COPY

original filed: 100 IHD Lab. Vaccine Mtg.

GKS GICS 100 Jaundice

THE ROCKEFELLER FOUNDATION
49 West 49th Street
New York, N. Y.

OCT 6 1942

APR 20 1942

AJW - [illegible]

RBF - RBF

WBS - [illegible]

April 11, 1942

Air Mail

Dear Dr. Sawyer:

When I got back I learned that Col. Simmons had sent word to Dr. Strode that he wanted to see me to find out more about our findings in California. I spent about 3½ hours at Col. Simmons' office yesterday in conference with him, Col. Lundeberg, Bayne-Jones, and Turner. I told them in a general way what we found in California up to the time I left. Col. Simmons is still very much impressed by the fact that there is no jaundice among the men vaccinated at Camp Callan on January 3 and since sent to Fort Bliss, Texas, and Camp Greeley, Alaska. The number of cases reported to the Surgeon General's Office is still increasing rapidly, and by yesterday there were approximately 2500 cases known, all in the Army. There is still no report of any cases in the Navy. Most of the cases seem to originate from Jefferson Barracks. I was told that in one day there at the end of December 8000 aviation cadets were vaccinated with Lot 335, and since then they have been dispersed all over the country, and where they have gone jaundice has appeared. There are 20 cases at Fort Jay, Governors Island from Jefferson Barracks. Bayne-Jones said that some of the men vaccinated at that time with the same material are still at Jefferson Barracks with cases of jaundice occurring among them. On the other hand new troops that have arrived there since have no cases.

There was one death at Perrin Field, Sherman, Texas. This man, James Eagan, was also vaccinated at Jefferson Barracks early in January. The case history and autopsy notes are very meager, but these are the essential facts I was able to learn regarding the case. I was unable to learn the lot number. He developed a severe attack of jaundice in the middle of March and died after a week in the hospital. He was afebrile throughout. Three blood counts were made on him. Two showed leukopenia and the third leukocytosis. He died rather suddenly. The autopsy notes, being scarce, showed nothing but that all tissues were deeply jaundiced, the spleen was of normal size, and the liver had shrunk to about two-thirds its normal size. After the body had already been embalmed, a piece of liver was removed at the undertaker's establishment and sent to the Pathological Museum of the Army Medical School for examination. Col. Ashland, pathologist, has diagnosed this as an extremely severe case of acute yellow atrophy. Col. Simmons promised to send us some slides from this case. Whether this case is the same type of jaundice as is prevalent at the present time, no one is sure, of course.

As you have learned from Dr. Strode's correspondence, the War Department has organized studies here in the East. Drs. Maxcy and Goodpasture are concentrating their efforts on Jefferson Barracks. Maxcy is studying the epidemiology and Goodpasture and Dawson are trying to determine the etiology of this disease.

I gained the impression that the men in the Surgeon General's Office are somewhat worried about the situation but not particularly alarmed. The difficulty, of course, is that no one can predict what proportions it will reach. They emphasized the difficulty they are facing - they do not know what provisions to make for additional beds to hospitalize these cases.

While I was there, they asked me numerous questions covering the history of the development of 17D virus, as well as the actual procedures involved in the preparation of the vaccine. Bayne-Jones asked most of the questions and made notes on everything I said. From the conversation I got the impression that Bayne-Jones is much more inclined to attribute the jaundice to the vaccine than the others are. However, all felt that vaccination should be continued by all means. Col. Simmons was particularly emphatic on this point and stated that if vaccination was once discontinued, it would be exceedingly difficult to start it again as he said that it took them a whole year to convince the general staff of the importance of this protective measure. Furthermore, as he said to you over the telephone, it would cause serious international complications. However, they are relying entirely on our advice in this matter. I told them that we have over 1 million doses of vaccine on hand, and we will continue to meet the requests for it until your return and we have a clearer picture of the whole situation.

If the jaundice is due to the vaccine, Bayne-Jones is inclined to attribute it entirely to the presence of human serum. He doesn't think the serum could be considered safe unless it was heated to near the coaggulation point, that is, about 70°C. He especially emphasized recent findings regarding the virus of poliomyelitis and stated that there is a virus that survives for long periods in sewers. He thinks it should be logical to assume that there might be other agents having high thermal resistance, especially in a medium containing a fair amount of fats, as serum sometimes does. He does not think that 58 or 60° should be considered safe unless this temperature was applied for a period of at least several hours.

Inasmuch as we have approximately 1,200,000 doses of vaccine on hand to meet requests from the Army and the Navy for a month at least, I have asked Dr. Goodner to discontinue making the present type of vaccine until you return. In the meantime we are carrying out investigations to determine, first, whether or not serum can be omitted from vaccine without increasing the amount of chick embryo appreciably; second, how much serum can be heated without coaggulation; and whether serum heated for long periods just below coaggulation point has the same properties as a protective colloid as that heated to 58 or 60°. There is no question that much denaturation will take place at a higher temperature, and the problem is to determine whether the denatured protein will have the same protective properties on the virus as the serum we have been using. A further point is to determine how much foreign protein reaction will give a heat-denatured human serum when injected into human beings.

Over this weekend Turner will get complete histories on all blood donors used in Baltimore since last summer. He said that last spring when he supplied serum to us, he inquired regularly regarding past history of jaundice among students who served as donors and found positive histories in a number of cases but that last fall he discontinued this procedure knowing that serum was inactivated before use.

We are also investigating our source of eggs. We all feel that it would be highly desirable to omit serum from future vaccines if possible. If for no other reason, it would eliminate an extra factor from the number of elements in the vaccine so that if jaundice should continue, we should then know definitely that it must originate from the eggs.

Since returning from California I have read again the literature, especially with regard to postvaccination jaundice observed in Brazil. The worst experience was observed with a vaccine containing no chick embryo. As you will recall, this vaccine was made with 17E virus grown in tissue cultures made of mouse embryo tissues in Tyrode solution to which either normal monkey or normal human serum was added. In making the actual vaccine, to the liquid tissue culture was added an equal amount of normal human serum before desiccation in frozen state. Dr. Lloyd took most of this vaccine with him from here although some of it was made in Brazil. The vaccine was given in conjunction with immune serum, of which three types were used - hyperimmune goat serum, hyperimmune monkey serum, or human convalescent serum. In one instance there were 61 cases of jaundice in 191 persons, vaccinated with the tissue culture virus put up as mentioned above and hyperimmune monkey serum, 2 to 8 months after vaccination. Among the 61 cases were 2 who later were found to have been immune before yellow fever vaccination. Whether the jaundice in this case originated from human or monkey serum, we do not know, of course, but it seems to exclude chick embryo.

I am enclosing herewith a copy of a questionnaire used by the Surgeon General's Office for the collection of data on cases of jaundice. They think that the questionnaire used on the Pacific Coast is too complicated.

Sincerely yours

J. H. Bauer

Dr. W. A. Sawyer
c/o Dr. M. D. Eaton
Research Laboratory
1392 University Avenue
Berkeley, California

JHB:MJH
Enc.
cc:Dr. Strode

Date _____

QUESTIONNAIRE FOR USE IN CONNECTION WITH CASES OF JAUNDICE WITHOUT KNOWN CAUSE

1. _____ _____ _____ _____
Name Grade A.S.N. Organization and present station

2. Inducted into Army: Date _____ Place: _____
Camp or station State

3. Subsequent stations (since Oct. 1, 1941):

	Name of station or camp	Date of arrival	Date of departure
(1)			
(2)			
(3)			
(4)			

4. Cities, towns or other places (outside of camp or station) visited on furlough or pass since Oct. 1, 1941. If frequent visits were made to any town near station, name the place, and frequency of visits; otherwise, name place and approximate date.

	Place	Date or frequency of visits
(1)		
(2)		
(3)		
(4)		

5. When was jaundice first observed?
How long did it last?
Has patient entirely recovered?

6. Immunization Record:

	Date	Place (Camp or station)
Typhoid	_____	_____
Smallpox	_____	_____
Tetanus Toxoid (completed)	_____	_____
Yellow Fever Lot No._____	_____	_____

7. Comments. History of contact with other cases, etc.

_____
Surgeon

NOTE: As very little is known of the pathological changes in the liver in this disease, all medical officers are requested to be on the alert for opportunities

(OVER)

of securing tissues for special studies. Tissues fixed in Zenker's fluid are suitable for histopathological examination and should be sent to the Army Medical Museum.

Small pieces of tissue placed in a Pyrex test tube and frozen by immersion of the tube in dry ice-alcohol mixture immediatsly after removal from the body are suitable for virus studies. They must be shipped in dry ice containers as described in paragraph 2b, S.G.O. Circular Letter No. 107, October 22, 1941. Such frozen tissue specimens should be shipped to Dr. Ernest W. Goodpasture, Professor of Pathology, Vanderbilt University, Nashville, Tennessee, member of the Board for the Investigation and Control of Influenza and Other Epidemic Diseases in the Army, who is prepared to undertake studies of this nature.

(1) _____
(2) _____
(3) _____
(4) _____

Complete and return to Office of The Surgeon General, Washington, D. C.

_____

(If additional copies of this form are needed they should be reproduced locally.)