June 5, 1951

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Dear Major Burns:

Thank you very much for sending me your preliminary draft of the report entitled "Demonstration of Residual Immunogenic Effects Produced by Japanese B Encephalitis Vaccine among Indigenous Personnel, Okayama, Japan 1950." Before saying anything else, I should like to commend you most highly for the tremendous amount of work that you are doing and for your inclination to write things up as quickly as they are done. I have just finished reading the 1950 Annual Historical Report of the 406th Medical General Laboratory and am simply amazed by how much work was done in your section.

With regard to the specific report which you sent me, I would like to say the following about its contents:

1. The reported cases in Okayama in 1950 — I have pointed out on several previous occasions, as well as in the original planning of this study, that any comparison on the incidence of Japanese B encephalitis in the vaccinated and unvaccinated groups must be based only on serologically proved cases. Your report says absolutely nothing at all about the serological confirmation of any of the reported cases. You state that a certain number of serum specimens were obtained, but nothing at all is said concerning the results. Although several hundred other sera were collected from Okayama and submitted to serologic study, the most important aspect of the work, namely serological confirmation of the diagnosis, is lacking. Accordingly, I cannot consider the conclusions drawn from the reported cases as having any significance. If the Japanese investigators had obtained those sera, you should report what results they had gotten with them. If you, yourself, have obtained such sera, you should state what the results have been. If you or Colonel Hullinghorst
had make no arrangements for the collection of such sera, it is highly regrettable.

2. The immune status of several groups of children in Okayama in 1950 — The presentation of your data on the neutralization tests would have been very much easier to digest if you had given the incidence of positives without forcing the reader to go through a series of calculations before he can arrive at what is actually there. Thus, if one compares the 3 groups of children (A - unvaccinated; B - children vaccinated at various times since 1946 and receiving boosters up to 1949; and C - children initially vaccinated in 1949) in the pre-epidemic period of 1950, one sees that 5 of 25, or 20%, were positive in Group A; 57 of 72, or 80%, were positive in Group B; and 41 of 66, or 51%, were positive in Group C. However the total number tested in Group A is too small for valid comparison, and, in view of the fact that Table 1 indicates that you had at least 105 sera in this group, it is regrettable that you did not test a larger number for neutralizing antibodies rather than for complement-fixing antibodies. Before further comparison is possible, I would suggest that you test at least another 50 of those sera in Group A. This is particularly desirable since in a post-epidemic sampling in 1950, Group A yielded 34 of 73, or 47%, positive, while Group B yielded 62 of 69, or 90%, positive, and Group C yielded 61 of 81, or about 50%, positive. The most reasonable interpretation of these data is that the immune status of Group A and Group C was probably about the same. Therefore, in order to be able to evaluate these data, it would be highly desirable if you could state the results of the neutralization tests on Group C in 1949. The question at issue is: Did the vaccine used in 1949 possess sufficient immunogenic potency to give rise to antibodies in those who had none? If it did give rise to such antibodies in 1949, the data you are reporting for 1950 could be interpreted as indicating that the antibodies did not persist through the winter. On the other hand, it is also possible that the vaccine used in 1949 was of such poor potency that it did not give rise to antibodies in an appreciable number of those who were without them before vaccination. I believe that that is a very important point to establish, and I hope very much that when you revise this report, you will include data to elucidate this question. On the other hand, it is very striking to me that the incidence of neutralizing antibodies in Group B was approximately twice as high as in the other groups and of an order not achieved in the unvaccinated population until a later age. This would suggest that the repeated boosters were highly effective in raising the immune status of these children, and the most
important question now is to what extent this immunity will be lost in subsequent years without further boosters. It would, therefore, be highly desirable to obtain blood specimens on the same children (not just another group) in Groups A, B and C who were positive in 1950 and see how many of them had become negative by June 1951.

With regard to acknowledgments in your report, it is not quite clear what portion of the work was done by yourself and what was done by others. What I mean is that it would be highly desirable to indicate the source of your information on data which obviously was not done by yourself. We all know that the serologic tests which you report were done under your direction, but who is responsible for providing all the information on the numbers of vaccinated and unvaccinated children in each community? Who checked all the cases and their diagnoses? Who provided you with the epidemiological data which are given in this report? If you obtained them from one Japanese source, I think it would be worth giving the name and affiliation of the Japanese investigators who had accumulated all of this information upon which you base so much of this report. From my own experience in Okayama I know how much of a job that is. On previous occasions when you sent me such preliminary drafts for presumably subsequent distribution, I never saw any final drafts nor did I have an opportunity to gauge to what extent my comments and suggestions influence your handling of the material, I would appreciate it very much if you could let me know what the ultimate distribution of this report you are writing is to be. If it is intended only for the records of the 406th Medical General Laboratory, I would appreciate it if you could supply me personally with answers to whatever questions I have raised in the discussion of your manuscript.

While you are answering some questions, I would also like to ask you to enlighten me on something which I find a little confusing in your section of the 1950 Annual Report. On Page 202 you indicate the complement fixation titers refer to the final serum dilution. Thus, a titer of 1:4 would be equivalent actually to undiluted serum. On the other hand, elsewhere in the report — Page 209 — your results suggest that you may be using original dilutions of serum for expression of the titer. Could you, please, let me know which it really is? I was also extremely interested in the high incidence of virus isolations that you obtained from mosquitoes in 1950. To what do you attribute the success in 1950 as compared to the very low incidence of positive isolations in previous years? Did the technique you used in 1950, namely, of grinding the mosquitoes in buffer of high pH plus antibiotics, differ from
that which you employed in 1949 and before 1949?

I am retaining the carbon copy of the report you sent me for my records but will return it to you if you should require it for other purposes.

With all good wishes,

Sincerely yours,

Albert B. Sabin, M. D.

P. S. Do you by any chance have a list of all the fatal Japanese B cases in American personnel since 1947 with their vaccination status? If you do, I would be very grateful to you if you could send me such a list.