Report of the Sub Committee on Japanese B. Encephalitis Studies, Virus and Rickettsial Commission, Armed Services Epidemiological Board

1. SUBJECT:


b. Future Participation of Virus and Rickettsial Commission in the Okayama Vaccination Program.


Committee members present: Drs. Paul, Sabin, Smadel, Hammon (chairman)

Committee members absent: Dr. Taylor, Lt. Col. Tigertt

Others participating in discussion: Dr. Casals, Major Eberhardt, Dr. Warren

On the 30 September, 1949, in Washington, D.C., the sub-committee held its second meeting. It had before it a request to make recommendations to the Armed Services Epidemiological Board on the question: should vaccine be purchased and furnished for the continued vaccination of Japanese children in the Okayama area. In order to have the most recent data available, the Commanding Officer of the 406th Medical General Laboratory had been requested to cable all the available pertinent data by 26 September.


In the report of the last meeting of the committee, dated 12 April, 1949, data from 1946 through 1948 were summarized and conclusions drawn as follows: "Over a three-year period Japanese B. encephalitis vaccine has been administered to 25,000 Japanese children who were between the ages of 3 and 5 years when the study began. Both the dosage schedule and type of vaccine have varied. During the first year (1946) only one case of encephalitis occurred in the entire prefecture in an individual outside the age group under study. During the second year a total of 6 cases occurred in the prefecture in the age group under study with none in the vaccinated group. During the third year (1947) 61 cases were observed in the entire area. One non-fatality occurred in the vaccinated group while case expectancy on the basis of the over-all occurrence in the age group under study was 5.27. On the basis of case occurrence in the non-vaccinated the anticipated number of cases in the vaccinated group was 7.6. The results are merely suggestive that the vaccine is of some value. The number of cases occurring has been too small to permit drawing more definite conclusions. This conclusion was unanimously accepted." In respect to future plans, the report read: "It was recommended that this vaccination program be extended to make a "five-year plan". Col. Tigertt indicated that he planned to increase the total size of the vaccinated group to 50,000 or 60,000, if possible, with retention of as many as possible of the old nucleus. Another phase of the study for the final year was suggested by Dr. Hammon - an attempt to determine whether annual vaccination decreased the rate of acquiring immunity through inapparent infection, consequently rendering it important to continue annual vaccination for the duration of life. Comparative post-epidemic antibody surveys among vaccinated and un-vaccinated might give this information."
In 1949 the program was continued as recommended and 54,200 children were vaccinated. This group represented approximately 50% of the children of the area who were between the ages of 5 and 10 years. A primary series was given to 33,200 and 21,000 were given recall doses. From data received in the message of 26 September from Lt. Col. Hullinghurst, and the previous data presented in the Annual Historical Report of the 406th Medical General Laboratory of 1948, by Lt. Col. Tigertt, Dr. Ross Gauld summarized the data which forms Appendix 1 of this report. It was pointed out that the most recent message concluded with the following statement, "Attention is again directed to the fact that epidemic not yet concluded. Data furnished are rough and subject to further study and correction".

After careful consideration of the data it was concluded that the preliminary data for 1949 showed a similar trend to that obtained in 1947 and 1948 and supported the previous conclusion that the vaccine probably had some protective value when given under these circumstances to children.

II. Recommendation Regarding Future Participation of Virus and Rickettsial Commission in the Okayama Vaccination Program.

Despite the recommendation made the previous year that the study be carried out for five years (one additional year after 1949), it was decided after thorough discussion by the Virus and Rickettsial Commission to recommend that the vaccination of Japanese children in Okayama be terminated in 1949 instead of in 1950.

1. Fairly reliable information regarding the effectiveness of the vaccine during the season immediately following its use has been obtained and evidence from just one more year would probably not adequately add to the evidence, particularly in view of the moderate incidence of the disease in 1948 and 1949 which might be expected to lead to a minimal number of cases in 1950.

2. Naturally developing antibodies in the non-vaccinated child population under study, as determined by tests prior to the last vaccinations, are rapidly reducing or eliminating the differences in susceptibility between the original groups.

3. Although the loss of certain American personnel (Colonel Tigertt, Captain Satterwhite, and the Prefectural Civil Affairs Team located in Okayama), whose work made possible the participation of the Virus and Rickettsial Commission in this program, influenced the decision to terminate the vaccination in 1949 instead of in 1950, it was not decisive - the chief reason being, rather, that it was not expected that much significant additional information could be obtained by continuing the vaccination for another year.

4. Should the Japanese investigators concur in the decisions reached by the Virus and Rickettsial Commission, it is recommended that the case incidence in the previously vaccinated and unvaccinated groups be carefully followed during the next two or three years to determine whether after cessation of vaccination the susceptibility of the vaccinated group as regards the clinically recognized disease will be different from that of the unvaccinated group.

5. Should the Japanese scientists engaged in this study, especially Professor K. Kitayama and Dr. M. Kitaoka, not concur in this decision, the Virus and Rickettsial Commission would continue to be interested in the further plans and results of further studies by these investigators even though it could not supply any direct help.
III. Application of Vaccination Study Conclusions to Program of General Vaccination of Japanese Children.

With the full realization that the reason for the wholehearted cooperation of Public Health and Welfare, SCAP, the Japanese investigators, physicians, and the Prefectural Civilian teams was to determine the effectiveness of the vaccine for use on Japanese children in all epidemic and endemic areas, this committee has given careful thought to the practical interpretation of the results. Deliberation was restricted to practical and scientific aspects of the problem with no consideration of political matters, or of questions of local expediency which it realizes it is not capable of evaluating. The committee reaffirms its previous conclusions stated in its report of 12 April 1949 addressed to the President of the Army Epidemiological Board and transmitted by him to the Surgeon General of the Army for General Crawford E. Sams in the memorandum of 22 April 1949 (Appendix 2). The chief reasons involved were that epidemics are unpredictable and vaccines should have to be administered annually for life to millions who were already immune, since no simple means of determining susceptibility is known. It is pointed out that for these reasons vaccines are not used for men in endemic encephalitis areas in the United States.

In respect to item (5) of the above report, although the results of one more year's survey have helped to convince us that the vaccine is of some effect as applied, it is not as yet clear whether the vaccinated children will attain through normal exposure as lasting and complete naturally acquired immunity as those not vaccinated. This, it is felt, is an important fact to establish. One study made on a heavily exposed group of American troops on Okinawa in 1947 suggested that vaccine had interfered with the development of naturally acquired immunity through apparent infection. Many unvaccinated and incompletely vaccinated individuals developed complement fixing antibodies during the season while this was not a characteristic of the completely vaccinated group. However, Colonel Biggert has reported (letter of 9 September 1949 to Dr. Smedal) that on the basis of surveys conducted early in 1949 it is difficult to demonstrate differences in the immunity pattern between the vaccinated and non-vaccinated groups. Recommendations for further studies to clarify this point are given below.

In addition, the committee feels strongly that production in Japan of a chick embryo vaccine of suitable potency in the quantities necessary is completely impractical. This is subject to change in the future. A suitable mouse brain vaccine would be far less difficult to prepare but its repeated use over a period of years might be dangerous from the standpoint of sensitization to brain tissue. For this reason mouse brain was replaced in the United States by the more costly, less potent, less stable, and more difficult to manufacture chick embryo type. It is possible that serious difficulties may eventually be encountered in Japanese horses through repeated subcutaneous vaccination with this product.

At the present time, therefore, the chief reason for not recommending vaccination of all Japanese children under 15 is that in the attempt to protect a relatively small number against the clinically recognized disease, it would be necessary to vaccinate yearly millions of individuals who do not need the vaccine, because they are already immune as a result of inapparent infection. Therefore, until a simple method becomes available to distinguish between those who are and those who are not immune, it is not considered practical to attempt vaccination of millions of people even if the vaccine for Japanese B encephalitis were very much better than it is and more readily and inexpensively prepared than is possible under present conditions.
IV. Recommendations for further study.

It is understood from Colonel Tigertt that sera have just recently been collected from a large group of vaccinated and unvaccinated children of comparable ages from the areas in which infection rates were high this year. These should be tested either in Dr. Hammon's laboratory or at the 406th Medical General Laboratory in a way comparable to the post-epidemic group from Okinawa in 1948, tested by Dr. Hammon. The same group should be bled again for neutralization tests in the spring of 1950. These tests will assist in determining whether vaccine has prevented, aided, or had no influence on the individual's development of naturally acquired active immunity as determined in vitro.

W. McD. Hammon, Chairman