



# POSNA

## The Core Curriculum

### **Rickets/osteomalacia**

#### **Objectives**

1. Outline the pathway of Vitamin D metabolism
2. Define: osteomalacia, rickets
3. Describe the clinical features of rickets
4. Describe the radiographic findings noted in patients with rickets, and their relationship with histologic findings
5. List causes of rickets in children
6. List 2 causes of Vitamin D resistant rickets
7. Discuss treatment regimens for nutritional rickets, and two forms of Vitamin D resistant rickets

#### **Discussion points**

1. What are Looser lines?
2. What would be the expected serum calcium and phosphorus levels in nutritional rickets? In phosphate diabetes? In end-organ insensitivity?
3. Why are children taking anticonvulsants predisposed to rickets?

#### **Discussion**

Rickets is probably the prototype of metabolic disease in children. The term, rickets, implies a decrease in calcium, phosphorus, or both, which is of such magnitude that it interferes with epiphyseal growth and mineralization. Osteomalacia is the adult counterpart of rickets, without the growth plate manifestations

A knowledge of vitamin D metabolism is necessary to understand the pathophysiology of rickets. Ultraviolet light acting on the skin transforms 7 dehydrocholesterol into vitamin D<sub>3</sub> (cholecalciferol). Vitamin D can also be ingested as a dietary supplement, vitamin D<sub>2</sub>. Both are hydroxylated in the liver to 25 hydroxyvitamin D<sub>3</sub>; serum levels of vitamin D<sub>3</sub> are the best indicators of total body stores of vitamin D<sub>3</sub>. With elevated PTH, or decreased serum levels of calcium or phosphorus, 25 hydroxyvitamin D<sub>3</sub> is hydroxylated again in the proximal tubules of the kidney to the active hormone metabolite 1,25 dihydroxyvitamin D<sub>3</sub>. In the presence of decreased PTH, or elevated serum levels of calcium or phosphorus, 25 hydroxyvitamin D<sub>3</sub> is converted to the metabolically inactive 24,25 dihydroxyvitamin D<sub>3</sub>. PTH acts with 1,25 dihydroxyvitamin D to facilitate transport of calcium from the diet across the gut wall. In the presence of hypocalcemia, PTH also acts independently of vitamin D to promote osteoclastic activity. PTH also

reduces the tubular reabsorption of phosphate (phosphate diabetes). Therefore, there are 3 organs involved with calcium metabolism - the gut, bone, and renal tubule - which are under control of two hormones - 1,25 dihydroxyvitamin D<sub>3</sub> and PTH. Causes of rickets are nutritional (unusual now in North America), which can be aggravated by chelators in the diet, and gastrointestinal causes, usually small bowel and/or hepatic in children. The chain of events is thus decreased vitamin D > decreased intestinal absorption of calcium > hypocalcemia > secondary hyperparathyroidism > decreased tubular reabsorption of phosphorus > hypophosphatemia > and a recurrent cycle begins.

The basic defect in bone and bone growth is a failure of mineralization. The so-called diagnostic feature histologically is the osteoid seam, a layer of unmineralized bone surrounding mineralized bone. The reserve and proliferative zones of the growth plate are relatively normal, but the hypertrophic zone is enormous, with unorganized cells piled on each other, and no recognizable seams of calcified matrix. Thus, tongues of cartilage can extend far into the metaphysis. The ring of LaCroix is deficient, and widening of the metaphysis is noted. Radiographic changes reflect these findings. The growth plate is widened with a fuzzy metaphyseal border secondary to the persistence of cartilage cells in this region and the lack of a zone of provisional calcification. The cortices and trabeculae are thin and fuzzy. Looser lines contain extensive collections of osteoid; these appear radiographically as transverse lucent lines, and are pathognomonic of osteomalacia. The serum calcium is generally low, but may be normal if secondary parathyroidism has captured enough calcium from bone to restore normal levels. The phosphorus is low.

Treatment is simple for nutritional rickets; for gastrointestinal rickets, elimination of the underlying cause is, of course, preferred, but supplemental vitamin D may sometimes be of value.

Rickets resistant to Vitamin D has long been recognized, now there are 4 general etiologies for this problem; phosphate diabetes, decrease in 1,25 dihydroxyvitamin D production, end organ insensitivity, and renal tubular acidosis. Children with phosphate diabetes absorb calcium, synthesis active vitamin 1,25 dihydroxy vitamin D, have no secondary hyperparathyroidism, but lack enough phosphate for normal bone production. Another type of vitamin D resistant rickets is secondary to an inability to synthesize active 1,25 dihydroxy vitamin D. Their blood chemistries will be similar to vitamin D dietary rickets except for a low serum 1,25 dihydroxyvitamin D. Patients with endorgan insensitivity appear to have a problem with the gut responding to 1,25 dihydroxyvitamin D. Their blood chemistries will show the effects of secondary hyperparathyroidism, and will have low serum calcium and phosphorus, elevated alkaline phosphatase and PTH. This group is obviously difficult to treat effectively. Patients may develop renal tubular acidosis from a variety of causes, with impaired resorption of phosphate in addition to other metabolic abnormalities. Children taking anticonvulsants may develop a form of rickets. There is apparently some injury to the hepatic cells which decreases synthesis of 25-hydroxyvitamin D; thus the precursor of the active form, 1,25 dihydroxyvitamin D is not available. Laboratory values will be similar to those accompanying nutritional rickets.

## References

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