Metabolic osteopathies

Metabolic osteopathies are diseases caused by imbalances between bone formation and resorption and disorders in bone mineralization → osteopenia and bone loss (osteoporosis, osteomalacia) or sclerotization of the bone and increase in bone mass (Paget's disease, osteopetrosis). These osteopathies are caused by dysfunction of bone cells, gene abnormalities (defects in collagen I synthesis, etc.), increased expression of bone morphogenetic proteins, renal dysfunction, endocrinopathies, tumor secretion of substances affecting bone metabolism.

Osteoporosis

Osteoporosis manifests itself as a reduction of normally mineralized bone mass with impaired bone microarchitecture. Causes an increase in bone fragility. The result is fractures of the forearms, femoral neck, compression fractures of the vertebrae, and others. Risk factors for osteoporosis are insufficient dietary calcium intake, vitamin D deficiency, disorders of its intestinal resorption, and other uncontrollable factors such as age and gender.

Classification

Osteoporosis is defined as a reduction in bone density below the T-score level of -2.5 standard deviations. **Osteopenia** is defined as a precursor to osteoporosis with a bone density level in the range of −1 to −2.5 standard deviations of the T-score.

Primary osteoporosis

Primary osteoporosis is a more common form of the disease, it does not occur as a result of another underlying disease.

- **Type I – Postmenopausal osteoporosis**: typical of women aged 55-65 years, associated with decreased estrogen hormone levels. It affects trabecular rather than cortical bone and threatens patients mainly with vertebral fractures.
- **Type II – senile osteoporosis**: is typical of patients over the age of 70, with women being affected twice as often as men. It is accompanied by an increase in immunoreactive parathyroid hormone (iPTH) and a decrease in intestinal Ca^{2+} resorption with a decrease in serum levels of active vitamin D. The type of osteoporosis affects the trabecular and cortical bones equally and is manifested mainly by fractures of long bones and femoral neck.
- **Idiopathic osteoporosis**: can occur in any age group, cause unknown.

Secondary osteoporosis

Secondary osteoporosis results from the underlying disease - most often of an endocrine nature, such as hyperparathyroidism, hyperthyroidism, hypercorticism. Other causes of secondary osteoporosis can be hereditary disorders, chronic diseases of the liver, kidneys, diabetes mellitus, malabsorption, tumors and iatrogenic stimuli (long-term use of glucocorticoids, long-term immobilization).

Risk factors

- positive family history, occurrence of fractures in older family members;
- premature menopause, secondary amenorrhea (longer than one year), primary hypogonadism;
- white race;
- intolerance to dairy products;
- sedentary lifestyle, lack of exercise, smoking, chronic alcohol intake.

Manifestations and complications

Manifestations of osteoporosis are non-specific. The disease can be asymptomatic for a long time. The diagnosis is often made by random X-ray examination. An important symptom is the gradual deformation of the figure. The curvature of the spine increases, the height of the figure decreases (even by 10 centimeters and more). Back pain is associated with spinal involvement, which can be severe, sudden, or nonspecific, exacerbated by movement or strain.

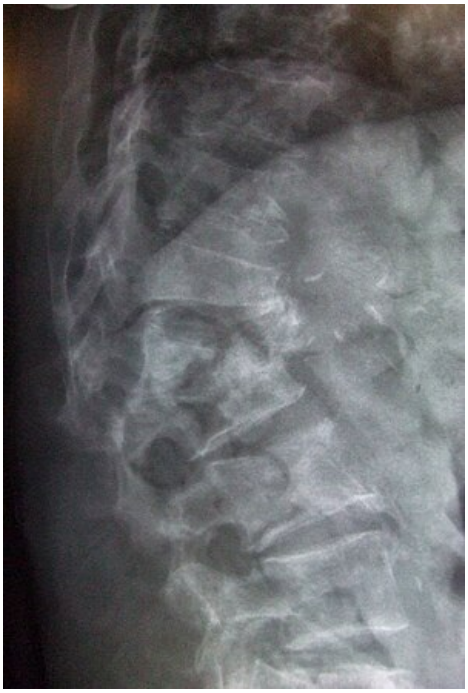
Pain is caused by irritation of the spinal roots due to compression of the vertebral bodies and reflex spasm of the paravertebral muscles. On X-ray, we observe a fracture of the cover plates of the vertebral bodies - a typical **image of fish vertebrae** or an image of a complete vertebral body fracture. In addition to vertebral fractures, fractures of the femoral neck, humerus and wrist often occur.

Examination

Early diagnosis of osteoporosis is very important for subsequent treatment.

Imaging methods

- Skeletal X-ray - changes noticeable with a loss of bone tissue of more than 30%, thinning of the corticalis on the long bones, vertebral bodies lose the trabecular structure on the side images.
  - Osteodensitometry - or **DXA** method (**two-energy X-ray absorption spectrometry**) provides information about the content of minerals in the bone. This is a non-invasive method that evaluates the degree of shading of an X-ray passing through the distal forearm, lumbar vertebrae or proximal femur. It is interpreted using Z-score and T-score values, see classification.
- Ultrasonodensitometry - ultrasonic measurement of bone density. It is performed on the heel bone.
- Quantitative Computed Tomography - **QCT** tells the most about trabecular bone condition. The disadvantage is the greater radiation exposure.



Skiagram of L1 / 2 vertebral compression fracture in osteoporosis

Biochemical indicators

- Calcemia, phosphatemia and alkaline phosphatase (ALP) activity are usually normal.
- Degradation products of type I collagen in urine: hydroxyproline, galactosyl-hydroxylysine, pyridinoline linkers, carboxy-terminal telopeptide CTx (osteoresorption markers).
- Calciuria in 24 hours (suitable as screening).
- Plasma tartrate-resistant acid phosphatase (TRAP) - an indicator of osteoresorption.
- Alkaline phosphatase bone isoenzyme - an indicator of bone formation (specific for osteoblasts).
- Procollagen type I propeptides (markers of bone formation, e.g. procollagen type I N-propeptide - PINP).
- Osteocalcin - an indicator of bone formation, a protein produced by osteoblasts.

Therapy

The goal of osteoporosis treatment is to stop or reduce bone loss by osteoclast activity. At the same time, we are trying to increase bone formation by osteoblast activity. Primary osteoporosis usually cannot be cured, only to stop its progression and alleviate the patient's difficulties. Treatment must be comprehensive and long-term. Non-pharmacological osteoporosis therapy is based on weight loss, rehabilitation exercises and adequate Ca^{2+} and vitamin D intake. In the case of bedridden patients, early mobilization is necessary if possible. Walking, cycling on a flat surface is recommended. Sports with jumps, wrestling, boxing are prohibited.

- **Calcium** – an important source of calcium is food (milk, cheese, **poppy seed**). The recommended daily dose of calcium is 1000-1500 mg.
- **Vitamin D** and its metabolites increase intestinal calcium resorption. The preparations are administered orally or by injection. The recommended daily intake is **800 IU** (20 µg) vitamin D daily.
- Calcitonin inhibits osteoresorption by reducing osteoclast activity. It is given by injection or nasally.

Hormone replacement therapy

Hormone replacement therapy is used to treat postmenopausal osteoporosis - the administration of estrogens and gestogens. By default, therapy lasts 5-7 years. Estrogen stimulates osteoblasts to form bone. In addition to bone effects, hormone replacement alleviates the symptoms of menopausal syndrome and has a beneficial effect on cardiovascular mortality. Replacement therapy carries a risk of thromboembolic complications. Extremely long-term substitution increases the risk of endometrial and breast cancer.

Bisphosphonates

Bisphosphonates are synthetic substances, osteoresorption blockers - pamidronate, alendronate. They also have an effect on the formation of trabecular bone. Bisphosphonate therapy has good effects on steroid osteoporosis.

Anabolic steroids

Anabolic steroids are androgen derivatives; increase osteogenesis, suppress osteoresorption. By altering the basic structure of the steroid, the virilizing effects are suppressed, and the anabolic effects are preserved, they have an analgesic effect.

Fluorides

NaF – increases bone formation and bone density in the axial skeleton. The therapy should last from two to five years. Treatment (with co-administration of Ca^{2+}) does not lead to the formation of new bone beams, it only strengthens existing beams.

Teriparatide

Teriparatide stimulates bone formation by the action of an endogenous PTH fragment.

Biological treatment

Studies are currently underway for antibodies to sclerostin, a protein that has catabolic effects on bone.

Prevention

It is important to identify patients at risk for future osteoporosis in a timely manner and to stop bone loss. Primary prevention includes a sufficient supply of calcium and vitamin D in the diet and a sufficient load on the bone with adequate movement.

Summary video

Rachitis

Rachitis *(rickets, English disease)* is one of the most common acquired diseases of the musculoskeletal system affecting children.

Etiopathogenesis and pathological anatomy

The disease corresponds to osteomalacia in adulthood.

Calciphenic rickets

The cause of this type of rickets is a lack of Ca or vitamin D, which can be caused by disorders of resorption of vitamins in the intestine, their insufficient supply, or lower exposure to sunlight. The result is insufficient osteoid mineralization. Furthermore, the bone beams are lined with strips of unosified matrix, the bone is dilated in the growth cartilage landscape, is soft and can bend. This results in characteristic changes in the growing skeleton.

Phosphopenic rickets

The cause of phosphopenic rickets is a lack of phosphates, which is caused by their increased losses in the kidneys.

Vitamin D-resistant rickets

This type is one of the inherited diseases that are caused by disorders of phosphate and calcium metabolism.

Clinical picture

The child is apathetic, sleepy, pale, irritated, also has an enlarged belly. Insufficient skeletal mineralization leads to a reduction in bone resistance.

Typical deformities of the growing skeleton

Craniotabes rachitica

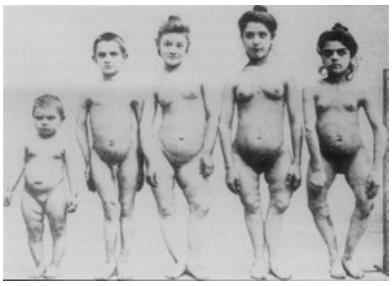
With this deformity, the fontanelles close late. The calf in the header is soft. Sometimes it is deformed by the pressure of the growing brain into the form of a caput quadratum, which is manifested by the prominence of the humps of the frontal and parietal bones.

Rachit's rosary

Deformity manifested by a symmetrical spherical extension of the transition of the bony and cartilaginous part of the ribs.

Harrison's groove

Another name for the *lacing groove* is a circular groove deforming the distal part of the chest.


Siblings with rickets

Sitzbuckel

These are deformities of the vertebrae, in which there is insufficient mineralization of the vertebral bodies. In severe cases, it causes a gibbus.

Crura vara rachitica

The manifestation is typical varus deformities of the lower legs.

Pelvic deformities

The pelvis is flattened, in the shape of a three-horned hat.

Fractures

Long bone fractures often occur.

Laboratory test

1. Alkaline phosphatase (ALP) is **elevated** (due to bone remodeling).
2. Serum calcium (Ca) is **slightly reduced** or **normal**.
3. Serum phosphate (P) levels are **reduced**.

X-ray image

On the X-ray, we find cup-shaped metaphyses, enlarged epiphyseal cartilage or angular deformities of the bones. The X-ray image is typical. We differentiate **4 X-ray stages:**

1st stage (acute)

The pineal gland and contour of the metaphysis are irregular. If the pineal gland already contains an ossification nucleus, then it is indistinct and irregular.

2nd stage

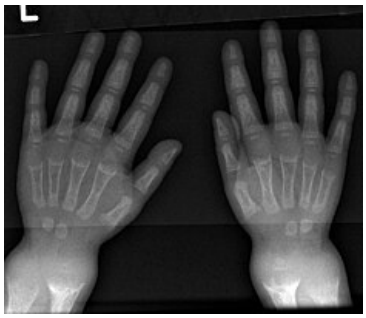
The pineal gland is irregular. The metaphysis is wider than normal due to "pushing" to the sides by loading, it also takes on a calyx-shaped shape. There is a loss of thickening of the periosteum, there is also a curvature of the compacts of the affected bones. Condensation of the cortex occurs in the concavity of the curve.

3rd stage

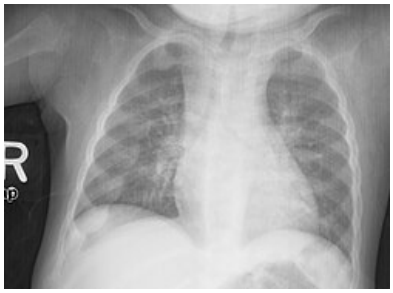
The shadow of the metaphysis thickens and characteristic **Looser zones** appear, which are condensation lines that run transversely to the end of the metaphysis. Furthermore, we can observe the difference in the width of the metaphysis and the pineal gland.

4th stage

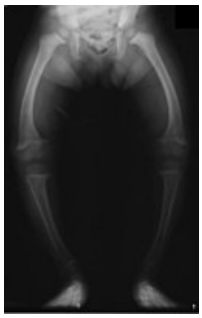
In the last stage, the normal bone structure is repaired and gradually restored, as well as its calcification.



Typical X-ray image of Florida rickets - rickets = cup-shaped extension at the distal ends of the ulna and radius



Rachit's rosary on X-ray (extended rib ends)



X-ray image of lower limb rickets

Therapy

High doses of **vitamin D** are given, and sufficient sunlight is recommended for a growing child (**heliotherapy**). In the Czech Republic, vitamin D is given from the 2nd week during the entire first year and in the winter months of the second year of life (prophylaxis is mandatory in our country). Early therapy leads to spontaneous correction of mild deformities.

Severe deformities that do not respond to treatment are corrected in long bones by **osteoclasia** or **osteotomy**, in the case of the chest and spine by exercise, a corset or a plaster bed.

Differential diagnostics

Differential diagnosis is usually trouble-free. In the beginning, the disease is similar to congenital syphilis, avitaminosis C (scurvy) and renal osteomalacia.

Osteomalacia

Osteomalacia means a loss of inorganic bone mass in adulthood, the amount of osteoid is maintained.

Osteodystrophia fibrosa cystica generalisata

Osteodystrophia fibrosa cystica generalisata **(*morbus Recklinghausen, primary hyperparathyroidism*) is a disease belonging to the group of acquired systemic diseases of the bone system.** Cave! **It should be distinguished from von Recklinghausen's disease, which is synonymous with neurofibromatosis - type 1.**

Etiopathogenesis

It mainly affects women (especially in the second decade of life). The cause is **parathyroid adenoma**, which leads to hyperproduction of PTH, PTH releases phosphates and calcium salts from the skeleton, thereby increasing phosphaturia and increasing calciuria (increases calcium resorption in the ascending arm of the Henle loop, but for high calcium values still occurs hypercalciuria). This leads to hypophostatemia and hypercalcaemia.

At the same time, osteoid formation (fibrous remodeling of cancellous bone) is increased. Cystic skeletal destruction and general osteoporosis occur. Fractures/infractions with intraosseous hemorrhages occur at the site of significant weakening of the supporting parts of the skeleton.

Clinical picture

Fatigue with decreased physical performance, occasional **pain** in the spine and limbs. In the later stage of the disease, minor **deformities of the limbs**, or. spontaneous fractures. **Renal impairment**: nephrolithiasis to nephrocalcinosis.

Laboratory test

- hypercalcemia
- hypercalciuria
- hypophosphataemia
- hyperphosphaturia

X-ray image

X-ray examination performed only after the occurrence of a spontaneous fracture (cystic deposits, thinning of compacts, dilation of the medullary cavity). Reducing the thickness of vertebral bodies, their expansion, and the occurrence of multiple compression fractures are common. Subperiosteal bone reduction, most commonly seen on the middle joints of the fingers. Structural changes in the calf are common.

In the advanced stages of the disease, there are multiple angulations and severe deformities of the supporting parts of the skeleton. Sometimes a parathyroid adenoma on CT.

Therapy

Causal treatment only **surgical** (removal of parathyroid adenoma). We treat hypercalcemic crises by hydration and adjustment of the mineral economy.

Orthopedic therapy consists in corrective osteotomy of deformities, ev. in combination with prolongation performances.

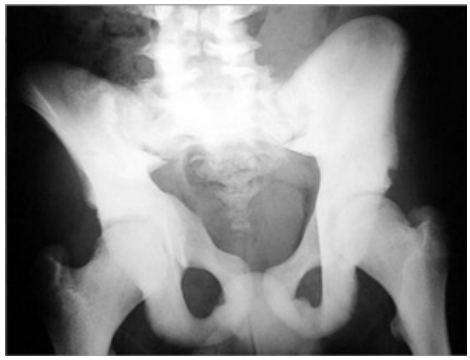
Differential diagnostics

Fibrous dysplasia (Jaffe-Lichtenstein), cortical fibrosis defect, juvenile solitary pseudocyst, myeloma. In all these diseases (with the exception of plasmacytoma) unilocular / monomelic occurrence, but in fibrous dysplasia affected the bones of almost the entire skeleton.

Albers-Schönberg Disease

Albers-Schönberg disease (*marble bone, osteosclerosis, osteopetrosis*) is a rare inherited disease with osteoclast dysfunction (bone resorption disorder). The **balance of osteoblasts and osteoclasts is disturbed** → bone becomes extremely compact (**bone sclerosis**). , strengthening of metaphyses and diaphyses The primary medullary cavity is filled with a homogeneous irregular bone substance → **extramedullary hematopoiesis**.

- 3 forms:
  - **Classical congenital form** (Albers-Schönberg disease) - malignant osteopetrosis (AR hereditary)
  - ***Osteopetrosis tarda*** – benign (AD hereditary).
  - **Osteopetrosis caused by renal tubular acidosis** (hereditary AR)


X-ray image of osteopetrosis.

Clinical picture

- various course and prognosis - mild to severe or deadly forms (eg early infantile form ending lethal to the 10th year of life),
- hematopoiesis disorders → anemia, immunodeficiency,
- macrocephaly, tooth defects, osteosclerosis, exophthalmos (compression of nerves in the bone canals),
- pathological fractures.

X-ray image

- increased bone density in the basic picture (cortical and spongiosis cannot be distinguished, filling of the bone marrow cavity),
- banded osteosclerotic zones of vertebral bodies and cover plates,
- thickening of the cortices of the long bones and the peripheral parts of the pelvis,
- radial thickening of the trabecular bone in the skeleton of the hand and foot,
- periosteal apposition to spicula, often in the traction zones of the skeleton (club-shaped metaphysis).

Laboratory test

- acid phosphatase increased in serum (possibly also alkaline phosphatase) ,
- calcium and phosphate levels normal,
- in the renal form manifestations of acidosis.

Prenatal diagnosis

- sonographically increased bone density,
- radiological card from the 25th week of pregnancy.

Therapy

- not causal
- **non-orthopedic treatment** - treatment of anemia or pancytopenia (bone marrow transplantation, corticoids, IFN-α),
- **orthopedic treatment** - pathological fractures (mostly transverse), bone healing prolonged, longer period of

immobilization of fractures necessary.

Differential diagnostics

- other sclerosing bone diseases (pycnodysostosis, progressive diaphyseal dysplasia, metaphyseal dysplasia, metal poisoning, syphilis, myelofibrosis) - they do not have severe anemia.

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