August 13, 1987

Dr. Albert Sabin  
3101 New Mexico Avenue, N.W.  
Apartment #1001  
Washington, D.C. 20016

Dear Albert:

Thanks very much for your letter of August 7th and the accompanying reprints. You raise three main points in your letter and I will address them in order.

You were the first to show that there was transitory cross protection between dengue serotypes and you also failed to observe evidence of disease enhancement with sequential infections. Subsequently, many other observers also have failed to note disease enhancement with sequential dengue infections under a great variety of circumstances. The reason that I have not quoted such studies in my reviews is that the proponents of the immune enhancement hypothesis say that enhancement occurs only at certain critical intervals of time between infections and only with certain strains of virus. Since they specify neither the intervals nor the characteristics of the viral strains, it is impossible to disprove the hypothesis—no matter how many observations one makes. As you can imagine, it is a frustrating situation to deal with. As for the in vivo and epidemiologic studies which purport to support the hypothesis, I know that in several instances, at least, data were "cooked" by adjusting the criteria for primary versus secondary infection or by eliminating certain observations to make the information "fit".

One of the unique problems of dealing with the immune enhancement hypothesis is that it is has been promulgated almost exclusively by workers associated at one time or another with the Army laboratories in Bangkok and at Walter Reed. Moreover, the scientific reputations of several senior investigators (including the general who presently heads the Army Medical R and D command) are tied to the hypothesis. As you can imagine, junior investigators in those institutions and outside arbovirus investigators dependent for research support on Army money are reluctant to criticize the hypothesis. The immune enhancement
hypothesis has been repeated so many times in reviews and
textbooks that most persons outside the field accept it as
established fact.

On the second point, you have mis-interpreted my position
on the subject of pathogensis. As indicated on pages 338 and
339 of the enclosed reprint labelled "1", I do think that the
clinical manifestations of dengue comprise a continuous
spectrum. The reason that I have had to discuss just the severe
end of the spectrum in my reviews is that the "World Health
Organization" claims that there are two distinct types of
dengue, and says that "dengue hemorrhagic fever" and "dengue
fever with hemorrhagic manifestations" are two different
entities! This bizarre conclusion is sponsored by WHO because
most hemorrhagic phenomena associated with dengue cannot be tied
to immune enhancement—no matter how hard one tries. The
definition became "official" by making sure that persons invited
to serve on WHO "expert" committees did not include outspoken
individuals with a contrary view.

On the third point, I plead guilty. I was aware of your
studies on the genetic basis of flavivirus resistance in mice
but did not know (or forgot) that you had related them to the
phenomenon of black resistance to yellow fever in Africa. Now
that you point it out, I think it very likely that that is the
basis of the resistance of the black population in Cuba to the
severe manifestations of dengue. I was reluctant to mention the
observations in mice since many would question their relevance
to man.

Don't feel bad. I am 20 years younger than you and I
also find that many of my earlier papers have been overlooked!
I will be leaving for Paris in about one week and consequently
if you wish to contact me in the next few months, please do so
at the following address:

Dr. Leon Rosen
26 Rue des Boulangers
75005 Paris, France

With best wishes,

Sincerely,

Leon Rosen