Children's Hospital Research Foundation  
Iland and Bethesda Avenues  
Cincinnati 29, Ohio

26 April 1944

Brig. General S. Bayne-Jones  
Division of Preventive Medicine  
Office of the Surgeon General  
U. S. Army  
1818 H Street, N.W.  
Washington, D. C.

Dear General Bayne-Jones:

Having heard from Dr. Paul that you have just returned and in view of the forthcoming meeting of the Board, I thought that you might be interested to have a preliminary report on the Hawaiian virus.

1. All of the six human subjects inoculated intracutaneously with 1 cc of a pool of the 6 Hawaiian sera developed a febrile disease with rash from which they all recovered.

2. Incubation period- 3 to 4 days, 1 subject  
   4 to 5 days, 2 subjects  
   5 to 6 days, 2 subjects  
   7 to 8 days, 1 subject

3. Duration of fever- 1 day fever, 1 subject  
   4 day fever, 2 subjects  
   5 day fever, 1 subject  
   7 day fever, 1 subject  
   8 day fever, 1 subject

4. Leukopenia- all subjects developed a leukopenia associated with changes in the neutrophile leukocytes compatible with that known to occur in dengue.

5. Rash- (a) Site of inoculation. All subjects developed a distinct zone of erythema at the inoculated site 3 to 4 days after injection of the serum. This type of inoculation reaction was never observed following intracutaneous inoculation of the phlebotomus fever virus.

   (b) Primary rash. 5 of the 6 subjects developed very striking morbiliform or scarlatiniform eruptions some hours preceding or simultaneously with the onset of fever. This rash in most instances lasted several days.
(c) Secondary rash. Three of the 6 subjects developed a distinct and rather marked petechial eruption over the feet, ankles, legs and in some instances over the hands and wrists toward the end of the febrile period, or after defervescence.

Photographs in color were taken of the reaction at the inoculated site, of the different types of primary rash and of the petechial rash. Lantern slides and transparencies are now available. Color prints have not yet been prepared.

6. Clinical course - The patients appeared very ill with this disease. Objectively the severity of this experimental disease was greater than any I had seen in patients with experimental phlebotomus fever. Only one of the 6 patients showed urinary changes, consisting of a transitory albuminuria, casts and few red blood cells on microscopic examination.

7. Pathogenicity of virus for laboratory animals and chick embryos -

(a) Laboratory animals. Guinea pigs - adult. Intraperitoneal inoculation of serum produced neither fever nor orchitis during the period of observation which lasted three weeks; newborn guinea pigs were inoculated intracerebrally and intraperitoneally with serum and whole blood respectively. One of 6 exhibited nervous signs 13 days after inoculation and focal cortical and meningeal lesions were found on histological examination of the brain. Passage of this brain into other newborn guinea pigs has not yielded anything as yet, although only 6 days have passed.

Infant mice, infant hamsters and full grown cotton rats inoculated with this virus have revealed nothing over a period extending for approximately 4 weeks.

(b) Chick embryos - Two series of chick embryos were inoculated, both into the embryo and yolk sac, with this virus. Series A - 7 day old chick embryos passaged at intervals of 7 days revealed no evidence of rickettsia on smear of the yolk sac, nor any evidence of pathogenicity for the embryos. Blind passages have been carried on and the material will be inoculated into human volunteers.

Series B - 9 day old embryos inoculated in the same manner as for yellow fever vaccine production and passaged every 4 days, have also revealed no pathogenicity for the embryos. This material will also be inoculated into human volunteers.

8. Weil-Felix and Rickettsial complement fixation tests - In view of the predominant dermotropic component in the clinical picture produced by this
virus it was deemed desirable to determine whether or not a rickettsial agent might have been present in it. The negative results in the yolk sac of the chick embryos, as well as in the guinea pigs which were inoculated intraperitoneally may be taken as evidence against the presence of a known rickettsial agent. Col. Plotz was good enough to carry out Weil-Felix and rickettsial complement fixation tests on sera obtained from the 6 subjects inoculated with the Hawaiian virus. All were completely negative with OX-2, and 5 of the 6 were completely negative against OX-19. One gave a partial agglutination of a titer of 1:40 with OX-19. In the complement fixation tests with epidemic and murine antigens, 5 of the 6 were negative and the 6th serum was anticomplementary.

9. Lack of immunologic relationship between Hawaiian virus and Middle East and Sicilian strains of phlebotomus fever- Two of the 6 subjects inoculated with the Hawaiian virus had recovered from, and could be considered to be immune to, infection with the Middle East strain, and two with the Sicilian strain of phlebotomus fever virus.

The data obtained on this Hawaiian strain of virus are not incompatible with the properties of dengue virus, although, of course, it would be wise to await the results of transmission by Aedes aegypti mosquitoes before putting the final stamp on it. I have several hundred cc of serum from six human subjects which is an adequate supply for future work. In addition to Dr. Hammon, Col. Plotz has expressed the desire to test dengue virus in certain types of tissue culture. I shall be guided by your directions with regard to the persons to whom this virus is to be released and with regard to the optimum time of its release. Personally, I would be inclined to withhold distribution of the virus, at least until transmission by Aedes aegypti has been demonstrated.

Sincerely yours,

Albert B. Sabin
Major, M. C.

ABS: EH B

cc. to General Simmons
Dr. Blake
Dr. Paul