SUBJECT: Interference and Immunologic Relationship between Dengue and Yellow Fever Viruses—Summary of Results Obtained in Studies on Human Beings, Rhesus Monkeys, and Aedes aegypti Mosquitoes.


Studies on Human Volunteers:

1. When virulent dengue virus, in amounts ranging from 10 to 1,000,000 human infective doses was inoculated simultaneously with, or 3 days after, yellow fever vaccine in human beings, the onset of dengue was delayed for 3 to 6 days, and the resulting disease was milder and of shorter duration.

2. When the dengue virus was injected 1 week after the yellow fever vaccine, the incubation period was unaffected, but the resulting disease was also milder and of shorter duration.

3. Neither the incubation period nor the duration or severity of dengue was modified in human volunteers who received the standard U.S. Army dose of yellow fever vaccine 5 weeks before being bitten by dengue-infected mosquitoes or the inoculation of 10 human infective doses of dengue virus.

4. Thirty volunteers were used in this study and the following conclusions seem warranted:
   a. Immunity to yellow fever neither protects against nor modifies the disease resulting from infection with dengue virus.
   b. While the simultaneous injection of yellow fever vaccine and dengue virus results in a rather mild and modified form of dengue, it cannot be regarded as a feasible method for the simultaneous immunization against both diseases.

Studies on Rhesus Monkeys:

1. Dengue virus in the form of highly infectious human serum inoculated intraabdominally or intracerebrally produced no apparent infection in rhesus monkeys. However, when it was injected 2 or 3 days before virulent, viscerotropic yellow fever virus, it interfered with the multiplication of the latter
virus and resulted in the survival of 6 of 7 monkeys (3 experiments) while all 9 controls inoculated with yellow fever virus alone died. When the interval between the dengue and yellow fever inoculations was 4 or 5 days, there was still demonstrable interference with the multiplication of the yellow fever virus, but death of the monkeys while postponed, was not prevented.

2. There was no evidence of cross immunity between the two viruses in monkeys receiving yellow fever virus one month after an inoculation of dengue virus.

Studies on Aedes aegypti Mosquitoes:

1. Aedes aegypti mosquitoes which first were proved to have become infected with dengue virus were allowed to feed on monkeys infected with the highly virulent, Asibi strain, of viscerotropic yellow fever virus. After a suitable interval these mosquitoes were tested for their capacity to transmit yellow fever, and 2 of the 3 monkeys bitten by them died of yellow fever.

2. Tests in which individual mosquitoes were inoculated in mice suggested, however, that some of the dengue infected mosquitoes did not become infected with the yellow fever virus, while all the normal mosquitoes did.

3. In view of the fact that in feeding on monkeys infected with the Asibi strain of yellow fever virus, each mosquito acquires about 10 million M.L.D. of the virus, a degree of infection which may not obtain in nature, further experiments are indicated in which the mosquitoes are allowed to feed on artificial mixtures containing varying amounts of yellow fever virus.

Note:

These studies have been carried out in collaboration with Drs. Max Theiler and J. H. Bauer of the Laboratories of The International Health Division of The Rockefeller Foundation.