Interrelationships Between the Key Elements of the Vitamin D Endocrine System: 25-OHD₃-1-Hydroxylase, Serum Calcium and Phosphorus Levels, Intestinal 1,25(OH)₂D₃, and Intestinal Calcium Binding Protein

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Calcium and phosphorus homeostasis is exquisitely regulated by the three hormones, calcitonin, parathyroid hormone, and cholecalciferol (vitamin D₃). The most notable advance in our understanding of the mechanism of action of vitamin D has been the elucidation of the complex metabolic pathway which has evolved to produce the biologically active form, 1,25-dihydroxyvitamin D₃ [1,25(OH)₂D₃]. Coupled with these developments concerning our understanding of the metabolic pathway of conversion of vitamin D into its active form, has been the realization that the mechanism of action of the fat soluble vitamin D is in reality similar to that of many of the classical steroid hormones, e.g. aldosterone, testosterone, estrogen, hydrocortisone, and ecdysterone. It should be noted that chemically vitamin D is in reality a steroid, in particular a seco steroid. Seco steroids are those in which one of the rings has undergone fission; in the instance of calciferol, this is ring B. It has been proposed (1,2) that vitamin D may generate its characteristic physiological response (5) by its ability to activate or stimulate the biochemical expression of genetic information which ultimately leads to the synthesis of functionally specialized proteins or the alteration of membrane structure necessary for calcium absorption. In this regard, it has been unequivocally established by Wasserman and colleagues that one of the primary biological responses of vitamin D or its active forms in the intestine is the generation of a specific protein which has the capability of binding calcium in a highly specific fashion (3). This protein has been termed vitamin D dependent calcium binding protein (CaBP).

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Calciferol, which may either be ingested dietarily or produced in the skin by a photochemical reaction, is first transported to the liver, where it is hydroxylated at the 25 position. 25-Hydroxy-vitamin D₃ [25-OH-D₃] is next transported to the kidney where it further undergoes metabolism to produce either 1,25-dihydroxyvitamin D₃ [1,25(OH)₂D₃] or 24,25-dihydroxyvitamin D₃ [24,25(OH)₂D₃]. These relationships are summarized in Figure 1. The 1,25-(OH)₂D₃ then proceeds by the circulatory system to its various organs, primarily the intestine and bone where it interacts and produces its characteristic physiological response. The key focal point in this endocrine pathway for production of the biologically active form of vitamin D is the kidney. The kidney also has the potential in some species and under some physiological circumstances to produce 24,25(OH)₂D₃; the physiological role of this steroid remains to be established. The reader is referred to Norman and Henry (4) and Coburn et al. (5) for the review of

Figure 1. Metabolic or endocrine pathway for the production of the hormonally active form of vitamin D, 1,25(OH)₂D₃. The central role of the kidney as it functions as an endocrine gland, related to vitamin D metabolism, is apparent.