

## **Treatment of Renal Bone Disease with 1alpha-Hydroxylated Derivatives of Vitamin D<sub>3</sub>.**

Kanis JA, Cundy T, Earnshaw M, Henderson RG, Heynen G, Naik R, Russell RGG, Smith R, and Woods CG. *Quarterly J of Med, New Series XLVIII, 1979; No. 190, p. 289-322.*

### Summary.

Forty patients with severe bone disease and chronic renal failure were treated with 1alpha-hydroxycholecalciferol (1alpha-OHD<sub>3</sub>) or 1,25-dihydroxycholecalciferol (1,25(OH)<sub>2</sub>D<sub>3</sub>) for 7-49 months (total = 738 patient months). There were symptomatic, biochemical and radiographic improvements in the majority of patients (>70 percent). Paired bone biopsies, taken before and during treatment in 26 patients, showed no change in bone matrix area, whereas matrix area decreased in a control group of 26 patients over the same period. There were small but consistent decreases in bone marrow fibrosis and in bone cell (osteoblast and osteoclast) counts in treated patients but not in controls. However, the proportion of patients who showed histological 'cure', in the sense of complete reversal of marrow fibrosis or excess osteoid was no greater in the treated than in the control group. In terms of the overall response, there were significant correlations between the improvement noted in symptoms, radiographs and plasma biochemistry, and these in turn were related to the smaller improvement in bone histology.

The major detectable factors before treatment which adversely influence its outcome were a high plasma level of calcium associated with high levels of parathyroid hormone, and the presence of marked osteomalacia without osteitis fibrosa. Other factors examined, which included the dose of agent used, initial plasma levels of phosphate and alkaline phosphatase, and dietary supplements of calcium, did not greatly influence the response. During the course of treatment, the dose of 1alpha-OHD<sub>3</sub> or 1,25(OH)<sub>2</sub>D<sub>3</sub> tolerated progressively decreased. In patients with poor histological response, hypercalcaemia occurred commonly at the start of treatment, whereas it occurred later in good responders when biochemical improvement was nearly complete. Hypercalcaemia could be rapidly corrected by stopping treatment. The rapid onset and reversal of action of 1alpha-OHD<sub>3</sub> and 1,25(OH)<sub>2</sub>D<sub>3</sub> confer therapeutic advantages over vitamin D. However, because these drugs do not invariably reverse bone disease and may give rise to unwanted effects, they should not be used indiscriminately in all renal patients. Their use demands adequate clinical, biochemical and radiographic supervision.

