Papers and Originals

EIGHTY-SIX CASES OF ADDISON'S DISEASE*

BY

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[With Special Plate]

Hypoadrenalism is a not uncommon condition nowadays: a defective function of the adrenals occurs as the result of hypopituitarism—a greater or less degree of which condition is more common than used to be supposed, and becoming more so as the result of the activity of the neurosurgeons in this sphere; adrenocortical activity, of course, ceases completely after bilateral adrenalectomy—an operation unknown till comparatively recent years, but now increasingly undertaken for Cushing's syndrome, metastatic mammary cancer, and even, occasionally, for hypertension; lastly, defective function for a variable and unknown period always follows long-continued corticosteroid therapy and constitutes one of the great problems of modern medicine. A knowledge of the diagnosis and management of hypoadrenalism is thus of importance nowadays, and creates one of the many new burdens which modern doctors have to assume and of which we were comparatively free in my young days.

It is not, however, of these types of hypoadrenalism which I wish to discuss here, but of the disorder first described so beautifully by Thomas Addison in 1855—a state of chronic adrenal insufficiency resulting from primary disease of the adrenals due to tuberculosis or idiopathic atrophy (possibly the result of an autoimmunizing reaction similar to Hashimoto's goitre); occasionally to infarction and malignant disease; and very rarely to syphilis, the reticuloses, and giant-cell granuloma. Since 1928 I have personally looked after 86 cases of Addison's disease, and hoped that an account of the experience so acquired might be of some interest, if only from a historical point of view.

Pathology

During 1928 to 1938 I saw 34 cases, but, though all these patients died, I was able to secure necropsies on only 24 of them (Table I). In 19 (79%) of these the disease had resulted from tuberculosis—a higher tuberculous incidence than in other published series. For example, Guttman (1930), reviewing 333 necropsies on patients with Addison's disease conducted in different centres between 1900 and 1930, reported a tuberculous aetiology in 68%, atrophy in 20, and other causes in 12; while Thorn *et al.* (1942), reviewing 64 necropsies on his own Addisonian patients between 1936 and 1942, recorded a tuberculous aetiology in only 22% of them. Edinburgh in those days, besides having a high incidence of pulmonary tuberculosis, was the home of extrapulmonary—usually bovine—tuberculosis due to our execrable dairy arrangements. I think that some of the cream on the top of the milk we drank was often composed of tuberculous pus, and in consequence tuberculous cervical adenopathy, bone and joint disease, and abdominal tuberculosis of all kinds were very common. I wonder how many of the younger members of my audience have ever seen even one case of ascites due to tuberculous peritonitis, which was a commonplace in the wards in my young days. This doubtless explains the high incidence of tuberculosis as a cause of Addison's disease in my series in comparison with the incidence of atrophy.

Table I.—*Findings in Necropsies on Patients with Addison's Disease*

	1928–38	1938–58
Tuberculosis	19 (79%)	14 (61%)
Atrophy	4	7
Infarction	1	—
Carcinomatous	—	2
	24	23

The ratio showed some diminution in the next 20 years, and, as anti-tuberculosis chemotherapy and a clean milk supply have become effective, we are seeing fewer cases. Thus I had 34 new cases during 1928 to 1938, 30 during 1938 to 1948, 18 during 1948 to 1958, and only four in the last four years. During the last 10 years we have had only one necropsy, as only one patient has died. One patient, who is still alive, had a strongly positive Wassermann reaction, but we have no means of telling whether or not his Addison's disease was due to syphilis.

Destruction of the adrenals by tuberculosis is usually complete. In one type almost the entire gland is converted into a necrotic caseating mass surrounded by a thick fibrous capsule; on careful search of serial sections remnants of adrenal cortical tissue may sometimes be found. In another type a predominantly proliferative lesion is present with many fibroblasts and connective-tissue cells, many tubercles, and only small areas of necrosis. Calcification occurs in this as in other tuberculous lesions.

In the atrophic cases the adrenals are sometimes completely absent. Occasionally small remnants of the cortex may be found and the medulla may or may not be preserved. One of our patients, who at necropsy was found to have atrophic adrenals, gave a convincing history that one of his brothers had died of Addison's disease. There are in the literature six accounts of this rare condition occurring in two or more members of a family (Neumann, 1916; Fahr and Reiche, 1919; Moehlig, 1947; Briggs *et al.*, 1951; Brøchner-Mortensen, 1956; Morse *et al.*, 1961), including Brøchner-Mortensen's remarkable report of four cases in two generations. When necropsies had been performed the disease was invariably found in these familial cases to have been due to atrophy of the adrenals and not to tuberculosis. Anderson *et al.* (1957) found complement-fixing antibodies to adrenal tissue in three patients with Addison's disease, and the concept that Addison's disease due to atrophic adrenals may be of autoimmune origin has recently been further supported by Blizzard *et al.* (1962), who demonstrated by the direct Coon technique circulating adrenal antibodies in the sera of 16 out of 30 patients suffering from Addison's disease.

Clinical Features

In this series the sexes were almost equally represented. The age incidence varied from 14 to 70 years, but Addison's disease is rare at the extremes of life and 80% of my patients were between 20 and 50 years old when first seen.

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In preparation for this lecture I have reviewed my old case records in an attempt to give a composite picture of the clinical features of Addison's disease. It was a disappointing experience—not uncommon with retrospective analyses of old case-sheets—as essential facts are often missing from the records, which goes to show that investigations need to be planned in advance if all important questions are to be answered. In addition, of course, our knowledge of adrenocortical function has increased enormously in recent years, and the earlier cases were not investigated as they are now.

Whatever the presenting symptom a feeling of tiredness and weakness was a feature of the history in every case (Table II), but these are very non-specific symptoms. The only other constant feature was loss of weight: where information was available regarding the patient's previous weight—which was not always the case—the loss was found to vary from 2 to as much as 15 kg. Some degree of

TABLE II.—*Incidence of Common Signs and Symptoms in 86 Cases*

	Insufficient Information	No. of Cases
Tiredness and weakness	—	86/86 (100%)
Loss of weight	24	62/62 (100%)
Skin pigmentation	—	80/86 (97%)
Systolic B.P. below 110 mm.	—	78/86 (91%)
Gastro-intestinal symptoms	10	66/76 (87%)
Early morning hypoglycaemia	30	40/56 (72%)
Buccal pigmentation	—	61/86 (71%)
Reactive hypoglycaemia	39	20/47 (43%)

pigmentation of the skin was almost invariable, though it must be confessed that in six of the patients this was either not present or so slight as to be diagnostically valueless. No other single feature is as useful diagnostically as pigmentation, to which further reference is made below, but the blood-pressure is usually of considerable aid. The highest systolic pressure recorded in an untreated patient—actually a few days only before he went into Addisonian crisis—was 132 mm. Doubtless he had been hypertensive before the onset of hypoadrenalism. Seven others had systolic pressures before treatment varying from 110 to 120 mm., but all the rest (91%) had pressures below 110 mm.—usually much below. A systolic pressure of over 110 mm. in an untreated patient is therefore strong but not absolute evidence against a diagnosis of Addison's disease.

Anorexia, nausea, and constipation were very common features which, in association with the loss of weight, had often raised the suspicion of gastric carcinoma. Abdominal pain and vomiting were symptoms of ominous significance as they usually heralded the onset of Addisonian crisis—the pain being very similar to the pseudo-peritonitis which so often accompanies diabetic ketoacidosis, and may result in some unexplained way from the dehydration and sodium depletion or the intestinal ileus common to both conditions. We knew nothing about the characteristic hypoglycaemia of Addison's disease in the early days, but since we became aware of it we have found that most of our patients untreated by cortisone are hypoglycaemic in the early morning, being difficult to rouse from sleep, and their attitude towards those who make the attempt being surly and resentful. I do not suggest, of course, that such behaviour is confined to Addisonian patients. It has been our experience that buccal pigmentation occurs only in patients whose skin is deeply pigmented and not in the less typical cases where its presence would be so diagnostically helpful. The 43% of patients in whom the information was available reacted to the unopposed insulin which they secreted in response to a meal rich in carbohydrate, so that an hour to two hours after taking such food they tended to become sleepy, to feel weak and faint, or to behave in the uninhibited manner of the mildly intoxicated.

Pigmentation

The typical brown pigmentation of the skin in Addison's disease results from an increased deposition of melanin in the deeper layers of the dermis. It is due to the melanophore hormone which is secreted along with corticotrophin when the latter is poured out by the anterior pituitary in a vain attempt to flog the dead horse of the adrenal cortex into renewed activity. A similar pigmentation was often induced in the days when corticotrophin was less effectively purified than it is now and when it was used in the prolonged treatment of certain conditions. Thus pigmentation does not occur in the hypoadrenalism resulting from hypopituitarism but does occur if bilateral complete adrenalectomy is performed for Cushing's disease when the syndrome has been due to a basophil adenoma of the pituitary. The basophil adenoma then tends to expand in spite of adequate corticosteroid replacement therapy, and to secrete an excess of corticotrophin and its melanophore contaminant with resulting deep pigmentation of the skin. Fig. 1 (Special Plate) is an example of such a condition.

The colour of the skin in Addison's disease varies from a not unattractive slight bronzing reminiscent of the olive, sun-kissed skin of the Mediterranean people to a deep almost negroid hue. The diagnosis of the condition must be more difficult in many parts of the world than it is in Scotland, where we so rarely have to consider physiological causes of pigmentation of the skin: it must be very difficult on purely clinical grounds, for instance, in an asthenic hypotensive Indian.

In the typical case the pigmentation is most conspicuous on the exposed parts, like the face, neck, and hands. On the dorsum of the hand it is most marked over the knuckles, and on the palms is usually limited to the creases of the skin, especially those over the interphalangeal joints. The nails assume a copper colour. The pigmentation is usually conspicuous on the nipples—like that which occurs in pregnancy—in the axillae and perineum, and on areas subjected to pressure, such as the elbows, knees, and spine. Fig. 2 (Special Plate) shows the pigmentation over the vertebrae and elbows of a young girl who had been in bed for a long time suffering from pulmonary tuberculosis as well as Addison's disease. Shortly after the picture was taken she developed contemporaneously tuberculous meningitis and Addisonian crisis. She was fortunate in that both streptomycin and cortisone had just become available, and she was rescued from two conditions each of which a short while previously had been invariably fatal. We were not then experienced in the use of cortisone, and undoubtedly overtreated her. Fig. 3 (Special Plate) shows that in consequence the pigment of hypoadrenalism largely disappeared, as the excessive secretion of corticotrophin and its accompanying melanophore contaminant had been inhibited, to be replaced by the striations characteristic of hypercorticism. I am glad to say she is now happily married and has two children.

Pigmentation of the buccal mucous membrane if not pathognomonic of Addison's disease is nearly so—I have seen it in only four patients who had not got the disease. It is blue-black in colour, rather like that seen on the gums of a black spaniel, best seen on the inner surface of the lip and cheek, on the gums and hard palate, but may be confined to the tongue. The pigmentation in Addison's

disease is characteristically patchy rather than uniform and occasionally alternates with leucodermic patterns, giving a very odd appearance (Special Plate, Fig. 4). After some months of adequate replacement therapy Addisonian pigmentation tends to fade.

A radiological examination should always be made. In a suspected case the demonstration of calcification of the adrenals gives unequivocal proof of the diagnosis of Addison's disease and usually of its tuberculous aetiology. Such calcification was noted in 53% of the present series owing to its unusually high tuberculous incidence. A negative *x*-ray examination does not, of course, exclude the diagnosis of Addison's disease nor even of its tuberculous aetiology. Radiological calcification in the adrenals is occasionally seen as a chance finding in patients with no other clinical or laboratory evidence of defective adrenal function—due to a partial infarction of the gland that has calcified, which sometimes occurs at birth, or to a calcified tuberculosis of one gland while the other continues to function normally.

Laboratory Tests

In 75% of my patients the clinical diagnosis presented no difficulty, and laboratory tests to confirm it were really superfluous. A quarter of the patients, however, presented a more difficult diagnostic problem, as they did not conform in all respects to the classical clinical pattern. Further, we are now anxious to diagnose adrenocortical insufficiency before it has advanced to the stage of complete failure which Addison's disease implies. There are doubtless a considerable number of cases in which destruction or atrophy of the cortex may be incomplete so that some degree of adrenocortical secretion may continue without, however, allowing for any reserve to meet the stresses of everyday life. Obviously a patient does not have normal adrenal function one day and Addison's disease the next. The accurate recognition of atypical cases of Addison's disease and of milder degrees of adrenocortical hypofunction is impossible without laboratory tests. The investigations available for estimation of adrenocortical function fall into two groups: indirect methods in which the metabolic consequences of the defective hormonal secretion are assessed; and direct methods depending on the measurement of hormone production.

Indirect Methods

Estimation of the level of sodium and chloride in the serum is a simple procedure, but, just as in chronic renal deficiency the concentration of the urea in the blood remains normal till an advanced stage of renal failure, so in hypoadrenalism the concentration of sodium in the serum is normal until the approach of adrenal crisis. Thus normal figures are often found in untreated Addison's disease, but low values are of serious significance. Such low values acquire greater diagnostic importance when they are associated with a normal or high excretion of sodium chloride in the urine.

When the question of hypoadrenalism is raised two quick screening methods are of value:

(1) If in an adult the excretion of 17-ketosteroids in the 24 hours is above 4 mg. the likelihood of severe hypoadrenalism is small; but the test is specific only in the negative sense, as the urinary output of 17-ketosteroids may be reduced in many debilitating conditions. Accurate estimations of the 17-ketosteroids have been available in our laboratory only during the last 14 years. During that time we have had 21 new cases of Addison's disease: only one of them has had a concentration of 17-ketosteroids in the 24 hours of above 4 mg. (5.8 mg.). An excretion above 4 mg. is therefore strong evidence against a diagnosis of Addison's disease, though it is compatible with lesser degrees of adrenal failure.

(2) The prompt and copious diuresis which normally follows the administration of a large quantity of fluid depends on a number of factors, including an adequate supply of adrenocortical hormones. Thus one of the most simple and reliable screening tests—though again non-specific—for adrenocortical insufficiency is the intravenous water-tolerance test carried out as follows: the patient fasts, taking neither solids nor fluids from 10 p.m. the previous night; at 8 a.m. the bladder is emptied as completely as possible; an intravenous infusion of 1,000 ml. of 5% glucose solution is then completed in 20 minutes and the bladder is again emptied; for four hours thereafter collections of urine are obtained every 20 minutes, care being taken to empty the bladder completely on each occasion. In health a total of at least 750 ml. should be secreted during the four-hour period following the infusion, and at some stage the flow of urine should exceed 3 ml. a minute. This has never occurred in the 14 cases of untreated Addison's disease in which we have carried out the test: in them the response to administration of fluid tends to be paradoxical—the volume of urine secreted during the night exceeding that passed during the day. The response can be restored to normal by the administration of cortisone. Nevertheless patients with milder degrees of hypoadrenalism may be able to deal with the water load normally.

The insulin-sensitivity test, which is a measure of the effect of the adrenal cortex on carbohydrate metabolism is valuable but may be upsetting to the patient and even dangerous if means are not immediately available to correct the alarming hypoglycaemia which may result from the intravenous injection of not more than 2 units of insulin in patients suffering from severe hypoadrenalism from any cause. In such cases a reactive hypoglycaemia usually becomes obvious following an ordinary glucose-tolerance test: some degree of hypoglycaemia occurs within two hours of the test dose of glucose being given and the return of the blood-glucose level to normal is delayed, indicating a deficiency of the glucocorticoids which normally counter any tendency to hypoglycaemia in such circumstances. As in the water-tolerance test these hypoglycaemic responses can be restored to normal by the administration of cortisone.

Direct Methods

The best direct assessment of adrenocortical function is the measurement of the 17-ketogenic steroid excretion, which in normal adults varies from 6 to 20 mg. in the 24 hours. The test has been performed only in the last five of my patients with Addison's disease and has always been below 6 mg. Nevertheless, in milder cases of hypoadrenalism the excretion may be in the lower part of the normal range and the diagnosis must eventually depend on the development of a suitable stimulation test of the adrenal reserve.

Urine should be collected for two or three 24-hour periods. Corticotrophin gel, 50 mg., is then injected intramuscularly twice a day for three days, and while this is given 24-hour urine collections are made. The average excretion of 17-ketogenic steroids during the control period is compared with the average excretion following stimulation, and in health the latter should exceed the former by at least three times. The response of the 17-ketosteroid excretion is less, especially in debilitated patients, and is hardly worth estimating.

The three patients with well-marked Addison's disease whom I have subjected to this test have shown no response. We have had inadequate experience of it as a test of lesser degrees of hypoadrenalism to enable us to dogmatize on what is a normal or subnormal response, but standards for this will doubtless emerge. For some years the standardiza-

tion of corticotrophin was unsatisfactory and it did not give very reliable results. Even now one has the impression that its potency is apt to deteriorate if kept much longer than six months. It may be that the amphenone-like compound metyrapone ("metopirone"), developed by Liddle *et al.* (1959) as a test of pituitary corticotrophin reserve and recently tested clinically by Brownie and Sprunt (1962), will prove of considerable value as a test of adrenal function, since it depends on a functioning adrenal cortex.

Treatment

Addison's disease is characterized by excessive loss of sodium chloride and water in the urine and retention of potassium due to deficient secretion of sodium-retaining hormones; as a result haemoconcentration, dehydration, and hypotension occur. The lack of glucocorticoid (hydrocortisone) secretion causes impairment of carbohydrate metabolism and a marked tendency to hypoglycaemia, together with an increased sensitivity to noxious stresses of all kinds. Treatment depends on redressing these disturbances by suitable mineralocorticoid and glucocorticoid replacement therapy.

For maintenance purposes the dose of cortisone, which for replacement therapy is very preferable to its modern analogues, varies from 25 to 37.5 mg. (1 to 1½ tablets) a day. Replacement doses of this order never give rise to the undesirable side-effects of hypercorticism, but, on the other hand, are usually insufficient to restore completely the sodium depletion of Addison's disease and to maintain the body fluids and blood-pressure at a normal level. The administration of larger doses of cortisone or the addition to the diet of 10 g. of extra sodium chloride a day will have this effect, but the supplementary use of a steroid with a greater sodium-retaining action than cortisone is preferable.

For many years the sodium-retaining steroid employed was the synthetic deoxycortone acetate (D.C.A.), which was indeed the sole treatment available before the introduction of cortisone. It could be given dissolved in ethyloleate by intramuscular injection, or, more economically and conveniently, by implantation of 200 to 300 mg. in the form of pellets into the abdominal wall. The effect of D.C.A. thus implanted was maintained for periods of time varying from five to ten months. Recently fludrocortisone, which has a sodium-retaining activity approaching that of aldosterone but only a weak glucocorticoid effect, has largely replaced D.C.A. It has the great advantage that, like cortisone, it is active when given orally, and for most patients the ideal treatment now seems to be the combination of 25 to 37.5 mg. of cortisone with 0.1 to 0.2 mg. of fludrocortisone daily.

It must always be remembered that maintenance treatment, quite satisfactory for ordinary purposes, may prove entirely inadequate at times of stress. Infections or intercurrent illnesses, traumata, and the administration of drugs such as morphine or anaesthetics—to which such patients are notoriously intolerant—may precipitate Addisonian crisis unless the protective replacement therapy is appropriately increased. Patients and their doctors should also be warned to have a supply of cortisone acetate and D.C.A. for injection, which should be substituted immediately for oral cortisone and fludrocortisone whenever a patient is unable from any cause to take and to retain medicines given orally.

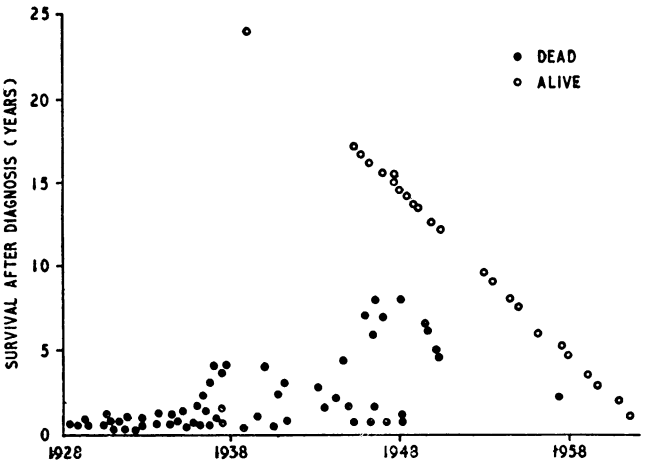
Addisonian crisis is a medical emergency which demands the most energetic treatment in hospital, where the patient can be given constant skilled nursing and medical care. The general measures employed for the treatment of shock should be initiated. Three to four litres of 5% glucose in normal saline should be infused in the course of 24 hours, at first rapidly and then, as improvement occurs, more slowly. Hydrocortisone hemisuccinate 100 mg. is added initially to the intravenous infusion, and thereafter, according to the state of the patient, from 50 to 75 mg. every six hours. This treatment should be supplemented by intramuscular injections of 10 mg. of D.C.A. twice in the first 24 hours. As the crisis is often precipitated by an infection it may be necessary to employ appropriate antibiotic therapy.

Prognosis

The story of the prognosis in Addison's disease falls into easily defined eras, dating from those landmarks in its history when each new therapeutic measure was introduced.

The first era, from the time in 1855 when Thomas Addison first described the disease until 1930, was a long period when attempts at treatment were all in vain, and the great majority of sufferers died within a year or at most two of the diagnosis of their malady.

In 1930 a cortical extract prepared by Swingle and Pfiffner was introduced for the first time and found to be of some value in the management of Addisonian crisis. With the emphasis which Loeb placed on the value of salt in maintenance treatment, this era can be called that of salt and cortical extract. However, between 1928 and 1938 (see Diagram) these measures did not greatly improve



the outlook, and 29 of my 34 patients died within two years of diagnosis, and only five lived for from two to five years.

The third era is that of D.C.A., which was synthesized by Reichstein in 1937 and first became available to us in 1939. The change in prognosis compared with the previous period is fairly obvious and several patients survived from that era and are alive to-day, including one who has lived with her Addison's disease for nearly a quarter of a century since its diagnosis. Nevertheless, the lives of the patients in the D.C.A. era were still very precarious. D.C.A. only corrected their disturbed mineral metabolism and did nothing to improve their hypoglycaemic state or to protect them from stress; in consequence there was still a high mortality. The fourth era, of course, started about 1948 when cortisone became available in very small supply, and this era may be called the cortisone–D.C.A. and ultimately the cortisone–fludrocortisone era. Since the supply of cortisone became adequate we have had only one death among our patients, in a woman who developed bronchopneumonia in the country a long way from Edinburgh and

whose doctor did nothing to supplement her maintenance treatment in order to help her meet the crisis. There are 24 surviving patients, and they are now in positively good health in contrast to their state of semi-invalidism in the preceding era. Many of them do hard labouring work without difficulty, and indeed were I faced as a young man with choosing whether I would rather have Addison's disease or diabetes I think I would choose the former. Its treatment is simpler than that of diabetes; with care the expectation of life should not be shortened, and so far as we know there are no Addisonian complications comparable to those of diabetes. There are few other conditions which illustrate more completely the triumphs of modern chemotherapy.

References

Anderson, J. R., Goudie, R. B., Gray, K. G., and Timbury, G. C. (1957). *Lancet*, **1**, 1123.
Blizzard, R. M., Chandler, R. W., Kyle, M. A., and Hung, W. (1962). Ibid., **2**, 901.
Briggs, J. N., Goodwin, J. F., and Wilson, A. (1951). *Brit. med. J.*, **1**, 115.
Brøchner-Mortensen, K. (1956). *Acta med. scand.*, **46**, 205.
Brownie, A. C., and Sprunt, J. G. (1962). *Lancet*, **1**, 773.
Fahr, T., and Reiche, F. (1919). *Frankfurt. Z. Path.*, **22**, 231.
Guttman, P. H. (1930). *Arch. Path.*, **10**, 742.
Liddle, G. W., Estep, H. L., Kendall, J. W., Williams, W. C., and Townes, A. W. (1959). *J. clin. Endocr.*, **19**, 875.
Moehlig, R. C. (1947). Ibid., **7**, 134.
Morse, W. I., Cochrane, W. A., and Landigran, P. L. (1961). *New Engl. J. Med.*, **264**, 1021.
Neumann, J. (1916). *Münch. med. Wschr.*, **63**, 488.
Thorn, G. W., Dorrance, S. S., and Emerson, D. A. Y. (1942). *Ann. intern. Med.*, **16**, 1053.

MALIGNANT LYMPHOMA OF THE TESTIS

BY

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[With Special Plate]

Malignant lymphoma is a collective term for all tumours of lympho-reticular origin, and, although many structural variations occur, they are generically sarcomas of the pluripotential reticular stem cell. Malignant lymphoma of the testis is a neoplasm presenting chiefly in later life, usually of rapid onset and commonly progressing to a fatal conclusion by generalized dissemination, becoming indistinguishable from generalized lymphosarcomatosis.

Relatively few cases of malignant lymphoma of the testis have been recorded. Curling (1878) mentions one seen by him in 1865 and two others, including that of Malassez (1877), who gave the first full description. More recently Ennuyer *et al.* (1960) have reviewed 34 cases from the literature and added two of their own.

It is the purpose of this paper to report 35 further cases, describe the natural history of the disease, and establish its existence as a primary condition of the testis.

Source of Material.—One of us (J. P. S.) has reviewed the pathology from 665 patients with testicular tumour registered at the Christie Hospital from the beginning of 1946 to the end of 1962. Of these, 35 (5.3%) have been recognized as falling into the lympho-reticular group of diseases.

Pathology

Malignant lymphomas of the testis are rapidly growing tumours and usually are large by the time they are first seen. The largest in our series measured 13 by 10 by 8 cm.

The tunica albuginea always appears to be intact, and may be smooth or lobulated. The cut surface shows soft white or cream-coloured tumour, usually destroying the body of the testis completely and often invading the epididymis. The tumour may be diffuse or divided into lobules by fibrous septa. Necrosis and haemorrhage may occur. Two of our cases show diffuse infiltration and two others nodular masses of tumour in the spermatic cord.

Microscopically, most of these tumours are composed of polymorphic, often angular, reticulum cells (Special Plate, Fig. 1) with considerable reticulin formation, almost to the extent of surrounding individual cells (Special Plate, Fig. 2). The typical tumour spreads in sheets between widely separated atrophic testicular tubules (Special Plate, Fig. 3). Mitoses are common, and invasion of the walls of veins is often seen. In two cases the appearances were of a more lymphocytic type of tumour, and in another they were those of a plasmacytoma.

Clinical Features

In 30 of the 35 patients the presenting feature was a testicular tumour which was usually painless. Of the remainder, the maxillary antra were affected at the onset in two (Cases 1 and 2), thigh muscle in one (Case 3), a vertebra in one (Case 4), and in another the disease was generalized throughout the lymphatic system when first seen (Case 5).

The mean age of the group is 59.8 years, which compares with a mean age of 33 years for the teratomas and 42.3 years for the seminomas in our series. The age distribution of these tumour types is shown in Fig A.

The left testis was involved in sixteen cases and the right in fourteen. In five the lesions were bilateral, three apparently of simultaneous onset and two affecting the right side two and four years before the left (Cases 6 and 7).

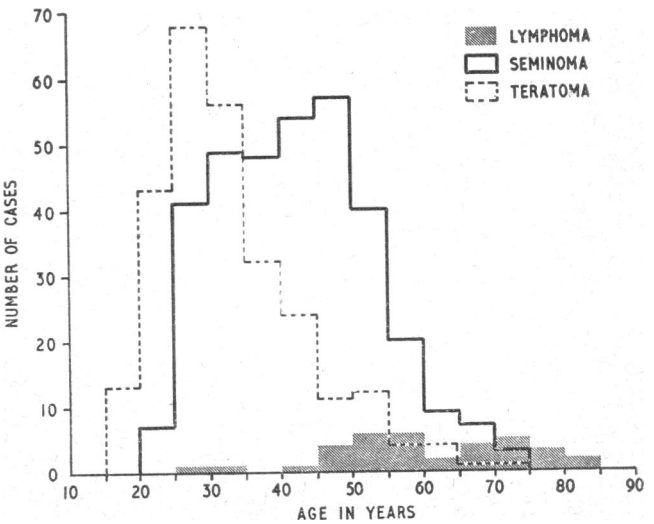

Fig. A.—Age distribution of malignant lymphoma, with seminoma and teratoma shown for comparison.

Sir DERRICK DUNLOP: 86 CASES OF ADDISON'S DISEASE

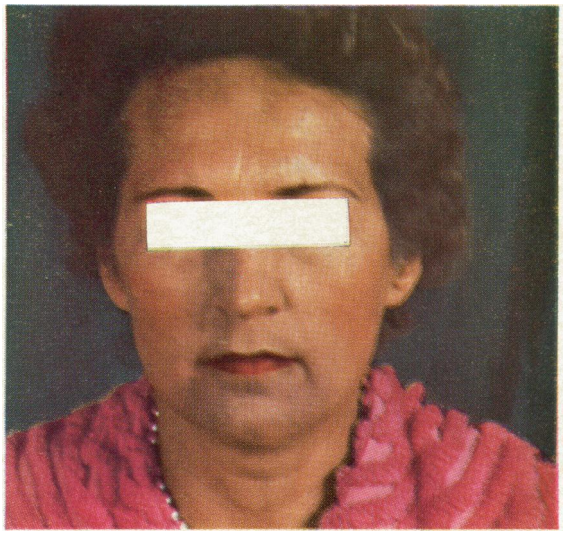

FIG. 1

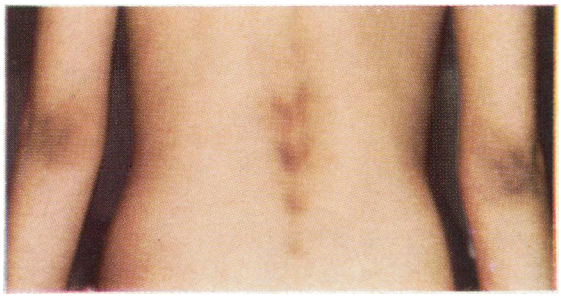

FIG. 2

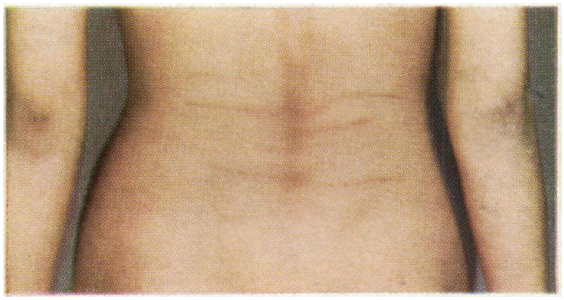

FIG. 3

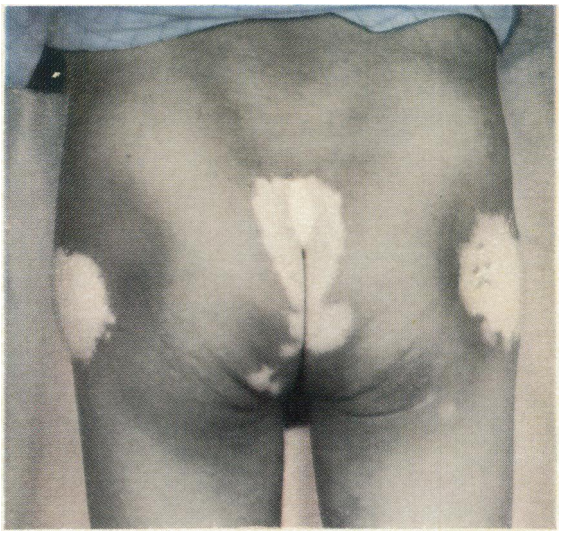

FIG. 4

H. ECKERT AND J. P. SMITH: MALIGNANT LYMPHOMA OF THE TESTIS

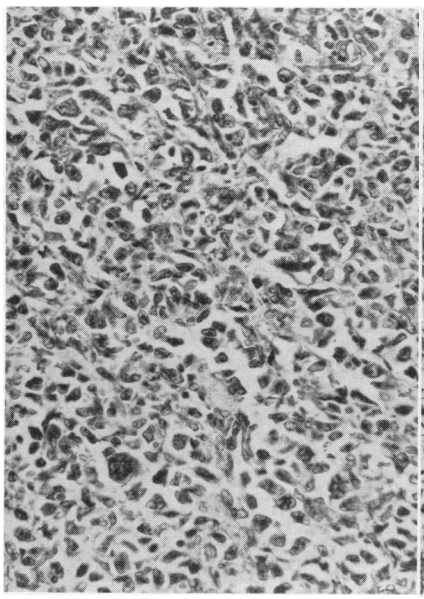

FIG. 1.—Section showing tumour composed of polymorphic angular cells. (H. and E. ×215.)

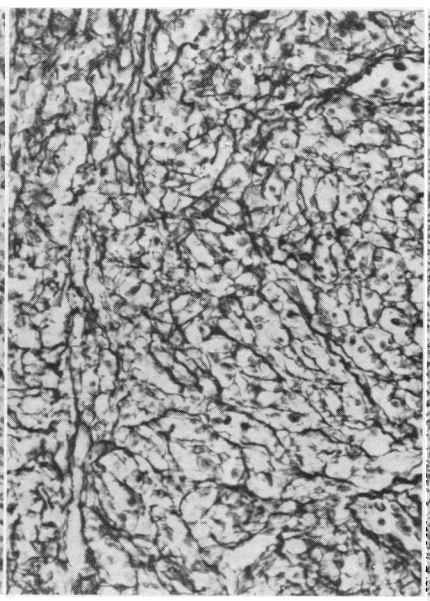

FIG. 2.—Section showing dense reticulin network. (Reticulin stain. ×215.)

FIG. 3.—Section showing diffuse infiltration of tumours amongst atrophic testicular tubules. (H. and E. ×60.)