THE 1957 STATUS OF YELLOW FEVER IN THE AMERICAS

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The professor of infectious diseases in a medical school, located in a city once the scene of a disastrous epidemic of yellow fever, inquired recently if the disease still exists in the Americas.

The statistics of the Pan American Sanitary Bureau list 77 cases officially reported during 1957, surely an insignificant number when related to the hundreds of millions of population of the Western Hemisphere. One might, then, be tempted to answer the query with a statement to the effect that yellow fever virus still exists in the Americas but that it is a public health problem of very minor importance. Such a reply would overlook these facts: these 77 cases come from seven countries, (Fig. 1), Bolivia, Brazil, Colombia, Guatemala, Panama, Peru and Venezuela; field studies have proven yellow fever virus to be present in British Honduras, where human cases were not observed during the year; and the range of the virus during 1957 from northwest to southeast has been over 3,500 miles.

A look at yellow fever in the Americas through the eyes of foreign health administrators might alter the indifference of the professor of infectious diseases.

The Committee on International Quarantine of WHO and the World Health Assembly, in meetings devoted to the preparation, adoption and modification of the International Sanitary Regulations, between 1949 and 1956, encountered greater difficulty in harmonizing the views of different countries, and groups of countries, on regulations for yellow fever than was encountered in the solution of all other differences.

During early 1956, the WHO sponsored a visit of representatives of Egypt, Philippines, Indonesia, British Africa, Belgian Africa, India, France, and Iraq to several countries in America to get first hand impressions of yellow fever here. After one day at the Pan American Sanitary Bureau in Washington the group visited Cuba where there is an active campaign for the eradication of the Aedes aegypti mosquito as a part of the continent-wide program to permanently prevent all urban yellow fever in the Americas. Then on to the then recently reactivated jungle fever zone of Honduras (Fig. 2) where it was learned that after an apparent silence of 15 months, yellow fever virus had not only persisted in Honduras but had moved northward into Guatemala (1).

In moving from Honduras to Guatemala yellow fever virus had left the range of its most widespread vector in the forests of South and Central America, Haemagogus spegazzini, and had demonstrated its adaptability to Haemagogus mesocondens (2) whose range extends well up into Mexico (Fig. 3).

In Costa Rica the group visited the San Juan de Dios Hospital where scores of cases of jungle yellow fever were under direct observation in 1951-52, and learned from those who had handled the cases that the clinical picture and high mortality of the jungle disease are in all ways similar to those of urban yellow fever.

In Panama the group learned the details of the cases of jungle yellow fever infected in 1948 only some ten miles from Panama’s International Airport at Tocumen, and of the 1949 to 1951 march of the epizootic through Western Panama to the frontier with Costa Rica. It was noted that the five hospitalized cases of 1948 were diagnosed post-mortem two months after the first case and two weeks after the last one, and then only because the Santo Tomas Hospital has a full time pathologist. The group could not but wonder how many similar episodes may
Fig. 1.—Number of cases of yellow fever from countries of the Americas, by political divisions and years, 1954 to 1957.
have passed unnoticed during the four decades yellow fever had been absent from the records of Panama and the Canal Zone. That this may have happened is suggested by the appearance in August 1956, of a case of yellow fever in the Santo Tomás Hospital (3), originating in the same jungle area which supplied the cases in 1948.

In Bogota, Colombia the visitors saw, at the Carlos Finlay Institute, the record of repeated and continuing incidence of yellow fever, year after year, and visited the yellow fever study area at San Vicente de Chucuri, Santander (Fig. 4), where in spite of repeated intensive vaccination campaigns, yellow fever cases have been confirmed in twelve of the last twenty-two years. San Vicente de Chucuri is apparently a permanent enzootic focus, in which, interestingly enough, monkeys are not present in numbers sufficient to maintain the virus unless there be some as yet unidentified reservoir or long-lived insect vector. Marsupials are suspected.

At Trinidad, B.W.I., the group learned of the early serendipitous discovery of yellow fever virus in jungle areas in April 1954, four decades after the last report of yellow fever from the Island, and of the urbanization of the jungle infection at Port-of-Spain some months later. Port-of-Spain was the first city in twelve years to report aegypti-transmitted yellow fever and the first maritime port in America to be infected in 25 years. Here, also, it was possible to see the intimate contact, through well paved roads, which exists between jungle and urban areas. The Aedes aegypti mosquito has been widespread in human habitations along the rural highways, near the infected forests. In Trini-
dad, reports were also heard of positive neutralization tests carried out in 1953 of young teen-age Trinidadians born long after the last reported yellow fever, indicating the possibility of previous unrecognized outbreaks on the Island.

The visiting group could not fail to note that in spite of evidence indicating the presence of yellow fever virus in Trinidad during a twelve-month period and its spread throughout the Island, less than a score of cases were reported internationally. Obviously many more must have occurred.

At Belém, the gateway to the Amazon Valley, the group from overseas learned of the isolation of yellow fever virus, also serendipitous, from six febrile persons in 1954 not far from the city, when yellow fever was not known to be active in the area. The group also learned of repeated isolations of virus from naturally infected Haemagogus mosquitoes captured in 1955 in the Utinga forest at the edge of the city.

At Rio de Janeiro, the terminal point of its American tour, the group visited the National Yellow Fever Service and heard the story of the 1928-to-1931 struggle to free South Brazil of endemic yellow fever, (Fig. 5), which followed the reinfection of Brazil's beautiful capital, 20 years after Oswaldo Cruz' first victory over the disease in 1908 (Fig. 4).

As stated, the objective of the trip was to give the group a first hand opportunity to see the conditions under which yellow fever occurs in the Americas, in order to judge the threat which yellow fever here may be to other regions. The hope that the trip might result in an immediate lessening of the fear in the Orient of infection from America was not fulfilled. On the eve of his departure one member of the group declared that his anxiety regarding the possibility of the infection of Asia with yellow fever had doubled during the trip. This may well have been the reaction of the entire group, visiting...
Following the confirmation in 1900 by the Reed Commission of Carlos Finlay’s theory of the transmission of yellow fever by the *Aedes aegypti* mosquito, dramatic results were obtained by the reduction of the breeding of this mosquito in endemic centers such as Havana, Panama, and Rio de Janeiro. There was a striking disappearance of the disease, not only from the cities where anti-mosquito measures were applied, but also from surrounding and tributary areas. And in 1915, on the basis of this experience, the International Health Board of the Rockefeller Foundation, under the leadership of Wickliffe Rose and General Gorgas, sponsored a program for the eradication of yellow fever from the Americas, (Fig. 6), based on the reduction of the *Aedes aegypti* breeding in the endemic centers until the disease should spontaneously disappear. As a result of this program, the last focus of self-sustain-
ing man- _aegypti_ -man yellow fever infection disappeared from the rural endemic area of northeast Brazil in 1934 (Fig. 7).

![Map of areas reported with yellow fever 1932 to 1957.](image)

**Fig. 7.—Areas reported with yellow fever 1932 to 1957.** (Courtesy The Jefferson Medical College of Philadelphia.)

As the man- _aegypti_ -man yellow fever was being eliminated, observation led to the discovery (4) in 1932 and succeeding years, of enzootic and epizootic yellow fever of the tropical forests of America. This was jungle yellow fever, the discovery of which gave a ready explanation of the source of virus for some previously unexplained _aegypti_ -transmitted outbreaks in cities and towns isolated from any known source of infection: Rio de Janeiro, Brazil, in 1928; Socorro, Colombia 1929; Guasapati, Venezuela 1929; and Santa Cruz de la Sierra, Bolivia 1932 (5).

This discovery showed that the dream of eradicating yellow fever VIRUS was chimerical. The almost simultaneous perfection of methods for the eradication of the highly domesticated _Aedes aegypti_ led inevitably to a program for the eradication of this African invader from the Americas.

Even though conditions in the period between 1900, when the _aegypti_ -transmission of yellow fever was confirmed, and 1931, when the last series of urban outbreaks ended, were quite different from those of the period following 1932, the year in which jungle yellow fever was confirmed and _aegypti_ -eradication begun, it is instructive to compare the distribution of yellow fever in these two periods.

The yellow fever reported between 1900 and 1931 (Fig. 6), was distributed around the periphery of South America, around the Caribbean Sea and the Gulf of Mexico, and along the Pacific Coast of Mexico, and Central America. It was almost entirely urban yellow fever although the contemporaneous description of the Trinidad outbreak of 1914 clearly identifies that episode as jungle yellow fever. The reports for this early period are almost entirely of outbreaks diagnosed clinically and epidemiologically, whereas the reports for the later period 1932 to 1955 (Fig. 7), have come in large part as the result of routine viscerotomy and the histopathological confirmation of unsuspected cases. This is true even of the few cases of _Aedes aegypti_ transmitted yellow fever which have been reported. Yellow fever has been found widely distributed in the interior of the continent and even when reported close to the coast has only in one instance (Port-of-Spain 1954) infected any international port. The _aegypti_ -transmitted yellow fever reported during this period was of two types: endemic rural yellow fever; and isolated urban outbreaks occurring very close, and secondary, to known infected jungle districts. The rural endemic yellow fever of northeast Brazil was terminated in 1934 by extending anti-_aegypti_ measures to large rural areas and has not recurred.

In the period from 1932 to 1955 a huge amount of epidemiological information about both urban and jungle yellow fever was collected and studied (6). This period includes the last three years...
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(1932–1934) of epidemic aegypti-transmitted yellow fever in northeast Brazil, and the period from 1935 to 1942 when urbanization of jungle virus occurred in 13 towns of Brazil, Paraguay, Bolivia and Colombia, in areas from which the aegypti mosquito has since been eradicated.

In order to bring the yellow fever situation of recent years into clearer focus, the distribution of the 1606 cases of yellow fever reported during the decade 1948–1957 have been brought together in Table I (Fig. 8). During this ten-year period, yellow fever occurred from Guatemala on the north to Argentina on the south and filled in many previous blank spots in the map of jungle yellow fever. The human cases were confirmed in 14 countries—Guatemala, Honduras, Nicaragua, Costa Rica, Panama, Colombia, Venezuela, British Guiana, Trinidad, Ecuador, Peru, Bolivia, Brazil and Argentina—without the occurrence of any aegypti-transmitted outbreaks! Brazil, Colombia and Bolivia reported cases in each of the ten years. In addition yellow fever in monkeys was confirmed in British Honduras, Venezuela in nine years and Peru in seven. Ecuador reported cases in the Amazon Valley in 1949 and on the Pacific slope in 1951. This is the first report of jungle yellow fever west of the Andes in Ecuador and the first yellow fever on the Pacific slope of South America to be reported since 1921.

In 1950 yellow fever extended much farther south in Bolivia than it had been found during 18 years of observation. In Brazil, the Southern States of Mato Grosso, Goias, Minas Gerais, São Paulo and Parana were invaded from the Amazon Basin, 1950 to 1953, for the third time since 1934. In late 1957 deaths in Mato Grosso and Goias indicated that a fourth epizootic wave was beginning.

In 1954, northeastern Venezuela, after apparent freedom from yellow fever for twenty years, was shown to be infected. This area was probably the source of virus for the outbreak of the same year in Trinidad, already referred to, and is also notable as originating the first infectious case of yellow fever known to travel by air from the jungle to a distant aegypti-infected urban center—Sucre State to Caracas. In 1955 and again in 1956, jungle yellow fever was reported in the State of Aragua in north central Venezuela, far

TABLE I.—Reported Cases of Yellow Fever in the Americas, 1948–1957

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*Jungle yellow fever, with the exception of 3 cases in Trinidad in 1954.
**All cases with laboratory confirmation.
***Evidence of activity of the virus of yellow fever in howler monkeys (Alouatta sp.)
Fig. 8.—Number of cases of jungle yellow fever from countries of the Americas, by political divisions and by years, 1946-1953. (Courtesy American Journal of Tropical Medicine and Hygiene.)
from any previous reported focus of infection and only some 50 miles from the capital.

In Panama, as already noted, yellow fever appeared in 1948 as a jungle infection east of the Canal, spread during the next five years across the Canal and up the Isthmus to Costa Rica and Nicaragua (7).

The events of the next three years, 1954, 1955, 1956, (Fig. 1), were to show that jungle yellow fever had not yet exhausted its ability to surprise the epidemiologists.

In Central America, in 1954, (Fig. 2), the enzootic which had previously been traced easily in Costa Rica and Nicaragua by the finding of sick and dead monkeys, was followed with difficulty across Honduras to the Ulua Valley near the frontier with Guatemala.

During 1955, no yellow fever activity, either in man or in monkeys, was reported in Central America. Surprisingly, early in 1956, activity among monkeys was reported in Honduras, in the same area where the activity had ceased 15 months before (1). Simultaneously, yellow fever among monkeys was observed across the border in Guatemala indicating progression of the epizootic wave. The year 1956 was one of considerable yellow fever activity in monkeys in Guatemala, without the occurrence of reported human cases. The activity in monkeys continued in 1957 in Guatemala and British Honduras; though human cases were confirmed in Guatemala.

The recurrence in Panama of jungle yellow fever in 1956 (3) and 1957 in the same districts where cases occurred in 1948, and the present epizootic wave, which has now reached Guatemala, when taken together raise the question of whether a second wave may follow the preceding one so soon in Central America where the susceptible monkey population was greatly reduced by mortality from yellow fever just a few years ago.

In Brazil, the 1950–53 outbreak in the Southern States stopped unexpectedly. Apparently drought conditions curtailed this epizootic before it completed its sweep through the forests of southern Brazil, practically all of which were invaded during the 1954 to 1956 epizootic. The only cases reported in Brazil during 1954 were found through routine virus isolations in an otherwise silent area near Belém at the mouth of the Amazon. In 1955 likewise yellow fever reported from Brazil was limited to this same area. In 1956 and 1957 there were a few scattered cases in the Amazon Valley.

The cumulative reports of yellow fever since 1932 and the unfolding picture of yellow fever since 1946, reveal clearly the absolute necessity of continuous observation and study if any appreciation, even approximate, of the sweep of epizootic cycles is to be obtained, for some of these cycles require a decade or longer for completion.

Even the 25-year period has been too short (Fig. 7), to give the whole picture of jungle fever in the Americas. This is due to the relatively long intervals which have occurred in certain areas between epizootic waves, as well as to the failure to recognize and report many, if not almost all, of the resultant human cases. The progress of a wave depends upon at least three coincident factors: the introduction of the virus; the existence of an adequate population of susceptible vertebrates; and weather suitable to multiplication and maintenance of adequate numbers of mosquito vectors. The study of the intervals between the appearance of yellow fever in specific areas indicates that yellow fever persists almost constantly in certain small areas, returns repeatedly after short periods of freedom in other areas, and recurs only after long and irregular absences in yet others.

Rio de Janeiro, already referred to as having been reinfected by jungle yellow fever virus in 1928, twenty years after the city had been freed of endemic yellow fever by Oswaldo Cruz, was again bombarded by jungle virus in a number of known infectious cases coming into the city from nearby infected areas in 1958.
During the past 19 years jungle yellow fever has not been observed in areas close to Rio nor have recognized cases appeared from further afield. Other areas have reported the recurrence of yellow fever after intervals of two or three years up to ten, twenty and even forty years.

This discussion of the status of yellow fever in 1957 has been largely limited to the official reports of the distribution of jungle yellow fever.

Since endemic aegypti-transmitted yellow fever no longer exists in the Americas, the problem of yellow fever during the past 20 years has been related to enzootic and epizootic yellow fever as a source of virus for jungle yellow fever cases, and to jungle yellow fever cases as a source of infection for Aedes aegypti-infested towns.

The questions to be answered in assessing the yellow fever situation as a threat to man are: What is the importance of jungle yellow fever to rural populations of tropical America? What is the threat of the urbanization of jungle yellow fever virus in cities and towns in enzootic and epizootic areas? What is the international threat of jungle yellow fever?

Jungle yellow fever is clinically and pathologically indistinguishable from urban yellow fever and is just as dangerous to the person infected in or near the forest as to the city victim. The jungle disease is however generally limited to those living or working in or very close to the tropical forest or entering the forest for recreation or travel. Figure 9 shows the transmission cycle of jungle yellow fever in tropical America.

Where the homes are closely surrounded by forest in a permanently enzootic focus (Ilheus, Brazil) or where the forest is being cleared for agriculture the disease becomes almost occupational in its distribution and attacks a high percentage of young adult males at their most productive period (Espírito Santo, 1949: 108 deaths, 100 in males over 16) (San Vicente de Chucuri, Colombia 1936-1955; 55 deaths, 45 farmers, 7 women, 3 children).

Where relatively light work, such as coffee picking, brings both women as well as men close to the forest, the disease tends to attack both men and women and even a considerable number of the children who accompany their parents to the fields. Thus it is clearly not necessary to chop down a tree to get yellow fever.

The development of a satisfactory yellow fever vaccine in 1936 greatly reduced the threat of jungle yellow fever, and has, in fact, practically eliminated it for those who are vaccinated.

The American nations are fortunate in having free access to vaccine, produced in the Oswaldo Cruz Institute, in Brazil, and in the Carlos Finlay Institute, in Colombia, in both with the collaboration of the Pan American Sanitary Bureau. Vaccination produces long lasting, probably permanent, immunity.

What is the threat of urbanization of
Status of Aedes aegypti eradication campaign in the Western Hemisphere—31 December 1957

Pv. 10.—Status of the Aedes aegypti eradication campaign in the Western Hemisphere on December 31, 1957. (From the Annual Report for 1957 of the Director, Pan American Sanitary Bureau.)
All observed urbanization of jungle yellow fever virus has occurred in towns relatively close to infected forests. The possibility of the introduction of yellow fever virus from forest to urban areas has been greatly reduced by the vaccination of large blocks of the populations living in jungle yellow fever areas: in Brazil, Colombia, Venezuela, Trinidad, Panama, Costa Rica, Nicaragua, Honduras, Guatemala and Mexico. However, vaccination is never complete, and absolute protection of towns can come only from the eradication of the \textit{Aedes aegypti} mosquito.

The program for the eradication of the \textit{Aedes aegypti} mosquito from the Americas has progressed to the point (Fig. 10), where there is very little opportunity for cases from infected jungle areas to infect cities without undertaking an international trip. From Argentina to Guatemala, the \textit{aegypti} mosquito has either been eradicated or is under heavy attack in all of the countries where jungle yellow fever has been reported in the past 25 years. To prevent reinfestation of those areas which have been, or are being, cleared of \textit{Aedes aegypti} it is essential that \textit{aegypti} be eradicated also from the United States, Cuba, the Dominican Republic, Haiti, Puerto Rico, Jamaica, and the other Caribbean islands—where conditions for jungle yellow fever do not exist—as well as from Mexico where jungle yellow fever could occur, and which also has \textit{Aedes aegypti}.

What is the international threat of jungle yellow fever? In its extra-human reservoir the virus of yellow fever apparently moves through contiguous or nearly contiguous forest areas quite independently of man. The forest areas may all be in one large country like Brazil, or in half a dozen small ones like the Central American countries. The virus takes cognizance only of ecological boundaries, not of national ones (8).

But in Venezuela in 1954 a man in the early—i.e. infectious—stage of jungle yellow fever traveled by plane from Sucre State to Caracas, a distance of several hundred miles. Facilities for both highway and air travel are constantly improving in the outlying areas of jungle yellow fever countries. This places these areas in closer contact, through man, with heavily used national and international routes of travel. \textit{Aegypti}-infested countries, that could formerly rely on relative isolation from virus-infested jungles to protect them from yellow fever, may soon find that they are no longer effectively isolated.

**Summary.** Yellow fever virus is always present, with variable year-to-year distribution, throughout the tropical and subtropical forests of America from Mexico to Argentina.

In the decade 1948–1957 there was laboratory evidence of virus activity in 15 countries and territories. From four to eight countries were known to be involved each year. In three instances the presence of the virus was observed only in howler monkeys (\textit{Alouatta sp}.). The countries involved were British Honduras, Guatemala and Honduras, in the years 1956 and 1957.

Jungle yellow fever is a serious threat to rural populations and is a permanent source of virus for the reinfection of such cities and towns, as may be infested with \textit{Aedes aegypti}, in the same country with infected forests and even of such cities and towns in other countries.

Maximum guarantees against yellow fever depend on the widespread vaccination of rural populations and on the eradication of the \textit{Aedes aegypti} mosquito from all of the Americas.

**References**

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The map for 1946 shows no yellow fever for south Brazil. As a matter of fact, no cases were reported there for the year. However, jungle yellow fever had moved from the Amazon Valley into the valley of the River Plate on the divide in Mato Grosso in 1944. This had spread into Goias and Minas Gerais, reaching to the Rio Grande on the frontier with Sao Paulo. The infection apparently died out during the year 1945, Sao Paulo being spared the next year.

However, viscerotomy revealed a very probable case of yellow fever at Dourados in southern Mato Grosso in 1946. This was given a diagnosis of leptospirosis—not yellow fever—at the time. Reexamination in 1947 by FLS led to the belief that this had been a case of yellow fever and that there was a possibility that yellow fever virus had moved through southern Mato Grosso into Paraguay and would eventually be manifested further south.

As a matter of fact, single cases were proven by viscerotomy for the province of Misiones in Argentina and the state of Rio Grande do Sul in Brazil in 1948.