

**2474** cardiovascular, and neuropsychiatric disease, even in mild hyperparathyroidism.

Two surgical approaches are generally practiced. The conventional parathyroidectomy procedure was neck exploration with general anesthesia; this procedure is being replaced in many centers, whenever feasible, by an outpatient procedure with local anesthesia, termed *minimally invasive parathyroidectomy*.

Parathyroid exploration is challenging and should be undertaken by an experienced surgeon. Certain features help in predicting the pathology (e.g., multiple abnormal glands in familial cases). However, some critical decisions regarding management can be made only during the operation.

With conventional surgery, one approach is still based on the view that typically only one gland (the adenoma) is abnormal. If an enlarged gland is found, a normal gland should be sought. In this view, if a biopsy of a normal-sized second gland confirms its histologic (and presumed functional) normality, no further exploration, biopsy, or excision is needed. At the other extreme is the minority viewpoint that all four glands be sought and that most of the total parathyroid tissue mass be removed. The concern with the former approach is that the recurrence rate of hyperparathyroidism may be high if a second abnormal gland is missed; the latter approach could involve unnecessary surgery and an unacceptable rate of hypoparathyroidism. When normal glands are found in association with one enlarged gland, excision of the single adenoma usually leads to cure or at least years free of symptoms. Long-term follow-up studies to establish true rates of recurrence are limited.

Recently, there has been growing experience with new surgical strategies that feature a minimally invasive approach guided by improved preoperative localization and intraoperative monitoring by PTH assays. Preoperative  $^{99m}\text{Tc}$  sestamibi scans with single-photon emission CT (SPECT) are used to predict the location of an abnormal gland and intraoperative sampling of PTH before and at 5-min intervals after removal of a suspected adenoma to confirm a rapid fall (>50%) to normal levels of PTH. In several centers, a combination of preoperative sestamibi imaging, cervical block anesthesia, minimal surgical incision, and intraoperative PTH measurements has allowed successful outpatient surgical management with a clear-cut cost benefit compared to general anesthesia and more extensive neck surgery. The use of these minimally invasive approaches requires clinical judgment to select patients unlikely to have multiple gland disease (e.g., MEN or secondary hyperparathyroidism). The growing acceptance of the technique and its relative ease for the patient has lowered the threshold for surgery.

Severe hypercalcemia may provide a preoperative clue to the presence of parathyroid carcinoma. In such cases, when neck exploration is undertaken, the tissue should be widely excised; care is taken to avoid rupture of the capsule to prevent local seeding of tumor cells.

Multiple-gland hyperplasia, as predicted in familial cases, poses more difficult questions of surgical management. Once a diagnosis of hyperplasia is established, all the glands must be identified. Two schemes have been proposed for surgical management. One is to totally remove three glands with partial excision of the fourth gland; care is taken to leave a good blood supply for the remaining gland. Other surgeons advocate total parathyroidectomy with immediate transplantation of a portion of a removed, minced parathyroid gland into the muscles of the forearm, with the view that surgical excision is easier from the ectopic site in the arm if there is recurrent hyperfunction.

In a minority of cases, if no abnormal parathyroid glands are found in the neck, the issue of further exploration must be decided. There are documented cases of five or six parathyroid glands and of unusual locations for adenomas such as in the mediastinum.

When a second parathyroid exploration is indicated, the minimally invasive techniques for preoperative localization such as ultrasound, CT scan, and isotope scanning are combined with venous sampling and/or selective digital arteriography in one of the centers specializing in these procedures. Intraoperative monitoring of PTH

levels by rapid PTH immunoassays may be useful in guiding the surgery. At one center, long-term cures have been achieved with selective embolization or injection of large amounts of contrast material into the end-arterial circulation feeding the parathyroid tumor.

A decline in serum calcium occurs within 24 h after successful surgery; usually blood calcium falls to low-normal values for 3–5 days until the remaining parathyroid tissue resumes full hormone secretion. Acute postoperative hypocalcemia is likely only if severe bone mineral deficits are present or if injury to all the normal parathyroid glands occurs during surgery. In general, there are few problems encountered in patients with uncomplicated disease such as a single adenoma (the clear majority), who do not have symptomatic bone disease or a large deficit in bone mineral, who are vitamin D and magnesium sufficient, and who have good renal and gastrointestinal function. The extent of postoperative hypocalcemia varies with the surgical approach. If all glands are biopsied, hypocalcemia may be transiently symptomatic and more prolonged. Hypocalcemia is more likely to be symptomatic after second parathyroid explorations, particularly when normal parathyroid tissue was removed at the initial operation and when the manipulation and/or biopsy of the remaining normal glands are more extensive in the search for the missing adenoma.

Patients with hyperparathyroidism have efficient intestinal calcium absorption due to the increased levels of  $1,25(\text{OH})_2\text{D}$  stimulated by PTH excess. Once hypocalcemia signifies successful surgery, patients can be put on a high-calcium intake or be given oral calcium supplements. Despite mild hypocalcemia, most patients do not require parenteral therapy. If the serum calcium falls to <2 mmol/L (8 mg/dL), and if the phosphate level rises simultaneously, the possibility that surgery has caused hypoparathyroidism must be considered. With unexpected hypocalcemia, coexistent hypomagnesemia should be considered, because it interferes with PTH secretion and causes functional hypoparathyroidism ([Chap. 423](#)).

Signs of hypocalcemia include symptoms such as muscle twitching, a general sense of anxiety, and positive Chvostek's and Trousseau's signs coupled with serum calcium consistently <2 mmol/L (8 mg/dL). Parenteral calcium replacement at a low level should be instituted when hypocalcemia is symptomatic. The rate and duration of IV therapy are determined by the severity of the symptoms and the response of the serum calcium to treatment. An infusion of 0.5–2 mg/kg per hour or 30–100 mL/h of a 1-mg/mL solution usually suffices to relieve symptoms. Usually, parenteral therapy is required for only a few days. If symptoms worsen or if parenteral calcium is needed for >2–3 days, therapy with a vitamin D analogue and/or oral calcium (2–4 g/d) should be started (see below). It is cost-effective to use calcitriol (doses of 0.5–1 µg/d) because of the rapidity of onset of effect and prompt cessation of action when stopped, in comparison to other forms of vitamin D. A rise in blood calcium after several months of vitamin D replacement may indicate restoration of parathyroid function to normal. It is also appropriate to monitor serum PTH serially to estimate gland function in such patients.

If magnesium deficiency was present, it can complicate the postoperative course since magnesium deficiency impairs the secretion of PTH. Hypomagnesemia should be corrected whenever detected. Magnesium replacement can be effective orally (e.g.,  $\text{MgCl}_2$ ,  $\text{MgOH}_2$ ), but parenteral repletion is usual to ensure postoperative recovery, if magnesium deficiency is suspected due to low blood magnesium levels. Because the depressant effect of magnesium on central and peripheral nerve functions does not occur at levels <2 mmol/L (normal range 0.8–1.2 mmol/L), parenteral replacement can be given rapidly. A cumulative dose as great as 0.5–1 mmol/kg of body weight can be administered if severe hypomagnesemia is present; often, however, total doses of 20–40 mmol are sufficient.

#### MEDICAL MANAGEMENT

The guidelines for recommending surgical intervention, if feasible (Table 424-2), as well as for monitoring patients with asymptomatic hyperparathyroidism who elect not to undergo parathyroidectomy