Aedes aegypti-transmitted yellow fever - aegypti yellow fever for short - long, one of the great scourges of tropical, subtropical, and even temperate regions of the Americas, has been brought under complete control in the Western Hemisphere. Only two small local outbreaks have occurred during the past 28 years, the first at Serra Madureira in the heart of the Amazon Valley in Brazil in 1942, the last at Port of Spain, Trinidad, in 1954. Whether the nations of the Americas are to be spared future epidemics of urban yellow fever depends on the completion of the present well-advanced programme for the eradication of Aedes aegypti.

The potential danger is clearly revealed by the 1963-1964-1965 outbreak of dengue in certain Caribbean islands and Venezuela. This outbreak has been dramatically limited to areas still infected with aegypti. So long as the eradication of aegypti is incomplete, the continuing threat of reinfection of eradicated areas is very real, as shown in recent years by the reinfections of Colombia and of British and French Guianas. The most recent break in the advancing eradication programme is the 1965 reinfection of El Salvador at a time when neighbouring countries are not known to be infested. (Initial investigation suggests this reinfection came through the importation from the United States of old automobile tyres, a favourite breeding place for aegypti in this modern age.)

Man’s victory of 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 aegypti-transmitted diseases
in other regions may gain much from a study of the struggle against yellow fever
since 1900. This date is chosen since it was the year in which convincing evidence
was produced incriminating Aedes 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 to completely eliminate aegypti to stop the transmission of yellow
fever; yellow fever disappeared rapidly when the breeding of aegypti occurred in
less than 5% of the houses. Further, once yellow fever disappeared in the large
endemic centres, after a period of some months or 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 aegypti
mosquito, and the availability of susceptible persons needed for continued transmis-
sion of yellow fever. This interrelationship may be disturbed by a drop in any of
these factors, which may occur readily because:

(a) the virus of yellow fever is available for the infection of the aegypti
mosquito only during the first three days of the disease in the individual
case;

(b) the infected aegypti must survive an extrinsic incubation period of nine
days or more, depending on the temperature, before becoming infective; once
infective, aegypti remains so for life, but does not transmit the virus to the
next generation; though it may survive for five or six months in the laboratory,
the effective epidemiologic survival period is generally not over six or seven
weeks; and

(c) persons of all races, both sexes, and all ages are susceptible, but the
rapidly acquired immunity is life long; there are no relapses, no carrier state,
and no second attacks.
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 (1913) and the recognition of the yellow-fever threat to Asia inherent in traffic through the Panama Canal beginning in 1914.

In 1915 the Rockefeller Foundation dedicated itself to the task of the eradication of yellow fever from the world; Surgeon General William G. Gorgas 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 the continent to identify endemic yellow-fever centres was to be followed by temporary intensive campaigns in such centres to reduce the *A. aegypti* index below the threshold needed 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 the endemic areas had been covered in this manner, yellow fever could not recur for lack of yellow fever-virus even though the campaign against the *A. aegypti* mosquito were abandoned.

In 1916 a reconnaissance of the historic yellow-fever regions of the Americas indicated very few remaining endemic centres and relatively easy victory was anticipated. After delays due to World War I, the eradication effort got underway in Ecuador in 1918. Victory in Ecuador was followed by successes in Peru, Colombia, Central America, Mexico and Venezuela, and by 1925 victory seemed near in Brazil.

The first suggestion of failure came with the appearance of yellow fever in north-east Brazil following the introduction of non-immune troops in 1926. An intensified attack on *A. aegypti* eliminated this threat, and during 1927-1928 a period of 12 months passed with a single reported sporadic case of yellow fever.

This calm was but the bull before the storm. In May 1928 yellow fever appeared in Rio de Janeiro where it had been unknown for 20 years. Yellow fever took full advantage of the high *A. aegypti* index in Rio de Janeiro, a busy tropical
seaport with a population of 1,700,000 people; 15 months were required to eliminate the disease from the city and three years 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 infection for Rio de Janeiro was not established at the time. The outbreak in Rio de Janeiro, however, emphasized the fact that yellow fever - in its classical, clinical manifestation a most dramatic disease - had been able to continue unobserved during a considerable period of time and to enter Rio de Janeiro without indication of the source of infection.

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 campaign of eradication.

The introduction in 1930 of routine microscopic examination of liver tissue from febrile cases dying after less than 11-days' illness revealed a latent endemic rural yellow-fever throughout a large area of north-east Brazil which had been unsuspected by the yellow fever workers in the nearby coastal port cities. This rural endemic yellow fever depended on an unusual distribution of the *Aedes aegypti* mosquito in this semi-arid area. The endemicity of yellow fever here was so high that most cases occurred in children under five years of age; practically no cases occurred beyond age 15. The attack on *Aedes aegypti* was carried to the rural areas with the result that yellow fever disappeared in August 1934. It is now 31 years since the disease has been found in this previously latent endemic area.

This latent endemic *Aedes aegypti* yellow fever explained the unexpected yellow fever among troops in 1928, but its limited extent and great distance from Rio de Janeiro made it unacceptable as the source of virus for the 1928 outbreak in Brazil's beautiful 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 *Aedes aegypti* in the Vale do Canaan, Espirito 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 mosquitoes other than *Aedes aegypti*. 
Observations were made on the invasion of several towns by jungle virus leading to 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.

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 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 mosquitoes to pinpoint the location of hidden breeding of aegypti not easily found by the search for larval foci.

The national eradication of aegypti as a permanent prevention of urban and maritime yellow fever was proposed and unofficially adopted as the objective of Brazil's Yellow Fever Service in 1934. Impossible as this task then appeared, experience was to show that eradication is actually easier than continuing effective aegypti control. Once a large city is free of 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 no increase of manpower beyond that previously used in aegypti-control work in the principal cities.

Aegypti eradication calls for the systematic attack on aegypti wherever it 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.

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1 Aegypti eradication became the official objective by Decree No. 8675 of 4 February 1942.
In 1964 the eradication of *aegypti* in Brazil had advanced to the point where reinestation across international frontiers was a major problem. In 1947 Brazil proposed, and the nations of the Americas became committed to, the eradication of *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 yellow fever confirmed for Trinidad and all the countries of the mainland, except Canada and the United States in North, El Salvador in Central, and Chile and Uruguay in South America. In spite of this widespread distribution of yellow-fever virus, a single series of only four 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 the *aegypti* mosquito from the remaining infested areas before "eradicated" areas become reinfested. The penetration of urban areas has become rare indeed since the 1930's (1942 and 1954), but the potential threat from the forest is permanent.

The eradication of *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 the *aegypti* 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 *aegypti* in Africa would be followed by ready reinestation with *aegypti* from the forest depends on the adaptability of the forest *aegypti* to domestic water containers. This has not yet been determined. Until it is, the *aegypti* yellow fever of Africa can be prevented by anti-*aegypti* measures in the large cities and by vaccination of the interior population. Neither method is wholly satisfactory.
Yellow fever has never travelled to Asia with man and 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.

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 infested with aegypti. Should 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.