BIOCHEMISTRY II - examination 4th Semester – **2015** **GENERAL MEDICINE**

Knowledge of the basic metabolic pathways gone through in Biochemistry I will be required.

Students are supposed to know the reference values of the analytes given below.
In other analytes, an appropriate orientation in physiological data is expected.

The list of analytes to Biochemistry II examination:

Serum / plasma

Cholesterol total

HDL-cholesterol

LDL-cholesterol

Triacylglycerols

Glucose

Creatinine

Urea

Bilirubin total

Proteins total

Albumin

Na^+

K^+

Cl^-

Ca^{2+}

pH

pCO_2

HCO_3^-

BE (base excess)

Osmolality

Buffer bases of plasma

Blood

Hemoglobin
Buffer bases of full blood

Urine

pH
Protein excretion
Albumin excretion

The examination consists of two parts, the computer test and oral examination.

The computer test - the first part of the examination

The test consists of 25 questions and is solved on computers in the computer room of Department of Biochemistry (time limit 45 min) (specific personal number /UCO/ and key-word for IS MUNI is necessary for entrance to the test):
As a rule, 10 questions are bent on the knowledge acquired in the practical exercises. Remaining 15 questions are bent on an essential knowledge ranging over all studied topics.
Only those students who gain 14 correct answers at a minimum will be permitted to sit for the oral examination.

The major topics for questions regarding practicals

- Principles of optical and electrophoretic laboratory techniques.
- Laboratory methods and assessment of the results. Sampling of blood, processing of samples.
- Basic calculations used in biochemical laboratories - diluting of solutions, converting molarities to mass concentrations and the other way round, calculations dealing with the 24h excretion of compounds into the urine.
- Total serum protein and albumin - the normal values in health, some states causing a decline or rise in serum albumin and total protein levels.
- Biochemical markers of heart infarction. Estimation of CK-MB activity, myoglobin, and troponins in the diagnosis of heart infarction.
- Electrophoretic separation of serum proteins: five major fractions and the typical pattern (approximate percentages), the dominant components in the globulin fractions.
- Bilirubin in blood serum - the unconjugated and conjugated bilirubin, the upper limit for normal concentrations of total serum bilirubin. Three main types of hyperbilirubinaemia with corresponding findings in serum, urine, and faeces.
- The causes of increased catalytic concentrations of ALP, AST, ALT, CK, LD, and amylase in blood serum, the clinical significance of the assays.
- Blood glucose - the mean concentration, the reactions involved in the enzymatic assay of glucose. The oral glucose tolerance test and the principle of the test evaluation. The significance of glycohaemoglobin determination. Late complications of diabetes – microalbuminuria.
- The serum lipids and approximate concentrations of the major lipid classes in blood serum. The major classes of lipoproteins and their relative sizes, constituents, and functions. Cholesterol concentration in serum, the significance of the HDL- and LDL-cholesterol concentration changes.
- Considering of the blood urea concentration and of its excretion: clinical significance, application to an estimate of the nitrogen balance (total nitrogen excretion).
- Serum creatinine and the urinary excretion of creatinine (mean values in healthy adults), clinical significance of the determination in serum and urine; calculations of the creatinine clearance and of tubular reabsorption of water from given data, the principle of calculating the clearances and the fractional excretions of other urinary constituents.
- The physiological values of the main parameters of acid-base balance in arterial blood and of concentrations of buffer bases in blood and plasma.
- Urinalysis (urine collection, pH, osmolality).The main "abnormal" urine components (the approximate amounts excreted into the urine of healthy individuals, principles of the chemical tests for urine proteins, glucose, ketone bodies, haemoglobin, bilirubin and urobilinoids), interpretation of the results in routine urinalysis.
- Renal calculi - the main components (calcium oxalate, uric acid, calcium phosphate), principles of the simplified chemical analysis based on the differences in the solubility of the components (in acidic or alkaline reagents).

- Principles of the main immunochemical assays used in clinical biochemistry (immunonephelometry and immunoturbidimetry, immunodiffusion methods, immunoelectrophoresis, competitive radioimmunoassays and enzyme immunoassays, ELISA).

The oral part of examination

Students select three questions from the sets (1-28, 29-58, 59-89) and have about 30 minutes for the written preparation. They should summarize their answers as concisely and accurately as possible. It is recommended to follow these items:

- to write a brief synopsis emphasizing the main ideas
- to draw metabolic pathways in structural formulas with a short comment
- where appropriate, to draw a picture

A good and concise preparation reflects the students' knowledge and understanding the biochemistry and will be considered in the final classification.

List of questions for the oral examination

1 Factors influencing results of laboratory examination (three phases of examination, biological and analytical factors, sample collection and handling of samples, interpretation of results, reference interval and its calculation, critical difference).

2 The significance of (both functional and non-functional) enzyme assays in blood serum. Isoenzymes - multiple forms of LD and CK.

3 Provision of glucose in different states, the factors increasing susceptibility of glucose (glucagon, adrenaline, cortisol). Glucosuria.

4 The basic metabolic disorder in diabetes mellitus: Hypoglycemia and hyperglycemia, the cause of ketoacidosis or of hyperosmolar coma. Long term complications of diabetes.

5 Lipids in blood plasma and the major classes of lipoproteins (differences in the lipid and apolipoprotein content, in size, in properties and in electrophoretic mobility, the origin in enterocytes and hepatocytes).

6 Transformation of chylomicrons and VLDL.

7 Metabolism of high-density lipoproteins.

8 The movements of cholesterol and its elimination. The balance of sterols and the bile acids transformation. Drugs affecting level of cholesterol.

9 The metabolic interrelationships among body organs predominating in a well-fed state (absorptive phase).

10 The metabolic interrelationships among body organs predominating after a brief fast (post-absorptive phase) and during prolonged fasting (starvation).

11 The main features of metabolism at overnutrition and obesity (production o adipokines, changes in metabolism of lipids and saccharides, insulin resistance, consequences)

12 The main features of metabolism at stress and metabolic stress

13 The main features of metabolism of adipous tissue at various conditions (after the meal, starvation, obesity). Main hormones of adipose tissue.

14 Proteins in human nutrition, parameters of quality, nitrogen balance and assessment of catabolic state

15 Metabolism of amino acids at various phases of metabolism (resorption phase, starvation, high-protein diet, hypercatabolic state, lack of dietary proteins)

16 Ammonium transport, the glutamine cycle and the glucose-alanine cycle.

17 Degradation of haemoglobin, formation of bile pigments.Metabolism and excretion of bile pigments. The main types of hyperbilirubinaemia.

18 Structure of contractile elements of skeletal muscle fibres (sarcomere, the proteins of thick and thin filaments, functions).Cycle of contraction and relaxation of skeletal muscle.

19 Provision of energy for muscle contraction and relaxation (substrates and pathways depending on the intensity as well as duration of muscular work or exercise).

20 Differences in mechanisms of cardiac and smooth muscle contraction. Biochemical markers of myocardial damage.

21 Synthesis of NO, isoenzymes of NO synthase, function of NO in organism, receptors of NO.

22 Nervous tissue – main types of cells and their function, myelin membrane, specific properties of endotel lining of vessels in brain, provision of energy and nutrient requirements, relationship of neurotransmitters to amino acids (a survey).

23 Cerebrospinal fluid – origin and composition

24 Membrane potential of a neuron, depolarization and the action potential propagation. Voltage-operated and receptor-operated (ligand-gated) ion channels - examples.

25 Adrenergic synapse (release and inactivation of the transmitter, the types of adrenergic receptors, signal transduction).

26 Cholinergic synapse (biosynthesis of the neurotransmitter and the release of it, two principal types of acetylcholine receptors and mechanisms of their function).

27 Acetylcholinesterase and its inhibitors (examples of organophosphate insecticides, typical signs of toxic effects, the first aid - the counteractive alkaloid).

28 Inhibitory GABAergic synapse ($GABA_A$ receptors, the effect of benzodiazepines and other ligands).

29 Composition and function of extracellular matrix. Fibrilar and interfibrilar components. Markers of ECM remodelation.

30 Collagen and elastin (structural features, biosynthesis of collagen). Lysine – the role of lysyl residues in connective tissue (covalent crosslinks of collagen fibrils, desmosine of elastin).

31 The bone – mineralization and remodelation, hormonal control. Biochemical markers of bone formation and of bone resorption.

32 Retinol and its derivatives - the biological role, biochemistry of visual excitation (activation of transducin, consequences in decrease of cGMP with hyperpolarization and in decreased Ca^{2+} stimulating guanylate cyclase).

33 Calciferols (calciols) - structure, sources, transformations, effects, mechanism of action.

34 Vitamin K - the biochemical function, significance for blood clotting, structural analogs and significance.

35 Digestion in the mouth and in the stomach (constituents of the saliva, the gastric secretion, secretion of HCl, humoral control of hydrochloric acid output).

36 The bile - formation, composition, functions of the constituents.

37 Digestion and absorption of saccharides (amylases and intestinal brush-border enzymes).

38 Digestion and absorption of lipids from the GIT (incl. chylomicrons, the fate of them).

39 Proteolytic enzymes of the digestive tract (secretion, activation, specificity), absorption of amino acids and peptides.

40 Biochemistry of small and large intestine, endocrine function

41 The specific functions of the liver in metabolism of nutrients and proteosynthesis. Metabolic zonation of liver.,

42 Function of liver in excretion.

43 Biochemical tests used for identification of liver injuries (detection of cell damage, cholestasis, reduced proteosynthetic capacity, etc.).

44 Distribution of body water, factors influencing the distribution of body water and its excretion (ADH, aldosteron, natriuretic peptides), consequences of retention or of dehydration.

45 Osmotic and oncotic pressure of blood plasma, plasma osmolality (values of the main parameters, empirical relations for a rough estimate of plasma osmolality) and osmolality regulation.

46 Electrolyte status of blood plasma. Relation of ion concentrations to acid-base balance (buffer base and strong ion difference, anion gap).

47 Alkali cations - distribution in various compartments, approx. daily intake and output, control of the excretion (angiotensin-aldosterone, natriuretic peptides), consequences of retention or of heavy losses of electrolytes.

48 Transport of CO_2 in blood: pCO_2 in arterial and venous blood, $[HCO_3^-]$, carbaminohaemoglobin, physically dissolved CO_2, the ratio $[HCO_3^-]/[CO_2+H_2CO_3]$.

49 Metabolic acidosis – causes and principle of compensation

50 Respiratory acidosis – causes and principle of compensation

51 Metabolic alkalosis – causes and principle of compensation

52 Respiratory alkalosis - causes and principle of compensation

53 Buffering systems in blood, blood plasma (components, concentrations), the main buffer bases in interstitial and intracellular fluids. Blood acid-base parameters (reference values, changes of the values in acute disturbances and in the course of their compensation).

54 The role of the kidney and of the liver in acid-base balance.

55 Filtration of the plasma through the glomeruli (composition and permeability of the filtration medium, glomerular filtration rate – creatinine clearance, glomerular proteinuria).

56 Reabsorption and secretion in the renal tubules (water, electrolytes - natriuresis, low molecular compounds – glucose, amino acids, uric acid, tubular proteinuria), the term fractional excretion E/F.

57 Transport processes in loop of Henle, distal tubulus and collecting duct. Main types of diuretics and principle of their effect.

58 Endocrine functions of kidney (erythropoetin, rennin-angiotensin system, aldosterone, calcitriol)

59 Nitrogenous low-molecular constituents of blood plasma and urine (alanine, glutamin, urea, creatinin, uric acid, NH_4^+,) – origin, main factors affecting their plasmatic concentration and excretion.

60 Major fractions of the plasma proteins, main components in electrophoretic fractions (albumin, haptoglobin, transferrin, examples of the acute-phase proteins, their origin and natural functions, principles of appreciating the alterations in individual plasma proteins).

61 Metabolism of iron (absorption, transfer and distribution in the body, functions, iron balance).

62 Antigens and antibodies (the terms complete antigen - immunogen, hapten, sequential and conformational immunogenic determinants - epitopes, classification of the human immunoglobulins and their molecular structures, specific roles of different Ig domains). The antibody-antigen reaction (formation of an immune complex, precipitation and agglutination as secondary reactions).

63 Blood clotting cascade. Fibrinogen, transformation to fibrin, and fibrinolysis.

64 Inhibitors of blood clotting - anticoagulants *in vivo* (function of heparin and coumarin derivatives) and *in vitro* (prevention of blood clotting, blood plasma).

65 Endothelium – function and special substances produced by endothelial cells

66 Red blood cells (metabolism, membrane, blood group determining structures).

67 Methaemoglobin in normal blood (origin, reduction to Hb), inherited and acquired methaemoglobinaemia (nitrates and nitrites in the environment).

68 Leukocytes – characteristic metabolic processes. Neutrophil granulocytes – interaction with endothelium, production of special proteins, selectins, secretion granula, phagocytosis, respiratory burst.

69 Principles of metabolism control (control of enzyme activity and of protein synthesis, control of transport across membranes, extracellular signals).

70 General features of hormone synthesis, secretion, transport, and inactivation in relation to signal intensity received by the target cell.

71 Membrane receptors cooperating with G-proteins (types of receptors and G-proteins, corresponding intracellular messengers).

72 Receptors with tyrosine kinase activity. The most important signal pathways (RAS and MAP kinase pathway)

73 Receptors cooperating with non receptor kinases (JAK/STAT signal pathway)

74 Intracellular hormones receptors, their activation and consequences.

75 Intracellular Ca^{2+} distribution - calcium channels, carriers, Ca^{2+}-dependent proteins (e.g. calmodulin) and enzymes, relations to cell functions.

76 Protein kinases (main classes) and phosphoprotein phosphatases, regulation of their activity

77 The role of hypothalamic and pituitary hormones – a brief survey, functions.

78 Synthesis of thyroid hormones (description, localization, secretion and its control).

79 Calcium and (inorganic) phosphate metabolism –intake, distribution in the body, mineral deposits and soluble forms, the role of PTH, calcitriol, calcitonin. Plasmatic concentration of calcium, factors affecting it.

80 Synthesis and inactivation of catecholamines, degradation products.

81 Glucocorticoids - structure, biosynthesis, function, regulation of secretion.

82 Mineralocorticoids - structure, biosynthesis, function, regulation of secretion, the renin-angiotensin system.

83 Sex hormones (structure, biosynthesis, function, sites of secretion and their regulation, inactivation).

84 Insulin (synthesis, regulation of secretion, fate, insulin receptor and results of its activation). Oral glucose tolerance test.

85 Insulin receptor and effects of its activation

86 The metabolism of xenobiotics - stage I of their biotransformation (various types of transformation, examples, mixed-function monooxygenases – function of *cyt* P450).

87 The metabolism of xenobiotics - stage II (conjugation). Reaction types, reactant activation, products – examples).

88 Alcohols and phenols as xenobiotics and their transformation (ethanol and ethylene glycol, salicylates and acetaminophen).