Reprinted from EXPERIMENTAL PARASITOLOGY, Academic Press Inc.
Volume V, No. 3, May 1956 *Printed in U. S. A.*

EXPERIMENTAL PARASITOLOGY V, 285-323 (1956)

PARASITOLOGICAL REVIEWS

The Epidemiology of Yellow Fever in Middle America

Harold Trapido and Pedro Galindo

Gorgas Memorial Laboratory, Panama, R. de P.

CONTENTS

INTRODUCTION

The Caribbean area is prominent in the history of yellow fever. From here came the first accounts of yellow fever recognizable as such. The large population centers of Panama, Veracruz and Havana were repeatedly visited by severe epidemics, and there were long periods when yellow fever remained endemic in these places. At the turn of this century the transmission of the disease by *Aedes aegypti* was proven. The control of *aegypti* which shortly followed in Havana and then Panama resulted in the disappearance of the disease from these cities. Urban yellow fever persisted, however, in Mexico and Central America until the first half of the twenties. In Panama the last urban yellow fever was reported in the fall of 1905. While several cases of the disease were brought to Panama by ship in subsequent years, there was no clinical recognition of autochthonous cases until 43 years later in the fall of 1948.

During this interval, continued work on the disease, particularly in Africa and South America, resulted in a number of important discoveries and developments. It was demonstrated by Stokes, Bauer and Hudson (1928) that primates other than man were susceptible to the disease, and that the etiological agent was definitely a filtrable virus. Bauer (1928), Philip (1929), and Davis and Shannon (1929) showed that in the laboratory, at least, the virus of yellow fever could be transmitted by mosquitoes other than *Aedes aegypti*. In Brazil and Colombia the recognition of yellow fever in areas in which the presence of *Aedes aegypti* could not be demonstrated brought a realization that other mosquitoes must in fact be natural vectors, and that animals other than man were involved in maintaining the virus in nature. The concept of a sylvan or jungle cycle of the disease was thus developed. This history has recently been summarized by Warren (1951).

This review will deal primarily with the epidemiology of yellow fever which appeared in Panama in 1948 and subsequently invaded the region to the west and north. For want of some better way to refer to the land mass extending from northwest to southeast, connecting the two American Continents, and including Panama, Central America, and Mexico, we have chosen the term "Middle America." Before attempting to deal with yellow fever in this area we must first give brief consideration to the physical environment.

Physiography, Climatology, and Vegetation Formations

Running the length of Middle America is a complex mountain system which is relatively narrow at the south, broadens in the area from southern Nicaragua to Chiapas, and expands to become the vast highland of Mexico. There are three gaps in this orographic chain, one at the Isthmus of Tehuantepec, a second in southern Nicaragua, and a third at the Isthmus of Panama. This third natural land feature was exploited for the construction of the Panama Canal. Thus the Canal is more than an incidental artifact on the landscape. It marks the location of an important physiographic feature. The terrain features of Middle America have an important influence on the climate, which in turn influences the vegeta-

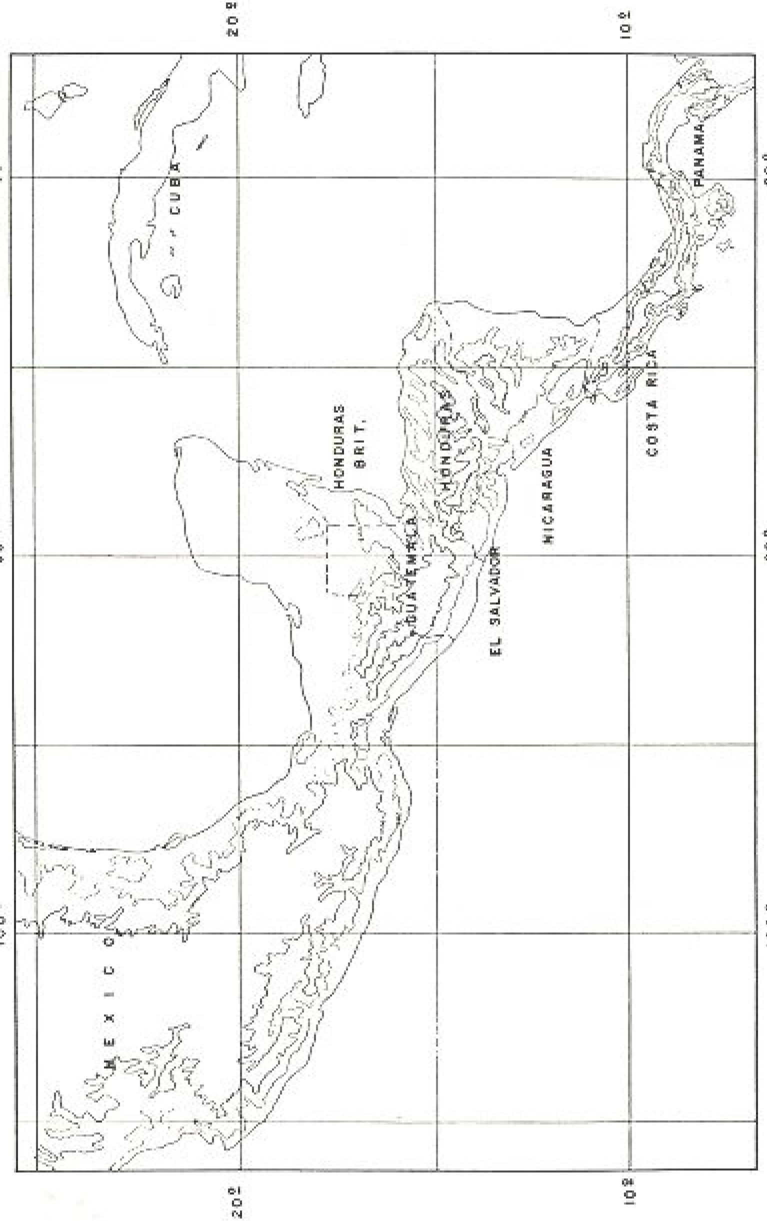

FIG. 1. Topography of Middle America. (Elevation contours shown are at 200 and 1000 meters.)

tion cover. Together, physiography, climate and vegetation have affected mosquito distribution and bionomics, and the geographic course of the yellow fever virus.

The yellow fever activity in Middle America has all occurred within what may climatologically be spoken of as the tropics, i.e., a region in which there is no month with a mean temperature below 18°C (64.4°F). The relatively constant high temperatures of the tropics produce high evaporation rates, so that there must be particularly abundant rainfall to maintain humid conditions. The climates of the tropics have been subdivided under the Koppen system according to the amount and annual distribution of rainfall (Trewartha, 1954). For our purposes the three principal tropical climatic types may be briefly characterized as follows: *Af*—rains throughout the year with no month having less than 6 cm. (2.4 inches) of precipitation; *Am*—there are months with less than 6 cm. of precipitation but these are compensated for by rains at other times of the year heavy enough to maintain high moisture conditions; *Aw*—the year marked by pronounced dry periods without sufficient precipitation during rainy seasons to avert drought.

In Middle America the movement of the air mass and the configuration of the land and mountain masses are such that, in general, high rainfall is experienced on the Atlantic side and lower rainfall on the Pacific. There are exceptional pockets of high rainfall on the Pacific slope such as those in southwestern Costa Rica and western Guatemala. There is also a special situation at the mountain gap in the Canal Zone which we will deal with later in discussing the course of the virus in this critical area. This general rainfall pattern is due to the fact that the trade winds, which blow from the north or northeast, are deflected upward by the mountain masses and in cooling precipitate their moisture along the Atlantic facing slopes and the lowlands immediately adjacent. There is also some spilling over of precipitation on the upper slopes of the Pacific face of the mountains.

In general the annual *cycle* of rainfall is a function of latitude. The rainy season is longest in lower Middle America and progressively shorter to the north, with the converse being true for the dry season. Thus in Panama the rainy season extends from May to December, while at Veracruz the principal rains are limited to the period from June through September. This pattern of wet and dry periods is more pronounced on the Pacific side.

The physical aspect of the vegetation cover is directly related to temperature and rainfall although soil type may also be a determining factor. The association of vegetation with climate is so intimate that climatologists often use vegetation cover to delimit climate types. Agreement is lacking among plant ecologists on the details of how the tropical plant associations should be classified, what they should be named, and the limits of the climatic conditions essential to their development. Certain general principles have impressed us, however, as being essential to understanding the relation of yellow fever to the Middle American forests. We need to characterize briefly two principal forest formations to be able to discuss later the epidemiology of yellow fever in the area.

"*Tropical rain-forest*" is notable for the great height (often 150 feet) of the trees of which it is composed, the heavy covering canopy which permits little or no direct sunlight to reach the forest floor, and the consequent lack of herbaceous ground cover. It is evergreen in the sense that at no time of year is there a general loss of leaves from the high covering canopy. The *Af* and *Am* climates of the Koppen system are capable of supporting evergreen tropical rain-forest of this sort, but it does not follow that rain-forest will everywhere be present where these climates prevail. While climatological maps show a band of *Af* and *Am* climates extending the length of the Atlantic slope of Panama, Central America and across the base of the Yucatan Peninsula to the Mexican Gulf coast, edaphic conditions intervene in parts of Nicaragua, Honduras, and Guatemala. The sandy soils there are clothed with pine forests which appear as islands in a sea of broad-leaved tropical rain-forest.

In "*tropical deciduous forest*" the trees do not attain the great height characteristic of tropical rain-forest, and during dry season there is a more or less general loss of leaves. The loss of leaves serves to reduce transpiration and conserve moisture for the trees, but it also permits the circulation of drying winds within the forest. The penetration of sunlight to the forest floor allows the development of a substantial ground cover. This forest formation is associated with the *Aw* climate which is generally distributed along the Pacific side of Middle America, with some exceptional areas as previously mentioned. By its association with a rainfall cycle of the *Aw* type, tropical deciduous forest is also an indicator of conditions unfavorable to the maintenance of yellow fever transmission during part of the year; the period of effective drought, which is implicit, reduces the number of tree holes with water available for larval development, and produces low humidites and high temperatures which limit the life span of adult mosquitoes.

Immunological Surveys Prior to 1948

During the thirties, the authorities of the Rockefeller Foundation undertook to make a world survey of the distribution of yellow fever immunity, utilizing the mouse protection test which had been devised by Sawyer and Lloyd (1931) following the discovery by Theiler (1930) that white mice were susceptible to yellow fever when the virus was introduced by intracerebral inoculation. Several immunological surveys were made in Panama, Central America, and Mexico.

Results from East of the Panama Canal

Human sera were collected from localities in Darien Province and along the San Blas coast of Panama (east of the Canal Zone and adjacent to the Colombian border) in 1936 and 1937 by Dr. Carl M. Johnson of the Gorgas Memorial Laboratory and by the Army Medical Research Board. The results of these tests were reported by Clark (1938) and Sawyer (1940). In addition to positive sera from adults, one 11-year-old and one 12-year-old of 117 children from Darien, and one 9-year-old of 95 children from the San Blas coast were positive. Sawyer concluded that "the evidence suggests that yellow fever was present at least as late as 1927." In 1941 and 1942, Kumm and Crawford (1943) collected additional sera in eastern Panama. They found six positives in the 10- to 14-year-age group and eight positives among children less than 9 years old. There were two positives in 7-year-olds, and at El Llano, which is but 50 miles east of Panama City, they found two positives in children born as late as 1928.

Results from West of the Panama Canal

In western Panama, Central America, and Mexico, Kumm and Crawford found no positives in persons under 25 years of age. Sawyer (1940) reported two fatal jaundice cases from the Pacific slope of Costa Rica in 1938 which clinically resembled yellow fever. But there was no necropsy in one case, and no histopathological study made of the other, so that no definitive diagnosis could be made. He also gave the results of neutralization tests on the sera of 396 persons in Costa Rica, collected in 1939 and 1940. All tests were negative and he concluded that yellow fever was not present there. The results of other surveys of human sera for yellow fever protective antibodies in the Middle American region were reported by Sawyer, Bauer, and Whitman (1937) and Bustamante, Kumm and, Herrera (1942). Sawyer *et al.* found immunity, as might have been expected, throughout the older age groups which would have been exposed to yellow fever when the *aegypti*-transmitted urban form was present in the area. But in Mexico there were also positive sera obtained in 1932 from three children reported to have been born 2 and 3 years subsequent to the last clinically recognized case of yellow fever in that country (at Panuco, Veracruz, February 1923). There was also one inconsistency in the sera from El Salvador. A child from Usulatan born in 1925 showed protection, although the last clinical yellow fever in the principal city, San Salvador, was recognized in 1924, and the last yellow fever recognized at Usulatan was in 1921. Several possible explanations for these aberrant positives were suggested, which we will consider later. Bustamante *et al.* collected bloods in the area along the Mexican-Guatemalan border and found no immunity in persons born subsequent to 1925.

Thus the general understanding of the distribution of yellow fever in the Americas, at the time the cases were diagnosed in Panama at the end of 1948, was that the sylvan or jungle phase of the disease was endemic in South America and possibly in eastern Panama adjacent to Colombia, or at least made periodic excursions into this last mentioned area. But Middle America, west and north of the Panama Canal, was free of the disease and had been so since 1925, prior to which urban *aegypti*-transmitted yellow fever had been present.

Appearance of Yellow Fever in 1948

Several papers have appeared dealing with the first recognition of clinical yellow fever in Panama during the last months of 1948. Herrera, Elton, and Nicosia (1949) give accounts of case histories, the pathology of five fatal cases and the clinical histories of four recovered cases from the Pacora area about 25 miles northeast of Panama City. Elton and Herrera (1949) summarize the histories, clinical courses and post mortem findings in three of the fatal cases. Elton and Johnson (1950) discuss the histopathological findings in these and several subsequent cases. Calvo and Galindo (1952), and Elton (1954) provide some background information on the circumstances under which the diagnosis of yellow fever was made. As is often the case in places where yellow fever has been absent for a long period, the disease was not diagnosed with certainty until several cases had accumulated. The appearance of yellow fever in Panama was officially notified in the Weekly Epidemiological Report of the Pan American Sanitary Bureau for January 17th 1949. Listed are eight cases and six deaths from the Pacora region. This report, which was based on a preliminary telephonic communication from Panama, is apparently in error as but five fatal cases and four recovered cases were known at this time (Herrera, Elton, Nicosia, 1949). On January 14th 1949, a firm histopathological diagnosis of yellow fever was made by Dr. Jose M. Herrera, Chief of Pathology at the Santo Tomas Hospital, and Dr. Norman W. Elton, Chief of the Board of Health Laboratory, and confirmed by Dr. Herbert C. Clark, Director of the Gorgas Memorial Laboratory. All agencies concerned were officially notified, and a conference of interested parties was held on January 17th. This resulted in the establishing of a cooperative program between the governments of the Republic of Panama and the Canal Zone. Included were plans for (1) the immunization of humans, (2) *Aedes aegypti* eradication, and (3) epidemiological studies. Courtney (1950) has reported the activities carried on under this program.

Course of Yellow Fever in Middle America After 1948

In the period from 1949 to 1954 there was a succession of yellow fever fatalities in both humans and monkeys in central Panama, western Panama, Costa Rica, Nicaragua, and Honduras. Human cases for which there is laboratory confirmation are reported internationally. The sequence of human cases and deaths, as officially notified, has been listed in the Weekly Epidemiological Reports of the Pan American Sanitary Bureau. The geographic location and timing of these cases are shown on the accompanying map. The Epidemiological Reports list 45 deaths and an additional six recovered cases for Costa Rica. But Elton, Romero and Trejos (1955) state that 206 yellow fever patients with 57 fatalities were seen in the San Juan de Dios Hospital in San Jose; during 1951 there were 157 cases, during 1952 46 cases, and during 1953 3 cases. In Nicaragua, the Epidemiological Reports list 11 deaths: five in 1952 and six in 1953. Trejos and Romero (1954) give the monthly distribution of 203 Costa Rican cases seen in 1951 and 1952. All but four of these occurred from June through December, the rainy season, when forest canopy *Haemagogus* are most prevalent. Three-quarters of the cases (154) were in August and September.

There were undoubtedly many more cases and deaths than came to the attention of health authorities. The poorly developed transportation system in most of the area in which the disease occurred, together with the rapid onset and short course of the disease, militate against patients

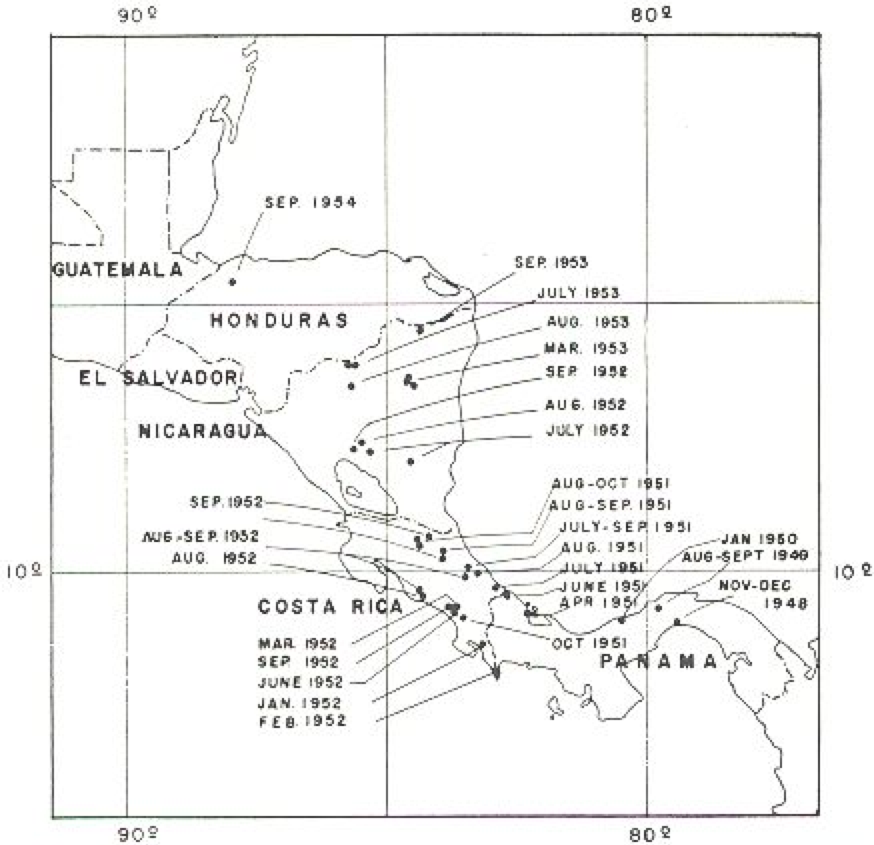

FIG. 2. Map showing the sequence of human yellow fever cases in Middle America from 1948 to 1954.

reaching a hospital where a diagnosis can be made. The substantial number of cases reported from Costa Rica is probably only indicative of the fact that the capital and principal hospital are centrally located, with a relatively good radiating net of roads and railroads. In Panama, no yellow fever activity was reported between January 1950, near the Canal Zone, and April 1951, from near Almirante close to the Costa Rican border. But the path of the virus between these two places would have been through the Atlantic side rain-forest where there are no roads and the predominantly Indian population can only travel by trails on foot or along streams in dugouts. The absence of reports from here, during a 15 month period, is more likely a reflection of the failure of cases to come to medical attention rather than any indication that humans were not involved. The cases at Almirante were diagnosed because a United Fruit Company hospital is there. The small number of cases recorded from the Atlantic side rain-forests of Nicaragua and Honduras may also be attributed to poor communication and transportation.

The last human case reported was a fatality which occurred at the hospital at San Pedro Sula, Honduras, in September 1954. San Pedro Sula is located in the valley of the Ulua River which is under intensive cultivation for bananas, and it is unlikely that the yellow fever was contracted there. Devastating floods were occurring at the time and communication lines were disrupted, so that it has not been possible to trace the source of the infection.

A prominent feature of the yellow fever episode in lower Middle America has been the frequency with which reports of fatalities in monkeys were noted. Massive monkey mortality was apparently not a regular feature of the yellow fever epidemiology in South America although it was remarked by Soper (1938) after the discovery of the sylvan cycle of the disease that, "there is a great deal of accumulated evidence, both scientific and hearsay, indicating that monkeys are infected in the jungle and that certain species, notably the howlers, die in large numbers at the time human infections are occurring in the forest." Other retrospective accounts from hearsay evidence of natives are those of Gaitan (1939) and Sanchez (1939) in Guatemala, Laemmert and Kumm (1950) in Brazil, and Gast-Galvis, Anderson, and Hill (1954) in Colombia.

As early as 1914 Balfour had called attention to reports by local residents of howler monkey mortality being associated with the appearance of yellow fever in Trinidad. He also noted the close association with the forest of several human cases in the outbreak of 1913.

There were no reports of monkey mortality at the time of the first human yellow fever cases in the Pacora area of Panama. Elton (1952a), however, called attention to the work of Collias and Southwick (1952) on the population density and social organization of howling monkeys on Barro Colorado Island, a biological reserve in Gatun Lake. These authors made a census of the howling monkeys on the island in March and April 1951 and found the number of individuals to be only about half that recorded in a study made 18 years previously by Carpenter (1934). While their interest was in social organization in these primates and its possible limiting effect on population growth, they also consider the possibility of population reduction by diseases, including yellow fever. They record the observation of Dr. Eugene Eisenmann, who had visited the island on several previous occasions, that the decrease in numbers of howling monkeys had happened shortly before 1951. Dr. Eisenmann also noted that in 1951 there was an apparent increase in numbers of *Cebus* monkeys. This would be a natural consequence of selective mortality in howling monkeys, had there indeed been a yellow fever epizootic. Elton (1952a and 1952d) pointed out that human cases of yellow fever occurred at Buena Vista, but ten miles from Barro Colorado Island, in August and September 1949, and attributed the reduction in numbers of howling monkeys on Barro Colorado to yellow fever. Early in 1951 there were word-of-mouth and newspaper accounts of monkey mortality in Chiriqui and Bocas Del Toro Provinces of western Panama, but no tissues positive by pathological diagnosis were obtained. In Costa Rica, Dr. Oscar Vargas-Mendez, Director General of Public Health, was alert to the significance of reports of monkey mortality, and a substantial series of tissues was obtained from sick and dead monkeys between July 1951 and September 1952, which formed the basis of the paper by Vargas Mendez and Elton (1953) on naturally acquired yellow fever in monkeys in Costa Rica. In the period from April to August 1952, Dr. Jorge Boshell, in charge of yellow fever epidemiological investigations for the Pan American Sanitary Bureau, obtained three spider monkeys and three howling monkeys in the Rivas area in southwestern Nicaragua in which histopathological diagnoses of yellow fever were made by Dr. Gast-Galvis, Director of the Carlos Finlay Institute, Bogotá, Colombia (Boshell Manrique, 1952). Dr. Boshell arrived in this area while the epizootic in monkeys was still in progress and has vividly described how the mortality was so extensive that the woods reeked with the odor of dead animals. He also traced reports by local people of monkey mortality in Chontales Province, east of Lake Nicaragua. We visited this area in 1953 and gathered reports from natives which were consistent in detailing how the howling monkeys, which formerly awakened the people by their calling at dawn, were no longer heard; how the bodies of monkeys which had died and fallen in streams fouled the water which was used for drinking and washing; and how the howling monkeys were most affected, the spider monkeys less affected, and the white-faced monkey populations were seemingly not disturbed. There were further reports of monkey mortality to the north in the Atlantic drainage of Nicaragua during 1953. Dr. Boshell also investigated a report of monkey mortality southwest of Managua on the Pacific slope in September and October of 1953, but he was unable to confirm the presence of yellow fever by histopathological diagnosis.

In June and again in August of that year we traveled widely in Honduras, to the north of Nicaragua, but nowhere did we hear of monkey mortality from local people. In December of 1953 there was a report of a human fatality with a clinical picture of yellow fever at Dulce Nombre in the basin of the Rio Patuca in southern Honduras. In tracing this Dr. Boshell went into the area in early January 1954. He obtained reports of monkey mortality there during the previous two months, but by the time of his arrival the dry season had become established and there was no current evidence of an epizootic. From February to July of 1954 the Department of Public Health of Honduras received reports of monkeys dying to the north, near Olanchito in the basin of the Rio Aguan, and at several other localities facing the north coast. In July fresh reports were received from the vicinity of La Masica, on the north coast between the port towns of Tela and La Ceiba. In this instance livers were obtained from two recently dead monkeys and a positive histopathological diagnosis of yellow fever established (Trapido and Galindo, 1955). There have been no further reports of monkey mortality in the 15 months which have since passed.

It will be noted from this summary covering a 6 year period, that all too often information on the events occurring in the primate populations in the forest was based only on the hearsay evidence of natives. It should be appreciated, however, that local reports were slow in coming to the attention of health authorities in capital cities, that valid reports were admixed in no small measure with baseless rumors, and that the areas involved were remote and difficult of access.

During the period of yellow fever activity extensive vaccination campaigns were carried on in Panama, Costa Rica, Nicaragua, and Honduras. Both Dakar and 17D vaccine were used. Eklund (1953) has reported on encephalitis associated with the use of the Dakar vaccine in Costa Rica and Honduras. Trejos and Romero (1954) give the details of yellow fever cases in vaccinated persons.

An extensive series of papers on various aspects of the yellow fever wave has been published by Elton (1952a, b, c, d, e, f, 1953, 1954, 1955) who projected schedules for its movement as far as the State of Veracruz in Mexico. In Costa Rica clinical aspects of cases were detailed by Miranda (1953) and Romero (1954), and a full clinical and laboratory account of hospitalized cases was given by Trejos and Romero (1954). A series of papers dealing with the forest mosquito fauna related to sylvan yellow fever in Middle America is that of Galindo, Carpenter, and Trapido (1949, 1951a, 1951b, 1952, 1955), Galindo, Trapido and Carpenter

(1950), Trapido, Galindo, and Carpenter (1955), Galindo and Trapido (1955) and Trapido and Galindo (1955). Recent review papers, based primarily on the literature are those of Benitez Armas (1951), Soper (1952) and Aldighieri (1954). The paper by Hanlan (1953) is a poorly evaluated review of the current status of yellow fever in Central America with questionable conclusions. Much informal information is included in the transcript of the yellow fever conference held in Washington in December 1954 (Anonymous, 1955).

Immunological Surveys in Middle America Subsequent to 1948

Humans

The only immunological survey of humans was that undertaken in Panama in 1949 and reported by Courtney (1950). Positives by the mouse protection test were found throughout the Republic. During World War II, however, extensive vaccination had been carried on by the Armed Forces, not only among their own personnel, but also in civilians employed in the area. It is, therefore, not possible to assess accurately the significance of the fact that positives were found in western Panama as well as the eastern part of the country.

Primates and Other Animals

Courtney (1950) and Clark (1952) have reported the results of mouse protection tests on the sera of primates and a variety of other arboreal animals which were collected by shooting. Courtney recorded positives from a number of localities in Panama, just east of the Canal Zone, among howling monkeys, spider monkeys, white-faced monkeys, marmosets, and kinkajous (*Potos flavus isthmicus*). These specimens were collected during 1949. The Clark paper summarized results obtained with animals collected in Panama during 1949 and 1950, and in Chiapas, the southernmost Mexican state, during 1951. In Panama, Clark found positives among primates at all localities from which he obtained specimens, throughout the length of the country. He also reported positives in kinkajous, an opossum (*Didelphis marsupialis etensis*), an ocelot, (*Felis pardalis mearnsi*), a three-toed sloth (*Bradypus grisens grisens*) and a conejo pintado (*Cuniculus paca virgatus*). Positives in more than 50% of the shot primates were not unusual. Protection tests on the monkey sera collected in Chiapas yielded positives in both howling and spider monkeys. There was some discrepancy in the results obtained with divided serum samples run at the laboratories of the Servico Nacional de Febre Amarela in Rio de Janeiro and at the Gorgas Memorial Laboratory.

Animals which have been collected with a shotgun usually have the vascular tree seriously ruptured, and it is not possible to obtain sterile blood from the heart or principal vessels. When serosanguineous fluid is taken from the thoracic or abdominal cavities there is often gross contamination which renders the serum unsatisfactory for use in neutralization tests. There is, therefore, some question of the validity of tests performed with serum from shot animals when it has not been possible to obtain sterile blood. In the monkeys from Panama obtained on the offshore island of Coiba and in the El Volcan area of Chiriqui Province, above 4,500 feet, the other epidemiological facts would not seem to be consistent with the finding of positives by neutralization tests. In the course of the epizootic wave here under review, there has been no overt evidence of yellow fever at elevations as great as those from which the Chiriqui highland monkeys were obtained. In six months of routine forest canopy mosquito collections just below the place where the El Volcan monkeys were gotten, only two specimens of *Haemagogus equinus* were captured (Trapido, Galindo, and Carpenter, 1955). The validity of the positive protection tests in the monkeys from Chiapas would also appear to be in question. In 1953 Dr. Jorge Boshell shot a second series of monkeys there using a small bore rifle which damaged the animals but little and permitted him to obtain sterile blood. The protection tests performed on these sera at the Carlos Finlay Laboratory, Bogotá, were negative and it has been concluded that the monkey population of that area of Mexico, at least, lacked immunity to yellow fever at that time (Anonymous, 1954). Caution should also be exercised in evaluating protection tests in animals other than primates, since various workers have raised the question of the presence of non-specific viricidal substances producing false positives. It has been pointed out by Laemmert, Ferreira, and Taylor (1946) that some species giving positive protection tests are highly resistant to experimental infection with yellow fever, and Koprowski (1946) found that the sera of marsupials and rodents which gave positive protection tests for yellow fever also neutralized certain other viruses.

A survey for yellow fever antibodies in live animals brought in to the Gorgas Memorial Laboratory from various localities in Panama during

1949, 1950, and 1951 has been reported by Rodaniche (1952). For these tests it was possible to obtain sterile blood, and in many cases to retest sera that gave doubtful or inconclusive results. Among 209 primates tested 12 gave positive results, (five marmosets, six spider monkeys and one night monkey). Fifty-eight other animals were also tested with a single positive being found in a pigmy anteater (*Cyclopes didactylus dorsalis*). All positives were in animals from localities east of the Canal.

Rodaniche (1956a) has continued the search for yellow fever antibodies in primates brought into the Laboratory alive. She has been able to demonstrate immunity in seven marmosets and one spider monkey obtained from late 1953 to the middle of 1955 at various localities in eastern Panama. In the case of the adults, there cannot be excluded the possibility that the immunity was acquired during the period that yellow fever is known to have been active in that region from 1948 to 1950. But she also found to be positive a juvenile spider monkey received in April 1954, a juvenile marmoset also received in April 1954, and a young adult marmoset received in June 1955. These would suggest that sylvan yellow fever is enzootic east of the Canal, or at least that it has persisted unrecognized for several years.

Middle American Fauna in Relation to Sylvan Yellow Fever

Mammal Hosts

The neotropical vertebrate fauna is so vast that the adequate exploration of the whole of it for possible involvement in the maintenance of yellow fever would be a staggering task. Investigations have therefore logically centered about the tree-inhabiting animals most likely to be in contact with the known arboreal mosquito vectors. Of greatest interest have been the primates and secondarily the marsupials. There are also fragments of information on other animals. Bugher (1951) has recently reviewed the knowledge of yellow fever hosts other than man. We here consider only the principal mammal groups for which there is some positive evidence of participation in the yellow fever transmission cycle in Middle America. The names used and the distributions given are based on the recent check list of Miller and Kellogg (1955).

Night Monkeys—Aotus. One species, *bipunctatus*, in Panama only. (records of other species from the area are considered erroneous.)

Howling Monkeys—Alouatta. The species *palliata* with seven subspecies ranges north to the state of Veracruz in Mexico.

Capuchin or White-Faced Monkeys—Cebus. Three subspecies of *capucinus* occur from Panama to northern Honduras.

Spider Monkeys—Ateles. Two South American species, *rufiventris* and *fusciceps* range into eastern Panama; nine subspecies of *geoffroyi* range north as far as southeastern San Luis Potosi, Mexico.

Squirrel Marmosets—Saimiri. This South American genus has a discontinuous distribution. It does not occur in eastern or central Panama, but there are two subspecies of *orstedii* in southern Costa Rica and the adjacent Chiriqui Province of Panama.

Marmosets—Marikina (also called *Oedipomidas* in the literature). The species *geoffroyi* ranges through Panama to the Costa Rican border.

In laboratory experiments all these genera of primates are susceptible to yellow fever to a greater or lesser degree, and it would appear that the virus levels attained are adequate to infect mosquitoes and maintain the monkey-mosquito transmission cycle. Differences in the outcome of the disease may be due to the strain of virus, as has been repeatedly shown in the laboratory, but also to the particular primate involved.

Of the widely distributed primary forest inhabiting monkeys, the disease is most often fatal in howling monkeys (*Alouatta*), less frequently fatal in spider monkeys (*Ateles*), and least often if at all fatal in white-faced monkeys (*Cebus*). This differential in the severity of the disease as determined in the laboratory appears to have been confirmed in the field in the course of the series of epizootics in Middle America. The reduction in numbers of howling monkeys in relation to white-faced monkeys reported by Collias and Southwick (1952) on Barro Colorado Island would be an expression of the differential effect. Less reliable but nevertheless impressive was the consistency with which the country people in the epizootic areas in Nicaragua remarked the severe mortality in the howling monkeys while the white-faced monkey populations were not noticeably affected. It has been suggested by Dr. Boshell, who has had extensive experience with yellow fever in the forests of both South and Middle America, that the populations of howling monkeys in Colombia, where sylvan yellow fever is endemic, were smaller than in Middle America prior to the present series of epizootics. Frequently recurring movements of yellow fever through the primate populations in Colombia would effect this difference by periodically reducing the howling monkey populations. This would also imply that sylvan yellow fever has not previously been active in the lower Middle American region for some long period. At Almirante, Panama, howling monkeys had been abundant in the rain-forest of the mountain slopes but also in the coastal mangrove swamps. After the yellow fever episode there in 1951, they could still be frequently heard in the mangrove, but not on the forested slopes. In this case the factor determining their survival in the mangrove appears to have been the restriction of the vector to the forested slopes.

Night monkeys (*Aotus*) are very susceptible to yellow fever but they sleep during the day in tree hollows, while *Haemagogus* mosquitoes are diurnal and feed most readily in bright sunlight. There would thus appear to be a behavior barrier between the two, although under other circumstances as at Muzo, Colombia, where yellow fever is endemic, *Aotus* monkeys are the only primates present and their involvement in the yellow fever cycle has been suspected there (Boshell Manrique and Osorno mesa, 1944). Should it be shown that arthropods other than diurnal mosquitoes are involved in transmission, the possible role of *Aotus* would have to be reevaluated.

In Colombia, Bates and Roca-García (1945) carried yellow fever virus through five cycles of transmission using *Saimiri* monkeys and *Haemagogus* mosquitoes, but in the area here considered these primates have a very restricted range in the Costa Rica and Panama border area, and could not have been generally involved.

The marmosets (*Marikina*) are very susceptible to yellow fever, with the disease frequently resulting in a fatal outcome. They are primarily inhabitants of scrubby second growth and thus are not in intimate contact with the preponderantly forest-dwelling arboreal mosquitoes which are the presently known vectors. Although they are common in the Pacora area where yellow fever appeared there was no evidence of mortality among them. However, Rodaniche (1952) found five of 64 individuals tested in this area during the period 1949 to 1951 possessed neutralizing antibodies for yellow fever. There is also some circumstantial evidence that they may have been affected by yellow fever on Barro Colorado Island, as Collias and Southwick (1952) found the population of this species to be lower in 1951 than that reported in 1929 to 1937 by Enders (1935, 1939). Their limited range eliminates them from consideration north and west of the Panama-Costa Rica border area.

Much work has been done in South America to assess the possible role of various marsupials as intermediate hosts of yellow fever in nature, with apparently conflicting results. The accumulated evidence has been critically reviewed by Bugher (1951). He concluded that all species studied were susceptible to the virus to some degree, but that the susceptibility varied due to a number of factors, particularly the strain of virus. In the case of the brown-masked opossum (*Metachirus*) a laboratory transmission cycle with *Haemagogus* mosquitoes has been accomplished (Bates and Roca-García, 1946). These workers also infected a woolly opossum (*Caluromys*) by bite with *Haemagogus*. Waddell and Taylor (1948) have carried on mosquito-marsupial transmission cycles in the laboratory using *aegypti*, murine opossums (*Marmosa*), and brown-masked opossums. While the opossums are active at night their daytime sleeping places include the crotches of trees as well as tree hollows, so they might well be exposed to the bites of diurnal arboreal mosquitoes. There are seven genera and numerous species present in Middle America: *Didelphis* (common opossums), *Marmosa* (murine opossums), *Monodelphis* (short bare-tailed opossums), *Philander* (grey-masked opossums), *Metachirus* (brown-masked opossums), *Caluromys* (woolly opossums) and *Chironectes* (water opossums). One genus, that of the common opossum, *Didelphis*, extends north through the eastern United States to the Canadian border. As mentioned previously, Clark (1952) found one positive *Didelphis* in his immunological survey in Panama.

Another group of arboreal inhabitants of the Middle American forests are the kinkajous (*Potos*) and olingos (*Bassaricyon*) which are closely related. There are seven races of *Potos flavus* ranging through Middle America to southeastern San Luis Potosi in Mexico, and three races of *Bassaricyon gabbii*, and two other species, *lasius* and *pauli*, in Panama, Costa Rica and Nicaragua. As is the case with the marsupials, they sleep during the day in trees where they are exposed to attack by diurnal arboreal mosquitoes. According to Bugher they are readily infected and circulate virus. He considers it probable that individuals giving positive protection tests are specifically immune to yellow fever. But it has apparently never been demonstrated whether or not they are capable of infecting mosquitoes. While these creatures are less conspicuous than monkeys because they are principally nocturnal, we are impressed that they are common animals in Middle America. Courtney (1950) and Clark (1952) both report positive mouse protection tests from shot animals collected in Panama.

Too little is known of the significance of positive protection tests in such animals as ocelots, sloths, anteaters, and cavies (conejo pintado) to be able to evaluate their possible roles in the epidemiology of yellow fever.

Mosquito Vectors

At the time that yellow fever appeared in Panama late in 1948 a DDT residual house spraying program for the control of malaria had already been carried on for several years. While the entire country had not been consistently sprayed, it so happened that the Pacora area had received treatment the previous September. One consequence of the appearance of yellow fever was an intensified DDT residual house spraying program which resulted in the apparent eradication of *Aedes aegypti* from Panama. Use of residual house spraying in the Central American countries also had a profound effect on *aegypti*. At the time yellow fever later appeared in Costa Rica, Nicaragua, and Honduras the urban vector of yellow fever had either been eradicated or reduced to such low levels that the possibility of urban transmission of the disease never arose in this area.

It may well be that there are as yet unsuspected cycles of yellow fever in environments other than the tropical forest canopy. But our studies in Middle America have been oriented toward learning enough about the distribution, ecology, and behavior of the mosquito associations of this situation to determine if the present general understanding of the epidemiology of the sylvan form of the disease can rationally be supported. In South America, mosquitoes of the aedine genus *Haemagogus* have repeatedly been implicated in the transmission of sylvan yellow fever, and we have accordingly paid particular attention to them in our studies in Middle America. Whitman (1951) has recently reviewed the knowledge of mosquito vectors of yellow fever. But since little has been known about the forest mosquitoes in Middle America, we give here a relatively full summary.

Haemagogus spegazzinii falco. This species ranges through Panama and Central America as far as the north coast of Honduras east of the Ulua Valley. Except for the Rivas Isthmus, southwest of Lake Nicaragua, it is known in Nicaragua and Honduras only from the Atlantic slope. It is characteristic of tropical rain-forest. In Middle America it appears most often on mountain slopes from 300 to 1500 feet in elevation, although we have taken it from as high as 4200 feet on the Atlantic side of the Chiriqui volcano. In dense rain-forest it is almost completely arboreal, but when it appears in deciduous forest or in cacao plantations, where the forest cover has been broken by thinning out the large trees, it also attacks on the ground. Yellow fever virus has been recovered from it in nature, by bite, a number of times in South America.

Haemagogus equinus. This is the widest ranging *Haemagogus* in Middle America, occurring throughout the region in suitable forest cover, but seldom above 4000 feet. We have recently been able to demonstrate that it even extends north to the United States where we collected it near Brownsville, Texas (Trapido and Galindo, 1956a). In habitat predilection it is the least discriminating *Haemagogus* of the region. It is present in numbers in deciduous tropical forest, and even in low thorny scrub, as well as in rain-forest. It may also be peridomestic, breeding in artificial water containers. Where coastal mangrove thickets have not been invaded by other *Haemagogus*, *equinus* also occupies this ecological niche. In most forest situations it is the commonest *Haemagogus* present. It is distinctly arboreal, but somewhat less so than *spegazzinii falco.* The species has repeatedly been shown to be capable of transmitting yellow fever in the laboratory. Although virus has never been recovered from it with certainty in nature, it has not been the subject of such intensive field studies as have been carried on in areas in which *spegazzinii falco* was shown to be a natural vector. It was the only *Haemagogus* present in the immediate area where a yellow fever epizootic occurred near La Masica, Honduras, in 1954 (Trapido and Galindo, 1955), but virus was not recovered from it (Rodaniche, 1956b).

Haemagogus lucifer and *iridicolor. Haemagogus lucifer* occurs in forests throughout Panama at elevations below 3500 feet. It is replaced near the Costa Rican border by the very closely related *Haemagogus iridicolor*, which extends into northern Nicaragua. Of the species of *Haemagogus* in the forests of Panama, *lucifer* is outnumbered only by *equinus*, but in areas in which yellow fever appeared in Costa Rica we found *iridicolor* to be more abundant than *equinus* (Galindo and Trapido, 1955). These species are somewhat less arboreal than *equinus*, about two-thirds to three-quarters of the specimens being taken in the canopy. Their ability to transmit yellow fever has never been tested.

Haemagogus mesodentatus complex. Morphologically these mosquitoes are closely related to *Haemagogus spegazzinii falco.* At the time we began our studies in Middle America the description of the type series from San Jose, Costa Rica (Komp and Kumm, 1938) and mention of their presence in El Salvador (Kumm and Zuñiga, 1942), was the only available information about them. We have since been able to establish that *mesodentatus* has a wide range from the mountain slopes of Bocas Del Toro Province in western Panama through the Atlantic side forests of Central America and Mexico to southeastern San Luis Potosi. We failed to find representatives of this group on the Pacific side of Nicaragua, but now know that there is a related but distinct species ranging from El Salvador through the Pacific versant of Guatemala and Mexico at least as far north as southern Sinaloa near Mazatlan. There is a third form replacing the other two in the highlands of Guatemala and extending at least as far north as the vicinity of Cuernavaca in Mexico. We have taken this form as high as 5000 feet in Chiapas. In lower Central America these mosquitoes are not particularly common, but in El Salvador, Guatemala and Mexico we have found them to be often a dominant element of the forest canopy fauna, in some places outnumbering even *Haemagogus equinus*. In recently performed experiments at the Gorgas Memorial Laboratory both *mesodentatus* from Peten and the companion species from the Pacific side of Guatemala (as yet undescribed) have been shown to be capable of transmitting yellow fever by bite.

Haemagogus of littoral situations. On the Pacific shores of Middle America there are three *Haemagogus* which sometimes breed in coconut husks, fallen palm spathes or rot holes of trees in coastal swamps, but whose primary habitat is tidal mangrove where they attack in numbers, both on the ground and in the trees. *Haemagogus boshelli* occupies this special habitat from Colombia to San Miguel Bay in eastern Panama. Replacing it in Panama, and extending to the Gulf of Fonseca in Honduras, is *Haemagogus chalcospilans*. Here it is in turn replaced by *Haemagogus regalis* which ranges north to the Pacific coast of Chiapas in southern Mexico. On the Atlantic side of Middle America we have found the coastal habitat to be occupied in British Honduras by an undescribed species, and in southern Veracruz by a form of uncertain status. Elsewhere this habitat is invaded by primarily forest-inhabiting species: in the Atlantic side mangroves of Costa Rica and westernmost Panama, *iridicolor*; in the coastal swamps of northern Honduras, *equinus*; and in the mangroves of the west coast of Mexico, *equinus*.

It has been proposed by Komp (1954) that *regalis* is conspecific with *lucifer*, but in light of the disconnected ranges, the different habitats, and morphological differences evident in newly collected material, we consider them quite separate species. Komp (1955) has also suggested that *Haemagogus boshelli* might be suspect as a yellow fever vector in eastern Panama. It is our view that *boshelli* as well as *chalcospilans* and *regalis* are essentially mangrove inhabitants, that they occur in numbers only in coastal situations, and that they therefore could not be involved in epizootics of the interior forests. The only coastal flatland where a yellow fever epizootic has been detected was that on the northern shores of Honduras where we found only *Haemagogus equinus* (Trapido and Galindo, 1955).

Haemagogus of deciduous forest and second growth. In lowland situations with relatively open deciduous forest and second growth there are two characteristic *Haemagogus* species. *Haemagogus argyromeris* is limited to the Pacific side of Panama where it breeds in artificial containers as well as tree holes and ground bromeliads. *Haemagogus anastasionis*, which is known from Colombia and Venezuela, apparently skips Panama but has been taken on the Pacific side from northwest Costa Rica to El Salvador, and on the Atlantic side of Mexico in Veracruz. It is morphologically related to *spegazzinii falco*. Both *argyromeris* and *anastasionis* are taken primarily on the ground. The ecological situations in which they occur together with their predilection for biting at ground level would seem to isolate them from possible involvement in epizootics among forest dwelling primates. Their ability to transmit yellow fever virus has not been tested.

Aedes leucocelaenus clarki and *leucotaeniatus*. *Aedes leucocelaenus clarki* is about as common as *Haemagogus spegazzinii falco* in similarly forested situations in Panama, but becomes uncommon in Costa Rica and rare in Nicaragua and Honduras. The northernmost record is from Yaruca, Honduras. Slightly more than half of those taken were in the forest canopy. Naturally infected specimens of *leucocelaenus* have been shown to transmit yellow fever by bite in South America. Closely related is *Aedes leucotaeniatus*, known from Panama and Costa Rica. It is less common than *leucocelaenus clarki* and is also less arboreal, fewer than half the individuals having been taken in the forest canopy. Its ability as a vector is unknown as it has not been the subject of experiments.

Other *Aedes*. *Aedes terrens* is a member of the same subgenus (*Finlaya*) as the preceding two species and might thereby be suspect as a yellow fever vector. But in Middle America there are probably several species or races passing under this name, and the form which readily feeds on man is abundant only at elevations of 2000 feet or more. It has not been a significant part of the mosquito fauna where yellow fever has appeared. *Aedes scapularis* which has been shown to be capable of transmitting yellow fever by bite in Brazil is present in Middle America, but it is a temporary ground pool breeding species which is spotty in distribution, erratic in numbers, and primarily attacks at ground level. In Middle America it has not appeared to be associated with the transmission of yellow fever. *Aedes fluviatilis* is another species which has been shown to be able to transmit by bite in South America and is present in Middle America, but it has been rare or absent where yellow fever has appeared.

Sabethini. A great diversity of the mosquitoes of this tribe is present in the American tropics. They breed primarily in water-holding plants but there are also some species which breed in tree holes. The eggs do not resist desiccation as do those of the aedines, so that they must either find breeding places throughout the year, or be very long-lived to survive the unfavorable dry season. One species has been consistently present in significant numbers wherever we have investigated sylvan yellow fever in Middle America, *Sabethes chloropterus*. It is an inhabitant of both tropical rain-forest and tropical deciduous forest, and ranges north to southern Mexico in both the Atlantic and Pacific drainages, but becomes uncommon at elevations above 3000 feet. It breeds in tree holes, is distinctly arboreal, and persists during the dry season when *Haemagogus* species and *Aedes leucocelaenus* become rare or disappear.

On the north coast of Honduras in 1954 very substantial numbers of *Trichoprosopon magnus* were encountered in the forest canopy where monkeys had died of histopathologically proven yellow fever (Trapido and Galindo, 1955). We consider this an exceptional circumstance, however, since the species breeds in a *Calathea* characteristic of swampy lowlands, and with the exception of this epizootic, the yellow fever recently experienced in Middle America has been confined largely to forested slopes where the species is rare.

The difficulty of maintaining sabethine mosquitoes in captivity has limited the laboratory study of their ability to transmit. Interest in the group has stemmed from the recovery of virus by inoculation from a mixed pool of this tribe in Brazil (Shannon, Whitman, and Franca, 1938). According to Waddell (1949) and Whitman (1951), one laboratory transmission by bite was obtained with a Brazilian species, *Trichoprosopon frontosus*. The survival of virus over dry season, when *Haemagogus* appear to be rare or absent as adults, requires the involvement of some other mosquito which is better able to persist through this unfavorable period. (This assumes that only mosquitoes are concerned, which is the conservative course to follow until proof to the contrary is forthcoming.) In our first studies of the forest mosquitoes associated with the appearance of yellow fever in Panama (Galindo, Trapido, and Carpenter, 1950) we were attracted by the fact that *Sabethes chloropterus* best fitted the theoretical requirements. Epidemiological studies in areas where yellow fever subsequently appeared in Central America further stimulated our interest in this species. After much effort a colony of *chloropterus* has been established at the Gorgas Memorial Laboratory, and in collaboration with Dr. Enid de Rodaniche we have recently been able to demonstrate the ability of this mosquito to transmit yellow fever by bite.

Epidemiological Discussion

Studies carried on in connection with the recent wave of yellow fever in Middle America have provided much new information of importance in reevaluating the epidemiology of the disease in the area. We will deal here with four principal problems: (1) Had sylvan yellow fever been present in Middle America prior to 1948? (2) Of what significance is the Canal Zone region in limiting the spread of sylvan yellow fever into Middle America? (3) How does the yellow fever virus survive over the dry season when the forest canopy mosquito fauna is at its lowest ebb? (4) Why did the sylvan yellow fever wave which recently passed through Middle America stop apparently on the north coast of Honduras in 1954?

Sylvan Yellow Fever in Middle America Prior to 1948

Events have shown that conditions for the support of a transient wave of sylvan yellow fever recently existed in Middle America at least as far north as the Caribbean coast of Honduras. The immunological surveys conducted prior to 1948, together with the obvious susceptibility of the primate population at the time yellow fever virus entered the area, would indicate that sylvan yellow fever was not present west and north of the Panama Canal for some considerable period. In the case of the monkeys the evidence covers the life span of the present population, while the immunity surveys among humans indicate the absence of yellow fever since 1925. These facts do not, however, exclude the possibility that sylvan yellow fever was present in Middle America at some previous time, masked by the more obvious urban cycle of the disease. To weigh the possibility of sylvan yellow fever having been present at some time in the past we must first consider certain historical evidence.

Of primary concern is the place of origin of the urban vector, *Aedes aegypti*. There is now general agreement that this mosquito is African in origin, and was introduced to the New World at the time of the Conquest or as a consequence of the slave traffic from Africa in the period immediately following. *Aedes aegypti* is a member of the subgenus *Stegomyia* which has numerous representatives in Africa but only *aegypti* in

America. In Africa *aegypti* is both sylvan and urban in habitat. The New World population is composed of only the domestic urban strain.

Secondly we must consider whether yellow fever originated in the Old or New World. This is a question which probably will never be settled with certainty. It was concluded by Carter (1931), in his careful and scholarly study of the early history of yellow fever, that both the historical and biological evidence pointed to Africa as the place of origin. More recently Taylor (1951) has summarized the evidence on both sides. He draws no conclusion, but the weight of the evidence he presents favors an African origin also. In recent papers on yellow fever in Middle America, Elton (1954, 1955) has unequivocally accepted certain references in the Mayan chronicles as proof of the presence of yellow fever in southern Mexico prior to the discovery of America. Carter (1931) had examined these records with meticulous care, but concluded that the first evidence of yellow fever recognizable as such was the Yucatan epidemic of 1648, some 120 years after the arrival of the Spaniards there.

If *Aedes aegypti* were not present in the New World prior to the Conquest, and yellow fever occurred among the Maya in southern Mexico before that time, the transmission cycle must have been sylvan. The evidence for pre-Conquest yellow fever is, however, too much in doubt to support firmly this conclusion.

By the time epidemics which can unquestionably be attributed to yellow fever appeared in Middle America, *aegypti* was firmly established. The fact that the control of *aegypti* resulted in the apparent disappearance of yellow fever from Middle America would favor the theory that only urban yellow fever existed here. But Elton (1953, 1955) has called attention to the native accounts recorded by Gaitan (1939) and Sanchez (1939) of monkey mortality being associated with yellow fever in Guatemala near the turn of the century.[1] Although we might like some more substantial evidence than these hearsay accounts which were not reported until after the existence of sylvan yellow fever was recognized in South America, they cannot be wholly disregarded.

We should also at this point reexamine the immunological studies outlined above. We have mentioned that there were certain minor inconsistencies in the survey of Sawyer, Bauer, and Whitman (1937). In

[1] Although mammals other than primates may be involved in the sylvan yellow fever transmission cycle, for the sake of simplicity we will refer only to them as hosts in the epidemiological discussion. What is said of them, however, would apply in general to other arboreal mammals which might be concerned.

Mexico they found positive protection tests in two children reported to have been born in 1924, and one born in 1925, but the last clinically recognized Mexican case was in February 1923. They suggest several possible explanations: (1) the ages of the subjects may have been incorrectly given; (2) the protection tests performed at that time may have been oversensitive; (3) mild and unrecognized yellow fever may have persisted for a period after the last apparent case was diagnosed. There was a similar difficulty in the case of a child from Usulatan, El Salvador. While the child was recorded as having been born in 1925, the last yellow fever recognized at Usulatan was in 1921.

Also of interest here are the details of the immunity survey made along the border between Mexico and Guatemala by Bustamante, Kumm, and Herrera (1942). They found positives only in the older age groups, but these were distributed far up the Usumacinta and Pasion Rivers, in an area of tropical rain-forest. Their explanation of the disappearance of yellow fever may be translated as follows. "The isolation of the villages of the Southeast, their few inhabitants and the lack of breeding places of *Aedes aegypti* explain the extinction of outbreaks of rural type with *A. aegypti*." The concept of rural yellow fever transmitted by *aegypti* was developed to explain a special situation in northeastern Brazil. Taylor (1951) has summed up this epidemiological pattern as follows. "Endemic rural yellow fever demands rather special circumstances, which in brief are: low rainfall, necessitating the collection and storage of water in artificial containers; a sufficient number of nonimmune travelers; and a wide dissemination of the mosquito vector among the villages and isolated inhabitants." The first requirement for rural *aegypti*-transmitted yellow fever is low rainfall with the attendant collection, storage and transportation of water in artificial containers. The area in which this yellow fever pattern appeared in northeastern Brazil is arid. The Usumacinta basin, on the other hand, has abundant rainfall which supports tropical rain-forest. It is not a region in which there is any cause to store water in artificial containers, for water is always close at hand. The climate and forest type support populations of *Haemagogus equinus* and *mesodentatus*, as well as howling and spider monkeys. This suggests that sylvan yellow fever rather than *aegypti*-transmitted rural yellow fever had been present in the Usumacinta basin.

When considered all together (the accounts of monkey mortality in Guatemala, the apparent persistence of yellow fever in Mexico and El Salvador after urban cases were no longer recognized, and the evidence of past yellow fever in the remote rain-forest of the Usumacinta basin) there is certainly suggested the possibility that yellow fever of non-urban type had been present.

But in reviewing the history of yellow fever we have not been able to find evidence of a sustained geographic sequence of outbreaks such as characterized the recent wave in its progress from Panama to Honduras. If sylvan yellow fever had occurred in the past in Middle America we must find some explanation of why such episodes were localized in nature.

While the South American tropical rain-forest habitat extends along the Atlantic slope of Middle America as far as Mexico, and the same generic elements of the mosquito fauna do likewise, there are distinct differences in details. Such details are: (1) the geographical limitations of the distribution of particular species; (2) quantitative differences in the relative densities of species; (3) quantitative differences in the annual cycles of abundance. Two forest mosquitoes which have been implicated in the transmission of sylvan yellow fever in South America we found in Panama and Costa Rica: *Haemagogus spegazzinii falco* and *Aedes leucocelaenus clarki*. But they are almost never present in the densities reported in South America (Galindo, Trapido, and Carpenter, 1950). These species become increasingly less common to the north (Trapido and Galindo, 1955). *Aedes leucocelaenus clarki* is rare north of Costa Rica, and its range ends in Honduras. *Haemagogus spegazzinii falco* is present in moderate numbers through Nicaragua, but the populations are sparse in Honduras. Its range appears to end near the place where the last yellow fever was reported on the north coast of Honduras. In the case of the *Haemagogus*, there are replacement species which extend to higher latitudes. On the Atlantic slope, *Haemagogus equinus* and *mesodentatus* follow the tropical rain-forest to its end in southeastern San Luis Potosi in Mexico, and *equinus* continues still farther north through tropical deciduous forest and even thorn scrub to southernmost Texas. Both these species have been shown in the laboratory to be capable of transmitting yellow fever, but they appear to be less efficient vectors than *spegazzinii falco*.

The effects of climatic changes which are related to latitude are also of great importance. In general, the greater the distance from the equator the more prolonged is the dry season with its attendant limiting influence on the forest canopy mosquito fauna during this part of the year. Temperature conditions also change with latitude. While the mean annual temperature at Belize (26.3°C) is very close to that at Colon (26.6°C) the departure from the mean is greater in British Honduras

(5.0°C) than in Panama (1.2°C) (Sapper, 1932). Characteristic of the climate of this region is the fact that the period of low temperatures coincides with that of low rainfall. Thus as one proceeds north the climatic conditions for the survival of virus over this critical time of year become increasingly less favorable. The low temperatures reduce the rate of virus multiplication in mosquitoes at the same time that the longer dry season limits mosquito survival. The chance for an infected mosquito to survive long enough to become infective during this unfavorable period lessens with increase in latitude.

The combination of these factors severely limits the opportunity for sylvan yellow fever to persist for long periods in endemic fashion in regions as far north as Guatemala and Mexico, on the Atlantic versant. The lower total precipitation on the Pacific versant, together with the more pronounced dry season militate against survival of virus over even a single dry season as far south as Panama.

In contrast to the unfavorable factors of climate and mosquito fauna, the large and wholly susceptible monkey population in Middle America favors the maintenance of sylvan yellow fever. But when the yellow fever virus enters the monkey population the situation deteriorates at once. With the available intermediate host pool shrunken through mortality and immunization by infection, the possibility of the virus cycle being continued is reduced.

In the regions of South America where sylvan yellow fever is permanently enzootic the factors are differently balanced. The available host population of primates is smaller due to the recurring passage of virus limiting the number of susceptibles. But the forest canopy mosquitoes are efficient vectors, they are present in large numbers, and the climatic cycle is more favorable, so that transmission is possible even when some substantial portion of the sylvan host population is immune. Herein the situation in Middle America differs. Efficient vector species have restricted ranges and are present in only limited numbers. Other species are wider ranging, but these too are usually present at densities lower than in South America, and in addition are less efficient vectors. Under these conditions a large and wholly, or almost wholly, susceptible primate population is necessary to support transmission.

In South America the sylvan cycle of yellow fever is thought to follow a monkey-mosquito-monkey or a monkey-mosquito-man cycle, and to wander through the vast forest indefinitely. The dangerous aspect of this sylvan cycle which has been repeatedly stressed has been that of a human infected in the forest coming into a nonimmune population center where *aegypti* is present, and setting off an urban epidemic.

Little attention has been given to the possibility of the reverse process; i.e., an *aegypti*-infected person going into the forest and being bitten by sylvan mosquitoes, thus releasing an epizootic in monkeys. But if yellow fever were brought to America with *aegypti*, this would have been the way by which permanently enzootic sylvan yellow fever became established in South America. When urban yellow fever was present in Middle America, prior to 1924 or thereabouts, the opportunity existed for the seeding of epizootics in areas peripheral to infected population centers. Such epizootics, however, would have been circumscribed in extent and duration by the marginal factors of climate, vectors and hosts previously outlined. They would have gone unrecognized at the time because the roles of vectors other than *aegypti* and hosts other than man were not suspected. There is thus suggested for Middle America, prior to 1924, a modification of the conventional sylvan yellow fever epidemiology. The transmission chain would have been human-sylvan mosquito-monkey, with a dead end in the forest after a period limited either by the intervention of particularly adverse climatic conditions, or the shrinking of the pool of susceptible primates, or a combination of both. Like the splash from a drop of water which dries up if more water is not added, yellow fever from urban reservoirs would have "splashed" into the forest and dried up there.

This leads us to the explanation of why there appear to have been no previous waves of sylvan yellow fever passing through Middle America such as that witnessed during the period from 1948 to 1954. When the virus entered from the south in 1948, this was probably the first time since the introduction of *aegypti*-transmitted yellow fever that a sustained transmission cycle was possible, because this was the first time that there had been opportunity for a nonimmune and abundant primate population to develop.

Significance of the Canal Zone Area as a Barrier to Sylvan Yellow Fever

It is plain from the immunological surveys cited, that sylvan yellow fever was present in eastern Panama long after urban yellow fever was eradicated. There is no satisfactory evidence that it had been west of the Canal for some long period. What then is the significance of the Panama Canal as a barrier? The Canal, as has been previously mentioned, marks a gap in the orographic system. To the east, toward the South American continent, the mountains are low and narrow, but to the west they broaden and increase in altitude to almost 12,000 feet at the Volcan de Chiriqui near the Costa Rican border. The gap at the Canal Zone permits the moisture laden trade winds access to the Pacific side. Thus the Atlantic side of the Canal Zone is deprived of a portion of rain which might fall there, and the Pacific gains in precipitation. To the west of the Zone, the mountain mass induces increased precipitation on the Atlantic and decreased precipitation on the Pacific. East of the Canal Zone, the low narrow ridges are less effective in screening out moisture from the trade winds.

These features produce tropical rain-forest on the Atlantic side of the Isthmus, and a band of this forest type along the lower slopes of the Pacific-facing ridges east of the Canal. To the west of the Canal, on the Pacific side, there is tropical deciduous forest or savannah. In the area of the Canal Zone and the country directly to either side of it, the intermediate rainfall produces a vegetation cover which is transitional between tropical rain-forest and tropical deciduous forest. This area is thus one in which conditions are marginal for survival of sylvan mosquitoes and virus over the dry season. The rainfall, however, varies substantially from year to year. For example, at Cristobal, at the Atlantic entrance to the Canal, annual rainfalls of as little as 86 inches or as great as 183 inches have been recorded (Esslinger, 1954). Our studies in the forest just east of Panama City, over a 6-year period, have shown that there are correspondingly great year to year fluctuations in the populations of forest canopy mosquitoes. This leads us to believe that what happened in the period 1948 to 1950 was that a virus wave arrived at this critical zone during a particularly good time for forest canopy mosquito production. The minimum conditions for sustained transmission were met, and the virus was able to pass across into the tropical rain-forest of the Atlantic slope west of the Canal. Once across this gap, climatic and forest cover conditions were favorable for the continued movement of the virus through an area with a wholly susceptible primate population.

Virus Survival During Dry Seasons

We are next faced with the problem of how the virus survived through dry seasons over a 6-year period. In the Atlantic side rain-forest, with the attendant *Af* or *Am* type climates, the "dry" season is in fact not very dry. At such Atlantic side localities as Limon, Costa Rica, and

Bluefields and Greytown, Nicaragua, the mean monthly rainfall at no time of year drops below 3 inches according to the data compiled by Reed (1923). Despite this lack of any completely dry period, our two year study of the forest canopy fauna in the tropical rain-forest at Almirante (Trapido and Galindo, 1956b) has shown that the rainfall fluctuations are sufficient to produce large swings in the abundance cycles of *Haemagogus* mosquitoes. In some months adults are so scarce that it is difficult to imagine the virus cycle being maintained by *Haemagogus* alone. Persisting throughout the year, however, is *Sabethes chloropterus*. While there may be other factors of which we are unaware, the recent proof that *Sabethes chloropterus* is capable of transmitting yellow fever virus seemingly provides the missing link in the transmission chain in the rain-forest. The Pacific side tropical deciduous forest with its *Aw* climate cycle and severe dry season apparently did not sustain the transmission cycle. There was no overt evidence of yellow fever along the Pacific versant of Panama west of the Canal Zone, with the exception of a human case at Burica Point on the Costa Rican border in an area which is, as previously mentioned, exceptional for the Pacific coast in that it is a pocket of high rainfall. The yellow fever here, like that on the Pacific side of Costa Rica and the Rivas Isthmus of Nicaragua, was the consequence of the excursion of virus from the Atlantic slope.

Why Did Yellow Fever Apparently Stop in Northern Honduras?

Finally we must deal with the question of why the yellow fever which passed through lower Middle America appeared to stop on the north coast of Honduras, after its last activity there during the rainy season of 1954. Perhaps too little time has lapsed (15 months) to say with certainty that it has indeed stopped. But the area of most recent activity is well populated, there are several hospitals in that part of Honduras and adjacent Guatemala, and an entire rainy season has passed without new evidence of yellow fever. For the purposes of this discussion we will adopt the working premise that we have seen the last of the recent yellow fever episode. There are three possible explanations of why yellow fever apparently stopped on the north coast of Honduras.

The Ulua valley, which lies just to the west of the place where the last epizootic was observed in 1954, may have been a barrier. This valley is almost completely cleared and under intensive cultivation for bananas. The inland bordering ridges are covered with pine forest which supports neither monkeys nor *Haemagogus* mosquitoes. There is, however, a narrow band of swampy broad-leaved forest at the head of the valley, between the bananas and the pines. It is possible that the clearing of the broad-leaved forest from most of the valley floor created a zone of artificial conditions sufficiently extensive to interfere with transmission.

Another consideration is that the place where yellow fever last appeared is very close to the end of the range of *Haemagogus spegazzinii falco*. It could well be that there is a causal relationship between the limits of the range of this efficient vector and that of yellow fever. But *spegazzinii falco* is not common here. Only 62 specimens were taken in a year of daily collecting in the canopy of the rain-forest at Lancetilla. These numbers are so small that it is difficult to imagine that *spegazzinii falco* alone could sustain transmission. Also, in our investigation of the epizootic on the north coast of Honduras in 1954, we found that the monkey mortality occurred in the forest of the swampy coastal plain where the only *Haemagogus* present was *equinus*. It would thus appear that *spegazzinii falco* was not exclusively involved in transmission. The range of *equinus* extends far to the north, and if it were a vector in this area, as seems likely, the yellow fever wave would not have stopped here.

Probably of greatest significance is the fact that the dry season of 1955 was exceptional, insofar as any climatological event can be called "exceptional." The climate of this Atlantic facing region is of the *Af* or *Am* type, without a severe dry season in most years, but during the first half of 1955 an unusual drought was experienced. This was severe enough to cause failure of the corn crop. In Guatemala it was necessary for the government to take emergency measures and import corn to avert famine. We have collected data from a series of representative localities on the Atlantic coastal plain to show the low rainfall during March, April, and May of 1955, in comparison with the averages for these places in previous years (Table 1). It will be seen that during these months of 1955 rainfall was only a fraction of that usually experienced. We have available 23 years of rainfall data from Lancetilla, Honduras, which is only a few miles from where the last epizootic occurred. In none of these years was there as little rainfall during March, April, and May, as in 1955. This unusual drought, through its effect on the sylvan mosquito fauna, appears most likely to have been the positive limiting factor.

The strong probability that it was the unusual deficiency of rainfall during the first half of 1955 which put an end to the progress of sylvan yellow fever, leaves us in doubt as to what might happen should another wave move through Middle America at some future time. It may take

TABLE I

Comparison of Total Rainfall during March, April and May of 1955 with the Average for these Months in Previous Years[a]

Honduras	*23 Yr. Av.*	*1955*
Lancetilla	17.56[b]	3.96
Guatemala	*21 Yr. Av.*	
Quirigua	11.67	1.90
Creek	13.43	5.02
Barrios	15.34	5.25
British Honduras	*10 Yr. Av.*	
Punta Gorda Agstat	13.29	3.75
Stann Creek Agstat	7.65	2.35
Orange Walk Town	6.31	0.67

[a] Data from Lancetilla are from the United Fruit Company Research Station; those from Guatemala are from the Guatemalan National Observatory; those from British Honduras are from the Department of Agriculture, British Honduras.

[b] Inches.

another quarter century, and observation of another such wave, to determine whether or not sustained sylvan yellow fever is capable of extending north to Guatemala and Mexico.

Summary

The history of yellow fever in Middle America and the events associated with the passage of a wave of the sylvan form of the disease from Panama to Honduras, during the period 1948 to 1954, are briefly given. The distribution and bionomics of the elements of the sylvan mosquito fauna and the mammals of the region, which are most likely to be related to the maintenance of the yellow fever cycle, are summarized.

The following epidemiological conclusions are suggested. (1) It is proposed that in the past there have been circumscribed and self-limiting episodes of sylvan yellow fever in Middle America, which were seeded from urban *Aedes aegypti*-transmitted epidemics. These epizootics were limited in extent and duration because of the marginal effectiveness of the sylvan mosquito fauna as vectors. (2) Localized outbreaks, by reducing the size of the susceptible primate pool, precluded the possibility of any general sustained wave of sylvan yellow fever. The elimination of urban yellow fever at about the end of the first quarter of this century permitted the susceptible primate host population to build up to densities capable of maintaining the recent wave of yellow fever during a 6-year period. (3) The passage of virus across the Canal Zone on to the Atlantic

slope of western Panama, and so into Central America, is attributed to the coincidence of the arrival of a virus wave at this zone of marginal ecology during a period of climatic conditions particularly favorable for forest canopy mosquitoes. (4) It is suggested that transmission of yellow fever by *Sabethes chloropterus*, which persists through dry season, is the key to the survival of virus during this unfavorable time of year. (5) The apparent end of the yellow fever wave in northern Honduras in 1954 is thought most likely to have been due to a severe and unusual drought during the first half of 1955.

Addendum

The manuscript of this paper was completed in early January 1956. Later in that month reports of monkey mortality during December and January reached the Central American Zone office of the Pan American Sanitary Bureau. Dr. Stanford F. Farnsworth, representative of the Pan American Sanitary Bureau in the area relayed this information as well as liver specimens from dead monkeys to Dr. Carl M. Johnson, Pathologist and Director of the Gorgas Memorial Laboratory. Dr. Johnson has reported a histopathological diagnosis of yellow fever in howling monkeys (*Alouatta*) received from two areas, the north coast of Honduras near Esparta, and the lower part of the Montagua River valley in adjacent Guatemala.

These events invalidate the working premise adopted in the last part of our epidemiological discussion and the derived suggestion of the severe dry season of 1955 as the probable cause of the end of the yellow fever wave. Both localities at which yellow fever has now appeared are of more than ordinary interest. The Honduras locality is the same swampy coastal forest in which monkeys died in July and August of 1954, and is in fact within a few miles of the last episode near La Masica. This demonstrates the ability of the virus to persist in a locality for almost a year and a half, a state of affairs known in some areas of South America, but novel insofar as recent observations in Middle America are concerned. The Guatemalan locality is beyond the limits of the range of *Haemagogus spegazzinii falco* as we now know it. Collections of forest mosquitoes by Dr. Boshell and his assistants in the Montagua valley and the Peten, to the west and north, have revealed only *Haemagogus equinus* and *mesodentatus*. That these other *Haemagogus*, already known to transmit yellow fever in the laboratory, may under some circumstances also be vectors in nature becomes an increased probability.

The virus has demonstrated its ability to pass across the intensively ultivated valleys of the Ulua and Montagua Rivers, to survive a severe dry season, and to be transmitted by vectors other than *Haemagogus spegazzinii falco*. It is now at the southern edge of the vast forest which extends across the Peten to the Mexican Gulf coastal plain. In this forest howling monkeys (*Alouatta*) and spider monkeys (*Ateles*) are abundant, as are *Haemagogus equinus* and *mesodentatus*. Also present, but apparently somewhat less abundant than to the south, is *Sabethes chloropterus*. The next several years will reveal how far north these elements are in good enough balance to sustain the yellow fever transmission chain.

References

ALDIGHIERI, R. 1954. Considérations sur l'épidemiologie de la fievre jaune en Amérique Centrale. *Méd. trop.* **14**, 286–301.

ANONYMOUS. 1954. Correction. Yellow fever in the Caribbean. *Bol. ofic. sanit. panamer.* **36**, 536.

ANONYMOUS. 1955. Yellow fever conference, 21-22 December 1954. Am. J. Trop. Med. Hyg. 4, 571–661.

BALFOUR, A. 1914. The wild monkey as a reservoir for the virus of yellow fever. *Lancet 1*, 1176–1178.

BATES, M. 1944. Experiments with the virus of yellow fever in marsupials, with special reference to brown and grey masked opossums. *Am. J. Trop. Med.* **24**, 91–103.

BATES, M., AND ROCA-GARCÍA, M. 1945. Laboratory studies of *Saimiri-Haemagogus* cycle of jungle yellow fever. *Am. J. Trop. Med.* **25**, 203–216.

BATES, M., AND ROCA-GARCÍA, M. 1946. Experiments with various Colombian marsupials and primates in laboratory cycles of yellow fever. *Am. J. Trop. Med.* **26**, 437–453.

BAUER, J. H. 1928. Transmission of yellow fever by mosquitoes other than *Aedes aegypti*. *Am. J. Trop. Med.* **8**, 261–282.

BENITEZ ARMAS, S. 1951. El pasado y el presente de la fiebre amarilla en Mexico. *Rev. med. mexicana* **31**, 451–455.

BOSHELL MANRIQUE, J. 1952. Personal communication.

BOSHELL MANRIQUE, J., AND OSORNO MESA, E. 1944. Observations on epidemiology of jungle yellow fever in Santander and Boyacá, Colombia, September, 1941, to April, 1942. *Am. J. Hyg.* **40**, 170–181.

BUGHER, J. C. 1951. The mammalian host in yellow fever. *In* Yellow Fever, G. K. Strode, ed., McGraw Hill Book Co., New York, pp. 299–384.

BUSTAMANTE, M. E., KUMM, H. W., AND HERRERA, J. R. 1942. Ausencia de fiebre amarilla en valle del Usumacinta (Guatemala y Mexico, 1942). *Rev. inst. salubridad y enfermedad. trop. Mex.* **3**, 255–271.

CALVO, A. E., AND GALINDO, P. 1952. Epidemiology of yellow fever in Panama (1949-1952). *1st Inter-Amer. Congr. Public Health, Havana*, 1–14. Mimeographed.

CARPENTER, C. R. 1934. A field study of the behavior and social relations of howling monkeys. *Comp. Psychol. Monographs* **10**, 1–168.

CARTER, H. R. 1931. Yellow Fever: An Epidemiological and Historical Study of Its Place of Origin. Williams & Wilkins Co., Baltimore pp. xii and 308.

CLARK, H. C. 1938. Annual report of the Gorgas Memorial Laboratory for 1937. *75th Congress, House Doc.* **467**, 1–24.

CLARK, H. C. 1952. Endemic yellow fever in Panama and neighboring areas. *Am. J. Trop. Med. Hyg.* **1**, 78–86.

COLLIAS, N. AND SOUTHWICK, C. 1952. A field study of population density and social organization in howling monkeys. *Proc. Am. Phil. Soc.* **96**, 143–156.

COURTNEY, K. O. 1950. Report on recent outbreak of jungle yellow fever in Panama. *Am. J. Public Health* **40**, 417–426.

DAVIS, N. C., AND SHANNON, R. C. 1929. Studies on yellow fever in South America; transmission experiments with certain species of *Culex* and *Aëdes*. *J. Exptl. Med.* **50**, 803–808.

EKLUND, C. M. 1953. Encefalitis infantil en Costa Rica y Honduras despues del empleo de la vacuna Dakar contra la fiebre amarilla. *Bol. ofic. sanit. panamer.* **35**, 505–516.

ELTON, N. W. 1952a. Public health aspects of the campaign against yellow fever in Central America. *Am. J. Public Health.* **42**, 170–174.

ELTON, N. W. 1952b. Sylvan yellow fever in Central America. *Public Health Repts. U. S.* **67**, 426–432.

ELTON, N. W. 1952c. Yellow fever in Panama: historical and contemporary. *Am. J. Trop. Med. Hyg.* **1**, 436–456.

ELTON, N. W. 1952d. Fiebre amarilla en America Central: la naturaleza de la fiebre amarilla selvatica y su antecedente historico. *Arch. med. panameños.* **1**, 189–195.

ELTON, N. W. 1952e. Anticipated progress of sylvan yellow fever in Nicaragua: plan for attempt to block its course in Honduras. *Military Surgeon* **111**, 157–162.

ELTON, N. W. 1952f. Progress of sylvan yellow fever wave in Central America: Nicaragua and Honduras. *Am. J. Public Health.* **42**, 1527–1534.

ELTON, N. W. 1953. Project to block the progress of jungle yellow fever in northern Honduras, and its calculated risks of failure. *Military Surgeon* **112**, 424–430.

ELTON, N. W. 1954. Yellow fever in Middle America. *Armed Forces Chem. J.* **8**, 24–29.

ELTON, N. W. 1955. Anticipated progress of yellow fever in Guatemala and Mexico, 1955-1959. *Am. J. Public Health* **45**, 923–927.

ELTON, N. W., AND HERRERA, J. M. 1949. Pathology of yellow fever in 1948 outbreak of sylvan form in Panama. *Am. J. Pathol.* **25**, 772–773.

ELTON, N. W., AND JOHNSON, C. M. 1950. Pathological features of yellow fever in Panama. *U. S. Armed Forces Med. J.* **1**, 596–601.

ELTON, N. W., ROMERO, A., AND TREJOS, A. 1955. Clinical pathology of yellow fever. *Am. J. Clin. Pathol.* **25**, 135–146.

ENDERS, R. K. 1935. Mammalian life histories from Barro Colorado Island, Panama. *Bull. Museum Comp. Zool.* **78**, 385–502.

ENDERS, R. K. 1939. Changes observed in the mammal fauna of Barro Colorado Island, 1929-1937. *Ecology* **20**, 104–106.

Esslinger, W. H. 1954. Annual summary, meteorological and hydrographic data. Panama Canal Co., Meteorological and Hydrographic Branch, Mimeographed.

Gaitan, L. 1939. Actas de la decima conferencia sanitaria Panamericana. *Ofic. Sanit. panamer.*, *Pub.* **136**, 84.

Galindo, P., Carpenter, S. J., and Trapido, H. 1949. Notes on forest mosquitoes of Panama. I. *Haemagogus spegazzinii falco* Kumm et al., *Haemagogus iridicolor* Dyar, *Anopheles* (*Lophopodomyia*) *squamifemur* Antunes, and *Anopheles* (*Anopheles*) *fausti* Vargas, four new records for the country. (Diptera, Culicidae). *Proc. Entomol. Soc. Wash.* **51**, 277–278.

Galindo, P., Carpenter, S. J., and Trapido, H. 1951a. Ecological observations on forest mosquitoes of an endemic yellow fever area in Panama. *Am. J. Trop. Med.* **31**, 98–137.

Galindo, P., Carpenter, S. J., and Trapido, H. 1951b. Westward extension of the range of *Haemagogus spegazzinii falco* Kumm *et al.* into Costa Rica. (Diptera, Culicidae). *Proc. Entomol. Soc. Wash.* **53**, 104–106.

Galindo, P., Carpenter, S. J., and Trapido, H. 1952. The taxonomic status of the *Aedes leucocelaenus* complex with descriptions of two new forms. (Diptera, Culicidae). *Ann. Entomol. Soc. Amer.* **45**, 529–542.

Galindo, P., Carpenter, S. J., and Trapido, H. 1955. A contribution to the ecology and biology of tree hole breeding mosquitoes of Panama. *Ann. Entomol. Soc. Amer.* **48**, 158–164.

Galindo, P., and Trapido, H. 1955. Forest canopy mosquitoes associated with the appearance of sylvan yellow fever in Costa Rica, 1951. *Am. J. Trop. Med. Hyg.* **4**, 543–549.

Galindo, P., Trapido, H., and Carpenter, S. J. 1950. Observations on diurnal forest mosquitoes in relation to sylvan yellow fever in Panama. *Am. J. Trop. Med.* **30**, 533–574.

Gast-Galvis, A., Anderson, C. R., and Hill, R. B. 1954. Natural yellow fever infection in a monkey. *Anales. soc. biol Bogotá* **6**, 147–150.

Hanlan, M. S. 1953. The current status and probable future of jungle yellow fever in Central America. *Northwest Sci.* **27**, 83–94.

Herrera, J. M., Elton, N. W., and Nicosia, J. 1949. La aparición en Panamá de un brote de fiebre amarilla en su forma "selvática" (1948–1949) descubierto por el examen postmortem. *Arch. hosp. Santo Tomas* (*Panamá*). **4**, 1–49.

Komp, W. H. W. 1954. *Haemagogus lucifer* H., D. & K., 1912, a synonym of *Haemagogus regalis* D. & K., 1906 (Diptera, Culicidae). *Proc. Entomol. Soc. Wash.* **56**, 193–195.

Komp, W. H. W. 1955. The occurrence of *Haemagogus boshelli* in Panama. (Diptera, Culicidae). *Proc. Entomol. Soc. Wash.* **57**, 181–182.

Komp, W. H. W., and Kumm, H. W. 1938. New species of *Haemagogus mesodentatus* from Costa Rica, and description of larva of *Haemagogus anastasionis* Dyar (Diptera, Culicidae). *Proc. Entomol. Soc. Wash.* **40**, 253–259.

Kumm, H. W. 1952. Periodicity in the annual incidence of reported cases of yellow fever during the past fifty years. *Am. J. Trop. Med. Hyg.* **1**, 210–219.

Kumm, H. W., and Crawford, P. J. 1943. The recent distribution of endemic yellow fever in Central America and neighboring countries. *Am. J. Trop. Med.* **23**, 421–431.

Kumm, H. W., and Zuñiga, H. 1942. The mosquitos of El Salvador. *Am. J. Trop Med.* **22,** 399–415.

Koprowski, H. 1946. Occurrence of nonspecific virus-neutralizing properties in sera of some neotropical mammals. *J. Immunol.* **54,** 387–394.

Laemmert, H. W., Jr., Ferreira, L. de C., and Taylor, R. M. 1946. Epidemiological study of jungle yellow fever in an endemic area in Brazil; investigations of vertebrate hosts and arthropod vectors. *Am. J. Trop. Med. Suppl.* **26,** 23–69.

Laemmert, H. W., Jr., and Kumm, H. W. 1950. The susceptibility of howler monkeys to yellow fever virus. *Am. J. Trop. Med.* **30,** 723–731.

Miller, G. S., Jr., and Kellogg, R. 1955. List of North American recent mammals. *U. S. Natl. Museum Bull.* **205,** xii and 954.

Miranda, G. 1953. Comportamiento de algunas pruebas de ictericia en la fiebre amarilla. *Rev. biol. trop. (Costa Rica)* **1,** 147–171.

Philip, C. B. 1929. Preliminary report of further tests with yellow fever transmission by mosquitoes other than *Aëdes aegypti. Am. J. Trop. Med.* **9,** 267–269.

Reed, W. W. 1923. Climatological data for Central America. *Monthly Weather Rev.* **51,** 133–141.

Rodaniche, E. C. de. 1952. Survey of live forest animals for protective antibodies against yellow fever in Panamá, R. P. *Am. J. Trop. Med. Hyg.* **1,** 789–795.

Rodaniche, E. C. de. 1956a. Virus studies. *Ann. Rept. Gorgas Mem. Lab.* **1955.** 84th Congress, House Doc. 287, 7–9.

Rodaniche, E. C. de. 1956b. Survey of mosquitoes captured in Honduras for yellow fever virus. *Am. J. Trop. Med. Hyg. 5* (3).

Romero, A. 1954. Fiebre amarilla en niños menores de doce años. *Rev. biol. trop. (Costa Rica)* **2,** 169–174.

Sanchez, G. 1939. La fiebre amarilla. "Lo que fue y lo que es." Conferencia dictada por le Doctor Guillermo Sánchez F., Profesor de Patalogía Tropical en la Facultad de Ciencias Médicas, Guatemala.

Sapper, K. 1932. Klimakunde von Mittelamerika. *In* Handbuch der Klimatologie, W. Köppen and R. Geiger, Eds., Gebrüder Borntraeger, Berlin, 2(J), pp. 1–74.

Sawyer, W. A. 1940. The yellow fever situation in the Americas. *Proc. 8th Scientific Congr., Washington* **6,** 297–312.

Sawyer, W. A. Bauer, J. H., and Whitman, L. 1937. Distribution of yellow fever immunity in North America, Central America, West Indies, Europe, Asia, and Australia, with special reference to the specificity of protection test. *Am. J. Trop. Med.* **17,** 137–161.

Sawyer, W. A., and Lloyd, W. 1931. Use of mice in tests of immunity against yellow fever. *J. Exptl. Med.* **54,** 533–555.

Shannon, R. C., Whitman, L., and Franca, M. 1938. Yellow fever virus in jungle mosquitoes. *Science* **88,** 110–111.

Soper, F. L. 1938. Yellow fever: the present situation (October, 1938) with special reference to South America. *Trans. Roy. Soc. Trop. Med. Hyg.* **32,** 297–332.

Soper, F. L. 1952. Yellow fever in the Caribbean. *Bol. ofic. sanit. panamer.* **32,** 197–205.

STOKES, A., BAUER, J. H., AND HUDSON, N. P. 1928. Experimental transmission of yellow fever to laboratory animals. *Am. J. Trop. Med.* **8**, 103–164.

TAYLOR, R. M. 1951. Epidemiology. *In* Yellow Fever, G. K. Strode, ed., McGraw Hill Book Co., New York, pp. 426–538.

THEILER, M. 1930. Susceptibility of white mice to virus of yellow fever. *Science* **71**, 367.

TRAPIDO, H., AND GALINDO, P. 1955. The investigation of a sylvan yellow fever epizootic on the north coast of Honduras, 1954. *Am. J. Trop. Med. Hyg.* **4**, 665–674.

TRAPIDO, H. AND GALINDO, P. 1956a. The genus *Haemagogus* in the United States. (Diptera, Culicidae). *Science*. **123**, 634.

TRAPIDO, H., AND GALINDO, P. 1956b. Mosquitoes associated with sylvan yellow fever near Almirante, Panama. In preparation.

TRAPIDO, H., GALINDO, P., AND CARPENTER, S. J. 1955. A survey of forest mosquitoes in relation to sylvan yellow fever in the Panama Isthmian area. *Am. J. Trop. Med. Hyg.* **4**, 525–542.

TREJOS, A., AND ROMERO, A. 1954. Clínica y laboratorio de la fiebre amarilla en Costa Rica. *Rev. biol. trop. (Costa Rica)* **2**, 113–168.

TREWARTHA, GLENN T. 1954. An Introduction to Climate. McGraw-Hill Book Co., New York, pp. vii and 402.

VARGAS-MENDEZ, O., AND ELTON, N. W. 1953. Naturally acquired yellow fever in wild monkeys of Costa Rica. *Am. J. Trop. Med. Hyg.* **2**, 850–863.

WADDELL, M. B. 1949. Comparative efficacy of certain South America *Aedes* and *Haemagogus* mosquitoes as laboratory vectors of yellow fever. *Am. J. Trop. Med.* **29**, 567–575.

WADDELL, M. B., AND TAYLOR, R. M. 1948. Studies on cyclic passage of yellow fever virus in South American mammals and mosquitoes; marsupials (*Metachirus nudicaudatus* and *Marmosa*) in combination with *Aedes aegypti* as vector. *Am. J. Trop. Med.* **28**, 87–100.

WARREN, A. J. 1951. Landmarks in the conquest of yellow fever. *In* Yellow Fever, G. K. Strode, ed., McGraw-Hill Book Co., New York, pp. 1–37.

WHITMAN, L. 1951. The arthropod vectors of yellow fever. *In* Yellow Fever, G. K. Strode, ed., McGraw Hill Book Co., New York, pp. 229–298.