INTRODUCTION

The Mosquito Hypothetically Considered as an Agent in the Transmission of Yellow Fever Poison

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On August 20, 1897, Ronald Ross, a British physician working in India, identified *Plasmodium* organisms in the gastrointestinal tract of the *Anopheles* mosquito and later proved that this insect is the transmitting vector of malaria in humans. He was subsequently elected to membership in the Royal Society, received the 1902 Nobel Prize in Physiology or Medicine, and was knighted. Almost sixteen years to the day earlier, on August 14, 1881, an obscure Cuban ophthalmologist, Carlos Juan Finlay (1833-1915), presented a paper to the Royal Academy of Sciences of Havana implicating mosquitoes in the transmission of yellow fever. His paper was destined to become a classic within the field of public health and infectious disease epidemiology. Because of its radical nature, however, his work received not adulation, honors, and awards, but scorn and derision. Finlay became the object of ridicule by his physician colleagues of Havana since, prior to his investigations, yellow fever was thought to be transmitted by either air-borne particles, direct human-to-human contact, through the agency of fomites, or, as Dr. John Snow, of cholera fame, doubly hypothesized, "a want of personal cleanliness" or "water (which)...contained the evacuations of patients with yellow fever..." It should also be noted that this presentation occurred 11 years before the discovery of viruses by the Russian microbiologist, Dmitri Ivanowski, who showed that the cause of tobacco mosaic disease could pass through a porcelain filter known to exclude bacteria.

While continuing to practice ophthalmology and general medicine in Havana, Finlay toiled for the next 20 years trying to prove his mosquito-borne hypothesis. His work paved the way for the eventual control of yellow fever (a disease with an approximately 50% mortality which, over time, has caused tens of millions of deaths) and, ultimately, the construction of the Panama Canal. His statue, one of many now honoring Dr. Finlay, clearly Cuba’s most famous physician, is located in the Plaza de Francia in the Casco Viejo district of Panama City.

Carlos Finlay was born in what is now Camagüey, Cuba, on December 3, 1833, one of seven children of Edward Finlay, a Scottish ophthalmologist and his French wife, née Eliza de Barrés. Finlay was initially home-schooled in Cuba by his paternal aunt but was later sent to France and Germany for his formal pre-medical education. During his time abroad, however, he contracted both cholera and typhoid fever, necessitating his returns to Cuba for convalescence. When he applied to medical school at the University of Havana, he was, ironically, rejected because that institution would not accept his foreign academic credits. Consequently, he enrolled at the Jefferson Medical School in

Philadelphia, PA, where he encountered Dr. John K. Mitchell, a vigorous advocate of the germ theory of disease and where he, undoubtedly, learned of the Philadelphia yellow fever epidemic of 1793, one of the most devastating epidemics in U.S. history.

After graduating with his medical degree in 1855, Finlay pursued additional training in Havana and Paris and eventually returned to Cuba to practice with his father. Working in his free time, he began to study yellow fever. He published his first of scores of papers on yellow fever in 1865, eleven years before Robert Koch proved the germ theory of disease in mammals by isolating *Bacillus anthracis* on potato slices, growing pure cultures in the aqueous humor of the ox's eye, injecting the organisms into mice thus producing a lethal anthrax infection, and re-isolating the pathogenic bacteria from the deceased rodents.

In this landmark paper, Finlay officially proposed his mosquito-borne theory of yellow fever transmission based on a combination of pure logical deductions, keen observations, brilliant epidemiological analyses, and elegant methodical research. He recognized that the conditions necessary for the propagation of the agent of yellow fever (which he variably called "poison," "morbigenus factor," "infecting particles," "tangible something," "pathogenic material" "material transportable cause," or "amorphous virus" [translated]) would also apply to the medium of its transmission.

In jurisprudence, the three aspects of identifying the perpetrator of a crime are to determine its means, motive, and opportunity. Finlay thus began a series of forensic-like studies in order to prove his hypothesis that the mosquito was, indeed, the culprit of yellow fever transmission. In so doing, he displayed an impressive knowledge of entomology, geography, meteorology, history (quoting, among others, Aristotle and Pliny), and research methodology. With his understanding of the pathophysiology of yellow fever, manifested clinically and histopathologically as "vascular lesions and physicochemical alterations of the blood," he deduced that "this agent could be found in the class of insects which, by penetrating into the interior of the blood vessels, could suck up the blood together with any infecting particles contained therein, and carry the same from the diseased to the healthy."

He investigated several varieties of mosquitoes and determined that the *Culex* mosquito (later designated *Aedes aegypti*) was the only species capable of transmitting yellow fever. He studied the anatomical structure of the female's proboscis and noted that it was of sufficient length to "reach with ease any capillary situated within a fifth of a centimeter from the cutaneous superficies." The *Culex* mosquito thus had the **means** to carry out its attacks. Why blood? During his meticulous mosquito breeding experiments, Finlay determined, apparently for the first time, that the blood sucking activity of the female *Culex* mosquito always followed her impregnation and was itself followed by the laying of eggs several days later. However, impregnated females denied access to blood meals die without ovulating and unimpregnated females emerging from the nymph state are incapable of stinging. He speculated that a temperature of $\geq 37^{o}C$ (human body temperature) was required for the maturation of the eggs within the mosquitoes' ovaries and that mammalian blood was a ready source for this thermal requirement. Finlay further recognized that febrile patients, due to infection with yellow fever, would be ideal targets for *Culex* mosquitoes and thus provide opportunities for spreading the causative agent of yellow fever, later recognized as a *Flavivirus,* the first human virus to be isolated. Finlay had now established the **motive**.

Finlay recognized the seasonal and ubiquitous geographical distributions of *Culex* mosquitoes and the meteorological, topographical, and ethnological determinants of the development of yellow fever. He articulated the observation that the female mosquito deposits her ova on the surface of water, thus explaining the relative scarcity of mosquitoes and, consequently, yellow fever, in dry and arid locations. He observed their preferred feeding times and temperature requirements for survival and noted that, while in Cuba the mosquitoes do not hibernate, they do so in colder climates. He witnessed that an impregnated, blood-satiated *Culex* female, placed in a glass tube for observation, would self-lubricate her body, presumably in order to facilitate the laying of eggs upon the surface of water. He, thus, proved that the conditions which most favored the incidence of yellow fever also favored the birth and propagation of mosquitoes. Therefore, Finlay documented the **opportunity**.

Following this theoretical discussion, Finlay proceeded to present his experimental mosquito transmission data. He permitted *Culex* mosquitoes to bite patients known to have yellow fever and those mosquitoes would then bite previously healthy individuals. Of the five previously healthy subjects so bitten (including himself), two developed jaundice (one with albuminuria), two became febrile, and one was completely asymptomatic. In the meantime, 20 control patients were all unaffected. Finlay considered these results consistent with his theory but acknowledged “the necessity of an irrefutable demonstration before a theory, so essentially different from all the prevailing ideas, can be generally accepted.” He concluded “that a single sting from the mosquito is insufficient to reproduce the grave forms of yellow fever…” Unfortunately for Finlay, the biological reality of two critical variables was not yet fully appreciated: [1] that yellow fever can be transmitted only in the first two to three days of a patient’s illness, and [2] that the mosquito's capacity to infect occurred no less than 11 days after contamination. Of the five transmission attempts described by Finlay, [1] the mosquitoes bit the yellow fever patients a mean of four days (range: 3-5 days) after the onset of their symptomatic illness, and [2] the time after biting the yellow fever patient until biting the previously healthy individual, what would later be termed the "period of extrinsic incubation," was a mean of only 3.2 days (range: 2-6 days).

In spite of his repeated inability to transmit yellow fever with absolute certainty, Carlos Finlay’s novel ideas and exhaustive subsequent work led, about 20 years later, to the ultimate proof provided by Walter Reed and the United States Army Yellow Fever Commission of 1900-1901. Finlay shared his expertise with them and supplied the mosquito eggs which they utilized in their trials. Lamentably, Walter Reed’s original report of the Yellow Fever Commission did not even mention Dr. Finlay’s assistance, prior mosquito theory, or research. Finally, however, Reed did acknowledge his contributions. Army general Dr. William C. Gorgas, later Surgeon General of the United States, himself credited with ridding the Canal Zone of yellow fever and malaria, honored Finlay as follows: “His reasoning for selecting the (*Culex* mosquito) as the bearer of yellow fever is the best piece of logical reasoning that can be found in medicine anywhere." He was praised further by U.S. Army General Leonard Wood, a physician and military Governor of Cuba in 1900 who said: "The confirmation of Dr. Finlay's doctrine is the greatest step forward in medical science since Jenner's discovery of the vaccination (of smallpox)."

THE MOSQUITO HYPOTHETICALLY CONSIDERED AS AN AGENT IN THE TRANSMISSION OF YELLOW FEVER POISON

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(An extract from the Annals of the Royal Academy of Sciences of Havana.)

Translated by Rudolph Matas, M.D.

Mr. President and Gentlemen -

Some years have now elapsed since I had the honor to communicate to you in this Academy the result of my alkalimetric experiments, through which, I believe, I have definitely demonstrated the excessive alcalinity which characterizes the atmosphere of Havana. Some of the gentlemen now present will doubtless remember also the conjectural relations which, at that time, I thought could be established between this atmospheric reaction and the development of yellow fever in this city. But much work has been done since; many and more exact data has been gathered, and the etiology of yellow fever has been more methodically studied than in previous years.

Through the knowledge which has been increasingly acquired since that time, I have had reason to become convinced of the untenable nature of any theory which may attribute the origin or propagation of yellow fever to atmospheric, miasmatic or meteorological influences, or of its equally weak character, if it appeals to filthy or neglected hygienic principles. I have thus been obliged to abandon my primitive beliefs, and in making this announcement here, I desire to justify, to a certain extent, this change in my opinions, by submitting to the appreciative criticism of my distinguished colleagues a new series of experimental studies, which I have undertaken, with the view of ascertaining the mode by which the yellow fever poison may be propagated.

I must state, however, that the subject of this paper has no relation whatsoever with the nature or form in which the morbigenus factor in yellow fever exists; in this regard I will limit my opinions to the following statement: that I admit the existence of a material transportable cause, which may be either an amorphous virus, an animal or vegetable germ, bacterium, etc., etc., but which consists in all cases of a tangible something, which has to be communicated from the sick to the healthy in order that the disease may be propagated. What I propose studying is the medium or agent by which the pathogenic material of yellow fever is carried from the bodies of the infected to be implanted in the bodies of the non-infected.

The necessity of admitting the intervention of an element foreign to the disease, in order that this may be transmitted, follows as a result of numerous observations, formulated in the early part of this century, by Rush and Humboldt, and confirmed by latter-day experience. Thus, yellow fever sometimes traverses the ocean, and is propagated in very distant cities, whose meterological conditions are widely different from those of the focus in which the infection originated; while at other times the same disease does not transgress the boundaries of a very limited epidemic zone, notwithstanding the fact that the meteorology and topography of neighboring localities reveal no differences which would explain so different a behavior of the same disease in two apparently similar places. Admitting the necessary presence of an agent of transmission whose behavior would explain the above anomalies, it is evident that the conditions now recognized as affecting the propagation of the yellow fever poison would also be applicable to this agent. In searching for the agent it was not probable that it would be found in the microzoa or zoophytes, for these minute forms of animated nature are little, if at all, influenced by the meteorological variations which most frequently affect the development of yellow fever. In order to meet the exigencies of this question it was found necessary to ascend as high up in the animal scale as the insect class, and keeping in mind, at the same time, that yellow fever is characterized clinically, and according to most recent labors, histologically, by vascular lesions and physico-chemical alterations of the blood, it seems natural that this agent could be found in that class of insects which, by penetrating into the interior of the blood vessels, could suck up the blood together with any infecting particles contained therein, and carry the same from the diseased to the healthy. Finally, on account of various reasons which it would be idle to relate, I asked myself if it was not the mosquito that transmitted the yellow fever poison.

Such, gentlemen, was the hypothesis which led to the series of experimental studies that I will now proceed to relate to you:

Let us begin by recalling, in a few words, the geographical distribution of the mosquito. In a general way it may be stated that the mosquito is found everywhere, excepting in elevated localities. In fact, the dipterous insect which now occupies us, the genus culex, which many believe the special plague of tropical regions, exists, on the contrary, in all latitudes. In the polar regions, the Laps, in common with the inhabitants of the inter-tropical regions of America, cannot eat or sleep in their huts without submerging themselves in a dense atmosphere of smoke, in order that they may escape the tormenting persecutions of this insect. In the open air the inhabitants of these (Polar) countries are equally harrassed by the mosquito which introduces itself into the mouth and nares at every inspiration; these people, in spite of their cuticles, already hardened by the cold of their eternal winter, barely manages to preserve themselves, by covering their exposed surfaces with veils saturated with foetid greases, and by anointing their bodies with lard or rancid oils. In Canada, England, France, Spain, in all Europe, Siberia, China, the United States, and all North as well as Central and South America, the atmosphere is infested with swarms of mosquitoes. In Central Africa a German traveler, Dr. Schweinfurst, was tormented by a species of mosquito with spotted legs, whose description might very appropriately be applied to the culex mosquito of Cuba, and also to that species observed in Batavia by Dr. Arnold, who, according to Kirby, regarded it as a species not yet described, and which resembled the Culex annulatus, only that it had no spots on its legs.

It is a noticeable feature in the geographical distribution of the mosquito, that this insect manifests a marked favoritism for continents rather than islands, confirming in this manner, Humboldt's observation that mosquitos are more prevalent on the banks of great rivers than on the islands situated within them, and that the harrassing presence of these insects is less perceptible in the middle of a stream than upon its banks. It may be owing to this fact, that the early historians of the discovery of America make no special reference to the presence of the mosquito in the West Indian Islands, during the first voyage of Columbus. I have found no direct allusion to this insect before the year 1538, when it is mentioned, by an ancient chronicler, in an excursion undertaken by Hernando de Soto, whose men, in crossing a river near Port aux Princes, were stung so severely by the mosquitoes, that they had large blotches of blood upon their backs. It is doubtless to this same relative insular immunity, that we owe the following fact related by an American traveler to the entomologist, Osten Sacken, (quoted by Dr. Taschenberg, Brehm, IX., page 446): About the year 1823, mosquitoes were not known in the Hawaiian Islands; but between 1828 and 1830, an abandoned ship from Mexico, stranded upon one of them. It was soon observed by the natives, that a swarm of insects which sucked blood and were unknown to them, had made its appearance upon and about the vessel. This drew the attention of the inhabitants to the spot, many of whom, impelled by curiosity, would board the vessel in the evenings, in order that they might be stung by these extraordinary insects. The mosquitoes, however, very soon spread themselves over the island, and in a short time became, as everywhere else, a veritable plague.

Although it is true that the mosquito exists in all latitudes, it is true also that the insect is not found in equal abundance in all localities. Humboldt and Bonpland, in their travels through equinoxial America, remark "that the tormenting presence of mosquitoes and gnats is not so generally felt in the torrid zone as is usually believed. On those plateaux, elevated 400 fathoms above the sea-level, and in the very dry and arid plains which are so distant from the great rivers, as the plains of Cumana and Calabozo, for instance, there are perceptibly no more mosquitoes than in the most inhabited parts of Europe." The influence of drought and distance from rivers or other water supplies, observed by these travelers, is easily understood, when we consider that the larva and nymph of the mosquito are aquatic, and that for its successful propagation the adult insect has to deposit its ova on the surface of the water. In regard to the diminished number of mosquitoes, observed in elevated regions, I believe this to be attributable to the rarer atmospheres of such localities which would offer a serious obstacle to the flight of the mosquito, particularly after gorging itself with blood, a difficulty particularly experienced by the Culex mosquito, the wings of which are so small that after its sanguinary performance, they hardly serve to lift the insect, even in ordinary atmosphere. In such cases it is easy to understand that the mosquito would instinctively avoid such localities. We are also told by these travellers that the good missionary, Bernardo Zea, constructed for himself an elevated habitation upon a platform on the trunks of palm trees, where they (the travellers) ascended at night to dry the plants which they had gathered during the day, and where they also wrote their diaries. "The missionary had rightly observed," they say, "that insects most abound in the lower atmospheric strata, at about 12 or 15 feet from the ground. Further on in their narrative these observers add: pari passu, as we approach the Andean plateau, these insects disappear, and we are permitted to respire a purer air . . . at a height of two hundred fathoms, mosquitoes and gnats are not to be feared. "

Chronologically considered, the mosquito is one of the most anciently known insects. Aristotle and Pliny alluded to its bill which serves to perforate the skin and suck up the blood. The Greek historian, Pausanias (quoted by Taschenberg) mentions the city of Nyas in Asia Minor. The harbor communications of this city with the sea were cut off, and in consequence a lake of fresh water was formed, from which such a plague of mosquitoes arose that the inhabitants were compelled to flee the city and emigrate to Miletus. Again, we read in the decades of Herrera, that

Juan de Grijalva, when he discovered the coasts of New Spain in 1518, had to disembark at the island now known as the Island of San Juan de Ulua where "the men were obliged to build their huts upon the highest sand hills of the island, in order that they might escape the importunities of the mosquitoes." He was obliged to leave this place at the end of seven days, "not being able to with stand the mosquitoes," and Berual Diaz del Castillo had to seek refuge in the temples of the Indians, "fleeing from the persecutions of the mosquitoes." Finally, in 1519, almost at the site of the modern city of Vera Cruz, "the long-legged mosquitoes," says Herrera, "and the small species which are much more troublesome, harrassed and fatigued the troops of Cortes." I have had occasion to observe two species of mosquitoes in Havana since the month of December, two years ago, when I began the study of these insects. The typical representative of one species is a large yellow-collored, long and thin-legged insect, without any distinct spots. I believe this insect to be the descendant of the identical mosquito which tormented Cortes and his men in 1519 on the sand bank of San Juan de Ulua, - in other words, the C.. cubensis described in La Sagra's work. Its body, measured from the base of the bill or proboscis to the anal extremity, is about 5 to 7 millimeters in length. This species is only active at night time, after 9 or 12, when it begins to practice its molesting evolutions, which it continues till daybreak. To this species belong most of the mosquitoes that I have found imprisoned within mosquito bars, where they usually remain part of the day, while they digest the blood they have sucked. The other species is the Culex mosquito, which our distinguished Cuban naturalist, Don Felipe Poey, brought to Paris in the years 1817 or 1820, where it was classified by M. Robineau Devoidy. I have observed two varieties of this species: one large, well-shaped and vigorous, of a dark greyish color, measuring a little less longitudinally than the long-legged or cubensis species; and the other, smaller in size, measuring from 4 to 4 1/2 millimeters in length. I have not busied myself in searching for the differential characters between the two varieties of the same species, as I found the difference in their sizes sufficiently distinctive for my present purpose.

The male of both species (C. cubensis and C. mosquito) is easily recognized by his plumy antennae, which present the appearance of moustaches, and by the trifid appearance of his proboscis. This appearance of the insect's bill is due to the palpi, which seem to be almost as long as the bill itself. They separate from the proboscis at its lower two-thirds, just before reaching the terminal extremity, contrasting in this manner quite notably with the smooth and even bill of the female, whose palpi do not seem to extend further than one-sixth of its length.

The two species of mosquitoes do not leave their resting places at the same time: the C. cubensis is active at night, and the C. mosquito at day time. Desirous of ascertaining the reason for this respective appropriation of day and night by the different species, and suspecting that the long-legged insect, in spite of its greater dimensions and more robust aspect, was, possibly, not organized to resist the heat of our tropical sun, whilst the C. mosquito with its stronger integument endured it better, I instituted the following experiments: On June 9th, 12 M., I exposed to the direct rays of the sun the two thermometers of my psychrometer; at the end of half an hour, the dry instrument measured 42.25°, and the damp thermometer 31.75°: The apparatus was then replaced by a glass tube, in which a long-legged mosquito (C. cubensis) was incarcerated, the insect had been captured 5 days previously,but was yet quite lively and active. Five minutes after exposure themosquito was dead.

It is known, that it is only the female mosquito that stings and sucks blood, whilst the male is only nourished with vegetable juices, principally with those of a sweet character; but, so far, I have not seen mentioned by observers who have written upon this subject, the additional fact that the female will not sting unless previously fecundated by the male. This at least, would appear to follow from these experiments:

A female of the C. mosquito species, captured at the moment of emerging from the nymph state, and imprisoned for 2 or 3 days, could not be made to sting. Many times have I repeated this experiment, and always my results have proved of a negative character.

The females imprisoned during the act of fecundation upon separating from the male sting at once, and fill up with blood.

Finally, almost all the females captured after they have satiated themselves with blood, lay eggs at the end of a few days; while the fecundated insects that are not able to satisfy their blood-thirst, through lack of opportunity, etc., die without ovulating.

It is, therefore , not that she may be nourished that the female mosquito eagerly searches for living blood, and in fact, it cannot be conceived how a body so minute as the mosquito, would require to sustain it, so enormous a quantity of as rich a food as pure blood. This reflection, leads me to the belief that the ingested blood is destined to other ends, related most propably to the genesis of the mosquito. I am inclined, besides, to the opinion, that the influence of the blood is due to its temperature; for if we conceive that for the satisfactory maturation of the ovules contained within the ovaries of the female mosquito, a temperature of 37° C. is required, this temperature, considering our meteorological condition, could hardly be secured with greater ease and certainty than by the means employed by the mosquito; and again, may not the blood of a pyretic patient, with a temperature of 39° or 40°, still more easily accomplish the ends which the mosquito is striving to attain, by increasing the activity of the ovulating period? We would also understand, how, in this way, the long-legged mosquito and other large species of the mosquito, would absorb, at one time, all the blood needed to mature with its heat, the 200 or 350 eggs which it lays at a single sitting; and again, how the smaller species (C. mosquito, etc.) have to sting and fill up several times, so that they may begin to lay eggs- this species not completing its period of ovulation before 2 or 3 sittings have been successfully accomplished.

Once a female mosquito has gorged itself with blood it requires 2 or 3 days, according to the species considered, to digest it; during this period, and hidden usually from indiscreet inspection, the insect passes hours in performing curious operation which Reaumur never could satisfactorily explain to himself, because he had occasion to observe it only while the insect was at liberty. When the mosquito is imprisoned within a glass tube it is easy to ascertain that this performance consists of movements which tend to lubricate the body with a viscid secretion which the mosquito collects from its anal extremity with its hind legs, and with which it besmears its entire body: each leg separately at first; the abdomen, wings, thorax, head and even its proboscis. As our distinguished fellow-academician, facile princeps among Cuban naturalists, D. Felipe Poey, has suggested to me, this manoeuvre may tend to render the female mosquito impermeable when she's ready to lay her eggs upon the surface of the water. It is also observable during the digestion of the injected blood that the mosquito discharges a quantity of sanguinolent particles which have the property of dissolving with extraordinary facility in water, even when they have been kept hard and dry for many months. This is duel doubtless, to the combination of the blood with the saliva which the insect drops into its sting, a procedure, designed, according to general opinion, to increase the fluidity of the blood at the time it is sucked from the sting. As a general rule, after sucking up all the blood which corresponds to an uninterrupted sting, the mosquito never pricks the skin again, and, on the contrary, rather avoids it (probably, because the heat of the skin is then disagreeable to it), until it has digested all the absorbed blood.

I will not repeat Reaumur's Classical description of the method by which the mosquitto of Europe constructs the elegant egg vessel which it floats upon the surface of the water. The same operation seems to be performed by the mosquito in Cuba. But as I have observed that the female mosquitoes, after launching their egg vessel, usually die upon the water, I have come to the conclusion that their bodies which Reaumur considered as the cadavera of so many drowned mosquitoes as they emerged from the nymph state are, in realty, the bodies of the mother insect, which permits itself to die by the side of its ova, that it may contribute to the future alimentation of the larvae.

To conceive, sting and ovulate are the three successive events which constitute the unvarying and unavoidable cycle within which the life of the mosquito may be said to revolve. The first of these functions, conception or fecundation, it is probable, takes place only once, as in most insects; a single impregnation of the seminal sac through the semen of the male, being usually sufficient to fecundate all the ova that in the future may pass through a corresponding part of the oviducts. In the Cuban bee, D. Felipe Poey has already told us, that a single impregnation of the female bee by the male is amply sufficient to fecundate all the thousands of ova that are to be laid during the 2 or 3 years life of this hymenopterous insect. In the females of the C. cubensis, there is no need of examining the prolonged fecundating power of the male sperm, as all the ova are discharged at one sitting; this does not obtain, however with the females of the C. mosquito species. They lay their eggs irregularly, or in layers of nine or fifteen eggs each, sometimes upon the water, at other times upon surrounding objects contiguous to the water, so that any slight rise in the water level may serve to bathe them. Whatever be the value of the hypothesis which I have propounded, in order to explain the necessity which impells the C. mosquito to sting several times and to fill itself with living blood, so that it may successfully hatch its eggs, it is a fact that the females of this species are always ready to sting again once they have digested the blood sucked up in a preceeding sting. In the case of the female insect captured in the month of January of the present year (1881), it was observed that she stung 12 times and that she spawned 3 times during the 31 days that she lived, death taking place in the United States, where the temperature was, at the time, below O° c.

It is evident that from the standpoint from which I am now considering the mosquito, that the species C. mosquito is admirably adapted to transmit from one individual to another any disease which might be communicated through the agency of the blood, particularly when we consider the numerous opportunities which it has of drawing blood from different sources, and also of infecting different individuals, thereby increasing the probabilities that its sting may combine the necessary conditions for the successful transmission of the infecting agent. On the other hand, as the C. cubensis may absorb on account of its larger size, a larger quantity of blood than the preceding species, and thereby retain upon its lancets a larger quantity of infecting material, it is apt to produce a more serious inoculation, particularly if this is effected a few moments after an interrupted sting. Through this mosquito we might, therefore, observe an infection of much graver character, but also of rarer occurrence.

It is impossible, however, to understand or properly appreciate the extraordinary facilities which the sting of the mosquito offers for the inoculation of any contagious particles which the blood may contain, without previously understanding the peculiar conformation and structure of the apparatus which the female mosquito employs to perforate the skin and suck up the blood of its victims. That part of the bill or proboscis of the mosquito, which is seen in normal conditions, is only the sheath, an envelope formed by the transformation of the lower lip; it springs from a pedicle implanted at the base of the head, beneath other oral structures; it is cleft in its superior portion throughout its whole length, until it reaches a terminal tubercle, which I consider analogous to the labial palpi of other insects, and from which the points of other organs are seen to emerge. The sheath of the C. mosquito, to which species I have limited my observations, measures about two and a half millimeters in length; a French line, according to Reaumur, would have measured the length of the bill of the species he investigated. Whatever be the manner in which our mosquito sometimes introduces its lancets to a point very near their insertions, it is easy to understand that it will reach with ease any capillary situated within a fifth of a centimeter from the cutaneous superficies. Within the sheath two tortuous tubes exist, which appear to lie loosely upon the floor of the cavity of the proboscis- the two tubes are united to a common trunk which occupies the cavity of the pedicle of the sheath. I believe it is through these tubes that the mosquito drops the acrid and irritating saliva, which produces the pruritus and pain of the sting, - a procedure designed, according to most observers, to increase the fluidity of the blood which is sucked up through the siphon. Five organs are to be found within the sheath: the principal structure, single in number, represents the superior lablum; it is of a horny consistence, and is prolonged in the form of a deeply grooved spur, perforated in its inferior portion throughout its whole length, till it reaches a terminal point somewhat like a tooth-pick, which has been cut from a long and narrow quill. This piece is tough and rigid, and throughout its external surface presents a figured appearance, as if a net were applied upon it, with its meshes brought out in relief, forming, thereby, innumerable small parallelograms, the most acute angles of which are directed towards the longitudinal axis of the organ. It is possible that, within the numerous spaces enclosed within the meshes, many particles of the sucked blood may be gathered and remain entangled. The other four pieces consist of two pairs of flexible lancets corresponding to the mandibuloc and maxilloc, implanted upon the root of the two maxillary palpi, which may be seen upon each side of the proboscis. The structure of these two classes of lancets is entirely distinct; the mandibular lancet is a curved piece with a tendency to maintain a curved form; its external surface is convex and presents throughout its whole extent a series of transverse and longitudinal crests; the external surface is also of a greenish color. The borders of the longitudinal fissure are armed with very sharply edged teeth; the point of the lancet is curved and convex, and also presents teeth upon its free borders up to its very terminal point. These teeth must be endowed with a very considerable degree of strength and sharpness, if we are to judge from their appearance.

The maxillary lancets, the origin of which is to be found lower down beneath the preceding, have the form of a riband with its edges curled inwardly; the free edges of the band, thus bent, are armed with a row of very fine and large teeth. This lancet, as a whole, bears a remarkable resemblance to the long and narrow leaves of some plants: the broad point, its double edge, and the central longitudinal ridge or raphe are strikingly similar. All these pieces are so nicely adjusted and moulded to fit the spur of the inferior labium that, upon removing the sheath, before dissociating the lancets, it would appear improbable that the rounded proboscis with its apparently single sharp point could be the result of a combination of the five pieces which I have just described.

It is well known that mosquitoes never disappear altogether from Havana7 there are certain seasons in the year in which they seem to be much more plentiful than at other times. Their number, it appears to me, augments progressively from April or May to August, from which time they steadily diminish till February or March, when they reach their minimum number. But there is a point in the natural history of the mosquito which is intimately related to the present study of this insect, and which it is highly important we should remember, in view of the numerous applications which it admits or in the explanation of the etiology of certain obscure yellow fever epidemics in localities apparently free from such pestilential visitations, and without any appreciable source of importation. I refer to the hibernation of the mosquito, a phenomenon which is not observed in our climate, at least in all its phases, but which constitutes, according to most authorities, the regular mode by which the species is propagated in cold climates. Dr. Taschenberg says, in regard to this particular: "the females, fecundated in the last generation, hibernate in all kinds of hiding places, principally in the cellars of houses, from which they escape in the following spring to multiply their species."

Concerning the conditions which favor mosquito genesis, I will mention heat, moisture, the presence of stagnant waters, low and dark localities, absence of winds and the summer season, but, in connection with this part of our study, it will not be amiss to quote Humboldt's observation: "The number of mosquitoes is not always regulated by determined meteorological or topographical conditions."

I have already spoken of the difficulty experienced by the mosquito in attempting an ascending flight, on account of the relatively small size of its wings, a difficulty specially observable immediately after it has gorged itself with blood. For the same reason the mosquito is not able to fly far from the site of its last sting, maintain itself suspended in the air for any considerable length of time, or transport itself for any great distance without stopping. But these facts do not militate against the possibility that the mosquito may, after it has stung, be transported hidden in the clothes, hat, valise, trunk, etc., of a traveler by whom it may be carried great distances, the insect carrying and possibly inoculating at its first opportunity the infecting germ which it may carry encrusted upon its lancets.

Finally we must keep in mind the preferences which the mosquito manifests towards certain races and individuals, noting in this particular the partial immunity enjoyed by the African and the especially active persecution of the recently arrived members of Northern races in the tropical regions of America. This favoritism evinced by the mosquito may depend upon the varying thickness of skin and upon the conditions which affect the cutaneous circulation, as these circumstances influence the facility with which the female mosquito may procure the blood which she needs to complete the cycle of her existence.

After this lengthy but necessary explanation of the habits of our Cuban mosquitoes, especially of the small Culex mosquito, we ask ourselves, supposing yellow fever to be an affection contagious through the blood, by what means could the mosquito transmit the disease? The most natural reply to this query would be that the infecting material might be transmitted through the agency of the blood which the insect might suck up from the vessels of a yellow fever patient, in quantities varying from 5 to 7 or 8 millimeters, which, if the mosquito were to die before digesting, would remain for a considerable length of time, in excellent condition to transmit its morbigenous properties. It is also quite possible, that the blood in form of excrement, which the mosquito deposits in drinking and other waters, could easily carry the virulent agent through this medium, and if the maladys is so communicable, it could thereby easily be transmitted. But Ffirth's experiments, and the consideration of other facts, which in my opinion are involved in the pathology of yellow fever, do not permit me to dwell longer on these two modes of disease propagation. I will now explain to you my reasons. When the United States yellow fever commission took its departure from our midst, about two years ago, and left in our possession a valuable collection of the microphotographs from the preparations made by our corresponding member, Dr. Sternberg, what more especially elicited my attention was the fact demonstrated in these photographs, that the red blood corpuscles were discharged entire in the hemorrhages of yellow fever. And, as these hemorrhages take place, at times, without any apparent rupture of the blood vessels, we came necessarily to the conclusion that this symptom (hemorrhage), being the most salient clinical feature of the malady in question, surely pointed to the vasular endothelium as the site of its principal lesion. Now, thinking over the peculiar facts presented to us by yellow fever, viz: That it is a transmissible disease, that it usually attacks but once in the life of an individual, and that it always presents in its manifestations a regular order of events, as in the case of the eruptive fevers, I came to frame an hypothesis in which the disease was considered as an eruptive fever, the eruption taking place in the vascular endothelium. Thus, the first period of the disease would coincide with the fever of invasion; the second stage of defervescence, with the eruptive stadium, and the last period with that of desquamation. If this (last stage) should be effected in favorable conditions, the patients will only present the indications of an exaggerated filtration of some of the blood elements through the new endothelium; if desquamation takes place under unfavorable systemic auspices, the new and weak endothelium will prove an insufficient barrier to the escape of the morphological blood elements, passive hemorrhages will follow, and the patient will be placed in imminent danger. Finally, in comparing this disease to small-pox or vaccinia ,it occurred to me that, in order that the disease might be inoculated, the inoculable material would have to be searched for in the blood vessels of the yellow fever patient, whence it could be carried to the interior of a healthy individual's blood vessels, who would be in a favorable condition for the reception of the infecting material. All the requisite conditions for the successful transportation of the inoculating virus are admirably combined in the mosquito, the sting of which it would be almost impossible for us to imitate with the comparatively rude and coarse instruments which could be manufactured by our most dexterous artizans.

According to this view, three conditions are therefore necessary in order that the yellow fever poison may be propagated: 1st, a yellow fever patient in whose capillaries the mosquito may bury its lancets, and impregnate them with the virulent particles at the proper period of the disease; 2nd, prolongation of the mosquito's life from the time of the original sting, from which the inoculable material was obtained, to the moment in which it is applied to the selected subject; 3d, coincidence of inoculable sting with favorable subject.

The first of these conditions has never been wanting in Havana, at least since Dr. Ambrosio G. del Valle has published his valuable mortuary statistics. In regard to the 2d and 3d, it is evident that the probabilities of their verification depend upon the abundance of the mosquitoes and upon the number of individuals susceptible to inoculation that are to be found in a given locality. I believe that, in Havana,the three conditions above mentioned have always coincided in the years of most marked yelloe fever mortaility.

Such is my theory, gentlemen, and doubtless, in listening to my argument, you have also remarked the singular corroboration which the historical, geographical, ethnological and meteorological coincidences have lent to my belief, through the data concerning the mosquito and the fever in history; I may also state that it is strengthened, furthermore, by the aid derived from it in the explanation of facts and occurances, so far inexplicable in the light of the prevailing doctrines. Yellow fever was not known in the white race until after after the discovery of America, and, according to Humboldt, it is a traditional belief, in Vera Cruz, that the disease has existed there since the Mexican shores were first visited by the Spanish Conquerors. We also notice that the Spaniards, in their earliest explorations, observed the presence of the mosquito, and that it was there also, on the sandy plains of San Juan de Uloa, that they were more especially harrassed by this insect. The races, also, which are most exposed to the influence of the yellow fever poison, are also most subject to attacks from the mosquitoes. The meteorological conditions which are most favorable to the development of yellow fever, are also those which favor the birth and propagation of the mosquito. In support of this assertion I might cite to you several partial epidemics, in which, as vouchsafed by competent physicians, the mosquitoes seemed to have been much more numerous than in former epochs; in fact, it is specified in one instance, that the mosquitoes were of a different species from those usually presented in the locality, on account of a peculiarly spotted appearance of the insects. In regard to topography, Humboldt, who has already told us the range of elevation which the mosquito can attain, has also informed us of the maximum altitude reached by the yellow fever poison. Finally, in the very notorious case of the U. S. steamship "Plymouth," on board of which two cases of yellow fever developed whilst on the open sea, after the thorough disinfection and congelation of the vessel during the previous winter, and after four months had elapsed since the occurrence of the last case of yellow fever of preceeding month of November, is perfectly explained by the hibernation of those mosquitoes, which may have stung the previous cases of yellow fever, and which, by returning to a tropical climate, were roused from their torpid state, stung again and gave rise to the two last apparently spontaneous cases of the disease.

With this basis to work upon, I determined to submit my theory to an experimental test, and after obtaining the consent of the interested parties, I proceeded as follows: On the 28th of June, one year ago, I carried an imprisoned mosquito to the Garcini infirmary where I permitted it to sting and fill itself with blood from the arm of a yellow fever patient, D. Camilo Anca, who at that time was laboring under a thoroughly characteristic attack of the disease. He was then in the fifth day of the illness, which proved fatal to him two days after. Having selected F. B., one of twenty unacclimated, now under my observation, for experimental purposes, I caused him to be stung by this mosquito two days after the insect had stung the yellow fever patient. Keeping in mind that the period of incubation of yellow fever, as has been ascertained by the observation of a few special cases, varies from one to fifteen days, I closely watched F. B. On the 9th day he began to feel unwell, and on the fourteenth he entered the hospital with a benign attack of yellow fever, well characterized, however, by icterus and the presence of albumen in the urine which persisted from the 3d to the 9th day of illness.

On the 16th of July I caused a mosquito to sting another patient with yellow fever-D. Domingo Rodriguez, who was lying in the same Garcini Infirmary in the third or fourth day of a serious attack of the disease. On the 20th I permitted myself to be stung by the same mosquito, and finally, on the 22d, I caused it to sting A. L. C., another one of the twenty unacclimated individuals subjected to my observation. At the end of five days he entered the hospital with fever, cephalalgia, pain in the loins, and flushed countenance. For three days these symptoms persisted, the patient passing into complete convalesence without icterus or albuminuria. This case was diagnosticated by the attending physician - Abortive yellow fever.

On July 29th I caused another mosquito to sting D. L. R., who was lying seriously ill on the third day of a yellow fever attack at the Garcini Infirmary. On the 31st T. F. was exposed to the sting of the same mosquito. On August 5th, 2, A.M., this patient was taken sick with all the symptoms of a light attack of yellow fever; he was somewhat jaundiced, but I do not believe that his urine ever contained any albumen. This case was also diagnosticated by the attending physician-Abortive yellow fever.

Finally, on July 31st, I exposed to the sting of another mosquito the same yellow fever patient, D. L. R.., who was lying as already stated at Garini's, in the 5th day of his illness, from which he died on the following day. On August 2d the same mosquito stung D.G.B., another individual, under my observation. Up to this moment the last inoculation does not seem to have inconvenienced this patient. Twelve days have only elapsed, however, and it is possible that he may yet be within the limits of the period of incubation. *

I must state that the cases I have just reported are the only instances in which I have attempted to inoculate the yellow fever poison directly through the mosquito, and that since June 22d (within the term of seven weeks) no cases of comfirmed or abortive yellow fever have occurred in any of the 20 unacclimated persons whose conditions I have closely watched, outside of the three first instances already mentioned.

These experiments are certainly favorable to my theory, but I do not wish to- incur the danger of considering as conclusively settled; a fact which is not proven, no matter how great the probabilities of its truth are in my favor. I appreciate only too well, the necessity of an irrefutable demonstration before a theory, so essentially different from all the prevailing ideas, can be generally accepted. But, whilst the data which are yet wanting are being gathered, permit me to submit to your consideration the following conclusions, in which you will find included the more essential points of what I have just attempted to demonstrate:

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* This patient, G.B. presented himself Aug. 17, complaining that for the last six days he had been suffering with Cephalalgia, Anorexia, and general malaise. On the 24th I found him with some fever (pulse 100; temp 38.02) and with a history of higher fever on the preceeding evening and on the same morning. The fever, however, was of a very ephemeral character, as the patient did not have to give up his occupation or require any immediate treatment. The fever ceased, but the headache continued a few days after.

Another person I.C., one of the twenty unaclimated who have submitted themselves to my observation, was stung on Aug. 15, by a mosquito, which had two days previously satiated itself with blood from a patient at the Military Hospital, in the fifth day of a yellow fever attack. This inoculation so far (Sept. 1st) has given rise to no apparent result. I was verbally informed that on the 24th and 25th (Aug.) that he had been unwell, but not to such an extent as to require his suspension from active service.

CONCLUSIONS.

1st. It is now a well attested fact that the Culex mosquito stings, as a rule, several times in the course of its existence, not only when its first sting has been accidentally interrupted, but also, where it has been able to satisfy its cravings; only that in the latter case, a lapse of two or more days interval between its stings is necessary.

2d. Besides the natural facilities for the retention of the particles contained in the liquids which the mosquito injects, which are revealed to us by the anatomy of this insect, the possibility cannot be denied that the mosquito may impregnate its lancet with a virus contained in a diseased blood, which the insect may inoculate into the persons successively exposed to its sting.

3d. The direct experiments made to determine if the mosquito could really transmit yellow fever in the manner indicated have been limited to the above five experimental attempts at inoculation, with a single sting in each separate instance; these attempts have been succeeded by the following results:

One case of benign yellow fever, characterized by icterus and albuminous urine; two cases, diagnosticated by the attending physicians, aborted yellow fever; and two light ephemeral fevers, without any definite character. From this we infer, that a single sting from the mosquito is insufficient to reproduce the grave forms of yellow fever, and that our final judgment in regard to the efficacy of mosquito inoculations must be postponed until we are corroborated by experimental evidence in absolutely decisive conditions, i. e. outside of the epidemic yellow fever regions.

4th. If the inoculation of yellow fever through the mosquito should finally be proved an incontrovertible fact, and that this mode of transmission of the disease is the usual and most common manner in which the yellow fever poison is transmitted; then the various conditions which affect the life and developement of this insect would explain the anomalies (so obscure and difficult of explanation otherwise) which have been observed in the history of the distribution of yellow fever, and we would have in our hands the means of avoiding or limiting, on one side, the extension of the disease, whilst on the other, we would preserve through benign prophylactic inoculations, those individuals who would be exposed to the risks of contracting this formidable malady.

My only wish, in presenting this communication, is that note be taken of my observations, and that the truth of my suspicions and conceptions be left to the decisive evidence furnished by direct experimentation. This does not signify, however, that I am at all desirous of evading the discussion of the views which I have just enunciated; on the contrary, it will be with great pleasure that I will listen to any remarks or objections which my distinguished colleagues may deem proper to make.

Havana, Aug. 11th, 1881.