ANXIETY; ALOPECIA AREATA; NEUROFIBROMATOSIS: AURICULAR FIBRILLATION**DESCRIPTION OF A PATIENT**

BY

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The following account of a patient is published because he displayed three disorders whose aetiology and pathogenesis are unknown. His fourth disorder—a psychological state dependent on an unusual personality—appeared to us to stand in aetiological relationship to two of his three abnormal physical states.

Case Record

The patient, a house-painter aged 39, was referred to the Derbyshire Royal Infirmary on May 5, 1943, by Dr. Eileen Crowley for treatment of auricular fibrillation.

Personal History

His childhood was quite normal, healthy, and happy. He does not recall any fears or anxieties as a boy. He was the leader of a small group of boys who were rather "young devils." At the age of 12 he passed the necessary examination to enable him to leave school, and he went to work as a riveter's mate. By the time he was 14 he had held a variety of jobs and was earning £2 15s. a week (1918). He was restless and ambitious, and had come to realize how many limitations there were in the life of his childhood; he saw no reason why he should not go a long way. He began to serve an apprenticeship in the carriage-and-wagon works (Midland Railway), but could not tolerate the attempts of the older men to put him in his place. He had a row with one of them and walked out, thinking that he could easily get another job. The post-war difficulties had then begun and he was unable to get work. His pride was hurt, so he falsified his age and joined the Grenadier Guards at 15 years. His father got him out again, but only by paying a forfeit. He was still unable to get a job, and was burning with resentment. He rejoined the Army to get back the forfeit, and then malingered until he was discharged by the Medical Board. He felt better after this, and came back home seeking work.

Then began a long and difficult period of partial employment. In 1922, aged 18, he married a girl two years older than himself whom he had got pregnant. She already had one illegitimate child. He had to live on 34s. a week, so they had a room in the house of her brother-in-law. Soon he found that she had had the illegitimate child by this man, and he became furiously jealous. He thought and dreamed of nothing else for weeks, and made scenes by following the brother-in-law about the streets. His pride was desperately hurt, and it was some years before he ceased to worry about his wife's conduct. At this time (in 1926), aged 22, he developed two small patches of alopecia areata on his head.

He made fresh efforts to overcome his difficulties, working partly as a painter and partly as a pianist (he had taught himself to play the piano). Financial worries, however, continued to press on him, and on one occasion he was in prison for failure to pay a debt. Gradually his health deteriorated, his finances grew worse, and his alopecia recurred. Shortly afterwards he got a job at a hospital as a painter, and so had regular work for the first time for years (1932—aged 28). His worries were apparently over, for he had every chance of getting out of his financial difficulties.

Presently he found that a new skin affliction was developing in the shape of nodules beneath the skin of the back of his neck. He became preoccupied with his condition, and after seeing a propaganda film thought he had syphilis. He went to several doctors and had repeated Wassermann tests before he was satisfied about this, and, even so, the doubts have recurred at intervals since then. His hair continued to fall out. He became very ashamed of his appearance; he would try to dodge people, and thought that they were looking curiously at him. This only served to increase his determination to make good and to show his real worth.

After about seven years' work at the hospital he started a house-painting business, and with characteristic energy was soon doing well (1939). When the air raids began he found that there was not much work for him to do, so he joined the A.R.P. He realized that he would get extra money if he could drive a lorry; so he bought a car, learned to drive it in one or two evenings, and passed the necessary test. When the raids died down he was able to go back to his painting business, which continued to do well. He put a

great deal of effort into every job he undertook, worrying greatly over the details of it. In April, 1942, one of his men stole a large sum of money from a firm for which he was doing a job. The man turned out to be a thief who had stolen from other clients of his, and the police had to make investigations all round the district where he worked. He was exceedingly distressed, and feared that no one would employ him any more. His heart began to beat irregularly and was shortly afterwards found by his doctor to be fibrillating.

Family History

The patient is either the sixth or the seventh of a family of twelve or thirteen children (doubtful about one older child who died). His mother was a fine woman who came from a healthy and highly respected family, and married rather beneath her. She was a great worker in good causes, was full of energy, and used to organize parades on behalf of the hospitals. She died of cardiac disease at 68 years. His father—a blacksmith—was a staunch teetotaler, and a good man. He suffered from rheumatism, and died of an unknown disorder when 65. The patient's paternal grandfather was blind during the latter part of his life and was extremely poor. Of the patient's brothers and sisters eight are still living. All have done very well. Three brothers are at present sergeants in the Middle East. He had no knowledge of any familial illness; nor does he know of any abnormalities of the skin or hair occurring in his parents or siblings.

His wife, aged 40, is in good health, but is a nervous woman. Of their three children, one daughter, aged 21, has a few small pigmented moles, but not café-au-lait patches or skin tumours. She bites her nails and has many night terrors. Otherwise her health is good. The other daughter, aged 18, has one small café-au-lait patch on the neck and many small pigmented moles, but no freckling or skin tumours. She has good health and a stable personality. The son, aged 14, has about 30 café-au-lait patches, the largest 5 in. by 4 in. on the back of the left thigh, diffuse freckling on the trunk, but no skin tumours. He has good health, and an impulsive, aggressive temperament, but his intelligence is poor. Under-development of sexual organs and a high palatal arch (speech defect) are other things of note.

Medical History and Habits

The patient's hair has been much in the condition described below for eleven years; it has grown slightly during the last two months. He now has to shave once a week, but for the preceding ten years had not shaved at all. The large tumour over the crest of the left

FIG. 1.—Back view of patient.

ilium has been present as long as he can remember, but he does not think it was there in infancy. The other skin tumours appeared in 1933 and increased steadily in size and numbers until 1939; few if any new ones have developed in the last four years. Although he was aware of his cardiac irregularity at its onset in June, 1942, yet he is now for the most part unconscious of it.

His habit for tobacco is 40 to 50 cigarettes a day and for alcohol 2 to 3 pints of beer a day. He has had no loss of libido at any

time. He is capable of great physical activity, and has had no other illness of importance in his life; no rheumatic fever or rheumatism. He well illustrated his impulsiveness by discharging himself from the hospital on the morrow of his admission and telephoning the following evening asking for readmission.

Examination showed him to be a healthy active man: height 5 ft. 10½ in., weight 11 st. 12 lb. *Hair*: Fine, sparse hair on scalp; no eyebrows; eyelashes very thin and poor; axillary hair very thin; no visible chest hair; pubic hair very thin and short. *Skin*: Diffuse freckling on the trunk and a few small café-au-lait patches on the abdomen and lower limbs. Nails are picked and bitten very short. There are no lesions on the mucous membranes. There is no detectable thickening of any nerves, nor are there any fibromata along their course.

Neurofibromata.—Hundreds of small skin tumours, varying in size from 1 mm. to 2 cm., are present on the face, scalp, neck, trunk, and limbs (Fig. 1). There is a larger one—a soft sessile tumour measuring 12 cm. across—just above the crest of the left ilium. These tumours occur with the greatest frequency on the scalp, face, neck, and trunk, but they are present in progressively diminishing numbers towards the periphery of the upper and lower limbs. The hands are practically free, and the feet have only one or two small nodules on the dorsum. Some of the tumours are under the skin, but the majority are on the surface of the skin as sessile tumours. They correspond well with the usual textbook descriptions of neurofibromata, which feel as if they were "herniated" through the fascia and can be "reduced" by pressure. The tumours are not painful.

Circulatory System.—The pulse is grossly irregular in force and frequency. The cardiac rate is 104 and the pulse rate 86; blood pressure 110/75. The retinal vessels are normal and there is no evidence of arteriosclerosis anywhere. There are no murmurs in the cardiac area, and the sounds are normal. The diagnosis of auricular fibrillation is confirmed by electrocardiogram (see Figs. 2 and 3), and radiographs show a heart shadow normal in size and shape.

The thyroid gland is not enlarged and there is no evidence of thyrotoxicosis: no tremor and no exophthalmos. There is no evidence of other endocrine disorder. Examination of the central nervous system revealed no abnormality, but he has very brisk muscle reflexes. The hands and feet are damp. The urine is normal. The blood sedimentation rate is 10 mm. in the first hour and 18 mm. in the second. His blood count shows: Hb, 103%; red cells, 5,480,000; white cells, 12,000, of which 2,440 are lymphocytes and 610 monocytes; the remaining 75% are neutrophils. His blood cholesterol is 115 mg. per 100 c.cm. of blood. His Wassermann reaction and

Psychiatric Summary

Coming from a superior working-class background, possessed of great drive and ambition, impulsive and resentful of failure, this patient suffered great frustration and anxiety, at the peak of which he twice developed alopecia areata. The second attack of alopecia progressed in spite of the partial relief of anxiety, and at this time he developed the multiple subcutaneous nodules. A third severe period of anxiety ten years later coincided with the development of auricular fibrillation. He is a well-spoken and obviously intelligent man who has educated himself beyond the level he would have attained when he left school at 12. His whole attitude indicates the possession of quite exceptional drive and ambition, with a keen sense of pride in his own achievements and strong resentment against the social and economic difficulties which have held him back and the disease which has disfigured him. His impulsiveness is well shown by his history. He is inclined to brood over his difficulties; his anxiety and desire for success reach an obsessional pitch at times. Some of his worries have definitely shown an obsessional character.

Diagnosis ; Progress

The case was diagnosed as one of anxiety, alopecia areata, neurofibromatosis, and auricular fibrillation.

Quinidine therapy was started soon after admission, and when the dose had reached 25 gr. a day the patient's cardiac rhythm switched to normal (Figs. 2 and 3). He was discharged on July 9, 1943, on a maintenance dose of 5 gr. of quinidine twice daily, which has been continued till now except for one month when, unknown to him, aspirin was substituted for his quinidine. He had no further fibrillation until Dec., 1943, when his cardiac rhythm became irregular again, after an attack of influenza. His heart was quickly converted to a normal rhythm with 20 gr. of quinidine in the day.

Comment

Von Recklinghausen's disease is characterized by neurofibromata and by abnormal pigmentation, as described in this man. These café-au-lait patches and diffuse frecklings are regarded as *formes frustes* of the disease (Parkes Weber, 1909) when they appear in the relations of those suffering from its fully developed forms. The disease is now thought to be inherited as a Mendelian dominant. More interesting than the disease itself are the abnormalities which are often associated with it. These are of great variety, and include mental, endocrine, autonomic, and skeletal disorders; they have been reviewed in a paper by Levin and Behrman (1940). Although defective development of pubic hair is mentioned in that review, there is no report, either in this or in other papers, of an associated alopecia areata. Auricular fibrillation has once before been described (Clarke and Wakefield, 1926) in association with neurofibromatosis, and these authors attribute it to an involvement of the vagus nerve by the tumours. No necropsy was obtained on their patient, but, according to them, the vagus nerve is the commonest of the cranial nerves to be involved by neurofibromata. It is difficult to believe that the auricular fibrillation in our patient could have been due to implication of any part of the autonomic system by the tumours, since quinidine has returned his heart's rhythm to normal, and the rhythm has remained regular even when the quinidine has been stopped. It is simpler to postulate that the auricular fibrillation and the alopecia areata are related to the neurofibromatosis in the same way as are the vast array of associated disorders already described in the literature—and that is, at a genetic level.

Levin and Behrman quote the views of Pende (supported by "many learned arguments"), who in 1910 suggested that neurofibromatosis has a place in a large group of endocrine-sympathetic dystrophies, among which he also included scleroderma and painful lipomatosis. For the production of these conditions two factors are required:

(1) A *constitutional factor*, represented by an abnormality of the endocrine-sympathetic system, which may be hereditary, intra-uterine, or extra-uterine during the period of growth; and

(2) A *precipitating factor*, such as shock, trauma, toxins, or infection, which through its effects on the endocrine-sympathetic system acts as a stimulus to embryonal elements of the autonomic system in the skin.

This appears to us as satisfactory an explanation of the aetiology of neurofibromatosis as can at present be attempted, and it can be similarly applied to alopecia areata and to idiopathic auricular fibrillation. Alopecia areata has been related to emotional disturbances by numerous observers. This association has been denied with equal frequency. In our

FIG. 2.—Electrocardiogram before quinidine therapy.

FIG. 3.—Electrocardiogram after 25 gr. of quinidine daily.

flocculation test are negative. A fractional test meal showed a histamine-fast achlorhydria in all specimens.

The report (Dr. G. R. Osborn) on the microscopical structure of a removed tumour from the back of the neck is: "The cutaneous nodule excised measures about 8 mm. in diameter. Microscopically this is a neurofibroma (fibroma molluscum). The most prominent nervous element is whorled groups of Schwann cells (schwannoma). Around these there is fibrous tissue with many small blood vessels. Nothing suggestive of malignancy seen. *Diagnosis*: neurofibroma."

experience of alopecia areata it has not been difficult, in both children and adults, to demonstrate a preceding emotional stress. Auricular fibrillation is associated with mitral stenosis, with thyrotoxicosis, and with myocardial degeneration. None of these conditions was present in our patient. Distinct from these varieties is another group called "paroxysmal auricular fibrillation." It is characteristic of these paroxysms that they last only a few hours or days, that they recur frequently, and that they are corrected to a normal rhythm with ease and safety by quinidine therapy. It is difficult to define as paroxysmal a condition which has persisted for eighteen months, as in our patient. When auricular fibrillation is unassociated with any organic disease and when it is preceded by adequate emotional tension, as in this man, it is reasonable to name it a cardiac neurosis.

This man's illness illustrates the varied factors—genetic, constitutional, psychological, environmental, and mechanistic—which we seek to assess in an evaluation of disease in man, but it also indicates how remote is the day of full comprehension. The link between the emotion which fails to find its appropriate physical discharge and the consequent physical disorder is usually assumed to be the vegetative nervous system; while this path is probable, the endocrine system offers an alternative mechanism. Both alopecia and auricular fibrillation are sometimes associated with endocrine disorder. We are far from a coherent conception of the mechanism by which emotional stress is translated into physical disorder. Not to seek this link, however, or, worse, to ignore its existence, is a heretical denial of the integrity of mind and body.

The present controversy between those who support the "biological" approach to aetiology ("What sort of man is this, and why did he become ill in the way he did?") and those who are preoccupied with mechanism ("What has the patient got?") implies a schism in diagnosis and therapy which is quite unreal. In our patient it was possible to define closely but one of the faulty mechanisms involved (i.e., auricular fibrillation), and here it was easy to intervene to the man's great advantage. While the biological approach to aetiology had in this case none of this immediate practical quality, yet it contributed to a fuller understanding of the sufferer and his disorder. The physician cannot disdain any approach which increases either his understanding or his capacity to help his patient.

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A MILK-BORNE OUTBREAK OF GASTRO-ENTERITIS DUE TO SALMONELLA DUBLIN

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On Aug. 19, 1943, the County Medical Officer of the West Riding of Yorkshire was informed that the practitioners in Knaresborough Urban District had throughout that day been called in to attend to numerous cases of sickness and diarrhoea. Inquiry by the local medical officer of health showed that all the cases had occurred in households supplied with milk from Farm G, situated at a village about two miles distant in an adjoining rural district. Simultaneously cases had occurred among residents at the farm. It therefore seemed that the disease was conveyed by the milk distributed from Farm G. Subsequent investigation proved that the outbreak was caused by *Salmonella dublin*, that the vehicle of infection was milk from Farm G, and that the source of infection was an apparently healthy cow which was a carrier of the organism.

Symptoms

The onset of the disease was sudden, with sickness or actual vomiting, diarrhoea, headache, and fever ranging from 100° to 102° F. The diarrhoea was profuse, but there was no blood or mucus in the motions. The febrile period lasted for about three days at the longest. A profuse herpetic eruption on the lips and nose was noted in a small proportion of cases. One patient complained of persistent headache for some days during convalescence. Many cases were very mild, and some patients were not confined to bed or were confined to bed only for a day. There were no deaths.

On Aug. 29 a baby 2 months old died of meningitis, but unfortunately no bacteriological or post-mortem examination was made. This child, which was breast-fed, did not suffer from diarrhoea. It was a member of a household of five persons supplied with milk from Farm G. One member of the household (not the mother) had been ill with diarrhoea about Aug. 19. This case is noted because Smith (1934) has described two sporadic cases of meningitis in children due to *S. dublin*.

Incubation Period

Cases occurred among the residents at a hostel for evacuee children, from particulars of which the duration of the incubation period was determined. The circumstances also confirmed the fact that the outbreak was milk-borne. At the hostel there were 7 children and a staff consisting of a matron, a nurse, and a cook. A daily charwoman was also employed. At the time of the outbreak a friend of the nurse was staying there. The hostel was supplied with milk from Farm G, and the residents, with the exception of the matron, and cook, had milk at about 11 a.m. on Aug. 18. The charwoman also had milk on that day. About 2 a.m. on the 19th three of the children complained of sickness and diarrhoea, and by 8 a.m. all the children, the nurse, and her friend were ill. The charwoman, on arriving at the hostel that morning, complained that she had suffered from sickness and diarrhoea during the night. The matron and cook, who did not take milk, remained well.

The interval of time between the consumption of milk and the onset of symptoms varied from 14 to 20 hours. This relatively long incubation period suggested infection with living *Salmonella* organisms.

Outbreak in the Urban District

As the practitioners were requested to notify cases of sickness and diarrhoea it was possible to estimate approximately the magnitude of the outbreak. The total number of cases notified was 162, and 79 households were involved. Some of the known cases were very mild, and it is therefore probable that there were many more cases, which did not come to light as a doctor was not called in. The date of onset of the illness was stated to be Aug. 18 in 2 cases, Aug. 19 in 143 cases, and Aug. 20 in 15 cases; in 2 cases the date was not given. The age and sex incidence is shown in Table I.

TABLE I.—Age and Sex Incidence of Cases of Gastro-enteritis notified in the Knaresborough Urban District

Age	Cases	Females	Males
Under 5	35	21	14
5-9	23	12	11
10-14	16	4	12
15-24	24	19	5
25-34	23	21	2
35-44	15	10	5
45 and over	26	17	9
Totals	162	104	58

Outbreak at Farm G

On making investigations at the farm it was found that six persons were resident there: the farmer H. F., aged 70; his son-in-law T. P., aged 36; his three daughters, R. P., aged 36, J. B., aged 32, and W. F., aged 23; and his granddaughter, J. P., aged 9. Two farm labourers—H. R., aged 40, and C. K., aged 35—were employed, but lived with their families in the village and were supplied with milk from the farm. The farmer, his son-in-law, and his granddaughter were ill with sickness and diarrhoea. The other residents and the two labourers were well, and remained well. All the members of