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Idiopathic Hypercalciuria

Frederic L. Coe, MD* and Murray J. Favus, MD*

Idiopathic normocalcemic hypercalciuria is certainly the commonest metabolic disorder observed in patients with calcium stones, and there is much evidence that hypercalciuria directly causes stones. The evidence relates high urine calcium levels to increased urine calcium oxalate supersaturation. High supersaturation to genesis of calcium stones, which is widely accepted, is reviewed in the following three papers.

A general consensus, drawn from many sources, indicates that reduction of urine calcium levels leads to a concomitant and impressive reduction of new stone production. At the moment, the principal uncertainties concern the mechanism by which urine calcium excretion is elevated and, in a related sense, the biochemical and clinical effects of measures taken to lower urine calcium in treatment of stone. Data that bear on the subject were presented by Lemann, et al (pp. 411 ff.). He and his colleagues have shown clearly that administration of slight excesses of 1,25(OH)2D3 to normal people causes fasting hypercalciuria and hypercalciuria on a low calcium diet. On a very low calcium diet, the urine calcium level may exceed dietary intake. These data suggest that a modest disorder of vitamin D metabolism, leading to a slight excess in the production of 1,25(OH)2D3, could easily give rise not only to hypercalciuria but to an intolerance of the low calcium diet. It could also give rise to fasting hypercalciuria, which could easily be confused with renal hypercalciuria.

Idiopathic hypercalciuria. F.L. Coe (403)
Separate pathogenetic origins for absorptive and renal hypercalciurias: Different responses to treatment. C.Y.C. Pak and J.E. Zerwekh (406)

Pak and Zerwekh (pp. 406 ff.) clearly indicated that, clinically, patients divide themselves into those with predominant overabsorption of calcium and those who have fasting hypercalciuria and appear to have a defective renal tubule calcium reabsorption. Clinical and laboratory observations clearly depict the heterogeneity of physiological response in the syndrome, and, interestingly, are compatible with the effects of 1,25(OH)2D3 administration in normals. In noting response to treatment, Pak pointed out that patients with reduced renal calcium conservation seem to do well with thiazide and those who present principally with intestinal hyperabsorption probably can be treated with sodium cellulose phosphate.

Material from our own group is consistent with the Pak data and with the Lemann experiments on 1,25D3 administration. We described (pp. 403 ff.) a continuous spectrum of behavior in hypercalciuric subjects. At one end are patients who conserve very well when challenged with a low calcium diet, and at the other end are patients who cannot conserve calcium well at all. Uniformly, hypercalciuric patients have low levels of serum PTH, and under conditions of low calcium diets the patients generally manifest a serum calcium level higher than that of normal subjects given the same diets. Despite the
higher calcium level in the blood and lower PTH, however, and equivalent levels of serum phosphorus, patients with hypercalciuria have the same levels of serum 1,25(OH)₂D₃. The best explanation for the spectrum of behavior observed in hypercalciuria in response to a low calcium diet is a subtle but persistent disorder of 1,25(OH)₂D₃ regulation.

From these three papers, and in the context of what is known about this disorder, the hypothesis emerges that a regulation disorder of 1,25(OH)₂D₃ may explain the complex and variable behavior of patients. Some can benefit from drugs that reduce calcium absorption and some benefit from thiazide. A final answer to treatment must await a definitive analysis of vitamin D metabolism, which is not yet available.