

## Correspondence

### GENETICS OF SCHIZOPHRENIA

DEAR SIR,

In the current discussion concerning the genetics of schizophrenia it should be remembered that mendelian genetics is a formal science and that for a particular scheme of inheritance, and given allelic frequencies, familial relations are automatically defined. In practice, the predictions from the simplest mendelian assumptions sometimes require modification to allow for such complications as selection effects, differential fertility, linkage, and gene mutation. Where diseases such as schizophrenia are concerned, interpretation of the familial evidence is further complicated by the problems of diagnosis and the variation of penetrance with age and to some extent with sex. Consider, however, the simple mendelian relation between the twins evidence and that concerning full sibs. Suppose the age- and sex-corrected concordance-rate of schizophrenia in monozygotic twins is  $S_M$ , and that in dizygotic twins it is  $S_D$ . Then, in a proband study, if one member of a family is a proved schizophrenic, the proportion of full sibs that will be genetically predisposed to schizophrenia should, on the average, be  $S_D/S_M$ . For the five major twins studies analysed by Essen-Möller (1963) this ratio is approximately 0.18. (It should be noted that this ratio is too small to be accounted for by any straightforward monogenic scheme of inheritance.) The observed risk in full sibs is 0.115 to 0.143, corresponding to average penetrances of about 61 to 76 per cent. This, and other familial evidence, is consistent with the hypothesis that predisposition to schizophrenia is governed by recessive inheritance at two autosomal loci (Burch, 1964). Furthermore, the sex- and age-distributions of schizophrenia as diagnosed in New York State, 1949 to 1951, indicate that the predisposed sub-population is homogeneous with respect to the two random, dependent-type events that appear to initiate the disease process (Burch, 1964). The high degree of internal consistency in the earlier evidence—including the extensive familial studies by Kallmann—strongly supports the genetic hypothesis. The critical analysis of Shields (1965) suggests that Tienari's (1963) subsequent twins study does not vitiate this hypothesis.

I recently proposed (Burch, 1964) that schizophrenia is either a spontaneous disturbed-tolerance autoimmune disorder involving cell-bound (lymphocytic) autoantibody as the primary pathogen, or that

it arises from spontaneous disturbances in an unidentified system that shares certain important genetical and statistical characteristics with the lymphoid system. On basic biological grounds described in detail elsewhere (Burch and Burwell, 1965) I now consider that the autoimmune interpretation is the more plausible.

P. R. J. BURCH

*Department of Medical Physics,  
University of Leeds,  
The General Infirmary,  
Leeds, 1.*

### REFERENCES

- BURCH, P. R. J. (1964). "Schizophrenia: some new aetiological considerations." *Brit. J. Psychiat.*, **110**, 818-824.  
BURCH, P. R. J., and BURWELL, R. G. (1965). "Self and not-self. A clonal induction approach to immunology." *Quart. Rev. Biol.*, in press.  
ESSEN-MÖLLER, E. (1963). "Twin research and psychiatry." *Acta psychiat. (Kbh.)*, **39**, 64-77.  
SHIELDS, J. (1965). "Psychiatric Genetics." (Book review.) *Brit. J. Psychiat.*, **111**, 777-781.  
TIENARI, P. (1963). "Psychiatric illnesses in identical twins." *Acta psychiat. (Kbh.)*, **39**, Suppl. 171.

### DEPRESSION : PSYCHOTIC/NEUROTIC ; ENDOGENOUS/EXOGENOUS

DEAR SIR,

Carney, Roth and Garside (*Journal*, Aug. 1965, p. 659) conclude that the separation of *endogenous* and *neurotic* depression is possible and useful; Mendels (*Journal*, Aug. 1965, p. 682) seem to regard it as neither possible nor useful.

Mendels claims that his results "lend support to the concept that there is always an endogenous element to depressive illness, and that the reactive element is more variable". Since the terms endogenous and reactive are exhaustive, this must mean that all reactive depressives are endogenous, but not all endogenous depressives are reactive. The distinction has, therefore, been made, but in terms of a "contained within" relationship.

The facts are not, however, supportive of this view. Table II (p. 685) can serve as the crux of the argument. In this Table the figures are given inaccurately, assessed incorrectly and interpreted arbitrarily.

Under A/E, all 11 subjects had a Steady Course; but 1 must have had a Fluctuating Course as well. Under B/E, 18 out of 19 subjects had an Adequate