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I would like to make a few remarks about active immunity, which has to be considered whenever the problem of latency and masking of animal viruses is discussed.

It is known that some viruses, especially those of the herpes, adeno and salivary group, persist in the body for very long periods of time, whereas others, such as the enteric viruses and the myxoviruses seem to disappear much more rapidly, as Huebner pointed out at the Madison Symposium on latency and masking. Representatives of the former group, which produce Type A intranuclear inclusions, can persist in the presence of antibody Their inclusions contain DNA. It is possible that these viruses are located in the altered nuclei, the hyperchromatic membranes of which cannot readily be penetrated by antibodies.

The virus of lymphocytic choriomeningitis, which does not produce intranuclear inclusions, may also persist for long periods of time in mice, particularly so when the infection occurs in the embryonic state. Such mice develop an immunological tolerance towards the virus, as Burnet has termed it. The virus content of their organs later in life is about equal to that of experimentally infected adult mice in the acute stage of the disease. The tolerant mice show minor histological changes in their organs, discharge considerable amounts of virus in the urine and nasal secretions for long periods and are the most efficient transmitters of the infection to normal mice by contact. Apparently the carriers discharge more virus than experimentally infected adult mice in the acute stage of the disease. The virus not only persists, but continuously multiplies in those animals for months or even years. It has not been possible beyond doubt to demonstrate antibodies in such mice.

In contrast to them, as shown years ago, the virus has a tendency, increasing with age at the time of infection, to disappear from the bodies of mice infected experimentally. Such animals develop complement-fixing antibodies, but the demonstration of neutralizing antibodies has been quite difficult. The results of more recent experiments, especially those of Rowe using the intraperitoneal neutralization test and the reinfection method, suggest that adult mice are capable of some antibody production. The neutralization titers, however, are very low compared with mice recovered from other virus diseases, and Rowe was unable to correlate these titers

with actual immunity in individual animals. Nevertheless, it is highly probable that antibody formation is primarily responsible for the gradual disappearance of the virus from the body.

More definite evidence, suggesting that antibodies can act upon intracellular virus both in vivo and in vitro, was obtained in recent experiments with EEE virus in mice. This agent has no tendency to persist long in recovered mice. Inapparent experimental infections occur, but are of short duration. Some results were reported at the recent Symposium on "Perspectives of Virology" in New York. I shall only briefly summarize the principal points:

(1) In mice infected subcutaneously and treated with powerful homologous immune serum 12 hours later, it was not possible to demonstrate active virus later than 24 hours after the serum treatment using highly sensitive techniques including tissue culture methods. Parallel animals not sacrificed failed to develop an active immunity. In mice treated with less potent immune serums and in the untreated controls virus was detected in various organs at least up to the 96th hour and the survivors in parallel groups kept for observation acquired an active immunity.

(2) Lung cells of mice cultivated in monolayers could be "cured" after 8 hours' contact with the virus, using potent hyperimmune mouse serum. Longer periods have not yet been tested. The cells were exposed to a 1:2 dilution of the serum for 48 hours. The result was the same when the cells were again trypsinized and cultured in monolayers after the treatment with immune serum.

(3) Kidney cells from hyperimmunized mice were highly susceptible to *in vitro* infection, but always slightly less so than normal kidney cells.

The observations made with EEE virus are similar to those reported in 1953 for the virus of Newcastle disease which is a potent antigen in chickens.

It appears to me that the conflicting results obtained by different investigators with immune serum in virus-infected tissue cultures are due in part to the fact that the serum was used in too low a concentration in many cases. Another contributing factor may have been the character of the virus itself. It is conceivable that a virus which multiplies exclusively or predominantly in the cytoplasm is more readily accessible to antibody than an agent which is located in the nucleus.

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I would like to say two things about Dr Burnet's statements We have been unable to demonstrate immunological tolerance in chicks hatched from eggs infected with influenza virus Another point, the more I collect experience with

lymphocytic choriomeningitis, the more I believe that it is not an intrauterine transmission but a transovarial one. The situation may be somewhat related to the situation with the insect viruses which are transmitted through the ova.