Note on the Pathogenesis of Diabetic Insanity.

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TRUE diabetic insanity is a rarity, and when it occurs does not always take the same form. But it is by no means uncommon to meet with certain lesser mental abnormalities in diabetes which are very constant in character; and what is usually regarded as the typical variety of diabetic insanity is simply an intensification of these abnormalities probably due to inherited or acquired cortical instability.(2) Hence this psychosis derives its interest from the definiteness of its ætiology and the constancy of its symptoms.

Many diabetic patients develop by degrees a morbid "listlessness and depression of spirits, weakness of mind, and peevishness of temper" (Saundby), and in some few instances this becomes accentuated into a form of insanity which, in the words of Maudsley, "is inclined to be of a whining and wailing character, tedious and chronic, largely hypochondriacal in its complexion,"—a description which I can corroborate in the main from observation of a case recently under my care.(3) This peculiar form of weak, lethargic melancholia, with impaired intelligence and peevish irritability, may therefore be accepted as the characteristic psychosis of diabetes; but it is not peculiar to that disease, being met with also in anæmias and states of general cachexy, and where, as in phthisis, emphysema, and some forms of heart disease, there is imperfect aëration of the blood. It may therefore be taken as the special psychosis of defective supply of nutriment, but particularly of oxygen, to the brain, this deficiency of oxygen being one to which the cortical nerve-cells have been shown, by experiments with carbon monoxide, to be peculiarly sensitive.(4)

The anatomical changes in diabetic brains support the conclusion, derived from the symptoms, as to the atrophic origin of the psychosis. Not only has chromatolysis been found in such brains by Marinesco and others, but still more numerous naked-eye observations show that wasting of the convolutions, with consequent widening of the sulci, enlargement of peri-

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vascular spaces, and other changes, are common occurrences; and these changes were found to a very marked degree in the brain of one of Clouston's two cases of diabetic melancholia which was examined, and which, though that of an adult woman, weighed only 38 oz.(5) Clearly, therefore, the mental symptoms are due to a gradual failure in function, ultimately leading to atrophy, of the brain; and as it is acknowledged that the changes in the central nervous system in diabetes are, with the exception of some rare focal lesions, of secondary origin, it may be instructive to inquire how they are produced.

Stress was laid above on the importance of a proper supply of oxygen to the brain, because it seems to me that it is the failure of such a supply to which the cerebral lesions and the symptoms may mainly be ascribed—a failure which I believe to be due, principally at least, to the appropriation of much of the oxygen by the glucose circulating in the blood. It is true that in some cases a marked reduction in the number of red cells has been found, but it is doubtful if this would, of itself, be sufficient to account for the symptoms, at all events in the majority of cases.

There is not wanting evidence in support of this hypothesis. In the first place, the presence in diabetic blood of a substance with marked reducing powers has been shown sufficiently by the fact, discovered by Williamson and confirmed by numerous others, that such blood is capable of decolourising methylene blue—a reaction attributed by nearly all observers to the glucose, which is the most powerful reducer of all the substances known to exist in such blood. Weak solutions of glucose, moreover, produce the same result, which I have obtained in a few minutes with a 0·4 per cent. solution rendered feebly alkaline with sodium bicarbonate. The reducing substance, therefore, is probably glucose. Supposing now, as seems almost certain, that glucose acts in the same way upon the hæmic oxygen, its effect might conceivably be to reduce some of the hæmoglobin. I have found that a solution of glucose as weak as 2 per cent., rendered slightly alkaline with sodium bicarbonate, and kept at about body temperature, will reduce the hæmoglobin in time, though not for many hours. As this solution contains much more glucose than has ever been found in the blood (the highest percentage

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detected by Naunyn being 0·7),[6] the result of these experiments does not at first sight seem to lend much colour to the hypothesis. But beyond the fact that a weak solution of glucose will reduce hæmoglobin, no conclusion can fairly be drawn from these results. The presence of numerous other bodies in the blood and its rapid motion render it incomparable with simple solutions *in vitro* (solutions, moreover, which were not in the first instance effectively deoxygenated, and which, in most cases, were exposed to the atmospheric oxygen); but in addition there is another consideration which must be taken to account. Every student of chemistry knows that in working with very dilute solutions a reaction is greatly delayed in its inception, but once started will progress rapidly. In the blood, the supposed reduction of hæmoglobin would be continuous. For these reasons the time and strength of solution required *in vitro* are not valid arguments against the occurrence of reduction under the ordinary conditions in the diabetic body, apart from the fact that the blood from the right side of the heart must contain an enormously larger amount of sugar than that of the general circulation. Lastly, it may be mentioned that some observers have found the red cells to stain badly with methylene blue, which may conceivably be due to the sugar which they contain,[7] though, on the other hand, the corpuscles, when separated from the plasma, are stated to have little or no effect upon methylene blue in solution.

There is therefore every probability that some reduction of the hæmoglobin does take place; but, in addition to this, it must be borne in mind that the glucose comes into intimate contact with the hæmic oxygen under two other conditions,—first, when the oxygen is free in the plasma of the pulmonary capillaries on its way to the corpuscles, and secondly, when it is redissolved after being liberated from the hæmoglobin, to be conveyed to the tissues; and there can be little doubt that a good deal of this free oxygen is absorbed by the sugar, more especially as, on leaving the hæmoglobin, the gas is in the energetic nascent state. The following would therefore be the order of events:—The blood from the right side of the heart, loaded with sugar from the hepatic and portal circulation, and 1° or 2° higher in temperature than that in the left side, encounters free oxygen in the pulmonary capillaries as it seeks to reach the corpuscles, and levies toll of it first. During the

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course of the blood through the brain and circulation generally, the hæmoglobin is being robbed of a certain amount; when the energetic nascent oxygen is set free in the systemic capillaries for the use of the tissues, a further portion is absorbed, and possibly combination may take place even in the tissues. There can therefore be little doubt that a sensible diminution takes place in the amount of oxygen available for use by the tissue cells, the vital activity of which is lowered in consequence; and, as the metabolism of the cortical cells is already very low,[8] they feel this deprivation more than those of other organs.

From all these considerations, then, clinical, pathological, and chemical, we are, I think, entitled to conclude that chronic reduction of the oxygen supply to the cortical cells is in all probability the principal cause of the characteristic insanity of diabetes, aided though it no doubt is by general malnutrition, due to the operation of the same cause on the other tissues (as shown by the numerous atrophies which are so marked a feature of the disease), and also by other influences.[9] One is tempted to assume that the resulting degeneration and ultimate atrophy of the nervous structures is simply due to disuse, or rather diminished use; but the process is probably more complex.

(1) Read at the General Meeting, July 24th, 1902. — (2) Under the latter head may be included exhaustion by mental work and worry.—(3) "Glycosuria and Insanity," Case I. *Med. Press and Circular*, Jan. 1st, 1902.—(4) L. Borri, *Rivista di Medicina legale*, ecc., Oct. 15th, 1897. (Recension by Chiozzi in *Riv. di Patolog. nerv. e ment.*, Dec., 1897, p. 552).—(5) *Lectures on Mental Diseases*, p. 657, 5th ed.—(6) "Der Diabetes mellitus," Nothnagel's *Spec. Pathol. u. Therap.*, Bd. vii, Th. vi, p. 150.—(7) Naunyn, op. cit., p. 243.—(8) L. Hill and D. N. Nabarro, *Journ. of Physiol.*, vol. xviii, p. 220.—(9) Raimann (*Wiener klin. Woch.*, 1901, p. 513) has found that the power of assimilating sugar is reduced in melancholia, so that alimentary glycosuria is more readily produced. It is thus possible that a sort of vicious circle may be established in diabetic insanity.

The Care of Idiots and Imbeciles. By J. H. SPROAT, M.B. (Lond.), Senior Assistant Medical Officer, Somerset and Bath Asylum.

THE question of better provision for the care of idiots and imbeciles has of late been one of some prominence in the more

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