Symposium: YELLOW FEVER

EPIDEMIOLOGY OF YELLOW FEVER IN PANAMA (1949 - 1952)

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I. Historical Introduction (1881 - 1948)

Panama is internationally known as an area where the existence of yellow fever has been proved in different periods. The yellow fever mortality statistics in Panama date from 1881. According to Elton (1932), from 1881 to 1904 there were 1,048 deaths from yellow fever among the employees of the French Canal Company, the figures varying from zero in several years to 308 in 1886. According to the same author, there were 1,461 deaths from yellow fever between 1885 and 1886 in the city of Panama, with a minimum of zero deaths in several years and a maximum of 231 in 1886, which was an epidemic year. The last case of locally- contracted yellow fever in the Republic of Panama and the Canal Zone before 1948 occurred in November 1905, and was reported by General Gorgas. From 1906 to 1919 there were 17 cases of yellow fever in Panama, but the patients had acquired the disease in other areas. Thirteen of these cases originated on the West Coast of South America; one in Cartagena, Colombia; two on the west coast of Mexico and Central America; and one was of uncertain origin. The last case diagnosed in Panama prior to 1949 died on 12 August 1919 in the Gorgas Hospital, Canal Zone.

During 1929, 1930, and 1931 the Gorgas Memorial Laboratory collected blood samples from a number of individuals who were living and working in Darién, near the Colombian border; these samples were sent to the Rockefeller Foundation to be submitted to the protection test for yellow fever, and two of them were found to be positive: one from a boy of 9, the other from a lad of 16. During 1935 and 1936 Dr. Carl M. Johnson, of the Gorgas Memorial Laboratory, obtained 270 blood samples in Darién, 7 of which were proved positive as a result of the protection test for yellow fever. Two of these samples came from boys less than 13 years old. Similar tests made at the same time in settlements along the Chagres River, near the Canal Zone, were negative. In 1943 Kumm and Crawford reported the results of a serological survey in the Republic of Panama, and came to the conclusion that in the eastern part of Panama, in the region between the Colombian border and the Bayano River valley, outbreaks of jungle yellow fever had occurred after 1925.
II. First epidemic outbreak (1948)

Unexpectedly, and with the physicians of the Republic of Panama totally unprepared for yellow fever, the first case that was later diagnosed as yellow fever appeared in November 1948 in Santo Tomás Hospital. The clinical diagnosis of this first case, because of the neurological manifestations, was originally malarial encephalitis. This first case was followed by four more within the period from 11 November to 28 December 1948. In view of the confusion prevailing in the medical analysis of these cases, it should be acknowledged that the first one to call attention to the possibility of yellow fever as the real diagnosis of these fevers of unknown origin was Dr. José María Núñez, Head of the Medical Department of Santo Tomás Hospital. It was then that the medical experts became alarmed and initiated more precise investigations that resulted in the definite establishment of the histopathologic diagnosis by Dr. Norman W. Elton, of the Public Health Laboratory of the Canal Zone, and Dr. José M. Herrera, Head of Pathology at Santo Tomás Hospital.

These first five cases occurred in men from 16 to 42 years of age who were farmers working in direct contact with the jungle 10 to 25 miles east of Panama City. The number of cases reported in this first outbreak (all diagnosed post mortem) does not show the real incidence of yellow fever, because subsequent investigations made in the same area revealed that other persons became ill during the same period with similar clinical symptoms. Dr. Herrera also reported (1949) that of ten patients who resided in the area where the fatal cases had occurred and who entered Santo Tomás Hospital during the period of the outbreak with fevers of unknown etiology, eight were subsequently found to have positive sera, as shown by the protection test for yellow fever, although they had not been vaccinated against the disease previously.

III. Second epidemic outbreak (1949)

From December 1948 to August 1949 no additional cases occurred, primarily because these are the months of the dry season in Panama, when the number of jungle mosquito vectors is very small. The first case of the second outbreak entered Santo Tomás Hospital on 5 August 1949 and died on the 7th. This was a 19-years old farmer born in Guabas, District of Penonomé, who had spent four months doing agricultural work in the area of Quebrada Grande, District of Colón, about 30 miles northwest of Panama City.
The second case entered Santo Tomás Hospital on 19 August 1949 and died two days later. This was a young man of 20, mestizo, who lived and worked in the town of Limón, located at the eastern shore of Gatún Lake, some 35 miles northwest of Panama City.

The third case occurred in January 1950 and involved a farmer who lived and worked in the District of Chagres, along the Atlantic coast of the Isthmus.

As can be clearly seen from the distribution of the cases during these first two outbreaks, the yellow fever virus spread first from east to west until it arrived at the eastern side of the Panama Canal. It continued in a northwestern direction and crossed the Panama Canal at Barro Colorado Island, in Gatún Lake, then reached the Atlantic coast a few miles west of the northern entrance to the Canal.

The large vaccination campaign against yellow fever begun in 1949 and intensified in 1950 was responsible for the temporary lack of data on the direction taken by the virus after the last case had occurred in the District of Chagres. Then, in January 1951, an engineer who was making surveys for a proposed trans-Isthmus highway between the Provinces of Chiriquí and Bocas del Toro, found ten dead Ateles monkeys along a trail in the jungles of Cerro Cuchara, in the Province of Bocas del Toro, at an altitude of 2,200 feet above sea level. In February of the same year, members of the party working under the supervision of this engineer reported finding other dead monkeys in the same area. On 9 April 1951, all members of the group were vaccinated against yellow fever by Dr. Gustav Engler of the United Fruit Company, who used batch No. 406 of vaccine prepared by the Carlos Finlay Laboratory in Bogota, Colombia. On 12 April, one of the members of this party, who had been vaccinated three days before, was admitted to Almirante Hospital with a clinical picture that indicated yellow fever; he died 24 hours later. The histopathologic diagnosis made by Dr. Carl M. Johnson, pathologist at the Canal Zone Public Health Laboratory, was yellow fever. In June 1951, another case of yellow fever was diagnosed clinically by Dr. Gustav Engler. The individual was discharged ten days after having entered the hospital. The yellow fever virus was isolated from the serum of this patient by Dr. Enid de Rodaniche, virologist of the Gorgas Memorial Laboratory. This was the first time that the yellow fever virus had been isolated from a human being in the Isthmus of Panama.

As can be seen, the yellow fever virus, once it had reached the Atlantic coast of the Isthmus, spread east-west along
the rain-jungles that extend from the western side of the Panama Canal to the border of Costa Rica, in the Province of Bocas del Toro.

The virus continued spreading along the Atlantic coast of Costa Rica and arrived at the northern boundary of that Republic in July 1951. In October of the same year, an isolated and sporadic outbreak occurred on the Pacific coast of Costa Rica, at Potrero Grande in the Province of Golfito, near the border of Panama. According to Elton, the transmission of the virus from the Atlantic to the Pacific possibly took place across the central mountain range by way of the trails used frequently by nomad farmers.

From Potrero Grande the yellow fever virus travelled in two directions: towards the north, and this is a movement we shall not discuss in this paper because it had no influence on the subsequent outbreak that occurred in Panama; and towards the southeast, causing another human death in the vicinity of the town of Golfito, Costa Rica, and still another at Punta Buria, within the borders of Panama, in February 1952. It should be noted that the movement of the virus toward the southeast apparently stopped near the border region of Panama and Costa Rica for reasons we shall try to explain further on.

Although the existence of any subsequent cases of yellow fever within the territory of the country could not be definitely ascertained, it should be mentioned that in July 1952 a report was received of approximately 100 deaths, caused by a fever of unknown origin but with a symptomatology similar to that of yellow fever, among the native population of the Alto Bayano and around the source of the Chucunaque River between the Provinces of Panama and Darién. It is significant that the deaths occurred precisely in villages beyond Aguas Claras in which yellow fever vaccination had never been carried out, owing to geographic difficulties and the resistance of the natives to this type of public health program. Investigations are being made at this time to determine conclusively the etiology and epidemiology of this fever of undetermined origin.

IV. Program against Yellow Fever (1949-1952)

Once the first outbreak of jungle yellow fever had been discovered in 1949, a cooperative program was established by the public health authorities of Panama, civil public health authorities of the Canal Zone, and the United States military and naval medical authorities stationed in the Canal Zone. Orientation for
this program was provided by technical personnel of the Pan American Sanitary Bureau and the program was organized personally by Dr. Fred L. Soper and his collaborators. The program included five phases, the first three of a strictly investigative nature and the last two of a public health nature, namely:

1. Serological surveys
2. Entomological surveys
3. Viscerotomy stations
4. Immunization of the susceptible population
5. *Aedes aegypti* eradication

V. Epidemiological Investigations

1. Geographic characteristics of the Isthmus of Panama: Panama forms part of the series of Central American Isthmuses that connect the two great continental land areas of North and South America.

The Isthmus of Panama is located between 8 and 9 degrees latitude North and between 78 and 83 degrees longitude West. It is therefore in the heart of the tropical zone, between the Tropics of Cancer and Capricorn. The topography of the Isthmus is generally rugged. The main characteristic of its mountains is the presence of many steep ridges and the almost total lack of high plains and valleys. The Pacific coast is distinguished by the presence of extensive level areas that are more or less swampy and that rise very gradually from the ocean to the slopes of the mountains, which serve as a river divide. On the other hand, the level areas along the Atlantic coast are not extensive, since there is only a narrow strip of lowland between the ocean and the mountains of the Continental Divide.

With the exception of the volcanic mass of the Barú, located in the Province of Chiriquí, with a maximum altitude of 3,478 meters above sea level, the Continental Divide does not reach any great height in the Isthmus of Panama. In certain places it rises less than 1,000 meters above sea level, especially in the depression existing in the central part of the Isthmus where the Panama Canal is located. Thus, the Panama Canal is more than just an artificial division, since it is a natural depression in the great continental mountain range and there are abrupt changes in flora and fauna.
2. Climatology. Since the Isthmus of Panama is in the heart of the tropical zone, the change of seasons typical of the temperate zones is not found in this region. There are only two seasons in the Isthmus, the rainy season or the so-called "winter", which generally lasts from May to December, and the dry season or "summer" from January to April.

The Isthmus can be divided into three principal zones in accordance with the abundance and distribution of rainfall, namely:

a) The Pacific Zone. The Pacific Zone is characterized by two well-defined seasons, the rainy season from May to December and the dry season from January to April. In normal years, there is almost no trace of rain during the dry season.

b) The Atlantic Zone. In this zone precipitation is more abundant and more evenly distributed throughout the year. Rainfall is most frequent from May to December, but some rain continues to fall during the so-called dry season.

c) Zone of the Continental Divide. In the regions of the steep ridges of the Continental Divide, rain is even more abundant, particularly beyond 3,000 feet above sea level. As in the case of the Atlantic Zone, there is rain all year.

3. Zoogeographic characteristics of the jungle regions of the Isthmus. There are four sharply defined jungle zones in the Republic of Panama, as follows:

a) The lowland jungles of the Pacific climatological zone. These jungles extend almost without interruption from the Colombian border to the eastern bank of the Panama Canal, disappearing into the large plains west of the Canal only to reappear in the Azuero Peninsula and the lowlands of the Provinces of Veraguas and Chiriquí. They are characterized by considerable humidity during the rainy season and relative aridity during the dry months. The flora is varied, having a predominance of certain species of foliaceous trees like the Anacardium exsulm and, along the coast at the mouth of swampy rivers, of plants typical of the semi-brackish area, especially trees of the Rhizophoraceae family.

These jungles are inhabited by monkees of the Alcuatta genus and, to a lesser degree, by simians of the Cebus genus. Among the jungle mosquitoes that might be connected with the transmission of jungle yellow fever, the Haemagogus equinus species is outstanding, accompanied by representatives
of the Haemagogus lucifer and Haemagogus chalcospilans species. The complete absence of the Haemagogus spagazzinii falco and Aedes leucocelaenus in this region is noteworthy; significant, too, are the facts that no cases of yellow fever among human beings have been reported in this zone and that the percentage of positive reactions to serological tests administered among the mammals of the region was extremely low.

b) The jungles extending along the slopes of the Central Cordillera. This zone includes the jungle regions that extend along the slopes of the mountains dividing the waters of the Isthmus of Panama, between 400 and 2,500 feet above sea level. In general, the relative humidity of these jungles is more constant than in the Pacific zone, because of scattered rainfall throughout the entire year, although the rains are more intense during the rainy season, from May to January. The canopy formed by the tree-tops is very high, sometimes 120 feet above the jungle floor. Here many monkies of the Alouatta, Marikina, Ateles, Cebus and Aotus genera live. Jungle mosquitoes, especially those that live in hollows in trees, are abundant in this zone, with the Haemagogus equinus, Haemagogus spagazzinii falco, Haemagogus lucifer and Aedes leucocelaenus predominating. It was here that the majority of jungle yellow fever cases reported in Panama had their origin.

c) Semi-tropical jungles with heavy rainfall in the highlands of the Isthmus, which extend along the Central Cordillera between 2,500 and 9,000 feet above sea level. These jungles are characterized by considerable humidity throughout the year, as evidenced by the great number of epiphytic plants found in the trees. Here, too, there are many monkies of the Ateles genus and, to a lesser degree, representatives of the Alouatta and Cebus genera, but the Culicid fauna are scarce insofar as variety of species is concerned. Among the Haemagogus we find only Haemagogus lucifer, while Haemagogus spagazzinii falco and Aedes leucocelaenus are conspicuous by their absence.

d) Jungles with heavy rainfall extending along the Caribbean Coast. These jungles are characterized by a constant relative humidity, due to intermittent rainfall almost the year round. These characteristics are more pronounced in the Province of Bocas del Toro, where there is no dry season. Here, as in the Zone of the Central Cordillera, can be found monkies of the Ateles, Alouatta, Cebus and Aotus genera. Leading among the possible jungle yellow fever vectors are
the Haemagogus spegazzinii falco and Aedes leucocelaenus species of mosquitoes, with fewer Haemagogus equinus and Haemagogus lucifer.

4. Serological surveys. Dr. Herbert C. Clark (1952) reported on the serological surveys he had made throughout the entire country. According to him, of 201 samples taken from 15 species of jungle mammals captured east of the Canal Zone, 104 proved positive when submitted to the protection test for yellow fever; that is, 51.7%. The species of mammals that showed the highest percentage of infection were the monkies of the Ateles and Alouatta genera, and the following species of mammals also showed some positive reactions: Cebus capucinus, Marikina geoffroyi, Actus sp., Potos flavus isthmicus, Bradypus grisens grisens, Cuniculus paca virgatus, Saimiri orstedii orstedii, Didelphis marsupialis etensis. In a similar survey carried out among mammals captured west of the Canal Zone, 68 of 224 samples obtained proved to be positive; that is, 30.3%. Of them, monkies of the Alouatta genus showed the highest rate of infection. According to Dr. Clark, the region producing the highest percentage of positive sera was the valley of Rio Tuira in the Province of Darién, followed by the zone of Cacique on the Atlantic coast of the Isthmus. It is noteworthy that Dr. Clark carried out his survey in the years 1949-1950, for the yellow fever virus had not yet reached regions like Bocas del Toro, where the captured mammals showed negative results. These serological surveys should be studied with great caution, since it is known that serum taken from animals that have been wounded by fire-arms develops virucidal substances that may distort the results of the tests and lead to entirely false conclusions.

Entomological Surveys. In January 1949, a few days after the discovery of the first outbreak of jungle yellow fever in Panama, Galindo, Trapido, and Carpenter were put in charge of entomological investigations in the jungles where the victims had contracted the disease, with the primary purpose of identifying the possible jungle vectors of the virus.

When the investigations were begun, only four species of Haemagogus were known in Panama, namely H. equinus, H. lucifer, H. argyromeris, and H. chalcospilans, none of which was known as an effective vector of the yellow fever virus.

The area chosen for the first studies was that of Cerro Azul or Cerro La Victoria, located some twenty miles from Panama City in a direction 50 degrees east of north. Three jungle stations were selected, at 400 feet, 1,000 feet, and 2,100 feet above sea
level, respectively. Each station consisted of a sturdy tree with a ladder nailed to its trunk to permit access to platforms constructed among the higher branches. Mosquitoes were caught weekly at each station, by trapping all that approached to bite, either at the level of the jungle floor or around the platforms.

A few weeks after these studies began it was possible to report the presence in these jungles of two species known as effective vectors of yellow fever in South America, namely Haemagogus spegazzinii falco and Aedes leucocelaenus.

These investigations were then broadened to cover the whole territory of the Republic and part of Costa Rica, and they are being reported in a series of publications by Galindo, Trapido, and Carpenter. Analysis of those publications leads us to the conclusion that the species Haemagogus spegazzinii falco and Aedes leucocelaenus undoubtedly were the principal vectors of the yellow fever virus in Panama. The former was probably responsible for maintaining the virus among the arboreal mammals, and the latter for transmitting it from those mammals to man, since Haemagogus spegazzinii falco rarely visits the jungle floor, gathering in large numbers in the upper branches of the trees, while Aedes leucocelaenus has the habit of moving freely although in smaller numbers, between the jungle floor and the canopy formed by the high branches of the trees, thus being in a better position to bite the men who invade its domains.

Efforts made to isolate the yellow fever virus from its probable jungle vectors. White mice were inoculated intracerebrally with a total of 4,395 mosquitoes captured in the jungles of Quebrada Grande, a little after the second outbreak. Of these mosquitoes, 2,198 belonged to the species Haemagogus lucifer, 589 were Haemagogus equinus, 395 Haemagogus spegazzinii falco, 506 Aedes leucocelaenus, and 707 Sabethoides chloropterus. All the inoculations gave negative results. In addition seven monkeys which did not show neutralizing antibodies for the yellow fever virus were exposed to the bites of 395 Haemagogus spegazzinii falco, 181 of which, it was proved, drew blood. The monkeys were kept under observation for a period of a month without showing the slightest evidence of infection, and their sera, tested 30 days after the last biting, did not show neutralizing antibodies for yellow fever.

A monkey of the genus Ateles, whose serum tested negative, was exposed to natural infection by being tied with a chain to a platform built in the branches of a tree sixty feet above the jungle floor in the region of Quebrada Grande, very near the spot where one of the human cases contracted the disease. This monkey remained on the platform from 5 December 1949 to 6 January
1950, without showing febrile temperatures or any other symptom that would make one suspect the presence of yellow fever, and his serum, when submitted to the protection test for yellow fever on 1 February, gave a negative reading.

Despite the negative results obtained in these experiments, we cannot reach any conclusion from them, because the number of mosquitoes used was small and the work did not begin until several weeks after the last report of death among the yellow fever cases that occurred in the experimental zone.

**Immunization of the Susceptible Population.** The immunization campaign, under the direction of Dr. K. O. Courtney, succeeded in vaccinating almost all the urban and rural towns in the Republic and the Canal Zone in a little more than a year, covering an estimated 80% of the total population of the Isthmus.

In view of the latest case of yellow fever on the Pacific coast, which occurred at Punta Burica in February 1952, a campaign of re-vaccination of the population of the provinces of Chiriquí and Bocas del Toro was immediately begun. In Panama City, the vaccination campaign has been kept active by the Panama City Health Department.

**Campaign for the eradication of Aedes aegypti.** When the first outbreak of yellow fever was discovered, there were more than thirty localities in the Republic where Aedes aegypti existed, particularly the urban towns with good sanitation, where it had not been considered necessary to spray with DDT for malaria control. The cities of Panama, David, and Chitré are examples of such localities.

The campaign against the aegypti consisted of two phases: one of vigilant observation to determine the presence of adults or larvae in the various towns; the other of eradication by means of spraying all the houses in the infested towns as well as all receptacles containing water with DDT.

After an intensive DDT campaign throughout the Republic, in September 1949 only two foci of aegypti could be located, and these were immediately eliminated. During 1951 an effort was made to determine the presence of aegypti in small communities of less than 20 houses, which had not been visited previously, and in August 1951 a new focus of aegypti was found in a small rural community in the Province of Bocas del Toro. This focus was eliminated, and since that date the search for this species in Panama has produced no additional specimens.
EPIDEMIOLOGICAL ANALYSIS AND INTERPRETATION

The sudden appearance of the first epidemic outbreak of yellow fever in Panamanian territory at the end of 1948 leads us to ask whether the yellow fever virus in its jungle form existed in the country in a latent state before that date. The work of Dr. Clark and Dr. Kumm demonstrates beyond doubt that there were cases of yellow fever in the territory of the Republic after the year 1925, which left in their wake a series of persons immune to this disease. The cases of immunity reported by Clark and by Kumm and Crawford were located east of the Panama Canal, in the valleys of the Tuira and Bayano Rivers, which made some investigators think that the Bayano River constituted a barrier to the spread of the disease to the western part of the Isthmus. However, it is to be noted that in the part of the Bayano River Valley where Kumm carried out his investigation, the river is no more than 10 meters wide, and his work was done in towns on the western bank of the river, which leads us to the logical conclusion that the Bayano River has never constituted a barrier to the spread of yellow fever virus to western Panama. It is possible that epidemic outbreaks of yellow fever may have occurred west of the Bayano River and that they passed unnoticed because of the fact that between 1920 and the discovery of the 1948 outbreak there was no consciousness of yellow fever among our national medical personnel.

If the distribution of human cases that occurred in Panama during the years 1948, 1949, and 1950 gives us a more or less exact picture of the course followed by the yellow fever virus through the jungles, we must come to the conclusion that this course closely followed the areas of distribution of two species of mosquitoes previously convicted of transmitting this disease in various South American countries, namely, Haemogogus spiegazzinii falco and Aedes leucocelaenus.

Let us remember that the original course of the virus during the first outbreak was from east to west, until it reached the eastern shore of the Panama Canal, where instead of continuing on across it headed north toward the Atlantic coast. It is noteworthy that Galindo, Trapido, and Carpenter have reported that Haemogogus spiegazzinii falco does not inhabit the jungles on the Pacific side west of the Panama Canal.

There are indications that the virus crossed the Canal in the neighborhood of Barro Colorado Island in Gatún Lake, for various censuses of the monkeys on that island, taken before and after 1949, indicate that during that year an epizootic of
considerable proportions killed 60% of the population of Alouatta monkeys, without appreciably affecting the population of Cebus; and everyone knows the great susceptibility of Alouatta monkeys to yellow fever and the high degree of tolerance the Cebus show to the virus of the same disease.

Once it had arrived at the Atlantic coast, the virus reached out toward the west along the coast without leaving evidence of human cases, due to the unpopulated condition of the region and the lack of means of communication between this zone and hospital centers.

The case reported from Punta Burica, on the Pacific coast of the Province of Chiriquí, in February 1952, requires special analysis. As we mentioned before, this case occurred at the extreme south of a spread of virus from Potrero Grande, Costa Rica, toward Panama. We believe that the reason the virus did not spread to the east in the province of Chiriquí is exclusively meteorological. It is well known that the region of Colfito, where this outbreak originated, is an area of heavy rainfall, while the Province of Chiriquí has much less precipitation, especially in the month of February when the case occurred in Punta Burica. This circumstance would mean a very low population density of Haemagogus at this time of year, which would account for the failure of the virus to continue spreading through the Province of Chiriquí.

In view of the fact that in various places in South America enzootic yellow fever zones have been recognized—as in Muzo, Colombia—where the virus is kept constantly active in the jungle reservoirs and vectors, it is necessary that a careful study be made in the Province of Darién to determine whether a similar enzootic area exists there. The high number of deaths from unknown causes reported from the towns east of the Bayano River not covered by yellow fever vaccination, and the fact that various serological surveys conducted in that region at different times have revealed children and adolescents who were immune to yellow fever, make this study indispensable, in order to determine the degree of vigilance that must be practiced in the neighboring communities.

In conclusion, we must state that conditions are favorable to future outbreaks of jungle yellow fever in the Republic of Panama, for which reason it is necessary to continue the campaign against this disease, above all in the three following phases:
a) To continue entomological investigation indefinitely, in order to locate and eliminate new foci of Aëdes aegypti.

b) To reorganize the viscerotomy service, which so far has been a total failure in the Republic of Panama.

c) To renew periodically the immunization campaign, particularly in those areas that offer the greatest chances of infection because of their contact with the jungle.
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