It is now accepted that the biologically active form of vitamin D is 1,25-
dihydroxycholecalciferol (1,25 (OH)2D3). There is good evidence for the
theory that 1,25 (OH)2 D3 is a "steroid hormone": its production is regula-
ted by an endocrine feed-back system, its action in the target tissue (in-
testinal mucosa) is in analogy with that of classic steroid hormones.
Theoretically hereditary disorders in hydroxylation of cholecalciferol and
end-organ responsiveness for 1,25 (OH)2 D3 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 OH D3 were normal and
increased after treatment with vit. D3 (2000 lU/d) and dihydrotachysterol
(up to 3.2 mg/d, equivalent to 320,000 IU vit. D3/d). Serum concentrations
of 1,25 (OH)2 D3 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
1α-OH vit. D3 (Etalpha Leo) 1.0-1.5 μg/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 sugges-
ted that diminished renal synthesis of 1,25 (OH)2 D3 in these patients is
cauased by an autosomal recessive defect in 25-OH D3-la-hydroxylase.
In patients with endorgan-unresponsiveness for 1,25 (OH)2 D3 both serum
concentrations of 25OH D3 and 1,25 (OH)2 D3 are elevated. The defect may
be a deficiency of (or a defect in) 1,25 (OH)2 D3 receptors in the cytosol,
in the nuclear factors or in some post-translational factor. Some of these
patients have alopecia.

In fish and some aquatic amphibians true parathyroid glands are lacking and hypercalcemnic
control is likely exerted by the pituitary gland. Two hormonal cell types have been impli-
cated: 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 es-
timated by ultrastructural morphometry and 1H-lysine incorporation rate, was inversely re-
lated to the external calcium concentration. Administration of ovine or tilapia prolactin
induced a significant hypercalcemia. In whole-body calcium uptake studies with 47Ca, pro-
lactin treated fish (0.15 lU/g/day) showed a significantly enhanced rate of uptake of cal-
cium from the water. The 47Ca-content of blood and bones was also elevated. Clearance of
47Ca from the body was not noticeably affected by prolactin.
Ultrastructural examination of bone-forming tissues did not show any changes in osteo-
blastic 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 20%, 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.