11
Magnesium, Bone Wasting, and Mineralization

11.1. Mobilization of Bone Magnesium

Relatively little attention has been paid to the importance of magnesium in bone metabolism, except to the degree that it affects the activity of the parathyroid glands and C cells and their secretion of parathyroid hormone (PTH) and calcitonin (CT), and the response of target organs. However, experimental magnesium deficiency causes abnormalities in skeletal structure, enzymes, and mineralization that resemble some of those seen in several clinical bone diseases. Depending on the degree and duration of the magnesium deficiency and concomitant dietary or iatrogenic imbalances (of magnesium with calcium, phosphates, vitamin D, and other calcemic agents), the pathologic skeletal findings can range from osteopenias to osteosclerosis. The effects of vitamin D, calcium, and phosphorus on magnesium requirements and on skeletal responses have been intensively studied, particularly in the 1930s, when vitamin D toxicity was the focus of much attention. Many of the results are conflicting, probably due to the dietary variations, and to species differences in requirements (i.e., of vitamin D). Only those portions of the PTH/CT/Mg data that deal directly with magnesium and bone are considered here. Much of that relating to gestational abnormalities has already been discussed. The relatively little information found on heteroionic magnesium/calcium exchange in bone, and on the magnesium interrelationships between the phosphatases that affect mineralization, alkaline phosphatase and pyrophosphatase, are brought into focus as possibly providing some insight into the conflicting and confusing data on mechanisms of pathologic skeletal processes.

Largely disregarded in the treatment of bone disease is the possibility that some of the therapeutic agents (used to increase bone mineralization) might adversely affect bone metabolism by causing loss of skeletal magnesium. Calcium, phosphorus, and vitamin D all increase magnesium requirements; the intakes of all have been rising during this century, while that of magnesium has been falling. Since plasma levels of magnesium are maintained within very narrow limits, even in the face of insufficient intakes or excessive losses, the magnesium is mobilized
from the tissue stores. Bone constitutes the largest total source; it contains two-thirds of the total body magnesium (Review: Heaton, 1971). Much of bone magnesium is quite labile, especially in young animals. Were the bone magnesium merely an inert storage depot, this would be a benign means of providing magnesium for the function and structure of life-preserving tissues (e.g., cardiovascular and renal), as well as preventing acute neuromuscular signs of magnesium depletion. For short periods of time, and more in young than in older individuals, availability of bone magnesium probably serves as a safety device that prevents serious systemic signs of magnesium deficiency. However, long-term loss of magnesium from the bone causes disturbances of bone modeling, remodeling, and turnover, with resultant bone abnormalities. Depending upon the supply of the calcemic agents or phosphate, it can give rise to formation of brittle chalky bones or to osteopenia. The mobilized bone constituents contribute to the renal damage of magnesium deficiency.

Because the amount of magnesium bone is only $\frac{1}{40}$ to $\frac{1}{50}$ that of calcium (Duckworth et al., 1940), relatively few investigators have given it much consideration as a significant bone mineral, either in bone metabolism or as a source of emergency magnesium supply. Bone magnesium is an important source, especially in young animals (McAleese et al., 1961), an observation supported by the drop in bone magnesium immediately after convulsions of magnesium deficiency (Orent et al., 1934; Martindale and Heaton, 1964). Differences in responses to vitamin D, PTH, and CT influence the mobilization of magnesium during magnesium deficiency and have led to diverse findings. Many of the studies have dealt with the influence of magnesium deficiency and repletion, with high and low calcium, phosphorus, and vitamin D intakes, on metabolic balance. They are not considered here, unless bone values are also given, since positive balances (e.g., of calcium and phosphorus) can be achieved by metastatic calcification, as well as by increased bone mineralization and can occur even with bone demineralization. Also, failure to exhibit negative magnesium balance under conditions that cause abnormal bone structure might be related to the initial shift of bone magnesium and calcium (e.g., the increase in bone magnesium/calcium ratio in rickets).

Some of the disparate findings in the different studies might well be the result of use of widely differing diets in the magnesium deficiency studies: diets that provide 3200 to 8000 parts per million (ppm) of calcium, 1900 to 5100 ppm of phosphorus, and 1150 to 1,000,000 IU of vitamin D per kilogram of diet mix, and 3 to 100 ppm of magnesium (Larvor and Durlach, 1971a). In some of the studies analyzed and tabulated by Larvor and Durlach (1971a), only the magnesium provided was indicated. Thus, the studies cited in the following sections are not strictly comparable.

11.2. Influence of High Vitamin D and High or Low Calcium Intakes

11.2.1. High Calcium: Decreased Mobilization

Most studies of hypervitaminosis D are in rats, which are commonly fed rations rich in calcium and phosphate, as well as in vitamin D. All three of these supple-