Fat Soluble Vitamins

Vitamin D

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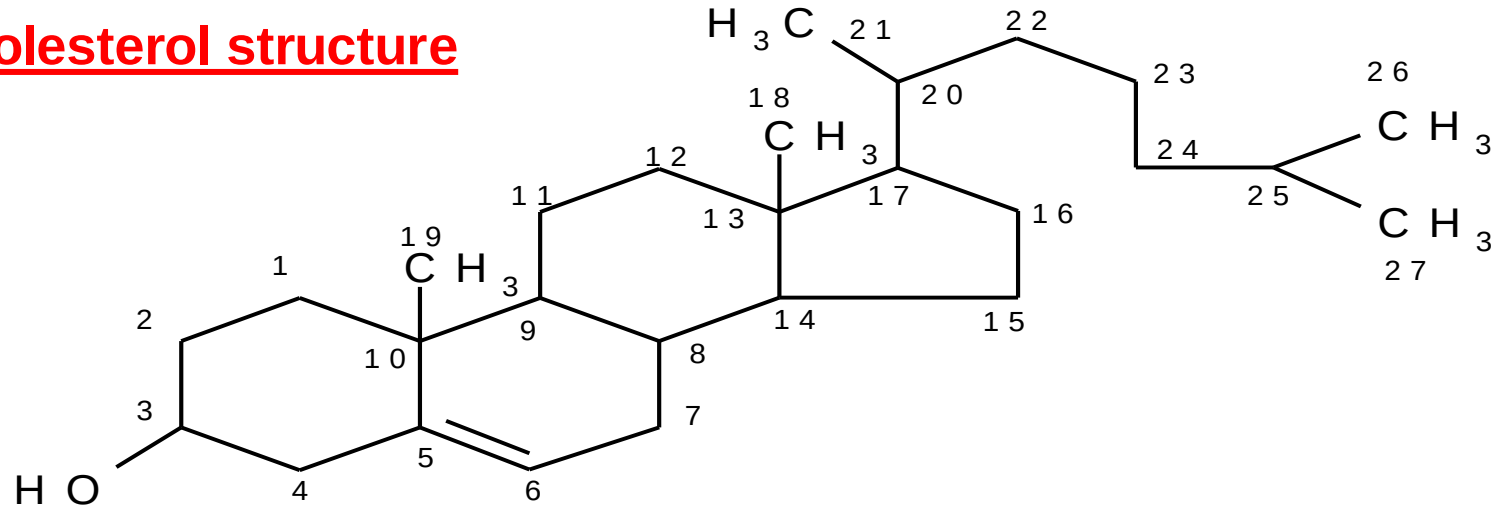
Vitamin D

- **Vitamin D is not strictly a vitamin since it can be synthesized in the skin.**
- **Only when sunlight exposure is inadequate, is a dietary source required.**

Chemical structure:

- **Vitamin D3 (cholecalciferol) is derived from 7-dehyro cholesterol (pro-vitamin D_3) by ultraviolet irradiation.**

Cholesterol structure



Vitamin D Sources

- Cholecalciferol is produced in the skin by U.V. (the cheapest source of vitamin D_3).
- Preformed vitamin D_3 from fish-liver oils, flesh of oily fish, egg yolk and liver.

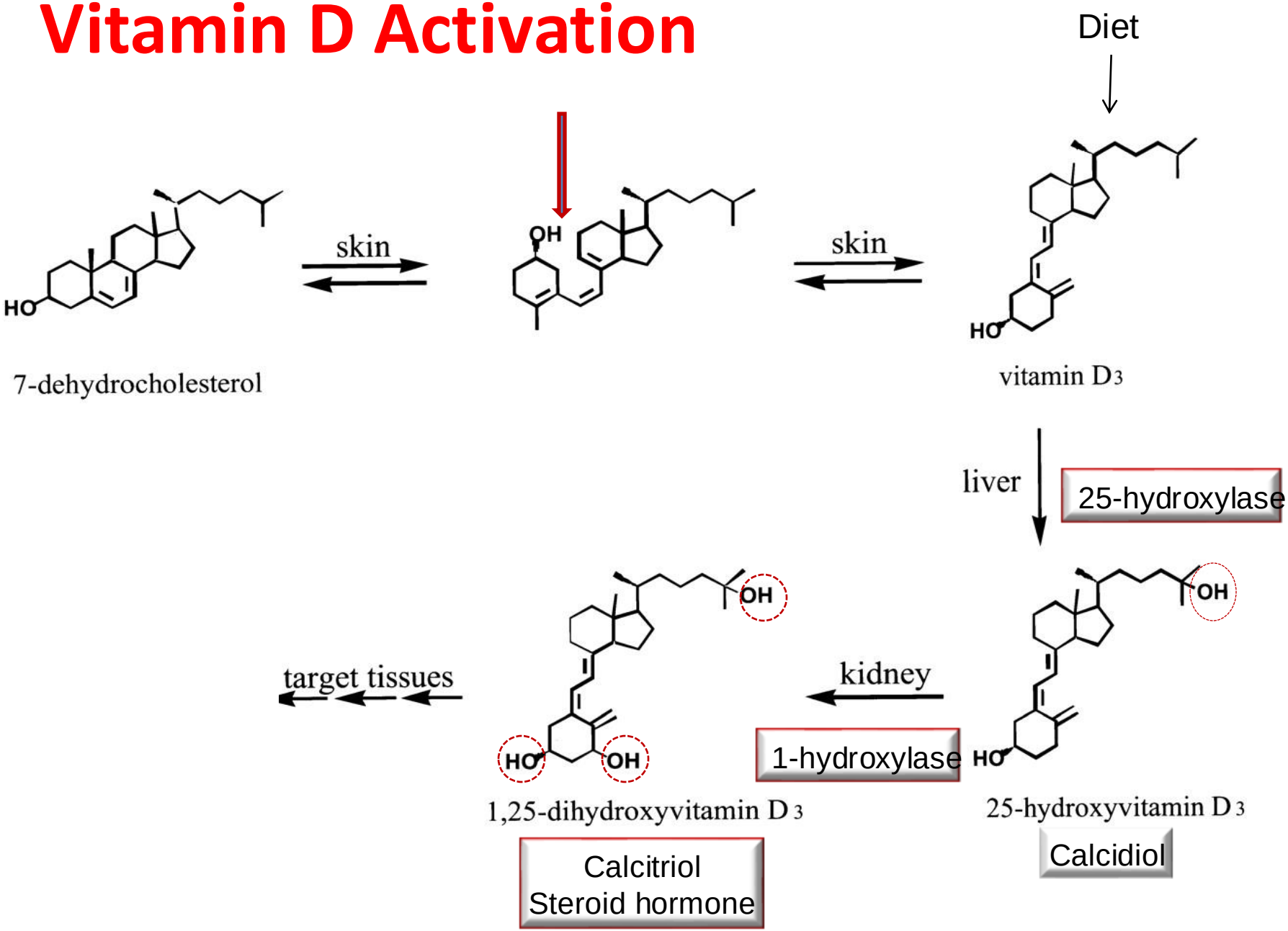
Activation:

- Activation of vitamin D starts in liver cells, where it is hydorxylated on the 25 position by specific microsomal enzyme.
- 25-hydroxy D can be further hydroxylated in kidney by a mitochondrial enzyme to produce 1,25 dihyroxy D_3 (calcitriol) which is the metabolically active form of the vitamin.
- 24,25-dihydroxy-D is another active form isolated. However, it is less active than 1,25 dihydroxy D3.

➢ 25-OH D_3 = storage form

➢ 1,25-$(OH)_2$ D_3 (calcitriol) = active form

Vitamin D Activation



Vitamin D Functions

I. Calcium homeostasis:

- **In the intestine:** it increases the absorption of calcium and phosphorus from the intestine (it induces the synthesis of specific mRNA responsible for synthesis of intestinal calcium binding protein).
- **In the bone:** It promote bone resorption (mobilization of calcium from bone) **at low Ca level**.
- **In moderate amount of Ca ,** 1,25 dihydroxy Vit D enhance deposition of calcium in bone.

  It promotes synthesis of osteocalcin which is needed for bone mineralization. It also promotes bone collagen synthesis.
- **In the kidney:** It enhances reabsorption of filtered tubular calcium & phosphate.

II. Reduce risk of:

- **Insulin resistance, obesity :** it is lower in obese individuals who are more likely to develop diabetes mellitus.

- **Cancer:** $1,25(OH)_2D$ can prevent cancer development or retard its progress/metastasis once developed by inhibition of the cell cycle, inducing apoptosis, and prevention of tumor angiogenesis.

- Vit. D derivatives are now used successfully in the treatment of psoriasis.

III. Vitamin D and immunity

- It exerts its effects on several immune-cell types, including macrophages, T and B cells.

1. Maintenance of tissue integrity:

- It helps to maintain firm intercellular junctions, and gap junctions (viruses can disturb junction integrity)
- It stimulates tight junction protein expression as E-cadherin.

2. Stimulation of synthesis of human cathelicidin:

- It induces the expression of cathelicidin (an antimicrobial peptide) by macrophages. Thus, reducing viral replication.

3. Vitamin D has anti-inflammatory effect (can weakening of Cs):

- It repressing production of inflammatory cytokines as interleukin-E2 (IL-E2).

[Cytokine storm; CS can be triggered by infectious diseases, and it generally presents as systemic inflammation and multiple organ failure].

III. Vitamin D and immunity

4. Anti-oxidant:

- **Vitamin D increases the gene expression of anti-oxidative enzymes, eg glutathione reductase (is suggested as a potential agent for fighting COVID-19).**

- **During COVID-19 pandemic, adequate vitamin D supplementation must be implemented in populations where vitamin D deficiency is prevalent.**

- **Even marginal deficiency may impair immunity. Although contradictory data exist, available evidence indicates that supplementation with vitamins C and D and zinc may improve immune function and reduce the risk of infection.**

METABOLIC DISEASES OF BONES

Because the functions of bone are numerous and complex, there are many disorders that require clinical care by a physician or other healthcare professional. These conditions include benign (non-cancerous) disorders, cancers that occur in bone, and cancers that affect bone.

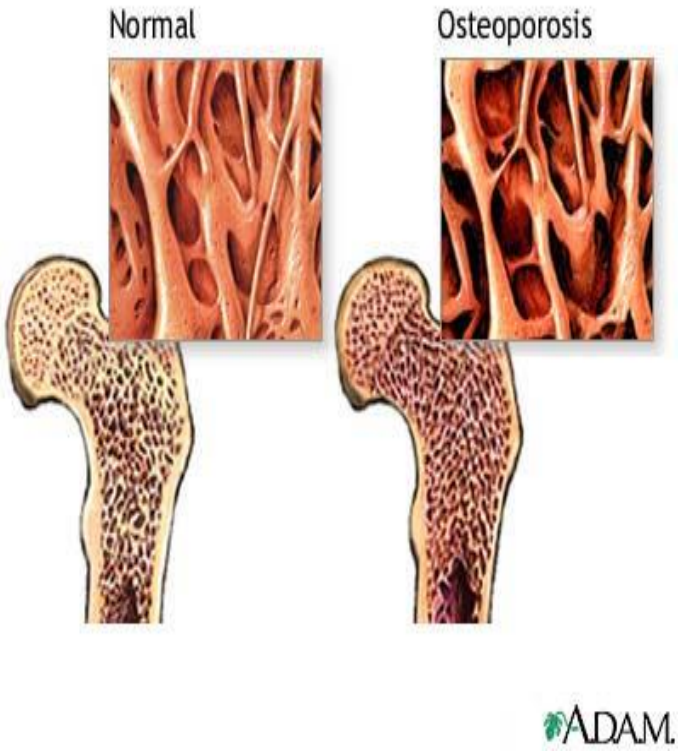
Bone disease is a condition that damages the skeleton and makes bones weak and prone to fractures. Weak bones are not a natural part of aging. While strong bones begin in childhood, people of all ages can improve their bone health.

Bone diseases are disorders and conditions that cause abnormal development and/or impairment in normal bone development. This can result in weakened bones, inflamed joints and pain.

Nutrient deficiencies such a lack of vitamin D or C, hormonal imbalances and cell abnormalities can also cause bone disorders in both children and adults.

Osteoporosis

Osteoporosis is a disease of bones that leads to an increased risk of fracture. In osteoporosis, the bone mineral density (BMD) is reduced, bone microarchitecture deteriorates, and the amount and variety of proteins in bone are altered.



The disease may be classified as :

primary type 1, and primary type 2.

The form of osteoporosis most common in women after menopause is referred to as primary type 1 or postmenopausal osteoporosis.

Primary type 2 osteoporosis or senile osteoporosis occurs after age 75 and is seen in both females and males at a ratio of 2:1.

Causes

Osteoporosis occurs when the body fails to form enough new bone, when too much existing bone is reabsorbed by the body, or both.

Calcium is one of the important minerals needed for bones to form. If you do not get enough calcium and vitamin D, or your body does not absorb enough calcium from your diet, your bones may become brittle and more likely to fracture.

A drop in estrogen in women at the time of menopause and a drop in testosterone in men is a leading cause of bone loss.

Lysosomal proteases present in ostecolasts deteriorate bone in order to stimulate resorption of calcium from bone to increase Ca^{2+} concentration in blood. A decrease in dietary calcium intake, usually as a result of decreased overall dietary energy intake, results in less calcium available for absorption and to maintain plasma calcium concentration. Low blood calcium stimulates parathyroid gland to release PTH. PTH promotes bone resorption leading to bone loss.

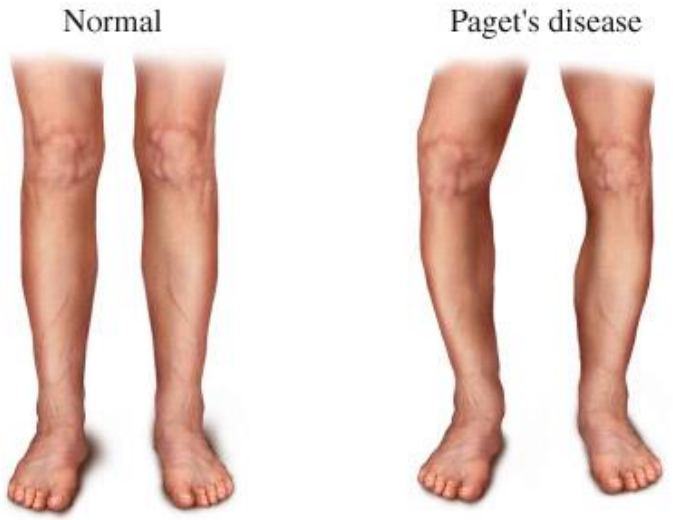
In addition, the amount of vitamin D3 synthesized in aging skin is significantly less than the amount produced in younger skin during exposure to UV rays moreover increases the chance of getting osteoporosis.

Paget's Disease

Paget's disease is a disorder of osteoblasts and osteoclasts that are responsible for breaking down, rebuilding and remodelling bone tissue.

Paget's disease causes bones to become thickened and enlarged but also brittle due to abnormal structural development.

Paget's disease typically is localized, affecting just one or a few bones.



Causes

1-Viral

Paget's disease may be caused by a slow virus infection

2-Genetic

There is also a hereditary factor

Symptoms

Sometimes, symptoms may be confused with those of arthritis or other disorders. In other cases, the diagnosis is made only after complications have developed. Symptoms can include bone pain.

Osteogenesis Imperfecta (OI)

This disease is a genetic disorder that is characterized by brittle bones that break or fracture easily.

It is caused by a gene defect in the production of collagen, a protein that is needed to make bones strong.

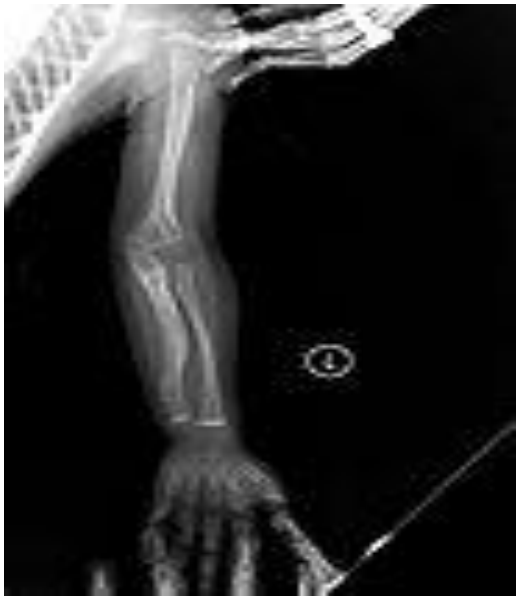
Osteogenesis imperfecta even affects the bones in the inner ear and can cause hearing loss, as well as weak teeth and a curved spine.

People with OI are born with defective connective tissue, or without the ability to make it, usually because of a deficiency of Type-I collagen. This deficiency arises from an amino acid substitution of glycine to bulkier amino acids in the collagen triple helix structure.

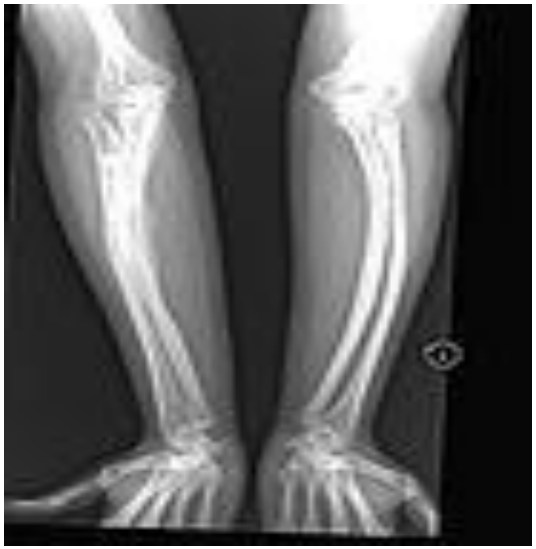
Types

There are eight different types of OI, Type I being the most common, though the symptoms vary from person to person.

Type	Description
I	mild
II	severe and usually lethal in the perinatal period
III	considered progressive and deforming
IV	deforming, but with normal scleras
V	shares the same clinical features of IV, but has unique histological findings
VI	shares the same clinical features of IV, but has unique histological findings
VII	associated with cartilage associated protein
VIII	severe to lethal



OI Type V in a Child



OI Type V in an Adult

Bone Cancers

bone cancer may be due to a primary cancer that begins in the bone or spreads to the bone as secondary cancer from another part of the body such as cancer in the lungs, breast or prostate. There are several types of primary bone cancers such as leukemia, osteosarcoma, Ewing sarcoma, and chondrosarcoma.

Bone cancer facts

The majority of cancer involving the bones is metastatic disease from other remote cancers. Primary bone cancer is much rarer.

The most common symptom of bone cancer is pain.

Bone cancer types

Osteosarcoma

is the most common primary malignant bone cancer. It most commonly affects males between 10 and 25 years old but can less commonly affect older adults. It often occurs in the long bones of the arms and legs at areas of rapid growth around the knees and shoulders of children.
This type of cancer is often very aggressive with risk of spread to the lungs.

Ewing's sarcoma

is the most aggressive bone tumour and affects younger people between 4-15 years of age.

It is more common in males and is very rare in people over 30 years of age. It most commonly occurs in the middle of the long bones of the arms and legs.

Chondrosarcoma

is the second most common bone tumour and accounts for about 25% of all malignant bone tumours. These tumours arise from the cartilage cells and can either be very aggressive or relatively slow growing.

Unlike many other bone tumours, chondrosarcoma is most common in people over 40 years of age. It is slightly more common in males and can potentially spread to the lungs and lymph nodes.

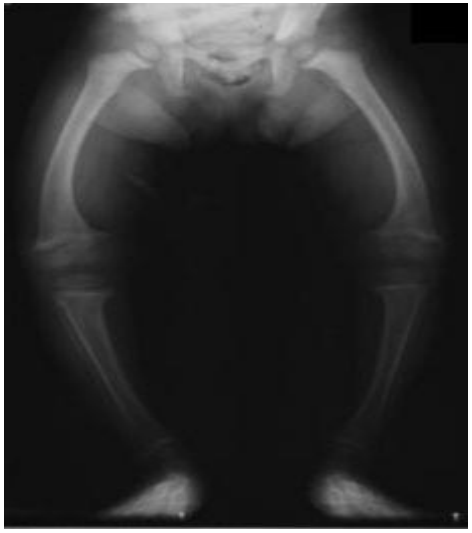
Chondrosarcoma most commonly affects the bones of the pelvis and hips.

Rickets

is a softening of bones in children due to deficiency or impaired metabolism of vitamin D, phosphorus or calcium, potentially leading to fractures and deformity.

Cause

The primary cause of rickets is a vitamin D deficiency. Vitamin D is required for proper calcium absorption from the gut. Sunlight, especially ultraviolet light, lets human skin cells convert Vitamin D from an inactive to active state.



Radiograph of a two-year old rickets sufferer

In the absence of vitamin D, dietary calcium is not properly absorbed, resulting in hypocalcaemia, leading to skeletal and dental deformities and neuromuscular symptoms.

Symptoms

Bone pain , Dental deformities (such as delayed formation of teeth)
Impaired growth, Increased bone fractures, Muscle cramps, Short stature (adults less than 5 feet tall), Skeletal deformities

Osteomalacia

Osteomalacia is similar to rickets because it is caused by a defect in vitamin D metabolism by the body, but it affects mainly adults. It is characterized by weakened bones and abnormal bone formation.

Osteomalacia in children is known as rickets, and because of this, use of the term *osteomalacia* is often restricted to the milder, adult form of the disease.

The softer bones in osteomalacia have a normal amount of collagen, which gives the bones its structure. However, they lack the proper amount of calcium.

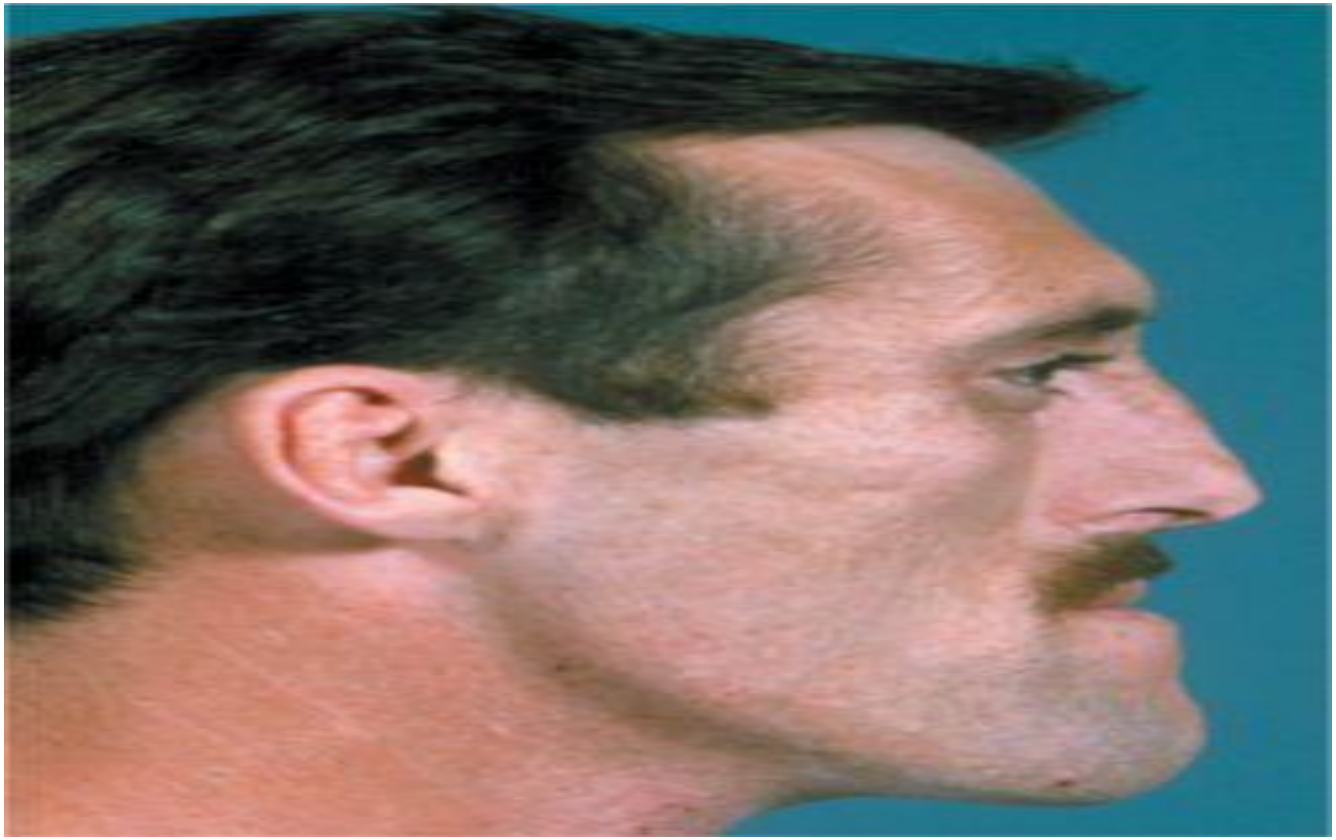
There are two main causes of osteomalacia:

(1) insufficient calcium absorption from the intestine because of lack of dietary calcium or a deficiency of or resistance to the action of vitamin D;
(2) and phosphate deficiency caused by increased renal losses.

Acromegaly

Acromegaly is a bone condition caused by excess of growth hormone production by the body.

Overgrown bones in the face, hands and feet characterize this disease. The most common cause of acromegaly is a benign tumour on the pituitary gland in the brain.



Fibrous Dysplasia

is an abnormal bone growth where normal bone is replaced with fibrous bone tissue. Fibrous dysplasia causes abnormal growth or swelling of bone.

Fibrous dysplasia can occur in any part of the skeleton but the bones of the skull, thigh, shin, ribs, upper arm and pelvis are most commonly affected.

The condition begins before birth. It is caused by a gene mutation that affects the cells that produce bone.

Causes

The cause of the gene mutation is not known. It is not inherited or passed on to the children of affected patients.

No dietary or environmental cause is known. It occurs equally among males and females of all races.

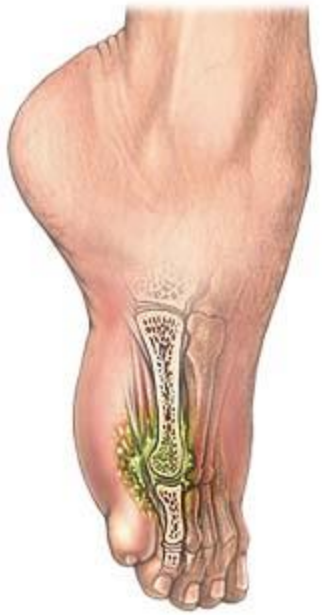
Osteomyelitis

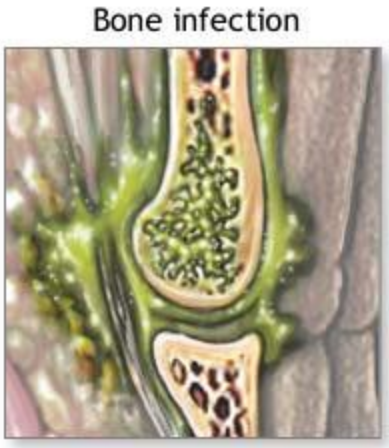
Osteomyelitis is a bacterial infection of bone, which can either be sudden and acute or chronic. Treatment may include antibiotics and in some cases, surgery to remove the infected bone tissue.

Causes

Bone infection is most often caused by bacteria, but it can also be caused by fungi or other germs.

Bacteria may spread to a bone from infected skin, muscles, or tendons next to the bone.





The infection can also start in another part of the body and spread to the bone through the blood.

A bone infection can also start after bone surgery.

Symptoms

Bone pain, Fever, ill-feeling , Local swelling, and redness.

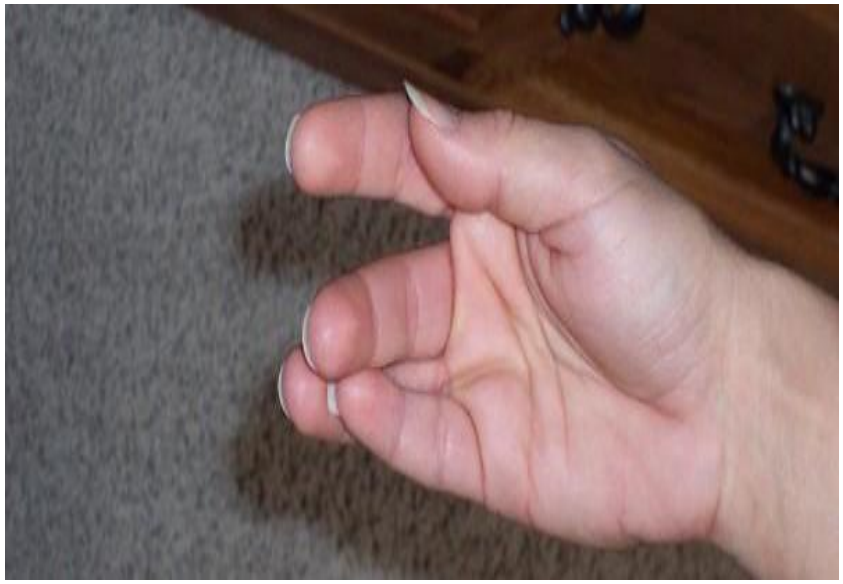
Hypocalcaemia

is the presence of low serum calcium levels in the blood

In the blood, about half of all calcium is bound to proteins such as serum albumin, but it is the unbound, or ionized, calcium that the body regulates

Causes

It manifests as a symptom of a parathyroid hormone [PTH] deficiency/malfunction,
a Vitamin D deficiency.



Symptoms

Numbness in hands, feet, around mouth and lips.

Hypophosphatasia

Hypophosphatasia is an inherited disorder that affects the development of bones and teeth. This condition disrupts a process called mineralization, in which minerals such as calcium and phosphorus are deposited in developing bones and teeth.

Causes

Mutations in the *ALPL* gene cause hypophosphatasia.

The *ALPL* gene provides instructions for making an enzyme called alkaline phosphatase. This enzyme plays an essential role in mineralization of the skeleton and teeth.

Signs and symptoms

Hypophosphatasia weakens and softens the bones, causing skeletal abnormalities similar to another childhood bone disorder called rickets.