The results support the belief that the adrenal inhibition test will prove of value in distinguishing Cushing's syndrome due to adrenal hyperplasia from cases of the syndrome due to carcinoma.

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ACUTE HYPERPARATHYROIDISM WITH ELECTROCARDIOGRAPHIC CHANGES

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Acute hyperparathyroidism is an extremely rare condition, and every case may therefore be regarded as worthy of record. Only isolated reports on definite or suspected cases are to be found in the literature. Seven proved cases have been reported, all of which were fatal (Hanes, 1939; Oliver, 1939; Arnold, 1940; Smith and Cooke, 1940; Mellgren, 1943). Doubtful cases were described by Dawson and Struthers (1923), Herxheimer (1926), and Herzenberg (1933). These four cases also ended fatally.

Acute parathyroid intoxication caused by a chief-cell adenoma of the parathyroid glands has a different clinical picture from that usually associated with chronic hyperparathyroidism. The main features are a rapid onset of anorexia, vomiting, constipation, loss of weight, and lassitude developing into increasing drowsiness and asthenia. Abdominal pains may be severe, almost resembling an acute abdominal disease. There may be slight fever, and the pulse rate is disproportionately rapid. This syndrome may be devoid of skeletal findings, while impaired renal function is regarded as characteristic (Mellgren, 1943; Spence, 1953). The acute crisis may supervene on long-standing chronic hyperparathyroidism as in our case. Death may ensue after several days; early diagnosis is therefore imperative, as treatment may be life-saving, as borne out in our patient.

The electrocardiographic findings have rarely been recorded (Ballin, 1932; Kellogg and Kerr, 1936). In our

patient the electrocardiographic changes, together with the clinical presentation, led to the correct diagnosis.

Case Report

A 57-year-old farmer was seen on July 4, 1955. Two weeks previously, while driving his car, he developed a sudden, momentary substernal chest pain which was so severe that he had to stop his car and rest. He consulted his doctor, who took an electrocardiogram which was sent to a consultant physician for an opinion. The physician advised bed rest and a further E.C.G. in one week.

The patient also complained of severe epigastric pain and a blown-up feeling in the abdomen over the past fortnight. He was very nauseated and had continuous headache. The chest pain recurred several times in these two weeks. He also noticed increasing weakness and lassitude and had a feeling of lameness in the arms.

For a number of years he had been slightly breathless on effort. He was always constipated, and said that his bowels had not acted for the previous week. Micturition was normal.

On further questioning he stated that 15 years ago he consulted a physician because of backache. Ten years ago he was diagnosed as having a peptic ulcer, confirmed by x-ray examination, and was treated in a country hospital for four weeks on a milk diet and alkalis. He volunteered the information that the treatment made him feel weak and gave him pins-and-needles in his hands. Although a subsequent x-ray examination showed healing of the ulcer, he felt worse after treatment. For two years thereafter he had paraesthesiae and weakness of his legs. Since then he has never had a milk diet for his ulcer.

Six years ago he was x-rayed again because of dyspepsia, and one year later he was admitted to a hospital for investigation of abdominal pain, backache, and heaviness in the chest. The x-ray picture showed no abnormality, but a gastric test meal revealed achlorhydria, and ever since then he has taken "acidulin" capsules with an occasional alkali powder.

One year ago he was treated by an orthopaedic surgeon for "chronic back strain." He had leg traction, but his backache did not improve.

Six months ago he had a complete dental clearance because the "infection was poisoning his system." Gum healing was greatly delayed. For many years he has had recurrent mild episodes of bronchospasm and sinusitis.

His usual diet included porridge with milk daily, cream and cheese three or four times a week, and two eggs for breakfast daily. He took fresh orange juice several times a week. He drank tea or coffee with milk about six times a day and occasionally took raw eggs for his weakness. He would often take a full glass of milk when the fresh milk came from the farm, but the milk tended to cause substernal heaviness, and he therefore did not drink the latter more than twice a fortnight. He had always been inclined to vomit after "sweet foods." There was no history of polyuria or polydipsia. He had lost 10 lb. (4.5 kg.) in weight in the past two weeks.

On physical examination the most striking features were the marked pallor and extreme asthenia. He could barely walk or talk and was very depressed. His temperature was 99.8° F. (37.7° C.) and pulse rate 100 a minute. His eyes were normal. An arcus senilis was present. He was edentulous. A doubtful fullness was present in the region of the right lower pole of the thyroid gland. The cardiovascular system was essentially normal. The blood pressure was 160/100, but the subsequent readings were in the neighbourhood of 130/80.

Surprisingly, the tendon reflexes were present and brisk, and apart from marked muscular hypotonia the central nervous system was normal. The rest of the examination was negative. Fluoroscopy showed some unfolding of the aorta.

The electrocardiogram showed a very short Q-T interval ($QTc=0.34$) with an almost absent ST segment (Fig. 1). This finding suggested hypercalcaemia and, together with the clinical features, indicated the diagnosis of hyperparathyroidism.

The Table shows all the biochemical investigations performed before and after operation, with follow-up studies. The noteworthy features on admission were the very high serum calcium of 21 mg. per 100 ml. and the normal plasma inorganic phosphate of 2.7 mg. per 100 ml. A full blood count was normal. The E.S.R. was 4 mm./hour (Wintrobe).

A complete skeletal x-ray survey did not reveal any demineralization. Radiography of the soft tissues, including the eyes and abdomen, showed no evidence of any metastatic calcification or nephrocalcinosis.

FIG. 1.—E.C.G. on admission. Lead 2 and V6 show general pattern of graph.

FIG. 2.—E.C.G. one day before operation. The ST segment is beginning to return. Lead 2 shows the general pattern.

Biochemical Results Before and After Operation, with Follow-up Data

	Blood (mg./100 ml.)						Urine			
	Calcium	Phosphate	Urea	Alk. Phos. K.-A. Units	Uric Acid	Creatinine	Electrolytes Na, Cl, K, CO ₂	Calcium (24-Hour Excretion)	Urea Clearance (% of Av. Normal)	Sulkowitch
4/7/55	21	2.7	54	6.5			Normal			
6/7/55	19.6						"			+ +
7/7/55			72							
8/7/55	18.7	3.2	82		11	2.1				
10/7/55								515	25	
12/7/55	19	2.7	46				"	450		
13/7/55							"			
15/7/55			36				"			
19/7/55	14		35				"		28	
22/7/55	13.8		31				"		30	
26/7/55	13.4	2.1	30				"	424	32	
Operation										
1/8/55	10.3	2.2	48	10.7			"			—
3/8/55	9.3	2.4	37					31	40	—
12/9/55	10.8	2.2	38	13.7					49	—
25/1/56	10.8	2.8	45	5.3	8.2				59	—

After admission to hospital his condition deteriorated alarmingly. Two days after admission he became confused and the aphonia and asthenia were more pronounced. Anorexia was extreme. His condition became critical. A low-calcium (100 mg. daily) and high-phosphorus diet was begun at this stage, together with intravenous therapy (1 litre of normal saline and 2 litres of 5% dextrose in water daily) with careful electrolyte studies.

At the beginning of this treatment the blood urea had risen to 82 mg. per 100 ml. from a previous level of 54 mg. and the plasma inorganic phosphorus had increased to 3.2 mg. per 100 ml. These findings, together with a uric acid level of 11 mg. per 100 ml., a creatinine level of 2.1 mg. per 100 ml., and a urea clearance of 25% of average normal indicated a severe degree of renal failure (see Table).

Subsequent progress on the above regime was extremely gratifying, and by the twelfth day the patient was able to take sufficient fluids orally for discontinuance of intravenous therapy. There was a considerable decrease in the serum calcium, phosphorus, and urea (see Table). Clinically the patient regained strength; the hypotonia, asthenia, and anorexia improved considerably; so that he was now considered fit enough for operation, 24 days after admission. The electrocardiogram taken the day before operation is shown in Fig. 2. Operation was purposely delayed to allow improvement of renal function, but had the amelioration of his condition not occurred we would have been forced to advise surgery much earlier.

The operation was performed on August 28 by Mr. A. Lee McGregor. An adenoma weighing 3.7 g. (2.6 by 1.5 cm.) was removed intact from the position of the right lower parathyroid gland. Inspection of the other parathyroid glands revealed no macroscopic abnormality. Histological examination showed a chief-cell adenoma of the parathyroid gland with a large cyst in the lower pole (Figs. 3 and 4).

The post-operative period was uneventful. Tetany was not observed. A dramatic decrease in the hypercalcaemia and hypercalciuria with a negative Sulkowitch test occurred within 48 hours after operation. The electrocardiogram taken five days after operation is shown in Fig. 5.

The patient was discharged from hospital 10 days after operation in excellent health.

Subsequent follow-up studies have revealed a consistently normal serum chemistry with a slowly improving urea clearance (see Table). When seen on January 25, 1956, he had gained 17 lb. (7.7 kg.) in weight and was asymptomatic apart from mild "hay-fever." He volunteered the fact that he was no longer constipated for the first time in many

years. The blood pressure was 120/80 mm. Hg. An intravenous pyelogram showed prompt excretion of the dye with no evidence of renal calcinosis or calculi. The urea clearance was 59% of average normal, indicating that renal function is still somewhat impaired.

FIG. 3.—Histopathological section of tumour. ($\times 3$.)

FIG. 4.—Typical cells of the parathyroid tumour. This also shows the vascularity and tendency to cyst formation. ($\times 150$.)

FIG. 5.—E.C.G. five days after operation. The pattern has returned to normal.

Discussion

The above case history makes it obvious that the diagnosis was that of acute hyperparathyroidism. From the clinical standpoint it is important to realize that a serum calcium of 21 mg. per 100 ml. is evidence of a dangerous degree of parathormone poisoning. Snapper (1930) has reported a calcium reading of 23.6 mg. per 100 ml. with eventual recovery. Apart from the hypercalcaemia, a rising serum phosphorus denotes an extremely grave prognosis (Albright and Reifenstein, 1948). In our case the initial phosphate level was not reduced owing to renal impairment, which also accounted for the subsequent rise. It is obvious that had this case not been diagnosed and treated a fatal outcome would have been inevitable.

The absence of radiological bony lesions in the presence of such a high serum calcium could be explained by the large amount of calcium in his diet, as is evidenced in the history. The marked hypercalciuria was probably responsible for the polyuria which the patient developed in hospital.

It is of interest to note that hypochlorhydria was found in the case reported by Herzenberg (1933), Morelle (1934), and Mellgren (1943). Chest pains were notable symptoms in the cases of Hanes (1939) and Oliver (1939).

On admission the patient's critical state, with increasing renal failure, made him a poor operative risk. The low-calcium, high-phosphorus diet, with sufficient fluids daily, temporarily improved the renal function, so that after three weeks on this regime he was fit for operation. The efficacy of this type of treatment is amply borne out in this case.

The literature contains very few references to the electrocardiographic changes in hyperparathyroidism. In 1932 Ballin reported that in one case the R-T interval increased from 0.22 second before parathyroidectomy to 0.27 second after removal of the tumour. He remarked that the electrocardiogram was a possible clinical method for measuring the muscular hypotonia. Kellogg and Kerr (1936) described the electrocardiographic changes in osteitis fibrosa cystica and showed that the QTc interval increased in both their cases after operation. In the one case the serum calcium was 19.2 mg. per 100 ml., and in the other 17.5 mg. before operation. Both electrocardiograms showed shortening of the QTc (Bazett) interval, with disappearance of the ST segment. The latter appears to fuse with the upstroke of the T wave, especially in their first case, with the higher serum calcium. This graph bears a striking resemblance to the tracing in our patient (Fig. 1), and it would appear to us that the conspicuous feature in these cases is not only the shortened Q-T interval but the virtual disappearance of the ST segment, which becomes one with the upstroke of the T wave. This gives the graph a characteristic appearance (Fig. 1). In our patient, when the calcium level decreased to 13.4 mg. per 100 ml. the QTc interval remained unchanged, but there was a partial return of the ST segment (Fig. 2).

After operation the ST segment and the QTc interval became normal (Fig. 5). Goldberger (1953) has remarked on the shortened Q-T interval and the RST segment, and has pointed out that these changes are more likely to occur in hyperparathyroidism with a normal serum potassium than in cases of hypercalcaemia of other origins. One of his tracings of a woman with hypercalcaemia due to testosterone therapy for breast carcinoma bears a close resemblance to our Fig. 1. In his case the serum calcium was 15.5 mg. per 100 ml. and the QTc interval 0.335 second. Hyperpotassaemia also causes a loss of the ST segment with widening of the S-ST angle (Herndon *et al.*, 1955), but the high pointed T waves differ greatly from the rounded T waves with the gentle incline of the downstroke of the T wave seen in the published cases of hypercalcaemia (Fig. 1). This downstroke appears to differ not only from the hyperpotassaemic downstroke but also from the normal (Fig. 5). Injection of calcium into patients with acute renal insufficiency has shown only a rough correlation between

the serum calcium level and the QTc interval (Herndon *et al.*, 1955), but these results can hardly be compared with the changes produced by hypercalcaemia due to hyperparathyroidism because of other concomitant electrolyte changes.

The relative shortening of the Q-T duration in hyperparathyroidism as opposed to other causes of hypercalcaemia has been described by Lepeschin (1951). Other electrocardiographic changes in cases of hypercalcaemia due to hyperparathyroidism include lengthening of the P-R interval, inversion of the T waves in leads 2 and 3, a slurred rSR in V1 and a peculiar broad rounded apex of the T wave rather similar to the appearances described by us (Fig. 1) (Kellogg and Kerr, 1936; Lepeschin, 1951; Goldberger, 1953). The present case showed no changes in the A-V conduction and no broadening of the QRS complex. The latter finding agrees with the observations of Herndon *et al.* (1955), who were unable to affect the QRS duration by raising the serum calcium. The only common factors which shorten the QTc interval are digitalis and its derivatives, hyperpotassaemia, high vagal tone, and anoxia (Lepeschin, 1951), but none of these produce the appearance of the T wave described above.

The prognosis has been discussed in a report by Rienhoff (1950). His follow-up of 25 cases of hyperparathyroidism due to adenomata revealed a mortality of 36% (9 cases) after three to eleven years following discharge from hospital. All the deaths were due to hypertension with or without renal insufficiency. All but one were in their fourth or fifth decade at the time of death. In four of these cases there was evidence of renal complications without bony lesions at the time of operation. The other five had skeletal complications but no renal abnormalities. Yet after removal of the parathyroid adenomata the nine patients appeared well and the blood chemistry returned to normal. Nevertheless there was a continuous degenerating process in the kidneys going on for a number of years that produced their ultimate death. This fact has also been stressed by Hellström (1950), and more recently by Simpson and Wilson (1955).

In our patient there has been a steady improvement in the renal status in the six months since operation, but this does not mean that complete recovery will ensue, as renal function is not yet normal. The outlook must remain uncertain.

It can be concluded that individuals who show least evidence of renal damage before operation have the best outlook for complete recovery. Once complications have developed to any extent, especially in the fourth and fifth decades, the secondary damage to the kidney may not be corrected in spite of successful operation and a complete cure of the hyperparathyroidism.

It must be emphasized that the main goal in treatment should be to make the diagnosis of hyperparathyroidism before obvious and serious complications have occurred (Rienhoff, 1950).

Summary

A case of parathyroid adenoma with parathormone intoxication is presented.

The rarity of acute hyperparathyroidism is stressed.

The electrocardiographic changes in hyperparathyroidism are discussed and their diagnostic value is emphasized.

The pre-operative management and prognosis of such a case are discussed.

The literature is reviewed.

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ANTISEPTICS IN MIDWIFERY

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For more than 20 years chloroxylenol has dominated the field of antiseptics in midwifery (Colebrook and Maxted, 1933), but manufacturers have been developing new antiseptics in this field and have reintroduced already known compounds in fresh formulations.

The possible use of quaternary ammonium compounds* has been considered at intervals, particularly since the paper of Domagk in 1935, and interest in their bactericidal power has recently revived. Direct comparison between the various types of compounds described in the literature is difficult because of the different methods which have been used for testing antiseptics. We felt, therefore, that it would be useful to compare "dettol" (chloroxylenol) with these antiseptics under the same conditions, and a series of experiments were undertaken to enable us to form our own opinion on which was the most suitable antiseptic for midwifery available at the present time. Shortly after the start of this investigation "hibitane" (chlorhexidine), a new British compound, described later by Davies *et al.* (1954), was made available to us and was therefore tested in the same way. The antiseptics which were selected for testing included those used by our clinical colleagues and some suggested by various manufacturers as likely to be of value for this particular field. Tests were carried out on nine substances in all, two of which were discarded after preliminary testing and are not, therefore, included in the results now reported. In the case of one further antiseptic, "milton," the investigation was discontinued after contact tests in the presence of organic matter had been completed. The six antiseptics which were fully tested are given in Table I. Trade names of substances have been used throughout this paper, since the long and cumbersome chemical names would not be so readily understood. In all these experiments the dettol used was the "new" formulation containing 4.8% *p*-chlor-*m*-xylenol.

*A full description of the properties and history of the quaternary ammonium compounds is given by Lawrence (1950).