CURRICULUM OF MEDICAL PHYSIOLOGY II  
2006/2007

Note: A. Fonyó: Principles of Medical Physiology, Medicina 2002 is the book recommended to study physiology. However, valuable complementary information can be found in R.F. Schmidt, G. Thews: Human Physiology; R.M. Berne & M.N. Levy: Principles of Physiology; A.C. Guyton: Textbook of Physiology. Topics in Physiological Practice (A laboratory guide) are also parts of the physiology curriculum.

GASTROINTESTINAL FUNCTIONS

Regulatory mechanisms in the gastrointestinal (GI) tract

Functions of the elements in the enteric nervous system (receptors, afferent neurones, “distributing” interneurones, excitatory and inhibitory interneurones, excitatory and inhibitory effector neurones). Local reflexes in the enteric nervous system, neurotransmitters and their receptors (acetylcholine, substance P, opioid peptides, VIP, NO, ATP).

Roles of the parasympathetic (vagal) preganglionic fibres, targeted and modulatory influences. Significance of the sympathetic innervation (postganglionic fibres, direct excitatory and indirect inhibitory actions). Short and long GI reflexes.

Endocrine and paracrine regulatory mechanisms. Signalling molecules and the (APUD) cells producing them. Gastrin (receptors, effects). Cholecystokinin (CCK; receptors, effects). Somatostatin, secretin, GIP, motilin. Role of histamine in the defense activity of the GI tract.

Motor functions of the GI tract

Mastication (chewing). Swallowing (innervation and peristalsis of the esophagus, roles of the vagal nerve, myogenic components).


Motor activity of the bile ducts, control of the gallbladder and the sphincter of Oddi (CCK, vagal nerve, VIP).

Secretory functions of the GI tract

General features of the exocrine glands in the GI tract. Composition and functions of the saliva. Transport processes during the primary secretion of the saliva and in the ducts. Correlation of the secretion intensity and the composition of the saliva. Sympathetic and parasympathetic control, neurotransmitters, receptors.

Composition of the pancreatic juice, transport processes in the acini and ducts. Neural and hormonal regulatory factors (vagal nerve, CCK, secretin), their effects on the acinar and ductal epithelial cells. Cephalic, gastric and intestinal phases of pancreatic juice production.
Composition of the bile. Transport systems of the liver cells. Secretion and enterohepatic circulation of the bile acids. Choleretics and cholagogues.

Secreting and absorbing intestinal epithelial cells. Intestinal juice secretion, its regulation. Effects of the cholera toxin.

Food breakdown, absorption

Breakdown of carbohydrates, transepithelial absorption of monosaccharides. Lactose intolerance.

ENERGY BALANCE, NUTRITION, THERMOREGULATION


Food intake: Requirement for energy uptake. Qualitative and quantitative requirements of food intake, nitrogen balance, daily protein minimum allowances. Vitamins, water and fat soluble vitamins. Feeding and satiety center.


SYNAPTIC TRANSMISSION, BASIC RECEPTOR FUNCTION

The processing of information in the nervous system. The types of neurotransmission, electric- and chemical synapses. Electric synapses. The general scheme of chemical transmission. The synthesis of the transmitter, the quantal aspect of transmitter release, its dependence on the external calcium concentration. The fate of the released transmitter. The
concept of EPSP and IPSP, the accompanying membrane potential change and the underlying mechanisms. The characteristics of chemical transmission (rectification, fatigue, summation, facilitation). The pharmacology of the chemical synapses (groups of neurotransmitters). Integrative function of neuronal networks.

The structure of the neuro-muscular junction (NMJ). The comparison of the neuronal synapse and the neuro-muscular junction. Properties of the postsynaptic membrane (nicotinic acetylcholine-receptor, end plate current, electrogren membrane surrounding the end plate, the "safety factor" of transmission). The concept of EPP, the comparison of EPP and EPSP. The pharmacology of the NMJ (agonists, antagonists, cholinesterase inhibitors). Myasthenia gravis.

The characterization of basic receptor function. The concept of the adequate stimulus. Primary, secondary and tertiary receptors. The transformation (generator potential) and coding (trains of action potentials) of information.

**PHYSIOLOGY OF MUSCLE**


**Properties of smooth muscle.** Smooth muscle types, their characteristics. Electrophysiological properties. Comparison of excitation-contraction coupling in skeletal and smooth muscles. Ligand-controlled mechanisms. Electro- and pharmaco-mechanical coupling (the inositol pathway, the role of intracellular calcium concentration increase, the regulation of actin and myosin interaction). Properties of the mechanical response, plasticity.

**Regulation of the intracellular calcium concentration**

Depolarization- and agonist-induced increase in intracellular calcium concentration, the role of the endoplasmic reticulum (IP$_3$- and ryanodine receptors). Positive and negative feedbacks (Ca induced calcium release, Ca dependent inactivation of calcium release channels). Calcium channels of the surface membrane (voltage- and ligand-gated channels, store-operated channels). Determination of the intracellular calcium concentration (fluorescent and absorbance dyes). Calcium binding proteins (parvalbumin, troponin C). Calcium removal mechanisms.

**Energetic aspects of muscle function**

Metabolic aspects of exercise (energy sources and metabolism in the striated muscle, metabolic features of fast and slow muscles. The ratio of anaerobic and aerobic metabolism, oxygen dept.
PHYSIOLOGICAL REACTIONS DURING EXERCISE

The adaptation of the cardiovascular and respiratory systems to exercise. The changes in the blood supply of a working muscle. Systemic changes, the redistribution of cardiac output. Changes in the venous and lymphatic flow. Respiratory changes during exercise.
PHYSIOLOGY OF EXCRETION

General aspects of renal function

Significance of renal function in homeostatic regulation. Isovolemia, isosmosis, isohydria, isoionia. Renal handling of plasma constituents, alien compounds and waste products. Endocrine function.

Nephron (morphology and function). General and specific characteristics of the tubular system. Parameters determining transport properties. Cortical and juxtamedullary nephrons.


Glomerular filtration


Factors influencing GFR. Components of the net filtration pressure. Filtration equilibrium, flow-limited transport. Special aspects of renal circulation.


Tubular transport


Transport properties of the loop of Henle and the distal nephron. Permeability characteristics and transport properties in specific tubular segments (thin descending and ascending limbs, thick segment, connecting and collecting ducts). Movement of Na⁺, K⁺, H⁺, bicarbonate, water and urea. Final processing of the filtrate in the collecting duct.

Mechanisms of Na⁺ transport in various tubular segments (driving force, carriers in the apical and basolateral membrane, inhibitors). Significance of tight junctions in the distal nephron, potential gradient as driving force. The origin and maintenance of the cortico-medullary osmotic gradient, contribution of cortical and juxtamedullary nephrons. Countercurrent multiplication in the loop of Henle. Countercurrent exchanger mechanism in the vasa recta system. Medullary recirculation of urea.
Osmoregulation, excretion of water


Water balance. Regulation of intake and excretion of water. Afferent and efferent mechanisms of osmoregulation (thirst mechanism, osmosodium receptor - ADH system). Control of ADH production, role of hypothalamus.

Defense of extracellular fluid volume, Na-homeostasis


Three basic mechanism of defense of ECF volume (GFR-mechanism, aldosterone, "third factor effects").

Complex regulation of ECF volume and osmolarity (differences in sensitivity, question of priority). Role of ADH and the mechanism of thirst in defense of ECF volume.

Acid-base balance

Acid-base buffers (chemical buffering). Buffer systems in the blood. Significance of H₂CO₃-HCO₃⁻ buffer system. Relationship between pH, pCO₂ and HCO₃⁻ concentration. Respiratory regulation of pH.


K-homeostasis

Calcium metabolism and bone physiology


MICTURITION


RENA L FUNCTION UNDER PATHOLOGICAL CONDITIONS

NEUROENDOCRINE FUNCTIONS

GENERAL PRINCIPLES OF ENDOCRINE REGULATION

Homeostasis. Comparison of the principles of chemical (humoral) and neural regulation. Differences (specificity, speed); common features (role of secretory processes, importance of the membrane potential and depolarization, endocrine and neurotransmitter role of the same compound, receptors); interactions (neural afferent/endocrine efferent, neurocrine actions, integrated behavioral responses).

Chemical structure, synthesis, storage and secretion of hormones. Factors determining the plasma level of hormones (secretion rate, binding to transport proteins, consequences of quantitative changes of the transport proteins, elimination, metabolism, excretion).

Regulation of hormone secretion (closed-loop feed-back systems, negative and positive feed-back, open-loop regulation).

Experimental studies and pathological aspects of hormone action (removal of endocrine glands, substitution, hypo- and hyperfunction).

Mechanisms of hormone action

Hormone-receptor interactions. Relationship of binding to biological response. Homologous and heterologous receptor desensitization. Peptide hormone and steroid hormone receptor structure and function.

Quantitative aspects of hormone action (description of the hormone/receptor interaction, role of the “spare receptors”, down- and up-regulation).


HYPOTHALAMO-HYPOPHYSSEAL SYSTEM


Feed-back loops in the hypothalamus - adenohypophysis - target gland chains. Possible roles of the hormones of the intermediate lobe.

HUMAN GROWTH HORMONE

Physiological significance of the chemical structure (specificity, difficulties in the substitution therapy). Somatomedins (IGF-I, IGF-II, relaxin). Effects of the growth hormone (mechanism of action at the cellular level, direct effects on the protein, lipid and carbohydrate metabolism, effects on the growth, roles of somatomedins, problems of growth hormone/insulin interaction (discussed in details at the regulation of the intermediate metabolism).
Regulation of the growth hormone production (feed-back loops, open-loop facilitatory and inhibitory factors - role of the metabolic substrates, endocrine interactions).

**Growth** and its endocrine regulation (growth periods, roles of growth hormone, thyroid hormones, androgens, estrogens, insulin).

Hypo- and hyperfunction of the pituitary gland (consequences of lack and excess production of growth hormone - dwarfism, gigantism, acromegaly).

**ENDOCRINE REGULATION OF MALE REPRODUCTIVE FUNCTIONS**

Roles of hormones in regulating reproductive functions (overview of hormones involved in male and female regulation, exposition of analogies and differences).

Effects of **testosterone** (free and bound form, conversion to dihydrotestosterone, anabolic effects, determination of the secondary male characteristics).

Endocrine control of **spermatogenesis** (blood/testis barrier, importance of environmental temperature, experimental proof of the roles of FSH and LH, significance of Leydig and Sertoli cells, plasma and local concentration of testosterone, paracrine interactions in the testis).

**Regulation** of the testis functions (interactions of LHRH, FSH, LH, testosterone and inhibin in the control, levels of the feed-back loops).

**HORMONAL CONTROL OF THE FEMALE SEXUAL FUNCTIONS**

Changes in the plasma hormone levels during the menstrual cycle.

Effects of **estrogens** (effects on the gonads, effects on the mammary gland, secondary female characteristics, behavioral effects, anabolic effects).

Effects of **progesterone** (effects on the gonads, effects on the mammary gland, anabolic effects).

**Interactions** of the hormones involved in female gonadal regulation (GnRH, FSH, LH, estrogens, progesterone, inhibin) at the level of granulosa cells, theca interna cells, luteinising cells and the anterior pituitary gland (with special emphasis on the newly described autocrine and paracrine interactions in the ovaries). Special features of the ovarial steroid hormone production (complementary interactions between granulosa and theca cells).

**Endocrine regulation of the female ovarial cycle** (interpretation on the basis of the hormonal interactions, development of the primary follicle, selection and development of the dominant Graafian follicle, ovulation, function of the corpus luteum).

**Pregnancy, parturition, lactation, puberty, menopause**

Endocrine activity of the **placenta** (changes in the plasma levels of hCG, progesterone, estrogens and hPL during the pregnancy, the role of the above hormones in maintaining
pregnancy and supporting the development of the fetus, short overview of other hormones produced by the placenta).

**Parturition** (possible endocrine signalisation of the start of the delivery process, hormonal preparation of the uterine muscle, role and regulation of oxytocin production).

**Lactation** (endocrine mechanisms involved in the development of mammary gland prior to and during the pregnancy, regulation of prolactin secretion, role of oxytocin in the neurohormonal milk ejection reflex).

Overview of endocrine changes during the **puberty** and **menopause**.

**ADRENAL MEDULLA**


**GLUCOCORTICOIDS**

**Physiological effects** of glucocorticoids on intermediary metabolism, water excretion, vascular reactivity and permeability, leukocytes and lymphatic system. **Permissive** effect. Mechanism of action.

**Pharmacological effects** (anti-inflammatory and anti-allergic effects).

**Regulation** of secretion, circadian rhythm, changes in adrenal responsiveness.


**THYROID HORMONES**

Functional aspects of the glandular structure. Chemistry of thyroid hormones. Iodine metabolism. Consecutive steps of hormone synthesis.

**Secretion** of thyroid hormones. Transport of thyroid hormones and tissue delivery. Metabolism and interconversions of thyroid hormones.

**Cellular mechanism** of thyroid hormone action.

**Feedback control** of thyroid biosynthesis and secretion. The hypothalamic-pituitary-thyroid axis. The immediate and long term effects of TSH.

**Clinical correlates.** Hypothyroidism, hyperthyroidism, cretinism, myxedema, Graves-Basedow disease, goiter and goitrogens.
ENDOCRINE REGULATION OF METABOLISM

Anabolic and catabolic pathways. Fate of carbohydrates, fats and proteins in catabolic and anabolic phases. Endocrine regulation of glycolysis, gluconeogenesis and ketone formation. Quantitative aspects of metabolic processes. The liver as a glycogen pool and glucose buffer.

HORMONES OF PANCREATIC ISLETS

Insulin

Biosynthesis and transport of the hormone. The structure of human and non-human insulin, therapeutic consequences. The structure of insulin receptor, regulation, signalization, Insulin Receptor Substrates. Long term and short term effects of insulin.
The transport of glucose through the cell membrane, role of Na+, K+. Insulin sensitive and insulin resistant glucose transport.
Effects of insulin on carbohydrate, fat and protein metabolism. Role of insulin in switching between carbohydrate and lipid metabolism.
NSILA, IGF-I and IGF-II: structure, function, the autocrine mechanism, the IGF-I and IGF-II receptor.
Glucose tolerance tests: normal and pathologic. Classification of decreased glucose tolerances.

Glucagon


Somatostatin and Pancreatic Polypeptide

Somatostatin: structure, function, metabolic effects. Action on intestinal motility and absorption. Regulation of somatostatin secretion. Pancreatic Polypeptide: structure and actions of the hormone.
Organization of the pancreatic islets.

METABOLIC EFFECTS OF EXTRA-PANCREATIC HORMONES