Міністерство охорони здоров'я України
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ЗАТВЕРДЖЕНО
на засіданні кафедри внутрішньої медицини №3
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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

Захворювання надниркових залоз. Хронічна недостатність кори надниркових залоз. Етіологія, патогенез, клініка, діагностика, профілактика та лікування. Гормонально-активні пухлини надниркових залоз

Харків 2016

Topic – «Chronic insufficiency of adrenal glands cortex. Etiology, pathogen, clinic, diagnostics, prophylaxis and treatment. Acute insufficiency of adrenal glands cortex . Hormonal-active tumors of adrenal glands»

1.The number of hours - 4

Actuality

The defeats of conduce to the heavy diseases the initial displays of which in most cases do not have a clear clinical picture, patients are under surveillance of doctors of different on specialty, which often are the reason of too late diagnostics and treatment. On occasion the disease can begin from the exigent state.

Addison's disease is characterized by chronic motion, needing lifelong hormonal therapy careful organization of clinical supervision, necessity of periodical correction of treatment. Diagnostics of diseases which are accompanied by hyper function of adrenal glands, can be extremely labored and needs differentiation with the numeral amount of other diseases. That is why it is necessary to study pathology of glandules to the doctors of all specialties.

Educational purposes:

- to acquaint students with *anatomic and physiologic information* about glandules;
- to teach the students of etiology, pathogenic, clinic, diagnostics, prophylaxis and treatment *of chronic insufficiency of adrenal glands (*Addison's disease*) and acute insufficiency of adrenal glands;*
- to acquaint students with *classification of tumors* of adrenal glands;
- to teach students to the clinic, diagnostics, differential diagnostics, treatment *of Cushing's syndrome (corticosteroms, glucosteroms*), *androsteroms and corticosteroms*, *primary hyperaldosteronism (Konn`s syndrome), ect.*;

What a student must know?

- *anatomic and physiologic information* of adrenal glands;
- prevalence, etiology, pathogen, clinic, diagnostics, prophylaxis and treatment *of chronic insufficiency of adrenal glands (*Addison's *disease) and sharp insufficiency of* adrenal glands*;*
- *classification of tumors* of adrenal glands;
- clinic, diagnostics, differential diagnostics, treatment *of Cushing syndrome (corticosteroms, glucosteroms*), *androsteroms and corticosteroms, primary hyperaldosteronism (Konn`s syndrome)*;

What a student must be able?

- to recognize clinical symptoms;
- to interpret laboratory information, results of determination of hormones, their predecessors and metabolite;
- to inculcate differential diagnostics;
- to work out a plan of inspection and treatment;
- to diagnose, treat, inculcate the clinical supervision at chronic insufficiency of adrenal glands, hormonal-active tumors of adrenal glands, adrenal-genital syndrome;
- to diagnose and treat sharp adrenal insufficiency and Addison's *disease* in the conditions of stress.

List of practical skills which a student must master

- to select main complaints at a patient, related to the diseases of adrenal glands;
- to set the possible etiologic factors of disease;
- to find out the presence of violations of internals and systems of organism, related to violation of the functional state of adrenal glands;
- right to interpret information of additional researches, in that number hormonal, roentgen logic and radiological;
- to diagrammatize inspection of this patient;
- to be able right to prepare biological material for hormonal research;

- to conduct differential diagnostics of this disease;
- to ground a diagnosis;
- to diagrammatize treatment of this patient;
- if necessary to set the plan of treatment to operation, in a period and after her;
- to set a possible prognosis;
- to write recipes on preparations of hormones of adrenal glands.

The topic contents: Chronic insufficiency of adrenal gland cortex. Etiology, pathogenic, clinic, diagnostics, prophylaxis and treatment. Acute insufficiency of adrenal glands cortex. Hormonal-active tumors of adrenal glands.

Anatomic and physiologic information of adrenal glands

Adrenal glands is double glands, right and left adrenal glands. Adrenal glands is complex, that consists of two headmen's - cortex and cerebral matter, that have the different embryo origin, different histological structure and synthesize the different types of hormones.

The cork matter is formed from the mesoderm cages located near-by the rudiment of sexual glands. *The cerebral matter* is derivative ectoderm cages of nervous comb. The permanent adrenal cortex begins in a postnatal period to be formed, and to the third year of life 3 areas of adrenal cortex concern expressly: glomerular, and reticulated, which abuts upon a cerebral layer.

At the grown man the adrenal glands have the form of triangles with dimensions 4x2x0,3 см and mass about 5-7 g. On a stake of cortex is been by about 80% mass of adrenal glands.

The cerebral matter of adrenal glands (as well as likeable nervous system) is derivative nervous comb, have the neuroectodermal origin, are the place of formation of catecholamine, to which take dopamine, noradrenalin and adrenalin.

The adrenal glands secretes corticosteroids which consist of a 21 atom of carbon. Steroid hormones divide into four groups: *glucocorticoides*, mineralocorticoides, *testosterone and estrogens.*

A cholesterol the particle of which at the adrenal glands makes a to 10% raw mass is the predecessor of steroid hormones. The large stake of cholesterol (80-90%) is related to fat acids, ethers of cholesterol of cytoplasm concentrated in lipid drops. A free cholesterol is only 10% his common maintenance in adrenal glands, is localized mainly in cytoplasm membranes and mitochondria. Addition to the supplies of cholesterol is under the control ACTH.

ACTH regulates speed of steroid genesis in adrenal glands, changing metabolism of cholesterol and his redistribution both into a cage and in mitochondries. *The biosynthesis of corticosteroids* begins in mitochondria.

Pregnanolon, that formed of cholesterol at mitochondria's, is a predecessor for most corticosteroids. Subsequent transformation of corticosteroids takes place in smooth and shiny cytoplasm reticulum.

The biosynthesis of mineralocorticoides controls the enzyme of P450-aldo, which is only in a glomerular area. That is why mineralocorticoides (aldosteron) appears only in the cell of glomerular area. Under the control the enzyme of P450-aldo there are all three lasts of peat-time of synthesis of aldosterone is synthesis from the 11-desoxycorticosterone ofcorticosterone, 18-hydroxycorticosterone and *aldosterone* (18-oxycorticosterone).

Formation of testosterones in the cortex of adrenal glands is carried out in its reticulated layer by conversion of 17-a-hydroxypregnanolon in *C-19 steroids* which a dehydroepiandrosteron and dehydroepiandrosteron sulfate belongs to. Androstendione appears with 17-a-hydroxyprogesterone with participation of enzyme of 17,20-desmolase. Androstendione can be converted to testosterone. At the men testosterone of adrenal origin is only small part from the general level oftestosterone, that circulates in a blood and exctrets with urine.

Biologically in the order of diminishing of activity cortisole, cortisone, corticosterone, 11-desoxycortisole and 11-pregnenoltrione is active *by glucocorticoides*.

Cortisole, that enters circulation of blood, associates a-2-globuline (*transcortine).* More than 95% cortisole blood is related to transcortine and is in a permanent equilibrium with free faction of hormone, that carries out a biological effect. Together with it cortisole contacts also with albumens which have to him low affinity in comparison with transcortine.

Free cortisole is filtered in the glomerulis of buds only, about 90% what reabsorbs in kidney tubules, and other part - about 330 nmol (120 milligrams) – excretes with urine for a day long.

A liver is the basic place of exchange of cortisole, but kidneys, intestine and lights, also take part in the exchange of corticosteroids. A half-period of cortisone is 80-110 min.

The secretion of cortisole, as well as ACTH, has characteristic day's rhythm. The maximum of secretion is on morning hours (6-8 г).

Glucocorticoides is important, vitally necessary hormones which take part in adjusting of exchange of matters in an organism:

- promote concentration of glucose in a blood due to the sharp increase of gluconeogenesis in a liver and decline of utilization of glucose on periphery (counterinsular action, peripheral antagonism of action of insulin);
- find out *catastatic action* on the exchange of albumens and fats - activate their disintegration and brake the synthesis;
- *activating of lipolyse* in fatty fabric results in freeing in the whey of blood of glycerin, free fat acids and other lipides (lipidemias andhypercholesterinaemia).
- repress all of the tools of inflammatory reaction and are natural counter-inflammation factors;
- jointly with aldosteron, catecholamins and other vasoactive peptids take part in support of orthoarteriotony. In addition, formation of angiotensinogen, which grows intoangiotensin, finds out own presor operates and simultaneously stimulates the secretion ofaldosterone, is here multiplied;
- *promote a diuresis,* stimulating speed of glomerular filtration and diminishing D-major of water (probably, as a result of oppression of formation of antidiuretic hormone).

Cortisole has small mineralocorticoidal activity - strengthens reabsorbtion of sodium in an exchange on the ions of potassium in the departments of tubulis of buds, that results in the delay of sodium in an organism, to the increase of volume of extracellular liquid and hypopotassiumaemia.

Cortisole is basic corticosteroid that carries out the control of secretion of corticoliberine and ACTH.

Biologically in the order of diminishing of activity of aldosterone, desoxycorticosterone, 18-oxycorticosterone and 18-oxy desoxycorticosterone is active by mineralocorticoides. Aldosterone is instrumental in the delay in the organism of sodium and water, stimulates the selection of potassium, and also finds out weak glucocorticoid operates.

Aldosterone, that secrets by adrenal glands contacts with specific cytoplasmatic receptors ephithelial cells of distal departments of tubulis of buds. The aldosterone-receptor complex then moves in a kernel and contacts with nuclear receptors, causing synthesis of enzyme of albumen, which carries out the enhanceable selection of potassium and delay of sodium, providing the exchange of ions of sodium on potassium in the distances departments of tubulis.

There is the secretion of sexual hormones in the reticulated layer of adrenal glands cortex (testosterone and estrogens).

Catecholamins appear in the chromaffin cells of adrenal glands cerebral layer, adrenergetic likable fibres of postganglionic neurons. Catecholamines simultaneously are both hormones and neurotransmitters which act leading part in adjusting of functioning of the cardiac system.

For formation of catecholamins *tyrosine* is an initial product. At first in mitochondries of chromaffin cells there is hydrolysis of *tyrosine* with participation of enzyme of *tyrosinehydroxylasa* with formation of dihydroxyphenylalanine *(DOPHA).* Activity of *tyrosinehydroxylasa* and hydroxylation of *tyrosine* is a basic link in the biosynthesis of catecholamins, limiting his speed. DOPHA is the predecessor of catecholamins, does not have biological activity, but easily passes through a blood-encephal barrier.

By *DOPHA*-decarboxylasa *DOPHA* grows into dehydrooxyphenilaethylamin. Decarboxylating of *DOPHA* and formation of dofaminum is carried out in a cytoplasm.

Dofaminum gets in the granules of chromaffin cells or terminal axons and in presence the enzyme of dophamin-b-oxydasa grows into *a noradrenalin.* Farther a noradrenalin again goes out in a cytoplasm and by the enzyme of noradrenalin-N-methyltransferasa is transformed in *adrenalin* which is repeatedly taken in by granules.

Granules execute the following specific functions: take in dophamin from a cytozole cell and convert him in a noradrenalin; granules are the place of "warehousing" of adrenalin and noradrenalin; guard them from action of monoaminooxydasa and destruction; in reply to nervous stimulation free catecholamines in a blood.

Freeing of catecholamines both from the cerebral layer of adrenal and from endings of the likable nervous system takes place under act of such physiology stimulant, as stress, physical and psychical loading increase of level of insulin in a blood, glucopenia, blood pressure and other. Freeing of catecholamins takes place with participation of ions of Ca2+, which enters cell or in ending of the likable nervous system. Catecholamines which enter blood achieve peripheral ткань, where accumulate or metabolize in direct ratio to likable innervation of tissue.

CHRONIC INSUFFICIENCY OF ADRENAL GLAND CORTEX (ADDISON`S DISEASE)

First the chronic insufficiency of adrenal glands cortex, caused by the tubercular disease, English physician Thomas Addison described in 1855.

Chronic adrenal insufficiency more frequent meets at men in age 20-40 years; correlation of men and women - 2:1.

Etiology

A primary form can be related to the defeat of cork matter by the adrenal glands destructive processes of different origin or with making progress atrophy of adrenal glands autoimmune genesis. Development *of the second form* of illness more frequent is related to the hypogenesis or atrophy of adrenal glands cork matter, hypothalamo-hypophysis system caused by the primary disease, and that results in an insufficient secretion of corticotrophin by hypophysis.

Before the principal reason of chronic insufficiency of adrenal glands was a tubercular infection, on its particle was to 80% all cases of disease.

On this time approximately in 50-65% cases primary chronic insufficiency of adrenal glands arises up as a result of autoimmune *adrenalitis.*

Often at the same patients next to the presence of autoantibody to the cell of adrenal glands cortex antibodies appear to the aits of pancreas. The autoimmune disease of adrenal glands cortex often meets as component of autoimmune polyglandular syndrome of I and II type.

The autoimmune polyglandular *syndrome of the I type* develops in child's age (about 10-12 years) and includes hypoparathyreosis, insufficiency of adrenal glands and candidomicose. The often indicated insufficiency of the transferred glands unites with hypogonadism, pernicious anaemia and chronic active hepatitis.

The autoimmune polyglandular *syndrome of the II type* is observed at adults, usually after 20-years-old age and is characterized by a triad: saccharine diabetes, autoimmune disease of thyreoid gland and adrenal insufficiency. At the autoimmune polyglandular syndrome of the II type the set association with the genes of the system HLA-DR3 and DR4, while at the autoimmune polyglandular syndrome of I as such association it is not.

Syndrome of Schmidt is characterized by the autoimmune disease of adrenal glands, thyreoid and sexual glands.

The second form of chronic insufficiency of adrenal glands cortex more frequent in all is conditioned by the inflammatory diseases of cerebrum and his shells (encephalitis, arachnoiditis). Addison's disease can also arise up as a result of the protracted corticosteroid therapy at rheumatism, collagenosess, illnesses of blood, bronchial asthma, as a result of what violation of functioning of the system is hypophysis- adrenal glands cortex, that results in a hypogenesis atrophy of adrenal glands cortex.

Pathogeny

The defease of adrenal glands cortex results in the decline of formation of *glucocorticoides*, in less degree mineralocorticoides and testosterone. The deficit of hormones causes difficult violations of exchanges processes in an organism, and also the functional state of many organs and systems.

The deficit of glucocorticoides draws heavy violation of carbohydrate exchange. Activity of processes of gluconeogenesis goes down, in intervals between a meal *there* are *the episodes of glucopenia*. The anabolic effect of *glucocorticoides* is not carried out on a liver - the supplies of hepatin go down in a liver, to the basic "depot" of carbonhydratess in an organism. Even on a background the carbohydrate loading

the level of glucose in a blood remains low is flat glucaemic curve. The low level of glucose in tissue causes the dystrophic changes and varied functional violations - in particular muscular weakness and adynamia.

Insufficiency of *glucocorticoides draws oppression of synthesis of albumens in a liver,* decline of activity of intracellular enzymes, an erythrogenesis and leucopoesis is slowed, adaptation diminishes to the stressing situations and to the infections. Deceleration of anabolic processes causes diminishing of volume of muscles.

Insufficiency of mineralocorticoides causes *the increased loss of sodium, dehydratation ,* diminishing of volume of circulatory blood (the loss of a 1 mmole sodium with urine conduces to the selection 6,5-8,5 ml of water, the additional loss of water on days can make on 300-850 ml). Diminishing of maintenance of sodium in the walls of arterioles reduces pressor activity of other vasoactive matters (noradrenalin and other). The decline of maintenance of sodium in plasma draws the decline of osmolality, *diminishing of volume of circulatory blood that also conduces to the decline of arteriotony.*

Insufficiency of testoids causes the parafunction sexual glands, worsens anabolic processes. Combination of these violations with *dehydratation,* diminishing of maintenance of hepatin in muscles, hypogenesis and atrophy of muscles conduces to the making progress loss of mass of body. Diminishing of synthesis of mineralocorticoides and glucocorticoides, and also testoids results in the parafunctions, hepato-biliar systems, ect.

Clinical displays

Patients, as a rule, can not define time of beginning of disease and specify on a constantly making progress general and muscular weakness that increases to the end of day.

1. Arterial blood pressure low appears in 88-90% patients and is one of early displays of chronic adrenal insufficiency. Diastolic and systolic pressure goes down - to 80/60 mm Hg and below. In special cases diastolic pressure can be in a norm. At presence of concomitant hypertensive disease or at patients after a bilateral adrenalectomy on an occasion Cushing's disease there is the normal or enhanceable arteriotony. Regardless of size of arteriotony patients have *an orthostatic hypotension* (Shellong's symptom).

Violation of all types of exchange causes deep dystrophic changes in myocardium, retractive ability of myocardium goes down here. Tachycardia. A pulse is soft, small.

The decline of indents voltage, decline of S-T interval, lengthening of P-Q, Q-T interval, expansion of QRS complex *on ECG.*

2. Psychical asthenisation is the expressed general weakness, indisposition, rapid fatigueability, apathy, loss of interest to life, depressed reactions. Together with it possible episodes of enhanceable crabbiness up to development of psychosis. An intellectual capacity, memory, capacity, goes down for concentration of attention. Nightly sleep does not bring the improvement of feel. Patients can not conduct the normal way of life, even the usual loadings are exhausting for them. During the expressed decompensation patients can not in the morning get up from a bed.

The attacks of leucopenia develop as a result of decline of secretion of cortisone, diminishing of gluconeogenesis, exhaustion of supplies of hepatin in a liver. A leucopenia appears as the attacks, which are characterized by a sharp weakness, crabbiness, psychotic reactions, feeling of hunger. Such attacks usually develop in the morning on empty a stomach or after the protracted interruption between a meal.

Psychical and emotional violations are conditioned by frequent glucopenias and high level of ACTH. Corticoid therapy normalizes the function and transferred symptoms diminish straight proportionally to normalization of level of cortisole in blood

3. Physical asthenisation is muscular weakness. Muscular force and volume of muscles goes down, the dystrophic changes develop in myofibrils. Dyselectrolyte violation, dehydration, low arterial blood pressure, and decline of formation of albumen and hepatin in muscles, diminishing of formation of macro ergs in tissue and decline of oxygen utilization by tissue, are the reason of dynamic and asthenia.

The decline of mass of body appears next to a general weakness. That takes place both due to dehydration and as a result of decline of appetite and joining of vomit. Mass of body goes down as a result of sharp oppression of anabolic processes with diminishing of amount of muscular tissue and loss of liquid. Speed of process can be different.

4. Hyperpigmentation of skin

A melanoderma is the specific symptom of primary defeat of adrenal glands, a symptom is never observed at the second insufficiency of adrenal glands. Very rarely a polychromia is absent at primary adrenal insufficiency is "white"Addisonismus.

Accumulation of melanin pigment foremost takes place on the opened parts of body, in the places of friction of clothes, on palms' lines, operation scars, on the mucuses shells of cavity of mouth, in the region of the anal opening and areolas of nipples, on external privy parts. A diffuse polychromia develops afterwards. The expressed of melanoderma correlates with grade of adrenal insufficiency is strengthening of expressed of melanoderma is an unfavorable prognostic sign precursor of development of Addison's crisis.

5. Abdominal syndrome is decline of appetite up to anorexia are the dystrophic changes of mucus shell of stomach draw the decline of pepsin and salt acid, often there are the displays of hypoacid gastritis.

In the period of decomposition of disease stomach-aches appear without clear localization, nausea, vomit, constipations which alternate with diarrhea, by the conditioned enhanceable secretion of chloride of sodium in the road clearance of intestine. Vomit and diarrhea strengthen the loss of sodium and result in development of sharp insufficiency of adrenal glands. The ulcerous disease of stomach and duodenum, colitis.

6. A nycturia is one of frequent symptoms of chronic insufficiency of adrenal glands.

Classification

On clinical motion:

1 – typical form is sharp weakness, fatigue ability, dynamic, anorexia, dyspepsia phenomena, hyper pigmentation.

2 –atypical forms:

а) mineral;

б)pigmentless;

в) diencephal, hypophysis- and other.

On the degree of weight:

Easy form (the feel is satisfactory, a capacity is stored, a systematic hormontherapy is not needed, enough dietary correction is addition of kitchen salt, limitation of products with high maintenance of potassium, and also reception of ascorbic acid);

Middle form (for achievement of clinical effect, renewal of the broken exchanges processes, diminishing of pigmentation and dynamic, normalization of arteriotony and mass of body, renewal of capacity, necessary hormontherapy);

Heavy form - Addison's crisis in anamnesis; a clinical effect is achieved only by permanent hormontherapy by glucorticoides in combination with mineralocorticoides.

Additional researches

The clinical blood test – anaemia, often difficult genesis, relative lymphocytosis is possible, sometimes leucopenia.

Biochemical researches – decline a level of glucose in a blood on empty stomach. During the leadthrough tolerance to insulin is the expressed falling of level of glucose in a blood.

Violation of balance of electrolytes. The deficit of glucorticoides and mineralocorticoides is the reason of surplus selection of sodium with urine, and the level of him in a blood goes down to 110 mmol/l, chlorides - below 98,4 mmol/l, and concentration of potassium is higher 5 mmol/l. Enhanceable coefficient of Na/K.

Sometimes enhanceable maintenance of calcium in a whey to 4,2 mmol/l. Absorption of calcium in an intestine and his exit from bones is increased. Normalization of calcium exchange takes place at adequate therapy.

There are the kidney parafunctions: speed of glomerular filtration and kidney blood stream goes down, the level of kreatinine rises in the whey of blood.

Typicalhypoalbuminaemia, sometimes alsohypoproteinaemia.

Violation of hormonal background.

The concentration of ACTH increases at primary insufficiency of adrenal glands and maintenance goes down ACTH at the second insufficiency. Day's rhythm of secretion is violated ACTH is high level and in the morning, and in the evening.

If level of corticosteroids in the blood taken in 8-10 o'clock morning, less than 170 nmole/l (6 mkg/100 ml), the diagnosis of insufficiency of adrenal glands does not cause doubting. Concentration goes down in the blood of cortizole, corticosterone, aldosterone.

The secretion of 17-OCS and 17-CS goes down with urine.

For more certain represents the functional state of adrenal glands leadthrough of stimulants tests.

1. Brief test with ACTH After determination of fluorogenic corticosteroids or cortizole level in plasma of blood intramuscular or intravenously inject 0,25 мg of synthetic ACTH. Through 30 min. concentration of corticosteroids is explored again. If the function adrenal gland cortex is not broken, is observed no less than double increase of corticosteroids in the blood of inspected. A negative test (there is no increase of maintenance of hormones in a blood) testifies to the decline of adrenal glands function. Test with synacthen it is expedient to connect with treatment by prednizolon, as he does not interfere with determination of fluorogenic cortizole.

2. Protracted stimulant test with ACTH characterizes potential backlogs of adrenal glands cortex, is used for differential diagnostics of primary and second insufficiency of adrenal glands. Enter preparation of the prolonged action of synacten-depot (1 mg) parenterally (intramuscular). Through 1, 4, 8 and 24 h after introduction of synacten-depot determines the level of corticosteroids in plasma of blood. At primary insufficiency of adrenal glands in all tests the level of cortizole will be low. At the second insufficiency through 4 h. the level of cortizole rises to 700 nmol/l (25 mkg/100 ml) and higher. In order to avoid sharp insufficiency of adrenal glands this test needs to be conducted, not breaking therapy by prednizolon.

At suspicion on acute insufficiency of adrenal glands to the patient simultaneously with introduction of synacten begin infusion of prednizolone solution (30-60 мг) and periodically 1 time per hour explore concentration of fluorogenic cortizole in blood. If through 4-6 h. she remains low, it is possible to talk about insufficiency of adrenal glands.

3. Test with lyzine-vasopressine. Execute intravenous infusion 4 IU lyzine-vasopressine during 2th hours. In a norm the level of corticosteroids of blood must rise in 3-3,5 times in comparison with initial one. Test contra-indicated at ischemic heart trouble.

4. Insulin-tolerance test. 0,1 IU of simple insulin are injecting in a dose on 1 kg of mass of body. Method of implementation of test and his interpretation similar to the test with ACTH. Insulin test contra-indicated to the persons with ischemic heart trouble, epilepsy, to the patients with the initial low level of fluorogenic corticosteroids in a blood (below 170 nmol/l).

For diagnostics of hypoaldosteronism determination of concentration of aldosteron is conducted in plasma of blood or his excretion with urine. For more certain, than one-moment determination of alsdosterone level, to estimate his balance in an organism allow pharmacodynamical tests.

5. Test with angiotenzine. 0,5 mg *angiotenzine* at 50-100 ml of isotonic sodium chloride solution or glucose inject intravenously during 50-60 min under the permanent control of arteriotony. Absence of aldosterone concentration increase at the end of infusion specifies on hypoaldosteronism.

6. A test with a низькосольовою diet is used for the exposure of the hidden insufficiency of secretion of aldosterone. Determination of aldosterone shows at primary chronic insufficiency of adrenal , that the level of aldosterone in blood can be in a norm, while maintenance of renin is enhanceable in connection with the decline of volume of plasma.

Visualization of adrenal glands.

Computer tomography, angiography, ultrasound echography, radioisotope scan-out, allows to define the topographical changes of adrenal glands and character of pathological process that caused their functional inferiority. X-ray-gramm of region of kidneys allows on occasion to discover a calciphylaxis in the region of adrenal glands .

Sometimes apply the transdermal aspiration biopsy of adrenal glands .

Change on EKG are conditioned by metabolic and electrolytes violations. The high-peak sharp indent of T appears usually. Possible deceleration of atrio-ventricular or intraventricular conductivity.

Immunological researches

Found out the specific marker of "autoimmune adrenalitis" are antibodies to the adrenal enzyme of 21-hydroxylasa (P450c21). Characteristic high titles of antibodies to the antigens of adrenal glands, violation of indexes of cellular immunity at autoimmune character of process.

Differential diagnostics must be conducted between primary and second insufficiency of adrenal glands, and also with the diseases, which are characterized by a hyperpigmentation, arterial hypotony and gastroenteric disorders.

A polychromia can be the inherited, national or caused individual sensitiveness to the sunbeams. She is observed also at a pellagra, dermatomyositis, at the metastases of melanoma, cirrhosises of liver, hemochromatosis, at the protracted use of preparations, which contain arsenic, silver, gold, bismuth.

A hemochromatosis is characterized by absence of polychromia on mucuses shells and characteristic by the presence of pigmental cirrhosis of liver and saccharine diabetes, grey-brown pigmentation of skin.

Porphyry is also accompanied by generall brown pigmentation, however characteristic presence of plenty of uroporfirine in plasma, urine and excrement.

Poisonings by salts of heavy metals (arsenic, zinc, lead, mercury and other) can be accompanied by pigmentation of skin and gums, but pigmentation of mucuses shells is absent.

Local pigmentation meets at an ulcerous colitis, cirrhosis of liver, melanosarcoma, acanthosis nigricans, neurofibromatosis.

At pellagra on pigmented areas skins which on extremities have the appearance of socks and gloves, the signs of dermatitis appear. In addition, at this disease constantly there is diarrhoea and dementia .

With arterial hypotony differential diagnosis is simple and conducted by laboratory tests.

Anorexia and gastroenteric disorders meets at the diseases of organs of digestion, pregnancy, nephrite, nervous breakdown.

Treatment

At hypocorticism a diet must be high-calorie, to contain enough albumens, enhance able amount of kitchen salt (8-10 g on a day) and vitamins, especially ascorbic acid.

I. Liquidation of causal factors which caused the disease of adrenal glands .

II. Substitute hormonotherapy.

Patients with primary chronic insufficiency of adrenal glands need permanent reception of corticosteroids. In most patients for complete indemnification enough introduction only glucocorticoids; on occasion necessary additional setting mineralocorticoids.

Hydrocortisone (cortisone) is preparation of choice and is appointed for 30 mg on a day (20 mg in the morning and 10 mg in the evening). *Cortisone* is usually used in a dose 40-50 mg (25 mg in the morning and 12-15 mg in the evening). Other synthetic glucocorticoids (prednisolone, dexametasone and other) is less wished, as they do not find out mineralcorticoid action.

At the easy degree of chronic adrenal insufficiency cortisone is used in a dose 12,5-25 mg on a day in combination with ascorbic acid for 1,0-1,5 g on a day during a meal.

At middle and heavy forms of chronic adrenal insufficiency additionally to glucocorticoids appoint mineralcorticoids, average daily necessity at a desoxycorticosterone acetate is 1 mg. *DOCSA* (desoxycorticosterone of acetate) in pills (5 mg) applies sub lingua, intramuscular appoint 1ml of the 0,5% oily solution; *a fluohydrocortisone* (cortinef, fluorinef) is applied for 0,05-0,1 mg one time on a day in the period of subindemnification and 2-3 times per a day in the period of disease decompensation.

The objective criteria of effective action of glucocorticoids are: increase of mass of body, disappearance or diminishing of dyspepsia, diminishing of skin and mucuses shells pigmentation, improvement of tolerance to glucose.

After **the adrenalectomy on an** occasion Cushing`s disease hormonal preparations are not appointed, after the delete of second adrenal gland in the first days apply 75-100 mg hydrocortisone intravenously and simultaneously intramuscular on a chart: 1-2th day - 50-75 mg every 3 hours, 3-th day - 50 mg every 4-5 hours, 4-5th day - for 50 mg every 5 hours, 6-7th day - 50 mg in 8 hours, 9-10th day - 50 mg 2 times per a day. From 8-9th day pass to the peroral use of corticosteroids, prednisolone is appointed for 5-10 mg on days, either 5 mg in the morning in combination with a 1 pill of DOCSA or a 1 pill of cortinef and 25 mg cortisone in the second half of day.

At operations, traumas, infections, stresses the dose of gluco- and mineralcorticoids is increased in 2-3 times in comparison with a supporting dose. At appearance of dyspepsia replace the peroral use of gluco- and mineralcorticoids parenterally. Surgical interference at patients with chronic insufficiency of adrenal glands conduct on condition of intravenous introduction of hydrocortisone (100-200 mg

depending on the type of operation). During the first 3-4th days of post operation period enter hydrocortisone also parenterally, and then gradually pass to the ordinary doses of preparations of substitute therapy.

Patients can not be engaged in hard physical work. The use of alcohol, reception of barbiturates, use of alkaline mineral waters is forbidden. Patients must know that any stressing state (infection, physical or mental overstrain and other) requires the increase of glucocorticoides reception. At appearance of weakness, indisposition, increase of temperature, stomach-aches, diarrhoea and other signs of worsening of the state it is necessary immediate to appeal for medical help.

ACUTE INSUFFICIENCY OF ADRENAL GLANDS

Sharp insufficiency of наднирків is a syndrome, that develops as a result of fall-off or complete exception of adrenal glands cortex function .

Etiology

1. Waterhouse-Frederickson's syndrome is primary acute insufficiency of adrenal glands cortex.

Waterhouse-Frederickson's syndrome, as well as primary chronic insufficiency of adrenal glands cortex, is related to destruction of their cortex.

Acute insufficiency of adrenal glands complicates some systems diseases (knot periarteritis and other). Presence in these terms of hemorrhage in adrenal glands or their acute ischemia conditioned by the thrombosis of central vein of adrenal glands by either (extraordinarily rarely) a thrombosis in arterial vessels of adrenal glands.

2. Addison's crisis is acute decompensation of primary chronic insufficiency of adrenal glands (Addison's disease).

Acute insufficiency of adrenal gland cortex can be complication of primary or second chronic insufficiency at inadequate hormontherapy, decline the dose of glucocorticosteroids. By factors which provoke Addison's crisis, there can be stressing situations: acute infections, intoxications, operations, pregnancy.

Addison's crisis develops gradually, during a few days. At latent chronic insufficiency of adrenal glands crises arise up on a background stresses. Precursors of crisis: asthenisation of patient, loss of weight, growths of polychromia and blood pressure low, pains in joints and muscles.

3. Bilateral adrenalectomy on an occasion Cushing's disease, glucorticosteroma.

Acute insufficiency of adrenal glands after a bilateral adrenalectomy develops as a result of inadequate therapy by corticosteroids or in the case of the use of contra-indicated preparations, which accelerate disintegration of corticosteroids in a liver.

4. Innate aplasia of adrenal glands.

Acute insufficiency of adrenal glands, related to innate violation of the enzymic systems in adrenal glands or with the change of sensitiveness to ACTH , usually develops in child's or early child's age.

Debre-Fiebiger`s Syndrome *is* the innate form of hyperplasia of adrenal gland cortex, this form related to the enzymic defect of hydroxylating of steroid ring in position 21. The deficit of glucocorticosteroids and mineralcorticoids, that is accompanied by the expressed metabolic (mainly electrolytes) violations, develops at this disease.

Shepard`s syndrome develops on 2th year of life and is characterized by the inferior secretory reaction of adrenal glands on endogenous stimulation ACTH, this is innate adrenal areactivity. Clinically syndrome shows up asthenisation, dermatomelasma, muscular weakness and adynamia. A syndrome is the rare pathology.

5. Metastases of tumor in adrenal glands.

6. Disfunction of adrenal gland cortex at the stressing states.

7. Syndrome of abolition on background of the protracted corticosteroid therapy.

8. Disease of hypothalamic-hypophisar region with a deficit of ACTH: hypopituitar syndrome, Schmidt`s syndrome, Simonds` syndrome, state after radial therapy of hypophysis, at Cushing`s syndrome, prolactinoma.

9. Disease of CNS: brain tumors, craniopharyngeoma, meningitis, encephalitis, eyeing nerve glyoma.

10. Adrenogenital syndrome.

11. Isolated insufficiency of aldosterone secretion.

Pathogeny

Acute deficit of glucocorticoids, mineralcorticoids.

1. The decline of cortisole concentration:

1) decline of adaptation of organism;

2) violation of all types of metabolism:

а) deceleration of gluconeogenesis from albumens and fats, glucopenia;

б) decline of albumens utilization;

в) decline of hepatin concentration in a liver and muscles.

2. The decline of aldosteron level draws:

1) decline of sodium reabsorbtion in kidneys with the increase of sodium and chloride loss with urine;

2) deceleration of chloride and sodium suction through an intestine

Heavy dehydratation develops. The volume of circulatory plasma goes down, shock develops.

Electrolyte balance is violated:

а) hypochloremia with incessant vomit, diarrhea;

б) delay of K in an organism with the increase of maintenance in cells, intercellular liquid blood with the decline of retractive ability of myocardium.

Clinical displays

Nausea, vomit, acute muscular weakness, high temperature, cardiac disorders, diarrhoea, abdominal syndrome and violation of psyche, is the most characteristic clinical signs of Addison's crisis.

1. The diseases of the nervous system is hallucinations, delirium, coma, paresthesias, violation of deep and superficial sensitiveness**.**

Clonic cramps are caused by heavy dehydratation.

Meningeal symptoms are formed in case of edema of brain.

Acrocyanosis, hyperhydrosis, hyperthermia, some abdominal and psychical symptoms is related to the increase of simpatico-adrenal system activity.

2. Disease of cardiac system

The expressed decline of arteriotony is the leading clinical symptom of acute insufficiency of adrenal glands.

Blood pressure low more frequent in all carries character of collapse or *shock, that is resistant* to standard countr-schock therapy, is not removed by catecholamins, that testifies to absence of their deficit even at a total adrenalectomy.

Acute cardiac insufficiency shows up a small, soft pulse, deafness of heart tones, diminishing of heart sizes.

On ECG: decline of voltage, ST below from isoline, T negative or diphasic, deceleration of conductivity of myocardium – lengthening of intervals PQ, QRS.

3. The gastroenteric diseases are nausea, incessant vomit, diarrhoea, great pains in a stomach, diminishing of peristaltic noises, symptoms of peritoneum irritation.

Abdominal pains, that simulate an acute stomach, can be caused by the spasms of muscles, peristalsis (intestinal colic).

Smell of acetone from a mouth is possible.

4. Disfunction of kidneys

Decline of glomerular filtration with accumulation of urea, remaining nitrogen.

5. Total dehydratation

There is the decline of turgor of skin and ophthalmotonus.

Hyperthermia of central genesis is also possible.

Clinical variants of acute adrenal insufficiency:

1.Cardiac.

A collapse, cardiac insufficiency. Cyanosys, hypothermia, deafness of tones, pulse of the weak filling.

2. Gastroenteric.

Nausea, vomit, quite often incessant vomit, diarrhoea, stomach-aches, symptomatic of "acute stomach".

3. nervous-psychical.

The edema of brain develops: adynamia, asthenia, depression, delirium with visual hallucinations. Possible meningeal symptoms, epileptic cramps. DOCSA removes the cramps effectively.

Syndrome develops quickly, for a few hours, runs across with lightning speed. Features of clinical displays of *Waterhouse-Frederickson's syndrome* syndrome: head pains, cramps, hyperthermia, dehydratation. Pains in a stomach. Cyanosys, heavy collapse with falling of temperature, edema of lights.

Laboratory confirmation of diagnosis

Glucopenia.

Possible increase of maintenance of ketonic bodies.

Violation of electrolyte balance:

1*) hyperpotassiumaemia (more than 5 mmol/l);*

2) hyposodiumemia (less than 140 mmol/l);

3) hypochlorinemia (less than 90 mmol/l);

correlation of Na/K exceeds 20.

Increase of urea concentration, remaining nitrogen.

Acidosis, decline of blood alkaline reserve.

Signs of haemoconcentration on the haemogramm : increase of haemoglobin, leucocytosis, eosinophilia.

In urine: acetone, proteinuria, cylindruria, leucocytosis, microhaematuria.

Treatment

1. Gluco- and mineralcorticoids substitute therapy.

After establishment the diagnosis of acute adrenal insufficiency massive corticosteroid therapy is a basic medical measure. Mainly use preparations of hydrocortisone, necessary by the method of intravenous infusion.

At first immediately one-moment inject in the vein 100 *mg hydrocortisone.*

For a day long intravenously inject additionally to 300-400-600 mg hydrocortisone together with infusion of isotonic sodium chloride solution and 5% solution of glucose.

Simultaneously with intravenous introduction the corticosteroids desired intramuscular injection of hydrocortisone acetate (for creation of stable muscular depot). At first inject 50-100mg, then repeat the injections every 4-6 hours 50-75 mg hydrocortisone.

At the adrenal coma day's dose of corticosteroids rises to 800-1500 mg. DOCSA enters hypodermic in a dose 2-4 ml, then - 1 мл 1 time per a day under the arteriotony control.

Additionally to infusion of cortisone it is recommended to inject mineralocorticoids. *DOCSA* inject hypodermic 1 мл a 0,5% oily solution, the injections repeat with an interval 4-6 hours. At uneffectiveness of measures with of out of control hypotony intravenously inject dopamin - 80 mg in 400 ml in 5% solution of glucose at a speed of 15-50 drops pro minute.

2. Removal of dehydratation and glucopenia.

In combination with a hormonotherapy the intravenous infusion therapy directed on correction of present violations of water-electrolyte, carbohydrate and proteometabolism is conducted.

In the first time the volume of intravenous infusions makes 3-4 l, during the first 2 hours inject to the 2th litres of solutions.

Use the isotonic solution of sodium chloride, solution of Ringer, 5% solution of glucose for the removal glucopenias and other solutions for correction of water-electrolytes violations.

3. Renewal of electrolyte balance.

It follows to pay the special attention to adequate correction under the careful laboratory control of electrolytes violations, as at sharp insufficiency of adrenal glands there is hyperpotassiumaemia very dangerous as a result of enhanceable sensitiveness of myocardium to surplus of potassium and propensity to development of heavy violations of excitability and conductivity, up to fibrillation of ventricles. Necessary monitoring on ECG.

Recommend to drink the added some salt water (10 g on 1l.). Possible intravenous infusion 20-30 ml a 10% solution of sodium chloride.

For the removal of hyperpotassiumaemia intravenously inject 30-40 ml a 40% glucose and 20 ml 10% solution of calcium gluconatis, at an insufficient effect - 30 ml of 10% solution sodium chloride.

4. Infusion of blood-substitute solutions. 200 мл 20% solution of albumen, 400 мл fresh-frozen or native plasma, ect. The volume correlation of the transferred solutions depends on the dynamics of clinical status and information of laboratory control.

From the 2th day of treatment the necessary amount of liquid is entered peroral. Day's dose of cortisone here goes down to 100-150 mg, and on a 3th day – to 50-75 mg, preparations inject intramuscular. In this period, if mineralcorticoid action of the indicated doses of cortisone appears insufficient, it follows to add hormones actually mineralcorticoid action (DOCA, 3-methyl-DOCA) or fluohydrocortisone (cortinef, fluorinef) in a dose 0,05-0,2 mg on a day.

Etiotropic treatment - it is directionally on the removal of adrenal insufficiency reason (antitoxic, countr-schock, haemostatic, antibiotic therapy, ect.). Symptomatic treatment consists in setting of analeptical, sedative, vitamins and other preparations.

PRIMARY ALDOSTERONISM (Konn`s syndrome)

In 1955 Konn described a syndrome, that is characterized by high arterial blood pressure and decline of level of potassium in the whey of blood, development of which is related to aldosteronoma.

A primary hyperaldosteronism more frequent meets at adults, more frequent are ill women (correlation 3:1) in age 30-40 years. Among children is the frequency of disease at girls and boys identical.

Basic ethiopathogenic, clinic variants of primary hyperaldosteronism.

1. Aldosteroma (Konn`s syndrome) - aldosteroneproducting tumor of adrenal glands (70% cases of primary hyperaldosteronism). Aldosteroneproducting adenoma adrenal cortex, as a rule, one-sided. Plural and bilateral adenomas meet exceptionally rarely. The cancer of adrenal glands as the reason of aldosteronism meets also infrequently - 0,7-1,2%. At presence of adenoma the biosynthesis of aldosterone does not depend on a secretion ACTH.

2. Bilateral hyperplasia of adrenal glands (30% cases) or plural *adenomatosis of adrenal cortex*(15%):

а) idiopatic hyperaldosteronism (hyperproducts of aldosterone, that is not repressed);

б) indefinite hyperaldosteronism (hyperproducts of aldosterone, that is preferentially repressed);

в) hyperaldosteronism, that is full repressed by glucocorticoids.

3. Aldosteroneproducting *adenoma, that is full repressed by glucocorticoids.*

4. Adrenal glands cortex carcinoma.

5. Extraadrenal hyperaldosteronism (tumor of ovaries, intestine, thyreoidal gland).

Malignant tumours are 2-6% all cases.

Clinical displays

1. Arterial hypertension.

A proof hypertension is sometimes accompanied by great head pains in the area of forehead. The hypertension is stable, but the presence of paroxysm is possible. Malignant hypertension is observed very rarely.

The hypertension *is irresponsive on the orthostatic loading*, resistant to the Valsalva test.

2. "Caliopenic kidney"

Almost in all cases primary aldosteronism is accompanied by hypopotassiumaemia as a result of surplus loss of potassium by kidneys under action of aldosterone. The deficit of potassium causes forming of « *Caliopenic kidney». The epithelium* of distal departments *of kidney tubulis is struck,* that in combination with a general hypopotassiumaemic alkalosis draws violation of mechanisms of oxidization and concentration of urine.

On the initial stages of disease kidney violations can be insignificant.

1) *polyuria* mainly nightly, 4 l arrives on days, *nycturia* (70% patients). Polyuria at a primary hyperaldosteronism is not repressed by preparations of vasopressine, does not diminish at limitation of liquid reception.

2) Characteristic *hypoisosthenuria* - 1008-1012.

3) Possible is a *moderate proteinuria.*

4) *Reaction of urine more frequent alkaline*.

Thirst, polydipsia develop as reaction on polyuria. Polydipsia and polyuria in a night-time next to the other displays (weakness, paresthesias, attacks of myoplegia) are the obligatory components of hypopotassiumaemic syndrome. Polydipsia has central genesis (hypopotassiumaemia stimulates the center of thirst) and reflex genesis (in connection with accumulation of sodium in cells).

Edematous not characteristic - only by 3% patients with the concomitant disease of kidneys or insufficiency of blood circulation.

3. Disease of muscles

Muscular weakness, periodic attacks of cramps of different intensity. Positive symptoms of Khvosteck and Trousseaux.

Characteristic paresthesias in different muscular groups.

4. Changes in the central and peripheral nervous system

A general weakness appears in 20% patients.

Head pains are observed in 50% patients, have intensive character is conditioned by the increase of arterial pressure and overhydratation of cerebrum.

5. Violation of carbohydrate exchange.

Hypopotassiumaemia represses the secretion of insulin, assists to development of tolerance to the carbonhydratess (60 % patients).

Additional diagnostic tests

1. Hypopotassiumaemia

Enhanceable excretion of potassium with urine (in a norm 30 mmol/l).

2. Hypersodiumaemia

3. Violation of hormonal background

The level of aldosterone in a blood more frequent is enhanceable at a norm 2-16 ng/100 ml to 50 ng/100 ml. Enhanceable concentration in the blood of aldosterone metabolits.

Enhanceable excretion of aldosterone with urine.

The mionectic unstimulated activity of renin in plasma is the cardinal symptom of primary hyperaldosteronism. The secretion of renin is repressed by a hypervolemia. In healthy maintenance of renin in a blood at horizontal position - 0,2-2,7 ng/ml/h.

Criterion of diagnosis of syndrome of primary hyperaldosteronism is *combination of small activity of rennin in plasma with hyperaldosteronaemia.* Differentially-diagnostic criterion from the secondary hyperaldosteronism at renovascular hypertension, chronic kidney insufficiency, to malignant arterial blood pressure high, when the level of renin and aldosterone is enhanceable.

4. Functional tests

1. Loading by sodium 10 g/daily during 3-5 days. At practically healthy persons with the normal adjusting of secretion of aldosterone the level of potassium of whey of blood will remain without the changes. At primary aldosteronism maintenance of potassium in the whey of blood fall to 3-3,5 mmol/l, the excretion of potassium is sharply multiplied with urine, the state of patient gets worse (acute muscular weakness, violation of cardiac rhythm).

2. 3th daily diet with low maintenance of sodium: the level of renin remains unchanging, the level of aldosterone can even go down.

3. Test with lasix. Before the leadthrough of test a patient must be on a diet with normal maintenance of chloride of sodium (about 6 g on days), within a week to get no hypotensions preparation. During the leadthrough of test a patient get inward 80 mg of lasix and during 3 h. walks. Through 3 h. takes a blood for determination of level of renin and aldosterone. At primary aldosteronism there is the considerable increase of level of aldosterone and decline of concentration of renin in plasma of blood.

4. Test with capothenum (captoprilum). In the morning at a patient is taking a blood for determination of maintenance of aldosterone and renine in plasma. Then a patient get inward 25 mg of

capothenum and during 2 h at him again is taking a blood for determination of maintenance of aldosterone and renin . At patients with primary aldosteronism the concentration of aldosterone is enhanceable, relation of aldosterone/renine activity more than 50.

5. Spironolactone test. A patient is on a diet with normal maintenance of chloride of sodium (6 g on days) and during 3 days gets the antagonist of aldosterone verospirone 100 mg 4 times per a day. On a 4th day in the whey of blood determine maintenance of potassium, and increase of its level of blood more than on 1 mmol/l in comparison with an initial level is confirmation of development of hypopotassiumaemia as a result of surplus of aldosterone. The level of aldosterone and renine in blood remains unchanging. Arterial hypertension is removed.

6. Test with no-aldosterone mineralcorticoids. A patient becomes 400 mcg of fluorcortisoleacetate during 3 days or 10 mg of desoxycorticosteroneacetate during 12 h. Level of aldosterone in the whey of blood and excretion of its metabolits with urine at primary aldosteronism does not change, while at the second hyperaldosteronism – diminishes considerably. In special cases there is some decline of level of aldosterone in a blood also at patients with aldosteroma.

7. Test with DOCSA. Appoint DOCSA for 10-20 mg/day during 3 days. At patients the level of aldosterone goes down with the second hyperaldosteronism, at the Konn`s syndrome - no. The level of glucocorticoids and testoids is normal.

8. Orthostatic test (walking during 4th hours). The level of aldosterone goes down paradoxically.

6. Topic diagnostics of adrenal function disease

Adenoms-aldosteroms have small sizes, at 80% patients less than 3 см in a diameter, more frequent is dislocated in left adrenal gland.

1. Computer tomography is the most informing research with a high sensitiveness. At 90% patients tumours appear 5-10 мм in diameter.

2. Scan-out of adrenal glands with I-^{131}-iodine-cholesterole on the background braking of glucorticoids function by dexamethasone (0,5 mg every 4 hours during 4th days). Characteristic asymmetry of adrenal glands. Sensitiveness - 85%.

3. Cannulation of adrenal veins with the researching of blood tests and determination at them level of aldosterone. A research sensitiveness rises after previous stimulation of adenoma by synthetic ACTH - the producing of aldosterone rises on the side of tumor sharply. Research sensitiveness - 90%.

4. X-ray-contrast venography of adrenal glands has test-sensitivity 60%: vascularisation of tumor is insignificant, sizes small.

5. Echography of adrenal glands.

6. X-ray-adrenalography in the conditions of pneumoperitoneum, combined with an intravenous urography or without it. Method informing is only for large tumours, more frequent false-negative results.

Differential diagnostics

1. Secondary aldosteronism are the states at which enhanceable formation of aldosterone is related to the protracted stimulation of his secretion by angiotensine II. For the secondary aldosteronism characteristic increase of level of renin, angiotensine and aldosterone in plasma of blood. Activation of the renin-angiotensine system takes place as a result of diminishing of effective volume of blood at the simultaneous increase of negative balance of sodium chloride. It develops at a nephrotic syndrome, cirrhosis of liver in combination with a hydroperitoneum, idiopatic edemata, which often meet at women in the period of premenopause, cardiac insufficiency, kidney acidosis.

2. Burther`s syndrome: hyperplasia and hypertrophy of juxtaglomerular vehicle of buds with a hyperaldosteronism. The surplus loss of potassium at this syndrome is related to the changes in ascending part of kidney tubulis and primary defect in the transport of chlorides. It is characterized midgetness, delay of mental development, presence of hypopotassiumaemic alkalosis.

3. T*umours, which product renin* (primary reninism), including the tumour of Williams (nephroblastoma) – the secondary aldosteronism runs across with a hypertension. Malignant hypertension with the disease of renal vessels and retina often unites with the increase of secretion of renin and secondary aldosteronism. The increase of renin formation is related to development of necrotizing arteriolitis. A hyperaldosteronism and hypertensions disappears after a nephrectomy.

4. *The protracted reception of tyazid diuretics* for treatmen of arterial hypertension lead to the secondary aldosteronism. That is why determination of rennin and aldosterone level in plasma of blood it is necessary to conduct only in 3 weeks or later after abolition of diuretics.

5. *Protracted reception of contraceptives* which contain estrogen, lead to the development of arterial hypertension, to the increase of renin level in plasma of blood and the secondary aldosteronism. The increase of formation of renin is here related to direct influence of estrogen on the liver and increase of synthesis of albuminous substrate –angiotensinogen.

6. *Pseudomineralcorticoid hypertension syndrome* is accompanied by hypertension, decline of rennin and aldosterone maintenance in plasma of blood.

7. *Syndrome of Liddle* is the inherited disease that is accompanied by enhance able reabsorbtion of Na in kidney tubulis with subsequent development of hypertension, the decline of K-, renin and aldosterone concentation in blood.

8. *The reception or surplus formation of desoxycorticosterone* in an organism results to the delay of sodium, surplus excretion of potassium and hypertension.

9. *Hypertonic disease* with low concentration of renin in plasma of blood is 20-25% all patients which suffer by this disease. Application of steroidogenesis inhibitors at patients with hypertension with low maintenance of renin resulted to normalization of arteriotony, while at patients with hypertension with normal maintenance of renin such treatment was uneffective.

Treatment

A diet is recommended with limitation of kitchen salt.

Aldosteronoms are subjects to surgical treatment - an one-sided adrenalectomy or adenomectomy is recommend. Obligatory preoperational preparation by the antagonists of aldosterone (verospirone and other). Preoperational therapy allows to normalize the arteriotony, pick up thread concentration of potassium in an organism, to normalize the renin-angiotensine-aldosterone system the function of which is repressed at this disease.

At primary aldosteronism in combination with bilateral *hyperplasia of adrenal cortex* rotined bilateral total adrenalectomy with subsequent vicar therapy by glucocorticoids. For the prophylaxis of acute adrenal insufficiency after the operation, especially in the case of bilateral adrenalectomy, necessary proper therapy by glucorticoids.

At *the patent with idiopatic hyperaldosteronism* give advantage of spironolactone to the therapy and only in a case of its uneffectiveness, is recommend the surgical treatment. At patients with idiopatic hyperplasia of adrenal cortex moreover spironolactone is amyloridum recommended, also 10-20 mg on a day, lasix. The additional use of the calcium canals blocators (adalat) gives the positive influencing by oppression of secretion of aldosterone and direct dilatating influence on arteriols.

Preparations of choice are *the antagonists of aldosterone* (verospirone, aldactone), which lock the peripheral effects of aldosterone. Systematic use high doses - 200-400 mg/day. Verospirone and other antagonists of aldosterone owns antitestoid properties and in cause of protracting their application at men develops hynaecomastia and impotence which is often observed at the doses of verospirone over 100 mg on a day and duration of the use more than 3 months.

Additionally appoint preparations of potassium, while monotherapy is not effective.

Dexamehtasone-dependend form of hyperaldosteronism does not require operative treatment, and, as a rule, the therapy by dexamethasone in a dose 0,75-1 mg on a day results to proof normalization of arteriotony, exchange of potassium and secretion of aldosterone.

FEOCHROMOCITOMA

Feochromocitoma (Feochromaffinoma, feochromoblastoma, chromaffinoma) is tumour from the cells of chromaffin tissue that secretes the surplus amount of catecholamins or other bioactive matters. Histological the tumor consists of cerebral layer cell of adrenal glands, which are painted by salts of chrome (chromos) in a brown-brown color (phaios) as a result of oxidization of catecholamins which are in the granules of cytosole.

Clinical displays

A clinical picture is conditioned by the surplus secretion of catecholamins. Hypertension, hypermetabolism and hyperglycaemia are the basic symptoms of disease.

The clinical displays of disease are very varied, feochromacitoma is the "chameleon"-disease.

Clinical variants:

1) *Paroxysmal (crisis) form* - in the period of crisis there is the acute increase of arteriotony with its normalization in a period between the attacks;

2) *permanent form* (without crisis, stable) - flows without crisis with a stably high arterial hypertension;

3) *mixed form* (stable with crises) - is characterized by the permanent increase of arterial blood pressure, which is the background for crises developing;

4) "*mute" tumors (*appear at the section at patients, that died on other reason, did not have hypertension, ect.).

I. Paroxysmal form of feochromocitoma

1. Arterial hypertension

Arterial pressure rises during a few seconds, measuring up 200 мм and anymore, to 300-350 мм. Typical very acute increase systolic and diastolic arterial pressure, quite often on a few minutes. Very rarely crisis develops on a background hypo- or normotony. Characteristic is the acute headache, already during the first attack possible development of stroke.

Reliable signs of feochromocitoma: young age of patient, duration of hypertension to 2th, years, paradoxical reaction of arteriotony on application of ganglioplegics.

2. Cardiac syndrome

Often take place *pains in a region hearts, tachycardia,* shortness of breath. Hypercatecholamineaemia, hypertony cause heavy changes in myocardium - on ECG tachycardia, violations of rhythm, ischemic-metabolic changes up to not-coronarogenic necrosises. Quite often symptomatic reminds the heart attack of myocardium – decline of segment of ST, negative T or high coronal T. Violations of rhythm appear at a day's monitoring - tachycardia, ventricular extrasystoles, migration of rhythm driver.

3. An abdominal syndrome is the variant of clinical display of catecholamine crisis. The symptomatic of "acute stomach" – pains in an abdominal region without clear localization, unconnected with character and time of meal, nausea, vomit. Possible is also the easy dyspepsia, declining of appetite, constipations. Most frequent variant are pains in epigastrium.

4. Neurovegetative syndrome

The typical expressed vegetative reaction is an abundant sweat, feeling of fear, expressed internal disturbance, nausea, sudden pallor of skin. In the moment of crisis in a peripheral blood there is a hyperglycaemia, neutrophilic leucocytosis.

5. The symptoms of hypermetabolism and violation of carbohydrate exchange are conditioned by surplus of secretion of adrenalin, which activates a glycogenolysis in a liver and muscles, brakes glucopenia action of insulin, stimulates lipolyze in fat tissue.

At patients with feochromocitoma are often the violations of tolerance to the carbonhydratess. Saccharine diabetes develops in 10% cases, in halves from them is insulin-depended diabetes (catecholamins repress the secretion of insulin).

The displays of hypermetabolism (enhanced basic exchange, tachycardia, diarrhoea) are unconnected with violation of the thyreoidea gland functions.

Catecholamine crisis at pheochromocitoma arises up suddenly, symptomatic is opened out very quickly. Crises more frequent develop spontaneously, possible provoking factors: change of position of body, physical or emotional overstrain, palpation of abdominal region, invasive researches, extraction of tooth, operation, trauma, reception of alcohol or medications (histamin or some anaesthetics). Palpation of abdominal region under the control of blood pressure as a diagnostic test is not practiced - there can be heavy crises.

Crisis appears *by a headache, disturbance, feeling of fear, crabbiness,, shortness of breath, nausea, vomit, stomach-ache*. Crisis can be the reason of death which comes as a result of hemorrhage in a brain, fibrillation of ventricles or acute cardiac insufficiency with the edema of lights.

The attack is halted similarly suddenly and quickly, as well as begins. The blood pressure goes back to initial sizes or even becomes below than them. The pallor of skinning covers will be replaced by hyperaemia. To 5 l. of light urine is selected with relative low-density. After the attack patients mark a somnolence, "wave of warm wave" to extremities, a general weakness is saved long time.

Catecholamine crisis is accompanied by a hyperglycaemia. In the period of crisis there is leucocytosis 1,0-3,0x10^6 with eosinophilia and lymphocytosis.

Catecholamine *shock* is the most heavy complication of feochromocitoma, develops by 10% patients, conditioned by the sudden change of sensitiveness of adrenoreceptors and violation of mechanisms of catecholamins inactivation. Except the basic symptoms of catecholamine crisis, the new state develops – this is ”*syndrome of out o thecontrol hemodynamics": frequent and disorderly change of episodes of hyper- and hypotension which badly or in general are not subject to therapeutic correction*. A tendency to the hypotension is the precursor of lethal result, is not removed by presor amines, steroids, cardiac glucozides and other counter-shock measures. Treatment: conservative (α-adrenoplegics) and surgical by uneffectiveness of medicinal therapy during 3-4 hours.

II. Permanent form of feochromocitoma

The clinical displays are polymorphic, often does not differ from arterial hypertension of other genesis. Proof hypertension without crises is the very rare phenomenon.

1. Cardiac syndrome

Pains in the region of heart, arrhythmia. Accent the second tone above an aorta. Changes of ECG: hypertrophia of the left ventricle, diffuse dystrophic changes. The changes of eyeground, cardiomegalia, coronar insufficiency, are developing quickly.

2. Neurovegetative syndrome

Headache, paresthesias. Expressed emotional weakness, feeling of death fear. Crabbiness, decline of memory, are developing afterwards. But the vegetative displays are absent quite often.

3. Abdominal syndrome

Pain in an epigastrium, nausea, periodic vomit, salivation or dryness in a mouth, diarrhoea or constipation. Reduction of tolerance to the carbonhydratess or obvious saccharine diabetes. Absence of typical crises make the diagnostics of feochromocitoma difficult.

III. Mixed form of feochromocitoma

On a background of permanent hypertension periodically there are characteristic crises.

Additional researches

Change of hormonal background.

The table of contents of catecholamins in plasma of healthy is 100-500 ng/l, at feochromocitoma their level rises to 800-1000 ng/l, and in the period of catecholamine crisis rises in 20-30 times. During the leadthrough of provocative tests concentration of catecholamins in plasma is multiplied in 5-15 times.

Increase of excretion with urine catecholamins and their metabolites –metadrenaline and metnoradrenaline. In a norm for days is selected with urine to 100 mcg of catecholamins (15-17 mcg is on adrenalin, 65-68 mcg – on a noradrenalin). In the period of attack the excretion of catecholamins exceeds 200 mcg after 24 h. Especially model comparison of concenrtation of catecholamins in portions of the urine collected to the attack, and their level in portion of the urine collected after the attack. Level of catecholamins and their metabolites rises very intensive.

The use *of* high-efficiency *chromatography* for determination of general catecholamins and their factions in urine is a sensible and specific test for diagnostics offeochromocitoma. At the use of this method in 95% cases of disease it is succeeded to find out the hypersecretion of catecholamins.

Catecholamine crisis is often accompanied by a hyperglycaemia and neutrophilic leycocytosis of peripheral blood.

Chromogranine frees oneself from the cerebral layer of adrenal glands and sympathic neuronal granules together with catecholamins. Chromogranine-A is also the marker of neuroendocrine tumors. Simultaneous determination of catecholamins and Chromogranine-A in the whey of blood rises the specificity of method to 95%, exactness – to 88% and positive prognosis of diagnosis – to 91%. The level of Chromogranine-A in the whey of blood is considerably increased at patients with feochromocitoma, while at patients with essential hypertension it can a little exceed its concentration at practically healthy persons.

2. Functional tests. The realizing of the special tests helps correct diagnostics of disease.

A. Provocation tests are used at the paroxysmal form of hypertension, at initial blood pressure not higher than 160 мм. Provocative tests do not have high specificity. Can cause heavy crises with heavy complications - fibrillation of ventricles, hemorrhage in a brain, edema of lights, heart attack of myocardium, that is why realize them in the conditions of hospital, at presence of means of the first aid: in case of occurring of heavy crisis injects tropaphenum.

Test with a histamin. To the patient, that is in horizontal position, realize the blood pressure measure, then injects intravenously 0,1 ml of 1% solution of histamin at a 5 ml of isotonic solution of sodium chloride. Measure the blood pressure every minute during 15 min. In the first 30 sec. after injection of histamin the arteriotony can go down, but in future it increases. Increase of numbers on 60/40 мм. in relation to initial numbers during first ones 4 min after injection of histamin specifies in the presence offeochromocitoma.

In the case of surplus increase of blood pressure a patient must become α-adrenoplegics phentolamine or tropaphenum (histamine-tropaphenum test).

Test with a tyramine. It is conducted in those terms, what test with a histamin. Injection 1 mg of tyramine intravenously and increase during 2 min systolic pressure on 20 мм. allows to suspect the presence of feochromocitoma.

Test with glucagone. It is conducted on empty stomach and in those terms: 0,5 or 1 мг of glucagone are injecting intravenously, the blood pressure is measured by each 30 sec during 10 min. Results of test the same, as by injection of histamine and tyramine.

Б. Curative tests are conducted at permanent hypertension and blood pressure not below than 160/110 мм

Test with clofeline. By the patient is entering in a vein a catheter and through 30 min takes a blood for determination of amount of noradrenalin and catecholamins in plasma. Then a patient accepts inward 0,3 mg of clopheline and through 3 h is blood again for determination of concentration of the indicated hormones explores. At patients with feochromocitoma maintenance of hormones in plasma of blood after the reception of clofeline does not change, while at patients with essential hypertension the level of noradrenalin goes down to the norm and even below.

Clofeline-glucagone test. To and through 3 h after the reception of clopheline from a calculation 0,3 mg/kg take a blood for determination of concentration in plasma of adrenalin, noradrenalin, dophamine, DOPHA, dihydrooxyphenylglicole. After it is injected 1мg of glucagone and in 2 minutes again take a blood for determination of level of catecholamins in plasma. Clonidinum reduces concentration of noradrenalin, while glucagone promotes concentration of noradrenalin in plasma of blood.

Test with a α-*adrenoplegics* phentolamine or tropaphenum. Conduct in those terms, what test with a histamin. Inject intravenously 5-10 mg phentolamine (1 ml 1% solution) or tropaphenum. Criterion of positive test is rapid decline of arterial blood pressure during 1-2 min no less than on 70/40 мм. in comparison with initial one, that allows to suspect the presence of feochromocitoma. It follows to take into account that after application α-adrenoplegics possible development of orthostatic collapse, that is why after the leadthrough of test patients must lie during 1,5-2 h.

4. Topical diagnostics is establishment of localization of tumor.

А. Visualisation of adrenal glands.

Computer tomography is method of choice in diagnostics of all tumours of adrenal glands. Exactness of diagnostics - 90-100%. Sizes are set tumours, its closeness, structure, correlation, with neighbouring organs vessels.

The method of magnetically-nuclear resonance has alike descriptions.

A Excretor urography allows to find only out the indirect signs of large tumor is considerable displacement of kidney, declining of ureter.

Suprarenography in the conditions of oxyretroperitoneum is informing in 60-80% cases.

Tomography of retroperitoneal space in the conditions of pneumoperitoneum: parasacral in an extraperitoneal cellulose injects to a 1500-3000 $см^3$ oxygen or nitrous oxide. Through 45 min executes tomography of adrenal region. A method allows to visualisate tumors more than 2 см in a diameter, informing 80%.

An aortography allows to find out the tumors of largenesses 3-4 см with good vascularisation. The image of tumor on angiograms goes out in 70% cases.

Veincavography, especially selective veingraphy of adrenal veins, has a greater sensitiveness.

The ultrasound scan-out (echography) is the method of scrinning inspection, uninvasive. A research sensitiveness is not very much high. Difficulties arise up at the expressed obesity small sizes of tumor.

Б. Research of extraadrenal tumors represents most difficulties for diagnostics. The program of inspection includes a cystoscopy, x-ray-inspection of organs of pectoral cavity.

Aortography, selective arteriography of adrenal arteries is most littleinforming as a result of low vascularisation of tumors.

The radioisotope scan-out with methylbenzylguanidine, trofic to chromaffin tissue, allows to find out all variants of paragangliomas and remote metastases.

Computer tomography is high-informing, but possible false-negative results at tumors which do not get in a tomographic "cut".

An echography is not invasive, but tumors do not appear by size to 2 см and metastases.

Treatment

At a catecholamine crisis parenterally injection of phentolamine is recommended for 2-4 mg each 5-10 min to liquidation of crisis. Possible positive effect and from the use of sodium nitroprusside. If achieved objective, adrenoplegics in the same dose continues to enter each 2 or 4 h (depending on the dynamics of pressure) during days. Then pass to the peroral setting of adrenolytics, which do not abolish to operation. To that end rotined application of α-adrenoplegics receptors for 20-40 mg on a day, and also prazozyne (minipres) for 2-5 мg 2-3 times per a day or labetolol for 200-600 mg 2 times per a day under the control the arteriotony.

β-adrenoplegics (propranolol, inderal, anaprilinum) is indicated at heavy tachycardia, especially if she is accompanied by arrhythmia. The peroral dose of inderal is 40-60 mg on a day. Application of *β-adrenoplegics* is possible only after introduction of α-adrenoplegics.

a-Methylparathyrozine in a dose 1-2 g on a day results in diminishing of tumor, decline of level of catecholamins in plasma and excretion them with urine, to normalization of arteriotony. It is recommended to begin treatment with a dose 250 mg every 6 hours, then a dose is multiplied on 250-500 mg on a day, sometimes to 4 g on days.

Establishment of diagnosis of feochromocitoma is absolute testimony for operation. Relative contra-indications for operation: acute violations of cerebral or coronal circulation of blood, expressed cardiac insufficiency kidney insufficiency, to the removal or diminishing of violations. At presence of remote metastases, to impossibility of complete radical oncotomy conduct palliative operations - delete basic part of tumor, that facilitates achievement of medicinal correction. Radical operation results in complete convalescence in most patients.

Preparation to operation: α-adrenoplegics (tropaphenum, phentolamine) and *β-adrenoplegics* (anaprilinum) under the control of blood pressure. The protracted application of these preparations is practiced only at inoperable tumors or presence of remote metastases.

At patients the delete of feochromocitoma is planned in which, risk of development of catecholamine crisis during operation it is possible to decrease by pre-operation preparation. In the last 3 days before operation daily conduct infuion of phenoxybenzamines (0,5 mg on 1 kg of mass of body of patient on 250 ml 5% solution of glucose during 2 h.). After the first infusion appoint anaprilinum 40 mg 1-2 times per a day. If hypertension is moderate, infuion of phenoxybenzamines can be replaced by the reception of that preparation inward for 10-15 mg 3-4 times per a day. The dose of anaprilinum remains the same. Phenoxybenzamine contra-indicated to the patients with feochromocitoma, in which took place the hypotensions states.

If as a result of the described conservative therapy of catecholamine crises during 2-3 h is not removed, it follows to resort to urgent surgical operation. After the feochromocitomectomy the blood pressure is quickly normalized.

CUSHING`S SYNDROME

***Cushing`s syndrome* is** the hypercorticoidism, conditioned by the primary tumour of adrenal cortex, that products glucocorticosteroids (glucocorticosteroma). More frequent in all glucocorticosteroms is localized in adrenal glands, sometimes in other organs (lights, bronchial tubes, pancreas ect.).

Clinical picture

1. Obesity

2. Arterial hypertension

3.Kidney diseases: glomerulonephritis with albumenuria and hematuria

4. The skinning changes are a hyperkeratinization, trophic violations.

5. steroid myopathy

6. Osteoporosis of spine, "fish vertebrae"

7. Violation of calcium exchange

8. Violation of carbohydrate exchange

Violations of tolerance to the carbonhydratess find in 50-90% out patients. The steroid diabetes caused by surplus of glucocorticoides is observed in 10-20% patients, differs by resistance to insulin, by the very rare exposure of ketoacidosis and it is comparative is easily regulated by a diet and setting of biguanids.

9.Involution of lymphoid tissue

Corticosteroids represses specific immunity, that results in development of the second immunodeficit and to formation of trophic ulcers, abscesses defeats of skin, chronic pyelonephritis. High risk of joining of sepsis.

10. sexual function disease: at children is early appearance of the second sexual signs, at women is amenorrhea, hypotrophy of uterus and milk glands.

11. Psycho-emotional violations

Astheno-dynamical syndrome: crabbiness, worsening of memory, decline of interest to circumferential, propensity to depression. Characteristic hypochondrias states. Sleep is violated. There can be the epileptiform attacks, psychoses.

12. Inclination to thromboses.

Diagnostics

Change of hormonal background. *The level of cortisone in the whey of blood is enhance able in 5-7 times* at the use of highly sensitive methods of research. Normal level in the whey of blood for children in more senior 1 year and adults on 7-9th a morning o'clock is made by 250 - 650 nmol/l.

Diminished concentration of corticotropine. Normal level in the whey of blood ACTH at adults in the morning at 8 o'clock - 5,5-24,6 nmol/l, in the evening in 18 – 0,2-6,0 nmol/l.

17-ketosteroids (17-KS) of urine is the androstan steroid hormones of adrenal cortex and products of exchange of testosterone. At men about 2/3 common amounts of 17-KS act with adrenal glands and 1/3 - from testicles. At women practically fully adrenal glands is the source of 17-KS, only wretched amount act from ovaries. At a hypercorticoidism maintenance of 17-KS can be enhanceable or normal.

The secretion of metabolites androgen-reactive ketosteroids rises considerably – etiocholanolone, dehydroepiandrosterone, androsterone. The coefficient of etiocholanolone /androsterone is multiplied.

Functional tests

Stimulants functional tests foresee introduction of pharmacological preparations, which stimulate adrenal glands –synacthen, corticotropine, metopyrone. After introduction of one of stimulator determine the change of level of blood cortizole or 17-OKS in urine. At a Cushing`s syndrome the level of cortizole and 17-OKC does not change are "deaf" adrenal glands, a tumor products hormones in the own rate.

Functional test, that repress the products of endogenous corticosteroids is test with dexamethasone (for 2 mg every 6 hours during two days. At the Cushing`s syndrome products of hormones by a tumor remain unchanging (test negative).

Visualization of adrenal glands disease

It is used ultrasound scan-out of adrenal glands or radioisotope scan-out with a cholesterol. Roentgenologic researches of adrenal glands - angiography, computer tomography are applied.

Hyperplasia of one adrenal gland appears at the Cushing`s syndrome, that is staggered by a tumor, and scray atrophy of the second adrenal gland. During the separate cannulation of adrenal veins concentration of hormones in a right and left vein will be different.

Angiography is the most informing *differentially-diagnostic test* with the selective drawning of blood from the adrenal veins for determination of maintenance at them cortizole. At second bilateral adrenal hyperplasia the concentrations of cortizone in the blood of adrenal veins is enhanceable on either side, *at tumours* – considerably enhanceable on the side of tumour and normal from an opposite side.

Differential diagnosis

*Cushing`s disease* on the clinical displays does not differ from the Cushing`s syndrome . Roentgenologic and radioisotopes methods allow to define a microadenoma in the region of sella turcica.

ANDROSTEROMA

Hormonal-active tumor of adrenal glands, that produce masculine sexual hormones. Androsteroma is localized in adrenal glands. In 60% of cases the tumour become malignant and have metastases. Arise up in young age and at children (more frequent at girls).

Clinic

1. *Anabolic effect*: strengthening of development of muscles, acceleration process of growth. Hyperandrogenia–low growth, short extremities, masculine type of body, atrophy of pectoral glands, amenorrhea, appearance of moustaches and beard.
2. *Virile syndrome*: at girls are the second sexual signs on a heterosexual type (making progress to the trichauxis, increase of clitoris, becoming rough of voice). The origin of androsteroma at women causes the making progress defemination. Patients acquire masculine phenotype, a clitoris is multiplied, voice is gruff; at boys is premature sexual development on a isosexual type.
3. Arterial hypertension.
4. Violation of carbohydrate exchange.
5. Dysplastic obesity.

Diagnostics

The acute increase of level of 17-KS in urine is the typical symptom of hormonal-active tumour of adrenal glands. The one-sided tumour of adrenal glands concernes at instrumental researches.

Treatment

Operative treatment with next steroid substitute therapy.

After operative intervention from malignant tumours, for a prophylaxis and treatment of metastases, at inoperable tumours the inhibitor of adrenal cortex –chloditane is used (2-4 g on days during 3-4 months). Preparation locks the synthesis of cortizone, reduces the secretion of testoids and does not influence on the products of mineralcorticoids.

ADRENOGENITAL SYNDROME

Congenital virilizing hyperplasia of adrenal glands, or adrenogenital syndrome, is the most widespread form of virilizing diseases. It is observed mainly at women.

Clinical displays

The clinical displays of adrenogenital syndrome are conditioned by the degree of blockade of the fermentative systems, which take part in the synthesis of cortizone is complete or incomplete block. Three clinical forms of a congenital disease develop at a complete block: *1) simple virilizing (congenital); 2) salt-losing; 3) hypertension*. At the incomplete block of the enzymic systems possible different clinical variants are varieties of simple virilizing form.

1. The simple virilizing *form* of adrenogenital syndrome is a congenital pathology, conditioned by the incomplete, genetically determined fermentative block, most widespread form of adrenogenital syndrome.

2. The salt-losing form of a congenital adrenogenital syndrome is accompanied by virilization and violation of water-salt exchange, caused by the expressed insufficiency of C-21-hydroxy. The synthesis of aldosteron goes down next to violation of synthesis of cortizole. The defect of the fermentative system appears on the stage of transformation of progesterone to a 11-desoxycorticosterone.

3. The hypertensive variant of adrenogenital syndrome is characterized by combination of virilism and arterial blood pressure high, delay of sodium and chlorides. Insufficiency of C-11-hydroxylasa in the organism of patient results in the hyperproducts of 11-desoxycortisole and considerable surplus of 11-desoxycorticosterone, that are expressed mineralcorticoid characteristics. The selection is thus sharply multiplied with urine of 11-desoxycortisole and ketopregnandiole.

Depending on the period of life, when the disease demonstrated, select the next forms of simple virilizing hyperplasia of adrenal glands.

A. Pubertat forms of adrenogenital syndrome

Conditioned *by the incomplete defect of the fermentative system* (deficit of C-21-hydroxylasa), the disease appears only in the period of the sexual ripening. In a pubertate period the deficit of hormonal backlogs of cortizole appears in an organism. The clinical displays of hypocortcism at this variant are absent. Before the sexual ripening an organism develops normally - outwardly patients have the expressed womanish signs sufficiently. But at anthropometric researches there are the signs *of masculinization of skeleton* is some increase of width of shoulders. External privy parts are usually changed little - there is only small hypertrophy of clitoris.

With beginning of the sexual ripening basic signs appear the diseases caused by the hyperproducts of testoids: *hypomenstrual syndrome*, that often carries anovulatory character, possible second ary amenorrhea. Characteristic primary fruitlessness.

As far as suppression of function of own gonade *there* is *the syndrome of defenemination*: subsequent development of milk glands is halted, *the symptoms of masculinization* appear. *Obesity* joins often.

Diagnostics

Excretion of 17-KS with urine is enhanceable, level of 17-OKS within the limits of norm (exhaustion of backlogs of glucocorticoid function of adrenal cortex is incomplete).

The differentially-diagnostic value has *the* large and small *test of oppression of adrenal cortex by glucorticoids.* More frequent during the leadthrough of dexamethasone test , that finds out most expressed braking influence on the selection ACTH is used. As a result of reception of dexamethasone quickly and considerably the selection goes down with urine not only total 17-KS but also androsterone, dehydroepiandrosterone and pregnandiole.

The expressed of androgenisation at this form of adrenogenital syndrome not always answers the egestions of 17-KS with urine. The degree of virilization depends on the increase of level of testosterone in a blood, egestions with urine in the surplus amount of metabolites 17-pregnenoldione and progesterone , that is why determination of testosterone in a blood and progesterone in urine acquires the diagnostic value.

By radioimmunological methods determine a level ACTH blood.

The excretion of estrogen with urine is usually enhanceable, but idle forms prevail physiological - oestrone and oestriole.

Б. Adrenogenital syndrome at adults

The first displays after completion of pubertate is hirsutism, hipooligomenorrhea, second fruitlessness, structure of privy parts and development of milk glands are normal.. Characteristic feature of adrenogenital syndrome adults have the hidden cortical insufficiency with general weakness, head and muscular pain, the hypotension in combination with the signs of vegetative-vascular dystonia.

Diagnostics

Although the level of excretion of 17-OKS can remain within the limits of norm, *reserves possibilities of adrenal cortex during the leadthrough of functional tests with ACTH (synacthen) are decrease.* By the dexamethasone test it is possible to specify the source of hyperproducts of testoids. At roentgenologic research of uterus, ovaries and adrenal glands substantial declining does not discover.

The level of 17-KS in urine at a congenital adrenogenital syndrome on the average even 140 mkmol/day (in healthy 33+5 mkmol/day), DEA - 22 mkmol/day (in healthy 2,4+1,0 mkmol/day), pregnandiole - 40 mkmol/day (in healthy 3,3+1,0 mkmol/day), pregnantriole - 60 mkmol/day (in healthy 1,6+0,3 mkmol/day), testosterone - 170 (nmol/day in healthy 21+2 mkmol/day). The selection of androsterone in three times exceeded a norm (in healthy 13 mkmol/day). Excretion of neutral 17-KS and products of metabolism of steroid hormones at the pubertat form of adrenogenital syndrome and adrenogenital syndrome of adults changed in 2 times and less, than at a simple virilizing form.

Differential diagnosis

Paratherapeutic androgenisation: the anomaly of organogeny sexual in new-born can be conditioned by the reception by a mother during pregnancy of testosterone, estrogens or progesterone. In subsequent the symptoms of virilisation do not make progress.

Androsteroma draws forming of virile syndrome at the children of senior age or at adults. The origin of androsteroma at women causes the making progress defeminisation.

The sharp increase of level of 17-KS in urine is the typical symptom of hormonal-active tumor of adrenmal glands. The one-sided tumour of adrenal glands concernes at instrumental researches.

Corticoandrosteroma causes forming of virile syndrome and premature sexual and somatic development, as there is the enhanceable secretion of both testoids and glucorticoids.

The tumours of adrenal cortex differ by a "noninteraction" is synthesis by them hormones is not controlled ACTH, that is why suppression of adenocorticoid function of hypophysis by exogenous of glucocorticoids does not result in the decline a steroidogenesis of tumour: dexamethasone test is negative.

The virilization tumours of ovaries are eliminated at gynaecological research, pelviography, leadthrough of the combined tests.

Treatment

Setting of glucocorticoids reduces products ACTH by a hypophysis and represses the secretion of testoids of adrenal glands, that is accompanied by regression of symptoms of virilisation: the second womanish sexual signs are formed, menstruations appear, milk glands and other signs of womanish phenotype develop.

Sexual development of boys also concernes sometimes to beginning of treatment. If the reception of glucocorticoids is begun with 3-4th, sexual development meets age-old standards. The Days' doses *of prednizolone* concerne by age of patients (1-3 years - 5 mg, 4-6 years - 5-7 mg, 7-14 years - 7-10mg, 15-18 years - 10-15 mg). At the innate forms of adrenogenital syndrome adopt prednizolone *for the term of life*, as even brief abolition of preparation causes renewal of displays of disease. In the case of joining of intercurrent disease multiply the dose of glucocorticoids. Treatments conduct under the control blood pressure, growth, "bone age" level of egestion of corticoids.

At the salt-losing form of adrenogenital syndrome also necessary use the mineralcorticoids - *desoxycorticosterone* for 5 mg on days. With the increase of age of patient possible indemnification only by prednizolone and sodium.diet In case of occurring of adrenal crisis the dose of preparations and salts solutions is multiplied.

Treatment of congenital forms of adrenogenital syndrome can include and implementation *of plastic operations* on forming of external privy parts.

Control of initial level of knowledges

1. The diagnosis of insufficiency of 21-hydroxylasa at a patient with a adrenogenital syndrome is confirmed by all indicated indexes, except:

   A. Increase the excretion of 17 CS with urine;
   B. Increase the level of 11-desoxycorticosterone in plasma;
   C. Increase the level of 17-hydroxyprogesterone in plasma;
   D. Increase the level of androstendione in plasma;
   E. Increase the excretion with urine of pregnandiol and pregnantriol

2. From transferred measures transfer those which are not necessary for the patient with Addison's crisis :
   A. Infusion the isotonic solution of sodium chloride;
   B. Infusion the hypotonic solution of sodium chloride;
   C. Infusion the solution of glucose

3. During the leadthrough of substitute therapy at hypocorticism what time is it better to appoint the evening reception of glucocorticosteroids?
   A. Before sleeping;
   B. in the evening;
   C. till 18.00

4. From the resulted clinical signs of hyporeninaemic hypoaldosteronism is not characteristic:
   A. hyperpotassiumaemia;
   B. Muscular weakness;
   C. Diseases of cardiac rhythm;
   D. Muscle cramps;
   E. Signs of kidney insufficiency

5. How does the secretion of aldosterone change at patients with a hypercorticoidism?
   A. Rises;
   B. Goes down;
   C. Stay within the limits of norm

6. What day's dose of dexametasone does use for the leadthrough of "small" dexametasone test for diagnostics of Cushing`s syndrome?
   A. 1 mg
   B. 2 mg
   C. 4 mg
   D. 8 mg
   E. 16 mg

7. The Konn`s syndrome is characteristic:
   A. oliguria;
   B. polyuria;
   C. Pollackiuria
   D. Nicturia

8. What level of active renin in plasma at the second hyperaldosteronism?
   A. increased;
   B. depressed;
   C. Stay without the changes

9. At presence of androsteroma at boys arises up:
   A. real isosexual premature sexual ripening;
   B. unreal isosexual premature sexual ripening;
   C. Unreal heterosexual sexual ripening

10. What preparations are contra-indicated at treatment of Addison's disease?
   A. prednisolone;
   B. DOCSA;
   C. ACTH;
   D. dexametasone

Endocrinology (initial level of knowledges)

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

Control of eventual level of knowledges

1. The low doses of adrenalin cause the following changes in the function of the cardiac system, except :
   A. Increase the minute volume of heart;
   B. Reduce peripheral resistance of vessels;
   C. Increase peripheral resistance of vessels;
   D. Activate β-receptors of vessels and heart

2. What action do catecholamins toward the exchange of carbonhydratess?
   A. activation of hepatin synthesis;
   B. activation of gluconeogenesis;
   C. activation of glucose metabolism intissues;
   D. activation of glucose transport

3. How do catecholamins influence on the exchange of lipids?
   A. Stimulate synthesis of fat acids;
   B. Activate processes of lipogenesis;
   C. Stimulate processes of adipocitis differentiation;
   D. Stimulate lipolise in fat tissue

4. How do catecholamins influence on the exchange of sodium in an organism?
   A. increase the excretion;
   B. Reduce the reabsorbtion;
   C. Increase the reabsorbtion;
   D. does not influence on exchange of sodium

5. How do catecholamins influence on the exchange of calcium in an organism?
   A. increase the level of calcium in plasma of blood;
   B. Reduce the level of calcium in plasma of blood;
   C. increase excretion of calcium with urine;
   D. Does not influence on exchange of calcium

6. What medicinal preparation is not used in treatment of feochromocitoma?
   A. Ganglioplegics;
   B. α-adrenoplegics;
   C. β- adrenoplegics;
   D. Chloditane

7. What electrolytes of blood and in what direction does change during the leadthrough of test with spironolactone at diagnostics of Konn`s syndrome?
   A. increase the level of sodium;
   B. Reduce the level of potassium;
   C. Increase the level of potassium;
   D. reduce the level of sodium

8. What differences in the level of hormones distinguish primary hypocorticism from the second?
   A. Низький level of glucocorticoids and the normal level of mineralcorticoids;
   B. Низький level of gluco- and mineralcorticoids;
   C. Normal level of glucocorticoids and mineralcorticoids

9. How will the level of aldosterone change in reply to loading by the chloride of sodium at presence of Konn`s syndrome?
   A. reduce to 50% and below;
   B. Will rise;

C. stay without the changes;
D. reduce less than on 50%

10. What from complications of metabolic character is often observed after the **delete** of feochromacitoma?
A. Lipidemia;
B. Violation the balance of electrolytes;
C. Glucopenia;
D. level of calcium in the whey of blood
E. Change the level of potassium in a blood

Endocrinology (eventual level of knowledges)

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

Situational tasks

1.A man, 36 years old, is ill 1-1.5 years. Complaints: expressed weakness, bad appetite, nausea. Became thin for 1 year on 10 kg. The skin of face, neck, overhead extremities is dark. Considerable pigmentation of skin folds, nipples. Pulse – 60/min. Arterial pressure 80/50 мм. Previous diagnosis ?
A. Chronicgastritis.
B. Cushing's disease .
C. Diabetes mellitus.
D. Chronic hepatitis.
E. Insufficiency of glands.

2. A woman, 42 years old. Complaints: periodic squeezing pain in the region of heart, expressed weakness at proximal muscles on extremities and cramp, pain in the back of head. Growth 176 см, mass of body is 80 kg. The scopes of heart are displaced to the left. EKG: sine rhythm, obliquely-descending decline of ST segment. Pulse – 92/min. Arterial pressure is 190/100 мм. Polyuria, nycturia with isosthenuria. Hyporeninaemia. Potassium – 2,8 mmol/l. What is the credible diagnosis?
A. primary aldosteronism.
B. hyperparathyreoidism.
C. essential hypertension.
D. feochromocitoma
E. Cushing's syndrome

3. A boy 7 years is hospitalized with the complaints of parents about speed-up physical and premature sexual development. After the inspection the diagnosis of aadrenogenital syndrome, virile form is set. What is appointed for substitute therapy?
A. prednisolon
B. fluorinef
C. cortinef
D. DOCSA
E. Vitamins A, E

4. A man, 32 years old, complains for a year about a weakness in muscles, thirst, polyuria, and headache. Growth is 180 см, mass of body – 76 kg, ps – 76/min, arterial blood pressure – 170/105 mmHg Skin of ordinary color. The edemata are absent. Hypopotassiumaemia, hypernatremia, hypochloraemia. Relative density of urine – 1007, reaction alkaline, proteinuria – 0,033 g/l. Diagnosis?
A.Konn`s syndrome.
B. Hyperparathyreosis.
C. Glomerulonephritis.
Д. Cushing`s syndrome.

5. A woman, 27 years old, with the satisfactorily compensated saccharine diabetes of type 1, complains about frequent glucopenias, nausea, disorders of intestine, arterial blood pressure diminished to 80/50 mm. Anaemia, НЬ-105 g/l. What can predefine the decline of pressure?
A. Diabetic enteropathy
B. Diabetic gastropathy
C. Chronic insufficiency of adrenal glands
D. Overdose of antidiabetic preparations
E. Unsaccharine diabetes

6. A man 28 years old complains about pain in a lumbar area with an irradiation in a left leg. Objectively: growth is 186 cm, weight is 92 kg. Arterial pressure -. 170/100 мм. Pulse - 84/min. It is present purple striae on a stomach and thighs. On a R-gram: osteoporosis, compression break of L-IV . In a blood: Er – 5.5 x 1012/l, НЬ -190 g/l, leuc - 9x10 $^{12л.}$ Calcium -3,3 mmol/l. What most credible reason of break?
A. Constitutional obesity
B. Trauma
C. Polycitaemia
D. Primary hyperparathyroidism
E. Cushing`s syndrome

7. Brothers 7 and 5 years old , hospitalized in connection with the complaints of parents about speed-up physical and premature sexual development. After the inspection a diagnosis is set: adrenogenital syndrome, virile form. What preparation does appoint?
A. DOCSA
B. Fluorinef
C. Cortinef
D. Prednisolone
E. Vitamins A, E

8. Woman 39 years old, complains about headache, weakness and paresthesias in extremities, polyuria. Objectively: tones of heart are muffled, ps - 94/min., arterial pressure- 105/90мм. Glucose of blood 5,5 mmol/l, sodium of plasma - 148 g/l, potassium of plasma - 2,7 mmol/l. relative density - 1012, albumen is reaction alkaline, leuc - 3-4. The most credible diagnosis:
A. Hypertonic disease
B.Amyloidosis
C. Diabetes mellitus
D . Chronic glomerulonephritis
E. Primary hyperaldosteronism

9. Endocrinologist was quickly caused to the urology clinic to sick, 46 years old, which was hospitalized with the attack of kidney colic**.** During the instrumental inspection a patient lost consciousness. The arterial blood pressure went down to 40/20 мм. In anamnesis the protracted (6 years) reception of glucocorticoids in connection with a pseudorheumatism. Halted the reception of glucocorticoids 3 days ago. Objectively: tones of heart deaf, pulse - 100/min., weak filling, rhythmic. Lights and organs of abdominal region without features. Diagnosis?
A. Addison's crisis

B. Adrenogenital syndrome
C. Acute adrenal insufficiency
D. Cushing's syndrome
E. Allergic shock

10. A woman, 32 years old, is ill 8 month and complains about a weakness in muscles, periodic cramps, attacks of acute general weakness, polyuria, nycturia. Tones of heart are muffled, accent II of tone above an aorta, arterial pressure is 170/100 мм. In a blood: potassium - 3,0 mmol/l, glucose - 5,3 mmol/l. In the general analysis of urine: alkalireaction of urine, albumen - 0,066 g/l, leuc - 3-5, hipoisosthenuria. Diagnosis?
A. Primary hyperaldosteronism
B. Hypertonic disease
C. Chronic pyelonephritis
D. Cushing's syndrome
E. Feochromocitoma

FAITHFUL ANSWERS

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

Controls questions

1. Acute insufficiency of adrenal glands cortex: ethiopatogeny, clinic and treatment.
2. Chronic insufficiency of adrenal glands cortex: etiology, pathogeny.
3. Classification of chronic insufficiency of adrenal glands cortex.
4. Basic diagnostic signs of Addison's disease
5. Differential diagnostics of Addison's disease .
6. Differential diagnostics of primary and secondary hypocorticism.
7. Treatment of chronic insufficiency of adrenal glands cortex.
8. Addison's crisis: ethiopathogeny, clinic, treatment.
9. Corticosteroma: pathogenic, clinical displays, treatment.
10. Laboratory diagnostics of Cushing's syndrome.
11. Differential diagnostics of Cushing's syndrome and its treatment.
12. Konn`s syndrome, determination. Basic diagnostic signs.
13. Primary aldosteronism: differential diagnostics and treatment.
14. Androsteroma: determinations, basic diagnostic criteria.
15. Differential diagnostics and treatment of Andre streams.
16. Feochromacitoma: determination, classification.
17. Basic diagnostic signs of feochromacitoma.
18. Differential diagnostics and treatment of feochromacitoma.
19. Adrenal genital syndrome, ethno pathogen, classification.
20. Basic diagnostic signs of adrenal genital syndrome.
21. Differential diagnostics and treatment of adrenal genital syndrome.

Practical tasks

- to select main complaints at a patient, related to the diseases of adrenal glands;
- to determine the possible etiologic factors of disease;
- to find out the presence of violations of internals and systems of organism, related to violation of the functional state of adrenal glands;

- to interpret right the information of additional researches (hormonal, roentgen logic and radiological);
- to realize inspection of this patient;
- to be able to prepare right biological material for hormonal research;
- to conduct differential diagnostics of this disease;
- to ground a diagnosis;
- to realize treatment of this patient;
- if necessary to set the plan of treatment to operation, in a period and after her;
- to determine a possible prognosis;
- to write recipes on hormonal preparations of adrenal glands.

Protocol of the clinical examination of the patient

Name, surname of the patient_____
Age_____ **Profession**_____

Complaints of the patient_____
_____
_____
_____
_____
_____

Anamnesis morbi
_____
_____
_____
_____
_____
_____

Last exacerbation_____
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_____

Anamnesis morbi
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Results of the physical examination:
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Preliminary diagnosis:
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Plan of investigation:

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Results of the additional methods of investigations:

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Rationale of the clinical diagnosis:

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Clinical diagnosis:
Main disease

_____
_____
_____

Accompanying disease

_____
_____
_____

Complications_____
_____
_____
_____

Treatment:
1. Regime_____
2. Diet_____
3._____
4._____
5…….

Literature:

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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 (змінами) _____

Завідувач кафедри Л.В. Журавльова