Міністерство охорони здоров'я України
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Кафедра Внутрішньої медицини №3
Факультет VI по підготовці іноземних студентів

ЗАТВЕРДЖЕНО
на засіданні кафедри внутрішньої медицини №3
«29» серпня 2016 р. протокол № 13
Зав. кафедри _____д.мед.н., професор Л.В. Журавльова

МЕТОДИЧНІ ВКАЗІВКИ
для студентів

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

Цукровий діабет, класифікація, етіологія, патогенез, клініка, діагностика

Харків 2016

Topic – «Diseases of the pituitary system. Obesity. Pathology of sexual glands»

1.The number of hours - 4

Whole lessons №9:

1. To teach the method of determination of etiologic and pathogenic factors of diseases of the hypothalamic-hypophysal system (HHS) and sexual glands (SG).
2. To work the method of research of the second sexual signs.
3. To acquaint students with classifications of diseases of HHS, SG.
4. Determination of variants of clinical picture of diseases of HHS, SG.
5. Acquaintance with the atypical clinical variants of diseases of HHS, SG.
6. Acquaintance of students with possible complications of diseases of HHS, SG.
7. Working off methodology of determination of basic diagnostic criteria of diseases of HHS, SG.
8. Drafting of plan of inspection of patients with the disease of HHS, SG.
9. Analysis of results of laboratory and instrumental researches which are used for diagnostics of diseases of HHS, SG.
10. Tactic of conducting of differential diagnostics of diseases of HHS, SG.
11. Technology of ground and formulation of diagnosis of diseases of HHS, SG.
12. Drafting of plan of treatment of patients with the disease of HHS, SG.
13. Deontological and psychological features of curation of patients with the disease of HHS, SG.

What must a student know?

1. Determination of concept of diseases of HHS, SG.
2. Epidemiology of diseases of HHS, SG.
3. Factors of risk of diseases of HHS, SG.
4. Mechanism of hormonal and metabolic violations at the diseases of HHS, SG.
5. Etiology and pathogenicity of diseases of HHS, SG.
6. Classification of diseases of HHS, SG.
7. Clinical picture of diseases of HHS, SG.
8. Typical clinical picture of diseases of HHS, SG.
9. Polyorganic complications of diseases of HHS, SG.
10. Diagnostic criteria of diseases of HHS, SG.
11. Choice of method of treatment of diseases of HHS, SG.

What must a student be able?

1. To define the factors of risk of diseases of HHS, SG.
2. To diagnose the disease of HHS, SG.
3. To carry out пальпаторне research of privy parts.
4. To determine the degree of development of the second sexual signs.
5. To define character of polyorganic complications of diseases of HHS, SG.
6. To analyze the results of hormonal researches and functional tests.
7. To estimate the results of ultrasound and roentgenologic research of privy parts and HHS.
8. To conduct differential diagnostics of diseases of HHS, SG.
9. Drafting of long-term plan of treatment of diseases of HHS, SG and their complications, technology of bringing in of patient to participation in a medical process.

10. Co-operating is with contiguous specialists (by a surgeon, gynecologist, ect.) on the stage of establishment of complete diagnosis, choice of method and tactic of treatment and protracted supervision

Table of contents of topic:

Cushing`s disease. Etiology and pathogenicity. Classification. Clinic. Diagnostics and differential diagnostics. Treatment.

Cushing`s disease is a neuroendocrine disease, conditioned violation of adjusting of the hypothalamic-hypophysal-adrenal system: the primary defeat of hypothalamus with the surplus products of corticoliberine stimulates the synthesis of hypophysis of corticotrophin a front particle, that causes second hyperplasia and hyperfunction of adrenal cortex, that clinically appears the syndrome of **hypercorticism**.

Women fall ill more frequent in 5-6 times, eyelids of manifestation - 20-40 years, but a disease meets for children, and people more senior 50 years.

From Cushing`s disease it follows to distinguish the syndrome of Cushing - **hypercorticism**, conditioned the primary tumor of adrenal cortex, that products glucocorticosteroides (glucocorticosteroma).

Etiology of disease is not set. For women Cushing`s disease more frequent arises up after births. In anamnesis patients regardless of floor have traumas of chairman, concussion of the brain, encephalitis and other defeats of the central nervous system. Most corticotrophin-secreting adenomas localized in the front particle of hypophysis (60%), other - in back and middle particles. Macroadenoma meet only in 10% patients, most characteristic micro adenoma (90%). Sometimes at Cushing`s disease a tumor at morphological research is not determined.

Pathogenic basis of Cushing`s disease is a change in the mechanism of control of secretion of corticotrophin.

An albumins exchange is violated: as a result of increase of level of cortisone the processes of disintegration of albumens are accelerated on a background the decline of their synthesis, the processes of dissimilation are accelerated.

Violation of carbohydrate exchange is conditioned relative insufficiency of insulin as a result of increase of level some counter-insular hormones -cortisone, glucagon, somatostatin.

Violation of electrolytic exchange is conditioned the increase of level of cortisone and especially mineralocorticoids of aldosterone: there is a delay of sodium in an organism, hypernatremia on a background the loss of potassium and hypokalaemia.

Clinical picture

1. Obesity

Observed in 92% patients. There is a redistribution of hypodermic-fatty cellulose on a dysplastic type (even if weight of patient remains unchanging) – fat accumulates in the area of person, neck, trunk, stomach. Quite often a fatty knoll appears in the area of overhead pectoral vertebrae. On extremities hypodermic-fatty tissue reduced.

2. Arterial hypertension

Early and proof symptom appears in 90% patients. Rises and diastolic arterial pressure, and systolic. High blood pressure is conditioned the increase of level of renin and hypernatremia. The accumulation of sodium in a vascular wall results in the increase of its sensitiveness to the endogenous pressor matters. hypernatremia promotes hypervolumeaemia. Arterial hypertension is accompanied the changes of vessels of retina and kidneys- hypertensive angiopathy of retina and. nephrosclerosis. Hypertrophy of the left ventricle of myocardium develops.

3. Electrolyte-steroid cardiopathy.

Metabolic and electrolytes changes, predominance in the cardiac muscle of processes of disintegration of albumen and hypokalaemia assist mushroom growth of insufficiency of circulation

of blood. Electrolyte-steroid cardiopathy which develops conduces to the structural defeats of myocardium and decline of retractive ability of cardiac muscle. Cardiopathy appears tachycardia, arrhythmias. Insufficiency of circulation of blood develops quickly – the shortness of breath, edema, multiplying a liver, appears.

4. Steroid myopathy

Caused violation of albumins exchange, dystrophic changes of muscles, diminishing of their mass and expressed changes of electrolytes – decline of concentration of intracellular potassium (so-called Steroid myopathy). There is the expressed muscular weakness, possible atrophy of muscles, especially extremities.

5. Change of skin (Steroid dermatopathy)

Atrophy of skin is conditioned violation of synthesis of albumens and collagen. A skin is refined, dry. As a result of x-raying of capillaries through derma there is the expressed «marble» vascular picture on a breast, extremities, red tint of skin of breasts, back, person. Often acrocyanosis.

Striae (bars of stretch) observed in 80% patients, conditioned the rapid deposit of fat. Striae wide, redder-violet, no communicative on a breast, stomach, internal surface of shoulders, thighs, in the area of pectoral glands. Striae lengths can arrive at 8-10 cm and width 2-3 cm. Coloring of striae changes on the different phases of disease: at reverse development of signs of illness they become whitishness's.

Hyperpigmentation of skin in the places of friction appears in 10% patients. A symptom is conditioned the increase of level of melanotrophic hormone.

Hypertrychosis, hyrsutism conditioned the increase of synthesis of androgens inadrenal glands. For women, becoming bald develops on a masculine type. The frequent pouring of abscesses out is on face, breasts, back.

6. Osteoporosis

Observed in 80% patients. A late symptom, expressed of osteoporosis, depends on weight of disease. Osteoporosis appears ostealgia, by the spontaneous breaks of compressions of pectoral and lumbar vertebrae, ribs, breastbone, and bones of skull.

In case of occurring of Cushing's disease in child's age there is lag in growth, braking of development of epiphyseal cartilages.

7. Violation of calcium exchange

Fixing of calcium in bone tissue and absorption of calcium goes down in a gastro-intestinal highway. Destroying of calcium is multiplied by kidneys, calcular pyelonephritis, develops quite often, nephrocalcinosis, chronic kidney insufficiency.

8. Violation of carbohydrate exchange

Violations of tolerance to the carbohydrates find out in 50-90% patients. Steroid diabetes, caused surplus of glucocorticoids, is observed in 10-20% patients, differs resistance to insulin, by the very rare exposure of ketoacidosis and comparatively easily regulated a diet and setting of biguanide.

9. Involution of lymphoid tissue

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

10. Violation of sexual function

Violation of sexual function takes place in 72% patients. Sexual disorders are early and permanent symptoms of disease, conditioned the decline of gonadotropic function of hypophysis and increase of secretion of testosterone by adrenal glands.

Women have violation of menstrual cycle (opsomenorrhea, amenorrhea), late sexual ripening, second fruitlessness. If pregnancy arises up, characteristic pathological motion. A typical small-cystic regeneration of ovaries is diminishing of primordial follicles with the origin of cysts in

a cortex and fibrosis of stroma. Other displays of virilisation are possible: hypertrychosis, growth of hairs on an overhead lip, chin, breasts, back, extremities, on the white line of stomach, now and then there is multiplying a clitoris. The expressed of virile syndrome is determined the measure of multiplying the synthesis of 17-CS.

A libido goes down for men, impotence develops.

11. Psycho-emotional violations

Asthenic dynamical syndrome is present in 97% patients, conditioned the promoted level of corticotrophin and serotonin. There are the expressed changes from the side of nerve-psychical sphere: crabbiness, worsening of memory, forgetfulness, and decline of interest to surrounding, propensity to depression. Sleep is violated.

Classification

Clinical classification foresees a division on the measure of weight of disease.

- Easy degree of weight: symptoms are moderately expressed, there is not osteoporosis.
- Middle weight: all symptoms are expressed, but complications are absent.
- Heavy degree: there are complications - insufficiency of circulation of blood, breaks of bones, nephrosclerosis, psychical violations, saccharine diabetes.

Ran across illnesses can be making progress or torpid.

- Making progress motion is characterized mushroom (during a few months) growth and subsequent growth of all symptoms and their complications. Patients lose a capacity quickly.
- There is slow gradual development of disease at a torpedo motion.

Diagnostics

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

Maintenance is promoted and corticotrophin, his day's rhythm of secretion is here changed – the decline of level of hormone is absent at night. Normal level in the whey of blood ACTH for adults in the morning at 8 o'clock - 5,5-24,6 pmol/l, in the evening in 18 – 0,2-6,0 pmol/l.

The level of mineralocorticoids of aldosterone is promoted in parts of patients. Normal level in the whey of blood of aldosterone- 100-400 pmol/l.

The excretion of hormones is changed and them metabolites with urine. The level of 17-OCS is sharply promoted, that determined a spectrophotometric method, which cortisone enter in the complement of, cortisone, them metabolites. 17-OCS urines are the sum of glucocorticoids of adrenal cortex and them metabolites, where enter:cortisol, cortisone, 11-desoxycorticosterone, tetrahydrocortisole and tetrahydrocortisone in free and linked forms. Determination of maintenance of 17-OCS allows to estimate glucorticoid activity of adrenal cortex.

17-ketosteroids (17-KC) urines – andro steroid hormones of adrenal cortex and products of exchange of testosterone. For men about 2/3 common amounts of 17-KC act from adrenal glands and 1/3 - from testicles. For women by the source of 17-KC practically fully there is adrenal glands, only wretched amount act from ovaries. At **hypercorticism** maintenance of 17-KC can be promoted or normal.

Functional tests

The functional tests of stimulants foresee introduction of pharmacological preparations which stimulate adrenal glands –synacten, corticotrophin, metopirone. After one introduction of stimulators determine the change of level of cortisone blood or 17-OCS in urine. At Cushing`s syndrome of adrenal "answer" on a stimulus - the level of cortisone or 17-OCS rises in 2-3 times. At

the Cushing`s syndrome (tumor of adrenal glands,glucocorticosteroma) the level of cortisone and 17-OCS does not change - "deaf"adrenal glands, a tumor products hormones in the own rate.

Functional test, that repress the products of endogenous corticosteroids is a test with dexamethasone (for 2 mg each 6 hours during two days). At Cushing`s disease of adrenal glands "answer" on introduction of exogenous glucocorticoids the decline of level of cortisone and excretion of 17-OCS more than on 50% from an initial level (a test is positive). At the syndrome of Cushing the products of hormones remain a tumor unchanging (a test is negative).

Roentgenologic research of skeleton - osteoporosis appears in 95% patients.

Visualization of defeat of the hypothalamic-hypophysal system

The macroadenoms of the Turkish saddle (10% cases) are diagnosed at sciagraphy of the Turkish saddle. Microadenoms do not appear at this research, application of computer tomography or magnetically-resonance tomography is needed. Researches informing in 60% patients. For the other patients topographical changes in the hypothalamic-hypophysal system are absent.

Visualization of defeat of adrenal glands

Used ultrasonic scanning of adrenal gland or the radioisotope scanning is with a cholesterol, marked radio-active isotope. Apply roentgenologic researches of adrenal glands – angiography, computer tomography, magnetically-resonance tomography.

In 50% patients there is bilateral hyperplasia of adrenal glands, secondary adrenal microadenomatosis is possible. In default of multiplying the sizes of adrenal glands there is multiplying the closeness of their cortex.

Hyperplasia of one adrenal gland appears at the Cushing`s syndrome (glucocorticosteroma), that staggered a tumor, and a compensate atrophy of secondadrenal gland. During separate catheterisation of adrenal veins maintenance of hormones in a right and left vein will be different.
The most informing differential-diagnostic test is angiography with selective taking of blood sample from the veins of adrenal glands for determination of maintenance in them cortisol. At second bilateral hyperplasia of adrenal glands maintenance of cortisol in blood of veins of adrenal glands is promoted on either side, at tumors – considerably promoted on the side of tumor and reduced or normal from an opposite side.
Computer tomography allows to define not only character of defeat of adrenal gland but also find out ectopic hormonal-active tumors.

Differential diagnosis

The Cushing`s syndrome on clinical displays does not differ from Cushing`s disease. Roentgenologic and radioisotopes methods allow to define localization of tumor. Tests from coricptropin, metopirone, does not cause change of maintenance of 17-0CS dexamethasone in urine, as products of hormones do not depend a tumor on the hypothalamic-hypophysal influencing.

For pubertal-youth dyspituitarismus characteristic even obesity, arterial hypertension. The hypertension can disappear spontaneously. Unlike Cushing`s disease, patients of always normal or high growth. At a disease the changes of bone structure, differentiation and growth of skeleton are absent speed-ups. All of it talks about predominance of anabolic processes at dyspituitarismus.

Treatment

For treatment the methods of pathogenic therapy are used, directed on normalization of hypophysal-adrenal relations, and methods of symptomatic therapy.
Pathogenic therapy. A medicinal method includes therapy, directed on the decline of function of hypophysis and adrenal glands under action of preparations which repress the secretion of corticotrophin (rezerpinum, dipheninum, ciproheptadinum, bromcriptinum, parlodelum), and matters which lock the biosynthesis of corticosteroids in the adrenal cortex (chloditanum). Rezerpinum is used in the dose of 1 мg on days and appoint during 3-6 months for normalization of

arterial pressure and decline of activity of hypophysis. Ciproheptadinum apply for 80-100 mg, parlodelum - for 5 mg on days during 6-12 months.

Conservative treatment of Cushing`s disease is conducted with the use of inhibitor of adrenal cortex - chloditanum. Preparation locks the synthesis of cortisol, reduces the secretion of androgens and does not influence on the products ofmineralocorticoids. At Cushing`s disease preparation is appointed in pills for 6-8 g on a day (0,1 g/kg the masses of patient). Clinical effect of chloditanum comes in 15-18 days – the common state gets better, pain diminishes in bones, mass of body goes down.

Effective combination of chloditanum from peritolum, inhibitor of synthesis of serotonin.

Symptomatic therapy is directed on indemnification and correction of albumins, electrolyte and carbohydrate exchange, arterial pressure and heard insufficiency, treatment ofosteoporosis, pyelonephritis and psychical violations.

Anabolic steroids is widely used (retabolilum for 0,5 g intramuscular 1 time per 10-15 days).

For treatment of hypokalaemia alkalosis it is expedient to combine preparations of potassium and verospirone.

At steroid diabetes biguanides are used, sometimes in combination with suflanilamids.

Heard insufficiency requires therapies cardiac glycosides. Application of diuretics it must be limited.

At septic displays appoint the antibiotics of wide spectrum of action taking into account a sensitiveness.

Treatment of osteoporosis is a very important purpose, because changes in bones are added reverse development slowly and not for all patients. The increase of suction of calcium is achieved setting of vitamin D3 and introduction to the organism of preparation of calcitonin, calcitrine and salts of calcium instrumental in the increase of calcination of bones. Treatment of osteoporosis must be conducted during 12-18 months. Calcitrine is appointed courses from 150-200 IU on a course, daily or in a day for 3-5 IU intramuscular. Preparations of calcium appoint for 3 g on days. Oxydevitum recommend to accept at a stretch during 4-6 months.

At the easy form of Cushing`s disease in 65% patients proof remission of disease is achieved by conservative methods.

At illness of easy and middle weight the irradiation of hypophysal area – controlled from distance radial therapy is used: gamma-therapy (dose 40-50 Gr) and proton bunch (dose 80-100 Gr on a course). The irradiation of hypophysal area leads or to disappearance of most clinical displays of disease, or part of symptoms. These changes come in 6-12 months upon termination of course of treatment. In most cases at middle weight of disease the combined treatment is used: operative delete of one adrenal gland and radial therapy of hypophysal area.

At heavy motion of disease, resistance to chloditanum conduct one-sided adrenalectomy. Before at a heavy form diseases executed an operative delete both adrenal glands in two stages. After the delete of one adrenal gland and cicatrisation of operating wound proceeded to the second stage - delete of second adrenal gland with autotransplantation of areas of adrenal cortex in a hypodermic cellulose. It was done for diminishing of dose of substitute therapy by hormones, which must be lifelong for patients after bilateral total adrenalectomy. However accompanied bilateral subtotal adrenalectomy often is the relapse of disease. Total bilateral adrenalectomy removes the symptoms of **hypercorticism** proof, but requires lifelong substitute therapy by steroid hormones. At 10% of these patients develops the syndrome of Nielsen – adenoma of hypophysis.

Hypopituitarism. Etiology and pathogenicity. Clinic. Diagnostics and differential diagnostics. Treatment.

Panhypopituitarism is a decline or fall of trophic functions of hypophysis, with second hypofunction of other peripheral endocrine glands. To the Hypopituitary syndromes belong hypophysal cachexia (Simmond`s disease) and Sheehan`s disease.

SIMMOND`S DISEASE

Hormonal insufficiency of the hypothalamic-hypophysal system develops on soil of infectious, toxic, vascular (at the diseases of the systems of connecting tissue), traumatic, tumors, allergic, autoimmune defeats of front particle of hypophysis and (or) hypothalamus. A similar clinical syndrome arises up also as a result of radial or surgical hypophysisectomy.

A flu, encephalitis, typhus, dysentery, festerings processes in different organs and tissues with embolic complications and necrosis of hypophysis, cranial-cerebral traumas which are accompanied intracranial hemorrhages in hypothalamus or hypophysis, can precede a disease.

One of the most frequent reasons of disease women have abortion and especially births, pregnancies, which was complicated an eclampsia, sepsis, embolic, massive (700-1000 ml) lose of blood which conduce to violations of haemocirculation in a hypophysis, to hypoxia and necrosis. In the row of patients of reason of hypopituitarism discovering is not succeeded (idiopathic hypopituitarism).

Morphological basis of this disease is atrophy of hypophysis with substituting for his ferrous elements by connecting tissue.

Clinical picture

Clinical symptomatic of disease is variable and consists of specific symptoms of hormonal insufficiency and polymorphic neurovegetative displays. Women are more frequent ill in age 30-40.

1. The syndrome of hypogonadism is conditioned a decline or complete fall of the gonadotropic adjusting of sexual glands. These violations quite often precede appearance of all other symptoms. A sexual desire (libido) is lost, potency goes down, hairs fall out on лобку and in западинах of arm-pits. External and internal privy parts atrophy gradually.

2. The syndrome of hypothyrose is conditioned diminishing of products of thyrotrohphin, formed quickly or gradually. There is a somnolence, adynamia, mental and physical activity goes down. Thyrose hypofunction results in violation of metabolic processes in myocardium. Contracting cardiac muscle is slowed, tones of heart become deaf, arterial pressure goes down.

3. The syndrome of **hypercorticism** is determined the degree of decline of function of adrenal glands. Heavy **hypercorticism** reduces resistance of patients to the undercurrent diseases and different stress situations, strengthens a general weakness, adynamia, low blood pressure and assists development of hypoglycaemia. Characteristic spontaneous morning hypoglycaemia is with the loss of consciousness.

4. The syndrome of exchange-trophic violations shows up by disappearance of hypodermic cellulose, atrophy of muscles, premature senescence. A skin is dry, atrophy, wrinkled, pale with an earthy tint, turgor is considerably reduced. Eyes fall back for patients. Hairs become fragile, loses the normal colouring, falls out. Fragility of nails appears. Teeth get shattered and collapse. A lower jaw atrophies, as in senile age. Develops diffuse decalcification of bones, that is accompanied feelings of pains in bones and phenomena of osteoporosis.

5. Hypothalamic component in clinical symptomatic can show up violations of thermoregulation more frequent with a hypothermia, but sometimes with subfebrility and vegetative crises (hypoglycaemia, chill, tetanic syndrome, polyuria). Quite often violations of the peripheral nervous system develop with polyneuritis,polyradiculoneuritis.

Psychical violations are observed at all variants of hypothalamic-hypophysal insufficiency. Characteristic decline of emotional activity, depression and other psychical rejections up to psychosis.

Some differences in clinical symptomatic can be related to the different etiologic factors. For example, at presence of tumor process the symptoms of the promoted intracranial pressure - head pain, worsening of sight and change of an eye bottom, vomit of central origin can come forward on the first plan. Viral meningoencephalitis gives the clinic of neurological symptomatic and chronic infection.

SHEEHAN `S DISEASE

The original form of polyglandular insufficiency is post-natal hhypopituitarism (Sheehan`s disease).

The primary factor of development of pathological process is a spasm of arterial vessels of front particle of hypophysis as a result of bleeding and collapse in the period of births, that results in violation of portal blood circulation of adenohypophysis. It is set that at a brief spasm (to one hour) take place only functional violations, at more protracted - the ferrous elements of adenohypophysis perish. An area of defeat can be different and is not in direct dependence on weight of bleeding.

Frequency of Sheehan`s disease, from data of different authors, one case makes approximately on 60-70 complicated births.

1. The symptoms of manifestation are observed already in the first 3-4 days. Head pains, dizziness's, episodes of loss of consciousness, eclipse of consciousness, stunned, increase of temperature of body, agalactia, appear. At the same time develop sharp general weakness, anorexia, quite often vomit, thirst, frequent urination with polyuria to 10 l. on days (transitory forms of diabetes insipidus). The period of post-natal stay in permanent establishment, as a rule, delays to 1-3 months.

2. An asthenia, decline of trophic, anorexia, is expressed, gradually increasing vegetative-trophic and exchange-endocrine violations accompany the flow of illness during next years. Patients are disturbed by a general weakness, indisposition, feeling of sensitiveness to the cold, absence of appetite, early decrepitude.

At an objective inspection pay on itself attention of progeria, decline of trophic, "alabaster" pallor, sometimes icteric coloring and dryness of skin, propensity to the edema, depigmentation of separate areas of skin, areoles. Hairs fall out, thus on a head their growth in sort recommences usually, and on pubes, it is fully absent of hairs in arm-pits. Other violations of trophic – fragility of nails, destruction of teeth and other appear

3. Syndrome of hypogonadism: pectoral glands atrophy, a menstrual cycle does not regular (menstruations are absent or are irregular and wretched). Secondary hypoplasia of sexual vehicle appears at gynaecological research

4. The syndrome of hypothyrose with all characteristic symptomatic can sometimes prevail in in a clinical picture.

5. The symptoms of adrenal insufficiency distinctly appear rarely. One of such signs there is propensity to hypoglycaemia, up to grave comatose conditions.

6. Insufficiency of antidiuretic function quite often takes place and shows up the transitory forms of diabetes insipidus or isosthenuria from relatively by the low relative closeness of urine (1006-1012) and moderate polyuria.

Hypopituitary violation can appear not right after the complicated births, but through the certain interval of time, being here provoked different stress situations - unfavorable terms of life, malnutrition. In such cases hypopituitarism can appear the comatose state.

Unlike the hypothalamic-hypophysal cachexy of Simmonds for illness of Sheehan there is not characteristic sharp exhaustion and heavy exchange-dystrophic violations. Typically combination of hypothyrose and **hypercorticism** at relatively less violation of function of sexual glands.

Diagnostics of hypopituitary syndromes

At clinical and biochemical laboratory researches for patients with hypopituitary syndromes normochromic anemia is determined quite often, sometimes leukopenia with the decline of amount of neutrophils. It can be microalbuminuria and hypoisostaenuria, mainly at hypothalamic localization of defeat and bringing in in the process ofneurohypophysis. The level of sugar in blood is on an empty stomach reduced or within the limits of low bound of norm, glycaemia. Something the level of sodium is reduced and to the chlorine in blood, maintenance of cholesterol is promoted, but these changes, as well as other biochemical indexes, not enough specific.

Hormonal researches testify to the considerable decline in blood of adenohypophysal hormones (corticotrophin, thyrotropin, follitriopine ,somatotropin). Maintenance of glucocorticoids is diminished in plasma of blood, thyroxin, and also iodine, related to the squirrel of blood. Day's excretion is reduced with urine of 17-CS, 17-OCS, to estrogen,gonadotropins. Fascination of radio-active isotope of iodine is reduced by a thyroidal gland.

The second character of hypothyrosis is confirmed a hasp from thyrotropin: after intramuscular introduction 10 IU of thyrotropin absorption of iodine rises by thyroidal gland during 1-3 days. A basic exchange is reduced.

For confirmation of the second character of **hypercorticism** conduct a test from corticotrophin: in reply to introduction of corticotrophin the level of 11-OKC and cortisol rises in plasma of blood, and also excretion of 17-OCS and 17-CS with urine.

On the measure of decline of level of hormones of peripheral glands, in reply reactions on introduction of trophic hormones (thyrotropin and corticotrophin), it is possible to judge about expressed of hypophysal insufficiency and, consequently, about weight of disease. Certain help is given by tests, directed on the exposure of functional backlogs of adenohypophysis. In particular, about backlogs of adrenocorticotrophic function a test gives an answer from metapirone, which electorally represses the synthesis of cortisol in the adrenal cortex: at the stored backlogs of hypophysis, on a background adopting metapirone (for 0,5 g 4 times per days) there is an increase of excretion of 17-OCS with urine. About backlogs thyrotrophic functions draw conclusion on the increase of level of thyrotropin in blood in reply to introduction of synthetic thyroliberine, about backlogs of somatotrophic function - for reactions in reply to introduction of arginine.

Differential diagnosis

A differential diagnosis is conducted with diseases, which are accompanied exhaustion (malignant new formations, chroniosrepsis, tuberculosis), Addison`s disease, hypothyrose, nervous anorexia.

At a somatic cachexia there is proper symptomatic and given laboratory researches of basic disease.

Primary insufficiency of adrenal glands is not accompanied a somatic cachexy, hypothyrose, by insufficiency of sexual glands and characterized typical pigmentation. A test from corticotrophin is negative – introduction of corticotrophin is not accompanied the increase of low level of corticosteroids in blood and urine.

At primary hypothyrosis more expressed and the isolated insufficiency of thyroidal gland. A test from thyrotropine is negative.

The expressed of anemia sometimes grounds for differential diagnostics with the diseases of blood, and heavy hypoglycaemia can simulate the tumors of pancreas -insulinoma.

Treatment of hypopituitary syndromes

Regardless of nature of disease at all forms of organic hypopituitarism treatment it must be persistent, systematic and conducted almost always during all life.

A diet of patients must be high-calorie with the promoted maintenance of albumens, carbohydrates, mineral salts and vitamins. Vitamins of A, E, C enter additionally. Setting of albumins preparations is shown.

Etiologic treatment depends on reason character of pathological process which lies in basis of disease. At the tumors of hypothalamic-hypophysal area their operative delete, criodestruction, radiotherapy, deep radial therapy, is recommended. The presence of inflammatory process requires setting of antibiotics, antihistaminic and other facilities. At chronic inflammation dehydratation facilities are shown. At suspicion on a tubercular damage, setting of specific therapy is needed.

Pathogenic treatment. Substitute hormonal therapy begins usually from preparations adrenal and sexual hormones and, in the last turn, thyroid hormones.

For the removal of hypocorticism use the medicinal matters of enteral introduction, but in heavy cases of treatment begin with parenteral facilities. Glucocorticoids are appointed: hydrocortisone (50-200 mg daily), prednisolone (5-15 mg) or cortisone (25-75 mg) is on days.

Mineralocorticoid insufficiency is removed a 0,5% desoxycorticosterone acetate (DOCSA) for 0,5-1 ml intramuscular daily, in a day or 1-2 times per a week, in future pass to the sublingual pills for 5 mg 1-2 times per a day. 2% suspension of desoxycorticosterone is used also of two-week prolongation. Effective hypodermic implantation of crystal of DOCSA, which contains 100 mg, by duration of action 4-6 months.

On a background substitute therapy add corticotrophin of short or (better) prolonged action corticosteroids (in 10-15 days from its beginning) (24-30 hours). Large efficiency and the best bearableness is observed at the use of "synacthen -depot" for parenteral introduction (1 ml (100IU) 1-3 times per a week).

Insufficiency of sexual glands is compensated for women by estrogen and progestagens, and for men - preparations of androgenic action. Treatment sexual hormones is combined with introduction of gonadotropins. For women a menstrual cycle is artificially reproduced substitute therapy; estrogen is 15-20 days entered, and in next 6 days – gestagens (pregnine, progesterone). At a Sheehan’s syndrome use the synthetic combined preparations with a substitute purpose (bisecurine, non-ovlon, rigevidonum, and other). Except for specific influence on a sexual vehicle, the proper hormones find out positive trophic and anabolic effects.

For men with a substitute purpose apply methyltestosterone for 5 mg 3 times per a day sub lingua, testosterone-propionas for 25 mg 2-3 times per a week intramuscular or preparations of the prolonged action: 10% solution of testenate for 1 ml each 10-15 days, sustanone-250 1 мл 1 time on 3-4 weeks.

Thyroid insufficiency is removed by thyroid hormones which are entered simultaneously with corticosteroid preparations, as strengthening of processes of exchanges strengthens hypocorticisms. Last years use the mainly synthetic combined preparations which contain thyroxin).

Appoint anabolic steroids to all patient: metandrostenolone (5 mg 2 times per a day), metandrostendiole sub lingua (25 mg 2 times per a day) or retabolilum (1 mg 1 time on 3 weeks).

In connection with the expressed dehydration in a diet add sodium chloride, intravenously enter isotonic solution of sodium of chloride (500-700 ml) in combination with a 5% solution of glucose (200-300 ml). The charts of treatment and dose of hormones which are entered pick up in the conditions of permanent establishment.

It does not follow to appoint patients with the purpose of stimulation of appetite insulin, because even small doses can cause him heavy hypoglycaemia.

Diabetes insipidus . Etiology and pathogencity. Clinic. Diagnostics and differential diagnostics. Treatment.

Diabetes insipidus is a neuro-endocrine disease, conditioned the deficit of antidiuretic hormone or insensitivity of peripheral tissues to him, clinically appears violation of water-electrolyte balance.

Prevalence of Diabetes insipidus: 0,5-0,7% endocrine diseases, with identical frequency meets for women and for men, more frequent in all – in age 20-40.

Etiology and pathogencity

A disease is drawn insufficiency (absolute or relative) of antidiuretic hormone (ADH, or vasopressin). ADH activates reabsorption of water in distal canals of nephron, due to what he got the name « antidiuretic hormone ». Insufficiency of ADH reduces реабсорбцію of liquid in kidneys and instrumental in the selection of plenty of hyperosmolar of the unconcentrated urine.

Central Diabetes insipidus (hypothalamic) is caused the absolute deficit of antidiuretic hormone as a result of his insufficient products hypothalamus. Reason of central forms of Diabetes insipidus can be degenerative, traumatic, tumors and other defeats of different areas hypothalamic-hypophysal systems (front kernels of hypothalamus, supraoptic-hypophysal highway, back particle of hypophysis) which result in the insufficient products of vasopressin. Acute or chronic infections can precede actual Diabetes insipidus: flu, mengoencephalitis, scarlatina, whooping-cough, all types of typhus, septic states, tuberculosis, lues, malaria, rheumatism. A flu with his neurotropic influencing meets more frequent than other infections.

A disease can arise up after a cranial (casual or surgical) trauma, psycho-emotional stress, supercooling, an electric trauma, and also during pregnancy, soon after births or abortion. Sometimes Diabetes insipidus arises up on a background the primary tumor of the hypothalamic-hypophysal system (adenoma, teratoma, glyoma) or metastatic defeat at the shrine of pectoral gland, thyroid, bronchial tubes.

The cases of autoimmune defeat of hypothalamus became more frequent. Diabetes insipidus quite often is combined with other endocrine diseases: hypophysal nanism, acromegaly, gigantism, adipose-genital dystrophy.

Peripheral Diabetes insipidus (nephrogenic, vasopressin-resistant) is conditioned the relative deficit of антидіуретичного hormone - insensitivity of receptors of kidney канальців to this hormone as a result of their genetic pathology. Peripheral Diabetes insipidus develops on a background the normal products of vasopressin, reason of disease is a sharp decline of sensitiveness of receptors of kidney canals to the hormone or vasopressin inactivation in a liver, kidney, placenta. The variant of Diabetes insipidus is given more frequent observed for children.

Heavy Diabetes insipidus with diuresis of 40-50 l/day can result in joining of nephrogenic Diabetes insipidus, especially at the use of unrefined immune preparations (especially adiurecrine). Formation of autoantibodies to preparation causes the autoimmune defeat of receptors to ADH; a kidney epithelium loses sensitiveness to exogenous vasopressin, that causes impossibility to modulate ability of kidneys to concentrate urine.

Clinical picture

Beginning of disease can be sudden or gradual. Gradual development is incident to the idiopathic forms.

1. Violation of waterhomeostasis. Polyuria to 3-15-40 and anymore l/daily, urine is colorless, with low specific gravity 1000-1005. For children the first symptom of disease can be enuresis.

Polydipsia adequate the loss of liquid with urine, imperative thirst is identically expressed and in the day-time, and at night. The amount of liquid which is drunk hesitates from 3 to 15 l., but sometimes for a satiation it is needed 20-40 and more liters of water. Limitation of liquid is not recommended a patient and even dangerously - can result in development of hyperosmolar crises. Expressed of polyuria and polydipsia depends on the degree of neuro-secretory insufficiency.

The symptoms of dehydration appear at the review of patient: a skin is dry, sweating is not even then, when the loss of water with urine is fully compensated adopting a liquid.

2. Asthenic syndrome. In connection with the necessity of frequent reception of liquid, in particular at night, patients have insomnia, crabbiness is promoted. Characteristic psychical and emotional violations: head pains, psychoses, declines of mental activity.

Physical asthenisation appears weight loss(very rarely there is obesity), to put fall behind in growth, physical and sexual development.

3. Dysfunction of gastric-enteral highway. The decline of ptyalism, intensive drinkable mode, draws the secondary violation of secretory function of stomach is anorexia, symptoms of hypoacidic gastritis.

4. Dysfunction of the cardiac system. At high polyuria with diminishing of volume of circulating plasma compensate tachycardia, arterial low blood pressure, violation of thermoregulation is formed.

The changes of internal organs are not expressed are lights, liver does not suffer usually.

5. Sexual dysfunction. For women - violation of menstrual function, fruitlessness. For men - decline of libido, potency.

6. Dysfunction of the central nervous system. At central Diabetes insipidus there can be neurological symptoms, related to the increase of intracranial pressure, squeezing of some departments of brain. At a intracranial tumor possible permanent head pain, bitemporal hemianopia, paralysis of eye muscles, was swollen disks of visual nerves, decline of sight. For xantomatosis characteristic defeat of bones of skull.

Hyperosmolar crises develops at inadequate renewal of the liquid lost with urine. The symptoms of dehydration appear: there is a sharp general weakness, nausea, vomit, diarrhoea, stomach-aches, head pains, cramps, psychical excitation, tachycardia, low blood pressure, collapse. During dehydration, not because of diminishing of volume of circulating blood and decline of kidney filtration, polyuria is saved.

Diagnostics

Simultaneous determination of osmolarity plasma and urine gives reliable information about violation of water гомеостазу, characteristic for Diabetes insipidus.

Typical hypoosmolarity of urine (100-200 mosmol/l). The osmolarity of urine is measured directly by osmometer or settles accounts on a formula.

Osmolarity of urine (mosmol/l) = (Specific gravity of urine – 1000) x 33,3.

Urine which is selected is discolored, contains no pathological elements. Characteristic hypoisosthenuria: a decline of specific gravity of urine is in all portions to 1000-1005.

The second major diagnostic criterion is hyperosmolarity plasma of blood of more than 290 mosmol/l. Osmolarity of plasma of blood is measured directly by osmometer or settles accounts on a formula (all parameters of whey are taken into account in mmol/l).

Osmolarity of plasma (mosmol/l) = 2 (Na of whey +K whey) +Glucose of whey +Urea of whey

Hypernatremia exceeds 150 mmol/l.

Diagnostic tests are conducted for differential diagnostics with psychogenic polydipsia.

1. Dehydration test

A test is provocative, conducted in the conditions of permanent establishment; duration must not exceed 6-8 hours, in exceptional cases 14 hours. All urine which is selected going hourly, its volume and specific gravity is exactly determined. The use of liquid is fully forbidden.

In healthy or patients with psychogenic polydipsia diuresis goes down, increased osmolarity of urine, in a 2-4 o'clock of osmolarity urine achieves the size of osmolarity of plasma and continues to be increased to 800 mosmol/l.

For patients with Diabetes insipidus the common state gets worse, thirst becomes sickly, the symptoms of dehydration appear, but amount of urine which is selected, and her osmolarity and relative closeness does not change substantially. Osmolarity of urine remains low (50-200 mosmol/l), and increased osmolarity blood to the dangerous sizes (more than 290 mosmol/l).

At the loss of weight on 2% from an initial level or a test must appearance of signs of heavy dehydratation (vomit, head pain, low blood pressure, and tachycardia) be halted immediately.

2. A test is with intravenous introduction of a 2,5% solution of chlore sodium.

On an empty stomach give to take an a swig at a patient water from the calculation of 20 ml on 1 kg of mass of body. In 30 minutes catheterize an urinary bladder for the receipt of tests of urine through each 15 minutes regardless of presence of urges on urination. After stabilizing of rate of diuresis intravenously tiny during 45 minutes enter a 2,5% solution of chloride of sodium – 0,2 ml on 1 kg of mass of body, continuing to collect 15-minute portions of urine.

In healthy or at psychogenic polydipsia diuresis goes down on a background the salt loading, specific gravity of urine, osmolarity of blood rises remains normal.

At Diabetes insipidus a volume and concentration of urine does not change substantially, saved hypoosmolarity of urine, here considerably rises osmolarity of blood.

3. A test is with preparations of vasopressin (desmopressin)

At introduction hypodermic 5 IU of desmopressin in 1 hour for patients the common state gets better with central Diabetes insipidus, diuresis goes down, specific gravity of urine, osmolarity urine rises increased more than on 10% from initial.

Water intoxication - head pain, diminishing of diuresis develops at psychogenic polydipsia. At nephrogenic Diabetes insipidus vasopressin is ineffective.

With the purpose of finding out of reason of disease it is necessary above all things to explore the state of the hypothalamic-hypophysal system (detailed roentgenologic, neurological and ophthalmology research). If necessary come running to computer tomography. A deciding value in diagnostics would have determination of basal and stimulated level of vasopressin in plasma.

Classification

On pathogenicity select Diabetes insipidus:

- True (primary, idiopathic, domestic).
- Symptomatic (purchased).

As a result of dehydratation test select a few types of central Diabetes insipidus.

1. Complete absence of secretion of ADH (an insignificant increase of osmolarity of urine is on a background growth of osmolarity of plasma).

2. Step growth of secretion of ADH (step increase of osmolarity of urine).

3. A delay of secretion of ADH is in reply to stimulation of osmoreceptors.

4. The secretory answer of ADH is reduced in reply to stimulation of osmoreceptors.

Differential diagnosis

Conduct with saccharine diabetes, psychogenic polydipsia, chronic diffuse glomerulonephritis in the stage of compensate polyuria, from hyperparathyrosis and primary aldosteronism.

At saccharine diabetes polyuria achieves such high level rarely, as at Diabetes insipidus. Polyuria is combined with glucosuria and high relative closeness of urine, increase of glycaemia. At combination of saccharine and Diabetes insipidus high polyuria is a stay after indemnification of saccharine diabetes and removal of glucosuria.

Psychogenic polydipsia (idiopathic or in connection with a psychical disease) is characterized primary thirst. She is conditioned functional or organic violations in the center of thirst, that lead to uncontrolled acceptance of plenty of liquid. Limitation of adopting a liquid and dehydration, that stimulate formation of endogenous vasopressin for patients on psychogenic polydipsia, unlike patients with Diabetes insipidus, does not violate the common state, amount of urine, which is selected, diminishes accordingly, and her osmolarity and relative closeness normalized. Adopting diuretic facilities at psychogenic polydipsia is accompanied multiplying the amount of day's urine, there is a paradoxical effect - decline of diuresis at Diabetes insipidus.

The chronic disease of buds in the stage of compensate polyuria is characterized comparatively small growth of amount of day's urine (to 3-5 l.), hypo- and isosthenuria within the limits of 1010-1012, proteinuria, presence of pathological urinary sediment and other symptoms of insufficiency of kidneys.

Hyperparathyrosis (Reklingshausen`s disease) also can flow with polyuria. However at this disease there is such expressed polydipsia and such low relative closeness of urine. The typical symptoms of hyperparathyrosis are changes of skeleton as osteoporosis, increase in blood of level of calcium and decline of maintenance of phosphorus.

Aldosteronism (increase of mineralocorticoid function of adrenal cortex) is accompanied, except for thirst andpolyuria, by other typical symptoms: by the weakness of muscles, cramps, paraesthesia, arterial hypertension, hypoglycaemia.

Treatment

The diet of patients with Diabetes insipidus foresees limitation of salt, albumens, exception of swizzles. A meal is appointed with plenty of vegetables, fruit, milk products. Etiopathogenic treatment is directed on liquidation of principal reason of disease (if she succeeds to be set). At the tumors of hypophysis or hypothalamus is surgical interference or radial therapy, introduction of radio-active yttrium, criodestruction. At inflammatory nature of disease are antibiotics, dehydration. At haemoblastosis is therapy by citostatics recommended.

The basic and very effective method of treatment of Diabetes insipidus is pathogenic substitute therapy by different preparations of back particle of hypophysis.

Adiurecrine is breathed in powder through a nose. In 20-30 minutes thirst diminishes after entering, urges to urination become rarer, the relative closeness of urine some rises, but however does not achieve normal numbers. The antidiuretic effect of Adiurecrine is saved 6-8 hours. Inhalation of preparation in the evening in most patients provides quiet nightly sleep. Initial dose of Adiurecrine – 0,03 г, at ineffectiveness a dose is multiplied to 0,05 g on a reception. At acute and chronic inflammation of mucus shell of nose the introduction of powder through a nose can be ineffective.

Adiurecrine is a synthetic analogue of vasopressin. Enter intranasal for 1-4 drops 2-3 times per a day.

Decompressing–gene-engineering arginine-vasopressin differs high efficiency. Decompressing enter intranasal for 1-2 drops (for 10 mkg 1-2 times per days) or pills (100-200 mkg) accept inward 1-3 times per a day..

When the intranasal use of preparations of back particle of hypophysis appears impossible or not enough effective (for example, as a result of rhinitis), come running to the injections of pituitrinum, extract of back particle of hypophysis. Pituitrinum (vasopressin with oxytocin) is entered hypodermic for 1 ml (5 IU) 2-3 times per a day. Preparation finds out the expressed antidiuretic action during 8-10 hours.

At overdosing of vasopressin and other preparations of antidiuretic action the symptoms of water intoxication can develop: excitation, head pain, consciousness, cramps, stomach-aches, diarrhoea, delay of liquid, is entangled, sometimes coma. These phenomena bind to swelling of brain as a result of delay of liquid.

For symptomatic treatment of Diabetes insipidus, especially at hypothalamic and nephrogenic Diabetes insipidus, use some diuretic preparations of thiazide group – hypothyzide for 100 mg/daily. For patients with Diabetes insipidus of hypothiazide finds out a paradoxical effect - reduces kidney filtration and excretion of sodium, the amount of urine which is selected goes down on 50-60%. Excretion of potassium increases thus. Preparation is effective not for all patients.

Enteral saccharine-decreading preparation chlorpropamidum also appears effective in the rows of patients with Diabetes insipidus, especially at combination of him with saccharine diabetes. Chlorpropamidum appoint in day's dose of 250 mg 2-3 times per a day. The mechanism of his antidiuretic action full is not found out, possibly, Chlorpropamidum potent the effect of endogenous vasopressin, promotes the sensitiveness of receptors of kidney to the hormone. An effect appears in 3-4 days of daily reception. In order to avoid hypoglycaemia and hypernatremia during the use of Chlorpropamidum, it is necessary to control the level of glucose and sodium in blood.

Hypopituitarism with somatotrophic insufficiency (hypophysal nanism). Classification. Etiology and pathogenicity. Clinic. Diagnostics and differential diagnostics. Treatment.

Nanism (nanosomia, microsomia) is a neuro-endocrine disease, conditioned violation of secretion of STH or his operating on peripheral tissues, that is characterized the delay of growth and physical development.

Nanism is the group of the heterogenic states which differ one from other on etiologic factors, on pathogenicity, on clinical displays and sensitiveness to therapy. Frequency of nanism is small – 1 on a 10 000 population, the masculine persons are ill in 2 times more frequent.

Etiology and pathogenicity

Reasons, which result in violation of secretion of STH and delays of growth, various. In most patients it is not succeeded to find out direct reason of violation of secretion of growth hormone. On occasion the etiologic factors of sporadic or purchased nanism are organic defeats of hypothalamic-hypophysal area (traumas, hemorrhages, meningitis's, glyoma, craniopharyngeoma, meningioma, angioma, vascular aneurysm, tuberculosis, lues and other). In development of insufficiency of STH quite often deciding part is acted by those or other traumatic factors: operating trauma of brain(births by pelvic praesentatio, multipregnancy, large fruit, etc). At considerable part of patients a disease is genetically conditioned.

Patients with violations of growth, conditioned insufficiency of STH, can be parted on 3 large groups: primary insufficiency of growth hormone; imperfectness of receptors to STH; insufficiency of education or action of IFG-1.

Born (genetic) insufficiency of STH

A. Insufficiency secretions of STH

1. Idiopathic, or sporadic form:

Idiopathic or a sporadic form of insufficiency of STH is a form of disease which most often meets in a clinic (60-70% all cases of delay of growth). She can be investigation of the isolated insufficiency of secretion of STH or be combined with insufficiency of other hormones of front particle of hypophysis.

1.1. Hypophysal insufficiency of STH:

а) isolated insufficiency of STH;

б) insufficiency of STH is in combination with insufficiency of other hormones;

в) syndrome of break of leg of hypophysis;

Introduction in clinical practice of computer tomography and nuclear-magnetic resonance tomography allowed to find out the special form of idiopathic insufficiency of STH, caused the break of leg of hypophysis and violation of physiology connection of front particle of hypophysis with hypothalamus which appears violation of function of adenohypophysis.

1.2. The isolated hypothalamic insufficiency of somatoliberine.

Isolated insufficiency of secretion of somatoliberine as a result of diminishing of amount of peptidergic cells, that secrets somatoliberine or to insufficiency of function of the neurotransmitter system which carries out adjusting of secretion and freeing of STH in the portal system of hypophysis. The deficit of somatoliberine causes insufficiency of secretion of STH and insufficient synthesis in the liver of IFG.

1.3. Psychosocial nanism.

Psychosocial nanism is caused the unfavorable emotional and social terms of development of child, by rough deviations from the physiology norms of feed (little albumins diet, polyvitamine insufficiency). The unfavorable terms of development, insufficiency of feed, result in transitory or functional hypopituitarism with the decline of secretion of STH.

Psychosocial nanism is characterized by the expressed delay of growth and signs of deficit of albumens and vitamins, dry inelastic skin, delay of sexual development, inadequate food and social conduct. At normalization of diet and social terms of development the state of the hypothalamic-hypophysal system gets better, the secretion of growth hormone quickly recommences to the norm.

2. Inherited, or domestic form:

2.1. Isolated insufficiency of STH of 1A of type.

Characteristic complete pre- and postnatal insufficiency of endogenous secretion of STH and antibodies to the hormone, which lock him anabolic effect, appear at introduction of exogenous STH (attempt of treatment).

The variant of nanism is given differs the low (not added determination) level of growth in the whey of blood hormone and high maintenance of antibodies to STH at treatment of patients by a growth hormone.

2.2. Isolated insufficiency of STH of 1B type

The table of contents of growth in the whey of blood hormone is reduced, but not full absent, as at a 1A type, there is not formation of antibodies to exogenous STH – therapy gives a good clinical answer to growth hormone.

2.3. Isolated insufficiency of STH of 2th type.

A type of inheritance is autosome-dominant. Patients are heterozygote on this sign, have one of parents, patient with this disease. The degree of expressed of delay of growth for children and parents is different. A genetic defect is mutations with the loss of amino acid tailings from 32 to 71 in the molecule of STH.

Characteristic low maintenance of STH is in the whey of blood, the level of hormone rises in reply to stimulation. Patients well answer on treatment of growth a hormone, for them formation of antibodies is absent on exogenous STH.

2.4. Isolated insufficiency of STH of 3th type

Type of inheritance – more frequent dominant, or autosome-recession, or coupled with a X-chromosome. Genetic defect - plural locules of deletion on the gene of STH. A disease is combined from hypogammaglobulinaemia (sometimes with agammaglobulinaemia).

2.5. Domestic panhypopituitary form of insufficiency of STH.

A panhypopituitary form is characterized by insufficiency of STH, and TTH, FSH, LH and ACTH. Characteristic is combination of undersizedness with the different on expressed displays of hypothyrosis (up to cretinism), violation of secretion of prolactin in reply to stimulation of thyroliberine.

A type of inheritance can be both a autosome-recession and X-coupled. Genetic defect – mutation and deletion gene of Pit-1, which activates the gene of STH, TTH and prolactin.

3. A domestic syndrome of high maintenance of STH-linking albumen is in the whey of blood.

Typical ever-higher level of STH-linking albumen in the whey of blood – STH-linking activity of whey in 30-110 times greater, than for healthy persons. STH-linking the albumen of whey of blood reduces speed of metabolic clearance and degradation of STH. A complex of growth hormone with STH-linking albumen is biologically the nonactive form of depositing of STH. Characteristic is partial resistance to the growth hormone.

4. A defect of receptors to the growth hormone – the Larone`s syndrome

Described by Larone in 1966. A type of inheritance is a autosome-recession. Reason of disease is insufficiency (or absence) of receptors to STH in a liver and other peripheral tissues at the simultaneous decline of level (or to complete absence) of STH-linking albumen in the whey of blood. High-affine STH-linking the albumen of whey of blood identical on amino acid composition to the extra-cell domain of diaphragm receptor to STH. The synthesis of STH-linking albumen and receptor of STH is encoded one gene.

A disease is characterized low maintenance of IFG -1 and compensate promoted level of immune-reactive of STH in the whey of blood. Typical resistance is to the exogenous growth which is entered with the purpose of treatment hormone. The level of insulin-factors of growth in the whey of blood is not multiplied in reply to introduction of exogenous STH, treatment of STH not effective. However observed a positive clinical effect (multiplying speed of growth) for these patients is at treatment of them IFG -1. Therapy of IFG -1 together with a growth acceleration results in diminishing of level of growth in the whey of blood which testifies to the presence of the stored feed-back in adjusting of secretion of STH hormone.

5. Insufficiency of IFG -1

5.1. Almost absolute absence of IFG -1 is at the normal level of IFG -2

In the certain amount of cases reason of undersizedness can be insufficiency of formation of IFG -1 at the normal level of IFG -2, which has low biological activity.

5.2. Hop-o'-my-thumb of the African pygmies.

Table of contents of STH in the whey of blood for pygmies within the limits of norm, but the level of IFG -1 is considerably reduced. Correlation of STH/ IFG -1 especially changes in a pubertal period, when healthy people have an acute increase of level of IFG -1 in the whey of blood, that provides the physiology «jump of growth» of pubertal period. A genetic defect is related to violation of gene which is responsible for the synthesis of IFG -1.

5.3. Absence of receptors is to IFG -1.

5.4. Postreceptory defect of action of IFG -1.

Reason of undersizedness can be insufficiency or absence of receptors to IFG -1 or defect at postreceptory level. A decline or absence of fastening of isotopic forms of IFG -1 in different tissues testifies to pathology of receptors. About the presence of postreceptory defect in operations IFG -1 testifies the normal fastening of IFG -1 of fibroblasts at a decline or absence of absorption of amino acid these tissues.

Б. Innate defects of development of hypophysis: anencephalic, absence of front particle of hypophysis, ectopic of front particle of hypophysis, hypoplasia of visual nerves, harelip or wolfish fall.

Insufficiency of STH is purchased

1. Tumors: craniopharyngeoma, germinoma, glyoma, sarcoma of adenohypophysis.

2. Traumas: births in facial or pelvic praesentatio, intracranial hemorrhages or thromboses, asphyxia, cranial-cerebral traumas, state after surgical interference on a hypophysis or basis of skull.

3. Vascular pathology: aneurysm of internal carotid arterial and vessels of hypophysis, angioma, infarct of hypophysis.

4. Infiltrative diseases: tuberculosis, lues, autoimmunehypophysitis.

5. Radio- or chemotherapy of leukemia, retinoblastoma, other tumors of brain and neck.

6. Arachnoideal cysts, syndrome of the "empty" Turkish saddle.

Clinical picture

1. Manifestation of nanism

At birth weight and growth of patients with insufficiency of STH does not differ from healthy children. In anamnesis many the patients are had place rejection in a neonatal period: more protracted icterus of new-born, hypoglycaemia.

The first signs of disease appear for children in age 2-3, when they begin to fall behind in growth from the yearlings. Speed of growth for patients with insufficiency of STH also acute reduced and not exceeding 3-4 cm in a year (in a norm 7-8 cm in a year).

2. Delay of growth

A hop-o'-my-thumb is consider growth for men below 130 cm and for women less then 120 cm. The criterion of nanism is diminishing of growth of child on 3 and more standard deviations from middle growth in population for this chronologic age.

3. Delay of physical development

Characteristic disparity between bone (roentgenologic) and passport age, delay of differentiation and ossification of skeleton. The lines of person are shallow, juvenile: a protuberant forehead, "falling" back bridge of the nose. Bones are thin, them cortical layer is refined; quite often there are structural alteration of bones, degenerative changes of cartilages, joints, subchondral departments of bones epiphyses. Development and change of teeth is violated – baby teeth can be saved to 15-years-old age.

The proportions of body are normal, but type of body is juvenile.

The skin of patients is tender, thin, juvenile. Hairs are thin, cilia are long, juvenile.

A hypodermic-fatty layer is developed not enough. Surplus of mass of body more characteristic for the Larone`s syndrome.

Development of the muscular system is weak, does not answer to the passport age. Hypotrophy of muscles is conditioned the deficit of natural anabolic– STH, androgens.

Voice is high, child – the juvenile structure of vocal is saved connection.

4. Dysfunction of internal organs

Internal organs of small sizes (splanchnomicria), but proportional to the grow of patients. Specifically for nanism functional changes of internal organs it is not described.

Characteristic propensity to arterial low blood pressure. Low blood pressure is especially expressed at concomitant insufficiency ofadrenal glands.

Tones of heart are muffled, hearkened to functional noises in connection with the trophic changes of myocardium and vegetative violations. On the ECG – low voltage of indents, especially at presence of hypothyrosis, sometimes bradycardia. .

Mental development of patients with insufficiency of secretion of STH more frequent normal, quite often it is people with good memory and developed intellect. Reactive asthenic, neurasthenic reactions are possible, the psyche of patients is very impressionable. At the delay of sexual development marked juvenile psyches, emotional infantilism. For patients with satisfactory sexual development psycho-emotional development is adequate. At presence of concomitant hypothyrosis and patients with the syndrome of Larone have a delay of mental development.

The signs of organic defeat of the nervous system appear at presence of tumor or defeat of the hypothalamic-hypophysal system of other genesis.

5. Infantilism

There is a delay of sexual development – infantilism in most patients. External and internal privy parts are underdeveloped. The second sexual signs are developed not enough. For boys, as a rule cryptorcism appears sometimes. For the female patients menstruations are absent, not enough the developed appendages, uterus, pectoral glands. Patients with the deficit of secretion of STH more frequent sterile.

Some signs of the sexual ripening appear at the high enough individual level of remaining secretion of STH, here observed and signs ripening of bone tissue, characteristic for pubertal (closing of areas of epiphyseal growth).

Diagnostics

Determination of initial level of STH is in the whey of blood. In most patients, which suffer on the delay of growth, caused insufficiency of secretion of STH, there is statistically a reliable decline of concentration of STH to 1,34±0,29 ng/ml at the norm of 3,82±0,2 ng/ml.

Conducting of tests, directed on stimulation of secretion of STH, substantially promote authenticity of diagnosis. A lot of physiology factors (sleep, physical loading, albumins feed) and pharmacological influencing (insulin, clonidine, L-dopa and other) stimulate freeing of STH from a hypophysis. During conducting of tests with stimulation maintenance of STH is estimated in blood, taken immediately in front of by introduction of stimulator and during 3 hours through each half a hour (0; 30; 60; 90; 120; 150 minutes).

A test with insulin. Insulin is entered intravenously from a calculation 0,075-0,1 IU on 1 kg of mass of body. At adequate hypoglycaemia (below 2,2 mmol/l) healthy children have an increase of level of STH higher 35-40 ng/ml. For patients with insufficiency of secretion of growth hormone the concentration of STH does not rise higher 5 ng/ml.

A test is dangerous: many patients, which suffer on insufficiency of secretion of STH, feed a weakness to spontaneous hypoglycaemia and promoted sensitiveness to insulin, - for them deep hypoglycaemia can develop at introduction of the indicated doses of insulin. In this case it is necessary to enter intravenously glucose and hydrocortisone to the removal of hypoglycaemia.

A test with clonidine. Clonidine belongs to α-adrenergic and is one of strongest stimulator of STH. At adopting clonidine inward (0,15 mg/м^2) stove the troop landings of STH observed on 90-120th research minute. Clonidine can be entered intravenously (0,2 mkg/kg), infusion is conducted slowly during 10 minutes. The maximal freeing of STH is observed on 30th minute. Effects of sides: somnolence and arterial hypotension.

A test with L-arginine. L-arginine is amino acid with the most strong stimulant influence on the secretion of growth hormone. The 10% solution of L-arginine monochloride is entered intravenously as infusion during 30 minutes (for adult - 30 g of dry powder, for a child or for patient with nanism– 0,5 g on 1 kg of mass of body). Maximum of the STH secretions observed on 60th minute. By-effects: hypoglycemia and hyperemia of face.

A test is from L-dopa. Dophaminergetic agonist is appointed inward (10 mg/kg). Maximum of the STH secretions observed on 60-120th minute. Indirect actions: nausea, vomit, head pain. The increase of answer of STH on adopting L-dopa is observed at the previous reception of inderal from the calculation of 0,75 mg on 1 kg of mass, but not more than 40 mg.

A test with glucagons. Glucagons in the dose of 100 mkg/м^2 (maximally for the children - 0,5 mg, for adults – 1 mg; for persons with mass of body over 90 kg – 1,5 mg) entered hypodermic or intramuscular. Maximum the secretions of STH observed on 120-180th minute.

A test with somatoliberine. Somatoliberine in the dose of 100 mkg (for children from the calculation of 1-1,5 mkg/kg of mass) enter intravenously. Maximum the increase of STH observed on 30-60th minute.

Criteria of estimation of tests are with stimulation of synthesis of STH.

Normal reaction: for practically healthy persons the level of STH in the whey of blood during conducting of the transferred tests rises higher 10 ng/ml, that eliminates the presence of insufficiency of secretion of STH.

"Partial" insufficiency of STH: an increase of concentration of growth hormone is in reply to stimulation from 7 to 10 ng/ml.

"Total" insufficiency of STH: an increase of concentration of growth hormone is in reply to stimulation from 5 to 7 ng/ml.

For diagnostics of insufficiency of secretion of STH, as a rule, are not used less than 2 resulted tests of stimulants. In 25% cases during conducting of the indicated tests pseudopositive results take place, what and a conducting necessity is caused a few the stimulants the secretion of STH of tests. In addition, in 10% practically healthy persons during conducting of one of tests the adequate increase of maintenance of growth which testifies to diminishing of backlogs of STH in a hypophysis hormone is absent.

Determination of rhythm of secretion of STH is in the period of sleep: in the 3-4th stage of sleep maintenance of growth in the whey of blood hormone rises considerably, for patients it is absent with insufficiency of secretion of STH of increase.

Determination of secretion of STH is in reply to the physical loading. After 10-15 minute physical loading (veloergometer, and other.) for practically healthy persons maintenance of growth in the whey of blood hormone for certain rises in 20-40 minutes in comparing to the initial level.

Determination of STH in morning portion of urine allows to get dynamic information about the secretion of growth hormone; a method is applicable for screening of insufficiency of STH secretion.

Level of IФР-1 and IФР-2 in the whey of blood - an index is integrated, more precisely in all characterizes the secretion of STH as compared to other indexes. The table of contents of IФР-1 and his basic linking albumen represents not only the absolute level of STH in blood but also his biological activity. Determination of concentration of these indexes is especially valuable at such violations, as a syndrome of Larone or states, at what secrets biologically nonactive STH.

A test with introduction of STH during 5 days is conducted for differential diagnostics of syndrome of Larone. At the syndrome of Larone the level of IФР-1 does not rise after trial therapy of STH, while there is a reliable increase of the indicated indexes at other types of insufficiency of STH.

The table of contents of vasopressin for healthy people (on the free water mode) at radio immunologic determination makes 0,6-4,3 ng/l, at the biological testing - 0,6-4 mIUd/l. Deprivation of water during 12 hours for healthy people causes the increase of concentration of вазопресину to 7,2 mIUd/l; excretion of vasopressin in healthy with the normal consumption of liquid makes 160-1075 mkIUd/g.

Roentgenologic research of skull and the Turkish saddle allow to visualise a form and sizes of the Turkish saddle which has the diminished sizes often. Osteoporosis and thinning of walls of the Turkish saddle, expansion of his entrance appears at craniopharyngeoma, supra- or intracellular hearths of deposit of limestone. Hydrocephaly is accompanied the presence of the digital deepening and divergence of cranial stitches.

Computer tomography allows to diagnose hypo-, aplasia and ectopic of hypophysis, syndrome of the "empty" Turkish saddle, defeat of hypothalamic-hypophysal area at the diseases (histiocitosis, xantomatosis) of the systems and other by volumes processes in a skull.

Differential diagnostics

It follows to differentiate insufficiency of secretion of STH from a delay and violations of growth, caused different reasons:

1) domestic low growth;
2) growth time-lagged
3) chromosomal illnesses (syndrome of agenesia and dysgenesia of gonads, syndrome of Turner and other);
4) violation of forming of bones (achondroplasia; hypochondroplasia; syndrome of plural epiphyseal dysplasia; disease of spine);
5) primordial nanism;
6) endocrine violations (primary hypothyrosis, adrenal cortex hyperplasia, syndrome of Moriac – heavy insulin deficit diabetes of child's age which is badly compensated, syndrome of Cushing of child's age, tumors of adrenal cortex, medicinal hypercorticism, diseases which are characterized surplus formation of estrogen or androgen and early closing of areas of growth).

The delay of growth is observed at the diseases of liver: the amount of cages diminishes, that secrets IФР-1 and IФР-2; level them in the whey of blood reduced, and STH-promoted. The delay of growth is possible at the heavy diseases of kidneys (Nitrogenaemia locks the mechanism of synthesis of IФР-1 in a liver).

Treatment

Pathogenic is therapy by a growth of man hormone. At the delay of growth, by the caused insufficiency of secretion of STH, therapy is directed on multiplying growth of patients. Therapy of STH must be lifelong – after completion of induction of growth substitute therapy prevents the rapid senescence of patient preparations of growth hormone.

On this time a growth of man hormone, got the method of gen-engineering technology, is used only. For the facilitation of exact dosage and painless introduction of STH, including sick, the syringes-pens of injections, similar to the syringes-pens for introduction of insulin, are developed. Preparations of growth hormone are made not many leading pharmaceutical firms of the world: norditropine (Denmark); genotropine (Sweden); chumatrop (THE USA); saizen(Switzerland). A cost of 1 mg preparation is 40-50$ and an year expenditure on treatment of one patient account for 20 000-35 000 $.

STH is usually appointed in the dose of 0,05 mg/kg mass of body (or 0,1 IU/kg) 3 times per a week as hypodermic or intramuscular injections. Repressing is hypodermic introduction of preparation – painless, simple in a technical relation and effective enough. The induced speed of growth - 8-12 cm is maximally possible on a year. In 1-1,5 years from the beginning of treatment speed of growth goes down to 6-7 cm on a year.

Lately apply more intensive therapy: appoint STH for 0,05 mg/kg daily. The acceleration of rates of growth here is not accompanied multiplying the effects of sides. In the pubertal period the dose of STH must be multiplied in 1,5-2 times.

By-effects of therapy: STH can entail the origin of different tumors.

Anabolic steroids was widely used in 60-80th for treatment of patients with insufficiency of STH. The medical doses of anabolic steroids for some patients promoted the concentration of STH in the whey of blood, but them a growth-stimulating action was insignificant. In addition, anabolic steroids have an androgenic effect, for girls draw development of virilisation.

Synthetic somatoliberine as hypodermics or permanent pulsating therapy used for treatment of delay of growth, secretion of somatoliberine caused insufficiency. The cost of somatoliberine is considerably higher, than preparations of STH.

Gene-engineering IFG -1 is shown for treatment of delay of growth of patients which suffer on the syndrome of Larone. First used this method of treatment with the positive clinical effect by Larone in 1992

Hexareline is the analogue of STH-freeing peptide-6 which is capable selective simulated the secretion of growth hormone. Hexareline proof to the enzymes and oxidizing degradation which

multiplies his bioaccess and allows to enter intravenously, hypodermic, intranasal and per os. At intravenous introduction a capacity of hexareline is for stimulation of STH in 2 times higher in comparison from somatoliberine.

A decline and insufficiency of secretion of gonadotropins requires the proper substitute therapy. Sexual steroids have most influence on initiation of pubertal growth acceleration in comparison from STH or IFG -1. Multiplying maintenance of estradiol in plasma for girls speed up the growth in a pubertal period. To the girls time-lagged to growth at bone age 11-12 years appoint ethinile-estradiole in day's dose of 0,1 mkg/kg inward.

Growth of boys with a constitutional delay in a pubertal period depends on the volume of testicular and level of testosterone in plasma of blood in a greater degree, what from the level of STH, IFG -1 or squirrel-3 which links IFG -1. A level of testosterone is in plasma of blood, necessary for a growth acceleration, must be higher 3,5 nmol/l. In the period of penetrate for boys the greatest speed of growth is observed at the index of volume of testicular 9,6±0,3 cm^2 and levels of testosterone in plasma of 6,6±0,7 nmol/l.

To the boys at bone age 11-12 years appoint testosterone intramuscular from the calculation of 50-100 mg/m^2 surface of body on a month.

Except for setting of sexual steroids, expedient setting of gonadotropins. Chorionic gonadotropin is appointed for boys in a dose 1000-1500 IU 2-3 times per a week during 3 months with a subsequent interruption on 8-9 months

At an incomplete effect from application of Chorionic gonadotropin appoint substitute therapy exogenousandrogens: methyltestosterone in the dose of 5 mg on the day sub lingua or preparations of testosterone intramuscular 25 mg each 15 days, which do not diminish final growth.

To the girls in age more 16 years treatment by estrogen and preparations of gestagen action is begun in cycles. During the first 16-20 days each month apply estrogen (microfolline for 20 mkg on a day or etinilestradiole for 0,05-0,1 mg 2 times per a day), and in the second phase of cycle are gestagen preparations (progesterone for 5-10 mg on a day intramuscular or pregnine for 10-30 mg sub lingua 3 times per a day).

At treatment of STH it follows to avoid application of glucocorticoids, as they lock the growth action of STH full. Only at expressed hypoglycaemia and low blood pressure, other signs of the expressed insufficiency of adrenal cortex it is possible to appoint the small doses of corticosteroids.

A psychosocially correction – help in the choice of profession, social adaptation is needed.

Acromegaly. Hypophysal gigantism. Etiology and pathogencity. Clinic. Diagnostics and differential diagnostics. Treatment.

Acromegaly is a disease of the neuroendocrine system, conditioned the promoted secretion of growth (STH), which clinically appears pathological disproportionate growth of bones of skeleton, soft tissues and internal organs, hormone.

Acromegaly in most cases develops for persons with the completed physiology growth and closed epiphysal growth areas, when growth of bones in length is already impossible. A disease appears pathological disproportionate growth of bones of skeleton, cartilages and soft tissues, violation of different types of exchange of matters.

Acromegaly and gigantism is diseases of one nature, age-old variants of the same process.

Gigantism is a juvenile variant of акромегалії, the hypersecretion of STH arises up early in life, there is proportional, but surplus growth of all skeleton and other organs and fabrics to closing of epiphysal areas of growth - gigantism develops. Clinically gigantism appears proportional surplus growth higher 190 cm. At the protracted presence of hypersecretion of STH without adequate therapy for patients with gigantism there can be signs of acromegaly. Very rarely the hypersecretion of STH in child's age at the opened areas of growth is accompanied not gigantism, but acromegaly.

Acromegaly is a rare enough disease, поширеність makes 40-70 cases on a 1 million population, and morbidity is 3-4 cases on 1 million Meets practically identically often both for men and for women. Most frequent age of manifestation of acromegaly - 35-45 years.

Etiology and pathogencity

Acromegaly is a syndrome reason of which can be a defeat of CNS at different levels and exceptionally rarely – not cerebral factors.

1. Somatotropinoma is a primary tumor of hypophysis with the autonomous hypersecretion of STH, is reason of акромегалії in 95% cases. Somatotropinoma – hormonal active tumor which consists the eosinophil's cells, that superfluously secrets STH. Genetic reasons of origin of somatotropin are activating of oncogens of dominants or inactivation of suppressing genes of tumors of recessions. In 50% cases of somatotropinoma there is deletion of 11-th chromosome or mutation of Gsp-gene.

2. Ectoped hormonal active tumors of different localization (APUD-oma), that secreting STH, are reason of acromegaly or gigantism in 1% cases. Retrohypophysary tumors which carry out the ectopic secretion of growth hormone can have various localization - cancer of pectoral gland, ovaries, lungs, pancreas, intestine. High maintenance of growth hormone is determined in tissue of such tumors, and after the delete of tumor maintenance of STH and IFG-1 in the whey of blood is normalized.

3. Primary pathology of hypothalamus is with second hyperplasia of cells of hypophysis. The cases of development of illness are described after a trauma, pregnancy, in a climacteric period; infectious processes have an especially large value in a hypothalamic area.

4. Increase of sensitiveness of peripheral tissues to STH or somatomedines is a clinic of acromegaly in 3% patients develops on a background normal maintenance of STH.

A basic metabolic effect of growth hormone is strengthening of synthesis of albumen. That is why at his hypersecretion there is strengthening of anabolic processes as intensive growth of bones of skeleton, multiplying the volume of muscles and internal organs (splanchnomegalia).

Clinical displays

1. Change of exterior.

For patients with acromegaly «distant » diagnostics is possible – a previous diagnosis can be set «at first blush» after the specific changes of exterior.

Facies acromegaly – the typical change of exterior is done patients alike on each other. Growth of bones of skull, especially face, appears – the bulge of superciliary arcs, bones of cheek-bones and chin is multiplied, a lower jaw is given out ahead, a nose is prolonged.

Macroglossia (multiplying a language) is with the imprints of teeth on lateral surfaces.

Mutation of voice – voice becomes low as a result of proliferation of cartilages of larynx and vocal connection.

A bite (prognatismus) is violated, dental intervals broaden (diastema).

Increased in the sizes of brush and foot - patients are forced often to change a shoe and gloves.

Brushes are wide, fingers are thickened and seem shortened. A width and length of foot is multiplied.

Deformations of skeleton of expressed arise up in heavy cases of disease: kiphoscoliosis, thorax acquires tubby form.

Acromegaly arthropathy is conditioned excrescence of cartilaginous tissue, appears pains in joints and their bulge, deformation.

2. Change of skin

Skin is thick, deep folds (especially on the back of head) appear as a result of active proliferation of components of connecting tissue. A skin on brushes and feet is considerably thickened, especially on palm's surface.

A skin is moist and fat, with the expressed pores as a result of гіпертрофії of glands of sweats and greasy.

Hypertrychosis is conditioned by hypertrophy of follicles of hairs.

Hyperpigmentation of skin is most shown in the area of folds of skin and in the places of the promoted friction, at acromegaly observed infrequently, as a rule, at concomitant relative adrenal insufficiency.

3. Myopathy

Real hypertrophy of muscular fibers is observed only at the beginning of disease, accompanied the of short duration increase of physical force and capacity.

Proximally myopathy develops to the measure of origin of dystrophic and fibrous changes in muscles, shows up a muscular weakness, gross violations of electric activity of myofibrils (from data ofelectromyography) and making progress morphological violations (from data of biopsy).

4. Peripheral neuropathy

Acroparaesthesia of different expressed is observed in 30-40% patients, conditioned squeezing of nervous barrels by the thickened fibrous vaginas, fillings out soft tissues.

Peripheral polyneuropathy is conditioned the bulge of perineural structures. Patients are disturbed by weakness in the separate groups of muscles, limitation and sickliness of motions is possible.

Carpal syndrome is a anesthesia fingers of hands as a result of squeezing of middle nerve in a carpal channel.

5. Defeat of the central nervous system.

There is an increase of intracranial pressure at the considerable sizes of tumor (3-5 cm is in a diameter). Going out outside the Turkish saddle and disposed supracellular, a tumor carries out pressure on the located alongside cerebral structures. The symptoms of violation of function of cranial nerves and departments of intermediate brain constrained a tumor appear on the measure of growth of tumor on leaving of her outside the Turkish saddle.

Head pain, at first episodic, gradually increases and can gain intensive, permanent character. Head pains are very strong now and then, take a patient to complete exhaustion. Head pain is localized usually in frontal-temporal areas, in the area of superciliary arcs, carried eyeballs. Pains are the tumors of hypophysis related to pressure on the diaphragm of the Turkish saddle, with tension of hard brain-tunic in the places of attachment of her to the bones of skull or with the increase of intracranial pressure.

Head pain can be combined with dizziness, by noise in ears, by violation of sleep.

An asthenic syndrome is typical enough are complaints about crabbiness, general weakness, broken, decline of capacity

Вогнищеві neurological symptoms are conditioned squeezing of near-by fabrics of cerebrum a tumor.

1. Violations of sight (decline of sharpness of sight, stagnant phenomena on an eye day, bitemporal hemianopsia on red, and then and on a white color) appear at squeezing of crossing of visual nerves. At ophthalmoscopy find out venous stagnation, was swollen atrophy of visual nerve, development of complete blindness is possible.

2. Violation of sleep (a somnolence is promoted), episodes of hyperthermia, symptoms of Diabetes insipidus (polyuria, thirst), appear in the case of growth of tumor in the direction of hypothalamus.

3. Epilepsy, homonymic hemianopsia is observed in the case of tumor invasion in a temporal

area.

4. Ptosis, ophthalmoplegia, neuralgias, the declines of ear are formed at development of tumor toward cavernous sinus and kernels III, IV, V, VI pair of brain nerves.

6. Splanchnomegalia.

Acromegaly is accompanied with hypertrophy of internal organs. Lungs, liver, stomach, kidneys on sizes and mass in 2-4 times exceed a norm. Multiplying parotid glands appears also.

6.1. Defeat of myocardium

Cardiomegaly - one of displays of splanchnomegalia. More than in 15% has patients place the expressed increase of sizes and mass of heart to 1-1,3 kg In 65-80% patients moderate hypertrophy of the left ventricle appears. “Acromegalic cardiomyopathy” is observed rarely enough, on the late stages of disease, characterized heavy cardiac insufficiency.

The mechanisms of defeat of myocardium at acromegaly are various.

1. Myocardial dystrophy and кардіосклероз is formed as a result of overwhelming excrescence of connecting fabric and inadequate hypertrophy of myofibrils.

2. Dysfunction of valvular vehicle is conditioned disparity of valvular structures the megascopic sizes of chambers of heart.

3. The blockades of heart are caused by fibrosis of atrio-ventricular partitions.

4. Arterial high blood pressure is observed in 25-35% patients and accompanied the increase of loading on myocardium. The increase of arterial pressure is conditioned narrowing of peripheral vessels as a result of proliferation of smooth and shiny muscles. Secondary hyperaldosteronism.

5. Making progress atherosclerosis is caused atherogenic violations of lipid exchange.

6.2. Defeat of breathing organs.

The decline of a vent function of lights is conditioned by kiphoscoliosis, limitation of mobility of ribs, decline of muscular force of respiratory muscles. A thorax takes бочкоподібної shape.

Hypertrophy of cartilages of bronchial tubes causes forming of syndrome of bronchial obstruction. A chronic bronchitis, emphysema of lungs, join easily. At acromegaly respiratory and lungs-cardiac insufficiency is quickly formed.

6.3. Defeat of gastro-enteral highway.

Hepatomegaly and fibrosis of liver can be accompanied hepatic-cellular insufficiency.

Polyposis of intestine is observed in 50% patients with acromegaly.

6.4. Endocrine violations

From the side of endocrine glands there is a diphasic reaction. At the beginning of illness the increase of formation of trophic hormones of hypophysis, which clinically appears hyperplasia and increase of function thyroid and parathyroid glands, and also hyperfunction of adrenal and sexual glands is possible..

Dysfunction of thyroidal gland.

A knot goiter, more frequent without violation of function of thyroidal gland, is observed in 50% patients with acromegaly.

Pseudothyrotoxicosis is clinical signs of increase of function of thyroidal gland (palpitation, crabbiness, increase of basic exchange) on a background normal absorption of radio-active iodine by a thyroidal gland and level of thyroidal hormones in blood observed quite often, but does not require an additional correction.

Hypothyrosis can develop after the conducted treatment of acromegaly (X-ray-therapy, implantation in the hypophysis of radioactive yttrium or gold, hypophysectomy, criotherapy, irradiation by proton bunch) with destruction of part of intact tissue of hypophysis which results in the decline of products of TTH.

Violation of carbohydrate exchange.

Violation of tolerance to glucose is observed in 60% patients withacromegaly. Reason of violation of carbohydrate exchange is stimulation of gluconeogenesis surplus of STH on a background normo- or hyperinsulinaemia.

20% patients with acromegaly have saccharine diabetes, as a rule, at motion of easy or middle weight. Typical isinsulin-resistance: diminishing of amount of receptors to insulin and relative insulin insufficiency cause a compensate increase of products of insulin (hyperinsulinism). The table of contents of immune-reactive insulin in the whey of blood of patients with acromegaly is promoted and on an empty stomach, and in reply to loading glucose. Hyperlipidaemia which locks glycolysis in peripheral tissues strengthens violations of exchanges. Diabetes at acromegaly is resistant to insulin-therapy, compensated by biguanids. Remission of disease is accompanied the improvement of motion of saccharine diabetes. Decompensation of carbohydrate exchange testifies to progress of acromegaly.

Dysfunction of sexual glands.

Violation of menstrual cycle up to amenorrhea is present in 70-80% women with acromegaly.

Lactorrhea appears in 30-40% women with acromegaly. A symptom is investigation of increase of secretion of prolactin or result of surplus of STH, which also has a lactogenic activity. Lactorrhea for men with acromegaly, meets extremely rarely.

The decline of potency and libido, violation of spermatogenesis and atrophy of testicles, take place in 30-45% men with acromegaly.

Features of motion of acromegaly.

Stages of development of acromegaly.

Preacromegalic the stage is characterized the most early signs diseases which usually are heavily diagnosed.

The hypertrophy stage is registered at presence for the patients of the characteristic for a disease phenomena of hypertrophy and hyperplasia of tissues and organs.

The tumor stage is characterized prevailing of signs of the pathological influencing of tumor of hypophysis on surrounding tissues - increases of intracranial pressure, eye and neurological violations.

Phases of disease: the active and stable phases of acromegaly distinguish on the measure of expressed of activity of pathological process. The criteria of activity of process is:

1 – renewal or growth of head pain;

2 – a subsequent increase of extremities (to the size of shoe);

3 – multiplying the sizes of the Turkish saddle (roentgenologic);

4 – an increase of maintenance of STH and inorganic phosphorus in the whey of blood.

Variants of motion of acromegaly: benignant and malignant.

Benignant more frequent appears for patients more than 45 years. A disease begins slowly, without the expressed clinic-laboratory signs of activity of process. Without treatment patients live from 10 to 30 and more years.

At malignant motion a disease arises up in junior age, characterized quickly making progress development of clinical symptoms, considerable increase of sizes of tumor of hypophysis with overrun of her the Turkish saddle and violation of sight. In default of timely and adequate treatment life-span patients makes 3-4 years.

The central forms of acromegaly are divided on hypophysal and hypothalamic. The benignant variant of motion is more frequent at the hypothalamic form of acromegaly, malignant - at a hypophysal form.

Additional researches

Biochemical researches.

Hyperlipidaemia. The acceleration of processes of lipolysis and oxidization of fats in peripheral tissues is accompanied the increase of maintenance in the whey of blood of non-aetherificated fat acids, cholesterol, lipoproteins, even ketone bodies. The increase of triglycerids and non-aetherificated fat acids in the whey of blood appears in 40% patients. Than disease makes progress as more active, as higher is level of non-aetherificated fat acids in blood.

The indexes of basic exchange rise: oxidization of substrates in basal terms at acromegaly is promoted in comparing to the norm, that is conditioned chronic surplus of STH and IФР-1.

Strengthening of synthesis of nucleic acids and albumen causes the delay of nitrogen in an organism.

Violation of mineral (phosphoric-calcium) exchange. Hyperkalaemia and hypercalcemia, that observed at the active phase of acromegaly, explained influencing of growth on the processes of reabsorbing of these elements hormone in kidney canals- by the increase of reabsorbing of phosphorus and diminishing of reabsorbing of calcium. In the active phase of disease maintenance of inorganic phosphorus in the whey of blood was for certain promoted 4,84±0,03 mg% (at the norm of 3,43±0,07 mg%). For patients which are in the phase of remission without the clinically expressed signs of progress of disease, maintenance of inorganic phosphorus in the whey of blood makes 3,71±0,19 mg%. For the active phase of disease a characteristic increase of excretion of calcium is with urine to 462,34±34,71 mg/day; while for patients stabilizing of disease appears in which, these indexes were at the level of 299,77±37,91 mg/day.

Roentgenologic researches.

Sciagraphy of bones of skeleton. Periostal appear hyperostosis in combination with osteoporosis.

Sciagraphy of skull. Characteristic bulge of bones of skull, conditioned hyperostosis of internal plate of bones of skull, especially in the area of frontal bone. The sizes of the Turkish saddle are substantially multiplied in 70-90% cases. Somatotropinoma practically in 100% cases are microadenoma (diameter 13 mm and anymore), that facilitates diagnostics – results in multiplying the sizes of the Turkish saddle which appears on the sciagrams of skull, instead of only at implementation ofcomputer tomography.

Sciagraphy of spine. Kyphoscoliosis is possible.

Sciagraphy of feet. Similar changes, excrescences of "spurs", are on the bones of heels. A characteristic increase of thickness of soft tissues of sole of foot, this symptom, is the diagnostic criterion of acromegaly. In a norm a thickness of soft tissues of foot is in an area of heel less than 22 mm, and for patients with acromegaly the thickness of soft tissues of foot always any more than 22 mm.

Change of hormonal balance.

A basal secretion of STH is a primary test. The table of contents of STH in blood is determined not less 3th times with an interval 1-2 days. The table of contents of growth in the whey of blood hormone for patients with the active phase of disease makes 20,51±2,06 ng/ml at the norm of 3,82±0,24 ng/ml.

The average daily level of growth in the whey of blood (the concentration of STH is integrated after 24h.) hormone at acromegaly in 3-10 times exceeds this index for practically healthy persons. In a norm maintenance of growth hormone for a day is near to the low bound of sensitiveness of method, and in midnight and a few subsequent hours there are lances of increase of concentration of STH. For patients with acromegaly this periodicity of secretion of STH is broken and the numbers of maintenance of growth in the whey of blood hormone for a day long remain high.

Monitoring of day's secretion of growth hormone foresees забір of blood for research each 5-10 minutes during 24 h by the special catheters. For patients with acromegaly day's rhythm of pulsating secretion of growth hormone is violated - the amount of discrete waves of pulses is times multiplied in 2-3.

Concentration of інсуліноподібного factor of growth -1 (IFG-1) in the whey of blood is the most adequate test for diagnostics of acromegaly. A level of ІФР-1 in the whey of blood is the integrated index of secretion of STH after 24 h, as there is direct correlation between the level of ІФР-1 in the whey of blood and level of day's secretion of STH. For acromegaly is characteristic increase of maintenance of ІФР-1 is in the whey of blood, which in a norm makes 0,4-2,0 IU/l.

As an increase of level of STH in the whey of blood meets at the neurogenic anorexia, chronic kidney insufficiency, cirrhosis of liver, insufficiency of albumins feed, is conducting of functional tests on stimulation and oppressing the secretion of growth hormone.

Functional tests which stimulate the secretion of STH.

A test is from insulin. Insulin is entered intravenously one-moment from a calculation 0,2-0,3 IU/kg of mass of body. Blood for determination of STH is taken 30 minutes prior to introduction of insulin, and through 15, 30, 60, 90 and 120 minutes after introduction of insulin. Hypoglycaemia, caused introduction of insulin, is powerful stimulator of secretion of STH for healthy people. During conducting of test from insulin for patients with acromegaly maintenance of growth in the whey of blood hormone to 60-th minute after introduction of insulin rises not enough (in relation to an initial size) and remains such to 120-th minute of research.

A test with thyroliberine. Intravenously one-moment enter 200-500 mkg of thyroliberine. Measure maintenance of STH 30 minutes prior to stimulation and through 15, 30, 60, 120 minutes after introduction.

For the practically healthy persons of introduction of thyroliberine practically does not influence on maintenance of STH. At acromegaly, especially in an active phase, the increase of level of STH appears during a test (in 30-120 minutes) on 200% and anymore in relation to a базального level (what in an initial test already substantially exceeded normal values). This change of sensitiveness of somatotrophes to thyroliberine for patients with aacromegaly so specific, that this test is used for diagnostics and differential diagnostics of aacromegaly, and also for the estimation of efficiency of treatment of acromegaly. Pseudopositive results take place for patients with heavy pathology of liver, kindeys, at nervous anorexia.

A test with somatoliberine. Enter intravenously one-moment 100 mkg somatoliberine. Measure maintenance of STH 30 minutes prior to stimulation and through 15, 30, 60, 120 minutes after introduction ofstimulator. For acromegaly a characteristic hyperergic reaction of secretion of growth hormone is on introduction of somatoliberine.

A test is with agonists of dopamine (L-Dopa, parlodel and other). Stimulators of dopaminergetic receptors in a norm stimulate the secretion of STH, while for patients with acromegaly there is a paradoxical decline of level of STH in the whey of blood under act of agonists of dopamine.

Agonists of dopamine appoint inward (L-Dopa - 500 mg, parlodel – 2,5 mg). In the morning on an empty stomach by patient twice is taking blood for determination of maintenance of STH. The repeated tests of blood take through 2 and 4 hours after adoptingof stimulator. During all test a patient does not adopt a meal and must be in horizontal position abed - there can be orthostatic low blood pressure at an attempt to get up, sometimes collapse, loss of consciousness.

Adopting agonists of dopamine in healthy or patients which have an increase of basal maintenance of growth in the whey of blood hormone without acromegaly, draws the considerable increase of concentration of STH through 2 and 4 hours after adopting preparations. At акромегалії adopting agonists of dopamine causes the paradoxical considerable decline of level of growth in the whey of blood hormone. A test is considered positive, if in 4 hours after a reception the level of growth hormone goes down on 50% and anymore from базального. A test with agonists of

dopamine allows simultaneously to define and efficiency of possible subsequent therapy by these preparations.

Functional tests are on oppressing the secretion of STH.

Glucose-tolerance test. Research is conducted on an empty stomach after finding sick at peace not less than 30 minutes, whereupon draw a sample of blood for determination of initial level of STH and glucose. After it a patient adopts solution which contains 75 g glucose, and through 30, 60, 90 and 120 minutes take the standards of blood for determination of those indexes (glucose and STH).

In a norm in the 60th minute in blood maintenance of growth in the whey of blood hormone goes down below 2 ng/ml. In the active phase of acromegaly the decline of level of hormone is absent below 2 ng/ml during 2-3 hours (a test is positive). Moreover, often there are the "paradoxical" troop landings of hormone in reply to loading glucose. A test carries double information: he allows also to estimate the state of carbohydrate exchange and find out violation of tolerance to glucose.

On ECG: find out the symptoms of violation of intraventricular conductivity, expansion of complex QRS, decline of interval of ST.

Differential diagnosis

Recklingshausen`s disease (hyperparathyrosis) develops at the adenoma of parathyroidal glands. Thus there is deformation of spine and tubular bones, increase and bulge of bones of skull. The distinctive signs of this disease is osteoporosis, presence of typical cystosis areas in bones, spontaneous breaks in default of multiplying the Turkish saddle and acromegaloid lines.

Padgett's disease (deforming osteoarthritis) is characterized a little facial particle and considerable increase of frontal and parietal bones (tower skull). The proximal particles of tubular bones are megascopic and thickened, Turkish saddle of normal sizes.

Hypertrophic osteoarthropathy is accompanied the phenomena of periosteal proliferation of bones, bulge of skin and some increase of nose, ears, feet.

Acromegaly: the exterior of "acromegaloid" patients is very alike with the exterior of most patients with acromegaly. Distinguishing features: the bulge of skin and multiplying the Turkish saddle is absent, level of STH in the whey of blood in a norm and stimulation of his secretion appears in reply to introduction of insulin, the function of other endocrine glands (sexual glands, pancreas,adrenal glands) is not broken.

Plural endocrine adenomatosis can flow with the presence of adenoma of hypophysis, and also adenoma of parathyroidal glands, which is accompanied the clinic ofhyperparathyrosis, as a rule, his domestic forms are adenomas of islets of pancreas with the clinic of insulinoma, and adenomas of hypophysis with the clinic of prolactinoma, to the syndrome of Cushing or acromegaly.

Cerebral gigantism can be inherited as a autosome-recession disease. Some clinical symptoms appear already at birth: dolichocephalic, high sky, prognatism, low blood pressure, different anomalies of skeleton. The table of contents of STH in the whey of blood does not differ from a norm. There is other type of "cerebral gigantism" which characteristic by macrocrania, large feet, signs of dysfunction of brain, mental backwardness. The secretion of STH also is not changed. Possibly, cerebral gigantism is related to violation of day's rhythm of STH or yet not identified peptides which have effects of IFG-1 and somatotropin.

The syndrome of Backwich-Widemann meets very rarely. Except for gigantism, there is exophthalmos, macroglossia, visceromegalia, hypoglycaemia is possible as a result of hyperinsulinism. The secretion of STH is not broken.

Treatment

Treatment of акромегалії is directed on the decline of level of growth in the whey of blood

hormone by oppression, destruction or delete of active STH-secreting of tumor which is achieved by radiological, surgical, pharmacological methods and by their combination. At the choice of method of treatment it is necessary to take into account the aggregate of factors: 1 – sizes and character of growth of adenoma; 2 – the state of sight; 3 – level of growth hormone; 4 – age of patient; 5 – presence for the patient of heavy high blood pressure, ischemic heart trouble and others.

A testimony is to surgical treatment of acromegaly: violation from the side of sight and neurological disorders, great head pains, propensity to progress of disease, ineffectiveness of medicinal therapy.

Medicinal therapy can be used at contra-indications to operative treatment or independently. Most expressed repressing operating on freeing of STH by adenoma of hypophysis discover the agonists of dopamine: l-dopa and especially parlodel.

Parlodel is the most popular in medical practice preparation, is the half-synthetic alkaloid of ergot, electorally and lasted locks a somatotrophic secretion. Taking into account that in the first days of adopting preparation there can be by-effects as nausea, low blood pressure. Parlodel recommend to accept, beginning from small doses. First day appoint 1,25 mg are 1/2 pills, in next 4 days the dose of preparation is multiplied to 10 mg on a day and before the week is out a patient accepts for 20-25 mg on a day: for 2 pills 4 times per a day with an interval at 6 h during a meal.

Other agonists of dopamine is used (metysergidum, pergolidum, and other).

Sandostatinum (octreotidum), analogue of somatostatin, the period of half-decay of which in the whey of blood makes about 90 minutes, lasted represses freeing of STH and in healthy, and for patients with acromegaly (more than 8 hours). At hypodermic introduction of sandostatinum more than to 20 times stronger represses freeing of growth hormone, than somatostatin. Decline of level of STH and IFG-1 in the whey of blood more than on 50% it is discovered for all curated patients with acromegaly, and almost in halves maintenance of growth hormone was below 5 ng/ml.

Sandostatinum appoint for 100 mkg hypodermic 3 times per a day. It should be noted that for some patients the effective dose of preparation (what normalize secretion of STH) makes 100 mkg on days, while in other its increase is needed to 1000 and even 1500 mkg on days, that it is related to the different amount of receptors to somatostatin on the membranes of cells of adenoma of hypophysis.

Treatment of sandostatinum can be accompanied by-effects as a decline of appetite, nausea, vomit, was ill in a stomach, promoted gasification in an intestine, diarrhoea, steatorrhoea and more rarely is swelling of stomach, great pain in a epigastric area. Sandostatinum apply before conducting of surgical treatment, and also in the case of relapse or ineffectiveness of the conducted radial treatment of acromegaly.

Obesity. Etiology and pathogenicity. Classification. Clinic. Diagnostics. Treatment. Children and teenagers have obesity.

Obesity is a disease which flows with violation of exchange of lipids and increase of mass of body.

Obesity of different degree appears at a 12% population, considerably more frequent for women (18,5%), than for men (7,8%), rarer among the people of manual labor (10,6%), than for engineer-technical workers (13,1%). Among school-age children obesity is observed in 11,2%. Surplus of mass of body on 20-55% diminishes life-span on 3,3.

Fat tissue is independent education which develops from the special reticular rudiment. There is education and deposit of fat in fat tissue. She executes three functions: a synthesis of triglycerids is from lipids and glucose; saving of them is in fatty depots; liberation of free fat acids (lipolysis).

In a mature fatty cage a cytoplasm is expressed round a kernel and contains the lipid including. The membranes of fat cages have highly sensitive receptors to all hormones.

Etiology and pathogenicity

External and internal factors, which result in disparity between the amount of energy which is outlaid, and receipt of power substrates, have a large value in an origin and development of obesity. A leading place occupies an alimentary factor, development of obesity as a result of surplus consumption of meal, foremost carbohydrates which are easily mastered in an organism. The surplus entering organism of food matters results, that they grow into a fat depot.

The most frequent obesity develops for adults after 40. Together with the change of activity of ductless glands and decline of oxidizing processes, a value is certain in development of obesity for seniors have violation in the enzymic systems.

Usually obesity for women develops in 2 times more frequent than for men.

Principal reason of obesity consists in violation of central nervous mechanisms of regulators, auxiliary factors is a surplus consumption of meal and hypodynamia.

Important part in development of obesity is acted by violation of hypothalamic centers: stress factors (supercooling, overheat), psychical traumas, traumas of skull, neuro-surgical interferences, intraperitoneal damages of skull, neuroinfections, rheumatism, quinsy, malaria, tubercular meningitis, epidemic parotitis. At the insufficient function of hypophysis the products of thyrotropin diminish and to lipotropin, the function of aits vehicle of pancreas rises, there is braking of mobilization of fat, passing of carbohydrates is increased to fats, the consumption of carbohydrates is multiplied tissues, in this connection the level of sugar goes down in blood and there is feeling of hunger.

There is expressed hyperlipidemia at the deficit of thyroidal hormones, Hypercholesterolemia and the deposit of fat increases in tissues.

Considerable influence on a fat exchange does adrenal cortex. The most substantial role belongs to glucocorticoids which are instrumental in multiplying maintenance of fat in an organism as a result of strengthening of processes of lipogenesis. At the protracted surplus of cortisol there is hyperlipidemia and Hypercholesterolemia. Disorder of water-salt exchange for patients with obesity in sort bind to violations the mineralcorticoid functions of adrenal cortex as a result of the promoted secretion of aldosterone.

There is intercommunication between development of obesity and insufficient function of sexual glands. Quite often obesity is observed for men which are ill on primary hypogonadism, adipose-genital dystrophy, syndrome of Kleinfelter. For women obesity more frequent meets at pregnancy and in a climacteric period.

Distinguish three as a segmental deposit of fat: overhead, middle and lower. Segmental obesity is bound to violation of trophic and regulative functions of the central nervous system (through likable and parasympathic systems).

Classification

Classification of obesity (Shurygin, Vositsky, Sidorov)

1. Forms of primary obesity:
1.1. Alimentary-constitutional obesity.
1.2. Neuro-endocrine obesity:
1.2.1. hypothalamic-hypophysal obesity
1.2.2. adiposo-genital dystrophy (for children and teenagers).
2. Forms of the second (symptomatic) obesity:
2.1. Cerebral.
2.2. Endocrine:
2.2.1. hypothyroid
2.2.2. hypoovarial
2.2.3. climacteric
2.2.4.adrenal.

3. Stages of obesity:
3.1. making progress;
3.2. stable.
4. Degrees of obesity:

- first degree (actual mass of body exceeds "ideal" no more than on 20%)
- second degree (surplus of mass of body is 30-49%)
- third degree (actual mass of body exceeds "ideal" on 50-99,9%)
- fourth degree (actual mass of body excels "ideal" on 100% and anymore).

Alimentary-constitutional form of obesity: there is overeating or asymmetric feed at the sharply limited physical loading, near relation suffer on by obesity.

Hypothalamic-hypophysary form of obesity: for patients surplus of mass, there is violation of function of hypothalamus (disorder of sleep, polydipsia, early violation of sexual function, proof high blood pressure). The deposit of fat is observed in the area of stomach, pelvic belt, trunk, pectoral glands, face. For patients the signs of syndrome of Cushing are absent, but the expressed high blood pressure appears.

An adipose-genital syndrome is characterized making progress obesity, delay of growth and development of the sexual system. To adipose-genital dystrophy those cases of disease belong for children and teenagers functional violations of the hypothalamic-hypophysary system lie in basis of which.

Clinical displays of obesity

For determination of middle (normal) mass of body and diagnostics of obesity the row of methods is offered.

1. Index of Broke: normal mass of body of person is in kg: growth (cm) - 100.
2. An index of Brateman: normal mass of body is even: [growth (cm) of x 0,7] minus 50.
3. Index ofDavenport: [mass of body (g) / growth (cm)] ^{2}
Index higher 3,0 testifies to the presence of obesity.
4. Index of Borogard [growth (cm) × volume of thorax (cm)] / 240
If exceeds a norm on 15-30 – obesity.

Indexes are indicated counted on men in age 25-30, which have a normosthenic constitution and middle development of musculature.

The method of determination of thickness of fold of skin (by A. Corovin) is used also in an infracostal area (in a norm she makes 1-1,5 cm). Thickness of basis of fold more than 2 cm testifies to obesity.

For practical aims at the calculation of ideal mass of body use tables, which are fixed in basis of the indexes of growth, age, feature of constitution.

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Periodically patients grumble about feeling of hunger, weakness, пітливість, shaking of extremities, dizziness, decline of physical and mental capacity, common indisposition, head pains, feeling of weight in a head, shortness of breath at the physical loading. Similar attacks more frequent arise up in the evening or at night.

There is thirst at the hypothalamic-hypophysal forms of obesity, an appetite, somnolence, is promoted.

A languor, apathy, sensitiveness to the cold, constipations, prevail at the hypothyroid forms of obesity.

At the defeat of the cardiac system there is a shortness of breath, palpitation, pains in the area of heart, edema. Sometimes patients complain on pain in joints, muscular pains and pains in a lumbar area.

At hypothalamic-hypophysal forms of obesity of deposit of fat determined mainly in the area of face, humeral belt, pectoral glands, stomach and extremities.

At hypoovarial obesity fat deposits are localized mainly in the area of pelvis and thighs, sometimes in a cervical area. At hypothyroidal obesity the division of fat is even.

Skin covers at obesity can be normal, pale or reddish coloring. For the persons of young age the narrow are sometimes determined, reddish color, atrophy character of striae, located on the skin of stomach, pectoral glands, on the internal surfaces of shoulders and thighs. As a result of stagnant character of circulation of blood there are changes of vascular network of skin and hypodermic cellulose, that appear development of telangiectasia.

As a result of local violation of blood circulation promoted loading on a joint vehicle atrophy of muscles and defeat of skeleton appears through large mass of body. Osteochondrosis develops, osteoarthritis, oosteoporosis.

As a result of considerable accumulation of fat and loosening the wall of stomach there are umbilical and inguinal hernia, divergences of direct muscles of stomach.

At obesity all organs and systems of organism are struck, but the cardiac system suffers more frequent in all. Arterial pressure rises for every fourth patient. The height of arterial pressure depends on the degree of obesity.

The increase of arterial pressure for burly patients is related to disparity of megascopic minute volume of blood and body volume of vascular river-bed not changed at multiplying mass. At the accumulation of fat mechanical resistance of current of blood and strengthening of metabolic processes is multiplied in an organism.

The deposit of fatty fabric conduces to the increase the area of vascular river-bed, hampering his adjusting and promoting origin of vascular dystonia.

For all forms of obesity characteristic increase of precapillary resistance of current of blood which can be caused the neurohumoral influencing (sympathicotonia) and mechanical obstacle (multiplying the volume of fat tissue).

In connection with high blood pressure, loading is multiplied on myocardium, the hypertrophy of the left ventricle, more liquid expansion of heart, appears in a diameter. Except for the overload of myocardium by high blood pressure, work of heart is laboured through mechanical obstacles (the high standing of diaphragm, fatty deposits is in an abdominal region, muscle of heart and pericardium). The deposits of fat between muscular fibers cause dystrophy of myocardium, and then and atrophy. Dystrophic changes in a heart meet in 23% burly patients and observed more frequent for women, than for men.

Obesity is instrumental in also atherosclerotic changes in the cardiac system. Consider that obesity in itself potent development of atherosclerosis. The amount of fat is megascopic multiplies loading on a heart and vessels and potent development of atherosclerosis. Brings dystrophic changes over in myocardium and atherosclerotic process to the noticeable decline of retractive ability of muscle of heart.

Obesity influences also on the functional state of lungs. A leading role in violation of function of lungs at obesity is played by a mechanical obstacle. Difficulty of breathing arises up not only in connection with the high standing of diaphragm, and also with squeezing of veins of back mediastinum which conduces to venous stagnation in a pleura and accumulation of liquid in the cavities of pleurae.

There is respiratory insufficiency with relative hypoventilation and as a result – hypercapnia with the insufficient satiation of arterial blood by oxygen and pulmonary hypertension. Obesity is accompanied diminishing of expiration volume of breathing and development of a vent insufficiency. Hypoventilation is the sign of lungs-cardiac insufficiency.

In 1956 the syndrome of Pickwick is described, which appears the expressed obesity, somnolence, cyanosis, periodic breathing, cramps, polycythaemia and hypertrophic of the left

ventricle. There is an idea, that a syndrome of Pickwick is a disease of diencephalon genesis. In behalf of it testifies circumstance that for children neuroinfection precedes development of syndrome of Pickwick.

For patients with obesity the diseases of digestive highway appear often. The increase of pressure is instrumental in it in an abdominal region, loosening the regulative influencing of muscles of abdominal press as a result of weakness of muscles, and also stagnation of blood in venous interlacements of organs of abdominal region.

Next to the signs of decline of concentration function of kidneys, almost in the halves of patients proteinuria appears with obesity, sometimes microhaematuria which is combined in a number of cases with leucocituria and cilindruria, which bind to the stagnant phenomena in kidneys.

The signs of defeat of the nervous system appear at all forms of obesity. At obesity consider direct influence of the promoted level of corticosteroids reason of neurological symptoms on nervous tissue, violation of cerebral circulation of blood on soil of hypertension and as a result of the promoted intracranial pressure. All neurological symptomatic can be divided into the row of syndromes:

а) syndrome of defeat of hypothalamic structures;

б) syndrome of dissipated organic microsymptomatic;

в) syndrome of irritation of peripheral nervous structures;

Hypothalamic-hypophysal obesity is investigation of diminishing of secretion of trophic hormones, increase of function of insular vehicle of pancreas, which results in braking of mobilization of fat, increased transition of carbohydrates in fats, megascopic consumption of carbohydrates by tissues, to the decline of sugar in blood and to the origin of feeling of hunger. The consumption of meal is promoted at the lack of physical activity conduces obesity to development.

A substantial role in pathogenicity of obesity belongs to the reduced function of thyroidal gland. Found out close intercommunication between obesity and saccharine diabetes. Burly persons often enough have violation of tolerance to the carbohydrates. Obesity is a diabetogenic factor, serves as a shove to the origin of the inherited saccharine diabetes.

Hematological changes are possible: basophilia, lymphocytosis, relative neutropenia, reticulocytopenia.

Treatment

Therapy of obesity must be complex with the use of medical feed, methods of physical therapies, medicinal and surgical treatment.

The main method of treatment is a dietary feed. Limitation of fats and carbohydrates is recommended at normal maintenance of albumen, vitamins and mineral matters. In all cases of development of hyperlipoproteinaemia it is necessary to eliminate food products, rich of cholesterol (liver, brains, caviar, yolks of eggs).

For the correction of violations in the exchange of lipids next to diet therapy apply hypolipoproteidaemic preparations (cholestiramide, nicotine acid, miscleronum), lipotropic matters, heparinum and heparinoids.

Diet №1 made calculating on 1 kg of mass of body - albumens of 1,5 g, 0,9 g of fat, 4,5 g of carbohydrates. An amount of liquid in day's ration is 2,5 l.

Diet №2 with sharp limitation of calorie content appointed in the conditions of permanent establishment during 25-35 days, and contained (calculating on 1 kg of mass of body) 1,5 g albumens, 0,9 g. fat, 1,5 g carbohydrates.

A diet is used also №8, that foresees limitation of general calorie content of meal due to carbohydrates and fat.

At the moderate increase of mass of body, when surplus of actual mass of body does not exceed 50% as compared to ideal, it follows to decrease in 2 times adopting products, rich in

carbohydrates and fats. For diminishing of feeling of hunger it is necessary to use products, rich in albumens (250-300 g of meat, 250-300 g of cheese, 2-3 glasses of kefir or milk). For prevention of avitaminosis it is necessary daily to accept for 2 drops of vitamin A, and vitamin D.

Necessary part of medical feed at obesity is application of unloading days - 1-2 days per a week, among which select:

a) hydrocarbons (mainly fruit-vegetable)

b) fat

c) albumens

d) combined and complex.

Complex unloading days include an unloading diet (carbohydrate, fat or albumen) in combination with the non-permanent reception of 50-100 mg Lasix.

Sometimes apply treatment hunger. However considered confessedly, that treatment hunger is unphysiology and possible only on occasion in the conditions of permanent establishment.

Physical methods, which are instrumental in the increase of tone of the central nervous system, strengthening of processes of exchanges in an organism and loosening his power holds, have a large value in therapy of obesity. One of physical factors of medical action there is a medical gymnastics, effective only at the alimentary-constitutional forms of obesity which is appointed taking into account the state of the cardiac system. It is possible to appoint swimming, walks, baths of suns and air.

Sexual hormones (male and female) apply at presence of hypofunction of sexual glands for patients with obesity. For women with obesity and decline of function of sexual glands apply estrogens, for men use androgens. Application of sexual hormones is shown at the adiposo-genital forms of obesity.

Wide distribution was got by anorexigenic preparations which repress an appetite.Phenamine (for 50-100 mg 30 minutes prior to a meal during 4-6 weeks) is used, which stimulates the central nervous system and reduces an appetite.

For burly patients with saccharine diabetes diet therapy is combined with application of biguands.

One of important moments there is limitation of adopting a liquid and application of diuretic preparations at treatment of obesity.

The methods of surgical treatment of obesity can be directed on the removal of etiologic reason of disease (tumor of hypophysis) and removal of external defects of figure (cosmetic surgery).

Agenesia of gonads (anorchia, agonadism, testicular regression, syndrome of absence of testicles).

The man has a masculine genotype and karyotype of 46XY, but phenotype indefinite: formation of external privy parts is broken. For patients privy parts is indefinite, practically absent. Violation of function of testicles takes place on to the 8-12th week of embryo development. On this term products testosterone by testicles yet insignificant, but the secretion of anti-Mueller`s hormone is already high. anti-Mueller`s hormone provides the sufficient level of stopping of development of derivative channels of Мюллера - uterus, uterine pipes, overhead third of vagina.

Turner`s Syndrome

It is a chromosomal disease, characteristic by karyotype of 45X (in 50%). In 25% find out mosaic without structural violations (46 XX/45 X), in other are structural violations of X-chromosome with mosaic or without him. Variant 45 X conditioned the loss of chromosome in the process of gametogenesis in dear from parents or by the error of mitosis at one of early divisions of

impregnated zygote. Somatic changes are investigation of loss of genetic material from the short shoulder of X-chromosome.

Phenotype is womanish. Patients differ a very specific exterior which got the name of «Turner`s phenotype ». Concomitant somatic anomalies touch foremost a skeleton and connecting tissue.

In child's age illness is diagnosed on the presence of lymphatic edema of brushes and feet, plicate necks, to the low line of growth of hairs, surplus of folds of skin on the back of head and insufficient mass of body at birth. Typical is persons with a little jaw, epicantus, low placed auricles, fish mouth and ptosis. In 20% are coarctation of aorta.

Growth for adults does not exceed 150 cm.

Characteristic undersizedness and the calculated is innate an anomaly: short neck with folds, high sky, the line of growth of hairs is low located on a neck, valgus-deformation of joints of elbows, great number of deformations of bones, violations of the cardiac, pectoral glands are not developed, nipple sexual chromatin pulled in, often negative, the second signs are undeveloped.

Characteristic is primary amenorrhea and sexual infantilism. Internal genitals: infantile uterine pipes and uterus.

The table of contents of FSH in the whey of blood in new-born is promoted, in child's age goes down to the norm, in age 9-10 goes down to the level to proper the emasculated persons. In this time maintenance of LH in a whey is promoted, and the level of estradiole in plasma is reduced (less, than 10 pg/ml).

Treatment. During the expected sexual ripening begin substitute therapy ofestrogens, that to induce growth of pectoral glands, privy parts, vagina. During the first year of treatment by estradiole speed of growth of skeleton is in length, ripening of bones is multiplied.

Syndrome of veritable hermaphroditism.

Veritable hermaphroditism is the state, about to which a patient have ovaries, and testicles or gonads with the histological features of male, and female.

Patients are divided into three groups:

1) In 20% from both sides present tissues: ovarian and testicular (ovotestis);
2) In 40% there is ovotestis on one side, on other is an or ovary, or testicle;
3) In 40% there is a testicle on one side, and on other is an ovary.

Patients have external privy parts on the different stages of transition from masculine to womanish. About 60% sufficiently are males. Normal male privy parts have only 10% patients, majority has hypospadia.

In 60% persons with female phenotype a clitoris is megascopic. Uterus is usually one-hornig. Ovaries occupy normal position, but testicles or ovotestis can will appear at dear level along the way of prolapses of testicle in embryogenesis and are often combined with hernia. In 30% testicular tissue is localized in a scrotum, in 30% - in an inguinal channel, in 30% - in the area of stomach.

The period of the sexual ripening is characterized by feminisation or virisation. In 75% of patients hynaecomastia, in 50% are menstruations. For persons with masculine phenotype the ovulation can show up pains in testicles. Fertile individuals with female phenotype, in which were remote an ovotestis, and also «men» which had children, are described. The defects of other systems are innate meet rarely.

In 60% patients the karyotype 46 XX, in 10% is karyotype 46 XY, in other is chromosomal mosaic at which a cellular line is present with a Y-chromosome. The enough body of genetic material of Y-chromosome is present in these cases, to induce development of testicular tissue.

As in ovaries more than 25% patients there are yellow bodies, for such individuals the female neuroendocrine system functions normally. Feminisation is conditioned the secretion of

esradiole by presentof ovarial tissue. For masculinized individuals the secretion of androgens prevails above the secretion of estrogens, and in spermatozoa appear some from them.

Treatment. If a diagnosis is set in new-born or child of junior age, the choice of sex depends on anatomic signs. At teens and adults it follows to delete gonads and their internal channels which do not answer prevailing phenotype and sex. In some cases accordingly change external privy parts.

«Clean» dysgenesis of gonads (syndrome of Swyer)

This syndrome was described by Swyer in 1955 as a case of masculinepseudohermafroditism. For patients karyotype is masculine - 46XY, but phenotype is female. Patients have gonads, that not secrets testosterone and anti-Mueller`s hormone. Absence of formation of anti-Mueller`s hormone creates terms for development of channels of Mueller in the period of embryonic life with forming of female genitals– uterus, labia-scrotal lips, vagina.

Growth is normal or slightly promoted. The second sexual signs are developed not enough (sexual infantilism). Characteristic primary amenorrhea.

Molecular-genetic researches show that at the syndrome of Swyer there or other variant of chromosomal anomaly:

1) deletion on the short shoulder of Y chromosome (Yp) which draws its functional inferiority;

2) translocation of XP fragment on normal Y chromosome (genotype of 46Yxp);

3) at the small number of patients deletion of short shoulder of Y chromosome appears with this pathology, where the gene of SRY is localized (gene which determines development of testicles);

4) at the family cases of partial 46XY dysgenesis of gonads not genes which determine a sex and located on Y chromosome are attracted in pathogenicity of disease, but some other genes which determine a sex, but non-communicative on a X chromosome.

For a disease is characteristic low level of sexual steroids in the whey of blood and maintenance of gonadotropin is promoted. In a pubertal period and later the substitute therapy by estrogens is recommended.

Cryptorchism.

A testicle goes down in a scrotum on 7-th months of pregnancy. Gonadotropin of mother and placentas, which influence on testicular tissue, induce formation of androgens and necessary both for the process of lowering of testicle and for functional activity of cages of Leidig and spermatogonies in new-born. If a testicle does not go down in a scrotum during the first year of life, this process stays too long to the period of the sexual ripening or a testicle does not go down in general.

At a review absence appears more frequent one testicle and rarer at bilateral cryptorchism – two testicles. At bilateral cryptorchism it is necessary to conduct differential diagnostics from anorchism by test with chorionic gonadotropin and by subsequent determination of level of testosterone in the whey of blood. A testicle which did not go down can be disposed in an inguinal channel or in an abdominal region.

Cryptorchism is reason of inferior development of testicle, that is why it is necessary as possible before to begin therapy by chorionic gonadotropin (for adults for 1500 MO twice for a week during 6 weeks) which improves circulation of blood in a testicle and lowering of testicle. Therapy of by chorionic gonadotropin is conducted in any age, beginning from multimonthly age, and if she appears ineffective, an operation is recommended (surgical report of testicles).

Syndrome of mono- and anorchism.

The defect of embryo development arises up after the 20th week of development. Born anorchia is investigation of violation of blood circulation of testicles with actual death of testicles of embryos. In a period after the 20th week of embryo development an urethra is already formed on a masculine type, but the normal forming of phallus and scrotum does not take place. For these patients a scrotum is underdeveloped, testicles are obsolete.

Phenotype and genotype is masculine. In a pubertal period the structure of skeleton is formed in default of the second sexual signs. Table of contents of testosterone in blood very low. In a pubertal period a level of gonadotropins is in blood та excretion them with urine promoted.

After the offensive of pubertal period the substitute therapy by androgens is recommended.

Syndrome of Kleinfelter

Development of syndrome is conditioned chromosomal violation - presence of additional X chromosome. Karyotype is possible at the syndrome of Kleinfelter: 47 XXY, 48XXXY, 48XXYY, inlaid variants of 46XY/47XXY and other. Sexual chromatin is positive, as there is two or anymore X chromosomes.

Before pubertal development such boys practically do not differ from yearlings. The delay of psychical development appears for some patients. The signs of androgenic insufficiency appear in a pubertal or postpubertal period. Growth of long tubular bones in length is halted at achieving puberty – sexual hormones close the epiphysaryl areas of growth. The deficit of androgens is accompanied multiplying time of storage of capacity for growth of long tubular bones with development of євнухоїдних proportions of skeleton is high growth, long in comparing to the sizes of trunk of extremity. The muscular system is developed not enough.

Insufficient development of the second sexual signs appears in a pubertal period. Penis of normal size or diminished in sizes. Testicles with hypoplasia- little, by a size from kidney bean and something sickly at palpation. The amount of cells of Leidig is diminished, the cells of Sertoly are obsolete, walls of seminal canals are gyalinized. Patients are sterile.

The level of testosterone in blood is reduced and after introduction of chorionic gonadotropin. Concentration of LH and especially FSH in plasma of blood compensate is promoted.

Substitute therapy is shown a patient with the syndrome of Kleinfelter by androgens. If the substitute therapy is begun by androgens in pubertal period, the processes of the sexual ripening are normalized, a libido rises, social adaptation of patients is provided. Therapy of gonadotropin is ineffective.

DELAY OF SEXUAL DEVELOPMENT

A delay of sexual development is undeveloping of the second sexual signs and absence or rare irregular menstruations in age 15 and more.

Does not follow to equate the delay of sexual development with primary amenorrhea- absence of menarche in age 16 and more years old. Delay of sexual development - a concept is wider and primary amenorrhea often is its symptom.

Cerebral form of delay of sexual development

A delay of sexual development is polyetiologic pathology. Reasons of delay of sexual development can be cerebral violations of organic character: traumatic, toxic, infectious defeats (encephalitis, epilepsy, tumors of hypothalamic area). This pathology of CNS next to expressed

nervous-psychical symptoms can entail the delay of sexual development, if the structures of mediobasal hypothalamus are attracted in a process.

To the cerebral forms belong delay of sexual development at psychoses, neuroses as a result of stresses (conflicts are in family, school, emotional overloads). One of cerebral forms of delay of sexual development is anorexia nervosa, that a waiver is of meal, which is considered as a neurotic reaction in reply to pubertal changes in an organism. This pathology, as a rule, appears for girls with the burdened psychical heredity, in this connection a careful inspection is shown for a psychiatrist.

Constitutional (genetic) delay of sexual development

A delay of sexual development is not the display of some pathology and has the constitutional, inherited, genetically conditioned character.

Girls time-lagged sexual development differ from coevals not only insufficient development of the second sexual signs and аменореєю but also absence of "feminisation of figure", that by the division of fatty and muscular tissue on a womanish type and changes in the structure of pelvis. For girls time-lagged sexual development anthropometric researches are set a eunuch`s build: lengthening hands and feet, relatively short trunk, diminishing of transversal sizes of pelvis. Grew them usually higher, than for coevals. Chronologic age passes ahead biological (bone) age usually.

Hypoplasia of privy parts appears at gynecological research (sexual infantilism is expressed). External and internal privy parts for patients time-lagged sexual development in 16-18 years answer the state of organs in age 10-11, that to the first phase of pubertal development. Ovaries are formed correctly, but the normal process of foliculogenesis and ovulation does not take place in them.

An exception is made by girls from hyperprolactinaemia (prolactinoma of hypophysis or functional hyperprolactinaemia). For these patients usually the sign of delay of sexual development is primary amenorrhea in combination with unsharply expressed hypoplasia of uterus. A build and length of body answer for them age-old norms, and pectoral glands are developed correctly.

Ovarial form of delay of sexual development

This form is least explored, obviously, in connection with its rareness. At her it is not set chromosomal pathology and changes of maintenance of sexual chromatin. In the structure of ovaries it is not discovered except for diminishing of follicle vehicle, changes. Ovaries are hypoplastic. Possibly, the infectious diseases of children's or toxic influencing which draw violation of follicle vehicle or innervations of ovaries have the defined value in pathogenicity of this pathology, that causes change of their sensitiveness to the hormones of stimulants of hypophysis.

For the clinical picture of delay of sexual development there are the personal intersexual touches of build at hypoplastic ovaries. Without regard to the delay of processes of ossification of epiphysis of tubular bones, length of body of girls does not exceed ordinary age-old norms. The second sexual signs are underdeveloped, appears also hypoplasia of external and internal privy parts. Characteristic primary amenorrhea, however there can be liquid and wretched menstruations.

Patients with the delay of sexual development speak to the doctor, as a rule, in age not early than 17-18-th years. To that time they, their parents and, unfortunately, even doctors wait appearances of signs of sexual development. At the inspection of girls time-lagged sexual development it is necessary to use the followings criteria:

- absence of menarche is in age of 16-th years;
- absence of signs of beginning of the sexual ripening in age 13-14-ти years and more;
- absence of menarche during 3th and anymore from the beginning of appearance of development of pectoral glands;
- disparity of indexes of growth and mass of body to chronologic age.

For patients with the delay of sexual development at suspicion on the cerebral forms of pathology a neurological inspection is needed:

- EEG, which allow to differentiate organic or functional violations of cerebral diencephalons structures;
- sciagraphy of skull and Turkish saddle, computer tomography of the Turkish saddle;
- ultrasonic research of organs of small pelvis is for clarification of sizes of uterus and ovaries;
- at presence of additional indexes is laparoscopic with the biopsy of gonads;
- determination of sexual hormones is in the whey of blood;
- sciagraphy of hands is for determination of bone age.

Treatment of central forms of delay of sexual development is a difficult task. In development of complex treatment must take part neurologist. Except for settings of neurologist, cyclic vitamin therapy, and also substitute hormonal therapy is used at hypoplastic ovaries.

PREMATURE SEXUAL DEVELOPMENT

Premature sexual development is appearance of the second sexual signs and menstruations for girls under age 8.

1. Isosexual form of premature sexual development - the signs of sexual development, that appear for girls.

2. Heterosexual form of premature sexual development - girls have signs, incident to masculine sexual development.

Isosexual premature sexual development can be true and erroneous.

1.1. Veritable premature sexual development (cerebral form) is the state, when structures which are responsible for adjusting of the reproductive system - hypothalamus and hypophysis are involved in a process.

Veritable premature sexual development for girls can have organic and functional character.

1. Organic cerebral premature sexual development - caused the organic defeat of CNS. At the organic defeat of brain premature sexual development, as a rule, develops after appearance or on a background cerebral and neurological symptomatic. Reasons of cerebral premature sexual development:

1. an asphyxia is in births, maternity trauma, hypotrophy of fruit, ketosis;
2. heavy intoxication and infection during the first year of life;
3. cerebral infections like meningitis, encephalitis;
4. brain tumors.

These reasons result in development of internal hydrocephalia- to the stretch and increase of pressure in the ventricles of cerebrum, pressure on hypothalamus, which forms the bottom of III ventricle, is the same carried out.

2. Functional cerebral premature sexual development - caused violations of CNS of functional character after carried in the first years of life (2 - 4 years) of infectious diseases, intoxications.

Cerebral premature sexual development runs across as a complete or incomplete form.

3. The complete form of cerebral premature sexual development is characterized development of the second sexual signs and menstruation.

4. The incomplete form of cerebral premature sexual development is characterized the different degree of development of the second sexual signs in default of menstruations.

An incomplete form of premature sexual development is the first phase of period of the sexual ripening stretched as though in time. Menarche for girls with the incomplete form of premature sexual development comes in 10 - 11 years.

Constitutional form of veritable premature sexual development.

At this form of premature sexual development it is not succeeded to find out neurological, cerebral pathology. Premature is age the process of the sexual ripening begins in which. A rate and sequence of this process is not violated. The inherited character of constitutional premature sexual development appears.

1.2. Ovarial form of premature sexual development.

Ovarial form of premature sexual development is conditioned the secretion of sexual hormones by tumor tissue of ovaries.

1.2.1. Hormonal active tumors of ovaries.

The first symptom of ovarian premature sexual development usually are menstrual-similar excretions of acyclic character at the poorly developed second sexual signs. Appearance of menstrual-similar excretions from sexual ways for girls under age 8 induces parents immediately to appeal to the doctor. That is why from the beginning of hormonal secretion to the address to the doctor passes tumor tissue little time and the second sexual signs do not have time to develop.

HETEROSEXUAL PREMATURE SEXUAL DEVELOPMENT

Name appearance of signs of the sexual ripening of opposite (masculine) sex heterosexual premature sexual development for girls on the first decade of life.

Adrenogenital syndrome

Most frequent clinical form of heterosexual premature sexual development.

An adrenogenital syndrome is born hyperplasia of adrenal cortex, erroneous womanish hermaphroditism or premature sexual development of girls on a heterosexual type. An adrenogenital syndrome is investigation of a born deficit of the enzymic systems which take part in the synthesis of steroid hormones of adrenal glands.

An adrenogenital syndrome is a genetic defect with the recession way of inheritance, the transmitters of imperfect gene can be and men, and women.

Hyperproducts of androgens in the adrenal cortex at a born adrenogenital syndrome are investigation of mutation of gene and born genetically conditioned deficit of the enzymic system. The synthesis of cortisol is violated - basic glucocorticoid hormone of adrenal cortex, formation of which diminishes.

Depending on character of deficit of the enzymic systems an adrenogenital syndrome divides in 3 forms, a general symptom for them is virilisation.

- An adrenogenital syndrome is with the syndrome of loss of salt: the deficit of 3-β-dehydrogenase results in the sharp diminishing of formation of cortisol, frequent vomit develops as a result, dehydration of organism with violation of cardiac activity. The symptoms of adrenogenital syndrome with the loss of salt appear at first time after birth.
- An adrenogenital syndrome with hypertension: the deficit of 11-hydroxylasa results in the accumulation of corticosterone hereupon to development of hypertension on a background violation of water and electrolyte exchange. The symptoms of adrenogenital syndrome with hypertension develop in the first decade of life. An adrenogenital syndrome with the loss of salt and hypertension meets rarely. Both these forms violate not only sexual development but also function of cardiac, digestive and other systems of organism. These patients make a general contingent for endocrinologist and pediatricians.

- adrenogenital syndrome, simple virilising form: the deficit of C-21- hydroxylase draws multiplying formation of androgens and development of symptoms of hyperandrogenia without the substantial decline of synthesis of cortisol. This form of adrenogenital syndrome is most frequent, not accompanied somatic violations of development. The deficit of C-21- of hydroxylase, without regard to a born character, can appear in different periods of life; depending on it select born, pubertal, post-pubertal forms.

Diagnostics

An objective diagnostic method is ultrasonic research of adrenal glands and magnetically-resonancetomography of adrenal glands. By an informing test for diagnostics maintenance of 17-ketosteroids (17-KC) and dehydroepiandrosterone is sharply promoted in urine and/or testosterone in blood, which are normalized after conducting of test with glucocorticoid preparations.

Treatment

Treatment of a born adrenogenital syndrome consists in application of glucocorticoid preparations. A dose depends on age, mass of body of child and degree of hyperandrogenia, which expressly correlates with the level of testosterone in blood or 17-KC and dehydroepiandrosterone in urine. Therapy is conducted lasted, because the deficit of the enzymic system has a born character. Abolition of treatment results in getting up of level of andogens in blood and to returning of all signs of virilisation.

ABSENCE OF SEXUAL DEVELOPMENT

Absence of sexual development is absence of menarche, absence of development of pectoral glands in age more than 16 years old.

Reason of this pathology is aplasia of gonads or violation of their development at which active hormone-producting tissue of ovaries is absent functionally. Sexual development does not come for girls to which by any testimony the delete of ovaries was conducted under age 8-10 years old. By other reason of absence of sexual development the defect of development of sexual glands, causedby dysgenesis of gonads, is genetically conditioned. Dysgenesis of gonads is rare pathology, with frequency 1 on 10 - 12 000 new-born.

Reason of development of dysgenesis of gonads is chromosomal violations as one loss of X chromosome or its part. More frequent in all there are four clinical forms of dysgenesis of gonads: typical, or classic (syndrome Turner), effaced, clean and mixed.

Climax by woman and men

Menopause is the appropriate stage of individual development of man, transitional period from maturity to old age, which is accompanied the loss of reproductive function. A climax can be physiology or pathological. Middle ages of offensive of climax – 49-51 year, for women - 45-55 years, for men - 47-60 years. Duration of menopause – 2-5 years. Frequency of pathological motion of menopause is 25-50%.

Climacteric syndrome, or a pathological climax is an aggregate of endocrine-vegetative violations which are formed for some people during climacteric hormonal alteration. A deciding value has a presence of premorbid background - presence of stress factors, psycho-emotional or sexual violations, sharp or chronic diseases of CNS, internal organs, genitals.

Pathogencity of climacteric syndrome consists in the "senescence of hypothalamus", violation of functioning of homeostatic centers, located in hypothalamus and limbic system which results in dysfunction of hypophysis and sexual glands.

PATOLOGICAL CLIMAX BY WOMEN

A climacteric syndrome is observed in 65-70% women. A premature (early) climax develops earlier than 45 years. A late climax appears after 55 years old.

Select a few variants of climacteric syndrome after the features of clinical displays:

1) typical form;
2) atypical form;
3) a combined form.

Medical tactic for the different forms of climacteric syndrome differs substantially.

1. **Typical form of climacteric syndrome**

Most frequent form of climacteric syndrome. More frequent observed for women which carry the protracted mental or physical overloads. Menopause comes in good time, but in postmenopause (in 2-6 months) there are typical climacteric symptoms, the expressed of which grows during 3-6 months, and then slowly diminishes for period 15-20 months.

A major diagnostic criterion is violation of menstrual function. At first the delays of monthly appear on 2-3 months (opsomenorrhea), quite often with the next uterine bleeding. Afterwards there is the proof stopping of menstruations (amenorrhea).

There are unsteady emotionally-psychical violations – nervousness, promoted fatigueability, tearfulness, feeling of fear. Characteristic general amotivational weakness, violation of rhythm of sleep.

Head pain also is a widespread enough complaint. Most characteristic moderately expressed, but practically permanent head pain, feeling of weight in a head. At a mental and physical overstrain, insomnia, overeating before sleep, intoxications brief pains appear in parietal and temporal areas.

Dizziness develops as a result of vegetative-vascular violations, atherosclerosis of vessels of cerebrum.

"Waves" of heat to the head and neck, pathological sweating is leading symptoms of climacteric syndrome. Type "waves" begin from the brief feeling of alarm, "pressure" in breasts and palpitation during a 30-60 sec. Then a face and neck blushes quickly, through 2-3 minutes hyperemia disappears, a face and neck is covered sweat. Frequency and expressed of "waves" is the basic (but not unique) criterion of weight of climacteric syndrome. At the easy form of climacteric syndrome the number of episodes of "waves" is small (to 10 on days), at middle- 10-20 on days, at heavy – more than 20 on days.

Pains are possible in bones and joints of different character and localization. The most characteristic pains are in a spine, large and shallow bones and joints. Oosteoporosis results in squeezing of vertebrae, diminishing of growth.

Obesity is a frequent sign of menopause, result of age-old change of hormonal background and exchange of matters

The symptoms of hypercriticism quite often are observed in an initial period of climax. Glucocorticoid and androgenic function of adrenal cortex rises, possibly, as an adaptation reaction on hypofunction of gonads. In menopause for patients with hypofunction of ovaries, which developed before time, the signs of hyperandrogenia- hirsutism can develop, pigment spot on the skin of face, hands, becoming rough of voice.

Violations of the functional state of щитоподібної gland are possible. There is insignificant гіпофункція of щитоподібної gland in 50% women, in 7% is гіперфункція.

Additional criteria of средньотяжкої form of climacteric syndrome: dizziness, head pain, worsening of memory and common state.

Additional criteria of heavy motion of climacteric syndrome: vegetative-vascular, endocrine, metabolic and trophic violations, dysfunction of the репродуктивної system.

2. **Atypical form of climacteric syndrome**

An atypical form develops for women, which carried psychical or physical traumas, heavy diseases (infectious, somatic, gynecological), operative interferences before, workings in the conditions of action harmful factors, protracted mental and physical overloads.

Characteristic violation of menstrual function (opso- or hypomenorrhea, and then proof amenorrhea). In 1-3 months typical climacteric symptoms (violation of rhythm of sleep, crabbiness, tearfulness, worsening of memory, decline of capacity promoted) which are combined with untypical appear after appearance of violation of menstrual cycle: by a general weakness, pains in the area of heart, palpitation, head pain, worsening of ear, sight, constipations or diarrhoea.

There is dryness of skin, fragility of nails, fall and fragility of hairs, appearance of pigmental spots on the skin of face, hands.

Almost all women have multiplying mass of body with the even or regional deposit of fat on a breast, stomach.

The symptoms of delay of liquid, edema, pains, are possible in bones, joints, sometimes sickly urination.

The state progressively gets worse with the decline of capacity or its complete loss.

For patients with the atypical form of climacteric syndrome can develop the attacks of bronchial asthma, Hypercholesterolemia, hyper- and hypoglycaemia. Hormonal cardiopathy, osteoporosis, osteochondrosis is formed quite often.

Typical development of crises.

Sympato-adrenal crisis. The exchange of matters is reduced. Asthenic constitution. Crises more frequent develop in the day-time or in the evening. Crisis begins from feeling of alarm, fear of death, chill. Promoted arterial hypertension, tachycardia. A skin is initial cold, pale, extremities are cold. With development of crisis a skin turns pale or blushes. Temperature of 37-39C°. Characteristic spasms of vessels of different localization, which squeeze pains in the area of heart. Head pains each evening, sleep is uneasy. Crabbiness is promoted. A capacity is higher in the evening. Pupils are extended. Dryness of mucous membrane of mouth, appetite reduced. Constipations. Liquid urination. The level of adrenalin in blood is promoted, hypokalemia. Duration of crisis 20-40 minutes, ends with intensive urination, sharp general weakness. Intervals between crises can have different duration.

Vagoinsular of crises. The exchange of matters is promoted. Constitution of picnic. Crises more frequent at night, in the morning. Skin is heat, rose. Extremities heat, hot. Temperature of 35,5-36C°, sweat is warm, liquid. Reduced arterial blood pressure, bradycardia. Characteristic prickly pains in the area of heart, head pains in the morning. Sharp weakness, episodes of fainting fit. Depression. Sleep is deep. Pupils are narrowed. Capacity higher in the day-time. Salivation. An appetite is promoted. Diarrhoea, nausea. Urination is frequent. The level of adrenalin in blood is reduced, hyperkalemia.

3. Combined form of climacteric syndrome.

The combined form develops for patients with chronic diseases of cardiac, hepato-billiary systems, by diabetes and other endocrine diseases, allergy.

Dysfunctional climacteric uterine bleeding – one of basic variants of pathological motion of menopause. Observed in 30% women which are in the period of pre-menopause. The origin of dysfunctional of the uterine bleeding is caused the age-old increase of hypothalamic activity with the increase of gonadotrophic function of hypophysis. In a pre-climacteric period a sensitiveness is to hormonal stimulation in peripheral organs normal or promoted, and as a result the promoted hormonal stimulation there is persistence of follicles in ovaries, in an uterus and pectoral glands are hyperplastic processes.

Dyshormonal climacteric cardiopathy.

Climacteric cardiopathy (myocardial dystrophy) is the atypical form of climacteric syndrome which runs across with pains in the area of heart for as cardialgia and by the defeat of myocardium of non-coronarogenic character.

Typical cardialgia is pains in the area of heart of non-coronal character. Pains are localized in the area of apex or in a pericardial area. An irradiation of pain can be absent, to be limited (in the left shoulder-blade) or widespread (the half of thorax engulfs all left). Variable intensity of the removed pain – from the easy aching to very great, unbearable pain. The typical bright emotional coloring of pain syndrome is feeling of the "killed nail", "stuck knife".

The signs of electrocardiographies are expressed moderately, unsteady, the expressed of rejections on ECG does not answer weight of pain syndrome.

Hormonal therapy results in reverse development of symptoms of disease - removal of cardialgia, normalization to the positive dynamics of ECG, normalization of indexes of lipid exchange, decline of secretion of lutropin and follitropin.

Diagnostics of climacteric syndrome by woman.

For diagnostics drawn on hormonal researches.

In development of climax for women select three stages.

I phase - the recurrence of excretion of estrogen is violated, there is relative hyperestrogenia, metabolism of estrogen is violated. The sensitiveness of tissues rises to estrogen, an allergy can develop to own estrogen. Excretion is promoted with urine of 17-КС and 17-ОКС.

II - excretion of estrogen with urine is reduced. Cytological reaction of vaginal stroke of 2-3 degrees. The phenomenon of crystallization of cervical mucus is poorly expressed. Mucus shells of body of uterus at histological research in the stage of atrophy.

III is the ahormonal stage. The secretion of gonadotropins is promoted. Correlation of lutropine / follitropine diminishes to 0,4-0,7 (in reproductive age even 1,0).

Treatment of climacteric syndrome.

Treatment must be complex, such, which sets rational mode of labour and rest, rational feed: hypocalorial ration with limitation of carbohydrates, enriched cellulose. Expedient psychotherapy, physiotherapy and medical physical education.

For the correction of vegetative-vascular violations apply tranquilizers, neuroleptics, antidepressants. The extracts of root of valerian normalize the function of hypothalamus. Effectively preparations which contain alkaloids remove vegetative dysfunction –belloidum, bellataminalum, bellasponum.

In more heavy cases use tranquilizers –elenium, sibazonum, andaxinum, trioxazinum. Treatments begin with small doses (1/2 pills 2-3 times per a day), gradually multiplying a dose to optimum. Course of therapy – 1-2 months.

Heavy symptoms of climacteric neurosis are a testimony for setting of neuroplegics– aminazinum, propazinum, etaperazinum. Apply small doses (1/2 pills 2-3 times per a day) during 2-4 weeks to development of proof effect, then a dose is gradually reduced. At presence of depression use antidepressants, for example, amitriptyline or azaphenum.

If violations of menstrual function appear in age 40-45, it is expedient to conduct a hormonal correction gestagen preparations with the purpose of proceeding in the reproductive system. Proceeding in hormonal homeostasis allows to normalize and functioning of privy parts, and all organism on the whole. Proceeding in a menstrual cycle in pre-menopause, with appearance of proof violations of menstrual cycle, favorably influences on the state of women: a feel gets better, "waves" are halted, sleep gets better.

Treatments begin from the periodic setting of gestagens during lengthening terms between menstruations. Gestagen preparations assign for the 18-20th day of the induced menstrual cycle at the positive phenomenon of "pupil" (-++) and (+++) during 6-8 days. The courses of treatment by gestagen preparations conduct until menstrual reactions are not halted (6-18 months). Testimonies for the repeated setting of gestagen is a delay of menstruation, the positive "phenomenon of pupil", high kariopicnotic index, is prolonged.

Norkolut (noretisteronum) accept for 1/2-1 pills (5 mg in a pill) daily in 20 minutes after a meal.

Turinal appoint for 2 pills on a day.

Pregnine accept on a 1 pill 3 times per a day sub lingua, or 1 injection of прогестерону for 1 мл of a 1% solution intramuscular daily.

Oxyprogesterone capronatis is the synthetic prolonged analogue of progesterone, enter intramuscular for 1 ml of a 12,5% solution on the 16-18th day of the created cycle.

In the hyperestrogenic phase of climax treatment is recommended by the combined estrogen-gestagen preparations. Application of the combined preparations imitates a normal ovarial cycle: primary estrogenic stimulation of endometrium is with a subsequent progestin-estrogen action. Rigevidonum, non-ovlonum appoint for 1/4-1/6 pills from the 5th day of spontaneous or induced menstruations during a 21th day and by a next interruption on 7 days. A continuous reception is practiced in small doses.

Divina removes the displays of climacteric syndrome and normalizes a lipid exchange. During the first it is 11 days accepted a cycle on a 1 white pill on a day (2mg estradiole), then 10 days on a 1 blue pill (2 mg estradiole and 10 mgmedroxyprogesterone), interruption 7 days.

The second and third phases of climax for women run across on a background of estrogenic insufficiency, in these phases it is recommended to apply estrogen. To the most active estrogenic preparations take estradiole and ethynilestradiole, less active estrone and estriole.

With средньотяжким motion of climacteric syndrome folliculinum is appointed patients for 5000 IU daily or for 10 000 IU in a day intramuscular during 15 days. Then conduct supporting therapy of synestrole for 1 mg (10 000 IU) 2 times per a day (10 days) and for 0,5 mg 1 time per a day (5 days).

The patent combined preparation which contains estrogen is climacterinum. On the course of treatment - 100 drops, accept for a 1 drop 3 times per a day in 1 hour after a meal. It is possible to move 3-4 courses with interruptions on 2-3 months.

Contra-indication is to application of estrogen: disease of liver and kidneys, tumor, mastopathia, vaginal bleeding of unknown etiology, endometriosis.

By a patient in the age 50 and more years, proceeding in a menstrual cycle does not follow. The symptoms of climacteric syndrome are removed the combined setting of estrogen and androgens. In one syringe enter intramuscular 0,5 ml of a 0,1% solution of estradiole dipropionatis(0,5 mg) and 2,5 ml of a 1% solution of testosterone propionatis (25 mg). Injections execute 1 time per 5-7 days during 5-7 weeks to the removal of symptoms of climacteric syndrome, then 1 time per a month during 6-12 months.

Amboseks, combined preparation of estrogen and androgen, enter intramuscular for 1 ml 1 time per a month during 6-12 months.

Contra-indication is to the use of androgen: gout, rheumatoid arthritis, hypertensive illness.

PATHOLOGICAL CLIMAX BY MEN

To the pathological variants of menopause for men take an early climax and climacteric syndrome. The symptoms of neuro-endocrine alteration accumulate on the displays of defeat of vessels atherosclerosis, which for men is formed on 7-10 years before, than for women.

Clinical picture

A hypertensive syndrome appears the unsteady increase of arterial blood pressure, typical transitory hypertension. Systolic pressure which brings an increase over of pulse pressure rises more considerable.

Cardial syndrome appears the attacks of cardial pains, unconnected with the physical loading, which are badly removed by coronarolithic preparations. Pains are removed on a background treatment by androgen.

Vasoasthenic syndrome is characterized the promoted fatigueability and muscular weakness. The attacks of muscular weakness appear suddenly, does not depend on the physical loading, are investigation of violation of regional circulation of blood.

Sexual and urinary dysfunction is related to the decline of tone of urinary bladder, violations of functioning of prostate: disturb indefinite dull pains in the area of urinary bladder and other dysuric phenomena. A libido is stored, but there can be violations of copulative cycle.

Diagnostics

And physiology, and pathological climax is accompanied the decline of formation of androgens in testicles. But a pathological variant is accompanied violation of metabolism of hormones: formation of active androgens (androsterone, dehydroepiandrosterone) goes down, the index of androsterone/dehydroepiandrosterone goes down.

A large value in pathogencity of pathological masculine climax has violation of balance of estrogens. At a physiology climax excretion of active estrogens (estrone, estradiole) goes down for men, prevails nonactive metabolite estriole. At a pathological climax for men a compensate decline of excretion of estriole is absent, active estrogen prevails (estradiole). Hypertensive and vasoasthenic syndromes are accompanied the expressed predominance of active estrogen, increase of relation of estradiole to estriole, diminishing of excretion of estriole.

Treatment

Therapy must be complex, to include psychotherapy, medical gymnastics, physical therapy treatment.

The purpose of hormonal therapy is creation of optimum hormonal background: androgens promote reactivity of spinal centers of erection, proceed in a libido, diminish expressed of vegetative violations. Treatment by androgens must not be continuous - development of atrophy of gonads is possible. Apply complex hormonal preparation of testobromlecitum, that consists methyltestosterone, bromuralum and lecithin. The course of treatment makes 6 weeks: 2 weeks on a 1 pill 3 times per a day under a language after a meal, 2 weeks - on a 1 pill 2 times per a day, 2 weeks - on a 1 pill 1 time per a day. Treatment can be picked up thread in 3-4 months.

Application of one андрогенів is possible. Methyltestosterone appoint on a chart: 1 week - on a 1 pill (5 mg) 2 times per a day sub lingua after a meal, 2 weeks - on a 1 pill 1 time per a day, 2 weeks - for 1/2 pills 2 times per a day. Sometimes appoint intramuscular injections 1% or to a 5% solution of testosterone propionates daily or in a day during 2-3 weeks. For the protracted therapy use the prolonged androgenic preparations - sustanon-250 or omnadrenum for 1 ml intramuscular 1 time per a month during 3-6 months.

Control of initial level of knowledge's:

Task 1

Hypothalamic-hypophysal insufficiency more frequent is investigation of the impression:

a) Hypothalamic areas;
b) hypophysis;
c) cortex of cerebrum

Task 2
What symptoms characteristic for Simmond`s disease?

a) muscular weakness; 0-pains in muscles;
b) pigmentation of skin;
c) acute diminishing of mass of body;
d) arterial low blood pressure;
e) all is higher marked

Task 3
What preparations is it expedient to use for patients by Simmond`s disease?

a) cortizole;
b) thyrotropine;
c) chorionic gonadotropin;
d) hormones of thyroid;
e) sexual hormones;
f) all is higher marked

Task 4
Sheehan`s disease on clinical motion differs from a hypothalamic-hypophysal cachexia:

a) absent of considerable loss of mass of body;
b) violation of function of sexual glands is less expressed;
c) all higher marked

Task 5
What violations of carbohydrate exchange are characteristic for patients with a hypopituitarism syndrome?

a) hypoglycaemia;
b) the reduced sensitiveness to insulin;
c) the reduced tolerance to the carbohydrates;
d) all is higher marked

Task 6
What pathogenic bases of nervous form of Diabetes insipidus?

a) resistance of receptors to the action of antidiuretic hormone;
b) kidney pathology;
c) sufficient products of antidiuretic hormone;
d) all is higher marked

Task 7
What most frequent etiologic factors of development of nervous form Diabetes insipidus?
a) **a** tumor of brain;
b) trauma of skull;
c) tubulopathy;
d) acute and chronic infections;
e) all is higher marked

Task 8
What from symptoms not peculiar for Diabetes insipidus?

a) polydipsia;

b) polyuria;
c) dysuria;
d) insomnia

Task 9
What diseases does it follow to conduct differential diagnostics of Diabetes insipidus?
a) diabetes mellitus;
b) hyperparathyrosis;
c) psychogenic polydipsia;
d) chronic pyelonephritis;
e) all is higher marked

Task 10
What from signs are characteristic for Nelson`s syndrome?
a) chronic adrenal insufficiency;
b) hyperpigmentation of skin;
c) tumors of the hypophysis;
d) all is higher marked

Task 11
At the Nelson`s syndrome develops the violation of:
a) day's rhythm of ACTH secretion;
b) mechanism of back connection of adjusting of secretion АКТГ;
c) both mechanisms of regulation

Task 12
How does the level of somatotrophic hormone change for healthy persons in reply to loading glucose?
a) any changes;
b) growth up;
c) sink down;
d) develops two-phase reaction

Task 13
What consequences do the hyperproducts of somatotropin lead to for adult persons?
a) to development of acromegaly;
b) to development of tallness;
c) to development of gigantism;
d) all is higher marked

Task 14
To what consequences do the hyperproducts of somatotropin for children?
a) to development of acromegaly; gigantism
b) to development of tallness;
c) all is higher marked

Task 15
To what consequences do the hyperproducts of somatotropin for teenagers (before closing of epiphysal areas of growth)?

a) to development of acromegaly**;**
b) to development of tallness;
c) to development of gigantism;
d) all is higher marked

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
B	C	D	C	C	C	A	C	E	D	C	C	A	A	B

Control of eventual level of knowledge's

Task 1
Pathology of what part of the neuro-endocrine system does take place at Simmond`s disease?
a) hypothalamus;
b) adenohypophysis;
c) primary defeat of peripheral endocrine glands;
d) secondary hypofunction of peripheral endocrine glands

Task 2
What reasons do lie in basis of development of hypopituitarism?
a) traumatic damages of head;
b) neuroinfections;
c) inflammatory diseases;
d) circulatory ischemic necrosis of the hypophysis

Task 3
What reason of development of Sheehan`s syndrome?
a) septic embolism;
b) neuroinfection;
c) tumor of hypophysis;
d) circulatory ischemic necrosis

Task 4
What clinical displays of somatotropine insufficiency?
a) low growth;
b) cachexy;
c) hypogonadism;
d) decrease of muscular mass;
e) all is higher marked

Task 5
What clinical signs of corticotrophin insufficiency?
a) arterial hypertension;
b) hyperpigmentation of skin;
c) reduced arterial pressure;
d) muscular hypotony; 0-all is higher marked

Task 6
What changes in the analysis of blood do take place at Simmond`s disease?

a) anaemia;
b) leucocitosis;
c) leucopaenia;
d) eosinopaenia;

Task 7
What biochemical indexes of blood most characteristic for Simmond`s disease?

a) hyperglycaemia;
b) inclination to hypoglycaemia;
c) hyperpotassiumaemia;
d) hypersodiumaemia;
e) hypernatremia;
f) hypokalemia

Task 8
What laboratory indexes are characteristic for partial hypopituitarism with insufficiency of secretion of thyrotropine?

a) decrease speeds of conducting on nervous fibers;
b) negative test with thyroliberine;
c) diabetoid " type of curve during conducting of test of tolerance to glucose

Task 9
What researches are recommended for differential diagnostics of primary and secondary hypogonadism?

a) large dexamethasone test;
b) test with chorionic gonadotropin;
c) determining of level of LH, FSH;
d) determining of excretion 17 – OCS;
e) determining of level of hormones of sexual glands

Task 10
What tests must be conducted for an estimation the function of hypophysis?

a) dexamethasone test;
b) metopirone test;
c) thyrotropine test;
d) thyroliberine test;
e) gonadoliberine test

Task 11
In what cases possible convalescence the patient with Diabetes insipidus ?

a) in case of development of disease after cerebral trauma;
b) in case of development of disease on a background of neuroinfection;
c) in both cases

Task 12
At nephrogenic Diabetes insipidus a sensitiveness to vasopressin:
a)promoted;

b) is stored;
c) absent

Task 13
What from the noted preparations do reduce the secretion of vasopressin?

a) oxytocine;
b) glucocorticoids;
c) alcohol;
d) noradrenaline;
e) all is higher marked

Task 14
What functional tests do use in diagnostics of Diabetes insipidus ?

a) with clophelinum;
b) with hypothyazidum;
c) with dexamethasone;
d) with limitation of liquid**.**

1	2	3	4	5	6	7	8	9	10	11	12	13	14
B	D	D	A	C	C	B	B	C	B	C	C	B	D

Tests

Task 1
What medicinal preparations is it expedient to use for treatment of Diabetes insipidus ?

a) **nalogs of arginine-vasopressin**;
b) pituitrinum;
c) hypothyazidum;
d) miscleronum;
e) clophelinum;
f) all is higher marked

Task 2
What predefined appearance "line-up" for patients with Cushing`s disease?

a) trombosis capillaries of skin;
b) **catabolic operating of glucocorticoids on the albumens of skin**;
c) haematoms;
d) all is higher marked

Task 3
What is condition changes from the side of lymphoid tissue for patients with Cushing`s disease?
a) plenty of androgens;
b) plenty of glucocorticoids;
c**) plenty of corticotrophin**;
d) promoted disintegration of albumens;
d) all is higher marked

Task 4
What does distinguish the endocrine-exchange of hypothalamic syndrome for patients with Cushing`s disease?

a) less expressed symptoms of hypocorticism;
b) osteoporosis;
c) **positive "small dexamethasone test";**
d) all is higher marked

Task 5
If a large dexamethasone test is positive, it more credible in all:
a) **Cushing`s disease**;
b) glucosteroma;
c) ACTH is an ectopic syndrome;
d) virilising hyperplasia of adrenal glands

Task 6
What from preparations do diminish a secretion of ACTH at patients with Cushing`s disease?

a) parlodel;
b) metopirone;
c) chloditane;
d) **ciproheptadinum;**
e) rezerpinum;
f) all is higher marked

Task 7
On what color in the first turn perception is violated at development of bitemporal hemianopsia for a patient with acromegaly:
a) white;
b) yellow;
c) red

Task 8
Function of adrenal cortex at patients with acromegaly:
a) normal;
b) promoted;
c) reduced;
d) **at first normal, and then on the measure of multiplying the term of disease can go down**

Task 9
At hypophysal nanism least the following suffers functions to the hypophysis:

a) thyrotrophic;
b) **adrenocorticotrophic**;
c) gonadotrophic

Task 10
At nanism of Larone patients have a secretion of STH:

a) **not broken**;
b) reduced;
c) promoted

Task 11
What clinical features of hypothalamic forms of obesity?
a) slow increase of mass of body;
b) **vegetative violations**;
c) even distributing fat tissue;
d) dysplastic obesity

Task 12
How does the basal secretion of growth hormone change for children with obesity?
a) increase;
b**) decrease**;
c) any changes

Task 13
What does stipulate polyphagia at patients with obesity?
a) increase concentrations ofendorphins;
b) hyperinsulinism;
c) all is higher marked

Task 14
How are external privy parts formed for a person with the chromosomal set of ХХУ?
a) to the female type;
b) **to the male type**;
c) to the intermediate type;
d) all is higher marked

Task 15
The boy 2 years old has bilateral cryptorchismus. Physical development and bone age correspond to the passport, karyotype 48 ХХУУ. Your diagnosis?
a) adrenogenital syndrome;
b**) syndrome of Kleinfelter**;
c) Reifenstein`s syndrome;
d) "poly-Y"-syndrome

Task 16
Except for ovaries the synthesis of estrogens is possible:
a) in adrenal glands;
b) **in fat tissue**;
c) in muscular tissue;
d) in all noted tissues

Task 17
What from the transferred products of steroidogenesis are made mainly in ovaries?
a) testosterone;
b) androstendione;
c) dehydroandrostendione;
d) cortisone;
e) all noted

Task 18

For a woman with a hirsute syndrome found out the high level of testosterone in plasma of blood at the normal level of dehydroepiandrosterone and dehydroepiandrosterone-sulfate. What origin of dysandrogenia does take place in concrete case?

a)adrenal;

b) ovarial;

c) mixed.

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
A	B	C	C	A	D	C	D	A	A	B	B	C	B	B	B	B	B

Questions of controls

1. Acromegaly. Etiology and pathogencity. Clinic. Diagnostics and differential diagnostics. Treatment.
2. Cushing`s disease. Etiology and pathogenicity. Classification. Clinic. Diagnostics and differential diagnostics. Treatment.
3. Hypopituitarism. Etiology and pathogenicity. Clinic. Diagnostics and differential diagnostics. Treatment.
4. Diabetes insipidus. Etiology and pathogenicity. Clinic. Diagnostics and differential diagnostics. Treatment.
5. Hypopituitarism with overwhelming somatotrophic insufficiency (hypophysal nanism). Classification. Etiology and pathogenicity. Clinic. Diagnostics and differential diagnostics. Treatment.
6. Hypophysarl gigantism. Etiology and pathogenicity. Clinic. Diagnostics and differential diagnostics. Treatment.
7. Obesity. Etiology and pathogenicity. Classification. Clinic. Diagnostics. Treatment. Children and teenagers have obesity.
8. Agenesia of gonads.
9. Turner`s syndrome.
10. Hermafroditism.
11. Cryptorchism.
12. Syndrome of mono- and anorchism.
13. Syndrome of Kleinfelter.
14. Sexual development violation at children.
15. Climax at women and men.

Practical tasks to the theme 9

1. To define the factors of risk of diseases of HHS, SG, the etiologic factors of disease are possible; retrospectively to set the initial signs of disease, estimate adequacy of applied diagnostic measures; to set pharmacological anamnesis; to define the basic stages of motion of disease.
2. To ground the diagnosis of diseases of HHS, SG.
3. To set character of complications of diseases of HHS, SG.
4. To estimate the results of clinic-laboratory and instrumental researches.
5. To define the degree of weight of diseases of HHS, SG.
6. To conduct the differential diagnosis of diseases of HHS, SG.

Protocol of the clinical examination of the patient

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

Complaints of the patient_____
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Anamnesis morbi
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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

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_____

Accompanying disease

_____
_____
_____

Complications_____
_____
_____
___

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

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Інформаційні ресурси

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

Методична вказівка складена:

Методична вказівка переглянута і затверджена на засіданні кафедри: _____

З доповненнями (змінами) _____

Завідувач кафедри Л.В. Журавльова