Calcium and vitamin D metabolism

Learning Objectives

At the end of lecture the student should able to:

- Recall scheme of vitamin D and Calcium metabolism
- Define Rickets
- Classify different types of Rickets and evaluate and manage a child with Rickets
- Recognize the clinical features of hypervitaminosis D

Rickets

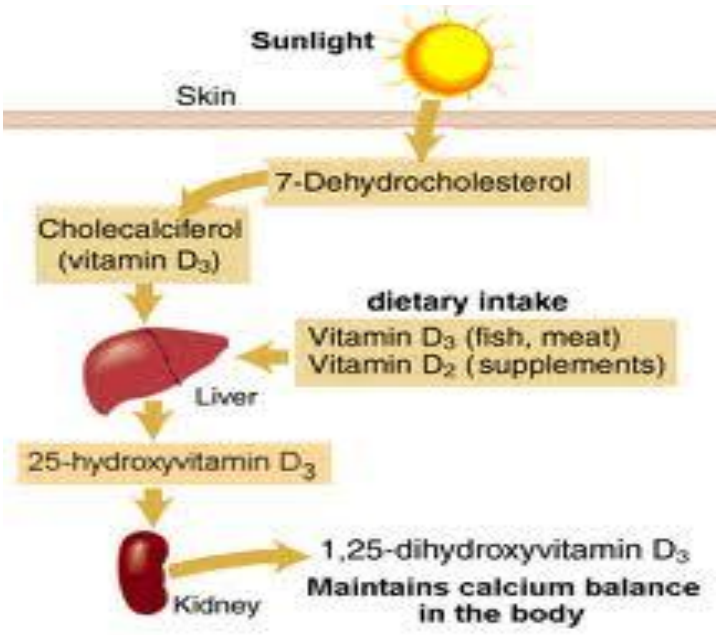
Bone consists of a protein matrix called *osteoid* and a mineral phase, principally composed of calcium and phosphate. Osteomalacia is present when there is inadequate mineralization of bone osteoid and occurs in children and adults.
Rickets is a disease of growing bone that is caused by unmineralized matrix at the growth plates and occurs in children only before fusion of the epiphyses.
Rickets is principally caused by vitamin D deficiency and may be secondary to nutritional vitamin D deficiency and inadequate intake of calcium.

Biochemical action of vitamin D

GI absorption of calcium; also increases absorption of phosphate, Direct actions on bone including mediating resorption .

Sources of vitamin D

- Exposure to sunlight(UV light)
- fish oils, fatty fish,
- egg yolks,
- and vitamin D– fortified formula, milk, cereals, bread



Causes of Rickets

VITAMIN D DISORDERS
Nutritional vitamin D deficiency
Congenital vitamin D deficiency
Secondary vitamin D deficiency
Malabsorption
Increased degradation
Decreased liver 25-hydroxylase
Vitamin D–dependent rickets type 1 A and B
Vitamin D–dependent rickets type 2 A and B
Chronic kidney disease
CALCIUM DEFICIENCY
Low intake
Diet
Premature infants (rickets of prematurity)
Malabsorption
Primary disease
Dietary inhibitors of calcium absorption
PHOSPHORUS DEFICIENCY
Inadequate intake
Premature infants (rickets of prematurity)
Aluminum-containing antacids
RENAL LOSSES
X-linked hypophosphatemic rickets*
Autosomal dominant hypophosphatemic rickets*
Autosomal recessive hypophosphatemic rickets (1 and 2)*
Hereditary hypophosphatemic rickets with hypercalciuria
Overproduction of fibroblast growth factor-23
Tumor-induced rickets*
McCune-Albright syndrome*
Epidermal nevus syndrome*
Neurofibromatosis*
Fanconi syndrome
Dent disease
Distal renal tubular acidosis

- Vitamin D disorders
- Calcium deficiency
- Phosphorus deficiency
- Renal losses and Distal renal tubular acidosis

Clinical Features of Rickets

GENERAL

- Failure to thrive
- Listlessness
- Protruding abdomen
- Muscle weakness (especially proximal)
- Fractures

HEAD

- Craniotabes : is a softening of the cranial bones and can be detected by applying pressure at the occiput or over the parietal bones. The sensation is similar to the feel of pressing into a ping-pong ball and then releasing.
- Frontal bossing
- Delayed fontanelle closure
- Delayed dentition; caries
- Craniosynostosis

CHEST

- Rachitic rosary
- Harrison groove occurs from pulling of the softened ribs by the diaphragm during inspiration
- Respiratory infections and atelectasis : Softening of the ribs also impairs air movement and predisposes patients to atelectasis and pneumonia

BACK

- Scoliosis
- Kyphosis
- Lordosis

EXTREMITIES

- Enlargement of wrists and ankles
- Valgus or varus deformities
- Anterior bowing of the tibia and femur

- Leg pain

HYPOCALCEMIC SYMPTOMS

- Tetany
- Seizures
- Stridor due to laryngeal spasm

Diagnosis of Rickets

Most cases of rickets are diagnosed based on the presence of classic radiographic abnormalities. The diagnosis is supported by physical examination findings and a history and laboratory test results that are consistent with a specific etiology. **The initial evaluation should focus on :**

- Dietary history, emphasizing intake of vitamin D and calcium.
- Cutaneous synthesis mediated by sunlight exposure. It is important to ask about time spent outside, sunscreen use, and clothing
- Maternal risk factors for nutritional vitamin D deficiency, including diet and sun exposure especially if the infant is breast-fed
- Medicationas : phenoba rbital and phenytoin, increase degradation of vitamin D, and aluminum-containing antacids interfere with the absorption of phosphate.
- Malabsorption of vitamin D is suggested by a history of liver or intestinal disease
- A history of **renal disease** as a cause of rickets. Polyuria can occur in children with chronic kidney disease or Fanconi syndrome.

Initial laboratory tests

- Serum calcium : low or normal
- Phosphorus : low
- Alkaline phosphatase : elevated
- Parathyroid hormone (PTH) : elevated
- 25-hydroxyvitamin D : low
- Urine Ca : low
- Urine phosphorus : elevated

Note: The above findings seen in nutritional vitamin D deficiency which is the commonest type

Radiological findings

- Thickening of the growth plate.
- The edge of the metaphysis loses its sharp border, which is described as fraying
- The edge of the metaphysis changes from a convex or flat surface to a more concave Surface which is termed cupping
- Widening of the distal end of the metaphysis
- Coarse trabeculation of the diaphysis and generalized rarefaction

Treatment of Rickets

There are 2 strategies for administration of vitamin D :

- With stoss therapy, 300,000–600,000 IU of vitamin D are administered orally or intramuscularly as 2–4 doses over 1 day.
- The alternative is daily, high-dose vitamin D, with doses ranging from 2,000–5,000 IU/day over 4–6 wk.
- Either strategy should be followed by daily vitamin D intake of 400 IU/day, typically given as a multivitamin.

Prognosis

Most children have an excellent response to treatment, with radiologic healing occurring within a few months.
Laboratory test results should also normalize rapidly

Prevention

Most cases of nutritional rickets can be prevented by universal administration of 400 IU of vitamin D to infants who are breastfed. Older children should receive 600 IU/day. Vitamin D may be administered as a component of a multivitamin or as a vitamin D supplement

HYPERVITAMINOSIS D

Hypervitaminosis D is secondary to excessive intake of vitamin D

Clinical Manifestations

- Nausea, vomiting, poor feeding, abdominal pain constipation,
- Hypertension, arrhythmias.
- Polyuria, dehydration and acute renal failure

Laboratory finding

- Hypercalcemia
- Elevated levels of 25-D (>150 ng/mL)
- Hyperphosphatemia
- 1,25-D are usually normal

Treatment

- Normal saline, with or without a loop diuretic
- Prednisone is 1–2 mg/kg/24 hr
- Calcitonin
- Bisphosphonates
- Hemodialysis