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Exposure –oriented Epidemiology

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Objectives:

- To describe types of Exposure –oriented Epidemiology
- The main principles of exposure-oriented Epidemiology

Types of Exposure-Oriented Epidemiology

1 Social Epidemiology
2 Occupational Epidemiology
3 Environmental Epidemiology
4 Nutritional Epidemiology
5 Reproductive Epidemiology
6 Molecular Epidemiology
7 Genetic Epidemiology
8 Clinical Epidemiology
9 Pharmacoepidemiology

Social Epidemiology

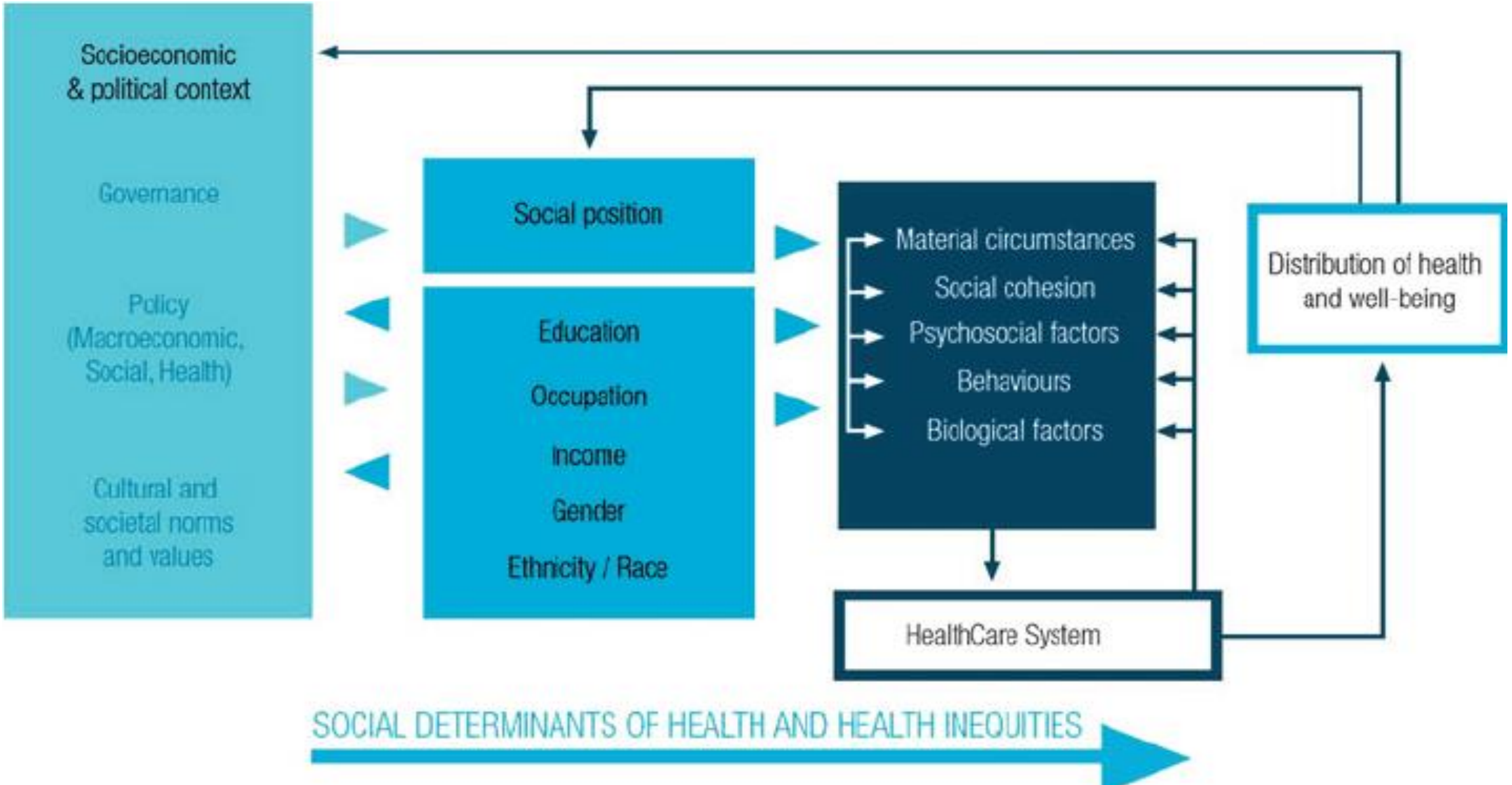
Definition: Social Epidemiology is a branch of Epidemiology that studies the social distribution and social determinants of health.

- Term “social” is used to contrast with the ‘individual’ and especially individuals theories of society
- Social Epidemiology and its social theories of disease distribution stand in contrast to individualistic epidemiology, which relies on individualistic theories of disease causation (Krieger, 2001)
- The idea that social conditions influence health is no new
- Insanitary conditions of the working classes and overcrowding, damp and filth contributed to their lower life expectancy (Chadwick, 1965)
- Social norms and conditions affect risks of suicide in the population (Durkheim, 1897)

The Social Determinants of Health

- If the social environment is an important cause of health, this is likely to be manifested as social inequalities in health.
- People from better social environments with greater access to socioeconomic resources are likely to have better health.
- Social inequalities in health documented for most countries for most causes of deaths and diseased, and in most age-groups.
- People from lower socioeconomic backgrounds are more likely to be unhealthier and have lower life expectancies.
- In Fig.1 *The socioeconomic and political context influences the structural determinants of inequalities (social class, gender, race,education)which in turn affect the conditions in which people live, work, grow, resulting in an unequal distribution of health in the population.*

The Social Determinants of Health



The Social Determinants

- **Health Behaviors:**

Smoking

Lung cancer
Chronic lung diseases

Alcohol

10% of adults
Phycology disorders
Depression
Car incidents
Intellectual Disability

Drug abusing

33% Psychiatric Disorders
Depression
HIV

Anabolic steroids

Cardiomiopathy
Osteoporosis
Hypertension
Diabetes
Depression etc.

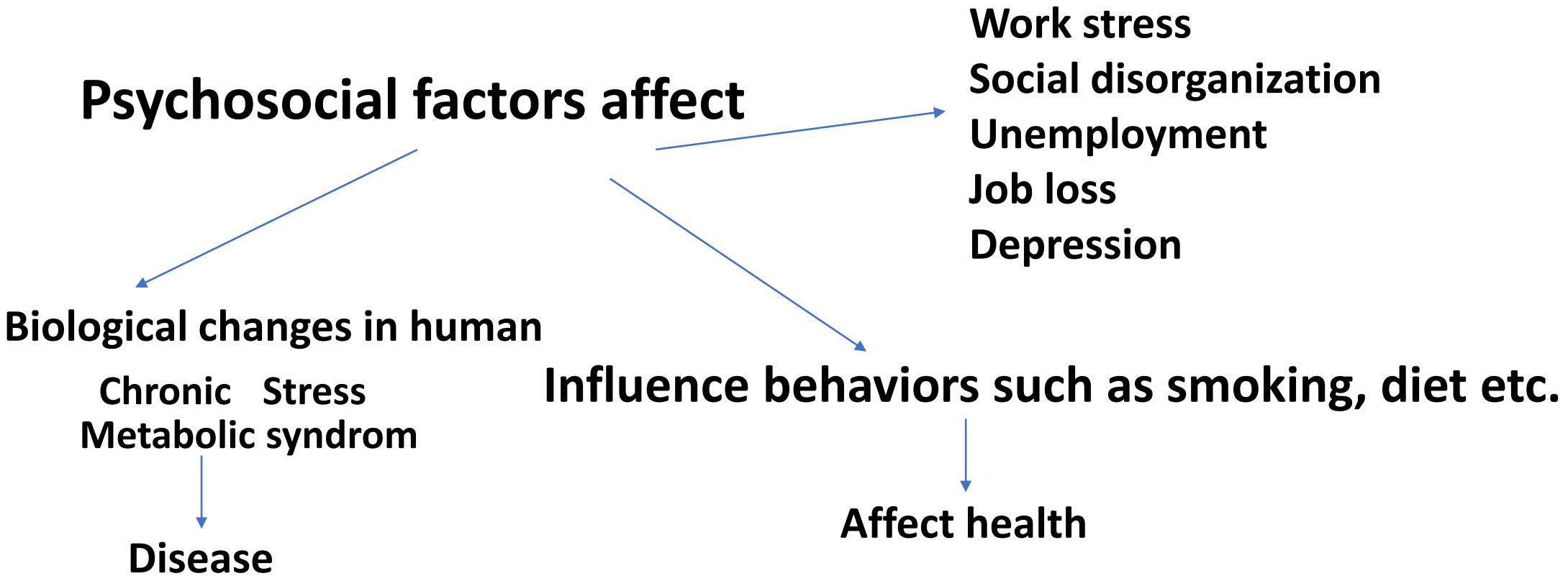
Sexual Behavior

By the 19 years 70% women and 80% men are non-virgins
Teenage pregnancy
250 000 babies born from girls aged 15-19 years old
70% of single mothers aged 15-19 years old

Sexually Transmitted Infections

Human Papiloma Virus
Syphilis
Gonorhea
HIV
Chlamidia

The social determinants



The social determinants create vulnerability or susceptibility to disease in population

Measures of Social Exposures

- Relationship between social factors (exposure) and outcomes (disease)
- Confounding effect from socioeconomic factors
- A Single crude measure of socioeconomic position (SEP)
  and different dimension of SEP in different population
- Most commonly education
- Income, wealth and assets are good indicators of a person's position in the labor market
- Material standards of living:
  proxy measures of car and house ownership, possession of consumer goods etc.
- Occupation is key variable in accumulation of advantages and disadvantages over of person's life course
- Occupation can be regarded as the means by which a person principal resource (education) is converted into an important reward (income)

Better measures of Health

- Health- related quality of life has come to mean a combination of subjectively assessed measures of health, physical function, social function, emotional or mental state, burden of symptoms, and sense of well-being
- DALYs or disability-adjusted life years, defines as lost year of "healthy“ life. The sum of the DALYs across the population, or the burden of disease is a measurement of the gap between current health status and an ideal health situation of population living at advanced age, free of disease and disability.
- QALYs – quality-adjusted life years
- YLL- Years of Life Lost to premature mortality
- YLD - Years Lost due to Disability

DALYs, YLL and YLD

DALYs for a disease or health condition are calculated as the **sum** of the **Years of Life Lost** (YLL) due to **premature mortality** in **the population** and the **Years Lost due to Disability** (YLD) for people living with the health condition or its consequences:

DALY = YLL + YLD

The YLL basically correspond to the **N** of deaths multiplied by the **standard life expectancy** at the **age** at **which death occurs**, is the following for a given cause, age and sex:

YLL = N x L

where: N = number of deaths, L = standard life expectancy at age of death in years

YLD - N of incident cases in the period is multiplied by the average duration of the disease and a weight factor that reflects the severity of the disease on a scale from 0 (perfect health) to 1 (dead).

YLD = I x DW x L

I = number of incident cases, DW = disability weight, L = average duration of the case until remission or death (years)

Methods

- Propensity Score matching, Oakes and Johnson, 2006
- Natural experiments and instrumental variables, Glymour, 2006
- Controlled community trials , Hannan, 2006
- Birth cohort studies - large scale representative samples population surveys
- Intervention and Cross National Comparative studies
  - inequalities, taxation, income

Occupational Epidemiology

- The goal of Occupational Epidemiology: to identify the causes of disease in a population in order to intervene to remove them; and prevention is a final goal
- Systematic study of illnesses and injuries related to the workplace environment (Checkoway et al.2004)
- Hippocrates wrote about the lifestyle habits and environment of populations and patients
- The first systematic description of occupational diseases and their causes in the book *De Morbis Artificum, Ramazzini, 1964*
  - different characteristics of skin ulceration in freshwater and sea fishermen, silicosis among stonemasons, ocular disorders among glassblowers and neurological toxicity among tradesmen exposed to mercury.

Goal of Occupational Epidemiology

- Scurvy in sailors (1753), scrotal cancer in chimney sweeps (1775), respiratory cancers in miners (1879) etc.
- New occupational hazards are in 1900s, when cohort study was designed (Doll, Case, 1952-1954) and occupational epidemiology developed as a discipline
- Rubber production, Bladder tumors among manufacturers and rubber workers, Birmingham, England, 1975. Rubber production let to exposure antioxidant the carcinogen 2-naphtylamine (Case and Hosker, 1954)
- Preventive measures to identify of specific causal agents “Occupational Hazards”
- Development of regulatory control

Methods using in Occupational Epidemiology

- Historical cohort study
- Case-control studies: multicenter, associations between laryngeal and hypopharyngeal cancer and smoking, alcohol, dietary, habits, and occupational factors (Tuyns et al.1988)
  - 6 centers in Italy, France, Spain and Switzerland
  - occupational history, lifestyle factors was obtained by face to face interviews with cases and controls
  - duration of years of work, specific tasks in work, company activity, specific products
  - 1,080 cases and 2,176 controls were coded
  - smoking and alcohol-adjusted OR were obtained by 2 approaches:
    first – 156 occupations and 70 industrials activities in which 9 individuals has been employed
    second – creation of job-exposure matrix (JEM) to categorize each combination of job and activity in terms of levels of probability, intensity and frequency of exposure to 16 occupational agents for which there was evidence of an association with laryngeal cancer risk.
  - The JEM was agent-specific by sensitivity and specificity *
- Cross –sectional studies
- Quantitative and Qualitative methods for assessing exposure as job-exposure matrices, job-specific questionnaire modules for assessment of experts, were developed by occupational epidemiologists and industrial hygienists

Table. Validation of the job exposure matrix (JEM) of the IARC case-control study on laryngeal and hypopharyngeal cancer: % of jobs entailing an exposure to specific agents according to an expert's assessment compared with the results from the JEM

JEM categories of intensity/probability of exposure								
Agent	N of job periods	1	2	3a	3b	3c	4	5
Asbestos	3220	96	83	79	73		68	
Solvents 1	2712	96	92	89	70	47	58	16
Solvents2	929	87	83	62	67	35	37	9
Formaldehyde	884	75	90	59	47	50	29	-d
Wood dust	863	95	-d	50	50	-d	8	0
PAH	2571	98	68	88	85	98	74	39

Mortality Odds Ration studies

- Case-control study, Miettinen and Wang, 1981. The cases comprise deats from the specific cause of interest, both exposed and unexposed, while the controls are other deaths, selected on the basis of a presumed lack of association with exposure.
- Proportionate mortality studies, frequency of death for the disease under study among exposed workers is compared with the corresponding figure calculated for a reference population(proportionate mortality ratio, PMR

Special Issues of Occupational Epidemiology

- **Dose –respond relationship**.
  - Exposure measured different metrics: duration, intensity, cumulative level, which based on mechanism of disease, development and nature of the exposure
  - cumulative exposure is the product of intensity and duration, is a correct metric for several types of diseases where risk directly proportional to dose.
  - duration of employment is a valid surrogate for cumulative exposure
- **3 reasons to use dose–response analysis:**
  - occupational exposures are time-, place specific
  - occupational exposures are well known Bradford Hill's criteria for establishing causality
  - one of steps of risk assessment, which aims at quantifying the health effects of environmental and occupational exposures which modifying new policies and technologies.

Special Issues of Occupational Epidemiology

- **Confoundng** related with internal comparison groups with general characteristics assumed to be similar to cases
- **Bias, Healthy worker effect (Fox and Collier, 1976):**
  - Phenomenon “healthy hire effect”
  - healthy worker survivor effect, related with long duration of employment (Arrighi, Hertz- Piccioto, 1994)
  - they depend on type of work, general social conditions
- **Data on exposure** in Occupational Epidemiology are summarized as qualitative or semiquantitative indices
  - JEMs produce indices of intensity and probability of exposure of an ordinal scale
  - if quantitative information is available, cumulative exposure can be estimated for each study
  - Categorical analysis, the exposure variable is subdivided into a certain number of categories on the basis of cut-points
  - when exposure is continuous- regression model with a term for a exposure (cumulative exposure)

Prevention

Result and application of epidemiological studies in Occupational Epidemiology is develop of prevention

Primary prevention is based on the application of basic industrial hygiene strategies at the industry level:

- Substitution with agents intended not to be as dangerous
- Fully enclosed processing
- Strict control of exposure by reduction of amounts used by local exhaust, by personal protection , by cleaning practices

To reduce the number of potentially exposed workers and their exposure level

At the community and country level. Primary prevention entails adopting regulations intended to favor preventive measures

The applications of occupational epidemiology in Public Health decision-making are broadening, providing inputs to risk assessment, evaluation of occupational guidelines , and extrapolation of findings from occupational settings to communities.

Environmental Epidemiology

- The ***human environment*** is the aggregate of surrounding things, conditions, or influences especially as affecting the existence or development of someone or something (Webster Encyclopedia)
- **Environmental Epidemiology** is the **study** of the **effect** on human health of physical, biological, and chemical factors in the external environment. By examining specific populations or communities exposed to different ambient environments, environmental epidemiology seeks to clarify the relation between physical, biological and chemical factors and human health .
- This idea is not new….Hippocrates sad “De aere aquis locis’ or Aristotle recommended that cites have no be located in a healthy environment and that air and water should be clean so as not to impair human well-being.
- More than 500 years ago, the very first observations were made of a possible relationship between “the air within the mine” and symptoms of disease and early mortality in the area of ancient ore mining around the village of Schneeberg in Saxony, Germany
- Outbreak of Cholera in London is a classic example for Environmental Epidemiology

Concepts of Environmental Epidemiology, 4 –step process

- Hazard identification: Does the agent have the potential to cause an adverse effect?
- Exposure assessment: What exposures are experienced or anticipated under relevant conditions?
- Exposure –outcome assessment: What is relation between exposure and outcome in humans?
- Risk characterization: What is estimated incidence and severity of an adverse effect in a given population?

Environmental Toxicology

- The field of environmental toxicology studies the consequences of industrial and agricultural chemical substances on human health and the environment.
- The process that is used to estimate this is called risk assessment.
- Risk assessment is an analysis that uses mathematical equations and scientific information (e.g. health and environmental) to determine the probability of an event occurring and the magnitude of the adverse effect over a specific time
- The risk assessment process comprises 7 Steps in vitro and animal experiments over a range of exposure intensities,
  - leading to NOEL (no observed effect level)
  - and the ADI (acceptable daily intake)

  that incorporates and appropriate safety factor …10. 100 or higher

Special methodological issues in Environmental Epidemiology

- Standardization of Study design
- Sample size
- Selection of study participants
- Choice of study area
- Measurements and exposure assessment of risk factor: technique, method and statistical evaluation

example:

Exposure effect relationship	**example**
Short-term exposure/short term effect	Traffic-related agents –acute respiratory symptoms Smog episodes – mortality or chronic respiratory diseases
Short-term exposure/long term effect	Fallout from nuclear weapon tests- cancer incidence Contaminated food – SARS, food poisoning
Long-term exposure/long term effect	Residential radon exposure – lung cancer

Pediatr Allergy Immunol. 2014 Oct;25(6):558-64. doi: 10.1111/pai.12271.

Risk factors and markers of asthma control differ between asthma subtypes in children.

Nordlund B[1], Melén E, Schultz ES, Grönlund H, Hedlin G, Kull I.

BACKGROUND: There is limited understanding about risk factors for asthma, and few studies have presented an overall picture of factors associated with asthma subtypes in schoolchildren. The aim of this study was to evaluate risk factors and markers of asthma control associated with asthma subtypes up to preadolescence.

METHODS:

A Swedish birth cohort of 3015 children was followed for 12 yr using repeated parental questionnaires. At 8 yr, clinical investigation was performed, specifically evaluating lung function, allergic sensitization (IgE > 0.35 kUA /l), and body mass index (BMI). Children were categorized into three subtypes: transient asthma - asthma at 4 and 8, but not at 12 yr (n = 71), late-onset asthma - asthma at 12 yr, but not earlier (n = 103), and persistent asthma - asthma at 4, 8 and 12 yr (n = 125).

RESULTS:

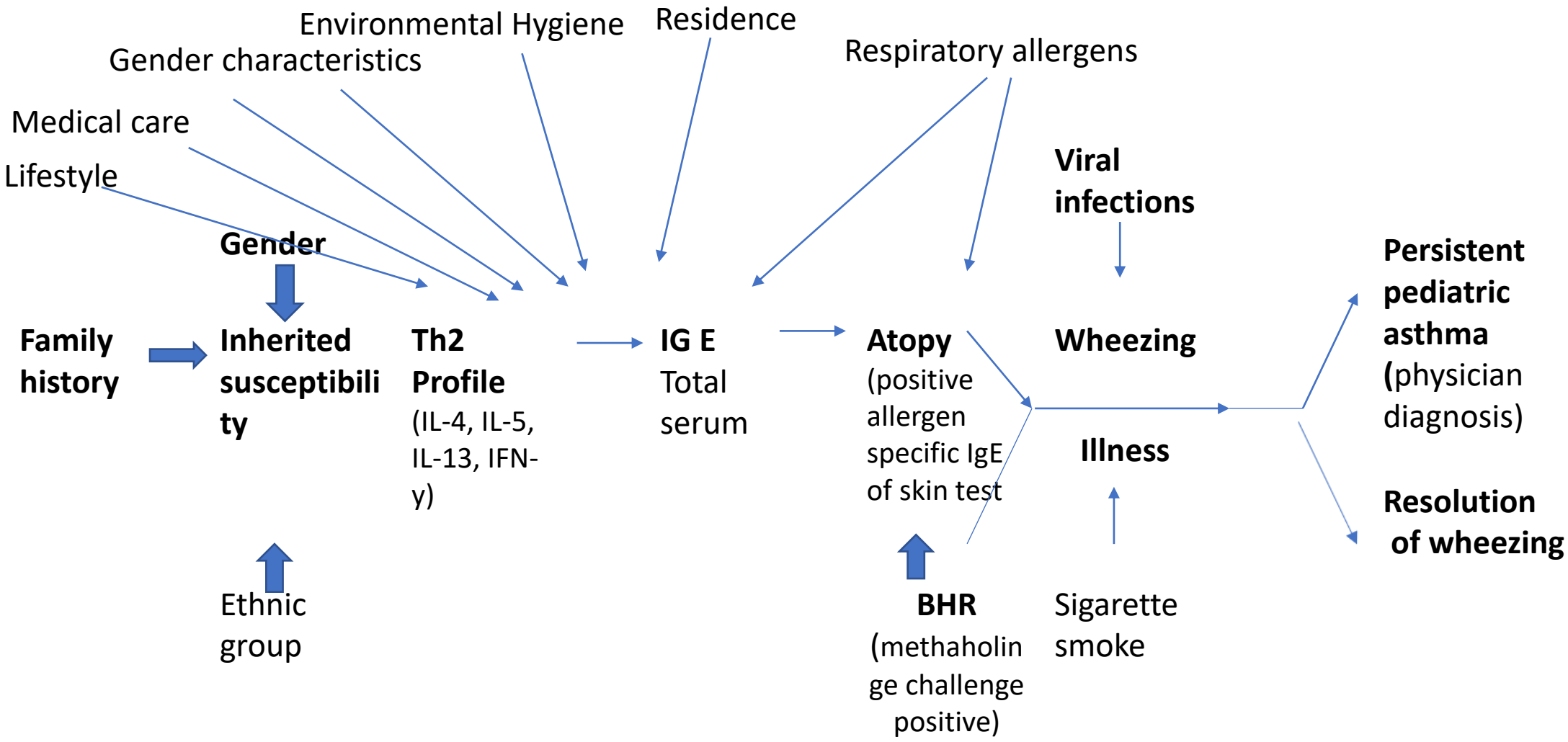
At 8 yr of age, high BMI (>85th percentile), sensitization, and rhinitis were significantly associated with late-onset asthma ($p < 0.05$). Prominent risk factors at birth associated with persistent, but not late-onset asthma, were male sex, tobacco exposure and, heredity for atopy ($p < 0.05$). Children with persistent asthma were also found to have significantly reduced lung function at 8 yr of age, more eczema/rhinitis, and were more atopic than non-asthmatics ($p < 0.05$). For persistent asthma, symptoms changed from 8 to 12 yr, with fewer nocturnal symptoms, less healthcare utilization, and less frequent wheeze at 12 yr ($p < 0.05$).

CONCLUSION:

Risk factors differ between asthma subtypes and markers of asthma control vary with age up to preadolescence.

KEYWORDS:

allergy asthma; asthma control; birth cohort; body-mass-index; children; population-based design; rhinitis; risk factors; symptoms



Factors and markers potentially associated with the development of persistent pediatric atopic asthma: Th T-helper cell, IL interleukin, IFN-y is interleukin gamma, BHR is bronchial hyperactivity, modified by Johnson et al, 2002

Nutritional Epidemiology

Nutritional Epidemiology is a science which study of distribution and variation in the nutritional behavior of individuals and relates that behaviors to health outcomes.

Purposes:

- understand the role of nutritional factors in causing various health outcomes
- In generic – to explore exposure –outcome relationship

Outcomes:

Well being, disease, disease markers, metabolic disturbance, level of Body mass index (BMI) to define obesity

Nutritional exposure: dietary or nutritional behavior (intakes, habits, knowledge, attitudes), biochemical markers, body composition or clinical signs of nutritional problems

Aim of epi studies:

Measuring Dietary Exposure:

- Population of Assessment
- Food record
- Food recalls: Interviewer administered 24-h- recalls
  Web –Based 24-h- recalls
- Dietary history method
- Food frequency Questionnaire (FFQ): traditional, Food propensity Questionnaire (FPQ),
  Screeners for Dietary Exposure, Web-Based

Versions of the FFQ,

FPQ and screeners

- Nutritional Biomarkers
- Dietary exposures
- Measurement of Dietary Behavior

Nutritional Epidemiology in Public Health Practice

- Nutrition Surveys: Assessing the Usual Intake of a Population
- Measuring Nutritional Exposures in Specific Groups
- References for Assessing Dietary Intake in Population
- Impact of Underreporting of Intake
- Consequences of Within –Person Variability in other areas

Reproductive Epidemiology

Reproductive Epidemiology is a science that studies problems of reproductive health: miscarriage, infertility, congenital malformations, time matters

DESIGH OF STUDIES:

- The Case-Parent Triad
- Describe of Fertility: recognition of pregnancy by clinical and biochemical measures, time to pregnancy (TTP), Twins
- Measuring Adverse Reproductive Outcomes: mortality, live births, fetal deaths, induced abortions (WHO)

Rates

live births – complete expulsion or extraction from the mother of a product of human conception, which breathes or shows any other evidence of life, such as a beating of the heart, pulsation of the umbilical cord, or define movement of voluntary muscles

fetal deaths – death prior to complete expulsion or extraction from the mother of a product of human conception, fetus and placenta, irrespective of the duration of pregnancy

induced termination of pregnancy – purposeful interruption of a intrauterine pregnancy with the intention other than to produce a liveborn infant and which does not result in a live birth

$$\textbf{induced termination of pregnancy rate} = \frac{\textit{N of induced terminations occurring during a specific time period}}{\textit{N of induced terminations+living births+reported fetaldeaths during the same period}} * 1{,}000$$

$$\textbf{induced termination of pregnancy rate (population)} = \frac{\textit{N of induced terminations occurring during a specific time period}}{\text{Female population aged 15- 44 years}} \textbf{* 1,000}$$

Rates

$$\textbf{Fetal death rate} = \frac{\textit{N of fetal deaths during a specific time period}}{\textit{N of fetal deaths +N of live births during the same period}} * 1{,}000$$

$$\textbf{Fetal death ratio} = \frac{\textit{N of fetal deaths during a specific time period}}{\textit{N of live births during the same period}} * 1{,}000$$

Rates

- Infant deaths
- Optimal Birth Weight
- Gestation Age
- Pregnancy complications: pregnancy produced hypertension, Pre-eclampia

Relative Prevalence Rate Measuremetn

Exposure	Cases	All births
+	2,000	100,000
-	1,000	100,000

$$PR = \frac{2{,}000/100{,}000}{1{,}000/100{,}000} = 2$$

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