DEPARTMENT OF VIRUS AND RICKETSIAL DISEASES
406th Medical General Laboratory
APO 500 c/o Postmaster
San Francisco, California

2 August 1951

Dr. Albert B. Sabin
The Children's Hospital Research Foundation
Elland and Bethesda Avenues
Cincinnati 29, Ohio

Dear Doctor Sabin:

Attached is an intra-mural report which I have written, entitiled "Comparable Clinical Evaluation of Japanese B Encephalitis Cases Among Indigenous and United Nations Personnel." This drafted manuscript is an addendum to the one forwarded to you in May ("Demonstration of Residual Immunogenic Effects Produced by Japanese B Encephalitis Vaccine Among Indigenous Personnel, Okayama, 1950"), and is presented primarily to show that American and Japanese clinicians are likely to make clinical (Japanese B encephalitis) selections yielding roughly the same degree of laboratory confirmations. This naturally should lend additional significance to the statistical data obtained in Okayama during 1950. Differences expressed in numbers of encephalic cases between the two above-named drafts and the 1950 Annual Historical Report represent the clinicians' final diagnoses. You will also note a change in population figures to accommodate the latest census findings.

I believe this draft will answer many of the questions posed in your letter of June 5. Specifically, I might add, in answer to your query regarding results in terms of final or original dilutions for expression of titre, that titration end points are estimated on the basis of the last tube, showing complete or 3-plus fixation, and the titre is taken as the dilution of serum originally added to that tube.

With regard to acknowledgements in the various drafts submitted, I have consulted numerous individuals in the past four years to gain the information accumulated in these reports. Obviously, a large part of the data was obtained through the Okayama Prefectural Health Unit. Even here, to mention the present departmental chief would be folly, since the titular head to this Department has changed three times during the period the studies were conducted in that area.

This will indicate to some extent the magnitude of the
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listing required to accommodate the named individuals who cooperated with us, since many of the "lesser personnel" transferred with their respective chief. I believe that most credit is due, accumulatively acknowledged, to the Welfare Ministry itself.

A reply to your official letter requesting information relative to the description of complement fixation tests conducted in this laboratory for serological diagnoses of infection with the virus of Japanese B encephalitis has been prepared. I have submitted this data, together with a list of fatalities due to Japanese B encephalitis among American personnel for the years 1947 through 1950 for Colonel Hullinghorst's approval which, in due course, will be forwarded to you through channels.

With all good wishes,

Sincerely,

KENNETH F. BURNS  
Major, VC  
Department Chief

1 Inc.
COmparable Clinical Evaluation of Japanese B Encephalitis
Cases Among Indigenous and United Nations Personnel

Intra-Mural Report Compiled by
Kenneth F. Burns, Major, MC

From the Department of Virus and Rickettsial Diseases
406th Medical General Laboratory
APO 500          c/o Postmaster
San Francisco, California

In Okyama Prefecture during 1950, 309 cases of Japanese B encephalitis were diagnosed clinically by Japanese clinicians. There were 137 deaths. Twelve of these cases were observed among a group of children to whom Japanese B vaccine had been previously administered, two of whom succumbed to the infection (Table 1).

In order to attempt evaluation of Japanese B encephalitis vaccine, or to what extent immunity as a result of vaccination will be lost in subsequent years without further boosters, it is desirable to know the accuracy of clinical diagnosis in the Okyama area as compared to American military hospitals. This can only be accomplished through the medium of either serologically proven cases or histologic findings. It is impossible to determine the number of unrecognized infections in retrospect, but a calculated estimate may be made by comparison of the degree of laboratory confirmation in the two groups.

Although the Japanese series of cases were not subjected to nearly as thorough laboratory evaluations as were the cases occurring in United Nation forces in Korea during the 1950 epidemic, it is possible to make certain comparisons regarding laboratory confirmation. Of the 309 clinically diagnosed Okyama cases, 137 were fatal. Among survivors (148 cases), complement fixation tests were performed on blood specimens from 137 convalescents. The complement fixation tests on both groups were conducted at the 406th Medical General Laboratory, according to a technique essentially identical to that described by Casals and Palacios (1) using
antigens prepared by the benzene extraction method of Yamaoka and Hamon (3). Two negative results were excluded because the specimens were not obtained on or after the 25th day of disease, leaving a total of 135 survivors with what was considered adequate serological representation. Of these, 94 or 69.6 percent exhibited complement-fixing titres of 1:4 or over.

According to Ando et al. (5) the incidence of complement-fixing antibodies against Japanese B encephalitis virus is very low (13.2%) among patients of infectious diseases other than Japanese B encephalitis during a Japanese B epidemic and a similar figure was obtained from among normal healthy individuals. A majority of these positive complement fixations were undoubtedly due to inapparent infection with virus of Japanese B encephalitis and were low in titre (1:2 or 1:4). A similar observation was also made by Kitaoka et al. (4).

By comparison, in the United Nations Korean series of 299 cases, in which 257 cases had adequate serological representation, 199 or 74 percent showed a complement-fixing titre of 1:4 or over. This demonstrates considerable discrepancy between the degree of serological confirmation among surviving cases in the two series.

However, the higher mortality among Japanese patients is an important factor in creating an apparently lower rate of serological confirmation in that group. In the Okayama series, 137 deaths occurred with a case fatality rate of 44.3 percent. In the United Nation group of 299, fatalities numbered 30, giving a case fatality rate of 10 percent. Of these 30, 3 were confirmed serologically before death and were included in the group of 199 serologically confirmed cases mentioned above. The remaining 27 died
too early to develop complement-fixing antibodies and were confirmed by
virus isolation or histological evidence or both.

Adjustment for these fatal cases brings the total United Nations
Korean series with adequate laboratory material to 364 (237 plus 27) and
the confirmed cases to 236 (199 plus 37) yielding a "confirmation rate"
of 65.6 percent of all clinically diagnosed cases.

In making a similar adjustment for the Okayama series, it must be
borne in mind that autopsies were not performed on the 137 fatal cases.
It seems reasonable to assume, however, that childhood fatalities due to
central nervous system infection in the face of a serologically confirmed
Japanese B encephalitis epidemic are due in the vast majority of instances
to the Japanese B encephalitis virus. Provided this assumption is accepted,
adjustment for fatal cases brings the total Okayama group under considera-
tion to 372 (35 plus 137) and the confirmed cases to 231 (94 plus 137),
yielding a "confirmation rate" of 64.8 percent of all clinically diagnosed
cases.

Certain other factors difficult to measure must be mentioned as
perhaps influencing the final percentage of confirmed cases. First,
American clinicians undoubtedly were faced with a greater number of mild
cases of central nervous system maladies, with a lower proportion of actual
Japanese B encephalitis infections, whereas Japanese clinicians are likely
to see only the more severe cases with cerebral manifestations. This would
tend to yield a greater proportion of confirmation in the Japanese groups.
Secondly, in the present series very few Japanese cases had to be excluded
on account of inadequate serum representation, while many American cases,
probably negative, were excluded because specimens of the 35th day or later
were not available. Had these negative cases been added, the percentage of
serological confirmation among United Nations cases would be appreciably lower.

Of the 148 Japanese cases, 130 sera were tested and found to be positive
for neutralizing antibodies. Two and eight of the remaining tested sera were
negative and equivocal, respectively. Sufficient quantities of serum were
not collected in 3 cases to test for neutralizing values.

Complement fixation tests conducted on the 8 non-tested cases for
neutralizing antibodies showed that 2 were negative, one exhibited a titre
of 1:4, another a titre of 1:8; two displayed a titre of 1:16 and the remaining
two showed titres of 1:128 and 1:256, respectively. Two convalescent sera
were negative for both neutralizing and complement-fixing antibodies and
among 6 sera displaying equivocal neutralizing results, 2 were positive
(1:4 and 1:8) and 6 portrayed negative complement-fixing results.

In view of the fact that a comparison of adjusted "confirmed rates" of
all clinically diagnosed cases suggests a similar trend, being almost
identical percentage-wise, it seems reasonable to assume that in a given
outbreak of Japanese B encephalitis, American and Japanese physicians are
likely to make clinical selections yielding roughly the same degree of
laboratory confirmation. This lends some significance to statistical data
obtained in Okayama during 1950 on the "Demonstration of residual
immunogenic effects produced by Japanese B encephalitis vaccine among
indigenous personnel" (5), and allows for further comparison on the
incidence of Japanese B encephalitis in the vaccinated and unvaccinated
groups.
TABLE I
CLINICALLY DIAGNOSED JAPANESE B ENCEPHALITIS CASES
IN PREVIOUSLY VACCINATED INDIVIDUALS
OKAYAMA, 1950

<table>
<thead>
<tr>
<th>Name</th>
<th>Age</th>
<th>Sex</th>
<th>Date of Case</th>
<th>Day of Disease</th>
<th>Serology</th>
<th>Vaccination Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>example1</td>
<td>6</td>
<td>M</td>
<td>25 Jun</td>
<td>102</td>
<td>1:4</td>
<td>16</td>
</tr>
<tr>
<td>example2</td>
<td>7</td>
<td>F</td>
<td>7 Aug</td>
<td>59</td>
<td>1:4</td>
<td>7000</td>
</tr>
<tr>
<td>example3</td>
<td>10</td>
<td>F</td>
<td>16 Aug</td>
<td>30</td>
<td>1:8</td>
<td>QNS</td>
</tr>
<tr>
<td>example4</td>
<td>8</td>
<td>M</td>
<td>15 Aug</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>example5</td>
<td>10</td>
<td>M</td>
<td>18 Aug</td>
<td>48</td>
<td>1:128</td>
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<td>example6</td>
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<td>F</td>
<td>23 Aug</td>
<td>44</td>
<td>1:8</td>
<td>16,000</td>
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<tr>
<td>example7</td>
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<td>M</td>
<td>25 Aug</td>
<td>33</td>
<td>QNS</td>
<td>16</td>
</tr>
<tr>
<td>example8</td>
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<td>M</td>
<td>6 Sep</td>
<td>39</td>
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<td>2500</td>
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<tr>
<td>example9</td>
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<td>16 Aug</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
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<td>example10</td>
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<td>F</td>
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<td>53</td>
<td>1:16</td>
<td>QNS</td>
</tr>
<tr>
<td>example11</td>
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<td>M</td>
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<td>1:33</td>
<td>5000</td>
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<tr>
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<td>57</td>
<td>1:33</td>
<td>16,000</td>
</tr>
</tbody>
</table>

* Died August 31, 1950 (autopsy not conducted).

Category I = One dose, initial series, 1949.
II = Complete course, 1949.
III = Complete course, 1948; recall in 1949.
REFERENCES


