

**WELCOME TO THE INSTITUTE
OF PATHOLOGICAL
PHYSIOLOGY
2016/17**

**Introductory lecture
Assoc. Prof. Martin Vokurka, MD, Ph.D.**

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Topics of the lecture

- Pathophysiology as a subject at the faculty but also a „method of thinking“ about medicine
- Teaching of pathophysiology
- Main basic terminology
- Case report – example of its use in pathophysiology teaching

Contents and aims of pathophysiology

Pathophysiology collects and provides data about *causes* and *mechanisms* of diseases.

Pathophysiology represents a theoretical basis for the medicine based on scientific knowledge.

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Pathophysiology knowledge

- **organs**
- **tissues**
- **cells and**
- **molecules**

The context and use in the clinical medicine

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Knowledge about causes and mechanisms of diseases is utilized for:

- **Prevention of diseases**
- **Diagnosis of diseases**
- **Rational therapy**

Pathophysiology

- Subject in medical curriculum – traditionally strong mainly in Central Europe
- Important part of medical thinking and knowledge – part of disease description (textbooks, web...)

Type 1 Diabetes Mellitus - Windows Internet Explorer

http://emedicine.medscape.com/article/117739-overview

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Type 1 Diabetes Mellitus

Author: Romesh Khadori, MD, PhD, FACP, Chief Editor: George T Griffing, MD more...

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Overview Presentation DDx Workup Treatment Medication

Updated: Aug 22, 2012

Background

Pathophysiology

Type 1 diabetes mellitus (DM) is a multisystem disease with both biochemical and anatomic/structural consequences. It is a chronic disease of carbohydrate, fat, and protein metabolism caused by the lack of insulin, which results from the marked and progressive inability of the pancreas to secrete insulin because of autoimmune destruction of the beta cells. (See Pathophysiology.) (See also [Glucose Intolerance](#).)

Etiology

Type 1 DM can occur at any age. It is most common in juveniles but can also develop in adults, especially in those in their late 30s and early 40s. (See Epidemiology.)

Prognosis

Unlike people with **type 2 DM**, those with type 1 DM usually are not obese and usually present initially with diabetic ketoacidosis (DKA). The distinguishing characteristic of a patient with type 1 DM is that if his or her insulin is withdrawn, ketosis and eventually ketoacidosis develop. Therefore, these patients are dependent on exogenous insulin. (See Presentation.)

Patient Education

Treatment of type 1 DM requires lifelong insulin therapy. A multidisciplinary approach by the physician, nurse, and dietitian, with regular specialist consultation, is needed to control glycemia, as well as to limit the development of its devastating complications and manage such complications when they do occur. (See Treatment and Medication.)

References

Despite the differences between type 1 and type 2 DM, the costs of the 2 conditions are often combined. In a study that focused on type 1 alone, Tao et al estimated that in the United States, type 1 DM is responsible for \$14.4 billion in medical costs and lost income each year.^[1]

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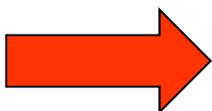
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Background Pathophysiology Etiology Epidemiology Prognosis Patient Education Show All

Pathophysiology

Type 1 DM is the culmination of lymphocytic infiltration and destruction of insulin-secreting beta cells of the islets of Langerhans in the pancreas. As beta-cell mass declines, insulin secretion decreases until the available insulin no longer is adequate to maintain normal blood glucose levels. After 80-90% of the beta cells are destroyed, hyperglycemia develops and diabetes may be diagnosed. Patients need exogenous insulin to reverse this catabolic condition, prevent ketosis, decrease hyperglucagonemia, and normalize lipid and protein metabolism.

Currently, autoimmunity is considered the major factor in the pathophysiology of type 1 DM. In a genetically susceptible individual, viral infection may stimulate the production of antibodies against a viral protein that trigger an autoimmune response against antigenically similar beta cell molecules.

Approximately 85% of type 1 DM patients have circulating islet cell antibodies, and the majority also have detectable anti-insulin antibodies before receiving insulin therapy. The most commonly found islet cell antibodies are those directed against glutamic acid decarboxylase (GAD), an enzyme found within pancreatic beta cells.

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Relation to other subjects

Previous knowledge mainly from:

- *physiology*
- *biochemistry*
- *biology and genetics*

In parallel it develops knowledge with:

- *microbiology, pathobiochemistry, pathology, immunology and pharmacology*

Historical development of pathological physiology

- Pathology (pathological anatomy)
- Clinical physiology
- Experimental pathology/pathophysiology
- Pathological physiology

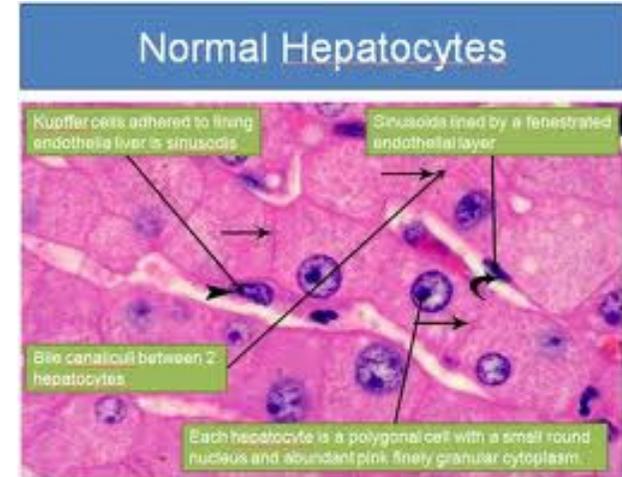
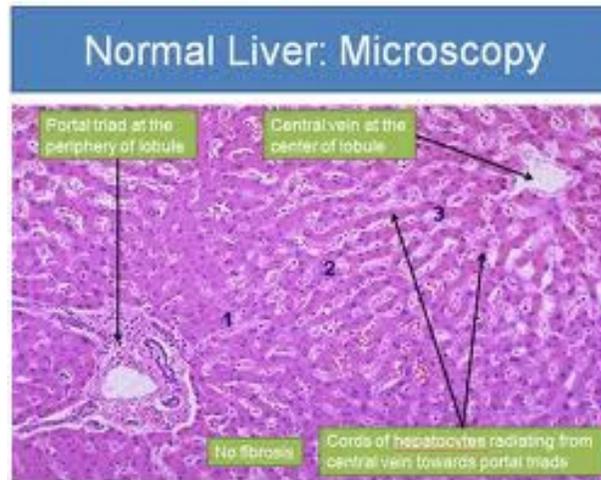
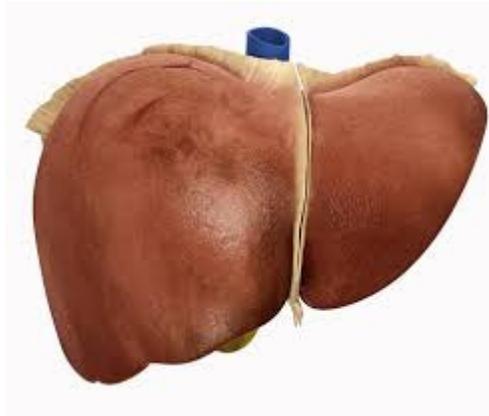
PATHOPHYSIOLOGY is not PATHOLOGY

- There is a significant difference between requirements of pathophysiology and pathology.
- Please do not underestimate the difference.

PATHOLOGY vs. PATHOPHYSIOLOGY

- Both disciplines - **PATHOLOGY** and **PATHOPHYSIOLOGY** are aimed at recognition and knowledge of etiology and pathogenesis of diseases.
- **PATHOLOGY** uses morphological methods while **PATHOPHYSIOLOGY** uses functional tests and methods.

Normal liver



NORMAL MORPHOLOGY

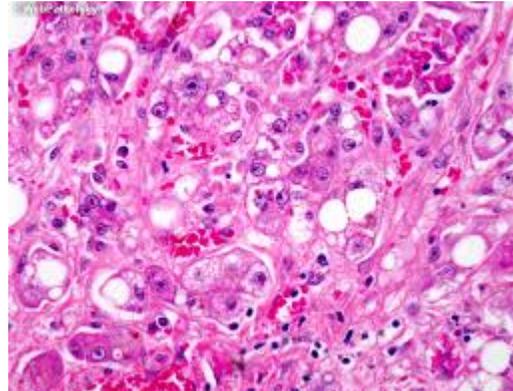
NORMAL FUNCTION

e.g. coagulation factors production

NORMAL COAGULATION

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Pathological liver



PATOLOGICAL MORPHOLOGY

IMPAIRED FUNCTION

e.g. decreased coagulation factors production

DECREASED COAGULATION

Hematomas, bleeding during the surgery or prolonged traumatic bleeding

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ORGANIZATION OF TEACHING

- **LECTURES**
- **SEMINARS** (functional tests, case reports, integrative seminars, – failure syndromes, case reports...)
- **essays, reports**
- **e-learning**
- **tests, examination**
- **final exam (including case reports)**

EXAM

- **Oral - four questions - one question is from seminar topics.**
- **Knowledge of a subject and understanding its links and significance.**
- **Ability to understand professors of the clinical subjects and communicate with them on medical problems.**

TEXTBOOKS

- **Pathophysiology of Disease.** An Introduction to Clinical Medicine.
Stephen J. McPhee et al.
Lange Medical Books/McGraw-Hill
- Some examination questions may require **other information sources.**

Robbins and Cotran PATHOLOGIC BASIS OF DISEASE Elsevier/Saunders

- is an excellent (absolutely superb) textbook in its full version
- **I do not think that its condensed version is good for studying pathophysiology**
though it could be helpful for studying pathology.

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People at the Institute of Pathophysiology

- Head: Assoc. Prof. M. Vokurka
- Deputy head for teaching:
Assoc. Prof. J. Živný
- English courses: Assoc. Prof. J. Živný
- Other teachers
- Teaching assistant: R. Korhoňová
- Consultations

Pathophysiology

- **General:** general principles of pathogenesis – genetic, immunological, molecular-biological...
- **Organ** („special“): pathophysiology of organ systems

Function and pathophysiology

- In this subject you will study (mainly during the seminars) the tests and methods to evaluate / examine the function of the organs and systems

Clinical examinations and tests

- Clinical physiology
- Regular seminars, necessary for case-report understanding, part of „practical“ exams
- Methods to examine **function**
knowledge of function (physiology)
testing of this function (e.g. heart activity)
pathological changes of the function and
how to reveal them in the testing

Case reports

- Description of a single case of a disease – interesting, rare or educative
- Used for understanding of pathophysiological principles and their use in real clinical situations
- To see how the disease, its causes and changes are reflected in the changes of the organ functions and their testing
- Part of the final exam is based to such case reports

Research at the Dept

- **experimental hematology**

*experimental bone marrow transplantation,
cell signalization and signal pathways,
leukemogenesis
experimental lymphoma treatment
tissue hypoxia,
iron metabolism*

- **proteomics**

- **computer simulations**

Basic terminology

- etiology, pathogenesis
- symptom, syndrome, disease, nosological unit
- Disease definition
- Latent and manifest phase of the disease
- Acute and chronic

Etiopathogenesis and pathophysiology

- You will study causes and mechanisms of the diseases development

Pathogenesis and etiology

- **Pathogenesis** – processes that lead to the development of the disease and its symptoms, and that are consequences of the pathological stimulus
- Can be the same regardless of the stimulus
- **Etiology** – cause of the disease
- **Etiopathogenesis**

**Causes of diseases = etiology,
etiological factors**

**Mechanisms of diseases =
pathogenesis**

Causes known and unknown...

- the difference depends on
 - time
 - knowledge
- unknown causes:
essential, cryptogenic, idiopathic...

Three factors of disease origin

- **external factor (pathogenic stimulus)**
- **Genetic background**
- **time**

Pathophysiological knowledge

- **organs**
- **tissues**
- **cells**
- **molecules**

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Symptom

- Felt or objectively seen
- One symptom is commonly not sufficient for the diagnosis
- Nonspecific symptom (fatigue, weakness...)
- **Patognomic** symptoms (typical for some disease)

Symptoms and pathophysiology

- During this subject you will study the mechanisms of the symptom origin

Syndrome – complex of symptoms

- Anemic syndrome: paleness, tiredness, dyspnoea, tachycardia...
- But anemie can itself can have many causes – diseases...

Disease

- ***Normative*** attitude: mainly stresses the subjective evaluation of the symptoms and the relationship to the aims of a human being
- ***Functionalistic*** attitude stresses the objective values, parameters, their measurement...

Causes of diseases

- Infection, vascular, inflammatory, tumors, genetic, psychogenic...
- Unknown = idiopathic, cryptogenic, essential...
- The medical research discovers etiology and pathogenesis of many diseases – molecular, (epi)genetic level...

Pathophysiology as a complex

- Disease origin – etiopathogenesis
- Symptoms of the diseases
- Diagnostic tests and methods
- The use for the clinical reasoning
- Case reports and their evaluation

Evidence based medicine

- Based on the results of large studies which evaluate the knowledge and theories on large samples of population

Personalised medicine

- customization of healthcare using molecular analysis and other information specific for a single person (patient)

Translational medicine

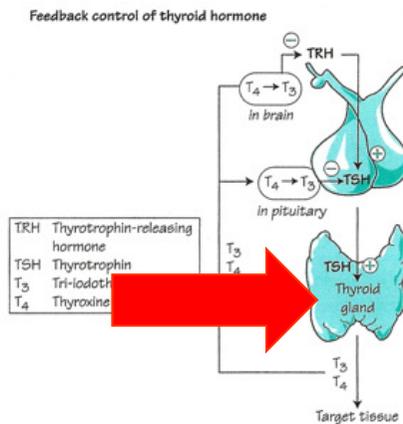
- Bench-to-bedside

Primary and secondary

- **Primary** means that the disease is caused directly by the damage of the organ itself (e.g. primary thyroid disease, primary polycythemia etc.)
- **Secondary** means that the problem is not in the organ itself but in its regulation (e.g. secondary thyroid disease, secondary polycythemia)

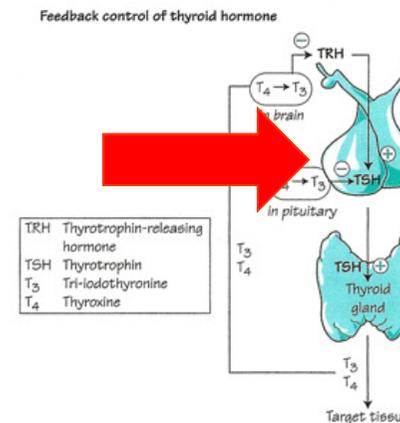
Thyroid diseases

- Primary



e.g. Thyroid inflammation (viral, autoimmune) or its tumor

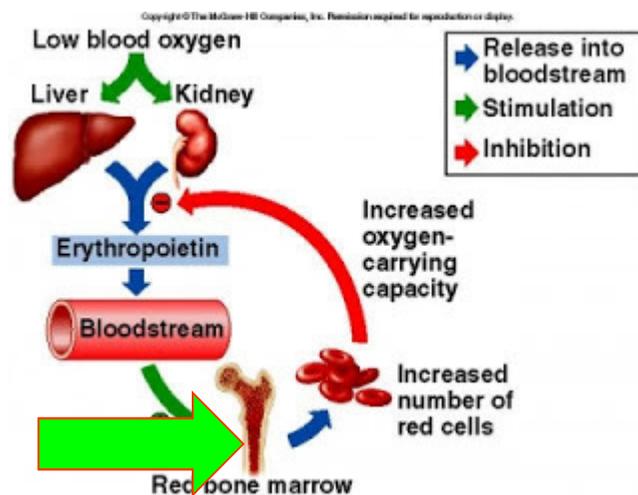
- Secondary



e.g. inflammation or tumor of the pituitary gland

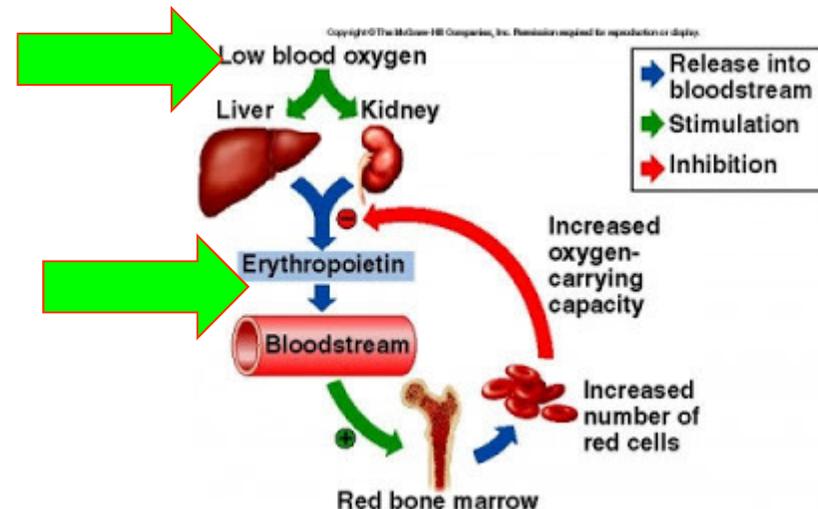
Polycythemia = increase in the number of RBC

- Primary



Bone marrow disease, RBC are produced out of the control, „uselessly“ lika a tumor

- Secondary



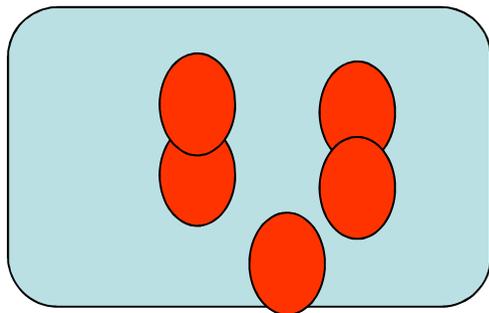
Bone marrow is normal but is overstimulated by erythropoietin, most often due to hypoxia

Damage, impairment of the function

- **Damage** = distinct disturbance of morphological (in the broadest sense of the word) properties of cells, tissues and organs (e.g. due to loss of blood flow, infection, autoimmunity, tumor...)
- **Function impairment** = deterioration or even loss of the function (of the organ)



FUNCTION
(e.g. blood pumping,
albumin production)



FUNCTION ?? DECREASED
(e.g. insufficient blood pumping,
decreased albumin production)

DAMAGE

ORGAN RESERVE
COMPENSATION

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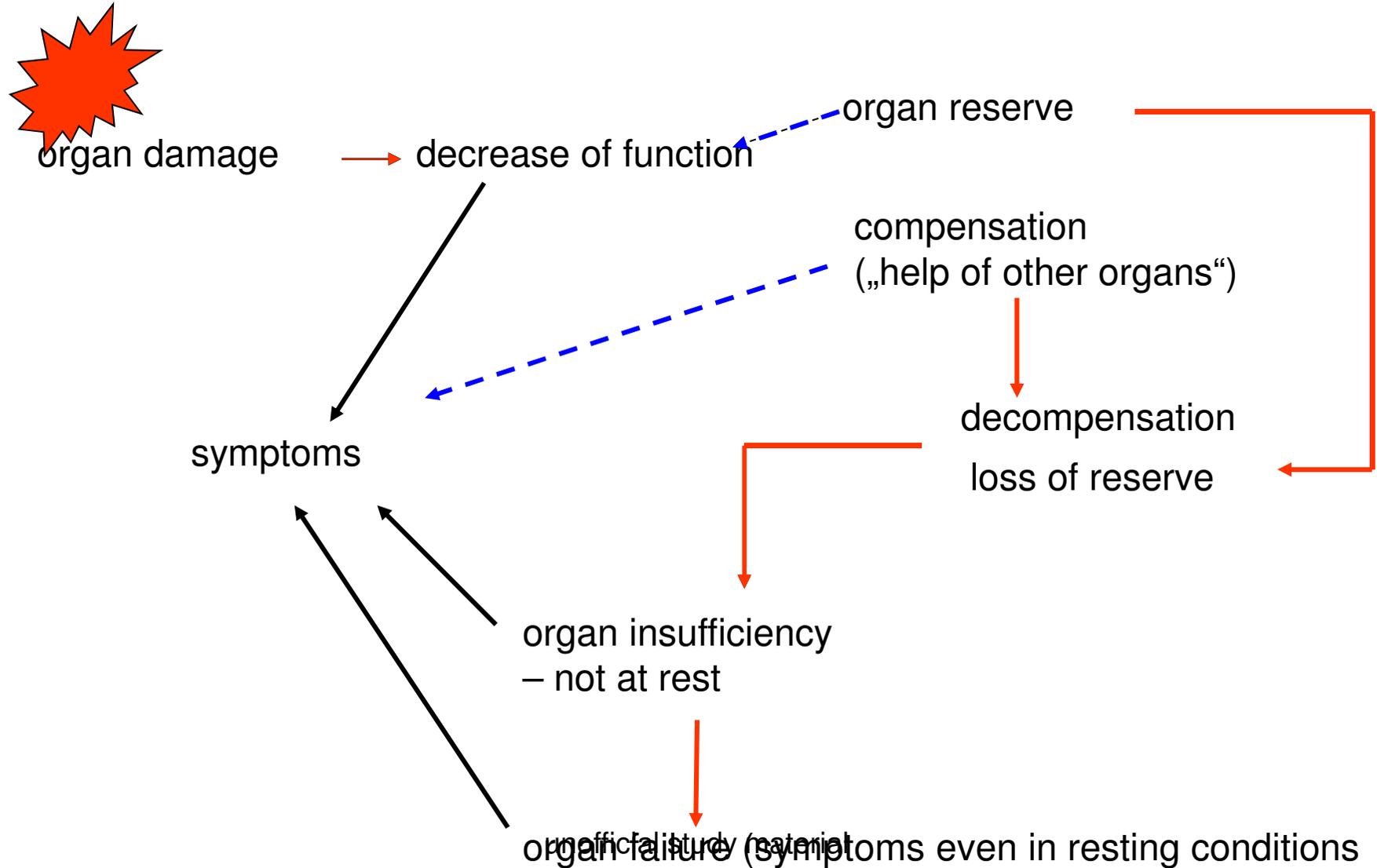
Reserve and compensation

- The organs have **reserve**, e.g. the liver can sustain basic functions even in the size of 1/7
- The organs and systems have the capacity of the **compensation**, that means they can increase the function of the remaining parts or can „help each other“
- Failing or exhausting of the compensation lead to the **decompensation**

Decreased functions

- If the organ is capable to sustain its functions only at resting situations, we speak about **insufficiency** – e.g. in lung disease the patient is not short of breath at rest, only during the exercise
- If the organ is not capable to sustain the functions event at rest, we speak about **failure** – e. g. the dyspnea even at rest

Disease sequelae



The end of the introductory lecture

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