FAMILIAL PSYCHOSES ASSOCIATED WITH ENDOCRINE DISORDER.

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ONE of the most striking characteristics of patients in a mental hospital diagnosed as suffering from schizophrenia, or dementia præcox, is their dissimilarity. It is easy to pick out cases in which the onset, course, symptomatology and outcome of the psychosis are different. There is thus a tendency to regard the schizophrenic group as possibly containing many different clinical entities. One of the current major problems of psychiatry is to clarify what constitutes schizophrenia and to subdivide the clinical material further in a way which will prove useful for study.

The following two case-records of a sister and brother suffering from schizophrenic-like psychoses exemplify these points. The woman, who had been diagnosed as a case of dementia præcox, was examined in the course of a survey of many patients in a large mental hospital. She suffers from an atypical psychosis associated with endocrine disorder. Her brother has a similar psychosis, but lives out of hospital. The parents were first cousins. I suggest that these two patients suffer from the same disease process, that the course and symptomatology are definite enough for the syndrome to be considered a clinical entity, and that the syndrome is in part determined by a recessive genetical factor.

A. B—, a female, now aged 60, was sent to hospital at the age of 49, because her behaviour was so disordered that she was unable to take care of herself.

The history of the illness was that, about the age of 40, hair began to grow on her face, and she became obese. Five years later, in response to an urgent letter, a relative visited the family and found the patient "very insane". She was "fat, lazy, stupid, irresponsible", and had not worked for some years. She and her brother were being cared for with much difficulty by their aged, widowed mother. Four years later the mother died. A relative found the house in a state of dirt and disorder. A. B— had been trying to force food down her mother's throat. She was sent to hospital that evening.

The history of her early life is scanty, but reliable as far as it goes. She was a healthy girl, of average intelligence, reached Standard 6 in school by age of 14, and later earned a living as a dressmaker. She is said to have been of a cheerful disposition. She took much interest in helping with "school-treats" for children. She did not marry. A photograph at the age of 35

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shows her to be a good-looking, well-proportioned, though short, woman, without any excess of hair or fat.

On admission, aged 49, she was 5 ft. 1 in. high, and weighed 11 st. 4 lb. Her body was dirty and neglected. She had a profuse beard, at least 6 in. long. She was very stout, and some years later she was operated on for a right femoral hernia. Menstruation had ceased before admission, and her menstrual history is unknown. The mental picture was one of gross inactivity, indifference, personal neglect, and preoccupation with a vague, unsystematized delusional system, of erotic trend.

She realized she was in hospital, and recognized doctors and nurses as such; yet she was "incapable of giving any account of herself". Her answers were often obscene and irrelevant, and she muttered much to herself. She was unemployable, defective in personal habits, hoarded rubbish in her clothes, and sat about, often "tailor-wise", in happy, preoccupied indifference. A "speech-defect" was noted.

She said she had one sweetheart and one husband and one wife, and that was all she wanted. She said she was 17 years old, and was related to royalty. She was older in the sun than in the shade. Some years later she maintained she was "born this morning", was married and had millions of children.

Her condition has changed very little in the eleven years since admission.

EXAMINATION.

Mental: Behaviour.

At the age of 60 she presents the same picture of inactivity and indifference. She can dress herself, but has to be washed. Her personal habits are frequently defective. On occasion she can do plain sewing quite well, but usually she sits muttering to herself or wanders about picking up rubbish. She recently hid a dead rat in her clothes. She rarely talks spontaneously to other patients, and she never looks at newspapers. She likes the radio music. She is quite observant of her surroundings. She is not nearly as inaccessible as her greatly disordered appearance might suggest. She at once obeys a request to come for examination, she understands questions well and can answer briskly and to the point. Frequently, however, she lapses into a low muttering on her delusional topics, from which it is hard to distract her. She often twiddles the fingers of both hands in front of her face, and is unable to give a coherent explanation of why she does this.

> Physician looks at her intently. Patient: Do you recognize me, sir? [laughs to herself].
>
> Dr.: What's your name? [Correct answer.]
>
> How old are you? Born this morning.
>
> What do you complain of? —— Nothing [laughs]; then, "My sweetheart" and other mutterings.

Affect and Content.

She is obviously happy. She sits smiling, enjoying the interview. In the ward she is usually content, sometimes elated or indifferent, but never obviously sad. She is irritable if crossed.

How are your spirits? —— Dull now and again.

How do you feel? —— I don't feel as if I'd like to go away from here. I think it's a nice place.

Are you happy? —— Yes.

Why? —— Perhaps because you're here [laughs]. I've been a gentleman in the army. I've been Lord Kitchener.

Are you a man or a woman? —— I'm a lady now. I've been a gentleman.

But why are you so happy? —— Because I am. Because I have a lovely husband and a true one.

She calls her husband "Mr. Algy", but can give no more facts about him. There is no evidence of hallucinatory visits from him.

Do any funny things happen to you? —— You mean about the Devil?

Yes? —— The Devil put his arm round my waist, and he said, Go in that way. He said Ha! Ha! Ha!

Do you ever feel as if people were speaking to you? —— Liberals out in the street voting.

Have you ever heard them? —— I have a lot of children, pretty girls.

She sometimes refers to herself as Queen Annie of Hyde Park and Piccadilly Circus. She cannot be exact about her delusions and hallucinations. They are vague and not formulated into any coherent system.

Sensorium.

Orientation.—She knows she is in hospital, but calls the hospital by her own name. She thinks she is in Birmingham [incorrect]. She gives the date as "28 March, 1881—no, 1889" [correct date is May 8]. There is thus much disorientation to time and place.

Memory: Remote.

How is your memory? —— Getting better. I lost my memory; I found it one day.

Where were you born? —— London [correct].

Patient then asked how old the doctor was and where he worked. She believes her parents are still alive and living in her old home.

When were you born? —— This morning.

Birthday? —— 25th October.

Year? —— 1881—no, 1884.

Day to-day? —— 28th March.

Where to school? —— G— Street [correct]. Oxford and Cambridge [incorrect].

How old on leaving? —— 14 [correct].

What work after leaving? —— Dressmaking [correct].

She can give some slight account of her work.

Did you like that? —— Yes. I got nervous debility. I've had nervous debility.

How does it affect you? —— Shaky legs. [She cannot explain this further.]

Recent Memory.

When did you come here? —— This morning—when we had our hair long.

How long been here? —— I don't know; since the day they asked me to come; about three years [eleven years].

What has been done for you to-day? —— Nothing—my face—a clean frock.

Name of charge nurse? —— [Correct].

Her memory is diffusely impaired, especially for events of more recent years since the onset of her psychosis.

Power of retention.—She can remember "a pencil and a green tie" after five minutes.

Intellectual functions.—She can repeat only 5 figures forwards and 3 backwards; yet she can perform Marie's Three Paper Test at once correctly.

She can count from 1 to 20, and from 20 down to 1, can repeat the ABC and the months of the year correctly. She gives the King's name as "Mr. Algy", the Prime Minister as Lord Salisbury, five large towns in Britain as "London, Islington, Great Euston Road, St. Pancras", and five rivers as "River Swee [correct], River Wye [correct], River Dover [incorrect]".

Asked to substract 7 from 100, she begins "93, 87, 82", and stops. Her reading age on Burt's reading test is 11½ years, with a big scatter from the eight-to thirteen-year levels. She reads a simple story slowly and correctly, but is able to repeat very little. She writes her name easily.

She cannot explain simple differences, such as tree and bush, wood and glass, etc.

Insight.

Any need for you to be in a mental hospital? —— No, not after you have done all these things.

Are you ill in any way? —— Well, I have a pain in my leg.

There is some intellectual defect, but owing to some lack of co-operation and delusional preoccupation the defect may not be as great as the results in the test suggest. The scatter in the reading test suggests deterioration. She has no insight into her present state, yet she knows she has had an illness; "lost my memory, nervous debility".

Physical.

Her habitus is abnormal (see Figs. 1 and 2). She is broad and short, with a large round head and small hands and feet. Her height is 5 ft. 1 in., and she weighs 11 st. 7 lb. The shoulders are broad, yet the pelvis is wide and the thighs incline inwards at a feminine angle. The legs are short. Her span is 4 ft. 7½ in. The limb muscles are small and flabby. Fat is excessive everywhere. It is deposited most profusely on the hips, abdomen and chest. The arms and legs, fingers and toes taper towards the periphery. She has a well-marked beard and moustache of coarse, thick, dark hair turning grey. Her head hair is profuse, but coarse and thick. Her beard is cut once a week. Axillary hair is profuse. Pubic hair is well developed and of feminine distribution. There is much hair down the inner side of the thighs and legs. The body-hair is not over-developed. The breasts and labia majora are well developed.

The clitoris is not enlarged, the uterus is not palpable. The skin is very dry. The dorsum of the forearms and hands acquires a marked sunburn in summer. This brown pigmentation is darker than her facial sunburn. It is absent in winter. She has had no dermatitis.

The ears are large, but well formed. The palate has a very high and narrow arch. She has about twenty small brown pigment-spots like dark freckles on the face, and four small pedunculated epidermal nodules on the right eyelids.

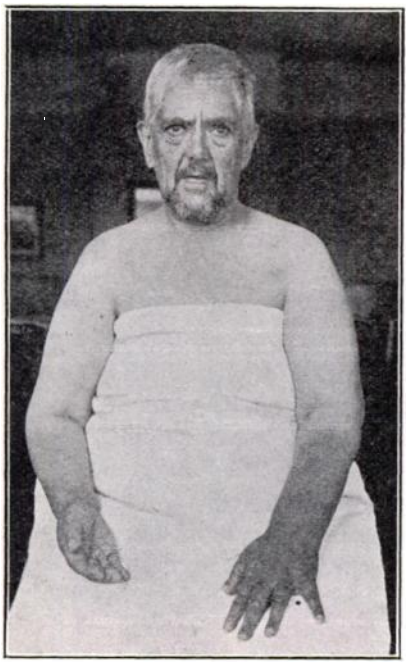

FIG. 1.

Female patient, A. B—, aged 60.

FIG. 2.

The heart-beat is regular in time and force, 82 per minute; the blood-pressure 252 systolic, 114 diastolic. There is no thickening of the radial or retinal arteries. Owing to the obesity it is hard to tell the size of the heart; it is certainly not grossly enlarged. There is a soft aortic systolic murmur, with an accentuation of the aortic second sound. The urine is acid, of specific gravity 1020, and contains a small quantity of albumen, but no sugar and no acetone. By microscope some leucocytes, epithelial cells and a few red blood-cells can be seen. There are no casts.

The abdomen is lax and protuberant. Striæ are prominent. No tumour can be felt. The liver and spleen are not enlarged, the kidneys are not palpable. The lungs are healthy.

No disorder can be made out in the nervous system. Her gait is slow and shuffling, but steady. She has a slight kyphosis. Her articulation is slurred,

but she is edentulous. The cranial nerves are normal. In particular there is no disorder of smell, the fields of vision are full, the retinæ healthy. Visual acuity is slightly reduced in both eyes, but is difficult to examine. The pupils are equal, circular, slightly irregular, but react well to light and on accommodation. The ocular movements are free, without nystagmus. There is no muscular weakness, inco-ordination or tremor.

The blood Wassermann is negative, blood urea 25 mgrm. per 100 c.c., blood cholesterol 298 mgrm. per 100 c.c. serum.

The glucose tolerance test is within normal limits:

Fasting blood-sugar level before breakfast												100	mgrm. sugar	per 100 c.c.
Blood taken	45 min.	after	feed of	100	grm.	glucose						136	,,	,, 100 ,,
,, ,,	1 hr.	15 min.	after	feed of	100	grm.	glucose					122	,,	,, 100 ,,
,, ,,	1 hr.	54 min.	,,	,,	100	,,	,,					115	,,	,, 100 ,,
,, ,,	2 hr.	16 min.	,,	,,	100	,,	,,					96	,,	,, 100 ,,

The blood-count showed: Red blood-cells, 6,120,000 per c.mm.; white cells, 6,200; hæmoglobin, 110%; colour index, 0·9. The differential count showed: Polymorphonuclear leucocytes, 69%; small lymphocytes, 26%; large lymphocytes, 4%; hyaline cells, 1%. A radiogram of her skull showed no abnormality of the pituitary region.

The case may be summarized thus: A healthy woman of cheerful, active disposition, at about age of 40, shows an insidious onset for no obvious cause, of hirsutism, obesity, increasing inactivity and emotional indifference, leading to a psychosis characterized at age of 60 by a gross deterioration of behaviour, personal neglect, emotional blunting, vague, poorly formulated, grandiose and erotic delusions, some intellectual decay, diffuse defect of memory, disorientation, and lack of insight into her present state, but a realization that she has had a "nervous debility".

Her physical state is characterized by a markedly broad and short habitus, a large head and small hands and feet, slight kyphosis and shuffling gait, obesity, hirsutism, marked hyperpiesia not of cardiac or renal origin, undue pigmentation of forearms and hands, an increase of blood cholesterol and of red blood-cells.

The brother, B. B—, presents a similar picture:

Only a scanty history is available. Born in London, a year before his sister, he reached the sixth standard at school and then worked in an umbrella factory for about eight years. Apparently he was a healthy boy. A deterioration of behaviour set in about the age of 23, since when he has never been out of the care of his relatives. A relative who saw him once in his later twenties found him at that time "a bit simple and soft". Boys used to tease him. His speech was slurred and he had a shake of the arms. He was not working and was cared for at home. In later years, apparently, his behaviour was worse than that of his sister, as his mother used to keep him locked in a room.

Since the age of 50 he has lived on a small farm and been cared for by a

cousin. She has noticed little change in his condition over the past eleven years. If anything, his behaviour has improved slightly under her strict discipline. Whereas formerly he used to roam about and smash windows, now he is more orderly, obedient, and does a little work.

Examination.

Mental : Behaviour.

There is, however, at the age of 61, a gross disorder of his behaviour. The limit of his work ability is to pump the well and clean out the stable. Over these jobs he will spend hours. Unless supervised, he will stand about doing

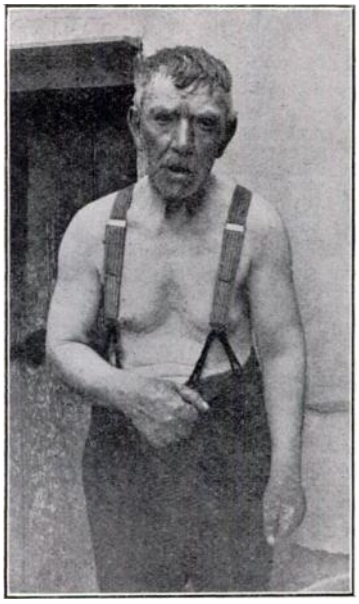

Fig. 3.—Brother, B. B—, aged 61.

nothing or muttering to himself, like his sister. He frequently puts his clothes on inside out. He rarely washes himself. Like his sister, he will defæcate and urinate anywhere. He used to urinate in his tea and drink it. He requires an almost constant supervision. He has a huge appetite. He can use a spoon and fork, but spills his food. He picks himself. He occasionally reads newspapers, and will comment on the horse-racing news. He can play a simple card game, which consists of pairing cards of like number. He recognizes the tunes of a few gramophone records. He often forgets what he is told to do. Usually dull, placid and contented, he will occasionally display a little querulous irritability. He is afraid of going out in the dark.

He recognizes the doctor as such, and he answers questions slowly and after delay.

Affect.

He says he is "all right" and "quite happy". There is no elation. He is dull, indifferent and contented. There is no evidence of delusion or hallucination.

Sensorium.

Orientation.—He knows the month and the year, but not the day or date. He knows what county he lives in, but not the name of the farm.

Memory.—He thinks his memory is "all right". He tells his full name correctly, but gives his age as 63, and does not know his birthday or birth year. He names the street in London where he was born, and the school he attended. He says he left school at age 16 (?), from the sixth standard. He can give only a slight description of his work in the umbrella factory ("a good trade, better than farming"), but he says he left because he "could not get work".

His memory for recent events shows similar defects. He can describe his work of to-day, but not of yesterday. He can remember the physician's name for three minutes, but not an address.

Intellectual functions.—He can repeat six figures forwards and four backwards. He does Marie's Three Paper Test on the second attempt. He can repeat the months of the year and the Lord's Prayer. He knows the name of the Prime Minister, and the names of five large towns, but of only one river. He can count from 1 to 20 and from 20 to 1. He subtracts 7 from 100 serially in 1 min. 45 sec., with six mistakes. He can write to dictation. His reading age on Burt's Reading Test is 13·2 years, with a scatter from 12 to 14. He can read a short story, and repeat it correctly. He can describe the difference between wood and glass, a mistake and a lie, but not between poverty and misery. He performs all these tests slowly and with effort. He has very little knowledge of current events.

Insight.

He does not appear to be aware of the abnormality of his behaviour, and he says he does not feel different from other people. He does not consider his defective personal habits unusual.

Physical.

There is a facial and bodily resemblance to his sister, but he is less broad and short. His height is 5 ft. 4½ in. His gait is clumsy, unsteady, irregular. He walks with a stoop, and sways a little.

His hands and feet are not small relatively to his limbs. His head is large. The ears are large and long. The palate has a high arch. The irides have a colouring very similar to those of his sister. The head hair is dark brown, coarse, plentiful. He has a fair, reddish moustache. The body hair is not excessive, and has a masculine distribution. The skin is very dry. Fat, though plentiful everywhere, is not excessive except in the breasts. The penis is small and short. The testicles are normally developed. The hands are darkly pigmented in summer, and show a severe dermatitis, which appears in summer and dies away in winter. The skin, both on the palms and on the back of the hands, is much thickened and fissured. In many places, especially on the back of the fingers and thumbs, are ulcers exuding serum and blood, and having thick, raised whitish edges.

The blood-pressure is 168 systolic and 88 diastolic. The heart is not enlarged, there are no cardiac murmurs, and no sclerosis of the radial or retinal arteries. The urine, S.G. 1030, contains 0·1% albumen, but no sugar or acetone. Blood and renal epithelial cells can be seen by microscope. There are no abdominal tumours. The liver is not enlarged. The kidneys are just palpable; they are not tender. For many years evidence of seminal emissions or of masturbation has been lacking. The nervous system shows little abnormality. His articulation is slightly thick and slurred. There is a slight coarse tremor of the protruded tongue and of the outstretched hands. The gait has been noted. There is no Rombergism, no inco-ordination, no loss of sensation, no muscle weakness. The tendon reflexes are active and equal, the abdominal reflexes present and equal, the plantar responses flexor. The cranial nerves are normal. In particular, the fields of vision are full, the vision normal, and the retinæ healthy. The pupils are round, regular, equal and react to light.

Neither patient has suffered from headaches, diplopia, somnolence or disturbance of urinary output.

To summarize: A healthy boy, of average intelligence, from age 23 onwards became increasingly inactive and indifferent, so that he was unable to work and had to be looked after at home. He developed slurred speech and a tremor, and his behaviour steadily deteriorated. At age 61 he is the victim of a psychosis characterized by a gross deterioration of behaviour, personal neglect, lack of initiative, emotional blunting, diffuse defects of memory, disorientation, a slight intellectual deterioration and a marked lack of insight.

Physically he is of a broad and short habitus, with a large head. He has a slight kyphosis, an unsteady gait, coarse tremor of the hands and tongue, and slurred speech. He also shows a moderate obesity, a lack of sexual activity, hyperpiesia and an undue skin pigmentation of the hands, associated every summer with a severe dermatitis.

The Family History.

Sibs of patient: One child died about 3 months old, cause unknown.

Parents:—Father: A horse slaughterer; a large, tall man, always healthy. Died, æt. 68, from "dropsy". He is described as "peculiar" in temperament. Although efficient at his work, he was very bad-tempered and unfriendly. In his later years he sat about the house doing nothing; often silent for hours.

Mother: A very small and short, hard-working woman, with a cheerful and stable personality. Died aged 86.

The parents were first cousins. The father's mother was sister to the mother's mother.

Paternal grandfather: Unknown.

Paternal grandmother: Died old; said to have been healthy.

Maternal grandfather: Normal; died 63.

Maternal grandmother: Normal; died 74. Sister of paternal grandmother.

Great uncles and aunts unknown.

Paternal uncles and aunts: Unknown. One uncle is said to have been "simple-minded".

Paternal cousins: Unknown.

Maternal uncles and aunts and first cousins:

(1) Uncle, healthy, died over 60. Several children, unknown.

(2) Uncle, healthy, died 74. Eleven children; 5 died in infancy; 3 normal males died, aged 36, tuberculosis; aged 46, tuberculosis; and aged 65, cancer. Two normal males alive, ages 45 and 48. One female, aged 58, married.

This female cousin was examined. Always a worrier, with obsessional trend; worse since menopause at 45. Has always worried about religion and about rightness or wrongness of her actions. Attended a London hospital intermittently for four years for treatment as out-patient. Is now preoccupied with question of whether she should be baptized, but wonders whether, if she were baptized, she would stop worrying or worry about something else. When worried, she often has "an awful pain and pressure on the top of the head, queer feelings, and tingling in the arms". She has always been able to manage her house for her husband and children.

(3) Uncle, alive, aged 78. Enlarged prostate removed at age of 71. Now mildly senile, with poor memory.

(4) Aunt, healthy, died 75. Three male and 2 female children alive and well, over age of 50. One male died from accident in the thirties.

(5) Aunt, healthy, died "middle life". Three children: boy and girl adult, alive and well; one girl died in childhood.

(6) Aunt, died over 70 years. In her later years she became much preoccupied with religion, shut herself in her house and refused to see anyone. This is said to have followed her finding that her husband was unfaithful. Children: Three boys and one girl, alive and well, all adult.

Commentary.

These two patients have similar psychoses. The onset is insidious. They both show a progressive deterioration of behaviour and an increasing emotional blunting, to such an extent that they cannot take care of themselves. Both show some intellectual decay, defect of memory, disorientation and lack of insight.

Both show a similar abnormal physique, a kyphosis and a shuffling gait. Tremor and slurred speech is observed in the man, and a speech defect was at one time noted in the woman. Both show other abnormalities strongly suggestive of an endocrine malfunction: obesity, hyperpiesia, skin pigmentation, diminished sexual activity in the man, and hirsutism, high blood cholesterol and increase of red blood-cells in the woman.

The psychosis in the woman began about fifteen years later than in the man, apparently ran a more acute course, and has progressed further. She shows a greater intellectual decay than her brother does, and, unlike him, she expresses delusions. These delusions are on the whole of quite a simple nature, and are little elaborated. Her remark that she is older in the sun than in the shade is at its face value typically schizophrenic; yet it may be the expression of a normal human striving. It is reminiscent of the attitude of the spinster in

W. S. Gilbert's verse who "may very well pass for 43, in the dusk with a light behind her". She is Queen Annie of Hyde Park, happily married to a Mr. Algy, with many children. Perhaps these delusions over-express the wish-fulfilment dreams of an unmarried woman, cursed in the prime of life with hirsutism and obesity, whose judgment is now disordered by a psychosis. Her delusions do not occupy a prominent position in the total clinical picture. Yet their presence, and her progressive apathy and deterioration of behaviour, have led her to a diagnosis of dementia præcox. It need hardly be emphasized that the application of the term "dementia præcox" to all cases showing this classical triad of symptoms has little more significance than that of a convenient diagnostic label.

In both patients the deterioration of behaviour is marked and of the same type. There is good evidence that this deterioration is not dependent on a decay of intellect. The degree of intellectual preservation stands in contrast to the disorder of conduct. The slump of behaviour is not secondary to active withdrawal into phantasy and delusional preoccupation. The picture, especially in the man, suggests the organic rather than the schizophrenic reaction type.

The principal symptom in both cases is the marked lack of emotional drive which is seen against a background of symptoms and signs indicative of endocrine malfunction. It is to be noted that the signs of endocrine disorder in the man might easily have been overlooked. Yet the dysplastic physique, obesity, hyperpiesia, pigmentation and loss of sexual activity, though not marked, are suggestive. It is perhaps unwise to speculate on the exact nature of the endocrine disorder. I hope some day to examine the endocrine glands histologically and to report on them. The clinical evidence suggests excessive activity of the adrenals or of the anterior pituitary or of both. Although, in the case of the woman, it is known that the psychosis began with endocrine disorder, that is not evidence that endocrine malfunction is the only, or even the principal, causal factor.

Such a psychosis is uncommon, perhaps rare. Notkin found only 8 patients showing evidence of gross endocrinopathy out of 6,000 mental hospital patients, and 3 of these patients were mental defectives.

The parents were first cousins. This finding is important. A disease determined by recessive Mendelian factors is manifest only in persons who receive a recessive contribution from both parents, in whose constitutions the factor may be only latent. When the disease is rare, the carriers are uncommon. In such a case, a person who is a carrier will be more likely to meet a similar carrier among his own family than among random acquaintances. The finding of a high incidence of blood-related parents among many cases of a rare constitutional disease is pathognomonic of a single recessive gene determination. According to Mendelian laws, a proportion approaching a quarter of the children of parents, both of whom are carriers, may be expected to

manifest the disease. The disease will have familial incidence; the parents and more distant relatives will generally be unaffected.

These conditions are fulfilled in this family. We find the familial incidence of a rare disease in the offspring of consanguineous parents. Such an association is unlikely to be due to chance. It is therefore probable that this psychosis is in part determined by a single recessive gene.

Summary.

A sister and a brother are described suffering from similar chronic, atypical and uncommon psychoses, characterized by the insidious onset of a progressive lack of emotional drive leading to gross deterioration of behaviour and secondary decay of memory and intellect, lack of insight, and, in one case, delusional formations; associated throughout the course with signs of endocrine malfunction, dysplastic physique, obesity, skin pigmentation, hyperpiesia, hypertrichosis in the woman, diminished sexual activity in the man. High blood cholesterol and increase of red blood-cells were found in the woman. The syndrome may be described as a chronic, progressive, deteriorative behaviour-slump, associated with endocrine malfunction suggestive of hyperactivity of the adrenals or of the anterior pituitary. The parents are first cousins. It is probable that this syndrome is in part determined by a single recessive Mendelian factor.

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