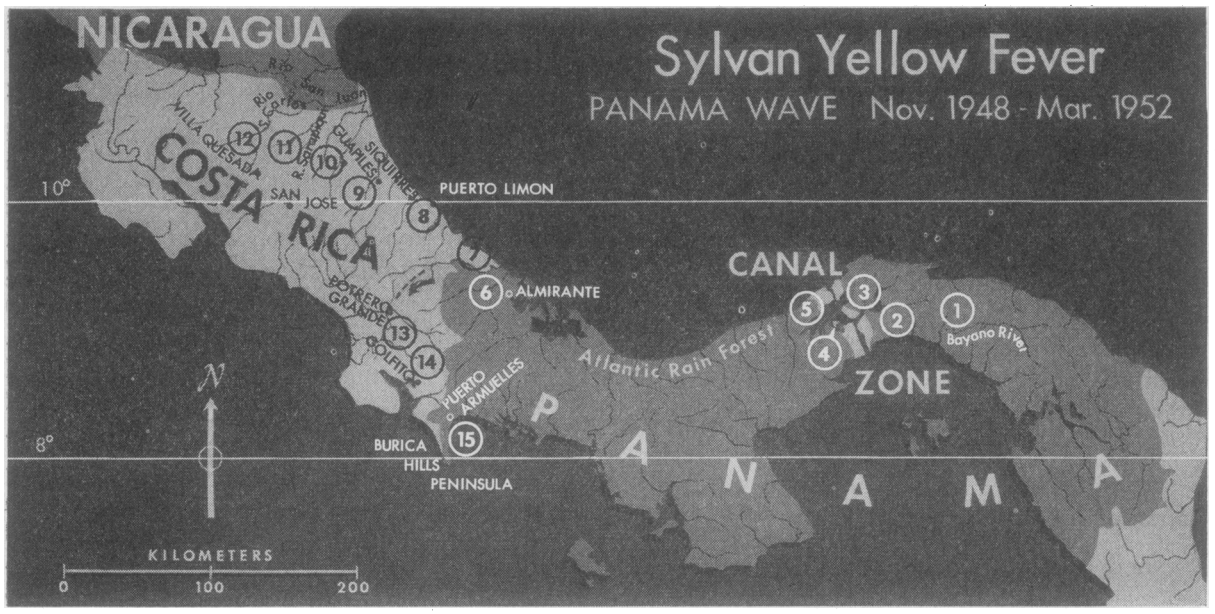

Sylvan Yellow Fever *in* Central America

By NORMAN W. ELTON, M.D.

A dramatic episode in the history of medicine is now being enacted in Central America. A wave of jungle yellow fever has moved from the long-established enzootic region of eastern Panama to the forested plains of northern Costa Rica, progressing some 450 miles since November 1948. In its wake it has left 41 proved human fatalities among the farming population, 8 in Panama and 33 in Costa Rica. Complete autopsies have been performed and the cause of death confirmed by several laboratories.

The velocity of this wave is only 12 to 15 miles per month, following a pathway delineated by forest continuity, tree-top mosquitoes, and arboreal mammals (especially the primates). Although advance areas in its projected path have been repeatedly alerted to anticipate its arrival—since the recognition of its existence as a wave in January 1950—sporadic cases and epidemic outbreaks have continued to occur in spite of control measures.

The wave appears to move in halts, by insidious infiltration, and in bursts, depending on natural conditions. Although their nature is still poorly understood, these movements are undoubtedly based on population density and

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Epidemic Centers and the Path of the Wave

The valley of the Bayano River ① and the region east of it have been recognized as an enzootic area for sylvan (jungle) yellow fever since 1929 (see map).

The Pacora area ② in November and December 1948 was the site of five fatalities among the farming population. These deaths may have been due to yellow fever. Histologic examination of the liver proved yellow fever to be the cause of death in two cases; in two others no liver tissue was saved for histologic study; and the remaining case exhibited an atypical liver lesion which was not diagnostic.

In August and September 1949, while it was still not realized that a yellow fever wave was in progress, three fatalities in which the typical liver lesion was confirmed occurred in the Buena Vista area ③.

In Gatun Lake, Barro Colorado Island ④, established in 1923 as a government reservation and wildlife preserve, is the home of about 30 clans of howling monkeys, which are particularly susceptible to yellow fever and suffer a high mortality. Early in 1951, studies indicated that some epizootic, probably shortly after the dry season of 1949 (January–April), materially reduced the population of these monkeys.

A human fatality from yellow fever occurred in the Chagres District ⑤ west of the Canal Zone on the Atlantic side in January 1950 and the pattern of the wave was recognized for the first time. Within 2 months the Minister of Public Health of Costa Rica was informed through diplomatic channels that the wave could be expected to reach Costa Rica in from 14 to 18 months. At the same time a fruit company subsidiary at Almirante ⑥ was alerted to watch for the wave after it had passed along the sparsely inhabited Atlantic rain forest.

Autopsy tissues, received in April 1951, confirmed the diagnosis of yellow fever in a chainman engaged in a highway survey in the forest about 10 kilometers west of Almirante. Within a week after this diagnosis was made, an intensive vaccination campaign was initiated in Costa Rica.

In June 1951, the virus of yellow fever was isolated from the serum of a patient admitted to the Almirante Hospital from a Costa Rican farm just across the border near Nievecita, Panama ⑦. This patient recovered.

Heralded by an initial fatality near Puerto Limon ⑧ on July 24, 1951, epidemic jungle yellow fever developed with explosive violence along a 100-mile front in Northern Costa Rica involving five epidemic centers ⑧ ⑨ ⑩ ⑪ ⑫ in rapid succession and almost simultaneously. These were as follows:

Epidemic center	*Proved fatalities*	*Date of first and last fatalities*
Puerto Limon	2	July 24; Aug. 1.
Pacuarito-Siquirres	3	Aug. 12; Aug. 20.
Roxana-Guapiles	3	July 27; Sept. 9.
Sarapiqui watershed	19	Aug. 13; Sept. 30.
San Carlos watershed	6	Aug. 19; October.

Early in October 1951 reports of the finding of many dead monkeys in the vicinity of Potrero Grande ⑬ were confirmed by the Director General of Public Health in Costa Rica. Panama was promptly informed. At the same time a serum specimen from a patient from this region, convalescing from clinically suspected yellow fever, reacted positively to the mouse protection test. Although skeptical about the significance of these findings, because of the high elevation of the continental divide in this region, an intensive revaccination campaign was immediately undertaken in western Panama on the Pacific side.

In January 1952, the Director of Public Health of the Republic of Panama was informed by Costa Rica that a mine laborer from the Coto District ⑭ had died in a Golfito hospital and a diagnosis of yellow fever had been histologically confirmed.

On February 10, 1952, a 23-year-old resident of the Burica Hills Peninsula died at a Puerto Armuelles hospital ⑮. This peninsula is hilly, forested, and populated by howling monkeys. The diagnosis of yellow fever was confirmed by two laboratories and the Armed Forces Institute of Pathology.

The probable location of the crossing of the continental divide is indicated by the arrow above Potrero Grande ⑬ where there is a heavily traveled trail leading from the Talamanca District on the Atlantic side to the valley of the Cabagra River on the Pacific side. Since the lowest elevation in the divide is between 5,000 and 7,000 feet at this point, it is considered likely that the virus was introduced, in May or June 1951, into the Pacific forest by a migrant farmer from the Atlantic side.

This offshoot of the main wave may move eastward after 2 or 3 months of rainy season (July–August 1952). It is now also moving northwest up the Pacific coast of Costa Rica as a secondary wave.

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terrain and seasonal factors, as well as on the efficiency of vaccination campaigns. During the past 3 years the wave has swept successively westward across Panama and Costa Rica, and has crossed the continental divide to the Pacific side of southern Costa Rica, threatening to return eastward through the Pacific watershed of Panama. There is no indication as yet that the main wave can be expected to stop until it reaches the forests of Vera Cruz and Tampico in Mexico.

At first glance the control of sylvan yellow fever seems simple, involving vaccination of the rural population as merely an administrative

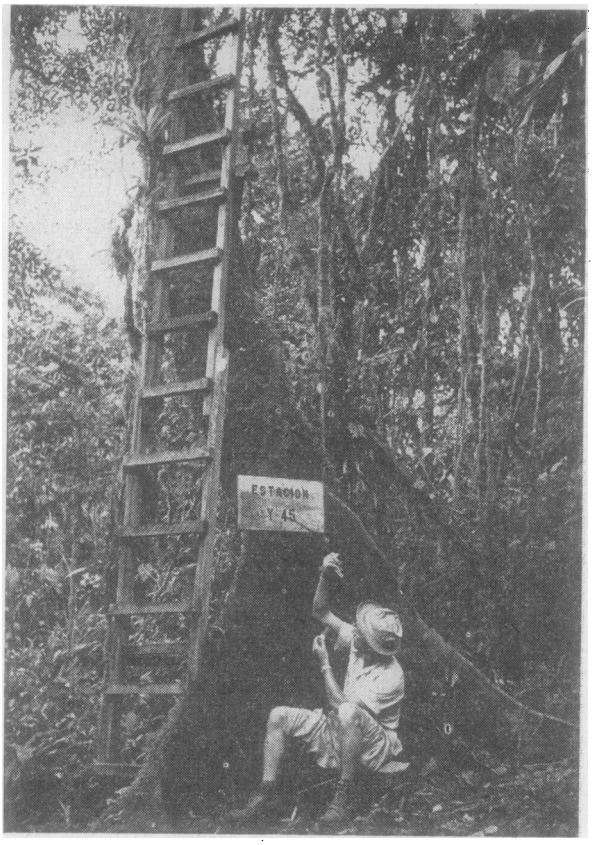
matter. Experience has clearly demonstrated, however, that this is not easily accomplished. Although the Dakar (mouse brain) and 17 D (embryonated) yellow fever vaccines rank among the most efficient ever developed for the prevention of any disease, there are numerous factors that contribute to failure in the field. Improper storage of the vaccine may cause rapid loss of potency. The vaccine must be kept in a deep-freeze until issued for immediate use, for even while still within the ampule it cannot be expected to stand up under ordinary environmental temperatures longer than 1 or 2 weeks. When the ampule is opened, its contents must be used within an hour.

Swollen streams, muddy trails, dispersion of habitations, and even deliberate concealment of habitations in isolated regions contribute to the difficulty in gaining access to the farmers of the agricultural areas of the forest. Cooperation and understanding on the part of the farmers themselves is being obtained but is not yet fully achieved. Preliminary educational campaigns and the establishment of vaccination stations scheduled to open for operation on specified dates are necessary. Helicopters facilitate the reaching of isolated localities, and when the people are properly informed, their signal fires, spontaneously prepared when neighborhood groups assemble, attract the helicopter to unscheduled landings. The tremendous morale effect of the helicopter used for this purpose has been demonstrated in Costa Rica (*3*).

Complacency in yellow fever control would breed disaster for the farming population. Even in Costa Rica, where the epidemic was anticipated months in advance, the outbreak placed a severe strain on the facilities of the health department and the hospitals. Had the country not been prepared, the episode might have been a holocaust. Brazil, which has been working on the control of this disease since 1932, reported 400 deaths and more than 3,000 clinical cases in the recent great epidemic of 1950. Jungle yellow fever easily can be dangerously underestimated.

Epidemiology

Jungle yellow fever, except in its epidemiology, is the same disease as urban yellow fever.



In studies on the mosquito vectors of jungle yellow fever, human subjects are stationed on the forest floor and also on platforms in the canopy. The subject is placing a catching tube over a mosquito feeding on his arm. The ladder leads to a platform 45 feet up in the canopy where a second subject is making simultaneous catches (photograph by Dr. Harold Trapido).

It occurs, however, in rural areas, and involves mainly the farming population. In the Western Hemisphere it is known as "woodcutters' disease," since it is transmitted by the tree-hole-breeding mosquitoes of the forest canopy. These mosquitoes are most active around midday, and descend to ground level at the edge of the forest or in cultivated clearings, roadways, or riverways. Working in these clearings or felling trees to enlarge a farm are hazardous undertakings when the canopy mosquitoes are infected. One of the principal vectors in Brazil is *Haemagogus spegazzinii falco* Kumm, a tree-top mosquito, which has been found to be present in Panama and Costa Rica (*7*).

Until the discovery of jungle yellow fever in 1932 (*16*), the sylvan and urban forms were epidemiologically indistinguishable to histo-

rians. Reorientation is essential before proper historical interpretations can be made. Urban outbreaks have been known to originate, through a chain of infection, from the sylvan form of the disease: natives infected by the forest mosquitoes transmitted the infection to the *Aedes aegypti*, known since 1900 as the vector of the urban form. The reverse procedure might just as readily have originated sylvan outbreaks in the past, the disease being transmitted from urban foci in port settlements.

One of the transient reservoirs of the virus is known to be present in the arboreal primates (monkeys and marmosets), and such a reservoir may also exist to some extent in other arboreal mammals. Although certain species of the tree-top mosquitoes, such as *Haemagogus spegazzinii falco* Kumm and *Aedes leucocelaenus*, are known to be vectors of the virus, other possible insect vectors are also being studied.

Ladder and platform in the forest canopy where *Haemagogus* mosquitoes, vectors of jungle yellow fever, are caught as they attack human subjects. There are large seasonal fluctuations in the numbers of these mosquitoes. Long-term studies of them are being made by the Gorgas Memorial Laboratory in Panama and Central America (photograph by Dr. Harold Trapido).

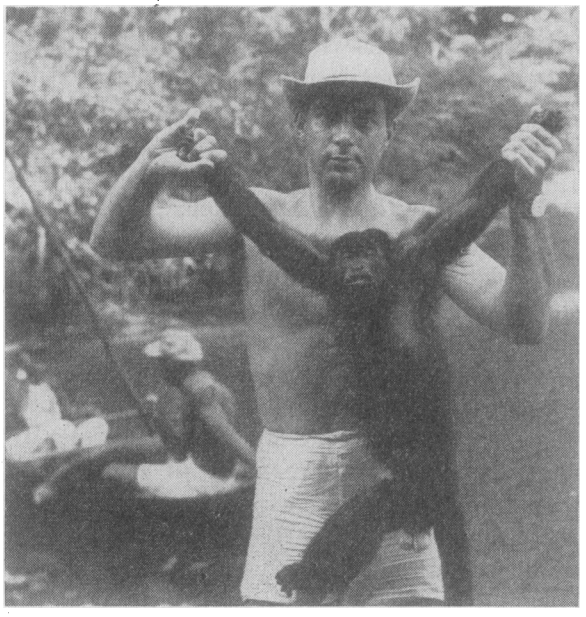
Sylvan yellow fever is primarily an enzootic or epizootic disease of the forest, with a high mortality for howling (*Alouatta*) monkeys. In fatal cases, these monkeys exhibit a liver and kidney pathology parallel to that found in rhesus monkeys and in man. During the recent outbreak of the disease in Costa Rica, specimens were studied from four howling monkeys, either shot or found recently dead. The kidneys exhibited a fully developed hemoglobinuric (lower nephron) nephrosis like that found in the human fatalities in Panama. The liver specimen from a monkey which was shot because it seemed ill exhibited the same type of convalescent yellow fever lesion encountered in rhesus monkeys during recovery after experimental infections. Of the other three liver specimens, two presented the classical, acute-phase liver lesion very much like that seen in man, and the third presented an acute lesion resembling that seen in experimentally infected rhesus monkeys. These diagnoses were made or confirmed at the laboratory of San Juan de Dios Hospital in San José, Costa Rica, and at the Board of Health Laboratory, Ancon, C. Z. The specimens are now among the accessions of the Armed Forces Institute of Pathology. The complete report on these wild "Vargas monkeys," in which the typical liver lesion of naturally acquired yellow fever has been observed, will be made at a later date.

Associated with the epizootic phase of jungle yellow fever, either simultaneously or lagging behind it by several weeks or months, is the epidemic phase involving the human population. That the epizootic phase is the precursor to the epidemic has long been known among the natives of Trinidad (*13*), and also in the lowlands of Guatemala (*6*). The howling monkey population in Brazil has been practically exterminated at times by waves of jungle yellow fever (*12*).

Pathological Anatomy and Clinical Pathology

During the westward passage of sylvan yellow fever across the Republic of Panama, complete autopsies were performed on the seven

proved fatalities from the disease. A complete autopsy also was performed on the most recent case occurring at Puerto Armuelles February 10, 1952. Three primary pathological processes appear to be involved in the mechanism of the disease, all of which may be considered interrelated: the hepatitis of yellow fever;



The black howling monkey, *Alouatta palliata aequatorialis* Festa.

the hemorrhagic diathesis undoubtedly resulting from this hepatitis; and the hemoglobinuric (lower nephron) nephrosis as a sequel of the hemorrhagic diathesis. Clinically these processes appear as (*a*) jaundice, (*b*) hemorrhages from mucous membranes, such as the vomiting of blood, and (*c*) uremia, frequently manifest by terminal convulsions and coma.

The hepatitis of yellow fever is diagnostic of the disease and has been accepted as the basis for the recognition of fatalities from yellow fever since 1930. Recognition of its histological specificity has evolved gradually since 1890 (*1, 2, 9, 11, 15*).

That the acidophilic material in the hepatic necrosis can be cleared from the polygonal cells with rapid regeneration of the liver cords (*1, 10*) was again noted recently in a Panamanian dying on the ninth day of illness, indicating that the liver lesion is a transient phenomenon. During its presence, however, the hemorrhagic diathesis develops to a degree indicative of a profound prothrombin deficiency (*4*) although this has not as yet been established clinically.

Among the hemorrhagic phenomena accompanying the liver damage are melena, hematuria, hematemesis, nasal and oral mucosal bleeding, cutaneous ecchymoses, hemorrhagic pneumonia, and hemoglobinuric (lower nephron) nephrosis (*5, 8*). The plugging of the tubules of the lower nephron by heme casts is a recognized phenomenon productive of uremia, and retention of nonprotein nitrogenous metabolites in yellow fever, due to hemorrhage, blood in the bowel, and the kidney damage, is not only to be expected but has already been demonstrated (*14*). This would lead to a state of uremia, with the typical oliguria, anuria, and termination in convulsions and coma encountered in the classical form of the disease. Occasionally a confluent bronchopneumonia is superimposed on the hemorrhagic reaction in the lung, as in two of the Panama cases.

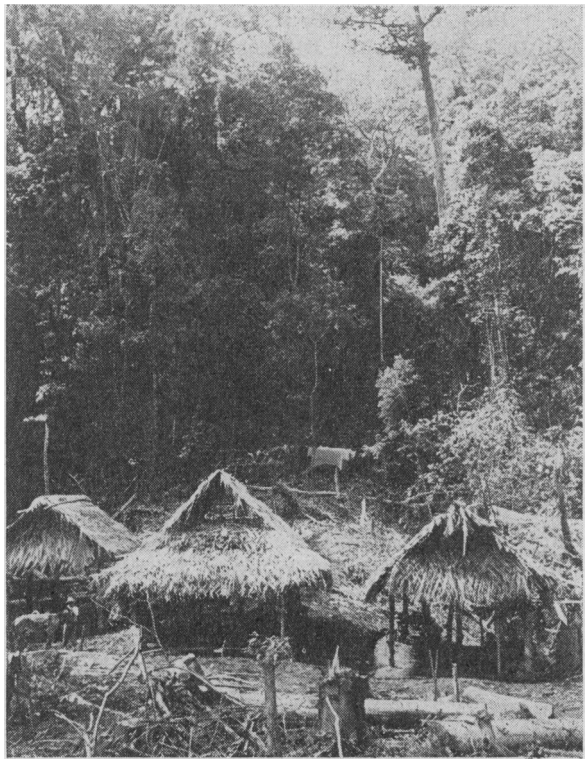
Death can occur, then, in either of two phases: (*a*) from the liver damage before the hemoglobinuric nephrosis and uremia are fully developed; or (*b*) from uremia due to the hemoglobinuric nephrosis after the hepatic lesion has begun to undergo involution. Liver and kidney specimens studied from the Panama cases support this concept of the major clinical pathological mechanism in yellow fever. Clinicians have long been more concerned about the development of renal failure than with liver failure in the disease. This interpretation awaits confirmation or modification from analysis of the extensive laboratory studies performed in Costa Rica by the staff of San Juan de Dios Hospital in San José during the recent epidemic in that country.

Outlook for Central America

Time seems generously disposed toward all concerned with the current wave of sylvan yellow fever in Central America. Presently, the main front of the wave appears stalled in the valley of the San Juan River between Costa Rica and Nicaragua, and its progress, if any, is insidious. There is no evidence as yet of an epidemic in Nicaragua, or of sporadic cases there. During this respite, the Ministry of

Health of Nicaragua has vaccinated more than 112,000 persons in the threatened areas.

Sporadic cases have been reported from the Pacific side of Costa Rica, mainly from the Cabagra zone, in the southern part of Puntarenas Province, close to the Panama frontier. This region first came under suspicion in October 1951, when dead monkeys were reported near Potrero Grande. On January 15, 1952, a confirmed human fatality occurred after an infection acquired in the Coto area, and on February 10 a resident of Burica Hills Peninsula died from the disease at Puerto Armuelles in the southwestern end of the Republic of Panama. This indicates that in some manner the wave has crossed the continental divide in southern Costa Rica, and is now threatening to recross the Republic of Panama, but this time on the Pacific side and moving eastward.



A new clearing in the otherwise unbroken rain forest northwest of Almirante, Bocas Del Toro Province, Panama, characteristic of the situation in which jungle yellow fever is contracted by humans. Two human cases occurred here in April 1951 in a group of men surveying a right-of-way through the forest for a projected road (photograph by Dr. Harold Trapido).

This is probably the first time in modern history that a wave of sylvan yellow fever has moved through Panama and Central America in its pure form and with a directional trend due to its canalization in a relatively narrow strip of land by two oceans. It developed its initial focus (November–December 1948) east of the Panama Canal, on the Pacific side of the continental divide. It then moved over the divide at a low point (600–700 feet) into the Chagres watershed (August–September 1949), crossing the Panama Canal and reaching the rain forest on the Atlantic by January 1950. Thence it ran westward to Almirante and the Costa Rican border, remaining entirely on the Atlantic side. The Atlantic watershed of east-central and northeastern Costa Rica were involved from July to October 1951. A seeding of the Pacific side of Costa Rica threatens to involve the Pacific watershed of Panama with an offshoot of the wave.

All of the proved human fatalities so far have acquired their infections at elevations below the 2,000-foot contour, and most of them have occurred definitely below the 1,000-foot contour. This implies that the continental divide can act as a barrier and also canalize the movement of the wave, as it did in Panama in 1949–51. Circumstances which might be conducive to the crossing of the divide are not well understood, for although the Cordillera in Costa Rica is higher than it is in Panama, a crossing has already actually occurred there.

Outbreaks in Nicaragua may not be encountered until April or even July or August in 1952. This is only an inference based on experience in Panama and Costa Rica, and may or may not be applicable to the pertinent climatic, seasonal, and terrain factors of Nicaragua. Probabilities suggest that the wave will keep on moving. As the lowlands and extensive valleys of eastern Nicaragua are involved, new enzootic foci may become established. Whether or not the Pacific watershed north of Costa Rica will be involved remains to be seen, for the divide is broken by Lake Nicaragua at the Costa Rican border.

If the disease does establish itself in Nicaragua this year, and if there are enough critically located population centers involved, the opportunity for a long-term study of the behavior of such a wave will be assured. This

would call for cooperative effort by scientific personnel in all fields of biology, public health, and medicine. On the other hand, the wave may lose itself in uninhabited regions and reveal its presence only sporadically in scattered localities at long intervals, thus not exciting public interest again until a large community is involved. Or it may vanish as did the second Brazilian wave of 1944–45. At its present velocity it may not reach Guatemala and Mexico for 5 or 6 years, but it will continue to constitute a cause of illness and death for the farming settlements in its pathway.

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Vineyard Haven Hospital Closed

A decline to about 40 percent of capacity has led to the recommended closing of the Vineyard Haven Hospital of the Public Health Service. The 30-bed facility on Martha's Vineyard, Mass., no longer admits patients and is to be closed as soon as provision can be made for the patients now in the hospital. Its principal beneficiaries are Coast Guardsmen and seamen for whom the Public Health Service will continue full responsibility, transferring all those requiring further hospitalization to the 300-bed Public Health Service Hospital in Boston.

The recent decision to close the hospital was based on the report of a special survey board that only 29 percent of the patients admitted in recent periods were local residents and that comparable Federal facilities were available nearby.