

## *Aedes aegypti* and Yellow Fever \*

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*Aedes aegypti*-transmitted yellow fever (referred to herein, for convenience, as *aegypti* yellow fever), long one of the great scourges of the tropical, the subtropical and even the temperate regions of the Americas, has been brought under complete control in the Western Hemisphere. All yellow fever that was recorded in the years 1900-31 (Fig. 1) is assumed to be *aegypti* yellow fever. Only two small and localized outbreaks have occurred in the last 28 years, the first at Senna Madureira in the heart of the Amazon Valley in Brazil in 1942, the second in Port of Spain, Trinidad, in 1954. Whether the Americas are to be spared further epidemics of urban yellow fever, sparked from widespread jungle outbreaks of the disease (Fig. 2) depends on the completion of the present well-advanced programme for the eradication of *A. aegypti*.

The potential danger is clearly revealed by the 1963-65 outbreak of dengue in certain Caribbean islands and Venezuela. This outbreak has been dramatically limited to areas still infested with *A. aegypti*. So long as the eradication of *A. aegypti* is incomplete, the continuing threat of reinfestation of areas from which it has been eradicated is very real, as shown by the reinfestations of Colombia, of French Guiana and of Guyana. The most recent break in the advancing eradication programme was the 1965 reinfestation of El Salvador at a time when neighbouring countries were not known to be infested. (Initial investigation suggests that this reinfestation came through the importation from the USA of old automobile tires, a favourite breeding-place for *A. aegypti* in this modern age.)

Man's victory over urban yellow fever in the Americas did not come easily, did not come rapidly, and did not come cheaply. The conquest of yellow fever was not complete with the initial glorious victories in Havana, Rio de Janeiro, Panama, Veracruz and New Orleans. Those facing the problems of diseases transmitted by *A. aegypti* in other

regions may gain much from a study of the struggle against yellow fever since 1900. This date is chosen because it was the year in which convincing evidence was produced that incriminated *A. aegypti* as the vector of yellow fever.

The attack on yellow fever began in Havana in 1901. The victory of Gorgas in Havana was followed by success in other cities of Cuba; in Santos and Rio de Janeiro, Brazil; in Veracruz and Tampico, Mexico; and in the cities of Panama.

Very early in the struggle against yellow fever, it became obvious that it was not necessary completely to eliminate *A. aegypti* to stop the transmission of yellow fever; it disappeared rapidly when the breeding of *A. aegypti* occurred in less than 5% of the houses. Furthermore, once yellow fever had disappeared from the large endemic centres, it was found that, after a period of perhaps only a few months to a year or more, the disease stopped spontaneously in the towns and villages of the entire tributary area.

These important observations are readily explained on the basis of the delicate interrelationship of the supply of yellow fever virus, the density of the *A. aegypti* mosquito, and the availability of susceptible persons needed for continued transmission of yellow fever. This interrelationship may be disturbed by a drop in any of these factors, which may occur readily for the reasons given below.

(1) The virus of yellow fever is available for the infection of the vector mosquito only during the first three days of the disease in the individual case.

(2) The infected *A. aegypti* must survive an extrinsic incubation period of nine days or more, depending upon the environmental temperature, before becoming infective. Once infective, however, *A. aegypti* remains so for life, but it does not transmit the virus to the next generation. Although *A. aegypti* may survive for five or six months in the laboratory, the effective epidemiological survival period is generally no more than six or seven weeks.

(3) While persons of all races, both sexes and all ages are susceptible, the rapidly acquired immunity is life-long; there are no relapses, no carrier states and no second attacks.

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FIG. 1  
AREAS OF THE AMERICAS IN WHICH YELLOW FEVER WAS REPORTED FROM 1900 TO 1931

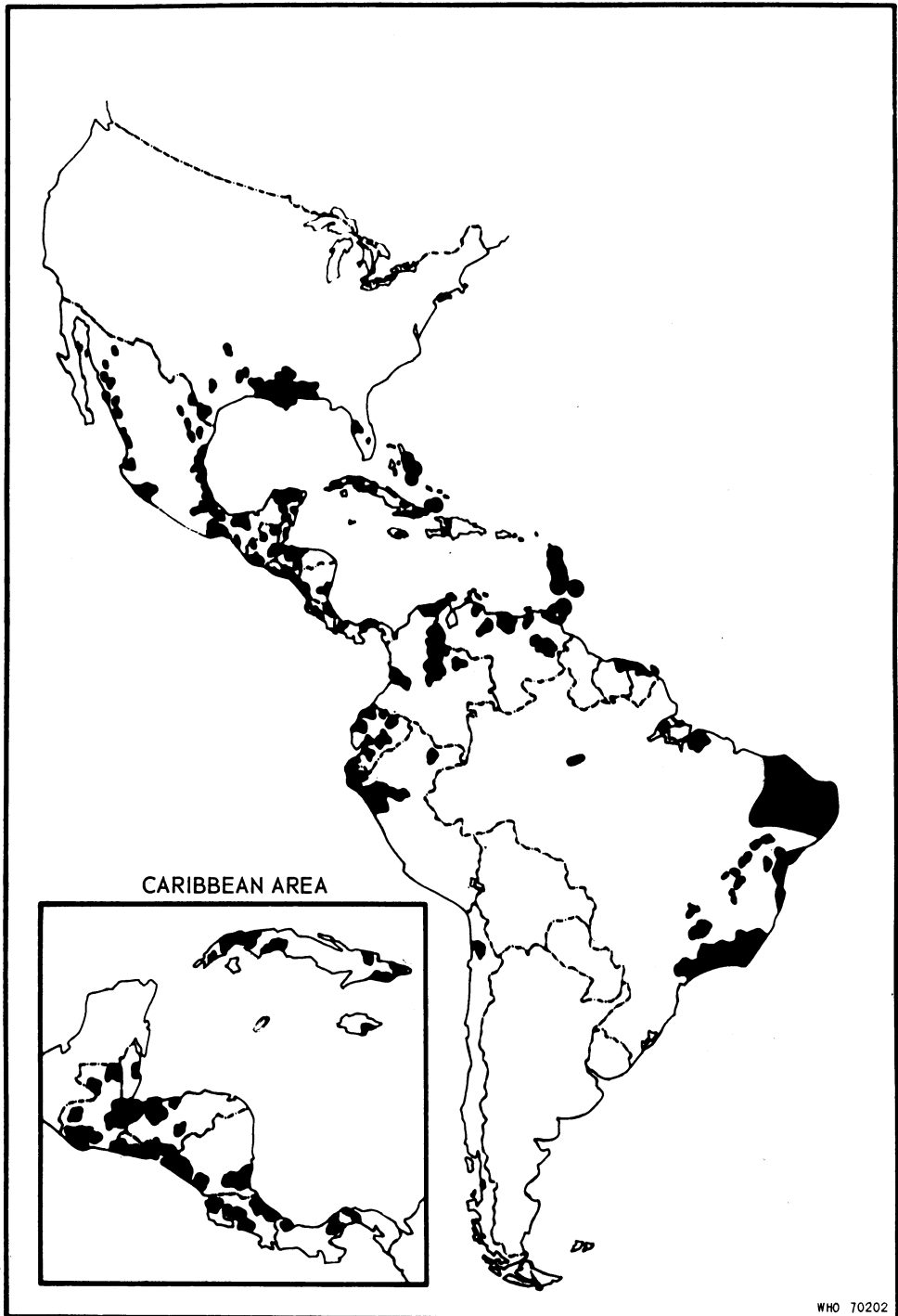
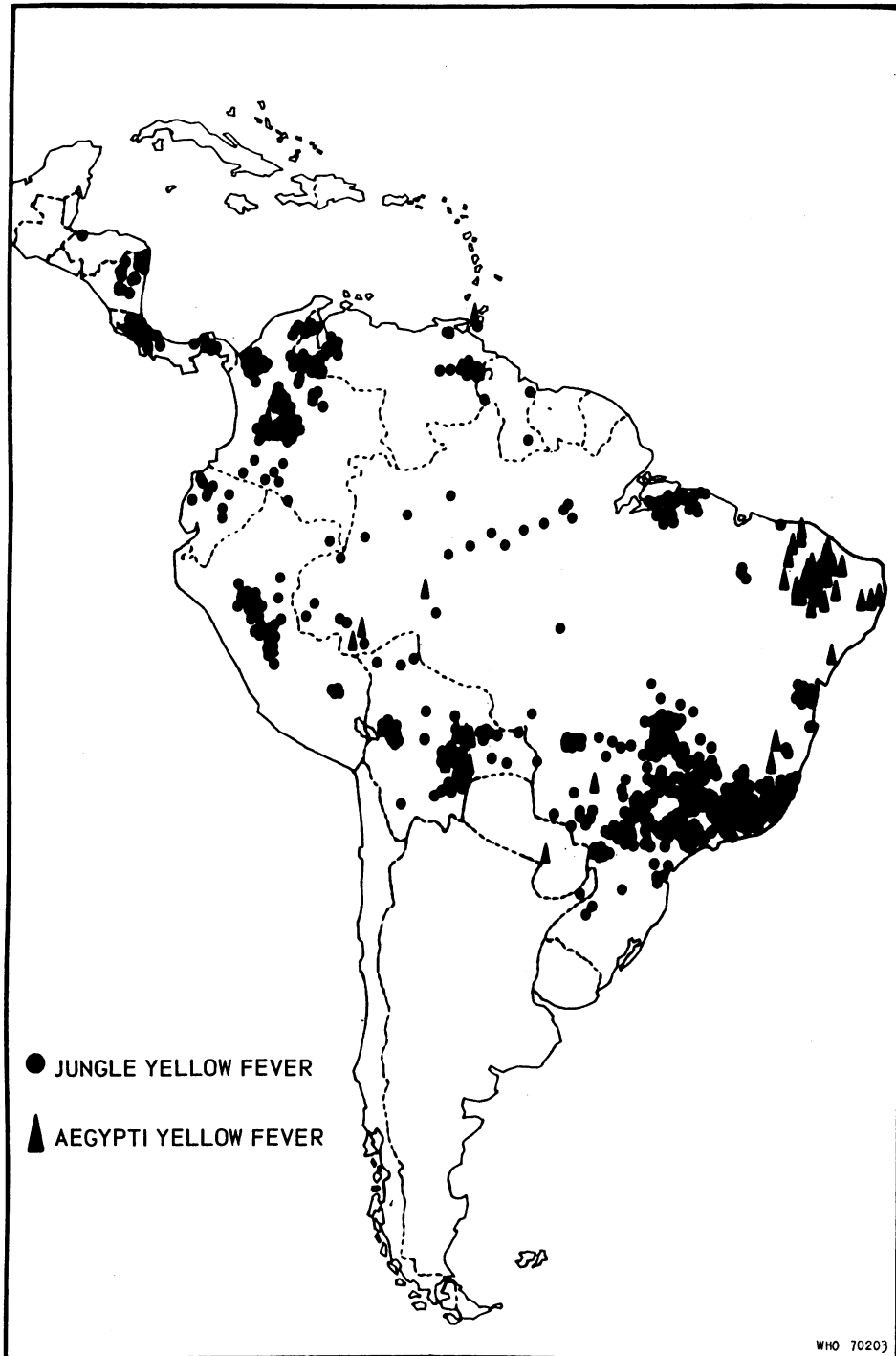


FIG. 2  
AREAS OF THE AMERICAS IN WHICH YELLOW FEVER WAS REPORTED FROM 1932 TO 1955



The unbroken series of victories led various workers, even before 1910, to dream of the eradication of yellow fever. The opportunity to undertake the task came with the creation of the Rockefeller Foundation in 1913 and the recognition of the yellow-fever threat to Asia inherent in the traffic through the Panama Canal that began in 1914.

In 1915, the Rockefeller Foundation dedicated itself to the task of eradicating yellow fever from the world. William C. Gorgas, Surgeon General of the USA, was chosen to lead this effort. The plan of action was fairly simple, based on the observations and experience of the previous 15 years. A reconnaissance of a continent to identify centres of yellow-fever endemicity was to be followed by temporary intensive campaigns in such places to reduce the index of *A. aegypti* below the minimum level for continued transmission of yellow fever. The campaign against *A. aegypti* would be maintained in each endemic centre until yellow fever spontaneously disappeared from the towns and villages of the surrounding area through exhaustion of the susceptible population by immunization. Once all areas of endemicity had been covered in this manner, yellow fever could not recur for lack of a reservoir of yellow fever virus, even though the campaign against *A. aegypti* were abandoned.

In 1916, reconnaissance of the historic yellow-fever regions of the Americas indicated that very few centres of endemicity remained, and relatively easy victory was anticipated. After delays caused by the First World War, the eradication effort got under way in Ecuador in 1918. Victory in Ecuador was followed by successes in Peru, Colombia, Central America, Mexico and Venezuela; by 1925, victory seemed near in Brazil.

The first suggestion of failure came with the appearance of yellow fever in north-eastern Brazil following the introduction there of non-immune troops in 1926. An intensified attack on *A. aegypti* eliminated this threat and, during 1927-28, a 12-month period passed with but a single case of yellow fever.

This calm was but the lull before the storm. In May 1928, yellow fever appeared in Rio de Janeiro, where it had been unknown for 20 years. The disease took full advantage of the high index of *A. aegypti* in that city, a busy tropical seaport which then had a population of 1 700 000. Fifteen months were required to eliminate the disease from the city itself, and three years to clear it from the towns and villages of the surrounding area. In the meantime, yellow fever had been recorded along the north coast of

Brazil and in the Amazon Valley at Belém and Manaus.

The source of the infection for Rio de Janeiro was not established at the time. This outbreak, however, emphasized the fact that yellow fever, which in its classical clinical manifestation is a most dramatic disease, had been able to continue unobserved during a considerable period of time and to enter the city with no indication of its source.

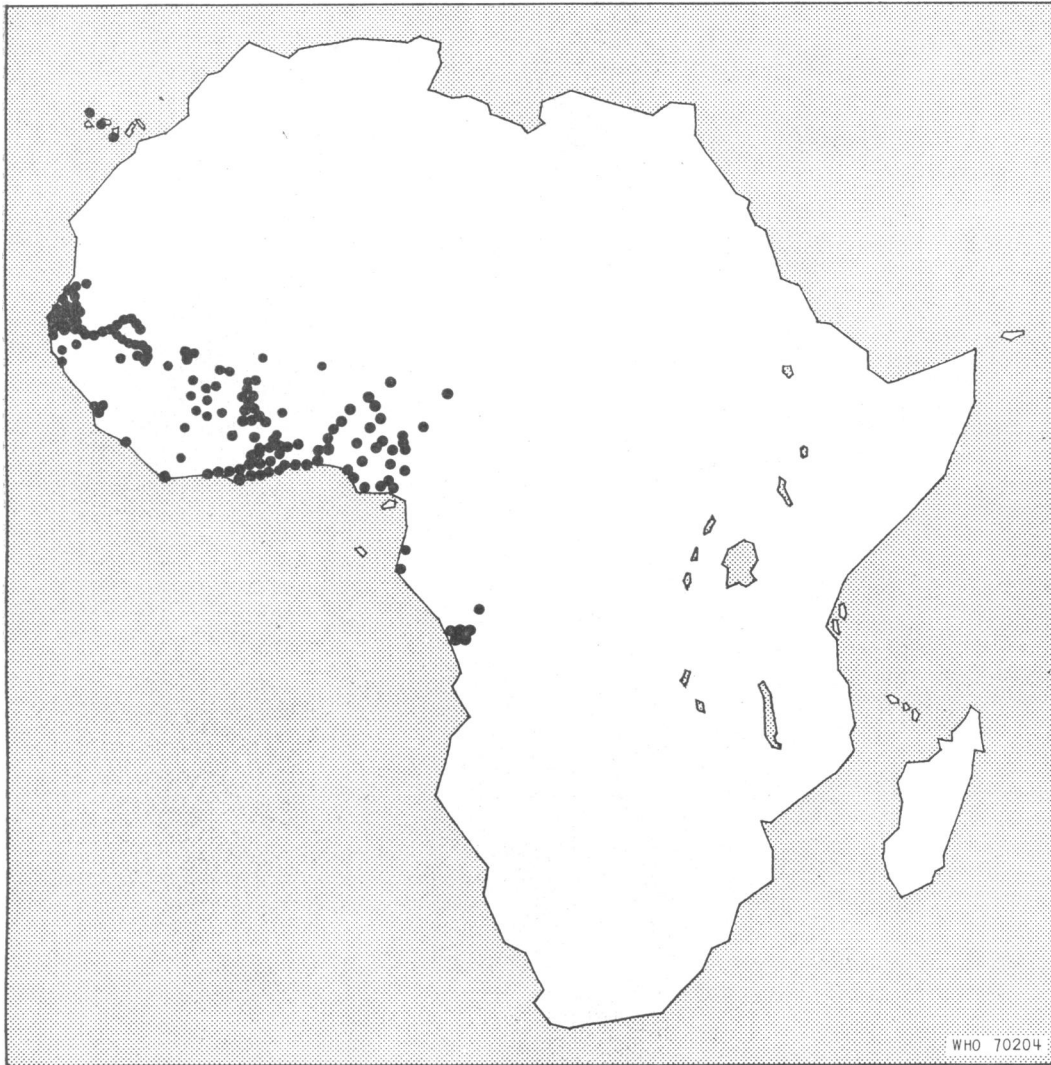
The events of the next few years were to reveal not one but two mechanisms for the persistence of yellow fever during the Rockefeller Foundation's campaign of eradication.

The introduction, in 1930, of the routine microscopic examination of liver tissue from febrile patients who died after less than 11 days of illness revealed a latent endemic rural yellow fever throughout a large area of north-eastern Brazil that had not been suspected by the yellow-fever workers in the nearby coastal port cities. This rural endemic yellow fever depended on an unusual distribution of the *A. aegypti* mosquito in this semi-arid area. The endemicity of yellow fever here was so high that most cases occurred in children under 5 years of age; practically no cases occurred in persons over 15 years of age. The attack on *A. aegypti* was carried to the rural areas, with the result that yellow fever had disappeared by August 1934. At this writing, it is 31 years since the disease has been found in this area of previously latent endemicity.

This silent endemic *A. aegypti* yellow fever explained the unexpected outbreak among troops in 1926, but its limited extent and great distance from Rio de Janeiro made it unacceptable as the source of virus for the 1928 outbreak in that beautiful city, then Brazil's capital.

The second unrecognized mechanism for the persistence of yellow fever was not so easily handled; in 1932 yellow fever was proven to occur in the absence of *A. aegypti* in the Vale do Canaan, Espírito Santo, Brazil. Following this revelation, continuing studies led to the recognition of jungle yellow fever as a disease of forest vertebrates, especially primates, transmitted by forest mosquitos other than *A. aegypti* (Fig. 2). Observations were made on the invasion of several towns by jungle virus leading to *A. aegypti*-transmitted outbreaks. Thus came an understanding of the origin of the 1928 yellow-fever invasion of Rio de Janeiro and the equally enigmatic outbreaks of *aegypti* yellow fever in Socorro, Colombia, and Guasapti, Venezuela, in 1929 and that in Santa Cruz de la Sierra, Bolivia, in 1932.

FIG. 3  
LOCALITIES IN AFRICA IN WHICH YELLOW FEVER WAS REPORTED FROM 1900 TO 1931



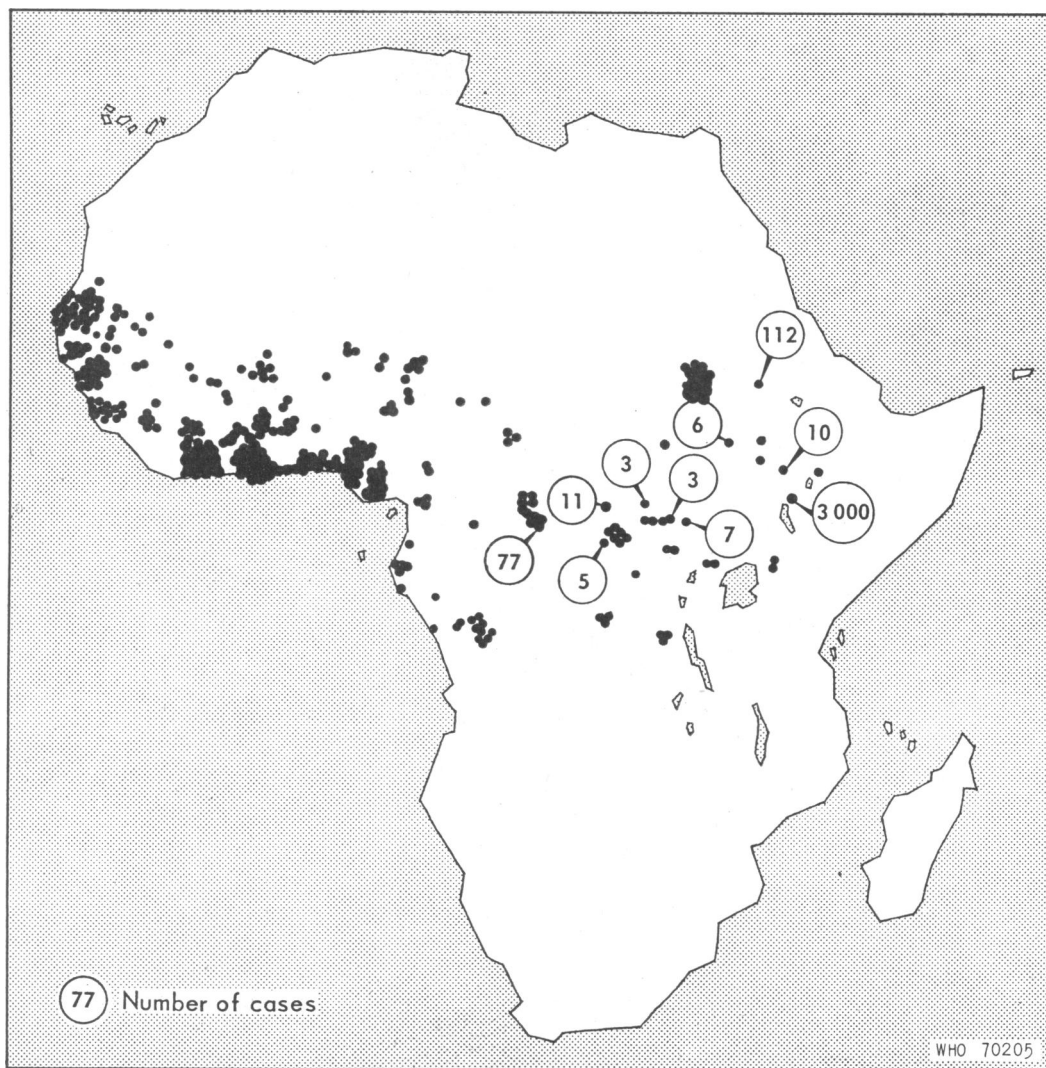
Since no means were known for preventing yellow fever among forest animals, it became obvious that the eradication of yellow fever, as planned by the Rockefeller Foundation, was impossible. The *aegypti* yellow fever of cities and towns could always recur through introduction of virus by persons infected in nearby forests.

Fortunately, in 1933, a year after the first observation of jungle yellow fever and before the gravity of its threat was fully apparent, it was shown that

*A. aegypti* had been eradicated in several Brazilian cities. This was not a result of deliberate planning for eradication; it occurred when not anticipated, as the result of meticulous administration and the introduction of the capture of adult mosquitos to pinpoint the location of hidden breeding of *A. aegypti* not easily found by the search for larval foci.

The national eradication of *A. aegypti* as a permanent preventative of urban and maritime yellow fever was proposed and unofficially adopted as the

FIG. 4  
LOCALITIES IN AFRICA IN WHICH YELLOW FEVER WAS REPORTED FROM 1932 TO 1963



objective of Brazil's Yellow-Fever Service in 1934.<sup>1</sup> Impossible as this task then appeared, experience was to show that eradication is actually easier than continuing effective *A. aegypti* control. Once a large city is free of *A. aegypti*, it is more economical to clean the suburbs and tributary villages than to maintain permanent control in the city. Continuing peripheral expansion was possible in Brazil with

<sup>1</sup> *A. aegypti* eradication became the official objective by Decree No. 8675 of 4 February 1942.

no increase of manpower beyond that previously used in *A. aegypti* control work in the principal cities.

*A. aegypti* eradication calls for systematic attack wherever this vector may be found, regardless of the immediacy of disease transmission. This policy has been most fruitful in Brazil. Several towns were infected by cases from nearby jungle outbreaks in 1934, 1935 and 1936, but only a single small outbreak has occurred in the last three decades.

In 1946, the eradication of *A. aegypti* in Brazil had advanced to the point where reinfestation across

international frontiers was a major problem. In 1947, Brazil proposed, and the nations of the Americas became committed to, the eradication of *A. aegypti* in the Western Hemisphere. This international development is a continuation of the phenomenon of peripheral expansion within the individual nation.

This effort was well timed; the intervening 18 years have seen the presence of yellow fever confirmed for Trinidad and all the countries of the mainland, except Canada and the USA in North, El Salvador in Central, and Chile and Uruguay in South America. In spite of this widespread distribution of yellow-fever virus, only a single series of but 4 cases of *aegypti* yellow fever has been recorded (Port of Spain, Trinidad, 1954).

Thus the endemic *aegypti* yellow fever of the Americas, the yellow fever of history, the only yellow fever known previous to 1932, has disappeared since 1934; whether it returns will depend on the completion of the eradication of *A. aegypti* from the remaining infested areas before "eradicated" areas become reinfested. The penetration of urban areas has become rare indeed since the 1930s (1942 and 1954), but the potential threat from the forest is permanent.

The eradication of *A. aegypti* in the Americas is possible because it has never adapted to life in the forest away from human habitation. Apparently this is also true for this vector in other parts of the world away from its original home in Africa, where it still breeds in the forest.

Whether eradication of the domestic *A. aegypti* in Africa would be followed by ready reinfestation

with *A. aegypti* from the forest depends on the adaptability of the forest *A. aegypti* to domestic water containers. This has not yet been determined. Until it is, the *aegypti* yellow fever of Africa can be prevented by measures against *A. aegypti* in the large cities and by vaccination of the population of the interior. Neither method is wholly satisfactory, because neither has a terminal point.

Yellow fever in Africa, previous to the discovery of jungle yellow fever (Fig. 3) was largely limited to West Africa between the Sahara Desert and the Gulf of Guinea, with extension down the coast to the mouth of the Congo River. Since 1932 (Fig. 4) yellow fever has been observed in a projection eastward of the previous range along the coast; this projection has stopped some distance from the coast. Even large outbreaks in the Sudan and Ethiopia lack the characteristics of the *aegypti* yellow fever of the West African coast and of the Americas.

Yellow fever has never travelled to Asia with man and *A. aegypti* by boat, probably because there has been no epidemic in the port cities of the east coast of Africa. The absence of yellow fever in these cities may not be equally important in preventing the movement of yellow fever by air, however.

Jungle yellow fever in the Americas and in Africa is a permanent source of yellow-fever virus, a potential threat to uninfected regions in these days of rapid travel, to all regions infected with *A. aegypti*. Should *A. aegypti* eradication in Asia and the Western Pacific be considered because of its transmission of other diseases, freedom from all threat of yellow fever can be cited as an added inducement.