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- 13 INBORN ERRORS OF VITAMIN D METABOLISM. By H.K.A. Visser, H.J. Degenhart and T. Hoogenboezem. Department of Pediatrics, Erasmus University and University Hospital/Sophia Children's Hospital, Rotterdam, The Netherlands.

It is now accepted that the biologically active form of vitamin D is 1,25-dihydroxycholecalciferol ( $1,25\text{ (OH)}_2\text{D}_3$ ). There is good evidence for the theory that  $1,25\text{ (OH)}_2\text{D}_3$  is a "steroid hormone": its production is regulated by an endocrine feed-back system, its action in the target tissue (intestinal mucosa) is in analogy with that of classic steroid hormones. Theoretically hereditary disorders in hydroxylation of cholecalciferol and end-organ responsiveness for  $1,25\text{ (OH)}_2\text{D}_3$  could be possible and indeed have been reported. We have studied three of four children in a family from the Cape Verde Islands, who showed clinical, chemical and radiological signs of severe rickets. Serum concentrations of  $25\text{ OH D}_3$  were normal and increased after treatment with vit.  $\text{D}_3$  (2000 IU/d) and dihydrotachysterol (up to 3,2 mg/d, equivalent to 320.000 IU vit.  $\text{D}_3$ /d). Serum concentrations of  $1,25\text{ (OH)}_2\text{D}_3$  were very low: 0,7; 0,6; 0,3 ng/100 ml; modified radio-receptor assay of Eisman et al. (Science 193, 1021, 1976). Treatment with  $1\alpha\text{-OH vit. D}_3$  (Etalpha Leo) 1,0-1,5  $\mu\text{g/d}$  gave rapid improvement in all signs of rickets. This type of rickets has been described in the literature as vit. D dependent rickets and pseudo vit. D deficiency rickets. It is suggested that diminished renal synthesis of  $1,25\text{ (OH)}_2\text{D}_3$  in these patients is caused by an autosomal recessive defect in  $25\text{-OH D}_3\text{-}1\alpha\text{-hydroxylase}$ . In patients with endorgan-unresponsiveness for  $1,25\text{ (OH)}_2\text{D}_3$  both serum concentrations of  $25\text{OH D}_3$  and  $1,25\text{ (OH)}_2\text{D}_3$  are elevated. The defect may be a deficiency of (or a defect in)  $1,25\text{ (OH)}_2\text{D}_3$  receptors in the cytosol, in the nuclear factors or in some post-translational factor. Some of these patients have alopecia.

- 14 PROLACTIN: A CALCIUM REGULATING HORMONE IN FRESHWATER FISH. By S.E. Wendelaar Bonga, Z. Kolar, and G. Flik. Department of Animal Physiology, Faculty of Science, University of Nijmegen, and Department of Radiochemistry, Inter-University Reactor Institute, Delft, The Netherlands.

In fish and some aquatic amphibians true parathyroid glands are lacking and hypercalcemic control is likely exerted by the pituitary gland. Two hormonal cell types have been implicated: the prolactin cells and the PAS-positive cells of the pars intermedia. In the tilapia *Sarotherodon mossambicus* the prolactin cells, but not the PAS-positive cells, responded to changes in the calcium concentration of the ambient water. Prolactin cell activity, as estimated by ultrastructural morphometry and  $^3\text{H}$ -lysine incorporation rate, was inversely related to the external calcium concentration. Administration of ovine or tilapia prolactin induced a significant hypercalcemia. In whole-body calcium uptake studies with  $^{47}\text{Ca}$ , prolactin treated fish (0.15 IU/g/day) showed a significantly enhanced rate of uptake of calcium from the water. The  $^{47}\text{Ca}$ -content of blood and bones was also elevated. Clearance of  $^{47}\text{Ca}$  from the body was not noticeably affected by prolactin.

Ultrastructural examination of bone-forming tissues did not show any changes in osteoblastic or osteocytic activity. Multinuclear osteoclasts were not observed. However, the mineral density of the bone increased considerably in the hormone-treated fish. After 9 days, the increase of the calcium concentration of the bones varied from 14 to 26%, and appeared to be log-dose related.

It is concluded that in freshwater fish blood calcium is controlled at the level of the gills, by stimulating the calcium uptake from the water. In terrestrial vertebrates, hypercalcemic control involves mobilization of calcium from bone by osteocytic osteolysis and osteoclastic activity. These processes are controlled by parathyroid hormone. This type of hypercalcemic regulation may have developed in ancestral tetrapods during the water to land transition, as an adaptation to a terrestrial way of live.