# FAULTY DETOXICATION IN SCHIZOPHRENIA.*

By J. H. QUASTEL, D.Sc., Ph.D., F.I.C., and W. T. H. WALES, M.R.C.S., L.R.C.P.,

(From the Cardiff City Mental Hospital).

[ABSTRACT.]

THE hippuric acid excretion test (after benzoate administration) has been used by previous workers, with the general result that it affords a reasonably accurate and satisfactory test for determination of parenchymatous hepatic damage and of various hepatic involvements. The test is also known to be indicative of hepatic disorder, even where no clear clinical signs of hepatic or renal derangements are observable. A series of 67 cases of mental disorder has been examined by the test, 45 of which belonged to the schizophrenic group; 18 of these were classed as catatonics. The average value of hippuric acid eliminated in the non-catatonic schizophrenic group, expressed in terms of benzoic acid, in 4 hours after administration of 6 grm. of sodium benzoate, was 3·4 grm. with an average deviation from the mean of $\pm$ 0·4 grm. This value agrees well with the values obtained by previous workers for normal cases having no hepatic damage. The average value of hippuric acid eliminated under the same conditions by catatonic patients was 2·2 grm. with an average deviation from the mean of $\pm$ 0·5 grm. All the catatonic patients studied, without exception, showed a diminished ability to excrete hippuric acid at a normal rate. It is inferred that a metabolic disturbance of the liver affecting benzoic acid detoxication may be a characteristic feature of catatonic patients.

Work on benzoic acid detoxication in catatonic patients before and after various shock treatments for schizophrenia is in progress.

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## Discussion

Prof. F. L. GOLLA said that the Association might congratulate itself on a remarkable session in which it had had two papers of importance, one of them giving an almost dramatic turn to their work as psychiatrists from the therapeutic point of view. One paper might be regarded as a pendant to some of Dr. Quastel's earlier work, all of which seemed to point in one and the same direction, namely, to some disturbance of the metabolic functions, probably attributable to a liver disturbance. There was one caution he desired to give. Some years ago he was using precisely the same method and gave it up, switching over to thiosulphate, with which he got very much the same results. But he went a little further. At about that time Hans Fischer had pointed out that the specific dynamic action of proteins was absent, and had said that that established a means of differentiating between schizophrenia and manic-depressive psychosis. Fischer's experiments accordingly were repeated, and there proved to be a much delayed absorption. This delayed absorption in the four hours he had given for the observation had led Fischer to suppose the absence of the specific dynamic action of proteins. With all diffidence he would suggest that in dealing with these phenomena it was necessary to make sure that they were not here investigating slow absorption. If they went back to the beginning of the pathology he thought the interpretation might well be that, as in every other process, whether $CO_2$, sugar curve, or anything else, these schizophrenics reacted very much more slowly than other people, but the reaction did eventually take place.

As regards Dr. Gjessing's paper, the feeling one had was that for the first time probably one had a definite somatic treatment based on somatic pathology for a certain—possibly very limited—class of patient. Dr. Gjessing had warned them that there was only a small number of people exhibiting particular symptoms in whom with the thyroid treatment it was possible to alter the course of the psychosis. Here again a word of caution was necessary. It would be the most unhappy thing that could result from such splendid work that people should run around talking about endocrine glands or endocrinology, as if they had to deal with this or that gland functioning improperly, and had only to use the proper hormone to improve the mental state of the patient. If the treatment they had heard about and were going to hear more about at the next day's session had any meaning at all, it seemed to him that it meant that in the majority of these psychotics their cortex radius was as good as in anybody else, but what had happened was that it had been possible to wake up the centres that governed the waking and sleeping activity of the cortex. As long as that was borne in mind it would be possible to put quite a different interpretation on such results as Dr. Gjessing had brought forward—not thinking of them in terms of disturbances of glands, but remembering that in the centres which governed cortical activity there were centres which governed water metabolism, oxygen metabolism, and the heat production of the body. These things should be recorded, in the careful and meticulous way Dr. Gjessing had done, and the disturbances looked upon as the outward and visible signs of disturbance of the diencephalon.

It was known that when asleep the body went on accumulating carbon dioxide, there was an inversion of the hydrogen-ion metabolism, various other bodily functions underwent a complete change, there was hyperactivity of the parasympathetic system—in fact during sleep there was a dropping off in very much the same way as in these cases. It was known that there was a centre in the hypothalamus which could be stimulated, in man by the giving of barbiturates, or in the cat by injections. The interpretation of all this was that here they were dealing with the outward and visible signs, not of glandular disturbance, but of disturbance of that part of the vegetative nervous system which innervated these glands and

looked after them and kept them up to their duties. They might go on cutting sections of the thyroid and the liver and so on, but he did not think very much would be found, because this was a functional disturbance due to imperfect control of part of the nervous system. As psychiatrists and neurologists they had to take the nervous system seriously.

Dr. P. K. McCowan confined himself entirely to Dr. Gjessing's paper. In the spring he had had the pleasure of visiting Dr. Gjessing's hospital in Norway, and was much impressed by the painstaking accuracy and patience with which he had carried out these researches over twelve or thirteen years. It was with much diffidence that he suggested any criticism of his paper, but it seemed to him that it was very important to ask whether there was any possibility that this work might not have the pathological significance which he was inclined to place upon it. Was there possibly some physiological explanation of some at least of the results he had been able to obtain? In such an extremely important subject as the pathology of schizophrenia everyone was intensely interested, and that was why he felt justified in putting forward just that faint suspicion.

With regard to the diet which Dr. Gjessing was giving his patients, was it possible that some of his results were due to the fact that, while his diets were sufficient for a normal individual, they became in fact starvation diets when the patient passed into his excited phase? He had mentioned the caloric value of his diet in his paper of 1932, and he thought that if it was the same diet this was a possible explanation. That explanation fitted in with some of the curves he had just shown. Some of them could be explained on the ground that the diet was sufficient in the normal phase, but not in the excited phase when the patient was using up his nitrogen excessively. He wished to know whether, having that in view, Dr. Gjessing had tried the effect of giving a much more abundant diet, and whether he had tried out normal individuals under the same experimental conditions, the excessive day and night restlessness of the excited patient being made up in the normal person by excessive expenditure of energy and perhaps artificially induced insomnia.

Dr. Gjessing replied, saying that he felt it very important, in the first place, that no research work of this kind should be carried out until all focal sepsis had been removed. In 1932, at the time of the publication of his earlier paper, this part of the subject had received inadequate attention, and patients had a good deal of infection. The other thing he wanted to point out was that in a disease so phasic and capricious as schizophrenia, so called, it was of very great importance to investigate the patient daily for a long period. He did not think this special work with catatonics was of such great value; the material was good, but the group was very limited.

With regard to Dr. McCowan's points, he himself was of opinion at first that these large nitrogen outputs in the excited state might be due to the excitement itself. But was this really the case? Amounts equal to 800, 1,000 or 1,200 calories more had been given and the patient's weight had risen 12 kilos, but nevertheless the same periodicity obtained. Even if the patient were given double the amount he needed, the periodicity of his psychical mood continued; but if the patient were given so many more calories then he was neither so well awake as before nor so deeply asleep as before—in other words, the case became more mixed, or less well defined. These catatonic stupor patients who were lying quiet and in whom the amount of movement day by day and week by week could be measured, nevertheless showed a bigger output of nitrogen. It might be said that there was some rigidity, but he did not think the rigidity could account for the bigger output. The degree to which the motor system acted on the output of nitrogen was, he confessed, an unsolved problem.

As to having normal controls, he had not had normal controls for these elaborate investigations, but nevertheless this work would have to be done some time when he had opportunity. But he did not think the normal controls would show the same

thing. They would not show stuporous or excited phases, as these patients did, nor that when more nitrogen was given in the food the periods were made shorter, and when less nitrogen was given, were made longer.

Dr. QUASTEL, in reply to Dr. Golla, said that he and his colleagues were quite aware of the fact that it had been stated that in schizophrenia there was a delayed absorption of glycine which had been held to account for this dynamic action. They had actually considered this question, whether their results could be interpreted by delayed absorption of either benzoate or glycine. In the case of one patient they had been giving increasing quantities of glycine without effect on the hippuric acid secretion. His own feeling was that from a study of Dr. Reed's papers and their own results, if there was a fault in absorption it lay, not with the glycine, but with the benzoate. Whereas in the past this question of absorption had been debated as applying to schizophrenics as a whole, in their own results it seemed to apply rather to catatonics. It seemed clear that catatonics showed a delayed absorption; the majority of schizophrenics did not. Among their own patients these catatonics did differ from other schizophrenic patients in regard to benzoate and the peculiar characteristics relating to absorption.