Chapter 66 – Parathyroidectomy for Sporadic Primary Hyperparathyroidism

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The incidence of sporadic primary hyperparathyroidism (HPT) has risen dramatically since the advent of chemical screening with an autoanalyzer in the 1960s, and most cases are discovered in asymptomatic patients with hypercalcemia. Patients may also present with nonspecific complaints of back pain, or they may have osteopenia, as depicted on radiographic studies. Primary hyperparathyroidism is the most common cause of hypercalcemia in the outpatient population, second only to malignancy in the inpatient population. Fortunately, primary HPT is usually easily and successfully treated by parathyroidectomy. The genetic etiology and risk factors for this disease have been described elsewhere.[1] Due to advances in localization[2] and widespread implementation of rapid biochemical hormone assays, failed exploration is rare. The success or failure of the procedure depends on the training, expertise, and experience of the operating surgeon. Reoperative parathyroid surgery is a considerably more complex operation with significantly greater failure and complication rates. Neck exploration and parathyroidectomy should not be undertaken by a surgeon who has not been trained specifically to localize abnormal parathyroid glands and to perform parathyroidectomies, or one who performs such operations infrequently.

PATIENT SELECTION

Parathyroidectomy is usually an elective operative procedure. Although urgent parathyroidectomy is seldom necessary, its indications include significant hypercalcemia in the second trimester of pregnancy and parathyrotoxicosis characterized by serum calcium levels greater than 15 mg/dL with or without symptoms of significant mental obtundation. The sensitivity and specificity of the clinical algorithm for the assessment of patients with suspected hyperparathyroidism are very high (>98%). Patients selected for parathyroidectomy should meet the following criteria: documented history of kidney stones, gastric symptoms (peptide ulcer or pancreatitis), depression, and/or bone pain. In addition, the National Institutes of Health (NIH) consensus conference statement in 1991 recommended surgery for asymptomatic patients with markedly elevated serum calcium levels (>11.4 mg/dL), low bone density (more than 2 standard deviations less than age, race, and gender-matched controls), reduced creatinine clearance (>30%), and hypercalciuria (>400 mg in 24 hours) who were 50 years of age or younger and who had inadequate follow-up care and no compelling contraindications to a general anesthetic.

PREOPERATIVE PLANNING

Preoperative parathyroid hormone (PTH) measurement confirms not only the diagnosis of primary HPT, but also provides a baseline with which intraoperative PTH levels can be compared. Although some variation between assay techniques may be observed, a value just above the normal range (i.e., 70) will need to drop below a value of 35, the lower limit of detection of some intraoperative rapid assays. Several radiologic procedures are available to localize an abnormal parathyroid gland preoperatively, including planar or three-dimensional single photon emission computed tomography (SPECT) sestamibi parathyroid scans, neck ultrasound, computed tomography and magnetic resonance imaging scans, selective arteriography, and highly selective venous catheterization to localize a PTH step-up. A combination of two of these techniques is occasionally useful, particularly in the setting of suspected, coincident thyroid disease. The sensitivity, specificity, and expense vary from procedure to procedure. Preoperative localization is currently standard-of-care and significantly assists in targeting the surgeon's exploration. Some surgeons employ intraoperative, radio-guided localization, using a hand-held gamma probe after systemic, intravenous ^{99}Tc-sestamibi infusion preoperatively. Others add the use of methylene blue injection,[3] which is said to concentrate in parathyroid glands, assisting their identification from surrounding lymph nodes and adipose tissue. The dye stains adenomas and hyperplastic glands a deep purple-blue color. Normal parathyroid tissue stains to a lesser extent or not at all.

Medications that cause perioperative bleeding (i.e., acetylsalicylic acid and ibuprofen, high-dose vitamin E) should be discontinued 7 to 10 days in advance. Because the procedure is generally elective, patients who are significantly overweight and are willing and capable of losing weight should be encouraged to do so. Related endocrinopathies should be ruled out when suggested by history or physical examination, and a positive family history of hypocalcemia should be sought. In particular, pheochromocytoma and medullary thyroid carcinoma can occur in the context of a multiple endocrine neoplasia (MEN) type IIa. Patients with pheochromocytoma should first undergo adrenalectomy, and patients with hypercalcemia and a solitary thyroid nodule that cannot be resolved by fine-needle aspiration biopsy for cytology should undergo a pentagastrin-stimulated calcitonin assay to rule out thyroid cancer of the medullary type. An abnormal 24-hour urine calcium measurement is useful to rule out familial

hypocalciuric hypercalcemia, although this condition is rare and the history usually elicits a familial calcium disorder.[4]

SURGICAL TECHNIQUE

Approach to the "Localizing Gland"

Following the induction of general endotracheal anesthesia or intravenous sedation and local anesthesia, the patient's neck is moderately hyperextended with the head adequately supported. A low anterior collar incision roughly 1 fingerbreadth above the clavicular heads is mapped out in a preexisting skin crease and is carried out from the lateral margin of one sternocleidomastoid muscle to the other. If clear identification of laterality is found on a localization study, the incision may be shifted toward that side and thus shortened. In the subplatysmal plane, the median raphe is dissected up to the thyroid cartilage and down to the manubrial notch. A self-retaining thyroid retractor is positioned beneath the strap muscles above and below to facilitate adequate exposure (Fig. 66-1). Thyroid and perithyroidal tissues are palpated *through* the strap muscles with an occasional palpation of an enlarged parathyroid gland, which is generally felt to be more firm than a rubbery lymph node. The overlying strap muscles are bluntly dissected from the ipsilateral thyroid lobe and retracted laterally, using compulsive hemostasis and control of any bridging vessels. The middle thyroid vein, if present, is doubly ligated with 4-0 silk suture and divided, facilitating medial mobilization of the thyroid lobe (Fig. 66-2). Blunt finger dissection at this juncture greatly facilitates the dissection up to the apex of the superior pole of the thyroid and down to below the inferior pole. During this maneuver, the surgeon may have an indication of the tumor location, corresponding to the preoperative localization, using digital palpation. With the assistant maintaining maximal medial traction of the thyroid lobe, the surgeon dissects the loose areolar tissue using a blunt dissector and nudging, spreading, and dividing to expose the carotid sheath, the inferior thyroid artery, and the recurrent laryngeal nerve (Fig. 66-3). The inferior thyroid artery is an invaluable landmark, in that nonectopic superior parathyroid glands lie above its junction with the recurrent laryngeal nerve and nonectopic inferior parathyroid glands lie below this structure (Fig. 66-4).

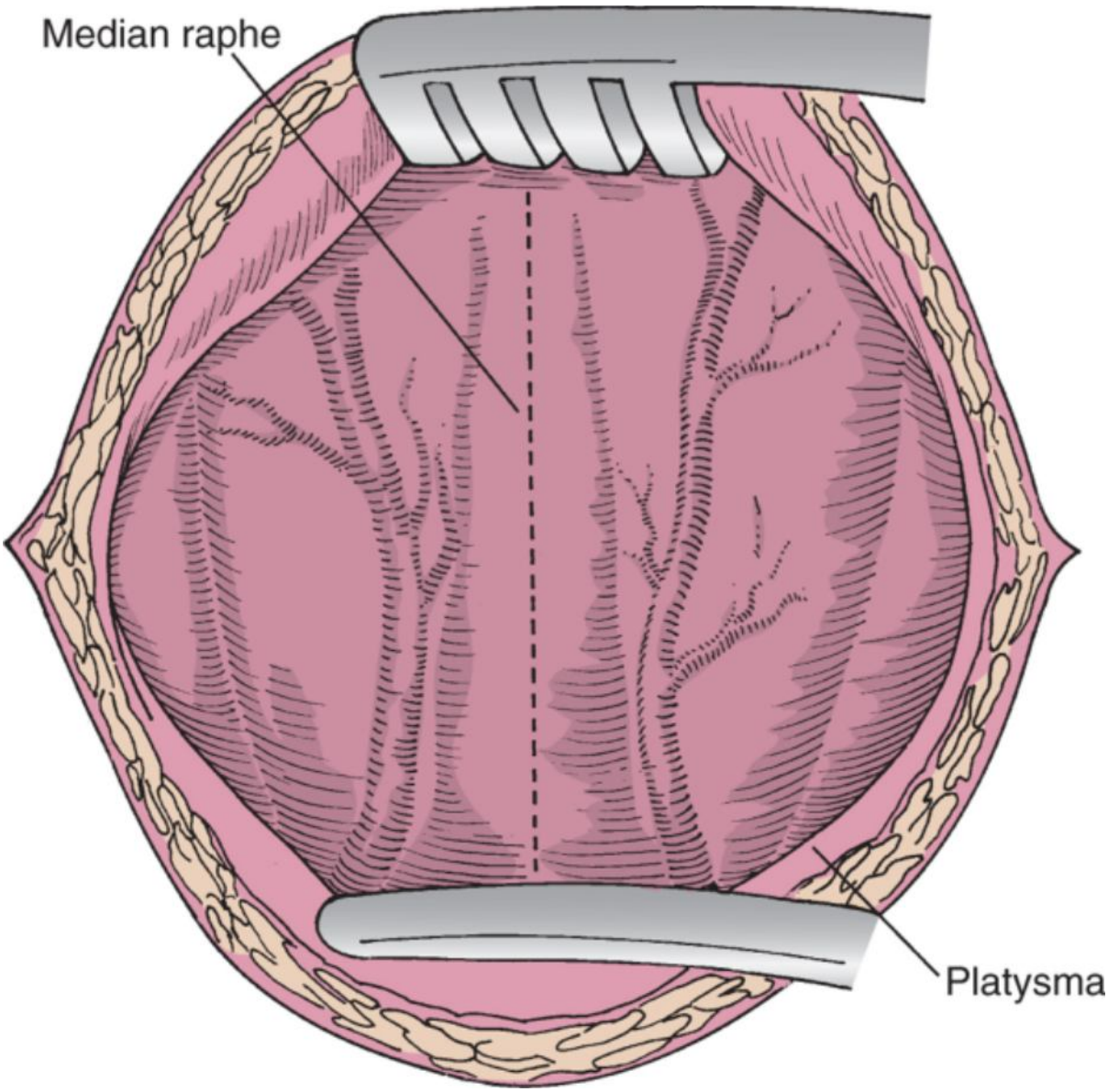

Figure 66-1 The undivided median raphe beneath the incised, retracted platysma.

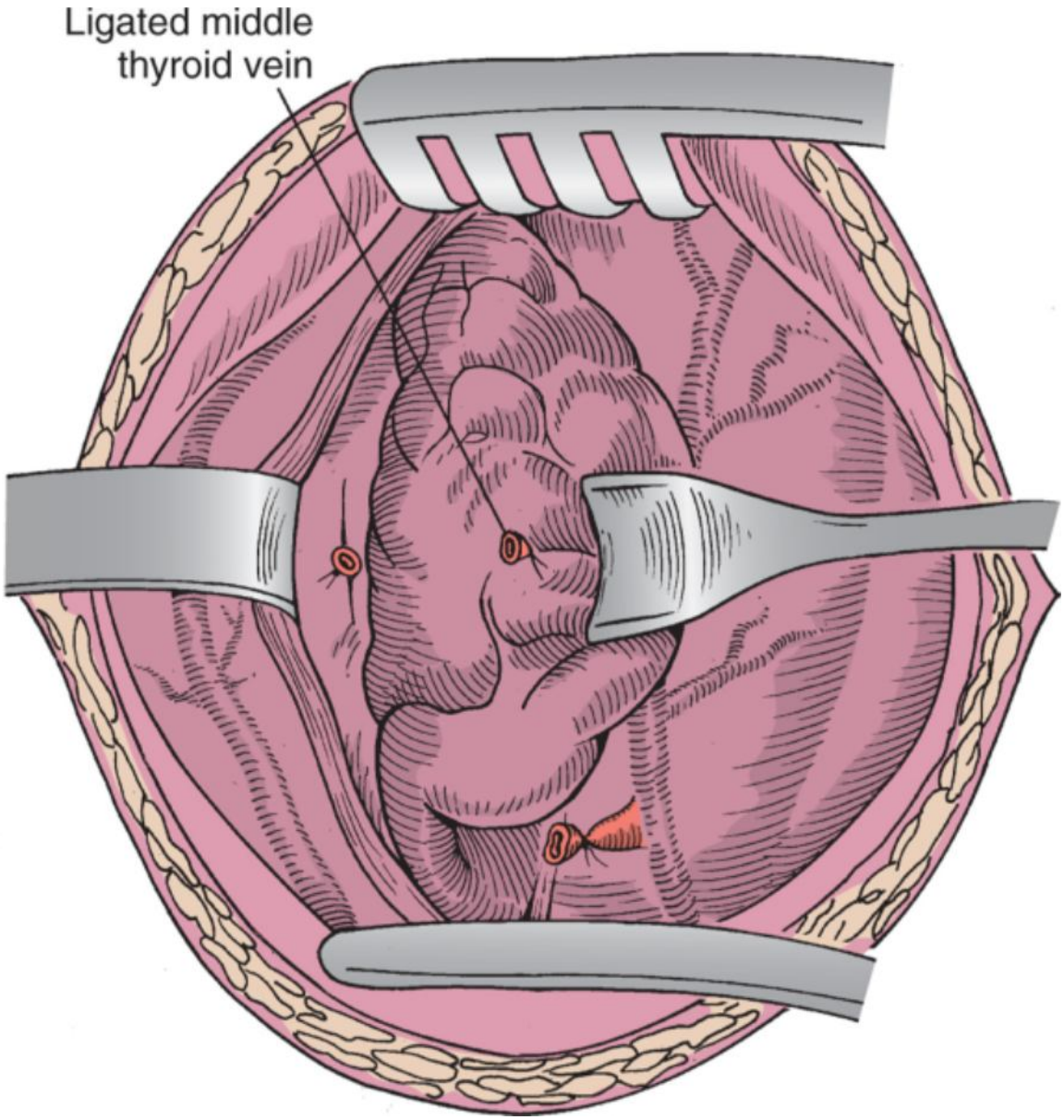

Figure 66-2 Middle thyroid vein ligation with medial traction of the right thyroid lobe.

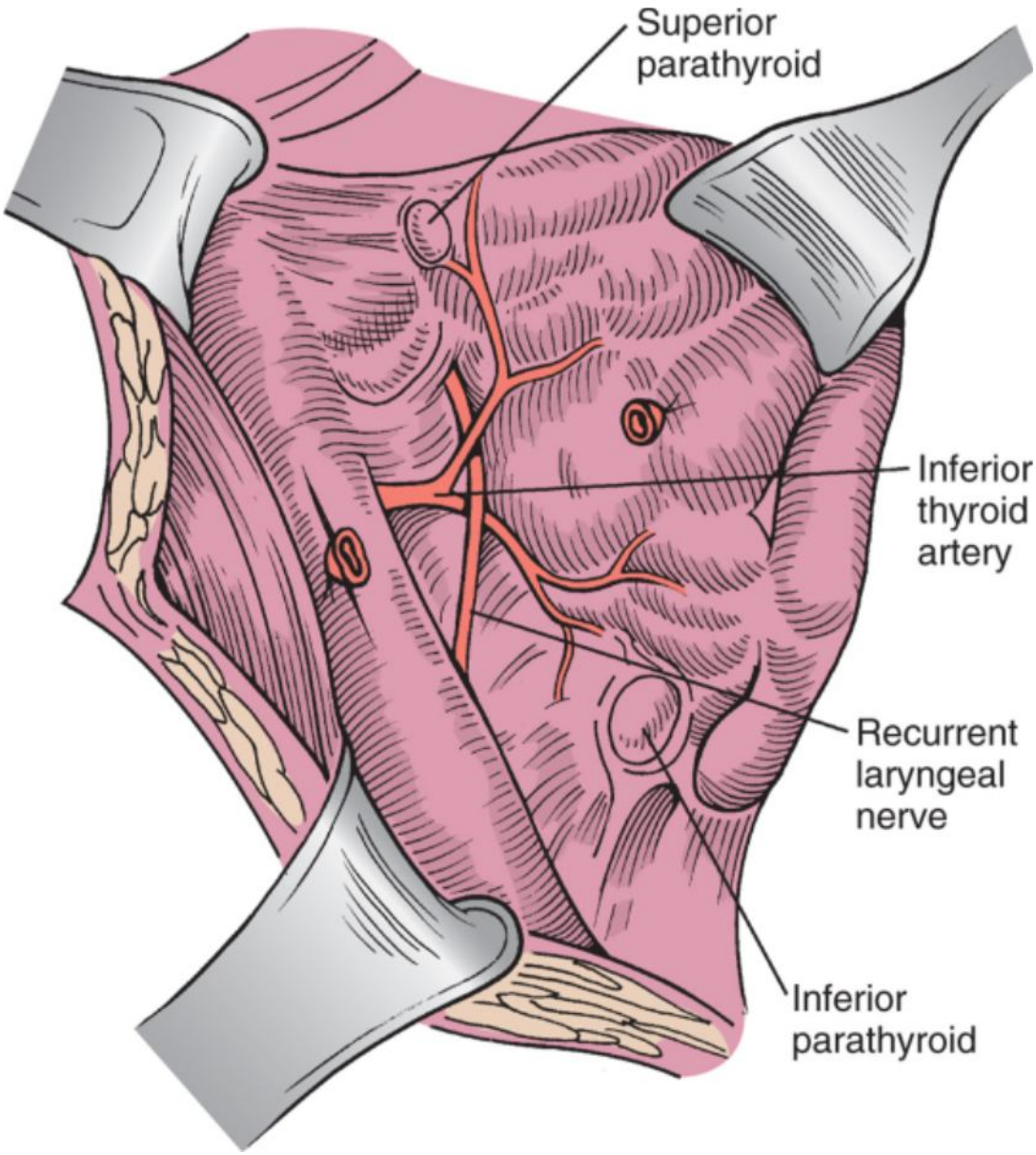

Figure 66-3 With medial thyroid lobe retraction and loose areolar tissue dissected away, the carotid sheath, inferior thyroid artery, recurrent laryngeal nerve, and parathyroid glands are exposed.

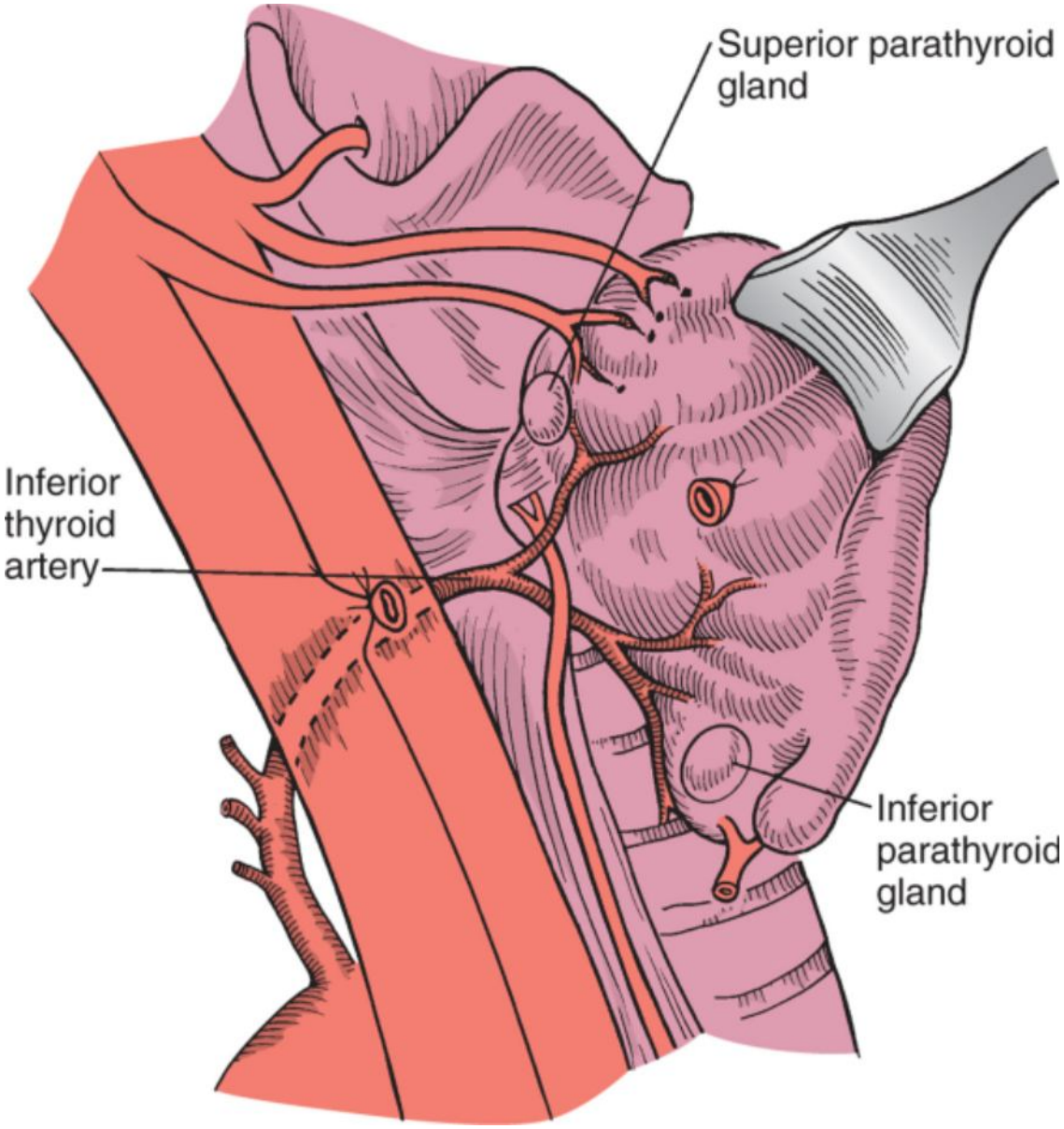

Figure 66-4 Nonectopic superior parathyroid glands lie above and inferior parathyroid glands lie below the inferior thyroid artery.

Approach to the "Nonlocalizing Gland"

If a nodule is palpated lateral or deep to the thyroid on one side and not on the other, the side of the palpated nodule is explored initially. Preoperative ultrasound may demonstrate an echogenic focus suggestive of an extrathyroidal or intrathyroidal nodule that merits intraoperative exploration. In the absence of such a finding, a bilateral exploration may occasionally be necessary, if laterality is not determined by a preoperative localization study. However, the surgeon may elect to explore one side first. This may be arbitrary or is occasionally guided by concomitant thyroid pathology. If an abnormal parathyroid gland is identified, and the other ipsilateral gland is grossly and pathologically (on frozen section) normocellular, the termination of the procedure is determined by the drop in intraoperative PTH of more than 50%. Four-gland exploration may be necessary if *all* of these criteria are not fulfilled, to ensure identification of the single or multiple abnormal parathyroid glands. Intraoperative localization using a hand-held gamma probe may also assist in this situation.[5] Because nonlocalizing glands may be of smaller volume (and thus emit less detectable ^{99}Tc), the use of intraoperative radio detection may be assisted by reducing the soft tissues preventing detection of the radioactivity. The collimated probe also may enable exclusion of one side from likely pathologic involvement. The modified procedure is as follows.

Ectopic and Nonectopic Parathyroid Tissue Locations

The parathyroid glands are subject to predictable patterns of descent during embryologic development. Therefore, those that fail to be localized within the commonly encountered position adjacent to the thyroid gland often can be found anomalously. When parathyroid glands are abnormally located, they pursue predictable patterns of descent

and may either hypodescend or hyperdescend along a specific route. Hence, familiarity with the embryologic origins and descent of the parathyroids is essential to the success of exploration (Fig. 66-5). The inferior parathyroid arises from the third branchial cleft along with the thymus and travels a greater distance than the superior parathyroid (which arises from the fourth branchial cleft with the lateral anlage of the thyroid); therefore, it is more likely to be ectopic in its location. Hypodescended superior and inferior parathyroids may be identified adjacent to the carotid bulb, but this is a most unusual finding. Roughly one half of abnormal superior parathyroids will lie beneath the capsule of the thyroid from the apex of the superior pole down to the insertion site of the inferior thyroid artery. The other (extracapsular) one half may be, and frequently are, ectopic, particularly the larger adenomas that descend *posterior* to the inferior thyroid artery along the tracheoesophageal groove and on occasion into the posterior superior mediastinum. Under such circumstances, a vascular pedicle arising from the inferior thyroid artery is identifiable and provides a critical clue to the location of the ectopic adenoma. Ectopic inferior parathyroids are frequently adjacent to or within the thymus within either the neck or the superior anterior mediastinum, usually identifiable and retrievable through the low anterior collar incision (Fig. 66-6).

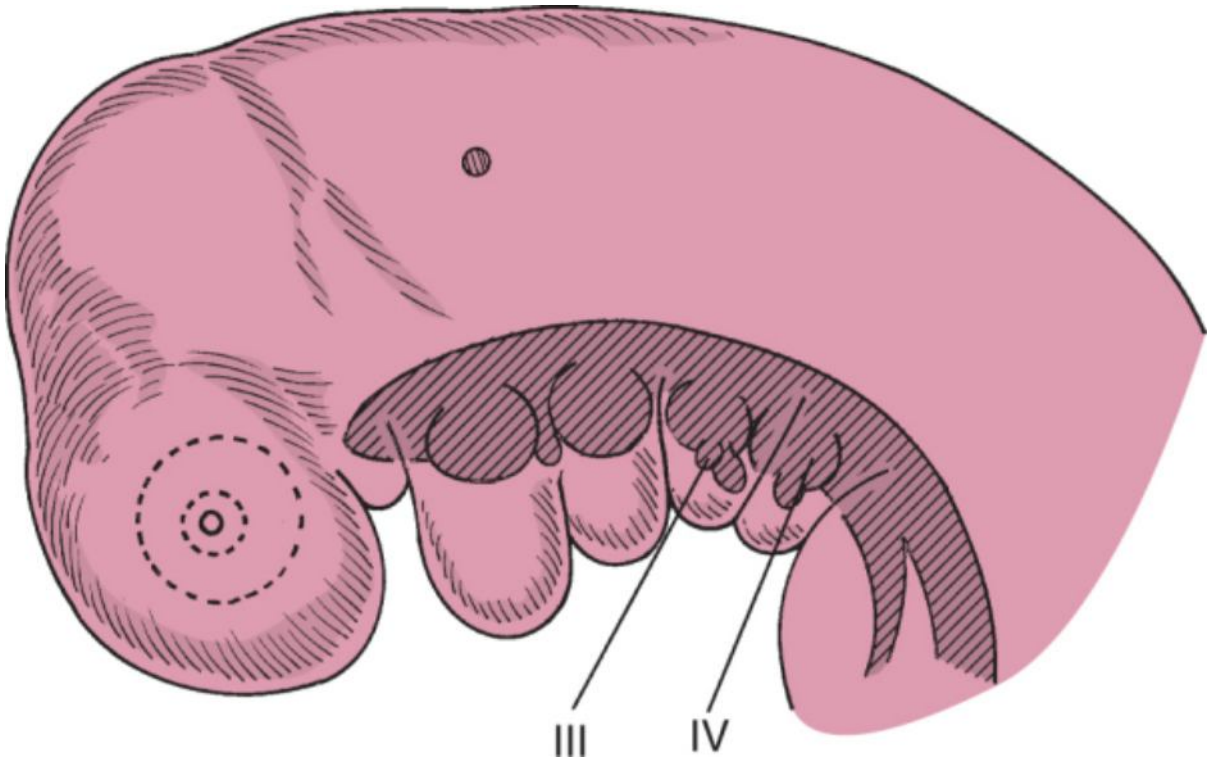

Figure 66-5 Embryologic pharyngeal origins of the inferior (III) and superior (IV) parathyroid glands.

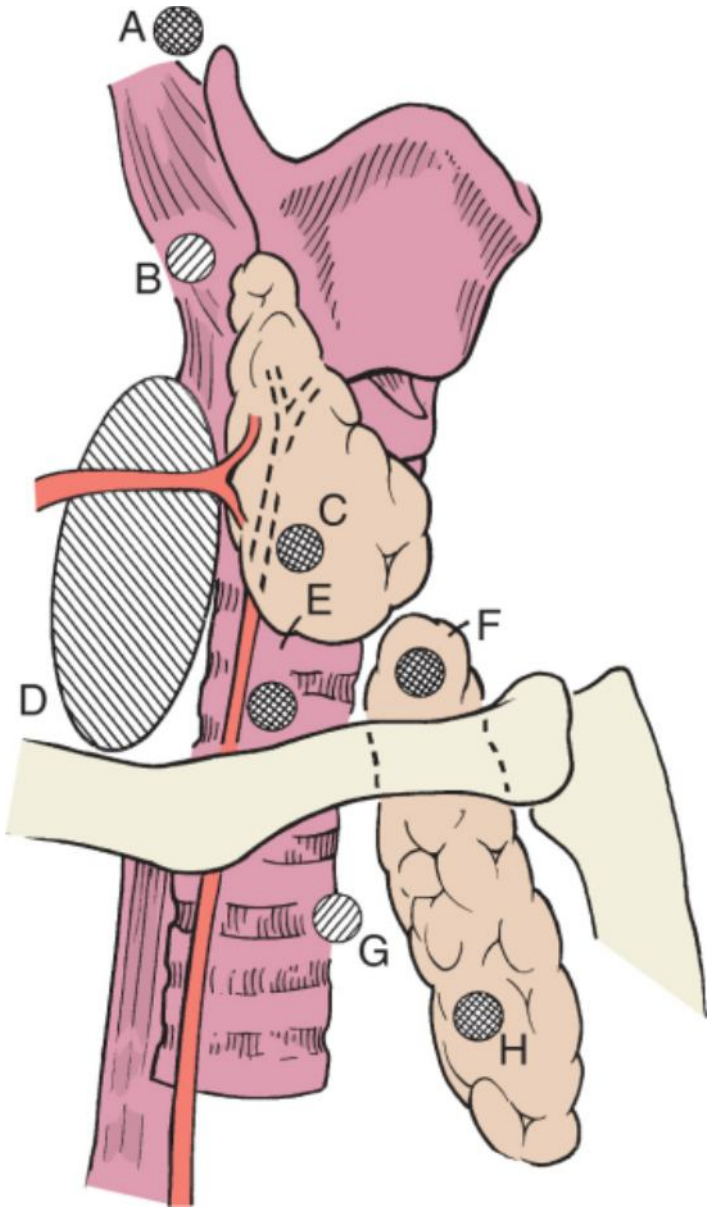

Figure 66-6 Ectopic locations of the superior (B, partially descended; D, tracheoesophageal groove; G, mediastinal) and inferior (A, undescended; C, intrathyroid; E, mediastinal outlet; F, intrathymic; H, anterior mediastinal) parathyroid glands.

Once an enlarged parathyroid is identified, every effort, short of removing the thymus, thyroid, and related soft tissues, should be made to identify the second ipsilateral parathyroid. When the ipsilateral gland is located and appears “normal,” its vascular pedicle is identified and preserved. We prefer biopsy of a normal-appearing parathyroid gland, using a stitch or surgical clip, to exclude multigland hyperplasia. Incisional biopsy has been shown to lead to “parathyrosis”[6] and provides complementary information in the era of intraoperative quick PTH measurement. If intraoperative PTH measurement is not available, biopsy confirmation (using a stitch or clip) of an “abnormal” parathyroid gland may be submitted for frozen section (hemolysin and eosin stain and oil red O staining) analysis. If the enlarged gland is not identified on the first side explored, the other thyroid lobe is mobilized and retracted as described previously, and the neck is thoroughly explored to identify the superior and inferior parathyroids, once again maintaining meticulous hemostasis to facilitate identification of the glands. If three normal glands are identified and the fourth (presumably adenomatous) gland is not, first a thymectomy and then a thyroid lobectomy (which may rarely contain an adenoma) are performed on the side of the “missing” gland. The pathologist immediately and thoroughly evaluates both structures. If the adenoma remains elusive and the intraoperative PTH levels remain elevated, the soft tissues of the neck from the level of the hyoid bone down to the arch of the aorta are removed, respecting the integrity of the superior and recurrent laryngeal nerves, vagus nerve, trachea, esophagus, common carotid artery, and internal jugular vein. Rarely will a parathyroid be identified in the carotid sheath, but as a final maneuver, exploration of this compartment superiorly to the carotid bulb should be included in the dissection.

If, after completing the more extensive dissection outlined previously, one still fails to locate the missing parathyroid adenoma and the operating surgeon is satisfied with the thoroughness of the supraclavicular

exploration, the location of each normal parathyroid should be marked with a metallic clip and the neck should be closed. Mediastinal exploration (via sternotomy) may be required later after a symptomatic patient is biochemically reevaluated with repeat serum calcium measurements, an intact PTH immunochemiluminometric assay, and a 24-hour urine calcium. A battery of localization tests should be repeated as well to assist in localization of the missing gland.

Approximately 10% of patients with sporadic primary hyperparathyroidism will have either the diffuse or the nodular form of parathyroid hyperplasia. A subtotal parathyroidectomy is performed to control the HPT in these patients. At least four parathyroids should be identified and at least 3½glands removed. The most accessible (usually an inferior) and smallest parathyroid should be selected for partial resection. In the course of dissecting out the gland, its vascular pedicle should be identified and avoided so as to avoid compromising the blood supply and therefore the viability of the remnant. A metallic clip should be placed across the midportion of the gland (Fig. 66-7) and the tissue distal to this removed with scalpel dissection and submitted for histologic confirmation. The remnant inferior gland can be tacked to the anterior trachea or other landmark for future safe identification if multigland hyperplasia develops. Before removing each one of the three remaining parathyroids, the viability of the remnant should be reassessed by observing its gross appearance.

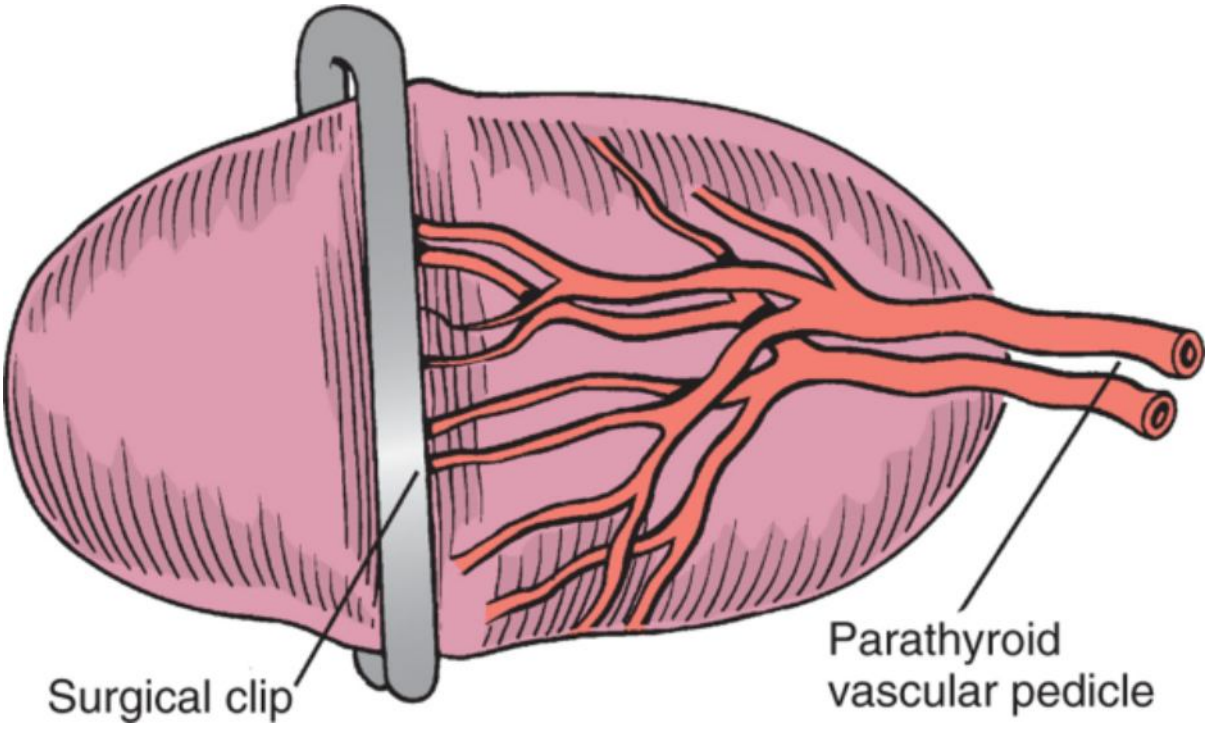

Figure 66-7 The parathyroid is clipped in preparation for transection on the avascular side of the surgical clip.

After the dissection is completed, hemostasis is achieved and a suction drain is brought out through a separate skin strap incision. The fascia overlying the strap muscles is reapproximated with interrupted 4-0 Vicryl sutures, the platysma is reapproximated in a similar fashion, and the skin is reapproximated with a running, fine, absorbable subcuticular closure and adhesive dressing strips. No neck dressing is applied to avoid obscuring hematoma formation.

POSTOPERATIVE MANAGEMENT

The head of the bed should be elevated at least 30 degrees for the first 12 to 18 hours to minimize venous oozing in the operative site. Significant postoperative hypocalcemia is rarely encountered in the absence of subtotal parathyroidectomy for hyperplasia or the removal of a parathyroid adenoma or carcinoma with a preoperative calcium greater than 12 mg/dL. A full preoperative diet and level of activity are resumed the evening of surgery. The majority of patients are discharged the day of or the first day after surgery.

PEARLS

- Successful parathyroidectomy depends on an accurate diagnosis, appropriate patient selection and preparation, and a thorough understanding of the embryology and anatomy of the parathyroid glands and related neck and mediastinal structures.

- Preoperative localization of abnormal glands should be standard procedure in all centers in which the surgery is to be performed. In our experience, three-dimensional SPECT acquisition using the ^{99}Tc isotope has enabled the localization of glands not identified by two-dimensional planar imaging (see Fig. 66-8). This is likely due to the ability to rotate the scan 360 degrees, reducing the tissue obstructing the emitting glands and the SPECT detector.
- Intraoperative PTH monitoring (not currently mandatory in confirming that the abnormal glands have been removed) substantially assists the surgeon and decreases dissection to the extent that patient safety and complications are positively impacted.
- When parathyroid carcinoma is present, it must be recognized early in the operative procedure. Optimal management consists of an en bloc resection of the carcinoma, adherent tissues, and ipsilateral thyroid lobe with at least a central compartment node dissection.

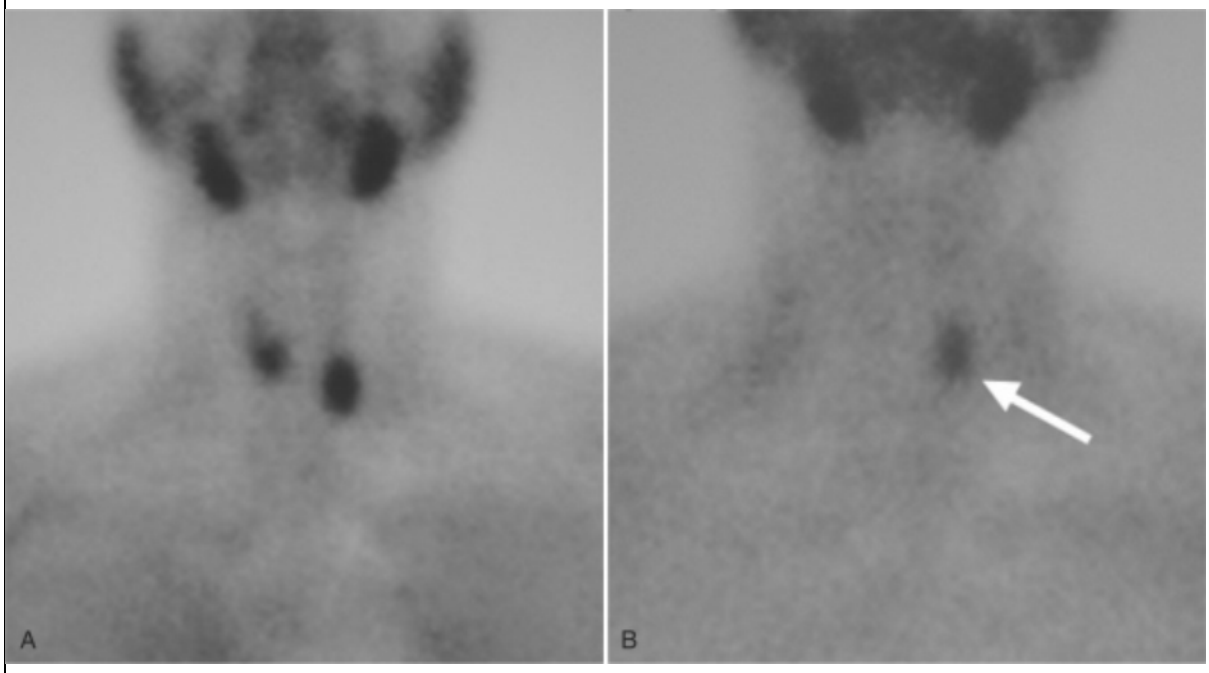

Figure 66-8 Two-dimensional planar ^{99}Tc images showing early **(A)** and delayed **(B)** images, localizing the adenoma in the left paratracheal region. A persistent focus of radiotracer activity is evident posterior to the right inferior thyroid lobe, consistent with a parathyroid adenoma. Ultrasound or three-dimensional single photon emission computed tomography techniques can be used (not shown) to localize the adenoma in the anteroposterior direction in addition to the left or right side.

PITFALLS

- The suspected malignant parathyroid must not be biopsied or its capsule violated, to avoid tumor seeding.
- In the absence of intraoperative circulating PTH decline of greater than 50% of the baseline value, an adenoma may not be differentiated from parathyroid hyperplasia. Confirmation depends on the accurate assessment (e.g., by fat-staining techniques) of the biopsied “normal” gland by the surgeon and the pathologist together. Failure to recognize hyperplasia inevitably results in persistent or recurrent hypercalcemia. Double adenomatas are uncommon (less than 2%).
- Ectopic thyroid tissue, lymph nodes, “brown fat,” and thymic tissue may grossly mimic a parathyroid gland, supporting the use of frozen section examination of all excised “parathyroid” tissue.
- The anatomic course and integrity of the recurrent and superior laryngeal nerves must be known and respected, so as to avoid impairing laryngeal function. Meticulous dissection is required to preserve the arterial supply and venous drainage of any retained parathyroid gland. Abnormal parathyroid glands are frequently ectopic. They may fail to descend from the retropharyngeal area, may descend within and therefore be concealed by the thyroid or thymus, or may hyperdescend into the anterior mediastinum (inferior parathyroid) or posterior mediastinum (superior parathyroid). Hyperdescended glands frequently carry their blood supply with them as derivatives of the inferior thyroid artery, and vascular pedicles should be carefully sought and dissected out.
- Although the reported half-life of circulating PTH is reported to be 10 minutes,[7] the surgeon should wait at least 15 to 20 minutes before the post-excision venipuncture is performed. Manipulation of the abnormal, enlarged glands may produce a temporary spike in circulating PTH after the preoperative PTH

value is drawn, temporarily confounding the greater than 50% decline rule for successfully terminating the procedure.