The Rockefeller Institute for Medical Research
Princeton, New Jersey

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SUBJECT: Penetration of Dengue Virus through Normal Nasal Mucosa with Resulting Modification in Clinical Type of Infection.


1. When it became evident that attempts to produce immunity against dengue by inactivated virus yielded negative results and did not offer, at this time, a practical approach to the problem, experiments were undertaken to determine whether or not there may be some way of administering active virus which might give rise to a sufficiently altered type of infection to lend itself for consideration as a method for immunization. Nasal instillation of the virus was tried as part of this program.

2. In the first experiment two volunteers received 0.5 cc. of undiluted dengue serum in each nostril. After an incubation period of 9 to 10 days both developed a modified infection in which the rash (dermotropic or endotheliotropic effect) was as marked as any seen with the Hawaiian strain of dengue virus and the usual leukocyte changes were present, while the fever and other manifestations were entirely negligible in one and reduced to a period of slightly more than 24 hours in the other. This is to be contrasted with the 5 to 7 days of fever, prostration and other severe clinical manifestations followed by a week or more of slow convalescence which almost regularly results from transmission of this virus by mosquito bites, parenteral inoculation, or even by rubbing into the scarified skin.
3. Dengue virus was demonstrated in the blood of these volunteers at the time the rash appeared, by subinoculation.

4. Another experiment was performed to determine the regularity of infection by the nasal route, the character of the resulting disease, and the effect of smaller amounts of virus. Two volunteers again received 1 cc. of undiluted dengue serum and two others 1 cc. of serum diluted 1:10. All became infected, but only two had the truly modified form of the disease.

5. It was, furthermore, established that in the modified disease following nasal instillation, enough virus is present in the blood at the onset of the rash to permit *Aedes aegypti* mosquitoes feeding at that time to acquire the capacity to transmit the infection.

6. About 5 weeks after nasal instillation, the three volunteers who exhibited the mildest symptomatic reaction were exposed to the bites of dengue infected mosquitoes and were found to be immune.

7. It still remains to be determined whether with a suitably small dose of virus, mild reactions may be obtained regularly.

8. Since it has been found previously that when yellow fever vaccine is given simultaneously with dengue, the rash is entirely prevented or markedly diminished, it is also planned to test the effect of combining nasal instillation of dengue virus with subcutaneous injection of yellow fever vaccine.

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