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ADRENALECTOMY IN MENTAL DISORDER

BY

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Although the endocrines have been largely employed in the practice of psychiatry, on the whole little progress has yet been made towards either improving the patients by their use or elucidating a relationship between glandular disturbances and mental disorders. Moreover, few of the diseases of the endocrine glands or the operative procedures connected with their relief have thrown any definite light on the relationship between psychiatry and endocrinology. At least seven cases of amelioration of mental symptoms following unilateral adrenalectomy have been reported (Allen *et al.*, 1939; Allen and Broster, 1945; Greene, Paterson, and Pile, 1945). It would seem equally important to describe two cases with well-marked mental abnormalities associated with characteristic glandular changes which were unimproved by this operation, whilst other findings of some interest have emerged from the investigations.

Case 1

A 44-year-old single woman was admitted to hospital in December, 1945. She was in an extremely neglected bodily state, and prior to her admission she was treated by the authorities as a person wandering at large. No history was available, and she was unable to give any details of her previous life until after the operation. She was completely apathetic, dull,

retarded, and disinterested. Although she answered questions, her replies were monosyllabic and hardly relevant. During the time she was in hospital before the operation she remained apathetic, and she either did not properly appreciate her position or was completely indifferent to it. It appeared that she had some intellectual impairment and at times a mild clouding of consciousness. Her physical state approximated closely to that described by Broster as "adrenal virilism," because it seems to have arisen in adult life many years after the development of menstruation and the female secondary sexual characteristics. She was a well-built woman, muscular rather than obese. The outstanding abnormality in the secondary sex characters was that the hair growth was male in distribution. The whole of the beard area—lip, chin, lower cheeks, and pre-auricular region—was covered with long coarse hair, the pubic hair extended up to the umbilicus, the thighs were hairy to a very marked degree. The hirsuties had been noticed for three or four years. The blood pressure was not raised: 135/125/95-75. Menstruation had ceased for about two years. The history suggests that the abnormality of suprarenal cortical function did not occur until about the age of 40, so that it was not surprising to find well-developed breasts and a female relationship between the respective widths of the pelvic and pectoral girdles. Preoperatively her urinary steroids measured as androsterone were 60 mg. in 24 hours (normal 9-12 mg.). Her blood sugar (Fig. 1, curve A) showed a flat curve of the pituitary

FIG. 1.—Case 1. Blood-sugar curve before operation, A, and after operation, B.

type as found in Broster and Vines's polyglandular type 3. The blood sedimentation rate fell 8 mm. in the first hour (200 mm. Westergren column). The differential blood count, blood cholesterol, urea, and serum chlorides were within normal limits. Intravenous pyelography did not give any indication of unilateral suprarenal enlargement, and therefore laparotomy was performed in April, 1946. The right suprarenal was much larger than the left. Examination revealed a normal development of the female pelvic organs. When, two days before the adrenalectomy, she was told that she was to have an operation in order to lose all her hair growth, the only remark she made was: "Rather far-fetched to operate on the tummy to lose hair on my face." Then she sank back into her apathetic condition again.

In May, 1946, right adrenalectomy was performed by Bernard Fey's costo-abdominal approach, which gave an excellent exposure of the suprarenal. Briefly, in the Bernard Fey approach an incision is made along the upper border of the eleventh rib to the tip and continued thence towards the anterior iliac spine in the line of the fibres of the external oblique. The eleventh rib is freed subperiosteally and displaced downwards. The posterior periosteum is incised, the common origin of the diaphragm and transversalis abdominis muscle divided near the tip of the rib, and the transversalis split in the direction of its fibres. This exposes the upper pole of the kidney and leads direct to the suprarenal. Mouat (1939) wrote: "I can find no record of Fey's costo-abdominal route having been used for operations other than those on the kidney and ureter, but inspection of the surrounding structures during operation, and my experience of it in the dissecting-room, lead me to suggest that this route might with advantage be used for operations on the adrenals or for repair from below of the hiatus in diaphragmatic hernia." Since 1939 Mr. John Everidge has strongly recommended to one of us (E. J. R. S.) the use of this route for operations on the suprarenal, and whatever its role may be in renal surgery it does appear to

give an ideal approach to structures superior to the kidney on either side of the body.

The operation was performed without difficulty and the blood loss was small. The patient's pulse was of good volume and between 80 and 90 a minute until the suprarenal was handled while being freed from its surrounding structures. The rate then suddenly rose to 150-160 with extrasystoles, although it was still described by the anaesthetist as a "good" pulse. The patient did not present the picture of surgical shock in that her colour remained good; she did not become cold, and the blood-pressure reading of 125/75 was little below her pre-operative figure. The injection of desoxycorticosterone, recommended in this operation, did not affect the rapid pulse, which persisted at about 150 for eight hours, after which it fell to 80. This strange reaction in pulse rate without other signs of shock is somewhat different from the results described by Zondek (1945) and others.

She had an uneventful post-operative convalescence. Four weeks after the operation she was slightly more alert mentally, gave a better account of herself, spoke about her mother's death and her solitary life in her own house, and expressed some concern regarding her present financial condition and other difficulties. She said that she lived in a house, which she inherited from her mother, but was entirely alone; the house fell to pieces, the ruins were infested with mice, and the bank clerks told her that she had no money. The next thing she remembered was that the authorities sent her to hospital. Her mental improvement did not materially progress after this, although she showed increased interests and was moderately sociable. She could not, however, fully appreciate her position; she smiled foolishly when asked questions, was hardly employable, lacked interest and initiative, and seemed to be indifferent to the operation and her future. She appeared to have a slight loss of her facial hirsutism.

Two months after the operation she asked whether she could be allowed to go out for short walks in the grounds as she felt bored. This was permitted, and on the first day she absconded. She was, however, readmitted three weeks later. When outside she was living in the ruins of her home, and as she did not have enough to eat she raided the pig-bins of the neighbours for food.

Four months after the operation it appeared that little if any hair had fallen out spontaneously, but there was the "painless depilation" described in adrenal virilism. The long coarse hairs on the beard area could easily be plucked out without pain. The absence of complaint could not be ascribed to her mental condition, as she showed obvious signs of pain when a hair of the eyebrow was pulled out, and stated that it hurt. Also, the beard hair came out easily without causing puckering of the skin, whereas it was difficult to avulse an eyebrow, and a cone of skin was drawn up before the hair came out. At this time she was menstruating irregularly, but her breasts and bodily configuration were of course unchanged.

Although the pathological investigations were repeated at weekly intervals the results were constant after the first six weeks. The steroids had fallen from 60 to 8.4 mg. of androsterone a day. The blood-sugar curve returned to normal (Fig. 1, curve B); the sedimentation rate was increased to 22 mm. in the first hour and it still had not changed a month later. Blood chlorides were decreased from 430 to 390 mg. per 100 ml. The cholesterol, urea, and differential blood count showed no change. Histologically the excised suprarenal gland revealed very marked adenomatous changes, the ponceaufuchsin staining was evident, and the cortex was remarkably enlarged and of abnormal pattern.

Case 2

A 43-year-old single woman, a typist, was admitted to hospital on Nov. 3, 1944, suffering from schizophrenia. The patient's paternal grandfather had died of senile dementia; he was always peculiar in his ways. The father died when the patient was quite a child. The mother dominated her. She has a normal sister. She was always a shy, sensitive child. When 10 years old she had a motor accident, when she was torn "from the front to the back passage." She was in hospital

for a short time. Her mother was constantly talking about this accident, and the patient became very self-conscious of it. She was brilliant at school and read a lot of good literature. As menstruation did not commence her mother insisted on her going to various doctors. Endocrine treatments were given without result, and it was agreed that her delayed maturity might be due to psychological shock. Meanwhile she started work, and on the encouragement of her sister she left home and lived independently in lodgings. She was then obviously in a "nervous state" and began psycho-analytical treatment; this, however, was unsuccessful, and was interrupted by her progressive psychosis. She became markedly eccentric, a pacifist, a feminist; she gave away her salary to fellow workers, and developed an involved teaching on sex theories. Ultimately she became progressively dissociated and had to be admitted to hospital.

One sample of the stream of talk should illustrate her mental state: "I am married to a motor-car since ages. I am as feminine as Elizabeth in Jane Austen's novel. I cannot talk to somebody who is having a stronger personality than I. I did not have sex appeal, but now I am having it. I had a car accident and my sexuality was lost, but I was pictorially guided and retained femininity. My body is feminine. When I do anything I see it pictorially; I saw myself going to school. My sex tells me that the feminine brain is different to the masculine brain. I used to have a male brain; I have been treated by women who always treated me as a male. In the factory where I was working there was a man who was my double. My mother wanted to make me into a man. I cannot look into your eyes; a man's eyes magnify everything and overpower everything. I never menstruated: I don't want to menstruate; I stopped it with will-power, but I still feel vibrating; the electricity is not where my 'feminine' is, and I cannot bear it. I am vegetarian; a vegetarian can live with a man without having a child and flirting. If I don't eat I don't get sexual." During her stay the mental picture was stationary; she had a full course of electric convulsion therapy without any apparent result.

Physically she corresponded to Broster's type 1, which he calls adrenal pseudo-hermaphroditism—that is, a woman in whom changes due to suprarenal cortical pathology arise before puberty and the development of the female secondary sexual characteristics. She had never menstruated. The breasts were not larger than those of a normal man. The hands were broad and bony. She was only of average height, but the pectoral girdle was wide compared with the pelvic. The hair was of male distribution and her upper lip was very hairy, but the whole beard area was not nearly as heavily clothed with hair as in Case 1. Her blood pressure before operation was 130/90.

Fig. 2.—Case 2. Blood-sugar curve before operation, A, and after operation, B.

The urinary steroids were equal to 20 mg. of androsterone in 24 hours. Her blood sugar (Fig. 2, curve A) showed an approximately normal curve; her sedimentation rate was 9 mm. in the first hour; and the differential blood count, blood cholesterol, urea, and chlorides were within normal limits.

Intravenous pyelography did not reveal any asymmetry, and in April, 1946, laparotomy was performed. This showed that the left suprarenal was larger than the right, although the difference between them was not as great as in Case 1. The female pelvic organs were palpated and the uterus found to

be minute. The uterine body was about 1 in. (2.5 cm.) long and the thickness of an ordinary lead pencil, which suggests that the endocrine abnormality began well before puberty. Five weeks after laparotomy the left suprarenal was removed by the Bernard Fey approach, which again afforded an easy and adequate exposure. The operation was completed without difficulty, and this patient did not show the peculiar behaviour of the pulse observed in Case 1 when the gland was handled, nor any signs of shock.

Four months after operation her physical condition remained unchanged, which is not unexpected, as the adrenal pathology had presumably been in operation for over thirty years, compared with three to four years in Case 1. She was completely indifferent to the operation. Her mental state remained untouched and completely stationary, and her physical condition was unchanged. The operation had, however, produced the anticipated biochemical changes. The urinary steroids had fallen from 20 to 7.4 mg. of androsterone six weeks after operation. The blood-sugar curve was normal (Fig. 2, curve B); the blood sedimentation rate showed a 22-mm. fall for the first hour; the blood chlorides dropped from 440 to 380 mg. per 100 ml. and remained unchanged after a further six weeks. The cholesterol, urea, and differential blood count values were unchanged. Histologically, the cortex of the excised gland showed some enlargement, but no other change.

Discussion

In the two cases described there is evidence of adrenal dysfunction. This was shown not only by their similarity to other cases that have been found to have abnormalities of these glands but also by their raised urinary ketosteroid excretions. Both had concurrent mental illnesses, and in the first case there seemed to be a definite relationship between the time of onset of the mental and physical symptoms. Neither, however, was notably improved by adrenalectomy.

Theoretically one may postulate a relationship between abnormality of a specific gland and mental illness in the following ways: (1) The mental illness may be the direct result of the glandular dysfunction; (2) the mental illness may cause the glandular dysfunction; (3) the mental illness and the glandular changes may coexist independently; (4) the mental illness may be psychogenic in response to worry over the physical changes induced by the gland; and (5) the mental illness may be the result of secondarily induced changes in other glands. Examples which are largely attributable to one or other of these causes may easily be found, though it is not possible for any one of them to be entirely divorced from the rest.

So far as adrenal abnormalities are concerned primary mental disturbances in paragangliomata of the medulla and in Addison's disease are known, and secondary disturbance due to sexual dysfunction in virilism. Other pathological conditions, however, particularly in regard to the various types of hyperadrenalism described by Broster, have not yet been associated with specific mental disturbances, although, as we have said, a number of cases of mental illness have been successfully treated by adrenalectomy. This suggests that the first form of relationship may be fulfilled, but no example of the second is known to have been cited. In regard to the fourth, severe emotional disturbances result from the growth of hair in women, and we have seen a patient other than those described in this paper in whom a very acute anxiety state and definite suicidal ideas developed as a result of her hirsuties. It is possible that some of the less successful results might be explained by the suprarenal overfunction being secondary to pituitary activity, as suggested in the fifth group. Thus an adenomatous gland (adrenal adenomata are common) might conceivably become overactive under undue pituitary influence, and its removal might not be

attended by the same relief of mental symptoms as if there was a primary dysfunction.

The first of our two patients developed her mental and physical symptoms at the same time, and it was believed that she belonged to the first group and had every chance of progressing favourably. The urinary androgens were certainly increased before and fell after operation, the chlorides and sugar-tolerance curves became normal, and a tumour giving a ponceau-fuchsin stain on section was removed; yet she did not improve. The second patient, on the other hand, had very long-standing abnormalities, a schizophrenic illness which was coloured by but not necessarily due to the physical changes and polyglandular disturbances. Perhaps, therefore, it was less likely that she would show an improvement after operation. It is interesting that in this case, too, in spite of the suprarenal removal, the reduction in the blood chlorides, the alteration in the sugar curve towards normal, and the post-operative reduction in ketosteroid excretion, there were no mental changes in keeping with this evidence. The raised sedimentation rates which developed subsequent to operation in both cases are unexplained.

Summary

A case of adrenal virilism with mental changes and another of adrenal pseudo-hermaphroditism, also with mental changes, are described.

Adrenalectomy (unilateral) produced the expected biochemical effects, and in Case 1 some physical change, but in neither was the mental picture materially affected.

The value of Bernard Fey's approach to the suprarenal is stressed.

A peculiar reaction of the pulse rate, apparently not due to surgical shock, during the removal of a large suprarenal is described.

An unexplained persistent rise in the blood sedimentation rate in both cases is noted.

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MISS RUTH THOMAS is one of those rare people who combine the possession of deep theoretical knowledge and wide practical experience with the power of clear and simple exposition. The seven pamphlets under review are the script of a series of broadcasts and a report prepared for the Curtis Committee. It is high praise to say that they read as well as they sounded. Miss Thomas deals with the early training of the infant and young child in an eminently sensible way, but it is a matter of dispute whether she is right when she forbids "potting" the infant under a year. She is correct in insisting that the child's anal eroticism, which is normal under a year, should not be frustrated and that too early insistence on cleanliness may result in trouble later on; but, by the establishment of a conditioned reflex to the pot, need the child be deprived of its pleasure and would not this save the mother much labour? Miss Thomas's description of the tragedies of homeless children is indeed harrowing; in this respect hell is paved as much by misdirected good intentions as by downright cruelty, and it is a relief to read of the real efforts by the better homes to provide the love and homeliness which these children so sadly miss. This brings out the urgent need for properly training those whose job it is to look after homeless children. These pamphlets should be bought from the National Association for Mental Health (39, Queen Anne Street, London, W.) and carefully studied by all those whether medical or lay who are concerned with children and the future welfare of the race. Their titles and prices are: *Children Without Homes: How Can They be Compensated for the Loss of Family Life?* (3s. 6d.) *Fears and Jealousies* (7d.), *Children's Fears* (7d.), *Children Who Dislike Their Food* (7d.), *Further Trying Habits* (7d.), *Habit Training* (7d.), *Temper Tantrums* (7d.).