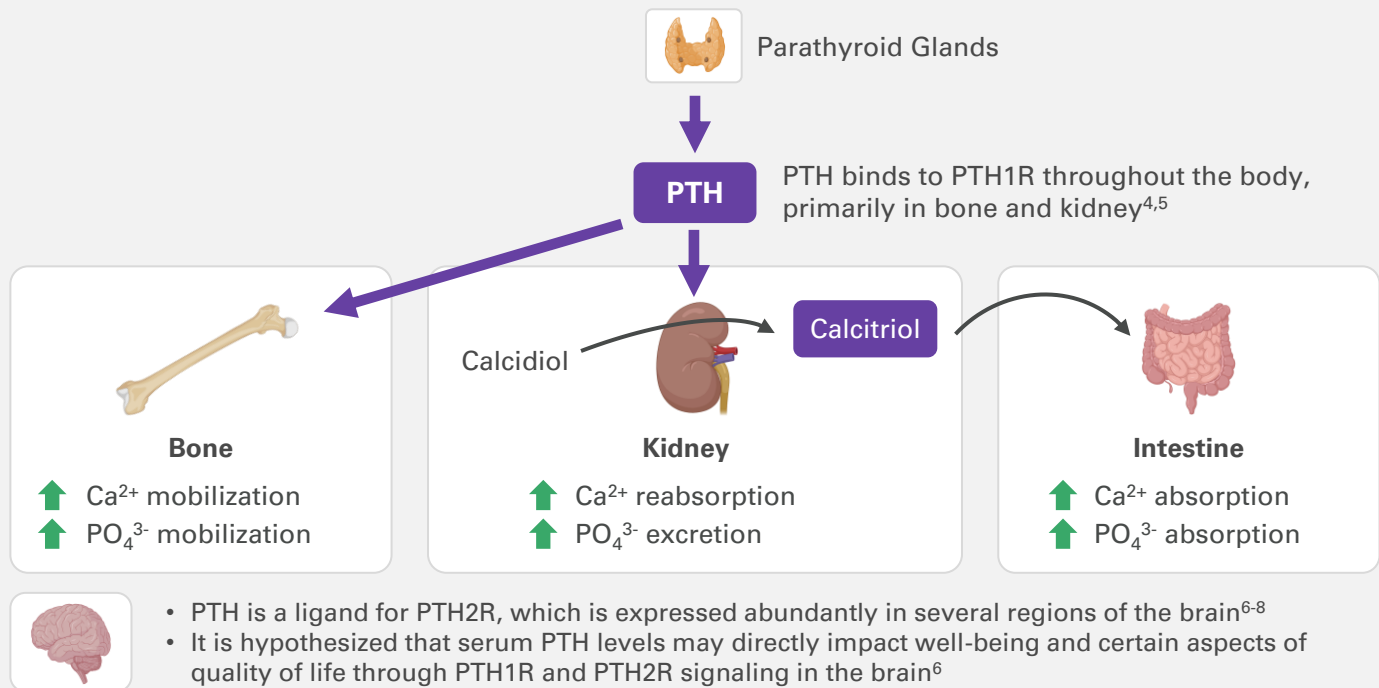


Hypoparathyroidism

Parathyroid Hormone (PTH) Physiology

PTH is the primary regulator of serum calcium and phosphate balance, acting directly on bone and kidney, and indirectly on the intestine¹⁻³



Hypoparathyroidism Introduction

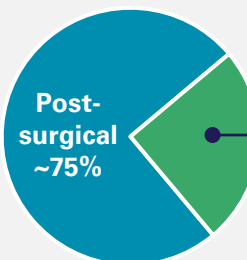
Hypoparathyroidism is an endocrine disease caused by insufficient levels of PTH⁹

Prevalence

United States:
~77,000 to
115,000 people^{10,11}

Europe:
~3.2 in 10,000
people¹²⁻¹⁵

Etiology^{2,10}



Other:

- Autoimmune
- Genetic
- Idiopathic

Diagnosis

Hypoparathyroidism is diagnosed when serum PTH levels are low or insufficient in the presence of hypocalcemia, confirmed twice at least 2 weeks apart.^{1,16} Elevated serum phosphate, reduced calcitriol, and elevated urinary FECa support diagnosis.^{2,16} Hypoparathyroidism may be considered chronic if it persists > 6 months after surgery^{1,17-18}

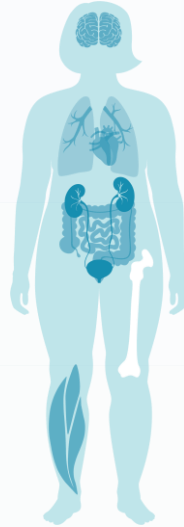
Abbreviations: Ca^{2+} , ionized calcium; FECa, fractional excretion of calcium; PO_4^{3-} , orthophosphate; PTH1R, PTH 1 Receptor; PTH2R, PTH 2 Receptor

References: 1. Brandi ML, et al. *J Clin Endocrinol Metab.* 2016; 2. Mannstadt M, et al. *Nat Rev Dis Primers.* 2017; 3. Shoback D.. *New England Journal of Medicine.* 2008; 4. Cheloha RW, et al. *Nat Rev Endocrinol.* 2015; 5. Lee M, et al. *Curr Opin Nephrol Hypertens.* 2009; 6. Dettori C, et al. *Pers Med.* 2023; 7. Bago AG, et al. *Neuroscience.* 2009; 8. Usdin TB, et al. *J Biol Chem.* 1995; 9. Shoback DM, et al. *Clin Endocrinol Metab.* 2016; 10. Clarke BL, et al. *J Clin Endocrinol Metab.* 2016; 11. Powers J, et al. *J Bone Miner Res.* 2013; 12. Smith A., et al. *Virtual European Congress of Endocrinology* 2020; 13. Underbjerg L, et al. *J Bone Miner Res.* 2015; 14. Cianferotti L, et al. *Calcif Tissue Int.* 2018; 15. Vadiveloo T, et al. *J Bone Miner Res.* 2018; 16. Khan AA, et al. *J Bone Miner Res.* 2022; 17. Bollerslev J, et al. *Eur J Endocrinol.* 2022; 18. Khan AA, et al. *Eur J Endocrinol.* 2019. November 2025, MED-US-TC-PTH-2500131

Hypoparathyroidism

Clinical Presentation

Individuals with hypoparathyroidism may experience a range of severe and potentially life-threatening short-term and long-term complications ¹⁻¹¹			
Neuro-psychiatric	Anxiety & Depression, Cognitive Impairment ("Brain Fog")	Cataracts, Papilledema	Ophthalmological
CNS	Seizures, Basal Ganglia Calcifications, Parkinsonism or Dystonia	Altered Tooth Morphology	Dental
Renal^a	Nephrocalcinosis, Nephrolithiasis, Chronic Kidney Disease	Vascular Calcifications, Cardiac Arrhythmias, Dilated Cardiomyopathy	Cardiovascular
PNS	Paresthesia, Muscle Cramps, Pain, Tetany	Laryngospasm, Bronchospasms	Respiratory
Derm-atological	Dry skin, Brittle Nails, Thinning Hair	Myopathy, Spondyloarthropathy	Musculoskeletal



The burden of hypoparathyroidism negatively impacts HRQoL, irrespective of serum calcium levels, as well as physical functioning and psychological well-being^{12,13}

Management of Hypoparathyroidism

Conventional Therapy (Active Vitamin D and Calcium) for Hypoparathyroidism

- Conventional therapy aims to alleviate hypocalcemia, but does not address insufficient PTH levels¹⁴
- High doses of active vitamin D and calcium may lead to hypercalciuria and predispose individuals with hypoparathyroidism to nephrolithiasis, nephrocalcinosis, and the development of chronic kidney disease^{2,9}
- Individuals with hypoparathyroidism receiving conventional therapy may still report reduced QoL and experience impaired physical functioning and well-being^{8,15,16}

PTH Therapy Considerations from the 2022 Guidelines from the Second International Workshop

- Consider the use of PTH when individuals with hypoparathyroidism are inadequately controlled with conventional therapy. Inadequate control of hypoparathyroidism is considered any one of the following: symptomatic hypocalcemia, hyperphosphatemia, renal insufficiency, hypercalciuria, or poor QoL¹⁷
- Individuals with hypoparathyroidism with poor compliance, malabsorption, or intolerance of large doses of active vitamin D and calcium may benefit from PTH therapy¹⁷

^aRenal complications occurring in hypoparathyroidism are primarily attributed to use of conventional therapy rather than the disease itself³

Abbreviations: CNS, central nervous system; PNS, peripheral nervous system; PTH, parathyroid hormone; HRQoL, health-related quality of life

References: 1. Shoback DM, et al. *Clin Endocrinol Metab.* 2016; 2. Brandi ML, et al. *J Clin Endocrinol Metab.* 2016; 3. Mannstadt M, et al. *Nat Rev Dis Primers.* 2017; 4. Brod M, et al. *Patient.* 2020; 5. Rubin MR, et al. *J Endocr Soc.* 2022; 6. Underbjerg L, et al. *J Bone Miner Res.* 2015; 7. Bilezikian JP, et al. *J Bone Miner Res.* 2011; 8. Hadker N, et al. *Endocr Pract.* 2014; 9. Rubin MR. *F1000Res.* 2020; 10. Underbjerg L, *J Bone Miner Res.* 2013; 11. Underbjerg L, et al. *J Bone Miner Res.* 2014; 12. Kontogeorgos G, et al. *Endocr Connect.* Jan 10 2022;11(1). 13. Brod M, et al. *Life Res.* Jan 2021;30(1):277-291. 14. Khan AA, et al. *Eur J Endocrinol.* 2019. 15. Büttner M, et al. *Endocrine.* 2017; 16. Bjornsdottir S, et al. *J Bone Miner Res.* 2022. 17. Khan AA, et al. *J Bone Miner Res.* 2022