dialysis produced an effective biochemical adjustment and ultrafiltration of excess fluid. A chest X-ray subsequent to this dialysis demonstrated no evidence of pulmonary œdema. Diuresis commenced 14 days after the ingestion of mercuric chloride and an uneventful recovery ensued.

Discussion

Pulmonary œdema complicating acute renal failure is subsequent to hypervolæmia produced by overhydration. Clinically, pulmonary œdema is recognised by tachypnœa, dyspnœa, cyanosis, the expectoration of frothy blood-stained sputum and the development of widespread crepitations throughout the lungs. The diagnosis may be confirmed by the characteristic radiological appearances. Both patients had initially developed an apical gallop rhythm and electrocardiographic evidence of left ventricular strain.

The initial treatment of pulmonary œdema is to allay anxiety, reduce pulmonary capillary pressure and increase alveolar oxygenation. Morphine, aminophylline and oxygen were used with some benefit. If, however, the pulmonary œdema is due to hypervolæmia following overhydration, the blood volume should be reduced directly. The rapid removal of blood by venesection or aterial puncture may be sufficient but this procedure exacerbates the anæmia which invariably develops in acute renal failure. Its application is therefore limited as the resulting severe anæmia impairs myocardial efficiency. The blood removed can be replaced by a smaller volume of packed cells in order to prevent the development of severe anæmia but such an exchange transfusion carries with it the danger of producing potassium intoxication. It is, however, possible to perform an exchange transfusion during dialysis, as in the first case, when the danger of hyperkalæmia is averted by the immediate removal of excess potassium. Hypervolæmia can be effectively corrected by ultrafiltration with the artificial kidney.

We found that ultrafiltration is best effected by the Skeggs-Leonards Artificial Kidney if the pressure in the blood circuit is artificially elevated to about 160 to 180 mm. Hg. on the venous side and if the dialysing fluid pressure is reduced by limiting its flow to about 400 to 500 ml/min.

The value of Dimercaprol given early in mercury poisoning has been pointed out by Longcope and Leutscher (1949). Augustine (1956) has found that the ingestion of more than 1 g. of mercuric chloride is fatal in 50% of patients. The survival of Case 2 after taking 2.84 g. of mercuric chloride was thought to be due to the early administration of dimercaprol and the use of the artificial kidney in the treatment of the pulmonary œdema.

Summary

1. Survival of two cases of poisoning producing acute renal failure complicated by pulmonary œdema is presented.

2. The management of pulmonary œdema by conventional methods, exchange transfusion and the artificial kidney is described.

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CRISIS FOLLOWING CORTICOTROPHIN IN ADDISON'S DISEASE WITHOUT PIGMENTATION

M. F. ALLISON, M.B., CH.B.
House Physician

I. S. BAILEY, B.Sc., M.D., M.R.C.P.
Senior Registrar

D. C. CURTIN, M.B., M.R.C.P.I., D.C.H.
Registrar

Crumpsall Hospital, Manchester

A PATIENT with Addison's disease developed a crisis during a diagnostic corticotrophin test. This, and the absence of oral and skin pigmentation, are sufficiently unusual to justify a brief report.

Case Report

A 33-year-old housewife was admitted to Crumpsall Hospital in August 1962. She gave a six-month history of lassitude and of loss of one stone in weight, but menstrual periods had remained regular. In 1957 she had a thyroidectomy for hyperthyroidism when examination of the excised gland showed a nodular colloid goitre with scattered small lymphadenoid foci.

On admission: Blood pressure 80/60 mm. Hg. There

was no goitre and she was euthyroid. Pubic and axillary hair were normal. There was no oral or skin pigmentation, and the urine was normal.

Investigations: Serum sodium 132 mEq./l., potassium 5.9 mEq./l.; 17-ketosteroid excretion 0.8 mg./24 hours and 17-ketogenic steroid excretion 0.9 mg./24 hours. After a water load of 1 litre, 420 ml. of urine excreted in 4 hours, maximum rate of flow 3.5 ml./min. X-ray chest, skull and abdomen normal. Radioactive iodine uptake normal (23% at 2 hours, 56% at 24 hours).

In the first week in hospital her clinical condition improved and blood-pressure rose to 100/70. A corticotrophin test was then performed by giving 30 units of corticotrophin gel twice daily by intramuscular injection.

During the first day of the test, she began to vomit, her blood pressure fell and twenty-four hours after the first injection she was shocked, with a systolic blood-pressure of 55 mm. Hg, and a serum sodium of 126 mEq./l. There was a good response to intravenous glucose saline and large doses of hydrocortisone. The steroid was gradually reduced over the next week to a maintenance dose of 50 mg. cortisone daily. After a few days this was replaced by fludrocortisone 1 mg. daily and three days later the corticotrophin test was repeated without ill effects. Her blood pressure remained steady at 105/70 mm. Hg. There was no significant rise in steroid excretion. (Table 1). She has since been maintained on 37.5 mg. of cortisone daily and is in excellent health with a blood-pressure 120/80 Hg and normal serum electrolytes. Repeat water diuresis while on maintenance cortisone shows an excretion of 900 ml. of urine within four hours of a water load of 1,200 ml., with a maximum rate of flow of 10 ml./min.

TABLE 1

	17-ketosteroids mg./24 hrs.	17-ketogenic steroids mg./24 hrs.
Control	3	2.5
Control	2	4
Corticotrophin	1.5	3
Corticotrophin	2	5
Corticotrophin	3	1

Discussion

The low serum sodium, the impaired excretion of a water load with restoration to normal by cortisone, the low steriod output and the crisis, indicate adrenal cortical insufficiency. The normal menstrual periods, normal axillary and pubic hair, normal thyroid function and failure to respond to corticotrophin, rule out hypopituitarism and establish the diagnosis of Addison's disease.

Lack of pigmentation in Addison's disease has been recorded (Wilks, 1862; Lawson, Beck and Murphy, 1943; Felix-Davies, 1955; Jores and Tamm, 1959; Fellows, Buchanan, Peterson and Stokes, 1962) but is unusual. Dunlop (1963) reported only six patients without pigmentation in a series of 86 patients with Addison's disease. It is not entirely clear why some patients should have no increase in pigment. It may be less marked in blondes and this is a possible explanation in our patient who has fair hair and fair skin and who has never tanned in sunlight. Fellows and others (1962) offer another explanation. In their two patients the plasma cortisol was in the low normal range but failed to increase on stimulation with corticotrophin, and they suggested that sufficient cortisol was produced to inhibit pituitary melanocyte-stimulating hormone, but insufficient for situations of stress.

Jenkins, Forsham, Laidlaw, Reddy and Thorn (1955) encountered six potentially serious anaphylactoid or febrile reactions to intravenous corticotrophin in the course of several thousand tests in patients with adrenal cortical insufficiency and commented that it is imperative that steriod should be administered immediately to avert adrenal crisis. These reactions occurred only in patients who had previously received corticotrophin: they became rare as the purity of the preparation improved and were probably produced by inert protein (Thorn, Jenkins, Laidlaw, Geotz, Dingman, Arons, Streeten and McCracken, 1953). It is unlikely that this mechanism accounts for the crisis in our patient, as this was her first injection. Stone and Jewel (1961) reported two deaths in crisis in a series of 17 patients given intramuscular or intravenous corticotrophin for suspected adrenal insufficiency and mentioned one further patient who suffered diarrhœa and vomiting. They suggested four possible explanations: adrenal exhaustion after stimulation of a partially functioning gland, thyroid stimulation by contaminating thyroid-stimulating hormone, water retention from contaminating posterior-pituitary extract, and salt loss from stimulation of a postulated salt-excreting adrenal steriod. We think the most likely explanation in our patient is exhaustion of a partially functioning gland.

Laidlaw, Reddy, Jenkins, Haydar, Renold and Thorn (1955) showed that fludrocortisone, 0.25 to 1.0 mg. daily, could by itself maintain a patient with Addison's disease in good health while making no appreciable contribution to urinary steriod excretion, and they also showed that this dose would protect the patient with Addison's disease from untoward reaction to corticotrophin. Stone and Jewel (1961) have since 1958 given 1 mg. of fludrocrotisone routinely during the corticotrophin test and have had no further fatalities. For these reasons we gave fludrocortisone during the second corticotrophin test and for these reasons we recommend the administration of 1 mg. fludrocortisone daily during a corticotrophin test in any patient suspected of Addison's disease.

Summary

A patient with Addison's disease but without pigmentation went into crisis during a diagnostic corticotrophin test. The patient was given fludrocortisone, 1 mg. daily, and the test was repeated without ill effect. It is suggested that fludrocortisone might be used routinely during a corticotrophin test in any patient suspected of Addison's disease.

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ATROPINE POISONING TREATED BY FORCED DIURESIS

BERNARD M. GRODEN, M.B., M.R.C.P.(GLASG.), M.R.C.P.(ED.)

Medical Unit, Glasgow Royal Infirmary

WILLIAM D. WILLIAMS, PH.D.(GLASG.)

Department of Pharmacy, The Royal College of Science and Technology, Glasgow.

A THIRTY-ONE-year-old male patient was admitted to hospital three hours after swallowing 7.5 ml. of 1% atropine sulphate eyedrops in a suicidal attempt.

Case Report

He was found to be hallucinated, irritable, and tremulous. His pupils were widely dilated; muscle tone was increased, with exaggerated reflexes and bilateral ankle clonus. His tongue was dry and furred. His pulse rate was 104/min., blood pressure 140/100 mm. Hg. He had not vomited prior to admission to hospital, and had not passed urine.

Treatment. A regime of forced diuresis, similar to that described by Ohlsson (1949) and Lassen (1960) for the treatment of barbiturate intoxication, was initiated. The actual technique was as follows:

Two pints of normal saline were given intravenously in one hour, followed by 0.5 g. chlorothiazide intravenously. Following this, two pints of 5% dextrose water were given over ninety minutes, and these were followed by 80 g. of urea in 200 ml. of water. Subsequently, one pint of 5% dextrose water was given hourly, and seven hours after starting the treatment a further 0.5 g. of chlorothiazide was given.

All the urine was collected by catheter and the atropine content was estimated by the Vitali Morin reaction. (Appendix, Table I).

Ten hours after commencing treatment the patient was rational and no longer hallucinated. His tremor had disappeared and his reflexes had returned to normal. His pupils, however, remained widely dilated for twenty-four hours, but gradually returned to normal during the subsequent twenty-four hours.

Discussion

Carter (1940) and Glaister (1957) describe patients who have recovered following consumption of similar quantities of atropine. Only symptomatic and supportive treatment have been available, however, and it seems agreed that chemical methods of treatment are ineffective (Goodman and Gilman, 1955; Graham, 1962).

Our results indicate that with forced diuresis 25.7 mg. of atropine sulphate, that is 34% of the ingested quantity, were excreted in the two hours following commencement of therapy or in the six hours after taking the drug. 30.9 mg. (41% of the ingested dose) were excreted in 10 hours following commencement of therapy, that is in the 14 hours after taking the drug. During this period the patient passed 5,800 ml. of urine. By comparison Tonnesen (1950) showed that humans, given doses of 2 to 5 mg. of atropine sulphate orally, excreted on average 12.7% of the ingested dose during the next two days.

We were able to detect atropine in the patient's urine for 24 hours after taking the drug, but no atropine could be detected chemically or by the cat's eye test (Sollmann, 1948; Krantz and Carr, 1961) after this.