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YELLOW FEVER IN CENTRAL AMERICA

The Post-War Spread as a Threat

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Among the triumphs which man occasionally shows in his relentless fight against the powers of a hostile environment, few have had more decisive historical repercussions over a wider geographical area than that which followed Carlos Finlay's trail-blazing discovery. Perhaps with the exception of plague, no scientific finding has ever resulted in such efficient, definitive methods of prevention.

The success of the campaigns which were undertaken, once the new notion of the insect vector was established, changed the destiny of the tropics: it allowed its inhabitants to plan their lives without the reservations which in the past the ever-existing possibility of the yellow fever epidemic imposed upon them. An era of optimism began, substantiated by the fact that the great tragedies of previous centuries became more and more rare. A few mysterious outbursts (happening away from the coastal areas or in the absence of any known source of contagion) failed to shake the belief that, by keeping the *Aedes aegypti* population below certain defined limits, the probability factor of urban epidemics was reduced to negligible proportions.

It was not until the discovery of a new epidemiological and epizootical mode of the disease that some dogmatic assertions had to be re-examined. On the one hand, the suddenly revealed evidence of permanent sources of infection in the forests of Africa and South America, and on the other hand the increase (both in speed and in intensity) of human traffic brought by air transportation, suggest that this is an opportune moment to reconsider some notions about preventive measures.

In the face of a permanent local and international menace, incomplete measures of partial control are perhaps no longer adequate. The probability factor is entirely different from that which might depend on intermittent infectious foci. And it has become dangerous, up to a certain point, to rely for one's safety on control measures taken by neighboring nations.

The past few years have emphasized the validity of this point of view. An unexpected epidemiological episode has shown to what extent conditions (believed until then to be limited to a specified geographical region) may suddenly break out and endanger other regions until then happily dozing in a state of false security. I am referring to the Middle American wave of yellow fever, which it is my purpose to relate briefly here. I shall endeavor to integrate it into the long story of which it is nothing but a chapter, and to underline the lessons which can be drawn from the observation of its course.

The theater of this event: the tropical rain forests and the deciduous forests of Panama, Costa Rica, Nicaragua and Honduras. The time: late 1948 to mid 1954.

Prior to 1948, there was evidence from immunological surveys of sylvan yellow fever in humans in the area east of the Panama Canal. On the other hand, the results of the surveys conducted west of the canal were interpreted as indicating the absence of the sylvan form of the disease in Middle America.

The first confirmed case of yellow fever west of the Canal occurred in January 1950. In April 1951 further cases were reported from Almirante, close to the Costa Rican border, and throughout that year the disease spread out in that country. In July 1952 confirmed cases occurred at the headwaters of the Rama river in Eastern Nicaragua.

From the beginning of the occurrence of human cases, a heavy mortality had been observed among the simian population of the countries involved. Livers of specimens pertaining to the genera *Alouatta* (howler monkey) and *Ateles* (spider monkey) found dead in the forest showed specific lesions of yellow fever. The primate fauna was virtually exterminated, with the exception of monkey species of the *Cebus* genus, which is susceptible to yellow fever, but survives the disease. The observation of manifestations among the monkey fauna became therefore the most efficient way of following the trajectory of the phenomenon, especially when it traversed large sectors of uninhabited forest.

Surveys of monkey immunity afforded good indications as to the immediate history of the region and permitted in certain cases to predict the future. The usefulness of this observation was enhanced by the fact that intense campaigns of vaccination were undertaken by the countries involved, with the result that human cases became more and more rare as the wave progressed towards the north.

As it reached Nicaragua the wave split in two fronts; one of them progressed through the deciduous tropical forests situated west of Lake Nicaragua, the other invaded the tropical rain forests of the East. The progression of these two waves was not comparable, since the seasonal and climatic conditions are different in the two geographical areas. Whereas the Pacific slopes

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of the West are in the theater of prolonged dry seasons lasting from October to May, the forests of the East show only a short interruption in the yearly curves of rainfall. Whereas the mosquito fauna of the West disappears for several months, in the East specimens of known vectors are to be found throughout the year. As was to be expected, the progression of the wave in the latter region was a continuous and uninterrupted phenomenon; on the Pacific side, on the contrary, there was at least one interruption in the course of the wave; it coincided with the disappearance of mosquitoes in the first months of 1953; the infection remained latent under conditions not yet quite clear and to be discussed later. Following the onset of rains, monkey mortality started anew at the very place where it had stopped several months earlier, and the local wave progressed northward for a while and died in the vicinity of Managua at the end of the same year. To the East the virus invasion raged along the foothills and headwaters, reached the Patuca valley and, by December 1953, emerged into Honduras, at the headwater of the Guampu, a northern affluent of the Patuca. From there on, it progressed during the first half of 1954 in a northerly and westerly direction, the wave reaching the Ceiba zone through Piedras Amarillas and Yaruca. In May, June, July and August, monkeys were dying on the flats of La Masica, Benque, and San Francisco, on the northern side of the coastal mountain range. The last positive monkey liver was obtained from that region in mid-August. No further evidence has been obtained north or west of that region, and it would seem now that the wave is stalled for the time being. Nevertheless, the experience gathered in Nicaragua (where, as we said before, the virus survived under incredible conditions for several months) makes one reluctant to utter a categorical affirmation, even at this stage, as to a possible cessation of the epizootic outburst.

A few special features of this episode should be pointed out, not simply for their historical interest but because of the conclusions which may be drawn from a series of facts peculiar to the ecology of the regions. These facts may throw a light on other epidemiological manifestations, not limited to Middle America and not restricted to the natural history of yellow fever. The features are related more especially to problems of transmission, extension and permanence of the virus and therefore come under two principal headings: Characteristics of the animal population, and characteristics and behaviour of the known and hypothetic vectors.

With regard to the animal populations involved it may be stated that never in our time, or in the time of our precursors, has a phenomenon of the intensity observed between 1949 and 1954 in Middle America been recorded. Two principal factors contributed to this. First was the fact of a universal susceptibility of the primate population (as suggested by the results of immunity surveys conducted west of the Panama Canal among sylvan humans). Secondly, there was the fact that the predominant species of this part of the world are extremely vulnerable to infection and non-resistant to it. A third

condition existed which certainly contributed to make the manifestations more dramatic and spectacular: the extraordinary density of the primate population in Middle America before the passage of the wave. One fact can give an idea of the numbers of those animals which could be found: preliminary immunity surveys conducted ahead of the wave allowed us to collect on several occasions over a hundred sera in five or six days (a record never attained in the forests of South America), and led us to the conclusion that these forests had not been visited by the virus for a very, very long time, in contrast to South America where the susceptible monkey populations are constantly whittled down by the enzoöty and are, therefore, reduced to scanty numbers of immune survivors.

To a large extent, these circumstances account for the massiveness, acuity and speed of the phenomenon; also, for its relatively short duration. It is well known that the proportion of insect vectors which become infected on a given animal is in direct relation to the titer of virus circulating in the infective host. It is further a well-known fact that highly susceptible animals such as the *Alouatta* and *Ateles* genuses multiply the infecting virus and carry it in high concentrations in their peripheral circulation for several days. A virus wave hitting any population of such animals has more chances to spread rapidly and extinguish itself for lack of fuel than if it had met another type of animal population, composed of less susceptible individuals, that is of less efficient infective hosts. This is important when we evaluate a given zone as to its endemic potentialities. The presence of animal species whose susceptibility is irregular and of low grade may be much more important from the standpoint of endemic permanence than the existence of populations of high susceptibility which can be instrumental in the outburst of spectacular manifestations, but which are not adequate to keep the menace latent for long periods—or forever. These remarks are not necessarily limited to yellow fever, but may well be extended to other infectious diseases.

Analogous considerations may apply to the vector problem. Theoretically, a highly efficient vector species may be defined as a species which, upon exposure to infection when biting an infected host, shows a high proportion of infection among the specimens exposed, with, consecutively, a short period of incubation for the transmitting ability to develop. Such a vector will have more probabilities to determine acute epidemiological or epizoötical accidents than a mediocre vector species, that is than one whose proportion of infection is lower and whose period of incubation is longer. Conversely, the mediocre vector is more liable to produce latent, prolonged, and occasionally ignored phenomena by killing or immunizing the susceptibles with slow tempo; and eventually, in the case of certain animal species, permitting their ranks to replenish before the process wears out. A combination of the ideal host with the most efficient vector is bound to provoke short-lived epidemic explosions. A combination of the mediocre host with the inefficient vector may well be the cause of prolonged endemic situations. It is not inconceivable that inter-

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mediate conditions may arise, and one state evolve into the other. All this seems rather obvious; and yet what an ingrained tendency there is among researchers to ignore or give scant consideration to animal hosts or insect vectors when the results obtained from them by experiment or by observation in nature are not clear-cut and spectacular!

The Middle American yellow fever wave, for one, appears to have been the result of a perfect combination of efficiencies. At a certain moment, at a certain place, three factors coincided: first, the infective agent—the yellow fever virus—hitting the Panama Canal in one of its periodical excursions out of the big South American reservoir. Second, the vector; fluctuation studies in mosquito fauna which were being conducted at the time by workers of the Gorgas Memorial Laboratory show a peak instant in a record year. Third, a dense and highly susceptible population of primates. The fire caught, covered eight hundred miles in less than five years.

Concerning the identity of the vector or vectors of Middle America, it is not within the scope of this paper to enter into taxonomical discussions or entomological long-drawn considerations. But we should mention the fact that, of the known tropical sylvan yellow fever vectors, three exist west of the Panama Canal as far as the Costa Rica-Nicaraguan border: *Haemagogus spegazzinii falco*, *Haemagogus equinus*, and *Aedes leucocelaenus*. The latter species disappears as one enters Nicaragua. As far north as the northern coast of Honduras and as far west as the Tela meridian (over 87° W.), the two former species persist. Then *Haemagogus spegazzinii* disappears, leaving *equinus* as sole representative of the tropical fauna. It is, I think, relevant here to mention a few facts concerning this interesting species. Its ability to transmit yellow fever by bite was demonstrated in Brazil under laboratory conditions. However, it has never been found infected in nature. In Colombia, at the experimental station of Volcanes, Caparrapi, it was found in small numbers in an infected area, together with *Haemagogus spegazzinii*. Several groups of the latter, ground up and inoculated intracerebrally into mice, showed a considerable amount of virus, whereas the *equinus* groups failed to show virus. A rhesus monkey bitten by over a thousand of these mosquitoes in a locality of Nicaragua where monkey mortality has been recently observed, did not show any sign of infection and failed to become immune. The fact that *Haemagogus equinus* is a universal mosquito which can be found at different altitudes, sometimes under severe and adverse conditions, had in the beginning led us to discard it as a potential vector, its universality being in disagreement with relatively localized manifestations. Then it was found, under laboratory conditions, that a great proportion of *equinus* do not have a life span compatible with the virus evolution, and die before the optimum incubation time is completed. All this seems to indicate that *Haemagogus equinus* may well be endowed with the characteristics which we ascribed to the theoretical "inefficient vector." I should like to add that this mosquito was present at the time and place where virus survived in Nicaragua

during the dry season of 1952-53. It is also present in Colombia, in some mysterious endemic areas where virus persists year after year, as shown by fatal human cases; areas of heavy human settlement where the simian population has been destroyed or reduced to such small proportions as to make it negligible as an epidemiological factor. Incidentally, those areas are densely populated by five genera of semi-domestic marsupials; of these, four (*Metachirus*, *Didelphis*, *Caluromys*, *Marmosa*) have been experimentally shown to be susceptible to yellow fever and many of their specimens have been found immune in nature in endemic areas. Muzo, Caparrapi, and San Vicente de Chucuri, in Colombia, may well be instances of the "combination of inefficiencies" which we mentioned above.

Other possible vectors of the *Haemagogus* genus and of the Sabethine tribe exist throughout Middle America and should be mentioned here. In Costa Rica and Nicaragua, we have *Haemagogus mesodentatus*, *Haemagogus irridicolor* and *Haemagogus anastasionis*. As one progresses towards the North, *mesodentatus* persists, and new forms appear. They are new to science and are at this moment being studied under laboratory conditions at the Gorgas Memorial Laboratory. About their ability to transmit yellow fever we can only conjecture. But we are in possession of a few facts which are highly suggestive. They appertain to the history of sylvan yellow fever in ancient times, towards the end of the last century, and in the first years of this one. In his article "Anticipated Progress of Yellow Fever in Guatemala and Mexico, 1955-59," *American Journal of Public Health* (vol. 45, number 7, July 1955) Colonel Norman W. Elton states: "Not only was the Mayan Empire swept by sylvan yellow fever in 1484, as indicated by the epidemic of 'xekik' (bloody vomiting) to which reference is made in the Books of Chilam Balam of Chumayel and Chilam Balam of Tizimin, but this form of the disease has also been noted in northern Guatemala early in the 20th century." Sanchez reports credible accounts of the ominous silence in the forests of the Verapaces due to the annihilation of the howler monkeys by yellow fever in 1901, followed by a great epidemic in that same region in 1902. Gaitan records an outbreak of the sylvan form close to the Hondurian frontier in the Motagua Valley of the Department of Izabel, in the vicinity of Los Amates, in 1920.

One of the best accounts of the antiquity of yellow fever in Mexico is given by Connor who recognized areas of endemicity, such as Campeche, Tabasco, Veracruz, the Valley of the Papaloapan, Ticul, and the vicinity of Mérida. He noted the frequency of the disease among the population of the upland regions, such as the Oaxacan hills, only after migration to the lowland river fronts. These people, as related in the chronicles, were free from the disease until they visited the coastal areas to make war or engage in the harvest. Carter, rather skeptical because he did not believe yellow fever could exist in the absence of *Aedes aegypti*, nevertheless comments on the periodic repopulation of the coastal areas by order of the Montezumas because of epidemics which at times wiped out the population of the lowlands. This was

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primarily the "matlazahuatl," characterized by the vomiting of blood and other manifestations of a hemorrhagic diathesis, which was carried back even into the highlands.

The supposition of epidemics having occurred in 1901 and 1902 and prior to that is substantiated by the few positive sera found by Bustamante in 1942 in the upper Usamacinta among the 40-49 as well as over 50 age-groups. Moreover, we were able in one particular instance to gather first-hand and precise information from an old man (now living in Flores, Peten) about the occurrence of a heavy monkey mortality which coincided with a human epidemic in the Guatemalan Peten. This information was obtained when we were beginning to despair of getting anything but legends and contradictory second-hand rumors, after having systematically interviewed all the older persons in different localities. One of our guides told us of an 82-year-old man, Felix Castellanos, who used to evoke in the family circle a tragic episode of his childhood. This took place when he was ten years old (therefore around 1882). He had accompanied his father to a lumber camp established by a Guatemalan and Mexican concern at the mouth of the river Lacantun, where it falls into the Pasion river. Labour in those days was recruited in Tenosique, and the crews, with their families, were driven on foot across the big plain to Libertad, Sayaxché and to the Rio Pasion, under conditions very similar to slavery. Roughly one month after the arrival of one of these contingents, while the camp site was still being cleared, people began to die. They were seized by a terrible fever, vomited "black ground coffee" and in the following days became intensely yellow. This man lost his two brothers and a sister in that manner.

The camp was abandoned by most of the terrified survivors. One day the boy was alone, nursing his sick siblings, when through the door of the hut he noticed a band of howler monkeys, which usually came to a guanacaste tree (*Higuronia*) close to the camp. Suddenly he was amazed to see one of the monkeys drop to the ground. Soon after, another fell from the tree, and this continued to happen throughout the day; the monkeys hung on to the tree for a while, then dropped, or else they fell while trying to move on the limbs of the tree. When his father came back from the forest, in the evening, the boy told him what he had observed. "Of course," answered the lumberman, "this has been happening for some time in the forest. The whole place reeks with the stench of them."

The old man still has a vivid image of the dying monkeys, which, as he relates it, is associated in his mind with the death of his siblings and other companions. I was able to verify this last August when I succeeded in contacting Felix Castellanos, and I heard him repeat a description of the incidents consistent with the second-hand story previously recounted to us. He struck me as being in full possession of his faculties.

I have placed what might seem an exaggerated emphasis on the history

of the Peten for several motives. In the first place it is reasonable to assume that an epidemical occurrence, given similar ecological conditions, may repeat itself. Now this region, remarkable for its geographical isolation, has scarcely changed since 1882, with the exception of its recent contacts with the outer world by air. To the southeast, the destruction of forests and the intensification of cultivation in the Motagua and Ulua valleys may perhaps have rendered more difficult the invasion of a sylvan epizoötic coming from the South. However, the possibility of its happening is not excluded. A yellow fever invasion of the Peten should open singular possibilities. It would mean, in the first place, that the various *Haemagogus* species present in its forests are very probably efficient vectors of the disease. These species, including *Haemagogus equinus*, have a wide range of distribution in Mexico and Belize. Particularly, the range of *equinus* has been recently found by workers of the Gorgas Memorial Laboratory to include the region of Brownsville, Texas. The epidemical and epizoötical consequences are easily seen. Nor would this state of things be a mere temporary menace. It is fully conceivable that the system of forests existing in this vast area may well harbour latent and rampant infections over a relatively long period. Apart from monkeys, in the Peten we have the very genera of marsupials which are strongly suspected of playing a role in the permanence of yellow fever in certain areas of Colombia. It is true that up to now, and with the exception of a positive *Metachirus* serum obtained in an epizoötic area of Nicaragua, there has been no evidence that the Middle American invasion may have affected the marsupials. Nevertheless, since the program of studies which was undertaken by us did not include a thorough investigation of this problem, we cannot afford to discard possibilities of this kind.

Conditions exist, therefore, of such a nature as to transform the forests of Peten, Belize and Mexico into a potential reservoir of infection.

All these facts lead to one all-important conclusion: the yellow fever threat has not disappeared from this hemisphere. As long as virus will persist in the big South American reservoir, as long as there persists the possibility of its periodical irruption into adjacent areas—such as happened from 1949 to 1954 in Middle America—the danger is there of epidemic outbursts in communities which still present the veritable anachronism of harbouring *Aedes aegypti*. The methods of control which followed Carlos Finlay's discovery reduced this danger to proportions which made life possible for urban populations where the awareness of the mosquito importance stimulated constant surveillance and where reduction of the indexes was maintained below a certain level. But the cessation of the dramatic episodes of the past produced as an understandable consequence a tendency to negligence in certain quarters. Permanent and rigorous measures of control in one place lose much of their efficiency when a neighbour is not as conscientious. Apart from that, any control which is based on indefinite routine procedures sooner or later is bound to slip; especially so in localities where public spirit has not attained the de-

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sirably high level of development, and where adequate personnel cannot be found in sufficiently large numbers. Moreover, permanent control measures are a constant drain on Public Health budgets, and the surveillance which they entail can never relax, nor is it possible to contemplate its abandonment in the foreseeable future. Several urban epidemics which occurred in South America long after the Finlay doctrine was demonstrated provide ample confirmation of this assertion.

The means at our disposal today have opened a new chapter in the history of the fight against epidemical hazards. It is possible now to envisage more radical measures and to set more definite goals.

The results which have been made possible by the advent of the chemical age in the warfare against insect pests can confine forever the everlasting menace to its sylvan boundaries.

The eradication from the Americas of the urban vector of yellow fever can be viewed as the logical and ultimate consecration of Carlos Finlay's work. And it will constitute the most eloquent tribute to his memory.

