# Rickets
# Spasmophilia
# Hypervitaminosis D

# Definition

**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 to ensure their delivery.

Characterized by impaired mineralisation of the rapidly growing bones and functions of the leading organs and body systems.

# 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 increased 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%)

# Frequency

- During the 1st year of life from rickets suffer  56% up to 80% of children.
- In Belarus, according to medical records, the frequency of rickets is 30-40%.
- The real frequency – is more than 50% (not all diagnosed and recorded cases).

# History

Rickets was known in antiquity.

The first mention of rickets found in the writings of Soranus of Ephesus (98-138 years) and Galen (131-211 yrs.)

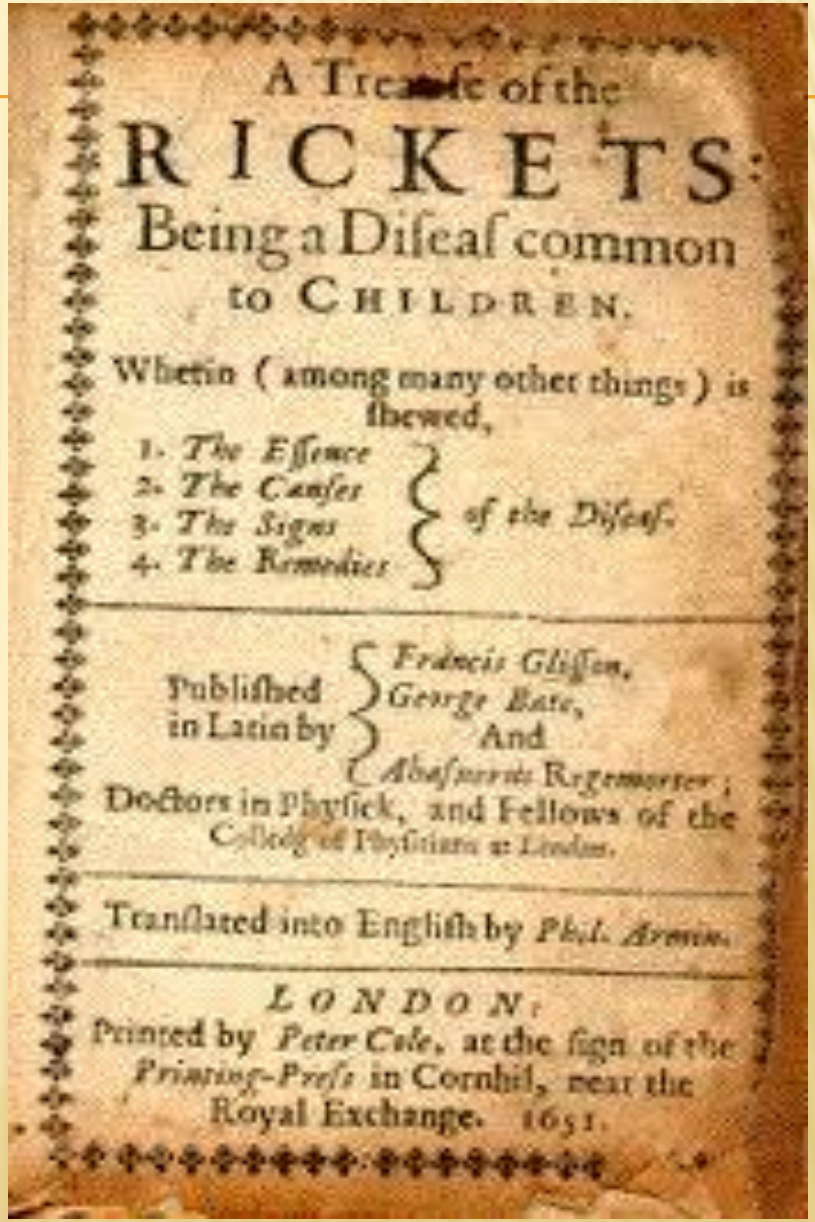
# History

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 called "the English disease», «rickets» (from old english «wrickken» - bend) or Glisson’s Disease.

# History

Later F. Glisson changed name to the Greek "rhachitis" (spine), based on the presence almost in all patients significant spinal deformation.


A Treatise of the
RICKETS:
Being a Disease common
to CHILDREN.
Wherein (among many other things) is shewed,
1. The Essence
2. The Causes
3. The Signs
4. The Remedies
of the Disease.
Published in Latin by Francis Glisson, George Bate, And Abasuerus Regemorter; Doctors in Physick, and Fellows of the College of Physicians at London.
Translated into English by Phil. Armin.
LONDON:
Printed by Peter Cole, at the sign of the Printing-Press in Cornhil, near the Royal Exchange. 1651.


Glisson, Francis. *A Treatise of the Rickets: Being a Disease Common to Children.....* London: P. Cole, 651.

http://www.mc.vanderbilt.edu/biolib/hc/nutrition/nh8.hml

# Durer A. “Madonna and Child”

# Da Vinchi “Madonna Lita”

# History

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.

# Influencing factors

- Deficiency of vitamin D or insufficient intake of vit. D with food (leads to the lack of formation of cholecalciferol (vit 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 Ca2+ and P3+ metabolism;
- variations in microelemental status etc.

# Predisposing factors

| From Mothers side | From Childs side |
|---|---|
| Maternal age less than 17<br>And more than 35 years | Time of birth – autumn, winter<br>(lack of sunlight) |
| Toxicosis of pregnancy | Prematurity, morpho-functional immaturity |
| Extra genital pathology<br>(metabolic diseases, gastro-intestinal tract pathology, kidneys diseases) | Large birth weight<br>(more than 4 kg) |
| Defects nutrition during pregnancy and lactation (protein deficiency, Ca, P, vit D, B1, B2, B6) | Large weight gain during the first 3 months of life |
| Day regimen (lack of insolation and physical activity) | Breast-feeding, but the human- and long standing milk of nurse |

# Predisposing factors

| Mothers | Childs |
|---|---|
| Complications during delivery | Early artificial and mixed feeding with non-adapted milk formulas |
| Poor socio-economic conditions | 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 and intestinal infections |
| | Anticonvulsant medications |
| | Large quantities of cereals and vegetables consuming. |

# Risk factors

Rickets develops when consuming large amounts of **cereals and vegetables** because cereals contain phytic acid which binds Ca2+ in the intestine and disturbs its absorption, and lignin, which blocks the action of vitamin D and its metabolites.

Vegetables contain excess of P3+, which inhibits the absorption of Ca2+.

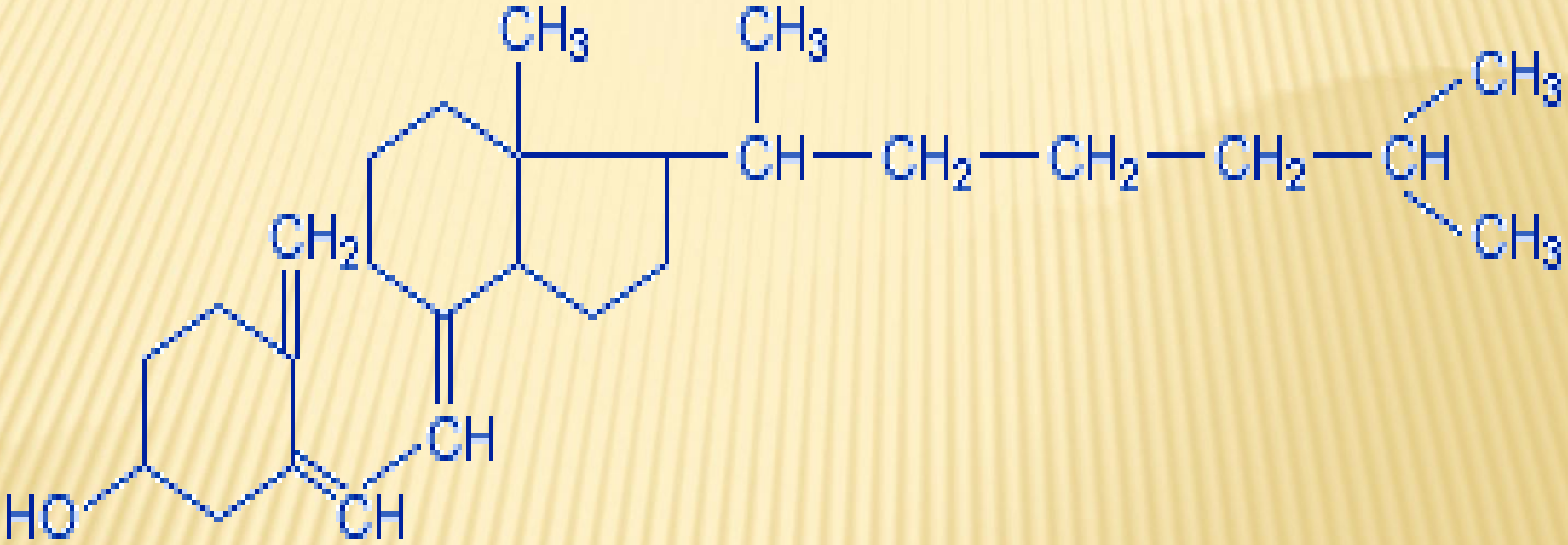
# Risk factors

- A special group of patients are premature babies. During the last trimester of pregnancy fetus receives from mother 80% of all the macro- and micronutrients, including Ca2+.
- Therefore, in premature babies the more pronounced osteopenia and predisposition to rickets are seen.
- After birth (due to the "catching up") preterm infants have increased demand especially in the salts of Ca2+ and vit. D.

# Endogen synthesis and transformation of vitamin D

- Under normal physiological conditions, about 80% of the body needs of vit. D can be synthesized in macrophage cells of the derma from provitamin D3(7-dehydrocholesterol).
- This process takes place only under the influence of sunlight on the skin (the most effective UV radiation with a wave length of 290 - 320 nm).

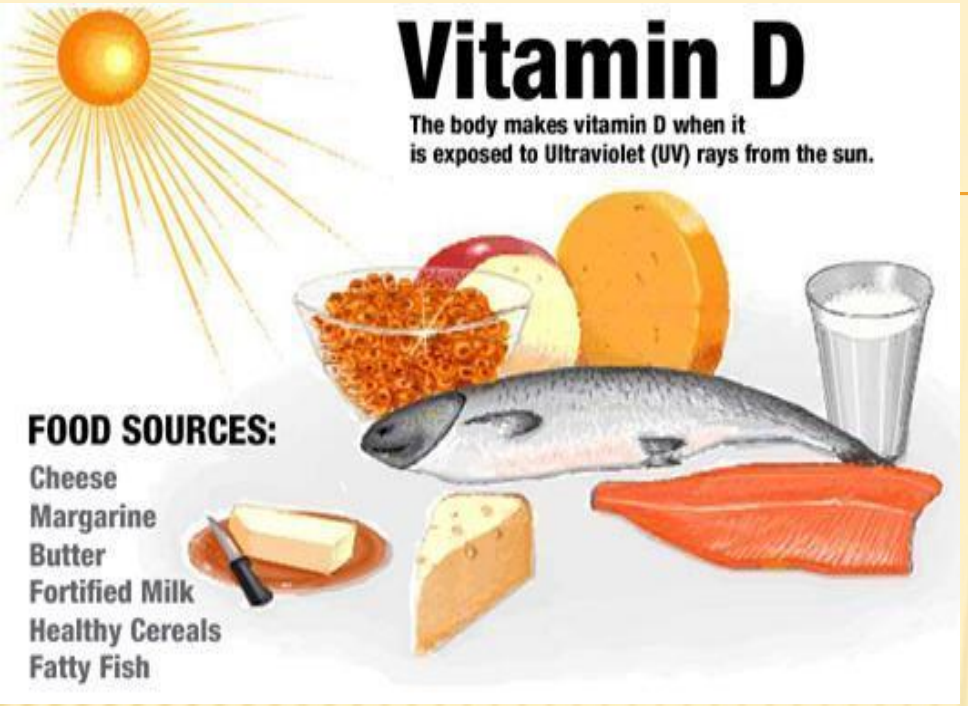
# Endogen synthesis and transformation of vitamin D

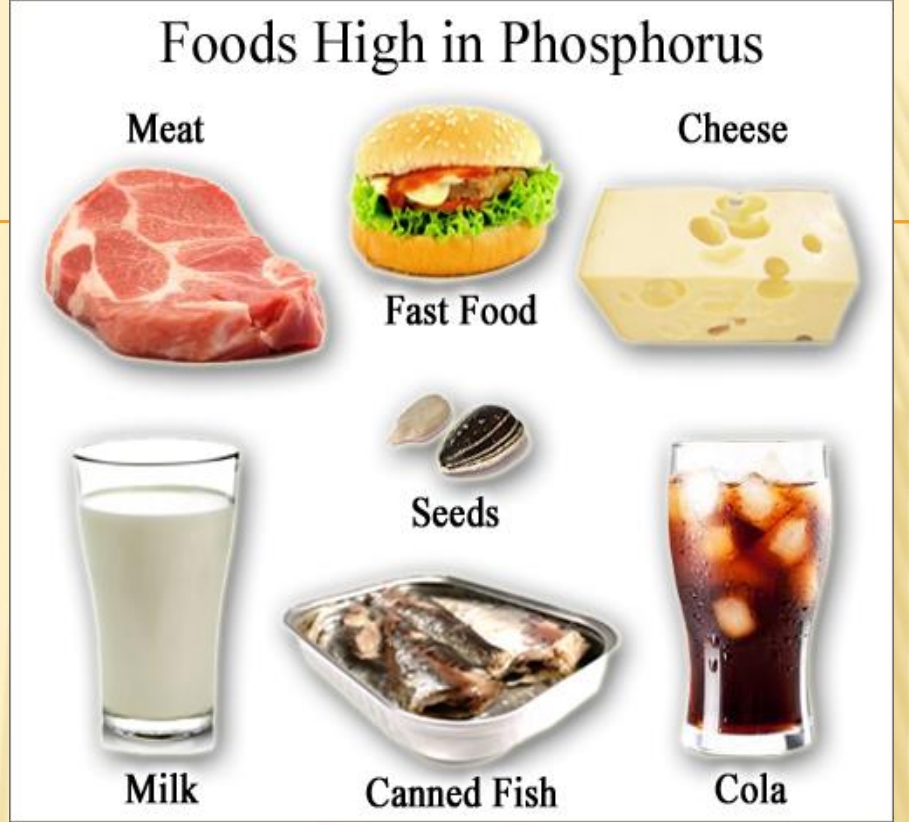


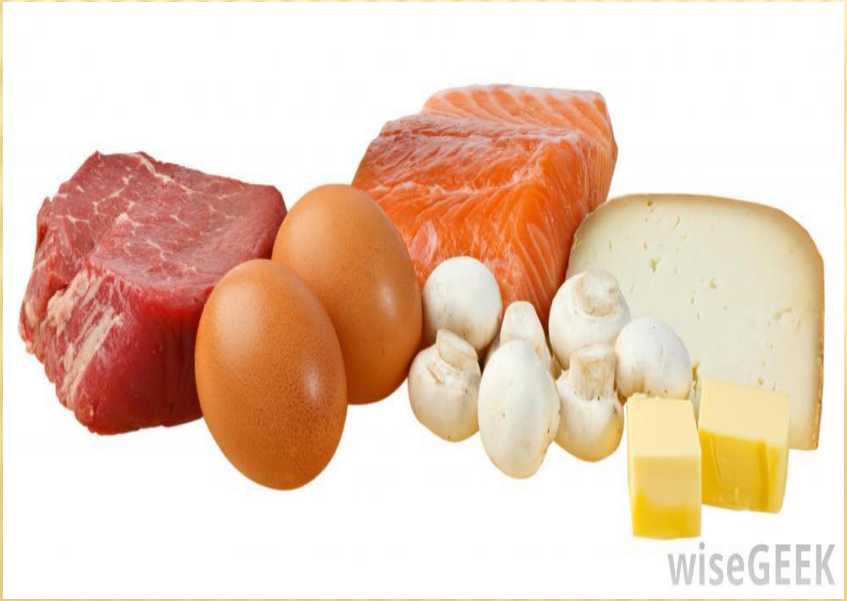

The remaining amount of vitamin D3 and all vitamin D2 come from foods of animal origin: egg yolk, milk, cheese, butter, caviar, fish.

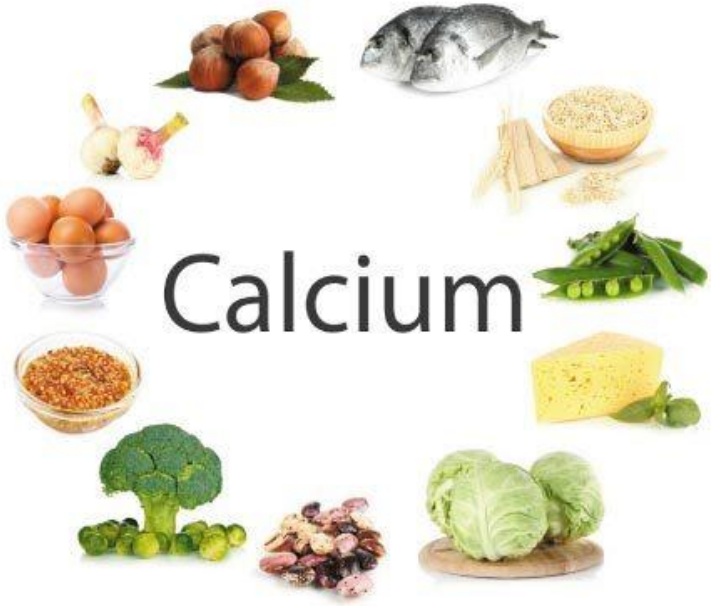
# Content of vitamin D in foods

- Fish oil — 150 ME/ml;
- egg yolk — 1,4–3,9 ME/g;
- vegetable oil — 0,08 ME/g;
- caviar — 3,2 ME/g;
- margarine — 1 ME/g.

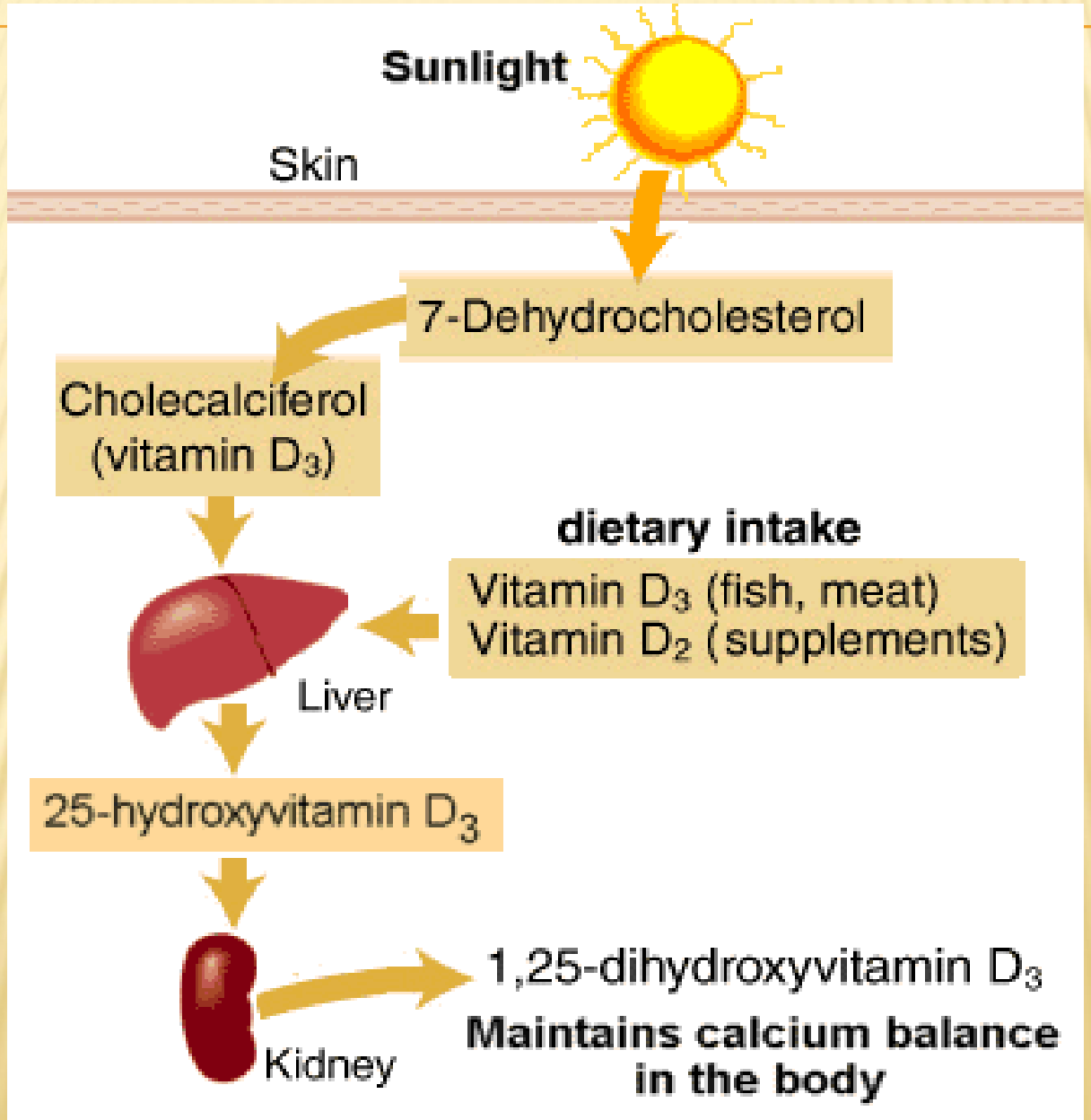

Vitamin D
The body makes vitamin D when it is exposed to Ultraviolet (UV) rays from the sun.
FOOD SOURCES:
Cheese
Margarine
Butter
Fortified Milk
Healthy Cereals
Fatty Fish


Foods High in Phosphorus
Meat
Fast Food
Cheese
Seeds
Milk
Canned Fish
Cola


wiseGEEK


Calcium

# Metabolism of vitamin D



# Metabolism of vitamin D

- Vit. D is absorbed in the proximal part of the small intestine, necessarily in the presence of bile.
- 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)D3 through the bile initially low, which leads to the accumulation of 25 (OH) D3 in the liver.

# Metabolism of vitamin D

- Our body produces several metabolites of vit. D, but only 2 of them actively influence on the metabolism of Ca2+ and P3+: 1,25 dihydroxycholecalciferol and 24,25 (OH)2 D3.
- In terms of normocalcemia and hyper-calcemia $24,25(OH)_2D_3$ (mainly synthesized in kidneys) is formed
- The formation of 1,25(OH) $_2D_3$ or calcitriol occurs under conditions of hypocalcemia.

# Metabolism of vitamin D

- 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).
- Activity of 1-hydroxylase, turning in the kidneys $25\ (OH)D_3$ to $1,25\ (OH)2D_{3,}$ depends on the presence of parathyroid hormone, as well as vitamins C, E, B2.
- Therefore, hypovitaminosis C, E and B group and parathyroid gland pathology contributes to the development of rickets.

# Metabolites of vitamin D:

- increased permeability of enterocytes cell membranes for Ca2+;
- stimulates the synthesis of Ca2+-binding protein, which provides transport of Ca2+ ions from enterocytes into the blood;
- stimulates the absorption of P3+ in the intestine;
- enhance the reabsorption of Ca2+ and P3+;
- stimulate the differentiation and proliferation of osteoblasts and chondrocytes, which leads to protein synthesis increasing by the cells of the connective tissue - collagen;
- stimulate osteocalcin synthesis - the basic non-collagenous protein of bone tissue.

# The amount of synthesized vitamin D depends on:

- the wave length of light (the most effective is medium wave spectrum, we get it in the morning and at sunset);
- original skin pigmentation (the darker skin, the less vitamin D is produced by the action of the sun);
- age (aging skin loses its ability to synthesize vitamin D);
- air pollution (industrial emissions and dust do not miss ultraviolet rays).

# Vit D: endocrinology system

- Currently vit. 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)2 D3 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 - important component of the anti-infectious immunity of the skin.

# Vit D: endocrinology system

- 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.

# Vit D: Calcium

- Ca2+ concentration in blood (2.1-2.8 mmol/l), did not vary by more than 3% due to hormonal control.
- The main mass of Ca2+ 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 Ca2+ in the blood bound to plasma proteins, mainly to albumin.

# Calcium in the cell: 3 conditions

- $Ca^{2+}$ localized in the cell organelles;
- Chelated Ca2 + associated with the cytoplasmic protein molecule;
- ionized Ca2 + concentration in serum is 1.1-1.4 mmol / l.
- Free Ca2 + is a regulator of a variety of intracellular processes, ensure the implementation of a specific transmembrane signal into the cell.

# Role of Ca2+ 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.

# Requirements for Ca2+ and vit D in the child

Breast milk contains Vitamin D (about 70 IU / L), as well as cow's (20 IU / L), but this amount can not satisfy the needs of the body of the growing child (about 400 -500 IU/day or 10 mcg).

The daily requirement for Ca2+ in infants is 50-55 mg / kg, in comparison to adults - only 8 mg / kg.

# Assimilation of Ca2+ and vit D in the child

- During breast-feeding healthy child assimilates about 70% of Ca2+ administered with food, and 50% phosphorus.
- During artificial feeding - only 30% of calcium and phosphorus 20-30%

# Regulation of the Ca2+ metabolism by calcitonin

Elevated levels of ionized Ca2 + is lead to the increase synthesis of calcitonin (thyroid hormone).

Calcitonin:

1.reduces the number and activity of osteoclasts;

2.enhances deposition of Ca2+ into the bone;

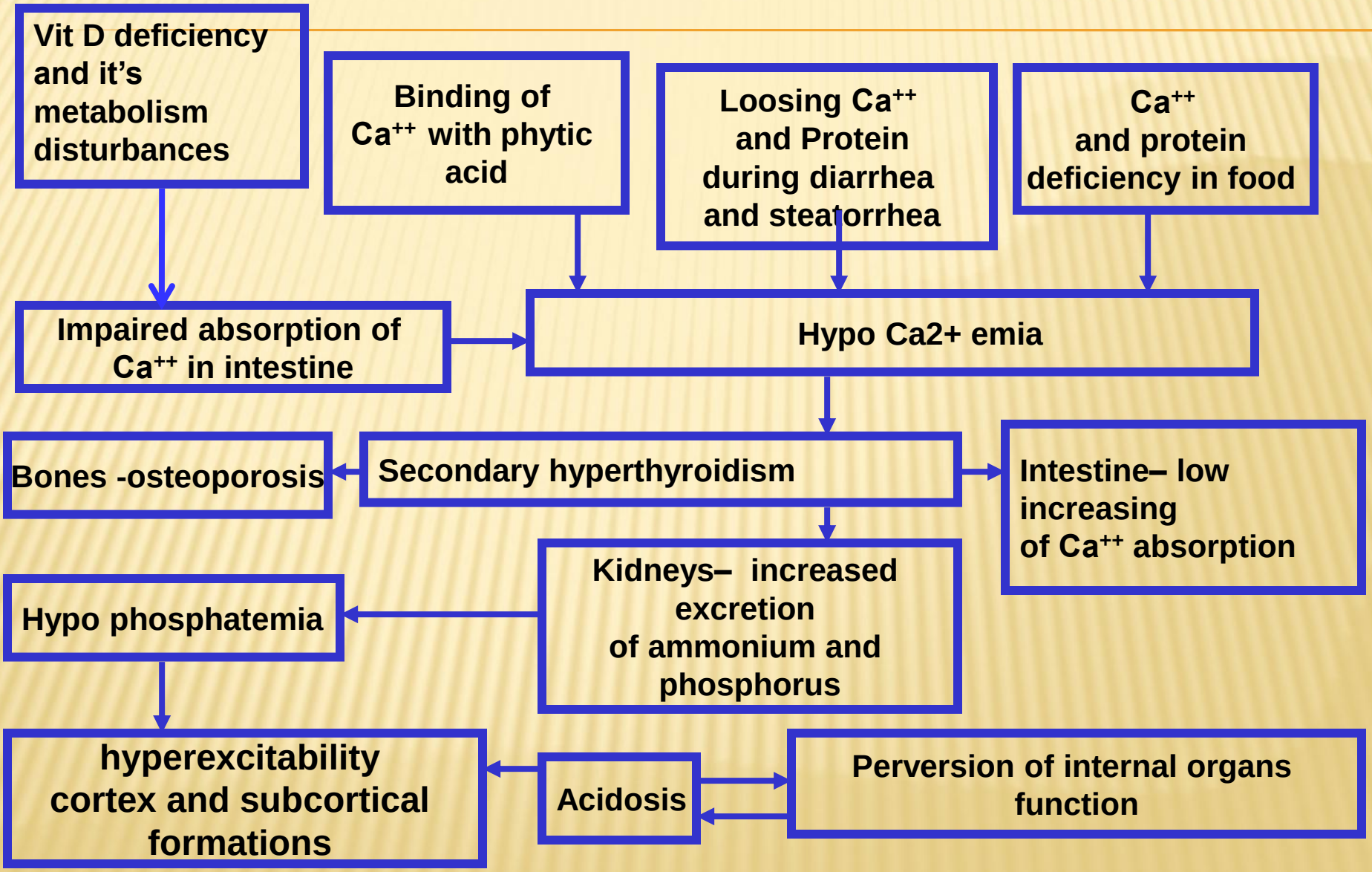
3. increases Ca2+ excretion by the kidneys,

4.works as the antagonist of parathyroid hormone.

# Participants of the Ca2+ - P3+ metabolism

- Thyroid's hormone
- Estrogens
- Androgens
- Somatotropic hormone
- Insulin
- Glucagon
- Steroids

# Rickets pathogenesis



# Parathhormone (PTH) and kidneys

- PTH increase the tubular reabsorption of Ca2+ and Mg2+;
- decrease reabsorption of potassium, non-organic P3+ and $HCO_3^-$;
- decrease excretion of protons and ammonium ions;
- increase the ability to form the active form of vitamin D-1,25 (OH)2

# Parathhormone (PTH) and bones

- 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 Ca2+ from the bone (release in the blood), and the depletion of matrix with collagen and proteoglicans.

# Pathogenesis

Acidosis retains P3+-Ca2+ 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 Ca2+ impairs the function of the central and autonomic nervous system and increases their excitability

# Rickets is accompanied with

- polyhypovitaminosis;
- disrurbances of protein metabolism;
- lipid metabolism;
- Impaired carbohydrate metabolism, in particular reduce the formation of piruvats from pyruvic acid

# Pathogenesis

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.

# Morphological composition of bone tissue is represented :

- cellular elements
- intercellular substance (matrix)
- mineral components.

- Bone matrix – is a collagen fibrils constituting about 90% of all proteins of bone tissue.
  Non-collagenous bone matrix proteins include osteocalcin and other proteins (osteopontin, fibronectin).

# Cellular elements include:

- **Osteoblasts** - large cells, the main enzyme of which is alkaline phosphatase (ALP). The main function is protein synthesis.
- **Osteoclasts** - giant multinucleated cells that produce acid phosphatase. The main function is bone resorption.
- **Osteocytes** - bone cells, "bricked" in calcified bone matrix, osteoblasts. The main function is the transport of nutrients and minerals.

# Remodeling of bone tissue

- During growth period the lengthening of the bone takes place due to the growth of the cartilage and its extension - for the deposition of the newly formed bone tissue in the subperiosteal bone space.
- The duration of a full cycle of the remodeling process on average of 5 months, 3 weeks of them takes the process of resorption.

# Morphological changes in bone tissue in rickets

- Impartment of endochondral ossification
- proliferation of osteoid;
- lack of bone mineralization;
- transformed bone softening

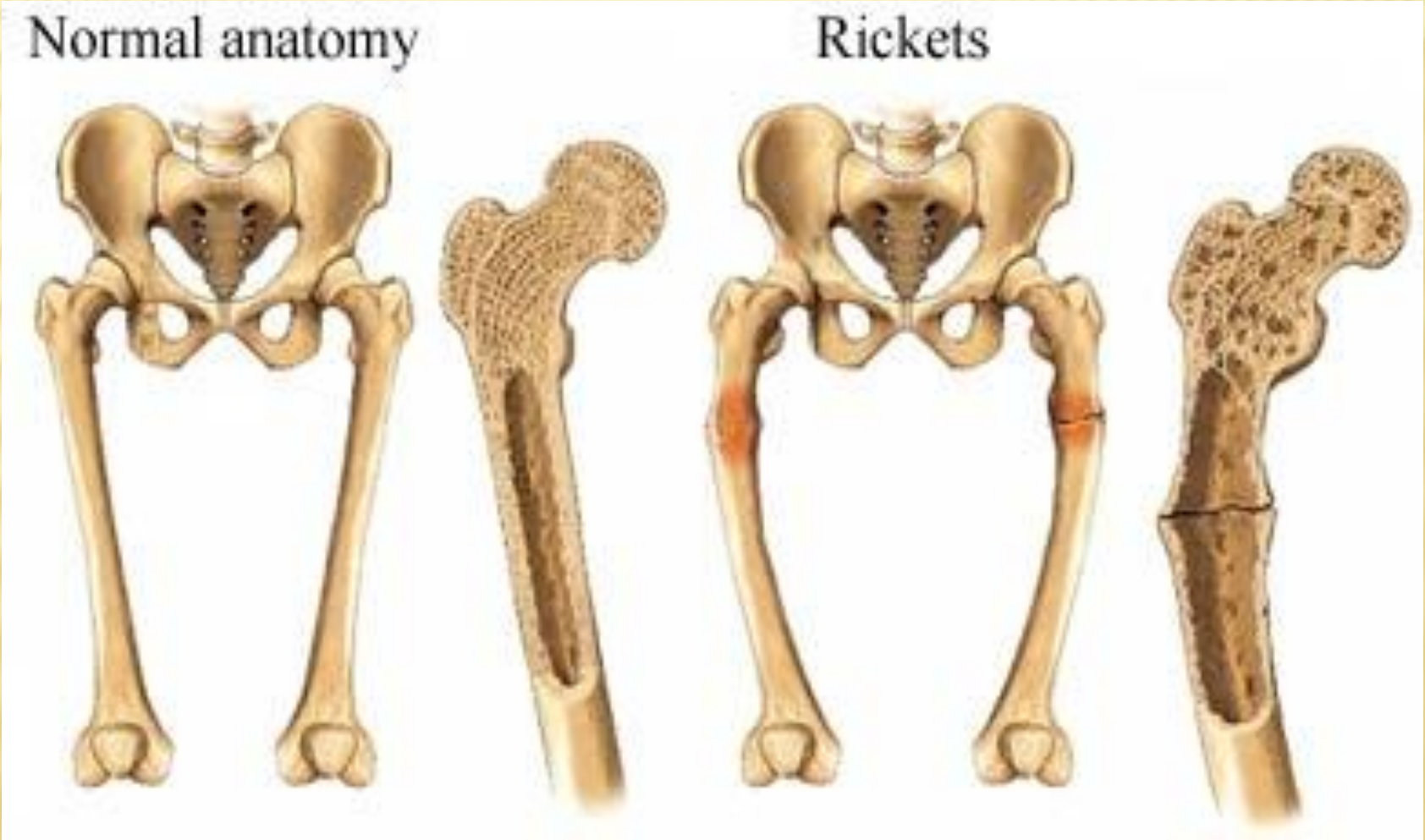
# Osteopenia

**Abnormaly low bone mass**

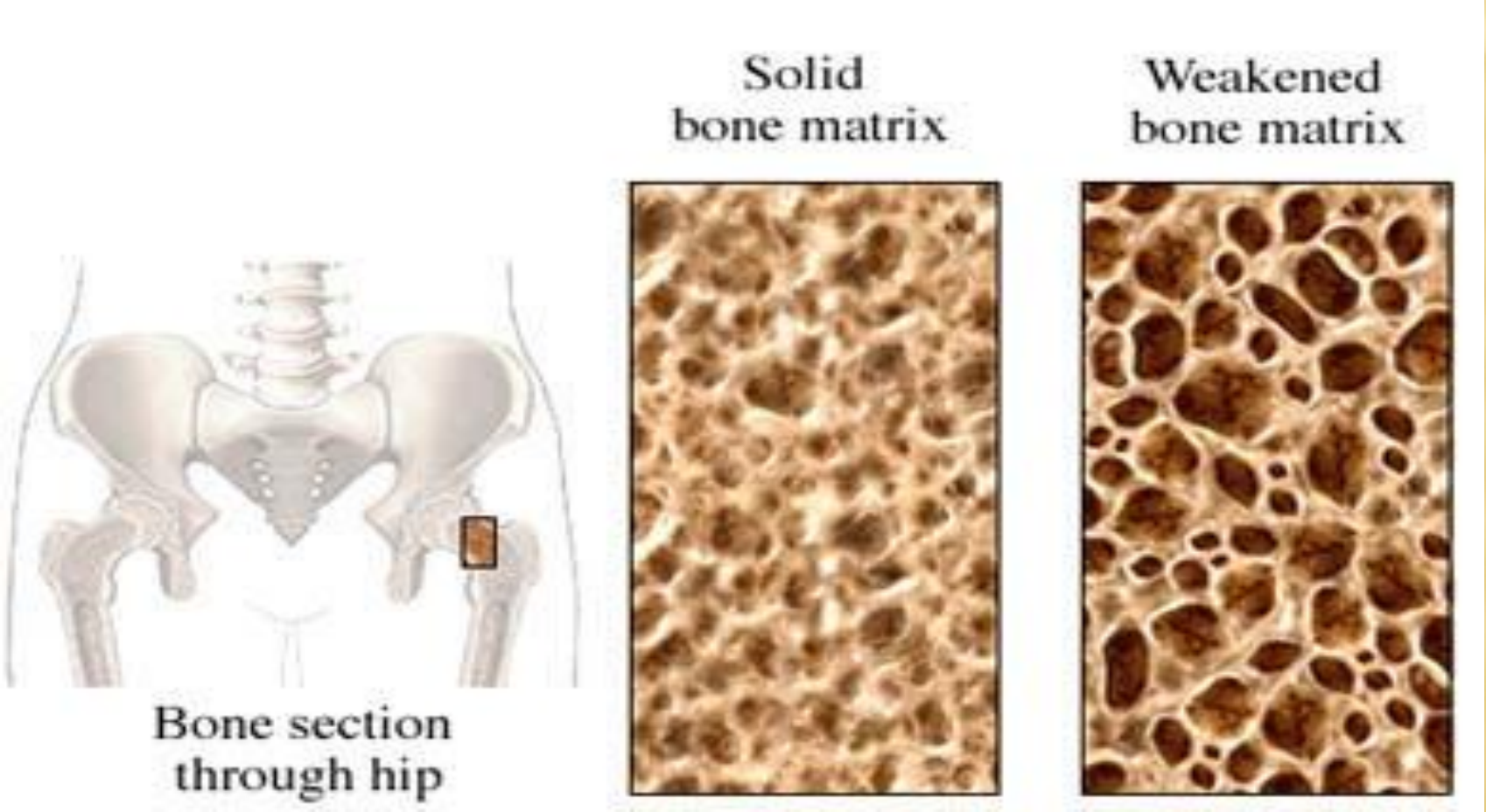
**Osteoporosis - simultaneous loss of the organic matrix and mineral substances due to low activity of osteoblasts, resulting in thinning of the beams sponge and compact bone substance = bone becomes fragile;**

**Osteomalacia - low bone mineralization. In low-mineralized bone organic matrix accumulates, ratio of mineral and organic substances decreases = bones lose toughness and become flexible;**

# Bone tissue changes in rickets



# Bone tissue changes in rickets




HTTP://WWW.EMPOWHER.COM/CONDITION/RICKETS

# Bone tissue changes in rickets

Proliferation of osteoblasts in bone metaphyses altered rickets, leads to the increase of alkaline phosphatase, which is the most sensitive biochemical marker for rachitic process and the level of which is normalized in the serum only after recovery from rickets.

# Rickets: Classification

| Stages of the disease | Grade of severity | Course | Biochemical option |
|---|---|---|---|
| Initial | I grade – mild course | Acute | Low Ca2+ level Ca-penic |
| Clinical signs | II grade – moderate | Sub-acute | Low P3+ level – P-penic |
| Recovery | III grade – severe | relapsing | Without Ca and P abnormalities |
| Residual signs | | | |

# Secondary rickets

Often occurs due to:

- malabsorption syndromes, chronic kidney disease or biliary tract pathology;
- metabolic diseases (tyrosinemia, cystinuria, and others.)
- prolonged use of anticonvulsants (phenobarbital), diuretics, corticosteroids, and parenteral nutrition.

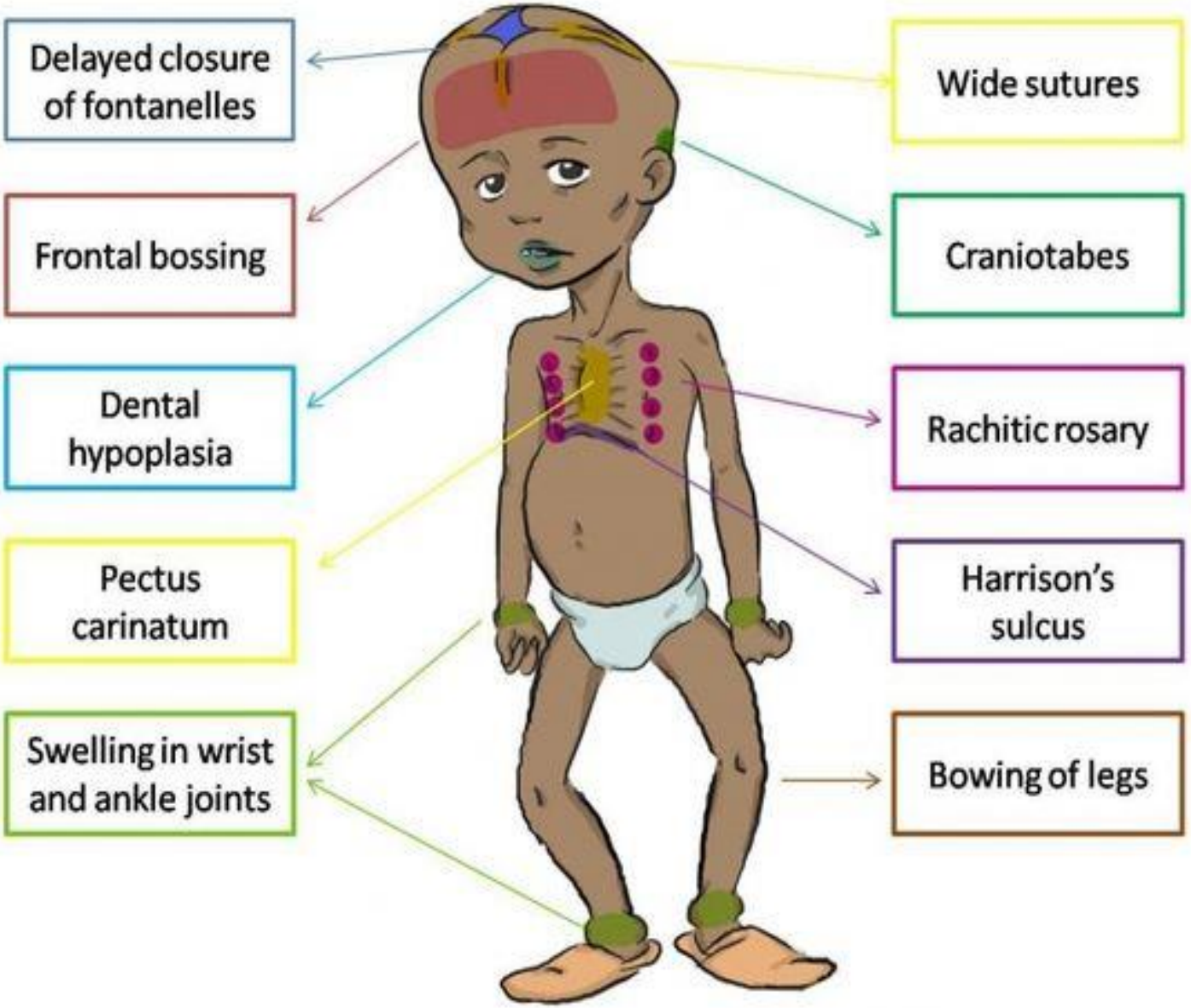
# Vit. D-dependent rickets

- Type I — genetic defect in the kidney in the synthesis of 1,25-dihydroxyvitamin D- $1,25(OH)_2D$.
- Type II — genetic resistance of target organs receptors to $1,25(OH)_2D$

**Vit.D- Resistant rickets**

- Phosphate diabetes
- Fanconi syndome
- Renal tubular acidosis

# 10 important clinical features in Rickets



# Clinical signs 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, flattening the occipital part of the head and a slight expansion in the areas of osteoid tissue growth (rosary).**

# Clinical signs of rickets – ping-pong ball sensation of the skull

# Clinical signs of rickets - flattening the occipital part of the head

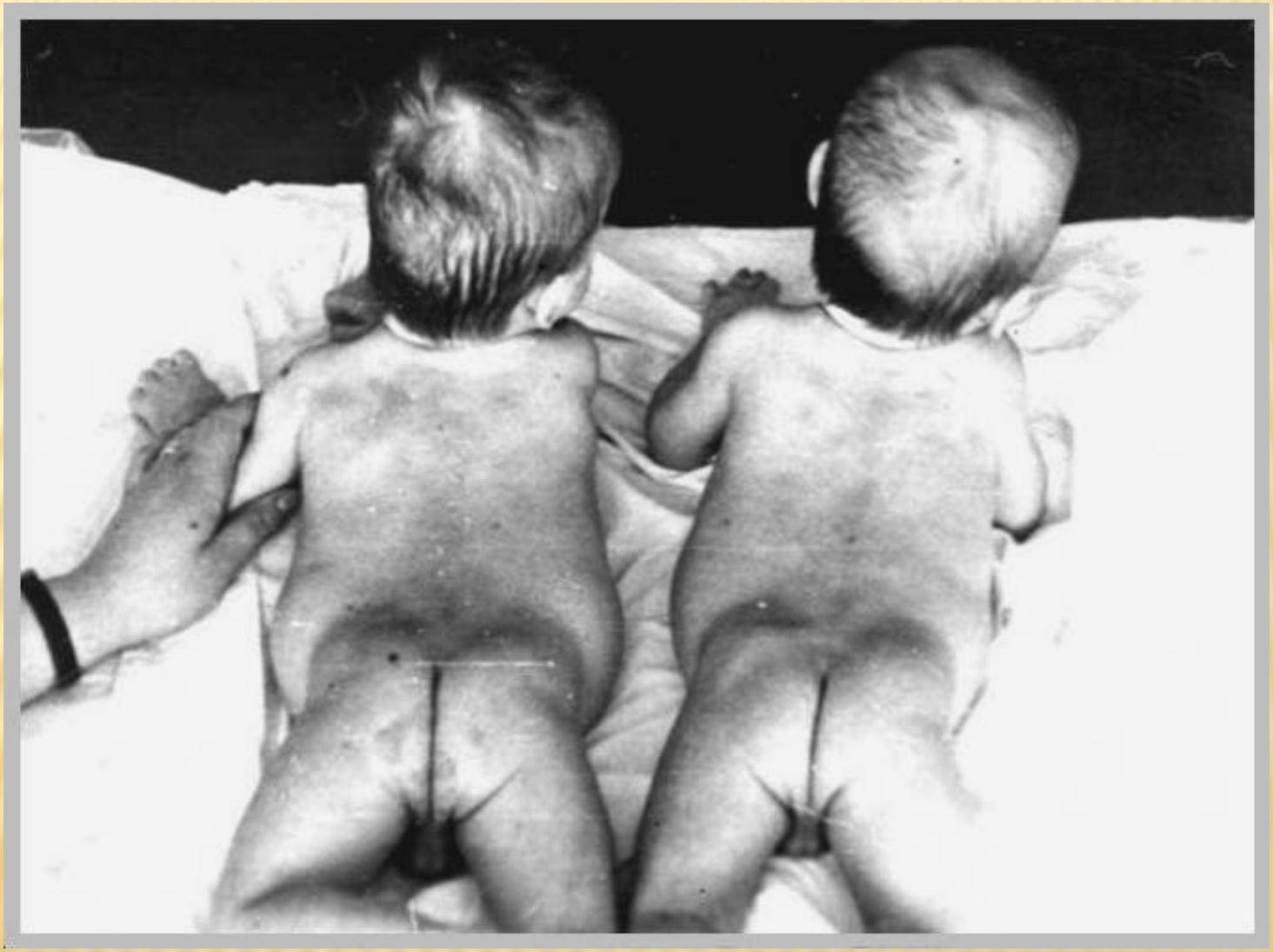
# Clinical signs of rickets

**Rickets II degree (moderate) is characterized by impaired general condition and moderate changes in the nervous, muscular systems: hypotension, enlarged "frog" belly, high standing of a diaphragm.**

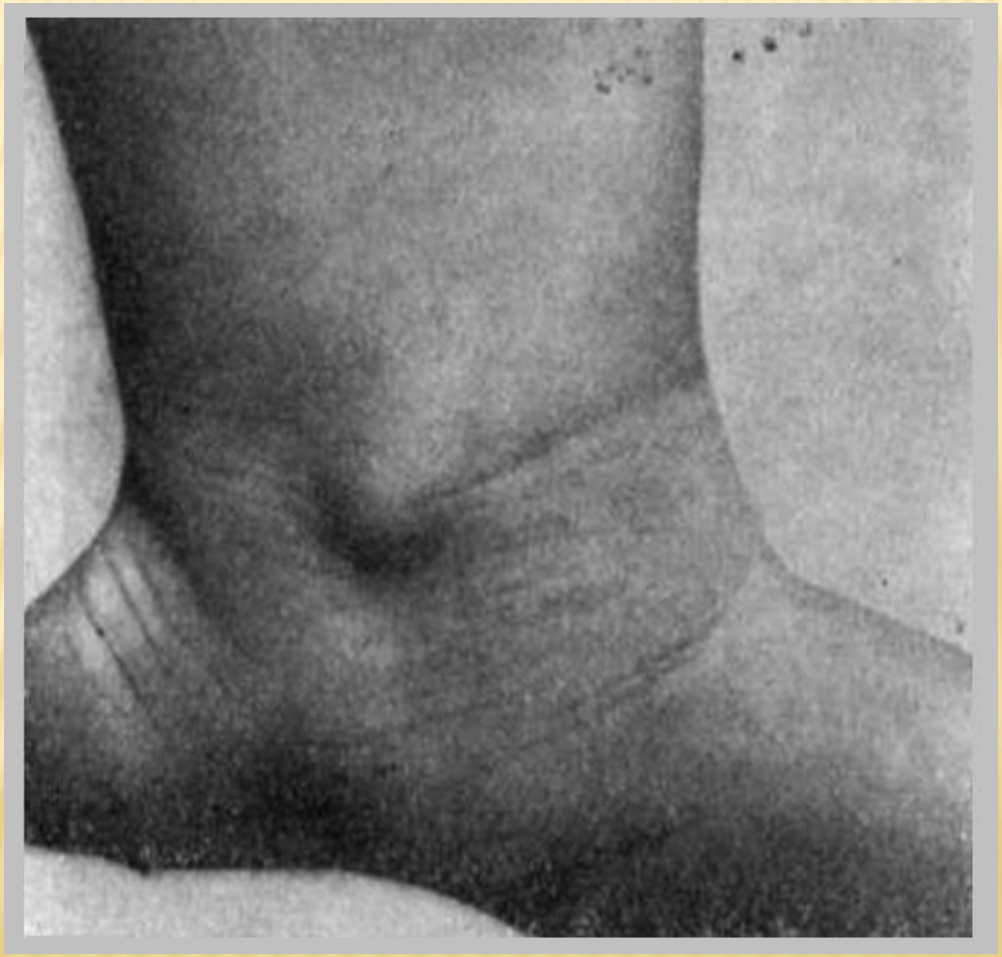
**slight enlargement of the liver and spleen, mild anemia, but more pronounced changes in the bones: parietal bumps, rachitic "beads"; "Bracelets", "string of pearls", spreads the lower thoracic inlet in the form of "hat brim", “Harrison’s" sulcus.**

# Clinical signs of rickets – “frog” belly

# Clinical signs of rickets – “frog” belly



# Clinical signs of rickets – dual wrists at the ankle

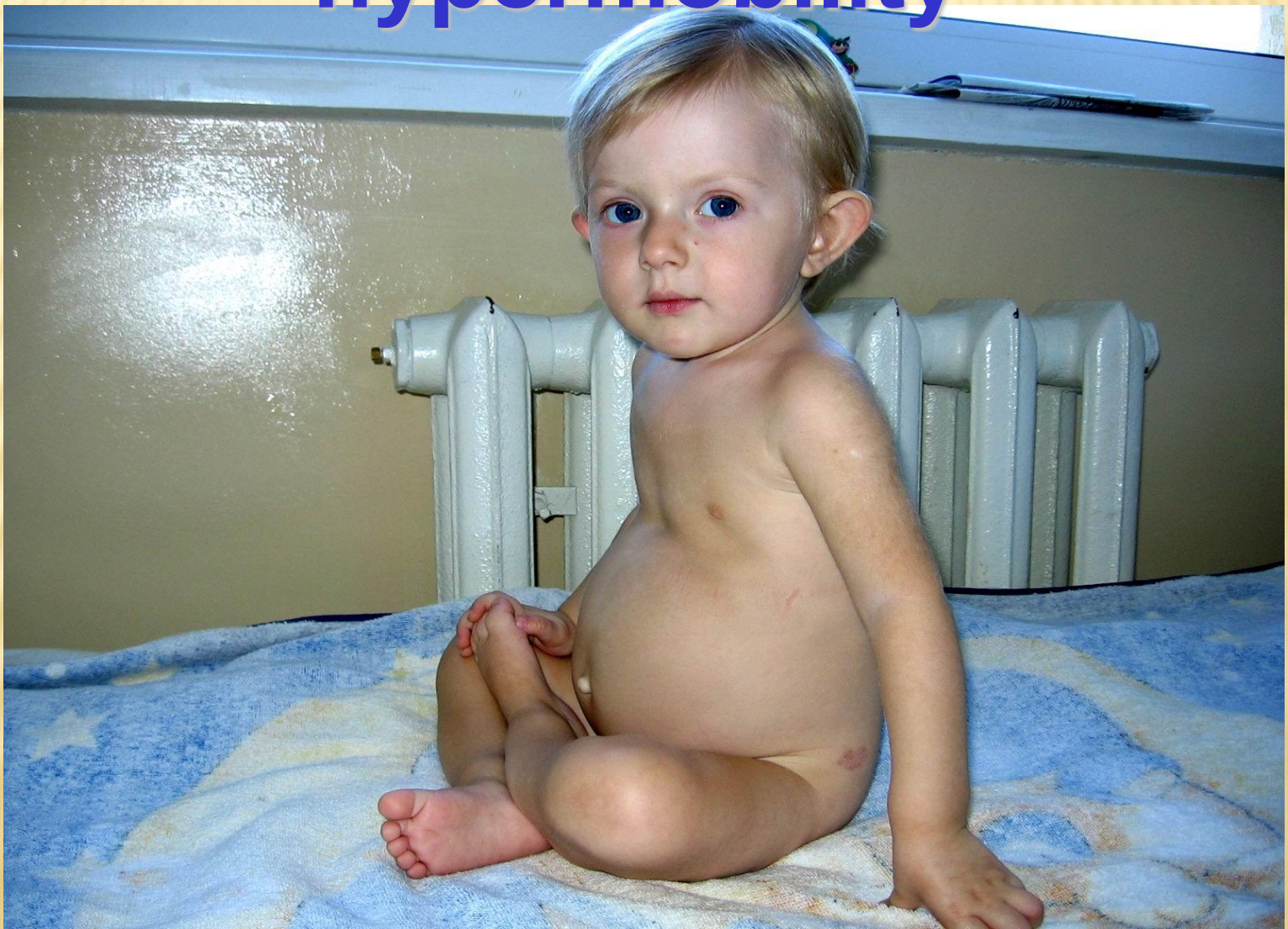


# Clinical signs of rickets

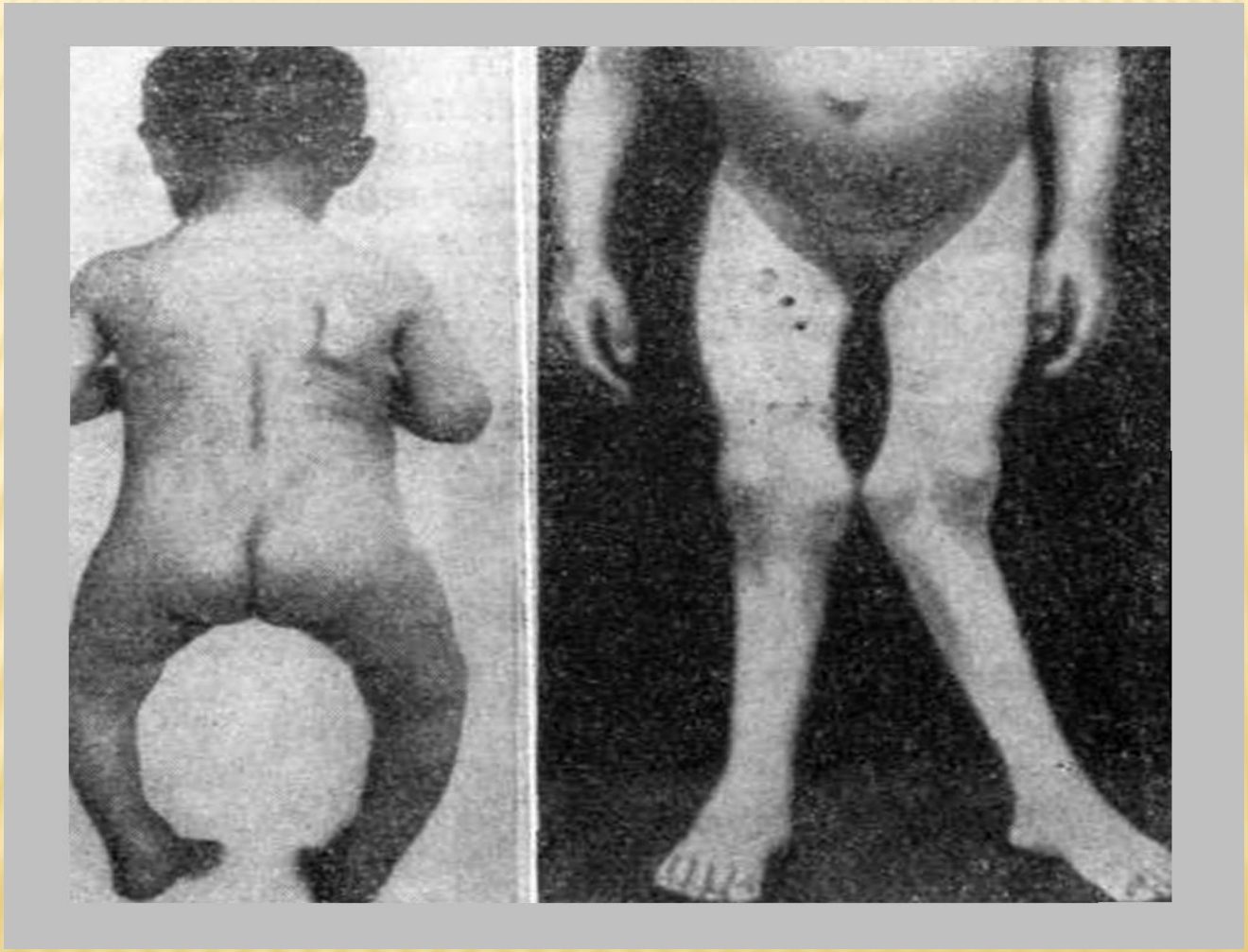
**Rickets III degree (severe) is characterized by severe skeletal deformities:**
**"square" shape of the skull, increasing the frontal, occipital tubercules, "Olympic" forehead, "saddle" nose, breaking the terms of teething, bite, chest deformity ("chest cobbler" "chicken" chest, kyphosis, lordosis,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

# Clinical signs of rickets – legs curvature, “frog” belly, short stature

# Clinical signs of rickets – musular hypotonia, joints hypermobility

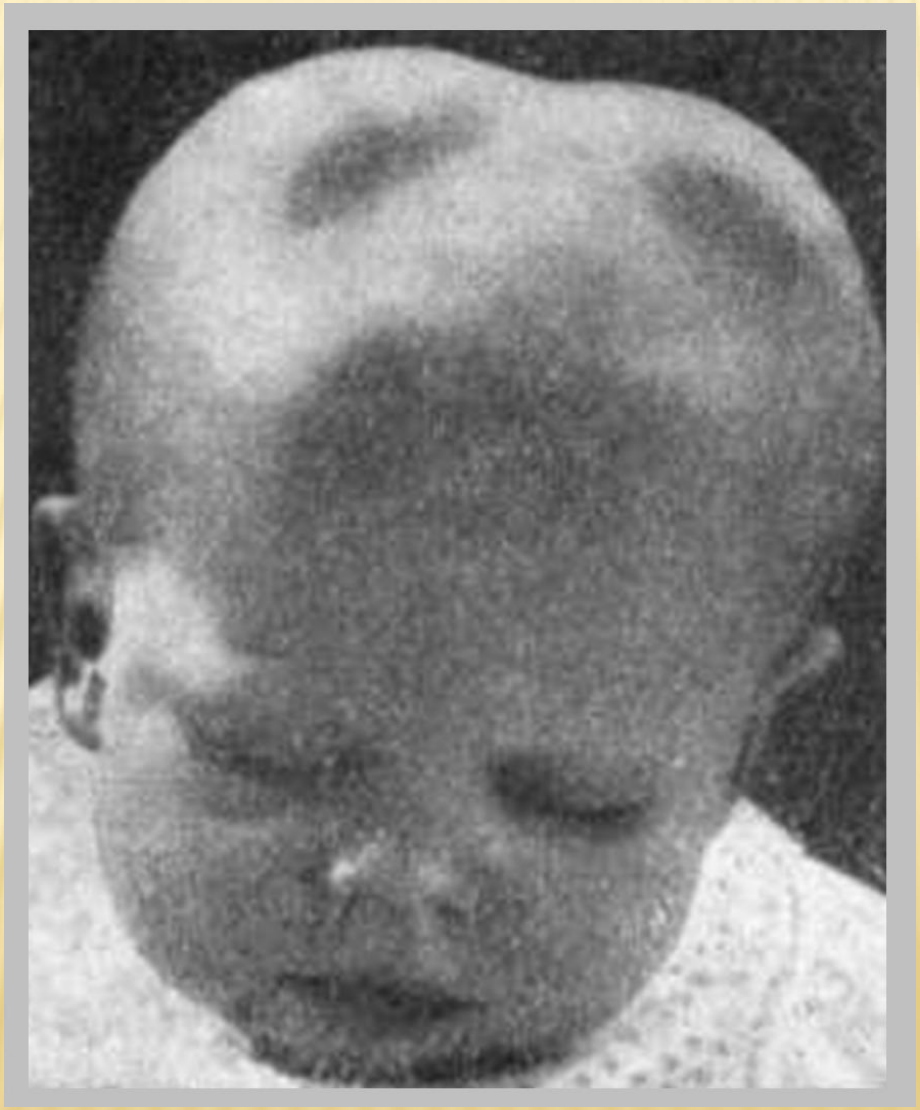


# Clinical signs of rickets – X and O-like bending the leggs

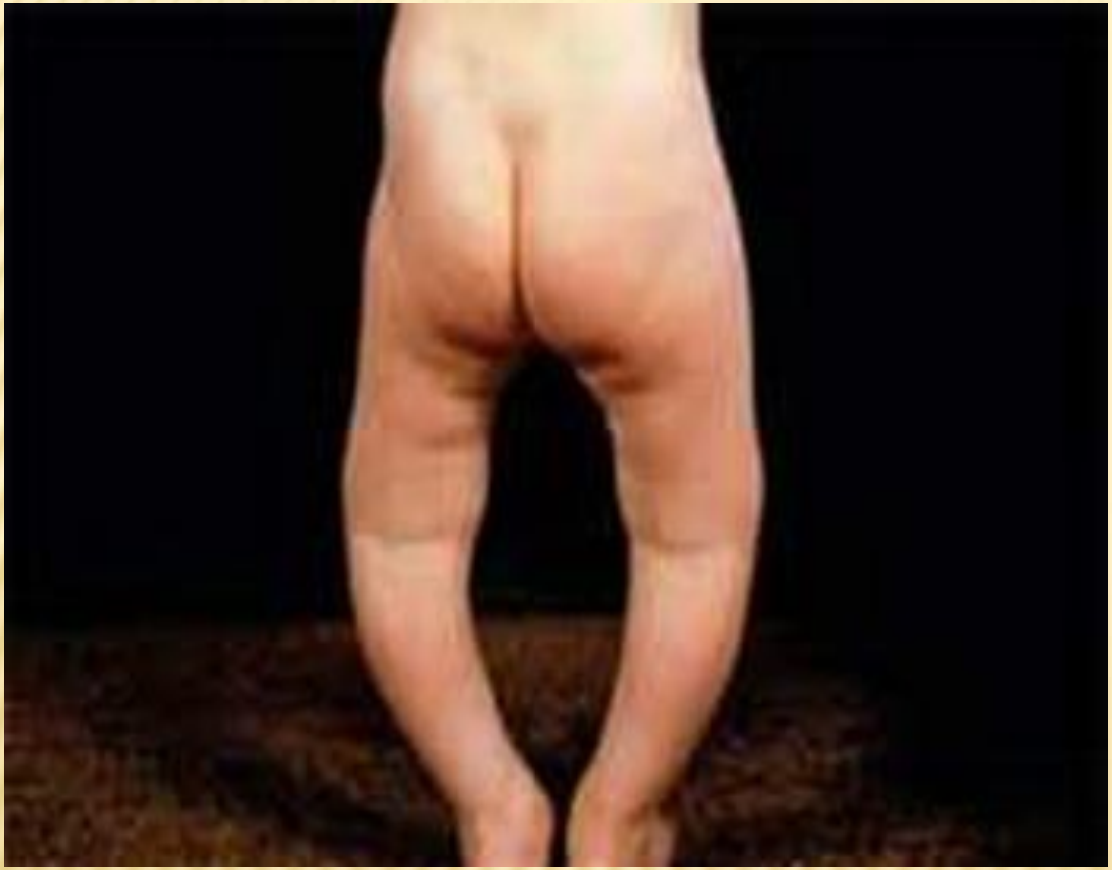


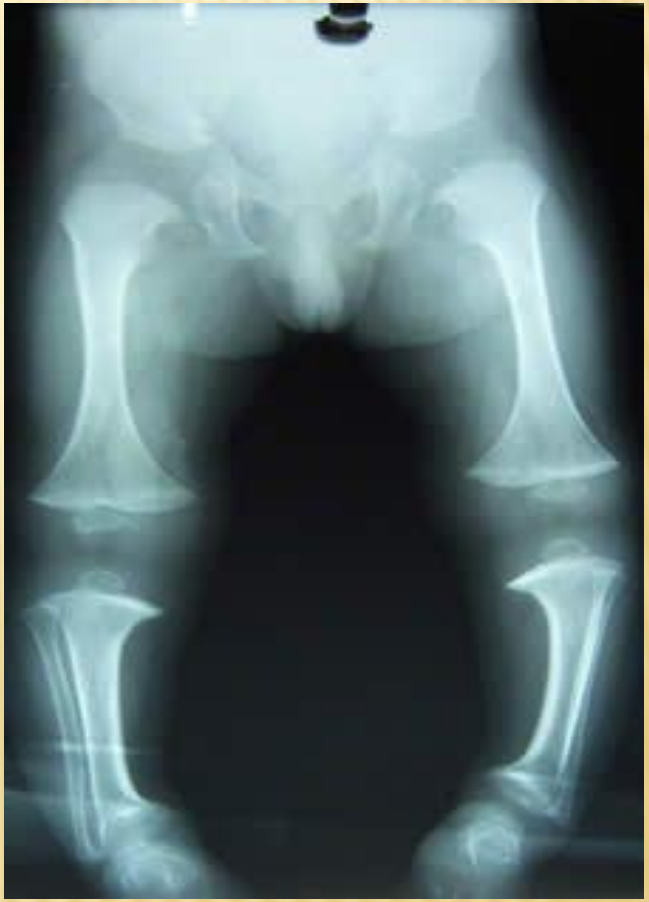
# Clinical signs of rickets – “Olympic forehead”

# «CAPUT NATIFORME»

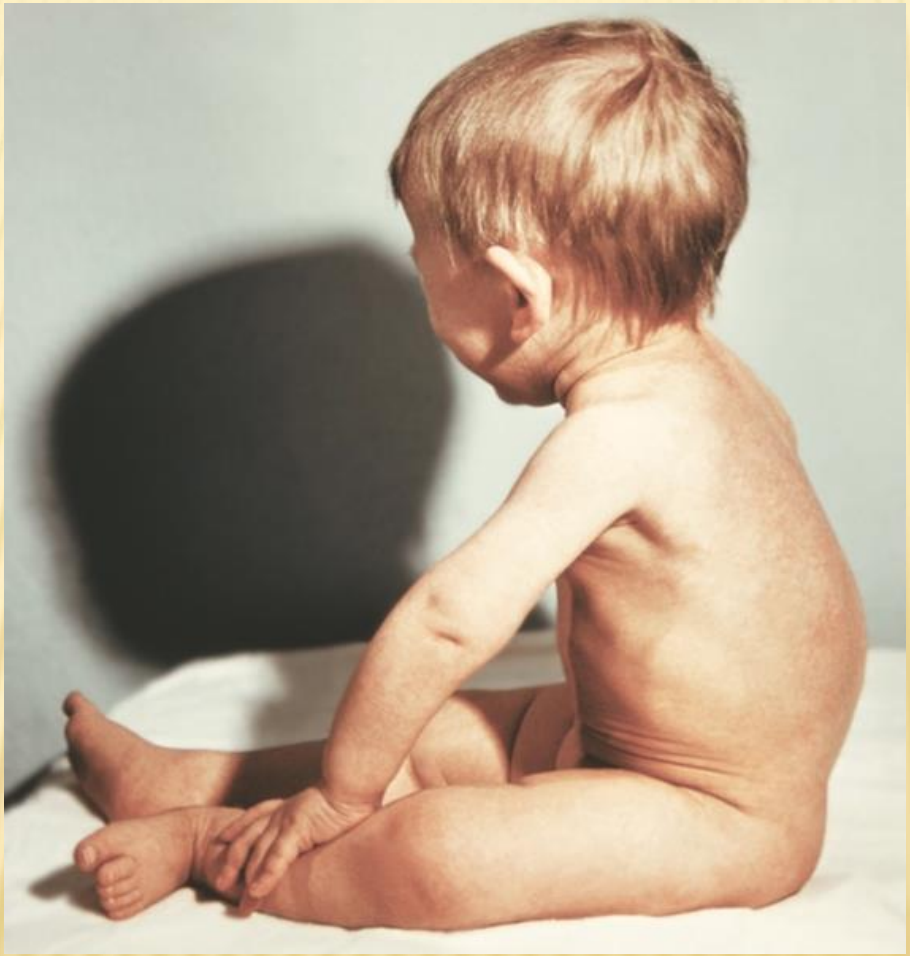


# Clinical signs of rickets – bone's changes





# Clinical signs of rickets



# Clinical signs of rickets – physical development retardation 100 years ago

# Clinical signs of rickets – physical development retardation - nowadays

# Clinical signs of rickets

- 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.

# Clinical signs of rickets

- 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.

# Clinical signs of rickets

- 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).
- Changes in the blood - decrease of Hb and red blood cell count, which is associated with dysfunction of the bone marrow.

# Course of rickets

- **Acute course observed mainly in children in the first 6 months of life, mostly in preterm and overweight, who did not receive vit. 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.**

# Course of rickets

**Relapsing course observed in frequently ill children, with inappropriate diet, when you stop to give vit. D after the treatment of rickets.**

**During recurrent course of rickets periods of exacerbation followed by periods of remission. Bone X-ray - reflects the formation of new bands of calcification in the metaphysis.**

# Biochemistry

***Ca-low 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. In the blood plasma - a significant reduction in ionized Ca2+, high levels of parathyroid hormone (PTH), decreased calcitonin.*

# Clinical signs of rickets - biochemistry

- ***P3+-low version of rickets is associated with significant bone deformities: a distinct thickening of the metaphyseal regions of long bones of hands, sternal ribs, 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, hyper-fosfaturia.***

# Biochemistry

**The absence of abnormalities in concentration of Ca2+ and P3+ in the blood**. is characterized by the severity of the frontal and parietal mounds in the absence of distinct changes in the nervous and muscular systems. Blood - a moderate increase in the level of PTH at normal rates of calcitonin. Ambiguous indicators of the level of Ca2+ and P3+ in the blood during the period of significant clinical signs are explained by multidirectional calcitonin concentration in the serum.

# 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 |

# Dynamics of biochemistry parameters depends of the stage of rickets

| Stage of the disease | Serum Ca2+ | Serum P3+ | 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 |

# Diagnostics

Laboratory normal levels – blood serum:

- Ca2+ level - **2,1-2,8 mmol/l**;
- ionized $Ca^{2+}$ level **1,1-1,4 mmol/l;**
- Non-organic P3+: 1,3-1,8 mmol/l;
- Alkaline phosphates activity 140-220 Un.

# Diagnostics

| Main methods: | Additional methods: |
| --- | --- |
| •Blood analysis (could be anemia).<br>•Urine (N).<br>• Blood biochemistry (Ca2+ and ionized, P, Alk P).<br>• Sulkoviths analysis (weekly positive or negative) | • Metabolic acidosis.<br>• 24 hours urinary excretion of Ca, P (elevated).<br>•Active vit D metabolites (calcidiol 25 –OHD) in blood serum 15-25 ng/ml).<br>•Serum level of PTH (increased) |

# Antenatal non-specific prevention

- 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 etc

# Antenatal specific prevention

- Prescribtion of women with 28-32 weeks of pregnancy vitamin D (in normal pregnancy 500 IU).
- When extragenital or obstetric pathology - 1000-1500 IU of vitamin D per day for 8 weeks, regardless of the time of year.
- Prescribtion of vitamin D for pregnant at an earlier date is impractical because it may contribute to damage to the placenta

# Postnatal non-specific prevention

- Breast feeding, when absence - prescribtion of 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

- Specific prevention of rickets 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.

# Postnatal specific prevention

- Children at risk for rickets recommended daily prescribtion of vitamin D at a dose of 1,000 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).

# Rickets prevention in preterm babies

- In prematurity of 1st degree vit D is assigned from the 10-14th day of life at dose 1,000 IU per day, every day for the first 3 years, except of summer months.
- In 2-3d degree of prematurity vit D is assigned from 10-20 days at dose of 1000-2000 IU daily for the 1st year of life, and for the 2nd-3$^{rd}$ year - at dose of 500-1000 IU, excluding summer months.

# Vitamin D: MEDICATIONS

| Medication name and form | The content of D |
|---|---|
| Acvadetrim Vitamin $D_3$ (cholecalciferol), aqueous solution (Medana Pharma Terpol group, Poland) | 1ml (20 dropps) – 15 000 IU, falcon – 10 ml ,1 drop – 500 IU |
| Videchol ($D_3$ oleosum solution) – 0,125% (Russia) | 1 drop – 500 IU, 1ml – 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 |

# Vitamin D: MEDICATIONS

| Medications | Vit D |
|---|---|
| Vit $D_2$ oleos 0,125% | 1 drop – 1 250 ME, Iмл – 50000ME |
| Vigantol (cholecalciferol), oleos (Merck KGaA, Германия) | 1 мл –20 drops (20 000 ME) |
| Oxidevit (synthetic analogue, 1,25 $[OH]_2D_3$) | 1 caps – 500 ME |

# Contraindications for vit D administration

- Absolute contraindication - idiopathic calciuria (Williams-Bourne disease).
- Organic disease of the central nervous system with symptoms of craniostenosis is a relative contraindication, because these children needs antiseizures therapy, which contributes to the development of osteopenia. Specific prevention of rickets is starting from 3-4 months life under normal growth of the head

# Specific therapy

**Vit 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 tests Sulkovich's.

Test is carried out before treatment and then every 7-10 days. Dose of 5000 IU is administered only when significant bone changes occured.

# Treatment – specific therapy

Total dose of vit 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 you see good results (normalization of muscle tonus and vegetetative 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 D3 at dose of 2000-5000 IU for 3-4 weeks, 3 months after the end of the first year, except for the summer months.

# Treatment – non-specific therapy

- 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).
- Pasty, sedentary children recommended salt baths (2 big spoons See Salt per 10 liters of water, the water temperature - 35-36 ° C, duration - 5 min), for irritable - conifers (1 tea spoon of Liter. Extract for 10 liters of water, water temperature - 36 ° C, duration - 10 min).
- At remission process in bone, but not earlier than 3 weeks after the start of therapy with vitamin D - massage.

# Treatment – non-specific therapy

- Magnesium in order to normalize the function of the parathyroid glands and reduce vegetative disorders - Asparkam, Pananginum

- antioxidants to normalize the process of lipid peroxidation (vit E, A, Vetoron, Qudesan

- Medications for improving metabolic processes: Potassium orotate

- Carnitine chloride (Elkar)

during 4-5 weeks.

# Treatment – non-specific therapy

- premature babies require the concomitant use of Ca2+ supplements - 55-60 mg / kg / day for 2-3 weeks, for children of the 2-nd year of life recommended a diet rich in calcium;
- 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;
- Physiotherapy, massage

# Spasmophilia (Infantile tetany)

- **Spasmophilia** (spasmophilia; Greek spasmos convulsions, + philia predisposition;
- Synonym: rickets or infantile tetany) - a pathological condition that occurs in patients with rickets in the first 6-18 months of life.
- Spasmofiliya is a special form of disorders of calcium and phosphorus, characterized by signs of increased neuromuscular excitability with a predisposition for spasms and convulsions (seizures).

# Spasmophilia: Pathogenesis

Decreased level of ionized Ca2+ on the background of hyperphosphatemia and alkalosis, seizures.

Seizures can be provoked by

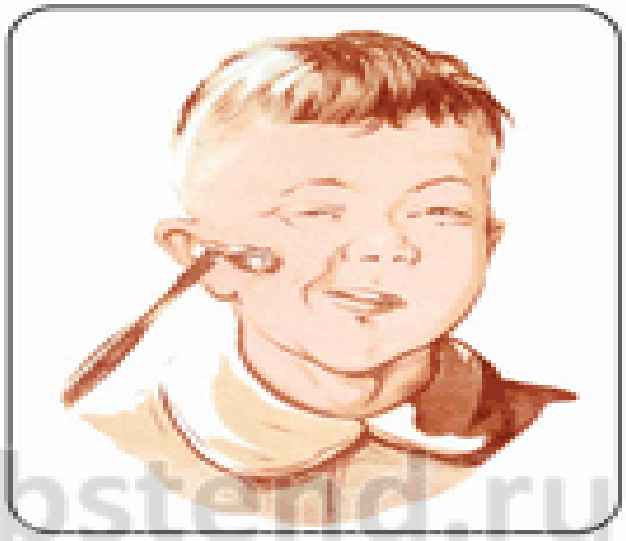
- any infectious process, high fever,
- hyperventilation (a shift to the alkalosis);
- repeated vomiting due to non-infectious and infectious diseases of the gastrointestinal tract;
- strong crying, irritation, fear and other factors that reduce the level of ionized Ca2+ in the blood.

# Asimptomatic form of spasmophilia

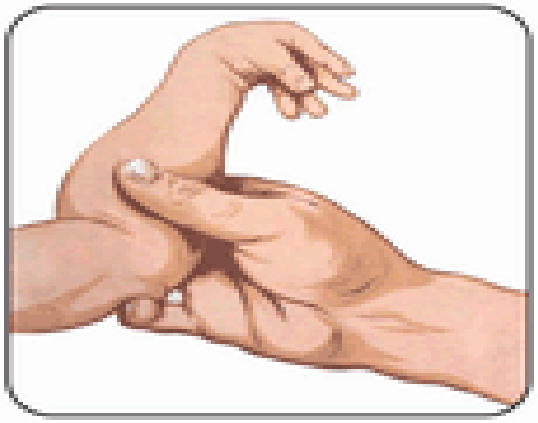


## Спазмофилия

"Рука акушера"



Симптом Хвостека



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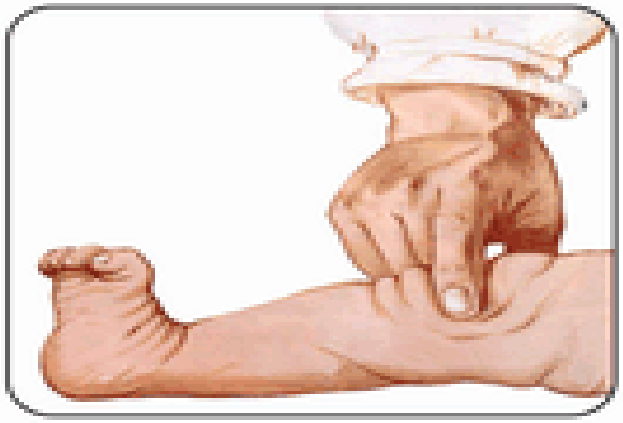

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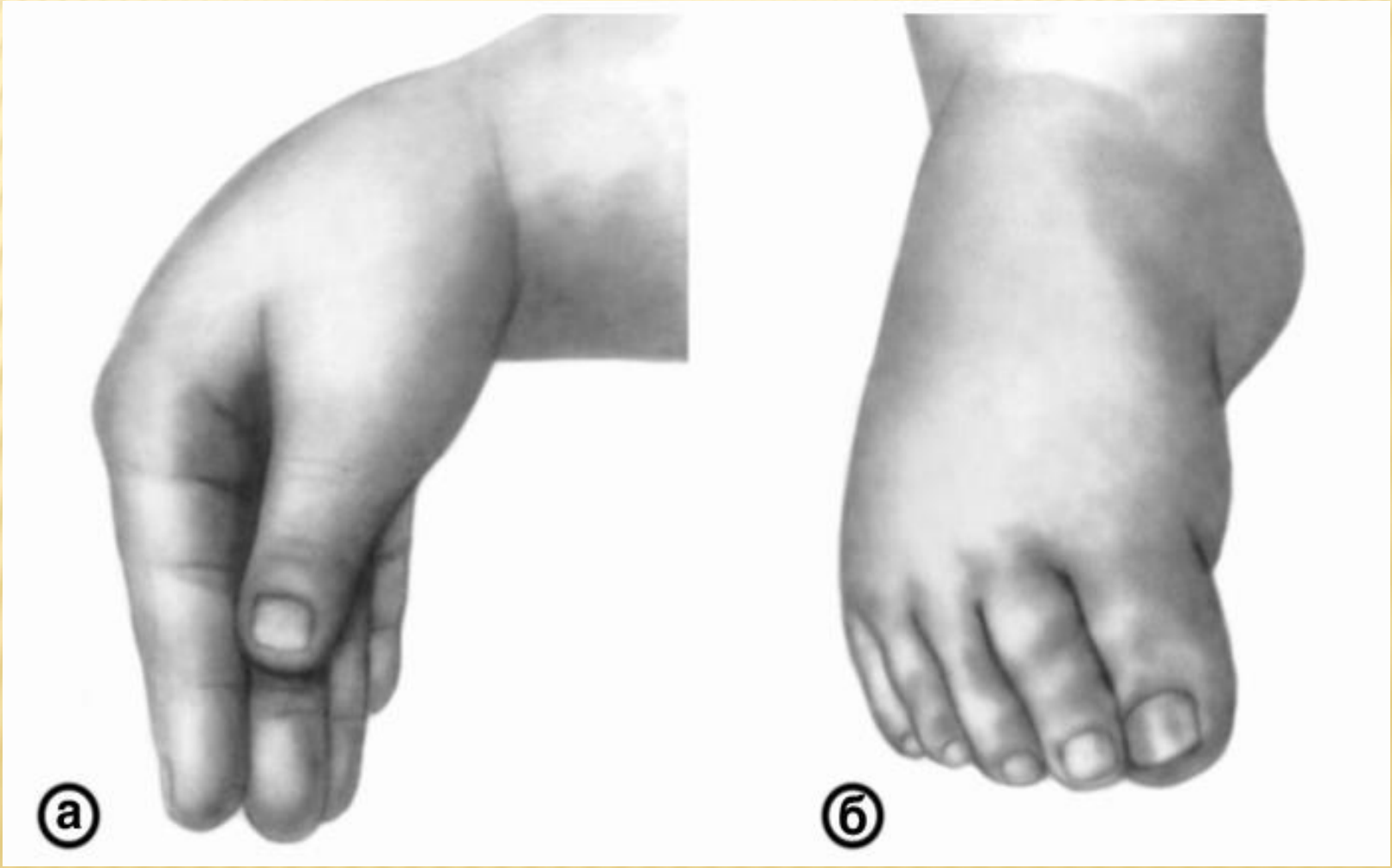
# Obvious spasmophilia – 3 forms

- **Laryngospasm** – convulsive spasm of the glottis on inspiration, accompanied by a "cock's cry" and cyanosis.
- **Carpopedal spasm** – tonic contraction of limb muscles mainly in the hands ("hand of obstetrician") and foot (“horse foot").
- **Tonic and clonic convulsions with loss of consciousness** that occur when the temperature rises or in a healthy condition

# Carpopedal spasms



# Differential diagnostics

Other hypocalcemic states, accompanied by convulsions or convulsive readiness:

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

# Treatment of spasmophilia

- Diazepam (0,5% - 0,1 ml / kg (no more than 2 ml per injection);
- Oxybutiric acid IV or IM at dose 0,25-0,5 ml /kg 20% solution
- Phenobarbitali per os or per rectum внутрь at single dose 0,005—0,015 g.
- Immediately determination of Ca2+ level in the serum and after - IV slowly 10% Calcium gluconate 0,5 ml/kg
- After 10% Calcium gluconate per os - 1 tea spoon 3 times daily after meal - 7-10 days.
- Therapeutic dose of vit D when the Ca level in blood came to normal

# Hypervitaminosis D

"It is better to have a major (large) rickets than hypervitaminosis D».

Hypervitaminosis D occurs when vitamin D overdosed or individual hyper sensitivity to it happened.

This condition is caused by a direct toxic effect of the drug on the cell membrane and increased concentration in the blood Ca2+.

Ca2+ salts are deposited in the blood vessels walls of internal organs, especially in the kidneys and heart.

# Pathogenesis

- Due to a significant increase in Ca2+ absorption in the intestine hypercalcemia and hypercalciuria developed. It is accompanied by deposition of Ca2+ in the vessel wall with irreversible calcification of internal organs
- Under the influence of the active metabolites of vitamin D Ca2+ and P3+ leached from the bones and formed osteoporosis (activates osteoclasts).
- Enhanced the accumulation of salts in the newly formed bone, cortical thickening, new nuclei of ossification, since excess vitamin D inhibits the activity of parathyroid glands.

# Pathogenesis

- 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.
- Both processes - a direct toxic effect on the cells of the endocrine glands and growing hyperCa2+ - leads to the involution of thymus and all lymphatic system, and later - to the gradual development of pluriglandulas failure. This causes a sharp decrease in the body's defenses and joining a variety of secondary infections.

# Clinical picture

- **Acute intoxication with vitamin D is more frequent in children of the first 6 months of life with an overdose of vit. 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).**
- **Could be tonic-clonic seizures.**

# Clinical picture

- **Chronic intoxication with vitamin D occurs on the background of long-term (6-8 months or more) of vit 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, changes in the cardiovascular and urinary systems**

# Treatment and prognosis

- Treatment of hypervitaminosis D is carried out in a hospital.
- Stop vitamin D, administered vitamins A and E
- infusion therapy in combination with diuretics (furosemide)
- In severe cases - a short course of prednisolone.
- Outcome is serious - development of nephrocalcinosis, chronic pyelonephritis with subsequent chronic renal failure

# Thank you very much for your attention!