inal flora[46,49]. Hoffer and Osmond[50] have recently reported an aromatic compound of uncertain identity staining mauve on paper chromatograms of urine in 75 per cent of schizophrenic patients examined. Since no dietary controls were used in this study, it is quite possible that these findings are also the result of a dietary-intestinal artefact.

Recently, 3,4-dimethoxyphenylethylamine, a compound which bears a striking resemblance to mescaline, has been reported to occur in the urine of schizophrenics more frequently than in normal urine[51]. The results of several studies have been quite variable (Table 1), and it is striking that in patients receiving plant-free diets no 3,4-dimethoxyphenylethylamine was detected.

Table 1. CHROMATOGRAPHIC DETECTION OF URINARY 3,4-DIMETHOXYPHENYLETHYLAMINE*

Schizophrenic	Normal	References
15/17	0/14	Friedhoff[51]
57/62 (on tranquillizers)		
13/16 (off tranquillizers)	21/46	Takesada *et al.*[52]
0/10 (plant-free diet)	—	Perry *et al.*[53]
4/22	0/1	Sen *et al.*[54]
5/12 (Friedhoff's patients)	0/10	Kuchl *et al.*[55]
2/10		
2/3	2/4	Baldessarini and Kopin[56]
0/2 (plant-free diet)	—	Gjessing[57]
98/154 (63%)	23/75 (31%)	

* Data are presented as the ratio of number of subjects in whose urine the compound could be detected to the total number of subjects studied.

It is clear that schizophrenia is a complex entity and that firmer and more precise diagnostic criteria are necessary. Greater caution is indicated in the interpretation of available genetic, pharmacological, biochemical, and psychological data which purport to describe differences between schizophrenic or pre-schizophrenic subjects and normal controls.

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OUR paper presented a hypothesis which we considered probable, and it was put forward with a view to encouraging further research on the various causation processes concerned in producing overt schizophrenia.

The primary basis for our view that schizophrenia is a genetic morphism is the fact that it clearly has a strong genetic component, and that its incidence is more than 1 per cent, a figure too high to be maintained by mutation alone. The distribution of schizophrenia in families is quite incompatible with the idea that the genetic basis is a single recessive gene, but gives a remarkably good fit with expectancy on the basis of the monogenic 25 per cent penetrance model suggested by us, though a poor fit with any polygenic model.

It next appears reasonably certain (*a*) that the genetic basis, whatever it be, is responsible for a marked 'error of metabolism', producing a number of physiological (biochemical, immunological, etc.) changes. The evidence for this is extensive, and is not merely "anecdotal" (see references 12–16 in our original paper); and (*b*) that the error of metabolism results in the production of some abnormal chemical compound which could be detected in the blood and/or urine. We realize that neither the precise compound nor the detailed steps in its formation have yet been conclusively identified, and merely mention that Hoffer and Osmond consider that it is adrenolutin, or some chemically related substance.

Further, it appears quite certain that schizophrenia involves interference with perceptual development, resulting in marked perceptual and eventually conceptual disorder. We realize that the precise nature of this interference has not yet been established, but emphasize that psychological tests have been devised which appear to distinguish schizophrenics from normal subjects.

Finally, we direct attention to the main implications of our hypothesis, and stress the need for more research in many fields before it or some modification of it is fully confirmed.

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