Present Knowledge of the World Problem of Yellow Fever, with Special Reference To South America and, More Particularly, To Brazil[1]

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As a result of the work carried out in Cuba, Rio de Janeiro, and São Paulo by the respective American, French, and Brazilian Committees appointed to study yellow fever, opinion on this disease generally accepted forty years ago may be summed up as follows:

(a) Yellow fever was a virus disease acquired by the bite of a mosquito that had sucked the blood of a patient within the first three days of illness, or by the inoculation of blood from a stricken person within the same limit of time.

(b) *Stegomyia calopus* (*Aedes aegypti*) was the only mosquito vector of the disease.

(c) The mosquito was not infectious until twelve days after feeding on a yellow fever patient but might remain so until the end of its life.

(d) Mosquitos could not become infected by feeding on such material as vomited blood, feces, or urine of patients, nor could they pass on the virus to other mosquitos, or to their own offspring.

(e) Yellow fever endemicity depended on the vitality of the vector, as Aëdes could not subsist at temperatures over 39° C. (102.2° F.) or under 15° C. (59° F.), the optimum temperature being between 27° C. (80.6° F.) and 32° C. (89.6° F.). The number of cases of yellow fever tended to increase towards the end of summer and to diminish with the onset of winter. (This was the general observation in Brazil.)

(f) The absence of clinical cases in a given region did not signify the absence of danger from epidemics.

After the remarkable sanitary campaign conducted by Dr. Oswaldo Cruz in Rio de Janeiro, it was thought that yellow fever might be wiped out from the whole world, an idea founded on the belief that urban centers—especially those on the coast—were the only reservoirs of the infection. During the last sixteen years, however, new methods of detecting the disease were disclosed which,

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when put into practice, showed that this erstwhile optimism was somewhat exaggerated. The more important of these discoveries were:

That the *Macacus rhesus* was susceptible to yellow fever and was a suitable laboratory animal for the study of the disease;[2]

Invention of the viscerotome, an instrument that permitted the taking of liver tissue samples for histologic examination without the need of autopsy;

Mouse protection test was a means of discovering past yellow fever infection in a given community.

It might be superfluous, at this point, to refer briefly to some of the refinements in the histologic diagnosis of this disease. The principal findings in yellow fever pathology are in the liver, where a coagulation type of necrosis, of hyaline appearance, selecting mainly the liver cells in the midzone of the hepatic lobule, takes place. There are normally staining liver cells undergoing fatty degeneration and containing small and medium-sized fat droplets irregularly and loosely scattered throughout the remainder of the hepatic lobule. Calcium impregnated casts in the renal tubules—the so-called Hoffman lesion—are also of diagnostic value.

When yellow fever suddenly reappeared in Rio (May 1928, to June 1929), only a few scientists and sanitarians like Sebastião Barroso and J. Pedroso were not surprised. Many years had elapsed since the yellow fever days of Havana, Guayaquíl, Veracruz, Panamá, and Dakar—also of the Brazilian epidemics of Belem, Manaos, Recife, Bahía, Rio and Santos—and most physicians were no longer intimately acquainted with the disease. Furthermore, during this period anti-mosquito measures had been lax and more than sixty percent of the population was no longer immune. The possibility of an outbreak of yellow fever depended only on the arrival of cases of the disease. The onset of the epidemic was therefore traced to soldiers who had just returned from the northeastern part of the country by way of the state of Minas Geraes (Pirapora). A similar outbreak, also caused by infected troops, occurred in Santa Cruz, Bolivia, in 1932.

As no cases of urban yellow fever had been known to exist in the region from which the soldiers were returning, an explanation had to be found. It was thought that there might be a rural modality of the disease—perhaps a sylvatic form. This surmise was later proved correct, and we now know that form of the disease as jungle yellow

2. A. Stokes, J. H. Bauer, and N. P. Hudson, Transmission of yellow fever to *Macacus rhesus*; preliminary note. J.A.M.A., 90:253–254, 1928.

fever. It was not, however, until the successive outbreaks (from 1932 to 1937) at San Ramón (Bolivia), Caparrapí, Muzo, and Restrepo (Colombia), Muchiri (Bolivia), and Valle do Chanaan (Espiríto Santo), Lauro Sodré (West Amazonia), in farms of Santa Rita, Umburana, Brasileiro (Ilhéus, Bahía), Coronel Ponce (Matto Grosso), Marajó Island, West Minas, South Goyaz and north of São Paulo (including the Sorocabana zone—Presidente Wemceslau and Cayuá), in Brazil, that scientists came to realize the danger of the jungle type of yellow fever and to understand certain aspects of the disease, which had previously been obscure.

Jungle yellow fever may be summarized as follows:

Jungle yellow fever is quite different epidemiologically from the urban variety. It has no connection with the latter type yet jungle yellow fever serves as a permanent source of infection for the rural, and even urban, zones whenever the index of *A. aegypti* is favorable.

Jungle yellow fever is an endemic disease; many vertebrates of the jungle (rodents, marsupials, monkeys) may serve as virus reservoirs.

Jungle yellow fever is not transmissible by *A. aegypti*, but it is by several species of wild mosquitoes (*Psorophora, Mansonia, Eretmopodites, Haemagogus*), by the *A. fluviatilis, A. leucocelaenus*, and, especially, by *A. scapularis*, which last shows a strong tendency to grow as a domestic species.

Contrary to the urban modality which is a thermophilic infection, endemic jungle yellow fever does not depend on the temperature, as the virus will maintain itself, and even increase, at a temperature below 15° C. (59° F.).

Jungle yellow fever may be considered an occupational disease, since it attacks almost exclusively those working in the jungle—males between the ages of 14 and 40 years.

As is the case with bubonic plague, cases of jungle yellow fever are generally preceded by an epizoötic among monkeys of different species (*guaribas* and *bugíos*). This aspect of the disease was observed long ago in Brazil and has become part of its folklore.

The virus is inoculated during the day and not at night as in urban yellow fever.

Jungle yellow fever may be considered an infection of the lower vertebrates which later became adapted to man. In its phylogenetic evolution it probably preceded the rural and urban varieties.

Jungle yellow fever is possibly less fatal than the urban or rural varieties, but this assertion has not yet been definitely proved.

The virus can also be probably transmitted by the feces of the mosquito when this is killed against the skin of a nonimmune person.

Man is the main agent in the propagation of yellow fever among the human species.

The fact that jungle yellow fever represents a reservoir from which adjacent rural zones may become infected, and the further fact that troops or other individuals, passing through the jungle, may carry the infection, makes this type of yellow fever extremely important from the epidemiologic point of view. The seriousness of the problem is in direct relation to the increasing facilities and to the rapidity of means of travel between rural zones, adjacent to jungle areas, and distant urban centers that are in communication with them.

SUMMARY AND CONCLUSIONS

Present day knowledge of yellow fever may be summarized as follows:

Yellow fever is an acute infectious disease caused by a filtrable virus and manifesting itself, in typical cases, by a relapsing febrile syndrome of rather short duration and serious course characterized by jaundice, albuminuria, asthenia, and hemorrhage.

Yellow fever may be of the urban and rural or jungle type.

Yellow fever is transmissible not only through the bite of several Culicidae, besides the well known *A. aegypti* that seems to be the only vector in urban centers and the main one in rural zones, but also by the feces of the vector when it is killed against the skin. (Infection of monkeys by the ingestion of ticks and other arthropods is a possibility that must be borne in mind.)[3]

Certain species of mosquitoes may transmit the disease in less than twelve days after they have become infected, if the insect is killed against the skin of a nonimmune person.

Certain species of mosquitoes must be accepted as possible vectors, though the presence of the virus in the salivary glands has not yet been demonstrated.

Primates, marsupials, rodents, and perhaps other vertebrates of the jungle, serve as virus reservoirs; different species of diptera and arthropods (ticks, for example) act as vectors in the jungle.

Man is a very important link in the epidemiological chain of urban and rural yellow fever infection, but not in that of the jungle variety, which is an endemic infection of the lower vertebrates.

Experimentation has proved that mosquitoes may become infected when placed together with mosquito vectors of the virus, and

3. H. Aragão, Epidemiologia e Prophylaxia da Febre Amarella, p. 24, 1937.

that infected mosquitoes may transmit the virus to their offspring. This last finding, however, may not necessarily be true under natural conditions.

The fact that no clinical cases are known to occur in a given region at a given time does not necessarily mean that yellow fever is absent from that community but only that no epidemic has broken out.

Besides the clinical examination, the following means may be utilized for the detection of yellow fever:

Microscopic examination of liver tissue obtained from fatal cases at autopsy or with the viscerotome. (Histologic examination of the kidneys may be also of value);

Protection tests by intracerebral inoculation of mice;

Xenodiagnosis utilizing uninfected *A. aegypti;*

Inoculation of rhesus monkeys with the blood of suspicious cases not later than the fourth day of illness, but preferably on the third.

Urban and extra-urban yellow fever are but modalities of the same disease. A clinical diagnosis is not always possible because of inapparent infections and abortive and atypical forms.

The treatment can only be symptomatic since there is no known specific drug (serum of convalescents is not as useful as may be expected).

Even though mortality may be as high as 50 percent in urban outbreaks, it is probably not higher than 10 or 20 percent when the different types of yellow fever and those inapparent, abortive, or undiagnosed cases are included in the computations.

At present the populations of the interior, especially those living close to jungle areas, are much more exposed to yellow fever than the ones along the coast or in large cities.

Prophylaxis should be instituted as follows:

(a) Public health authorities must be relentless in their fight against *A. aegypti* in an attempt to keep its index at less than one. This will soon be possible in Brazil. There are already states like Maranhão, Minas, Matto Grosso, Goyaz, Espiríto Santo, Parañán, Santa Catarina, and the Distrito Federal, where this species is no longer found.

(b) All patients and suspected cases should be kept under netting or in screened rooms at least during the first three or four days of illness, while the virus is still in the peripheral bloodstream.

(c) During epidemics all of the population should use mosquito netting or screen their homes and bedrooms.

(d) All persons working in jungle areas, as well as dwellers of adjacent rural areas, should be vaccinated. Vaccination of inhabitants is compulsory in rural areas where it may be impossible to eliminate the vector. Tourists, troops, and other persons who may have to visit jungle areas should not be permitted to do so unless they are immune or have been previously vaccinated.

(e) All means of transportation, such as carriages, automobiles, boats, and airplanes, coming from, stopping in, or passing near endemic areas, including infected jungle areas, should be carefully disinfected. Since 1937 Pan American Airways has been taking the following precautions:

Vaccination of all members of airplane crews;

Issuance of certificates of origin to all passengers, said certificates stating starting point, destination, and stops with respective dates, name of the localities visited during the previous six days before starting on the trip, and so forth. (These certificates are not required of those who have already had yellow fever or who have been previously vaccinated);

Disinfection of all airplanes.

Not only sanitary authorities and physicians but also military officers and the people, in general, should be kept informed at all times regarding means of prevention in those countries where the disease is still considered a public health menace.

We might close with the words of the well-known authority on yellow fever, Dr. Fred Soper, of the International Health Division of the Rockefeller Foundation, "The time has come when the occurrence of cases of yellow fever due to transmission of *Aedes aegypti* should be considered a public health crime reflecting on the competence of health authorities."[4]

4. F. L. Soper, Jungle yellow fever. A new epidemiological entity in South America. Rev.de Hyg.e Saude Publica, Rio de Janeiro, **10**:107–144, 1936.