YELLOW FEVER INSTITUTE, BULLETIN No. 9.

Treasury Department, Public Health and Marine-Hospital Service.

WALTER WYMAN, *Surgeon-General.*

Are Vessels Infected with Yellow Fever

SOME PERSONAL OBSERVATIONS.

By Surgeon H. R. CARTER

JULY, 1902.

WASHINGTON:
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Section C.—TRANSMISSION. J. H. WHITE, Asst. Surg. General, Chairman of Section.

ARE VESSELS INFECTED WITH YELLOW FEVER?—SOME PERSONAL OBSERVATIONS.

By Surgeon H. R. CARTER.

JULY, 1902.

In a paper read before the American Public Health Association at Buffalo, September 18, 1901, Dr. Doty, the quarantine officer of New York, affirms the absence of secondary cases of yellow fever aboard vessels—i. e., that while cases of this disease contracted ashore develop aboard vessels, yet none are contracted aboard the vessel itself—that is, the vessel does not become "infected" with yellow fever.

The experience of other quarantine officers has been different, and it may be of service then to group some cases already of record in which the contrary was observed. It is not proposed to collate a number of examples of vessels aboard which yellow fever was contracted, from the literature of the subject, but to give very briefly the history of some such vessels personally observed by the writer, from his own notes, during a four years' service (1888 to 1891, inclusive) at the quarantine of the Gulf, Chandeleur and Ship islands. Here were received all vessels believed to be infected with yellow fever bound for all of the Gulf ports, except for New Orleans and from Tampa south. Consequently our clientele was considerable. The bulk of them, however, although certainly the worst class of vessels which entered the Gulf of Mexico, were not, in my opinion, "infected" when I received them—i. e., yellow fever could not then have been contracted aboard them.

I will premise here that I accept without reservation the conveyance of yellow fever by an infected mosquito of a certain kind, and that to me a vessel "infected" with yellow fever is simply one which is harboring these infected mosquitoes. Whether they came aboard already infected or, being aboard, became infected by feeding on cases of yellow fever developing aboard ship but contracted ashore, can in general be determined from the history of the spread of the infection. Indeed, it was primarily the history of these and other ships which led to the (tentative) formulating of the laws of the "interval between the infecting and secondary" cases of yellow fever and the "period of extrinsic incubation of places" of that diease, which, and much else, are so clearly explained by the conveyance by a mosquito host.

The deductions as to the disease being contracted aboard the vessels, when such deduction is made, are, however, independent of the assumption of any theory of conveyance. I do assume, however, that the period of incubation of yellow fever, rarely, if ever, exceeds six or six and one-half days.

1888.—SHIP ISLAND.

I. Norwegian bark *Magnolia*, 946 tons, fifty-six days from Rio de Janeiro via Pensacola Bar, rock ballast. Left Rio de Janeiro May 20; left 2 men sick in hospital and had 1 aboard, considered yellow fever. Master sick third day out, May 22; died, May 27. All well till June 1, then several (3) got sick at once. First mate sick, June 11; died, June 17; black vomit. All were sick on the way up except 2; 21 on crew list including the 2 men left in Rio de Janeiro. One of these who escaped fever had had yellow fever, and the other was a lad from Dantzig on his first deep-sea voyage. In all 17 men were sick of fever en route, of whom 5 died. The last case, Elias Eliasen, developed June 14. Here, save the captain, all sickened not less than eleven days after leaving Rio de Janeiro, and the first mate and Eliasen on the twenty-third and twenty-sixth day, respectively. They then contracted yellow fever aboard ship.

The picture is that of an infection introduced aboard the vessel by the men who sickened in Rio de Janeiro—i. e., there were uninfected stegomyiæ aboard which were infected from these cases and conveyed yellow fever to the remainder of the crew, except the captain, who contracted it ashore. I did not record the dates of the cases of the men left at Rio de Janeiro; it was shortly before clearing. The interval between an infecting and a secondary case is almost always fourteen days or over.

II. Italian bark *Riagino*, Rio de Janeiro, for Pensacola, fifty-one days out; rock ballast, 560 tons. No sickness in Rio de Janeiro until just before leaving, then sent 2 men to hospital. Left five days after. Log shows men were taken June 4 and June 6 and removed on June 6. Sailed on June 10. No one had been ashore save master and steward, using a harbor boat.

First case reported sick en route June 21; 1 next day; 6 sick en route;

3 deaths, June 28, June 29, and July 14, all with black vomit. Crew refused duty at second death. Last case well July 13. Sixteen on crew list; 2 in Rio de Janeiro. Master had had yellow fever; steward sick just after leaving, not considered yellow fever.

Six cases developed ten days after leaving Rio de Jáneiro. Same remarks as were made of the *Magnolia* apply here.

No record is made of where these 2 vessels lay in Rio de Janeiro, the writer not then appreciating the importance of this.

1889.

My notes for 1889 are lost, and indeed there may have been in 1888 more than the 2 vessels given above, which should have been included in this paper; but my notes, taken at first solely with the view of determining the period of incubation of yellow fever, give data on only these two sufficiently definite to determine that they were infected—i. e., that yellow fever was contracted aboard.

1890.

III. British ship *Avon*, in rock ballast; 22 in crew, 4 immune to yellow fever. Sailed from Rio de Janeiro April 20. All well in port and en route until thirty-eight days out, when a boy in port watch sickened with yellow fever. Taken to hospital, Gulf Quarantine, on third day, and died on sixth day. Another case developed two weeks later in a quarantine attendant who helped me clean up the room, sail locker, in which the boy was sick aboard ship.

It is remarkable that there should have been only 1 case of yellow fever among the crew aboard this vessel. At the time it was ascribed to the fact that this boy, the only one on the port watch, helped a man, shipped in Rio de Janeiro and immune to yellow fever, overhaul his chest a few days before the boy was taken sick. Whether there was an infected mosquito in the chest which had survived this length of time, or whether there was any relation between the chest and the fever, may be a question. It in no wise affects the present question, that the disease was contracted aboard. It was the first case seen at this station that year.

IV. British ship *Curlew*, from Rio de Janeiro, with rock ballast. No sickness was reported en route, in port, or on arrival. She was cleaned July 22 to July 23, 1890, and disinfection completed July 25, in the afternoon. One case of yellow fever developod July 27, the sixty-fourth day out, in the early morning before day.

V. British ship *Chippewa*, from Rio de Janeiro, with rock ballast. No sickness was reported in port, en route, or on arrival. She was cleaned July 26 and July 27, and disinfection completed July 28. One man, the quartermaster, developed yellow fever July 29, at night, sixty-eight days out from Rio de Janeiro.

The *Avon* made no port after leaving Rio de Janeiro and communicated with no vessel en route. The other 2 made no port save Pensacola Bar, and communicated with no vessel save the pilot boats there and off Mobile Bar. The infection in these 3 vessels, then, must have been contracted aboard. They lay in open roadstead at my station, 1½ miles off shore and about ½ mile apart, and there was no visiting between them and none of their crews was ashore.

VI. Spanish bark *Castilla*, fifteen days from Cienfuegos via Round Island Quarantine, in rock and earth ballast; 14 in crew. Eight days out from Cienfuegos to Round Island. All well in port, en route, and on arrival. Mate sickened fourth day after arrival at Round Island while discharging ballast. Vessel sent here in tow August 22. Mate had yellow fever; died on the sixth day of illness. Captain developed yellow fever day after mate's death; taken to hospital. No other cases of sickness aboard; the remainder of the crew are, save 1, Manila men, and all probably immune to yellow fever, being mainly residents of Cuba for many years.

Here 2 men developed yellow fever, 1 twelve and 1 seventeen days after leaving Cienfuegos. The infecting mosquitoes may well have been harbored in the hold, which the mate would probably not have visited until he anchored at Round Island and began discharging ballast, and in which the master would not be apt to go while the mate was on duty.

VII. Spanish bark *Grand Canaries*, seven days out from Havana July 7. All well in port, en route, and on arrival and while in quarantine. Crew probably all immune to yellow fever, being mainly Manila men and old residents of Havana.

O. F., quarantine employe, went aboard as ballast master; next day developed yellow fever, July 11. This man had been exposed to no possible source of infection for the six months previous except this vessel. A case nearly similar to the above occurred in 1889, but I have no notes of it.

VIII. Norwegian bark *Queen of the Seas*, in rock ballast, Rio de Janeiro for Pensacola, fifty-four days out. Left Rio de Janeiro with 17 men; 6 deaths en route. All well in Rio de Janeiro. Lay at Mocanque, a healthful part of harbor. None save master allowed ashore, but he went in ship's boat. Left 1 man at Rio de Janeiro—consumption. Shipped 1 man, a negro, in his place. Sailed April 23; master sick April 26; second mate sick night of May 10; 2 men May 11; 1 man May 12; 2 men morning of 13th; 2 during day of 13th; 1 man sick and 1 died 15th; 1 man died 17th; 2 sick 17th; 1 died 19th; 2 died 21st and 22d; 1 sick 21st; 1 died 25th; 13 sick en route, 5 died. The man shipped in Rio de Janeiro (negro) and 1 of the others immune by previous attack. The picture is very clear of a clean ship, infected by the illness of the master contracted ashore—i. e., had uninfected mosquitoes aboard, which became infected from the master sick of yellow fever, and conveyed it to the crew.

1891.

IX. British ship *Curlew*, fifty-seven days from Rio de Janeiro for Pensacola. Lay in the Gamboa last eight days. Two men sick February 27, taken to hospital that day; sailed March 1. Master sick March 1; 5 men besides him that night. Two men March 4, 1 March 5, and 2 more during the day. Two men sick March 7. Two men died the 19th, sickening the 13th and 15th, respectively, both with black vomit. All aboard here, 19, were sick en route except 1, a Barbados negro; but don't believe all had yellow fever, the crew having been badly frightened. The earlier cases and the 3 who died were undoubtedly yellow fever, as were the steward and mate. Here we have 2 cases, at least, developing thirteen and fifteen days after leaving Rio de Janeiro.

X. Swedish ship *Condoren*, seventy-nine days out from Rio de Janeiro via Pernambuco for Mobile. Rock and earth ballast; 18 in crew. All well in port. Lay in Gamboa last five days. No shore leave allowed, but took ship's boat to go ashore. Sailed March 3; 3 men sick March 5; 16 men sick, all told, up to March 26, and 6 deaths. Last man got sick March 26, when she put into Pernambuco short-handed and sent 3 sick men to hospital. Two men sick March 20; 4 men sick March 18; 1 man sick March 26 (really night of 25th). At Pernambuco she lay eleven days and was disinfected by sulphur. Shipped 8 new men, 4, probably 5, of them immune to yellow fever. Developed no sickness on the rest of the way up. Here 4 men developed yellow fever fifteen days from Rio de Janeiro.

XI. German ship *Gustav and Oscar*, Rio de Janeiro for Pensacola. Lay at Cobras, a healthful place. One case yellow fever at Rio de Janeiro, March 22, sent to hospital March 24. No shore leave allowed. Sailed from Rio de Janeiro April 1; first case sickness April 7, 2 men; 3 next day; 1 next morning, and 2 during the day of the 9th. One death on the 10th, leaving 6 men sick. Captain sick on the 10th at night after supper. Last case on 14th. Two deaths on 11th; 1 on 12th. Crew list shows 21 men left Rio de Janeiro; 14 sick and 4 deaths en route. It is reasonably certain that 4 of the remaining crew were immune to yellow fever by previous attack.

XII. Norwegian bark *Crown Prince*, fifty-eight days out from Rio de Janeiro for Ship Island. Lay at Moncanque. No sickness aboard in Rio de Janeiro. No shore leave granted, and did not use ship's boat to go ashore. Sailed April 29. Master sick second day out (April 30). Next case May 16; 3 (2 aft and 1 forward) became sick. May 17, 2 sick in morning, 1 in the day. May 18, 3 men in forecastle sick. May 20, 2 sick, 1 death. May 21, 1 death, 1 sick. May 23, 2 deaths. May 24, 1 sick. May 28, 1 death last night. May 29, 1 sick this morning. M 0, 1 death. The 1 case on the 29th was the last case taken sick. There were 14 men aboard and every man had fever, 6 dying. She put into Barbados on June 10, disinfected and shipped (in quarantine) 4 new men, 1 probably unacclimated. No more sickness en route. All of these cases except the captain's were not less than sixteen days from Rio de Janiero before developing.

XIII. French ship *Emily Postel*, twelve days from Vera Cruz via Pensacola quarantine. Had "sickness" aboard just before leaving Vera Cruz, 1 man. Sailed from Vera Cruz July 28; no sickness since until crew went to discharge ballast, August 12. One man sick yellow fever August 15, 2 men the same, August 19, and 1 man August 20. Disinfection by sulphur was done on the appearance of the first case of yellow fever and no case occurred save the above. All were developed more than sixteen days after leaving Vera Cruz, hence from infection on board. The history points to infection (infected mosquitoes) in the hold.

The picture given by the *Curlew* and *Conderen* are those of disease conveyed by mosquitoes coming aboard already infected just before they sailed. The infection was not introduced by the men who first sickened, the interval between them and the next cases was too short. Observe that they lay in the Gamboa, directly in the lee of a town badly infected. The other two give the usual history of a clean place (town or vessel) infected by some one developing yellow fever, contracted elsewhere, in it.

XIV. Dr. G., assistant surgeon U. S. Marine-Hospital Service, developed yellow fever June 18 at the Gulf Quarantine Station, and died June 29. He was immediately from New York, where he had been on duty some months, and had been at the station but fourteen days when he was taken ill. There had been no case of yellow fever at the station that year. There were a number of vessels in quarantine, but the *Gustav and Oscar* (No. XI) was the only one I judged to be infected. On this vessel, as on the others, he had been with me inspecting, opening up drawers and boxes, and going into every compartment, etc., for the disinfection. I thought his infection was from this vessel. It was certainly from some vessel.

I think it will be granted from the above that the ability of a vessel to carry the infection of yellow fever is no myth. Here are 13 vessels which did so carry it collated from only three years' observation at a single station. Such vessels are indeed rarer, much rarer, now than they were before 1894, yet they still come. I saw 2 at Tortugas in 1894. Other cases are reported by Geddings and by Echemendia at the same place and at Port Tampa quarantine. Rosenau reports a case contracted aboard the steamship *Vigilancia*, from New York, plying between New York and Vera Cruz via Havana, in 1899. The steamship *Bodo*, last year (1900), from Bocas del Toro, for Mobile, developed 3 cases of yellow fever, seven, eight, and nine days out from Bocas del Toro. It would not be difficult, I think, to multiply instances of recent date. yet that they are rarer is without question. On the factors which have brought this about we can barely touch.

Obviously there are two methods by which vessels can become infected. (*a*) A case of yellow fever contracted elsewhere may develop aboard a vessel already harboring stegomyia mosquitoes which become contaminated from it. (*b*) The stegomyia mosquitoes may come aboard already contaminated. In the first case, there being nearly always over two weeks between the infecting and the first secondary cases of yellow fever, it results that, if the first case occurs after leaving port, vessels, even sailing vessels, from Cuba and the Caribbean Sea will generally reach quarantine and (if at a southern station) be disinfected—i. e., mosquitoes killed, before it is time for the secondary cases to develop, or, indeed, to be contracted. This agrees with all observation. In vessels infected in the second way, cases of yellow fever may occur after a very short or no interval from leaving port. The causes, then, which have lessened the number of infected vessels at United States ports, are—

1. The very great falling off of vessels from Rio de Janeiro and Santos since the establishment of the Brazilian Republic. This does away with the bulk of the "long-trip vessels" we used to have, which are the only ones developing secondary cases en route if infected by a case of yellow fever developing aboard. (Vide *a*.)

2. The replacing of sailing craft by steamships. That steamers convey yellow fever less frequently than sailing vessels has long been known. This is because they lie a much less time in an infected port, and the discipline of their crews is better; no shore leave means no man goes ashore. They also make quicker trips, and thus are not apt to develop secondary cases en route, even if yellow fever contracted elsewhere develops aboard and they have the stegomyia aboard. It is also to be noted that the worst parts of the harbors of Havana and Rio de Janeiro, above San Jose wharf and the Gamboa, have never been berths for steamships. Note, too, that the sailing vessels displaced are the foreign sailing vessels; the American schooner was less often infected than foreign vessels.

3. Especially since 1893, and to some extent before supervision had been kept by United States sanitary inspectors in the more dangerous yellow-fever ports over vessels bound for the United States, especially of passenger vessels. Certain anchorages have been recommended as safe, others have been forbidden, notably the Gamboa at Rio de Janeiro and certain wharves and parts of the harbor at Havana. Passengers who it is believed will develop infection aboard have been barred; shipment of new men in the infected port carefully supervised; vessels in which yellow fever has occurred in port are disinfected before leaving, and many other measures taken to have the vessel leave port clean, or as nearly clean as commercial considerations allow. In general, the vessel owners, especially of the regular lines, have given hearty cooperation in these measures, as well as in keeping the crew aboard and in confining the visits of such officers as must go ashore to daylight.

These restrictions, especially the last, have by no means been absolute for all classes of vessels, but are well observed, in Cuban and Mexican ports at least, by probably over five-sixths of the tonnage. The sanitary measures to avoid infection (3) and the proportionate substitution of foreign sailing vessels by steamships (2) are without doubt the main factors acting in cooperation in lessening the infection of ships. No one can read Burgess' list of infected vessels in Havana Harbor (Report, U. S. Marine-Hospital Service, 1896) without noting how great has been that decrease in recent years.

We have said that if a case of yellow fever develops aboard a vessel harboring the stegomyia mosquito (proper conditions of temperature being premised) that they may become contaminated by feeding on him and infect others. A vessel which has no stegomyia aboard is like "noninfectible territory" and will not communicate infection, even if cases of yellow fever develop aboard. I think it fair to say that vessels plying to and from southern ports of the United States will, during the summer season, generally have the stegomyia aboard, independently of its berth in tropical harbors, and may at times breed them in their water supply. This mosquito, however, seems to be rare north of Virginia Beach (its distribution has not been sufficiently investigated, however), and a vessel plying to and from a northern port of the United States would not harbor this mosquito unless it came aboard in the tropical port. Now how far this mosquito goes or is borne from shore has not, I think, been directly investigated, but we do know that the crews of vessels moored off from shore (say 200 or more fathoms) in that part of Havana harbor seaward from the line between the Sta. Catalina warehouses and the Machina wharf do not develop yellow fever (unless close to some vessel which is infected). This means that contaminated stegomyia, at least, do not go so far from shore. Lying then at the anchorages accounted safe in Havana harbor, where the passenger vessels for the United States lie, one would think that the probability of any stegomyia coming aboard would be small. At Vera Cruz the vessels must lie nearer shore (although to windward of it), and experience shows that the crews of vessels lying there are not entirely safe, as I believe them to be in Havana, although infection in the part of the harbor picked out as safe is decidedly rare. The anchorages in both harbors regarded as safe are well to the windward of the town all summer. A direct investigation of this matter—i. e., the presence of the stegomyia aboard vessels from northern ports in different parts of the harbor of Havana and other tropical harbors, should be made.

To sum up—

1. Vessels aboard which yellow fever had been contracted—i. e., vessels infected with yellow fever have not been rare, at least at southern quarantine stations.

2. Such vessels are much rarer since 1893, and are not very common now.

3. That the diminution of the number of infected vessels reaching United States ports is due mainly to the sanitary measures for avoiding exposure to infection in the foreign port, and to the substitution of steam for sailing vessels. To some degree the falling off of the vessels from Brazilian ports is also a factor.

4. That a case of yellow fever developing aboard a vessel plying between southern ports of the United States and the tropics will probably infect the vessel so that other cases can, if time be given, be contracted aboard her.

5. Such vessels, however, if short-trip vessels, not more than ten or twelve days en route after the occurrence of the case of yellow fever, will in general be disinfected at southern quarantine stations before any other cases have been contracted aboard, although harboring infected mosquitoes.

6. That a case of yellow fever so occurring aboard a vessel from a northern port of the United States would be able to infect her or not according to whether she had acquired the mosquitoes *stegomyia fas.* in the tropical port.

7. It is, in general, then necessary to disinfect all vessels running between southern ports of the United States and tropical ports if a case of yellow fever occurs aboard, no matter where it be contracted; while vessels running between northern ports and the tropics may, through precautions in tropical harbors, have no stegomyia aboard and are thus not infectable by cases of yellow fever occurring aboard.

8. Some vessels giving no history of yellow fever in port, en route, or on arrival—even when many days en route—are nevertheless infected and communicate the yellow fever to those who go aboard, vide Nos. IV, V, VI, VII. Note, also, the first case aboard the *Avon*, No. III, was thirty-eight days out from Rio de Janeiro. This is probably due to the infection (infected mosquitoes) in parts of the vessels unfrequented by the crew while en route, or to the crew being all immune to yellow fever.

YELLOW FEVER INSTITUTE, BULLETIN No. 11.

Treasury Department, Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

VESSELS AS CARRIERS OF MOSQUITOES,

BY

Passed Asst. Surg. S. B. GRUBBS.

MARCH, 1903.

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Section C.—TRANSMISSION. Asst. Surg. Gen. J. H. WHITE, Chairman of Section.

VESSELS AS CARRIERS OF MOSQUITOES.

By S. B. GRUBBS,

Passed Assistant Surgeon, United States Public Health and Marine-Hospital Service.

At the present time, when evidence is pointing with more and more clearness to the mosquito as the sole means of transmitting yellow fever, nothing is of greater interest to the quarantine officer than to decide to what extent and under what circumstances these infecting insects may be carried by vessels.

This subject may be approached in three different ways: First, by observations on the length of time after leaving infected ports vessels may develop yellow fever; second, by experiments with mosquitoes under artificial conditions made to simulate as much as possible those of nature; and third, by actual observation of vessels arriving from ports at the time infected or where the presence of the *Stegomyia fasciata* render them liable to infection.

While it will require data obtained by all these means and extending over a long period to arrive at any conclusions sufficiently accurate to allow them to influence quarantine procedure, still I believe the last method of observation cited will throw more light on the subject than the first two.

It is for this reason that every vessel arriving at Gulf Quarantine Station from Stegomyia-infected ports has, since the 1st of July last, been carefully examined to ascertain if mosquitoes were present on board, and, if present, their variety, where and when they came aboard, and under what conditions.

Gulf Quarantine Station is an especially good point for these observations, from the fact that it is 10 miles from the mainland, and because vessels bound here do not pass near land, and so but rarely take on mosquitoes en route, and even these, as will be seen, are always the marsh-bred varieties of *Culex*. Besides, the examination of at least a thousand mosquitoes on Ship Island has convinced me that there are no *Stegomyia* here.

Each vessel inspected was carefully searched, the inspector being armed with a cyanide killing bottle, and in addition the captain was asked the following questions:

1. Were there any mosquitoes on board on your outward voyage, consisting of —— days?

2. If so, did they come aboard before departure from home port or at sea, and under what circumstances?

3. Were there any mosquitoes on board at your destination or on homeward voyage?

4. If in port—

(*a*) How far were you from shore?

(*b*) Prevailing wind and weather?

5. If on homeward voyage (consisting of —— days)—

(*a*) Were they from port?

(*b*) Did they come aboard at sea, on what day, and how far were you from land?

(*c*) Were there wigglers in any of your tanks at any time?

During the five months from June 1 to November 1 observations were made on 82 vessels, all arriving from ports where the *Stegomyia* is believed to exist in quantities. Of these 78 were sailing vessels and 4 were steamers.

Of these 82 vessels 65 claimed to have had no mosquitoes aboard at any time during the voyage or at port of departure, and their absence having been confirmed by search, we can dismiss them from consideration and pass to the remaining 17.

Five of these had mosquitoes on board at their ports of departure, 2 being rid of them as soon as they were well at sea, while 3 others carried them two days and were then no more troubled, except one schooner on which they reappeared in quantities five days before she reached this port, when she was 20 miles from shore.

Nine sailing vessels, having no mosquitoes on board before sailing, had them appear at sea, in one case from the water casks in which the captain found larvæ. But in the other cases they doubtless came from land which was at the time distant—20 miles in one case, 15 miles in three cases, 10 miles in one case, and 2 miles in the last two instances. In all these vessels the mosquitoes found on board on arrival at this station were the common varieties of *Culex*, there being no *Anopholes* or *Stegomyia* among them.

Stegomyia fasciata were found on board and were identified in the remaining three cases, as follows:

The schooner *Susie B. Dantzler* arrived from Vera Cruz, Mexico, on July 16, 1902, after a voyage of fifteen days. The captain stated that mosquitoes came aboard in large quantities at Vera Cruz, although he lay a half mile from shore and there were variable winds with squalls and rain all the time. The number of the insects decreased on the voyage but were always in evidence, and we caught four or five of them here. No larvæ were found in any of the tanks, and as the captain had repeatedly examined them without result in his efforts to be rid of the mosquitoes, I believe the insects found on board here came all the way from Vera Cruz.

The schooner *Eleanor* arrived from Vera Cruz on July 17, 1902, thirteen days out. She had no mosquitoes on board before reaching Vera Cruz, but there quantities came on board. Her moorings were half a mile from shore and the winds were variable. The captain stated that he could not get rid of the insects after sailing, although the number decreased very much and there were no larvæ in any of the tanks. At the time of her inspection here we caught and identified a number of *Stegomyia.*

The brigantine *John H. Crandon* arrived at the station July 27, 1902, twenty-two days from Vera Cruz, where she had one case of yellow fever on board. At that port she lay a half mile from the sea wall, three-eighths of a mile from an infected prison, and within 200 yards of an infected vessel. *Stegomyia fasciata* were found on board by Acting Assistant Surgeon Hodgson before she sailed, as well as larvæ in the tanks. All during the trip there were mosquitoes in abundance, and a veritable plague of *Stegomyia* was found on board on her arrival here. There was a constant buzz in the forecastle, and anyone entering was sure to be attacked by several mosquitoes. Specimens were caught in almost every protected part of the vessel, and all were found to be the *Stegomyia fasciata.* The captain had emptied several water barrels because he found they were breeding mosquitoes, but the water remaining had no live larvæ, although many old moults were seen. As breeding was surely going on in the tanks during a part of the voyage at least, it would be impossible to say how long any particular mosquito had been aboard or if any of them had been brought here from the infected port.

SUMMARY.

The above facts may be summed up as follows:

Vesssels having no mosquitoes on board at any time	65
Vessels having mosquitoes on board in port of departure	5
Vessels on which mosquitoes (*Culex*) appeared en route	9
Vessels arriving with *Stegomyia fasciata* on board	3

Three and a half per cent, then, of all vessels brought *Stegomyia* on a voyage averaging seventeen days.

CONCLUSIONS.

From but one season's observations at a single quarantine station we can not assume to draw any hard and fast conclusions regarding the probability of *Stegomyia*, infected or not, being carried by vessels. Nevertheless, I think we may conclude, first, that mosquitoes can come aboard vessels under favorable conditions when the vessel is not over 15 miles from shore; second, that *Stegomyia* can be carried from Mexican or West Indian ports to those of our Gulf States; third, that they can board a vessel lying at anchor a half mile or less from shore, being conveyed by the open lighters used or flying aboard, and finally, that a vessel moored a short distance from land may become infected with yellow fever, our old beliefs to the contrary notwithstanding.

I wish to acknowledge the aid of Assistant Surgeons Burkhalter and Ebersole in collecting data and specimens.

YELLOW FEVER INSTITUTE, BULLETIN No. 12.

Treasury Department, Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

THE EARLY HISTORY OF QUARANTINE:

ORIGIN OF SANITARY MEASURES DIRECTED AGAINST YELLOW FEVER,

Passed Asst. Surg. J. M. EAGER.

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The Early History of Quarantine:

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Section D.—QUARANTINE AND TREATMENT. Asst. Surg. Gen. W. J. PETTUS, Chairman of Section.

THE EARLY HISTORY OF QUARANTINE—ORIGIN OF SANITARY MEASURES DIRECTED AGAINST YELLOW FEVER.

By P. A. Surg. J. M. EAGER.

FEBRUARY, 1903.

The public sanitary measures included in the comprehensive term "quarantine" have been more extensively applied in America against yellow fever than against any other disease. Most of these measures had their origin long before yellow fever was known to the world. The way they came into existence and how they were later used as a protection against yellow fever is one of the most interesting topics in sanitary history—one without which no account of the prophylaxis of yellow fever would be complete. In the present writing the term "quarantine" is not limited to its narrower sense, but is taken to mean any restraint, owing to contagious disease, of intercourse on land or by sea. It includes such incidental measures as disinfection.

The history of quarantine is closely interwoven with that of medicine in general and of shipping. We read of these practices being applied against leprosy in biblical times, and Captain Cook, the English navigator, tells us that the savages of the South Sea Islands, who had not advanced beyond the stone age at the time of his visit to those islands, resorted to rude sanitary precautions in the case of arrivals from neighboring places.

The story of the beginnings of quarantine is associated particularly with the epidemiology of leprosy, pest, and syphilis. Cholera and yellow fever were later considerations. The first reported prevalence of yellow fever was at Bridgetown, Barbados, in 1647, the year before the great pest of Habana. At this time quarantine measures had been practiced against other malignant contagious diseases, a maritime quarantine station having been in operation at Venice in 1403, nearly a century before the discovery of America. It was only necessary to include yellow fever in the category of contagious exotic diseases and apply against the malady the procedures already in vogue. The first appearance of yellow fever in Europe occurred at Lisbon in 1723, and is described in the article "Yellow fever in Portugal" (Bulletin No. 4, Yellow Fever Institute, United States Public Health and Marine-Hospital Service). It was not, however, until 1821, following an extensive epidemic in Spain, that quarantine was applied in Europe against yellow fever. The Spanish academies were interpellated as to the nature of the disease, and as a result of their replies yellow fever was declared quarantinable. Inquiry in England in 1823 and 1824 was followed by an act of Parliament directing quarantine against yellow fever in the same way as against plague. Quarantine theory and practice have from the beginning followed medical dogma. Religion, astrology, and crude or false doctrines of etiology extended their influence. Like most branches of practical medicine, the practice of quarantine passed from the hands of priests into those of empiricists. It took ages for public sanitation to establish itself on a scientific basis.

LEPROSY AND LAND QUARANTINES.

The first quarantines of which any mention is made in literature were land quarantines used as a protection against leprosy. The ancients regarded this disease as of African origin, and Lucretius states positively that it first came from Egypt. In the Old Testament the first indications are found of precautions taken against contagious maladies. Leviticus, Numbers, and the First Book of Samuel give directions for the sequestration of lepers, first in the desert, then outside the camp, and afterwards without the walls of Jerusalem. In these books the inspection of persons for the detection of leprosy is detailed. Persons afflicted with skin diseases were directed to present themselves before the priests. An observation of each case was made, and, according to minutely described symptoms, isolation of the patients was ordered for a prescribed period.

The crusaders on their arrival outside the walls of Jerusalem found lazarettoes still in existence, and after taking the city from the Mussulmans sent all contagious maladies to these isolated places. The name Hospital of St. Lazarus was given to the place of sequestration. Returning to Europe, the members of the military expeditions brought back with them not only numerous diseases, but also the word "lazaretto," as applied to a place for the isolation of the victims of communicable maladies. As a result lazarettoes were built outside the gates of nearly all the principal cities of Europe. Leprosy itself had, however, been introduced into Europe many centuries earlier. It is spoken of as a foreign disease by the earlier Greek and Latin writers. Pliny thinks that leprosy was introduced into Europe by Pompey returning to Rome from Syria after his celebrated triumph over fifteen nations in Asia. It is implied that leprosy walked with the three hundred princes before the triumphal car of the conqueror. These surmises give rise to the interesting query whether leprosy was not the first quarantinable disease introduced by sea. As a quarantinable disease leprosy takes precedence in several ways. For instance, it was the first quarantinable disease (quarantinable from the point of view of the United States quarantine regulations) of which the causative germ was discovered.

During the epoch of the crusades leprosy became widespread in Europe and resulted in the extensive establishment of isolation stations. Leper houses existed at Metz, Verdun, and Maestricht as early as the seventh century, for long before the crusades the disease had spread from Italy into the Roman colonies of Gaul, Britain, and Spain, and thence into the most remote countries. Mathew Paris estimates that at the time of the great epidemic of leprosy in western Europe succeeding the movement against the Mohammedans 19,000 lazarettoes were in operation in Europe. Religious orders conducted the houses bearing the name of St. Lazarus, but in northern Europe many dedicated to St. George were under secular supervision. Not only were persons suffering from leprosy and other contagious diseases sent to such asylums, but the insane and individuals whose separation from society was deemed an advantage to the populace or the ruling powers were also confined there. In these places of isolation quarantine measures, that afterwards had their application at maritime stations and ultimately were directed against yellow fever, developed primarily. Lepers were not strictly confined to the leper houses. They were, however, required to wear a special costume, to limit their walks to certain roads, to give warning of their approach by sounding a clapper, and to forbear communicating with healthy persons and drinking from or bathing in any running stream.

PEST AND EARLY VIEWS OF ETIOLOGY.

In connection with pest and later with syphilis the greatest advances of mediæval times took place in public sanitary methods, leading to the establishment of maritime and land quarantines. During the Middle Ages more attention was given to the isolation of leprosy than of other diseases now known to be virulently contagious, for the reason that the minds of medical men were hampered by accepted doctrines. One of the first of these dogmas was founded on the fact that, while in the sacred Scriptures minute attention is given to precautions against leprosy and skin diseases, no measures are prescribed against pest. Yet most disastrous epidemics are recorded in the Old Testament.

By the word pest is understood not only bubonic plague, but the different epidemic diseases, whatever they may have been, that were formerly included under that term. In their application to this group of maladies the various docrines of etiology had a most important bearing on etiology. The history is preserved in a great number of documents, many of them obscure and quaint, but all interesting as showing the gradual development of public sanitation. From an etiological standpoint the history of public hygiene in its relation to epidemiology is divided into four periods, during all of which widely diverse views of causation of epidemic disease were held, the state of knowledge in each successive epoch advancing nearer the truth. First came a chaotic period up to the time of Hippocrates, secondly the centuries that intervened from the time Hippocrates set forth his views of etiology to the middle of the sixteenth century, when Fracastoro, basing his observations on the epidemic prevalence of syphilis that extended throughout Europe, announced a theory of contagion. Then followed an interval lasting until the evidence of a living contagion gained credence. Lastly came the time when specific germs were found to be the cause of epidemic disease. The last era, however, brings the history of quarantine to such a recent time as to be outside the scope of the present writing.

The word plague as well as pest was given by ancient medical writers to any epidemic disease that wrought an extensive destruction of life. Oalen, for example, used the word in this sense. History is replete with epidemics. Instances of ancient prevalences are the disastrous disease, recorded in II Kings, causing the destruction of the Assyrian army; the plague of Athens, described by Thucydides; the great pestilence in the reign of Marcus Aurelius, that extended over almost the whole of Europe, and the plague of Justinian, descriptions of which are given by Procopius and Evagrius. The plague of Justinian lasted for fifty years and has a decided interest in connection with the present subject, having been introduced in all probability largely by sea. It began at Pelusium, in Egypt, 542 A. D. After spreading through Egypt it appeared the next year at Constantinople. In subsequent years it advanced over the entire Roman world, making its initial appearance in seaboard towns and radiating inland. Frequent epidemics occurred in succeeding centuries, one of the most important of which was the great cycle of epidemics in the fourteenth century, which has been given the name of the "black death." Throughout all this extensive period notions and practices relating to public sanitation were being evolved in accordance with the prevalent tenets of causation. In the earliest period religion, superstition, and stellar influence took the principal place in the confused ideas of etiology. Ill-ordered doctrines led to all sorts of irrational practices. Among the Greeks, in the rites of Æsculapius, the sick were not permitted to enter the temples, where they underwent treatment, without first being purified by various baths, frictions, and fumigations. All this was accompanied by ceremonies similar to those practised within the temples, namely, magical performances and fervent prayers recited in a loud voice, often with musical accompaniment. As an accessory to the purification preliminary to being admitted, the patient was required to pass the night stretched on the skin of a sheep that had been offered as a sacrifice. Here he was ordered to compose his mind for sleep and await the arrival of the physician. Throughout these ages as well as in more recent times a fanciful association between the phenomena of the material world and the destinies of mankind closely linked the doctrine of etiology with astrology. The persistent belief of learned men in the relation of stellar conditions to epidemics is in part explained by the fact that astrologers who predicted epidemics wrought charms against the impending pestilence, thus saving their credit, in event the disaster did not materialize, by claiming that it had been averted through their efforts. These primitive views of the origin of epidemics did not necessarily place the cause of the disease outside the earth and its immediate surroundings. Winds, thunder and lightning, fogs, and other meteors were blamed for causing pestilence, and the flight of birds and insects were supposed to be dependent phenomena. Xanaphanes, five hundred or six hundred years before Christ, expounded an idea that the sun was a torch and the stars candles that were put out from time to time. According to his notion, which was seriously accepted, the stars were not heavenly bodies in the wider sense, but meteors thrown off from the earth. So a belief in stellar influence did not carry the mind outside worldly ranges. For this reason other practices than prayers and sacrifices were believed to be effective. They consisted chiefly in efforts to dissipate the meteors, such as huge and numerous fires, and to avoid meteoric influence by confinement in closed or otherwise protected places.

During the period under consideration, the promptings of superstition were paramount and the epidemiologists of the times confined themselves principally to interpreting the signs of the heavens. More advanced views came as the result of reasoning, but the path of discovery by experimental science was not entered upon until after many centuries.

ETIOLOGY ACCORDING TO HIPPOCRATES.

The doctrines of etiology took a more determinate form under the teachings of Hippocrates. According to Hippocrates, disease has its origin either in the régime of life or in the air that surrounds the living body and enters into it. He made therefore a twofold etiological division of diseases, those dependent on the personal régime, and those dependent on the quality of the air. Regarding the latter class, when many individuals are attacked by the same disease at the same time, he supposed the cause to be a common one, namely, the air breathed. Hippocrates believed that a régime of life, which differs with different persons, could not be the cause of a malady that attacks alike the young, the old, men and women. On the other hand, when diseases of different sorts occur, it was clear to him that the cause is individual. Epidemic disease, according to the Father of Medicine, is often promoted by a specific, unknown, and extraordinary condition of the air due to the presence of the *quid divinum*, which may also exist in miasms and certain other impure things. This *quid divinum* has given much trouble to the followers and commentators of Hippocrates, and the judgment as to what he conceived it to be must be left to the fancy of the student of his writings. It seems probable, however, that Hippocrates meant the scourge of divine wrath. It was this very idea that for centuries prevented the application of sanitary measures to epidemic disease. Men regarded pestilence as a punishment inflicted by the Almighty on delinquent humanity and an attempt to turn aside a weapon borne in the divine hand was considered vain and impious.

The influence of Hippocrates's views, with their bearing on sanitation, extended with slight abatement almost to the time when Fracastoro announced his doctrine of contagion. Throughout all this period, moreover, the controlling power of Platonism held experimental inquiry in check. It was believed that the true nature of things could be discovered by the action of reason and not in any important degree by experience and observation. Thus, it will be seen, the measures directed against epidemic disease were often misguided, ineffective, and dependent on all sorts of false doctrines.

GALEN'S VIEWS OF EPIDEMIOLOGY.

Galen, not dissenting from the views of Hippocrates, was of the opinion that any disease that caused the almost simultaneous death of a large number of people should be regarded as of the nature of pest. He did not hold to any view of contagion in these maladies, that is, of their direct communication of man to man, though he evidently believed that the corruption of the air was more intense in the neighborhood of the sick than elsewhere. Pest, he declared, was born of a pollution of the atmosphere and assailed man by way of respiration. This doctrine was accepted by the pupils of Galen. In the commentaries of the books of Hippocrates on epidemics, or popular diseases, as they were called, it is asserted that pestilential maladies proceed from a special condition of the heavens. These commentaries, at one time attributed to Galen, have since been demonstrated to be the production of his disciples. The long line of Greek, Latin, and Arabic medical writers down to the time of Avicenna, the Mohammedan physician, adhered to the teaching of Hippocrates and Galen, and when they speak of contagion the term must always be understood to mean contracting a disease by breathing altered air. The masters of medicine of the middle ages held similar opinions. Bernardo Gorgonio, professor of medicine at Montpellier, France, in 1300, and Arnaldo da Villanova, who lived toward the end of the twelfth century, gave the name of pestilent fever to every deadly fever and maintained the cause to be a corruption of the air. Guglielmo Varignara, professor of medicine at Bologna in 1302, not only denied the contagious nature of measles and smallpox but declared that the buboes of plague were not contagious. Gentile, who died of pest at Foligno, Italy, in 1348, believed that the poison of pest existed in the air and was due to a putrefaction of this medium. John Godesden, a leading English physician of the fourteenth century, announced the same views. De Chauliac, an eminent French physician of Avignon, who observed the terrible epidemic of 1348–1361, recorded casually his idea that pest could be contracted by contact with the sick, but assigned as a primary cause decomposition of the air due to the conjunction of planets whereby a certain subtle substance is evolved capable of producing epidemics. Another famous physician of those times, Raimondo da Vinario, who was a spectator of the epidemics of pest in 1348–1361 and 1373, says that it is a very dangerous thing to have to do with persons stricken with pest; that one person sick with pest may infect an entire city; that those employed in public hygiene in times of epidemic prevalence take the malady by contagion; that physicians more than any other class are likely to catch the disease; and that monks are generally exempt from pest because they are isolated in monasteries and thus free from outside exposure. Still there is not room to believe that this master of medicine had any precise conception of the nature of contagion. Like so many others, he put his faith in corruption of the air brought about by an influx of stars, planets, and constellations, and in poisonous exhalations emanating from the earth. The danger of contact with the sick he conceived to be due to the air filled with pestilential poison that had been inspired and afterwards exhaled by the victims of the disease. Da Vinario held also that garments worn by the sick and other fabrics in close contact with them contained the infective principle, and hence should be transported with the sick to a distant and isolated place. Notwithstanding all this, he does not mention the necessity for purification of infected things nor ever suggest the caution of destroying fomites. There can be no stronger evidence than this of the tenacity with which the physicians of the middle ages adhered to the accepted doctrines of their predecessors.

THE BEGINNINGS OF RATIONAL ETIOLOGY.

It took centuries of involuntary observation to shake the idea that epidemics are of celestial origin and to be combated by prayers, fasting, and processions. The first advances toward broader ideas were not made by medical men. The record of reformed views is found in works on jurisprudence and in the narratives of travelers. In the books of jurisprudence of the emperors of the East it is noticed that care should be exercised in having relations with persons arriving from places where pest reigns. It was ordered, in consequence, that those so exposed should be separated from others for the purpose of observation. The term of forty days (whence the word quarantine) is named, this being the supposed maximum period of the duration of acute maladies. Whether this isolation was practiced in a particularly selected place or in the houses of the suspects is not known.

Merchants traveling in the East and detained at Alexandria or Cairo during the prevalence of pest observed that cloistered monks did not contract the disease. Many of these merchants, exiled by pestilence, staid constantly within the boundaries of their residences, transacting all business through barred windows and from terraces that crowned the house tops. The stubbornness with which medical men held to the doctrine of aerial corruption of celestial origin is shown by the report made to the Marseille government in 1720 by a body of distinguished physicians, in which the condition of the air was pronounced to be the sole cause of pest, the idea of communicability from man to man being absolutely rejected.

One of the most ancient edicts commanding the segregation of sufferers from pestilential maladies had for its authors two laymen, Sagacio and Pietro de Gazata, and is found in the chronicles of Reggio d'Emilia. The document, dated 1374 and written in low Latin, orders that all persons sick with pest be taken outside the city, into the open country, a camp, or the woods, there to remain until dead or cured. The parish priests are required to promptly report all cases of pest under pain of death by fire. After registering these historical facts, the chronicler adds:

> And I saw in this same year that these orders were observed in Reggio, for which cause all were grieved and terrified more than by the fear of the illness which, when God permits, can not be averted.

ORIGIN OF THE DOCTRINE OF CONTAGION.

The credit of having created the doctrine that pest is contagious by contact with the sick and their effects is chiefly due to Jacobo della Torre, known also by the name of Jacopo da Forli, from the name of a city in central Italy, where he was born in the second half of the fourteenth century. Contagion had been referred to obscurely and timidly from Aristotle down, but now the idea took a practical form. The old notion was that fomites were a sort of tinder that caught from the air an infection existing independently of the sick. Many writers, including Galen, believed there was an extreme degree of atmospheric pollution in the vicinity of the sick, rendering such neighborhoods dangerous, but this was considered a primary cause of the illness rather than a direct emanation from the sick.

Della Torre's doctrines were not accepted by the various schools of medicine and were for a time absolutely forgotten. Fracastoro proclaimed the same theories at a later period, when they were better received, and to him is generally given the honor of announcing the theory of contagion. Jacobo della Torre advised the magistrates of his native town to remove outside the city all persons affected with pest and to isolate them, as well as all persons who had been with them. The authorities were warned against delay, for it was avowed that every precaution would be futile should the disease become diffuse throughout the city. In his recommendations no mention is made of purification, but he asserted his disagreement from the accepted belief in the stellar origin of the infective principle. Della Torre's disciple, Michele Savonarola, attained greater eminence than his master, and so far vindicated the honor of his school as to declare that even persons in good health may transport the pestilential virus to distant places, and that those who are not brought in association with the victims of pest or with pest-bearing things escape the disease. But Savonarola did not fully indorse the teachings of his preceptor. He could not shake off a belief in astrology and admitted that the origin of pest resided in a disorder of the air generated in consequence of planetary contact.

Giovanni da Concorrezzo, toward the second half of the fourteenth century, was so profoundly convinced that pest came exclusively from universal aerial pollution that he denounced as useless every precaution to check the advances of the disease and affirmed that all measures designed to avert contagion are inefficacious.

At this period, when the world had about decided that in epidemics sanitation was not worth while, three observing men lent their influence to broader views and thus gave a potent stimulus to the doctrine of contagion. These writers were Alessandro Benedetti, Marsilio Ficino, and Gerolamo Fracastoro.

BENEDETTI AND FICINO.

Alessandro Benedetti, anatomist and military surgeon, wrote a treatise on pest, published in the last decade of the fifteenth century, in which is presented a résumé of his doctrine concerning pest. Pest, he declared, is not only catching by contact with the sick, but by fomites. The latter, he believed, are capable of receiving and preserving the contagion for long periods. Convalescents from pest, and the things that have been in relation with them, should, he said, be purified before being brought in touch with healthy persons.

Marsilio Ficino was born in Florence in 1433, and passed his childhood in the court of Cosmo de' Medici. He was a priest as well as a physician. Pest had, in Ficino's time, tormented Tuscany, and in 1479 broke out in Florence. The Grand Duke Cosmo de' Medici requested Ficino to prepare a book treating of the pest with the scope of instructing the people how to protect themselves from the scourge. The book, published about 1480, was written in Italian. In writing it, Ficino was associated with Tommaso del Garbo, Mengo da Faenza, and others, and the volume bore the title of Counsel Regarding the Pest. The book is a rare one in its original tongue, but fortunately was translated into Latin and is still preserved in different libraries. The list of the works of Ficino refers to this treatise by the title of Antidotus, and it is so cited in many medical books printed in later years. The theories given in this work as to the origin and nature of epidemic disease are the same fantastic stuff that antecedent writers dealt out, but the ideas as to how the disease may be imparted are of a much better sort. The view is advanced that pest can be communicated from man to swine, and that cats and dogs convey the disease. The reader is informed that pestilential poison may abide in the air for long periods and may infect food. Advice is given to boil all drinking water, or to impregnate it with iron rust; to dilute wine with water so prepared; to add an acid sauce to the food; to choose dry food and fruit grown in balsamic and elevated regions, and to dwell on hills or in the mountains. Treating of prophylaxis and dietetics during times of pest, there is a long list of injunctions relative to exercises of the body and the quality of the food. For example, it is enjoined to shun the heat of the sun and of fires; to avoid sweating and the drying of sweat on the body; not to eat fish, or if needs be, to eat small fish from some clear running stream with a rocky bed, and to fry them in oil and treat them liberally with lemon juice, pepper, and cinnamon; and, lastly, there is an enumeration of fruit and vegetables to be chosen or avoided. Overeating and overdrinking are admonished, and it is advised to cook all meat well and prepare it with aromatic condiments. To preserve the health of those in attendance on the sick, it is directed to keep as far apart as may be from the bed-side; to ventilate the sick rooms; to fumigate the house with burning terebinth wood; to carry in the hand a firebrand, a pot of lighted charcoal, or a sprig of rue, mint, sage, or myrtle; and to bathe the body, morning and evening, with warm vinegar. Directions are given to sprinkle the house with preparations of terebinth, juniper, sandal, rose, rosemary, laurel, and similar herbs. The reader is informed that walls, partitions, and all structures made of wood are capable of preserving the contagion for more than a year, and that their disease-bearing qualities should be corrected by washing, fumigations, and fire; that garments of wool and similar stuffs, if not exposed to the air and sun, fumigated often, and well washed, may still contain contagion after three years. The statement is made that the morbid principle can diffuse itself through division walls and enter neighboring habitations. Caution is prescribed in moving animals, money, furniture, and bundles from place to place because of the danger of conveying disease.

FRACASTORO AND SYPHILIS.

Gerolamo Fracastoro is generally credited with being the author of the theory of contagion, but, as has been seen from a review of the works of previous writers, it can only be claimed for him that he elaborated the theory, presented it in a popular form, and lent to the idea the influence of his high authority.

An important event at this period of history was the extensive prevalence of syphilis in Europe, a spread of the disease that gave it every likeness to a general pestilence. The chroniclers of this occurrence were convinced that the disease could propagate itself at a distance, and that it could be communicated by intercourse not more intimate than conversation and social commingling. The malady diffused itself through all classes of society, and history names a king and other potentates among the victims. In Italy the belief prevailed that the disease had gained access to the country with the invading army of Charles VIII, of France. The Italians called it the "morbo Gallico." In France it took the name of the Neapolitan disease. Wide credence was gained by another theory to the effect that the malady had come in by sea with the naked savages of America. In this case it must have spread and taken root very speedily, for it is said that when Columbus went to Barcelona on his way to pay homage to Ferdinand and Isabella, of Spain, syphilis flourished in that seaport; public prayers were being offered as in times of pest, and precautions were being taken against the disease as in case of leprosy.

Laws were made in France for the regulation of syphilis. By an act of the Senate at Paris, dated March 6, 1496, persons affected with the disease were forbidden under pain of the halter to have any dealings with well persons, and it was ordered that the sick should be segregated in places set aside for their reception in the Faubourg St. Germain. Notwithstanding the rigor of the ordinance, many stricken persons eluded the vigilance of the sanitary guards and moved about in the city of Paris, thereby spreading the disease. The provost then found it necessary to make public cry, warning all persons that thereafter pretensions of ignorance would be disregarded by the authorities, and any individual, native or stranger, afflicted with syphilis and found within the city would be summarily cast into the river and left to his fate.

Some years later there was similar trouble in the Italian part of the Tyrol, trouble which so interfered with one of the most important ecclesiastical gatherings of the times that Pope Paul III, by advice of Fracastoro, removed the Council of Trent to Bologna. Fracastoro had previously written a dignified and graceful medical poem, in Latin, entitled "Syphilidis sive Morbus Gallicus," after whose hero, the shepherd Syphilus, the disease received its name.

His interest in this prevalence of syphilis influenced Fracastoro to publish, in 1546, the work "De Contagionibus." The great feature of this writing is the presentation of the subject in such a catching way that it took hold on the popular mind, and even had decided effect in loosening the deep-rooted medical opinion of the times. The lesson of contagion was taught by a number of clever similes. For example, Fracastoro divides contagious diseases into three classes, namely, disease catching by contact, in which he compares the mode of communicability to the way in which one decayed fruit spoils another perfect one; disease carried by fomites, a process likened to the persistence of soot on a smoky wall; and disease conveyed to a distance, in which manner the virus is carried just as the volatile essence of garlic or of an onion is borne through space, affecting the nostrils and causing the eyes to water. Fracastoro taught that the poison of disease consists in corpuscles, and that it affects first the minute particles of the animal body. He says that this poison persists in the body, in fomites, or in the air, in proportion to a kind of stickiness existing between the conveying medium and the poisonous corpuscles; and that woolen fabrics and the like absorb, retain, and transport contagion with ease, because they contain interspaces to lodge the corpuscles, and are of a nature to protect the poison from the light, heat, cold, air, dampness, and other conditions injurious to it.

So we see that, with the acceptance of the views of Della Torre, Benedetti, Ficino, and Fracastoro, things were fairly in the way for a beginning of quarantine on a practical basis.

MARITIME QUARANTINE.

Maritime quarantine originated in connection with the Levantine trade. Its early history is associated with that of shipping in the Mediterranean, especially with that of the traffic of Venice, Genoa, and Marseille. Although commercial activity in these waters was initiated by the Phœnicians, the maritime pioneers, records of disease introduced by sea are not found bearing earlier date than the period when Roman navigation was well established. As has been seen, the practice of isolation was first applied against communicable disease by the Hebrews, but their lazarettoes, it appears, were little used in connection with foreign trade, leaving out of the question commerce by sea. In the exchange of commodities with foreign countries the Hebrews were largely dependent on the Phœnicians and Arabs. Had the Jews been active in outside commerce, we should probably read in the Old Testament of sanitary laws applicable to caravans and vessels.

As has been already mentioned, Pliny implies that leprosy was introduced into Europe by Pompey on his triumphal return from the East. It is altogether probable that the Roman ships, laden with spoil from Syria, and bringing many prisoners of war to Italy, carried in leprosy.

In connection with the question of the first recorded introduction of disease by sea a curious error has entered into writings on the subject. J. Freind, adducing evidence in his History of Medicine that Procopius was a physician, quotes a translation of Procopius's works by Dr. Howel, and says that the great Byzantine historian describes the pest at Constantinople (A. D. 534) as having originated at Pelusium, in Egypt. This is indeed what Procopius wrote. But it happens that later writers—evidently reading Freind's history—say that Procopius states the epidemic in question was carried to Constantinople by ships and that this invasion of disease became later the foundation of the quarantine establishments on the Mediterranean coast. It is, however, true that the Italian epidemics of the sixth century began in the maritime towns and thence spread inland; but it does not follow that the writers of the time considered the intervention of ships essential to the introduction of disease by sea. For example, Francesco Alfano, professor of medicine at the University of Salerno, which in those days was reputed to be the greatest medical school in the world, writing in 1577, says that the corrupt air capable of introducing pest may be blown over sea and land for long distances; otherwise how could it be explained, he asks, that pest was transported from Ethiopia to Athens and to all Attica? It was considered, moreover, that a ship might easily be pestridden. Even by going to sea a vessel with all well aboard at the time of departure could not always escape the scourge. The infection extended over the water. Matteo Villani, of Florence, writing in 1581 of the epidemic of 1346, which spread from Asia into Turkey, Egypt, Russia, Greece, and Italy, says that in those evil days numbers of Italian galleys flying from the pest left the stricken ports for healthier harbors. Their crews perished miserably at sea. Some reached Sicily, Pisa, and Genoa, and the disease went with them.

EARLY MARITIME SANITARY LAWS.

There is but little known of ancient laws relating to maritime commerce, and even this little was lost to the world until 1147. The story is an interesting one. Justinian, during his reign, confided to ten jurisconsults the task of collecting and adjusting the numerous Roman laws, together with the various sentences and rulings of judges and magistrates. A compendium of these documents and of the laws promulgated during the rule of Justinian was published. It is known by the name of the Codex of Justinian. The only part of this code that treats of ships is called the *Digestum*, and it was lost for hundreds of years. Finally, in 1147, the papers were discovered at Amalfi and made public. The *Digestum* treats of the reciprocal rights of the owners and renters of ships, but no mention is made of sanitary matters. During the long period when this important legal instrument was lost, the Venetians, Genoese, and other Latin maritime nations supplied the deficiency in part from the initial sources of Roman law and in part by custom and agreement. Of this sort are two collections, one known by the name of *Recognoverunt Proceres* and the other called the *Consolato del Mare*. Besides these, there is a great number of documents, such as constitutions, decrees, ordinances, sentences, and the like, which pertain to maritime rights. It is a remarkable fact that, notwithstanding the detailed attention given to most maxims relating to shipping, the *Recognoverunt* and the *Consolato del Mare* are silent too on the subject of sanitation. Therefore, in the Middle Ages, in event of contagious prevalences, it rested with each individual city or country to make such provisions as were deemed opportune. Such an edict is the one, said to be the most ancient of its kind, already mentioned as having originated at Reggio d'Emelia, in 1374, and commanding notification and segregation of cases of plague.

The Venetians were, it is generally admitted, the first to make provision for maritime sanitation. As far back as the year 1000 there were overseers of public health, but at first the office was not a permanent one. The incumbents were appointed to serve during the prevalence of an epidemic only. The first information we have of this kind of public office is under date of 1348, when Nicolaus Venerio, Marinus Querino, and Paulus Belegno (their Christian names given in the Latin of the text) were appointed overseers of public health.

These officers were authorized to spend public money for the purpose of isolating infected ships, goods, and persons at an island of the lagoon. A medical man was stationed with the sick. As a later result of these arrangements, the first thoroughly constituted maritime quarantine station of which there is historical record was established in 1403 on the island of Santa Maria di Nazareth, at Venice. The island had previously belonged to the hermit monks of the order of St. Agostino. The record of the foundation of the first maritime quarantine is found in a Venetian manuscript written by Giovanni Tiepolo, a patrician. The chronicle reads:

1403. The pest began at Venice. A place for a lazaretto was seized from Friar Gabriel, of the order of Hermits, and Santo Spirito was given to him.

Neighboring States engaged in commerce in the Mediterranean speedily followed the example of Venice. The first maritime quarantine station at Genoa was founded in 1467, and at Marseille in 1526. The Marseille quarantine, one of the most complete of its kind, occupied the island of Pomique. This establishment had, in former times, been a leper house, but, in 1476, was converted into a plague hospital, and later became a maritime quarantine station.

It was not until 1459 that a public bureau of sanitation existed in the Republic of Venice. In that year officers, called conservators of sanitation, were regularly appointed. This information was handed down by a contemporary seafarer, Ser Domenico Malipiero, a Venetian patrician, an expert in commerce and diplomacy, who, in 1488, commanded the men-of-war under Captain-General Ser Jacopo Marcello at the celebrated naval battle of Gallipoli. In the contest against the Ottoman fleet the captain-general was killed, and Malipiero (who had a grade relative to that of vice-admiral at the present time) took command and was victorious. Malipiero wrote certain annals of his life which he bequeathed to his son-in-law. This interesting diary, in Venetian dialect, remained secret until 1844, when it was published in the Italian Historical Archives.

The city of Barletta became at one period of the Middle Ages the richest commercial port, next to Venice, in the Adriatic. This was owing to certain concessions granted the city whereby the traffic of a large territory was compelled to enter and leave by her gates. The privilege was not without its drawbacks. Barletta underwent three pestilences of a particularly aggravating character. The first, in 1384, was a strange malady that caused the sufferers to lose their skins like a molting snake. The other two epidemics (1498 and 1656) were probably bubonic plague, and in the last 35,000 souls, almost the entire population of the city, perished. These afflictions gave rise to the practice at Barletta of absolutely refusing entry to any infected vessel until the expiration of a long period of observation at a place outside the entrance of the port.

During all this period land quarantines were in operation at times of pest. Offenses against quarantine, both land and maritime, were severely punished. Pietro Follerio, a great Neapolitan jurisconsult of the sixteenth century, mentions whipping, the mill, exile, and death as penalties for infringement of sanitary regulations. A quarantine proclamation and command made by Don Carlo d'Aragona imposes rigorous punishment for surreptitiously entering the city of Palermo during a prevalence of pest. Torture, long service in the galleys, and work among the sick in a pest hospital are named among the penalties. Even the nobles were subject to heavy fines and long imprisonment in the castle.

BILLS OF HEALTH.

Sanitary bulletins were incident to quarantines and cordons. They were so called because they were stamped with the "bollo" or seal of the authority issuing them. When the system of sanitary bulletins was fully developed these patients, in their connection with ships, were designated as clean, when beyond suspicion; touched, when from a noninfected place in active communication with infected places; suspicious, without sickness aboard, but having received goods from places or from ships or caravans from places where pest prevailed; and dirty, when from a place where disease existed.

Professor Bo, a member of the council of health of Genoa, in making researches relative to ordinances of sanitation proclaimed in France in 1850, found an interesting document in the archives of the "Conservatori di Mare di Genoa," a body of officials to whom in mediæval times was confided the vigilance over public health. This writing, dated 1300, makes mention of bulletins of health (*bullettones sanitatis*) with which ships from the littoral of Corsica and Sardinia were required to be provided. Prior to 1300 there is a record in a rubric of the statutes of the city of Urbino, Italy, in which, referring to precautions against pest, it is written that no person shall leave the gate of the city without a proper bulletin, and that, to this end, watch shall be kept day and night at the city gates and walls. During the pest at Naples, in the year 1557, citizens, usually merchants, were stationed at the gates of the city to examine bills of health. Corruption and lack of diligence on the part of these persons were punishable by death. Sentinels, some on foot and some on horseback, made a patrol about the city walls to prevent clandestine entrance. Bills of health to be acceptable had to be stamped with the seal of the university of the place from which the traveler came. They gave not only the day but the hour of departure, together with a description of the traveler. Sanitary bulletins were also issued to accompany merchandise, but in times of severe pest all articles except aromatics and medicaments were considered suspicious. The facts here given are taken from the instructions written by Pietro Follerio, an eminent jurisconsult, who was assigned by the viceroy of Naples to superintend the province of Campania during the prevalence of pest with the special duty of indicating means for the betterment of public hygiene. It is worthy of notice that the provisions of public sanitation in those times are usually found, not in books of medicine, but in treaties on jurisprudence. This is explained by the fact that the medical profession was looked to for scientific indications only, and that the application of sanitary measures founded thereon, limiting or compromising as they often did the rights of the public or the constitutional privileges of citizens, was a matter for legal consideration and action.

AN EARLY SANITARY CONGRESS.

The efforts of some of the pioneers of quarantine were at times ill-advised, did not always meet with general approval, and sometimes, indeed, occasioned strong outbursts of popular indignation. The experience of Girolamo Mercuriale (called the Æsculapius of his time) and of his colleague Capodivacca is an instance. In the summer of 1576 the frequence of strange febrile diseases, often very mortal, was observed at Venice. The supreme magistrate of health of the Republic of Venice, suspecting pest, called a conference of great physicians, among others Girolamo Mercuriale, Capodivacca, and Nicola Massa. As for the verdict Massa wavered, and the other members were divided into two camps, one body for and the other against pest. Mercuriale and Capodivacca asserted decidedly that the malady was not pest, but an epidemic of fever, due to the excessive heat of the season. This opinion carried the day, and no precautions were taken against the spread of the disease. Unfortunately for the optimistic diagnosticians, the illness increased, and speedily took on all the characters of pest. The populace uprose and made an effort to lynch Mercuriale and Capodivacca and burn their houses. Both the physicians, fortunately for them, escaped by flight, their property being saved by prompt action of the authorities.

EARLY EFFORTS AT DISINFECTION.

The armament of disinfection in early days was full of oddities. In the process of purification time was more trusted than anything else. Gian Filippo Ingrassia, appointed by Philip II of Spain to establish a public sanitary service in Sicily, begins his book on pest and contagious disease with the following distich by Martello:

Lana, aura et linum captant contagia pestis;
Ignis, furca, aurum sunt medicina mali.

Before reviewing the different means besides fire, the gallows, and money used against contagion, it is interesting to make a survey of the things, in addition to wool, the air, and garments, that were reckoned infectible. Animals were considered capable of conveying disease. During the pestilence at Palermo in the year 1575 Ingrassia caused all the dogs in the city to be brought together alive on a certain day and cast into a common pit, where they were covered with quicklime and then with earth and stones. As to cats, they were allowed to live, so as "not to have worse war with rats," says Ingrassia, but all cats that had been near suspected houses were required to be kept closed up. There were similar restrictions for fowls and pigeons. Elsewhere geese and cattle were banished from the cities during epidemics. Habitations, ships, and even the sails and cordage with which vessels were rigged belonged to the category of infectible things. Nicola Massa, a Venetian physician, who published in 1556 a book on pestilential fevers, names the following as fomites: Wool, hair, cotton, linen, hemp, silk, thread, and all things made from these substances; skins, feathers, and the like; and all merchandise, as well as sacks, baskets, boxes, casks, and cords that cover them. Massa considered as noninfectible all metals and objects made of them, including arms and cooking utensils; precious stones and marble; grain, flour, and meal; vegetables, fruit—fresh and dried—and nuts, wine, oil, and vinegar; and all drugs and aromatics. In regard to metallic money he said that those who held it in suspicion might allay their fears by receiving it in a vessel of vinegar.

Exposure for many days to the air in selected places and to the dew was looked upon with great favor. The dew of the dead of night was supposed to be particularly efficacious. This practice originated in the more or less accurate observation that during the season when the mists of the Nile were thickest the pest in Lower Egypt began to diminish.

The vapors of volatilized aromatic substances, known technically as "perfumes," were credited with great virtues in correcting the alteration of the air generated by pest. Cloves, cinnamon, cedar bark, camphor, mints, resinous wood, and similar substances were kept boiling in pots of vinegar and rosewater for long periods. One recipe containing garlic and known as the "vinegar of the four thieves" enjoyed high repute. Fumigations in summer differed from those in winter. Aromatic wine was added in fumigations for cold weather, being assumed to have a special property of correcting air at a low temperature. It was also considered advisable to lengthen the period of isolation in winter because cold was thought to have a tendency to conserve the contagious principle. Sulphur fumigation was not regarded with favor in early days. The strong sulphurous fumes were said to alter the air unfavorably rather than rectify it; but sulphur came more into vogue in the eighteenth century. The burning of gunpowder was also thought useful.

Huge fires, kept burning for weeks, were used from the most ancient times. The physician Acron is reputed to have rendered great service by the use of fires at Athens during the pest at the beginning of the Pelopennesian war. Fires made of shavings and chips were thought preferable, because they produce a clear flame, without smoke. Aromatic wood was added to these fires, but special caution obtained against burning anything producing an offensive odor, such as the wood of certain nut trees, for fear of liberating vapors likely to add to the disturbed condition of the air. Not only were garments and similar articles burned, but sometimes houses and ships as well. Opposition often existed against such measures on the ground of further deteriorating the atmosphere.

Mixtures of lime were favorably regarded and whitewashing of infected apartments was habitually practiced. Acid fumigations are spoken of in the eighteenth century. Muriatic acid fumes, suggested as a disinfectant in 1774 by Guyton Morveau, of Paris, were used in 1800 to disinfect rooms, garments, mattresses, and the like, after the epidemic of yellow fever in Spain ("Yellow fever in Spain," Yellow Fever Institute, United States Public Health and Marine-Hospital Service, Bulletin No. 5). With all these measures, great stress was laid in cleaning up infected cities during and after epidemics, giving special attention to sewers, wells, cesspools, and disposing properly of dead bodies. In reading the chronicles of the middle ages the conviction can not be avoided that, were it not for occasional epidemics, public sanitation would have fallen entirely into disuse.

MEASURES ADOPTED IN A PEST-STRICKEN CITY.

To gain a precise knowledge of what measures were usually practiced in places afflicted with an epidemic in early days, it is instructive to examine specifically the provisions adopted in a particular city. A suitable instance is presented in the Treatise on Plague, by Alessandro Massaria, who was in charge of sanitary measures at Vicenza, Italy, during a prevalence of bubonic plague of one year's duration in 1577. The first death was attributed to garments clandestinely introduced from Padua, where plague prevailed. After a necropsy establishing the diagnosis the furniture in the house was burned and every exposed person stripped, given new clothes, and removed outside the city. The house was purified by aromatic fumigations and painted with milk of lime. All infected vestments and bedding received a treatment with strong lye. The disease, however, spread, and in one year the city, with a population of 30,000, suffered 1,908 deaths from plague. As soon as the epidemic established itself the city was divided into 32 sections and a daily house-to-house inspection made by 64 trustworthy citizens, two to each precinct. All cases of sickness were reported to one of four public physicians. These physicians served for periods of fourteen days. Infected habitations received the same treatment as in the initial case, except that the furniture was not burned in all instances, but washed instead with lye and left in the sun and open air for thirty days. All garments were put in running water for two days. Persons exposed or under suspicion went to the Campo di Marte, outside the city walls, where wooden houses had been built. A river separated the isolation camp from the lazaretto, where the sick were lodged and where physicians and nurses were in attendance. Suspects developing plague in the isolation camp were taken across the river to the lazaretto, and convalescents from the latter place were transferred to the former. Those who kept well in the Campo di Marte for twenty-two days returned to their disinfected homes in the city, there to remain under observation for an additional twenty-two days. Convalescents from the lazaretto passed twenty-two days in the isolation camp, and were afterwards confined to their houses in the city for another twenty-two days. At the height of the epidemic all the houses in the city were closed for forty days, and none but the guards were allowed in the streets. At this time 5,000 persons were fed from public funds, and there were about 400 persons in the lazaretto and 500 on the Campo di Marte.

EARLY MARITIME QUARANTINE STATIONS.

The maritime quarantine stations of the sixteenth century consisted of an anchorage, barracks for suspects and convalescents, and a place where purification could be applied. The practice, with obvious modifications, was the same as in the case of an infected city. The personnel of these stations consisted in many places, at the earliest times, of surgeons and their assistants, for plague, being regarded as a surgical disease, did not fall clinically into the hands of physicians. At a later period the physicians conducting the stations were aided by surgeons, barbers, and experts in aromatics, because, as Massa says, the physicians were so limited in their acquirements as not to know how to do manual operations or treat external maladies.

With a view to learning how the various methods of disinfection were practically applied at early maritime quarantine stations, it will be interesting to relate what was done to a Catalan ship that arrived at Palermo from Barcelona on the way to Naples at the time Ingrassia was chief of sanitation in Sicily. The account at least shows that the sanitarians of the sixteenth century were thoroughgoing. This vessel had 97 persons aboard, 18 of them passengers. Three seamen and two passengers had died of a disease suspected of being pest. The deaths occurred while the vessel was taking on cargo in the harbor where she lay at anchor. The cargo consisted of barrels of salted fish, cases of sugar (destined for Palermo, and already disembarked and in store), salted cheese, salt in bulk, a quantity of sumac, and merchandise, including many bales of cloth from Barcelona, a port not under suspicion. The master of the vessel was at once required to give 20,000 scudi security not to leave the harbor until given pratique. To make assurance doubly sure, the rudder was taken away from the ship and a watch set. All persons, except the sick and a sufficient number of seamen to guard the ship, were sent ashore to a place known as the Borgo, where all garments were taken from them and they themselves exposed to the fumes of boiling pitch and afterwards washed with vinegar. Some of the clothing was burned and some washed, aired, and perfumed for fifty days.

The sick were sent to a lazaretto, the Cuba, a huge stone building, which still stands at Palermo as a monument of early quarantine.

The treatment given the cargo was as follows: Barrels of salted fish, washed outside, first with sea water and then with vinegar; cases of sugar, salted cheese, and sumac, coverings removed and burned and the commodities without further treatment delivered to the owners; salt, no treatment, not being considered infectible; merchandise, aired and perfumed ashore for 50 days, and the cloth unrolled and hung from the rigging of the ship for 50 days. The sails and cordage of the ship were taken down, submerged in the sea for a week, and then hung from the masts, yards, and booms in the air, sun, and dew, by day and night, as long as the ship remained in quarantine. Fumigation was made in the interior of the ship by boiling pitch in caldrons between decks. Fifty days were set as the period of detention, instead of forty, because the season was winter.

FURTHER HISTORY OF QUARANTINE.

Without touching on quarantine in America, which is another and interesting story, it is profitable to take a view of the further history of quarantine in Europe. Following the discovery by Anthony van Leeuwenhoek, in 1675, of bacteria, called by him "animalcules," there was a wide belief in the casual connection of microscopic creatures with disease, a belief supported by the doctrine of living contagion enunciated by Marcus Antonius Plenciz, of Vienna, in 1762, but it was without marked effect on quarantine procedure. The theory, in fact, lost hold on the public and medical minds to such an extent that in the early part of the nineteenth century the doctrine of a living contagion was looked upon as an absurd assumption. It was not until the middle of the last century, following the investigations of Pasteur, Pollender, and Bavaine, that quarantine practice became established on its modern scientific basis.

English quarantine procedure prior to 1800 did not differ much from that of the Mediterranean ports. English vessels, which did not begin to enter the Mediterranean until the time of the Crusades, were usually, in early years when engaged in the Levantine trade and from infected ports, sent to Mediterranean quarantines for treatment. In 1710, under the reign of Queen Anne, a rigorous quarantine act was passed in England, and in 1721 two ships with cargoes of cotton goods from Cyprus, where plague prevailed, were burned by the sanitary authorities in English waters. A quarantine station was established in 1741 in Stangate Creek, on the Medway. Here vessels, not treated at Mediterranean quarantines, were submitted to practically the same procedures as were in vogue at French and Italian ports. Floating hulks were also used as quarantine stations in England from about the middle of the eighteenth century. The act of Queen Anne's reign was qualified by later enactments, and during the pest in Poland, in 1780, vessels bound for England from the Baltic were compelled to undergo a typical old-fashioned quarantine. A few years later there was an order in effect directing all vessels on the way to England and liable to quarantine to show a yellow flag at the mainmast head when in sight of other vessels at sea during the day and a distinctive light at night. From the beginning of the nineteenth century quarantine restrictions were, by changes in the laws and their application, materially relaxed in Great Britain, and as a substitute for former practice it has not been the custom in modern times to detain any vessel unless there has been communicable disease aboard during the voyage, or such exists on arrival. Following the decision of the Spanish Government in 1821, that yellow fever was to be considered quarantinable, an inquiry on the subject was made in England in 1823 and 1824, which resulted in the passage of a law directing the same procedures to be applied against yellow fever as against plague.

In France, until the year 1821, vessels from the Levant were not allowed to enter at any ports except Marseille and Toulon. The sanitary regulations of these ports were fortified by royal edicts. With the appearance of yellow fever on the frontier of Catalonia in 1821, an appalling epidemic that spread from Barcelona and killed 25,000 people in five months, a law was passed by the French Chambers, March 5, 1822, making a uniform sanitary code for all France, which, with certain subsequent modifications, formed the basis of French maritime sanitary practice.

Quarantine in the different continental European maritime countries during the eighteenth century was practically on a uniform basis, and during the first half of the succeeding century quarantine was practiced on the same lines in all European countries engaged in Eastern, American, and African trade, England excepted.

The international sanitary conferences at Paris in 1851 and 1852, in which participated the different European powers having interests in the Mediterranean, marked the close of the old régime of quarantine.

Delegates were present from France, Austria, the two Sicilies, Spain, the Roman States, Greece, Portugal, and Turkey. England was not signatory. Regulations were adopted much less restrictive than former ones, it being admitted that the efficacy of many measures formerly practiced was doubtful or negative, science having proclaimed that, for the most part, pestilential maladies are not contagious. This surprising declaration was followed by a revolution in quarantine methods on the Continent and resulted in the general adoption of practices based on the limited communicability of epidemic diseases. These changes, with which the early history of quarantine closes, were brought into effect at the beginning of the new era, during which the doctrine of specific living causes of epidemic diseases have been built up on the substantial basis of experimental medicine.

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BIBLIOGRAPHY.

[The whole title-page of many of the works consulted and some subtitles are given because of the interest attaching to the writings as documents in which the early history of quarantine is preserved.]

Historiæ Ecclesiasticæ Scriptores Græci. Coloniæ Allobrogrum. Petrus de la Rouviére. MVCXII. Book III. Chap., XXVIII. Evagrii Scholastici Epiphaniensis et ex præfectis oriundi. Historiæ Ecclesiasticæ. De pestilente morbo.

Jacobi Foroliviensis, medici singularis. Expositio et quæstiones in primum canonem Avicennæ & Venetiis, 1547. I Can: Fen: 2. Doctr. I. Chap. 8.

Ovid. Metamorfosi. Lib: VII.

Procopii (Cæsariensis). De bello Persico. Raphælem Volaterranum conversus. Romæ apud Iacobum Mazochium. Romanæ Academie Bibliopolam. Anno MDXVI. Die XXIX, mensis Februari. Triumphante Divo Leone X Pontifice Massimo. Anno ejus tertia. Lib: II. De novo genere pestilentiæ (an: 534).

Muratori, Rerum Italicarum Scriptores. Vol. 18. Milan, 1731. The edict of Reggio d'Emilio is found on page 82, letter D, year 1374.

Tractatus singularis doctissimi viri Marsilii Ficini de epidemiæ morbo, ex italico in latinum versus. Cum privilegio imperial. Augustæ Vindelicorum in Sigismundi Grim Medici et Marci Vuyrsung officina excusoria. Anno virgine partus MDXVIII.

Joannis Baptista Van Helmont. Ortus Medicinæ id est Initia Physicæ inaudita. Progressus Medicinæ novus. In morborum ultionem ad vitam longam: Lugduni. Sumptibus Joannis Baptistæ Devenet. In Vico Mercatorio. Sub signo Crucis aureæ. 1640. Tumulus pestis.

Honorati Fabri, S. J. Tractus duo. Quorum prior est de Plantis et de generatione animalium. Posterior de Homine. Parisiis. Apud Franciscum Muget, Regio ac Illustriss: Archiepiscopi Parisiensis Typographum, ad insigne Adorationis trium Regum. 1666. Cum privilegio et permissu. De Homine. Liber VI. Propositio XII. Page 38. Explicantur ea quœ pertinent ad febres.

Ioannis Fernellii, Ambiani. De abditis rerum causis. Libri duo postremo ab ipso auctore recogniti, compluribusque in locis aucti, ad Henricum Franciæ Christianissimum. Lagduni, apud Bartholomæum Vincentium. 1605.

Hieronymi Fracastorii. De contagionibus et contagiosis morbi, et eorum cura. Libri tres. Ad Alexandrum Farnesium Cardinalem Amplissimum.

Ioannis Francisci a Ripa, papiensis. Comentaria ad jus canonicum. Item Tractus de Peste et Responsa: summo studio et labore, collatis manuscriptis exemplaribus &. Augustae Taurinorum. Apud haeredes Nicolai Bevilaquae. 1574.

Nicolai Massa, Veneti, Artium et Medicinae Doctoris. Liber de febri pestilentiali, ac de Pestichiis, Morbillis, Variolis et Apostematibus pestilentialibus, aeorumdem curatione, necnon de modo quo corpora a peste praeserveri debeant. Opus sane utilissimum, cui nuperrime auctor tum pleraque alia, tum praecipue doctrinam addidit de rebus quae pestilentem contagionem suscipere, vel non suscipere possint &. Venetiis, apud Andream Arrivabenum. Ad signum Putei. 1556.

Ad Instructiones Urbanas et Regias pro custodia pestis. Brevis apparatus, praefectis sanitatis non inutilis. Auctore Petro Follerio, I. C. Ad admodum Illustrem D. Regentem Salazar, Praefectissimum sanitatis. Romae, apud baeredes Antonii Bladii impressores camerales. 1577. Cum licentia superiorum.

Hierönymi Mercurialis Poroliviensis, medici praeclarissimi. De pestilentia. Lectiones habitae Patavii, 1577, mense Januarii. In quibus de peste in universum, praesertim vero de Veneta et Patavina, singulari erudictione tractatur &. Patavii, apud Paulum Meietum. 1560.

Francisci Alphani, philosophi ac medici Academiae Salernitanae. Opus de Peste, Febre pestilenti et Febri maligna, nec non de variolis et morbillis, quatenus nondum pestilentes sunt. Neapolis, apud Horatium Salvianum. 1577.

Danielis Sennerti uratislaviensis, Doctoris et Medicinae Professoris in Accademia Vittembergensi. Operum in Quinque Tomos Divisorum. Lugduni, sumptibus Joannis Antonii Huguetan et Marci Antonii Ravaud. MDCLXVI. Institutionum Medicinae. Liber II. Pars II. De causis morborum. Caput XII. De causis morborum tortius substantiae. Vol. I.

Archivio Storico Italiano. 1844.

Statuta Civitatis Urbini. Impressa Pisauri per Bartholomaeum Caesanum. Anno Incarnationis Domini nostri Jesu Christi 1559.

Opera Ambrosii Parei. Regis Primarii et Parisiensis chirurgi, a docto viro plerisque locis recognita, et Latinatate donata. Jacobi Guillemeau, Regii et Parisiensis chirurgi labore et diligentia. Ad clarissimum virum Marcum Mironem, Regis Archiatrum dignissimum. Parisis apud Jacobum Du Puys, sub signo Samaritanae, MDLXXXII. De Peste. Liber Vigesimusprimus.

Informatione del Pestifero et Contagioso morbo. Il quale affligge et have afflitto questa città di Palermo, et molte altre città e Terre, di questo Regno di Sicilia, nell'Anno 1575 et 1576. Data allo invittissimo et Potentissimo Re Filippo Re di Spagna & Col regimento preservativo et curativo. Da Giovan Filippo Ingrassia, Protofisico per Sua Maestà in Questo Regno. Cum privilegio decennium.

Alexandri Massariae, Vicentini, Antiq: et celebri gymnasii Patavini Doctoris primarii Opera Medica &. Lugduni, Sumptibus Joannis Amati Candy. 1534.

Bando et Comandamento da parte dello Illustrissimo & Eccellentissimo Sig. D. Carlo d'Aragona, Principe di Castelvetrano, Duca di Terra Nuova & Luogotenente & Capitan Generale per Sua Maestà in questo Regno di Sicilia. Promulgated in Palermo, November 28, 1575.

Istorie di Matteo Villani, cittadino fiorentino, che continua cuella di Giovanni suo fratello. In Firenze nella stamperia de' Giunti. 1581.

Thucydides. De bello Peloponnesiaco. Translation in Italian by Peyron. Turin, 1861.

Grand Dictionnaire Universe du XIXme Siècle, par Pierre Larousse. Encyclopedia Brittanica.

J. Freind. Histoire de la Medicine dupuis Calien jusq' au 16me Siècle. Trad. de l'Anglais par Etienne Coulet, A. Leide, J. A. Langerak, 1727.

Joannis Astruc. De morbis Venereis & Venetiis. 1740. Vol. I. Lib. I. Cap. 15.

La Grande Encyclopedie. Vol. 27me. Police sanitaire. Quarantaines.

Dictionnaire des Science Médicales. Par une Société de Médecins et de Chirurgiens. Paris. C. L. F. Panckoucke. Edit. 1818.

Gauthier, L. R. A. Recherches historique sur l'exercise de la médicine dans les temples chez les peuples de l'antiquité. Paris. 1844.

Ferdinando Gregorovius. Storia della Città di Roma nel medio evo dal Secolo V al XVI. Prima traduzione Italiana sulla secunda edizione Tedesca dell' Avv. Renato Manzato. Venezia, 1875.

Loffredo, Savino. Storia della città di Barletta. Napoli, 1895.

Delle Instituzione di Sanità Marittima del Bacino del Mediterraneo. Studio Comparativo di Giovanni Bussolin, Birettore dell' I. R. Lazzaretto Marittimo in Valle San Bartolomeo, Segretario di Governo. Edito dall' I. R. Governo Marittimo. Trieste, 1881.

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WORKING PARTY NO. 2,

YELLOW FEVER INSTITUTE.

EXPERIMENTAL STUDIES IN YELLOW FEVER AND MALARIA AT VERA CRUZ, MEXICO.

BY

M. J. ROSENAU, PASSED ASSISTANT SURGEON.
HERMAN B. PARKER, PASSED ASSISTANT SURGEON.
EDWARD FRANCIS, ASSISTANT SURGEON.
GEORGE E. BEYER, ACTING ASSISTANT SURGEON.

MAY, 1904.

WASHINGTON:
GOVERNMENT PRINTING OFFICE.
1905.

YELLOW FEVER INSTITUTE, BULLETIN No. 14.
Treasury Department, U. S. Public Health and Marine-Hospital Service.
WALTER WYMAN, *Surgeon-General.*

REPORT

OF

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PREFACE AND ACKNOWLEDGMENTS.

Working Party No. 2, Yellow Fever Institute, consisting of Passed ist. Surg. Herman B. Parker, Asst. Surg. Edward Francis and Act-g Asst. Surg. George E. Beyer, was detailed by the Surgeon-eneral U. S. Public Health and Marine-Hospital Service, with the proval of the Secretary of the Treasury, to Vera Cruz, Mexico, pril 27, 1903, for the purpose of making further studies upon the use and methods of transmission of yellow fever.

Doctor Parker returned to Washington upon official business June 1903, and on September 13, 1903, returned to Vera Cruz with Passed sst. Surg. M. J. Rosenau, Director of the Hygienic Laboratory, who d in the meantime been appointed chairman of the commission, th instructions to repeat that part of the work of Working Party o. 1 relating to the *Myxococcidium stegomyiæ.*

Professor Beyer left for New Orleans on October 4 to resume his ties at the Tulane University of Louisiana.

The remaining three members of the working party continued work Vera Cruz until November 28, 1903, when, on account of the sub-lence of the yellow fever epidemic and scarcity of material, they turned to Washington.

The commission made a brief report to the Surgeon-General, signed all of its members and published in the Public Health Reports r January 15, 1904, as follows:

ndings of Working Party No. 1, Yellow Fever Institute, not all corroborated by Working Party No. 2.

WASHINGTON, *December 18, 1903.*

RGEON-GENERAL.

SIR: We have the honor to report that, as a result of our studies at Vera uz, Mexico, this summer, we have not been able to corroborate all the findings Working Party No. 1, Yellow Fever Institute, Public Health and Marine-spital Service, having found phases of the organism described by them as *xococcidium stegomyiæ* in normal mosquitoes.

Respectfully,

M. J. ROSENAU,
Chairman Working Party No. 2.
H. B. PARKER,
EDWARD FRANCIS,
GEO. E. BEYER.

The commission was now, January 18, 1904, dissolved, and its embers permitted to publish individually any further matter bear-g on the summer's work.

This bulletin, therefore, has been prepared by two members of the mmission, Doctors Rosenau and Francis, who have continued cer-in phases of the work, but who here wish to make full acknowledgment of the services rendered by their colleagues. Especial mention should be made of the fact that the mosquitoes which fed on yellow-fever cases and subsequently were used to produce the initial case of experimental yellow fever (Marcos Cruz) were handled by Professor Beyer.

Credit is also due to Professor Beyer for the scheme of experimentation which was partly carried out. This plan was published by him in full in the New Orleans Medical and Surgical Journal for May, 1904, entitled "The mouth parts and salivary glands, normal and otherwise, of the yellow-fever mosquito." Professor Beyer was a member of Working Party No. 2 from May 5, 1903, to January 18, 1904, and was in charge of the laboratory at Vera Cruz from June 8 to September 17, 1903, during the absence of Doctor Parker.

Asst. Surg. Joseph Goldberger was associated with us throughout the entire summer, having been detailed to Vera Cruz to supervise the sanitation of vessels leaving for the United States. He helped us find suitable cases of yellow fever and malaria in the hospitals from which he infected a large collection of mosquitoes, and he also made many of the observations which we have embodied under "Miscellaneous observations on mosquitoes."

The plans of the commission were laid before Governor Dehesa, of the State of Vera Cruz, who was always most zealous in furthering the scientific investigation of yellow fever, and offered us many facilities.

To Mr. Alexander M. Gaw, of Jalapa, Mexico, we desire to express our particular appreciation of many thoughtful kindnesses and material assistance.

To Dr. Eduardo Licéaga, president of the superior board of health of Mexico, and to his representatives in Vera Cruz, Doctors del Rio, Iglesias, and Garcia, we wish to express our thanks for their interest in the work and for many courtesies, thoughtful kindnesses, and material assistance.

The United States consul, Mr. W. W. Canada, and Acting Asst. Surg. S. H. Hodgson, U. S. Public Health and Marine-Hospital Service, were always ready to assist us in every way possible.

Finally, we wish to express our appreciation to the Surgeon-General of the Public Health and Marine-Hospital Service for his continued interest and support which made the work possible.

M. J. Rosenau,
Passed Assistant Surgeon, Chairman.
Herman B. Parker,
Passed Assistant Surgeon.
Edward Francis,
Assistant Surgeon.
Geo. E. Beyer,
Acting Assistant Surgeon.

YELLOW FEVER INSTITUTE.

Treasury Department, Bureau of Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

BULLETIN No. 14.

Section B.—ETIOLOGY. P. A. Surg. M. J. ROSENAU, Chairman of Section.

EXPERIMENTAL STUDIES IN YELLOW FEVER AND MALARIA.

By M. J. ROSENAU, *Passed Assistant Surgeon,*
HERMAN B. PARKER, *Passed Assistant Surgeon,*
EDWARD FRANCIS, *Assistant Surgeon,*
GEORGE E. BEYER, *Acting Assistant Surgeon.*

THE CAUSE OF YELLOW FEVER.

The cause of yellow fever is not known, but we have to consider the *Myxococcidium stegomyiæ* of Parker, Beyer, and Pothier. These authors described in some detail the life cycle of a supposed animal parasite in infected mosquitoes closely resembling coccidia.

It was our first duty to investigate the merits of this announcement. We therefore first sectioned about one hundred normal mosquitoes, *Stegomyia* and *Culex*, both male and female. A study of these slides soon convinced us that bodies resembling *Myxococcidium stegomyiae* may be found in normal mosquitoes and that for the most part these bodies were yeast cells in various stages of reproduction. Carroll had called our attention to this in a conversation and subsequently discussed it in an article published in the Journal of the American Medical Association for November 28, 1903.

Since then the French commission, working at Rio de Janeiro,[a] has come to the same conclusion.

[a] Marchoux, Salimbeni, and Simond: La fièvre jaune; rapport de la mission française. Ann. de Inst. Pasteur, tome XVII, November, 1903.

EXPLANATION OF PLATE 1.

Wild yeasts in pure culture isolated from banana at Vera Cruz, Mexico, in the summer of 1903. Stained with hematoxylin and eosin.

All the specimens show deeply stained granules.

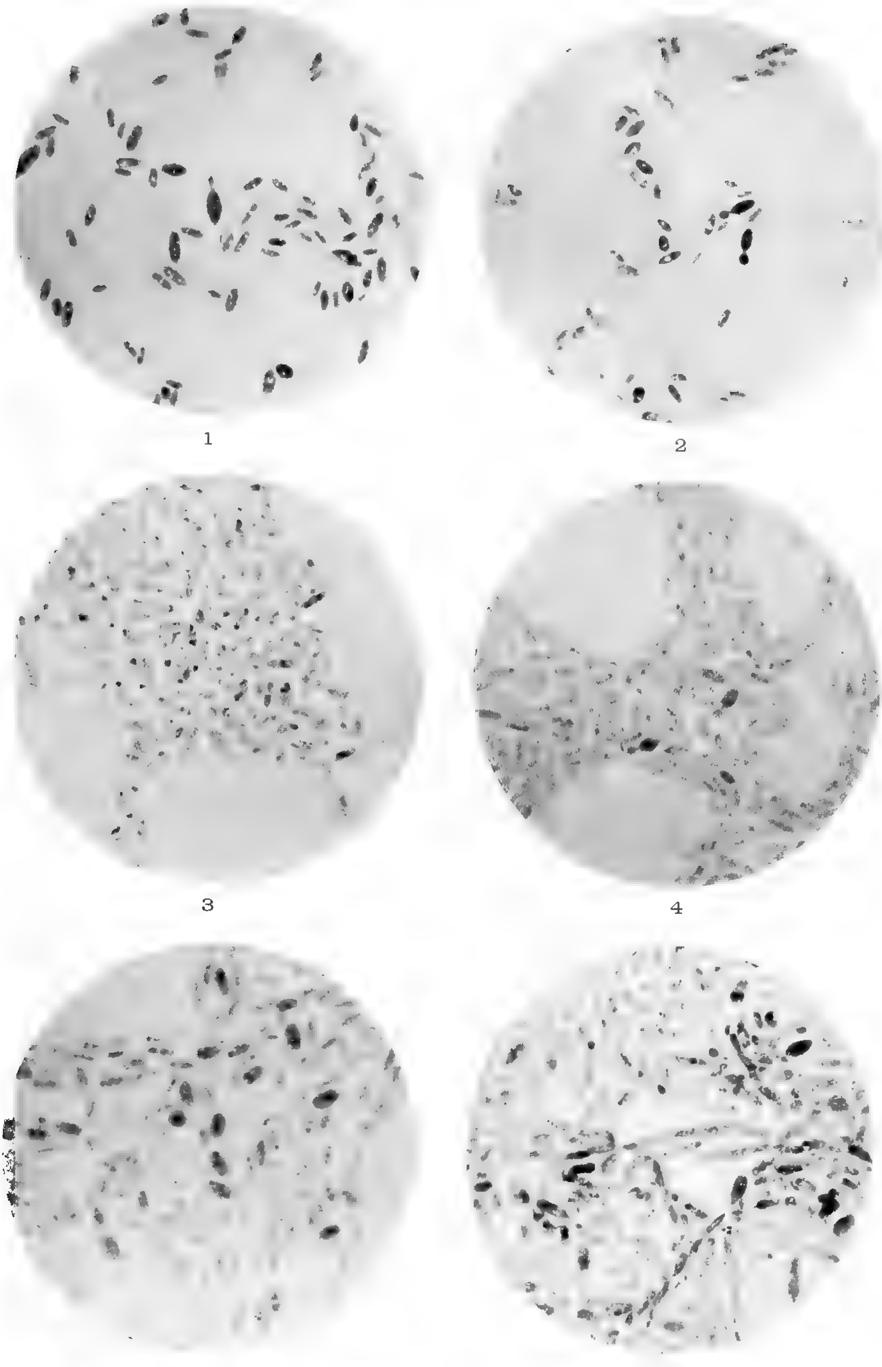
1. Shows the lemon-shaped budding forms of *Saccharomyces apiculatus*.

2 and 4. Other budding forms.

3. Well marked granules.

5. Ovoid forms with granules.

6. Filamentous yeast.



WILD YEAST IN PURE CULTURE ISOLATED FROM BANANA AT VERA CRUZ, MEXICO, IN THE SUMMER OF 1903. STAINED WITH HEMATOXYLIN AND EOSIN. ALL THE SPECIMENS SHOW DEEPLY STAINED GRANULES.

:haudinn[a] considers yeasts as normal commensals of all mosquitoes believes they play an important part in the physiology of the ct, generating the gas that is almost always found in the eso- geal diverticulum and also producing an enzyme or other irritat- substance which, when injected under the skin of man, causes the ımmation resulting from mosquito bites. Schaudinn considers e yeast cells to play a very important part in the economy of the ct and believes them to be hereditarily passed from the adult ›ugh the egg to the larvæ and pupæ.

:osquitoes fed upon fruits have many more yeast cells in their .es than those fed upon blood or other material. This we were to confirm. We also fed mosquitoes upon pure cultures of l yeasts growing upon banana, and found that the insects fed on ı a fermenting diet would soon be so swelled up with gas that r bodies looked like transparent air bubbles. Insects so fed do 7 badly and it is difficult to keep them alive over a week in trop- temperatures.

ome of these wild yeasts are very interesting; one in particular— *Saccharomyces apiculatus*, which is found widely spread through- nature especially on fruit. This particular yeast assumes at times racteristic spindle or lemon shapes, with a bud at the pointed , somewhat resembling one of the conjugating forms of protozoan ınisms with which it has been confused.

/e were enabled to isolate this yeast in pure culture from the anas at Vera Cruz only after some difficulty. The ordinary plate hods failed because the other saccharomyces overgrew the small nies of *S. apiculatus*. The following expedient finally succeeded: overripe and fermenting piece of banana containing the mor- logic forms desired is planted into orange juice. This culture .ium was made by simply squeezing the oranges, taking care not et any of the oil of the peel, then filtering until clear, and steriliz- by heat in test tubes. As the *Saccharomyces apiculatus* is a bot- yeast, the growth which appears at the bottom of the test tube in lve to eighteen hours is examined under the microscope and, if the ɔer forms are found, transferred to another tube containing ıge juice. This is repeated until a number of subcultures are le, and as the *Saccharomyces apiculatus* grows better in the orange e than the other yeasts, the latter are quickly left behind until ıre culture is obtained.

/e have noted in stained preparations of these wild yeasts that r sometimes show red chromatin (?) granules in a blue protoplasm

[a] Schaudinn, Fritz 1904, Generations- und Wirtswechsel bei *Trypanosoma* und *ochaete* (vorläufige Mitteilung.). Arb. a. d. k. Gesundheitsamte, Berl., 4°.

when stained with polychrome methylene blue, such as Goldhorn's. We call atention to this, for isolated yeast bodies of this character stained thus might lead to errors of interpretation.

THE BLOOD IN YELLOW FEVER.

We are fully justified in concluding that in the blood of yellow-fever cases there is a living entity floating free in the plasma and capable of reproducing the disease. The positive results obtained in the filtration and inoculation experiments done by Reed and Carroll, corroborated by the French commission and ourselves, is sufficient proof of that statement.

We carefully examined many blood smears stained with polychrome methylene blue of Wright and Goldhorn, and failed to see the presence of any body which could be considered to stand in any causal relation to the disease.

The smears were taken from 17 cases at periods of five hours to six days after the onset of the disease. In every case blood was taken within the first three days of sickness. In several cases the blood was taken daily or on alternate days. The corpuscles and plasma were carefully searched. The red cells often showed minute blue bodies, usually round and sometimes slightly irregular, which resemble those ascribed to cell degeneration or nuclear rests in anemia.

The mononuclear leucocytes and polymorphonuclear neutrophiles often showed in their protoplasm small, round, clear spaces having a punched-out appearance. These spaces could not be made to take up any one of several stains employed. They were also found in malarial and normal blood.

In making our blood preparations we used a method devised by one of us (Rosenau) about four years ago, which has been in constant use in the Hygienic Laboratory since, and as it has proven so satisfactory in our hands we will describe it. The technique was suggested by the glass slides commonly used for this purpose. The instrument consists of a little glass apparatus we call the "spreader," made by simply welding two pieces of solid glass rods together, as shown in fig. 1. The short arm should be true, so as to lie flat when applied to the slide, and should be several millimeters shorter than the width of the slide. A drop of blood is taken from the ear or finger tip and placed upon one end of the slide in the usual manner. The spreader is then applied to the drop, and if the glass is clean the blood will at once be drawn by capillary attraction across its whole length; it is then spread by a gentle, even stroke, without undue pressure, along the le. Very beautiful prèparations, with the corpuscles lying singly, thus obtained.

This little apparatus can readily be made at the blowpipe.

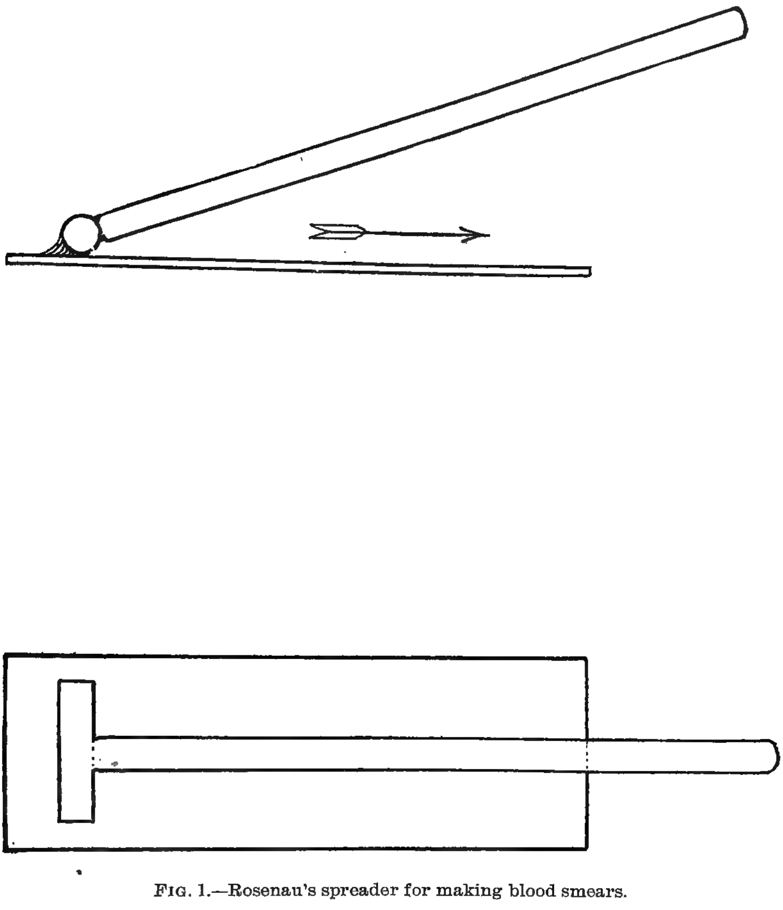


FIG. 1.—Rosenau's spreader for making blood smears.

THE PERIOD OF INCUBATION OF YELLOW FEVER.

The exact period of the incubation of yellow fever is a matter of eat importance in quarantine and public-health work. For years quarantine regulations of the Marine-Hospital Service required letention of five days, which was considered amply safe to cover period of incubation of the disease. The regulations of the Pub- Health and Marine-Hospital Service, promulgated August 10,)3, lengthened the time of observation in special cases to six days, sing this action upon the recent experimental work which has made possible to determine the period of incubation of yellow fever with eat exactness.

We have collected from the literature all the cases in which the period of incubation may be stated with precision. These are of course for the most part experimental cases in which the exact time of the mosquito bite is known, and in which the onset of the disease has been carefully observed.

The disease usually begins sharply with a chill, pains, and rise of temperature. In such cases the precise hour of onset may be stated, but sometimes the attack begins vaguely or at night. Then the period of incubation can be stated only approximately. In the following table the onset of the disease is considered from the time the temperature rises, thus omitting the prodromal symptoms of lassitude, headache, etc, which sometimes send a patient to bed twenty-four hours before the fever sets in.

Of course from a practical standpoint in public health work only those cases infected in a "natural" way—that is, by the bites of mosquitoes, can be considered. Subjoined is a table of 40 such cases.

TABLE 1.—*Period of incubation in yellow fever, resulting from bites of infected mosquitoes.*

[Carter: "The period of incubation of yellow fever," Med. Rec., Mar. 9, 1901; also, private correspondence. Observations of the disease following one short exposure in the infected region at Orwood, Miss., during the epidemic of 1898.]

Case No.—	Bitten.	Attack.	Incubation.
1			3 days.
2			Do.
3			Between 3 and 4 days.
4			Do.
5			Do.
6			Do.
7			Do.
8			Do.
9			4 days.
10			Do.
11			4½ days.
12			5¼ days.

In these observations, which were of a clinical nature, no attempt was made to determine the period of incubation within hours, anything less than one-fourth of a day being disregarded.

[Reed, Carroll, Agramonte, and Lazear: "The etiology of yellow fever; a preliminary note," Phila. Med. Journ., Oct. 27, 1900.]

Case No.—	Bitten.	Attack.	Incubation.
13 (10)	Aug. 27, 2 p. m.	Aug. 31 (?) a. m	3 days 17-22 hours (about).
14 (11)	Aug. 31, 11 a. m	Sept. 6 (?) p. m.	6 days (about). According to the authors, 6 days 2 hours.

TABLE 1.—*Period of incubation in yellow fever, etc.*—Continued.

eed, Carroll, and Agramonte: "The etiology of yellow fever; an additional note," Journ. Am. Med. Assoc., Feb. 16, 1901.]

Case No.—	Bitten.	Attack.	Incubation.
(1)	Dec. 5, 2 p. m	Dec. 8, 11.30 p. m	3 days 9½ hours.
(3)	Dec. 8, 4 p. m	Dec. 14, 9 a. m	4 days 20 hours, took to bed; 5 days 17 hours, onset of fever.
(4)	Dec. 9, 10.30 a. m	Dec. 12, 9.30 p. m	3 days 11 hours (about).
(5)	Dec. 11, 4.30 p. m	Dec. 15, noon	3 days 19½ hours (bed).
(7)	Bitten several times—Dec. 21, noon, and Dec. 22, 4.30 p. m.	Dec. 25, noon	2 days 19½ hours since shortest, and 4 days since longest exposure.
(6)	Dec. 30, 11 a. m	Jan. 3, 10.30 a. m	3 days 22½ hours.

[Reed: "Experimental yellow fever," Am. Med., July 6, 1901.]

Case No.—	Bitten.	Attack.	Incubation.
	Jan. 19, 3.30 p. m	Jan. 23, 3 p. m	3 days 23½ hours.
	Jan. 31, 9.30 a. m	Feb. 3, noon	3 days 2½ hours.
	Jan. 6, 11 a. m	Feb. 9, 5 p. m	3 days 6 hours.
	Jan. 7, 2 p. m	Feb. 10, noon	2 days 22 hours.

eed and Carroll: "Etiology of yellow fever; a supplemental note," Am. Med., Feb. 22, 1902.]

Case No.—	Bitten.	Attack.	Incubation.
(1)	Sept. 16, 4 p. m	Sept. 19, 4.30 p. m	3 days ½ hour.
(2)	Oct. 9, 4 p. m	Oct. 13, midnight	3 days 8 hours (about).

[Guitéras: Revista de Med. Trop., vol. 2, No. 10, 1900-1901.]

Case No.—	Bitten.	Attack.	Incubation.
(2)	Feb. 23, 2.45 p. m	Feb. 26, (?) p. m	3 days 10 hours (about).
(30)	Aug. 8, 8.30 p. m	Aug. 12, (?) p. m	4 days 5 hours.
(31)	Aug. 8, 9.30 p. m	Aug. 11, (?) p. m	3 days 3 hours.
(33)	Aug. 9, 9 a. m	Aug. 14, (?) p. m	5 days 3 hours.
(37)	Aug. 13, 1.45 p. m	Aug. 17, (?) 8.45 p. m	3 days 19 hours.
(39)	Aug. 14, 9 a. m	Aug. 18, (?) 6 a. m	3 days 21 hours.
(40)	Aug. 14, 10.15 a. m	Aug. 20, forenoon	5 days 21 hours (about).
(41)	Aug. 22, 4.30 p. m	Aug. 25, (?) 4.30 p. m	3 days.

arker, Beyer, and Pothier: "A study of the etiology of yellow fever," Yellow Fever Institute, Bull. No. 13, March, 1903.]

Case No.—	Bitten.	Attack.	Incubation.
	Sept. 4, 9.30 a. m	Sept. 7, (?) a. m	3 days 2 hours (about).

[archoux, Salimbeni, and Simond: "La fievre jaune," Rapport de la Mission Francaise, Institut Pasteur, Annales, November, 1903.]

Case No. —	Bitten.	Attack.	Incubation.
(2)			3 days 18 hours.
(17)*a*			3 days 22 hours.
(20)			5 days 22 hours.
(22)*b*			7 days 5 hours.

Before being bitten by infected mosquitoes patient had received injections of blood from llow fever cases to induce immunity: 5 cc. blood twelve days old; followed fifteen days later same quantity eight days old.

This man previously had been given 20 cc. serum taken on the eighth day and passed through a rkefeld filter; six days later 20 cc. of same serum not filtered; subsequently bitten by infected squitoes. The serum injections may have induced a partial immunity, which delayed the set and modified the disease, for he had a mild attack.

TABLE 1.—*Period of incubation in yellow fever, etc.*—Continued.

[Francis and Beyer.]

Case No.—	Bitten.	Attack.	Incubation.
40	Sept. 11, 9 a. m., and Sept. 12, 2.30 p. m.	Sept. 14, 3.30 p. m.	3 days 7 hours, or 2 days 1 hour.

A study of the 40 cases in this table discloses the fact that yellow fever usually begins about three days after the mosquito bites.

The period of incubation resulting from this natural method of conveying the disease is rarely under three days. We have but one such authentic instance, namely, two days twenty-four hours (case No. 24).

The longest period observed was seven days five hours, but it must be noted that the man who had this unusually long period of incubation had previously been treated with injections of immunizing sera, which may have delayed the onset and modified the disease, for he had a mild attack.

Leaving this case (No. 39) out of consideration, the longest period of incubation resulting from the bites of mosquitoes is the case (No. 14) of Reed. Carroll, Argamonte, and Lazear, in which an incubation period of six days two hours was observed. This corresponds strikingly to Carter's clinical observations in which he reports a case with an incubation period of five and three-fourths days. See case No. 12 in Table 1.

The French commission, working in Rio de Janeiro, came to the concluson that the period of incubation of the disease may be much longer than this; but we find on analyzing their work that they drew their inferences largely from the disease produced by such artificial means as the inoculation of modified blood serum.

One of the conclusions of this commission was that yellow fever may not infrequently incubate for twelve days before symptoms declare themselves.

They state that "this incubation of twelve days is not absolutely rare. We have had occasion to see that the natural infection may also present an incubation equally lóng."

With this statement we must take issue, for the long experience of the Public Health and Marine-Hospital Service in the many wars it has waged against yellow fever has amply demonstrated that for practical purposes five days is sufficient to cover the period of incubation of the great majority of cases. An analysis of all the cases reported in Table 1 supports this view.

The French Commission reports several cases in support of their contention. One, a young man 18 years old, who took yellow fever ten days after having arrived in Petropolis from Rio de Janeiro. Petropolis is a village free from yellow fever. Another instance was a girl 12 years old, who was taken with yellow fever ten days after returning from Rio, her father having sent her to Petropolis because his wife and three other children had the fever.

We do not doubt that Petropolis is "indemne," free of *Stegomyia fasciata*, and that the disease has never been known to spread there; but the communication with Rio is close, and if yellow fever cases are brought to Petropolis it is conceivable that infected mosquitoes may also be carried. There are many other "loopholes" which weaken observations of this kind, and we have therefore refrained from placing them in our table.

The last case cited by the French commission is as follows:

On board the vessel *Messageries*, returning to Europe, having taken passengers from Rio de Janeiro, an isolated case of yellow fever declared itself among the latter passengers between Dakar and Lisbonne; that is, nine to fourteen days.

It was our experience that some cases of yellow fever are so mild that they are detected with difficulty, especially under such unfavorable conditions as on board ship. "The isolated case" on board the *Messageries* may have been the second case, especially as the fourteen days is sufficient to cover the "extrinsic incubation" of the disease. The literature has several instances of such cases. They should be carefully considered before drawing definite conclusions.

It is interesting to compare the period of incubation resulting from exposure to infection in the "natural" way with the period of incubation resulting from experimental yellow fever, produced by the inoculation of blood or blood serum. The following table shows 17 such cases:

TABLE 2.—*Period of incubation in yellow fever, resulting from the injection of blood.*

[Reed, Carroll, and Agramonte: "Experimental yellow fever," Am. Med., July 6, 1901.]

Case No.—	Inoculated.	Attack.	Incubation.
1	Jan. 4, 11 a. m.	Jan. 8, 9 a. m.	3 days 22 hours.
2	Jan. 8, 9 a. m.	Jan. 11, 9 a. m.	2 days 12 hours.
3	Jan. 22, 1 p. m.	Jan. 24, 9 a. m.	1 day 19 hours.
4	Jan. 25, 12.45 p. m.	Jan. 28, 1.15 p. m.	3 days 1 hour.

No. 1 received subcutaneously 2 cc. blood taken on second day.
No. 2 received subcutaneously 1.5 cc. blood taken 12 hours after beginning of attack.
No. 3 received subcutaneously 0.5 cc. blood taken on second day.
No. 4 received subcutaneously 1 cc. blood taken 27¼ hours after commencement of disease.

[Reed and Carroll; "The etiology of yellow fever; a supplemental note," Am. Med., Feb. 22, 1902.]

Case No.—	Inoculated.	Attack.	Incubation.
5 (3)	Oct. 15, 4 p. m.	Oct. 20, 6 p. m.	5 days 2 hours.

Case 5 received subcutaneously 0.75 cc. partially defibrinated blood 15¼ hours old.

TABLE 2.—*Period of incubation in yellow fever, etc.*—Continued.

[Reed and Carroll: "The etiology of yellow fever; a supplemental note," Am. Med., Feb. 22, 1902.]

Case No.—	Inoculated.	Attack.	Incubation.
6 (7)	Oct. 15, 11 a. m	Oct. 19, 3 p. m	4 days 4 hours.
7 (8)	Oct. 15, 11.05 a. m	Oct. 19, noon	4 days 1 hour.

Cases 6 and 7 were inoculated subcutaneously with 3 cc. of an equal volume of water and serum filtered through a Berkefeld filter.

[Marchoux, Salimbeni, and Simond: "La fievre jaune," Rapport de la mission française, Institute Pasteur, Annales, November, 1903.]

Case No.—		Incubation.
8 (1)	1 cc. serum	5 days 5 hours.
9 (3)	5 cc. serum heated to 55° for ten minutes; five days later, 10 cc. heated to 55° for ten minutes; seven days later, 1 cc. blood. This was a "remarkably benign case," and as the man had been injected previously with heated yellow fever serum, the immunity produced probably explains the long period of incubation as well as the mildness of the attack.	12 days 12 hours.
10 (4)	5 cc. serum heated to 55° for twenty minutes; seven days later, 10 cc. serum heated to 55° for ten minutes; eight days later, 1 cc. serum heated to 55° for five minutes. Then 1 cc. serum. The same explanation for this unusually long period of incubation as above, especially as a parallel case similarly treated showed an immunity.	8 days 5 hours.
11 (7)	1 cc. serum filtered through a Chamberland F filter	5 days 18 hours.
12 (8)	do	12 days 18 hours.
13 (13)	0.1 cc. (1 drop) of serum	4 days 18 hours.
14 (15)	5 cc. blood, 5 days old	2 days 21 hours.

[Francis and Beyer.]

Case No.—	Inoculated.	Attack.	Incubation.
15 (2) [a]	Sept. 15, 4 p. m	Sept. 17, (?) a. m	1 day, 15 hours (about).
16 (3) [b]	do	do	Do.
17 (4) [c]	do	Sept. 17, 9 a. m	1 day, 17 hours.

[a] Intravenous injection of 1.75 cc. serum diluted with an equal volume of salt solution and filtered through a Chamberland B filter.
[b] Intravenous injection of 2.5 cc. serum diluted with an equal volume of salt solution and filtered through a Chamberland B filter.
[c] Intravenous injection of 2.5 cc. serum diluted with an equal volume of salt solution and filtered through a Chamberland B filter.

It will be noted from these 17 cases that the period of incubation of yellow fever produced by the inoculation of blood or blood serum is not so constant a factor as in Table 1, in which the disease was induced by the bites of mosquitoes.

The shortest time in this table is one day fifteen hours, and the longest twelve days eighteen hours.

Surg. H. R. Carter, Public Health and Marine-Hospital Service, has given special attention to this phase of the subject, and we are indebted to him for valuable suggestions.

THE FILTRATION OF YELLOW-FEVER BLOOD.

Reed and Carroll (Am. Med., Feb. 22, 1902) were the first to filter yellow-fever blood and prove the infectiousness of the filtrate. They passed it through a Berkefeld filter, which on testing held back the *Staphylococcus pyogenes aureus*.

The filtrate showed no growth in bouillon, and yet when injected into nonimmunes produced yellow fever. The blood from the latter was also shown to be capable of producing yellow fever when injected into a third subject.

That the men inoculated with the filtrate suffered from yellow fever induced by a morphologic entity which passed the filter, and not from a toxemia, was shown not only by their rather long periods of incubation, but was conclusively shown by carrying their experiment to the third degree.

The following experiments were planned in order to determine among other things whether the organism of yellow fever, as it exists in the blood serum, is capable of passing the pores of the Pasteur-Chamberland B filter:

An investigation of the literature of the other filterable viruses shows that the South African horse sickness is the only one which has yet been reported as having passed the Chamberland B filter.

In the filters of the Pasteur-Chamberland system those marked "B" are finer, more compact, with thicker walls, and consequently less porous than those marked F. We have been informed by Assistant Surgeon-General H. D. Geddings, who has recently inquired about this in Paris, that only two grades—B and F—are now being made.

The subjects used for our experimentation were all volunteers, nonimmunes, and carefully selected from among the native Mexicans at Jalapa and the adjacent mountainous country, taken by train to Vera Cruz, and immediately placed within the screened wards of our hospital. All cases recovered.

Jalapa is a town having an elevation of about 4,000 feet, where yellow fever has never been known to spread and has not existed, except for the cases occasionally imported from the coast (tierra caliente).

In order that the case from which we drew the blood for filtration should be one in which there was the highest degree of confidence as to the diagnosis of yellow fever, we decided to produce the disease through the bites of infected mosquitoes rather than to select a case by clinical evidence alone from the yellow-fever wards.

Mosquitos which had been allowed to feed upon typical cases of yellow fever in San Sebastian Hospital, Vera Cruz, were applied in succession to the hands of four persons whom we had selected as being nonimmunes. The first three failed to become infected, but the fourth took sick with what proved typical yellow fever. The histories of the three negative cases are here given in brief:

G. M., age 22, Mexican.—On August 13 he was taken to Vera Cruz and placed in our screened ward. August 15, at 3.20 p. m., he was bitten by two mosquitoes which had fed twelve days previously, at 9.30 a. m., on J. R., a fatal case of yellow fever. Nothing unusual was noticed in the patient during the period of observation, which continued until August 28.

J. O., age 18, Mexican.—He was taken to Vera Cruz August 13 and placed in the mosquito-proof ward. On August 28, at 9.30 a. m., he was bitten by four mosquitoes, two of which had fed sixteen days previously, at 4 p. m., on A. L., a fatal case of yellow fever, forty hours after the onset of the disease, and the other two had fed fifteen days previously, at 10.30 a. m., on the same case fifty-eight hours after the onset of the disease. The patient remained perfectly well throughout the following month while under observation in the screened room.

M. R., age 21, Mexican.—He was brought to Vera Cruz August 28 and kept in the screened ward. On September 1, at 6.30 p. m., he was bitten by two mosquitoes which had fed nineteen days before, at 10.30 a. m., on A. L., a fatal case of yellow fever, fifty-eight hours after the onset of the disease. The patient continued in his usual health during Sepember 2 and 3. On September 4, at 2 p. m., on going into the ward the patient was found wrapped in his blanket and said he felt chilly and complained of slight temporal headache. There was no elevation of temperature.

The next case succeeded:

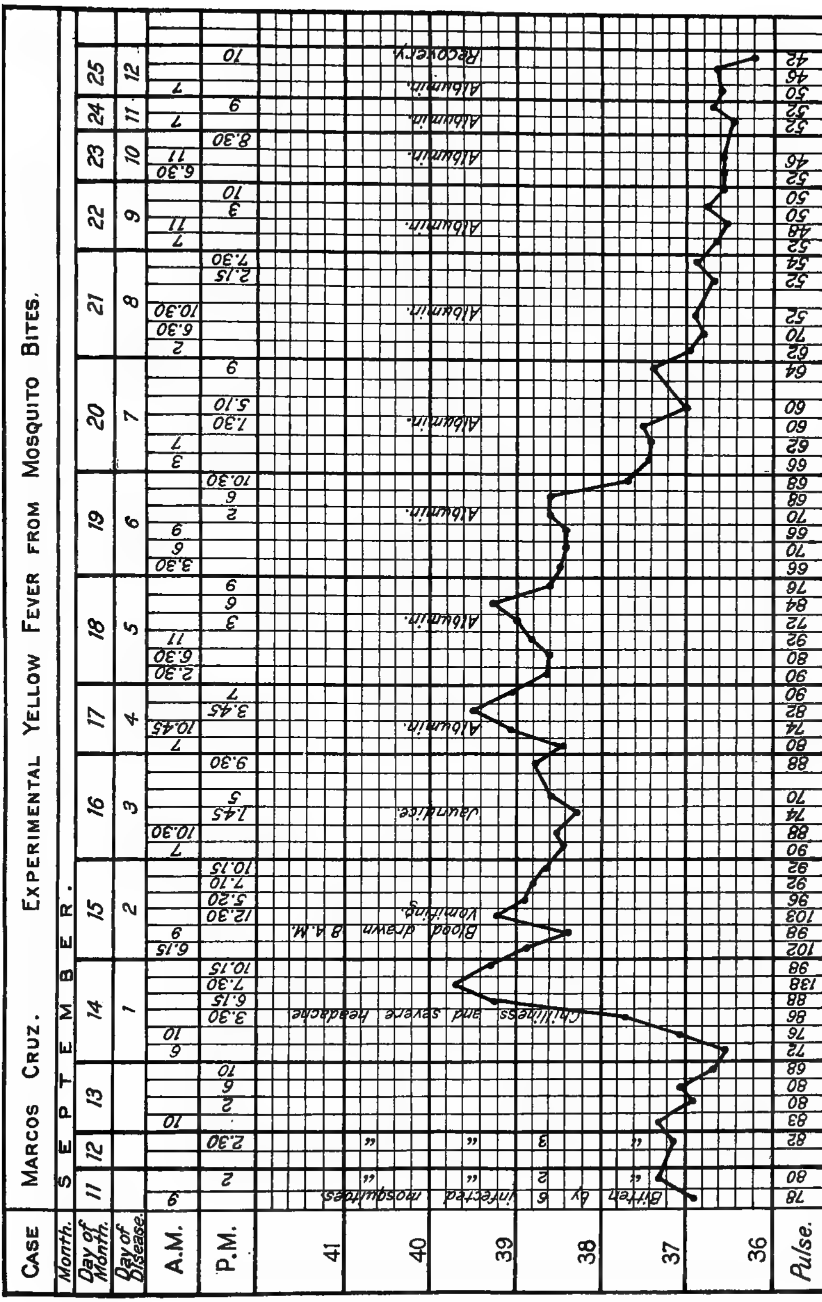
Yellow Fever Produced by the Bites of Mosquitoes.

Marcos Cruz (case XLII), age 21, born in Perote, a mountain town free from yellow fever, where he has always lived. States that he never had fever of any kind. He was physically sound on examination, and brought to Vera Cruz, where he was immediately placed in a mosquito-proof room and kept under observation for fourteen days, when he was bitten by 11 mosquitoes, as follows:

On September 11, at 9 o'clock a. m., 3 mosquitoes which had fed fifteen days previously, at 9.30 a. m., upon Trinidad Martinez, a fatal case, fifty-one hours after the onset. At the same time, 3 other mosquitoes, which had fed fourteen days previously, at 2.30 p. m., upon Hipolito Vasquez, a fatal case, sixty-nine hours after the onset of the disease. At 2 p. m. of the same day he was bitten by 2 more mosquitoes, which had fed fourteen days previously, at 2.30 p. m., on Hipolito Vasquez, sixty-nine hours after the onset.

The next day, September 12, at 2.30 p. m., he was bitten by 3 mosquitoes, 2 of which had fed fifteen days previously, at 2.30 p. m., on Hipolito Vasquez, sixty-nine hours after the onset of the disease, and the other had fed sixteen days previously, at 9.30 a. m., on Trinidad Martinez, fifty-one hours after the onset of his disease.

On September 12 and 13 the patient had no symptoms, and his temperature remained normal.



Temperature chart of Marcos Cruz.

September 14, at 4 p. m., Cruz complained of feeling chilly and had frontal headache. The chilly sensation lasted for several hours and the headache became so severe that he was given ice caps to his forehead for the relief of this symptom. The conjunctivæ became injected; the gums turgid and red.

The case continued clinically with typical symptoms of yellow fever.

On September 15, at 8 a. m., there was a slight icterus of the eyes; at 10 a. m. there was marked vomiting; at 7 p. m. the gums were very much swollen. Urine contained no albumin.

September 16: Eyes injected and yellowish, skin jaundiced; no albumin.

On September 17, the third day of the disease, albumin first appeared in the urine and was found daily until September 25, after which examination was discontinued.

On September 15, at 8 a. m., 16 hours after the onset of the disease 80 cc. of blood were drawn into a sterile flask by means of an aspirating needle from the median basilic vein of his left arm.

The flask was set aside in the lower part of the ice chest, at a temperature of from 16° to 19° C., for five hours in order to allow the blood to coagulate.

Thirty-five cubic centimeters of the clear serum were then drawn off, and to it was added an equal volume of physiological salt solution.

The mixture was transferred with all due precautions to the inside of a Pasteur-Chamberland B bougie and filtered from within outward by means of vacuum, which was applied to the outer surface of the filter in a reverse manner to that shown in fig. 2, omitting the paraffin cup.

It required one hour to obtain 13.5 cc. of filtrate, which was used for the injection of three nonimmunes, Bonifacio Orea, German Ramos, and Guadalupe Gomez.

Orea and Ramos each received 5 cc. of the filtrate, injected intravenously into one of the veins of the arm. As the same was diluted with an equal volume of salt solution, each man received 2.5 cc. of the original blood serum.

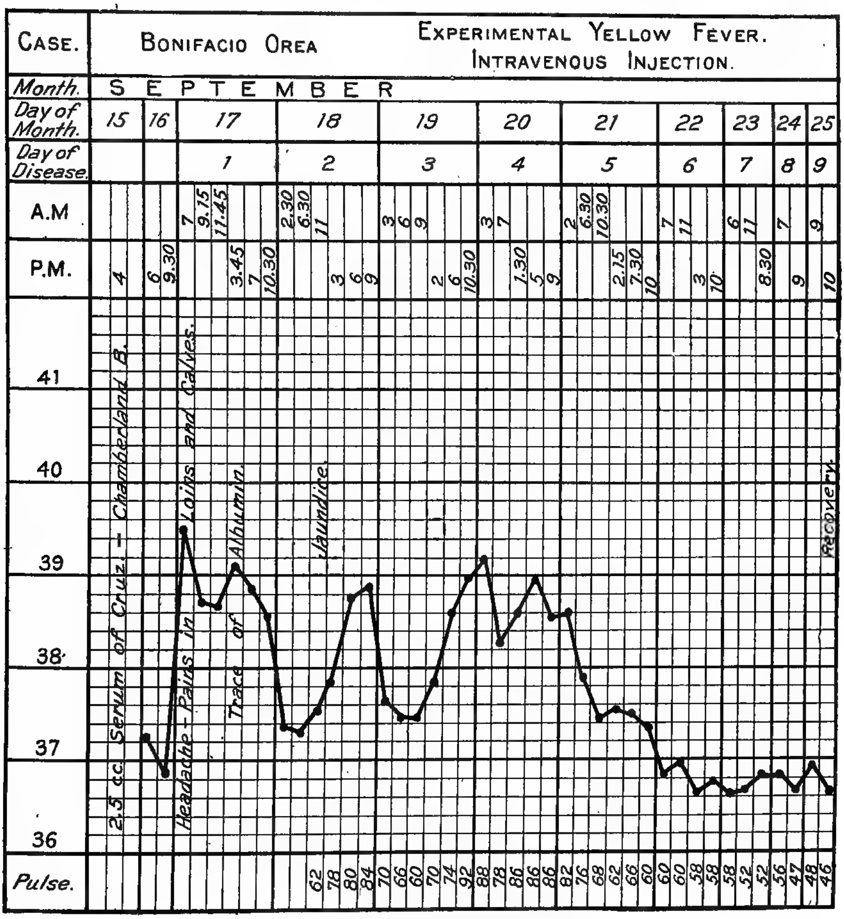
Gomez received 3.5 cc. of the mixture, representing 1.75 cc. of the original serum.

These injections were made at 4 p. m. September 15, which was just eight hours after the blood had been drawn from Cruz, the blood having kept five hours at a temperature of 16° to 19° C. and three hours at room temperature.

Yellow Fever Produced by the Inoculation of Blood Serum.

Bonifacio Orea (case LXV), aged 33, single; born in the mountains near Puebla; said that he had never been on the coast and never had any sickness of any kind. He was physically sound on examination; blood and urine negative.

He was brought to Vera Cruz August 28 and kept in a mosquito-proof room under observation for eighteen days.



Temperature chart of Bonifacio Orea.

On September 15, at 4 p. m., he was given an intravenous injection into one of his arm veins of 5 cc. of Marcos Cruz's diluted serum filtered through a Chamberland B bougie. As the serum had been diluted with an equal quantity of physiological salt solution Orea actually received 2.5 cc. of the blood serum of Cruz. (For details of this filtration, see p. 62.)

On September 16 there were no symptoms.

September 17, at 7 a. m., he was found with a temperature of 39.5° C., with marked frontal headache, pains in the loins and calves of the legs. His gums were slightly swollen and he had injection of the ocular conjunctivæ. The patient said that at 1 o'clock in the morning he felt like stretching and had a chill. The blood showed no malarial parasites. Urine showed a trace of albumin.

September 18: Eyes and body jaundiced.

The patient made a rapid recovery after a mild but definite attack of yellow fever.

German Ramos (case L), aged 22, single; has always lived in the mountains near Puebla. He was given a careful physical examination August 26. Blood and urine negative. He was brought to Vera Cruz August 28 and immediately placed in a mosquito-proof room, where he was kept under observation eighteen days, when he was given an injection of filtered serum, as follows:

On September 15, at 4 p. m., he was given an injection into the right median basilic vein of 5 cc. of diluted serum of Marcos Cruz, filtered through a Pasteur-Chamberland filter B. This serum having been diluted with an equal volume of physiological salt solution, Ramos received 2.5 cc. of the serum of Cruz. (For details of this filtration, see the records of Marcos Cruz, page 62.)

September 16, no change.

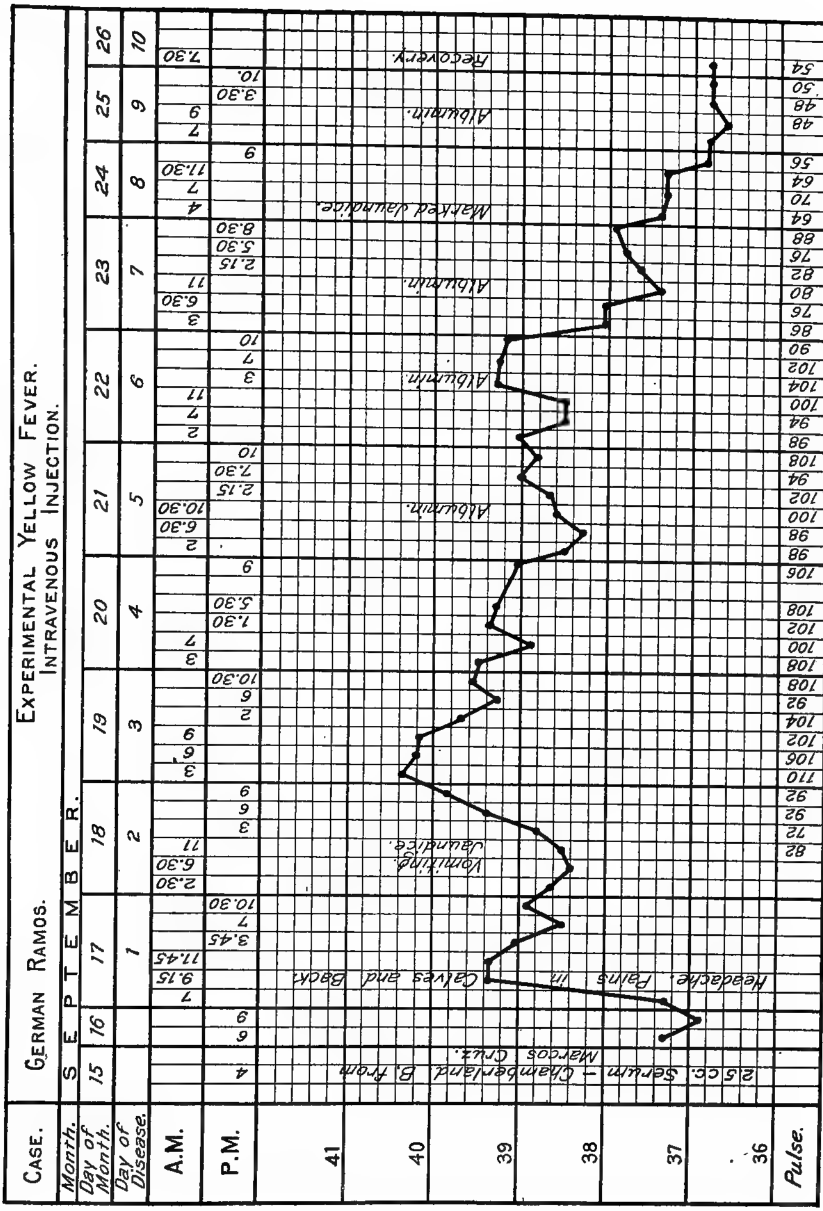
September 17, at 7 a. m., his temperature was 37.3° C., and he did not feel at all unusual; but at 9.15 a. m. his temperature was 39.4°. He had frontal headache, pains in the back and calves of the legs. The blood was negative for malaria.

September 18, the eyes were injected and the body jaundiced. Patient vomited twice. He exhibited a typical clinical picture of yellow fever.

His temperature on the third day was higher than at the onset of the disease, which is rather unusual, and in Vera Cruz is considered a grave sign. It will also be noted that his febrile period, which lasted seven days, did not show the characteristic remission. Albumin first appeared on the 21st and continued until the 25th, when examination was discontinued.

Patient recovered.

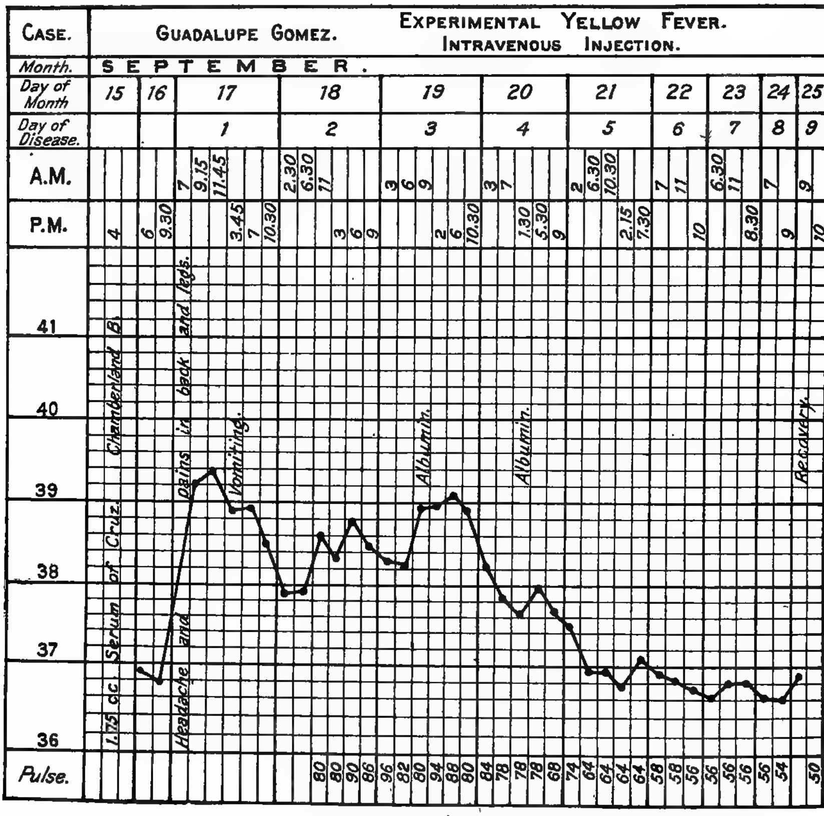
Guadalupe Gomez (case LI); born in Jalapa, aged 17, had never been on the coast, and states that he never had any kind of fever. He was physically sound when examined; blood and urine negative. He was brought to Vera Cruz August 28 and placed in a mosquito-proof room, where he was kept under observation eighteen days.



Temperature chart of German Ramos.

On September 15 at 4 p. m. he was given an injection of 3.5 cc. of diluted blood serum from Marcos Cruz, filtered through a Pasteur-Chamberland B filter. As this serum had been diluted with an equal quantity of physiological salt solution, he actually receved 1.75 cc. of Cruz's serum. The injection was given into one of the superficial veins of the arm.

September 16, no symptoms.



Temperature chart of Guadalupe Gomez.

September 17, 7 a. m., had a temperature of 38.1° C., frontal headache and pains in the back and in the calves of the legs. Says he first felt chilly at 10 o'clock of the previous night Vomited yellowish fluid. No malaria, no albumin.

September 18, no albumin, no malaria, gums swollen. Bleeding from right nostril.

September 19 and 20, urine shows albumin, but none subsequently. Patient made a rapid and uneventful recovery.

REMARKS ON FILTRATION EXPERIMENTS WITH YELLOW-FEVER BLOOD.

We have been careful to give with some minuteness all the details of the manner in which the blood was filtered in these experiments. We know that the filtration of micro-organisms or other small particles through porcelain or diatomaceous earth is influenced very much by the length of time the filtration is continued, the pressure used, by the character of the fluid in which the particles are suspended, the temperature, and other factors which are perhaps less known.

Our review of the literature on the filtration of blood and body juices containing the infectious material of diseases, the causes of which are unknown and which are believed to be ultramicroscopic, disclosed reports of successful and unsuccessful filtration with such meager details that it is difficult to draw proper conclusions. Those factors which control the power of a given filter to allow an organism to pass or to hold it back also account for the different results which various experimenters have obtained in certain cases.

For instance, we succeeded in passing diluted yellow-fever serum through the closest-grained Pasteur-Chamberland B filter that we could obtain, whereas the French commission—Marchoux, Salimbeni, and Simond—working at Rio de Janeiro, failed to pass the infective agent of yellow fever through a Chamberland B filter, though they found that it did pass through the Chamberland F filter,. As the French commission used undiluted blood and we used diluted serum, the apparent discrepancy in results is accounted for; for it is a well-known fact that particles suspended in an albuminous medium filter with more difficulty than particles suspended in water, alcohol, or other limpid menstra of this character.

Nocard, Roux, and Dujardin-Beaumetz, in 1899, endeavored to repeat Löffler's experiment with aphthous fever. They first failed to pass the infective agent contained in the lymph of this disease through a Berkefeld filter because they used an albuminous fluid, viz, "Martin's serum-bouillon," in order to dilute the lymph with a nutrient medium, thus hoping to obtain cultures without the danger of contamination in the filtrate. They found, however, that the albuminous matter contained in the diluting fluid clogged the pores of the filter, so that the filtrate was not virulent.

They repeated the experiment, using water to dilute the lymph in the proportion of 1 to 50, when they found the organisms causing aphthous fever readily passed through a Berkefeld filter, and gave the disease by intravenous injection to young and old cattle.

It is also a well-known fact that filters which successfully hold back certain bacteria will permit them to pass if the filtration is continued long enough. In this case the organisms are believed to grow through the pores of the filter.

It is also evident that the passage of small particles through the pores of a filter depends directly upon the pressure used, and in all filtration experiments the exact pressure, whether positive or negative, should be stated.

It is further necessary to call attention to the very great discrepancy in filters. We have made a careful study of various filters found upon the market and find that there is no satisfactory method by which they can be accurately graded, although we find in certain makes an attempt to graduate the power of the filter. Filters of course should always be tested under water with air pressure for pin holes and cracks, and also with small bacteria for permeability. It is only in this way that we may determine approximately what a particular filter is capable of doing.

The Berkefeld filters, made of diatomaceous earth, are more porous and variable than the Pasteur-Chamberland bougies, made of unglazed porcelain, which have finer pores and are more constant in their ability to filter micro-organisms.

After filters have been tested they must be dried and sterilized with the greatest care in order to prevent cracking, and should always be tested for porosity with microbes after filtration in order to insure this point.

We have found in testing various filters that the weakest part is apt to be the joint, and that in any mechanical arrangement of the filter and flask there is the greatest danger of contamination and untrustworthy results if either the liquid that is being filtered or any other fluid comes in contact with a joint.

It will be noted that in the arrangement which we had for filtration by pressure (fig. 2), the fluid was simply passed into the Pasteur-Chamberland candle and withdrawn by means of a pipette in such a manner that contact between the two fluids was eliminated, and that no dependence was placed upon the security of any joints except those necessary to retain the air pressure. In the case of the small Berkefeld filter (fig. 3), in which the filtration was done by the pressure of the atmosphere produced by a vacuum, the joint between the filtering candle and the metal top was kept well out of the liquid, so that here again was avoided the possibility of error from this source.

TESTING OF FILTERS WITH OBJECTS OF "ULTRAMICROSCOPIC" SIZE.

Four filters of the Pasteur-Chamberland system, letter B, were tested to determine whether they would allow particles of microscopic size to pass into the filtrate.

At the outset we were confronted with the difficulty of finding a substance suitable for such a purpose. The substance should be in a very fine state of division, composed of particles grading gradually in size from the ultramicroscopic to those of definite microscopic size The substance should be insoluble in the menstrum, so that a particle recognized in the filtrate would not represent a precipitate formed after passing the filter.

We finally selected carbon on account of its insolubility, the very fine state of division into which it can be brought, and the ease with which the small particles may be recognized because of their black color and violent Brownian movement.

To 60 cc. of distilled water we added 40 drops of Higgins's American india ink, bought on the market, and this suspension was placed into each of the four Chamberland B filters and drawn through the walls from within outward by a vaccuum in a reverse manner to fig. 2. The first water to come through was pale, but gradually it became slightly brown and later the surface of the filter took on a distinctly dark color. About one and a quarter hours was required for the 60 cc. to pass through each filter.

The filtrates of the four filters were examined with Zeiss microscopes, using objectives of 1.5 and 2 mm. and oculars 4 to 12, and there was not the slightest difficulty to see in the hanging drops small particles of carbon in active Brownian movement. Dried specimens of the filtrate showed small particles plainly visible.

These filters were new and were tested under pressure beneath the surface of water and found free from cracks and pin holes. Before testing with the india ink they were washed with distilled water, about 200 cc. being put through each one.

The filters first became black in disseminated points on the surface. The black areas were of irregular shape, having a diameter of one-eighth to one-fourth inch. As the filtration continued these areas became larger. At the end of the filtration the filter had a distinctly mottled appearance, showing streaks of white, small circumscribed areas of deep black, and larger areas less deeply stained. That these areas of black are carbon may be demonstrated by burning them in the flame.

This shows a lack of uniformity in the structure of each individual filter, which only confirms what may be seen after breaking a filter into pieces. At places air spaces may be seen which may extend through almost the entire thickness of the wall, thus reducing the real thickness of the filter to a mere shell.

Two new Berkefeld filters, $2\frac{1}{4}$ by $\frac{5}{8}$ inches, were tested with the dilute ink solution. Neither pressure nor vacuum was used. The filtrate came in drops in rapid succession and was as black as the test fluid and showed the particles of carbon under the microscope.

These same filters were tested with a bouillon culture of *Staphylococcus pyogenes aureus* in a reverse manner to fig. 2. From three to four hours were taken in passing 150 cc. of the bouillon culture through each filter. The filtrates remained sterile after twelve days in the incubator.

The Berkefeld filters were rigged with the glass cylinders which come with them and a vacuum was used. About four hours were required to run 150 cc. of the bouillon culture through each filter.

THE FILTRATION OF CERTAIN VIRUSES.

Peripneumonia of cattle, rinderpest, foot-and-mouth disease, South African horse sickness, exudative typhus of chickens, mosaic disease of the tobacco leaf, yellow fever, epithelioma contagiosum of fowls, hydrophobia, clavelee, and hog cholera have each been shown to be due to a virus which passes the pores of certain porcelain and diatomaceous filters which hold back the ordinary bacteria.

With the exception of peripneumonia we know nothing of the character of the infective agent in these filtrates, which by direct microscopic examination and by cultural methods have yielded no morphological entity.

The outlook for finding in the body fluids, the specific cause of any one of these diseases, by the microscopes in present use is encouraging as long as we can say that we have a filter which will not allow the virus of the disease to pass, but which does allow the particles of some test substance to be plainly seen in the filtrate.

It is far more important to know what particular filter a certain virus can *not* pass through than it is to know what brands of filter it does pass through. Given a filter that will not permit the virus of a disease to pass through its pores, and if on testing that filter we find that we can put through it visible particles of some test substance, there is plenty of hope that the infective agent of that virus may be visible with our present oil-immersion systems.

On the other hand, if we can find a filter which will not transmit particles of microscopic size and yet will allow the virus of a certain disease to pass into the filtrate, we can not expect to see the individual entities in the virus.

Several factors influence the filterability of a virus, namely, the kind of filter used, the character of the menstruum in which the virus is suspended, the degree of pressure or vacuum used, the amount of time allowed to the process, the temperature, the motility of the particles, and other factors. Unfortunately, in the study of the literature of the various filterable viruses we sometimes fail to find exact data on all these points.

Peripneumonia.—Peripneumonia[a] of cattle is the only filterable virus which has so far given a visible growth on artificial media. Collodion sacs were filled with Martin's peptone bouillon, to which was added a little serum of the rabbit or cow in the proportion of 1:20. The sac was then inoculated with peripneumonia and placed in the peritoneal cavity of rabbits and cows for fifteen to twenty days. The fluid became turbid and in it, under a magnification of 2,000 diameters, could be seen the most extremely small, moving, strongly refractile points. In a series of subcultures made from such a growth the last of the series was virulent.

The colonies on agar mixed with bouillon-serum, were transparent, small, and made up of exceedingly fine particles whose form it was impossible to determine. The microbe of this disease was made to pass the Berkefeld and Chamberland F filters, but when an albuminous diluting liquid was used, it could not be made to pass either.[b]

Foot-and-mouth disease.—Loeffler and Frosch[c] state that lymph was taken from the blebs of calves suffering with this affection, diluted with 35 parts of water, and then passed through a filter candle. The filtrate, in amounts which correspond to one-tenth to one-fortieth cubic centimeter of the original lymph, when injected into calves caused them to sicken in two days, the same as the control animals into which were injected equal amounts of unfiltered fluid.

McFadyean says that foot-and-mouth disease passes the Berkefeld filter when in watery suspension, but is arrested when in an albuminous fluid.

Nocard[d] says that aphthous fever passes through Berkefield, Chamberland, and Kitasato filters.

South African horse sickness.—Nocard[a] succeeded in passing the virus of this disease through a Berkefeld filter only.

McFadyean[e] reports that pure blood taken from an animal sick with the disease was passed through the Berkefeld filter under a pressure of 26 inches of mercury and the filtrate, when inoculated into a horse, produced the disease.

When the blood serum was diluted with four parts of water and

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[a] Nocard, Roux, Borrel, Salimbeni et Dujardin-Beaumetz: Le microbe de la peripneumonie. Ann. de l'Inst. Pasteur, vol. 12, 1898, p. 240, etc.

[b] Nocard, Roux, and Dujardin-Beaumetz: Etudes sur la peripneumonie. Recuil de med. vet., 1899, 8e. serie, Oct. 26, 1899, p. 441.

[c] Loeffler and Frosch: Bericht der kommission zur erforschung der maul und klauenseuche bei dem Inst. f. Infek.-krank. in Berlin. Centbl. f. bakt. u. infek., 1898, bd. 23.

[d] Nocard: La "horse sickness" ou "maladie des chevaux de l'Afrique du Sud. Bull. de le soc. centr. de med. vet., n. s., vol. 19, 1901, p. 37.

[e] Journ. comp. path. and therap., 1900, XIII.

filtered through a Chamberland B filter for two hours under a pressure of 29 inches of mercury, the filtrate was infective to a horse into which it was injected. After an incubation of three days and a clinical course of six days the horse died.

Exudative typhus of chickens.—Magiora and Valenti[a] made experiments with the emulsions of the blood, lungs, liver, spleen, kidneys, and heart. They used the Berkefeld filter and Chamberland F. Dilutions were made with 40 and 60 parts of physiological salt solution and a pressure of 1½ atmospheres was employed.

Bacteriological examination of the filtrate proved negative, but chickens injected with 5 cc. of the filtrate died in about two days, presenting the same clinical and pathological picture as the naturally infected ones.

Another set of chickens injected with the blood of the ones which had received the filtrate developed typical symptoms and post-mortem changes of the disease.

An exposure of five minutes at 65° C. sterilizes the virus.

These investigators found that the filtrates had very much less virulence than the unaltered blood. Four cubic centimeters were found to represent the minimum fatal dose of a filtrate from a mixture of blood and water in the proportion of 1:160, whereas 4 cc. represented the minimum fatal dose of an unfiltered mixture of blood and water in the proportion of 1:1,500,000.

It is interesting to note how the filtration experiments cleared up an error which former students had made in regard to the loss of virulence in pure cultures of organisms which they had isolated in this disease. They had found a cocco bacillus in the internal organs. The culture tubes inoculated from the body fluids showed growths of this organism. Inoculations into chickens from colonies on the first set of cultures caused the disease, but subcultures from the first set of cultures were not virulent. Into the first set of cultures there had evidently been carried some of the invisible virus along with the cocco bacillus.

Mosaic disease of the tobacco leaf.—Beijerinck[b] pressed the sap out of diseased plants and passed it through very thick porcelain filters, and the filtrate was free from bacteria, but virulent for the tobacco leaf.

Epithelioma contagiosum of fowls.—It was found by Marx and Sticker[c] that the infective agent suspended in sodium chlorid solution passed through a Berkefeld filter, but not through a porcelain filter. The filtrate gave no growth on media; it was carried through a series

[a] Magiora and Valenti: Ueber eine seuche von exsudativen typhus bei hühnern. Zeit. für hyg. und infekkr., vol. 42, 1903, p. 198.

[b] Centrbl. für bakt., Abt. 2. bd. 5. 1899. p. 27.

[c] Deut. med. wochenschr., bd. 28, 1902, p. 892.

of 16 generations in fowls; it resisted 60° C. for three hours, and after one hour in a vacuum tube at 100° C. it was virulent.

Hydrophobia.—Remlinger and Riffat-Bey [a] ground up a rabbit's brain in water together with a bouillon culture of chicken cholera and filtered it by aspiration through a Berkefeld V filter. The filtrate inoculated into rabbits caused rabies.

Celli and de Blasi [b] ground the brain and spinal cord in sand under 300 atmospheres pressure. A suspension in distilled water, when subjected to a small Berkefeld filter under a vaccuum of 570 mm. for half an hour, gave an infective filtrate.

Remlinger (Ann. de l'Institut Pasteur, v. 17, No. 12, 1903, p. 834) confirmed his earlier work with Riffat-Bey mentioned above. He showed that the virus of hydrophobia can not be made to pass through a Chamberland filter nor through a Berkefeld N or W. It can only be forced through a Berkefeld V, which filter is the most porous of the Berkefeld system.

Hog cholera.—De Schweinitz,[c] in a preliminary note, mentions a disease peculiar to hogs, indistinguishable clinically and at post-mortem from hog cholera, but which can be transferred from hog to hog by inoculation with certain body fluids which have been rendered free from bacteria by filtration through the finest porcelain filters. This filtrate was shown to contain no organisms of hog cholera or swine plague, because when inoculated into rabbits and guinea pigs the animals remained healthy.

Rinderpest.—Nicolle and Adil-Bey [d] passed the virus of this disease through a Berkefeld filter, but not through a Chamberland F.

Clavelee (sheep pox).—Borrel [e] filtered a suspension of the pustules in water. The filtrate from the Berkefeld filter was infective, but that from the Chamberland F was not.

Nonfilterability of vaccine and smallpox.—Parke [f] crushed vaccine virus with fine sand, using 25 tons of pressure to the square inch. One portion of the suspension of crushed virus was passed through a Berkefeld filter and another portion through a Chamberland filter. Both filtrates were evaporated over sulphuric acid in a vacuum.

Calves and rabbits inoculated with the filtrate before and after

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[a] Remlinger and Riffat-Bey: Le virus rabique traverse la bougie Berkefeld. Compt. rend. heb. des Sec. de la Soc. de Biol., vol. 55, 1903, p. 730.

[b] Deut. med. wochenschr., vol. 29, p. 945.

[c] U. S. Dept. of Agriculture, Bur. Animal Industry, Circular No. 41, Sept., 1903.

[d] Nicolle et Adil-Bey: Études sur la peste bovine. Ann. de l'Inst. Pasteur, vol. 16, 1902, p. 56.

[e] Borrel: Experience sur la filtration du virus claveleux. Compt. rend., Soc. de Biol., vol. 54, 1902.

[f] Assn. Am. Physicians: Trans., vol. 17, 1902.

evaporation failed to show any reaction. Control animals inoculated with the crushed material before filtration always had successful vaccinations. The object of the crushing was to liberate the organisms from epithelial cells or other tissues which might retain them.

Smallpox virus from three fatal cases failed after crushing to pass into the filtrate, as determined by the inoculation of monkeys.

Filterable bacteria.—Von Esmarch [a] sought to determine whether there are such things as ultramicroscopic organisms among the saprophytes.

We readily believe that the virus of a filterable infectious disease is made of very small organisms, possibly ultramicroscopic, and that if these organisms could be made to multiply the resulting mass would have an appreciable size. If there are ultramicroscopic saprophytes he thought that all conditions were in the highest degree favorable for their multiplication, and that on the ordinary laboratory media they ought to find their most suitable conditions of growth and give an appreciable evidence of their existence.

He used 40 different kinds of fluids, including sewage, rich vegetable infusions, decomposing urine, emulsions of sputum, cavaders, and feces. The clear filtrates from these suspensions were planted on all the laboratory media and these plants kept under different conditions showed no growth.

During the first week's observations of the original filtrate no growth was noted; but after ten days this fluid showed a turbidity which was due to a very fine motile organism (*Spirillum parvum*), which grew as vibrios and spirilla, which were recognized only by the greatest magnification. It passed the Berkefeld, Chamberland F, Reischel, and Pukall filters and appeared in the first 200–300 cc. of filtrates. No other bacteria were found in the filtrates. Its size is about the same as that of the influenza bacillus, being 1 to 3 micra in length and 0.1 to 0.3 micra in width.

Von Esmarch grew bacteria through filters which hold them back in ordinary filtration work. He used Berkefeld, Kitasato, and Maassen filters.

These filters were filled with plain bouillon and were placed in a vessel containing bouillon inoculated with an organism, and the whole was kept at 37°, or room temperature.

Typhoid grew through the Kitasato filter at 37° in twenty-four hours, and at room temperature in two days.

Cholera went through a Maassen filter at 37° in two days, but a control kept at room temperature did not grow through after thirteen days.

A small Berkefeld filter allowed *Bacillus prodigiosus* to pass in

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[a] Centbl. fur bakt., bd. 32, 1902, p. 561.

from one to three days, and a large Berkefeld allowed *pyocyaneus* and *prodigiosus* to pass in seven days.

Wherry [a] states that the bacillus producing pneumonia in guinea pigs (0.5 micron wide and 0.7 micron in length) passed the small Berkefeld No. 5, but was not found in the filtrate from the thicker walled Berkefeld No. 8, nor in the filtrate from the Chamberland F. It, however, grew through the walls of all three.

FOMITES.

While we made no experiments directly designed to determine the part played by fomites in transmitting the infection of yellow fever, still our work strongly bears on this point, and we can fully corroborate the conclusions of Reed and Carroll that fomites or inanimate objects are not dangerous in this respect.

Nonimmunes whom we kept for weeks under observation in our mosquito-proof rooms slept on the same beds, used the same clothing, washed from the same bowl, ate the same food, drank the same water, and breathed the same air as those sick with yellow fever; nevertheless they remained free of all fever except that which was purposely given them by mosquito bites or blood inoculations.

As these experiments were done in the summer time at Vera Cruz, a badly infected city where the disease prevailed at the time in epidemic form, it removes some of the objections which were made at the time to the work of the Army Commission, which for the most part was done during the winter months in an otherwise healthful locality—Camp Lazear.

THE FILTRATION OF MALARIAL BLOOD.

The filtration experiments with malaria were undertaken with the hope that they would throw light upon yellow fever, which bears so many analogies to malaria. Both diseases are transmitted by mosquitoes, and it is therefore natural to suppose that yellow fever is due to an animal parasite, perhaps similar to the well-known plasmodium of Laveran. However, as the one disease is filterable and the other is not; and as the parasite of the one is visible and the other can not be seen with the highest powers of the microscope at present at our command, either in the mosquito or in man; and as the one produces an immunity and the other does not, we find the analogy is not after all so very striking and that it does not seem helpful in solving our problem.

The malarial rosette breaks and liberates spores (*merozoites*) which are exceedingly minute, and in order to carry out the analogy in an

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[a] Journ. med. research, vol. 8, 1902, p. 322.

experimental way we filtered malarial blood in order to determine whether there might be forms of the malarial parasite which are even smaller than this spore.

We know from the work of Novy that a trypanosome (*Trypanosoma Lewisi*), which is a colossal organism when compared with a malarial spore, has forms which are so minute that they pass a Berkefeld filter, for he has succeeded not only in artificially cultivating the adult trypanosome parasite, but in infecting animals with the filtrate from these cultures. We also know from the recent work of Schaudinn[a] that some of the animal parasites (*Spirochaeta*), multiply by reducing division; that is, each time cleavage takes place the organism is reduced in size, and this process continues until the divided forms become too small to be seen as individuals and can be made out only as clusters.

We therefore reasoned that if the malarial parasite has an ultramicroscopic form minute enough to pass the pores of a filter, it would encourage us very much to look for a visible form of the yellow fever organism in the blood and tissues of man and the mosquito by the aid of technique that had not previously been employed.

Our filtration experiments with malarial blood resulted negatively so far as demonstrating the presence of a minute or ultramicroscopic form of this parasite was concerned, but there developed unexpectedly what appears to be a demonstration of the malarial toxin. We produced a definite paroxysm by the inoculation of blood serum freed of the malarial parasites by filtration; and it is reasonable to suppose that the same substance circulating in the blood, which caused the chill, fever, and sweat in one man, caused a precisely similar chain of symptoms in the other two into whom this serum was transferred.

We found that if the blood is drawn after the height of the paroxysm and while the fever is declining this poison is not manifest; but if the blood is taken during the chill and while the temperature is rising, it is present.

If this poison is the toxin causing a malarial paroxysm it is remarkable that it should be present in the blood serum in such a considerable quantity and disappear so very rapidly. Still, the clinical symptoms of the disease would indicate the sudden production of a large quantity of toxin and its rapid elimination, neutralization, or destruction. So far as we know, this is the first time that a poison has been demonstrated which is capable of reproducing the symptoms of a disease due to an animal parasite of microscopic size.

It would be folly from a few observations to claim that we have discovered the malarial toxin. The only conclusion justified is that we have demonstrated the existence of some poison in the blood which is

[a] Loc. cit.

capable of reproducing the symptoms of the disease when injected into the veins of other men.

We are not unmindful of the fact that chemical substances derived from the hemoglobulin or other proteids in the blood may be toxic, and we are of course familiar with the work of Gauldi, Montesano, Mannaberg, Celli, and others, who failed to demonstrate a pyrogenic toxin in malarial blood from similar experiments. The length of time the blood was exposed to the air between the time it was drawn from the malarial patient until it was injected into the person experimented upon may account for the discrepancies in results. The time the blood is drawn in relation to the paroxysm and many other factors should also be taken into account.

Mannaberg[a] drew blood during the attack in a case of ordinary tertian malaria. He centrifugalized it and injected the clear serum subcutaneously into two healthy people.

One received 1 cc. of serum at 4 p. m., when his temperature was 36.7° C. The temperature at 4.30 p. m. was 37° and at 6 o'clock 36°.

The other patient was given 0.7 cc. of the serum and his temperature rose within fifteen minutes after the injection from 36.5° to 37.6° C.

Celli[b] took during the cold stage a small quantity of blood from each of many malarial patients.

Young children were inoculated with 50 cc. of the serum subcutaneously and 50 cc. intravenously.

Another child was given the concentrated serum remaining after treating 260 cc. of serum in a vacuum apparatus at low temperature. The child was injected intravenously and subcutaneously.

From a hemorrhage in a case of severe comatose pernicious malaria 25 cc. of serum were obtained and injected into another patient.

None of the patients into whom the serum was injected showed pyrexia. There was in several instances, however, a slight rise of temperature which the experimenter says may occur after the injection of normal serum.

Rievel and Behrens[c] studied a sarcosporidium of the llama. They removed ten of the sacks and ground them up with physiological salt solution in a mortar, and injected 2 cc. of the fluid subcutaneously into a rabbit. After seven hours the rabbit died. The autopsy revealed nothing unusual.

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[a] Mannaberg, Julius: Die malaria krankheiten. Nothnagel's Specielle Pathologie und Therapie, Bd. 2, 1899.

[b] Celli, Angelo: Malaria. Transl. by J. J. Eyre. Longmans, Green & Co., New York and London, 1900.

[c] Rievel and Behrens: Beiträge zur Kenntnis der Sarcosporidien und deren Enzyme. Centralblatt für bakt. u. parasit. (orig.). Bd. 35, no. 3, s. 341.

Another rabbit received by mouth the contents of several sacks rubbed up in salt solution. This rabbit was given at the same time a subcutaneous injection of 1 cc. of the fluid. The animal died after eight hours. From a gross examination of his internal organs and a bacteriologic examination of the same, nothing abnormal was found.

Blood from the spleens of the above-mentioned rabbits, when injected into three other rabbits, caused no abnormal symptoms.

Pieces of the flesh of the llama were cut up in salt solution and the fluid part was injected into two rabbits subcutaneously. Both remained sound.

A rabbit inoculated subcutaneously with a suspension of the contents of sarcosporidia sacks in salt solution died after seven hours. The post-mortem was negative.

Two other rabbits treated in the same way remained alive six hours. Another died after seven hours.

A suspension was subjected to dialysis and it was found that the dialysat, when injected into a rabbit, caused death within twenty-four hours. The cooked dialysat was inactive.

Our experimental cases in malaria follow:

Filtration Experiments with Estivo-Autumnal Fever.

Filomena Martinez (case LXIII), 35 years old, born in Mexico City, lived in Vera Cruz about one year.

The patient was admitted to the hospital of Working Party No. 2 October 27, at 10 a. m. He had been under observation the previous day and early that same morning at San Sebastian Hospital.

As he showed a heavy infection with malarial parasites he was transferred to our laboratory.

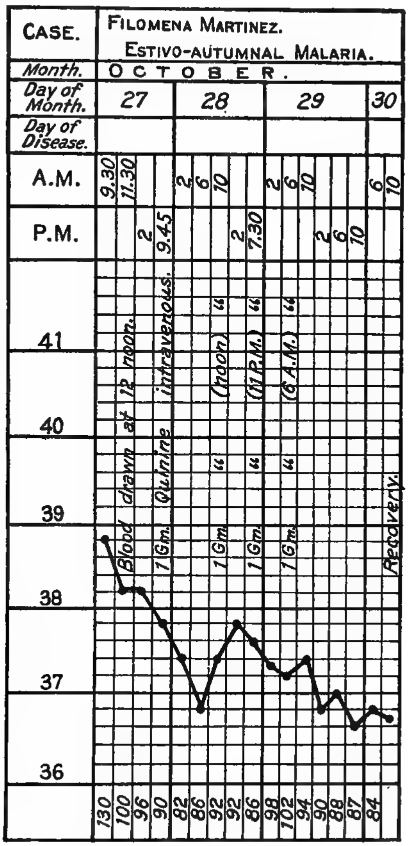
He gives a history of having had yellow fever about six months ago. His present illness, according to his statement, began some two weeks ago with fever, but he says he did not have chills. The patient's mental condition when seen was below par, and he was unable to give consistent answers. He seemed somnolent and was evidently beginning to show the effects of his infection upon the brain.

An examination of his blood, taken at 4.15 p. m., October 26, showed very many young ring forms, some of them with active amœboid shapes. None appeared pigmented in the smears stained with Goldhorn's polychrome methylene blue. Crescents and ovoids also present.

At 12 o'clock noon, October 27, a trifling incision was made through the skin over the median cephalic vein on the right side. A needle was introduced into the vein and 100 cc. of blood were quickly drawn into a sterile flask. The wound was covered with a sterile dressing and healed without complications.

The blood was immediately put into the ice chest, the temperature of which registered between 16° and 19° C. Clotting took place rapidly. The red cells settled to the bottom of the flask, the upper part of the clot being composed of a firm yellowish buffy coat. The serum separated well and was very clear.

The blood serum was drawn off and diluted with an equal volume of an isotonic salt solution and then divided into two portions.



Temperature chart of Filomena Martinez.

One portion was passed through a Chamberland B filter and injected into José Ojeira.

The other portion was passed through a Berkefeld filter and injected into Luis Peredo.

Blood smears made from the blood which was drawn from the vein showed in stained specimens crescents and the young small ring forms of estivo-autumnal malaria. Some of the stained parasites showed one chromatin point, others two. A few were irregular in outline,

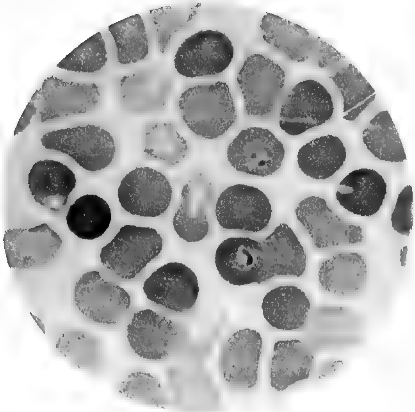
EXPLANATION OF PLATE 2.

Estivo-autumnal malaria.

The character of the malarial parasites in the blood of Filomena Martinez at the time it was filtered.

Stained with Goldhorn's polychrome methylene blue.

1. Small ring forms.
2. Young ameboid forms.
3, 4, 5, and 6. Ovoids.



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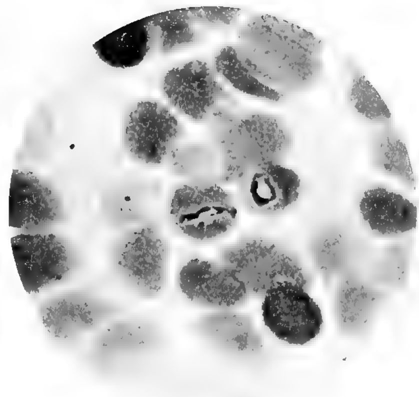

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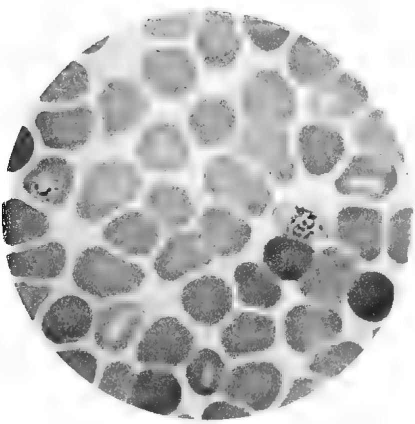

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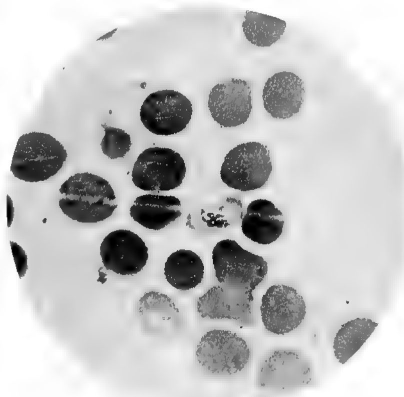

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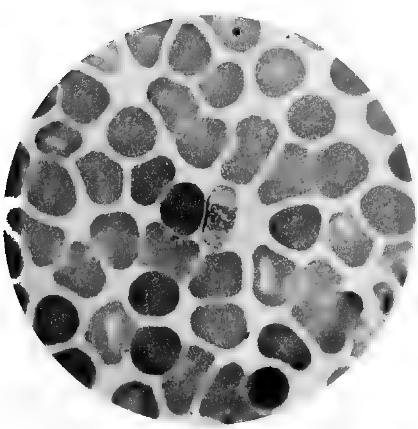

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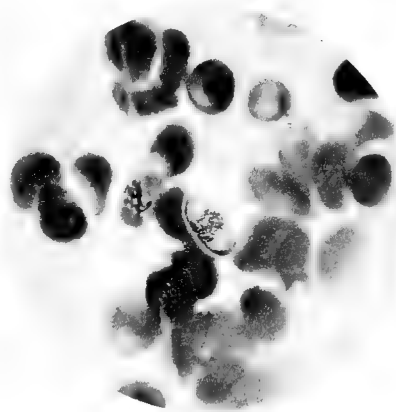

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CHARACTER OF THE MALARIAL PARASITES IN THE BLOOD OF FILOMENA MARTINEZ AT THE TIME IT WAS FILTERED.

indicating older parasites with amœboid motion. These latter were two or three times the size of the small ring forms. (See plate 2.)

These irregularly shaped parasites had two and some three chromatin points. In the blood taken at subsequent periods similar forms were seen, the older or younger forms predominating, depending upon the time of day the blood was examined.

The details of diluting and filtering the blood serum of Filomena Martinez follow:

At 5.30 p. m. the blood was taken from the ice chest, having been there just five and one-half hours, and 27 cc. of the clear serum were pipetted off. This serum contained a few flakes and very few red blood cells.

To this serum was added an equal amount (27 cc.) of physiological salt solution (0.6 per cent).

The mixture was transferred to a filter flask and a Chamberland B filter was carefully lowered into the fluid and securely fastened in position. This was a new filter marked as follows: "B. filtre Chamberland système Pasteur H. B. Cie., Choisy-le-Roi. BTE S. 6.O.G. Contrôlé."

The filter was tested before using with an air pressure of 30 pounds, after which it was lowered into water. When first lowered into the water the air came from every part of the surface of the filter in very fine bubbles, but nowhere was there evidence of a crack or pinhole. As soon as the filter became wet no air could be forced through it with a pressure of 30 pounds. This particular candle was considered to be tighter than the other Chamberland-Pasteur filters which we had similarly tested.

The filter was then thoroughly washed by allowing 200 cc. of water to pass through it under 20 pounds pressure. It was sterilized in the hot air sterilizer for one hour on the day before the blood was filtered, at a temperature of 150° C. for one hour.

The filtration was begun at 6 p. m., October 27, and was conducted in accordance with the diagram (fig. 2) by means of pressure from an air pump. This air pump was worked by hand and the diluted blood serum filtered under a pressure of 15 pounds. The pressure was controlled by the gauge, as shown in the sketch.

Very slight variations occurred both above and below 15 pounds, owing to the difficulty of exact control with hand power.

The pressure was kept up for one hour, and the filtrate was drawn from the inside of the bougie with a long sterilized pipette. In this manner it will be noticed that there was no possible chance of contact between the filtrate and the blood serum, and throughout the process the greatest care was taken in order to prevent such a contamination. The filtrate as it came through the filter was clear and of amber color.

At 7.20 p. m. 20 cc. of the filtrate were injected by means of an appropriate syringe with hypodermic needle into the left median cephalic vein of José Ojeira with entirely negative results.

A second portion of the blood serum of Filomena Martinez was

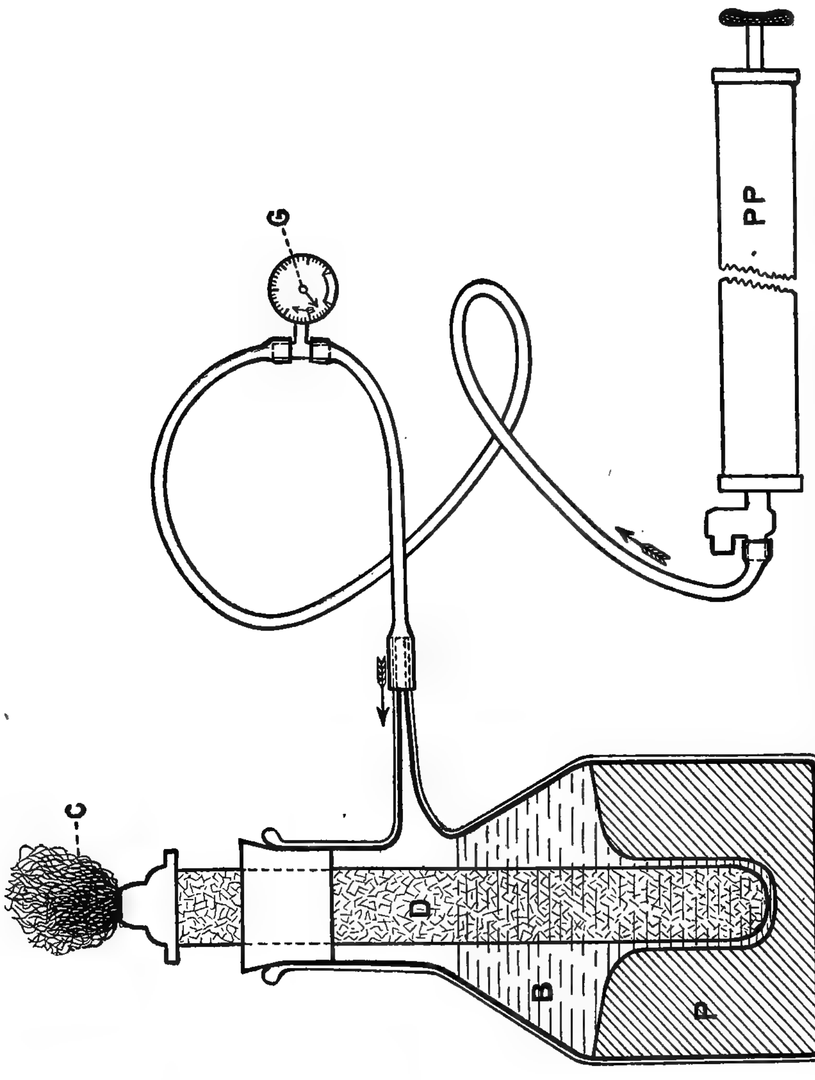


FIG. 2.—The arrangement used for filtering through a Pasteur-Chamberland bougie B. PP, pressure pump. G, pressure gauge. D, Pasteur-Chamberland bougie, stopped with cotton and sterilized; held in place by a rubber stopper. P, a molded cup of paraffin to keep the small quantity of blood in contact with the surface of the filter. B, the blood serum.

pipetted off and diluted with an equal quantity of physiological salt solution, and filtered through a small Berkefeld filter, as follows:

A new Berkefeld filter was prepared by thoroughly washing by allowing water to pass through it for several hours, and then sterilized in dry heat.

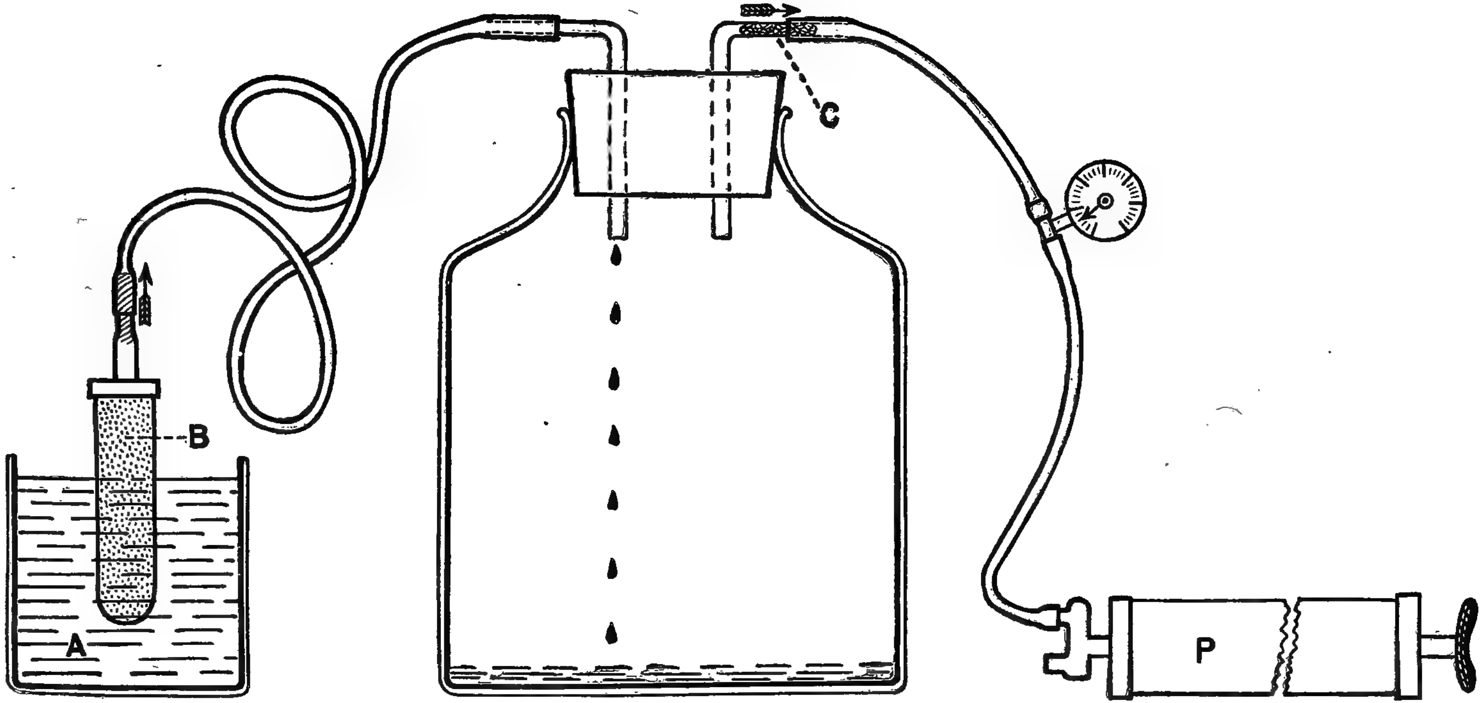


FIG. 3.—Showing the method of filtering through a Berkefeld filter by means of a hand vacuum pump. A, flask containing the blood serum. B, Berkefeld bougie. C, cotton plug. P, hand pump.

This filtration was also done from without inwards, as may be seen by reference to the sketch (fig. 3), but by using vacuum instead of direct air pressure, as in the case of the filtration through the Pasteur-Chamberland bougie. The filtrate was carried over to a sterile bottle, as shown in the sketch, and drawn out with a pipette, so that, care being taken, there could be no chance of contamination. It required about twenty minutes to filter 46.5 cc. of diluted serum, and at 8.15 p. m., viz, eight and one-fourth hours after the blood was drawn, twenty cubic centimeters of this filtrate, which represented 10 cc. of the original serum, were injected into the left median basilic vein of Luis Peredo with entirely negative results.

This filter was then thoroughly washed with water which ran through in drops under atmospheric pressure, and was preserved for further testing, with the following results:

On March 1, 1904, this filter was tested with a bouillon culture of *Staphylococcus pyogenes aureus*. The filtrate remained sterile after ten days in the incubator.

At 10 p. m. Martinez was given 1 gram of bimuriate of quinine directly into one of the veins of his arm. This was repeated at noon on October 28, and again at 11 p. m. on the same day.

On the 29th he received another gram into the vein, with marked improvement in his symptoms and a notable reduction in the number of intracorpuscular forms in the blood, as will be seen by the following notes of the case:

October 27, 10 p. m.—One gram bimuriate of quinine intravenously. Blood examination, 3 crescents in one field; some fields have as many as half a dozen small ring forms.

October 28, 2 a. m.—Blood examination. Some fields have 5 and 6 small ring forms, some irregular amœboid shapes, also ovoids.

6 a. m.—Blood examination. One or two ring forms to each field; also crescents.

10 a. m.—Blood examination. About 1 organism to each field; some young ring forms; some amœboid shapes; also ovoids.

12 noon.—One gram bimuriate of quinine intravenously.

2 p. m.—Blood examination. About 1 intracorpuscular form to each field.

11 p. m.—One gram bimuriate of quinine intravenously.

October 29, 2 a. m.—Ten-minute search of a slide stained with polychrome methylene blue showed no intracorpuscular forms; crescents not diminished in numbers.

6 a. m.—Only 2 intracorpuscular rings seen; crescents in moderate numbers.

10 a. m.—Given 1 gram bimuriate of quinine into a vein. Five-minute search of a stained blood smear shows 5 ovoids and only 1 intracorpuscular ring form.

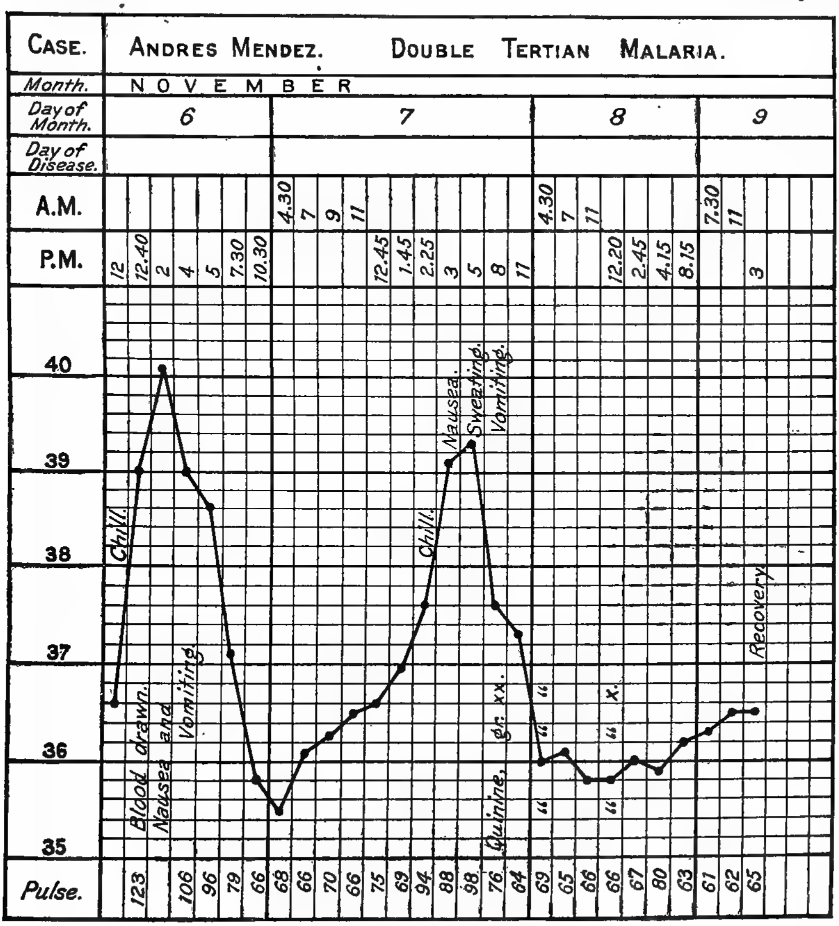
2 p. m.—No intracorpuscular forms.

10 p. m.—No intracorpuscular forms.

October 30, 6 a. m.—Blood examination shows no intracorpuscular forms. A large mononuclear leucocyte has much brown pigment. Ovoids still present in apparently undiminished numbers. Patient has very much improved in his general condition. His mind is better, appetite has returned, and he was returned to San Sebastian Hospital.

Filtration Experiments with Tertian Fever.

Andrez Mendez (case LXVI), 39 years old; born in La Luz, Estado de Guanajuato; never had fever in his native place. In 1878 had yel-



Temperature chart of Andres Mendez.

low fever (?) in San Antonio, Estado de Guanajuato, with which he says he was sick about one month. He came to Vera Cruz three years ago and has had fevers five or six times since.

Present illness dates from about November 3, but states that he has been troubled with mild attacks of fever for a month, which he describes as coming on alternate days, but not sufficiently severe to keep him from his work.

The fever which initiated his present sickness began with a severe chill, and was followed by fever and sweat, and was associated with some nausea and vomiting. He states that these paroxysms were repeated daily until his admission to San Sebastian Hospital, November 6, 1903.

Blood examination showed that he had a heavy infection with tertian parasites, and he was immediately transferred to the laboratory of Working Party No. 2, Yellow Fever Institute.

The man was physically robust, but very anemic, mucous membranes particularly pale, skin cold and damp.

At about noon on this date (November 6), the patient was seized with a chill.

By 12.30, half an hour later, the rigor was very marked; he lay in bed with a blanket drawn over his head, and was shaking violently; he could not hold a thermometer in his mouth, and the pulse was taken with difficulty. During this time the temperature was rapidly rising, it being now 39.1° C.

At 12.40 blood was drawn from one of the superficial veins at the bend of the elbow. On account of the rigor there was some difficulty in introducing the needle. The blood flowed freely; 125 cc. were quickly drawn. It was permitted to flow into a porcelain dish and immediately defibrinated by whipping with sterilized forks. Clotting took place very quickly, so that the fibrin was readily and quickly separated from the fluid.

Judging from the size of the clot and color the fibrin had enmeshed a number of corpuscles. The defibrinated fluid showed no further tendency to clot, and on microscopical examination looked like fresh blood containing a normal number of corpuscles.

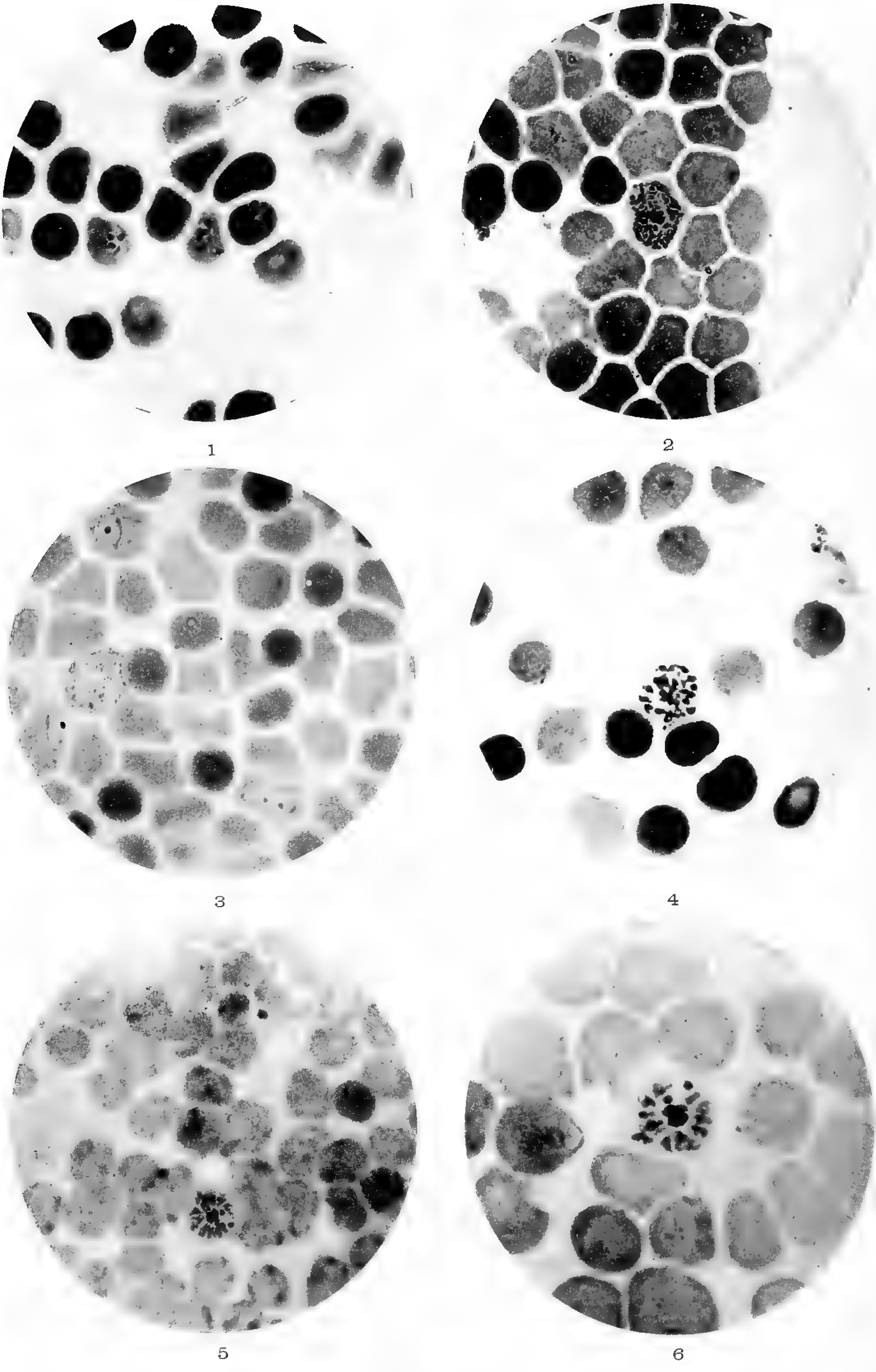
To 25 cc. of defibrinated blood was added 25 cc. of physiological salt solution, and this diluted blood was filtered through the same Berkefeld filter in the same manner as was done with the blood of Filomena Martinez (see p. 84). This filter, when tested later, March 1, 1904, held back *Staphylococcus pyogenes aureus*.

Nine cc. of the filtrate were injected into the right basilic vein of Luis Peredo as soon as this amount could be obtained. This injection took place at 1.40 p. m. It only took about forty minutes to defibrinate and filter the blood, which process was done as rapidly as possible.

Stained smears of the filtrate showed no morphologic elements. The filtrate had a distinct red color. For the method by which this filtration was done, see fig. 3.

As a control, José Ojeira, at 2 p. m., was given an injection into

Plate 3.



CHARACTER OF THE MALARIAL PARASITES IN THE BLOOD OF ANDRES MENDES AT THE TIME IT WAS FILTERED.

EXPLANATION OF PLATE 3.

Double tertian malaria.

The character of the malarial parasites in the blood of Andres Mendez at the time it was filtered.

Stained with Goldhorn's polychrome methylene blue.

1. Young ameboid forms.
2. Older pigmented parasite.
3. Young and old forms in the same field.

4, 5, and 6. Segmenting forms.

his left basilic vein of 4 cc. of the *unfiltered* mixture. As the blood was diluted with equal parts of salt solution, he therefore received 2 cc. of Mendez's blood.

The unfiltered mixture of defibrinated blood and salt solution, upon microscopic examination shortly after Ojeira received his injection, showed amoeboid tertain organisms with dancing pigment. For the character of the malarial parasites infecting the blood of Mendez, see illustration, plate 3.

After drawing the blood from Mendez he continued to have a chill, with severe rigor and chattering of the teeth, accompanied by nausea and vomiting. His temperature continued to rise after the blood was drawn until it reached 40.2° C. The febrile period was followed by drowsiness and moisture of the skin.

As will be seen by reference to the temperature chart, Mendez was kept under observation without quinine, and had another typical malarial paroxysm the next day. All the evidence in his peripheral blood, which was examined frequently, pointed to a severe double infection with the tertian parasite.

He was then given quinine, which entirely controlled the disease, and caused the complete disappearance of the parasites from his peripheral blood.

The results caused by the injection of the blood of Andres Mendez into Peredo and Ojeira follow:

Luis Peredo (case LXIV), a volunteer, aged 25, born in Jalapa, State of Vera Cruz, where he has always lived. When examined at Jalapa, August 26, he was found to be physically sound; urine contained no albumin; peripheral blood showed no plasmodium.

He was brought to Vera Cruz August 28 and taken from the station directly to the laboratory, from which time he was kept constantly within a mosquito-proof room.

On October 27, after having been under daily observation two months, during which time he remained in normal health, he was injected with the filtered blood of Filomena Martinez (page 84), who at the time was suffering with a paroxysm of malarial fever of the estivo-autumnal type, his blood containing many young ring-forms and crescents.

It will be noted by reference to the records of Filomena Martinez that the blood was drawn during the decline of the paroxysm. It was then allowed to clot in the ice chest; the clear serum was pipetted off and diluted with an equal quantity of isotonic salt solution, and this filtered through a new Berkefeld filter.

Twenty cubic centimeters of the filtrate, which on account of the dilution represented 10 cc. of the blood serum, were injected into the left median basilic vein of Peredo.

For further details of the manner in which the blood serum was obtained and the filtration performed, see the above records of Filomena Martinez.

Peredo was carefully watched from the hour he was injected, but he remained in good health, and no deviation from the normal was detected.

His temperature was taken every four hours during the night and day, both before and following the injection, as will be seen by the temperature chart. No symptoms developed.

His blood was examined daily for plasmodium, but none was found. The result of this injection must therefore be considered negative.

Ten days later he was again injected with filtered malarial blood under different circumstances, and with positive results.

At 1.40 p. m., November 6, he was given an intravenous injection of the blood of Andres Mendez, passed through the same Berkefeld filter as before. Mendez was suffering with a double tertian infection; his blood was drawn during his chill and before the height of the paroxysm, as will be seen by reference to the temperature chart (page 85).

Thinking that allowing the blood to clot four or five hours in the ice chest in order to obtain a clear serum for filtration might be too severe a tax upon the vitality of the malarial parasite, we this time defibrinated the blood as quickly as possible, diluted it as before with an equal volume of physiological salt solution, and filtered it through the same Berkefeld filter in the same manner as was done with blood of Filomena Martinez.

As soon as 9 cc. of the filtrate could be obtained it was injected into the basilic vein of the right arm of Louis Peredo. This injection took place at 1.40 p. m.

About thirty-five minutes after receiving the injection he began having chilly sensations and headaches, and presently went to bed covering himself with his blanket (2.25 p. m.). Five minutes later (2.30) he was having a violent chill, his teeth chattering so that we could not trust the thermometer in his mouth. The rigor of the entire body was so marked that there was difficulty in taking the radial pulse. The face was pale, and at this time he vomited most of the dinner he had eaten a short time before receiving the injection.

The patient complained of headache, which he localized at the forehead and occiput; says he felt cold and had pains in the knees. At this time the skin was dry. The chill lasted somewhat over half an hour.

At 3 p. m. the patient had transient chilly creeps, very slight rigor.

At 3.15 p. m. he said he felt "warm inside," and all sense of chilliness had disappeared; still has headache.

At 3.25 p. m. he complained of marked pain in the legs.

At 3.30 p. m. vomited the remainder of his dinner.

It will be seen from the temperature chart that during this time his temperature was rapidly rising and reached its highest point (38.7° C.) at 4 o'clock p. m., just two hours and twenty minutes after receiving the injection.

The pains in the knees and back continued, and nausea and vomiting now became a distressing feature of the paroxysms for the patient.

The fever gradually subsided, and reached normal at 4.30 a. m. that same night. (See temperature chart.)

As the fever subsided the skin became moist, the nausea and pains gradually disappeared, so that by 6 o'clock p. m. the patient was quiet and dozing. The entire paroxysm, therefore, according to the temperature record, lasted about eight hours, although the patient was sleeping quietly five hours after receiving the injection.

It is interesting to note that this man Peredo had what seemed to be a typical malarial paroxysm beginning with a distinct rigor associated with a rise of temperature and followed by slight sweating. It is of particular interest to note that his paroxysm, so far as symptoms were concerned, was very much like the paroxysm from which Andres Mendez suffered, especially the nausea and vomiting.

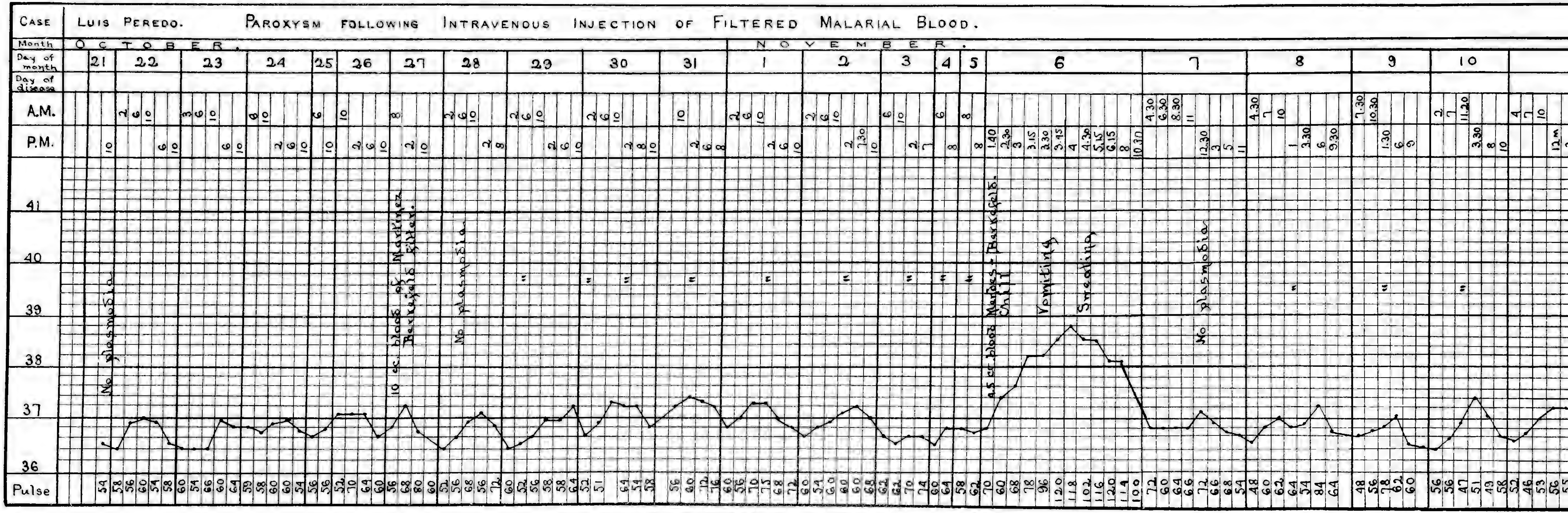
Peredo was kept under very close scrutiny until November 24, eighteen days following the injection, during which time he remained entirely normal and no plasmodium appeared in his peripheral blood, which was frequently examined, as follows:

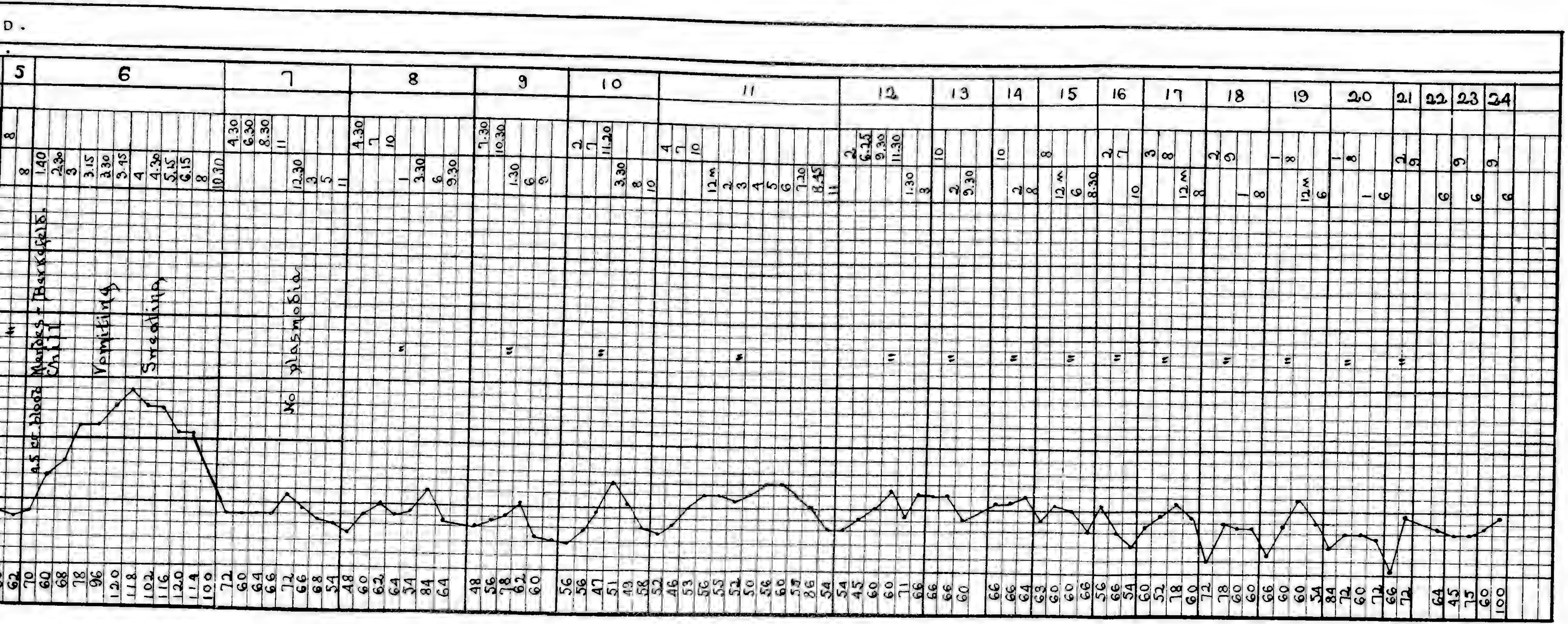
Blood examination.—Goldhorn's stain.

November 6.—4.30 p. m., 8 p. m. No malaria.
November 7.—4.30 a. m., 8.30 a. m., 12.30 p. m., 5 p. m., 11 p. m. No malaria.
November 8.—7 a. m., 1 p. m., 6 p. m., 9.30 p. m. No malaria.
November 9.—7.30 a. m., 1.30 p. m. No malaria.
November 10.—2 a. m., 3.30 p. m., 8. p. m., five minutes each. No malaria.
November 11.—4, 7, 10 a. m., 2, 6, 11 p. m., five minutes each. No malaria.
November 12.—1.30, 6.25 a. m,, five minutes each. No malaria.
November 13.—7 a. m., 9.30 p. m., five minutes each. No malaria.
November 14.—8 a. m., 8 p. m., five minutes each. No malaria.
November 15.—8 a. m., 8.30 p. m., five minutes each. No malaria.
November 16.—7 a. m., 9.30 p. m., five minutes each. No malaria.
November 17.—8 a. m., 8 p. m., five minutes each. No malaria.

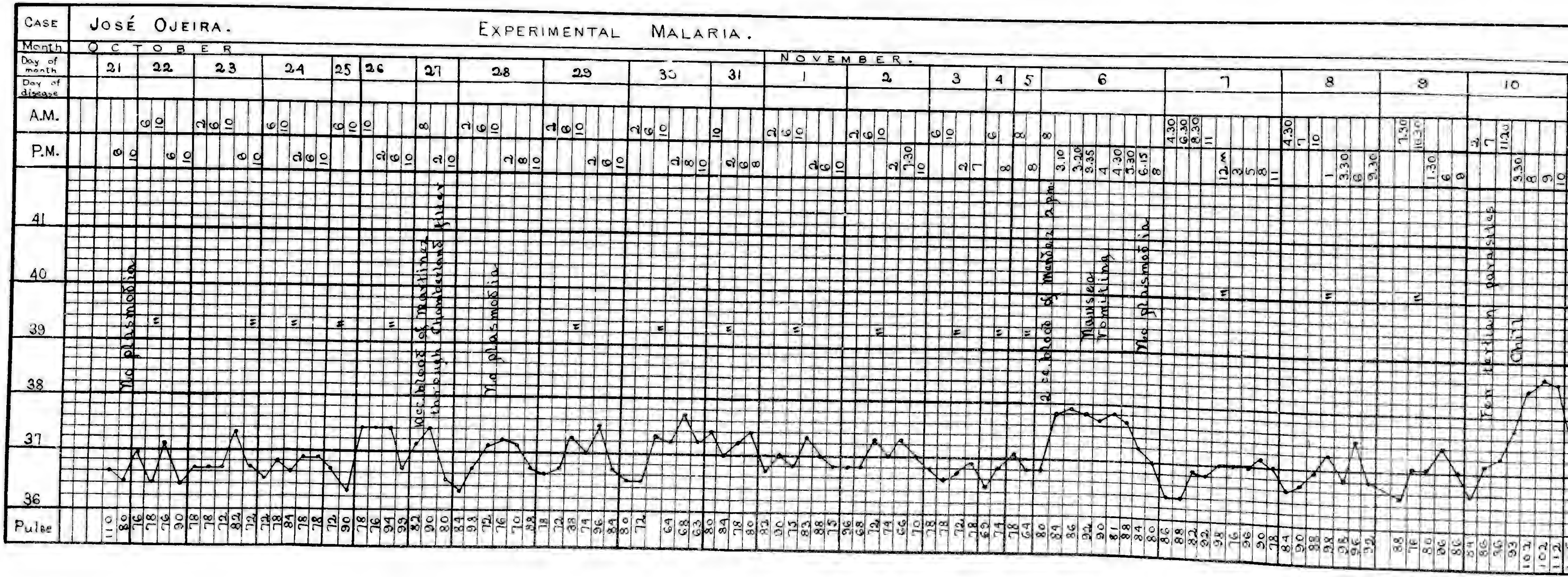
José Ojeira (case XXIII), a volunteer from Jalapa, 18 years old; had never lived on the coast, and says he never had fever of any kind. On examination in Jalapa, August 11, he was found to be physically sound, of robust physique; urine showed no albumin, and blood examination for malaria was negative.

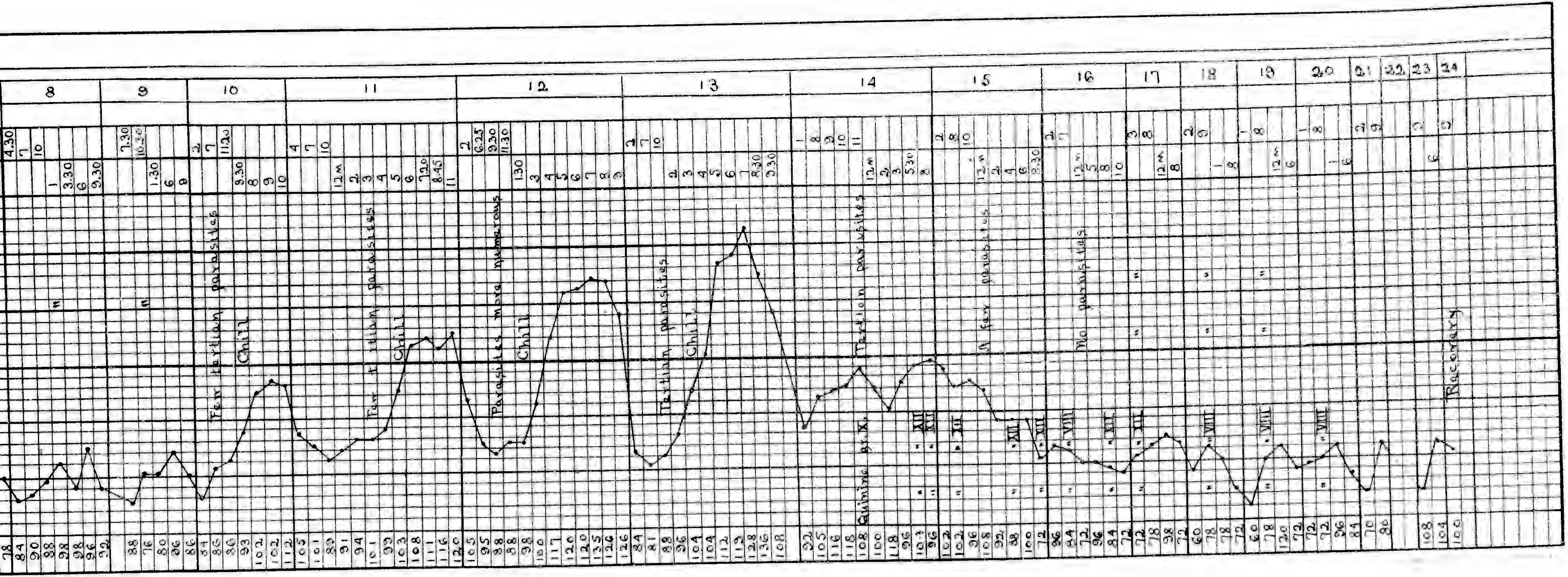
He was taken to Vera Cruz August 13, and immediately transferred to a mosquito-proof room in the laboratory, where he was kept under close observation.


Case
Luis Peredo.
Paroxysm following Intravenous Injection of Filtered Malarial Blood.
Month
October.
November.
Day of month
Day of disease
A.M.
P.M.
41
40
39
38
37
36
Pulse
No plasmodia
10 cc. blood of Martinez Berkefeld filter.
No plasmodia
2.5 cc blood Marques - Berkefeld.
Chill
Vomiting
Sweating
No plasmodia



D.
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
4.5 cc blood Marders - Berkefeld.
Chill
Vomiting
Sweating
No plasmodia


Case
José Ojeira.
Experimental Malaria.
Month
October
November.
Day of month
Day of disease
A.M.
P.M.
Pulse
41
40
39
38
37
36
No plasmodia
10cc blood of Martinez through Chamberland filter
No plasmodia
2 cc blood of Maddox 2 p.m.
Nausea
Vomiting
No plasmodia
Few tertian parasites
Chill



8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
Few tertian parasites
Chill
Few tertian parasites
Chill
Parasites more numerous
Chill
Tertian parasites
Chill
Tertian parasites
Quinine gr. X.
A few parasites
No parasites
Recovery

On August 28, at 9.30 a. m., he was bitten by four mosquitoes, two of which had bitten Antonio Leal (case XXXV), a yellow-fever patient fifteen days seventeen hours previously; and the other two had bitten the same case fourteen days twenty-three hours previously.

The man was kept under close observation in a mosquito-proof room, but showed no reaction. There was no rise of temperature, nor did he present any untoward symptoms.

On October 27, 7.20 p. m., he received intravenously 20 cc. of diluted blood serum of Filomena Martinez (æstivo-autumnal infection), passed through a Pasteur-Chamberland filter B. This represented 10 cc. of blood serum. For detals of this filtration see Filomena Martinez (p. 81).

Ojeira showed no reaction whatever as a result of this injection.

It will be noted that the blood of Martinez was drawn after the height of the paroxysm, and while the temperature was on the decline. Martinez was suffering with a very severe æstivo-autumnal infection at the time the blood was taken.

Ojeira's blood was carefully examined several times daily, both before and following this experiment, and at no time was anything resembling a malarial parasite seen in his peripheral blood.

On November 6, the patient having continued in good health since the last experiment, was used as a control for the experiment made on Peredo.

On this date, at 2 p. m., he was given an intravenous injection of 4 cc. of the *unfiltered*, diluted, and defibrinated blood of Andres Mendez. At the time the blood was drawn from Mendez it contained a heavy infection of a double tertian malaria, and the blood was taken from him during a chill and before the height of his paroxysm. It was at once defibrinated, diluted with an equal volume of physiological salt solution, and filtered through a Berkefeld filter. Nine cc. of the filtrate were given intravenously to Peredo, causing a malarial paroxysm without, however, the presence of the malarial parasite, and due, as we believe, to the toxin (?) in the blood of Mendez.

Ojeira, who received 2 cc. of unfiltered blood (4 cc. dilution), reacted within an hour, with a slight rise of temperature and nausea, and four days following developed a typical malarial paroxysm, with many tertian parasites in his peripheral blood.

There can be no doubt that the reaction to the 2 cc. of defibrinated blood injected into the vein of Ojeira caused a slight paroxysm, which it is reasonable to suppose was due to the same poison present in the blood of Mendez, and which also caused the reaction in Peredo.

It will be noticed that 2 cc. of this blood caused but a slight reaction in the case of Ojeira, while 4.5 cc. caused a more marked reaction, with a rise of temperature to 38.7° C., in the case of Peredo, indicating in a very definite manner that the severity of the symptoms were directly due to the quantity of poison introduced. Ojeira did not have a chill or other manifestations of a malarial paroxysm, other than a rise of temperature and nausea. He vomited gastric mucus several times.

On November 10, the fourth day following the injection, Ojeira had a typical malarial paroxysm, with tertian parasites in his peripheral blood. He suffered with a double infection, having a chill every day, as will be noticed by reference to the temperature chart. The character of the parasites in his blood and the clinical course of the disease resembled in all respects those of Mendez, from whom the blood was taken. Both cases were entirely controlled by quinine.

MISCELLANEOUS OBSERVATIONS ON MOSQUITOES.

In association with Doctor Goldberger we made some miscellaneous observations upon the life history and biology of the *Stegomyia fasciata* and *Culex pipiens*, some of which were of sufficient interest to record.

We found that the female *Stegomyia* does not always lay her eggs at one time. More often she deposits them in groups at intervals of several days. The maximum number laid by any one insect observed by us was 101. The female *Stegomyia* sometimes dies, apparently from exhaustion, after laying her eggs, but we noted several instances in which this was not the case. The insect which laid 101 eggs was alive and vigorous until killed by us five days later.

The manner in which the female *Stegomyia* lays her eggs is of some interest. She bends her abdomen ventrally, and as the genital orifice comes in contact with the sides of the vessel or with the water or other object the egg is deposited. The insect moves along and repeats the performance.

The eggs are sometimes laid on the water, sometimes on the side of the vessel above the water line, and sometimes on a leaf floating on the water.

In accordance with the few observations which we made on this particular point, *Stegomyia fasciata* females that are fed solely on banana or sugar do not lay eggs. They seem to require a feeding of blood for ovipositing. Unconjugated females also do not lay eggs.

The longest life that we observed was in a female *Stegomyia*, which we kept for sixty-four days, and then killed for sectioning.

We found, as has been often noted by other observers, that the greatest activity of the *Stegomyia fasciata* is during the daytime, but we have observed them flying at night. We have also observed them feeding on us at night by artificial light. We have noticed on several occasions that they are especially voracious early in the morning, about sunrise. On several occasions a number of noninfected insects were let loose in the laboratory and we observed that upon rising at sunrise they attacked us viciously.

It may be noted that this fact apparently explains the danger to persons sleeping in an infected house and the comparative freedom from danger in daylight communication with an infected town, especially if the person remains in the open air and sunlight and avoids houses, and confines his visits to the streets and parts of the town free from the disease.

A number of experiments were made with the female *Culex pungens*, but they could not, under any circumstances, be induced to feed upon blood while in confinement. It was found that they preferred death.

MOSQUITOES MAY BITE CADAVERS.

The female *Stegomyia fasciata* will bite a cadaver, and, if on a dependent portion, can draw blood. We have two observations on this point.

Narciso Nadal (case XX). A number of *Stegomyiæ* were applied twelve hours after death, only one of which apparently obtained blood.

Trinidad Martinez (case XXII). A number of female *Stegomyiæ fasciatæ* were applied one-half hour after death, and three insects succeeded in feeding with blood.

As it has been shown by the work of the French commission that the blood of yellow fever is not infective after the third day, the danger of conveying the infection by means of mosquitoes feeding upon cadavers must be exceedingly remote.

LONGEVITY.

Several experiments were undertaken to determine the fact whether the male *Stegomyia fasciata*, as has been stated, has a brief life history. We have one experiment showing that the male mosquito may live and thrive over a month.

Observation.—A number of male mosquitoes were placed in a cage October 10 and subsequently fed on sirup. They were all alive and in good condition on November 15, when they were killed and used for experimental purposes, having lived thirty-six days.

OVIPOSITING.

Sometimes the female *Stegomyia fasciata* will lay a considerable number of eggs at one time and then die.

Observation.—(Mosquito XLIII. Francis, Re. No. 4.) This female *Stegomyia fasciata* was taken from the breeding jar on October 3, fed on normal blood October 4, 6, 7, 8, and 10, then placed in a jar with water to tempt ovipositing, and banana feeding begun. On October 19 four males were added to the jar. On October 23 the female was given another blood feed. On the 26th she laid 54 eggs and was found exhausted and dying on the surface of the water.

More often the female *Stegomyia* lays groups of eggs at intervals of several days, and sometimes lives after the last laying.

Observations.—(Mosquito XLIII–38. Francis, Rc. No. 1.) This female *Stegomyia* was taken from the breeding jar October 3; fed on normal blood on October 4, 6, 7, 8, and 10; then placed in a jar to tempt ovipositing and given banana; laid eggs on October 10 and 11; given another blood feed October 16; found apparently dying on the surface of the water on October 18.

(Mosquito XLIII–68. Francis, Rc. No. 3.) This female *Stegomyia* was taken from the breeding jar on October 3 and fed on normal blood October 4, 6, 7, 8, and 10. It was then placed in a jar to tempt ovipositing and given banana. On October 11 she laid a considerable number of eggs. On October 19 again given blood feed and three males placed in the jar. October 25 she laid 29 eggs. On October 26 laid 12 more eggs. On the 30th the insect was removed in a dying condition.

(Mosquito XLIII–67. Francis, Rc. No. 5.) This female *Stegomyia* was taken from the breeding jar October 3. Fed on normal blood October 4, 6, 7, 8, and 10. Then placed in a separate jar with water to tempt ovipositing and given banana. On October 13 she laid some eggs. On the 19th given a blood feed and three males added. She laid 11 more eggs on October 23, 16 on the 25th, and 37 on the 28th, when she was found dying on the surface of the water.

(Mosquito XLIII–69. Francis, Rc.) This female *Stegomyia* was taken from the breeding jar when less than forty-eight hours old and fed upon normal blood October 4, 6, 7, 8, and 10, and subsequently at intervals of one or two days up to October 23, when she was placed in a cage by herself with a beaker of water to tempt ovipositing. At the same time given banana to feed upon. October 25 two males were added to the cage. October 25 she laid 51 eggs; November 7, 24 eggs; November 8, laid 26 eggs; total, 101 eggs.

She was given another feed of blood November 10.

Was killed November 13 while apparently vigorous.

Female *Stegomyia fasciata* that have fed on the blood of yellow-fever patients on the second, fourth, and sixth days of the disease may subsequently lay eggs that hatch in a normal manner, and the larvæ develop into pupæ and imagoes.

Observations.—(Mosquito XLVII–36. Marcial Lujan, Rx. a.) This insect was separated from the breeding jar October 8 and fed on Marcial Lujan, a typical case of yellow fever on the sixth day of his illness. She was subsequently fed on normal blood October 11, 13, 16, 17, and 19. On October 22 a beaker of water was placed in the cage in order to tempt ovipositing, and banana feeding begun. She laid 15 eggs on October 25 and 15 more on October 26. Both sets hatched.

(Mosquito XLVII–37. Marcial Lujan, Rx. b.) This female *Stegomyia* taken from the breeding jar October 8. Fed on blood of Marcial Lujan on the sixth day of his illness, October 9, and subsequently on normal blood October 11, 13, 16, 17, and 19. On October 22 given a beaker of water to tempt ovipositing and banana feeding begun. She laid 31 eggs on October 26, 9 on the 27th, and 12 on the 30th. The eggs laid on the 26th and 27th hatched on the 29th.

(Mosquito XLII–122. Marcos Cruz, Rn. a.) This insect was separated from the breeding jar October 14 and allowed to feed on Marcos Cruz, one of our experimental cases of yellow fever October 15, that is, on the second day of his illness. She was subsequently fed on sirup. On November 1, placed in a cage with a beaker of water and two males. She laid 12 eggs on November 4, which subsequently hatched.

(Mosquito LVIII–32. Sesoleda Martinez, Rx. b.) This female *Stegomyia* was separated from the breeding jar October 19. Fed upon the blood of Sesoleda Martinez, a fatal case of yellow fever October 20, the fourth day of his illness. Subsequently this insect was given banana. October 28 a normal blood feed. On November 5 a beaker of water was placed in the cage to tempt ovipositing. Four days later, November 9, she laid 26 eggs, which subsequently hatched.

The statement has been made that the female *Stegomyia fasciata*, and mosquitoes generally, require a feeding on blood in order to lay eggs. In three experiments tried by us we are able to confirm this statement so far as the *Stegomyia fasciata* is concerned. The insects were fed on sirup and banana, but could not be tempted to lay eggs.

Observations.—Banana feeding. A large number of male and female *Stegomyia fasciata* that had been fed on banana for fourteen days were given a beaker of water to tempt ovipositing. They were left nine days. No eggs laid. They were then killed for section.

Sirup feeding. A large number of male and female *Stegomyiæ* that had been fed on sirup for fourteen days were given a beaker of water to tempt ovipositing. They were observed twenty-one days later. No eggs were laid.

Banana and sirup feeding. A large number of male and female *Stegomyiæ* were given alternate feedings of banana and sirup for thirty-two days, at which time a beaker of water was placed in their cage to tempt ovipositing. They were observed nine days later. No eggs were laid.

Unconjugated females do not lay eggs.

Observations.—Stegomyiæ pupæ were isolated and placed in separate small bottles so that the imagoes could not be kept in strict quarantine. Six of these unconjugated females were given a feeding of blood twenty-four hours after birth, and were subsequently fed on banana. They were kept in a cage with a beaker of water to tempt ovipositing. Five days subsequently they were given a second feeding on blood. Twenty-five days later they were killed, not having laid eggs.

Size of Screening.

It is of considerable practical importance in quarantine and public health work to know the size of screening that will keep out the *Stegomyia fasciata*, and as no accurate observations upon this subject had been made, with which we were familiar, we conducted a few experiments to determine this point.

Screens with a varying number of meshes to the inch were placed over breeding jars, and banana, sirup, and other food placed on the other side so as to tempt the hungry insects to pass through. These experiments were arranged by placing the fruit and food in a jar which was inverted over the breeding jar. A piece of gauze or netting was inserted between the two jars so that the *Stegomyiæ* would have to pass through its meshes in order to apear in the upper jar.

We found that both male and female *Stegomyiæ* may pass a wire gauze containing 16 strands or 15 meshes to the inch, but could not pass 20 strands or 19 meshes to the inch.

It is therefore evident that the large-meshed mosquito bars ordi-

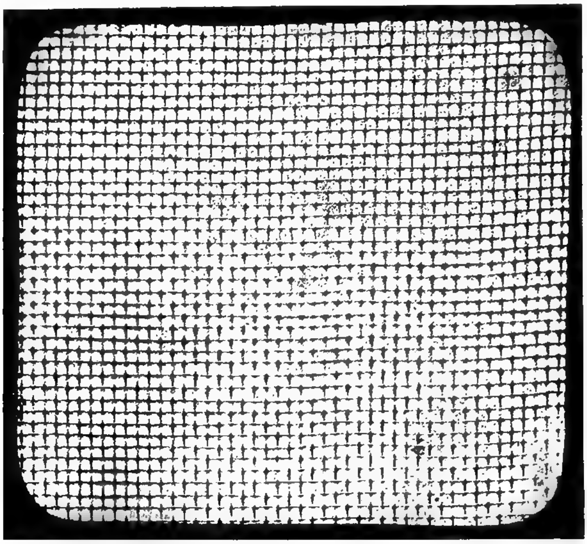


FIG. 4.—Showing screen containing 16 strands or 15 meshes to the inch. Allows male and female stegomyia fasciata to pass.

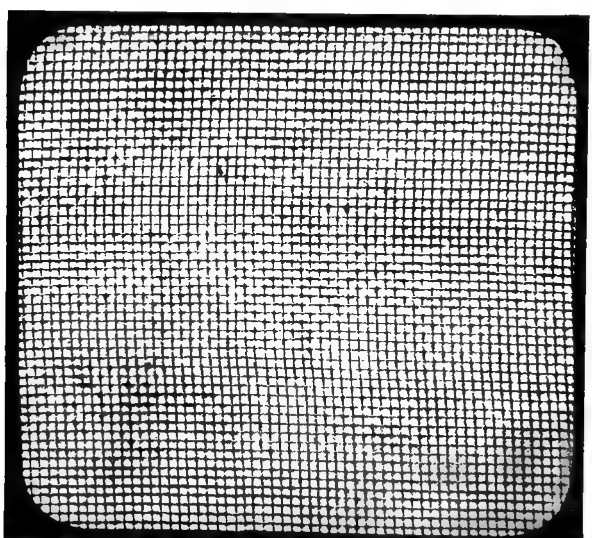


FIG. 5.—Showing screen containing 20 strands or 19 meshes to the inch, through which stegomyia fasciata can not pass.

narily used in this latitude would not offer proper protection, and that window screening must also be of a finer wire than is sometimes employed.

DISINFECTION EXPERIMENTS.

A few tests were made to determine the relative efficiency of sulphur dioxid, tobacco smoke, and pyrethrum as insecticides with particular reference to the *Stegomyia fasciata.*

A small room and hallway containing 1,200 cubic feet of air space were used in these experiments. The room contained a large window and one door, which were made reasonably tight to prevent the escape of the fumes, and the mosquitoes were exposed in cages in various parts of the room.

Experiment No. 1—Tobacco.—One pound of tobacco per 1,000 cubic feet; exposure, one hour; result, some mosquitoes survived.

Six hundred and twenty-five grams of tobacco, which is about the proportion of 1 pound per 1,000 cubic feet, were burned in a pan in the center of the room. The cages containing the mosquitoes were placed on the floor, near the ceiling, and on a chair.

The room was opened one hour after the tobacco was lighted, which was done by means of alcohol. The mosquito cages were immediately removed and placed in a current of fresh air in order to give the mosquitoes a favorable opportunity to revive.

All the mosquitoes in the cage which was near the ceiling were dead. Of those in the cage on the chair, one female was flying actively about; the other females and another male were all dead. Those in the cage that stood on the floor were stupefied, but none was killed, most of them flying actively about.

The tobacco was completely consumed in this process, and the fumes upon opening the door were very strong. The unpleasant odor was very persistent and disagreeable.

Experiment No. 2—Tobacco.—Two pounds per 1,000 cubic feet; exposure, two hours; result, all mosquitoes killed.

The mosquito cages were immediately removed after two hours had elapsed, at which time none of the insects showed apparent signs of life; but after remaining in the fresh air for three hours a few of them moved their wings and tarsi. None, however, revived.

Experiment No. 3—Pyrethrum.—Two pounds per 1,000 cubic feet; exposure, 2 hours; result, all mosquitoes killed.

The pyrethrum was burned in a brazier placed upon some sand on the floor.

Three cages containing many mosquitoes were distributed, one on the floor, one near the ceiling, and one in an open box on the table. The cages had a piece of crumpled gauze upon the bottom and a folded handkerchief hanging in the cage, in order to give the insects retreats in which to hide from the effects of the fumes and to test the penetrating action of the gas.

All of the mosquitoes were killed.

Experiment No. 4—Pyrethrum.—Two pounds per 1,000 cubic feet; exposure, two hours; result, all mosquitoes killed.

Mosquito cages were placed in several parts of the room. At the end of the experiment some of the insects showed signs of life, but none revived.

Experiment No. 5—Pyrethrum.—One pound per 1,000 cubic feet; exposure, two hours; result, all mosquitoes killed.

The pyrethrum was burned in an open brazier upon the floor in the same room used for the preceding experiments. The mosquitoes were freely exposed to the effects of the fumes in appropriate cages, which were placed upon the floor, near the ceiling, and one inside a box laid upon a table.

At the end of the experiment the cages were immediately taken to the fresh air and many of the *Stegomyia* showed signs of life, but none revived.

Experiment No. 6—Sulphur.—Three and one-fourth pounds per 1,000 cubic feet; exposure, two hours; result, all mosquitoes killed.

In this experiment four large rooms and the hallway of our laboratory building were fumigated to destroy some mosquitoes that had escaped. The rooms communicated with each other and with the hallway through large openings. No attempt was made to seal the doors and windows or to paste cracks.

Three pots of sulphur were distributed at points of vantage, each pot containing 20 pounds, the total space to be fumigated being 12,280 cubic feet.

Two hours after the sulphur was lighted the house was opened and it was found that only about two-thirds of the sulphur had burned; that is, about 3¼ pounds per 1,000 cubic feet. In this experiment the pots containing the sulphur were not placed in water, the object being to obtain a dry gas and thereby minimize the destructive action of the fumes upon the fabrics and pigments.

Four cages containing mosquitoes were placed in different parts of these rooms and all were killed.

As a result of these disinfection experiments we conclude that: While we found tobacco smoke efficacious in destroying the insects, we also found that the method is exceedingly objectionable on account of the persistent and disagreeable odor that it leaves, as well as on account of the yellow stains which remain. Tobacco smoke in concentrated form stains fabrics, paint work, and other surfaces, but the stains may be removed by washing; still, this forbids its use in parlors and the rooms of fine houses.

We found that the burning of 1 pound of tobacco per 1,000 cubic feet, with an exposure of one hour, was only sufficient to stupefy the insects. All *Stegomyia fasciata* were killed by an exposure of two hours to the fumes of tobacco burned in a proportion of 2 pounds per 1,000 cubic feet.

We found 1 pound of pyrethrum per 1,000 cubic feet, with an exposure of two hours, sufficient to kill *Stegomyia fasciata*, and, although many of them still showed signs of life after this exposure, none revived. Two pounds per 1,000 cubic feet, with an exposure of two hours, was sufficient to kill them outright.

We made only one experiment with sulphur dioxid in order to kill some *Stegomyia fasciata*, which had escaped in the laboratory. We selected sulphur on account of our confidence in the insecticidal value of this substance. In this experiment we used about 3 per cent of the gas, generated by burning in open pots, with an exposure of two hours. The previous work of one of us[a] showed that 1 per cent, with an exposure of one hour, is quite sufficient in a small inclosure, but we used the excess on account of the peculiar construction of the house.

When burning sulphur for its insecticidal effects care should be taken to keep the gas as dry as possible, while the contrary is necessary in order to obtain its germicidal action.

The small percentages of sulphur dioxid kept dry are not sufficient during short exposures to bleach pigments or injure fabrics; and this, in our opinion, is the best of the poisonous gases to insure the destruction of such vermin in houses. Formaldehyde gas is utterly untrustworthy in this connection. It is not an insecticide.

We made no experiments with hydrocyanic-acid gas. While recognizing its great insecticidal power, we considered it entirely too poisonous a substance to use in the household or other inhabited places. In our opinion the use of this gas should be limited to greenhouses, railroad cars, granaries, and other isolated and uninhabited places.

SUMMARY AND CONCLUSIONS.

The cause of yellow fever is not known.

The *Myxococcidium stegomyiae* is not an animal parasite. Yeast cells sometimes simulate the coccidia in form and staining reaction.

The infection of yellow fever is in the blood serum early in the disease. No abnormal elements that bear a causal relation to the disease can be detected in the serum or in the corpuscles with the best lenses at our command.

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[a] Disinfection against mosquitoes with formaldehyde and sulphur dioxid, M. J. Rosenau. Bull. No. 6, Hyg. Lab., U. S. Pub. Health & Mar.-Hosp. Serv., Wash., Sept. 1901.

The infective principle of yellow fever may pass the pores of a Pasteur-Chamberland B filter.

Particles of carbon visible with Zeiss lenses pass through both the Berkefeld and Pasteur-Chamberland B filters.

Because the virus of an infectious disease passes a Berkefeld or Pasteur-Chamberland B filter it does not necessarily follow that the parasite which passed the filter is " ultramicroscopic," or that it may not have elsewhere another phase in its life cycle of large size.

The filtration of viruses may succeed or fail, depending upon the character of the filter, the diluting fluid, the pressure, time, temperature, motility of the particles, and other factors.

The period of incubation of yellow fever caused by the bites of infected mosquitoes is usually three days, sometimes five days, and in one authentic instance six days and two hours; but when the disease is transmitted by such artificial means as the inoculation of blood or blood serum the period of incubation shows less regularity.

Yellow fever may be conveyed to a nonimmune by the bite of an infected *Stegomyia fasciata;* but the bites of *Stegomyia* which have previously (over twelve days) bitten cases of yellow fever do not always convey the disease.

Fomites play no part in the transmission of the disease.

The tertian and estivo-autumnal malarial parasites will not pass the pores of a Berkefeld filter.

We have demonstrated a poison in the blood during the chill of tertian infection which, when injected into another man, caused chill, fever, and sweating. This poison, while present in a case of tertian during the rise of temperature, could not be demonstrated in the blood of a case of estivo-autumnal fever during the decline of the paroxysm. While this poison reproduced the symptoms of the disease, still the data are too limited to consider it the malarial toxin.

Stegomyia fasciata is a domestic insect. It is most active during the day, but will bite at night under artificial light. The female lays eggs at intervals; the maximum number of eggs laid by one insect observed by us was 101. The mosquito does not always die directly after ovipositing.

Stegomyia fasciata may bite and draw blood from cadavers, although the danger from spreading the infection from this source is remote.

Male and female *Stegomyia fasciata* may pass a screen containing 16 strands, or 15 meshes to the inch, but not one of 20 strands, or 19 meshes to the inch.

Tobacco smoke produced by burning two pounds per 1,000 cubic feet with an exposure of two hours is sufficient to kill *Stegomyia* *fasciata.* This method is objectionable on account of the yellow stains and disagreeable odor.

Pyrethrum burned in the proportion of 1 pound per 1,000 cubic feet with an exposure of two hours will stupefy *Stegomyia fasciata;* it requires 2 pounds to kill them outright.

From the limited number of experiments made and from previous experiments we consider sulphur dioxid the best of the gaseous insecticides for this purpose.

Formaldehyd gas is not an insecticide, and therefore not applicable.

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YELLOW FEVER INSTITUTE, BULLETIN No. 15.
Treasury Department, U. S. Public Health and Marine-Hospital Service.
WALTER WYMAN, *Surgeon-General.*

REPORT

OF

WORKING PARTY NO. 3,

YELLOW FEVER INSTITUTE.

ATTEMPTS TO GROW THE YELLOW FEVER PARASITE.

THE HEREDITARY TRANSMISSION OF THE YELLOW FEVER PARASITE IN THE MOSQUITO.

BY

M. J. ROSENAU

AND

JOSEPH GOLDBERGER.

JANUARY, 1906.

WASHINGTON:
GOVERNMENT PRINTING OFFICE.
1906.

LETTER OF TRANSMITTAL.

PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE,
Washington, January 8, 1906.

SURGEON-GENERAL
PUBLIC HEALTH AND MARINE-HOSPITAL SERVICE,
Washington, D. C.

SIR: We have the honor, in compliance with your instructions, to submit herewith a report of part of the work done by us in New Orleans during the latter part of the epidemic of 1905 in the study of some problems connected with yellow fever.

This report covers two points, namely, an attempt to grow the yellow fever parasite and some experiments on its hereditary transmission in the mosquito.

In a future report we hope to cover the results of our study of the mosquito material collected by us. This material consists of mosquitoes (*Stegomyia fasciata*) some of which were permitted to feed on yellow fever cases in the first three days of the disease and others (controls) which stung a series of healthy subjects or such as were suffering from some affection clearly not yellow fever.

We desire here to express our appreciation of the invaluable assistance rendered us by Surgeon J. H. White.

To Surgeon A. C. Smith we are indebted for the loan of apparatus and for placing at our disposal the hospital laboratory. Passed Assistant Surgeon T. F. Richardson rendered us valuable help in many ways. To Passed Assistant Surgeons Rupert Blue and Thomas D. Berry and Assistant Surgeon Wm. C. Rucker our thanks are due for collections of mosquito larvæ. To Dr. H. P. Jones, Dr. Birney Guthrie, and Prof. P. E. Archinard, of New Orleans, our thanks are due for numerous courtesies at the Emergency Hospital. Finally, we desire to acknowledge our indebtedness to many of the other officers of the Service on duty at New Orleans for material assistance on numerous occasions.

Respectfully,

M. J. ROSENAU,
Passed Assistant Surgeon.
JOS. GOLDBERGER,
Passed Assistant Surgeon.

YELLOW FEVER INSTITUTE.

Treasury Department, Bureau of Public Health and Marine-Hospital Service.

WALTER WYMAN, Surgeon-General.

BULLETIN No. 15.

Section B.—ETIOLOGY. P. A. Surg. M. J. ROSENAU, Chairman of Section.

ATTEMPTS TO GROW THE YELLOW FEVER PARASITE.

THE HEREDITARY TRANSMISSION OF THE YELLOW FEVER PARASITE IN THE MOSQUITO.

By M. J. ROSENAU, *Passed Assistant Surgeon,*
and
JOSEPH GOLDBERGER, *Passed Assistant Surgeon,*
U. S. Public Health and Marine-Hospital Service.

ATTEMPTS TO GROW THE YELLOW FEVER PARASITE.

In view of the fact that the infective principle causing yellow fever may pass through the close-grained pores of a Pasteur-Chamberland B filter, it seemed to us hopeless, with the limitations of the present microscope, to expect to see the causative agent of this disease by direct examination of the blood.

Novy's work with trypanosomes, both his success in their artificial cultivation and his filtration experiments indicating the possibility of an "ultramicroscopic" phase in their developmental cycle, suggested to us the possibility of cultivating by similar methods the yellow fever parasite and thus perhaps developing a stage in its life cycle which might readily be visible. We attempted, therefore, to grow the parasite of yellow fever in the "water of condensation" of blood-agar tubes.

The culture tubes were prepared in several different ways; both human blood (nonimmune) and rabbit's blood were used. Some tubes were prepared with the whole, and some with the defibrinated blood. When the whole blood was used it was quickly added while fresh to melted agar, at 42° C., in the proportion of about 2 parts of blood to 1 of agar. After mixing, the tubes were slanted and allowed to set. The defibrinated blood was prepared by whipping in the usual way, and then it was added to the melted agar in about the same proportions as above stated. After standing a short while the blood-agar slants, thus prepared, developed from several drops to about 1 cc. of "water of condensation."

A drop or two of blood from typical cases of yellow fever taken from the arm vein during the early stages of the disease was planted into this "water of condensation."

Other cultures were prepared with much larger quantities of the yellow fever blood, using the yellow fever blood itself as a part of the culture medium. To tubes containing about 2 cc. of melted agar, about 4 cc. of fresh yellow fever blood was added as quickly as possible after its withdrawal from the vein. Other tubes were similarly prepared with the defibrinated yellow fever blood.

Some of the cultures were kept in the incubator at 37° C., and others at room temperature. Of the latter, some were kept in the dark and others exposed to the light in order to simulate the conditions as they appear to occur in the mosquito.

The water of condensation was examined from time to time both in hanging drop and in stained smears. It was found to contain large numbers of bodies of various sizes and shapes, some of them exhibiting curious and exaggerated Brownian motion. All of the particles were interpreted as degeneration products, mostly from the cellular elements of the blood.

HEREDITARY TRANSMISSION OF THE YELLOW FEVER PARASITE IN THE MOSQUITO.

The question of the herditary transmission of the yellow fever parasite from the *Stegomyia fasciata* to its progeny is of interest both biologically and practically.

Reasoning by analogy such transmission can not be regarded as impossible, as it is known to occur in some, probably closely allied diseases, namely through the tick in Texas fever[a] and canine piroplasmosis[b]. Schaudinn[c] has satisfied himself that hereditary transmission of the tertian malarial parasite (*Plasmodium vivax*) occurs in *Anopheles*, and recently Dutton and Todd[d] have shown that the spirochaete of the tick fever of the Congo is passed from tick to tick through the egg.

To the sanitarian the question is of interest in its bearing on the problem of the recrudescence of yellow fever.

The recrudescence of epidemics of yellow fever has heretofore been explained in one of two ways: (1) Either a *Stegomyia fasciata* that had become directly infected by feeding on a case of the disease had survived (as they are experimentally known to be able to do), or (2) the infection had in the interval between the epidemics been continued by unrecognized cases and on the recurrence of favorable conditions the disease would reassume epidemic proportions.

From time to time a third explanation has been advanced, namely, the transmission of the infection from the mother mosquito through the eggs to its progeny[e] which, under favorable circumstances, were

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[a] Smith and Kilborne, 1893, U. S. Department of Agriculture, Bureau of Animal Industry, Bulletin No. 1.

[b] Lounsbury, C. P., Transmission of Malignant Jaundice of the Dog by a Species of Tick. Reprint Cape of Good Hope Agricultural Journal, November 21, 1901.

[c] Schaudinn, Fritz, Generations und Wirtswechsel bei Trypanosoma und Spirochaete. Arbeiten aus dem Kaiserlichen Gesundheitsamte, Berlin, Band XX, Heft 3, 1904, p. 428.

[d] Dutton and Todd, Liverpool School of Tropical Medicine, Memoir xvii, 1905.

[e] Finlay (Medical Record, N. Y., May 27, 1899, p. 738), inspired by the discovery of Smith and Kilborne of the hereditary transmission of the parasite of Texas fever in the tick, was the first to suggest the hereditary transmission of the yellow fever parasite in the mosquito. In 1901 Reed, Carroll, and Agramonte (American Medicine, Phila., July 6, 1901, p. 19) reported the negative results of an inoculation experiment with 14 mosquitoes hatched from the ova of a *Stegomyia fasciata* that had already shown itself capable of conveying the disease, and Guiteras (American Medicine, Phila., Nov. 23, 1901, p. 810) reports two experiments. In both the mother

capable without themselves directly having had access to a case yellow fever, of giving the disease to a susceptible individual. Tl explanation has now received the support of an experimental case yellow fever induced by the sting of a *Stegomyia fasciata* apparent hereditarily infected. This case is reported by Marchoux and Simoı in a paper on "The hereditary transmission of the yellow fever vir in the *Stegomyia fasciata*," a translation of which we give in appendi p. 114.

Against this one positive case we submit the negative results inoculations attempted in 13 nonimmunes.

In an endeavor to account to ourselves for the divergence of o results from that of the French workers we have considered sever factors in the problem, failure to comply with any of which mig readily be productive of negative results. We believe, howeve that our work, so far as we can judge from the details in the paper, closely parallels the work of Marchoux and Simond. Natu ally the first factor which arises for consideration is whether tl mothers of the *Stegomyia fasciata* used by us for the inoculation our nonimmunes were infected. Marchoux and Simond state that tl mother of the insect whose sting produced the positive case fever had been made to feed on *several* (number not stated)[a] of the

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mosquitoes were experimentally proved to be infected. In the first the progeny one mother were tried without results upon three nonimmunes; in the other a lar brood from several mosquitoes was kept in a breeding jar and was fed upon noni munes with impunity.

[a] During the progress of this bulletin through the press the second report of t French Commission to Rio de Janerio (Marchoux and Simond, Annales de l'Instit Pasteur, Paris, XX, 2, Jan. 25, 1906, p. 16) came to our hands, giving full details the positive experimental case of yellow fever produced by the sting of a *Stegomy fasciata* apparently hereditarily infected, as follows:

"Experiment.—A female *Stegomyia fasciata* born in the laboratory and arriving the adult stage January 19 (*probably means January 9*), 1905, was paired from the 9 to the 11th. It stung a yellow-fever patient presenting a severe attack in the seco day of the disease, on the 11th of January, and laid the first batch of eggs Janua 17. On the 25th of January it stung another patient in the second day of the disea who presented an attack of moderate severity, and laid the second batch of eg January 28. This latter batch hatched out from the 3rd to the 4th of February, a the larvæ cared for in the laboratory produced perfect insects February 16.

"Two females from this batch were isolated in tubes and fed with sirup up March 2. At this date—that is to say, 14 days after completing their metamorphos these mosquitoes were made to sting subject A. This subject, a Portuguese, h arrived in Brazil only a few days before and had never had yellow fever. He show no reaction to this inoculation. After an interval of eight days, March 10, the sa subject was stung a second time by one of the two mosquitoes, the other having ac dentally died. Four days later, March 14, he presented symptoms of yellow feve

It will be noted, therefore, that the eggs giving rise to the progeny that apparen caused an attack of yellow fever were laid by the mother mosquito 17 days af the first and 3 days after the second feed of yellow-fever blood. (Compare mosquitoes Nos. 3 and 4, Group II, of Set 1, p. 107.)

cases of yellow fever in order to determine a heavy infection. In our work mother mosquito of Set 1 had three feedings of yellow fever blood from two severe cases.

Mother mosquito of Set 2 and that of Set 3 each had one feed of yellow fever blood early in the disease.

That the interval between the infecting feed and oviposition must enter as an important element in the transmission of the infection through the eggs to the progeny—if such transmission ever takes place in yellow fever—must be evident. Marchoux and Simond do not report clearly on this point;[a] they state simply that their mosquito was 20 days old at the time of oviposition and that some time prior to the laying it had been made to sting several cases of yellow fever.

In our experiments the intervals were as follows:

SET 1.

Group I, mosquitoes Nos. 1 and 2.—The eggs producing these mosquitoes were laid 13½ days from the first, 11½ days from the second, and about 2½ days after the third feed of yellow fever blood.

Group II, mosquitoes Nos. 3 and 4.—The eggs giving rise to this group were laid 16 days from the first, 14 days from the second, and about 5 days from the third feed of yellow fever blood. (Compare footnote ([a]), page 106.)

SET 2.

Group I, mosquito No. 5.—The eggs giving rise to this group were laid 15 days after one feed of yellow fever blood.

SET 3.

Group I, mosquito No. 6.—The eggs giving rise to this group were laid 14 days after one feed of yellow fever blood.

Groups II, III, and IV, mosquitoes Nos. 7, 8, 9, 10, 11, 12, 13, and 14.—The eggs giving rise to these groups were laid 15 days after one feed of yellow fever blood.

Another important factor in the problem, and one to which Marchoux and Simond call attention, is the time needed by the hereditarily infected mosquito to become infective. In their case this was twenty-two days. In our work the inoculations were carried up to and including at least the forty-ninth day, as shown in Table 1.

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[a] See note [a] on page 106.

TABLE 1.—*Summary of inoculations of nonimmunes by hereditarily infected (?) mosq toes—subjects kept under observation at least seven days after each inoculation.*

[The mosquitoes are designated by numbers from 1 to 14; nonimmunes by capital letters.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Remarks.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Remarks
		Days.				*Days.*	
No. 10	B	2	No reaction.	Nos. 6 and 10	G	26	No reacti
Nos. 7, 8, and 9	B	3	Do.	No. 14	[a] L	26	Do.
No. 2	A	6	Do.	Nos. 5 and 9	F	27	Do.
No. 1	B	9	Do.	No. 6	H	28	Do.
No. 2	C	10	Do.	Nos. 3 and 4	G	29	Do.
No. 2	A	12	Do.	Nos. 12, 13, and 14	[b] M	30	Do.
Nos. 1 and 2	C	13	Do.	No. 6	J	31	Do.
Nos. 3 and 4	B	13	Do.	Nos. 1, 11, and 12	B	32	Do.
Nos. 1 and 2	B	20	Do.	No. 3	J	33	Do.
No. 3	E	21	Do.	No. 6	M	34	Do.
Nos. 11 and 12	H	22	Do.	Nos. 12, 13, and 14	G	34	Do.
No. 4	E	23	Do.	No. 1	H	35	Do.
Nos. 13 and 14	J	23	Do.	Nos. 12 and 13	J	36	Do.
Nos. 1 and 2	D	24	Do.	No. 3	[b] L	37	Do.
No. 6	F	24	Do.	No. 1	K	39	Do.
Nos. 5 and 9	F	25	Do.	Nos. 13 and 14	N	39	Do.
Nos. 11 and 12	J	25	Do.	No. 12	N	40	Do.
No. 13	G	25	Do.	No. 3	G	45	Do.
No. 3	F	26	Do.	No. 3	N	49	Do.

[a] Subject passed from observation after 6 days.
[b] Subject passed from observation after 5 days.

A factor in the problem which is of prime importance and whic must always be reckoned with in estimating the value of negativ results is the susceptibility to the disease of the subject used for th inoculations. We were careful to select only those who we were sa isfied never had had the disease.

Another factor which must be considered is temperature. No mer tion is made in the paper of Marchoux and Simond at what tempera ture their mosquitoes were kept. Our mosquitoes were kept unde artificial conditions at a temperature of between 80° and 90° F. (Se p. 109.)

Many other factors which we shall not discuss undoubtedly ente into and affect this problem.

DETAILS OF EXPERIMENTS.

In our study we used three sets of *Stegomyia fasciata*, comprisin fourteen insects, the progeny of three mothers that had fed on yellov fever. The history of these mosquitoes is as follows:

Set 1, Groups I and II, mosquitoes Nos. 1, 2, 3, and 4.

Mother mosquito.—The mother mosquito of this set was one of number raised from the larval stage in our laboratory, and, withou any prior feeding, was made to sting, on October 3, at 5.20 p. m., patient (Melancon) with a severe case of yellow fever, 14½ hours afte the initial chill; about 42 hours later this mosquito was again mad to sting the same patient, now about 56 hours after the onset. On October 14, at 3.55 p. m., this insect was made to sting a second yellow fever patient (Kippers), suffering from a severe attack of the disease, about 48 hours after the onset of the first symptoms.[a] In all, then, this mosquito had three feedings of yellow fever blood from two severe cases in the early stages of the disease. This, as well as all our mosquitoes, was kept in a room in which the temperature was artificially kept between 80° F. and 90° F. Four or five times throughout the course of these experiments the temperature in this room fell to 70° for six or eight hours at a time.

Group I.—On October 17, at 8.30 a. m. (13½ days from the first, 11½ days from the second, and about 2½ days from the third feed of yellow fever blood), this mosquito deposited eggs from which there were hatched between November 4 (4 p. m.) and November 5 (8.30 a. m.) two[b] adult female *Stegomyia fasciata*, which comprise our Group I of Set 1, and were numbered 1 and 2.

Group II.—On October 19, at 4.30 p. m. (16 days from the first, 14 days from the second, and about 5 days from the third feed of yellow fever blood), this same mother insect laid a second batch of eggs from which were hatched between November 7 (8 a. m.) and November 8 (8.30 a. m.) two adult female *Stegomyia fasciata*, which comprise our Group II of Set 1, and were given the numbers 3 and 4.

Set 2, Group I, mosquito No. 5.

Mother mosquito.—The mother mosquito of this set was one of a number raised from larvæ and for some time fed on immune blood.

On October 4, at 9 a. m., this insect was made to sting a severe case (Melancon) of yellow fever 30 hours after the initial chill.[c]

Group I.—October 19, at 4.30 p. m. (15 days after the feed of yellow fever blood), this insect laid a batch of eggs from which there was hatched between November 7 (8.30 a. m.) and November 9 (8.30 a. m.) one adult *Stegomyia fasciata*, which was given the number 5 and was the only one comprised in this set.

Set 3, Groups I, II, III, and IV, mosquitoes Nos. 7, 8, 9, 10, 11, 12, 13, and 14.

Mother mosquito.—The mother mosquito of this set was one of a number of *Stegomyia fasciata* raised from larvæ in our laboratory

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[a] On Oct. 8, 10, and 12, it was permitted to fill itself by stinging an immune. After Oct. 16, fed with sirup.

[b] We mention only the mosquitoes that survived and were used for inoculation; others, including males, are ignored in this report.

[c] On Oct. 6, 8, 10, 12, and 15, fed by stinging an immune. After Oct. 16, fed with sirup.

and, without any prior feeding, was made to sting on October 4, at 9 a. m., a severe case of yellow fever (Melancon) 30 hours after the initial chill.[a]

Group I.—October 18, at 4.20 p. m. (14 days after the feed of yellow fever blood), this insect deposited some eggs, from which there was hatched November 12, at 9 a. m., an adult female *Stegomyia fasciata*, which formed Group I of this set and was given the number 6.

Group II.—October 19, at 4.30 p. m. (15 days after the feed of yellow fever blood), this mother mosquito laid another batch of eggs, from which there were hatched between November 7 (8.30 a. m.) and November 9 (8.30 a. m.) three female *Stegomyia fasciata*, numbered 7, 8, and 9, which form Group II of this set.

Group III.—November 12, at 9 a. m., there was hatched an additional adult female *Stegomyia fasciata*, which was numbered 10 and forms Group III of this set.

Group IV.—Between November 13 (8.30 a. m.) and November 18 (8.30 a. m.) there were hatched four additional females, numbered 11, 12, 13, and 14, which comprise Group IV of this set.

At stated intervals these fourteen *Stegomyia fasciata*, the progeny of mothers (Sets 1, 2, and 3) that had fed on cases of yellow fever as above indicated, were made to sting nonimmune subjects, and during the intervals fed upon sirup.

Mosquitoes Nos. 1 and 2 (Set 1, Group I) were applied to and stung seven nonimmunes (A, B, C, D, G, H, K) at various invtervals between the sixth and thirty-ninth day after completing their metamorphoses, as shown in Table 2.

TABLE 2.—*Inoculation with mosquitoes Nos. 1 and 2.*

[Nonimmunes are designated by capital letters.]

Mosquito.	Stung nonimmuue—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		Days.			*Days.*
No. 2	A	6–7	Nos. 1 and 2	B	20–21
No. 1	B	9–10	Nos. 1 and 2	D	24–25
No. 2	C	10–11	No. 1	G	32–33
No. 2	A	12–13	No. 1	H	35–36
Nos. 1 and 2	C	13–14	No. 1	K	39–40

Of these inoculations, four were made after the twenty-second day (the mosquito incubation period in the successful case reported by Marchoux and Simond), namely, at age periods of 24, 32, 35, and 39 days.

[a] On Oct. 6, 8, 10, 12, and 14, fed by stinging immune. After Oct. 15, fed with sirup.

Mosquitoes Nos. 3 and 4 (Set 1, Group II) were made to sting eight nonimmune subjects (B, E, F, G, J, L, M, and N) ten times at intervals between the thirteenth and forty-ninth day after emergence as adult insects, as shown in Table 3.

TABLE 3.—*Inoculation with mosquitoes Nos. 3 and 4.*

[Nonimmunes are designated by capital letters.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		Days.			*Days.*
Nos. 3 and 4	B	13–14	No. 3	J	33–34
No. 3	E	21–22	No. 3	aL	37–38
No. 4	E	23–24	No. 3	M	42–43
No. 3	F	26–27	No. 3	G	45–46
Nos. 3 and 4	G	29–30	No. 3	N	49–50

a Subject passed from observation at the end of 5 days.

Mosquito No. 5 (Set 2) was made to sting subject F on two separate days; the first time 25 and the second 27 days after reaching the adult stage, 3 and 5 days, respectively, later than in the positive case reported by the French workers as shown in Table 4.

TABLE 4.—*Inoculations with mosquito No. 5.*

[Nonimmune is designated by a capital letter.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		Days.			*Days.*
No. 5	F	25–27	No. 5	F	27–29

Mosquito No. 6 (Set 3, Group I) was made to sting at age periods of 2, 4, 6, 9, and 12 days longer than in the successful case reported by Marchoux and Simond. In all, five subjects were used.

TABLE 5.—*Inoculation with mosquito No. 6.*

[Nonimmunes are designated by capital letters.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		Days.			*Days.*
No. 6	F	24	No. 6	J	31
No. 6	G	26	No. 6	M	34
No. 6	H	28			

Mosquitoes Nos. 7, 8, and 9 (Set 3, Group II) were made to sting subjects B and F. Subject B was stung by all three insects 3 (to 5) days after completing their metamorphoses. Subject F was stung by insect No. 9 on the twenty-fifth (to twenty-seventh) and again on the twenty-seventh (to twenty-ninth) day after its metamorphosis.

TABLE 6.—*Inoculation with mosquitoes Nos. 7, 8, and 9.*

[Nonimmunes are designated by capital letters.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		Days.			*Days.*
Nos. 7, 8, and 9	B	3-5	No. 9	F	27-29
No. 9	F	25-27			

Mosquito No. 10 (Set 3, Group III) stung subjects B and G, 2 and 26 days respectively after emergence from the pupal shell, the latter inoculation being 4 days after the 22-day period.

TABLE 7.—*Inoculation with mosquito No. 10.*

[Nonimmunes are designated by capital letters.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		Days.			*Days.*
No. 10	B	2	No. 10	G	26

With mosquitoes Nos. 11, 12, 13, and 14 we made one inoculation at least 22 days after completing their metamorphoses, and nine inoculations of seven subjects (B, F, G, J, L, M, and N) at varying intervals after this period up to and including the fortieth day after attaining the adult stage, as shown in Table 8.

TABLE 8.—*Inoculation with mosquitoes Nos. 11, 12, 13, and 14.*

[Nonimmunes are designated by capital letters.]

Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.	Mosquito.	Stung nonimmune—	Age of mosquito at time of stinging.
		Days.			*Days.*
Nos. 11 and 12	H	22-27	No. 11	F	32-37
Nos. 13 and 14	J	23-28	No. 12	B	32-37
Nos. 11 and 12	J	25-30	Nos. 12, 13, and 14	G	34-39
No. 13	G	25-30	Nos. 12 and 13	J	36-41
No. 14	[a] L	26-31	Nos. 13 and 14	N	39-44
Nos. 12, 13, and 14	[b] M	30-35	No. 12	N	40-45

[a] Subject passed from observation after 6 days.
[b] Subject passed from observation after 5 days.

We have recorded above our work with particular reference to the mosquitoes. Below (Table 9) we tabulate it with reference to the nonimmunes who were the subjects of the inoculations.

TABLE 9.—*Nonimmunes and inoculations to which they were subjected.*

Subject, age, and nationality.	Stung by mosquito—	Age of mosquito at time of inoculation.[a]
		Days.
A, nonimmune, 23 years, Canadian	No. 2	6
	No. 2	12
B, nonimmune, 44 years, Dalmatian	Nos. 6 and 10	2
	Nos. 7, 8, and 9	3
	No. 1	9
	Nos. 3 and 4	13
	Nos. 1 and 2	20
	No. 12	32
C, nonimmune, 16 years, Austrian	No. 2	10
	Nos. 1 and 2	13
D, nonimmune, 26 years, Norwegian	Nos. 1 and 2	24
E, nonimmune, 21 years, American	No. 3	21
F, nonimmune, 23 years, American	No. 6	24
	Nos. 5 and 9	25
	No. 3	26
	Nos. 7 and 9	27
	No. 11	32
G, nonimmune, 23 years, American	No. 13	23
	Nos. 6 and 10	26
	Nos. 3 and 4	29
	No. 2	32
	Nos. 12, 13, and 14	34
H, nonimmune, 34 years, American	Nos. 11 and 12	22
	No. 6	28
	No. 2	35
J, nonimmune, 45 years, Irish	Nos. 13 and 14	23
	Nos. 11 and 12	25
	No. 6	31
	No. 3	33
	Nos. 12 and 13	36
K, nonimmune, 27 years, Norwegian	No. 2	39
L, nonimmune, 38 years, American	No. 14	26
	No. 3	37
M, nonimmune, 20 years, American	Nos. 12, 13, and 14	30
	No. 6	34
N, nonimmune, 31 years, Irish	Nos. 13 and 14	39
	No. 12	40
	No. 3	49

[a] Ages given in this table are minimal. For further details consult previous tables.

In all, thirteen subjects were used. After each inoculation they were kept under observation for at least 7 days, except in three instances, in two of which the observation period was 5 and in the third 6 days.

Our results were uniformly negative, no reaction of any kind being observed in any of the subjects of our inoculations.

CONCLUSION.

In view of the negative results recorded by us in our efforts to confirm the positive work of Marchoux and Simond, we feel that additional work will be necessary to settle the question of the hereditary transmission of the parasite of yellow fever in the *Stegomyia fasciata*. Nevertheless, the sanitarian will do well to continue his measures of mosquito destruction after the suppression of an epidemic.

APPENDIX.[a]

THE HEREDITARY TRANSMISSION OF THE VIRUS OF YELLOW FEVER IN THE STEGOMYIA FASCIATA.

By E. Marchoux and P. L. Simond.

Among the new facts concerning yellow fever which we gathered in Brazil there is one the importance of which obliges us to publish at once. It concerns the question of the possibility of the hereditary transmission of the yellow fever virus from mosquito to mosquito.

Since 1903 our attention has been turned to the fact that in certain foci of an epidemic zone it is at times difficult to find a case of yellow fever of recent date as the origin of the new cases which spring up at a given time. There being no doubt that the lighting up of these foci was due to the presence of infected *Stegomyia fasciata*, we were forced to conclude that one or several of these mosquitoes had in some way been imported from a distant point where the disease existed from which they had drawn the virus. This undoubtedly occurs frequently. We, nevertheless, were led to ask ourselves if, under certain circumstances, eggs derived from a Stegomyia infected in the course of an epidemic some months prior to the one observed could not have given birth to Stegomyias hereditarily infected.

Several experiments were made in 1903 to confirm this hypothesis. We had some Stegomyias lay eggs that had stung some cases early in the disease. The eggs were hatched into larvæ, and the adult insect raised from these was made to sting a human subject.

These experiments did not give us positive results at that time, although the subjects that had been bitten by these mosquitoes were not immune to the disease, for subsequently it was possible to give it to them by injections of fresh virulent serum.

We resumed these experiments in February, 1905. We collected a number of eggs of one laying from a Stegomyia 20 days old which had stung several of our cases in order to determine a heavy infection, and the larvæ which were hatched the 4th of February were placed in a jar to be reared. The adult insects began to emerge February 16. These, isolated in tubes from the time of emergence, were fed with

[a] Translated from Comptes Rendus, Société Biologie, Paris, Vol. LIX, No. 27. August 4, 1905, p. 259.

sirup until March 2. At this date, 14 days after the metamorphosis, two of these Stegomyia stung subject A, a Portuguese, who had arrived in Brazil a few days before, and had up to that time never had yellow fever. The subject showed no reaction following this inoculation.

He was stung again by one of these two mosquitoes (the second having died in the meantime) on the 10th of March, 8 days after the first inoculation. Four days later, March 14, he developed a typical though mild attack of yellow fever. The character of the period of invasion, the vomiting, the pains, the course of the temperature, the icterus, and the progress of convalescence permitted no doubt as to the nature of the disease.

We deemed it a duty, nevertheless, to confirm our diagnosis experimentally. After recovering, this subject was twice submitted to the stings of several Stegomyia infected by a case of yellow fever. He showed himself absolutely refractory to these inoculations, as do all individuals recently immunized by a first attack.

Let us add that the conditions under which he was observed by us from the time of his arrival in Brazil do not permit that any source of contamination, other than the hereditarily infected mosquito by which he had been stung, could have brought on the attack of yellow fever which he had presented.

It may be concluded from this experiment that under conditions which can not as yet be precisely defined the *Stegomyia fasciata*, the progeny of a mother directly infected by a case of yellow fever, are themselves infected hereditarily. It follows from the various experiments done on this subject that the time needed by the mosquito hereditarily infected to become capable of discharging the virus with its salivary secretion is longer than in the case of the mosquito which has drawn the virus directly from the blood of a patient. This period was 22 days in the positive case.

It follows likewise, both from experiments and from epidemiologic facts, that this hereditary transmission can not be considered as the general rule but rather as an exceptional occurrence.

The mildness of the attack suffered by A warrants the belief that the passage of the virus from one generation of Stegomyia to another is accompanied by a certain amount of attenuation. This may be a new field open to research with reference to vaccination against yellow fever.

The knowledge of this mode of propagation explains one of the most obscure points in the history of yellow fever, that of the recurrence of certain epidemics under conditions where a primary case can not be found that is sufficiently recent to explain the infection of the Stegomyia.

Finally, its importance can not be disregarded from the point of view of prophylaxis.

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YELLOW FEVER INSTITUTE, BULLETIN No. 16

Treasury Department, U. S. Public Health and Marine-Hospital Service

WALTER WYMAN, *Surgeon-General*

YELLOW FEVER

ETIOLOGY, SYMPTOMS AND DIAGNOSIS

BY

JOSEPH GOLDBERGER

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YELLOW FEVER INSTITUTE, BULLETIN No. 16

Treasury Department, U. S. Public Health and Marine-Hospital Service

WALTER WYMAN, *Surgeon-General*

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ETIOLOGY, SYMPTOMS AND DIAGNOSIS

BY

JOSEPH GOLDBERGER

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By JOSEPH GOLDBERGER, *Passed Assistant Surgeon, U. S. Public Health and Marine-Hospital Service.*

ETIOLOGY.

The claims, by various authors up to 1890, of having discovered the specific cause of yellow fever, were all effectually disposed of by the investigations of Sternberg. Since that time several investigators have reported finding the specific causative agent; but it is notable that no two of the micro-organisms for which this claim was made were identical, and since only one could be the specific organism, it is evident that the others could have no real claim to specificity.

Of the organisms referred to, that described by Sanarelli (1897) as the *Bacillus icteroides* attracted most attention and, indeed, was at first hailed as the long-looked-for germ.

A series [a] of epoch-making investigations and discoveries by a commission composed of Walter Reed, James Carroll, Aristides Agramonte, and Jesse W. Lazear, medical officers of the United States Army, which have been fully confirmed and in some respects amplified by independent workers—Cuban [b], Brazilian [c], American [d], French [e], German [f]—have resulted in establishing:

1. That yellow fever is transmitted, under natural conditions, only by the bite of a mosquito (*Stegomyia calopus*) that at least 12 days

[a] Reed, Carroll, Agramonte, and Lazear, 1900; Reed, Carroll, and Agramonte, 1901a, and 1901b; Reed and Carroll, 1902.

[b] Guiteras, 1901. [c] Barreto, de Barros, and Rodrigues, 1903. [d] Ross, 1902; Parker, Beyer, and Pothier, 1903; Rosenau, Parker, Francis, and Beyer, 1904; Rosenau and Goldberger, 1906. [e] Marchoux, Salimbeni, and Simond, 1903; Marchoux and Simond, 1906a, 1906b, 1906c. [f] Otto and Neumann, 1905.

before has fed on the blood of a person sick with this disease during the first 3 days of his illness.

2. That yellow fever can be produced under artificial conditions by the subcutaneous injection of blood taken from the general circulation of a person sick with this disease during the first 3 days of his illness.

3. That yellow fever is not conveyed by fomites.

4. That the *Bacillus icteroides* Sanarelli stands in no causative relation to yellow fever.

As all preventive measures are based on the foregoing fundamental propositions, a somewhat more detailed consideration of each is desirable.

A.—*Yellow fever is transmitted, under natural conditions, only by the bite of a mosquito* (Stegomyia calopus) *that at least 12 days before has fed on the blood of a person sick with this disease during the first three days of his illness.*

The unusual prevalence of insects during some epidemics of yellow fever was noted more than a century ago. It was not until 1848, however, that any suggestion was made as to their etiological connection. In that year Josiah C. Nott of Mobile, Ala., reasoning from certain epidemic peculiarities of the disease, expressed it as "probable that yellow fever is caused by an insect or animalcule bred on the ground," and mentioned "mosquitoes, flying ants, many of the aphides" as illustrations of insects whose general habits were such as to fulfill the requirements as transmitters of the disease. At about this time there appears to have prevailed a fairly widespread belief in the existence of some relation between mosquitoes and yellow fever, for Dowler, writing in 1855, states that many persons regarded "any increase in the number of mosquitoes as a certain prelude or precursor to a yellow-fever epidemic."

The first to definitely assert that the mosquito is the medium of transmission and to specifically indicate the mosquito concerned was Carlos J. Finlay. In 1881, at a meeting of the Royal Academy of Medical and Physical Sciences of Habana, he stated that three conditions were necessary for the propagation of yellow fever, namely: "(1) The existence of a yellow fever patient into whose capillaries the mosquito is able to drive its sting and to impregnate it with the virulent particles, at an appropriate stage of the disease. (2) That the life of the mosquito be spared after its bite upon the patient until it has a chance of biting the person in whom the disease is to be reproduced. (3) The coincidence that some of the persons whom the same mosquito happens to bite thereafter shall be susceptible of contracting the disease." During the succeeding twenty years Finlay continued, tenaciously, to maintain his theory which, in collaboration with Delgado, he attempted, though unsuccessfully, to prove.

To Reed, Carroll, Agramonte, and Lazear is due the credit for the masterly experiments which converted a discredited hypothesis into an established doctrine.

The transmission of the disease by the mosquito is not, as Finlay thought, a simple mechanical transfer from one individual to another, such as occurs at times in plague through the instrumentality of fleas or in surra through biting flies. In these diseases neither the flea nor the fly is necessary, but in yellow fever not only is the mosquito necessary, but it is essential that the mosquito be of a particular species or at least of a particular genus. Thus, attempts to transmit the disease by means of mosquitoes of other than the genus *Stegomyia*[a] have not been successful.

It has been found, furthermore, that in yellow fever, unlike either surra or sleeping sickness, a certain period must elapse after the infecting feed before the mosquito is capable of communicating the disease.[b] Experimentally this interval appears to be not less than 12[c] days, so that a susceptible individual may expose himself with impunity to repeated stings within the first 10 or (?) 11 days[d] after the mosquito has fed on a person sick with the disease. This is the period of "extrinsic incubation" of Carter, whose painstaking observations at Orwood and Taylor, Miss., in 1898, resulted in his tentatively fixing this interval as "usually in excess of 10 days" and served, in the light of the then recent discovery of the mosquito transmission of malaria, to direct the attention of the Army Commission to Finlay's mosquito as a possible "intermediary host" for this disease.

The duration of this period of "extrinsic incubation" is decidedly influenced by the temperature of the air. It is at its minimum at temperatures above 26° C (80° F), but becomes progressively longer as the temperature declines below this point.

The period of the disease at which the mosquito bites is another essential factor in the latter's power to transmit the disease. Thus all attempts to produce an attack by means of the bites of mosquitoes that had previously fed on cases after the third day of the

[a] No experiments have as yet been recorded with any species of this genus other than *S. calopus*.

[b] In surra and sleeping sickness for example, no such interval exists. On the contrary, it is only during the two days immediately following the infecting feed that the tsetse flies concerned can transmit these diseases. After the third day their bite is perfectly harmless. In dengue this interval appears likewise to be absent.

[c] I say "appears to be," because the recorded experimental evidence is not sufficient to prove that it may not under favorable conditions be a (very) little shorter than 12 days.

[d] Nor do such bites during this period confer, as Finlay believed, an immunity from subsequent attack.

disease have failed,[a] whereas all successful attempts have been with such mosquitoes as had been allowed to feed on cases during the first three days.

There are some who, while granting that the mosquito is capable of transmitting the disease directly by biting, maintain that the disease may also be acquired by ingesting water in which the body of an infected mosquito has disintegrated. Again, there are others who, while admitting that the mosquito is the sole medium of transmission, hold, nevertheless, that there may be sources other than the one mentioned from which this insect may acquire its infection, and suggest black vomit or articles soiled by yellow-fever patients as pertinent illustrations. But neither the results of experiments especially designed to test these hypotheses nor the indirect evidence furnished by a large mass of observations give the slightest support to these assumptions. After the mosquito has become infective it probably remains so for life.

B.—*Yellow fever can be produced under artificial conditions by the subcutaneous injection of blood taken from the general circulation of a person sick with this disease during the first 3 days of his illness.*

The subcutaneous injection of a drop[b] (0.1 cc.) of yellow fever blood serum from a case in the first day of illness has produced an attack of yellow fever, whereas five times this amount from a case in the fourth day of the disease produced no symptoms.

C.—*Yellow fever is not conveyed by fomites.*

Before the demonstration by the Army Commission of the transmission of yellow fever through the mosquito it was very generally believed, notwithstanding a large mass of evidence to the contrary, that the disease was communicated by the exhalations of the sick, by contact with their excretions, or with articles that had been exposed to or been soiled by them.

In order to put this almost universal belief in fomites to a rigorous test, the Army Commission exposed each of a series of seven non-immunes to clothing and bedding which had been used by cases of yellow fever and which had become soiled with blood, urine, feces, and black vomit. The house in which the experiment was carried out was especially constructed for the purpose in an isolated place near Habana. In order to prevent access of mosquitos and to simu-

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[a] The recorded experimental evidence is not sufficient to show that this infective period may not at times extend into the fourth day. This is of considerable practical importance. A case of yellow fever should be protected from mosquitoes during four full days at least.

[b] Parker, Beyer, and Pothier (1903) induced an attack of yellow fever by the subcutaneous injection of 0.033 cc. of filtered serum from a case in the third day.

late the conditions thought most favorable to infection by fomites, the windows and doors were screened and so placed as to prevent free ventilation, special pains were taken to exclude sunlight, and provision was made for heating during the day so that an average temperature of 72.6° F. was maintained throughout the entire period. The men were exposed in squads for periods averaging 21 nights each. Each squad entered the house at night, removed the soiled articles from the boxes in which they were packed, shook them out, hung some about the room, and used some for making up the beds in which they slept. In the morning the various garments and articles of bedding were repacked and the men left the room to occupy a near-by tent during the day. The result of this experiment was entirely negative; the men remained in perfect health. Subsequently some of them submitted to mosquito inoculation and promptly sickened with the disease, showing conclusively that they were not immune.

It may be of interest to observe that the first experiments to determine the infective power of fomites were made over a century ago. In 1800 Cathrall reported having repeatedly applied black vomit to his tongue and lips and to the skin of various parts of the body without experiencing any ill effects. In company with a friend he had, besides, exposed himself to the fumes of heated black vomit, both in the open air and in a confined space, likewise without harm. In 1804 Ffirth, imitating Cathrall's example, went so far as to repeatedly swallow several ounces of fresh black vomit; he rubbed some into incisions in his arms and dropped some into his eye without experiencing any but momentary disagreeable effects.

In view of the foregoing, one can not but admire the acute reasoning of La Roche,[a] who, half a century ago, in discussing the evidence in support of transmission through the agency of clothes, bedding, merchandise, etc., concluded that "we may well infer" that in the record of such instances "some error has crept in—something has been omitted or overlooked—and that the production of the disease was really due to some other agency than the one contended for," a conclusion which will be concurred in by anyone who will take the pains to critically examine the recorded instances of alleged transmission by such means.

D.—*Experiments to show that the* Bacillus icteroides *Sanarelli stands in no causative relation to yellow fever.*

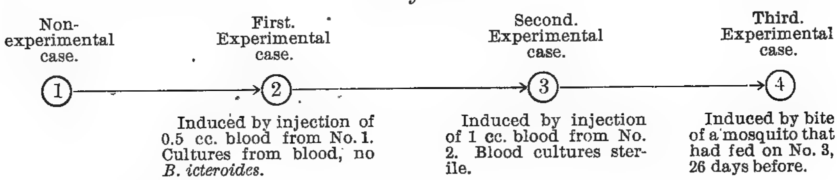
The fact that the Army Commission was able to produce three cases of yellow fever by the subcutaneous injection of blood which was shown to be sterile by the culture method is sufficient to eliminate

[a] Vol. 2, p. 522.

B. icteroides from consideration. That the attacks of fever so produced were not simply such as might be caused by the injection of a soluble toxine circulating in the blood is shown by the following chain of experiments:

The first link in the chain was a fatal nonexperimental case of yellow fever which furnished the Army Commission[a] with blood that culturally showed the absence of *B. icteroides*, but 0.5 cc. of which injected subcutaneously into a nonimmune (W. F.)[a] induced an attack of fever having all the characters of yellow fever. From the latter case blood was drawn and 1 cc. injected into a second nonimmune (J. H. A.)[a]; culturally this blood was sterile, but nevertheless it caused an attack in all respects similar to yellow fever. Eight hours after the onset of this man's illness some mosquitoes were allowed to bite him, one of which, 26 days later, was applied to a nonimmune (Vergara)[b], who developed an attack of yellow fever 3 days, 10 hours later (see diagram).

Diagram.



The only possible explanation of this chain of events is that there was present in the blood used for the subcutaneous injections an organism that can not be cultivated on ordinary media—*B. icteroides* grows readily on all ordinary media—and that the mosquito that bit the second of the experimental cases became infected with this organism and 26 days later transmitted this infection to a nonimmune. It is inconceivable that a toxine alone could infect a mosquito in such a way as to enable the latter, 26 days later, to reproduce the disease by biting a nonimmune. It may be observed in this connection that a person who has suffered from an attack of the disease, acquired naturally or experimentally through the bite of a mosquito, is immune to injections of virulent yellow fever blood serum and, vice versa, an attack of the disease induced by the injection of yellow fever blood protects against subsequent inoculation by means of infected mosquitoes.

The parasite.—While the organism of yellow fever has not yet been discovered, we are, nevertheless, in possession of some facts which enable us to form some idea of its character. The disease has been found to occur in nature only in man and the mosquito, so that it is

[a] Reed, Carroll, and Agramonte, 1901b, p. 16.
[b] Guiteras, 1901, p. 812.

inferred that the parasite is one of those that requires for the complete evolution of its life cycle a mammalian and an arthropod host. We have familiar analogies in *Piroplasma bigeminum* of Texas fever and the *Plasmodium* of malaria. Because of these analogies it is inferred that biologically it may be grouped with them as a protozoon. On the basis of these and other analogies, both Schaudinn (1904) and Novy & Knapp (1906) have suggested that it may be a *Spirochæta*. Stimson's recent discovery of a spirochæte-like organism in the tubules of a yellow fever kidney is, therefore, exceedingly interesting and suggestive.

The cycle in man is represented clinically by a stage of incubation and by a stage of fever. Some attempts to infect mosquitoes by allowing them to bite subjects during the stage of incubation, in one instance as late as 6 hours before the onset of the stage of fever, have been unsuccessful; whereas a mosquito that bit a case of the disease 8 hours after the onset became infected and conveyed the disease to a nonimmune 26 days later. This would indicate that the parasite does not appear in the circulating blood until the onset of the disease. We already know that it remains in the blood only during the first three days of the disease or, at least, it is only during those three days that it exists in a form capable of continuing its life cycle in the mosquito or in a fresh nonimmune.

In the circulation it exists in a form so minute as to be capable of passing through the finest grained porcelain filters, such as the Chamberland B and the Chamberland F.

Its resistance to deleterious influences is feeble when withdrawn from the circulation. When kept in a test tube exposed to the air in the dark, at a temperature of 24° C. (75° F.) to 30° C. (80° F.), it loses its virulence in 48 hours. Under the same conditions, but protected from the air by keeping under oil, it retains its vitality somewhat longer—up to between 5 and 8 days. Heating for 5 minutes at 55° C. (132° F.) apparently suffices to kill it. The effect of low temperatures has not been studied.

The cycle in the mosquito requires at least 12 (?) days[a] for its completion. As to the changes which it undergoes during this period we are in complete ignorance.

The French commission has recorded one experiment which would indicate that the parasite may, under certain circumstances, be transmitted to the progeny of an infected mosquito through the egg. An attempt by Rosenau and Goldberger to confirm this resulted negatively. The same commission attempted, but without success, to transmit the parasite from one mosquito to another by feeding larvæ with cadavers of infected adults; they appear, however, to have succeeded in trans-

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[a] See page 5, footnote c.

mitting the parasite to a mosquito by feeding it with sirup in which the body of an infected insect had been crushed.

Judging from the variations in the virulence of different epidemics it is fair to infer that there is a corresponding variation in the virulence of the parasite. The variation in severity of individual cases appears, however, to be largely influenced by the susceptibility or resistance of the subject, for the bite of the same mosquito or mosquitoes will be followed in one instance by a severe and in another by a mild attack. Nor does there appear to be any appreciable difference in severity between attacks induced by the bite of a single as compared with those induced by the bites of several insects.

Susceptibility.—Attempts to induce the disease in the ordinary laboratory animals have been unsuccessful. Marchoux and Simond (1906a) caused a mild febrile attack in one orang-outang and in one chimpanzee by bites of infected mosquitoes. Thomas (1907) induced a mild febrile attack with albuminuria in a chimpanzee following an inoculation by infected mosquitoes.

All persons are naturally susceptible, but there is a difference in the degree of this susceptibility in different races. Thus the mortality in the negro is less than in the Caucasian. Age has a distinct influence on susceptibility, as is shown by the mildness of attack and relatively low mortality in children. Nativity and long-continued residence in an endemic focus were supposed at one time to "acclimatize" and thus protect against the disease, but it is now believed that this protection was obtained not by the occult influence of climate but by having had during childhood or at some other age a mild and unrecognized attack of the disease.

THE YELLOW FEVER MOSQUITO.

This insect has been known by a variety of names of which *Culex mosquito*, *Culex tæniatus*, and *Culex fasciatus* were in most common use up to 1901. In that year Theobald, having observed that some sixteen species of *Culex*, while agreeing amongst themselves, differed from the others of this genus in certain peculiarities of scale arrangement, separated these into a group to which he applied the name *Stegomyia*. In this group was included the yellow-fever mosquito whose name thereupon became *Stegomyia fasciata*. Blanchard (1905), however, has pointed out that the specific designation *fasciata* is not applicable to this insect, as it had first been applied to another, so that *calopus*, suggested by Meigen in 1818, has the right of priority. Therefore, under the rules of zoological nomenclature, the correct name is *Stegomyia calopus* (Meigen, 1818) Blanchard, 1905.

Adult.—The *Stegomyia calopus* (figs. 1 and 2) is readily recognized. It is a handsome insect—a study in black and white. The distinction

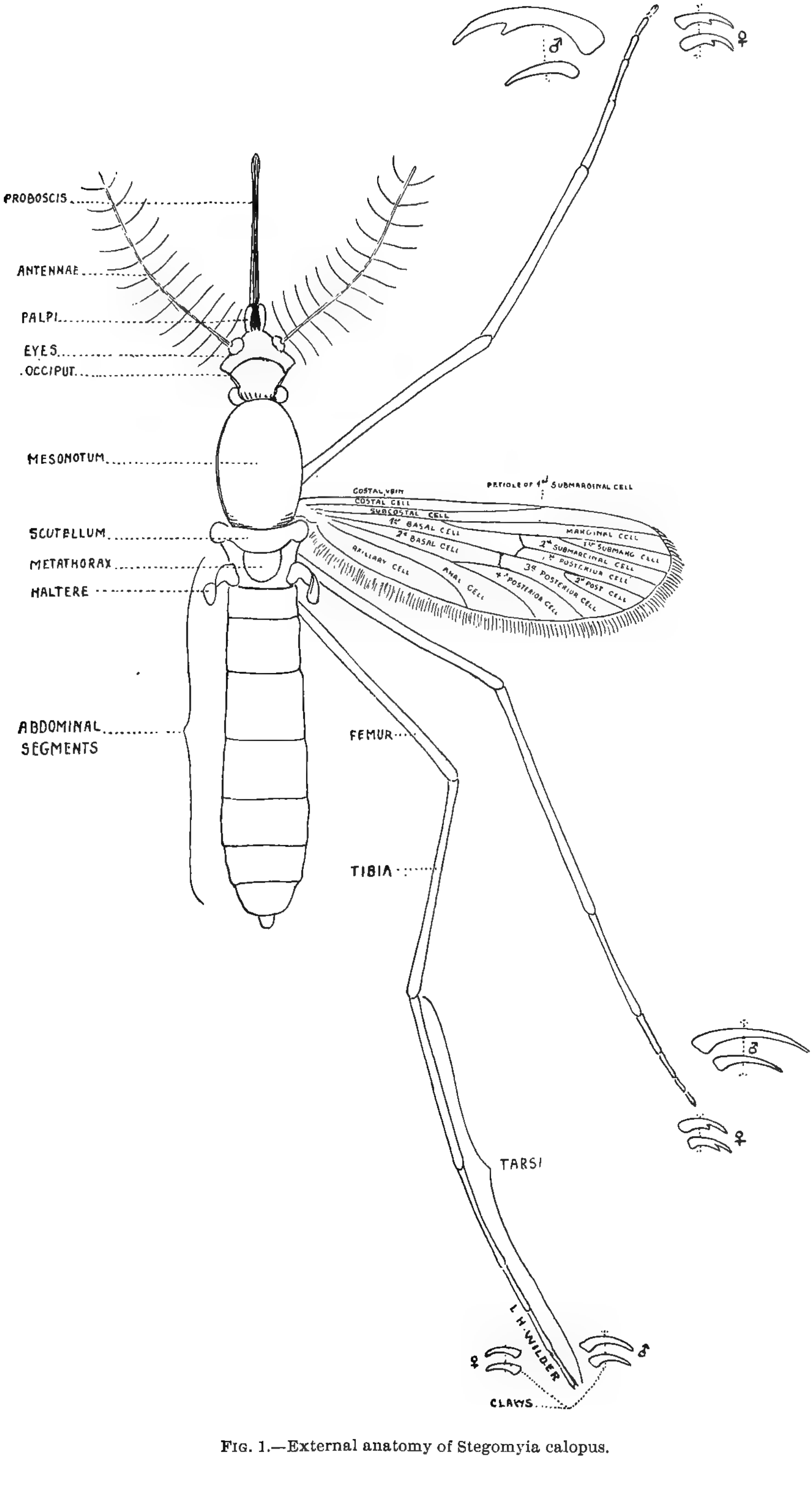

FIG. 1.—External anatomy of Stegomyia calopus.

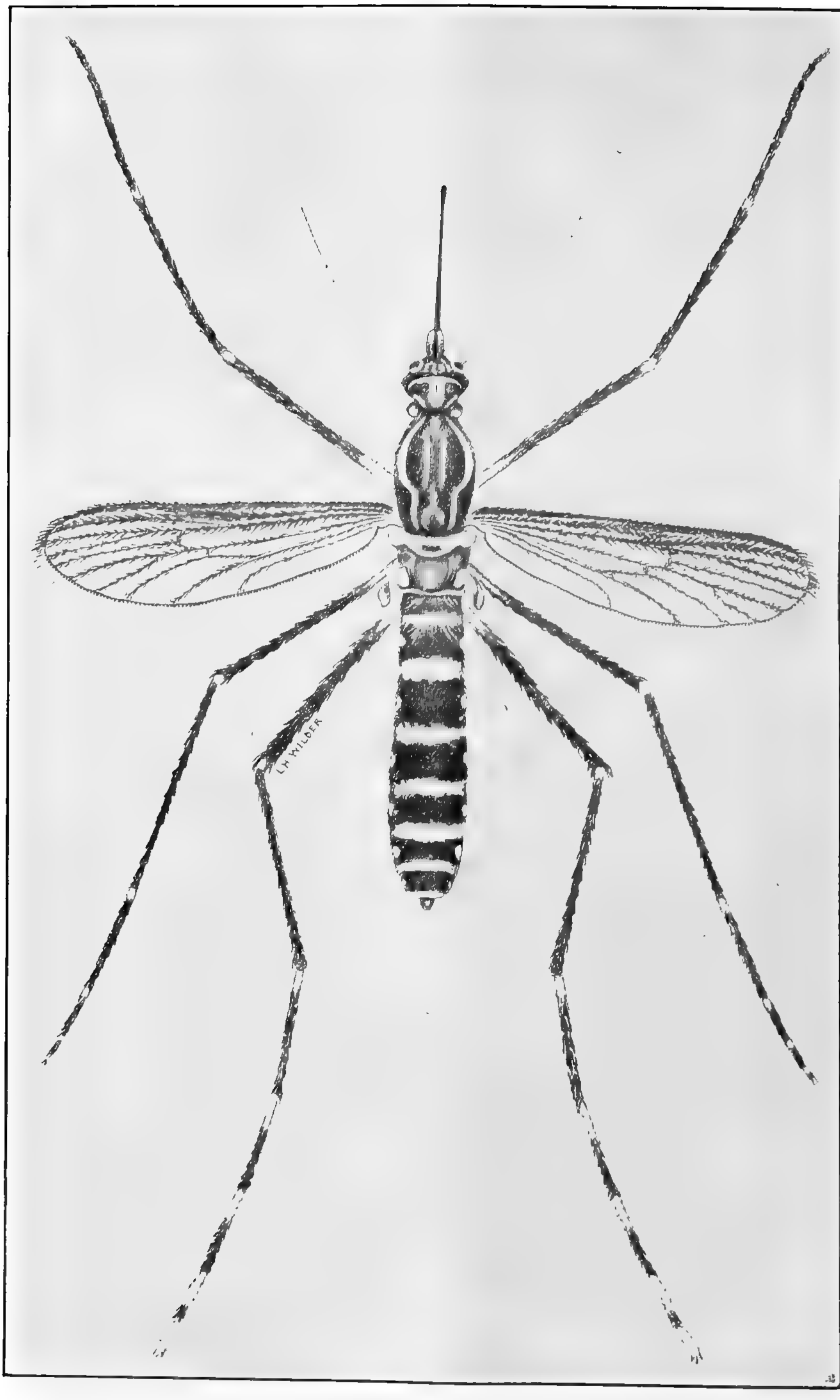

Fig. 2.—Stegomyia calopus (female).

tween the male and the female is readily discernible in the characters the antennæ; in the former (fig. 3) these organs are prominent and ıthery—decidedly hirsute. Another prominent point of difference ists in the length of the palpi; in the male they are long—almost as ıg as the proboscis, but in the female they are short—less than one-.rd the length of the proboscis.

The palpi in both sexes are black, but are ornamented with white ıles which, in the male, are arranged as four narrow bands, while in e female they are collected into a white tuft at the tip.

The proboscis is black and is devoid of ornamentation, differing in is respect from both *Culex tæniorhynchus* and *Culex sollicitans*, ch of which has the proboscis marked by a pale band in the middle. ıese two insects bear a superficial resemblance to *S. calopus*, for ıich they are not infrequently istaken by the uninformed.

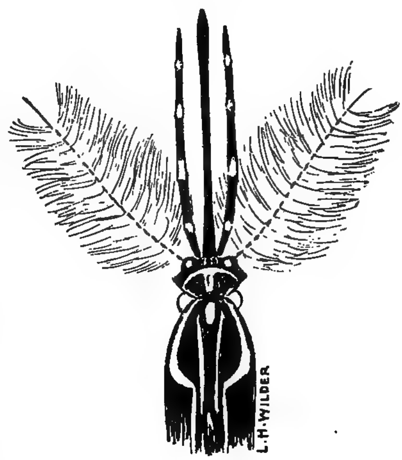

FIG. 3.—Appendages of head of Stegomyia calopus (male).

The head is clothed by the broad .t scales characteristic of the ›nus. These scales are black, ex-pt for a line of white down the iddle extending to the neck and narrow white border to the eyes.

The thorax is dark brown, almost ack, ornamented with silvery hite patches and lines of which ıe following are peculiar to and stinctive of this species, and en-ɔle one to recognize it at a glance: . well marked, easily recognizable, ure white curved line on either de of the back (mesonotum) be-veen which, but less obvious to the naked eye, are two delicate ıedian parallel lines; a prominent transverse white line of scales n the scutellum.

The abdomen is clothed with black and white scales, the latter col-ıcted in bands at the bases of the abdominal segments, and in distinct atches at the sides.

The legs are black scaled, except for white bands which are arranged ı follows: A basal band on the first joint of the fore, on the first and ›cond of the mid, and on all of the hind tarsi except the last, which ·, as a rule, all white. Each leg is provided with a pair of claws ·hich are equal in size in the female but unequal in the male. They iffer in other respects in the two sexes; in the female those of the fore nd of the mid legs are provided with one tooth, those of the hind ›gs are simple; in the male all the claws are simple except the larger ne of the forefoot.

The veins of the wings are clothed with dark brown scales. The first submarginal cell is longer than the second posterior cell and the base of the former is nearer the root of the wing.

Biting.—The male insect does not bite; it lives almost exclusively on vegetable and fruit juices. In the females, however, a feed of blood is a necessary condition precedent to egg laying. At summer temperatures this insect will digest a full meal of blood in about 48 hours. If disturbed in the act of feeding it will fly away, but will return and attempt to finish its interrupted meal. In this way one infected mosquito in its efforts to obtain one full meal may bite several individuals, and so may, almost simultaneously, produce more than one case of yellow fever.

It has long been observed that communication with an infected town is distinctly safer during the day than after dark. In an effort to explain this phenomenon the French yellow fever commission first suggested, then made some experiments which appear to show that under natural conditions the yellow fever mosquito, after the first week, ceases to bite during the day and bites only at night—that is, between 5 p. m. and 7 a. m. These results are not, however, altogether in harmony with the observations of others, and there are cases recorded showing that yellow fever may be contracted by visiting an infected house during the day.[a] We must conclude, therefore, that the *Stegomyia calopus*, young or old, may bite at any time during the 24 hours, though probably it is most vicious about dusk and about dawn. The female is impregnated almost immediately after her birth, and then proceeds to seek a blood feed; 3 or 4 days after this she is ready to lay her eggs.

Breeding places.—The *Stegomyia calopus* appears to be strictly a house mosquito—a domestic though not domesticated animal. Her breeding places, therefore, may be expected, and actually have been found to be any collections of water in and about habitations, such as cisterns, wells, water barrels, tubs or jars with or without water plants, sagging roof gutters, more or less broken and discarded crockery, bottles and tins, fountains (not containing fish), cemetery vases, baptismal and other fonts in churches, chicken or horse troughs, grindstone troughs, and tubs or barrels containing water which has been softened and made more or less alkaline by the use of ashes. The larvæ have been found in tin cans containing fecal matter, in cesspools, and in some natural collections of water formed by leaves of certain tropical plants, such as the palm and century plant. Ordinarily, she does not seek street puddles or gutters, favorite breeding places for *Culex tæniorhynchus* and *Culex pipiens* (=*pungens*), though her larvæ have been found in these situations.

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[a] Carter, 1901b, p. 936.

Egg.—The female lays her eggs (fig. 4) on the surface of the water or on the sides of the container at or just above the water line. The eggs do not adhere one to the other to form the compact boat-shaped masses characteristic of *Culex* (fig. 5), but lie on their sides more or less isolated, though frequently grouped into clumps. At the moment of laying the eggs are of a cream color but rapidly become jet black; they are somewhat cigar shaped with one end slightly broader and more bluntly rounded than the other. They measure on an average about 0.55 mm. in length and 0.16 mm. in width at the broadest part. Under the microscope the apparently cylindrical egg is seen to be slightly flattened on one side. The eggs are most commonly laid during the night or early morning, but they may be laid at any time during the 24 hours. The total number of eggs laid varies, the average being about 65 to 70; the maximum recorded is 144.[a]

FIG. 4.—Eggs of Stegomyia calopus (after Stephens & Christopher, 1904).

The act of ovipositing appears to greatly exhaust the mosquito, so that it may fall on the surface of the water and die immediately after even the first egg laying. There are numerous exceptions, however, and the act may be repeated several times and the mosquito survive for some time after.

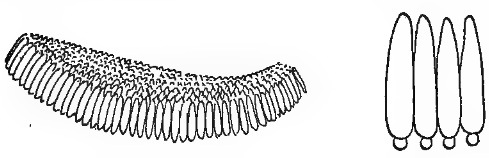

FIG. 5.—Eggraft and eggs of Culex (after Stephens & Christopher, 1904).

If laid on the surface of the water the egg floats, being supported by the surface film. Disturbance of the water surface may cause the egg to become wet and sink to the bottom, but this does not prevent its hatching out into the larva. The egg shows marked powers of resistance to unfavorable influences. Thus it may be kept dry for from two or three to six and one-half months[b] and still retain its vitality and hatch out when put back into the water. Reed and Carroll[c] have shown that freezing does not destroy its vitality. The egg probably plays the leading rôle in the hibernation of this mosquito.

Under the most favorable conditions as to temperature (30° C. (86° F.) and over) eggs hatch out in about 36 hours after they are laid, but with a lowering of the temperature this period becomes progressively longer until 20° C. (68° F.) is reached, below which they will not hatch at all.

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[a] Marchoux and Simond, 1906b. [b] Francis, 1907. [c] Reed and Carroll, 1901.

Larva.—The egg hatches into the larva ("wiggle-tail") (fig. 6), which can be distinguished readily from the larva of *Culex pipiens* (fig. 7), its most common messmate, by the color and proportions of the breathing siphon (air tube). In the *S. calopus* the respiratory siphon is black and somewhat barrel-shaped, with its greatest transverse diameter equal to about one-half of the length; whereas in *Culex pipiens* the air tube is brown, longer, more slender, and with the greatest transverse diameter less than one-third of the length of the tube. The larva, though it lives in the water, is strictly an air breather and must come to the surface for air. It thrusts its breathing tube up into the surface film and remains suspended head down, at an angle somewhat less than 45°, for a variable time. A film of oil on the surface of the water is sufficient to obstruct the air tube, and thus cause the death of the larva by suffocation. The larva is very timid, so that a very slight jar or a sudden shadow will cause it to move rapidly to the bottom of the container where, indeed, it may very commonly be observed to feed.

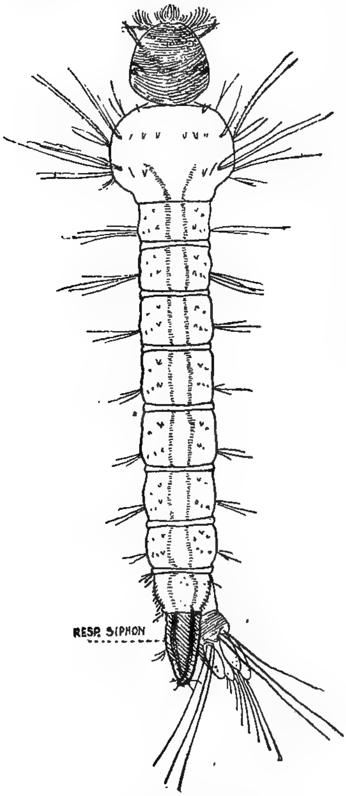

FIG. 6.—Larva of Stegomyia calopus (after Howard, 1901).

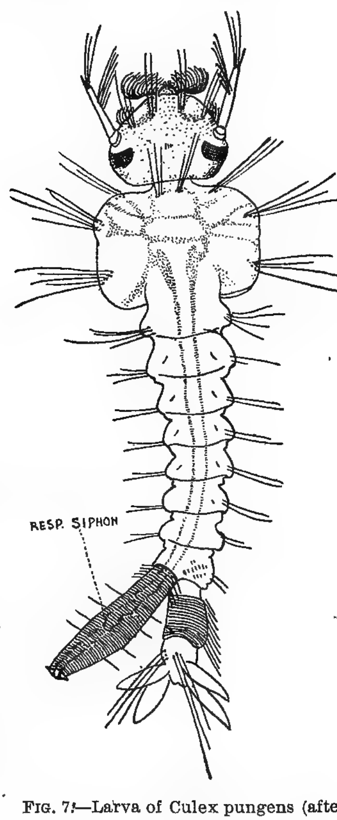

FIG. 7.—Larva of Culex pungens (after Howard, 1901).

The duration of the larval stage is influenced by food supply and temperature. With an abundant supply of food and under favorable conditions of temperature this stage lasts not less than 6 or 7 days; under conditions where the supply of food is scanty or the temperature reduced the duration of this stage may become very much prolonged (weeks) or development may altogether cease. In the latter case the larva may die without completing its metamorphosis or, with the return of favorable conditions, it resumes its development. Freezing for short periods does not appear to injure it.

Pupa.—After several moults the larva changes into the pupa (fig. 8). The pupa is not provided with a mouth and does not feed. It spends its time at the surface of the water for, like the larva, it is an air breather, and is provided with two trumpet-shaped breathing tubes which spring, not from the tail as in the larva, but from the dorsum of the thorax. It moves only when disturbed, and then rather rapidly and jerkily downwards into the depths. The pupal stage lasts at least 36 hours, during which time important changes take place in its internal organization preparatory to the emergence of the perfect insect or imago. The pupal, like the larval stage, is normally passed in the water. Berry has shown, however, that the pupa may be spilled on the ground without its metamorphosis being interfered with. Under the most favorable conditions it takes at least 9 days from the time the egg is laid to the appearance of the imago.

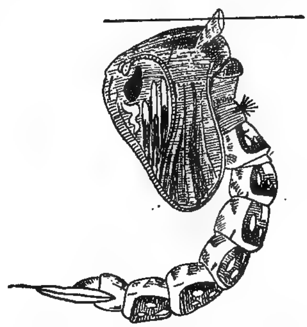

FIG. 8.—Pupa of Stegomyia calopus (after Howard, 1901).

Longevity.—The length of life of the adult female under natural conditions probably varies greatly. Experimentally, Guiteras (1904a) succeeded in keeping a presumably infected one alive for 154 days at the fall and winter temperatures of Habana. At summer temperatures, deprived of water, it does not usually survive longer than 3½ to 4 days, and only very exceptionally 5 days. This fact has a bearing on the possibility of transporting the mosquito in bandboxes or trunks.

Its activity, which is greatest at about 30° C. (86° F.), distinctly diminishes as the temperature declines and approaches 20° C. (68° F.). Below the latter point and as the temperature of 15° C. (59° F.) is approximated the insect seeks obscure corners for protection, becomes very sluggish, and can only exceptionally be induced to bite. In a refrigerator at 8° to 10° C. (46.5° to 50° F.) Guiteras (1904a) was able to keep some mosquitoes alive without food or water for 87 days. How much longer they mave have lived it is impossible to say, because the experiment was terminated at the end of this time by some ants that gained access to and destroyed the mosquitoes. A freezing temperature kills the mosquito rather quickly.

In the influence of variations in temperature on the rate of multiplication, on the activity and on the duration of life of the mosquito we have a satisfactory explanation of the peculiarities of seasonal prevalence of the disease in endemic foci, of the decline of epidemics with the advent of cool weather, and of their abrupt cessation on the occurrence of a severe frost. The occurrence of cases even after a killing frost is explained by the fact, already mentioned, that the *S. calopus* is peculiarly a house mosquito, and it is for this reason occasionally able to escape the full rigors of the climate.

Aërial conveyance.—On this subject I can do no better than quote Carter (1904), who has given it a great deal of attention.

Although direct observations on this problem are few, yet there are certain indirect ones bearing, however, entirely on the aërial conveyance of the *Stegomyia* infected with yellow fever. It is notorious that yellow fever is usually conveyed but a short ways aërially "across the street" or more often "to the house in the rear," which is about as far as it was expected to be thus conveyed. This represents a distance of about 75 yards. The two longest distances recorded in recent times of aërial conveyance, one of 225 meters (Melier) and one of 76 fathoms—456 feet (the writer)—are entirely exceptional. So much for the distance which the "infected" *Stegomyia* is conveyed—or, rather, usually conveyed—aërially.

On the other hand, it is known that vessels moored in certain districts of the Habana harbor did not develop yellow fever aboard except in those who had been ashore or unless they lay close to other vessels which were infected. This experiment has been made on so large a scale, with so many vessels, and for so many years that we must accept as a fact that an infected *Stegomyia* was not conveyed aërially from the Habana shore to those vessels, or, allowing for errors, was very rarely so conveyed. The distance which had been found safe was something over 200 fathoms—1,200 feet. The prevailing wind was generally slightly on shore, but was not constantly blowing. Whether there is any difference in the distance to which infected or noninfected mosquitoes are conveyed is, of course, entirely a matter of surmise. There is no apparent reason why there should be. Yet the infected *Stegomyiæ* have almost certainly become so in a house, and with their very domestic habits must be found out of doors, where they would be subject to conveyance by the wind in much smaller numbers than the uninfected insects, and consequently a lesser *number* of them would be conveyed aërially. Observation is needed on this subject—the distance (across water) that *Stegomyiæ* are aërially conveyed.

Conveyance by railroads and vessels.—The yellow fever mosquito may be conveyed from one place to another in the railway car. I captured one in a day coach en route between Donalsonville and Bainbridge, Ga., in August, 1905. My experience in traveling by rail, both in Mexico and in the southern part of the United States, leads me to believe that the number thus conveyed is very small, so that the chance of conveying one that is infected is probably very slight.

Distribution by vessels may not infrequently be observed. They have been found on steam vessels, but much more commonly and in greater numbers on sailing vessels, because the latter are more likely to present easily accessible breeding places. It can hardly be doubted that the outbreaks of yellow fever in such northern cities as Baltimore, Philadelphia, New York, Boston, and Quebec were due to the importation on sailing vessels of infected mosquitoes. These in proportion as they found conditions favorable, multiplied more or less rapidly and abundantly and produced epidemics which were more or less closely confined to, or in the neighborhood of, the shipping.

Geographic distribution.—The *Stegomyia calopus* has been found to be one of the most widely distributed of mosquitoes. It is primarily a tropical insect, but has extended north and south along lines of travel, establishing itself permanently wherever the conditions of temperature and moisture are favorable. Speaking broadly, it belts the globe between 38° north and 38° south latitude.

Within the United States the points at which it has been found, with few exceptions, "fall within the limits of what are known as the tropical and lower austral zones. These life zones include practically all of the southern United States which border on the Atlantic Ocean and the Gulf of Mexico, with the exception of those portions of Virginia, North and South Carolina, Georgia, and Alabama which constitute practically the foothills of the Appalachian chain; in other words, western Virginia and North Carolina, the extreme northwestern corner of South Carolina, the northern part of Georgia, and the extreme northeastern corner of Alabama. Further than this, the lower austral zone includes the western half of Tennessee, the western corner of Kentucky, the extreme southern tip of Illinois, the southeastern corner of Missouri, and all of Arkansas except the northern portion. It also includes the southern portion of Indian Territory, southern Arizona, and some of northern Arizona, and southern strips in Utah, Nevada, and California.

"In the greater part of the territory thus indicated, and *where the climate is not too dry*, *Stegomyia fasciata* will, with little doubt, upon close search, be found.

"All the rest of the lower austral territory just indicated, and *where the climate is not too dry*, will constitute a region where the yellow-fever mosquito, if once introduced, will undoubtedly flourish. Even in the dryer portions of western Texas, southern New Mexico, southern Arizona, southern California, and southern Nevada, where the climate is exceptionally dry, there is a possibility that this species, if once introduced, will breed in the water supply of ranches, except, possibly, where the water is impregnated with alkali."[a]

INCUBATION.

In 29[b] cases of experimental yellow fever, recorded in the literature, produced by mosquitoes *in nonimmunes that had not been subjected to*

[a] Howard, 1903.

[b] This does not include one case apparently induced by mosquitoes that had acquired their infection by feeding on sirup in which the bodies of infected mosquitoes had been crushed. In this case the incubation period would appear to have been not less than 9 nor more than 12 days.

previous inoculations with blood serum, the period of incubation varie from not less than 2 days 1 hour to 6 days 2 hours. In 25 of thes cases the incubation period did not exceed 5 days, leaving four cases or 13.8 per cent of the total, in which this period was in excess of days. There is some reason for believing that this period may, excep tionally perhaps, be prolonged to 8[a] or 10[b] days.

The limits of variation of this period in the experimental cases pro duced by blood injection were from 1 day 15 hours to 12 days 1 hours in subjects that had not been subjected to other than the on blood inoculation.

The length of the period of incubation appears to bear no direc relation to the number of mosquitoes used for the inoculation; no does it appear to bear any direct relation to the age of the insect o insects or to the character (mild or severe) of the case from whic they obtained their infection or which they induce.

SYMPTOMS.

Yellow fever is a disease that manifests itself in all grades of severity from an attack suggesting a "slight attack of grippe" or "indiges tion" of such mildness as hardly to interfere with one's daily routine and not calling for medical attention, to an attack of such malignanc that the physician finds himself powerless to stay its course to a fata termination. Besides this great difference in the virulence of indi vidual attacks, there is considerable variation in their duration and i the relative prominence of certain symptoms. These differences hav been used by different writers in various ways as a basis for dividin the disease into different clinical types. As these divisions are of n practical use they will not be considered.

Onset.—In most cases the transition from a state of well being i abrupt and may be marked by the occurrence of a chill or chilliness or by the appearance of a severe frontal headache, or pain in the lum bar region of such severity as to suggest an attack of smallpox or occasionally, in children by the occurrence of convulsions. In thes cases close questioning will not infrequently elicit a history o indisposition for perhaps 12 to 24 hours before the occurrence of th symptom or symptoms that definitely mark the onset of the disease In a smaller proportion of cases the patient takes to his bed in conse quence of a rapidly increasing lassitude with or without headache.

The disease may be ushered in at any time during the 24 hours, s that one not infrequently obtains a history of the patient's havin been awakened at night by the occurrence of a chill, or awakening i the morning with fever, headache, and nausea.

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[a] Carter, 1901a, p. 366.

[b] Marchoux, Salimbeni and Simond, 1903, p. 674, footnote.

Pains.—Pain in some form is one of the earliest and one of the most constant symptoms. It is usually marked, but at times, in children, and occasionally in mild cases in adults, it may be slight, and in the former sometimes altogether absent. Frequently marking the onset or, if not, appearing soon after, are headache, pain in the back and limbs. After two or three days, with the decline in the fever, the severity of these usually diminishes. The headache is usually frontal, but it is sometimes temporal or occipital; there is usually associated with it more or less aching of the eyes. The pain in the back is sometimes described as if it had been produced by blows with a rod, on which account the French in the West Indies have called it the *coup de barre;* in some instances it is not unlike the lumbar pain of smallpox. The aching in the limbs has its seat in the muscles, and affects more particularly the muscles of the thighs and calves of the legs.

Facies.—With the onset of the disease the face usually becomes flushed and somewhat swollen. The flushing may be slight or occasionally altogether absent, or it may be so marked as to suggest the initial rash of dengue, especially if it extends, as it sometimes does, down the neck to the upper part of the chest. The amount of swelling varies; it may be inappreciable or it may be sufficient to smooth out somewhat the lines of expression. Coincident with the flushing of the face the eyes become congested and red and sensitive to light. In mild cases the injection of the conjunctiva may be shown only as an abnormally prominent capillary mesh; in the severe cases the conjunctiva may appear as if inflamed, and in rare instances it may become raised around the cornea from infiltration of serum and blood. The flushing of the face and the injection of the eyes usually diminish as the temperature begins to decline.

In certain grave cases, coincident with the appearance of black vomit, the face becomes pale, the lips cyanosed, the eyes sunken, and the redness of the conjunctivæ becomes replaced by a more or less distinct tinge of yellow.

Skin.—At first the skin is warm to the touch and usually, but by no means always, dry; sometimes, indeed, it is covered with perspiration which may persist throughout the disease. Later, in some cases, with the occurrence of black vomit, the skin becomes cool and clammy. Jaundice occurs in all but some mild cases; it usually appears first about the third day as a slight tinging of the ocular conjunctiva. At almost the same time, or very soon after, it may be noticed that the skin also has acquired a pale yellow tint. Its early detection may be facilitated by pinching up a fold of skin and causing a momentary local anæmia.

As the case progresses the icteric tint, which at first is faint, gradually becomes more pronounced. The depth of color attained varies from a pale lemon to an orange or a saffron hue. In some cases th jaundice may appear somewhat earlier than the third day; in other somewhat later, or not until convalescence. In some fatal cases i may not present itself until after death. After convalescence is estab lished the icterus more or less rapidly fades away.

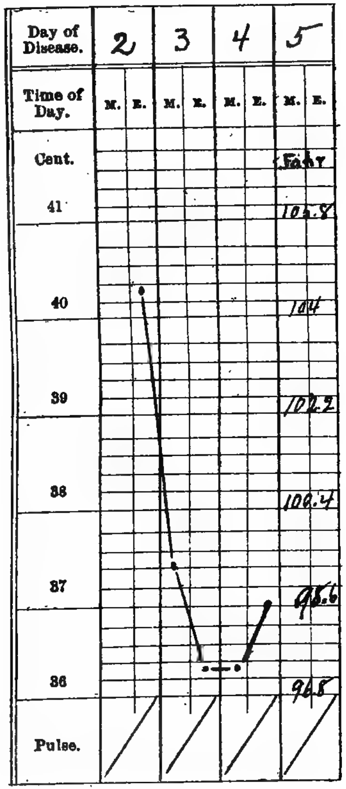
Various accidental eruptions, such as sudamina, herpes, and echy motic patches are occasionally observed.

Odor.—An odor variously described has been noted by many writ ers. Some have considered the odor so peculiar as to be almost path ognomonic. While I have myself never detected any odor that could differentiate from that which may occasionally be noted in othe diseases, and while I can conceive that as the result of pathologica changes volatile odorous matters may be given off by the skin (o lungs) that are peculiar to the disease, I am, nevertheless, constraine to believe that some, at least, of the observers who have noted thes "characteristic" odors have deceived themselves, especially when read that the odor was detected "twelve days before the developmen of the fever."

Temperature.—With the onset of the disease the temperature rise and usually continues its ascent for from 24 to 48 hours. During thi initial rise the fever frequently reaches the highest point which i attains during the disease. This does not commonly exceed 40.2° C (104.5° F.). A temperature above 41° C. (105.5° F.) is but rarel recorded. Its subsequent course varies considerably, but on scrutin it will, speaking broadly, conform to either of two general types: I one the fever having reached its acme the temperature declines pro gressively and more or less rapidly, with or without evening exacer bations until it reaches normal (charts 1, 2, 3, and 4). In the othe the temperature continues with more or less marked oscillations fo 3, 4, or 5 days at or near the point to which it first rose, and then more or less rapidly, declines to the normal (charts 10 and 11). Th cases which conform to the latter type are usually the more grav and more likely to be fatal; but some of the most rapidly fatal case (chart 2)—the so-called *foudroyante* cases of the French—belong i the former category.

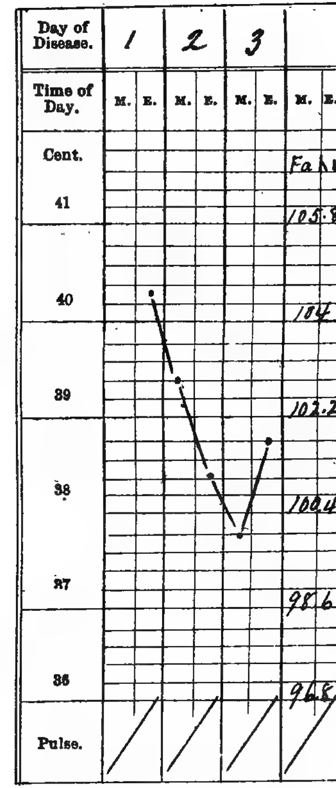
The initial rise is occasionally interrupted by a decided, though short remission or by a complete intermission which may last 6 to 10 hours I have seen an intermission lasting at least 6 hours occur 14 hour after the onset (chart 6). Both the remission and the intermissio may be, and more commonly are, delayed until the completion of th initial rise and are then, particularly the remission, somewhat mor prolonged (charts 5, 7, 8, and 9). The remission may be repeate (without the occurrence of black vomit) so that the temperature curv assumes a distinctly remitting character (charts 8 and 9). A fall i temperature frequently marks the onset of black vomit. It is for thi

CHART 1.



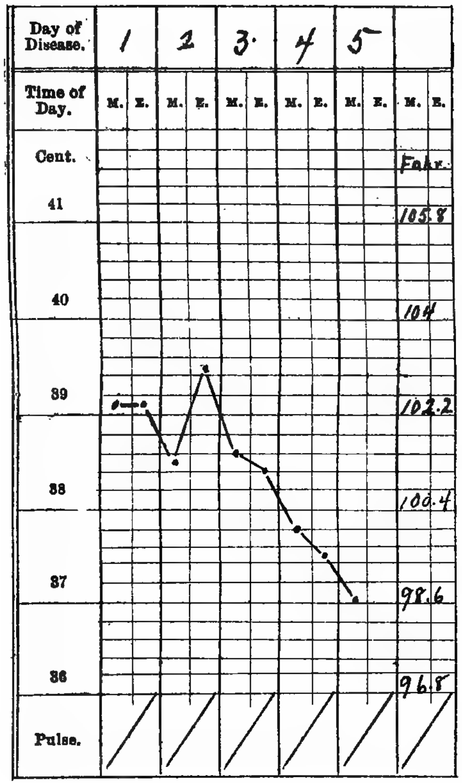
Yellow fever, descending type; very mild.

CHART 2.



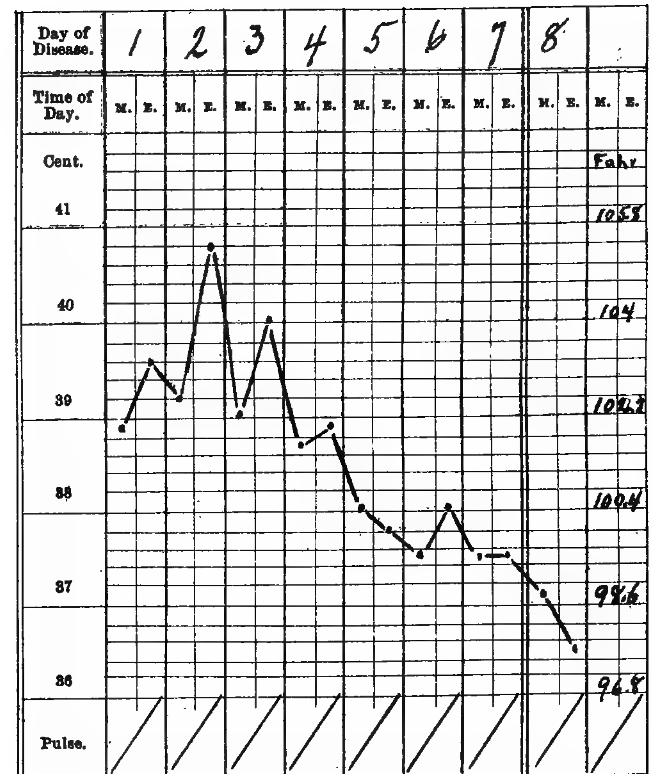
Yellow fever, descending type; fatal in 2 days 20 hours.

Chart 3.



Yellow fever, descending type; mild; duration, 5 days;

Chart 4.



Yellow fever, descending type; medium severity; duration, 8 days; recovery.

Chart 5.

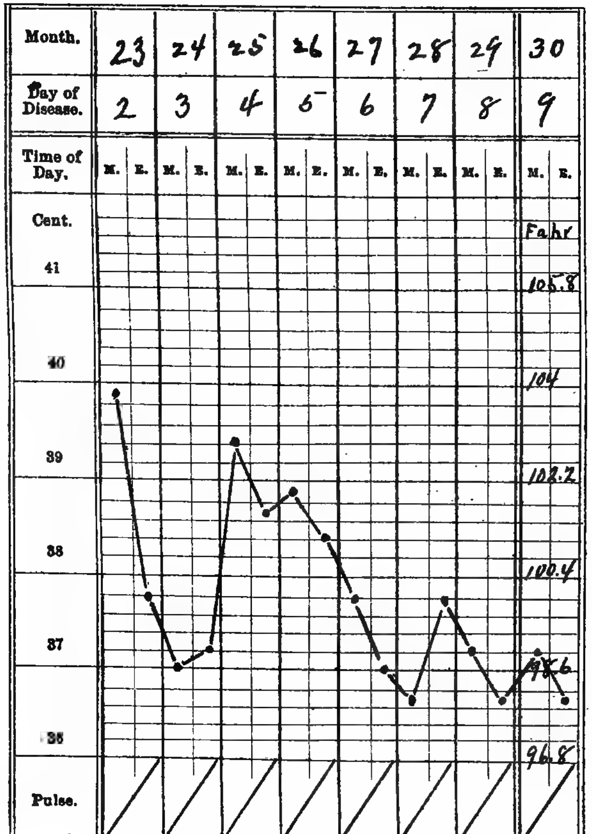


Chart 6.

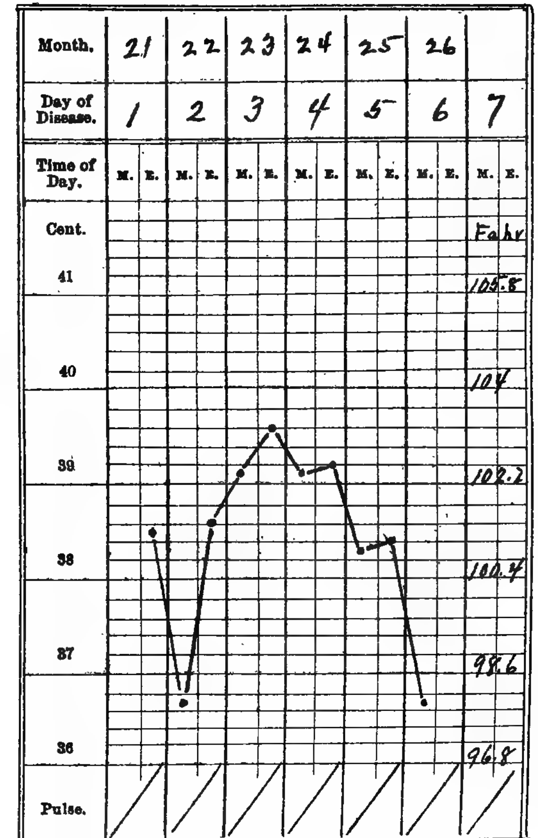
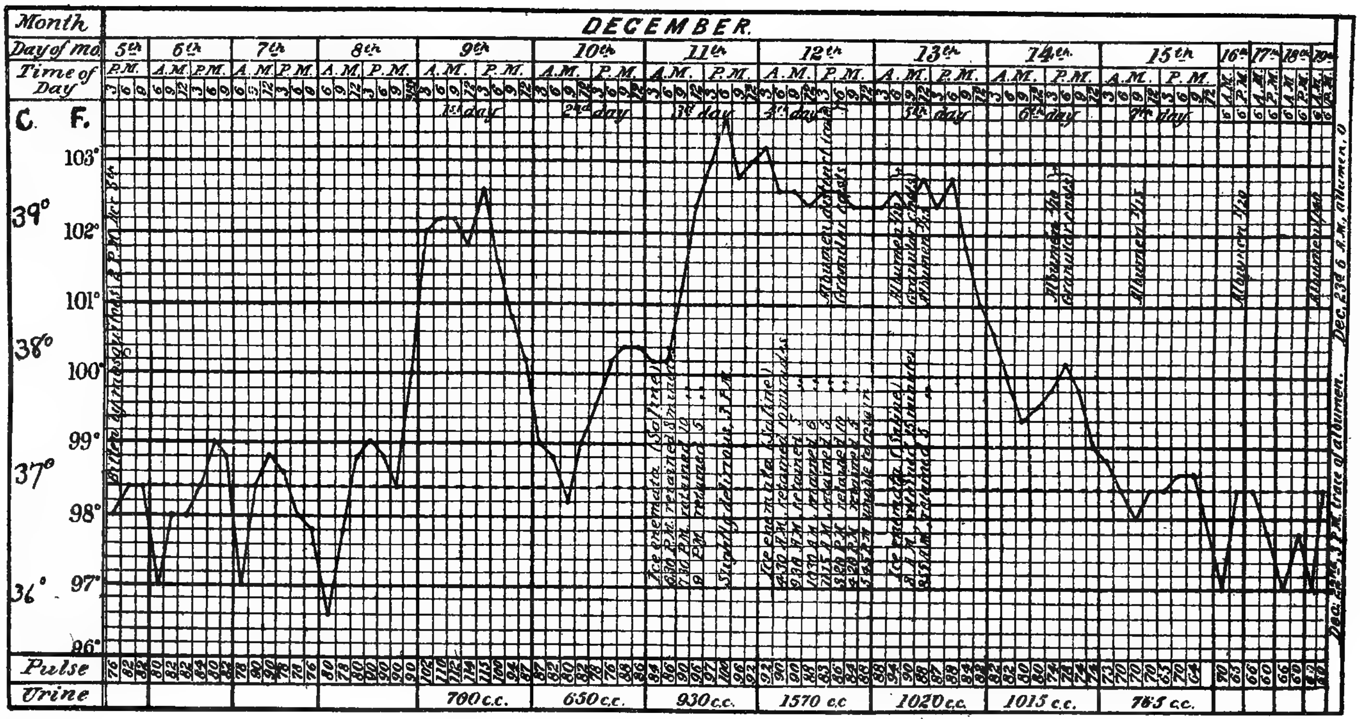
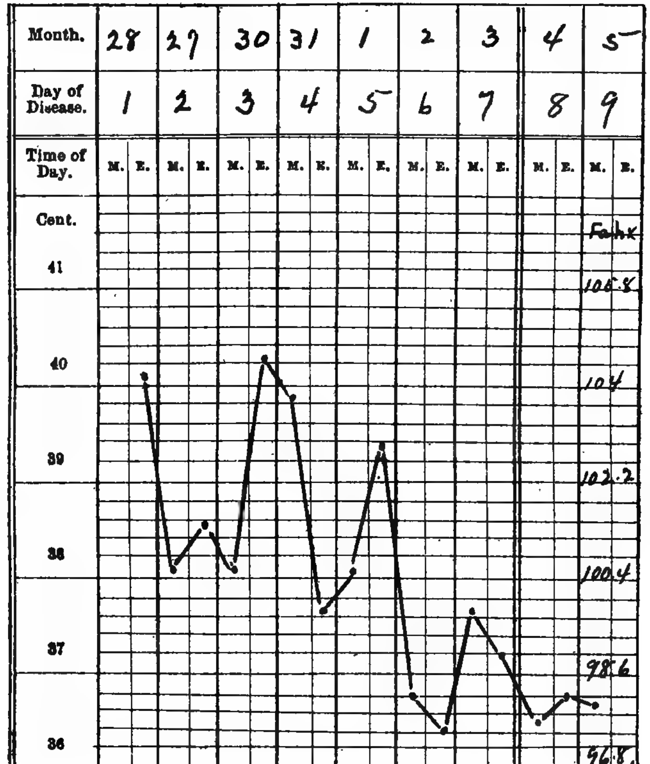


CHART 7.

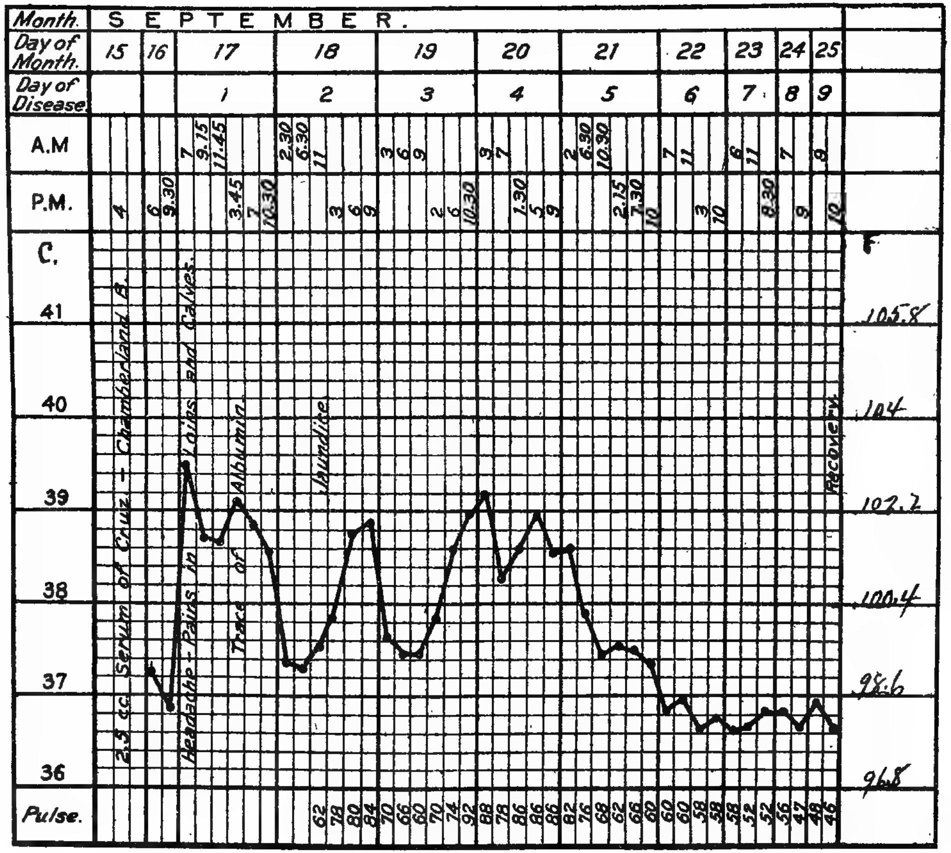


Yellow fever, intermitting type; intermission, 34¼ hours after onset. Experimental, by bite of *Stegomyia calopus*. (Reed, Carroll, and Agramonte. 1901.)

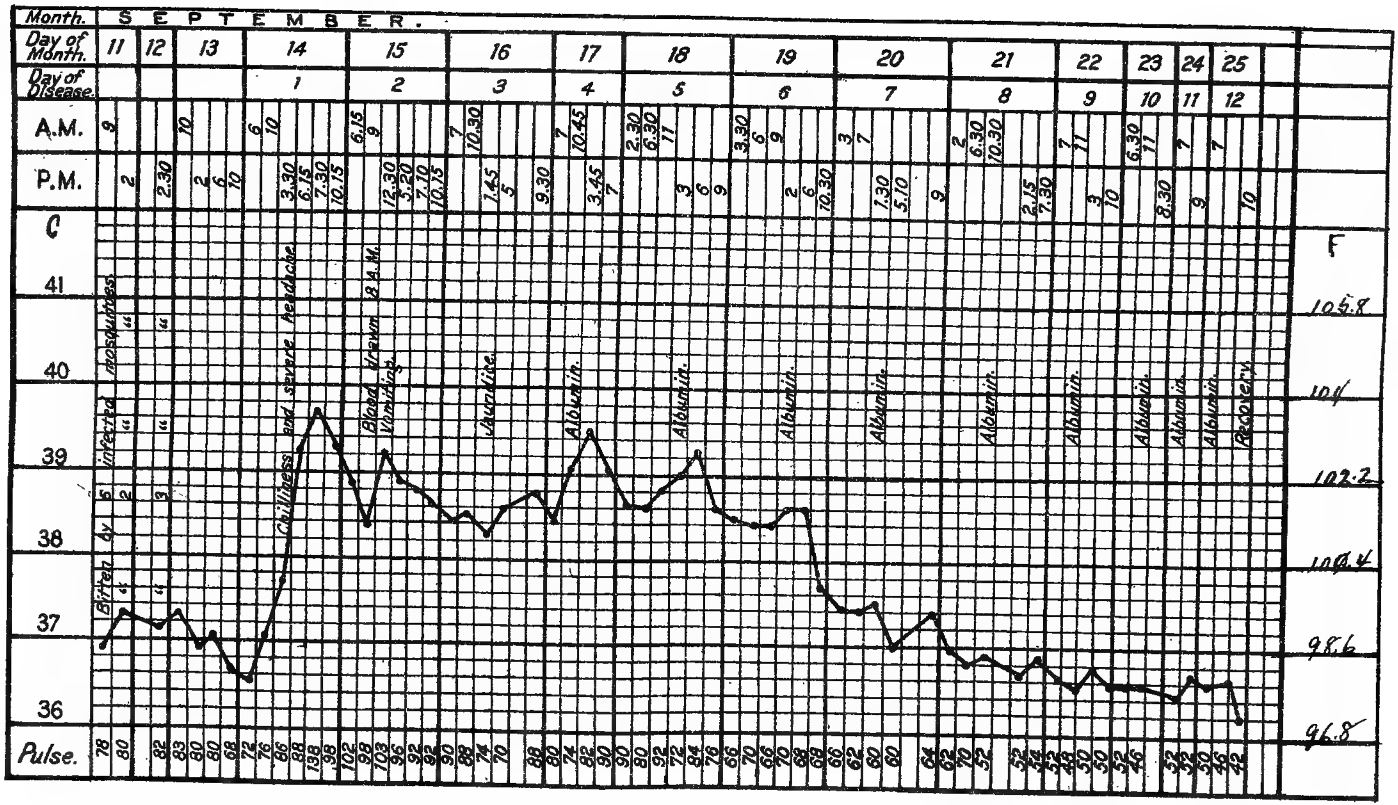
CHART 8.



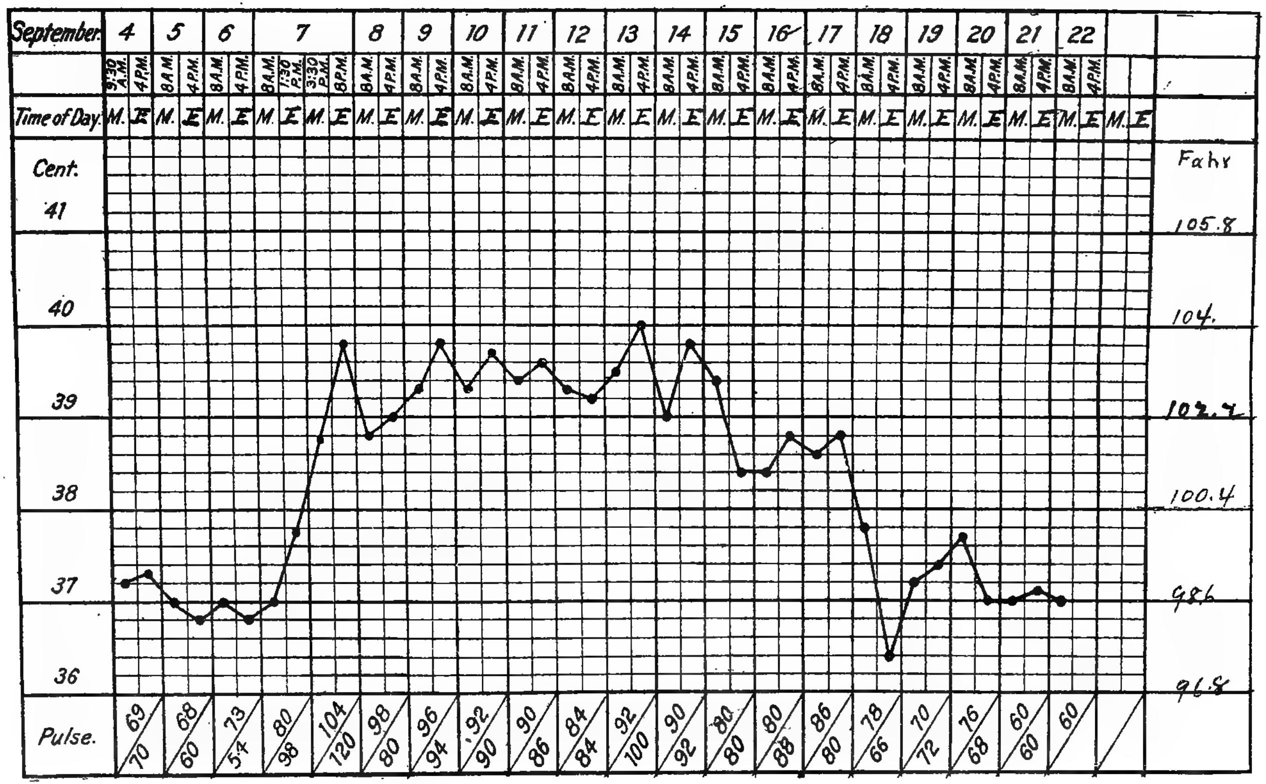
Yellow fever, remitting type; severe.



Yellow fever, remitting type; mild, with remission 24 hours after onset. Experimental by intravenous injection of filtered blood serum. (Rosenau, Parker, Francis, and Beyer. 1904.)



Yellow fever, continued type; moderate severity. Experimental by bites of *Stegomyia calopus*. (Rosenau, Parker, Francis, and Beyer. 1904.)



Yellow fever, continued type; very severe. Experimental by bites of *Stegomyia calopus*. (Parker, Beyer, and Pothier. 1903.)

reason that there may be observed in many cases a progressive lowering of the temperature with the approach of a fatal termination, so that at the end the temperature may be little if any above normal. In some fatal cases, however, the temperature remains elevated to the end; or, if it has fallen, rises acutely before death and may continue its ascent for some minutes after. Agonic and post-mortem temperatures of 42.5° and 43° C. (108.5° and 109.5° F.) have been observed. During the first days of convalescence the temperature is usually somewhat below normal.

Pulse.—At the outset the pulse is usually full and bounding, and the number of its beats may register 120 or 125 per minute. As the fever progresses the tension and the rapidity of the pulse diminish. At intervals in the course of the disease the pulse may be distinctly dicrotic. At the close, in fatal cases, it becomes rapid and feeble; in those terminating favorably the pulse not infrequently falls to 50 and occasionally even less. It is often stated that slowness is a peculiar characteristic of the pulse in yellow fever, but this is not altogether correct. While, to be sure, the pulse in this disease is not a rapid one, its peculiar character consists in the sluggishness with which it responds to the stimulus of a rise in the temperature. This sluggishness at times amounts to an actual irresponsiveness which is so marked, early in many cases, that there is witnessed the phenomenon of a stationary or falling pulse rate with a rising temperature, or a falling pulse with a stationary temperature. This is not simply a lack of correlation such as is sometimes observed in typhoid, but an actual divergence between the two. Attention was first called to this phenomenon by Faget, of New Orleans, who considered it pathognomonic.

Unfortunately this sign is not always present and, when present, it is not always as well defined as could be wished. Its minor manifestations are occasionally observable in other febrile affections, such as pneumonia, malaria, dengue, and septicemia.

Respiration.—The number of the respiratory movements is usually not notably increased. The character of the respiration is, in many cases, altered somewhat. Many patients experience a feeling of thoracic oppression so that at variable intervals their breathing is punctuated by a sighing respiration. In the latter stages of some cases hiccough appears; it is always an ominous sign.

Blood.—The results of blood examination are characterized chiefly by their negative character. Morphologically the cellular elements show no alteration. In uncomplicated cases the number of the red corpuscles and the percentage of hemoglobin are not, as a rule, reduced, but, on the contrary, frequently show an increase above the normal. The number of the white corpuscles is somewhat diminished, and the proportion of the different forms is slightly altered. The chief alteration consists in an increase in the percentage of the polymorphonuclear leucocytes and a diminution in the eosinophiles. Sometimes there is a slight increase in the large mononuclears. There is usually a noticeable increase in the number of the blood platelets. The coagulability of the blood does not undergo any material change.[a] With the onset of convalescence there is a fall in the number of the red corpuscles and in the percentage of hemoglobin.

Hemorrhages.—A tendency to hemorrhage is one of the marked characteristics of the disease. As a rule, this does not manifest itself before the third day. The most common and, in a very large proportion of the cases, the only manifestation of this tendency is bleeding from the gums. The gums become more or less swollen and the blood may ooze from them spontaneously or, more commonly, only after some traumatism, such as a slight pressure of the examining finger. Epistaxis is almost as frequent a symptom as bleeding from the gums; it may occur at the onset, but more commonly, like bleeding from the mouth, does not appear until the fourth or fifth day. In women, menorrhagia or metrorrhagia are common manifestations. During pregnancy death of the fetus and miscarriage are of common, though not invariable, occurrence.

Hemorrhage from the stomach, appearing as black vomit, occurs in the graver cases only. It varies considerably in amount; in the lighter grades it may be barely perceptible, as dark streaks or specks in the vomited matter, but in the severer forms it may be so profuse that the vomitus is uniformly dark red or black, like coffee grounds. Blood originating in a hemorrhage from the nose or mouth which has been swallowed may give to vomited matter precisely the same character as blood which has its origin in the stomach. Black vomit, therefore, does not necessarily mean gastric hemorrhage. Melæna may result from passing altered blood which had its origin in the stomach, or it may be due to hemorrhage from the intestine. The quantities of black vomit ejected and melæna discharged per rectum are at times surprisingly large.

Digestive tract.—In some of the severer forms the lips become dry and cracked and bleeding. In almost all cases the gums become more or less swollen, and at first covered with a white epithelial coating which rapidly wears off, leaving them red and spongy and disposed to bleed on slight pressure. The tongue at first is commonly moist, with a gray coating over the center and dorsum and with red tip and edges. As the disease progresses, in severe cases, the tongue becomes dry, red, fissured, and more or less streaked with blood. The appetite is lost from the first, but returns rapidly with convalescence. Thirst is frequently marked. Nausea and vomiting are commonly, but not invariably, present. In general, they appear with or soon after the onset, and, as a rule, become more or less accentuated with the prog-

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[a] Marks, 1906.

ress of the disease. There is nothing peculiar about the character of the vomited matter in any but some of the grave or the fatal cases. At first it may consist of food remnants or of such liquids as may have been swallowed; later it consists of a thin mucus, which soon becomes bile-stained. In some grave cases, about on the third day, sometimes on the second, but more commonly on the fourth or fifth, streaks of red or black may be detected in the vomited matter. These streaks are more or less altered blood and are the first signs of black vomit. In some cases it does not go beyond this, but in some very severe cases and in most of the fatal ones the vomited matter soon becomes more or less uniformly black in color. In some fatal cases black vomit does not manifest itself during life, but is found post-mortem. In the severer cases there is sometimes associated with the vomiting or retching more or less distressing hiccough. In the cases terminating favorably the gastric irritability gradually diminishes and disappears. The bowels are usually constipated. The movements are at first natural in color and remain so in all but some of the grave cases, in which they may become dark and tarry. Some tenderness, especially in the severer cases, can usually be elicited by pressure in the epigastric region as early as the second day. Abdominal pains of a colicky character are occasionally complained of; sometimes they are very severe and cause the patient intense suffering.

Urine.—In mild cases and in those of moderate severity the urine may show but slight alteration in character as regards quantity and density. In severer cases it becomes reduced in volume and somewhat in specific gravity. Complete suppression is not a rare occurrence in fatal cases. The suppression may, however, only be apparent and due to retention, as may be demonstrated by catheterization.

In all but the mildest cases albumin appears in the urine at some time in the course of the disease. It may appear within 24 hours after the onset, though usually not until the end of 48 hours; or it may delay its appearance until after the subsidence of the fever. At first it appears only in small amounts—a slight trace, perhaps—which in some cases is not increased, while in others it rapidly augments in volume up to 80 to 90 per cent. In favorable cases the amount begins to diminish almost at once or very soon after the maximum has been recorded, and will be found to have disappeared in from three or four days to two or three weeks from the time it first appeared. In some cases, however, the albuminuria is very transitory and may not be detected unless every specimen of urine passed be examined. When jaundice is present, biliary pigment appears in the urine, as may frequently be noted when making the nitric-acid test for albumin. Albertini and Guiteras[a] report the absence of the diazo

[a] Guiteras, 1904b, p. 594.

reaction in this disease. Haylin, granular and epithelial casts, which may be bile-stained, are commonly encountered in the sediment.

Liver.—Except jaundice, which has already been discussed, there appear in uncomplicated cases no symptoms referable to this organ, the dimensions of which are, as a rule, not materially altered.

Spleen.—In uncomplicated cases the spleen does not undergo any material change in size.

Nervous system.—Sleeplessness, more or less marked, is a frequent symptom. Delirium is of common occurrence; in many cases it is only a slight mental wandering during the first or second night after the onset. In some of the grave cases this wandering gives place to a muttering or an active maniacal delirium; toward the end in some fatal cases unconsciousness, more or less profound, supervenes and the scene is closed with tonic convulsions involving particularly the muscles of the face and flexors of the arms. In all mild, in many grave, and in some fatal cases the mind is clear and alert throughout the course of the attack.

Duration.—The great majority (75 per cent) of all cases terminate before the ninth day. A fatal termination rarely occurs before the third day, but it has been recorded as late as the twenty-second.

Complications.—In the vast majority of cases yellow fever runs its course without any disturbing complications. Occasionally, however, a deep-seated muscular abscess or an inflammation of the parotids may occur.

The most common complication is malaria, which may manifest itself either during the febrile period or, and more commonly, during convalescence.

Yellow fever may occur as a complication in the course of some chronic diseases such as pulmonary tuberculosis, cirrhosis of the liver, dysentery, malarial cachexia and ankylostomiasis, or some acute infections such as typhoid fever and gonorrhea.

Convalescence.—With the termination of the fever the patient finds himself, even after a relatively mild attack, markedly depressed in strength. As a rule, however, recuperation is rapid. Occasionally convalescence is retarded by the occurrence of complications such as malaria, furunculosis, and peripheral neuritis.

Relapse and second attacks.—A return of the fever and other symptoms characterizing an attack of yellow fever after convalescence has been established is rare. Cases of relapse have, however, been observed after an interval of 2 or 3 days to 2 weeks or a month. It is a question whether so-called relapses occurring after an interval of 2 weeks or a month should not more properly be considered second attacks.

As a rule with but very rare exceptions one attack of the disease confers immunity on the individual for life. Nevertheless, there are on record some fairly convincing instances of a second more or less grave attack a year or longer after the first.

DIAGNOSIS.

The increase in knowledge concerning the etiology of various communicable diseases and the improvement in methods devised for their recognition have been followed, among other things, by a broadening of our conceptions relating to the degrees of severity which they may assume. Thus when, for example, we speak of typhoid or cholera we think not only of the severe classical types, but we have in mind also those mild and irregular forms which are recognizable only because of the improved tests which are at our command.

We now know that, like cholera and typhoid, yellow fever also manifests itself in all grades of severity; but unfortunately, unlike the former, we have no test whereby in any particular case we can say definitely that this is or is not yellow fever. The recognition of this fact is of the very highest importance with respect to prevention, for it makes it imperative that in infectible regions every case of fever, however mild, should be considered as potentially yellow fever until this disease can positively be excluded.

On taking charge of a case of fever the practitioner, in the South, should therefore start with the assumption that he is dealing with a case of yellow fever, and in formulating his final, definite diagnosis, in which this disease is excluded, he must use the greatest care and caution. The clinician must fix it firmly in his mind that yellow fever is not excluded simply because he knows of no other previous case; obviously he may be dealing with the first case himself, or several cases may have occurred in such as, for one reason or another, had received no medical attention. Nor is yellow fever eliminated from consideration because he fails to detect *any* so-called "characteristic" sign or symptom.

Ordinarily the *combination* of an *acute fever* with *albuminuria, jaundice*, an *irresponsive* or *divergent pulse*, a *tendency to hemorrhage* from the mouth, and *gastric irritability*, with no material alteration in the size of the liver and spleen, should leave no doubt in the observer's mind as to the nature of the disease with which he is dealing.

The diseases with which yellow fever may be confused are malaria, hemoglobinuric fever, dengue, grippe, bubonic plague, typhoid fever, acute yellow atrophy of the liver, Weil's disease, and relapsing fever.

Malaria.—Yellow fever at times simulates certain irregular forms of malaria very closely, and in the absence of any known infection the grave error of mistaking it for malaria has, not rarely, been committed. On the other hand, during epidemic seasons the mistake is not infrequently made, both within and without the infected zone, of calling malaria yellow fever.

Careful examination of stained blood smears will show an absence of the plasmodia in the former group and their presence in the latter; but while the absence of the plasmodium from the blood excludes malaria in the first instance, its presence in cases of the second group does not eliminate yellow fever from consideration. In these cases, yellow fever should be excluded only after a careful study of the case. Careful observation for several days after the adminstration of a few doses of quinine, preferably subcutaneously[a] or intravenously, may be necessary. The abrupt decline in the fever coincident with the disappearance of the parasites from the circulation following the exhibition of the quinine in the manner indicated, with absence of albumen from the urine or its presence only as a trace, with no jaundice and no tendency to hemorrhage, may generally be interpreted as probably excluding yellow fever. The mere decline of the fever after the administration of quinine without a previous examination of the blood to determine the presence of the malarial parasite does not exclude yellow fever.

Hemoglobinuric fever.—This grave manifestation of malaria resembles yellow fever in its abrupt onset, bilious symptoms, jaundice, and albuminuria, but differs in being characterized by a rapid blood destruction and enlargement and tenderness of the liver and spleen. The blood destruction manifests itself by a reduction in the number of the red corpuscles, low hemoglobin percentage, and by the red or black color of the urine, due to the elimination of hemoglobin.

Dengue.—The differentiation between well-marked types of dengue and yellow fever is a matter presenting no serious difficulty after the first two or three days. The points of difference most to be relied on are the presence of an eruption and the absence of jaundice in dengue. Albuminuria, which is so prominent a sign even in relatively mild attacks of yellow fever, is slight and commonly altogether absent in even quite sharp attacks of dengue. In the latter disease the percentage of the polymorphonuclear leucocytes is reduced whereas in yellow fever it is more or less increased.

When, however, we come to deal with cases that are ill-defined, cases that present no eruption (or in which none has been detected), in which jaundice is doubtful or absent, and in which no albumin or only a dubious trace of it can be detected, we encounter a very real and serious difficulty in deciding as to which of the two diseases we have before us. While it is of the very greatest importance to recognize that we have no means of surely identifying individual cases of

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[a] The injection should be given into a muscle, not into the subcutaneous cellular tissue. With good aseptic technique the intravenous injection is preferable. Give 1 gram (15 grains) of the bimuriate dissolved in 1 cc. (15 minims) of distilled water and repeat three times at 12-hour intervals; the solution and syringe must, of course, be sterile.

this type, nevertheless a clue to their nature will, as a rule, be discovered if a careful study of a series of cases be made. In a group some individuals are very likely to be found that will show, if they are yellow fever, unmistakable jaundice and a degree of albuminuria quite out of proportion to the mildness of the attack, whereas, if they are dengue, some cases will be found that will exhibit the characteristic rash. In isolated instances, or until cases presenting distinctive symptoms are encountered, the observer will do well to suspend judgment and not assume, as is too frequently done, that mildness of attack and a failure to die are pathognomonic of dengue. He should remember, also, that the two diseases may occur side by side, thereby multiplying the difficulties of the problem and rendering caution imperative.

Grippe.—An attack of influenza is characterized, as a rule, by symptoms referable to a catarrhal condition of the upper air passages. Cases in which these symptoms are marked hardly come into consideration in the diagnosis of yellow fever. As with dengue it is the less well-defined cases of influenza that counterfeit and are simulated by mild and ill-defined cases of yellow fever; and much that has been said concerning the diagnosis from dengue is here also applicable.

Bubonic plague—In localities where yellow fever and plague prevail, and at quarantine stations in connection with vessels from such ports, the question of differentiating the two diseases may arise. Clinically there is only a very superficial resemblance between the two, but in all cases of doubt a careful bacteriological examination should be made of the sputum, blood, or aspirated juice from enlarged glands; the latter, by the way, are but very rarely met with in uncomplicated yellow fever, while in plague they are not only enlarged but inflamed and the surrounding tissue infiltrated.

Typhoid fever.—Early in the disease typhoid may be mistaken for yellow fever, but the resemblance is slight and observation of the patient for 3 or 4 days will be certain to resolve any doubts. At this stage the general appearance and the increasing apathy of the patient are distinctive. The temperature is a gradually ascending one or has reached the fastigium, and the pulse, though not fast, follows the daily oscillations of the fever and does not, as in yellow fever, tend to become slower from day to day. Jaundice is, at best, but a rare complication of typhoid and may be said almost never to occur early in the disease. The urine frequently gives the diazo reaction, and at this time is usually free of albumin, though occasionally traces of the latter constituent may be met with; nephritis is a late and not common complication of typhoid fever. The bacillus of Eberth may be isolated from the blood.

In an attack of yellow fever of three or four days duration and with a corresponding elevation of temperature the combination of symptoms distinctive of a well-defined attack of this disease would be clearly manifested. In some of the severer forms of yellow fever the tem perature is occasionally prolonged for two to three weeks, and som of the accompanying symptoms are, in some of these cases, suggestiv of typhoid. Typhoid fever, in the second or third week, will giv the Widal reaction and Eberth's bacillus may be isolated from th blood. These are, of course, absent in yellow fever.

Acute yellow atrophy of the liver.—This is a very rare disease. I occurs most commonly in women, and in these more particularly dur ing pregnancy. The disease is ushered in like a case of catarrha jaundice. A marked and rapid reduction in the size of the liver i distinctive.

In yellow fever the size of the liver is unaffected. In malignan jaundice albuminuria is of frequent occurrence, but it is not as marke nor as constant as in cases of yellow fever of the same degree of viru lence. The duration of over 75 per cent of the recorded cases o malignant jaundice has been in excess of seven days; the duration o almost 75 per cent of the cases of yellow fever does not exceed seve days. An early fatal termination in such a case would decidedly favo a diagnosis of yellow fever, but a later termination should not, how ever, be regarded as excluding yellow fever.

Weil's disease.—This disorder is characterized by fever, intens jaundice, swelling and tenderness of the liver, diarrhea, notabl enlargement of the spleen, and nephritis. In yellow fever neithe liver nor spleen are enlarged, a tendency to constipation is the rule and in cases of a corresponding grade of severity, the hemorrhagi symptoms are likely to be more marked and to appear earlier.

Relapsing fever.—The presence of the *Spirochæta* of Obermeier i the blood is distinctive.

Catarrhal jaundice.—This may in some instances have to be consid ered. In this condition the jaundice appears with little or no elevatio of temperature, preceded by slight, if any, symptoms of indigestio and accompanied by clay-colored stools. In yellow fever the jaundic appears after at least two or three days of fever and will be accom panied by the other symptoms characterizing a well-defined attack the stools are not clay colored.

REFERENCES.

Blanchard (R.).
1905.—Les moustiques. Paris.

Barreto de Barros and Rodrigues.
1903.—Experiencias realisadas no Hospital de isolamento de S. Paulo, etc. Rev med. de São Paulo, February 28, v. 6, p. 69–73.

Berry (T. D.).
1905.—Ability of the larvæ and pupæ of the *Stegomyia fasciata* to withstand des iccation. Pub. Health Rep., Washington, v. 20, part 1, p. 1148.

Carter (H. R.).
1900.—A note on the interval between infecting and secondary cases of yellov fever, etc. New Orl. Med. & Surg. Journal, May.

CARTER (H. R.)—Continued.

1901a.—The period of incubation of yellow fever. Med. Record, N. Y., March 9, v. 59.

1901b.—A note on the spread of yellow fever in houses. Med. Record, N. Y., June 15, v. 59.

1904.—Some characteristics of *Stegomyia fasciata*, etc. Med. Record, N. Y., May 14, v. 65.

CATHRALL (I.).

1800.—Memoire on the analysis of black vomit. Phila.

DOWLER (B.).

1855.—On the natural history of the mosquito. New Orl. Med. & Surg. Journ., v. 12, p. 187.

FAGET (J. C.).

1875.—Monographie sur le type et la spécificité de la fièvre jaune établis avec l'aide de la montre et du thermomètre. Paris and New Orleans.

FFIRTH (STUBBINS).

1804.—A treatise on malignant fever with an attempt to prove its non-contagious nature. Inaugural dissertation. Phila.

FINLAY (CARLOS J.).

1881.—El mosquito hipotéticamente considerado como agente de transmisión de la fiebre amarilla. Ann. de la Real Academia de ciencias med. . . . de la Habana, Aug. 14, v. 18, pp. 147–169.

FINLAY and DELGADO.

1890.—Estadística de las inoculaciones con mosquitos contaminados en enfermos de fiebre amarilla. Ann. de la Real Academia de ciencias med. . . . de la Habana, v. 27, pp. 495 and 591.

FRANCIS (EDWARD).

1907.—Observations on the life cycle of *Stegomyia calopus*. Pub. Health Rep., Washington, Apr. 5, v. 22, p. 382.

GUITERAS (JUAN).

1901.—Experimental yellow fever. Am. Med., Phila., Nov. 23.

1904a.—Notes from the laboratory. Rev. de Med. tróp., Habana, v. 4, p. 64.

1904b.—Yellow fever. Buck's Ref. Handbook Med. Sciences, v. 8, p. 590.

HOWARD (L. O.).

1901.—Mosquitoes. New York.

1903.—Concerning the geographic distribution of the yellow fever mosquito. Pub. Health Rep. (Supplement), Washington, November 13, v. 18, No. 46.

LA ROCHE (R.).

1855.—Yellow fever. Phila.

MARCHOUX, SALIMBENI, and SIMOND.

1903.—La Fièvre jaune, Rapport de la mission française. Ann. de l'Inst. Pasteur, Paris, Nov., v. 17, p. 665.

MARCHOUX and SIMOND.

1906 a.—Études sur la fièvre jaune. Ann. de l'Inst. Pasteur, Jan., v. 25, p. 16.

1906 b.—Idem. Idem, Feb., v. 25, p. 104.

1906 c.—Idem. Idem, March, v. 25, p. 161.

MARKS (LEWIS HART).

1906.—The coagulability of the blood in yellow fever. Am. Journ. Med. Sciences, November.

NOTT (JOSIAH C.).

1848.—Yellow fever contrasted with bilious fever, etc. New Orl. Med. and Surg. Journ., p. 590.

NOVY & KNAPP.

1906.—Studies on *Spirillum obermeieri* and related organisms. Jour. Infect. Diseases, Chicago, v. 3, No. 3, p. 29.

Otto & Neumann.
1905.—Studien über Gelbfieber in Brasilien. Zeit. f. Hyg. u. Infectionsk., v. 5: p. 357.

Parker, Beyer, and Pothier.
1903.—A study of the etiology of yellow fever. Yellow Fever Inst., U. S. P. H and M. H. S., Washington, March, Bull. No. 13.

Reed and Carroll.
1901.—The prevention of yellow fever. Med. Record, N. Y., Oct. 26, v. 6(p. 641.

1902.—The etiology of yellow fever. A supplemental note. Am. Med., Phila Feb. 22, v. 3, p. 301.

Reed, Carroll, and Agramonte.
1901a.—The etiology of yellow fever. An additional note. Journ. Am. Med Assn., Feb. 16, v. 36, p. 431.

1901b.—Experimental yellow fever. Am. Med., Phila., July 6, v. 2, pp. 15–2:

Reed, Carroll, Agramonte, and Lazear.
1900 a.—The etiology of yellow fever. A preliminary note. Phila. Med. Journ. Oct. 27, v. 6, p. 790.

Rosenau and Goldberger.
1906.—The hereditary transmission of the yellow fever parasite in the mosquito Yellow Fever Inst., U. S. P. H. and M. H. S., Washington, Jan., Bull. No. 15

Rosenau, Parker, Francis, and Beyer.
1904.—Experimental studies in yellow fever and malaria. Yellow Fever Inst. U. S. P. H. and M. H. S., Washington, May, Bull. No. 14.

Ross (John W.).
1902.—Yellow fever contracted from the mosquito. New Orl. Med. & Surg Journ., May.

Sanarelli (Dr. J.).
1897.—Étiologie et pathogénie de la fièvre jaune. Ann. de l'Inst. Pasteur v. 11, p. 433.

Schaudinn (Fritz).
1904.—Generations- und Wirtswechsel bei *Trypanasoma* und *Spirochæte.* Ark a. d. Kaiser. Gesundheitsamte, v. 20, part 3, p. 435.

Stephenson and Christophers.
1904.—The practical study of malaria. 2d ed., London.

Sternberg (George M.).
1890.—Report on the etiology and prevention of yellow fever. Washington.

Stimson (A. M.).
1907.—Note on an organism found in yellow fever tissue. Pub. Health Rep Washington, May 3, v. 22, No. 18, p. 541.

Theobald (Fred. V.).
1901.—A monograph of the culicidæ or mosquitoes, &c. London, vols. 1, 2, an plates.

1903.—Idem. vol. 3.

Thomas (H. Wolferstan).
1907.—Yellow fever in the chimpanzee. Br. Med. Journ., Jan. 19.

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YELLOW FEVER INSTITUTE, BULLETIN No. 17

Treasury Department, U. S. Public Health and Marine-Hospital Service

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THE PROPHYLAXIS OF YELLOW FEVER.

By G. M. GUITERAS, *Surgeon, U. S. Public Health and Marine-Hospital Service.*

The study of yellow fever has ever been an interesting one from the time it was first observed in the Western Hemisphere to the present day.

Whether the disease is indigenous to America or was introduced from the west coast of Africa, is a mooted question. From the historical data which we have on the subject it would appear as though the latter opinion was the correct one.

The disease has been a scourge to the fair and fertile regions of tropical and subtropical America and has greatly retarded their material progress. Its existence in an endemic form at various points, such as Habana, Rio de Janeiro, and Vera Cruz, has given these ports an unenviable reputation with travelers and seriously hampered their commercial interests, and carried from these foci to other infectible territory it has caused widespread epidemics resulting in great loss of life, interference with commerce, and financial disaster.

The peculiar characteristics of the disease and the mystery which shrouded its etiology and method of propagation have invested it with remarkable interest, and in our day the solution of this mystery, in so far as the method of propagation is concerned, has given us one of the most important advances in modern science.

The work of the United States Army Board in establishing beyond a doubt the hypothesis enunciated by Carlos Finlay, in 1881, as to the transmission of yellow fever by the mosquito, was indeed brilliant. I had the pleasure of being present at the International Sanitary Congress held in Habana when Doctor Reed presented his memorable report proclaiming the new dogma. The work ther described was so thorough and the results so clearly established as leave no doubt in the minds of his hearers as to the truth of his co clusions. Considering the number of able men who had been stuc ing the subject, it is remarkable that a period of nearly twenty ye should have elapsed before Finlay's ideas were seriously conside and finally accepted. It is still more remarkable when we consi that since the early part of the nineteenth century various observ had indicated the mosquito as in some way related to the dise under consideration. There is no doubt but that the interesting wo of Dr. Henry R. Carter, of the Public Health and Marine-Hospi Service, in establishing, in 1898, the "extrinsic" period of incubati of yellow fever—that is, the interval between the infecting and s ondary cases—gave renewed impetus to the study of the mosquito a factor in yellow fever and indirectly brought about the confirn tion of the truth of the hypothesis of Doctor Finlay.

PRINCIPLES OF PROPHYLAXIS.

The prophylaxis of yellow fever, which up to a few years ago w founded on ideas so uncertain and insecure, is to-day firmly bas on the discovery of the transmitting agent of the disease. This age can be destroyed and may be prevented from becoming itself inoc lated and, if inoculated, from transmitting the disease to the we

In the abstract the measures necessary to accomplish this are p fectly feasible. No extraordinary means or intelligence is requir to make them effective; only a careful attention to details. But practice, when the peculiarities of human nature, the rights of t individual as guaranteed by the law, and the ignorance of the peo have to be taken into account, the problem becomes both difficult a onerous.

The subject of the prophylaxis of yellow fever has been thorough thrashed out during the last few years, and as the matter is so sim in itself there is but little that may be added to what has alrea been said. Within the time stated the writer has been connect with the two epidemics which have occurred in the United States— Laredo, Tex., in 1903, and at New Orleans and Vicksburg in the ge eral epidemic of 1905—and has carried out with success the princip of prophylaxis which will be referred to in this article. It is n however, the purpose to enter herein into the minutiæ of the met ods of prophylaxis, but rather to invite attention to some of t difficulties to be encountered and to suggest some of the mea whereby, in the opinion of the writer, the obstacles found in t practical application of the principles involved may be lessened eliminated.

IMPORTANCE OF EARLY DIAGNOSIS.

The knowledge that we now have of the transmission of yellow fever gives us a secure basis upon which to lay our plans against the introduction of the disease or to prevent its spread when introduced. There is, however, one link wanting to give us absolute control of the disease, and that is the etiological factor. The consensus of opinion up to the present time is that it is a micro-organism, ultramicroscopic, and as yet beyond our means of detection. The importance of determining this causative agent is apparent from every point of view, but especially so as an aid to diagnosis, for the prompt and positive diagnosis of yellow fever is one of the most important factors in the prophylaxis of the disease, especially when it appears in a locality where it was previously unknown or that has been free of it for some time.

In order to take measures against the spread of a disease it is first of all necessary that we should be aware of its presence. In the case of yellow fever considerable embarrassment presents itself in determining this fact, both on account of the inherent difficulty in making the diagnosis and the natural fear of the attending physician of the alarm and other unfortunate consequences which will usually follow a declaration of its presence, and especially the fear that he may be, after all, mistaken in the diagnosis. This applies particularly to those localities where yellow fever is a new or an infrequent visitor and where there exists an unreasonable fear of the disease.

It is foreign to the purpose of this paper to enter into a discussion of the differential diagnosis of yellow fever, but I desire to impress upon the reader the importance, from a prophylactic point of view, of the early diagnosis of all cases of this disease. We know that the *Stegomyia calopus* can only become infected by biting the patient during the first three days of the illness; hence the diagnosis should be made in its very incipiency. Frequently it is not easy to do this, especially in mild cases. It is here that our knowledge is at fault and all our energies should be bent to discover some means of making a positive diagnosis, one which can not be controverted. When this is achieved the citadel will have been won and the last vestige of danger from this disease removed.

USUAL CONDITIONS WHEN YELLOW FEVER IS DECLARED.

Under present circumstances the following conditions almost invariably confront us in an outbreak of yellow fever in a locality usually free from it, such as, for instance, our South Atlantic and Gulf coast: A case of fever presents itself to a physician who is not on the lookout for yellow fever and who perhaps has never seen the disease. If it be a mild case of yellow fever, it will probably get well without his suspicions being even aroused. If, however, it be of moderate severity and the physician careful and observant, he will soon note symptoms which do not square with the fevers which he has been accustomed to see. He may then suspect that all is not right and begin to think of the possibility of yellow fever. Immediately the purely medical and scientific character of the case becomes clouded by the material considerations involved. Is the diagnosis positive? Shall the case be reported or not? From where could the infection have come? This last question is always given undue weight, with fatal results, because as a rule it is impossible to answer, and its consideration leads to uncertainty and delay. But why should we pause to answer? Do we do so in a case of measles, scarlatina, or smallpox? Why not make the diagnosis on the symptoms of the disease as presented to us and not bother at that critical moment with the abstruse study of its possible origin? That surely would be the most rational and practical way to proceed. In any case, it is indeed a heavy responsibility to satisfactorily answer these questions under the conditions at present affecting our Southern States or other localities similarly placed. The usual course of action is as follows: The attending physician will consult with his confrères. Some will opine that it is, others that it is not, yellow fever. One who has had some experience with the disease, a so-called expert, is finally called in and, we will presume, verifies the diagnosis of yellow fever. As an immediate result of this declaration the physicians of the place, and with them the public, divide into two antagonistic camps, one maintaining that the disease is yellow fever, the other that it is not. And thus, with much wrangling and disorder and under the most discouraging circumstances, the work of preventing the spread of the disease is inaugurated. The effort to stamp it out then becomes a veritable campaign, not only against the mosquito, but against a usually small but determined party of opposition among the people. Such a condition of affairs would not exist if the diagnosis could be promptly established beyond question or cavil.

To attain this being impossible with the diagnostic means at present at our command, I pass on to speak of what seems to me a most important indirect prophylactic measure, one which may do much to offset the results of our present inefficiency to promptly establish an absolutely correct diagnosis—and that is education.

EDUCATION AS A PROPHYLACTIC FACTOR.

The people in general, and the medical profession as well, should be taught the truth about yellow fever, its comparatively low mortality as treated at present, and the facility with which the disease may be avoided and controlled. In a community which is well informed on these points the presence of a case of yellow fever could be announced without any fear of alarm or panic and the measures to prevent its propagation put in force at once without clamor or delay. The physician could act simply on the merits of the case from a professional standpoint. If the disease under observation presented the symptoms of yellow fever, he would announce it as such without stopping to consider or, for the time being, trying to determine from whence it came or obscure his judgment with considerations as to the effect of his diagnosis on the business interests of the locality or on his own personal interests. Such a condition of affairs is much to be desired and with patience and preserverance may be attained.

The education of the public on this subject acts not only in this indirect manner, but directly as well, for it will so guide public opinion that it will be possible to practically eliminate the transmitting factor of the disease, the mosquito, the *stegomyia calopus*. And as it is impracticable to select only the *stegomyia calopus* for destruction, a campaign against this mosquito must be a general one, and also include those responsible for the transmission of malaria, filaria, etc., thus removing from the Tropics and subtropics some of the most important causes of morbidity and mortality, and which heretofore have been serious obstacles to their political, commercial, and industrial progress. Education on this subject, therefore, I consider of prime importance in the prophylaxis of yellow fever, and it is surprising how little has been done or is being done on this line.

The writer in his report to the surgeon-general on the yellow fever epidemic at Laredo, Tex., in 1903, said:

"Insistent and continued efforts should be made through the public press and other available means to educate the people within the sphere of influence of the *stegomyia fasciata* (*calopus*), so that they will learn to protect themselves against the invasion or spread of yellow fever among them by destroying the means for the propagation of said mosquito and by protecting themselves against the mosquito by efficient screening. Above all, to eradicate the existing fear in the medical profession as well as among the laity, of declaring the presence of yellow fever. If the first case presenting the slightest suspicious symptoms of that disease were promptly made public and the proper modern precautions taken, there would be no danger of the disease spreading. In fact, the public should be taught to acknowledge the existence of yellow fever in their midst with the same equanimity as they do in the case of measles or scarlatina."

And again, in the report of the epidemic in Vicksburg, Miss., in 1905, the writer stated:

"There is still much ignorance and skepticism (on the subject of the method of transmission of yellow fever). An effort should be made to overcome this by widely distributing pertinent literature on the subject. And as it is reasonable to suppose that in spite of the progress already made and being made to eradicate this disease from Tropical and subtropical America, it will continue to harass us for many years to come, it is believed that a campaign of education should be begun with the young. All important facts pertaining to the transmission of yellow fever by the *stegomyia fasciata* (*calopus*), and the mode of propagation of this mosquito should be taught in the public and private schools and colleges in infectible territory. There may be seen in this way a good chance to completely destroy the *stegomyia* in its present habitat, and even if not successful in entirely destroying it, the great advantage will have been gained that when yellow fever should make its appearance in a locality the work of the sanitarian in checking or stamping out the disease would be made easy indeed and the usual panic with its discomforts and financial losses avoided."

My experience in these two epidemics and what I have seen elsewhere has confirmed in my mind the importance of this matter. I believe and would recommend that the method of transmission of yellow fever, and malaria as well, be taught in the schools wherever these diseases are liable to occur. The subject should be taught in the primary grades, for what children then learn they will retain. To obtain the desired result the most elementary teaching would suffice. Children may be taught to dread a mosquito as they now do other insects that are less harmful. In the higher grades, with little labor or time, the reasons for this fear of the mosquito may be demonstrated, as also the methods of exterminating the insect and of protecting one's self against its bite.

ULTIMATE RESULTS OF EDUCATION.

With the above idea disseminated among the people it would not be long before public opinion would demand with irresistible force the drainage of swamps and lowlands and the inspection of houses and premises to see that they were free of breeding places for mosquitoes.

To have open cisterns, water barrels, bottles, broken crockery, or, in fact, any receptacle capable of holding water exposed for any length of time, would be considered as much a nuisance and a menace to the public health as ill-ventilated and crowded tenements, dirty streets, defective sewerage, and the many other dangers which at present excite the social and political activities of national, state, and municipal authorities. Such a system would, within a comparatively short time, eliminate all danger from both yellow fever and malaria.

PROPHYLACTIC MEASURES INDICATED IN INFECTIBLE TERRITORY.

We will now consider more in detail the prophylactic measures that should be observed in infectible territory. These may be divided into two classes, to wit: (*a*) Measures directed against the introduction of yellow fever from abroad; (*b*) those looking to the prevention of its spread when it has been introduced.

Maritime quarantine.—Measures employed to prevent the entrance of infection from abroad are usually included under the term "maritime quarantine" and are at present well provided for in the United States by an efficient national quarantine establishment, which is an integral part of the United States Public Health and Marine-Hospital Service.

The measures ordained against the introduction of yellow fever by the quarantine regulations of this service are based on its well-known period of incubation and the processes of disinfection on the mosquito transmission of the disease, and are directed to the destruction of this insect both in its larval and adult stage. These measures may be stated briefly as follows:

Vessels which may possibly be infected are detained at the port of arrival five days after disinfection; vessels known to be infected, six days. The service has medical officers stationed at all the important ports within the yellow-fever zone, and if the vessel is disinfected at the port of departure under the supervision of this officer, the vessel on arrival at a port of the United States within the infectible area is subject to the following modified treatment: If arriving in five days or less, she may be admitted to pratique without disinfection or further detention than is necessary to complete the five days. If arriving after five days and within ten days, she may be immediately fumigated and admitted without detention. If arriving after a longer voyage than ten days, she will be considered as not having been subjected to any previous treatment. This last disposition is based on the possibility that a case of yellow fever may have occurred aboard and recovered within the time mentioned.

Passenger traffic from infected ports, without detention, is also permitted by these regulations under the following conditions:

Vessels carrying such passengers must be in the best sanitary condition and must lie at approved moorings in the open harbor. The crew must not be allowed ashore at the port of departure. The entrance of mosquitoes into the vessel must be prevented, and if they do find ingress must be destroyed. Passengers and crew must be certified as immune by the medical officer issuing the bill of health. The evidences of immunity which may be accepted are proof of a previous attack or ten years' residence in an endemic focus of yellow fever. These regulations apply, of course, only during the close quarantine season—that is, from the 1st of May to the 1st of November.

It will be noted that the above restrictions are liberal enough and at the same time give adequate protection.

Referring for a moment to the evidence upon which certificates of immunity are based, the writer is of the opinion that a ten years' residence in an endemic focus should no longer be considered sufficient, for with our present knowledge of the method of transmission of yellow fever it is quite clear that any intelligent person taking certain simple precautions might very well live a lifetime in an endemic focus and yet never be exposed to infection.

Measures against the spread of yellow fever.—With reference now to class *b*—that is, preventive measures against the spread of yellow fever once it has been introduced, we find that as a rule we are not so well equipped. The principle of prophylaxis is, of course, precisely the same, but is much more difficult of application because we have to deal with local and conflicting interests and the ignorance of the people. Municipalities usually have a sufficiency of ordinances and regulations covering prophylactic measures against yellow fever, but unfortunately these are completely ignored except when menaced by an epidemic, and then enforced with difficulty. These ordinances have been enacted during a period of stress and excitement, when yellow fever was present or dangerously near, and quickly forgotten once the danger had passed. Now, this should not be, for there is no reason why every port in infectible territory should not be so administered as to make it noninfectible, so that if yellow fever should gain an entrance from abroad its spread would be impossible. To attain this I would outline the following plan: Education and the formation of a public opinion that would look upon the mosquito not only as a disagreeable pest but a very dangerous one as well; proper drainage; a corps of inspectors to examine all premises every ten days, preferably once a week, to see that they are free from water containers capable of harboring mosquito larvæ; the screening or covering with oil of water containers which can not be destroyed, or the use of small fish where the above methods are not available; the removal of unnecessary vegetation; the screening of dwellings and other buildings.

In carrying out the above measures there is nothing that requires any great expenditure of money or labor, and if efficiently performed and consistently kept up it would be but a short time before the introduction of a case of yellow fever into a locality so governed would be unattended with danger and scarcely cause a ripple of excitement.

GENERAL PLAN FOR HANDLING AN EPIDEMIC.

Where the ideal conditions above mentioned do not prevail there is, of course, imminent danger of the disease spreading. Steps must be taken at once to prevent this. The bases of preventive measures may be stated succinctly as follows: To prevent the infection of Stegomyia mosquitoes by properly protecting all persons ill with yellow fever during the first three days of the illness; to protect the well from the bite of the mosquito; and, as a corollary to the above, the destruction of all mosquitoes and their means of propagation. Given the requisite personnel, sufficient funds, and the necessary authority to enforce measures to this effect and there would be little danger of the disease spreading. These desiderata, however, are usually wanting or only imperfectly supplied. The practical adaptation of the above propositions may be considered under the following heads:

1. Detection of cases or inspection.
2. Yellow fever hospital.
3. Martial law.
4. Detention camp.
5. Protection against the bite of the mosquito; screening, etc.
6. Extermination of mosquitoes, including oiling, fumigation and the screening or destruction of water containers.

The details of the two latter are so well known and, in fact, so simple that it seems unnecessary to take up the reader's time with a discussion of them. Relative to the first three, which I consider of great importance and which, in a way, form the tripod on which the others rest, it is well to say a few words.

1. *Detection of cases or inspection.*

In order to put in force efficient prophylactic measures it is absolutely necessary that all cases be reported immediately. For reasons before stated this is difficult, and to those already given we may add that during an epidemic many cases of fever do not call a physician at all. To surmount these obstacles, as well as the difficulty of definitely recognizing the disease in its early stages, all cases of pyrexia in which the reason of the abnormal temperature is not manifest should be treated prophylactically during the first three days as though they were yellow fever, or until a positive diagnosis to the contrary is made. For the purpose of reaching all cases of fever a thorough inspection is required. Every dwelling in the infected area must be inspected daily, or, better, twice a day, by competent inspectors, persons capable of reading the clinical thermometer. All cases of pyrexia discovered by the inspectors should be immediately reported to the officers in charge of the screening and fumigating parties for proper action. The patient having been protected against the bite of the mosquito by screening and his dwelling and the surrounding houses fumigated for the purpose of destroying any possibly infected mosquitoes, the question of diagnosis may safely be left to be determined later. Whenever possible the patient should be removed to the hospital.

2. *Yellow-fever hospital.*

This brings us to the second prophylactic measure advocated above—the advantage, and indeed necessity, of a yellow-fever hospital in dealing successfully with an epidemic.

There is a prejudice among the people against the term "yellow-fever hospital," hence it would be as well to yield to this prejudice and call it an "isolation" or "observation" hospital. The important point is that this hospital be absolutely mosquito proof, and that it be made attractive, be clean and well managed, so that the people may be drawn to it and feel that they will be as well or better cared for in the hospital as in their own homes. The greater the number of fever patients that can be removed to the hospital the easier will be the task of stamping out the disease.

Such cases as in the opinion of the sanitary officer can not be properly screened in their homes should be compelled to go to the hospital. The transfer of the patient must be accomplished with such precautions as will prevent the possibility of his being bitten by a mosquito—under a mosquito-bar or in a screened ambulance.

3. *Martial law.*

To make the inspection thorough and effective and to compel the transfer of the sick to the hospital when necessary, authority is required. In a republican form of government this authority is usually wanting and these measures have to be carried out inefficiently and in the face of great opposition.

To obviate this the writer would advocate that martial law be declared in epidemics when the conditions are such as to warrant it. This legal procedure is frequently invoked when the menace to life and property is not nearly so great as in an outbreak of yellow fever or other infectious or contagious disease.

With martial law to support the sanitary officer the prophylactic measures herein advocated could be enforced in every detail and an outbreak of yellow fever effectually controlled. It is easy to understand why this agent was not invoked prior to the demonstration of the transmitting factor of yellow fever, when our efforts to control the disease were rather vague and uncertain; but to-day, when our system may be made so precise and certain it seems almost criminal not to take advantage of such a powerful auxiliary.

In our epidemics the sanitarian, unsupported by authority, is obliged to lose much precious time and energy in his efforts to gain the good graces and plaudits of the populace, so that he may be permitted to perform his work untrammeled.

4. Detention camp.

In most epidemics it is necessary to provide means to permit persons to leave the infected district without danger of carrying the disease elsewhere. This may be accomplished by a so-called "detention camp," where those wishing to leave the infected locality may do so after being detained under observation for the time requisite to assure their freedom from infection.

With our present knowledge of the transmission of yellow fever it is unnecessary to establish these "camps," as heretofore, in out-of-the-way or inconvenient places. On the contrary, they may be located with perfect safety within the infected district so long as the detained persons are kept in mosquito-proof quarters and, when their period of observation has terminated, are taken to their destination in mosquito-proof conveyances while within the infected area.

It is plain, however, that in a properly educated community where the measures above advocated can be put in practice, there will scarcely be any necessity for a detention camp.

In the foregoing pages the writer has endeavored to outline a scheme or plan of prophylaxis which he feels quite sure will do the work expected of it. The machinery is there, but where is the power to set it in motion? To start it successfully, smoothly, and without friction, some central authority with the necessary means and power, acting surely and swiftly, must be provided. This should be the function of the Government.

PROPHYLACTIC MEASURES SUGGESTED BY THE FRENCH COMMISSION OF THE PASTEUR INSTITUTE.

Much interest is attached to the means of prophylaxis suggested by the results obtained by the French commission of the Pasteur Institute in their report on the investigation of yellow fever, published in the Annals of the Institute in November, 1903, to wit:

1. An injection of virulent blood serum which has been heated for five minutes at a temperature of 55°C. confers a relative immunity, which may become complete if followed by the injection of a very small quantity of virulent serum.

2. The injection of defibrinated blood which has been kept under liquid vaseline for eight days confers a relative immunity.

3. The serum of a convalescent is endowed with preventive properties.

4. The immunity conferred by the serum of the convalescent is still in evidence at the end of twenty-six days.[a]

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[a] Abstract of Report, French Yellow Fever Commission; Annual Report, U. S. Public Health and Marine-Hospital Service, 1904.

Further study on this line may give us an immunitive serum which will be of great value in controlling yellow fever.

However, even though we attain this and, furthermore, discover the etiological factor in yellow fever we will still, in a great measure, have to depend on the means of prophylaxis herein outlined, and I desire, therefore, to impress upon the reader the importance of education as a prophylactic factor and the necessity of clothing the sanitary officer with the requisite power and authority to enforce the measures that we now have at our command, which are simple and efficient.

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