ADRENAL GLAND.*

By S. LEVY SIMPSON, M.A., M.D., M.R.C.P.

(Physician to Willesden General Hospital; Asst. Physician, Princess Louise Kensington Hospital for Children; Research Worker, Dept. of Endocrinology, Lister Institute.)

Addison's disease is due to insufficiency of the hormone produced by the cortex of the adrenal gland, although the medulla may play a minor part. In seventy-five per cent. of the cases the lesion is tubercular and it is not infrequent to have a previous history or a family history of tubercular adenitis, or abdominal tuberculosis, etc. Some twenty per cent. of cases are due to an idiopathic atrophy, sometimes following acute infection, and comparable to acute yellow atrophy of the liver. Other rare causes are syphilis and secondary neoplasm. Myxoedema, hyperthyroidism, or diabetes mellitus are occasionally associated.

Some fifty symptoms and signs are described. The major ones are wasting, weakness, pigmentation and low blood pressure. The latter may, however, be late in developing. An interesting group of minor symptoms, of diagnostic importance, is yawning, conjunctivitis, photophobia and hiccups. Other causes of pigmentation are pernicious anæmia, exophthalmic goitre, chronic arsenic poisoning, idiopathic steatorrhœa, carcinomatosis, pregnancy, hæmochromatosis, pellagra, acanthosis nigricans, familial, racial, argyria, and Simmonds' cachexia. Pigment inside the mouth occurs only in Addison's disease and in some families where negro blood has crept in, perhaps many generations ago. Simmonds' pituitary cachexia differs from Addison's disease in the absence or slowness of the pigmentation, in the marked lowering of the basal metabolic rate even in the chronic phase of the disease, in the early atrophy of, or failure to develop the sex organs and secondary sex characteristics, and sometimes in the slowness of the pulse.

The pigment in Addison's disease is an increase of the normal melanin. Bloch thinks that if tyrosine is not converted to adrenaline by the diseased adrenal it changes into melanin. Heudorfer, however, believes that the pigment is a compensatory increase and functions as the chromaffine cells of the adrenal.

The low blood sugar of Addison's disease is associated with a decrease in the liver and muscle glycogen, due to a deficiency of cortin. The latter, however, cannot prevent insulin hypoglycæmia. The impaired carbohydrate metabolism is an important factor in the inability to withstand cold. All the features of Addison's disease can now be produced in the adrenalectomised animal maintained on an inadequate dose of cortin. The raised blood urea is partly due to a concentration of blood, and to some functional interference with the kidneys, but actual degeneration of the kidney tubules can occur.

The rational treatment of Addison's disease is cortical extract. Some patients may maintain health on 5 ccs. daily, intramuscularly, or less, but for the very severe cases a daily dose of 30 ccs. makes the treatment impracticable. In crisis intravenous saline and glucose and large doses of cortin are necessary. Salt is of definite value in treatment, but the degree of improvement obtained in this way is not comparable to that produced by cortin; its chief value is to permit

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the use of a smaller dose of cortin. The rationale of salt is the fact that the blood sodium is low and its excretion high, producing a negative balance. It should be given in large doses by mouth, twelve grams a day, and the phosphate, bicarbonate and citrate can be mixed with the chloride. Adrenaline is of slight therapeutic value.

Cortin has been advocated for a large number of conditions in which the function of the adrenal is thought to be temporarily depressed. In our experience it is of some value in dehydration of infants, and where the vomiting of pregnancy is associated with asthenia and pigmentation.

Tumours of the adrenal cortex (or hyperplasia) produce the characteristic adreno-genital syndrome with amenorrhoea, hirsuties, and perhaps enlargement of the clitoris. All the features of Cushing's basophil syndrome may be present and pathologically, secondary basophilia or hyalinisation of the basophil cells may be found. The urine may contain an excess of "male" comb growth and prostate stimulating hormone. Histologically identical cortical tumours in the male, however, produce impotence and feminisation with an excess of oestrin in the urine. Testicular and ovarian hormones are very similar chemically. Although adrenal cortical tumours sometimes cause pseudohermaphroditism, true hermaphroditism and many types of pseudohermaphroditism are probably determined by genetic factors. Precocious puberty occurs with adrenal cortical tumours, but is also caused by pineal tumours, ovarian tumours, and occasionally by pituitary tumours and small tumours in the region of the tuber cinereum. In spite of the close connection between the adrenal cortex and sex, there has been no convincing evidence of an effect of cortical extract on the sex organs of animals, although such extracts contain the life-maintaining factors.

Tumours of the medulla are of two kinds. The paragangliomata (also called phæochromocytoma) consist of chromaffine cells and secrete adrenaline. They produce hypertension and vaso-motor crises, with nausea, pallor, acrocyanosis, palpitation, tremors and glycosuria. The ganglioneuromata or sympathoplastomata produce no endocrine symptoms, but are very malignant and metastases occur early. The orbit metastasis in the child was described first by Robert Hutchison and simulates chloroma.

Denervation of the adrenals has been advocated by Crile for neuro-circulatory asthenia, hypertension, hyperthyroidism and gastric ulcer. Marine holds the view that the adrenal cortex inhibits the thyroid. Lymphoid hyperplasia is common to Addison's disease and Grave's disease.