

for many minutes without moving. The dog hungered for twenty-four hours. I put a cloth-covered muzzle around his head and injected 100-150 c.c. of salt solution with the addition of grape seeds, globules of tinfoil, little granules of kaolin and Arminian bole into the rectum. I did not wish to kill the animal and so resorted to the hypodermic use of apomorphin. The before-mentioned mulatto willingly aided me in experimenting on the dog, which I tied very short. Seven experiments were made on this animal. Of 5 made with physiologic salt solution 4 proved positive, 1 negative. The sixth and seventh with distilled water, were negative.

Series 3.—I made the third series of experiments in August and September, 1899, in the course of treatment of a woman suffering from mechanical insufficiency of the stomach with a subacid condition (total acidity: Phenolphthalein, 24; HCl, .04 per cent. Toepfer). I excluded any food or drink by the mouth, and nutritive enemas were administered for eleven succeeding days; the result of the treatment was everything that could be wished for. The first enemas—all given in the knee-elbow position—were evacuated very soon, undoubtedly on account of the nervous condition of the patient. But from the third day on the remainder of the enemas were not expelled before five or six hours had passed; frequently no movement of the bowels followed from the evening to the morning. The quantity of the enema was 250 to 300 c.c. in general three times a day, in intervals of six to seven hours. The woman had been treated by lavage before she came under my treatment and was well used to the stomach tube. The enema itself consisted of a mixture of 250 c.c. of milk and cream, 2 eggs, 1 tablespoonful of a mixture of tropon and cornstarch and a pinch of sodium chlorid. and was brought up 15 to 22 inches into the rectum. A part of the treatment was also the injection of cottonseed-oil—250 c.c.—emulsified with oleic acid or rather sodium oleate (eunatrol). Several times, a few hours after the injection of the enemas the patient complained of eructations and a sensation of tasting eggs, other times tasting of grease or oil. These complaints induced me to start the experiment, the experimental additions being without the knowledge of the patient. To the nutriment enemas I added small, dried, uncooked whortleberries, which I knew would as a rule pass the alimentary canal quite unaffected by the digestive juices of the intestines. Four experiments were made and, by means of the stomach-tube, through which I introduced 1 quart of water, I twice recovered whortleberries; the other two times I could not discover any. Two experiments were made with oil emulsion, to which menthol—validol—was added. One time the patient noted a marked peppermint flavor, and both times I recovered, during lavage of the stomach, about 10 c.c. of the emulsified oil with a marked flavor of menthol. The stomach lavage occurred between five or six hours after the injection of the enema.

Reviewing the series of experiments, we find: One spontaneous experiment on a patient, 6 experiments on the mulatto, 7 experiments on the dog, 6 experiments on the woman patient—a total of 20. Of these 3 made with oil and 10 made with NaCl solution proved positive; 4 made with the latter solution proved negative, as far as the stomach is concerned, while 3 made with distilled water also proved negative.

The result of my experiments may be put down as positive in the meaning of Grützner, Swiezynski and Riegel. In this matter we can better understand the good effect of the nutritive enemas, especially when we consider cases in which patients have been nourished exclusively by rectal feeding, not only for days or weeks—among others, Donkin, up to 23 days; Boas, up to 14 days; D. D. Stewart, 23 days; the writer, 11 days—but also for months—Leube 6, and Riegel 10 months. The occasions of temporarily suspending the ingestion of food into the stomach are not too rare, particularly in cases of stenosis of the esophagus, cardia and pylorus, gastric ulceration and hemorrhage, certain poisonings.

when the mucous membranes are destroyed, gastric hyper-irritation and dilatation of the stomach; besides these, rectal injections can be effectively used as carriers of medicine in cases of intestinal affections.

In conclusion, I should like to suggest to my colleagues that they make further experiments along this line, so that no doubt will prevail whether antiperistalsis is the rule or the exception.

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THE ETIOLOGY OF YELLOW FEVER.

AN ADDITIONAL NOTE.*

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At the Twenty-eighth Annual Meeting of the American Public Health Association,¹ held in Indianapolis, Ind., Oct. 22-26, 1900, we presented, in the form of a preliminary note, the results of our bacteriologic study of yellow fever, based on cultures taken from the blood in eighteen cases, at various stages of the disease, as well as on those which we had made from the blood and organs of eleven yellow fever cadavers. We also recorded the results obtained from the inoculation of eleven non-immune individuals by means of the bite of mosquitoes (*Culex fasciatus*, Fabr.) that had previously fed on the blood of patients sick with yellow fever. We were able to report two positive results, in which the attack of yellow fever followed the bite of a mosquito within the usual period of incubation of this disease.

In one of these cases all other sources of infection could be positively excluded. From our several observations we drew the following conclusions: 1. *Bacillus icteroides* (Sanarelli) stands in no causative relation to yellow fever, but, when present, should be considered as a secondary invader in this disease. 2. The mosquito serves as the intermediate host for the parasite of yellow fever.

*Read at the Pan-Am. Med. Cong., held in Havana, Cuba, Feb. 4-7, 1901.

1. Phila. Med. Jour., Oct. 27, 1900.

Since the publication of our preliminary note, we have continued our investigations, especially as regards the means by which yellow fever is propagated from individual to individual, and as to the manner in which houses become infected with the contagium of this disease. The results already obtained are so positive and striking that, with the permission of Surgeon-General Sternberg, we have concluded to present to this Congress an additional note, in which we will record these later observations. We desire to here express our sincere thanks to the Military Governor of the Island of Cuba, Major General Leonard Wood, U. S. V., without whose approval and assistance these observations could not have been carried out.

In order to exercise perfect control over the movements of those individuals who were to be subjected to experimentation, and to avoid any other possible source of infection, a location was selected in an open and uncultivated field, about one mile from the town of Quemados, Cuba. Here an experimental sanitary station was established under the complete control of the senior member of this Board. This station was named Camp Lazear, in honor of our late colleague, Dr. Jesse W. Lazear, Acting Assistant-Surgeon, U. S. A., who died of yellow fever, while courageously investigating the causation of this disease. The site selected was very well drained, freely exposed to sunlight and winds, and, from every point of view, satisfactory for the purposes intended.

The personnel of this camp consisted of two medical officers, Dr. Roger P. Ames, Acting Assistant-Surgeon, U. S. A., an immune, in immediate charge; Dr. R. P. Cooke, Acting Assistant-Surgeon, U. S. A., non-immune; one acting hospital steward, an immune; nine privates of the hospital corps, one of whom was immune, and one immune ambulance driver.

For the quartering of this detachment, and of such non-immune individuals as should be received for experimentation, hospital tents, properly floored, were provided. These were placed at a distance of about twenty feet from each other, and were numbered 1 to 7 respectively.

Camp Lazear was established Nov. 20, 1900, and from this date was strictly quarantined, no one being permitted to leave or enter camp except the three immune members of the detachment and the members of the Board. Supplies were drawn chiefly from Columbia Barracks, and for this purpose a conveyance under the control of an immune acting hospital steward, and having an immune driver, was used.

A few Spanish immigrants recently arrived at the Port of Havana, were received at Camp Lazear, from time to time, while these observations were being carried out. A non-immune person, having once left this camp, was not permitted to return to it under any circumstances whatever.

The temperature and pulse of all non-immune residents were carefully recorded three times a day. Under these circumstances any infected individual entering the camp could be promptly detected and removed. As a matter of fact only two persons, not the subject of experimentation, developed any rise of temperature; one, a Spanish immigrant, with probably commencing pulmonary tuberculosis, who was discharged at the end of three days; and the other, a Spanish immigrant, who developed a temperature of 102.6 F. on the afternoon of his fourth day in camp. He was at once removed with his entire bedding and baggage and placed in the receiving ward at Columbia Barracks. His fever, which was

marked by daily intermissions for three days, subsided upon the administration of cathartics and enemata. His attack was considered to be due to intestinal irritation. He was not permitted, however, to return to the camp.

No non-immune resident was subjected to inoculation who had not passed in this camp the full period of incubation of yellow fever, with one exception, to be hereinafter mentioned.

OBSERVATIONS.

Having thus sufficiently indicated the environment of Camp Lazear and the conditions under which its residents lived, we will now proceed to a narration of the observations thus far made at this experimental station. At the time these inoculations were begun, the several tents were occupied as follows: Tent No. 1 by 1 immune and 1 non-immune; No. 2 by 1 immune and 2 non-immunes; No. 3 by 2 immunes; No. 4 by 3 non-immunes; No. 5 by 3 non-immunes; No. 6 by 2 non-immunes; and No. 7 by 1 non-immune.

For the purpose of experimentation subjects were selected as follows: from Tent No. 2, 2 non-immunes, and from Tent No. 5, 3 non-immunes. Later, 1 non-immune in Tent No. 6 was also designated for inoculation.

CASE 1.—Private John R. Kissinger, Hospital Corps, U. S. A., aged 23, a non-immune, occupant of Tent No. 2, with his full consent, was bitten at 10.30 a. m., Nov. 20, 1900, by a mosquito—*C. fasciatus*—that had bitten a severe case of yellow fever on the fifth day, eleven days previously; another severe case, on the third day, six days before, and a third severe one on the third day, three days before. As Kissinger had not absented himself from Columbia Barracks for a period of more than thirty days, it was considered safe to inoculate him without waiting for his period of incubation to pass.

Nov. 23, 1900, Kissinger was again bitten by the same mosquito. The result of both inoculations was negative. The mosquito, therefore, was incapable of conveying any infection on the eleventh or fourteenth day after it had bitten a severe case of yellow fever on the third day of the disease. This insect had been kept at ordinary room temperature and died November 26, 1900.

Dec. 5, 1900, at 2 p. m., twelve days after the last inoculation. Kissinger was again bitten by five mosquitoes—*C. fasciatus*—two of which had bitten fatal cases of yellow fever, on the second day, fifteen days before; one a severe case on the second day, nineteen days previously, and two a mild case on the third day, twenty-one days before.

The record of temperature and pulse, taken every three hours, following this inoculation, showed that the subject remained in his usual state of health during the following three days, except that on December 8, on the third day, Kissinger had slight vertigo, upon rising, which soon passed away. At 4.30 p. m.—commencement of fourth day—he complained of frontal headache; otherwise he felt well and partook of supper with appetite; at 9 p. m., temperature was 98.4 F., pulse 90; at 11.30 p. m., he awoke with a chill, his temperature 100 F., pulse 90; he complained of severe frontal headache and backache; his eyes were injected and his face suffused. December 9 at 3 a. m., his temperature was 102 F., pulse 102; he had violent headache and backache with nausea and vomiting. He was then removed to the yellow fever wards. His subsequent history was that of a case of yellow fever at moderate severity. Albumin appeared in the urine on the fourth day, increased to one-fifth by volume on the sixth day and disappeared on December 22. Granular casts were present in considerable numbers from the fourth to the eighth day. The conjunctivae were jaundiced on the third day. The diagnosis of yellow fever in this case was made by Drs. Juan Guitéras, Carlos Finlay, W. C. Gorgas, and A. Diaz Albertini, the board of yellow fever experts of the city of Havana, who saw the patient on several occasions during his illness. (See Chart I.) The period of incubation in this case was 3 days, 9½ hours.

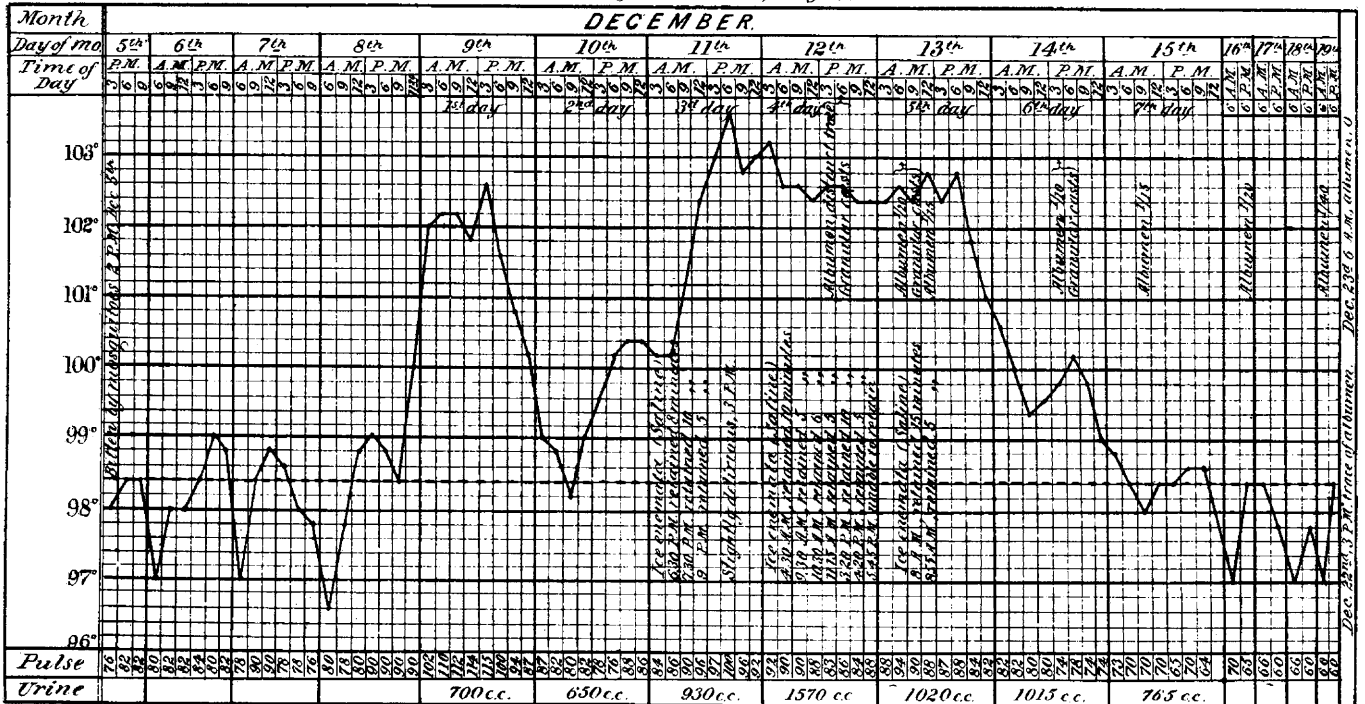
CASE 2.—John J. Moran, aged 24, an American, non-immune occupant of Tent No. 2, with his full consent, was bitten at 10 a. m., Nov. 26, 1900, by a mosquito—*C. fasciatus*—which twelve days before had bitten a case of yellow fever of moderate severity, on the third day of the disease. This insect had also bitten a well-marked case of yellow fever—second day—ten days previously.

to speak of the infection of a building by means of contaminated mosquitoes.

CASE 3.—A Spanish immigrant, aged 26, a non-immune occupant of Tent No. 5, with his full consent, was bitten at 4 p. m., Dec. 8, 1900, by four mosquitoes—*C. fasciatus*—which had been contaminated as follows: one by biting a fatal case of yellow fever, on the third day, seventeen days before; one a

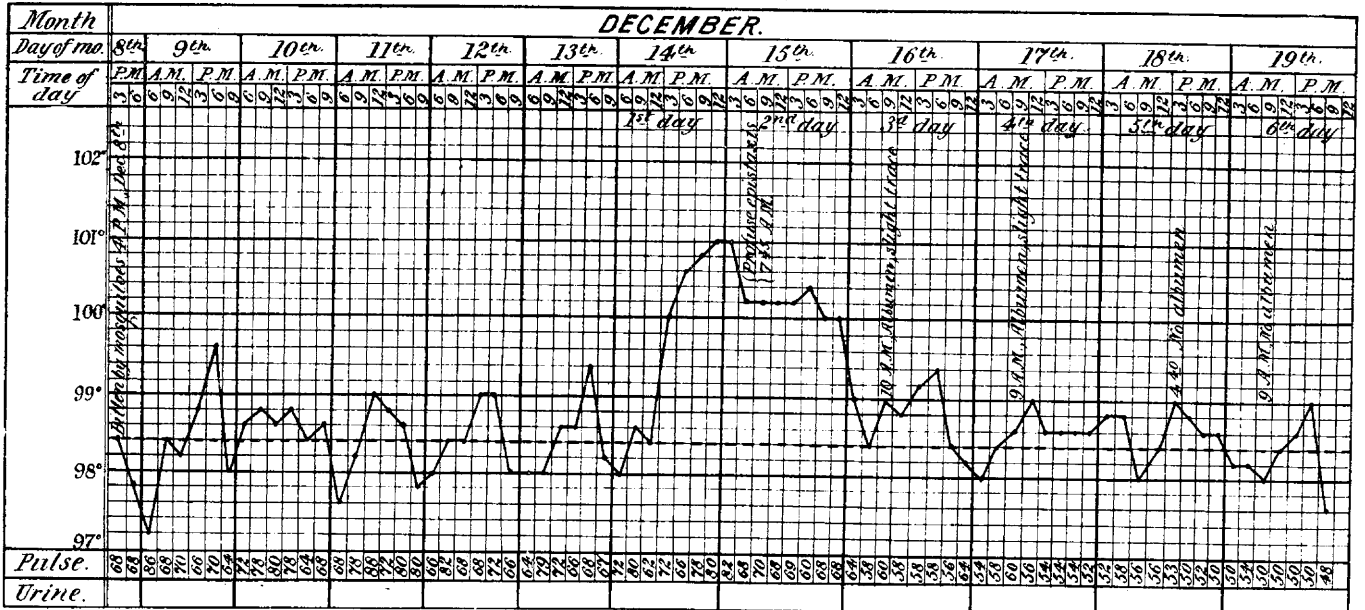
Yellow fever, produced by the bite of Culex fasciatus
Period of incubation, 3 days 9½ hours.

Chart I.



Yellow fever, produced by the bite of Culex fasciatus
Period of incubation, 4 days 20 hours.

Chart II.



November 29, at 2.20 p. m., Moran was again bitten by the same mosquito. The result of both of these inoculations was negative. This insect was, therefore, incapable of conveying the infection fifteen days after having bitten a case of yellow fever of moderate severity on the third day, and thirteen days after it had bitten a well-marked case of this disease on the second day. This mosquito had been kept at room temperature. Moran's case will be again referred to when we come

severe one, on the third day, eighteen days before; one a severe case, on the second day, twenty-two days before, and one a case of moderate severity, on the third day, twenty-four days previously.

The record of temperature and pulse, taken every three hours after the inoculation, shows no rise of temperature above 99 F. until 6 p. m., December 13, on the sixth day, when 99.4 F. is recorded; pulse 68. The subject, who was of a very lively

disposition, retained his usual spirits until noon of the 13th, although he complained of slight frontal headache on the 11th and 12th. He took to his bed at noon of the 13th, the fifth day, complaining of increased frontal headache and a sense of fatigue. At 9 p. m., his temperature was 98.2 F., pulse 62.

December 14, at 6 a. m., temperature was 98 F., pulse 72, and he still complained of frontal headache and general malaise. Profuse epistaxis occurred at 7.45 a. m.; at 9 a. m., temperature was 99.6 F., pulse 80; at 1.15 p. m., temperature was 100 F., pulse 80, and he complained of a sense of chilliness, with frontal headache increased, and slight pain in the back, arms and legs; at 3 p. m., temperature was 100 F., pulse 80; at 4.15 p. m., temperature 100.7 F., pulse 68; his face flushed and eyes congested. He was removed to the yellow fever wards. A trace of albumin was found in the urine passed at 3.30 p. m., December 15; a few hyaline casts were present. He was seen at this time by the Havana board of experts and the diagnosis of mild yellow fever confirmed. (See Chart No. 2.)

The period of incubation in this case was four days and twenty fours, counting from the time of inoculation to the hour when the patient took to his bed; if reckoned to the onset of fever, it was 5 days and 17 hours.

CASE 4.—A Spanish immigrant, aged 27, a non-immune occupant of Tent No. 5, with his full consent, was bitten at 10 a. m., Nov. 26, 1900, by a mosquito—*C. fasciatus*—which had bitten a severe case of yellow fever, on the second day, ten days before. Three days later, November 29, he was again bitten by the same insect. December 2, after an interval of three days, he was again bitten by the same insect, and also by a second mosquito—*C. fasciatus*—which, twelve days before, had been contaminated by biting a fatal case of yellow fever on the third day. No unfavorable effects followed any of these attempted inoculations. The first-mentioned mosquito, therefore, was incapable of conveying any infection on the seventeenth day after biting a severe case of yellow fever on the second day; the other also failed to infect on the twelfth day after biting a fatal case of yellow fever on the third day. Both of these mosquitoes had been kept at ordinary room temperature.

December 9, after an interval of seven days, the subject was again bitten, at 10.30 a. m., by one mosquito—*C. fasciatus*—which had been infected nineteen days before by biting a fatal case of yellow fever on the second day of the disease. He remained in his usual health until 9 a. m., December 12, the third day, when he complained of frontal headache; his temperature was 98.8 F., pulse 96. This headache continued during the entire day. At 6 p. m., temperature was 99 F., pulse 94; at 9 p. m., temperature 99 F., pulse 84; at 9.30 p. m., temperature 99.4 F., pulse 82. Severe headache and backache was complained of; his eyes were injected and his face suffused. The following morning he was sent to the yellow fever wards. Urine passed at 4.20 p. m., December 15, the third day, gave a distinct trace of albumin. Many hyaline casts were present on the same date. The conjunctivæ were jaundiced on the third day.

The patient was seen by the board of experts on December 14, and the diagnosis of yellow fever made. (See Chart No. 3.)

The period of incubation in this case was 3 days, 11½ hours.

CASE 5.—A Spanish immigrant, aged 26, a non-immune occupant of Tent No. 5, with his full consent, was bitten at 10 a. m., Nov. 26, 1900, by a mosquito—*C. fasciatus*—that had bitten a well-marked case of yellow fever, on the third day, twelve days before. November 29 he was again bitten by the same insect. December 2 he was for the third time bitten by two mosquitoes—*C. fasciatus*—both of which had bitten a well-marked case of yellow fever, on the third day, eighteen days before. As no bad results followed any of these inoculations, it follows that these mosquitoes were incapable of conveying any infection eighteen days after they had bitten a well-marked case of yellow fever on the third day. Both of these insects had been kept at room temperature.

December 11, after an interval of nine days, the subject was again, at 4:30 p. m., bitten by the same mosquitoes, four in number, that had been applied to Case 3, three days prior to this time, with positive results.

The record of temperature and pulse, taken every three hours following the inoculation, showed no change till December 13, the second day, at 9 a. m., when the temperature was 99 F., and the pulse 78. From this hour till 6 p. m. the temperature varied from 99.2 to 99.6 F. The subject complained of frontal headache, slight in degree, during the entire day. At 9 p. m. his temperature was 98.4 F., pulse 62.

December 14, the third day, he complained of slight frontal headache during the entire day, and was indisposed to exertion. From 6 a. m. to 6 p. m. the temperature averaged 99.2 F., and the pulse varied from 64 to 90; at 9 p. m. it was 98.4 F., the pulse 78. December 15, the fourth day, at 6 a. m., temperature was 98.2 F., pulse 78. He still had frontal headache. At 9 a. m., temperature was 99.2 F., pulse 80; at 12, noon, the former was 99.2 F., the pulse 74. The subject now went to bed, complaining of headache and pains throughout the body. At 2 p. m., the temperature was 100 F., the pulse 80; eyes much congested; face flushed. At 6 p. m. his temperature had risen to 102 F., and the pulse to 90. He was then transferred to the yellow fever wards. Albumin appeared in the urine at 7:30 a. m., December 17. Bleeding from the gums and roof of the mouth occurred on the sixth and seventh days of his illness.

This case was examined by the board of experts on the 16th and 19th, and the diagnosis of yellow fever made.

Albumin disappeared on the sixth day, the temperature falling to normal on this date, and remaining near this point till December 23, the ninth day of sickness, when a relapse occurred, attended with bleeding from the gums on December 24 and 25, with the appearance of red blood cells and pus cells in the urine in moderate numbers. Fever subsided on December 26, and the urine became normal on December 29. (See Chart iv.)

The period of incubation in this case, if reckoned from the time of inoculation to the hour when the patient took to his bed, was 3 days, 19½ hours.

The four patients whose histories we have given above were also examined by a number of physicians of Havana, among whom we may mention Dr. Bango, of "La Covadonga," Dr. Sanchez, of "La Benéfica," and Dr. Moas, of "La Purissima Concepcion," by all of whom the diagnosis of yellow fever was confirmed. Let us now rapidly review the circumstances attending these cases of experimental yellow fever, in order to emphasize certain points of interest and importance in connection with their occurrence. (We omit any reference to the clinical histories.)

It should be borne in mind that at the time when these inoculations were begun, there were only 12 non-immune residents at Camp Lazear, and that 5 of these were selected for experiment, viz., 2 in Tent No. 2, and 3 in Tent No. 5. Of these we succeeded in infecting 4, viz., 1 in Tent No. 2 and 3 in Tent No. 5, each of whom developed an attack of yellow fever within the period of incubation of this disease. The one negative result, therefore, was in Case 2—Moran—inoculated with a mosquito on the fifteenth day after the insect had bitten a case of yellow fever on the third day. Since this mosquito failed to infect Case 4, three days after it had bitten Moran, it follows that the result could not have been otherwise than negative in the latter case. We now know, as the result of our observations, that in the case of an insect kept at room temperature during the cool weather of November, fifteen or even eighteen days would, in all probability, be too short a time to render it capable of producing the disease.

As bearing upon the source of infection, we invite attention to the period of time during which the subjects had been kept under rigid quarantine, prior to successful inoculation, which was as follows: Case 1, fifteen days; Case 3, nine days; Case 4, nineteen days; Case 5, twenty-one days. We further desire to emphasize the fact that this epi-

demic of yellow fever, which affected 33.33 per cent. of the non-immune residents of Camp Lazear, did not concern the 7 non-immunes occupying Tents No. 1, 4, 6 and 7, but was strictly limited to those individuals who had been bitten by contaminated mosquitoes.

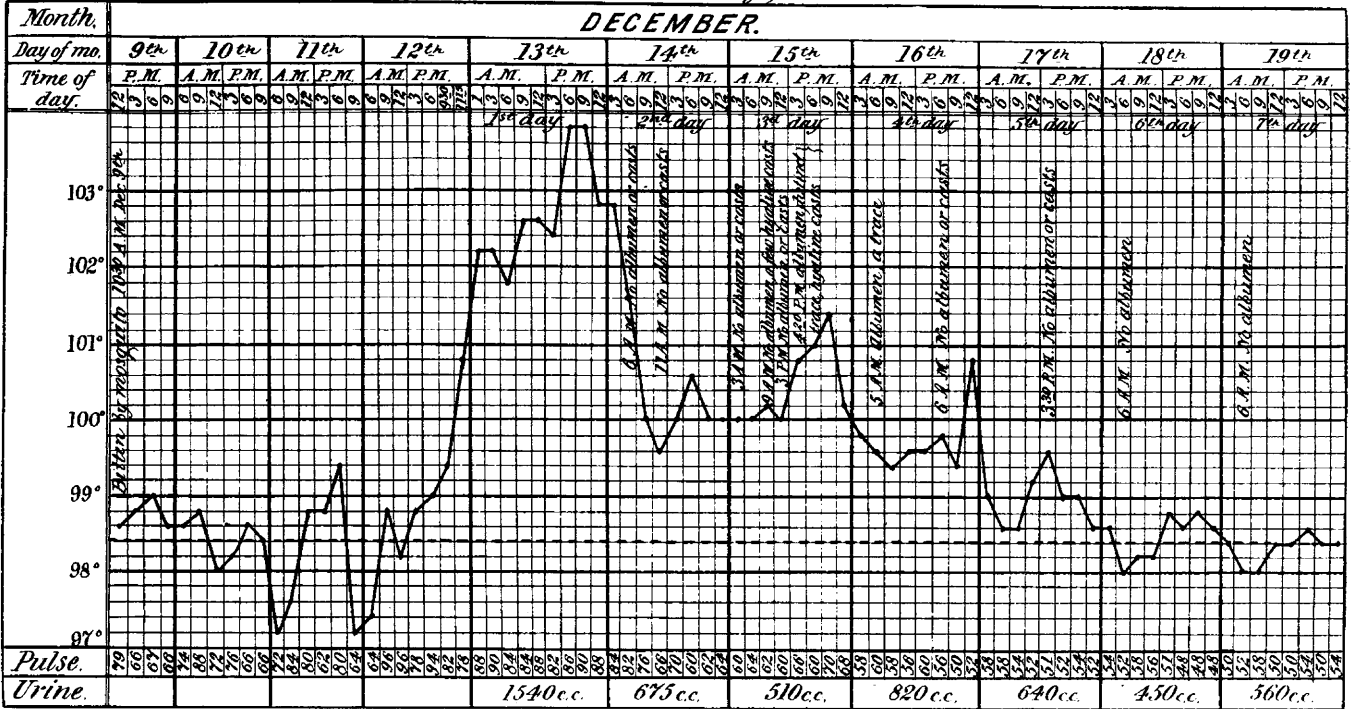
Nothing could point more forcibly to the source of this infection than the order of the occurrence of events at this camp. The precision with which the infection of the individual followed the bite of the mosquito left

a mild case of yellow fever on the first day of the disease (Case 4). These insects had been kept at a temperature of 82 F.

The subject remained in his normal condition until the evening of Jan. 2, 1901, the third day, when he complained of frontal headache. At 6 p.m., his temperature was 99 F., pulse 64. He slept well, but still complained of headache on the following morning, January 3. He partook sparingly of breakfast, and afterward lay on his bed, being disinclined to exert himself. At 9 a.m., the temperature was 99 F., the pulse 96; at 10:30 a.m., temperature 100 F., pulse 80. A

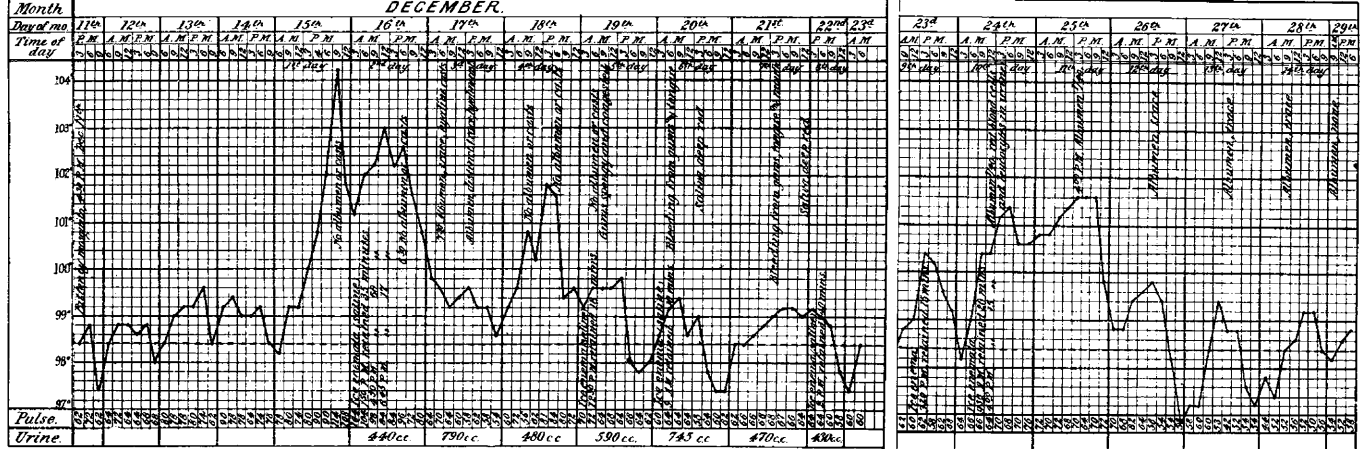
Yellow fever produced by the bite of *Culex fasciatus*.
Period of incubation 3 days, 11 hours.

Chart III.



Yellow fever, produced by the bite of *Culex fasciatus*.
Period of incubation, 3 days 19 1/2 hours.

Chart IV.



nothing to be desired in order to fulfill the requirements of a scientific experiment.

The epidemic having ceased on Dec. 15, 1900, no other case of yellow fever occurred in this camp until we again began to expose individuals to inoculation. Thus fifteen days later we made the following observation:

CASE 6.—A Spanish immigrant, aged 27, a non-immune occupant of Tent No. 6, with his full consent, was bitten at 11 a.m., Dec. 30, 1900, by four mosquitoes—*C. fasciatus*—that had been contaminated seventeen days previously by biting

sense of chilliness and sharp frontal headache was complained of, and at 3 p.m. his temperature was 100.8 F., his pulse 89, and his eyes were congested and face flushed. He was removed to the yellow fever wards. A specimen of urine passed at midnight, January 4, contained a distinct trace of albumin. Slight bleeding from the gums occurred on the fifth and sixth days. The patient was seen by the board of experts on the second and seventh days of his attack, and the diagnosis of yellow fever confirmed. (See Chart v.)

The period of incubation in this case was three days, 22 1/2 hours. The subject had remained in strict quarantine for twenty-two days preceding his inoculation.

In considering the character of the attacks and the course of the disease in these five cases of experimental yellow fever, it must be borne in mind that these infected individuals were all young men, in good general physical condition and placed amid excellent hygienic surroundings. Further, it must not be forgotten that, upon the earliest manifestation of an approaching infection, they were each and all put to bed at once, and were even carried to the yellow fever wards while occupying the same bed. In other words, these men were kept at absolute rest from the first inception of the disease. Just what bearing this may have had on the subsequent course of the fever, we can not say, but since so much stress is laid on absolute rest of the patient by those having most experience in the treatment of yellow fever, the influence of this enforced rest, in our cases, upon the subsequent course of the attack, was doubtless of much importance. We reserve a consideration of the clinical side of these cases for a future report.

In our opinion the experiments above described conclusively demonstrate that an attack of yellow fever may be readily induced in the healthy subject by the bite of mosquitoes—*C. fasciatus*—which have been previously contaminated by being fed with the blood of those sick with yellow fever, provided the insects are kept for a sufficient length of time after contamination before being applied to the person to be infected.

Our observations do not confirm Finlay's statement that the bite of the mosquito may confer an abortive attack of yellow fever, when applied to the healthy subject two to six days after it has bitten a yellow fever patient. We have always failed to induce an attack, even of the mildest description, when we have used mosquitoes within less than twelve days from the time of contamination, although the insects were constantly kept at summer temperature. We could cite instances where we have applied mosquitoes at intervals of two, three, four, five, six, nine, and eleven days following the contamination of the insect with the blood of well-marked cases of yellow fever, early in the disease, without any effect whatever being produced by the bite. Thus in one case no result followed the bite of fourteen mosquitoes which four days previously had been contaminated by biting a case of yellow fever on the first day. Again, seven days later, or eleven days after contamination, the surviving seven of these insects failed to infect an individual. On the seventeenth day after contamination, however, the bite of four of these mosquitoes—all that remained of the original fourteen—was promptly followed by an attack of yellow fever in the same individual. These insects had been kept, during the whole of this time, at an average temperature of 82 F.

Our observations would seem to indicate that after the parasite has been taken into the mosquito's stomach, a certain number of days must elapse before the insect is capable of re-conveying it to man. This period doubtless represents the time required for the parasite to pass from the insect's stomach to its salivary glands, and would appear to be about twelve days in summer weather, and most probably about eighteen or more days during the cooler winter months. It follows, also, that our observations do not confirm Finlay's opinion that the bite of the contaminated mosquito may confer immunity against a subsequent attack of yellow fever. In our experience, an individual may be bitten on three or more occasions by contaminated mosquitoes without manifesting any symptoms of disturbance to health, and yet promptly sicken with yellow fever within a few

days after being bitten by an insect capable of conveying the infection.

ACQUIREMENT OF THE DISEASE.

Having shown that yellow fever can be conveyed by the bite of an infected mosquito, it remains to inquire whether this disease can be acquired in any other manner. It has seemed to us that yellow fever, like the several types of malarial fever, might be induced by the injection of blood taken from the general circulation of a patient suffering with this disease. Accordingly we have subjected four individuals to this method of infection, with one negative and three positive results. Reserving the detailed description of these cases to a subsequent occasion, we may state that in one of the positive cases, an attack of pronounced yellow fever followed the subcutaneous injection of 2 c.c. of blood taken from a vein at the bend of the elbow, on the first day of the disease, the period of incubation being three days and twenty-two hours; in the second case, 1.5 c.c. of blood, taken on the first day of the disease, and injected in the same manner, brought about an attack within two days and twelve hours; while in our third case, the injection of 0.5 c.c. of blood taken on the second day of the disease, produced an attack at the end of forty-one hours.

In the case mentioned as negative to the blood injection, the subsequent inoculation of this individual with mosquitoes already proved to be capable of conveying the disease, also resulted negatively. We think, therefore, that this particular individual, a Spanish immigrant, may be considered as one who probably possesses a natural immunity to yellow fever.

It is important to note that in the three cases in which the injection of the blood brought about an attack of yellow fever, careful cultures from the same blood, taken immediately after injection, failed to show the presence of Sanarelli's bacillus.²

Our observations, therefore, show that the parasite of yellow fever is present in the general and capillary circulation, at least during the early stages of this disease, and that the latter may be conveyed, like the malarial parasite, either by means of the bite of the mosquito, or by the injection of blood taken from the general circulation.

CAN YELLOW FEVER BE PROPAGATED IN ANY OTHER WAY?

We believe that the general consensus of opinion of both the medical profession and the laity is strongly in favor of the conveyance of yellow fever by fomites. The origin of epidemics, devastating in their course, has been frequently attributed to the unpacking of trunks and boxes that contained supposedly infected clothing; and hence the efforts of health authorities, both state and national, are being constantly directed to the thorough disinfection of all clothing and bedding shipped from ports where yellow fever prevails. To such extremes have efforts at disinfection been carried, in order to prevent the importation of this disease into the United States, that, during the epidemic season, all articles of personal apparel and bedding have been

2. A fourth case of yellow fever, severe in type, has been produced by the subcutaneous injection of 1 c.c. of blood taken from the general circulation on the second day of the disease, the period of incubation being three days and one hour. The patient from whom the blood was obtained was an experimental case which was in turn produced by the injection of blood—0.5 c.c.—derived from a non-experimental case of fatal yellow fever. As "controls," Cases 1, 4, 6 and 7 of this report were also injected subcutaneously with 1 c.c. of the same blood without manifesting any symptoms whatever. The blood which produced this fourth case of yellow fever, when transferred at the same time to bouillon tubes in considerable quantities, gave no growth whatever.

theory of the conveyance of yellow fever by fomites, since we know of no other way in which this question can ever be finally determined.

For this purpose there was erected at Camp Lazear a small frame house consisting of one room 14x20 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 ceiled within with "tongue and grooved" boards, and was well battened on the outside. It faced to the south and was provided with two small windows, each 26x34 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 .5 mm. mesh. In addition sliding glass sash were provided within and heavy wooden 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, 3x5 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 to 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 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-slips, 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 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 series of twenty days, this room was occupied each night by these three non-immunes. Each morning the various soiled articles were carefully packed 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 12, a fourth box of clothing and bedding was received from Las Animas Hospital. These articles had been used on the beds of yellow fever patients, but in addition had been purposely soiled with the bloody stools of a fatal case of this disease. As this box had been packed for a number of days, when opened and unpacked by Dr. Cooke and his assistants, on December 12, the odor was so offensive as to compel them to retreat from the house. They pluckily returned, however, within a short time and spent the night as usual.

December 19 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; undershirts, 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 have 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 days, has proved an absolute failure. We think we can not do better here than to quote from the classic work of La Roche.³ This author says: "In relation to the yellow fever, we find so many instances establishing the fact of the non-transmissibility of the disease through the agency of articles of the kind mentioned, and of merchandise generally, that we can not but discredit the accounts of a contrary character assigned in medical writings, and still more to those presented on the strength of popular report solely. For if, in a large number of well authenticated cases, such articles have been handled and used with perfect impunity—and that, too, often under circumstances best calculated to insure the effect in question—we have every reason to conclude, that a contrary result will not be obtained in other instances of a sim-

3. R. La Roche: Yellow Fever, vol. ii, p. 516, Philadelphia.

ilar kind; and that consequently the effect said to have been produced by exposure to those articles, must—unless established beyond the possibility of doubt—be referred to some other agency.

The question here naturally arises: How does a house become infected with yellow fever? This we have attempted to solve by the erection at Camp Lazear of a second house, known as "Building No. 2," or the "Infected Mosquito Building." This was in all respects similar to "Building No. 1," except that the door and windows were placed on opposite sides of the building so as to give through-and-through ventilation. It was divided, also, by a wire-screen partition, extending from floor to ceiling, into two rooms, 12x14 feet and 8x14 feet respectively. Whereas, all articles admitted to "Building No. 1" had been soiled by contact with yellow fever patients, all articles admitted to "Building No. 2" were first carefully disinfected by steam before being placed therein.

On Dec. 21, 1900, at 11.45 a.m., there were set free in the larger room of this building fifteen mosquitoes—*C. fasciatus*—which had previously been contaminated by biting yellow fever patients, as follows: 1, a severe case, on the second day, Nov. 27, 1900, twenty-four days; 3, a well-marked case, on the first day, Dec. 9, 1900, twelve days; 4, a mild case, on the first day, Dec. 13, 1900, eight days; 7, a well-marked case, on the first day, Dec. 16, 1900, five days—total, 15.

Only one of these insects was considered capable of conveying the infection, viz., the mosquito that had bitten a severe case twenty-four days before; while three others—the twelve-day insects—had possibly reached the dangerous stage, as they had been kept at an average temperature of 82 F.

At 12, noon, of the same day, John J. Moran—already referred to as Case 2 in this report—a non-immune American, entered the room where the mosquitoes had been freed, and remained thirty minutes. During this time he was bitten about the face and hands by several insects. At 4.30 p.m., the same day, he again entered and remained twenty minutes, and was again bitten. The following day, at 4.30 p.m., he, for the third time, entered the room, and was again bitten.

CASE 7.—On Dec. 25, 1900, at 6 a.m., the fourth day, Moran complained of slight dizziness and frontal headache. At 11 a.m. he went to bed, complaining of increased headache and malaise, with a temperature of 99.6 F., pulse 88; at noon the temperature was 100.4 F., the pulse 98; at 1 p.m., 101.2 F., the pulse 96, and his eyes were much injected and face suffused. He was removed to the yellow fever wards. He was seen on several occasions by the board of experts and the diagnosis of yellow fever confirmed. (See Chart 6.)

The period of incubation in this case, dating from the first visit to "Building No. 2," was three days and twenty-three hours. If reckoned from his last visit it was two days and eighteen hours. There was no other possible source for his infection, as he had been strictly quarantined at Camp Lazear for a period of thirty-two days prior to his exposure in the mosquito building.

During each of Moran's visits, two non-immunes remained in this same building, only protected from the mosquitoes by the wire-screen partition. From Dec. 21, 1900, till Jan. 8, 1901, inclusive—eighteen nights—these non-immunes have slept in this house, only protected by the wire screen partition. These men have remained in perfect health to the present time.

December 28, after an interval of seven days, this house was again entered by a non-immune American, who remained twenty-five minutes. The subject was bitten by only one insect. The following day he again

entered and remained fifteen minutes, and was again bitten by one mosquito. The result of these two visits was entirely negative. As the mortality among the insects in this room, from some unknown cause, had been surprisingly large, it is possible that the subject was bitten by insects not more than thirteen days old, in which case they would probably not infect, since they had been kept for only five days at a temperature of 82 F., and for eight days at the mean temperature of the room, 78 F.

Be this as it may, nothing can be more striking or instructive as bearing upon the cause of house infection in yellow fever, than when we contrast the results obtained in our attempts to infect Buildings No. 1 and No. 2; for whereas, in the former *all* of seven non-immunes escaped the infection, although exposed to the most intimate contact with the fomites for an average period of twenty-one nights each; in the latter, an exposure, reckoned by as many minutes, was quite sufficient to give an attack of yellow fever to one out of two persons who entered the building—50 per cent.

Thus at Camp Lazear, of 7 non-immunes whom we attempted to infect by means of the bites of contaminated mosquitoes, we have succeeded in conveying the disease to 6, or 85.71 per cent. On the other hand, 7 non-immunes whom we tried to infect by means of fomites, under particularly favorable circumstances, we did not succeed in a single instance. Out of a total of 18 non-immunes whom we have inoculated with contaminated mosquitoes, since we began this line of investigation, 8, or 44.4 per cent., have contracted yellow fever. If we exclude those individuals bitten by mosquitoes that had been kept less than twelve days after contamination, and which were, therefore, probably incapable of conveying the disease, we have to record eight positive and two negative results—80 per cent.

CONCLUSIONS.

1. The mosquito—*C. fasciatus*—serves as the intermediate host for the parasite of yellow fever.
2. Yellow fever is transmitted to the non-immune individual by means of the bite of the mosquito that has previously fed on the blood of those sick with this disease.
3. An interval of about twelve days or more after contamination appears to be necessary before the mosquito is capable of conveying the infection.
4. The bite of the mosquito at an earlier period after contamination does not appear to confer any immunity against a subsequent attack.
5. Yellow fever can also be experimentally produced by the subcutaneous injection of blood taken from the general circulation during the first and second days of this disease.
6. An attack of yellow fever, produced by the bite of the mosquito, confers immunity against the subsequent injection of the blood of an individual suffering from the non-experimental form of this disease.
7. The period of incubation in thirteen cases of experimental yellow fever has varied from forty-one hours to five days and seventeen hours.
8. Yellow fever is not conveyed by fomites, and hence disinfection of articles of clothing, bedding, or merchandise, supposedly contaminated by contact with those sick with this disease, is unnecessary.
9. A house may be said to be infected with yellow fever only when there are present within its walls contaminated mosquitoes capable of conveying the parasite of this disease.

10. 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.

11. While the mode of propagation of yellow fever has now been definitely determined, the specific cause of this disease remains to be discovered.

[For discussion see p. 461.]

THE METRIC SYSTEM.*

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"Frenchmen have beheaded their king, declared there is no God, and are now trying to enforce the metric system!" said a member of the English parliament in the course of an alleged argument against the system. This is a fair sample of the arguments advanced against it. It is not my purpose to make any extended argument in favor of it, taking it for granted that THE ASSOCIATION is already, theoretically at least, converted to it. If there are any who are still in doubt upon the subject, I ask them to consider the following résumé:

The system is recommended: 1, because it is simple; 2, it saves time; a good authority on the subject estimates that its employment would save one year of school life for each child; 3, it is cosmopolitan; 4, it is scientific; 5, it is in use in the United States Coast Survey Service, in the Marine-Hospital Service and in the U. S. Navy.

Against its use are the following considerations: 1, it discards an old and familiar system; 2, it is impossible to forget the old system; 3, the accuracy of the standard meter has been questioned by some mathematicians.

Leaving the question here, I propose to consider its present status in the medical profession, and suggest some measures that would hasten its general adoption. Although legalized in 1866, and advocated by a very large majority of the scientific men of the country, a very small number of medical men make use of it to-day. After a somewhat extended investigation in regard to its use in Boston and vicinity, I am of the opinion that Whelply, of St. Louis, was entirely safe when he made the statement in Washington recently that 5 per cent. or less of those writing prescriptions to-day employ the decimal notation.

An inquiry regarding the standing of the men using the metric system was universally answered by the statement that they are the leading men in the profession. So I am inclined to think that while numerically the percentage is perhaps disappointingly small, if we consider quality rather than quantity the showing is quite satisfactory. And when we consider the radical nature of the change, and that natural inertia of which we are all more or less victims, perhaps we shall agree that the progress is as great as we could reasonably expect.

What can we do as individuals to increase this percentage? First, learn to think in the new system, and teach others to do the same. Just so long as we spend our time comparing the new system with the old, and devising rules for their easy interconversion, just so long shall we make slow progress. The equivalent of a grain in terms of the new system is, in my judgment, enough to remember, and when the new system is fully established, forget even that.

There are, besides this individual action, three important factors that would help to a solution of the problem. Let the Association of Medical Colleges and the Pharmaceutical Association, and the Association of Dental Schools, insist that hereafter no one shall receive a degree either in medicine, dentistry or pharmacy, until he has a working knowledge of the system. Let all three associations urge on the writers of text-books the exclusive use of the system. Let the manufacturers of pharmaceutical products label their packages exclusively in the new system. If these conditions could be fulfilled, a tremendous stride would be made toward the universal use of the metric system. Of these three propositions, I am inclined to think the latter is the most important. So universal has become the use of tablets, that if they were all labeled as suggested, almost every practicing physician would be taking daily lessons. In talking with drug houses on this subject, they say if it could be brought about by general agreement, it would be a good thing, but if one or two firms only should adopt the plan, loss of trade is feared. E. R. Squibb & Sons have for many years adopted this method, and the firm deserves much credit, not only for this, but for their persistent and intelligent presentation of the subject in their publications.

DISCUSSION.

DR. E. H. BARTLEY, of New York City, by invitation, opened the discussion. He has been using the metric system in writing his prescriptions for twenty years, and adopted a prescription blank with a vertical line near the right hand margin, to take the place of the decimal point. To the left of this line he had printed "gram," and, to the right, "milligram," and is in the habit of filling out all the three places, if necessary, using ciphers. He uses only these two denominations. He thinks the use of the terms centigram and decigram is confusing and unnecessary and they ought to be dropped. Having been a chemist before he studied medicine, he has learned to use the metric system, prefers it for prescription writing, and has always used it. He has learned the doses of remedies in the English system, and has continued to do so because it is difficult to carry in the mind the doses in two different systems and it increases the danger of errors. He thinks it much safer, for the present at least, to carry in the mind the dosage in grains and minims and make the conversion at the time of writing the prescription. This is very easy if we adopt the plan of always writing for two, three, or four ounces. When he first began writing prescriptions, he learned a rule which has worked very well, viz.: In 60 c.c., or ℥ii, the number of grams to be written for will equal the number of grains or minims of the active ingredient in each teaspoonful of the mixture. Thus, if you wish to give ten grains of iodid of potassium at a dose, you would write

Potassii iodidi	10 000
Aquæ q. s. ad.....	60 000
M. ft. sol. To be given in dram doses.	

Each dram contains ten grains of the salt. This prescription contains fifteen doses. In a three-ounce mixture, or 90 c.c., the number of grams to be taken would be $1\frac{1}{2}$ times the dose, and in a four-ounce mixture, 120 c.c., it would be double the dose, in grains, in each dram, or just equal to it if the dose be increased to two drams, or a dessertspoonful.

As regards the liability of mistakes on the part of the pharmacist in dispensing a prescription written in metric form, he has only twice in twenty years, had a pharmacist make a mistake in the quantity prescribed. In one case the pharmacist put in double the quantity of water ordered, and the patient got less than the prescribed dose, and the other was similar to it. But the danger of this is getting less every year. The pharmaceutical schools now make the use of the metric system compulsory with their students, so that all druggists will soon be familiar with it, and the danger, from their side, will become extremely small. The dangers even now are very little from that source. The only one is that arising from physicians

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