THE INTER-RELATIONSHIPS OF MENTAL DISORDERS AND DIABETES MELLITUS.

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THE relationship between mental disorders and diabetes is studied as shown by 30 cases of mental disorder associated with diabetes, 93 cases of uncomplicated diabetes and 400 uncomplicated cases of mental disorder. This study covers, first, the psychological picture in diabetes ; second, the types and courses of mental disorder associated with diabetes ; and third, the mental symptoms with hypoglycæmia.

In a previous paper (1) the psychological factors in the ætiology of diabetes have been considered. There, also, " emotional glycosuria " and opinions as to the emotional factors in the origin of diabetes were discussed. From case studies it was concluded that psychological influences in some instances may be of ætiological significance in diabetes, as well as greatly influencing the course of an established diabetic condition.

PSYCHOLOGICAL PICTURE IN DIABETES.

Careful studies of the psychological picture in a large series of uncomplicated diabetic cases are lacking. There are, however, many references to the mental picture in diabetes. There is a preponderance of observations pointing to depression, of varying degree, and anxiety as being the most common mental state associated with diabetes (Savage (2), Stone (3), Masson (4), Neilson (5)). However, actual psychoses are comparatively rare in this metabolic disorder if one is to accept Masson's figures that 1·2 to 1·7% of diabetics develop psychoses. The source of these figures is not given, but the psychoses represent a small percentage of the possible mental disorders if one includes psychoneuroses and personality deviations which are seen in diabetics.

CLINICAL PICTURE.

Certainly, in the eyes of the internist, who sees the great majority of cases of diabetes, there is no predominance of mental symptoms present. In fact the majority of such cases do not present any conspicuous psycho-pathology

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—certainly no more so than the average group of cases referred to hospital. However, the lack of description of psychopathology in diabetics by internists may, in part, be explained by their interest in treating the disease and not the person. Consequently, unless the patient emphasizes his mental difficulties, no notice or investigation of this field is usually made. From clinical experience, it seems likely that there is a greater tendency to neurotic symptoms in diabetes than in some other large groups, but there are no figures to substantiate this impression.

In the more severe cases of diabetes, and in many of the less severe occurring in neurotic individuals, there is frequently a mental picture, which, however, varies to some extent in the age-groupings. These symptoms are most frequent in the middle period of life, less frequent in children, and less pronounced in the aged.

Perception.—The only conspicuous difficulty in this field is the tendency to *diminished alertness* and awareness of the environment, although the individual may be much more alert to his own condition and events affecting himself. This may, in part, be due to the necessary training that every diabetic patient should have to take care of himself. In the toxic diabetic patient, the most conspicuous mental symptoms are perceptional disorders—confusion, disorientation and hallucinosis.

Intellection.—In this field there are four common difficulties: (1) *Memory disorders* are most frequent. The patient complains, " I can't remember as well as I used to ", and the relatives often report on the patient's " absent-mindedness ". While these are subjective complaints in most cases, there is some evidence that memory defect and the delayed psychic response are more pronounced in diabetic patients than in non-diabetic individuals. (2) *Inability to concentrate*, with delayed response to questioning, is very frequently the complaint of the diabetic patient. (3) *Sluggish mental activity*, particularly the " mental laziness " of moderately severe diabetic patients, is often both a subjective and an objective observation. Perhaps directly associated with their emotional apathy, they lose interest in mental activities, prefer to avoid them if possible, and lack the quickness and precision of former accomplishments. (4) *Hypochondriasis*, in some form, is very frequent. They may complain of " brain pressure ", a sense of fullness in the head, heart pounding, alternating feelings of being hot or cold, directly relating every ache or pain to their diabetic condition, and innumerable other vague " functional " complaints. It is a frequent observation, specially mentioned by Joslin (16), that diabetes often occurs in children of superior intelligence.

Emotion.—As has been stated above, the most frequent mental symptoms associated with diabetes by most observers has been some form of (1) *depression.* While certainly this is very common, it does not seem to stand out in the average case of diabetes more than perhaps the earlier symptoms of memory defect and inability to concentrate. It is my impression that diabetes frequently

occurs in moody individuals, and the tendency to obesity places them most characteristically in the pyknic habitus group. Mood changes are frequent, with probably a stronger tendency to depression and moroseness, with only occasional spurts of gaiety and elation. (2) In severe cases there is *fear*, most often of their condition, with associated threatened ruin or being forsaken by friends. Occasionally cases develop *suicidal ideas* without necessarily being psychotic. Stone (3) mentions briefly two extreme cases: "A mother deliberately allowed a 13-year-old daughter, who could not control her desire for food, to go into her second attack of coma and die. In this instance the chief mental aberration was in the mother, but the child, who was quite intelligent, as diabetic children usually are, often told me she would rather die than live such a restricted life. Her preference prevailed. I know a young diabetic widow and mother, whose mother is a so-called Christian Scientist. The patient is reasonably amenable to her physician's directions, but she is more amenable to her mother's suggestions. The result has been diabetic coma five times in the last few years." (3) *Irritability* is very common, sometimes associated with temper tantrums. The relatives notice this feature in many cases as being more pronounced than prior to the diabetic state. Mothers will report it in their diabetic children as being more noticeable than in their healthy children. (4) *Apathy* and *indifference*—an emotional "flattening"—is not uncommon. The patients experience more difficulty in making themselves interested in their surroundings, activities, family and friends. (5) *Anxiety*, especially as concerns their own health, is often present. This is particularly true immediately after they have learned of their diabetic state, and have not yet accustomed themselves to the routine of weighing diets and administering insulin. The natural concern is encouraged by the very regime which they must follow—the difficulties in taking a trip, eating in restaurants, unavoidable delays. (6) Occasionally the diabetic becomes *seclusive*, even when depression may not be accountable for such a reaction. Where previously a good mixer, they gradually prefer to remain at home and away from their social contacts.

Volition.—(1) The physical condition may, in part, explain the *weakness*, with the resulting "tired feeling" and what is manifested externally as *physical laziness*. They are to some extent prohibited from very active physical activity, but much more often apparently prefer a more sedentary life than they have previously lived. They appear to shun physical effort, and not for physical reasons. (2) *Somnolence*, or at least an increased desire to sleep, is present in many cases, and rarely insomnia. (3) Ordinarily there is an increase in the *appetite*, though with emotional indifference and depression the patient frequently loses his interest in food, and with it his appetite. Rarely he may develop an aversion to food. (4) *Impotence* and *frigidity* are sometimes associated with the diabetes, though certainly not caused by it, except in extremely severe cases. The patient with such difficulties associates them

directly and causally with the diabetes, and they serve as an additional worry and source of fear. Occasionally one finds *erotic impulses*, particularly in women, which might be due to the pruritus with an unusual amount of attention and manipulation of the genitals, and occasionally to masturbation, with subsequent reactivation of guilt feelings.

To date, no psycho-analytic investigations have been made in diabetic persons. Consequently nothing is known as to the unconscious motives or associations in diabetes. The very nature of the disease in which the conscious person labours to keep himself "sweet" by metabolizing sugar, and the natural tendency of his body to make itself "sour" (acidosis), lends itself to ready associations with every individual's struggle in life. Furthermore, in view of the fact that the ætiology is largely speculative and the emotional life plays so important a rôle in its course, one may expect to learn a great deal from psychological studies of the unconscious.

Psychological Investigation of Diabetics.

In addition to the psychiatric approach, there have been two additional lines of investigation of the psychological state in diabetes—psychological tests and hypnosis. Neither of these have been illuminating, so far as they have gone. Miles and Root (6) carried out a careful study, giving psychological tests covering cancellation of digits, memory span for digits, memory span for four-letter words, and addition of one-place numbers. These tests were given to 39 diabetic patients, along with a series of controls, and it was found that the diabetic patients with hyperglycæmia and glycosuria at the beginning of treatment show a decrement of 15% or more in memory and attention tasks. This loss is in amount rather than in quality. With treatment they found rapid improvement in psychologic status, approaching but not quite reaching normal. In five long-standing treated cases of diabetes, they noted that the accuracy and quickness of movements was 20% below normal. Dashiell (7), working with one diabetic, who lent himself for the experiments, found that for strength, adding, serial reactions, and colour naming, experimentally produced hyperglycæmia and hypoglycæmia entail alterations (deficiencies) of the psychological efficiency in the same rather than opposite directions.

The criticism of such experiments, in part at least, is the fact that the psychological functioning in such tests is likely to be decreased in any physically sick individual. One is justified in saying that such findings represent the status at the time of examination, and in view of their improvement on treatment, that the inefficiency was due to the illness. It does not indicate positively that it was due to the toxic effect of the hyperglycæmia. The toxic effect producing depression, which Cowie, Parsons and Raphael (8) noted as being conspicuously relieved in diabetic children treated with insulin, led

them to give a series of depressed patients glucose and insulin. Their results were not convincing, though they found that the degree of depression may be measured by the amount of insulin necessary to bring the glucose utilization curve to that of a normal individual.

By hypnosis, Gignon, Aigner and Brauch (9) in four patients with grave diabetes who had previously been treated with insulin, were able to lower the blood sugar by the suggestion of an injection or of a better preparation of insulin. In one case the blood sugar was reduced to 0·12% and the urine became sugar-free. In six non-diabetic cases Nielson and Geert-Jorgensen (10) were unable to influence the fasting blood sugar with suggestions that the liquid given was a strong sugar solution, nor did any change appear after suggested shock.

Psychological factors producing diabetes.—In a previous paper this subject is discussed at length. In summary, Savage and Maudsley (2) believed that emotional stress could produce diabetes. Emerson (11) states that " diabetes will sometimes follow intense emotional crises, but more often is the result of long-continued worry. This in part explains, according to Solis-Cohen, the frequency of this disease in his own race ". Nielson (5) regards diabetes as a neurological disease with the disturbances in metabolism as end-results and, as such, " emotional upsets and severe mental strain apparently initiate diabetes ". Allen (12) states, " Since diabetes is presumably in most cases a functional disease of the nervous system, the possibility exists that a sufficiently intense functional influence may give rise to the disease ". Strouse and Soskin (13) infer psychological influences in the ætiology of diabetes, and go so far as to state that no diabetic patient can be successfully treated by therapeutic arithmetic, and that the diabetic diet limits must be set by a clinical and laboratory study of the individual patients. Other writers do not go this far, though there is a unified opinion that mental factors may greatly influence the disease once it has become established (Kissinger (14), Stragnell (15), Stone (3), Allen (12), Joslin (16), Foster (17), Woodyatt (18), Nielson (5), Pike (19), Cammidge and Howard (20)).

The influence of emotional factors on the carbohydrate tolerance is well shown in the following case :

CASE 19.—A woman, æt. 40, whose three siblings are all subject to headaches, one sister has a transient diabetes, and one brother had depressions. She grew up on a farm, having attended grade school with a creditable record. She married at 19 a man 57 years of age. He died 12 years later and she had a " nervous breakdown ", lasting 4–5 weeks. She developed a second nervous breakdown at 35, a lighter attack than her first, and became concerned over business worries. She married again at 38, and her husband is living, but is thoughtless of her, frequently staying away all evening, or even all night without telling her of his plans or giving any explanation. She has been unhappy much of the time since her recent marriage, and unsatisfied sexually. She has had two pregnancies, one a miscarriage, and a second with a Cæsarian operation, the baby dying. About 18 months following her marriage she developed an urticaria of her genitals, followed by thirst, frequent

polyuria, and pruritus. She became extremely irritable, and cried frequently. Four months later glycosuria was discovered which, with a diet excluding sugar, cleared. Every time, however, that her husband remained away an evening or night, or if she became emotionally upset otherwise, she excretes sugar—a fact of which she has been aware. Physically she is 38 lb. underweight, but otherwise is physically and neurologically normal. She has a hæmoglobin of 70%; other blood and serology tests are normal. Glucose tolerance curve showed a fasting blood-sugar of 0·116% with a slight accompanying glycosuria. Hourly blood-sugars thereafter were 0·354, 0·551, 0·460, 0·333, and 0·287%, all of which were accompanied by glycosuria. With diabetic education, a restricted diet and many psychotherapeutic interviews she became sugar-free, except for an occasional trace. Eight months later she reports, " I get nervous when my husband goes out at nights, but I try not to, because I know it means a set-back ".

Abstract.—An unstable neurotic woman of 40, who first married a man 40 years her senior, developed two " nervous breakdowns " in six years following his death. Remarried, unhappily, was nervous and emotionally upset frequently, and developed a severe diabetes, which, however, only showed glycosuria following emotional stimuli.

Ætiological rôle of psychic trauma in diabetes.—Allen (12) quotes Naunyn and Lépine as frequently reporting diabetes beginning with a mental shock, and Allen himself states that a latent diabetes may undoubtedly be made active by a psychic trauma. One of Joslin's (16) reported cases followed an emotional strain. Foster (17) briefly mentions Seegan's case (1870) of an officer who, acting as second in a duel for a friend who was killed, developed a depression and diabetes; and Dickinson's case (1875) of a mother who, after seeing her child fall from a window, developed depression, insomnia, anorexia, and died of diabetes ten months after. He states that he has seen cases, usually in young individuals, where the onset of the disease dated from a fright or excessive anxiety.

In the present series of 93 cases of diabetes mellitus uncomplicated by any conspicuous mental disorder, only two cases had a psychic trauma preceding the diabetic onset. One man developed diabetes four months after the death of a daughter from tuberculosis, with a second daughter critically ill with the same disease and a wife becoming helplessly crippled with inflammatory rheumatism. In a second case the patient developed his diabetes while under great stress in taking care of his sick wife. None of these 93 cases was studied from a psychological angle, yet in 10 of the cases the anxiety, worry or depression was sufficiently conspicuous to have been noted in the record.

However, as has been pointed out, these are all conscious events in the life of the individual, and in no way explain or throw light on any possible unconscious factors that might account for the origin of diabetes in certain cases. In psychiatry we have learned that many of the strange phenomena seen in hysteria, obsessional neuroses and often in the psychoses have their origin, not in the obvious external conscious life, but entirely in the unconscious.

What may be the cause of the psychological picture accompanying diabetes? In part, in severe cases with hyperglycæmia, it is probably due to actual toxic effect, though this is by no means proved. It seems possible that in some cases

there is a deviation of the individual's personality, and the diabetes is a part of that expression. The personality characteristics marking such physical illnesses as gastric ulcer, thyroid disease, hypertension, tuberculosis, are not due to the illnesses. More and more evidence is accumulating to suggest that the first three of these may be caused chiefly by emotional difficulties. From a study of the cases at hand, I concluded that the psychological picture above described, so often associated with diabetes, is perhaps sufficiently characteristic to be regarded as a " diabetic personality " reaction. Such a concept should emphasize that the diabetes is an expression of the personality rather than that the personality is an expression of the diabetes.

Relationships of Mental Disorders and Diabetes.

Hyperglycæmia and glycosuria in mental disorders.—Dealing indirectly with the subject of diabetes and mental disorder, and more directly with the problem of emotional glycosuria, several investigators have made studies of the blood-sugar and the frequency of glycosuria in various mental disorders. Kooy (21) (1919) in nineteen cases of melancholia found an average fasting blood-sugar of 0·112%, with a tendency for slight spontaneous hyperglycæmia to be present. In ten cases of schizophrenia he found values from 0·076 to 0·116—figures slightly lower than in melancholia. Wuth (22) (1921) reported fifteen cases of increased fasting blood-sugar among forty cases of schizophrenia, the average value for all cases being 0·107%. Raphael and Parsons (23) (1921), studying both schizophrenia and manic-depressive psychoses, reported that " fasting levels are well within normal range, and they, in themselves, carry little diagnostic value ". In 1923 Bowman (24) examined 229 consecutive admissions to Bloomingdale, and found the sugar content not increased except in cases of paresis and psychoses due to cardiovascular disease. In a subsequent study (1929) Bowman and Kasanin (25) examined 148 cases of varying kinds of mental disease, manifesting various emotional reactions. The blood-sugar ranged from 0·08 to 0·12%. Only nine cases, all women, showed a blood-sugar over 0·12%. Other than in these cases there was no correlation between mood and high blood-sugar content. Furthermore, in some cases an abnormally low amount of blood-sugar occurred with excitement, depression and other emotional conditions.

The conclusion from these studies is that the fasting blood-sugar level is little, if at all, disturbed by the mental illness. They might be interpreted as contradicting the emotional glycosuria theory of Cannon except that emotional states, as seen in psychopaths, are not necessarily comparable with emotional states in the normally mentally healthy individual. In both the theory and in the psychopaths, the specificity of the emotion and the unconscious motives for the response are not known, and hence the apparent, though superficial, contradiction.

That the carbohydrate metabolism is disturbed in mental disease seems well established by three sets of workers. Raphael and Parsons (23), Lorenz (26) and Henry and Mangam (27) have all shown that the glucose tolerance curve in depressions and acute cases of schizophrenia indicates a definite retardation in glucose metabolism. In marked contrast to the retardation found in these disorders is the definite acceleration of glucose metabolism in cases of manic-depressive excitement. Cowie, Parsons and Raphael (8) found they could measure the degree of depression by the amount of insulin necessary to bring the glucose utilization curve to that of a normal person. Mann (76) has reported a study of the blood sugar in 152 psychotic patients and found a sustained hyperglycæmia to be the general rule, though not specific for any type of mental condition. He found it more frequently associated with melancholia and stupor. McCowan and Quastel (77) studied the sugar-tolerance curves in 85 psychotic patients, 52 of whom were in the manic-depressive group. They defined a hyperglycæmic index to be used as a quantitative measure of departure of the sugar tolerance from normal limits. In the depressions they found the closest parallelism between the magnitude of the hyperglycæmic index and the emotional tension. They found a low hyerpglycæmic index in schizophrenia and in benign stupor ; in the manic state it was low except when the excitement was coloured with paranoid or aggressive trends. Northcote (78) found only 6 of 27 psychotic patients investigated to show a return of the blood sugar to the fasting level in two hours. In the most recent similar study by Katzenelbogen and Friedman-Buchanan (28), of 116 psychotic patients tested by the blood-sugar tolerance curves, they found a similar disturbance in all types of cases. This disturbance was regarded as a physiological accompaniment of a psycho-biological reaction.

Glycosuria produced from emotional stimuli has been repeatedly shown in animals (Boehm and Hoffmann (29), Cannon, Shohl and Wright (30), Hirsch and Reinbach (31), Fujii (32)), and seems established as occurring in man (Folin, Denis and Smillie (33), Malmivirta and Mikkonen (34), Hackebusch (35), though denied by MacLeod (36)). It seems definitely more frequent in mental disorders than in mental health. Allen (12) states that " glycosuria is admittedly frequent among the insane " and Savage states that it is " rare in insanity". Williams (37) states that " the work of an impressive company of physicians warrants the conclusion that ' alimentary glycosuria ' appears more frequently in schizophrenia than in normal individuals '', in contrast to the opinion of Reiter (38) and Hofman-Bang (39), who have rarely found glycosuria in schizophrenia. It should be added that in contrast to the opinion of these last writers, who regard the association of diabetes with schizophrenia as being very rare, several of the cases reported in the literature as well as five of the present series were definitely in that group.

The statistics available regarding the frequency of glycosuria in mental disease are more convincing. Bond (40) (1895) found 12 cases (6·85%)

in 175 new admissions showing glycosuria. Schultze and Knauer (41) noted 67% of 14 cases of manic-depressive depressions to show glycosuria, as well as frequent association of glycosuria and the depressions occurring in imbecility, schizophrenia and general paralysis. They regarded this glycosuria as of neurogenic origin " beginning with the psychic findings ". Folin, Denis and Smillie (33) found 22 (12%) cases in 192 patients examined at the McLean Hospital to show glycosuria, and in 664 urine specimens examined at the Danvers State Hospital, 58 (8·7%) showed positive sugar reactions.

The examination of a large number of urine specimens does not indicate the percentage of mental patients who showed transient glycosuria. In the examination of the admission specimen of urine in 400 consecutively admitted patients to the Menninger Sanitarium, only 12 patients showed glycosuria (3%), none of whom turned out to be true diabetics. However, in a group of 115 cases of manic-depressive psychoses, depressed phase, 7 (6%) showed transient glycosuria, suggesting a more frequent occurrence of glycosuria in pronounced emotional disturbances.

The production of glycosuria by an emotional stimulus, the disturbed carbohydrate metabolism in psychoses and the frequent occurrence of glycosuria in mental disease indicate a very close association between psychological functioning and metabolism. These associations lend suggestive evidence towards a possible psychogenic ætiological factor in diabetes.

Clinical mental pictures associated with diabetes.—A distinction must be made between those cases of mental disorder which are associated with diabetes but are not produced by the diabetes, and those cases which are toxic and probably due to the diabetes—diabetic psychoses.

There are many cases reported of associated diabetes and mental disease, and there is no uniformity in the mental picture. In the present series there are ten different mental diagnoses :

Psychoneuroses and neuroses :
- Neurasthenia, 4 cases.
- Simple depression, 1 case.
- Anxiety state, 1 case.
- Obsessional, 2 cases.
- Hysteria, 1 case.

Neurotic character, 1 case.
Senile psychoses, 5 cases.
Toxic psychoses, 3 cases.
Paretic neuro-syphilis, 1 case.
Tabo-paretic neuro-syphilis, 1 case.
Schizophrenia, paranoid type, 5 cases.
Paranoid state, 3 cases.
Manic-depressive psychoses, manic phase, 1 case.
" " depressed phase, 1 case.

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The majority of opinions and cases reported in the literature have been associated with *depression*, and, as has been stated previously, the majority of writers on diabetes have been most impressed with the occurrence of mild depression in the diabetic. The opinion that melancholia is the most common mental picture is expressed by Savage (2), Pike (19), Nielson (10), Craig (42), Janota and Stříetský (43). Masson (4) states that the form of insanity is usually depression with morbid fears for the future, delusions of worthlessness, while hallucinations are not uncommon. None of his five cases, however, were conspicuously depressed, and none of them was diagnosed as a manic-depressive psychosis. Two cases of depression are reported by Porot (44), two by Schultze and Knauer (41), one by Obarrio and Petre (45)—though associated with morphinism—and four of the cases observed by Scherer (46) were manic-depressive depressions. One case (Case 23 of this series) was manic-depressive depression, abstracted below to illustrate an indirect causal relationship, and Case 18 was a "senile agitation", with depression, which recovered. Case 3 had a mild depression, and one of the toxic cases (Case 22) had had depressed periods. The paretic neuro-syphilis (Case 13) mental picture was depression and suicidal tendency.

The *manic phase* of the manic-depressive psychosis is shown only in Janota and Stříetský's (43) report, and in that instance, with anti-diabetic treatment, the mental picture changed to a paranoid state. One case in the present series was in a manic phase, and also serves to illustrate the importance of heredity in both the mental disturbance and the diabetes (emphasized specially by Savage (2), Masson (4) and Sherer (46)):

CASE 24.—A woman, æt. 53, who has a very nervous diabetic mother, two insane sisters, and three brothers and one sister described as nervous. Two maternal first cousins were insane. She attended school until ten years of age, and then worked as a nurse girl till her marriage at 18. She has had ten children, eight of whom are living and well. She had a depression at 24, and manic attacks at ages 33, 34, 35, 37, 39 and 50. Her present illness is a manic state, the same as previous attacks, with over-activity, irritableness, restlessness. She is distractible, flighty and mischievous. She weighs 191 lb., but otherwise is physically normal. Her diabetic state was discovered at age 50 during a manic episode. It was readily controlled with dietary treatment until the present illness, when it reappeared with fasting blood-sugars ranging from 0·150 to 0·200%, and a constantly positive glycosuria. She developed a genital pruritus with much masturbation, and her conversation was continuously overtly erotic with proposals, invitations and braggadocio of her prowess. Her diabetes was again readily controlled, but with little, if any, improvement of the mental state.

Psychoneuroses are frequently associated with diabetes, though practically no reference to this is made in the literature. This may be in part explained by the fact that practically all papers on this subject have either dealt with the emotional factors in diabetes or psychoses associated with the disease, with the result that the great psychoneurotic group has only been hinted at in discussing the more extreme mental states of diabetic patients. Stone (3)

casually mentions "certain unusually unstable individuals" with diabetes whom he has treated. The remarkable case of Newburgh and Camp (47) was certainly in the psychoneurotic group. The patient was diagnosed and treated for diabetes for four months, but even though sugar-free, she had a recrudescence of mental symptoms. She was treated by Dr. Camp psychoanalytically and recovered. The whole picture was subsequently regarded as the effect of an anxiety state which had produced all the symptoms of diabetes, including the glycosuria, retarded glucose utilization curve, fasting hyperglycæmia and physical symptoms. Kauffman (cited by Klieneberger (48)) reported a case of anxiety state in the sense of Wernicke, which, however, was probably more psychotic than neurotic. Nine cases in this series were primarily neuroses or psychoneuroses.

CASE 3.—A man, æt. 49, always in good health. At the age of 32 he began having periodic attacks, once a year or less, of numb feeling in the tongue and hands, which would "go to his head" to produce a headache. He did nothing medically for this condition. About a year ago, following a hard day's work in the harvest field, he became "absent minded" in the evening; he has continued to have varying degrees of this incapacity since, though physically well. His local physician obtained no abnormal findings at first, but at a subsequent examination discovered a mild glycosuria on one urine analysis. The patient was placed on some symptomatic medication and told to refrain from eating carbohydrates. An ulcerated tooth was extracted and for a short period he was a little improved, only to have his mental symptoms become more pronounced, necessitating hospitalization. Physically he was 28 lb. under weight, and showed a definite sluggish pupillary response to light, though an entirely negative serology. His fasting blood-sugar was 91·2%, though with a definite glycosuria. With an intake of 124 grm. of glucose his hourly blood-sugars were 169·2, 129·4, 104·0 (all accompanied by glycosuria), 67·7, and 84·6 without glycosuria. Mentally he was concerned over a sister who was feebleminded and died in a mental hospital, identifying himself with her. Under expressive psychotherapy he seemed relieved of this concern, his memory cleared, and his depression disappeared. He was placed on a diabetic diet and the urine became and remained sugar-free. By the end of the month he tolerated a very liberal diet, without showing glycosuria. A second glucose tolerance test at this time showed a fasting blood-sugar of 79·7 mgrm., and hourly specimens 145·6, 42·5, 66·0 and 84·6, the first two of which showed an accompanying glycosuria, but the latter two did not.

Schizophrenia is less frequently associated with diabetes, and some authors place the chief emphasis on the infrequency with which diabetes is associated with the asthenic body constitution (Reiter (38), Scherer (46)). Cases are reported, however, by Reiter (38), Hofman-Bang (39), Klieneberger (48), Scherer (46), and Katz (79). Several of the cases mentioned below under the toxic psychoses present schizophrenic pictures. Four of the five cases of Masson's (4) report were of a paranoid state, and by many psychiatrists would have been regarded as schizophrenia. Five schizophrenic cases (5, 10, 14, 16, 17) are included in the present series, all of which were of the paranoid type.

CASE 17.—A male, æt. 44, whose heredity is unknown except that his father was alcoholic and his mother had "dropsy". He had had no schooling, having always worked as a labourer. He married at 36 and had no children. He was

moderately alcoholic and gave a history of a penis sore. He rather suddenly developed mental symptoms at 43, believing people were after him, making signs with their hands, and wanting to kill him. At times he was anxious and lacrymose, though his conversation was usually relevant and coherent. His weight was 168 lb., with a height of 5 ft. 8½ in. Physically he was well. Two blood Wassermann tests were negative, and the spinal fluid negative. Basal metabolism was + 1. His diabetes was unknown, and the urine was normal for four years following his admission to the hospital. He became more disturbed than usual and his urine showed glycosuria 2·2%. The fasting blood-sugar was as high as 250 mgrm., but was 192·3 mgrm. two weeks after treatment was initiated, and fell at successive examinations over the following three months to 144·9, 122·17 and 109·3 mgrm. At first insulin was given, 10 units daily, but gradually this was eliminated. Shortly after this time he was given a hospital job fitted to his capacity, which he accepted, became much interested and improved remarkably. With his mental improvement his diabetic picture improved, and his discharge was effected nine months after his diabetes had appeared, at which time his delusions as well as diabetes were not apparent.

Senile psychoses are occasionally associated with a diabetes, usually of a mild type. The diabetes is regarded as promoting the arterio-sclerosis, and the most prominent diabetic authorities (Joslin, Woodyatt) do not regard arterio-sclerosis as causing diabetes. Redlich (49) in 1903, and more recently Masson (4), calls attention to the fact, however, that arterio-sclerosis produces the mental failure quite apart from the diabetes. This is undoubtedly the case in many instances, though not invariably. Reiter's (50) case, which had at first been diagnosed as an incurable arterio-sclerotic affection, recovered, and improvement was associated with diabetic improvement under dietary care. A very remarkable case in the present series of five cases (7, 8, 18, 25, 26) is very similar.

CASE 5.—A woman, æt. 63, well-educated and a social leader, but self-centred and with poor judgment regarding her financial management. A depression with suicidal threats was precipitated by a refusal on the part of her relatives to give her more money without a better accounting. The depressive mental picture on hospitalization at about three months after the onset of her illness was one of agitation, perplexed anxiety, restlessness, insomnia and delusions that ruffians, Indians or negroes were coming after her to carry her away, mistreat her, torture her, perhaps kill her. For six months after the onset of the illness there was no evidence of diabetes, when suddenly, during a very excited episode, she developed marked glycosuria, which continued in varying degrees with fluctuations in her mental picture despite dietary measures and varying dosages of insulin. The diabetic state never remained under satisfactory control during several months of episodic excitement and agitation. Unfortunately a satisfactory glucose tolerance curve could not be made until some eight months after her admission, at which time she was much improved and co-operative, but still receiving 10 units of insulin three times a day. At this time the fasting blood-sugar was ·110% without glycosuria; at subsequent hourly examinations ·263%, ·241%, ·150% and ·079%, with all of which she showed glycosuria. From the 20th to the 24th month she was much improved mentally, and did not require insulin, but became more agitated and required insulin again for the following twelve months in varying dosages. With many psychotherapeutic contacts she became free of her fears, agitation and delusions, and re-established social contacts and became happy. During the last six months she returned to her normal mental picture, received no insulin, and her diabetes disappeared. She showed no glycosuria on a diet free in

carbohydrates. Two years after her discharge, when last heard from, she was happy, managing her own affairs, and showing neither mental nor diabetic symptoms.

Paranoid state is at best an unsatisfactory psychiatric diagnosis, and yet serves to indicate the predominant mental pathology. It is particularly important in this study to find three cases (4, 9, 15) with such a diagnosis, and, in addition, all five of the schizophrenic cases were of a paranoid nature, three of the senile psychoses cases were primarily paranoid in their mental content, and two of the three toxic cases presented paranoid delusions. In all, 12 of the present series of 30 cases showed a paranoid set of delusions as the conspicuous mental content. Further, four of the five cases reported by Masson (4) were decidedly paranoid, as was Sherer's (46) case, both cases reported by Singer and Clark (51), one of Schim van der Loeff and Barnhoorn (52), that of Klieneberger (48), and Janota and Stříetský's (43) case became paranoid with anti-diabetic treatment. White (53), in discussing diabetic psychoses, states that " although the mental picture is usually a depression, persecutory delusions are frequently developed ".

CASE 16.—A woman, æt. 51, without hereditary taint of either diabetes or mental disease. She was fourth of a family of eight. She had a common school education, and married happily at 29, having two children, who are both well. She had been failing in her mental efficiency for ten years before admission, and for the last fifteen months believed some one was going to kill her. Voices have told her she was to be killed, and also instructed her to kill her daughter. She would awake at night screaming and cursing. Physically she was well, weighing 133 lb. Blood and urine examinations were normal until she had been in the hospital for nine years. Glycosuria was then noted, and for the next two years her urine was constantly positive, with 5·5% to 0·65% glucose, despite dietary efforts. The next year it became slightly less, and the fourth year usually negative. The fasting blood sugar varied during this time from 180 to the highest of 319 mgrm. per 100 c.c. The patient would never adhere to her diet, and there was no conspicuous change in her mental picture. She died at 65 years of age, 14 years after her admission to the hospital and five years after the onset of her diabetes. The immediate cause of death was a cardiac embolism, and the pancreas showed the typical pathology of diabetes mellitus.

The high incidence of paranoid delusions in this series, as well as in reported cases, is very unlikely mere coincidence, but only a very large number of observations can elucidate this point. Schim van der Loeff and Barnhoorn (52) conclude that paranoid symptoms should be included in the characteristic mental picture, believing their origin to be in an exaggeration of trends in this direction prior to the existence of the psychoses. Their significance is certainly not clear, and until a group of such cases can be studied with a view of ascertaining the unconscious motives and associations, the relationship to diabetes will be obscure.

Toxic psychoses associated with, and presumably due to the diabetes, are regarded as being rare (Bonhoeffer (54), Ewald (55), Klieneberger (48), Masson (4), Scherer (46), Singer and Clark (51)). All of these writers have reported

such cases, as has also Laudenheimer (56), Janota and Stříetský (43) and Schim van der Loeff and Barnhoorn (52) (four cases). Harris (80) explained this rarity on the basis that the brain oxidizes and hence utilizes the available carbohydrate more effectively than other tissues, and hence mental symptoms in diabetes are rare. Sittig (57) describes a case of Korsakoff's syndrome on the basis of the acidosis associated with diabetes. The criteria for so classifying such a case, according to Schultze and Knauer (41), are: (1) the diabetes must have been present before the psychosis; (2) other essential causes for the psychosis must be absent; (3) the psychosis must run parallel with the diabetes; (4) through anti-diabetic treatment the diabetes must improve and the psychosis must recover. Not many of the above reported cases adhere strictly to these criteria, particularly as to the recovery of the psychosis. Further, the "essential causes of a psychosis" are rarely obvious, certainly if we are going to refer to schizophrenic and cylothymic disturbances. Ewald (55) suggests differentiation by an energetic use of insulin, but some cases remain distinctly toxic with delirium, even though the diabetes is under control.

Much of the literature regarding diabetes and mental disorders centres around this important, though narrow, aspect of the disease, i.e., whether diabetes can cause a mental disorder of a psychotic nature. Most of the reports of such cases are based on the obvious toxic state of the patient, with the characteristic perceptual disorders (confusion, disorientation, hallucinations and delirium, often with delusions), rather than conforming to the criteria that the diabetes and psychosis must run parallel. There are cases of both types, i.e., those in which the mental picture runs parallel with the diabetes, and those in which it does not, but it cannot be proven that the latter are not toxic psychoses related to the diabetes. This group of toxic cases, to be regarded as diabetic psychoses, represents a small percentage of the number of cases in which diabetes and mental disease are associated.

There were three cases (20, 21, 22) in the present series regarded as belonging to the toxic psychoses, as exemplified by the following:

CASE 21.—A man, æt. 57. A college education, married, but much marital unhappiness. Found to have diabetes seven years previous to his examination, but having felt well, took no treatment. He developed leg pains and came for treatment. A glucose tolerance showed very high blood sugar levels—331 mgrm., one hour 647 mgrm., two hours 579 mgrm., three hours 628 mgrm., four hours 524 mgrm., and five hours 415 mgrm. per 100 c.c. He was treated with diet and insulin, and symptoms disappeared. For eighteen months he continued treatment and then again neglected himself. After five months of neglect he reported with gangrenous left toe. He was hospitalized, but lived only two months. There was a slight extension of the gangrene, which then dried, but with some sloughing of the side of the foot. Despite insulin and diet, his blood sugar repeatedly fluctuated above normal—as high as 300 mgrm. For approximately two weeks prior to his death he became very confused, disoriented and delusional. His delusions centred chiefly around his clothing, believing he had lost it, that someone had stolen it a year ago. His remote memory remained fairly intact, but recent memory was very unreliable. He developed pneumonia and died. Autopsy findings disclosed no

brain changes, but those of pneumonia and diabetes. The possibility of toxic absorption from the gangrenous area as the cause of his mental symptoms seemed unlikely to several physicians who saw him at this time. Except for the last two days he was afebrile. The day prior to his death his urine was free from sugar and acetone, although his blood sugar mounted to 415·0 mgrm.

Causal relationships of mental disorder and diabetes.—In considering the question of causal relationships between these two conditions, a sharp distinction must be made between the time of onset of each disorder and the relation one may have to the other as a causal factor. There are three relationships with regard to the time of onset: (1) the mental disorder and the diabetes appearing together; (2) a mental disorder appearing in a diabetic individual; and (3) diabetes appearing during the course of a mental illness. In the first instance it is possible that the mental disease may cause the diabetes, that the diabetes may initiate the mental disease, or that they both may appear as the expression of a common cause in the form of some organic disturbance. In the second relationship, certainly many of the mental disorders so appearing are not due to the diabetes, and in the third type it is equally true that the mental disorder does not necessarily give rise to the diabetes.

Several classifications of the causal relationships have been suggested, though some of these are confused by consideration of the time of origin. Laudenheimer (56) made four groups: (1) Diabetes and a psychosis occurring together, unassociated, and more or less accidentally; (2) diabetes following a psychosis; (3) diabetes causing a psychosis; and (4) diabetes and a psychosis from a common cause. Masson (4) suggested three groups: (1) Diabetes as a passive accompaniment or complication of a psychosis; (2) psychoses due to diabetes; and (3) cases in which diabetes exists and through arterio-sclerosis causes cerebral deterioration. He is considering the possible relationships with psychoses only, and not less severe mental disturbances. Pike (19) suggests three groups: (1) Cases where brain disturbance is the common cause of both conditions; (2) diabetes as purely a physical complication of the mental disorder; and (3) toxic psychoses due to the diabetes.

It should be pointed out that all these groupings consider only the severe types of mental disorders, and for this reason are inadequate. That diabetes may be merely a passive accompaniment or purely a physical complication to a mental disorder is within the range of possibility, but is based chiefly on the findings that the course of mental disorder does not run parallel with the diabetic picture. Cases are reported which show an inverse and even alternate relationship between the two conditions, and so the fact that we are unable to demonstrate a correlation between the conditions in some cases does not justify the assumption that there is no relation, and that they are merely co-existing independent entities. The facts that both conditions are gross total-organism reactions, and that the effects of the metabolic disorder of diabetes, even "uncomplicated", as well as any major mental disorder, are

felt and reflected by every organ system of the body, would strongly suggest a definite, even though obscure, inter-relationship.

In the light of information gained in the present study, as well as from a fairly complete study of the literature, the following groups based on causal relationship are suggested :

1. Diabetes as a result of psychological disturbances, appearing either with the mental disorder or during its course. This condition might more accurately be designated as a carbohydrate metabolism disorder rather than diabetes.

2. Mental disorders due to diabetes, particularly the autotoxic reactions, occurring during the course of a diabetes.

3. Mental disorders and diabetes arising from a common organic cause, particularly tumours, injuries or hæmorrhage, affecting either the brain or pancreas.

4. An indirect causal relationship, in which the worry, concern and expense of a diabetic condition initiates a psychopathic process, or, on the other hand, a narcissistic individual ignores a known pre-diabetic tendency and develops his diabetes.

5. A group of cases in which the two illnesses are associated, but the relationship between them is obscure because of indefiniteness or ignorance of their time of onset, the lack of information regarding the psychological and physical factors at the time of their original association, or difficulties in establishing co-relationships in their subsequent courses. In this group must fall the cases in which extraneous factors have an obscure influence—heredity, arterio-sclerosis, involution, indirect thyroid and pituitary influences and probably others.

Group 1 : *Mental disturbances causing diabetes.*—This group has been discussed in the preceding paragraphs on the psychological factors in diabetes. In this study there were five cases (3, 4, 10, 17, 18) in which the mental disturbance appeared to be an important ætiological factor in the diabetes, and conformed to the arbitrary requirements (in a previous report (1)) of such a relationship : (1) Obvious psychopathology was evidenced prior to the development of the diabetic state ; (2) the mental picture was quite different from the toxic state occasionally seen in either hyperglycæmia or hypoglycæmia ; (3) the course of improvement of the mental picture was paralleled by the glycæmic and glycosuria levels, with fluctuations in these as emotional upsets occurred in the psychic life ; (4) the metabolic disorder was indicated by a persistent glycosuria (without dietary control or insulin), retarded glucose utilization curves of the blood-sugar, and a response to dietary, and in some cases insulin therapy ; (5) with mental recovery, the diabetic condition cleared, requiring neither insulin nor rigid dietary treatment.

At present, other than these five, there are no similar cases of diabetes reported in the literature in which the psychogenic factors have been considered, except following emotional shock. The cases studied lent themselves particularly well because of the obvious psychopathology. That more subtle

and less conspicuous psychological pathology may be a causative factor in many cases of diabetes seems possible. Except for the case of Newburgh and Camp (47) (from which they subsequently withdrew the diagnosis of diabetes) no reported case of diabetes has been investigated psycho-analytically. Until a series of such have been so investigated, the psychological ætiology will not be entirely proved or refuted.

Group 2: Mental disorder caused by diabetes.—In a previous paragraph on toxic psychoses, it was pointed out that occasionally diabetes does produce a toxic mental state. The cases reported, however, both the three in this series (Cases 20, 21, 22) and others, were all severe mental disturbances. Case 21 is abstracted above to illustrate the toxic psychoses. The other two are herewith abstracted:

CASE 20.—A woman, æt. 50, with migrainous mother, sister, brother and aunt, and "nervous" mother and sister. The patient has had no serious physical illnesses, but diabetes for seven years, treated only with diet. Four weeks previous to the onset of mental symptoms she had influenza which marked the onset of a neuritis of the shoulders. Two weeks following the influenza (and two weeks before her admission to the hospital) she began to wander about the house seeing that everyone was in bed. She thought her son-in-law and the maid were too interested in each other. A week before her admission she became more seclusive, mentioned that she thought someone was abusing her, and although religious, ceased saying her prayers. She worried about money spent on her, felt sure she would not get well, and might as well die. She complained of dysuria. Physically she was fat, and had a discolouration of the skin, burnt sienna colour, especially in the folds of her body and extremities. She had a left convergent strabismus (of years' standing). The thyroid was enlarged, but showed no evidence of hyperactivity, and she was never sufficiently co-operative to obtain a basal metabolism. Mentally she was confused, disorientated, unco-operative, and although no sedatives were given her, remained sluggish, somnolent. Because she was known to be diabetic, she was given a diabetic diet immediately on admission, and only showed glycosuria the first day. However, she presented a blood sugar of 0·2% even without glycosuria. The clinical picture is further confusing because she persistently showed a small amount of albumen in her urine with no casts, but many pus-cells. She was shortly transferred to another hospital, where the treatment was continued, and she recovered entirely. Because of the previous influenza attack the diagnosis of encephalitis was considered, but was not borne out by physical findings. At the second hospital she was diagnosed as psychosis with somatic disease.

CASE 22.—A farmer, æt. 68. A brother died of paralysis at 35. He has used alcohol moderately for years. He has had headaches lasting a few hours for a year. Until a year ago has farmed actively, although for years has had difficulty in getting along with his neighbours. Ten days before his admission he consulted his doctor because of weakness and shortness of breath. His blood-pressure at that time was 70/35, and his urine negative for albumen and sugar, though he had repeatedly shown sugar. Eight days before admission he had a severe chill, but no other disturbance. Four days before admission he rode into the town, having decided he would go to the hospital, and was clear mentally. He showed sugar on this next day. He became delirious and violent the next two days and was transferred to our hospital. Physically he was weak, showed a chronic blepharitis and marked hyperæmia of the sclera; teeth extremely unhealthy, erythema and œdema of the meatus urinarius and adjacent area, and a blood-pressure of 165/80. He was unable to stand, and the right pupil was larger than the left. There was hyperæsthesia to touch, pain and temperature in hands and feet below the knees (not

paralleling any nerve distribution). He was confused, disorientated, talked of his family having poisoned him, and showed decided emotional dulling. His urine showed much and consistent glycosuria. A glucose tolerance curve two weeks after his admission showed a fasting blood sugar of 0·204% and 0·272% in one hour and 0·250% at the second hour. Spinal fluid examination was entirely normal. There was marked anæmia, varying as low as 40% hæmoglobin. With dietary treatment he improved, and in five weeks was clear mentally, though keeping strictly to his dietary therapy. He was discharged as mentally recovered, and a year subsequently we learned that he was driving his own car, looking after his business, and was generally well.

To what extent diabetes may be responsible for the personality deviations so often associated with it is not yet conclusively shown.

Group 3 : *Mental disorder and diabetes from a common cause.*—Ever since Claude Bernard in 1855 demonstrated that injury in the floor of the fourth ventricle could produce a diabetic picture, it has been repeatedly noted that tumour, hæmorrhage, or injury to this or even associated areas gave rise to a marked glycosuria. (An example of such a case is given in a recent clinical-pathological study (58) of a ruptured cerebral aneurysm, which, because of lack of localizing signs, was at first diagnosed as diabetic coma and the patient given insulin.) Tumours of the pancreas also give rise to both mental and diabetic symptoms. Yaskin (59) reported a series of four cases of carcinoma of the pancreas, in all of which the conspicuous first symptoms were mental—depression with crying spells, anxiety, insomnia and anorexia. Joslin (60) has recently stated that 4% of all carcinomata occurs in the pancreas, but 13% of carcinomata occurring in diabetes is of the pancreas.

Group 4 : *Indirect causal relationship*, where the concern about the diabetes precipitates the mental disturbance, or the unstable individual with a known diabetic tendency permits it to develop. In this apparent relationship between the two conditions it appears that one of them precipitates the other. The superficial evidence, however, in both instances possibly only serves to hide an unconscious motive of self-destruction—" focal suicide " (61). This is often suspected by the physician, but probably could not be definitely proved except by minute scrutiny of both the conscious and particularly the unconscious motives.

Case 23.—A woman, æt. 57, unmarried, and a factory worker all her life. Her leg had been amputated because of diabetic gangrene a year previous to her mental breakdown. Five months after the leg amputation, her niece, with whom she lived, married, and the patient became depressed, accusing the niece of not caring for her any more. She expressed suicidal wishes. She was financially pressed, and the expense of her insulin, lack of funds for special food, and her forced inactivity on account of her leg, are given as the cause of the manic-depressive depression which developed. (In this case the method of obtaining her expressed wish of suicide seems to be very definitely *via* her diabetes.) In this connection suicidal attempts in diabetics by taking excess of insulin have been reported by Secher (62) and Beardwood (63).

Group 5 : *A group of cases in which the relationship* between the mental disorder and diabetes is *obscured* by lack of information regarding the history,

psychological and physiological data ; and further, by an inability to evaluate other possible ætiological factors, such as heredity, involution brain changes, with or without cerebral arterio-sclerosis, thyroid and pituitary factors. With regard to heredity, we are confused by a mass of statistics, both in the fields of diabetes and mental disorder. In psychiatry the recent tendency of opinion is to place far more importance on the environmental factors in development than on heredity, but this may be due in part to the impossibility of evaluating the importance of heredity and in any way altering it. But the facts themselves do not conclusively prove the inheritance of mental disease according to Mendelian laws. Heredity in diabetes is also regarded as an important ætiological factor, and yet heredity studies in adult diabetic patients are unreliable and practically worthless, since it is very rarely possible to obtain the data regarding the relatives. In Joslin's (60) studies of diabetic children treated over some ten years, he found a history of hereditary influence in 53% of the cases. But this still leaves nearly half the cases without this factor, and no measurable factor of its actual ætiological significance in the cases where it is present. So the state of our knowledge of hereditary influence in these conditions separately, to say nothing of their associated picture, contributes to cloud and confuse the ætiological relationship.

Mention has been made, under the discussion of the senile psychoses associated with diabetes, of the possible rôle of arterio-sclerosis.

Disturbances of the thyroid have been recognized by even conservative surgeons to be, in many cases, psychological in origin. But the thyroid picture is sometimes confused with diabetes, and " often only therapy distinguishes between thyroid and pancreatic glycosuria " (Rabinowitch (64)). Contrary to the more widely accepted opinion, John (65) makes no distinct differentiation between the thyroid and pancreatic glycosuria. But that the two may fuse and complicate the picture is indicated by Joslin (16), who states that " hyperthyroidism precedes diabetes so much more frequently than diabetes precedes it, that its (hyperthyroidism) place in diabetic ætiology is assured ". There are undoubtedly many cases scattered through the literature similar to one reported by Emerson and that of Newburgh and Camp (47), in which there is a close relationship between a psychogenic thyroid disturbance and a diabetic picture.

Pituitary disturbances and relationships are also recognized as having a very close association with glycosuria and diabetes. Approximately 25% of acromegaly cases have an associated diabetes, and many without glycosuria have a high sugar-tolerance curve. Recent experimental work has demonstrated even a closer relationship between the pituitary and pancreas. Houssay and Biasotti (66) showed that hypophysectomized dogs were extremely sensitive to insulin, and that a minimal dose might induce hypoglycæmic shock ; and, further, that pancreatectomy in a hypophysectomized dog produces only a mild form of diabetes. Barnes and Regan (67), following

up the same idea, prepared such a dog in which no glycosuria appeared after removal of the pancreas, and found that the administration of one of several pituitary extracts would cause glycosuria, which disappeared when injections were discontinued. The associations of mental disturbances with pituitary disorders (68) are less distinct than with diabetes, and the psychological factors entering into their production seem much less evident.

Inter-relationship between Psychic and Diabetic Disorders in the Progress of the Diseases.

A study of the relationships of the courses of the two conditions throws some light on the ætiological relationship between them. The course relationship between the mental disorder and diabetes sifts the cases into five groups: (1) Parallel improvement and fluctuations; (2) inverse relationship in which the one disease improves as the other becomes more severe; (3) alternate relationship, in which one of the conditions disappears as the other appears; (4) a change in the type of mental picture with treatment of the diabetes; (5) no apparent relationship, in which the mental disease may improve without changing the diabetic state, or, as more often occurs, the diabetic picture is controlled without apparent effect on the mental picture.

Group 1.—Parallel improvement and fluctuations in the course of the mental disorder and the diabetes. In the present series of cases this relationship was used as one of the essential criteria of a possible psychogenic diabetes. It has been made the chief criterion for the diagnosis of a true diabetic psychosis by Schultze and Knauer (41), and Schim van der Loeff and Barnhoorn (52). Cases showing such a parallelism are reported by these writers, in addition to the case of Klieneberger (48), two by Masson (4), and two by Porot (44). An opinion that parallelism is the most frequent relationship in the course of the two conditions is expressed by Pike (19) and Nielson (5). This opinion may, in part, be influenced by the very frequently cited evidence of diabetic specialists that, in the average diabetic patient, the course of the disease is parallel to the emotional events in his life.

As inferred from the discussion in the last paragraph, parallelism in the course of the condition may be regarded as indicating a primary causal rôle to either condition. Consequently it is chosen as *prima facie* evidence for a possible psychogenic diabetes as well as for a diabetic psychosis. So far as the psychogenics of diabetes is concerned this evidence is not entirely valid, as will be pointed out in the discussion of the alternate relationship. In many cases there is only a slight, though definite, parallelism between the two conditions. In the present series of 30 cases there were 14 cases showing parallelism, 2 of which were much less closely parallel in their course than the others. This might be assumed to be possible, because it would be expected that the mental picture might slightly improve with a correction, by treatment,

of the diabetes, and yet it is apparent in the larger group of cases that control of the diabetes does not necessarily change the mental picture.

Group 2.—Inverse relationship in which the mental symptoms or the diabetes may improve as the other condition becomes more pronounced. The evidence is not entirely clear as to the exact nature of this relationship, since, in the cases reported, the diabetes has been judged entirely by the amount of glycosuria, which does not necessarily indicate the state of the blood sugar. Singer and Clark (51) reported two cases of diabetes with a toxic brain disturbance, in both of which the acute toxic symptoms coincided with diminution in the amount of sugar in the urine.

CASE 25.—A woman, æt. 73, whose family history, so far as known, is negative for both mental disorder and diabetes. She married a drug addict at 17, and, after the birth of two children, divorced him. The diabetic history is vague, but it was known to exist for several years, with various treatment efforts, and at least two "cures". Since the age of 60 she has been irritable, cantankerous and forgetful, and has written to high governmental officials accusing her relatives of plotting to kill her. She has shown periodic excitement and intense irritability. She is physically well except for a marked general arterio-sclerosis. Her weight is 9 st. 9 lb. She presents extensively systematized delusions of persecution toward her children and friends. During her hospitalization the insulin dosage had to be changed many times, varying from 10 to 60 units daily. She fluctuated between periods of being calm, quiet and pleasant (at which times the amount of insulin necessary to control the glycosuria had to be increased) and periods of extreme agitation and noisiness, at which times the urine was sugar-free on from 10 to 20 units less of insulin.

The mechanism in this case, as well as those of Singer and Clark, is not clear. Psycho-analytically one might postulate that the re-direction of the libido to external objects, in her excited periods, decreased the amount directed towards her body metabolism, which occurred in the absence of provocative external irritating stimuli. However, the most provocative stimuli were entirely within her own psychological life, for she did not see her friends nor relatives. Other patients and attendants did serve as immediate identifications, whom she accused of being agents and co-persecutors.

Group 3.—Alternate relationship, in which the diabetes or the mental disorder disappears on the appearance of the other disease, and thus one seems to replace the other. There were no such cases in the present series, but Savage and Masson both report them. Savage (2) cites the details of four such cases, two in which the diabetes alternated with melancholia, one in which the patient had neuralgia and diabetes, both of which disappeared during a severe depression, only to reappear following the mental recovery. A fourth case of general paralysis had a diabetic condition of long standing, which disappeared with the development of the organic brain disease, but reappeared before the fatal termination of the disease. One of Masson's (4) cases (No. 2) developed acute mental symptoms of a paranoid delusional type slightly before the disappearance of a diabetic affection, and these seemed to be a substitute for it.

This group might be regarded as the extreme example of the inverse relationship described above, in which the one disease has entirely replaced the other. The same psycho-analytic explanation is here clearer—that in such cases the libido is entirely directed in one instance upon the psyche and in the other on the metabolic disease. That such cases might be due to psychological conflicts is supported by the kaleidoscopic picture-changes seen in hysteria, where one body manifestation, such as a stocking anæsthesia, may be entirely replaced by another manifestation, such as a body or facial tic.

Group 4.—A change in the type of mental picture with treatment of the diabetes. That the diabetes and the mental disease are directly causally related seems positive in such a case as related by Janota and Střítesk̀ý (43). A 34-year-old woman, of the asthenic type, developed a hypomanic mental picture shortly after the first symptoms of diabetes, although the diabetes was not recognized until after the onset of the psychosis. With treatment of the diabetes with insulin and diet, the mental picture became paranoid and depressed, the entire illness lasting three and a half months. The authors regarded it as a true diabetic psychosis, even though it did not conform to the diagnostic criteria of Schultze and Knauer of parallel improvement in the two conditions.

Group 5.—No apparent relationship between the mental disorder and the diabetes, and either may improve without changing the status of the other condition. Because diabetes lends itself to a very direct control with diet and insulin, the great majority of cases in this group are those in which the mental symptoms were not apparently influenced by the improvement in the diabetes. Theoretically, it might be expected to find diabetic cases in which the mental symptoms cleared without this influencing the severity of the diabetes. Practically these are not permitted to occur, because the diabetc symptoms can be controlled, and not to do so would be gross neglect.

In the large group of cases (of which there are thirteen in this series) in which the mental symptoms are not influenced by the diabetic improvement, there are five instances in which the diabetes was inadequately controlled. Not only did the mental state of the patient preclude co-operation in the treatment of his diabetes, but often he made active efforts to violate his diet. In these cases, consequently, the relationship between the progress of two conditions might have been changed had it been possible effectively to treat the diabetic condition. In four other cases of this series the diabetic condition was adequately controlled, however, without changing the mental picture, and in one the diabetes became a negligible factor without requiring even dietary care, without change in the mental picture. It should be pointed out that if the diabetic condition were possibly psychogenic, it might be expected to clear or at least be controlled, without changing the mental picture. In four cases in this group only a clinical study was made in the office, and there was no opportunity for either an observation period or follow-up examinations or reports.

Mental Picture in Hypoglycæmia.

In five cases previously reported, in which it was concluded that the diabetes was due to psychological conflicts, it was noted that the sugar threshold of the blood in three of the cases was around 100 mgrm. per 100 c.c. and 125 in a fourth. These seem to correspond with similar cases reported in a study by Hoxie and Lisherness (69). In a series of 307 cases in which routine glucose tolerance curves were made, they found 95 cases with a fasting blood-sugar below 0·07%, and in 50 of these 95 cases the glucose curve did not rise above 0·2%. In 23 cases they found a blood sugar below 0·07% in which sugar appeared in the urine. Mental disturbances were present in 36 of the 50 cases, 3 of whom showed glycosuria and 33 did not. Besides pointing out that the glycæmic level is independent of the glycosuria, they concluded that the hypoglycæmia is the result of the general nervous state rather than the cause of it. The same point is made by Ashe, Mosenthal and Ginsberg (70), and they illustrate by case studies that there may be no symptoms with a very low blood-sugar (0·3%), and yet there may be symptoms of hypoglycæmia with the blood-sugar at accepted normal levels (0·75 to 0·83%).

The mental picture in hypoglycæmia is a conspicuous part of the syndrome. In an extensive though rather uncritical review of the behaviour aspects of hypoglycæmia, Kamper (71) quotes Leyton that in a study of 500 cases of hypoglycæmia the more important symptoms are the mental changes. Several good studies have been made of the nervous and mental manifestations in hypoglycæmia (Bassoe and Traut (72), Meignant (73)), and their relation to hyperglycæmia is suggested by the psychological observations of Dashiell (7) on an experimental subject, from which he concluded that the psychological efficiency is altered in these two conditions in the same rather than opposite directions. Harris (81) has contributed much to define the clinical types of hyperinsulinism, including the report of one case of psychosis, and Stone (82) has recently reported a spectacular case of hypoglycæmia with psychotic episodes.

So-called " insulin psychoses " have been described, as the result of insulin therapy in diabetics. Oppenheimer (74) reports two types of hypoglycæmic reactions which have occurred in 2·7% of his insulin-treated diabetics: (1) An organic focal reaction with motor aphasia, apraxia, rigidity, perhaps laughter or crying; and (2) true psychotic forms resembling hysteria, manic reaction or schizophrenia. Gravano (75) goes so far as to classify the types of insulin psychoses into the four most frequently encountered clinical forms: (1) Those characterized by a manic attack, which are most frequent and are attended by motor and mental excitement. He reports three such cases. (2) Hysteria-like manifestations. (3) A confusional form, resembling a delirium. (4) A form characterized by automatisms. This last type is described also by Ashe *et al.*, in which the patient loses conscious control with resultant

irresponsible actions, such as getting lost, exposing himself to great dangers, wandering about a theatre during the performance, eccentric and senseless remarks. Scherer (46) regarded his case as a possible example of the insulin psychosis, with a history of three transient psychotic episodes associated with hypoglycæmia, following the last of which the prolonged schizophrenic reaction occurred.

Conclusions.

1. Certain fluctuations of a specific type occur with sufficient frequency in diabetic individuals to suggest a descriptive picture of the " diabetic personality ".

2. Diabetes does not determine the type of frank mental disturbance that may be associated with it, except in a small percentage of cases referred to as toxic psychoses or true " diabetic psychoses ".

3. That psychological conflicts may be an important ætiological factor in many cases of diabetes seems very probable. That they may actually cause the diabetes in some instances is unproven, but suggestive.

4. Gross psychological trauma may initiate diabetes, but the more important unconscious conflicts might conceivably be the cause of the entire picture, even in these cases, and possibly operate in some instances to produce diabetes in the absence of any external event or situation.

5. Mental disorder and diabetes never occur independently in the same individual. They may occur independently at different times, but once associated, they bear a relationship to each other.

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