Ministry of Education and Science of Ukraine
V. N. Karazin Kharkiv National University

RICKETS, SPASMOPHILIA, HYPERVITAMINOSIS D

Methodical recommendations
for students of 4th course of medical faculty

Kharkiv – 2021

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Methodical recommendations are worked out on the basis of the Programs disciplines «Pediatrics» for students of higher medical educational institutions of III–IV levels of accreditation, authorized by the Ministry of Health of Ukraine. These recommendations are intended for English-speaking medical students of the 4th year.

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CONTENTS

LIST OF ACRONYMS

Ca–calcium
ECG – electrocardiography
Mo – month
P – phosphorus
Vit C – vitamin C
Vit D –vitamin D
1.25(OH)2D3 – calcitriol
25(OH) D3 – calcidiol

INTRODUCTION

Rickets is a disease of growing organism, which appears as a result of polyhypovitaminosis with primary insufficiency of vitamin D, that leads to disturbances in metabolism of phosphorus and calcium and processes of ossification with changes of organs and systems function. Its diagnostics is based on clinical manifestations involving nervous, osseous, muscular systems and laboratory and instrumental investigations. The incidence of rickets in Europe is similar to that in the United States. In sunny areas, such as in the Middle East, rickets may occur when infants are bundled in clothing and are not exposed to sunlight. In some parts of Africa, deficiency of calcium, phosphorus, or both in the diet may also lead to rickets, especially in societies where corn is predominant in the diet. The frequency of rickets has been increasing internationally. Possible reasons include recommendations for children to wear sunscreen while outdoors and a tendency for children to spend more time indoors, watching television or playing electronic games, instead of playing outdoors.

Diseases such as spasmophilia and hypervitaminosis D are pathogenetically associated with rickets. Spasmophiliais characterized by the predisposition of children 6-18 months of age to seizures and spastic conditions that occur in connection with the acute development of hypocalcemia on the background of electrolyte imbalance and alkalosis.

Hypervitaminosis D occurs due to an overdose of vitamin D and due to their individual intolerance. The urgency of studying this problem is also due to the proven in recent years the effect of vitamin D deficiency on the immune system of children of any age and the quality of the child's body's response to infectious agents on the background of these pathological conditions.

RICKETS

Rickets is a group of diseases of the child's body associated with an insufficient intake of vitamin D or a violation of its metabolic processes, leads to a violation of various types of metabolism (primarily phosphorus-calcium), and causes damage to many organs and systems, but mainly to the bone skeleton.

Etiology. There are the following predisposal factors for appearance of rickets:

1. Deficiency of UV irradiation and staying out-doors, because 90% of endogenously created vit D_3 in organism is synthesized in skin under influence of sun beams. It is necessary to take into account that because of pollution of atmosphere of big towns, only minimal quantity of sun beams having antirachitic activity reaches the earth.

2. Food factors. Increase of frequency and severity of rickets was confirmed in groups of children receiving:

a) non-adapted mixtures (to which vit D is not added);

b) milk feeding only for a long time (1L of woman's milk contains 40–70 IU of vit D, cow's milk – 5–40 IU), late prescription of additional food (1 g of egg's yolk contains 140-390 IU of vit D);

c)–vegetarian additional food predominantly (vegetables, porridges) without sufficient quantity of animal proteins and fats.

3. Perinatal factors. Prematurity predispose to rickets because the most intensive income of Ca and P from mother to fetus takes place during last months of pregnancy, so a baby born earlier than 30 weeks of gestation very often has osteopenia – more low content of mineral substances in bone. At the same time, they are need in greater quantity of Ca and P in food because of greater rate of postnatal growth comparatively with mature children. Besides, prematurity, as well as placental insufficiency, is combined with much more low reserve in organism and more low level of vit D and its metabolites in cord blood.

4. Insufficient motor activity.

5. Dysbacteriosis with diarrhea.

6. Anticonvulsive prolonged therapy, which leads to speeding up metabolism of active forms of vit D.

7. Syndromes of malabsorption, chronic diseases of liver and kidney, which lead to disorders of formation of active forms of vit D.

8. Hereditary anomalies of metabolism of vit D, Ca and P.

9. Ecological factors. Excess of strontium, zinc and other metals in soil, water, food leads to partial substitution of Ca by these substances.

10. Pigmentation of skin decreases intensity of creation of cholecalciferol in skin.

Pathogenesis. Endogenous vit D_3 (cholecalciferol) is synthesized in skin from 7-dihydrocholesterin under influence of ultraviolet rays. More than 60 its

metabolites are created in organism later, but nowadays, only 2 of them are considered to influence actively upon metabolism of Ca and P – 1.25-dihydrocholecalciferol and 24.25-dihydrocholecalciferol. Both of them are created in kidneys, and intermediate metabolit (25-hydrocholecalciferol) – in liver. The main effects of active metabolites of vit D_3 are stimulation of absorption of Ca and P in intestine and stimulation of bone's mineralization. They activate synthesis of Ca-bounding proteins and increase activity of adenilatcyclase; that's why we consider vit D_3 to be hormone.

Hypocalcemia leads to increased function of parathyroid glands. Parathormone decreases (and vit D increases) reabsorption of phosphates in kidney tubules, stimulates absorption of Ca in intestine, resorbtion of Ca from bone and thus – liquidates hypocalcemia.

Insufficiency of vit D provokes aminoaciduria, leads to disorder of structure of organic matrix of bone (collagen). Disorder of ossification is seen in epiphysis, in metaphysis we see excessive growth of osteoid tissue.

Classification. There are different ways of classifying types of rickets, the most commonly used is to be classified as calciopenic and phosphopenic rickets.

Calciopenic rickets is due to nutritional deficiency of vitamin D and or calcium and rarely due to vitamin D defect in its cellular action or its metabolism to active metabolite-calcitriol or due to excess loss of calcium in urine.

Phosphopenic rickets is mainly due to renal phosphate wasting either due to primary renal tubular defect or excess generation of phosphatonin, compounds that inhibit phosphate reabsorption from renal tubules but unusually related to dietary phosphate deficiency that is wide available. It also determines rickets without significant variations in calcium and phosphorus levels.

Table 1

Classification of rickets

Vitamin D-deficient rickets, classic	**Vitamin D - dependent rickets**	**Vitamin D-resistant rickets**	**Secondary rickets**
options: Calcipenic, Phosphopenic, Without deviations of the Ca and P content in serum from normal. *By character of course:* acute, subacute, recurrent	1.Type 1-genetic defect synthesis in the kidneys 1.25 (OH) 2D 2.Type II genetic resistance of target organ receptors to 1,25 (OH) 2D	1. Familial congenital hypophosphatemic rickets or phosphate diabetes 2. Debre-de Toni-Fanconi syndrome (glucosoamino phosphate diabetes - complete, incomplete variant)	1. In case of kidney diseases, biliary obstruction 2. With malabsorption syndromes 3. With metabolic diseases substances (cysteinuria, tyrosinemia etc.)

Continuation of table 1

Severity: I – light II - moderate III - severe *Disease periods:* Initial period, Peck period, period of convalescence, residual effects		3. Renal tubular acidosis Hypophosphatasia *Phases of the disease:* active, clinical and laboratory remission (complete, incomplete)	4. Induced phenobarbital or others against convulsive drugs, glucocorticoids

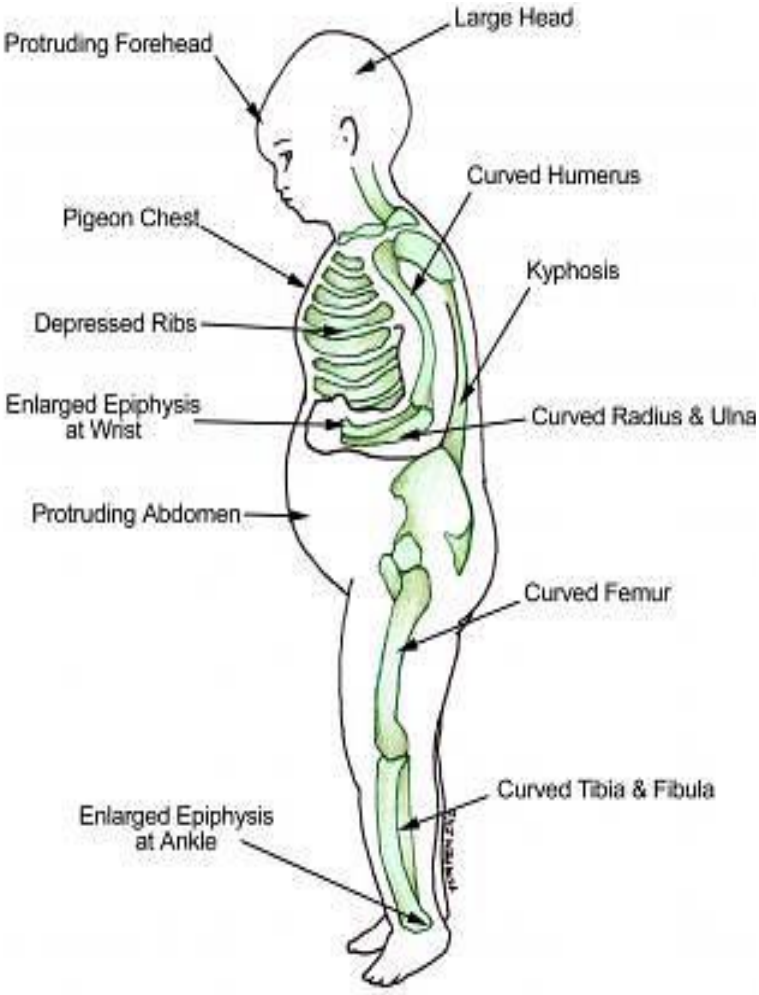

Figure 1.Clinical signs of rickets

Hereditary (congenital) anomalies of metabolism of Vitamin D, Ca and P

• *Vit D-dependent rickets of I type* (pseudovitamin D-deficiency rickets) – defect in the gene coding of renal 1-alpha-hydroxylase. Autosomal recessive disease.

• *Vit D-dependent rickets of II type* (hereditary 1-alfa, 25-dihydroxyvitamin D-resistent rickets) – mutation exists in the vitamin D receptors (VDR). Autosomal recessive disease.

• *Vit D-resistent rickets* (familial hypophosphatemic rickets and hereditary hypophosphatemic rickets with hypercalciuria) – mutations of the phosphate-regulating gene on the X chromosome.

Clinical manifestations

The symptom complex of bone changes is associated with the main pathomorphological processes that occur in the bones.

– *Symptoms of osteomalacia:* softening of the bones of the skull, craniotabes, an increase in the size of the large fontanelle, non-closure of the small and sometimes lateral fontanelles, brachycephaly (Fig. 1), deformities of

the bones of the skull, limbs, clavicle, flattened pelvis, erosion and caries of teeth, Garison's sulcus. Spine changes are kyphosis, lordosis, scoliosis, deformity of the lower extremities.

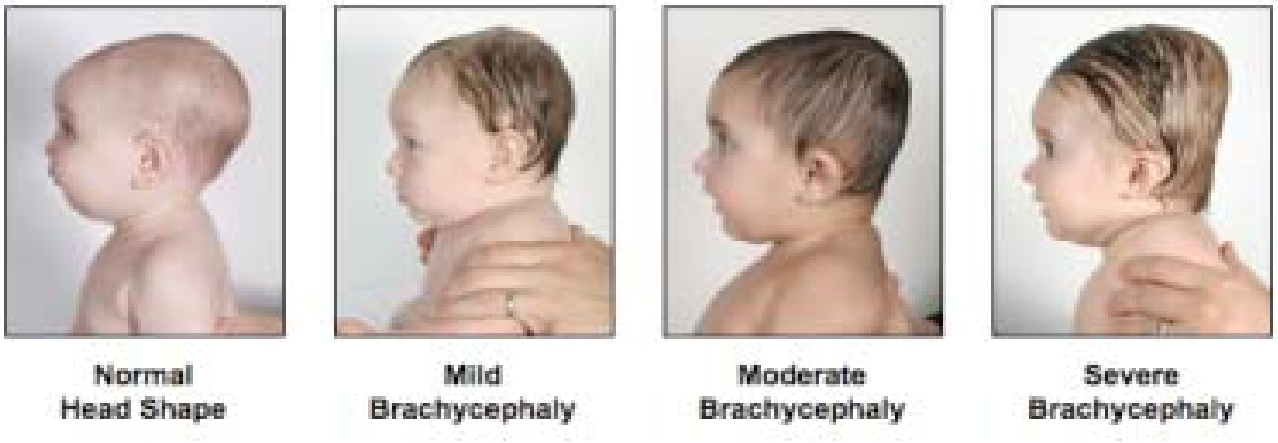

Figure 2. Defomation of skull

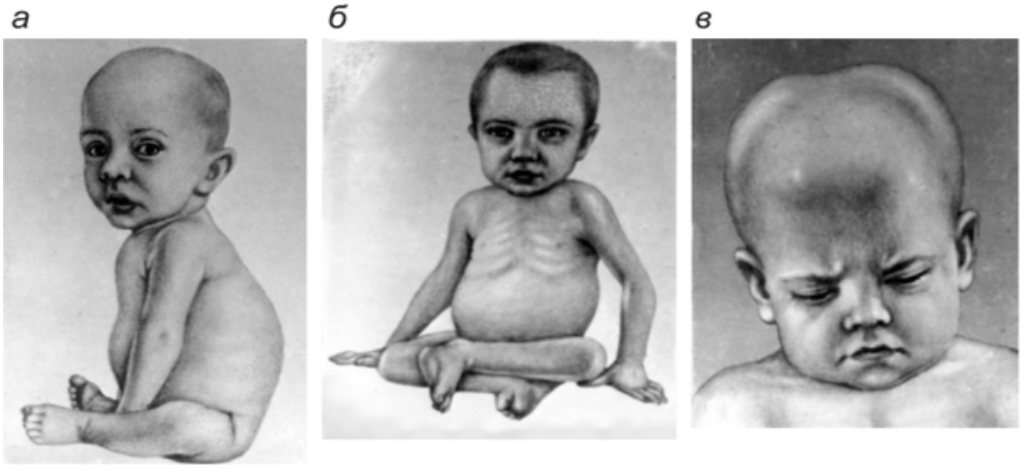

Figure 3. Kyphosis(a,b); Caput quadratum (b)

– *Symptoms of osteoid tissue hyperplasia:* enlargement of the frontal and parietal tubercles (caput quadratum, caput succedaneum, Olympic forehead) (Fig. 3 (b)), rickety rosary (Fig.4) at the junction of the bone and cartilaginous parts of the ribs, thickening of the epiphyses of the forearm bones (rickets bracelets) (Fig.4), phalanges of the fingers (threads of pearls).

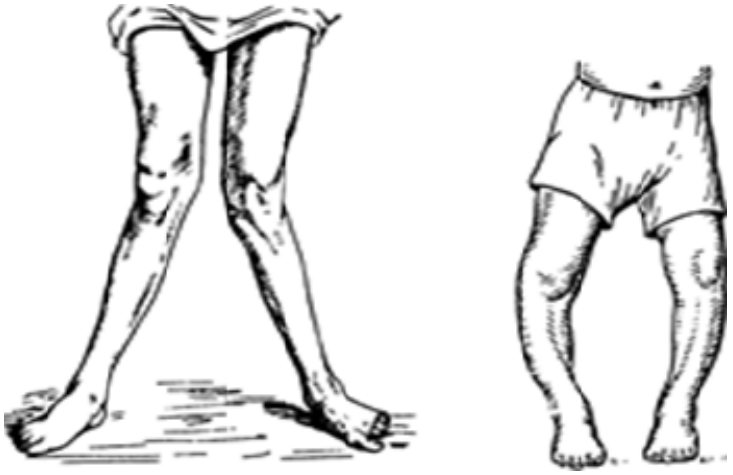

Figure 4. Deformation of low extremities ("O", "X" shaped deformities)

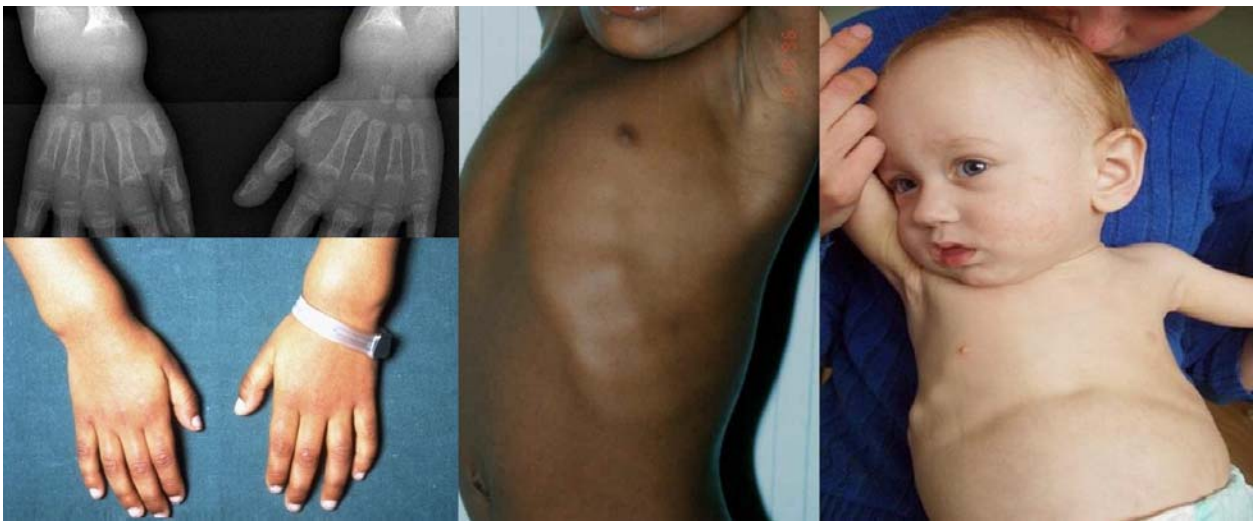

Figure 5.Rickets bracelets, rickety rosary

– *Symptoms of bone hypoplasia:* delayed closure of fontanelles, delayed teething, enamel hypoplasia, fractures (especially green-branch fractures), lagging in the growth of tubular bones in length in severe cases.

Other symptoms. Signs of muscle hypotension: Hypotension of the abdominal muscles and intestinal hypotension causes an increase in the abdomen, giving it the shape of a toad. Muscular hypotension and weakness of the ligamentous apparatus are manifested by laxity of the joints, general motor inhibition, delayed static functions - children begin to sit, stand, walk late. The child has anemia, occipital alopecia.

On the side of the cardiovascular system, muffling of heart sounds, tachycardia, systolic murmur is observed. On the part of the respiratory system, there is an increased risk of respiratory infections, areas of atelectasis in the lungs and the development of protracted pneumonia. There is a hepatolienal syndrome. Constipation, neurological abnormalities (irritability, interrupted sleep, sweating), hypocalcemic convulsions may occur.

Clinical symptoms depending on the period, severity and course of rickets.

Initial period.

From the side of nervous system, irritability, anxiety, and disturbed sleep are noted. The child has sweating, especially of the head, baldness of the occiput. Severe symptoms of osteomalacia: softness of the bone margins in the region of the large fontanelle, muscle tone is reduced. The calcium content in the blood remains normal, the phosphorus level decreases slightly. There is phosphaturia.

The peak period.

Sweating, weakness, hypotonia of muscles and ligaments become more expressive. The child lags behind in psychomotor development.

Symptoms of osteomalacia are increasing: softening of the flat bones of the skull, the appearance of craniotabes, flattening of the occiput, asymmetric

head shape, kyphosis, lordosis, scoliosis. There are overgrowths of symptoms of hyperplasia of osteoid tissue at the points of ossification of the flat bones of the skull – the formation of frontal and occipital tubercles (square head, "Olympic" forehead, costal "rosary", rickety bracelets appear). At the level of the diaphragm from the outside on the chest, a deep depression is formed – "Harrison's groove".

Deformities of the facial part of the skull (saddle nose, malocclusion) may occur. Teeth erupt later, inconsistently, easily affected by caries.

During the *period of convalescence*, signs of active rickets are not detected, vegetative and neurological symptoms gradually disappear: general well-being improves. The concentration of calcium and phosphorus in the blood is normalized. The duration of the period is from 6 months. up to 2 years.

Period of residual effects. During the period of residual effects, bone deformities, anemia, hepatolienal syndrome may occur.

For rickets of the first degree: changes in the autonomic nervous system are poorly expressed: increased sweating, worsening sleep, irritability, anxiety, decreased appetite, dyspeptic symptoms are possible; – changes on the part of the skeletal system are poorly expressed: compliance and soreness on palpation of the skull bones, areas of softening of the skull bones (craniotabes), deformation of the skull bones (flat, asymmetric occiput, frontal and parietal tubercles). To diagnose mild rickets, it is necessary to have changes in the skeletal system.

For rickets of the II degree – changes from the side of the vegetative nervous system - moderately pronounced, - changes on the part of the skeletal system - moderately pronounced: thickening on the ribs, at the junction of the bone and cartilaginous parts of the ribs – "rosary", softening of the ribs "Garison's groove", deformation of the sternum, expansion of the lower aperture, curvature of the spine – kyphosis, scoliosis, "O", "X" shaped deformities of the lower extremities, decreased motor activity, *the presence of moderate changes* – on the part of the muscular, circulatory, cardiovascular, digestive systems: – moderate enlargement of the liver, spleen, hypotonia of the muscles of the ligamentous apparatus, joint laxity, an increase in the size of the abdomen, the presence of anemia . For rickets of the second degree, lesion is characteristic bones in two or even three parts of the skeleton, pronounced changes in the nervous, bone, muscular systems, moderate changes in the internal organs.

For rickets of the III degree – significant disorders on the part of the nervous, bone and other systems: general motor retardation, delay in the development of static functions, pronounced bone deformities, decreased muscle tone, joint laxity, enlarged liver, spleen, functional disorders on the part of the cardiovascular, respiratory, digestive, circulatory systems.

Acute rickets is accompanied by signs of osteomalacia of the skeletal system, pronounced neurological symptoms.

Subacute rickets is characterized by pronounced symptoms of osteoid hyperplasia, the simultaneous presence of bone lesions in a child (with rickets, the skull is affected in the first 3 months of life, chest deformities occur at 3–6 months, and deformities of the lower extremities – in the second half of life).

*Recurrent rickets*is diagnosed if there are clinical, laboratory and radiological signs of active rickets identified in a child with previous rickets (presence of calcification stripes).

Table 2

Laboratory diagnostics of rickets

Indicators	Periods of rickets		
	Initial period	Peck period	Period of convalescence
Phosphorus, mmol / l N = 1.29-1.62 mmol / L	0,8	0,65–0,48	N
Calcium, mmol / l N = 2.25-2.75 mmol / L	2,62	2,2–2,0	2,3–2,4
Citric acid, μmol / l N = 156-208 μmol / L	160,0	52–104	154
Phosphatase, m.o. N = 200 m.o.	300	1000–1700	200
acid-base composition	Subcompensated acidosis	Decompensated acidosis	Moderate alkalosis

*Calcium:*normal level of serum Ca (total) in the blood is 2.25–2.5 (2.75) mmol/L, ionized Ca N = 1.1-1.4 mmol/L

*Phosphorus:*Normal level of P in blood is 0.97 – 1.62 mmol/L (1,45–2,1)

- for infants (5.0–7.5 mg/dL)
- for adults (2.7–4.5 mg/dL)

Alkaline phosphatase (ALP) level is 20–140 IU/L (140-220 IU, 4–6 mmol/l). Elevated ALP indicates that there could be active bone formation occurring as ALP is a byproduct of osteoblast activity.

Sulkovich's test- this test gives approximate presentation about Ca content in blood from is presents in urine. *Assessment of result:* "+" – normal level, "++, ++++" – hypercalcaemia and hypercalciuria.

X-ray examination.*Classical radiological changes* manifested in the form of osteoporosis, but of the greatest practical interest are changes primarily in the pineal glands (the heads of the tubular bones). In the bones of the extremities, there is a radiologically visible darkening of the edge line of the bone, delayed development of bone growth points; decreased density, stratification of the periosteum or curvature of the diaphysis of the tubular bones.

In the chest: classic "champagne corks" referring to a swelling in the form of rickety "rosary"; the image of the lungs with rickets creates the appearance of a fogging of both pulmonary fields.

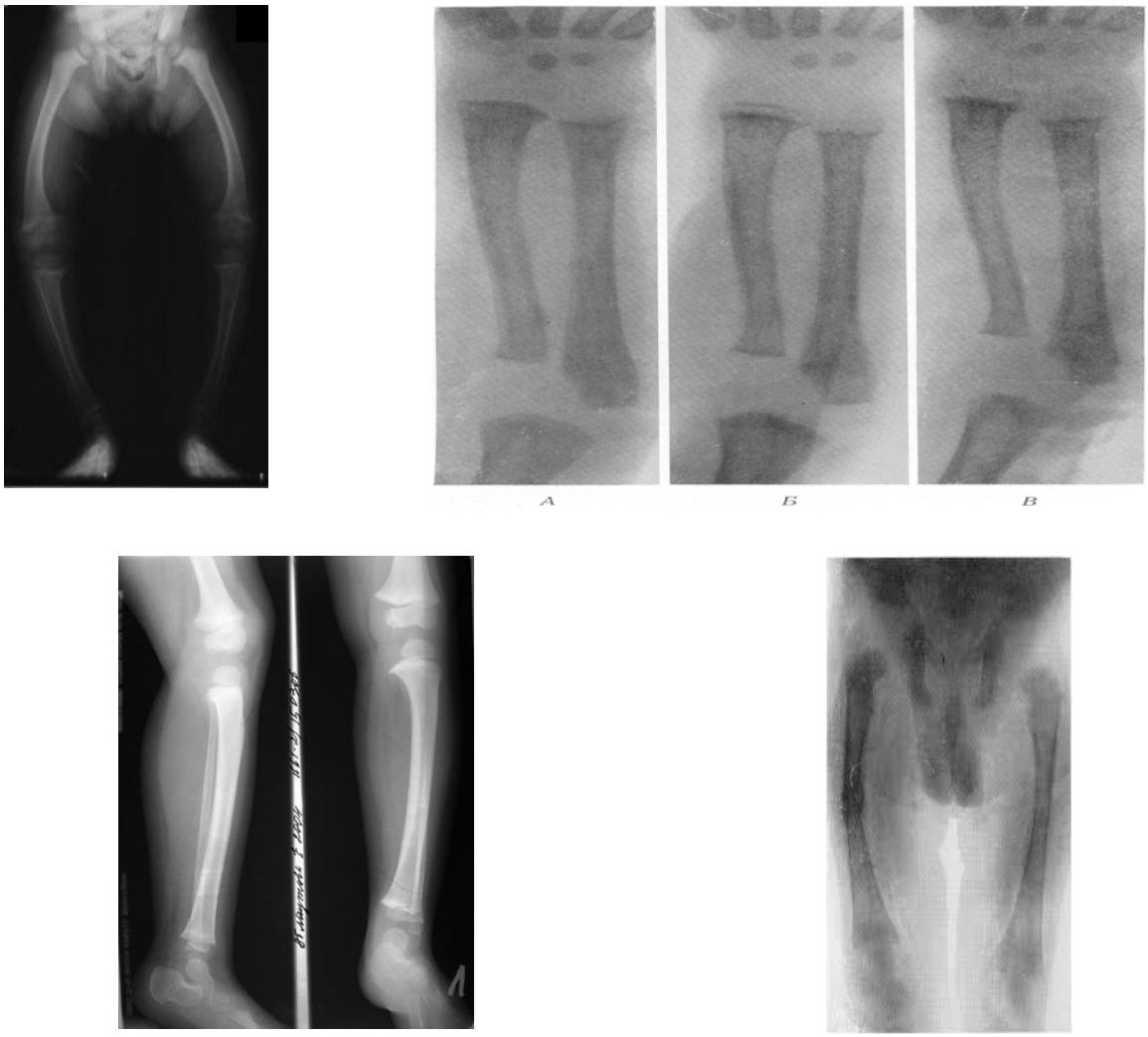

Figure 6. X-ray signs of rickets

Diagnosis of rickets.

a) Symptoms from the nervous, bone, muscular system;
b) characteristic deformities of the skeleton;
c) the staging of the pathological process;
d) biochemical changes in blood;
e) X-ray changes in bones.

Second level investigations:

– Bone densitometry;
– Bone mineral content;
– Receptor vitamin D interaction – in vitro study to assess VDDR type 2;
– Estimation of vitamin D metabolites to differentiate VDDR type 1 from type 2

Tertiary level investigations

– 25 (OH) D_3 level ng/ml

– Deficient Vit D level in serum – < 10 mmol|l

– Insufficient 10–20 mmol|l

– Optimal 20–60 mmol|l

– High 60–90 mmol\l

– Toxic > 90 mmol\l

Differential diagnosis. In *hypothyroidism*, in contrast to rickets, there is dry skin and pasty subcutaneous tissue, especially in the neck. There is never any softening of the bones of the skull: the bones are dense, there are no "beads" and thickening of the epiphyses. The child's face becomes peculiar: a low bridge of the nose, a half-open mouth with a large tongue, which does not fit in the oral cavity. There is a slow mental development. X-ray examination reveals a sharp delay in the appearance of ossification points and the presence of clear contours of the epiphyseal surfaces, characteristic of hypothyroidism.

In *chondrodystrophy*, the main symptom is a sharp shortening of the limbs. Disproportionate parts of the body: short limbs and a normally developed trunk. The limbs are clumsy, often somewhat curved and thickened due to the shortening of the phalanges, the hands have a peculiar trident shape. Despite the slow growth of bones in length, the growth of skin and subcutaneous tissue occurs normally, due to this, the skin on the limbs gathers in folds and hangs over the joints.

X-ray examination: all bones give an intense shadow, they are shortened, the cortical layer is thickened, there are no changes in the metaphyseopiphyseal region that characteristic of rickets.

Vit D-dependent rickets of I type: defect of 25-hydroxyvitamin D-I-hydroxylase in kidney lays in its basis. Laboratory signs are following:hypocalcemia, hypophosphatemia, high levels of parathormone in blood, increased activity of alkaline phosphatase, aminoaciduria, glucosuria. Usual doses of vit D are ineffective.

Vit D-dependent rickets of II type: almost the same, but total alopecia and retarded growth are present; level of 1,25 $(OH)_2$ D_3 is normal, but hypocalcemia and hypophosphatemia are preserved.

Phosphat-diabetes – defect is not quite clear, but it concerns reabsorption of phosphates in renal tubules and decreased activity of convertion of 25 (OH) D_3 in 1,25 $(OH)_2$ D_3. There are O-shaped legs; hypophosphatemia may be revealed by chance from the 1st month of life, signs of hypocalcemia, hyperplasia of osteoid tissue, myopathy are absent, level of blood Ca is normal or slightly decreased, parathormone in blood is normal, alkaline phosphatase elevated a little bit.

Hypophosphatasia – the length of tubular bones is diminished, disorders of ossification of all skeletal bones, activity of alkaline phosphatase in blood is very low. Hypercalcemia, nephrocalcinosis, renal insufficiency may be seen.

Treatment. Treatment of rickets in children should be long-term and aimed at eliminating hypovitaminosis D, normalizing phosphorus-calcium metabolism, correcting the acid-base state, restoring the functions of all organs and systems.

Non-specific treatments: diet, outdoor walks, massage and gymnastics.

For the specific treatment of rickets, the use of water-soluble vitamin D_3 (cholecalciferol) can be recommended.

Treatment is carried out with vitamin D_2 in doses, depending on the severity of the disease: with mild – 2000 IU, with moderate – 4000 IU, severe – 5000 IU during 30–45 days. In the future, to prevent exacerbations and relapses of the disease, 2000 IU for 30 days 2–3 times a year with intervals between them at least 3 months up to 3–5 years of age.

Prevention. Prevention may be antenatal and postnatal, specific and non-specific.

Non-specific antenatal prophylaxis of rickets: the main non-specific measures for the prevention of rickets in the antenatal period should be aimed at ensuring the normal course of pregnancy, preventing premature birth, intrauterine fetal hypoxia, gestosis, diseases; improvement of living and working conditions, everyday life. Special attention should be paid to the organization of the correct motor regime, sufficient stay in the fresh air, rational nutrition. The daily diet of a pregnant woman should include foods that are able to provide the need for vitamins, minerals, proteins, polyunsaturated fatty acids: meat, fish, milk or dairy products, soft cheese, hard cheese, raw vegetables, fruits.

*Specific antenatal prophylaxis*is carried out with vitamin D_3 (water or oil solution) or Videin.

Antenatal prophylaxis is carried out for healthy pregnant women from 28 to 32 weeks of pregnancy, 500 U daily for 6–8 weeks. Pregnant women from risk groups (gestosis, diabetes mellitus, rheumatism, hypertension, chronic liver disease, kidney disease, clinical signs of hypocalcemia and bone mineralization disorders) carry out antenatal prophylaxis from 28–32 weeks of pregnancy with 1000–2000 IU daily for 8 weeks.

*Specific postnatal prophylaxis*can be carried out*continuously or in a course method.*

Full-term healthy children start from 2nd month of life till 3 years old at 500 U daily, with the exception of 3 summer months (course dose per year – 180,000 IU).

It is also possible to carry out at the 2nd, 6th, 10th months of life, 2000 IU daily for 30 days. In the future, up to 3 years of age, should be provided 2–3 courses per year with intervals between them in 3 months (course dose per year – 180,000 IU).

Children at risk of rickets (children born to women with obstetric and chronic extragenital pathology, children suffering from malabsorption syndrome,

with congenital pathology of the digestive system, from twins and from repeated births with short intervals between them, as well as children on early artificial feeding, postnatal prophylaxis begins at 2–3 weeks of life 500–1000 IU daily until reaching 3 years of age, with the exception of the summer months.Or prophylaxis is carried out in the 2nd months of life at 1000–2000 U per day, at the 6th and 10th months of life, 2000 IU daily for 30 days. In the future, up to 3 years of age, 2–3 courses per year with intervals between them not less than 3 months.

For young children, who are often sick, postnatal prophylaxis is carried out at 4000 IU daily for 30 days. In the future, at 2000 IU for 30 days, 2–3 courses per year.

For children who receive long-term anticonvulsant therapy (phenobarbital, seduxen, diphenin) , corticosteroids or heparin postnatal prophylaxis is carried out at the 2nd, 6th, 10th month, at 4000 U daily for 30–45 days. In the future, 2–3 courses per year with intervals between them at least 3 months.

For premature infants of the 1st degree, postnatal prophylaxis is carried out from 10–14 days of life at 500–1000 IU every day during the first half of life. In the future, 2000 IU per day months 2–3 times a year with intervals between them 3–4 months.

For premature infants of II and III degrees, postnatal prophylaxis is carried out from 10–20 days of life at 600-1000 IU every day during the first half of life. In the future, 2000 IU per day for a month 2–3 times a year with intervals between them 3–4 months.

SPASMOPHILIA

Spasmophilia is a disease of young children, characterized by a tendency to tonic and tonic-clonic seizures, increased neuromuscular excitability due to a decrease of the level of ionized calcium in the extracellular fluid against the background of alkalosis. In the most severe cases of this disease, cardiac arrest (tetany of the heart) is possible, as well as respiratory arrest on expiration (bronchodilation).

Mostly children from 2 months to 2 years old are ill. Premature babies suffer from spasmophilia more often. The disease usually develops in early spring.

Etiology and pathogenesis. It is based on a violation of phosphorus-calcium metabolism against the background of deficiency of ergocalciferol, its metabolism and the function of regulatory systems. Major biochemical changes: hypocalcemia, relative hyperphosphatemia, alkalosis.

In the spring, the formation of ergocalciferol in the skin increases, phosphate reabsorption increases, calcium is deposited, and hypocalcemia may occur in a child with impaired mineral metabolism against a background of calciferol deficiency. Excessive formation of calciferol can contribute to the occurrence of hypofunction of the parathyroid glands, which also leads to

hypocalcemia.When the serum calcium concentration falls below 7–7.5 mg / dl, muscle irritability occurs, apparently due to a loss of inhibitory control, since the deficiency of ionized serum calcium affects the neuromuscular junctions.

Clinical picture. Latent spasmophilia. The symptoms are not obvious, but they can be detected by identifying the symptoms of Chvostek, Trousseau and Erb. Serum calcium levels are less than 7–7.5 mg / dL.

1. *Facial phenomenon of Chvostek* – when tapping with a finger in the fossa canina area, facial muscles contract from the corresponding side.

2. *Symptom Trousseau* - when the shoulder is compressed with an elastic tourniquet after 3 minutes. there is a convulsive contraction of the hand, the hand takes the form of an obstetrician's hand.

3. *Erb's symptom* – irritation of the median nerve in the elbow by galvanic current contributes to the contraction, the current strength is less than 5 A (normally more than 5 mA).

4. *Maslov's phenomenon* – characterized by short-term cessation of breathing due to painful irritation with a needle, this does not happen in a healthy child.

Manifest spasmophilia. Spontaneous clinical manifestations include carpopedal spasm, laryngospasm, and seizures. Serum calcium levels are often well below 7 mg / dL.

*Laryngospasm*is manifested by a slight spasm of the glottis or its complete but short-term closure. After the spasm a noisy breath comes – "cock crow". The attack lasts from a few seconds to 1–2 minutes and is repeated throughout the day.

Carpopedal spasm – tonic contraction of the muscles of the feet and hands. It can last for hours, sometimes several days. If the spasm lasts a long time, swelling may develop on the dorsum of the feet and hands. There is no soreness.

The most severe manifestation of spasmophilia is*eclampsia*- an attack of tonic-clonic seizures with loss of consciousness.

Diagnostics. The diagnosis is based on the presence of combined signs of rickets with low serum calcium levels and symptoms of tetany:

• decrease in the concentration of ionized Ca in the blood serum (0.9 mmol / l and below at a rate of 1.1–1.4 mmol / l),

• alkalosis (respiratory, less often metabolic),

• ECG - signs of hypocalcemia (lengthening of the QT complex> 0.3 s).

• Serum phosphorus levels are usually low;

• Serum alkaline phosphatase is elevated.

• In the differential diagnosis, it is necessary to exclude the causes of tetany, such as hypoparathyroidism, hypomagnesemia and phenothiazine intake.

Emergency care for spasmophilia. Emergency measures are necessary for general clonic-tonic seizures, laryngospasm and loss of consciousness with

impaired breathing. When breathing stops, artificial respiration is performed by the mouth-to-nose method, oxygen therapy to eliminate hypoxia (preferably mask inhalation with 40 % oxygen).

To relieve seizures, anticonvulsants are administered: 0.5 % seduxen solution intramuscularly to children aged 6–12 months – 0.5–0.7 ml each, older – 0.8–1 ml each or 20 % solution of gammaoxybutyric acid (GHB) at the rate of 100 mg per 1 kg of body weight (0.5 ml per 1 kg of body weight). GHB can be administered intravenously, intramuscularly, or rectally. In severe cases of seizures, both drugs can be used simultaneously.

After an urgent determination of the level of calcium in the blood, a 10 % solution of calcium chloride or gluconateis administered to children aged 6–12 months – 10 % calcium gluconate solution, 10 % calcium chloride solution 3–4 days. After the appointment of calcium preparations, anti-rickets therapy is prescribed.

Forecast: favorable. An attack of general tonic convulsions is dangerous – respiratory arrest and weakness of the heart. If the attack of eclampsia lasted for a long time, mental retardation is possible in the future.

Prevention: breastfeeding; timely prevention of rickets.

HYPERVITAMINOSIS D

Hypervitaminosis D occurs in children as a result of an overdose of ergocalciferol or because of its individual intolerance (due to the treatment and prevention of rickets). An overdose of ergocalciferol causes the development of severe, often irreversible disorders in the body as a result of hypercalcemia and pathological calcification of vital organs and tissues – vascular calcification, nephrocalcinosis, calcium deposits in the myocardium, alveoli, stomach wall, intestines, less often in the cornea and conjunctiva of the eye). The organs in which ergocalciferol is metabolized are most susceptible to damage – these are the liver and kidneys.

A direct toxic effect on the cell is manifested by increased lipid peroxidation, the formation of free radicals and, as a consequence, a violation of the stability of cell membranes.

In the initial period, there are anxiety, irritability, fearfulness of children or, more often, lethargy, weakness, sleep disturbance, increased thirst if the child refuses milk, decreased appetite up to anorexia, regurgitation, repeated vomiting. In the future, the body temperature rises (from subfebrile to high), the phenomena of toxicosis with exicosis, and malnutrition increase.

Early closure of the sutures of the skull and fontanelles, shortness of breath, increased blood pressure, muffled heart sounds, systolic murmur, tachycardia, enlarged liver and spleen, loose stools or constipation are observed. There may be meningeal and encephalic symptoms.

Kidney function is impaired (polyuria, nicturia, subsequently oliguria, anuria, uremia).

In the blood, hypercalcemia, hyperkalemia, hypercholesterolemia, increased urea levels.

The phosphorus content in the blood can be high, normal or low, in the urine – high.

Sulkovich'stest is sharply positive (hypercalciuria).

Calcium deposition in areas of bone growth is determined by X-ray. Increased absorption of calcium in the intestine leads to hypercalcemia followed by metastatic tissue calcification.

Hypercalciuria is a persistent symptom of hypervitaminosis D, which may be the cause of secondary pyelonephritis. The metabolism of phosphorus is impaired, citric acid accumulates in the blood, metabolic acidosis develops.

Lipid peroxidation and impaired oxidative phosphorylation leads to damage to cell membranes, leading to degenerative changes in tissues. Dysfunction of the endocrine system is observed, liver parenchyma is damaged.

Acute vitamin D intoxication often develops in children of the first half a year of life with a massive intake of vitamin D for a relatively short period of time (2–3 weeks) or individual hypersensitivity to the vitamin. At the same time, signs of neurotoxicosis or intestinal toxicosis appear: appetite is sharply reduced, the child is thirsty, vomiting often occurs, body weight rapidly decreases, dehydration develops, constipation appears (unstable and loose stools are possible). In some children, short-term loss of consciousness is recorded, tonic-clonic seizures are possible.

Chronic vitamin D intoxication occurs against the background of prolonged (6-8 months or more) use of the drug in moderate doses, but still exceeding the physiological need. The clinical picture is less pronounced and includes increased irritability, poor sleep, weakness, joint pain, a gradual increase in dystrophy, premature closure of the large fontanelle, changes in the cardiovascular and urinary systems.

Clinical classification of hypervitaminosis D in children (according to N. P. Barmebaeva, V. I.Strukov, 1984):

Light – there are no manifestations of toxicosis, there is a decrease of appetite, sweating, irritability, sleep disturbances, delayed weight gain, increased urinary calcium excretion; Sulkovich test (++),

Moderate – moderate toxicosis, decreased appetite, vomiting, delay or possible weight loss, manifestations of hypercalcemia, hypomagnesemia, hypercitremia; Sulkovich's test is sharply positive (+++ or ++++),

Severe – severe toxicosis, persistent vomiting, significant weight loss, complications (pneumonia, pyelonephritis, myocarditis, pancreatitis), a sharp change in biochemical parameters.

II. *By periods.*

1. Initial period.

2. Peak period.

3. The period of convalescence.

4. Residual effects: calcification of various organs and blood vessels, their sclerosis with the development of coarctation of the aorta, pulmonary artery stenosis, urolithiasis, chronic renal failure.

III. *By duration.*

Acute – up to 6 months,

Chronic – more than 6 months.

Treatment. Prescribe vitamin D antagonists:

vitamin A (5000-10,000 MO per day), the metabolism of which forms taurine, which inhibits the deposition of calcium in tissues;

vitamin E (tocopherol acetate 5–10 mg per day for infants, 10–15 mg per day for older children) – inhibits lipid peroxidation processes,

phenobarbital (3–5 mg / kg per day).

To reduce the absorption of calcium in the intestine, *prednisolone*is prescribed 2 mg / kg per day by mouth for 10–14 days with a gradual decrease in the dose,

15 % solution of *magnesium sulfate* 5–10 ml 3 times a day inside.

Furosemide 1 mg / kg is administered to increase renal calcium excretion,

syntheticthyrocalcitone in drops of 2–4 IU / kg every 6–12 hours for 3–4 days to reduce the concentration of calcium in the blood.

Infusion therapy using 5 % albumin solution – for hypoproteinemia, 5 % glucose solution, 0.9 % sodium chloride solution.

QESTIONS FOR SELF-CONTROL

1. Anatomical and physiological peculiarities of the musculoskeletal system in children.

2. Rickets. Determination, epidemiology, etiology, pathogenesis, classification, clinical picture, diagnostics, treatment, prophylaxis.

3. Spasmophilia, classification, clinical manifestations, diagnostics, treatment.

4. Hypervitaminosis D. Etiology, pathogenesis, clinics, diagnostics, treatment, emergency in acute hypervitaminosis D, prophylaxis.

Control tests

1) Which substances except hormones regulate metabolism of calcium and phosphorus in child’s organism?

A. Alkaline phosphatase.

B. Adrenaline.
Д. Ultraviolet irradiation.
E. Vitamin C.
C. Vitamin D.

2) What level of calcium is considered to be hypocalcemia?
A. 2 μmol/l
B. 2 mmol/l
Д. 2,5mmol/l
E. 3,2mmol/l
C. 1,5mmol/l

3) How parathyroid hormone influences upon the blood serum level of phosphorus?
A. Increases.
B. Doesn't change.
C. Dicreases.

4) What is the difference between muscles composition of children and adults?
A. Presence of fetal myosine.
B. Presence of ATA.
C. Absence of Ca.
Д. Increased content of myofibrallar proteins.
E. Increased content of alkalinephosphotase.

5) At what age big fontanel must be closed?
A. At 3 years.
B. At 1-1,5 years.
Д. At 7 mo.
E. At 2 years.
C. At 4 mo.

Standard answers: 1) C, 2) B, 3) C, 4) A, 5) B

Situational task 1. Fearfulness, agitation, irritability, bad sleep, sweating, baldness of occiput are present in a child of 1,5 mo. Level of serum calcium is 2,05 mmol/l. Formulate the diagnosis.

Correct answer. Rickets of I degree.

Situational task 2. In a child of 3mo from twins at examination is revealed: he doesn't support head well, craniotabes is present, lower aperture of the chest is opened, circumference of the head is increased, liver is palpated

+2 cm under the rib's arch. Level of serum calcium is 1,9mmol/, alkaline phosphotase – 7,5 μmol/l. What disease does the child have?

Correct answer. Rickets of III degree.

Situational task 3. A child of 4mo has impression of occiput, rachitic rosary on ribs, increase of frontal and occipital tubers, enlargement of fontanel. What additional examinations are necessary for formulation of diagnosis?

Correct answer. Calcium and phosphorus of blood, functional liver tests.

Situational task 4. A child of 3 years has rachitic rosary on ribs, O-shaped deformation of legs. Results of additional analyses: Ca – 2,6mmol/l, P – 1,9 mmol/l, alkaline phosphotase is normal. What disease does the child have?

Correct answer. Rickets, period of residual phenomena.

Situational task 5. A girl of 6mohas increased circumference of the head, rachitic rosary on ribs, "bracelets", opened lower aperture of the chest, muscular hypotonia. Liver is palpated +2-2,5 cm under the rib's arch. Results of additional analyses: Ca – 1,8mmol/l, P – 1,1 mmol/l. What disease does the child have?

Correct answer. Rickets of II degree, subacute course, period of height.

REFERENCES

Main sources of information

1. Nelson textbook *of Pediatrics* / R. M. Kliegman, R. E. Behrman, H. B. Jenson et al. – 20th ed. – Philadelphia, Pa : Saunders Elsevier, 2015. – 2615 p.

2. Propaedeutics of children's diseases and nursing of the child / T. Capitan. –Vinnisa, 2010. – 807 p.

3. Propedeutics of paediatrics / V. A. Fjoklin, V. A. Klymenko et al. – Kharkiv, 2010. – 346 p.

4. Pediatrics: Manual on Faculty Pediatrics for Foreign Students / Y. V. Odinets, A. F. Ruchko, I. N. Poddubnaya. – Kharkov: Kruk, 2003 .

5. Pediatrics. Textbook / O. V. Tiazhka, T. V. Pochinok, A. N. Antoshkina et al./ edited by O. Tiazhka. – Vinnytsia: Nova Knyha Publishers, 2011. – P. 36–49.

6. Rudolph's Pediatrics / A. M. Rudolph, C. D. Rudolph, M. K. Hostetter. – McGraw-Hill, 2003.

Additional sources of information

1. Contemporary Pediatrics/ O. Ozdemir – Croatia, 2012, 432 p.

2. The Harriet Lane handbook: a manual for pediatric house officers/ the Harriet Lane Service. Children's Medical and Surgical center of the Johns Hopkins Hospital. – 19th ed. /editors, Megan M. Tschudi, Kristin M. Acara. 2012,1132 p.

3. Molin A, Wiedemann A, Demers N, Kaufmann M, Do Cao J, Mainard L, et al. Vitamin D-Dependent Rickets Type 1B (25-Hydroxylase Deficiency): A Rare Condition or a Misdiagnosed Condition. J Bone Miner Res. 2017; 32: 1893–1899.

4. Pediatrics / H. Bauchner, R. Vinci, M. Kim, CambridgeUniversity Press. 2010 – http://ebooks.cambridge.org

5. http://www.emedicine.com

6. https://www.healthline.com/health/rickets

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