Parathyroid Adenoma:

Problems in Diagnosis and Management

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ALTHOUGH the first successful operation for parathyroid adenoma was performed by Felix Mandl [15] in Vienna in 1925, the tumor was encountered rarely at Charity Hospital of Louisiana at New Orleans for many years. Three-fourths of the 53 cases collected during almost a quarter century at that institution have occurred during the past eight years. As might be expected at a large general Charity Hospital, problems have arisen in diagnosis and treatment of these patients. Analysis of these cases and presentation of illustrative cases should emphasize the need for early recognition and appropriate operation.

Clinical Data

From January 1942 through July 1966, 53 patients with parathyroid adenoma have been admitted to the Charity Hospital. The cases have been identified through the Tumor Registry, records of which begin in 1948, and the Record Room, in which a coding system can identify diagnoses made since 1942. During this same period, admissions to Charity Hospital have averaged 60,000 per year.

Forty-six patients had single adenomas, four had double adenomas, and two had triple adenomas. Multiple adenomas were described in one patient at necropsy.

Surgical Cases. In 33 patients the diagnosis of adenoma was established at operation. The first operation was performed by Dr. Michael E. De Bakey in 1942 when he was a member of the Tulane faculty. For a number of years, the late Dr. Rawley Penick supervised a number of operations performed on the Tulane service. Since 1959, one of us (E. T. K.) has performed or supervised the operations on the Tulane service, and for the past three years Dr. Norman Nelson has supervised the operations on the Louisiana State University service. One patient had two operations for parathyroid adenoma at another hospital before being transferred to Charity Hospital, where residual tumor was found at necropsy.

Solitary adenomas were discovered incidentally in five surgical patients during other operations. None of these had signs or symptoms of hyperparathyroid disease. Three were operated upon because of thyroid nodules and one for hyperthyroidism. The fifth patient had carcinoma of the tonsil, and thyroid and parathyroid adenomas

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were removed during a radical neck dissection.

Postmortem Cases. Twenty diagnoses were made at necropsy, 16 on the Tulane service, two on the Louisiana State University service, and two by the now-discontinued Independent service. Ten patients had no symptoms of parathyroid disease. Thus, in 15 patients, adenomas were found incidentally at operation or necropsy without evidence of hyperfunction. Wilson and associates [23] recorded 10 incidental cases among 51 at the Peter Bent Brigham Hospital.

Year of Diagnosis. Only one diagnosis was made before 1951 in a patient who was operated upon successfully in 1942 (Fig. 1). During the 1950's 11 patients had operations, and four adenomas were discovered at necropsy. Since 1960, interest in this disease had mounted, and adenomas have been discovered at 16 necropsies and in 21 operative patients.

Distribution by Age. Sixteen patients were in the sixth decade, and 37 (seven-tenths) occurred in the fifth through seventh decades (Fig. 2). The youngest patient was a 20-year-old woman in whom diagnosis was made after she was found to have renal stones, and the oldest patient was a 92-year-old woman whose adenoma was found incidentally at necropsy, after operation to relieve intestinal obstruction. The postmortem cases represent a much older age group (average 65.9 years) than the surgical group (average 50.2 years).

Distribution by Race and Sex. Of 19 white patients, three were men and 16 women, and of the 34 Negro patients nine were men and 25 women (Fig. 3). During the same period, Negro admissions to the hospital comprised about 70% of the total. If obstetrical, premature and newborn admissions are excluded, the average number of Negro admissions was 59% which closely approximates the 64% Negro patients in the adenoma series. Sixty-one per cent of the hospital admissions were women as compared to 77% of the adenoma patients.

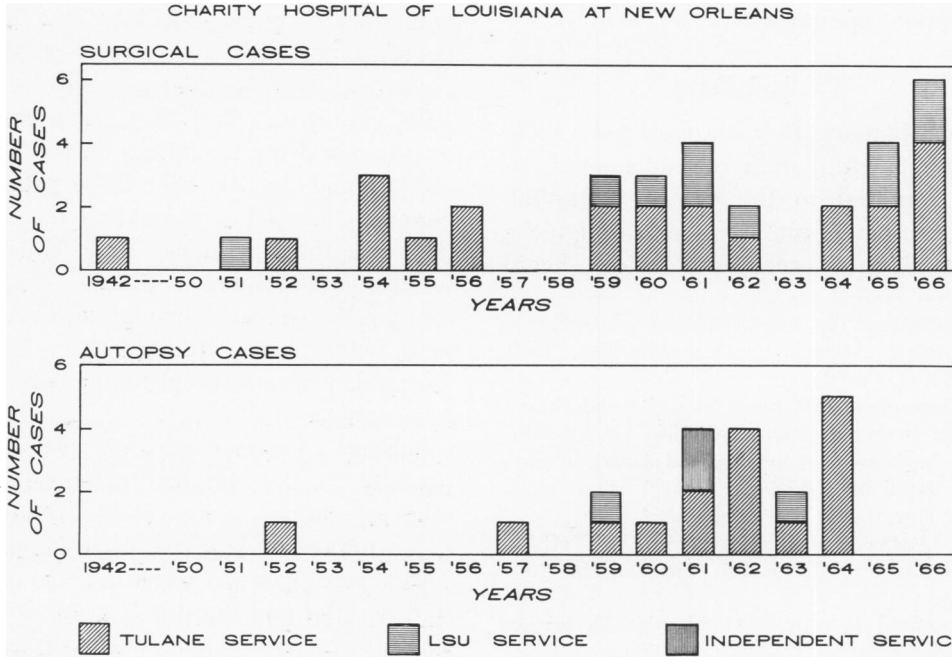


FIG. 1. Distribution of 53 parathyroid adenomas by type of case, service, and year of diagnosis.

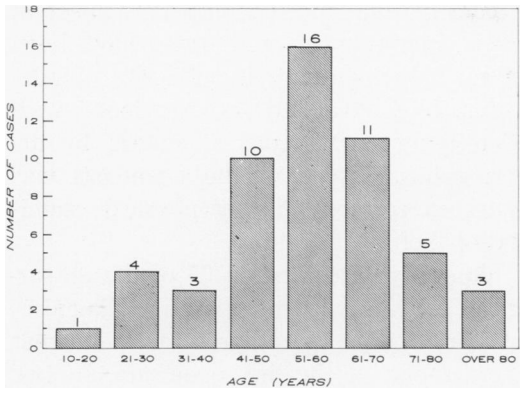


FIG. 2. Age incidence in 53 cases of parathyroid adenoma.

Anatomic Site. The anatomic position of the adenomas has been difficult to determine accurately from the hospital records, particularly in the postmortem cases. In 31 of the 33 surgical patients the site of adenoma was recorded (Fig. 4), but in only five of the 20 postmortem cases. Three patients, all surgical, had tumors in the superior mediastinum, one of which was removed through a thyroidectomy incision. In two other patients, the sternum had to be split to find the adenomas; one overlay the junction of the innominate veins in close association with the thymus gland, and the other lay in the left upper mediastinum behind the cartilagenous portion of the first rib.

Of adenomas found in the neck at operation and necropsy, 22 were located posterior to the lower lobes of the thyroid gland,

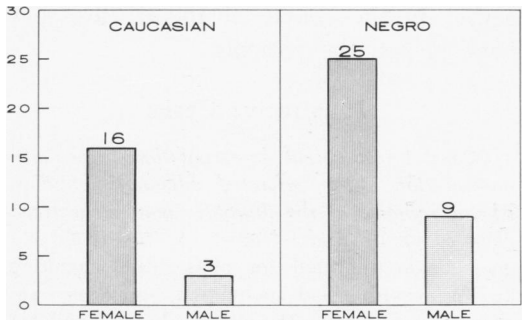


FIG. 3. Parathyroid adenoma, race and sex incidence in 53 cases.

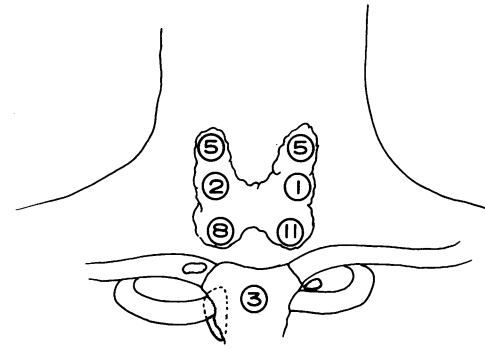


FIG. 4. Localization of 35 parathyroid adenomas in 31 surgical cases.

nine on the right and 13 on the left. Ten were posterior to the upper lobes of the thyroid, five on each side. Three adenomas were found on the left and two on the right, posterior to the middle thyroid region so that it was not possible to identify the origin of the adenomas. In two patients adenomas were found within the thyroid capsule; one was found by the pathologist following routine thyroidectomy, and the other was found within the right lobe of the thyroid after subtotal thyroid resection for persistent hypercalcemia after earlier exploration of the neck yielded no signs of tumor.

Histologic Characteristics. Of the 53 patients with adenomas, 35 were reported by the pathologists to have no dominant cellular type. In ten, the histologic appearance was primarily that of chief cells; in five, oxyphil cells; and in two, clear cells. In one patient with an original diagnosis of adenoma, the postmortem diagnosis was revised to low-grade parathyroid carcinoma. Seven of the chief-cell and both clear-cell adenomas were considered functional. The oxyphil adenomas, all found at necropsy, were considered non-functional.

Other Types of Cancer. In addition to one patient with parathyroid carcinoma, eight patients had diagnoses of cancer, three of the pancreas, two of the thyroid, one of the tonsils, one of the gallbladder and one of the ovary. The two thyroidal

and the tonsillar cancers were discovered at operation. No explanation is immediately forthcoming for the apparent increased incidence of cancer in this group of patients.

Initial Complaints. Of the 53 patients, 38 (28 surgical and ten postmortem) had complaints suggestive of adenoma. Complaints referable to renal stone or nephrocalcinosis were primary in 17 patients and an additional seven also had similar renal complaints in addition to primary symptoms from other organs. Nine patients had complaints referable to peptic ulcer, associated in three with gastrointestinal bleeding. Five had complaints of osteitis fibrosa cystica, one of whom was originally thought to have Paget's rather than von Recklinghausen's disease. Another had a bone cyst resulting in a pathologic fracture. Six had nonspecific complaints of weakness, nervousness, nausea, and vomiting, and four had these complaints in addition to other more prominent symptoms. Four patients had strokes secondary to hypertension. Only one patient had a previous history of pancreatitis.

Diagnostic Tests. The most important diagnostic test was measurement of serum calcium; serum phosphorus was also helpful. All patients who had exploratory operations had persistent serum calcium of 5.6 mEq./L. or more. After operation, calcium levels returned to normal in all but one patient, a man in whom a second parathyroid adenoma and islet cell adenomas of the pancreas were discovered at necropsy, after death from peptic ulcer and bleeding. Persistent minor elevations in serum calcium in three patients warrant further study, one of whom may have Boeck's sarcoid. Other chemical determinations such as urinary calcium and phosphorus, alkaline phosphatase, cortisone suppression tests of serum calcium, and tubular reabsorption of phosphorus have not proved consistently helpful. Soft tissue planograms, roentgenograms after ingestion of barium, and scanning after injection of selenium-tagged methionine have been of no help in identifying the site of adenoma. We have had no experience with identifying parathyroid adenomas by arteriograms.[21] None of the adenomas was detected correctly during physical examination before operation.

Operative Results. In 25 of the 28 surgical patients with preoperative diagnoses of primary hyperparathyroidism, adenomas were found at the first operation. In two of three who had second operations, adenomas were found in the mediastinum, in the third, subtotal thyroidectomy performed a month after negative neck exploration revealed an intracapsular parathyoid adenoma. In another patient one adenoma was found, but a second undetected adenoma contributed to the patient's death. In one postmortem case, residual parathyroid cancer was found after parathyroid tissue had been removed during two previous operations elsewhere.

Postoperative Complications. One patient had a laryngeal nerve injury and developed hypoparathyroidism, which required continuing treatment with calcium and vitamin D. Two other patients had temporary hypoparathyroidism that required medication. One patient had a severe wound infection that necessitated drainage, and two have persistent renal calculi.

In six postmortem cases, recognition of the diagnosis and removal of the tumors earlier in the course of the disease may have helped the patients.

Illustrative Cases

Case 1. *Recurrent hyperparathyroidism after regeneration of an infarcted adenoma; papillary adenocarcinoma of the thyroid; homologous transplant of parathyroid adenoma.* A 45-year-old Negro woman admitted for nausea and vomiting, had previously had polydipsia, polyuria, and chronic constipation. Hematuria, dysuria, and frequent urination were also noted, and roentgenograms showed a calculus in the left kidney.

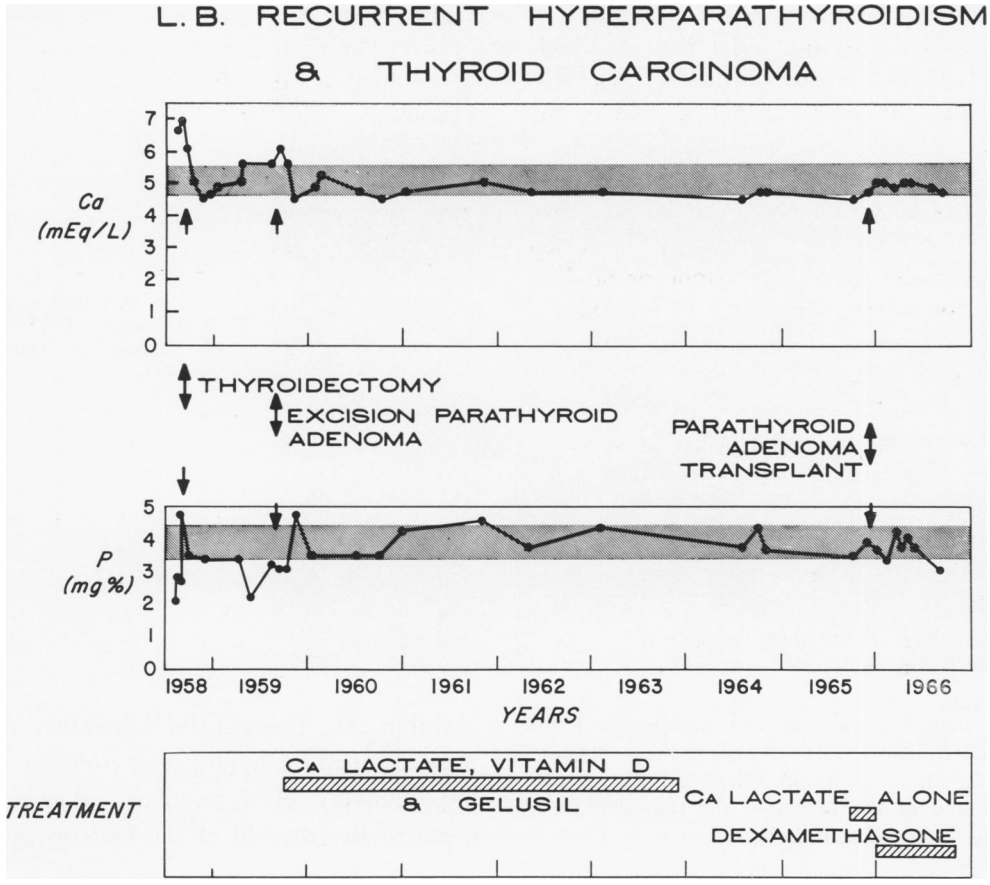


FIG. 5. Case 1. Serum calcium and phosphorus determinations following regeneration of infarcted parathyroid adenoma after resection of carcinoma of the thyroid.

The patient received antibiotic drugs for urinary infection. Six months later she was admitted again for pain in her knees, shoulders, and hands. Serial roentgenograms of the upper gastrointestinal tract showed a narrowed gastric antrum suggestive of old scarring and fibrosis. Serum calcium ranged from 6.5 to 6.7 mEq./L., and serum phosphorus from 2.3 to 2.7 mEq./L. (Fig. 5). Alkaline phosphatase was reported as 6.8 Bodansky units. Renal tubular reabsorption of phosphorus ranged from 70 to 82%. Diagnosis of hyperparathyroidism was made and exploratory operation was done the following month. Operation disclosed two apparently normal right parathyroid glands. A nodule 1 cm. in diameter was removed from the lower anterior portion of the left lobe of the thyroid; frozen section showed adenocarcinoma (Fig. 6). Total left lobectomy, isthmusectomy, and subtotal right lobectomy were therefore done; the inferior arteries were ligated in continuity. The left parathyroid glands were never identified.

After operation, serum calcium and phosphorus returned to normal levels, but within seven months the patient had recurrent symptoms, and serum calcium rose to 5.7 and phosphorus was 2.7 mEq./L. The neck seemed normal, and no evidence of metastatic thyroid cancer was detected.

About a year after operation, the neck was explored again by one of us (E. T. K.). The bed of the thyroid gland was dissected with considerable difficulty, and no residual carcinoma or parathyroid tissue was found. The upper sternum was split, and after tedious dissection a nodule, $1.1 \times 0.6 \times 0.6$ cm. was found behind the junction of the first rib and the sternum. Frozen section proved it to be a parathyroid adenoma (Fig. 7). After operation, serum calcium fell to 3.6 mEq./L., and oral calcium lactate and vitamin D were required to maintain normal serum calcium levels.

Six years later, a portion of a parathyroid adenoma removed from another patient at Charity Hospital was implanted in the patient's left calf.

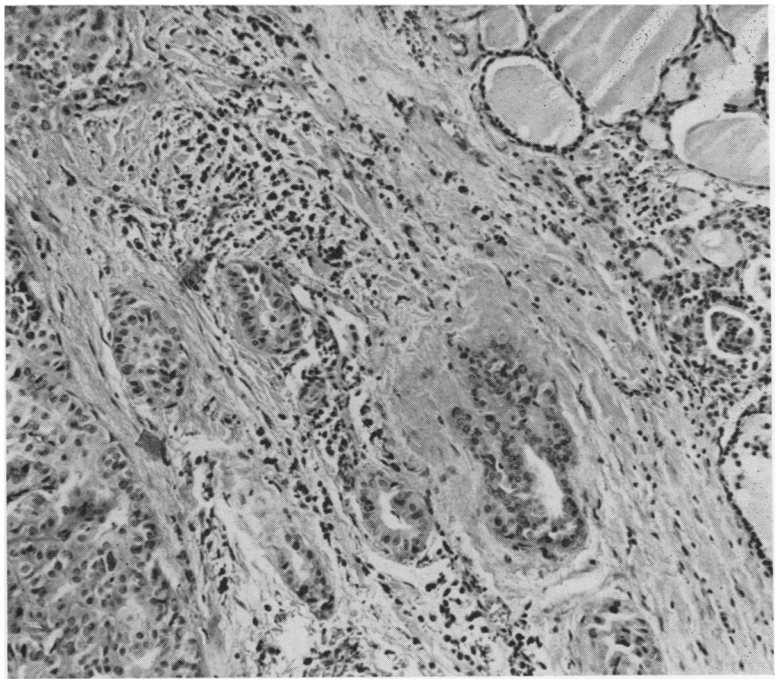


FIG. 6. Papillary adenocarcinoma in left lobe of thyroid of Case 1 (×140).

Since then her calcium and phosphorus levels have remained normal, although she does not take oral calcium or vitamin D. Selenium-tagged methionine scan of the region of the transplant later showed no uptake of isotope.

Comment. The clinical laboratory data were classical for hyperparathyroidism, but the discovery of a papillary adenocarcinoma of the thyroid at the first operation

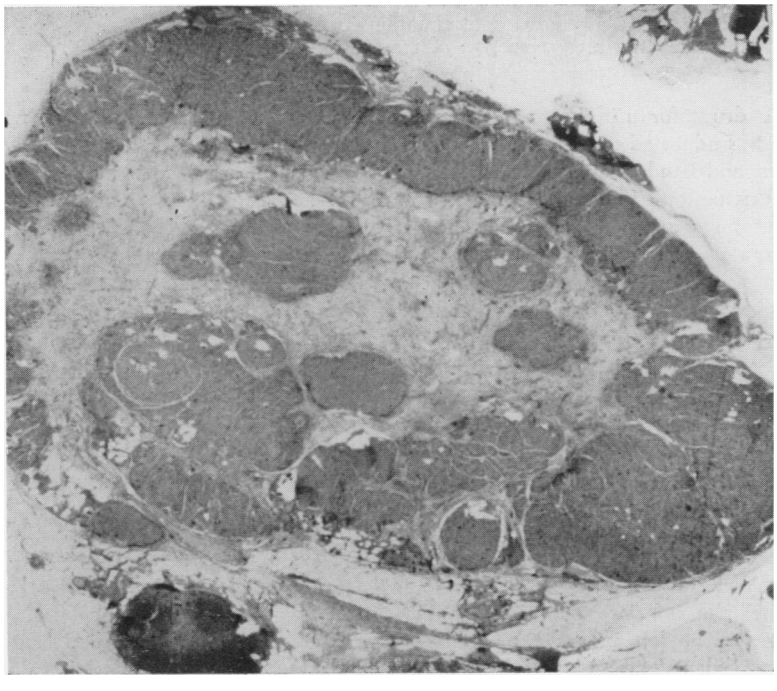


FIG. 7a. Case 1. Low-power photomicrograph showing infarcted parathyroid adenoma with central necrosis and peripheral regeneration.

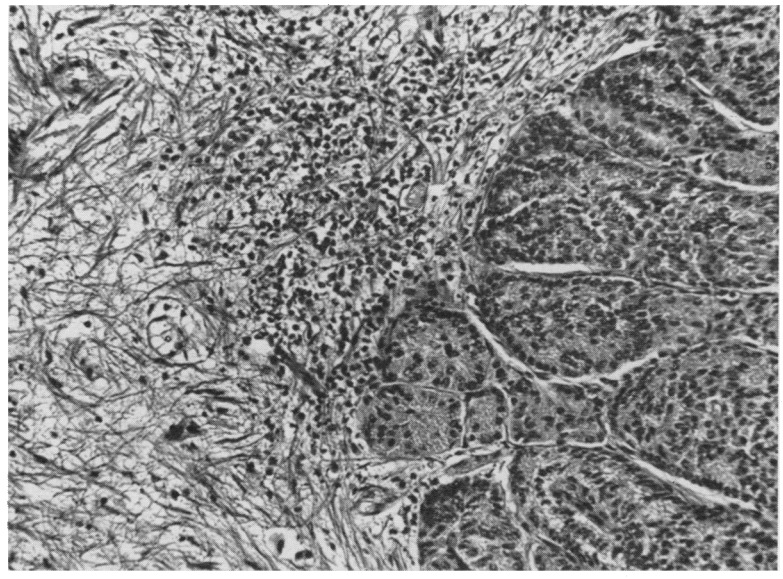


FIG. 7b. High-power photomicrograph of Fig. 7a showing regenerating parathyroid and granulation tissue.

resulted in treatment for cancer, and further search for a parathyroid adenoma was abandoned. The ligation of the inferior thyroid artery routinely done for thyroid lobectomy undoubtedly caused infarction of the parathyroid adenoma in the upper mediastinum, which later regrew. Microscopic examination showed large areas of fibrous granulation tissue containing nests of regenerating adenoma in the central portion of the tumor, with active regenerating adenomatous cells in the periphery.[18] Howard and colleagues [11] described a patient with spontaneous remission of hyperparathyroidism due to necrosis of adenoma and found evidence of old hemorrhagic necrosis in adenomas thought to be caused by infarcts in three of 35 patients.

Homologous transplantation of embryonic, adult, or adenomatous parathyroid tissue for relief of hypoparathyroidism has long interested physicians,[12] but it is difficult to determine whether a transplantation has been successful. A common factor for success seems to have been use of embryonic, newborn, or adenomatous parathyroid tissue, either for direct transplantation or after conditioning in tissue culture with the recipient's serum. Retrospectively, in our patient use of calcium should have been discontinued to find out if parathyroid deficiency existed before transplantation. Although transplantation in this patient cannot yet be labeled successful, calcium levels have remained normal without supplementary treatment.

Case 2. *Parathyroid adenoma with occult sclerosing carcinoma of the thyroid.* A 65-year-old white man was admitted for evaluation of hyper-

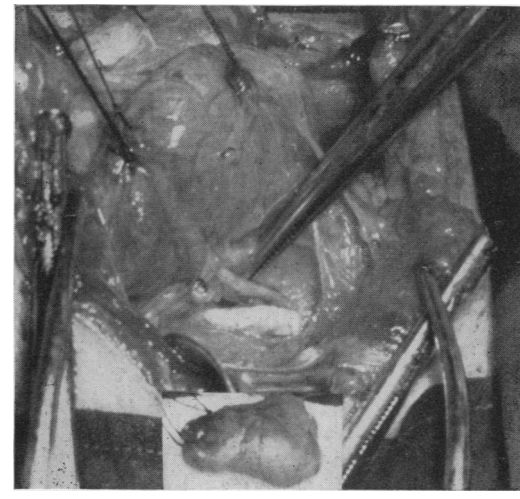


FIG. 8. Case 2. Parathyroid adenoma removed from a site posterior to the inferior thyroid artery and recurrent laryngeal nerve. Gelfoam placed in site of adenoma.

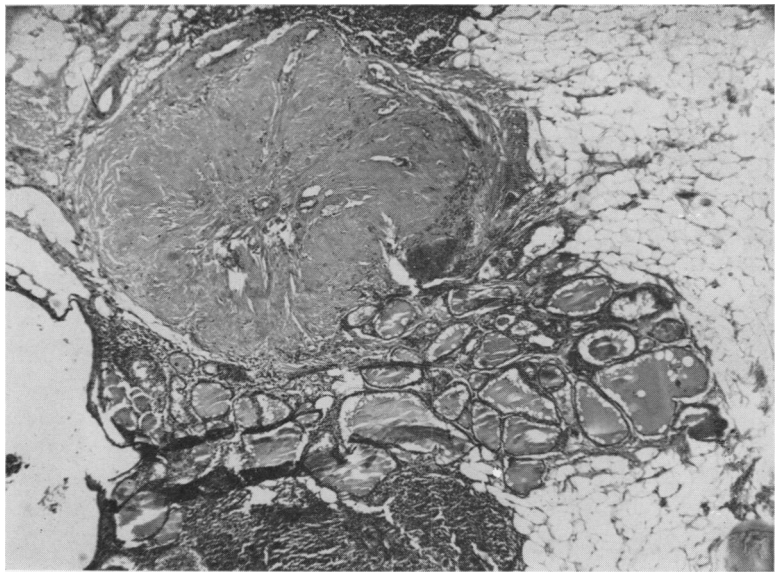


FIG. 9. Case No. 2. Thyroid follicles present in peripheral sinus of Delphian lymph node and adjacent fat-hyalinized nodule was interpreted as thrombosed, recanalized vein (×50).

parathyroidism. Eleven years previously he had been admitted for prostatic hypertrophy, vesical calculi, and small renal calculi, for which transurethral resection was done. Five years previously he had had repeated episodes of renal colic. Measurements of serum calcium and phosphorus and tubular reabsorption of phosphorus were inconclusive. Later the same year a second transurethral prostatectomy was done, and still later a left nephrectomy for nephrocalcinosis.

On the present admission, serum calcium ranged from 5.6 to 6.0 mEq./L., and phosphorus from 2.3 to 2.8 mEq./L. A parathyroid adenoma, 2 × 2 × 1 cm., posterior and inferior to the right lobe of the thyroid, was found and resected (Fig. 8). During the operation an enlarged Delphian node lying above the isthmus of the thyroid was removed. The left inferior parathyroid gland was identified, but the superior parathyroid glands were not found. After operation, serum calcium and phosphorus levels returned to normal. The Delphian node showed metastatic follicular carcinoma from the thyroid gland (Fig. 9). About seven weeks later, the entire left lobe and isthmus, and almost all the right lobe were removed. Step sections of the thyroid gland showed occult scleros-

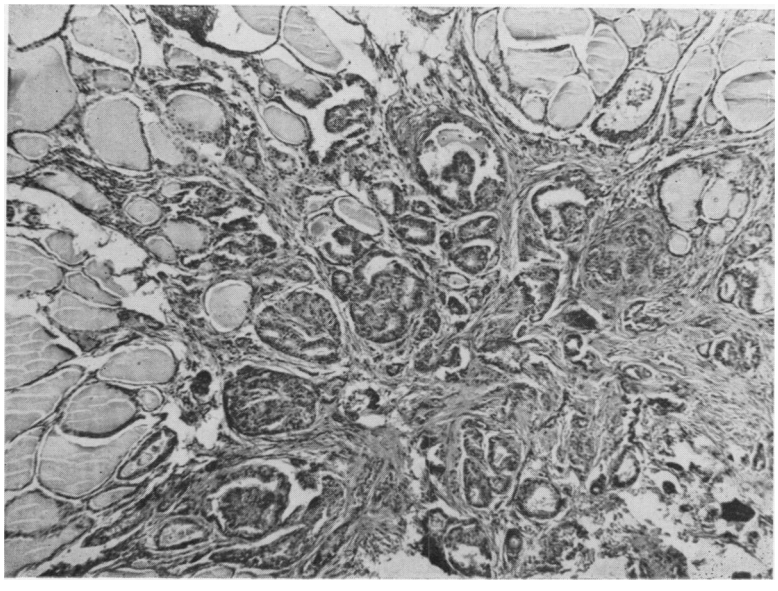


FIG. 10. Case 2. Occult sclerosing follicular thyroid carcinoma in left lower lobe (×50).

ing follicular carcinoma within the left lobe (Fig. 10).

Comment. Diagnosis by frozen section of the node at the first operation would have obviated the second operation. Occasionally frozen sections are unreliable in diagnosis of thyroid carcinoma, and the surgeon decided that the tissue should be saved for permanent section. Whether the diagnosis could have been made on frozen section remains moot, but with the cryostat now available, frozen section examination should be obtained.

Presence of thyroid tissue in cervical lymph nodes opens the question of whether a malignant or benign process exists.[4, 13] Careful sectioning of the thyroid glands in most patients shows occult thyroid carcinoma.[19]

Case 3. *Mediastinal parathyroid adenoma.* A 28-year-old white housewife was admitted to Hotel Dieu with a history of bilateral renal calculi of six years' duration. Ten years earlier, bilateral pyelolithotomy was done for magnesium and calcium stones. Two years before this admission, nephrocalcinosis was detected in the right kidney. At that time calcium was 5.7 and phosphorus was 3.1 mEq./L. A year later the uneventful delivery of the patient's first child occurred. Eight months prior to admission a second child developed hypocalcemic tetany ten days after birth. The infant responded to calcium therapy and is now normal. Six months before the present admission, nephrocalcinosis of both kidneys became worse. The patient had episodes of nausea and vomiting, paresthesia of the face and hands, and felt nervous and tired. She was referred to Dr. George E. Burch, Professor of Medicine at Tulane, who made a diagnosis of primary hyperparathyroidism, probably due to adenoma.

After admission, the neck and superior mediastinum were thoroughly explored through a collar incision. The thyroid gland was small and symmetric and contained no nodules. Both inferior parathyroid glands were small and on biopsy revealed atrophic tissue. Biopsy of a small nodule of tissue behind the left lower lobe showed parathyroid tissue. Subtotal thyroidectomy was done because of the possibility of an adenoma within the gland. After operation serum calcium levels did not change.

Three weeks after the first operation the patient was admitted to the Tulane Clinical Research Center at Charity Hospital, and mediastinotomy was done by splitting the entire sternum. A mass, $5 \times 3 \times 1$ cm., was noted adjacent to the right thymus gland overlying the junction of the innominate veins (Fig. 11). The tumor was removed, and a piece of the adenoma, $1 \times 1 \times 1$ cm., was implanted in the intercostal muscles in the second right interspace. By the sixth day after operation, serum calcium had dropped to 4.0 mEq./L., and

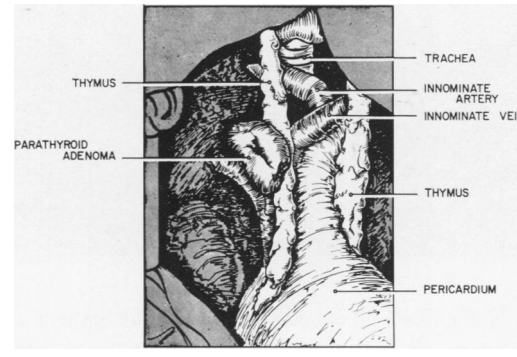


FIG. 11a. Case 3. Drawing of parathyroid adenoma lying over junction of innominate veins.

FIG. 11b. Photograph of adenoma in situ (Case 3).

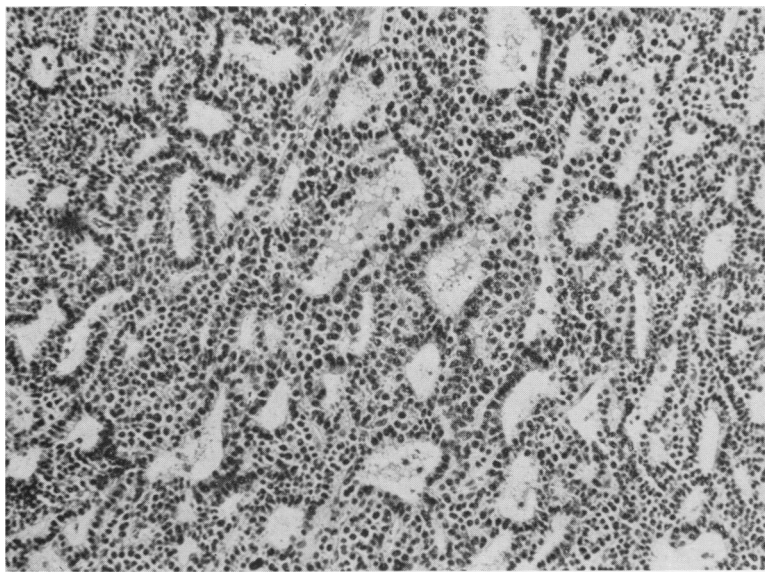


FIG. 11c. Photomicrograph of parathyroid adenoma in Case 3 (×140).

has remained about 4.8 mEq./L. The patient is now an alert, energetic, attractive young woman, in sharp contrast to the tired, lethargic, emotionally labile patient with multiple physical complaints before operation. A pyelogram eight months after operation showed no change in the nephrocalcinosis.

Comment. This patient had typical hyperparathyroidism. The operations were done in stages so that the results of permanent sections and examination of the thyroid could be known before mediastinotomy was done. At the second operation, a large parathyroid adenoma found in the mediastinum explained atrophy of the parathyroid glands in the neck and the temporary inadequate function of the parathyroid tissue of the patient's second child. Because it was feared that the previous exploration may have interfered with the blood supply of the atrophic parathyroid glands in the neck, a portion of parathyroid adenoma was transplanted into an accessible region on the anterior chest wall, by the technic suggested by Cope. Although this transplanted tissue can conceivably enlarge enough to produce symptoms, it is accessible for removal if evidence of hypercalcemia develops.

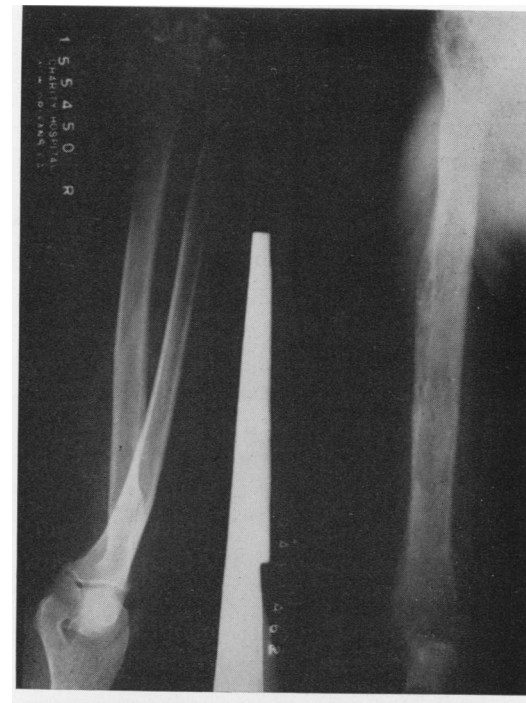
Case 4. *Acute parathyroid crisis.* A 69-year-old Negro woman was admitted because of nausea, vomiting, and increasing mental confusion. She had visited the Charity Hospital Clinics often over the past twenty years and was known to have hypertension, heart disease, and syphilis with gummatous lesions in the region of the olecranon bursa. She had been taking digitalis for the past four years for heart failure.

On this admission, the patient appeared acutely ill, was disoriented, and was salivating profusely. Electrocardiogram showed tachycardia, left ventricular hypertrophy, and myocardial ischemia. Blood urea nitrogen was 71 mg./100 ml. Calcium was 8.0 and phosphorus 4.2 mEq./L. Alkaline phosphatase was 18 sigma units. Urine showed 2 plus albumin, with a positive Sulkowitch's test. Roentgenograms were interpreted as Paget's disease of the humerus and skull (Fig. 12). A diagnosis of renal failure, nephrocalcinosis and chronic pyelonephritis was made. The medical staff considered hypercalcemia due to hyperparathyroidism a strong possibility. The surgical consultants believed that an operation on a patient as ill as she would be extremely hazardous and that renal failure and Paget's disease could explain the hypercalcemia at least in part. Operation was deferred, and the patient was given intensive medical treatment, including antibiotics, hydration, sodium versinate by infusion, and cortisone, but she died five days after admission. Necropsy showed chronic pyelonephritis, nephrocalcinosis, diffuse parathyroid hyperplasia and adenoma, adrenal hyperplasia, pituitary adenomas, and osteitis fibrosa cystica.

Comment. Recent reports have pointed out the necessity for awareness of acute parathyroid crisis, particularly in patients with hypercalcemia associated with renal failure.[8, 14, 17, 22, 23] Excision of the parathyroid adenoma is the most effective treatment, but the operative fatality rate is high, and failure to find an adenoma almost automatically results in death of the patient. Although this patient's death was due in part to parathyroid poisoning, she also had multiple endocrine abnormality syndrome.[20] It is doubtful whether the renal disease and other pathologic changes present would have permitted recovery had the adenoma been successfully removed at operation.

One other patient died of parathyroid poisoning; a parathyroid adenoma had been removed in another hospital in 1957.[18] In 1959 a second operation was performed because of persistent hypercalcemia, and a large parathyroid gland, thought to be a second adenoma, was removed from the left side of the neck. Histologic examination when reviewed indicated that the tissue represented a normal parathyroid gland. Because of persistent symptoms, the patient was transferred to Charity Hospital, where she died from parathyroid poisoning. At necropsy a nodular mass, 2 × 2 × 2 cm. was found in the region from which the right parathyroid adenoma had been removed two years before. Sections showed a low-grade parathyroid carcinoma.

We have continued to consider acutely ill patients with hypercalcemia possible candidates for exploratory operation, but have not since encountered such a patient.



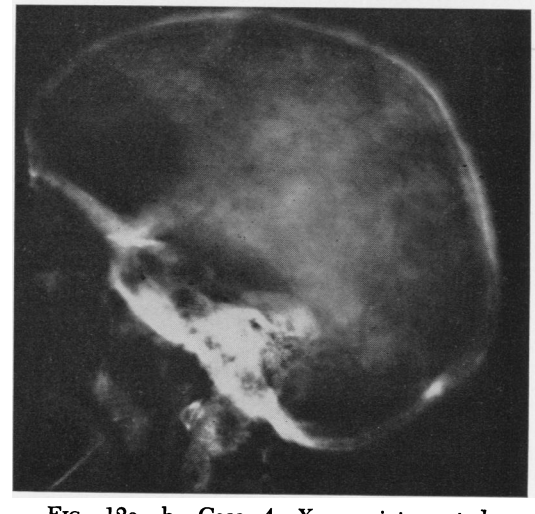


FIG. 12a, b. Case 4. X-rays interpreted as Paget's disease of humerus and skull, later revised to osteitis fibrosa cystica.

Case 5. *Multiple endocrine adenoma syndrome*[20] *(MEA Syndrome).* A 59-year-old white woman was admitted for congestive heart failure. The patient had signs and symptoms of endocrine, bone, renal and gastrointestinal diseases. She received intensive medical care, but continued to have fibrillation and died of cardiorespiratory disease seven weeks later. The necropsy performed by pathologist Dr. Louis H. Stern, was a classic demonstration of the multiple endocrine adenoma syndrome. Pertinent findings included an eosinophilic adenoma of the pituitary gland, parathyroid hyperplasia and clear cell adenoma, islet cell hyperplasia of the pancreas, and adrenal cortical hyperplasia (Fig. 13). Secondary diseases due to the adenomas were manifested by acromegaly and megaduodenum, osteitis fibrosa cystica, multiple renal calculi, and hemorrhagic duodenitis with superficial ulceration.

Comment. In addition to this patient, three others had MEA syndrome, including Case 4. The third patient in this series, reported elsewhere,[18] was a 35-year-old man with masked hyperparathyroidism, milk-alkali syndrome, and multiple endocrine adenoma. The parathyroid gland was explored for adenoma, and although one adenoma was discovered, a second was missed. After the operation a duodenal ulcer developed, with severe gastrointestinal hemorrhage; subtotal gastrectomy did not control the bleeding. The remaining adenoma in the neck may have contributed to exacerbation of the peptic ulcer leading to the patient's death, but the islet cell adenomas in the pancreas and duodenum can also be implicated. In retrospect, a total gastrectomy should have been performed as well as complete extirpation of the parathyroid adenomas.

The fourth patient with MEA syndrome was a 56-year-old man with a bleeding duodenal ulcer, who was admitted in coma. The patient died shortly thereafter, and necropsy disclosed an adenoma of the islets of Langerhans, three clear cell parathyroid adenomas, and adrenal cortical adenomas.

Patients with multiple endocrine adenomas are problems in treatment. Functioning adenomas of islet cell, duodenum, and pituitary, parathyroid and adrenal glands may all be present, and successful removal at one site may result in exacerbation of symptoms caused by adenomas at another site. Treatment of this syndrome has no simple answers, but the presence of ade-

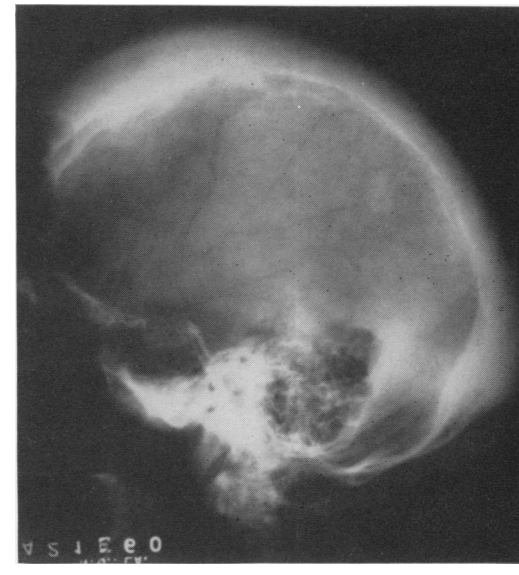


FIG. 13a. Case 5. Skull showing enlarged pituitary fossa, acromegaly, and osteitis fibrosa cystica in patient with multiple endocrine adenoma syndrome.

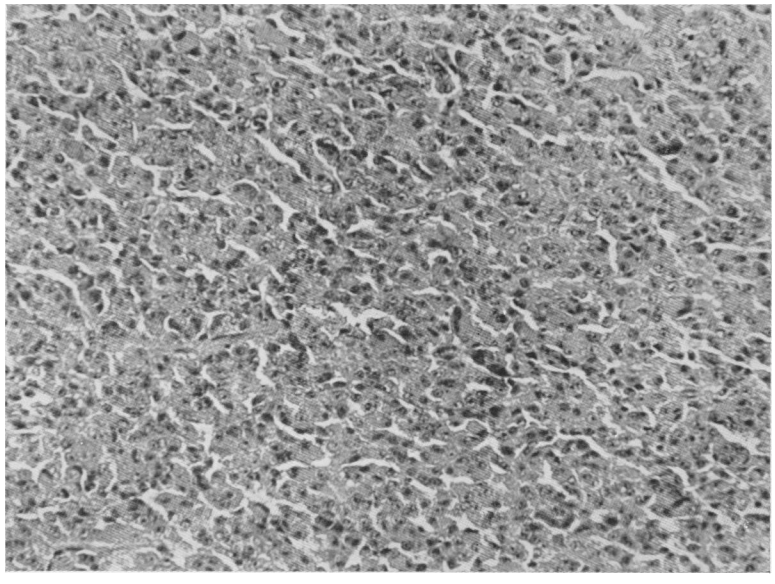


FIG. 13b. Photomicrograph of eosinophilic pituitary adenoma (×140).

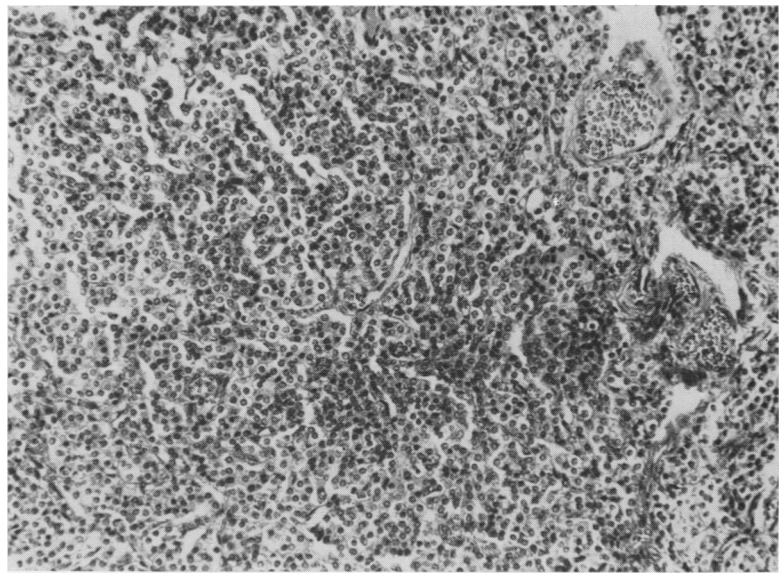


FIG. 13c. Photomicrograph of hyperplasia of parathyroid (×140).

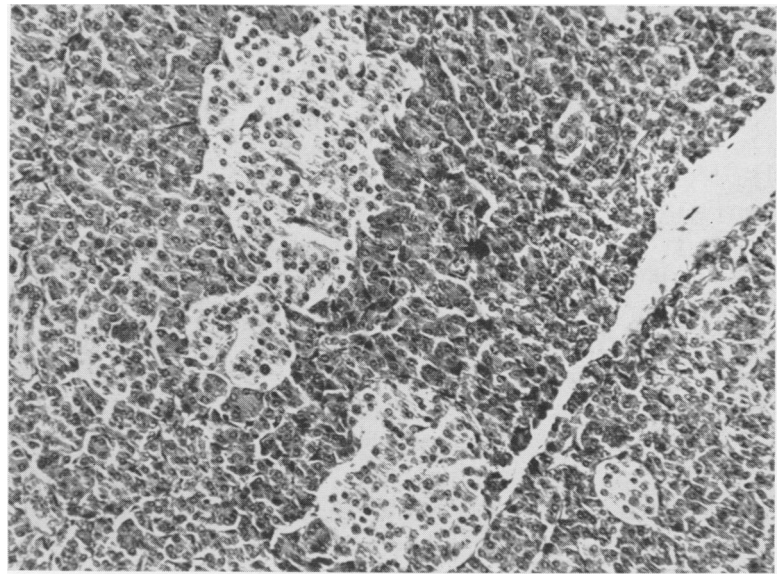


FIG. 13d. Photomicrograph of focal islet cell hyperplasia of pancreas (×140).

nomas in other endocrine glands should be kept in mind when the diagnosis of parathyroid adenoma is made.

Discussion

Successful management of parathyroid adenomas requires the combined skills of the internist, endocrinologist, pathologist, and surgeon. Our policy has been to have a senior staff surgeon perform or supervise these operations, for although the straightforward case represents a simple surgical exercise, the difficult case can try the skill of the most experienced surgeon.

The surgical technic for removal of parathyroid adenoma has been adequately described.[2, 3, 5, 10] Each case must be individualized, but excellent exposure is always required and is usually not difficult to obtain, as the thyroid gland is rarely enlarged. Careful dissection is necessary, with complete hemostasis. The glands and suspected

adenomas should be identified, and frozen section of all tissue should be obtained before resection. As thorough exploration takes considerable time, a two-stage procedure is recommended; if no adenoma is found in the neck a subtotal thyroidectomy should be done in case the adenoma lies within the thyroid gland. The pathologic examination should be completed and the clinical ressponse noted before a second-stage mediastinotomy is done.

The indication for operation in patients with primary hyperparathyroidism is hypercalcemia after exclusion of other causes of elevated serum calcium. Serum calcium of 5.5 mEq./L. or greater deserves evaluation, although patients with serum calcium between 5.2 and 5.5 mEq./L. for extended periods may also have parathyroid adenomas.

Elevated serum calcium in patients with multiple myeloma, sarcoidosis, and vitamin D intoxication will fall to 5.2 mEq./L. or less after 150 mg. of cortisone acetate has been given by mouth for seven to ten days. Serum calcium of 5.2 mEq./L. or less on two consecutive days after the second dose has been given is significant. Cortisone does not consistently suppress hypercalcemia in patients with the milk-alkali syndrome or malignant disease. Suppression of hypercalcemia of primary hyperparathyroidism is rare. Primary hyperparathyroidism should be suspected in milk-alkali syndrome if the serum calcium does not fall to 5.2 mEq./L. within two weeks after adequate hydration and withdrawal of alkali and remain below that level for the next several months.

The tubular reabsorption of phosphorus test aids diagnosis of hyperparathyroidism in patients with borderline hypercalcemia and should be done before the cortisone suppression test, as use of cortisone may affect renal function. This four-hour test should be done in the morning after the patient has had three days of high phosphate intake to exaggerate renal loss of phosphate. Values below 78% are considered abnormal.

The possibility of a specific and sensitive immunoassay[1] seems good with the isolation of pure parathyroid hormone.[7] Even this measurement may not replace present laboratory procedures, however, as experience with specific assays in other hyperfunctioning endocrinopathies has not always shown significant increases in circulating hormones.

No test of function or immunologic assay differentiates hypercalcemia due to parahormone from that due to a parahormone-like substances. At present a thorough search must be made for malignant disease as a cause of hypercalcemia before operation is done for parathyroid adenoma.

Our experience with selenomethionine (75_{Se}) scintograms to identify the site of hyperfunctioning parathyroid tissue has been disappointing. Seven attempts to identify parathyroid tissue before operation have been unsuccessful. Although we have observed uptake of isotope in several specimens, the amount has not been sufficient to identify the site on the scintogram. These results do not necessarily reflect the experience of others,[9, 16] as many factors may have been responsible for our lack of success. The principal difficulty is that ratio of the concentration of 75_{Se}, determined by specific activity in the parathyroid tissue, to that of surrounding thyroid or thymic tissue has never exceeded three to one. Because of the relative size of the masses present, selective concentration in the parathyroid tissue must be at least tenfold that elsewhere before differentiation on the scintogram is satisfactory.

Summary

Among 53 patients with parathyroid adenomas at the Charity Hospital of Louisiana from January 1, 1942 to July 31, 1966, 33 diagnoses were made at operation and 20

at necropsy. Five adenomas found incidentally at operation and the ten discovered at necropsy gave no clinical clues of hyperfunction.

More than three-fourths of the cases were found during the past eight years. Three adenomas were in the mediastinum and 50 in the neck; 46 were single, and seven were multiple. Renal stones, peptic ulcer, weakness, fatigue, and mental confusion were prominent complaints. One patient had parathyroid cancer and eight other patients had various concurrent cancers. Of 28 patients with diagnosis before operation, 24 were cured at the first operation and three at the second. The other patient died after operation in which a second adenoma was overlooked; he was one of four who died of multiple endocrine adenoma syndrome. In six patients with postmortem diagnoses of hyperparathyroidism contributing to death, all may have been benefited if the diagnosis had been established earlier and corrective operation had been performed.

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