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Best practice recommendations for the diagnosis and management of hypoparathyroidism

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ABSTRACT

Background: Hypoparathyroidism (HypoPT) is characterized by low serum calcium due to insufficient parathyroid hormone (PTH). This manuscript builds upon the 2022 international HypoPT guidelines and three systematic reviews, which have been further informed by updated narrative reviews and expert consensus. This paper presents current best practice consensus recommendations for the diagnosis and management of HypoPT.
Methods: An International Panel of Experts updated the previous systematic reviews (SR's), conducted narrative reviews, developed, and subsequently approved these best practice recommendations at the Parathyroid Summit, held as a pre-Endocrine Society meeting in May 2024 (Boston, USA).
Results: Diagnostic criteria for chronic HypoPT require hypocalcemia with inappropriately normal or low PTH levels. Conventional therapy is recommended as first line therapy and includes calcium supplementation, active vitamin D, correction of vitamin D inadequacy and correction of abnormalities in serum magnesium. Monitoring is required to achieve optimal serum calcium while avoiding hyperphosphatemia, hypercalciuria and declines in renal function. Assessment of HypoPT complications is required including skeletal health assessment in postmenopausal women and men over the age of 50 years. Specific strategies are provided for managing HypoPT during pregnancy and lactation as well as in children. PTH replacement with palopegteriparatide has been approved and is an important therapeutic option, especially when conventional therapy is inadequate or not tolerated.
Conclusion: These best practice recommendations provide a framework for HypoPT diagnosis and management, emphasizing individualized care, role of DNA analysis in the diagnosis of nonsurgical HypoPT, and role of PTH or PTH analogue therapy as appropriate. They complement the 2022 international guidelines and incorporate updated therapeutic recommendations from the past 3 years including the positioning of the newly approved molecule palopegteriparatide based on recent clinical trial data and expert consensus.

1. Introduction

Hypoparathyroidism (HypoPT) is a rare endocrine disorder diagnosed by low serum albumin corrected or ionized calcium, in the presence of low or inadequate parathyroid hormone (PTH) levels [1–3]. Chronic HypoPT is associated with multisystem complications, including renal (nephrolithiasis, nephrocalcinosis and/or renal insufficiency), neurologic (paresthesias, cognitive impairment, seizures), cardiovascular (prolonged QT interval, arrhythmia, hypocalcemic heart failure), as well as cataracts and an increased risk of infections [4,5]. All-cause mortality is also significantly higher in chronic HypoPT with an adjusted HR/OR (95 % CI) of 1.80 (1.49–2.17) [4,6,7].

These best practice consensus statements, developed by leading international experts in HypoPT, provide a comprehensive approach to the diagnosis, management, and monitoring of HypoPT. This work builds upon the 2022 international guidelines [8] and three systematic reviews (SRs) [4,9,10] which were completed and has been further informed by updated narrative reviews and expert consensus (Table 1).

The initiative was launched by the Canadian Society of Endocrinology and Metabolism (CSEM) in partnership with multiple international endocrine societies (see acknowledgements for list of endorsements). CSEM convened an international panel of experts to develop updated best practice recommendations through a structured, consensus-based process. This document provides a practical clinical framework that guides the use of PTH replacement therapy with palopegteriparatide in the management of chronic HypoPT.

These recommendations are intended to guide individualized, decision-making across diverse patient populations and clinical contexts. The recommendations address practical clinical concerns including postsurgical risk assessment, genetic evaluation in nonsurgical HypoPT, comprehensive management of complications, sick day protocols, dose titration with PTH therapy, transitioning between conventional therapy and PTH, as well as considerations for pregnancy, lactation, and care of children.

2. Methods

The 2022 international guidelines and three systematic reviews have been further updated with narrative reviews covering the time period of 2022 to March 2025 and expert consensus. These recommendations were developed through expert collaboration and updated narrative reviews addressing clinical challenges and incorporating guidance on the newly approved PTH replacement therapy, namely palopegteriparatide [4,8,9]. The previous 2022 Global HypoPT guidelines were endorsed by over 65 international and regional endocrine or surgery societies. The International Task Force had previously conducted three systematic reviews, the first identifying symptoms and complications associated with chronic HypoPT, and the second assessing the predictive value of early postoperative PTH and calcium measurements for developing chronic HypoPT after total thyroidectomy [4]. The third systematic review evaluated the efficacy and safety of PTH therapy compared with conventional therapy [9]. The International Task Force found that PTH therapy can improve physical health-related QoL and reduced the need for active vitamin D and calcium supplementation, however, it may increase the risk of hypercalcemia [9]. Additionally, a clinical practice survey by the International Task Force explored global expert practices [10]. It highlighted variations in clinical approaches and identified key areas for future research. The current Best Practice Recommendations provide practical guidance regarding evaluation and management based on new findings and provide a framework for improving patient care and monitoring protocols for chronic HypoPT.

3. Narrative review framework

This process involved:

- **Literature Search:** An updated literature search was conducted (by methodologist H.A.) to identify relevant evidence published from May 2022 to March 2025. Searches were performed across MEDLINE/PubMed, Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL). Search strategies were developed individually for each of the nine clinical domains addressed in the

Table 1
Summary of best practice consensus statements.

1. Diagnosis	a. Postsurgical Hypoparathyroidism (HypoPT) • Measure PTH 12–24 h post total thyroidectomy, if serum PTH (measured by 2nd or 3rd generation assay) is >10 pg/ml or 1.05 pmol/L, the patient is unlikely to develop permanent HypoPT. • Follow-up is advised by the surgeon and endocrinologist or family physician if PTH is <10 pg/ml (<1.05 pmol/L), as a significant number of these individuals (still <50 %) may develop permanent HypoPT. A close follow-up with laboratory assessment (including calcium and PTH) within the first week post-surgery is advised, or earlier in the presence of symptoms or severe hypocalcemia. Subsequent follow up dependent on the severity of the hypocalcemia and symptomatology • A diagnosis of chronic HypoPT is confirmed ≥12 months after surgical intervention in the presence of hypocalcemia (albumin-corrected or ionized calcium) determined on two separate occasions with inappropriately normal or low PTH levels performed at least two weeks apart. • To reduce the risk of developing postsurgical HypoPT, an experienced surgeon is required with a high-volume surgical practice at a specialized center. The following risk factors are associated with a higher risk of developing HypoPT: • Obesity >40 kg/m^2 (surgery is more complicated, both technically and metabolically). • Vitamin D deficiency (25(OH) D ≤25 nmol/L) as transient hypocalcemia may be of longer duration and more severe. • Children have smaller glands, higher potential for reactive lymph nodes and bulky thymus requiring greater surgical expertise. • Graves' disease as the hypervascularity of the thyroid makes surgery technically challenging. • Presence of thyroid malignancy and central neck dissection requires removal of surrounding tissues which can lead to devascularization of parathyroid glands. • Concomitant thyroid and parathyroid surgery as the uninvolved parathyroid glands may be suppressed and smaller and may inadvertently be removed during thyroidectomy. • Repeat surgery. • Need for autotransplantation of parathyroid tissue into the lateral neck or forearm. b. Nonsurgical HypoPT
2. Etiology	• Diagnosed in the presence of a low albumin-corrected or ionized calcium – confirmed on two separate occasions with inappropriately normal or low PTH (either 2nd or 3rd generation assay) at least two weeks apart • Check serum magnesium levels and correct/normalize if abnormal • Biotin use (if >5 mg daily) should be stopped for at least three days prior to testing, as it may falsely lower PTH due to interference with some PTH assay • Genetic testing is advised for all patients with idiopathic HypoPT, especially in the presence of a family history of HypoPT and in those under the age of 40 years • Syndromic HypoPT: evaluate the following genes for pathogenic or likely pathogenic variants: • Autoimmune: APECED (*AIRE1*) HypoPT, mucocutaneous candidiasis, adrenal insufficiency, GI dysfunction and malabsorption. • Congenital: DiGeorge (*TBX1*, *NEBL*) (cardiac abnormalities, cleft palate, thymic aplasia, autoimmune disease, ocular complications, hearing loss, developmental delay) • CHARGE (*CHD7*, *SEMA3E*), Kenny-Caffey, Sanjad-Sakati (short stature, small hands and feet, dysmorphic facies) (*TBCE*, *FAM111A*) • HDR (HypoPT, Deafness, Renal dysplasia): *GATA3* (Barakat syndrome) • Mitochondrial Disorders: MELAS, KSS, MTPD • Nonsyndromic HypoPT: • Isolated: *GCM2*, *PTH*, X-linked *SOX3* • Associated with other conditions: ADH and Bartter Syndrome (*CASR*, *GNA11*)
3. Assessment of HypoPT Complications:	• Renal complications - evaluate 24-h urine for calcium, creatinine, oxalate, and citrate; assess eGFR; perform renal US or other abdominal imaging modality • Ocular complications – conduct an eye exam assessing for cataracts • Neurologic complications - CT of brain in presence of neuropsychiatric symptoms and duration of HypoPT >5 years – at baseline and follow-up - if clinically indicated • Cardiac complications – EKG and may need cardiac monitoring in the presence of cardiac symptoms or significant hypocalcemia; also evaluate other cardiovascular risk factors • Skeletal complications - Markers of bone turnover, spinal radiographs, BMD with DXA and TBS if available • Psychiatric complications - screen for depression, anxiety and neuropsychiatric manifestations; evaluate QoL • Infectious complications - recognize increased risk of infections in HypoPT with increased incidence of URI, UTI, and urogenital infections
4. Conventional Therapy	• Recommend taking calcium supplements with meals to serve as phosphate binder and to improve calcium absorption • Calcium citrate preferred in presence of PPI use, and may also reduce urinary oxalate • Multiple daily dosing preferred for optimal calcium absorption and sustained serum calcium and phosphorus levels • Start calcitriol typically at 0.25 μg daily, given the short half-life (5–8 h) higher and/or divided doses may be needed; similarly alfacalcidol (starting dose 0.5 μg daily) also has a short half-life (3–6 h). Close follow-up in 2–3 days after making dose changes is advised. • Correct low 25(OH)D – tissues other than kidneys are able to synthesize 1,25$(OH)_2$D and normalizing 25(OH)D with parent vitamin D is advised. • Correct serum magnesium levels: inadequate intracellular magnesium levels result in PTH resistance, as magnesium is a cofactor for adenylate cyclase; also high serum magnesium can lower PTH synthesis and secretion as it binds to the CaSR. • Recognize that intracellular magnesium deficiency is significant in the presence of a low measured serum magnesium and replace accordingly. • Thiazide diuretics: off label, useful in the presence of hypercalciuria as renal calcium reabsorption is enhanced; recommended dose is 25–100 mg daily along with low Na^+ diet and monitoring of serum magnesium and potassium. • Encourage low phosphate diet in adults – limit dairy, beans, meat, nuts, seeds, grains, boxed and canned foods may be of value in lowering serum phosphorus -avoid consuming excess bioavailable phosphorus via food additives (can elevate dietary phosphorus content by 41 % increase) • Encourage a calcium enriched diet.

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Table 1 (*continued*)

	• Phosphate binder may be given if high serum phosphorus and maybe of value in the presence of soft tissue calcifications aiming for a normal serum phosphorus and normal calcium phosphate product (4.4 $mmol^2/l^2$ or 55 mg^2/dL^2)
	• Cautious use of antiresorptive therapy is advised if necessary for osteoporosis due to the potential risk of hypocalcemia with antiresorptive therapies. The dose of active vitamin D may need an upward adjustment to avoid hypocalcemia.
	• Conventional therapy is challenging in the presence of bariatric surgery, any malabsorptive state or in the presence of NG tube feeding
	• Does not avoid fluctuations in serum calcium.
5. Limitations of Conventional Therapy	• Need to adjust during exercise, menses, times of increased calcium requirements. • Active vitamin D increases serum phosphorus and urine calcium further. • May not fully relieve symptoms or improve QoL and is associated with high pill burden and side-effects. • May increase risk of long-term complications.
6. Monitoring	• Check labs every 3–12 months depending on clinical stability – monitor serum calcium, albumin, phosphorus, magnesium and eGFR • Check serum 25(OH)D every 6–12 months after achieving values in the target range; until then approximately every three months. • Check serum PTH at baseline assessment. • Limited value in measuring serum $1,25(OH)_2D$. • Monitor 24-h urine calcium and creatinine every 6–24 months – and try to normalize to minimize risk of CKD, nephrolithiasis and nephrocalcinosis.
7. Acute Hypocalcemia management	• Target low normal albumin-corrected serum calcium, 24-h urine calcium <250 mg /24 h for women and 300 mg/24 h for men. • Check albumin corrected serum calcium, serum magnesium, 12 lead EKG for QTc prolongation. • Indications for IV calcium supplementation – life-threatening hypocalcemia (albumin corrected serum calcium <1.9 mmol/l or < 7.5 mg/dL) • Monitor for cardiac arrhythmia, laryngospasm, or tetany. • For IV treatment, use calcium gluconate bolus [1 g of calcium gluconate (90 mg elemental Ca)] over 10 mins followed by infusion (10 g of calcium gluconate in 1 l of D5W at 100 ml/h and titrate with cardiac monitoring. • Give oral calcium and activated vitamin D. • Note that injectable activated vitamin D requires more research and PTH and PTH analogues may be of value postoperatively in postsurgical HypoPT in the presence of unstable refractory hypocalcemia, however these options are not FDA approved.
8. Pregnancy and Lactation considerations	• Always measure albumin-corrected calcium or ionized calcium, as total calcium may be lower due to hemodilution in pregnancy. • PTHrP produced by placenta and breast and PTH-independent increases in $1,25(OH)_2D$ starting in the first trimester may impact dose of conventional therapy required. • Recognize maternal complications including pre-eclampsia, PROM (premature rupture of membranes), seizures, arrhythmias, hypercalciuria and renal stones, diabetes mellitus, chronic kidney disease, and preterm labor. • Recognize fetal complications including neonatal seizures, hyperparathyroidism if maternal serum calcium low during pregnancy; HypoPT if maternal serum calcium is high, lower birth weight • Avoid hyper and hypocalcemia with close monitoring of serum calcium, magnesium, phosphorus, and creatinine frequently (e.g. every 2–4 weeks). • There are no safety data regarding use of PTH and PTH analogues during pregnancy. • Discuss PTH therapy prior to planning pregnancy. • If on PTH, switch to conventional therapy and try to achieve mid to low normal serum calcium. • Stop thiazide diuretics. • Preconception education and optimize control. • Discuss risk of transmission in mothers with a genetic cause for HypoPT and plan follow up of infant. • Consider pre-implantation genetic testing of the embryo in those with known genetic etiology. • Team approach advised with endocrinologist, obstetrician and neonatologist. • Achieve low normal to mid normal serum calcium • normal serum phosphorus, magnesium, 25(OH)D and 24 h urine calcium. • There is often greater need for calcium and active vitamin D with cessation of lactation and loss of PTHrP and changing needs for treatment should be anticipated by the treating endocrinologist. • If there are changes in doses of calcium or activated vitamin D, recommend repeating albumin-corrected calcium measurement in 4–7 days later. • Serum phosphorus, magnesium and 25(OH)D and 24-h urine calcium should be monitored and maintained in normal reference range.
9. Consensus Statements for Children	• Conventional therapy dosing is based on age. • Age < 4 years: liquid calcitriol (0.02–0.1 μg/kg/day) and supplemental calcium carbonate (40–60 mg/kg/day) divided 3 times daily. • Age 4–10 years: oral calcitriol dose is titrated in increments of 0.25 μg to calcium levels in the low-normal range, along with calcium carbonate 800–1000 mg daily (liquid or chewable tablets), both divided 3–4 times daily. • Age > 10 years are treated with adult doses of calcitriol along with 1000 mg calcium supplements divided 3–4 times daily. • Monitor spot urine for calcium, magnesium and creatinine. • Renal US annually.
10. PTH Replacement in Adults	• Recombinant human PTH (1–34) (teriparatide) may be given by sc injection or pump if available (not FDA approved) in doses of 0.34–1.4 μg/kg/day either continuously (by pump) or in twice daily doses (for injection). • Correct vitamin D deficiency (25(OH)D < 25 nmol/L) or insufficiency (25(OH)D 25–75 nmol/L). • Palopegteriparatide (TransCon PTH, TCPTH) in adults (approved by EMA and FDA) – titration of dosing from an initial dose of 18 μg sc daily a. If albumin corrected serum calcium is below the target range – increase palopegteriparatide by 3 μg every 7 days - Before 7 days – increase calcium and activated vitamin D b. If albumin corrected serum calcium is normal – continue palopegteriparatide to day 7 - At day 7 – decrease activated vitamin D + increase palopegteriparatide by 3 μg daily - If not on active vitamin D, then decrease calcium by 1500 mg daily + increase palopegteriparatide by 3 μg

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Table 1 (*continued*)

c. If albumin-corrected serum calcium is high – stop or decrease activated vitamin D

- If not on activated vitamin D, then decrease calcium
- If off activated vitamin D and calcium, then decrease palopegteriparatide

Sick Day or Missed Dose of PTH Therapy:

- Check serum calcium and albumin preferably fasting or with symptoms - monitor daily for 3–5 days under medical supervision.
- PTH (1–34) (teriparatide) – take missed dose if <12 h from scheduled time and check serum calcium and albumin and take extra dose of PTH if necessary.
- Palopegteriparatide – do not take the missed dose, check albumin corrected serum calcium and take extra calcium carbonate or citrate 600 mg BID, TID, or four times a day (QID) as needed with physician supervision.

PTH Therapy Cessation with Initiation of Conventional Therapy

- Careful tapering of PTH with gradual up titration of conventional therapy and close monitoring to avoid hypocalcemia or hypercalcemia is required to ensure a smooth transition to conventional therapy. The following steps are recommended:
  a. Gradually reduce the dose of PTH (1–34) (teriparatide) over several days, as abrupt cessation may lead to hypocalcemia.
  b. Monitor serum calcium levels daily during the transition, particularly in patients with unstable calcium levels.
  c. Anticipate higher requirements for conventional therapy compared to pre-PTH therapy due to activated bone remodelling.
  d. Palopegteriparatide can be tapered off and conventional therapy can be reintroduced and titrated with daily monitoring of serum albumin-corrected calcium.

Best practice – goals of therapy

- Relieve symptoms while avoiding hypercalcemia and symptomatic hypocalcemia (serum ionized Ca <1.00 mmol/L).
- Aim for a normal urine calcium.
- Aim for a normal serum phosphorus.
- Aim for a normal serum magnesium.
- Aim to preserve renal function.
- Avoid renal stones and/or nephrocalcinosis.
- Aim to improve QoL.

Promising new therapies are currently in phase 3 trials and data regarding efficacy and safety is expected shortly with PTH1R agonists and calcilytic therapy.

Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED) Autoimmune Regulator Gene (AIRE1) Bone Mineral Density (BMD) Calcium-Sensing Receptor (CASR) Coloboma, Heart defects, Atresia choanae, Retardation of growth and development, Genital and Ear anomalies (CHARGE) Chronic Kidney Disease (CKD) Computed Tomography (CT) Dual-energy X-ray Absorptiometry Trabecular Bone Score (DXA TBS) Estimated Glomerular Filtration Rate (eGFR) Electrocardiogram (EKG) Food and Drug Administration (FDA) Hypoparathyroidism, Deafness, Renal Dysplasia (HDR) Kearns-Sayre Syndrome (KSS) Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like Episodes (MELAS) Musculoskeletal (MSK) Nasogastric (NG) Proton Pump Inhibitor (PPI) Parathyroid Hormone (PTH) Parathyroid Hormone-related Protein (PTHrP) Quality of Life (QoL) Tubulin-Specific Chaperone E (TBCE) Ultrasound (US) Upper Respiratory Infection (URI) Urinary Tract Infection (UTI).

narrative reviews (see Supplementary File 1). Structured search strategies combined both controlled vocabulary (e.g., MeSH terms in MEDLINE, EMTREE terms in Embase) and free-text keywords to maximize sensitivity and comprehensiveness. Searches were restricted to human studies, English language publications, and excluded conference abstracts, case reports, editorials, letters, and commentaries.

Search strategies combined terms for the underlying condition (e.g., "hypoparathyroidism"), and domain-specific concepts, including etiology, diagnosis, (e.g., "PTH assay," "parathyroid hormone measurement"), standard of care treatment (e.g., "calcitriol," "active vitamin D analogs"), complications and organ effects (e.g., "nephrocalcinosis," "fractures," "kidney failure"), management in special populations (e.g., "pediatric hypoparathyroidism," "pregnancy," "lactation"), and emerging therapies (e.g., "PTH1 receptor agonist," "calcilytic therapy").

Titles and abstracts of retrieved records were independently screened for eligibility by two reviewers (H.A. and D.A.). Full-text articles of potentially relevant studies were then independently assessed to determine inclusion. Discrepancies between reviewers were resolved through discussion to reach consensus.

- **Inclusion Criteria:** Studies were selected based on their relevance, methodological rigor, and contribution to understanding best practices. The narrative reviews updated findings from the three systematic review conducted by the International Task Force [4,9], noting that no major new studies had been published in the past 2 years. This justified the use of narrative reviews tailored to each domain by the respective expert groups.
- **Synthesis:** Each section of the narrative review was updated with a focus on new knowledge and the development of current best practice recommendations.

4. Expert consensus approach

This structured approach included multiple phases to ensure comprehensive and robust conclusions, as detailed below:

1. **Expert Identification and Selection**: An International Panel of experts in HypoPT was convened, consisting of clinicians, researchers, and specialists with experience in the diagnosis and treatment of HypoPT in adults and/or children. Experts were identified and invited by the Summit co-chairs (A.A.K and M.L.B) and selected based on their credentials, clinical and research experience, publications and contributions to the field. Patient perspective was incorporated throughout the development of the best practice recommendations with the two representatives of the HypoPARAthyroidism Association (M.R, P·K). See Supplementary table 1 for team composition.
2. **The International Expert Panel structure**: The panel was divided into 9 teams focusing on specific domains including diagnosis, management, and monitoring of HypoPT. Each team conducted

narrative reviews to update evidence and developed best practice recommendations addressing common clinical challenges.

3. **Virtual Meetings and Feedback:** The purpose of the meetings was to establish the learning objectives and define the key questions to be addressed in the best practice recommendations, establish standards for best practice, discuss progress, and finalize the recommendations to be presented at the global consensus conference. Four virtual meetings were held on January 27, March 9, April 6, and May 4, 2024 to facilitate discussion amongst panel members
4. **Global Meeting and Presentation of current evidence:** The global consensus meeting was held prior to the Endocrine Society Annual Meeting on May 31, 2024 at which time each team of international experts presented the summary of advances in their respective area of review as well as best practice recommendations. These were open to discussion and critique by all panel members. Best practice recommendations were modified to reflect consensus amongst the International Expert Panel. Consensus statements were approved by the International Panel of Experts addressing advances in the diagnosis, management, and monitoring of HypoPT. While no formal voting occurred, agreement was reached through iterative discussions.
5. **Consensus Circulation:** Following the global consensus meeting, the document summarizing the best practice consensus statements was circulated three times (dates June 28, July 19, and October 4, 2024) amongst the International Expert Panel for their review and approval and all recommendations were incorporated into the final approved best practice recommendations manuscript. This manuscript underwent 3 rounds of circulation on January 1 and February 1, and February 18, 2025, allowing the International Expert Panel to provide feedback and suggest further modifications. The iterative nature of this process was designed to refine the recommendations based on collective expert insights.
6. **Consensus Gathering:** To ensure a robust consensus, the International Expert Panel engaged in discussions throughout the process. Feedback was integrated from all contributors to facilitate transparent collaborative decision-making leading to evidence-based, best practice consensus statements and recommendations.

4.1. Section 1: approach to the etiology of HypoPT

4.1.1. Etiology and prevalence of HypoPT

Chronic HypoPT is defined as hypocalcemia accompanied by an undetectable, low, or inappropriately normal intact PTH level on two occasions at least two weeks apart [8]. Prevalence of the disease ranges from 6.4 to 37 per 100,000 [11]. Incidence ranges from 0.8 per 100,000 (Denmark) to 2.6 per 100,000 (India) [11]. HypoPT is due to post-surgical (~75 %) and nonsurgical (~25 %) etiologies in adults.

4.1.2. Nonsurgical HypoPT

Nonsurgical HypoPT may be due to genetic or autoimmune causes which are the most common causes of nonsurgical HypoPT. Genetic testing is advised for patients with idiopathic HypoPT, particularly those with syndromic features, positive family history, or age $\leq$ 40 years [7,8,12]. There are a number of causes for syndromic HypoPT including APECED, which is commonly associated with additional autoimmune disorders, most notably mucocutaneous candidiasis, adrenal insufficiency and gastrointestinal (GI) dysfunction [7]. Other genetic causes of HypoPT are listed in (Table 2). A detailed history and physical assessment as well as a lab profile is helpful in determining the presence of a genetic or autoimmune cause for HypoPT.

Ab against NLRP5 (NACHT Leucine-rich-repeat protein 5) have been associated with HypoPT in APECED [13]. The presence of a Calcium Sensing Receptor (CaSR) Ab can impact parathyroid function and requires further evaluation [13]. Currently there are no clinically validated gold standard assays for CaSR Ab.

4.1.3. Postsurgical HypoPT

Chronic postsurgical HypoPT is more likely to develop if the intact PTH level is <10 pg/ml (<1.05 pmol/L) in the first 12–24 postoperative hours [8,12]. The diagnosis of chronic HypoPT is confirmed if HypoPT is present 12 months or longer following neck surgery. Causes include devascularization of the parathyroid pedicle(s), damage to parathyroid parenchyma via hematoma or bruising, or inadvertent removal. Surgical experience and training make this less likely due to the acquired ability to easily distinguish parathyroid glands (glands (which are normally 30–50 mg in weight and 1 × 3 mm in size) from surrounding fat, thymus, lymph node or thyroid tissue. Risk factors for the development of postsurgical HypoPT include Graves' disease due to increased thyroid blood flow with subsequent ligation of vessels having a more profound effect on the perfusion of the glands. Concomitant central neck dissection requires greater exploration and resection of surrounding tissue in the compartments containing these lymph nodes, increasing risks of disruption of the parathyroid vascular supply. Children have smaller glands of differing color dependent on age and a prominent thymus, and/or enlarged and/or reactive lymph nodes all of which can make the identification and preservation of tiny parathyroid glands more technically challenging. Patients undergoing thyroid surgery are at risk as the vascular supply to the parathyroids can be compromised or all parathyroid tissue may be inadvertently removed. When a single parathyroid adenoma is removed, transient HypoPT may occur until the normal, suppressed parathyroid glands become active.

Several studies have reported that parathyroid function can recover even after many years of HypoPT, although this remains a rare occurrence [14–17]. For example, patients initially diagnosed with permanent post-surgical HypoPT have been shown to regain parathyroid function 8 to 16 years later, with normalization of serum calcium and PTH levels and reduction or discontinuation of calcium and vitamin D supplementation [18]. This phenomenon highlights the importance of ongoing monitoring and clinical vigilance in patients receiving both conventional therapy and PTH replacement.

4.2. Section 2: current challenges in diagnosis of HypoPT

In making the diagnosis and in management of chronic HypoPT, serum calcium is accurately assessed by using either albumin-corrected calcium calculations or direct ionized calcium measurements. Formulas to adjust for albumin may have limitations, especially in CKD and severe acid-base disturbances [7].

Commonly used formulas for calcium adjusted for albumin are below:

$$\text{adjusted calcium (mg/dL)} = \text{total calcium (mg/dL)} + 0.8\ [(4.0 - \text{albumin (g/dL)}]$$

$$\text{adjusted calcium (mmol/L)} = \text{total calcium (mmol/L)} + 0.02\ \text{x}\ [40\ \text{g/L} - \text{patient albumin (g/L)}\ ].$$

Table 2
Genetic causes of hypoparathyroidism [7].

Category	Disorder	Inheritance	Chromosomal locus	Genetic alteration	OMIM phenotype number (#)	Abnormalities associated with chronic hypoparathyroidism
Disorders of Parathyroid Gland Formation	DiGeorge Syndrome Type 1 (DGS1)	AD	22q11.2	del. (*TBX1*)	188400	Thymic hypoplasia with immune deficiency, conotruncal heart malformations, cleft palate, dysmorphic facies, short stature, developmental delay, gastrointestinal issues, thrombocytopenia, cognitive impairment, psychiatric disorders
	DiGeorge Syndrome Type 2 (DGS2)	AD	10p14-p13	del. (*NEBL*)	601362	Similar to DGS1 with cardiac/parathyroid anomalies
	CHARGE Syndrome	AD	7q21.11 / 8q12.2	*SEMA3E* / *CHD7*	214800	Choanal atresia and malformations of the heart, inner ear (deafness), and retina (coloboma), poor growth, genital hypoplasia
	Hypoparathyroidism-Sensorineural Deafness-Renal Dysplasia (HDR)	AD	10p14	*GATA3*	146255	Deafness, renal dysplasia
	Hypoparathyroidism-Retardation-Dysmorphism Syndrome (HRDS/Sanjad-Sakati)	AR	1q42.3	*TBCE*	241410	Growth retardation, dysmorphic facial features, developmental delay
	Kenny-Caffey Syndrome Type 1 (KCS1)	AR	1q42.3	*TBCE*	244460	Severe proportionate short stature, cortical thickening with medullary stenosis of the tubular bones, craniofacial abnormalities, eye abnormalities
	Kenny-Caffey Syndrome Type 2 (KCS2)	AD	11q12.1	*FAM111A*	127000	Similar to KCS1, however, patients with AD KCS2 have normal intelligence
	Gracile Bone Dysplasia (GCLEB)	AD	11q12.1	*FAM111A*	602361	Gracile bones with thin diaphyses, premature closure of basal cranial sutures, microphthalmia
	Kearns-Sayre Syndrome (KSS)	Mitochondrial		mtDNA	530000	Ophthalmoplegia, pigmentary degeneration of the retina, cardiomyopathy
	Pearson Marrow-Pancreas Syndrome	Mitochondrial		mtDNA	557000	Bone marrow failure (altered hematopoietic precursors), diabetes, malabsorption
	Mitochondrial Encephalomyopathy with Lactic Acidosis and Strokes (MELAS)	Mitochondrial		mtDNA	540000	Myopathy, encephalopathy, lactic acidosis, stroke-like episodes, seizures, cortical blindness, hemianopsia, episodic vomiting
	Mitochondrial Trifunctional Protein Deficiency Syndrome (MTPD)	AR	2p23.3	*HADHA*	609015	Hypoglycemia, cardiomyopathy, myopathy with hypotonia, episodic vomiting, liver disease, peripheral neuropathy
	Medium-chain acylCOA dehydrogenase deficiency (ACADMD)	AR	1p31.1	*ACADM*	201450	Hypoglycemia, lethargy, vomiting, fatty infiltration of liver, seizures, developmental delay if undiagnosed or untreated
	Long-chain 3-hydroxyacylCoA dehydrogenase deficiency (LCHAD)	AR	2p23.3	*HADHA*	609016	Recurrent hypoglycemia, rapidly progressive myopathy, cardiomyopathy, hepatomegaly, cholestatic liver disease, fatty liver, hepatic failure
	Smith-Lemli-Opitz syndrome (SLOS)	AR	11q13.4	*DHCR7*	270400	Multiple congenital malformations (microcephaly, abnormal genitalia and nostrils), mental retardation, adrenal insufficiency
Disorders of Parathyroid Hormone Secretion	Familial Isolated Hypoparathyroidism Type 2 (FIH2)	AD/AR	6p24.2	*GCM2*	618883	Seizures, hypocalcemic
	Hypoparathyroidism X-linked recessive (HYPX)	XLR	Xq27.1	del./ins. (*SOX3*)	307700	–
	Autosomal Dominant Hypocalcemia Type 1 (ADH1)/ Bartter Syndrome Subtype 5	AD	3q13.3-q21.1	*CASR*	601198	Hypomagnesemia, hypercalciuria; possibly associated with Bartter syndrome
	Autosomal Dominant Hypocalcemia Type 2 (ADH2)	AD	19p13.3	*GNA11*	615361	Hypomagnesemia, hypercalciuria
	Familial Isolated Hypoparathyroidism Type 1 (FIH)	AD/AR	11p15.3	*PTH*	146200	Cataracts
Hypomagnesemia Syndromes	Hypomagnesemia 1, Intestinal (HOMG1)	AR	9q21.13	*TRPM6*	602014	Hypercalciuria, nephrocalcinosis
	Hypomagnesemia 2, Renal (HOMG2)	AD	11q23.3	*FXYD2*	154020	Hypocalciuria
	Hypomagnesemia 3, Renal (HOMG3)	AR	3q28	*CLDN16*	248250	Progressive loss of kidney function, amelogenesis imperfecta
	Hypomagnesemia 4, renal (HOMG4)	AR	4q25	*EGF*	611718	Mild to moderate psychomotor retardation
	Hypomagnesemia 5, Renal (HOMG5)	AR	1p34.2	*CLDN19*	248190	Progressive renal failure, nephrocalcinosis, and severe visual impairment, amelogenesis imperfecta

(*continued on next page*)

Table 2 (*continued*)

Category	Disorder	Inheritance	Chromosomal locus	Genetic alteration	OMIM phenotype number (#)	Abnormalities associated with chronic hypoparathyroidism
	Hypomagnesemia 6, renal (HOMG6)	AD	10q24.32	*CNNM2*	613882	–
	Gitelman Syndrome (GTLMNS)	AR	16q13	*SLC12A3*	263800	Hypokalemic metabolic alkalosis, hypocalciuria
	Episodic Ataxia Type 1 (EA1)	AD	12p13.32	*KCNA1*	160120	Spells of incoordination and imbalance, often associated with progressive ataxia
	Hypomagnesemia, hypertension, and hypercholesterolemia syndrome	Mitochondrial		mtDNA	500005	Hypertension, hypercholesterolemia
	Hypomagnesemia, seizures, and mental retardation 1 (HOMGSMR1)	AD/AR	10q24.32	*CNNM2*	616418	Seizures, delayed psychomotor development
	Hypomagnesemia, seizures, and mental retardation 2 (HOMGSMR2)	AD	1p13.1	*ATP1A1*	618314	Significantly impaired intellectual development
Damage to Parathyroid Glands	Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED/APS1)	AD/AR	21q22.3	*AIRE*	240300	Chronic mucocutaneous candidiasis, adrenal insufficiency, autoimmune diseases (e.g., celiac disease, vitiligo, type 1 diabetes, hypogonadism)
	Other autoimmune polyendocrine syndromes	–	–	(Polygenic, HLA-related)	–	Association of organ-specific autoimmune diseases

Abbreviations: AD = Autosomal Dominant, AR = Autosomal Recessive, mtDNA = mitochondrial DNA; del./ins.: deletion/insertion.
Adapted from Mannstadt et al. JBMR 2022. (Mannstadt, M., Cianferotti, L., Gafni, R.I., Giusti, F., Kemp, E.H., Koch, C.A., Roszko, K.L., Yao, L., Guyatt, G.H., Thakker, R.V., Xia, W. and Brandi, M.-L. (2022), Hypoparathyroidism: Genetics and Diagnosis. J Bone Miner Res, 37: 2615–2629. https://doi.org/10.1002/jbmr.4667).

Table 3
Prevalence of complications of HypoPT in adult patients from a recent systematic review and meta-analysis conducted by the International Task Force on Hypoparathyroidism [4].

Complication	Adjusted HR/OR (95 % CI)
Nephrocalcinosis/nephrolithiasis	1.88 (1.68–2.12)
Renal insufficiency	3.67 (2.44–5.52)
Cataract	2.13 (1.65–2.75)
Seizures	3.22 (2.51–4.11)
Arrhythmia	1.37 (1.05–1.79)
Ischemic heart disease	1.26 (1.02–1.56)
Depression	1.89 (1.37–2.61)
Infection	2.30 (1.75–3.02)
All-cause mortality	1.80 (1.49–2.17)

Second-generation PTH assays are standard practice. Potential interferences are rare and can affect their accuracy. High-dose biotin intake can falsely lower PTH readings, and factors such as human anti-mouse antibodies or rheumatoid factor may also interfere [7]. Biotin interference is specific to assays utilizing biotin-streptavidin binding and alternative testing methods are available when biotin interference is suspected [19–21].

Additional biochemical abnormalities supporting the diagnosis of HypoPT include elevated serum phosphorus, increased fractional excretion of calcium, decreased levels of $1,25(OH)_2D$, and reduced bone turnover markers [22].

The diagnosis of postsurgical HypoPT may be delayed if patients are unaware of the symptoms associated with hypocalcemia [23]. Clinicians should consider measuring serum calcium in patients presenting with neuromuscular irritability, cognitive disturbances, or those at risk due to genetic conditions (see Table 2) [4,23].

Genetic testing is recommended for patients with idiopathic HypoPT. Gene panel testing, encompassing all known candidate genes, is of value. However, a negative result does not exclude a genetic cause due to technical limitations [7]. Isolated autoimmune HypoPT lacks definitive clinical tests and thus should be classified as idiopathic.

4.3. Section 3: target organ effects and quality of life

The complications of HypoPT may be due to the disease itself (e.g., hypocalcemia, PTH deficiency, hyperphosphatemia), and may also be exacerbated by the use of conventional therapy which can further increase serum phosphorus, as well as hypercalciuria and hypercalcemia and contribute possibly to declines in renal function (see Table 3) [4,24,25]. HypoPT is associated with multisystem organ involvement as noted in the recent systemic review and meta-analysis conducted by the International Task Force on HypoPT (Table 4) [4].

4.4. Section 4: conventional therapy: challenges and limitations (children and adults)

4.4.1. Conventional therapy

Conventional therapy consists of oral calcium supplements and active vitamin D in conjunction with dietary recommendations to increase calcium intake (Table 5) [8,26–29]. In Europe, higher doses of active vitamin D are usually prescribed with lower doses of calcium supplementation in comparison to North American practice. We recognize that high doses of calcium supplements may be difficult to tolerate, inconvenient, and add to the pill burden [30–34]. However, calcium supplements are also very effective as phosphate binders. Conventional therapy requires titration of calcium and active vitamin D with individualized therapy aiming to alleviate symptomatic hypocalcemia while keeping urinary calcium excretion and serum phosphorus within the normal range.

Activated vitamin D analogs are required as the 1a-hydroxylation of 25(OH) vitamin D is diminished in the absence of adequate PTH. Active vitamin D increases serum calcium levels and serum phosphorus, as well as the filtered calcium load and urinary calcium levels [8,11]. Calcitriol is commonly prescribed, starting at 0.25 μg per day. If higher doses are required, it can be given at 0.25 μg twice daily. Due to its short half-life, it is preferred to administer in divided doses during the day [8]. In postsurgical HypoPT with severe hypocalcemia higher doses may be required depending on the severity of hypocalcemia following neck surgery (e.g. calcitriol 0.25–0.5 μg twice daily) [35] (Table 5). The elimination half-life of calcitriol from serum is 3–6 h. Alfacalcidol, is initiated at 0.5 μg per day. For alfacalcidol the onset of activity is 6 h, as it requires 25-hydroxylation. The 1,25 (OH)2 D formed reaches

Table 4
Multisystem complications of hypoparathyroidism.

Complication	Clinical presentation	Comments
Renal [41,102]	Hypercalciuria, nephrocalcinosis/ nephrolithiasis, renal failure	Preservation of renal function is a critical treatment goal; risk increases with age, disease duration, hypercalcemia and hypercalciuria are risk factors
Neurologic/ Psychiatric [25,103,104]	Seizures (generalized and focal), Intracranial calcifications (basal ganglia, cerebellum, thalamus)	The prevalence of intracranial calcifications is 25–78 %. They are associated with longer disease duration, hyperphosphatemia, and extraskeletal calcification at other sites (e.g.: lens with the presence of cataracts). Intracranial calcifications do not appear to correlate with neurological symptoms.
Reduced Quality of Life (QoL) [30,44,45,105]	Persistent cognitive issues ('brain fog') [45,106], depression, MRI data: reduced volume of the hippocampus area or the size of the thalamus	QoL may be impaired even with normal calcium; QOL may reflect direct CNS effects from PTH deficiency. Age, gender, etiology, laboratory values, medication and disease duration all appear to influence QoL. Depression is more prevalent in HypoPT [4]
Skeletal [103,107]	Low bone turnover, high BMD values (above healthy, age-matched controls). CNHR data: 35 % of postmenopausal women had osteoporosis by BMD or prior fragility fracture, and 4 % had both. Three of 9 men ≥50 years had osteoporosis by BMD or fragility fracture criteria (33.3 %).	Monitoring bone health is critical, especially in postmenopausal women and older men (≥50 years) with HypoPT, as this population demonstrates a high prevalence of osteoporosis by BMD and/or prior fragility fracture. However, the relationship between BMD and fracture risk in HypoPT remains poorly understood and long-term prospective data is required to understand the relationship between BMD and fracture risk in HypoPT. While some data suggest that osteoporosis by BMD criteria may not be more prevalent than in age-matched controls, individuals with nonsurgical HypoPT appear to have a higher risk of vertebral fractures, suggesting compromised bone quality despite preserved bone density. In contrast, findings remain inconsistent across studies, particularly in postsurgical HypoPT. In a large cohort study of patients with HypoPT matched to eucalcemic controls, vertebral fracture risk was higher (HR 1.55; 95 % CI: 1.12–2.14), while femoral fracture risk was lower (HR 0.70; 95 % CI: 0.50–0.98) [108,109]. Another study involving 44 women with postsurgical HypoPT reported a higher proportion of Genant grade II and III vertebral fractures (11.4 %, 5 out of 44) compared to mostly Genant grade I fractures in the control group (6.8 %, 3 out of 44) [110]. These heterogeneous findings highlight the uncertainty regarding fracture risk in chronic HypoPT.
Cardiac [27,29]	Arrhythmias, prolonged QT interval due to hypocalcemia	QT interval prolongation due to hypocalcemia appears to be both a function of the actual serum calcium level and its rate of decline. Ischemic heart disease is more prevalent in HypoPT.
Ophthalmic [28]	Increased cataract incidence, earlier need for cataract surgery (younger age)	Cataracts often non-nuclear; related to disease duration and brain calcification
Infections and Immune Function [29,30]	Frequent infections in respiratory, urinary tract, and urogenital system	Immune effects may reflect inadequate levels of PTH, 1,25(OH)2D, or hypocalcemia; immune lineage cells have PTH1 receptors, it is possible that the lack of PTH is a predisposing factor for immune dysfunction.

Table 5
Conventional therapy [8].

Medication	Dose	Comments/half-life
Calcium carbonate or calcium citrate	Ranges from 500 to 3000 mg three times daily preferably with meals to enhance phosphate binding effects	Calcium citrate preferred in presence of proton pump inhibitor (PPI) use
Vitamin D3 (cholecalciferol)	1000 to 100,000 IU daily based on 25(OH)D level	4–6 h plasma half-life
Vitamin D2 (ergocalciferol)	50,000 IU weekly to daily based on 25(OH)D level	4–6 h plasma half-life
Calcitriol	0.25–3 μg daily total dose administered in divided doses	5–8 h plasma half-life
Alfacalcidol	0.5–6 μg daily total dose administered in divided doses	3–6 h plasma half-life
Thiazide diuretics (Hydrochlorothiazide)	25–100 mg daily	6–12 h plasma half-life

Table 6
Monitoring frequency.

Testing	Frequency	Comment
Ca, Albumin, Creatinine /eGFR, Phosphorus, Magnesium	3–12 months	Within 7–10 days of dose change Note timing of calcium check (pre/post- calcium intake)
PTH		Only in first year post-op to establish chronicity
25(OH)D	6–12 months	At 3 months if insufficient Limited value of measuring 1,25 $(OH)_2D$
24 h urine calcium and creatinine	6–24 months	Monitor for presence of hypercalciuria

maximum serum concentrations after 12 h due to the conversion steps occurring in the liver [36].

Ensuring adequate levels of 25(OH)D is critical, even when activated vitamin D is used, as 25(OH)D provides the substrate for tissue-specific production of $1,25(OH)_2D$. Vitamin D supplementation is provided in order to achieve a normal 25 (OH)D level (75–125 nmol/L; 30–50 ng/mL). Supplementation with cholecalciferol or ergocalciferol is titrated

and the doses required may range from 1000 IU of cholecalciferol daily to ergocalciferol 50,000 IU once a week or more frequently if required to achieve a normal 25(OH)D level. High-dose vitamin D alone is occasionally used but can lead to wide fluctuations in serum calcium levels and is not advised.

Magnesium deficiency must also be addressed, as the absence of PTH can impair magnesium uptake in the distal convoluted tubule. Both magnesium excess and deficiency are associated with functional HypoPT [37,38].

Thiazide diuretics lower urinary calcium excretion by enhancing calcium reabsorption in the distal tubule. Doses for hydrochlorothiazide range from 25 to 100 mg/day and may cause side effects including postural hypotension. Treatment may necessitate potassium and magnesium supplementation. Optimal efficacy requires a low-sodium diet, often with dietary guidance from a dietitian. Additionally, studies have shown a slight increase in the incidence of nonmelanoma skin cancer with thiazide diuretic use [39], prompting some experts to recommend sunscreen for patients.

Managing hyperphosphatemia with conventional therapy can be challenging. While reducing dietary phosphate intake is a reasonable approach, it is often difficult to achieve due to the widespread presence of phosphate in many foods. Additionally, evidence supporting the effectiveness of dietary restriction is limited. Encouraging a low-phosphate diet, includes limiting sources such as dairy, beans, meat, nuts, seeds, grains, and processed foods such as boxed and canned foods which contain phosphorus as food additives. These additives can increase phosphorus content by up to 41 %, and should be avoided [40]. Calcium supplements taken with meals can help reduce serum phosphate by also serving as a phosphate binder [8,27]. For refractory cases of hyperphosphatemia, such as those associated with a high calcium-phosphate product or soft tissue calcifications, phosphate binders may be considered. However, the evidence supporting their use in managing hyperphosphatemia in HypoPT is sparse.

Hypercalciuria is a common complication in HypoPT, arising from an increased filtered load of calcium in the absence of PTH-mediated calcium reabsorption in the kidneys. Correcting hypercalciuria may reduce the risk of nephrocalcinosis and nephrolithiasis. These renal complications are seen in approximately one-third of HypoPT patients and significantly elevate the risk of chronic kidney disease by 3-fold in post-surgical cases and 6-fold in nonsurgical cases [41,42]. In the presence of autosomal dominant hypocalcemia (ADH) hypercalciuria is often exacerbated with calcium and active vitamin D administration [43]. It is recommended to maintain albumin-corrected serum calcium levels in the lower half of the normal range or slightly below normal while avoiding symptomatic hypocalcemia in order to minimize the risk of hypercalciuria which increases with conventional therapy. While this carefully balanced strategy is effective for some patients on conventional therapy, achieving and maintaining a low normal serum calcium with a normal urine calcium can be challenging in the presence of inadequate PTH levels.

The frequency of monitoring in HypoPT depends on the patient's stability. A survey of clinicians experienced in managing HypoPT revealed that 70 % of cases adhere to the monitoring schedule outlined in Table 6. This includes assessing serum calcium, albumin, phosphorus, and magnesium, and eGFR every 3–12 months [10]. For unstable patients, serum calcium should be rechecked within several days following any significant changes in the pharmacologic intervention. [8]. When interpreting serum calcium results, it is important to consider the timing of calcium supplements or active vitamin D administration relative to the blood draw, as this can affect serum calcium levels. Additionally, a single blood test may not reflect fluctuations in calcium levels. Monitoring 24-h urine calcium and creatinine is also essential and should be performed every 6–24 months [8].

While conventional therapy is effective in raising serum calcium levels, this approach has several limitations. Conventional therapy often does not consistently maintain stable serum calcium levels and requires

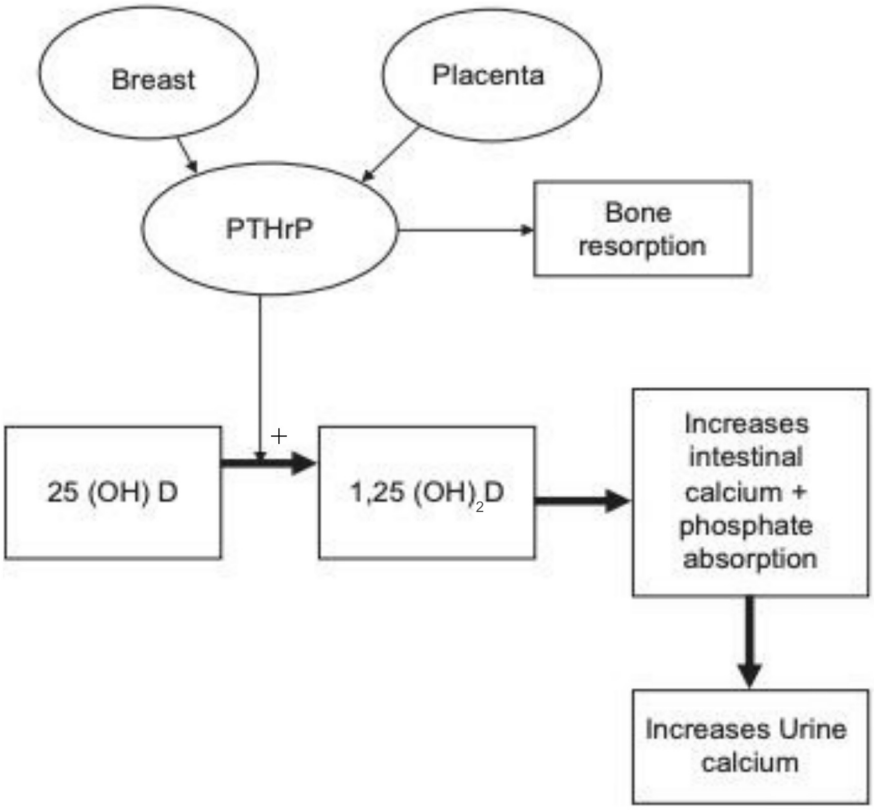

Fig. 1. Calcium homeostasis during pregnancy.
(Reproduced with permission from Khan et al. (2019) [51].)

close monitoring to accommodate changes in dietary calcium intake or physical activity. Additionally, conventional therapy may increase urinary calcium and/or serum phosphorus, which may elevate the risk of renal complications and ectopic calcifications. Conventional therapy often fails to fully alleviate symptoms or significantly improve QoL [44–46]. The regimens can be highly burdensome for patients with large doses of calcium supplements and active vitamin D taken multiple times during the day. High pill burden, complex dosing schedules, and side-effects can impact QoL [12,30] and contribute to poor treatment adherence [46,47].

4.4.2. Acute hypocalcemia

Acute hypocalcemia can be a life-threatening emergency and requires urgent intervention. The presentation and severity of symptoms depend on the absolute serum calcium level, the rate of its decline, and the duration of hypocalcemia. Calcium therapy (IV and oral) is generally indicated if severe symptoms are present (such as seizure, laryngospasm or severe tetany) but may also be needed when albumin-corrected serum calcium falls below 7.5 mg/dL (1.9 mmol/L) [2,48] although no universally accepted threshold exists. IV calcium is warranted, regardless of the serum calcium level, in the presence of complications including a prolonged corrected QT (QTc) interval on EKG (>0.45 s in men, >0.47 s in women), laryngospasm, bronchospasm, seizures, or tetany. It is further indicated for patients unable to take oral supplements or with a history of seizures. One gram of IV calcium gluconate (90 mg elemental calcium) is the preferred treatment due to its lower risk of soft tissue necrosis compared to an infusion of calcium chloride (272 mg elemental calcium) should extravasation occur. Treatment begins with an IV bolus of 90–180 mg elemental calcium administered over 10–20 min via a durable and secure IV with a large bore needle and with cardiac monitoring. Rapid infusion of IV calcium can result in cardiac arrest. Following bolus doses of IV calcium, a slower rate of continuous IV calcium infusion and oral calcium and calcitriol therapy can be initiated [8].

The infusion is prepared by mixing 10 ampules (900 mg elemental calcium) into 1 l of 5 % dextrose or normal saline. Bicarbonate or phosphate should not be added to the solution, as they can form insoluble calcium salts. The infusion is started at a rate of 100 mL/h and adjusted based on serum calcium levels, albumin corrected serum calcium (or preferably ionized calcium if available). The serum calcium can be monitored every 6 h and then daily until stable, with the goal of restoring calcium levels to just below the normal reference range. An IV dose of 15 mg/kg elemental calcium over 4–6 h can increase serum calcium by approximately 0.5–0.75 mmol/L [8]. Concurrently, active vitamin D metabolites are introduced. Oral calcitriol is typically started at 0.25–0.5 μg twice daily, or alternatively, alfacalcidol 0.5μg daily may be used. If hypomagnesemia is present, it must be corrected to ensure effective treatment of hypocalcemia.

4.5. Section 5: HypoPT and pregnancy: maternal and fetal considerations

4.5.1. Calcium homeostasis in pregnancy

Changes in the calcium-regulating hormones during pregnancy are designed to meet the needs of the developing fetal skeleton, while preserving the integrity of the maternal skeleton. Calcium, phosphorus, and magnesium are delivered against a concentration gradient from the placenta to the fetus [49]. However, the maternal ionized or albumin-adjusted calcium levels remain stable and normal during pregnancy in the euparathyroid woman [49]. PTH-related protein (PTHrP) produced by the placenta and breast increases between 3 and 13 weeks of gestation [49]. This increase in PTHrP enhances the conversion of 25(OH)D to 1,25(OH)$_2$D [50–53] (Fig. 1). Endogenous 1,25(OH)$_2$D enhances intestinal calcium and phosphorus absorption from the maternal gut. These rises in PTHrP and 1,25(OH)$_2$D may be sufficient to meet the increasing needs of calcium and phosphorus of the developing fetal skeleton. However, in some women with HypoPT these increases in PTHrP and 1,25(OH)$_2$D may not be sufficient and an increase in conventional therapy with calcium and activated vitamin D analogues may be required. Yet, in others, a reduction in the dose may be necessary. It is not possible to predict the dose requirements for calcium and active vitamin D in pregnancy and close monitoring of serum calcium adjusted albumin, and phosphorus is advised during pregnancy with lab tests every 3–4 weeks. During pregnancy intravascular volume expansion results in hemodilution and a reduction in the concentration of albumin. Therefore, accurate calcium measurement requires either a direct ionized calcium or albumin-corrected level [49]. During lactation, estrogen withdrawal leads to an increase in bone resorption in addition the production of large amounts of PTHrP from the breasts lead to increases in serum calcium and endogenous 1,25dihydroxyvitamin D necessitating further modification in the doses of conventional therapy required. Weaning may result in a dramatic decline in PTHrP and also requires close monitoring with adjustments made to the doses of conventional treatment.

4.5.2. Pregnancy complications

Retrospective studies have reported an increased incidence of comorbidity including the development of diabetes, chronic kidney disease, pre-eclampsia, and PROM during pregnancy in women with HypoPT [54–58] (Fig. 2). These complications may be attributable to HypoPT due to fluctuations in serum calcium levels; however, a causal relationship cannot be confirmed without randomized controlled studies.

4.5.3. Preconception considerations

Women with HypoPT can proceed with pregnancy and should be informed about the risks of hyper- and hypocalcemia and the need for close monitoring. The healthcare provider needs to be informed about the pregnancy as soon as possible to enable close monitoring. During

Maternal Serum Calcium	Fetus	Mother
High Maternal Ca^{+2}	Hypoparathyroidism, polyhydramnios, and neonatal seizures	Hypercalciuria and kidney stones
Low Maternal Ca^{+2}	Hyperparathyroidism, increased bone resorption, intrauterine fragility fractures, subperiosteal bone resorption, osteitis fibrosa cystica, and respiratory distress	Miscarriage, preterm labor, seizure, and arrhythmia

Fig. 2. Reported maternal and fetal adverse events in Hypoparathyroidism.
(Reproduced with permission from Ali et al. (2021) [111].)

pregnancy planning, it is important to target a serum calcium level just below or in the low reference range. Treatment adjustments should be made before conception to ensure stable serum calcium levels. PTH therapy should be switched to conventional therapy due to the lack of safety data with PTH therapy, and thiazides should be discontinued before pregnancy. For genetic forms of HypoPT, the risk of transmission to the offspring should be discussed. Counselling should include discussion of the role of pre-implantation genetic testing.

4.5.4. Monitoring during pregnancy and lactation

Pregnant women with HypoPT should be educated regarding the signs and symptoms of hypo and hypercalcemia as well as its management. Monitoring should involve a multidisciplinary team, including endocrinologists, obstetricians, and neonatologists. Biochemical monitoring is recommended every 2–4 weeks [1,8,59] and following dose changes within 4–7 days. Neonatal surveillance with serum calcium measurements in the first days of life is recommended, especially if the baby is lethargic, irritable, or showing signs of failure to thrive [59].

Close follow-up is also required just after delivery and during lactation. It is important to notify the endocrinologist regarding plans for weaning due to the risk of hypocalcaemia.

4.5.5. Management during pregnancy and lactation

It is recommend to maintain albumin-corrected serum calcium level in the low normal to mid normal reference range with normal serum phosphorus, magnesium and 25(OH)D. Avoidance of maternal hypo- and hypercalcaemia is advised due to the complications listed in Fig. 2 [1,8,59].

4.6. Section 6: PTH and PTH analogues in children

HypoPT in children usually has a genetic etiology [22,60]. For a child with new-onset HypoPT, determining the underlying cause is critical as it alerts the treating physician to the possibility of the potential emergence of comorbidities, such as adrenal insufficiency in APS-1, or electrolyte imbalances, such as hypomagnesemia, and calcifications in the kidney and brain in patients with activating variants in the *CASR* [61,62].

As in other chronic childhood illnesses, the therapeutic approach ultimately focuses on achieving optimal linear growth, weight gain, and bone accrual [22,60,61]. Conventional therapy with calcitriol and calcium supplements in infants and children with HypoPT, under the age of 4 years, includes liquid calcitriol (0.02–0.1 μg/kg/day) along with supplemental calcium carbonate (40–60 mg/kg/day) in 3 divided daily doses. For children ages 4–10 years, the oral calcitriol dose is titrated in increments of 0.25 μg to reach and maintain calcium levels in the low-normal range, along with calcium carbonate 800–1000 mg daily (liquid or chewable tablets), both divided into 3–4 doses daily. Children older than 10 years are treated with adult doses of calcitriol along with 1000 mg calcium supplements, both divided into 3–4 doses daily.

Many pediatric patients with HypoPT are resistant to conventional therapy. Large doses of oral calcitriol and calcium are not effective in APECED, which is often associated with malabsorption. In these individuals large doses of conventional therapy required to achieve a serum calcium close to the normal reference range may lead to calcifications in the kidney with reduced renal function [22,60,61]. For more than a decade, human PTH (1–34) has served as a safe and effective replacement therapy for children and adults who are refractory to conventional therapy [22,60,61,63–69]. PTH given by twice-daily injections normalizes serum and urine calcium in most adults with post-surgical HypoPT [60]. Individualized dosing of subcutaneous PTH (1–34) in children has demonstrated that smaller, more frequent, doses avoids fluctuations in serum and urine calcium which may occur directly after a subcutaneous PTH injection, thus avoiding transient elevations in urine calcium, and increased markers of bone turnover [65,66]. Additionally, PTH injections are associated with normal growth and bone accrual in children with HypoPT [61]. PTH (1–34) delivered through a pump is the method of choice for children whose urine calcium excretion or bone markers are intermittently above the normal range despite 2–3 daily doses of PTH (1–34) injections [66]. Delivery of PTH by pump enabled lower total daily doses for PTH (1–34) (teriparatide) in comparison to twice- daily PTH injections in children with familial hypoparathyroidism (0.32 vs 0.85 μg/kg/d; pump vs BID PTH) [66]. Pump delivery of PTH 1–34 leads to simultaneous normalization of blood and urine calcium and markers of bone turnover in adults with post-surgical HypoPT and in children with APECED or gain-of-function *CASR* variants [65–69].

4.7. Section 7: PTH and PTH analogues in adults

While this section focuses on the use of PTH and its analogues in adults, it is noteworthy that long-term studies involving both adults and children have demonstrated the safety and efficacy of synthetic hPTH (1–34) in HypoPT.

4.7.1. PTH therapy

PTH replacement therapy has been evaluated in HypoPT with synthetic hPTH (1–34) as well as rhPTH (1–84). Synthetic human PTH (1–34) is marketed as teriparatide and is still available on the market. Production of rhPTH (1–84), formerly marketed as Natpara, has been halted by the FDA in September 2019 due to the potential of rubber particles present in solution with chronic use of the pen device [70]. Palopegteriparatide, also known as TransCon PTH, is an inactive prodrug with PTH (1–34) linked to polyethylene glycol that prolongs the half-life of PTH (1–34) to approximately 60 h providing PTH in the physiologic range for 24 h at steady state and has now been approved by both the FDA and the EMA for HypoPT [71,72].

4.7.2. PTH (1–34)

Synthetic human PTH (1–34) (hPTH) given once or twice daily, maintained eucalcemia, reduced urine calcium excretion and increased phosphorus excretion. In controlled studies, synthetic hPTH (1–34) has been found to be safe and effective over a 3-year period in both adults and children [64,73]. Adults and children receiving PTH (1–34) subcutaneous injections have been followed for up to 19 years [60]. In one study hPTH (1–34) use was associated with hypocitraturia, and an increased risk of renal calcification in spite of a lowering of urinary calcium [74]. Administration of hPTH (1–34) by a subcutaneous infusion pump compared to twice-daily injections was evaluated in a randomized cross-over study and led to normalization of serum calcium, with less fluctuation in serum calcium, phosphorus, and magnesium and with reduced urine calcium and normalization of bone turnover markers. The infusion pump also reduced the total daily dose required for hPTH (1–34) in comparison to twice daily hPTH (1–34) injections [65,66]. Although synthetic hPTH (1–34) is not clinically available, similar findings have been observed with rhPTH (1–34) in children and adults [67,68,75–78].

4.7.3. PTH (1–84)

Although rhPTH (1–84) is no longer available, it is briefly discussed here to reflect prior clinical experience with PTH-based therapy. In a 24-week, double-blind, placebo-controlled study, 53 % of patients on rhPTH (1–84) met the primary endpoint compared to 2 % on placebo [79–81]. Conventional therapy requirements decreased however in controlled studies a reduction in urine calcium has not been observed in comparison to conventional therapy. Long term observational studies have shown reductions in urine calcium excretion [80,82]. Serum phosphorus and the calcium/phosphorus product decreased in the REPLACE and extension studies [9,10,79,82], findings not replicated in the fixed- or adjusted-dose studies [80,81]. Renal function was found to be stable [79–82]. Bone turnover markers rose then plateaued, BMD was stable except for decreases noted at the 1/3 radial site, and increased

cortical porosity was observed, however its impact on fracture risk is not known at this time [65–67,81–84].

4.7.4. Palopegteriparatide

Palopegteriparatide, consists of PTH (1–34) linked to a polyethylene glycol moiety [71]. With exposure to physiologic temperature and pH, the linker is slowly cleaved, releasing the PTH molecule and the polyethylene glycol moiety is cleared separately by the kidney [71]. This formulation of PTH (1–34) extends its half-life to approximately 60 h and provides a sustained release of active PTH [71]. In both phase 2 and 3 trials, palopegteriparatide resulted in eucalcaemia, with >90 % of participants being able to achieve independence from conventional therapy at 24 weeks of treatment with demonstrated reductions in urinary calcium excretion and serum phosphorus compared to placebo [85,86].

The PaTHway trial was a phase 3 trial with a 26-week, double-blind, placebo-controlled evaluation in 84 patients randomized to receive once-daily palopegteriparatide (18 μg daily or placebo) co-administered with conventional therapy [86] followed by a 182-week open label extension phase. At week 26, 93 % (57/61) of participants treated with palopegteriparatide achieved independence from conventional therapy. Participants receiving palopegteriparatide showed normalization and greater reduction in urine calcium excretion than those on placebo from baseline to Week 26. Also at week 26, 79 % (48/61) of participants treated with palopegteriparatide vs 5 % (1/21) treated with placebo met the composite primary efficacy endpoint achieving a normal serum calcium adjusted for albumin, independence from conventional therapy, and stable study drug dose for at least 4 weeks before week 26 ($p < 0.0001$).

Patients on palopegteriparatide demonstrated significantly improved QoL a key secondary endpoint as measured by both the Hypoparathyroidism Patient Experience Scale (HPES) domain scores (all scores with p values <0.01) and the 36-Item Short Form Survey Physical Functioning subscale score ($p = 0.035$) compared with placebo. Overall, palopegteriparatide was well tolerated, although some patients did experience mild or moderate adverse events [86]. Treatment-related adverse events in the palopegteriparatide group included injection site reactions (31.1 %), hypercalcaemia (9.8 %), and headache (9.8 %). No

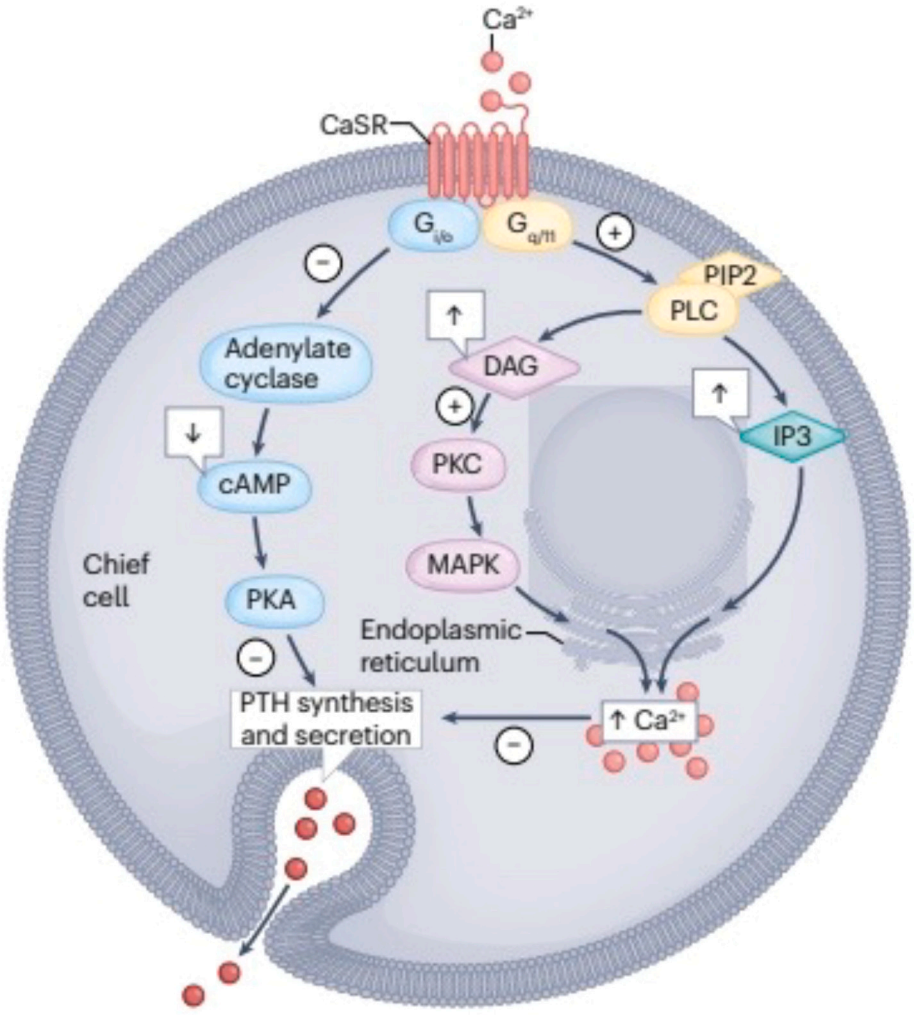

Fig. 3. Parathyroid chief cell physiology.
Calcium binds to the calcium-sensing receptor (CaSR), which is a G-protein-coupled receptor bound to the heterotrimeric guanine nucleotide-binding proteins (G-proteins) Gα11 and Gαq. Calcium bound to CaSR activates Gαi/o which leads to inhibition of adenylate cyclase [112,113]. This binding decreases cAMP production and prevents activation of protein kinase A (PKA), leading to reduced parathyroid hormone (PTH) synthesis and secretion. Activation of CaSR also activates Gαq, through which phospholipase C (PLC) cleaves phosphatidylinositol-4,5-bisphosphate (PIP2) into diacylglycerol (DAG) and inositol 1,4,5-trisphosphate (IP3). IP3 binds to receptors on the endoplasmic reticulum and triggers the release of increased intracellular calcium which subsequently inhibit PTH synthesis and secretion. DAG activates protein kinase C (PKC), which leads to activation of the mitogen-activated protein kinases (MAPK) signaling pathways. Activation of MAPK pathways also results in increased intracellular concentrations of calcium and inhibition of PTH synthesis and secretion.
Reproduced with permission from Khan et al. (2025) [3].

participants withdrew from the trial for drug-related concerns. A post-hoc analysis of the 1-year data from the PaTHway trial showed that palopegteripartide was associated with a statistically significant mean increase in eGFR from baseline of 9.3 ml/min/1.73 m^2 suggesting that palopegteriparatide improves renal function in patients with chronic HypoPT [87]. The underlying mechanism for the increase in renal function requires further study and may reflect both the impact of palopegteriparatide as well as cessation of conventional therapy.

The 3-year results from the phase 2 PaTH Forward trial with data up to week 162 have been presented [88]. This trial was a 4-week randomized, double-blind, placebo-controlled study followed by an ongoing open-label extension period.

At week 162, 91 % of participants achieved the primary end-point; 24-h urinary calcium excretion was maintained within normal range at week 162 with palopegteriparatide [88]. Bone turnover markers initially increased with palopegteriparatide treatment, P1NP peaked at 26 weeks and CTx peaked 12 weeks after initiation of TransCon PTH therapy and thereafter trended downward over 3 years. As measured by T-scores, BMD declined however it remained within the normal range over 162 weeks and stabilized after 26 weeks of treatment. Mean *Z*-scores declined from the high baseline levels reflective of chronic HypoPT towards age-matched and sex-matched norms and remained above zero. Higher baseline BMD T-scores and Z-scores were associated with greater declines in BMD over time [88].

Palopegteriparatide has been demonstrated to be well tolerated, and efficacious and long-term safety and efficacy data continue to be evaluated in the ongoing phase 3 long-term clinical extension trial. Palopegteriparatide has now been approved by both the EMA and the FDA as a treatment for HypoPT. The recommended starting dose for palopegteriparatide is 18 μg daily and the drug is titrated to achieve eucalcaemia.

5. Emerging therapies

5.1. Section 8: PTH1R agonists

Eneboparatide is an injectable long-acting 36 amino acid PTH/PTHrP hybrid peptide with prolonged intracellular signaling despite a short-life. This PTHR1 agonist has been shown to increase serum calcium for >24 h after injection and reduce serum phosphorus in a thyroparathyroidectomized rat model of HypoPT and also had prolonged effects on serum calcium in monkeys [89].

By targeting a specific conformation of the PTH1R, called R0, eneboparatide remains bound to the PTH1R following internalization and continues to signal from intracellular compartments. Eneboparatide is administered as a once-daily injection. In a Phase 2 placebo-controlled open label trial in patients with hypoparathyroidism, 88 % of patients achieved independence from conventional therapy while maintaining serum calcium levels within the target range. Eneboparatide also led to a rapid and sustained decrease in mean 24-h urinary calcium excretion by about 50 % [90]. These effects were associated with reduced symptoms of HypoPT, the prevention of the progressive declines in renal function and the preservation of bone integrity [90].

The FDA granted a fast track designation to Eneboparatide for the treatment of patients affected by HypoPT and multicenter, randomized, placebo-controlled, double-blind, phase 3 CALYPSO trial, designed to evaluate the efficacy and safety of the treatment in adult HypoPT patients, is ongoing [91].

5.2. Section 9: calcilytic therapy

The CaSR's are expressed in high concentrations in parathyroid and renal tubule cells, where they are important regulators of calcium homeostasis (Fig. 3).

Signaling by the CaSR decreases PTH synthesis and secretion and increases urinary calcium excretion to maintain blood calcium in a narrow physiologic range [92,93].

ADH1 is a rare form of HypoPT caused by activating pathogenic or likely pathogenic variants in the *CASR* [94,95]. It is associated with significant hypercalciuria because of two synergistic effects on the parathyroid glands with lowering PTH and on the kidneys with activation of the *CASR*. The hypercalciuria is further exacerbated with conventional treatment, and is even more prominent than in other forms of hypoparathyroidism, leading to nephrolithiasis, nephrocalcinosis, and chronic kidney disease [96].

Calcilytics are negative allosteric modulators of the CaSR that have been shown to increase PTH levels in patients with ADH1 and reduce urinary calcium effectively [97]. In a Phase 2B study, encaleret, an oral investigational calcilytic, was administered to 13 patients with ADH1 [98]. It was well tolerated with no serious adverse events. Encaleret treatment increased PTH robustly into the normal range and normalized the serum calcium. Over 24 weeks of outpatient treatment, the serum calcium remained in the normal range [98]. Importantly, despite higher levels of serum calcium, the average 24-h urine calcium decreased into the normal range and remained normal throughout the study [98]. Encaleret is currently in Phase 3 trials for the treatment of ADH1 (NCT05680818).

Because of its profound effect on renal calcium handling, encaleret is also under investigation in a Phase 2 trial in patients with postsurgical HypoPT (NCT05735015) to assess its ability to decrease urinary fractional excretion of calcium and increase serum calcium in these patients who do not have a *CASR* mutation.

5.2.1. Other novel therapies

A PTH peptide prodrug, MBX 2109 is being evaluated for HypoPTH in phase 2 clinical trials. This molecule has a long half-life of 184–213 h which would support once-weekly administration [3,99].

An oral small molecule PTH1 receptor agonist is currently being evaluated as a potential treatment for HypoPT [100].

6. Best practice recommendations: strengths and limitations

These global best practice recommendations reflect the collective expertise of international clinicians and researchers with extensive experience in the diagnosis and management of HypoPT. Through a structured, consensus-based process informed by narrative review and current evidence, this work provides practical, clinically relevant recommendations to address persistent challenges in the care of individuals with HypoPT and updates the 2022 global guidelines on HypoPT. A major strength of this initiative is its emphasis on clinical applicability. It addresses clinical concerns including postsurgical risk assessment, genetic evaluation for nonsurgical HypoPT, comprehensive management of complications, sick day protocols, dose titration with PTH therapy, transitioning between conventional therapy and PTH, and considerations for pregnancy, lactation, and care of children. Limitations include the reliance on expert consensus in domains where high-quality evidence is limited, and potential variability in implementation due to differences in healthcare resources and regulatory approvals across jurisdictions. Additionally, narrative reviews may introduce selection bias and lack the transparency and reproducibility of systematic reviews, as they do not follow structured methods for literature identification and appraisal [101].

The translational value of these recommendations is their potential to inform clinical pathways, guide individualized decision-making, support the development of monitoring protocols, and optimize the integration of PTH replacement therapy as well as emerging therapies in the management of HypoPT.

7. Summary/conclusions

HypoPT is a rare disease associated with multisystem complications and significantly impacts QoL and morbidity. The diagnosis of HypoPT

requires meticulous biochemical evaluation, awareness of assay limitations and potential interferences, and a high index of suspicion, particularly in nonsurgical cases. Early and accurate diagnosis is crucial for initiating appropriate management and improving patient outcomes.

Conventional therapy can normalize serum calcium and alleviate the symptoms of hypocalcemia; however, it has many limitations. These include high pill burden, and further exacerbation of hyperphosphatemia, hypercalciuria and potentially further impairment of renal function. Conventional therapy may not improve QoL or the neuropsychiatric manifestations of HypoPT. It may also be ineffective or not practical in those with malabsorption or intolerance to large doses of calcium and/or active vitamin D. PTH replacement therapy is now available with palopegteriparatide which has a long half-life of 60 h, and results in a sustained activation of the PTH-R1. This molecule has been shown to achieve eucalcemia, while lowering urine calcium and serum phosphorus, improving QoL and in a post-hoc study has been shown to improve renal function. It also reestablishes normal bone remodelling. Long-term safety data are being evaluated in phase 3 clinical trials.

Emerging therapies include eneboparatide, a long-acting PTH/PTHrP analog that has been shown to achieve eucalcemia and lower urine calcium and normalize bone remodelling and is currently being evaluated in phase 3 clinical trials.

Encalaret, a calcilytic and a negative allosteric modulator of the CaSR, has been shown to normalize the CaSR sensitivity in ADH1 and can correct hypocalcemia, hypercalciuria, and low PTH in individuals with the condition. This molecule is also very promising and is currently in phase 3 clinical trials. The use of encalaret in postsurgical HypoPT may also be of value, however it remains investigational and requires further study to determine its safety and efficacy in this distinct patient population.

Long-term safety and efficacy data are being evaluated, and it is expected that PTH replacement will enable significant improvements in morbidity with reductions in the long-term complications of HypoPT.

Close monitoring of serum calcium in pregnancy and during lactation is required in order to achieve optimal maternal and fetal outcomes.

Management of HypoPT in children is also an area of clinical research and PTH replacement in children is also expected to improve disease outcomes with reductions in long term complications.

These best practice recommendations review current evidence and provide guidance for management based on international consensus. Updates are expected in 5 years with availability of further long-term data.

8. Future direction

Research is required to understand the mechanisms for the long-term multisystem complications of HypoPT as well as the impact of PTH replacement on these complications.

Further research is also required to improve the availability of real-time measurements of serum calcium as this technology can dramatically improve the QoL in HypoPT and enable improved titration of drug therapy. It is expected that long acting PTH and PTH analogues as well as PTH receptor modulators will enable effective PTH replacement in HypoPT for all patient populations. Calcilytic molecules may also be of value in postsurgical HypoPT, as well as in ADH1, and further research is exploring these opportunities of intervention. It is expected that the outcomes for HypoPT will dramatically improve with the availability of physiologic PTH replacement.

Abbreviations

$1,25(OH)_2D$	1,25-Dihydroxyvitamin D
25(OH)D	25-Hydroxyvitamin D
Ab	Antibody
ADH	Autosomal Dominant Hypocalcemia
AIRE	Autoimmune Regulator
AIRE1	Autoimmune Regulator 1
APECED	Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy
APS-1	Autoimmune Polyglandular Syndrome Type 1
BID	Twice Daily
BMD	Bone Mineral Density
Ca	Calcium
Ca(i)	Ionized Calcium
CaSR	Calcium-Sensing Receptor (protein)
CASR	Calcium-Sensing Receptor (gene)
CHD7	Chromodomain Helicase DNA Binding Protein 7
CHARGE	Coloboma, Heart defects, Atresia choanae, Retardation of growth and development, Genital abnormalities, Ear abnormalities (a syndrome)
CI	Confidence Interval
CKD	Chronic Kidney Disease
CNS	Central Nervous System
CT	Computed Tomography
CVS	Cardiovascular System
D5W	5 % Dextrose in Water
DCT	Distal Convoluted Tubule
eGFR	Estimated Glomerular Filtration Rate
EKG	Electrocardiogram
EU	European Union
FAM111A	Family with Sequence Similarity 111 Member A
FDA	Food and Drug Administration
FP	Family Physician
GATA3	GATA Binding Protein 3
GCM2	Glial Cells Missing Homolog 2
gms	Grams
GNA11	Guanine Nucleotide-Binding Protein Subunit Alpha-11
HDR	Hypoparathyroidism, Deafness, Renal Dysplasia
HR	Hazard Ratio
Hr	Hour
Hrs	Hours
HypoPT	Hypoparathyroidism
IV	Intravenous
kg	Kilogram
Kg/m^2	Kilograms per Square Meter
KSS	Kearns-Sayre Syndrome
mcg	Microgram
MD	Medical Doctor
MELAS	Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like Episodes
MRI	Magnetic Resonance Imaging
MTPD	Mitochondrial Trifunctional Protein Deficiency
Na+	Sodium
NEBL	Nebulette
NG	Nasogastric
OR	Odds Ratio
postop	Postoperative
PPI	Proton Pump Inhibitor
PROM	Premature Rupture of Membranes
PTH	Parathyroid Hormone
PTH1R	Parathyroid Hormone 1 Receptor
PTHrP	Parathyroid Hormone-related Peptide
pg/ml	Picograms per milliliter
Q	Every
QID	Four Times Daily
QoL	Quality of Life
QT	Quartile
QTc	Corrected QT Interval
REPLACE	Efficacy and safety of recombinant human parathyroid hormone (1–84) in hypoparathyroidism
RX	Prescription
SC	Subcutaneous

SEMA3E	Semaphorin 3E
SI	International System of Units
SOX3	SRY-Box Transcription Factor 3
TBCE	Tubulin-Specific Chaperone E
TBS	Trabecular Bone Score
TBX1	T-Box Transcription Factor 1
TID	Three Times Daily
UCa	Urine Calcium
Ug	Microgram
URTI	Upper Respiratory Tract Infection
US	Ultrasound
UTI	Urinary Tract Infection

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6. Emirates Diabetes Endocrine Society (EDES)
7. Endocrine Society of India
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14. India Society for Bone and Mineral Research (ISBMR)
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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.metabol.2025.156335.

Data availability statement

The data that support the findings in this consensus paper are openly available in PubMed, MEDLINE, EMBASE and the Cochrane databases.

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