March 25, 1958

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Dear Chris:

I have been away from the laboratory a good deal and regret the delay in replying to your letter of 12 March. We have now completed our study with the alleged Russian multiple sclerosis virus of Shubladze et al. The questions that I asked and the answers I obtained are as follows:

1) Is Shubladze virus only related to rabies or is it antigenically indistinguishable? Quantitative serum dilution cross neutralization tests with antirabies serum and antiShubladze virus serum against both rabies and the Shubladze virus indicated that the two viruses are not merely related but are indeed antigenically indistinguishable.

2) Is it true as claimed by Shubladze and co-workers that sera from patients with multiple sclerosis will neutralize the virus while normal sera will not? Instead of testing the sera against a fixed amount of virus (as Dick did) I determined the neutralization index of the various sera by testing undiluted serum against varying amounts of virus. In the very first test in which 5 sera from patients with multiple sclerosis were compared with 5 normal sera I was able to confirm the findings of Shubladze et al. However, I remembered that years ago I found that freshly obtained sera from human beings who had never been vaccinated against rabies very often yielded neutralization indexes in the range of 100. In the tests just mentioned the multiple sclerosis sera had been in the deep freeze for only about 2 weeks while the normal sera had been in the deep freeze for about a year. In a series of subsequent experiments it was possible to show that fresh normal human sera also neutralized the virus to the same extent as the sera from the MS patients and that the neutralizing principle in both was completely destroyed by heating at 56°C.
for one-half hour while specific antirabies and anti-Shubladze virus antibodies were not affected by heating at 56°C. Our final conclusion was after a series of tests on normal and MS sera that the neutralizing activity of MS sera is due to this nonspecific factor rather than to antibody and that there is no difference between MS sera and normal sera when proper precautions are taken to handle and store them in the same manner. I am somewhat puzzled that Dick failed to find this in his tests unless the handling of the sera prior to the time that they reached him was such as to inactivate this heat labile factor. At any rate while Dick's studies failed to find an explanation for the Russian observations I believe that our tests indicate where they might have been misled.

3) Was the pathology produced by the Shubladze virus any different from that produced by fixed rabies virus? The only difference that I found was that the Shubladze virus still produced Negri bodies in mice while the strain of fixed rabies virus that I used did not. There was no significant or specific demyelinization with either strain.

The results that I have just mentioned will be submitted for publication very shortly and you may quote them if you like. Now as regards your question about the attitude of reliable investigators in the Soviet Union, I don't know of anything in print that indicates the widespread skepticism that I encountered both among virologists and clinicians. I also spent some time with Professor N. I. Graschenkov who was a neurologist and neurophysiologist in charge of the Botkin Hospital and also President of the Scientific Advisory Board to the Ministry of Health. I made rounds with him one day at the hospital and he showed me patient after patient with multiple sclerosis who had been treated with the so-called multiple sclerosis vaccine without effect. Professor Graschenkov worked in England with Lord Adrian in 1936 and Adrian visited him in Moscow about 2 years ago. It is possible that if Lord Adrian wrote to Graschenkov he might obtain an expression of opinion in writing that might not be available in print. I think it is well to remember that the Russian government had used
this vaccine as a propaganda tool for some time and I can understand the hesitation of some investigators in the Soviet Union to publish anything against it - at least up to the present time.

With best wishes and kindest regards.

Sincerely yours,

Albert B. Sabin, M. D.

ABS: meh