

ways in order to please and make them happy without forgoing the general rules of the hospital and society. All these things work satisfactorily towards the speedy progress of the sick. But above all, the patient should have absolute faith and confidence, and the nurse in charge, with the co-operation of the other staff, should cultivate this attitude.

ADDISON'S DISEASE

1. The Treatment of Addison's Disease

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In 1849, Thomas Addison of London read before the South London Medical Society a paper on "The Constitutional and Local Effects of Disease of the Suprarenal Capsules" which gave the first description of the disease now known by his name.

The disease is comparatively rare. Sir William Osler is said to have observed only seventeen cases in the United States. Among 150,000 admissions to Barnes Hospital, thirty-six patients were diagnosed as having Addison's disease, while nine others, apparently less typical, were classed as adrenal insufficiency. About sixteen patients per 100,000 admissions to the Mayo Clinic have had Addison's disease.

The symptoms of Addison's disease occur as the result of destruction of the cortical portions of the adrenal glands. This may follow tuberculosis, the commonest cause. Simple atrophy with fibrosis is found almost as frequently. Destruction by tumour tissue, haemorrhage, thrombosis, or embolism is less frequent. As the result of the diminution in adrenal cortex tissue, the endocrine secretion of its cells is so diminished as to cause serious disturbance in a number of the body's metabolic processes. Complete absence of this secretion causes death. Partial insufficiency results in weakness, apathy, skin pigmentation, weight loss, dehydration, weak heart action with low blood pressure, and gastro-intestinal disturbances such as loss of appetite, vomiting and diarrhoea.

Better knowledge of the anatomical, physiological, and chemical disturbances present in Addison's disease has led to more successful treatment of a condition previously considered entirely hopeless. For about ten years adrenal cortex extracts made from animal adrenals have been used, and it is now evident that many lives have been at least temporarily saved and considerably prolonged. It has been found that the disease is characterised by loss of sodium and chloride, with a consequent loss of fluid, and that urea and potassium tend to be retained. Giving sodium salts to these patients causes improvement, while potassium is detrimental.

Proper treatment with adrenal cortical extracts causes retention of the sodium and chloride and excretion of the potassium.

Blood sugar in adrenal insufficiency is low and is restored to normal with treatment. During the past year a synthetic adrenal cortex hormone, desoxycorticosterone, has become available. It will raise the blood pressure of patients with adrenal insufficiency and restore the salt balance to normal. At present it seems likely that several hormones may be secreted by the adrenal cortex, and that they may be concerned in various combinations with salt, water, and sugar metabolism.

Laboratory studies may be useful in diagnosing Addison's disease. Frequently however, a patient with typical signs may fail to exhibit the chemical changes expected. The following table gives the normal blood chemical findings as contrasted with those in a typical case of severe Addison's disease.

Milligrams per 100 cubic centimetres.			
		Normal.	Addison's Disease.
Sodium	...	315—330	260
Chloride (NaCl)		570—620	440
Potassium	...	16—22	36
Urea	...	10—40	120

The Clinical Picture

In its fully developed form the clinical picture is unmistakable and striking. The colour of the patient's skin is brownish, varying from light brown in some cases to much darker hues in others, even to shades approaching black. The tongue and mucous membranes of the mouth may show patchy dark brown pigment. Usually this brownish pigmentation is most marked on the face, neck and upper extremities, and in the folds of the axilla and groin. There may be freckles of darker brown or black, and especially heavy pigment may be deposited about scars. In some cases the pigment is patchy and may alternate with depigmented or whitish areas. Excessive fatigue is evident after the slightest exertion, and the patient is usually thin, with the skin dry and wrinkled from loss of body fluid.

The onset of the disease is usually gradual and insidious. Loss of energy usually occurs first. Later, pigmentation may appear, and it may be so slow in development that it is mistaken for sun tan, and be unnoticed by friends or relatives. Loss of appetite and weight appear. In women there is usually amenorrhoea. Alternate constipation and diarrhoea are common. Dizziness, headache, backache, sensitivity to cold, and nervous symptoms, especially irritability and apprehension, are frequent. Vomiting is a late and dangerous occurrence, often heralding the approach of the so-called "Addisonian crisis". The earlier insidious symptoms have usually been present from one to three years when the loss of strength may become actual prostration. Vomiting and diarrhoea may occur, often with abdominal pain, and the patient may collapse into semi-consciousness or complete coma.

Treatment of Addisonian Crisis

No illness is more serious or acute than the crisis of Addison's disease. The patient must be protected from over-zealous friends, relatives, nurses and doctors. The physical examination is limited to the minimum necessary to determine the diagnosis. The usual admitting routine is omitted, the patient being put to bed in a quiet room with the least possible fuss.

The examining physician finds—in addition to the pigmentation, dehydration, evidence of weight loss, and prostrated or comatose state—that the patient has the signs and symptoms usually spoken of as occurring with "shock". The heart beat is feeble and rapid and the pulse at the wrist may be imperceptible.

The blood pressure is very low, with a systolic pressure of 80 millimetres or less, sometimes 70, 60 or unobtainable. The tongue is dry, and there may be an acetone odour on the breath. The temperature is variable, sometimes subnormal, sometimes very high, especially if the patient is in extremis.

Treatment must be instituted at once. The patient is not moved about. He is covered with blankets to conserve body heat. Venous blood is obtained for determination of its content of chloride, glucose, urea, and perhaps sodium and potassium. Through the same needle, physiological saline solution containing 10 per cent glucose is administered, and to this is added twenty to forty cubic centimetres of the most potent adrenal cortex extract obtainable. The intravenous solution is given very slowly to give the body time to absorb the fluid, salt and glucose it so badly needs. During the first twenty-four hours from four to six litres of ten per cent glucose in saline solution may be given, and from forty to one hundred cubic centimetres of the adrenal cortex extract is given intramuscularly or intravenously. The patient is apt to show prompt response to this therapy, regaining consciousness, and he may be able to take food and water.

It may be necessary to continue this emergency treatment for days, however, if the patient relapses whenever the intravenous salt and the hormone therapy is interrupted or decreased. It is probably of value to start the patient on intramuscular injections of desoxycorticosterone acetate ten to fifty milligrams daily during this period. This new synthetic adrenal cortex hormone is capable of maintaining patients with chronic adrenal insufficiency in fairly good health. Its usefulness in crisis is uncertain. Apparently it is absorbed rather slowly from its oily solvent and takes several days to produce a notable effect. It would seem best therefore to rely in crisis upon adrenal cortex hormone, salt, glucose and adequate water, but to start the synthetic material at once so that the patient may have any advantages it offers; and treatment may be continued with it should he recover from the crisis.

Maintenance Treatment

One cannot predict how long the intensive crisis treatment may be necessary. As the patient's strength improves he is given water by mouth, then a light diet, and one-gram enteric-coated sodium

chloride tablets, ten or twelve daily. When food, salt and water intake by mouth becomes sufficient, intravenous therapy is stopped. Maintenance therapy is instituted at a level arrived at by gradually tapering off to it from the intensive crisis treatment. If the patient's strength remains good, the blood pressure rises to 100 or above, vomiting and diarrhoea stop, and he is able to take food and fluids by mouth, the adrenal cortex hormone is dropped gradually from forty to thirty, then twenty, ten, five cubic centimetres or even less daily. Sodium chloride by mouth is usually contained in doses of four to twelve grams in tablets, and a maximum amount of salt is used in a shaker on the food (usually three to six grams daily). Sodium citrate, five grams twice daily, in orange juice, helps in getting in additional sodium.

The maintenance doses finally arrived at vary a great deal between patients. Some patients with the milder forms of the disease may be maintained in fairly good health upon a high salt intake without hormone therapy. Restriction of the potassium in the diet is sometimes of distinct value, especially when large doses of salt cannot be tolerated, or when the adrenal cortex extract is not used or is only used in small doses. Miss Fisher, in her accompanying article, discusses more fully the low potassium diet. The treatment of the patient recovered from the crisis becomes that employed in the chronic form of the disease.

Patients with chronic adrenal insufficiency may occasionally be maintained upon a high salt and low potassium diet alone, but optimum strength and weight gain and a normal blood pressure are seldom obtained without the use of adrenal cortical extracts or the synthetic hormone, desoxycorticosterone. Unfortunately adrenal cortex hormone is largely destroyed in its passage through the intestinal tract, and oral treatment is not practical because of the very large amounts of hormone which must be given. Intravenous hormone injection exerts only a transient effect and is used only in crisis. Daily subcutaneous doses of five to twenty cubic centimetres of potent extract are usually sufficient for maintenance. Smaller doses of the expensive extract are sufficient if sodium chloride intake is high. Diets very low in potassium are seldom necessary in patients treated with salt and hormone. A high potassium intake is detrimental, and should be avoided.

Desoxycorticosterone acetate in sesame oil, five to twenty-five milligrams intramuscularly per day, seems to act in general like the glandular extracts and will keep patients with true Addison's disease in relatively good condition for many months. Overdosage with the synthetic material, especially when salt is being given, may cause oedema and higher than normal blood pressure. The synthetic hormone has been used for only a year and much remains to be learned about it.

Implantation of hard sterile pellets of desoxycorticosterone acetate subcutaneously in the sub-scapular region has been shown to be a practical way to allow the patient to absorb small amounts of the hormone constantly without the necessity of repeated injections. Such pellets will remain in place, slowly becoming smaller



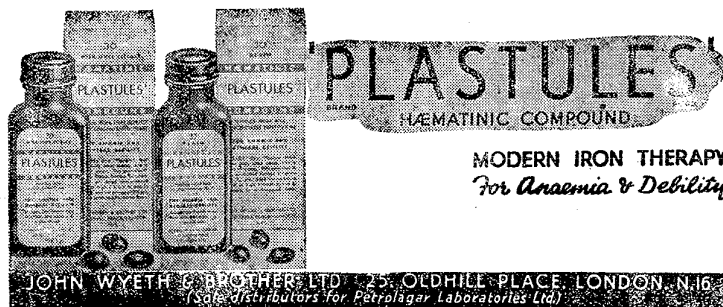
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in size, and may furnish enough hormone to last a year or more when four to seven such pellets are used.

With adequate doses of the natural or synthetic hormone supplemented by a high salt intake the patients we are now treating who have chronic Addison's disease are looking and feeling better than such patients ever have before. Fewer patients are dying in crisis. One of our patients works as a railroad car inspector; another as a busy housewife and mother of two; another is an active helper on the farm. All three were in crisis during the past year when first seen. Patients must be taught to take their salt and hormone as religiously as a well trained diabetic takes his diet and insulin. The patient should be taught to recognise the danger signs of increasing weakness, vomiting, and diarrhoea, just as the diabetic is taught the symptoms warning of hypoglycaemia or impending coma. Physicians now have a greater responsibility to patients with adrenal insufficiency since more can be done for them today than ever before. Nurses, because of their longer contact with patients, may detect the signs which will determine the course treatment shall take. Alert observation and attention to the details of treatment and nursing care are of paramount importance.

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2. Desoxycorticosterone in Addison's Disease

By MR. EDGAR S. GORDON, M.D.

Since the preponderance of evidence at present points to some other substance or group of substances as the true adrenal cortical hormone, it is important to determine in which direction these investigations are leaning. Corticosterone still remains a possibility, in spite of its relatively low potency in certain respects in the hands of some investigators. The "cortin fraction" of Kendall, which has not been crystallised, is extremely potent in most of the measurable functions of the adrenal cortex. Furthermore, Grollman has announced the preparation of a new compound from the cortex, which has a higher potency than any heretofore obtained. Little about its chemistry has been reported to date. Until these matters have been settled, the entire question of the adrenal cortical hormone will be in an unsatisfactory and unsettled state. The known complications which may arise from the clinical use of desoxycorticosterone make its application to therapy a procedure involving some risk, except in the hands of clinicians provided with adequate facilities for identifying and controlling any difficult situations which may arise. Until many details of its action are more thoroughly understood, its use should probably be restricted.

*From the Council on Pharmacy and Chemistry Report,
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