

RECENT RESEARCHES CONCERNING THE ETIOLOGY,
PROPAGATION, AND PREVENTION OF YELLOW
FEVER, BY THE UNITED STATES ARMY COM-
MISSION.

(Three Charts.)

By WALTER REED, M.D.,

Surgeon, U.S. Army, President of the Commission.

THE efficient control of the spread of yellow fever is a matter of such vast practical importance, both from the hygienic and commercial point of view—not only for the countries where this disease prevails as an epidemic, but also for those in which, after importation, it may assume epidemic proportions—that it has seemed appropriate to bring together in this paper a summary of the work thus far accomplished by the United States Army Commission¹ on the Island of Cuba, during the years 1900 and 1901, in order that English and Colonial readers who have not, perhaps, had access to the original contributions published in different American journals, may be able to form an intelligent opinion concerning the permanent value of this work. It will also afford opportunity for recording the more recent confirmatory observations made by others concerning the mode of transmission of yellow fever discovered by the Commission, and for calling attention to the results already obtained by the U.S. Army Medical Department in the suppression of this disease, especially in the city of Havana, through the enforcement of sanitary measures based on these later researches.

The American Commission was organized in May 1900, and began its investigations during the following month (June), being equipped with suitable laboratory facilities for practical work, both at the

¹ The members of this Commission were Major Walter Reed, Surgeon, U.S. Army, and Drs James Carroll, A. Agramonte, and the late Dr Jesse W. Lazear, Contract Surgeons, U.S. Army.

military garrison of Columbia Barracks, near Quemados, Cuba, and also in the city of Havana. As yellow fever was already prevailing at the time of our arrival in Cuba suitable material for the scientific study of this disease was immediately available.

The Etiology of Yellow Fever.

Before giving the results of our investigations it may be well to recall the situation as regards the etiology of yellow fever at that time. Briefly it may be said that the claims of all investigators for the discovery of the specific agent of yellow fever—since modern bacteriological methods had come into use—had been disproved by the exhaustive observations of Sternberg⁽¹⁾, published in 1890, except that made by Sanarelli⁽²⁾ for a small, motile bacillus isolated by him from the blood drawn during life in two of six cases of yellow fever, and from the blood and organs after death in seven of twelve cases of this disease (58%), studied at Montevideo and Rio de Janeiro, Brazil. The results obtained, however, by those who had promptly undertaken to investigate Sanarelli's claim for the specific character of *Bacillus icteroides*, seemed to show a lack of agreement such as has never been reported, as far as the writer can recall, in connection with the supposed specific cause of any of the other acute infections. Thus while Achinard and Woodson⁽³⁾ had, during the epidemic of 1897 in New Orleans, La., isolated a bacillus, claimed by them to be identical with *B. icteroides*, from the venous blood in 4 out of 5 cases, and from yellow fever cadavers in 32 out of 39 cases (82%), Portier⁽⁴⁾, working in the same city and during the same epidemic, could only obtain this bacillus 3 times in 51 autopsies, and failed to obtain it at all in cultures made from the venous blood during life in 10 cases. Again, while Wasdin and Geddings⁽⁵⁾, in the city of Havana, were able to cultivate *B. icteroides* from blood withdrawn from the lobe of the ear, "not earlier than the third day of the disease" in 13 of 14 cases (92·8%), and to find it in 85·7% of their necropsies, Agramonte⁽⁶⁾, studying the disease on the Island of Cuba, failed to isolate *B. icteroides* in a single instance from blood drawn from the lobe of the ear in 37 cases or from the blood drawn from a vein at the bend of the elbow in 31 cases, at various stages of the disease. The latter observer, however, reported finding this bacillus at autopsy in 11 of 35 cases (31·4%). Without going further into detail, we may say that the results obtained by Lutz⁽⁷⁾ and

de Lacerda and Ramos⁽⁸⁾ in Brazil, and by Matienzo⁽⁹⁾ in Mexico, were equally conflicting and unsatisfactory.

Under these circumstances it seemed to the members of the Commission of the first importance to give their entire attention to the bacteriological study of the blood of those sick with yellow fever and of the blood and organs of yellow fever cadavers, having especially in view the isolation of *B. icteroides*. We were thus able during June, July, and August to take repeated cultures from the blood during life in 18 cases of yellow fever, adopting the usual method employed in withdrawing blood from a vein at the bend of the elbow, and transferring the blood, at once, in quantities of 0.5 c.c. to each of several tubes containing 10 c.c. of nutritive bouillon which were afterwards incubated at 37° C. for a period of one week. In seven cases, four of which were designated as "mild" yellow fever and three as "well-marked" yellow fever, only one culture was made from the blood in each case, viz.: in two cases on the 1st day; in one case on the 2nd day; in three cases on the 3rd day, and in one case on the 4th day. In the remaining eleven cases, diagnosed as "severe" yellow fever, of whom four died, more frequent cultures were taken from the blood, these varying from two to six cultures on as many different days of the disease. In two of the fatal cases, cultures were made each day from the commencement of the attack and including the day on which death occurred.

The negative result of these numerous cultures taken from the blood of cases of yellow fever, as regards the presence of *B. icteroides*, was reported in a "Preliminary Note" presented at the meeting of the American Public Health Association⁽¹⁰⁾, held in Indianapolis, Indiana, October 22nd—26th, 1900. To these eighteen cases we can now add six other cases, or a total of twenty-four, from which blood cultures have been made during life with negative results.

The importance of this negative finding as regards the growth of any specific bacterium will be better appreciated when it is seen, as I shall soon have occasion to point out, that yellow fever may be produced in non-immune human beings by the subcutaneous injection of a small quantity (0.5—2 c.c.) of blood withdrawn from the venous circulation of a patient suffering with this disease.

In addition to the results above recorded, the careful study of eleven autopsies was equally barren as to the presence of any particular micro-organism, although the quantity of material with which our tubes were inoculated was greater than is usually made use of at autopsies.

In a word, then, the careful bacteriological study which the Commission had made in cases of yellow fever had given no indications as to the presence of the specific agent of this disease. The same may be said concerning the result of numerous microscopic examinations of fresh and stained specimens of blood which we had in the meanwhile studied with the view of finding possibly some intracellular or extracellular body. Apparently no body, bacterial or protozoan, which could be brought into view with a $\frac{1}{12}$ Zeiss immersion objective, was present in the blood of these cases.

Although displaced from the order in which the following observations were made, it will be best to present, at this time, the results of the experiments which were later carried out by the Commission on non-immune human beings by means of the subcutaneous injection of blood, withdrawn during the active stage of the disease, as these results bear so directly upon the subject which we are now considering, viz. the etiology of yellow fever.

The only reference that I can find in the literature relative to an attempt to convey yellow fever in this way is cited by Sternberg⁽¹⁾, who states that at Vera Cruz, Mexico, in 1887, he saw Dr Ruis inject into a non-immune individual a hypodermic syringe of blood drawn from a case of yellow fever on the eighth day of the disease. The result was negative, as was also the result of two other attempts related to him by Ruis.

Our own observations, undertaken for the purpose of ascertaining whether an attack of yellow fever could be induced in a second individual by the injection of a small quantity of blood, embrace experiments made on twelve American soldiers and Spanish immigrants, all non-immune individuals.

These observations may be divided into the following classes :

1. Injection of the fresh blood taken from a vein at the bend of the elbow.
2. Injection of partially defibrinated blood.
3. Injection of partially defibrinated blood heated for ten minutes at 55° C.
4. Injection of blood-serum previously diluted with sterilized water and filtered slowly through a Berkefeld laboratory filter.

The following Table, I., gives the results of these several inoculations :

TABLE I.

No. of case	Quantity and material used	Day of disease	Date of inoculation	Result	Date of attack
I	2 c.c. fresh blood	Second	Dec. 26, 1900	Negative	
II	2 " "	"	Jan. 4, 1901	Positive	Jan. 8, 1901
III	1.5 " "	First	" 8 "	"	" 11 "
IV	0.5 " "	Second	" 22 "	"	" 24 "
V	1 " "	"	" 25 "	"	" 28 "
VI	0.75 c.c. partially defibrinated blood	Third	Oct. 15 "	"	Oct. 20 "
VII	1.5 c.c. partially defibrinated blood heated for 10 minutes at 55° C.	"	" 15 "	Negative	
VIII	Same as No. VII	"	" 15 "	"	
IX	" "	"	" 15 "	"	
X	1.5 c.c. of filtered blood serum	"	" 15 "	Positive	Oct. 19, 1901
XI	Same as No. X	"	" 15 "	"	" 19 "
XII	{ Same as No. X { 2 c.c. fresh blood	Fourth	" 15 "	{ Negative { Positive	" 23 "

By an examination of this table it will be seen that of the seven individuals who received subcutaneously the fresh or partially defibrinated blood in quantities of 0.5--2 c.c., six (85.7%) developed an attack of yellow fever within the usual period of incubation of the disease.

These results are of very great interest as demonstrating that the *specific agent of yellow fever is present in the blood, at least during the first, second, and third days of the attack.*

Another important point brought out by these experiments was that *the blood which conveyed the disease did not contain any bacterium which would grow on our usual laboratory media.*

In order to establish this fact, as soon as blood had been injected into the non-immune subject, additional blood was, at once, withdrawn in considerable quantity and transferred to tubes of nutritive bouillon. In one instance, where 2 c.c. of blood had been drawn into the syringe, 0.5 c.c. of this sufficed, when injected, to produce a severe attack of yellow fever, after seventy-three hours' incubation, while the remaining 1.5 c.c. transferred immediately to four tubes of bouillon gave no growth, except that from one tube we isolated on the 4th day *Staphylococcus pyogenes citreus*, found by us to be a common skin-contaminating organism in Cuba.

Table I further shows that the specific agent contained in the blood is destroyed or attenuated by heating the latter at 55° C. for 10 minutes,

so that the injection of 1.5 c.c. of this heated blood was harmless (cases VII, VIII, and IX), while the injection of 0.75 c.c. of the same blood unheated sufficed to promptly induce an attack of yellow fever in a "control" individual (case VI).

Of not less interest was the fact brought out by these observations that yellow fever can be produced by the injection of a small quantity of bacteria-free serum filtrate, obtained by passing the diluted serum through a Berkefeld laboratory filter (cases X and XI), and further that the blood of a case of yellow fever, thus produced, when injected into a third non-immune subject will promptly bring about an attack of this disease (case XII); thus demonstrating that the specific agent of yellow fever can find its way through the pores of a filter which ordinarily serves to prevent the passage of all known bacteria.

I have elsewhere⁽¹²⁾ in conjunction with one of my colleagues (Carroll) discussed the facts here presented more at length and will limit myself, therefore, to the remark that these experiments appear to indicate that yellow fever, like the foot and mouth disease of cattle, is caused by a micro-organism so minute in size that it might be designated as ultra-microscopic.

The Propagation of Yellow Fever.

Prior to the time at which the foregoing observations were made the Commission had already turned its entire attention to the possible solution of the problem of the propagation of yellow fever, being induced thereto, not only by the fruitlessness of the investigations made thus far along bacteriological lines, but, also, by reason of certain facts which seemed to call for a better interpretation than had hitherto been accorded them.

Without entering into details, I may say that, in the first place, the Commission saw, with some surprise, what had so often been noted in the literature, that patients in all stages of yellow fever could be cared for by non-immune nurses without danger of contracting the disease. The non-contagious character of yellow fever was, therefore, hardly to be questioned.

In the second place, it had been observed that patients discharged from the wards during early convalescence could be brought into intimate association with non-immune individuals without thereby establishing fresh foci of the disease. This did not seem to indicate that any specific agent was present in the excreta of the sick.

Again, it had been noted that in certain cases of this disease no growth had been obtained on the ordinary laboratory media, either by frequent cultures from the blood during life or from the blood and organs after death.

Further, in the course of an investigation which the Commission were able to make during the last week of July, 1900, concerning the origin and spread of a small epidemic of yellow fever that had appeared in a military garrison, numbering about 900 men, at Pinar del Rio, Cuba, they had seen that by reason of the false diagnosis of "pernicious malarial fever" which had been given to these cases no disinfection of bedding or clothing had been carried out; and yet there was no indication that this neglect had contributed in the least to the spread of the disease; nor had any harm come to those non-immunes who had slept in the beds vacated by the sick, or washed the supposedly infected garments of those who had recovered or died of this disease.

Putting these various data together, it seemed probable that more progress might be made if attention should be turned to the mode of transmission of yellow fever, especially as our own observations had caused us to seriously doubt the usually accepted belief of the conveyance of this disease by means of *fomites*.

Then, too, the endemic curve of yellow fever in the city of Havana, and its well-known epidemic curve in the United States, appeared to be more intimately associated with and more affected by the rise and fall of the annual temperature curve than was to be seen in any of the acute infections, except malarial fever. The peculiar behaviour of this disease (if I may use the expression) in rapidly spreading in certain localities, when introduced, as contrasted with its failure to propagate itself in other places, where the conditions for its increase were apparently just as favourable, seemed to point in the strongest manner to the necessity for some special agent or intermediate host in the dissemination of its specific cause. If malarial fever—a disease so much affected by temperature conditions—required the agency of a special genus of mosquito for its propagation, as had in recent years been so brilliantly worked out by Ross, Grassi, Bastianelli, Bignami and others, it did not seem unreasonable to suppose that yellow fever—a disease so plainly controlled by seasonal conditions—might also depend on some such agent for its spread. Influenced by this line of reasoning, the Commission began, during the second week of August, 1900, its observations relative to the propagation of yellow fever by means of the bite of a certain species of mosquito—*Stegomyia fasciata*.

The work along this line was carried forward so rapidly that, within thirty days, eleven individuals had been bitten by infected *Stegomyia*, of whom two¹ developed well-marked attacks of yellow fever within the usual period of incubation, and under such circumstances as to positively exclude, in one case, any other possible source of infection.

Appreciating fully the importance of this discovery and in order to exclude all other possible sources of infection in our future observations, it was now determined to establish a Special Experimental Station where further observations could be made on non-immune human beings, both as to the propagation of yellow fever by means of the bite of the mosquito as well as by exposure to the most intimate contact with infected clothing and bedding, and this under the strictest enforcement of military quarantine. With the approval and assistance of the *Military Governor of the Island of Cuba*, this Experimental Station was ready for occupancy on November 20th, 1900, and was continuously occupied until March 1st, 1901.

As the results obtained at this station have already been published⁽²⁾ in full elsewhere, I will here only present a brief account, first of the experiments with fomites and afterwards of those made with infected mosquitoes.

Attempts at Infection by Fomites.

I quote from a paper which the writer presented for the Commission at the meeting of the Pan-American Medical Congress², held in Havana, Cuba, Feb. 4-7, 1901: "For this purpose there was erected at Camp Lazear a small frame house consisting of one room, 14 × 20 feet, and known as 'Building No. 1,' or the 'Infected Clothing and Bedding Building.' The cubic capacity of this house was 2800 feet. It was tightly sealed within with 'tongued and grooved' boards, and was well battened on the outside. It faced the south and was provided with two small windows, each 26 × 34 inches in size. These windows were both placed on the south side of the building, the purpose being to prevent, as much as possible, any thorough circulation of the air within the house. They were closed by permanent wire-screens of 0.5 mm. mesh. In addition a sliding glass sash was provided within and heavy wooden

¹ One of these cases was that of Dr James Carroll, Contract Surgeon, U.S.A., a member of the Commission.

² *Loc. cit.*

shutters without; the latter intended to prevent the entrance of sunlight into the building, as it was not deemed desirable that the disinfecting qualities of sunlight, direct or diffused, should at any time be exerted on the articles of clothing contained within this room. Entrance was effected through a small vestibule, 3 × 5 feet, also placed on the southern side of the house. This vestibule was protected without by a solid door and was divided in its middle by a wire-screen door, swung on spring hinges. The inner entrance was also closed by a second wire-screen door. In this way the passage of mosquitoes into this room was effectually excluded. During the day, and until after sunset, the house was kept securely closed, while by means of a suitable heating apparatus the temperature was raised to 92°—95° F. Precaution was taken at the same time to maintain a sufficient humidity of the atmosphere. The average temperature of this house was thus kept up at 76.2° F. for a period of sixty-three days.

“Nov. 30, 1900, the building now being ready for occupancy, three large boxes filled with sheets, pillow-cases, blankets, etc., contaminated by contact with cases of yellow fever and their discharges were received and placed therein. The majority of the articles had been taken from the beds of patients sick with yellow fever at Las Animas Hospital, Havana, or at Columbia Barracks. Many of them had been purposely soiled with a liberal quantity of black vomit, urine, and fecal matter. A dirty ‘comfortable’ and a much soiled pair of blankets, removed from the bed of a patient sick with yellow fever in the town of Quemados were contained in one of these boxes. The same day, at 6 p.m., Dr R. P. Cooke, Acting Assistant Surgeon, U.S.A., and two privates of the Hospital Corps, all non-immune young Americans, entered this building and deliberately unpacked these boxes, which had been tightly closed and locked for a period of two weeks. They were careful at the same time to give each article a thorough handling and shaking, in order to disseminate through the air of the room the specific agent of yellow fever, if contained in these fomites. These soiled sheets, pillow-cases and blankets were used in preparing the beds in which the members of the Hospital Corps slept. Various soiled articles were hung around the room and placed about the bed occupied by Dr Cooke.

“From this date until Dec. 19, 1900, a period of twenty days, this room was occupied each night by these three non-immunes. Each morning the various soiled articles were carefully repacked in the aforesaid boxes, and at night again unpacked and distributed about the

room. During the day the residents of this house were permitted to occupy a tent pitched in the immediate vicinity, but were kept in strict quarantine.

“December 19th these three non-immunes were placed in quarantine for five days and then given the liberty of the camp. All had remained in perfect health, notwithstanding their stay of twenty nights amid such unwholesome surroundings.

“During the week December 20—27 the following articles were also placed in this house, viz. pajamas suits, 1; under-shirts, 2; night-shirts, 4; pillow-slips, 4; sheets, 6; blankets, 5; pillows, 2; mattresses, 1. These articles had been removed from the persons and beds of four patients sick with yellow fever and were very much soiled, as any change of clothing or bed-linen during their attacks had been purposely avoided, the object being to obtain articles as thoroughly contaminated as possible.

“From Dec. 21, 1900, till Jan. 10, 1901, this building was again occupied by two non-immune young Americans, under the same conditions as the preceding occupants, except that these men *slept every night in the very garments worn by yellow fever patients throughout their entire attacks*, besides making use exclusively of their much-soiled pillow-slips, sheets and blankets. At the end of twenty-one nights of such intimate contact with these *fomites*, they also went into quarantine, from which they were released five days later in perfect health.

“From January 11 till January 31, a period of twenty days, ‘Building No. 1’ continued to be occupied by two other non-immune Americans, who, like those who preceded them, have slept every night in the beds formerly occupied by yellow fever patients and in the night-shirts used by these patients throughout the attack without change. In addition during the last fourteen nights of their occupancy of this house they had slept each night, with their pillows covered with towels that had been thoroughly soiled with the blood drawn from both the general and capillary circulation, on the first day of the disease, in the case of a well-marked attack of yellow fever. Notwithstanding this trying ordeal these men have continued to remain in perfect health.

“The attempt which we have therefore made to infect ‘Building No. 1’ and its seven non-immune occupants, during a period of sixty-three nights, has proved an absolute failure.”

Infection by Mosquitoes.

While the experiments with *fomites* were being carried out in "Building No. 1," certain non-immune individuals who were lodged in tents, in a separate part of the camp, were being subjected, with their full consent, to the bites of mosquitoes which had previously fed on the blood of cases of yellow fever occurring in the city of Havana. Thus during the period from December 5th, 1900, to February 7th, 1901, we had subjected to this method of infection twelve non-immune subjects, who had previously passed their full record of quarantine in this camp. Of these 10, or 83.3%, experienced attacks of yellow fever and always within the period of incubation of this disease.

The following Table II. gives the necessary data concerning these observations:

TABLE II.

No. of case	Days in quarantine	Inoculation		Method of inoculation	Period of incubation in hours	Result	Order of occurrence	Date of occurrence
		Hour	Date					
I	15	2 p.m.	Dec. 5, 1900	Mosquito	81½	Positive	I	Dec. 8, 1900
II	9	4 p.m.	" 8 "	"	137	"	III	" 13 "
III	19	10.30 a.m.	" 9 "	"	83½	"	II	" 12 "
IV	21	4.30 p.m.	" 11 "	"	91½	"	IV	" 15 "
V	32	12 noon	" 21 "	"	95	"	V	" 25 "
VI	31	10 a.m.	Jan. 8, 1901	"	—	Negative	VI	—
VII	22	11 a.m.	Dec. 30, 1900	"	94½	Positive	VII	Jan. 3, 1901
VIII	69	8.30 p.m.	Jan. 19, 1901	"	95½	"	VIII	" 23 "
IX	74	10.30 a.m.	" 25 "	"	—	Negative	IX	—
X	6	9.30 a.m.	" 31 "	"	74½	Positive	X	Feb. 3, 1901
XI	78	11 a.m.	Feb. 6 "	"	78	"	XI	" 9 "
XII	25	2 p.m.	" 7 "	"	70	"	XII	" 10 "

The positive results obtained, therefore, by this mode of infection stand in striking contrast to the negative experiments made with *fomites*. Indeed, cases VIII and XI of Table II had each slept twenty-one nights in the garments of yellow fever patients while occupants of Building No. 1. As they had remained in perfect health at Camp Lazear for yet thirty days longer, they were at the expiration of this time bitten by infected mosquitoes solely for the purpose of testing their immunity and with the result that an attack of yellow fever promptly followed in each case.

It should be borne in mind, also, that of the non-immune residents at Camp Lazear, while all lived under the same hygienic conditions,

only those individuals developed yellow fever who were purposely bitten by contaminated mosquitoes, or injected with the blood of those sick with this disease. Moreover, the precision with which the infection of the individual followed the bite of the mosquito left nothing to be desired in order to fulfil the requirements of a scientific experiment.

Case V of Table II is of especial interest, when taken in connection with the failure to induce the disease by contact with *fomites*.

This individual, having been quarantined for thirty-two days at Camp Lazear, volunteered to enter a newly erected building in which fifteen contaminated mosquitoes had just been freed. His first visit was at noon, December 21, 1901, and the length of his stay thirty minutes. At 4.30 p.m. the same day he again entered this building and remained twenty minutes. The following day at 4.30 p.m. he, for the third time, visited this room and remained twenty minutes. During each of these visits he was bitten by mosquitoes. He did not enter the building again, nor was he exposed to any other source of infection. Nevertheless at the expiration of three days and twenty-three hours, or at 6 a.m. December 25, 1900, he was suddenly seized with an attack of yellow fever, which proved to be severe in character. That the infection was occasioned by the bites of contaminated mosquitoes was plainly shown by the immunity from the disease enjoyed by two non-immunes "controls," who, protected only by a wire-screen partition, had been present at each of the subject's visits and who, under the same conditions of security against the bites of the infected mosquitoes, continued to sleep in, and breathe the common atmosphere of this room for yet eighteen nights.

To the positive cases contained in Table II, which were produced at Camp Lazear, we are now able to add four other cases of yellow fever occasioned by the bites of infected mosquitoes, thus making a total of fourteen cases, in each of which happily recovery followed.

A very important point brought out by these observations is that an interval of about twelve days or more after contamination appears to be necessary before the infected *Stegomyia* is capable of conveying the disease to a susceptible individual. Repeated experiments made with insects which had bitten yellow fever patients two to ten days previously were always negative, although these same insects were proven capable of conveying the disease after having been kept until 17 to 24 days had elapsed. Our observations⁽⁴⁾ further demonstrate that mosquitoes that have been kept for periods varying from 39 to 57 days after contamination are still capable of conveying the disease, and

further that infected *Stegomyia* may survive for a period of at least 71 days. This will explain how the contagion of yellow fever may cling to a building, although it has been vacated for a period of two or more months.

Bearing in mind that the observations made by means of blood injections (Table I) were only undertaken *after* we had succeeded in demonstrating that the disease could be conveyed by the bites of infected *Stegomyia*, it will be seen that our study of the method of propagation of yellow fever, at Camp Lazear, sufficed to prove very definitely that, while the natural mode of transmission of this disease is through the bites of infected mosquitoes, yellow fever may also be conveyed, like malarial fever, by the injection of a small quantity of blood taken from the veins of an individual suffering with this disease.

Per contra, our observations show that, notwithstanding the common belief in this mode of transmission, yellow fever cannot be induced in the non-immune individual even by the most intimate contact with contaminated articles of clothing and bedding.

Although the investigations made at Camp Lazear were only concluded one year ago, already confirmatory evidence of the strongest character has been furnished in a series of experiments carried out by Guitéras⁽¹⁵⁾ at the Inoculation Station of the Sanitary Department of Havana.

I may be pardoned for quoting the paragraph with which Guitéras begins his contribution. He says: "The favourable results obtained by the United States Army Commission in their experiments with yellow fever, the continued series of mild cases resulting from these experiments without a death, suggested very naturally the continuation of their work on a larger scale; not with a view to control or confirm the conclusions of the Commission, for anyone who had followed their work with unprejudiced attention must have concluded that their solution of the problem of the etiology of yellow fever was final; but rather in the hope of propagating the disease in a controllable form, and securing amongst the recently arrived immigrants immunization, with the minimum amount of danger to themselves and the community."

Of a total of 42 individuals inoculated by Guitéras 25 were rejected by him by reason of having been bitten by insects that had been applied to cases of fever about which the diagnosis was in doubt. The following table, therefore, only includes 17 persons who were bitten by *Stegomyia* that had previously fed on unmistakable cases of yellow

fever at intervals of 14 to 36 days before being applied to the non-immune subject.

TABLE III.

No. of case	Date of inoculation	Mode of inoculation	Result	Period of incubation
1	Feb. 23, 1901	Mosquito	Positive	3 days, 10 hours
2	Aug. 4, 1901	"	Negative	
3	" 4 "	"	"	
4	" 7 "	"	"	
5	" 8 "	"	Positive	4 days, 5 hours
6	" 8 "	"	"	3 " 3 "
7	" 7 "	"	Negative	
8	" 9 "	"	Positive	5 " 3 "
9	" 10 "	"	Negative	
10	" 10 "	"	"	
11	" 10 "	"	"	
12	" 13 "	"	Positive	3 days, 19 hours
13	" 13 "	"	Negative	
14	" 14 "	"	Positive	3 " 21 "
15	" 14 "	"	"	5 " 21 "
16	" 22 "	"	"	3 days
17	" 24 "	"	Negative	

A more complete confirmation of the results obtained by the American Commission could not be furnished than the data contained in the foregoing table, since they show that of 17 individuals who were bitten by infected *Stegomyia fasciata*, eight (47 %) developed the disease. Most unfortunately in three of these cases very grave symptoms ensued, such as black vomit and suppression of the urine, which eventuated in the death of the patients. I may add that in the hands of Guitéras *fomites* failed to exert any effect on non-immunes.

Whether other species of mosquitoes than *Stegomyia* are capable of conveying the parasite of yellow fever has not as yet been determined by the Commission: nor have we been able to ascertain whether the parasite passes from the mother insect to daughter insects. The experiments which we have thus far been able to make for the purpose of determining these important points, although negative, have been too few in number to warrant any definite expression of opinion.

The Prevention of Yellow Fever.

The definite determination of the way in which yellow fever is transmitted from the sick to the well, furnishes a solution at last of that much vexed problem of how to prevent the spread of the disease.

Even in the absence of more definite knowledge concerning its specific agent—knowledge greatly to be desired from the scientific standpoint—we are now able, as sanitarians, to direct our efforts along certain well-defined lines, with a feeling of security heretofore unknown.

From the point of view of prevention the situation may be briefly summed up in the following conclusion, which was presented by the American Army Commission to the Pan-American Congress of 1900¹, viz. "The spread of yellow fever can be most effectually controlled by measures directed to the destruction of mosquitoes and the protection of the sick against the bites of these insects."

This conclusion was the logical outcome of the observations that had been made by the Commission at its Experimental Station near Quemados, Cuba.

The importance of the discovery that yellow fever is transmitted by the bite of a certain species of mosquito did not fail to attract the prompt attention of the Military Governor of the Island of Cuba, himself a physician and formerly a distinguished member of the Medical Department of the United States Army. By his direction the theory was at once subjected to a practical test in the city of Havana, in which city yellow fever had not failed to make its yearly appearance during the past one hundred and forty years.

Under the efficient management of the Chief Sanitary Officer, Surgeon-Major Wm. C. Gorgas, U.S. Army, the sanitary regulations were so far modified as to require that every patient having yellow fever should not only be quarantined, but that his room should be promptly protected with wire-screens, so as to prevent the possibility of mosquitoes becoming infected by sucking the blood of the patient. As a second important measure, a systematic destruction of all mosquitoes in other rooms of the patient's house, as well as in adjoining houses, was at once begun, the fumes of *pyrethrum* being relied upon to stupefy the insects, after which they were carefully swept up and burned. In other words, Surgeon-Major Gorgas relying upon the well-known slow progress of yellow fever sought to destroy all mosquitoes, infected or non-infected, within a given radius of each case, while at the same time he effectually excluded all mosquitoes from access to the sick. If a secondary case occurred, the same hygienic measures were vigorously enforced along the lines above indicated.

As an illustration of what has been accomplished by these newer

¹ *Loc. cit.*

CHART I.
 Showing monthly mortality from Yellow Fever in the City of Havana, for the twenty years, 1880—1899,
 and for the years 1900—1901.

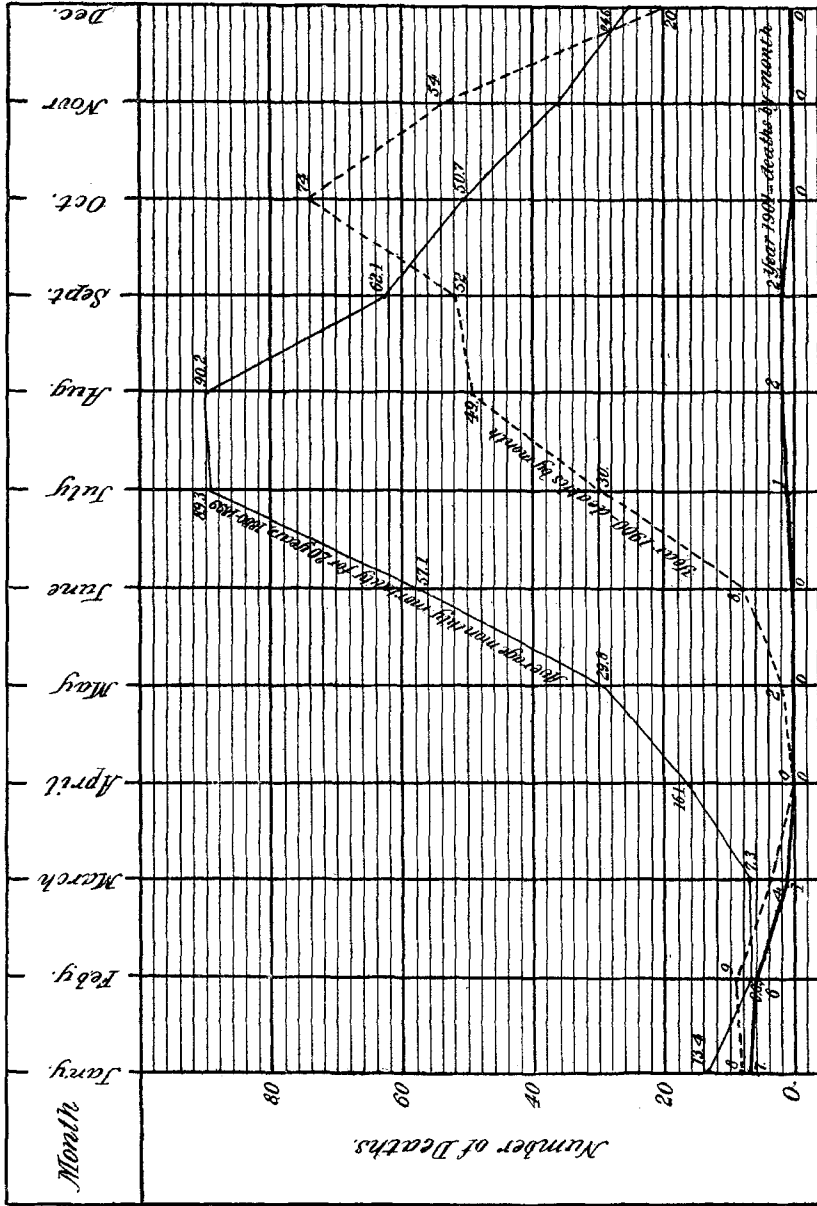


CHART II.

Cases and Deaths from Yellow Fever in the City of Havana, for the Epidemic year, March 1, 1900, to March 1, 1901 (by month).

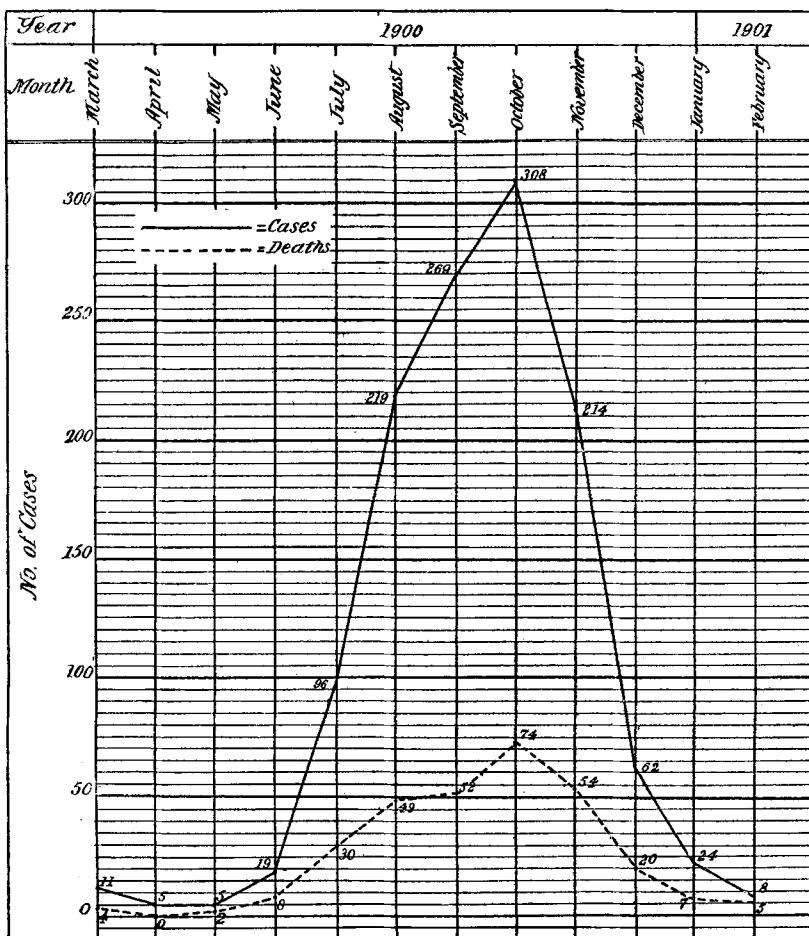
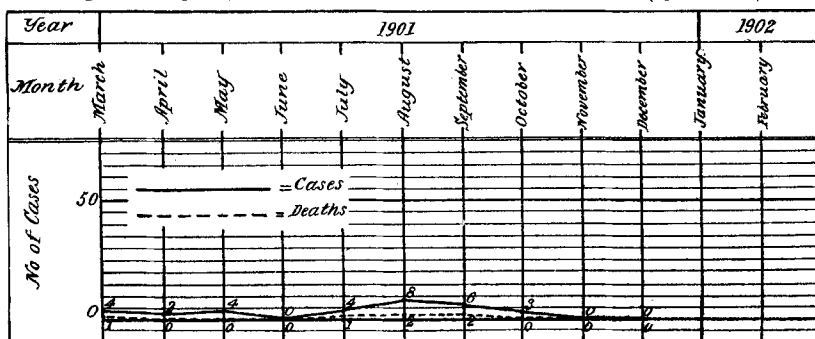


CHART III.

Cases and Deaths from Yellow Fever in the City of Havana, for the Epidemic year, March 1, 1901, to March 1, 1902 (by month).



sanitary regulations, I may state that counting from the date when they were put into force, viz. February 15, 1901—Havana was freed from yellow fever within ninety days; so that from May 7th to July 1st—a period of fifty-four days—no cases occurred. Notwithstanding the fact that on the latter date and during the months of July, August, and September, the disease was repeatedly reintroduced into Havana from an inland town, no difficulty was encountered in promptly stamping it out by the same measures of sanitation intelligently applied both in the city of Havana as well as in the town of Santiago de las Vegas, whence the disease was being brought into Havana.

As a further illustration of the remarkable sanitary victory accomplished over a disease whose progress we had heretofore been powerless to arrest, I will close this paper by inviting the reader's attention, first to the accompanying Chart I, which shows the average monthly mortality from yellow fever in Havana for the twenty years, 1880—1899, inclusive, and also the mortality by month for the years 1900 and 1901. I will then ask him to examine Chart II, which shows the progress of yellow fever in Havana during the epidemic year, ending March 1, 1901, when the sanitary authorities were putting forth every effort known at that time to sanitary science in order to control the march of the disease; and when he has satisfied himself that no effect whatever was produced upon the epidemic of that year, I will invite his attention to Chart III, which shows the occurrence of this disease in Havana for the epidemic year March 1st, 1901, to March 1st, 1902, during which year yellow fever was fought on the theory that the specific agent of this disease is transmitted solely by means of the bites of infected mosquitoes. By carefully comparing the figures both as to deaths and cases in these two Charts, and recalling that between the years 1853 and 1900 there have been recorded in the city of Havana 35,952 deaths from yellow fever, he will then be able to more clearly appreciate the value of the work accomplished by the American Army Commission.

BIBLIOGRAPHY.

1. Report on the Etiology and Prevention of Yellow Fever. Washington, 1890.
2. La Fiebre Amarilla. Conferencia dada en la Universidad de Montevideo, el 10 Junio 1897. Reprint.
3. Bacteriological Study in the Etiology of Yellow Fever. *New York Medical Journal*, Jan. 28, 1899, pp. 109—114.
4. Summary of Pathologic and Bacteriologic Work, at Isolation, New Orleans, La. *Journal of the American Medical Association*, April 16, 1898, pp. 884—888.
5. The Etiology of Yellow Fever. Abstract of Report, &c. *N.Y. Med. Journal*, August 26, 1899, pp. 299—302.
6. Report upon Bacteriological Investigations in Yellow Fever. *The Medical News*, N.Y., February 10 and 17, 1900.
7. *Revista d' Igiene e Sanita Publica*, xi. No. 13, July, 1900, pp. 474—475.
8. La Bacille Ictéroïde et Sa Toxine. *Archives de Médecine Expérimentale &c.*, xi., 1899, pp. 378—398.
9. Nota para Servir al estudio bacteriológico de la Fiebre Amarilla. *Gaceta Medica de Mexico*, xxxvi., 1899, pp. 218—230.
10. The Etiology of Yellow Fever. A Preliminary Note. *The Philadelphia Med. Journal*, October 27, 1900.
11. Yellow Fever. *Buck's Reference Hand-book of the Medical Sciences*, Vol. VIII., 1889, p. 48.
12. The Etiology of Yellow Fever. A Supplementary Note. *American Medicine*, Vol. III., No. 8, February 22, 1902, pp. 301—305.
13. The Etiology of Yellow Fever. An Additional Note. *Journal of the American Medical Association*, February 16, 1901.
14. Experimental Yellow Fever. *Transactions of the Association of American Physicians*, Vol. XVI., 1901.
15. Experimental Yellow Fever at the Inoculation Station of the Sanitary Department of Havana. *American Medicine*, Vol. II., No. 21, 1901, pp. 809—817.