

used properly. Freyman (1963) reported how older children often sabotaged the parents' efforts to make them use the apparatus, and, in others, the mother's anxiety would be transferred to her child, who would then refuse to use the apparatus. In this series there were 23 such failures (11.5%)—namely, 12 children would not co-operate, in four cases the alarm kept everyone awake, and seven children failed to awaken with the alarm. Of the 12 who would not co-operate, 10 refused point-blank to sleep with the apparatus. Some authors would exclude children who refused, but we feel that all cases should be included. The failure rate compares favourably with that obtained by other authors—namely Wickes (1958) 26%, Taylor (1963) 19%, and Young (1965) 35%.

Relapses.—In this series 30 patients relapsed—28 within six months of discontinuing treatment and 2 between 6 and 12 months. Of these 30 patients, 17 were cured by a second course of treatment. The overall relapse rate was 6.5%.

Complications.—A rash consisting of red papules or punched-out ulcers has been described by Gillison and Skinner (1958), Borrie and Fenton (1966), and Greaves (1969). These have been thought to be due to electrolysis of sodium chloride in the urine with the production of sodium hydroxide at the cathode. One of the following may be the cause: too small a

quantity of urine leaking on to the bed and thus failing to set off the alarm, a run-down battery, or the bell failing to waken the patient. In this series no ulcers occurred: it has been suggested that buzzer ulcers are more likely to occur with metal-foil electrodes. In our experience metal-foil electrodes are unsatisfactory, often disintegrating after 8 to 10 weeks' use, and for this reason we have not used them for several years. Freyman (1963) stated that foil-type sheets do not activate the bell as quickly as the wire-type.

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Medical Memoranda

Severe Hypercalcaemia from Hyperthyroidism with Unusual Features

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Mild disturbance of calcium metabolism in hyperthyroidism is well recognized but severe hypercalcaemia is rare. We report here a further case of pronounced hypercalcaemia from hyperthyroidism with several unusual features.

CASE REPORT

The patient, a 50-year-old nursing sister, presented in September 1967 with a six-month history of weakness, nausea, vomiting, and intermittent epigastric pain unrelated to meals, with loss of appetite and of 4 st. (25 kg.) in weight. Because of progressive breathlessness on exertion she could walk only 10 yards (9 metres) on the flat. Her previous illnesses included migrainous vomiting as a child and intermittent attacks of nausea, vomiting, and epigastric discomfort for the previous four years; a barium meal examination in 1964 showed nothing abnormal. She had rheumatic fever when aged 16 and 26, but there had been no limitation of her exercise tolerance until latterly.

Her present illness had been investigated in June 1967 elsewhere by barium studies, cholecystogram, and urography, all of which gave normal results, and in July she was referred to a psychiatric day hospital, from which she discharged herself after a few weeks.

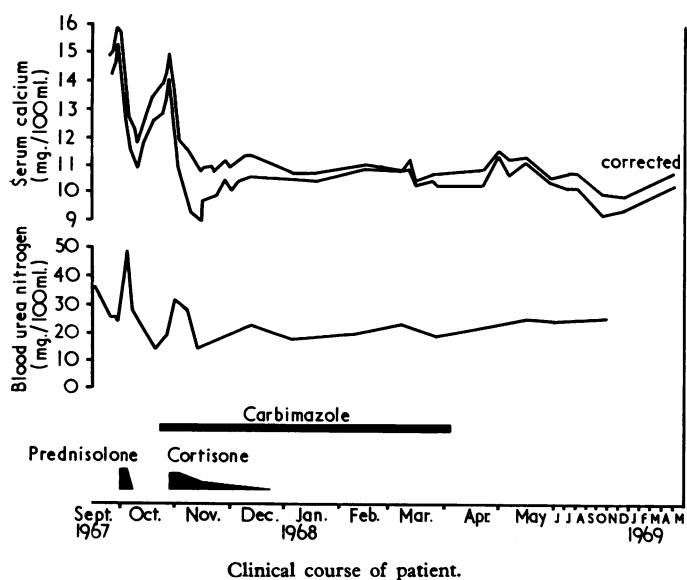
On examination she was ill, pale, and dehydrated. She was pyrexial (99-101°F.; 37.2-38.3°C.) with a tachycardia of 130 and a soft mid-diastolic apical murmur. There was pronounced upper abdominal tenderness and generalized muscle weakness and wasting.

Initial investigations failed to reveal a definite diagnosis: haemoglobin 9.4 g./100 ml., E.S.R. 80 mm./hour (Westergren),

W.B.C. 6,900/cu.mm. with normal differential, microcytic red cells, and blood urea nitrogen 38 mg./100 ml. Electrolytes: Na 146, K 2.2, Cl 88, alkali reserve 39 m.Eq/l. Bilirubin 0.7 mg./100 ml., alkaline phosphatase 24 K.A. units/100 ml. Serum aspartate aminotransferase 85 units and serum alanine aminotransferase 210 units (normal range 20-110 units.) Flocculations and turbidities normal. Plasma protein total 7.1 g./100 ml. (albumin 2.9, globulin α_1 0.6, α_2 1.4, β 0.7, γ 1.5 g./100 ml.). Midstream specimen of urine showed pyuria and coarse granular casts with 0.05 g./100 ml. of protein. Examination of faeces showed persistent occult bleeding. Gastroscopy (21 September) revealed normal gastric mucosa with normal motility, and a barium meal examination showed only a slowly emptying stomach. Therapy was instituted with intravenous fluids, phenothiazines, ampicillin, and, later, potassium chloride by mouth when vomiting had stopped.

At this stage gross hypercalcaemia was present (corrected levels* 14.9-15.8 mg./100 ml.), with a normal serum phosphate (2.9-3.4 mg./100 ml.). Bleeding and clotting times were normal and there was no shortening of the Q-T interval of the E.C.G., though non-specific T-wave inversion was noted. The commoner causes of hypercalcaemia were considered. There was no history of excessive alkali, milk, or vitamin-D ingestion, and protein electrophoresis showed no abnormal proteins. The raised alkaline phosphatase suggested hyperparathyroidism, but the subsequent clinical course and steroid suppression negated this diagnosis. The protein electrophoresis and high E.S.R. with negative Mantoux reaction (to 100 units of old tuberculin) were suggestive of sarcoidosis, but a Kveim test was subsequently shown to be negative. The clinical picture, anaemia, high E.S.R., and persistent occult gastrointestinal bleeding raised the possibility of a gastrointestinal neoplasm.

It was decided, in view of the risk of serious renal damage, to try the diagnostic and therapeutic effect of steroids (prednisolone 80 mg./day). The result was dramatic, clinically and biochemically (see Chart).



The diagnosis of hyperthyroidism was now reconsidered and, though there were no clinical features to support it, this was confirmed by ^{131}I uptake (61.6% of dose at four hours). The scan showed a small gland with even uptake. The protein bound iodine was raised at 9.8 $\mu\text{g}/100 \text{ ml}$. but thyroid antibodies were absent. The serum thyroxine level was 7.0 $\text{mg}/100 \text{ ml}$. and T₃ binding capacity 173%. Carbimazole therapy 10 mg. eight-hourly was started—steroids having been stopped—to see if control of the hyperthyroidism would restore the calcium metabolism to normal. Hypercalcaemia and vomiting recurred after 6 and 22 days respectively, necessitating reintroduction of steroid therapy (cortisone 600 mg. daily), again with complete control of hypercalcaemia. When the patient was euthyroid steroids were stopped and she remained normocalcaemic and symptom-free. A therapeutic dose of ^{131}I 6 mCi was given and she remained well and with normal serum calcium values over the next 18 months, but required a small dose of thyroxine—0.1 mg. daily.

COMMENT

Comparison of hyperthyroid and euthyroid patients has shown a mean increase in serum calcium in the hyperthyroid group (Adams *et al.*, 1967), and if total serum calcium is normal ionized calcium is probably always raised (Frizel *et al.*, 1967). All patients are in negative calcium balance with consistently high urinary calcium and in most cases an increased faecal loss of calcium (Cook *et al.*, 1959), but ^{47}Ca absorption is variable (Adams *et al.*, 1967). ^{47}Ca absorption studies were performed on this patient (see Table) when she had been

Blood Levels of ^{47}Ca After Oral Dose of 20 μCi at 0 Hours

	Euthyroid Normocalcaemic 25/3/1968 %	Hyperthyroid Hypercalcaemic 22/4/1968 %
1 hour	..	1.66
2 hours	..	1.91
3 "	..	1.53
4 "	..	1.44
6 "	..	1.45
24 "	..	1.04
Net absorption by stool count	42.9	38.2

rendered euthyroid with carbimazole and again one month after stopping that drug. On both occasions ^{47}Ca absorption was within normal limits, but though she was clinically hyperthyroid, the serum calcium was only just above the normal range—quite unlike the presenting state when ideally ^{47}Ca studies should have been done. It was, however, not felt justified to withhold treatment further.

Although the tendency to hypercalcaemia is common, cases of severe hypercalcaemia are rarely reported (Bortz *et al.*, 1961; Guyer, 1965; Buckle *et al.*, 1969). The mechanism of severe hypercalcaemia may be a relative deficiency of calcitonin—possibly with most hyperthyroid cases an increase in calcitonin copes with the tendency to hypercalcaemia. Parathyroid hormone levels seem to remain unchanged (Buckle *et al.*, 1969). With the next case of severe hypercalcaemia serial estimations of plasma calcitonin should be made before, during, and after treatment. There is some evidence (in pigs) that the calcium-lowering potential of the thyroid is considerably impaired by antithyroid drugs (Duncan and Care, 1967), so allowance must be made for this if such drugs are used. It is difficult, however, to see how their use can be avoided in such a serious situation. Unfortunately, animal experiments (Yasamura *et al.*, 1967), in which hyperthyroidism is induced by thyroxine administration and calcitonin levels are studied, cannot reproduce the rare occurrence of spontaneous hyperthyroidism with pronounced hypercalcaemia.

A striking feature of the present case was the sensitivity and rapidity of response of the hypercalcaemia to cortisone and prednisolone. While the action of these steroids is not as rapid as that of the sodium salts of phosphate and sulphate, the dose we used produced a more rapid response than that seen by Gleckler (1956). In this case of hypercalcaemia due to sarcoidosis, in which he used just over 100 mg. of cortisone daily, normal calcium levels were not attained until about five weeks, the initial calcium level being 15.6 $\text{mg}/100 \text{ ml}$. They should therefore be more useful than indicated in a recent leading article (*Lancet*, 1967) and may be as effective as calcitonin (Buckle *et al.*, 1969), which is not widely available.

Gastrointestinal symptoms with normal radiology of the gastrointestinal tract in association with hypercalcaemia are well recognized, but a worrying feature in this case was the persistent evidence of occult gastrointestinal bleeding, which did not clear up until December 1967 (when serum calcium was normal).

An unexplained finding was the persistently raised serum alanine aminotransferase, which had not returned to normal until one year after the initial illness. Serum bilirubin and flocculation and turbidity tests were consistently normal, bromsulphalein sodium excretion showed no retention of dye, and creatine kinase was normal.

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*If normal total plasma protein is taken as 7.2 g./100 ml., a difference of 0.1 g./100 ml. from the normal = 0.069 mg. of calcium, and this correction is added to total calcium if total protein of the sample is under 7.2 g./100 ml. and subtracted if over 7.2 g./100 ml.

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