

# Metabolic osteopathy

This article has been translated from WikiSkripta; ready for the **editor's review**.

<sup>[1]</sup>Metabolic osteopathies are diseases caused by disturbances in the balance between bone formation and resorption and disturbances in bone mineralization → osteopenia and decreased bone mass (osteoporosis, osteomalacia) or bone sclerotization and increased bone mass (Paget's disease, osteopetrosis). These osteopathies are caused by bone cell dysfunction, genetic abnormalities (defects in the synthesis of collagen I etc.), increased expression of bone morphogenetic proteins, kidney function disorders, endocrinopathies, tumor secretion of substances affecting bone metabolism<sup>[2]</sup>

## Osteoporosis

### Osteoporosis

### Definition of Osteoporosis

Osteoporosis, or porous bone, is a disease in which bone tissue is normally mineralized but the mass or the density of the bone is decreased and the structural integrity of trabecular bone is impaired.

### Types of Osteoporosis

1. Postmenopausal or primary osteoporosis Postmenopausal osteoporosis occurs in the middle-aged and older women. It can occur due to estrogen deficiency as well as estrogen -independent age-related mechanisms. Hormonal deficiency also can increase with stress, excessive exercise, and low body weight. Postmenopausal changes include a substantial increase in bone turnover, which, an imbalance between the remodeling activity of osteoclasts and osteoblasts. Sex hormones, especially estrogen and testosterone, are significant in premenopausal bone maintenance, however, when estrogen levels drop after menopause; it appears that circulating androgens become significant effectors on bone metabolism. Poor nutrition and insufficient intake or malabsorption of dietary minerals, including calcium is factors in the development of osteoporosis. Calcium absorption from the intestine decreases with age, and studies of individuals with osteoporosis show that their calcium intake is lower than that of age-matched controls. Deficiencies of vitamins, particularly vitamins C,D, E and K, also contribute to bone loss. 2. Secondary osteoporosis Secondary osteoporosis is caused by hormonal imbalances (endocrine disease, diabetes, hyperparathyroidism, hyperthyroidism), medications (such as heparin, corticosteroids, phenytoin, barbiturates, lithium), and other substances (including tobacco and ethanol). Other conditions include rheumatoid disease, human immunodeficiency virus (HIV), malignancies, malabsorption syndromes, liver or kidney disease; also increase the risk for developing osteoporosis. Secondary osteoporosis sometimes develops temporarily in individuals receiving large doses of heparin. Heparin promotes bone resorption by decreasing collagen synthesis or by increasing collagen breakdown. Another form of transient osteoporosis of the hip is associated with the third trimester of pregnancy or the immediate postpartum period.

## Pathophysiology

Osteoporosis develops when the remodeling cycling or the process of bone resorption and bone formation is disrupted leading to an imbalance in the coupling process. The explosion of the new information in field of bone biology has led to new understanding of the roles of hormones, growth, and signaling factors, and cellular biology in osteoporosis. The osteoclast differentiation pathway is directed by a series of processes that include proliferation, differentiation, fusion and activation. These processes are controlled by hormones, cytokines, and paracrine stromal-cell microenvironment interactions. Therefore the intercellular communication in bone and the key molecular regulators are necessary for bone homeostasis. Certain transcript factors known as Forkhead box (FoxO) help protect against the effects of OS by preventing excess accumulation of ROS and regulating certain genes that affect DNA repair and cell life span. Normal bone homeostasis is dependent on the balance between the cytokine receptor activator of nuclear factor, ligand (RANKL), its receptor RANK, and its decoy receptor osteoprotegerin (OPG); understanding this has led to a tremendously increased knowledge of osteoclast biology and pathogenesis of bone loss. Postmenopausal osteoporosis is characterized by increased bone resorption relative to the rate of bone formation, leading to sustained bone loss resulting from estrogen deficiency. Bone loss resulting from estrogen deficiency also contributes to osteoporosis in men. Sex steroids exert anti-apoptotic effects on osteoblasts but exert pro-apoptotic effects on osteoclasts; in both scenarios this is accomplished by activating the extracellular signal regulated kinases (ERKs). Estrogen activates ERKs outside the nucleus; ERKs then accumulate in the nucleus and activate downstream transcription factors. Glucocorticoid induced osteoporosis is characterized by increased bone resorption and decreased bone formation. Glucocorticoids increase RANKL expression and inhibit OPG production by osteoblasts. The use of immunosuppressive drugs such as cyclosporine A, to reduce rejection of transplanted organs also alters the OPG/RANKL RANK system and can lead to posttransplantation osteoporosis. Age related bone loss begins in the third to fourth decade. The cause remains unclear, but it is known that decreased

serum growth hormone and IGF levels along with increased binding of RANKL and decreased OPG affect osteoblast and osteoclast function. Loss of trabecular bone in men proceeds in a linear fashion, with thinning of trabecular bone rather than complete loss as is noted in women.

## Genetics

In recent years there has been progress made in studies understanding the genetic basis to osteoporosis. Genetic factors that contribute to osteoporosis by influencing not only bone but mineral density but also bone size, bone quality and bone turnover. Meta-analysis has been used to define the role of several candidate genes in osteoporosis. Some qualitative trait loci that regulate bone mass identified by linkage studies in humans and experimental animals have been replicated in multiple populations. Genes that cause monogenic bone diseases also contribute to regulation of bone mass in normal population. Genome wide association studies and functional genomics approaches have recently begun to apply to genetic studies of osteoporosis.

- Family history
- White/Asian Race
- Increased Age
- Female Gender

## Epidemiology

- 200 million people worldwide suffer from osteoporosis
- Approximately 30% of all postmenopausal women have osteoporosis in the United States and in Europe.
- At least 40% of these women and 15-30% of men will sustain one or more fragility fractures in their lifetime.
- An increased risk of 86% for any fracture has been demonstrated in people that have already sustained a fracture.
- Fewer than 10% of vertebral fracture results in hospitalization even if they cause pain and substantial loss of quality of life.
- In Europe, the prevalence defined by radiological criteria increases with age in both sexes and is almost as high in men as in women: 12% in females (range 6-21%) and 12% in males (range 8-20%).
- Hip fracture rates are more common in Scandinavian and North American than these observed in Southern European, Asian and Latin American

Countries.

- In women over 45 years of age, osteoporosis accounts for more days in the hospital than any other diseases, including diabetes, myocardial infarction and breast cancer.
- In Sweden, osteoporotic fracture in men account for more hospital bed days than those due to prostate cancer.
- By 2050, the worldwide incidence of hip fracture in men is projected to increase by 240% in women and 310% in men.
- The estimated number of hip fractures worldwide will rise from 1.66 million in 1990 to 6.26 million in 2050, even if age-adjusted incidence rates remain stable.

## Disease Described

Disorders of Bone Metabolic Bone Disease is characterized by abnormal bone structure that is caused by altered or inadequate biochemical reactions resulting in disorders of bone strength. Abnormalities include genetic, mineral, vitamin, and structural abnormalities.

## Signs and Symptoms

Clinical manifestations of osteoporosis depend on the bones involved. The most common is bone deformity. Pain tends to occur only when there is a fragility fracture. Fractures are likely to occur because of the trabeculae of spongy bone become thin and sparse and compact bone becomes porous. As the bones lose volume, they become brittle and weak and may collapse or become misshapen. Vertebral collapse causes kyphosis and diminished height. Fracture of long bones particularly the femur and humerus, distal radius, ribs, and vertebrae are most common. The most serious fractures are hip fractures because of their resultant chronic pain, disability, diminished quality of life, and premature death. Fatal complications of fractures include fat or pulmonary embolism, hemorrhage, and shock

## Diagnosis

The World Health Organization has defined osteoporosis based on bone density. Normal bone mass is greater than 833 mg/cm<sup>2</sup>. Osteopenia or decreased bone mass is 833 to 648 mg/cm<sup>2</sup>. Osteoporosis is bone mass less than 648 mg/cm<sup>2</sup>. DEXA Scan (Dual X-ray Absorptiometry) The most common osteoporosis test is dual X-ray absorptiometry -- also called DXA or DEXA. It measures people's spine, hip, or total body bone density to help gauge fracture risk. Read more. Beyond DEXA: Other Bone Mineral Density Tests Various methods can check bone density, including ultrasound and quantitative computed tomography (QCT). Bone density scores and cost may vary by testing method.

## Blood Test Markers

Whether you're being screened or treated for osteoporosis, your doctor may order a blood or urine test to see the metabolism of bone. This provides clues to the progression of your disease. Bone Densitometry Bone densitometry is a test like an X-ray that quickly and accurately measures the density of bone.

# Treatment

Treatment is more common and is focused on preventing fractures and maintaining optimal bone function. The role of calcium intake to prevent and treat osteoporosis is controversial. It is well accepted that oral calcium intake sufficient to maintain normal calcium balance is necessary during adolescence to ensure development of peak bone mass and that calcium-deficient diets can aggravate bone loss associated with menopause and aging. Recommendations have been established for young women of 1000 mg of calcium daily and for postmenopausal women of 1500 mg daily with vitamin D. Other nutrients that appear to have a positive impact on bone health include magnesium, Vitamin K and docosahexaenoic acid or DHA. Regular moderate weight bearing exercise can slow the rate of bone loss and in some cases reverse demineralization because the mechanical stress of exercise stimulates bone formation. An exercise program can enhance muscle strength as well. Bisphosphonates are a class of inorganic pyrophosphate derivatives that bind bone mineral and improve osteoblast and osteocyte survival while promoting osteoclast apoptosis, thus slowing the bone remodeling process. Another treatment is the use of denosumab, a monoclonal antibody that binds the cytokine receptor activator of RANKL. RANKL inhibition blocks the maturation, function, and survival of osteoclasts, thus reducing bone resorption. Teriparatide also called PTH 1-34 is a biosynthetic form of parathormone and contains the first 34 amino acids of parathyroid hormone. Given subcutaneous injection, PTH reduces vertebral fractures but use is limited to a period of 24 months because the development of osteosarcoma.

Medicines Approved to Prevent and/or Treat Osteoporosis Class and Drug Brand Name Form Frequency  
Bisphosphonates Alendronate Generic Alendronate and Fosamax® Oral (tablet) Daily/Weekly Alendronate Fosamax Plus D™ (with 2,800 IU or 5,600 IU of Vitamin D3) Oral (tablet) Weekly Ibandronate Boniva® Oral (tablet) Monthly Ibandronate Boniva® Intravenous (IV) injection Four Times per Year Risedronate Actonel® Oral (tablet) Daily/Weekly/Twice Monthly/Monthly Risedronate Actonel® with Calcium Oral (tablet) Weekly Risedronate Atelvia™ Oral (tablet) Weekly Zoledronic Acid Reclast® Intravenous (IV) infusion One Time per Year/Once every two years Calcitonin Calcitonin Fortical® Nasal spray Daily Calcitonin Miacalcin® Nasal spray Daily Calcitonin Miacalcin® Injection Varies Estrogen\* Estrogen Multiple Brands Oral (tablet) Daily Estrogen Multiple Brands Transdermal (skin patch) Twice Weekly/Weekly Estrogen Agonists/Antagonists Also called Selective Estrogen Receptor Modulators (SERMs) Raloxifene Evista® Oral (tablet) Daily Parathyroid Hormone Teriparatide Forteo® Injection Daily RANK ligand (RANKL) inhibitor Denosumab Prolia™ Injection Every 6 Months

- Estrogen is also available in other preparations including a vaginal ring, as a cream, by injection and as an oral tablet taken sublingually (under the tongue). The vaginal preparations do not provide much bone protection.

## Links

International Osteoporosis Health Organization (<http://www.iofbonehealth.org>) [1]  
(<http://www.iofbonehealth.org>)<http://www.iofbonehelath.org>

## References

McCance, K. H. (2014). Pathophysiology The Biologic Basis for Disease in Adults and Children. St Louis, Missouri: Elsevier Mosby. National Osteoporosis Foundation. (2014, January). Retrieved from [www.nof.org](http://www.nof.org) Uitterlinden, A. v. (2006). Identifying genetic risk factors for osteoporosis. Musculoskeletal Neuronal Interact, (6)1:16-26. World Health Organization . (2014, January). Retrieved from World Health Organization - Osteoporosis : [www.who.org](http://www.who.org)

## Rickets

Rachitis

## Osteomalacia

## Ostoemalacia

### Definition of Disease

Osteomalacia/ Rickets is a metabolic bone disease characterized by inadequate bone mineralization. The remodeling cycle proceeds normally through osteoid formation, but mineral calcification fails to occur. Rickets is the term used to describe the condition prior to the closing of the physis. Osteomalacia is used after physis closure.

### Pathophysiology

Crystallization of minerals in osteoid requires adequate concentrations of ionized calcium and phosphate. Vitamin D influences these levels after its dihydroxylation into calcitriol (hepatic position 25 and renal position 1). When concentrations are too low crystallization does not proceed normally. Vitamin D disrupts mineralization because it normally regulates and enhances the absorption of calcium in the intestine. A lack of vitamin D causes plasma calcium concentrations to fall. Low plasma calcium levels stimulate parathyroid hormone (PTH). PTH raises calcium concentration but also increases renal clearance of phosphate. When phosphate decreases below a critical level, mineralization cannot proceed normally.

## Genetics

Hereditary forms of osteomalacia include:

- Hypophosphatemic vitamin D resistant rickets, an X-linked, autosomal dominant disorder,
- Hypophosphatemic rickets with hypercalciuria autosomal recessive
- Vitamin D dependant rickets caused by a mutation in the renal tubular 25-hydroxyvitamin D hydrolase

Hereditary forms of vitamin D deficiency and resistance, identified in childhood, are associated with osteomalacia in adults, but these disorders are rare.

## Epidemiology

Osteomalacia is rare in the United States and Western Europe. There is a growing prevalence of vitamin D deficiency in many countries, which when severe and prolonged results in hypocalcemia, secondary hyperparathyroidism, secondary hypophosphatemia, and osteomalacia. Populations at risk include:

- The homebound elderly who have little sun exposure and insufficient dietary calcium and vitamin D
- Patients with malabsorption related to gastrointestinal bypass surgery, crohns, or celiac disease
- Vegetarian diets without vitamin D supplementation
- Women who wear traditional veils or dresses that prevent sun exposure
- Patient on long term anticonvulsant therapy i.e. phenytoin and phenobarbital
- Rifampin and glucocorticoids
- Tumor induced osteomalacia i.e. paraneoplastic syndrome of renal phosphate wasting by tumor secretion of phosphatonin

## Disease described

The principle abnormality associated with Osteomalacia/ Rickets is a defect in the mineralization of the osteoid matrix. It can be definitively diagnosed by bone biopsy. The clinical syndrome associated with osteomalacia consists of pain, myopathy, and fracture.

## Sign and Symptoms

- Pain, sometimes severe, in bones, particularly in the pelvis, lower back and legs. Tenderness may sometimes be felt in the shins and in other bones.
- The patient usually walks with feet rather widely separated and may appear to waddle. Deformities of the pelvis and long bones may be obvious.
- Tetany is manifested by involuntary twitching of the muscles of the face or by carpopedal spasm.
- Spontaneous fractures may be a feature. Before the deformities are clinically detectable, diagnosis may be made by X-ray examination, which will show rarefaction or decalcification of bones all over the body.

## Diagnosis

- Blood and urine tests. In cases of osteomalacia caused by vitamin D deficiency or by phosphorus loss, abnormal levels of vitamin D and the minerals calcium and phosphorus are often detected.
- X-ray. Slight cracks in bones that are visible on X-rays, referred to as Looser transformation zones, are a characteristic feature of osteomalacia.
- Bone biopsy. High specificity in detecting osteomalacia, it's not often needed to make the diagnosis.
- ALP and PTH may be done to rule out renal disorders causing the problem.

## Treatment

Osteomalacia is managed by treating the underlying cause. If vitamin-D deficiency is diagnosed, repletion can be accomplished with:

- Oral vitamin D, 1000 IU per day.
- Neutral phosphate salts, 500 mg four times daily.
- Long-term anticonvulsant therapy may be supplemented with 400 to 800 IU of vitamin D daily.

- Hepatobiliary disease or chronic renal failure is managed with supplemental 25(OH)D ( calcifediol) and 1,25(OH)2D ( calcitriol) (Lexicomp, 2014).

## Links

<http://www.mayoclinic.org/diseases-conditions/osteomalacia/basics/definition/con-20029393>

<http://my.clevelandclinic.org/orthopaedics-rheumatology/diseases-conditions/hic-osteomalacia.aspx>

## Related current articles

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1819593/>

<http://onlinelibrary.wiley.com/store/10.1111/j.1753-4887.2008.00100.x/asset/j.1753-4887.2008.00100.x.pdf?v=1&t=hta9wzlo&s=bd3005296b46d52d150162df20d17a80f485c5da>

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# 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. **It must be distinguished from morbus von Recklinghausen, which is synonymous with neurofibromatosis - type 1.**

## Etiopathogenesis

It mainly affects women (mainly in the 2nd decade of life). **The cause is an adenoma of the parathyroid glands** , which leads to hyperproduction of PTH , PTH releases phosphates and calcium salts from the skeleton, thereby increasing phosphaturia and increasing calciuria (it increases calcium resorption in the ascending limb of the loop of Henle, but due to high calcium values, hypercalciuria still occurs) . This results in hypophosphatemia and hypercalcemia .

At the same time, there is an increased formation of osteoid (fibrous remodeling of cancellous bone). Cystic destruction of the skeleton and generalized osteoporosis occur . Fractures/infractures with intraosseous hemorrhages occur at the site of significant weakening of the load-bearing parts of the skeleton .

## Clinical picture

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

## Laboratory finding

- hypercalcemia
- hypercalciuria
- hypophosphatemia
- hyperphosphaturia

## X-ray image

X-ray examination performed only after the occurrence of a spontaneous fracture (cystic deposits, thinning of the compacts, enlargement of the medullary cavity). A decrease in the thickness of the vertebral bodies, their expansion, and the occurrence of multiple compression fractures are common . Subperiosteal bone reduction, most commonly seen on the middle phalanges 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 load-bearing parts of the skeleton. On CT sometimes parathyroid adenoma.

## Therapy

Causal treatment only **surgical** (removal of parathyroid adenoma). Hypercalcemic crises are treated with hydration and adjustment of the mineral economy.

Orthopedic therapy consists in corrective osteotomy of the resulting deformities, possibly in combination with prolongation performances .

## Differential diagnosis

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

## Links

### Related Articles

- Metabolic osteopathy
- Osteoporosis
- Osteomalacia
- Rickets

### References

1. ↑ Jump up to: a b c d e f g SOSNA, A., P. VAVŘÍK and M. KRBEC, et al. *Basics of orthopedics*. 1st edition. Prague: Triton, 2001. ISBN 80-7254-202-8 .

## Albers-Schönberg disease

Morbus Albers-Schönberg

## Links

### Related Articles

- Metabolic bone disease of immaturity

### References

1. GALLO, Jiří, et al. *Ortopedie pro studenty lékařských a zdravotnických fakult*. 1. vydání. Olomouc : Univerzita Palackého v Olomouci, 2011. ISBN 978-80-244-2486-6. ↑ Skočit nahoru k: a b c d e f g KLENER, Pavel. *Vnitřní lékařství*. třetí vydání. Praha : nakladatelství Galen, 2006. 1100 s. s. 886 – 892. ISBN 80-7262-430-X. ↑ KRAUSE, Carola, Olexandr KORCHYNSKYI a Karien DE ROOIJ, et al. Distinct modes of inhibition by sclerostin on bone morphogenetic protein and Wnt signaling pathways. *J Biol Chem* [online]. 2010, vol. 285, no. 53, s. 41614-26, dostupné také z <<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3009889/?tool=pubmed>>. ISSN 0021-9258 (print), 1083-351X. ↑ Skočit nahoru k: a b c d e f g h i j k l m n o DUNGL, P., et al. *Ortopedie*. 1. vydání. Praha : Grada Publishing, 2005. ISBN 80-247-0550-8. Chybná citace: Neplatná značka <ref>; název „Dungl“ použit vícekrát s různým obsahem ↑ Skočit nahoru k: a b c d e f g h i j k l m n o p q r s t u v w x y z aa ab ac ad ae SOSNA, A., P. VAVŘÍK a M. KRBEC, et al. *Základy ortopedie*. 1. vydání. Praha : Triton, 2001. ISBN 80-7254-202-8. Chybná citace: Neplatná značka <ref>; název „Sosna“ použit vícekrát s různým obsahem ↑ KOUDELA, K., et al. *Ortopedie*. 1. vydání. Praha : Karolinum, 2004. ISBN 80-246-0654-2.
2. GALLO, George, et al. *Orthopedics for students of medical and health faculties*. 1. edition. Olomouc : Palacký University in Olomouc, 2011. ISBN 978-80-244-2486-6.