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AUTOSOMAL DOMINANT HYPOCALCIURIC HIPERCALCEMIA

Abstract : Identification and cloning of the membrane receptor through which a number of target cell types sense extracellular ionized calcium concentration (Ca^{2+}–sensing receptor– CaSR) have provided incontrovertible evidence that calcium ions, in addition to serving their well–recognized function as an intracellular second messenger, can also serve a hormone–like role as an extracellular "first messenger". Therefore, calcium ions serve as a calciotropic hormone modulating functions of target tissues (parathyroid glands, kidney tubular cells, and other cell types) through their own membrane receptor in a manner totally analogous to the more classical calciotropic hormone, parathyroid hormone. This receptor, together with receptors for the most of the polypeptide hormones, neurotransmiters and glycoproteins, belong to the family of G–protein coupled receptors (guanin nucleotid binding proteins). Cloning of the CaSR has also enabled the identification of inherited diseases with inactivating or activating mutations of this receptor that cause hypercalcemic and hypocalcemic disorders, respectively. Autosomal dominant hypocalciuric hypercalcemia or familial benign hypercalcemia is a condition produced by a loss–of–function (inactivating) mutation of the CaSR gene, with an increase in the set point of the extracellular calcium ion sensing mechanism, and consequent parathormone overproduction, together with increased renal tubular calcium reabsorption, due to the existence of the same mutation in tubular cells. Generally, surgical treatment is not necessary for this condition as compared to other variants of primary hyperparathyroidism. In this paper, clinical characteristics of this relatively rare disorder have been presented.