Learning Objectives

Dear Students,

The learning objectives below summarize the most important concepts required on the exams (written and oral). They consist of 3 parts: 1. title 2. learning objectives 3. reference values. The title is the same as the respective topic of the oral final exam. The learning objectives consist of tasks and questions, and in some cases they also contain useful hints for the answers. The learning objectives that appear in **bold RED color** indicate those objectives and reference values that will serve as questions in the entry part of the exam. Not knowing or giving inadequate response to these objectives or reference values during any part of the exams will result in a failed (1) exam. The reference values usually appear where they are first encountered, but they might be important for any later topic as well. For those reference values, where value ranges are given, the student is expected to be able to give at least a value that is WITHIN the reference range along with the CORRECT unit. Important: on the oral exams the picked topic (card) will contain ONLY the title, not the detailed objectives.

On behalf of the teaching staff of the department I hope that these objectives will assist you in preparing for a successful exam.

Sincerely yours

Ferenc Domoki

1. Principles of control theory

Define the term of internal environment (milieu intérieur) and explain the importance of its control?
Define the terms homeostasis and homeostatic parameters. List at least 5 controlled functions and/or parameters in human.
Distinguish between guidance and control.
Describe the major forms of physiological controlling circuits (humoral, neuronal).
Describe the parts of the neuronal reflex arch and explain their respective functions in control (receptor, afferent branch/pathway, center, set point, efferent branch/pathway, effector).
Define negative and positive feedback control. Give examples for processes controlled by negative feedback, positive feedback. Explain feed-forward control.
Characterize endocrine, paracrine and autocrine humoral control based on the release site of the mediators and their path to the target cells.
Define „behavioural control" and explain its importance/necessity. Give examples!
How can the efficiency of control systems be expressed quantitatively? **Define gain!**
Define the term servo-control mechanism.

2. Passive transport mechanisms of the cell membrane

Describe and make a schematic drawing of the molecular structure of the plasma membrane (fluid mosaic model). Explain how the distribution of phospholipids and proteins influences the membrane permeability of ions, hydrophylic and hydrophobic compounds. Describe lateral diffusion in the membrane.
Contrast the following units used to describe concentration: mM, mEq/l, mosm/kgH_2O.
Define simple diffusion and explain how changes in the driving forces (chemical and electrical gradient, in steady state situation) and membrane properties will influence the transport rate. **State Fick's law of diffusion.**
Describe the role of water channels (**aquaporins**) in the water permeabiliy of the cell membrane.

Define: osmosis, osmol, osmolarity, osmolality and tonicity, and reflection coefficient. Explain how the different permeability of the cell membrane to water and solutes will generate an osmotic pressure.
Characterize facilitated diffusion. Define the types of the carriers: (uniporter, symporter, antiporter). Define the terms: transport maximum, saturation, competitive and non-competitive inhibition.

Reference values: **blood plasma osmolality: 290 mosm/kgH_2O**, osmotic pressure: 660 kPa = 4950 mmHg

3. Active transport mechanisms of the cell membrane.
Define the terms primary and secondary active transport. Define the terms: transport maximum, saturation, competitive and non-competitive inhibition.
Describe how energy from ATP hydrolysis is used to transport ions such as Na^+, K^+, Ca^{2+} and H^+ against their electrochemical differences via examples.
Explain how energy from the $Na^+$and K^+ electrochemical gradients across the plasma membrane can be used to drive the net „uphill" (against gradient) transport of other solutes (e.g., Na^+/glucose co-transport; Na^+/Ca^{2+}-exchange).
Explain the role and significance of ATP-binding cassette (ABC) transporters via examples.
Define the term vesicular transport: endocytosis, exocytosis, transcytosis. Give examples for specific and aspecific vesicular transport processes.

4. The resting membrane potential
Explain the origin of the resting membrane potential, the electric and chemical forces that determine the diffusion of ions.
State the Nernst equation used to determine the equilibrium potential of ions, and apply the equation to determine the equilibrium potential for K^+ in the cell membrane (E_{K^+}).
Using the Nernst-equation predict the direction of net ion movement, if the membrane potential is a) equal), b) lower, c) higher than the ion's equilibrium potential. Give the typical equilibrium potential values for Na^+, K^+, Cl^-, and Ca^{2+}.
Using the Nernst-equation calculate E_{K^+} if the extracellular K^{+-}-concentration increases by 5 mmol/l, and E_{Na^+} if the extracellular Na^+-concentration increases by 5 mmol/l.
Determine the resting membrane potential (for instance in striated muscle fibers) using the Goldman-Hodgkin-Katz-equation. Explain how the membrane potential is affected if the membrane permeability to Na^+, K^+, and Cl^- decreases.
Characterize the dynamic equilibrium („steady state") in the resting membrane. Explain the importance of the simultaneous passive ion currents (eg. Na^+, K^+) and active ion pumping (Na^+-K^+-ATPase) in determining the membrane potential and cellular volume. **Explain the consequence of the inhibition of the Na^+-K^+-ATPase.**

Reference values: extracellular ion concentrations: Na^+: 138-151 mM, K^+: 3.4-5.2 mM, HCO_3^- 21-28.5mM, Cl^-: 101-111 mM, Ca^{2+}: ionized 1.5 mM; typical intracellular (cytoplasmic) ion concentrations: Na^+: 12 mM; K^+: 155mM; HCO_3^-: 8 mM; Cl^-: 4mM; Ca^{2+}: 10^{-5}-10^{-4} mM

5. The electric properties of neuronal membranes.
Define the following terms regarding ion channels: selectivity, gating, activation, inactivation.
Compare the gating mechanisms of intra- and extracellular ligand-gated, voltage-gated, and mechanical-gated ion channels.
Explain the importance of the „voltage clamp" technique to study ion channel function.

Define and compare the electrotonic (local, graded) **potentials with the action potential** (direction of potential change, graded or not, propagation velocity, change in the amplitude of the potential change during grading). Describe the regions of the neuronal membrane where these potentials typically occur.
Make a schematic drawing of the membrane potential changes during an action potential recorded in the giant squid axon. Using the drawing, identify the phases of the action potential. Explain the terms threshold and the "all or none" principle. Define the terms rheobase and chronaxia.
Characterize the voltage-gated Na^+-, K^+- and Ca^{2+}-**channels functionally** (gating, activation, inactivation). Describe the role of voltage-gated Na^+-, K^+- and Ca^{2+}-channels in the phases of the neuronal action potential (depolarisation, „overshoot", repolarisation, afterhyperpolarization).
Define and explain the terms absolute and relative refractory periods.

6. The axonal propagation of the action potential. Axon classification.
Describe the propagation of the action potential in myelinated and unmyelinated axons. Explain saltatory conduction.
Define the terms membrane space constant and time constant.
Define membrane capacity. Explain how membrane capacity affects the propagation of the action potential in myelinated and unmyelinated axons.
Action potential propagation in mixed peripheral nerves: The compound (extracellular recorded) action potential.
Explain how axonal diameter and myelinisation determines the action propagation velocity of different axons in the same peripheral nerve. **Describe the various axon classes based on the Erlanger-Gasser-classification.**

Reference values: action potential duration in nerves: 1 ms, typical action potential propagation velocities in the axon classes of peripheral nerves (Erlanger-Gasser classification): Aα: 100, Aβ: 50, Aγ: 20, Aδ: 15, B: 7, C: 1 m/s

7. Receptors, signal transduction mechanisms.
Describe the main types of signaling molecules (mediators): autocrine and paracrine signaling molecules, hormones, neurotransmitters, neurohormones.
Define the terms: receptor, ligand, agonist, antagonist (competitive, non-competitive).
Classification of receptors: 1. based on localization (cell membrane receptors, cytosolic receptors, nuclear receptors, intracellular membrane receptors (IP_3, ryanodin), **2. based on function** (ionotropic receptors, metabotropic receptors, receptor enzymes, and enzyme-linked receptors).
Ionotropic receptors: selective and non-selective receptors, cation and anion channels. Give 1-1 examples.
Metabotropic receptors: types (G-protein coupled receptors, tyrosin-kinase receptors etc).
Heterotrimer G-proteins, types (G_s/G_i/G_q), functions.
Define the term second messengers, describe the most important members (cAMP, cGMP, calcium, IP_3/DAG).
Explain the importance of posttranslational modification (eg. phosphorylation) to control the activity of cellular proteins.
Explain the function of receptor enzymes and enzyme-linked receptors through 1-1 example.
Signal transduction via intracellular receptors: the general structure and function of cytosolic and nuclear receptors explained through 1-1 example.
Describe the following terms related to membrane receptors: activation, inactivation, internalization, up-regulation, down-regulation, sensitization, desensitization.

8. Fluid compartments of the body. The blood plasma.

Define the terms extracellular and intracellular fluid. List the compartments of extracellular fluid.
Describe the indicator dilution technique and its use to determine plasma volume, blood volume, extracellular fluid volume, and total body water.
Describe the fractions obtained by centrifugation (cells, plasma).
Define the term hematocrit.
List the anorganic and organic constituents of the blood plasma. Give the reference values.
Identify the protein fractions of blood plasma, explain the method (electrophoresis) used for their measurement. **Give 1-1 example from each fraction**.
Identify and characterize the lipoproteins found in the blood plasma.

Reference values: **total body water: ~60% of body weight, (intracellular 40%, extracellular 20%), interstitial fluid volume: 11 l, blood volume: 5-6 l (80 ml/kg body weight), plasma volume: 3 l, hematocrit: 0,44-0,46, plasma osmolality: 290 mosm/kgH_2O, plasma Na^+: 138-151 mM, plasma K^+: 3.4-5.2 mM, plasma HCO_3^- 21-28.5mM, plasma Cl^-: 101-111 mM, plasma Ca^{2+}: 2,4-2,8 mM (total), 1.5 mM (free, ionized), plasma glucose: 4,2-5,9 mM, plasma urea: 2,5-10,3 mM, plasma bilirubin: 5,0-17,0 µmol/l, plasma proteins: 60-80 g/l, plasma albumine: 34-45 g/l, plasma total cholesterol: <5,17 mM, plasma total lipids: 4,5-10 g/l**

9. The general features of red blood cells.

Describe the following parameters of the red blood cells: count, size, shape, life span.
What is the fate of the cell organelles in mature red blood cells?
Define the following terms and give the formula of their calculation: MCH, MCHC, MCV.
Describe the Price-Jones curve.
Enlist and describe the types of anemias and explain their mechanism.
Characterize the osmotic resistance of the red blood cells.
Describe the mechanism of blood sedimentation, the method of its measurement, significance and normal value.
Describe the membrane of the red blood cells. Enlist three important membrane proteins.

Reference values: **count: 4.3-5.2 million/µl, diameter: 7-8 µm, life span: 120 days, sedimentation rate: <20 mm/hour, blood hemoglobin concentration: 135-160 g/l, MCV: 94 fl, MCH: 29 pg, MCHC: 333 g/l, osmotic resistance: 0.45-0.50% NaCl solution**.

10. Erythropoesis.

Describe the red bone marrow and enlist the main progenitors of red blood cells. **Provide the definition of reticulocyte, its staining and the significance of reticulocyte count.**
Describe the main stages and mechanisms of iron metabolism: absorption (ferroportin), transport (transferrin), storage (ferritin, hemosiderin), regulation (hepcidin).
The role of vitamin B_{12} and folic acid in the formation of red blood cells.
Erythropoietin: production (kidney), **trigger, function**.
Enlist some important hormonal influences on erythropoiesis (e.g., growth hormone, testosterone).

Reference values: **serum iron: 9-27 µM, iron RDA (recommended dietary allowance): 10-20 mg**, daily iron loss: 1-3 mg, **Vitamin B_{12} RDA: 1-2µg, Folic acid RDA: 200 µg, relative reticulocyte count: 0.4-1.5%**

11. Hemoglobin degradation, bilirubin metabolism.

Describe the fate of old erythrocytes, release of hemoglobin, binding proteins of hem and hemoglobin, and the uptake into the macrophages.
Describe the steps of the degradation of hemoglobin, the fate of iron, globin chains, and the porphyrin ring.
The release of bilirubin from macrophages, transport in blood, uptake in liver, conjugation and secretion into the bile.
Provide the definition of direct and indirect bilirubin.
The fate of bilirubin in the intestines, the enterohepatic circulation and secretion. Urobilinogen (UBG), and the significance of its detection in the urine.
The definition of icterus (jaundice) and some of its main forms.

Normal value: **plasma bilirubin: 5.0-17.0 µM**

12. The physiology of white blood cell.
Give the normal value of leukocyte count, and the sites where white blood cells are produced.
Describe the differential leucocyte count, starting with the method of staining. Describe the morphological features of white blood cell types and enlist the reference values of the differential white blood cell count (%).
Describe the main functions of white blood cell types:
Describe phagocytosis: the roles of the monocyte/macrophage system and the neutrophil granulocytes.
Describe the types of lymphocytes and their major functions. Define the concept of antigen and delineate the process of antigen presentation. **Describe the role and structure of immunoglobulins and their subtypes and functions.** Expound the main elements and the functions of the complement system.

Reference values: **white blood cell count: 4000-10000 cell/µl, neutrophils: 60-80%, lymphocytes: 20-30%, monocytes: 2-6%, eosinophils: 1-5%, basophils: 0-1%.**

13. The AB0 and Rh blood groups.
Describe the antigens and the circulating antibodies of the ABO blood group (Landsteiner-rules).
Describe the pattern of inheritance of the ABO blood group. What kind of proteins are coded by the genes responsible? What is the cause of the development of antibodies?
Describe the antigens of the Rh blood group.
Describe the pattern of inheritance of the Rh blood group. What kind of proteins are coded by the genes responsible? Why does the Rh blood group NOT follow the Landsteiner-rule?
What is the prevalence of AB0 and Rh phenotypes?
Describe the process of the blood group determinations. Compatibility tests before blood transfusion (major and minor test, biological test).
Expound the process of Rh-sensitization (anti-D prophylaxis, erythroblastosis foetalis).
What are the definitions of agglutination and hemolysis? What is the consequence of hemolysis?

14. Primary hemostasis.
What is the difference between hemostasis and blood coagulation? Compare the white and the red thrombus.
Describe the basic steps of thrombopoesis.
What is the normal value of thrombocyte count?
Describe the most important morphological features of the thrombocytes, size, types of granules.
Elaborate the role of primary hemostasis, enlist its major processes.

Explain the adhesion, aggregation and activation of thrombocytes. Give some of the molecular mechanisms of these process (von Villebrand factor, the glycoproteins involved in platelet adhesion/aggregation, the mediators, receptors and signal transduction pathways involved in platelet activation).
What is the role of the endothelial cells in the regulation of hemostasis?

Reference values: **platelet count: 150000-300000/µl, bleeding time (Ivy's method): 3-5 min**

15. Secondary hemostasis: blood clotting (coagulation).
Define the coagulation factors, their nomenclature, site of synthesis, and the mechanism of their action.
Describe the extrinsic pathway.
Describe the intrinsic pathway and the contact phase.
Expound the common phase of blood coagulation (convergence of extrinsic and intrinsic pathways) and the formation of the stable fibrin mesh.
Explain the role of vitamin K in the synthesis of the so-called vitamin K-dependent coagulation factors.
What is the "placenta sanguis"? Define the process of clot retraction, define the term serum and compare its composition with the blood plasma.
Compare prothrombin time and coagulation time.
Define INR, its calculation and significance.

Reference values: **prothrombin time: 18-20 s, INR: 0.8-1.2, coagulation time (Lee-White method): 5-8 min**, fibrinogen: 3 g/l

16. Fibrinolysis. Inhibition of clotting in vitro and in vivo.
Expound the activation and regulation of the plasmin system.
Describe the following systems and their regulation: thrombomodulin/protein C/protein S; heparin/antithrombin.
Enlist substances that can be used to inhibit blood coagulation *in vitro* (EDTA, citrate) and define their mechanism of action.
Enlist substances and drugs that can be used *in vivo* to inhibit thrombocyte activation and blood coagulation or to facilitate fibrinolysis (inhibitors of cyclooxygenase, heparin, vitamin K antagonists, plasminogen activators).

17. Neurotransmission.
Characterize electric synapses including the description of the molecular structure of gap junction operating in these synapses. **Compare transmission between electric and chemical synapses** (direction of information, speed of transmission).
Describe the consecutive events of chemical neurotransmission (starting with the depolarization of presynaptic membrane ending with the development of the graded electric response of the postsynaptic membrane (postsynaptic potential, PSP). Describe the ion currents involved in the development of the following local potentials: excitatory postsynaptic potential (EPSP), inhibitory postsynaptic potential (IPSP), end plate potential (EPP), and receptor potential.
Describe the temporal and spatial summation of postsynaptic potentials (EPSPs and IPSPs), and their role to trigger an action potential
Describe the common features of classical neurotransmitters.
Group the classical and non-classical neurotransmitters based on their chemical structure: 1. **acetyl-choline**, 2. amino acids (**glutamate, glycine, GABA**), 3. biogenic amines (**dopamine, noradrenaline,**

adrenaline, histamine, serotonin), 4. gases (**NO**, CO), 5. lipids (endocannabinoids, 6. peptides (endophins, encephalins, dynorphins, substance P, CGRP, VIP).
Characterize the neurotransmitters in bold based on their synthesis, inactivation, receptors and signal transduction mechanisms. Define the terms ionotropic and metabotropic neurotransmitter receptors.
Describe the role of intraneuronal (axonal) transport mechanisms in the maintenance of interneuronal communication.
Nonsynaptic neurotransmission. Volume transmission.

Reference values: synaptic delay: 1-1,5 ms.

18. The peripheral nervous system: primary sensory neurons.
Make a schematic figure of a primary sensory neuron and indicate its major parts: peripheral axon, central axon, cell body. Give the anatomical location of primary sensory neurons (spinal dorsal root ganglia, and the sensory ganglia of cranial nerves).
On the schematic figure of the primary sensory neuron indicate the most likely sites of the generation of the receptor potential, the propagation of the action potential and the release of neurotransmitters.
Define the terms: receptor sensitivity (activation threshold), receptor specificity (modality), and receptive field.
Group the somatosensory receptors based on the origin of the sensory stimulus (extero-, intero-, and proprioceptors) **and on their modality** (mechano-, thermo, uni- and polimodal nociceptors).
Describe the steps of sensory signal transduction processes in mechanoreceptors, thermoreceptors and nociceptors, and how the action potential is generated. Give the important neurotransmitters released by primary sensory neurons.
Define the terms slow-adapting and fast-adapting receptors.
Explain how the axonal diameter and myelinisation determines the action potential propagation in sensory axons. **Group the sensory axons according to the Lloyd-Hunt (Ia, Ib, II, III and IV)-, and the Erlanger-Gasser classification (Aα, Aβ, Aδ, and C).**
Define the term secondary sensory cell, and describe its connection to the primary sensory neuron. Give at least one example.

19. The parasympathetic division of the autonomic nervous system.
Characterize the structural organization of the parasympathethic nervous system: give the location of the cell bodies and axons of preganglionic neurons, also of the cell bodies and axons of ganglion cells.
Classify the axons of the autonomic nervous system found in peripheral nerves according to the Erlanger-Gasser classification (B and C fibers).
Characterize the synaptic connection between the preganglionic axon and the ganglion cell.
Define the term autonomic ground plexus. Describe the structure and function of axon varicosities.
Describe the biosynthesis, synaptic release, and elimination of acetyl-choline. Describe the effects of acetyl-choline of the receptors of target cells. Give examples of parasympathethic effects mediated by cholinergic receptors.
Give further neurotransmitters released by parasympathetic nerves, and give examples of parasympathetic effects mediated by such neurotransmitters.
Define the term autonomic tone.

20. The sympathetic division of the autonomic nervous system. The adrenal medulla.

Characterize the structural organization of the sympathethic nervous system: give the location of the cell bodies and axons of preganglionic neurons, also of the cell bodies and axons of ganglion cells.
The sympathetic adrenergic system: describe the biosynthesis of noradrenaline and adrenaline, the synaptic release and elimination of noradrenaline.
List the adrenergic receptor types found on target cells along with the respective signal transduction pathways. Give examples of adrenergic effects mediated by each receptor type.
Describe the anatomical structure of the adrenal medulla and the regulation of hormone release.
Describe the transport of catecholamines in the circulation, their metabolism and excretion.
Give examples of sympathetic cholinergic effects, and also of non-adrenergic–non-cholinergic (NANC) sympathetic effects.

21. The peripheral nervous system: motor neurons, neuromuscular junction.
Make a schematic figure of a motor neuron, and indicate the following parts: dendrite, axon, axon hillock, cell body. Give the anatomical locations of the cell bodies (ventral horn of the spinal cord gray matter, motor nuclei of cranial nerves), and classify the motor axons found in peripheral nerves according to the Erlanger-Gasser classification (Aα and Aγ fibers).
Using the schematic figure, indicate the sites of the generation of IPSP, EPSP, the action potential and the release of neurotransmitter.
Make a schematic figure of the neuromuscular junction found in striated muscles, and indicate the consecutive steps of neuromuscular transmission.
Compare the differences between the end plate potential (EPP) and the muscle fiber's action potential.
List the inhibitors of the neuromuscular junction (curare, succinylcholine, botulinum toxin), give their targets and mechanisms of actions.
Define the term motor unit. Describe motor recruitment during various levels of muscle activity.

22. Skeletal muscle: structure, electromechanical coupling, the biochemistry of contraction.
Describe and name the parts of the skeletal muscle at different anatomical levels (bundle of fibers, fibers, myofibrils, myofilaments, sarcomere).
Characterize the thick and thin filaments and enlist their proteins. Draw a myosin molecule and show its subunits (heavy and light chains), define their functions.
Describe the steps of the electromechanic coupling in striated muscle. Define and explain the function of the following terms: sarcolemma (cell membrane of the muscle cell), T-tubules, sarcoplasmic reticulum (L-tubules), troponin-tropomyosin, and calcium ions.
Describe the cycles of actin-myosin bridges and their binding, and explain how it results in muscle contraction (the sliding filament model). Describe the mechanism of relaxation.
Summarize the role of ATP in muscle contraction and relaxation. What is the mechanism of rigor mortis („stiffness of death")?

23. Skeletal muscle: the mechanics and energetics of muscle contraction.
Define and compare the isometric, isotonic, and auxotonic contractions.
Explain the connection between preload, afterload, and total load during isotonic contraction.
Draw the muscle length - tension diagram, describe the active, passive and total tension, and their molecular mechanism. Explain the relationship between the length of the sarcomere and the shape of the active tension curve (bell shaped curve).
Explain the relationship between force (load) and shortening velocity. Define the muscle power.

Characterize the difference between muscle twitch and tetanus (complete and incomplete), and explain the contraction summation. Explain how muscle twitch turns into tetanus by the increasing of the stimulation frequency.
Define the term of muscle fatigue and enlist intracellular processes that play a role in fatigue.
Compare the three types of skeletal muscle in a table (fast-anaerobic, fast-oxidative, slow-oxidative) with a special reference to their structure, energy sources, and function.
Describe the energy sources of the working muscle, and rank them according to the speed and amount of ATP production during the contraction. Describe the differences between muscle types.

24. Smooth muscle physiology.
Define the terms and compare single-unit and multi-unit smooth muscles.
Describe the intracellular pathways that control contraction and relaxation in smooth muscle.
Distinguish between electromechanical coupling and pharmacomechanical coupling.
Describe the differences in actomyosin regulation of, respectively, smooth and skeletal muscle and indicate the structural similarities in their respective contractile units.
Explain the sources, movements and roles of Ca^{2+} in smooth muscle during contraction and relaxation.
Describe the mechanisms responsible for myofilament Ca^{2+} sensitization and desensitization.
Explain why smooth muscles can develop and maintain force with a much lower rate of ATP hydrolysis than skeletal muscle
Distinguish between muscle relaxation from the contracted state and the phenomenon of stress relaxation and give examples of each process.

25. Respiratory mechanics 1: Static mechanics of the lung and the chest.
Draw a normal spirogram, indicating the various lung volumes. Explain how the different lung capacities are determined by the summation of lung volumes. Explain which lung volumes and capacities CANNOT be determined directly with a spirometer.
Draw the static transpulmonary pressure – lung volume curve both during inflation from the residual volume to total lung capacity, and during deflation.
Define lung compliance, and give two examples of lung pathologies where lung compliance is smaller or higher than the normal value, respectively
Draw the transmural pressure – volume (compliance diagram) of the lung, the chest wall, and the combined respiratory system (lung+chest) plotted in the same graph. Show and explain the significance of the equilibrium points of the diagram.
Enlist the factors determining total lung capacity, functional residual capacity and residual volume.
Describe the forces responsible for the development of negative pleural pressure (elastic recoil of the lung, and expansion tendency of the chest wall). Describe the consequence of pneumothorax (air getting into the pleural space).
Define surface tension, and describe its effect on pulmonary mechanics, including the effect on alveolar size and the role of surfactant. Define the term atelectasis, and the role of surfactant in its prevention. What does the term mean: alveolar interdependence?
Describe the source and the composition of surfactant. Explain the regulation of surfactant secretion.

Reference values: static lung volumes and capacities male/female (ml): **TV: 500/500**, IRV: 3100/1900, ERV: 1200/800**, RV: 1200/1000, FRC: 2400/1800, VC: 4800/3200, TLC: 6000/4200; lung compliance: 0,2 l/cmH_20, chest+lung compliance 0,1 l/cmH_20.**

26. Respiratory mechanics 2: Ventilation.

Draw a diagram showing how pleural pressure, alveolar pressure, air flow, and long volume changes during the respiratory cycle. Indicate the beginning and the end of inspiration, and the end of expiration. Describe how the pressure gradient between intrapulmonal and athmospheric pressure drives air movement in and out of the lung.
Describe the factors constituting dynamic lung resistance against lung volume changes (airway resistance and viscous tissue resistance). Describe based on the segmental differences in individual airway diameters, total cross sectional area of parallel coupled airways, and the occurrence of turbulent as well as laminar flow, WHY the upper airways and the great bronchi contribute principally to airway resistance.
Define and explain the following terms: anatomic and physiologic dead space, respiratory rate, respiratory minute volume, dead space ventilation, alveolar ventilation.
Describe the method to determine physiologic dead space.
Draw a spirogram of a forced expiratory effort. Indicate the forced vital capacity (FVC), the forced expiratory volume in 1 second **(FEV_1)**. **Define the Tiffeneau-index** (FEV_1/VC). Define peak expiratory flow (PEF), and forced expiratory flow 25-75 (FEF25-75; between 25 and 75% of FVC).

Reference values: pleural pressure at the end of inspiration/expiration: -8/-5 cmH_20, alveolar pressure at the peak of inspiratory/expiratory flow: -1/1 cmH_20, air flow at the peak of inspiratory/expiratory flow -0,5/0,5 l/s, maximal expiratory pressure: 100 cmH_20, PEF: 10 l/s, **Tiffeneau-index (FEV_1/VC): 75-80%, anatomic dead space: 150 ml, respiratory rate: 14 breaths/min, minute ventilation: 7 l/min, alveolar ventilation: 5 l/min.**

27. Pulmonary gas exchange.
Explain the concept of partial pressure of gases.
Give the reference values of partial pressures for oxygen and carbon dioxide in inspired air, alveolar air, arterial blood and mixed (central) venous blood?
Enlist the factors determining diffusion between the alveolar gas and the capillary blood, apply Fick's law of diffusion. Define diffusion-limited, and perfusion-limited gas transport.
Define the term diffusion capacity.
By using the ventilation equations ($P_{AO2}= P_{iO2}- V_{O2}/V_A*863$ Hgmm; $P_{ACO2}= V_{CO2}/V_A* 863$ Hgmm) determine the factors affecting the alveolar/arterial pO_2 and pCO_2 (inspired oxygen concentration, oxygen uptake/metabolism, alveolar ventilation, and carbon dioxide production and alveolar ventilation, respectively). Define the terms hypoventilation, hyperventilation.
Describe the dynamics of oxygen transport from the alveolus to the capillary blood, define capillary reserve (the amount of red blood cell capillary transit time, where there is no further net gas diffusion).
Give the normal value of total ventilation/perfusion quotient (V/Q) in healthy lungs, and explain how local V/Q is modified by the vertical distribution of ventilation and perfusion.

Reference values: **partial pressure values (mmHg) of respiratory gases: inspired air / alveolar air / arterial blood / venous blood: pO_2: 149/100-104/95-98/40, pCO_2: 0,3/40/40/46**; partial pressure of water vapour in alveolar air: 47 mmHg; **ventilation/perfusion quotient (V/Q): 0,9-1,1.**

28. Oxygen transport in blood.
Describe the chemical structure of the hemoglobin molecule. Enlist and define special/pathological hemoglobin forms (HbF, methemoglobin, carboxy-hemoglobin) and give their functional characteristics.
Draw the hemoglobin oxygen-dissociation curve. Explain the connections between pO_2, hemoglobin-saturation. Define P_{50} and give its normal value.

Compare the contribution of hemoglobin-bound and physically dissolved O_2 to blood oxygen content.
Give the oxygen binding capacity of hemoglobin (Hüfner-number).
Describe how the oxyhemoglobin dissociation curve is affected by changes in pCO_2 (Bohr-effect), plasma pH and red blood cell 2,3-DPG concentration. Explain the functional significance of these changes.
Give 5 causes of hypoxia. Types of hypoxia: 1. hypoxic hypoxia (low inspired air pO_2, alveolar hypoventilation, disturbed diffusion across the alveolocapillary membrane), 2. transport hypoxia (anemia, methemoglobinemia, carbon-monoxide poisoning), 3. ischemic hypoxia (low cardiac output, vascular occlusion), 4. histotoxic hypoxia (inhibition of mitochondrial respiration).
Define the term cyanosis (deoxyhemoglobin > 50 g/).
Explain how the oxyhemoglobin dissociation curve, arterial pO_2 and oxygen saturation are affected by anemia and carbon-monoxide poisoning, respectively.

Reference values: **HbA P_{50}: 26 mmHg; arterial/mixed venous blood oxygen saturation: 97-98/75%; Hüfner-number: 1,34 ml/g; oxygen concentration in arterial/venous blood: 200/150 ml/l; arteriovenous oxygen difference ($AVDO_2$): 50 ml/l; resting oxygen uptake/metabolic rate: 250-280 ml/min.**

29. Carbon-dioxide transport in blood.
Describe the CO_2 transport mechanisms in blood and the percentage contribution of these mechanisms to transport: (1. physically dissolved, 2. chemically dissolved as bicarbonate anions, and 3. hemoglobin-bound with carbamino bonds)
Name the critical enzyme required for CO_2-transport, and its cellular location.
Explain the importance of chloride-shift (Hamburger-shift) in the blood CO_2-transport.
Give the reference values for the dissolved CO_2 concentration as well as the plasma bicarbonate levels both in arterial and in mixed venous blood.
Explain the effect of hemoglobin oxygen dissociation on the uptake of CO_2 (the Haldane effect).

Reference values: **CO_2 concentration in arterial/venous blood: 480/520 ml/l; bicarbonate concentration arterial/venous blood: 24/27 mM; arteriovenous difference CO_2 ($AVDCO_2$): -40 ml/l; CO_2 production at rest: 210 ml/min**.

30. The rhythmogenesis of breathing, ventilatory reflexes elicited from the lung.
List the muscles used in quiet breathing, and the additional muscles involved in forced respiration.
Give the anatomical localization of the motoneurons involved in the breathing effort (C3-5, Th1-11).
Describe the phases of motoneuron activity during the respiratory cycle (inspiratory, postinspiratory, exspiratory).
Describe the brainstem regions involved in the rhythmogenesis and regulation of breathing movements: DRG, VRG, pre-Bötzinger complex and its importance, PRG (medial parabrachial and Kölliker-Fuse nucleus).
List and characterize three reflexes originating from pulmonary receptors controlling tidal volume and respiratory rate. Describe the respective reflex arches. (1. **Hering-Breuer reflex**, 2. reflexes elicited by irritant receptors, 3. chemoreflexes elicited by J-receptors)
Define the following terms: eupnoe, hypopnoe, hyperpnoe, dyspnoe.
Define the following breathing patterns: Kussmaul breathing, Cheyne-Stokes breathing, apneusia, gasping.

31. The chemical control of ventilation.

Describe the anatomical locations of chemoreceptors monitoring the blood pO_2, pCO_2, and pH levels, explain their respective importance for detecting the changes in blood gases.
Describe the structure and function of peripheral chemoreceptors.
Describe the function of central chemoreceptors.
Explain how alveolar ventilation is changed by changes in pO_2, pCO_2, or by combined changes. When does CO_2 narcosis develop?
Describe the respiratory drive following the adaptation of central chemoreceptors. Explain the consequence if oxygen is given to this patient.
Describe the changes in alveolar ventilation 1. immediately after traveling to high elevation, 2. after 2 weeks of acclimation at this high elevation, and 3. immediately after returning to sea level.
Describe the importance of feed-forward control of ventilation during physical exercise, and its effect on arterial pCO_2, pO_2, and pH values.

Reference values: maximal O_2 uptake: 4000 ml/min, maximal CO_2 production: 3200-4000 ml/min, maximal voluntary ventilation (MVV): 100-200 l/min

32. Biology of the airways. Metabolic and endocrine functions of the lung.
Describe the function of the nasal turbines. Characterize the sneezing and the coughing reflex.
Define the term mucociliary clearance.
Protection of the lung and the airways: describe functions alveolar macrophages, Clara-cells, tissue mast cells.
Describe the control of airway diameter and secretory activity: Define the term bronchomotor tone. Adrenergic effects. Describe the effects mediated by adrenergic receptors. Describe the effect of inflammatory mediators (histamine, prostanoids, leucotrienes).
Describe the clearance of vasoactive substances by the pulmonary circulation. Give examples for substances that are virtually fully "cleared" (local mediators: leucotrienes, prostanoids, bradykinin, VIP, endothelin, serotonin, and also for substances that pass effectively unchanged (the vasoactive hormones: adrenaline, vasopressin).
Describe the importance of pulmonary vascular endothelium in the production of angiotensin II (ACE expression).

33. Hemodynamics: basic biophysical principles
Define and compare flow and velocity of flow in terms of concept and unit. Understand the relationship between flow, velocity, and cross-sectional area.
Know the factors that determine the total energy of the flowing blood (Bernoulli's law).
Understand the relationship between pressure gradient, flow, and resistance (Ohm's law) and be able to calculate for one variable if the other two are known.
Describe the systemic and the pulmonary circulation as serially connected systems, and use Ohm's law to describe the hemodynamics in both.
Define resistance and conductance. Understand the effects of adding resistance in series vs in parallel on total resistance and flow.
Explain the factors determining hydraulic resistance using the Hagen–Poiseuille's law. Explain the deviations from Hagen–Poiseuille's law predictions that occur in the circulatory system (blood and blood vessels)
Explain the terms laminar and turbulent flow. List the factors that shift laminar flow to turbulent flow. Reynolds number. Describe the relationship between turbulent flow with the audible events, such as murmurs and bruits.

34. Hemorheology

Explain and give the units of the followings: shear stress, shear rate, viscosity. Give Newton's law of viscosity, and **define Newtonian** and non-Newtonian fluids.
The anomalous viscosity of blood: **which factors affect blood viscosity?** (hematocrit, shear thinning and the Fåhræus–Lindqvist effect)
Describe the mechanisms of shear thinning (dispersion of red blood cell aggregates, and red blood cell adaptations).
Describe the dependence of the structural viscosity (red blood cell aggregation, money roll formation) on the composition (ratio) of plasma albumine and globuline fractions.
Characterize the flow adaptations of red blood cells. (axial migration, orientation, shape changes)
How will the apparent blood viscosity change in microvessels? Describe the Fåhræus–Lindqvist-effect and its mechanisms.

35. Cardiac muscle: structural and functional characterization, regulation of contractile force
Compare the cardiac and the skeletal muscle with respect to: fiber size, electrical connections between cells, and arrangement of myofilaments. **Based on ion permeability and electrical resistance describe the role of gap junctions in creating a functional syncytium.**
Contrast the duration of the action potential and the refractory period in a cardiac muscle and skeletal muscle. Sketch the temporal relationship between an action potential and the resulting contraction (twitch) in a cardiac muscle cell and in a skeletal muscle fiber. Based on this graph, explain why cardiac muscle cannot remain in a state of sustained (tetanic) contraction.
State the steps in excitation-contraction coupling in cardiac muscle. Outline the sequence of events that occurs between the initiation of an action potential in a cardiac muscle cell, the resulting contraction and then relaxation of that cell. Provide specific details about the source of intracellular Ca^{2+} increase and the special role of Ca^{2+} in the modulation of contraction force and relaxation of cardiac muscle.
How do the following factors increase the power of contraction (positive inotropy) in the cardiac muscle: increasing the length of muscle fibres (heterometric control), partial inhibition of the Na+-K+-ATPase and increasing the extracellular Ca^{2+}?
Explain the positive lusitropic effect induced by stimulation of the adrenergic receptors?

36. Cardiac cycle. The jugular pulse.
Draw, in temporal relationship, the pressure changes in the left atrium, ventricle and in the aorta, the volume changes of the left ventricle, and the valve positions during the mechanical cardiac cycle.
Identify the phases of the cardiac cycle on the graph.
Define stroke volume, cardiac output, cardiac index, and ejection fraction and give their reference values.
Know the factors that contribute to the formation of cardiac sounds. Describe the timing, causes and location of the 1st and 2nd heart sounds.
Explain the push-pull characteristic of the cardiac pump and the valve-plane mechanism.
Explain the pressure changes in the right atrium during the cardiac cycle and how these changes contribute to the jugular pulse.

Reference values: **duration of the systole/diastole 270/530 ms (at 75 beats/min heart rate); left ventricular pressure (systole/diastole): 120/6-8 mmHg; right ventricular pressure (systole/diastole): 24/0-2 mmHg; left atrial pressure: 6-8 mmHg; right atrial pressure: 0-2 mmHg; heart rate at rest/at maximal work 70-180/min; stroke volume at rest/at maximal work: 70-80/125 ml; left ventricular end-systolic volume: 40-80 ml; left ventricular end-diastolic volume: 110-160 ml, left ventricular ejection fraction: 0.5-0.7; cardiac output at rest/maximal work: 5.5-24 l/min, cardiac index: 3.2 l/min/m^2.**

37. Preload and afterload, the Frank-Starling law of the heart.
Draw and describe the length-tension relationship in a single cardiac cell. Correlate the cellular characteristics of length, tension, and velocity of shortening with the intact ventricle characteristics of end diastolic volume, pressure, and dP/dt. Draw the ventricular function curve into the volume-pressure graph.
Define preload. (the maximal tension of the ventricular wall BEFORE the systole). Why can end-diastolic ventricular pressure, atrial pressure and central venous pressure be used for estimating the preload, and why is the ventricular pressure the most reliable method for the estimation?
Define afterload. (the maximal tension of the ventricular wall DURING the systole). Why can systolic arterial pressure be used for estimating the afterload?
Describe the Starling heart-lung preparation and use it to demonstrate how a denervated (transplanted) heart can adapt to changes in the preload and afterload. **Phrase the Frank-Starling law of the heart.**
What is the role of the Frank-Starling law of the heart in keeping the cardiac output of the left and right ventricles equal?

38. Cardiac muscle: cellular electrophysiology
Sketch a typical action potential in a ventricular muscle and a pacemaker cell, labeling both the voltage and time axes accurately. Describe how ionic currents contribute to the four phases of the cardiac action potential. Use this information to explain differences in the shapes of action potentials recorded from different cardiac cells.
Describe the ion channels that contribute to each phase of the cardiac action potential. How do differences in channel population influence the shape of the action potential in the nodal tissue and in the working myocardium?
Explain what accounts for the long duration of the cardiac action potential and the resultant long refractory period. What is the advantage of the long plateau of the cardiac action potential and the long refractory period?
Explain the ionic mechanism of pacemaker automacy and rhythmicity.
Beginning in the SA node, diagram the normal sequence of cardiac activation (depolarisation) and the role played by the specialized conducting system.
Explain why the AV node- His bundle is the only normal electrical pathway between the atria and the ventricles, and explain the functional significance of the slow conduction through the AV node.
Contrast the sympathetic and parasympathetic nervous system influence on heart rate and cardiac excitation in general. Define the terms: positive and negative chronotropy and dromotropy, and explain the ionic background of the effects in the SA node and in the AV node.
How does hyperkalaemia affect the excitability of the cardiac muscle?

Reference values: **duration of the myocardial action potential: 200-300 ms. Frequency of the intrinsic pacemaker, the SA node: 100 AP/min**, conduction speed in the AV node: 0.02-0.05 m/s, in the Purkinje fibers: 2-4 m/s.

39. Electrocardiography, other methods for the assessment of cardiac function.
Define the term electric dipole. Describe the characteristics that define a vector. Describe how dipoles generated by the heart produce the waveforms of the ECG.
Describe the electrode conventions used by clinicians to standardize ECG recordings. Know the electrode placements and polarities for the 12 leads.
Name the parts of a typical bipolar (Lead II) ECG tracing and explain the relationship between each of the waves, intervals, and segments in relation to the electrical state of the heart.

Define mean electrical vector (axis) of the heart and give the normal range. Determine the mean electrical axis from knowledge of the magnitude of the QRS complex in the standard limb leads.
Cardiac catheterization.
Echocardiography and other imaging methods

Reference values: **Standard paper speed for ECG recording: 25mm/s (1mm=40ms); standard amplitude 1cm=1mV; P wave: <100 ms; PQ interval: 120-200 ms; QRS complex: 80 ms (<100 ms); QT interval: 320-390 ms; normal electric mean axis position: 30-60°.**

40. Cardiac work and metabolism. The coronary circulation

Describe the components of the external work of the heart (pressure-volume work and kinetic work) and the mechanical efficiency of the cardiac work.
Characterize the substrates supplying the energy metabolism of cardiac muscle fibers, and describe quantitatively the contribution of the cardiac muscle to resting oxygen consumption.
Describe the phasic flow of blood to the ventricular myocardium through an entire cardiac cycle. Contrast this cyclic variation in myocardial flow a) in the walls of the right and left ventricles and b) in the subendocardium and the subepicardum of the left ventricle.
Give the reference values of oxygen extraction and arteriovenous oxygen difference in the coronary circulation, and explain how these values are unique when compared with other body organs.
Explain the mechanism whereby coronary blood flow is coupled to myocardial workload, and identify the humoral mechanisms that cause coronary vasodilation and increased blood flow
Explain how sympathethic stimulation alters cardiac activity and coronary vascular resistance.
Identify the importance of direct and indirect sympathethic nervous system effects in determining coronary blood flow during exercise?

Reference values: **coronary blood flow at rest: 250 ml/min, 4-5% of resting cardiac output; heart $AVDO_2$: 114 ml/l (more than double of the body average).**

41. Hemodynamics: the functional categorization of blood vessels

Explain the concept of transmural pressure of blood vessels.
Explain the concept of vascular compliance, give the formula for its determination ($C=\Delta V/\Delta P$).
Which two main factors determine vascular compliance (starting volume and distensibility)?
Characterize the different vascular segments based on their compliance.
Explain the concept of critical closing pressure.
Describe the relationship among wall tension, transmural pressure, vessel radius and wall thickness using the equation of Laplace's law. Based on the relationship, in which vessel segment is the rupture of the vessel due to high wall tension most likely?
Give the definitions of hydraulic resistance and conductance. Explain the effects of adding resistance in series vs. in parallel on total resistance.
Characterize the contribution of arteries, arterioles, capillaries, venules, and veins to peripheral vascular resistance. Contrast blood pressure, cross sectional area, flow velocity, and blood volume in these vascular segments.

Reference values: **perfusion pressure (pressure gradient) in the systemic / pulmonary circulation: 92/6 mmHg**, total peripheral resistance (at rest): 16,5 mmHg × min/l, pulmonary vascular resistance: 1,5 mmHg × min/l; blood pressure drop in the systemic resistance vessels (arterioles): 60 mmHg, average flow velocity in the aorta: 22.5 cm/s, in the capillaries: 0,03 cm/s, cross sectional area of the aorta 4 cm^2, total cross sectional area of capillaries: 3000 cm^2.

42. The function of the aorta and the arteries

Describe the invasive and non-invasive methods of arterial blood pressure determinations (catheter + pressure transducer, and sphygmomanometry).

Draw the blood pressure curve of the aorta. Give the definitions and reference values of arterial systolic, diastolic, mean, and pulse pressures.

Describe the Windkessel function of the aorta.

Describe the effects of changes in a) stroke volume, b) arterial compliance, and c) total peripheral resistance, on arterial systolic, diastolic, mean, and pulse pressure values.

Describe the propagation of the pressure pulse, the changes in the shape of the pressure waveform from the aorta to the peripheral arteries. Contrast the pressure pulse with the flow pulse.

Describe the arterial pulse qualities assessed with palpation.

Reference values: **arterial systolic/diastolic/mean pressures: 120/80/93 mmHg; pulse pressure: 40 mmHg**

43. The microcirculation: capillary solute exchange and fluid dynamics

Describe the vascular elements of the microcirculation (arterioles, mertarterioles, precapillary spincters, capillaries, venules)

Describe the main types of true capillaries: continuous, fenestrated, discontinuous and barrier endothelium.

Describe the diffusion across the capillary wall using Fick's law.

Contrast capillary permeability of small molecule solutes and proteins based on their respective reflection coefficients (σ).

Define oncotic (colloidosmotic) and hydrostatic pressures, and give the reference values of these (the Starling forces) in both the capillary blood and the interstitial fluid compartments.

Define the Starling equation and discuss how each component influences fluid movement across the capillary wall.

Using the components of the Starling equation, explain why fluid does not usually accumulate in the interstitium of the lungs. (the low hydrostatic pressure protects from pulmonary edema)

Reference values: average systemic capillary hydrostatic (blood) pressure: 17,3 mmHg, interstitial hydrostatic pressure: -3 mmHg, **plasma oncotic (colloidosmotic) pressure: 28 mmHg**, interstitial oncotic (colloidosmotic) pressure: 8 mmHg; average pulmonary capillary hydrostatic pressure: 10-11 mmHg

44. The microcirculation:lymphatic circulation and edema formation

Describe the lymphatics, and explain how the structural characteristics of terminal lymphatics allow the reabsorption of large compounds, such as proteins. Contrast the structure of lymphatic capillaries and systemic capillaries. What is the significance of the smooth muscle in the walls of lymphatic vessels?

Identify critical functions of the lymphatic system: clearance of proteins from the interstitium, reabsorption of filtered fluid, fat absorption, lymphocyte recirculation "patrolling".

Diagram the relationship between interstitial pressure and lymph flow. Explain why edema does not normally develop as interstitial pressure increases.

Explain how edema develops in response to a) venous obstruction, b) lymphatic obstruction c) increased capillary permeability, and d) malnutrition.

Reference values: **lymph flow: 3-4 l/day**.

45. The characteristics of the venous circulation.

Characterize the veins, contrast them to arteries of similar size (number of vessels, wall distensibility). Explain why the volume of the venous system increases significantly with the changes of hydrostatic pressures related to standing up (orthostasis).

Describe the factors promoting venous return (heart pumping: „vis a tergo" and „vis a fronte", dynamic muscle pump, venoconstriction, respiratory pump). Explain why the insufficiency of venous valves deteriorates the function of the muscle pump.

Describe the sympathethic innervation of the veins eliciting vasoconstriction. Define venomotor tone.

46. The regulation of local blood flow.

Define the autoregulation of blood flow. Distuinguish between short-term and long-term autoregulatory responses.

Describe the contribution of myogenic tone to local regulation of blood flow. Describe the Bayliss effect.

Enlist the vasoactive mediators released from vascular endothelium. **Describe the biosynthesis of nitric oxide and its actions on the vascular smooth muscle.**

Describe how the theory of metabolic regulation of blood flow accounts for active hyperemia and reactive hyperemia. Identify the role of P_{O2}, P_{CO2} , pH, adenosine, PGE_2, and K^+-ions in the control of local blood flow.

Starting at the post capillary venule, describe the process of angiogenesis, including the stimulus that initiates new vessel growth. Describe the role of angiogenesis in providing a long-term match of tissue blood flow and metabolic need.

Describe how histamine released from mast cells, bradykinin, prostanoids, and neuropeptides (SP, CGRP) released from polymodal nociceptors contribute to the inflammatory hyperemia. **Describe the triple response of the skin, and the contribution of the axon reflex to it.**

47. Factors determining cardiac output, the Guyton diagram.

Understand the principles underlying cardiac output measurements using the Fick principle, dye dilution, and thermodilution methods.

Know how cardiac function (output) curves are generated and how factors which cause changes in contractility in the heart can alter the shape of cardiac function curves.

Understand the concept of "mean vascular filling pressure", its normal value, and how various factors can alter its value.

Define venous return. Understand the concept of "resistance to venous return" and know what factors determine its value theoretically, what factors are most important in practice, and how various interventions would change the resistance to venous return.

Construct a vascular function curve. Predict how changes in total peripheral resistance, blood volume, and venous compliance influence this curve.

Explain why the intersection point of the cardiac function and vascular function curves represents the steady-state cardiac output and central venous pressure under the conditions represented in the graph.

Use the intersection point of the cardiac function curve and vascular function curve to predict how interventions such as hemorrhage, heart failure, autonomic stimulation, and exercise will affect cardiac output and right atrial pressure. Predict how physiological compensatory changes would alter acute changes.

Reference values: **mean vascular filling pressure: 7 mmHg, cental venous pressure: 0-2 Hgmm**.

48. Short-term control mechanisms of arterial blood pressure.
Define the resting, neurogenic, basal and myogenic tone of resistance vessels.
Describe the sympathethic vasomotor tone: its origin, the neurotransmitter and receptor responsible for the effect. What is the physiological significance of the sympathethic tone? Give examples to organ circulations where the sympathethic vasomotor tone is significant (skin, skeletal muscle splanchnic circulation) and where is negligible (coronary circulation, brain, kidney)
Characterize the reflex circuit elements of the high pressure baroreceptor reflex: 1. activity of the baroreceptors of the carotid sinus and the aortic arch along with their afferent nerves, 2. the connections of the medullary neuronal groups playing a role in the central integration of the reflex, 3. the activity of the sympathethic and the parasympathethic efferents, 4. the effects on the target organs (heart, arterioles, veins)
Describe the significance of the high pressure baroreceptor reflex.
Explain the function of the baroreceptor reflex during postural changes (lying down, standing up).
Blood pressure regulation during emergency situations: 1. describe the circulatory reflexes evoked by hypoxia and/or hypercapnia, and 2. characterize the CNS ischemic pressor response (Cushing reflex).

Reference values: when standing up (orthostasis) the increase of venous blood volume in the lower extremity: 500 ml.

49. Long-term control of arterial blood pressure.
Contrast the siginificance of the renal regulation of extracellular volume and blood volume and the baroreceptor reflex in the regulation of arterial blood pressure
Describe the concept of pressure diuresis.
Explain the neurohumoral reflex mediated by cardiopulmonary (volume) receptors that occur after an acute increase or decrease in arterial blood pressure. Include receptor response, afferent nerve activity, CNS integration (hypothalamus), and effects on target organs (kidney)
Describe the effects of angiotensin II, vasopressin, and atrial natriuretic hormone on arterial blood pressure: direct vascular and indirect renal mechanisms. Give the respective receptors and signal transduction mechanisms mediating the effects of these hormones.

50. Pulmonary circulation.
Compare the pulmonary circulation with the systemic circulation: blood pressure values, vascular resistance, response to hypoxia.
Describe the regional distribution of pulmonary blood flow in a standing human subject. Explain the differences among zones I, II, III in terms of pulmonary vascular pressures and intraalveolar pressures.
Describe how the pulmonary vascular resistance changes with the change in cardiac output and pulmonary arterial blood pressure. Explain the changes with the mechanisms of vascular distension and capillary recruitment.
Describe how pulmonary vascular resistance changes with lung volume. Explain the phenomenon with the changes occurring in extraalveolar and alveolar blood vessels.
Describe the pulmonary hypoxic vasoconstriction, and its role in the regulation of blood flow distribution in the lungs (Euler-Liljestrand reflex).
Describe the effect of inhaled NO on hypoxic vasoconstriction and pulmonary vascular resistance.
Characterize the bronchial circulation.

Reference values: **pulmonary artery systolic/diastolic/mean pressure: 24/9/14 mmHg, pulmonary artery pulse pressure: 15 mmHg, left atrial pressure: 6-8 mmHg.**

51. Skeletal muscle blood flow, the cardiovascular adaptation to work and exercise.

Explain the relative importance of systemic neural and local control mechanisms in the skeletal muscle circulation.

Describe the cardiovascular consequences of exercise on peripheral resistance, cardiac output, A-V oxygen difference, and arterial pressure. Give the contribution of skeletal muscle blood flow to the cardiac output at rest and during exercise.

Describe the redistribution of cardiac output during exercise to the CNS, coronary, splanchnic, cutaneous, and skeletal muscle vascular beds during sustained exercise (distance running).

Contrast the effect of phasic and sustained skeletal muscle contraction on extravascular compression of blood vessels and on central venous pressure. Explain the importance of the muscle pump.

Predict the changes in cardiac output and arterial pressure during the initial and the sustained phases of the Valsalva maneuver.

52. Glomerular filtration: the factors determining the volume and composition of filtrate

Identify the following structures of the glomerular tuft: the afferent and efferent arterioles, glomerular capillary network, mesangium, Bowman's capsule, and the juxtaglomerular apparatus (including the specialized juxtaglomerular arteriole cells and the macula densa).

Describe the three layers comprising the glomerular filtration barrier, and identify podocytes, foot processes, the capillary endothelium, and the basement membrane. Which layers impede the filtration of water, Na^+, inulin, albumin, and red blood cells, respectively?

Define glomerular filtration rate (GFR), renal plasma flow (RPF), and filtration fraction (FF) and give their reference values.

Given the capillary and Bowman's capsule hydrostatic and oncotic pressures, calculate the net filtration force (the effective filtration pressure) at the glomerular capillaries. Describe the changes in net filtration force that occur as blood travels along the glomerular capillary and hydrostatic pressure falls and colloid osmotic pressure increases.

Define the filtration coefficient at the glomerular capillary, describe the factors determining it and explain its role in determining GFR.

Reference values: **GFR: 120-125 ml/min, RPF: 660 ml/min, FF: 0.2**

53. Renal blood flow. The regulation of GFR and RBF.

Describe in sequence the blood vessels through which blood flows when passing from the renal artery to the renal vein, including the glomerular blood vessels, peritubular capillaries, and the vasa recta.

Define renal blood flow (RBF), give its normal value and its contribution to the cardiac output at rest.

Compare blood flow to, and oxygen consumption by, the kidneys with that of skeletal muscle and cardiac muscle. Describe the renal structure, where anaerobic conditions prevail.

Describe the effect of change in the resistance of the afferent arteriole on GFR and RBF, and RPF.

Describe the autoregulation range of RBF/RPF/GFR. From the mechanisms of RBF, RPF, and GFR autoregulation **describe the role of the tubuloglomerular feedback**, the local vasoactive metabolites (paracrine angiotensin II, prostaglandins), and the myogenic response (Bayliss effect).

Describe the effect of low hydrostatic and high colloid osmotic pressures in peritubular capillaries on net proximal tubular fluid reabsorption.

Reference values: **autoregulation range: 80-180 mmHg, RBF 1320 ml/min, RBF is 20-23% of resting cardiac output, normalized renal blood flow 420 ml/min/100g** (cardiac muscle 84, skeletal muscle 2.7, brain 54 ml/min/100 g)

54. The general features of epithelial transport mechanisms in the renal tubuli.

Describe in sequence the tubular segments through which ultrafiltrate flows after it is formed at Bowman's capsule to when it enters the renal pelvis. Identify each structure as being located in the renal cortex or renal medulla. Based on the glomerulus location and the length of the loop of Henle, distinguish between cortical and juxtamedullary nephrons.

Describe the contribution of the major nephron segments to the reabsorption of the filtered load of solute and water (transport capacity, production of concentration gradients).

Make a schematic drawing of the renal epithelium labeling the tight junctions, the apical membrane, and the basolateral membrane. Trace the movement of a compound that travels across an epithelium by a transcellular pathway and a compound that travels via a paracellular pathway. Indicate how water movement is driven by solute movement.

Explain the functional importance of the asymmetric distribution of transport proteins between the apical and the basolateral membrane.

Explain the role of the tight junction in leaky and tight epithelia. Give examples of renal tubular segments with leaky and with tight epithelia.

55. Tubular reabsorption and secretion. Renal clearance.

Define tubular reabsorption and secretion.

Calculate the filtered load, the excretion rate, and the net tubular reabsorption or the net tubular secretion of a freely filtrated X substance, given its plasma and urine concentrations, the GFR and the urine flow rate (minute diuresis).

Explain the clearance principle. Use the clearance equation and appropriate compounds (inulin/creatinine, PAH) to determine the glomerular filtration rate, renal plasma flow, and renal blood flow.

Give the reference values of the clearance for inulin, creatinine, PAH, and glucose. Distinguish between the use of inulin and creatinine clearances as measures of the glomerular filtration rate. Describe the effect of GFR reduction on plasma creatinine concentration and plot the function.

How much is the clearance of a freely filtrated X substance if 1. it is fully reabsorbed (glucose type reabsorption), 2. only partly reabsorbed, 3. there is a net tubular secretion (PAH type transport). (Answers: 1.: Cl=0; 2. 0<Cl<GFR; 3. GFR<Cl≤RPF). Give one-one example for such substances.

Reference values: **inulin clearance=GFR, plasma creatinine: 50-150 µM**, endogenous creatinine clearance: 90-150 ml/min, **PAH-clearance=RPF**

56. Renal tubular transport of organic solutes: glucose, amino acids, ketone bodies, proteins, uric acid, urea, UBG.

The organic solutes reabsorbed with glucose-type reabsorption (monosaccharides, amino acids, ketone bodies).

Renal tubular glucose reabsorption: characterize the luminal and basolateral transport mechanisms.

Define the renal threshold of glucose and tubular maximum (Tmax) glucose. Define glucosuria, and describe the laboratory tests used to detect glucose in the urine.

Describe the osmotic diuresis induced by glucosuria associated with diabetes mellitus.

Describe the fate of the filtered peptides and proteins in the proximal tubuli. Define proteinuria and describe the laboratory tests used to detect protein in the urine.

Describe the active tubular secretion of organic anions in the proximal tubuli.
Describe the transport of uric acid in the proximal tubuli.
Describe the urea reabsorption in the proximal tubuli, and the urea recirculation in the distal nephron segments.
Describe the laboratory tests to detect Bilirubin, UBG, and ketone bodies in the urine.

Reference values: **renal threshold of glucose: 10 mM**, plasma uric acid: 150-500 µM

57. Renal tubular transport of NaCl and water, production of the medullary osmotic gradient.
Calculate the amount of filtered Na^+. Identify the main driving force of Na^+-reabsorption (the basolateral Na^+–K^+-pump).
Describe the luminal mechanisms of Na^+-reabsorption in the proximal tubulus (Na^+-solute, Na^+–H^+-antiporter, paracellular mechanisms), **in the thick ascending limb of the loop of Henle** (Na^+–K^+–$2Cl^-$-symporter), **in the distal convoluted tubulus** (Na^+–Cl^--symporter) **and the collecting duct** (Na^+-channel). **Which transport is under hormonal control?**
Identify the targets of the following diuretics: carbonic anhydrase inhibitors, loop diuretics (furosemid), thiazids, K^+-sparing diuretics (aldosterone-antagonists).
Characterize the renal tubular segments based on their water permeability. **Identify the tubular segment where water permeability is under hormonal control.**
Define glomerulotubular balance. Describe the proximal tubular reabsorption responsible for glomerulotubular balance.
Describe the changes of osmolarity in the tubular fluid and in the interstitial fluid from the loop of Henle, and its importance for the dilution and concentration of urine.
Explain the countercurrent multiplier mechanism of the loop of Henle: what is the role of the countercurrent design and the different transport mechanisms in the descending and the ascending limbs in the production of the medullary hyperosmotic gradient? Contrast the mechanism of NaCl reabsorption in the thick ascending limb with the thin ascending limb of the long-loop juxtamedullary nephrons, and explain the role of urea.
Describe the role of the countercurrent organization of renal medullary blood flow through the vasa recta on retaining the medullary osmotic gradient (countercurrent exchanger).

Reference values: **maximal osmotic concentration** in the outer medulla (short-loop nephron): 600 mosmol/l**, in the inner medulla (long-loop nephron): 1200 mosmol/l; max. urea concentration in inner medulla: 600 mM.**

58. The physiology of the urinary tract. Micturition.
Describe the motor functions of the upper urinary tract.
Explain the visceral sensory, autonomic (sympathethic and parasympathethic) and somatic motor innervation of the urinary bladder and the urethral sphincters. Identify the structures critically important for urine continence as well as for micturition located in the lumbar and sacral segments of the spinal cord, and in the pons.
Make a schematic drawing of a cystometrogram. Show on the plot the receptive relaxation of the urinary bladder, and explain its mechanisms.
Describe the reflex arc of the micturition reflex. What is the significance of the measurement of urine flow rate (uroflowmetry)?
Define the terms passive and active incontinence.

59. Principles of the regulation of the gastrointestinal tract.

Describe the general functions of the gastrointestinal system (GIS) (motility, secretion, digestion, absorption). Starting from the oral cavity, describe where the above listed functions of the GIS are predominantly regulated by the central nervous system (oral cavity, salivary glands, esophagus, proximal stomach, rectum) or by local neural/humoral as well as by hormonal mechanisms (distal stomach, small intestine, colon)!
Describe the major anatomical characteristics of the enteric nervous system and the major cellular divisions of enteric ganglia (sensory nerves, interneurons, and motor neurons). Given a cross section of the bowel wall, identify the anatomical positions and major characteristics of the myenteric and submucosal plexi.
Explain the interactions between the enteral nervous system and the sympathethic/ parasympathethic divisions of the autonomic nervous system.
Describe the reflex types of the GIS (local, short, and long-looped reflexes). Describe the respective reflex arches, the pathways and neurotransmitters involved in the neuronal regulation of GIS function.
Give the locations and the cell types of the endocrine cells, responsible for the production of the major GIS hormones: gastrin, secretin, CCK, GIP, GLP, and motilin.
Understand how the physical and chemical compositions of luminal contents are sensed and the cellular and systemic responses to luminal stimuli.

60. Special functional features of the gastrointestinal smooth muscle.
Describe the characteristics of the spontaneous and stimulated electrical activity of GI smooth muscles (electrical slow waves, action potentials, and contraction).
Describe the anatomical locations and role of interstitial cells of Cajal as slow wave pacemakers and mediators of inputs from the enteric nervous system.
Describe major motor patterns in the GI tract and their functions during fasting (migrating motor complex or MMC) and during digestion.
Describe the nervous regulation of peristaltic movement. **Define the Bayliss-Starling law of the gut.**
Describe how extrinsic nerves (sympathetic and parasympathetic) affect motor patterns.
Describe the functional importance of tonic inhibitory input from enteric motor neurons in the GI tract and how loss of this form of regulation might cause inappropriate GI motility.
Describe how distension of organs affects GI reflexes and alters responses to other regulatory inputs.
Understand how abnormal distension can cause GI pain and lead to abnormal motility.

61. The splanchnic circulation
Give the percent contribution of splanchnic blood flow from the resting cardiac output. Contrast the local and neural control of the splanchnic circulation.
Describe the role of the hepatic portal system in the function of the GIS, and the hepatic artery in providing flow and oxygen to the liver. **Describe the hepatic microcirculation**, the morphological and functional features of the sinusoid capillaries. Describe how the increase in venous pressure will lead to the development of ascites.
Describe how the GI circulation is adapted for secretion and absorption. Describe the role of the autonomic nervous system in the adaptation of blood flow to GI secretion.

62. Functions of the upper GI tract: chewing, salivation, swallowing.
Describe the motor mechanisms of food intake: sucking, biting, chewing (mastication).
Describe the volume and composition of salivary fluid coming from major salivary glands. Understand how acinar secretions are modified by duct cells to produce the final salivary fluid.
Describe the physiological function of the components of saliva. State the components of the saliva important in oral hygiene.

Describe the stimuli and neural pathways involved in promoting salivary secretion. Explain why the the composition of saliva will be different in response to sympathethic or parasympathethic stimulation.
Know the normal range of resting luminal esophageal pressures, how esophageal pressure is measured in the clinic, and why luminal pressure varies with the respiratory cycle.
Describe the afferents that initiate swallowing, the motor pathways and general targets for innervation that accomplish the swallowing reflex, and major nuclei of in the brain stem that integrate these afferent inputs.
Understand the differences in the neural and muscular composition and function in the upper versus lower esophagus. Explicitly consider the upper and lower esophageal sphincters (UES and LES). What is the mechanism of the sphincter tone in the UES and the LES, respectively? What is the mechanism of the peristaltic wave in the upper and the lower esophagus?
Distinguish between primary and secondary esophagus peristalsis. Define the terms: dysphagia, achalasia, aspiration.

63. Motor functions of the stomach. Vomiting (emesis).
Describe the functional divisions of the stomach concerning gastric motility patterns.
Describe gastric motility in the interdigestive periods: MMC.
Describe gastric filling: the short-loop and long-loop (local and central) neural reflexes eliciting the receptive relaxation of the proximal stomach.
Describe gastric emptying: describe the frequency and the progression of peristaltic waves across the body and antrum of the stomach. Explain the functions of gastric peristalsis (mixing, grinding, propulsion).
Describe how the physical and chemical composition of a meal is sensed by the stomach and duodenum to affect the rate of gastric emptying (neural and hormonal mechanisms).
Describe the mechanism of vomiting. List some stimuli that can trigger vomiting.

64. The mechanism and regulation of gastric juice secretion.
Describe the functional divisions of the stomach concerning gastric juice secretion (HCl producing oxyntic region, mucus producing antral region).
Describe the products of different cell types in the glands of the oxyntic area: the parietal cells (HCl, intrinsic factor), chief cells (pepsinogen), and mucosal cells (bicarbonate rich mucus)
Describe the cellular mechanism of HCl production.
Explain the role of HCl in the digestion of proteins and carbohydrates. How is the activation of pepsinogen triggered? What is the role of HCl in the defense against infections?
Enlist the neurotransmitter (Ach), **the paracrine substance** (histamine), **and the hormone** (gastrin) **directly stimulating the parietal cells**: their source, receptors, and signal transduction mechanisms.
Describe how **the regulation of gastrin secretion** integrates the information from the central and enteral nervous system as well as from the gastric contents. Describe the role of GRP and somatostatin.
Describe the role of duodenal contents in regulating gastric secretion. Give the neuronal and hormonal mechanisms of the intestinal inhibition.
List the mechanisms contributing to gastric mucosal defense.
Describe the reference values of esophagus and gastric pH, their determination (24 pH testing)

Reference values: **gastric juice secretion: 1-1.5 l/day; gastric juice H^+ concentration: 70-80 mmol/L; gastric juice pH: 1.10-1.15**; esophagus pH >4.0 >95% of the day.

65. The exocrine pancreas: secretion and regulation.

List the major components secreted by the exocrine pancreas and the principal cell types involved in this secretion.
Describe the main digestive enzymes of the pancreas and the mechanism by which pancreatic zymogens are activated in the small intestine. Explain the role of the duodenal enteropeptidase (enterokinase).
Describe the process of digestive enzyme synthesis and packaging and how this process maintains the integrity of the pancreas.
Describe the mechanisms by which chyme from the stomach is neutralized in the duodenum.
Describe the mechanisms by which HCO_3^- is secreted by pancreatic ductal cells.
List the stimuli that release secretin and CCK and explain the route by which these regulatory peptides stimulate the pancreas.
State the effects of the autonomic nerves to the pancreas and vago-vagal reflexes on pancreatic secretion.

Reference values: **pancreatic juice production: 500-700 ml/day**

66. The bile: secretion, storage, mobilization, regulation.
Describe the cellular mechanisms for the hepatic uptake, conjugation, and secretion of bile salts and bilirubin.
List the water, ionic, bile salt, phospholipids, cholesterol, bicarbonate, xenobiotics and bilirubin components of bile as secreted by the liver and after modification by the gallbladder.
Explain the mechanisms stimulating gall bladder contraction and the secretion of bile through the sphincter of Oddi into the small intestine.
Describe the amphipathic structure of bile salts, and describe how this property assists the solubilization and digestion of fats.
Explain the mechanism of reabsorption of bile acids/salts in the small intestine (ileum).
Describe the enterohepatic circulation, including any different handling among primary and secondary bile salts and bile acids.
Describe the secretory function of the hebatobiliary epithel and how bile participates in the control of duodenal pH. How is HCO_3^- secretion controlled in the hepatobiliary system (secretin)?.

Reference values: **bile secretion: 600 ml/day**

67. The small intestine: digestion and absorption.
Describe how rates of absorption are affected by the macroscopic and microscopic architecture of the gut epithelium. Explain the importance of the unstirred water layer on the surface of the brush-border.
Describe the renewal of the GI cells and explain how these cells form a barrier and a selective gate in the secretory and absorption processes.
Describe the sequential digestion of ingested starch by enzymes of the salivary glands, pancreas, and the intestinal apical membrane. Membrane transport mechanisms for carbohydrates in the enterocytes.
Describe the sequential digestion of ingested proteins by gastric pepsin, pancreatic enzymes, and enzymes at the intestinal apical membrane. Membrane transport mechanisms in the absorption processes.
Describe the mechanisms and molecules mediating the solubilization and digestion of lipids in the small intestine. **Describe the mechanisms for the uptake, processing and release of lipids by the small intestinal epithelium.**
Describe the composition and formation of chylomicrons, their movement across the enterocyte basolateral membrane, and the route of entry into the cardiovascular system.

Describe common causes of steatorrhea, and predict effects of steatorrhea on absorption of fat-soluble vitamins.
Describe the location and the mechanisms that mediate the intestinal absorption (trans-epithelial movement) of water, the major electrolytes, iron and calcium.

Reference values: **intestinal juice secretion: 2-3 L/day, intestinal fluid reabsorption: 5-6 L/day**

68. The functions of the colon. Defecation.
Describe the motility patterns in different regions of the colon: haustration, antiperistalsis, mass-peristalsis, defecation.
Explain how motility of the colon affects the reabsorption of water and electrolytes.
Describe the mechanisms, localization and regulation of colonic sodium and chloride absorption.
Describe the mechanisms mediating colonic bicarbonate and potassium transport.
Describe the role of the colon in forming the normal intestinal microbiota.
Defecation: Describe the defecation reflex and voluntary control of the reflex, define the terms passive and active incontinence.

Reference values: **fluid reabsorption in the colon: 1.5-2 L/day, water-content of the faeces: 75-150 ml/day**

69. Nutrition: energy metabolism, the role of macronutrients in energy intake.
Name the types of macronutrient compounds (carbohydrates, proteins and lipids). Compare the energy content of the macronutrients – biological caloric values.
Explain the strategies for the measurement of the energy production of the body. (direct- and indirect calorimetry).
Define the respiratory quotient (RQ) and the caloric equivalent for oxygen values. Caloric equivalent values of different macronutrient compounds. Respiratory quotient and caloric equivalent values measured after consumption of normal mixed food.
Define the basal metabolic rate (BMR). Describe the standard conditions for measurement of the BMR. List the major factors affecting the BMR of individuals (age, gender, endocrine status).
Explain the effect of food ingestion on the metabolic rate (specific dynamic effect – diet-induced thermogenesis (DIT)). Describe the effect of protein-rich diet on the metabolic rate.
List the factors determining the daily energy expenditure (BMR+DIT+physical activity). Describe the effect of physical activity on the metabolic rate, leisure rate, limits of maximal energy expenditure.
Introduce the concept of energy balance of the body.
Dietary proteins: **Describe sources and minimal daily allowance of proteins**, importance of the essential amino acids, biological value (grade) of the dietary proteins. Compare the protein content and quality of food of animal and plant origin.
Dietary carbohydrates: Describe types of carbohydrates (sources), biological importance, their anti-ketogenic effect, their contribution to the energy production of the body.
Dietary lipids: Describe the sources of lipids, essential fatty acids, their biological importance, their contribution to energy production of the body.

Reference values: conversion of Calorie/kcal values to Joule values: 1 Cal/kcal=4.2 kJ; biological caloric values of carbohydrates/proteins/lipids: 17.2/17.2/39 kJ/g; **RQ values** of carbohydrates/proteins/lipids/**mixed food**: 1.0/0.8/0.7/**0.82**; **caloric equivalent values for oxygen:** carbohydrates/proteins/lipids/**mixed food**: 21.2/19.2/19.7/**20.2 kJ/L O_2**; **BMR adult male/female: 7100/6300 kJ/day**; leisure rate of adult male/female 9600/8400 kJ/day corresponds to 115-100 W; recommended daily allowance of proteins/carbohydrates/lipids: 60-80/300/50-150 g/day; WHO recommendation for optimal protein intake: 1-1.5 g/kg b.w./day

70. Nutrition: water, minerals, vitamins, dietary fibers.

Give the normal range of dietary water intake, and the sources of water getting into the GIS.
Describe the concept and give the definition of trace elements. Explain the biological/biochemical significance of trace elements. List and describe the physiological role of some of the major trace elements such as Fe, Zn, Cu, Se, I, F etc.
Describe the vitamin concept, and give the definition of vitamins. List the major classes of the vitamins. Define the terms provitamin, antivitamin, and provide some examples for such compounds used in the medical praxis.
Describe the concepts of hypo- and hypervitaminosis, and the importance of recommended daily allowance (RDA) values.
Water soluble vitamins: list the RDA values, major biochemical roles and the symptoms of vitamin deficiencies for thiamin (B1), niacin (B3), cyanocobalamin (B12) and ascorbic acid (C).
List the types, sources, biological significance of lipid soluble vitamins. **Describe the symptoms of vitamin** A**, D and K deficiencies**.
Dietary fibers: Describe the sources, their biological role (gut motility, effects on the microbiota of the colon).

Reference values: d**ietary water intake: 1.5-2 L/day; secreted fluid volume in the whole GIS: 6-8 L/day; RDA values of vitamins: thiamin (B1): 1-1.5 mg/day; niacin (B3): 15-25 mg/day; cyanocobalamin (B12): 1.5-3 µg/day; ascorbic acid (C): 65-75 mg/day; retinol (A): 0.8-1.1 mg/day**

71. Principles of endocrine control systems.

Give the definitions of hormone and hormonal control, **describe the classification of hormones based on their chemical structure** (eg amino acids, biogenic amines, peptides, proteins, steroids) and also the classification of hormone receptors (membrane receptors and intracellular receptors). **Give 1-1 examples from each group**.
Explain the types of hormonal effects using 1-1 example (stimulatory, inhibitory, permissive effects. Define intracrine effect, give an example of such effect.
Understand the effects of plasma hormone binding proteins on access of thyroid hormones and steroid hormones to their sites of action and degradation and on the regulation of hormone secretion.
Explain the bases of hormone measurements and assessment of biological activity.
Explain the effects of secretion, excretion, degradation, and volume of distribution on the concentration of a hormone in the blood plasma.
Explain the importance of patterns of hormone secretion, such as pulsatile, diurnal, and menstrual. Give examples.

72. Characterization of the hypothalamo-hypophyseal (neuroendocrine) system.

Describe the anterior and posterior pituitary lobes with respect to cell types, vascular supply, development, and anatomical connection to the hypothalamus. Define neurosecretion.
Describe the 3 major families of the anterior pituitary hormones and their biosynthetic and structural relationships.
Identify appropriate hypothalamic factors (releasing and inhibiting hormones) that control the secretion of each of the anterior pituitary hormones, and describe their route of transport from the hypothalamus to the anterior pituitary.
Understand negative feedback control of anterior pituitary hormone secretion at multiple levels.

73. Thyroid hormones: biosynthesis, regulation, effects.

Describe the enteral absorption and the uptake of iodide in the thyroid gland.

Identify the steps in the biosynthesis, storage, and secretion of tri-iodothyronine (T3) and thyroxine (T4).

Describe the function of the hypothalamus-anterior pituitary-thyroid gland axis, the negative feedback regulation of T4/T3 secretion. Describe the trophic effect of TSH on the thyroid gland.

Describe the plasma transport proteins involved in blood transport of thyroid hormones. Explain the importance of thyroid hormone binding in blood on free and total thyroid hormone levels.

Understand the significance of the conversion of T4 to T3 in extra-thyroidal tissues, give the name of the enzyme responsible for the conversion. Define intracrine effect.

Describe the localization of thyroid hormone-receptors, the molecular mechanism of ligand-receptor interaction.

Describe the physiologic effects and mechanisms of action of thyroid hormones on energy metabolism, carbohydrate, fat and protein metabolism.

Describe the effect of thyroid hormones on the cardiovascular system that enable the metabolic effects.

Understand the causes and consequences of a) over-secretion and b) under-secretion of thyroid hormones. Explain what conditions can cause an enlargement of the thyroid gland.

Reference values: iodide RDA: 0,5 mg/day

74. Hormone synthesis in the adrenal cortex. The glucocorticoids: biosynthesis, regulation, effects.

Identify the functional zones (one medullary and three cortical zones), innervation, and blood supply **of the adrenal glands and the principal hormones secreted from each cortical zone** (mineralocorticoids, glucocorticoids, androgens).

Describe the biosynthesis of the adrenal steroid hormones (glucocorticoids, mineralocorticoids, and androgens).

Describe the components of the neuroendocrine (hypothalamo-pituitary-adrenal, HPA) axis that control glucocorticoid secretion. The corticotroph cells of the anterior pituitary. POMC.

Understand the differential regulation of cortisol versus aldosterone release. Describe the trophic effect of ACTH on the adrenal cortex and its significance concerning drug therapies involving glucocorticoid treatments.

Understand the cellular mechanism of action of adrenal cortical hormones. Describe the mechanism of the so-called pre-receptor specificity responsible for the selective effect of mineralcorticoids.

Identify the major physiological and pharmacological actions of glucocorticoids on energy metabolism, on the carbohydrate, fat and protein metabolism, on the cardiovascular system, on the immune system , on the central nervous system, an on other endocrie systems that complement the metabolic effects to promote survival of the organism.

Identify the consequences of a) over-secretion and b) under-secretion of glucocorticoids.

75. The endocrine pancreas.

Identify the major hormones secreted from the endocrine pancreas, their cells of origin, and their chemical nature. Describe the functional organization of the Langerhans islet.

List the major target organs or cell types for insulin, the major effects of insulin on each, and the consequent changes in concentration of blood transport nutrients.

Identify the time course for the onset and duration for the biological actions of insulin. Describe the methods assessing insulin secretion and insulin sensitivity.

Understand the relationship, between blood glucose concentrations and insulin secretion. Define the term „incretin", and describe the glucose-dependent release of an incretin and its effects.

Describe the roles of neural input and gastrointestinal hormones on insulin secretion. List the factors that modulate the secretory response.
Describe the control of glucagon secretion.
List the target organs or cell types for glucagon and describe its principal actions on each.
Describe the consequences of over-secretion or under-secretion of insulin. Diabetes mellitus.

76. The integrated endocrine control of metabolism. Stress and general adaptation syndrome.
Identify the normal range of plasma glucose concentrations, and list the chemical forms and anatomical sites of storage pools for glucose and other metabolic substrates.
Identify the hormones that promote the influx and efflux of glucose, fat, and protein into and out of energy storage pools and their impact on the uptake of glucose by tissues. Establish specific roles for insulin, glucagon, growth hormone, leptin, ghrelin, and catecholamines.
Describe the changes in metabolic fuel utilization that occur in long- and short-term fasting and in acute and sustained exercise. Understand how increases or decreases in hormone secretion produce these changes.
Describe the role of appetite and metabolic rate in the maintenance of long-term energy balance and fat storage. **Identify the factors that regulate appetite and fuel oxidation.**
Give the definitions of stress and stressor. Describe the 3 phases of the general adaptation syndrome (GAS) during the stress response.
Describe the interactions of adrenal medullary and cortical hormones in response to stress.

77. Nutrition: The internal control of food intake.
Describe how does energy intake and the metabolic rate affect the energy balance of the body and the deposition of fat into the adipose tissue. Name the major factors influencing the food uptake and catabolic processes.
Describe the evaluation of the body composition, evaluation of the grade of obesity (BMI, lean body mass)
Define hunger and satiety.
Name the hypothalamic centers involved in the regulation of food intake: localization and neurochemical phenotype of orexigenic and anorexigenic neuron groups. Name orexigenic and anorexigenic mediator substances (neuropeptides: NPY, MSH, CART, AgRP). Describe the role of central and peripheral glucose sensors.
Describe the peripheral signals affecting the central regulation: mediators released from the GI tract (ghrelin, CCK, insulin). Describe the role of the chemosensitive vagal afferents. Characterize the biological effects of signal molecules produced by the adipocytes: leptin and related adipokines.
What are the physiological correlates of carbohydrate and fat appetite?
Describe the central regulation of water (thirst) and salt intake.

78. The concentration and dilution of urine. Osmoregulation.
Identify major routes and normal ranges for water intake and loss.
Describe the changes in body fluid volume and osmolality caused by a net water loss in the body. Predict how this disturbance would alter the rate of urine production and the osmotic composition of urine?
Describe the changes in body fluid volume and osmolality caused by a net NaCl loss in the body. Predict how this disturbance would alter the rate of urine production and the osmotic composition of urine?
Localize the cells producing arginine-vasopressin (AVP), and describe the mechanism of neurosecretion from the posterior pituitary gland.
Describe the stimuli and mechanisms that control AVP secretion.

List the target cells for vasopressin and explain why AVP is also known as antidiuretic hormone (ADH).
Identify the tubular segment, where AVP increases water and urea permeability, and describe the cellular mechanism of its action (V_2-receptor, aquaporins, urea transporter). Explain how these affect urine concentration/dilution.
Predict the consequence on urine concentrating ability if the medullary osmotic gradient is disrupted. Following disruption, describe how the osmotic gradient would be re-established.
Given urine and plasma osmolarities and urine volume, calculate osmolar and free water clearance.
Identify expected free water clearance for an individual producing either a dilute or a concentrated urine.
Distinguish between central and nephrogenic diabetes insipidus and explain the difference between the polyuria elicited by diabetes insipidus and by osmotic diuresis.

Reference values: **urine osmotic concentration: 70-1200 mosmol/L; urine specific gravity: 1001-1030 g/l (blood plasma 1012 g/l); diuresis and its interpretation: <100 ml/day: anuria; 100-600 ml/day: oliguria, 600-2500 ml/day: normal range, >2500 ml/day: polyuria**, in diabetes insipidus can reach 18-25 l/day!; minimal daily excreted osmotic activity: 650 mosmol.

79. Volume regulation (the regulation of Na^+ metabolism and extracellular fluid volume).
Identify the normal range of dietary Na^+ intake and major routes of Na^+ loss from the body. Define the role of Na in maintaining extracellular fluid volume.
Identify the the alterations in Na+ reabsorption in conditions of volume depletion (hypovolemia), and volume expansion (hypervolemia).
Describe the mechanisms involved in the monitoring of ECF volume (e.g., high-pressure baroreceptors, low-pressure cardiopulmonary stretch receptors, the juxtaglomerular apparatus, ANP producing atrial cardiomyocytes).
Explain the regulation of renin secretion. Diagram the activation of the renin-angiotensin system (RAS).
Describe the effects of angiotensin II.
Identify the major mineralocorticoid hormone, describe its production, its target cells and its major biological actions.
List the physiological stimuli regulating aldosterone secretion. Contrast these stimuli with the effects of aldosterone on renal excretion of Na^+ and K^+, respectively.
Describe the causes and the consequence of reduced or elevated secretion of aldosterone.
Describe the regulation of ANP secretion, and the renal as well as the extrarenal effects of ANP.
Describe the integrated regulation of renal tubular Na^+-reabsorption. Give details on the role of angiotensin II, aldosterone, ANP and sympathethic activity.

Reference values: **Na^+ dietary intake/loss: 100-400 mmol/day**, this corresponds with ~5-30g table salt consumption.

80. The regulation of K^+ metabolism.
Identify the normal range of dietary K^+ intake and major routes of K^+ loss from the body.
Define the role of extracellular K^+ in maintaining normal nerve, heart muscle and skeletal muscle function.
Describe K^+ distribution within the body, extrarenal K^+ homeostasis, and the role insulin, epinephrine, and aldosterone play in the movement of K^+ between intracellular and extracellular pools. Describe the K^+ shift caused by acidosis.
Calculate the normal filtered load of K^+. Identify the tubular sites of K^+ reabsorption and secretion.

Describe the factors that regulate K^+ secretion in the collecting duct (i.e., aldosterone, plasma K^+) **and distinguish these from factors that alter secretion at this site** (i.e., luminal fluid flow rate, acid-base disturbances, anion delivery).

Reference values: **K^+-intake/loss 50-100 mmol/day**

81. The regulation of Ca^{2+} and phosphate metabolism.

Identify the normal range of dietary Ca^{2+} and phosphate intake, major storage pools of Ca^{2+} and phosphate, and major routes of Ca^{2+} and phosphate loss from the body.
Calculate the normal filtered load of Ca^{2+}. **Identify the tubular sites of Ca^{2+} reabsorption**. Calculate the normal filtered load of phosphate. Identify the tubular sites of phosphate reabsorption. Identify the tubular transport mechanisms that are hormonally regulated.
Know the cells of origin for parathyroid hormone (PTH), its biosynthesis and degradation.
Describe the regulation of PTH secretion and the role of the Ca^{2+}-sensing receptor.
List the target organs and cell types for PTH and describe its effects on each.
Understand the causes and consequences of a) over-secretion, and b) under-secretion of PTH, as well as its therapeutic use. Explain the symptoms of latent tetany (Chvostek's and Trousseau's sign).
Identify the sources of vitamin D and diagram the biosynthetic pathway and the organs involved in modifying it to the biologically active 1,25(OH2)D3 (1-25 dihydroxycholecalciferol, calcitriol).
Identify the target organs and cellular mechanisms of action for calcitriol.
Describe the negative feedback relationship between PTH and calcitriol.
Describe the consequences of vitamin D deficiency and vitamin D excess.
Name the stimuli that can promote secretion of calcitonin, its actions, and identify which (if any) are physiologically important.

Reference values: **Ca^{2+} intake/absorption 1000/200 mg/day**, also 25/5 mmol/day; Ca^{2+} loss: 2,5-7,5 mmol/day, **vitamin D RDA: 600 IU/day** (between 1-70 years of age)

82. Acid-Base Balance

Identify the normal range of pH values. Describe the role of buffers in maintaining pH, including the roles of the lungs and kidneys.
Describe the respiratory and renal regulation of the CO2/$HCO3^-$ buffer system, which allows a buffer with a pK of 6.1 to be physiologically important in the maintenance of the normal plasma pH of 7.4.
Distinguish between CO2-derived (volatile acid) and nonvolatile acid, the amounts produced each day through dietary intake / cellular metabolism, and the normal routes of loss from the body.
Identify the major sites of $HCO3^-$ reabsorption (and secretion) along the nephron, emphasizing the importance of H+ secretory mechanisms in this process. Describe the cellular mechanisms responsible for net transepithelial movement of $HCO3^-$.
Describe the adjustments in $HCO3^-$ reabsorption (H^+ secretion) by alterations in systemic acid-base balance.
Describe net acid excretion by the kidneys, titratable acid, the importance of urinary buffers, and the production and excretion of ammonium. Distinguish between the reclamation of filtered bicarbonate and the formation of new bicarbonate.
Given a sudden increase or decrease in pH, identify the magnitude and the time course of the compensations that act to minimize change in pH of the body fluids, including a) buffers, b) respiratory adjustments, and c) renal adjustments.
From blood values, identify simple and mixed metabolic and respiratory acid-base disturbances.
Distinguish between increased and normal anion gap metabolic acidosis.
Describe the renal and respiratory compensations of acid-base disturbances.

Reference values: **arterial blood pH: 7,37-7,43, standard bicarbonate: 24 mmol/L, buffer base (BB): 44-49 mmol/L, base excess (BE): +2,5– -2,5 mmol/L**, anion gap: 8-12 mmol/l; acid productions (nonvolatile)): 50-100 mmol/day, urine pH: 4.0-8.0; tubular bicarbonate „ reabsorption": 4300 mmol/day, new bicarbonate production: 50-100 mmol/day

83. Thermoregulation, cutaneous blood flow.

Diagram the thermal balance for the body, including metabolic heat production, heat exchange mechanisms (convection, conduction, radiation), and heat loss through evaporation.
Contrast the stability of body core with the variability of body shell (skin) temperature. Give the reference values of core body temperatures in humans, the circadian changes in core temperatures and also the dependence of core temperature on the menstrual cycle.
Define the thermoneutral comfort zone.
Enlist the major physiologic mechanisms preventing from the development of either hypethermia or hypothermia.
Metabolic heat production: the respective contributions of basal metabolic rate, physical exercise, and shivering to heat production. The Van't Hoff's rule. Non-shivering thermogenesis: the structure and function of brown adipose tissue, the control of its activity.
The control mechanisms of cutaneous blood flow: specific features of the microcirculation in acral and non-acral regions. Contrast local and neural control of cutaneous blood flow. Discuss the unique characteristics of skin blood flow that are adaptive for body temperature regulation.
Describe the structure, function, and neuronal control of eccrine sweat glands. Describe the cellular mechanisms of fluid secretion by the secretory coil and the ductal NaCl reabsorption.
Describe the neuronal components of thermoregulatory reflexes: peripheral and central thermoreceptors, the neuronal groups in the preoptic area, the hypothalamus, the brain stem and the spinal cord and their connections to form negative-feedback thermoregulatory control circuits.
Define the thermoregulatory „set point" .
Explain how the change in core temperature that accompanies exercise or passive heat accumulation differs from fever produced by infections (such as influenza), which alter the thermoregulatory set point.
List and describe the physiological changes that occur as a result of acclimatization to heat and cold.

Reference values: **core body temperature: 37 °C (36,2-37,5 °C), thermoneutral zone (naked man): 25-27 °C.**

84. Sports physiology.

Describe the possible energy sources, basic pathways of energy metabolism and hormonal regulation of metabolism of the exercising skeletal muscle.
Classify muscle fibers according to their bioenergetics.
Explain how the duration and the intensity of exercise determine the predominant metabolic pathway and the main fuels of striated muscle.
Outline the connection between the ratio of the various muscle types and the predicted athletic success of an individual.
Explain different methods for the measurement of energy expenditure during exercise. Define fatigue and exhaustion and mention some of their possible underlying mechanisms.
Characterize quantitatively the acute cardiorespiratory effects of exercise (heart rate, cardiac output, blood pressure, respiratory rate, lactate threshold, ventilation and oxygen uptake (V_{O2})).
Describe the cardiovascular, respiratory and muscular effects of training. Compare the above mentioned parameters in untrained and trained subjects at rest and during exercise.

List the factors determining performance in sports! (natural endowment = genetic factors, training, physiological status = neuromuscular and cardiorespiratory systems, psychological factors = motivation and tactics).
Explain the impact of food and fluid intake (amount, composition and timing) in optimizing performance. List some ergogenic substances.

Reference values:

variable	pretraining	posttraining	world class endurance runner
Heart rate HR_{rest} (beats/min)	75	65	45
Heart rate HR_{max}(beats/min)	185	183	174
Stroke volume SV_{rest} (ml)	60	70	100
Stroke volume SV_{max} (ml)	120	140	200
Systolic arterial BP at rest (mmHg)	135	130	120
Blood volume (L)	4,7	5,1	6
Max. ventilation V_{max} (L/min)	110	130	190
Max. blood lactate level (mmol/L)	7,5	8,5	9
Max. oxygen uptake Vo_{2max}(mL/bwkg/min)	40	50	80

85. The development and physiology of the male reproductive system
Define chromosomal, gonadal and somatic sex.
Compare and contrast the actions of testosterone, dihydrotestosterone, estradiol, and Müllerian inhibitory factor in the development of the male and female reproductive tracts.
Describe the physiological functions of the major components (testis, epididymis, ductus deferens, seminal vesicle, prostate) of the male reproductive tract.
Describe spermatogenesis and the role of Sertoli cells, Leydig cells and the basement membrane in this process. Describe the blood-testis barrier.
Describe the endocrine regulation of testicular function: the role of the GnRH pulse generator, FSH, LH, testosterone, and inhibin.
Describe the, biosynthesis, mechanism of transport within the blood, metabolism and elimination of testosterone and related androgens.
List the major target organs and cell types for testosterone and other androgens. **Describe the actions and cellular mechanisms of testosterone** and related androgens.
Identify the consequences of over-secretion and under-secretion of testosterone for a) prepubertal and b) postpubescent males.

86. The physiology of the female reproductive system, the menstrual cycle.
Describe oogenesis and its relationship to changes in the ovarian follicle. Explain the roles of FSH, LH, estradiol, and inhibin in oogenesis and follicular maturation.
Describe ovulation and the formation and decline of the corpus luteum and the roles of hormones in each of these processes.
Describe the hormonal regulation of estrogen and progesterone biosynthesis and secretion by the ovary. Identify the cells responsible for their biosynthesis, the mechanism of their transport in the blood, and how they are degraded and removed from the body.
List the major target organs and cell types for estrogen action and describe its effects on each.
Describe the actions and cellular mechanisms of estrogen.

List the principal physiological actions of progesterone, its major target organs and cell types, and describe its effects on each.
Describe the actions and cellular mechanisms of progesterone and other progestins.
Graphically illustrate the timing of changes in blood levels of FSH, LH, estradiol, and progesterone, and correlate these with structural changes in the endometrium and the ovary seen during the menstrual cycle.
Describe how the changes in ovarian steroids produce the proliferative and secretory phases of the uterine endometrium and menstruation and the changes in basal body temperature during the menstrual cycle.
Explain the physiological basis of steroid hormone contraception.

Reference values: length of menstrual cycle is 25-30 days; length of menstruation 4-6 days; duration of LH surge: 10-12 hours.

87. The physiology of the sexual act, fertilization, and implantation.
Describe the neural, vascular, and endocrine components of the erection, emission and ejaculation response.
Describe the neural vascular, and endocrine components of the changes in the female reproductive organs associated with sexual arousal and orgasm.
Describe the process of fertilization, including capacitation and the acrosome reaction, and the movement of the blastocyst to the uterus. Describe the process of implantation.

Reference values: volume of semen: 1,5-5,0 ml, sperm concentration >15 (20-40) million/ml, >60% motile; duration of oocyte migration 1-2 days; implantation of the blastocyst: 7 days after ovulation.

88. The neuroendocrine control of pregnancy, parturition and lactation.
List the protein hormones secreted by the placenta and **describe the role of human chorionic gonadotropin (hCG) in the rescue of the corpus luteum in maintaining pregnancy early post-implantation.** Explain the hormonal basis of pregnancy tests
Describe the interactions between the placenta and the fetus in the pathway for production of estrogens during pregnancy (the so-called fetoplacental unit).
Describe further hormonal systems determining intrauterine development of the fetus (insulin, thyroid hormones).
Discuss the roles of sex steroids, oxytocin, relaxin, and prostaglandins in the initiation and maintenance of parturition.
Explain the role of hormones in mammary gland development during puberty, pregnancy, and lactation.
Explain the basis for the inhibition of milk secretion during pregnancy and the initiation of lactation after parturition.
Describe the neuroendocrine regulation of milk secretion and milk ejection. Enlist the stimuli responsible for the release of oxytocin, and the effects of oxytocin (Ferguson-reflex).

Reference values: length of pregnancy: 40 weeks.

89. The fetal circulation, the cardiorespiratory adaptation of the neonate.
Describe the progressive changes in maternal blood volume, cardiac output, and peripheral resistance during pregnancy and at delivery.
Contrast the blood flow pattern in the fetus with that of a normal neonate, including the source of oxygenated blood.

Describe the function in utero of the fetal ductus venosus, foramen ovale, and ductus arteriosus. Explain the mechanisms causing closure of these structures at birth.
Discuss the relative differences in oxygen saturation and pressure for blood in the major blood vessels and cardiac chambers of the fetus. Explain how these values change at birth.
Explain the cause of neonatal jaundice (icterus neonatorum).

90. Physiology of growth and puberty.
List the hormones and paracrine mediators that play an important role in extrauterine somatic growth (growth hormone, IGF1, sex steroids, calcitriol, thyroid hormones, glucocorticoids).
Describe the relationship between growth hormone and the insulin-like growth factors and their binding proteins in the regulation of growth.
Explain the regulation of growth hormone secretion. Identify the roles of hypothalamic factors, glucose and IGF-I. Describe the circadian rhythm of growth hormone secretion.
Identify the target organs or cell types for insulin-like growth factors that account for longitudinal growth.
Describe the metabolic and growth promoting actions of growth hormone.
Describe the consequences of growth hormone overproduction a) before and b) after the cessation of longitudinal bone growth.
What is the effect of hypothyroidism or stress on somatic growth?
Describe developmental changes in the male and female reproductive systems during puberty.
Describe the stages of puberty in females: adrenarche, thelarche, pubarche, menarche. What do these expressions mean? What effects are responsible for these?
Define acceleration.
What are the effects of sex steroids on somatic growth?

91. The control of cerebral blood flow, the cerebrospinal fluid, barrier systems of the brain.
Give the normal value of cerebral blood flow, and its percentage to the resting cardiac output.
Contrast the significance of local and systemic neural control of cerebral blood flow. Discuss the relative importance of PO2, PCO2, pH and blood glucose level in regulating cerebral blood flow.
Describe the mechanisms of local cerebral metabolism- blood flow coupling and its significance in relation to fMRI.
Explain the role of astrocytes in maintaining neuronal milieu.
Describe formation and reabsorption of cerebral spinal fluid (CSF), including the anatomy and function of the choroid plexus.
Describe the normal pressure, flow, volume, and composition of the CSF.
Describe the structural components of the blood brain barrier and how this barrier impedes the movement of various substances from the blood to neurons. Contrast the barrier mechanisms between the blood brain barrier and the blood CSF barrier.
Locate and identify the brain regions outside the blood-brain barrier, and describe the function of circumventricular organs.

Reference values: **cerebral blood flow (adult): 750 ml/min**, 15% of resting cardiac output. **CSF volume: 140 ml; CSF secretion rate: 500 ml/day. CSF pressure: 5 mmHg (8-10 cmH_2O); CSF composition: white blood cell: 0-5 cells/µL**, protein concentration: 0.35 g/l; $Na^+/K^+/Cl^-/HCO3^-$: 149/3/128/26 mmol/kgH_2O (molal concentration), glucose concentration: ~ 2/3 of plasma concentration.

92. The somatosensory nervous system: receptors.

Characterize the somatosensory receptors according to their 1. modality (mechano-, thermo-, nociceptors), **2. source of the stimulus** (extero-, proprio-, interoceptors) **and 3. histological structures** (encapsulated, free nerve endings).
Describe the cutaneous mechanoreceptors and their functions: Pacinian corpuscles, Meissner's corpuscles, Ruffini endings, Merkel cell, free nerve endings.
Define the concept of a dermatome and explain the dermatomal organization of the head and body.
Define the concept of a somatosensory receptive field and explain how dermatomes and receptive fields are related.
Define the terms receptor sensitivity, receptor specificity, and receptive field. Explain how the peripheral innervation density is related to receptive field size.
Define rapidly and slowly adapting sensory reception.

93. The somatosensory nervous system: the dorsal column ascending pathways.
Describe the submodalities of somatic sensibility subserved by the Dorsal Column-Medial Lemniscus system.
List the neural components of the Dorsal Column-Medial Lemniscus system and its Trigeminal analogs.
Describe the functional properties of the Dorsal Column-Medial Lemniscus system.
Describe the topographic representation of the body at the level of the dorsal column nuclei, the ventrobasal thalamus, and the somatic sensory cortex.
Define two-point discrimination and tell how it is related to peripheral innervation density and receptive field size.
Describe the factors that contribute to the high somatic sensory acuity of the hands and face.
Describe signs and symptoms of dorsal column-medial lemniscus system dysfunction.
Describe how lateral inhibition improves spatial two-point discrimination.
Explain how peripheral innervation density influences the size of the representation area in the postcentral gyrus.
Discuss what is meant by the Fine Touch System and be able to trace its connections to the cerebral cortex.

94. The somatosensory nervous system: the anterolateral (spinothalamic) ascending pathways.
Describe the submodalities of somatic sensibility subserved by the spino-thalamic system. Describe the ascending sensory pathways and their connections with the cerebral cortex conveying nociceptive, thermal and tactile (coarse touch) sensory information.
Describe the difference between the modality specific and wide dynamic range type interneurons/projection neurons in the spinal dorsal horn.
Describe the connections of the anterolateral pathway with the brainstem and the hypothalamus. Provide examples to illustrate the functional importance of these anatomical connections (sensory stimulus-evoked cardiorespiratory and other autonomic reactions, arousal, changes in the muscle tone, thermoregulatory reflexes).
List the neural components of the spino-thalamic system and its trigeminal analogues.
List the functional properties of the spino-thalamic system.
Describe the deficits caused by lesions in the spino-thalamic system.

95. The somatosensory nervous system: nociception and pain.
Describe the concepts of nociceptor and nociception. Definition of pain.
Describe the cellular mechanisms of nociceptor activation.

Differentiate between fast and slow pain and identify the peripheral nerve fibers and central connections that account for these different types of pain.
Describe the reactions of the body evoked by noxious stimulation (motor and autonomic responses, affective reactions).
Describe the components of the descending pain control (endogenous analgesic) system (PAG, LC, raphe nuclei, spinal gate control mechanisms). List the types of neurotransmitters involved. Describe how endogenous opiates may modulate the pain experience.
Compare nociception with itch sensation.
Describe the key features of visceral nociception. Describe the mechanism of referred pain of visceral origin. **Describe the concept of Head zones, list 3 characteristic localizations of referred visceral pain**.
Describe the main mechanisms of development of inflammatory pain. **Explain the terms hyperalgesia and allodynia.**

96. The visual system: protection of the eye, image formation, refraction errors.
Describe the function and importance of tear secretion, the composition of tear, the control of tear secretion (parasympathetic innervation).
Describe the so called palpebral-reflexes (corneal-, conjunctiva-, supraorbital-, nasal-, acustico-palpebral reflexes). Integration of the palpebral reflexes in the CNS (upper brainstem motor reflexes).
Describe the gross anatomical structure of the eye and basic physiological optics.
Describe the refraction of light as it passes through the eye to the retina, identifying the eye components that account for refraction of light.
Define „refractory power" and its unit.
Describe the process of accommodation, contrasting the refraction of light by the lens in near vision and in far vision. **List the components of the accommodation triad.**
Define the "near point".
Explain the method of measuring visual acuity using the Snellen/Csapody chart and the normal value of visual acuity (visus).
What is the Javal-Schiøtz ophthalmometry used for?
Describe the refractive deficits that account for myopia, hyperopia, presbyopia, astigmatism and their correction.
Explain the production, circulation and absorption of the aqueous humour. Give the normal value of intraocular pressure and explain what tonometry is. Explain glaucoma.

Reference values: **visus: 5/5** (m) or 20/20 (feet), spatial resolution: 1', **, total refractory power of the eye: 60 D, refractory power of the cornea: 40-43 D, refractory power of the lens (far accommodation): 17-20 D**, near point: 7-10 cm, physiologic astigmia: 0.5 D, **intraocular pressure: 10-20 mmHg (mean: 16 mmHg)**.

97. The visual system: the function of the photoreceptors, retinal signal processing.
List the structure and cell types of the human retina. Understand the intrinsic circuitry of the retina and its functioning.
Describe the basic biochemistry of the photo-transduction process, the "dark current", and the photoreceptor response to capturing a photon.
Explain the properties of the different photoreceptor types: number, distribution in the retina, chromatic and luminance properties (scotopic and photopic vision), critical flicker fusion frequency.
Explain the phenomenon of the Purkinje shift.
Explain how adaptation to darkness and light works.
Understand the connectivity and synaptic interactions of photoreceptors, horizontal cells and bipolar cells in the construction of center-surround antagonistic receptive fields.

Describe how different post-synaptic receptors create depolarizing or hyperpolarizing responses and how they are organized to create different ON-center and OFF-center responses and the antagonistic surrounds.
Describe the electrical responses produced by bipolar cells, horizontal cells, amacrine cells, and ganglion cells, and comment on the function of each.

Reference values: critical flicker fusion frequency: 22-25 Hz (scotopic), 40-50 Hz (photopic), Purkinje shift: 500-555 nm (the difference in the maximum of spectral sensitivity of the retina under scotopic and photopic conditions).

98. The visual system: the visual field and the visual pathways.
Trace the projections of the visual hemifields onto the retina (nasal/temporal), describe the retino-thalamo-striate pathway. Explain how the crossing of optic nerve fibres accounts for visual field representations at each stage.
Predict the visual field deficits resulting from the following lesions in the visual pathway: retinal lesion, optic nerve lesion, optic chiasm, optic tract, LGN (lateral geniculate nucleus), optic radiations and primary visual cortex. In your response use the terms bitemporal (heteronymous) hemianopia, contralateral homonymous hemianopia, macular sparing.
Explain the method of perimetry for the determination of the visual field. Explain why people have a physiological scotoma (blind spot).
Describe the extrageniculate projections (suprachiasmatic nucleus, superior colliculus, pretectum) of retinal ganglion cells and their importance.
Review the midbrain path for the pupillary light reflex. How do you interpret the presence / absence of the direct and consensual reflex?

99. The visual system: the control of eye movements.
List the extraocular muscles and the innervating motor nerves.
Classify the eye movements based on the relationship of the optical axes and on speed.
Explain the importance of the pursuit eye movements.
What are saccadic eye movements and what is their biological function? What is the function of the fixation periods between saccades? Explain the importance of microsaccades.
Explain optokinetic nystagmus.
Describe the structures involved in controlling eye movements: cortical (posterior parietal cortex, frontal eye fields), subcortical (medullar and pontine reticular formation, motor eye nuclei, e.g., NOT (nucleus of the optic tract), superior colliculus).

Reference values: speed of the pursuit eye movements: up to 60 °/s, saccadic eye movements: > 60 °/s (max: 1000 °/s).

100. The visual system : cerebrocortical mechanisms.
Describe the structural and functional specializations of the lateral geniculate nucleus (LGN).
Describe the receptive field characteristics of the cells in the primary visual cortex.
Explain the general functional organization of V1. Describe the topographic representation of the visual field within the primary visual cortex including the topics of retinotopic organization, orientation selectivity, ocular dominance and cortical blobs.
Recognize how centre-surround antagonistic receptive fields are combined to report complex parameters, such as orientation specificity and motion detection.
Differentiate between the general organization and functional specializations of the dorsal and ventral extrastriate visual streams.

Describe the processing of information in the visual cortex and in the higher visual association areas. Differentiate the retino-thalamo-cortical pathway from extrastriate visual projection systems.

101. The visual system : binocular vision, color vision.

Explain the followings: corresponding retina points, horopter; describe binocular disparity and its relationship to stereopsis.
Describe monocular cues supporting spatial vision.
Explain the neuronal mechanisms for colour vision and the following terms: achromatopsy, protanopy, deuteranopy, tritanopy, protanomaly, deuteranomaly, tritanomaly.
Explain how colour vision can be tested (Ishihara plates).

102. Hearing: the function of the outer and the middle ear. Hearing tests.

Define the following categories: pure (basic) tone, sound (musical tone), noise. **Define** the frequency, the loudness and intensity of the sound, propagation of the sound, **sound pressure level (dB)**, subjective loudness (phon), equal loudness curves (isophones)
Draw the human audibility curve and explain the changes that occur with aging.
Describe the function of the outer, middle, and inner ear structures in the mechano-electrical transduction process of sound energy into nerve impulses. **Describe the acoustic impedance matching. Describe the differences between bone and air conduction.**
Describe the nerves and muscles in the middle ear and explain their role in withdrawal reflexes.
Define the difference between conductive, sensory and neural loss of hearing. **Introduce the following hearing tests** and explain how they contribute to the diagnosis of hearing disorders: **audiometry, Weber test, Rinne** test and tympanometry. Presbyacusis.

Reference values: **frequency range of human hearing: 20-20000 Hz, sound pressure level of human hearing: 0-120 dB, reference sound pressure level: 20 µPa, threshold of human hearing: 0 dB, frequency range of human speech: 250-4000 Hz, reference frequency of the phon scale: 1000 Hz**

103. Hearing: the function of the inner ear, auditory pathways.

Explain the frequency analysis performed by the cochlea on the basis of its physical properties (Békésy theory, tonotopy).
Identify the neuronal elements of the organ of Corti. Define the endocochlear potential. Explain the function of inner and outer hair cells. Define the otoacoustic emission.
Explain how deformations of the basilar membrane are converted into action potentials in auditory nerve fibers.
Describe the auditory pathway and explain the role of analysis of auditory evoked potentials in the examination of its elements.
Describe how pitch, loudness, and localization of sounds in space are coded by central auditory neurons. Describe the role of frequency code and population code in hearing and explain the binaural hearing.

104. The physiology of olfaction.

Describe the location, structure, and afferent pathways of smell receptors.
Describe the olfactory cilium and the family of olfactory receptors housed in its membrane.
Explain how olfactory receptors are activated and explain the mechanism of olfactory transduction.
Explain the term molecular receptive range.

Explain the terms topography, spatial topography, and functional topography in the olfactory system.
Describe the structure and functions of the first central relay station for olfactory
Information (the olfactory bulb), its afferent input, and efferent output.
Describe the structure and function of the central olfactory centers beyond the olfactory bulb, the cortical representation of olfaction.
Define the following terms: anosmia, hyposmia, dysosmia.

105. The physiology of taste sensation.
Describe the location, structure, and afferent pathways of taste receptors.
Describe the cells of a taste bud.
Name the basic taste sensations, i.e., identify the five distinct gustatory modalities.
Explain how taste receptors are activated and explain the mechanism of taste transduction for each taste quality.
Identify the three cranial nerves that transmit taste information to the cerebral cortex.
Describe the structure and function of the central taste centers**.**
Define the following terms: ageusia, dysgeusia.

106. The motor reflex. The structure and function of muscle proprioceptors.
Define motor reflexes, describe the reflex arc from stimuli to reflex actions.
What is the difference between exteroceptive and proprioceptive reflexes?
Define the notion of proprioception and describe the proprioceptors.
Define the main functions of muscle spindles and Golgi tendon organs.
Delineate the localization, structure, and sensory/motor innervation of muscle spindles and Golgi tendon organs.
Describe the intrafusal and extrafusal muscle fibers and provide a classification for intrafusal fibers.
What is the difference between Ia, II, and Ib afferents?
Define the structure and function of gamma and alpha motoneurons.

107. The myotatic and the inverse myotatic spinal reflex.
Define the notion of myotatic and inverse myotatic reflexes, describe the receptors and the adequate stimuli.
Trace the path of neuronal activity during the knee-jerk (patellar) reflex and describe the reflex arc.
Compare the reflex arc of the knee-jerk reflex with that of the inverse myotatic reflex.
Describe the agonist and antagonist muscles and the mechanism of reciprocal innervation.
Describe the biceps, triceps, and Achilles-tendon reflexes and the corresponding segments of the spinal cord.
What is the Jendrassik maneuver? What are hyporeflexia, hyperreflexia, and clonus?

108. The gamma fusimotor servomechanism (gamma-loop).
Define the gamma motoneurons and the muscle fibers that are innervated by these neurons.
What happens to the structure and sensitivity of the muscle spindle when the alpha motoneurons are activated and the extrafusal fibers are contracted?
Explain how the activity of gamma motoneurons is able to compensate the changes in the structure and sensitivity of muscle spindles due to the contraction of the extrafusal muscle fibers (alpha-gamma coactivation).
Define the notion of muscle tone and explain the role of the gamma loop in the maintenance of muscle tone and in the regulation of deep tendon reflex intensity.

109. Exteroceptive spinal reflexes.
Describe the receptors and their adequate stimuli.
Describe the reflex arc of the flexor-extensor reflex.
Compare the nociceptive and non-nociceptive exteroceptive reflexes.
Describe the abdominal skin reflex and the plantar reflex.

110. The spinal integration of rhythmic locomotive movements. The spinal interneurons.
Enlist the types of rhythmic locomotive movements.
Explain the cyclic alteration of the activity of flexors and extensors during these movements and the role of intersegmental integration.
What is the notion and function of central pattern generator (CPG)?
What is after discharge and rebound?
Describe the localization, types and functions of interneurons in the spinal cord (interneurons of descending pathways, Ia and Ib interneurons, CPGs, Renshaw cells).
What are the inhibitory neurotransmitters in the spinal cord (GABA, glycine)? Explain the mechanism of action of muscle relaxants and strychnine.

111. The consequences of spinal cord hemisection and transection.
What is the spinal shock? What are the sensory, motor, and vegetative consequences of the total spinal cord transection?
Define the following terms: tetraplegia, paraplegia, hemiplegia and paresis.
Enlist the functions that can and cannot be recovered after spinal shock in humans.
What is the lower (alpha) motoneuron? What kind of alterations can be observed in muscle tone, power, muscle mass, and tendon reflexes after the injury of lower motoneurons?
What is atrophy and fasciculation?
Explain the symptoms of the Brown-Sequard syndrome.

112. The control of muscle tone.
Define muscle tone and its alterations: hypotonia, atonia, rigidity, and spasticity.
Explain the role of alpha and gamma motoneurons in the regulation of muscle tone.
Enlist the brainstem neuronal structures participating in the regulation of muscle tone (nucl. ruber, nucl. vestibularis Deitersi, pontin and medullar reticular formation) **and explain their role in flexor and extensor tone.**
What is the effect of cortical and cerebellar lesion on muscle tone?
Enlist the pathways and functions of the lateral (cortico- and rubrospinal) and medial (vestibulo-, reticulo-, tectospinal) descending system.
What are the symptoms of decerebration and decortication (upper motoneurons lesion)? How will the muscle tone, power, muscle mass, and tendon reflex activity change? What is the mechanism?

113. The control of body posture. The vestibular system.
Define the statotonic and statokinetic reaction and enlist the sensory mechanisms implicated in the control of posture and gait (vestibular, proprioception, visual).
Delineate the elements of the vestibular system (semicircular canals and otolith organs).
Explain the function of hair cells. Endolymph, perilymph, receptor potential, activity of the vestibular nerve.
Compare the functions of the semicircular canals and otolith organs.

Describe the reflexes of the vestibular system: sustaining postural reflex, vestibulocollic and vestibuloocular reflex.
Define and describe the types of nystagmus: optokinetic, rotatoric, postrotatoric, and caloric nystagmus and their mechanisms.
Explain the significance of neck proprioceptors in the regulation of gait and posture and give some examples (e.g., flexion of upper and lower limbs in the case of forward head movements).

114. The cerebrocortical control of movements.
Enlist the parts and localization of the motor cortex (primary motor, premotor, and supplementary motor cortex).
Describe the functions of the primary motor cortex (force, direction, speed; encoding muscle and joint movements from egocentric reference frame). Somatotopic organization and plasticity.
Describe the origin, path, and function of the corticospinal tract. Consequences of lesions (Babinski sign).
Explain the „long-loop" reflexes.
Enlist the functions of the premotor cortex.
Enlist the functions of the supplementary motor cortex.
Compare the mechanisms of stimulus-driven actions and internally generated, planned actions.
Explain the role of the multimodal sensory cortex (posterior parietal lobe) and prefrontal cortex.
Mention some of the symptoms caused by the lesion of the motor cortex and posterior parietal cortex (initiation and inhibition of movements, alien hand, apraxia, neglect, loss of proprioception).

115. The cerebellum.
Enlist the main parts of the cerebellum (anterior, posterior, flocculonodular lobe, vermis, paravermis, lateral hemisphere) and the histological layers.
Delineate the functional network of the cerebellum (climbing fibers, mossy fibers, granular cells, parallel fibers, basket cells, Purkinje cells, deep nuclei).
Describe the mechanism of excitation and inhibition in the cerebellar network. Describe the electrophysiological properties of the Purkinje cell (complex action potential, climbing fiber LTD and motor learning).
Describe the parts of the vestibulocerebellum, afferents, efferents, function.
Describe the parts of the spinocerebellum, afferents, efferents, function.
Describe the parts of the cerebrocerebellum, afferents, efferents, function.
Mention a few symptoms caused by the lesion of the cerebellum (nystagmus, ataxia, dysdiadochokinesis, dysmetria, hypotonia, telegraphic speech).

116. The basal ganglia.
Enlist the parts of the basal ganglia (neostriatum, pallidum, nucl. subthalamicus, substantia nigra) **and their anatomical localization.**
Describe the main neurochemical systems in the basal ganglia (glutamate, GABA, dopamine, acetylcholine, peptide cotransmitters).
What is the function of the direct pathway?
What is the function of the indirect pathway?
Discuss the sensory, motor, and cognitive functions of the basal ganglia.
Describe the clinical conditions associated with hypokinesis (**parkinsonism**) and hyperkinesis (chorea, ballism, athetosis, tic).

117. The integration of autonomic functions in the CNS. Functions of the hypothalamus.

Functional anatomy of the autonomic nervous system. Characterization of the autonomic innervation of visceral organs. Autonomic reflexes.
Hierarchical organization of the autonomic nervous system. Walter Hess and the integrative action of the hypothalamus.
Functional anatomy of the hypothalamus. Afferent and efferent neurohumoral connections of the hypothalamus. **Hypothalamic control of visceral functions.**
Central nervous integration of sensory, motor and autonomic functions and behavior. The autonomic nervous system and the limbic system. Cortical control of autonomic functions.

118. The functions of the limbic system. Emotions.
Describe the neuronal structures belonging to the limbic system, and list their functions.
Explain the importance of the connection between the cerebral cortex and amygdala in cognitive and emotional behaviour.
What is the function of the olfactory system within the limbic system?
What is the connection between the limbic system and the autonomous nervous system?
Describe emotions as adaptive mechanisms, their central representations and their effect on the homeostasis.
Explain the connection between homeostatic need, motivation and the cerebral reward system.

119. Electroencephalogram (EEG) and the physiology of sleep-wake cycles.
Describe the origin (the electrophysiological basis) of the electroencephalogram.
Describe the EEG waves (frequency ranges, amplitude) of the EEG, and identify the brain states typically associated with these different waveforms.
Describe the conceptual basis of recording evoked potentials, and describe the importance of evoked potentials in neuroscience.
Describe the changes of the brain electrical activity (EEG) during shifts from wakefulness to non-REM, and then to REM sleep phases.
Describe the features of human sleep (length and number of sleep cycles during the sleep, changes in the duration of non-REM/REM phases in consecutive sleep cycles).
Outline the current understanding of regulatory mechanisms regulating the appearance of NREM, REM and wake states. Include the brain structures and neurotransmitters involved and the mechanism of the circadian rhythm underlying the sleep-wake cycle.
Describe how respiration, cardiovascular, renal, gastrointestinal, eye movement, muscle, and endocrine function change from wake to NREM and REM states.
Define the term: polysomnography.
Reference values: **EEG wave frequency ranges: delta: 0.5-4 Hz, theta: 4-7 Hz, alpha: 8-12 Hz, beta 13-30 Hz**

120. The circadian rhythm and the pineal gland.
Define and describe the most important features of circadian rhythms (biological changes that are 1) genetically determined, 2) generated by an internal self-sustaining pacemaker that can be entrained (synchronized) by external signals , and 3) have an app. 24h periodicity).
Give examples of physiological changes characterized by circadian rhythmicity (body temperature, growth hormone secretion, cortisol secretion etc.
Explain the features of the suprachiasmatic nucleus (SCN) that make this nucleus suitable to function as a circadian pacemaker (Zeitgeber).

Describe the role of the retinohypothalamic pathway in synchronizing SCN activity with the light-dark cycling.
Describe the structure and autonomic innervation (nervi conarii) of the pineal gland, and the biosynthesis of melatonin – the hormone secreted by the pinealocytes.
Describe the neuronal pathways connecting the SCN to the pineal gland in order to give explanation for the circadian changes in melatonin secretion.
What is our current understanding of the physiological functions of melatonin? (melatonin receptors, endocrine circadian transducer)

121. Cognitive functions, neuronal correlates of language
Define the term of cognition and enumerate the main functions included.
Define the levels of language organization.
Define the term dominant hemisphere, Wada-test.
Describe the classic model of language localization in the brain (Wernicke-Geschwind).
Explicate the limitations of the Wernicke-Geschwind-model, and provide some alternative explanations.
Define the term of aphasia, describe the main types and typical brain lesions.
Specify the term of agnosia, describe the main types and typical brain lesions.
Define the Gerstmann syndrome and its neuronal basis.
Define the neglect syndrome and its neuronal basis.
Describe the main principles of human hemispheric specialization.

122. Neuronal plasticity, learning and memory
Define the terms of learning and memory and enumerate the main types of learning.
Compare habituation and sensitization.
Compare classic (Pavlovian) and operant conditioning.
Compare episodic and semantic learning.
Describe working memory and its neuronal correlates.
Specify the neuronal basis of explicit (declarative) memory.
Specify the molecular mechanisms of long-term potentiation (LTP) and long-term depression (LTD) (initiation, specific receptors and enzymes, localization in the central nervous system).
Specify the neuronal basis of implicit (non-declarative) memory.