

RECENT CONCEPTS OF CALCIUM METABOLISM
IN HEALTH AND DISEASE

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I N T R O D U C T I O N

INTRODUCTION

Functions of calcium:

Calcium is present in the body in larger amounts than any other mineral element. It is of great importance in blood coagulation and in activation of certain enzymes. Calcium promotes excitation contraction coupling in skeletal, cardiac and smooth muscles. Calcium is also required for release of neurotransmitters from synaptic vesicles and for secretion of granular material from exocrine glands and from endocrines such as the adrenal medulla, B-cell of pancreas (insulin) and ADH from neurohypophysis. Calcium is also important for synthesis of nucleic acids and proteins (Bringham and Patts, 1979).

Requirements:

In Europe and U.S.A. the average daily calcium intake is 800-1000 mg/day. In developing countries the intake is often less (200-400 mg/day). The need for calcium is increased during the growth period of infancy and childhood and in mothers during pregnancy and lactation (Bringham, et al., 1979).

Sources:

The main sources of calcium are milk and cheese. Egg yolk, beans, lentils, nuts, figs, cabbage and green vegetables contribute smaller amounts (Bringham, et al., 1979).

PHYSIOLOGY OF CALCIUM METABOLISM

INTESTINAL ABSORPTION OF CALCIUM

This mechanism has been extensively studied experimentally in rats. Calcium absorption in the rat occurs by active transport in the upper part of the small intestine just distal to pylorus. The transport depends on a process of oxidative phosphorylation and the production of high energy phosphate bonds. Calcium also diffuses across the intestinal wall at all levels of the small intestine and even to some extent in the large intestine (Lengemann, Comar and Wasserman, 1967).

Wills (1973) found that in an adult, calcium can be absorbed from all parts of the small intestine by an active transport mechanism. The greatest calcium absorbing capacity is in the duodenum where there is an active transport mechanism controlled by vitamin D. In the jejunum and ileum, calcium absorption takes place by passive or facilitated diffusion.

The rate and extent of calcium absorption depend on many factors. The most important factor is vitamin D. Other factors also play a role such as body requirements, previous dietary calcium intake, and the availability of calcium in the gut including the effects

of bile, fatty acids, pH of the gut contents and hormonal influences (Keele, Neil and Joels, 1982).

(1) Vitamin D:

Several different compounds derived from sterols, belong to the vitamin D family, and they all perform more or less the same functions. The most important of them, called vitamin D₃ is cholecalciferol. Most of this substance is formed in the skin as a result of irradiation of 7-dehydrocholesterol by ultraviolet rays from the sun (Kodicek, 1974).

Vitamin D has a potent effect on increasing calcium absorption from the intestinal tract. It also has an important effects on both bone deposition and bone resorption. However, vitamin D itself is not the active substance that actually causes these effects. Instead, the vitamin D must first be converted through a succession of reactions in the liver and the kidney to the final active product, 1,25 dihydroxycholecalciferol (Kodicek, 1974).

The first step in the activation of cholecalciferol is to convert it to 25-hydroxycholecalciferol which occurs in the liver by the activity of 25-hydroxylase,

a microsomal enzyme in the liver. The process, however, is a limited one because the 25-hydroxycholecalciferol itself has a feedback inhibitory effect on the conversion reactions. This feedback effect is extremely important for two reasons; first, the feedback mechanism regulates very precisely the concentration of 25-hydroxycholecalciferol in the plasma. The intake of vitamin D_3 can change 10-fold, and yet the concentration of 25-hydroxycholecalciferol still remains within a few percent of its normal mean value. Obviously, this high degree of feedback control prevents excessive action of vitamin D_3 when it is present in too high concentration (Fraser, 1980). Second, this controlled conversion of vitamin D_3 to 25-hydroxycholecalciferol conserves the vitamin D_3 for future use, because once it is converted, it persists in the body for only a short time, whereas in the vitamin D form it can be stored in the liver for as long as several months (Fraser, 1980).

The compound 25-hydroxycholecalciferol is transported from the liver bound to an α -globulin of plasma. In the kidney 25-hydroxycholecalciferol is further hydroxylated by 1- α -hydroxylase in mitochondria to form 1,25-dihydroxycholecalciferol which is the active form of

vitamin D. This conversion requires parathyroid hormone. Therefore, PTH exerts a potent effect in determining the functional effects of vitamin D in the body specifically its effects on calcium absorption in the intestines and its effect on bone (Fraser, 1980).

1,25-dihydroxycholecalciferol has several effects on the intestinal epithelium in promoting intestinal absorption of calcium. Probably the most important of these effects is that it causes formation of a calcium-binding protein in the cytoplasm of the intestinal epithelial cells. The rate of calcium absorption seems to be directly proportional to the quantity of this calcium-binding protein. Furthermore, this protein remains in the cells for several weeks after the 1,25-dihydroxycholecalciferol has been removed from the body, thus causing a prolonged effect on calcium absorption (Guyton, 1982).

Other effects of 1,25-dihydroxycholecalciferol that might play a role in promoting calcium absorption are these: (1) it causes the formation of a calcium-stimulated ATPase in the brush border of the epithelial cells and (2) it causes the formation of alkaline phosphatase