SPECIAL ARTICLES

SUSCEPTIBILITY OF WHITE MICE TO THE VIRUS OF YELLOW FEVER[1]

IT has been found that if yellow fever virus is injected into the brains of white mice, a certain number become ill and die. The virus can be propagated in mice indefinitely by the intracerebral injection into normal mice of the brain of an infected mouse. Once established in mice the passage virus invariably produces death after an intracerebral injection. In the early passages death usually took place on the seventh or eighth day. In subsequent passages there was a gradual shortening of the incubation period, so that by the sixtieth passage death occurred on the fifth day.

The virus is highly neurotropic in mice. Infection can be produced by the injection of the virus into the brain, spinal cord or eye. Other routes of injection, such as intraperitoneal, subcutaneous, etc., very seldom cause illness and death, though a considerable proportion of such mice are rendered immune to a subsequent intracerebral injection of the passage virus.

At death the virus can be demonstrated to be present in large amounts in the brain, spinal cord, peripheral nerves and the adrenal glands. The blood, liver, spleen, kidney and testis contain very little if any virus.

Continuous passage of the virus through mice leads to a gradual loss of virulence for rhesus monkeys. Monkeys were injected with the third, twenty-ninth and forty-second passages in the mice. The animal injected with the third generation died of typical yellow fever on the fifth day. The monkey which received mouse virus from the twenty-ninth generation developed a febrile reaction on the sixth and seventh days and recovered. This monkey was subsequently shown to be immune to virulent yellow fever virus derived from another monkey. The third monkey was injected with the forty-second generation of mouse virus and remained well. It was found dead on the forty-eighth day, death being due to some intercurrent disease.

The mouse virus can be preserved in 50 per cent. glycerine, at 2°–4° C., for at least fifty-eight days but not for one hundred days. Infective brain kept in a frozen condition at −8° C. retains its virulence for at least one hundred sixty days.

The mouse virus is neutralized by immune yellow fever serum derived from monkey or man. This effect can be shown by mixing infective mouse brain with the serum to be tested and injecting the mixture intracerebrally into normal mice. Normal serum has no protective action.

There are very few macroscopic changes in mice dying of an infection with yellow fever virus. Hemorrhage into the stomach, in about 50 per cent. of the mice, is the only abnormal finding sufficiently common to warrant the conclusion that it is caused by the virus.

Microscopical examination of the brain shows in the early stages a definite proliferation of the endothelium of the capillaries with an accumulation of mononuclear cells in the perivascular spaces, while in the late stages the picture is distinctly reminiscent of encephalitis lethargica. The ganglion cells undergo necrosis and there are invariably present eosinophilic nuclear changes resembling those present in the liver of man and monkey dead of yellow fever and described as inclusions by Torres[2] and Cowdry.[3]

The neurotropic character of yellow fever virus in mice and the nature of the pathological lesions produced are factors giving strong support to the theory that the infectious agent of yellow fever should be classified with the filtrable viruses.

In relation to these experiments it is of some interest to add that Dr. A. W. Sellards informs me that Dr. Laigret in the study of yellow fever patients in Senegal noted in exceptional cases minor neurological symptoms and suggested the importance of testing the central nervous system for the presence of virus and to observe the effect of inoculating the virus into the central nervous system.

A detailed account of which the above is a summary is in preparation and will be published in the near future.

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AN INTERPRETATION OF MASS CONJUGATION IN PARAMECIUM

WHEN freshly gathered material for the study of Paramecium is assembled at the spring of the year shortly after the great thaw in this latitude, it may be observed after a few days that a strong tendency to conjugation manifests itself in the wild culture. Under these conditions the presence of one hundred to

[2] C. M. Torres, Supplemento das Memorias Instituto Oswaldo Cruz, 1929, No. 6.

[3] E. V. Cowdry and S. F. Kitchen, SCIENCE, 69: 252, 1929.