Pathophysiology
Analytic Programme

**Theoretical Pathophysiology** – represents a part of discipline that studies the general laws, origin of diseases, its evolution and final phases Foundation Concepts of Pathology.

**General Pathophysiology** - studies the general laws, origin of typical pathologic processes, its evolution and final periods. These processes are common for all types of biological species and a human organism.

**Special Pathophysiology** - studies the general characteristics and origin of typical pathologic processes in different organs and body systems.

**Clinical Pathophysiology** – studies the laws of evolution of the concrete nozologic forms of human diseases.

**Introduction**
Definition of Pathophysiology. Subject, aims and methods in Pathophysiology. Structure of the learning courses.

I. **Theoretical Pathophysiology. General Nozology.**
   1.1. General Etiology. Causes and conditions. General Characteristics.
   1.2. General Pathogenesis. Biological essence. Structural lesions and functional disturbances as the basic substrate of a disease. Interrelations “cause – effect” in pathogenesis. Vicious circle. The main pathogenetic link. Adaptive, compensatory, reparative and protective reactions.
   1.3. General Nozology. Notion. Norma. Health. Pathological reaction. Pathological process. Pathological state. Disease. Notion. Phases and outcomes.
   1.4. General Sanogenesis. Notion. Sanogenetic mechanisms (primary and secondary). Interrelations between pathogenetic mechanisms and sanogenetic ones during disease evolution. Complete and incomplete recovery.
   1.5. General Tanatogenesis. Death. General causes. Terminal states. Preagonia. Agonia. Clinical death. Biological death. Pathogenetic aspects of resuscitation. Complications.

II. **General Pathophysiology. Typical pathologic processes.**
2.1. Typical cellular pathologic processes.
   Cell nucleus lesion. Disturbances of the accumulation and transmission of the genetic information. Mutagenesis. Mutations. Congenital diseases (hereditary and non-hereditary). Chromosomal and genetic disorders. Pathology of the cell membrane receptors and intercellular transmission. Modifications in synthesis of the membrane and cytoplasmic receptors.
   Cell membrane lesion. Disturbances of the transmembrane transport. Changes in the transport between cells and interstitial space: diffusion, osmosis, active and passive transport. Typical electrolyte disorders: loss of intracellular potassium and extracellular sodium accumulation. Electrogenesis disturbances.
Intracellular dehydration. Intracellular overhydration (cell swelling). Cellular acidosis and alkalosis. Buffer systems. Hyperenzymemia. Cell membrane lipid peroxidation and oxidative shock.

Cell mitochondria lesion. Energy genesis disturbances. Cellular hypoxia. Oxidation and phosphorilation disorders.

Endoplasmic reticulum lesion. Disturbances of the cell protein synthesis processes.

Complex Golji lesion. Cell excretion disorders.

Cell microsomal system disturbances. Disturbances of the cellular detoxication processes.

Cell lysosomes lesion. Oxigendependent and oxigenindependent protective cell systems disorders. Intracellular and extracellular release of lysosomal enzymes. Cell autolysis.

2.2. Typical tissue pathologic processes.

Cell differentiation disorders. General mechanisms of the tumoral progression. Anaplasia. Hyperplasia. Metaplasia. Morphologic, biochemical and functional modifications.

Cell regeneration disorders. Hyporegeneration and atrophy. Complete and uncomplete regeneration. Sclerosis. Fibrosis. Morphologic, biochemical and functional modifications.

Cell proliferation disorders. Aplasia. Hypoplasia. Hyperplasia. Morphologic, biochemical and functional modifications.

Typical cell metabolic disturbances. Parenchimatous distrophy. Protein distrophy. Fat distrophy. Morphologic, biochemical and functional modifications.

Cellular hyperplasia. Morphologic, biochemical and functional modifications.

Connective tissue disorders. Cells and intercellular matrix affections.

Necrobiosis. Necrosis. Apoptosis. Cellular and tissue reparative processes.

2.3. Typical pathologic processes in organs.

Inflammation. Definition. Biological essence. Exterior signes. Primary and secondary alteration. Mediators. Biological effects. Vascular reactions. Exudation. Leukocyte emigration. Phagocytosis. Proliferation. Regeneration. General manifestations.

Peripheral blood circulation disorders. Arterial hyperemia. Venous hyperemia. Stasis. Ischemia. Blood rheology disturbances. Thrombosis. Embolia as a cause of peripheral vascular disorders. Pathogenesis.

Capillary and interstitial fluid exchange disorders. Filtration and resorbtion disorders. Oedemas. Classification. Pathogenesis of the cardiac, renal (nephritic and nephrotic), allergic, toxic oedemas.

Lymphogenesis and lymph circulation disorders. Lymphostasis.

Organs denervation. Morphologic, biochemical and functional modifications.

2.4. Integral typical pathologic processes.
Thermic balance disturbances. Hypothermia. Hyperthermia. Etiology. Pathogenesis. Compensatory reactions and functional disorders.

Fever. Pyrogens (exogenous and endogenous, primary and secondary). Pathogenesis of the Fever. Periods. Functional modifications. Biological essence.

Hypoxia. Classification due to etiology and pathogenesis. Adaptive, compensatory and pathologic reactions. Hyperoxia and hyperbaric oxygenation. Pathogenic effects.

Stress. Biological essence. Mechanisms. Adaptive and pathologic reactions.

Complete and incomplete starvation. Protein, lipid and carbohydrate, vitamin insufficiency.

Shock. Etiology. Pathogenesis. General characteristics of the different types of shock: traumatic, cardiogenic, anaphylactic, hemotransfusional, endotoxic.

Dehydration of an organism: intravascular, interstitial, intracellular, isoosmolal, hypoosmolal, hyperosmolal. Compensatory reactions. Pathologic modifications.

Overhydration of an organism: intravascular, interstitial, intracellular, isoosmolal, hypoosmolal, hyperosmolal. Fluids redistribution between liquid spaces. Compensatory reactions. Pathologic modifications.

Typical electrolyte concentration deviations: hyper- and hyponatriemia, hyper- and hypokaliemia, hyper- and hypochloremia, hyper- and hypomagneziemia, hyper- and hypocalciemia. Functional disorders.

Acidosis: respiratory, metabolic, excretory, exogenous, compensated, noncompensated. Compensatory reactions. Pathologic modifications.

Alkalosis: respiratory, metabolic, excretory, exogenous, compensated, noncompensated. Compensatory reactions. Pathologic modifications.

III. Special pathophysiology. Pathologic processes in organs and body systems.

3.1. Pathologic processes in central nervous system.

Neuronal functions disorders: electrogensis and rest potential formation disturbances. Excitability. Inhibition.

Transsynaptic transmission disturbances – synaptopathology. Disturbances of synthesis, deposition, release, degradation and recapture of neurotransmitters. Postsynaptic structure lesion.

Sensitivity disorders. Nociceptive and antinociceptive system disturbances. Pain. Physiologic mechanisms. Anaesthesia. Hypostesia. Hyperstesia, parestesia.

Central motoric functions disorders. Central and peripheric paralysis. Hyperkinesis piramidic and extrapiramidic. Spinal hyperkinesis.

Vegetative nervous system disorders. Vagotonia and sympaticotonia.

Reflectory functions disorders in the central nervous system. Neuroses. Parhogenetic mechanisms.

Consciousness disorders. Sleepiness, sopor, stupor, coma.

Sleep disorders. Sleeplessness. Narcolepsia.

Liquorogenesis and liquorodynamics disorders. Intracranial hypertension.
3.2. Pathologic processes in endocrine system.
   Neuro-endocrine hypothalamic disorders. Neurosecretion disturbances.
   Anterior Pituitary disorders. Growth hormone hypersecretion and hyposecretion. ACTH hypersecretion and hyposecretion. Thyrotropic hormone hyper and hyposecretion. Gonadotropic hormones secretion disturbances. Prolactin hyper- and hyposecretion. Posterior Pituitary disorders: vasopressin hypo- and hypersecretion
   Peripheral endocrine glands secretory disorders. Glucocorticoids hyper- and hyposecretion. Catecholamines hyper- and hyposecretion. Thyroid hormones hyper- and hyposecretion. Insuline hyposecretion. Hyper- and hypoparathyroidism. Male hypogonadism. Female hypogonadism.
   Sexuality disorders. Intersexualismus, transsexualismus, homosexualismus. Hypersexuality, hyposexuality. Male impotention. Female frigidity.
   Peripheral endocrine disorders. Hormonal transport and interaction with receptors disturbances.

3.3. Immunologic pathologic processes.
   Humoral, cellular and mixed immunodeficiency. Immediate hypersensitivity. Delayed hypersensitivity. Types I, II, III, IV and V of allergic reactions. Autoimmunity.

3.4. Pathologic processes in digestive system.
   Nutritional motivation disorders. Hypo- and hyperrexia, anorexia, polyphagia, dysrexia, polydypsia.
   Mastication disorders. Teeth pathologic processes. Caries, paradontosis. Oral mucous disorders: stomatitis.
   Salivary secretion disorders. Hypersalivation, hyposalivation.
   Swallowing disturbances. Dysphagia. Gastro-esophageal reflux.
   Gastric secretion disorders. Gastric hypersecretion and hyperchlorhydria. Gastric hyposecretion and hypochlorhydria. Achlorhydria. Ahylia.
   Disturbances of gastric motoric functions. Gastric hyper- and hypotonia. Gastric hypo- and hyperkinesia. Nausea. Physiologic and pathologic vomiting.
   Gastric protective functions disorders. Gastric and duodenal ulcerogenesis
   Gastric digestion disorders. Gastric maldigestion. Operated stomach syndrome.
   Exocrine pancreatic secretion disturbances. Pancreatic insufficiency. Pancreatic autolysis. General modifications.
   Bile secretion disorders. Hypo- and acholia. Maldigestion due to acholia.
   Intestinal digestion disturbances. Intestinal malsecretion. Intestinal maldigestion. Intestinal malabsorption. Intestinal hypotonia. Ileus.
   Large intestines disorders: hypotonia and hypokinezia, atonic constipations, coprostasis, intestinal meteorism, gastrointestinal autointoxication. Hypertonic constipations. Diarrhea. Dysbacteriosis.

3.5. Pathologic processes in Liver.
   Metabolic disorders due to liver affections. Carbohydrate, protein and fat metabolism disturbances. Glycogenoses. Protein synthesis disorders: hypoalbuminemia.
Blood coagulation factors synthesis disorders. Transamination and deamination disorders. Disturbances of lipoproteine, phospholipids, cholesterol synthesis. Fatty liver.

Vitamine metabolism disorders due to liver affections.

Bile pigments hepatic metabolism disturbances. Hyperbilirubinemia. Hepatic jaundice.

Bile formation and excretion disorders. Cholestasis. Acholia. Choleemia. Cholelalemia. Hyperbilirubinemia. Mechanical jaundice. Cholelytiasis.

Liver insufficiency.

3.6. Pathologic metabolic processes.

Carbohydrate metabolism disorders. Carbohydrates insufficiency. Carbohydrate maldigestion and intestinal malabsorption. Hypoglycemia. Hyperglycemia. Glycogenogenesis, glycogenolysis, gluconeogenesis disturbances.

Protein metabolism disorders. Nutritional protein insufficiency. Protein maldigestion and intestinal malabsorption. Hypoproteinemia, hyperproteinemia, dysproteinemia. Hyperurikemia. Goute.

Lipid metabolism disorders. Nutritional lipid insufficiency. Excessive lipid consumption. Lipid maldigestion and intestinal malabsorption. Hyperlipidemia. Hypercholesterolemia. Obesity. Fatty infiltration and fatty distroiphy. Ketogenesis and hyperketonemia.

3.7. Pathologic processes in red blood.

Changes in the circulating blood volume. Hypervolemia. Hypovolemia.

Red blood cells differentiation and maturation disorders. Erythroblastic leukoses.

Red blood cells proliferation disorders. Erythropoietin insufficiency. Aplasia and hypoplasia of bone marrow.

Aplastic anemia. Hypoplastic anemia. Vitamine B_{12} – deficiency anemia. Red bone marrow hyperplasia. Erythrocytoses.

Genetic defects in the erythrocytary system: membranopathies, enzymopathies. Hereditary hemolytic anemias.

Genetic defects of hemoglobin synthesis. Hemoglobinopathies. Iron deficiency anemia. Protein deficiency anemia.

Hemorrhage. Hypovolemia. Posthemorrhagic anemia (acute and chronic).

Acquired hemolytic anemias. Intravascular hemolysis. Intracellular hemolysis. Anemias and jaundice with intracellular hemolysis. Hereditary hemolytic anemias. Hypersplenism.

Hemic hypoxia. Compensatory reactions and clinical manifestations.

3.8. Pathologic processes in white blood.

Mieloid, monocytic and lymphoid cells differentiation and maturation disorders. Leukoses.

Leukocytes differentiation and maturation disorders. Mieloid and lymphoid hypoplasia. Leukopenia. Agranulocytosis. Biological essense.

Mieloid and lymphoid hyperplasia. Leukocytosis. Biological essense.
Leukopenia and leukocytosis due to white blood cells redistribution.

3.9. Pathologic processes in thrombocytic system. Pathology of hemostasis.
Megacariocytes differentiation and proliferation disturbances. Megacarioblastic leukoses. Hypoplasia. Absolute thrombocytopenia. Thrombocytopenias. Thrombocytopenia. Coagulopathies. Thrombosis. Disseminated intravascular coagulation. Hemorrhagic diateses.

3.10. Pathologic processes in cardiovascular system.
Cardiac functions disturbances. Cardiac automatism disorders: tachycardia, bradycardia and sinus arrhythmia. Extrasistolia, cardiac fibrillation (atrial and ventricular). Cardiac blocks.
Coronary insufficiency. Miocardial hyperfunction: volume and resistance overload. Cardiac hypertrophy.
Valvular affections. Congenital and acquired cardiac vices. Septal defects sepal: interatrial and interventricular comunicion.
Cardiac and circulatory insufficiency. Hemodinamic changes and compensatory reactions.
Pericardial affections, pericarditis, hydropericardium, hemopericardium, cardiac tamponade. Intrapercardial hypertension.
Blood vessels disorders. Arterial hypertension (small and large circles). Cor pulmonale. Chronic arterial hypotensionca. Collapse. Shock. Compensatory reactions. Regional circulatory disturbances in the brain, liver, kidney. Cardiac venous return disorders.
Circulatory hypoxia. Compensatory reactions and functional disturbances.

3.11. Pathologic processes in respiratory system.
Atmospheric pressure modifications: hypobaric and hyperbaric conditions, hypoxia and hyperoxia. Exogenous hypercapnia.
Pulmonary ventilation disturbances. Respiratory center disorders. Respiratory muscles paralysis.
Air pathways disorders: obstruction, stenosis. Asphyxia. Dispneas. Atelectasis. Alveolar hypoventilation and hyperventilation.
Bronchiolar disorders: obstruction, bronchiolospasmus. Expiratory dyspnea. Obstructive respiratory insufficiency. Compensatory recations.
Changes of the diffusion of gases in lungs. Alveolar dysfunction. Pulmonary emphysema. Alveolitis. Pneumofibrosis. Pulmonary oedema.
Pleural disorders. Pleuritis. Hydrothorax. Pneumothorax. Intrapleural hypertension. Restrictive respiratory insufficiency. Compensatory reactions. Respiratory hypoxia. Compensatory reactions.
Hemoglobin oxigen affinity disorders. Hemoglobinopathies.
Small circulation disorders. Pilmonary arterial trunk obstruction. Ventilation / perfusion ratio modifications.

3.12. Pathologic processes in excretory system.
Renal glomerular dysfunction. Glomerular filtration disturbances of the renal, subrenal and suprarenal origin.

Renal tubular disturbances. Dtubular genetic defects. Reabsorption disorders (water, electrolytes, glucose, proteins, free amino acids). Hypo-stenuria, isostenuria, hyperstenuria.

Water and elecrrolytes imbalanse of the renal origin. Renal qedemas (nephrotic and nephritic).

Tubular secretion disorders (potassium, H+-ions, uric acid). Acidogenesis and ammoniogenesis. Renal acidosis.

Endocrine renal function disturbances. Activation of the renin-angiotensin-aldosterone system. Renal hypertension.

Erythropoietin secretion disorders. Nephrogenic anemia.

Quantitative and qualitative urine modifications: polyuria, oligo-anuria, nicturia. Pathologic components in the urine: proteinuria, glucosuria, hematuria, hemoglobinuria, leukocytes presence (piuria), bilirubinuria, cylindruria.

Urine elimination disturbances. Renal tubular block. Pielonephritis. Urolythiasis.

Renal insufficiency. Hyperazotemia, overhydration, oedemas, acidosis, arterial hypertension, anemia, autointoxication.

IV. Clinical Pathophysiology.

Pathogenesis of clinical syndromes and different nozologic forms

4.1. Pathologic syndromes in the central nervous system (CNS). Meningitis. Encephalitis. Chronic brain ischemia. Brain strokes. Intracranial hypertension. Brain edema. Changes of liqurodynamics.

4.2. Pathologic syndromes in endocrine system. Pituitary gigantismusr and nanisms. Simmonds’s disease. Diabets mellitus. Bazedow – Graves’s disease. Hypothyroid states. Cushings syndrome. Feochromocytome. Adreno-genital syndromes. Hyper- and hypoparathyroidism. Asexual disorders: male impotention, female frigidity. Phertility disorders.

4.3. Nozologic forms in immunology. Bruton’s disease. Swiss imunodeficiency. Anaphylaxy. Serum sickness. Collagenoses. Rheumatism.

4.4. Syndromes and Nozologic forms in digestive system. Gastritis. Gastric and duodenal ulcers. Hepatitis. Hepatosis. Liver cyrrhosis. Protal hypertension. Liver insufficiency. Pancreatitis. Enteritis. Colitis. Hemolytic, parenchimatou and mechanical jaundice.

4.5. Metabolic syndromes and Nozologic forms. Glycogenoses (glycogen storage diseases). Lipidoses. Atherosclerosis. Obezity. Fatty infiltration and fatty distrophy of organs.

4.5. Pathologic syndromes and Nozologic forms in red blood system. Aplastic anemia. Iron deficiency anemia. Vitamin B_{12} and folic acid deficiency anemia. Posthemorrhagic anemia. Toxic hemolytic anemia. Erythremia.
4.6. Pathologic syndromes and Nozologic forms in white blood system. Leukoses.

4.7. Pathologic syndromes and Nozologic forms in thrombocytes system. Thrombocytopathies. Thrombocytopenias.

4.8. Pathologic syndromes and Nozologic forms in cardiovascular system. Valvulopathies. Ischemic heart disease. Myocardial infarction. Myocarditis. Myocardiosclerosis. Pericarditis. Acute cardiac insufficiency. Arterial hypertension. Atherosclerosis. Shock.

4.9. Pathologic syndromes and Nozologic forms in respiratory system. Bronchial asthma. Pneumonia. Pulmonary emphysema. Pulmonary oedema. Pulmonary artery embolia

4.10. Syndromes and Nozologic forms in the kidney pathology. Acute diffuse glomerulonefritis. Nephrotic syndrome. Pielonefritis. Urolythiasis.

Practical courses

Finishing to study Pathophysiology students must know: definitions, etiology, pathogenesis, manifestations, consequences, biological essence of 200 pathologic processes. Students of the IV-th year must know: pathogenesis of 90 clinical syndromes and nozologic forms, must possess experimental work on animals such as anaesthesia, immobilization, drugs administration (intramuscular, intraperitoneal injections), blood collection, thermometria, blood vessels preparation, frog peritoneum preparates; they must be able to do simple surgical interventions and possess experimental models of inflammation etc. Students must be able to investigate blood smears, to account the number of red and white blood cells, cytologic exudate analysis, osmotic resistance of red blood cells, to explain ECG modifications in the different types of cardiac arrhythmias and myocardial infarction, to analyse spermograms, blood picture in various anemias and leukoses, bile pigments changes in different types of jaundice. Students must be able to appreciate the functional state of kidneys (clearance, urine analysis).

References

1. V.Lutan, Tatiana Zorkina, and oth. Medical Pathophysiology. Vol.I Chisinau, 2002. Redaction (engl.) by Tatiana Zorkina, 2006.
2. Veronica Colev (red.). Pathophysiology. Iasi, 2001.
3. Handbook of Practical Pathophysiology. Ed. By Veronica Colev. Iasi, 1999.
4. Tim D. Spector, John S. Axford. An introduction to General Pathology. Churchill Livingstone, London, New-York, 1999.
5. Cotran R., Cumar V., Robbins S.L. Basic Pathology, Saundfers, 1997.
6. Cotran R., Cumar V., Robbins S.L. Pathologic Basis of Disease. 5th Edition. W.B. Sauanders Company, Philadelphia, 1994.
7. Guyton AS.C. Textbook of medical physiology. W.B. Sauanders Company, Philadelphia, 1986.