

PARATHYROID GLAND DISEASES

A Clinical and Surgical Review for Postgraduate Students

Applied Anatomy & Calcium Homeostasis • Primary Hyperparathyroidism
Localization & Surgical Management • MEN Syndromes
Parathyroid Carcinoma • Secondary & Tertiary Hyperparathyroidism
Postoperative Complications • Hypoparathyroidism

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A concise, examination-oriented text for postgraduate trainees in general surgery, endocrine surgery
and ENT–Head & Neck surgery

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Learning Objectives

- Describe the applied surgical anatomy, embryology and common ectopic locations of the parathyroid glands.
- Outline the physiology of calcium homeostasis and the role of parathyroid hormone (PTH).
- Classify the parathyroid disorders and describe the aetiology and pathology of primary hyperparathyroidism.
- Interpret the biochemical and imaging workup of hypercalcaemia, and distinguish primary hyperparathyroidism from its key differentials.
- Apply current criteria for surgery in primary hyperparathyroidism and describe the surgical options, including intraoperative PTH monitoring.
- Recognise the hereditary hyperparathyroidism syndromes (MEN1, MEN2A, HPT-JT) and their surgical implications.
- Describe the diagnosis and management of parathyroid carcinoma, secondary and tertiary hyperparathyroidism, and hypoparathyroidism.
- Anticipate and manage the common postoperative complications of parathyroid surgery.

1. Introduction and Applied Surgical Anatomy

Most individuals have four parathyroid glands — two superior and two inferior — although supernumerary glands (a fifth gland or more) are found in a meaningful minority of patients and single-gland agenesis is occasionally encountered. Each gland is normally 3–6 mm in size and weighs 30–50 mg, with a characteristic yellow-brown colour that distinguishes it from surrounding fat and lymph nodes at operation.

Embryological Origin

The superior parathyroid glands arise from the **fourth pharyngeal pouch** (alongside the ultimobranchial body and thyroid) and undergo a short migration, giving them a relatively constant location posterior to the upper pole of the thyroid, near the cricothyroid junction. The inferior parathyroid glands arise from the **third pharyngeal pouch** together with the thymus, and undergo a longer caudal migration — this shared embryological journey explains both their more variable final position and their association with intrathymic ectopic glands.

Gland	Typical location	Common ectopic sites
Superior	Posterior to the upper thyroid pole, at the level of the cricothyroid junction, dorsal to the recurrent laryngeal nerve.	Retro-oesophageal or retropharyngeal (undescended too far); rarely within the carotid sheath or posterior mediastinum.
Inferior	Posterolateral to the lower thyroid pole, ventral to the recurrent laryngeal nerve; more variable in position.	Within the thymus or thyrothymic ligament (most common ectopic site), undescended (high, near the carotid bifurcation), or intrathyroidal.

Blood Supply and the Recurrent Laryngeal Nerve

Both superior and inferior parathyroid glands are supplied almost exclusively by the **inferior thyroid artery** (a branch of the thyrocervical trunk), regardless of gland location — a fact of practical importance, since ligating the inferior thyroid artery close to the thyroid capsule preserves the terminal branches supplying the parathyroids. The recurrent laryngeal nerve typically passes deep (anterior) to the inferior parathyroid gland and superficial (posterior) to the superior gland — the classic "superior dorsal, inferior ventral" relationship used to help orientate dissection and protect the nerve.

2. Physiology of Calcium Homeostasis

Parathyroid hormone (PTH) is the principal minute-to-minute regulator of extracellular ionised calcium. It is secreted by chief cells in response to a fall in serum ionised calcium, detected via the **calcium-sensing receptor (CaSR)**, a G-protein-coupled receptor on the parathyroid cell surface that forms the physiological basis of both hyperparathyroidism and familial hypocalciuric hypercalcaemia.

Actions of PTH

- **Bone** — stimulates osteoclastic bone resorption (via osteoblast-mediated RANKL signalling), releasing calcium and phosphate into the circulation.
- **Kidney** — increases distal tubular calcium reabsorption, decreases proximal tubular phosphate reabsorption (phosphaturic effect), and stimulates renal 1α -hydroxylase to increase conversion of 25-hydroxyvitamin D to active **1,25-dihydroxyvitamin D (calcitriol)**.
- **Intestine** — increases calcium absorption indirectly, via calcitriol-mediated upregulation of intestinal calcium transport.

The net effect of these three actions is to raise serum calcium and lower serum phosphate — a biochemical signature (hypercalcaemia with hypophosphataemia and an inappropriately normal or elevated PTH) that underlies the diagnosis of primary hyperparathyroidism. PTH-related peptide (PTHrP), secreted by certain malignancies, binds the same PTH/PTHrP receptor and produces a similar biochemical picture but with a suppressed (rather than elevated) native PTH level — a key discriminator in the workup of malignancy-associated hypercalcaemia.

3. Classification of Parathyroid Disorders

Disorder	Core defect
Primary hyperparathyroidism	Autonomous, PTH-dependent hypercalcaemia arising from intrinsic parathyroid pathology (adenoma, hyperplasia or carcinoma).
Secondary hyperparathyroidism	Appropriate physiological PTH elevation driven by a chronic hypocalcaemic/hyperphosphataemic stimulus, most commonly chronic kidney disease.
Tertiary hyperparathyroidism	Autonomous PTH hypersecretion that persists (with hypercalcaemia) after long-standing secondary hyperparathyroidism, typically once the original stimulus is corrected (e.g., after renal transplantation).
Parathyroid carcinoma	Rare (<1% of hyperparathyroidism) malignant parathyroid neoplasm, often presenting with markedly elevated calcium and a palpable neck mass.
Hypoparathyroidism	Deficient PTH secretion or action, producing hypocalcaemia; most commonly iatrogenic, following thyroid or parathyroid surgery.

4. Primary Hyperparathyroidism — Aetiology and Pathology

- **Single parathyroid adenoma** — the cause in approximately 80–85% of cases; a benign monoclonal proliferation of a single gland, with the remaining glands normal or suppressed.
- **Multigland hyperplasia** — accounts for around 10–15% of cases; all four glands are enlarged, and this pattern should prompt consideration of a hereditary syndrome (MEN1, MEN2A) even in an apparently sporadic case.
- **Double adenoma** — a less common intermediate pattern (roughly 2–5%), with two enlarged glands and two normal/suppressed glands.
- **Parathyroid carcinoma** — rare (<1%), discussed separately in Chapter 12.

Genetic Associations

Most primary hyperparathyroidism is sporadic, but a meaningful minority is hereditary, arising as part of Multiple Endocrine Neoplasia type 1 (MEN1, due to *MEN1* tumour-suppressor mutations), MEN2A (due to *RET* proto-oncogene mutations), or the hyperparathyroidism-jaw tumour syndrome (HPT-JT, due to *CDC73/HRPT2* mutations, which also predisposes to parathyroid carcinoma). Multigland disease, young age at presentation, or a family history of endocrinopathy should prompt genetic counselling and testing (discussed further in Chapter 11).

5. Primary Hyperparathyroidism — Clinical Features

The classical mnemonic "bones, stones, abdominal groans and psychic moans" describes the features of overt, longstanding disease, but in current practice the great majority of patients in regions with routine biochemical screening present with mild, asymptomatic or minimally symptomatic hypercalcaemia detected incidentally.

System	Manifestations
Bones	Osteopenia/osteoporosis (preferentially cortical bone), bone pain, pathological fractures, and — in advanced, longstanding disease — osteitis fibrosa cystica (subperiosteal resorption, bone cysts, "brown tumours").
Stones (renal)	Nephrolithiasis, nephrocalcinosis, and impaired renal function from chronic hypercalciuria.
Abdominal groans	Peptic ulcer disease, constipation, and (less commonly) acute pancreatitis.
Psychic moans	Fatigue, depression, cognitive difficulty ("brain fog"), anxiety, and in severe hypercalcaemia, confusion or coma.
Cardiovascular	Hypertension, left ventricular hypertrophy, and in severe/acute hypercalcaemia, arrhythmia.
Neuromuscular	Proximal muscle weakness and fatigability.

A useful clinical distinction is between **symptomatic** disease (overt bone, renal or neuropsychiatric manifestations) and **asymptomatic** disease (biochemical hypercalcaemia alone, now the presentation in the majority of patients), since this distinction — together with defined biochemical and organ-specific criteria — determines surgical candidacy (Chapter 9).

6. Diagnosis and Biochemical Evaluation

The diagnosis of primary hyperparathyroidism is biochemical. The classic pattern is an elevated (or inappropriately "normal") intact PTH in the presence of hypercalcaemia — PTH should be appropriately suppressed by hypercalcaemia from any other cause, so a non-suppressed PTH in a hypercalcaemic patient is diagnostic of PTH-dependent disease.

Initial Workup

- Serum calcium (corrected for albumin) and ionised calcium.
- Intact PTH.
- Serum phosphate — typically low or low-normal.
- Renal function (creatinine, eGFR) and 24-hour urinary calcium excretion.
- 25-hydroxyvitamin D — vitamin D deficiency should be corrected before surgical decision-making, as it can exaggerate PTH elevation.
- Bone mineral density (DXA) at the lumbar spine, hip and, importantly, the **distal one-third radius** — a site preferentially affected by cortical bone loss in primary hyperparathyroidism and often the first to show osteopenia.
- Renal imaging (ultrasound or CT) to assess for nephrolithiasis/nephrocalcinosis when clinically indicated.

Normocalcaemic Primary Hyperparathyroidism

A recognised variant in which PTH is persistently elevated with consistently normal albumin-corrected and ionised calcium, in the absence of a secondary cause (vitamin D deficiency, renal impairment, malabsorption). A subset of these patients will progress to overt hypercalcaemic disease over time and warrant periodic biochemical and skeletal surveillance.

7. Differential Diagnosis of Hypercalcaemia

Primary hyperparathyroidism and malignancy together account for the great majority of hypercalcaemia in clinical practice — malignancy predominates among inpatients, while primary hyperparathyroidism predominates in ambulatory, otherwise well patients.

Category	Examples
PTH-dependent	Primary hyperparathyroidism (adenoma, hyperplasia, carcinoma); tertiary hyperparathyroidism; lithium therapy; familial hypocalciuric hypercalcaemia (FHH).
PTH-independent (PTH suppressed)	Malignancy (PTHrP-mediated humoral hypercalcaemia of malignancy, osteolytic bone metastases, or myeloma); vitamin D intoxication; granulomatous disease (sarcoidosis, tuberculosis — extrarenal calcitriol production); thyrotoxicosis; immobilisation; milk-alkali syndrome; thiazide diuretics.

Familial Hypocalciuric Hypercalcaemia (FHH)

FHH is an important benign mimic of primary hyperparathyroidism, caused by an inactivating mutation of the calcium-sensing receptor gene, resulting in a higher physiological "set point" for calcium and mild, lifelong, asymptomatic hypercalcaemia with a normal or mildly elevated PTH. It is distinguished by a low **urinary calcium-to-creatinine clearance ratio (typically <0.01)**, a family history of similarly mild, asymptomatic hypercalcaemia, and — critically — the absence of benefit from parathyroidectomy, which does not correct the biochemical abnormality. Recognising FHH prevents inappropriate surgery.

8. Localization Imaging

Once the biochemical diagnosis of primary hyperparathyroidism is established, imaging is used to localise the abnormal gland(s) — it plays no role in making the diagnosis, which remains purely biochemical. Localization guides the choice between a focused, minimally invasive approach and a bilateral exploration.

- **Cervical ultrasound** — widely available, operator-dependent, useful for both parathyroid localisation and concurrent assessment of the thyroid gland for coexisting nodular disease.
- **Sestamibi ($^{99m}\text{Tc-MIBI}$) scintigraphy** — exploits differential washout kinetics between overactive parathyroid tissue and thyroid tissue; sensitivity is highest for a single adenoma and lower for multigland disease. Dual-phase and SPECT-CT protocols improve anatomical localisation.
- **4D-CT (four-dimensional CT)** — adds a temporal (contrast enhancement/washout) dimension to standard multiplanar CT; increasingly used, particularly for reoperative cases or when ultrasound and sestamibi are discordant or negative.
- **Selective venous sampling** — an invasive, highly specialised technique reserved for reoperative surgery after non-localising or discordant non-invasive imaging.

Concordant localisation on two modalities is generally required before proceeding to a focused, minimally invasive operation; discordant or negative imaging favours a bilateral neck exploration.

9. Indications for Surgery in Primary Hyperparathyroidism

Parathyroidectomy is curative and is recommended for all symptomatic patients. For asymptomatic patients, guidance from the Fifth International Workshop on the Evaluation and Management of Primary Hyperparathyroidism (2022) and the American Association of Endocrine Surgeons defines criteria under which surgery is recommended even without overt symptoms, given the demonstrated benefit for bone density and the prevention of disease progression.

Indications for Parathyroidectomy in Asymptomatic Primary Hyperparathyroidism

Age <50 years.

Serum calcium >1 mg/dL (0.25 mmol/L) above the upper limit of normal.

Skeletal involvement: T-score $\leq$ -2.5 at the lumbar spine, hip, femoral neck or distal one-third radius, and/or a vertebral fracture on imaging.

Renal involvement: eGFR <60 mL/min/1.73 m², 24-hour urinary calcium >400 mg (10 mmol) with increased stone risk on biochemical stone-risk analysis, or nephrolithiasis/nephrocalcinosis on imaging.

Any patient for whom medical surveillance is neither desired nor feasible.

Surgery is also indicated regardless of these criteria in patients with any classical symptom of hyperparathyroidism, in pregnancy with significant hypercalcaemia (with appropriate timing considerations), and in confirmed or suspected parathyroid carcinoma.

10. Surgical Management of Primary Hyperparathyroidism

Focused (Minimally Invasive) Parathyroidectomy

With concordant preoperative localisation, a focused parathyroidectomy — targeting only the imaging-identified gland through a small, often unilateral incision — is the procedure of choice for sporadic single-adenoma disease, offering shorter operative time, reduced morbidity and comparable cure rates to bilateral exploration.

Intraoperative PTH Monitoring

Because PTH has a short circulating half-life (a few minutes), intraoperative PTH (IOPTH) monitoring is used to confirm biochemical cure before closing. The most widely used criterion, the **Miami criterion**, defines a successful excision as a fall in PTH of more than 50% from the highest of the pre-incision or pre-excision baseline, measured 10 minutes after excision of the abnormal gland(s). Failure to achieve this drop should prompt continued exploration for additional hyperfunctioning tissue.

Bilateral Neck Exploration

A traditional four-gland exploration remains indicated when preoperative imaging is negative or discordant, when multigland disease or a hereditary syndrome is suspected, in reoperative surgery, and when parathyroid surgery is combined with a concurrent thyroidectomy for coexisting thyroid pathology.

Reoperative Surgery

Persistent or recurrent disease after an initial operation requires careful re-review of biochemistry (excluding FHH), repeat and often complementary localisation studies (4D-CT, repeat sestamibi, selective venous sampling), and referral to a high-volume endocrine surgical centre, given the increased technical difficulty and complication risk of reoperative neck surgery.

11. MEN Syndromes and Hereditary Hyperparathyroidism

Hereditary hyperparathyroidism differs from sporadic disease in typically presenting at a younger age, with multigland involvement, and a higher risk of persistent or recurrent disease after limited surgery — surgical strategy therefore differs fundamentally from the sporadic single-adenoma case.

Syndrome	Key features and parathyroid implications
MEN1 (<i>MEN1</i> gene)	Primary hyperparathyroidism (the most common and often earliest manifestation, seen in the great majority of gene carriers by middle age), pituitary adenomas, and pancreatic neuroendocrine tumours ("the three Ps"). Parathyroid disease is virtually always multigland — subtotal parathyroidectomy (3½ glands) or total parathyroidectomy with immediate forearm autotransplantation is favoured over a focused approach, alongside cervical thymectomy given the risk of supernumerary/ectopic thymic glands.
MEN2A (<i>RET</i> proto-oncogene)	Medullary thyroid carcinoma (near-universal penetrance, usually the dominant management priority), pheochromocytoma, and primary hyperparathyroidism (less common and generally milder than in MEN1, often single- or double-gland).
Hyperparathyroidism-jaw tumour syndrome (<i>CDC73/HRPT2</i>)	Primary hyperparathyroidism (with an elevated risk of parathyroid carcinoma — up to 15% in some series), ossifying fibromas of the jaw, and renal cysts/tumours. Any patient with this genetic background warrants a surgical approach mindful of the carcinoma risk (see Chapter 12).

Genetic counselling and testing should be offered to patients with multigland disease at a young age, a personal or family history suggestive of an associated endocrinopathy, or histology raising concern for hereditary disease.

12. Parathyroid Carcinoma

Parathyroid carcinoma is a rare cause of primary hyperparathyroidism, accounting for well under 1% of cases, but should be actively considered when hypercalcaemia is severe. It is associated with *CDC73/HRPT2* mutations, either sporadically or as part of the hyperparathyroidism-jaw tumour syndrome.

Features Raising Suspicion of Carcinoma

- Markedly elevated serum calcium (often >14 mg/dL) and PTH levels several-fold above the upper limit of normal — substantially higher than typical adenoma-related disease.
- A palpable, firm neck mass — unusual in benign parathyroid disease, where the gland is rarely palpable.
- Vocal cord palsy from recurrent laryngeal nerve invasion, or fixation to surrounding structures at operation.
- Definitive diagnosis is often only possible on histology, given overlapping features with atypical adenoma; capsular, vascular or perineural invasion and unequivocal invasion of adjacent structures are the key diagnostic criteria.

Management

When carcinoma is suspected pre- or intraoperatively, **en bloc resection** of the gland with the ipsilateral thyroid lobe and any adherent structures is the treatment of choice — meticulous avoidance of capsular rupture is essential, since tumour spillage seeds the operative field and markedly increases the risk of local recurrence. Fine needle aspiration and preoperative parathyroid biopsy should be avoided if carcinoma is suspected, for the same reason. Prognosis is relatively favourable with complete initial resection but recurrence — often manifesting years later as recurrent hypercalcaemia — is common, and long-term biochemical surveillance is required.

13. Secondary Hyperparathyroidism

Secondary hyperparathyroidism is an appropriate physiological response of the parathyroid glands to a chronic hypocalcaemic or hyperphosphataemic stimulus. The overwhelming majority of cases occur in the context of **chronic kidney disease-mineral and bone disorder (CKD-MBD)**.

Pathophysiology

As glomerular filtration declines, phosphate retention and reduced renal 1α -hydroxylase activity (with consequently low calcitriol) combine to lower serum calcium and raise fibroblast growth factor 23 (FGF-23). These changes chronically stimulate parathyroid hormone secretion and, over time, drive parathyroid gland hyperplasia — initially diffuse and polyclonal, but with progression to nodular, increasingly autonomous hyperplasia that becomes less responsive to medical therapy.

Medical Management

- Dietary phosphate restriction and phosphate binders.
- Active vitamin D analogues (e.g., calcitriol, paricalcitol) to suppress PTH secretion.
- Calcimimetics (cinacalcet, etelcalcetide) — allosteric activators of the calcium-sensing receptor that lower PTH without raising serum calcium, now central to KDIGO-guided medical management.

Indications for Parathyroidectomy

Surgery (discussed further in Chapter 15) is reserved for secondary hyperparathyroidism refractory to optimised medical therapy, characterised by persistently and severely elevated PTH with associated hypercalcaemia and/or hyperphosphataemia, progressive bone disease, calciphylaxis (calcific uraemic arteriolopathy), or intractable pruritus/bone pain attributable to hyperparathyroidism.

14. Tertiary Hyperparathyroidism

Tertiary hyperparathyroidism describes autonomous, PTH-driven hypercalcaemia that persists despite correction of the original stimulus for secondary hyperparathyroidism — classically after a successful renal transplant, when chronically hyperplastic parathyroid tissue continues to secrete PTH autonomously even though the uraemic stimulus has resolved. It reflects the same nodular, increasingly monoclonal transformation of hyperplastic parathyroid tissue seen in advanced secondary disease, now manifesting as hypercalcaemia rather than the hypocalcaemic/normocalcaemic biochemistry of pre-transplant secondary disease.

A period of observation (often 12 months) after transplantation is reasonable in mild, asymptomatic cases, since some degree of gland involution and biochemical normalisation can occur as renal function stabilises. Persistent, symptomatic, or progressively worsening hypercalcaemia, particularly with a risk of nephrocalcinosis threatening the transplanted kidney, is an indication for surgery.

15. Surgical Options in Renal Hyperparathyroidism

Unlike sporadic primary hyperparathyroidism, renal (secondary/tertiary) hyperparathyroidism virtually always involves all four glands, so a focused, single-gland approach is inappropriate. Three recognised operative strategies exist.

Procedure	Description and considerations
Subtotal parathyroidectomy (3½ glands)	Removal of three glands and most of a fourth, leaving a well-vascularised remnant in situ; avoids the risk of graft non-function seen with autotransplantation, but re-exploration for recurrence is technically more difficult.
Total parathyroidectomy with autotransplantation	All four glands removed, with a portion of the most normal-appearing gland minced and autografted (typically into the non-dominant forearm brachioradialis muscle); recurrence, if it occurs, is more accessible for re-excision under local anaesthesia from the graft site.
Total parathyroidectomy without autotransplantation	Reserved for selected patients, particularly some transplant candidates, given the risk of adynamic bone disease from over-suppression of PTH; used more cautiously and less commonly than the other two options.

The choice between these approaches depends on the patient's transplant candidacy, surgeon and institutional preference, and the anticipated ease of future re-exploration should recurrent disease develop.

16. Postoperative Complications

Hungry Bone Syndrome

A profound, prolonged hypocalcaemia occurring after parathyroidectomy in patients with severe, longstanding hyperparathyroidism (particularly renal hyperparathyroidism or marked pre-operative skeletal disease), caused by a sudden reversal of osteoclastic bone resorption and rapid remineralisation of chronically demineralised bone. It is distinguished from routine postoperative hypocalcaemia by its severity, duration and often accompanying hypophosphataemia and hypomagnesaemia, and it requires aggressive, sustained calcium and active vitamin D replacement.

Hypocalcaemia

Transient hypocalcaemia is common after successful parathyroidectomy, reflecting temporary suppression of the remaining normal glands, and is managed with oral (and, if symptomatic, intravenous) calcium supplementation, tapering as remaining gland function recovers. Permanent hypoparathyroidism is uncommon after focused surgery for sporadic single-adenoma disease but carries a higher risk after extensive bilateral or reoperative surgery.

Other Complications

- Recurrent laryngeal nerve injury, causing transient or permanent vocal cord palsy.
- Neck haematoma — rare but potentially airway-threatening, requiring prompt recognition and, if compromising the airway, emergency bedside decompression.
- Persistent hyperparathyroidism — hypercalcaemia that fails to resolve or normalise within six months of surgery, usually reflecting a missed hyperfunctioning gland.
- Recurrent hyperparathyroidism — new hypercalcaemia after a documented period of postoperative normocalcaemia, raising concern for a missed supernumerary gland, parathyromatosis, or (rarely) malignancy.

17. Hypoparathyroidism

Hypoparathyroidism results from deficient PTH secretion (or, rarely, peripheral resistance to its action) and produces hypocalcaemia with hyperphosphataemia. The most common cause overall is **iatrogenic** — inadvertent removal of, or vascular injury to, the parathyroid glands during thyroid or parathyroid surgery.

Other Causes

- Autoimmune (isolated, or as part of autoimmune polyglandular syndrome type 1).
- DiGeorge syndrome (22q11.2 deletion) — congenital parathyroid aplasia/hypoplasia alongside cardiac and thymic anomalies.
- Severe hypomagnesaemia — impairs both PTH secretion and peripheral action, and must be corrected before hypocalcaemia will respond to calcium/vitamin D therapy alone.
- Infiltrative disease (haemochromatosis, Wilson's disease) and neck irradiation (rare causes).

Clinical Features and Diagnosis

Features reflect neuromuscular irritability from hypocalcaemia: perioral and acral paraesthesiae, muscle cramps, and tetany (including carpopedal spasm). Two classic bedside signs are **Chvostek's sign** (facial muscle twitching on tapping over the facial nerve anterior to the ear) and **Trousseau's sign** (carpal spasm induced by inflating a blood pressure cuff above systolic pressure for several minutes) — the latter is more specific. Severe or acute hypocalcaemia may cause laryngospasm, seizures, and a prolonged QT interval predisposing to arrhythmia.

Management

Acute, symptomatic hypocalcaemia is treated with intravenous calcium gluconate, with cardiac monitoring, followed by oral calcium and active vitamin D (calcitriol, which does not require renal activation and acts more rapidly than native vitamin D) for maintenance therapy. Coexisting hypomagnesaemia must be corrected. Recombinant human PTH is available in selected health systems for chronic hypoparathyroidism poorly controlled on conventional calcium/vitamin D therapy, though access varies by region and conventional replacement remains first-line.

18. Summary of Current Guidelines and Evidence

Management recommendations in this review are aligned with the Fifth International Workshop on the Evaluation and Management of Asymptomatic Primary Hyperparathyroidism (2022), the American Association of Endocrine Surgeons Guidelines for Definitive Management of Primary Hyperparathyroidism (2016, with subsequent literature incorporated), and KDIGO guidance on the management of CKD-mineral and bone disorder. Key evidence-based practice points include defined biochemical, skeletal and renal criteria for surgery in asymptomatic disease, the role of intraoperative PTH monitoring (Miami criterion) in confirming biochemical cure, the preference for calcimimetic-based medical therapy before surgical referral in secondary hyperparathyroidism, and en bloc resection as the standard of care for suspected or confirmed parathyroid carcinoma.

As with all endocrine surgical guidance, recommendations continue to evolve; trainees should confirm current protocol details against the latest published guideline versions and their institutional multidisciplinary policies before applying them in clinical decision-making.

Key Points for Revision

High-Yield Summary

All parathyroid glands, wherever located, are supplied by the inferior thyroid artery; the recurrent laryngeal nerve passes deep to the inferior gland and superficial to the superior gland.

The diagnosis of primary hyperparathyroidism is biochemical — an elevated or inappropriately non-suppressed PTH in the presence of hypercalcaemia; imaging localises but never diagnoses.

A single adenoma accounts for roughly 80–85% of primary hyperparathyroidism; multigland disease should raise suspicion of a hereditary syndrome (MEN1, MEN2A, HPT-JT).

Familial hypocalciuric hypercalcaemia is distinguished by a low urinary calcium-to-creatinine clearance ratio (<0.01) and does not benefit from parathyroidectomy.

Surgical criteria for asymptomatic primary hyperparathyroidism: age <50 , calcium >1 mg/dL above the upper limit of normal, eGFR <60 , T-score ≤ -2.5 or fragility fracture, or urinary calcium >400 mg/24h with increased stone risk.

The Miami criterion ($>50\%$ PTH fall at 10 minutes post-excision) confirms biochemical cure intraoperatively.

Markedly elevated calcium and PTH with a palpable neck mass should raise suspicion of parathyroid carcinoma — manage with en bloc resection and avoid capsular rupture or preoperative biopsy.

Secondary hyperparathyroidism is a physiologically appropriate response to CKD-MBD; tertiary hyperparathyroidism is autonomous disease persisting after the original stimulus resolves (e.g., post-transplant).

Hungry bone syndrome causes severe, prolonged hypocalcaemia after parathyroidectomy for longstanding severe disease, especially renal hyperparathyroidism.

Chvostek's and Trousseau's signs are the classic bedside features of hypocalcaemic neuromuscular irritability; correct coexisting hypomagnesaemia for hypocalcaemia to respond to treatment.

Further Reading and Key Sources

The following primary sources informed this review and are recommended for deeper study:

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8. Williams N, O'Connell PR, McCaskie AW, eds. *Bailey & Love's Short Practice of Surgery*, 28th ed. Boca Raton: CRC Press.

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