

The etiology of hypercalcemia can be divided into 2 major categories: parathyroid hormone–mediated and non–parathyroid hormone–mediated. These diuretics also block sodium and chloride transport, leading to increased passive absorption of sodium, water, and calcium in response to decreased arterial volume.[5] Excessive use of calcium carbonate for treating stomach reflex disease or indigestion may lead to milk–alkali syndrome, resulting in hypercalcemia, renal dysfunction, and metabolic alkalosis.[8] Prolonged use of retinoic acid causes an increase in bone resorption, which can also increase calcium levels.[9] Hypercalcemia of malignancy: This condition is most commonly caused by excessive production of parathyroid hormone–related protein by tumors, which act on parathyroid hormone receptors due to their structural similarity. However, high levels of parathyroid hormone can also lead to severe hypercalcemia, osteoporosis, bone fractures, nephrolithiasis, and renal failure.[2] Tertiary hyperparathyroidism: This condition also results in elevated levels of calcium and high levels of parathyroid hormone but is due to parathyroid hyperplasia from chronic overstimulation, most often in patients with renal failure or a history of renal transplant.[3] Familial hypocalciuric hypercalcemia: This condition is caused by a loss–of–function mutation in the calcium–sensing receptor gene and is inherited in an autosomal dominant manner. Lithium use leads to hypercalcemia by altering the set point at which calcium suppresses parathyroid hormone, requiring higher levels of calcium for parathyroid hormone suppression.[5] Teriparatide is a recombinant human parathyroid hormone used to treat osteoporosis that can cause transient hypercalcemia.[6] Aboloparatide is a synthetic peptide analog of parathyroid hormone–related protein that binds to the parathyroid hormone receptor type 1, potentiating the actions of parathyroid hormone and parathyroid hormone–related protein. Consequently, it can similarly increase serum calcium levels.[7] Non–Parathyroid Hormone–Mediated Medication–induced: Thiazide diuretics increase calcium reabsorption in the distal convoluted tubule of the nephron, resulting in parathyroid hormone–independent hypercalcemia. Parathyroid Hormone–Mediated Primary hyperparathyroidism: This condition results in elevated levels of calcium with high or inappropriately normal parathyroid hormone levels and is typically caused by a parathyroid adenoma. This condition also results in elevated levels of calcium and parathyroid hormone but can be distinguished by the low levels of calcium in the urine.[4] Medications can also cause hypercalcemia. Malignancy can also cause metastatic disease to the bone and increase osteoclast activity, leading to increased bone resorption and hypercalcemia. Patients most commonly present with asymptomatic high–normal calcium or mild hypercalcemia.