410 Disorders of the Parathyroid Gland and Calcium Homeostasis

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PARATHYROID GLAND DISORDERS

■ INTRODUCTION

Four parathyroid glands are located posterior to the thyroid gland. They produce parathyroid hormone (PTH), which is the primary regulator of calcium physiology. PTH acts directly on bone, where it induces calcium (and phosphate) release, and on the kidney, where it enhances calcium reabsorption in the distal tubules. In the proximal renal tubules, PTH increases excretion of phosphate and the synthesis of 1,25-dihydroxyvitamin D ($1,25[OH]_2D$), a hormone that increases gastrointestinal calcium absorption. Serum PTH levels are tightly regulated by a negative feedback loop. Calcium, acting through the calcium-sensing receptor, and vitamin D, acting through its nuclear receptor, reduce PTH release and synthesis. Additional evidence indicates that fibroblast growth factor 23 (FGF23), a phosphaturic hormone, can suppress PTH secretion. Understanding the hormonal pathways that regulate calcium and phosphate levels as well as bone metabolism is essential for effective diagnosis and management of a wide array of hyper- and hypocalcemic disorders.

Hyperparathyroidism, characterized by excess production of PTH, is a common cause of hypercalcemia and is usually the result of autonomously functioning adenomas or hyperplasia. Surgery for this disorder is highly effective and has been shown to reverse some of the deleterious effects of long-standing PTH excess on bone density. Humoral hypercalcemia of malignancy (HHM) is also a common cause of hypercalcemia, which is usually due to the overproduction of parathyroid hormone–related peptide (PTHrP) by cancer cells. The similarities in the biochemical characteristics of hyperparathyroidism and HHM, first noted by Albright in 1941, are