2 cm in diameter in right upper zone. Multiple cystic areas in ribs, left clavicle, left humerus, right hand, pelvis, femora and tibiæ. Radiograph of skull showed a 'pepper pot' appearance and plain film of abdomen nephrocalcinosis. Serum protein-bound iodine and total ^{131}I uptake normal. Thyroid scan demonstrated diminished uptake over left lobe. Edrophonium test negative. No malignant cells in sputum on repeated examination. Biopsy of cyst over left tibial tuberosity was suggestive of the 'brown tumour' of hyperparathyroidism.

Exploration of neck (Mr A J Heriot) revealed an irregularly hyperplastic thyroid gland with some cystic changes. A chief cell parathyroid adenoma weighting 8 g was removed and a partial thyroidectomy performed. No other parathyroid tissue identifiable.

Progress: Within a few hours of operation, her serum calcium fell to 8·8 mg/100 ml, and twenty-four hours later to 7·8 mg/100 ml when oral calcium supplements were started. Within two days of the operation she was in extremely positive calcium balance and the urinary excretion of hydroxyproline had fallen to 26 mg/24 h. Three months after parathyroidectomy, her muscle weakness had disappeared and there was radiological evidence of healing of the cysts and of the skull. The opacity in her right lung remained unaltered in size on serial measurement.

Discussion

This woman presented with an opacity in her lung, severe myopathy and multiple, expanded cysts in her bones. She had hypercalcæmia but no hypercalciuria.

In view of the negative sputum cytology, the 'pepper pot' appearance of the skull, the histology of the tibial cyst and the presence of a nodule in the neck, the diagnosis was thought to be primary hyperparathyroidism with myopathy (Vicale 1949, Murphy *et al.* 1960, Prineas *et al.* 1965). The lung lesion is unlikely to be a bronchial carcinoma producing parathyrotrophic-like substances (Stone *et al.* 1961, Krane 1964, Strickland *et al.* 1967), as one would have expected to find hyperplasia of all the parathyroids rather than a solitary adenoma.

REFERENCES

Krane S M (1964) *New Engl. J. Med.* **270**, 898

Murphy T R, Remine W H & Murbank M K (1960) *Proc. Mayo Clin.* **35**, 629

Prineas J W, Mason A S & Henson R A (1965) *Brit. med. J.* i, 1034

Stone G E, Waterhouse C & Terry R (1961) *Ann. intern. Med.* **54**, 977

Strickland N J, Bold A M & Medd W E (1967) *Brit. med. J.* iii, 590

Vicale C T (1949) *Trans. Amer. neurol. Ass.* 74, 143

Familial Multiple Endocrine Adenopathy (Primary Hyperparathyroidism and Zollinger-Ellison Syndrome) in Two Siblings

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Case 1 Mrs J S, aged 39. Sister of Case 2

History: First had symptoms of duodenal ulcer in August 1964 and was treated by antacids. No ulcer was demonstrated on barium meal examination but nephrocalcinosis was noticed. Serum calcium was normal. Five months later she developed pain in her bones and radiography showed osteoporosis of mandible and skull and subperiosteal erosion of phalanges. She was hypercalcæmic and her serum alkaline phosphatase was 52·5 K-A units.

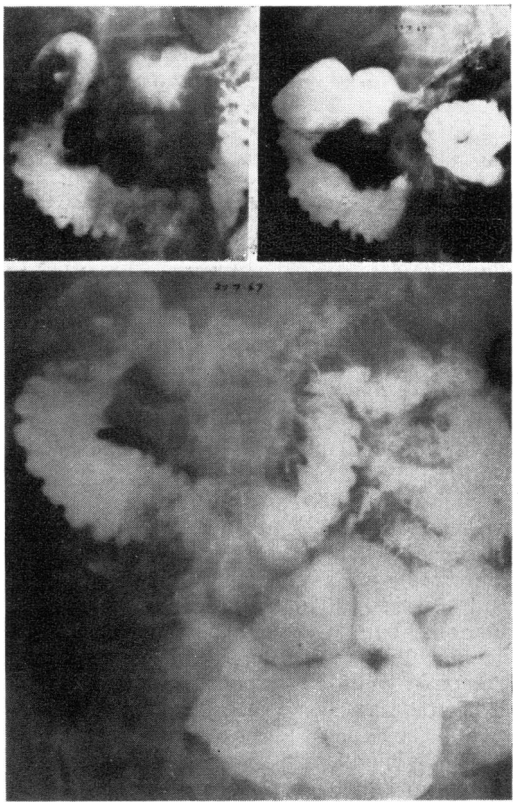

Fig 1 **Case 1** *Barium meal radiography showing a large ulcer crater in the second part and dilatation with prominent spiky mucosa of the second and third parts of the duodenum and dilatation with 'feathery pattern' of the jejunum*

First operation (30.3.65): Right parathyroid adenoma removed. Normal left upper parathyroid gland seen and left *in situ*. No other parathyroid tissue seen. Post-operative serum calcium fell to normal and remained normal until February 1967 when she first complained of diarrhœa and was found to be hypercalcæmic again (Fig 2).

In July 1967 she had severe abdominal pain and diarrhœa and was readmitted to hospital.

Investigations: Hypercalcæmia; serum alkaline phosphatase 9 K-A units. Tolbutamide tolerance test normal. Radiography: healing of previous osteoporotic lesions in bone; nephrocalcinosis; normal pituitary fossa. Barium meal suggestive of Zollinger-Ellison syndrome (Fig 1). Gastric secretion: overnight juice 1,384 ml (159·2 mEq H^+). Basal hour 32·4 mEq H^+; with maximal gastrin stimulation 27·6 mEq H^+/hour.

Second operation (3.8.67): Laparotomy – total gastrectomy and splenectomy. Large inflammatory mass found in head of pancreas in direct relation to a large ulcer crater felt in second part of duodenum. An adjacent lymph node showed metastatic islet cell carcinoma and pyloric mucosa showed parietal cells on frozen section.

Third operation (12.10.67): Re-exploration of neck and removal of left upper parathyroid adenoma. No other parathyroid gland could be seen. Post-operative serum calcium fell to normal and has remained normal (Fig 2) without any calcium or vitamin D supplement.

Comment: This patient had clear evidence of islet cell carcinoma with lymph node metastasis, gastric hypersecretion, peptic ulceration and adenomas of two parathyroid glands. She must still have parathyroid tissue to maintain the post-operative serum calcium at normal level and this makes it imperative to follow her serum calcium level in order to detect the appearance of any further parathyroid tumour. The metastatic lymph node was assayed for gastrin by Professor R A Gregory of Liverpool, but the result was negative.

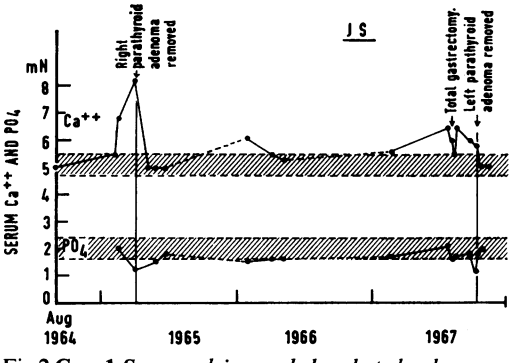

Fig 2 Case 1 *Serum calcium and phosphate levels*

Case 2 Mr R P H, aged 35. Brother of Case 1

History: Passed two stones per urethram following attacks of right renal colic in January 1967. Three months later he had hæmaturia and left renal colic and was found to be hypercalcæmic with 24-hour urinary excretion of calcium of 32·5 mEq. He also had a history of mild diarrhœa for abour a year.

Investigations (June 1967): Serum calcium level could not be suppressed with cortisone for 10 days. Tolbutamide tolerance test normal. Plasma cortisol and urinary excretion of steroids normal. Urinary 5-hydroxyindole acetic acid excretion 26 mg/day (normal 3–17 mg/day).

Radiography: Normal pituitary fossa and skeletal survey. Barium meal: no ulcer; second and third parts of duodenum looked slightly dilated with spiky mucosal folds – suspicious of Zollinger-Ellison syndrome.

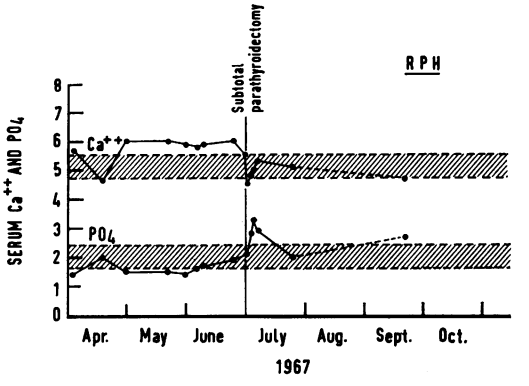

Fig 3 Case 2 *Serum calcium and phosphate levels*

Operation (29.6.67): Subtotal parathyroidectomy. All four parathyroid glands were hyperplastic and lobulated, especially the upper ones. Half of the right lower parathyroid was left *in situ*. Histology: primary nodular hyperplasia of chief cells (Dr E Dillwyn Williams).

Post-operatively his serum calcium has been maintained normal with oral calcium since operation (Fig 3).

Comment: With this patient with nodular hyperplasia of all four parathyroids the problem now is, should he have a laparotomy in order to discover a possible islet cell carcinoma while it is still completely removable? His increased urinary excretion of 5-HIAA also raises the suspicion of

an associated carcinoid tumour, which has been reported in relation to multiple endocrine adenopathy (Williams & Celestin 1962).

Family History
The father of these two patients died at the age of 59 from 'coronary' and the mother is now 64 and well. They have two other siblings, a sister aged 41 and a brother aged 23, who are apparently well. Mrs J S has two children and Mr R P H has one, all of whom are well. One of their paternal aunts, aged 63, has had renal stones and her daughter, aged 16, was in hospital with 'pyelitis'. A child of another paternal aunt died of 'kidney trouble' at the age of 2½ years.

Discussion
Total gastrectomy was performed on Case 1 as the primary carcinoma was irremovable and total gastrectomy has been advocated under such circumstances even in the presence of residual malignant tumour (Jordan *et al.* 1963), since the tumour is slow growing.

POSTSCRIPT (20.5.68)
Case 2 (Mr R P H) was reinvestigated in January 1968. Gastric acid secretion: basal 15·1 mEq H^+/h; maximal pentagastrin stimulation 54·3 mEq H^+/h (basal before parathyroidectomy 46·8 mEq H^+/h). Gastrin activity in serum normal (Dr C J Thomson), in urine slightly positive (Professor S Bonfils). Urinary 5-HIAA excretion 5 mg/day.

Laparotomy (15.2.68): One nodule palpated in the body of the pancreas. No ulcer found in stomach or duodenum. Splenectomy and distal pancreatectomy were carried out. Histological examination revealed multiple non-beta islet cell tumours of the pancreas (3–8 mm in size) and many incipient foci of tumour.

Post-operative course: Pulmonary embolism was diagnosed on the fourth post-operative day and on the ninth post-operative day he started to bleed from the gastrointestinal tract. On the twelfth post-operative day he collapsed and died.

Post-mortem findings: Bilateral massive pulmonary emboli, bilateral femoral vein thrombosis, prominent mucosal folds of stomach and duodenum with six recent bleeding ulcers in the latter, a small subphrenic abscess and two minute islet cell tumours in the wall of the lower duodenum. The adrenal glands were overweight but histologically normal. – P D; M R W.

REFERENCES
Jordan G L jr, Law S W & Foster R P (1963) *Amer. J. Surg.* **105**, 80
Williams E D & Celestin L R (1962) *Thorax* **17**, 120

Hypernatræmia in a Patient with Ectopic Pinealoma

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The patient is a 19-year-old girl with hypopituitary dwarfism and diabetes insipidus. A craniotomy was performed under steroid cover in 1966 and an ectopic pinealoma removed. Post-operatively she was given radiotherapy and the steroids tailed off. Three months later she developed lassitude and hypernatræmia without thirst or clinical evidence of dehydration. She was shown to have evidence of diabetes insipidus, hypopituitarism and impairment of renal function.

In this patient the hypernatræmia probably resulted from damage to the hypothalamic thirst centre with consequent adipsia in a patient already suffering from diabetes insipidus, so that she failed to respond to plasma hyperosmolality by drinking. The administration of cortisone resulted in a return of thirst perception.

[This case will be reported more fully in the *British Medical Journal.*]