SUCCESSFUL GRAFTING OF ADRENAL GLAND IN A CASE OF ADDISON'S DISEASE*

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The results of transplantation of adrenal tissue in numerous animal experiments do not, on the whole, encourage the use of this method in cases of adrenal insufficiency in man. Moreover, the operation on the animal is carried out under ideal conditions, whereas in man the recipient of the graft is usually extremely ill and the choice of donor is also necessarily limited. Clinical reports of unsuccessful attempts to treat Addison's disease by transplantation of the adrenals are frequent in literature, and even the few reports of successful transplantations are not above criticism.

In the first place, unmistakable proof is needed that the case is one of Addison's disease. Thus, in one case which had been apparently cured by transplantation treatment the eventual necropsy showed that the adrenals were healthy while the graft had decayed (Conybeare and Millis, 1924). Again, in view of the well-known clinical variations in the course of the disease, short periods of improvement with increased blood pressure should not be considered to be the result of transplantation therapy. Transplantation should not be looked upon as clinically successful unless there is a definite improvement extending over a period of months in a case of undoubted Addison's disease. So far as we are able to judge there are no more than five cases in the literature which fulfil this requirement. These are the cases of Reinhart (1928), Halperin and Arkuschenko (1927), Leschke (1928), Beer and Oppenheimer (1934), and Goldzieher and Barishaw (1937). The periods over which these cases were observed subsequent to operation varied from five months to one year.

We are able to add a sixth case to this list—a successful grafting in an indisputable case of Addison's disease, although an atypical one owing to the absence of pigmentation. The patient was under our observation for nearly three years before operation and for fifteen months since operation.

Case History

The patient, a woman aged 56, had undergone hysterectomy at the age of 34 on account of persistent haemorrhage due to myoma. Apart from this she had apparently been healthy, and had had two normal pregnancies. The disease for which she was eventually treated by grafting began very gradually ten years earlier, progressed slowly, and was interrupted by periods of improvement. She became languid and easily fatigued, took less interest in her environment, and became indifferent even with regard to her own health.

The physical symptoms during the course of years included intermittent intestinal disturbance accompanied by painless diarrhoea, which had been mistaken for and treated as enterocolitis. X-ray examination of the intestinal tract revealed nothing abnormal. The blood pressure, which had

not been taken before the onset of the disease, was always low—between 80 and 90 mm. Hg—and during the more severe phases it was below even this level. The disturbances of temperature were characteristic. The Egyptian winter, generally regarded as agreeably temperate, seemed to her unpleasantly cold. Her body temperature under normal conditions was low—about 97° F. taken rectally—and even during acute infectious illnesses it hardly ever rose above 100.4°. Moderate wasting became unmistakable, even in the early stages of the disease, and increased rapidly in the later stages. The patient lost 22 lb. in the course of six years, half of it in the first six months of 1935. She often suffered from nausea, though vomiting did not actually occur, and she complained of "rheumatic" pain in the musculature of the back.

Two incidents in this history were noteworthy. In June, 1935, she had severe pain in the upper abdomen, the stools assuming a whitish sheen, but there was no jaundice, and the urine on examination was normal. This condition persisted for a week, and was treated as "liver colic" by her doctor. Some months later an attack of "oppression of the heart" occurred, the pain radiating into the left arm. During both these incidents the blood pressure was found to be below 80 mm.

For a time the patient had intravenous injections of glucose, and always felt particularly well for some hours subsequently. To combat the emaciation insulin was given, but even 3 units gave rise to symptoms of overdosage—profuse sweating, tremor, dizziness, and faintness—and had to be discontinued. Such attacks, which resembled angina pectoris, were treated by withdrawal of salt, but the effect of this measure was a rapid increase of weakness, somnolence, muscular pain, and nausea, so that the patient had to return to her usual food, which contained salt at random.

During 1935 all the above symptoms became more pronounced. Malignant tumour was suggested, but examination revealed only a trophic ulcer of the vagina, which on histological examination gave no sign of malignancy.

It was at this time that we first saw the patient. Her bad general condition and cachectic fatigued appearance were noted. There was no abnormal pigmentation or distribution of hair. The blood picture was as follows: erythrocytes, 3,900,000 (later 3,400,000) per c.mm.; haemoglobin, 75% (later 68%); leucocytes, 7,500 per c.mm.—neutrophils 55%, lymphocytes 41%, eosinophils 1%, monocytes 2%, band-like polymorphs 1%. The Wassermann reaction was negative. The blood sugar was 100 to 115 (later 91) mg. per 100 c.cm. The electrocardiogram showed no marked deviation from the normal, and a radiograph of the renal area gave no indication of calcified glands.

Treatment with anterior pituitary extract over several weeks was without result. The administration of cortical extract was then started, the patient receiving daily, and later every second or third day, intravenous injections of 10 c.cm. The result was immediate and impressive: the weakness, muscular pain, and somnolence disappeared, and within two months the patient had put on 11 lb. in weight.

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For one year all went well, and it was possible to reduce the extract to 20 to 30 c.cm. a week, given intramuscularly. Then a severe crisis occurred following some days of over-exertion and domestic worry. There was nausea with frequent vomiting and fatty diarrhoeic stools, and the abdominal musculature was rigid and painful to pressure. Blood pressure dropped to 70 mm. In view of the patient's very thin veins and the collapsed circulation, intravenous administration of considerable amounts of fluid could not be undertaken. Fluids (1,200 c.cm.) with 20 grammes of salt were given daily, mostly by mouth and to a small extent rectally. The patient received daily 80 c.cm. of adrenal extract (cortin and eschatin), and with eventual improvement the amount was reduced to 70 and later to 50 c.cm. a week, given intravenously. But the former condition of comparative ease could not be regained. The patient's complexion became more yellowish, with a clay-coloured tinge, and freckle-like spots appeared on the backs of the hands and on the face; but the typical Addison pigmentation was not shown, nor was there at any time pigmentation of the mucous membrane of the mouth.

The Operation and After

This was the condition until August, 1938, when a severe Addisonian crisis occurred, due immediately to the damp heat prevailing at that time in Alexandria (86°, with 95% humidity). The amount of extract was increased to 40 c.cm. daily, but the blood pressure dropped to 70 mm.

In this crisis it was decided to graft into the patient the left adrenal gland of a man who had died just previously from a cerebral tumour. The donor was 52 years of age, and belonged to the same blood group as our patient. The graft was made in the abdominal musculature on the left side, under local anaesthesia.

[Here followed in the complete paper a detailed description of the operation.]

Soon after the operation the symptoms of adrenal insufficiency reached their climax—increased somnolence, uncontrollable vomiting, frequent diarrhoeic stools, collapse of circulation, and fall of blood pressure to 60 mm., this in spite of the fact that the daily administration of extract had been increased to 80 c.cm. and that of salt to 50 grammes. Within three days of the operation, however, the condition improved, the dose of extract was reduced, and no more was given after the seventh day, and the patient declared that she felt absolutely well. She left hospital on the sixth day after the operation. During the next two months the blood pressure varied between 115 and 135 mm., the colour of the skin became lighter, and the freckle-like spots were no longer so intensely coloured. But any great exertion or excitement always produced slight somnolence and pain in the back, and during an influenza attack, when the blood pressure was lowered to 80 mm., it was necessary to give 10 to 20 c.cm. of extract for some days.

Comment

From the results of experiments on animals it seems irrelevant to the success of the operation where the grafting takes place (ovary, testis, kidney, musculature), nor does the type of transplantation (whether the organ is cut into slices or grafted as a whole) seem to be of significance. As the operation has been shown to be more likely to succeed in some species of animals than in others, it may be that in man the conditions are exceptionally unfavourable. It has been demonstrated in a great number of animal experiments (Loeb, 1930, 1937) that transplantation in general is more successful the closer the blood relationship between donor and recipient, and in respect of the adrenal gland in particular this has been recently emphasized by several workers (Ingle and Higgins, 1938; Ingle, Higgins, and Nilson, 1938). When selecting the donor the utmost the surgeon can do is to consider the blood group.

The result of the grafting operation must be largely dependent on the bodily condition of the recipient, and in Addison's disease particularly it must not be lost sight

of that the insignificant surgical procedure of grafting endangers the patient's life. Treatment by extract before, during, and after the operation has therefore undoubtedly improved the prospects of success.

In our patient the adrenal graft is able to meet the requirements of normal life, but if the demand is above normal it fails. This cannot be due to the fact that there is only one adrenal gland fully functioning, because such symptoms of insufficiency are not met with in cases in which one adrenal gland has been removed by operation. On the contrary, there is complete accordance between our observations and those on the functional behaviour of grafted adrenals in the animal (Ingle, 1937; Perla and Gottesman, 1931a, 1931b; Wyman and tum Suden, 1937).

Summary

In a severe case of Addison's disease the adrenal gland of a patient belonging to the same blood group, who had just died, was grafted into the abdominal musculature. The functional results, as observed over a period of fifteen months after operation, are excellent. A state of compensation has been produced so long as the patient lives under normal conditions. Only after special exertion or during a transitory infection, with increased demand on the adrenal gland, are slight signs of insufficiency noted.

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TREATMENT OF 100 WAR WOUNDS AND BURNS

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During recent enemy activity over this country 100 wounded men have been under our care in a military hospital. The great majority were admitted within six hours of injury, unlike those described in previous articles on surgery in the present war (Cohen and Schulenberg, 1940; Brown, Dennison, Ross, and Divine, 1940).

Some 50 of our patients were airmen, both Allied and German. They were brought in within an hour or two of their injury. Excited, with nerves still keyed to the highest pitch, with heads still spinning from the swift rush earthwards, and with wounds bleeding freely from the battle, they formed a striking contrast to the Dunkirk soldiers with their grimy and inflamed wound holes often several days old.

These cases afforded an opportunity of carrying out modern treatment and, as some were in for several weeks, for observing their clinical progress. The preliminary anti-shock measures—warmth, morphine, hot fluids—were necessary in all except trivial cases. Some patients required either blood or plasma. When salines were indicated we often used the intramuscular route for injection in order to eliminate the risk of oedema of the lungs (Billimoria and Dunlop, 1940). The problem of assessing