SHORT REPORTS

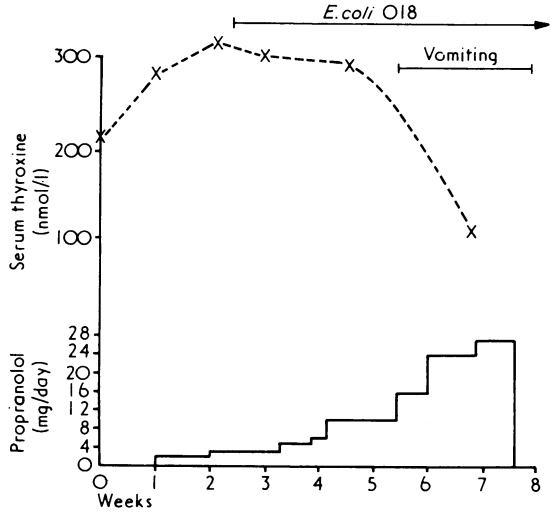
Propranolol treatment of thyrotoxicosis in a premature infant

Advances in the treatment of neonatal thyrotoxicosis are important because, although rare, this disease has a 12% mortality.[1] Pemberton, McConnell, and Shanks[2] reported the first case of neonatal thyrotoxicosis successfully treated by beta-blocking drugs alone. We have used propranolol for the first time in a premature infant and confirm that this is a safe and easy method of treating toxic symptoms.

Case report and comment

Thyrotoxicosis was diagnosed in the twenty-fourth week of pregnancy in a 28-year-old gravida II patient who presented with tachycardia, goitre, and exophthalmos. Treatment with carbimazole, 15 mg daily, controlled her symptoms. Labour started spontaneously but prematurely and was followed by a normal delivery of a baby boy weighing 1625 g on 23 September 1976, who at birth was assessed to be at 34 weeks gestation. There was no antenatal record of fetal tachycardia and he was apparently normal at birth with no goitre. The cord blood thyroxine concentration was 216 nmol/l (16·8 μg/100 ml) (normal adult range for our laboratory 60-135 nmol/l (4·7-10·5 μg/100 ml)). No carbimazole was detected in the cord blood, although the mother had been receiving this regularly prior to delivery.

On the seventh day the baby became irritable and hyperactive, with an apex beat of 200 per minute. He was jittery, showing fine tremor of the limbs especially on handling, but there was no evidence of cardiac failure. He had been fed via a nasogastric tube and had lost 55 g since birth. His serum thyroxine concentration had risen to 279 nmol/l (21·7 μg/100 ml). Propranolol suspension, 0·5 mg thrice daily, started via the nasogastric tube on the seventh day, produced a definite symptomatic improvement and the apex beat fell to 150-160 per minute. Over the next five weeks the dose of propranolol was increased by gradual stages to a maximum of 7 mg four times daily, in order to maintain the apex beat at 150-160/min. This progressive increase in dosage of propranolol required to control symptoms has been previously noted.[2] The serum thyroxine concentration rose to a maximum of 312 nmol/l (24·3 μg/100 ml) at fifteen days of age and then gradually fell to within the normal range at 49 days (see figure). At 38 days he started to vomit and this continued until twenty-four hours after propranolol had been stopped. He vomited two to four times every day, either during or shortly after feeds. The amount vomited varied from small regurgitations to large projectile vomits. Despite this he continued to gain weight. The results of investigations, including a barium meal, urinary pregnanetriol concentration, and 11 oxygenation index, and screen for infection were all normal. From the age of 17 days onwards *Escherichia coli* 018 was repeatedly grown from his stools. This organism was epidemic on the baby unit during this period. All infants carried this strain of *E coli* asymptomatically, but none of the others vomited. At 53 days of age the propranolol was stopped, his vomiting subsided, and he was discharged home two days later weighing 2560 g. Vomiting has been reported as a rare side effect of propranolol therapy in adults (Committee on Safety of Medicines), with an incidence of 0·21%.[3]



Relationship of serum thyroxine concentration to age in weeks.

Conversion: SI to traditional units—Thyroxine: 1 nmol/l ≈ 0·078 μg/100 ml.

Discussion

Carbimazole is known to cross the placenta,[4] and has been used in the mother in an attempt to prevent neonatal thyrotoxicosis.[5] In our case the baby did not show early signs of toxicity, but these developed one week postpartum despite maternal treatment with carbimazole. We can not explain the absence of carbimazole in our cord-blood sample. This baby did not need iodides, digoxin, carbimazole, or sedatives since the toxic symptoms were adequately controlled with propranolol alone. We suggest that beta-blockade should now be considered as a treatment of choice for neonatal thyrotoxicosis.

We thank Dr W S George for serum thyroxine and carbimazole estimations, and Mrs Betty Patterson for secretarial help.

[1] Samuel, S, *et al*, *American Journal of Diseases of Childhood*, 1971, **121**, 440.
[2] Pemberton, P J, McConnell, B, and Shanks, R G, *Archives of Diseases in Childhood*, 1974, **49**, 813.
[3] Conway, J, *Modern Trends in Cardiology*, London, Butterworth, 1975.
[4] Dassault, J, *et al*, *Journal of Clinical Endocrinology and Metabolism*, 1969, **29**, 595.
[5] Ramsey, I, *British Medical Journal*, 1976, **2**, 1110.

(*Accepted 6 May 1977*)

Special Care Baby Unit, Derby City Hospital, Derby DE3 3NE
K N PEARL, MD, DCH, paediatric registrar (present address: New Charing Cross Hospital, London W6 8RF)
T L CHAMBERS, MRCP, DCH, consultant paediatrician

Cardiac arrest due to liquorice-induced hypokalaemia

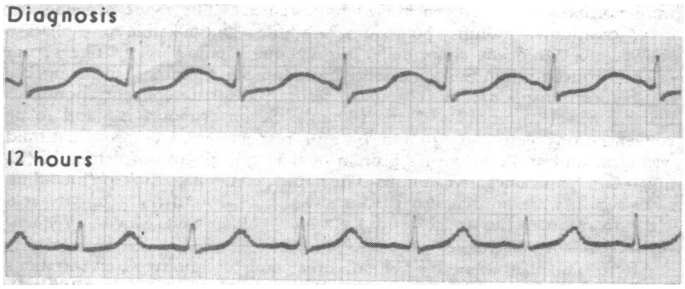
Although liquorice and related compounds have been in therapeutic use for many years it is only in the past 10 years that they have been shown to cause clinically significant hypokalaemia.

Case report

A 58-year-old woman had noticed tiredness and weakness in her limbs for a year and began taking a bottle of tonic wine daily. After a mild attack of diarrhoea, the weakness increased, and she was found on the floor, unable to get up. Her only medication was a monthly injection of vitamin B_{12} for pernicious anaemia.

On admission her rectal temperature was 35°C but although she soon became normothermic, the weakness worsened. By the next morning her limbs were flaccid and tendon reflexes absent, though plantar reflexes remained flexor. She had bilateral ptosis, a weak voice, and rapid shallow breathing. The abdomen was distended and silent, but without tenderness. The cardiovascular system was normal; her pulse was regular at 80 beats/min and blood pressure was 140/80 mm Hg. Other results were: plasma potassium 1·3 mmol(mEq)/l; bicarbonate 34 mmol(mEq)/l; magnesium 0·53 mmol/l (1·3 mg/100 ml) (normal 0·7-1·0 mmol/l (1·7-2·4 mg/100 ml)); sodium chloride, calcium, and haemoglobin levels normal; aspartate transaminase 104 U/l (normal 5-40 U/l); and alkaline phosphatase 51 U/l (normal 15-35 U/l). A chest radiograph was normal, and an abdominal radiograph showed a distended gas-filled bowel. The electrocardiogram is shown in the figure.

Immediately after hypokalaemia had been diagnosed the patient developed ventricular fibrillation. This was successfully treated with external cardiac massage, and 60 mmol of potassium chloride given intravenously in 100 ml 1/5 isotonic saline over five minutes. An episode of tetany occurred, which lasted about one minute, and calcium chloride 10 mmol was given intravenously. She received 420 mmol of potassium chloride intravenously and



Electrocardiogram at diagnosis and 12 hours later showing disappearance of large U waves and appearance of normal T waves.

24 mmol of magnesium sulphate intramuscularly over the next 24 hours. Then 115 mmol daily of effervescent potassium chloride was given orally for the next two days. Muscle power returned to normal within 12 hours, and it was then found that the patient had been eating about 1·8 kg of liquorice sweets per week. Three months after stopping liquorice she remained well, and all laboratory values were normal.

Comment

Liquorice has long been known to cause sodium retention with oedema and hypertension, and more recently it has been shown to cause clinically significant hypokalaemia. Sometimes the hypokalaemia is very severe and associated with muscle weakness, raised muscle enzyme levels in the blood, and myoglobinuria.[1]

The aldosterone-like effects of liquorice are due to its glycyrrhizinic acid fraction,[2] and liquorice consumption in normal people will cause sodium retention, potassium loss, and suppression of aldosterone levels in the blood.[3]

Our patient had the now well-described syndrome of hypokalaemia and myopathy,[4] though without myoglobinuria. She also suffered a cardiac arrest, an event which has not been described in previous reports of liquorice toxicity.

We thank Dr Gillian Hanson and Dr Peter Wright for their interest in this case and for their encouragement.

[1] Cumming, A, *Nursing Times*, 1976, 11 March, p 367.
[2] Conn, J W, Rovner, D R, and Cohen, E L, *Journal of the American Medical Association*, 1968, **205**, 497.
[3] Epstein, M T, *et al*, *British Medical Journal*, 1977, **1**, 488.
[4] Epstein, M T, *et al*, *British Medical Journal*, 1977, **1**, 209.

(*Accepted 22 April 1977*)

Medical Unit, Whipps Cross Hospital, London E11 1NR
BARBARA BANNISTER, MRCP, medical registrar (present address: Royal Free Hospital, London)
ROBERT GINSBURG, MB, BS, house physician (present address: London Hospital, London)
JOHN SHNEERSON, DM, MRCP, medical registrar

Acquired ichthyosis and toxic epidermal necrolysis and mesenteric reticulum cell sarcoma and malabsorption

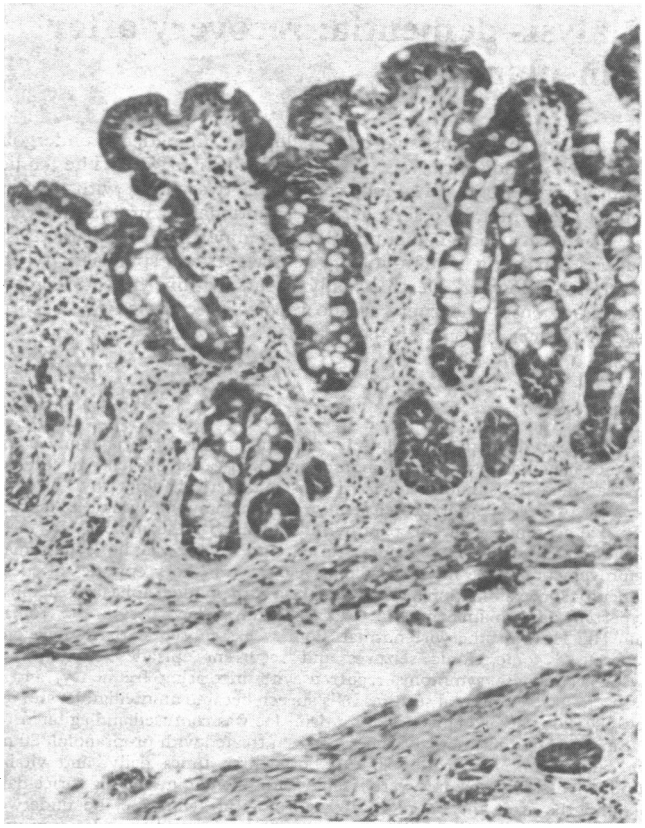
Here we describe a patient with malabsorption with small intestinal subtotal villous atrophy initially diagnosed as having coeliac disease, but not responding to gluten withdrawal, and in whom reticulum cell sarcoma of the mesenteric lymph nodes developed. Ichthyosis appeared and toxic epidermal necrolysis was a terminal complication.

Case report

A 61-year-old woman presented in July 1973 with diarrhoea and 12-kg weight loss in 6 months. Her bowels had been open five times daily, with bulky, greasy, and offensive motions. At the age of 6 months she had had an illness termed "consumption of the bowels," which had resolved spontaneously, and since then she had had one normal daily bowel action. She was of normal stature, but had lost weight, and had a pale, smooth skin. There was no evidence of longstanding malabsorption. The results of relevant investigations were as follows. Faecal fat excretion was 20 g stearic acid daily: serum albumin 32 g/l; haemoglobin 12·2 g/dl; and serum folate 2·2 μg/l (2·2 ng/ml). Sigmoidoscopy and barium enema results were normal, while barium follow-through showed a non-specific malabsorption pattern. Peroral jejunal biopsy showed subtotal villous atrophy, with an infiltrate of lymphocytes and plasma cells. The patient was started on a gluten-free diet. In twelve months she regained 7 kg and her bowel habit and stools returned to normal. Repeat biopsy, however, showed persistent subtotal villous atrophy and a heavier cellular infiltrate with increased submucosal collagen.

In November 1974 she was readmitted with a relapse of steatorrhoea and weight loss, despite adhering to the diet. She appeared ill, grossly wasted, and had a generalised ichthyosis. There was no hepatosplenomegaly, but enlarged, firm, inguinal lymph nodes were palpable. Throughout this admission she had intermittent peaks of fever to 40°C. Barium follow-through now showed an irregularly narrowed small bowel around an enlarged mesenteric root. Bipedal lymphangiography demonstrated filling defects in the inguinal and intra-abdominal lymph nodes. The results of bone marrow examination and liver biopsy were normal, but reticulum cell sarcoma had replaced much of an inguinal lymph node. A third jejunal biopsy again showed subtotal villous atrophy. Cytotoxic treatment was started with single doses of mustine (4·5 mg) and vincristine (2 mg), and a 14-day course of procarbazine (75 mg daily), and prednisolone (40 mg daily). She was discharged taking 20 mg prednisolone daily. Two weeks later the ichthyosis was less appreciable. The white cell count was $7{\cdot}0 \times 10^9$/l (7000/mm^3), lymphocytes $0{\cdot}21 \cdot 10^9$/l (210/mm^3); and platelet count 115×10^9/l (115 000/mm^3). She was given mustine (9 mg) and vincristine (2 mg) intravenously. Five days later toxic epidermal necrolysis developed, spreading from the buttocks on to the trunk. The white cell count had fallen to $0{\cdot}8 \times 10^9$/l (800/mm^3) and platelets to 15×10^9/l (15 000/mm^3). After 10 days she developed bronchopneumonia and died.

Direct immunofluorescence on a skin biopsy during life showed IgG cryoglobulin in dermal blood vessels. (A serum IgG cryoprecipitate of 4 g/l was present.) At necropsy the small bowel mucosa was flattened, but there was no macroscopic or microscopic evidence of lymphoma. Mesenteric lymph nodes contained large neoplastic lymphoreticular cells, representing reticulum cell sarcoma modified by chemotherapy. The spleen weighed 100 g and contained similar cells.



Jejunal biopsy at time of diagnosis of reticulum cell sarcoma, showing subtotal villous atrophy and chronic inflammatory infiltrate after 16 months' gluten withdrawal. (H and E. ×100.)