Learning guidelines for Immunology (AOK-OAK061-1)

<u>1. Lecture:</u> The structure and working principle of the immune system. Central and peripheral lymphoid organs.

Describe the history, importance and role of immunology in the biomedical sciences.

Explain the concepts of immunity and antigen. Describe the tasks and operating principles of the immune system. Define the terms: immunogen, antigen, hapten, epitope. Explain the concepts of innate and adaptive immunity. Explain the concepts of innate and adaptive immunity. Explain the concept of immune homeostasis. Describe the types and generation of immune cells. Also describe the tissues and organs of the immune system. Talk about the role of bone marrow, thymus, spleen, lymph nodes, and other secondary lymphatic organs. Describe immune-privileged sites. Describe the concept of mucosal-associated immune defense. Talk about the immunological role of the skin.

Normal values:

Cell types	**%**	**Cell number/mm ^{3}**
Leukocytes		3.8-10.5 x 10^3
neutrophil granulocytes	45 – 65	1.8-7.3 x 10^3
eosinophilic granulocytes	1-3	80-360
basophilic granulocytes	<1	20-110
Lymphocytes	20-30	1.5-4 x 10^3
Monocytes	5-10	160-720
dendritic Cells	1	60
NK	10	200-400
Red blood cells (Erythrocytes)		3.9-5.7 x 10^6
Thrombocytes		1.4-3.5 x 10^5

2. Lecture: Characteristics of innate immunity. The relationship between innate and adaptive immunity.

Define the innate immunity, its main characteristics and functions. Compare the innate and adaptive immunity according to their antigen recognition, receptors, kinetics of the immune response, and quality of secondary immune response. Characterize the receptors of the innate immunity and the molecular patterns they recognize. List the soluble effector molecules of the innate immune system. Classify the cytokines according to their origin and functions, and give several examples to each group. Define the following terms: autocrine, paracrine, endocrine, pleiotropic, redundant, synergic, antagonist. List the cells of the innate immune system; describe their development from hematopoietic stem cells. List the main characteristics of monocytes and macrophages. Name the types of macrophages and their functions in different tissues. Characterize the neutrophil granulocytes, explain their functions. Compare the antimicrobial mechanisms of phagocytes. Describe the origin, types and tasks of dendritic cells. Describe briefly the characteristics of basophil and eosinophil granulocytes and mast cells. Introduce the natural killer (NK) cells and point out the differences between NK cells and specific lymphocytes. Characterize the innate lymphoid cells.Explain the relationship between the components of the innate and adaptive immune system, the communication between their cells and their dependency on each other.

3. Lecture: The structure of MHC molecules, polymorphism. Antigen presentation. Development of T and B cells.

Describe the MHC gene region. List the genetic reasons for the diversity of MHC molecules. Explain the significance of polymorphism of the MHC gene complex at the individual and population level. Outline the clinical implications of MHC polymorphism. Compare the structure of the two main proteins coded in the MHC region (MHCI and MHCII) and their binding to antigenic peptides. Name the rules of MHC-peptide binding.Describe the cellular and molecular steps of intracellular or vesicular derived peptide antigen processing on MHC class I and MHC class II. Describe the roles of antigen presentation on MHC class I and MHC class II in the immune system. Provide examples of intra- and extracellular antigen presentation, also give examples of the following effector T-cell responses. Define the cross-presentation.

Describe the common mechanisms in B- and T-cell maturation. Explain the concept of gene recombination of the immunoglobulin superfamily. Describe the mechanisms of V/D/J recombination. Describe the process of early lymphocyte development, list the checkpoints and define the outcomes. Explain the mechanism of central B-cell tolerance. Compare the negative and positive selection of thymocytes. Explain the affinity hypothesis and discuss the formation of regulatory T cells. Give at least 3 examples of immunodeficiency caused by mutations in genes involved in lymphocyte development.

4. Lecture: B lymphocytes. B cell activation, antigen-dependent differentiation of B cells. The structure of antibodies, antibody-mediated effector functions

Describe the subtypes of B lymphocytes and describe the main characteristics of each subtype! Describe the process of positive selection of B lymphocytes! Describe the circulation of mature B lymphocytes between the blood circulation - secondary lymphoid organs / tissues - lymphatic circulation! Describe the conditions under which the activation of B lymphocytes can take place without the involvement of T cells! Describe where the antigen recognition by B lymphocytes occurs! Characterize the follicular dendritic cells! Describe the role of B-cell receptors and B-cell co-receptor in B lymphocyte activation! Describe the possible consequences of the interaction between antigen-exposed B lymphocytes and follicular helper T cells (T_{FH})! List the most important processes in the germinal center! Compare the major features of short- and long-lived plasma cells! Compare the structure of B-cell receptors and antibodies! Describe the mechanisms behind affinity maturation!

Describe the molecular mechanism of isotype switching! Compare the process of isotype switching and that of somatic gene rearrangement! Describe the effector functions of antibodies! Describe the different isotypes of human antibodies! Compare the major features of naive and memory B cells!

Describe how an already produced antibody can inhibit the activation of a naive B lymphocyte capable of recognizing the same antigen! Demonstrate this mechanism through a clinical example!

5. Lecture: Antigen recognition function of T lymphocytes. The T cell mediated immune response. T cell types, their effector functions.

Characterise the antigen recognition of T-cells and define MHC restriction. Explain the TCR complex structure and the role of TCR, CD3, CD4 and CD8 co-receptors in T-cell signalling. Know the structure of the CAR T-cell. Give three T-cell signalling pathways activating in response to antigen presentation. Specify the steps of T-cell activation after infection, including the location and kinetics of these steps. Explain the process of APC costimulation and also the T-cell response in the absence of this costimulation. Name two costimulation mechanisms involved in the activation of naïve T-cells. Define immunological synapse. Show the role of IL-2 in T-cell activation. Characterise the types and subtypes of effector T-cells. Explain what polarization means during their differentiation. Explain the activation and mechanism of action of cytotoxic T-cells in the immune response. Specify four subtypes of effector helper T-cells. Broadly explain the role of TH1/TH2/TH17 cells in the immune response and name the effector cells activated by each subtype. Name a few cytokines for each Th subtype. List three primary immunodeficiencies that cause disease through loss of T cell function.

6. Lecture: Complement system. Cell types and mediators involved in inflammation and acute phase response.

Underline the importance of the complement system. List the components of the complement system and its main activation pathways. Explain how the classical pathway is initiated by activation of the C1 complex and specify the steps of the complement cascade. List the members of the alternative pathway. Explain the activation of the mannose-binding lectin

pathway and its joining to the complement cascade. Draw the late steps and the terminal phase of the complement activation. Describe the regulation of the complement activation and the consequences of its defects. What are the functions of the complement system in the immune response against pathogens, in the B cell activation, in the clearance of immune complexes and apoptotic cells? List the complement receptors and describe their co-operation with Fc receptors. Name the cell types involved in inflammation and describe their functions. Tell the process of leukocyte extravasation. List the main types of inflammatory mediators. Name the inflammatory cytokines and draw the signalling pathways leading to their expression. What are the local and systemic effects of inflammatory cytokines? Give examples of acute phase proteins. Explain the generation of lipid mediators and their roles in inflammation. Describe the plasma enzyme cascades involved in inflammation. What are the differences between acute and chronic inflammation? Summarize the possibilities of reducing inflammation.

7. Lecture: 1 MTO

8. Lecture: Autoimmunity. Peripheral and central immune tolerance.

Principles of immune tolerance, its distinction from immunodeficiency and immunosuppression
Comparison of effector and tolerant immune response
Principles and sites of the development of central tolerance, positive and negative selection
Principles and sites of the development of peripheral tolerance, key mechanisms of peripheral tolerance-induction (intercellular communication, cytokines)
Definition of regulatory T-cells, the development, function and subtypes of regulatory T-cells
Compare the two subtypes of T reg cells acccording to their development
Principles of autoimmunity and autoimmune diseases
The role of a polygenic background in the development of autoimmune diseases
The role of environmental factors in the development of autoimmune diseases
Potential ways of the breach of peripheral tolerance during the development of autoimmune diseases
Knowledge of the examples presented in the lecture relating to the pathomechanism of selected autoimmune diseases

9. Lecture: Immune responses against extracellular pathogens. Immune responses against intracellular pathogens. Immunescape. Immunological memory. Vaccination.

List the phases of the immune response and describe the temporal course of the immediate, early induced innate, and adaptive immune responses. Describe the defense mechanisms against pathogens (innate and adaptive immune system defense mechanisms) and present the immune effector modules (types 1, 2, and 3).
Describe the general characteristics of the immune response against intracellular pathogens. Compare the defense mechanisms against intravesicular and cytosolic pathogens. Describe the main steps of the immune response during viral infections and explain the role of type I and II interferons. Explain the phenomenon of antibody-dependent enhancement (ADE). Describe the characteristics and consequences of the immune response against unicellular parasites. Describe the steps of the immune response against multicellular parasites (helminths), emphasizing the importance of the Th2 type response. List the main mechanisms of defense

against extracellular pathogens and explain the dominance of the humoral immune response. Describe the process of elimination of extracellular pathogens from recognition to removal of the pathogen. Define the concepts of phagocytosis, opsonization, and neutralization.
Give examples of immune escape strategies used by viruses, parasites, and extracellular bacteria, and explain the concepts of antigenic drift and antigenic shift.
Explain the development and significance of immunological memory. Compare the kinetics of primary and secondary immune responses. List and describe the types of memory T cells. Describe the subpopulations of B cells and explain the formation of memory B cells (germinal center reaction) and their main characteristics. Explain the basic principle of vaccination and list the main types of vaccines. Compare the characteristics of active and passive immunization. List the mandatory vaccinations in Hungary.

10. Lecture: Types and characteristics of hypersensitivity reactions. Allergic reactions.
Types of hypersensitivity reactions, their classification, what are the main characteristics of each type, examples.

Type I. hypersensitivity reaction (allergy): What are allergens, characteristics and examples for common allergens. Mechanism of activation of mast cells and basophile granulocytes, their major characteristics. List the cellular and molecular steps and characteristics of immediate and late phase responses of allergy. What are the cellular events after the first and second allergen exposure? What are the mediators of Type I. hypersensitivity reaction? What is the effect of mastcell degranulation on the gut, lung and veins? Local and systemic anaphylaxis. How can you prevent allergic reaction, what are the therapeutic possibilities? Definition of pseudoallergy, similarities and differences to true allergic reactions.

Type II. hypersensitivity reaction: What is the definition of Type II. hypersensitivity reactions? What is the meaning of ADCC? List examples for type II. hypersensitivity reactions. Present the causes and symptomps of hemolytic disease of the newborn (HDN) and therapeutic interventions. Describe the transfusion reaction that occurs after an incompatible ABO blood group transfusion. Types of autoimmune diseases belonging to type II hypersensitivity reactions; examples of autoimmune diseases with and without tissue damage. Presentation of the pathomechanism of myasthenia gravis and autoimmune hyperthyroidism. Definition of frustrated phagocytosis. Describe the transplantation rejection reactions that belong to type II hypersensitivity reactions.

Type III hypersensitivity reaction: What is the definition of type III hypersensitivity reaction? What are the cellular mechanisms involved in type III hypersensitivity reaction? Definition of frustrated phagocytosis. Causes and mechanisms of immune complexes formation and accumulation? Provide examples of type III hypersensitivity reactions (serum disease, SLE, polyartheritis nodosa. What are antidotes, where do they originate? Describe the Arthus reaction.

Type IV. hypersensitivity reaction: What is the definition of Type IV. hypersensitivity reactions?What are the cellular events during type IV. hypersensitivity reactions? What are the most common antigens causing type IV. hypersensitivity reactions? Describe the mechanism of

chronic DTH reactions, tuberculin reaction and contact dermatitis. Explain the pathomechanism of celiac disease. Describe the transplant rejection reaction belonging to type IV. hypersensitivity: acute and chronic rejection and graft-vs-host disease.

11. Lecture: Transplantation, pregnancy immunology.

Define the following basic concepts: graft, donor, recipient, rejection. Define the concepts of autologous, allogeneic, and xenogeneic grafts. Define the concepts of auto-, allo-, and xeno-transplantation. Classify transplantation antigens. Describe alloantigen recognition by T cells, as well as activation and effector functions of alloreactive T and B cells. Describe the innate immune responses elicited by allografts. Present the types of rejection reactions. Classify the types of host-versus-graft (HvG) reactions. Present the pharmacological options for the treatment of organ rejection. Describe the immunological aspects of pregnancy. Present the stages of pregnancy from an immunological perspective. Describe the structure of the maternal–fetal interface and the immune cells present there. Describe the distinct immunological processes across the different stages of pregnancy. Describe the systemic and immunological basis of feto-maternal tolerance. What are the immunological roles of the placenta?

12. Lecture: Tumor immunology. Immunotherapies and their role in tumor therapy.

Please outline the concept of tumor generation, present the molecular basis of their development. Know the chemical, physical, biological carcinogens. Describe the antigenicity of tumors. Describe the role of elements of innate immunity in tumor defense. Outline the role of elements of adaptive immunity in defense. Describe the escape mechanisms of tumors from immune defense. Group cancer therapies. List biological therapies. Describe the role and types of Complementary Alternative Medicine in tumor therapies.

13. Lecture: Basic immunology methods. Monoclonal antibodies, Immunodiagnostics.

Determine the definition of enzyme immunoassay, and types of ELISA method. Give the definitions of controls, standards, index, cut-off value, concentrations, and titre.
Show the types of quantitative and qualitative detections of immunoglobulins.
Determine the definitions of precipitation and agglutination. Please determine the basics of complement fixation and hemagglutination inhibition tests and their use in infectious-disease diagnostics.
Describe the basics of immunfluorescence methods in infectious-disease diagnostics.
Give the basics of immunserological methods in infectious-disease diagnostics.
Explain the basics of Western-blot and Line Immunoassay in infectious-disease diagnostics.
Describe the basics of immunohistochemistry.
Provide the production of monoclonal antibodies and their use in diagnostics and therapy.