Bone Growth and Development

When crystals of hydroxyapatite (a complex of calcium, hydroxyl and phosphate ions) are laid down between collagen fibers, bone calcification occurs. These ions in bone are in dynamic equilibrium with ions present in the bloodstream, an equilibrium which is regulated by *Vitamin* D and by two peptide hormones, Parathyroid hormone (PTH) and calcitonin. As late as the 1930's and 1940's, when the role of dietary *Vitamin D* in normal bone growth and development was not recognized, rickets was an all too common feature of community life, particularly in areas with the sun exposure.

The role of *Vitamin* D is largely played at the site of the mucosal cells of the intestine, where it stimulates calcium absorption and retrieval to the blood stream from food passing through the gut, as well as in the proximal tubgles of the kidney, where it promotes re-absorption of phosphate which would otherwise be excreted in urine.

The constant turnover (dynamic equilibrium) of the ions of bone crystal between those in the bloodstream and those stored in bone itself, is a important feature both in formation and in repair of bone. Three types of cells work together in this process: osteoblasts, osteocytes, osteoclasts. The osteoblasts synthesis the matrix upon which bone crystals are laid down; the osteocytes interlink this matrix with long filaments; the osteoclasts, which sit on the surface of bone crystals, are important in maintaining calcium and phosphate ion equilibrium with the blood stream. How these cells actually interact in the calcification of bone is an area of intense research and many theories abound. It is known that PTH acts directly on osteoblasts, facilitating their interaction via other chemical activators with osteoclasts.

In particular, the role of bone-specific alkaline phosphatase, which releases free phosphate for combination with calcium in hydroxyapatite crystals, is still unclear. What is clear, however, is that individuals who present with *Vitamin D – resistant rickets* have abnormally high levels of alkaline phosphatase in their bloodstream, but little phosphate, presumable because their natural 'active' *Vitamin D* as well as calcium in these individuals usually indicate normal or only sightly lower than normal concentrations. Research into these questions, as reported for example, at the 2nd European Kidney Research Forum, continues apace.

It should be clear that the typical therapy for individuals suffering from Familiar Hypophoshatemia is a combination of the active form of *Vitamin D* (called dihydrocalciferol, ergocalciferol or just calciferol, this drug also goes under the proprietary name of Rocatrol) and supplements of phosphate and/or calcium. Under this

sort of therapy, measured phosphate and alkaline phosphatase levels in the bloodstream return to normal levels; there is now enough free phosphate (either as supplied as free ions, or as correctly re-absorbed in the kidneys) to inhibit further production of the bone-specific alkaline phosphatase). Furthermore, calcium is absorbed and retrieved correctly by the intestinal cells under the influence of good, active *Vitamin D* (or is also supplied as free ions). Bone growth then proceeds, with the appropriate laying down of bone crystal as can be seen by a chronological series of X-rays.

The dramatic role of the dynamic equilibrium of progressive bone growth under theraph is illustrated in real cases of *Vitamin D* – resistant rickets, where the bowed legs of growing children can be observed to straighten, over the course of several years, against the influence of gravity.