VIRUSES

Persistent Infections

from a Correspondent

A SYMPOSIUM on host–virus reactions with special reference to persistent agents was held in London on February 17 and 18 under the auspices of the Royal College of Pathologists. Persistent virus infections include slow viruses which after a long latent period lead to progressive disease (for example, scrapie and visna) or malignancy (for example, leukaemogenic viruses), viruses which following an acute infection remain latent and are occasionally reactivated after a long interval (for example, varicella-zoster and measles in subacute sclerosing panencephalitis), and viruses which persist without reactivation (for example, adenoviruses in lymphoreticular tissue).

Several contributions were devoted to scrapie and conditions which produce similar lesions in the nervous system—kuru and Creutzfeld-Jacob encephalopathy of man and mink encephalopathy. Dr D. C. Gajdusek (NIH, Bethesda) reviewed the transmission to chimpanzees and some other primates of kuru (formerly a common disease among the Fore highlanders of New Guinea) and Creutzfeld-Jacob encephalopathy (a rare disease of Europeans). Dr R. M. Barlow (Animal Diseases Research Association, Edinburgh) described the transmission of mink encephalopathy to goats and mice. It is now clear that the scrapie agent replicates in culture.

All of these conditions are characterized by a long latent period followed by spongiform encephalopathy, with neuronal degeneration and astrocytic proliferation. None of the causative agents seems able to stimulate an immune response, either humoral or cell mediated; their remarkable properties as usual aroused discussion. Dr T. Alper (Hammersmith Hospital, London) thought that the small target size (<7 nm) shown by resistance to ionizing radiation and greater sensitivity to shorter-wave ultraviolet than to radiation of 260 nm was difficult to reconcile with a nucleic acid-containing virus. Dr Gajdusek quoted observations that certain plant viruses, such as potato spindle virus, have a ribonucleic acid content of only 50,000 daltons, a target size of <7 nm and are not readily sedimentable by centrifugation. Perhaps association with membranes might account for the relative resistance of the scrapie agent to radiation, heat and certain chemicals. Unpackaged and unassembled viruses are known, and Dr Gajdusek felt that this was a more likely explanation for scrapie-like agents than postulating the existence of replicating agents of an altogether different nature.

The role of measles virus in subacute sclerosing panencephalitis is firmly established (Dr J. H. Connolly, Queen's University, Belfast), although the factors allowing the progressive spread of infection in the brain are not yet understood. Patients with multiple sclerosis sometimes have measles antibody levels in the cerebrospinal fluid higher than would be expected from blood levels, and Dr Françoise Cathala (Hôpital de la Salpêtrière, Paris) reported the finding of gamma globulin spikes (three or more bands on electrophoresis) in the cerebrospinal fluid of some multiple sclerosis patients. This would be consistent with antibody production within the nervous system.

Several herpesviruses can establish latent infections in man. Thus EB virus can remain in lymphoreticular tissue after infectious mononucleosis and be recovered from conditions like Burkitt lymphoma. Dr B. G. Achong (University of Bristol) discussed their possible role in the aetiology of the lymphoma. Several herpesviruses of animals are tumour inducing, as reviewed by Dr P. M. Biggs (Houghton Poultry Research Station, Huntingdon). Herpes simplex and varicella-zoster persist in nerve ganglion cells and can be reactiviated under certain conditions. Dr A. C. Allison (Clinical Research Centre, Harrow) reviewed evidence that once infections with these viruses are established antibody is insufficient to prevent viral spread, and that cell-mediated immunity plays a major part in controlling these infections. Sometimes a general failure of cell-mediated immunity (for example, patients with lymphoreticular malignancy treated with cytotoxic drugs) allows the infection to emerge; in other cases the effect may be virus-specific, for example, antibody blocking cell-mediated immunity. Dr Allison also suggested that growth of viruses in macrophages may explain other progressive infections in which viral antigen and antibody are both present in peripheral blood. Immune complexes deposited in kidneys and blood vessels can cause glomerulonephritis and panarteritis. One such infection is lymphocytic choriomeningitis in mice infected as newborns, reviewed by Dr F. Lehmann-Grubbe (University of Hamburg); infected adults have severe and often fatal cell-mediated immunopathological reactions.

Dr P. A. Pálsson (University of Iceland, Reykjavik) described visna and maedi, progressive infections of the central nervous system or lungs of sheep produced by the same myxovirus-like agent. Visna virus and foamy viruses contain RNA and RNA-dependent DNA polymerases, which might allow them to persist as DNA proviruses. There is, however, no evidence that they ever induce cancer. Visna-maedi virus again replicates in spite of the presence of neutralizing antibody, and infected tissues show marked mononuclear cell infiltration.

CORRESPONDENCE

Transfer of DNA

SIR,—The interesting results of Ledoux and his collaborators on the incorporation of bacterial DNA in plant cells were featured in a recent editorial (*Nature New Biology*, **234**, 161; 1971). I would like to comment on two questions raised, namely, whether DNA can replicate and become functional in foreign cells, and whether this whole line of investigation may not be a red herring "which in no way enhances our understanding of biology".

Stroun, Anker and their colleagues (for references see Stroun *et al.*, *J. Bact.*, **106**, 634; 1971) found by hybridization experiments that bacterial DNA can indeed replicate as well as produce its RNA in plant and animal cells. All precautions were, of course, taken to exclude the possibility of artefacts through bacterial contamination. These findings in themselves show that it is not all a "red herring".

Some of the results can be understood on the hypothesis of metabolic DNA. It has been amply documented that two kinds of DNA exist, stable genetic DNA and labile DNA which is metabolically active. It seems likely that initially foreign DNA is regarded by cells as metabolic DNA, can become self-replicating and transcribe to RNA. Occasionally a molecule may well be able to "slip in" with the genetic DNA. Differentiated cells produce appreciable amounts of expendable DNA (for reviews see S. R. Pelc, *Exper. Gerontol.*, **5**, 217; 1970; and *Intern. Rev. Cytol.*, **32**, 327; 1972). For example, 1 to 3 per cent per day of the total DNA in mouse liver and muscle is expendable. Therefore communication between cells by means of transfer of DNA is possible as all the steps necessary have now been demonstrated. In fact such a process has recently been suggested to explain the interaction between responsive cells in the immune reaction (S. R. Pelc, G. Harris, and I. Caldwell, *Immunology*, in the press).

Yours faithfully,

S. R. PELC

Division of Cellular Biology,
Kennedy Institute of Rheumatology,
Bute Gardens, Hammersmith,
London W6 7DW