Disorders of Phosphate Balance

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The physiologic concentration of serum phosphorus (phosphate) in normal adults ranges from 2.5 to 4.5 mg/dL (0.80–1.44 mmol/L). A diurnal variation occurs in serum phosphorus of 0.6 to 1.0 mg/dL, the lowest concentration occurring between 8 AM and 11 AM. A seasonal variation also occurs; the highest serum phosphorus concentration is in the summer and the lowest in the winter. Serum phosphorus concentration is markedly higher in growing children and adolescents than in adults, and it is also increased during pregnancy [1,2].

Of the phosphorus in the body, 80% to 85% is found in the skeleton. The rest is widely distributed throughout the body in the form of organic phosphate compounds. In the extracellular fluid, including in serum, phosphorous is present mostly in the inorganic form. In serum, more than 85% of phosphorus is present as the free ion and less than 15% is protein-bound.

Phosphorus plays an important role in several aspects of cellular metabolism, including adenosine triphosphate synthesis, which is the source of energy for many cellular reactions, and 2,3-diphosphoglycerate concentration, which regulates the dissociation of oxygen from hemoglobin. Phosphorus also is an important component of phospholipids in cell membranes. Changes in phosphorus content, concentration, or both, modulate the activity of a number of metabolic pathways.

Major determinants of serum phosphorus concentration are dietary intake and gastrointestinal absorption of phosphorus, urinary excretion of phosphorus, and shifts between the intracellular and extracellular spaces. Abnormalities in any of these steps can result either in hypophosphatemia or hyperphosphatemia [3–7].

The kidney plays a major role in the regulation of phosphorus homeostasis. Most of the inorganic phosphorus in serum is ultrafilterable at the level of the glomerulus. At physiologic levels of serum phosphorus and during a normal dietary phosphorus intake, approximately 6 to 7 g/d of phosphorous is filtered by the kidney. Of that

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amount, 80% to 90% is reabsorbed by the renal tubules and the rest is excreted in the urine. Most of the filtered phosphorus is reabsorbed in the proximal tubule by way of a sodium gradient-dependent process (Na-P_i cotransport) located on the apical brush border membrane [8–10]. Recently two distinct Na-P_i cotransport proteins have been cloned from the kidney (type I and type II Na-P_i cotransport proteins). Most of the hormonal and metabolic factors that regulate renal tubular phosphate reabsorption, including alterations in dietary phosphate content and parathyroid hormone, have been shown to modulate the proximal tubular apical membrane expression of the type II Na-P_i cotransport protein [11–16].

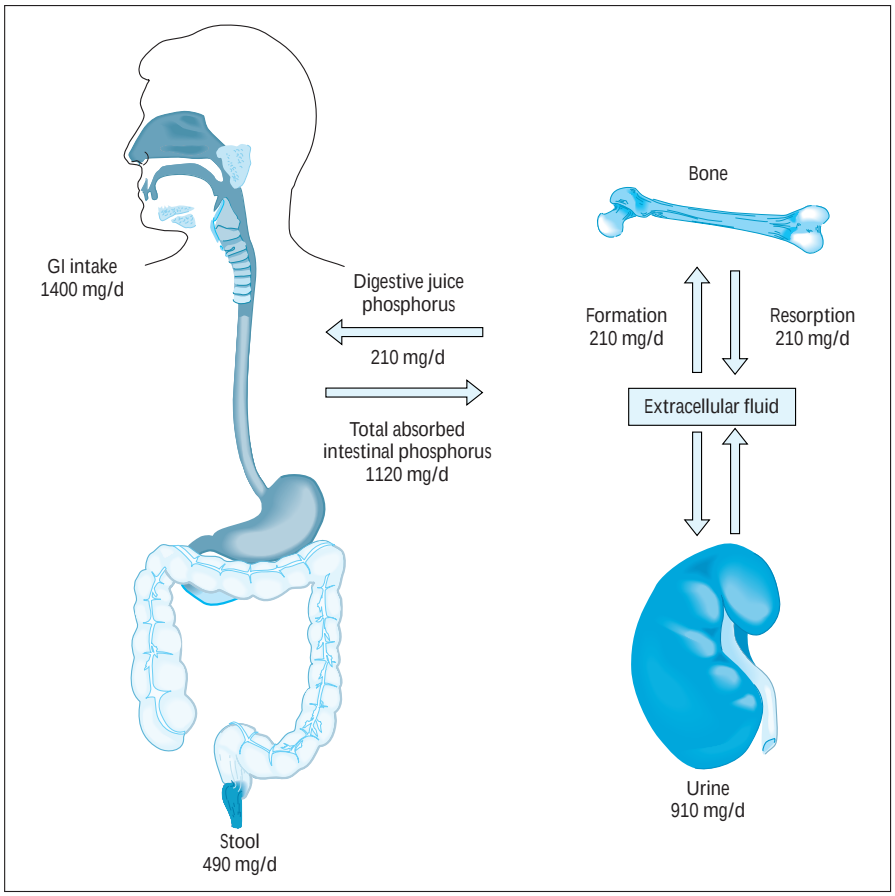

FIGURE 7-1
Summary of phosphate metabolism for a normal adult in neutral phosphate balance. Approximately 1400 mg of phosphate is ingested daily, of which 490 mg is excreted in the stool and 910 mg in the urine. The kidney, gastrointestinal (GI) tract, and bone are the major organs involved in phosphorus homeostasis.

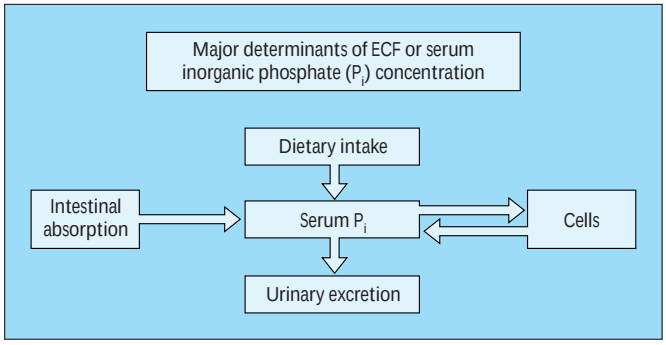

FIGURE 7-2
Major determinants of extracellular fluid or serum inorganic phosphate (P_i) concentration include dietary P_i intake, intestinal P_i absorption, urinary Pi excretion and shift into the cells.

Renal Tubular Phosphate Reabsorption

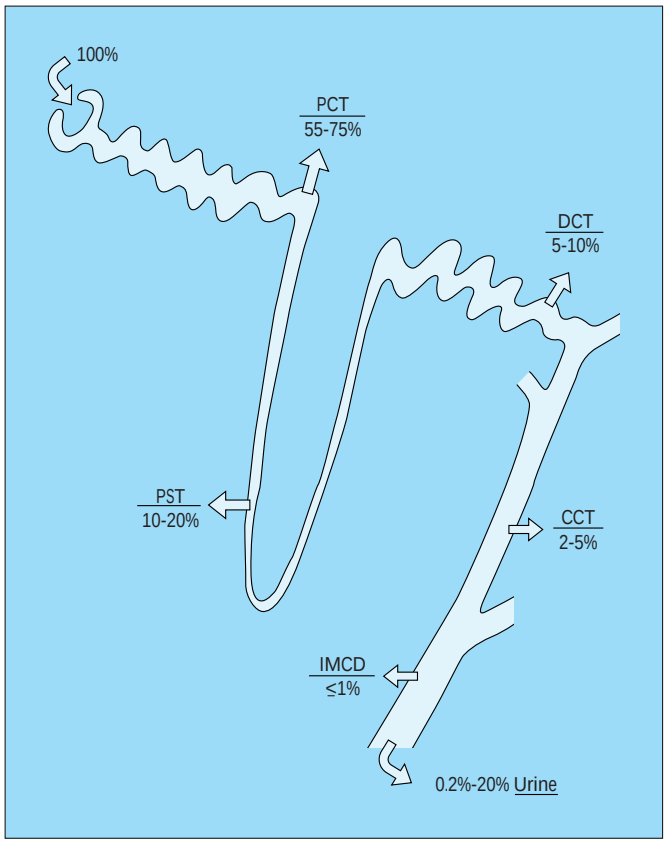

FIGURE 7-3

Renal tubular reabsorption of phosphorus. Most of the inorganic phosphorus in serum is ultrafilterable at the level of the glomerulus. At physiologic levels of serum phosphorus and during a normal dietary phosphorus intake, most of the filtered phosphorous is reabsorbed in the proximal convoluted tubule (PCT) and proximal straight tubule (PST). A significant amount of filtered phosphorus is also reabsorbed in distal segments of the nephron [7,9,10]. CCT—cortical collecting tubule; IMCD—inner medullary collecting duct or tubule; PST—proximal straight tubule.

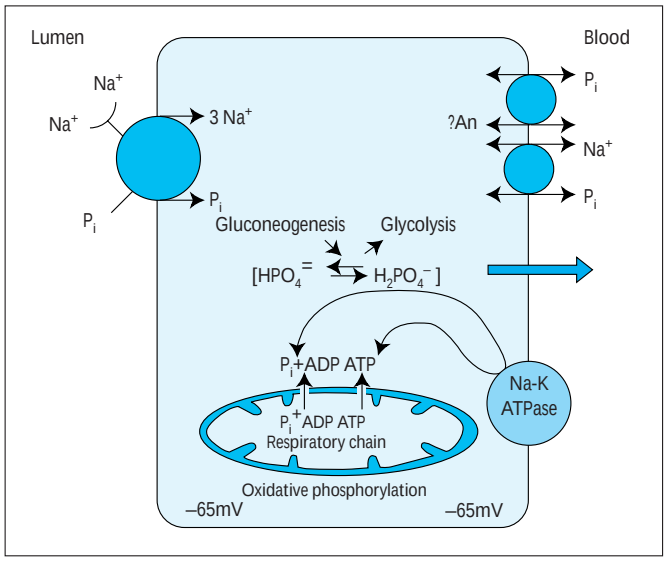

FIGURE 7-4

Cellular model for renal tubular reabsorption of phosphorus in the proximal tubule. Phosphate reabsorption from the tubular fluid is sodium gradient–dependent and is mediated by the sodium gradient–dependent phosphate transport (Na-P_i cotransport) protein located on the apical brush border membrane. The sodium gradient for phosphate reabsorption is generated by then sodium-potassium adenosine triphosphatase (Na-K ATPase) pump located on the basolateral membrane. Recent studies indicate that the Na-P_i cotransport system is electrogenic [8,11]. ADP—adenosine diphosphate; An—anion.