1) the region of the gall bladder (its projection on the skin); (2) epigastrium; (3) pancreato-biliary-cystic point; (4) shoulder zone; (5) point of the scapular angle; (6) paravertebral points to the right of the 8th to 11th thoracic vertebra; (7) phrenic nerve site (tender to pressure in the region between the anterior heads of the right sternocleidomastoid muscle (phrenic symptom, or de Mussy-Georgievski symptom).

Some laboratory and instrumental studies reveal signs of cholelithiasis in the full absence of its symptoms. Blood test shows an increased cholesterol content. Duodenal probing (carried out in remission) can sometimes reveal fine stones (microliths) and a large quantity of cholesterol crystals. The most important diagnostic technique in cholelithiasis is contrast roentgenography (cholecysto- or cholangiography and echography studies). These techniques help reveal stones in the gall bladder and the bile ducts.

Course and complications. The course of cholelithiasis is quite varied. Non-complicated cholelithiasis can manifest itself by only one attack of gall-stone colic. The attacks however are usually recurrent. They follow

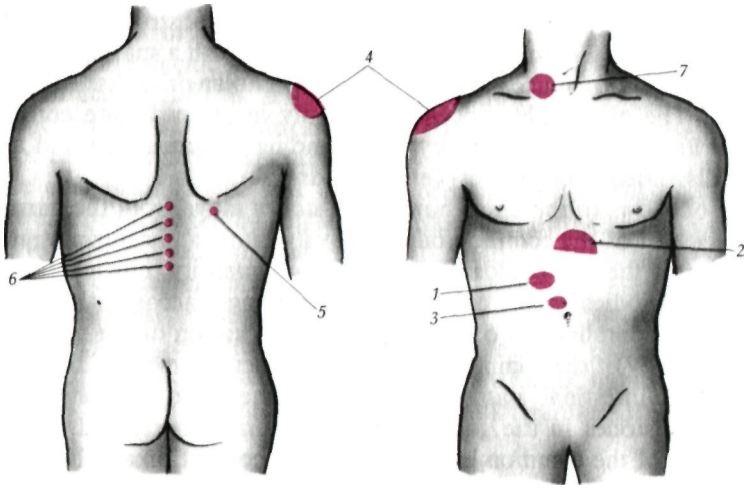


Fig. 100. Points and zones of pain in cholelithiasis.

one another at short intervals or can occur once in 1 or 2 years, and even less frequently. Rare cases are known when the patient recovers spontaneously with the discharge of a small stone into the intestinal lumen. Long-standing cholelithiasis is usually attended by infection. The main disease is then aggravated by symptoms of cholecystitis or cholangitis.

Obstruction of the gall-bladder neck is a complication of the disease. It can cause hydrops. Obstruction is manifested by a most severe pain attack. Following several weeks, an enlarged gall bladder can be palpated. It is elastic and painless. In the absence of gall-bladder adhesion to the neighbouring organs (due to pericholecystitis) the bladder can easily be displaced together with the liver during deep respiration and by palpation.

In hydrops, the gall bladder is filled with a yellowish or colourless fluid (white bile) which is formed due to absorption of bile elements in the gall-bladder walls and effusion of serous exudate from the gall-bladder mucosa. If an infection joins, empyema of the gall bladder develops and the patient's condition is sharply deteriorated. The patient feels chills; the body temperature is high; pain in the right hypochondrium develops again. Neutrophilic leucocytosis and increased ESR are characteristic. If the gall-bladder entrance is fully obstructed by a stone, the bladder may become gradually affected by cirrhosis and its walls become sclerosed.

The common bile duct may be obstructed by a stone that passes from the gall bladder. As a rule, the stone is retained at the sphincter of the hepatopancreatic ampulla. Soon after the pain subsides, signs of obstruc-

tive jaundice develop. The common bile duct is obstructed completely when a mechanical closure (by a stone) combines with a spasm and inflammatory oedema of mucosa of the bile duct (cholangitis) that hinder bile outflow. The gall bladder does not usually increase despite congestion because its walls are affected by the attending inflammation and are no longer distended (Courvoisier-Terrier syndrome).

Bile outflows to the duodenum when stones move from the narrow to the wider part of the common bile duct (valve stones), or during transient relaxation of the gall-bladder walls. Jaundice intensity thus increases and decreases periodically; the colour of faeces changes accordingly.

Another complication of the disease is perforation of the gall bladder (less frequently of the common bile duct) with development of the outer or inner vesico-intestinal passages and sometimes bile peritonitis. Long presence of stones in the gall bladder can cause cancer, and prolonged obstruction of the common bile duct with bile congestion and infection of the bile ducts often provoke biliary (cholestatic) cirrhosis of the liver.

Treatment. Conservative treatment provides better outflow of bile and decreases the tendency to further formation of stones. The patient is recommended to lead a more active life, and prescribed frequent meals with restricted intake of cholesterol-containing foods, mineral water, and cholagogues. Various antispastic and pain removing preparations are prescribed (atropine, papaverin, warmth, etc).

Surgical treatment of cholelithiasis is indicated in the presence of hydrops or empyema of the gall bladder, obturation of the common bile duct with obstructive jaundice, perforation of the gall bladder with development of fistulae or bile peritonitis, or in the presence of frequent attacks of gall-stone colics that fail to be removed by conservative treatment.

Prophylaxis consists in removal of metabolic disorders and causes of bile congestion. The patient is recommended regular meals, exercises, active mode of life, rational diet, and measures to prevent constipation.

Cholecystitis

Cholecystitis is the inflammation of the gall bladder. The incidence of the disease is rather high; women are mostly affected.

Aetiology and pathogenesis. Various infections, autolytic affections of the gall-bladder mucosa associated with regurgitation of pancreatic juice into the gall bladder, and helminthic invasions are important factors provoking cholecystitis. Virus aetiology of cholecystitis has been recently proved (Botkin's disease virus). Cholecystitis of toxic and allergic nature also occur. The aetiological role of infection in development of cholecystitis is confirmed by bacteriological studies of microbial flora of B bile obtained

during operation or by duodenal probing. Infection may enter the gall bladder by enterogenic (from the intestine), haematogenic (from remote foci of infection such as affected tonsils, carious teeth, etc.) and lymphogenic routes. The aetiological importance of lamblia in the development of cholecystitis is disputable.

Bile congestion in the gall bladder predisposes to cholecystitis. The disease can be provoked by gall stones, dyskinesia of the bile ducts (under the effect of various psychoemotional factors, endocrine disorders, dysfunction of the vegetative nervous system, numerous nerve reflexes of the pathologically changed organs of the digestive system, etc.), anatomical properties of the gall bladder and bile ducts, ptosis of the internal organs, pregnancy, inactive mode of life, rare meals, habitual constipation, etc. Acute and chronic cholecystites are differentiated.

ACUTE CHOLECYSTITIS

Pathological anatomy. Acute catarrhal cholecystitis is characterized by a mildly enlarged gall bladder containing serous or seropurulent exudate. The mucosa is swollen and plethoric. The inflammation affects the submucous layer as well (it is infiltrated by leucocytes). In purulent forms of cholecystitis, the lumen of the gall bladder is filled with purulent exudate; its walls are richly and diffusely infiltrated by leucocytes. The mucosa is oedematous, hyperaemic; erosion is frequent; deep ulcers or necrotic affection of the entire depth of the bladder wall occur in graver cases, gangrenous cholecystitis (gangrene of the gall bladder).

Clinical picture. Acute cholecystitis begins vigorously: sharp pain arises in the left hypochondrium which involves the entire upper abdomen and radiates into the right side of the chest, the neck, and sometimes into the heart. Pain may resemble biliary colic, but it is less intense. Pain continues for a few days; if not treated, it may continue for longer time. Pain is often attended by nausea and vomiting with a small amount of bile. Pain arises as a result of inflammation of the wall and serous coat of the gall bladder and distension of the overlying peritoneum. The temperature rises to 38 and even 40 °C and the patient feels chilly. Sometimes a mild jaundice develops due to inflammatory oedema of the mucosa of the common bile duct and obstructed bile outflow. The tongue is dry and white-coated. The abdomen is distended, the movements of the anterior wall are limited, or the wall is not involved in the respiratory act at all.

Surface palpation first reveals local and then diffuse tension in the abdominal wall and sharp tenderness in the right hypochondrium. Acute cholecystitis is also characterized by some other symptoms: Zakharyin's symptom (sharp pain in the region of the gall bladder when it is tapped or pressed), Vasilenko's symptom (sharp pain in the region of the gall bladder when it is tapped over at the height of inspiration), Obraztsov-Murphy

symptom (sharp pain in the right hypochondrium when the examiner's hands press the gall bladder at the height of inspiration), Ortner's symptom (pain during tapping over the right costal arch by the edge of the hand). If inflammation extends onto the peritoneum overlying the gall bladder, Shchetkin-Blumberg symptom is positive. In this case, in the presence of gangrenous cholecystitis (gangrene of the gall bladder) and possible perforation of the gall-bladder wall, a dangerous sign appears, i.e. the peritoneum friction sound at the point of its projection onto the abdominal wall. In moderate tension of the abdominal muscles it is sometimes possible (especially in purulent cholecystitis) to palpate an enlarged and very tender gall bladder. The liver does not usually increase, but its tender edge can sometimes be palpated. The de Mussy-Georgievsky symptom (tenderness at the point of the phrenic nerve, between the heads of the sternocleidomastoid muscle) can often be positive. Zones of skin hyperaesthesia (Zakharyin-Head symptom) can be found below the inferior angle of the right scapula and in the region of the 9th—11th interspaces. Leucocytosis is shifted to the left and the ESR increases.

Duodenal probing (that can only be done during abatement of the process) often fails to obtain B bile; or a cloudy whitish exudate poor in bilirubin can only be obtained. Bile samples contain much leucocytes, mucus, and cells of desquamated epithelium. The corresponding flora can be revealed in bile cultures.

Course. Patients with catarrhal cholecystitis recover comparatively soon. But the disease may convert into the chronic form. Acute purulent cholecystitis has a graver course, with signs of toxicosis, peritoneal irritation, high neutrophilic leucocytosis and considerably increased ESR. Signs of general toxicosis are more vivid in gangrene of the gall bladder, while in its perforation the symptoms of peritonitis join the picture.

Treatment. The patient must be admitted to hospital. Extirpation of the gall bladder is indicated in purulent and gangrenous forms of acute cholecystitis. Strict bed rest and abstention from taking food during the first two days following the attack are prescribed to patients with catarrhal cholecystitis. Later food should be given in small portions, 5-6 times a day, according to Pevzner. Broad-spectrum antibiotics (oletetrin, 100 mg, 2-'3 times a day intramuscularly, during 5-7 days) and spasmolytics (papaverine hydrochloride, 2 ml of a 2 per cent solution, 3 times a day subcutaneously) should be given.

CHRONIC CHOLECYSTITIS

Chronic cholecystitis may develop after acute cholecystitis but in most cases it develops gradually as an independent disease.

Pathological anatomy. The inflammatory process affects all layers of the gall-bladder wall in chronic cholecystitis. The bladder wall gradually scleroses, grows thicker, and calcium is deposited in the tissue. The gall bladder diminishes in size and adheres to the neighbouring organs. The adhesions deform the bladder to interfere with its normal function and to provide conditions for inflammation with periodic exacerbations.

Clinical picture. The patient complains of dull boring pain in the right hypochondrium which usually develops 1-3 hours after taking abundant (especially fat and roasted) food. The pain radiates upward to the region of the right shoulder, neck and the scapula. If cholecystitis concurs with cholelithiasis, sharp pain may arise (like in biliary colic). Dyspeptic signs are also present: bitter and metallic taste in the mouth, eructation, nausea, abdominal flatulence, and alternation of diarrhoea with constipation. The disease is sometimes not attended by pain except that the patient feels heaviness in the epigastrium or right hypochondrium, and dyspepsia develops. The temperature is often subfebrile.

The appearance of the patient and his nutrition are usually normal. Moderate obesity is sometimes observed. Examination of the abdomen can reveal its flatulence (either uniform or predominantly in the upper portion).

Surface palpation of the abdomen reveals sensitivity and sometimes pronounced tenderness in the region of gall-bladder projection. Muscular resistance of the abdominal wall is usually absent. De Mussy-Georgievsky, Ortner's, Obraztsov-Murphy, and Vasilenko's symptoms are positive. The liver is usually of normal size but in the presence of complications, such as hepatitis or cholangitis, the liver may be slightly enlarged with firm and tender (to palpation) edge. The gall bladder is impalpable.

The blood changes (during exacerbation) are characterized by moderate leucocytosis and mildly increased ESR.

Signs of inflammation (mucus, leucocytes, desquamated epithelium) can be found in B bile. If inflammation involves bile ducts (cholangitis), C bile contains the same signs of inflammation. The vesical reflex (B bile) is sometimes impossible to obtain even by repeated probing. This indicates disordered contractility of the gall bladder which is typical of chronic cholecystitis. Bacteriological studies of B bile reveal the character of microbial flora. Polarographic study of bile can reveal signs of inflammation.

Cholecystography shows changes in the configuration of the gall bladder and the absence of its distinct contours. This indicates upset concentrating capacity of the gall-bladder mucosa. After taking a stimulating meal the gall bladder contracts insufficiently.

Course. The course of the disease is characterized by alternation of exacerbations and remissions. The disease can be exacerbated by abuse of

fatty or fried foods, smoked meat and fish, condiments, alcoholic drinks, etc., by acute intestinal infections, and other factors. The process continues for many years and even decades. Cholecystitis is often complicated by inflammation of the bile ducts (cholangitis) or of the pancreas (pancreatitis).

Treatment. Patients with exacerbated chronic cholecystitis must be treated in in-patient conditions (like in acute cholecystitis). In interparoxysmal period, treatment should be given 1-2 times a year in anti-relapse courses: periodic duodenal probing or giving cholagogues in 3-4 week courses (e.g. allochol per os, 1—2 tablets 3 times a day after meals, cholagogic species in the form of infusions, 10—20:200 ml, half-glass 3 times a day, 30 minutes before meals). Sanatorium and health-resort therapy is also indicated.

Prophylaxis. The disease and recurrent exacerbations should be prevented by taking measures to control bile congestion (exercises, walks and trips, regular and frequent meals with certain restriction) and treat focal infections.

PANCREAS

Methods of Examination

Inquiry

Pain, dyspepsia, jaundice, general weakness and wasting are the main complaints of patients with diseases of the pancreas.

Pain may vary in intensity and character. Attacks of paroxysmal pain, like in biliary colic, arising 3-4 hours after meals (especially after taking fatty food) are characteristic of calcareous pancreatitis. Pain is usually localized in the epigastrium or left hypochondrium to radiate into the back. Pain is sometimes so severe that can only be removed by spasmolytics or even narcotics.

Pain is especially severe in acute pancreatitis. It develops suddenly and persists for a few hours or days and even weeks. The pain is usually localized in the upper abdomen and is often girdling in character. Severe pain and its vigorous onset in acute pancreatitis are explained by a sudden obstruction of the main pancreatic duct as a result of spasm and inflammatory oedema with subsequent sharp increase in pressure in small pancreatic ductules and irritation of the solar plexus.

Pain is very severe and prolonged in tumours of the pancreas. If the head of the pancreas is affected, pain is localized in the right hypochon-

drium and radiates into the back. If the tumour extends onto the body and tail of the pancreas, pain is felt in the entire epigastrium, left hypochondrium, and its character may be girdling. Pain is intensified when the patient is in the recumbent position because the tumour presses on the solar plexus. The patient would therefore assume a forced (half-bent) posture to lessen the pain. Boring pain is characteristic of chronic pancreatitis, although this form of the disease may be attended by severe pain as well.

Nausea and vomiting more frequently attend acute pancreatitis and are of reflex character. Chronic pancreatitis and tumour of the pancreas are characterized by *dyspepsia* which is due to upset enzymatic activity of the pancreas. Patients with chronic pancreatitis often complain of poor appetite, aversion to fatty foods, nausea, meteorism, diarrhoea with ample liquid lustrous (fatty) and fetid faeces. Upset intestinal digestion causes rapid *cachexia* and general weakness.

Cancer of the head of the pancreas is characterized by the following symptoms*: jaundice* is of the obstructive type, progressive; the skin is dark-brown (with a greenish hue); there are severe itching, and haemorrhages. The tumour presses the terminal portion of the common bile duct to obstruct bile outflow. Jaundice may develop in sclerosis of the head of the pancreas as well. This is the result of chronic pancreatitis.

Anamnesis. It is necessary to pay attention to certain factors that may stimulate the development of inflammatory diseases of the pancreas. Abuse of alcohol and fatty food, as well as a long-standing cholecystitis are among the predisposing factors.

Physical Examination

INSPECTION

The general inspection of the patient may reveal general cachexia and jaundice with skin scratches and haemorrhages into the skin that attend cancer of the pancreas. Acute pancreatitis is characterized by pallidness of the skin with cyanotic areas which appear as a result of respiratory and circulatory disorders developing in grave toxicosis. In long-standing chronic pancreatitis, in connection with digestive disorders, the patient may develop cachexia; his skin is dry and turgor decreases. Inspection may, in rare cases, reveal distension of the upper abdomen (cysts of the pancreas). Acute pancreatitis may be attended by abdominal flatulence.

Percussion over the pancreas can reveal dulled tympany or complete dullness in cases with considerable enlargement of the pancreas (in the presence of cysts or tumours).

PALPATION

Surface palpation of the abdomen of a patient with acute pancreatitis reveals tenderness and strain of the prelum muscles in the epigastrium, sometimes in the left hypochondrium or over the pancreas (Korte symptom).

Palpation of the pancreas is very difficult because of the deep position and soft consistency of the gland. Normal pancreas can only be palpated in 4-5 per cent of women and 1-2 per cent of men affected by cachexia with relaxed prelum and ptosis of the internal organs. The pancreas is only palpable when enlarged considerably. Consolidated pancreas affected by cirrhosis, newgrowth, or cyst can be easier palpated.

The pancreas should be palpated in the morning, after giving purgatives (with the empty stomach). The greater curvature should first be palpated; then the position of the pylorus should be determined and the right knee of the transverse colon palpated. The horizontal portion of the duodenum should preferably be outlined by palpation in order to find the point where the head of the pancreas might be better palpated. The head of the pancreas is easier to palpate than its body or tail because of its greater size and frequent consolidation. Palpation is deep and sliding, usually above the right part of the greater curvature of the stomach. The Obraztsov-Strazhesko rule should be followed during palpation. The palpating hand is placed horizontally, 2—3 cm above the preliminarily found lower border of the stomach. The skin is pulled upwards and then the palpating hand presses gradually into the abdominal cavity with each expiration. As soon as the posterior wall is reached, the hand should slide in the downward direction.

A normal pancreas is a soft transverse cylinder, 1.5-3 cm in diameter. The organ is immobile and painless. In the presence of chronic pancreatitis and tumour of the pancreas, it can sometimes be palpated as a firm, irregular, and slightly tender band. Conclusions should be derived very carefully, because part of the stomach, the transverse colon, a pack of lymph nodes and some other formations can easily be mistaken for the pancreas.

Laboratory and Instrumental Methods

LABORATORY STUDIES

Coprological studies. Upset exocrine function of the pancreas has its effect mainly on assimilation of food (mainly fats and proteins). Faeces become ample and of pasty consistency. Their colour is greyish; the smell is

rancid. Microscopic study of faeces reveals considerable amount of neutral fat and muscular fibres with preserved striated pattern. These coprological changes are revealed in cases with pronounced disorders in secretion of the pancreatic juice which occur, for example, in pancreatic duct obstructed by a stone or a tumour. Moderate pancreatic dysfunction can be compensated for by intestinal digestion and the action of microbial enzymes.

Insufficient digestion of food can be due to other causes. Then, in order to assess the pancreatic function, it is necessary to use methods by which the composition of the pancreatic juice can be studied directly, or the condition of the pancreas should be assessed by the blood and urine enzyme content. "Spontaneous" pancreatic juice, or juice liberated in response to special stimulation should be used for these studies. The latter method is more reliable since it reveals functional possibilities of the pancreas. Stimulants of pancreatic secretion can be administered to the duodenum or parenterally. The stimulants can be divided into two groups by their action on the pancreas. Some of them mostly intensify secretion and increase hydrocarbonate content in the secreted juice. Other stimulants do not increase the volume of secretion while the enzyme content increases significantly. Stimulants of the first group are hydrochloric acid, secretin, vegetable juices, and ether. Vegetable fat, pancreozymin, and insulin belong to the other group.

Hydrochloric acid and secretin (physiological stimulants) are most widely used in practical studies. As hydrochloric acid passes the stomach and enters the duodenum, it stimulates formation of secretin which is carried with the blood to the pancreas to activate its secretory function. The disadvantage of hydrochloric acid is that its presence in the duodenum stimulates formation not only of secretin but also of cholecystokinin, which in turn stimulates secretion of bile whose presence in the pancreatic juice distorts the results of the studies. Pure secretin introduced intravenously (one clinical unit/kg body weight) is devoid of this disadvantage. Hydrochloric acid is however more readily available. Pancreozymin is often used in combination with secretin, which is administered 60 minutes later.

Procedure. The duodenal contents are obtained by a tube. A double-tube should be used: its one end opens in the stomach and the other in the duodenum. Better results are obtained with this tube because extraction of gastric juice during this procedure ensures better purity of the pancreatic juice. The position of the tubes should be controlled by X-rays. A water-jet pump is used for continuous suction of the gastric and duodenal contents. After a 30-minute aspiration of "spontaneous" pancreatic juice, 30 ml of warmed 0.5 per cent hydrochloric acid solution are introduced through the duodenal tube. The tube is then clamped for 5 minutes, and then six or

eight 10-minute portions of the juice are collected. If secretin is used as a stimulant, the juice is pumped immediately after the injection (10-minute portions as well) and studied.

The volume, colour, transparency, bilirubin concentration, hydrocarbonate alkalinity, and enzyme activity are then determined in the obtained samples. Hydrocarbonate alkalinity is determined gasometrically (Van Slyke's apparatus). Bilirubin is determined by the icterus index. Amylase, trypsin, and lipase are determined in the pancreatic juice. Normally the enzyme concentration in the juice decreases after administration of hydrochloric acid or secretin because the liquid fraction of the juice thus increases. But in 60—90 minutes, the concentration returns to initial. In insufficiency of the pancreas the initial enzyme concentration is restored more slowly. The content of separate enzymes sometimes changes as well. The pancreatic function is assesed not only by enzyme concentration, but also by the quantity of enzyme units isolated per unit time.

Study of enzymes in duodenal contents. Activity of amylase is determined by the *Wohlgemuth test* — by the quantity of millilitres of a 1 per cent starch solution that can be split by 1 ml of pancreatic juice. The duodenal contents are diluted in an isotonic sodium chloride solution in geometrical progression from 1:10 to 1:20 240. To 1 ml of each solution added are 2 ml of a 1 per cent starch solution. After a 30-minute incubation on a water bath at 37 °C, a drop of 1/50 N iodine solution is added to each test tube. The maximum dilution is determined by the absence of the blue colour which indicates that all starch has been split. Multiplying this dilution by 2 (2 ml of starch solution were added) the quantity of amylase units is determined (normal, 640-1280).

Determining trypsin by the Fuld-Goss method. The procedure is the same as that used for determining amylase. The duodenal contents are diluted and 2 ml of a 0.1 per cent alkaline caseine is added to each 1-ml portion of the diluted solutions. After a 24-hour thermostatting at 37 °C, the solution in which all caseine has been split is found by the absence of cloudiness after adding a few drops of a 5 per cent acetic acid solution. The calculation is the same as in determining amylase. The normal activity of trypsin is 160-2500 units.

Determination of lipase by the Bondi method is based on the formation of fatty acids from fat split by lipase. Lipase activity is expressed by the quantity of millilitres of the alkali spent to neutralize fatty acids formed from olive oil by the action of 100 ml of the duodenal juice. Normal activity of lipase is 50-60 units.'

Study of the pancreatic enzymes in the blood and urine. The so-called deflection of pancreatic enzymes is of certain diagnostic importance. In some pathologies of the pancreas mainly associated with abnormal secre-

tion outflow, the pancreatic enzymes enter the blood and then the urine. Since urine and blood are easier obtained than the pancreatic juice, the clinical study of the pancreatic function usually begins with blood and urine tests. Amylase and lipase are first determined in them; trypsin and antitrypsin are determined in rare cases.

Amylase can be determined *in blood and urine* by the Wohlgemuth test as in the analysis of the duodenal juice, except that a weaker solution of starch (0.1 per cent) is used. More accurate results are obtained with the Smith-Roe method which is based on decomposition of starch by amylase (normally, 80-150 units in blood). The intensity of colour of the starch-iodine solution changes depending on the degree of starch hydrolysis (determined absorptiometrically).

Blood lipase is determined by the stalagmometric method which is based on the change in the surface tension of tributyrin solution under the action of fatty acids formed by the action of lipase. But several types of lipase are present in the blood; pancreatic and hepatic lipases prevail. Pancreatic lipase is stable to atoxyl but is decomposed by quinine, while hepatic lipase is on the contrary stable to quinine and decomposed by atoxyl. The increased content of atoxyl-resistant lipase is important for the diagnosis of pancreas affections.

The endocrine function can also be affected in diseases of the pancreas. For special tests see "Diabetes Mellitus".

X-RAY EXAMINATION

Survey radiographs of the abdominal cavity reveal only separate stones in the pancreatic ducts or calcified tissues of the pancreas (due to chronic pancreatitis). These are projected in accordance with the anatomical location of the organ at the level of the 2nd-3rd lumbar vertebrae; or a large cyst is projected as a uniform distinctly outlined formation.

X-ray examination of the stomach and the duodenum can sometimes reveal indirect signs of tumours, cysts, and sometimes chronic pancreatitis. For example, in the presence of cancer, a cyst of the head of the pancreas or in pancreatitis attended by enlargement of the head, contrast radiography reveals dilation, deformation, and displacement of the duodenal loop. If a tumour (cyst) is localized in the body or tail of the pancreas, the changes appear as defective filling in the region of the posterior wall or the greater curvature of the stomach due to pressure on it from the enlarged pancreas. Changes in the duodenum can be especially vivid if the gland is first relaxed (relaxation duodenography). To that end the patient is given intravenously 2 ml of a 0.1 per cent atropine sulphate solution and, intraintestinally (through a duodenal tube), barium sulphate suspension.

X-ray studies of the pancreas can also be carried out during duodenoscopy (retrograde pancreatography, wirsungography). A contrast substance is administered into the pancreatic duct. Depending on the character of the affection, non-uniform stenosis, dilation, or rupture of the bile duct can be seen on the X-ray picture.

To diagnose affections of the pancreas (tumours, cysts), angiography is also used with administration of the contrast substance through a tube into the coeliac artery, through the femoral artery, and further to the aorta.

RADIOISOTOPE METHODS OF STUDY

Methionine labelled with radioactive selenium (^{75}Se—selenomethionine) is used for scanning the pancreas. The radioactive solution (250μCi) is given intravenously and scanning is taken in 30 minutes. The rate of accumulation, time of the presence of the isotope in the pancreas, and the time of its delivery to the intestine together with the pancreatic secretion are also assessed.

In the presence of diffuse inflammatory and dystrophic changes in the pancreatic parenchyma, the absorption of labelled methionine in the pancreas considerably decreases and a scanogram shows uneven (spotted) distribution of the isotopes; vast defective accumulation of the isotope in the pancreas is revealed in cysts and tumours of the pancreas.

ECHOGRAPHY

Echography is widely used in the study of the pancreas. One- and two-chamber techniques are used. The special value of echography in the study of the pancreas is that the gland is deeply located inside the abdomen and other methods of examination are inapplicable, except angiography and retrograde (through an endoscope) wirsungography, which furnish valuable diagnostic information. Echographic diagnosis is complicated by the great individual variability of position and size of the pancreas, pronounced meteorism, and obesity. Because of these difficulties, the pancreas can be "seen" and examined only in 90 per cent of patients. The reflected echo-signals give the examiner the idea of the position, size, and condition of the pancreas. Echography is used to confirm the presence of acute or chronic pancreatitis, to establish the diagnosis, or to suspect the presence of a tumour (depending on the size, character and position, tumours are revealed in almost 80 per cent of cases). Cysts of the pancreas over 1.5—2 cm in size are revealed in almost 100 per cent of cases.

One-dimensional apparatus is used to examine the patient from his back; three groups of echo-signals appear on the screen: (1) generated im-

pulse; (2) impulses reflected from the skin, subcutaneous fat, and long muscles of the back; and (3) signals reflected from the pancreas appear on the oscilloscope screen as vertical peaks located above the zero line.

Major Clinical Syndromes

Exocrine Pancreatic Insufficiency

This symptom complex is characterized by disordered secretion by the pancreas of its juice containing the main digestive enzymes, such as trypsin, lipase, amylase and others (over 15 altogether), and also hydrocarbonates that ensure the optimum medium for the activity of these enzymes. Exocrine insufficiency of the pancreas can be primary (congenital) and secondary (acquired). Primary exocrine insufficiency of the pancreas can be due to its underdevelopment and mucoviscidosis (congenital systemic cystofibrosis of the exocrine glands, e.g. the pancreas, bronchial, salivary or sweat glands, which is manifested by increased viscosity of their secretion due to high mucopolysaccharide content). The secondary exocrine insufficiency of the pancreas arises in the presence of any disease attended by the affection of a considerable part of the pancreatic parenchyma (pancreatitis, cysts, etc.), and by obstruction of the secretion outflow (obstruction of the duct by a stone, tumour, etc.).

If the pancreatic juice is delivered to the intestine in deficient quantity (normally from 1.5 to 21 per 24h) or if the amount of the main enzymes in the juice is deficient, normal digestion is upset and conditions for accelerated reproduction of microorganisms in the small intestine are created to cause dysbacteriosis which upsets digestion to a greater extent. Rumbling and sounds of pouring liquid are heard in the abdomen; the patient suffers from meteorism and characteristic pancreatogenic diarrhoea (polyfaecalia, yellowish faeces with fatty lustre). Coprological studies reveal steatorrhoea, creatorrhoea, and amylorrhoea. But early stages of pancreatic insufficiency can proceed without marked intestinal dysfunction because of the high reserve potentialities of the pancreas.

Owing to the upset intestinal function, undigested food particles can be determined coprologically. Apart from the cavitary digestion the parietal intestinal digestion (affected mainly by the intestinal enzymes) and the absorption of the products of enzymatic hydrolysis are also upset. The patient develops cachexia, signs of polyhypovitaminosis, symptoms of deficiency of the major microelements (iron, manganese, ions of calcium, sodium, potassium etc.) are observed. The function of many endocrine glands is upset secondarily. The patient complains of general weakness and

decreased work capacity. Hypoproteinaemic oedema can develop in patients with cachexia.

Pancreatic secretion is studied for the diagnosis of the syndrome of pancreatic exocrine insufficiency. Activity of trypsin, antitrypsin, lipase, and amylase in the blood serum, and also amylase in the urine is studied simultaneously. Upset intestinal digestion, which is characteristic of pancreatic insufficiency, is determined in grave cases by the typical disorders in stools (pancreatogenic diarrhoea) and coprogram. Since in most diseases of the pancreas its endocrine apparatus is also involved (pancreatic islands) determination of blood sugar (with a fasting stomach), the level of glycaemia and glucose tolerance (single and double loads) is diagnostically important (see "Diabetes Mellitus").

It should be remembered that the exocrine pancreatic insufficiency occurs in many diseases. The diagnosis of the main disease (by direct examination and laboratory studies) is therefore of primary importance for further treatment of the patient.

Three stages of exocrine pancreatic insufficiency are differentiated: the first stage (initial, latent) becomes only manifest when the requirement for the digestive enzymes increases (overeating, especially intake of much fats); the second stage is a pronounced pancreatic insufficiency (frequent or permanent diarrhoea, steatorrhoea, creatorrhoea, amylorrhoea); and the third stage, dystrophy; it is characterized by considerable wasting (to cachexia) due to severe disturbances in the intestinal digestion and absorption, polyhypovitaminosis, and dystrophic changes in various organs and tissues.

Treatment. The following three principles are observed: (1) treatment of the main disease; (2) mechanically and chemically sparing diet: food must be easily hydrolysed by the enzymes and contain much protein, vitamins, and limited quantity of carbohydrates (depending on the pancreatic incretory function); (3) substitution enzyme therapy including preparations containing pancreatic enzymes: pancreatin, pansinorm, and others.

Prophylaxis. Timely detection, treatment and also prevention of diseases of the pancreas (rational diet, abstention from alcohol).

Special Pathology

Pancreatitis

Pancreatitis is inflammation of the pancreas. Acute and chronic pancreatitis are differentiated.

ACUTE PANCREATITIS

Aetiology and pathogenesis. Most often there exists connection between acute pancreatitis and inflammation of bile ducts, cholelithiasis in particular. This connection is explained by possible penetration of bile (usually infected) into the pancreatic duct and activation of the enzymes (trypsin and lipase) of the pancreatic juice. This condition can arise when the common bile duct and the pancreatic duct have a common ampulla, e.g. in spasm of the sphincter of the hepatopancreatic ampulla, obstruction of the ampulla by a stone, increased pressure in the duodenum (during coughing, vomiting, etc). Upset outflow of the pancreatic juice in obstruction of the duct by a stone, oedema of the duct mucosa, etc. is also important.

Among the other aetiological factors are alcoholism, poisoning with chemicals, such as lead, cobalt, phosphorus, arsenic, etc., and alimentary disorders (overeating or inadequate nutrition), certain infectious diseases (e.g. epidemic parotitis, virus hepatitis), local circulatory disorders in the pancreas due to spasms of the vessels, embolisms and thrombosis arising due to general changes in the vascular system.

Activation of proteolytic enzymes in the pancreas is important in the pathogenesis of pancreatitis irrespective of its aetiology. This causes enzymatic digestion (autolysis) of the pancreatic parenchyma with haemorrhages and fat necrosis. The developmental mechanisms of pancreatitis depend also on secondary infection of the excretory ducts that develops by ascending haematogenic or (less frequently) lymphogenic routes.

Pathological anatomy. Inflammation, necrosis, and in later periods atrophy, fibrosis and calcification of the pancreas are revealed. Abscesses of variable size are found in purulent inflammation of the pancreas, or diffuse melting of the pancreatic tissue develops with subsequent fibrosis of the pancreas (in favourable outcome). Mild forms of pancreatitis are only manifested by inflammatory oedema of the gland.

Clinical picture. Acute pancreatitis occurs mostly in women with disordered fat metabolism (aged 30 to 60). The disease usually begins by a sudden pain in the upper abdomen which arises after taking ample and fat food or alcohol. In mild cases the pain is not severe and is mainly localized in the epigastrium. It may also be girdling with radiation into the lumbar region, the left shoulder blade, and sometimes the retrosternal region. Grave cases (acute necrosis of the pancreas) are manifested by excruciating pain which ends in collapse and shock. Pain is attended by nausea, painful vomiting, salivation, constipation or, less frequently, diarrhoea.

Inspection of the patient reveals pallid and sometimes icteric skin and mucosa due to difficult bile outflow from the common bile duct. In grave cases, general cyanosis is possible, or cyanosis may be local, on separate parts of the anterior abdominal wall or the lateral parts of the abdomen. Cyanosis is connected with pronounced toxicosis. The abdomen is often inflated. Surface palpation of the patient with the early initial stage of the disease reveals a soft and tender abdomen; the left part is more sensitive. Later, when peritonitis joins the process, the muscles become strained and symptoms of peritoneal irritation develop. Ascites can be revealed in acute haemorrhagic pancreatitis. The pancreas is usually impalpable. Cases with skin hyperaesthesia in the upper left quadrant (corresponding to segments VII-XII) often occur.

The temperature is subfebrile, high in necrotic or purulent pancreatitis, and subnormal in collapse.

The blood tests show neutrophilic leucocytosis with a shift to the left, lymphopenia, aneosinophilia, and increased ESR. During the very first hours of the disease, increased quantities of the pancreatic enzymes (diastase and lipase) are contained in the blood and urine. The blood and urine amylase content can nevertheless remain normal in necrotic pancreatitis (or amylase content may even be decreased). In these cases, the decreased blood calcium content and increased activity of aspartate aminotransferase are of certain diagnostic importance. At-

tacks of tetany can develop in marked hypocalcaemia. Hyperglycaemia and glucosuria are not infrequent.

Course. Acute pancreatitis lasts several weeks and can end by complete recovery or acute disease may convert into chronic and relapsing pancreatitis. If pancreatitis is severe, the patient may die during the initial period of the disease from a collapse and shock, or later from grave complications (cysts and abscesses of the pancreas).

Treatment. The patient must be taken to hospital. The conservative therapy includes: (1) control of shock (intravenous drop infusion of 2-3 l of a 5 per cent glucose solution, transfusion of blood or plasma); (2) physiological rest for the pancreas with abstention from food during 2-4 days; (3) administration of antienzymatic preparations (trasilol, etc.) for inactivation of proteolytic enzymes; (4) inhibition of pancreatic secretion and removal of pains (atropine sulphate, promedol, paranephric or paravertebral block); (5) prevention of secondary infection (prescription of antibiotics). Surgical treatment is indicated in suppuration of the pancreas, in peritonitis, and haemorrhagic pancreonecrosis.

CHRONIC PANCREATITIS

Chronic pancreatitis occurs mostly in women aged 30 to 70. It can develop after acute pancreatitis or directly as a chronic condition due to the same aetiological factors upon which the onset of acute pancreatitis depends. Chronic pancreatitis in men occurs mostly due to chronic alcoholism.

Pathological anatomy. Morphological changes occurring in pancreatitis are oedema of the pancreas, small haemorrhages, necrosis and proliferation of connective tissue with gradual atrophy of cell elements. Reparation of the pancreas occurs simultaneously (areas of hyperplasia and formation of adenoma). Sclerosis develops in the interstitial tissues and in the parenchyma of the pancreas. Therefore the insular cells, which remain intact for a long time, are later atrophied and sclerosed. At the early stage of the disease the pancreas is only mildly enlarged and dense; cicatrices, calcification, and obstruction of the ducts develop later. The pancreas diminishes in size and becomes dense and cartilaginous.

Clinical picture. Patients with chronic pancreatitis complain of pains that come in attack or are permanent. Pain usually occurs in the upper abdomen or in the epigastrium and radiates to the left shoulder, shoulder blade, neck, or to the left iliac bone; it can sometimes be girdling and radiate from the epigastrium, along the left costal edge, to the spine. Pain intensifies significantly after taking fatty food. The patient complains of poor appetite, aversion to fats, regurgitation, nausea, vomiting, abdominal flatulence, diarrhoea (constipation in some cases), and loss of weight. The characteristic symptom of chronic pancreatitis is ample grey and fetid fatty faeces (steatorrhoea) which is connected with developing exocrine pancreatic insufficiency.

The skin and the sclera of the patient are sometimes icteric due to compression of the common bile duct by an enlarged head of the pancreas. Deep palpation of the abdomen reveals tenderness in the region of the pan-

creas. The gland can sometimes be palpated in emaciated patients as a dense band. Zones of hypersensitivity of the skin can also be revealed (Zakharyin-Head zones in the region of VIII-X segments on the left).

Neutrophilic leucocytosis and increased ESR are observed in the blood in grave cases. The content of the pancreatic enzymes in the blood and urine during exacerbation increases, but remains normal or even decreases in the atrophic process. The enzyme content in the pancreatic juice in patients with severe affections of the pancreas is decreased. Hyperglycaemia and glycosuria can occur in some cases. Coprological studies show signs of inadequate digestion of proteins and fats (steatorrhoea, creatorrhoea; etc.) which is connected with pancreatic hyposecretion.

X-ray examination of the duodenum in conditions of artificial hypotonia (duodenography) reveals dilation and deformation of the duodenal loop due to enlargement of the head of the pancreas. Diagnosis is confirmed by echography.

Course. The disease is usually protracted, with periodic remissions and exacerbations. But the prognosis is usually favourable in the absence of pronounced pancreatic dysfunction or complications such as diabetes mellitus, etc.

Treatment. Bed-rest, rational and sparing diet that does not stimulate pancreatic secretion but contains sufficient amount of proteins and vitamins should be recommended during exacerbations; antibiotics and anti-enzyme preparations (trasilol and others) should also be given. Pancreatin, pansinorm and other enzyme preparations should be given in substitution therapy.

Prophylaxis. This includes timely treatment of diseases that might be aetiologically significant in the origin of chronic pancreatitis (diseases of the bile ducts, etc.) and control of alcoholism.

Chapter 8

URINARY SYSTEM

Methods of Examination

Inquiry

Complaints. Patients with diseases of the kidneys most commonly complain of pain in the lumbar region, disordered urination, oedema, headache, and dizziness. They may also complain of deranged vision, pain in the heart, dyspnoea, absence of appetite, nausea, vomiting, and elevated body temperature. But diseases of the kindeys may also proceed without any symptoms of renal or general clinical insufficiency.

If the patient complains of *pain,* its location should first of all be determined. Pain of renal origin often localizes in the lumbar region. If the ureters are affected, the pain is felt by their course. If the bladder is involved, pain is suprapubical. Radiation of pain into the perineal region is characteristic of an attack of nephrolithiasis.

The character of pain should then be determined. It is necessary to remember that the renal tissue is devoid of pain receptors. The pain is felt when the capsule or the pelvis is distended. Dull and boring pain in the lumbar region occurs in acute glomerulonephritis, abscess of the perirenal cellular tissue, in heart decompensation ("congestive kidney"), in chronic pyelonephritis (usually unilateral) and less frequently in chronic glomerulonephritis. Pain arises due to distension of the renal capsule because of the inflammatory or congestive swelling of the renal tissue. Sharp and suddenly developing pain on one side of the loin can be due to the renal infarction. The pain persists for several hours or days and then subsides gradually. The pain is rather severe in acute pyelonephritis: inflammatory oedema of the ureter interferes with the normal urine outflow from the pelvis and thus causes its distension. The pain is usually permanent. Some patients complain of attacks of severe piercing pain in the lumbar region or by the course of the ureter. The pain increases periodically and then subsides, i.e. has the character of *renal colic*. Obstruction of the ureter by a calculus or its bending (movable kidney) is the most common cause of this pain, which is usually attended by spasmodic contraction of the ureter, retention of the urine in the pelvis, and hence its distension. The spasmodic contractions and distension of the pelvis account for the pain. Pain in renal colic is usually unilateral. It radiates into the corresponding hypochondrium and most frequently by the course of the ureter to the

bladder and to the urethra. This radiation of pain is explained by the presence of nerve fibres (carrying the impulses from kidneys, ureters, sex organs and the corresponding skin zones) in the immediate vicinity of the relevant segments of the spinal cord (D_X-D_{XII} and L_I-L_{II}). This facilitates propagation of the excitation. Patients with renal colic (like those with colic of other aetiology) are restless; they toss in bed. Patients with severe pain of other aetiology would usually lie quiet in their beds (movements may intensify the pain).

The conditions promoting pain should be established. For example, pain in nephrolithiasis can be provoked by taking much liquid, jolting motion, or the like; pain is provoked by urination in cystitis. Difficult and painful urination is observed in stranguria. Patients with urethritis feel a burning pain in the urethra during or after urination.

It is necessary also to establish the agent that lessens or removes the pain. For example, atropine sulphate, hot water-bottle or warm bath help in renal colic. Since these remedies only help in spasmodic pain by removing spasms of the smooth muscles, their efficacy in renal colic confirms the leading role of the ureter contraction in the pathogenesis of this pain. Pain of the renal colic-type in patients with movable kidney may lessen with changing posture: urine outflow improves with displacement of the kidney. Pain slightly lessens in patients with acute paranephritis if a bag with ice is placed on the lumbar region and if the patient is given amidopyrine or other analgesics.

Many renal diseases are attended by *deranged urination*: changes in the daily volume of excreted urine and in the circadian rhythm of urination.

Secretion of urine during a certain period of time is called *diuresis*. Diuresis can be positive (the amount of urine excreted exceeds the volume of liquid taken) or negative (the reverse ratio). Negative diuresis is observed in cases of liquid retention in the body or its excess excretion through the skin, by the lungs (e.g. in dry and hot weather). Positive diuresis occurs in resolution of oedema, after administration of diuretics, and in some other cases. Deranged excretion of urine is called *dysuria*.

Increased amount of excreted urine (over 21 a day) is called *polyuria*. It can be of renal and extrarenal aetiology. Polyuria is observed in persons who take much liquid, during resolution of oedema (cardiac or renal), and after taking diuretics. Long-standing polyuria with a high relative density of urine is characteristic of diabetes mellitus. In this case polyuria arises due to a deranged resorption of water in renal tubules because of increased osmotic pressure of the urine rich in glucose. Polyuria occurs in diabetes incipidus because of insufficient supply of antidiuretic hormone secreted into blood by the posterior pituitary. Polyuria also occurs in the absence of sensitivity of the tubules to the ADH, in affected interstice of the renal

medulla of various nature, in hypokaliaemia, and hypo- and hypercalcaemia.

Persistent polyuria with low specific gravity of urine (hyposthenuria) is usually a symptom of a severe renal disease, e.g. chronic nephritis, chronic pyelonephritis, renal arteriolosclerosis, etc. Polyuria in such cases indicates the presence of a neglected disease with renal insufficiency and decreased reabsorption in renal tubules.

Decreased amount of excreted urine (less than 500 ml a day) is called *oliguria.* It can be not connected directly with renal affections (extrarenal oliguria). For example, it can be due to limited intake of liquid, during staying in a hot and dry room, in excessive sweating, intense vomiting, profuse diarrhoea, and during decompensation in cardiac patients. But in certain cases oliguria is the result of diseases of the kidneys and the urinary ducts (renal oliguria), such as acute nephritis, acute dystrophy of the kidneys in poisoning with corrosive sublimate, etc.

A complete absence of urine secretion and excretion is called *anuria.* Anuria persisting for several days threatens with possible development of uraemia and fatal outcome. Anuria may be caused by the deranged secretion of urine by the kidneys (secretory anuria) which occurs in severe form of acute nephritis, nephronecrosis (poisoning with sublimate or other nephrotoxic substances), transfusion of incompatible blood, and also some general diseases and conditions such as severe heart failure, shock, or profuse blood loss.

In certain cases the secretion of urine is normal but its excretion is obstructed mechanically (obstruction of the ureters or the urethra by a calculus, inflammatory oedema of the mucosa, proliferation of a malignant tumour). This is called excretory anuria. It is usually attended by strong pain in the loin and the ureters due to distension of the renal pelves and the ureters. Exctretory anuria is often attended by renal colic.

Renal (secretory) anuria can be of reflex origin, e.g. in severe pain (contusion, fractures of the extremities, etc). Anuria should be differentiated from *ischuria,* when the urine is retained in the bladder and the patient is unable to evacuate it. This occurs in compression or other affection of the spinal cord, and in loss of consciousness.

Pollakiuria (frequent micturition) is observed in certain cases. A healthy person urinates from 4 to 7 times a day. The amount of excreted urine during one micturition is from 200 to 300 ml (1000-2000 ml a day). But frequency of micturition may vary within wider range under certain conditions: it may decrease in limited intake of liquid, after eating much salted food, in excessive sweating, in fever, and the like, or the frequency may increase (polyuria) if the person takes much liquid, in getting cold, and the like circumstances. Frequent desire to urinate with excretion of

meagre quantity of urine is the sign of cystitis. A healthy person urinates 4—7 times during the day time; a desire to urinate during night sleep does not arise more than once. In the presence of pollakiuria the patient feels the desire to urinate during both day and night. In the presence of chronic renal insufficiency and if the kidneys are unable to control the amount and concentration of excreted urine in accordance with the amount of liquid taken, physical exertion, the ambient temperature, or other factors important for the liquid balance in the body, the patient urinates at about equal intervals with evacuation of about equal portions of urine. This condition is called *isuria.*

Under certain pathological conditions, the frequency of urination is normal during the day time but increases during night. The amount of urine excreted during night often exceeds the amount of daily urine *(nycturia).* Nocturnal enuresis (nycturia) and oliguria during day time occur in cardiac decompensation and are explained by a better renal function at night, i.e. at rest (cardiac nycturia). Nycturia may concur with polyuria in renal dysfunction, at the final stage of chronic glomerulonephritis, chronic pyelitis, vascular nephrosclerosis, and other chronic renal diseases (renal nycturia). In the presence of isuria and nycturia of renal origin, which arise due to the loss by the kidneys of their concentrating ability, the specific gravity of the urine is monotonous. The condition is known as *isosthenuria.* The specific gravity of urine is usually decreased *(hyposthenuria).* The specific gravity of urine varies from 1.009 to 1.011, i.e. approaches the specific gravity of primary urine (plasma ultrafiltrate) in patients with pronounced nephrosclerosis, which is the final stage of many chronic renal diseases.

Some diseases of the bladder and the urethra are attended by difficult and painful urination. The patient would complain of change in the colour of the urine, its cloudiness, and traces of blood.

Oedema is observed in acute and chronic diffuse glomerulonephritis, nephrotic syndrome, amyloidosis, and acute renal excretory dysfunction (anuria). It is important to ask the patient about the site that was the first to be attacked by oedema, the sequence of oedema spreading, and the rate of intensification of this phenomenon (see "Renal Oedema").

Headache, dizziness, and *heart pain* may result from kidney affections. These symptoms occur in those renal diseases which are attended by considerable increase in the arterial pressure, e.g. in acute and chronic glomerulonephritis or vascular nephrosclerosis. A pronounced and persistent increase in the arterial pressure can be among the causes of deranged vision (neuroretinitis).

Patients with diseases of the kidneys can complain of weakness, indisposition, impaired memory and work capacity and deranged sleep. Vi-

sion may be deranged along with skin itching and unpleasant breath. Dyspeptic disorders sometimes join in: loss of appetite, dryness and unpleasant taste in the mouth, nausea, vomiting, and diarrhoea. All these phenomena are associated with retention in the body of protein decomposition products due to renal insufficiency (see "Renal Insufficiency") which develops at the final stage of many chronic renal diseases, and sometimes in acute diseases attended by retention of urine during several days.

Fever is the common symptom of infectious inflammatory affections of the kidneys, the urinary ducts and perirenal cellular tissue.

History of the present disease. When questioning the patient, it is necessary to establish the connection of the present disease with previous infections (tonsillitis, scarlet fever, otitis, acute respiratory diseases). This sequence is especially characteristic of acute glomerulonephritis. But it is sometimes difficult to establish the time of onset of the disease because some chronic affections of the kidneys and the urinary ducts can for a long time be latent. Moreover, when questioning the patient, it is necessary to find out if he had deranged hearing or vision in his childhood that might be suggestive of congenital renal pathology.

Special attention should be given to the presence in the patient's past history of diseases of the kidneys and the urinary ducts (acute nephritis, pyelitis, cystitis) or symptoms that might suggest them (dysuria, haematuria, oedema, arterial hypertension, attacks of pain in the abdomen or loin resembling renal colics), since these symptoms can be connected with the present renal pathology. In certain cases the cause and the time of onset of grave kidney affections (necronephrosis) can be established by revealing industrial or domestic poisoning, intentional (or by mistake) taking of some poisons (corrosive sublimate, preparations of bismuth, phosphorus, silver, large doses of sulpha preparations, or of some antibiotics, e.g. aminoglycosides, expired tetracyclines, phosphorus compounds), transfusion of incompatible blood, etc. Amidopyrin, phenacetin, barbiturates, camphor, and some other medicines can cause allergic changes in the kidneys.

The patient must be asked about the character of the disease course: it may be gradual (arteriolosclerosis, chronic diffuse glomerulonephritis, amyloidosis of the kidneys), or with periodical exacerbations (chronic pyelonephritis, chronic diffuse glomerulonephritis). It is necessary to establish the cause of exacerbations, their frequency, clinical signs, the character of therapy given and its efficacy, the causes inducing the patient to seek medical help.

Anamnesis. Special attention should be given to the factors that might provoke the present disease or have effect on its further course. For example, a common factor promoting development of acute and chronic

nephritis and pyelonephritis is chilling and cooling (poor housing or working conditions, drafts, work in the open, acute cooling of the body before the disease). Spreading of genital infection onto the urinary system can be the cause of pyelonephritis. It is necessary to establish the presence or absence in the past of tuberculosis of the lungs or other organs. This helps establish the tuberculous nature of the present disease of the kidneys.

It is necessary to establish if the patient has some other diseases that might cause affections of the kidneys (collagenosis, diabetes mellitus, certain diseases of the blood, etc.). Various chronic purulent diseases (osteomyelitis, bronchiectasis) can be the cause of amyloidosis of the kidneys. Occupations associated with walking, riding, weight lifting, etc., can have their effect on the course of nephrolithiasis and provoke attacks of renal colic. Some abnormalities of the kidneys, nephrolithiasis, amyloidosis, etc., can be inherited. It is also necessary to record thoroughly the information on past operations on the kidneys or the urinary ducts.

When examining women, it is important to remember that pregnancy can aggravate some chronic diseases of the kidneys and be the cause of the so-called nephropathy of pregnancy (toxaemia of late pregnancy).

Physical Examination

INSPECTION

Inspection of the patient should give the physician the idea of the gravity of the patient's condition. Very grave condition with loss of consciousness may be due to severe affections of the kidneys attended by renal insufficiency and uraemic coma; the condition may be satisfactory or of moderate gravity (in milder cases). It is necessary to pay attention to the patient's posture in bed: active (at initial stages of many diseases of the kidneys), passive (in uraemic coma), or forced (in paranephritis; the patient may lie on his side with the leg flexed, bringing the knee to the abdomen on the affected side). In the presence of renal colic the patient is restless, tosses in bed, groans or even cries from pain. Convulsions are observed in the presence of uraemic coma, renal eclampsia, and nephropathy of pregnancy (toxaemia of late pregnancy with involvement of the kidneys).

Oedema is characteristic of acute and chronic glomerulonephritis, nephrotic syndrome, and amyloidosis of the kidneys. The appearance of the patient with oedema of the renal origin is quite specific (Fig. 101). The face is pallid, swollen, with oedematous eyelids and narrowed eye-slits (facies nephritica). In patients with more pronounced signs of pathology, oedema affects the upper and lower extremities and the trunk (anasarca).

The colour of the patient's skin is also important. Oedematous skin in

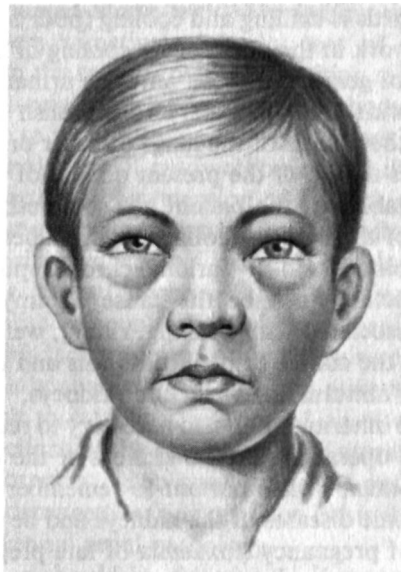


Fig. 101. Patient with renal oedema.

chronic nephritis is pallid due to the spasm of skin arterioles, and anaemia which attends this disease. The skin is wax-pallid in amyloidosis and lipoid nephrosis. It should be remembered that in cardiac oedema (as distinct from renal oedema) the skin is more or less cyanotic.

When inspecting a patient with chronic nephritis, it is possible to observe scratches on the skin and coated dry tongue; an unpleasant odour of ammonia can be felt from the mouth and skin of the patient (factor uremicus). All these signs characterize chronic renal insufficiency (uraemia).

Inspection of the abdomen and the loin does not usually reveal any noticeable changes. But in the presence of paranephritis, it is possible to notice swelling on the affected side of the loin. In rare cases, an especially large tumour of the kidney may be manifested by protrusion of the abdominal wall. Distended bladder can be protruded over the pubic bone in thin persons. The distension can be due to overfilling of the bladder, for example, due to retention of urine in adenoma or cancer of the prostate.

PALPATION

The posterior location of the kidneys, and also the absence of anterior approach to them due to the interference of the costal arch, makes palpation of the kidneys difficult. Relaxation of the prelum and pronounced

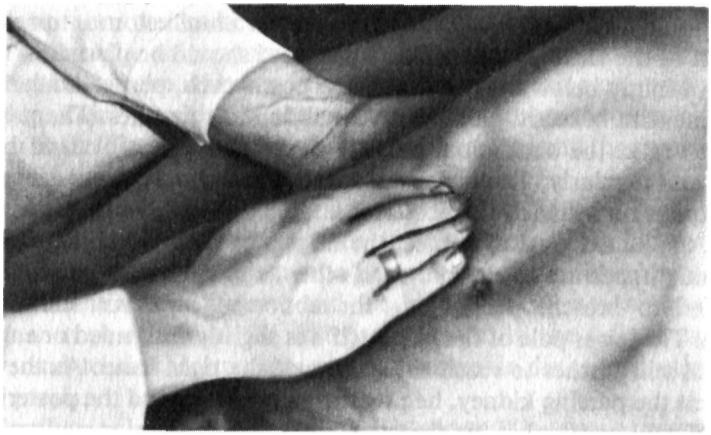


Fig. 102. Palpation of the right kidney of the lying patient.

cachexia can be attended by certain ptosis of the kidneys and make them accessible to palpation even in healthy subjects. But the results of palpation can only be reliable in considerable enlargement of the kidneys (at least 1.5—2 times, e.g. due to formation of a cyst or a tumour), or their displacement by a tumour, or in cases with a floating kidney. Bilateral enlargement of the kidneys is observed in polycystosis.

It is necessary to remember that the kidneys can move about in the range of 2—3 cm in the proximal and distal directions when the subject changes his position from horizontal to vertical, and also during respiratory movements of the diaphragm. Passive movements of the kidneys transmitted from the diaphragm during inspiration and expiration should be taken into consideration during palpation: the Obraztsov-Strazhesko palpation method should be used. The patient should be palpated in the lying or standing position. When the patient is in the horizontal position, his kidneys ate better palpated because the strain of the prelum is absent. But the movable kidney can be palpated in the standing patient because it hangs by gravity and is displaced downward by the pressure of the low diaphragm.

During palpation of the patient in the lying position (Fig. 102), his legs should be stretched and the head placed on a low pillow; the prelum is relaxed and the arms are freely placed on the chest. The physician should assume his position by the right side of the patient with his left hand under the patient's loin, slightly below the 12th rib so that the finger tips be near the spinal column. During palpation of the left kidney, the physician's

hand should be moved further, beyond the vertebral column, to reach the left part of the lumbar region. The right hand should be placed on the abdomen, slightly below the corresponding costal arch, perpendicularly to it and somewhat outwardly of the rectus abdominis muscles. The patient is asked to relax the abdominal muscles as much as possible and breathe deeply and regularly. The physician's right hand should press deeper with each expiration to reach the posterior abdominal wall, while the left hand presses the lumbar region to meet the fingers of the right hand. When the examining hands are as close to each other as possible, the patient should be asked to breathe deeply by "the abdomen" without straining the prelum. The lower pole of the kidney (if it is slightly descended or enlarged) descends still further to reach the fingers of the right hand. As the physician feels the passing kidney, he presses it slightly toward the posterior abdominal wall and makes his fingers slide over the anterior surface of the kidney bypassing its lower pole. If ptosis of the kidney is considerable, both poles and the entire anterior surface of the kidney can be palpated. The physician should assess the shape, size, surface (smooth or tuberous), tenderness, mobility, and consistency of the kidneys. Bimanual palpation of the kidney can also be done with the patient lying on his side.

In contrast to other organs, an enlarged or ptosed kidney can be examined by ballottement (Guyon's sign): the right hand feels the kidney while the fingers of the left hand strike rapidly the lumbar region in the angle between the costal arch and the longissimus thoracic muscles: the fingers of the right hand feel vibration of the kidney. In deranged urine outflow through the ureter and in pronounced distension of the renal pelvis by the accumulated urine or pus, liquid fluctuation can be felt during palpation of the kidney.

If the physician palpates some formation where he expects to find a kidney, he must check reliably if this is actually a kidney because it is easy to mistake for the kidney an overfilled and firm part of the large intestine, tumor of perirenal cellular tissue (lipoma, fibroma), an enlarged right lobe of the liver, the gall bladder (during palpation of the right kidney), or an enlarged or displaced spleen (during palpation of the left kidney). The kidney is a bean-shaped body with a smooth surface, slipping upwards from under the palpating fingers and returning to normal position, tossed up by ballottment and giving tympany during percussion over the kidney (by overlying intestinal loops). Protein and erythrocytes appear in the urine after palpation. But all these signs are of only relative importance. For example, if a malignant tumour develops, the kidney may lose its mobility due to proliferation of the surrounding tissues; its surface becomes irregular and the consistency more firm; if the tumour is large, the kidney moves apart the intestinal loops and percussion gives dullness. But the

kidney can nevertheless be identified by the mentioned signs by differentiating it from the neighbouring organs and other formations.

Palpation of the kidneys in the standing patient was proposed by S. Botkin. During palpation the patient stands facing the physician who sits on a chair. The prelum muscles should be relaxed and the trunk slightly inclined forward.

Palpation can be used to diagnose ptosis of the kidneys. Three degrees of nephroptosis can be distinguished: the lower pole of the kidney can be palpated in cases with ptosis of the first degree; the entire kidney can be palpated in the second degree; and the kidney freely moves about in all directions to pass beyond the vertebral column, to the side of the other kidney, and to sink downwards to a considerable distance, in the third-degree ptosis.

Palpation is also used to examine the bladder. If it contains much urine, especially in persons with thin abdominal wall, the urinary bladder can be palpated over the pubic bone as an elastic fluctuating formation. If the bladder is markedly distended, its superior border reaches the umbilicus.

Tenderness in palpation of the ureter along its course and sensitive loin over the kidneys (sensitive to pressure exerted in the angle between the 12th rib and the longissimus thoracic muscles) is of certain diagnostic importance. The area overlying the ureter extends on the anterior abdominal wall between the superior ureter point (at the edge of the rectus abdominis muscle at the level of the umbilicus) and the inferior point (at the intersection of the bi-iliac line and the vertical line passing the pubic tubercle).

PERCUSSION

It is impossible to percuss the kidneys in a healthy subject because they are covered anteriorly by the intestinal loops which give tympany. Dullness can only be determined in the presence of very marked enlargement of the kidneys.

A much more informative method for examination of the kidneys is *tapping*. The physician places his left hand on the patient's loin and using his right hand (palm edge or fingers) taps with a moderate force on the right hand overlying the kidney region on the loin (Fig. 103). If the patient feels pain, the symptom is positive (Pasternatsky's symptom). This symptom is also positive in nephrolithiasis, paranephritis, inflammation of the pelvis, and also in myositis and radiculitis. This decreases the diagnostic value of Pasternatsky's symptom.

A full urinary bladder gives a dull sound on percussion of the suprapubic region. The percussion is carried out from the umbilicus downward, along the median line; the pleximeter-finger is placed parallel to the pubic bone.

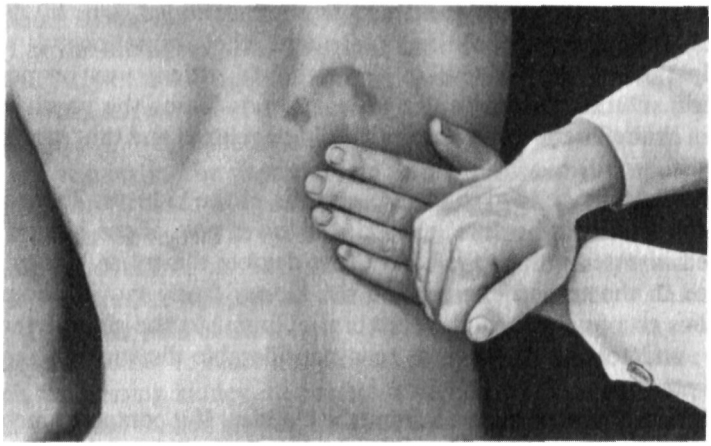


Fig. 103. Determining Pasternatsky's symptom.

Instrumental and Laboratory Methods

URINALYSIS

The study of urine is important for establishing a diagnosis of and concluding on the course of the pathology. Various pathological processes occurring in the kidneys and the urinary tracts have their effect on the properties of urine. Pathological metabolites may be released into the blood in various diseases. Excreted by the kidneys, these metabolites are also found in the urine and their determination is therefore important diagnostically. Urine samples taken after night sleep are usually studied. The analysis begins with the study of its **physical properties.**

The normal *daily amount of urine* (daily diuresis) excreted by an adult varies from 1000 to 2000 ml, the ratio of the urine evacuated during the day to the nocturnal diuresis being 3:1 or 4:1. The daily amount of urine below 500 ml and over 2000 ml can be considered pathological under certain conditions.

The *colour* of normal urine depends on its concentration and varies from straw-yellow to the colour of amber. Concentration of urochromes, urobilinoids, uroerythrin and of some other substances accounts for the colour of urine. The most marked changes in the urine colour depend on the presence of greenish-brown bilirubin, large quantity of erythrocytes (appearance of meat wastes), reddish-brown urobilin, and medicines (acetylsalicylic acid and amidopyrine give pink colour to the urine, methylene blue colours it blue, and rhubard greenish-yellow). Normal

urine is clear. *Cloudiness* may be due to salts, cell elements, mucus, fats, and bacteria.

The *smell* of urine is specific and not pungent. When decomposed by bacteria in- or outside the bladder, urine smells of ammonia. In the presence of ketone bodies (in grave forms of diabetes mellitus), urine smells "fruity" (the odour of decomposing apples).

The *specific gravity* of the urine varies from 1.001 to 1.040. It is measured by an urometer (hydrometer) with the scale reading from 1.000 to 1.050. Determination of the specific gravity of the urine is of great clinical importance because it gives information on the concentration of substances dissolved in it (urea, uric acid, salts) and characterizes the concentrating and diluting capacity of the kidneys. It should be remembered that specific gravity depends not only on the amount of particles dissolved but mainly on their molecular weight. High-molecular substances (e.g. proteins) account for increased specific gravity of the urine without influencing substantially the osmotic concentration of the urine. The osmotic concentration of the urine depends mainly on the presence of electrolytes and urea. Osmotic concentration is expressed in mosm/l. The maximum osmotic concentration of urine in a healthy person is 910 mosm/1 (maximum sp. gravity, 1.025-1.028). The specific gravity of the urine may exceed 1.030-1.040 in the presence of high quantity of glucose (glucosuria), because the concentration of 10 g/l increases gravity of the urine by 0.004.

Chemical analysis of urine. *Reaction of the urine.* The kidneys are important for maintaining acid-base equilibrium in the body. The kidneys are capable of removing the ions of hydrogen and hydrocarbonate from the blood and this is a mechanism by which pH of blood is maintained constant. The concentration of the hydrogen ions is the true reaction of urine (active acidity or pH of the medium). The sum of dissociated and undissociated hydrogen ions is the titration (analytical) acidity. The true reaction of urine may vary from pH 4.5 to 8.4. The pH of urine can be determined colorimetrically and electrometrically. Colorimetry includes methods employing litmus paper, bromthymol blue, and other indicators, by which the pH is determined only tentatively. More accurate determination of pH is done by comparing colour intensity of test solutions with standard solutions (the Michaelis method).

Special indicator papers can also be used for sufficiently accurate determination of the pH of urine in the range from 5.0 to 9.0. The mean pH value of the urine in healthy subjects (with normal nutrition) is about 6.0. The value of pH is affected by the use of medicinal preparations (diuretics, corticosteroids). Acidity of urine can increase in diabetes mellitus, renal insufficiency, tuberculosis of the kidneys, acidosis, and hypokaliaemic alkalosis. Urine reacts alkaline in vomiting and chronic infections of the urinary tracts due to bacterial-ammoniacal fermentation.

Determination** of **protein in urine. Normal urine does not practically contain protein. The small quantity of plasma proteins (to 150 mg/day), that is present in the urine, cannot be determined by qualitative tests used in practical medicine. The appearance of protein in the urine in concentrations determinable by qualitative methods is called *proteinuria.* It can be of renal and extrarenal origin. Organic renal proteinuria occurs in kidney affections due to increased permeability of glomeruli which is underlain by vascular inflammation or structural disorganization of the basal membrane. Glomerular permeability is upset by the "molecular sieve" mechanism, i.e. low-molecular proteins are lost in the first instance. This proteinuria is called selective. As the process progresses, high-molecular proteins are also lost (non-selective proteinuria). Selectivity of proteinuria is an important diagnostic and prognostic sign.

Functional renal proteinuria is connected with the permeability of membranes in the renal filter in the presence of strong stimulation, slowing of the blood flow in the glomeruli, etc. Functional proteinurias include emotional, athletic (effort), cold, and orthostatic (a condition characterized by the appearance of protein in the urine when the patient is in the erect posture; hence the name). In cases with extrarenal proteinuria, proteins enter the urine from the urinary and sex ducts (admixtures of inflammatory exudate); extrarenal proteinuria does not exceed 1 g/1. Tests intended to reveal protein in the urine are based on its thermal or acid coagulation (the urine sample should first be filtered).

Acetic-acid test. The test gives reliable results provided the pH of the medium is 5.6. If the urine contains much phosphates, a few drops of acetic acid, which is usually added in this test, do not decrease the pH of the medium significantly and the proteins remain dissolved as alkalalbumins. In other cases it is enough to add a few drops of acetic acid to decrease the pH much below 5.6, and the proteins form acid albumins without giving cloudiness. The test should be better carried out with the Bang buffer (56.5 ml glacial acetic acid and 118 g of sodium acetate dissolved in 1 1 of water). To a 5-ml sample of urine added are 1-2 ml of the Bang buffer and the mixture is boiled for 30 s. The solution turns cloudly in the presence of even insignificant amount of protein.

Sulphosalicylic acid test. This is one of the most sensitive and popular tests. To 3-4 ml of filtered urine added are 6—8 drops of a 20 per cent solution of sulphosalicylic acid. Cloudiness develops if the test is positive.

Quantitative determination of albumin. A modified Heller's test is now popular: a white ring appears at the interface between the test liquid containing albumin and nitric acid. A thin but distinct ring appears by the end of the third minute to indicate the presence of 0.033 g/1 of albumin in the test urine. Filtered urine is layered on 1-2 ml of a 50 per cent nitric acid and the time is marked. If the white ring forms earlier than in 2 minutes,

the urine sample should be diluted with water so that the white ring should be formed during the course of the second or third minute. The amount of albumin contained in the urine is determined by multiplying 0.033 g/l by the dilution degree.

Turbidimetric tests are widely used for determining protein in the urine. The sulphosalicylic acid is used for the purpose. Since turbidity is proportional to protein concentration in the urine, protein can be determined from the calibration curve after determining extinction (optical density) of the solution.

Rapid-diagnosis methods are very popular now. They are used for prophylactic large-scale examination of the population (with special paper indicators). Protein error of some acid-base indicators is used as the working principle. The paper is impregnated in bromphenol blue and citrate buffer solution. As the paper is wetted, the buffer dissolves to ensure the required pH of the medium for the indicator reaction. Amino groups of protein react with the indicator at pH 3.0—3.5 to alter its initial yellow colour to greenish-blue. By comparing the new colour with a special scale of standards, it is possible to assess tentatively protein concentration in the test urine.

Protein concentration in urine expressed in grammes per litre does not express the absolute amount of protein lost. It is therefore recommended to express it in grammes per day. The protein concentration in the urine collected during 24 hours should first be determined, diuresis measured, and the amount of protein lost per day finally calculated.

Determining Bence-Jones proteins. Bence-Jones proteins occur in myeloma and Waldenstrom's macroglobulinaemia. These are light (L) polypeptide chains, which pass an intact renal filter because of their relatively small molecular weight, and are determined by thermal precipitation and electrophoretic study of urine.

Determining glucose in urine. The urine of a healthy person contains very small quantity of glucose (0.03—0.15 g/1) which cannot be detected by common qualitative tests. Glucose in the urine *(glycosuria)* can be both physiological and pathological. In the presence of normal renal function, glycosuria occurs only in increased concentration of sugar in the blood (normal sugar content of blood is 4.6—6.6 mmol/l or 0.8—1.2 g/1), i.e. in the presence of hyperglycaemia. The so-called renal glucose threshold (sugar concentration in the blood) does not usually exceed 9.9 mmol/1 (1.8 g/1); higher concentration of sugar indicates glycosuria.

Physiological glycosuria can be observed in persons whose diet is rich in carbohydrates (alimentary glycosuria), following emotional stress, and administration of some medicines (caffeine, corticosteroids). Less frequent is renal glycosuria associated with disturbed resorption of glucose in the

tubules: glycosuria develops in the presence of normal amount of sugar in the blood. As a primary disease, glycosuria occurs in the form of renal diabetes. Secondary renal glycosuria occurs in chronic nephritis, nephrotic syndrome, and in glycogen-storage disease. Pathological glycosuria occurs most frequently in diabetes mellitus, less frequently in thyrotoxicosis, in pituitary insufficiency (Itsenko-Cushing syndrome), and in liver cirrhosis.

In order to assess correctly glycosuria (especially in patients with diabetes mellitus), it is necessary to calculate the daily loss of sugar with urine. Most qualitative tests used to detect glucose in urine are based on the reducing power of glucose.

Haines' test for sugar in the urine is based on the property of glucose to reduce copper hydroxide in an alkaline medium to yellow cuprous hydroxide or red cuprous oxide.

Nylander's test. The reaction is based on reduction of bismuth nitrate by glucose to bismuth metal. In the presence of sugar, the colour of solution changes from brown to black. The test urine should be free from protein. Extraneous reducing substances (antipyrin, benzoic acid, etc.) giving a false reaction should be removed by adding 1 ml of 95 per cent alcohol and a small amount of animal carbon to 9 ml of urine.

Glucose oxidase (notatin) test. This is a highly specific and very simple enzyme test. Glucose oxidase (notatin) is β-d-glucose dehydrogenase. At its first stage, the enzyme acts on glucose to liberate hydrogen peroxide. At the second stage, the presence of hydrogen peroxide is established by a redox indicator (like in the benzidine test).

The principle of the glucose oxidase test is used in the indicator paper method. A paper strip impregnated with glucose oxidase, peroxidase and a benzidine derivative is dipped in urine: if the urine contains glucose the paper turns blue in 30-60 seconds.

Quantitative determination of glucose in urine. The amount of glucose contained in a given sample of urine can be determined by the angle of rotation of a polarized beam of light: glucose rotates the polarized light to the right.

Althausen colorimetric method. The method is based on the colour reaction occurring during heating a glucose solution with alkali. To 4 ml of urine added is 1 ml of 10 per cent sodium hydroxide (or potassium hydroxide) solution and the mixture is boiled for a minute. The solution is allowed to stand for ten minutes and its colour compared with this of colour standards (either visually or photometrically).

Determining ketone (acetone) bodies. The presence of ketone bodies (acetone, acetoacetic and β-oxybutyric acid) in the urine is called *ketonuria.* Ketonuria is usually observed in severe diabetes mellitus but it can also develop due to carbohydrate deficit (in grave toxicosis, long-

standing gastro-intestinal disorders, etc.); it may develop postoperatively. Ketone bodies in the urine occur simultaneously and their separate determination is therefore clinically impracticable. The *Lange test* is most commonly used for the detection of ketone bodies in the urine. The test urine sample is mixed with acetic acid and nitroprusside, and then ammonia is layered: a violet ring is formed at the interface of the liquids if the test is positive.

Determination of bilirubin. Normal urine is practically free from bilirubin. Increased amounts of bilirubin in the urine at which common qualitative bilirubin tests become positive (bilirubinuria) occur in hepatic and subhepatic jaundice at which the concentration of bound bilirubin (bilirubin glucuronide) in the blood increases. Most qualitative tests for bilirubin are based on its conversion into green biliverdin under the action of oxidizers.

Rosin's test. Lugol (1 per cent iodine solution) is layered upon 4-5 ml of urine: a green ring appears at the interface between the liquids if the test is positive.

Fouchet's test. To 10—12 ml of urine added are 5-6 ml of a 15 per cent barium chloride solution; the mixture is stirred and filtered. Barium chloride precipitates bilirubin. The precipitate is separated on a filter and 2—3 drops of Fouchet's reagent (100 ml of a 25 per cent trichloroacetic acid solution mixed with 10 ml of a 10 per cent ferric chloride solution) are added: green-bluish or light-blue spots appear on the filter if the test is positive. The Fouchet test is more sensitive.

Determining urobilinoids. Urobilinoids are urobilin (urobilinogens, urobilins) and stercobilin (stercobilinogens, stercobilins). Urobilin and stercobilin bodies are not determined separately. Excretion of large amounts of urobilinoids in the urine is called *urobilinuria* which occurs in diseases of the liver (hepatitis, cirrhosis), haemolytic anaemia, and in intestinal diseases (enterites, etc.).

Neubauer's test. The test is based on the reaction between urobilin bodies and the Ehrlich reagent (2 g of p-dimethylaminobenzaldehyde + + 100 ml of a 20 per cent hydrochloric acid solution). To a few millilitres of urine (freshly taken and cooled to room temperature) added are a few drops of the Ehrlich reagent: colouration of the liquid during the first 30 seconds indicates increased content of urobilin bodies (positive test), while development of colour at later period indicates either their absence or the presence of their normal quantity.

Florence' test. Urobilinoids are extracted from the urine acidified with sulphuric acid by ether (8-10 ml of urine and 3 ml of ether). The ether extract is then layered upon 2-3 ml of concentrated hydrochloric acid. The advantage of this test is that it is also positive in the presence of normal

quantity of urobilinoids and can therefore be used to establish their complete absence.

Bogomolov's test. To 10 ml of urine added are 2—3 ml of a saturated copper sulphate solution. Next, a few drops of hydrochloric acid are added to clarify the solution. The mixture is allowed to stand for 5 minutes, 2—3 ml of chloroform are added, and the mixture is shaken: chloroform turns pink in the presence of urobilin bodies.

Quantitative determination of urobilinoids is based on their colour reaction (pink) with p-dimethylaminobenzaldehyde or with hydrochloric acid.

Rapid diagnosis (by indicator paper) of ketonuria, bilirubinuria, urobilinuria is based on the employment of the same chemical reactions with subsequent colorimetry.

Microscopy of urine sediment. A urine specimen is stirred thoroughly and its 10 ml are transferred into a centrifugal test tube. After centrifuging, the supernatant is decanted while the precipitate transferred onto an object glass for microscopy. The precipitate is first examined at small and then at large magnification to study the formed elements, cylinders, and salts.

Erythrocytes (red blood cells) can be altered and unaltered. Unaltered erythrocytes contain haemoglobin and appear as greenish-yellow discs. Altered erythrocytes are free from haemoglobin and are colourless one- or two-contour rings (Plate 21). These erythrocytes occur in the urine of low specific gravity; erythrocytes shrink in the urine of specific gravity. The urine of a healthy person can have single erythrocytes.

Erythrocytes may be liberated either from the kidneys or from the urinary tract. The presence of erythrocytes in the urine is called *haematuria.* Haematuria that can only be established by microscopy is called microhaematuria, while haematuria revealed by macroscopy is called macrohaematuria. It is important practically to decide whether haematuria is of glomerular or non-glomerular origin. In the latter case blood is liberated into the urine from the urinary tract due to the presence of stones in the pelves, urinary bladder or ureters, and because of tuberculosis or malignant newgrowths of the urinary bladder. In the presence of glomerular haematuria, the urine usually contains much protein. Proteinoerythrocytic dissociation (i.e. haematuria with insignificant proteinuria) usually suggests haematuria associated with pathology of the urinary tract. An intermittent character of haematuria (with strongly varying intensity) is another evidence of non-glomerular haematuria.

A *three-glass test* is used for differential diagnosis of haematuria. The patient urinates into three vessels. If the blood originates in the urinary tract (urethra), the highest amount of blood is present in the first portion

of the urine; if bleeding occurs in the urinary bladder, haematuria is the highest in the last portion. If the source of haemorrhage is located in other parts of the urinary system, all three portions of the urine contain equal quantity of erythrocytes.

Leucocytes are found in the urine as small granular rounded cells. They swell in the urine of low specific gravity. Leucocytes in the urine of a healthy person are usually neutrophils and their amount is insignificant (to 1—2 in the microscope's vision field). Increased quantity of leucocytes in the urine *(leucocyturia*) indicates inflammation in the kidneys or urinary tract (urethritis, prostatitis, cystitis, pyelonephritis). *Thompson's test* is used for differential diagnosis of leucocyturia. The firts portion of an early morning urine specimen is collected in the first glass, the main bulk of the urine in the second glass, and only the residue in the third glass. If prevailing quantity of leucocytes is found in the first portion, it indicates the presence of urethritis and prostatitis. If the main quantity of leucocytes is found in the third portion, this suggests the disease of the urinary bladder. Uniform distribution of leucocytes in all portions of the urine may suggest affection of the kidneys. Cell structures are quickly destroyed in alkaline urine; it is therefore difficult to judge about the degree of leucocyturia. Eosinophils are sometimes found in the urine; they differ from other leucocytes by ample uniform refracting granularity. The presence of eosinophils suggests an allergic character of the disease.

The degree of leucocyturia does not always correspond to the gravity of affection in chronic pyelonephritis. In the absence of active inflammatory process, the quantity of leucocytes in the urine may remain normal. The method of supravital staining is widely used now. It was proposed in 1949 by Sternheimer and Malbin. Depending on their morphological properties, leucocytes (Plate 22) are coloured either red or pale-blue by a special stain (water-alcohol mixture of 3 parts of Gentian violet and 97 parts of safranine). Leucocytes that are coloured blue in the urine of low specific gravity are greater in size and contain vacuolized cytoplasm with granules that are set in Brownian movement. They are found in patients with pyelonephritis. Leucocyte cells (Sternheimer-Malbin cells) can be found in the urine of patients with iso- or hyposthenuria with any location of the source of inflammation in the urinary tract. These cells are more often called "active leucocytes". They are determined by adding distilled water to urine precipitate to create low osmotic pressure.

Increased number of "active leucocytes" suggest activation of inflammation in the urinary tract or exacerbation of pyelonephritis.

Microscopy can reveal cells of squamous, transitional, and renal *epithelium* (Plate 23). Squamous epithelium cells are rounded or polygonal; they are large, colourless, and contain a small nucleus; they

enter the urine from the external genitalia and the urethra; their diagnostic importance is low. Cells of transitional epithelium line the mucosa of the urinary tract; their configuration is quite varied; they are smaller than squamous epithelium cells; the nucleus is rounded. The presence of large amount of transitional epithelium in the urine indicates inflammatory process in the pelves or the bladder. Cells of renal (cuboidal) epithelium of tubules are rounded or polyhedral; they are small (slightly larger than leucocytes) and have a large, eccentrically located nucleus; their granularity is coarse. They are often found in hyaline cylinders. The presence of renal epithelium in the urine is a specific sign of acute and chronic affections of the kidneys, and also of fever, toxicosis, and infectious diseases.

Casts are proteinous or cell formations of tubular origin; they have cylindrical configurtion and variable size (Plate 24). *Hyaline casts* are proteinous formations of indistinct contour with smooth and slightly granular surface; they are found in acute and chronic nephritis, nephrotic syndrome, and also in physiological transient albuminuria. Hyaline casts can be found in the urine of practically healthy people when the pH of the urine decreases sharply along with increasing specific gravity of the urine, which is characteristic of dehydration. It is believed that hyaline casts are formed by glycoprotein secreted in the tubules; but there are no reliable data that would confirm this conjecture. *Granular casts* have distinct contours; they consist of dense granular mass formed by degraded cells of renal epithelium. Their presence indicates dystrophic processes in the tubules. *Waxy casts* have distinct contours and a homogeneous yellow structure. Their presence is characteristic of chronic diseases of the kidneys. The urine can also contain epithelial, erythrocytary, haemoglobin and leucocyte casts, and cylindrical formations of amorphous salts, which are diagnostically unimportant.

"Non-organized sediment" of the urine consists of salts that precipitate as crystals and amorphous substances. Their character depends on the colloidal composition of the urine, its pH, and other properties. Acid urine contains uric acid (yellow rhomboid-type crystals), urates (yellowish-brown amorphous salt), oxalic lime, or oxalates (colourless octahedral crystals that may also occur in alkaline urine) (Plate 25). Alkaline urine contains ammonium urate, calcium carbonate, triple phosphates, amorphous phosphates, and neutral calcium phosphate (Plate 26). The sediment is diagnostically insignificant but pathological urine can contain crystals of cystine, thyrosine, and leucine. The presence of thyrosine and leucine is especially characteristic of subacute dystrophy of the liver and of phosphorus poisoning. The presence of lipoids in the urine is characteristic of nephrotic syndrome. In a polarizing microscope, lipoids give a dual reflection and appear as lustrous crosses.

Addis-Kakovsky test. The test is used for quantitative determination of the formed elements in the urinary sediment. Urine collected during ten hours is stirred thoroughly, its amount is measured and a 12-minute aliquot (1/50th of the full volume) is placed in a graduated centrifugal test tube. After centrifuging for 5 minutes at 2000 rpm the supernatant is removed by a pipette, while the remaining 0.5 ml sediment is stirred and transferred into **a** cell for counting blood formed elements. Leucocytes, erythrocytes, and casts are counted separately. The quantity of cells counted in one microlitre is multiplied by 60 000 to find the quantity of the formed cells of the urine excreted during the day. The normal counts are 1 000 000 for erythrocytes, 2 000 000 for leucocytes, and 20 000 for casts.

Nechiporenko 's method is now widely used to count erythrocytes and leucocytes in 1 ml of urine. The main advantage of this method is that an average sample of urine is taken for analysis and the presence of pus from the sex organs is thus excluded. A disadvantage of the method is that it does not account for diuresis. The normal counts are 1000 erythrocytes, 4000 leucocytes, and 220 hyaline casts.

Bacterioscopic and bacteriological study of urine. Urine cultures are used to establish the infectious nature of a disease of the urinary system. Sterile glassware should be used for the purpose. Whenever necessary, the urine is studied bacterioscopically for the presence of tuberculosis mycobacteria. A smear is prepared from the urinary sediment withZiehl-Nielsen staining. The urine is studied bacteriologically to determine qualitative and quantitative composition of its microbial flora. In the presence of bacteriuria, it is very important to determine its degree and microorganism sensitivity to various antibiotics.

FUNCTIONAL TESTS FOR KIDNEYS

Assessing the renal function by specific gravity and amount of the urine excreted. In conditions of water deficit, a normal person excretes a small amount of the urine with high specific gravity; and vice versa: if excess liquid is taken, the amount of the urine excreted increases while its specific gravity decreases. The kidneys thus maintain equilibrium in the bodily fluids, i.e. they maintain constancy of osmotic concentration and volumes of the fluids. If the body is dehydrated, osmotic concentration of extracellular fluid increases and the amount of released antidiuretic hormone (ADH) increases to increase tubular resorption of water. If the amount of taken liquid increases, osmotic concentration of extracellular fluid decreases; this decreases secretion of ADH and water resorption to increase diuresis. In pathology, the kidneys are incapable of ensuring the required osmotic gradient in the medulla and the concentrating power of the kidneys

is thus upset. The impaired power of the kidneys to resorb the osmotically active substances without water disturbs their diluting capacity.

Zimnitsky's test. The main advantage of this method is that the renal function is tested without interfering with the normal life of the patient. The patient collects his urine at 3-hour intervals (8 portions during 24 hours). The volume of each portion and specific gravity of the urine are determined. The volumes of daily and night urine are compared and a conclusion is derived concerning daily and nocturnal diuresis. Fluctuations in specific gravity of the urine during the course of the day and its maximum value are thus determined. Normally the daily diuresis exceeds the nocturnal one; volumes of urine portions can vary from 50 to 250 ml, and their specific gravity from 1.005 to 1.028. Nocturnal diuresis (nycturia) prevails in renal insufficiency to indicate longer work of the kidneys because of their impaired functional capacity. If renal insufficiency is pronounced, decreased specific gravity becomes permanent *(hyposthenuria*). Combination of polyuria with low specific gravity of the urine and nycturia is a specific sign of renal dysfunction.

Dilution test. The patient is given to drink 1-1.5 1 of water or thin tea within 30-45 minutes and then the urine is collected at 30-minute intervals during 4 hours. The portions are measured and their specific gravity determined. A normal individual would eliminate about 75 per cent of the taken liquid during four hours, while the specific gravity of the urine decreases to 1.003-1.001. The first portions will be larger and their specific gravity lower. A more accurate method includes also calculations where the amount of liquid taken is referred to the body weight: 22 ml of liquid is given per kg body weight.

If the excretory function of the kidneys is decreased, the amount of urine excreted during 4 hours is markedly less than that of liquid taken; the specific gravity in all portions is about the same, but not below 1.006-1.007. If the renal function is upset significantly, the specific gravity of the urine in all portions is 1.009-1.011, which corresponds to the specific gravity of the primary urine. The dilution test is contraindicated in oedema and hypertension.

Urine concentration test. The patient receives no fluids for 36 hours (nor food containing much liquid). Urine is collected at 3-hour intervals during 24 hours (8 specimens). The volume and specific gravity of each specimen is determined. The specific gravity of the urine of a healthy individual will in these conditions be not lower than 1.028. If the specific gravity of thus obtained urine does not rise over 1.022, this indicates impaired renal function.

The urine concentration test is valid when applied to cases where the daily diuresis does not exceed 400 ml. The test is contraindicated in acute

inflammatory processes in the kidneys, in cardiovascular and renal insufficiency, and in essential hypertension.

The renal function can be assessed by studying glomerular filtration, renal plasma flow, tubular transport of certain substances (e.g. glucose reabsorption), secretion of extraneous substances, urea and electrolyte excretion in the urine. It is possible to reveal and assess the degree of renal insufficiency by studying *concentration of urea, indican, residual nitrogen, creatinine, potassium, sodium, calcium, magnesium and phosphates in the blood* (see Tables 7 and 8 of the "Appendix").

Renal insufficiency arises in cases where the mass of the active parenchyma is 20 per cent (and lower) of the normal weight. The determination of the mass of the active nephrons is thus important to assess the renal function. The measure of active nephrons is the maximum reabsorption of glucose (normal 300-500 mg/min) and the glomerular filtration rate (normal, 65-120 ml/min).

Clearance tests are now widely used to study the renal function according to Van Slyke. Glomerular filtration and tubular reabsorption of water can be measured by clearance tests with substances that are not resorbed or liberated in the tubules. This means that these substances enter urine only by glomerular filtration. Once we assume that a given substance contained in a minute volume of plasma passes entirely into a minute volume of urine, i.e. the plasma is completely cleared of this substance, the filtered amount is then equal to the amount passed with urine. The filtered quantity of substance is equal to the product of glomerular filtration (F) and its concentration in plasma (P). The quantity excreted with urine is equal to the product of the urine minute volume (*V)* and the concentration of this substance in the urine *(U),* i.e, $FP = UV$. Hence

$$F = \frac{UV}{P}.$$

The *U, V,* and *P* values can be found clinically and used for the determination of *F* that characterizes the volume of plasma which is completely cleared of the given substance during one minute. This volume is called clearance.

If a substance that is filtered in the glomeruli but is not reabsorbed or liberated in the tubules is used for the assessment of renal function, the clearance of this substance is actually equal to glomerular filtration. Using this phenomenon, Rehberg proposed a test for studying the amount of filtration by endogenic or exogenic creatinine.

If one assumes that creatinine content of plasma and glomerular filtrate is the same, it is possible to determine the degree of concentration of the glomerular filtrate as it passes the tubules. In other words, not only the

amount of filtration but also of reabsorption can thus be determined (percentage of reabsorbed water):

$$\frac{(F - V) \times 100}{F}.$$

In healthy individuals the amount of glomerular filtration is 65—125 ml. The percentage of reabsorbed water is 98.5-99.

The Rehberg test can be carried out with additional administration of creatinine and liquid, or without it. The second version is used more frequently. Blood is taken from the vein of the patient on a fasting stomach and creatinine concentration is determined. Urine is collected during 2 or 24 hours. Diuresis is measured thoroughly and creatinine content determined. Next, using the formula given above, the amount of glomerular filtration and reabsorption percentage are calculated.

As renal failure develops, glomerular filtration decreases gradually to attain as low values as 5-2-1 ml/min. Tubular reabsorption changes less markedly to decrease in cases of pronounced insufficiency to 80-60 per cent.

Substances that are not only filtered in the glomeruli but also secreted in the tubules give a mixed clearance, e.g. filtration-reabsorption or filtration-secretion clearance. This clearance is used to assess the renal function in general (rather than its separate function). Clearance of some substances (diodrast, phenol red, para-aminohippuric acid, etc.) is so high that practically approaches the renal blood flow, i.e. the amount of blood that passess the kidneys during one minute. The renal blood flow can thus be determined by the clearance of these substances.

The determination of glomerular filtration is of great clinical significance and is one of the most popular methods for quantitative study of the renal function. The prognostic value of the method increases if it is used in follow-up studies. Thus, persistent decrease in glomerular filtration to 40-50 mg/min during 18-24 months following acute glomerulonephritis suggests the conversion of the acute process into the chronic disease.

X-RAY EXAMINATION

The kidneys are normally not seen on X-ray pictures, except in thin individuals (oval silhouettes can frequently be seen by sides of the spinal column, between the 11th thoracic and 3rd lumbar vertebrae). Stones in the kidneys and the ureters are visualized by X-rays. Best seen are stones containing calcium salts (oxalates and phosphates); stones containing urates are usually not seen. In suspected tumour, X-raying is done after placing

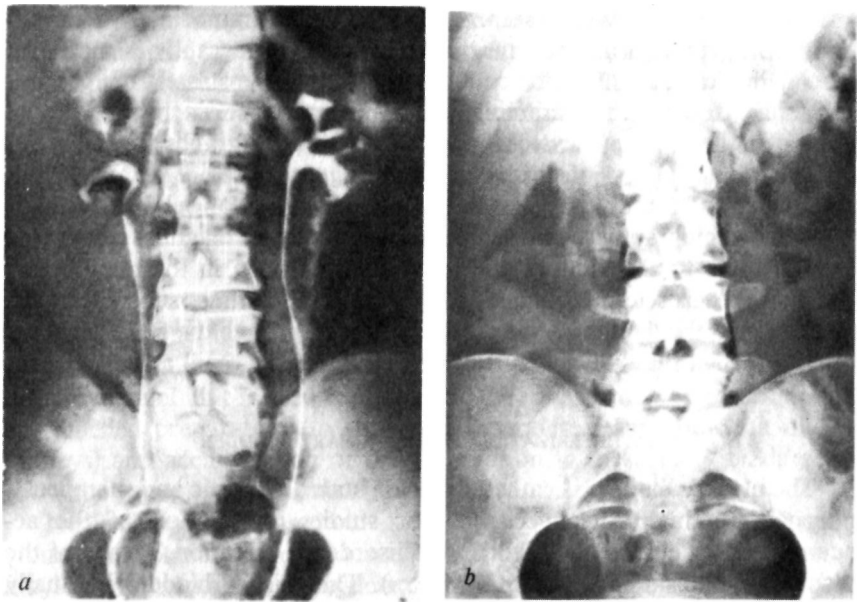


Fig. 104. Pyelograms in norm *(a),* and in pyelonephritis *(b).*

pneumoren or pneumoretroperitoneum (administration of oxygen into the retroperitoneal and perirenal space).

Excretory urography is carried out in hospitals: the patient is given intravenously a contrast substance that is readily excreted by the kidneys (25-40 ml of a 30-50 per cent solution of iodine preparation verographin, urotrast, or the like) and then a series of pictures are taken by which determined are the size, position and functional capacity of the kidneys (by the readiness with which they excrete the contrast substance), the size and configuration of the pelves, position of the ureters, and the presence of concrements (Fig. 104a and *b).* If the renal function is strongly upset, the contrast substance is poorly excreted, and the procedure fails to give the wanted results. Drop-infusion urography is used for diagnosis of complicated cases. The patient is given 200—250 ml of a 25 per cent solution of a contrast substance by drop infusion during 10-15 minutes. The dose of the infused preparation may be increased with this method while the safety of the procedure is higher since the infusion can immediately be discontinued if first signs of allergic response to the contrast substance appear. The pictures of the kidneys and the ureters obtained by this technique are much better even in decreased renal function. The silhouettes of the

kidneys are especially well seen on pictures taken immediately after administering the contrast substance. Retrograde pyelography is made for special indications. Liquid contrast substance (urotrast) or gaseous substance (oxygen, air) is administered into the renal pelvis through special ureteral catheter using a cystoscope. Retrograde pyelography is carried out in cases when findings of the excretory pyelography are not reliable or not sufficiently informative to establish correct diagnosis of pelvic affection.

Renal angiography (nephroangiography) is used to diagnose disordered blood supply to the kidneys due to upset circulation in the renal artery (stenosis, atherosclerotic plaque, etc.). A special contrast substance (cardiotrast, and the like) is injected into the aorta (through the femoral artery using a special tube) at the level of branching of the renal arteries.

CATHETERIZATION OF THE URINARY BLADDER

The urinary bladder is catheterized for both diagnostic and therapeutic purposes (taking urine specimens for studies, evacuation of the accumulated urine from the bladder, in disordered urination, lavage of the bladder with disinfectant solutions, etc.). The urinary bladder is usually catheterized by a soft elastic tube which is sterilized and coated with vaseline oil before use.

CYSTOSCOPY

Cystoscopy is the inspection of the urinary bladder by a cystoscope. The procedure is used to inspect the bladder mucosa, to reveal the presence of ulcers, papilloma, tumours, stones, and also to carry out some therapeutic manipulations. Using a special thin catheter, it is possible to take urine specimens from each kidney and to study the renal function (chromocystoscopy). In chromocystoscopy, the patient is given intravenously 5 ml of a 0.4 per cent indigo carmine solution, and then the time of the appearance of coloured urine from the orifice of the ureter is noted by observation through a cystoscope. In a healthy individual, the urine coloured by indigo carmine begins passing from the ureters in 3-5 minutes following the stain administration. The appearance of the coloured urine from the affected kidney will be delayed, or the urine will not be discharged at all.

KIDNEY BIOPSY

Transcutaneous biopsy of the kidneys is now practised at nephrological departments. A piece of the kidney tissue is taken for histological, histochemical or other examinations by a long needle provided with a syr-

inge (for aspiration). The puncture is made on the side of the loin, over the kidney. In order to reveal the causative agent of pyelonephritis, the obtained sample is cultivated on a nutrient media and the microbial sensitivity to antibiotics is determined. Transcutaneous nephrobiopsy is used to establish the character of the tumour, to diagnose chronic glomerulonephritis, amyloidosis, and in some other cases, but always only for special strict indications, because of the great danger of this procedure.

RADIOGRAPHIC STUDIES

Radioisotope nephrography is used to study the kidney function. The patient is given intravenously diodrast or hippuran labelled with ^{131}I. Then, a multichannel unit is used to determine the rate of blood clearance from the labelled preparation (to show the general secretory function of the kidneys) and accumulation of the preparation in the urinary bladder (to show the general urodynamics in the upper urinary tract).

Nephrography is used to study the renal function in chronic glomerulonephritis, tuberculous affection of the kidneys, pyelonephritis, amyloidosis, to diagnose disordered urine outflow from one kidney, and to facilitate differential diagnosis of hypertension (Fig. 105).

Scanning of the kidneys is sometimes used. In this case accumulation of the labelled radioactive preparation (e.g. ^{203}Hg labelled neohydrin) in the kidneys is determined by a special apparatus, gamma-topograph or a scanner. Kidney silhouette is recorded on a paper in the form of a scanogram (Fig. 106). The renal function is assessed by the intensity of accumulation

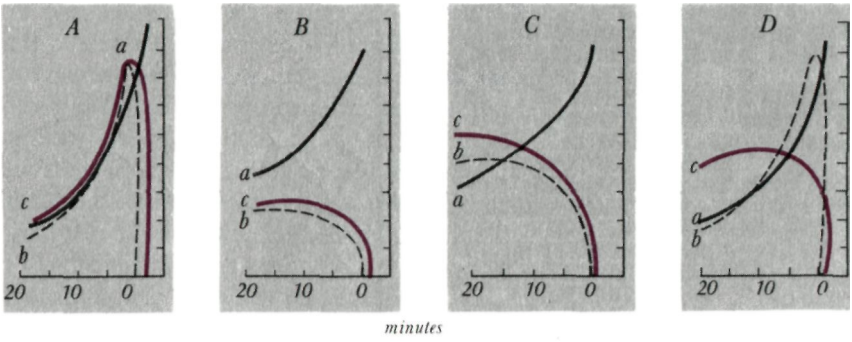


Fig. 105. Radionephrograms in norm *(A),* in chronic glomerulonephritis with upset nitrogen excretory function of the kidneys *(B),* bilateral hydronephrosis (C), chronic pyelonephritis (a stone in the left kidney) *(D).*

a—blood clearance; *b*—radionephrogram of the right kidney; c—radionephrogram of the left kidney.

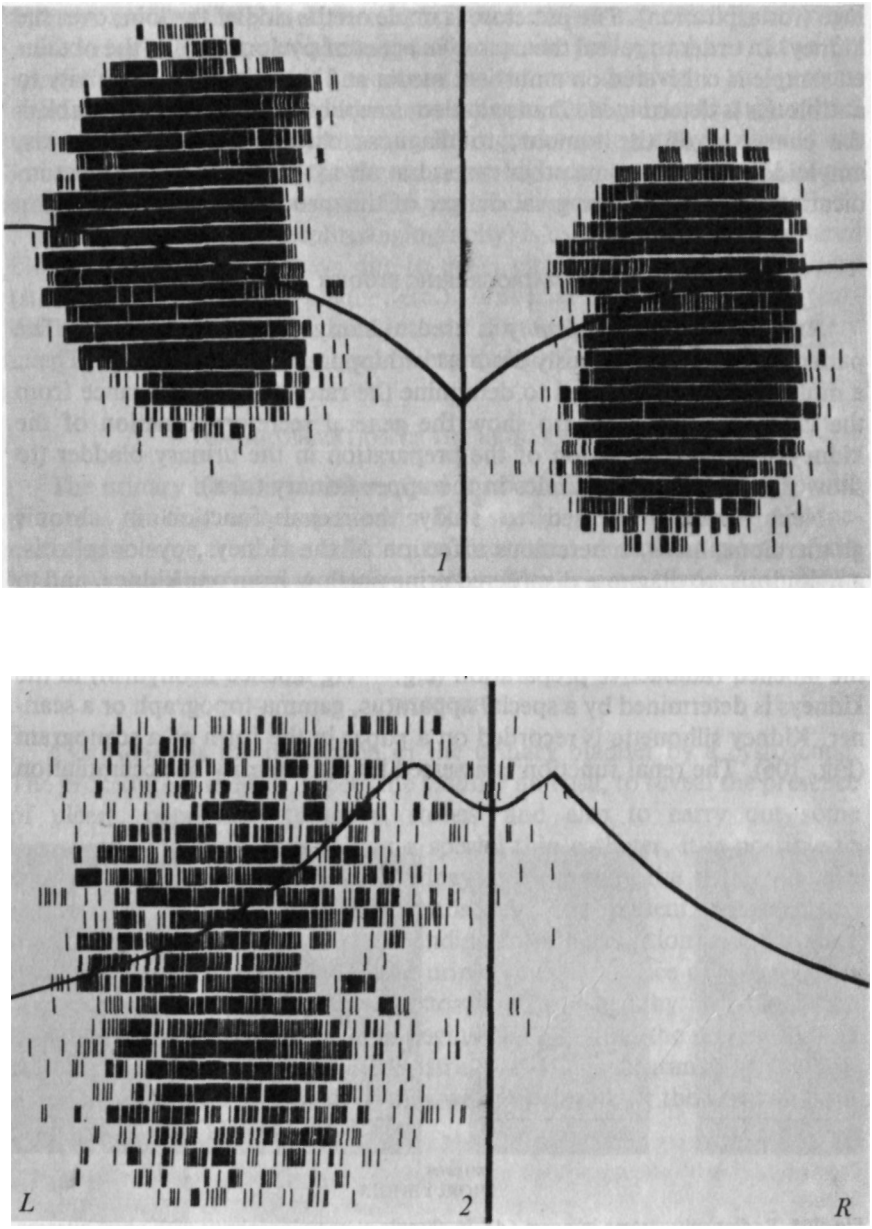


Fig. 106. Scanograms.
1—normal kidneys; *2*—the right kidney affected by hypernephroma.

of the preparation (intensity of the silhouette). The presence of focal accumulation defects indicates tumours, cysts, tuberculous affections of the kidneys, and other destructive processes. The shape and size of the kidneys can be determined from a scanogram.

Echography. Echography (ultrasonography) is widely used in nephrology to determine the size and position of the kidneys, the condition of the renal tissue, to reveal cysts, tumours of the parenchyma, stones in the pelves, etc.

Main Clinical Syndromes

Renal Oedema

Oedema of renal aetiology is quite specific in most cases and can easily be differentiated from oedema of other origin, e.g. cardiac oedema, by the affection of loose connective tissue (the eyelids, the face) rather than of the lower extremities. Renal oedema can develop and resolve quickly. In pronounced cases, oedema is usually uniform over the entire trunk and the extremities (anasarca). Not only the skin but also subcutaneous fat and the internal organs become oedematous. The liver usually becomes oedematous and enlarged, but in renal diseases the enlargement of the liver is usually proportional to enlargement of the other ograns, and is never so pronounced as in cardiac oedema. Greater or lesser amount of fluid is accumulated in the serous cavities, e.g. in the pleural, abdominal, and pericardial cavities. Oedema can be revealed by palpation. It can also be confirmed by the McClure-Aldrich test: 0.2 ml of isotonic sodium chloride solution is injected into the skin on the median surface of a forearm and the time of disappearance of the resulting weal is noted. In a healthy subject, the weal is resolved within one hour. In the presence of a marked oedematous syndrome, the dynamics of oedema during treatment can be better assessed by repeating the test in several days with measurement of girths of the extremities and the abdomen at the same level, by determining the fluid level in the pleural and abdominal cavities, by weighing the patient, and also by determining daily diuresis and water balance of the body (the ratio of the taken and eliminated liquid during 24-hour period).

Oedema, like the general disorder in the water-salt metabolism, arises due to various causes in renal diseases.

1. Diffuse *increased permeability of the capillary wall* is important in development of oedema in many diseases of the kidneys attended by the oedematous syndrome. Great importance in this process is attributed to auto-immune processes and increased hyaluronidase activity of the blood serum, which as a rule, attends many diseases of the kidneys.

Hyaluronidase intensifies depolymerization of hyaluronic complexes of mucopolysaccharides that form the intercellular substance (interendothelial "cement") and the basal membrane of the capillary wall. Porosity of the wall thus increases. The decreased blood serum content of calcium is also important because calcium compounds with protein (calcium proteinate) is a component part of the intercellular "cement"; change in the blood pH (acidosis) is important as well. Because of the generalized increase in capillary permeability, not only water and the dissolved substances, but also much protein pass from the blood to the tissues. Depolymerization of mucopolysaccharides of the intercellular substance of tissues increases the quantity of molecules in the intercellular fluid and raises its colloidal-osmotic pressure.

It follows that the nephrotic syndrome is characterized not only by increased permeability of the capillary wall that facilitates fluid transport to the tissues, but also conditions are provided for fluid retention in the tissues, because the increased colloidal-osmotic pressure of the intercellular fluid accounts for its hydrophilic property: the intercellular fluid easier absorbs water and gives it back with difficulty. The comparatively high protein content in the oedema fluid (transudate) explains the higher density and lower mobility of oedema in the presence of deranged capillary permeability compared with oedema associated with hypoproteinaemia.

In the presence of increased capillary permeability, transudate is accumulated in the subcutaneous fat and other highly vascularized tissues. Serous cavities usually contain low amounts of fluid. Disordered capillary permeability in the glomeruli causes proteinuria and promotes development of hypoproteinaemia. Oedema of this type occurs not only in diseases of the kidneys but in some other diseases as well, e.g. it can also be allergic or angioneurotic (Quincke's oedema), in cases with bee stinging, etc.

2. *Colloidal-osmotic (hypoproteinaemic) mechanism* of oedema development is also important in the nephrotic syndrome. It is manifested in a decreased plasma oncotic pressure due to high proteinuria which usually occurs in such patients, and also in protein passage through the porous capillary walls into the tissues. Oedema of predominantly colloidal-osmotic origin obeys the laws of hydrostatics and tends to develop in the first instance in the lower extremities in walking patients and in the loin of bed-ridden patients. Hypoproteinaemic oedema usually occurs in cases where the blood protein content is less than 35-40 g/l (3.5-4 g/100 ml) and albumins are contained in the quantity below 10-15 g/1 (1—1.5 g/100 ml). Qualitative changes in the composition of the blood proteins are very important. Highly dispersed proteins (albumins) are mainly lost in the urine in nephritis patients; the amount of globulins decreases to a lesser extent. Osmotic pressure is determined by the quantity

of molecules contained in a unit volume of blood plasma rather than by their molecular weight. The loss of highly dispersed albumins, whose specific colloidal-osmotic pressure is about three times that of coarse-dispersion globulins, therefore substantially decreases oncotic pressure of the blood.

Hypoproteinaemic oedema arises not only in the nephrotic syndrome; it can also develop in long starvation (hunger oedema), deranged absorption in the small intestine (disordered absorption syndrome), cancer cachexia, and in some other diseases attended by a decreased protein content in the blood plasma.

3. *Hypernatriaemic oedema* (to be more exact, hypernatriahistic oedema) is explained by the retention of the highly hydrophilic sodium ions in the blood and especially in the tissues. Administration of sodium chloride in large doses can thus cause this oedema. Hypernatriahistia attending diseases of the kidneys is an additional factor intensifying the effect of increased capillary permeability and hypoproteinaemia. Hormone factors, and in the first instance hypersecretion of aldosterone (the adrenal cortex hormone) and antidiuretic hormone (the posterior pituitary hormone), are very important in the accumulation of the sodium ion in some diseases.

Any oedema, irrespective of its intensity, indicates upset osmoregulation in which the hormone link (aldosterone-antidiuretic hormone system) is the decisive one. This hormone system is mainly responsible for maintaining constant volume and ionic composition of the blood. As the volume of circulating blood decreases even insignificantly (which can occur in renal diseases when part of the liquid passes from the blood to tissues due to increased porosity of the capillary wall or decreased oncotic pressure of the blood), the volume receptors, located mainly in the walls of the right atrium and the common carotids, are stimulated. Protective mechanisms respond to this stimulation to maintain the intravascular volume. Aldosterone secretion by the adrenal cortex is intensified to increase sodium reabsorption in the walls of the renal tubules and its concentration in the blood, and to promote its accumulation in tissues. According to some authors, the quantity of aldosterone excreted in the urine during 24 hours increases in the nephrotic oedema from 2-10 to 25-200 μg and more. Sodium excretion in the urine thereby decreases considerably. Secondary hypersecretion of aldosterone that develops as a compensatory reaction, e.g. in oedema or a sudden loss of water from the body, is called secondary hyperaldosteronism as distinct from the primary hyperaldosteronism that occurs in tumours or hypertrophy of the adrenal cortex. Increased sodium reabsorption in the renal tubules is followed by increased reabsorption of water. High concentration of the sodium ions in

the blood (due to its intensified reabsorption in the renal tubules) stimulates osmoreceptors and intensifies secretion of the antidiuretic hormone by the pituitary gland, which in turn intensifies the facultative reabsorption of water in distal tubules still more. If the primary cause of oedema (increased capillary permeability, decreased oncotic pressure of plasma) is still active, fluid is not retained in the blood vessels and continues its passage from the blood to the tissues to intensify oedema.

4. Oedema can occur in *acute anuria* of the kidneys in acute poisoning (e.g. with corrosive sublimate), hypovolaemic reduction of blood circulation in the kidneys (profuse blood loss, shock), and also in the terminal stage of certain chronic renal diseases (retention oedema). But decreased glomerular filtration becomes only important in the presence of other forerunners of oedema rather than an independent factor. For example, in severe renal insufficiency attended by pronounced filtration disturbances, oedema is often absent or even resolved, if any.

It should also be noted that none of the above mechanisms of renal oedema develops independently but becomes only a dominating factor in this or that case.

Nephrotic Syndrome

The nephrotic syndrome (symptom complex) is characterized by pronounced proteinuria, hypoproteinaemia (mainly due to hypoalbuminaemia), hyperlipidaemia (hypercholesterolaemia), and oedema.

The nephrotic syndrome occurs in chronic glomerulonephritis, amyloidosis, malaria, sepsis, tuberculosis, collagenosis, diabetes mellitus, and certain other diseases. Less frequently the cause of the nephrotic syndrome cannot be established immediately, but in most cases a detailed analysis of anamnestic data and a thorough examination of the patient reveal chronic glomerulonephritis. These forms of the nephrotic syndrome occur mostly in children. Cases where the cause of renal dystrophy is unclear are identified as lipid nephrosis.

It is believed that the nephrotic syndrome is caused by metabolic disorders, mostly upset fat and protein metabolism, with subsequent derangement of trophies and capillary permeability in the glomeruli. Protein and lipids contained in large quantity in primary urine of these patients infiltrate the tubular wall to cause drastic dystrophy in the epithelial cells. The auto-immune mechanism is of great significance for the development of the chronic nephrotic syndrome. It has been proved by animal experiments: small doses of nephrotoxic serum provoke nephritis in rabbits; a picture characteristic of the nephrotic syndrome develops on administration of large doses.

Pathological anatomy. The following morphological signs of the nephrotic syndrome develop, in addition to the changes characteristic for the main disease. The kidneys are enlarged ("large white kidneys") and their capsule is easily removed. Histological studies reveal dystrophic changes in the epithelium of the tubules, especially of the convoluted tubules. Lipid deposits can be found in the basal parts of the epithelial cells. The glomeruli are affected by dystrophy; especially specific are changes in podocytes and endothelial cells with which the disordered permeability of the glomerular membrane is associated.

Clinical picture. The main, and often the only complaint of patients is persistent oedema. It is especially pronounced on the face which becomes swollen and pallid, the eyelids are only a narrow slit, and the patient opens his eyes in the morning with difficulty. The legs, the loin, the skin of the abdomen and the hands are also affected by oedema. The oedema is mobile: when the skin is pressed by the finger, a depression remains in it which soon disappears. Fluid is accumulated also in the internal organs and the serous cavities. In typical cases the arterial pressure remains unchanged or even decreased.

As the oedema progresses, diuresis usually decreases and the patient often eliminates only 250-400 ml of urine a day. The specific gravity of the urine is high (1.030-1.040) and it contains much protein, to 10-20 g/l and more. Cases were reported where the urine contained 24 g/1 of protein. Fine dispersed molecules of albumins prevail among protein. It is believed that the increased filtration of the plasma protein through the glomerular capillary wall and also disordered reabsorption of protein molecules by the affected tubular epithelium are important in the aetiology of proteinuria in the nephrotic syndrome. Great quantity of hyaline, granular and waxy casts, and cells of renal epithelium are found in the urinary sediment. The presence of leucocytes and erythrocytes in the urinary sediment is not characteristic for the nephrotic syndrome. Doubly refracting cholesterol crystals are usually found, which are, as a rule, absent in renal diseases proceeding without the nephrotic syndrome.

A long-standing and persistent proteinuria causes protein depletion of the body and a stable reduction of its content in the blood plasma (1.5 and even 2 times). The albumins become especially deficient, and the albumin to globulin ratio, which is normally 1.2-2.0, decreases significantly. The content of α_2-globulins, and also γ-globulins, slightly increases. Proteinuria and hypoproteinaemia (especially hypoalbuminaemia) largely account for oedema that develops in the nephrotic syndrome (see "Renal Oedema"). It has been established that the loss of protein in the urine is aggravated by the renal catabolism of plasma proteins (proteolysis of part of serum protein during its reabsorption in the tubules) and also, probably, by the increased protein loss through the alimentary tract.

Among the constant symptoms are pronounced hyperlipidaemia, in-

creased blood serum concentration of cholesterol (to 13—15 mmol/1, i.e. 2 or 3 times as great), phospholipids, and neutral fat. These changes are probably secondary to upset protein metabolism and hypoproteinaemia. Laboratory studies reveal three characteristic signs of the nephrotic syndrome: proteinuria, hypoproteinaemia, and upset lipid metabolism (hypercholesterolaemia).

The blood clearing function of the kidneys is not substantially affected in the nephrotic syndrome, and azotaemia does not develop for a long time. The main functional renal tests remain normal for a long time, but the tubular secretion can decrease. Biopsy of the kidneys supplies valuable information concerning the nature of the nephrotic syndrome in chronic renal diseases.

Course. If the main disease does not progress, the nephrotic syndrome lasts for years. Oedema and the urinary syndrome intensify at times usually when provoked by an attending infection. Patients with the nephrotic syndrome are sensitive to coccal infection. They often develop recurrent pneumonia and erysipeloid inflammation of the skin. These patients usually died before antibiotics were discovered. Vascular thrombosis is likely to occur in patients with the nephrotic syndrome. The prognosis depends mostly on the main disease and the attending infections.

Treatment. The main disease should be treated. In the presence of pronounced hypoproteinaemia, the patient is prescribed a diet rich in proteins (2-2.5 g/kg body weight without reference to oedema) and poor in sodium chloride. Plasma or concentrated human albumin is given intravenously. Corticosteroids (prednisolone) and immunodepressants (imurane, etc.) are prescribed. If oedema is pronounced, the patient is given diuretics: furantril (furocemid), 0.04 g per os every other or third day, in combination with verosperon (0.075-0.15 g/day per os) to remove oedema. Sanatorium and health-resort therapy in dry climate (Central Asia) is recommended during relative remissions.

Renal Hypertension

Renal arterial hypertension is a symptomatic hypertension caused by the affection of the kidneys or renal vessels and upset renal mechanism of arterial pressure regulation. Among all cases of arterial hypertension, renal hypertension makes about 10-15 per cent.

Many diseases of the kidneys, in the first instance acute and chronic glomerulonephritis, pyelonephritis, nephrosclerosis and various affections of the renal blood vessels are attended by elevated arterial pressure. This is underlain by the important role that the kidneys play in the regulation of arterial pressure. The juxtaglomerular apparatus of the kidneys, which is

an accumulation of special cells at the vascular pole of the glomerulus at the point where the artery nears the proximal end of the distal convoluted tubule, produces renin in the presence of ischaemia of the renal parenchyma. Renin acts on the liver-produced hypertensinogen, which is a fraction of α_2-globulin of plasma, to convert it into angiotensinogen. The latter is converted enzymatically into angiotensin (hypertensin). Angiotensin stimulates hypersecretion of aldosterone, stenosis of arterioles, and increases arterial pressure. The current literature contains reports on the development of renal hypertension which is associated with renal hyposecretion of special hypotensive substances (e.g. prostaglandins).

It should be noted that due to diffuse spasm of arterioles, essential hypertension also provides conditions for atherosclerosis of the arteries, disordered blood supply to various organs, the kidneys included, and hence for the increased secretion of renin (see "Essential Hypertension"). Therefore, at a certain stage of essential hypertension, further elevation of pressure in the arteries depends largely on the renal mechanism. As distinct from hypertension of other genesis, renal hypertension often tends to run an especially rapid and malignant course (in about 20 per cent of cases).

Like any other hypertension, renal hypertension is manifested by some annoying subjective symptoms, such as headache, dizziness, and noise in the ears (see "Essential Hypertension"). Headache is especially severe in marked elevation of the arterial pressure. It is often attended by vomiting, and paraesthesia. As a rule, the work capacity is impaired and sleep deranged. The increased arterial pressure can be determined by feeling the pulse which appears to be tense. More accurately arterial pressure should be measured instrumentally. Both systolic and diastolic pressure should be measured; the latter pressure is sometimes very high. The second sound is usually accentuated over the aorta.

High and persistent hypertension affects the heart. First, the left-ventricular muscle is hypertrophied due to constant overload. This can be determined by the increased apex beat, specific changes detectable by X-rays (rounded heart apex) and electrocardiographically (deviation of the heart's electrical axis to the left, a certain increase in the R_1 wave, and later descent of the S-T_1 segment below the zero line, and the negative or two-phase $T_{1,2}$ wave).

At later stages, dystrophic changes occur in the myocardium because its vascularization lags behind the growth of the muscle weight to account for the deficient blood supply; next, cardiosclerosis develops. At the same time, atherosclerosis of the coronary vessels may develop due to upset lipid metabolism, which is characteristic for arterial hypertension and many other renal diseases attended by the nephrotic syndrome. The coronary disease impairs blood supply to the myocardium to an even greater extent.

Heart pain, like that of angina pectoris often occurs. Further progress of renal diseases can provoke circulatory insufficiency.

Certain acute diseases of the kidneys attended by a rapid and pronounced elevation of the arterial pressure, mainly acute glomerulonephritis, are attended by the condition at which the left ventricle is not hypertrophied enough to compensate for the markedly increased load. Acute ventricular failure can therefore develop. It is manifested by attacks of cardiac asthma and even by a lung oedema.

Renal arterial hypertension involves specific changes in the fundus oculi (renal retinopathy). But these changes, attending kidney diseases, are often due not only to the spasms of arteries and arterioles of the retina but also, in a certain measure, to the upset permeability of retinal capillaries; they also occur during final stages of chronic diseases of the kidneys that end with nephrosclerosis, uraemic toxicosis, and haemorrhagic syndrome.

Certain stenosis of arteries and arterioles of the retina, tortuosity of fine veins of the yellow spot, and flatness of the veins at their crossing with the arteries, with small ampoule-like dilatation before the crossing (Hann-Salus symptom), are observed during the first period (first degree). The patient does not complain of deranged vision; the changes are only transient and functional. Further, due to a continuing spasm and hyalinosis of the arteriolar walls, their lumen narrows, larger arteries become stenosed and tortuous, the veins are compressed by the crossing arteries, and their ampoule-like dilatations before the crossing point become more pronounced (second degree). In the final stage, the arteries and arterioles are highly tortuous and markedly affected by spasms; they resemble silver wires; small veins of the retina are consolidated and sclerosed, they bend at the point of crossing with the arteries and are impressed into the retina to simulate a rupture (the third degree). Greyish-white and yellow foci of oedema and retinal dystrophy and haemorrhages are revealed; the papilla of the optic nerve is oedematous. Foci of dystrophy radiating in the area of the yellow spot often have a stellar shape. Vision is deranged due to dystrophic changes in the fundus oculi and haemorrhages.

It should be noted that the fundus oculi is a very convenient site where fine vessels can be visualized, as well as changes occurring in them and the surrounding tissues (in the retina) during the course of the disease. The study of the fundus oculi is therefore very informative for the diagnosis and prognosis of a renal disease. In certain cases, the patient consults first the ophthalmologist for his impaired vision, because renal diseases can for a long time develop without vivid symptoms. The specific changes in the fundus oculi help in such cases suggest renal pathology (which is later confirmed by the appropriate studies).

Finally, disorders in cerebral circulation with paralysis, deranged sen-

sitivity, dysfunction of the pelvic organs, and also myocardial infarction can develop as a result of arterial hypertension and atherosclerosis.

It follows therefore that in certain kidney diseases, the renal hypertension syndrome can be of primary significance in the clinical picture of the disease and can be decisive for its course and outcome.

Renal Eclampsia

Eclampsia (Gk *ek lampein* to flash) usually develops in acute diffuse glomerulonephritis, but can also arise in aggravated chronic glomerulonephritis and nephropathy of pregnancy. The pathogenesis of eclampsia is largely underlain by increased intracranial pressure, oedema of the cerebral tissue and cerebral angiospasm. Eclampsia in all these conditions usually arises in pronounced oedema and increased arterial pressure. Attacks of the disease are provoked by salted food and excess liquid.

The first signs of approaching eclampsia are often unusual somnolence and flaccidity. These are followed by severe headache, vomiting, temporary blindness (amaurosis), aphasia, transient paralysis, mental confusion, and a rapid rise in the arterial pressure. Convulsions develop unexpectedly, sometimes after uttering a cry, or after a noisy deep inhalation. The convulsions are first strong tonic spasms, which are followed (in 0.5-1.5 minutes) by strong clonic contractions. Less frequently only twitching of some muscles is observed. The face becomes cyanotic, the neck veins swell, the eyes turn aside or roll up, the tongue is bitten, and foam emerges from the mouth. The pupils are dilated and do not respond to light; the eyeballs are firm. The pulse is tense, slow, the arterial pressure increases. The body temperature rises in frequent attacks. Involuntary defaecation and urination often occur.

Attacks of renal eclampsia usually last for a few minutes, rarely for longer time. Eclampsia occurs in some cases as a series of two or three attacks which follow one another. The patient then calms down to stupor, deep sopor or coma; consciousness is then regained. After recovery from the state of stupor the patient sometimes remains in amaurosis (blindness of the central origin) and aphasia (mutism).

This is the classical picture of an eclampsia attack. But it should be-remembered that attacks of eclampsia may also be atypical; they may occur without loss of conciousness or occur in an obliterated form, as a transient aphasia, amaurosis, and mild muscular twitching.

Renal eclampsia should be differentiated from convulsions of other origin. Convulsions in eclampsia are the same as in epilepsy (a congenital or post-traumatic nervous disease). But oedema or other signs of renal in-

sufficiency are absent in epilepsy; attacks of convulsions usually occur in the course of many years. Convulsions develop also in uraemic coma, but the patient has a typical anamnesis in this case (chronic renal insufficiency), signs of uraemic toxicosis, slow (in the course of several days) development of the convulsive state; the character of convulsions is different as well: convulsions develop as slight fibrillary twitchings.

Treatment. An attack of renal eclampsia can be removed immediately by a suboccipital or cerebrospinal puncture with extraction of a small portion of the cerebrospinal fluid: the intracranial pressure decreases and the patient regains consciousness. The extraordinary efficacy of cerebrospinal puncture proves the importance of increased intracranial pressure for the pathogenesis of attacks of renal eclampsia. Phlebotomy and intravenous injection of magnesium sulphate (10 ml of a 25 per cent solution) remove attacks of eclampsia, effectively decrease the arterial pressure and lessen cerebral oedema.

Renal Failure

Renal failure is toxicosis of the body caused by renal dysfunction (self-poisoning). Uraemia is a severe form of renal failure. Renal failure and uraemia occur in acute and chronic cases. Acute uraemia develops in poisoning with nephrotoxic substances (compounds of mercury and lead, carbon tetrachloride, barbiturates, etc.), in transfusion of incompatible blood, profuse haemolysis, and shock. Chronic uraemia develops in the final stage of many chronic renal diseases, such as chronic glomerulonephritis, pyelonephritis, amyloidosis, affections of the renal vessels, tumours of the kidneys, etc.

Pathogenesis. It consists in profound homeostatic disorders. It has been established that products of protein decomposition are accumulated in the blood of patients with uraemia. These are nitrogenous slags, such as urea, uric acid, creatinine, and other guanidines. The content of indican, phenol and other aromatic substances that are formed in the intestine and pass into the blood through the intestinal wall (normally, these substances are eliminated from the blood by the kidneys) increases. Various compounds of sulphur, phosphorus, magnesium, and other substances are accumulated; the ionic equilibrium is upset. Acidosis develops as a result of the accumulation of acid products and disordered production by the kidneys of ammonia that neutralizes the acids. Uraemia is attended by a grave affection of the liver and metabolic disorders.

Acute renal failure and *acute uraemia* develop due mainly to shock and the accompanying circulatory disorder (mostly in the kidneys). Anoxia develops to cause dystrophic changes in the renal glomeruli and tubules. In

other cases, when acute renal failure is due to poisoning or a grave infectious disease, its pathogenesis is largely determined by the direct action of poisons and toxins on the renal parenchyma. In both cases glomerular filtration is deranged, diuresis decreases and oliguria develops; in severe cases anuria may occur. Salts of potassium, sodium, phosphorus, nitrous products and some other substances are retained in the body.

Acute renal failure rapidly develops and the patient's condition becomes grave: vomiting, mental confusion, deranged respiration and upset heart activity are observed. The glomeruli are affected by ischaemia to raise the arterial pressure; oedema develops in anuria. The patient may die unless anuria and azotaemia are removed during the first few days. If the course of the disease is benign, diuresis increases but the concentrating capacity of the kidneys remains impaired for some time; the renal function gradually normalizes and the patient recovers.

Clinical picture. Acute renal failure varies slightly, depending on the character of the main disease. In many cases it proceeds with some general symptoms which make a syndrome. Four stages of acute renal failure are distinguished: (1) *initial stage* lasting from several hours to 6—7 days; its clinical picture is characterized by the main symptoms of the disease (traumatic or transfusion shock, severe infectious disease, poisoning, etc.); (2) *oligoanuric stage* characterized by changes in diuresis (to complete anuria), uraemic toxicosis, and water-electrolyte disorders. Proteinuria, cylindruria, and erythrocyturia are revealed on examination. The oligoanuric stage can end with death of the patient or his recovery. In the latter case, diuresis suddenly or gradually increases (the third or *polyuric stage).* The specific gravity of the urine is low, the concentration of residual products of protein metabolism in the blood decreases, water-electrolyte balance is restored and the pathological changes in the urine disappear. The fourth stage, *recovery,* begins with normalization of diuresis; it lasts from 3 to 12 months.

Development of *chronic renal failure* is determined by the progressive affection of the kidney parenchyma. The latent period of chronic renal failure, when renal dysfunction has no clinical symptoms and can only be revealed by special laboratory methods, and the manifested period, characterized by the marked clinical picture of uraemia, are distinguished.

The *latent period* can only be revealed by special tests carried out for concentrating capacity of the kidneys and cold food and by the Zimnitsky test. The patient's urine is usually of low specific gravity (below 1.017). Variations in specific gravity are only insignificant (isohyposthenuria). The clearance tests reveal disordered reabsorption in the renal tubules and in glomerular filtration. Mild renal dysfunction can be revealed by radioisotope nephrography. It is believed that the first signs of renal failure

in patients with chronic renal diseases only appear when the functioning parenchyma diminishes to at least one fourth of its normal size.

Progressive renal failure is attended by changes in the circadian variations in urination: isuria or nycturia are observed. The concentration and dilution tests reveal significant disorders in the concentrating capacity of the kidneys, pronounced isohyposthenuria (the specific gravity of all urine specimens varies from 1.009 to 1.011, i.e approaches the specific gravity of plasma ultrafiltrate, the "primary" urine). More pronounced disorders in reabsorption and glomerular filtration are determined by the clearance tests and nephrography. Concentration of nitrogenous substances in the blood gradually increases. Residual nitrogen increases several times (its normal content is 14.2-28.5 mmol/l or 20—40 mg/100 ml). Laboratory studies reveal increased concentration in the blood of various products of protein decomposition: urea (3.23-6.46 mmol/1 in norm and 10-15 and more times higher in renal failure), creatinine (0.088-0.176 mmol/1 in norm and 1-1.3 mmol/1 in renal failure), indican (0.68-5.44 μmol/1 in norm). It should be noted that the increased blood indican content is often the first and the most reliable sign of chronic renal failure, because its blood content does not depend on the protein concentration of food and because it is not accumulated in tissues.

Moderately increased concentration of products of nitrogenous decomposition in the blood *(azotaemia)* may have no effect on the subjective condition of the patient for a certain period of time. But later some external changes become manifest and they can be used for the diagnosis of uraemia. Certain symptoms of uraemia depend on partial compensation of renal failure by a more active involvement of the skin, mucosa, and the digestive glands in the excretory processes. Decomposition of the urea (excreted by the mucosa of the air ways and the mouth) to ammonia by the bacteria accounts for the specific uraemic breath. In serious cases, the uraemic breath can be felt by the physician as he approaches the patient's bed. It is believed that the uraemic breath can be felt when the concentration of residual nitrogen in the blood exceeds 70 mmol/1 (about 100 mg/100 ml).

The nitrogenous substances, and in the first instance urea, are liberated by the gastric mucosa and decomposed to form ammonia salts. These salts irritate the mucosa of the stomach and the intestine to stimulate nausea, vomiting (uraemic gastritis), and diarrhoea (uraemic colitis). Irritation of the respiratory mucosa causes laryngitis, tracheitis, and bronchitis. Severe stomatogingivitis develops. The mucosa becomes affected by ulcers and necrosis. Urea crystals (as a white powder) can sometimes be seen on the patient's skin. This is especially noticeable at the orifices of the sweat glands (at the base of hairs). Strong itching develops and the patient scrat-

ches his skin. Poisons accumulated in the blood are also liberated by the serous membranes. *Uraemic pericarditis* is especially characteristic. It can be revealed by auscultating the heart using a stethoscope: the specific coarse pericardial friction can be heard. This friction appears in the terminal period and is a sign of approaching death.

Memory and sleep become deranged due to general poisoning; weakness, dull headache, somnolence, apathy and deranged vision are characteristic. Examination of the fundus oculi reveals narrowed arteries and dilated veins, oedema of the papilla of the optic nerve, and whitish local foci (retinopathy). Development of retinopathy is explained by trophic disturbances due to the vascular spasm of the fundus oculi vessels and uraemic toxicosis which intensifies these changes. The pupils are usually narrowed.

Metabolic disorders are pronounced: the patient develops cachexia; the liver and bone marrow functions are affected by dystrophy; toxic uraemic anaemia develops which is usually attended by leucocytosis and thrombocytopenia. The tendency to haemorrhages develops due to a decreased blood platelet count, disorders in the blood coagulating system and increased capillary permeability (as a result of toxicosis). Haemorrhages of the gastro-intestinal tract, urinary tract, uterus, and the nose may develop. Skin haemorrhages also occur. The body temperature slightly decreases.

Later, toxicosis increases, the patient's consciousness becomes dimmed, and *uraemic coma* develops. Periods of stupor alternate with periods of excitation, hallucinations, and noisy slow breathing with very deep inspirations (Kussmaul's breathing); respiration with alternating periods of hyperpnoea and apnoea (Cheyne-Stokes respiration) occurs less frequently. At the terminal stage the patient is in a deep coma; muscular twitchings occur at times and the patient dies.

There is no universally accepted classification of chronic renal failure at the present time. Three stages are usually differentiated: (1) the initial stage with insignificantly increased residual nitrogen and creatinine and moderately decreased glomerular filtration; (2) pronounced stages (IIA and IIB) with marked azotaemia and electrolyte disorders and (3) terminal stage with a pronounced clinical picture of uraemia.

Main principles of treatment. Patients with acute renal failure should be immediately taken to hospital. Treatment should be begun as early as possible and aimed at eliminating the main aetiological factors (removal of nephrotoxic substances or their detoxication, giving large doses of plasma or blood substitutes for hypovolaemic shock). The electrolyte equilibrium should be corrected simultaneously. Mannitol or furocemid should be given intravenously in the initial functional stage of acute renal failure to restore diuresis. Haemodialysis (artificial kidney) or peritoneal dialysis are necessary in grave cases.

The protein content of the diet is controlled in patients with chronic renal failure. Therapeutic action on the aetiological factor and pathogenic mechanisms should be attempted (antibacterial therapy in pyelonephritis, immunodepressants in chronic glomerulonephritis, etc.). The water-electrolyte equilibrium and acid-base balance are corrected simultaneously. The necessary symptomatic therapy with hypotensive, cardiovascular and other preparations should be carried out. In severe cases, permanent chronic haemodialysis is carried out or the kidneys are transplanted to prolong the patient's life.

Special Pathology

Diseases of the urinary system come among the first in the list of diseases the most frequently occurring. In some cases the kidneys may be the locus of primary pathology. These are comparatively rare congenital abnormalities and genetic nephropathies. Inflammatory affections of the renal parenchyma, such as diffuse glomerulonephritis of infectious allergic nature, pyelonephritis arising in inflammatory processes of the urinary tract (cystitis, pyelitis) due to extension of inflammation onto the renal parenchyma, and focal nephritis in sepsis occur more commonly. The group of metabolic-dystrophic diseases of the kidneys includes their acute affections in various poisonings with nephrotoxic substances, in shock, and also chronic diseases such as amyloidosis and, to a certain extent, nephrolithiasis. The kidneys are often the site of tumours (especially frequently hypernephroid cancer or hypernephroma). Affections of the renal vessels are not infrequent. Traumatic affections of the kidneys often occur in surgery and treatment of urinary diseases.

The other group includes affections of the kidneys that are secondary to diseases of the other organs and systems: essential hypertension, atherosclerosis, diabetes mellitus, gout, collagenosis, general infections, etc.

In many untreated or improperly treated cases, primary or secondary affections of the kidneys cause dystrophic changes in nephrons, development of connective tissue with its subsequent cicatrization and cirrhosis of the kidneys (nephrosclerosis) which is manifested clinically by signs of progressive renal failure (see "Renal Failure").

Diffuse Glomerulonephritis

Diffuse glomerulonephritis is the general infectious allergic disease with predominant affection of the glomerular vessels. Acute and chronic glomerulonephritis are distinguished.

ACUTE GLOMERULONEPHRITIS

Aetiology. Acute diffuse glomerulonephritis usualy develops after acute infectious diseases, such as tonsillitis, scarlet fever, acute respiratory diseases, pneumonia, and otitis. Especially important are diseases caused by group A haemolytic streptococcus, most frequently of type XII. But nephritis can arise also after infectious diseases caused by other bacteria, e.g. pneumococci or staphylococci. Acute nephritis sometimes develops following overcooling, especially in damp weather. Cases were reported of acute nephritis developing after vaccination.

Pathogenesis. Acute nephritis typically arises not during an infectious disease but only following a period of time, usually 2-3 weeks later. Attempts to isolate the streptococcus from the kidney tissue end in failure. Thus, the onset of acute nephritis usually coincides with the period when antibodies to streptococcus are produced. This indicates that acute nephritis is not simply an infectious disease but an infectious allergic disease.

It is suggested that bacterial antigens, that get into the blood during infection, injure the kidney tissue, whose affected proteins act as an antigen to stimulate the production of the corresponding antibodies in the reticuloendothelial system. The antigen-antibody complexes are fixed in the endothelial and epithelial cells of the renal glomeruli and also in the basal membrane of the glomerular capillaries to cause their injury. Both kidneys are always involved in acute diffuse glomerulonephritis and all glomeruli are equally affected. This distinguishes the affection from focal nephritis and confirms its allergic nature.

It is necessary to note that both the glomerular capillaries and vessels of the other organs and tissues are affected in acute glomerulonephritis. Nephritis is thus the general vascular disease. Cases have been described when in the presence of a marked clinical picture of the disease (oedema, hypertension), the urinary symptoms were insignificant or absent. But as a rule, the glomerular apparatus of the kidneys is affected in acute nephritis which is explained by the specific character of their function as the excretory organ.

Pathological anatomy. The kidneys of those who died from acute nephritis are of normal size or slightly enlarged; their colour is brown or greyish-brown. Malpighi corpuscles, in the form of small tubercles, can be seen on section. Microscopy of the renal tissue in the initial stage of the disease reveals enlarged and hyperaemic glomeruli; during further progress of the disease, microscopy reveals ischaemia of the glomeruli due to spasm of the capillary loops, fibrinoid swelling of the capillary walls, proliferation of their endothelium, accumulation of coagulated proteinous exudate in the space between the capillary loops and the glomerular capsule, blood stasis, thrombosis of the capillary loops, and haemorrhages. Pathological changes occur in both kidneys in all cases. Epithelium of the renal tubules is affected less

markedly. Intra- and extracapillary glomerulonephritis is mostly differentiated; depending on the character of the inflammation, glomerulonephritis may be exudative (serous, fibrinous, and haemorrhagic) and productive.

At later stages of the disease, inflammatory phenomena subside in renal tissue, proliferation of endothelium in glomerular loops decreases, and patency of the capillaries is restored.

Clinical picture. The clinical picture of acute glomerulonephritis is quite specific and is determined by the main three syndromes: oedema, arterial hypertension, and changes in the urine (haematuria and proteinuria). The patients would usually complain of oedema, which arise first on the face, under the eyes, and then extend onto the entire body and the extremities. Development of oedema is explained by disordered capillary permeability and aldosterone hypersecretion by the adrenal cortex. Headache and heaviness in the head are frequent symptoms. They are explained by increased arterial pressure and, in some cases, intracranial pressure. Vision can be deranged due to spasm of the retinal vessels and haemorrhages into the retina. Many patients complain of general fatigue and reduced work capacity.

In the presence of a pronounced oedema and massive pleural effusion, and when the heart muscle is overloaded due to markedly increased arterial pressure, patients with acute nephritis suffer from severe dyspnoea, sometimes with attacks of asphyxia (like in cardiac asthma).

The patient with acute nephritis would often complain of dull lumbar pain. The gravity of the disease depends on the degree of oliguria. The diuresis decreases while the patient may have frequent tenesmus. Complete anuria occurs in some cases. If haematuria is marked, the urine looks like meat wastes.

Inspection of the patient reveals his specific appearance: pallid skin, oedematous face, swollen eyelids, and oedema of the trunk. Some patients assume the forced semireclining or sitting position because of pronounced dyspnoea. Renal eclampsia occurs in grave cases. The onset of an eclampsia attack is heralded by increasing arterial pressure and a severe headache.

The extent and the character of oedema can be established by palpation. The pulse of the patient should also be felt. Acute nephritis is characterized by a tense pulse which is sometimes slow. The apex beat is somewhat shifted to the left and increased due to myocardial hypertrophy which soon develops in the presence of arterial hypertension.

Percussion of the chest in the presence of generalized oedema reveals free fluid in the pleural cavity (transudate) and congestion in the lung root region (dulled tympany). The left border of the heart extends beyond the corresponding midclavicular line.

Normal or harsh respiration is heard by auscultation. In the presence of pronounced congestion, dry and moist congestive rales are heard.

Auscultation of the heart reveals bradycardia (due to the reflex transmitted in increased pressure from the aorta onto the vagus nerve through n. depressor).

The first sound is sometimes decreased at the heart apex. If the heart muscle is much overloaded, the gallop rhythm is heard. The second sound is usually accentuated over the aorta due to increased arterial pressure.

X-ray studies of the chest confirm the presence of pleural effusion and congestion in the lung roots. Dilatation and hypertrophy of the left ventricle are clearly determined (the heart apex is rounded). Sphygmomanometry is of great help in establishing a diagnosis. It reveals one of the main symptoms of acute nephritis, i.e. arterial hypertension. Systolic pressure increases to 200-220 mm Hg, but in some cases it is not so high. Diastolic pressure increases to 100-160 mm Hg almost in all cases.

Electrocardiography reveals signs of hypertrophy and overload of the left-ventricular myocardium. The amplitude of ECG waves decreases in pronounced oedema of the trunk.

Changes in the urine are characteristic of acute nephritis. During development of oedema, diuresis usually decreases to oliguria. The urine of patients with acute nephritis usually contains much protein and erythrocytes due to the increased permeability of the renal capillaries. If haematuria is pronounced, urine can be reddish-brown (the colour of meat wastes). Microscopy of the urinary sediment usually reveals the presence of casts (mainly hyaline casts) and cells of renal epithelium. The nitrogen excretory function of the kidneys is usually not affected in acute nephritis. Nitrogenous slags can only accumulate in the blood in serious cases attended by anuria. The clearance tests reveal more or less considerable reduction of glomerular filtration.

The infectious allergic character of acute glomerulonephritis is confirmed by immunological shifts: the content of α_2- and γ-globulins in the blood increases during the acute period.

Acute glomerulonephritis often proceeds without pronounced symptoms which make it difficult to identify it and hence to prescribe the appropriate treatment. But mild and indistinct forms of glomerulonephritis, like acute forms of this disease with classical clinical symptoms, give rise to chronic glomerulonephritis, unless the appropriate therapy is given.

The gravest and even dramatic (Tareev) complication of acute glomerulonephritis is renal eclampsia which occurs in 4—l0 per cent of patients (mostly in children and women). During a convulsive attack, the patient may be heavily contused or his ribs may be fractured. Cases were reported where patients died from cerebral circulatory disorders or lung oedema; true, such cases are rare. Attacks of eclampsia usually leave no consequence. It is interesting to note that eclampsia sometimes serves as a stimulus to a rapid regress of the disease and patient's recovery.

Course. Acute glomerulonephritis usually lasts only a few weeks or months. The first sign of beginning recovery is resolution of oedema and further decrease in arterial pressure. Small haematuria and proteinuria can persist for months following disappearance of the main symptoms. Some patients do not recover completely and the disease becomes chronic.

Treatment. Patients with acute nephritis should be taken to hospital. It is important that the air in the ward should be warm and dry; drafts should be absent. Sodium chloride intake should be restricted to 0.5—1.5 g a day, which promotes resolution of oedema and normalization of arterial pressure. Protein intake should also be slightly decreased (at the expense of meat protein).

Prednisolone and other corticosteroid hormones having anti-allergic and anti-inflammatory properties are efficacious means of pathogenetic therapy of acute nephritis. Rauvolfia is given to control hypertension; furocemid and other diuretics should be given to remove oedema.

Prophylaxis. Hardening of the body and also thorough sanation of the infection foci (carious teeth, chronic tonsillitis, sinusitis, and the like) are required.

CHRONIC GLOMERULONEPHRITIS

Aetiology and pathogenesis. Chronic diffuse glomerulonephritis is a relatively common disease. It is often secondary to the acute form of this disease if the patient is not timely and properly treated. In other patients, chronic glomerulonephritis occurs suddenly, without acute nephritis in their anamnesis, but it can be suspected that the chronic disease was preceded by acute nephritis which however was latent, without manifest symptoms, and therefore not identified in proper time.

Chronic diffuse glomerulonephritis can sometimes be secondary to nephropathy of pregnancy which was not treated properly. Chronic nephritis is one of the three classical forms of Bright's disease.

Great importance is now attached to the auto-immune mechanism in the pathogenesis of chronic glomerulonephritis. Antibodies to altered proteins of the renal tissue are probably formed in patients with the disease, in addition to formation of antibodies to streptococcus. This maintains the inflammatory process in the kidneys and is the cause of chronic progressive course of the disease.

Pathological anatomy. The kidneys are not enlarged, or enlarged only slightly during the first period of the disease, which lasts several years. In the final stage of the disease, the kidneys are markedly diminished in size, their surface is granular, the renal tissue firm (arteriosclerotic kidney). Microscopy in chronic nephritis reveals mostly intracapillary inflammation in the glomeruli with gradual obliteration of the capillary loops and the capsule cavity and conversion of the glomerulus into a scar or a hyaline node. Dystrophic changes occur in the epithelium of the renal tubules.

Clinical picture. Two periods can be easily distinguished in the course of the disease: the first period, when the nitrogen secretory function of the kidneys is impaired only insignificantly *(the stage of renal compensation*), and the second period, during which this function is affected substantially *(the stage of renal decompensation).*

The symptoms of the first period are the same as in acute nephritis. The patient may complain of weakness, more or less persistent headache, vertigo, and oedema. But the gravity of these symptoms is usually less significant than in acute nephritis. The disease is often asymptomatic and is only revealed accidentally, during out-patient examination. Objective studies help establish increased arterial pressure and hypertrophy of the left ventricle. Urinalysis reveals proteinuria and cylindruria. The presence of waxy casts is especially important diagnostically. The urinary sediment usually contains a small quantity (less frequently, considerable quantity) of leached erythrocytes. The blood serum cholesterol content is increased. More or less significant hypoproteinaemia is observed due to permanent proteinuria.

Symptoms of the second, or final, period of the disease develop gradually due to the progressive nephrosclerosis. Low indices of clearance tests (especially insulin and PAH clearance tests) indicate decreased quantity of functioning kidney tissue. The filtration capacity of the kidneys remains unchanged for a long time and only decreases during exacerbation of the process. The concentration capacity of the kidneys gradually decreases along with the decrease in the specific gravity of the urine. Removal of nitrogenous slags from the body is maintained during this period by polyuria (evacuation of much liquid from the body). Nocturnal diuresis increases by the compensatory mechanism as well: it is two thirds one half of the daily diuresis (nycturia). As the concentration capacity of the kidneys is affected to a greater extent, the specific gravity of the urine becomes low and its variations between 1.009 and 1.011 during the course of the day (and under the effect of dry food) are insignificant (isohyposthenuria). The content of nitrogenous slags in the blood of patients (urea, creatinine, indican) increases during this period.

Symptoms of uraemia develop: weakness becomes more considerable, the patient complains of lassitude, headache, nausea, skin itching, unpleasant ammonium breath, and impaired vision. Not long before death, the patients develop uraemic coma.

Course. Chronic nephritis usually lasts from 2-3 to 10-15 years. The first period of the disease (renal compensation) is long; the second period (decompensation) is shorter. During the course of the disease, there occur more or less prolonged periods of exacerbation, which are usually provoked by cooling or infections; exacerbations are followed by remissions.

Several clinical forms of chronic glomerulonephritis are differentiated

by the character of its course and prevailing symptoms. The *nephrotic form* is characterized by oedema, the urinary syndrome, and a comparatively rapid course. The *hypertensive form* is comparatively benign and is characterized by the hypertensive syndrome and insignificant changes in the urine. The *mixed form* is characterized by oedema, changes in the urine, and arterial hypertension. This form of glomerulonephritis is the gravest and comparatively rapid: a pronounced renal failure develops in 2—3 years. Finally, there is the *latent form* of the disease, which is not manifested by oedema or pronounced hypertension; the changes in the urine are only insignificant; renal failure develops at late terms, often only in 10-15 years. As a rule, the patient dies of renal failure.

Treatment. Patients with exacerbations are prescribed bed-rest, a dairy and vegetable diet with restricted sodium chloride (to 1.5-2.5 g/day) and containing at least 1 g/kg protein. The daily protein intake in the nephrotic form and hypoproteinaemia should be slightly increased. Foci of chronic infection (carious teeth, tonsillitis, etc.) should be treated. Infectious foci are treated with antibiotics. Good effect in the treatment of exacerbated nephritis (nephritic form of diffuse glomerulonephritis) is attained with prolonged use of chloroquine diphosphate (in the absence of marked hypertension or azotaemia). The course of treatment continues for several months. Stable clinical remission and even recovery of patients can sometimes be obtained with this therapy.

Symptomatic therapy in hypertensive and oedematous forms of chronic nephritis includes hypotonics (reserpin) and diuretics (hypothiazide, furocemid). Sanatorium therapy is often very helpful to patients with hypertensive and nephrotic forms of glomerulonephritis with compensated renal function.

Control of azotaemia is important in the treatment of uraemia. The intake of animal protein (meat) should be limited to 18-30 g/day. Broad spectrum antibiotics and also sour milk products (yoghourt, sour milk) are given to inhibit the putrefactive process in the intestine. In the absence of tendency to oedema, ample liquid is indicated. Group B vitamins, ascorbic acid, glucose, repeated blood transfusions, gastric lavage with sodium hydrocarbonate, sodium hydrocarbonate enema are used to control toxicosis. Peritoneal dialysis and haemodialysis (artificial kidney) are more effective means to control uraemic toxicosis. These means do not remove the cause of uraemia but only prolong the patient's life. More prospective treatment of severe forms of chronic nephritis is transplantation of the kidneys.

Prophylaxis. Prophylaxis consists in timely treatment of acute and chronic focal infections (tonsillitis, sinusitis, carious teeth, paradontosis, etc.). Patients with chronic glomerulonephritis should be regularly inspected.

Toxic Kidney

Toxic kidney (acute nephrotic syndrome, acute nephrosis, necronephrosis) occurs in acute infectious and toxic diseases, such as typhus, malaria, influenza, ingestion of some nephrotoxic substances (corrosive sublimate, carbon tetrachloride), in transfusion of incompatible blood, massive burns, and some other cases.

Pathological anatomy. In milder cases, insignificant dystrophy of epithelium of the proximal tubules occurs in the form of opaque swelling and fat infiltration in the tubular cells. In severe cases, the kidneys are slightly enlarged and flaccid. In poisoning with corrosive sublimate, the kidney is first red (large red kidney) due to pronounced plethora. Its vessels are then affected by the spasm and the kidney contracts (small white kidney). Histology reveals proteinous dystrophy and necrosis of the tubular cells and their desquamation; the glomeruli are often affected as well (acute necronephrosis).

Clinical picture. Symptoms of the disease vary greatly. Mild forms are practically asymptomatic; protein can only be detected in the urine. Febrile albuminuria occurring in infectious diseases can be used as an illustration. In severe forms of the disease, the urine excretion is upset, and oliguria develops. Hypertension and oedema are absent in typical cases. The urine is concentrated and its specific gravity is high; it contains protein, various casts, erythrocytes, cells of renal epithelium, and leucocytes. Renal dysfunction is aggravated by the disordered haemodynamics which attends shock (e.g. in burns, injuries). Anuria attends most severe cases; nitrogenous slags are accumulated in the blood. The patient dies within a few days unless excretion of urine is not restored.

Treatment. The main disease which is aggravated by the kidney affection should be treated. If oliguria or anuria persists, peritoneal dialysis or haemodialysis are indicated to prevent uraemia.

Amyloidosis of the Kidney (Amyloid Kidney)

Renal amyloidosis (amyloid nephrosis, amyloid dystrophy of the kidneys) is a manifestation of the general disease, amyloidosis.

Aetiology and pathogenesis. Congenital (hereditary), primary, and secondary congenital amyloidosis are distinguished. Secondary amyloidosis develops in the presence of pronounced protein metabolic disorders, mostly in patients with chronic inflammatory diseases such as tuberculosis, osteomyelitis, or bronchiectasis. Less frequently amyloidosis develops in deforming polyarthritis, lymphogranulomatosis, and some other diseases. It is believed that in all these diseases, in connection with chronic action of infection and toxins, and also decomposition of tissues and leucocytes, synthesis of proteins is distorted in the reticuloendothelial system. The auto-immune mechanism is actuated at a certain stage, and the production of antibodies to the altered own proteins is initiated. The antigen-antibody complexes, in the form of a specific firm amyloid substance, which is a combination of globulin and mucopolysaccharides, are deposited in various organs and first of all in the walls of fine vessels and capillaries under the argyrophilic membrane, under the tunica propria of the glands, and in the reticular stroma of various organs. Metabolism in

the adjacent cells is upset due to deposition of amyloid. The cells and other tissue elements become compressed and atrophied. Genetically determined amyloidosis is the result of congenital defects of the enzyme systems responsible for the protein synthesis. Aetiology of sporadic primary amyloidosis is uncertain.

Pathological anatomy. Insignificant changes are found in the spleen, kidneys, liver, adrenal glands, and the gastrointestinal tract (less frequently in lymph nodes and other organs) in amyloidosis. Amyloid kidneys are enlarged, consolidated, and grey ("large fatty kidney"). Histology reveals amyloid grains under the argyrophilic membrane of the arteries and capillaries. Capillary loops become obliterated, the glomeruli are replaced by amyloid grains or connective-tissue scars. Dystrophic changes in the tubular epithelium are also observed. Amyloid-affected (contracted) kidney is the result of a severe process.

Clinical picture. The clinical picture of all types of amyloidosis is the same. The clinical picture of secondary amyloidosis is largely determined by the main disease (pulmonary tuberculosis, osteomyelitis, etc.) and also (in all types of amyloidosis) by the degree of affection with amyloidosis of the other organs, e.g. the gastro-intestinal tract, the liver, the heart, and other organs and systems. Amyloid kidney usually occurs with the nephrotic syndrome (see "Nephrotic Syndrome"), which has its effect on the clinical picture of the disease. In the initial period of the disease the patient's general condition is not affected. The study of the urine can only reveal proteinuria (to 10—15 g/l). As distinct from a "purely" nephrotic syndrome, the urine contains not only albumins but also globulins. Single casts (hyaline, granular, waxy, epithelial cells, leucocytes) can be found in the urinary sediment. The erythrocyte content is usually low, but some patients have a pronounced nephrotic syndrome with typical changes in the urine.

The blood study reveals hypoproteinaemia with a specific prevalence of globulins (the albumin to globulin ratio decreases to 1.0 and more), and with the prevalence of α_2- and γ-globulins. Hypercholesterolemia may also occur.

The differential diagnosis between amyloid kidney and other chronic diseases of the kidneys is often facilitated by the test with intravenous administration of Congo red. The method with subcutaneous injection of 1 ml of a 1 per cent methyl blue solution is commonly used. One-hour specimens of the urine are taken during 5 or 6 hours following administration. Normally, all specimens should be coloured green. In the presence of amyloidosis, the colour changes insignificantly or does not change at all. But negative tests with Congo red or methylene blue do not rule out the presence of amyloidosis because the degree of affection may be insufficient to ensure reliable retention of the dye. An accurate diagnosis of amyloidosis can only be established by the results of nephrobiopsy.

Persistent oedema develops at later periods of the disease. Despite the affection of the renal vessels arterial hypertension is a rare symptom in amyloidosis. Glomerular filtration in patients with amyloid kidney becomes upset during the early period. At the final stage, a picture of pronounced renal failure arises; it is characterized by azotaemia and uraemia, from which the patient usually dies. Less frequently the patient dies of cachexia or other causes.

Treatment. Treatment of secondary amyloidosis can only be successful if the main cause of the disease is removed before severe changes have taken place in the organs, in the kidneys in the first instance. Treatment includes a protein-rich diet (provided the nitrogen-excretory function of the kidneys is satisfactory) and containing limited quantity of sodium chloride; the therapy also includes vitamins and control of oedema and azotaemia (in the presence of renal failure).

Prophylaxis. It consists in timely revealing and treating chronic inflammatory processes and purulent diseases to which amyloidosis is secondary.

Nephrolithiasis

Calculi are formed in the renal pelves in nephrolithiasis. The chemical composition of calculi is quite varied. They usually contain phosphates (calcium and magnesium salts of phosphoric acid). Less frequently calculi consisting of salts of oxalic acid (oxalates), uric acid (urates), and carbonic acid (carbonates) are encountered. Calculi may contain proteins, xanthine, cystine, and sulphonamide.

Aetiology and pathogenesis are uncertain. But it has been established that formation of calculi is stimulated by the infection of the urinary tract, injuries to the kidneys, and haemorrhages into the renal tissue, urinary congestion, and some avitaminoses (A, D). Metabolic disorders (hyperparathyroidism) and sharp changes in the pH of the urine also promote calculi formation.

It is believed that precipitation of salts from the urine and calculi formation occur around an organic "nucleus" which may be desquamated cells of pelvic epithelium, accumulation of leucocytes, a blood clot, etc. But salts may precipitate if their concentration in the urine is increased or their solubility decreases due to changes in the pH of the urine, or if the concentration of the so-called protective colloids in the urine, which ensure stability of supersaturated solutions, decreases. For example, concentration of the uric acid in the urine is usually 15-20 times higher than its solubility in water.

Clinical picture. The disease is characterized by attacks of nephrolithiasis (renal colic) which are followed by interparoxysmal periods.

Most patients do not complain of anything in the *interparoxysmal* period. Only dull pain in the lumbar region occurs in some of them. The Pasternatsky symptom is as a rule positive. The study of the urine sometimes reveals transient haematuria; salt crystals are often found.

The first sign of the disease is usually an *attack of renal colic,* which develops during the passage of a calculus via the ureter. The attack occurs suddenly, often after jolting or long walking. The pain is localized in the lumbar region with radiation downward, by the course of the ureter, and into the sex organs. The pain is very severe and the patient is restless; he changes his posture continually. Pain intensity may lessen for a short time but then it intensifies even to a greater extent. The attack is attended by frequent and painful urination and various reflex symptoms (nausea, flatulence of the abdomen, retained stools). Erythrocytes and protein are found in the urine. The attack ends when the calculus passes into the urinary bladder. Sometimes the calculus passes the urethra and is excreted. Attacks recur at various intervals, from several attacks during one month to one during many years.

In the presence of typical attacks of renal colic, it is easy to diagnose nephrolithiasis. But it is sometimes difficult to differentiate renal colic in the right side from an attack of pain occurring in cholelithiasis. It should be remembered that pain in attacks of renal colic radiates downwards, whereas in attacks of hepatic colic it radiates upwards, into the right shoulder, shoulder blade, and the diuretic symptoms are absent. An attack of hepatic colic may end with jaundice.

Diagnosis in remission can be facilitated by X-ray examination (pyelography). The calculus can rarely be revealed on a survey X-ray picture of the kidneys (Fig. 107). Oxalates, phosphates, and carbonates give an intense shadow on the X-ray patterns.

Course and complications. Long-standing presence of concrements in the renal pelvis has its specific effects: pyelitis (inflammation of the renal pelvis) usually develops, which can later transform into pyelonephritis (see "Pyelonephritis", below).

If a calculus is retained in the ureter to obliterate its lumen, the renal pelvis becomes distended by the accumulated urine to cause hydrops of the kidney (hydronephrosis) which causes future atrophy of the renal tissue. Pyonephrosis (acute purulent inflammation of the pelvis with involvement of the kidney tissue) develops if urine is infected. Pyonephrosis is characterized by a grave general condition of the patient, hectic fever with profuse sweating, dull pain in the corresponding side of the loin, neutrophilic leucocytosis with shift to the left, and markedly increased ESR.

Treatment. All measures should be taken to remove spasm and pain in

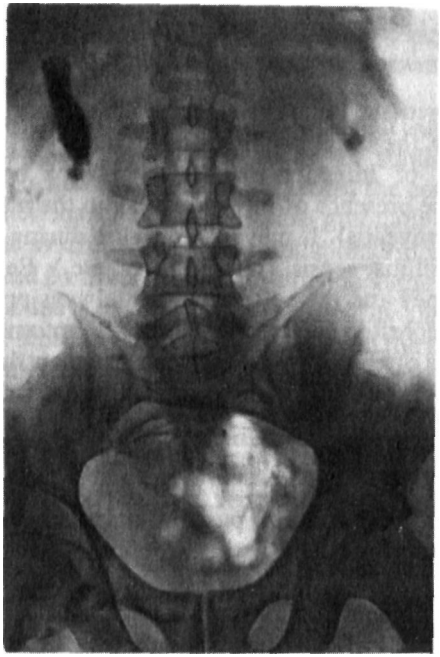


Fig. 107. Stones in both kidneys (scout radiograph).

attacks of renal colic. A hot-water bottle should be placed on the loin and atropine given subcutaneously. Hot water baths are also helpful. Procaine block in the lumbar region is given.

In the interparoxysmal period patients are recommended to drink much liquid. In the presence of urates, alkaline mineral water is desirable (Borzhomi, Essentuki mineral water). Great importance is given to the diet. Food rich in calcium chloride (milk, curd cheese, potatoes) and other substances that compose stones should be taken in limited quantity. In the presence of oxalates, green lattuce, beans, tomato and other foods containing oxalic acid should be excluded from the diet. If urates are present, meat, fish and foods rich in purine bases should be ruled out.

If small stones are found in the pelvis, long walks, ample liquid intake, and antispasmodics containing essential oils (enathine, cystenal) should be prescribed to stimulate the excretion of the stones. If pyelonephritis joins the process, antibiotics and nitrofuranes should be given. Infected large stones should be removed surgically. This, however, does not eliminate the cause of stone formation and they can be formed again.

Pyelonephritis

ACUTE PYELONEPHRITIS

Aetiology and pathogenesis. Acute pyelonephritis arises as a result of infection spreading from the renal pelvis onto the kidney tissue in acute pyelitis, or as a result of infection of the kidney or its pelvis via haematogenic route in the presence of infectious foci in the patient's body (chronic tonsillitis, osteomyelitis). It may also develop during acute infectious diseases (acute tonsillitis, sepsis, typhoid fever, etc.). Penetration of the bacteria into the kidney and the pelvis does not always provoke acute pyelonephritis or focal nephritis: bacteriuria without symptoms of involvement of the renal tissue is often observed. Difficult urine outflow from the kidney (stone in the ureter, twisting of the ureter) stimulates development of pyelonephritis.

Pathological anatomy. The kidneys are slightly enlarged, the mucosa of the renal pelvis is inflamed and oedematous, ulceration is possible. If urine outflow is obstructed, the pelvis contains pus. Inflammatory infiltration of the renal tissue develops and purulent foci can be found in some parts of the kidney.

Clinical picture. The patient's condition is grave: high irregular fever, chills, dull lumbar pain. If inflammation spreads over onto the urinary bladder and the urethra, the patient feels tenesmus and sharp pain during urination.

Study of the urine reveals pyuria and bacteriuria. In complete obstruction of the ureter and unilateral affection there may be no changes in the urine. Obliterated forms of acute pyelonephritis may also be observed (usually in the presence of grave general diseases). In such cases the kidney affection can only be suspected from the urinalysis.

Treatment. Antibiotics, sulpha and nitrofuran drugs (furadonin) are recommended.

CHRONIC PYELONEPHRITIS

Aetiology and pathogenesis. Pyelonephritis often arises in patients with chronic pyelitis due to transition of the inflammatory process from the renal pelvis onto the renal tissue. Nephrolithiasis facilitates fixation of the infection in the pelves and its spreading onto the renal tissue. Chronic pyelonephritis is usually caused by conventionally pathogenic flora, intestinal escherichia; less frequently the disease is provoked by enterococcus, Proteus, or other infection. As infection spreads from the renal pelvis onto the renal parenchyma, the papillae are first affected, and then the

medullar and cortical layers of the kidney. The kidney contracts as a result. The process is often unilateral. If both kidneys are involved, the extent of affection may differ.

Clinical picture. Involvement of the renal tissue in the process alters the clinical picture of pyelitis to make it similar to that of chronic glomerulonephritis: hypertension develops, the concentrating and nitrogen excreting functions of the kidneys are gradually deranged, and uraemia develops. But as distinct from chronic glomerulonephritis, pyelonephritis is characterized by involvement of only one kidney or asymmetrical affection of the kidneys. This can be revealed by intravenous or retrograde pyelography, separate study of the urine from the right and left kidneys obtained by catheterization of the ureters, and also by separate studies of some substances excreted by the kidneys. Clearance tests are useful, since they can reveal early signs of involvement of the distal tubules by the delayed excretion of phenol red and decreased excretion coefficient. Radiographic methods, such as renography and scanning, are also used for the purpose.

Pyelonephritis is characterized by the signs of infectious inflammation of the renal pelves, i.e. by the presence of bacteriuria, leucocyturia (especially the presence of active leucocytes known as Sternheimer-Malbin cells in the urinary sediment), and also deformation of the renal pelves as revealed by pyelography. Bacteriological study of the urine is of great significance: (cultivation of the urine on a nutrient media, and determination of bacterial sensitivity to antibiotics). It should be remembered that urine specimens from women should only be taken by catheterization of the bladder. Differential diagnosis is facilitated by puncture biopsy of the kidneys.

At the terminal stage, due to involvement of both kidneys and development of nephrosclerosis, all functional tests for kidneys are not informative. Death of patients is in most cases caused by uraemia.

Treatment. Infection is treated by antibiotics, sulpha drugs, and nitrofuran derivatives. Symptomatic therapy is given to control hypertension and azotaemia (at the terminal stage).

Chapter 9

DISEASES OF THE BLOOD

Methods of Examination

Inquiry

Complaints. Some general complaints, such as weakness, fatigue, vertigo, exertion dyspnoea, palpitation, and loss of work capacity can be symptoms of anaemia. But the same symptoms are characteristic of leukaemia and myeloid hypoplasia (aplasia). In acute and profuse haemorrhage (e.g. gastro-intestinal), the patient develops acute weakness, vertigo, and syncope.

Many diseases of the blood system are attended by *fever*. Temperature elevates to subfebrile in haemolytic and vitamin B_{12} deficiency anaemia, which is explained by the pyrogenic effect of the erythrocyte decomposition products. Subfebrile temperature can be observed in other types of anaemia due to compensatory intensification of basal metabolism. Moderate and high temperatures often occur in acute and chronic leucosis, especially in leukaemic forms due to intense decomposition of leucocytes, during which great quantity of pyrogenic purine bases are released. This also explains increased sweating of leukaemia patients. And finally, elevated temperature may be the result of necrotic-ulcerous processes and concurrent secondary infections, especially in acute leucosis, in the terminal stage of chronic leucoses, and also in myeloplastic syndrome (panmyelophthisis, agranulocytosis). Fever in lymphogranulomatosis is undulant, with gradual (in the course of 8-15 days) elevation and lowering of temperature.

The patient often complains of *skin itching*. Intense itching in lymphogranulomatosis can be the first symptom of the disease, which develops long before the other symptoms of the disease appear. Skin itching is also characteristic of erythraemia and chronic lympholeukaemia.

Patients with many diseases of the blood system complain of *poor appetite* and loss of weight. Wasting is especially pronounced (cachexia) in chronic leucoses and malignant lymphoma, e.g. in lymphogranulomatosis, lymphosarcomatosis, etc. Vitamin B_{12} deficiency anaemia is characterized by burning sensation in the tip and edges of the tongue. Iron deficiency anaemia, especially the so-called early and late chlorosis, is characterized by perverted taste: the patient readily eats chalk, clay, earth, coal (pica chlorotica). The olfaction changes as well: the patient finds pleasure in smelling ether, petrol, and other substances with unpleasant odour.

Haemorrhagic diathesis, myeloaplastic syndrome and leucosis are attended by *increased bleeding*. Haemorrhagic eruptions on the skin and mucosa develop spontaneously or due to insignificant causes (pressure, mild contusion). Bleeding from the nose, gums, gastro-intestinal tract, lungs, kidneys, and the uterus also develop. Slightest injuries to the skin and mucosa stimulate prolonged bleeding in haemophilia and in overdosage of anticoagulants.

Diseases with intense proliferation of cells of the bone marrow and its hyperplasia (e.g. acute leucosis, chronic myeloleucosis, erythraemia) are often attended by pain in the bones, especially in flat bones. The pain can be spontaneous, but it becomes especially pronounced, when pressure is exerted on the bone or it is slightly tapped over. Acute leucosis is often attended by pain in the throat during swallowing because of developing necrotic and ulcerous tonsillitis.

Many diseases are manifested by *severe pain in the left hypochondrium* due to involvement of the spleen. The spleen is quickly enlarged and its capsule is overdistended to cause dull pain in cardiac decompensation and thrombosis of the splenic vein. Pronounced enlargement of the spleen, e.g. in chronic myeloleucosis (and in some forms of liver cirrhosis), is attended by the feeling of heaviness and distension in the left hypochondrium. Sharp pain develops in perisplenitis. It is intensified during deep breathing and coughing. But the most severe pain develops in massive infarction of the spleen, torsion of the vascular-ligamentous bundle (if the spleen is mobile) and spleen rupture. If enlargement of the spleen is significant, it may be ruptured by a slight injury.

Considerable enlargement of the liver, e.g. due to myeloid or lymphoid metaplasia in chronic leucosis, can be the cause of a subjective *feeling of heaviness and pain in the right hypochondrium*. Right hypochondriac pain of the colic type is characteristic of haemolytic anaemia. It can also be caused by pigmented stones in the gall bladder and bile ducts that are formed due to pronounced hyperbilirubinaemia and hypersecretion of the bile pigment.

History of the present disease. When inquiring the patient it is necessary to obtain information concerning his general condition in the period preceding the onset of the present disease and also the conjectured causes of the disease. It is necessary to establish the time of the appearance of the symptoms, to study thoroughly the dynamics of the disease, to establish if the patient had his blood examined in the past, and the results of these studies. It is also necessary to find out if the patient was treated for the present disease and the results of this treatment.

Anamnesis. When collecting the anamnesis, it is necessary to remember that improper way of life, insufficient time spent in the open air, inade-

quate nutrition and vitamin deficit can be the cause of anaemia. Acute and chronic industrial poisoning with mercury salts, lead, phosphorus and other noxious substances, and also exposure to radiation due to neglect of safety regulations, often become the cause of affection of the haemopoietic system.

Past medical history can be quite valuable to establish the aetiology of the present disease. Diseases of many organs that can be complicated by obvious or latent haemorrhages (e.g. tumours or ulcers of the gastrointestinal tract, bronchiectasis, pulmonary tuberculosis, etc.) can be the cause of anaemia. Atrophy of the gastric mucosa and removal of the stomach or even its partial resection can impair assimilation of iron and vitamin B_{12}, which are prerequisites for normal erythropoiesis. Chronic diseases of the liver are often accompanied by the haemorrhagic syndrome due to upset production of some coagulating factors, e.g. prothrombin and fibrinogen. Severe anaemia may develop against the background of chronic diseases of the kidneys attended by renal insufficiency. Prolonged uncontrolled intake of medicinal preparations without doctor's prescription (amidopyrin, butadione, chloramphenicol, sulpha drugs, cytostatics, etc.) can inhibit the function of the bone marrow and provoke haemolytic or aplastic anaemia and the haemorrhagic syndrome.

Some diseases of the blood system can be hereditary. These are haemolytic anaemias and haemophilia. It is therefore necessary to inquire the patient about his relatives, paying special attention to the presence in them of signs of anaemization or increased tendency to haemorrhages.

Physical Examination

INSPECTION

Inspection reveals the *general condition of the patient* and his *consciousness.* Many diseases of the blood system are characterized by a very grave condition and loss of consciousness at their terminal stages. These are progressive anaemia, myeloid aplasia, and leucoses.

The skin and mucosa should be inspected at diffused daylight. Their colour is important: anaemia is characterized by *pallor of the skin and visible mucosa,* the hue differing in various types of anaemia. For example, the skin of patients with juvenile chlorosis is "alabaster" pallid, sometimes with a greenish hue. The skin of patients with vitamin B_{12} deficiency is slightly yellowish and waxy. The yellow hue of the skin and visible mucosa are more pronounced in haemolytic anaemia. It should be remembered that a mild yellow hue can be easier revealed on the sclera. Pallid skin does not always indicate anaemia and can also be due to special anatomic properties of the skin (deep vascularization), spasm of the peripheral vessels

(collapse, nephritis), and some other factors. Moreover, pallor of the skin can also be masked by its hyperpigmentation (tan due to exposure to the sun). A more informative sign is therefore pallor of the mucosa. Anaemization can easier be revealed by inspecting the conjunctiva of the upper and lower eyelids. In chronic leucoses the skin becomes greyish. Erythraemic patients have "plethoric" cherry-red skin, the colour being especially marked on the face, the neck, and the hands.

Haemorrhagic spots of various size and shape (from petechia and ecchymoses) develop on the skin and mucosa of patients with haemorrhagic diathesis; large haemorrhagic spots are called bruises. Haemorrhagic lesions are first red but as haemoglobin converts into biliverdin, bilirubin or its other coloured products of oxidation, the colour changes to cherry-blue, green, and yellow (before the ecchymosis resolves). In contrast to inflammatory rash and telangiectasia, haemorrhagic spots do not disappear when they are pressed upon.

Trophies of the skin is also important. The skin is dry and sometimes scaling in patients with iron deficiency anaemia. Hairs become brittle and their ends break.

Changes characteristic of some diseases of the haemopoietic system can be revealed during inspection of the mouth. Pronounced atrophy of the tongue papillae is characteristic of vitamin B_{12} deficiency anaemia: the tongue surface becomes smooth, as if varnished (Hunter's glossitis). Intense caries of the teeth and inflammation of the mucosa round dental necks (alveolar pyorrhoea) often occur in patients with iron deficiency anaemia. Nectoric ulcerous tonsillitis and stomatitis are frequent symptoms of acute leucosis.

Regional swelling on the neck, above the clavicles, in the armpits and the groin, less frequently swelling of other location can be revealed by inspection of patients with certain forms of leucosis. This is explained by a considerable enlargement of the corresponding lymph nodes that become palpable (see below). The left part of the abdomen is distended in considerable enlargement of the spleen (e.g. in chronic myeloleucosis), which can also be confirmed by palpation.

PALPATION

Patients suspected for leucosis or some forms of anaemia should be palpated to examine the bones: palpation of flat bones or epiphyses of tubular bones (and also tapping over them) is painful in the presence of marked hyperplasia of the bone marrow.

Palpation of the *lymph nodes and the spleen* is however more informative. Enlargement of lymph nodes is most pronounced in lympholeucosis, lymphogranulomatosis, and lymphosarcoma. These diseases

are characterized by regular and multiple affection of the lymph nodes. The lymph nodes of only one group are first affected, but later other groups become involved too (both surface and deep nodes of the mediastinum and the abdominal cavity). It should be remembered that lymph nodes can be enlarged not only in diseases of the blood system but also in some other diseases, such as tularaemia, tuberculosis, cancer metastases, etc.

Enlarged lymph nodes in leucoses and malignant lymphomas are painless, they never fuse with the skin, do not suppurate or form fistulae, as distinct from affections of other aetiology (e.g. in tuberculosis). The nodes are pasty and elastic in lymphoid leucosis; in lymphogranulomatosis, and especially in lymphosarcoma, they are firm and fuse into conglomerates, sometimes as large as 15-20 cm in diameter.

The spleen should be palpated with the patient in the recumbent position or on his right side. In the former case the patient should lie on a low pillow, the arms and the legs being stretched. If the patient lies on his right side, his head should be slightly down, the left elbow bent and resting freely on the chest; the right leg should be stretched and the left knee bent and drawn up to the chest. The prelum is relaxed to a maximum. In this position, the spleen is displaced anteriorly to facilitate its palpation even if it is slightly enlarged. The physician sits on the right side of the patient and faces him. The left hand of the physician is placed on the left part of the patient's chest, between the 7th and 10th ribs in the axillary lines and slightly presses on the chest to limit its respiratory movements. The physician's right hand is placed on the anterolateral surface of the patient's abdominal wall at the edge of the costal arch, at the point of junction of the costal arch and the 10th rib, or (if preliminary inspection and percussion suggest enlarged spleen) at the antero-inferior edge of the spleen. During expiration the physician moves his hand gradually into the abdomen to form a pouch and the patient is asked to make a deep inspiration. If the spleen is palpable (and provided the palpation is performed correctly), it is displaced during inspiration by the descending diaphragm to come in contact with the palpating fingers of the right hand and to slip over them. This manipulation should be repeated several times in order to examine the entire palpable edge of the spleen. The size, shape, sensitivity, density, mobility, and configuration of the anterior edge of the spleen should be determined by palpation.

One or several notches on the anterior edge of the spleen can be palpated if its enlargement is considerable. The notches are used to identify the spleen (to differentiate it from other organs, e.g. from the left kidney). The anterior surface of the enlarged spleen emerges from under the costal arch and also becomes palpable.

A normal spleen is impalpable. It can only be palpated in rare cases of

extreme ptosis, and more frequently in enlargement of the organ. The spleen is enlarged in some acute and chronic infectious diseases (enteric and recurrent fever, Botkins's disease, sepsis, malaria, etc.), in liver cirrhosis, thrombosis or compression of the splenic vein, and also in many diseases of the haemopoietic system (haemolytic anaemia, thrombocytopenic purpura, acute and chronic leucosis). A considerable enlargement of the spleen is called splenomegaly. The greatest enlargement of the spleen is observed at the terminal stage of chronic myeloleucosis: it often occupies the entire left part of the abdomen, while its lower pole is found in the small pelvis. After the size of the spleen is determined by palpation and its contours marked on the skin of the abdomen by a dermograph, a skin test is sometimes performed with subcutaneous injection of 1 ml of a 0.1 per cent adrenaline solution (Frey test) by which the contractile function of the spleen is determined. In most cases the smooth muscles of the spleen contract in response to adrenaline to diminish 2-3 times. The spleen does not diminish appreciably in this test in the presence of its fibrosis, in perisplenitis, or in the presence of its tumours or cysts.

The spleen is not firm in acute infectious diseases; it is especially soft (the consistency of dough) in sepsis. In chronic infectious diseases, liver cirrhosis, and leucosis the spleen is firm, especially in amyloidosis.

In most diseases the spleen is insensitive to palpation. It becomes tender in infarction, perisplenitis, and in distension of the capsule, due to the rapid enlargement, e.g. in venous blood congestion due to thrombosis of the splenic vein. The spleen surface is usually smooth; the edges and the surface are irregular in perisplenitis and old infarctions (depressions in the surface). In syphilitic gummas, echinococcosis, cysts and very rare tumours of the spleen its surface is tuberous.

The spleen is normally quite mobile, but the mobility becomes limited in perisplenitis. A markedly enlarged spleen remains motionless during respiration but it can however be displaced by the palpating fingers.

Not only the spleen but also the liver sometimes becomes enlarged due to metaplasia (as determined by palpation).

PERCUSSION

Percussion is not important for the study of the haemopoietic organs; it is only used to outline tentatively the spleen. Since the spleen is surrounded by hollow organs (the stomach, the intestine), which give loud tympany during percussion, it is impossible to determine accurately its borders by percussion.

During percussion, the patient stands upright or lies on his right side. Light percussion should be used with transition from clear resonance to

dullness. Obraztsov's percussion is recommended. In order to determine the transverse dimensions of the spleen dullness, percussion is carried out in the line passing 4 cm laterally of the left costoarticular line (the line connecting the sternoclavicular articulation with the free end of the 11th rib). Normally spleen dullness is determined between the 9th and 11th ribs. It is 4-6 cm wide. The long axis of the spleen is percussed by the 10th rib; normally the anterior edge of the spleen does not extend beyond the costoarticular line; its dullness zone is 6— 8 cm long.

AUSCULTATION

Auscultation is used to study the spleen: peritoneal friction sound can be heard in perisplenitis in the region overlying the spleen.

Instrumental and Laboratory Methods

MORPHOLOGICAL STUDY OF THE BLOOD

Total blood counts are widely employed. Blood studies include quantitative and qualitative determination of the composition of the formed blood elements: counting erythrocytes and determining their haemoglobin contents, total leucocytes and their separate forms, and platelets. Additional counts are sometimes necessary depending on the character of the disease (counting reticulocytes, deriving the thrombocyte formula, etc.).

The concept of a reticular cell as a source of all cell elements of the blood has undergone a substantial revision in recent years in connection with advances in haematology. The haemopoietic scheme is now described as follows.

The first class of polypotent precursor cells is represented by the stem cell. The stem cells are self-sustaining, characterized by rapid proliferation and differentiation.

The *second class* of partly determined polypotent precursor cells is represented by precursors of lymphopoiesis and haemopoiesis; their self-sustaining power is limited; the cells are found in the bone marrow.

The *third class* of unipotent precursor-cells includes colony-forming cells (precursors of granulocytes and monocytes), erythropoietin-sensitive cells, precursors of B-lymphocytes and T-lymphocytes precursors.

The *fourth class* includes morphologically identifiable proliferating cells; the *fifth class* includes maturating cells and the *sixth class* mature cells with a limited life cycle. The cells of the sixth class are mainly delivered to the peripheral blood.

The cell composition of the blood of a healthy individual is constant and any changes are therefore diagnostically important. But minor changes in the blood can be observed during the 24-hour period: after meals, exercise, etc. In order to remove these interfering factors, blood specimens should be taken under the same conditions.

Taking blood specimens. The study of blood begins with obtaining its specimen. Blood is taken from the 4th finger of the left hand. The finger is first disinfected by a mixture of alcohol and ether. The skin on the side of the first phalanx is then punctured by a blood lancet to a depth of 2.5-3 mm. Blood should issue freely because any pressure on the finger will express other tissue fluids to impair the accuracy of studies. The first emerging drop of blood should be wiped off with dry cotton wool.

Determining haemoglobin. There are the following three major groups of methods for determining haemoglobin: colorimetric (widely used in practical medicine), gasometric, and determination by the iron contained in the haemoglobin molecule. Sahli's method of estimating haemoglobin (1895) was widely used until recent times.

The cyanmethaemoglobin method has now been universally accepted as the most accurate and objective technique, which was approved by the International Standardization Committee (in haematology). The method is based on oxidation of haemoglobin (Hb) to methaemoglobin (MetHb or Hi) by potassium ferricyanide. Methaemoglobin reacts with CN-ion to form a stable red complex, cyanmethaemoglobin (CNMetHb) or haemoglobin cyanide (HiCN). Its concentration can be measured on a spectrophotometer, photoelectrocolorimeter, or haemoglobinometer.

According to this method, 0.02 ml of blood taken from the finger is transferred into 5 ml (dilution 1:251) of a transforming solution consisting of acetone cyanhydrine, potassium ferrocyanide, and sodium hydrocarbonate; the mixture is stirred thoroughly, allowed to stand for ten minutes, and the optical density of the solution is measured at 500—560 nm (a green optical filter) against a blank solution (the transforming solution or pure water). Concentration of haemoglobin is determined from a calibration curve. Concentration of haemoglobin in healthy people varies from 120—140 g/l in women and from 130—160 g/l in men.

Erythrocyte counting. In order to count erythrocytes in the chamber, blood is diluted to 1:200 in 3.5 per cent sodium chloride solution. To that end 0.02 ml of blood is added to 4 ml of the diluting solution. The mixture is stirred thoroughly and transferred into the counting chamber.

The counting chamber is a glass plate with one or two counting grids. Burker haemacytometers are usually used for the purpose. Three elevated strips, separated from each other by grooves pass across the main plate. The middle strip is divided into halves by another groove. Each half has a graduated counting grid. The lateral strips are 0.1 mm higher than the middle one. The cover glass rests on the elevated lateral strips to ensure a 0.1 mm spacing between the grids and the cover glass (the depth of the counting chamber). In order to ensure the accurate spacing, the cover glass should be pressed tightly against the strips. A well-washed and wiped glass is ground-in by reciprocating sliding movements until the iridescent (Newtonian) rings and lines appear over the lateral strips. A drop of diluted blood is placed by a

pipette under the ground-in cover glass. The fluid is sucked in by capillary force to fill the space over the grid.

If the blood was diluted in a test tube, the mixture should be first jolted, then a glass rod dipped into the fluid and a hanging drop transferred onto the slit between the counting chamber and the cover glass. Counting should be done one minute later (when the erythrocytes precipitate to the chamber bottom).

There exist many counting grids but they all employ one principle. They consist of larger and smaller squares with the area of 1/25 and 1/400 mm^2, respectively. Goryaev's grid is commonly used in the Soviet Union. It consists of 225 greater squares, 25 of which are divided into smaller ones, 16 squares in each greater square. Erythrocytes are counted in 5 greater squares (divided into smaller ones). A certain rule is followed in counting: cells are counted in each square in one direction, and then this direction is reversed in the next row of squares, as shown by the arrow in Fig. 108. Counted are not only the cells inside the square but also those lying by two lines (e.g. the left and the upper line) without counting blood cells lying on the right and lower line. The quantity of erythrocytes counted in 5 greater squares is recalculated with reference to one litre.

Normal erythrocyte counts in women are $3.9\text{-}4.7 \times 10^{12}$ and in men $4\text{-}5 \times 10^{12}$ per 1 l of blood.

There are instruments by which the counting procedure is either simplified or automated. These are *erythrohaemometres* and *absorptiometres* where concentration of erythrocytes is assessed by the amount of absorbed or scattered light passed through a suspension of erythrocytes, or directly reading automatic instruments. In the latter case blood cells pass a narrow capillary to change resistance of an electric circuit. Each cell gives a

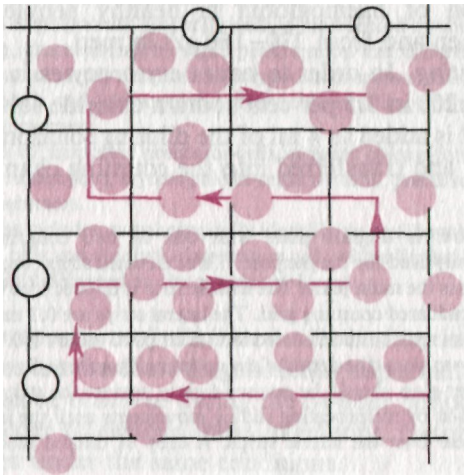


Fig. 108. Counting red blood cells.

pulse on the screen of an oscilloscope and is recorded on the instrument scale.

Once the quantity of erythrocytes and haemoglobin in a given blood specimen is known, it is possible to calculate the haemoglobin content of each erythrocyte. There are many methods by which haemoglobin saturation can be determined. One of them is the calculation of the *colour index.* This is a conventional value derived from the ratio of haemoglobin to the number of erythrocytes. This value is found by dividing a tripled quantity of haemoglobin in grams by the first three figures expressing the quantity of erythrocytes. Normally this value approaches 1. If it is less than 1, the erythrocyte saturation of haemoglobin is insufficient; if the value exceeds 1, the volume of erythrocytes is higher than normal. Oversaturation with haemoglobin is impossible. A normal erythrocyte is saturated with haemoglobin to the utmost limit.

At the present time, in accordance with the general tendency to express blood constants in absolute values, the weight percentage of haemoglobin in erythrocytes is calculated, instead of determining the colour index of the blood. To that end haemoglobin content in one litre is determined and the found quantity divided by the number of erythrocytes in the same volume. Normally one erythrocyte contains 33 ng of haemoglobin.

Leucocyte counting. Blood for counting leucocytes is diluted either in a special mixer or a test tube. A 3-5 per cent solution of acetic acid destroying erythrocytes is mixed with a small amount of a suitable aniline dye to stain leucocyte nuclei. The counting chamber is filled as for counting erythrocytes. It is convenient to count leucocytes in 100 greater (undivided) squares. A constant factor is found from the dilution of blood and the volume of fluid in each square. With 1:20 dilution it is 50. When test tubes are used for dilution, 0.02 ml of blood is added to 0.38 ml of the diluting liquid in the test tube. Saponin is used for haemolysis of erythrocytes in automatic counting instruments. The normal leucocyte counts are 4000-9000 in 1 μl or $4.0\text{-}9.0 \times 10^9$ per 1 l of blood.

The *leucocyte formula* is counted in stained smears. An adequate smear meets the following requirements: it is thin and the formed elements are arranged in one layer; the smear is yellow and semitranslucent. The width of the smear is 2-3 mm narrower than the glass, while the length, 2/3-3/4 the length of the glass. A good smear is uniform and the cells are intact (not damaged during their application to the glass). In order to ensure an even layer, the glass is first defatted over a gas burner or in a mixture of alcohol and ether. A small drop of fresh blood is touched by the glass edge and spread immediately over the entire glass surface. A polished cover glass of the counting chamber or another object glass with polished edges and made slightly narrower than the main object glass can be used for the purpose.

This glass is positioned behind the blood drop at an angle of 45° to the plane of the first glass and moved back to bring it in contact with the blood. As soon as the blood spreads over the entire width of the polished edge, the glass is moved forward along the surface of the object glass. Blood is thus spread in an even layer over the object glass. Before staining, the smear is fixed in methanol for 3 minutes, or in ethanol or a mixture of ethanol and ether for 30 minutes. Other fixing agents can also be used. When the smear is dry it is covered with a layer of stain.

Differential staining is used for blood cells. Romanovsky-Giemsa staining method is commonly used. The stain is a mixture of weakly acid (eosin) and weakly alkaline (azure II) stains. Depending on the reaction of the medium, the cells and their parts differently accept the stain: acid (basophilic) substances are coloured blue by azure, while alkaline (oxyphilic) substances are coloured red by eosin. Neutral substances accept both dyes and turn violet. Azure II, which is generally blue, contains a small quantity of azure I. In some cells the cytoplasm contains grains which selectively accept red azure I. The grains are called azurophilic.

Romanovsky-Giemsa stain is diluted before use with distilled water, 1-2 drops per 1 ml of water. Smears are placed on glass rods fixed in the sides of the cell and the stain is added in the maximum quantity that can remain on the glass. The staining time (15-30 min) depends on concentration of the stain, quality of water (neutral) and temperature; it is determined empirically. The stain is then removed by a jet of water and the smears are placed in the vertical position to dry.

Differential blood count is the percentage of separate forms of blood leucocytes. In order to ensure accuracy, it is necessary to observe not less than 200 leucocytes using the immersion system. Since the cells are not evenly distributed over the surface (larger cells tend to move toward the edges) it is necessary to follow a certain rule in counting, so that both the centre and the peripheral parts of the smear might be inspected. The smear can be moved from its upper edge to the lower one, then in the lateral direction, through 2 or 3 fields of vision, then back, from the lower to the upper edge, and so on. According to another method, the smear is moved from the edge, through 5 or 6 vision fields toward the centre, then the smear is moved in the lateral direction through the same distance, then again to the periphery, and so on, until 50 cells are counted. Four sites by the four angles of the smear should be thus inspected. Each cell should be identified and recorded. A special 11-key counter is convenient for cell counting. When 200 cells are thus counted, the number of each leucocyte is divided by two.

Leucocytes quickly respond to various environmental factors and changes inside the body. Shifts in their counts are very important diagnostically. But individual variations in leucocyte composition are quite significant and it is therefore necessary to compare individual findings not with the average values, but with a certain range within which these variations are normal (see Appendix, Table 6).

When assessing the composition of leucocytes, it is necessary to bear in mind that changes in percentage ratios can give an incorrect picture of the shifts occurring in the blood. For example, an increase in the absolute amount of a given type of cells in the blood decreases the percentage of all other cell elements. The picture is reverse with decreasing absolute amount of this given type of blood cells. A correct conclusion can be derived not from relative (percentage) but absolute values, i.e. the quantity of a given type of cells contained in 1 μl (in 1 l of blood, according to the SI).

The total quantity of leucocytes alone is of great diagnostic significance, because it characterizes the condition of the haemopoietic system and its response to harmful effects. The increased number of leucocytes *(leucocytosis)* is the result of activation of leucopoiesis. The decreased number of leucocytes *(leucopenia*) depends on the inhibition of the haemopoietic organs, their exhaustion, increased decomposition of leucocytes under the effect of antileucocytic antibodies, etc.

Neutrophils are the most changeable group of leucocytes. Their number increases in many infections, intoxication, and tissue decomposition. Neutrapoiesis is characterized not only by the increased total number of neutrophils but also by the appearance in the blood of immature forms: the quantity of stab neutrophils increases; juvenile neutrophils and even myelocytes appear. This rejuvenation of the neutrophil composition is called the blood shift to the left, because the figures grow on the left side of the laboratory blank where leucocyte counts are normally recorded. Regenerative and degenerative shifts are distinguished. In the regenerative shift to the left the mentioned changes are observed, while in the degenerative shift to the left, the number of stab neutrophils only increases along with the degenerative changes in neutrophils in the absence of leucocytosis (vacuolization of cytoplasm, nuclear pyknosis, etc.). The regenerative shift indicates active protective response of the body, while the degenerative one indicates the absence of this response. The protective role of neutrophils consists in phagocytosis, bactericidal action, and production of proteolytic enzymes promoting resolution of necrotized tissue and healing of wounds.

The regenerative shift to the left occurs most frequently in the presence of an inflammatory or necrotic focus. An especially marked shift to the left (to promyelocytes and even myeloblasts in the presence of significant leucocytosis) is called *leucaemoid reaction.* The number of neutrophils decreases *(absolute neutropenia*) in the presence of the inhibiting action of toxins of some microbes (e.g. causative agents of typhoud fever or brucellosis) and viruses, ionizing radiation, and some medicinal preparations.

The absolute number of lymphocytes increases less frequently. Lym-

phocytosis occurs during recovery in acute infectious diseases, infectious mononucleosis, infectious lymphocytosis, lymphoid leucosis, rubella, brucellosis, and thyrotoxicosis. More frequently lymphocytosis is only relative, associated with a decreased number of neutrophils (like relative lymphopenia in the presence of increased number of neutrophils). Absolute lymphopenia occurs in radiation sickness and systemic affections of the lymphatic system: lymphogranulomatosis and lymphosarcoma.

Eosinophils are present in the blood in relatively small quantity but their number increases, and sometimes significantly, in allergic processes (serum sickness or bronchial asthma), in helminthiasis, and itching dermatosis. Eosinophilia in allergic processes is associated with the role played by eosinophils in removal of toxic substances produced in these reactions. Decreased number of eosinophils (eosinopenia), to their complete absence, occurs in sepsis, severe forms of tuberculosis, typhus, and poisoning.

Basophils are carriers of important mediators of tissue metabolism. Their number increases in sensitization of patients and decreases markedly during decomposition caused by the repeated administration of the allergen.

Increased number of monocytes (monocytosis) indicates development of the immune processes. Monocytosis occurs in some chronic diseases (e.g. chroniosepsis, tuberculosis, malaria, visceral leishmaniasis, syphilis) and in infectious mononucleosis. Monocytopenia sometimes occurs in severe septic (hypertoxic) forms of typhoid fever and other infections.

Leucocyte counting procedure requires special skill. The laboratory technician should be able to differentiate between various blood cells (Plate 27). Granulocytes have specific segmented nuclei (violet like in all leucocytes) and oxyphilic (pink) cytoplasm containing grains. Grains of a neutrophilic leucocyte (10-15 μm) are small, their size varies; they are stained brown-violet. The nucleus has a rough structure, with alternation of intense- and light-coloured sites; it consists of 2 to 5 (mostly 3 or 4) segments of various size and shape connected by thready bridges. The nucleus of a stab neutrophil is about the same size and colour, but it is a uniform curved band which never thins to a thread. The eosinophil nuclei consist mostly of two symmetrically arranged segments of about the same size (three segments can also be present); their structure and colour are similar to those of neutrophil segments. Eosinophils are highly granular. Grains are large, round, bright-orange and of equal size; they stuff the entire cytoplasm. The diameter of the cell is about 15 μm. A basophil is slightly smaller than the other granulocytes (9-14 μm). The nucleus can be segmented. Often it has an irregular oval shape and is stained intensely. The grains are large and dark-violet; their size varies. Due to metachromasia, their dark-blue colour makes them look violet.

Agranulocytes are characterized by a non-segmented nucleus and basophilic (blue) cytoplasm. The lymphocyte is the smallest of all leucocytes; its diameter usually varies between 7 and 12 μm, but some lymphocytes are as large as 12-15 μm. The nucleus is round, oval, or bean-shaped; it occupies almost the entire cell and is intensely coloured. The cytoplasm of most lymphocytes surrounds the nucleus by a narrow circle; it is pale-blue and becomes lighter toward the nucleus. In addition to these "small" lymphocytes, there are "medium size" ones having a large sky-blue zone of a cytoplasm. Some lymphocytes have several large cherry-red (azurophilic) grains in their cytoplasm. A monocyte is the largest blood cell. Its diameter is 20 μm. Its large nucleus is of irregular shape and relatively light-coloured. The cytoplasm is greyish-blue and smoky; the colour intensity does not diminish toward the nucleus. If stained well, dust-like azurophilic granularity is revealed in some cells.

In rare cases, apart from the mentioned cells, normal blood contains *plasma cells.* Their number increases in pathology. The cells have an eccentrically arranged dense nucleus (often a wheel-like structure) and a markedly basophilic vacuolized cytoplasm. Their number increases in certain infectious diseases, wound sepsis, hypernephroma, myeloma, etc. These cells are probably responsible for the production of gamma globulins.

When counting leucocytes, it is necessary to pay attention to both quantitative and qualitative shifts in the formed elements. The degenerative shifts were discussed above. In grave toxicosis, granularity of neutrophils becomes even more pronounced, the granules become larger and coloured; this granulation is called toxicogenic. Indistinct spots are sometimes revealed in blood smears; they are stained like the nuclear substance of leucocytes. These are Botkin-Gumprecht shadows, the remains of nuclear chromatin characterizing brittleness of leucocytes due to which they decompose (leucocytolysis).

Erythrocytes are studied in the same smears (Plate 28). The size, shape, colour and cell inclusions should be assessed. Normal erythrocytes in the smear are rounded, their diameter varying from 6 to 8 μm (the average diameter, 7.2 μm). The size of erythrocytes often changes in anaemia of various nature. Various erythrocytes change differently. Excessive variation in the size of erythrocytes is called anisocytosis. Prevalence of smaller erythrocytes (microcytosis) occurs in iron deficiency anaemia. Macrocytosis develops in haemopoietic dysfunction of the liver. *Megalocytes* (large, over 12 μm, oval hyperchromic erythrocytes formed during maturation of megaloblasts) appear in the blood of patients with vitamin B_{12} deficiency (vitamin B_{12} deficiency anaemia). In pathological conditions of erythrocyte maturation, along with anisocytosis, the change in the shape of erythrocytes (*poikilocytosis)* is also observed; in addition to

round erythrocytes, blood contains also erythrocytes of oval, pear-shaped and other configurations. If erythrocytes are undersaturated with haemoglobin (colour index less than 0.85) they are poorly stained to become *hypochromic;* in vitamin B_{12} deficiency they are coloured intensely, i.e. *hyperchromic* (colour index higher than 1). A mature erythrocyte is oxyphilic, i.e. coloured pink. An immature erythrocyte is *polychromatophilic.* In supravital staining these erythrocytes appear as *reticulocytes* (see below). Normal blood contains polychromatophilic erythrocytes in meagre quantity: single cells per 1000 erythrocytes. Since they are less noticeable than reticulocytes, the latter are counted to assess the number of juvenile polychromatophilic cells. The importance of this count is that the number of reticulocytes in the blood is a measure of the activity of the bone marrow. Normally this number is 2-10 per 1000 erythrocytes. Erythropoiesis is activated in blood loss and haemolysis, and the number of reticulocytes in normal bone marrow and peripheral blood increases. The absence of this increase indicates decreased function of the bone marrow and conversely reticulocytosis in the absence of anaemia indicates latent but well compensated loss of blood. High reticulocytosis is observed in effective treatment of vitamin B_{12} deficiency anaemia.

In erythropoietic hypofunction of the bone marrow, more immature nuclear (but still containing nuclei) elements of the red blood, i.e *normoblasts* and *erythroblasts,* are delivered into the blood from the bone marrow. During maturation of erythrocytes in pathological conditions, nuclear remnants, known as *Jolly bodies,* may be preserved. These are round chromatin formations 1-2 μm in size, stained cherry-red. Red *Cabot rings* (thread-like rings or convolutions) may also remain. They are believed to be the remnants of the nuclear envelopes, and occur mostly in vitamin B_{12} deficiency anaemia.

Basophilic granulation of erythrocytes is also the result of their abnormal maturation. Blue granules are seen against the pink background during ordinary staining of a fixed smear. It should not be mistaken for reticulocyte granulation which is revealed only in supravital staining. Basophil-granular erythrocytes occur in pernicious anaemia and some intoxications, especially in lead poisoning.

Reticulocytes are stained in unfixed smears of fresh blood in which erythrocytes are still alive. Various alkaline dyes are used to stain smears by various techniques. Best results are attained with brilliant cresyl blue. A drop of a saturated alcoholic solution of the stain is applied to a defatted object glass and a smear is made by the usual way. As soon as the stain dries up, a thin blood film is smeared over it and the glass is transferred to a moist chamber (a Petri dish containing a piece of wet blotting paper). The smear is kept there for 5 minutes and then removed and allowed to dry.

The smear is inspected with an immersion system. Mature erythrocytes are stained green. Against this background, reticulocytes (depending on their maturity) have blue granules, filaments, or other formations that may resemble a crown, a ball, or a network. Filaments and grains are more mature forms and they usually predominate in reticulocytes.

When counting reticulocytes, their number per 1000 erythrocytes is determined. For convenience of counting, the vision field of the microscope is diminished by placing a special window in the eye-piece. The total number of erythrocytes and reticulocytes is counted in the field of vision. Counting is continued till the number of erythrocytes is 1000.

Thrombocytes (platelets) have a diameter of 1.5-2.5 μm. Their normal number is 180.0-320.0 $\times$ 10^9 per 1l (180 000-320 000 per 1 μl) of blood. Using the Romanovsky-Giemsa staining technique, the central part, the granulomere with intense azurophilic granulation, and non-granular hyalomere around it are distinguished. If the number of thrombocytes decreases significantly *(thrombocytopenia),* a tendency to haemorrhages develops. The critical figure at which haemorrhage occurs is believed to be 30 $\times$ 10^9 per 1 l (30 000 per 1 μl). Thrombocytopenia occurs in affection of the bone marrow by infectious causative agents, some medicinal preparations, ionizing radiation, and in auto-immune processes. *Thrombocytosis* occurs after haemorrhage, in polycythaemia, and malignant tumours.

In order to determine the number of thrombocytes, it is necessary to prevent their agglutination. To that end, a drop of a 14 per cent magnesium sulphate solution is placed over the puncture point on the finger. The blood issuing from the wound mixes with the solution and smears are made from this mixture, which are then fixed and stained after Romanovsky-Giemsa. The fixing and staining time should be doubled (compared with the blood smear staining time). Using a window to restrict the field of vision (like in counting reticulocytes), 1000 erythrocytes and all thrombocytes that occur among them are counted in vision fields. Once the number of erythrocytes in 1 μl is known, the number of thrombocytes can be calculated in 1 μl and in 1 l of blood.

Apart from the described indirect counting of thrombocytes, they can also be determined directly in a counting chamber. The blood is diluted by a suitable solvent, e.g. by a 1 per cent ammonium oxalate solution. A phase contrast microscope is used for counting. This method is more accurate than indirect counting. In certain diseases of the haemopoietic organs, thrombocyte counts are also necessary. Juvenile, mature, and old thrombocytes are distinguished. They also differ in size, shape, colour and structure; their degenerative forms appear sometimes.

Changes in the morphological composition of the blood should be used

to establish diagnosis of a disease together with the other findings of examination of the patient.

Erythrocyte sedimentation rate (ESR). Erythrocytes do not clog together in the stream of blood because they are all negatively charged. If a blood specimen is placed in a vertical vessel and an anticoagulating agent is added to it, erythrocytes gradually settle by gravity. Then they agglomerate into heavier groups which precipitate at a faster rate. Agglomeration is promoted by some protein components of the plasma (globulins, fibrinogen) and by mucopolysaccharides. Therefore, the processes which increase their accumulation in the blood are attended by acceleration of erythrocyte sedimentation. This condition occurs in most inflammatory processes, infections, malignant tumours, collagenoses, nephroses, and tissue decomposition; to a certain measure, this acceleration is proportional to the gravity of the affection. In certain diseases erythrocyte sedimentation is not accelerated in their initial stage (epidemic hepatitis, typhoid fever); in other pathological conditions erythrocyte sedimentation rate is slowed (heart failure).

Erythrocyte sedimentation rate is not an independent diagnostic symptom; it only indicates the activity of the process. It is important in this aspect in the diagnosis of tuberculosis, rheumatism, and collagenosis. Changes in the erythrocyte sedimentation rate do not always agree with other signs of activity. For example, ESR lags behind the rate of temperature elevation and leucocytosis in appendicitis or myocardial infarction; its normalization is also slower than normalization of the mentioned symptoms. The normal ESR does not rule out the presence of disease which would be usually attended by an increased erythrocyte sedimentation rate. But it should be remembered that ESR does not increase in healthy people.

The *Panchenkov method of ESR determination* is widely used in the Soviet Union. A Panchenkov capillary graduated in 1 mm (100 divisions) is used for the purpose. It is filled with a 5 per cent sodium citrate solution to a half of full capacity (50 divisions). The solution is blown out onto a watch glass or into a test tube. Using the same capillary, 100 mm of blood is taken from the punctured finger (2 times). To that end, the capillary is held horizontally and brought in contact with the issuing drop of blood: the blood is drawn in by the capillary force. The blood is then mixed with the reagent in the 4:1 ratio. The mixture is taken into the capillary, to the mark 0 (100 divisions), and placed in a Panchenkov stand, in a strictly vertical position. The number of millimetres of a settled plasma column is noted in 60 minutes. The normal rate for men is 2-10 mm/h and for women 2-15 mm/h.

PUNCTURE OF HAEMOPOIETIC ORGANS

The morphological composition of the blood does not always show the changes occurring in the haemopoietic organs. For example, the cell composition of blood remains almost unaltered in aleukaemic form of leucosis despite significant changes in the bone marrow. M. Arinkin (1928) proposed a *sternal puncture* for intravital study of the bone marrow. Owing to the simplicity and safety of the procedure, it is used for the study of almost all patients with diseases of the haemopoietic system. The Kassirsky needle is used for the purpose in the Soviet Union. This is a short thick-walled needle with a mandrin and a stopping device that prevents deep penetration of the needle. After the skin, subcutaneous fat and the periosteum are anaesthetized, the soft tissues are punctured over the sternum, at the level of the second or third intercostal space (or above the manubrium). Then the stopping device is fixed at a distance of 5 mm from the skin surface and the anterior plate of the sternum is punctured: the operator's hand has a feeling of entering a cavity. The mandrin is now removed and a dry 10-20 ml syringe is attached to the needle. About 0.5 or 1 ml of bone marrow is now aspired into the syringe and transferred onto a watch glass. If the bone marrow is mixed with an unknown quantity of blood, its composition cannot be definitely determined. Using a blotting paper (or by inclining slightly the watch glass), the blood is separated, and the small grains of bone marrow are carefully pressed against the glass to prepare a smear of the crushed marrow. After fixation and staining (Romanovsky-Giemsa), not less than 500 elements containing nuclei are counted in the smear. A myelogram is then derived (see Appendix, Table 13).

The marrow specimen can show upset maturation of the cells: increased number of juvenile forms or prevalence of primary undifferentiated elements, upset proportion between the red and white cells, changes in the total number of cells, presence of the pathological forms, etc. Apart from the sternum, other bones (e.g. iliac bone) can also be used for taking the bone marrow.

More accurate information on the composition of the bone marrow is given by *trepanobiopsy*. A special needle (troacar) is passed into the iliac crest to cut out a column consisting of the bone-marrow tissue, which is then used for making histological preparations. The structure of the bone marrow remains unchanged in the preparations while the absence of blood makes it possible to evaluate its cells composition and to reveal focal and diffuse changes in it.

Enlarged lymph nodes are often punctured. It makes it possible to establish the character of changes in the cell composition and to verify the diagnosis of some systemic diseases of the lymph apparatus (lymphoid

leucosis, lymphogranulomatosis, lymphosarcomatosis), to reveal metastases of tumours, etc. More accurate data can be obtained with *biopsy of the lymph node*. The puncture is made without anaesthesia, by a simple injection needle attached to a 10-ml syringe. The obtained material is used to prepare smears. The spleen is punctured by the same method. The patient is asked to keep breath at the inspiration height to prevent possible injury of the spleen during respiratory movements. Combined study of cell composition of the bone marrow, spleen and lymph nodes reveals the relations between these organs of the haemopoietic system and the presence of extramedullar haemopoiesis which develops in some affections of the bone marrow.

ASSESSMENT OF HAEMOLYSIS

Evaluation of haemolysis becomes necessary mainly in anaemia of the haemolytic character. Erythrocytes undergo constant decomposition in physiological conditions (haemolysis). In pathological haemolysis, haemoglobin destruction is intensified to increase formation of unbound bilirubin and excretion of stercobilin with faeces and urine. This is an important symptom of pathological haemolysis (see "Liver and Bile Ducts").

Another sign suggesting haemolysis is the *degree of osmotic stability* (resistance) of erythrocytes. Congenital microspherocytic haemolytic anaemia is characterized by decreased osmotic stability of erythrocytes. This anaemia is diagnosed by mixing blood specimens with sodium chloride solutions whose concentration increases in 0.02 per cent gradient from 0.2 to 0.7 per cent (1 ml of each solution). The mixtures are shaken and the test tubes are allowed to stand for 5-20 hours to complete sedimentation of erythrocytes (or the liquids are centrifuged after 1-hour standing). The test tubes where haemolysis takes place are separated. The minimum resistance is determined by the test tube where the concentration of sodium chloride is the highest and the pink colour becomes appreciable. The maximum resistance is determined by the test tube where the concentration of sodium chloride is the lowest and in which there is no sediment. Normally haemolysis begins at sodium chloride concentrations from 0.42 to 0.46 per cent and terminates at 0.30 to 0.36 per cent. In haemolytic anaemia haemolysis begins at 0.54—0.70 per cent and ends at 0.40-0.44 per cent concentration of sodium chloride.

The third sign of haemolysis (also only relative) is *reticulocytosis*. Increased decomposition of erythrocytes stimulates erythropoiesis. The number of reticulocytes increases although the increase is not always proportional to the degree of haemolysis.

STUDY OF THE HAEMORRHAGIC SYNDROME

Blood in the human body is liquid because of the physiological dynamic equilibrium of the coagulation and anticoagulation systems. If the activity of any procoagulant decreases or is lost, or the activity of anticoagulants increases, there develops a tendency to haemorrhage (haemorrhagic diathesis). If the relation is reversed, the tendency develops to increased coagulability of the blood and formation of thrombus. Bleeding in haemorrhagic diathesis is associated with haemorrhage of fine capillaries, while haemostasis is effected by a series of sequential mechanisms which protect the body from profuse loss of blood.

The first event leading to haemostasis is formation of a white thrombus consisting of thrombocytes which have undergone the so-called viscous metamorphosis. This term is used to describe a series of consecutive phases in the transformation of the thrombocyte: after a blood vessel is injured, thrombocytes stick to the injured site (adherence) and fuse (aggregation). Blood platelets stick together to lose their usual shapes and to turn into a clot that arrests bleeding from the injured capillary or a larger vessel before a red thrombus is formed. The platelets then dissolve to liberate substances promoting coagulation of blood, contraction of the vessel (serotonin), and consolidation of the clot. The event following formation of the white thrombus is activation of plasmic, tissue, and thrombocytic factors which cause precipitation of fibrin threads, coagulation of blood, and formation of a red thrombus, which is larger and stronger than the white thrombus.

Coagulation of blood is a complicated enzymatic process, in which 13 plasma factors (I-XIII) and 12 thrombocytic factors (1-12) are involved. The plasma factors of blood coagulation are as follows: I-fibrinogen-fibrin, H-prothrombin-thrombin, III-thromboplastin, IV-Ca ions, V-proaccelerin, VI-accelerin, VII-proconvertin, VIII-antihaemophilic globulin, IX-plasma thromboplastin component, X-Koller factor, XI-plasma thromboplastin antecedent, XU-contact factor, and XIII-fibrinase (fibrin-stabilizing factor). According to the activation sequence ("the cascade theory"), each plasma factor of the coagulation system is a proenzyme which is activated by the preceding factor and, in turn, activates its successor, thus to ensure a kind of a chain reaction.

The blood coagulation process can be divided into three phases. The first begins at the moment when the blood contacts the rough surface of the injured vessel to activate the first link in the chain (contact factor, XII) and to complete formation of thromboplastin (factor III). Thromboplastin is formed from the antihaemophilic globulin of plasma (VIII) with participation of plasma factors XII, XI, X, IX, V, and three platelet factors in the presence of the calcium ions.

The second phase of blood coagulation begins with formation of thromboplastin: the blood prothrombin (produced by the liver with involvement of vitamin K) is activated by thromboplastin in the presence of the calcium ions, plasma factors VII and VI, and the I thrombocytic factor to convert into an active thrombin. Thrombin acts on the fibrinogen of blood to form fibrin. This is the third phase which ends by formation of a blood clot, i.e. the red thrombus. The next stage is the action of the fibrin-stabilizing factor of the fibrin. Under the action of the 6th platelet factor, retractozyme, fibrin threads shorten to contract and consolidate the clot, which accounts for a complete discontinuation of the bleeding.

In addition to the factors promoting coagulation, the blood contains also anticoagulants or inhibitors of blood coagulation which are responsible for the liquid state of normal blood. Each component of the coagulation system has its opponent inhibitor (antithromboplastin,

antithrombin, anticonvertin, etc.). There are inhibitors to anticoagulants too. In physiological conditions, a change in any factor causes a corresponding change in its antagonist; the equilibrium of the two systems is thus maintained. Imbalanced increase in anticoagulant activity results in bleeding. Heparin is the most powerful anticoagulant. It inhibits all phases of blood coagulation, especially conversion of prothrombin into thrombin. Thrombocytic factors play an important role in the described processes. Some of them promote coagulation of blood, and others activate anticoagulants.

After the blood clot fulfils its purpose, the reverse process is started, its dissolution. It is attained through the action of a complicated enzymatic fibrinolytic system, which in many respects is similar to the coagulation system. Fibrin of the clot is dissolved by the proteolytic enzyme fibrinolysin which circulates in the blood as an inactive profibrinolysin. It is activated by fibrinokinase (plasmic, tissue, and bacterial). There are the corresponding inhibitors of fibrinolysin and fibrinokinase: antifibrinolysin and antifibrinokinase.

It is clear that haemostasis is a very complicated phenomenon and it is sometimes difficult to find the defective link in this chain of processes. There are many tests that can reveal predisposition to bleeding or thrombus formation and to find their causes. Classical tests are distinguished by which the general coagulation trends of a given blood can be determined and which are used to examine all patients with haemorrhagic diathesis. There are also differential tests by which a missing factor can be found. The classical tests are used to determine (1) blood coagulation time; 2) thrombocyte count; (3) bleeding time; (4) retraction of blood clot; and (5) permeability of capillaries.

Coagulation time characterizes coagulability of blood in general without accounting for separate phases of the coagulation process. Coagulation time increases in increased anticoagulation activity of blood or decreased concentration of procoagulants and shortens in the presence of the tendency to thrombus formation. The longest coagulation time (to several hours) is observed in haemophilia A. It does not change in certain haemorrhagic diatheses.

In order to evaluate coagulability of blood, a venous blood specimen is placed in a test tube and kept on a water bath at a temperature of 37 °C. At 30-second intervals, the test tube is inclined and inspected to see if the liquid level is mobile. In physiological conditions, the blood coagulates in 5-10 minutes (Lee and White method).

Drop tests are widely used to determine coagulability of blood. A specimen of blood is taken either in a capillary pipette and the time when it loses mobility is determined, or a drop is placed into a moist heated chamber onto a paraffin-coated watch glass and the time, when the drop does not flow toward the edge of the inclined glass, is determined.

Estimation of bleeding time (by Duke's method). The finger tip or an ear lobe is punctured by Franke's needle or a blood lancet to a depth of 3 mm. The spontaneously issuing blood is removed at 30-second intervals by touching it with blotting paper. The normal bleeding time is 2-4

minutes. Since discontinuation of bleeding is associated with formation of a white thrombus, the test results depend on the number of thrombocytes and the ability of the vascular wall to contract, which is promoted by liberation of the vasoconstricting factor, serotonin, by thrombocytes. The bleeding time in trombocytopenia is considerably prolonged and the number of blood drops removed by the blotting paper increases many times (Plate 29, *a* and *b).* If the capillary tone is abnormal the size of blood drops increases.

Clot retraction also depends on the number and activity of thrombocytes since it occurs under the effect of retractozyme liberated by the blood platelets. A specimen of venous blood (3-5 ml) is placed in a graduated centrifuge test tube and placed in a thermostat at a temperature of 37 °C. The serum separated in 24 hours is removed and its volume is divided by the volume of the blood specimen to calculate the retraction index which is normally 0.3-0.5.

Capillary permeability. *Konchalovsky-Rumpel-Leede sign.* A tourniquet is applied to the forearm and changes occurring in the skin are assessed. If petechiae appear on the skin below the tourniquet, the test is positive. Application of a sphygmomanometer cuff and the appearance of more than 1 petechiae on the skin area of 1 cm^2 at a pressure of about 100 mm Hg is interpreted in the same way.

Cupping glass test. Air is evacuated from a cup applied to the skin (rarefaction of about 200 mm Hg) for two minutes. If the test is positive, petechiae develop on the skin under the cup. The number of petechiae shows the degree of affection of the vascular wall.

Pinch test. A haemorrhagic spot appears at the site of a pinch, which gradually increases in size and becomes more intense.

Mallet symptom. Ecchymosis develops on the skin after tapping with a percussion mallet.

Determining activity of the 1st phase of blood coagulation. The simplest test is the determination of *time of plasma recalcification.* The time of coagulation of oxalate plasma, after adding an optimum quantity of calcium chloride to it, is determined. (The oxalate plasma is prepared by mixing 9 parts of plasma with 1 part of a 1.34 per cent sodium oxalate solution and separation of plasma by centrifuging.) The test characterizes blood coagulability in general. Its results somewhat differ from those of the whole blood coagulability tests, in which the formed element factors are also involved. The normal time of recalcification is 60—70 seconds.

The *prothrombin consumption test* characterizes the activity of those plasma factors which utilize prothrombin in the process of thrombin formation. The prothrombin time of plasma (see below) and serum is determined. The higher the prothrombin consumption during plasma coagula-

tion, the less is its amount in the serum and the longer it takes to coagulate, and vice versa. It follows that shorter time of prothrombin consumption test indicates disordered formation of thromboplastin.

Determining activity of the 2nd phase of blood coagulation. The activity of the 2nd phase of blood coagulation (formation of thrombin) depends on prothrombin concentration. Its determination is difficult; the overall activity of the prothrombin complex (factors II, V, VI, VII, and X) is therefore established. The method consists in determination of the rate of oxalate plasma coagulation after adding excess thromboplastin and calcium chloride (Quick's time). Since the time of coagulation depends on some conditions (thromboplastin concentration, temperature, etc.), the *prothrombin index* is usually determined: percentage ratio of the prothrombin time of the donor's plasma to the prothrombin time of the patient's plasma (normally it is 80—100 per cent).

Heparin tolerance test characterizes the same phase of coagulation. The test consists in determining the deviation (with respect to norm) in the time of oxalate plasma coagulation after adding heparin with subsequent recalcification. As the activity of the coagulants increases (tendency to thrombosis) the plasma tolerance to heparin increases, and the time of plasma coagulation decreases. If the activity of the anticoagulants predominates (tendency to bleeding), the time increases.

Determining activity of the 3rd phase of blood coagulation. This is the determination of fibrinogen by an equivalent content of fibrin.

Additional tests. Apart from the mentioned relatively simple methods, there are many complicated tests by which the activity of components of the coagulation and anticoagulation systems are determined. Two of them are now commonly used for the determination of the general coagulation tendency of blood (tendency to hypo- or hypercoagulation). The methods are known as thrombotest and thromboelastography.

Thrombotest. A 0.1 ml specimen of oxalate plasma is placed in 5 ml of a 0.5 per cent calcium chloride solution. Sedimentation of fibrin after a 30-minute incubation at 37 °C varies in character (from slight opalescence or the appearance of minutest fibrin grains to the formation of a firm clot), depending on the coagulating properties of blood. Seven degrees of thrombotest are distinguished, from which three correspond to hypocoagulability, two (4th and 5th) normal coagulability and two (6th and 7th) hypercoagulability of blood.

Thromboelastography. The test gives a graphic representation of the entire process of spontaneous coagulation of unaltered (native) blood or plasma. A blood specimen is taken from the vein by a silicon-coated needle and placed into a small cell into which a rod bearing a disc is immersed. The cell is vibrated by an electric motor. The disc remains motionless till

the blood specimen remains liquid. As the blood thickens, the disc becomes engaged, and the rod with a mirror attached to it begins vibrating. A beam of light is reflected from the mirror and recorded on a sensitive paper in the form of a zig-zag curve (thromboelastogram). By measuring its separate portions it is possible to assess some properties of the coagulation process, for example, the "reaction time", which corresponds to the length of the 1st and 2nd phases of blood coagulation, the time of clotting (the 3rd phase), elasticity and strength of the clot, and some other indices characterizing hyper- or hypocoagulability of blood (see Appendix).

Summation of the findings of all mentioned tests gives a coagulogram characterizing the condition of the blood coagulation system.

X-RAY EXAMINATION

X-rays can be used to reveal enlargement of the mediastinal lymph nodes (lymphoid leucosis, lymphogranulomatosis, lymphosarcoma) and also changes in the bones which occur in some types of leucosis and malignant lymphoma (focal destruction of bone tissue in myeloma, bone destruction in lymphosarcoma, consolidation of bones in osteomyelosclerosis). Changes in the bone tissue are better revealed by X-rays. The spleen is not seen during common X-ray examination. *Splenoportography* is a special technique which is used for examining the vessels of the spleen (see section on splenoportography).

RADIOISOTOPE METHODS OF STUDY

The spleen function is studied by administering plasma or erythrocytes labelled with radioactive iron (^{59}Fe) into the circulatory system. Foci of erythropoiesis, e.g. in erythraemia and other affections, can be established by this method.

The spleen can also be scanned with the patient's erythrocytes labelled by radioactive chromium (^{51}Cr) or a colloidal solution of gold (^{198}Au) which is captured by the reticuloendothelial cells. This method is suitable for determining the spleen dimensions and for revealing focal affections in it.

Special Pathology

Anaemia

Anaemia is a pathological condition characterized by decreased number of erythrocytes and/or haemoglobin content in a blood unit volume due to their general deficiency (Gk *an* not, *haemia* blood, i.e. deficient of blood).

Anaemia should be differentiated from hydraemia (abnormally watery

blood) in which the erythrocyte and haemoglobin are deficient as well, but not at the expense of their absolute reduction but due to dilution of blood in renal, cardiac and other oedema. Anaemia should also be differentiated from oligohaemia, which is the reduction of the total volume of blood, e.g. immediately after a profuse haemorrhage. The total mass of circulating blood can be normal in anaemia (normovolaemia), increased (hypervolaemia) or decreased (oligohaemia or hypovolaemia). Thickening of blood in persistent vomiting and profuse diarrhoea can mask anaemia because the total amount of plasma decreases and the number of erythrocytes and haemoglobin in a unit volume of the circulating blood can be normal or even increased.

Anaemia is often characterized not only by quantitative changes in the red blood composition, but also qualitative changes in the structure of erythrocytes and haemoglobin molecules. These changes are important for the transport function of blood and tissue respiration, and can be the cause of additional pathological changes in the body. For example, a congenital defect of erythrocytes in some hereditary haemolytic anaemia may (due to their intense haemolysis) cause haemosiderosis of the internal organs, formation of pigment stones in the gall bladder, etc.

Anaemia has a pronounced effect on the vital activity of the body. Anaemization causes oxygen hunger of organs and tissues (hypoxia) and their dystrophy. For example, if the blood haemoglobin content is halved (70—80 g/l), initial symptoms of myocardial dystrophy develop. If the haemoglobin content decreases to 50 g/1, the dystrophic changes become pronounced. Unoxidized products of metabolism (lactic acid, in the first instance) accumulate in the body due to hypoxia. The alkaline reserve of blood decreases. In grave cases, a tendency to acidosis develops which causes further dystrophy of tissues. Severe anaemias attended by marked disorders in tissue metabolism are incompatible with life.

Anaemia of any origin is accompanied by some compensatory processes, which partly remove or lessen its consequences: (1) blood circulation is intensified, i.e. stroke and minute volumes increase, tachycardia develops, and the rate of blood flow increases; (2) blood distribution is altered, blood depots in the liver, spleen, and muscles are activated, and the blood supply to the peripheral tissues becomes limited at the expense of the increased blood supply to the vital organs; (3) oxygen utilization in tissues is intensified and the role of anaerobic processes in tissue respiration increases (anaerobic respiration with glutathione); (4) the erythropoietic function of bone marrow is stimulated. More than 50 types of anaemia are now differentiated.

According to their origin, the following types of anaemia are distinguished.

1. *Anaemia due to loss of blood* (acute and chronic).

2. *Anaemia due to disordered haemopoiesis* in deficiency of iron (necessary for the production of haemoglobin), in vitamin B_{12} deficiency (necessary for normal erythropoiesis), in inhibition of the bone marrow by endogenous or exogenous toxicosis, radiation, or by some unknown factors, and also in cases where red bone marrow is replaced by other tissue, e.g. myeloma or multiple metastases.

3. *Anaemia due to excessive haemolysis.* This type of anaemia is subdivided into: (a) anaemia with prevalent extravascular (intracorpuscular) haemolysis of erythrocytes in macrophages of the spleen, and, to a lesser extent, in the bone marrow and liver. These are anaemia caused by hereditary morphological and functional erythrocyte deficiency (spherocytic and ovalocytic anaemia), and auto-immune haemolytic anaemia. They are all characterized by hyperbilirubinaemia and splenomegaly; (b) anaemia with intravascular, usually acute haemolysis (in various poisoning, transfusion of incompatible blood, cold and effort anaemia) attended by release into the plasma of unbound haemoglobin and by haemoglobinuria; haemosiderosis of the internal organs is observed also in chronic haemolysis (e.g. in Marchiafava-Micheli disease). This classification is only conventional because both intracorpuscular and vascular haemolysis can occur in one and the same form of haemolytic anaemia.

Haemolytic anaemia is also often subdivided as follows: (a) hereditary (congenital) anaemia, which includes membranopathy of erythrocytes (associated with abnormality of protein or lipid complexes of erythrocyte envelope, causing changes in their shape and premature decomposition; microspherocytic anaemia, ovalocytic anaemia, etc.); enzymopenic anaemia (due to deficiency of various enzyme systems of erythrocytes, which promotes their accelerated decomposition) and haemoglobinopathy in which the structure of haemoglobin or its synthesis are disturbed (sickle-cell anaemia, thalassaemia); (b) acquired anaemia (auto-immune haemolytic and iso-immune anaemia, and also anaemia caused by mechanical injury to erythrocytes, acquired membranopathies, toxic anaemia, etc.).

Apart from the pathogenetic classification, there are classifications based on other principles. Three groups of anaemia, for example, are distinguished in accordance with haemoglobin saturation of erythrocytes (by the colour index): *normochromic* (0.8-1.0), *hypochromic* (less than 0.8) and *hyperchromic anaemia* (more than 1.0). The group of hypochromic anaemia includes iron-deficiency anaemia: chronic (less acute) posthaemorrhagic anaemia, gastrogenic iron-deficiency anaemia, and juvenile chlorosis. Hyperchromic anaemia is caused by the deficiency

of vitamin B_{12}. This is Addison-Biermer anaemia, bothriocephalus anaemia, and also achrestic anaemia (due to defective utilization of vitamin B_{12}). Other anaemias proceed without considerable changes in the colour index of blood and are therefore normochromic.

It is very important to assess the regenerative capacity of the bone marrow upon which (to a certain degree) depend treatment and prognosis of the diseases. Distinguished are *regenerative* anaemia, i.e. anaemia in which the bone marrow preserves its capacity to produce new erythrocytes; *hyporegenerative* anaemia, in which this capacity is impaired; and *aregenerative* or aplastic anaemia, in which bone marrow function is completely or almost completely lost. The regenerative function of the bone marrow is assessed by the rate at which the quantity of reticulocytes increases in the peripheral blood and by the proportion of the erythro- and leucoblastic elements in the sternal punctate. Their normal ratio is 1:3 or 1:4, while in regenerative anaemia, in which erythropoiesis dominates in the compensatory function of the bone marrow, this ratio becomes 1:1,2:1 and even higher. This shift is absent in hypo- or aregenerative anaemia, while the reticulocyte content of the peripheral blood is low.

ACUTE POSTHAEMORRHAGIC ANAEMIA

Anaemia caused by an acute blood loss (acute posthaemorrhagic anaemia) occurs mostly in various injuries associated with traumatized large vessels (extrauterine pregnancy, delayed placental detachment during labour, etc.). Acute posthaemorrhagic anaemia occurs in diseases that can be attended by profuse bleeding, e.g. in gastric and duodenal ulcer, degrading tumour of the stomach, kidneys, or the lung, in tuberculosis and abscess of the lung, bronchiectasis, varicose dilation of the oesophageal veins in liver cirrhosis, haemorrhagic diathesis, and especially in haemophilia.

Clinical picture. In cases with external haemorrhage, the physician can often locate the source of bleeding at first sight (e.g. in injury). The patient's grave condition can in these cases be directly attributed to profuse blood loss. Haemorrhage from the internal organs can be manifested by blood vomiting (unaltered blood originates from the oesophagus; brown blood from the stomach), by expectoration of blood (scarlet foaming liquid), by the presence of blood in faeces (melaena in haemorrhage from the stomach or the small intestine; dark or scarlet blood originates from the large intestine, especially from its terminal part) and by blood presence in the urine (haematuria). It should be remembered that in gastro-intestinal haemorrhage, the blood can only be discharged into the environment in a.certain lapse of time (with the vomit or excretions). Moreover, haemorrhage caused by the rupture of the spleen, liver, or by the internal injury to the chest can be difficult to establish because blood will accumulate in the abdominal or pleural cavity.

The first sign of a sudden haemorrhage is the feeling of weakness, dizziness, noise in the ears, palpitation of the heart, nausea, and in rare cases vomiturition. In severe cases with profuse blood loss, the patient is in the state of shock (if the bleeding is caused by an injury) or collapse (if haemorrhage is due to affection of the internal organs). The patient's condition depends not only on the amount of blood loss, but also on the rate at which blood is lost. Inspection reveals pronounced and in some cases deadly pallidness; the skin is covered with

sticky cold sweat, the skin temperature is subnormal. Respiration is superficial and accelerated. The pulse is fast, small, and (in severe cases) thready. Arterial pressure (both systolic and diastolic) is low. Auscultation of the heart reveals marked tachycardia.

The pathological and compensatory changes in acute blood loss with benign outcome can be divided into three stages (or phases). First oligohaemia develops. It causes a reflex spasm of the vessels to decrease the volume of the vascular system and to recover blood from its reserves (depots). For this reason, the blood haemoglobin and erythrocyte content may remain normal within the first hours (or even within 1 or 1.5 days) following the blood loss. Tissue fluids are drawn into the vessels to cause hydraemia in 2 or 3 days: the erythrocyte and haemoglobin content in unit volume decreases. Signs of marked activation of erythropoiesis appear on the third to seventh day. Anaemia becomes hypochromic in the loss of considerable amount of blood due to exhaustion of the iron store.

Treatment. Bleeding should be arrested as soon as possible by placing a tourniquet or by a tamponade of the external haemorrhages in wounds. Surgical intervention is indicated in continuing haemorrhage from the internal organs. Measures to prevent shock or collapse should also be taken. Blood loss should be compensated for by infusion of whole blood or its substitutes; cardiac and vascular medicinal preparations should be administered. Iron preparations should be given to patients with profuse blood loss in several days after the haemorrhage has been arrested.

IRON DEFICIENCY ANAEMIA

Iron deficiency anaemia (anaemia sideropriva gastroenterogenica) arises in the deficit of iron which is necessary for the production of haemoglobin in erythrocytes. This type of anaemia develops in patients with decreased iron absorption due to resection of the stomach ("agastric anaemia"), removal of a considerable part of the small intestine, especially of its proximal part, in intestinal diseases attended by abnormal absorption, and in the iron deficit in food. The latter occurs mostly in children with prolonged milk diet and copper deficit. Increased iron demands occur during intense growth of the body. During establishment of the menstrual cycle in young girls (menstrual loss of blood and iron ions) juvenile iron deficiency anaemia (juvenile chlorosis) may develop. Chronic haemorrhage also causes iron deficiency anaemia.

Repeated (not profuse) loss of blood cause anaemization due to exhaustion of the iron store which is necessary for the production of haemoglobin in erythrocytes. Daily intake of iron with food is small, about 11-28 mg, and one fourth of this quantity is only absorbed. This is equivalent to the iron content of 15 ml of blood. Daily loss of 15 ml (or even smaller amount) of blood therefore inevitably exhausts the iron store to cause iron deficiency anaemia.

Chronic blood loss and chronic posthaemorrhagic anaemia attends many diseases of the internal organs, and in the first instance, of the gastro-intestinal tract. In most cases these are gastric or duodenal ulcer, cancer, polyposis of the stomach and intestine, haemorrhoids, and certain types of helminthiasis. Chronic posthaemorrhagic anaemia often occurs in

tumours of the kidneys, cavernous tuberculosis of the lungs, and in uterine haemorrhage.

Some other factors promote anaemia. These are mainly those factors which can decrease the iron stores of the body. For example, patients with secondary gastric hyposecretion and enteritis develop anaemia sooner and it runs a more severe course in the presence of even insignificant chronic haemorrhage. Gravity of chronic posthaemorrhagic anaemia arising in patients with degrading tumours of the gastro-intestinal tract, kidney, or the uterus, is intensified by the toxic effect of the tumour on the haemopoiesis and by multiple metastases into the bone marrow, etc. Hydrochloric acid of the gastric juice promotes reduction of trivalent iron to its divalent form, which is easier assimilated. But recent studies show that hydrochloric acid does not play a decisive role in activation of iron absorption.

In the absence of adequate iron supply to the body or its utilization from the store, the synthesis of haemoglobin, myoglobin, and iron-containing enzymes of various cells involved in the oxidation processes is upset. This impairs nutrition of tissues and accounts for the development of many symptoms of the disease. The clinical picture of iron deficiency anaemia is explained by insufficient oxygen transport to tissues due to anaemia on the one hand, and by disordered cell respiration on the other.

Clinical picture. Slow development (within months and years) of iron deficiency anaemia accounts for actuation of the compensatory mechanisms. Most patients therefore are well adapted to the disease and can satisfactorily stand even significant anaemia.

We shall not discuss patient's complaints associated with the main disease, to which anaemia is secondary (e.g. the cause of chronic haemorrhage). The specific complaints of anaemic patients will only be emphasized: weakness, dizziness, dyspnoea (especially exertional), increased fatigue, noise in the ears, and fainting. Many patients develop various dyspeptic symptoms: decreased appetite, perverted taste, slight nausea, heaviness in the epigastrium after meals, and regurgitation. Diarrhoea is also frequent. Slight paraesthesia (tingling and pricking) is possible. Excruciating dysphagia sometimes develops during swallowing dry or solid food in especially severe cases. This sideropenic dysphagia was first described by Rossolimo and Bekhterev in 1900-1901. Later this syndrome was described by Plummer and Vinson. The dysphagia is explained by extension of the atrophic process from the stomach onto the oesophageal mucosa, and sometimes by its development in the proximal part of the soft connective-tissue membranes and bridges.

Inspection of the patient reveals pallor. Certain trophic changes in the skin, its appendages, and mucosa can be due to the general iron deficit. The skin is dry and sometimes slightly scaling. The hair is brittle, early

grey, and showing the tendency to falling. The nails become flat, sometimes spoon-like, opaque, marked by transverse folds, and brittle (koilonychia). The mouth angles often have fissures (angular stomatitis), the papillae of the tongue are levelled (atrophic glossitis). The teeth lose their luster and quickly decompose despite a thorough care. If iron preparations are taken for a long time, the teeth may blacken due to formation of black iron sulphite (by the reaction of iron with hydrogen sulphide which is liberated by the carious teeth). Purulent inflammation of the gum mucosa around the tooth necks develops (alveolar pyorrhoea).

Physical examination can reveal a slight indistinct enlargement of the left ventricle, systolic murmur at the heart apex, and nun's murmur over the jugular vein (mostly on the right). Lymph nodes, liver and spleen are not enlarged.

Study of the blood reveals decreased erythrocyte and even more decreased haemoglobin content of the blood. The colour index is less than 0.85; in grave cases it is 0.6-0.5, and even lower. Microscopy of blood (Plate 30) reveals pallid erythrocytes (hypochromia), anisocytosis, and poikilocytosis. The average diameter of erythrocytes is less than normal (microcytosis). The number of reticulocytes is small. Anaemia is usually attended by thrombocytoleukopenia, sometimes relative monocytosis, lymphocytosis, and eosinopenia. The iron content of the serum is decreased (1.5-2.5 times and more). The percentage of transferrin saturation also decreases (below 15).

Decreased activity of the iron-containing enzymes of tissue respiration provokes (or intensifies) atrophy of the gastro-intestinal mucosa. The study of gastric juice reveals in most cases achlorhydria or even achylia; the total amount of the excreted juice is much decreased. X-rays reveal levelled folds of the oesophageal and gastric mucosa. Oesophagoscopy and gastroscopy confirm atrophy of the oesophageal and gastric mucosa.

Course. The course of the disease is chronic and gradually progressive if the iron deficit in the body increases.

Treatment. Iron preparations (haemostimulin, etc.) are given. If the patient has gastritis or peptic ulcer, the iron preparations should better be given intramuscularly or intravenously (ferbitol, fercoven, etc.). The therapy gives a comparatively rapid and permanent effect: work capacity is rapidly restored, erythrocyte and haemoglobin of blood normalize in 3-5 weeks. The patient should however be regularly (several times a year) given prophylactic courses of therapy with iron preparations in order to prevent possible relapses of the disease. The diet of patients with iron deficiency anaemia should be rich in iron salts, e.g. liver, meat, eggs, apples, dried fruits. Efficacy of treatment of anaemia caused by chronic loss of blood depends on removal of the source of blood loss.

VITAMIN B_{12} (FOLIC ACID) DEFICIENCY ANAEMIA

Aetiology and pathogenesis. Vitamin B_{12} (folic acid) deficiency anaemia was first described by Addison in 1855. One of its forms was later given the name of Addison-Biermer anaemia. In 1868, Biermer published a more detailed description of the disease, which he called pernicious or malignant anaemia, because its prognosis was then grave and patients usually died in a few months or years after the appearance of the first symptoms.

The disease was effectively treated for the first time by Minot and Murphy (1926). The patients were given raw calf liver in large amounts every day. Minot and Murphy noted that distinct remissions followed in patients who were given this diet and conjectured that raw liver contained a certain substance which is necessary for normal haemopoiesis, and whose absence or deficit causes pernicious anaemia. The next stage in the study of this disease is connected with experiments carried out by Castle (1929). He noted that meat treated with gastric juice (containing various amounts of hydrochloric acid) produces an anti-anaemic effect when administered into the stomach of patients with the Addison-Biermer anaemia. Gastric juice alone, untreated meat, or meat treated with gastric juice of patients with the Addison-Biermer anaemia have no anti-anaemic effect. Castle suggested that a special substance, haemopoietin, was necessary for normal maturation of erythrocytes. Haemopoietin is produced by combination of a certain extrinsic factor supplied with food and the intrinsic factor contained in normal gastric juice.

At the present time, Castle's conjecture concerning the pathogenesis of Addison-Biermer anaemia has been proved experimentally and clinically. The extrinsic and intrinsic factors and their biological role have been studied sufficiently well. The factor is vitamin B_{12} (cyanocobalamin) discovered by Smith in 1948 which is contained in calf liver, kidneys, meat, eggs, and gastromucoprotein produced by the accessory cells of the glands found in the fundus of the stomach. In healthy subjects, vitamin B_{12} combines with gastromucoprotein in the stomach to give a sufficiently stable complex which protects vitamin B_{12} from intestinal microflora to ensure adequate absorption of vitamin B_{12} (mainly in the ileum). Gastromucoprotein is absent from the gastric juice of patients with the Addison-Biermer anaemia due to pronounced atrophic gastritis. In the absence of gastromucoprotein, vitamin B_{12} delivered with food is decomposed by intestinal flora and is not assimilated by the body to cause vitamin B_{12} deficit. In other cases, vitamin B_{12} (folic acid) deficiency anaemia is the result of vast resection of the stomach, severe enteritis, increased demands for vitamin B_{12} in pregnancy, its consumption by helminths (bothrioce-

phaliasis), and in disordered assimilation of this vitamin by the bone marrow (achrestic anaemia).

An important biological effect of vitamin B_{12} is activation of folic acid. Like vitamin B_{12}, folic acid belongs to substances included in the group of vitamin B. It is contained in leaves of various plants, fresh vegetables, beans, liver, and kidneys of animals. Folic acid is deposited in the human body mainly in the liver, where it is present in inactive state. Vitamin B_{12} promotes formation of folic acid derivatives, folates, which are probably the factor necessary for haemopoiesis in the bone marrow. In conditions associated with vitamin B_{12} and folate deficiency, the synthesis of DNA is disordered; this in turn causes disorders in cell division; the cells become large and qualitatively inadequate. Erythroblasts are affected most severely: large cells of embryonal haemopoiesis, megaloblasts, are found in the bone marrow instead of erythroblasts. They are not only larger than erythroblasts; they also differ in the structure of their nuclei and protoplasm, earlier and more intense saturation with haemoglobin during their differentiation (at the stage of reticular structure of the nucleus), retarded mitotic division, and mainly in their inability to grow to normal erythrocytes. Most megaloblasts are decomposed in the bone marrow before they reach the stage of a nucleated cell. Only a small quantity of megaloblasts are differentiated to anuclear cells (megalocytes) and enter the blood vessels. Megalocytes are larger and more saturated with haemoglobin than erythrocytes and differ from them by morphological and functional inadequacy. Megalocytes have no such high oxygen-transport capacity as the erythrocytes and are quickly decomposed by reticuloendothelial cells: the average life of megalocytes is about three times shorter than of erythrocytes.

The absence of gastromucoprotein in gastric juice (like achlorhydria which usually attends this disease) is due to atrophy of the gastric mucosa. Some investigators believe that atrophy of gastric mucosa is not inflammatory in its origin as it was believed earlier (atrophic gastritis) but is a result of congenital insufficiency of its glandular apparatus which is manifested with time. In the opinion of other authors, the atrophy of gastric mucosa is caused by antibodies produced by the patient's body to the gastric glandular cells, which can however be slightly altered by toxic effects or inflammation (auto-immune mechanism).

If the second coenzyme of vitamin B_{12}, desoxyadenosylcobalamin, is deficient, fat metabolism becomes upset with accumulation of methylmalonic acid, which is toxic for the nervous system (provokes funicular myelosis).

The Addison-Biermer anaemia attacks commonly the aged; the incidence among women is higher than in men.

Pathological anatomy. The skin and the organs are pallid. Small haemorrhages are possible. Haemosiderosis of the liver, kidneys, bone marrow and dystrophic changes in them are characteristic. These changes are observed also in the myocardium, the brain, and the spinal cord (mostly in the lateral cord). Bone marrow is affected by hyperplasia; it is bright-red, the foci of extramedullar haemopoiesis are seen in the spleen and the lymph nodes. Histological studies show prevalence of red blood cells; many young forms, myeloblasts are seen. Megaloblasts, the large cells of perverted erythropoiesis, are especially numerous.

Clinical picture. The onset of the disease is insidious. The patient grows weaker, he complains of heart palpitation, dizziness, and dyspnoea, especially during exercise or brisk movements; the work capacity is impaired, the appetite becomes poor; slight nausea is possible. The first complaint is often the burning sensation in the tongue. This is explained by the

development of atrophic glossitis (see below) which usually attends this disease. The patient often develops achylic diarrhoea or, on the contrary, persistent constipations. Dystrophic changes in the nervous system cause skin anaesthesia and paraesthesia; the gait is often affected in grave cases: spastic paresis develops (incomplete spastic paralysis of the lower extremities); the knee reflex disappears, the function of the urinary bladder and the rectum can also be affected. All these symptoms are known as the funicular myelosis which develops due to the predominant affection of the lateral spinal columns. Symptoms of the disordered activity of the central nervous system (deranged sleep, emotional lability, etc.) become apparent.

Inspection of the patient reveals pallor of the skin and mucosa, usually with a yellowish tint due to increased decomposition of megalocytes and formation of bilirubin from the released haemoglobin, and a slight swelling of the face. The patient is not thin. Quite the reverse: most patients are well fed. The bright-red smooth and glossy tongue (because of the pronounced atrophy of the papillae) is quite characteristic of the Addison-Biermer anaemia. This symptom is known as Hunter's glossitis (W. Hunter was the first to describe this symptom). The mouth mucosa and the posterior wall of the throat are also atrophied. The tip and edges of the tongue, and also the mouth mucosa can be ulcerated. The tendency to caries is often seen in the teeth.

Pressing or tapping on the flat and some tubular bones (especially the tibia) is often painful. This is the sign of bone marrow hyperplasia. Palpation can reveal a slight enlargement of the liver and the spleen.

The cardiovascular system is usually involved as well. The left border of the heart is displaced to the left, tachycardia develops, "anaemic" systolic murmur is heard at the heart apex in 75 per cent of cases; the nun's murmur is often heard over the jugular veins. The pulse is soft and accelerated. Most patients develop hypotension. ECG shows a certain decrease in the general voltage, the decreased *T* wave and the *S-T* interval.

Changes in the gastro-intestinal tract are pronounced. Especially characteristic is atrophy of gastric mucosa which can be revealed by X-ray examination, and more distinctly by gastroscopy. The atrophy is often focal, and the affected sites (mostly in the fundus of the stomach) can be seen as iridescent spots. Atrophy can combine with polyps in the folds of gastric mucosa and its polypous thickening. It should be remembered that anaemia, including pernicious anaemia, can be a symptom of a malignant tumour in the stomach. Cancer of the stomach occurs in patients with the Addison-Biermer anaemia 8 times more frequently than in healthy persons. Patients with this disease should therefore be systematically inspected by X-rays (by gastroscopy whenever possible). Almost all patients develop achlorhydria. In 98 per cent of cases it has the histamine-resistant

character. The total amount of juice produced during the study is usually significantly diminished; the pepsin content of the juice is very low or it cannot be determined at all (achylia). Usually achlorhydria develops many years before the first symptoms of anaemia develop.

Elevated temperature is a common symptom of vitamin B_{12} (folic acid) deficiency anaemia; the temperature is usually subfebrile.

Blood plasma contains slightly increased amounts of free bilirubin due to increased haemolysis of the red cells, especially megalocytes; the plasma iron content increased to 30-45 mmol/l (170-200 *μg/ml).*

The blood picture (Plate 31) is characterized by a sharp decrease in the quantity of erythrocytes (to 0.80×10^{12} per 1 1) at a comparatively high haemoglobin saturation. Despite the decreased total haemoglobin content of the blood, the colour index remains high (1.2—1.5). Red blood cells differ in size (anisocytosis), with prevalence of large erythrocytes (macrocytes). Especially large slightly oval and intensely red megalocytes appear (in many cases megaloblasts are also seen). The volume of each cell increases. Many erythrocytes are oval, or they have the shape of a sickle and other shapes (poikilocytosis). Megalocytes often have remnants of the nucleus or its envelope in the form of Jolly bodies or Cabot rings. The content of reticulocytes is not high. The number of reticulocytes sharply increases (reticulocytic crisis) during vitamin B_{12} therapy to indicate the beginning remission. Blood leucocytes decrease mostly at the expense of neutrophils. Eosinopenia, relative lymphocytosis, and thrombocytopenia are observed. Large neutrophils with polysegmented nuclei also occur.

The quality of erythroid precursors in a specimen of bone marrow sharply increases, by 3—4 times compared with the number of leucopoietic cells (the proportion being reverse in physiological conditions). Megaloblasts are observed in varying amounts among the erythroid precursors; in grave cases they are found in prevailing quantity. Both erythropoiesis and leucopoiesis are disordered. Megakaryocytes are also large, with a multi-lobed nucleus: thrombocyte separation is disordered.

Course. If untreated, the disease progresses. Before Minot and Murphy proposed their effective treatment of the disease, patients rarely survived more than 3 years. At the terminal period, many patients developed coma (coma perniciosum) with loss of consciousness, arephlexia, decreased arterial pressure and temperature, vomiting and involuntary urination.

At the present time the patient recovers from the Addison-Biermer anaemia if treated properly and if adequate prophylactic measures against relapses of the disease are taken.

Treatment. Vitamin B_{12} is given. In most cases treatment begins with moderate doses of the vitamin (100-300 μg) which is given once a day intramuscularly or subcutaneously. Considerable shifts in the bone marrow

punctate toward normalization of erythropoiesis are observed already in 24 hours after the first dose of the vitamin is given. Cells produced by division and differentiation of juvenile forms are very much like the cells produced at the corresponding stages of normal erythropoiesis. Erythropoiesis normalizes completely in 2 or 3 days. In 5 to 6 days of the therapy, the newly formed erythrocytes enter the blood vessels in considerable amounts: the reticulocyte crisis occurs. The number of reticulocytes in the peripheral blood increases to 20—30 per cent and then gradually decreases. General weakness lessens, work capacity is regained, and gastric secretion normalizes in certain cases.

Signs of funicular myelosis are eliminated much slower and do not always disappear completely. After the blood picture normalizes and the symptoms of the disease markedly subside, the patient is given maintenance therapy with small doses of vitamin B_{12} (100 μg weekly, or 2-3 times a month). This therapy should be maintained for the rest of the patient's life. Clinical blood counts should be done periodically. The treatment ensures adequate subjective condition of the patient, his work capacity is regained, and relapses of the disease are prevented.

AUTO-IMMUNE HAEMOLYTIC ANAEMIA

Aetiology and pathogenesis. The pathogenesis of acquired auto-immune haemolytic anaemia (anaemia haemolytica chronica) is underlain mainly by the immunopathological shifts, which are manifested by the production of antibodies to own erythrocytes (autoagglutinins). This condition may be caused by acute infections, poisoning, medicamentous intoxications, especially severe forms of malignant lymphomas and collagenosis, and by some other factors. These antibodies belong to the immunoglobulin fraction and are incomplete or "weak" antibodies. Erythrocyte-bound antibodies do not cause agglutination in the blood vessels but block erythrocytes to promote their deposition in the reticulohistiocytic system (mostly in the venous sinuses of the spleen) and their capture and destruction by macrophages.

Sometimes auto-immune haemolytic anaemia is associated with the appearance of cold antibodies which are bound (together with the complement) to erythrocytes. Their action is manifested in the peripheral parts of the body (finger tips, ears) in overcooling. In addition to auto-agglutinins, autohaemolysins are also found in some patients. The disease may proceed in them with signs of both extra- and intravascular haemolysis.

Clinical picture. The disease develops either gradually and incidiously or acutely with a haemolytic crisis. The main complaints of the patient are weakness, dizziness, fatigue, and slightly elevated temperature. All these symptoms intensify during the haemolytic crises. Skin itching is absent. The skin is pallid with a slightly icteric hue. Applying pressure to the sternum and its percussion are painful. Palpation reveals enlarged and consolidated spleen; the liver is enlarged only slightly.

The blood erythrocyte and haemoglobin content is low, while the colour index remains normal. Erythrocytes vary in size, shape, and colour (poikilocytosis, anisocytosis, anisochromia). The average size of the erythrocytes is slightly smaller than normal (microcytosis). As distinct from congenital haemolytic anaemia, the erythrocytes of healthy individuals, as well as of patients with acquired anaemia, are less intensely coloured in the cen-

tre than by the periphery, which depends on their form (planocytes). The number of reticulocytes is high; reticulocytosis is especially marked in considerable anaemization and after the haemolytic crisis. The osmotic resistance of erythrocytes is not substantially changed. The blood serum of patients is yellowish. Study of the blood confirms increased content of unbound bilirubin on which the colour depends. Hypergammaglobulinaemia is also determined. The iron content of the serum is increased. Iron is liberated in large amounts during haemolysis of erythrocytes. Owing to increased liberation of bilirubin, bile obtained by duodenal probing is very dark. The urine and faeces of the patient are darker than normal; daily excretion of stercobilin with faeces and of urobilin with urine is increased. Study of specimens of bone marrow indicates more or less significant intensification of erythropoiesis.

Both cell-bound (blocking) antibodies and those found in the free state in the plasma (conglutinins) are revealed in the blood of patients with auto-immune haemolytic anaemia. Coombs' test is used to reveal them. A direct Coombs' test is used to reveal cell-bound (blocking) antibodies. A suspension of the patient's erythrocytes washed in isotonic sodium chloride solution is added to the serum of a rabbit immunized by human blood globulins. Erythrocytes agglutinate if anti-erythrocytic antibodies are present on their surface. Erythrocytes of individuals without acquired haemolytic anaemia are not agglutinated. Conglutinins in the serum of patients are revealed by adding erythrocytes of a healthy individual (donor) in order to absorb the antibodies on them. The cells are washed and carried through the test as described above. This is the indirect Coombs's test.

Course. The course of the disease is usually undulant. The disease is exacerbated by infections, big doses of some medicines, e.g. salicylates, and by some other transient factors. In grave and long-standing cases, the patient's bone marrow may be exhausted and anaemia becomes hyporegenerative. In some cases the activity of the bone marrow may also be inhibited by the production of auto-antibodies to erythroblastic precursors. Formation of the pigment stones in the gall bladder is a complication of the disease. Thrombophlebitis, and thrombosis of the splenic vein are other possible complications.

Treatment. Corticosteroids inhibit the production of antierythrocytic auto-antibodies. Blood transfusion should be carried out in rare cases because it can markedly enhance haemolysis.

MYELOPLASTIC SYNDROME (PANMYELOPHTHISIS)

The myeloplastic syndrome or panmyelophthisis is a large group of conditions of various aetiology and pathogenesis, whose main clinical symptoms are determined by the inhibition of blood formation in the bone marrow. Congenital (genetically determined) and acquired forms of myeloid aplasia are distinguished by the origin, and acute and chronic forms—by the course of the disease. There are also forms characterized by incomplete inhibition of the regenerative capacity of the bone marrow (hypoplasia), and complete functional inhibition (aplasia).

Various clinicohaematological variants of myeloid hypo- and aplasia are differentiated by partial (in one direction) or total (in all directions) inhibition of the regenerative capacity of the bone marrow. Most specific forms are hypo- and aplastic anaemia (in which the erythropoietic function of the bone marrow is inhibited in the first instance), agranulocytosis (inhibition of the granulocytopoietic function of the bone marrow), and also panmyelophthisis in which the regenerative function of the bone marrow is inhibited in all directions (the production of erythrocytes, granulocytes and thrombocytes is deranged more or less uniformly).

Hypo- and aplastic conditions of the bone marrow (especially hypoplastic anaemia) should not be mistaken for the hyporegenerative conditions which develop for example in chronic

posthaemorrhagic anaemia, grave haemolytic anaemia, and in some other conditions. As distinct from hypoplastic anaemia, a sufficiently large amount of the erythroid precursors are preserved in the bone marrow of patients with hyporegenerative anaemia; the course of the disease is not steady; if the cause of the bone marrow exhaustion is removed, its function is restored. The myeloplastic conditions do not also include cases where the decreased content of the formed elements (erythrocytes, neutrophils, thrombocytes) in the peripheral blood is explained by their increased destruction in the spleen (hypersplenism) which occurs when the spleen is significantly enlarged (e.g. in cirrhosis of the liver) because the activity of the bone marrow is not decreased in these conditions but is, on the contrary, increased. Cytopenia due to metaplasia of the bone marrow (in malignant lymphomas and leucosis) and due to displacement of myeloproliferative tissue (in multiple myeloma, multiple metastases of cancer, etc.) does not belong to this group either.

Aetiology and pathogenesis. The aetiological factors of myeloid hypo- and aplasia are varied. These may be endogenous factors, e.g. thymus hypofunction, hereditary predisposition, etc. But the exogenous factors are as a rule decisive. Among them the most important are (a) chemical poisoning, e.g. with benzene, tetraethyl lead; (b) prolonged and uncontrollable medication with some drugs, e.g. amidopyrin, butadion, cytostatic preparations (embichin, TEPA, 6-mercaptopurine), methylthiouracyl, sulpha drugs, some antibiotics (chloramphenicol), or increased sensitivity to them; (c) infectious and toxic effects (tuberculosis, sepsis, syphilis); (d) vegetable food that may, under certain conditions, contain toxic substances (wheathered corn, etc.); (e) ionizing radiation (radioactive substance, X-rays, etc.). It is believed that the above factors act mainly by inhibiting the nucleoproteid enzymes to slow down the mitotic cell division.

A special importance is now attached to auto-aggressive mechanism in the development of some forms of myeloid hypoplasia. This mechanism consists in production of antibodies to own blood and bone marrow cells. It is possible however that the auto-antibodies are not the triggering mechanism of the disease, and their production is only secondary to the changes in the cells. Causes of myeloid aplasia remain unknown in some cases.

Pathological anatomy. Pronounced anaemia of organs, dystrophic changes and traces of multiple haemorrhage in them are revealed in classical cases. The territory of red bone marrow is markedly contracted due to its replacement by fat tissue.

Clinical picture. The clinical picture of the disease varies depending on the prevailing direction of the inhibition of the bone marrow function. But the most characteristic symptoms are caused by anaemization, haemorrhagic diathesis, necrotization of tissues, and secondary infection (e.g. in agranulocytosis). As the disease progresses, certain changes can be seen in the clinical picture: a certain syndrome may dominate during the initial stage of the disease but later other syndromes join to indicate the total inhibition of the regenerative capacity of the bone marrow. If the disease develops gradually and remains unnoticed by the patient his first complaints are weakness, dyspnoea, rapid unmotivated fatigue, and decreased work capacity. Haemorrhagic signs are possible in thrombocytopenia: nasal bleeding, multiple ecchymoses on the skin caused by the slightest injuries and sometimes spontaneously, gastrointestinal and uterine haemorrhages. Fever is also characteristic.

Inspection of the patient reveals pallor; signs of resolving subcutaneous haemorrhages can be seen as bluish-purple spots, which later turn brown, and finally yellow. The skin is moist, its turgor is slightly decreased. The tourniquet and pinch tests are positive in pronounced thrombocytopenia. Changes in the heart, lungs, kidneys and the gastro-intestinal tract are usually not pathognomonic, but haemorrhages into various organs and internal and external haemorrhages are possible in the haemorrhagic syndrome. The lymph nodes, the liver and the spleen are usually not enlarged.

The blood picture shows various degrees and directions of changes in the regenerative capacity of the bone marrow. *Hypo-* and *aplastic anaemia* are characterized by markedly

decreased erythrocyte counts (to 1×10^{12} per 1 1 and below). As a rule, erythropenia is attended by more or less pronounced leuco- and thrombocytopenia. The number of reticulocytes decreases considerably.

Neutropenia is most pronounced in agranulocytosis: the number of leucocytes decreases to 1.5×10^9-1×10^9 and even to 0.2×10^9 per 1 l. The number of granulocytes decreases in the first instance. Their percentage content does not exceed 1-5 of the total number of leucocytes. This accounts for relative lymphocytosis and monocytosis although the absolute content of these cell forms usually remains unaltered or decreases only insignificantly. Younger forms of neutrophil leucocytes (stab neutrophils) are practically absent from the peripheral blood. Eosinophils cannot be revealed either. Some pathological changes in the nuclei and cytoplasm of neutrophils are seen: pyknosis of the nuclei and toxic granulation of the cytoplasm. Anaemia and thrombocytopenia are not pronounced during the initial period but later they become more pronounced.

In certain cases, anaemia, leucopenia and thrombocytopenia develop almost simultaneously which corresponds to the clinical picture of panmyelophthisis. When the number of thrombocytes falls below 30×10^9 per 1 1, the haemorrhagic syndrome develops.

The sternal punctate is not substantially changed during the early stages of the disease. The number of erythroid or myeloid precursors may be relatively decreased. In marked cases, the sternal punctate can contain only meagre quantity of cell elements (with prevalence of the reticular and plasma cells). Since the course of marrow aplasia is not uniform, sternal punctate may occasionally contain portions of bone marrow in which the changes are only insignificant. This may mislead a physician in his assessments of the disease gravity. A more correct and accurate picture of marrow haemopoiesis gives trepanobiopsy of the iliac bone by which histological preparations of the bone marrow can be obtained.

Course. Acute, subacute, and chronic forms are distinguished. The acute disease may have a fulminant course: cases were reported in which patients died in two days. The course of the forms with inhibited leucopoiesis is usually more rapid than that with the prevalent inhibition of erythropoiesis. This to a certain degree depends on a different life span of white and red blood cells.

The prognosis of the congenital and genuine myeloid aplasia is quite unfavourable. The disease progresses and the patient dies in a certain period of time. The progress of the myelotoxic form of the disease, e.g. caused by overdosage of amidopyrin, butadion or cytostatics, can often be arrested if the intake of these preparations is discontinued in due time. The patient may thus recover. The frequent cause of death in agranulocytosis is sepsis.

Treatment. The patient must be taken to hospital. In order to act on the auto-immune mechanism of the disease, corticosteroids (e.g. prednisolone) are given. If anaemization is pronounced, repeated transfusions of blood and erythrocytic mass are indicated. Blood and specially prepared leucocytic and platelet mass are transfused to patients with leucopenia and thrombocytopenia. In order to stimulate leucopoiesis, sodium nucleate, pentoxyl, and anabolic steroid hormones are given. Large doses of vitamins (especially of vitamin B_{12}) are indicated in all cases. Antibiotics are given in septic complications. Bone marrow transplantation is now used to treat myeloid aplasia.

Haemoblastosis

Haemoblastosis is proliferation of the haemopoietic tissue; it can be diffuse and focal.

Haemoblastosis is a disease of the whole blood system characterized by (1) progressive cell hyperplasia in the haemopoietic organs with

pronounced prevalence of proliferation of certain cells (which determine the morphological essence of the disease in each particular case) over their differentiation (maturation), and the loss of their typical morphological and functional properties; (2) substitution (metaplasia) of these pathological cells for normal cells of the haemopoietic organs; (3) development of pathological foci of haemopoiesis in various organs.

Haemoblastosis is a comparatively rare disease. Its mortality rate is 1.7-8.1 per 100 000 population. The share of leucosis among therapeutic cases is 1.5-2.6 per cent. However the incidence of haemoblastosis, especially of acute forms, has recently increased in all countries.

Aetiology and pathogenesis. Most authors regard haemoblastosis as tumours whose morphological basis are haemopoietic cells of various organs. This has been proved by numerous observations and experiments. For example, some factors can provoke the growth of tumours and haemoblastosis. These factors are cancerogenic substances (3,4-benzpyrene, methylcholanthrene, etc.) and radiation. There are common features in the character of tissue proliferation in haemoblastosis and tumours. Metabolic disorders in haemoblastosis-affected cells and tumour cells have been proved to be of the same type (anaerobic glycogenosis prevails in them). Concurrence of haemoblastosis and tumour is not infrequent. Administration of an extract of tumour tissue to experimental animals causes haemoblastosis in some of them; and vice versa, administration of the bone marrow or lymph node punctates of haemoblastosis patients may provoke the growth of tumours.

There are two main theories explaining the aetiology of haemoblastosis and tumours. These are the virus and the genetic theory. At the present time more than 20 viruses have been isolated that can cause haemoblastosis in animals. Attempts at isolating the virus of the main forms of haemoblastosis in man end in failure. According to the genetic theory, haemoblastosis develops due to the congenital or acquired damage to the chromosome structures of low differentiated cells of the haemopoietic organs. A clone theory has been launched recently, according to which haemoblastosis arises due to primary chromosome mutation in one of the haemopoietic cells with its subsequent multiplication and formation of a clone of blast cells.

Nomenclature and classification of haemoblastosis. All types of haemoblastosis are designated in accordance with the name of cells which determine the cytomorphological essence of the disease. For example, acute myeloblasts leucosis, chronic erythromyelosis, lymphoid leucosis, etc. The traditional names of certain types of haemoblastosis describe the major syndrome of the disease, e.g. osteomyelosclerosis, macroglobulinaemic haemoblastosis, etc. Certain types of haemoblastosis have a second

name (the name of the author who was the first to study or describe the disease), e.g. Waldenstrom disease, Cesaris disease, etc. Like other tumours, haemoblastoses can be benign and malignant.

More than 30 forms of haemoblastosis have been well studied. Recent advances in haematology have made it possible to improve the classification of the diseases.

The following two groups of haemoblastosis are distinguished: leucosis and haematosarcoma (malignant lymphoma).

*Leucosis** is the disease of the haemopoietic cells with the primary locus of the tumour in the bone marrow. The release of tumour (leucosis) cells into the blood cause leukaemia as a symptom of the disease. The following forms of leucosis are distinguished.

1. Acute leucosis in which haemopoiesis is transformed at the expense of low differentiated blast cells or precursor cells of the 3rd and even 2nd series. Haemocytoblastosis is now absent from the modern classification because it has been proved that the "youngest" cell of haemopoiesis is not the haemocytoblast but three consecutive series of precursor cells. Various forms of acute leucosis are differentiated mainly by the cytochemical characteristics of leukaemic cells. In adult patients, acute myeloblastic leucosis occurs in 60 per cent and lymphoblastic leucosis in 25-30 per cent of cases. Other forms occur less frequently.

2. Chronic leucosis, in which haemopoiesis is transformed at the expense of more mature cells of differentiated haemopoiesis. Separate forms are differentiated quite easily by cytomorphological signs of leukaemic cells: chronic myeloid leucosis, chronic lymphoid leucosis, chronic erythromyelosis, erythraemia, etc.

It should be remembered that differentiation between acute and chronic leucosis first of all depends on the cytomorphological sign (the degree of cell maturity) rather than on the clinical course of the disease, although both these signs coincide in most cases. Acute leucosis may continue for a year or even longer, while a patient with chronic leucosis may die within a few months. Therefore, the diagnosis, in addition to the definition of the type of leucosis (acute, chronic), should also determine its course. It is also important to remember that acute leucosis almost never transforms into the chronic form because it is characterized by anaplasia (the cells lose ability to further maturation) of the initial elements of haemopoiesis. Quite the reverse, chronic leucosis can be exacerbated with formation of non-differentiated elements (blasts) in the foci of haemopoiesis and in the

* Translator's note: the term "leukaemia" is generally used in western literature while "leucosis" is the accepted usage in the USSR. In view of the authors' preference we have retained their usage, while both terms are used more or less synonymously.

peripheral blood. Exacerbations may be spontaneous or provoked by some causes of progressive anaplasia of leukaemic cells. Chronic leucosis in the stage of blast crisis is similar to acute leucosis.

Leucosis can have the following three variants: with considerable increase in the quantity of pathological cells in the peripheral blood (*leukaemic form),* with moderate increase in their number *(subleukaemic form*), and without appreciable leukaemic shift in the presence of normal or decreased quantity of white blood elements *(aleukaemic form).*

Leukaemic forms of leucosis are sometimes difficult to differentiate from leukaemoid reactions (extreme leucocytosis to 0.1×10^{12} per 1 1 of blood) which are observed in some infectious diseases. In leukaemoid reactions, the leucocyte counts can be shifted to the left, to myeloblasts. But this leucocytosis in leukaemoid reactions is characterized by its potential reversibility (provided the causes are removed) and by preservation of the functional and morphological properties of leucocytes. Although leukaemic cells are called normal haemopoietic cells, in fact they cannot perform their usual function, and patients with leucosis have decreased immunity. The cells cannot differentiate into more mature cells; they decompose at a quicker rate. It has been established that leukaemic cells have an inhibiting effect on normal haemopoiesis.

Leucosis is characterized by lability, pronounced ability to transformation with exacerbation of the process (with the progress of anaplasia to less differentiated cells) and with involvement of other haemopoietic cells. Moreover, both morphological and clinical changeability of the process are characteristic. In some cases more or less long remissions can occur spontaneously or under certain effects (infectious disease, treatment). Remissions are then followed by exacerbations (to blast crisis).

Each type of leucosis is a static expression of the specific features of clinico-cytomorphological picture of the diseases and at the same time can also include certain elements of the dynamic process. This should be taken into consideration during establishing a diagnosis and in prescribing the appropriate therapy.

Haematosarcoma (malignant lymphoma, or regional tumours with their possible generalization) is also a tumour of haemopoietic cells but its localization is mostly extra-marrow and focal. Lymphogranulomatosis is the most common haemoblastosis. Paraproteinaemic haemoblastosis (mutliple myeloma, Waldenstrom's disease) is a special form arising from precursors of B lymphocytes and characterized by production of pathological globulins. Reticulosarcoma and some other diseases are also special forms of paraproteinaemic haemoblastosis.

Leucosis can also transform into some types of malignant lymphomas, except lymphogranulomatosis. The reverse process is also possible: ample

leukaemic cells appear in the blood and bone marrow in malignant lymphomas, i.e. the blood picture and the course of the disease are similar to those observed in leucosis.

ACUTE LEUCOSIS

Acute leucosis is characterized by profuse proliferation of the youngest (blast) elements of blood with their subsequent disturbed differentiation and also with development of foci of pathological haemopoiesis in various organs. Lympho- and myeloblastic forms of the disease are common.

Acute leucosis occurs at any age, but men and women from 20 to 30 are mostly affected.

Pathological anatomy. The skin and the internal organs are anaemic. Mucosa (especially in the fauces and mouth) and often the skin are affected by necrotic ulcers and multiple haemorrhages. Haemorrhages into the internal organs also occur. Lymph nodes, the spleen and the liver are moderately enlarged. Histological studies of these organs and of the bone marrow show that they are as if "stuffed" with non-differentiated cells of blood (blasts).

Clinical picture. The onset of the disease is in most cases acute or subacute: high temperature (remittent or hectic), profuse sweating, chills, pronounced weakness, pain in the bones, and other general symptoms resembling those of acute septic affections. Pain in the throat is often one of the first complaints: swallowing becomes painful because of necrotic ulceration of the throat and fauces. For this reason the disease is often mistaken for necrotic tonsillitis and only further observation of the patient and the study of the bone marrow and blood help the physician establish a correct diagnosis. Fever, chills and sweating, which are so characteristic of acute leucosis, are explained by the pyrogenic effect of purines released in great quantity during the decomposition of immature leucocytes. Fever can also be caused by secondary infections; despite the markedly increased production of white blood cells, their function is inadequate, and resistance of leucosis patients to various infections decreases.

In some cases the onset of the disease is gradual, with non-pronounced general symptoms: slight weakness, indisposition, rapid fatigue, and subfebrility. The condition then worsens and a complete clinical picture of the disease develops. Anaemia and various haemorrhagic complications and secondary infection develop.

Inspection of the patient usually reveals grave condition from the very onset of the disease. In the terminal period the condition is particularly grave: the patient is passive, answers the doctor's questions with difficulty, or is unconscious. The skin is pallid, sometimes with yellowish or greyish hue, and moist; its turgor is decreased. Traces of subcutaneous and in-

tracutaneous haemorrhages can be seen. The tourniquet and the pinch tests are positive; haemorrhage is considerable at points of injections. Necrosis and bed-sores are possible. Necrosis of the mucosa, especially of the mouth and throat, is especially pronounced. Ulcerous and necrotic tonsillitis, gingivitis, and stomatitis are quite characteristic of the disease. Necrotized surfaces are covered with a poorly removable grey or yellowish coat. When removed, it reveals bleeding ulcers. The breath of the patient is putrefactive. Palpation reveals enlargement of separate groups of the lymph nodes, spleen, and the liver. The heart borders are broadened; tachycardia, systolic murmur at the heart apex (due to dystrophic processes in the heart muscle), and anaemia are revealed. Pericarditis and pleuritis are possible. Each haematological form of leucosis is characterized (though not necessarily) by some special clinical features.

The blood of patients contains increased number of white blood cells: to 1×10^{11} and even 2×10^{11} per 1 1 (in rare cases even this figure may be exceeded) (Plate 32). Subleukaemic forms of the disease can occur. Leucopenia can develop in some cases at the early stage of acute leucosis. Leucopenia is then succeeded by leucocytosis. The most specific haematological sign of the disease is the presence of blast cells in the peripheral blood. All blast cells are similar morphologically but special cytochemical reactions can be used to differentiate between them. Prevalence of their certain forms is determined by the haematological variant of leucosis (acute lymphoblastic, acute myeloblasts, acute monoblastic leucosis, etc.). The immature forms may amount to as high as 95 and even 99 per cent. Leukaemic cells often have some specific defects in their nuclear and cytoplasmic structure. Only the youngest and the most mature cells can be revealed in the blood of most patients with acute leucosis, while intermediate forms are absent (hiatus leucaemicus). Eosinophils and basophils are absent; other cell forms are decreased significantly not only relatively but also absolutely. Thrombocytopenia and anaemia are observed which can be explained by the displacement of megakariocytes and erythroblasts from the bone marrow by vigorously proliferating blast cells and also by the prevalent development in the direction of leucopoiesis. Anaemia may intensify due to haemorrhage (characteristic of this disease) and also due to the intensified haemolysis of erythrocytes. Coagulability of blood and the bleeding time are abnormal in most cases; ESR sharply increases.

The bone marrow punctate contains 80-90 per cent of leukaemic blast cells, which displace all other cell elements.

Course. The course of the disease is progressive. Prognosis is unfavourable. The average life expectancy of patients with acute leucosis is about 2 months; in separate cases from 2 days to 18 months. But modern

therapy can prolong the patients' life to 2-3 years; in rare cases to 5 years and more.

Treatment. Combined therapy, including 3-5 preparations, depends on the clinico-haematological variant of the disease. Corticosteroids (e.g. prednisolone) in large doses are prescribed together with cytostatic (6-mercaptopurin, vincristin, methotrexate, etc.). Anaemia is removed by blood transfusion and by preparations preventing haemorrhagic complications (vicasol, calcium chloride, aminocaproic acid). If secondary infection arises, antibiotics are indicated. Intense vitamin therapy is also useful.

CHRONIC MYELOLEUCOSIS

Chronic myeloleucosis is the most common variety of leucosis. It develops from precursors of myelopoiesis. It is characterized by myeloid hyperplasia of the bone marrow attended by delayed maturation of the myeloid elements at a certain stage of their development and by myeloid metaplasia of the spleen, liver, lymph nodes and other organs. Karyological studies reveal, in the overwhelming majority of cases, the so-called Philadelphia (Ph^1) chromosome in the myeloid precursors. Chronic myeloleucosis occurs at any age but its incidence at the age of 20-45 is higher.

Pathological anatomy. The internal organs are pallid and anaemic. The spleen is markedly enlarged, consolidated; it has traces of past ischaemic infarctions and new infarctions. Microscopy does not reveal spleen follicles; diffuse proliferation of the myeloid tissue can be seen. The liver is enlarged and myeloid proliferation can be traced by the course of the liver capillaries and the periportal layers. The lymph nodes are somewhat enlarged; their section is greyish-red. Myeloid tissue can be seen in them (as well as in the other organs).

The bone marrow is juicy, bright-red or greyish-red; it displaces fat marrow in the tubular bones to a lesser or greater extent. Red bone marrow is represented mainly by the myeloid elements; the more acute the process, the greater the prevalence of less differentiated elements.

Clinical picture. The initial symptoms of the disease are not specific: weakness, fatigue, excess sweating, and subfebrile temperature. The symptoms become more pronounced with time and the patient consults a doctor. The work capacity decreases appreciably, weakness increases, sweating becomes profuse, the body temperature rises periodically to 37.5-39 °C; cachexia develops. A common symptom is the feeling of heaviness in the left part of the abdomen which depends on the pronounced enlargement of the spleen. Pain may be due to a considerable distension of the spleen capsule. Splenic infarction is manifested by piercing pain which intensifies during breathing. Pain in the bones is not infrequent. It is due to hyperplasia of the myeloid tissue.

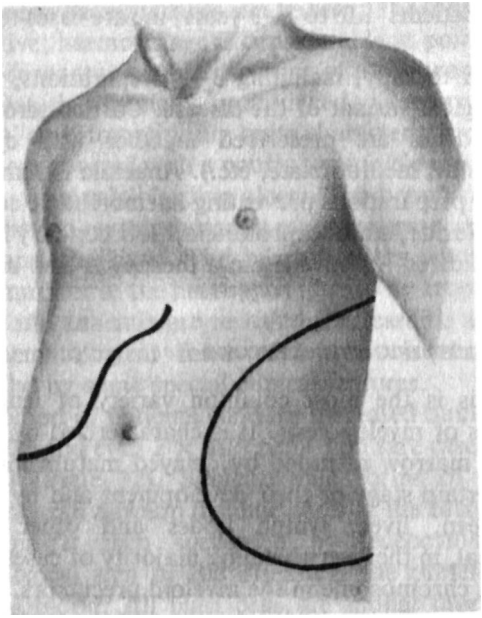


Fig. 109. A patient with chronic myeloid leucosis (marked are the borders of the enlarged spleen and liver).

Myeloid infiltration in various internal organs can be the cause of some additional symptoms, such as dyspeptic signs in affections of the gastrointestinal tract, coughing in the presence of infiltrations in the lungs and the pleura, neurological changes due to affection of the brain, the spinal cord, nerve radices, etc. In the terminal period of the disease, the heart is overloaded due to pronounced anaemization; dyspnoea and oedema develop (their origin being dependent also on hypoproteinaemia). Thrombocytopenia and shifts in the blood coagulation system cause haemorrhagic complications. Inspection of the patient helps physician assess his general condition and determine (approximately) the stage of the disease (stage I—the initial symptoms, stage II—pronounced symptoms, and stage III—dystrophy; this is the terminal stage). The terminal stage is characterized by pronounced cachexia and considerable enlargement of the abdomen due to markedly enlarged liver and spleen (Fig. 109). The skin is pallid, with a yellowish or greyish hue; it is flaccid and moist. The legs are affected by oedema. Gingivitis and necrosis of the mouth mucosa are possible. Palpation reveals moderate enlargement of the lymph nodes of various groups. The liver and especially the spleen are markedly enlarged. It is believed that no other disease is attended by enlargement of the spleen to the extent to which it is enlarged in the terminal stage of chronic

myeloleucosis. The liver and the spleen are firm. In the presence of infarctions of the spleen it is tender to palpation. Peritoneal friction sound can be heard over the spleen by auscultation. Applying pressure to the bones and tapping over them are painful.

The leucocyte count is markedly high (Plate 33). It can be 3×10^{11} and even 6×10^{11} per 1 1. Leucocyte count can first only slightly exceed the normal level but later it increases, gradually or suddenly. Temporary remissions are possible, especially in the appropriate therapy. In addition to the main form of myeloleucosis characterized by a considerable increase in the white blood cells count (leukaemic), there may be cases with their moderately increased (subleukaemic) and normal counts (aleukaemic). Study of the blood smears reveals mainly cells of granulocytic series which make 95-97 per cent of all white blood elements. There are many immature forms among them (myelocytes, promyelocytes, and even myeloblasts). During exacerbation, the number of young forms markedly increases. Only the youngest cells, myeloblasts, and a relatively small number of mature granulocytes (stab and segmented ones) can be revealed in the blood, while the intermediate forms are absent (hiatus leucaemicus). Basophils and eosinophils are usually present in the smear; their percentage can even be increased. Basophilia in 4—5 per cent of cases is regarded as a sign of myeloleucosis. The number of lymphocytes and monocytes decreases to 3-0.5 per cent in grave cases with significant leucocytosis, but their absolute amount in the blood does not change substantially. Red blood changes are only observed at stages II and **III** of the disease, when anaemia joins the process and progresses. Erythrocyte and haemoglobin content of the blood decreases synchronously. The colour index therefore remains within the normal range (0.8-1.0). Thrombocytopenia develops as the terminal period approaches. ESR usually increases to 30—70 mm/h.

The content of the erythroid precursors markedly decreases in the bone marrow (especially when the disease approaches its terminal stage). Cells of the myeloid series prevail (especially juvenile forms: promyelocytes, myelocytes, and myeloblasts). Megakaryocyte count slightly increases in the first half of the disease. Characteristic also is the increase in the number of basophilic and eosinophilic promyelocytes and myelocytes.

Course. The course of the disease is progressive, sometimes with transient spontaneous remissions. Before modern methods of treatment of the disease were introduced into clinical practice, the average life expectancy of patients was 2.5—3 years (sometimes to 10 years). Today the life of patients is prolonged more significantly. Patients die of cachexia, anaemization incompatible with life, haemorrhagic complications, or from a joining infection.

Treatment. Myelosan and other cytostatics are prescribed, usually in

combination with 6-mercaptopurine, prednisolone, etc. Patients with a marked splenomegaly are given radiotherapy or dopan. Repeated transfusions of blood or packed red cells are indicated in cases with pronounced anaemization.

CHRONIC LYMPHOID LEUCOSIS

Chronic lymphoid leucosis is now regarded as a benign tumour of the immunocompetent tissue. Its haematological basis is mainly B-lymphocytes (morphologically mature but functionally inadequate). Chronic lymphoid leucosis is characterized by systemic hyperplasia of the lymphoid apparatus, lymphoid metaplasia of the spleen, bone marrow, and other organs. Chronic lymphoid leucosis is a common form of leucosis. It usually occurs in the middle-aged and aged individuals (from 35 to 70), mostly in men.

Pathological anatomy. The lymph nodes of various groups are enlarged significantly. Their section is grey or greyish-red. The pattern of the lymph nodes is blurred; microscopy reveals accumulation of lymphoid cells, among which juvenile forms occur. The tonsils are enlarged, their structure is indistinct; microscopy reveals large accumulations of lymphocytes and lymphopoietic cells. The spleen is markedly enlarged but not to the extent to which it is enlarged in chronic myeloleucosis. Its structure is indistinct because of diffuse hyperplasia of the lymphoid tissue. Lymphatic infiltrations are seen in the liver, the stomach wall, pancreas, kidneys, and the skin; in other words, all organs can be affected. Lymphoid metaplasia of the bone marrow is observed.

Clinical picture. The initial symptoms are general weakness, indisposition, and rapid fatigue. The first symptom which troubles the patient and makes him feel like consulting a doctor is usually enlargement of the subcutaneous lymph nodes. General weakness gradually increases, excess sweating develops along with subfebrile temperature. Depending on a particular enlarged lymph node group and the organ affected by lymphoid infiltration, additional symptoms develop: dyspepsia, diarrhoea (in affection of the gastro-intestinal tract), dyspnoea and attacks of asphyxia (in compression of the trachea and bronchi by the bifurcation lymph nodes), erythema, dryness and itching of the skin (in leukaemic lymphodermia), etc. Lymphoid metaplasia of the bone marrow may cause haemorrhagic symptoms (due to thrombocytopenia) and anaemia. Leukaemic infiltration can cause radicular pain and exophthalmos. Diffuse lymphatic proliferation in the nasopharynx can develop.

Enlarged lymph nodes can often be revealed during inspection of the patient. Lymph nodes of one or several groups are often enlarged; later all other lymph nodes become also involved. The tonsils can be enlarged too.

Skin infiltration is attended by its consolidation, reddening, dryness and scaling. At the terminal stage, the patients are extremely thin (cachexia).

Palpation is used to assess accurately the enlargement of the lymph nodes and their properties. The lymph nodes are elastic-pasty; they do not fuse with the skin or with one another, and are painless in most cases. They can grow to the size of a hen egg. Even markedly enlarged, the lymph nodes never ulcerate or suppurate (as distinct from tuberculosis affection of the nodes). The liver and the spleen are enlarged and consolidated. Infarctions of the spleen can occur; its palpation then becomes tender.

Leucocyte counts in the leukaemic form of the disease are as high as 3×10^{11} per 1 l, and more. Lymphocytes make 80—95 per cent of the white blood (Plate 34); they are mostly mature. The structure of their nucleus and cytoplasm is sometimes quite peculiar: the cells are very soft and are easily destroyed when preparing a smear; specific Botkin-Gumprecht shadows are formed. Small amounts of juvenile cells, prolymphocytes and lymphoblasts, occur. During exacerbation their number increases. The relative quantity of neutrophils is much decreased (to 20-4 per cent). The blood picture is less specific in subleukaemic and aleukaemic forms of the disease, where lymphocytosis is usually less pronounced. Anaemia and thrombocytopenia (mainly of the auto-immune genesis) join at the terminal period.

Study of the punctate of the bone marrow reveals its lymphoid metaplasia: great quantity of lymphoid cells are found (to 50 and even 90 per cent in especially grave cases). The number of cell elements of the granulocytic and erythroid precursors is decreased. The results of studying the lymph node punctate are less convincing because lymphoid cells are common elements of its parenchyma while the hyperplastic character of the lymphoid tissue is sometimes difficult to determine.

Course. The disease progresses in cycles or gradually. The average life expectancy of patients is 4—5 years. Some survive for 10—12 years and over. The patients die of secondary infections, usually pneumonia (which is promoted by inhibition of humoral immunity), of haemorrhagic complications, and cachexia.

Treatment. Active treatment is not given during the initial period of the disease (like in chronic myeloleucosis). Special attention is given to normalization of conditions of work and rest of the patients, who must be fed an adequate diet rich in vitamins and proteins. The patient should walk in the open air. X-ray therapy is given in the presence of toxicosis or if the disease is rapidly progressing. The enlarged lymph nodes and the spleen are irradiated. Leukeran, prednisolone, cyclophosphane and other chemical cytostatics are given. Blood transfusion is indicated in anaemia and thrombocytopenia.

ERYTHRAEMIA

Erythraemia (chronic erythromyelosis, Vaquez' disease) is a benign myeloproliferative disease characterized by total hyperplasia of the bone marrow cell elements, which is more pronounced in the erythroid precursor. Erythraemia was first described by the French clinicist Luis Vaquez in 1892. Aged males are mostly affected.

Erythraemia should be differentiated from erythrocytosis which may be a symptom of some other diseases (chronic diseases of the lungs and the heart, essential hypertension, some kidney diseases, etc.) and erythrocytosis developing in the presence of hypoxia (at high altitudes, e.g. in highland; less frequently in pilots). The symptoms of the main disease prevail in the clinical picture of symptomatic erythrocytosis. During remission, or in cases of recovery, the erythrocyte count in the peripheral blood normalizes. Symptomatic erythrocytosis is not attended by neutrophilic leucocytosis or thrombocytosis, or else splenomegaly, which are common in erythraemia.

Pathological anatomy. Pronounced hyperaemia of the organs and the presence in them of old and new haemorrhages are characteristic. Red bone marrow is affected by hyperplasia; it displaces fat from the diaphysis of the tubular bones. Histological studies reveal increased number of the erythroid series cells. The liver and the spleen are mildly enlarged and plethoric. The left ventricle of the heart is often hypertrophied (in arterial hypertension).

Clinical picture. The onset of the disease is slow and indistinct. When the symptoms are activated, the patient complains of headache, heaviness in the head and noise in the ears, exertional dyspnoea, impaired memory, and skin itching. Vision and hearing function are also impaired in some cases. Pain in the abdomen can develop, probably due to excess blood delivery to the internal organs. Unbearable and burning pain can transiently develop in the finger tips (erythromelalgia), which can be explained by transient vascular spasms.

Inspection of the patient reveals peculiar plethoric redness of the exposed skin (face, neck, hands). The tongue and the lips are bluish-red, the eye conjunctiva is hyperaemic. This peculiar colour of the skin and mucosa is due to overfilling of the surface vessels with blood and its slow movement in the vessels. The greater part of haemoglobin is thus converted into its reduced form. Palpation reveals moderately enlarged spleen and liver. Tapping over flat bones and exerting pressure on them are painful, which is characteristic of bone marrow hyperplasia.

Arterial pressure (both systolic and diastolic) is often increased. It is believed that arterial hypertension is a compensatory reaction of the vessels to the increased viscosity of blood. In these cases palpation of the apex beat and electrocardiography reveal left-ventricular hypertrophy.

The erythrocyte count increases and is usually from 6×10^{12} to 8×10^{12} per 1 l, and more; haemoglobin increases to 180—220 g/l; the colour index is less than 1. The total blood circulatory volume increases significantly (1.5-2.5 times) mainly at the expense of increased erythrocyte count. The blood reticulocyte content increases to 15—20‰ which indicates intensified regeneration of erythrocytes. Polychromasia of erythrocytes is observed; separate erythroblasts can be found in the smear. The number of white blood cells also increases (1.5-2 times) at the expense of neutrophils, whose content is 70-85 per cent. The nuclear shift to the left is observed. The number of eosinophils, less frequently of basophils, increases. The number of thrombocytes increases sharply to 1.5×10^{12}-2×10^{12} per 1 l of blood. ESR is slow, blood viscosity increases significantly, while coagulability of blood and the bleeding time remain normal.

Histological study of the bone marrow (obtained by trepanobiopsy) shows significantly increased number of cells of the erythroid series. The number of juvenile cells of the granulocytic series and of megakaryocytes is also increased.

Course. The disease progresses slowly. The average life expectancy of patients is 10—14 years. The outcome of the disease is myelofibrosis with progressive hypoplastic anaemia or transformation into myeloleucosis. Most frequent complications are thrombosis of the cerebral vessels, spleen, lower extremities, and less frequently of other parts of the body. Tendency to bleeding also develops which is due to both functional inadequacy of thrombocytes and the low relative content of fibrinogen in the blood. Erythraemia patients often develop gastroduodenal ulcer.

Treatment. Radioactive phosphorus (^{32}P) is the best therapeutic means for erythraemia. It produces a cytostatic effect on haemopoiesis in the bone marrow. Clinical remission, lasting from 1 to 3 years is attained in most cases. New cytostatics (myelosan and marcofan) are also used. Symptomatic therapy includes phlebotomy (500 ml) at 5—7 day intervals.

LYMPHOGRANULOMATOSIS

Lymphogranulomatosis is a systemic disease in the group of malignant lymphomas and is characterized by the specific malignant affection of the lymph nodes, the spleen, and other organs. The disease was first described by Thomas Hodgkin in 1832. Hence another name, Hodgkin's disease.

Aetiology and pathogenesis. It is believed that the disease is underlain by lymphogenic metastasis from the primary focus, which obeys the law of tumour propagation. Lymphogranulomatosis is possibly a tumour of histiocytes in which the chromosome set is disordered (Melburn chromosome).

Pathological anatomy. The main changes are enlargement of various lymph nodes. Their histological studies reveal focal three-stage growths of the granuloma cells. The stage of diffuse hyperplasia of the lymph node is followed by focal, and then diffuse proliferation of the reticular and endothelial cells, and also of the cells of juvenile connective tissue. The presence of the Berezovsky-Sternberg cells is especially characteristic. These giant cells have 1, 2 or 3 large nuclei with large nucleoli. Fibrosis develops at the third stage. Necrotic foci are sometimes observed. Lymphogranulomatosis is characterized by a varied histological picture and simultaneous presence of various phases of lymphogranulomatous growths in various lymph nodes. The spleen is enlarged and firm; the section shows many light-grey foci of lymphogranulomatous proliferations which account for the porphyritic texture. Proliferation of lymphogranulomatous tissue can be seen in other organs, e.g. in the stomach, intestine, liver, etc.

Clinical picture. Weakness and general indisposition are in most cases the first appreciable signs of the disease. Skin itching is among them. It can be excruciating and the patient scratches the skin. The temperature elevates and hidrosis develops. Attacks of fever are first infrequent, but later become more constant. The temperature curve has a specific pattern, to reach 38-39.5 °C at its peaks. The difference between the morning and evening temperatures is 1-2 °C. The main symptom for which the patient would first consult the doctor is gradual swelling of some part of the body, mostly of the neck (due to growth of the lymph nodes). Both surface and deep-seated lymph nodes become enlarged. Considerable enlargement of the lymph nodes of any internal group can involve some additional changes in the patient's condition and cause complaints. For example, when the lymph nodes grow to compress the mediastinum, the trachea or bronchi the patient develops dyspnoea, cough, pain and the pressing sensation in the chest. If the recurrent nerve is compressed, the corresponding vocal cord is affected by paresis and voice becomes hoarse. Lymphogranulomatous affection of the stomach causes symptoms of dyspepsia (abdominal pain, regurgitation, vomiting, etc.). If the abdominal lymph nodes and the intestine are involved, persistent constipation may develop.

Findings of physical examination show enlargement of the lymph nodes which is the most characteristic sign of the disease. The cervical lymph nodes (mostly on the right side of the neck) become enlarged in more than 50 per cent cases; the nodes of the other side of the neck become involved later. Next involved are submandibular, supra- and subclavicular, axillary, femoral, and inguinal lymph nodes; less frequently the lymph nodes of the other regions (occipital, ulnar, etc.) are involved.

Newly involved nodes are soft, while the old ones become very firm. They fuse together to form conglomerates but do not adhere to the skin. The nodes are painless, they do not suppurate or open, as distinct from actinomycosis- or tuberculosis-affected nodes (scrofuloderma). If a group of lymph nodes is enlarged considerably, the overlying skin becomes dark-

red and then bronze due to disordered circulation; it does not however get thin.

Inspection of the patient reveals some symptoms caused by compression of the vessels and nervous trunks by the enlarged lymph nodes (regional cyanosis, dilatation of the veins, Horner's symptom, etc.). Abdominal lymph nodes can be palpated if their enlargement is considerable. A tuberous tumour can be felt in the mesogastric region round the umbilicus. The spleen is enlarged and firm; it is tender in the presence of perisplenitis. Enlargement of the liver is less characteristic. Enlargement of the mediastinal lymph nodes can best of all be revealed by X-rays.

Hypochromic anaemia and neutrophilic leucocytosis are usually found; lymphocyte counts (absolute and relative quantities) are low. Eosinophilia and thrombocytopenia may also occur. ESR is increased: at the terminal stage it is 50—70 mm/h. Study of the punctate of the bone marrow is not quite informative but the Berezovsky-Sternberg cells may often be observed.

Histological study of lymph node bioptates (Plate 35) reliably confirms the diagnosis of lymphogranulomatosis. The cell composition of the lymphogranulomatous tissue is as a rule quite varied but its most specific element are granulomas with giant cells to 30—80 μm in diameter (Berezovsky-Sternberg polynuclear cells which do not occur in other diseases). Study of the content of lymph nodes is more accessible but less informative.

Course. The disease is progressive; remissions are followed by exacerbations. Anaemia and cachexia develop gradually. The prevalent affection of a particular group of lymph nodes accounts for the clinical picture of the disease. In some cases compression of a vital organ can accelerate the disease and its outcome. The patient may also die of a secondary infection. The average life expectancy of the patients is from 3 to 4 years; some patients however survive for 6-8 years and more.

Treatment. Radiotherapy is quite effective. It can give remissions lasting as long as several months (after irradiation of the enlarged lymph nodes). Chemical cytostatics (usually their combinations) are used.

Haemorrhagic Diathesis

Haemorrhagic diathesis is the disease characterized by the tendency to bleeding and repeated haemorrhages; they may occur spontaneously and may be caused by injuries; injury can be quite insignificant, which otherwise would never provoke bleeding in a normal individual.

Aetiology and pathogenesis. These are quite varied. Some types of haemorrhagic diathesis are hereditary but many of them can be caused by some external factors.

Avitaminosis (deficit of vitamins C and P) is an especially predisposing factor. Some infections (long-standing sepsis, louse-born typhus, virus haemorrhagic fevers, icterohaemorrhagic leptospirosis), allergic conditions, some diseases of the liver, kidneys, and of the blood system can also provoke the onset of haemorrhagic diathesis.

Haemorrhagic diathesis can be classified by the pathogenesis into two major groups: (1) haemorrhagic diathesis due to disordered capillary permeability (haemorrhagic vasculitis, vitamin C deficiency, some infectious diseases, trophic disorders, etc.); (2) haemorrhagic diathesis due to disorders in the blood coagulation and anticoagulation system. The latter group is further subdivided into the following conditions:

A. Haemorrhagic diathesis caused by disordered blood coagulation system:

(1) first phase: congenital deficit of plasma components of thromboplatelet formation (factors VIII, IX, XI), haemophilias A, B, C, etc.; deficit of thrombocyte components (thrombocytopathy, e.g. thrombocytopenic purpura; see below);

(2) second phase: deficit of plasma component of thrombin formation—factors II, V, X, the presence of antagonists to them and of their inhibitors;

(3) third phase: deficit of plasma components of fibrin formation—factors I (fibrinogen) and XII.

B. Haemorrhagic diathesis caused by accelerated fibrinolysis (due to increased synthesis of plasmin and insufficient synthesis of antiplasmin).

C. Haemorrhagic diathesis caused by disseminated intravascular coagulation (thrombohaemorrhagic syndrome or coagulopathy of consumption) in which all procoagulants are utilized during massive intravascular coagulation and the fibrinolysis system is activated.

This concise classification of haemorrhagic diathesis is only conventional because several pathogenic factors are often involved. This classification covers a very large group of diseases, both hereditary and acquired, and also secondary syndromes arising against the background of the main disease (metastasizing malignant tumour, burn disease, etc.)

Clinical picture. The general clinico-morphological symptoms of haemorrhagic diathesis are haemorrhages into various organs and tissues, external and internal haemorrhages (from the gastro-intestinal tract, lungs, uterus, kidneys, etc.) and secondary anaemization. The disease is complicated by dysfunction of the haemorrhage-affected organs, by hemiparesis in disordered cerebral circulation, regional paralysis and paresis in compression of large nervous trunks by haematomas, haemarthrosis in repeated haemorrhages into the joints, etc.

Despite the great variety of haemorrhagic diatheses and certain diagnostic difficulties, accurate diagnosis is quite important for efficacious

therapy in each particular case. The aetiological and pathogenetic factors of the disease should be properly considered for an accurate diagnosis. Haemorrhagic diathesis is the subject of special study of senior medical students. Here we shall only acquaint the reader in general with thrombocytopenic purpura (Werlhof's disease).

The **prophylaxis** of hereditary (familial) haemorrhagic diathesis includes medico-genetic studies that may give the wife and husband the necessary information and advice concerning possible complications in their offspring; if haemorrhagic diathesis is not hereditary but acquired, measures should be taken to preclude development of diseases that may promote the onset of haemorrhagic diathesis.

Thrombocytopenic purpura (Werlhof's disease). Thrombocytopenic purpura is a haemorrhagic diathesis due to the deficit of blood platelets. The disease was first described by Paul Werlhof in 1735. Thrombocytopenic purpura occurs mostly in young females.

The **aetiology and pathogenesis** of the disease are unknown. It has only been established that the immune-allergic mechanism is positively involved in about 50 per cent cases: anti-thrombocytic antibodies are produced and fixed on the surface of thrombocytes to damage them and to prevent their normal separation from megakaryocytes. The triggering factors (the impetus to production of auto-antibodies) may be infection, toxicosis, individual hypersensitivity to certain foods and medicines. In some cases the disease is caused by hereditary insufficiency of certain enzyme thrombocyte systems which is probably activated by some additional factors.

Pathological anatomy. Multiple haemorrhages in the skin and the internal organs are characteristic. The spleen may be considerably enlarged. Separation of thrombocytes from megakaryocytes in the bone marrow is disordered (according to histological findings).

Clinical picture. The main symptom of the disease is the appearance on the skin and mucosa of multiple haemorrhages in the form of small dots (petechiae) or large spots (ecchymoses). Haemorrhage may be spontaneous and due to insignificant injuries, mild contusion, pressure on the skin, etc. Haemorrhagic lesions are first purple, then they darken to cherry-red and brown, and then lighten to yellow and disappear in several days. But new lesions develop to succeed the disappearing ones. Bleeding from the nose, gastro-intestinal tract, kidneys or uterus are not infrequent; haemorrhages into the internal organs (brain, fundus oculi, myocardium, etc.) are also possible. Grave and prolonged bleedings arise in extraction of teeth or in other minor operations. The tourniquet test (and especially the pinch test) are positive. The spleen and the lymph nodes are usually not enlarged; tapping on the bones is painless.

Thrombocyte counts are usually less than 50×10^9 per 1 l; in some cases only single blood platelets can be found in preparations. The degree

of bleeding can be assessed by the degree of thrombocytopenia. Hypochromic anaemia can develop after profuse bleeding. The clotting time is normal in most cases, but it can be slightly longer (due to the deficit of thromboplastic factor III of blood platelets). The bleeding time increases to 15-20 min and more; clot retraction is disordered. Thromboelastography reveals greatly increased reaction and clotting time.

Course. Both acute and chronic recurrent forms of the disease are observed. The patient dies of profuse bleeding and haemorrhages into the vital organs.

Treatment. Removal of the spleen is indicated in grave cases: the number of thrombocytes increases in the blood of a patient and haemorrhage stops in a few days following the operation. The effect of splenectomy is probably explained by decreased decomposition of blood platelets in the spleen and by the removal of the inhibiting effect that the spleen has on thrombocytopoiesis. Blood transfusion is useful for haemostasis and blood substitution. Repeated transfusion of thrombocytic mass gives positive haemostatic effect. Vitamin P, vitamin C, calcium chloride and vicasol are given to strengthen the vascular walls. Since the allergic factor is involved in the pathogenesis of the disease, corticosteroid hormones are quite effective in certain cases.

Chapter 10

ENDOCRINE SYSTEM AND METABOLISM

Methods of Examination

Inquiry

Complaints. The endocrine system has multiple effects on various bodily functions and the patient's complaints are therefore varied. The patient may complain of increased excitability, interrupted and superficial sleep, impaired memory, irritability, hyperhidrosis, chills, heart palpitation, noise in the ears, blood rush to the head, skin itching, increased thirst, and considerable wasting. When inquiring the patient, the physician can reveal some features of his nervous and psychic character that may suggest some endocrine diseases: e.g., fussiness, rapid movements, hasty speech, apathy, and flaccidity suggest thyroid dysfunction, while mental underdevelopment, and its degree—infantilism and cretinism.

Anamnesis. It is important to establish the direct cause of the disease. Strong emotions, fear, and psychic traumas are the predisposing factors for thyrotoxic goitre. Endocrine diseases often develop during sexual maturation, after childbirth, and during menopause.

The hereditary factor is also important in endocrine diseases, e.g. in diabetes mellitus. The endocrine function can be affected by some other diseases. Tuberculosis of the adrenal glands, for example, is the cause of their hypofunction (Addison's disease).

Physical Examination

INSPECTION

Inspection of the patient is a valuable diagnostic procedure. Sometimes the diagnosis becomes clear at first sight. The patient's appearance and some special features of his behaviour are quite characteristic in diffuse thyrotoxic goitre, myxoedema, acromegaly, nanism (dwarfism), pituitary cachexia, Itsenko-Cushing syndrome, Addison's disease, upset fat metabolism, etc.

Endocrine diseases, especially affections of the thyroid and pituitary glands, can alter the *expression of the patient's face.* Patients with thyroid hyperfunction have large, wide open, protruded eyes; winkling is rare, the eyes are lustrous, and the patient's face has the expression of horror or fear. The face of patients with thyroid hypofunction (myxoedema) is

round, without wrinkles, with motionless eyes; the general expression is dullness and apathy. The acromegalic face is characterized by protruding superciliary arches, abnormally large nose, lips, tongue and the chin; the abnormally large lower jaw has widely set teeth (diastema). Pituitary hypofunction is attended by obesity which gives the woman-like expression to the male face.

Neck. Inspection of the anterior surface of the neck can reveal the size of the thyroid gland (its enlargement).

Height. Gigantism (over 195 cm) is mostly the result of anterior pituitary hyperfunction (acromegalic gigantism) or hypofunction of the sex glands (hypogonadal gigantism). Dwarfism (the height below 135 cm) can be due to hypofunction of the anterior pituitary lobe with preservation of childish proportions of the body, underdevelopment of the sex organs, and the absence of the secondary sex characters. The same symptoms can be observed in marked thyroid hypofunction with signs of myxoedema and mental retardation (to idiotism).

Skin. Pallid face with a yellowish hue is characteristic of myxoedema; the face is hyperaemic in Itsenko-Cushing syndrome (anterior pituitary hyperfunction); the mucosa and skin are bronze (especially skin folds, the palms) in patients with Addison's disease (adrenal hypofunction). Dry and scaling skin is characteristic of thyroid and parathyroid hypofunction; the skin is dry and cold in hypothyroidism. The skin is smooth and moist in patients with hyperthyroidism. Thickening of the skin associated with hypertrophy of its papillar layer is found in acromegaly. Oedema of the skin which is characteristic of hypothyroidism is due to its impregnation with mucinous substance. The Itsenko-Cushing syndrome is characterized by atrophy of the skin on the femur and the abdomen (red-violet striae). Scratching of the skin and furunculosis, cholesterol deposition in the skin of the eyelids is often observed in diabetes mellitus. Nails are brittle in hypothyroidism and tetany.

Hair. Changes in hair is an important diagnostic sign in endocrine diseases. A female pattern of hair growth in men is typical of eunuchoidism, while male-type pilosis in women occurs in acromegaly and Itsenko-Cushing syndrome; falling of hair from the eyelids, brows, mustaches, and the head is characteristic of myxoedema.

Subcutaneous fat. Uniform distribution of fat over the entire body is characteristic of thyrogenic obesity, while deposition of fat mostly in the pelvic region (lower abdomen, buttocks, thighs) occurs in pituitary and pubertal obesity. Excess fat on the face and trunk is a sign of the Itsenko-Cushing syndrome. Excess wasting is observed in some forms of diabetes mellitus and thyrotoxic goitre. Cachexia is a sign of Simmonds's disease which is due to the affection of the pituitary gland (pituitary cachexia).

Bones. Eunuchoidism is characterized by a delayed growth of the epiphyseal ends of long tubular bones. Acromegaly is marked by abnormal thickening of the enlarged bones of the skeleton.

Muscles. The hormone of the parathyroid glands is produced in deficient quantity and the blood calcium content is thus decreased. As a result, patients develop tonic convulsions (mostly of the flexor muscles). The patient's hand is flexed to give the specific appearance of the "obstetrician hand". When the facial muscles are affected by convulsions, the face acquires the expression of a forced smile. The muscles are developed in excess in acromegaly.

The thyroid and the testes are the only endocrine glands that are accessible to direct inspection.

PALPATION

The thyroid gland is studied by palpation. Tentative palpation assesses the density of the organ, the character of its surface, and the presence of nodes. Then follows special palpation. The examiner places four flexed fingers of both hands deep beyond the posterior edges of the sternocleidomastoid muscle, and the thumbs beyond the anterior edges of this muscle. The patient is now asked to make swallowing movements: the thyroid together with the larynx moves between the examiner's thumbs. This method is used to reveal even insignificant enlargement of the thyroid gland that cannot be detected by common palpation. Mobility of the gland during swallowing, the presence or absence of pulsation, and tenderness of the thyroid can also be determined by this method. Palpation of one lateral lobe of the gland can be facilitated by pressing the thyroid cartilage on the opposite side. The thyroid isthmus is palpated by the sliding movements of the examining fingers in the direction of the sternal manubrium. The lower portion of the thyroid, which is concealed behind the sternal manubrium, may be affected by nodes. In order to palpate them (for outlining their borders and assessing their consistency), the patient is asked to make swallowing movements, while the examiner's fingers palpate the thyroid in the suprasternal notch.

In order to follow up changes in the size of the thyroid gland, it is important to determine its size. The girth of the neck, the transverse dimension of the thyroid and the size of its separate nodes should be determined. When measuring the girth of the neck, one end of the measuring tape should be fixed on the crest of the 7th cervical vertebra, the tape being passed over the most prominent part of the thyroid. When taking transverse measurements, the tape is placed beyond the outer posterior edges of the sternocleidomastoid muscles and passed over the anterior sur-

face of the thyroid gland. The diameter of separate lymph nodes of the thyroid gland is determined by bow compasses with rounded ends.

Palpation gives a more detailed information on the structure of the skeleton and the condition of the skin of patients with endocrine diseases that were first revealed by visual examination.

Percussion can reveal a retrosternal struma (goitre).

AUSCULTATION

Sounds and murmurs can be heard over the enlarged thyroid in patients with thyrotoxicosis. These are explained by accelerated flow of blood and its intensified supply to the thyroid gland.

Laboratory studies

Determination of protein-bound *iodine* (PBI) in the blood serum is widely used to study the thyroid function because 90-95 per cent of protein-bound iodine is the iodine of thyroxin. The level of the protein-bound iodine in healthy adults varies from 315 to 630 nmol/1 (4-8 mg/100 ml). Figures below 275 nmol/1 (3.5 mg/100 ml) indicate hypothyroidism, and above 670 nmol/1 (8.5 mg/100 ml) hyperthyroidism. If high PBI persists for a year and does not vary with increasing content of thyroid hormones in the blood, it may be due to administration of contrast iodine-containing substances (for X-ray examination) and iodine therapy (saiodin, enteroseptol, mexase, etc.). The blood serum of patients with parathyroid hypofunction is examined for *calcium* and *phosphorus;* the content of these elements decreases in tetany.

Aldosterone and *hydroxycorticosteroids* are found in decreased quantity in patients with diseases of the adrenal glands (Addison's disease); the content of *potassium* and *sodium salts* increases in these patients. In suspected diabetes mellitus (and also in the presence of this disease) the *blood* and *urine* are tested for *sugar* (see below).

DETERMINING BASAL METABOLISM

Basal metabolism is the amount of energy produced by the body at rest which is only necessary to maintain the vitally important processes, such as respiration, circulation of blood, body temperature, the function of the kidneys, etc. The produced energy is the result of oxidation of proteins, fats, and carbohydrates taken with food with the corresponding consumption of oxygen. Once the amount of oxygen consumed by the body is known, the released energy (in calories) can be determined by multiplying the amount of oxygen by its heat equivalent. The heat equivalent of oxygen is different for combustion of proteins, fats, and carbohydrates. It has been found that it agrees with the respiratory quotient *(RQ):*

$$RQ = \frac{\text{CO}_2 \text{ volume produced in respiration}}{\text{O}_2 \text{ volume consumed}}.$$

Therefore, *RQ* is calculated in addition to the determination of consumption of O_2 and production of CO_2.

Basal metabolism is determined in the morning before the breakfast. The patient is in the lying position, at complete rest, in a warm and silent room. After the patient has adapted to the conditions of the experiment the gas exchange is studied for 5-10 minutes.

There are two systems (open and closed) for the determination of gas exchange. With the open system, the patient breathes with atmospheric air while the expired air is collected in a closed reservoir where O_2 and CO_2 are determined and *RQ* is then calculated. Oxygen breathing is used in the closed system. The patient's nose is clamped and a mouth-piece is introduced into his mouth. The mouth-piece is provided with the inlet and outlet valves; it is connected with a spirometer containing oxygen and provided with a CO_2 absorber. During inspiration, oxygen passes into the lungs and the expired air is returned to the spirometer. The decrease in the initial volume of oxygen is recorded automatically on a moving chart. The amount of carbon dioxide is not determined by this method, and a protein-free diet should therefore be given to the patient, three days before the examination. In this *caseRQ* nears 0.8. This quotient is adopted conventionally as a constant for calculations. Automatic recording instruments of the closed type (metabolimeters) are much simpler and therefore widely used in practical medicine. Oxygen consumption during 5 or 10 minutes of the experiment is recalculated for 24 hours with reference to the calorific value of oxygen, atmospheric pressure, and the ambient temperature (the latter two factors are important for the volume of gas).

The results of the determination of basal metabolism are assessed by comparing the findings with the amount of energy that a healthy individual of the same body-build spends in conditions of basal metabolism. Basal metabolism depends on the weight of an individual, his height, age, and sex. The reference values can be found in standard tables. In a healthy individual the findings are usually close to the reference (tabulated) ones and only differ by not more than ± 15 per cent.

Basal metabolism in patients with pronounced thyrotoxicosis usually increases by 30-100 per cent and in patients with myxoedema it decreases by 20—30 per cent and more. But basal metabolism depends also on some other pathological conditions. It increases in diabetes mellitus, fever of any aetiology, leucosis, polyglobulia; it decreases in anaemia, especially in pernicious anaemia, and in Addison's disease. Increased oxygen demands in patients with heart failure do not indicate increased basal metabolism but oxygen deficiency.

RADIOISOTOPE STUDIES

Absorption of ^{131}I by the thyroid gland. Accumulation of radioactive iodine in the thyroid gland during 2—24 hours is determined either by a contact method using the Geiger-Mueller counter, or by scintillation instruments (at a distance of 10-30 cm). Remote measurements are more accurate because they do not depend on thickness of the tissues overlying the thyroid gland, its configuration, or structure. A DSU-60 unit is used in the Soviet Union for the purpose. It can be used not only to diagnose thyroid dysfunction but also to locate tentatively the tumour metastases and the degree of accumulation of ^{131}I in the right and left lobes of the thyroid gland.

Normal accumulation of ^{131}I in the thyroid gland during two hours is 7-12 per cent, and during 24 hours 20-29 per cent. In patients with thyrotoxicosis, these figures are 9.5—72 and 11-89 per cent, respectively,

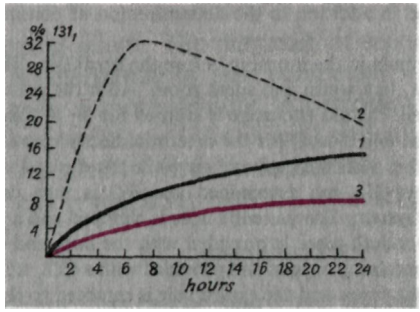


Fig. 110. Accumulation *of* iodine in the thyroid gland. 1—in norm; *2*—in thyrotoxicosis; *3*—in hypothyroidism.

while in patients with myxoedema 1-2 and 1-2 per cent, respectively. A more reliable test for thyrotoxicosis is the determination of the rate of absorption and removal of ^{131}I by the thyroid gland. The ^{131}I content in the thyroid gland is determined in 2, 4, 6, 8, and 24 hours following its administration. The follow-up studies of radioactive iodine accumulation in the thyroid gland can be shown graphically where the thyroid function is described by a curve (Fig. 110).

Excretion of ^{131}I in the urine. This is another valuable method of evaluating the thyroid function. Healthy individuals excrete 31—63 per cent of radioactive iodine in the urine during the first 24 hours, while patients with thyrotoxicosis excrete 3—22.5 per cent and with hypothyroidism 36—71 per cent.

Scanning. This technique is used to determine the shape, size, location, and functional condition of the thyroid gland. Scanning is also used to reveal hyperfunctioning "warm" and "cold" nodes in the thyroid tissue, and to determine metastases of tumours (Fig. 111).

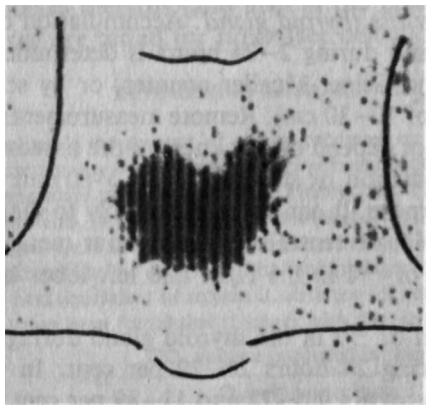


Fig. 111. Scanogram of a normal thyroid.

X-RAY STUDY

X-rays are used to detect bone thickening and the enlarged sella turcica in patients with acromegaly. These are indirect evidence of pituitary affection (usually by tumour). Angiograms and retropneumoperitoneum reveal tumours of the adrenal glands; radiographs can reveal retrosternal goitre, deposition of calcium in the thyroid, and displacement and compression of the trachea and oesophagus by the thyroid gland.

THERMOGRAPHY

Thermography is the method of recording infra-red radiation by an instrument sensitive to heat. Intense local infra-red radiation can be detected on a thermogram during the study of patients with thyroid cancer. It is recommended to combine thermography with scanning for diagnosis of tumours of the thyroid gland.

Special Pathology

Diffuse Toxic Goitre

Diffuse toxic goitre (thyrotoxicosis, Basedow's disease) is caused by thyroid hyperfunction. The disease most commonly occurs in women between the ages of 30 and 50; the incidence in men is 5-10 times lower.

Aetiology and pathogenesis. Psychic trauma, infection (tonsillitis, rheumatism, etc.), dysfunction of other endocrine glands (pituitary) are important for the development of the disease. Familial factors are also important: toxic goitre can often be found in close relatives.

Secretion of hormones by the thyroid gland is intensified in stimulation of hypothalamic centres which stimulate secretion of the thyrotropic hormone by the anterior pituitary lobe. The hypothalamic centres can be stimulated by various factors, by psychic traumas in the first instance. Investigations of V. Baranov and other authors demonstrate the essential role of the central nervous system in the pathogenesis of diffuse toxic goitre. The authors have proved that in many patients the development of toxic goitre was preceded by neurocirculatory dystonia which interferes with ^{131}I capture by the thyroid gland. This form of neurosis is now given great significance in the pathogenesis of diffuse toxic goitre and is regarded as a precursor of this disease.

Hyperthyroidism causes changes in various tissues and organs and disturbs various types of metabolism: protein-carbohydrate, fat, mineral, water metabolism, etc. Upset function of the sympathico-adrenal system is

also a very important factor which accounts for many symptoms of the disease. The role of the pituitary gland in the pathogenesis of thyrotoxicosis cannot be ruled out completely because patients with thyrotoxic goitre suffer from exophthalmos, while the exophthalmic factor is secreted by the pituitary gland.

Pathological anatomy. The thyroid gland enlarges uniformly or by focal hyperplasia; hence diffuse or nodular goitre. Microscopy shows intense blood filling in the thyroid gland and reconstruction of follicular epithelium into columnar or polymorphous epithelium. Sometimes the affected thyroid gland differs only insignificantly from the normal one by the character of its epithelium and follicles; the follicles may only have cyst-like dilatations and contain little colloidal substance. Lymphocytes are accumulated and lymphoid follicles are formed.

Clinical picture. The onset of the disease may be acute or gradual, with slow development of the symptoms. The main signs of the disease are enlargement of the thyroid gland, ocular signs, and heart palpitation. The patients complain of increased psychic excitability, non-motivated anxiety, deranged sleep, hyperhidrosis, tremor of the fingers or in the entire body, frequent defaecation, wasting, and muscular weakness.

Inspection of the patient immediately reveals the special features in his behaviour: fussiness, hasty speech; sometimes the patient drops the subject quite unexpectedly and starts discussing another subject. Ophthalmopathy and some other ocular symptoms suggest hyperthyroidism. Despite preserved or even increased appetite, the patient may lose much of his weight (to cachexia). The patient's skin is smooth, warm and moist to the touch. Some patients develop diffuse pigmentation of the skin which however does not colour the mucosa. The pigment is sometimes deposited selectively in the skin of the eyelids. The hair of the head becomes thin and soft.

During inspection special attention should be paid to the size of the thyroid gland and symmetry of its enlargement. If the thyroid gland is enlarged significantly, the patient's breathing becomes stridorous. Inspection of the patient should be followed by palpation of the thyroid gland. Five degrees of thyroid enlargement are distinguished: I—enlarged thyroid gland is difficult to palpate; II—enlarged thyroid gland is clearly seen during swallowing; III—clearly visible thickening of the neck due to goitre; IV—marked goitre; V—large goitre. Enlargement of the second and third degree occurs most frequently.

Ocular symptoms. A common symptom of diffuse toxic goitre is bilateral dilation of the eye slits which gives an expression of astonishment to the patient's face. Another frequent manifestation is Graefe's sign: a white strip of sclera between the edge of the eyelid and the upper margin of

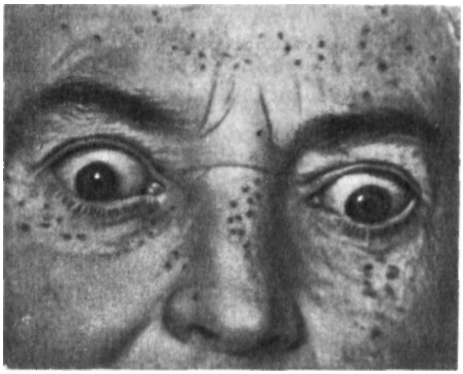


Fig. 112. Positive Graefe's symptom in thyrotoxicosis.

the cornea which appears as the eyeball moves downward (Fig. 112). Among other symptoms are Stellwag's sign (infrequent blinking), Kocher's sign (exposure of the sclera between the lower edge of the upper eyelid and the upper edge of the iris when the eyes are fixed on an upwardly moving object), and the exophthalmic symptom (protruded eyeballs). The protrusion is usually more or less uniform but asymmetry is also possible. One eye can only be involved in some cases. In grave exophthalmic goitre, keratitis, ulcers of the cornea can also develop and the patient's power of vision can thus be endangered. The eyelids can swell, and weakness of convergence can be observed; the eyeball can move aside when attention is fixed on a slowly approaching object (Moebius' sign). This symptom is associated with upset function of the oculomotor muscles.

Cardiovascular system. Tachycardia is one of the most frequent symptoms of the disease. Pulse rate varies within the range of 90 to 120 and in grave cases to 150 beats per minute. Systolic and minute volumes, the mass of the circulating blood and the rate of the blood flow increase, systolic pressure grows, diastolic pressure falls, and the pulse pressure increases. Auscultation of the heart reveals a snapping first sound and systolic murmur at the apex and over the pulmonary artery which are due to increased blood flow rate and low tone of the papillary muscles. A most frequent and serious complication is atrial fibrillation (tachysystolic form) due to the toxic effect of the thyroid hormones on the myocardium. Circulatory insufficiency can also develop. Electrocardiograhic studies reveal a slightly increased amplitude of all waves (especially of the *T* wave), sinus tachycardia, extrasystole, and atrial fibrillation. X-rays examination reveals a slightly enlarged left ventricle of the heart.

Gastro-intestinal tract. The appetite increases. The increased motor

function of the intestine accounts for diarrhoea. Hepatic dysfunction can have various effects: from slight disorders (that can only be revealed by functional tests) to cirrhosis.

Nervous system. The clinical symptoms of disorders in the higher nervous activity are excitability, increased reactivity, general motor restlessness, fidgetiness, and fine tremor of the fingers of the stretched arms (Marie's syndrome).

Endocrine system. A pronounced clinical picture of the disease is attended by a marked hypofunction of the sex glands (amenorrhoea) and of the adrenal cortex (hypoadrenocorticism); diabetes mellitus can join the process.

Study of the peripheral blood can reveal hypochromic anaemia, leukopenia, and lymphocytosis. Biochemical studies of blood reveal the tendency to hypocholesterolaemia and hyperglycaemia.

Basal metabolism increases by 50 and sometimes by 100 per cent. Tests with ^{131}I show accelerated and increased absorption of radioactive iodine by the thyroid gland, an increased content of protein-bound iodine, and decreased excretion of iodine in the urine. The body temperature is usually subfebrile.

Course. The course of the disease depends on the gravity of thyrotoxicosis and is divided into three degrees: I degree thyrotoxicosis is characterized by the absense of complications; wasting is not marked, tachycardia is moderate (to 100 beats per min), basal metabolism increases not more than by 30 per cent; the symptoms are pronounced in II degree of thyrotoxicosis (wasting is considerable, symptoms of nervous disorders are marked, tachycardia from 100 to 120 beats per min, basal metabolism increases by 30-60 per cent); III degree thyrotoxicosis: grave forms of the disease with pronounced symptoms (rapidly developing cachexia, marked psychic excitability and other nervous symptoms, pronounced tachycardia, over 120 beats per min, basal metabolism increased by more than 60 per cent). Forms of the disease complicated by atrial fibrillation, heart failure, affections of the liver, and psychoses are also referred to **III** degree thyrotoxicosis.

The main complications in thyrotoxicosis are affections of the internal organs, e.g. the heart or the liver, and also psychoses, hypoadrenocorticism, and thyrotoxic crisis.

Treatment. The patient should be given calm and rest; sleep should be normalized. The diet must be adequate, rich in proteins and vitamins. Antithyroid preparations should be given: iodine, thiouracyl, and imidazole derivatives. Transition from the second to the third degree is a positive indication for surgical intervention, irrespective of the length or gravity of the disease.

Hypothyroidism

Hypothyroidism is the pathological condition associated with thyroid hypofunction. Hypothyroidism can be primary and secondary. Primary hypothyroidism is the primary pathology that arises in the thyroid gland, while secondary hypothyroidism depends on dysfunction of other organs that can affect the thyroid gland function. Grave forms of hypothyroidism are usually called myxoedema.

Aetiology and pathogenesis. Factors causing the onset of primary hypothyroidism are hypoplasia or aplasia of the thyroid gland, iodine deficiency in the body, subtotal thyroidectomy, overdosage of ^{131}I (which is given in hyperthyroidism) or preparations of thiouracil group, acute (in the past) or chronic thyroiditis. Hyposecretion of thyroxine and triiodthyrosine upsets normal metabolism and causes changes in tissues, organs, and systems of the body.

Pathological anatomy. Morphological changes in the thyroid gland are marked hypoplasia, aplasia, or atrophy. Hyperplastic changes occur in the thyroid gland in hypothyroidism caused by disordered synthesis of the hormones associated with the defective enzyme systems.

Clinical picture. The main complaints are apathy, lack of interest in the surroundings, impaired memory, decreased work capacity, somnolence, flaccidity, and chills.

The patient's appearance is quite specific: the eye slits are narrow, the face is puffy, the neck oedematous, the skin is pallid with a yellowish hue, sometimes with blush on the cheek bones. The skin is rough to the touch, thick, dry, cold, and scaling. The skin is thickened due to accumulation in it of mucopolysaccharides which give the impression of oedema. As distinct from oedema, pressure on the skin does not leave depressions. Hair on the head is rare; it falls off from the brows. Movements are slow and speech is monotonous.

Central and peripheral nervous systems. The mentioned complaints are associated with changes in the function of the central nervous system. Psychosis may develop in long-standing hypothyroidism. Disorders in the peripheral nervous system are manifested by strong severe radicular pain in the extremities, paresthesia, cramps, and shaky gait.

Cardiovascular system. Bradycardia develops; the minute blood volume decreases and the blood flow rate is slow. The heart sounds are dulled. Fluid containing much protein and mucinous substances if often accumulated in the pericardium; it can be accumulated also in the pleural and abdominal cavity. Systolic pressure falls while diastolic pressure remains normal. ECG shows low voltage, especially in *P* and *T* waves. Heart failure develops in rare cases.

Gastro-intestinal tract. Hypo- and achlorhydria often develops. The intestinal motor function is decreased, constipation and meteorism develop.

Metabolism. Protein synthesis is decreased. Blood cholesterol is usually increased. Moderate hypoglycaemia is observed. Electrolyte level remains unchanged in most cases. Blood calcium sometimes decreases, and ESR increases.

Reduction of basal metabolism to 50 per cent and also of the protein-bound iodine is of great diagnostic significance. Absorption of ^{131}I in the thyroid gland is low.

Myxoedema coma may develop in grave cases.

Treatment. Thyroid preparations are mainly used to treat hypothyroidism and coma.

Diabetes Mellitus

Diabetes mellitus is characterized by metabolic disorders associated with absolute or relative deficiency of insulin production. Diabetes mellitus is a frequently occurring disease. People between the ages of 40 and 60 are mostly affected.

Aetiology and pathogenesis. Organic or functional affection of beta cells of the pancreas islets is the main factor in the pathogenesis of diabetes mellitus. This affection accounts for insufficient synthesis of insulin. Primary insufficiency of these cells can arise after infection, psychic trauma, removal of the pancreas, its destruction by a tumour, sclerosis of the pancreatic vessels, in pancreatitis, regular overeating, or insufficient intake of substances required for the normal function of the insular apparatus. Familial predisposition (genetically determined functional insufficiency of beta cells) is a background against which the diabetogenic effect of the named factors is realized.

Secondary insufficiency of beta cells can be due to endocrine dysfunction: pituitary, adrenal and thyroid hyperfunction. Somatotropic and thyrotropic hormones, corticotropin, glucocorticoids and glucagon have diabetogenic properties and are called contrainsulin hormones. The pathogenesis of diabetes mellitus also depends on the presence of excess insulin inhibitor, i.e. enzyme insulinase (which is produced in the liver and is activated in the anterior pituitary hyperfunction) and also insulin antagonists and antibodies to insulin contained in the blood of patients.

Hyperglycaemia is a symptom of disordered carbohydrate metabolism. Increased blood sugar content is associated with a slowed glucose supply to the muscles and fatty tissue and its slow phosphorylation. This interferes with glucose decomposition, synthesis of glycogen, and conversion of carbohydrates into fats. High blood sugar depends also on intensified glucose

supply from the liver to the blood and formation of glucose from glycogenic amino acids. Hyperglycaemia is usually attended by glycosuria, which in turn depends on an increased amount of glucose in the glomerular filtrate and its complete reabsorption in the tubules. Upset protein metabolism is manifested by the inhibited synthesis of protein. Clinically it is manifested by formation of trophic ulcers and slow healing of wounds.

Disorders of fat metabolism are delayed formation of higher fatty acids and neutral fats from carbohydrates, and ample supply of free fatty acids to the blood. Clinically this is manifested by wasting of the patient. Fat infiltration of the liver is the sign of upset fat metabolism. A severe disorder in fat metabolism is ketosis. This is an accumulation in the blood of acetone bodies and ketones (β-hydroxybutyric acid, acetoacetic acid, acetone) which are intermediate products of oxidation of higher fatty acids in the liver. Diabetic coma, a fatal complication of diabetes mellitus, can develop in this disorder of fat metabolism.

Polyuria, loss of sodium and partially of potassium are symptoms of upset water-salt metabolism in diabetes mellitus. The pathogenesis of polyuria is associated with glycosuria which elevates osmotic pressure in the tubules to decrease reabsorption of water. Reabsorption of sodium in the kidneys is also decreased.

A long-standing and incompletely compensated diabetes mellitus results in vascular changes (retinopathy, nephropathy, or Kimmelstiel-Wilson syndrome) and atherosclerosis. Pronounced fluctuations in the blood sugar increase pituitary activity, cause spastic atonia of the vessels, which, in turn, affects the structure of their walls, accelerates the destruction of elastic fibres, and promotes sclerosis and calcinosis.

Insulin deficit inhibits phosphorylation of vitamin B_6 which often causes neuropathic complications of diabetes mellitus.

Pathological anatomy. Diabetes mellitus is responsible for the decreased number of beta cells of the pancreatic islets, for their degranulation and hydropic degeneration. Hyaline and fat may be deposited in beta cells. This is not however a specific symptom of diabetes mellitus. At early stages of the disease, especially in young persons, morphological changes in these cells are absent.

Clinical picture. The symptoms of diabetes mellitus are excessive thirst (polydipsia), increased appetite, polyuria, hyperglycaemia, glycosuria, wasting, weakness, decreased work capacity, and skin itching, especially in the perineal region.

Inspection of the patient reveals rubeosis (reddening of the face, the cheeks, supraciliary arches, and the chin due to dilated cutaneous vessels) and xanthosis (yellowish decolouration of the palms and soles associated with upset conversion of carotin into vitamin A in the liver and accumula-

tion of carotin in the skin). The patient's skin is dry, rough, easily scaling, covered with traces of scratching (due to skin itching). Furuncles, exematous and ulcerous lesions can also be found. At points of insulin injection, there are zones where fat is absent (insulin lipodystrophy).

Muscles and bones. Muscular atrophy and osteoporosis are observed in decompensated diabetes mellitus.

Cardiovascular system. Atherosclerosis of various arteries with the corresponding clinical symptoms, angina pectoris, gangrene of the feet, etc. is not infrequent.

Respiratory organs. Diabetes mellitus often concurs with bronchitis, pneumonia, and pulmonary tuberculosis.

Gastro-intestinal tract. Mouth mucosa and the tongue are dry. Paradontosis and pyorrhoea frequently occur. Appetite is very good and sometimes voracious (bulimia). Study of the gastric juice reveals the presence of hypo- or achlorhydria. Fat dystrophy of the liver and its cirrhosis develop in some patients with long-standing decompensated diabetes mellitus.

Kidney diseases. Arteriolosclerosis of the kidneys and intracapillary glomerulosclerosis (Kimmelstiel-Wilson syndrome) may occur. They are manifested by hypertension, retinopathy, and albuminuria. Pyelonephritis is not infrequent.

Retinopathy. Retinopathy in diabetes mellitus is manifested by the presence of exudate in the retina, haemorrhages, and pigment abnormality in the yellow spot. Cataracts often occur.

Changes in the nervous system. Polyneuritis is frequent. Headache, deranged sleep, and decreased work capacity are the symptoms of affection of the central nervous system.

The main laboratory methods used to diagnose diabetes mellitus and assess its gravity are based on determination of sugar and ketone bodies in the urine, determination of sugar in the blood on a fasting stomach and during the day, and glucose tolerance tests.

When a patient suspected for diabetes mellitus is examined, his blood and urine are in the first instance tested for sugar. Sugar in the urine of a diabetes mellitus patient may be 5-8 per cent and more. Morning urine of patients with latent diabetes mellitus may be free from sugar, and daily urine should therefore be better studied. Urine taken after giving the patient a test meal or sugar can also be studied.

Blood of a healthy individual (with a fasting stomach) contains 4.4-6.6 mmol/1 (80—120 mg/100 ml) of glucose. This concentration increases to 28-44 mmol/1 (500-800 mg/100 ml) and more in diabetes mellitus patients. But in the mild forms of the disease the blood sugar may remain normal (especially so if the test is done on a fasting stomach). In such cases

blood sugar should be determined 3 or 4 times a day with a normal diet given. If glycaemia appears to exceed normal in repeated glucose tolerance tests, the diagnosis of diabetes mellitus can be considered proved. After determining blood sugar on a fasting stomach, the patient is given to drink 50 g of glucose in 200 ml of water. Blood specimens are then taken at 30-minute intervals for 3 hours. The blood sugar in a healthy individual increases by about 50 per cent (but not over 9.4 mmol/l or 170 mg/100 ml) during the first hour, while during the second hour the initial blood level is restored (or it may drop below normal). The rise in the blood sugar is higher in diabetes mellitus patients, the increase in sugar concentration is delayed, while the initial level is not restored even in three hours. There is a variant of the glucose tolerance test in which another portion of glucose is given to the patient in one hour following the first dose. The first glucose dose intensifies the secretion of insulin in healthy persons, and the second dose does not therefore increase the sugar concentration in the blood, while sugar curve of diabetes mellitus patients gives another ascent (two-peak curve).

Glucose oxidase and Samogyi-Nelson tests are now used for determining blood sugar. The glucose oxidase method is used to determine true glucose of the blood and it is therefore most specific, but the normal glucose level is slightly underestimated compared with the Hagerdon and Jensen method (3.3-5.5 mmol/1, or 60-100 mg/100 ml). The sugar concentration in the blood depends also on the technique by which the blood specimen is taken: glucose level is higher in capillary than in the venous blood. Increased blood sugar does not always indicate diabetes mellitus since it may be the result of emotional excitation. Glucosuria is an indirect sign of hyperglycaemia. The presence of sugar in the urine in the absence of hyperglycaemia cannot be used as an evidence of diabetes mellitus either, since glucosuria can be due to decreased sugar permeability of the kidneys (renal threshold). In the presence of kidney pathology (nephrosclerosis), glucosuria may be absent even when the blood sugar is abnormally high.

Tests for urine sugar are qualitative and quantitative. Sugar can be determined in the urine by special indicator papers (glucotest) and tablets (for rapid determination of urine sugar). Determination of acetone and acetoacetic acid (acetone bodies) is obligatory. It should however be remembered that acetonuria can occur also in healthy individuals during fasting and in toxaemia of pregnancy.

Patients with clear signs of diabetes mellitus do not require glucose tolerance testing. Prednisolone or corticoglucose test should be carried out in persons predisposed to diabetes mellitus and with normal results of glucose tolerance test. The results of glucose tolerance test depend on various factors: fasting, pathological processes in the liver parenchyma, in-

juries, infections, acute disorders in cerebral circulation, and strong emotions.

Determination of the alkali reserve of the blood helps predict the approaching grave complication of diabetes mellitus, i.e. diabetic coma. The alkali reserve decreases sharply in moderate acidosis. It decreases not only in diabetes mellitus but also in acidosis of other aetiology, e.g. in fasting or in kidney diseases.

Course. The onset of the disease may be acute or gradual. The first signs of diabetes mellitus may be persistent itching and furunculosis. By the course and severity of the symptoms, and also by the body response to the therapy given, the clinical picture of diabetes mellitus is differentiated into light, moderate, and grave. The degree of hyperglycaemia, glycosuria, the presence of ketone bodies in the urine, and the gravity of acidosis should also be taken into consideration. In addition to the mentioned forms of diabetes mellitus, the following three stages are distinguished in its course: prediabetes, masked diabetes, and true diabetes mellitus. Prediabetes cannot be diagnosed by the existing methods. This can be defined as hereditary predisposition, obesity, and cases where newborns (both dead and alive) weigh over 4.5 kg. Masked diabetes mellitus can be detected by the glucose tolerance test. True diabetes mellitus is diagnosed by clinico-laboratory findings.

Diabetic coma is a grave and sometimes fatal complication of diabetes mellitus. It occurs if diabetes mellitus is treated improperly or if the disease is complicated by acute infections, injuries, or nervous stress. Toxic symptoms develop gradually in most cases and the onset of coma is preceded by its precursors (precomatose state). Excessive thirst develops along with polyuria, epigastric pain, dyspepsia, headache, and loss of appetite. The patient's breath smells of acetone (odour of rotten apples). Precomatose state is followed by the first phase of coma which is characterized (in addition to the mentioned symptoms which are gradually intensified) by a strong nervous excitement: insomnia, restlessness, clonic convulsions, and Kussmaul's respiration. The excitement is followed by a marked inhibition, the second phase of diabetic coma: the patient develops dizziness, shows no interest in surroundings, and finally loses consciousness. When in a deep coma, the patient is motionless, the face may be pink or pallid, the skin dry, the muscle tone and tendon reflexes are decreased, pathological reflexes sometimes develop, the eyeball tone decreases, the eyeballs are soft to the touch, the pupils are narrow. Kussmaul's respiration is heard at a considerable distance. The pulse is low and fast; the arterial pressure falls. Hypothermia, oliguria, and sometimes anuria develop. Blood sugar markedly increases (from 22 to 55 mmol/l or from 400 to 1000 mg/100 ml). The alkali reserve of blood decreases to 15-30 per cent

(v/v), the number of ketone bodies increases along with increased content of non-protein (residual) nitrogen; the chloride content decreases. Leucocytosis in coma can be as high as 50×10^9 per 1 l of blood with a neutrophilic shift to the left. Ketone bodies and considerable amounts of sugar are found in the urine. But gradual development of diabetic coma and distinct stages of this process are not always observed, and the terminal phase of diabetic coma may come suddenly, without precursors.

The pathogenesis of diabetic coma is associated with acidosis mainly on account of accumulation of ketone bodies and their toxic effect on the central nervous system.

Hypoglycaemic coma arises in patients treated with insulin for diabetes mellitus, if their diet lacks carbohydrates or as a result of insulin overdosage. Hypoglycaemic coma develops rapidly, sometimes within a few minutes. Coma is preceded by a sudden feeling of hunger, weakness, sweating, tremor in the entire body, psychic and motor excitement. Comatose state is characterized by pallor and moist skin, increased muscular tone and tendon reflexes, and convulsions; the pupils are dilated, the eyeballs remain firm. The blood sugar is low; sugar and acetone are absent from the urine. The patient quickly responds to treatment: after an intravenous infusion of a hypertonic solution of glucose, the patient quickly regains consciousness.

Treatment. In the absence of malnutrition, ketosis, or concomitant diseases, and if there were no precomatose or comatose state, the patient may be given a diet therapy alone. Otherwise, and also if the antidiabetic preparations prove ineffective, or else if there are contraindications to their use, the patient should be given insulin.

The dose of insulin to treat diabetic coma depends on the gravity of the patient's condition and the length of the disease. In order to prevent the development of hypoglycaemic coma, a glucose solution in a hypertonic sodium chloride solution should be administered by drop infusion in 90-120 minutes following the administration of insulin.

Obesity

Obesity (adiposis) is excessive deposition of fat in subcutaneous and other tissues, which is associated with metabolic disorders.

Aetiology. Overeating is the main aetiological factor. Hypodynamia, hereditary and constitutional predisposition are also important. Pregnancy, lactation, and menopause are among other factors responsible for obesity in women.

Obesity can be regarded as an independent disease in cases with an excessive caloric intake (alimentary obesity). Obesity can also be a symptom

of endocrine diseases (thyroid or pituitary dysfunction) or diseases of the central nervous system (infection, injury, tumour).

Pathogenesis. The main pathogenic mechanism of obesity is dysfunction of the central nervous mechanisms, i.e. the cerebral cortex and hypothalamic centres (the ventromedial and ventrolateral nuclei of the hypothalamus) that regulate fat and carbohydrate metabolism. The result of these disorders is upset equilibrium between the caloric intake and the amount of energy spent by a living body. The role of the endocrine factors and also changes in the local tissue metabolism with increased deposition of fat should also be considered in various types of obesity. Changes in insulin content in obese individuals are of special practical interest: at the early stage of obesity, these patients have hyperinsulinism, which is followed by hypoinsulinaemia on account of exhaustion of the insular apparatus in long-standing obesity. Hypoinsulinaemia impairs tolerance to carbohydrates which occurs in most obese persons, and often causes diabetes mellitus. Obesity can thus be regarded as prediabetes.

Pathological anatomy. Fat deposition is more pronounced in subcutaneous tissue, omentum, around the kidneys, and in the mediastinum. In the epicardium, fat is mainly deposited at the apex of the heart and around its right chambers. Fat can grow into the depth of the heart to separate muscle fibres, which thus grow thinner. The liver is enlarged at the expense of fatty (adipose) infiltration, which also affects the pancreas. Fat loosens the pancreatic parenchyma and causes atrophy of pancreatic islets.

Classification. Two types of obesity are distinguished, primary and secondary. Primary obesity includes alimentary obesity whose primary pathogenetic factors are unknown. Secondary obesity includes the following forms: (a) cerebral (hypothalamic obesity due to affection of the central nervous system, e.g. by a tumour, infection, or injury); and (b) endocrine obesity which is connected with dysfunction of the pituitary and thyroid glands, or the ovaries.

There is a type of obesity in which fat is deposited in tender tumour-like growths (lipomatosis).

Clinical picture. The clinical picture of obesity is quite varied, depending on the degree of the condition, length of a pathological process, and the presence of changes in other organs and systems.

The degree of obesity is determined by Broca's formula (weight of individual = height - 100). The obesity is first degree if the patient's weight exceeds that calculated from the formula by 30 per cent; the second degree—from 30 to 50 per cent; the third degree—from 50 to 100 per cent; and the fourth degree of obesity is characterized by more than 100 per cent excess in weight. Individuals with the first and second degree of obesity do not complain of their disease. They attend the doctor only for aesthetic consideration. Patients with obesity of the third and fourth degree com-

plain of dyspnoea (which develops first under considerable load and later during light exercise), fatigue, impaired memory, hyperhidrosis, flaccidity, constipation, and menstrual disorders. General inspection of the patient alone is enough to establish the diagnosis of obesity. The colour of the skin may be normal; the skin can also be pallid or hyperaemic. White, red, or violet stripes (striae) can be seen on the skin of the abdomen and the thighs. Sometimes the skin sags together with the subcutaneous fat to resemble an apron. Because of hyperhidrosis, obese patients often have skin diseases, such as eczema, pyodermia, and furunculosis. The diaphragm is high and for this reason obese patients often develop bronchitis and pneumonia.

Long-standing and pronounced obesity provokes changes in the cardiovascular system. Hypertension and atherosclerosis are frequent. These pathological changes and also mechanical factors (accumulation of fat in the mediastinum, decreased respiratory excursions, high diaphragm) interfere with normal work of the heart and cause chronic circulatory insufficiency.

Patients with obesity have increased appetite. They develop tendency to constipation and meteorism. Cholelithiasis, cholecystitis, cholangitis, and acute pancreatitis occur in obese patients more frequently than in normosthenic individuals. Sex and pancreatic function decreases in obesity.

Treatment. Low-calorie diet is recommended to decrease the weight of obese patients to the normal level, after which the diet should be normalized. The meals should be taken at regular intervals; the patient should lead an active life (remedial exercises). Treatment of obesity by starvation or by decreasing significantly the ration is not recommended on account of possible serious disorders.

Preparations decreasing appetite (anorexigenics) should be given to patients on a fasting diet who suffer severely from hunger.

Prophylaxis. Health education and sports are effective.

Vitamin Deficiency

Vitamins are low-molecular chemical compounds contained in foods. They are necessary to maintain biocatalysis of separate biochemical and physiological processes in a living body. Vitamins are synthesized in man and animals in insufficient quantity and therefore they should be taken with food.

If food lacks vitamins, its assimilation is disordered and symptoms of vitamin deficiency develop. Pathological conditions occurring in full absence of vitamins are called avitaminosis. Types of avitaminosis depend on the lack of a particular vitamin (e.g. vitamin A, B_1, B_2, etc.) and are designated avitaminosis A, avitaminosis B_1, etc., respectively. If deficiency

of vitamins is only partial, this condition is called hypovitaminosis, the insufficiency is usually functional.

Aetiology and pathogenesis. Depending on the cause of vitamin deficiency, two forms are distinguished: exogenous and endogenous. *Exogenous or primary* vitamin deficiency is caused by the low vitamin content of food. This is primary vitamin deficiency which develops in monotonous and irregular meals and imbalanced diet (with prevalence of carbohydrates, small amounts of animal proteins and fats, and in the absence of fresh vegetables and fruits).

Exogenous or *secondary* vitamin deficiency is caused by various factors. These may be disordered absorption of vitamins in the gastrointestinal tract (alimentary diseases), in helminthiasis, acute and chronic liver diseases, malignant newgrowths, leucoses, familial enzymopathies, endocrine dysfunction (thyroid or pituitary dysfunction), ingestion of foods containing antivitamin properties (thiaminase, avidin, etc.). Vitamin deficiency can develop in prolonged use of medicinal preparations with antivitamin properties (streptomycin, chloramphenicol, sulpha drugs, etc.). Vitamin deficiency can arise with adequate intake of vitamins but in the presence of increased demands for these substances, for example at high or low ambient temperature, during intense exercise, nervous or psychic overstrain, and in oxygen deficiency.

Demands in vitamins, especially for ascorbic acid, pyridoxine, folic acid, calcipherols, and tocopherols especially increase in pregnancy and nursing. Vitamin deficiency can develop also in prolonged use of a diet lacking vegetables, fruits, rye bread, etc. Avitaminosis develops during wars and other disasters, in long sea voyages, in polar regions where people feed on dry or canned foods, etc. Beri-beri *(B_1* avitaminosis), pellagra (PP avitaminosis), scorbutus (scurvy, or C avitaminosis) occur now in developing countries of Asia, Africa and South America. Population in developed countries usually suffers from hypovitaminosis, which arises due to improper storage of foods, seasonal variations in vitamin content of foods, or incorrect processing of foods.

Clinical picture. Pure hypovitaminosis occurs comparatively rarely. More frequent are deficiencies of various vitamins, with prevalence of symptoms characteristic for the lack of a particular vitamin. General vitamin deficiency develops in practically healthy individuals early in spring and it is manifested by rapid fatigue, decreased work capacity, poor appetite, and deranged sleep. Table 5 gives clinical signs of separate hypovitaminoses in deficit of separate vitamins. Diagnosis of avitaminosis (in the presence of specific pathological symptoms) can be confirmed by testing the blood and urine for the presence of vitamins or their metabolites. Biochemical tests are also used to obtain indirect evidence of

Table 5

Main Clinical Symptoms of Diseases in Vitamin Deficiency

Lacking vitamin	Clinical signs of hypovitaminosis
Ascorbic acid (vitamin C)	Loose and bleeding gums, petechial lesions, dry skin
Nicotinic acid (vitamin PP)	Scarlet tongue, tender and cracked. Burning sensation in the tongue. Diarrhoea without mucus or blood. Skin scaling, hyperpigmentation. Neurasthenic syndrome (irritability, insomnia). Muscular pain.
Pyridoxine (vitamin B_6)	Increased excitability, loss of appetite, nausea. Hypochromic anaemia. Seborrhoeal dermatitis. Insomnia. Depression.
Retinol (vitamin A)	Pallid and dry skin. Cornification of hair follicles. Acme. Tendency to pyodermia. Conjunctivitis. Photophobia. Night blindness. Brittle and reedy nails. Frequent respiratory affections.
Riboflavin (vitamin B_2)	Dry lips. Vertical fissures on the lips. Fissures and crusts in the mouth angles (angular stomatitis). Seborrhoeal dermatitis of the face, ears, and the neck. Conjunctivitis. Reedy and brittle nails.
Thiamine (vitamin B_1)	Decreased appetite; nausea, constipation. Muscular dystonia. Distractedness, loss of self-confidence, non-motivated fears. Tender palpation of the calf muscles. Heart palpitation. Dyspnoea during light exercise. Rapid fatigue (mental and psychic).
Tocopherol (vitamin E)	Muscular weakness. Sex disorders.
Phylloquinone (vitamin K)	Nasal and gum bleeding. Intracutaneous and cutaneous haemorrhages. Gastro-intestinal haemorrhages.
Folic acid	See vitamin B_{12} (folic acid) deficiency anaemia
Cyanocobalamin (vitamin Bl2)	See vitamin B_{12} (folic acid) deficiency anaemia

vitamin metabolic disorders. For example, tryptophan is given to a patient and excretion of xanthurenic acid in the urine is determined. This gives information of the pyridoxine supply of the body.

Determination of eye sensitivity to light helps establish deficiency of retinol and riboflavin. Immunobiological tests are also used: phagocytic reaction, complementary activity test, gamma-globulin concentration test, etc.

Radio-indicative method is also used to determine vitamin deficiency. It can be used to determine distribution, transport, conversion, and excretion of vitamins.

Treatment. Diet containing much vitamins and vitamin preparations (in doses several times exceeding normal daily demands) should be prescribed. Hypervitaminosis and toxic complications are however possible in prolonged therapy.

Prophylaxis. Health education of population is important. People should be taught to feed properly, and instructions should be given how to cook and store foods. General knowledge of vitaminology is useful. Special measures must be taken by the appropriate governmental institutions. These measures include increased production of foods rich in vitamins, and of preparations (vitamins and polyvitamins). Foods for sale should be stored and processed properly at public catering enterprises. Vitamin content of food should be increased by selection of agricultural crops and rational animal breeding.

Chapter 11.

DISEASES OF BONES, MUSCLES, AND CONNECTIVE TISSUE. ACUTE ALLERGOSES

This is a very large group of diseases. In certain cases, affections of the osteo-articular apparatus, muscles or connective tissue are primary and their symptoms prevail in the clinical picture of the disease (although signs of affections of other organs or systems may join). In other cases, affections of the bones, muscles or connective tissue are only secondary to some other diseases (metabolic disorders, endocrine diseases, etc.), and their symptoms only supplement the clinical picture of the main disease. Systemic affections of the connective tissue, diseases of bones, joints, and muscles make a special group known as collagen diseases (collagenosis, diffuse connective tissue disease). These diseases are characterized by allergic inflammation of the connective tissue and its derivatives. Immune and auto-immune disorders are of certain importance in the pathogenesis of many diseases, but they are decisive in the pathogenesis of the collagen diseases.

Collagen diseases are divided into four major collagenoses: rheumatoid arthritis, systemic lupus erythematosus, systemic scleroderma, and dermatomyositis. Rheumatism is close to these diseases with respect to its pathogenesis.

Among diseases of the osteo-articular apparatus, muscles and connective tissue, differentiated are diseases of inflammatory nature of various aetiology (arthritis, myositis, etc.), mostly metabolic and dystrophic affections (arthrosis, certain myopathies, etc.), tumours, and congenital developmental abnormalities.

Methods of Examination

Inquiry

Complaints. Patients with diseases of the bones and muscles and with systemic affections of the connective tissue can produce various complaints. These would be commonly pain in the joints, spine, or muscles, hindered movements in the morning, sometimes muscular weakness, and elevated temperature. Symmetrical affections of minor joints of the hands

and soles, their tender articulation (active and passive) and also tender palpation are characteristic of rheumatoid polyarthritis. Major joints (wrist, knee, elbow, hip) are affected less frequently in this disease. Pain becomes more intense by night, in cold and damp weather. At later periods of the disease, the joints are distinctly disfigured, and their articulation is limited (to ankylosis). A frequent complaint is difficult and limited articulation and movement in the morning; the movements become easier by the end of the day. Rheumatism and arthrosis deformans are characterized by a distinct tendency to affection mainly of the major joints. In arthrosis deformans, pain develops mainly under load on the affected joint (in walking, stepping on the affected leg). Pain intensifies by the evening as a result of daily exercise. In ankylosing spondylarthritis (Bekhterev's disease), pain is localized in the spine and the sacrolumbar articulations. Pain develops after a long stay in a fixed position (usually during night sleep). At later stages of the disease when changes in the spine become pronounced, pain becomes permanent; it occurs not only during night but also in physical exertion and during weather changes. Specific changes in the spine of a patient can be revealed by the physician at first sight. In rare cases, the joints are also involved in this disease.

Rheumatoid polyarthritis is characterized by the predominant affection of the major joints and by the "wandering" character of affection: various joints are involved one after another, while pain in the previously affected joint disappears (within a few days or weeks) and articulation is restored. Another specific feature of rheumatoid polyarthritis is that all changes in the affected joints and periarticular tissues disappear and leave no trace after the acute rheumatic process abates.

Acute attacks of pain, mainly in the metatarsophalangeal joints of the great toes (less frequently in other joints), which arise mainly during night and predominantly in the aged and middle-aged males, can be a symptom of gout, the disease in which the purin metabolism is upset.

Thus, if a patient complains of pain and difficult movement of joints, the character of this pain should be studied thoroughly to determine its location, intensity, lenght, effect of exercise and other factors that can provoke pain, etc.

Muscular pain also differs in its character. Pain can be disseminated to indicate involvement of the entire muscular tissue. Acute attacks of pain in this or that group of muscles that last for several days (often after exposure to cold) suggest myositis. Pain in the calf muscle during walking (usually in the presence of marked atherosclerosis of the arterial vessels in various organs, in frost-bitten legs, in heavy smokers) is characteristic of stenosing arteries of the lower extremities (due to atherosclerosis, obliterating endarteritis, and certain other diseases). Pain discontinues when the patient

stops walking (the syndrome of intermittent claudication). The patient would often complain of cold in the legs which makes him wear woolen socks and winter boots even in warm weather. Muscular pain is also a symptom of trichinelliasis, cysticercosis, or myositis of infectious, occupational (chronic exposure to low or high ambient temperature, vibration or other harmful industrial factors), and traumatic origin. It is important to determine localization, intensity, character, and duration of the pain.

Elevated temperature and *various skin lesions* (petechia, erythema, urticaria, etc.) are frequent symptoms of systemic diseases of the connective tissue, the so-called collagenoses, and also allergoses. A rapidly developing (without apparent cause) *local oedema of the skin and subcutaneous tissue* is frequent in Quincke's disease (allergic oedema attended by skin itching and burning; this may be caused by food, bacterial or other allergy).

Muscular weakness (hypotonia) develops not only in prolonged rest (immobilized patients with grave diseases) but also in some neurological diseases (myatonia, myasthenia, progressive muscular dystrophy, etc.). Each of these diseases has its special features. Myasthenia, for example, is characterized by pathological muscular fatigue. Contractions of a muscle may first be quite normal, but in repeated movements the muscular force decreases to complete loss of contractile power. After a short rest, the muscle again becomes capable of contracting. Muscles lifting the upper eyelid and muscles participating in swallowing and mustication are usually affected in the first instance.

Weakening of active muscular movements is called paresis, while a complete loss of power to perform movements is known as paralysis.

Paresis and paralysis may affect any muscle or group of muscles in the presence of impaired innervation. Clinicists (internists included) would commonly observe patients with affected innervation of muscles of only one extremity (monoplegia); sometimes both legs are paralysed (paraplegia), or the extremities on one side are only affected (hemiplegia). Tetraplegia (paralysis of all four extremities) occurs in rare cases. Paralysis and paresis can develop due to affection of peripheral nerves, spinal cord (injury, compression, tumour growth, etc.), of certain parts of the brain (in thrombosis of the cerebral vessels, e.g. in atherosclerosis, embolism, or cerebral haemorrhages). Spastic paralysis with subsequent atrophy of the paralysed muscles occurs in affection of the central neuron.

The patient sometimes complains of *cold and pale fingers* (in rare cases of the ear or nose). This may occur at low ambient temperatures, injuries, and psychic stress. This is attended by pain and hyposensitivity of the skin to pain and temperature variations; this condition may develop after an attack of hyperaesthesia. Such attacks are characteristic of Raynaud's

disease (vasomotor neurosis). This condition is often the first symptom of a grave collagen disease, systemic scleroderma.

Anamnesis. Information concerning the onset and development of the disease should be collected. Many chronic diseases of bones and muscles develop insidiously and progress slowly. The disease becomes apparent only at later periods. Acute vigorous onset is characteristic of rheumatism (often in 2—2.5 weeks following tonsillitis, scarlet fever or acute respiratory infection), some forms of rheumatoid arthritis, and infectious arthritis (caused by brucellosis, dysentery, gonorrhoea, etc.). Acute affection of muscles occurs in myositis, acute paralysis, including paralysis unassociated with injuries. Hemiparesis in patients with atherosclerosis or arterial hypertension of any origin occurs not infrequently. Hemiparesis develops due to thrombosis of the cerebral vessels, cerebral haemorrhages in mitral heart diseases concurrent with cardiac fibrillation and thromboendocarditis (due to embolism and arterial obstruction) and in some other diseases. Nodular periarteritis (mainly in the young) and systemic lupus erythematosus begin acutely only in rare cases.

In some cases, it is possible to establish the factor that provoked the disease of the joints and systemic affections of the connective tissue. In most cases, these diseases are preceded by an infectious disease or overcooling of the body; sometimes the disease follows irrational use of medicinal preparations (sulpha drugs, antituberculosis preparations, antibiotics, vaccines, sera, etc.), or develops due to perverted hypersensitivity to these preparations.

Anaphylactic shock may develop in patients with acquired or congenital hypersensitivity to certain medicines given parenterally or when carrying out some tests, e.g. Pirquet, or Mantoux test. Some medicines can cause anaphylactic shock due to a contact with the mucosa (eye conjunctiva, mouth mucosa). But a slow development of an allergic reaction to medicinal preparations (antibiotics, sulpha drugs, butadione, thiamine, procaine, etc.) is more frequent: skin itching, dermatitis, urticaria, fever, arthralgia, myalgia, lymphadenopathy and other types of medicamentous allergy develop in several days. The remarkable advances in pharmacology help control many diseases, but they also bring along some negative effects, e.g. development of the so-called medicamentous diseases. Therefore, when questioning the patient, it is necessary to find out if he took some medicines, and if he did, then for what diseases, and what was the allergic reaction, if any.

A certain (unknown) role belongs to the hereditary predisposition of the patient to certain diseases of the bones and muscles, systemic diseases of the connective tissue, and various allergic affections (bronchial asthma, urticaria, etc.).

Physical Examination

INSPECTION

A glance at a patient can sometimes be enough to assess his health and diagnose the disease, e.g. anaphylactic shock, an attack of asthma, skin lesions such as erythema, urticaria, or local angioneurotic oedema (usually localized on the face), and suggest the allergic nature of the affection. Changes in the skin become more pronounced in grave cases: vesicles and even necrotic lesions develop on the skin and mucosa.

The posture of the patient, e.g. a marked kyphosis of the chest in combination with lumbar lordosis and limited mobility of the spine (the trunk of the patient is fixed in the inclined "position of a beggar") suggests ankylosing spondyloarthritis (Bekhterev's disease). Affections of the spine, joints, acute inflammation of muscles (myositis) limit the patient's mobility and sometimes immobilize him completely. The *gait of the patient* is quite informative for diagnosis. The paralytic gait of a patient with hemiplegia is characterized by the dragging limb. Paretic gait is characterized by slow movements of the patients and shuffling. It occurs in contracture of the extremities, paresis of the spinal origin. Unilateral affection of joints of the lower extremities makes the patient spare the affected limb (limping on account of pain). It should be remembered that the hip joint is commonly affected in tuberculosis (tuberculous coxitis) usually in children; at later stages of the disease, ankylosis develops, the growth of the affected extremity is delayed, and the muscles become atrophied. Acute gonitis in adults can be of gonorrhoeal nature. Deranged innervation of muscles (paralysis, paresis of various nature), congenital myopathy (a group of diseases that are the subject of detailed discussion in the course on nervous diseases) are also important for the gait of a patient. Patients with grave disorders of muscular innervation are completely immobilized.

Marked deformation of small joints of the hand and foot is characteristic for rheumatoid arthritis. Disfigured terminal phalanges of the fingers with sclerotically changed skin on them (with necrosis in grave cases), or specific stretching folds round the mouth, especially in young women, suggest systemic scleroderma (collagen group of diseases). Cramped muscles (usually flexor muscles) are sometimes revealed on inspection of the patient (development of contracture).

Erythema of the face skin, butterfly distribution of eruptions on the forehead (also mostly in young women) suggest a grave systemic disease of the connective tissue—systemic lupus erythematosus. Focal sclerotic changes on the skin of variable size are characteristic of local scleroderma.

PALPATION

When examining the skin by palpation, the physician can reveal *increased dryness,* e.g. in systemic scleroderma, indurative *oedema,* and (at later stages of the disease) atrophy of the skin and focal calcinosis of soft tissues, mainly of the fingers and around major joints. *Consolidation of muscles* may occur in systemic scleroderma and dermatomyositis. The muscles are also consolidated and become tender in ordinary myositis. In the presence of Raynaud's syndrome, palpation confirms abnormally low temperature of the skin of the extremities, especially of the terminal phalanges of the fingers.

Palpation of the joints reveals *hyperthermia and oedema* of the skin around them (in acute affections), tenderness and deformities of the joints. A thorough palpation can show whether only the joint or the surrounding soft tissues are also involved. In some cases, palpation can reveal that, despite tenderness of the joints and pain in them during movements, the joints are not affected by pathology.

Palpation is also used to study *passive mobility of various joints;* limited activity of joints can be due to pain in arthritis or arthrosis, and also in ankylosis (i.e. in articular immobility). In the presence of incomplete ankylosis, the movement may first be unobstructed, but then suddenly discontinue as if hindered by some insurmountable barrier. Special diagnostic techniques are sometimes used. In cases suspected for coxitis (inflammation of the hip joint), overextension of the stretched leg should be tried. The patient lies in the prone position. The movement of the affected leg is limited in coxitis due to developing pain and reflex muscular contracture. Flexion and rotation in the affected joint should be tried with the patient lying on his back. In order to measure accurately the angle between two articulating bones through which an affected leg can move, a special instrument, known as a goniometer, is used. It should be remembered that the joint function can also be limited by cicatricial shrinkage of muscles or tendons due to past myositis, inflammation of tendons or their sheaths, or wounds. Inspection of the skin of the extremities, palpation of the muscles and tendons can reveal the cause of limited articulation. Palpation of the joint can reveal fluctuation in the presence of acute inflammation with ample transudate in the joint, or in the presence of purulent exudate.

By giving passive movements to all joints one after another and by palpating the muscles, it is possilbe to determine their tension. *Contractile muscular tension,* which depends on dysfunction of the lower motor neuron, and *plastic tension* which shows the condition of the internal medium of myofibrillae, are distinguished. Muscular hypotension and

hypertension are possible. Hypotonic muscles are flaccid to the touch, the belly of long muscles is not pronounced, passive movements are possible in the full extent, and sometimes even in a greater extent than of normal muscle. The joints are loose. When the muscle is passively stretched, the examiner does not feel any muscular resistance. Muscular hypotension occurs mostly in affections of the peripheral nerves and prolonged muscular inactivity (e.g. when the patient keeps his bed for a long period for some grave disease). Muscular hypertension arises as a result of increased reflex muscular tension in the presence of affected pyramidal tracts; the muscles are firm and difficult to stretch passively; muscular resistance increases with the speed and abruptness of passive movements.

In order to obtain a complete impression of the muscular condition, the *force of muscles* should be assessed. Two methods are used for the purpose. The patient may actively resist the physician's attempt to flex or extend his extremity (static force), or, on the contrary, the patient tries to overcome the resistance of the physician's hand (dynamic force). There are special instruments, dynamometers, and dynamographs which determine the muscular power of various groups of muscles.

Instrumental and Laboratory Methods

LABORATORY DIAGNOSIS

Laboratory diagnosis of systemic affections of the connective tissue is used mainly for determining activity of inflammatory or destructive processes in collagen tissue.

An active pathological process in these systemic diseases alters the concentration and qualitative compostition of glycoproteins in the blood serum. *Glycoproteins* are biopolymers of protein and carbohydrate groups. Glycoproteins are component parts of the cell membrane; they circulate in the blood as transport molecules (transferrin, ceruloplasmin). Some hormones, enzymes, and immunoglobulins are also glycoproteins.

Glycoproteins are determined by chemical and electrophoretic methods. Most chemical methods are based on the determination of the carbohydrate component of the glycoprotein molecule by using various colour reactions with subsequent colorimetry. The principle of the electrophoretic determination of glycoproteins is the same as in electrophoretic separation of protein fractions of the blood serum. Schiff's reagent (containing basic fuchsine) is used for staining in the determination of glycoprotein fractions on electrophoregrams. The relative content of glycoprotein fractions in the blood of a healthy individual is as follows (in per cent): ablumins 10.4-16.6, α_1-globuhns 14.2-18.3, α_2-globulins 24.8-31.8, β-globulins 21.7-25, and γ-globulins 16.0-19.2. The highest glycoprotein content is thus found in α_1-, α_2-, and β-globulins.

Increased contents of these *globulins* indicate an active process. The highest increase in the α_2-globulins is observed in acute rheumatic diseases, and of α_1-globulins, in long-standing pathologies.

Determination of *seromucoid* in the blood is informative though not specific for an active rheumatic process. The total amount of seromucoid (which contains several mucoproteins) is determined by the proteinous component (the biuret test). Normally it is 0.75± 0.025 g/1. At the present time nine separate proteins are known to compose seromucoids. *Haptoglobin* is a seromucoid protein. It is a component part of α_2-globulin and can combine with haemoglobin. The haptoglobin-haemoglobin complex is absorbed by the reticuloendothelial system and prevents loss of iron during destruction of erythrocytes. The normal content of haptoglobin is 1.0 ± 0.032 g/1. In acute phase of collagenosis, the concentration of this protein sharply increases in proportion with the activity and dissemination of the process. This is a more permanent sign than the increased ESR. Quantitative determination of haptoglobin is done by electrophoresis. At the present time several variants of haptoglobin have been discovered but their diagnostic value is unknown.

The determination of *ceruloplasmin,* the copper-containing glycoprotein of blood, in rheumatoid patients has a certain diagnostic significance. Ceruloplasmin is an α_2-globulin transporting plasma copper. It is determined in deproteinized serum by paraphenylene diamine. Its normal content is 0.2 ± 0.05 g/1; its content increases in the active phase of inflammation.

The activity of inflammation in collagen diseases is determined not only by concentration of protein components in the blood serum but also by the concentration of the *carbohydrate components of glycoproteins:* hexoses (D-galactose, D-mannose, D-glucose), pentoses (D-xylose, L-arabinose), desoxy-sugars (L-fucose, L-ramnose) and neuraminic (sialic) acid.

Determination of hexoses. The method is based on a colour reaction of orcinol or resorcinol, with subsequent colorimetry of coloured solutions and determination of concentrations from calibration curves. Normal concentration of hexoses in healthy individuals is 1.25 ± 0.025 g/1; the hexose level increases in collagen diseases.

Determination of fucose. A product of reaction between glycoprotein and sulphuric acid is mixed with cysteine hydrochloride. Normal fucose concentration is 0.09 ± 0.01 g/1.

Determination of sialic (neuraminic) acids by Hess's method. The reaction is based on the formation of a coloured product of sialic acids eliminated from the serum glycoproteins with aceto-sulphuric reagent, and subsequent colorimetry of the coloured solution. Normal concentration of sialic acids is 0.56 ± 0.025 g/1. Their concentration increases during maximum activity of a rheumatoid process.

Concentration of *fibrinogen* in the patient's blood can increase during the maximum activity of a pathological process.

C-reactive protein appears in the blood serum of rheumatoid patients. This protein is absent from the blood of healthy individuals. Its name C-reactive protein owes to its ability to precipitate with C-polysaccharide of pneumococcus. During electrophoresis, it moves with α_2-globulins. It is determined by the Anderson and McCarthy method (by precipitation with specifically immune serum). This test is not specific either: C-reactive protein appears in the blood of patients with pneumonia, streptococcal and staphylococcal infections, and in myocardial infarction.

A *rheumatoid factor,* which is a class M inmmunoglobulin, can be found in the blood of patients with systemic lupus erythematosus and rheumatoid polyarthritis. But it has been recently proved that class G and A immunoglobulins are also present in the blood of these patients and it is therefore more correct to speak about rheumatoid factors. The latex fixation test is used for the purpose. The blood serum is tested by the agglutination reaction with human γ-globulin adsorbed on latex particles. Another method is based on the *Waller-Rose reaction,* where rabbit 7-globulin is adsorbed on sheep erythrocytes. The results are determined by the maximum dilution of the serum (titre) at which the rheumatoid factor can be detected. The maximum titre in healthy individuals does not exceed 1:64. The discovery of the rheumatoid factor is only of relative diagnostic significance, since the factor can be detected also in the presence of some other diseases (hepatitis, syphilis, tuberculosis, tumours).

Blood, bone marrow, and exudate of patients with systemic lupus erythematosus can contain the *lupus erythematosus factor (LE phenomenon, lupus erythematosus cells).* Because of the presence in the blood serum of the LE factor of the globulin nature, the nuclei of blood and tissue cells swell, the chromatin structure is destroyed and chromatin converts into an amorphous mass. This material is foreign to the body and is therefore destroyed by leucocytes. LE cells are detected microscopically. These are phagocytes (usually neutrophilic leucocytes) whose cytoplasm contains one or several homogeneous red-violet (azure-eosin) formations. Free bodies of the same colour and structure can be seen. LE cells surrounded by neutrophils (rosettes) can also be found. LE cells should be differentiated from neutrophilic leucocytes which have phagocytosed nuclear remnants with preserved contours of the chromatin network. LE cells are detected in high-leucocyte smears stained after Romanovsky. The incidence of LE cells in patients with systemic lupus erythematosus varies from 40 to 95 per cent. The LE phenomenon can also be observed (although much less frequently) in patients with grave liver affections, acute leucosis, rheumatism, tuberculosis, certain types of anaemia,

nodular periarteritis, but the LE cells are not detected permanently in them, and they only occur as single cells.

Antinuclear reactions are now used for diagnostic purposes. Reactions for *determination of antibodies to DNA, desoxyribonucleotide, and to cell nuclei* are among them. The immunofluorescence method is used for the purpose.

Systemic affections of connective tissue are attended by increased ESR and sometimes by neutrophilic leucocytosis. Leucopenia with shift to the left (to myelocytes) can be seen in patients with systemic lupus erythematosus. Hypo- or normochromic anaemia can be revealed in patients with long-standing and continually relapsing forms of rheumatism, rheumatoid arthritis, and systemic lupus erythematosus.

Increased titres of antistreptococcal antibodies, i.e antistreptohyaluronidase and antistreptokinase (more than 1:300) and antistreptolysine (more than 1:250) are characteristic immunological changes in collagen diseases. Increased titres of the antistreptococcal antibodies is a particularly serious factor in the absence of infectious foci in the body, especially so if the titres are very high (1:1500 and over). The streptococcus antibodies can however sometimes remain at the same level in diseases which otherwise would be attended by their increased level.

X-RAY EXAMINATION

X-rays reveal calcification of soft tissues, e.g. in systemic scleroderma. But the X-ray examination is most valuable in diagnosis of diseases of bones and joints. Radiographs of bones and joints are usually taken. A new technique known as *electroroentgenography* is now used by which the picture is taken not on an X-ray film but on special paper. In order to reveal pathological changes, pictures of symmetrical bones and joints are usually made at least in two projections. The analysis of X-ray pictures reveals the proportions of the bones, their shapes, inner structure, and the condition of the joint slit. Osteoporosis (rarefaction of bone tissue), the presence of focal defects of the bones (in tumours, their metastases, etc.), osteosclerosis (consolidation of bone tissue in chronic haematogenic osteomyelitis, etc.), deformities of bones, changes in their articulation (narrowing or dilatation of the joint slit, dislocation, incomplete dislocation, etc.) and other pathological conditions can be detected by X-rays.

Each disease is characterized by a certain X-ray picture of changes in bones and joints. It should be remembered that bones are also affected in some endocrine diseases (hyperparathyroidism, acromegaly), prolonged treatment with glucocorticosteroids (osteoporosis develops), in the last term of pregnancy, in metabolic disorders, and in many other cases which,

at first sight, might have no direct relation to skeletal affections. Systemic scleroderma, for example, is characterized by osteolysis (resorption of bones) of distal phalanges of the fingers and toes, and osteoporosis, mainly epiphyseal one. This sign sometimes helps differentiate this disease from other collagen diseases.

Biopsy

Biopsy is indicated in cases suspected for tumour, for the determination of the character of muscular affections in systemic myopathies and in collagen diseases. In systemic lupus erythematosus study of bioptate of the synovial membrane of the joints, liver, and kidneys helps reveal changes typical of a given disease. Lupus nephritis, haematoxylin bodies, and the "wire-loop" phenomenon are especially specific. Biopsy of the synovial membrane of joints, rheumatoid nodes (rheumatoid granuloma) is of great importance for diagnosis of rheumatoid arthritis. Amyloidosis, which is secondary to this main disease, can be revealed by biopsy of the kidney, gum or rectal mucosa. Biopsy of the skin, and in some cases of the lymph nodes, is of great importance for the diagnosis of collagen diseases.

Major Clinical Syndromes

Anaphylactic Shock

Anaphylactic shock is a symptom complex of acute grave general allergic reactions of immediate type, characterized mainly by the initial stimulation and subsequent inhibition of the function of the central nervous system, bronchospasm, and a marked arterial hypotension.

Aetiology. An anaphylactic shock may be caused by repeated intake of substances which sensitize the body when taken for the first time. Usually these are medicinal preparations such as penicillin, streptomycin, procaine, vitamin B_1, some other antibiotics, sulpha drugs, vaccines, sera, extracts of pollen of some plants, etc. It is important to note that an anaphylactic shock may develop after administration of small doses of the preparation which was given earlier in larger doses, e.g. in intracutaneous injection of only a few units of penicillin (in diagnostic test for allergy). An anaphylactic shock may develop from using a syringe which was sterilized together with syringes and needles that were used to inject penicillin to other patients. Inquiry of patients predisposed to anaphylactic shock can often reveal allergic reactions in the past history. An anaphylactic shock usually

arises in parenteral administration of medicines but it can also develop when these substances contact the mucosa. In some cases, an anaphylactic shock may occur from insect bites.

Pathogenesis. The pathogenesis of anaphylactic shock consists in sensitization of the body during the first intake of the antigen (medicinal substance, vaccine, etc.) and production of antibodies, which are partly fixed on various tissue cells. On repeated intake of the same substance, a reaction occurs by which an antigen-antibody complex is produced. Biologically potent substances, such as histamine, bradykinin, serotonin, etc., are released immediately from the cells into the blood in large quantities. These substances produce various effects on the organs and systems of the body to cause spasms of smooth muscles and to increase vascular permeability, while combination of the antigen with the circulating antibodies activates the complement and causes formation of anaphylatoxin. In atopy (hereditary allergy characterized by congenital presence of antibodies to certain allergens), an anaphylactic shock may develop during the first contact with this substance.

Clinical picture. In addition to the described general symptoms, anaphylactic shock may have some specific features. Anaphylactic shock develops rapidly, in a few seconds or minutes (to 30 minutes), following the intake of the allergen. The first symptoms are usually vertigo, headache, fear, cold sweat, dyspnoea, anxiety, pressure in the chest, and paroxysm of cough. In some cases, skin itching develops simultaneously. Some patients develop allergic urticaria, allergic oedema, tachycardia, abdominal pain, vomiting, diarrhoea, and often convulsions. The further picture varies: rapidly developing oedema of the throat and asphyxia, progressive hypotony, oedema and haemorrhages into the internal organs (which are especially dangerous if they affect the brain). In grave cases, the patient soon loses consciousness; this is an unfavourable prognostic sign.

Despite the varied clinical picture of anaphylactic shock, its diagnosis is not difficult: the main sign is the rapid response of the patient to the administration of the medicine. The shock may occur immediately. A routine systemic examination of the patient is impossible and urgent measures should be taken to recover the patient from the shock. This done, the physician may proceed with verification of the diagnosis.

Prognosis. The prognosis is serious in all cases: the patient may die within the first minutes or hours of asphyxia, cardiovascular insufficiency, or irreversible affections of the vitally important organs. The latter may develop and become the cause of death at later terms (in several days). After the patient has been drawn from the critical state, he should be given a thorough medical observation and examination by laboratory and in-

strumental methods (as indicated). This enables the physician to diagnose the affection of this or that organ at the early stage of the process.

Treatment. It is necessary to stop the allergic effect, e.g. to apply a tourniquet to the extremity into which the medicine was injected or which was bitten by an insect. This should be followed by administration of adrenaline (as a vasoconstrictive agent) to arrest the allergen supply from the tissues into the blood. Antihistamine preparations (dimedrol, suprastin, etc.), glucocorticosteroids and their analogues (prednisolone, etc.), having pronounced anti-allergic and anti-inflammatory action, should also be given. Depending on the special character of each particular case, symptomatic treatment should be given: oxygen therapy, cardiac glycosides, angiotonics, etc.

Prophylaxis. A thoroughly collected allergic anamnesis is very important. The patient should be asked to what preparations he might have allergic response, or if he has atopy or hereditary predisposition to allergic reactions. If this information is available, the physician should exclude those preparations to which the patient has the allergic reaction. Any room, where patients are given injections of medicinal preparations, should be equipped with all necessary means to recover patients from possible anaphylactic shock.

Allergic Oedema

Allergic oedema (angioneurotic oedema, Quincke's oedema) is characterized by attacks of transient circumscribed oedema of the skin, subcutaneous connective tissue, and mucosa.

Aetiology and pathogenesis. This is an allergic reaction to various allergens. Vascular reactions, and in the first instance increased vascular permeability, are important factors causing allergic oedema.

Clinical symptoms. The angioneurotic oedema develops acutely, a few seconds or minutes following the intake of the allergen (usually without any precursors). As a rule, oedema affects the lip, the cheek, the eye, but it can also develop in any organ (oedema of the throat, stomach, etc.). The oedema persists from a few minutes to several hours. The size of the swollen area varies, but it rarely exceeds the size of the palm. The allergic oedema may recur, not infrequently on the same organ.

Treatment. Intravenous infusions of a 10 per cent calcium gluconate solution, administration of antihistaminic preparations, glucocorticosteroids (prednisolone, etc.). Symptomatic therapy is also recommended (e.g. in oedema of the laryngeal mucosa).

Prophylaxis. Medicines or foods which are known to cause the allergic reactions should be excluded.

Special Pathology

Rheumatoid Arthritis

Rheumatoid arthritis (infectious allergic polyarthritis, infectious nonspecific deforming polyarthritis) is a systemic disease of the joints, first and foremost of small joints. The incidence among women is higher than in men. Young and middle-aged individuals are usually affected. The incidence of the disease is rather high: according to various authors, from 0.8 to 5 per cent of the population are affected by the disease.

Aetiology and pathogenesis are unknown. The onset of the disease is usually associated with the presence of chronic infectious foci (streptococcal infection, unknown viruses, possibly mycoplasm). The disease is regarded as an infectious and allergic and is referred to the group of larger collagen diseases. The rheumatoid factor (antibodies to the Fc fragment of immunoglobulin and mainly to the class M immunoglobulin) and antibodies to DNA, collagen, and to the formed blood elements are regularly found in the blood of patients with rheumatoid arthritis. It is believed that the rheumatoid factor arises in response to the production of autoantigens, the proteins of the affected synovial membrane of the joints. The reaction between the antigen and the antibody causes a progressive affection of the joints with further development of pathological proteins (autoallergens). Hereditary predisposition to the disease is also important.

Pathological anatomy. Osteosynovitis is characteristic of the initial period. Later the cartilages and periarticular tissues are involved in the process. Fibrous-sclerotic changes develop which finally result in complete or incomplete dislocation of the joints, development of ankylosis and marked deformation of the joints (hence another name: deforming polyarthritis). In addition to pronounced affections of the joints, connective tissue and vessels are also affected in various organs which makes it possible to regard rheumatoid arthritis as a systemic disease.

Clinical picture. Polyarthralgia with mostly symmetrical affection of minor joints of hands and feet, limitation of movements, which is especially pronounced after prolonged inactivity, and progressive deformation of the affected joints are symptoms characteristic of the disease. But all other joints can also be involved. In some cases, the disease is monoarthritis. The onset of the disease is usually subacute, but it may be acute or prolonged Pain in the joints is especially severe in the morning; it decreases at rest. After a night sleep or prolonged inactivity, the movements are especially limited, and articulation is difficult (this symptom is explained by oedema of periarticular tissues). By the night, movements of the joints become easier. The patient may also complain of general fatigue, fever, indisposition, weakness, and loss of appetite.

Inspection of patients with pronounced arthritic changes reveals specific deformation of the joints, their subluxation and ankylosis. The most typical signs of the disease are deviation of the hand in the ulnar direction (seal's fin deformity), flexion contracture of proximal and hyperdistension of distal interphalangeal joints (button-hole deformity), flexion contracture of the metacarpophalangeal joint with hyperdistension in the proximal and flexion in the distal joint (swan-neck deformity of the finger). Inspection is supplemented by palpation of the joints to determine their tenderness, the degree of limitation of active and passive movements.

The typical changes in the hand of patients with rheumatoid arthritis are a peculiar "visiting card" of the disease. It is an important diagnostic sign. Changes in the other joints are difficult to differentiate from similar changes occurring in arthritis of other aetiology.

Palpation reveals a greater or lesser degree of muscular atrophy (due to lack of exercise, i.e. atrophy due to inactivity and due to specific muscular affection). Sometimes firm rheumatoid nodules, 0.5-1.5 cm in diameter, usually mobile and not adherent to the surrounding tissues, can be palpated in subcutaneous connective tissue around the elbow, over the ulnar bone, Achilles tendon, and in the occipital aponeurosis.

Lymphadenopathy, spleno- and hepatomegaly are observed in juvenile rheumatoid polyarthritis. In 80 per cent of cases, rheumatoid arthritis occurs in the form of joint affections. The arthrovisceral form of the disease occurs less frequently. In this case, direct examination of the patients and laboratory-instrumental methods reveal changes specific for affections of various organs (subacute or chronic myocarditis, pleuritis, diffuse fibrosing alveolitis, glomerulonephritis, or amyloidosis of various organs, e.g. kidneys, liver, etc., which attend rheumatoid arthritis).

Laboratory studies reveal increased ESR (to 50-60 mm/h), not infrequently normochromic anaemia, and also positive non-specific biochemical tests showing the activity of inflammatory processes such as dysproteinaemia (hypergammaglobulinaemia, increased alpha globulins and fibrinogen in the blood serum), and high seromucoid and C-reactive protein in the blood. Detection of the rheumatoid factor in the blood serum and synovial fluid is a more specific laboratory test for rheumatoid arthritis.

X-raying of the joints reveals their specific changes: osteoporosis of bone epiphyses, narrowing and erosion of the joint slit, formation of microcysts in the epiphyses, osteophytes growing by the articulation surfaces. Complete and incomplete dislocation, marked deformities of the joints, and also complete overgrowth of certain articular slits can be revealed at later stages of the disease.

Course. The disease is chronic and progressive. In most patients, it is characterized by periodic exacerbations (provoked by infections, overcooling, etc.) and remission. The patient can die of a concurrent amyloidosis, affection of the vitally important organs (heart or renal failure), and also complications associated with prolonged (sometimes, uncontrolled) administration of strong medicinal preparations. These complications may be perforation of steroid ulcer of the stomach, or hypertonic and diabetic complications in prolonged use of glycocorticosteroids and their analogues.

Treatment. Therapy includes: (1) sanation of chronic infection foci (carious teeth, tonsillitis, sinusitis, etc.); (2) using non-steroid anti-inflammatory analgesics (acetylsalicylic acid, butadione, bruphen, and the like); (3) using chloroquine derivatives (delagil, plaquenil); (4) using glucocorticosteroids. and their analogues (prednisolone and the like) in grave cases; this should also be supplemented by local therapy (given into the joint cavity); (5) remedial exercises and physiotherapy (mainly thermotherapy); (6) in individual cases, surgical treatment (synovectomy).

Prophylaxis. Prophylactic measures are not well developed. But it has been shown that timely diagnosis and sanation of chronic infection foci (sanation of the mouth, tonsils, ears, etc.) are very important.

Osteoarthrosis

Osteoarthrosis (deforming arthrosis) is a chronic dystrophy of the joints and periarticular tissues which causes deformation of the joints. The disease usually attacks aged and middle-aged women.

Aetiology and pathogenesis are not yet known. It is believed that osteoarthrosis is associated with metabolic disorders in the cartilage due to its premature ageing. General endocrine and metabolic disorders, chronic microtrauma of the joints, and hereditary predisposition are also important. Synovitis, the reactive inflammation, is secondary to irritation of the synovial membrane by articular detritus (minute grains of necrotized cartilage). Compensatory irritation of the cartilage occurs also with formation of osteophytes; subchondral osteosclerosis develops.

Pathological anatomy. Dystrophic changes in the cartilage impair its elasticity. The cartilage surface becomes dry, opaque and rough. In grave cases, the cartilage may be affected by necrosis and ulceration, deformation of the joint surface, formation of osteophytes, perichondral osteosclerosis, and finally secondary arthroses. Inflammation in the cartilage and periarticular tissues is usually mildly pronounced.

Clinical picture. The patient complains of pain during exercise (walking, stepping on the affected leg) in the spinal column, the large joints of

the lower extremities, and in distal interphalangeal joints of the hands. The pain is abated at rest.

Deformation of the joints and swelling around them can only be revealed in grave forms of the disease. Palpation can reveal mild tenderness of tissues surrounding the affected joint. Movements of the joints are difficult only at the last stage of the disease. It concerns mostly the hip joint (coxarthrosis): patients develop waddling gait due to difficult articulation of the bones. As the disease progresses, walking becomes impossible because of dislocation or marked deformation of the hip joint. Laboratory studies do not reveal any significant changes, except a mildly increased ESR. X-rays reveal narrowing of the joint slit, the presence of osteophytes, subcartilaginous osteosclerosis in combination with cyst-like areas of diminished density in the epiphyses, deformities of the joints of various degrees, and in some cases dislocation of the joint.

Course. The disease is chronic and gradually progressive. Dislocation of the damaged joint is the possible complication.

Treatment. Therapy includes prescription of (1) analgesic and anti-inflammatory preparations; (2) intra-articular injection of trasylol (inhibitor of the proteases that are involved in the degenerative changes in the cartilage) and arteparon (to inhibit splitting of cartilage mucopolysaccharides); (3) remedial exercises and physiotherapy (mainly thermotherapy).

Haemorrhagic Vasculitis

Haemorrhagic vasculitis is an immuno-allergic disease characterized by affection of the capillaries, minor blood vessels, with subsequent multiple haemorrhages. The disease was first described by Schoenlein in 1832 and then by Henoch in 1868.

Aetiology. Aetiology of the disease is uncertain, but it has been long noticed that haemorrhagic vasculitis often attends certain infectious diseases (influenza, tonsillitis, tuberculosis, etc.) or develops in the presence of hypersensitivity to some foods and medicines. Specific antibodies to endothelial cells of the vascular wall are found in the blood of patients with haemorrhagic vasculitis.

Pathological anatomy. There are multiple haemorrhages in the skin, the wall of the gastrointestinal tract, and less frequently, in other organs. Histological studies of tissues in the zone of haemorrhage reveal affections of the capillaries and minor vessels, necrosis of their vascular wall, thrombosis, proliferation of the intima with narrowed lumen of the vessel, and focal perivascular infiltration.

Clinical picture. The disease is characterized by a sudden multiple haemorrhages in the skin, often at symmetrical points of the right and left

part of the trunk and the extremities. The joints may be affected: this is attended by pain, limited movements, and swelling of the periarticular tissues. In the abdominal form of vasculitis, haemorrhagic lesions appear on the gastro-intestinal and peritoneal mucosa; the patient complains of severe pain in the abdomen, which is attended by bloody vomiting and stools; the belly is tensed, the general condition grave, like in the acute abdomen syndrome. In certain cases, haemorrhagic vasculitis can proceed with affections of the kidneys (subacute or chronic glomerulonephritis) and other organs.

In mild cases, there are no changes in the blood, but severe haemorrhage is attended by hypochromic anaemia. The thrombocyte and fibrinogen content of blood is normal. Blood coagulability, bleeding time and clot retraction time remain normal. The tourniquet and pinch tests, and also the Bittorf-Tushinsky symptom are positive in most cases.

Course. The disease may be acute and continue for several days or weeks, or it may be chronic, with periodic exacerbations. The patient may die of profuse bleeding or haemorrhage into vitally important organs; necrosis of the intestine and kidney affections can be other causes of death.

Treatment. Treatment should be symptomatic. Calcium chloride is given intravenously to cause a weak anti-allergic effect and to strengthen the vascular wall. Salicylates and butadion are given in cases with affected joints. Corticosteroids are effective. They decrease substantially the allergic response of the body. Dimedrol, diprazine and other antihistamine preparations are also efficacious.

APPENDIX

Developments in Laboratory Diagnosis

Improvement of methods to diagnose internal diseases is related to the advances in science and technology. Wide-scale application of new diagnostic techniques in various branches of medicine helps in making the most accurate diagnosis. Highly informative laboratory and instrumental methodologies are currently being used at large research medical centres and major clinics and hospitals.

Application of computers has radically broadened the possibilities of the existing medical equipment and promotes automation of many processes such as control, recovery, and storage of the necessary diagnostic information in computers. This enables simultaneous recording and processing of various parameters of the body organs and systems performance to reveal the presence (or alternately the absence) of a syndrome, and also provides models of body functioning in various conditions, critical ones included.

Microprocessors may be used for automated history taking in several patients simultaneously. The patient has only to answer questions that are displayed on the TV screen by pressing an appropriate button on the keyboard. Depending on the answer, the microprocessor presents new questions that verify and detail the collected data. Such apparatus have become an invaluable diagnostic aid in routine medical examinations of the population. Computers help automate many labour-taking processes in laboratory diagnosis (e.g. counting blood cells, their distribution by size, determining motility of various microorganisms) which is especially important in rapid diagnosis. Data banks that are to contain exhaustive information on each patient are being established in the clinic, each physician and researcher having a personal computer at hand. Using computers on a wide scale would, in many respests, change our current concepts of physicians' labour and the peculiarities of the diagnostic process.

Instrumental diagnostic techniques are being constantly improved. New methods of X-ray studies are actively incorporated into everyday medical practice. These techniques include large-frame photofluorography, angiography, etc. The accuracy and reliability of radionuclide diagnostic techniques have been substantially improved and new gamma-chambers have been developed. Computed tomography (CT) has become a routine technique to visualize the internal structure of organs with rapid and precise mathematical processing of the obtained findings. This technique can, for example, reveal minutest tumorous lesions in the internal organs, and thus is of great diagnostic value. Nuclear magnetic resonance (NMR) is now being effectively used for the diagnosis of various diseases. This is a tech-

nique for sectional imaging of the body based on the chemical analysis (absorption of specific radio frequencies by atomic nuclei).

Ultrasonography has also become a very important diagnostic modality. One- and two-dimensional echography, and also Doppler sonography reveal some lesions of the internal organs (e.g. tumours) and structures that fail to be detected radiologically.

Endoscopic examination is another diagnostic modality that undergoes further improvement. This technique is used to visualize the internal organs under natural illumination. Combined use of various diagnostic methods (e.g. endoscopy under echographic control, endoscopy with subsequent administration of contrast medium and X-ray examination) is being introduced on a wider scale. Thermography and thermovision have also been widely used for detection of pathological processes (e.g. inflammation) in various organs by variation of temperature in definite areas of the patient's body.

Biopsy sampling of various internal organs is being used more intensively. A new branch of medicine has developed—clinical morphology. Its main object is the clinical, rather than the pathologico-anatomic diagnosis aimed at timely detection of the disease, determination of its characteristic features, and choosing of optimal therapy.

Clinical immunology, genetic engineering, and medical genetics have become of major importance in the diagnosis of internal diseases. Current techniques of laboratory diagnosis make it possible to detect the slightest changes in the internal environment of the organism, its homeostasis. The existing laboratory and instrumental methods to diagnose diseases of the lungs are undergoing further improvement. Greater attention is given to identification of causative agents of inflammation (including the agents of the new generation, such as viruses, fungi, etc.). Comprehensive bacteriological studies with new elective nutrient media facilitate the correct diagnosis. Methods for rapid aetiologic diagnosis of pneumonia are being developed. Immunoassay techniques help reveal such causative agents as *Chlamydia, Legionellae,* or viruses.

The study of the immune status of the body has become a major item in revealing allergic pulmonary disorders. This includes detection of specific and non-specific antibodies, determining the immunoglobulin and immune response mediator levels, studying the structure and functional characteristics of immunologically competent cells using monoclonal antibodies, etc.

Methods of functional diagnosis of pulmonary diseases has been used on a wider scale too. Computers help better estimate the parameters of the external respiration. The flow-volume analysis makes it possible to determine the patency of large, medium, and small bronchi and this provides

for differentiated approach to the management of patients. Rheographic methods for determining the contractile function of the right ventricle, vascular resistance to the blood flow, and pressure in the pulmonary artery system are used in haemodynamic studies of pulmonary circulation.

Diseases of the pleural cavity, subpleural portions of the lungs, and the anterior mediastinum are more commonly diagnosed by ultrasonography. Thermography is more frequently used for rapid diagnosis of these conditions by detecting local changes in body temperature.

Roentgenotomography is now widely used for differential diagnosis of pulmonary diseases. Diseases of the lungs and the mediastinum, that are difficult to diagnose by common radiologic techniques, may be identified more reliably by computed tomography and scintigraphy. Radiocardiography and radiopulmonography are more frequently used for haemodynamic studies of the lesser circulation.

The diagnosis of various bronchopulmonary diseases is facilitated by endoscopy (fibrobronchoscopy, mediastinopleuroscopy) combined with biopsy of the bronchial mucosa and transthoracic needle biopsy of the lungs with subsequent cytologic, histologic, and bacteriologic studies of the obtained specimens. Percutaneous target biopsy of thoracic pathological formations is performed under the control of computed tomography or ultrasonography. The diagnosis of circulatory disorders is commonly made with employment of enzyme immunoassay methodologies to reveal atherosclerotic lesions of the blood vessels. High plasma lipoprotein levels are determined both quantitatively and qualitatively. The genetic councelling methods are commonly used to reveal a familial predisposition to atherosclerosis. Electrocardiography is commonly used for differential diagnosis of cardialgias and early diagnosis of ischaemic heart disease (pedalling tests with the determination of tolerance to exercise, and drug tests to correctly interpret changes in the ECG).

A new generation of computerized electrocardiographs have been introduced into clinical practice. Depending on the object of investigation, an automatic ECG analyzer is able to differentiate ECG changes in detail and give to 120 variants of conclusions. Computerized electrocardiographic systems have become an invaluable aid in regular medical population checkups. The ECG findings can also be deciphered in the form of simple conclusions, such as 'health', 'pathology', 'additional examination required', etc.

Day-round monitoring with stationary or portable apparatus is widely used to diagnose diseases of the heart. This provides important information on the character of cardiac arrhythmias and ischaemic disorders in the myocardium that develop in the patient in various situations (at rest or during exercise) during a 24-hour period. Cardiac monitoring reveals latent changes that cannot otherwise be detected during common short-duration electrocardiography.

Remote control of ECG is being further improved and special consultation centres are being established where ECG are deciphered in different cases. Computers are also used for integrated assessment of the course of myocardial infarction.

Rheographic methods of examination (bi- and tetrapolar rheography) are used to measure the main parameters of the central haemodynamics (stroke and minute volumes in particular). Using multifunctional polycardiographs enables electrocardiographic, phonocardiographic, and sphygmographic examination to be performed simultaneously with rheography.

Ultrasonography is an effective means of diagnosis of cardiac pathology. It helps to verify the character and severity of pathological changes in the heart valves and in the myocardium (heart defects, dilatation of the heart chambers, contractile dysfunction), to reveal the changes in the interventricular septum, dysfunction of the papillary muscles, prolapse of the mitral valve, postinfarction aneurysms, pericardial effusions, and newgrowths (Fig. 113). Two-dimensional echocardiography helps accurate determination of the myocardial dysfunction and the volume of the heart

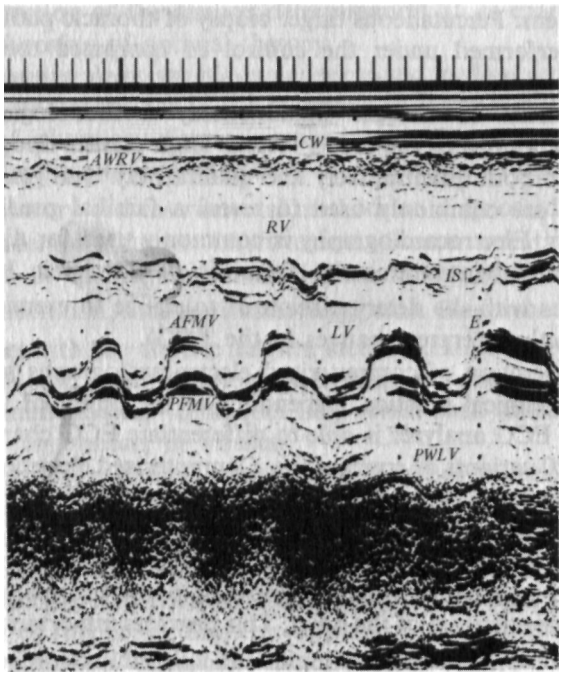


Fig. 113. Echocardiogram of the anterior flap of the mitral valve in mitral stenosis.

CW—chest wall; AWRV—anterior wall of the right ventricle; RV—right ventricle; IS—interventricular septum; LV—left ventricle; AFMV—anterior flap of the mitral valve; PFMV—posterior flap of the mitral valve; PWLV—posterior wall of the left ventricle.

chambers. Doppler echocardiography, which is based on the changing frequency of the echoed signals, is also used for the examination of cardiac performance, determination of the effective stroke volume, regurgitation and shunting volumes, and the linear velocity of the blood flow in the arteries, and for detection of atherosclerotic lesions in large arteries and thrombosis of deep veins. Catheterization with subsequent ventriculography and biopsy of the myocardium is performed to reveal the cause of myocardial lesions.

New methods of studying blood vessels have been developed. A system for studying microcirculation during biomicroscopy of capillaries is provided with a special device by which the image is transmitted on the TV screen to supply comprehensive information about the condition of the microcirculatory bed. Peripheral microcirculation (e.g. in the hands) is commonly estimated by thermography. Coronarography is used for special indications to verify the morphological changes in the coronary arteries in living subjects.

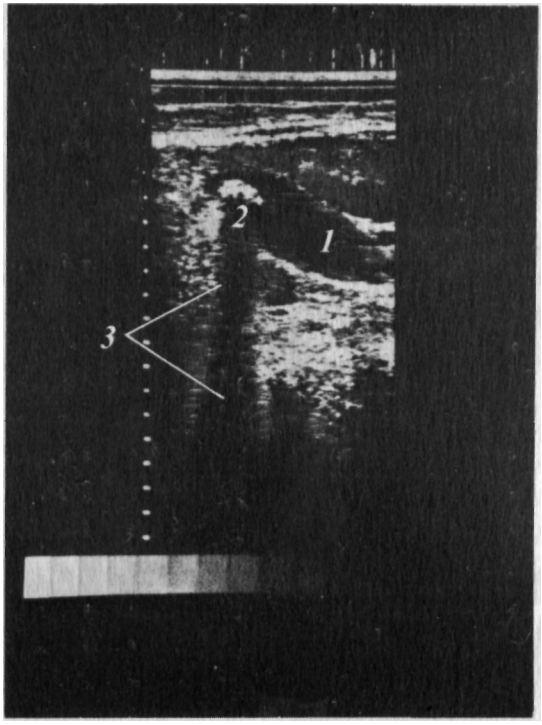


Fig. 114. Sonogram of a patient with cholelithiasis.
1—gall bladder cavity; 2—calculus; 3—'acoustic path' (a characteristic sign).

Noninvasive methods of examination of blood vessels (dynamic scintigraphy, ultrasound examinations, computed tomography) are widely used.

In gastroenterology, ultrasound is commonly used to diagnose diseases of the pancreas and liver, and also lesions of hollow organs such as the stomach and the colon (Fig. 114) (also combined with endoscopy). Newgrowths are detected by computed tomography (CT) and nuclear magnetic resonance (NMR). Computed tomography is a technique of diagnostic radiology that uses a narrow collimated X-ray beam, that is passed through the body (scanning), to produce an image of the studied tissue (organ) with the aid of the computer. This very precise technique makes it possible to differentiate between tissues with only slightly differing attenuation coefficients without using any contrast, and thus to detect pathological changes in them, e.g. hepatomegaly and tumour of the liver (Fig. 115), hydatid disease (ecchinococciasis) (Fig. 116), the gall bladder lesions (Fig. 117). Diagnostic percutaneous aspiration biopsy of a pathological focus may be performed under CT control to assess the cellular composition of a tumour (morphologic studies), to drain an abscess and introduce antibiotics into its cavity (Fig. 118), or to administer drugs inhibiting the malignant tissue growth into a tumorous node.

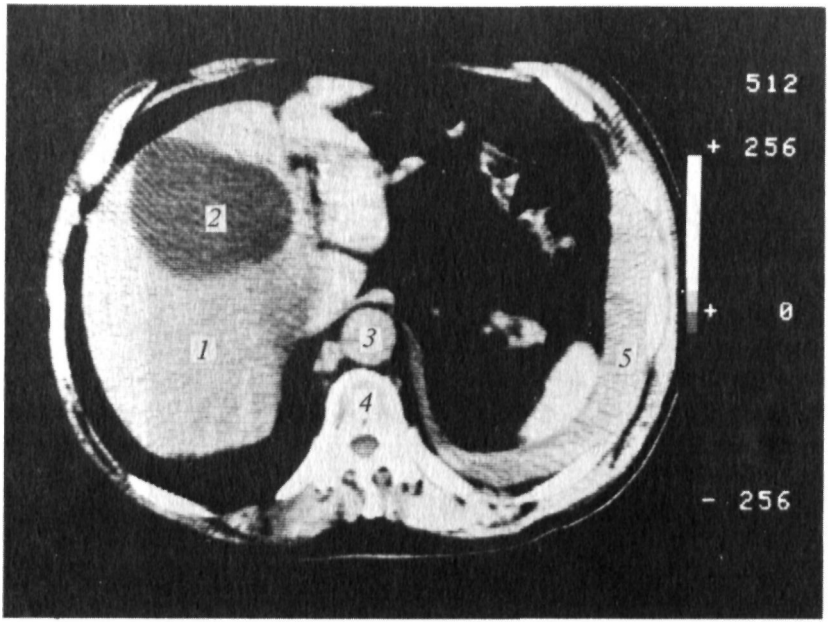


Fig. 115. CT scan of hepatic tumour.
1—liver; 2—tumour node; 3—aorta; 4—vertebra; 5—spleen; 6—intestinal loops.

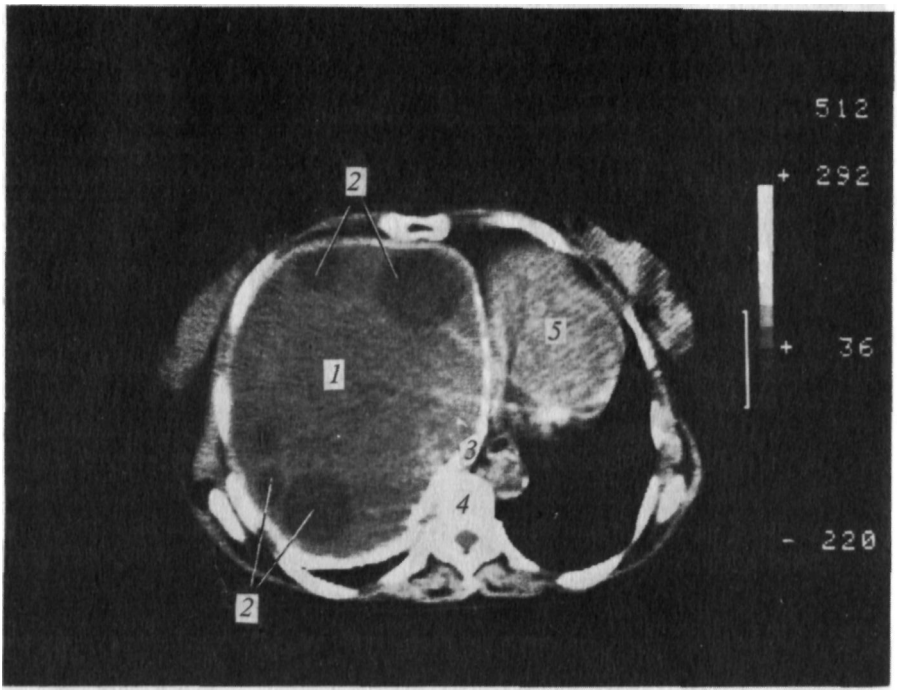


Fig. 116. CT scan of a patient with severe hydatid disease.
1—hydatid cyst in the right lobe of the liver; 2—daughter hydatids in the cyst's depths; 3—calcification line in the periphery of the cyst; 4—vertebra; 5—stomach.

Diagnostic radiology now includes large-frame fluorography of the stomach and percutaneous cholangiography. Angiography is more intensively used to reveal tumours of the gastrointestinal tract.

Endoscopy has also broadened the field of its application. TV endoscopy, endoscopy employing microelectronic devices, and luminescent endoscopy has been widely used in clinical practice. Endoscopic retrograde cholangiopancreatography is used to verify the condition and patency of the extrahepatic bile ducts. Inflammation of the internal organs is diagnosed thermographically (endoscopic thermography). Complex automated instruments employing microelectronic devices and also multichannel recorders of bioelectric processes in the gastrointestinal tract are being devised.

Histochemical, immunochemical, genetic, historadiographic, and electron microscopic techniques are widely used for the diagnosis of gastrointestinal pathology. The determination of concentration of gastrointestinal peptides in tissues, the activity of various enzymes in the pancreatic juice, and studies of upset digestion and absorption in the small intestine also help the diagnosis.

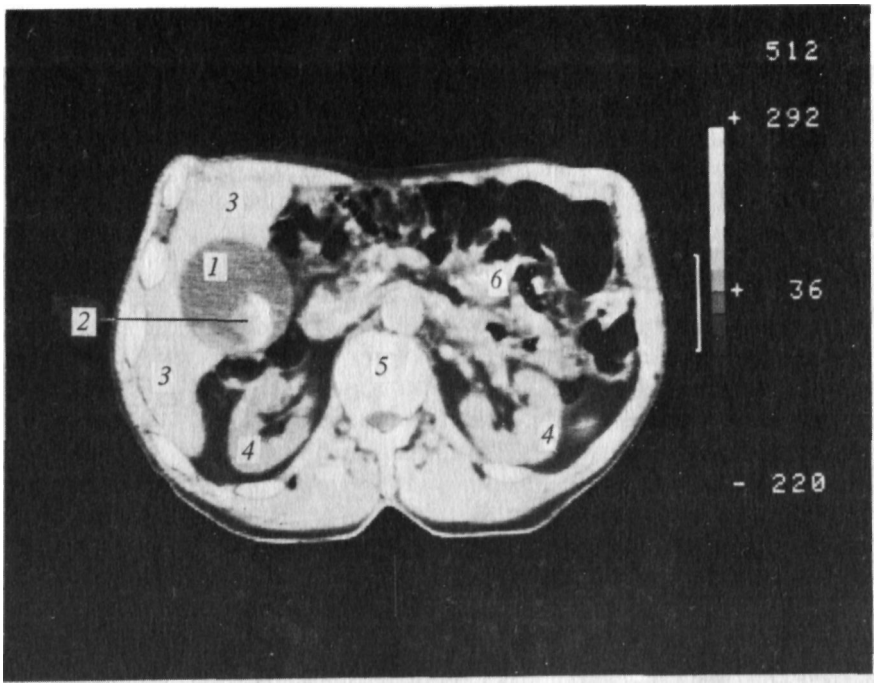


Fig. 117. CT scan of a patient with cholelithiasis.
1—enlarged gall bladder; 2—concretion of uneven density; 3—liver; 4—kidneys; 5—vertebra; 6—intestinal loops.

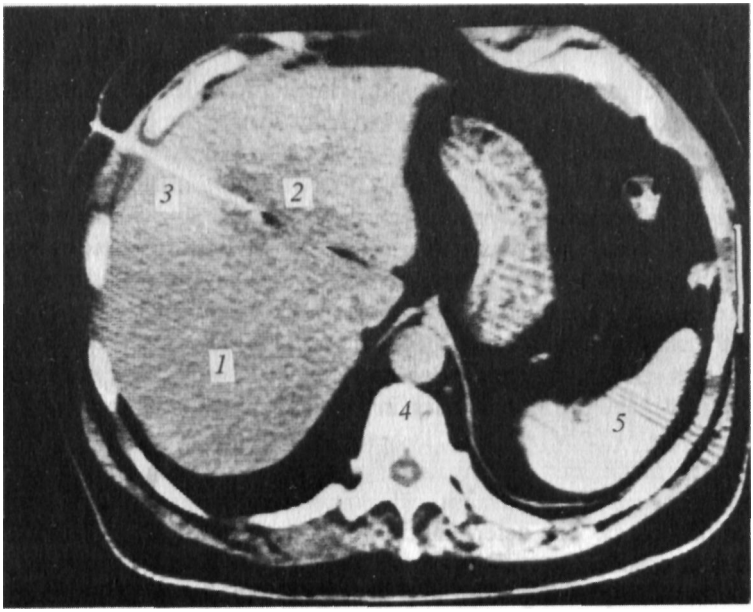


Fig. 118. CT scan of puncture of liver abscess.
1—liver; 2—liver abscess; 3—puncture needle; 4—vertebra; 5—spleen.

Clinical practice has been enriched by highly informative methods of studying the kidney performance. Immunologic diagnosis of various glomerulopathies and bacteriologic studies in pyelonephritis undergo further development. Ultrasound and radionuclides, computed tomography and selective angiography of the renal vessels are widely used in the diagnosis of nephrogenic arterial hypertension, tumours and cysts of the kidneys, and nephrolithiasis (Fig. 119). Nuclear magnetic resonance and tomography facilitate assessment of the kidney function by producing separate images of the cortex and medulla. The condition of the retroperitoneal space may also be better assessed.

Computed tomography is commonly used to diagnose endocrynological disorder, e.g. abnormalities of the adrenals (Fig. 120). Diseases of the thyroid (neoplasms, cysts) are well detected by echography which is also helpful in detecting enlargement of the adrenals.

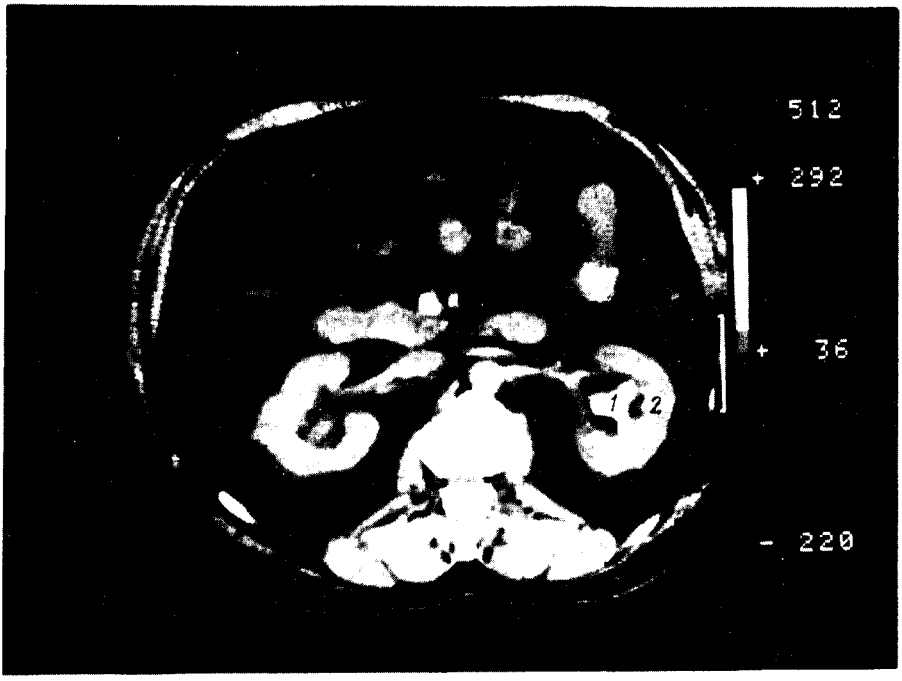


Fig. 119. CT scan of a patient with nephrolithiasis.
1—dense pathological formation with irregular outlines (calculus); 2—pelvis of the left kidney.

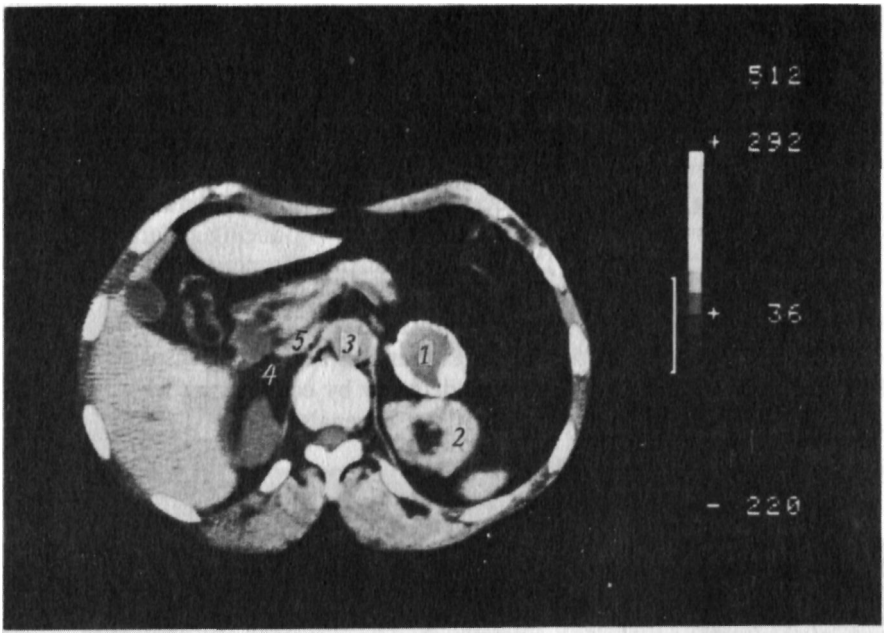


Fig. 120. CT scan of a patient with tumour of the left adrenal gland.
1—tumorous masses with signs of calcification in front of the left kidney; 2—left kidney; 3—aorta; 4—normal right adrenal gland; 5—inferior vena cava.

Advances in the diagnosis of internal diseases in the forthcoming decades largely depend on the development of new diagnostic techniques based on recent scientific and technical progress, and on equipment of tus, the physician can sometimes underestimate the importance of subjective hospitals and policlinics with new apparatus and instruments. At the same time, such technization of medicine has some adverse effects. Being supported by accurate and highly sensitive laboratory instruments and apparasymptoms of the disease and the informative value of such techniques as palpation, percussion and auscultation. Meanwhile, each physician must be able, in case of emergency and in conditions where such instruments and apparatus are not available (e.g. at patient's bedside), to establish the diagnosis and render appropriate medical aid. The physician must not entirely depend on an X-ray apparatus or a laboratory; such a physician is then only a dispatcher who refers the patient to the laboratory for additional examination.

A correct diagnosis can be established only on the condition that the physician has adequate clinical thinking and is able to analyze and correlate the patient's complaints, history, and physical examination findings with numerous additional information obtained in the laboratory and by instrumental examination.

Normal Laboratory Findings

Table 6

Normal Blood Counts

Item	Quantity
Haemoglobin:	
men	130.0-160.0 g/l
women	120.0-140.0 g/l
Erythrocytes:	
men	4.0-5.0 × 10^{12} per 1 l
women	3.9-4.7 × 10^{12} per 1 l
Colour index	0.85-1.05
Haemoglobin content of one erythrocyte (average)	30—35 pg
Reticulocytes	2—10%
Thrombocytes	180.0-320.0 × 10^{9} per 1 l
Leucocytes	4.0-9.0 × 10' per 1 1
Neutrophils:	
stab	1-6%
	0.040-0.300 × 10^{9} per 1 l
segmented	47-72%
	2.000-5.000 × 10^{9} per 1 l
Eosinophils	0.5-5%
	0.020-0.300 × 10^{9} per 1 l
Basophils	0-1%
	0-0.065 × 10^{9} per 1 l
Lymphocytes	19-37%
	1.200-3.000 × 10^{9} per 1 l
Monocytes	3-11%
	0.090-0.600 × 10^{9} per 1 l
Erythrocyte sedimentation rate (ESR):	
men	2-10 mm/h
women	2-15 mm/h

Table 7

Residual Non-Protein Nitrogen and Bound Nitrogen in Blood Serum

Substance	Quantity
Residual nitrogen	14.28-28.56 mmol/1
Urea (60, 06)*	3.23-6.46 mmol/1
Uric acid (168.11)	0.118-0.413 mmol/1
Creatinin (113.12)	0.088-0.176 mmol/1
Indican (295.30)	0.68-5.44 µmol/l or 0.2-0.8 mg/l

* Here and in tables which follow parenthesized are molecular or atomic weights.

Table 8

Ionogram of Blood Serum .

Element	Quantity
Sodium	138-148 mmol/1
Potassium	3.8-5.2 mmol/1
Calcium	0.75-2.75 mmol/1
Magnesium	0.75 -1.4 mmol/1
Chlorine	95-105 mmol/1

Table 9

Chemical Composition of Blood Serum

Substance	Quantity
Bilirubin (Jendrassik method) (75% free bilirubin)	8.55-20.52 μmol/l
Iron (55.847)	12.53-25.06 μmol/l
Total protein	60-80 g/l
Glucose (Hagedorn-Jensen method) (180.16)	4.4 - 6.6 mmol/l
Total lipids	3400-6000 g/l
α-lipoproteins	25 - 30%
β-lipoproteins	65-70%
Total cholesterol (386.64)	3.9-5.2 mmol/l

Table 10

Coagulogram

Item	Normal finding
Bleeding time (Duke)	to 4 min
Coagulation time (Lee-White)	5-10 min
Thromboelastrogram	R 9-14 min K 5-8 min Max. amplitude 50-60 min
Recalcification time	60-70 s
Plasma fibrinolytic activity	3-4 h
Plasma fibrinogen (Rutberg)	2-4 g/l
Prothrombin index in capillary and venous blood	80—100%
Antithrombin activity	90-110%
Prothrombin time	28-32 s
Heparin tolerance of plasma	7-11 min
Clot retraction	44-65% (retraction index, 0.3-0.5)
Prothrombin consumption	80-100%

Table 11

Hormones and Mediators of Blood

Substance	Normal finding, µg/l
Corticotropin	2500-7000
11-Hydroxycorticosteroids	140-230
Corticosteroids:	
(a) protein-bound	130-203
(b) free	11-32
Hydrocortisone	90-200
Corticosterone	10-50
Protein-bound iodine	30-70
Histamine	20-70
Serotonin	100-300
Adrenaline	11.2-1.4
Noradrenaline	12.7-2.6
Renin	5.5 - 7.9
Acetylcholine	5-15

Table 12

Blood Enzymes

Enzyme	Normal activity
Aspartate aminotransferase	10-35 IU
Alanine aminotransferase	10-30 IU
Creatine phosphokinase	10-110 IU
α-Hydroxybutyrate dehydrogenase	40-140 IU
Lactate dehydrogenase, total	120-140 IU
Urea-stable fraction	45-50%
Malate dehydrogenase	48-96 IU
γ-Glutamine transferase	4-28 IU
Cholinesterase	2000-4000 IU
Leucine aminopeptidase	8-22 IU
Alkaline phosphatase:	
total	20-60 IU
thermally stable	20-25%
Acid phosphatase:	
total	to 11 IU
prostatic fraction	to 4 IU
Glutamate dehydrogenase	8-16 IU
Fructose-1-monophosphate aldolase	to 1.4 IU
Fructose-1,6-diphosphate aldolase	to 8 IU
Sorbitol dehydrogenase	0-0.4 IU
a-Antitripepsin in ai-globulin	86%
in co-globulin	14%
Tripsin inhibitor	300-600 IU
Amylase	12-30 mg/ml/h

Table 13

Normal Myelogram (Gribova, 1979)

Cell	Mean value, %	Normal variation, %
Reticulocytes	0.9	0.1 -1.6
Blasts	0.6	0.1 - 1.1
Myeloblasts	1.0	0.2-1.7
Neutrophils:		
promyelocytes	2.5	1.0-4.1
myelocytes	9.6	7.0-12.2
metamyelocytes	11.5	8.0-15.0
stab neutrophils	18.2	12.8-23.7
segmented neutrophils	18.6	13.1-24.1
total	60.8	52.7-68.9
Eosinophils (all generations)	3.2	0.5-5.8
Basophils	0.2	0-0.5
Erythroblasts	0.6	0.2-1.1
Pronormocytes	0.6	0.1 -1.2
Normocytes:		
basophilic	3.0	1.4-4.6
polychromatophilic	12.9	8.9-16.9
acidophilic	3.2	0.8-5.6
Erythroid cells	20.5	14.5-26.5
Lymphocytes	9.0	4.3-13.7
Monocytes	1.9	0.7-3.1
Plasma cells	0.9	0.1-1.8
Myelokaryocytes (thous. in 1 /μl)	118.4	41.6-195.0
Leucocyte: erythrocyte ratio	3.3	2.1-4.5
Maturation index:		
erythrokaryocyte	0.8	0.7-0.9
neutrophil	0.7	0.5-0.9

Table 14

Normal Lymphadenogram
(calculated for 1000 cells, after Lucas)

Cell	%
Lymphoblast	0.1-0.9
Prolymphocyte	5.3 -16.4
Lymphocyte	67.8-90.0
Reticulocyte	0-2.6
Plasmacyte	0-5.3
Monocyte	0.2-5.8
Mast cell	0-0.5
Granulocytes:	
neutrophilic	0-0.5
eosinophilic	0-0.3
basophilic	0-0.2

Table 15

Normal Splenogram
(calculated for 1000 cells, after Meshlin)

Cell	%
Lymphoblast	0-0.2
Prolymphocyte	1 -10.5
Lymphocyte	57-84.5
Reticulocyte	0.5-1.8
Plasmacyte	0-0.3
Erythroblast	0-0.2
Myelocyte	0-0.4
Metamyelocyte	0-0.1
Granulocytes:	
neutrophilic	1.0-7.0
eosinophilic	0.2-1.5
basophilic	0.1 -1.0

Table 16

Normal Gastric Acid Secretion (after Fishzon-Ryss)

Secretion	Total acidity	Free HCl	Total HCl output	Free HCl output	Pepsin concentration, in mg/100 ml (after Tugolukov)	Pepsin output, in mg/h (after Tugolukov)	Gastric juice, in ml/h
	in titration units (mmole/l)		in milliequiv. or mmol				
Fasting stomach	to 40	to 20	to 2	to 1	to 20	to 10	to 50
Basal secretion	40-60	20-40	1.5-5.5	1-4	20-40	10-40	50-110
Stimulated after Leporsky	40-60	20-40	1.5-6	1-4.5	20-45	10-50	50-110
Histamine stimulated (submaximal) secretion	80-100	60-85	8-14	6.5-12	50-65	50-90	100-140
Histamine stimulated (maximum) secretion	100-120	90-110	18-26	**16-24**	50-75	90-160	180-220

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SUBJECT INDEX

291,

УДК 616.1/4—07(075.8)=20

Учебное издание

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ПРОПЕДЕВТИКА ВНУТРЕННИХ БОЛЕЗНЕЙ

Контрольные редакторы Е. Г. Кольцова, Т. М. Соколова
Редактор С.И. Соустина
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Технический редактор М. А. Анциферова. Корректор Т. В. Гончарова

ИБ № 8578

Подписано к печати 19.07.90. Формат 60х90 1/16. Бумага офсетная №1.
Гарнитура тайме. Печать офсетная. Объем 20,75 бум. л.
Усл. печ. л. 41,50 в т. ч. 1 печ. л. цв. вкл. Усл. кр.-отт. 85,87.
Уч.-изд. л. 49,23. Изд. № 11/6942. Тираж 7900 экз. Зак.1556 . Цена 4 р. 60 к.

ИЗДАТЕЛЬСТВО «МИР»
В/О «Совэкспорткнига» Государственного комитета СССР по печати.
Набрано в Межиздательском фотонаборном центре издательства «Мир».
129820, ГСП, Москва И-110, 1-й Рижский пер., 2.

Можайский полиграфкомбинат В/О «Совэкспорткнига»
Государственного комитета СССР по печати.
143200, г. Можайск, ул. Мира, 93.

П $\frac{4108040000—268}{056(01)—90}$ 81—90