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# RICKETS. SPASMOPHILIA AND HYPERVITAMINOSIS D

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МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РЕСПУБЛИКИ БЕЛАРУСЬ
БЕЛОРУССКИЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ
1-я КАФЕДРА ДЕТСКИХ БОЛЕЗНЕЙ

**И. А. Козыро, А. В. Сукало, А. Г. Белькевич**

# РАХИТ. СПАЗМОФИЛИЯ И ГИПЕРВИТАМИНОЗ Д

# RICKETS. SPASMOPHILIA AND HYPERVITAMINOSIS D

Учебно-методическое пособие

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Освещены вопросы этиологии, патогенеза, классификации, клинических проявлений рахита, спазмофилии и гипервитаминоза Д у детей. Приведены современные рекомендации по диагностике, лечению и профилактике данных заболеваний.

Предназначено для студентов 4-го курса медицинского факультета иностранных учащихся, изучающих педиатрию на английском языке.

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# RICKETS

## Definition and history

Rickets is a disease of early-aged children, caused by a temporary mismatch between the needs of the growing body of the child in phosphorus and calcium deficiency and systems which ensure their delivery. Rickets is characterized by impaired mineralization of the rapidly growing bones and functions of the leading organs and body systems.

Rickets was known in antiquity. The first mention of rickets was found in the writings of Soranus of Ephesus (98–138 yrs.) and Galen (131–211 yrs.). The first medical description of rickets belongs to the British anatomist and orthopedic F. Glisson (1650). Due to the high prevalence of rickets in England this disease was called «the English disease», «rickets» (from old English «wrick-ken» — bend) or Glisson's disease. Later F. Glisson changed name to the Greek «rhachitis» (spine), based on the presence almost in all patients significant spinal deformation. Vitamin D was discovered in 1922 by Mc. Collum, later the opportunity to study its specific action on bone, muscle, intestine and renal tubules was found.

## Frequency

Rickets is «a disease of the growing organism» as it affects children during one of the «fastest growing» age periods — from 2 months to 3 years old.

During the 1st year of life child increase body weight from birth weight 3–3,5 kg till 10–12 kg (triple) and body length from birth length 50–54 sm till 75–78 sm (50 %).

During the 1st year of life from 56 to 80 % of children suffer from rickets.

According to medical records, the frequency of rickets in Belarus is 30–40 %. But the real frequency is more than 50 % because of not all cases are diagnosed and recorded.

## Etiology

Currently, rickets is understood as a polyethological metabolic disease. Its development is caused by the combined influence of many endogenous and exogenous causes as well as predisposing factors acting both prenatally and postnatally, both on the mother's and the child's side.

**Influencing factors:**

– deficiency of vitamin D or insufficient intake of vitamin D with food (leads to the lack of formation of cholecalciferol (vitamin D3) in the skin);

– insufficient intake of calcium and phosphorus;
– increasing function of the parathyroid glands;
– impairment of renal function;
– disturbances in the endocrine system which regulates $Ca^{2+}$ and $P^{3+}$ metabolism;
– variations in microelemental status.

**Predisposing factors:**

1. *From mother's side:*
– maternal age less than 17 and more than 35 years;
– gestosis of pregnancy;
– extra genital pathology (metabolic diseases, gastrointestinal tract pathology, kidney diseases);
– defects nutrition during pregnancy and lactation (protein deficiency, Ca, P, vit D, B1, B2, B6);
– day regimen (lack of insolation and physical activity);
– complications during delivery;
– poor socio-economic conditions.
2. *From child's side:*
– time of birth — autumn, winter (lack of sunlight);
– prematurity, morpho-functional immaturity;
– large birth weight (more than 4 kg);
– large weight gain during the first 3 months of life;
– breast-feeding, but the human-and long standing milk of nurse;
– early artificial and mixed feeding with non-adapted milk formulas;
– lack of exposure to fresh air;
– lack of physical activity (tight swaddling, lack of exercise therapy and massage);
– perinatal encephalopathy with lesions of the III ventricle;
– skin, liver, kidney diseases, malabsorbtion syndrome;
– frequent respiratory tract and intestinal infections;
– anticonvulsant medications;
– large quantities of cereals and vegetables consuming.

## Endogen synthesis and transformation of vitamin D

Adequate Vitamin D intake, positive calcium balance and outdoor physical activity are essential for appropriate skeletal growth and bone mineralization. These environmental factors also show a liability to reduce risk of several diseases. A diverse diet rich in food containing large amounts of Vitamin D, including oily fish, is important (table 1).

*Table 1*

**Sources of vitamin D**

| Sources | Vitamin D content |
|---|---|
| Fish oil | 150 IU/ ml |
| Egg yolk | 20–50 IU/yolk |
| Vegetable oil | 0,08 IU/g |
| Caviar | 3,2 IU/g |
| Cow's milk | 0,4–1,2 IU/100 ml |
| Infant formula (beginning formula) | 40–50 IU/100 ml |
| Infant formula (follow-up formula) | 40–80 IU/100 ml |

If the additive effect of dietary Vitamin D consumption and sunlight-induced Vitamin D synthesis in the skin is insufficient, taking supplements becomes essential to achieve optimal Vitamin D status. Most Vitamin D in the human body is produced in the skin after exposure to sunlight, specifically solar ultraviolet-B irradiance. In Central Europe, solar angle and weather conditions suitable for Vitamin D synthesis occur between late April and early September; whereas skin synthesis does not occur from October to March. The efficacy of skin synthesis basically depends on two factors: the degree of skin pigmentation and age. For optimal effect, Central Europeans should expose, without sunscreen, 18 % of the body surface (i.e. uncovered forearms and partially exposed legs) to a half of one minimal erythemal dose two or three times per week. In practical terms, exposing 18 % of the body to the sun without sunscreen for approximately 15 minutes a day between 10 a.m. and 3 p.m. is likely to be adequate for fair-skinned Central Europeans.

## Metabolism of vitamin D

Our body produces several metabolites of vitamin D but only 2 of them actively influence on the metabolism of $Ca^{2+}$ and $P^{3+}$: 1,25 dihydroxycholecalciferol and 24,25$(OH)_2D_3$. In terms of normocalcemia and hypercalcemia 24,25$(OH)_2D_3$ (mainly synthesized in kidneys) is formed. The formation of 1,25$(OH)_2D_3$ or calcitriol occurs under conditions of hypocalcemia. The process of vitamin D synthesis has some stages (fig. 1):

1. Vitamin D is absorbed in the proximal part of the small intestine, necessarily in the presence of bile.

2. In the liver under the influence of 25-hydroxylase 25-hydroxyvitamin D or calcidiol is formed. The stock accumulates in muscle tissue and fat layer, the excretion of 25$(OH)D_3$ through the bile initially low, which leads to the accumulation of 25$(OH)D_3$ in the liver.

3. At the kidney level the formation of 1,25$(OH)_2D_3$ occurs under the influence of 1-hydroxylase enzyme (in the kidneys proximal tubular cells).

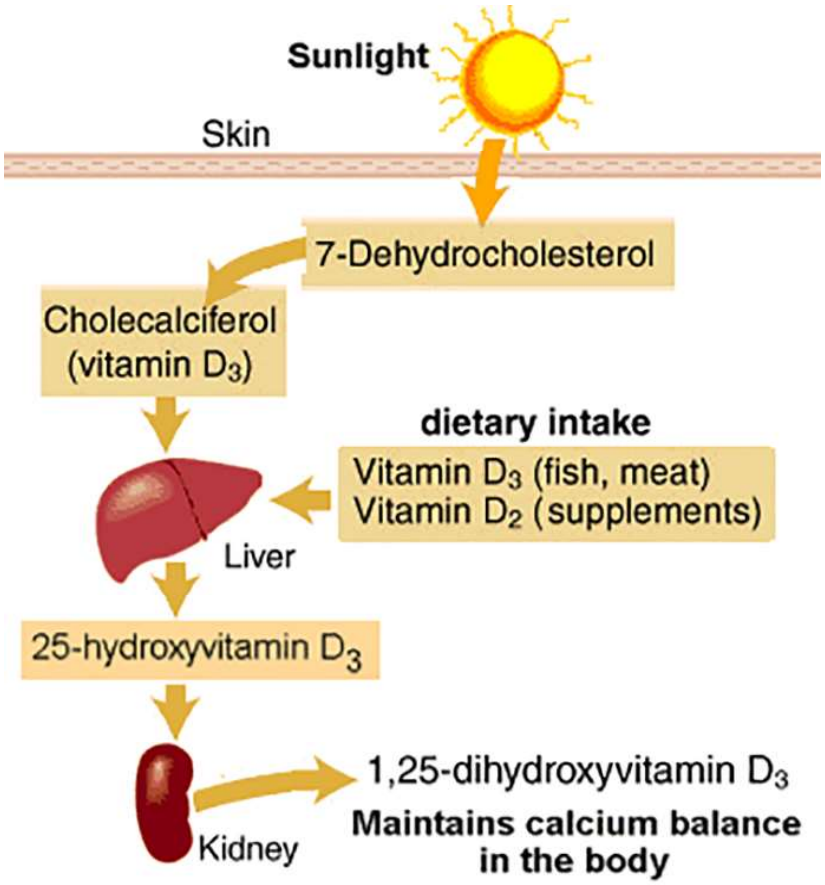



*Fig. 1.* Metabolism of vitamin D

**Role of metabolites of vitamin D:**

– increases permeability of enterocytes cell membranes for $Ca^{2+}$;

– stimulates the synthesis of $Ca^{2+}$-binding protein which provides transport of $Ca^{2+}$ ions from enterocytes into the blood;

– stimulates the absorption of $P^{3+}$ in the intestine;

– enhances the reabsorption of $Ca^{2+}$ and $P^{3+}$;

– stimulates the differentiation and proliferation of osteoblasts and chondrocytes which leads to protein synthesis increasing by the cells of the connective tissue — collagen;

– stimulates osteocalcin synthesis — the basic non-collagenous protein of bone tissue.

**Role of $Ca^{2+}$ in the body:**

– is the basis of the skeleton;

– involved in processes of blood clotting; protein synthesis, cell division and differentiation; immunogenesis;

– involved in myocardial contraction, automatism of the heart;

– transmission of nerve impulses;

– regulation of membrane permeability;

– stimulation of the activity of certain enzymes;
– secretion of hormones.

$Ca^{2+}$ concentration in blood is *from 2,1 to 2,8 mmol/l* and don't vary by more than 3 % due to hormonal control. The main mass of $Ca^{2+}$ is concentrated in the bone skeleton where the Ca phosphate (85 %), carbonates (10 %), salts of organic acids (citric and lactic (about 5 %)) are represented. 50 % of the $Ca^{2+}$ in the blood bound to plasma proteins, mainly to albumin. Ionized $Ca^{2+}$ concentration in serum is *from 1,1 to 1,4 mmol/l*. Free $Ca^{2+}$ is a regulator of a variety of intracellular processes and it ensures the implementation of a specific transmembrane signal into the cell. Elevated levels of ionized $Ca^{2+}$ is lead to the increase synthesis of calcitonin (thyroid hormone) which reduces the number and activity of osteoclasts, enhances deposition of $Ca^{2+}$ into the bone, increases $Ca^{2+}$ excretion by the kidneys and works as the antagonist of parathyroid hormone (PTH).

Currently vitamin D is considered as steroid pregormon. Its activity is provided by specific receptors (VDR) in many organs and tissues, suggesting about integrated D-endocrine system in the body. Recently synthesis of the active form $1.25(OH)_2D_3$ is discovered. It directly exposed to ultraviolet irradiation in the skin. It promotes the synthesis of the antimicrobial protein cathelicidin with eliminating effect on Gr- microflora which is the important component of the anti-infectious immunity of the skin.

**Main functions of vitamin D:**

– maintaining mineral homeostasis;
– involved in the metabolism of lipids;
– maintaining the concentration of electrolytes and energy metabolism;
– participation in the maintenance of adequate bone mineral density;
– regulation of hair growth;
– stimulation of cell differentiation;
– inhibition of cell proliferation;
– implementation of immunological reactions;
– regulation of blood pressure.

A whole cascade of metabolic disorders develops with insufficient intake of vitamin D from food or its low synthesis. Scheme of pathogenesis of rickets is in the fig. 2.

An important role in the pathogenesis is assigned to PTH which is activated in rickets. Its effect on kidneys and bones is as follows:

– increasing the tubular reabsorption of $Ca^{2+}$ and $Mg^{2+}$;
– decreasing reabsorption of potassium, non-organic $P^{3+}$ and $HCO_3^-$;
– decreasing excretion of protons and ammonium ions;
– increasing the ability to form the active form of vitamin D — $1,25(OH)_2$;
– inhibition of collagen synthesis in active osteoblasts;
– activation of osteoclasts osteolysis;

– acceleration of maturation of osteoblasts and osteoclasts progenitor cells;
– the consequence of these effects is the mobilization of $Ca^{2+}$ from the bone (release in the blood) and the depletion of matrix with collagen and proteoglicans.

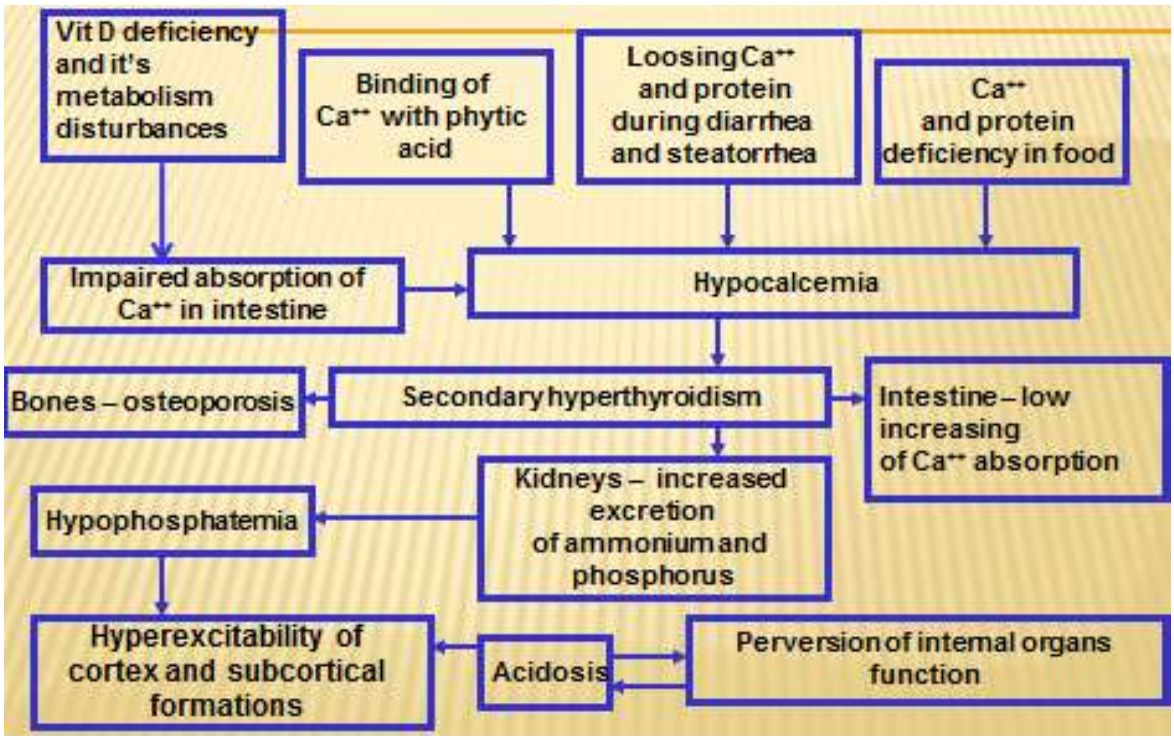



*Fig. 2.* Pathogenesis of rickets

It should be noted acidosis retains $P^{3+}$-$Ca^{2+}$ salts in the dissolved state, than prevents impregnation of cartilage and osteoid tissue. Accumulation in the blood serum of acidic products of metabolism at the same time with decreasing the level of $Ca^{2+}$ impairs the function of the central and autonomic nervous system and increases their excitability. Upon cleavage of the pyruvic acid is formed a series of intermediate oxidized products, one of which is the citric acid. Citrates form soluble compounds with $Ca^{2+}$ and transport it from the bone into the blood and back again. Citric acid is also enhances the reabsorption of $P^{3+}$ in the kidneys.

## Classification of rickets

There are some points in classification of rickets:
1. *Stages of the disease:*
– initial;
– clinical sings;
– recovery;
– residual sings.

2. *Grade of severity:*
– I grade — mild;
– II grade — moderate;
– III grade — severe.
3. *Course:*
– acute;
– sub-acute;
– relapsing.
4. *Biochemical option:*
– low $Ca^{2+}$ level (Ca-penic);
– low $P^{3+}$ level (P-penic);
– without Ca and P abnormalities.

Some diseases and conditions can lead to secondary rickets, e.g. malabsorption syndromes, chronic kidney disease, biliary tract pathology, metabolic diseases (tyrosinemia, cystinuria), hereditary diseases (vitamin D-resistant rickets), prolonged use of anticonvulsants (phenobarbital), diuretics, corticosteroids, parenteral nutrition.

## Clinical signs of rickets

Clinical signs of rickets depend on grades, course and biochemical changes but there are basic signs (fig. 3).

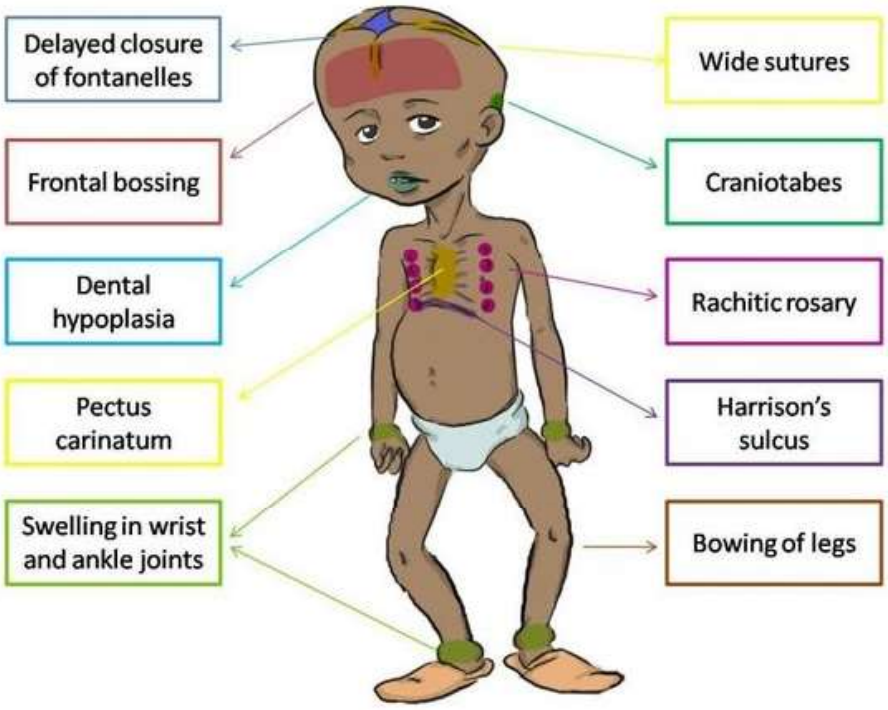


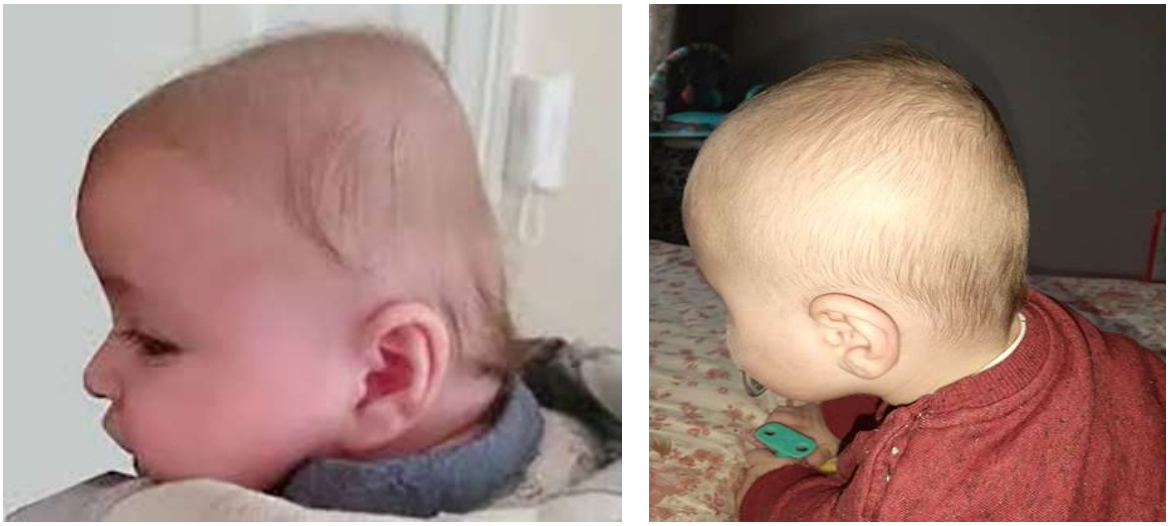

*Fig. 3.* Ten important clinical features of rickets

**Rickets I grade (mild)** is characterized by a minor disturbance of the general state:

– restlessness; sweating; red dermographism;

– moderate hypotonia (constipation);

– initial bone changes — craniotabes (fig. 4, *a*), flattening the occipital part of the head (fig. 4, *b*) and a slight expansion in the areas of osteoid tissue growth (rosary).



***a*** ***b***

*Fig. 4.* Initial bone changes in children with rickets:
*a* — craniotabes; *b* — flattening the occipital part of the head

**Rickets II degree (moderate)** is characterized by:

– impaired general condition and moderate changes in the nervous, muscular systems: hypotension, enlarged «frog belly» (fig. 5), high standing of a diaphragm, slight enlargement of the liver and spleen, mild anemia;

– but more pronounced changes in the bones: parietal bumps, rachitic «beads»; «bracelets», «string of pearls», spreads the lower thoracic inlet in the form of «hat brim», «Harrison's sulcus».

**Rickets III degree (severe)** is characterized by severe skeletal deformities: «square» shape of the skull, increasing the frontal, occipital tubercules, «olympic» forehead, «saddle» nose, breaking the terms of teething, bite, chest deformity («chest cobbler» and «chicken» chest (fig. 6, *a*), kyphosis, lordosis, scoliosis), the curvature of the long bones (fig. 6, *b*), «flat» pelvis, atony of muscles, joint laxity and ligaments, and static disorder of motor function.

Enlargement of the liver and spleen in rickets is associated with metabolic disorders, anemia and stasis (congestion) in the portal and splenic veins. Heart and diaphragmatic muscles hypotonia, degenerative changes in the myocardium and electrolyte disturbances lead to a weakening of the heart, decreased blood pressure,

tachycardia, moderate expansion of the heart borders, soft systolic murmur. Due to severe hypotension of intercostal muscles, diaphragm and muscles of the bronchi hypoventilation develops what together with acidosis creates a predisposition in children with rickets to develop pneumonia. Changes in immunobiological properties of the organism get children sick easily with infectious diseases which occur for a long time and in a more severe form. Decrease in activity of gastrointestinal enzymes leads to poor appetite and malabsorption of nutrients from intestine which together with abdominal muscles hypotension causes an increase of the abdomen volume («frog belly») and slow bowel movement (constipation). A change in the blood (decrease of hemoglobin and red blood cell count) is associated with dysfunction of the bone marrow.

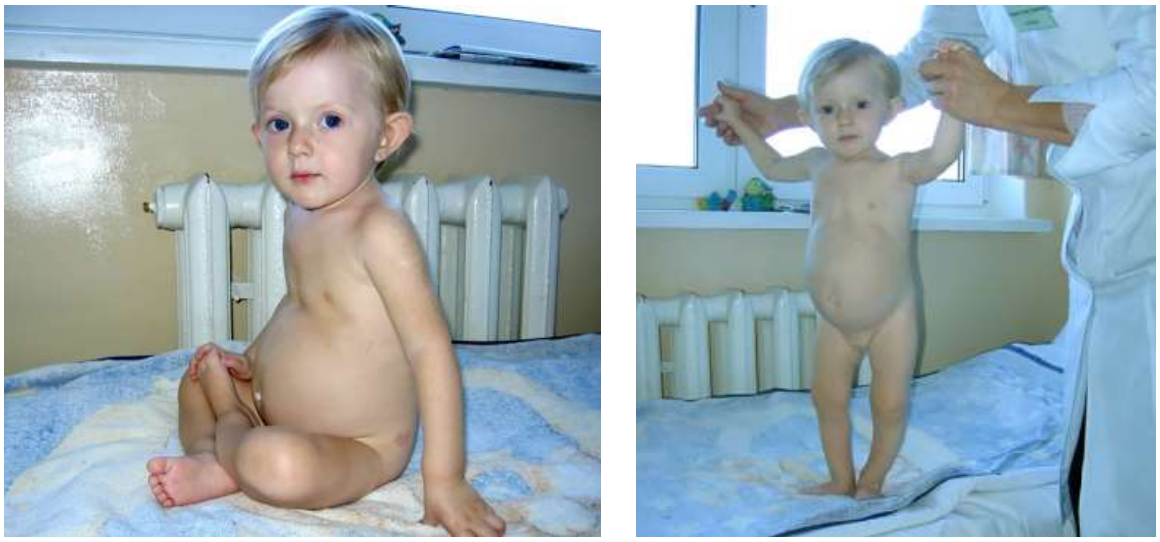
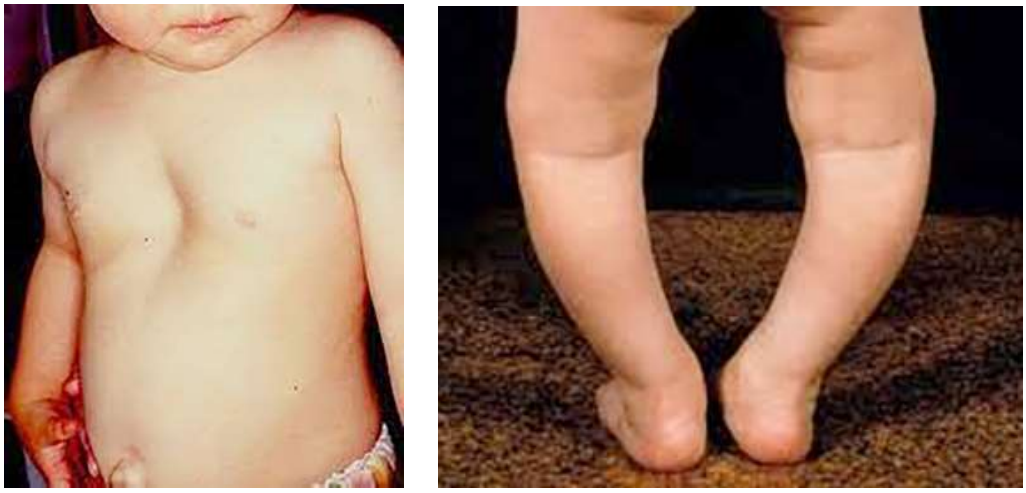


*Fig. 5.* Musular hypotonia and «frog belly»



***a*** ***b***

*Fig. 6.* Bone changes of skeleton:
*a* — «chest cobbler»; *b* — O-like bending the legs

*Acute course* observed mainly in children in the first 6 months of life, mostly in preterm and overweight, who did not receive vitamin D as a prophylactic measure.

*Subacute course* characterized by a slow development of symptoms, mild neurological and autonomic disorders, prevalence of osteoid hyperplasia on osteomalacia and deviations of biochemical parameters. This usually occurs in children older than 6 months.

*Relapsing course* observed in frequently ill children with inappropriate diet when you stop to give vitamin D after the treatment of rickets. This type of course is characterized by periods of exacerbation followed by periods of remission. Bone X-ray reflects the formation of new bands of calcification in the metaphysis.

**Ca-penic version** of rickets is characterized by severe disorders of the autonomic nervous system (sweating, red dermographism, tachycardia), increased neuro-reflex excitability (hand tremor, sleep disturbances, unwarranted anxiety, vomiting, bowel dysfunction). There is an acute variant. There is in the blood plasma a significant reduction in ionized $Ca^{2+}$, high levels of PTH, decreased calcitonin. **P-penic version** of rickets is associated with significant bone deformities: a distinct thickening of the metaphyseal regions of long bones of hands, sternal ribs and the presence of different strains of the skull. Motor retardation, severe hypotonia, abdominal enlargement, weak ligaments and articular apparatus, expressed hypophosphatemia, high levels of PTH and calcitonin, hyperfosfaturia also are typical. **Without Ca and P abnormalities version** is characterized by the severity of the frontal and parietal mounds in the absence of distinct changes in the nervous and muscular systems. In blood there is a moderate increase in the level of PTH at normal rates of calcitonin. Ambiguous indicators of the level of $Ca^{2+}$ and $P^{3+}$ in the blood during the period of significant clinical signs are explained by multidirectional calcitonin concentration in the serum.

## Diagnostics of rickets

There are 2 groups of diagnostic methods:

1. Main methods:
– blood analysis (could be anemia);
– urine (normal);
– blood biochemistry: $Ca^{2+}$ and ionized ones, $P^{3+}$ (normal 1,3–1,8 mmol/l), alkaline phosphates (normal 140–220 U/l);
– Sulkovich's analysis (weekly positive or negative).
2. Additional methods:
– pH blood;
– 24 hours urinary excretion of Ca, P (elevated);
– active vitamin D metabolites ($25(OH)D_3$ in blood serum 15–25 ng/ml);
– serum level of PTH (increased).

Changes in indicators depend on the stage of rickets and are presented in the table 2.

*Table 2*

**Dynamics of biochemistry parameters**

| Stage of the disease | Serum $Ca^{2+}$ | Serum $P^{3+}$ | Alkiline phosphates | pH blood | pH urine |
|---|---|---|---|---|---|
| Initial | N | N or moderate↓ | ↑ | Metabolic acidosis | ↑ |
| Clinical signs | ↓ | ↓ | ↑ | Metabolic acidosis | N or ↑ |
| Recovery/ residual signs | Moderate ↓ or N | N or ↑ | N | Metabolic acidosis | N |

Instrumental methods, e.x. X-ray bones, also can be used for diagnostics of rickets. X-ray signs of rickets are presented in table 3.

*Table 3*

**X-ray signs of rickets**

| Stage of the disease | X-ray changes |
|---|---|
| Initial | Absent |
| Clinical signs | Osteoporosis, goblet metaphyseal extension, blurred and fuzzy zones prior to (preliminary) calcification, the epiphysis becomes saucer-shape, the nucleus of ossification identified indistinctly |
| Recovery/residual signs | Uneven sealing growth zones (fringed), the appearance of lines prior to (preliminary) ossification |

## Differential diagnosis of rickets

Rickets is manifested by quite vivid clinical symptoms and specialists are well acquainted with this disease that allows in most cases to timely and correctly verify the diagnosis. But there are diseases with phenotypic similarity to rickets which requires differential diagnosis:

- vitamin D-resistant rickets;
- vitamin D-dependent rickets;
- renal tubular acidosis;
- de Toni-Debre-Fanconi disease;
- hyper- and hypophosphatasia;
- chondrodystrophy;
- Blount's disease;
- hypothyroidism.

## Therapy of rickets

Treatment of rickets should be comprehensive, timely, long-term and individually selected. Today, various schemes for the treatment of rickets are used in the world. But there isn't single and internationally recognized program of treatment. An integrated approach to the treatment of rickets includes the elimination of vitamin D deficiency, the normalization of P-Ca metabolism, the elimination of metabolic disorders and the correction of vegetative disorders.

**Specific therapy:** vitamin D at dose 2000–5000 IU daily during 30–45 days. Treatment starts with 2000 IU for 3–5 days and after if tolerated, increase the dose to an individual aspect under the supervision of medical Sulkovich's test. Test is carried out before treatment and then every 7–10 days. Dose of 5000 IU is administered only when significant bone changes occurred. Total dose of vitamin D for the whole course of treatment:

– in mild severity — 150 000–300 000 IU;
– moderate — 300 000–600 000 IU;
– severe — 600 000–800 000 IU.

When results is good (normalization of muscle tonus and vegetative nervous system, levels of alkaline phosphatase, Ca and P in the serum, disappearance of craniotabes) treatment is discontinued and the dose is reduced to preventive. Antirecurrent treatment is carried out at risk children (vitamin $D_3$ at dose of 2000–5000 IU for 3–4 weeks) 3 months after the end of the first course, except for the summer months. Medications of vitamin D which can be used for therapy of rickets are presented in table 4.

*Table 4*

**Medications of vitamin D**

| Name and form of medication | The content of D |
|---|---|
| Aqvadetrim Vitamin $D_3$ (cholecalciferol), aqueous solution (Medana Pharma Terpol group, Poland) | 1ml (30 drops) — 15 000 IU, flacon — 10 ml, 1 drop — 500 IU |
| Videchol ($D_3$ oleosum solution) — 0,125 % (Russia) | 1 drop — 500 IU, 1 ml — 25 000 IU |
| Ergocalciferoli oleosum soluion (vit $D_2$) 0,0625 % | 1 drop — 625 IU, 1 ml — 25 000 IU |
| Ergocalciferoli oleosum soluion (vit $D_2$) in capsules | 1 caps. — 500 IU |
| Vit $D_2$ oleos 0,125 % | 1 drop — 1 250 IU, 1 ml — 50 000 IU |
| Vigantol (cholecalciferol), oleos (Merck KGaA, Germany) | 1 ml — 20 drops (20 000 IU) |
| Oxidevit (synthetic analogue, $1,25(OH)_2D_3$) | 1 caps. — 500 IU |

**Non-specific therapy:**

1. For children older than 6 months in the complex of therapeutic interventions should be included therapeutic baths (alternate day, 10–15 procedures on the course).

2. Pasty, sedentary children recommended salt baths (2 big spoons of see salt per 10 liters of water, the temperature of water 35–36 °C duration 5 min), for irritable — conifers (1 tea spoon of extract for 10 liters of water, temperature of water 36 °C duration 10 min).

3. At remission process in bone but not earlier than 3 weeks after the start of therapy with vitamin D massage is recommended.

4. Magnesium in order to normalize the function of the parathyroid glands and reduce vegetative disorders (Asparkam, Pananginum).

5. Antioxidants to normalize the process of lipid peroxidation (vitamin E and A, Vetoron, Qudesan).

6. Medications for improving metabolic processes (Potassium orotate, Carnitine chloride (Elkar)) during 4–5 weeks.

7. Premature babies require the concomitant use of $Ca^{2+}$ supplements in dose 55–60 mg/kg/day for 2–3 weeks, for children of the 2nd year of life a diet rich in calcium is recommended.

8. Citrate mixture (acidi citrici 2.1; natrii citrici 3.5; aquae destillatae ad 100) 1 tea spoon 3 times per day for 10–14 days.

## Prevention of rickets

Prevention of rickets can be antenatal (non-specific and specific) and postnatal (non-specific and specific).

*Antenatal non-specific* prevention includes observation of pregnant women in antenatal clinics, correct day regimen enough (at least 2–3 hours a day) stay of pregnant woman on the fresh air, proper nutrition with adequate dietary vitamins, calcium, protein and etc. *Antenatal specific* prevention inserts prescription for women with 28–32 weeks of pregnancy vitamin D (in normal pregnancy 500 IU). When woman has extragenital or obstetric pathology she must take 1000–1500 IU of vitamin D per day for 8 weeks regardless of the time of year. Prescription of vitamin D for pregnant women at an earlier date is impractical because it may contribute to damage of the placenta.

*Postnatal non-specific* prevention includes breast feeding or adapted formulas (only in breast milk ratio of Ca:P is optimal 2 to 1), admission for the whole lactation period multivitamin medications (Pregnavit, Materna), introduction of complementary foods in time, active movements (massage, gymnastics), sufficient exposure to the fresh air, day regimen, adequate dressing baby, tempering. *Postnatal specific* prevention in term infants is held till 3 years of life. Vitamin D is prescribed for full-term children who are breast-fed from 3–4 weeks of age in

the autumn-winter-spring period at a dose of 500–1000 IU daily. Children at risk for rickets recommended daily prescription of vitamin D at a dose of 1000 IU in the autumn-winter-spring period during the first 3 years of life. In case of artificial feeding daily prophylactic dose is prescribed considering vitamin D, contained in the formula (only 1 liter of a formula contains 10 micrograms of vitamin D which is equivalent to 400 IU).

## SPASMOPHILIA

**Spasmophilia** / rickets or infantile tetany (from Greek «spasmos» — convulsions and «philia» — predisposition) — a pathological condition that occurs in patients with rickets in the first 6–18 months of life. Spasmophilia is a special form of disorders of Ca and P characterized by signs of increased neuromuscular excitability with a predisposition for spasms and convulsions (seizures).

### Pathogenesis

The main reason of spasmophilia is decreased level of ionized $Ca^{2+}$ on the background of hyperphosphatemia and alkalosis that leads to seizures.

Seizures can be provoked by:

– any infectious process, high fever;

– hyperventilation (a shift to the alkalosis);

– repeated vomiting due to non-infectious and infectious diseases of the gastrointestinal tract;

– strong crying, irritation, fear and other factors that reduce the level of ionized $Ca^{2+}$ in the blood.

### Classification and clinical symptoms

There are two clinical forms of spasmophilia: asimptomatic and obvious. *Asimptomatic spasmophilia* usually precedes obvious ones so it must be diagnosed in a timely. Chvostek's, Erb's, Trousseau's, Maslov's and Lust's symptoms are the most common symptoms of asimptomatic spasmophilia.

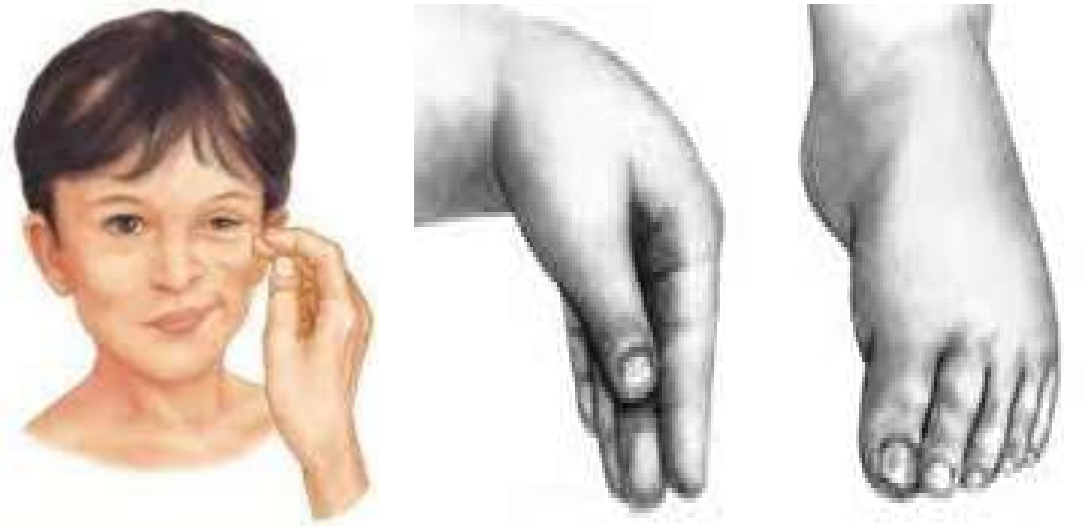
Chvostek's symptom — a contraction of the facial muscles appears when tapping between the zygomatic arch and the corner of the mouth (fig. 7, *a*).

Erb's symptom — a muscle contraction when the cathode applied to the area of the median nerve is opened.

Trousseau's symptom — a convulsive contraction of the fingers occurs in the form of an «obstetrician's hand» when the neurovascular plexus on the shoulder is compressed (fig. 7, *b*).

Maslov's symptom — a respiratory arrest is noted at the height of inspiration with a slight prick of the skin.

Lust's symptom — a rapid abduction of the foot outward with its dorsiflexion when tapping below the head of the fibula (fig. 7, *b*).



***a*** ***b***

*Fig. 7.* Symptoms of asimptomatic spasmophilia:
*a* — Chvostek's symptom; *b* — Trousseau's and Lust's symptoms

*Obvious spasmophilia*, as a rule, manifests in the form of laryngospasm, carpopedal spasm and eclampsia (sometimes in combination with each other).

Laryngospasm — a convulsive spasm of the glottis on inspiration, accompanied by a «cock's cry» and cyanosis.

Carpopedal spasm — a tonic contraction of limb muscles mainly in the hands («obstetrician's hand» and «horse's foot»).

Eclampsia — tonic and clonic convulsions with loss of consciousness that occur when the temperature rises or in a healthy condition.

## Differential diagnostics

Differential diagnostics is carried out with convulsions of another etiology:

- febrile convulsions;
- hypoglycemia;
- hypoparathyroidism (congenital or acquired);
- pseudohypoparathyreosis;
- hypomagnesemia;
- epilepsy.

### Treatment of spasmophilia

Treatment of spasmophilia:

– diazepam (0,5 % 0,1 ml/kg (no more than 2 ml per injection);

– oxybutiric acid (intravenously or intramuscularly 20 % at dose 0,25–0,5 ml/kg);

– phenobarbitali per os or per rectum внутрь at single dose 0,005–0,015 g;

– immediately determination of $Ca^{2+}$ level in the serum and after intravenously slowly 10 % calcium gluconate at dose 0,5 ml/kg;

– after 10 % calcium gluconate per os 1 tea spoon 3 times daily after meal 7–10 days;

– therapeutic dose of vitamin D when the Ca level in blood came to normal;

– with laryngospasm provide access to fresh air and create a dominant focus of excitation by irritating the nasal mucosa, skin, vestibular apparatus and changing body position.

## HYPERVITAMINOSIS D

**It is better to have a major (large) rickets than little hypervitaminosis D.**

Hypervitaminosis D is a multi-organ disease resulting from both the direct toxic effect of the vitamin on cell membranes and the consequences of hypercalcemia. Hypervitaminosis D occurs when vitamin D overdosed or individual hyper sensitivity to it happened.

### Pathogenesis

Due to a significant increase in $Ca^{2+}$ absorption in the intestine hypercalcemia and hypercalciuria developed. It is accompanied by deposition of $Ca^{2+}$ in the vessel wall with irreversible calcification of internal organs. Under the influence of the active metabolites of vitamin D $Ca^{2+}$ and $P^{3+}$ leached from the bones and formed osteoporosis (activates osteoclasts). The accumulation of salts in the newly formed bone, cortical thickening and new nuclei of ossification is enhanced since excess vitamin D inhibits the activity of parathyroid glands.

Vitamin D in high dose has a direct toxic effect on cells, enhancing lipid peroxidation and free radical formation which gives the instability of cell membranes including lysosomal and mitochondrial ones. Both processes — a direct toxic effect on the cells of the endocrine glands and growing hypercalcemia — leads to the involution of thymus and all lymphatic system and later to the gradual development of pluriglandulas failure. It causes a sharp decrease in the body's defenses and joining a variety of secondary infections.

## Classification

Classification:

1. *Stages of the disease:*
– initial;
– clinical sings;
– recovery;
– residual sings.
2. *Grade of severity:*
– I grade — mild;
– II grade — moderate;
– III grade — severe.
3. Course:
– acute (up to 6 months);
– chronic (more 6 months).

## Clinical picture

**Acute intoxication** with vitamin D is more frequent in children of the first 6 months of life with an overdose of vitamin D in a relatively short period of time (2–3 weeks) or individual hypersensitivity to vitamin D. There are signs of neurotoxicity or exicosis: reduced appetite, thirst, vomiting, severe dehydration and rapidly decreased body weight, toxycosis, constipation (possible unstable and loose stools). Tonic-clonic seizures also can be.

**Chronic intoxication** with vitamin D occurs on the background of long-term (6–8 months or more) of vitamin D usage in moderate doses. The clinical picture includes increased irritability, poor sleeping, fatigue, joint pain, poor weight gain, premature closure of the large fontanelle and changes in the cardiovascular and urinary systems.

## Treatment

Treatment:

– treatment of hypervitaminosis D is carried out in a hospital;

– stop vitamin D, administered vitamins A (5 000–10 000 IU/per day) and E (5–10 mg 1–2 time per day) 10–12 days;

– infusion therapy in combination with diuretics (furosemide 0,5–1 mg/kg per day);

– in severe cases a short course of prednisolone can be used (5 mg/kg intravenously slowly until the patient's condition improves, then 1–2 mg/kg per day per os).

## Prognosis

Outcome is serious: development of nephrocalcinosis, chronic pyelonephritis with subsequent chronic renal failure.

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