Learning guidelines for Immunology (AOK-OAK061-1)

1. Lecture: 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.

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. Describe the origin, types and tasks of dendritic cells. Characterize the neutrophil granulocytes, explain their extravasation and functions. 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.

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.

Compare the innate and adaptive immunity according to their antigen recognition, receptors, kinetics of the immune response, and quality of secondary immune response. 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: 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 mannan-binding lectin pathway and its joining to the complement cascade. Draw the late steps of the complement activation. Name the complement receptors. 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? Describe the regulation of the complement activation and the consequences of its defects.

Name the cell types involved in inflammation and describe their functions. 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. Describe the plasma enzyme cascades involved in inflammation. Explain the generation of lipid mediators and their roles in inflammation. What are the differences between acute and chronic inflammation? Summarize the possibilities of reducing inflammation.

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

Compare the structure of the two main proteins coded in the MHC region (MHCI and MHCII) and their binding to antigen peptides. Describe the cellular and molecular steps of peptide antigen processing on MHCI and MHCII. Name the rules of MHC-peptide binding. 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 genetic reasons of MHC diversity: polygenic coding, polymorphism, haplotypes and codominant inheritance. Explain the importance of HLA genetic variation on the individual and the population level. Outline the clinical consequences of MHC polymorphism.

Describe the common mechanisms in B- and T-cell maturation. Explain the main steps of gene recombination of the immunoglobulin superfamily. Describe the mechanisms (with enzymes) of V/D/J recombination in T-cell receptor and B-cell receptor. Describe the process of early lymphocyte development, list the checkpoints and define the outcomes. Explain the mechanism of central B-cell tolerance. Give at least 3 examples of immunodeficiency caused by mutations in genes involved in lymphocyte development.

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. 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 the activation and mechanism of action of cytotoxic T-cells in the immune response. Specify four subtypes of effector helper T-cells and explain what polarization means during their differentiation. Broadly explain these subtypes' role in the immune response and name the effector cells activated by each subtype. Name a few cytokines for each Th subtype.

6. 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!

7. Lecture: Test for recommended grade

8. Lecture: Immune responses against extracellular pathogens. Immune responses against intracellular pathogens. Immunescape. Immunological memory. Vaccination.
Draw the kinetics of the immune response against pathogens. Classify the pattern recognition receptors based on their structure and ligands. Name the Toll-like receptors (TLRs) and their ligands. Draw the signalling pathways of TLRs.
List the cellular and humoral elements of the immune response against pathogens. Explain step-by-step the immune response against extracellular pathogens: antigen recognition, antigen processing, antigen presenting and elimination of the pathogen. Define the following terms: phagocytosis, opsonization and neutralisation. Describe the steps of immune response against multicellular parasites.
Describe the steps of immune response against intracellular pathogens (intravesicular and cytosolic), name the cellular and humoral elements involved. Present the anti-viral immune response from recognition to elimination, give an example.
List several examples how extracellular bacteria can escape from immune response. Classify the escape mechanisms of viruses, give examples.
Describe the origin and the main properties of memory T and B cells. Characterize the kinetics of the secondary immune response. Define the fundamentals of vaccination. Compare the main types of vaccines. Point on the main differences between active and passive immunization.

9. 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

10. 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.

11. 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?

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.

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, RA, 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 tuberculin reaction and contact dermatitis

12. Lecture: Transplantation, pregnancy immunology.

Describe the immune tolerance, what are the basics of B cells and T cell tolerance! Describe the molecular mechanisms of central and peripheral tolerance. What does HLA typing mean and what is its significance for transplantation? Define the following terms: graft, donor, autograft, allograft, xenograft. How are the transplant antigens classified? Describe the classification of the rejection reactions. Describe the host-versus-graft rejection reactions, describe the cellular and molecular mechanisms of hyperacute, acute and chronic host-versus-graft reactions! Describe the role of T cells in rejection reactions. Describe the graft versus host rejection reactions. What are the therapeutic options to avoid the rejection reactions?
Describe the systemic and immunological basis of feto-maternal tolerance. What are the immunological roles of the placenta? Describe the cause and consequences of fetal erythroblastosis and the therapeutic options!

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

Basic immunological methods. Monoclonal antibodies. Diagnostic immunology.
Please determine the definition of enzyme immunoassay, and types of ELISA method. Please determine the definitions of controls, standards, index, cut-off value, concentrations, and titre.
Please show the types of quantitative and qualitative detections of immunoglobulins.
Please 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.
Please show the basics of immunfluorescence methods in infectious-disease diagnostics.
Please show the basics of immunserological methods in infectious-disease diagnostics.
Please show the basics of Western-blot and Line Immunoassay in infectious-disease diagnostics.
Please show the basics of immunohistochemistry.
Please show the production of monoclonal antibodies and their use in diagnostics and therapy.