МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

DISEASES OF ENDOCRINE SYSTEM «CHRONIC COMPLICATION OF DIABETES MELLITUS: DIABETIC RETINOPATHY, NEPHROPATHY, NEUROPATHY AND DIABETIC FOOT. THE PECULIARITES OF CLINICAL COURSE AND TREATMENT OF DIABETES MELLITUS IN SURGICAL PATIENTS AND PREGNANT WOMEN»

Methodological recommendations
for students of IV course

«ЗАХВОРЮВАННЯ ЕНДОКРИННОЇ СИСТЕМИ. ХРОНІЧНІ УСКЛАДНЕННЯ ЦУКОРОВОГО ДІАБЕТУ: ДІАБЕТИЧНВ РЕТІНОПАТІЯ, НЕФРОПАТИЯ, НЕЙРОПАТІЯ ТА ДІАБЕТИЧНА СТОПА. ОСОБЛИВОСТІ КЛІНІЧНОГО ПЕРЕБІГУ ТА ЛІКУВАННЯ ЦУКОРОВОГО ДІАБЕТУ У ХІРУРГІЧНИХ ХВОРИХ ТА ПРИ ВІГІТНОСТІ»

Методичні вказівки
для студентів IV курсу

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Захворювання ендокринної системи. Хронічні ускладнення цукрового діабету: діабетична ретинопатія, нефропатія, нейропатія та діабетична стопа. Особливості перебігу та лікування цукрового діабету у хірургічних хворих та при вагітності: метод. вказ. для студентів IV курсу / укл. Л.В. Журавльова, В.О. Федоров, Л.Р. Бобронніков а та ін.– Харків:ХНМУ, 2013.- 36с.

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Module №1 "The fundamentals of diagnostics, treatment and prevention of main diseases of the endocrine system"

Topic "Chronic complications of diabetes mellitus: diabetic retinopathy, nephropathy, neuropathy, and diabetic foot. The peculiarities of clinical course and treatment of diabetes mellitus in surgical patients and pregnant women"

Topicality

Vascular injuries are the one of the leading syndromes in diabetes mellitus. In most cases their intensity determines patient's capacity for work, prognosis and duration of his life. In this regard the timely and accurate diagnostics as well as treatment of diabetic angiopathies becomes the leading value in diabetology. The problem of angiopathies has an interdisciplinary character and isn't a purely diabetologic issue. This problem has multiple links to ophthalmology, neurology, and surgery. The knowledge of clinical peculiarities and therapeutical tactics at different stages of angiopathies of different localization allows maintaining the patient's capacity for work for longer time.

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, diagnosis, prophylaxis and treatment of diabetic retinopathy;
- to acquaint students with diagnosis and treatment of diabetic neuropathy;
- to acquaint students with the diabetic foot infections: their classifications, diagnosis, algorithm of treatment;
- to teach students the principles of treatment of pregnant women, who suffer from diabetes mellitus;
- to acquaint students with diagnosis and surgical treatment of diabetic angiopathy of lower extremities;
- to familiarize students with timely diagnostics of diabetic gangrene, with peculiarities of urgent and planned surgical interferences for patients with diabetes mellitus.

What student should know?

- classification of diabetic angio- and neuropathies;

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

What student should be able to do?

- to analyze data, received during questioning and examination of patients suffering from diabetes mellitus, select a leading syndrome;
- to interpret the data of ophthalmoscopy, conjunctiva biomicroscopy, capillaroscopy, thermography, ECG, urine analysis, state of nitrogen-generating renal function, renal blood flow, tubular secretion and reabsorption;
- to correct the diet and pharmacological 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 for pregnant women suffering from diabetes mellitus;
- to appoint differentiated treatment for patients with lower extremities complications.

List of practical skills which students should possess:

- A questioning of patients: to identify complaints that testify the presence of vascular and neurologic lesions, clearly explain the order of symptoms appearance and their stability, the results of therapeutic interventions; define the stability of carbohydrate metabolism compensation, the presence proteinuria, its stability, the nature of sediment in the urine and applicable treatment; presence of hypoglycemic episodes in

anamnesis, their frequency, intensity; vascular events; function of digestive system, genitourinary system;

- Examination of patients: the external appearance, presence of edema, muscles atrophy, skin condition, the nature of fluctuations on the distal sections of arteries, muscle strength, reflex character, state of all kinds of sensitivity, visual acuity, the rhythm of cardiac activity, blood pressure level , character of intervals on the ECG, intensity of ECG changes, capillaroscopic picture, rheography data, volume sphygmography, common urine test, proteinuria, the presence leucocytes and erythrocytes; hemoglobin concentration in blood, lipid level, cholesterol, urea, protien fractions; the character of renal blood flow, glomerular filtration rate and tubular reabsorption; analysis of ophthalmoscopic data;

- substantiation of diagnosis; if necessary- appoint additional diagnostic procedures and explain your choice;

- The plan of treatment at present time, medications, doses and terms of their application, use of other means of influence; prognosis and medico-social assessment.

Topic contents

Chronic complications of diabetes mellitus: diabetic retinopathy, nephropathy, neuropathy, and diabetic foot infections. The peculiarities of clinical course and treatment of diabetes mellitus in surgical patients and pregnant women.

A long time of badly controlled hyperglycemia leads to multiple, primarily vascular complications that affect small vessels (microvascular), large (macrovascular) vessels, or both. The mechanisms by which vascular disease develops include glycosylation of serum and tissue proteins with formation of advanced glycation end products; superoxide production; activation of protein kinase C, a signaling molecule that increases vascular permeability and causes endothelial dysfunction; accelerated hexosamine biosynthetic and polyol pathways leading to sorbitol accumulation within tissues; hypertension and dyslipidemias that commonly accompany DM; arterial microthromboses; and proinflammatory and prothrombotic effects of hyperglycemia and hyperinsulinemia that impair vascular autoregulation. Immune dysfunction is another major complication and develops from the direct effects of hyperglycemia on cellular immunity.

Microvascular disease underlies the 3 most common and devastating manifestations of DM:

- Retinopathy
- Nephropathy

- Neuropathy

Microvascular disease may also impair skin healing, so that even minor breaks in skin integrity can develop into deeper ulcers and easily become infected, particularly in the lower extremities. Intensive control of plasma glucose can prevent or delay many of these complications but may not reverse them once established.

Diabetic retinopathy

Diabetic retinopathy is a major cause of blindness, particularly among working-age adults. The degree of retinopathy is highly correlated with

- Duration of diabetes mellitus
- Glycemic control
- Hypertension

The stages of retinopathy development:

Nonproliferative retinopathy: Nonproliferative retinopathy (also called background retinopathy) develops first and causes increased capillary permeability, vascular microaneurysms, dot and blot hemorrhages, exudates (hard and soft), macular ischemia, and macular edema (thickening of the retina caused by fluid leakage from capillaries).

Proliferative retinopathy: Proliferative retinopathy develops after nonproliferative retinopathy and is more severe; it may lead to vitreous hemorrhage and traction retinal detachment. Proliferative retinopathy is characterized by abnormal new vessel formation (neovascularization), which occurs on the inner (vitreous) surface of the retina and may extend into the vitreous cavity and cause vitreous hemorrhage. Neovascularization is often accompanied by preretinal fibrous tissue, which, along with the vitreous, can contract, resulting in traction retinal detachment. Neovascularization may also occur in the anterior segment of the eye on the iris; neovascular membrane growth in the angle of the eye at the peripheral margin of the iris can occur, and this growth leads to neovascular glaucoma. Vision loss with proliferative retinopathy may be severe.

Clinically significant macular edema can occur with nonproliferative or proliferative retinopathy and is the most common cause of vision loss due to diabetic retinopathy.

Symptoms and Signs

Nonproliferative retinopathy: Vision symptoms are caused by macular edema or macular ischemia. However, patients may not have vision loss even with advanced retinopathy. The first signs of nonproliferative retinopathy are

- Dot and blot retinal hemorrhages
- Capillary microaneurysms
- Cotton-wool spots (soft exudates)
- Hard exudates

Hard exudates are discrete, yellow particles within the retina. When present, they suggest chronic edema.

Cotton-wool spots are areas of microinfarction of the retinal nerve fiber layer that lead to retinal opacification; they are fuzzy-edged and white and obscure underlying vessels.

Signs in later stages are the following:

- Macular edema (seen on slit-lamp biomicroscopy as elevation and blurring of retinal layers)
- Venous dilation and intraretinal microvascular abnormalities

Proliferative retinopathy: Symptoms may include blurred vision, black spots or flashing lights in the field of vision, and sudden, severe, painless vision loss. These symptoms are typically caused by vitreous hemorrhage or traction retinal detachment.

Proliferative retinopathy, unlike nonproliferative retinopathy, causes formation of fine preretinal vessel neovascularization visible on the optic nerve or retinal surface. Macular edema or retinal hemorrhage may be visible on funduscopy.

Diagnosis

The following procedures are used for the diagnosis of diabetic retinopathy:

- Funduscopy
- Color fundus photography
- Fluorescein angiography
- Optical coherence tomography

Diagnosis is made mainly by funduscopy. Color fundus photography is done. Fluorescein angiography is used to determine the extent of retinopathy, to develop a treatment plan, and to monitor the results of treatment. Optical coherence tomography is also useful to assess severity of macular edema and treatment response.

Screening: Because early detection is important, all patients with diabetes should have an annual dilated ophthalmologic examination. Pregnant patients with diabetes should be examined every trimester. Vision symptoms are indications for ophthalmologic referral.

Treatment

- Control of blood glucose and BP
- For macular edema, intraocular injection of antivascular endothelial growth factor (antivascular EGF) drugs, intraocular corticosteroid implants, focal laser, and/or vitrectomy
- For high-risk or complicated proliferative retinopathy, panretinal laser photocoagulation and sometimes vitrectomy

Control of blood glucose and BP are critical; intensive control of blood glucose slows progression of retinopathy. Clinically significant diabetic macular edema is treated with intraocular injection of antivascular EGF drugs (ranibizumab, pegaptanib, bevacizumab) and/or with focal laser photocoagulation. In some countries, an intraocular fluocinolone implant is available for patients with chronic diabetic macular edema. Vitrectomy can help in recalcitrant diabetic macular edema. In select cases of severe nonproliferative retinopathy, panretinal laser photocoagulation may be used; however, usually panretinal laser photocoagulation can be delayed until proliferative retinopathy develops.

Proliferative diabetic retinopathy with high-risk characteristics of vitreous hemorrhage, extensive preretinal neovascularization, or anterior segment neovascularization/neovascular glaucoma, should be treated with panretinal laser photocoagulation. This treatment significantly reduces the risk of severe vision loss.

Vitrectomy can help preserve and often restore lost vision in patients with any of the following:

- Vitreous hemorrhage that persists for 3 months
- Extensive preretinal membrane formation
- Traction retinal detachment
- Recalcitrant diabetic macular edema

Prevention

Glycemic and blood pressure control; intensive control of blood glucose delays onset of retinopathy.

Diabetic nephropathy

Diabetic nephropathy (DN) is glomerular sclerosis and fibrosis caused by the metabolic and hemodynamic changes of diabetes mellitus.

DN is the most common cause of nephrotic syndrome in adults and of end-stage renal disease in the Europe, accounting for up to 80% of cases of the latter. The prevalence of renal failure is probably about 40% among patients with type 1 diabetes mellitus. The prevalence of renal failure among patients with type 2 diabetes mellitus is usually stated as 20 to 30%,

but this figure is probably low. Renal failure is particularly common in certain ethnic groups, such as blacks, Mexican-Americans, Polynesians, and Pima Indians. Other risk factors include the following:

- Duration and degree of hyperglycemia
- Hypertension
- Dyslipidemia
- Cigarette smoking
- Certain polymorphisms affecting the renin-angiotensin-aldosterone axis
- Family history of diabetic nephropathy
- Genetic variables (decreased number of glomeruli)

Renal failure usually takes ≥ 10 years after the onset of nephropathy to develop; however, because type 2 diabetes is often present for several years before being recognized, nephropathy often develops < 10 years after diabetes is diagnosed.

Pathophysiology

Pathogenesis begins with small vessel disease. Pathophysiology is complex, involving glycosylation of proteins, hormonally influenced cytokine release (transforming growth factor-β), deposition of mesangial matrix, and alteration of glomerular hemodynamics. Hyperfiltration, an early functional abnormality, is only a relative predictor for the development of renal failure.

Hyperglycemia causes glycosylation of glomerular proteins, which may be responsible for mesangial cell proliferation and matrix expansion and vascular endothelial damage. The GBM classically becomes thickened.

Lesions of diffuse or nodular intercapillary glomerulosclerosis are distinctive. There is marked hyalinosis of afferent and efferent arterioles as well as arteriosclerosis; interstitial fibrosis and tubular atrophy may be present. Only mesangial matrix expansion appears to correlate with progression to end-stage renal disease.

DN begins as glomerular hyperfiltration (increased GFR); GFR normalizes with early renal injury and mild hypertension, which worsens over time. Microalbuminuria, urinary excretion of albumin in a range of 30 to 300 mg albumin/day, then occurs. Urinary albumin in these concentrations is called microalbuminuria because detection of proteinuria by dipstick on routine urinalysis usually requires > 300 mg albumin/day. Microalbuminuria progresses to proteinuria > 0.5 g/day at a variable course, usually over years. Nephrotic syndrome (proteinuria ≥ 3 g/day) precedes end-stage renal disease, on average, by about 3 to 5 years, but this timing is also highly variable. Other urinary tract abnormalities commonly occurring with DN that may accelerate the decline of renal function include papillary

necrosis, type IV renal tubular acidosis, and UTIs. In DN, the kidneys are usually of normal size or larger.

Symptoms and Signs

DN is asymptomatic in early stages. Sustained microalbuminuria is the earliest warning sign. Hypertension and some measure of dependent edema eventually develop in most untreated patients. In later stages, patients develop symptoms and signs of uremia (nausea, vomiting, anorexia) earlier (with higher GFR) than do patients without DN, possibly because the combination of end-organ damage due to diabetes (neuropathy) and renal failure worsens symptoms.

In the natural history of DN, **Mogensen** identified 5 stages of renal dysfunction:

Stage 1: Renal hypertrophy and hyperfiltration – glomerular filtration rate may be increased 20 - 40%

Stage 2: Is clinically 'silent' but hyperfiltration persists and is correlated with mild hyperglycaemia

Stage 3: Microalbuminuria is present

Stage 4: Overt nephropathy with proteinuria, hypertension and progressive renal failure

Stage 5: End-stage renal failure develops

These are more clearly defined in type 1 diabetics, mainly because they often present with metabolic complications early after onset of diabetes, while type 2 diabetics may have a very insidious onset and they may have been exposed to a much longer period of hyperglycaemia before the diagnosis is made.

Diagnosis

- Screening of all patients with diabetes with random urine albumin/creatinine ratio
- Urinalysis for signs of other renal disorders (hematuria, red blood cell casts)

The diagnosis is suspected in patients with diabetes who have proteinuria, particularly if they have diabetic retinopathy (indicating small vessel disease) or risk factors for DN. Other renal disorders should be considered if there are any of the following:

- Heavy proteinuria with only a brief history of diabetes
- Absence of diabetic retinopathy
- Rapid onset of heavy proteinuria
- Gross hematuria
- RBC casts
- Rapid decline in GFR

- Small kidney size

Urinary protein: Patients are tested for proteinuria by routine urinalysis; if proteinuria is present, testing for microalbuminuria is unnecessary because the patient already has macroalbuminuria suggestive of diabetic renal disease. In patients without proteinuria on urinalysis, an albumin/creatinine ratio should be calculated from a mid-morning urine specimen. A ratio ≥ 0.03 mg/mg (≥ 30 mg/g) indicates microalbuminuria if it is present on at least 2 of 3 specimens within 3 to 6 months and if it cannot be explained by infection or exercise. Some experts recommend that microalbuminuria be measured from a 24-h urine collection, but this approach is less convenient, and many patients have difficulty accurately collecting a specimen. The random urine albumin/creatinine ratio overestimates 24-h collection of microalbuminuria in up to 30% of patients> 65 due to reduced creatinine production from reduced muscle mass. Inaccurate results can also occur in very muscular patients or if vigorous exercise precedes urine collection.

For most patients with diabetes who have proteinuria, the diagnosis is clinical. Renal biopsy can confirm the diagnosis but is rarely necessary.

Indications for renal biopsy or other investigations in diabetic renal disease:

• The absence of retinopathy, specifically in type 1 diabetics

• Rapid onset of severe proteinuria, with a short duration of diabetes (< 5 years) (type 2 diabetics may have proteinuria soon after the diagnosis is made)

• With macroscopic haematuria – microscopic haematuria does occur in diabetic nephropathy, but macroscopic haematuria may indicate papillary necrosis or a glomerulonephritis (IgA)

• Active urinary sediment, particularly red cell casts

• Rapid decline in renal function without significant proteinuria, particularly in type 2 diabetics when atherosclerotic renovascular disease should be considered; usually a Doppler investigation of renal arteries, or an MR angiography are done as screening tests

• If serological tests suggest another disease (such as antinuclear factor (ANF), antineutrophil cytoplasmic antibody (ANCA), etc.)

Screening: Patients with type 1 diabetes without known renal disease should be screened for proteinuria and, if proteinuria is absent on routine urinalysis, for microalbuminuria, beginning 5 years after diagnosis and at least annually thereafter.

Patients with type 2 diabetes should be screened at the time of diagnosis and annually thereafter.

Prognosis

Prognosis is good for patients who are meticulously treated and monitored. Such care is often difficult in practice, however, and most patients slowly lose renal function; even prehypertension (BP 120 to 139/80 to 89 mm Hg) or stage 1 hypertension (BP 140 to 159/90 to 99 mm Hg) may accelerate injury. Systemic atherosclerotic disease (stroke, myocardial infarction, peripheral arterial disease) predicts an increase in mortality.

Treatment

- Maintenance of glycosylated Hb (HbA1c) ≤ 7.0
- Aggressive BP control, beginning with angiotensin inhibition

Primary treatment is strict glucose control to maintain HbA1c ≤ 7.0; maintenance of euglycemia reduces microalbuminuria but may not retard disease progression once DN is well established. Glucose control must also be accompanied by strict control of BP to < 130/80 mm Hg. Some experts suggest BP should be 110 to 120/65 to 80 mm Hg, particularly in patients with protein excretion of > 1 g/day; however, others claim that BP values < 120/85 mm Hg are associated with increased cardiovascular mortality and heart failure. Dyslipidemia should also be treated.

Angiotensin inhibition is first-line therapy. Thus, angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor blockers are the antihypertensives of choice; they reduce BP and proteinuria and slow the progression of DN. ACE inhibitors are usually less expensive, but angiotensin II receptor blockers can be used instead if ACE inhibitors cause persistent cough. Treatment should be started when microalbuminuria is detected regardless of whether hypertension is present; some experts recommend drugs be used even before signs of renal disease appear.

Diuretics are required by most patients in addition to angiotensin inhibition to reach target BP levels. Dose should be decreased if symptoms of orthostatic hypotension develop or serum creatinine increases by more than 30%.

Nondihydropyridine Ca channel blockers (diltiazem and verapamil) are also antiproteinuric and renoprotective and can be used if proteinuria does not meaningfully decrease when target BP is reached or as alternatives for patients with hyperkalemia or other contraindications to ACE inhibitors or angiotensin II receptor blockers. In contrast, dihydropyridine Ca channel blockers (nifedipine, felodipine, amlodipine) are relatively contraindicated because they may worsen proteinuria and renal function. ACE inhibitors and nondihydropyridine Ca channel blockers have greater antiproteinuric and renoprotective effects when used together, and their antiproteinuric

effect is enhanced by Na restriction. Nondihydropyridine Ca channel blockers should be used with caution in patients taking β-blockers.

Dietary protein restriction yields mixed results. The American Diabetic Association recommends that people with diabetes and overt nephropathy be restricted to 0.8 g protein/kg/day. Significant protein restriction should be done only with close dietary monitoring to ensure a balanced supply of amino acids, because undernutrition may be a significant risk.

Kidney transplantation with or without simultaneous or subsequent pancreas transplantation is an option for patients with end-stage renal disease. The 5-year survival rate for patients with type 2 diabetes receiving a kidney transplant is almost 60%, compared with 2% for dialysis-dependent patients who do not undergo transplantation (though this statistic probably represents significant selection bias). Renal allograft survival rate is > 85% at 2 years.

Diabetic neuropathy

Diabetic neuropathy is the result of nerve ischemia due to microvascular disease, direct effects of hyperglycemia on neurons, and intracellular metabolic changes that impair nerve function. There are multiple types, including

- Symmetric polyneuropathy (with small- and large-fiber variants)
- Autonomic neuropathy
- Radiculopathy
- Cranial neuropathy
- Mononeuropathy

Symmetric polyneuropathy is most common and affects the distal feet and hands (stocking-glove distribution); it manifests as paresthesias, dysesthesias, or a painless loss of sense of touch, vibration, proprioception, or temperature. In the lower extremities, these symptoms can lead to blunted perception of foot trauma due to ill-fitting shoes and abnormal weight bearing, which can in turn lead to foot ulceration and infection or to fractures, subluxation, and dislocation or destruction of normal foot architecture (Charcot joint).

Small-fiber neuropathy is characterized by pain, numbness, and loss of temperature sensation with preserved vibration and position sense. Patients are prone to foot ulceration and neuropathic joint degeneration and have a high incidence of autonomic neuropathy.

Predominant large-fiber neuropathy is characterized by muscle weakness, loss of vibration and position sense, and lack of deep tendon reflexes. Atrophy of intrinsic muscles of the feet and foot drop are common.

Autonomic neuropathy can cause orthostatic hypotension, exercise intolerance, resting tachycardia, dysphagia, nausea and vomiting (due to gastroparesis), constipation and diarrhea (including dumping syndrome), fecal incontinence, urinary retention and incontinence, erectile dysfunction and retrograde ejaculation, and decreased vaginal lubrication.

Radiculopathies most often affect the proximal L2 through L4 nerve roots, causing pain, weakness, and atrophy of the lower extremities (diabetic amyotrophy), or the proximal T4 through T12 nerve roots, causing abdominal pain (thoracic polyradiculopathy).

Cranial neuropathies cause diplopia, ptosis, and anisocoria when they affect the 3rd cranial nerve or motor palsies when they affect the 4th or 6th cranial nerve.

Mononeuropathies cause finger weakness and numbness (median nerve) or foot drop (peroneal nerve). Patients with DM are also prone to nerve compression disorders, such as carpal tunnel syndrome. Mononeuropathies can occur in several places simultaneously (mononeuritis multiplex). All tend to affect older patients predominantly and usually abate spontaneously over months; however, nerve compression disorders do not.

Diagnosis of symmetric polyneuropathy is by detection of sensory deficits and diminished ankle reflexes. Loss of ability to detect the light touch of a nylon monofilament identifies patients at highest risk of foot ulceration. Alternatively, a 128-Hz tuning fork can be used to assess vibratory sense on the dorsum of the first toe. Electromyography and nerve conduction studies may be needed for all forms of neuropathy and are sometimes used to exclude other causes of neuropathic symptoms, such as nondiabetic radiculopathy and carpal tunnel syndrome. Management of neuropathy involves a multidimensional approach including glycemic control, regular foot care, and management of pain. Strict glycemic control may lessen neuropathy. Treatments for relief of symptoms include topical capsaicin cream, tricyclic antidepressants (imipramine), SNRIs (duloxetine), anticonvulsants (pregabalin, gabapentin,carbamazepine), and mexiletine. Patients with sensory loss should examine their feet daily to detect minor foot trauma and prevent it from progressing to limb-threatening infection.

Lower extremities complications

Diabetic angiopathy of lower extremities most often has a combined character and includes macro-and microangiopathy. It is often the first manifestation of diabetic angiopathy.

Clinical signs of angiopathy of the lower extremities:

1) intermittent claudication;
2) extremities are cold;
3) absence of arterial pulsation on the foot;

4) shiny skin;
5) loss of hair on the feet and legs;
6) nail thickening, often fungal infections;
7) atrophy of subcutaneous fat.

In patients with diabetic angiopathy of the lower extremities and polyneuropathy a "silent" ischemia is observed – the pain syndrome is absent due to the loss of pain sensitivity.

Classification of diabetic angiopathy of lower extremities:

Stage 1 (pre-clinical) is not accompanied by any subjective symptoms or physical symptoms. Diagnosis of vascular lesions is only possible when using additional research - capillaroscopy, rheovasography. Capillaroscopy determines the increase in the number of capillaries, arterial narrowing and shortening, the appearance of granular flow. The data of oscillography show increasing velocity of pulse wave, increasing the average pressure.

Stage 2 - functional, clinically manifests as pain in the legs after prolonged walking, coldness of feet, paresthesias, leg cramps. An objective examination reveals some weakening of pulsation in the feet arteries, lowering of skin temperature by 2-3 C °. Capillaroscopy data show deformation of capillaries, turbidity of background, discontinuous blood flow. According to oscillography - increased velocity of pulse wave. There are three possible types of disorders revealed on rheovasography: hypertonicity of vessels, hypotonicity and atony.

Stage 3 - organic, characterized by addition of trophic disorders: dry skin at feet and legs, pallor or cyanosis, "marble" pattern of skin.The intensity of pain syndrome is increasing - spastic pain in the calf muscles cause the patient to stop during walking of usual intensity (intermittent claudication). Physical examination helps to determine a significant weakening or absence of pulsation in the arteries of the foot. Capillaroscopy detects emptying of capillaries, oscillography reveals falling of oscillator index until no oscillations. The functional tests (cold, nitroglycerin) - show distortion of reactions or no reaction.

Stage 4 - ulcerative-necrotic, gangrenous, characterized by the presence of venous ulcers and gangrene of the toes or other sites.

Classification of the degree of ischemia of the lower limbs:

1. Asymptomatic, no pain during exercise.
2. Intermittent claudication.
3. Pain at rest (cold feet).
4. Gangrene

Diagnosis

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

By using I or III fingers press in different distal sections of foot until blanching of the skin. Normally pink color is restored after 2-3 seconds.

3. "Lifting test."

The patient lies on his back, holding one foot raised above the level of the trunk for 30 sec., then puts it down. Normally, the color of both feet becomes equal in 15 seconds. In case of low blood flow equalization of color takes more than 40 seconds., the skin becomes pale or cyanotic.

4. Pulse on a.dorsalis pedis, a. tibialis posterior. Variations of pulse disorders:

0 - no pulse;

I - fibular pulse (determined only by Doppler test);

II - threadlike;

III - weak;

IV - normal;

V - atherosclerotic (solid).

5. Pulse by ultrasound Doppler.

Doppler study provides insight into the turbulent movement and volume of blood flow. The sound that arises in the study depends on the distance from the heart vessels, caliber, elasticity, damage of arteries. Ultrasonic wave while reaching erythrocytes is reflected and partly shifted (the degrees of displacement is proportional to the velocity of blood flow). The signal is formed by the difference between the two frequencies.

In a normal Doppler study a three-phase rhythm is revealed:

1) rise of the pulse wave in tension of the vascular wall in diastole;

2) decline in pulse wave during the backflow of blood from the arteries to the heart in diastole;

3) a new rise of the pulse wave from the venous valves of the aorta.

6. Determination of systolic blood pressure on the feet by ultrasound Doppler.

7. Research ankle-brachial (ischemic) index.

Ischemic index = systolic pressure on a.tibialis / systolic pressure on a.brachialis. Normally, the ratio exceeds 1.0. In severe ischemia ischemic index is below 0.8.

8. "Stress test" for the detection of latent ischemia.

Ischemic index is determined. Then patient walks for 4 minutes (or until severe pain) and again the ischemic index is determined. Repeated measurements are done every minute until return to their original values. Reduced ischemic index is a sign of latent ischemia.

Treatment of angiopathy of lower extremities

1. Complete compensation of diabetes.

2. Normalization of the metabolic processes.

3. Elimination of dyslipidemia.

4. Angioprotectors and antiplatelet drugs.

5. Vasodilator drugs.

6. Magnetic therapy, local barotherapy; bromine, hydrogen and sulfide baths.

7. Stimulation of trophic processes – Solcoseryl, intramuscular injections, 2 ml 2 times a day (20-30 days).

8. Intra-arterial administration of a mixture of 100 ml of 0.5% solution of novocaine, 1 ml of 2.5% solution of nicotinic acid, 5000 IU of heparin. Infusion is performed 1 time in 3-5 days, altogether 7 infusions.

Diabetes mellitus and pregnancy

Diabetes in pregnancy is associated with risks to the woman and to the developing fetus. Miscarriage, pre-eclampsia and preterm labour are more common in women with pre-existing diabetes. In addition, diabetic retinopathy can worsen rapidly during pregnancy. Stillbirth, congenital malformations, macrosomia, birth injury, perinatal mortality and postnatal adaptation problems (such as hypoglycaemia) are more common in babies born to women with pre-existing diabetes.

Gestational diabetes (or gestational diabetes mellitus, GDM) is a condition in which women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy. It can develop in overweight, hyperinsulinemic, insulin-resistant women or in thin, relatively insulin-deficient women. Gestationaldiabetes occurs in 1 to 3% of all pregnancies, but the rate may be much higher in certain ethnic groups.

Independent risk factors for gestational diabetes:

- body mass index above 30 kg/m^2
- previous macrosomic baby weighing 4.5 kg or above
- previous gestational diabetes
- family history of diabetes (first-degree relative with diabetes)
- family origin with a high prevalence of diabetes:
    - South Asian (specifically women whose country of family origin is India, Pakistan or Bangladesh)
    - black Caribbean
    - Middle Eastern (specifically women whose country of family origin is Saudi Arabia, United Arab Emirates, Iraq, Jordan, Syria, Oman, Qatar, Kuwait, Lebanon or Egypt).

The 2-hour 75 g oral glucose tolerance test (OGTT) should be used to test for gestational diabetes and diagnosis made using the criteria defined by

the World Health Organization. Women who have had gestational diabetes in a previous pregnancy should be offered early self-monitoring of blood glucose or an OGTT at 16–18 weeks, and a further OGTT at 28 weeks if the results are normal. Women with any of the other risk factors for gestational diabetes should be offered an OGTT at 24–28 weeks.

Women with gestational diabetes should be instructed in self-monitoring of blood glucose. Targets for blood glucose control should be determined in the same way as for women with pre-existing diabetes.

Women with gestational diabetes should be advised to choose, where possible, carbohydrates from low glycaemic index sources, lean proteins including oily fish and a balance of polyunsaturated fats and monounsaturated fats.

Women with gestational diabetes whose pre-pregnancy body mass index was above 27 kg/m^2 should be advised to restrict calorie intake (to 25 kcal/kg/day or less) and to take moderate exercise (of at least 30 minutes daily).

Hypoglycaemic therapy should be considered for women with gestational diabetes if diet and exercise fail to maintain blood glucose targets during a period of 1–2 weeks.

Hypoglycaemic therapy should be considered for women with gestational diabetes if ultrasound investigation suggests incipient fetal macrosomia (abdominal circumference above the 70th percentile) at diagnosis.

Hypoglycaemic therapy for women with gestational diabetes (which may include regular insulin, rapid-acting insulin analogues (aspart and lispro) and/or oral hypoglycaemic agents (metformin and glibenclamide) should be tailored to the glycaemic profile of, and acceptability to, the individual woman.

If it is safely achievable, women with diabetes should aim to keep fasting blood glucose between 3.5 and 5.9 mmol/litre and 1-hour postprandial blood glucose below 7.8 mmol/litre during pregnancy.

Intrapartum care:

Pregnant women with diabetes who have a normally grown fetus should be offered elective birth through induction of labour, or by elective caesarean section if indicated, after 38 completed weeks.

Women with diabetes and comorbidities such as obesity or autonomic neuropathy should be offered an anaesthetic assessment in the third trimester of pregnancy.

If general anaesthesia is used for the birth in women with diabetes, blood glucose should be monitored regularly (every 30 minutes) from induction of general anaesthesia until after the baby is born and the woman is fully conscious.

During labour and birth, capillary blood glucose should be monitored on an hourly basis in women with diabetes and maintained at between 4 and 7 mmol/litre.

Women with type 1 diabetes should be considered for intravenous dextrose and insulin infusion from the onset of established labour.

Intravenous dextrose and insulin infusion is recommended during labour and birth for women with diabetes whose blood glucose is not maintained at between 4 and 7 mmol/litre.

Postnatal care: women who were diagnosed with gestational diabetes should be offered lifestyle advice (including weight control, diet and exercise) and offered a fasting plasma glucose measurement (but not an oral glucose tolerance test) at the 6-week postnatal check and annually thereafter.

Management of Diabetes Mellitus in Surgical Patients

Diabetes is associated with increased requirement for surgical procedures and increased postoperative morbidity and mortality. The stress response to surgery and the resultant hyperglycemia, osmotic diuresis, and hypoinsulinemia can lead to perioperative ketoacidosis or hyperosmolar syndrome. Hyperglycemia impairs leukocyte function and wound healing. The management goal is to optimize metabolic control through close monitoring, adequate fluid and caloric repletion, and judicious use of insulin.

Patients with diabetes undergo surgical procedures at a higher rate than do nondiabetic people. Major surgical operations require a period of fasting during which oral antidiabetic medications cannot be used. The stress of surgery itself results in metabolic perturbations that alter glucose homeostasis, and persistent hyperglycemia is a risk factor for endothelial dysfunction, postoperative sepsis, impaired wound healing and cerebral ischemia. The stress response itself may precipitate diabetic crises (diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar syndrome (HHS)) during surgery or postoperatively, with negative prognostic consequences. HHS is a well-known postoperative complication following certain procedures, including cardiac bypass surgery, where it is associated with 42% mortality.

Furthermore, gastrointestinal instability provoked by anesthesia, medications, and stress-related vagal overlay can lead to nausea, vomiting, and dehydration. This compounds the volume contraction that may already be present from the osmotic diuresis induced by hyperglycemia, thereby increasing the risk for ischemic events and acute renal failure. Subtle to gross deficits in key electrolytes (principally potassium, but also magnesium) may pose an arrhythmogenic risk, which often is superimposed on a milieu of endemic coronary artery disease in middle-aged or older people with diabetes.

It is therefore imperative that careful attention be paid to the metabolic status of people with diabetes undergoing surgical procedures. Elective surgery in people with uncontrolled diabetes should preferably be scheduled after acceptable glycemic control has been achieved. Admission to the hospital 1–2 days before a scheduled surgery is advisable for such patients. Even emergency surgery should be delayed, whenever feasible, to allow stabilization of patients in diabetic crises.

The actual treatment recommendations for a given patient should be individualized, based on diabetes classification, usual diabetes regimen, state of glycemic control, nature and extent of surgical procedure, and available expertise. Some general rules can be applied, however. Whenever possible, ketoacidosis, hyperosmolar state, and electrolyte derangements should be searched for and corrected preoperatively, and the surgery itself should be scheduled early in the day, to avoid protracted fasting.

The review of the stress response and glucoregulation

Anesthesia and surgery cause a stereotypical metabolic stress response that could overwhelm homeostatic mechanisms in patients with pre-existing abnormalities of glucose metabolism. The invariant features of the metabolic stress response include release of the catabolic hormones epinephrine, norepinephrine, cortisol, glucagons, and growth hormone and inhibition of insulin secretion and action.

Anti-Insulin Effects of Surgical Stress

In addition to insulin resistance induced by circulating stress hormones, surgical stress has a deleterious effect on pancreatic β-cell function. Plasma insulin levels fall, and insulin secretory responses to glucose become impaired during surgery. The mechanism of the impaired β-cell responsiveness during surgery is unclear, and the defect is poorly correlated with ambient intraoperative catecholamine levels. Postoperatively, however, there is a close inverse correlation between plasma epinephrine and insulin secretion.

These anti-insulin effects of the metabolic stress response essentially reverse the physiological anabolic and anti-catabolic actions of insulin. The important anabolic actions of insulin that may be reversed or attenuated during the stress of surgery include: *1*) stimulation of glucose uptake and glycogen storage, *2*) stimulation of amino acid uptake and protein synthesis by skeletal muscle, *3*) stimulation of fatty acid synthesis in the liver and storage in adipocytes, and *4*) renal sodium reabsorption and intravascular volume preservation. The anti-catabolic effects of insulin include: *1*) inhibition of hepatic glycogen breakdown, *2*) inhibition of gluconeogenesis, *3*) inhibition of lipolysis, *4*) inhibition of fatty acid oxidation and ketone body formation, and *5*) inhibition of proteolysis and amino acid oxidation. Thus, inhibition of insulin secretion and action shifts

the perioperative milieu toward hypercatabolism through a variety of mechanisms.

Direct Catabolic Effects of Stress Hormones

The neuroendocrine response to the stress of general anesthesia and surgery leads to activation of potent counterregulatory hormones. The catecholamines (norepinephrine is augmented mostly during surgery and epinephrine postoperatively) stimulate gluconeogenesis and glycogenolysis, inhibit glucose utilization by peripheral tissues, and inhibit insulin secretion. Activation of phosphoproteins by cAMP-dependent protein kinases accounts for the stimulatory effects of catecholamines on liver and muscle glycogen breakdown, whereas phosphorylation of glycogen synthase accounts for the decreased glycogen synthesis.

These effects predispose to severe hyperglycemia, which is further exacerbated by the stimulatory effect of epinephrine and norepinephrine on glucagon secretion. Other catabolic effects of catecholamines include stimulation of lipolysis and ketogenesis. Epinephrine increases adipocyte cAMP levels, leading to phosphorylation and activation of hormone-sensitive lipase. The activated hormone-sensitive lipase promotes lipolysis and release of free fatty acids into the circulation.

Glucagon, whose levels are augmented by catecholamines, exerts catabolic effects similar to those of the catecholamines: stimulation of hepatic glucose production and ketogenesis and inhibition of insulin action in peripheral tissues. Growth hormone and glucocorticoids potentiate the catabolic effects of catecholamines and glucagon. Glucocorticoids increase hepatic glucose production and induce lipolysis and negative nitrogen balance by stimulating proteolysis. The products of lipolysis and proteolysis (e.g., free fatty acids, glycerol, alanine, glutamine) provide substrates for increased gluconeogenesis by the liver.

Clearly, the combination of relative hypoinsulinemia, insulin resistance, and excessive catabolism from the action of counterregulatory hormones is a serious threat to glucose homeostasis in all patients with diabetes, particularly those whose preoperative metabolic control is less than perfect. The logical conclusion is that insulin therapy will be needed perioperatively in the majority of patients with diabetes undergoing surgery.

Management

Operationally, all patients with type 1 diabetes undergoing minor or major surgery and patients with type 2 diabetes undergoing major surgery are considered appropriate candidates for intensive perioperative diabetes management. The management approach in these categories of patients always includes insulin therapy in combination with dextrose and potassium infusion. Major surgery is defined as one requiring general anesthesia of $\geq$1 h. Type 2 diabetic patients undergoing minor surgery are managed based on

their usual diabetes regimen, their state of glycemic control, the nature and extent of the surgical procedure, and available expertise.

Patients Managed With Diet Alone

People whose diabetes is well controlled by a regimen of dietary modification and physical activity may require no special preoperative intervention for diabetes. Fasting blood glucose should be measured on the morning of surgery, and intraoperative blood glucose monitoring is desirable if the surgical procedure is lengthy (>1 h). If surgery is minor, no specific therapy is required. If surgery is major or if diabetes is poorly controlled (blood glucose >11 mmol/l), an intravenous infusion of insulin and dextrose should be considered (see below), and hourly intraoperative glucose monitoring is recommended.

Patients Treated With Oral Antidiabetic Agents

Second-generation sulfonylureas should be discontinued 1 day before surgery, with the exception of chlopropramide, which should be stopped 2–3 days before surgery. Other oral agents can be continued until the operative day. Although metformin has a short half-life of ∼6 h, it is prudent to temporarily withhold therapy 1–2 days before surgery, especially in sick patients and those undergoing procedures that increase the risks for renal hypoperfusion, tissue hypoxia, and lactate accumulation.

At a minimum, blood glucose should be monitored before and immediately after surgery in all patients. Those undergoing extensive procedures should have hourly glucose monitoring during and immediately following surgery. Bedside capillary blood glucose meters are adequate for these monitoring requirements. However, extremely high or low values should immediately be repeated before instituting remedial action, and a simultaneous blood specimen should be sent for laboratory corroboration.

For minor surgery, perioperative hyperglycemia (>11 mmol/l) can be managed with small subcutaneous doses (4–10 units) of short-acting insulin. Care must be taken to avoid hypoglycemia. After minor procedures, most usual antidiabetic medications can be restarted once patients start eating. Patients treated with metformin should withhold the drug for ∼72 h following surgery or iodinated radiocontrast procedures. Metformin therapy can be restarted after documentation of normal renal function and absence of contrast-induced nephropathy. The recommended treatment for patients undergoing major surgery and for those with poorly controlled type 2 diabetes is intravenous insulin infusion, with glucose, using one of two standard regimens (see below).

Insulin-Treated Patients

Minor surgery

Patients treated with long-acting insulin (ultralente, glargine, protamine zinc insulin) should be switched to intermediate-acting forms 1–2 days

before elective surgery. Close perioperative blood glucose monitoring is crucial to avoid extremes of glycemia. Intravenous insulin/glucose/potassium should be commenced before surgery. Blood glucose levels should be monitored hourly intraoperatively and immediately after surgery. The infusion should be stopped and usual insulin treatment resumed once oral intake is established. There should be a 1h overlap between stopping intravenous insulin and re-instituting subcutaneous insulin.

Major surgery

Insulin-treated patients undergoing major elective surgery should preferably be admitted 2–3 days before surgery, if glycemic control is suboptimal (hemoglobin A_{1c} >8%). If admission is not feasible, a physician or diabetes nurse practitioner should work with the patient to optimize self-monitoring of blood glucose (SMBG) values in the days preceding the planned surgery. In such circumstances, SMBG should be performed at least before each meal and at bedtime, with target preprandial values of 4.4–6.7 mmol/l and bedtime values of 5.6–7.8 mmol/l.

The preoperative evaluation should include a thorough physical examination (with particular focus on autonomic neuropathy and cardiac status), measurement of serum electrolytes and creatinine, and urine ketones. The presence of autonomic neuropathy mandates increased surveillance for hypotension, respiratory arrest, and hemodynamic instability during surgery. Gross metabolic and electrolyte abnormalities (hyponatremia, dyskalemia, acidosis) should be corrected before surgery.

Intravenous Insulin, Glucose, Potassium, and Fluids

Intravenous infusion of insulin, glucose, and potassium is now standard therapy and has replaced subcutaneous insulin therapy for the perioperative management of diabetes, especially in type 1 diabetic patients and patients with type 2 diabetes undergoing major procedures. Several reports have emphasized the advantages of the insulin infusion regimen over subcutaneous delivery.

It is not necessary to add albumin to the insulin infusion to prevent nonspecific adsorption of insulin to the infusion apparatus; flushing ~50 ml of the insulin infusion mixture through the tubing will accomplish the same purpose.

Adequate fluids must be administered to maintain intravascular volume. Fluid deficits from osmotic diuresis in poorly controlled diabetes can be considerable. The preferred fluids are normal saline and dextrose in water. Fluids containing lactate (Ringer's lactate, Hartmann's solution) cause exacerbation of hyperglycemia.

Insulin

Two main methods of insulin delivery have been used: either combining insulin with glucose and potassium in the same bag (the GIK regimen) or giving insulin separately with an infusion pump.

The combined GIK infusion is efficient, safe, and effective in many patients but does not permit selective adjustment of insulin delivery without changing the bag. The glucose component can be either 5 or 10% dextrose. The latter provides more calories.

Regardless of whether separate or combined infusions are given, close monitoring is required to avoid catastrophe during these infusion regimens. These recommendations must be interpreted flexibly, given the individual variability in insulin requirements and metabolic profiles. In the absence of strict evidence-based guidelines, the consensus approach is to avoid extremes of glycemia (aiming for 6.7–10.0 mmol/l) and to tailor therapies to individual patients based on feedback from glucose monitoring.

The initial insulin infusion rate can be estimated as between one-half and three-fourths of the patient's total daily insulin dose expressed as units/h. Regular insulin, 0.5–1 unit/h, is an appropriate starting dose for most type 1 diabetic patients. Patients treated with oral antidiabetic agents who require perioperative insulin infusion, as well as insulin-treated type 2 diabetic patients, can be given an initial infusion rate of 1–2 units/h.

An infusion rate of 1 unit/h is obtained by mixing 25 units of regular insulin in 250 ml of normal saline (0.1 unit/ml) and infusing 10 ml/h. Alternatively, 50 units of regular insulin is made up to 50 ml with saline and given by syringe pump at 1–2 ml/h. Adjustments to the insulin infusion rate are made to maintain blood glucose between 6.7 and 10.0 mmol/l.

The duration of insulin (and dextrose) infusions depends on the clinical status of the patient. The infusions should be continued postoperatively until oral intake is established, after which the usual diabetes treatment can be resumed. It is prudent to give the first subcutaneous dose of insulin 30–60 min before disconnecting the intravenous line.

Glucose

Adequate glucose should be provided to prevent catabolism, starvation ketosis, and insulin-induced hypoglycemia. The physiological amount of glucose required to prevent catabolism in an average nondiabetic adult is ~120 g/day (or 5 g/h). With preoperative fasting, surgical stress, and ongoing insulin therapy, the caloric requirement in most diabetic patients averages 5–10 g/h glucose. This can be given as 5 or 10% dextrose. An infusion rate of 100 ml/h with 5% dextrose delivers 5 g/h glucose. If fluid restriction is necessary, the more concentrated 10% dextrose can be used. Many now prefer to give 10% dextrose at a starting rate of ~100 ml/h.

The usual range of perioperative blood glucose that clinicians are comfortable with is ~ 6.7–10.0 mmol/l. The insulin and glucose infusion

rates should be adjusted accordingly if blood glucose monitoring shows marked deviation from the acceptable range. The convention is to administer ~0.3 units of insulin/g glucose in most otherwise stable patients. However, insulin requirements are higher in septic, obese, or unstable patients and in those treated with steroids or undergoing cardiopulmonary bypass surgery. If the GIK regimen is to be used, then 15 units of insulin in 500 ml 10% dextrose containing 10 mEq potassium is the usual starting solution given at 100 ml/h.

Potassium

The infusion of insulin and glucose induces an intracellular translocation of potassium, resulting in a risk for hypokalemia. In patients with initially normal serum potassium, potassium chloride, 10 mEq, should be added routinely to each 500 ml of dextrose to maintain normokalemia if renal function is normal. Hyperkalemia (confirmed with repeat measurement and electrocardiogram) and renal insufficiency are contraindications to potassium infusion.

Emergency Surgery

Approximately 5% of people with diabetes will require emergency surgery over their lifetime. The commonly performed surgeries include general procedures (laparotomy, appendectomy, cholecystectomy, and so forth) and diabetes-related procedures, such as abscess drainage, ulcer care, and lower-extremity amputation.

By definition, the time of occurrence of these emergencies cannot be predicted, and appropriate surgical care must not be unduly delayed. Nonetheless, particular care must be taken to exclude DKA and other conditions that are likely to be mistaken for surgical emergencies. Many patients with DKA and prominent abdominal symptoms have undergone needless surgical exploration for a nonexistent acute abdominal emergency. Functional syndromes due to diabetic autonomic neuropathy of the gastrointestinal tract (gastroparesis, gastroenteropathy, intractable or cyclical vomiting) may mimic anatomical surgical emergencies. Similarly, the rare diabetic pseudotabes syndrome, characterized by sharp neuropathic pain along thoracolumbar dermatomes, can be confused with visceral disorders. Patients with pseudotabes typically have pupillary and gait abnormalities from associated cranial and peripheral neuropathy. The initial evaluation of a diabetic patient with a suspected surgical emergency must, therefore, include a thorough medical history and physical examination directed at excluding the aforementioned diagnostic pitfalls.

Unfortunately, many patients who require emergency surgery will have suboptimal glycemic control. However, this is not necessarily a contraindication to the timely performance of potentially life-saving surgery. An intravenous access should be secured and immediate blood specimens should be sent for glucose, electrolyte, and acid-base assessment.

Gross derangements of volume and electrolytes (e.g. hypokalemia, hypernatremia) should be corrected.

Surgery should be delayed, whenever feasible, in patients with DKA, so that the underlying acid-base disorder can be corrected or, at least, ameliorated. Patients with HHS are markedly dehydrated and should be restored quickly to good volume and improved metabolic status before surgery. Blood glucose should be monitored hourly at the bedside, and insulin, glucose, and potassium infusion should be administered, as appropriate, to maintain blood glucose in the 6.7 –10.0 mmol/l range. Serum potassium should be checked frequently (every 2–4 h), and potassium supplementation should be adjusted to ensure that the patient remains eukalemic throughout surgery and postoperatively.

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 artery disease
D. Autonomous cardiac neuropathy
E. Hypokalemia

2. The most typical kidney injury in diabetes mellitus is:

A. Nodal glomerulosclerosis
B. Diffuse glomerulosclerosis
C. Amyloidosis
D. Chronic pyelonephritis

3. What type of neuropathy is the most common one in patients with diabetes mellitus?

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

4. The most typical derangement of organs of visions in patients with diabetes mellitus is:

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

5. What treatment is the most appropriate one in case of diabetes mellitus of pregnant women?

A. Short-action insulin
B. Biguanides

C. Sulfanylamide glucose-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 in 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 to resolve problems in areas of:
A. Microaneurysms localization
B. Minor hemorrages
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. Disorders of intrarenal hemodynamics
C. Both symptoms

9. Disorders of intrarenal hemodynamics at the early stages of diabetic nephropathy are characterized by:
A. Hyperfiltration
B. Hyperperfusion of kidneys
C. Intraglomerular hypertension
D. All above mentioned

10. Normal daily urinary albumin excretion is:
A. up to 30 mg;
B. 40 mg
C. 50 mg
D. up to 300 mg
E. up to 400 mg

Endocrinology (initial level of knowledge)

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

Control of final level of knowledge

1. The laboratory symptoms of marked diabetic nephropathy are:

A. Proteinuria
B. Changes in the glomerular filtration rate
C. Increased azotemia
D. Progress of arterial hypertension
E. All mentioned above

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

A. Microaneurysms
B. Point hemorrhages
C. Retinal edema
D. Exudation focuses
E. All mentioned above

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 mentioned above

4. Proliferative 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 mentioned above

5. Panretinal laser photocoagulation is used mainly in:

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 derangements of

sensitivity, first of all:

A. Oscillatory
B. Pain
C. Tactile
D. Temperature

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

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

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

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

10. Diabetic macroangiopathies include injuries of all listed below organs, except of one:

A. Aorta and coronary arteries
B. Kidneys
C. Cerebral vessels
D. Peripheral vessels
E. General atherosclerosis

Endocrinology (final level of knowledge)

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

Case-based questions

1. The patient K. has been suffering from diabetes mellitus for 28 years. During the last year the dose of insulin was reduced by 14 units. The urine test: protein – 1.7 gram/l, sugar – 0.8 %, a great amount of red blood cells, cylinders. The given symptoms are the 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 type 2. Diabetes is compensated by a diet and maninil. The patient has to undergo an inguinal hernia operation. What medical tactic should be applied to this patient?

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 normal by 36%. AT reaches 150/90 mm of mercury. Blood sugar is 5.9 mmol/l, general cholesterol – 4.9 mmol/l, urinary acid – 0.211 mmol/l. Which existing risk factor primarily requires elimination in the process of secondary prevention?

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

4. Evaluate the glucose tolerance test for a 17-years-old boy: fasting glucose – 5.78 mmol/l, in an hour after taking 75 g of glucose – 7.21 mmol/l, in two hours – 5.68 mmol/l.

A. Diabetes mellitus, latent form
B. Diabetes mellitus, moderate severity
C. Glucose tolerance is not impaired
D. Diabetes mellitus, mild form
E. Symptomatic hyperglycemia

5. The urine test data of a 17-year old boy for the first time showed glucose presence – 5 gram/l. Fasting glycemia is 5.4 mmol/l. No complaints. Which test would reliably exclude diabetes mellitus?

A. Glucose tolerance test
B. Daily glycemia fluctuation
C. Insulin level in plasma
D. Daily glucosuria
E. After-meal glycemia

6. A man of 20 years old complains on thirst, increased urination, general weakness, decrease of body weight. Objective data: skin is dry, red cheeks, vesicular respiration sounds. Cardiac sounds are normal. The tongue is dry. No symptoms of peritoneal irritation. What would be the most informative test to make the diagnosis?

A. Fasting glucose test
B. Complete blood count
C. Urine test
D. Zimnitskiy's test
E. Liver function test

7. A patient of 30 years old with the satisfactorily compensated diabetes mellitus of type 1 has frequent hypoglycemia episodes, nausea, intestinal disorders, skin hyperpigmentation, low BP - 80/50 mm of mercury, progressing anemia Hb -105 gram/l. What may be the reason of the low BP?

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 noticed itching of skin. Her height is 167 cm and weight is 89 kg. Fasting glycemia – 8.1 mmol/l. What diagnosis is the most probable one?

A. Diabetes mellitus, type 1
B. Diabetes mellitus, type 2
C. Impaired glucose tolerance
D. Steroid diabetes mellitus
E. Neurodermatitis

9. A woman of 35 years old, got sick with a flu, has a fasting glycemia of 11.3 mmol/l, glucosuria – 25 gram/l. Her height is 168 cm, and weight is 67 kg. What is the most informative study to clarify the diagnosis?

A. Daily glucosuria fluctuation
B. Daily glycemia fluctuation
C. Determination of C-peptide
D. Glycemia in an hour after meal
E. Glucose tolerance test

10. The 29-years old patient K. complains on thirst, polyuria (up to 5 L per day), weakness. Blood glucose is 8.5 mmol/l. What is the preliminary 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. Diagnosis of angiopathies of lower extremities.
4. Classification of diabetic retinopathies.
5. What is the reason for the development of diabetic encephalopathy?
6. Diagnosis of diabetic glomerulosclerosis.
7. Classification of diabetic neuropathies.
8. The peculiarities of kidneys injury in patients with diabetes mellitus.
9. What are the manifestations of the urogenital system disfunction in diabetic patients?
10. Which processes influence the heart disfunction of diabetic patients?
11. Symptoms of diabetic autonomous cardiac neuropathy.
12. What symptoms are typical for the angiopathy of lower extremities?
13. Diabetic foot. What are the reasons for its development?
14. Stages of diabetic nephropathy.

15. Diagnosis of peripheral polyneuropathies.
16. Medications for treatment of angiopathies.
17. List pharmaceutical preparations, that have angioprotective action.
18. Methods of treatment of diabetic neuropathy.
19. Methods of physical therapy of patients with angio- and neuropathies.
20. Modern means of treatment of proliferative retinopathy.
21. Principles of treatment of diabetes in pregnancy.
22. Peculiarities of management of surgical patients with diabetes mellitus.
23. Prevention of diabetic angiopathies.

Practical tasks

1. To supervise patients with diabetes mellitus: to analyze the data, obtained at questioning and examination;
2. To interpret data of ophthalmoscopy, conjunctiva biomicroscopies, capillaroscopy, thermography, ECG, urine test, state of nitrogen-releasing function of kidneys, renal blood flow, canalicular secretion and reabsorption ;
3. To prescribe a diet, medical treatment for diabetic patients with different stages of vascular injuries;
4. To define a presence and a type of neuropathy during the clinical examination of patients, prescribe treatment for the certain type of neuropathy;
5. To prescribe treatment for pregnant patients with diabetes mellitus;
6. To prescribe treatment for patients with diabetic foot.

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