26 January 1945

SUBJECT: Neutralizing Antibodies in Dengue and the Capacity of Different Strains of the Virus to Stimulate their Production.


1. Attempts by other investigators in former years to demonstrate neutralizing antibodies in convalescent dengue serum were unsuccessful.

2. It has been possible to demonstrate that the serum of volunteers convalescent from infection with the Hawaiian strain of virus was capable of neutralizing 1,000, but not 100,000 minimal human infective doses. This means that when 0.9 cc. of convalescent serum is mixed with 0.1 cc. of acute dengue serum diluted 1:100, and the mixture is injected intracutaneously in a human volunteer, no local lesion develops and no disease results; the acute dengue serum used is of such potency that mixed with normal serum it regularly produced local skin lesions and unmodified dengue in a final dilution of 1:100,000, while the 1:1,000,000 dilution produced no, or negligible, local lesions and clinical infection in 3 of 4 volunteers tested.

3. Neutralizing antibody against 1,000 human infective doses has now been demonstrated in the serum of volunteers convalescent from infection with the Hawaiian strain of virus, 1 week, 1 month, 2 months, 3 months and 8 months after defervescence.

4. The serum of a U. S. Army medical officer who had dengue in the Philippines about 20 years ago failed to neutralize 1,000 and also 10 minimal infective doses.
5. The serum of a volunteer who 7 weeks before recovered from infection with the "New Guinea--\[redacted\]" strain of dengue and was proved to possess a partial though definite immunity to the Hawaiian strain (via infected mosquito bites), failed to neutralize 10 as well as 1,000 minimal infective doses.

The possibility that this represented evidence for the existence of immunologically distinct types of dengue virus was dispelled when it was found that this serum could not neutralize a minimal amount of the homologous virus, i.e., the "New Guinea--\[redacted\]" strain.

6. Additional tests revealed that 3 of the 4 available New Guinea strains (\[redacted\] and \[redacted\]) did not give rise to neutralizing antibodies against the Hawaiian strain. The fourth New Guinea strain (\[redacted\]) represented by a convalescent serum obtained from a volunteer approximately 6 months after infection, did produce such antibodies.

7. The evidence now available suggests that some strains of dengue virus stimulate the production of neutralizing antibodies, while others do not, and that some strains give rise to more complete active immunity than others.

8. It is of interest to note that tests with known sera have indicated that a large number (20 to 40) different sera may be tested for neutralizing antibodies on a single volunteer, on the basis of the appearance of a local skin lesion.

9. On the basis of these results a positive neutralization test can be
can establish that dengue infection has occurred at some time in the past, while a negative test cannot exclude it.

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