July 18, 1949

Dr. John R. Paul
333 Cedar Street
New Haven, Connecticut

Dear John:

I have received your letter of July 12th with the enclosed memorandum for General Sams on the subject "Anti-mosquito measures most likely to break transmission chain of virus of Japanese B encephalitis to human beings", written by Dr. Sabin and signed by Albert and yourself. I shall forward Col. Bauer's copy to him as you requested but am returning the original to you with my comments in this letter rather than adding them to the original memorandum, and forwarding all to Col. Bauer for transmission to General Sams.

Albert had sent me a copy of the memorandum which arrived a few days before your letter. His came while I was in Bakersfield and I went directly from there to Yakima and have just returned recently to San Francisco to find both on my desk. Unfortunately, Dr. Reeves is in Bakersfield and I have not been able to talk this matter over with him and although I have tried to contact Dr. Meiklejohn, I have failed to do so. Dr. Sasa, however, has just been with me and I have talked it over with him.

It is my opinion and that of Dr. Sasa that the recommendations being made are premature and result from drawing conclusions on a series of hypotheses not sufficiently supported by facts which, if carried out, would divert efforts being made at present which may be equally as important or more important in the control of Japanese B encephalitis than those more limited methods proposed. It would take a twenty page paper with many references to present all of the reasons and evidence for making the above statement. I will point out just a few of the most conspicuous points in the following paragraphs.

In a series of two papers published in the American Journal of Hygiene, 71:82-102, 1948, can be found a story from our unit of a concept of the importance of Culex tarsalis found within chicken houses. This concept was based on more factual information and on a longer period of investigation than that suggested in the current memorandum. No recommendation was made, at the time this concept matured, to any official health organization that control measures be carried out to break the cycle at what appeared to us to be a very likely vulnerable link. Instead, a carefully planned field experiment was undertaken to determine whether the concept was correct. It proved to be wrong and we were glad that we had not recommended control procedures to be applied only in the form of residual DDT to the walls of chicken houses.

No one has any data at present to prove that the principal source of infection of mosquitoes during the typical explosive epidemics of Japanese B encephalitis as observed in man is not man himself. We know nothing about the titer of virus in the blood of man prior to the onset of the clinical disease. The blood of man at this time may very possibly be more important than that of his domestic animals. I agree in all probability that "chickens are out of this cycle", but "our studies on the ecology of the mosquitoes in Okayama" are of such a sketchy nature and are so incomplete that they are of suggestive value only, so I cannot agree that "birds may probably also be left out of consideration", although there is a good possibility of such. Many of the carefully planned studies that are being carried out this summer under Col. Tigertt's directions are aimed at throwing more light on this particular phase of the subject and it appears to me to be
undue to draw conclusions and institute far reaching administrative procedures without the aid of these current studies. In any case, there is no valid evidence to cause us to conclude at this time that man's domestic mammals are the only important source of mosquito infection.

In regard to the statement "available evidence suggests Culex pipsiens can, for all practical purposes, be eliminated from consideration"; this is diametrically opposed to the opinion of Dr. Sasa who carried out the mosquito studies which I believe are the principal basis for the knowledge on which Dr. Sabin draws his conclusions. Dr. Sasa points out to me that there are no Culex tritaeniorhynchus within the city of Tokyo, yet there has been epidemic after epidemic of the disease attacking the population within the metropolitan area of the city. On the periphery of the city there are areas where C. tritaeniorhynchus breed and can be found in numbers. My own experience is of too scanty a nature to present for evidence, although in so far as it goes it agrees with Dr. Sasa's statement. We shall also recall that there are no C. tritaeniorhynchus on Guam but that Culex quinquefasciatus, a very close relative of Culex pipsiens, is the only mosquito found in large numbers in the homes of natives on Guam. There are also large numbers of these on Okinawa. I feel as Dr. Sabin does and pointed it out in early 1946, that the activity curve of C. tritaeniorhynchus as we have seen it presented by Japanese entomologists suggest that this mosquito should be more important than C. pipsiens. Both mosquitoes appear to be able to transmit equally well, both of them have been found infested by Japanese workers and although we have now found C. tritaeniorhynchus infected nine times, the numbers of C. pipsiens collected in the same area were so small to be of no significance. The collectors limited themselves to large animal shelters and so found C. tritaeniorhynchus and Anopheles hyrcanus sinensis and did not look in human habitations and elsewhere where C. pipsiens might have been found in large numbers.

The statement "our studies on the ecology of the mosquitoes in Okayama reveal that Culex tritaeniorhynchus and Anopheles hyrcanus sinensis rarely became engorged with blood after biting human beings" does not conform at all with the observations made by any of us including Dr. Sasa. When these mosquitoes bite man, they engorge very readily.

Since writing the above, I have been in communication with Dr. Reeves by telephone and he agrees in general with the above and has pointed out the following which I was also about to record: the fact that Culex tritaeniorhynchus are "found to remain in dark and humid corners of the animal shelters in which they engorged with blood the night before" is a perfectly valid observation which I have made, Dr. Reeves has made, and Dr. Neiklejohn has made in Japan or in Okinawa or in both places. However, this does not mean that this represents a high proportion of the potentially infected population of this mosquito. We again tentatively drew this same conclusion, which proved to be erroneous, in Kern County, believing that Culex tarsalis was principally a domestic mosquito accounted for in a large part by the adults which we found in chicken houses and in other shelters near domestic habitation. We did not find them in the fields or in hollow trees or in bushes at a distance from human habitations and concluded that their activity was limited almost entirely to the area of human habitations. However, when we found that 99% of the wild birds were infected with avian malaria and that C. tarsalis was the principal vector it was necessary to acknowledge that this was a "wild" mosquito, very active in areas distant from human habitations and hiding out during the day time in very large numbers in places we did not as yet recognize.
Observations made by all of us suggest that C. tritaeniorhynchus is present in large numbers hiding in places we have not yet recognized. There is no doubt about it that the easiest place to find them in the daytime is on the walls of large animal shelters. A high proportion of these are engorged, heavy and have not flown any great distance, explaining why these are to be found there. However, once the blood is digested, they probably take off for other places. Not until 7 to 10 days after the blood has been digested from the animal from which they become infected are the mosquitoes infective. We have gone to Japanese village after village where there has been but one shelter containing horses or cows and C. tritaeniorhynchus were found in large numbers in these shelters. And, we found them in very small numbers or absent in any other type of shelter. Yet, when a light trap was hung out at night at a considerable distance from the barn, thousands of C. tritaeniorhynchus were caught. A fair proportion of these contained eggs indicating that they had had a previous blood meal. It is just as possible that they had received this previous blood meal from a rat, a mouse, another rodent, a dog, a cat, a goat or a horse or a man and from all we know yet, a bird. Spraying only the interior of shelters of mammalian domestic animals is probably not going to noticeably decrease the numbers of C. tritaeniorhynchus in any one area any more than spraying chicken houses for C. tarsalis. Furthermore, it is quite likely not to effectively reduce the number of potentially infected mosquitoes, since as yet we have no idea as to what species of animals serves as the most important source of virus infection. I would like also to point out that Dr. Meiklejohn, Dr. Rees, Lt. MacIaren and I have gone through village after village on Okinawa in the epidemic year of 1947 and found not a single large domestic mammal in the village, yet cases of encephalitis. These animals were scarce in Okinawa after the war. An occasional village had one, two or three domestic mammals such as Dr. Sabin feels are principally responsible for the infection of mosquitoes, but by the results of our tests and by the tests made by Dr. Sabin back in 1945, it is known that practically 100% of these domestic mammals are immune and that probably not more than one or two out of a hundred of these sparsely scattered animals on that island are still susceptible and could serve as a source of mosquito infection. I might also point out that horses and even dogs are very scarce at present in Tokyo and that the percentage not immune makes the number potentially available quite insignificant.

I feel there are too many uncertainties in regard to item #5 being correct, I do not concur in #6 and would expect that if this measure were carried out on a large scale as suggested in #7, results would probably not "show that this is either the simplest method for controlling Japanese B encephalitis or that there is something radically wrong with our present concepts of the transmission of the infection". It would probably not show anything because it would not be carried out in the form of an experiment. It might be possible to plan a carefully conducted experiment such as that of Kern County with control areas so that an answer might be obtained. However, I would like to know the results of some of the current studies of this year before feeling that such an experiment was even justified as yet.

My recommendations are that mosquito larval control measures be carried wherever practicable together with residual DDT applications in the habitations of human beings and their domestic animals as is the current practice, until we have gained more fundamental epidemiologic information.
I would like also to suggest that it would be only courteous to give Col. Tigertt an opportunity to comment on something like this before it is turned over to General Sams. At the moment Col. Tigertt has more information on this and is probably closer to the situation than any of us here. He has at least three of my field personnel on loan working on these problems and he is currently very interested in collecting and analyzing data to render control measures more specific and effective.

Very sincerely yours,

W. McD. Hammon, M. D.
Professor of Epidemiology

H/r

cc: Dr. Albert Sabin
    Dr. Colin MacLeod
    Lt. Col. Frank Bauer