GENETIC INVESTIGATIONS IN TWINS.*

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I am very grateful for the invitation of the Association to speak about the work I have been doing with twins, as it is an opportunity to thank the very many members who have helped in it. Without your kindness and co-operation the work would not have been possible. Medical Superintendents have put themselves out to make it possible for me to see patients and examine records ; medical officers have discussed cases with me ; I have been able to see the invaluable reports on family visits by social workers, and P.S.W's. have even made special inquiries on my behalf ; hospital secretaries have made visiting books and other records available, and have rummaged through dusty files for ancient case-notes, and they have added to their labours routine inquiries about twinship which have considerably enlarged my series. This help has been given not only to me personally, but also to other workers collaborating with me. For all this and more, which I have no time to mention, I want to say thank you very much.

A full account of the results of the twin study will be published in due course as a Medical Research Council Report. What I should like to do to-day is to sketch some of the findings, and discuss some special points in the interaction of heredity and environment in the causation of mental illness. Particular reference will be made to schizophrenic twins.

It has been repeatedly argued, especially in the U.S.A., but most recently by Bleuler (1951), that the contribution which twin studies can make to the aetiology of mental disorder is so limited as to be negligible. The main argument put forward in favour of this view is that incidents which occur very early in the life of the individual, especially the emotional attitude shown by the mother in his infancy, must be held critical for his later development, and for laying the foundation of a predisposition to mental disorder. As uniovular twins are more alike than binovular ones, the attitude of the mother will be the same to both of a pair of uniovular twins, different to each of a pair of binovular twins. If uniovular twins are then found to be more alike than binovular twins in respect of mental illness later in life, then this is a reflection of the greater similarity in their early upbringing.

The reply which can be made to this argument is fourfold. It is not true that in early infancy uniovular twins are more alike than binovular cases ; there is no evidence that mothers differentiate significantly in their emotional attitude to twins of the same sex ; there is no evidence that differences in the early emotional environments of twins are related to differences in the tendency to psychotic illness in adult life ; the argument itself is tendentious, and is admittedly dictated by an emotional bias.

To take the last point first : Those who advance the argument openly express the fear that, if heredity were regarded as a cause of mental illness, we should look on all such illness as predestined, and abandon hope of treating it. This is, of course, scientifically not a valid point of view to take : we should try to be guided by evidence and not by our desires. However, the fear itself is illusory. If we assign some part in the aetiology of the psychoses to heredity our enthusiasm in treatment should be unaffected. Furthermore, an examination of the facts shows that in all forms of mental illness environmental influences have to be allowed for, even if heredity also plays a part ; and it should be of practical help to discover what aspects are predominantly determined by heredity, or predominantly by the environment.

To return to the factual basis of the argument : Contrary to what might be expected, there are rather greater differences at birth between uniovular than between binovular twins. There is above all a greater average difference in weight. Owing to the fact that they commonly share the same placenta and the same blood supply, uniovular twins tend to compete with one another. If one obtains a slight

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advantage, then with a more strongly acting heart it may come to get more than its fair share of the total blood supply. Binovular twins, on the other hand, are isolated from one another, and have a better chance of reaching each its own norm. At the time of birth it is more likely that the mother will tend to differentiate between members of a uniovular than between members of a same-sexed binovular pair.

The question arises whether she does in fact differentiate between twins. My series consists predominantly of adult twins, providing evidence only of a retrospective kind; more valuable information could be obtained from the current observation of infantile twins. For what it is worth, in no case in my series is there information about any sharp differentiation made by the mother between the twins. Parents, especially fathers, sometimes take a partial attitude to their children, favouring one and not the other. This partiality is much more probable with children born at different times and children of opposite sex; mothers are much less likely than fathers to react in this way. Even fathers, however, usually regard a pair of same sexed twins in much the same way. The only likely difference to be made by the mother is in giving more personal attention to the smaller or weaker of a pair of twins, a difference, that is to say, which will be of more frequent occurrence in the first year of life in uniovular than binovular pairs.

The second point to arise is that it does not seem very likely that the psychological environment of infancy and early childhood bears much relation to the eventual development of an endogenous psychosis, such as schizophrenia. It may be a very different matter with such abnormalities as neurotic traits and psychopathic personality. In the schizophrenic twins, when the concordant are compared with the discordant uniovular pairs, there is no sign of greater similarity in the very early lives of the former than in those of the latter. A large degree of early dissimilarity may go with later concordance in respect of mental disorder.

The pair of twins in whom there was the most striking degree of early difference is a case in point. These twins, Lily and Mary, came from a psychiatrically normal family. Their father was a policeman. There were in all 11 children, our twins being the eldest, one other pair of twins dying at birth. Lily weighed 9 lb. at birth, Mary only 3½. Not unnaturally it was Mary who was breast-fed, while Lily was given the bottle. Mary was never so strong as her twin, but neither had any serious illnesses. At school they were average, but Mary won prizes. They are described as not at all alike in their ways. Mary was her dad's girl and took after him, Lily after her mother. Lily was more placid, Mary more fiery. Lily thought herself a fine lady and didn't like housework or hard work; Mary enjoyed housework and gave herself no airs. Mary would mix with anyone, Lily was too much of a madam. Both were fond of children; Mary liked animals, Lily disliked them, cats particularly. Lily hated looking after sick people and was not kind to the father, but Mary was of kinder disposition and looked after him when he was ill. Lily never liked the cold, Mary did not mind it. Both preferred men to women friends and have had many love affairs.

Both twins left home at about the age of 20, and lived thereafter together. At the same age they began to go deaf. They rather shut themselves up together, with little outside contact, and lived on very little money. They were very fond of one another, and either would be uneasy with the other away. When they were 46 Mary left her job and Lily found her another with her own firm, a caterer's. Although, unlike Lily, Mary never became psychotic to the point of requiring hospital treatment, the medical records of the firm show that at this time Mary was suffering from delusions. She had the idea that the Chief Accountant and the Assistant Chief Accountant took a passionate interest in her, and she talked of going out to dinners, dances and theatres with them. On account of these and other strange things she said she had to leave. However, she found herself other work and settled down. When she was visited eight years later she was at work and not mentally ill, but she showed some strange mannerisms, and a discrepancy of affect of a type one might expect in a post-schizophrenic patient

Lily's illness began two years after Mary's, in 1942 She had been worried by air raids, and had lost a good deal of sleep; but the proximate cause of her breakdown was an unhappy love affair. She was found one day wandering in the courtyard of her firm. She said that inner feelings told her not to go into the office to work; she was "persecuted by men" and "all men were cads." Taken to an observation ward and to a mental hospital, it was found difficult to get in contact with her because of her deafness. Her mood was bewildered and her memory for recent events was vague. She said that voices told her "don't go in there," and that she was forced to do certain things. Delusions and hallucinations persisted, she chattered to herself, gradually went downhill into a state in which she was noisy, incoherent and unemployable, but always kept herself clean and tidy. Seen in hospital in the sixth year of her illness she was entirely inaccessible, shouting incomprehensible things which themselves showed a marked degree of schizophrenic incoherence.

Now the problem arises how the similarities and the differences in the psychotic pictures shown by Mary and by Lily are to be related to differences in their early upbringing. Is it in the least plausible to say that as Mary was breast-fed and Lily was not we can attribute to that fact the greater gravity of Lily's illness ? Although the mother had a greater physical intimacy with Mary than with Lily, it was Lily who was her mother's girl, while Mary was her dad's. Both women fell ill in menopausal years, at a time when they were both suffering under a variety of stresses, the anxieties of war, employment difficulties, poor circumstances and, in the case of Lily, an unhappy love affair. Surely it is more reasonable to attribute the difference in the degree (though there is none in the quality) of their psychoses to temporally immediate rather than to temporally remote events ?

The total collection of twins consisted of 297 pairs, of which 67 were uniovular and 6 of doubtful ovularity. It was possible to use the material as a whole to test some of the factors which are commonly supposed to have a predisposing influence in the causation of mental disorder. This was done by marking in each pair one as more and one as less severely affected. The members of discordant pairs who never developed a mental illness were, of course, taken as the less severely affected ; but even in concordant pairs one member either had a milder illness, or became ill somewhat later in life. It was possible then to correlate differences in severity with differences in the incidence of predisposing factors. Very often the relevant information was lacking, so that for the examination of any single point many pairs of twins had to be left out of account. Enough were left to provide statistically significant information about several points.

The first factor which has to be examined is that of the birth itself. The stillbirth rate, neonatal death-rate and infantile death-rate are all higher in twins than in the singly born, largely because twins are on the average underweight, but also because twinship may cause difficulties in parturition. It is usually felt that the first-born of the twins has the more difficult passage, though I know of no conclusive statistical data. In any case among the first-born in my series there were 119 who had the more and 103 who had the less severe illness in later life. The difference, which is to the advantage of the second-born, is quite insignificant.

If, however, difficulties were known to have occurred during the birth, which was not often the case, a significant difference was found. Of those who had the more difficult birth more than twice as many (37 : 17) had the severer than the less severe illness later.

This is highly suggestive evidence that a minor degree of organic cerebral impairment, suffered at birth, may predispose to mental disorder. The disadvantage of those who had gone through a difficult birth was even more marked in the uniovular pairs (9 : 3) than in the binovular pairs (28 : 14). Furthermore this difference showed up in each of the four main clinical groupings, schizophrenic, affective, psychopathic and organic.

Oddly enough birth weight did not seem to be important. Those who were lighter at birth tended on the whole to do slightly better than their heavier twins. Little information was obtainable about differences in breast-feeding—as a rule either both twins or neither were breast-fed—and numbers are too small for a test.

The evidence obtained about minor physical illness was inconclusive. This is a subject to which considerable interest attaches. It may be recalled that Galton drew attention to it on the basis of his own observations of twins. He noticed that when two similar twins did develop differently it was nearly always because one of them suffered from a physical illness or accident. He wrote :

> " The effect of illness . . . is great, and well deserves further consideration. It appears that the constitution of youth is not so elastic as we are apt to think, but that an attack, say of scarlet fever, leaves a permanent mark, easily to be measured by the present method of comparison " (of twins).

Much interest in this subject has recently been shown by Swedish psychiatrists. They claim to have observed mild but prolonged neurasthenic states in both adults and children after specific fevers and other physical illnesses, and even slight but semi-permanent changes of personality. To this sort of condition they have given the name " hypophrenia." More work might well be done in other countries upon this important problem. In my material I have not distinguished between the illnesses of childhood and those of later life ; but taking together all sorts of illness occurr-

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ing well before the onset of the mental illness, it was found that of those members of twin pairs who had had more illness 44 had the graver mental state, 28 the less grave. The difference just fails to reach statistical significance.

I am not, of course, discussing here the significance of physical illness in precipitating mental illness, to which more importance attaches.

Among the predisposing causes of mental illness I should now like to mention two psychological constitutional aspects. By constitutional I do not mean necessarily genetically determined. Even with uniovular twins it is sometimes quite possible to point to one as the more and one as the less unstable or neurotic. If we confine ourselves to childhood, those who were the more neurotic at that time twice as often as not had the severer illness later on (40 : 19). The difference, however, is shown only in the binovular pairs, and so cannot be regarded as independent of genetical differences. If we take neurotic traits over the whole of the premorbid life, the difference, from one which is noteworthy and significant, becomes overwhelming. Nearly five times as often as not (72 : 15) the more neurotic had the severer illness. In the individual clinical groups the figures are schizophrenia 35 : 10, affective psychoses 6 : 2, neurotic and psychopathic states 18 : 1, organic states 3 : 2. The difference is shown just as much in the uniovular (18 : 4) as in the binovular pairs (54 : 11).

Obviously, if the uniovular pairs show this influence as much as the binovular pairs, genetical factors alone provide no satisfying explanation. Somewhere or other we must postulate the effects of environmental factors which have a double effect, first in reducing stability and giving a touch of the neurotic to the personality, secondly in prejudicing natural powers of resistance to mental illnesses such as schizophrenia.

An effort was made to classify personality differences so as to show which neurotic traits were principally at fault, and four showed up as more important than the rest : emotional lability, paranoid, unsociable and hysterical traits of personality. All these were highly significant, had their effect on schizophrenic as well as other forms of illness and, with the exception of unsociable traits, showed marked effects within the uniovular as well as within the binovular pairs.

Further than this it is not possible to go, and on the question of the nature of the environmental factors at work, physical or psychological, Freudian or Pavlovian, my guess is no better than anyone else's.

There is a second aspect of the psychological constitution which is interesting. A pair of twins of the same sex, brought up together, almost inevitably become close companions and rivals. This ambiguous relationship is not so acute in binovular twins, where there will be genetical differences leading to differences of personality, interests and activities. The more different they are the more they will tend to lead different lives, and the less acute the rivalry will be. With uniovular twins it is otherwise. They too may solve the emotional tension by choosing different paths. Lange has pointed out that one may see the gradual development of antithetical aspects of personality, even a polar difference, one, say, becoming boastful, the other shy, or one extravagant, the other economical. Relatives share in the process by emphasizing slight differences between the twins when one is compared with the other. This is a factor in the twin situation which itself leads to the development of differences, and which is stronger in uniovular than binovular pairs. Another way in which the situation may be solved is by one of the twins emerging as the dominant partner, the other as his follower. One is reminded of the interesting observations on a " pecking order " in domestic poultry, and the development of mutual dominance and submission in married couples. To a certain extent the same sort of thing, which we notice sometimes to a marked degree in uniovular twins, may develop also in binovular twins. In them too one may become relatively dominant, the other relatively submissive.

This particular trait of personality seems to be, more than other traits, susceptible to modification by environmental and psychogenic influences. Wartime experience at Sutton showed that when neurotic patients were classified by personality traits, the contrast was not so much between the dominant and submissive types as between the dominant-submissive and the independent. A man of the dominant-submissive type would tend to be dominant in one set of circumstances, submissive in another, subservient to officers, say, and domineering to men of lower rank. Whether this is true or not, the development of a general tendency to dominance or submission certainly has an influence on any mental illness which occurs.

In my material the more submissive of the two twins did conspicuously less well when assailed by either an affective or a schizophrenic psychosis. In 35 pairs the submissive twin had the more severe, in 12 pairs the less severe state. The difference was shown just as much in the uniovular pairs, though the numbers are smaller (9 : 3). In the neurotic and psychopathic pairs, however, the contrary was true. In this group submissive twins did better than their dominant partners. What is the explanation of this ?

A likely hypothesis is that the dominant one of a pair of twins develops a psychological and perhaps psychophysical constitution endowed with greater energy and assertiveness, and may thereby be better able to withstand the predominantly mentally debilitating effects of a schizophrenic illness or a depression. One might perhaps find him less well able than his more submissive partner to remain socially adjusted during an attack of hypomania—but one must remember that manic and hypomanic illnesses are much less common than depressions.

When we come to neurotics and psychopaths this extra energy of personality may not always be helpful to the subject. The Gluecks (1950), for instance, found that juvenile delinquents, when compared with a control series, were physically better built and stronger, and mentally were more energetic and aggressive. Submissiveness is an essential feature of social adaptation.

We may turn now from predisposing, and especially the pathoplastic, factors which influence mental illness to the more specific pathogenic factors. In my series there were 41 pairs of uniovular twins of which one member, the propositus, was schizophrenic. In 28 cases the other member of the pair was also schizophrenic. Making the fairest possible adjustment for age, the concordance figure can be calculated as 76 per cent. The concordance rate in binovular pairs was 14 per cent. Although Kallmann, on the basis of his immense material, finds a substantially higher concordance in uniovular pairs, our figures are not in conflict. My figures also agree quite well with those found previously by Luxenburger. Reviewing all the published material, including that of Essen-Möller, who found on a small series a lower rate, these investigations show beyond all reasonable doubt the great importance of heredity factors in the aetiology of schizophrenia. Those who insist on rejecting this evidence do so on grounds which convince one of nothing but their lack of open-mindedness. If we accept this evidence, that genetical aetiological factors must be ranked high, where does it lead us ? Does it lead us, for instance, to a fatalistic view, that the illness is predestined and nothing whatever can be done about it ?

Such a conclusion would be extremely superficial. Uniovular twins are to some extent a special case. The two members of the pair are alike in every one of their genes. If one becomes schizophrenic, not only must the other have any hypothetical specific schizophrenic genes, but he must have also all the other genetical constitutional factors which may have contributed to the outbreak of the disease in his partner. Even then in something like one case in four he will escape mental illness. Even against this heavy adverse genetical loading favourable factors of an environmental kind have been sufficient to protect him. It would be of the most immediate value to psychiatry if we could discover what these favourable features have been. Unfortunately history-taking proves a very blunt instrument for their exploration. Kallmann has pointed out how desirable it would be, on discovering uniovular twins of which one was and one was not schizophrenic, to admit both to hospital and carry out on both of them all the biological and laboratory tests which experience suggests might be productive.

Other workers who have interested themselves in schizophrenic twins have connected discordance, the health of one and the illness of the other, predominantly with physical differences. One twin bore children and developed a puerperal schizophrenia, while the other remained a spinster ; or one had a head injury or an infective illness which the other escaped. Very seldom has a marked difference in the psychological situation been held responsible. In my material I have one pair in which the schizophrenic twin had an attack of meningitis at the age of 4 which the healthy twin escaped, and another pair in which both twins had congenital syphilis, but the twin who had earlier treatment remained well while her partner became schizophrenic. In yet another pair the eventually schizophrenic twin was a heavier beer-drinker than his brother. I have one pair only in which there was a marked degree of difference in the psychological situation.

These were a pair of Austrian girls, Poldi and Friedel. Birth was normal and both were healthy as children, but Poldi was always the heavier and stronger. Nevertheless they were extremely alike and were often mistaken for one another. They were brought up in a Catholic nunnery school and were equally forward, but Poldi had more ambition and learned better. They were much alike in character and were extremely fond of one another, but Friedel was more dreamy and romantic. She was fond of reading and writing and once composed a film scenario. She did not make friends so readily as Poldi, and was less ready to trust herself, or others. However, she had no nervous symptoms till her illness. The two girls came to England from Austria together in 1935, then being 24, and took positions in families. Poldi was very happy and was treated like one of the family. Friedel was less fortunate. Her mistress was nervous and hysterical, and was always having rows with Friedel or her husband or her servant. She told Friedel she was just an ordinary maid and must not give herself airs over music. Her husband was a little kinder. At last there was such a scene that Friedel gave in her notice. Poldi went to see her and found her excited but normal. Two days later, however, she had been admitted to a mental hospital. Some months later Poldi returned to Austria, and such evidence as we have shows she has remained well. Friedel, however, never fully recovered from her initial acute catatonic state, and is at the present time deteriorated, manneristic, foolish and impulsively destructive.

The evidence suggests that the chance whether a predisposed person is or is not subjected to a physical or psychological stress may be critical for his later career. I would not like to exclude the possibility of psychoses of schizophrenic type of purely environmental causation, but would imagine that they are rare. In the majority of schizophrenic psychoses the heredity predisposition has probably played an essential role. Those without this hereditary factor would therefore be practically immune to the disease. This is essentially a much more optimistic view than that of American environmentalists, who would regard us all as equally liable to schizophrenia. Having the predisposition, however, one will not develop the disease unless other factors, environmental and genetical, conspire against one. If an effective environmental stimulus is applied, then the disease begins, but without that stimulus one may escape for good. Furthermore, the evidence suggests that once the disease has started it will progress or remit in a way that is decided mainly by factors which have nothing to do with heredity. The ultimate outcome shows no close resemblance within uniovular pairs, and other workers, such as Bleuler, have found that it is not often similar within pairs of sibs or other relatives. These ideas lead one to emphasize strongly the significance of precipitation and the importance of treatment.

A pair which illustrates the significance of certain possible precipitants, and also shows the very great difference in age of onset which may exist, is that of two twins, one of whom fell ill at 16 while the other remained well until 49.

In this case there is a family history of mental illness. The father was extremely religious and strict in his views. One of the brothers started to have epileptic fits at the age of 13, and at 25 was picked up when wandering in a confused state and taken to a mental hospital. His state in hospital seems to have been a prolonged epileptic twilight state which took some months to recover.

The two twins were girls, Connie and Ada. When they were children they were so alike that the teachers had to ask who was who. Connie was more mischievous as a child but in later years was quieter, and then also differed a little physically, being rather more of a pyknic habitus. Connie was also of a more sensitive disposition than her twin, and was more given to worrying. She was much upset when Ada left home to work, and still more so when her mother died. She was then 16. Very gradually after that her behaviour became more and more peculiar, and she took to wandering away from the house and would be found by the police in distant spots. When she was admitted to a mental hospital at the age of 27 her illness was said to have already lasted 8 years.

On admission to hospital she was depressed. She spoke vaguely of mysteries connected with her illness and of influences controlling her. She grimaced and her gesticulation was odd. At times it was clear that she heard hallucinatory voices, and she then became restless and excited; but as a rule she was dull and slow. In the course of years she became more and more withdrawn, mute, vacant, even stuporose. The hebephrenic picture took on some catatonic features.

Ada went out to work instead of staying at home like Connie. She did well and became forewoman at a printing works, but continued to live at home with her father, a quiet, respectable woman. Her father died when she was 49, and though she then moved into a flat on her own and seemed to settle down she gradually became more and more peculiar. She had difficulty in keeping jobs and had an increasing number of disputes with her neighbours. She told others that she was followed around in the streets by a man in a mackintosh, and that she could see "lights." She gave up work entirely, neglected her appearance, would throw water down the stairs in the early hours of the morning and threw milk bottles out of the window. Eventually a flying milk bottle struck a passer-by in the street and the police forced an entry into her apartment. She was admitted to a mental ward at the age of 55, twenty-eight years after her twin.

In hospital she said she could see traffic lights and posts with cross-arms travelling about the room; she was pursued by police in cars and aeroplanes; she heard voices saying "crafty old thing"; she was "intimidated for lantern-slides" and heard remarks about television. She showed herself an angry paraphrenic. Gradually in the course of years her behaviour deteriorated and she became as incoherent and inaccessible as her sister.

The similarities and differences in this pair of twins are instructive. There is a suggestion of psychogenesis in each of them, the one starting to go downhill after the loss of her mother, the other after the death of her father. The onset in one is associated with the endocrine and emotional changes of adolescence, in the other with those of the menopause. The one has an insidious hebephrenic psychosis, the other a more stormy paranoid psychosis. The final state of each is the same.

Another instructive case is that of Barbara and Ellen, girls of rather dull intelligence who went into domestic service after leaving school. Ellen is said to have contracted syphilis at 25, but she was treated and discharged cured. At some time after that she was put on probation for annoying a clergyman. At 29 she showed the first signs of mental disorder when she had been working very hard, and was admitted to an observation ward. There she said she could hear the voice of Christ Jesus telling her to be a good girl; the voice came through the window. The doctor had put electricity on her head. She had written letters to the vicar as she loved him. Transferred to a mental hospital, she continued to hear the voice of Jesus, and would preach to those around telling them how wicked they were. Within a few weeks she ceased to be hallucinated, settled down to an orderly life and was a willing worker. She remained like this for the next 11 years, without deterioration, but with occasional attacks of excitement, usually caused by a fracas in the ward. When I saw her in 1937 she was still in the mental hospital, but seemed to me to have made a complete recovery. Affective *rapport* was normal. She was willing to discuss her past delusional and hallucinatory experiences, said she had long been free from them, and put them down to mental illness. The next year she was discharged to mental after-care, and after that got a job. In 1948 the mistress who had employed her for the past five years reported she had been well all that time.

Barbara, who had also gone into domestic work, after a time gave it up and worked in a factory. Like Ellen, with whom she had little contact, she became interested in religion. At one time she assumed the name of a local Canon, and called herself Mrs. R—. She is said to have caused clergymen in her neighbourhood some annoyance, but she did not fall ill until 1947, twenty years after her twin. She then became depressed and quiet, and one day was found looking "vacant and mad" and saying that she was going to marry the parson and would next day be dead. In the observation ward she was depressed, restless, suspicious, aggressive and auditorily hallucinated. In the mental hospital she refused to answer questions, saying it was none of her doctor's business. She pointed to veins in her leg, saying that that was where "they" injected the Indian drug. Asked who "they" were, she replied, "Bear my cross, it doesn't matter." Three months after admission she was becoming more grandiose. She said she was a queen, married to the Bishop of Birmingham. She had had 26 children since she had been in hospital, having got the man's seed in a cup of spirits of salt. When I saw her in 1948 Barbara was still showing a florid paranoid picture, and talked in even and equable tones in an incoherent grandiose and bizarrely paranoid way. The flight of ideas recalled a manic state, but her manner was haughty and resentful as that of a woman who has been insulted.

The striking points about this pair are, on the one hand the considerable symptomatic resemblance in the clinical picture, on the other hand the great disparity in age of onset, and the great difference in outcome. Rather surprisingly, it is the psychosis that comes on late in life which proves much the more malignant.

One is constantly meeting such mixtures of similarities and dissimilarities in twin material, and it is not often possible to find much rhyme or reason behind it. Statistical analysis helps a little. In certain sorts of symptoms twins and other blood relatives tend to resemble one another, and in other types of symptom they do not. My case-material is rather old, and case-notes were nothing like as good in mental hospitals when the work began as they are to-day.

To take such a symptom as depersonalization, for instance. This is a rather unusual but far from rare symptom, of more than common interest. What medical officer, however, would pay it the slightest interest in the old days? It was enough for his purpose to write down the symptoms which proved the patient to be indisputably mad. Yet I have two pairs, one uniovular and one binovular, of which both members complained specifically of this symptom. Taking symptoms as a whole, there was a greater degree of resemblance between twins in respect of positive symptoms than negative ones. A depressive or manic colouring, for instance, can be regarded as a positive affective symptom, and both twins and other sorts of relative tended to resemble one another in showing or not showing such affective change. Flattening, and inappropriateness of affect, however, can be regarded as negative symptoms, and there was little resemblance between relatives here. This is all to be considered in relation with the point I have already mentioned—that the outcome of the illness and the degree of schizophrenic deterioration do not seem to be caused by hereditary factors.

Finally there is one more point I would like to mention—the difficulties of diagnosis which constantly face us. Some psychiatrists pour scorn on diagnosis, regarding it as entirely secondary in importance to psychodynamic study of the personality. I am sure that when we are dealing with the psychotic patient this is a mistaken view. The conclusion we reach about the nature of the illness from which he suffers, whether it is organic or functional, endogenous or reactive, schizophrenic, affective or epileptic, provides the fundamental basis of prognosis and treatment. In one discordant pair of uniovular twins the patient during her stay in the mental hospital was regarded as a schizophrenic. Yet I have now, never having seen her myself, no hesitation in retrospectively revising the diagnosis.

These twins are described as " alike as two peas "; they were of the same build, colouring and facial appearance and could even wear each other's spectacles. Pamela has never had any nervous symptom of any kind, and was still healthy and normal when last seen at the age of 29. Beatrice first became nervous at 13, when she developed a fear of going to bed at night. She had done extremely well at school, and was advanced two classes on returning to school from the holidays. However, she had a breakdown, and was admitted first to a general and then to a neurological hospital. While in hospital she had a violent attack, which was not considered to be epileptic. She returned home, but became worse and was admitted to a mental hospital. There she was sullen and had fits of biting herself. She tried to swallow safety-pins, coins and pencils, and she spoke of monsters looking through the windows. Consciousness was clouded and her conversation was incoherent. She recovered and went home, but soon had first a mild and then a severe relapse, in which she tried to strangle herself and to throw herself into the canal. In hospital again she would sit and stare, or scream, bite her arms and beat her head and limbs on the floor. She was thought to be hysterical. For some time after that she was quiet and inaccessible ; but she would also have hallucinated phases in which she was violent. Once more she recovered to return to school. Before she was 16 she relapsed again with a twitching in one arm. Admitted to a neurological hospital, she was thought to be suffering from chorea. Once more she went into a state of hallucinosis and violence and was transferred to a mental hospital, where attacks of clonic spasm of the muscles succeeded one another. Once again she made a complete recovery after a few weeks. Some months after recovery she attended a psychiatric clinic, where intelligence tests showed a superior intelligence but marked scatter, or irregularity of performance, suggesting an organic change. She was, however, regarded as suffering from hysteria and was treated by psychotherapy. She tried clerical work but did not do well, and became a probationer nurse. At the age of 20 her symptoms returned. She started to have shaking fits, and then passed into a state of panic terror in which she was admitted again to a mental hospital. Further attacks of violence occurred, and she was thought to be a case of Gjessing's periodic catatonia. In lucid intervals she was rational but had an affected manner. She completely recovered and was discharged. She worked as a telephonist for two years, but then had to return to hospital for attacks of violence and attempted suicide. Then, for the first time, she had a series of major epileptic attacks, culminating in *status epilepticus*; with 60 fits in 24 hours. Her life was saved by treatment, but her doctors still did not think of her as an epileptic. Describing her own feelings, she said that a queer feeling came over her in which she felt she " must do something "; she felt then as if she were in another world ; everything was confused and she saw flashes of light, dark patches, kaleidoscopic colours—" indescribable." She was given insulin treatment, which was, however, interrupted when she had another major fit. Once more she recovered, but relapsed again, sometimes smashing windows, or trying to injure herself (she bit off the terminal phalanx of one finger) or having an occasional epileptic fit. At the age of 26 she was subjected to prefrontal leucotomy, and she then improved much, becoming cheerful and rational though somewhat fatuous. She went home, but a year later she became depressed, smashed windows, and was taken to hospital, where she shortly died in *status epilepticus*.

I think that there can be no reasonable doubt that all this girl's recurrent short-lived psychotic phases were epileptic twilight states. Despite many characteristic features, especially her own description of her subjective feelings, and despite the occurrence of major epileptic fits, every diagnosis but that of epilepsy was made, and every treatment given but the appropriate medication. Gruhle has pointed out that the psychotic states of epileptics are often phenomenologically indistinguishable from schizophrenia. Epileptic fits of an occasional kind are often observed in chronic schizophrenics, especially catatonics, without doubt being aroused of the diagnosis of schizophrenia. We should perhaps be more alert than we are to the possibility of simulation of a schizophrenic state by an epileptic one.

I hope that from the sketch I have provided it will be seen how twin investigations can take us some if only a little way into the problems of aetiology. Certain broad indications emerge, but conclusive answers to precise questions of detail are not to be obtained. There is, for instance, a good deal to indicate the significance of endocrine factors, but none at all to show which aspect of endocrine metabolism is worth special investigation. This is because the data with which I worked had not been subjected to special lines of inquiry, and not because of a weakness in the twin method of investigation. It would be perfectly possible to pursue the same method with much more precision and power on material which had been carefully investigated along either biological or psychologically analytical lines.

Reference.

Bleuler, M., (1951): *Fortschr. Neur. Psychiat.*, **19**, 385.