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Харківський національний медичний університет**

Кафедра Внутрішньої медицини №3
Факультет VI по підготовці іноземних студентів

ЗАТВЕРДЖЕНО

на засіданні кафедри внутрішньої медицини №3

«29» серпня 2016 р. протокол № 13

Зав. кафедри _____ д.мед.н., професор Л.В. Журавльова

**МЕТОДИЧНІ ВКАЗІВКИ
для студентів**

з дисципліни «Внутрішня медицина (в тому числі з ендокринологією)
студенти 4 курсу I, II, III медичних факультетів, V та VI факультетів по підготовці
іноземних студентів

**Гострі та хронічні ускладнення цукрового діабету. Особливості перебігу та
лікування цукрового діабету у хірургічних хворих, при вагітності**

Харків 2016

Topic – «Acute and chronic complications of diabetes mellitus: diabetic retinopathy, nephropathy, neuropathy, and diabetic foot. Progress and treatment of diabetes mellitus of surgical patients and pregnant women»

Number of hours - 4

Topicality

Vascular injuries are among the leading syndromes of diabetes mellitus manifestations. In most cases, their intensity determines the patients' efficiency, prospects as to the disease progress and the duration of their life. In this connection, timely and exact diagnostics and treatment of diabetic angiopathy acquire a leading value in diabetology. The problem of angiopathies is interdisciplinary, as it is not purely a matter of diabetology, but also of ophthalmology, surgery, and nephrology. Knowledge of clinic and therapeutic approach at the different intensity of differently located angiopathies allow prolonging patients' efficiency.

Educational aims:

- to acquaint students with classification of diabetic angiopathies and neuropathies;
- to teach students the stages of development, diagnostics, differential diagnosis, treatment and prevention of diabetic nephropathy;
- to teach students the stages of process, diagnostics, prophylaxis and treatment of diabetic retinopathy;
- to acquaint students with diagnostics and treatment of diabetic neuropathy;
- to acquaint students with the diabetic foot infections: their classifications, diagnostics, algorithm of treatment;
- to teach students the principles of treating pregnant women suffering from diabetes mellitus;
- to acquaint students with diagnostics and surgical treatment of diabetic angiopathy of lower extremities;
- To acquaint students with timely diagnostics of diabetic gangrene, with peculiarities of urgent and planned surgical interferences for patients with diabetes mellitus.
- to acquaint students with classification of urgent conditions in diabetes;
- to teach students the stages of development, diagnostics, differential diagnosis, treatment and prevention of acute complications of diabetes mellitus;

What must a student know?

- classification of diabetic angio- and neuropathies;
- stages of diabetic nephropathy, retinopathy, and angiopathy of lower extremities;
- diagnostics and differential diagnostics of diabetic nephropathy, retinopathy, and angiopathy of lower extremities;
- treatment and prevention of diabetic nephropathy, retinopathy, and angiopathy of lower extremities;
- classification, diagnostics and treatment of diabetic neuropathy;
- diabetic foot infections: classification, diagnostics, algorithm of treatment;
- classification, diagnostics, differential diagnosis, treatment and prevention of acute complications of diabetes mellitus;
- principles of treating pregnant women suffering from diabetes mellitus;
- Diabetic gangrene, peculiarities of urgent and planned surgical interferences for patients with diabetes mellitus.

What must a student be able to do?

- to analyze data, received during questioning and examination of patients suffering from diabetes mellitus, select a leading syndrome;
- to interpret data of ophthalmoscopy, conjunctiva biomicroscopy, capillaroscopy, thermography, ECG, urine analysis, state of nitrogen-generating kidneys function, kidney blood flow, canalicular secretion and reabsorption;
- to coordinate the diet and chemical treatment of patients suffering from diabetes with different stages of vascular injuries;
- to write prescriptions, prescribe physical therapy procedures and physical activity mode;
- to determine the presence and type of neuropathy during clinical examination of patients, to appoint treatment for the certain type of neuropathy;
- to appoint treatment of pregnant women suffering from diabetes mellitus;
- To appoint differentiated treatment of patients in the "Diabetic foot" room.

List of practical skills which should be mastered by a student

- interrogation of patients: to find out complaints which testify to vascular and neurological injuries, specifying the order of symptoms appearance, their stability, results of therapy; to determine stability of carbohydrate exchange compensation, presence of proteinuria, its stability, character of sediment in urines and actual treatment; presence of hypoglycemia in the anamnesis, their frequency, intensity; vascular catastrophes; digestive apparatus and urinary organs functioning;
- examination of patients: appearance, presence of edemata, muscular dystrophy; state of skin and its appendages; character of pulsation on the distal sections of arteries, muscular strength, reflexes, state of all of types of sensitiveness, visual activity; cardiac rhythm, AT level and its changes in orthostasis, character of intervals on the ECG, intensity of changes on the ECG; capillaroscopic picture, data of rhenography, rheoplethysmography, and volume sphygmography; bulk urine analysis, proteinuria, cylindruria, presence of leucocytes and red corpuscles; specific gravity of urine and its dynamics within 24 hours, correlation of daily and nightly diuresis; blood haemoglobin concentration, levels of lipids, cholesterol, urea, albuminous factions; character of renal plasma flow, glomerular filtration and canalicular reabsorption; analysis of ophthalmoscopic data;
- substantiation of diagnosis, prescribing additional necessary diagnostic procedures, with grounding their necessity;
- Plan of immediate treatment, stage treatment, medicines, dose and terms of their taking, use of other ways of influence; forecast and medical and social examination.

Theme Contents

Chronic and acute complications of diabetes mellitus: diabetic retinopathy, nephropathy, neuropathy, and diabetic foot infections. Progress and treatment of diabetes mellitus of surgical patients and pregnant women

Clinical classification of diabetic angiopathies

1. Microangiopathies:

- a) Nephropathy;
- b) Retinopathy;
- c) Microangiopathy of lower extremities;
- d) Generalized microangiopathy, in particular microangiopathies of skin, muscles and Internal.

2. Macroangiopathies (atherosclerosis) of:

- a) aorta and coronaries;
- b) cerebral vessels;
- c) peripheral vessels;
- d) general atherosclerosis.

3. Universal diabetic angiopathy (combination of macro- and microangiopathies).

Diabetic nephropathy

Basic types of kidney glomerular injuries due to diabetes:

1. *Diffuse glomerulosclerosis* (intracapillary) progresses rather slowly and rarely (and rather lately) lead to renal insufficiency. In most cases, within 4-5 years after manifestation of diabetes, kidneys show the phenomena of diffuse diabetic glomerulosclerosis, and within 15-20 years from the beginning of illness 43-45% patients have these changes.

2. *Knotted glomerulosclerosis* is observed, as a rule, more frequently in case of diabetes mellitus type 1. Simultaneously with the displays of knotted glomerulosclerosis there are symptoms of diffuse diabetic glomerulosclerosis. About 25% of diabetes patients have knotted injuries, they appear almost at the beginning of disease, make quick progress with the development of diabetic glomerular and capillary microaneurysms.

Microaneurysms are located on periphery or in the center of the knot, and narrow or fully occlude the capillary bore. Microaneurysms are transformed in *the knots of Kimmelstiel-Wilson* (hyaline knots), which contain a significant number of nucleuses of mesangium cells and the hyaline matrix.

Progress of diabetic nephropathies and their diagnostics

The clinical practice uses the classification of diabetic nephropathy stages by *S.E. Mogensen (1983)*.

Stage 1: hyperfunctional hypertrophy. It appears at the diabetes manifestation, conditioned by the adaptation renal hypertrophy with the increase of size and number of glomeruli.

It is characterized by *hyperperfusion, hyperfiltration and normoalbuminuria* (less than 30 mg/day). Microalbuminuria is reversible, which occasionally happens in case of adequate insulinotherapy. The speed of glomerular filtration is high, but it is reversible as well.

Methods of microalbuminuria express diagnostics: dipsticks for urine "Micral-Test" by "Boehringer Mannheim" (Austria), absorbing pills of "Micro-Bumintest" by "Bayer" (Germany), etc. With these methods, it is possible to quickly (during 5 minutes.) define the presence of albumin microconcentrations in urine with sufficient precision.

Stage 2: initial structural changes. The morphological signs of this stage appear in 2-5 years after manifestation of diabetes and are characterized by thickening of the basal membrane of glomeruli and increase of mesangium volume.

Clinically this stage shows only in *hyperfiltration and normoalbuminuria* (less than 30 mg/day). Microalbuminuria appears periodically, more frequently during diabetes decompensation and in case of physical activity. Speed of glomerular filtration is increased.

Stage 3: beginning of nephropathy. It appears in over 5 years from the beginning of disease, as a rule, it is 10-15 years.

Microalbuminuria becomes permanent, from 30 to 300 mg/day. Speed of glomerular filtration is either significantly increased or normal. Blood pressure tends to rise, especially and in case of physical activity.

Stage 4: clinical nephropathy. It appears in 30-40% cases of diabetes mellitus type 1 in 15-20 years from the beginning of disease.

Microalbuminuria is transformed in *clinical proteinuria* (protein loss with urine exceeds 0.5 gram a day). Renal compensatory ability is exhausted, and the speed of glomerular filtration gradually, but steadily decreases. Hypertension becomes almost permanent, and peripheral edemata appear.

Stage 5: the stage of renal (uremic) insufficiency. It is characterized by a very low speed of glomerular filtration (less than 10 ml/min.), the creatinine level of blood serum exceeds 200

mmol/l. There are rough morphological changes of kidneys - total diffuse or knotted glomerulosclerosis.

The first three stages of diabetic nephropathy are pre-clinical and proceed without clinical symptoms. The only objective sign of nephropathy is microalbuminuria. At these stages the nephropathy can still be stabilized and decelerated provided careful control of glycemia. The prevention of nephropathy subsequent progress includes elimination of intra-glomerulus hypertension, normalization of intrarenal hemodynamics and kidneys volume which is achieved by prolonged use of inhibitors of angiotensin converting enzyme.

Appearance of proteinuria testifies to the serious and irreversible destructive changes in kidneys: for instance, about 50-75% of glomeruli are already sclerosed and morphological and functional changes became irreversible. From the beginning of proteinuria the speed of glomerular filtration progressively decreases at a speed of 1 ml/min. per month (about 10 ml/min. per year) which leads to the final stage of kidney insufficiency in 7-10 years from the beginning of proteinuria. Efficiency of treatment on the stage of clinically apparent nephropathy is low - practically no therapeutic facilities are able to slow down the nephropathy progress and the term of the uremia stage significantly.

Treatment of diabetic microangiopathies

1. The compulsory condition of prophylaxis and treatment of diabetic microangiopathies is *good compensation of diabetes mellitus*, normalization of carbohydrate, lipid, albumin metabolism indices, and elimination of polyvitaminic insufficiency.

2. Course treatment with *vitamin medications* ensures the stable normalization of metabolic processes.

Coccarboxylase is injected intramuscularly 500-100 mg 1 time a day in courses of 20 days.

Riboflavin-mononucleotide is injected intramuscularly or hypodermically 1 ml of a 1% solution during 20 days.

Flavinatum is prescribed intramuscularly 2 mg 1-3 times a day in a course of 15-20 days.

Vitamin E has antioxidant action, improves the indexes of lipid metabolism. It is prescribed in the dose of 100 mg per day.

Nicotinamidum has also antioxidant action, decreases the activity of polyol shunt in tissues, boosts the B-cells regeneration. It is prescribed in the dose of 75 mg per day.

3. *Angioprotectors* improve vascular walls and reduce its increased permeability. *Anginin* (prodectin, paramidin) reduces the increased permeability of vessels, blocks the bradykinin activity, diminishes vascular wall infiltration by atherogenic lipoproteins, decreases thrombocyte aggregation, improves microcirculation, assists in hemorrhages involution, diminishes trophic violations. It is prescribed in pills of 250 mg, up to 6 pills per day during 2-5 months.

Dicinon (etamsylat) significantly boost capillaries firmness, improves microcirculation, it has a hemostatic action, without increasing the coagulative properties of blood. It is especially effective in case of diabetic retinopathies with hemorrhages. The pills of 250 mg are taken 3 times per day during 2-3 weeks or the medicine may be prescribed intramuscular at the dose of 2 ml of a 12.5% solution 1-2 times per day. In case of intravenous injection the hemostatic effect comes in 7-15 minutes with duration of 4-6 hours.

Doksium (Calcium dobesilat) reduces the capillaries permeability and thrombocyte aggregation, as well as exudation and hemorrhagic effects. It has the highest effect in case of diabetic retinopathies. It is taken in pills of 250 mg 3-4 times per day during 4-6 months with the course repetition during 5-6 years.

Emoksipin represses the peroxidation processes; it has angioprotective and anticoagulating action and assists in hemorrhages resorption. For retinopathies treatment it is injected retrobulbarly with the dose of 0.5 ml of a 1% solution per day (10-15 days), subconjunctivally and parabolbarly with the dose of 0.5 ml per day (10-30 days), the therapy course is repeated 2-3 times a year.

Endotelon reduces the capillaries permeability, stabilizes the collagen and mucopolysaccharides system. It is taken in pills of 50 mg 2 times per day.

Divaskan (iprazochrome) represses prostaglandins of group E and serotonin activity, normalizes permeability of vessels, and blocks thrombocyte aggregation. It is taken in pills of 2.5 mg 3 times per day during 1-3 months.

Komplamin (teonicol, xantinol nicotinate) improves microcirculation and histohematogenous exchange, reduces the capillaries permeability; it has antiaggregant and antiatherogenic action, increases the fibrinolytic blood activity. It is prescribed inwardly in pills of 150 mg 3-4 times per day during 1-2 months.

4. *Antiagreganti* reduces thrombocytes aggregation and microthrombosing in the microcircular channel which greatly improves the microcirculation as a whole. *Heparinum* has anticoagulating and antiaggregant properties. It is injected hypodermically in the abdomen in the dose of 5000 UN. 4 times per day during 2-3 weeks with the gradual decline of dose.

Trentalum (pentoxiphilin) is taken by 2 pills (of 0.1 gram or 0.3 gram) 3 times per day (during 1 month), then by 1 pill 3 times per day during 1-2 months. Parenteral introduction (up to 100 or 300 mg) often causes fever and hyperemia.

Curantylum (dipyridamole) is prescribed in pills of 25 mg (1-2 pills) 3 times per day during 1-2 months.

Acetylsalicylic acid has in small doses of 160-300 mg per day an antiaggregant action.

Tiklid (ticlopidine) is taken in pills of 200 mg 1-2 times per day (for 3-4 weeks).

Reopoliglyukin is injected intravenously drop-by-drop in the dose of 400 ml 2-3 times per week, with 6-8 infusions within a course.

5. *Vasorelaxants* eliminate vasospastic reactions and increase an interstitial blood flow.

Nicotine acid not only relaxes vessels but also activates fibrinolysis. It is prescribed intramuscularly in the dose of 2 ml of a 1% solution 1 time per day for 20 days.

Nicospanum is taken by 1-2 pills 3 times per day for 3-4 weeks.

Andekalin (angiotrofin) is taken by 2 pills (5 mg each) 3 times per day (for 1 month) or intramuscularly in 10-40 UN. 1 time per day (during 2-4 weeks).

Treatment and prophylaxis of diabetic nephropathy

Stable microalbuminuria is an indication for beginning of active specific therapy of diabetic nephropathy.

The main principles of treatment of diabetic nephropathy at Stages I-III are the following:

- 1) optimal compensation of metabolic violations (including the dislipidemy correction);
- 2) renal and systemic hypertension relief.

An important role is played also by the *angiotensin converting enzyme (ACE) inhibitors*. The ACE inhibitors at diabetic nephropathy are able to relieve intraglomerular hypertension, in this way influencing the leading mechanism of kidneys affection progress, and they have the great *nephroprotective effect* at diabetes mellitus. These medicines block formation of the vasoconstrictive angiotensin II eliminating the morbid action of this factor on kidneys, which results in renal angiospasm, activation of sclerotic processes in renal tissues, and increase of permeability of renal filter for proteins. Blockade of angiotensin II action with the ACE inhibitors allows maintaining the normal structure of renal tissue and preventing the progress of diabetic glomerulosclerosis. Significant *antihypertensive action* complements the nephroprotective one of ACE inhibitors at diabetes mellitus.

It is necessary to prescribe ACE inhibitors as a prophylaxis of diabetic nephropathy progress at the microalbuminuria stage.

A new approach to treatment of diabetic nephropathy is use of *glycosaminoglycans*. The medicine discovered a considerable nephroprotective effect of glycosaminoglycans, which is conditioned by their ability to slow down the sclerotic processes in kidneys and restore the heparitin sulphate generation, which is the main structural element of basal renal membrane.

Sulodexid (*Vessel Due F*) is a medication of the glycosaminoglycans group; it contains heparin-like substances. The medication is taken orally by 2 capsules 2 times per day, if there is no effect (according to the albuminuria level) in a month it is possible to increase the dose up to 3 capsules 2 times per day. A capsule contains 250 LSU (liposome units).

Principles of treatment of diabetic nephropathy, Stage IV:

- 1) low-protein and sodium-free diet: restricted consumption of animal protein to a 0.6 – 0.7 gram per 1 kg of the body weight per day and restricted consumption of salt to 3 – 5 gram per day;
- 2) normalization of arteriotony: it is preferable to prescribe ACE inhibitors, it is possible to take other antihypertensive drug with them.

The speed of diabetic nephropathy progress in case of treatment with ACE inhibitors slows down in 5-6 times, while in case of traditional antihypertension therapy (β -adrenoceptor blocking agents and diuretics) - in 2 times.

If the monotherapy with ACE inhibitors is ineffective, a good hypotension effect can be achieved by combining ACE inhibitors with *loop diuretics, calcium channel blockers or selective β -adrenoceptor blocking agents*.

It is necessary to correct lipidemia – by a hypolipidemic diet; if the general cholesterol level exceeds 6.5 mmol/l (norm is up to 5.2 mmol/l) and the serum triglycerides amount exceeds 2.2 mmol/l (norm is up to 1.7 mmol/l), it is recommended to add medications, normalizing the lipid blood spectrum (it concerns mainly statins).

Principles of treatment of diabetic nephropathy at Stage V:

- 1) symptomatic therapy, directed at the maintenance of satisfactory compensation of metabolic violations;
- 2) elimination of nitrous intoxication symptoms ;
- 3) hypertension correction ;
- 4) normalization of phosphoric-calcium exchange;
- 5) correction of renal anemia.

It is necessary in cooperation with a nephrologist to decide if it is possible to use the conservative treatment for such patients, and also to prepare the patients to the extracorporeal treatment modes (hemodialysis, peritoneal dialysis) or surgical methods (a kidney transplantation).

Prophylaxis of diabetic nephropathy

It is necessary to start prophylaxis of diabetic nephropathy progress from the first days of diagnosing diabetes mellitus. At the early stages of diabetes mellitus the prophylactic measures consist in the careful correction of metabolic violations.

The optimal level of carbohydrate violations compensation at diabetes mellitus, which allows prevention of diabetic nephropathy progress, is maintenance of support of glycemia of *not more than 7 mmol/l* on an empty stomach, and *not more than 10 mmol/l* after meal, and of glycohemoglobin (HbA1c) – *not more than 7%* (at a norm of 6.5%).

For patients, receiving intensive insulinotherapy with optimal compensation of metabolic violations (level of HbA1c not more than 7%), the frequency of diabetic nephropathy progress in 2–2.5 times lower than for patients with the badly compensated diabetes mellitus, which receive traditional insulinotherapy.

Diabetic retinopathy

Classification of diabetic retinopathy (stages of process)

1. *Inproliferative stage* is characterized by varicose veins, limited amount of microaneurysms, separate intraretinal lipid focuses and microhemorrhages. The stage is characterized by venulopathy, i.e. by dilatation and sinuosity of venues, and appearance of microaneurysms. Microaneurysms of capillaries and venues are the specific symptoms of diabetic retinopathy. Visual functions are not violated. This stage is a compensatory reaction on the tissue hypoxia, it foresees opening of additional capillaries. The angiopathy may be benign, without a tendency to progress.

2. *Preproliferative stage:* all above mentioned symptoms increase in character. *The changes of veins* are characterized not only by their dilatation but also by irregular caliber, and sometimes by over-tightening, beaded appearance, sinuosity, and formation of loops. Sharp changes of venous vessels testify to the goal over-tightening on their flow. Appearance of *exudates* – white and yellow areas of retinal opacity, either dense or looking like "flakes of

cotton wool", they are formed in place of hemorrhages and thromboses as a result of lipids and hyalinoid substance deposit.

In addition to solid exudate focuses, there appear soft ones, caused by a sharp focal ischemia in the layer of the retina nervous fibers. There is a rise in number of hemorrhages, which can be both intraretinal superficial, striped and even preretinal. After localization of hemorrhages in the central area of eye fundus, the sharpness of sight declines, and the scotomas of different intensity appear. The fluorescent angiography of the eye fundus shows unperfused by blood areas of retina and arteriovenous shunts, leakage of fluorescein from retinal vessels and microaneurysms, and reduction of paramacular capillaries.

3. *Proliferative stage* is noted for appearance of newly formed vessels on the disk of optic nerve, near it or in the course of large branches of retinal vessels, for formation of fibroglial films. The stage is characterized by addition of processes of retinal vessels formation (*neovascularization*) and *retinal fibrosis*. The process of neovascularization in a retina greatly violates photoreception, and it can lead to aneurysms. Newly formed vessels are very thin, with frequent repeated hemorrhages.

A serious complication of diabetic retinopathy, which can arise at any stage, is *macular retinopathy* which leads to a decline of central sight. Macular retinopathy can be caused by an edema, deposits of lipid exudate in parafoveal capillaries, traction action of the hyaline membrane or epiretinal membrane on the retina, or marked reduction of capillary network (ischemic macular retinopathy).

The consequences of proliferative diabetic retinopathy include *preretinal hemorrhages*, *hemophthalmia* (a hemorrhage in the vitreous body), *retinoschisis* (*stratification of retina*), *traction lamination of retina* and neovascular glaucoma. Serious complications which result in the complete loss of sight – retina lamination and rupture, atrophy of the optic nerve, the iris rubeosis, *secondary glaucoma*, and *secondary cataract*. The vitreous body may have extended and numerous hemorrhages. The hemorrhages in the vitreous body are accompanied by formation of intraretinal fibrosis, which penetrate from the retina into the vitreous body, and wrinkling of which can cause the retina lamination.

Diagnosics

The examination includes the biomicroscopy of eye ground, retinography and fluorescent angiography of retina (according to indications), in addition to traditional examination of patients suffering from a disease of eyes. Eye ground examinations with the scanning laser ophthalmoscopy are especially informative. Biomicroscopy and fluorescent angiography show the state of vessels of the front eye segment. The ultrasonic and electro-physiology methods of analysis are especially useful if a detailed visual examination of eye ground is impossible (for example, in case of a cataract, hemorrhages or the vitreous body opacity).

Prophylaxis

There are no reliable methods of primary prophylaxis of diabetic retinopathy for patients suffering from diabetes mellitus. At the same time, early manifestation of diabetes mellitus, regular medical check-up of a patient (including self-control), timely and adequate treatment of both basic and concomitant diseases allow to detain the diabetic retinopathy, slow down its progress and in most cases to prevent blindness and sight disability. Patients with diabetes mellitus without clinical signs of diabetic retinopathy must be examined by an ophthalmologist every 1–2 years. After appearance of diabetic retinopathy symptoms it is necessary to fix the individual terms of visits to the ophthalmologist, but not rarer than 1–2 times per year. If the sight declines, it is necessary to visit an oculist immediately. A great importance is attached to educating patients with diabetes mellitus of self-control methods, correct diet, physical exercises, giving up smoking and use of alcohol, reducing stresses.

Treatment of diabetic retinopathy

Positive influence on diabetic retinopathy is characteristic to *angioprotectors*, *antioxidants*, medications, which normalize *hemostasis* processes and *flow properties* of blood, improving protein and lipid metabolism.

Noticeable improvement of the retina state and visual functions of patients suffering from preproliferative diabetic retinopathy is achieved thanks to a course treatment with *heparin*

inhalations in combination with the intravascular laser blood irradiation and intramuscular *low-molecular heparin injections*. Injections of recombinant *prourokinase* also boost the efficiency of hemophthalmia therapy.

The medicine also uses herbal drugs: for instance, *mirtilene forte*, which contains whortleberries anthocyanosides, improves the retinal trophism and sight sharpness in bad illumination. At diabetes, mirtilene forte also slows down cataract progression .

The aminoguanidine medication represses the process of glycosylation of structural proteins.

It is customary to use *the aldose reductase inhibitors* – an enzyme which participates in glucose metabolism along polyol course with accumulating sorbitol in insulin-independent cells.

The RKC-beta medication is an inhibitor of vascular endothelial growth factor (mitogen, which participates in formation of new vessels and provides for their increased permeability due to diabetic retinopathy).

The purpose of *surgical operations* in case of diabetic retinopathy is prophylaxis and treatment of complications which are the main reasons of decline of sight or blindness. These include macular retinopathy, preproliferative stage of disease with risk factors, proliferative retinopathy and its complications, such as preretinal hemorrhages, hemophthalmia, formation of fibrovascular membranes, traction retina lamination, neovascular glaucoma.

The retina photocoagulation is performed with lasers which work in a green, yellow, red or infra-red band of light spectrum. Argon or krypton lasers are used especially often. These operations coagulate microaneurysms, areas of diffuse permeation of fluorescein from microvessels and destroy lipid focuses.

The most effective treatment method for proliferative diabetic retinopathy is *panretinal photocoagulation (PRPHC)* which is performed in several sessions. In successful cases, PRPHC leads not only to cessation of neovascularization and gliosis processes, but also to partial or complete disappearance of new vessels which were formed before. The positive results frequency of timely PRPHC reaches 80–70%. However, some cases require additional laser interferences or vitrectomy.

Photocoagulation complications include hemorrhages, macular edema, vitreoretinal tractions, and uveitis. At the same time, focal and dissipated retina photocoagulations are selection methods which allow to save the patient's sight.

It is impossible to use PRPHC in case of opacity of the transparent eye medium, especially with hemophthalmia. In such cases, it is recommended to use transconjunctival or *transscleral retina cryocautery*. This procedure speeds up the hemorrhages resorption and ceases or slows down the progress of proliferative diabetic retinopathy.

In the most serious cases of proliferative diabetic retinopathy complicated with bad hemophthalmia, formation of glial and fibrovascular membranes, traction macular retinopathy or retina lamination, it is customary to use *vitrectomy* with extraction or segmentation of epiretinal and posterior hyaline membrane, focal or panretinal *endolaser photocoagulation* and if necessary gas or *silicon tamponade*.

Diabetic angiopathy of vessels in lower extremities

In most cases, diabetic angiopathy of vessels in lower extremities has a combined character - both macro-, and microangiopathies, are often the first symptom of diabetic angiopathies.

Clinical signs of angiopathies in lower extremities:

- 1) remittent lameness;
- 2) extremities are cold;
- 3) absence of arteries pulsation on the foot;
- 4) shiny skin;
- 5) psilosis on feet and shins;
- 6) bulge of nails, often with mycosis;
- 7) atrophy of subcutaneous fat.

Patients with diabetic angiopathy in lower extremities and polyneuropathy have latent ischemia – the pain syndrome is absent as a result of pain sensitivity loss.

Classification of diabetic angiopathy in lower extremities

Stage 1 (pre-clinical) is not accompanied by any subjective displays or physical symptoms. Diagnostics of vessels disease is possible only with additional researches - capillaroscopy, tachooscillography, rheovasography. Capillaroscopy shows the increase of the number of capillaries, narrowing and shortening of arterial branch, and appearance of grainy blood flow. Tachooscillography data reveal an increase in speed of the pulse wave propagation and increase of middle pressure.

Stage 2 - functional, clinically it shows in onychalgia after a long walk, sensitiveness to cold of feet, paresthesias, cramps of gastrocnemius muscles. An objective examination reveals certain weakening of pulsation on feet arteries, decline of the skin temperature by 2-3 °C. Capillaroscopy shows deformation of capillaries, background opacity and blood flow discontinuity. Tachooscillography data reveal an increase in speed of the pulse wave propagation. Rheovasography may show three types of violations: vessels hypertonia, hypotonia, and spastycoatony.

Stage 3 - organic, it is characterized by adding trophic violations: dryness of skin on feet and shins, pallor or cyanosis, "marble" skin pattern. Intensity of pain syndrome is increased - spastic pains in gastrocnemius muscles force patients to stop while usual walking (syndrome of remittent lameness). Physical examination shows a considerable weakening or absence of pulsation on the foot arteries. Capillaroscopy reveals desolation of capillaries; tachooscillography data show falling of oscillometric index to absence of oscillation. Functional tests (cold, nitroglycerine) determine the absence or twisting of reaction.

Stage 4 – marked necrotic, gangrenous, is noted for trophic ulcers and gangrene of toes or other localization.

Classification of degree of lower extremities ischemia

1. Asymptomatic, without pain at the physical loadings.
2. Remittent lameness.
3. Pain at rest (cold foot).
4. Gangrene

Diagnostics

1. Determination of the skin temperature.
2. Test of capillaries filling.

Press with the I or III finger in different distal sections of the foot up to skin blanching. Normally, the rose discoloration recommences in 2-3 sec.

3. "Lifting test".

A patient, lying on the back, holds one leg lifted over the trunk level during a 30 sec., then let it down. Normally, the discoloration of both feet becomes identical in 15 secs. In case of reduced arterial blood flow, the discoloration smoothing occupies over 40 sec; the skin becomes pale or cyanotic.

4. Pulse examination of a.dorsalis pedis, and tibialis posterior. Variants of pulse violations:

- 0 - is absence of pulse;
 - I - fibular pulse (determined only by the Doppler sensor);
 - II - thready pulse;
 - III - weak;
 - IV - normal;
 - V - atherosclerotic (tense).
5. Pulse examination with ultrasonic Doppler.

Doppler examination accounts for the turbulent motion and volume of blood flow. A sound generated during the examination depends on the remoteness of the vessel from the heart, and caliber, elasticity, and damage of arteries. An ultrasonic wave, hitting red corpuscles, is reflected and partly displaced (the displacement degree is proportional to the blood flow speed). A signal is generated as a result of difference between two frequencies.

Normally, Doppler examination determines the three-phase rhythm:

- 1) raise of a pulse wave during the stretch of vascular wall in the diastole;
 - 2) falling of a pulse wave during reverse blood flow from arteries to the heart in the diastole;
 - 3) new raise of a pulse wave from crescent aortic valves.
6. Determination of systolic pressure on feet with an ultrasonic Doppler.
7. Examination of tibial-humeral (ischemic) index.

Ischemic index = systolic pressure on a.tibialis/systolic pressure on a.brachialis. normally, the correlation exceeds 1.0. In case of bad ischemia, the ischemic index falls below 0.8.

8. "Stress-test" for revealing of hidden ischemia.

An ischemic index is determined at ease. A patient walks during 4 minutes (or up to feeling an intense pain), afterwards the ischemic index is calculated once more. The repeated measurements are carried out every minute up to returning to the initial values. A decline of ischemic index is the sign of hidden ischemia.

Program of treatment of angiopathies in lower extremities

1. Complete compensation of diabetes mellitus.
2. Normalization of metabolism.
3. Elimination of hyperlipoproteinemia.
4. Angioprotectors and antiaggregant.
5. Vasodilators.
6. Magnetotherapy, local barotherapy, turpentine, iodide-bromine, and hydrogen sulfide baths.
7. Stimulation of trophic processes – *solcoseryl* intramuscularly by 2 ml 2 times per day (for 20-30 days).
8. Endarterial injection of a mixture with 100 ml of a 0.5% novocaine solution, 1 ml of 2.5% nicotine acid solution, 5 000 UN. of heparin. The infusion is performed 1 time per 3-5 days, with 7 infusions in the course.

Diabetic neuropathy

Classification of diabetic neuropathy (S.Kotov and al., 2000)

Peripheral neuropathy

1. Symmetric, mainly sensory and distal polyneuropathy.
2. Asymmetric, mainly agile and in most cases proximal neuropathy.
3. Radiculopathy.
4. Mononeuropathy, especially multiple.
5. Autonomous (visceral) neuropathy.

Central neuropathy

1. Diabetic encephalopathy, encephalomyelopathy.
2. Acute nervous and mental disorders on the background of metabolism decompensation (ketoacidosis, hyperosmolarity, lactic acidosis, hypoglycemia).
3. Acute violation of cerebral blood flow (transient, stroke).

1. Symmetric sensory (or sensorimotor) distal polyneuropathy

Character of subjective and objective displays of neuropathy depends on the type of most staggered nervous fibers. Affection of large fibers shows in violation of oscillation and haptic sensitivity, while of small ones – in pain and fever. Motor violations, such as weakness and atrophy of foot and hand muscles, are observed at later stages. In typical cases, sensory violations (violation of sensitivity) are combined with motor violations (moderate muscular weakness) and symptoms of vegetative dysfunction.

First of all, sensory fibers suffer with formation of *sensory violations*: pain hyperesthesia appears, and oscillation sensitivity and reflexes reduces. As a rule, the violation degree of

various types of sensitivity does not coincide. Violation of pain, temperature, deep sensitivity is symmetric. Usually diabetic proximal neuropathy develops gradually. In the course of neuropathy progress, there is a “falling out” of some types of sensitivity and reflexes, above all Achilles ones.

Typical *paresthesias* include feeling of “formication”, feeling of “beaten glass in a shoe”, by a “pin stings”, “scorching”, numbness, sensitiveness to the cold. Localization of sensory violations: toes, then all feet and the lower third of shins («*socks*»). Sometimes paresthesias spread on the hands («*gloves*»). Polyneuropathy begins with affection of distal sections of feet and then it spreads proximally. Sometimes, there are affections of peripheral nerves of trunk which show in the hypesthesia of chest and stomach skin. In serious cases paresthesias gain permanent megalgia increasing at night.

Affection of mainly small fibers results in painful neuropathy, with *pain* being a dominant symptom in the clinical picture. The pain may have different character, it may be both acute, “lancinating”, “tearing”, and dull, or “aching”. Pain is permanent, considerably increasing at night. Pain sensation may acquire hyperpathic trace: a slightest touch of the skin leads to aggravation of pain. Painful neuropathy may sometimes develop into debut diseases, more frequently - at later terms of diabetes. Pains are often resistant to treatment, and remain for months, even for years.

Objectively neuropathy shows in sensory and trophic violations – thin skin on feet and shins, psilosis, hyperhidrosis or anhidrosis, callosities. The characteristic symptoms include muscular atrophy, thinning of interosseous muscles, and dangle foot. Neuropathies are crucial in formation of ulcers on feet: neuropathic ulcers make up 50-80% all of ulcers in diabetic patients. *Neurotrophic ulcers* can be formed even with sufficient pulsation in foot arteries.

A. Diagnostics of sensory violations.

1. Analysis of oscillation sensitivity with a tuning fork of frequency 128 Hz.
2. Analysis of proprioceptive sensitivity: a patient’s hallux is moved upwards, then downwards. The patient is asked to define blindly a direction of motion.
3. Analysis of algesthesia is conducted by a pin: light pricks are made from the distal sections of a lower extremity upwards.
4. Analysis of haptic sensitivity is performed with a cotton lump.
5. Analysis of discriminatory sensitiveness. The foot skin is touched simultaneously with two thin sticks. In presence of the discriminatory sensitivity a patient distinguishes two touches at the distance of up to 2 cm one from the other. In case of violation of this sensitivity, - two touches at the distance over 2 cm are perceived as one touch or not perceived at all.
6. Analysis of temperature sensitivity is conducted an alternating placing a warm palm and a cold metallic object on the patient’s shin and foot.

V. Diagnostics of agile violations.

1. Estimation of volume of shin and foot muscles.
2. Analysis of muscle resistance.
3. Revealing of contractions.
4. Analysis of tendon reflexes, such as patellar, Achilles, plantar ones.

The origin of permanent pain syndrome is conditioned by affection of the sympathetic nervous system (*sympathalgia*). Sympathalgias are often combined with neurosis-like, psychopathy-like and depressed violations. Combination of pain neuropathy with drastic loss of body weight and depression is called *diabetic cachexia*.

Osteoarthropathy (neuroosteoarthropathy, “Charcot's joint”) is conditioned by a simultaneous violation of somatic and autonomous innervation (with violations of autonomous innervation playing a leading role). Neuroosteoarthropathy is a rather rare complication of distal polyneuropathy, characterized by a progressive destruction of one or more foot joints. This complication is characteristic mainly for aged patients suffering from diabetes mellitus for over 15 years.

2. *Asymmetric agile proximal neuropathy (proximal neuropathy, “diabetic amyotrophy”)*

In case of proximal neuropathy, the structural defect is localized in the area of cells in ventricornus, trunks and roots of peripheral nerves and conditioned by multifocal ischemic,

metabolic and traumatic affections of these structures or their combination. They lead to spondylosis deformans and bulging of intervertebral cartilages.

A clinical picture consists of the following triad: *atrophy, pains and fasciculation* in the pelvic girdle muscles, which are the most frequent in the quadriceps muscle of thigh. Occasionally, there may be weakness and atrophy of the shoulder girdle muscles. This process is usually asymmetric with the subsequent affection of muscles on the other side.

There are two variants of progress of "proximal diabetic neuropathy" – acute and subacute, when a clinical syndrome is formed within several weeks.

3. Radiculopathy

Radiculopathy shows up in *acute, intensive pains*. In most cases, pains are localized on one side at the level of thoracic or lumbar spine. Variants of localization: intercostal neuralgia, brachioplexalgia, lumbo-abdominalgia, ischialgia. At first radiculopathy reminds a vertebragenous process - there is connection with motions and symptoms of nerve trunks tension. Pains increase at night. The intensity of pain syndrome can constantly grow, acquiring a symptomatic character. In some cases, radiculopathy can imitate acute pathology in the thoracic or abdominal cavity. Paresthesias are not characteristic. The pain area, as a rule, has *hypertension*. Typical paradoxical sensitivity (feelings dissociation): rough palpation or active motions do not increase the pain sensations, while a tender touch is accompanied by a flash of widespread pain. The oligotrophy of muscles appears sometimes, that is innervated by the proper counterfoil. The disease has a gradual improvement within 1 – 3 months.

4. Diabetic mononeuropathy

Affection of a single nerve (mononeuropathy) or several nerves (plural mononeuropathy) is rather often observed of diabetic patients (1 – 4% of patients).

Affection of separate peripheral nerves is caused by the initial imperfect state of nerves in case of diabetes, due to violation of their metabolism and blood supply, when even a minor center of ischemia or a microhemorrhage result in the expressed nerve parafunction. The most frequent reason of mononeuropathy is mechanical injury or nerve entrapment in physiologically narrow sections ("trap" or tunnel mononeuropathy).

Medicine distinguishes mononeuropathy of craniocerebral and peripheral nerves.

Neuropathies of cranial nerves. All cranial nerves may have isolated affections, the principal reason being nerve ischemia.

Tolosa-Hunt syndrome is a peculiar form of plural mononeuropathy of craniocerebral nerves for patients with diabetes mellitus. It is conditioned by aseptic periphlebitis in the area of cavernous sinus affecting trunks of the III, IV, V (branch I) and VI pairs of craniocerebral nerves.

Tunnel mononeuropathy of peripheral nerves (compression neuropathy, repetitive stress injury) is much more frequent for patients with diabetes mellitus than for the population on the whole. At one or another section all peripheral nerves pass anatomically narrow channels formed by bones, copulas and muscles, where they can be easily compressed. Patients with diabetes mellitus suffer from reduced peripheral nervous system resistance to harmful factors (mechanical, toxic, and dysshemic).

Repetitive stress injuries feature pains which increase at night. In the area of the affected nerve innervation hypersensitivity is with time transformed in hyperesthesia. If the nerve has sensible and motor fibers, lingering injuries lead to loss of weight weakness of muscles.

The carpal tunnel syndrome is conditioned by affection of median and ulnar nerves. *The tarsal tunnel syndrome* is characterized by entrapment of tibial nerve in the Richet's calcaneal tract. *Morton's neuralgia* is accompanied by entrapment of the fourth plantar nerve of toes in the area of metatarsophalangeal articulation.

5. Autonomous (visceral, vegetative) neuropathy

It is conditioned by affection of central and/or peripheral sections of the vegetative nervous system, vegetative neuropathy is caused by violation of parasympathetic and sympathetic innervation of internals and the cardiovascular system.

The autonomous neuropathy sharply declines the chances of diabetic patients to survive. Reduced tolerance to the physical activity, nightly arterial hypertony, heat regulation violation, a painless myocardial infarction are the principal causes of diabetic patients "oxymortia".

The clinical displays of autonomous neuropathy are determined by major affections of certain sections of the vegetative nervous system.

Sympathalgias represent a symptom of autonomous neuropathy, conditioned by violations of sympathetic innervation and adaptation to pain. Sympathalgia is included in the symptom complex of different forms of peripheral neuropathy. It is characterized by burning, extended, having no clear localization, persistent pains which are dominant complaints of diabetic patients.

The symptoms of autonomous neuropathy can be divided into cardiovascular, gastrointestinal and urogenital systems.

The cardiovascular *variants* of autonomous neuropathy include monotonous tachycardia, orthostatic hypotension, painless myocardial infarction, and oxymortia.

1. *Monotonous (permanent, persistent) tachycardia* is caused by parasympathetic insufficiency, heart denervation. A cardiac rhythm is fixed - the variation of RR intervals at ease is diminished and the heart rate reaches 90-100-130 beats per minute. It is rather often for diabetic patients. The tachycardia intensity does not change with a different position of body, physical activity, during rest, sleep, in reaction to different vagotonic tests ("fixing" of the cardiac rate).

In order to reveal the violation of the parasympathetic system it is customary to use tests with electrocardiography registration of changes in cardiac rhythm at ordinary and deep breathing (the Ewing test which is a modified Valsalvi test).

In the course of the vegetative heart denervation progress, the heart rate may slow down to the standard values, but reactions on activity and vagotonic tests are not normalized.

2. *Orthostatic hypotension*. At transition from the horizontal to vertical position AT falls by 30 mm of mercury and more. The cause of orthostatic hypotension is an affection of sympathetic efferent endings (sympathetic denervation) of smooth muscles of arteries walls in internals and extremities. A vasoconstrictive reaction is blocked in the basic pools – muscles and conjunctive tissue of internals. Diabetic patients with autonomous neuropathy have inversed physiological arteriotony rhythm, when nightly values substantially exceed daily ones.

Clinically, the orthostatic hypotension shows in dizziness, "black veil", and fainting after standing up. Sometimes a patient is bed-ridden as he cannot get up. Orthostatic hypotension can imitate hypoglycemia, especially if it develops after prescription of insulin. Often hypotension is not accompanied by compensatory tachycardia, but by the decline of systolic blood emission from the left ventricle of heart.

Vasomotor violations. Imperfectness of sympathetic innervation of minor feet blood vessels results in an increase of arteriovenous blood shunt. An intensive arteriovenous shunt can lead to a massive stagnation of venous blood, plasma diapedesis and formation of the "neuropathic edema" in extremities.

Vasomotor violations with venous stagnation and capillaries drainage in combination with sweat-glands dysfunction cause the significant dryness and fissures of the sole skin, which contributes to formation of ulcers of feet.

Oxymortia is the most tragic display of autonomous neuropathy; it can be a consequence of violations in the cardiac rhythm, painless myocardial infarction, and sleep apnea. The cardiac denervation is the major cause of painless myocardial infarctions of diabetic patients. There is a positive correlation between the presence of autonomous neuropathy, the QT interval, and patients' oxymortia.

Typical violations are painless forms of coronary heart disease (CHD), in particular myocardial infarctions, sometimes oxymortia. The reason of predominance of painless CHD forms for diabetic patients is affection of visceral nerves which determine the algesthesia of myocardium.

Violations of pupil reactions show in a reduced diameter of pupils at adaptation to darkness on the early stages and by no or very slow pupil dilatation in future. These violations hamper orientation at night time.

Diabetic neuropathy of the central section of the optic tract (the optic nerve and chiasma) is one of displays of cerebrovascular complications of diabetes. The reason of disorders is a local ischemic or hemorrhagic affection of chiasma with development of *chiasmatic syndrome*, which clinically shows in symmetric scotomas and hemianopsia.

Violation of sweat production. Violation of sympathetic innervation of sweat-glands results in a symmetric decline or absence of sweat production on feet and palms with the compensatory increase of sweat production in the upper torso and on the head which sometimes is perceived as a sign of hypoglycemia by patients.

A rare variant is *gustatory hidrosis* - voluminous sweat production on the face, neck, upper torso in several seconds after reception of some food products - alcohol, marinade, vinegar, and cheese. Strengthening of local sweat production is linked with violation of function of superior cervical sympathetic ganglion.

Violation of hypoglycemia sensation (asymptomatic neuroglycopenia)

Hypoglycemia states are frequent complications of sugar-reducing therapy of diabetes mellitus, especially with intensive insulinotherapy. At adequate activity of adaptation mechanisms hypoglycemia results in activating of the contrinsular system - to stress emission of glucagon, adrenaline and glucocorticoids. The emission of contrinsular hormones shows in alarm, hunger, shaking, motor disturbance, hyperhidrosis, tachycardia, and increase of arteriotony.

Respiratory violations. At hypoxia state patients with diabetes and autonomous neuropathy suffer from violation of the respiratory center activation with possible development of sudden apnea. Sometimes the parasympathetic insufficiency violation shows in the pneumocardial insufficiency which is characterized by the sudden cardiac arrest and respiratory failure. It is considered, that a cardiopulmonary failure is conditioned by a decline of the respiratory center sensitiveness and by hypoxia, which leads to hypotension and decline in the central blood flow.

Urogenital violations show in sexual disorders and acraturessis.

The atony of urinary bladder (neuropathy of urinary bladder, "diabetic bladder") is caused by the decline of the detrusor sensitivity to the nervous impulses which stimulate contraction of the urinary bladder fibers and provide for its emptying. As a result, the bladder contractions become weaker, which leads to weakening of urine stream, incomplete emptying of the bladder, and uroschesis in the bladder.

Impotence, conditioned vegetative neuropathy, is observed in 40-50% cases of male patients with diabetes mellitus. Yet, the gonadotropic hypophysis function is not reduced, and the level of testosterone in plasma is normal. At first, violation of sexual function is temporal, it appears at decompensation of diabetes mellitus, but gradually becomes permanent. Clinically it shows in a decline of libido, orgasm weakening, inadequate reactions, sterility. Violation of the reproductive function is often related to retrograde ejaculation - supply of sperm to the urinary bladder as a result of weak sphincteric function of the urinary bladder.

A basic display of impotence is insufficient erection or its absence. Many patients may have violations of anal or testicular reflexes simultaneously with erectile impotence, conditioned by the autonomous neuropathy. For women, the autonomous neuropathy can result in a dry vagina and discomfort during sexual intercourse.

Variants of central neuropathy

1. Diabetic encephalopathy

The decline of patient's memory (amnesic disorders are especially typical for patients who transmitted frequent Hypoglycemia states), is accompanied by violation of psychical activity - fatigability, crabbiness, tearfulness, parahypnosis, and apathy. Heavy violations of psychical activity at diabetes mellitus are quite rare.

Aged diabetic patients more often suffer from encephalopathy with the mixed vascular-metabolic character, and is accompanied by a focal neurological deficit, macrostructural

cerebrum changes. The computer tomography and magnetically resonance tomography reveal atrophy and postinsult changes, which are the display of characteristic for diabetes mellitus macroangiopathies, atherosclerosis and hypertension. Strokes and transient ischemic attacks of these patients should be considered as displays of the central diabetic neuropathy.

2. Diabetic myelopathy

It develops simultaneously with diabetic encephalopathy of patients with a long experience of disease, and appears in easy conduction sensible disorders, reflex pyramid insufficiency, disfunction of arbitrary urination and defecation. It is not always possible to distinguish the symptoms of affection of cerebrum and spinal brain, that is why the term "encephalomyelopathy" is used.

3. Acute neuropsychic disorders

All types of diabetes decompensations (ketoacidotic, hypoglycemic, lacticidic, hyperosmolar) feature serious progressive disorders of cerebral metabolism and even acute neuropsychic violations. In certain cases they occupy a central place in the clinical picture, and in others they are disguised by intensive somatic disorders.

Basic neuropsychic syndromes at acute metabolism decompensation are the following: decline of consciousness level from light stunning to comma, psychomotor agitation, inadequate behavior, dysphoria, morning unawakening (characteristic for hypoglycemia), epilepsy.

Diabetic foot infections are a complex of anatomic and functional changes of feet, conditioned by diabetic neuropathy, osteoarthropathy, and angiopathy, which are often complicated by the purulo-necrotic process.

Classification of diabetic foot infections (I. Dedov (1999))

- 1) neuropathic: a) without osteoarthropathy; b) diabetic osteoarthropathy;
- 2) neuroischemic (mixed);
- 3) ischemic.

In every case there is a combination of displays of sensory and autonomous neuropathy with ischemic disorders.

Clinical displays of neuropathic violations, conditioned by the diabetic proximal neuropathy are the following: a decline or withdrawal of all types of sensitivity, a decline of heat and cold sensation, violation of sweat production, sensitiveness to the cold of the feet, discoloration of skin, reflex and motor insufficiency.

Typical displays of vegetative (autonomous) neuropathy are as follows: atrophy of soft foot tissues, deformation of joints, skin cyanosis, "pigeon" toes, callosities on soles.

Characteristic signs of ischemic disorders include: discoloration of skin on extremities after changing their position (acrocyanosis at lowering, and pallor at raising), change of coloration and temperature of the feet skin, and asymmetry of pulse.

A decline or withdrawal of all types of sensitiveness on feet, as well as violation of supporting function of feet increase the traumatism risk with formation of ulcers on feet.

Trophic ulcers are minor (1-2 cm in diameter), almost painless deep defects of soft tissues, the ulcers bottom are tendons, joints surfaces, and bones.

The typical localizations of ulcers are the feet area, with protruding metatarsus condylus, the medial surface of the I finger, a heel, dorsum and pillows of toes. Ulcers on feet of patients with diabetes mellitus are classified into neuropathic, neuroischemic and ischemic ulcers.

In case of isolated peripheral neuropathy the foot of warm, hyperemic, hydropic, sweat production is broken (at first increased with later anhidrosis), fissures appear on the skin. Hyperemia is caused by the arteriovenous shunt. An ischemic foot is characterized by a pale or cyanotic coloration, dry shining skin, psilosis, bulge of nails, atrophy of subcutaneous fat.

The provocative factors of an ulcer formation include microtraumas, disregarded by patients due to hypesthesia, increase of pressure on a sole surface while walking, limitation of joints mobility, and callosity.

Treatment of diabetic neuropathy

Treatment of diabetic neuropathy includes adequate control of glycemia, vasoactive and metabolic therapy. *Permanent compensation* of diabetes mellitus is necessary, but not sufficient condition of prevention and treatment of diabetic neuropathy.

Metabolic therapy – lately the medicine widely uses *antioxidants*. Priority in this group of means is given to medications *α-lipoic (thioctic) acids* (espa-lipon, thioctacid, thiagamma, berlition) which have marked anti-oxidant action and occupy one of central places in metabolic therapy. Due to its positive influence on the basic links of diabetic neuropathy pathogeny, treatment with thioctic acid results in the improvement of energy metabolism of nervous tissues, in the increase of ATP production and in transmembrane ion transportation as a result of activating of mitochondrial oxidizing processes, that determines the perspective of its use in treatment and prophylaxis of late diabetes complications.

In serious forms of neuropathy, *thioctacid* is prescribed by 300-600 mg (12-24 ml) intravenously dropwise for 2-4 weeks, with the subsequent transition to peroral intake of the medication in the dose of not less than 600 mg per day. In relatively light forms of disease the medication is prescribed orally by 200 mg three times a day on a term for not less than 4 weeks. For the prophylaxis of diabetic neuropathy it is customary to prescribe monthly courses of treatment twice a year.

The complex therapy of diabetic neuropathy widely uses *vitamins A, C, E, having antihypoxic action*. *Vitamins B₁, B₆, B₁₂* have neurotropic action. Repeated courses of treatment should be taken not rarer than twice per year. The medicine uses new, highly effective forms of these medications, in particular - biologically active liposoluble form of thiaminum (vitamin B₁) - *benphothiaminum*, activity of which is 8-10 times higher than of water-soluble forms of thiaminum, and chances to penetrate into a nerve cell and be converted in an active thiaminum metabolite are even higher.

Another modern highly active medication is *milgamma 100* (100 mg of benphothiaminum + 100 mg of hydrochloride pyridoxin) for oral intake.

Neurodiabetology widely uses a combined medication which includes all vitamins of group U in a necessity medical dosage, - *neuromultivit*.

Vasoactive therapy of diabetic neuropathy. One of main places in micro- and macroangiopathy therapy is occupied by *pentoxifylline (trental)*, the action of which lies in normalization of blood flow at a capillary level due to reduction of the mold blood elements aggregation, viscosity lowering and increase of deformation ability of red corpuscles. It improves microcirculation, contributes to excretion of metabolic products and toxins, increase of circulating liquid volume and diuresis normalization. The prolonged form of pentoxifylline (*trental 400, flexital 400, vasonit 600*) ensures a protracted and more even satiation with the medication. Use of trental is limited for patients with diabetic retinopathy due to a danger of hemorrhages.

Among other medications which have less expressed *antiaggregant* characteristics, it is possible to use *curantyl and complamin*, which have mainly peripheral vasorelaxant action, that is why they are the most effective in the distal forms of diabetic neuropathy.

In treatment and prophylaxis of cerebral blood circulation disorders the medicine uses *vasoactive medications* of different groups with mainly central action: *cavinton, stugeron* (cinnarizine), *sermion (nicergolin)*, *nimodipine (nimotop)* and *instenon* – a medication with combined (nootropic and cerebral vasodilating action) etc.

An important role in prevention of late diabetes complications progress (discirculatory encephalopathy, stroke, CHD, lower extremities macroangiopathy, etc.) is given to treatment of arterial hypertension and atherosclerosis. The complex approach using methods of unmedicinal and medicinal therapy is optimal. For patients with diabetes mellitus it is preferable to treat arterial hypertension with *ACE inhibitors* (captopril, enalapril, fosinopril, perindopril) and *calcium channels inhibitors* (amlodipine, nitrendipine, nisoldipine, felodipine).

It is necessary to restrict prescription of *diuretics* usually used in treatment of all forms of arterial hypertension for patients with diabetes mellitus, as quite often side effects of their use

can considerably exceed their positive influence and even contribute to progress of acute metabolism decompensation.

Medications from the *group of fibrates of the 3rd generation*, such as *Liponor*, to treat *hypercholesterolemia*.

Treatment or prevention of pain. Intensive pain syndrome demands parenteral introduction of medications.

In order to relief somatic pains it is possible to use *nonsteroid resolvents*. An important condition of analgesia achievement is use of neuroprotective medications and vitamins of group B.

Carbamazepine medications (Finlepsin, Carbatol) show the best effect in case of marked *sympathalgias*. Taking into account marked psychoemotional and depressed disorders, it is appropriate to include *tranquilizers* with sedative action, *neuroleptics* and *antidepressants* in the therapy complex of patients with persistent pains.

The physical methods of treatment of diabetic neuropathy include hyperbaric oxygenation, electrophototherapy, magnetotherapy, electrophoresis of proserin and vascular medications, diadynamic currents on the area of the sympathetic trunk, electrostimulation of paretic muscles, acupuncture, and other methods of non medicinal therapy.

Treatment of acute neuropsychic disorders which complicate the diabetes mellitus progress is primarily directed at normalization of pathometabolism, as elimination of acute metabolism decompensation results in recovery of consciousness and removal of focal neurological symptomatology.

The comatose conditions in patients with diabetes mellitus.

Glucopenia coma

A glucopenia coma is sharp complication of saccharine diabetes, conditioned the fall-off of maintenance of sugar in blood with the subsequent decline of utilization of glucose by cerebral fabric and *гипоксією* of brain.

Etiology

1. Overdose of insulin preparations (clorpropamide, tolbutamide), disparity between the dose of insulin and requirement in him.
2. Insufficient reception of carbonhydrates.
3. An interruption lasted in a meal.
4. Surplus muscular work.
5. Decline of insulin proactive ability of liver and buds as a result of decline of activity of insulinase at combination of saccharine diabetes with the diseases of liver or buds.
6. Labil'niy motion of saccharine diabetes.
7. The state is after ketoacidosis.
8. Alcoholic intoxication.
9. Adenoma of V-klitin (nesidioblastoma).

Pathogeny

A glucopenia is accompanied by activation of the sympathoadrenal system, increase of level of adrenalin, Noradrenalinum. A glucopenia also results in the irritation of hypothalamus, increase of activity of hypophysis and bark of adrenal with the increase of level of hormones is ACTH, STG, glucocorticoidis.

A glucopenia causes heavy violation of trophism of cerebrum is hypoxia, hypofunction of bark and diencephalis area. Development of irreversible changes is possible. Paresis of vessels of cerebrum develops, was swollen cerebral matter, thromboses.

Clinical displays of glucopenia coma

A glucopenia coma develops quickly, quite often suddenly.

The expressed of clinical displays depends on the sensitiveness of CNS to the glucopenia.

Easy glucopenia state

Feeling of hunger. Disturbance, anxiety, crabbiness, aggressiveness. Sharp general weakness, pallor, hyperhidrosis, chill, tremor. Head pain, dizziness, hyperesthesia. Feeling of numbness of language, lips. Palpitation. Nausea, vomit.

The glucopenia state is expressed

Sharp excitation, aggressiveness, hallucinations, fear, inadequate conduct. The stunned, entangled consciousness develops quickly. Increase of tendon, periosteal reflexes. Positive symptom of Babinskogo. Tonic, clonic cramps. Development of meningeal syndrome - decline of tendon reflexes, low blood pressure of muscles is possible, anisocoria, nystagmus, languid reaction of pupils. Pupils are wide, tone of eyeballs is normal. Temperature, breathing without features. A pulse is normal or speed-up. The attacks of stenocardia can be transformed in the heart attack of myocardium. Strokes are possible.

Deep glucopenia coma

Dead faint, deep comma. Arefleksiya. Stopping of cramps. Stopping of sweating. Hypothermia. Breathing is superficial. Bradikardiya, low blood pressure.

Differential diagnostics is conducted with undiabetic glucopenias.

A hyperinsulinism is primary (organic, absolute): heavy insufficiency of circulation of blood, inflammatory and destructive defeats of liver, kidney insufficiency.

A hyperinsulinism is second (functional, symptomatic): operative interferences on a gastroenteric highway are a gastrectomy, gastrostomy with speed-up suction of carbonhydrates and extrass of insulin.

A surplus meal is after the protracted starvation.

A hypersensitiveness is to insulin.

Glucopenias are possible at some endocrine diseases : syndrome of Simmondsa, syndrome of Shiena, hypophysial nanism, hypothyroidism, to illness of Addisona, born hyperplasia of bark of adrenal.

The deficit of insulinis hormones can be observed at a kidney glucosuria, malnutrition, pregnancy, lactation, cirrhosis of liver, cholangitiss, cholecystitiss.

Laboratory diagnostics

The glucopenia state can develop and at the normal values of glycemia - at the fall-off of level of sugar in the whey of blood, adaptation of CNS to the high levels of sugar in blood.

On a background a glucopenia a "hungry" ketosis and acidosis can develop as a result of activating of gluconeogenesis.

Treatment

1. Intravenously enter a stream a 40% glucose of 20-40-100 ml. The criterion of sufficientness of dose is proceeding in consciousness. Then pass to infusion of a 5% glucose - glucopenias can recur.

2. Effective intramuscular introduction of 1 ml 1% glucagon, repeated introduction in 10 minutes.

3. Hypodermic enter 0,5-1,0 ml of a 0,1% solution of *adrenalin*, intravenously or intramuscular to 150-200 mg hydrocortisone. At recurrent glucopenias each 2 hours enter 1-2 ml glucagon intramuscular, and also glucocorticoidis (to 75 mg hydrocortisone or 30 mg prednisolone) - intravenously tiny 4 times per days.

4. For the improvement of cerebral circulation of blood intravenously enter 5-10 ml of a 25% solution of *sulfate of magnesium*.

5. Through the danger of edema of cerebrum at the protracted glucopenia comma appoint intravenous tiny introduction of a 15-20% solution of *manitol* (0,5-1,0 grammes are on 1 kg of mass of body).

6. For the improvement of metabolism of glucose enter intramuscular 100 mg cocarboxylase and 5 ml of a 5% solution of *ascorbic acid*.

Oksigenoterapiya is conducted by water-wet oxygen.

After testimonies apply cardiac and vascular facilities.

Ketoacidic coma

Ketoacidic coma is sharp complication of saccharine diabetes, conditioned an accumulation in the organism of ketonic bodies, dehydration and acidosis. Ketoacidotichna comma is the most frequent variant of sharp violations of carbohydrate exchange, observed in 1-6% patients with saccharine diabetes. Lethality from ketoacidotichna commas in the specialized medical establishments - 5%, as an organism can carry considerable hyperketonemia - to 170 mmol/l.

Ketoacidoz is the isolated biochemical changes without clinical symptoms.

Ketoacidotic state - biochemical changes and row of conditioned are expressed by them clinical symptoms.

Etiology

1. Late diagnostics of sugar diabetes.
2. Inadequate treatment of sugar diabetes is declension of insulin or disparity of dose of insulin to the requirement in preparation.
3. A sharp increase of requirement is in insulin which causes decompensation of carbohydrate exchange:
 - a) physical stress (traumas, operations, burns, chilblain);
 - б) psychical stress;
 - в) heavy intercurrent diseases (infections, inflammations, vascular catastrophes);
 - г) fatty infiltration of liver;
 - д) lipidian diet.
4. Vomit of different genesis lasted.

Pathogeny

In pathogeny of diabetic comma a basic role is played by the deficit of insulin, which reduces utilization of glucose fabrics, increases a gluconeogenesis in a liver which results in a hyperglycaemia and glucosuria. The deficit of insulin is instrumental in the increase of lipolysis and accumulation in blood of triglycerides, phosphotides, cholesterol of acids. Formation of ketonic bodies is enhanceable in a liver during mionectic utilization in hepatic fabrics results in ketoacidosis and ketonuria.

A hyperglycaemia increases an osmolality in a extracellular liquid which is instrumental in the receipt of water and cellular electrolytes, especially potassium and phosphorus from cages in intercellular spaces, the process of cellular dehydration develops. The increase of concentration of glucose in the glomerular filtrate of buds hinders its D-major in tubulis, drawing an osmotic diuresis. The loss of extra- and intracelularis liquids can arrive at a 10% mass of body.

The accumulation of acids in a extracellular liquid strongly displaces the bicarbonate buffer system toward diminishing of pH, that causes the increase of partial pressure of carbon dioxide and accumulation of hydrogen ions. These changes of chemical composition of blood result in the irritation of respiratory center appearance of breathing of Kussmaulya, characteristic for diabetic acidosis. Consider that a leading role in pathogeny of acidosis is played by the increase of concentration of hydrogen ions, but not ketonic bodies, as their level does not correlate weight of clinical displays with a degree. The removal of surplus of hydrogen ions is arrived at oxidization of ketonic bodies and leadingout of hydrogen ions by buds as an ammonia or by the exchange of hydrions on the ions of sodium in kidney tubulis.

As utilization of ketonic bodies at a diabetic comma is sharply mionectic, the equilibrium of hydrogen ions is arrived at as a result of leadingout their buds. Functional violations of buds are the characteristic features of diabetic acidosis. As a result of dehydration glomerular filtration and receipt of amino acid goes down in the cages of kidney tubulis, where their deamination and formation of ammonia is.

The change of concentration of hydrogen ions violates the gradient of electrolytes between a cellular and extracellular liquid, which results in the loss of ions of potassium, magnesium and phosphorus with urine. At the deficit of potassium in the cages of kidney fabric

the leading out of hydrogen ions of, is violated which creates a pathological circle which results in subsequent exhaustion of supplies of sodium and potassium.

An osmotic diuresis, as well as vomit, is instrumental in the loss of sodium and chlorine. Research of water-electrolyte balance rotated at a diabetic comma, that the loss of extra- and intracellular liquids arrived at 6 litres, to sodium - about 500 mekv, chlorides - 390 mekv, potassium - 350 mekv. Lowering of utilization of glucose by cerebral fabric which is combined with cellular dehydration, cerebral anoxia and acidosis, is reason of loss of consciousness at a diabetic comma. Together with the expressed hyperglycaemia maintenance of bicarbonate of sodium diminishes to 15 mekv/l and decline of pH to 7,3-6,8.

Chart of pathogeny of ketoacidosis coma

Decline of level of immunoreactive insulin.

A decline of amount of receptors is to insulin.

A decline of affinity receptors is to insulin.

Decline of activity of hexokinase.

Increase of activity of glucose-6-phosphatase.

A decline of utilization of glucose is in fabrics

growth of power deficit is in fabrics.

Scary increase of secretion of insuline hormones

(STG, ACTH, catecholamins).

Activation of lipidic exchange:

activity of lipolysis rises

the expressed of lipogenesis goes down.

Basic power substance in an organism is become by Nezhk.

Disintegration of Nezhk increases in a liver.

Formation of acid rises in a liver.

Resintez of acid goes down in fat acids.

Oxidization of acid goes down in the loop of Krebsa.

Activating of gluconeogenesis: disintegration of hepatin is in a liver;

disintegration of albumens is with amination of amino acid in a liver.

Acute hyperglycaemia. A glucosuria is expressed.

Increase of osmolality of extracellular liquid, polyuria.

intracellular dehydration, lost to 10% b.w. (6-7 l).

Acidoz is metabolic, respiratory, kidney (a kidney blood stream goes down, glomerular filtration and leading out the buds of N⁺ goes down).

Forecasters of ketoacidosis coma

The period of decompensation of saccharine diabetes, which shows up polyuria, Polydesum, diminishing of weight, anorexia, nausea and vomit, is preceded the clinical displays of comma. The period of precursors can last a few days, sometimes even weeks - the displays of decompensation of saccharine diabetes grow (polyuria, Polydesum, anorexia, decline of b.w.).

At growth of ketoacidosis the initial displays of intoxication appear by ketonic bodies (there is nausea, vomit, stomach-aches, smell of acetone from a mouth), the signs of dehydration of organism make progress.

Clinical displays of ketoacidosis coma

Defeat of CNS. Head pain of pulsating, holding apart character.

Violation of consciousness:

1 stage (*easy ketoacidosis state*). Somnolence, weakness, languor, fatigueability, apathy, but a patient can adequately answer a question.

2 stages (*the ketoacidosis state is expressed*). Stunned: reactions are slow, inadequate, a contact with a patient is laboured. Reflexes are stored.

3 stages (*grave ketoacidosis condition*). Sopor: consciousness absents, awakening a patient is possible only by strong irritants, a linguistic contact with a patient is impossible.

Tendon reflexes mionectic, congratulatory reflexes (swallowing, corneous) are stored. An algesthesia is stored.

4 stages (*ketoacidosis coma*). Comatose state: dead faint, irresponsive on any irritants. The fall of tendon, periosteal, skin reflexes, congratulatory reflexes, is hyposthenic.

Defeat of breathing organs. Liquid loud breathing as Kusmaulya (inhalation, short exhalation, is prolonged, a pause lasted), conditioned acidosis. Smell of acetone in mid air, which a patient breathes out.

Defeat of the cardiovascular system. An arteriotony goes down or normal. A pulse is frequent, weak filling. Violations of rhythm, conditioned hypokaliemia (gastric extrasystole, twinkling of auricle).

Defeat of gastroenteric highway. A language is assessed a brown raid, dry. Nausea, anorexia, swelling of stomach is expressed. Vomit sometimes by "coffee-grounds" Stomach-aches, sometimes symptomatology of sharp stomach.

Pathogeny of symptoms is paresis of smooth and shiny muscles as a result of hypokaliemia with expansion of stomach and enteroplegia; spasms of sphincter, conditioned acidosis; sharp ketonosis ulcers of mucus shell of stomach are with the gastroenteric bleeding.

Defeat of buds. Poliuriya which changes oliguria and anury.

Changes of skin. A person is pale, the lines of person are sharp. A skin is dry, languid, inelastic, with a mionectic turgor. The temperature of skin is mionectic. Mucus shells are dry.

Eyeballs. Tone of eyeballs is mionectic, pupils are narrowed; cross-eye which meets or goes away.

Defeat of muscles. Low blood pressure, muscles are languid, weakened (display of hypokaliemia); pains in extremities are neurimialgia.

Clinical signs of hypokaliemia: pallor, muscular and general weakness, carelessness, apathy, lethargy, hyporeflexia, atony of smooth muscles of stomach and intestine, which is accompanied flatulence, vomit, impassability of intestine.

Electrocardiography signs of hypokaliemia: tachycardia, high indent of P, lengthening of interval of R-q, decline, decline of segment of S-T, pathological indent of U.

Electrocardiography signs of hyperkaliemia: decline of indent of P, high sharp indent of T. increase of interval of S-T.

Clinical variants of ketoacidosis comma:

1) encephalopathic - the clinical displays of violation of cerebral circulation of blood prevail;

2) cardiovascular is a collapse, cardiac insufficiency;

3) gastroenteric - sharp stomach, choleroïd syndrome;

4) kidney is dysuria, changes of urinary sediment.

Laboratory diagnostics

Clinical blood test: the level of haemoglobin, red corpuscles, hematocrit, leukocytosis, thrombocytosis, is enhanceable (polycythemia is caused condensing of blood).

Clinical uranalysis: glucosuria, ketonuria, increase of specific gravity of urine (4 grammes of glucose - 0,001 units of absorbancy), the reaction of urine, proteinuria, cylindruria, microhematuria, acid.

The level of immunoreactive insulin in blood is considerably mionectic.

Hyperglycaemia to 16-50 mmol/l.

A ketosis is an increase of maintenance in blood of ketonic bodies (N 0,9-1,7 mmol/l); a kidney threshold for ketonic bodies is 2,5-3,5 mmol/l.

Acidoz is diminishing of size of pH (N 7,35-7,45), fall-off of alkaline reserve to 5% (N of 55%-75%), decline of standard bicarbonate (SB) (N 20-27 mmol/l).

Giperosmolyarnist' is moderato expressed or absents.

Violation of lipidic exchange is as a result of activating of lipolysis: increase of level of NEZHK, hypertriglyceridemia, hypercholesterolemia.

Violation of proteometabolism is as a result of acceleration of proteolysis: increase of kreatinine, increase of level of urea, increase of level of remaining nitrogen.

Violation of electrolyte exchange: the decline of level of Na and SI is possible. A level κ to beginning of інсулінотерапії normal or enhanceable as a result of migration κ from cages. Late гіпокаліємія develops after the beginning of insulinotherapy (in 4-6 hours) .

Fibrinolytic activity of blood is enhanceable.

Complication of ketoacidosis coma

1. Glucopenia coma.
2. It was swollen a brain.
3. Gіpokaliєmichniy of crises.

Differential diagnosis of ketoacidosis

Reasons of undiabetic ketoacidosis:

- 1) alcoholic intoxication;
- 2) massive korticosteroidis therapy;
- 3) incessant vomit;
- 4) deficit of coferment of A-transferazi.

Reasons of undiabetic acetonuria:

- 1) fever;
- 2) intoxication;
- 3) incessant vomit;
- 4) protracted starvation.

Treatment of ketoacidosis comma

1. Filling of deficit of insulin.

Insulinotherapy is conducted only *preparations of short action*. Apply the mode of small doses of insulin - the gradual decline of level of glycohemіa prevents development of edema of cerebrum, relative glucopenias, vascular catastrophes.

Insulins enter hourly intravenously tiny, sometimes by a stream. In exceptional cases at impossibility of intravenous introduction intramuscular injections are possible. For the removal of adsorption of insulin add 7 ml of a 10% solution of albumin the elements of the system or a few ml of blood of patient with each 500 ml of solution.

The calculation of dose of insulin is conducted hourly, coming from weight of patient - 0,1 ODES/kg. Dose of insulin (ODES) = *weight of patient (kg) of x 0,1(ODES/kg)*. If there is not a decline of level of glycohemіa in 2 hours, the dose of insulin is increased in 2 times is a coefficient of calculation of dose 0,2 ODES/kg.

Under reaching glycohemіa *less than 14 mmol/l* dose of insulin which is entered in a hour, reduce in 2 times (a coefficient of calculation of dose is 0,05 ODES/kg). As a environment is utilized not solution, but 5% glucose. The increase of intervals is possible between the injections of insulin - each 2 hours.

At glycohemіa *less than 11 mmol/l* pass to fractional introduction of insulin one time on 3-4 hours hypodermic or intramuscular. Fractional introduction of short insulins is continued during 1-2 weeks after a leadingout sick from a ketoacidosis comma - a circumstance is given related to that day's requirement in insulin can go down in 2 times, and the daily correction of dose is needed.

2. Regidrataciya.

If blood normal - enter solution of Ringera, if enhanceable (more than 320 mmol/l) blood, as a environment is utilized low blood pressure solution 0,45% NaCl to normalization of index, then pass to solution .

It is important to provide adequate expressed of dehydration of proceeding in the lost liquid - during the first 6 hours enter for 0,5-1,0 l/hour to diminishing of signs of dehydration, then amount of liquid which is entered, diminish to 0,2-0,3l/hour. Total amount of infusion -

about 6-10 l/days. At presence of signs of decompensation of the cardiovascular system the dose of infusion must not exceed 2-3 l/days.

3. *Correction of the acidis state.*

At pH less than 7 intravenously enter solution of bicarbonate of sodium for 100 mmol/hour (1 gramme of NaHCO₃ = 12 mmol) to achievement of pH 7 (340 ml/hour of a 2,5% solution or 200 ml of a 4% solution). On each 100 mekv of NaHCO₃ additionally enter 13-20 mekv of Ksl - 10-15 ml of a 10% solution.

The overdose of sodium of hydrogen carbonate can cause was swollen a brain, of hypokaliemia and hypernatremia, alkalosis.

The necessary dose of bicarbonate is expected on a formula: normal level of bicarbonate of sodium in blood (20 mmol/l or 20 mekv/l) minus is present level of bicarbonate, increased on the volume of extracellular liquid (15-20 l).

Other formula: mass of body in kg, increased on 0,3 and increased on VE (deficit of meadows). Utilize a coefficient 0,15 and enter the half of the expected dose. Introduction of bicarbonate of sodium can be repeated 2-3 times per days with an interval at 2 o'clock.

Sometimes this solution is entered in an enema, wash a stomach or give to drink. For a fight against acidosis and dehydration apply glutaminis acid also (1,5-3,0 grammes are on days).

4. *Correction of hypokaliemia.*

Conducted with the use of chloride of potassium, as equivalent doses of pananginum will cause hypermagnesemia (a 1 gramme of Ksl contains 17 mmol).

At hypokaliemia less than 3 mmol/l enter 39 mmol/hour of Ksl (3 grammes of Ksl are at o'clock), about 30ml of a 10% solution.

At normokaliemia conduct the prophylaxis of late hypokaliemia.

At kaliemia 3-4 mmol/l - enter for 26 mmol/hour of Ksl (2 grammes of Ksl are on a hour), about 20 ml of a 10% solution.

At kaliemia 5-6 mmol/l - enter 13 mmol/hour of Ksl (a 1 gramme of Ksl is on a hour), about 10 ml of a 10% solution.

At hyperkaliemia more than 6 mmol/l or introduction of preparations of potassium is halted development of anury.

5. *Prophylaxis of DVS-SINDROMU.*

Heparinum for 5000 ODES intramuscular 4 times per days or more high dose under control to the prothrombin index - retain at the level of 70%.

6. *For the improvement of oxidizing processes* intravenously tiny enter 100 mg cocarboxylase, 5 ml of a 5% solution of ascorbic acid, 200 mcg to the vitamin of V12, 1 ml of a 5% solution of vitamin of V6.

7. *At insuperable vomit* for filling of deficit of albumens and fight against starvation in 4-6 hours from the beginning of treatment enter 200-300 ml plasma. In order to avoid the hypochloremic state intravenously enter 10-20 ml of a 10% soluble-sodium chloride.

8. *For prevention of cardiovascular insufficiency* hypodermic enter Cordiaminum for 2 ml or a 20% solution of caffeine for 1-2 ml each 3-4 hours. At mionectic AT appoint plasma, dextrane, integral blood intravenously, intramuscular 1-2 ml of a 0,5% solution of DOKSA. At expressed tachycardia intravenously enter 0,25-0,5 ml of a 0,05% solution of strophanthin or 1 ml of a 0,06% solution of korgliconum on isotonic soluble-sodium chloride.

9. *Oksigenoterapiya* is carried out by introduction through the nasal catheter of water-wet oxygen with speed not more than 5-8 l/min.

10. The diuretic appoint *at development of oliguria or anury*, at unefficiency is hemodialysis.

11. *Development of signs of edema of cerebrum* is a testimony for intravenous introduction of hydrocortisone of 400 mg.

12. *Antibiotics are* after testimonies.

13. For proceeding in metabolic violations to the ration add carbonhydratess which are easily mastered, assign a fat free diet for 10 days, much to drink liquids (to 1,5-3,0 l on days), alkaline mineral water. From a 2-3th day a diet is extended.

Hyperosmolar coma

A hyperosmolar coma is sharp complication of sugar diabetes, conditioned blood with sharply expressed intracellular dehydration in default of ketosis.

A hyperosmolar coma meets rarely - 0,23% patients with sugar diabetes. Most often this complication develops for patients more senior than 50 years, with concomitant obesity or for children (teenagers). Lethality is high - 50%.

Provoking factors:

- 1) sharp dehydration of organism is vomit, diarrhoea, hemorrhage, a diuresis, burns, frostbite, is enhanceable;
- 2) surplus introduction of solutions of glucose and salt solutions;
- 3) intercurrent diseases, infections;
- 4) surgical interferences;
- 5) protracted treatment by the diuretic, massive doses of immunodepressants.
- 6) leadthrough of hemodialysis, peritoneal dialysis.

Chart of pathogeny of hyperosmolaris comma

A sharp hyperglycaemia blocks a ketogenesis.

Decline of excretive function of buds with the decline of leadingout of Na, SI and urea with urine: hypernatremia, chloruremia, hyperazotemia.

Dehydration intracellular, intercellular.

hypovolemia.

Thickening of blood. Thromboses, thromboembolism

Dehydration of fabrics of organism

Clinical displays of hyperosmolaris coma

A *hyperosmolaris* coma develops gradually, during a few days, rarely - for a day long. Predecessors of coma are polyuria, Polydipsia, sometimes polyphagia. An asthenia, signs of dehydration, somnolence, entangled consciousness, joins then.

Hyperosmolaris of blood is accompanied the expressed propensity to formation of thrombus, by heavy violation of microcircularis in different fabrics - foremost in a cerebrum and buds. Clinical displays are conditioned violation of cerebral circulation of blood is characteristic early and expressed functional neurological symptomatology. Thromboses of kidney vessels are reason of sharp kidney insufficiency.

The signs of dehydration of fabrics - dryness and decline of turgor of skin, low blood pressure of muscles, decline of tone of eyeballs are especially expressed.

Neurological violations. Bilateral spontaneous nystagmus, hemianopsia. Aphasia. Cramps, epileptic attacks. Hemiparesis, paralyzes. Tendon reflexes absent, pathological reflexes appear (Babinskogo and else.). Muscular hypertone or low blood pressure of muscles. Vestibular violations. Hallucinations are possible. Violation of consciousness is a somnolence, stunned, copor, comma. Hyperthermia of central genesis.

Defeat of buds: early, frequent oliguria, anury.

Change of peripheral fabrics. Sharp dryness of skin, mucus shells; decline of turgor of skin.

Change of eyes: decline of tone of eyeballs; pupils are narrowed, languidly react on light.

Change of breathing organs: breathing is superficial, speed-up; there is not breathing of Kusmaulya, there is not a smell of acetone.

Defeat of the cardiovascular system. Tachycardia, arrhythmia. Low blood pressure, collapse, shock. Thromboses of peripheral arteries and veins. The edemata of lower extremities and scrotum are possible.

State of gastroenteric highway: there is vomit, flatulence, stomach-aches; intestinal impassability is at late hypokaliemia.

Laboratory diagnostics

There are signs of thickening *in a clinical blood test*: haemoglobin, hematocrit, leukocytosis, is enhanceable.

In a clinical uranalysis: glucosuria, proteinuria, cylindruria, hematuria.

Hyperglycaemia 50 - 200 mmol/l.

Giperosmolyarnist' to 500 mosmol/l at the norm of 285-295 mosmol/l.

Osmolyarnist' of blood is determined on a formula: Osmolyarnist' (mosmol/l)= glycohemia (mmol/l)+ urea (mmol/l)+2(K+na)(mmol/l)+((albumen of gramme/l of x 0,243): 8)

Chloruremia.

Gipernatriemiya.

Giperkaliemiya to beginning of treatment of insulinomas or normokaliemiya.

Gipokaliemiya after the beginning of insulinotherapy.

Giperproteinemiya.

Giperazotemiya.

pH, the level of bicarbonates, ketonic bodies is normal.

Treatment of hyperosmolar coma

1. Regidrataciya.

Enter low blood pressure solution of NaCl 0,45% for 2 l/hour during the first 2th hours, then for 1 l/hour to normalization of blood and venous pressure. At achievement of glycohemia 14 mmol/l pass to инфузю of a 2,5% solution of glucose. For days enter 8-12 l of liquid.

2. Correction of hypokaliemia.

Introduction of preparations of potassium is carried out only at the decline of glycohemia to 14 mmol/l. If level of potassium in blood less than 3,5 mmol/l and there is not an anury, enter for 10-20 mmol of Ksl (7,5-15 ml 10% Ksl) on a 1 litre of solution of NaCl on a hour.

3. Insulinotherapy.

Insulinotherapy is carried out only by intravenous tiny introduction for 8-12-16 FROM insulin hourly to the decline of glycohemia below 14 mmol/l.

At achievement of глікемії 14 mmol/l (250 mg%) pass to fractional introduction of insulin for 6-8 ODES each 3 hours.

4. For the prophylaxis of edema of cerebrum and improvement of his metabolism enter intravenously 50 ml 1% glutaminis acid.

5. Oxygen therapy.

6. A prophylaxis of thromboses is a heparin for 5000-6000 dose 4 times per a day intramuscular.

7. Symptomatic therapy.

At cardiac insufficiency is Cordiaminum, strophanthin or corgluconum.

At low blood pressure - 1-2 ml 0,5% DOKSA or other mineralocorticoids, plasma solutions (Haemodesum, albumin, reopoliglukin). Antibiotics are after testimonies.

hyperlactacidemic coma

hyperlactacidemic a coma is sharp complication of sugar diabetes which develops as a result of accumulation in the organism of suckling acid and origin of metabolic acidosis. Meets rarely, differs high lethality - 50%.

Etiology

1. Sear and yellow leaf (propensity is to hypoxia).
2. Concomitant diseases are with hypoxia (defeat of heart, lights, chronic alcoholism).
3. Sharp hypoxia (shock is traumatic, cardiogenic, toxic, sharp infectious or inflammatory diseases, bleeding, collapse, heart attack of myocardium).
4. Endogenous intoxications (hepatic or kidney insufficiency, leucosis, heavy infections).
5. Exogenous intoxications (methanol, ethanol).
6. pharmacogenic lactacidosis at the use of biguanids, fructose, polyols, salicilatis, to the lactat of sodium.

Provoking factors:

- 1) surplus physical loading (suckling acid is synthesized in a working muscle);
- 2) hypovitaminosis, especially to the vitamin of V1;
- 3) deficit of magnesium;
- 4) sharp intoxications.

Chart of pathogeny of hyperlactacidemic coma

hypoxia.

Hypersecretion of catecholamins, STG, glucocorticoidis.

Oppression of aerobic glycolysis.

Stimulation of anaerobic glycolysis.

the products of suckling acid are enhanceable.

decline of activity of pyruvate dehydrogenase, that converts

PVK in an ethanoly-KOA is a blockade of oxidization of PVK.

An accumulation of PVK is with proceeding in it to suckling acid.

Blockade of secretion of N⁺ by buds.

Violation of correlation of oxidization NADF and picked up a thread NADF N2.

Violation of transport of PVK is in chondriosome.

Clinical displays of hyperlactacidemic comma

A coma can develop quickly, during a few hours.

A prodromal *period* is sometimes accompanied by dyspepsia phenomena (anorexia, nausea, vomit), speed-up breathing, stenocardia and muscular pains (suckling acid is strong "muscular poison"), violations of psychoemotion sphere. Lethality is high - 50-80%, as already at the increase of level of suckling acid to 7 mmol/l irreversible changes develop in fabrics.

Defeat of CNS: apathy, somnolence. Excitation, delirium, insomnia, motive disturbance, is possible. A coma develops gradually.

Defeat of the cardiovascular system: a blockade of receptors of peripheral vessels is the expressed and proof low blood pressure, collapse, hypothermia. A blockade of receptors of myocardium is proof bradycardia, decline of retractive ability of myocardium, development of making progress cardiac insufficiency, resistantto therapy. Vnutrishnesudinni thromboses.

Defeat of buds: oliguria, then anuria.

Defeat of gastroenteric highway: dyspepsia, nausea, vomit.

Change of muscles: muscular pains, low blood pressure of muscles.

Breathing organs: the shallow breathing a speed-up, then breathing of Kusmaulya, conditioned of acidosis.

Laboratory diagnostics

Hyperglycaemia or normoglicemia.

Increase of level of suckling acid (in a norm 0,6-1,2 mmol/l; 2 mmol/l is a kidney threshold).

Decline of level of acid (in a norm 0,06-0,12 mmol/l).

Sharp increase of index suckling acid (in a norm 10 : 1).

Acidosi is a decline of pH at the norm of pH 7,35-7,45.

Decline of level of standard bicarbonate (SB) at a norm 20-27 mmol/l.

Decline of level of reserve lugnesis at a norm 55-75%.

hypercaliemia.

hyperazotemia.

Treatment of hyperlactacidemic comma

1. *Correction of acidosis.*

At pH less than 7 intravenously enter 1-2 l of a 2,5% solution of **bicarbonate** of sodium for 100 mmol/hour (340 ml of a 2,5% solution in a hour). Introductions halt at achievement of pH 7.

2. Stimulation of transition of suckling acid in acid by 1% methylene dark blue in an amount 50-100 ml, for 2,5 mg on 1 kg of weight of patient.

3. *Insulintherapy.*

Conducted even at presence of normoglicemia - intravenously tiny enter for 6-8 FROM insulin of short action in 500 ml of a 5% glucose.

4. A correction of low blood pressure is plasma substitute and hydrocortisone for 250-500 mg.

5. *Oxygen therapy.*

6. *Gemodializ is* after testimonies at an anury.

Diabetes mellitus and pregnancy

Diabetes of pregnant women

This group include only persons whose violated tolerance to glucose was firstly determined during pregnancy. The group does not include women who suffer from diabetes before pregnancy. This state is accompanied by an increased frequency of different perinatal complications, and a risk of diabetes progress in 5-10 years after the delivery. Diabetes of pregnant women develops in 1-2% of pregnancies, and in most cases tolerance to glucose returns to normal after delivery. It should be taken into account that the more greater violation of tolerance to glucose is during the pregnancy, the greater is the risk of diabetes mellitus (and in a less time) after it.

Indications to the analysis of tolerance to glucose during pregnancy include glycosuria, diabetes of relatives, as well as anamnestic data which contain spontaneous abortions, innate injuries of children from previous pregnancies, giving birth to many living or dead children with the body weight over 4.5 kg, the pregnant woman's obesity, middle age, the fifth and more delivery. Presence of more than one of the mentioned factors means a great risk of pathological tolerance to glucose.

One of DM progress risk groups is formed by women who have diabetes of pregnancy in the anamnesis. Over 34% of such women are taken ill within 10 after the pregnancy.

The estimation of dynamics insulin content in blood plasma shows that certain changes are expressed at gestational DM in comparing to physiology pregnancy. The insulin level on an empty stomach was higher at gestational DM and exceeded this index is at physiology pregnancy by 46 % ($24,3 \pm 2,42$; against $16,6 \pm 2,34$; $p < 0,05$). The maximal increase of the insulin level in blood was determined in 60 min.

Insufficient control of diabetes during the last weeks of pregnancy can cause large problems for a child: Large weight at birth and low level of sugar of blood (hypoglycemia).

The placenta penetrable for blood sugar – the pregnant woman's hyperglycemia is accompanied by the fetus's hyperglycemia. The increase of blood sugar of the fetus stimulates generating a great amount of the fetus's own insulin. Hyperinsulinemia causes deposit of surplus fat in subcutaneous fat – and a large fetus is formed. The great weight of child at birth hampers the delivery and can lead to serious consequences. The fetus's high sugar level in blood and hyperinsulinemia can result in the baby's hypoglycemia immediately after birth. The child has increased insulin generation in order to reduce surplus sugar in blood. At birth, when the child separates from the mother, the source of surplus sugar disappears, and hyperinsulinemia leads to a drastic fall of the child's blood glucose level.

In the second half of pregnancy the present complications of diabetes, such as retinopathy, nephropathy, arterial hypertension, require a more frequent and careful control.

Hyperglycemia in the 3rd trimester of pregnancy, when formation of the fetus's pulmonary tissue ends, can result in the delay of pulmonary tissue development and cause respiratory insufficiency after birth. For pregnant women with diabetes mellitus, there is a high

risk of premature detachment of placenta and intrauterine fetal death. At a threat of detachment of placenta the delivery is scheduled 1 - 2 weeks before the calculated term. Insufficient control of diabetes in the last weeks of pregnancy enhances the risk of jaundice of the newborn.

Women with diabetes more disposed to the development of preeclampsia. Preeclampsia is the most severe form of toxicosis at the second half of pregnancy, often requiring hospitalization. It is characterized by increase of arteriotony, edemata of hands and face and presence of albumen in urine, which chiefly affects functioning of kidneys, liver and placenta, as well as the general state of mother and child.

The pregnancy hormones reach a maximum in the third trimester, in time of the maximal hormonal activity of the placenta. Placental hormones are contrinsular in their influence on the carbohydrate metabolism, cause an increase of glucose in the blood serum and reduce the tissue sensitivity to insulin. In this period pregnant women have an enhanced need in insulin. A general unit need in insulin during 26th-36th weeks of pregnancy arrives at 0,9 un./kg. At the end of the third trimester, the dose of insulin can go down, especially before supper and before sleep due to the high consumption of sugar from the mother's organism by the child for its growing needs.

In the third trimester a pregnant woman should: visit endocrinologist and gynecologist no less than 1 time per 7-10 days; to carry out a careful control of blood sugar; to execute the second examination by an oculist.

The method of aid in delivery depends on the child's sizes and state and the woman's state - level of AT, presence of edemata, albumen in urine, degree of intensity of the diabetes complications.

During the delivery the need in insulin of the woman in childbirth changes considerably. The placenta ceases generation of hormones, and the need in insulin falls sharply, that requires the decline of insulin dose. Besides, delivery is rough labor, when blood sugar spontaneously goes down. Often delivery requires introduction of glucose solution for prophylaxis of hypoglycemia. In case of diabetes mellitus of type I, some amount of insulin will be needed during the delivery, but usually it much less, than before pregnancy. In case of diabetes of type II, women can do without insulin during the delivery. During a puerperal period a need in insulin is increased, usually to the level which existed before pregnancy.

According to Pedersen classification, the risk of unsuccessful outcome of pregnancy is greater for women with diabetic ketoacidosis, preeclampsia, pyelonephritis, and also for women, deprived of the necessary attention.

Almost 80% of pregnancies with diabetes mellitus of type 1 are complicated with at least one mother's infectious disease (against 26% for women not suffering from diabetes). Frequency of urogenital, respiratory and endometrial complications is increased. Frequency of post-natal infections is 5 times higher than for healthy women in childbirth.

In the high-risk group (IDDM, complicated with neuropathy and hypertension) it is recommended to use small doses of aspirin for prophylaxis of preeclampsia.

Nephropathy (NP) occurs in 5% of pregnancies. The risk of unfavorable outcome can be forecast in case of the daily proteinuria over 300 mg in the first 3 months of pregnancy.

In the first 3 months hypertension appears in 30% of pregnant women with diabetic NP and by the moment of births the number reaches 75%. More than in a half of all cases of NP the delivery come before the 37th week of pregnancy, and in 50 - 60% of cases it is necessary to perform a Cesarean section. Other complications include serious edemata due to hypoalbuminemia, as well as resistant to treatment normochromic and normocytic anemia.

In case of kidneys disfunction it is often necessary to carry out hemodialysis (HD) and even transplantation of kidneys. HD almost always leads to premature delivery.

Difficulties of therapy of kidney complications come into a question. Regardless of the previously said, the outcome of pregnancy with NP is successful in 90% cases. However, a bad perinatal outcome is possible in case of:

- proteinuria over 3 gram/day;
- creatinine content in serum over 30 mmol/l (1,5 mg/dl);
- mean arterial pressure over 107 mm of mercury.

Even if the pregnancy is developing well, the level of the prolonged post-natal sickness rate is high.

Treatment and prophylaxis of diabetic retinopathy and diabetic neuropathy is thoroughly examined.

Control of diabetes during pregnancy

Above all, before pregnancy a woman with IDDM must be thoroughly instructed about a diet during the pregnancy; it is worthwhile to conduct insulinotherapy and achieve euglycemia; it is necessary to estimate the function of kidneys and conduct an ophthalmology examination.

The pregnancy should be postponed until achievement of HbA1c concentration less than 8% (0.08 units SI).

Ideally, a concentration of glucose in plasma must be below 5 mmol/l (100 mg/dl) on an empty stomach and below 7.8 mmol/l (140 mg/dl) after-meal. (NB! Indicated values of various glucometers for domestic purposes are 15% lower).

The recommended diet. General daily amount of energy should make up 30-35 kkal per 1 kg of ideal body weight at a 6-time days' meals. Carbohydrates should make up 55%, proteins – 20%, and fats – 25% (no less than 10% of them saturated). The questions of insulinotherapy are thoroughly considered. If the pregnancy is complicated by ketoacidosis, a risk of loss of the fetus is 20%, which mainly happens in the first 3 months of pregnancy. Therefore, ketoacidosis requires as early correction as possible.

Peculiarities of surgery for patients with diabetes mellitus

Correction of metabolism and surgical pathology

1. Treatment of diabetes at the large volume of surgical interferences

At the large volume of surgical interference regardless of diabetes severity it is necessary to introduce short-action insulin during the whole patient's stay in hospital.

A. Preoperative preparation.

In case of a planned operation the doctor prescribes dietotherapy taking into account the concomitant disease. For instance, patients with pathology of the hepatobiliary system should be prescribed the diet # 9 by type of the diet # 5, with ulcerous illness – the diet # 9 by type of the diet #1, with the kidneys affection – the diet # 9 by type of the diet # 7 and so on.

If the patients cannot meal enterally, they should be provided with nutritional support. It is known that during starvation the heptatin supplies in the liver are exhausted within 24 hours even for healthy people. Denutrition at diabetes and surgical disease increases catabolism and immunodeficiency.

As a nutritional support it is possible to use glucose (5-10 % solution) to 200.0 dry substance per day at the maximum infusion speed of 0.5 gram/kg/g. Too fast introduction of glucose leads to its incomplete utilization, to the increased content of lactate, urea and bilirubin in plasma. Day's amount of glucose is evenly distributed within 24 hours in 2-4 portions. Insulin is added into the vial with glucose for infusion at 1 UN. per 4 gram of dry glucose, if necessary – potassium muriate is added as well.

Introduction of sugars slows down formation of ketone bodies and proteolysis. Liquidation of the increased albuminolysis takes place at consumption of 150-200 mcode of carbohydrates per day.

To maintain speed of proteometabolism at the optimal level it is necessary to introduce a complex of amino acids. The amino acids are more actively used for synthesis of proteins in case of simultaneous introduction of calories carriers (infusion solutions of carbohydrates, lipophilics). The optimal supply for 1 mcode of amino acids makes up approximately 25-30 kkal.

Lipophilics have favourable influence, especially at the prolonged nutritional support (during 3-4 weeks). Adults are recommended to receive 1-2 gram of fat per 1 kg of the body weight per day. 30-40 % general amount of calories should be provided by fats. After infusion of 500.0 lipophilic it is necessary to make a break for 2-3 days. Lipophilics are not indicated at considerable affection of flow blood properties.

Insulinotherapy. The correction of carbohydrate metabolism during preparation and a planned operation should maximally approximate to the criteria of diabetes compensation. If a surgical disease is accompanied a pain syndrome or an inflammatory process, it is necessary to try to achieve a level of glycemia within 7-9 mmol/l for a day. An exception is made for patients who had high indexes of glycemia and glucosuria for a long time (over 2-3 months) before their hospitalization. In these cases it is sufficient to moderately reduce the indexes of carbohydrate metabolism under control of the patient's health.

The most reliable calculation of insulin dosage is glycemia on an empty stomach and the next control according to the day's indexes of glycemia and glucosuria, taking into account the patient's health.

On the day of admission to hospital (if glycemia on an empty stomach is unknown) it is necessary to account for the action of taken sugar-lowering preparations and concentration of sugar in blood. In necessary, insulin is immediately introduced hypodermically at 6 UN. per every 2.8 mmol/l of sugar concentration in blood, if it exceeds 10 mmol/l. Taking into account the next meal, 4 UN. of insulin are added to the mentioned dose. In future, all insulin injections are made in the same time according to a diet. The number of injections per day depends on the need in insulin.

Patients *with a light form of diabetes* in a state of compensation, who used only dietotherapy before admission to the surgical department, it is necessary to prescribe insulin 3 times per day in 3-7 days prior to the operation (before breakfast 4-5 UN., before dinner — 3-4 UN., before supper — 2-3 UN.).

If on the background of surgical pathology (more usually during operations or at once after surgery) the level of sugar in blood increases moderately for the first time on an empty stomach (up to 5.5 – 6.6 mmol/l) and during a day (up to 9.5- 10 mmol/l), insulinotherapy is carried out as for treatment of the light form of diabetes. These patients may have the insular apparatus restored in the anabolic phase of postoperative period. In this case insulin is cancelled. The patient continues to keep to diets of the type Board 9 until a complete healing of the postoperative wound. In future, if necessary, glycemia is tested with loading glucose. If there is no violation of tolerance to glucose, the clinical form of diabetes mellitus is excluded, i.e. “Oppel minor surgical diabetes” is confirmed, that falls in the reliable risk class under the classification of WHO.

It is necessary to cancel the intake of sugar-lowering peroral medications with introduction of the prolonged insulin by patients with *moderate diabetes* and to prescribe treatment with short-action insulin. Usually, these patients' glycemia on an empty stomach without the sugar-lowering action of medications and any stress fluctuates within the limits of 8-12 mmol/l. In this case, as a rule, it is necessary to make 4 injections of insulin: at 6:00 — 3-4 UN., before breakfast — 8-10 UN., before dinner — 6-8 UN., before supper — 4-6 UN. At 6:00 insulin is introduced to normalize the level of sugar on an empty stomach without the following meal. It should be noted, that nightly glycemia, as a rule, is a bit lower than in the morning according to the circadian rhythm of insulin activity (the “dawn” phenomenon)

In case of *the serious form of diabetes mellitus* the prolonged insulin is substituted with the short-action insulin, which should be introduced in 5 injections: at 6:00 — 5-8 UN. (without the following meal), before breakfast — 12-16 UN., before dinner— 12-14 UN., before supper — 8-10 UN., at 24:00 — 3-4 UN. (without the following meal).

In case of urgent operations the correction of metabolism is performed in 3-4 hours before, and during the operation. Insulin is injected hypodermically at 6 UD of the hormone per every 2.8 mmol/l of glycemia, after deduction of 10 mmol/l from its laboratory index. At the same time, 5 % solution of glucose is injected intravascularly drop-by-drop at the speed of 200 mol/hour with insulin at 1 UN. of the hormone per 3 gram of dry glucose. Glycemia control is carried out hourly from the beginning of operation with the next correction of intravenously injected insulin dose. In case of ketoacidosis it is necessary to immediately begin its removal by intravenous drip-by-drop introduction of 2 % solution of sodium bicarbonate (50-100 mol). Strict control of the acid-base state is needed to avoid transition to alkalosis. As a rule, ketoacidosis elimination takes place synchronously with disappearance of Kussmaul breathing and marked

arterial hypotony. If it is possible to postpone the operation for several hours, it is advisable at first to eliminate ketoacidosis, to reduce the glycemia level to 14-15 mmol/l, and then with infusion of glucose with insulin and potassium preparations it is possible to proceed to the operative interference. In the case of the diabetic coma, the operation is postponed until the patient's rallying from the comatose state.

B. Metabolic correction during the operation

At the light form of diabetes mellitus insulin is not introduced in the morning before the operation. During the operative interference such patient is introduced 5 % solution of glucose with insulin at 1 UN. of the hormone per 3 gram of dry glucose.

Patients with a moderate or a serious form of diabetes mellitus receive the usual dose of insulin at 6:00, and then 1/2-2/3 of the next morning insulin dose — hypodermically in the operating-room, immediately before the operation. During the whole surgical period patients receive intravenously drop-by drop a 5 % solution of glucose with insulin. It is also possible to use the preserved blood and electrolyte solutions without glucose.

In the day of the operation (planned), glycemia is maintained at a level, exceeding former indexes by 2-3 mmol/l, i.e. within the limits of 9-11 mmol/l. If possible, diabetic patients should be operated in the morning and at the beginning of the week in order to provide the best control.

A danger during surgery lies chiefly not in hyperglycemia but in undetected hypoglycemia. The latter may be suspected judging by increased sweat production and delayed awakening after anesthesia. The given metabolism disorder is quickly removed by introduction of carbohydrates, with the subsequent reducing of the insulin dose. With the observance of the mentioned insulinotherapy tactic, the frequency of hypoglycemic reactions is minimized.

C. Treatment of diabetes in the post-surgical period

The levels of glycemia and glucosuria are carefully controlled immediately after the operation, as the diabetic patients' need in insulin during the first days after surgery can be increased. To prevent decompensation of diabetes mellitus, the insulin dosage is constantly corrected. If the operated patient can receive nutrition in full measure, insulin is prescribed in a dose, equal to that before the surgery with certain corrections in accordance with the laboratory indexes of the current carbohydrate metabolism. If the nutrition is limited, the amount of insulin is reduced accordingly, and with restoration of meals it is smoothly passed to the residual dosage.

In need of parenteral nutrition in the early post-surgical period, it is customary to use a solution of amino acids, fructose, glucose with insulin at a rate 1 UN. of the hormone per 3-4 gram of dry glucose. Any post-surgical complications or intensifying of concomitant disease are also accompanied by growth of hyperglycemia and glucosuria. Proinflammatory cytokines contribute to ketoacidosis in the catastrophic phase of a surgical pathology. Alkalescence with sodium bicarbonate during this period envisages maintenance of satisfactory hemodynamics, and not a complete elimination of acidosis (which has a risk of passing to the alkalosis). Taking into account the antiketogenic action of carbohydrates during their oral introduction, it is necessary to achieve early setting of nutrition the easily digested carbohydrates.

In the anabolic phase of the post-surgical period, the insulin activity recommences, consequently, it is necessary to proceed with the correction of its dosage (the danger of hypoglycemia boosts immediately after removal of suppurative foci).

2. Treatment of diabetes is at minor surgical interferences.

Patients with *compensated* diabetes mellitus have «minor» operations (on the skin and ENT-organs, teeth extraction, etc.) in their ordinary nutrition mode. On the first days after the operation the content of sugar in blood is actively controlled. If necessary, the carbohydrate metabolism is corrected by additional introduction of simple insulin.

At *decompensated* diabetes, per oral sugar-lowering preparations or prolonged insulin are substituted by the short-action insulin.

After healing of wounds, both after minor and grave surgery interferences it is possible to return to the former mode of treatment of diabetes mellitus, if it was effective. In the opposite case, the patient should be moved to the endocrinological department for prescribing of the optimal therapy.

Correction of metabolism at suppurative diseases

The suppurative-necrotizing pathology (abscesses, phlegmons, furuncles, carbuncles, gangrene of lower extremities, cholecystitis, appendicitis, etc.) is accompanied by swift decompensation of diabetes mellitus. At the grave flow of the suppurative pathology even an increase of the dose of hypodermically injected insulin in 3-4 times does not have the desired effect for the patients with diabetes mellitus. It is possible to avoid the considerable destruction of insulin at a purulent infection is possible, by using intravenous and intramuscular injections, which allows to shorten the time of transportation of the hormone to tissues. It is necessary to take into account that the action of simple insulin at hypodermic introduction lasts for 6-8 hours, at intramuscular – 3-4 hours, at intravenous – about 2 hours.

If a diabetic patient with a suppurative pathology goes to hospital in the state of the expressed intoxication, the medical staff immediately begin *infusion detoxication therapy*, intravenous drop-by-drop introduction of insulin (approximately 6-10 UN./hour at glycemia 18-25 mmol/l) and potassium preparations. The level of sugar in blood is obligatory controlled before introduction of insulin, and later every hour. Thus the correction of the insulin dose is carried out so that the speed of glycemia decline does not exceed 4-5 mmol/l/h. In order to avoid hypoglycemia after removal of purulent content, the dose of insulin is reduced by 1/3 or by half of the previous one with the subsequent control of its effectiveness.

The level of sugar in blood on the first day of the patient's stay in the surgical department should not fall below 9-10 mmol/l or indexes present before the development of purulent process. After ceasing infusion therapy it is customary to switch to intramuscular introduction of insulin *until* complete disappearance of the purulent process. A dose for the first injection is calculated, by increasing in 3 times the previous amount of insulin, which was injected intravenously during one hour with deduction of the hormone activity which was used for glucose utilization (if it was introduced).

Taking into account the next meal (300-400 kkal) 6-8 UN. are added to the calculated dose. The correction of subsequent insulinotherapy is carried out according to glycemia indexes, without changing a single dose more than by 4 UN. Intramuscular injections are made every 3 hours (it is possible to observe an interval within 2 or 4 hours between certain introductions of insulin in accordance with a diet in the department) at 6:00, 8:00, 11:00, 14:00, 18:00, 21:00, and 24:00. At 24:00 it is possible to introduce insulin hypodermically in order to spare the patient from an injection at 3:00. The meal is taken after injections at 8:00, 11:00, 14:00, 18:00, and sometimes — at 21:00. Control of glycemia is performed before every introduction of insulin (preferably 7 times per days) 2-3 times per week depending on the character of diabetes and the surgical disease. Normalization of carbohydrate metabolism indexes is carried out not only by modification of the insulin dosages but also by the patient's nutrition.

An increase of sugar in blood at a stable nutrition and insulinotherapy can be a symptom of abscess metastases or the ineffective draining of abscess.

On the other hand, in the course of reducing activity of the purulent process, the need in insulin decreases. In this period there must be a caution of hypoglycemic reactions (sensation of hunger, hyperhidrosis, headache, heartaches, worsening of sight, inadequate behavior and so on) which diminish or disappear after the meal. After liquidation of the suppurative inflammation the hypodermic introduction of insulin is restored with further switching to the ordinary treatment mode of the given form of diabetes in ambulatory conditions.

In the case of generalization of the purulent process there is a growing threat of an unfavorable result. Unefficiency of therapy requires the immediate revision of the surgical tactic, careful correction of carbohydrate metabolism, and a complex of medical measures concerning the septic patient's management.

Control of the initial level of knowledge

1. The most probable reason of stable tachycardia of patients with diabetes mellitus, type 1 is:

A. Combination of diabetes mellitus with thyrotoxicosis

- B. Diabetic cardiomyopathy**
- C. Coronary heart disease**
- D. Autonomous cardiac neuropathy**
- E. Hypokalemia**

2. The most characteristic kidneys affection at diabetes mellitus is:

- A. 100-nodal glomerulosclerosis**
- B. Diffuse glomerulosclerosis**
- C. Amyloidosis**
- D. Chronic pyelonephritis**

3. Which type of neuropathy is the most frequent for patients with diabetes mellitus?

- A. Radiculopathy**
- B. Encephalopathy**
- C. Peripheral polyneuropathy**
- D. Vegetative neuropathy**

4. The most characteristic organs of visions affection of patients with diabetes mellitus is:

- A. Accommodation disorder**
- B. Diabetic retinopathy**
- C. Cataract**
- D. Glaucoma**

5. Which treatment is the most appropriate at diabetes mellitus of pregnant women?

- A. Short-action insulin**
- B. Biguanides**
- C. Sulfanylamide sugar-reducing preparations**
- D. Prolonged types of insulin**
- E. Prolonged types of insulin in combination with short-action insulin**

6. A daily fluctuation of the glycemia level of a pregnant woman suffering from diabetes mellitus should not exceed:

- A. 3.5 to 7.5 mmol/l;**
- B. 3.5 to 8.5 mmol/l**
- C. 3.5 to 9.5 mmol/l**
- D. 4.5 to 8.5 mmol/l**
- E. 4.0 to 8.0 mmol/l**

7. Focal laser photocoagulation is used for coagulants introduction in areas of:

- A. Microaneurysms localization**
- B. Minor hemorrhages**
- C. Exudations**
- D. All mentioned cases**

8. An early marker of diabetic nephropathy is:

- A. Appearance of microalbuminuria (from 30 to 300 mg per day)**
- B. Violation of intrarenal hemodynamics**
- C. Both symptoms**

9. Violation of intrarenal hemodynamics at the early stages of diabetic nephropathy is characterized by:

- A. Hyperfiltration**
- B. Hyperperfusion of kidneys**
- C. Intraglomerular hypertension**
- D. All above mentioned**

10. In a norm, the almunin urinary excretion per day reaches:

- A. up to 30 mg;**
- B. 40 mg**
- C. 50 mg**
- D. up to 300 mg**
- E. up 400 mg**

Endocrinology (initial level of knowledge)

1. D
2. A
3. C
4. B
5. E
6. A
7. D
8. C
9. D
10. A

Control of final level of knowledge

1. The laboratory symptoms of marked diabetic nephropathy is:

- A. Proteinuria (without changes of urocheras)**
- B. Changes in the speed of glomerular filtration**
- C. Increase of azotemia**
- D. Progress of arterial hypertension**

E. All above mentioned

2. Neoproliferative diabetic retinopathy is characterized by the presence of:

- A. Microaneurysms**
- B. Punctuate hemorrhages**
- C. Retina edema**
- D. Exudation focuses**
- E. All above mentioned symptoms**

3. Preproliferative diabetic retinopathy is characterized by the presence of the followings symptoms:

- A. Venous anomalies**
- B. Big amounts of solid and "cotton-wool" exudates**
- C. Numerous large retinal hemorrhages**
- D. All above mentioned**

4. Prolifeative diabetic retinopathy is characterized by the presence of the followings symptoms:

- A. Neovascularisation of the disk of visual nerve**
- B. Hemorrhages in the vitreous body**
- C. Formation of fibrous tissue in the area of preretinal hemorrhages**
- D. All above mentioned**

5. Pararetinal laser photocoagulation is used mainly at:

- A. Preproliferative retinopathy**
- B. Nonproliferative retinopathy**
- C. Proliferative retinopathy**
- D. Diabetic nephropathy**
- E. Diabetic neuropathy**

6. Barrier laser photocoagulation is used mainly at:

- A. Nonproliferative diabetic retinopathy in combination with edema of the macular area**
- B. Preproliferative diabetic retinopathy**
- C. Proliferative diabetic retinopathy**
- D. Diabetic nephropathy**
- E. Diabetic neuropathy**

7. Diabetic neuropathy is accompanied by violation of sensitivity, above all:

- A. Oscillatory**
- B. Pain**
- C. Haptic**
- D. Temperature**

8. Which early symptom is the most characteristic for diabetic nephropathy?

- A. Selective albuminuria
- B. Orthostatic proteinuria
- C. Transient arterial hypertension

9. Which stage of development is not characteristic for diabetic angiopathy of lower extremities?

- A. Marked necrotic
- B. Functional
- C. Organic
- D. Ischemic
- E. Preclinical

10. Diabetic macroangiopathies include all listed below, except for one:

- A. Aorta and coronarias
- B. Kidneys
- C. Cerebral vessels
- D. Peripheral vessels
- E. General atherosclerosis

Endocrinology (final level of knowledge)

1. E
2. E
3. D
4. D
5. C
6. A
7. A
8. A
9. D
10. B

Situational tasks

1. The patient K. suffers from diabetes mellitus for 28 years. During the last year the dose of insulin was reduced by 14 UN.. In the urine analysis: protein – 1.7 gram/l, sugar – 0.8 %, a great amount of red corpuscles, casts. The given symptoms are a manifestation of:

- A. Resistance to insulin
- B. Diabetic nephropathy
- C. Decompensation of diabetes mellitus
- D. Pyelonephritis

E. Insulin chronic overdosage syndrome

2. A 62-year old patient suffers from diabetes mellitus of type 2. Diabetes is compensated by a diet and maninil. The patient has to undergo an inguinal hernia operation. What must the tactic be?

- A. To substitute maninil with glymepiride**
- B. To substitute maninil with glurenorm**
- C. To prescribe short-action insulin preparations**
- D. To prescribe prolonged-action insulin preparations**
- E. To prescribe biguanides**

3. A patient had a large-focal myocardial infarction. His body weight exceeds a norm by 36%. AT reaches 150/90 mm of mercury. Blood sugar makes up 5.9 mmol/l, general cholesterol – 4.9 mmol/l, urinary acid – 0.211 mmol/l. Which of the given risk factors requires removal first of all in the process of the secondary prophylaxis?

- A. Hyperglycemia**
- B. Arterial hypertension**
- C. Obesity**
- D. Hypercholesterolemia**
- E. Hyperuricemia**

4. How is it necessary to estimate the tolerance to glucose test for a 17-years-old boy: on an empty stomach – 5.78 mmol/l, in an hour after taking 75 m of glucose – 7.21 mmol/l, in two hours – 5.68 mmol/l.

- A. Diabetes mellitus, latent form**
- B. Diabetes mellitus, moderate severity**
- C. Tolerance to glucose is in order**
- D. Diabetes mellitus, light form**
- E. Symptomatic hyperglycemia**

5. The urine of a 17-year old boy for the first time showed glucose – 5 gram/l. Glycemia on an empty stomach is 5.4 mmol/l. No complaints. Which analysis will reliably exclude diabetes mellitus?

- A. Test to tolerance to glucose**
- B. Daily glycemia fluctuation**
- C. Insulin level in plasma**
- D. Daily glucosuria**
- E. Glycemia after-meal**

6. A man of 20 years complains about thirst, increased uropoiesis, general weakness, diminishing of body weight. Objective data: a skin is dry, red cheeks, vesicular respiration. Cardiac sounds are sonorous. The tongue is dry. No symptoms of peritoneum irritation. Which is there the most informative analysis to establish the diagnosis?

- A. Glucose blood test**
- B. General blood test**
- C. General urine analysis**
- D. Urine testing by Zemnitskiy**
- E. Hepatic blood test**

7. A patient of 30 years old with the satisfactorily compensated diabetes mellitus of type 1 has frequent hypoglycemia, nausea, intestine disorders, dermatomelasma, AT fell down to 80/50 mm

of mercury, anaemia was progressing, Hb -105 gram/l. What may be the reason of the tension drop?

- A. Diabetic enteropathy**
- B. Diabetic gastropathy**
- C. Chronic adrenal insufficiency**
- D. Overdose of antidiabetic preparations**
- E. Progress of diabetes insipidus**

8. A woman of 53 years old after a psychical trauma felt itching of skin. Her height is 167 cm and weight is 89 kg. Glycemia on an empty stomach – 8.1 mmol/l. Which diagnosis is the most probable?

- A. Diabetes mellitus, type 1**
- B. Diabetes mellitus, type 2.**
- C. Violated tolerance to glucose**
- D. Steroid diabetes mellitus**
- E. Neurodermatitis**

9. A woman of 35 years old, taken ill with a flu, has a glycemia on an empty stomach of 11.3 mmol/l, a glucosuria – 25 gram/l. Her height is 168 cm, and weight is 67 kg. Which analysis is the most informative for specification of diagnosis?

- A. Daily glucosuria fluctuation**
- B. Daily glycemia fluctuation**
- C. Determination of C-peptide**
- D. Glycemia in an hour after-meal**
- E. Test to tolerance to glucose**

10. The 29-year old patient K. complains about thirst, hydruria (up to 5 l per day), weakness. Blood sugar makes up 8.5 mmol/l. What is the provisional diagnosis?

- A. Chronic glomerulonephritis**
- B. Psychogenic polydipsia**
- C. Diabetes mellitus**
- D. Primary aldosteronism**
- E. Diabetes insipidus**

CORRECT ANSWERS

1. B	5. D	9. C
2. C	6. A	10. C
3. C	7. C	
4. C	8. B	

Control questions

1. Classification of angiopathies of diabetic patients.
2. Nosotropic mechanisms of diabetic angiopathies development.
3. Diagnostics of angiopathies of lower extremities.
4. Classification of diabetic retinopathies.
5. What is the development of diabetic encephalopathy related to?

6. Diagnostics of diabetic glomerulosclerosis.
7. Classification of diabetic neuropathies.
8. Peculiarities of kidneys affections of patients with diabetes mellitus.
9. What are manifestations of the urogenital system dysfunction of diabetic patients?
10. Which processes influence the heart dysfunction of diabetic patients?
11. Symptoms of diabetic autonomous cardiac neuropathy.
12. What symptoms testify to angiopathy of lower extremities?
13. A notion of "diabetic foot". What contributes to its development?
14. Stages of diabetic nephropathy.
15. Diagnostics of peripheral polyneuropathies.
16. Medications for treatment of angiopathies.
17. List pharmaceutical preparations, that have angioprotective action.
18. Ways of diabetic neuropathies therapy.
19. Methods of physical therapy treatment of patients with angio- and neuropathies.
20. Modern means of treatment of proliferative retinopathy.
21. Modes of physical activity in patients with diabetes mellitus' treatment from angiopathies.
22. Principles of diabetes treatment of pregnant women.
23. Peculiarities of surgery for patients with diabetes mellitus.
26. Prophylaxis of diabetic angiopathies.

Practical tasks

1. To conduct supervision of patients with diabetes mellitus: to analyze the data, obtained at questioning and examination;
2. To interpret data of ophthalmoscopy, conjunctiva biomicroscopies, capillaroscopy, thermography, EKG, urine analysis, state of nitrogen-releasing function of kidneys, renal blood flow, canalicular secretion and reabsorption ;
3. To prescribe a diet, treatment with medical preparations of diabetic patients with different stages of vascular injuries;
4. To write out prescriptions, prescribe physical therapy procedures and a mode of physical activity;
5. To define a presence and a type of neuropathy during the clinical examination of patients, to prescribe treatment for the certain type of neuropathy;
6. To prescribe treatment for pregnant patients with diabetes mellitus;
7. To prescribe treatment for patients in the cabinet "Diabetic foot infections".

Protocol of the clinical examination of the patient

Name, surname of the patient _____

Age _____ Profession _____

Complaints of the patient _____

Anamnesis morbi

Last exacerbation _____

Anamnesis morbi

Results of the physical examination:

Preliminary diagnosis:

Plan of investigation:

Results of the additional methods of investigations:

Rationale of the clinical diagnosis:

Clinical diagnosis:

Main disease

Accompanying disease

Complications

Treatment:

1. Regime _____
2. Diet _____
3. _____
4. _____
5.

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Інформаційні ресурси

сайт кафедри внутрішньої медицини № 3 ХНМУ <http://www.vnmed3.kharkiv.ua/>, встановлене інформаційно-освітнє середовище Moodle на піддомен сайта <http://distance-training.vnmed3.kharkiv.ua>

Методична вказівка складена:

Методична вказівка переглянута і затверджена на засіданні кафедри:

З доповненнями (змiнами) _____

Завiдувач кафедри

Л.В. Журавльова