

University of Szeged, Medical Faculty
Dept. Biochemistry

SCHEMES OF LECTURES
II. semester

LEUKOCYTE

General characteristics of neutrophil granulocytes

- main types of granulocytes
- neutrophil granulocytes as microphages (essence and importance of phagocytosis, activation and degranulation)
- general metabolism of neutrophils

Oxidative stress

- ROI: reactive oxygen intermediates (types and reactivity)
- role of Fe and Cu ions (Fenton and Haber-Weiss reaction)
- ROI-producing physiological processes/reactions and their localizations
- endogenous and exogenous antioxidant compounds (uric acid, bilirubin; vitamins and vitamin-like substances)
- antioxidant enzymes and their functions (SOD, catalase, GSH-peroxidase)
- essence of oxidative stress and states associated with it
- consequences of oxidative stress (lipid peroxidation, protein , carbohydrate and nucleic acid damages)

Special pathogen-killing mechanisms in neutrophils

Oxidative mechanisms

- respiratory burst (basics, lokalization during phagocytosis, properties and function of NADPH-oxidase)
- ❖ chronic granulomatous disease (CGD)
- myeloperoxidase (lokalization, function)

Non-oxidative mechanisms

- breakdown /digestive/ enzymes (proteinases, glycosidases); antiproteinases and their importance
- ❖ α -1 antiproteinase deficiency
- bakteriostatic and baktericid proteins (lactoferrin and defensins; lysozyme)

Chemotaxis

- steps of chemotaxis and receptors involved in adhesion
- importance of chemotaxins (examples)
- ❖ leukocyte adhesion defect (LAD1) /see: also at the material on adhesion/

FUNCTIONS OF PLATELETS, HEMOSTASIS, FIBRINOLYSIS

Steps of hemostasis (vasoconstriction, platelet aggregation and formation of the thrombus, retraction procedure)

Functions of platelets

- formation, structure of platelets, important organelles, special metabolism
- α -granules, lysosomes (lambda granules) and dense bodies (delta granules): composition, platelet specific proteins
- molecular mechanism of platelet activation, important cell-surface receptors, signaling pathways, importance of Ca^{2+} , role of prostaglandin derivatives, role and action of TxA_2 and PGI_2
- inhibition of platelet activation
- primary adhesion: definition and its regulation, direct and indirect collagen binding (β_1 integrin/ GpIa-IIa and von Willebrand factor and its receptor (GpIb-IXa))
- ❖ Bernard-Soulier syndrome
- platelet aggregation: definition and its regulation (GPIIb/IIIa-receptor ($\alpha_{IIb}\beta_3$ integrin) receptor)
- ❖ Glanzmann-type thrombasthenia
- ❖ In vivo inhibition of platelet aggregation (therapy/ prophylaxis):
 1. GPIIb/IIIa-receptor ($\alpha_{IIb}\beta_3$ integrin)-inhibitors
 2. ADP-receptor antagonists
 3. acetyl-salicylic acid, mechanism of action
- role of platelets in activation of coagulation cascade and formation of thrombus

Coagulation system

- coagulation factors: synthesis, biochemical characterization, their role in the cascade
- types and processes of coagulation cascade (intrinsic, extrinsic), way of activation of coagulation factors (contact activation, limited proteolysis, serin proteases, activation complexes, role of Ca^{2+})
- role of vitamin K, synthesis of vitamin K dependent factors (II, VII, IX, X, protein S and C), formation of gamma-carboxy –glutamate
- anticoagulants: vitamin K antagonists (kumarin-derivatives)
- structure and function of thrombin
- structure of fibrinogen, formation of fibrin net, stabilization of fibrin, mechanism of transglutaminase (Laki-Lóránd factor) reaction
- laboratory testing of coagulation system: (Prothrombin-time PT (Quick-probe), Activated partial thromboplastin time APTI, Thrombin time TT), INR (International Normalized Ratio)
- ❖ coagulation factor deficiencies:
 - ❖ inherited lack of factor VIII, IX, XI: hemophilia A,B és C; characterization, symptoms
 - ❖ inherited lack of factor Von Willebrand
 - ❖ secondary lack of coagulation factors (for ex.: liver disorders)
 - ❖ disseminated intravascular coagulation (DIC): biochemical background, symptoms

- biochemical basics of anticoagulation: mechanism of antithrombin III, role of vitamin K
- in vivo anticoagulation and prophylaxis: 1. Heparin; LMWH: low molecular weight heparin 2. vitamin K antagonists (kumarin derivatives), mode of action, importance, advantages/disadvantages
- in vitro anticoagulation: heparin, citrate, oxalate, EDTA; mode of action

Fibrinolysis

- mechanism of fibrinolysis, biochemical importance
- plasminogen, activation of plasmin system
- role of plasma kinins, complement, strepto- and urokinase system in activation of fibrinolysis
- fibrin degradation procedure, (FDP: fibrin degradation products), importance
- ❖ in vivo fibrinolytic therapy and its importance (acute dissolving of thrombi)
- ❖ DIC

RED BLOOD CELLS

Characterization of red blood cells (erythrocytes)

- shape, changes in shape, size, cell count, life-time
- formation of erythrocytes, importance of enucleation
- factors required for production of red blood cells /synthesis (folic acid, vitamin B₁₂, erythropoietin)
- ❖ megaloblastic anemia
- general functions
- response to hypo- and hyperosmolarity

Structural composition of red blood cells

- membrane structure
- components of cytoskeletal system, and characterization
- ❖ inherited spherocytosis, elliptocytosis (see: actin-cytoskeleton)
- membrane transporters (Na-K ATPase, Band 3 protein)
- specific antigens (ABO and Rh blood groups)

Special metabolism of red blood cells

- GLUT-transporter
- anaerobic glycolysis, Cori-cycle
- ❖ glycolytic enzyme deficiencies: hemolytic anemias
- synthesis and role of 2,3 DPG (Rapoport-Luebering shunt)
- HMP-shunt, NADPH production
- ❖ glucose-6-phosphate dehydrogenase enzyme deficiency and its consequences
- components of the antioxidant system and their action; production and regeneration of glutathione, antioxidant role of glutathione

Metabolism of iron

- iron content of the human body and its tissue distribution, daily iron requirement
- characterization of iron absorption and its regulation
- storage: ferritin
- transport: transferrin
- cellular uptake: receptor-mediated endocytosis
- ❖ iron deficiency anemia

Hemoglobin and myoglobin

- structure and function in details
- position of the hem functional group and its structural changes during oxygenation and deoxygenation
- R and T conformation, kinetics of conversion of two conformation into each other, factors influencing the stability
- factors influencing the oxygen binding affinity of hemoglobin (shift of sigmoid curve to right and left)
- binding of 2,3-DPG, its effect on oxygen affinity
- molecular background of Bohr-effect, its role in the oxygen supply of tissues
- changes in oxidation state of iron ion, formation and regeneration of methemoglobin
- ❖ methemoglobinemia
- ❖ carbon monoxide poisoning
- shift in expression of globin genes during human development
- differences in between fetal and adult hemoglobin
- ❖ thalassemia
- ❖ sickle cell anemia

PLASMA PROTEINS

Composition of blood

- blood cells
- main components of the plasma
- differences between blood serum and plasma

General characterization of plasma proteins

- synthesis (location, general characteristics)
- role of oligosaccharide side chains
- reference range of plasma total protein, pathological increase and decrease
- ❖ malnutrition, kwashiorkor

Separation of plasma proteins

- separation methods
- characterization of native electrophoresis, its application in clinical practice
- plasma protein fractions, pattern, serum levels
- ❖ pathological electrophoretic patterns: nephrosis, liver cirrhosis (β - γ bridge formation), hypogammaglobulinemia, monoclonal gammopathy, acute and chronic inflammation (iron deficiency anemia, hemolytic anemia)

Characterization of plasma proteins

- names of proteins in albumin, alpha1, alpha2, beta, gamma fractions
- detailed characterization (synthesis, main characteristics, physiological-biochemical functions, disorders):
- albumin
- ❖ analbuminemia
- alpha-1-acidic glycoprotein
- alpha-1-lipoprotein (HDL)
- alpha-1-antitrypsin
- alpha-fetoprotein
- ❖ inherited alpha-1-antitrypsin deficiency (emphysema)
- ceruloplasmin (+ copper metabolism)
- ❖ Wilson and Menkes disease
- alpha-2-macroglobulin
- haptoglobin and hemopexin
- ❖ hemolytic anemias
- beta-lipoprotein (LDL)
- prebeta-lipoprotein (VLDL)
- transferrin, ferritin (+iron metabolism)
- ❖ iron deficiency anemia
- fibrinogen
- immunoglobulins

Acute phase proteins

- characterisation and importance of acute phase response
- positive and negative acute phase proteins