

8695 P

Development of Antiviral Properties Within Lymph Nodes.

PHILIP D. McMASTER AND JOHN G. KIDD.

From the Rockefeller Institute for Medical Research, New York City.

Every intradermal injection is intralymphatic and infectious agents introduced by way of a skin wound may reach the lymphatic glands directly.^{1, 2} Specific bacterial agglutinins are formed in the nodes draining the ears of mice into which killed cultures of bacteria have been injected intradermally.³ Experiments now show that the lymph nodes elaborate a principle capable of neutralizing a virus draining to them.

Rabbits were inoculated intradermally in one ear with a standard amount of vaccine virus and in the other with typhoid bacterin. Thirty-two experiments were done. In half of these the ears were amputated after an hour, while in the others the ears were left intact. After later intervals of from 2 hours to 15 days the cervical lymph nodes of both sides, inguinal nodes, bone marrow and spleen were removed and extracts of them were inoculated separately into 3 or 6 normal rabbits (as was serum procured from the same animals at the same time) to test for their content of virus (titration tests). In addition neutralization tests were set up to learn whether these extracts possessed antiviral properties.

Only the extracts of the ears and cervical lymph nodes of the virus-injected side gave rise to virus lesions. A few hours after the injection of standard amounts of virus in the ears equal amounts of virus were recovered from the lymph nodes. By the second or third day an increase in virus was demonstrable in the extracts of the nodes on the virus-injected side. A rapid decline took place thereafter and by the 7th to the 9th days the extracts failed to produce lesions. At no time did the serum or extracts from other nodes or organs give evidence of virus.

Tests showed an early appearance of neutralizing ability in the extracts of the nodes from the virus-injected side. By the 4th day the 10% extracts of these nodes inactivated fresh vaccine virus diluted to 10^{-5} and 10^{-6} (10-100 infective doses) to a greater degree than did whole serum. Serum of the same animal, similarly diluted, possessed no neutralizing power, nor did the extracts of inflamed

¹ Hudack, Stephen S., and McMaster, Philip D., *J. Exp. Med.*, 1933, **57**, 751.

² McMaster, Philip D., and Hudack, Stephen S., *J. Exp. Med.*, 1934, **60**, 479.

³ McMaster, Philip D., and Hudack, Stephen S., *J. Exp. Med.*, 1935, **61**, 783.

cervical lymph nodes from the other side, nor the extracts of spleen or bone marrow or of either ear. The lack of neutralizing power of the extracts of the inflamed nodes on the side injected with typhoid bacterin served to control the possibility that a concentration of antiviral bodies formed elsewhere in the body and circulating in the blood had taken place in the nodes of the virus-injected side. After longer intervals, for example 7 days, the serum and extract of lymph nodes from the virus-injected side, similarly diluted, showed equal neutralizing ability; whole serum possessed even more.

Experiments were done to test whether or not a neutralizing principle might be formed in the tissue of the injected ear, and reach the node by drainage. Extracts of the tissues of both ears (the virus-injected one showing a typical vaccinia lesion) as well as of the cervical nodes of both sides 4 days after inoculation were separately filtered through Seitz pads and tested. The filtration separated virus from antiviral principle in the extract of the cervical nodes from the virus-injected side in which both were present together, only the antiviral properties passing the filters. The ear extracts and filtrates totally lacked antiviral power and so too did those of the lymph nodes on the control side, whereas those of the glands on the injected side possessed it. Virus was present only in the ear extract from the virus-injected side. The experiment was repeated with similar findings.

The results from day to day with serum and extracts of other organs than the lymph nodes indicate that the latter were a major source of the neutralizing power of the serum.

The circumstances of our experiments were much like those when natural infection with a virus takes place by way of cuts or abrasions of skin or mucous membrane. The resemblance to the conditions obtaining in the case of ordinary Jennerian vaccination is especially close. The neutralizing power of the blood is probably of lymph node origin.