phosphate, becoming phosphate depleted based on inadequate dietary intake is difficult. However, in settings of severe caloric deprivation, inadequacies can occur. Examples include anorexia nervosa, prisoner-of-war camps, prolonged ICU care, malabsorption syndromes, and chronic alcoholism. In the first three disorders, caloric intake is scant, and little phosphate is consumed. In alcoholism, caloric intake may be high, but alcohol is devoid of phosphate. The use of phosphate-binding antacids such as aluminum hydroxide gels may lead to severe phosphate deficiency, hypophosphatemia, and osteomalacia.

Excessive Renal Phosphate Losses

Disorders involving excessive losses are associated with a low TmP. PTH is phosphaturic, and all types of HPT are associated with hypophosphatemia as long as renal function is normal. This situation is widely appreciated for primary HPT but is less well appreciated for secondary HPT, particularly in the setting of vitamin D and calcium malabsorption. A low serum phosphate level may be the first and only noticeable clue to severe vitamin D deficiency. This fact has led to the diagnosis of celiac sprue in unsuspected cases on many occasions.

PTHrP (see Malignancy-Associated Hypercalcemia) is phosphaturic, as is PTH, and patients with humoral hypercalcemia of malignancy are commonly hypophosphatemic for this reason as long as their renal function is intact. Thiazide and loop diuretics are potent phosphaturic agents, and their use without phosphate replacement therapy leads to hypophosphatemia. Ethanol is also in this category.

Certain genetic disorders may lead to severe renal phosphate wasting (see Chapter 74). These disorders include X-linked hypophosphatemia (XLH), also called *vitamin D–resistant rickets*, and autosomal dominant hypophosphatemic rickets (ADHR). Another renal phosphate-wasting syndrome is oncogenic osteomalacia, also called *tumor-induced osteomalacia* (see Chapter 74). Acquired or inherited diffuse renal proximal tubular disorders, such as Fanconi's syndrome, may lead to hypophosphatemia as a result of renal phosphate wasting.

Excessive Skeletal Mineralization

Increased bone mineralization with respect to bone resorption results in large amounts of phosphate entering the skeleton, leading to hypophosphatemia. One example is the hungry bone syndrome that occurs after parathyroidectomy (see Hypocalcemia). Other examples are osteoblastic metastases and the treatment of vitamin D–deficient rickets or osteomalacia with vitamin D.

Phosphate Shift into Extracellular Fluid

Phosphate can be shifted from serum into the intracellular compartment by a rise in ECF pH. Recovery from a metabolic acidosis (e.g., diabetic ketoacidosis) and development of a respiratory alkalosis lead to hypophosphatemia. One of the most stunning examples of this phenomenon is the shift of phosphate into cells after administration of oral carbohydrate or parenteral glucose to victims of starvation or anorexia nervosa. Insulin increases the rate of glucose uptake into cells and its subsequent phosphorylation to glucose-6-phosphate. In the setting of significantly depleted phosphate reserve, rapid consumption of oral carbohydrate or parenteral glucose may lead to profound hypophosphatemia and sudden death due to respiratory or circulatory failure. Refeeding of starvation victims should be accomplished slowly and with attention to phosphate repletion.

Treatment

Phosphorus replacement is best accomplished through the oral route and usually is given in two to four divided doses that deliver 2000 to 4000 g/day. Doses greater than 1000 to 2000 mg/day often cause diarrhea initially (phosphate is used as a purgative), but with gradual increments, larger doses may be well tolerated. Intravenous phosphate should be given only with a clear understanding of the quantities involved (see Chapter 72) and to patients for whom oral administration is not an option. Frequent monitoring of serum phosphorus, calcium, and creatinine levels is required. Intravenous dosages up to 500 to 800 mg/day may be required.

HYPERMAGNESEMIA

Symptoms and Signs

Clinically significant hypermagnesemia is uncommon. The symptom is drowsiness, and the signs are hyporeflexia and eventual neuromuscular, respiratory, and cardiovascular collapse. It may also lead to hypocalcemia (see Hypocalcemia). Hypermagnesemia is seen in two settings: severe renal failure accompanied by the administration of magnesium-containing antacids and after the intravenous administration of large doses of magnesium sulfate for eclampsia or preeclampsia.

Differential Diagnosis

The differential diagnosis of hypermagnesemia is brief and is limited to the two disorders previously described (Table 73-5). Mild hypermagnesemia is common in patients on dialysis, but severe hypermagnesemia occurs only in the settings of renal failure accompanied by parenteral or oral magnesium salt administration, such as the use of magnesium-containing antacids or phosphate binders. Hypermagnesemia occurs commonly but in a controlled fashion in the treatment of eclampsia.

HYPOMAGNESEMIA

Symptoms and Signs

Hypomagnesemia is common, particularly in the ICU setting, but as with hypophosphatemia, it is often overlooked or ignored. Magnesium is essential for a broad range of biologic processes,

TABLE 73-5 CAUSES OF HYPERMAGNESEMIA AND HYPOMAGNESEMIA

Hypermagnesemia	Diuretics
Renal failure accompanied by magnesium antacid use	Saline infusion
Parenteral magnesium sulfate administration for eclampsia	Secondary aldosteronism
Hypomagnesemia	Cirrhosis
Inadequate intake	Congestive heart failure
Starvation	Osmotic diuresis, hyperglycemia
Malabsorption	Cisplatin, aminoglycoside antibiotics, amphotericin
Alcoholism	Hypokalemia
Vomiting, nasogastric suction	Hypercalcemia, hypercalciuria
Excessive renal losses	Proximal tubular diseases
	Genetic defects