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Report on the etiology, and the preventive vaccination of yellow fever.

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REPORT ON THE ETIOLOGY, AND THE PREVENTIVE VACCINATION OF YELLOW FEVER.

BY DR. L. GERERD.

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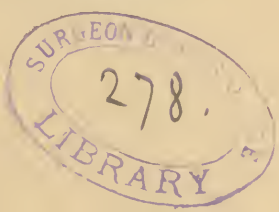
Translated from the French by Dr. Wolfred Nelson, late of Panama, S. A.

Whence comes yellow fever, how does it propagate itself, and what is our etiological knowledge of its nature? Can that knowledge produce some prophylactic means or measures, easy to apply and sufficient to give absolute protection against this formidable plague?

Such were the problems that I had undertaken to solve after my arrival on the Isthmus of Panama. I shall now briefly give the results of my experiments and studies:

I.

In the month of June, 1882, in a report to the Superior Agent of the Interoceanic Canal Company resident in the City of Panama, S. A., I had the honor to inform him, that I had found in the blood of yellow-fever patients, some microscopic organisms,—some filiform, others resembling a string of beads (*chaplets*), and, lastly, brilliant little bodies. That the organisms were constant in appearance, and could thus serve as elements for diagnosis.



After some trials and a great many failures I succeeded in isolating the microbes, and obtained them in great quantity without the human body, by artificial cultivation, in liquids suitable for their nutrition and reproduction.

I was then enabled to study the mode of existence of the microbes. If one observes the filiform bodies attentively for a given time he perceives in their transparent and homogeneous substance, a series of small corpuscles, that refract light more than the other parts of the microbe. Little by little these corpuscles arrange themselves around a central axis or core, giving the organism the appearance of a string of beads, *chaplet*. (This French word signifies the string of beads "told" by devout Catholics while praying.) Soon other changes follow, the string-like formation separates and in place thereof nothing remains but a mass of brilliant little points. The size of little points is about the thousandth of a millimetre. These corpuscle germs have great resistance. *They do not perish by drying, and can after many years serve to propagate the disease, by regenerating the filiform bodies, when placed under favorable conditions.*

But what *rôle* can we attribute to the microbes in the production of yellow fever? To elucidate this question I have had recourse to experiments on animals. At the beginning of my work I experimented on a number of rabbits, later with dogs, poultry, rats and monkeys, but these animals did not show any predisposition to the disease.

At length a result was obtained by inoculating a guinea pig with half a *gramme* (a *gramme* is equal to 15 1-3 grains) of blood taken from the heart of a man an hour after his death from spe-

cific yellow fever. The animal sickened and after two days' fever died in great agony.

At the autopsy on the little cadaver, I found the characteristic lesions of yellow fever, shown with sufficient clearness to establish the identity of the disease, notwithstanding the difference in the organisms.

These direct inoculation experiments were repeated a great many times, the same results were produced in nine cases out of ten. The cadaveric lesions were always the same.

Examinations of blood taken from the ears of a guinea pig suffering from the disease invariably gave the same results, *i.e.*, the recognition or presence of the same microbe met with in man suffering from specific yellow fever.

Having thus established that yellow fever was transferable by inoculation, or vaccination from man to the guinea pig, it became easier to study the *rôle* of the microbe itself in the production of the disease.

More animals were inoculated with the culture liquids peopled with the microbes. They all died in the same manner, presenting the same symptoms as those infected by the direct inoculation of blood.

The periods of incubation in the various experiments declared themselves with varying phases in from one to nineteen days. Figures that correspond with those resulting from observation of the disease at Panama.

As a whole, the knowledge acquired by the experiments just related may be summarized thus :

1st. Yellow fever is a disease that is always characterized by the presence in the blood of the patients of a special microbe, which can be multi-

plied outside of the bodies of men or animals, by artificial culture.

2nd. The microbes give birth to germs endowed with great resistance to destructive causes, and are capable of reproducing the disease.

3rd. Yellow fever can be transmitted to a guinea pig by the inoculation of blood in its sub-cellular tissues.

4th. Finally, the animals inoculated with cultures charged with the parasites, contract yellow fever and die. Post-mortem, the same lesions are found as in those directly inoculated with blood.

II.

Vaccination.

"In 1880 M. Pasteur discovered the first in-
"stance of a disease, produced by a special mi-
"crobe, which, by special treatment, could be de-
"prived of a part of its virulence, and that fowls
"could be inoculated with it without danger. By
"using the attenuated virus, the disease could be
"communicated to fowls, and after a light attack
"they were protected against the fatal disease.

"Later, several microbic diseases were recog-
"nized or defined. Their microbes having the
"same properties.

"M. Pasteur, with marvelous sagacity, could not
"help but remark that the process which had ena-
"bled him to lessen or attenuate the action of the
"microbe of chicken cholera, ought to be a pro-
"cess of diminishing or attenuating the virulence
"of microbes generally that cause other diseases."*

Such were the antecedents that encouraged one to search out a method for attenuating the microbe

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* Chamberland de la Vacination Charbonneuse.

of yellow fever. In my experiments already related I noticed that three of the inoculated animals that were dangerously ill recovered. That circumstance permitted me to submit to experimental proof, the important theoretical problem, as to whether they were still susceptible to the yellow fever poison. The three guinea pigs were re-inoculated some time afterwards to demonstrate if they were susceptible to the disease *de novo*. They did not present any abnormal symptoms after the inoculation, nor the slightest elevation of temperature.

Thus, we should admit in principle that yellow fever cannot be taken anew. And in this again the experiments were in perfect accord with clinical observations.

This fact accepted rendered my later experiments perfectly legitimate in the alternation of the virus of yellow fever poison for the production of a vaccine-virus capable of protecting man against the terrible effects of the disease.

The problem, thus stated, to me seemed susceptible of receiving a favorable solution by following in the steps traced out with so much perfection by M. Pasteur, in his search for the virus of charbon or malignant pustule.

This *savant* showed that he easily could obtain microbes of various degrees of virulence. From the deadly virulence, that is to say, that killed one hundred times in a hundred the animals experimented upon, such as guinea pigs, rabbits and sheep, passing thence by a number of intermediate steps down to the most inoffensive attenuation of the virus. The method of preparing this attenuated or lessened virus thus becomes one of marvelous simplicity.

My conjectures were confirmed by experiment, and now, after the usual experiments, trials and inevitable reverses, I have obtained the microbe of yellow fever in different degrees of attenuation which can be reproduced indefinitely by cultivation.

A guinea pig inoculated by this attenuated virus not only runs no danger of death from the inoculation itself but is placed beyond the dangers and death that invariably follows the injection of virulent blood in animals that have not been protected by the preventive vaccination, or inoculation.

The illustrious *savant* whose methods I have followed said: "We now possess some virus-vaccine from charbon, capable of protecting against "that fatal disease without being fatal in itself, a "living vaccine, cultivated at will, transportable "everywhere, without alteration, at length prepared by a method that we may believe susceptible of generalization."

I shall now apply his words to yellow fever, and it remained for me carry my experiments from the animal to man.

The experiment was made last week on myself. Some months ago I was inoculated with an extremely attenuated culture. Fifteen days ago by a second and stronger culture, and, finally, guided by special reasons, I allowed myself to be bitten by mosquitoes that had just bitten a man suffering from specific yellow fever. He was in the fifth day of the disease.

In view of my experiments it became easy to analyse what obtains in the human body, inoculated, as I was, with a virulence of maximum intensity, direct from the body of a patient.

Twenty-four hours after the above direct inocu-

lation I felt sudden pains in the regions of the kidneys, a feeling of bruising or soreness in all my extremities, a sensation of tearing in my eyeballs. Two hours after these first sensations my temperature was taken in the mouth and was found to be 39°C. (36 9-10° centigrade being equal to 98½° Fahrenheit). That evening it was 40° C. The next morning also 40°C. That evening 39° C. and on the morning of the 3rd day 39°. Then it kept falling to normal.

Tongue creamy white, gums bleeding, the amount of urine was diminished by one-third. On the fourth day I had got back to my normal condition.

Thus, the preventive inoculation of yellow fever is proven. This was what I had been searching for, a virus capable of transmitting a mild type of the fever without danger.

The first step, the most difficult and the most laborious, because it was filled with the uncertainty of unknown factors, was over. The rest will surely follow in time.

A number of courageous friends having full confidence in the method, and who fully understood the importance of the experiments, and their great utility for mankind, have declared themselves ready to be vaccinated by me. I shall vaccinate them soon, with all the care that such a serious matter requires, and with all the precautions exacted by rigorous experiments.

In conclusion, I may add that the theoretica question of the preventive vaccination of yellow fever is thus solved. The practical question has now entered on a course of experimentation, and promises to be a fact and a safeguard to mankind.

(EDITORIAL FROM THE CANADA MEDICAL RECORD.)

July, 1886.

YELLOW FEVER AND ITS PREVENTION.

In this issue our readers will find a timely and highly important communication on the etiology and prevention of yellow fever by inoculation. We are indebted to Dr. Gererd for having prepared it as a special contribution to the RECORD, and to our old friend, Dr. Wolfred Nelson, late of Panama, South America, for its translation.

For many years—1826 to date—the city and Isthmus of Panama have been recognized hot-beds of yellow fever. In 1868 there was a serious epidemic in the city of Panama. It appeared again as an epidemic in 1880, and it remained endemic and endo-epidemic up to the summer, when, in May and June, it assumed the proportions of an epidemic of the first class, killing forty victims daily. This fact was first announced in the *New York Herald*, and later by the American papers, generally in May. Later the *New York Herald* stated that the mortality of forty per diem understated the truth.

The filthy condition of the cities of Panama and Colon, in the American Isthmus, may be imagined, but the reality is almost incredible. The city of Panama—modern Panama—was built in 1688 as a strongly-walled, massively-constructed city. To-day, speaking of it and its suburbs—now extensive—it is without water supply or drainage, properly so-called. Its water is derived from deep wells, built by the early Spaniards, the majority on the outskirts of the suburbs. Three of the

largest wells, from which watermen purchase water to sell in the city, are at Cocoa Grove. The wells are within three hundred feet of a new cemetery, they are in a ravine many feet below its surface, while they drain a level fully sixty feet below the cemetery. The cemetery is, without exception, the most flourishing bonanza in the Isthmus. The owner of the wells, Senor Don Nicanor Obcarrio, has a special concession from the Government of the State of Panama to bury the dead. Whether they are buried in his cemetery or in the foreign Jewish or Chinese cemeteries he exacts his fee. Regarding the cemetery, at the edge of the wells, between July 15th, 1884 and April 12th, 1886, it had actually received 3,884 bodies for interment in the ground, apart from several hundreds buried in the *bovedas* or stone vaults. In the month of November, 1884, the Canal Company alone buried 652 officers and men on the Isthmus, principally from yellow and malarial fevers, tropical dysentery, &c., &c. The Canal hospitals in Panama have had as many as seventeen deaths in a single day.

Such is Panama, well and fitly named the Gate to the Pacific, by Captain Bedford Pim, R.N., in one of his interesting books. The Isthmus of Panama is a constant producer and distributer of yellow fever. The Mexican West Coast epidemic of 1883 and 1884 was traced to a yellow fever corpse landed by a steamer from Panama.

That death has such a monopoly can easily be understood, when the drainage and water-supply, so-called, are considered. In both Panama and Colon over-crowding has obtained to an incredible extent, but in Colon the inhabitants have pure drinking water, and not cemetery drainage as in Panama. In Panama proper the natives throw all

kinds of filth over the sea-walls ; as it is not washed away by the tides, there it remains, an insult to the eye, a foul, reeking, death-dealing mass. In the suburbs the inhabitants throw their excretæ and filth into lanes and vacant lots, this, plus heat and moisture, generates poisons best left to the understanding of our *confreres*. God forbid that it should ever reach their nostrils. A few drains within and without the city are never flushed except by the rains. During the dry season, December to May, they are simply so many receptacles for excretæ. The odors that pour forth from them are unbearable.

It ceases to be a matter of wonder that, under such conditions, the Canal hospitals offered a rich field for clinical observation for Dr. Gererd and his Canal *confrères*, Drs. Meurrisse, Didier, Vernial and the late George W. Nelson.

Dr. Gererd's special observations on yellow fever and its specific microbe extended over three years. He had an able staff of assistants, and the finest of appliances that science could suggest, and it was his singular good fortune to recognize and isolate and cultivate the special microbe. Its propagation was brought about by Pasteur's well-known methods and apparatus.

With Dr. Gererd it was more than a mere matter of scientific enquiry pushed to a successful issue—with him it was a matter of absolute faith, and he abundantly proved it by inoculating him self with culture-microbes, and finally resorted to a crucial test, in allowing himself to be bitten by mosquitoes, that had just fed on a yellow-fever patient. Dr. Finlay, of Havana, we believe, was the first yellow fever expert to point out the propagation of yellow fever by mosquitoes. Dr. Gererd's experiments are a highly important contribution to

tropical medicine. His three years of persistent labor were crowned with success, and he deserves all the praise that science and his Government (he is a Parisian) may accord him.

Yellow fever is one of those fearful scourges in whose dread presence physicians feel powerless. So little is known of the cause producing it and the great variety of treatments are a silent but tacit admission that our tropical *confrères* hitherto have been working in darkness, some epidemics killing 75 and 80 per centum, others 8 and 10. The last great epidemic at New Orleans and vicinity is credited with having swept away 30,000 victims.

Yellow fever on the Isthmus of Panama is nearly always fatal, that is true specific yellow fever. Of twenty-seven admissions to the Canal hospital, Panama, for a series of weeks but one recovered.

The Dingler Expedition to Panama—fully endorses the above. M. Dingler, Chief of Works of the Panama Canal, accompanied by his wife, and family, in all a party of thirty-three, including Canal engineers, arrived at Colon on the 29th of October, 1883 ; up to January, 1885, or in fourteen months, fourteen of the party had had yellow fever with but a single recovery, M. Dingler losing his whole family, wife, son and daughter. The recoveries truly are the exceptions that prove the rule. The malignancy and intensity of the disease there destroys the blood. Intense malarial poisoning is supposed to be an important factor, no doubt increased by the unsanitary conditions already described.

Dr. Domingo Freire, if we remember rightly, was the first observer to recognize a microbe in yellow fever and to conduct experiments and publish the

results. One of his first contributions on this subject was translated from the Spanish by Dr. Wolfred Nelson, and published in the RECORD some three years ago. *Science* in a recent issue refers to Dr. Domingo Freire's excellent work at Rio de Janeiro, Brazil, and states that in 7,000 inoculations by him, only eight died of the disease, while 3,000 inoculated persons living under the same conditions were victims to the disease.

Dr. Joseph Holt, the very able and indefatigable President of the New Orleans Board of Health, whose quarantine regulations are undoubtedly the best known, recently has used his influence to secure the passage in Congress of a Bill to enable an American Commission to visit the yellow fever centres and study the disease, and the methods of skilled men like Dr. Domingo Friere and Dr. L. Gererd. Should the Commission verify the experiments of the gentlemen named, preventive medicines in the tropics will have entered on the grandest discovery of modern times, one that will protect millions of people.

The RECORD has been promised a series of original papers on yellow fever, by physicians of recognized standing in Brazil, Mexico, and at Panama. They will appear as received, as well as a series to be written in Cuba, the hot-bed *par excellence* of the disease.

John S. Billings, M.D.

Compliments of

Joseph Holt, M.D.

A phase of the Y. F. investigation that might be interesting to.
It reminds me of your suggestion in regard to the use of guinea pigs.