Lack of Evidence for Retrovirus Infection in Schizophrenic Patients

DEAR SIR,

We read with interest the publication of Dr T. J. Crow's hypothesis associating retroviral infection with the development of schizophrenia (*Journal,* September 1984, **145,** 243–252). In view of the familial occurrence, indirect evidence for an infectious aetiology, and data suggesting immune dysfunction in some schizophrenic patients, we found this hypothesis plausible and worth investigating. No evidence exists, however, to suggest that retroviruses, rather than other classes of viruses, are involved. One of the unique properties common to all retroviruses is that they contain an enzyme, reverse transcriptase, which can transcribe DNA from RNA. The presence of this foreign enzyme in host cells may stimulate the production of antibodies directed against reverse transcriptase, which can be detected by standard immunological laboratory techniques. If an individual has, or previously had, an active retroviral infection, elevated titres of serum IgG specifically directed against reverse transcriptase may then be present, as has been recently reported in patients with the autoimmune disorder, systemic lupus erythematosus (Okamoto *et al,* 1983). We therefore examined sera from schizophrenic patients for the presence of antibodies to this protein, as well as others, that might provide evidence for Dr Crow's proposal.

Fifteen hospitalised DSM-III diagnosed chronic schizophrenics, all with evidence of active positive symptoms of psychosis, and 15 age-and gender-matched normal controls had serum samples drawn and blindly assayed for antibodies to reverse transcriptase. However, since reverse transcriptase is only weakly antigenic, and thus some individuals with retroviral infections may be missed if screening is limited to antibodies against this protein, we have also examined antibodies to Human T Cell Leukemia Virus antigens (HTLV I and III), the only class of retroviruses known to infect humans. The assay procedures have been described in detail elsewhere (Kalyanaraman *et al,* 1981; Saxinger and Gallo, 1983). At serum dilutions of 1:300 or greater no antibodies (IgG) to reverse transcriptase or any of the other viral proteins were found in either the schizophrenic or control groups. In contrast, almost 100 percent of human T cell leukemia patients have titres several fold greater to at least some of the viral proteins (Sarin & Gallo, 1983), as do patients with acquired immune deficiency syndrome (AIDS; Sarngadharan *et al,* 1984).

We, therefore have failed to find evidence that would be consistent with the presence of a retrovirus infection in schizophrenia. If schizophrenia is associated with periodic activation and reproduction of the retrovirus, particularly during an exacerbation of psychosis, then we would expect that at least a few of our 15 patients would have shown some antibody response to the enzyme, reverse transcriptase.

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References

KALYANARAMAN, V. S., SARNGADHARAN, M. G., BUNN, P. A., MINNA, J. D. & GALLO, R. C. (1981) Antibodies in human sera reactive against an internal structural protein of human T-cell lymphoma virus. *Nature,* **294,** 271–273.

OKAMOTO, T., TAMURA, T. & TAKANO, T. (1983) Evidence in patients with systematic lupus erythematosus of the presence of antibodies against RNA-dependent DNA polymerase of baboon endogenous virus. *Clinical and Experimental Immunology,* **54,** 747–755.

SARIN, P. S. & GALLO, R. C. (1983) Human T-cell leukemia-lymphoma virus (HTLV). In *Progress in Hematology, volume XIII* (ed. E. B. Brown). New York: Grune & Stratton.

SARNGADHARAN, M., POPOVIC, M., BRUCH, L., SCHUPBACH, J. & GALLO, R. C. (1984) Antibodies reactive with human T-lymphotropic retroviruses HTLV-III. *Science,* **224,** 506–508.

SAXINGER, W. C. & GALLO, R. C. (1983) Application of the indirect enzyme linked immunoabsorbent assay microtest to the detection and surveillance of human T cell leukemia-lymphoma virus. *Laboratory Investigation,* **49,** 371–377.

Dr Crow replies

DEAR SIR,

The observations of DeLisi and Sarin, along with those of Robert Guroff and colleagues, (*Journal,* March 1985, **146,** 326), are obviously relevant to the retrovirus/transposon hypothesis of schizophrenia and are a welcome attempt to subject this theory to experimental test.

However while one might have interpreted a positive finding (i.e. an excess prevalence of antibodies to reverse transcriptase in a group of patients with psychosis by comparison with an appropriate control group) as support for the hypothesis, there are a number of reasons why a negative outcome may be less damaging than at first sight appears to be the case. One of these (alluded to indirectly by DeLisi and Sarin) is the antigenic variability of the class of retroviruses. Unless a virus very closely resembling HTLVI or III were postulated, antibodies to these viruses would not be expected. Therefore the force of the test relies heavily upon reverse transcriptase and, as DeLisi and Sarin note, this enzyme is only weakly antigenic. Moreover it is not entirely clear that if the virus were integrated in the genome that an antibody response would be elicited. For example retroviral sequences as detected by