

1 in 3 patients. Wetterberg cannot support the suggestion that either schizophrenia-like or manic-depressive syndromes are predisposed to by AIP; nor does the presence of the gene tend to mental retardation.

Contrasting with the sober garb of Wetterberg's report, the second book under review is a profusely illustrated glossy brochure in a purple cover. In it Dr. Macalpine, Dr. Hunter, and Professor Rimington put forward the interesting theory that the mental illness which affected George III was a form of porphyria. There are four contributions to this book, and in the first, by the two first-named authors, acute intermittent porphyria is offered as the true diagnosis of the King's psychosis which has previously generally been taken to be manic-depressive. With admirable enterprise and industry the authors sought out and studied authentic historical documents which have been passed over, it seems, by the historians. The case they make is a plausible one; it could perhaps have been improved if they had given us more detail of each of the attacks of illness separately. The psychiatrist will, however, be inclined to concede that the King's mental symptoms do fit a psycho-organic syndrome better than a manic-depressive one. In the second chapter Professor Rimington joins the two psychiatric authors to show that two descendants of George II who have been traced can be definitely identified as porphyrics. The diagnosis for them and for George III is now varied to one of porphyria variegata, which is the South African and not the Swedish variant. In the third chapter a professional historian, Dr. John Brooke, acclaims the significance of the findings in the historical context; in the fourth Professor Goldberg gives a short and pithy statement, which could with benefit have been considerably expanded, on the porphyrias in clinical and metabolic aspects. All these contributions appeared originally as articles in the *British Medical Journal* or were commissioned by it. Since their appearance there has been a very lively debate in the correspondence columns of that journal and some searching re-examination of the evidence. This, on the whole, has not supported the hypothesis put forward by the authors.

This is certainly very entertaining, but one should remember a clinical diagnosis is one thing, and a historical diagnosis another. The latter cannot be substantiated in the way that the first can. It is not for the reviewer to express any opinion on a matter on which Professor Rimington and Professor Dent are unable to agree; but two comments may be made. From the point of view of the geneticist, the genealogical links, which join Mary Queen of Scots down the ages via George II and George III with the contestably porphyric representatives of the House of Hanover living today, offer little substance for the repeated diagnosis of porphyria. From the point of view of the psychiatrist, if the historian thinks that varying a psychiatric diagnosis from manic-depression to porphyria, from a 'mental' to a 'physical' malady, should cause him to review his entire view of the man's personality, and to re-allot his estimates of praise- and blame-worthiness, then he mistakes the nature of psychiatric evidence.

ELIOT SLATER

Biological Psychiatry. A Review of Recent Advances.

By J. R. Smythies, with the collaboration of Alec Coppen and Norman Kreitmann. (Pp. viii + 112; 21 figures + 6 tables. 30s.) London: William Heinemann Medical Books. 1968.

In this book J. R. Smythies gives a further account of the tantalizing search for a biochemical lesion in schizophrenia, and in particular he reviews the present status of the methylation hypothesis. The methylation hypothesis is based on the twin facts that 3, 4-dihydroxyphenylethylamine (dopamine) and related catecholamines are present in the mid-brain where they are thought to act as neurohumours, and that 3, 4, 5-trimethoxyphenylethylamine (mescaline) produces a state not dissimilar to schizophrenia. Support was given to the hypothesis when it was shown that methylation of one of the hydroxy groups (at the 3 position) is the normal method of inactivating catecholamines at their site of action, and further evidence was provided by reports that 3, 4-dimethoxyphenylethylamine (DMPE) was excreted in the urine of schizophrenics and not of normals (the pink spot). Disappointment came when it was shown that the pink spot was not in fact DMPE, and that in any case DMPE was inert in man in large doses. Now, however, it appears from work on structure/activity relations which Smythies and his colleagues are carrying out in Edinburgh that DMPE does in fact have a mescaline-like action if it is protected from amine oxidase by a methyl group on the terminal carbon of the side chain, as is the case with amphetamine. However, the body has not yet been shown to be capable of methylating catecholamines at the 4 position, and a methyl group here appears to be necessary (though not sufficient) for mescaline-like action. The author suggests that the 4-methylated derivatives may act by inhibiting the enzyme which normally methylates at the 3 position, thus leading to a rise in free catecholamines at the active sites.

Further tantalizing facts concern methylation at the other end of the aromatic amine molecules: that mammalian tissues are capable of N-methylating tryptamine, and that N-dimethyltryptamine is another member of the group of psychotomimetic drugs. Moreover, the N-methylating mechanism is strongly inhibited by chlorpromazine. These and other pieces of evidence for a disorder of methylation in schizophrenia are reviewed in a lucid style, and one is left with a strong sense of optimism that a practical application of the theory to therapy is not far away.

The author is assisted by Alec Coppen in a review of evidence concerning disorders of amines and electrolytes in affective disorders, in both of which studies some promising clues are being energetically followed up; and by Norman Kreitman in a review of epidemiological data. Outstanding in the latter is a clear discussion of work on the effect of the family as a possible predisposing factor in schizophrenia (double-bind, marital skew, etc.), and a description of the WHO ten-year programme of research into social psychiatry and epidemiology. The final chapter is a brave attempt to build a bridge between biological psychiatry and psychoanalysis.

JOHN PRICE