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Introduction

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The 7th 'Neuroscience of HIV infection' meeting will be held on March 6 to 9, 1996 in Paris and will gather scientists working on different clinical and biological aspects of HIV and related opportunistic infections in the nervous system. All the abstracts from this meeting are published in this issue of the Journal of NeuroVirology, preceded by short overviews on recent clinical, virological and immunological developments, written by the invited speakers.

After 10 years of research on HIV infection in the nervous system, where do we stand? In terms of the pathophysiology of the disease, several points are now generally accepted: (1) It is agreed that HIV1 invades the CNS soon after primary infection; (2) it is also agreed that different types of virally-induced CNS insults are likely to take place at different times during disease progression; (3) it is clear that HIV1-induced encephalopathy is directly dependent on the presence of HIV1 within the CNS and that brain macrophages are infected by HIV1; (4) evidence now shows that CNS macrophages are in a state of hyperactivation. As discussed in several presentations in this meeting, this macrophage hyperactivation modulates the ability of brain macrophages to replicate the virus and induces the production of cytokines, NO° and other soluble factors which participate in neuronal death; (5) the presence of neuronal apoptosis is also generally accepted and is discussed in terms of its frequency and mechanisms by several speakers. Yet there are other points that are still unclear: the molecular mechanisms of regulation of viral replication and of neurotropism, the interaction between HIV1 and astrocytes and its consequences on astrocyte functions, the final mechanism(s) of neuronal death and its relationship with intraneuronal calcium homeostasis, the role of cytotoxic T cells especially in the induction of early and reversible neurological lesions, the role of autoimmunity, etc. Most of these subjects are discussed by the participants. It should also be recognized that research is limited by the relatively small number of scientists working on Neuroscience of HIV infection and by the scarcity of experimental models. The two main models are cultures of human embryonic, fetal or adult CNS or neural cell lines and the SIV model, both of which have their limitations but, as demonstrated in the papers presented, can provide very accurate answers. Perhaps the use of transgenic mice or xenograft of human CNS tissue in SCID mice could open new avenues of research.

In the clinical sciences, the frequencies of the main neurological symptoms are now clarified for both the central and peripheral nervous systems. Some studies are now being performed specifically in HIV1-infected drug users. Such results are also important to obtain in Africa and south-east Asia. The large number of presentations related to peripheral neurological manifestations and their pathophysiology is new. Nevertheless, it is interesting to note that experimental studies on HIV1-related peripheral nerve lesions and on spinal cord lesions are extremely rare, although some of the presentations in this meeting offer new hypotheses. A major problem remaining in the clinical sciences is to define surrogate markers of CNS involvement, which would allow easier evaluation of the efficacy of antiviral treatments. In this respect, several groups have explored the use of functional brain imagery: brain spectroscopy gives interesting results but the final answer is clearly not obtained. Other groups are working on correlations between CNS symptoms and the detection of cytokines, other soluble factors or viral products in CSF or blood, but here again no perfect marker has been found. This absence of good surrogate markers of nervous system lesions might be one explanation for the relatively small number of therapeutic trials, which are also impeded by the need for large collaborative studies. Finally, the diagnosis of opportunistic infections of the nervous system and of CNS lymphoma has been facilitated by PCR techniques although, as shown by several presentations at this meeting and at previous ones, their sensitivity is relatively low.

HIV1-infected persons are expecting results from us. A very large concerted action between neuroscientists in basic research, neuropathologists and clinicians in different fields is obviously essential to bring out new ideas and approaches leading to new therapeutic possibilities.