

Chapter 11

Metabolic Diseases

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1) Vitamin D deficiency:

Vitamin D deficiency occurs when systemic levels of calcidiol (25-hydroxyvitamin D) fall below the physiological threshold required for optimal calcium and phosphorus homeostasis, directly impairing bone mineralization and neuromuscular function.

• Diagnostic Benchmarks

Serum concentration of 25-hydroxyvitamin D [25(OH)D] is the standard diagnostic marker:

Deficient: < 20 ng/mL (< 50 nmol/L)

Insufficient: 21– 29 ng/mL (52.5–72.5 nmol/L)

Sufficient: 30 –50 ng/mL (75–125 nmol/L)

Toxicity risk: > 100 ng/mL (> 250 nmol/L)

• Primary Causes

Limited UVB Exposure: Modern indoor lifestyles, sunscreen usage, geographical latitude, and atmospheric pollution prevent the photochemical conversion of 7-dehydrocholesterol to pre-vitamin D₃ in the skin.

Reduced Skin Synthesis: Higher melanin concentration acts as a natural sun filter; aging skin also produces significantly less provitamin D.

Malabsorption Syndromes: Celiac disease, Crohn's disease, ulcerative colitis, and bariatric surgery impair the absorption of fat-soluble vitamins in the small intestine.

Organ Dysfunction: Chronic liver disease impairs 25-hydroxylation, while end-stage renal disease inhibits

1-alpha-hydroxylase, the enzyme responsible for creating active calcitriol ($1,25(\text{OH})_2\text{D}$).

• Symptoms and Complications

Early and Mild Cases: Frequently asymptomatic, though patients may present with nonspecific fatigue, symmetric low back pain, proximal muscle weakness, and frequent upper respiratory infections.

Pediatric Complications (Rickets): Defective growth-plate mineralization causing bowed legs, knock-knees (genu valgum), widened wrists, delayed fontanelle closure, and frontal bossing.

Adult Complications (Osteomalacia & Osteoporosis): Incomplete mineralization of bone matrix leads to dull, throbbing bone pain and severe fragility fractures. Secondary hyperparathyroidism often develops to scavenge calcium from the skeleton, accelerating bone loss.

• Treatment and Correction

Reversing a documented deficiency typically requires short-term therapeutic repletion:

High-Dose Loading: A standard clinical regimen is 50,000 IU of Vitamin D3 (Cholecalciferol) orally once per week for 6 to 8 weeks, preferred over Vitamin D2 due to superior bioavailability.

Daily Maintenance: Following normal serum recovery, ongoing supplementation of 1,000 to 2,000 IU daily maintains adequate levels.

Co-factors: Co-administration of calcium (1,000–1,200 mg daily from diet or supplements) and adequate magnesium intake is necessary for proper hormonal activation and bone remineralization.

2) OSTEOPOROSIS:

This is characterized by a combination of an abnormally low bone mass and defects in bone structure. These factors produce usually a fragile bone which has greater than

normal risk of fracture in a person of that age, sex and race. Bone depletion can be caused by either of two factors like increased bone resorption, decreased bone formation or combination of these. This reduction of bone mass causes loss of bone strength. Loss of structural connectivity between bone plates alters mechanical properties of bone leading to loss of strength out of proportion to diminution in bone mass. As a consequences of these, stress or strain fractures may be seen around the diaphyseo- metaphyseal junctions in tubular bones and in cancellous vertebral bodies. African population is consideredably less prone to these effects.

Osteoporosis can be generalized, regional, postmenopausal, involuntional, or may be secondary due to hypercortisonism, gonadal hormone insufficiency, hyperthyroidism, alcohol abuse and immobilization.

3) RICKETS:

This metabolic disease has inadequate mineralization of bone with defective calcification, producing softened bones. This may be due to defective metabolic pathway of Vitamin D. The causes may be nutritional deficiency, less sunlight exposure, intestinal malabsorption, decreased 25 hydroxylation (liver diseases and anticonvulsants) and reduced 1-alpha hydroxylation (renal diseases and enzyme deficiency). There will be defective calcification in deeper layer of physis. In proliferative zone, cells pile up irregularly instead of arranging in orderly column. This produces physeal plate thickness, poor mineralization of bone and less bone formation in zone of calcification.

The affected child is listless, failure to thrive, and flaccid. Bone changes may be in form of deformity of skull (craniotabies), thickening of knee, ankle and wrist(physeal thickness), ricketic rosary (costochondral junction enlargements) and layeral indentation of chest. (Harrison's sulcus). A child may have bowing of distal tibia and lower limb deformities.

On X-rays, a child may have thickening and widening of growth plate, cupping of metaphysis and bowing of the diaphysis.

There will be diminished levels of serum calcium and phosphate and increased levels of alkaline phosphates.

Treatment consists of treat the underlying cause. Dietary intake of Vitamin D has to be increased along with sun exposure. Treatment with Vitamin D in dose of 400-1000IU per day and calcium supplementation is effective. The use of sun blocking lotions should be discontinued.

4) OSTEMALCIA:

This is of insidious onset and patients usually complain of bone pain, back ache and muscle weakness.

It is due to dietary deficiency of Vitamin D and insufficient sun exposure in adults. It manifests as inadequate mineralization of bone producing an osteoid which is incompletely calcified leading to softened bones. The changes are AWAY from physis. There are islands of bone lined by wide defective osteoid producing unmineralized ghost trabeculae. These are not strong enough for effectively weight bearing. The bone cortices are thin than normal and new bone formation or stress fractures.

On X-rays, there may be

- # Looser zone - transverse band of rarefaction usually in long bones due to incomplete stress fractures healing with callous lacking calcium.

- # biconcave vertebrae due disc pressure

- # trefoil pelvis – lateral indentation of acetabula or

- # spontaneous fractures of ribs, pubic rami Or femoral neck

Serum calcium and phosphate levels will be decreased and increased alkaline phosphate. The calcium phosphate product is diminished in rickets and osteomalacia (< 2.4 are diagnostic).

Treatment: Dietary intake of Vitamin D has to be encouraged in adults which was common in vegetarians. Sun exposure should be sufficient and sun blocking lotions should be avoided. Vitamin D 400-1000IU per day should be taken along

with dietary recommendations. The long bone deformities should be corrected surgically.

Osteomalacia	Osteoporosis
Unwell	Well
Chronic ache	Pain after fracture
Muscles weak	Normal
Loosers zone	Not present
Alk phosphate increased	Normal
Serum phosphate decreased	Normal
$\text{Ca} \times \text{P} < 2.4 \text{ mmol/L}$	$\text{Ca} \times \text{P} > 2.4 \text{ mmol/L}$

5) RENAL OSTEODYSTROPHY:

This is a manifestation of chronic renal failure and decreased glomerular filtration. Bone changes develop due to decreased mineralization and bone formation. Patients developed a picture of secondary hyperparathyroidism.

Patients may have stunted and pasty face with marked rachitic deformities and myopathy. There will be widened and irregular epiphyseal plates. Long standing cases may have displacement of epiphysis called epiphysiolysis. Spine may have rugger Jersey appearance (alternative bands of increased and decreased bone density.)

On serology, there will be low calcium, high phosphate and elevated Alkaline phosphate. PTH levels may be increased.

Treatment consists of treating the hyperphosphataemia and secondary hyperparathyroidism by restricting intake of phosphorous and administering Vitamin D. Recently, a calcimimetic drug (Cinacalcet) has been introduced.

6) PAGETS DISEASE (OSTEITIS DEFORMANS):

Patients are usually asymptomatic and diagnosed incidentally. The pain may be dull ache, worse in bed when the patient wake up.

Pagets disease is characterized by increased bone over but internal architecture is abnormal. There is enlargement and thickening of bone. It usually seen after 50 years with prevalence of 3% in people's over the age of 40years. It is rare in Asia and Africa. The disease may be localized or whole of one bone is involved. Tibia and pelvis are commonly affected, but may be seen in femur, skull and spine.

It starts at one end of bone and progress towards diaphysis with marked increase in osteoclastic and osteoblastic activity. Serum alkaline phosphate and urinary excretion of hydroxyproline is increased when bone turn over is accelerated. In osteolytic phase, there this s resorption of bone by osteoclasts producing large excavations filled with vascular tissue. Adjoining area shows osteoblastic activities. This alternative activity produces thickened, but weekend bone. Gradually eroded areas fill with new lammelar bone producing irregularly pattern. Long standing cases Long bone deformities along mechanical stress are present. Tibia bows anteriorly while femur bows anteriolaterally. The limbs look bent and feel thick and skin is warm termed as osteitis deformans. Patient may have short neck due to flattening of skull (Platybasia). Patients looks shorter and ape like with bent bones and arms hanging in front of him.

On Xrays, there may a flame shaped lesion extending along shaft of bone or a circumscribed area of osteoporosis in skull. Occasionally, patients presents with pathological fracture.

Serum calcium and phosphate are usually normal, but serum alkaline phosphate is raised. Urinary N telopeptide is a sensitive marker of bone resorption.

Mostly patients don't have any symptoms and require no treatment. The indications for specific treatment are:-

- Persistent bone pain
- Repeated fractures
- Neurological complications

Drugs that suppress bone turnover, mainly calcitonin and bisphosphonates are effective when disease is active and bone turn over is high.