Arthropod-Borne Encephalitides in Japan and Southeast Asia

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It is likely that the report of this unusual investigation will be followed with interest—regardless of the reader's particular professional concern—and that it will leave him with a heightened regard for the essential ingeniousness of scientific research.

The arthropod-borne, viral encephalitides, specifically Eastern, Western, and Venezuelan equine encephalitis, and the St. Louis, Japanese, Murray Valley, and Russian spring-summer encephalitis, are a group of clinically and epidemiologically related infections which are distinguished from one another chiefly on immunologic and geographic grounds.

The results of hemagglutination-inhibition tests show that the viruses causing these diseases, as well as certain other insect-borne agents, may be classified into two broad groups, designated A and B by Casals and Brown.[1] The geographic distributions of these viruses do overlap somewhat, viz., St. Louis and the equine encephalitides in this country and Japanese and Russian spring-summer encephalitis in northeast Asia.

Historically, knowledge of these diseases began with the clinical and pathologic studies which defined them as central nervous system infections and was extended by virologic and epidemiologic investigation which established the nature of the infectious agents and their mode of transmission. Epidemiologic studies of several of these diseases, including Japanese encephalitis (JE), revealed that a wide variety of vertebrate and invertebrate hosts are infected in nature. Such observations raise the question of where man and the other hosts fit into the picture. The work to be presented here deals with the ecology of JE virus and follows logically from the extensive earlier work of both Japanese and American investigators. This report is a summary of the efforts of the scientific staff of the 406 Medical General Laboratory in Tokyo. Much of it remains to be published formally, but the data in epitomized form are given in the Annual Reports of that laboratory for the years 1950–1954.

JE in the main islands of Japan is a seasonal disease limited to the months of August and September. Human epidemics have occurred at irregular intervals in various parts of Japan, but outbreaks involving a thousand or more cases appear in metropolitan Tokyo (which includes rural as well as crowded urban areas) every second or third year.[2] Encephalitis in the domestic animals of rural areas was frequently observed simultaneously with the occurrence of human disease in nearby cities. The close association of epidemic disease with the seasonal abundance of culecine mosquitoes suggested to Japanese epidemiologists in the early 1930's that the encephalitis was mosquito-

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borne. In succeeding years Mitamura and his associates recovered JE virus from several culecine species,[3, 4] including Culex tritaeniorhynchus Giles. Moreover, in 1948 Hammon, et al., reported the isolation of the virus from C. tritaeniorhynchus collected in Okayama.[5]

In recent years studies of the Army group in Tokyo demonstrated that of all suspected species C. tritaeniorhynchus is the sole vector in the Tokyo area (and probably in all Japan as well). Moreover, these workers found that outbreaks of human or animal encephalitis first appear well after peak numbers of these particular mosquitoes have been attained in the environment. Further, the occurrence of clinical encephalitis tended to parallel the frequency with which virus was detected in these mosquitoes. Thus, when mosquito infection rates were high more overt disease was observed than in seasons when mosquito infections were minimal.[6] Sometimes infections occurred in horses and pigs without involvement of human beings[7] and, conversely, epidemics were encountered without associated epizootics.

The source of JE infection for the culecine mosquito was unknown when the present ecologic studies were begun. However, it was known that C. tritaeniorhynchus in Japan was a strictly seasonal mosquito, being present in the Tokyo area only for five-eight weeks beginning about mid-July.[6] During this short interval the population increased rapidly to peak about the first week in August and declined as quickly. In these few weeks C. tritaeniorhynchus acquired, propagated, and transmitted its infection. Virus was rarely detected in them until after their peak population was attained, but thereafter was demonstrated frequently. This suggested that the mosquito population was seeded with virus very rapidly and almost simultaneously over a wide area.

When this question came to serious study in 1952 man and his domestic animals seemed unlikely sources for the rapid, mass, mosquito infection. Most of the human and domestic animal populations were immune to JE; hence, very few were capable of developing the viremia which could serve as a source of infection for mosquitoes. Attention was therefore directed to certain of the Japanese wild birds which in earlier studies by Hammon and his associates[8] had presented serologic evidence of previous experience with JE virus. Birds were particularly appealing as potential sources of mosquito infection because they are short-lived and prolific. Thus, there was a rapid turnover of population with large numbers of new susceptibles each year. In addition, viremia of two- to five-day's duration consistently followed experimental infection of a variety of recently hatched wild and domestic birds. Hence, birds seemed to provide a reasonable source for infection of large numbers of mosquitoes.

Such observations as these prompted a search for naturally occurring viremia in the nestlings of a heron-egret rookery near Tokyo. Begun in 1952 the birds and mosquitoes of this rookery were studied for infection at regular intervals throughout the summer of each year. The resulting data show that both birds and mosquitoes of such a habitat were infected simultaneously in early August each year. Moreover, the frequency of mosquito infection tended to parallel that of the nestlings. Thus, in 1952 when active infection was experienced by many of the rookery's herons (but not the egrets) virus was recovered from mosquitoes almost daily during the same interval (July 29–August 11). The following year heron infection was not demonstrable. Instead virus was recovered from a single egret, and mosquito infection was correspondingly less frequently detected than in the preceding year.[9]

An explanation for the selective in-

fection of herons in 1952 was suggested by the feeding behavior of the vector mosquito in the rookery. Both direct observation and controlled experiments with bird-baited traps in the field showed that herons attracted 10 to 20 times more C. tritaeniorhynchus than did egrets. Thus, even though nestling egrets were as abundant as were young herons during this year in the rookery, the species most frequently infected was that with the greater mosquito attack rate. It should be emphasized that in 1952 the vector mosquito had ample opportunity both to acquire and to further transmit virus to these birds.

The selective biting behavior of the vector would not explain the failure to demonstrate heron infection in 1953. The absence of heron infection and the over-all low incidence of avian infection that year might be attributed to the high incidence of immunity in the nestling population. Thus, the majority of heron nestlings hatched throughout the summer of 1953 possessed neutralizing antibody to JE virus. This occurred long before virus was detected in mosquitoes. Only 28 per cent of the egret nestlings had this neutralizing substance that year. Further study showed that this antibody was transovarially transmitted from the parent hen and that such passively immunized young birds failed to develop viremia when inoculated in the laboratory with JE virus.

These careful observations of avian viremia in a single rookery cannot be extrapolated to embrace infection of the bird population of Tokyo. Nevertheless, preliminary data obtained in 1954 and 1955 in other areas suggested that the findings were representative for the Tokyo area. Further, other adult birds living in different habitats (cormorants, magpies, thrushes, bulbuls) had as high an incidence of neutralizing antibody as did the herons of the original rookery. It seemed logical to postulate that certain wild birds played a significant role in the rapid seeding of the vector population with virus in the Tokyo area. Added weight for this hypothesis, and against that of domestic animals being of importance, was the absence of epizootic disease in the Tokyo area in recent years.

It is possible at the present time only to speculate upon the relationship of these observations to the occurrence of JE in man. In the years 1952–1953 avian and mosquito infection preceded by two- to four-weeks the peak occurrence of human encephalitis in Tokyo proper. The incidence of human disease paralleled the frequency of bird-mosquito infection being highest in 1952 when infection in the lower forms was most frequently demonstrated.

The mechanism for the perpetuation of virus from one season to another is unknown, but there are many interesting possibilities which deserve further study. Thus, virus might overwinter in hibernating mosquitoes. Or, an auxiliary infection cycle involving birds and their endoparasites, similar to that of the lungworm and pigs in the ecology of swine influenza [10] might be operative. It is conceivable that the hormonal stress experienced by actively ovulating birds might in some way reactivate latent infection with a recurrence of viremia which could then initiate the nestling infection cycle. Finally, the potential of infected birds carrying JE virus during migration must be considered. The spring migratory flight northward is composed exclusively of adult birds; adult birds are extremely resistant to experimental infection with JE virus and rarely develop viremia unless overwhelmed by massive inoculation.[11] The possibility of viremic adult birds seeding areas in their spring migration northward is therefore remote. On the other hand, because widespread dissemination of virus in young birds occurs just prior to the fall migration, the possibility exists of migrating

viremic juveniles carrying virus south. It is apparent that careful study is indicated on the problem of overwintering JE virus.

In conclusion, it may be noted that none of the concepts tested in this work were entirely new. However, older ideas resulting from investigation of other arthropod-borne viruses in different geographic areas have been successfully integrated with careful observation of JE virus in the field. This approach has implicated wild birds in the ecology of JE. Moreover it led to the hypothesis that this avian infection serves as the most likely source for the widespread rapid seeding of the C. tritaeniorhynchus with virus in Japan.

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Alabama Association Organized

The Alabama Public Health Association was organized at an initial meeting on March 2. It began life with 111 members, nearly two-thirds of whom are members or Fellows of the American Public Health Association. This new association hopes to qualify for APHA affiliation.

Officers elected are:

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Margaret Cotton, executive secretary, Alabama Heart Association
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