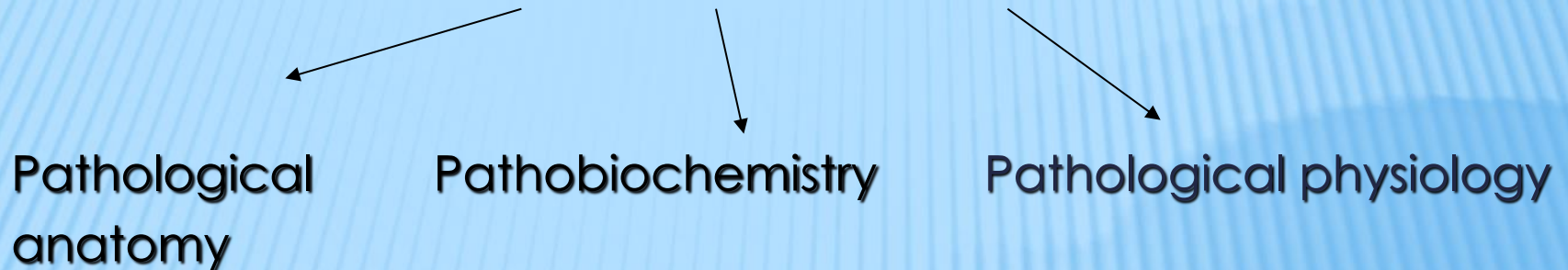


PATHOLOGICAL PHYSIOLOGY AS A SCIENCE

September 19, 2017

General teaching on diseases



Pathological physiology is a teaching on diseased functions, i.e. on etiology and pathogenesis of diseases based on experimenting and clinical observations including functional diagnostics.

Connection between a premorbid organism and a disease

Etiology

Etiology – is the assignment of causes or reasons for phenomena. A description of the cause of a disease includes the identification of those factors that provoke the particular disease.

e.g. tuberculosis

In the etiology of particular disease, a range of **extrinsic (exogenous) factors** in the environment must be considered along with a variety of **intrinsic (endogenous)** characteristics of the individual.

Pathogenesis

Pathogenesis of a disease refers to the development or evolution of the disease.

To continue with the above mentioned example, the pathogenesis of tuberculosis would include the mechanisms whereby the invasion of the body by the tubercle bacillus ultimately leads to the observed abnormalities.

A given disease is not static, but it is a **dynamic phenomenon with a rhythm and natural history of its own.**

It is essential to keep in mind this concept of natural history and the range of variation among different diseases with respect to their natural history.

General pathophysiology

A: Health and disease.

1. Definition of health and disease
2. Pathogenic factors (physical, chemical and biological) and response of organism for them (adaptation, dysadaptation).
3. Types and degree of disease.
4. Death (clinical, biological, cerebral).

General pathophysiology

B: Cellular mechanisms in pathological stages

C. Reaction on damage of tissue integrity and infection.

1. Non-specific (innate) immunity: **inflammation**

2. Specific (acquired) immunity, acquired immune diseases (**immunodeficiency, hypersensitivity and autoimmunity**)

General pathophysiology

D: Growth and proliferation

1. Induction of proliferation and wound healing
2. Malignant proliferation
3. Tumour growth

E: Genetic background in etiopathogenesis of disease

monogenic diseases

polygenic disease (complex)

Special pathophysiology

- × Pathophysiology of organ systems
- × Pathophysiology of organs
- × Pathophysiology of tissue
- × Pathophysiology of molecules
- × Pathophysiology of genome

Definition of health

- ✘ Health – is a component of a general quality of life
- ✘ To declare a person or a group diseased ⇒
fateful consequences, broad social effects
- ✘ Law presupposes a definition of health

Concept of normality

- × Most people have some notion of normal and would define disease or illness as a deviation from or an absence of that normal state.
- × However, on closer scrutiny, the concept of normality turns out to be complex and cannot be defined succinctly, correspondingly, **the concept of disease is far from simple.**

Normality as health may be defined on various levels:

- **Biological (physical) normality:** A whole of undisturbed functions. There are, however, non-reflected presumptions: it is not said what is the aim of an organism. A "humanistic" definition must precede.
 - **Psychological normality:** A well balanced result of an adequate self-esteem (self-confidence), of spontaneity and excitability
Realistic attitude towards the aims of life and realistic individual desires, an ability to draw lessons from experience, sociability
 - **Sociological normality:** An ability to fulfill expectations and roles in the frame of the existing social system
- Normality of mind (spiritual):** An advancement of objectivity and reason, independency and finding ones identity, ability to love and creativity

Normality as viewed by law (*juridical*): Ability to work, lack of the necessity to be cared for.

„*Ecological*“ definition of WHO:

State of perfect physical, psychical and social wellbeing, not only an absence of disease and infirmity.

Definition of disease

Disease can be defined as

a contradiction to health = „alternative model“
or only as

a contrary term – than, there is a whole array of intermediate steps:

- ideal health
- reasonably acceptable health
- predispositions
- feeling not well
- subclinical forms
- clinical forms
- fatal courses of disease

Normal and abnormal processes represent different points on the same continuous spectrum.

DISEASES

- × Diseases are clinically *individualized entities*. When a physician says that her patient has some disease, she is classifying some observable clinical entity and categorizing it as the exemplification of a nosological theoretical entity, *that is, as an exemplification of some pathology*.
- × Pathology, following this approach, is an abstract entity, but individual diseases are not abstract. Diseases are observable entities.

DISEASES

- × **Pathologies** are the general theoretical categorizations of **events (acute diseases)** or **states (chronic diseases)**.
- × **Pathologists** look for the pathological features of some specific pathology, and they usually look for them *in cells, tissues and organs*.
- × **Pathophysiology** describes and explains dynamics of events and/or states (diseases)

DISEASES

- × **Clinics** look for the clinical features of some or several diseases or morbid conditions *in their patients*. Patients are possibly diseased, sick individuals and they are objects of medical attention. It is not by chance that clinicians use ‘disease’ (the term) and not ‘pathology’ in their professional practice. Etymologically, ‘disease’ comes from the Middle English (and from Old French, *desaise*) as a fused word of ‘dis’ and ‘ease’.

DISEASES

- × Diseases are happenings in the course of some individuals' lives. This is just what makes it possible to describe their **epidemiology in two different ways**: we can describe the distribution of diseases numerically in a given population at a specific time (**the prevalence of the disease**) and we can also describe numerically the occurrence of new appearances, emergences or happenings of some disease after some time (or up to some time, like up to the present time).

DISEASES

- ✘ This second kind of epidemiological description, **incidence**, is possible just because diseases are (or at least can be) *events*.
- ✘ Diseases are things that happen in (or with) living beings (animals or plants). Following the Aristotelian jargon, diseases are things that occur or happen in or with living individual substances: human beings, individual animals or plants.

DISEASES

- × Diseases can be **local** (restricted to tissues or organs) or **systemic**, and they can also be **acute or chronic**. Acute diseases can be serious or not, **benign or malignant**, the same with chronic diseases.
- × But chronic diseases have the special characteristic that once they install themselves in the organism they **persist** over time. This is not a matter of convention. It is an essential (real) characteristic of chronic diseases that they represent changes in the physiology of the individual that worsen her capacity to fight against several other external or internal threats. The consequence is **actual unhealthiness**.

DISEASES

- × Chronic diseases sometimes represent an **actual significant persistent change in the organism's general state**; they can change the organism's state from a healthy to an unhealthy one. In the case of acute diseases, the change is not necessary; it is a matter of probability.
- × Acute diseases are causes of unhealthy states, but in some cases, the acute disease is a healthy and functional process (**acute gastroenteritis and food poisoning diseases, for example, are acute processes that represent the organism's attempt to eliminate poisons or microorganisms, so as to prevent chronic damages and illness; so the aim of those diseases is to re-establish physiology**). Acute diseases are causes of unhealthiness only if the outcome is death, a chronic disease or other chronic harm. In this case, the disease ceases to be acute.¹³ Chronic diseases are also causes of unhealthiness, but the difference is that they remain actual in the organism during the now dysfunctional state. In the case of acute diseases, once one has changed the actual state of an individual from a healthy to an unhealthy one, the acute disease has transformed itself into another condition: a chronic injury, some chronic disease or a permanent disability.

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Definition of disease (BUCHBORN)

- × „Feeling of bad health as a result of subjective and/or objective somato-psychical derangement, with/without subjective, medical or social need for help, as a result of disturbances in harmonic cooperation of individual functional parts and subsystems of an organism“

A superposition
of three aspects of
a disease in
medical practice
(together: "morbus")

a patient's point of view
(aegritudo, illness)

a doctor's point of view –
objective in a medical
description (nosos, disease)

a point of view of the social
milieu (a state of need and
deficiency)

The concepts of health and disease relate
to both natural and cultural phenomena

Stages of disease development

- × Symptoms (prodromal stage)
- × Acute disease (1-21 days)
- × Chronic disease (above 40 days):
 - following after acute disease (chronic bronchitis in smokers)
 - primary chronic (e.g. Wegener's granulomatosis)

A **complication** of a disease – is a new or separate process that may arise secondarily because of some change produced by the original entity

Recovery

Remission

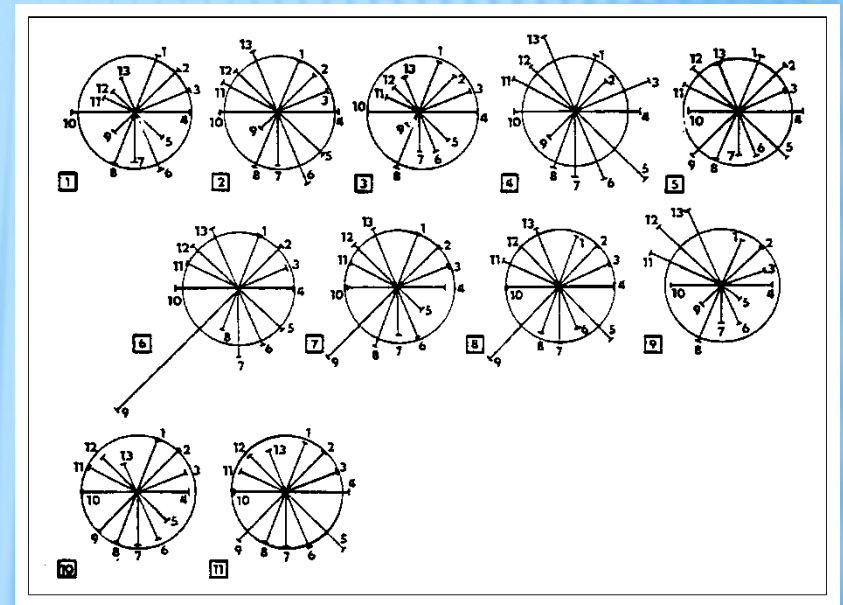
Exacerbation

Relaps

Residual disease

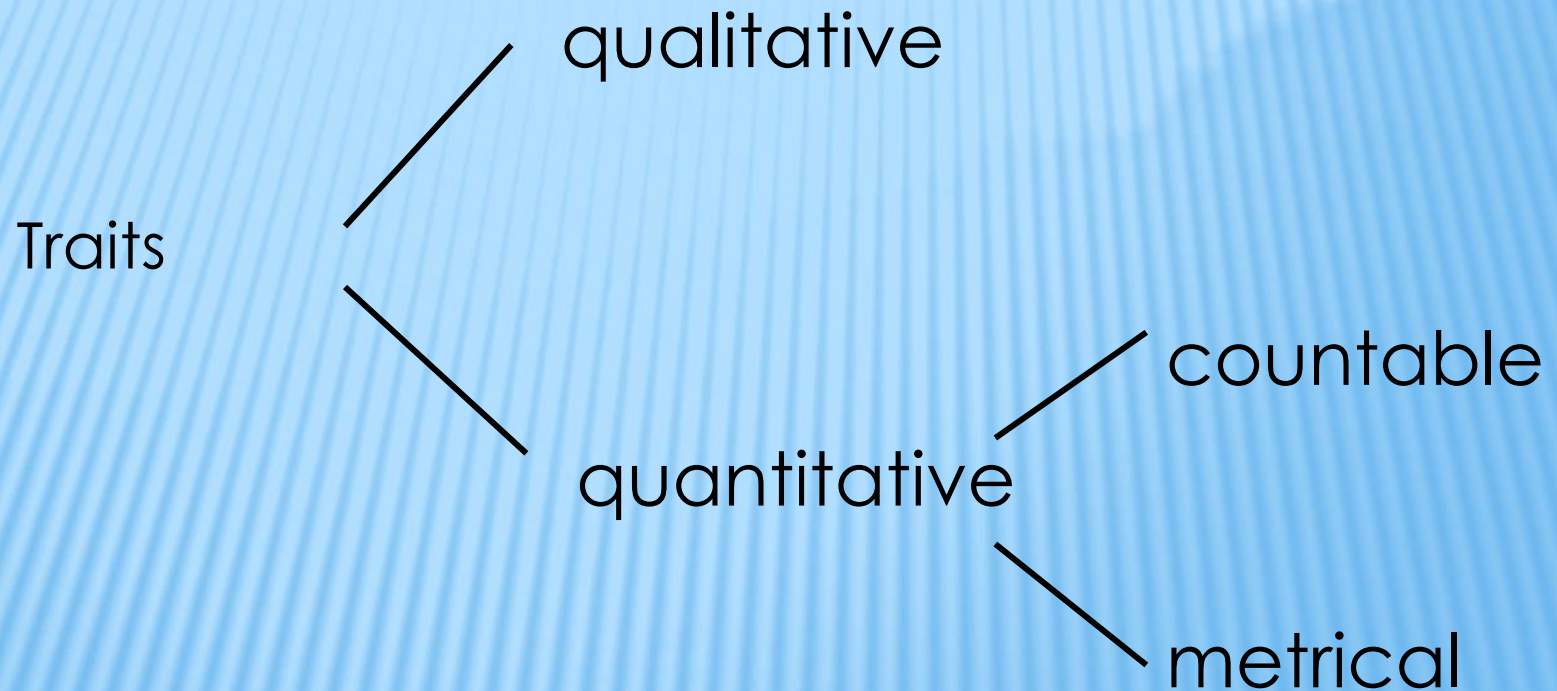
Identification of health and disease

- ✘ Interindividual variability → health and disease are probabilistic, not strictly deterministic phenomena;
- ✘ a diagnosis is a task of a statistical type.



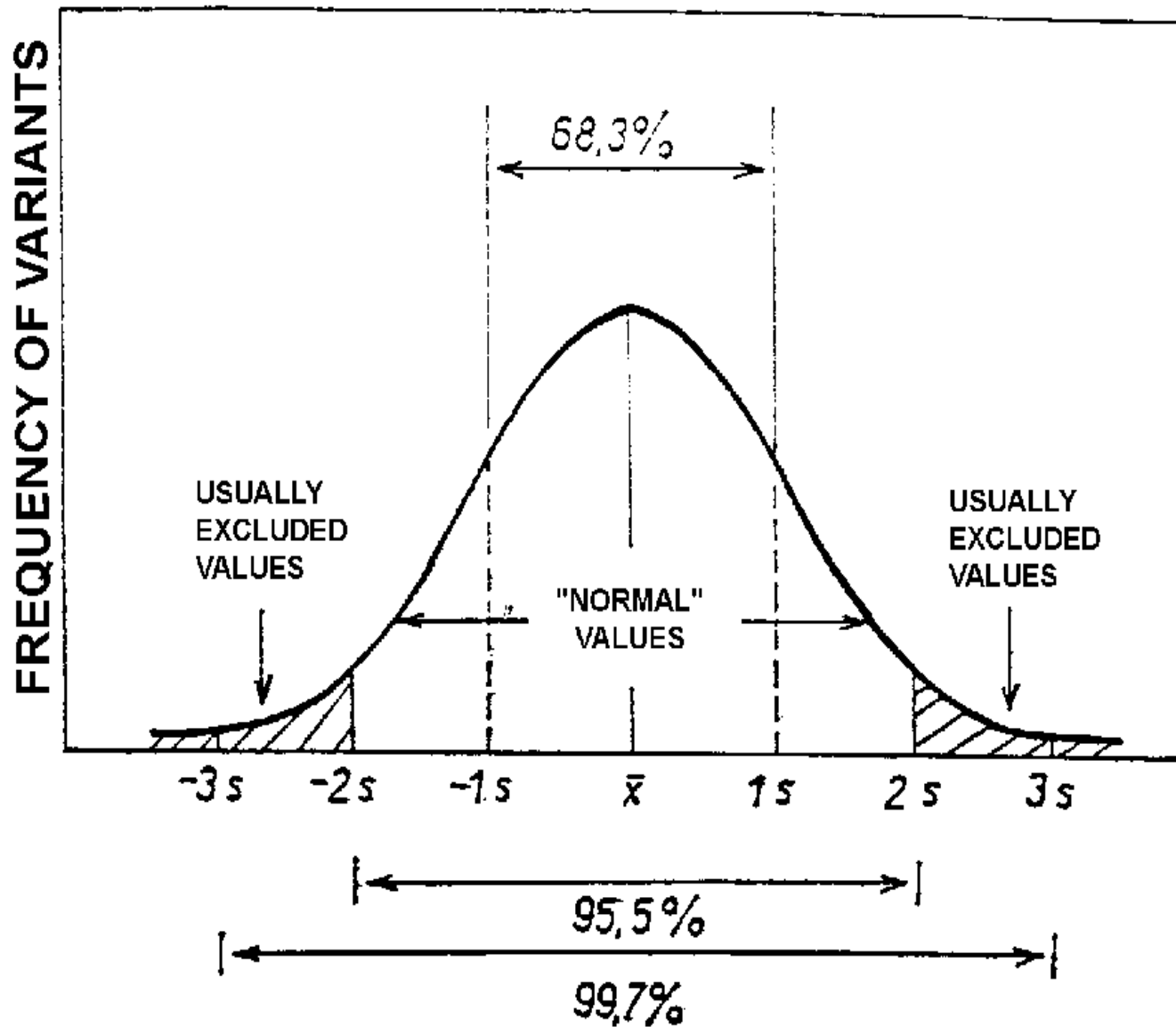
If only because of diagnostic aims, we must be well aware of the enormous extent of **the interindividual variability** among people.

Qualitative and quantitative traits in population



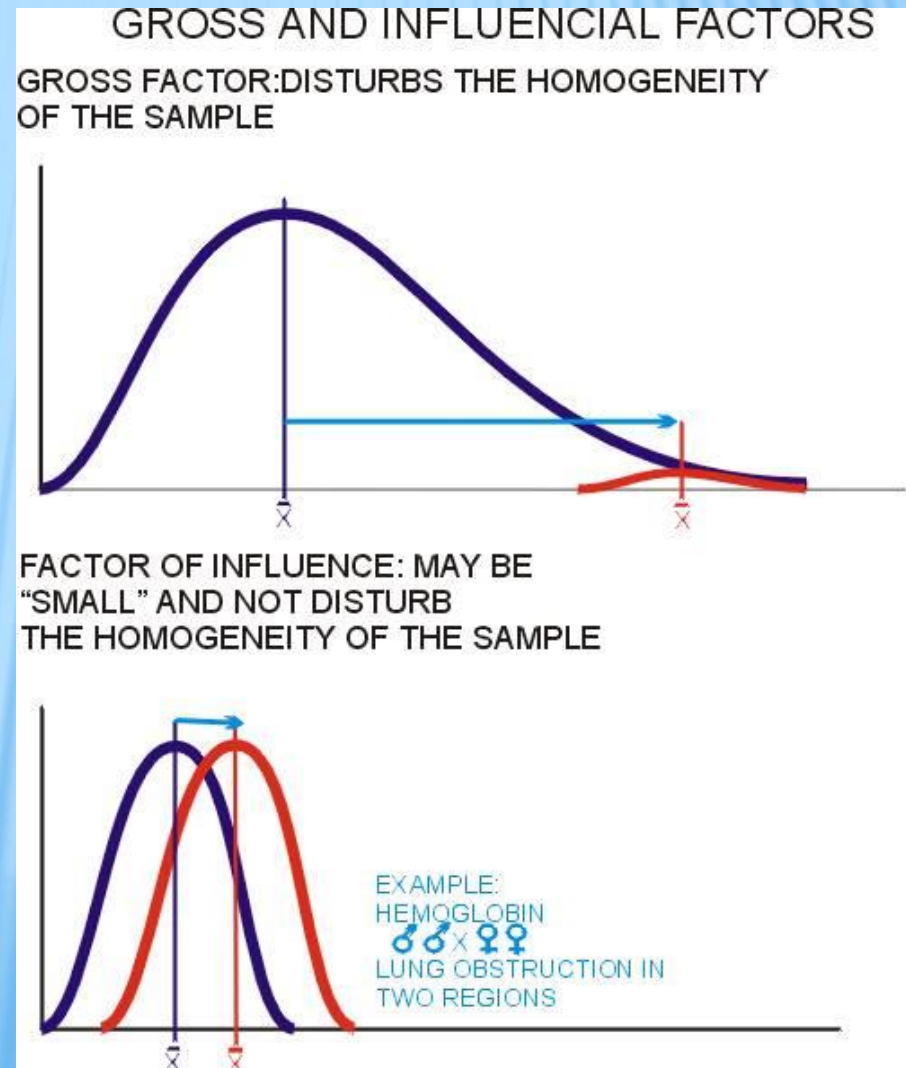
We are interested in **frequency distributions** of quantitative traits – a starting point for determining s.c. normal (= reference) values

A way of determining reference („normal“) interval



Large and small factors, influential and non-influential factors, homogeneity of samples.

If only small factors are at play, one can speak on a **homogeneous set**. The difference between „large“ and „small“ factors is only relative, depending on the total number of the factors involved.



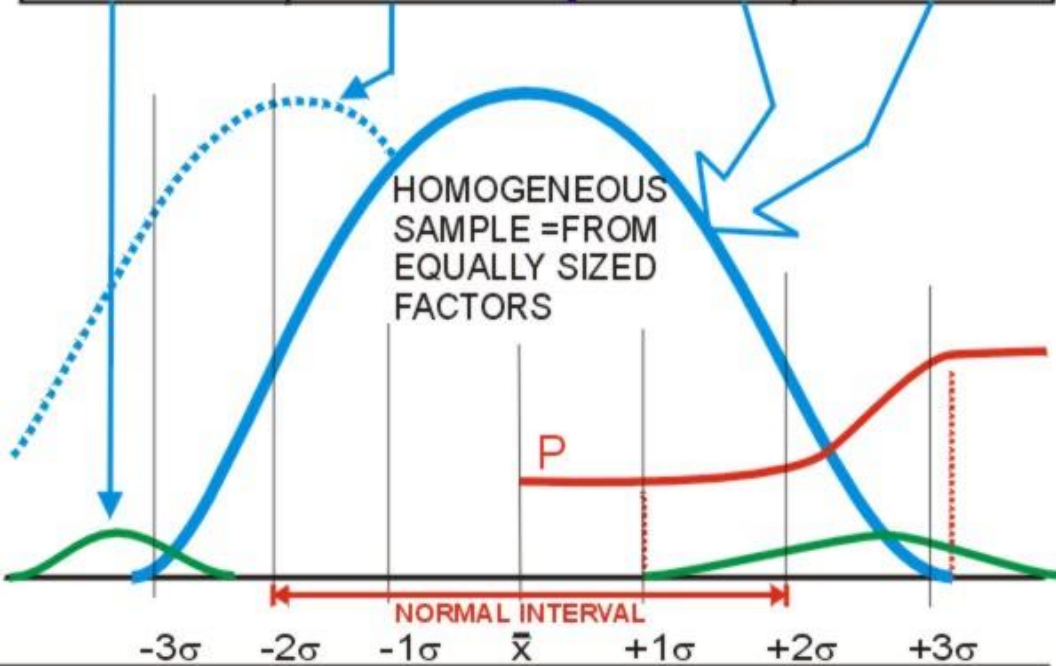
It is advisable to distinguish **large** and **small** factors creating the distributions.

A **large (big)** factor is something what acts beyond the mechanism of the origin of a normal distribution. It disturbs the homogeneity of factors prescribed by this mechanism. One of the levels of the large factor must have a gross effect upon the trait, it must "move" the position of the trait in the affected individual strongly "to the right" or "to the left". Now, because of the blurring effect of the other factors, the result is as if the large factor created "its own" distribution, sometimes hidden in the general population.

Small factors correspond roughly to the prescription for the normal distribution. Their set creates something as a homogeneous set and correspondingly a homogeneous distribution arises

FACTORS

LARGE		SMALL	
RARE (NON-INFLUENTIAL)	COMMON (VERY INFLUENTIAL)	RARE (NEGLIGIBLE)	COMMON (INFLUENTIAL)
RARE SERIOUS TRAUMAS INTOXICATIONS INFECTIONS	HARMFUL INFLUENCES ON LARGE POPULATION SEGMENTS	NOT INTERESTING	COMMON INFLUENCES OF ENVIRONMENT, FOOD, MUSCLE ACTIVITY
RARE ALLELES ↓ MONOGENIC DISEASES	(COMMON ALLELES) ↓ SERIOUS DISEASE (SICKLE CELL ANEMIA)	NOT INTERESTING	COMMON ALLELES NEUTRAL (SEX, BLOOD GROUPS, PLASMA LIPOPROTEINS)

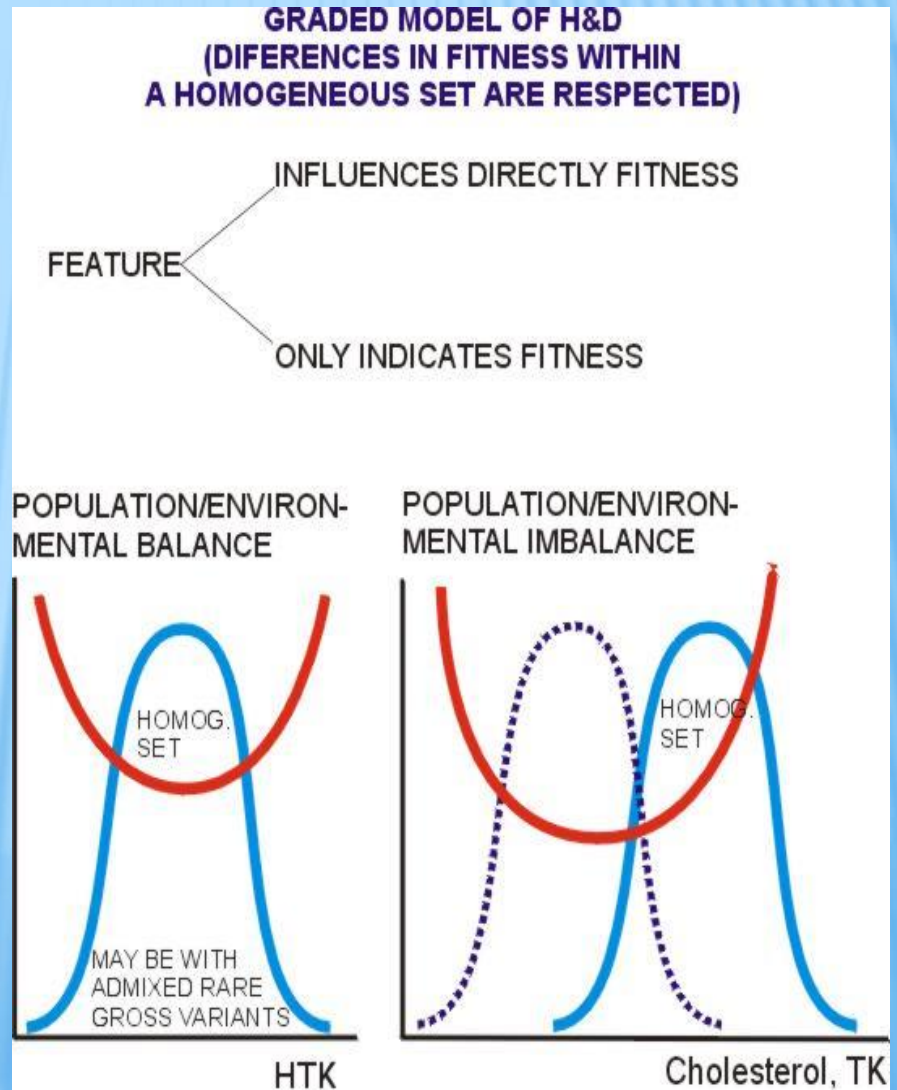


Large rare factors form small distributions on the sides of the general distribution, a large common factor would strongly „move“ a large segment of the population (a rare situation – e.g., G6PD polymorphisms); small factors produce by their combinations a homogeneous subset of the whole population. A „philosophy“ of the normal = reference interval of the diagnostic signs leans on an idea that the given disease acts as a large factor producing its own subdistribution. Ideally, we should know a probability (P) with which a specific level of a sign falls into „healthy“ or „pathological“ distribution

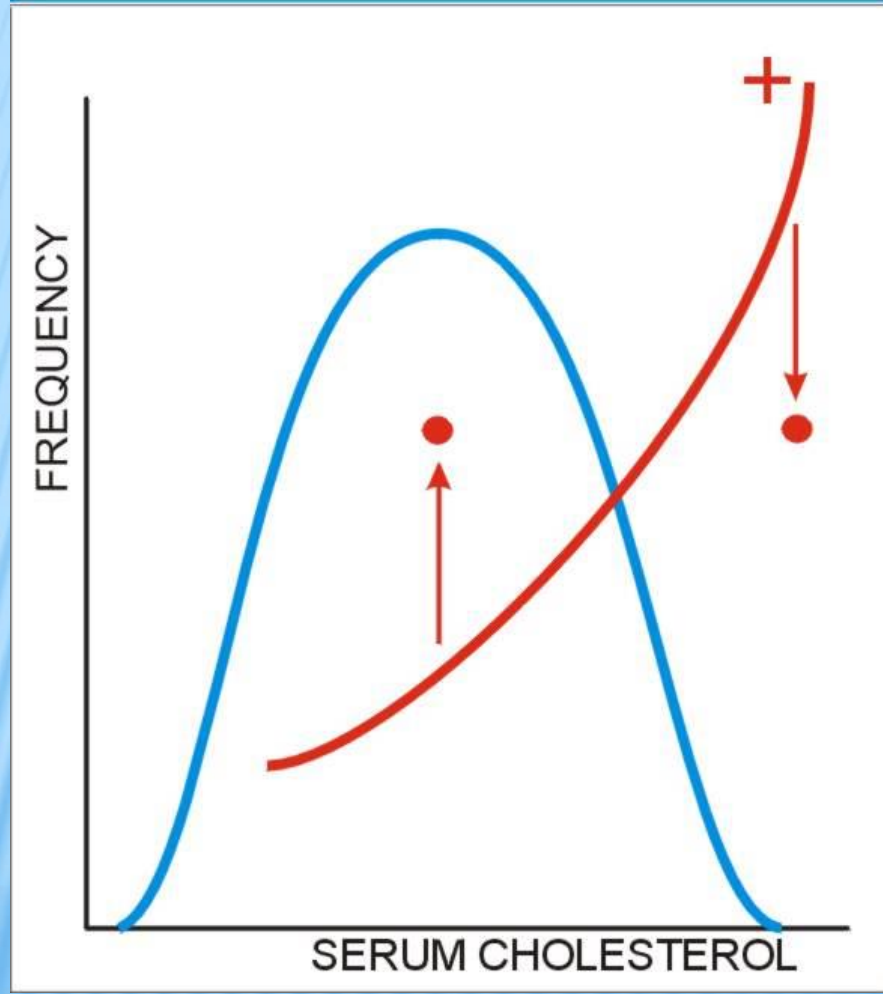
Features relevant from the point of view of health/adaptation are exposed to selection pressures.

A population may get beyond the adaptation optimum after the conditions have changed – typically in s.c. **complex diseases**

As far as the population is not too far from the optimum (of the feature given), typical U-curves may take place: either symmetrical around the population modal value (e.g., mortality as dependent on hematocrit), or shifted beyond the modal value (a genotyp in imbalance with the environment in civilization diseases – blood pressure, plasma cholesterol etc.)



PRESENCE OF EUFUNCTIONAL EXTREME VALUES AND OF DYSFUNCTIONAL MEAN VALUES IS A CONSEQUENCE OF HIDDEN PARAMETERS OF AN ORGANISM



Normality conception and its role in diagnostics

„Normal“ is currently a condensed term for „common and therefore healthy“: it is used so when we try to define health in a descriptive-statistical way. Those who derive health according to value criteria could do without it easily, using independently terms „healthy“ and „common“ according to the circumstances.

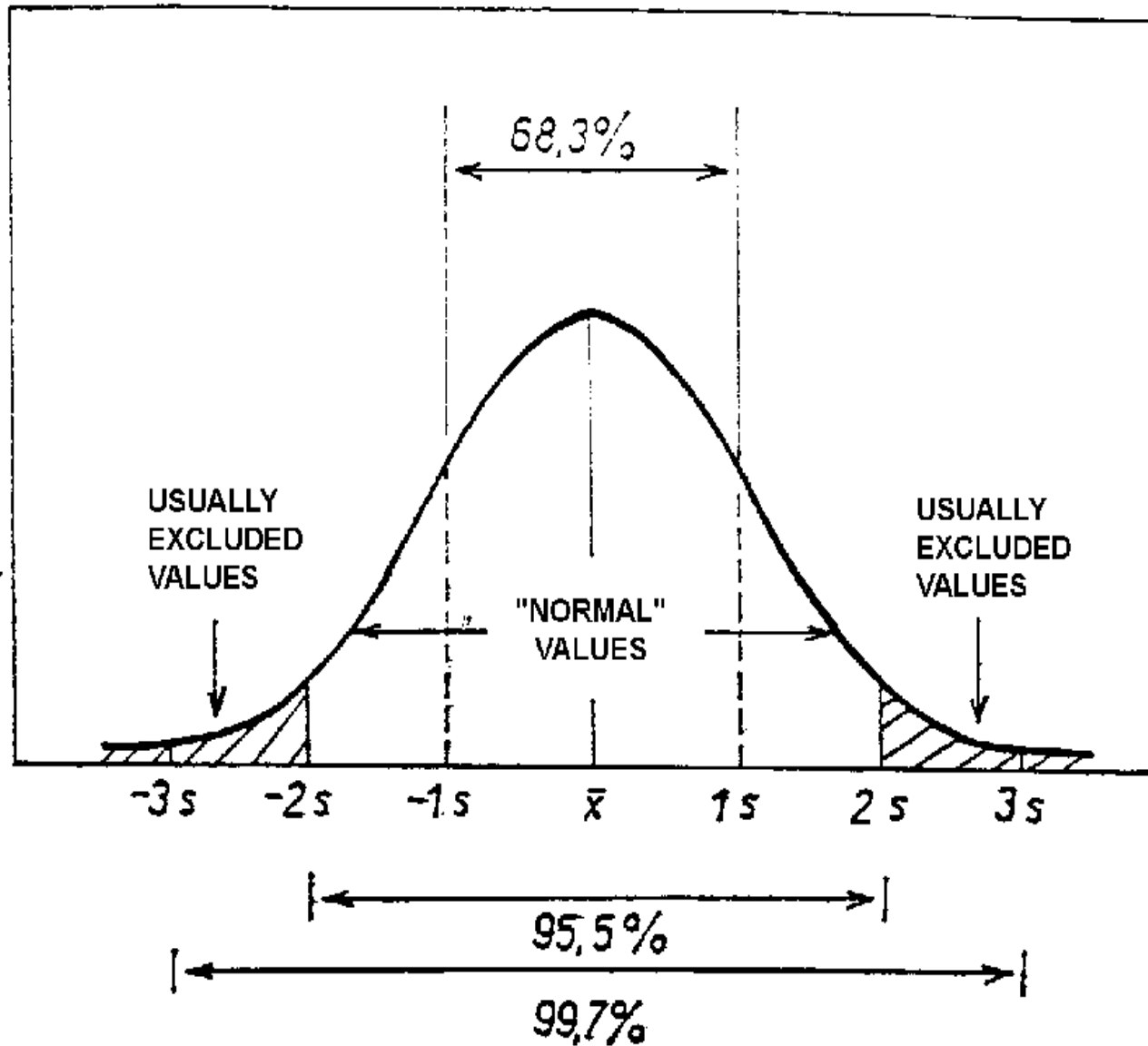
Statistical norms for health are set according to the value criteria valid in the particular time and place; it is a secondary step following the value decision.

There is some arbitrariness in the normative definition, namely according to the shared *interests* prevailing in the particular era and place, and according to different viewpoints:

- of **insurance medicine** (expected life span)
- of **preventive medicine** (prophylaxis of complications)
- of **epidemiology** (weighting of risk factors) etc.

A way of determining reference („normal“) interval

FREQUENCY OF VARIANTS



Factors leading to deviations from normal interval

- **Preinstrumental error** (e.g., a way of blood withdrawal)
- **Instrumental error** (dispersion of readings and/or systematic error, e.g.,
 - with a spectrophotometric determining of stuff concentrations)
- **Intraindividual fluctuations** of the variable measured. The person counts to the 5% of healthy individuals who are used to be excluded from the reference interval definitively
- **Eufunctional extreme** (individual norm cannot be defined)
- **A real pathology**

Essential pathophysiology questions:

- × How?
- × Why???

<http://www.med.muni.cz/patfyz>

