for acting as independent assessor of x-ray films, and to the Medical Research Committee of the United Birmingham Hospitals for financial assistance.

APPENDIX

1. *Definitions.*—*Post-primary pulmonary tuberculosis* includes all intrapulmonary lesions regarded by us as tuberculous except the primary complex and single calcified shadows in the lung. *Significant pulmonary tuberculosis* has been used in Table VI. Its meaning must vary according to the observer. We have included all post-primary tuberculous lesions requiring any further observation or treatment: this, in fact, includes all lesions not entirely calcified.

2. *Reading Chest X-ray Films.*—(1) Mass x-ray films were read independently by us (P. A. T. and V. S. B.) and Dr. L. A. McDowell; all suspects were recalled for a large film. If this film showed post-primary pulmonary tuberculosis then the film taken before partial gastrectomy was inspected. (2) The pre-operative films of the 14 patients who subsequently developed radiological pulmonary tuberculosis after a normal x-ray film before operation were inspected by Dr. Springett. In order to minimize the likelihood of bias he was given a pile of films containing the 14 films we regarded as normal, together with a number of other films showing minor abnormalities. Using this technique, Dr. Springett confirmed that these 14 films were normal. (3) The film of all patients whose x-ray films we classed as abnormal before operation were inspected and accepted by Dr. Springett as showing post-primary pulmonary tuberculosis.

POSTSCRIPT.—A mass x-ray survey of hospital in-patients was carried out at the Central Middlesex Hospital during 1953-4, and by courtesy of Dr. F. Pygott we show the result of this survey: only the males are quoted for comparison with Table VI. Accurate comparison of the results with those in the present survey should be cautious, because the figures were obtained in a different area and the films were interpreted by different observers. Nevertheless there is a wide discrepancy between the two prevalence rates, especially in the older age groups.

Age in Years	Total No.	Significant P.T.
Under 25	388	1 (0.3%)
25-34	348	—
35-44	356	8 (2.2%)
45-54	432	4 (0.9%)
55-64	360	1 (0.3%)
65 and over	376	5 (1.3%)
Total	2,260	19 (0.8%)

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ADDISON'S DISEASE PRESENTING IN HYPOGLYCAEMIC COMA

BY

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It is well known that patients with Addison's disease may be easily precipitated into crisis, sometimes presenting as hypoglycaemic coma, by intercurrent infection. Such patients also manifest hypoglycaemic symptoms at relatively higher blood-sugar levels than normal persons.

The Literature

Simpson (1932), while treating a patient in Addisonian crisis whose fasting blood sugars were always under 80 mg. per 100 ml. and as low as 62 mg. per 100 ml., found that 600 ml. of 5% glucose, given intravenously, brought much improvement. He stated (Simpson, 1953a, 1953b) that a common cause of death in Addisonian patients stabilized on deoxycortone is hypoglycaemic coma. Thorn *et al.* (1940) reported the case of a patient stabilized on deoxycortone who, on the third day of a low-carbohydrate diet, went into a hypoglycaemic coma. The blood sugar was 55 mg. per 100 ml. and the patient was promptly restored with intravenous glucose. Serum sodium and potassium levels and the carbon dioxide combining power were normal. A slightly raised serum potassium was thought to be associated with the low blood sugar. They stressed that the reaction was a specifically "carbohydrate" one. There was no loss of sodium or chloride ions or any dehydration as evidenced by the normal haematocrit and normal body weight.

Magnusson (1934) described hypoglycaemia occurring in a patient suffering from Waterhouse-Friderichsen syndrome. Banks and McCartney (1943) noted immediate improvement in the pulse and blood pressure following 10 g. of intravenous glucose in patients with this syndrome and presumed hypoglycaemia, though no blood-sugar estimations had been done.

Rushton *et al.* (1940) described the case of a paranoid patient who on three occasions had spontaneous hypoglycaemic attacks when she refused food. In one of these attacks there was limb flaccidity with bilateral extensor plantar responses. The blood sugar was 40 mg. per 100 ml. The intravenous injection of 20 ml. of 50% glucose caused prompt recovery. At post-mortem examination bilateral adrenal atrophy was found. In this case there was no abnormal pigmentation. They go on to state that, though hypoglycaemia is not common in Addison's disease, in a limited number of cases hypoglycaemic episodes are an outstanding feature, and that in such cases salt and water metabolic disturbance may not necessarily parallel that of the carbohydrate.

Welty and Robertson (1936) reported two cases of Addison's disease, proved by post-mortem examination, presenting in hypoglycaemic coma. The coma was promptly relieved by intravenous glucose. The blood-sugar values were 50 and 40 mg. per 100 ml. The serum sodium potassium and chloride values were within normal limits.

It is more usual, however, to find low values for serum sodium or serum chloride, or both, in Addisonian hypoglycaemic coma. Normal values may be due in some cases to the associated dehydration resulting in a falsely high figure.

The following case report describes a case of Addison's disease presenting in hypoglycaemic coma.

Case Report

A woman aged 48 was admitted at 8.15 p.m. on October 4 in deep coma. The only available history was that, for the 24 hours prior to admission, she had complained of severe headache and thirst and had vomited several times, and that she had been found unconscious at 5.30 p.m.

On recovery, the following additional history became available. There had been three pregnancies. The last, nine years previously, had been normal, with no post-partum haemorrhage, and the pubic hair had regrown after shaving for the confinement. For two years before admission there had been a gradual loss of pubic hair, together with a loss of axillary hair. A gradual onset of hypomenorrhoea had occurred, and for 14 months before admission she had had amenorrhoea. For four months she had noticed great prostration if she missed a meal. There was a three-months history of fatigue. The day before admission she had a burning dysuria, with frequency, urgency, and strangury. This was later shown to be a *Bact. coli* pyelitis. Associated with this were vomiting and headache. She had no recollection of the events of the day of admission.

Examination showed a thin, dehydrated woman with a marked generalized dusky pigmentation of the skin, and a brown patch of pigmentation on the buccal aspect of the right cheek. A ring of brown pigment was present on the garter-pressure areas of both thighs. The areolae and genitalia were hyperpigmented but otherwise normal. Axillary hair was absent, and pubic hair was sparse. Eyebrow and head hair was normal. There was a right-sided seventh nerve weakness of upper motor neurone type, and the left pupil was larger than the right. Reaction to light and accommodation was normal. Kernig's sign was positive and neck stiffness was pronounced. All the limbs were flaccid and there was a bilateral extensor plantar response. All tendon reflexes were absent, except those of the right arm and the left biceps. The pulse was 80 a minute and the temperature less than 97° F. (36.1° C.). Blood pressure was 90 mm. Hg systolic—diastolic unrecordable. Other systems were normal to clinical examination.

A tentative diagnosis of subarachnoid haemorrhage in an Addisonian patient was made, and lumbar puncture was performed. The cerebrospinal fluid was biochemically normal, and the W.R. negative; glucose was not estimated. At this stage it was thought that the patient might be in an Addisonian crisis. Biochemical investigations were then found to be as follows: blood sugar, 38 mg. per 100 ml.; blood urea, 53 mg. per 100 ml.; serum potassium, 15.2 mg. per 100 ml.; serum chlorides, 574 mg. per 100 ml. (as NaCl); serum sodium, 332 mg. per 100 ml.

At 11 p.m., three hours after admission, 50 ml. of 50% glucose was given intravenously, with dramatic lightening of coma. In three minutes the patient could answer questions and was able to take 30 g. of glucose by mouth. The central nervous system was now normal to clinical examination. The diagnosis was changed to Addisonian crisis with hypoglycaemic coma.

During the next 24 hours she received 30 mg. of deoxycortone intramuscularly, 150 mg. of cortisone intramuscularly, and 70 ml. of "eucortone" intravenously, with 5 pints (2.8 litres) of 20% glucose by mouth, in addition to 3½ pints (2 litres) of normal saline intravenously. Penicillin, 1 mega unit six-hourly, was given by intramuscular injection for five days.

The day after admission, investigation showed: blood sugar, 102 mg. per 100 ml.; white-cell count, 8,600 per c.mm. (polymorphonuclear neutrophils 75%, lymphocytes 21%, monocytes 4%, eosinophils 0%, basophils 0%). Subsequently she was given 100 mg. of cortisone daily until October 11, with marked clinical improvement.

On October 6 the haemoglobin was 65% (Haldane); packed cell volume, 30%; blood Wassermann reaction, negative; blood Kahn test negative. On October 7 a catheter specimen of urine contained numerous pus cells and coliform organisms were grown on culture. The blood sugar was 366 mg. per 100 ml., and the blood urea 31 mg. per 100 ml. On October 8 the blood cholesterol was 115 mg. per 100 ml., and 17-ketosteroid excretion 2.73 mg. a day. The basal metabolic rate was $\pm 0\%$ on October 9. Next day the chest x-ray examination showed nothing abnormal, with no evidence of tuberculosis.

A straight x-ray film of the abdomen was normal: no supra-renal calcification. X-ray films showed skull and pituitary fossa to be normal.

On October 12, 13, and 14 she received 50 mg., 25 mg., and 12.5 mg. of cortisone respectively, and none at all from the 15th to the 18th inclusive. Oral glucose-tolerance test (40 g. of glucose) on the 15th showed a flat curve with a fasting blood sugar of 107 mg. per 100 ml. and a maximum blood sugar of 133 mg. per 100 ml. after half an hour. No glucose was present in the urine. On October 18 the fasting blood sugar was 77 mg. per 100 ml.; eosinophil count, 350 per c.mm.; Kepler's index 9. On October 19 the Thorn test was positive. The eosinophil count was 250 per c.mm.; four hours after 25 mg. of corticotrophin intramuscularly it was 212 per c.mm. At noon on the fifth day (October 19) the patient complained of weakness and malaise and her blood pressure was 70 mm. Hg systolic. She had lost 5½ lb. (2.6 kg.) in weight. At 2 p.m. 150 mg. of cortisone was given orally. By 6 p.m. she looked and felt much better, and her blood pressure was 95 mm. Hg systolic.

During her stay in hospital the patient gained more than 14 lb. (6.4 kg.), and was stabilized on a maintenance dose of 50 mg. of cortisone daily by mouth. Her blood-sugar values have since remained within normal limits and her blood pressure at 120/80 mm. Hg.

She is now able to miss a meal without prostration, her pubic hair is gradually increasing, and the pigmentation is gradually decreasing. She says that she has "never felt better."

Comment

There were two fundamental problems causing difficulty in diagnosis and treatment: the hypoglycaemia and the exclusion of hypopituitarism. Diagnosis was delayed by the absence of any suggestive history on admission and by the neurological signs due to the hypoglycaemic coma.

Thorn *et al.* (1951), reviewing the principal signs and symptoms of 94 cases of Addison's disease, do not specifically mention hypoglycaemia. It is therefore worth stating that hypoglycaemic coma may be the presenting feature of an Addisonian crisis. The urinary tract infection was thought to be the precipitating factor.

Under treatment the patient was alert and co-operative. She was not hypersensitive to cold. Her eyebrow and head hair was normal. The skin was also normal. The basal metabolic rate was normal and the blood cholesterol a low normal; there was no evidence of hypothyroidism. The menopause could in part account for the sparsity of the pubic and axillary hair together with the amenorrhoea. Hair loss is a late sign in Addison's disease though an early one in hypopituitarism. However, in retrospect the patient thought that she had been in poor general health for at least one year, possibly two years. Clinically her genitalia were normal and she had a long history of successful reproduction.

Maddock *et al.* (1953) described four male patients with depressed gonadal and adrenocortical function due to selective pituitary failure. Two had hypoglycaemic manifestations and, in both, pigmentation was deficient. All the cases had a long history of hypogonadism. Thorn *et al.* (1951) state that "the integrity of the pituitary gland is essential for the development of Addisonian pigmentation." Pigmentation of the buccal mucous membrane does not occur in hypopituitarism, and is the most important point in the differential diagnosis.

The 17-ketosteroid level of 2.73 mg. a day also favours the diagnosis of Addison's disease, as it is usually less than 2 mg. a day in hypopituitarism severe enough to cause hypoglycaemic coma.

The absence of an eosinophilia was due to treatment having been started 12 hours before the blood was taken. This factor and the presence of a *Bact. coli* urinary infection account for the absence of a lymphocytosis.

The presence of classical Addisonian pigmentation and the absence of hypothyroidism and hypogonadism excluded a diagnosis of hypopituitarism. In view of this, and the

predominantly "carbohydrate" defect, cortisone alone was used for maintenance therapy.

As soon as the hypoglycaemia was recognized the patient was restored to consciousness with the intravenous administration of glucose. After this, oral glucose feeding sufficed to maintain adequate blood-sugar levels.

It is suggested that the possibility should be borne in mind that hypoglycaemia may be contributing to loss of consciousness in the Addisonian patient. It would therefore seem worth while to estimate the blood-sugar level as a routine in this type of case.

Summary

The case of a woman with Addison's disease presenting in hypoglycaemic coma is described. The coma responded immediately to the administration of intravenous glucose. The differential diagnosis is briefly discussed.

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LOW TERMINATION OF THE INTERNAL SAPHENOUS VEIN

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The Trendelenburg* operation for varicose veins, usually in combination with ligation of the main communicating vessels above and below the knee, is one of the most commonly performed in surgery. In terms of alleviation of symptoms, both annoying and incapacitating, a countless multitude of patients must have derived benefit from its effects. In all centres where the operation is performed carefully in the classical method surgical complications are few. When such a complication does occur, however, it is often a tragedy, and may result in the crippling of a young and healthy person undergoing a relatively minor operation for a non-urgent condition.

Accidental ligation of the femoral vein would be expected as a recognized hazard of the operation in

*The high ligation of the internal saphenous vein at the sapheno-femoral junction was first described by Homans in 1916. The operation actually recorded by Trendelenburg (1890) was simple ligation of the internal saphenous in the mid-thigh. The term "Trendelenburg operation" as denoting the high ligation is retained in this paper as it still receives widespread acceptance. The internal saphenous vein of this paper is the vena saphena magna of the *Nomina Anatomica* (1955 revision).

view of its relation to the internal saphenous vein, but has rarely been reported. Daseler *et al.* (1946) record one case in which the femoral vein was ligated and severed, but give no details of the anatomy or subsequent procedure. Wells (1948) describes the immediate repair of a femoral vein tied off in the course of a high ligation operation for varicose veins, with no deleterious effects. McPheeters (1945) reports a femoral vein and artery ligated together. Luke and Miller (1948), in their paper entitled "Disasters following the ligation and retrograde injection of varicose veins," review 21 cases with 4 fatalities; these are divided into two groups, operative and thrombotic. In the former no femoral vein ligation is recorded and no abnormal anatomy mentioned. Homans (1949) stresses that interruption of the femoral vein tends to result in chronic oedema, venous engorgement, and post-phlebitic induration and ulceration.

This report presents four cases, all of which have been admitted on or transferred to the same unit during the past three years.

Case 1

A man aged 23 gave a history of bilateral varicose veins for four years. He underwent operation on December 27, 1952. An uncomplicated Trendelenburg procedure was carried out on the left side with venous ligations in the thigh and leg. On the right side the internal saphenous vein entered the femoral at a lower level than normal, at the apex of Scarpa's triangle, and the femoral vein was accidentally tied. In the post-operative period the superficial veins remained tightly distended and the leg became oedematous. However, the patient was discharged on January 10, 1953, with the wounds healed and the swelling controlled by a blue-line bandage.

He was readmitted on May 29, 1954, with chronic oedema of the leg and small ulcers on the anterior and medial aspects of the ankle. Varicosities were present in the distribution of the internal saphenous vein. With rest in bed and eusol dressings the ulcers healed and he was discharged on June 15. On his third admission on February 5, 1955, the areas of ulceration were again present, the varicosities more obvious although less tense, and the swelling of the leg had become less over the previous year. Trendelenburg tests showed that the deep venous return was functioning. A further operation was performed on February 14 in which the varicosities in the calf and above the knee were ligated without post-operative increase in the oedema. He was discharged on February 23 with the ulcers healed.

Case 2

A housewife aged 38 was admitted on May 27, 1955, from another hospital where on the previous day the left femoral vein had been accidentally ligated following a haemorrhage in the course of a bilateral Trendelenburg operation. The foot was warm but pulseless, a little cyanosed, and anaesthetic. The patient was mentally confused. The wound was immediately opened under general anaesthesia, when it was confirmed that the femoral vein had been ligated and divided, and it was seen that the saphenous vein entered the femoral vein a good 5 cm. below the groin. The femoral artery was in marked spasm, but there was no sign of damage to its wall. After this second operation the patient developed oliguria, albuminuria, and uraemia, which was felt to be due to lower nephron nephrosis. The possible causative factors of this condition could have been one or more of the following: (1) prolonged hypotension following the severe haemorrhage of the first operation, leading to renal anoxia; (2) trauma to the limb and ligation of the femoral vein causing spasm of the femoral artery, which extended proximally to involve the renal arteries (Trueta, 1947); and (3) congestion and necrosis of the muscles consequent on ligation of the femoral vein with effects similar to the crush syndrome. The blood urea had risen to 430 mg. per 100 ml. on June 3.