and verified by examination under conventional low-power microscopy. This allows for the elimination of false readings associated with radioactivity of ELISA counters.

Table 1 lists the origin and clinical state of the sera and CSF and shows that we failed to detect antibodies to the oncoviruses (ATLV/HTLV-I, HTLV-II) or to the lentiviruses (LAV/HTLV-III) in any of the 46 sera and 15 CSF from MS patients.

In our preliminary studies we also tried to isolate a retrovirus from the peripheral white blood cells (WBC) of two patients with MS. The WBC were separated on Ficoll before being divided into two parts. One part was co-cultivated with fresh human cord WBC and the other part was cultured with the Karpas T cells[3]. If ATLV/HTLV-I or HTLV-II were involved in MS, one might expect the cord WBC to become infected and express the viral antigen. In contrast, if an AIDS-like lentivirus was involved, one would have expected cell lysis of both the cord T cells and our T-cell line, or at least development of an antigen that reacted with sera containing antibodies to LAV/HTLV-III or ATLV/HTLV-I.

Table 1 Results of retrovirus tests

	ATLV/ HTLV-I	HTLV-II	LAV/ HTLV-III
UK: Paired, MS sera	0/15	0/15	0/15
MS CSF	0/15	0/15	0/15
Paired, OND sera	0/20	0/20	0/20
OND CSF	0/20	0/20	0/20
Sweden: MS sera	0/21	0/21	0/21
Germany: MS sera	0/10	0/10	0/10
Japanese ATL sera	5/5	5/5	0/5
British black ATL sera	3/3	3/3	0/3
British homosexuals' sera	0/61	0/10	61/61

MS, multiple sclerosis; CSF, cerebrospinal fluid; OND, other neurological diseases, including suspected but not confirmed MS; ATL, adult T-cell leukaemia.

The two cultures of cord cells, and the two cultures of our T-cell line, which were co-cultivated with the WBC from the MS patients, were tested for the expression of ATLV/HTLV-I and LAV/HTLV-III after 2 and 4 weeks in culture, using the IP method. Neither the cord WBC nor our T-cell line expressed any antigens that reacted with human sera containing antibodies to ATLV or to LAV. Since sera of patients with ATLV contained antibodies which cross-reacted with HTLV-II, one would expect these sera to react with HTLV-II-infected cells if a related virus is involved in MS.

In summary, we failed to detect any antibodies against ATLV/HTLV-I and HTLV-II or LAV/HTLV-III in the sera and CSF samples from MS patients, nor could either of these viruses be isolated from the WBC. The claim to the presence of antibodies which react with the known human retroviruses is based on ELISA tests. We now know that some of the ELISA systems may give a high rate of false-positive results. The report that 37% of Israeli Falashas were ATLV/HTLV-I-positive has turned out to be wrong, probably due to the ELISA method[4]. Similarly, it has been repeatedly reported that some of the ELISA test kits used for AIDS screening give a high rate of false-positives[5,6]. The results of such ELISA methods might cause premature claims to the involvement of HTLV in MS.

The possible viral aetiology of MS remains enigmatic; should a retrovirus eventually prove to be a pathogenic factor, it is likely to be distinct from the known human retroviruses.

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KOPROWSKI *ET AL.* REPLY: We are pleased that other investigators[1,2] have undertaken the difficult task of searching for the involvement of retroviruses in multiple sclerosis. However, it is difficult for us to compare the results of our study[3] with the data presented by Hauser *et al.*[1] and Karpas *et al.*[2]. The first study used a commercially prepared kit for HTLV-I antibody while the second used visual detection of HTLV-I antibody by immunoperoxidase on infected cells. The drawback of both these assays is that the concentration of the HTLV group-specific (*gag*) antigen p24 in the kit is unknown and is considerably lower in cells than that used for our antibody determinations by ELISA. Despite this, the results of Hauser *et al.*[1] with MS sera and normal controls are almost identical to the results shown in our Fig. 2[3]. The discrepancy between our results and theirs with other neurological disease (OND) patients may be explained if we knew which OND patients were tested by Hauser *et al.*[1]. While Karpas *et al.*[2] may find their immunoperoxidase test sensitive enough to detect antibodies in extremely high-titred AIDS[4] and in eight leukaemia sera, we expect that this assay would not detect low-titred (HTLV-I cross-reactive) antibody found in MS patients. Because of the fluctuation of the HTLV p24 antibody levels, it does not make sense to search with low-sensitivity assays for antibodies in a single sample of either serum or cerebrospinal fluid of MS patients. 'False-positives' in our ELISA were excluded by specific competitive inhibition assays[3].

The inability of Hauser *et al.*[1] to detect retroviral sequences by *in situ* hybridization may be due to several factors: (1) use of complementary DNA probes rather than the much more sensitive riboprobes[5,6]; (2) the stringency conditions under which the test was run (not mentioned by Hauser *et al.*[1] but crucial in our assay); (3) restriction of sensitivity of the test by nonspecific hybridization with pBR322 plasmid alone. Hauser *et al.* provide neither positive controls showing the limitation of the sensitivity of the test nor controls confirming the presence of hybridizable RNA in the lymphocytes.

In the light of the considerable time and effort invested in the isolation of the human retroviruses I, II and III, it is not surprising that Karpas *et al.*[2] failed to isolate the 'MS virus' from two randomly chosen MS samples in 4 weeks. We also emphasize points repeatedly made in our report that detectable antibodies are: present in low titre; cross-reactive, that is, not reactive specifically against the test HTLV; and, most importantly, present only sporadically in cerebrospinal fluid and sera during the course of disease. Karpas *et al.*[2] made a point that if HTLV is involved in MS, it is "distinct from the known human retroviruses". We agree and that was precisely our conclusion.

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