

# PRIMARY HYPERPARATHYROIDISM

## A Diagnostic and Operative Problem

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### Historical Note

In 1903 Askanazy discovered a parathyroid tumour in a patient with Von Recklinghausen's disease and used the term adenoma to describe it. In 1907 Erdheim was the first to describe the relationship between calcium metabolism and the parathyroid glands. Collip in 1925 discovered parathyroid hormone and thus the anatomical and physiological relationship of parathyroid disease was established. In 1926 Mandl removed a parathyroid adenoma from a patient with Von Recklinghausen's disease. In a later report Mandl described the patient as having recurrent renal calculi and hypercalcaemia. The patient was re-explored in 1933.

### Anatomy

In a study of the normal anatomy of the parathyroid glands Gilmour (1938) found the 2 superior parathyroids above the lower one-third of the thyroid gland on the posterior or medial surface in 90% of those studied. He also found the 2 inferior parathyroid glands were adjacent to the inferior pole of the thyroid in 95%. 3% of the inferior parathyroid glands not so positioned can be found 3 to 6 cms below the inferior pole of the thyroid.

Approximately 80% of individuals have 4 parathyroid glands, the inferior occupying less constant positions (Cope, O. 1960). A given patient may very rarely have only 3 parathyroid glands. Cadaver dissections have disclosed that 3 parathyroid glands were present in 20-30% of human beings (Goss, C.M. 1954).

The normal weight of a parathyroid gland is 40-50 mgm. The largest diameter of a normal parathyroid is 0.5 cms. (Mazzei *et al.* 1966).

### Pathology

A single adenoma is the cause of hyperparathyroid states in about 80% of cases; double adenomas occur in 4%, hyperplasia in 12% (Norris, 1947). 5% of parathyroid adenomas are found in the mediastinum. Of these 65% are found in the anterior mediastinum (Pochter, 1963). The author maintains, however, that a careful search is necessary once the mediastinum is opened. Carcinoma is responsible for 4% of cases (Norris, 1947). Beahrs *et al.* (1963) give a figure of 3%. Everybody is agree with Cope (Cope *et al.* 1953) that local invasion or distant metastases together with hypercalcaemia must be present for the diagnosis of carcinoma.

As for the size of the adenoma, Cope (1960) stated that the amount of adenomatous tissue found should be roughly proportional to the severity of the disease, and therefore exploration should be terminated when an adenoma of sufficient size to account for the disease is found. If the findings are equivocal he counsels waiting, observation and re-exploration if necessary. This view is opposed by Glenn (1960), Adams (1963), Coffey (1965) and Mazzei (1966). Since 10% of parathyroid adenoma are multiple, any unidentified gland may be yet another adenoma. It is not possible to exclude this unless a thorough search is made of all 4 parathyroid glands. Nobody disagrees that a normal parathyroid gland may be difficult to identify. It may be desirable and necessary to remove many pieces of tissue for frozen section. There is also no general agreement that the size of the adenoma is related to the severity of the disease. The parathyroid glands differ from other endocrine glands in that an adenoma affecting one or

more parathyroids does not cause atrophy of the others (Wyndham, 1965, Mazzei 1966). Adenoma and hyperplasia may co-exist in the same patient, although in different glands, especially in the presence of azotemia accompanying nephrolithiasis or other kidney disorder.

The confusion extends to the microscopic appearances of the tumour where chief cells may predominate (Mazzei, 1966), or clear cells (Woolser, 1952). Histologically adenomatous and hyperplastic glands are similar if not identical. Thus it is also necessary for the pathologist to know the condition of the remaining parathyroid glands, which should be identified and if questionable biopsied to rule out hyperplasia (Judd, 1966).

### Clinical features

#### 1. Nephrolithiasis

The majority of symptoms of primary hyperparathyroidism are related to nephrolithiasis. This may show up on a routine plain X-ray of the abdomen. Renal calculi may be a consequence of a parathyroid adenoma in the absence of an elevated serum calcium (D. Martin, 1964). They may show up on the routine investigation of a case with azotemia. The nephrolithiasis need not necessarily be a cause of the renal dysfunction. Of course looking for a renal stone or calcium deposits in the kidneys is part of the investigations required when the suspicion is aroused of a parathyroid adenoma. A plain x-ray and I.V.P. will demonstrate nephrolithiasis although the true extent of calcific deposition and renal damage will require some refined investigations, such as creatinine clearance studies and renal biopsies. It is interesting to note that the first case of parathyroid adenoma operated upon by Mandl developed recurrent renal calculi and hypercalcaemia and was re-explored in 1933.

#### 2. Peptic ulceration:

The association between parathyroid adenoma and peptic ulceration is very disputed. Although Mazzei *et al.* (1966) maintain that the association is well known,

Lee *et al.* (1955) found a 24% incidence. Ostrow *et al.* (1960) quote a figure of less than 10%. Wilder *et al.* (1961) reported 7 cases with a combination of hyperparathyroidism and peptic ulcer and reviewed 45 cases from the literature. Of these 52, 35 had active and "intractable" ulcers at the time of operation on the parathyroid. Of 28 patients fully studied, 23 sustained an improvement in their ulcer symptoms after excision of the parathyroid adenoma. Chojecki (1965) performed a series of biological investigations in patients with gastro-duodenal ulcer, and failed to demonstrate a real relation between the two conditions.

### Polyendocrine adenomatoses

A 49 year old male was reported in the Proceedings of the R.S.M. in 1964 as having a parathyroid adenoma, excessive gastric secretion consistent with Zollinger Ellison syndrome. He had 2 adenomas of the pancreas. All the adenomas were removed at operation.

Another case was reported in the Rev. Int. Hepat. (1965). This was a 39 year old woman with renal lithiasis, recurring peptic ulcers with gastric acid hypersecretion and biological signs of parathyroid hyperfunction. She had an adenoma of the left inferior parathyroid gland and pancreatic adenomatosis. The latter consisted of 5 nodules of non-beta cell adenomas. The authors made some remarks about this case and others in the literature which makes one wonder if the Zollinger Ellison syndrome must not be integrated in the larger framework of the polyendocrine adenomatoses.

### Joint Manifestations

#### *Chondrocalcinosis:*

There is disagreement as to whether this condition is familial (Eengelman *et al.* 1967, Mintz *et al.* 1960, 1964). It is usually recognised in the 6th decade or later. It affects the weight bearing joints usually, particularly the knees (Engelman and Shearn, 1967). Other joints have also been reported as manifesting calcification, e.g.

ankles, symphysis pubis (Wood, 1958, Hosking and Clennar, 1960). The upper limbs can also be affected, particularly the elbows and the articulation of the wrist (Bogdonoff, 1956). A personal case presented with a central type of polyarthritis affecting the large joints responsible for movements of the upper limb. Chondrocalcinosis is associated with raised or normal urate levels (Engelman and Shearn, 1967). Unlike gout it is not benefitted by the administration of Colchicine.

Joints affected are swollen and painful. Radiologically the calcification is recognisable. In the presence of an effusion the joint aspirate reveals calcium pyrophosphate crystals (Jackson, 1965, Zitman and Sit Aj, 1963). Synovial biopsy reveals a mild synovitis (Bywaters, Scott, Dixon, 1963).

### **Bone Disorders**

Effects of decalcification and abnormal recalcification may be found on X-ray films. The classical picture of Von Recklinghausen is seldom seen at present. Cystic bone changes represent a late stage in the disease. Gross cystic changes may be accompanied by skeletal deformities and pathological fractures. The more usual and earlier manifestations are disappearance of the lamina dura as seen on dental films, subperiosteal reabsorption of bone, especially of the phalanges, and generalised rarefaction of bone, including a ground glass appearance of the skull.

Bone pain is a relatively common symptom. Progression of the disease leads to progressive deformity like kyphosis, bowing of the limbs. The brown tumour in the jaw produces an expansion which erupts to produce an epulis like swelling beneath the gum. Most if not all patients have some degree of bone involvement affecting one or more bones (Fraser, Harrison and Ibertson, 1960, Miravet *et al.*, 1965). X-ray study may help to exclude other causes of hypercalcaemia such as sarcoidosis, metastatic disease of bone or the presence of occult neoplasm.

### **Renal dysfunction and Hypertension**

Although renal dysfunction can give rise to secondary hyperparathyroidism,

the association between azotemia and primary hyperparathyroidism is not very clear. Obviously, bilateral renal calculi or severe nephrocalcinosis would interfere with renal function, but Hellstrom and Ivemark (1962) confirmed the view that the most severe impairment of renal function occurred in patients with osteitis fibrosa, whether calcium deposits were present in the kidney or not. In these cases there is microscopic damage to the tubules with blockage of their lumina and sclerosis of nephrons. Moreover nephrocalcinosis in hyperparathyroidism is often associated with secondary pyelonephritis. In the older age group the renal vessels are affected by arteriosclerosis, independently of hyperparathyroidism.

Hypertension frequently complicates the intermediate and later stages of the disease. It is interesting to observe that in cases presenting with renal stone or nephrocalcinosis there was a lower incidence of hypertension than in those presenting with osteitis fibrosa.

### **Mental Symptoms**

Psychiatric changes do not follow a set pattern. They vary from catatonic stupor (Hockaday *et al.*, 1966) to aggressive behaviour and change of character (Nielsen, 1955). Acute depressive illness with suicidal tendencies was reported by Reinfrank (1961). Other patients presented with hallucinations, confusion, impairment of memory, fits of rage. The symptoms cleared up or improved after removal of the parathyroid adenoma.

### **Acute hyperparathyroidism and tetany**

Hyperparathyroidism with severe hypercalcaemia and large tumours may present with weakness, anorexia, nausea, vomiting, constipation, polyuria, polydipsia and disturbances in behaviour and state of consciousness. This extreme case of hyperparathyroidism has been called hypercalcaemia crisis and is a medical and surgical emergency. This problem of acute parathyroid intoxication was the subject of study by Wilson *et al.* (1964) Payne and Fitchett (1965) reviewed 68 reported cases

of hyperparathyroid crisis and added 2 of their own. In 60 of these 70 patients the crisis was due to single or multiple adenomas. No operation was carried out on 28 cases; they all died. In the remaining 32, excision was followed by survival in 26.

Tetany follows spontaneous infarction of an adenoma (Johnston, 1961). But such a happening, unless following a neck operation is rare. On the other hand tetany has been reported in children born of mothers with undiagnosed primary hyperparathyroidism. The first observation was made by Friedrichsen in 1938. Other cases were reported by Walton (1954), Hutchin and Kessner (1964) and others. These children presented with neonatal tetany. In a case reported by Bruce and Strong (1955) symptoms of hypoparathyroidism developed when the child was 1 year old; diagnosis of hypoparathyroidism was not made until it was  $7\frac{1}{2}$  years of age. Neonatal tetany may be the only clinical lead to diagnosis of the mother. In Hartenstein's case (1966) history taking revealed that the mother had a kidney stone during the pregnancy. In Van Ardel's case (1955) the mother had the first symptoms of renal calculus 3 years after her infant had tetany of the newborn. The conclusion is that one must investigate the mother of a case of tetany of the newborn, as the adenoma of the mother may be asymptomatic. The complication of hyperparathyroidism are not confined to the foetus. Ludwig (1962) reported an increased incidence of complications of pregnancy and recommended exploration for the adenoma when the diagnosis is made during pregnancy.

### Muscular System

Muscular weakness is not uncommon (Vicale, 1949). Muscular hypotonia was reported by Pyrah (1966). Generalised muscle weakness unassociated with atrophy or tenderness but associated with hypoactive reflexes was reported by Karpati and Frame (1964).

### Other Abdominal Manifestations

Anorexia, constipation, nausea and vomiting may be additional signs (Cope,

1957). Pancreatitis may be acute, presenting as an acute abdomen and diagnosed on a raised serum amylase report. Recurrent attacks of pancreatitis with pancreatic calculi may be associated with primary hyperparathyroidism. Alteration in calcium metabolism as a result of the steatorrhoea of chronic pancreatic disease may lead to the development of secondary hyperparathyroidism. A long standing hyperplasia of this type may eventually lead to the formation of autonomous parathyroid tissue. The term tertiary hyperparathyroidism has been introduced to describe the phenomenon. The presence of pancreatic adenoma in relation to the polyglandular syndrome has already been referred to. It is interesting to note that acute pancreatitis can follow parathyroidectomy (Mixer, 1962).

### Eye Changes

The eye can be affected by hypercalcaemia (Walsh and Howard, 1947). Calcific deposits may be present in the conjunctiva and cornea.

### Cardiovascular changes

Hypertension, decreased Q-T intervals, decreased action potentials are detected on E.C.G. recordings (Hellstrom *et al.*, 1958).

### Biochemistry

1. Exploration of the neck is undoubtedly called for in the presence of one or more clinical features of hyperparathyroidism and positive biochemical findings. There are cases that manifest intermittent function of parathyroid adenomas in which the serum calcium is within normal range at times and at other times significantly elevated (Veenema, 1961, Whitby, 1958). In cases of renal calculi with normal renal function, a figure persistently in the upper limits of normality should arouse suspicion and is commonly reported. McGeown (1959) states that the level of serum calcium fluctuates, though this is denied by some. The level of serum calcium at which a suspicion of hyperparathyroidism is aroused has dropped

through the years, mainly because of findings of "occult" parathyroid adenoma, such as a case reported by Martin and Turner (1964), where 5 estimates varied from 10.7 to 10.4. Black (1953) published a series of cases from the Mayo Clinic which showed a level less than 11.0 mgm% and expressed the opinion that a figure greater than 10.5 mgm% must be viewed with suspicion. Routine serum calcium analyses will help to unearth unsuspected hyperparathyroidism. Boonstra and Jackson (1965) discussed 31 cases of parathyroid adenoma with no definite clinical manifestations in this way. Patients with no definite biochemical or clinical evidence of hyperparathyroidism need prolonged, repeated study before a decision is taken to operate. But unexplained elevated serum calcium measurements in the presence of normal serum phosphorus measurements are sufficient evidence to warrant surgical exploration of the neck (Mazzei *et al.* 1966). True hypercalcaemia does not occur in uncomplicated secondary hyperparathyroidism, no matter how long the duration or how severe the degree of osteitis fibrosa generalisata (David *et al.*, 1962, Albright *et al.*, 1934).

2. Increased calcium excretion in the urine occurs in primary hyperparathyroidism. In the presence of normal renal function, the absence of hypercalcuria rules out hyperparathyroidism. Albright (1934) suggested a modified diet; on that basis calcium excretion should not exceed 150 mgm..

3. Phosphorus/creatinine clearance ratio is very helpful. The basis of this test lies in the action of parathyroid hormone that mobilises calcium from bone and increases absorption of calcium from the alimentary canal (Horwith *et al.*, 1966, Caniggia *et al.*, 1966). It also decreases reabsorption of phosphate from the renal tubules. The normal figure is about 0.07. A ratio of 0.2 is strong evidence of hyperparathyroidism. The creatinine clearance should be not less than 60 mls. per minute. The reabsorption of phosphate is low in metastatic bone disease, osteomalacia, myelomatosis and Cushing's syndrome.

4. Serum phosphate level is low in

hyperparathyroidism: 1-3 mgm per 100 ml. The normal level is 3-4 mgms per 100 ml. It is normal or increased in primary hyperparathyroidism with renal failure or renal failure with secondary hyperparathyroidism. A similar level is present in non-acidosis or acidotic osteomalacia, and is raised in hypophosphatasia, considerably raised in hypoparathyroidism.

5. Phosphate excretion index is calculated from a correction of the phosphorus/creatinine clearance ratio from the level of serum phosphorus (Nordin and Fraser, 1954). Its value is very much doubted.

6. Serum uric acid level may be raised in middle-aged patients presenting with gout, calcification of joints and joint pains and effusion.

7. Serum alkaline phosphatase is usually increased in the presence of clinical or radiological bone involvement. It is diminished in hypophosphatasia and is raised, although not to such a high level as in primary hyperparathyroidism, in osteomalacia. It is interesting to note that Norman Wyndham (1965) maintained that obvious skeletal decalcification coupled with a high serum alkaline phosphatase is a warning of possible post-operative difficulties in controlling the fall of serum calcium level.

8. Plasma protein level estimation will help in differentiating primary hyperparathyroidism from other causes of hypercalcaemia.

9. Results of calcium infusion tests have a degree of overlap such that a differentiation between hyperparathyroidism and other conditions simulating it is not possible (Horwith *et al.*, 1966). The general consensus of opinion favours this view. Martin and Turner (1964) suggested that this test was of value in diagnosing two of their cases of occult hyperparathyroidism.

10. Phosphate deprivation test suffers from the same defect as the previous one.

11. Hydroxyprolinuria is a measure of osteoblastic activity. Hence serum alkaline phosphate levels are also raised, and usually it is accompanied by radiological changes. Normal hydroxyprolinuria does

not exclude a diagnosis of hyperparathyroidism.

12. Studies of  $^{45}\text{Ca}$  dynamics and intestinal absorption of  $^{45}\text{Ca}$  (or  $^{47}\text{Ca}$ ) demonstrate increased absorption of Ca. (Horwith, 1966). Bone absorption of radio Ca. suggests this to be a more sensitive index of bone involvement than serum alkaline phosphatase.

13. The ultimate test is a measure of circulating parathormone (Rasmussen, 1961). It is a polypeptide, molecular weight 7000, bound to beta and gamma globulins in the plasma (Thasjian, 1963). Its estimation is complicated and suitable only for specialised centres.

The first and still the most important biochemical test is the level of the serum calcium. More elaborate tests already mentioned may and will in varying degree help to distinguished primary hyperparathyroidism from other causes of hypercalcaemia, e.g. Paget's disease, sarcoidosis, malignancy, multiple myeloma, Vitamin D intoxication, osteoporosis, milk alkali syndrome, idiopathic hypercalcaemia of infants, hyperthyroidism, chronic renal disease and acute adrenal insufficiency.

## Localisation

### A. Radiography

#### 1. Oesophageal cine-roentgenography

An ordinary barium swallow may not demonstrate a defect that may be present only momentarily. Hence cine-radiography is carried out, using barium of normal consistency and films exposed with 35 mm at a minimum rate of 15 frames a second. The signs to watch are the following:

a) Straightening of the pharyngo-oesophageal angle on one side. The angles are normally obtuse and symmetrical on each side.

b) Deviation of the oesophagus. This is seen in enlargement of the thyroid gland and with a very large parathyroid adenoma.

c) Defect in the oesophageal wall. A defect at the level C.6-7 interval or the upper part of the body of C.7 indicates a lesion of the upper pole; one at the lower

part of C.7 or T. localises the lesion to the lower pole. The level may be erroneously shown on the roentgenogram due to the tumour altering its position with the posture of the patient.

d) Loss of normal distensibility of the oesophageal wall is another sign less readily seen.

Such a study was used to localise parathyroid adenoma in 2 cases described by Scatliff and Scibetta in 1963. In a serum calcium survey of 26,000 individuals, cine-radiography was used to demonstrate the site of the adenoma in 31 affected individuals, (Stevens and Jackson, 1967).

2. Chest X-ray may show a mediastinal mass, as in the case of a mediastinal parathyroid adenoma lying both within and without the pericardial sac, described by Maurer *et al.* (1965). Hardy *et al.* (1964) removed a parathyroid adenoma from a patient in whom a mediastinal mass has been observed 4 years previously.

3. A technique of pneumo-mediastinography has been described by Posen *et al.* (1964) for the localisation of a mediastinal tumour.

4. Arteriographic demonstration of parathyroid adenomas has been reported by Seldinger (1954), Steiner *et al.* (1956), Born and Werner (1964), Hardy *et al.* (1964) and more recently Newton and Eisenberg (1966).

The arterial supply to the parathyroid glands is normally derived from the branches of the inferior parathyroid arteries (Halsted and Evans, 1907). An angiographic diagnosis depends primarily on the distortion and displacement of the inferior thyroid artery. But the position of the artery relative to the adjacent structures varies greatly even normally. A goitre may widen the loop of the inferior thyroid artery. Abnormal and increased vascularity can sometimes be demonstrated in a normal thyroid. Therefore a differential diagnosis between thyroid and parathyroid tumours may not be possible using arteriography. Moreover, the localisation of one adenoma does not absolve the surgeon from the responsibility of looking for other adenomas in the remaining parathyroid glands.

Angiography is usually accomplished by a bilateral transaxillary percutaneous approach to the subclavian artery. By this means 9 of 14 cases were correctly predicted by Newton and Eisenberg (1966). 13 out of 17 cases were correctly localised by Byron and Werner (1964); Hardy *et al.* (1964) advocate arteriography via the brachial artery with the tip of the catheter in the innominate artery or the aortic arch. This would have outlined their V parathyroid tumour supplied by an anomalous artery arising from the innominate artery. Angiography may be carried out pre-operatively or during operation. At this point it is worth noting that there is by no means an agreement as to the size of the inferior thyroid artery in the presence of an adenoma. State (1964) on the one hand maintained that the difference in the size of the inferior thyroid arteries helped to establish the diagnosis of adenoma and its site. The branches of the inferior thyroid artery also had an unusual distribution. Wyndham (1965) found it impossible to trace or demonstrate a specific branch from the inferior thyroid artery to the adenoma.

#### B. Scintigraphic visualisation with SE-75 methionine

Bartelheimer (1965) reported on a 22-year old woman who was operated upon 5 times, including a thoracotomy, unsuccessfully. Only after a selective isotope labelling was the adenoma found and removed. Of 4 patients examined by scintiscanning by Conte *et al.*, only one was accurately located behind the left thyroid lobe.

This substance is avidly taken up by hyperactive parathyroid tissue, especially adenoma. The more active, the larger and the more easily accessible the tumour, the better is the result of scanning, the easier the diagnosis and localisation. The limitations of this method are admirably described by Centi Colella and Pignorini (1965). A positive result is strongly indicative of hyperfunctioning parathyroid tissue, especially adenoma, although a retrosternal tumour gives a wrong count because of

interposition of the bone marrow which absorbs it and cannot be suppressed like, for example, thyroid tissue. A negative result does not exclude the presence of hyperfunctioning parathyroid tissue.

#### Operative Difficulties

Exploration of the neck is via a collar incision as for partial thyroidectomy. It is made easier by division of the infrahyoid muscles above their nerve supply. Gentleness and absolute haemostasis are essential. Considering the size of a normal parathyroid gland, identification may be extremely difficult. Tracing the branches of the inferior thyroid artery may lead the surgeon to such a gland. The significance of an abnormally large inferior thyroid artery has already been discussed. If there is any question about a possibly abnormal parathyroid gland, a biopsy should be taken and examined by frozen section. If all parathyroid glands are found and one is abnormally large, it is excised and submitted for frozen section. When an adenoma is hard to find, one must remove or examine all the areolar tissue of the neck in an area bounded by the upper extremity of the superior pole of the thyroid gland above, the lateral border of the carotid sheath and lowest point that can be reached. It may then be necessary to remove many pieces of this areolar tissue for frozen section. A neck exploration is never completed unless all four glands are identified. The reason lies in the not inconsiderable incidence of multiple adenomas and in the rarer presence of adenoma and hyperplasia in the same individual. Of course it would also avoid multiple operations and persistence of the disease.

The problem as to how much adenomatous tissue should be removed has already been discussed in the section of pathology. In cases of hyperplasia affecting all four parathyroid glands Cope (1960) removed 3 glands and one third of the fourth. Hardy *et al.* (1964) resected two thirds of each gland opposite the hilum at which the arterial supply entered the gland, thus preserving a good supply to the rest of the gland.

If after a neck exploration the serum calcium drops temporarily, the neck should be re-explored. The danger of such a procedure are obvious. Feind (1964) suggested a lateral posterior approach to avoid scar tissue and the ever present danger of injuring the recurrent laryngeal nerve. He suggests dissecting out the sternomastoid muscle and carotid sheath and its contents. The omohyoid muscle is divided and the dissection is carried down to the prevertebral fascia. The inferior thyroid artery is identified as it pierces the pre-vertebral fascia and followed medially. The recurrent laryngeal nerve is identified as it curves around the subclavian artery and followed upwards.

It is the custom to carry out a mediastinal exploration, when indicated, at a second operation, partly because the combined operation is necessarily a large one, partly because the surgeon has a breathing time for a review of the biochemical diagnosis. Cope (1941) is a strong advocate of this procedure. Norman Wyndham (1965) disagrees. He maintains that the combined operation should take no longer than many other major operations and that the original neck exploration should in any case not have been undertaken without positive diagnostic proof. Judd (1966) advocates a thorough search for an adenoma at the initial procedure including mediastinal exploration through a sternum splitting incision. Manner (1965), as a result of a chest X-ray and barium swallow, approached an adenoma directly through the sternum with a mediastinal exploration. Although approximately 65% of mediastinal parathyroid adenomas are found in the anterior mediastinum, a thorough search is necessary once the mediastinum is opened (Pochter, 1963).

The last straw is reached if a functioning tumour affects a Vth parathyroid gland. Cope (1941) reported a case with four normal parathyroid glands in the neck and a fifth and hyperfunctioning tumour within the thorax found at a second operation. In 1960 he reported finding unmistakable hyperplasia of all 4 glands in the neck. Resection of 3 glands and one third of the 4th resulted in a slight

fall in the level of the serum calcium. A much larger Vth parathyroid gland was found within the capsule of the thymus gland. After its removal the serum calcium returned to normal. Rose (1959) reported 4 normal cervical glands and a mediastinal adenoma. One of the lowest mediastinal Vth parathyroid adenomas was that reported by Hardy *et al.* (1964). It was at the level of D.8 and had its own independent arterial supply from the innominate artery.

### Prognosis

Surgery, that is, the removal of the adenoma or adenomata is the only possible treatment than can be offered. Emergency parathyroidectomy is mandatory in a hypercalcaemic crisis. Its effectiveness is best shown in patients suffering from renal or musculo-skeletal disorders, provided they are not too far advanced. Peptic ulceration is a very common condition. It may resolve completely and may undergo spontaneous remission. Although improvement in ulcer symptoms has been reported after excision of a parathyroid adenoma, it can be argued that the result was just a happy ending to an unfortunate co-incidence. The association with pancreatitis is less fortuitous. Recurrent attacks of pancreatitis can be stopped by removal of the parathyroid adenoma. Pancreatic adenomata revealed by an augmented histamine test or at laparotomy require removal. The response of hypertension does depend on the age of the patient and the degree and the length of time over which it has been present. The prognosis of a patient presenting with mental symptoms is even more guarded, because the response may be dramatic, disappointing or disastrous in the sense of a worsening or a complete change in the behavioural pattern.

### Conclusion

Early diagnosis and early surgery are of paramount importance. Various aids are available for both and have been discussed. Whatever the presenting feature or features of primary hyperparathyroid-



ism, the adenoma or adenomata must be removed. Parathyroid adenoma will eventually cripple the patient and kill him. An endeavour has been made to show pitfalls and disagreements in the laborious progression from clinical suspicion, biochemical confirmation of the diagnosis to surgical extirpation.

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