

Ministry of Health of Ukraine  
Bogomolets National Medical University

METHODOLOGICAL RECOMMENDATIONS

to practical classes for students

Academic discipline OK25 Pediatrics with children's infectious diseases

Branch of knowledge: 22 «Health care»

The specialty: 222 «Medicine»

Department of Pediatrics № 2

APPROVED at the meeting of the Department of Pediatrics No. 2 from August 28 , 2023, protocol №1

Reviewed and approved by: Center for Pediatric Disciplines

from August 28 , 2023, protocol № 1

**Lesson topic:** Diseases of the hypothalamic-pituitary system and gonads in children. Obesity in children.

**The goal of the lesson:** the formation of professional competences for achieving program learning outcomes on diagnosis, treatment and prevention of pituitary dwarfism, diabetes insipidus, disorders of sex development (Turner syndrome, Klinefelter syndrome, congenital hyperplasia of the adrenal cortex, ovotesticular disorder of sex development), hypogonadism, cryptorchidism, premature puberty, delayed puberty, obesity in children.

**Competencies:**

- collect medical information about the patient and analyze clinical data in children with pituitary dwarfism, diabetes insipidus, disorders of sex development (Turner syndrome, Klinefelter syndrome, congenital hyperplasia of the adrenal cortex, ovotesticular disorder of sex development), hypogonadism, cryptorchidism, premature puberty, delayed puberty, obesity;
- determine the necessary list of laboratory and instrumental studies and evaluate their results in pituitary dwarfism, diabetes insipidus, disorders of sex development (Turner syndrome, Klinefelter syndrome, congenital hyperplasia of the adrenal cortex, ovotesticular disorder of sex development), hypogonadism, cryptorchidism, premature puberty, delayed puberty, obesity;
- make a preliminary and clinical diagnosis of pituitary dwarfism, diabetes insipidus, disorders of sex development (Turner syndrome, Klinefelter syndrome, congenital hyperplasia of the adrenal cortex, ovotesticular disorder of sex development), hypogonadism, cryptorchidism, premature puberty, delayed puberty, obesity;
- determine the nature of nutrition in the treatment and prevention of pituitary dwarfism, diabetes insipidus, disorders of sex development (Turner syndrome, Klinefelter syndrome, congenital hyperplasia of the adrenal cortex, ovotesticular disorder of sex development), hypogonadism, cryptorchidism, premature puberty, delayed puberty, obesity;
- determine the principles and nature of the treatment of pituitary dwarfism, diabetes insipidus, disorders of sex development (Turner syndrome, Klinefelter syndrome, congenital hyperplasia of the adrenal cortex, ovotesticular disorder of sex development), hypogonadism, cryptorchidism, premature puberty, delayed puberty, obesity;
- to diagnose emergency conditions in diabetes insipidus, congenital hyperplasia of the adrenal cortex;
- determine tactics and provide emergency medical care in case of complications of diabetes insipidus, congenital hyperplasia of the adrenal cortex;
- perform medical manipulations (blood pressure measurement, ECG, height measurement, weighing, measurement of waist and hip circumference);
- keep medical records;
- adhere to the bioethical principles of a medical specialist.

**Equipment:** portable personal computer, stethoscope, tonometer, medical scales, height meter, centimeter medical tape, centile graphs of growth, body weight, body mass index for boys and girls, tables of standard deviations of body mass index for boys and girls, disposable gloves, antiseptic for hands.

**Lesson plan and organizational structure**

| Stage name | Description of the stage | Levels of assimilation | Timing |
|------------|--------------------------|------------------------|--------|
|------------|--------------------------|------------------------|--------|

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| Preparatory | <p><i>Organizational issues</i></p> <p><i>Learning motivation:</i></p> <p>The pituitary gland, together with the neurosecretory nuclei of the hypothalamus, forms the hypothalamic-pituitary system, which controls the activity of the peripheral endocrine glands. The pituitary gland secretes somatotropic hormone, adrenocorticotrophic hormone, prolactin, luteinizing hormone, follicle-stimulating hormone, and thyroid-stimulating hormone. Neurosecretory nuclei of the hypothalamus secrete releasing hormones (somatotropin releasing hormone, gonadotropin releasing hormone, corticotropin releasing hormone, thyrotropin releasing hormone), dopamine, oxytocin, vasopressin. Gonads – male (testicles) and female (ovaries) are the main elements of the human reproductive system, which perform exocrine (formation of sperm and oocytes) and endocrine (production of sex hormones (androgens and estrogens)) functions. Obesity is a risk factor for the development of severe comorbidity, which leads to a decrease in the quality and length of life. Diseases of the hypothalamic-pituitary system, gonads and obesity significantly affect the growth and development of the child. Early diagnosis and timely treatment of diseases of the hypothalamic-pituitary system, gonads and obesity are the key to recovery or achieving compensation and thus ensure the normal development of the child.</p> <p><i>Control of the initial level of knowledge (test control and oral questioning):</i></p> <p><b>1) Diabetes insipidus develops as a result of deficiency:</b></p> <p>A. Antidiuretic hormone<br/> B. Luteinizing hormone<br/> C. Adrenocorticotrophic hormone<br/> D. Oxytocin<br/> E. 11-hydroxylase</p> <p><b>2) What stimulated level of somatotropin indicates its total insufficiency?</b></p> <p>A. &lt; 5 ng/ml<br/> <b>B. &lt; 7 ng/ml</b><br/> C. &lt; 9 ng/ml<br/> D. &lt; 11 ng/ml<br/> E. &lt; 12 ng/ml</p> <p><b>3) At what age does the level of gonadotropins increase in girls with Turner syndrome?</b></p> <p>A. After 3 years<br/> B. From the age of 6<br/> <b>C. After 9 years</b></p> | <p>Introductive</p> <p>Reproductive</p> | 25 min |
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|             | <p>D. From the age of 12<br/>E. After 15 years</p> <p><b>4) Select the karyotype in Klinefelter syndrome.</b><br/>A. 47, XXY<br/>B. 48, XXXY<br/>C. 49, XXXXY<br/>D. 50, XXXXXY<br/><b>E. All answers are correct</b></p> <p><b>5) IV degree of virilization of the external genitalia according to the Prader scale in girls corresponds to:</b><br/>A. Small hypertrophy of the clitoris, partial fusion of the labia majora (high posterior commissure).<br/>B. Hypertrophy of the clitoris and a wide entrance to the urogenital sinus.<br/>B. Well-developed corpus cavernosum and a formed head of the clitoris, a narrow entrance of the urogenital sinus.<br/><b>G. Penis-like clitoris, urogenital sinus opens on the shaft of the clitoris.</b><br/>D. Penis-like clitoris, the urogenital sinus opens on the head of the clitoris.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                    |         |
| <b>Main</b> | <p><i>Performance of practical tasks:</i></p> <ul style="list-style-type: none"> <li>- Demonstration of a thematic patient in the pediatric department.</li> <li>- Taking medical history of children with pituitary dwarfism, diabetes insipidus, congenital hyperplasia of the adrenal cortex, hypogonadism, cryptorchidism, disorders of puberty and sex development (Turner syndrome, Klinefelter syndrome, ovotesticular disorder of sex development), obesity, conversing with the relatives of the sick child.</li> <li>- Taking family anamnesis from relatives of a sick child.</li> <li>- Clinical examination of children with pituitary dwarfism, diabetes insipidus, congenital hyperplasia of the adrenal cortex, hypogonadism, cryptorchidism, disorders of puberty and sex development (Turner syndrome, Klinefelter syndrome, ovotesticular disorder of sex development), obesity.</li> <li>- Interpretation of clinical examination data of children with pituitary dwarfism, diabetes insipidus, congenital hyperplasia of the adrenal cortex, hypogonadism, cryptorchidism, disorders of puberty and sex development (Turner syndrome, Klinefelter syndrome, ovotesticular disorder of sex development), obesity; determination of the main clinical syndromes; making a preliminary diagnosis.</li> </ul> | <p>Introductory</p> <p>Reproductive</p> <p>Reproductive<br/>Reproductive</p> <p>Reconstructive</p> | 145 min |

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|              | <ul style="list-style-type: none"> <li>- Setting up a plan of examination of children with pituitary dwarfism, diabetes insipidus, congenital hyperplasia of the adrenal cortex, hypogonadism, cryptorchidism, disorders of puberty and sex development (Turner syndrome, Klinefelter syndrome, ovotesticular disorder of sex development), obesity; interpreting the results.</li> <li>- Substantiation and formulation of the final clinical diagnosis according to classification on the basis of anamnesis data, complaints, objective and laboratory-instrumental examination, differential diagnosis.</li> <li>- Prescription and substantiation of the treatment of children with pituitary dwarfism, diabetes insipidus, congenital hyperplasia of the adrenal cortex, hypogonadism, cryptorchidism, disorders of puberty and sex development (Turner syndrome, Klinefelter syndrome, ovotesticular disorder of sex development), obesity taking into account age-dependent doses of drugs.</li> <li>- Practicing medical manipulations (measurement of blood pressure, weighing, measurement of waist circumference, measurement of hip circumference); evaluating the results of research.</li> </ul>                                                                                                                                            | <p>Creative</p> <p>Creative</p> <p>Creative</p> <p>Reconstructive Creative</p> |        |
| <b>Final</b> | <p><i>Control of the final level of preparation (situational tasks):</i></p> <p>Task 1</p> <p>The girl is 9 years old. Complaints of weight gain, headache, weakness, drowsiness, increased fatigue, increased appetite. The child was born from the 3rd pregnancy (physiological), 3rd physiological childbirth. Body weight at birth was 3300 g, body length 50 cm. At an early age, grew and developed according to age norms, body weight was at age norms. Past diseases: influenza, chicken pox. Body weight and height of parents and older sister are within normal limits. The child's weight gain began 3 weeks after surgery for acute appendicitis (endotracheal anaesthesia).</p> <p>Objectively: body temperature 36.6 °C, respiratory rate 18/min., heart rate 80/min., blood pressure on the right arm 165/95 mmHg, on the left - 155/90 mmHg. Height 140 cm, body weight 42 kg 140 g. The distribution of the subcutaneous fat layer is unequal, mainly in the abdomen (in the form of an "apron"), hips, chest, shoulders. The skin is dry, cyanotic with a marble pattern, bright red striae in the abdomen, thighs, chest, and shoulders. In the lungs, breathing type is vesicular. Heart sounds are rhythmic, a bit muffled. The abdomen is soft, painless on palpation. The liver protrudes from beneath the edge of the costal</p> | Creative                                                                       | 30 min |

arch by 1 cm. The spleen and kidneys are not palpable. Sexual development corresponds to passport age. Appendix. Table for evaluation of BMI in a 9-year-old girl.

| Age<br>,<br>y.o. | Number of standard deviations (SD) |          |          |                 |         |      |      |
|------------------|------------------------------------|----------|----------|-----------------|---------|------|------|
|                  | -3<br>SD                           | -2<br>SD | -1<br>SD | Me<br>-dia<br>n | 1<br>SD | 2 SD | 3 SD |
| 9                | 12,1                               | 13,1     | 14,4     | 16,<br>1        | 18,3    | 21,5 | 26,5 |

CBC. Hemoglobin 124 g/l, erythrocytes 3.1 T/l, reticulocytes 3%, platelets 270 g/l, leukocytes 6.9 g/l, myelocytes 0%, metamyelocytes 0%, banded neutrophils 3%, segmented neutrophils 55%, basophils 1%, eosinophils 4%, lymphocytes 29%, monocytes 8%, ESR 4 mm/h.

Biochemical analysis of blood. Total protein 79.7 g/l, glucose 5.3 mmol/l, total bilirubin 19.1  $\mu$ mol/l, direct bilirubin 3.6  $\mu$ mol/l, cholesterol 5.1 mmol/l, creatinine 69.2 mmol/l, urea 5.7 mmol/l, uric acid 0.23 mmol/l, ALT 34 units/l, AST 31 units/l, alkaline phosphatase 170 units/l, CRP (-), rheumatoid factor (-), amylase 89 units/l, potassium 4.4 mmol/l, sodium 142 mmol/l.

Urine analysis. The color is straw-yellow, the reaction is weakly acidic, the specific weight is 1024, the transparency - transparent. Chemical research: protein was not detected, sugar was not detected, acetone was not detected. Microscopy of the sediment: epithelial cells (flat 1-2 in the field of vision, polymorphic 0-1 in the field of vision, renal epithelium was not detected), leukocytes 2-4 in the field of vision, erythrocytes 0-1 in the field of vision, cylinders not detected, salt not detected, mucus not detected, bacteria not detected.

X-ray of the bones of the hands: bone age is 9 years.

Questions: 1) Your diagnosis. 2) What diseases should be differentiated from this child's disease? 3)

Examination plan for this disease. 4) Principles of the treatment of this disease.

Answer standard: 1) Hypothalamic obesity, 1st degree. Secondary arterial hypertension. 2) Differential diagnosis is carried out with various clinical forms of obesity (exogenous constitutional obesity, genetic syndromes and defects accompanied by obesity, brain tumors and injuries, hormonally inactive tumors of the pituitary gland, «empty sella» syndrome, obesity at the background of mental illnesses, hypothyroid obesity,

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|  | <p>hypoovarian obesity, hypercorticotoid obesity). 3) Determination of height and body weight, calculation of BMI, waist and hip circumference and their ratio, sexual development, blood pressure, general blood and urine tests, determination of fasting blood glucose, blood lipid spectrum, x-ray of hands to determine "bone" age; if necessary - MRI or computer tomography of the brain, consultation of a neurosurgeon, ultrasound of the thyroid gland, adrenal glands, organs of the abdominal cavity, if necessary for girls - ultrasound of the pelvic organs; in case of the presence of endocrine disorders - examination according to the relevant protocols; if possible - the level of insulin, leptin in the blood; if the signs of pseudohypoparathyroidism are present - calcium, blood phosphorus, parathormone. ECG, with a persistent increase in blood pressure - echocardiography. Consultations: neurologist, ophthalmologist, geneticist, infectionist. 4) Hypocaloric diet; dosed physical activity, physical therapy; dehydration therapy (with signs of liquor hypertension) 25% solution of magnesium sulfate, diacarb in age-related doses in the combination with potassium preparations; in case of severe obesity, signs of hyperinsulinism, metformin is prescribed in an initial dose of 500–750 mg per day (250 mg 2–3 times a day), the dose may be increased to 1000–1500 mg per day. Sanation of foci of chronic infection. Symptomatic treatment: a) with hyperlipidemia - lipoic acid; in case of the presence of cerebrovascular pathology and cerebrospinal fluid dycirculation - treatment according to the recommendation of a neurologist, according to the relevant protocol; with persistent arterial hypertension - hypotensive agents, preference is given to herbal preparations or ACE inhibitors and <math>\beta</math>-adrenergic blockers.</p> <p>Task 2</p> <p>On the 12th day of life, in a newborn girl with an abnormal structure of the external genitalia lethargy developed, repeated projectile vomiting (fountain) that was not related to eating, loose stools, gradually increasing dehydration, and no weight gain. A child from the first pregnancy (physiological), physiological childbirth. Body weight at birth was 3100 g, body length - 51 cm.</p> <p>Objectively: body temperature 36.5 °C, respiratory rate 60/min., heart rate 180/min., blood pressure 50/28 mmHg. Body weight 3100 g, body length 51 cm. The general condition is severe, the child is restless, projectile vomiting (fountain). The skin is dry, earthy-gray with a marble shade. Tissue turgor is reduced, severe hypotension, hyporeflexia. Big fontanelle and eyes are sunken. Breathing is shallow.</p> |  |  |
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|  | <p>Heart sounds are rhythmic, weakened. The abdomen is distended, the lower edge of the liver protrudes from below the edge of the costal arch by 2 cm. The spleen and kidneys are not palpable. An irregular structure of the external genitalia is determined (penis-like clitoris, folded labia majora, incomplete fusion of the labia, incomplete separation of the urethra and vagina, urogenital sinus), hyperpigmentation of the external genitalia, the white line of the abdomen. Excretions are loose, without pathological impurities.</p> <p>CBC. Hemoglobin 170 g/l, erythrocytes 5.1 T/l, reticulocytes 10%, platelets 200 g/l, leukocytes 8.9 g/l, myelocytes 0%, metamyelocytes 0%, banded neutrophils 4%, segmented neutrophils 37%, eosinophils 10%, lymphocytes 42%, monocytes -7%, ESR 8 mm/h.</p> <p>Biochemical analysis of blood. Total protein 65 g/l, glucose 1.7 mmol/l, total bilirubin 66 µmol/l, direct bilirubin 7.7 µmol/l, ALT 37 U/l, AST 29 U/l, alkaline phosphatase 140 U/l, LDH 1520 U /l, amylase 90 U/l, cholesterol 2.9 mmol/l, creatinine 47 mmol/l, urea 3.5 mmol/l, uric acid 0.26 mmol/l, CRP (–), rheumatoid factor (–), potassium 8.8 mmol/l, sodium 115 mmol/l.</p> <p>Urine analysis. The colour - colorless, the reaction is weakly acidic, the specific weight is 1004, the transparency - transparent. Chemical research: protein was not detected, sugar was not detected, acetone was not detected. Microscopy of the sediment: epithelial cells (flat 2–4 in the field of vision, polymorphic 1–2 in the field of vision, renal epithelium not detected), leukocytes 1–3 in the field of vision, erythrocytes 0–1 in the field of vision, cylinders not detected., salt not detected, mucus not detected., bacteria not detected.</p> <p>Questions: 1) Your diagnosis. 2) What diseases should be differentiated from the diseases of this child? 3) Examination plan for this disease. 4) Principles of treatment of this disease.</p> <p>Answer standard: 1) Congenital hyperplasia of the cortex of the adrenal glands, salt-wasting form, state of decompensation, exicosis, hypoglycemia, hyperkalemia, hyponatremia. 2) Differential diagnosis is carried out with other forms of intersexuality, diseases accompanied by vomiting and dehydration (pylorospasm, pylorostenosis, intestinal infections, diabetes insipidus, sepsis, hereditary enzymopathy, brain tumors, etc.). 3) Assessment of physical development (height, body weight), body structure, examination of the external genitalia, determination of the degree of virilization, assessment of the stage of sexual development, examination of blood pressure, blood electrolytes (potassium, sodium, chlorine), blood glucose, blood pH (at salt-wasting form), x-ray of hands to determine bone</p> |  |  |
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|  | <p>age, sex chromatin, karyotype, consultation of gynecologist for girls, ultrasound of pelvic organs, adrenal glands; hormonal tests: cortisol level or urinary excretion of free cortisol; 17-hydroxyprogesterone; testosterone; 17-ketosteroids in daily urine; carrying out a test with dexamethasone, the level of ACTH in the blood; plasma renin activity. 4) Intravenous hydrocortisone or prednisolone. After stopping of the vomiting, mineralocorticoid drugs (fludrocortisone) are administered. For the purpose of rehydration, a 5% glucose solution in a 0.9% sodium chloride solution is prescribed. In severe hypoglycemia, a 10% glucose solution is used. Dopamine is prescribed in case of a significant drop in blood pressure. After stabilization of the patient's condition, the dose of glucocorticoids is gradually reduced for 5 days to the maintenance dose. In case of hyperkalemia, 10% calcium gluconate is administered. Sodium bicarbonate 7.5% is prescribed to improve the entry of potassium into cells. Lifelong treatment with glucocorticoids and mineralocorticoids. During the dose titration of mineralocorticoids, table salt is additionally introduced. Surgical treatment (correction of the abnormal structure of the external genitalia) is indicated for girls with virilization according to Prader 3–5 degree.</p> <p><i>General evaluation of the student's educational activity during the class</i></p> |  |  |
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### Questions for student self-preparation for practical classes

- Etiology, pathogenesis, clinical features, diagnostic methods, differential diagnosis, treatment and prevention of pituitary dwarfism in children.
- Etiology, pathogenesis, clinical features, diagnostic methods, differential diagnosis, treatment and prevention of diabetes insipidus in children.
- Etiology, pathogenesis, clinical features, diagnostic methods, differential diagnosis, treatment and prevention of hypogonadism in children.
- Etiology, pathogenesis, clinical features, diagnostic methods, differential diagnosis, treatment and prevention of cryptorchidism.
- Etiology, pathogenesis, clinical features, diagnostic methods, differential diagnosis, treatment and prevention of premature puberty in children.
- Etiology, pathogenesis, clinical features, diagnostic methods, differential diagnosis, treatment and prevention of delayed puberty in children.
- Etiology, pathogenesis, clinical features, diagnostic methods, differential diagnosis, treatment and prevention of Turner syndrome.
- Etiology, pathogenesis, clinical features, diagnostic methods, differential diagnosis, treatment and prevention of Klinefelter syndrome.
- Etiology, pathogenesis, clinical features, diagnostic methods, differential diagnosis, treatment and prevention of ovotesticular disorder of sex development.
- Etiology, pathogenesis, clinical features, diagnostic methods, differential diagnosis, treatment and prevention of congenital hyperplasia of the adrenal cortex in children.

- Etiology, pathogenesis, clinical features, diagnostic methods, differential diagnosis, treatment and prevention of obesity in children.

**Recommended literature:**

**Main:**

- Nelson Textbook of Pediatrics, 2-Volume set, 21-th edition. By Robert M. Kliegman, Bonita M.D. Stanton, Joseph St. Geme and Nina F Schor. – Philadelphia, PA : Elsevier Inc., 2020. 4264 p. (P. 2876–2889, 2892–2912, 2970–2979, 2982–2985, 2993–2997, 3001–3019)

**Additional:**

- Clausena CS, Ljubicica ML, Maina KM et al. Congenital Adrenal Hyperplasia in Children: A Pilot Study of Steroid Hormones Expressed as Sex- and Age-Related Standard Deviation Scores. *Horm Res Paediatr* 2020; 93 (4):226–238. [www.karger.com/hrp](http://www.karger.com/hrp). doi: 10.1159/0005090

- Duicu C,<sup>1</sup> Pitea AM,<sup>1</sup> Oana Maria Săsăran OM et al. Nephrogenic diabetes insipidus in children (Review). *Exp Ther Med*. 2021;22(1): 746. doi: 10.3892/etm.2021.10178

- Korkmaz HA, Kapoor RR, Kalitsi J et al. Central diabetes Insipidus in children and adolescents: Twenty-Six Year Experience from a Single Centre. *Int J Endocrinol*. 2022 (6): 1–6. Article ID 9397130. <https://doi.org/10.1155/2022/9397130>

- Ronan L, Alexander-Bloch A, Fletcher PC. Childhood Obesity, Cortical Structure, and Executive Function in Healthy Children. *Cereb. Cortex*. 2020; 30 (4): 2519-2528 Volume 30, Issue 4, April 2020, Pages 2519–2528, <https://doi.org/10.1093/cercor/bhz257>

- Soliman A, Rogol AD, Elsiddig S et al. Growth response to growth hormone (GH) treatment in children with GH deficiency (GHD) and those with idiopathic short stature (ISS) based on their pretreatment insulin-like growth factor 1 (IGFI) levels and at diagnosis and IGFI increment on treatment. *J Pediatr Endocrinol Metab*. 2021; 34(10):1263–1271. doi: 10.1515/jpem-2021-0389

**Methodical guidelines have been created**

Associate professor of Pediatric Department No 2

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