MPMV, showed a Mg^{2+} preference with the synthetic templates poly(rA)·oligo$(dT)_{12-18}$ and poly(rC)·oligo$(dG)_{12-18}$, but a Mn^{2+} preference with poly$(rC)_m$·poly$(dG)_{12-18}$.[10]

We have transmitted SAIDS to two healthy female rhesus monkeys (E-427 and B-959), 17½ months of age, by inoculating them with IDB-1 virus grown in vitro in fourth-passage bone marrow fibroblasts from normal healthy rhesus monkeys. The virus used as inoculum was purified by discontinuous and continuous density gradient centrifugation in neutral sucrose and had an isopyknic density of 1·15 g/ml. Peak absorbance at 254 nm and reverse transcriptase activity coincided in the pooled fractions used as inoculum. Only type D retrovirus particles were seen by electron microscopy in negative stains of the inoculum.

Both inoculated monkeys had early manifestations of SAIDS (neutropenia, lymphadenopathy, and splenomegaly) 2 to 4 weeks after the inoculation. More severe disease was noted in monkey E-427 and, 5 weeks after inoculation, an enlarged right inguinal node was removed from this animal for histopathological examination. The normal architecture of the nodular cortex was effaced by extensive atypical proliferation of lymphoblasts and immunoblasts. The only suggestion of follicles was a few subcapsular aggregates of small lymphocytes. Plasma cells were rare. This histopathology is consistent with that seen in previously studied animals with early to intermediate SAIDS.

Both animals (E-427 and B-959) died 8 weeks after inoculation with clinical and pathological disease similar to that described previously in experimentally and naturally infected rhesus monkeys with SAIDS.[1,3,4] Death in both animals was from pneumonia caused by an opportunistic invader, probably a virus, since the infection was unresponsive to antibiotics.

These results provide strong evidence that the causative agent of SAIDS is a type D retrovirus related to MPMV. Our collaborators from the California Primate Research Center of the University of California, Davis, have arrived at the same conclusion in independent experiments which will be published elsewhere. Fine and co-workers[11] previously reported that newborn rhesus monkeys inoculated with MPMV died of an immunosuppressive disease resembling SAIDS, providing further support for this conclusion. Several other retroviruses have been associated with immunosuppressive disease in animals and man.[12-15] Our results add another to this list.

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MASON-PFIZER MONKEY VIRUS AND SIMIAN AIDS

SIR,—In 1983 Henrickson et al[1] described a syndrome resembling acquired immunodeficiency syndrome (AIDS) in a group of sixty-four rhesus monkeys at the California Primate Research Center in Davis, California. This syndrome, designated simian AIDS (SAIDS), manifests as generalised lymphadenopathy, chronic wasting, and severe opportunistic infections, and is often fatal. The most recent disease outbreak, which has lasted for two years now, is the fourth manifestation of apparent acquired immunodeficiency in *Macaca mulatta* and *M arctoides* at this primate research centre. The current outbreak of SAIDS has all the hallmarks of a disease observed in *M mulatta* (rhesus monkeys) inoculated at the Litton Bionetics Primate Facility, Kensington, Maryland, with purified Mason-Pfizer monkey virus (MPMV) or MPMV-infected cells.[2] No AIDS-like disease was observed in rhesus monkeys inoculated with uninfected rhesus cells, Burkitt's lymphoma tissue, rubella virus, simian sarcoma virus, or DNA viruses (including Epstein-Barr and *Herpes simplex*). MPMV was recovered from tissue of virtually all diseased, MPMV-inoculated animals.

Macaques with the spontaneously arising disease[1] and macaques inoculated with MPMV[2] had in common the following clinical signs: lymphadenopathy, weight loss, diarrhoea, hypoproteinaemia, neutropenia, anaemia, pneumonia, generalised gastrointestinal tract lesions, and infections with *Klebsiella* spp, *Staphylococcus aureus, Candida* spp, *Pseudomonas* spp, *Entamoeba histolytica,* and *Cryptosporidium* spp. The transmission of SAIDS from diseased to normal *M mulatta* with heparinised blood or plasma filtered through a 0·45 μm filter[3] implies a viral aetiology for the disease seen at the Davis centre.

Our seroepidemiological studies of the expression of natural antibodies to horizontally transmitted (MPMV) macaque retroviruses[4] also support this hypothesis. Macaques in all seven primate colonies studied had antibodies to MPMV. The highest frequencies of seropositive sera were 26% and 43% in *M mulatta* and *M radiata,* respectively, at Davis. These seroepidemiological studies and the close similarity between the SAIDS seen at the California Primate Research Center and the syndrome characterised by us at the Litton Bionics Primate Facility suggest that a common aetiological agent, possibly MPMV, is responsible for both diseases. SAIDS in the Davis colony may be associated with the presence and transmission of MPMV or a closely related type D virus.

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SUBCLINICAL HEPATITIS A IN NORTH INDIAN CHILDREN

SIR,—More than 90% of the population of India is positive for IgG antibody against hepatitis A virus (HAVAb-G),[5] which suggests a past infection by hepatitis A virus (HAV).[6] Detailed history-taking, however, does not reveal clinical hepatitis in the past, and it has been assumed most individuals have had subclinical infection early in life. This hypothesis now can be tested.

IgM anti-HAV (HAVAb-M; Abbott Laboratories) as a marker of acute or recent infection by HAV has been sought in 90 healthy children below the age of 10 years and in 60 adults aged 17–30. 25

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4. Fine DL, Arthur LO. *Virology* 1981; **112:** 49–61.
5. Gandhi BM, Joshi YK, Tandon BN. Prevalence of virus A exposure and viral hepatitis A in India. *Lancet* 1981; ii. 374.
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(28%) of the children but none of the adults were positive for HAVAb-M. HAVAb-G was tested in sera from 17 of the IgM-positive children: 6 had titres of 75 or more and 3 of these had titres of 2000. In the general population in our laboratory where HAVAb-G is positive titres of 75 or more are usual.[3] Transaminase levels were two to three times normal in 3 of the 16 HAVAb-M positive children tested for these enzymes.

The presence of HAVAb-M and high titres of IgG antibody confirm that, in this part of north India, almost 30% of children below the age of 10 have subclinical acute virus A hepatitis. This group will be a continuing source for the spread of HAV infection in the community, and these findings also explain the high positivity rate for HAVAb-G in individuals over the age of 10 who have no history of a clinical attack of acute viral hepatitis.

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WHAT CAUSES PARKINSON'S DISEASE?

SIR,—Professor Calne and Dr Langston (Dec 24/31, p 1457) are probably correct, insofar as they suggest a multifactorial causation for Parkinson's disease. They emphasise the importance of environmental insults such as occult viral and/or toxic factors and the contribution of normal ageing as a "threshold" trigger that produces symptoms only when the other trigger factors are also operative.

I would like to comment on ageing in Parkinson's disease. The mean age of onset is between 55 and 60 and the incidence declines after that. Dementia seems to be much more common in Parkinson's disease than in an age-matched population, and dementia is thought to be an Alzheimer type degeneration. The prevalence of Alzheimer's disease increases linearly with age, and early onset (before age 65) has suggested premature or faster ageing. The high concurrence rate of parkinsonism and presumed Alzheimer's disease (40–50% of parkinsonians) further supports the notion that ageing of the brain, if it is an important factor in Parkinson's disease, takes place at an accelerated rate, leading to the combined impact of parkinsonism and dementia. This hypothesis is flawed because it is not universal: many patients get Parkinson's disease early in life, others have persistently unilateral disease, and still others probably acquire parkinsonism from unknown viral infections. However, the value of Calne and Langston's hypothesis is that it deflates the idea of a strictly hereditary basis for the disease and focuses our attention on the more probable importance of the environment influencing the individual genome.

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SIR,—Professor Calne and Dr Langston do not take into account some epidemiological findings that may be relevant. In 1963 Poskanzer and Schwab[1] found that the mean age of Massachusetts General Hospital patients with parkinsonism had increased by 27 years from a group with onset of the illness in the years 1920–24 to a group with onset in 1955–59. They postulated that most parkinsonism of the previous 60 years had stemmed from the 1915–37 outbreak of epidemic encephalitis. In my neurological practice all patients in whom parkinsonism developed in the 12 years after 1970 were 50 years old or more at the time of the onset. In 1950–70 onset of parkinsonism before age 50 was common, accounting for more than 20% of my cases. There seems to have been no change in referral pattern to account for this finding. The files of the Massachusetts General Hospital for the years 1972–82 contain 860 cases of parkinsonism (all types except drug-induced). Only 2 patients had had the onset of their illness in that 10-year period while under the age of 50—a patient born in 1930 had symptoms at the age of 45 and another, born in 1937, had symptoms at the age of 39. No one with parkinsonism was born after 1937. This decrease in early-onset parkinsonism supports the epidemic encephalitis hypothesis. The illustrations of Parkinson's disease in Kinnear Wilson's textbook are not of old people.

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SIR,—Since 1974 we have investigated the effect of seven dopamine agonistic drugs in 2100 patients with Parkinson's disease.[1] The first compound we studied was bromocriptine. We possess accurate histories for 424 cases. In only 20 (4·8%) was there a family history of Parkinson's disease. This argues against a genetic origin for this disease. 365 patients (86%) were non-smokers, 12% of whom had smoked previously. The number of non-smokers, therefore, is higher among parkinsonian patients than in the healthy population (48–58%), a finding that accords with a comment in Professor Calne and Dr Langston's paper. We know of only 1 case of a toxic reaction to meperidine analogues. This patient, however, did not have typical parkinsonian symptoms. Besides periodic akinesia and rigor the patient exhibited typical ballistic movement disorders. Among four squirrel monkeys injected with methylphenyltetrahydropyridine (MPTP) we also found a hemiballistic syndrome. These toxins may cause extrapyramidal symptoms not always typical of Parkinson's disease.

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SIR,—Professor Calne and Dr Langston argue that Parkinson's disease is caused by selective damage, by a presumably non-viral environmental factor, to dopaminergic cells in the substantia nigra, that this is aggravated by the normal ageing process, and that the other brain lesions found are secondary to degeneration of the nigral dopaminergic neurons. Underlying this hypothesis is the observation that the neurotoxin methylphenyltetrahydropyridine (MPTP) causes specific lesions of the dopaminergic neurons in the substantia nigra.[1] There are difficulties with this idea.

(1) Calne and Langston's hypothesis fits quite well with post-encephalitic parkinsonism in which symptoms follow, immediately or after a latent period, a viral attack to which the dopaminergic neurons of the substantia nigra are especially sensitive. The gradual evolution of this disease is generally considered to reflect additional neuronal loss due to ageing. It is difficult, however, to fit idiopathic Parkinson's disease to this model, which predicts that after the initial insult—viral in the post-encephalitic form, toxic (?) in the idiopathic form—the evolution of the disease should be similar, due to normal ageing. This is not borne out by clinical experience. In post-encephalitic Parkinson's disease severe lesions of the nigral dopaminergic neurons are accompanied by slowly progressing and mild symptoms; in the idiopathic form the patients deteriorate rapidly although the lesions may be less severe.[2]

(2) If the other lesions are secondary they should be the same in the two forms of Parkinson's disease. They are not.[2] Moreover, although the decreased peptide concentrations in the basal ganglia of patients with idiopathic parkinsonism[3] could conceivably be

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