1. INTRODUCTION

Over the past several years, considerable progress had been made in understanding the basic mechanism of calcium absorption and the role of vitamin D in this process (cf. ref. 1 for earlier review). Physiological studies had demonstrated that vitamin D affected, directly or indirectly, at least two processes in the transfer of Ca\(^{2+}\) from intestinal lumen through the intestinal cell to the lamina propria (1,2). One process is the movement of Ca\(^{2+}\) into the intestinal mucosa and the other, the transfer out of the intestinal mucosa in the parenteral direction. This dual action of vitamin D\(_3\) is illustrated in Figure 1. In the experiment shown, the effects of vitamin D on the absorption of \(^{47}\text{Ca}\) by the intestine of rachitic chicks, and on the transient accumulation of \(^{47}\text{Ca}\) by the intestinal mucosa, were determined. The data in the upper panel (Figure 1) verified the accepted fact that vitamin D considerably increases the rate of \(^{47}\text{Ca}\) absorption, in this case by rachitic chicks. Further, both the uptake and release of \(^{47}\text{Ca}\) by the intestinal mucosa were greater in vitamin D\(_3\) replete chicks as compared to untreated chicks (Figure 1, lower panel). The primary role of vitamin D\(_3\), in physiological perspective, was considered to be an alteration of the calcium permeability of the brush border membrane, with other effects secondary to this event. It was also accepted that the intestinal cell can actively transport Ca\(^{2+}\) across the intestinal epithelium (3–5) and that Ca\(^{2+}\) can also be absorbed by a non-saturable, diffusional process (6,7).

Over the past fourteen years substantial emphasis has been given to understanding the processes by which the calcium ion is absorbed in the intestine. This has occurred concurrently with related developments in the metabolism and synthesis of vitamin D metabolites and the clinical application of this knowledge.
Figure 1. Effect of vitamin D₃ on the duodenal absorption and mucosal uptake of ⁴⁷Ca by rachitic chicks. Four week old rachitic chicks were dosed per os with 500 I.U. vitamin D₃ 72 hours before experiment. The ⁴⁷Ca dose (150 mM NaCl, 1 mM CaCl₂, pH 7.2) was injected into the ligated duodenal loop of the chicks under ether anaesthesia. At various times, the loop was excised and counted for ⁴⁷Ca activity. The loop was then rinsed free of a luminal ⁴⁷Ca and the scraped mucosa counted for ⁴⁷Ca activity. Chicks per group = 6.

For ease of understanding, it is advantageous to consider the absorptive process as comprised of three distinct processes: (a) the transfer of calcium across the brush border membrane, (b) the transit of calcium through the intracellular milieu and (c) the exit of calcium from the cell. As shown in Figure 2, the thermodynamic parameters indicate that Ca⁺² can enter the cell by a diffusional process, down a thermodynamic gradient. However, the exit step necessarily requires energy since this cation must be driven uphill against a concentration gradient. As mentioned, vitamin D increases both processes, and current information bears on the molecular basis of each of these processes, as well as possible pathways of transfer of calcium through the intracellular milieu.