refers to a paper by De Souza and himself.[4] They injected sugars into the blood stream, and collected the urine passed immediately afterwards. The one merit of the method employed is that the blood is not extravascular, but as a means of demonstrating the presence of such an enzyme in the blood the method does not lend itself to any conclusions. It is unlikely that more than a proportion of the injected sugar would be changed into a reactive form in the time allowed (five minutes); further, the sugar excreted would presumably be that which was unchanged, and therefore useless to the body during that period; further, if any change was observed it could not be a proof that an enzyme was present in the blood.

After a careful study of the figures given by Hewitt and Pryde in their paper,[3] it is reasonable to conclude that the rotations observed with isotonic and hypertonic solutions were of the same degree as those observed with hypotonic. It is stated that in the case of hypertonic and isotonic solutions a specific rotation below +40° was not recorded. No figures are given, but this statement implies that changes of that order were observed. In the absence of fuller details, it would appear from the figures 1 and 2 that only about a quarter of the sugar originally introduced into the intestine was present when the fluid was removed for polarimetric examination. Supposing that a quarter of the sugar remains in the intestine when an isotonic or hypertonic solution is introduced, then the observed alteration in rotation required to change the *specific* rotation from +52.5° to +40° would be 0.34° for the isotonic solution, and 0.50° for the hypertonic solution of glucose employed, or alteration of rotation (not *specific* rotation) very similar to, or even larger than was observed, according to the figures, which are stated to "show the optical changes most markedly." It is a curious fact that marked changes should have been observed in hypotonic, and not in isotonic solutions. The authors state: "Contact with the mucous membrane of the living intestine probably effects the production of γ glucose in excess of any amount normally present in glucose solutions which have attained a permanent specific rotation." Were it a genuine effect due to an enzyme in the intestinal cells, it would be likely that the most marked change would be observed in the isotonic solution in the short time allowed (five minutes), since, presumably, changes in the body preferably occur in fluids isotonic with the tissues—for example, perfusion experiments are always performed with approximately isotonic solutions. On the above reasoning precisely similar alterations in *observed* rotation (not *specific*) must have taken place in hypo-, iso-, and hyper-tonic solutions of sugars, but only in the case of hypotonic solutions do these differences lend themselves to the elaborate treatment which they have received in this paper, owing to the fact that a small difference in *observed* rotation of a hypotonic solution makes a large difference in *specific* rotation. A conclusion derived from neglecting inconvenient facts with the acceptance of others is of questionable use. The conclusions drawn from these facts were only given in the following paper,[4] in which they state: "It may be presumed on *a priori* grounds that a structural change of the nature referred to has some fundamental reason."

Further doubt is thrown on the work by the admitted difficulty in seeing through the fluid for polarimetric observation, a difficulty which becomes obvious when the wide variations in the successive readings are noted; incidentally, the readings are given to three places of decimals. Small reliance therefore can be placed on the one laevo-rotation observed. No copper-reducing value of the sugar is given; the statement is merely made that it agreed remarkably well with the final rotation.

The one experiment recorded in which fructose was used may be adequately explained by temperature variations, to which this sugar is notoriously sensitive. There is evidence that fructose is more rapidly utilized in the body than glucose, presumably because it is more rapidly converted into normal blood sugar. It is remarkable therefore that Hewitt and Pryde attained such little success with the use of fructose.

Hewitt rightly observes: "The dangers attending the use of permanganate with biological material are obvious." The technique adopted by these authors when using permanganate has been briefly referred to by us as being not above suspicion.[8] They omitted to perform the only conclusive test—namely, a comparison between the rates of decolorization at the beginning of the experiment, and at the end when the sugar had attained equilibrium. The italics used in discussing their experimental method hence have not the importance the authors attach to them.

We may conclude that the experimental evidence put forward by Hewitt and Pryde does not support Hewitt's recent contention[2] that "they showed with some certainty that γ glucose and γ fructose are formed and can be detected when the stable α and β isomerides are in contact with living intact intestine." We are glad to note that the possible significance of their experiments performed three years ago has not escaped Hewitt, and that experiments are now in progress on the diabetic organism. We feel that it is necessary to point out the above facts in order to correct any doubt on our work which Hewitt's criticism may have caused.

Summary.

1. There is definite evidence that a reactive sugar is present in the blood.

2. There is no chemical evidence that γ glucose is formed in the body.

3. There is definite evidence that some of the blood sugar of diabetics is fundamentally different from that of normal persons.

4. No evidence at present exists that the intestine plays an essential part in the causation of this difference.

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THE TREATMENT OF GENERAL PARALYSIS BY MALARIA.

BY

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A SHORT account of the treatment of general paralysis of the insane by infection with malaria was given by Dr. E. W. Scripture at a meeting of the Medico-Psychological Association on November 23rd, as reported in the BRITISH MEDICAL JOURNAL of December 9th, 1922 (p. 1121). The principle depends on the fact that remissions in chronic disease may occur after an attack of an acute specific fever. Many methods of producing fever artificially have been tried, with varying results, but Wagner-Jauregg, quoted by Pilcz,[1] has drawn up a scale of efficiency of the various methods used as follows: (1) chemical substances—for example, sodium nucleinate; (2) toxalbumins—for example, tuberculin, staphylococci; (3) acute disease; the last is the most efficient. With tuberculin treatment Pilcz[3] obtained a remission in 26 per cent. of his cases, and eight remained well three years after treatment. The treatment by malaria gives a much higher percentage of remissions. During a recent residence in Vienna as a post-graduate I had an opportunity of seeing some of the clinical results, which are very encouraging.

The method consists in the withdrawal of from 2 to 4 c.cm. of blood from the vein of a patient suffering from benign tertian malaria (whether the patient be in the febrile stage or not), and in its subcutaneous injection into the subject of general paralysis, who will develop within about a week typical attacks of malaria. He is allowed to have ten to twelve such attacks, when the malaria is cured by the administration of quinine in doses of 1 gram for three days in succession; then in doses of 0.5 gram for fourteen days. In no case did the malaria persist; it invariably cleared up after the first few doses of quinine. During the febrile attacks and occasionally after, there is very often an exacerbation of mental

symptoms, consisting chiefly of auditory hallucinations and delusions of persecutions. In the majority of cases these symptoms promptly disappear when the febrile attacks have terminated. Following upon the febrile attacks and going parallel with the quinine treatment, weekly doses of neo-salvarsan are administered intravenously, commencing with 0.3 gram; six doses in all are given, in the scale of 0.3, 0.4, and four of 0.6 gram.

Of the 350 cases treated down to February, 1923,[2] complete observations were made in 296 only. Of these, no fewer than 202 showed remissions of varying degree, and 112 showed complete remission with the disappearance of former mental disturbances and a return of former business capacity; 68 per cent. showed remissions, and 38 per cent. complete remissions, and this in spite of the fact that many advanced cases were included.*

Of especial practical importance is the time during which remissions persisted. Of the patients who had complete remissions, 3 treated in 1917 are still actively employed at business and show no evidence of relapsing. These remissions are therefore of five years' duration. In 17 the remissions have already lasted two to three years, and in a further 34 treated correspondingly later the remission has persisted for one to two years. Of the total for whom complete remission has at any time been claimed 3 only have relapsed or have shown any tendency to relapse. Of those for whom incomplete remission has been claimed the majority were far advanced forms of the disease, and yet even here much benefit was seen, particularly in the cessation of acute symptoms and in the non-progression or even regression of the dementia. Of those showing all the signs of an already present dementia many again became sociable and inoffensive, and regained a certain degree of occupational ability.

Several of the German clinics have already made a trial of the method, with good results. Weigandt[4] reports that of 50 cases treated by this method remissions were obtained in 88 per cent., and good remissions in 48 per cent. The remissions do not follow immediately upon the febrile attacks, but very often show a gradual progressive course over a period of weeks and even months, so that cases which at first seemed incomplete, when re-examined months later showed complete absence of symptoms. One very remarkable fact is that there is no parallelism between the clinical and serological findings. Many who show a complete remission of symptoms still give a positive reaction in blood serum and cerebro-spinal fluid, and yet the same cases, when examined months later, have shown a negative Wassermann result in both. In connexion with this Gerstmann[2] quotes a case treated by the tuberculin-mercury method in 1909 in whom a complete remission still persists. When examined recently the report was: Wassermann reaction positive in the blood and cerebro-spinal fluid; globulin test positive; lymphocytes 186.3.

In this country and in some others the difficulty consists in obtaining suitable cases of benign malaria for purposes of inoculation. Once a single case has been inoculated there is then no difficulty in transferring the infection to other paralytics, and though this involves the transference of syphilitic blood, yet, in cases which have been thoroughly examined and found positive for syphilis, this is of little consequence. The method of continuous transference has been practised in Vienna, where two strains of plasmodia are being used—one after having been passed through 58 hosts, and the other through 38, in both cases without any reduction in the virulence of the infection. Attempts are being made to keep the parasite alive outside the body; so far it has not survived for more than eight hours. The latest report[2] from the Wagner-Jauregg clinic contains an interesting account of the histological findings in the case of a patient treated by malaria who died of intercurrent disease. The authors seek to draw conclusions from the greater infiltration of the temporal lobes as to some extent explaining the occurrence and persistence of the auditory hallucinations mentioned. In general the histological changes in cases which had shown remission under malarial treatment were those of the so-called stationary paralysis of Alzheimer, with an almost complete absence of the changes usually found in progressive general paralysis.

* These figures are given in a personal letter from Dr. Gerstmann, and differ slightly from those in the *Zeit. f. d. ges Neur. und Psy.*

The proportion of complete remissions (38 per cent.) is high for general paralysis, but it is certain that with cases treated at an earlier stage than many of those included in the Vienna figures this percentage would be much higher. Professor Wagner-Jauregg[5] goes so far as to say that in cases of short duration entire success can be predicted with almost absolute certainty. Whether this be justified or not can only be determined by a widespread trial of the method.

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Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

A SMALL EPIDEMIC OF PLAGUE.

THE epidemic here reported occurred on an India-going vessel. It began on March 7th, 1922, nine days after the ship left Karachi, the last port of call. There were six cases, all among the lascar crew of the ship; no Europeans were affected.

Case 1.—A Goanese steward, aged 32, was taken ill on March 5th, 1922; he was first seen on the morning of March 7th. He complained of intense pain in the small of his back, with severe frontal headache, and had vomited twice during the night. His temperature was 103°, his pulse rate 120. His temperature rose the same night to 104.2°, and he became slightly delirious. There were no physical signs in the chest or abdomen. Towards evening vomiting became incessant. Next day the patient's general condition somewhat improved, but vomiting was still incessant. On examination an exquisitely tender small bubo was found in the left groin. The diagnosis of plague was made on discovery of this bubo. Towards evening the patient became markedly worse, and was delirious at intervals. He continued so until death occurred on the afternoon of the following day.

Case 2.—A native sailor, aged 32, first seen on March 15th, had a large bubo, which was hard and somewhat tender, in the left groin. The constitutional disturbances were very slight; fever was absent, the pulse rate 90. Next day his temperature rose to 100°, and the patient showed some degree of lethargy. Without his condition apparently altering he died suddenly soon after midnight.

Case 3.—A native sailor, aged 35, was seen first on March 15th, but had apparently been ill for two days before. He was obviously very ill when first seen, with a temperature of 103°. There was some enlargement of the inguinal lymphatic glands on both sides, but no tenderness. He died suddenly the same evening.

Case 4.—A Goanese steward, aged 37, reported sick on March 19th, just as we were going into port at Port Said. His temperature was 100.8°, his pulse rate 100. There was a small tender bubo in the left axilla. He was sent ashore as a case of suspected bubonic plague and died three days later.

Case 5.—A native sailor, aged 35, was taken ill on March 24th, and was first seen on the morning of March 26th. He had a temperature of 104°, pulse rate 124. In his left groin was a large, exquisitely tender bubo. He was seen on the following morning by Dr. Duval, assistant M.O.H. for Dunkirk, who confirmed the diagnosis and supplied serum, which was given daily in doses of 50 c.cm. This was the first supply of serum which we had had. On March 27th the patient was very weak, and in the evening he sank into a low delirium. Next day he was in a typhoidal condition, having a weak irregular pulse, muttering constantly, and taking food and stimulants only with much persuasion. On March 29th he was still in a very collapsed state, and on March 30th the Dunkirk authorities consented to take him into hospital, where he died the following day.

Case 6.—This case may have been a virulent pneumonia, but I have added it under the impression that it was really a case of pneumonic plague. The patient, the galley cook, aged 41, was taken ill during the night of March 29th; he was first seen on the morning of March 30th, when his temperature was 104°, his pulse rate 132. He had a slight, often repeated cough, with expectoration of blood-stained sputum; there was marked cyanosis and embarrassment of breathing (respiration rate 42). In the chest there was nothing to be detected, save a few râles at the bases of both lungs. The temperature continued to rise to 106°; by evening the patient became worse, and died at two o'clock the following morning.

The origin of the outbreak was not traced; very few rats, dead or alive, were seen on the ship, and even after fumigation with sulphur dioxide at Dunkirk only about half a dozen rats were discovered. If the infection were from man to man, which is said by the Royal Commission on Plague to occur only in 3 per cent. of cases, the first patient had a much longer incubation period than usual, as he had not been ashore for thirteen days previously (in Karachi), whereas the usual incubation period is said to be from two to five days.