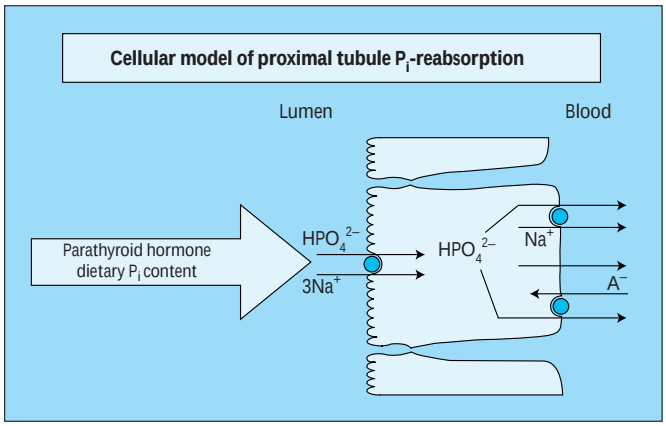

FIGURE 7-5

Celluar model of proximal tubular phosphate reabsorption. Major physiologic determinants of renal tubular phosphate reabsorption are alterations in parathyroid hormone activity and alterations in dietary phosphate content. The regulation of renal tubular phosphate reabsorption occurs by way of alterations in apical membrane sodium-phosphate (Na-P_i) cotransport $3Na^+$-HPO^{2-}_4 activity [11–14].

FACTORS REGULATING RENAL PROXIMAL TUBULAR PHOSPHATE REABSORPTION

Decreased transport	Increased transport
High phosphate diet	Low phosphate diet
Parathyroid hormone and parathyroid-hormone–related protein	Growth hormone
Glucocorticoids	Insulin
Chronic metabolic acidosis	Thyroid hormone
Acute respiratory acidosis	1,25-dihydroxy-vitamin D_3
Aging	Chronic metabolic alkalosis
Calcitonin	High calcium diet
Atrial natriuretic peptide	High potassium diet
Fasting	Stanniocalcin
Hypokalemia	
Hypercalcemia	
Diuretics	
Phosphatonin	

FIGURE 7-6

Factors regulating renal proximal tubular phosphate reabsorption.

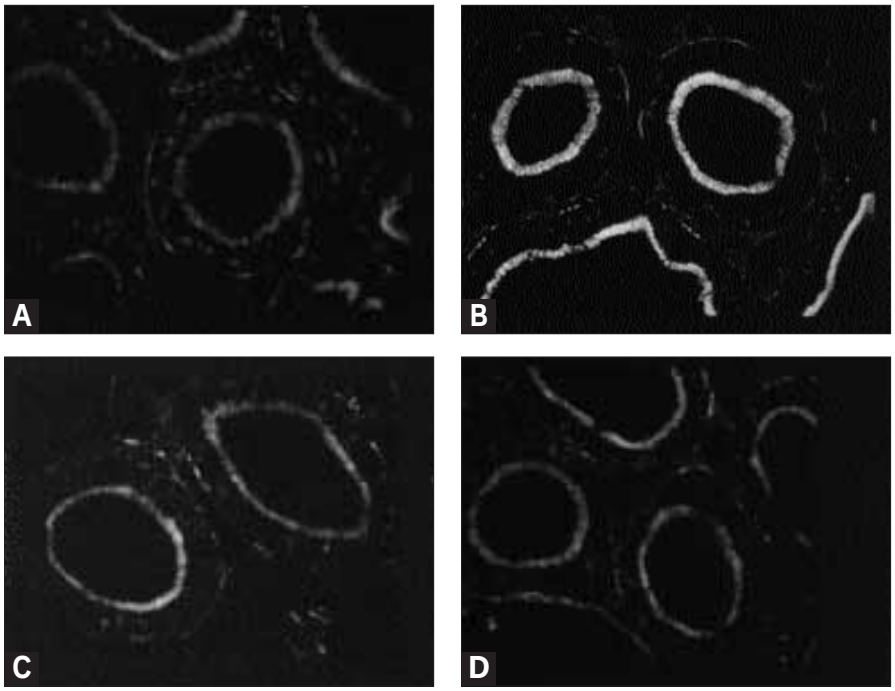

FIGURE 7-7 (see Color Plate)

Effects of a diet low in phosphate on renal tubular phosphate reabsorption in rats. **A,** Chronic high P_i diet. **B**, Acute low P_i diet. **C**, Colchicine and high P_i diet. **D**, Colchicine and low P_i diet. In response to a low phosphate diet, a rapid adaptive increase occurs in the sodium-phosphate (Na-P_i) cotransport activity of the proximal tubular apical membrane (**A**, **B**). The increase in Na-P_i cotransport activity is mediated by rapid upregulation of the type II Na-P_i cotransport protein, in the absence of changes in Na-P_i messenger RNA (mRNA) levels. This rapid upregulation is dependent on an intact microtubular network because pretreatment with colchicine prevents the upregulation of Na-P_i cotransport activity and Na-P_i protein expression (**C, D**). In this immunofluorescence micrograph, the Na-P_i protein is stained green (fluorescein) and the actin cytoskeleton is stained red (rhodamine). Colocalization of green and red at the level of the apical membrane results in yellow color [14].

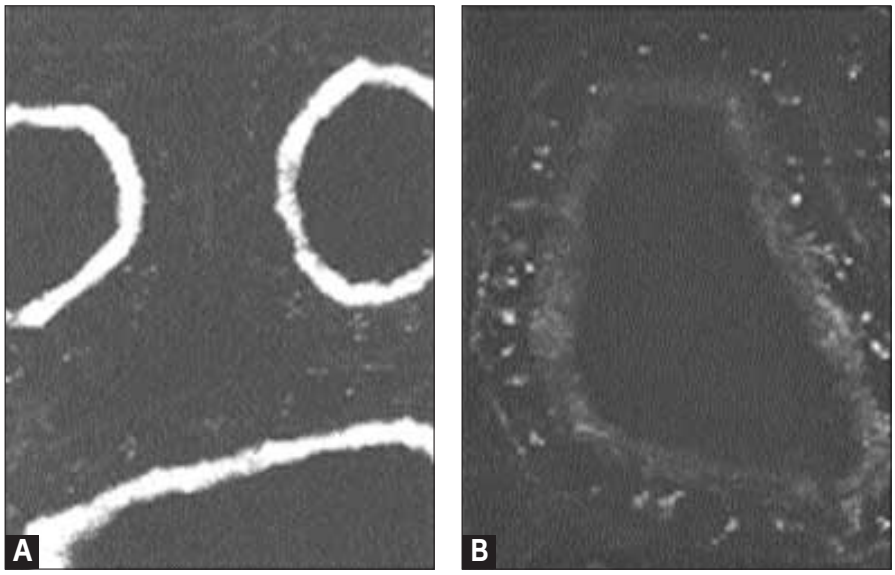

FIGURE 7-8 (see Color Plate)
Effects of parathyroid hormone (PTH) on renal tubular phosphate reabsorption in rats. In response to PTH administration to parathyroidectomized rats, a rapid decrease occurs in the sodium-phosphate ($Na\text{-}P_i$) cotransport activity of the proximal tubular apical membrane. The decrease in $Na\text{-}P_i$ cotransport activity is mediated by rapid downregulation of the type II $Na\text{-}P_i$ cotransport protein. In this immunofluorescence micrograph, the $Na\text{-}P_i$ protein is stained green (fluorescein) and the actin cytoskeleton is stained red (rhodamine). Colocalization of green and red at the level of the apical membrane results in yellow color [13]. **A**, parathyroidectomized (PTX) effects. **B**, effects of PTX and PTH.

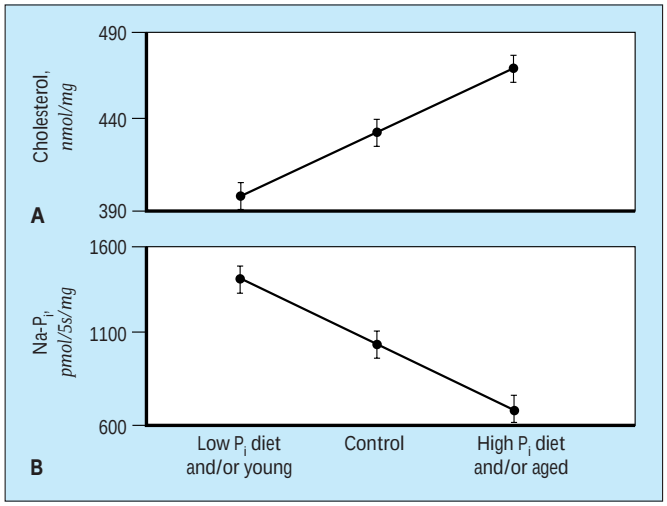

FIGURE 7-9
Renal cholesterol content modulates renal tubular phosphate reabsorption. In aged rats versus young rats and rats fed a diet high in phosphate versus a diet low in phosphate, an inverse correlation exists between the brush border membrane (BBM) cholesterol content (**A**) and $Na\text{-}P_i$ cotransport activity (**B**). Studies in isolated BBM vesicles and recent studies in opossum kidney cells grown in culture indicate that direct alterations in cholesterol content *per se* modulate $Na\text{-}P_i$ cotransport activity [15]. CON—controls.

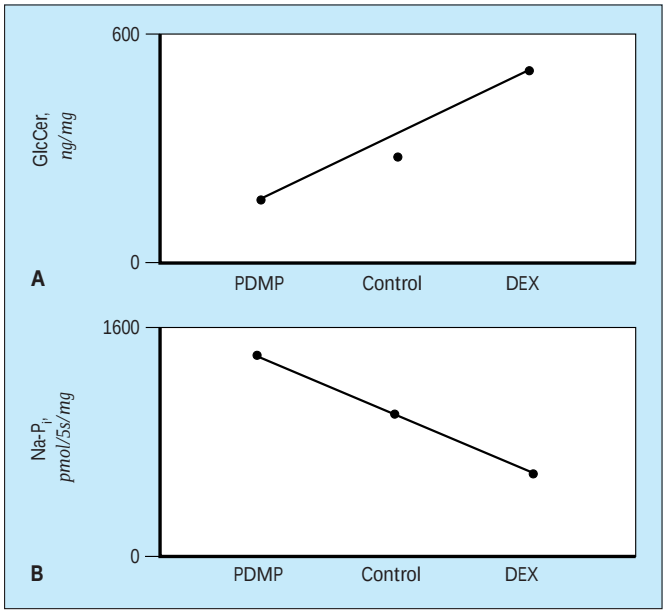

FIGURE 7-10
Renal glycosphingolipid content modulates renal tubular phosphate reabsorption. In rats treated with dexamethasone (DEX) and in rats fed a potassium-deficient diet, an inverse correlation exists between brush border membrane (BBM) glucosylceramide (GluCer)—and ganglioside GM_3, content and $Na\text{-}P_i$ cotransport activity. Treatment of rats with a glucosylceramide synthase inhibitor PDMP lowers BBM glucosylceramide content (**A**) and increases $Na\text{-}P_i$ cotransport activity (**B**) [16].

Hypophosphatemia/Hyperphosphatemia

MAJOR CAUSES OF HYPOPHOSPHATEMIA

Internal redistribution	Decreased intestinal absorption	Increased urinary excretion
Increased insulin, particularly during refeeding	Inadequate intake	Primary and secondary hyperparathyroidism
Acute respiratory alkalosis	Antacids containing aluminum or magnesium	Vitamin D deficiency or resistance
Hungry bone syndrome	Steatorrhea and chronic diarrhea	Fanconi's syndrome
		Miscellaneous: osmotic diuresis, proximally acting diuretics, acute volume expansion

FIGURE 7-11
Major causes of hypophosphatemia. (*From* Angus [1]; with permission.)

CAUSES OF MODERATE HYPOPHOSPHATEMIA

- Pseudohypophosphatemia
  - Mannitol
  - Bilirubin
  - Acute leukemia
- Decreased dietary intake
- Decreased intestinal absorption
  - Vitamin D deficiency
  - Malabsorption
  - Steatorrhea
  - Secretory diarrhea
  - Vomiting
  - PO^3_4-binding antacids
- Shift from serum into cells
  - Respiratory alkalosis
    - Sepsis
    - Heat stroke
    - Neuroleptic malignant syndrome
    - Hepatic coma
    - Salicylate poisoning
    - Gout
    - Panic attacks
    - Psychiatric depression
- Hormonal effects
  - Insulin
  - Glucagon
  - Epinephrine
  - Androgens
  - Cortisol
  - Anovulatory hormones
- Nutrient effects
  - Glucose
  - Fructose
  - Glycerol
  - Lactate
  - Amino acids
  - Xylitol
- Cellular uptake syndromes
  - Recovery from hypothermia
  - Burkitt's lymphoma
  - Histiocytic lymphoma
  - Acute myelomonocytic leukemia
  - Acute myelogenous leukemia
  - Chronic myelogenous leukemia in blast crisis
  - Treatment of pernicious anemia
  - Erythropoietin therapy
  - Erythrodermic psoriasis
  - Hungry bone syndrome
  - After parathyroidectomy
  - Acute leukemia
- Increased excretion into urine
  - Hyperparathyroidism
  - Renal tubule defects
    - Fanconi's syndrome
    - X-linked hypophosphatemic rickets
    - Hereditary hypophosphatemic rickets with hypercalciuria
    - Polyostotic fibrous dysphasia
    - Panostotic fibrous dysphasia
    - Neurofibromatosis
    - Kidney transplantation
    - Oncogenic osteomalacia
    - Recovery from hemolytic-uremic syndrome
  - Aldosteronism
  - Licorice ingestion
  - Volume expansion
  - Inappropriate secretion of antidiuretic hormone
  - Mineralocorticoid administration
  - Corticosteroid therapy
  - Diuretics
  - Aminophylline therapy

FIGURE 7-12
Causes of moderate hypophosphatemia. (*From* Popovtzer, *et al.* [6]; with permission.)