mixed with a moderately thick dough, the disengagement of carbonic acid taking place throughout, fills it with innumerable minute interstitial bubbles, or makes it spongy, as the housewives say, or light. If baked in this condition these bubbles expand with the heat, making the bread still "lighter," or more porous, and in a condition for more ready disintegration in the stomach and intestine than breads made without yeast, and depending upon the vaporization of water only for their lightness. The alcohol is mostly dissipated in the baking and cooling of the bread; the cooked yeast itself is probably of no special dietetic consequence.

In medicine yeast is now scarcely used. It has been given in indigestion, dyspepsia, etc., but is of little consequence (there are yeast cells in or upon our food almost always). Dose of liquid yeast, 15 or 20 gm. (ʒ ss.). It still survives to a moderate extent as a poultice (*Cataplasma Fermenti*), which is simply a thin raised dough.

Take of beer yeast, 6 fluidounces; wheaten flour, 14 ounces; water heated to 100° F. (37.8° C.), 6 fluidounces. Mix the yeast with the water and stir in the flour. Place the mass near the fire till it rises.

Yeast poultice is a light, agreeable application, and is thought to overcome the odor and reduce the decomposition of sloughing sores. It is seldom used in this country.

W. P. Bolles,
Revised by *Henry H. Rusby.*

YELLOW FEVER: HISTORICAL SKETCH OF THE DISEASE, ITS ETIOLOGY AND MODE OF PROPAGATION.—History.—The remotest records about epidemic diseases in the Old World fail to show that yellow fever or any other disease presenting similar epidemiological features had ever been observed previous to the discovery of America in 1492; while in the newly discovered lands it soon became apparent that every expedition of European settlers that came to the Antilles or to the Spanish Main had to pay a heavy tribute to an unknown pestilence, during the first summers of their residence, suffering thereafter no further trouble from the climate. Was this pestilence yellow fever?

In order to answer that question Bérenger-Féraud and I, independently of each other, undertook minute historical researches, some fifteen years ago. We both came to the same conclusion: that the disease mentioned in the old Spanish chroniclers as the "peste," "contagio," or "epidemia," was no other than our modern yellow fever; and that, at the time of the discovery, it was endemic on the coast of Mexico, at the present site of Vera Cruz, as well as on the Atlantic side of the isthmus, and on the Spanish Main along the coast of Colombia and Venezuela inhabited by the Carib Indians. These warlike Indians were constantly plying across the Caribbean Sea in their canoes, and through them yellow fever appears to have been sometimes conveyed to their own Isles of Dominica, Guadeloupe, Porto Rico, and to the eastern end of Hispaniola (the Province of Higuey in Santo Domingo) which was often visited, if not held in actual subjection by that fierce Indian tribe. The disease was called "Poulicantina" by the Caribs (Bérenger-Féraud) and "Cocolitzle" by the Mexicans (see my "Epidemiologia primitiva," in Cronica Medico-Quirurgica de la Habana, Mayo 15, 1897).

The Caribs maintained in captivity upon their own isles a number of women and youths captured by them from the peaceful and even timorous tribes who dwelt upon the greater Antilles, the male adult prisoners having been disposed of to satisfy the cannibal instincts of the captors. Being born or bred in the endemic foci on the mainland, the Caribs must have been immune against the Poulicantina, just as the natives of Cuba have been hitherto against yellow fever; but the presence of the non-immune captives may have supplied the required material for the occasional development of poulicantina epidemics in the Carib Isles, and also in the Higuey district of San Domingo; and in this way the disease could readily have reached any foreigners who chanced to visit those islands. This is indeed what seems to have happened to the Spaniards, newly arrived in Hispaniola, during a long succession of summers ever since their first settlement in 1494; and to the French ever since their first attempts to colonize the Carib Isles, one and a half centuries later. The French missionaries, less reticent than the Spanish colonists had been, made no mystery of the symptoms of the epidemic disease which attacked them, and which, they said, was known in the Spanish Islands under the names of "peste" or "epidemia"; so that the identity between our modern yellow fever and the poulicantina as well as with the "peste," "contagio," "epidemia," of the Spanish colonies, could no longer be doubted, after the description of Du Tertre, who witnessed the epidemic of Guadeloupe in 1648, and Cogolludo's minute account of that of Yucatan the same year.

First Names Given by the Spaniards to the Pestilential Disease which Attacked the Spanish Settlers Newly Arrived in Hispaniola and Darien.—On the 2d of February of 1494, two months after the arrival of Columbus at Hispaniola, on his second voyage, bringing with him the first European expedition (fifteen hundred men) that ever set foot on American soil, twelve of the seventeen vessels on which that expedition had come sailed away, under command of Antonio Torres, for Spain, taking, no doubt, the route through the Canary Islands which was still followed in those days. At the port of departure where the colonists, by order of the admiral, were building the town of Ysabela, most of the men had been falling sick since the last week of January; but though many were on the sick list only few died. Critics are mostly agreed in attributing to malarial fevers the illness which attacked the men at this time, the admiral himself having been one of the sufferers. It is possible, however, that some of the fatal cases may have been yellow fever. At any rate, as the year advanced, the situation became more critical, and by the end of May, when the admiral's brother, Bartolomé Colon, arrived with three vessels laden with provisions from Spain, sickness and death had been rife among the Spanish settlers in Hispaniola, not only at the port of Ysabela, but also in the interior of the island where forts had been constructed near the gold mines. The Indians then began to run away from their masters, deserting the culture lands, perhaps in order to preserve themselves from a contagion with which they were already familiar; but the Spaniards attributed their dispersion to a preconcerted plan for starving the foreign invaders out of their country by not planting at the proper season the vegetables upon which the inhabitants were most dependent for their subsistence. Oviedo attributes to this action of the Indians the great mortality which followed. From two-thirds to one-half of the Spaniards died, but innumerable were also the deaths among the Indians themselves, whose cadavers lay strewn in the fields, producing, says the chronicler, a most horrible and pestilential stench. Columbus, in the mean time, had been absent from the island since the end of April, exploring the coasts of Cuba and Jamaica, and intending also to visit Porto Rico. About the middle of September, on his way from Jamaica to Porto Rico, he came close to the shore on the south coast of Hispaniola, holding intercourse with the Indians and landing nine men of his crew to convey information about his own movements to his people at Ysabela, across the island. He was detained by a severe hurricane during seven or eight days in a narrow pass between the coast and the islet of Saona, close to the Higuey district. On the 25th or 26th of September, as he was proceeding toward Porto Rico, he was suddenly attacked by a grave illness, which deprived him of his senses and so much alarmed the crew that they turned from their intended course and brought the admiral and the other two vessels back to Ysabela, where they arrived on the 29th. He continued several days ill, and had a long convalescence, probably prolonged by a return of his malaria infection, as often happens in Cuba in the convalescence of yellow fever. In a letter which the admiral wrote to the King, he states that his illness on that occasion had been a "modorra pestilencial," probably the name which Dr. Chancas, the physician attached to the expedition, had given to the disease which had been causing so many deaths on the island since the admiral's departure in April. This same pestilential disease appears also to have been carried from Hispaniola to the Canary Islands, either by the vessels of Antonio Torres, or, more probably, by the three which returned to Spain after having landed D. Bartolomé Colon at Ysabela; for Humboldt and Bonpland inform us that "what remained of the Guanches on the Island of Teneriffe perished mostly in 1494, in the terrible epidemic called the "Modorra." Though every subsequent expedition which landed at Hispaniola lost one-third or more of their contingent from the same pestilence during the first summers of their residence on that island, the chroniclers, warned by the panic which had been created in Spain by rumors of the first epidemic, were silent as to the name and symptoms of the disease, always attributing the great mortality to the bad quality of the food and to the change of climate. But in 1514, when Pedrarias Davila landed at Darien with a splendid expedition, among whom were the Chronicler Oviedo and Andagoya, both of whom had lived in former years in Hispaniola, a terrible epidemic broke out among the newcomers, causing seven hundred deaths in one month, and each of the above-mentioned authors declares that the cause of it was the "modorra sickness"; adding that after the newcomers had gone through that ordeal, the climate proved as salubrious to them as that of Spain. The name of "modorra" was, however, soon abandoned, probably because the stupor or coma which characterizes some particular epidemics of yellow fever (see Cornillac, ed. 1875, p. 423) was found to be a less constant symptom than Dr. Chancas had imagined. In subsequent years the uncompromising terms of "peste," "pestilencia," "epidemia," "contagio," were substituted, and continued in use till the end of the seventeenth century.

The names of vomito negro and yellow fever were first given to the disease in the early part of the eighteenth century. In 1753, a surgeon of the Spanish navy, Dr. Josef Gastelbuondo, who had settled in private practice at Cartagena de Indias, published a book on the "vomito negro," stating in his preface that he had been studying the disease and investigating its causes during the previous forty years, and had performed several autopsies. Strange to say, he attributes the disease to the same causes which had been constantly invoked by the early Spanish colonists of the two previous centuries, namely, to the change of climate and to the poor quality of food for which the newcomers were unprepared. Other names such as typhus amaril, typhus ictérode, hæmogastric pestilence, malignant remittent, putrid fever, etc., continued, however, to be used conjointly with that of "vomito negro," yellow fever, fièvre jaune, febre gialla, till the commencement of the nineteenth century.

During the first two hundred years after the discovery of America the ports of Santo Domingo, Cartagena de Indias, Porto Bello, Darien, Vera Cruz, where the "flotas de Indias" brought each year, during the summer months, a large number of non-immunes from Spain, yellow fever assumed the character of a permanent endemic, while on the Island of Cuba, owing perhaps to its cooler climate and to the fact that its communication with Spain was less direct, the disease obtained a permanent foothold only in 1761, after the occupation of Havana by the English and the subsequent opening of Cuban ports to general commerce. Since that time and until 1901 Havana has been considered a constant menace of yellow-fever infection for the United States and for European ports. Rio de Janeiro, Brazil, on the other hand, has become an endemic focus only since 1850.

New Orleans also was at one time considered an endemic focus of yellow fever, not less than forty-eight epidemics having been recorded in the first sixty years of the nineteenth century; but the success which has followed the observance of strict quarantine measures after the civil war plainly shows that the infection of that port had in reality been derived from repeated importations from Vera Cruz, Havana, Central America, or from the West Indies. The propensity of yellow fever to spread into neighboring countries, along the lines of traffic, and to be carried in ships to far distant ones when certain climatic and topographical conditions are realized, has been verified again and again, causing innumerable victims as well as serious financial distress, and spreading terror over large areas in North and South America, on the western coast of Africa, in the Canary Islands, in the southwest part of Europe, and at times reaching as far north as Quebec and Swansea, and as far south as Montevideo and Buenos Aires. The climatic and topographical conditions to which reference has been made are essentially those which are compatible with the existence and functional activity of the insect which, as will be seen, assumes the rôle of a natural transmitter of the yellow-fever infection; the principal ones being the prevalence of temperatures between 70° and 90° F., low levels above the seaboard, proximity to the sea or to watercourses, and protection from strong winds. There is, however, another condition which must be inferred by reason of the geographical distribution of the disease, but for which no satisfactory explanation has yet been offered. I refer to the fact that while yellow fever is so frequently carried over the waters of the Atlantic Ocean, and, very exceptionally, far into the Mediterranean Sea, it is a remarkable fact that there is no record of the disease having ever been conveyed over the waters of the Pacific Ocean beyond the western coast of America, where epidemics have often occurred. Whether or not this fortunate state of things will continue after the Panama canal is thrown open, must be a matter of conjecture; but the bare possibility that it might not so continue should be borne in mind and act as a stimulus for all nations interested in the matter to urge the stamping out of yellow fever from the Caribbean Sea and the Gulf of Mexico, as well as from the western shores of America, before free communication is established between the waters of the two oceans in the very heart of the yellow-fever territory *par excellence.*

For a detailed account of yellow-fever epidemics in different countries the readers must be referred to Bérenger-Féraud's valuable chronology of the disease ("La Fièvre Jaune," Paris, 1890), and to Dr. G. M. Sternberg's article in the first edition of this Handbook.

Etiology and Mode of Propagation.—In the first edition of this Handbook, Dr. G. M. Sternberg expressed himself in the following terms regarding the etiology of yellow fever.

"As to the nature of the *specific cause* of the disease there can scarcely be two opinions. The present state of science justifies the belief that it is a living micro-organism; and facts relating to the origin and extension of epidemics show that, as in cholera and in typhoid fever, this micro-organism is capable of development outside of the human body under conditions which will be discussed hereafter. Unfortunately, the present state of science does not enable us to give an account of the deadly microbe which we assume to be the cause of the disease under consideration. We know to-day the morphological and physiological characters and the habitat, within the body of an infected individual, of the specific cause of cholera, of typhoid, and of relapsing fever, but the researches made up to the present time have failed to demonstrate the 'germ' of yellow fever" (Reference Handbook of Medical Sciences, Vol. VI., 1887).

My tetragenus febris flavæ (M. tetragenus versatilis Sternberg) fared no better under Dr. Sternberg's keen criticism than did the *germs* of Freire, Carmona, or Gibier, nor shall I at present renew my claim as to its etiological significance; but I think it worth while recording the following remarkable coincidence. In 1895, in a paper on "Tetracoccus Versatilis," which was published in the *Edinburgh Medical Journal* (December, 1895), I called attention to the curious circumstance that pure cultures of my tetragenus, which had been filtered through Kitasato filters, had on two occasions given evidence that some of the tetragenus germs had passed

through the pores of the filter; while in 1901, in the last experiments performed by the United States Army Board, we are informed that the blood serum of a yellow-fever patient, after being passed through a Berkefeld filter, gave evidence that the germ had passed through the filter, for positive results were obtained when the filtrate was injected into non-immunes, and Drs. Reed and Carroll infer that the said germ must be ultra-microscopic (see the article published by Drs. Reed and Carroll in *American Medicine*, February 22d, 1902, p. 304). Should the fact be confirmed that my tetragenus possesses ultra-microscopic spores besides the coarser forms which it develops in our artificial culture media, most of the objections which have been raised against its etiological significance would fall to the ground.

In 1897 Dr. Sanarelli discovered in his cultures from yellow-fever material collected in Brazil a new bacillus which he still considers the specific germ of the disease. This discovery attracted a good deal of attention, having been confirmed by some other observers, while others again strenuously denied that it had any etiological significance. The unquestionable competence of the discoverer and his previous good record at the Institut Pasteur added considerable weight to his claim. A final verdict, however, was given against him after it was averred that his bacillus icteroides never developed in any of the bouillon tubes that were planted, by Drs. Reed, Carroll, and Agramonte, with samples of yellow-fever blood which, inoculated into non-immunes, invariably reproduced the disease. I believe, however, that the bacillus of Sanarelli may be one of the promoters of the secondary infections which characterize the hæmogastric forms of yellow fever, and in that capacity it may yet be found to constitute an important factor in the development of the worst complications which are apt to occur in the course of an attack of yellow fever.

However much it may be regretted, that up to the present day the specific germ of yellow fever has not been identified, so that the diagnosis of some abortive or atypical cases must often be considered problematic, it is, however, a great source of satisfaction that we positively know the manner in which the disease is transmitted in nature, and that this knowledge enables us to control with great success its propagation and to stamp it out, as has been done in Havana during the last sixteen months.

Discovery of the Yellow-fever Mosquito.—Apart from the historic interest which the matter might afford, I think it proper to acquaint the reader with the arguments which led to the discovery of the particular mosquito by which yellow fever is transmitted, inasmuch as, considered from an *a priori* point of view, those same arguments should prove more convincing than when they are presented merely as a sequel to the demonstration.

In 1880, after receiving the valuable report given out by Prof. Stanford Chaillé as president of the Havana Yellow-fever Commission of 1879, I undertook a careful revisal of all the facts which had been collected since 1853 in the United States, and arrived at certain conclusions which are here summarized in the form of propositions, and which afforded a solid foundation for my future investigations.

Proposition A. Though yellow fever must be considered to be a germ disease, it is transmissible only under certain topographical and climatological conditions which are realized at all seasons of the year only in certain localities along the Atlantic shores of tropical America, where the disease is considered endemic, and of which Havana might be considered a type.

Proposition B. Even within the infected foci, the disease is apparently not contracted through contact with the patient or his secretions, nor by breathing the air of the sick-room, nor by the use of contaminated food or drinks.

Proposition C. The pathological lesions pointed out by Crevaux, Gama Lobo, and other competent observers, in the walls of the blood capillaries of yellow-fever cadavers, and the hemorrhagic tendency which, as a rule, develops in the course of the attack, even in mild cases, suggested the idea that the mesoblastic tissue from which the vascular endothelium is formed might prove to be the most appropriate source from which the infective material could be obtained.

From proposition A, I had inferred that, for the production of a case of yellow fever, a third factor was required besides the yellow-fever patient and a person susceptible to the infection—a factor which, though indispensable for the transmission, might exist independently of the patient and of the disease. It should, however, be essentially dependent for its existence and for its functional activity on the topographical and climatological conditions which favor the transmissibility of yellow fever.

From proposition B, I inferred that the only unexplored channel by which the virus or germ might prove pathogenic for human beings must be by a process of inoculation.

From proposition C, I surmised that in order that the inoculation should prove effective, the infectious material might be obtainable only from the blood or from the walls of the blood capillaries of a yellow-fever patient, and might require also to be inserted into the capillaries of a non-immune.

I was thus led to conclude that the transmission was effected through the agency of some blood-sucking insect which was peculiar to yellow-fever countries, and which was able to retain upon its mouth parts the living germ so as to inoculate it afterward into those whom it chanced to bite. In searching for such an insect I came across the day mosquito of Havana (culex mosquito Desv., Stegomyia fasciata Theo.), in which I had observed certain peculiarities in the manner of laying its ova, and in its readiness to renew its bites whenever the digestion of a previous meal of blood had been completed, both of which peculiarities seemed to differentiate it from other species of gnats and to make it particularly well suited for the purpose of reproducing a disease in an epidemic form. Upon investigation I found that this insect was benumbed and unable to bite under the influence of temperatures of 15° C. (59° F.), at which degree of cold epidemics of yellow fever were known to cease in New Orleans, in Rio Janeiro, and in Havana; and also that after being kept for a while in a rarefied atmosphere corresponding to altitudes of four thousand to six thousand feet, at which elevation yellow fever is intransmissible, the insect lost to a great extent the power of driving its sting into the flesh.

My next step was to submit my theory to an experimental test by applying to non-immunes mosquitoes of that species which had been made to bite, two or three days before, a severe case of yellow fever. Among twenty non-immune soldiers who were set apart and kept under observation during two months, five were on different dates bitten by a mosquito which had been contaminated in that manner. Three of the five were taken sick after their inoculation, one after fourteen days with a mild but characteristic attack of albuminuric yellow fever, two were attacked on the fifth day after the inoculation with an abortive form of yellow fever, while neither of the other two showed any symptoms characteristic of the disease. None of the fifteen who had not been inoculated suffered any similar attack of fever during the two months that they remained under observation. After the lapse of four years I ascertained that none of my five inoculated soldiers had been reported again as suffering from yellow fever.

During the next twenty years I continued to perform that mild form of inoculation, my object being to ascertain whether or not some degree of immunity might thereby be obtained even when no immediate pathogenic effect had followed the inoculation. The principal data concerning each of the mosquito inoculations that were performed either by me or by my collaborator, Dr. Claudio Delgado, have been set down in Table I., so that the reader may judge for himself and draw his own conclusions. Two of the inoculations (No. 3 and No. 104 of

Tables of Mosquito Inoculations Performed in Havana.

Abbreviations which are used in these tables:

"eph."....Ephemeral fever without characteristic symptoms.
"Abort."....Abortive yellow fever, with albuminuria.
"abort."....The same without albuminuria.
"N-a"....Non-albuminuric yellow fever with well-marked fever curve and other symptoms.
"n-a."....The same with milder symptoms.
"y-f."....Yellow fever about which particulars are not given, but not fatal unless so expressed.
"Alb."....Regular albuminuric yellow fever.
"alb."....The same of mild type.
"Hg."....Hæmogastric yellow fever, with black or bloody vomit or melæna, of fatal termination.
"hg."....The same, not fatal.
"s."....Severe.
"f."....Fatal.
"m."....Mild.
"vm."....Very mild.

Symbol of contamination. The figures to the left of the oblique stroke express the days that have elapsed since the insects have bitten the infecting patient. To the right of the oblique stroke are expressed, in abbreviation, the type of the disease, and, in Roman numerals, the day of the attack when this patient was bitten.

Table I.—Inoculations with Recently Contaminated Mosquitoes.

No.	Inoculation.	Mosquitoes.	Contamination.	Result in first twenty-five days.	Ulterior yellow fever.	Subsequent residence.
1	30 June, 1881.	1	2/Hg., iv.	14 July, 1881, alb.	0.	4
2	22 July, 1881.	1	6/Alb., v.	27 August, 1881, abort.	0.	4
3						
4	31 July, 1881.	1	2/Hg., iii.	5 August, 1881, abort.	0.	
5	2 August, 1881.	1	3/Hg., v.	17 August, 1881, eph.	0.	4
6	15 August, 1891.	1	2/Hg., vi.	0.	0.	2
7	7 August, 1891.	1	2/Alb., iii.	0.		4
	11 September, 1881.	1	2/Hg., vii.	0.	10 September, 1882, N-a.	10
8	22 June, 1883.	2	2/Hg., vi.	9 July, 1883, N-a.	0.	10
9	15 July, 1883.	1	2/Alb., vii.	0.		
	17 August, 1883.	1	2, 4/Hg., v.	26 August, 1883, N-a.	0.	12
10	15 July, 1883.	1	2/Alb., vii.	0.		
	17 August, 1883.	1	2, 4/Hg. v.	0.	0.	3
11	21 August, 1883.	1	6, 8/Hg. v.	0.	5 June, 1884, hg.	3
12	16 July, 1883.	1	3/Alb., vii.	0.	0.	9
13	16 July, 1883.	1	2, 4/Alb., vii.	0.		
	18 August, 1883.	2	3/Hg. v.	9 September, 1883, alb.	0.	10
14	26 September, 1883.	2	2, 3/Alb., v.	0.	?	9
15	29 November, 1883.	1	3/Alb., iii.	0.	21 July, 1884, Hg.	x
16	29 November, 1883.	2	4/Alb., iv.	0.		
	30 May, 1884.	1	3/Hg., vi.	0.	7 August, 1884, y-f.	14
17	1 December, 1883.	1	4/Alb., v.	0.		
	6 May, 1883.	2	4/Alb., iv.	0.		
	23 February, 1887.	2	2/Alb., v.	0.	? July, 1890, y-f.	14
18	25 January, 1884.	1	?/Hg., vi.	0.	?	?
19	16 June, 1884.	2	4/Hg., v.	0.	6 June, 1885, alb.	7
20	26 June, 1884.	1	3/Hg., v.	0.	28 September, 1884, Abort.	10
21	27 June, 1884.	1	3/Hg., v.	0.	23 November, 1884, N-a.	14
22	26 June, 1884.	1	3/Hg., iii.	0.	0.	14
23	28 August, 1884.	2	3/Hg., iv.	0.	0.	4
24	29 August, 1884.	2	4/Hg., v.	0.	0.	1
25	2 September, 1884.	1	2/Hg., iv.	0.	0.	4
26	27 August, 1884.	1	2/Hg., iv.	0.	0.	4
27	14 September, 1886.	1	2/ ?	0.	22 June, 1887, alb.	4
28	7 September, 1886.	1	6, 4/ ?	23 September, 1886, N-a.	0.	5
29	14 September, 1886.	1	2/Hg., vi.	0.	0.	4
30	21 May, 1887.	1	2/Hg., vi.	0.	8 July, 1887, alb.	6
31	21 May, 1887.	1	2/Hg., vi.	0.	15 July, 1887, alb.	15
32	16 June, 1887.	2	2/Hg., iv.	11 July, 1887, alb.	0.	14
33	? July, 1887.	2	2/Hg., vi.	0.	? August, 1889, y-f.	14
34	11 September, 1887.	2	2/Alb., iii.	0.	17 September, 1893, Hg.	x
35	11 September, 1887.	2	2/Alb., iii.	0.	0.	4
36	13 September, 1887.	2	2/Alb., iv.	0.	0.	4
37	14 September, 1887.	2	2, 3/Alb., vi.	0.	0.	4
38	12 September, 1887.	2	3/Alb., ii.	0.	30 August, 1889, alb.	4
39	14 September, 1887.	2	3/Alb., vi.	0.	30 August, 1893, alb.	11
40	18 September, 1887.	2	2/Alb., vi.	0.	? August, 1888, N-a.	10
41	30 September, 1887.	1	3/Alb., vii.	0.	? January, 1889, Alb.	?
42	8 June, 1888.	1	3/Hg., iv.	1 July, 1888, N-a.	4 November, 1888, N-a.	14
43	12 September, 1888.	1	2/Alb., iv.	0.	18 June, 1890, n-a.	4
44	12 September, 1888.	1	2/Alb., iv.	0.	21 September, 1889, Abort.	3
45	22 October, 1888.	1	3/Alb., vi.	0.	0.	4
46	22 October, 1888.	1	3/Alb., vi.	0.	13 September, 1891, N-a.	4
47	23 October, 1888.	1	4/Alb., vi.	0.	23 September, 1889, n-a.	8
48	16 November, 1888.	1	2/N-a., ii.	0.		
	29 January, 1889.	1	3/Hg., iii.	0.	24 November, 1889, n-a.	8
49	16 November, 1888.	1	2/N-a., ii.	0.		
	28 January, 1889.	1	2/Hg., iii.	0.		
	26 April, 1889.	2	?/Alb., iv.	0.	30 October, 1889, N-a.	7
50	16 November, 1888.	1	2/N-a., ii.	0.	? July, 1889, Abort.	4
51	11 April, 1889.	1	?/Alb., v.	0.	0.	3
52	16 August, 1889.	2	3/Alb., iv.; Hg. v.	0.		
					10 September, 1892, N-a.	
53	16 August, 1889.	2	3/Alb., iv.	0.	13 May, 1893, N-a.	4
54	16 August, 1889.	1	2/Alb., iv.	0.	16 August, 1893, alb.	5
55	17 August, 1889.	2	3/Alb., iv.	26 August, 1889, Abort.	0.	2
56	16 August, 1889.	1	3/N-a., v.	0.	0.	5
57	22 May, 1890.	2	2/Hg., iii.	0.	0.	5
58	23 May, 1890.	2	2, 3/Hg., iii.	0.	17 November, 1890, N-a.	7
59	24 May, 1890.	2	3/Hg., iii.	0.	0.	7
60	27 May, 1890.	2	7, 6/Hg., iii., v.	0.	5 November, 1890, alb.	3
	13 October, 1890.	1	2/Hg., v.	0.		
61	13 August, 1890.	1	2/Alb., iv.	0.	16 August, 1892.	5
62	13 August, 1890.	1	2/Alb., iv.	0.	0.	3
					4 September, 1893, alb.	5

TABLE I.—INOCULATIONS WITH RECENTLY CONTAMINATED MOSQUITOES.—*Continued.*

No.	Inoculation.	Mosquitoes.	Contamination.	Result in first twenty-five days.	Ulterior yellow fever.	Subsequent residence.
63	13 August, 1890.	1	2/Alb., iv.	0.	14 September, 1898, alb.	3
64	13 August, 1890.	1	2/Alb., iv.	0.	0.	5
65	13 August, 1890.	1	2/Alb., iv.	0.	0.	7
66	14 August, 1890.	1	3/Alb., iv.	21 August, 1890, Abort.	4 July, 1895, Abort.	12
67	13 October, 1890.	1	2/Hg., iv.	0.		
	12 June, 1891.	1	2/Alb., v.	0.	19 September, 1895, Abort.	9
68	12 June, 1891.	2	2/Alb., iii.	0.	4 July, 1896, Hg.	4
69	15 June, 1891.	2	3/Alb., v.	0.	0.	3
70	15 June, 1891.	1	3/Alb., v.	0.	0.	3
71	16 June, 1891.	1	4, 3/Alb., iv.	0.	0.	5
72	16 August, 1891.	1	3, 2/Alb., iv.	0.	0.	3
73	16 August, 1891.	1	3, 2/Alb., iv.	0.	0.	5
74	16 August, 1891.	1	3, 2/Alb., iv.	0.	0.	5
75	16 August, 1891.	1	3, 2/Alb., iv.	0.	0.	4
76	25 August, 1892.	1	2/Hg., v.	0.	8 September, 1893, Alb.	6
77	27 August, 1892.	1	2/Hg., iv.	0.	0.	1
78	27 August, 1892.	1	2/Hg., iv.	0.	0.	5
79	17 April, 1893.	2	2/Hg., v.	0.		
80	17 May, 1893.	1	2/Alb., iv.	22 May, 1893, eph.	18 October, 1893, N-a.	
					26 August, 1895, hg.	5
81	28 May, 1893.	1	2/Alb., iv.	0.	20 September, 1893, n-a.	5
82	28 May, 1893.	1	2/Hg., iii.	11 June, 1893, eph.	1 September, 1893, hg.	8
83	17 June, 1893.	1	6, 3/Alb., v.	0.	23 November, 1893, Hg.	x
84	12 August, 1893.	1	3/Hg., v.	17 August, 1893, N-a.	0.	5
85	12 August, 1893.	1	2/Alb., iii.	0.	0.	1
86	12 August, 1893.	2	2/Alb., iii.	0.	0.	5
87	5 September, 1893.	2	2/Alb. vi.	0.	13 December, 1894, abort.	8
88	2, 3 December, 1893.	1	2/Hg., iv., v.	0.	25 February, 1894, Alb.	4
89	12 May, 1894.	1	4, 2/Alb., iv.	0.	17 September, 1895, eph.	3
90	6 June, 1894.	2	3/Hg., iv.	22 June, 1894, Abort.	18 August, 1895, Abort.	4
91	15 August, 1894.	2	2/Hg., iv.	0.	? February, 1898, y-f.	4
92	8 August, 1894.	1	3/Hg., vi.	0.	? June, 1896, y-f.	4
93	20 August, 1894.	1	2/Alb., iv.	0.	? June, 1896, y-f.	4
94	20 August, 1894.	1	2/Hg., iv.	0.	0.	4
95	20 August, 1894.	2	2/Alb., iv.	0.	0.	4
96	20 August, 1894.	1	2/Alb., iv.	0.	0.	4
97	21 August, 1894.	1	3/Alb., iv.	0.	0.	4
98	21 August, 1894.	1	3/Alb., iv.	0.	14 July, 1895, alb.	4
99	8 December, 1894.	1	3/Hg., iv.	0.	18 July, 1895, Alb.	4
100	19 January, 1895.	1	2/Alb., vi.	0.		
101	7 October, 1895.	1	3/Alb., ?.	0.	12 August, 1897, N-a.	6
	11 November, 1895.	1	4/Hg., viii.	0.	0.	4
102	2 September, 1896.	1	3/Hg., iv.	0.	16 September, 1900, Alb.	3
103	10 July, 1900.	1	2/Hg., vi.	0.		

my former tables) have been omitted, because the mosquito in those two cases had not previously bitten any yellow-fever patients.

I was fully aware, at the time, of the shortcomings in my mode of proceeding, the principal ones being: 1. That I had neither leisure nor other facilities for breeding my mosquitoes from the ova or from the larvæ, but had to rely on the outward appearance of the winged insects and on the conditions of the locality where they had been caught, in order to exclude as far as possible the chances that the insects might have been already infected at the time when they were caught. 2. That with the exception of one case (No. 9 of Table I.), in none of my cases had I been able to exclude altogether the possibility that the inoculated person might have been infected from some other source after my own inoculation. 3. That I could not assume the responsibility of attempting to produce severe, perhaps fatal experimental attacks by applying more than two or three recently contaminated insects at one time, or even one mosquito whose contamination dated back from several days or weeks, by either of which processes I had assumed that a dangerous experimental result might follow.

The outcome of my continued study had led me, in 1898, to the following conclusions:

1. That the germ of yellow fever is only pathogenous for human beings when introduced by inoculation. 2. That the regular process by which the inoculation of the germ is accomplished, in nature, is through the bites of the culex mosquito (Stegomyia fasciata Theo.), the insect having previously become contaminated through the act of biting a yellow-fever patient within the first five days of his attack. 3. That although the bites of a recently contaminated mosquito can produce at most only a very mild attack of yellow fever, or simply confer latent immunity without eliciting any obvious pathogenic manifestation, the bites of the same insect, when its contamination dated back from several days or weeks, might produce severe or fatal attacks. 4. That the yellow-fever mosquitoes, after they have once become contaminated, retain the power of inoculating the disease during the rest of their lives. 5. That yellow fever might be stamped out of Havana by just such a method as the one which was adopted by Major W. C. Gorgas, with signal success, in 1901.

EXPERIMENTAL DEMONSTRATION OF THE MOSQUITO THEORY AND NEW FACTS BROUGHT TO LIGHT BY THE UNITED STATES ARMY YELLOW-FEVER COMMISSION* IN HAVANA.

A most eventful period in the history of yellow-fever investigation opened in the month of July, 1900, when the yellow-fever commission, which had been sent from Washington to study that disease in Havana, undertook to investigate the mosquito theory of yellow-fever transmission with a brood of those insects developed from ova of the culex mosquito (Stegomyia fasciata Theo.) which I had preserved and placed at their disposal.

In the course of twenty days, from August 11th to 31st, 1900, they tried the mosquito inoculations upon eleven non-immunes. The results were negative in their first nine attempts, which consisted in applying to a non-immune one or two insects which had bitten a case of yellow fever (mostly of a mild type) two, three, four, five, six, eight, or thirteen days before biting the non-immune. Their next two attempts, however, proved successful beyond their expectations. The first of these

* This commission was composed of Walter Reed, M.D., Surgeon, U. S. A., James Carroll, M.D., and A. Agramonte, M.D., Jesse W. Lazear, M.D., Acting Surgeons, U. S. A. Dr. Lazear died of yellow-fever while Dr. Carroll was barely convalescent of his experimental attack. He attributed his own attack to the circumstance that during a visit to the yellow-fever ward of Las Animas Hospital, four or five days before he was taken sick, he had noticed a mosquito biting his hand, and being already a believer in the mosquito theory he had refrained from driving away the insect and had allowed it to fill itself completely in order to watch the result.

was made upon a member of the commission, Dr. Carroll, who applied to his own arm a mosquito which had bitten four yellow-fever patients (two of them severe cases) two, four, six, twelve days before the inoculation. Three days and seven hours after the bite of the contaminated mosquito, Dr. Carroll was taken sick with a severe attack of well-characterized albuminuric yellow fever (see No. 1, Table II.). The second successful inoculation was obtained upon a non-immune American, who offered himself for the trial. He was bitten by four mosquitoes which, between them, had previously bitten ten yellow-fever patients (two of them fatal and two severe ones) at different intervals varying between two and sixteen days before the inoculation. This American was attacked at the end of six days and two hours with high fever, and presented all the characteristic symptoms of yellow fever, the albuminuria and jaundice continuing till several days after convalescence (No. 2 of Table II.).

In neither of these two cases had the inoculated subjects been isolated or kept under close observation until the first symptoms of the attack had declared themselves; but the circumstance that their insects were home-bred, that the attack had commenced within the classical limits of the yellow-fever incubation, and that the symptoms were very characteristic, convinced them not only of the fact that the mosquito was indeed the transmitter of the disease, but also, by reason of their first negative results, that an interval of at least ten or twelve days must elapse after the insect has bitten a yellow-fever patient before it acquires the faculty of inoculating the disease. They decided, therefore, to act in accordance with this principle in all their future experiments.

After delivering their preliminary report with a minute account of their two successful inoculations, the same commission returned to Havana with instructions to carry out to a close the demonstration of the important question involved: Whether or not the Stegomyia mosquito is the natural transmitter of yellow fever. For this purpose they were provided by Gov.-Gen. L. Wood with ample means, and permitted to repeat their mosquito inoculations upon any non-immune who, after being informed of the risks, should consent to be experimented upon.

After a careful preparation of the premises and the adoption of many ingenious devices to exclude chances of error, the commission started a series of mosquito inoculations which, under the circumstances in which they were performed, left no room for a doubt as to the fact that the experimental attacks which followed the inoculations could be attributed only to the bites of their contaminated mosquitoes.

By adhering to the rule of using in their experiments only mosquitoes having more than ten or twelve days of contamination, and which had been kept at summer temperatures (80° to 82° F.), they had no difficulty in obtaining well-marked results, the failures having been the exception. They were thus able to contaminate their fresh mosquitoes from previous experimental cases of their own, and, on some occasions, to confirm a doubtful clinical diagnosis by applying to a non-immune mosquitoes which had bitten the patient.

The fourteen successful mosquito inoculations obtained by the Army Board during the years 1900 and 1901 have been tabulated for future references (see Table II.), leaving their other valuable experiments with the injection of yellow-fever blood, and others also for the purpose of demonstrating that fomites and air-borne germs have no share in the propagation of the disease, to be considered after I have completed the record of all the inoculations with mosquitoes that have so far been published.

TABLE II.—SUCCESSFUL MOSQUITO INOCULATIONS BY THE UNITED STATES YELLOW-FEVER BOARD, 1900 AND 1901.

No.	Subject.	Inoculation.	Mosquitoes.	Contamination.	Incubation.	Experimental Attack.
1	Dr. C.	27 August, 1900	1	12/4/s., ii. 6/2/m., ii.	3 days 7 hours	August 31: s. Alb.
2	X.	31 August, 1900	4	12/f., i., ii. 12/16/6/4/2/s., i., ii. 10/6/2/m., i., ii.	6 days 2 hours	September 7: Alb.
3	J. R. K.	5 December, 1900	5	15/f/i., 19/s., ii. 21/m., ii.	3 days 9 hours	December 9: Alb.
4	Sp. a.	8 December, 1900	4	17/f., iii., 19/22/s., iii. 24/m., iii.	5 days 17 hours	December 14: alb.
5	Sp. b.	9 December, 1900	1	19/f., ii.	3 days 11 hours	December 12: alb.
6	Sp. c.	11 December, 1900	4	20/f., iii. 25/s., iii. 27/m., iii.	3 days 10 hours	December 15: alb. tr.
7	Sp. d.	21 December, 1900	?	Mosquito house.	3½ days ?	December 25: alb.
8	Sp. e.	30 December, 1900	4	17/(case 5), i.	3 days 22 hours	January 3: alb.
9	L. F.	19 January, 1901	3	39/s., iii.	4 days	January 23: Alb.
10	C. W.	31 January, 1901	2	51/s., iii.	3 days 2 hours	February 3: alb. tr.
11	J. H.	6 February, 1901	2	57/s., iii.	3 days 6 hours	February 9: Alb.
12	C. S.	7 February, 1901	3	16/f., ii.	2 days 22 hours	February 10: N-a.
13	Sp. f.	16 September, 1901	4	53/f., iii. 34/f., ii.	3 days	September 10: Alb.
14	Sp. g.	9 October, 1901	8	18/(case 13), ii.	3½ days	October 13: alb. tr.

The following series of Prof. John Guiteras will show the advantage of including in such reports not only the successful experiments, but also the negative ones.

During the spring and summer of 1901 Professor Guiteras, being in charge of the Experimental Station at Las Animas Hospital, undertook to ascertain whether the mosquito inoculation could be safely used as a means of conferring immunity upon new comers. His experiments at Las Animas were performed according to the rules set down by the Army Board, and the same precautions were taken to exclude sources of error. In the course of nine months, from February to October, 1901, he performed forty-nine inoculations upon twenty-three subjects who were supposed to be non-immunes, but two of them apparently were not. Nine of the forty-nine attempts were followed by a well-marked attack of yellow fever within three to six days after the bites of the infected mosquitoes. The first successful inoculation (No. 2, Table III.) was performed with a mosquito which had been presented to me by Dr. Carroll, of the Army Board, and which had bitten only once an experimental blood case (No. 4, Table IV.) about nine hours after the invasion. This insect was applied on the 23d of February to a non-immune Spaniard who was taken sick on the 26th at midnight with a mild but characteristic attack of albuminuric yellow fever (No. 2, Table III.).

Seven of Dr. Guiteras' successful inoculations were obtained with mosquitoes which had been contaminated from a particular patient (Alvarez), while other mosquitoes which had bitten different yellow-fever patients coming from the same locality, and who had been attacked about the same time as Alvarez, all gave negative results, even when applied to subjects who afterward succumbed to the Alvarez mosquitoes. The attack in the infecting patient (Alvarez), though severe, had not been fatal; yet the insects which had bitten him only once acquired such a virulent contamination that out of