August 11, 1950

Dr. W. Neil Harmon
Graduate School of Public Health
University of Pittsburgh
Pittsburgh 13, Pa.

Dear Bills:

Many thanks for the confidential mimeographed report dealing with the possible existence of Japanese encephalitis virus in California. It all had a very familiar ring to me and you have all my sympathy for the headaches it must have caused you and the tremendous amount of work this sort of thing, of necessity, engenders.

In view of my own experience, dating back to 1942 relative to "neutralizing antibodies" for Jap B virus among Cincinattians and to 1946-1947 relative to its occurrence in arthropods from Japan, I put my finger on two important facts in your very detailed report:

1) Jap B (Nakayama) virus was centrifuged in the room (A) just prior to harvesting the mouse inoculated with the Aedes dorabilis mosquitoes from California.

2) The data on patients and horses listed in Tables 6 and 7, contain no information regarding complement fixation tests with Jap B antigen on the sera which were tested for neutralizing antibodies.

I think you will agree that Jap B C-F data on these sera are of crucial importance in deciding whether or not infection with Jap B virus had occurred, and I hope that the sera are still available for such tests. With regard to the significance and interpretation of the Jap B neutralizing capacity occasionally exhibited by certain American sera let me first refer you to my discussions in the enclosed reprints (Sabin, Corder and Nakamato, Difference in dissemination of the virus of Japanese B encephalitis among domestic animals and human beings in Japan, Am. J. Hyg., 1947, 46, 341-355; Corder, Nakamoto, Schlesinger and Sabin, Neutralizing and complement-fixing antibodies for Japanese B encephalitis virus in vaccinated U.S. personnel in Japan, Proc. Soc. Exp. Biol. and Med., 1947, 65, 130-135). You will note that the Japanese first encountered it in 1930 among sera sent from New Haven, Canadians also in 1938 in a patient with encephalitis in Manitoba (sera tested at Rockefeller Institute), then my own experiences in Cincinnati and Tokyo, which were triple-checked. Although I think that the C-F test by itself can clarify the situation in individual patients...
who may exhibit such neutralizing capacity there is something else which might also prove to be helpful.

In 1942, I observed that the sera of "normal" Americans which neutralized Jap B virus (and the range of neutralization indexes was similar to that recorded in your table 6) became completely negative after heating at 56°C for 30 minutes. Although such heating may reduce the titer of specific Jap B antibodies, a number of tests with human sera indicated that neutralization is not completely abolished and occasionally not even significantly reduced. I think now, that it is most important to test the possibility of "reviving" the specific activity by undiluted (fresh or frozen) human or guinea pig sera which contain heat-labile accessory factors. My experience with dengue and especially with toxoplasma neutralization suggests that this procedure may prove useful in distinguishing specific from non-specific neutralization for certain other infectious agents as well.

The irregularity with which the "nonspecific" neutralizing substance may be encountered in the same individual, especially in relation to an acute infection, was brought home to me in a study with Newcastle virus carried out by Beatrice Howitt on acute and convalescent sera, kept frozen in dry ice throughout, which I sent her from patients with epidemic pneumonitis in Cincinnati. You will note in the enclosed confidential summary (please return it to me after you have seen it), that in many instances the acute serum failed to neutralize while the convalescent serum neutralized in very high titer. It would have been easy on the basis of the neutralization tests to report this as an epidemic of pneumonitis caused by Newcastle virus. However, I insisted on other tests including heating of the sera, and complement fixation. Heating at 56°C completely abolished these high neutralization indexes and the C-F tests were entirely negative. It is not impossible that you may find the same thing in relation to Jap B among the patients listed in your Table 6.

I will withhold my final verdict on the presence of Jap B virus in the U.S.A. until you have had an opportunity to test those sera in the manner discussed above. The present evidence, however, does not, in my opinion, warrant the suspicion that Japanese B encephalitis virus has been introduced in the U.S.A.

With all good wishes for your success in unravelling this business,

Sincerely yours,

cc: Dr. John R. Paul
Dr. Colin MacLeod
Lt. Col. Frank L. Bauer
Dr. W. C. Reeves

Albert B. Sabin, M.D.