Measuring ionized calcium directly is important if the authentic ionized serum calcium concentration is needed.

Sepsis

Gram-positive and gram-negative sepsis have been associated with hypocalcemia that usually is mild. The mechanisms are poorly understood. Hypocalcemia occurring in the setting of sepsis appears to confer a particularly adverse prognosis.

Hypermagnesemia

Magnesium is a divalent cation, as is calcium, and in very high concentrations, it may mimic the actions of calcium to suppress PTH. In so doing, it leads to a functional type of hypoparathyroidism and hypocalcemia. In practice, this condition is uncommon.

Hypomagnesemia

Hypomagnesemia is one of the most common causes of hypocalcemia. It is encountered often in patients with alcoholism, malnutrition, cisplatin therapy for cancer, and intestinal malabsorption syndromes. Hypomagnesemia inhibits PTH secretion (i.e. magnesium adenosine triphosphatase is required for PTH secretion) and prevents the calcemic actions of PTH on the kidney and skeleton. Magnesium deficiency causes a functional form of hypoparathyroidism and resistance to PTH. The treatment is straightforward: magnesium replacement, which corrects the syndrome in minutes to hours. Intravenous calcium or vitamin D is ineffective.

Rapid Bone Formation

Increased rates of bone mineralization that are out of proportion to the rate of bone resorption lead to net calcium entry into the skeleton and, if these rates are large, to hypocalcemia. This state occurs in several clinical settings. One condition is the hungry bone syndrome that may follow parathyroidectomy, usually performed for HPT. Preoperatively, the rates of bone turnover (i.e., resorption and formation) are very high but are approximately coupled. Postoperatively, the rate of osteoclastic bone resorption abruptly declines with the decline in PTH, but the elevated rate of mineralization continues for days. Because of this acute postoperative imbalance, the skeleton becomes a sink for calcium, and hypocalcemia ensues.

Rapid bone formation also may occur in patients with vitamin D deficiency who have severe osteomalacia or rickets and large amounts of unmineralized osteoid. When these patients are treated with vitamin D, rapid mineralization of unmineralized osteoid occurs, the skeleton becomes a sink for calcium, and hypocalcemia ensues. Another example of this phenomenon occurs in the setting of extensive osteoblastic bone metastases, such as in prostate or breast cancer and occasionally in other malignancies.

Hyperphosphatemia

Disorders that lead to hyperphosphatemia may cause hypocalcemia as a result of exceeding the calcium-phosphate solubility product in serum. Examples of disorders that may cause the kind of severe hyperphosphatemia required include rhabdomyolysis (e.g., crush injuries), renal failure, and the tumor lysis syndrome. Severe hyperphosphatemia may be seen after ingestion of large amounts of phosphate-containing purgatives in preparation for colonoscopy, inadvertent perforation of the rectum during the administration of phosphate enemas, and overzealous administration of intravenous phosphate. In these examples, the onset of hyperphosphatemia is relatively abrupt, and the hypocalcemia is immediate and severe. Commonly, the first sign of this sequence of events is a seizure.

Treatment involves reducing the serum phosphorus level by whatever means necessary. Giving intravenous calcium should be avoided because it is precipitated into soft tissues.

Medications

Certain medications may cause hypocalcemia, including those used to treat hypercalcemia. Fluoride compounds (e.g., anesthetic gas), chelating agents such as ethylenediaminetetraacetic acid (EDTA) and citrate (i.e., in stored blood), radiographic intravenous contrast agents, and the antiviral drug foscarnet may cause hypocalcemia.

Pancreatitis

When pancreatitis causes hypocalcemia, it is a poor prognostic sign. The classic mechanism involves the formation of calcium-free fatty acid soaps by lipases that are released from the inflamed pancreas. The free lipases then autodigest omental and retroperitoneal fat into negatively charged ions that tightly bind calcium in the ECF, causing hypocalcemia. The hypocalcemia is reversible by calcium infusion, and it self-terminates when the pancreatitis improves.

HYPERPHOSPHATEMIA

Symptoms and Signs

Hyperphosphatemia produces no specific signs. It is usually identified incidentally on routine chemical screens or as a result of the induction of hypocalcemia.

Pathophysiology

Hyperphosphatemia develops as a result of two mechanisms. One is a large load of phosphate delivered into the ECF through the GI tract, intravenous medications, or endogenous sources such as muscle or tumor. The second mechanism is the inability to excrete phosphate, as occurs in acute or chronic renal failure. Essentially all natural foods contain phosphate, and therefore almost any diet contains substantial quantities of phosphate (see Chapter 72). Normally, phosphate is easily cleared by the healthy kidney, but this ability is lost as the GFR declines below 20 to 30 mg/dL.

Differential Diagnosis

The differential diagnoses of hyperphosphatemia are listed in the following sections and in Table 73-3.

Artifactual Occurrence

Hyperphosphatemia may occur artifactually as a result of hemolysis in blood collection tubes. One clue is that the same phenomenon occurs with potassium. The occurrence of unexplained hyperkalemia and hyperphosphatemia should trigger the