
YELLOW FEVER CONFERENCE

(Washington, D. C., December 21-22, 1954)

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PAN AMERICAN SANITARY BUREAU
Regional Office of the
World Health Organization
1501 New Hampshire Avenue, N.W.
Washington 6, D. C.

YELLOW FEVER CONFERENCE¹

21-22 December, 1954

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¹ A Spanish translation of these proceedings will appear in the July issue of the *Boletín de la Oficina Sanitaria Panamericana*.

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INTRODUCTION

A conference was called by the Director of the Pan American Sanitary Bureau, for the purpose of discussing and reviewing the present status of yellow fever in the Americas. The conference highlighted certain gaps in the present knowledge concerning seedbeds of the disease and its survival in certain jungle areas, and the administration of control measures.

Among those present were leading authorities in the U. S. Public Health Service, the Divisions of Preventive Medicine of the U. S. Army, Navy and Air Force, the Rockefeller Foundation, the Gorgas Memorial Institute, the U. S. Department of State, the Carlos Finlay Institute of Bogotá, Colombia, and members of the staff of the Pan American Sanitary Bureau.

The Conference met in the International Conference suite of the U. S. Department of State, December 21 and 22, 1954, with Dr. Fred L. Soper presiding.

PROCEEDINGS

(Tuesday, December 21, A. M.)

THE CHAIRMAN: Today's meeting is entirely unofficial and informal, and the objective is purely informational. There are no prepared papers to be read, the purpose being to have an opportunity for an informal discussion with some of the people who know the most about yellow fever in the Americas.

Yellow fever is not a "dead duck". Yellow fever is not a disease which has been conquered. It is not a disease which has been eliminated from consideration as a permanent threat, and one of the important things that can be done here today is to attempt to take a long-term view of yellow fever and see what has been happening over the years.

Too many health authorities get alarmed about yellow fever only when it becomes an urban disease, overlooking entirely the fact that, for the jungle populations and for rural workers who have to go into the forest, yellow fever carries the same threat that it previously had for the people in the cities.

Yellow fever is one of the diseases which have varying epidemiological characteristics under different circumstances. It is a disease which, when studied under a given set of conditions, oftentimes leads to very definite beliefs and con-

victions related to these specific conditions. From personal experience I have some convictions of my own that are quite different from those of people who have observed the disease under other conditions.

Yellow fever has been, in the past, one of the most important of the virus diseases to investigate. It has a number of characteristics which make it very useful for study. All of the strains of virus are apparently homologous. It is possible to make a diagnosis, a pathological diagnosis, in fatal cases. We do have susceptible animals, so the isolation of virus is readily carried out, and the immunity reactions, particularly in primates, are very clearcut.

The yellow fever virus has served as the basic virus on which a great deal of the preliminary work was done, much of which has been applied to other viruses. However, at the present time, we do not find the reverse taking place. The developments and discoveries that are being made with other viruses are not being carried back actively into the field of yellow fever virus.

Yellow fever, as an international problem, receives very little attention until yellow fever appears in an urban community, such as happened recently in Trinidad, and then it is surprising how the picture can change overnight; everybody becomes excited and extreme measures tend to be taken. The last three or four years have seen discussions of grave importance in the international field as to the measures which should be taken to avoid the possibility that yellow fever might be carried to Asia. It is interesting at this point to note that the original activity of the Rockefeller Foundation on yellow fever, beginning about 1915, came as a result of a trip which Dr. Wyckliffe Rose made to Asia, where he found that the health authorities in India were very much concerned over the possibility of yellow fever being introduced there following the opening of the Panama Canal. Today the development of air services has created an even greater concern. The threat, however, is not only to Asia but to all cities and ports where the mosquito vector of yellow fever persists.

In the Americas, a decision was taken by the Pan American Sanitary Organization in 1947 to attempt the eradication of the *Aedes aegypti* mosquito from the continent. Later in the day, we will hear how that campaign is progressing.

It is to be hoped that from this meeting today we will have an appreciation of yellow fever as a disease and as it exists in the Americas at the present time, and that we will recognize the importance of the continued measures for limiting yellow fever as much as possible through the vaccination of all rural populations in the forested areas of the tropics and subtropics of the Americas, and through the complete eradication of *aegypti* in the hemisphere.

It is also important that we face up to the practical nonexistence of serious continued studies on yellow fever at the present time, which represents a real scientific and practical loss to American medicine. These are the principal thoughts which led to the calling of this meeting.

Turning now to the maps you will note that Maps 1 and 2, taken from the last four-year report of the Pan American Sanitary Bureau, consist of eight small maps giving the number of cases of jungle yellow fever in countries of the Americas, by political subdivisions and by years—1946 to 1953.

In 1946 the entire area of Brazil showed only two cases of yellow fever; in 1947, four cases; in 1948, five cases; in 1949, six cases and, in 1950, there were seven cases. From 1951 to 1953, we see an extensive invasion of the disease to different points in southern Brazil with many more cases than are reported here; but in 1954 Brazil once more has reported no yellow fever.

In considering these maps, attention should be given to the fact that yellow fever reporting is different from that of other diseases in that only laboratory confirmed cases generally get listed. When jungle yellow fever was first identified, the reluctance of the medical profession to accept its existence was such that no cases were reported without laboratory proofs; so practically all of the figures on yellow fever in the Americas during the past two decades when urban yellow fever has been practically non-existent are based on cases identified by examination of liver tissue.

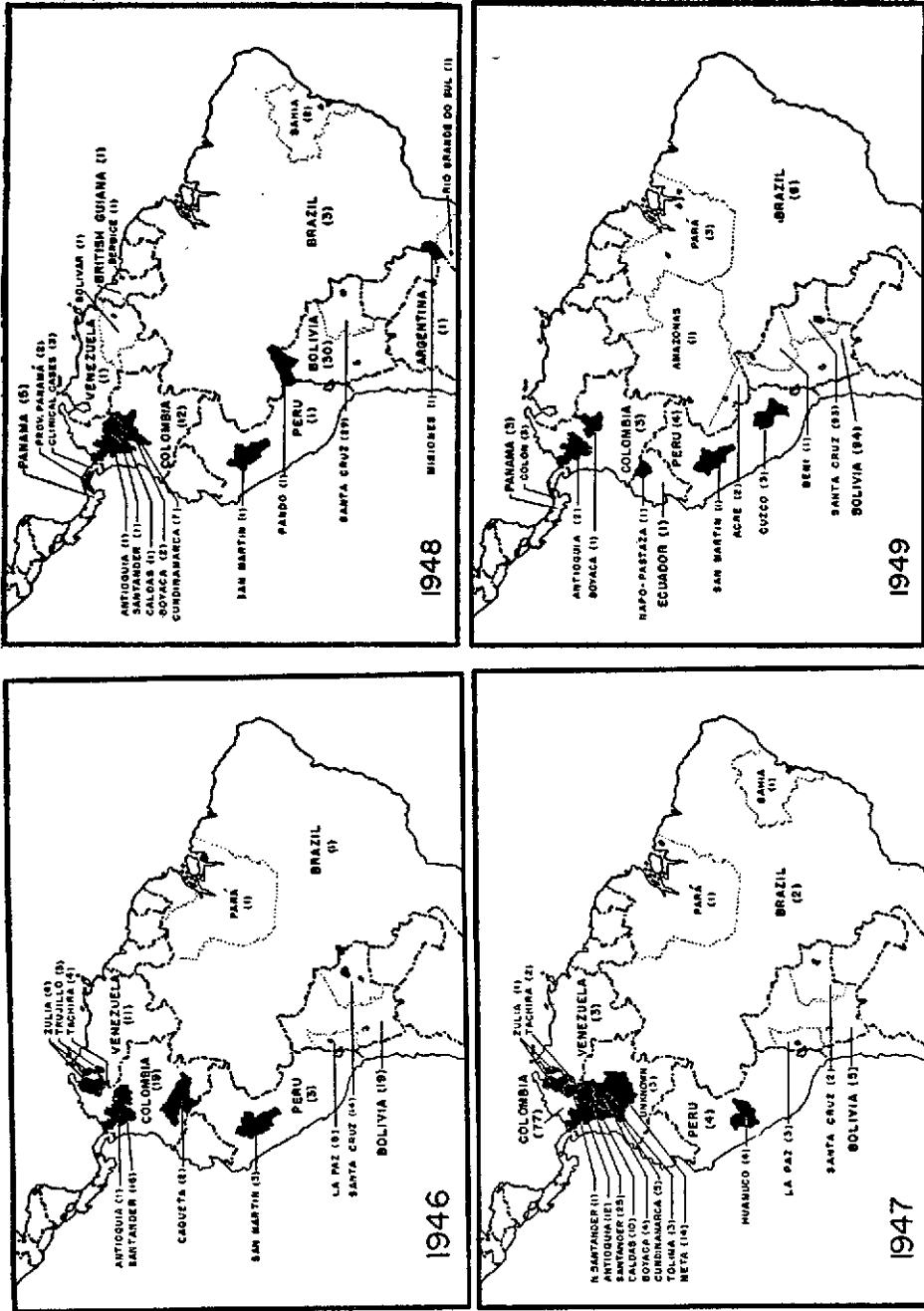
As contrasted with Brazil, we may consider Colombia where there has been a constant appearance of at least some cases every year. It is important to realize that year after year, year after year, yellow fever is a constant and continuous problem in various parts of Latin America.

Map 3 gives the yellow fever picture for 1954. Cases have occurred continuously in Colombia and in western Venezuela in an area which had yellow fever ten years ago. In eastern Venezuela, in the area labeled Sucre and Monagas, yellow fever is occurring again after a period of twenty-one years during which it had not been identified there.

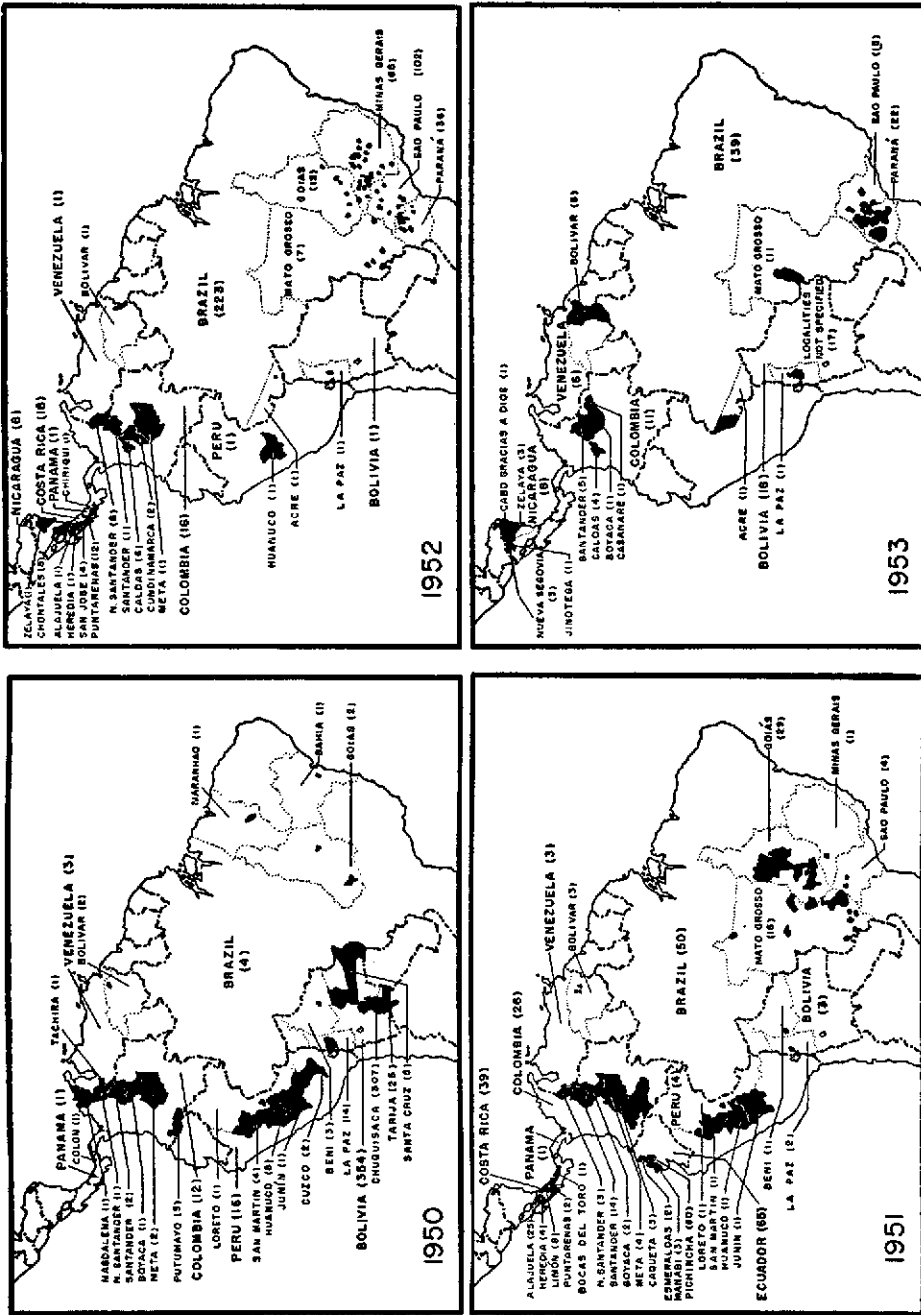
The map of Trinidad shows the distribution of proven cases this year, representing the first notification of yellow fever in that island since 1914—a forty-year period. The infection in Port of Spain with *aegypti*-transmitted yellow fever breaks a twenty-five year record of no yellow fever in any maritime port in the Americas. Not since the invasions of Rio de Janeiro in 1928 and 1929 has there been a maritime threat of yellow fever dissemination through infection of a port. Truly we must take a long-term view of the yellow fever problem.

Map 4, with a great number of names and dates, delineates the areas in Central America and the Caribbean where jungle yellow fever has occurred from 1948 to November, 1954. The year 1948 marks the period when the first cases were identified in the present sweep of virus up through Panama and Central America. Only the northern part of South America has been included to give just the regional picture of contemporary yellow fever activity. By considering the dates in various areas, one gets a clear view of the differing epidemiological picture in different areas. In the Central America area, there is a gradual progression of dates from east of the Canal in 1948 up to September of 1954 in north-eastern Honduras; on the other hand, there are repetitions of dates occurring in Colombia at fairly frequent intervals in the same places, quite contrary to what has occurred in Central America. In eastern Venezuela, south of the Orinoco River, lies an area in which yellow fever recurs at fairly frequent intervals, whereas in the northeastern section close to Trinidad there was no recorded activity until 1954.

The intervals between the recorded appearances of yellow fever in specific

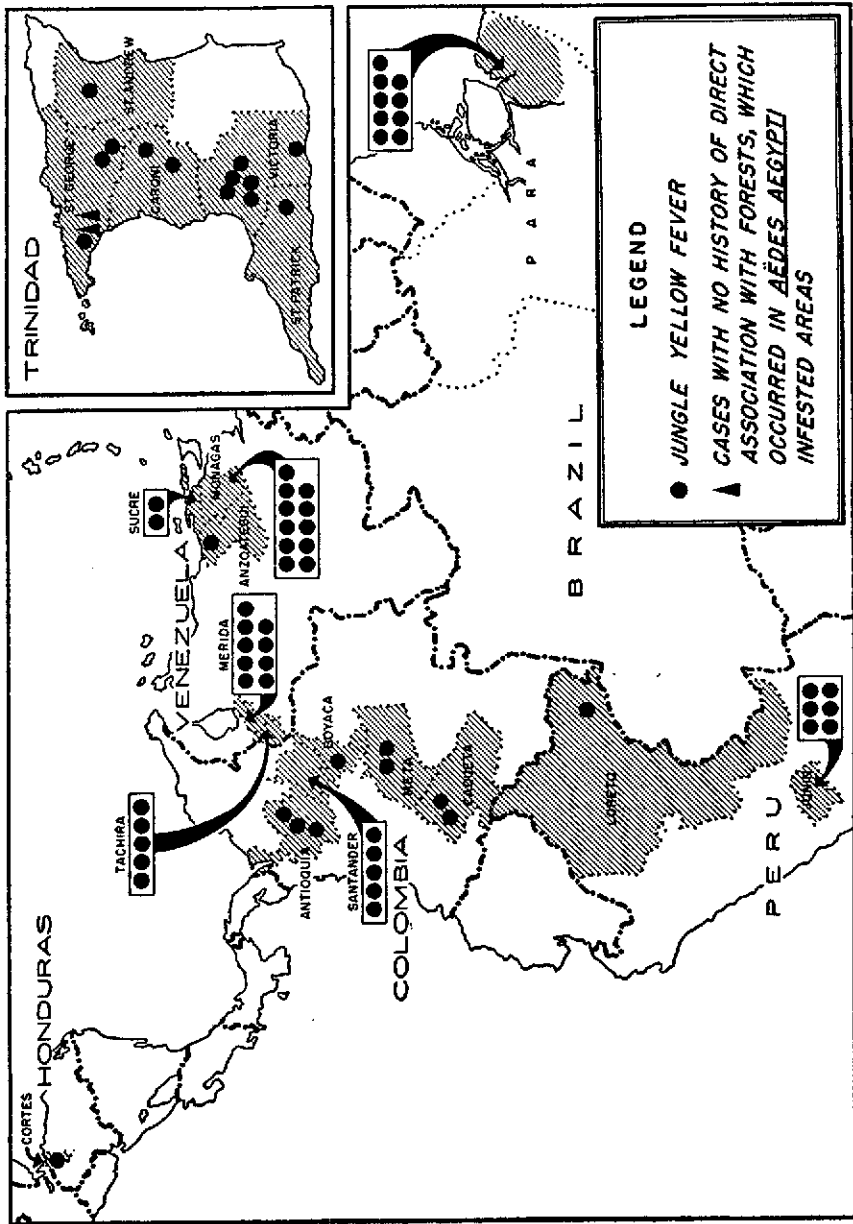


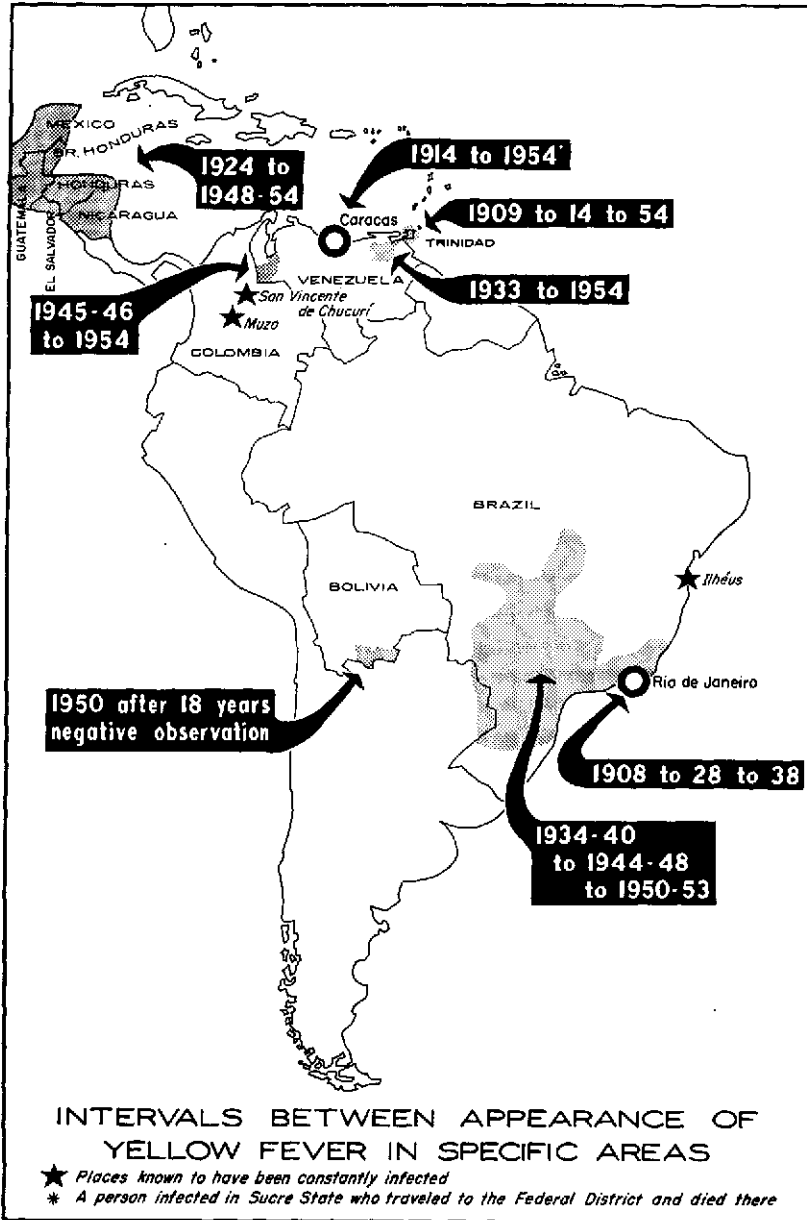
MAP 1.—Areas with number of cases of jungle yellow fever in countries of the Americas, by political subdivisions and by years, 1946-1949



Map 2.—Areas with number of cases of jungle yellow fever in countries of the Americas, by political subdivisions and by years, 1950-1953

MAP 3
 REPORTED CASES OF YELLOW FEVER IN THE AMERICAS, BY MAJOR
 POLITICAL DIVISIONS OF EACH COUNTRY, 1954





MAP 5

areas appear in Map 5, which emphasizes both the cyclical movement of jungle yellow fever in many areas—the long periodicity between outbreaks—and the continued existence of yellow fever virus in certain areas where apparently it is constantly present. Among these permanently infected areas, Ilheus on the east coast of Brazil, and San Vincente de Chucuri and Muzo in Colombia, are the most notorious. There was no reported yellow fever in Rio de Janeiro from 1908 to 1928, with a blank period from 1929 to 1938, when some infective cases came into the city from nearby jungle yellow fever areas without, however, giving rise to any locally infected cases. Since then, there has been no yellow fever reported in Rio.

In southern Brazil there was an extensive outbreak from 1934 to 1940, then a free period, after which yellow fever reappeared in 1944 in the areas where it had been in 1934, and in 1945 in the district invaded in 1935. This second wave failed to prosper, although the virus was able to progress through Mato Grosso (1936) and penetrate to Rio Grande do Sul (Brazil) and to Misiones in Argentina (1948). From 1950 to 1953 a third wave was observed, which was less extensive than the first (1934–1940), but considerably greater than the second (1944–48). The second and third waves were apparently sharply curtailed at a certain point by unfavorable weather conditions.

In southern Bolivia, an area under observation since 1932 where no yellow fever had been recorded had a severe outbreak in 1950. The cycle in this particular area lasted more than 18 years. In the same way, the present wave of jungle yellow fever in western Venezuela is occurring after a ten year period of freedom from the disease. And in eastern Venezuela the area close to Trinidad was known to be infected in 1933, but was later apparently free until 1954. Yellow fever was notified in Trinidad in 1909 and 1914, then nothing further until 1954. In Caracas, where the last previous cases of jungle yellow fever had been reported in 1914, an infective case of yellow fever came into the city from eastern Venezuela in 1954. This is the first specific known case of an infective yellow fever case being transported by air from a jungle district to a receptive urban center. The picture in Central America is one in which there is no history or evidence of yellow fever in this area between 1924 and the present outbreak, which has been continuous from 1948 to 1954.

Little by little, cumulative evidence indicates that *jungle yellow fever* is a problem of all the American countries on the mainland, with the exception of the United States and Canada in North America and of Uruguay and Chile in South America. Cases have been confirmed in Argentina and in Rio Grande do Sul—the most southern state of Brazil—and, with the movement into Central America, there is a great probability of its continuing into Guatemala and Mexico. Jungle yellow fever is not a threat to the Islands of the West Indies, in most of which monkeys are not found.

The continental character of yellow fever and its characteristic periodicity require and justify the organization of international study programs. It is obvious that many countries are not in a position to study their yellow fever problems. Yellow fever, coming into Central America once in twenty-five or thirty years,

sweeping through, as it did through Costa Rica, in two consecutive years and then disappearing, offers little opportunity for Costa Rica to undertake long-term studies.

It may be well, at this point, to get more direct information of what has been happening recently in the two areas that are most interesting to the United States at the moment: Trinidad and Central America. I am going to ask Dr. Wilbur Downs, of the Rockefeller Foundation, to outline for us the picture of what has happened in Trinidad. Dr. Downs has, during the past two years, been operating a tropical diseases laboratory in Trinidad, established for the express purpose of *not* studying yellow fever.

DR. WILBUR G. DOWNS (ROCKEFELLER FOUNDATION): We ran into yellow fever quite by accident in Trinidad. The Rockefeller Foundation had decided several years ago to establish a virus laboratory in Trinidad with the intention of studying the distribution in Trinidad, in the northern part of South America and in the islands to the north, of a number of the virus agents which had been picked up largely in the course of yellow fever work elsewhere in earlier years.

While we were getting the laboratory established, we made a serum survey of certain selected areas of Trinidad and sent the specimens to New York, to Dr. Theiler at the Laboratories of the Division of Medicine and Public Health of the Rockefeller Foundation. In all, I think there were some seven hundred specimens that went up. Dr. Theiler ran through a number of neutralization tests to a variety of agents including of course yellow fever, and came back with the information that along with a number of positive sera in older people—which would be expected in the Trinidad population—he had several positives, five or six, on individuals between the ages of fifteen and twenty. This did not tie in with the known yellow fever history in Trinidad, namely, that the last reported outbreak was in 1914.

This report was based on sera collected in the months of June, July and August 1953, and Dr. Theiler's report of positive yellow fever reactors came down to us in about October or November, 1953. At that time, we told the director of Medical Services of the Trinidad Government that there were some positive young people, and that here was a problem which would certainly have to be studied as time went along. So it was then that our suspicions were aroused.

We started off on a program of seeing fever cases. This was not in connection with yellow fever, but just to study fever cases as they came. We wanted to pick up dengue or Ilheus infections. Dr. Theiler had found a high index of immunity to a virus known as Ilheus in neutralization tests run on the Trinidad sera, and we were blindly exploring in an attempt to pick up the as yet unrecognized human disease.

On April 23, 1954, Dr. Spence, a young doctor assigned to us by the Trinidad Government, saw a lad in the Arima Hospital in central Trinidad who was almost not sick enough to attract his attention. The chap had come in with a fever the day before and, by the time Dr. Spence saw him, his temperature was only 100½. I believe Spence actually debated whether he would take a specimen on him or

not. We were then getting more specimens than we had animals for but, as luck would have it, he took a specimen on that individual. It must have been some eight or nine days later that Dr. Charles Anderson, who runs the laboratory service of the Trinidad Regional Virus Laboratory, asked "What about this fellow from Arima by the name of Houllier? What did he have?" We looked back in the clinical records, couldn't even remember him, didn't have anything that particularly struck our notice. Dr. Anderson continued, "There is something here that is certainly killing the mice." And in a very short time, not more than ten or fifteen days later, Dr. Anderson, who had had considerable experience in yellow fever work in Colombia and elsewhere, was quite certain that it was a yellow fever case; that the virus we were dealing with was yellow fever. At that time, we made a preliminary announcement to the Health Department—this was early in May—that we had a suspect yellow fever case.

The situation was serious enough actually to warrant a very careful check and, in the laboratory end of it, the patient's virus was identified by running it against pre- and post-monkey yellow fever immune serum that Dr. Theiler's laboratory supplied to us; and the reverse test was run in which the patient's pre- and post-serum was run against the French neurotropic strain of yellow fever virus. It checked through both ways that the agent that had been isolated was indeed yellow fever virus.

It must have been very early in June by the time we had this two-way specificity test completed. The Health Department was at that time notified officially that we had made an isolation of yellow fever virus, and the international wheels started turning rather rapidly from that time on.

With the experience of this case in April, and particularly early in May when we began to suspect that something very good was at hand, we started off in several directions. The first was to try to see, with our limited facilities, as many clinical cases as we could around the island. The second was to attempt to hop in on the monkeys as quickly as possible and find out what was going on in the monkey population of the island. And the third was to start a mosquito collection and inoculation program in the immediate area of the mountainous, wooded part of Trinidad from which this case had come.

The human case aspect ran along rather slowly through June and July. We saw a number of cases of illness, but did not make any virus isolations from any of them.

We started out on an intensive monkey hunting program and, almost as soon as we started questioning hunters around the island, it became evident we were on a good lead with the monkeys. Hunters—certainly dozens, possibly a hundred or so with whom we talked—had no recollection of dead monkeys before January 1, 1954. The first good story is a rather remarkable one, and one which I obtained from three hunters independently.

A little group decided they would go on an annual New Year's hunt which they had carried out for years, and went into part of the Nariva Swamp in eastern Trinidad on January 1, 1954. The first one I picked this up from I didn't believe. He said, "We ran into hundreds of dead monkeys." I attempted to shake

him on this with "You saw five dead monkeys? You saw ten? twenty? thirty?" It certainly developed that that man had seen a plenty, and the stench of the dead monkeys in this rather limited area of forest, a little island in the swamp area, was sufficient to throw the dogs' noses off and they had to abandon their hunt.

I thought this was remarkable and marked it down as a questionable story until I encountered a companion of his, a dignified, white-bearded East Indian—of social level sufficient to be called 'baboo'—who went through the same story with me, without having previously talked to the first fellow. The story was later confirmed from yet a third hunter. So this is the earliest date I have been able to pick up, January 1, 1954, in this story of dead monkeys.

None of the other stories have I been able to fix so specifically in time, but there have been dozens of stories from hunters in all of the areas of the island in which monkeys exist. Monkeys in Trinidad are of two species, *Cebus apella* and *Alouatta seniculus insulans*. The monkey stories are almost all concerned with *Alouatta*, by the way. In all of the areas in which I have been able to determine that monkeys exist, I have picked up stories of dead monkeys during the course of 1954. Usually the hunter questioned would have seen three or four, and a couple of chaps had seen as many as a dozen or so scattered over a period of several months.

We started out ourselves on a program of monkey shooting, attempting to pick up bands of monkeys in the various areas of the island, knocking down the monkeys and taking an immediate blood specimen. We carried our thermos right into the woods with us so that as soon as a specimen had clotted we were able to put it on ice. We got quite respectable specimens back, usually from the heart, but in some cases from exsanguination into the pleural cavities and, in rare instances, from the abdominal cavities. The specimens thus obtained are at the present time being tested in neutralization tests, and we are finding a number of positives.

We put out a feeler for monkeys. We wanted recently dead monkeys and let it be known, through the eastern part of the island particularly, that we would pay \$35 British West Indian (about \$21 U. S.) plus taxi fares for any sick monkeys, live but sick, that should be brought in; or we would pay \$20 and taxi fares for any recently dead monkeys which showed no sign of having been shot or thus killed. Surprisingly enough, over a period of several months, we got in six monkeys recently dead.

Dr. Theiler had been down to Trinidad on a visit and unfortunately his visit fell in this dead period between the first case and when we began to run into trouble. The day after he left Trinidad, July 30, 1954, in came the first dead monkey.

Now, this monkey, apparently dead less than twenty-four hours when we opened it, presented a very interesting picture. The liver was pale, fitting more or less the occasional color picture that is seen of a yellow fever liver. The abdominal cavity had over 100 cc., possibly as much as 200 cc., of blood and clot. This monkey had evidently exsanguinated into his abdominal cavity. The question arose,

what was the cause of death here? Would this be a yellow fever monkey or was this some injury? Did the monkey fall out of a tree and provoke this hemorrhage? We looked around carefully and found that near the attachment of the hepatic ligaments, up on the diaphragm, there had been a tear of the liver. Apparently, this was the spot from which the exsanguination into the abdominal cavity had occurred. This material in the abdominal cavity had separated into blood and clot quite nicely, so we took off a good bit of serum, at least 50 cc.; inoculated some of that serum into mice; also ground up liver and spleen, and got yellow fever virus from all three of the materials inoculated.

A neutralization test later run on that monkey serum showed that it is strongly protective, and we hope to titrate the protective level of antibody in the serum and also to titrate the virus level. We have material and we can titrate the actual circulating virus level that was there. It may give us some interesting information.

The second monkey that came in a few days later showed an identical pathological picture, as luck would have it. We opened it up and there was hemorrhage into the abdominal cavity, ruptured liver and clot. The virus also was isolated from that monkey.

We wonder whether these animals may not get very sick up in the tree and, at the time, virtually collapse from the yellow fever infection; whether they may not drop and hit the ground with a thud and rupture their liver already made very friable by the pathological process going on in it. It seems logical. Or when making a stretch from tree to tree, they may tear their friable liver. In either case, hemorrhage would appear to be, and actually would be, the immediate cause of death, although yellow fever would be the underlying cause.

The remaining monkeys from which virus was isolated did not have associated hemorrhage. Four other monkeys come in through the end of September and we succeeded in isolating virus from the livers of all of them. A couple of these animals were in an advanced state of decomposition; they were not yet liquefied, but their liver was soft with gaseous blebs over the surface. There was a decided stench when the abdominal cavity was opened; yet from these livers it was possible to isolate virus.

The mosquito program that Dr. T. H. G. Aitken started when the first human case was seen resulted in the capture and inoculation of over 100,000 mosquitoes—not many *Haemagogus* by the way—with nothing at all coming out of all this work. It was quite a heavy program we put in there and got very little out of it. We did not collect in trees on this occasion. We were as interested in finding something other than yellow fever as we were in finding yellow fever. We were just about getting a mosquito collecting program started on a large scale in connection with some of the other viruses, and we decided that here was a chance to go ahead with the added possibility of picking up yellow fever from mosquitoes other than *Haemagogus spegazzinii* (*Haemagogus* were not in high density in this area), so we went ahead on that gambit and did not succeed in getting anything—yellow fever or other viruses. All inoculations, by the way, were made into adult mice in the case of the mosquito collections. From the human and the

monkey material we routinely made inoculations into baby mice and found they were more sensitive as indicators of the presence of virus than the adult mouse inoculation, although trickier to handle, of course.

The human cases began to come shortly after we had seen the first dead monkey early in August. The first rumor of trouble came from the Director of Medical Services himself, who telephoned the laboratory one day and said: "I have a funny bit of information. A nurse who had been working with the Department, but had married an oil worker in southern Trinidad several years ago, came to see me two or three days ago and asked me for a job. I asked why, thinking that she had been taken care of, but she said her husband had died the week before and that she had to start to work again. I inquired what her husband had died of and she responded, 'Typhoid fever with jaundice.'"

Interestingly enough, all the hospitals and all the government medical officers in Trinidad had been advised of the presence of yellow fever on the Island. We were actively scouting the hospitals as far as our limited facilities—namely, Dr. Spence and myself—permitted, and the local doctors were supposed to be on the lookout. Well, this case went into the San Fernando Hospital and was diagnosed typhoid fever with jaundice. We later determined that he had quite a typical yellow fever history, dying on about the seventh day of illness, but he was interred without the possibility of obtaining any specimens, pathological or virological.

Then on Bank Holiday, which is the first of August in the British tradition, a sugar cane supervisor, an Englishman, went hunting in a forested area in central Trinidad with four native companions. On the fourth of August he began to feel sick, got sicker and sicker. His company doctor decided he couldn't handle him; sent him into the colonial hospital in San Fernando, and he died of "malaria with jaundice." I still remember enough about malaria to know that jaundice can occur as a complication of malaria. This case had no malaria parasites in the blood and although they did not get a fresh specimen of liver to inoculate, they did get a specimen in formalin which was sent to Dr. Gast Galvis. His telegraphic report came back from Bogota that this was yellow fever.

The next fatal case in the San Fernando Hospital was an "acute yellow atrophy," on which we did get a liver specimen for inoculation, and Dr. Gast Galvis got a liver specimen for pathological section. This turned out surprisingly enough to be yellow fever also, both by virus isolation from the liver specimen and by pathological examination.

There followed another fatal case which was reported as infectious hepatitis with possibility of yellow fever. This was a positive one also, by virus isolation and pathological examination. These were all from the same hospital, mind you.

Finally, a small child died and we received this telephone call from San Fernando Hospital, "We think we have had a yellow fever death." So it took five hits in the same place, with the same man seeing every one of the patients, with the presence of the disease notified on the Island, and the medical men alerted, before a positive diagnosis was made by anyone other than our own personnel. We by the way, coincidentally with this, had been seeing other cases which I will dwell upon a bit later.

This last case is an exceedingly interesting one. We should like to get together with Dr. Gast Galvis and see what can be done with it. Dr. Anderson saw liver sections and said, "This liver is interesting; I think I choose to regard it as suspicious. We will see what Dr. Gast Galvis says. My guess is that he won't dare to call this a positive case, but I'll bet we will get a report back from him that it is suspicious." Dr. Gast Galvis's report on the case was that there were suspicious lesions in the liver. Possibly he will be able to elaborate a bit upon that. But we got virus from that liver, which sews the matter up quite nicely.

There was one further fatal case in the San Fernando Hospital. After that, they got on the hyperacute side and there were a series of cirrhosis and actual cases of infectious hepatitis that weren't yellow fever, and from which the pathological reports and the biological reports, attempts at isolation, were also negative.

In the meantime, Dr. Spence and I had been scouring the hospitals in northern Trinidad and some in southern Trinidad, and were seeing a number of cases of nondescript fevers. There are a great many fevers in Trinidad, of that I am quite aware now. When malaria parasites are found, it is just lovely, you have a diagnosis. If malaria parasites are not found, you really don't know what you are dealing with. We had to rely upon the parasitological examination there. Albuminuria did not help. It is nice when it is present, but when it is not, that doesn't exclude the diagnosis of yellow fever. Jaundice is seen occasionally in yellow fever cases, but is not infrequent in other illnesses, including infectious hepatitis.

In our experience, the majority of cases from which virus was isolated did not have either jaundice or albuminuria and could be called dengue, malaria or early typhoid. The low white count was a constant feature. We never saw any of them with a leukocytosis, but that was about the only constant feature we could pick out.

We succeeded in getting virus from ten other human cases of varying degrees of illness, several of them from cases of jaundice but a goodly number from cases without jaundice and cases which would be most difficult to diagnose even in retrospect. So, all told, fifteen human cases were seen and identified as yellow fever, either by pathological examination which accounted for five of them, or by virus isolation which was successful in fourteen of the fifteen.

On August 8, 1954, a case of undiagnosed fever was seen in Port of Spain. Suspicion of yellow fever did not run high, but the virus of yellow fever was isolated from this patient's blood. This case has been considered as a proven urban case in the present outbreak. No secondary cases around it could be located, nor could antecedent cases leading up to it be located. This is the only proven urban case in the present outbreak.

Now, in addition to that, we have a large number of undiagnosed human cases running to well over a hundred, seen in this same period. It is evident that among these were many more yellow fever cases which are now showing up in the neutralization tests on pre- and post-sera. Just how long the list will be, I really do not know; and it is complicated because a number of individuals received yellow fever inoculation between their early and late specimens. Whether we shall be able to untangle the immunological mess that occurs under such situations will

remain to be seen. In many of these cases we may be forced to suspend diagnosis, possibly for a long time.

The Cumaca mosquito collecting program that I mentioned earlier was abandoned about the end of July. Early in August we became aware of a focus in central Trinidad in an area near Tabaquite, Victoria County. A recently dead monkey and two human cases, from both of which virus was isolated, came from this region. A mosquito collecting program was set up in a region known as the Charuma Forest. Dr. Aitken's crews collected entirely on the ground. Mosquitoes and all other biting arthropods encountered were collected and inoculated. Mosquitoes were broken down into two groups: *Haemagogus* and not *Haemagogus*, and were thus inoculated. We should have liked to break the collections down into the 15 to 20 component species, and to inoculate each species separately, but we did not have enough mice to do that. Virus was isolated twelve times from the ground-collected *Haemagogus*. Shannon, Whitman and Franco, in their original *Haemagogus* virus isolation in 1938, found virus in ground collected *Haemagogus*. Later work in Colombia and elsewhere went up into the trees and, for the past few years, I believe it has been quite customary to consider *Haemagogus* in connection with tree collecting.

Another collecting station was established at the same time in the Melajo Forest, St. Andrew's County, in eastern Trinidad. A sick monkey that had just fallen, alive, out of a tree on top of a wood cutter was brought in from there. By the time the animal reached the laboratory it was dead. Our immediate pathological observation was that it was undoubtedly a yellow fever monkey. The liver looked like the rest we had seen, so we immediately started a localized mosquito collecting service right in and under that tree. We only had two men collecting, one on a platform in the tree and the other on the ground. Virus was isolated nine times from those collections, eight of the times from *Haemagogus* mosquitoes. Unfortunately the tree and ground collections were mixed and inoculated as one, so we don't know whether the eight *Haemagogus* isolations are from tree-platform or ground-captured mosquitoes. The ninth isolation came from ground-captured mosquitoes, a pool of some fifteen species, among which the genera of *Anopheles*, *Aedes*, *Limatus*, *Wyeomyia*, *Psorophora* and *Mansonia* were all represented. We cannot know what mosquito or mosquitoes in that group may have been carrying the virus.

Also from that same station we have an isolation of another virus agent which is interesting us greatly. It is not yellow fever and we have high hopes that it may be the elusive Ilheus virus coming through.

We stopped this mosquito collecting, by the way, through shortage of mice and of funds in general at a time when positive captures were still occurring. We got positive virus isolations from about the middle of August clear through to the end of September. We stopped the program while we were still getting virus from both of these two localities, and have no idea how much longer we might have continued collecting infected mosquitoes from these areas.

The last human case we saw was in early October, and have seen no more since then. The last infected monkey was brought in sometime late in September,

and we have seen no more monkeys since then, although I have what I think is a sound report of a dead monkey as late as November 6, 1954, from the Charuma Forest area.

THE CHAIRMAN: Thank you very much, Dr. Downs, for your instructive and significant report. We are all delighted with your vivid description of finding yellow fever in Trinidad.

Please note that even after yellow fever was known to be present, it was impossible to get the local doctors to diagnose and declare it. Yellow fever, known only from the textbook description of a typical clinical case, appears to be a disease which should be readily spotted on the appearance of the first case. This is not true because many of the cases are mild cases that would never be—cannot be under any circumstances—diagnosed clinically. Furthermore, the classical clinical case is so similar to cases of other diseases with symptoms of intoxication that they do not stand out individually nearly so clearly as they do in the textbook.

The remarks which Dr. Downs has made on Trinidad, and the difficulties of getting a diagnosis, offer the opportunity to show the viscerotome, an instrument designed by the late Dr. E. R. Rickard of the Rockefeller Foundation for the removal of liver tissue, post mortem, without autopsy. I am going to pass this viscerotome around. As you can observe, it is very rapid in its action. It is a simple instrument; with the blade closed it is introduced through the body wall into the liver; then the blade is retracted about half an inch, the instrument is forced further into the liver, and lastly, with a plug of liver tissue in the channel, it is closed and withdrawn. The whole operation requires less than a minute.

This instrument has been the principal key to the recognition of yellow fever when it has been present in the rural communities of South America during the last twenty-five years. The viscerotome does not have the same value in Africa as in South America because there it has served the medical officers very largely as a means of avoiding autopsies on suspect cases. In the Americas, the viscerotome has been used by local lay representatives who are paid so much for each liver specimen sent in. The viscerotomist has instructions to puncture the body of each person dying in the community after less than eleven days of any acute febrile illness, no matter what the apparent cause of death may be. It is the routine systematic use of viscerotomy which has given the outline of the space and time distribution of yellow fever in the Americas during the past quarter of a century, as shown on Maps 1 to 5.

The planning of control measures to be undertaken after the introduction of yellow fever into a community, on the assumption that the first or any one of the early cases there will be diagnosed in the absence of viscerotomy, is dangerous. When yellow fever returned to Rio de Janeiro in 1928, after an absence of twenty years, it was not diagnosed until four separate foci of infection had been established in different parts of the city. It is almost certain that in Trinidad yellow fever would not have been recognized in time to prevent a serious urban outbreak had it not been for the existence of the virus laboratory there at the time and

under the circumstances related by Dr. Downs. The first fatal case was found entirely by accident, because the victim's widow had to go back to work and asked for a job with the Director of Medical Services.

The history of yellow fever in Trinidad, during recent decades, is significant in the light of the 1954 findings. The thirteen black spots and the two triangles on Map 3 showing the distribution of cases in 1954, refer only to the individual cases mentioned by Dr. Downs. When the Rockefeller Foundation made a survey of immunity to yellow fever in Trinidad, some twenty years ago, little was known about jungle yellow fever, with the result that Trinidad, on the basis of urban surveys, was given a clean bill of health as not having had yellow fever since the previous reported outbreak in 1914. One of the earliest suggestions in medical literature that yellow fever might involve monkeys was reported by Dr. Andrew Balfour at that time, after a short visit to Trinidad in 1914, in his article entitled *The Wild Monkey as a Reservoir for the Virus of Yellow Fever*, which appeared in the *Lancet*, (London, 1914, I, 1176-8).

Following the 1914 outbreak, there is no official report of yellow fever in Trinidad until 1954, although Trinidad, as shown on Map 4, lies just a few miles off the coast of Venezuela. In 1933, during an attempt to get information on yellow fever from Venezuela, a viscerotome was left at the Standard Oil Hospital at Quiriquire, not far from the coastline facing Trinidad, and a single positive liver was received that year. In spite of continued viscerotomy in this area, there is no evidence of yellow fever here from 1933 to 1954, when cases were confirmed again at Quiriquire and later at other points.

One point omitted by Dr. Downs is that some of the old hunters in Trinidad reported that they had seen similar monkey mortalities about 1934, but not in the interval between 1934 and 1954.

DR DOWNS: Well, there is one story now from 1932 and another which dates from 1933 or 1934.

THE CHAIRMAN: This story of dead monkeys in Trinidad from 1933 to 1934 may be correlated with the fact that on the nearby mainland a positive liver was obtained in 1933. And now in eastern Venezuela, after a gap of twenty-one years, a series of some fourteen fatal cases of yellow fever were reported at the time Trinidad had the infection in monkeys and in men just off the coast. Apparently, there was an unrecognized invasion of Trinidad about 1933 or 1934. There may have been periods of complete freedom from yellow fever between 1914 and 1934 and between 1934 and 1954.

To complete the story in Trinidad, as related to the *Aedes aegypti* situation, it can be stated that representatives of the Pan American Sanitary Bureau have repeatedly called attention, since early 1948, to the need for eradication of *aegypti* in Trinidad as part of the Bureau's program for the elimination of this species from the Americas. The authorities have, however, placed the greatest emphasis on malaria control with very little attention to the problem of *aegypti* eradication, with the result that *aegypti* breeding has continued practically unhindered in

recent years. In some districts, the 1954 house breeding index of *aegypti* was almost 100 per cent. And *aegypti* infestation is not limited to the urban districts, but extends well out through the so-called rural areas.

Information on the occurrence of jungle yellow fever came to the Bureau in June, and measures were taken to collaborate with the government in the control of *aegypti* and in the vaccination of the exposed population. In August, Dr. Downs isolated virus in Port of Spain itself from a case with no history of contact with the forest. Thus, for the first time in a quarter of a century, yellow fever once more invaded a maritime port in the Americas.

In the meantime, anti-mosquito services had been started in the city, based very largely on residual spraying of the houses, which is a slow but highly effective anti-*aegypti* measure; and fortunately the house spraying was begun in exactly the area in which the first confirmed urban case was found. Later, another case was found; and there are stories of other cases which may have been yellow fever.

With the declaration in early September that Trinidad was an infected port, a considerable disruption of traffic, of commerce, even of airplane traffic, occurred; and there has been a considerable financial loss to the colony, running into some millions of dollars. The manager of the Queens Park Hotel in Trinidad reported greatly reduced income, and there has been no difficulty in getting reservations during recent months. The tourists simply haven't been going to Trinidad, and the tourist ships haven't been stopping; altogether it has been quite a loss. Trinidad is an outstanding example of the loss which can occur to a community through the necessity of declaring an area infected. Had a fraction of the money which has been spent under emergency conditions been invested on a well-planned *aegypti* eradication program, this quarantine problem would have been solved without difficulty years ago.

Dr. Bayne-Jones has raised, for later discussion, the question of the urbanization of jungle yellow fever. What are the conditions under which it occurs? Why doesn't it occur more frequently? What is the threat that jungle yellow fever presents to the areas with *aegypti*?

I suggest we leave the *aegypti* program in Trinidad for later discussion and, turning for a moment to the Panama-Central American area, ask Colonel Norman Elton to give us briefly the story of how the cases of yellow fever, which had occurred in Panama in 1948, were diagnosed and reported in 1949; also the story of later developments up to and through the Costa Rica episode of 1951 and 1952.

COLONEL NORMAN W. ELTON (MEDICAL CORPS, U. S. ARMY): I have with me reprints of a paper on yellow fever in Central America, "Yellow Fever in Middle America" just published in the November-December 1954 issue of the Armed Forces Chemical Journal, which I should like to distribute to shorten the discussion and bring the story up-to-date. You will find two maps in the last two pages. I will attempt to cover merely the salient points of the topic about which Dr. Soper has asked me to speak.

During the months of November and December, 1948, there were five fatalities

in Santo Tomás Hospital, Panama City, following a febrile illness of short duration. Autopsies were performed on all of them by Dr. Juan M. Herrera, pathologist at Santo Tomás and well known especially as an expert in neuropathology, who had trained under Ramón y Cajal in Spain before the Spanish Civil War.

The first case was studied thoroughly, but the liver lesion was not very typical. It was not that of yellow fever as we know it, nor was it the lesion of any familiar pathologic entity. The lobules exhibited a peripheral zone fatty necrosis of a rather unique character. He diagnosed it as a form of acute yellow atrophy. The next case appeared grossly like the first, and he took no liver tissue for microscopic examination. A third similar case occurred during November, and he again assumed from the gross that it fell into the same category. The fourth—a death early in December—caused him to examine a liver specimen by frozen section, and he saved some liver tissue for further study. However, he diagnosed this again as acute yellow atrophy.

By this time a good deal of discussion had arisen among the intern and resident staff at Santo Tomás and also among some of the residents and interns at Gorgas Hospital about the possibility of yellow fever. This, however, was an old story in the Canal Zone, and had been known to recur repeatedly since 1919, when the last imported case of yellow fever, that of Kenneth Thomas, terminated fatally in 1919.

When Dr. Herrera was confronted with his fifth autopsy in December, and encountered the same lesion as in the fourth, although at that time he again considered the diagnosis to be acute yellow atrophy, he was worried for several reasons. Egypt had just declared Panama and the Canal Zone under quarantine for yellow fever, effective December 12, 1948 (*Relevé Epidémiologique Hebdomadaire*, No. 104), and a rumor was abroad that an Egyptian had contracted yellow fever in the vicinity of the Tocumen Airport and died after returning to Egypt. The Republic of Panama wired back to the World Health Organization early in January, 1949, protesting this action, denying that any yellow fever existed in the Republic of Panama. It was ascertained only recently that this curious coincidence occurred only because of the mouse protection test surveys conducted by Henry Kumm, in 1942, revealing that jungle yellow fever existed as far as the Bayano River in Eastern Panama, and it was customary to consider an entire country quarantinable if any part of it was involved. There was no other reason for this action by Egypt, and the rumor about the Egyptian citizen was without any basis in fact.

About this same time (after the fourth autopsy) Dr. Herrera had sought a consultation on his microscopic slides and asked for any known slides of the liver lesion of yellow fever from institutions in Panama City, but got no help. When the fifth case occurred late in December, 1948, he found himself in an extremely delicate position and in need of a consultation. The situation first came to my attention on January 13, 1949, when I was asked by Colonel Karl Lundeberg, Assistant Chief Health Officer of the Canal Zone, to call on Dr. Herrera and ask to be permitted to look at the slides of these cases that had been dying in November and December, "although they were probably hepatitis". I went down to

Santo Tomás that afternoon, taking with me a set of brain tumor slides to discuss with him, and also a slide of a typical yellow fever liver which I had acquired for my collection from Dr. Carl Johnson some years before. Dr. Herrera was out, so I left the slides on his bench.

The next morning I went again and found the laboratory very busy, so I started discussing the training of medical technologists with Dr. Mario Rognoni. Dr. Rognoni then mentioned that Dr. Herrera would like to have me look at some liver slides he had. Dr. Herrera placed a slide under the microscope. I noted that he had on his desk a number of books and reprints with photomicrographs of the liver lesions of yellow fever and hepatitis. He said he was puzzled about this slide and thought it might be yellow fever. After about 20 seconds I agreed with him most emphatically, for it was about the same as being asked to identify the full moon in a starlit sky.

He wanted to know why I was so sure, and pointed out similarities with certain hepatitis lesions. Since he had not yet noted the typical slide I had left the previous afternoon, I called his attention to it, and he studied it for a while under his microscope. A few minutes later he called me over again and said, "Look, tell me just why this is a yellow fever liver." So I looked at the slide under the microscope, which was a typical slide, and began describing it as a lesion which could rarely be confused with that of any other entity. I then remarked that that was "why I brought this slide". He then said, "But that isn't your slide, that's another case of mine you haven't seen before." I could only say "Well, then, you have two cases of yellow fever", and he retorted, "Now I know I have". Thus Dr. Herrera and I were initiated in the histopathology of the yellow fever liver. From that time on we collaborated with each other in diagnosing the cases that occurred subsequently in Panama.

The next morning a conference was held at the Board of Health Laboratory, comprising all the public health officials of the Canal Zone, the Armed Forces and the Republic of Panama, at which a decision was made to take appropriate action based on our diagnoses. On Sunday, January 16, 1949, the newspaper headlines blazed forth that yellow fever had returned to Panama. Shortly afterwards Congress appropriated \$600,000 for the control of yellow fever in Panama and the Canal Zone. I might remark, perhaps facetiously, that 20 seconds of a pathologist's time at a microscope activated this grant. That amounts to a million eight hundred dollars a minute for a pathologist's work without risking materially the reputation of the specialty. The \$600,000 was expended in a blanket vaccination of the entire Republic of Panama and the Canal Zone.

From then on, the study of yellow fever as it passed up through Central America was a pathologist's job, monitored and documented mainly by the field application of pathologic anatomy in the study of primate livers. At first it was not known that a wave was in progress, although I was suspicious of it very early because of my contacts with scientists who had had experience in South America with the Brazilian waves of the 1930's and 1940's. We sat tight and waited. Then, in August and September 1949, Dr. Herrera and I diagnosed three more human fatalities from the Buena Vista area between the transisthmian highway and the

east Canal Zone boundary. A slight progression westward had occurred, but still not enough to be sure it was a wave phenomenon.

This, incidentally, occurred in an area that had been covered by vaccinating teams. Revaccination was immediately undertaken and, in what might be considered a rather sparsely populated region, 2,000 more people were vaccinated who had been previously overlooked. I mention this merely to indicate the difficulties inherent in vaccinating rural populations. Fortunately the majority of the farmers in this area were Negroes, who are much less susceptible to the disease than Caucasian or Indian stock, or the impact of the epidemic would have been far more serious.

We may skip Barro Colorado Island for the moment, because it was not recognized as the obvious stepping stone of the wave in its crossing of the Panama Canal until some two years later. The monkeys did die on Barro Colorado at the right time, but this was not known until a survey of the howler monkey clans on the island was made by Drs. Collias and Southwick of the University of Wisconsin during the dry season of 1951.

In January 1950, a farmer died of yellow fever in the Chagres District west of the Canal on the Atlantic Side—locality No. 5 on Map 1 of the reprints of the paper on yellow fever in Central America. Here at last was strong evidence of a constant westward movement, indicating that a wave was actually in progress, and the calculated risk involved stimulated the spirit of prophecy.

It was, however, difficult to estimate the velocity of the wave and to determine its past and future pathway. Because of the complex nature of the Gatun (Chagres) Watershed, the path of the wave to this point west of the Canal was not clear until further data were acquired, but it was later apparent that the involvement of the Chagres District was by a backlash of the main axis with the true wave front well on its way westward toward Costa Rica through the Atlantic rain forest of western Panama at that time.

About this time I met Gerardo Jimenez, Consul General of Costa Rica to Panama, at a cocktail party and discussed the yellow fever situation with him. I don't recall exactly what was said, but do remember telling him it was not just cocktail party conversation and that he could quote me. As of March 20, 1950 he informed his Minister of Public Health in San José that the Atlantic side of Costa Rica would be involved in from 14 to 18 months. Not only was this a sheer guess on my part, but I didn't learn that such a letter had been written until August 1951.

The Chiriqui Land Company, a subsidiary of the United Fruit Company at Almirante, was also alerted on the Atlantic side of Western Panama near the Costa Rican border to watch the monkeys and expect human cases by September 1951. This was not such a good guess, because the death of René Ramírez from yellow fever occurred in that vicinity in April, 1951, well ahead of schedule. Now for the first time sufficient data were at hand to make a fairly accurate estimate of the wave's velocity, and the proper corrections for the tortuous pathway caused by the Gatun Watershed in the crossing of the Panama Canal. Also on this occasion Costa Rica instituted an all-out alert.

In June 1951, Dr. Enid de Rodaniche, at Gorgas Memorial Laboratory, iso-

lated the yellow fever virus from a serum specimen from a recovery case from Nievecita, just across the boundary in Costa Rica, a little to the northwest of Almirante. Then, with explosive violence, beginning with the initial fatality on July 24, 1951, a series of five epidemic centers flared up in northern Costa Rica lasting from July to October, the main details of which you will find in the reprint.

This was a true "front", and not a directional extension of the main axis, but at right angles to it, like a whiplash, probably building up along the 500 meter contour and sweeping down broadside into the plains of northern Costa Rica on a hundred-mile front.

Then a phenomenon occurred which was not supposed to happen. Monkeys began dying in the Cabagra River Valley in Puntarenas north of Golfito on the Pacific side of Costa Rica in October 1951. This seemed unbelievable at first because up to this point the Continental Divide had been crossed only in the vicinity of the Canal Zone and had acted as a barrier at elevations of 3,000 feet. Now a crossing had occurred where the minimum elevation was at least 5,000 feet. However, the Golfito Plantation of the United Fruit Company had already vaccinated its labor force in spite of having been advised that they were probably protected by the Divide.

A possible explanation of this phenomenon may be human carrier importation of the virus across the Talamanca trail by a migrant farmer fleeing the epidemic on the Atlantic side and seeding the forest mosquitoes on the Pacific side. At this point it is appropriate to point out that all the 206 human cases of yellow fever in Costa Rica acquired their infections at elevations not over 500 meters above sea level, and that this was the maximum elevation at which monkeys died of the disease as proven by liver examinations of 36 specimens.

This secondary wave then began expanding northwestward and southeastward in two spurs at about the same velocity as the main axis—13 miles/month—leaving in its trail dead monkeys and human cases and deaths. The southeast spur died out in the Burica Hills Peninsula at Puerto Armuelles in western Panama, failing to reenter the heretofore uninvolved Pacific watershed west of the Canal.

At the time the northern Costa Rica epidemic centers were still active from July to October, 1951, the main axis, in the form of an epizootic precursor, was moving northward and monkeys were beginning to die along the San Juan River east of the great Lake Nicaragua. Early in 1952 the main axis split at Lake Nicaragua and a daughter wave swept northward into the lower part of the Isthmus of Rivas and its western spur began moving down the Pacific side of northwestern Costa Rica, leaving a trail of dead monkeys in a southeastern direction. In southern Rivas Dr. Boshell states that the forest reeked with the stench of the carcasses of dead monkeys. This contrasts significantly with the rather quiet manner in which the epizootic phase involved the monkeys of Barro Colorado in 1949, with a much lower mortality in the howler monkey clans, and suggests that the virus may be undergoing enhancement in virulence, at least for the arboreal primates.

The Rivas spur of the daughter wave did not reach Managua, although there

was so much apprehension that it might do so that people went out shooting monkeys in a frantic effort to check the wave. Evidently a natural barrier existed here and the spur died out. However, the southeast spur of this daughter wave from the northwest corner of Costa Rica kept progressing until it met the northwest spur of the secondary wave from southern Puntarenas in the vicinity of the Tarcoles Valley west of San José on the Pacific side in March 1953.

In the meanwhile the main axis kept moving up the Atlantic side of Nicaragua roughly following the 1000-foot contour. The initial Nicaraguan outbreak was accurately predicted as to its precise time and general locality (July, 1952, in the Mico Valley), and the projection for northern Nicaragua and Honduras has proven quite accurate up to the present time.

Before Dr. Boshell presents the story of Nicaragua and Honduras, I should like to stress the importance of jungle yellow fever to the rural population, since much of the emphasis seems to have been on the urban component. It can be just as devastating to the farmers. The people of Central America must raise food crops but, since much of the arable land is planted with coffee and other pay crops, the average farmer must raise his subsistence crops by developing a forest-type of agriculture, and his clearings lie in close proximity to the forest and to yellow fever. The importance of this disease to the rural population must not be overlooked. Furthermore, it is very difficult to vaccinate the people in the bush. Many hundreds of square miles with primitive communication channels are involved. Their habitations are dispersed and difficult of access. Far more than just an administrative problem is involved.

In conclusion, I should like to express a debt of gratitude to the people of Costa Rica, to the medical profession of that country and to its Health Director, Dr. Oscar Vargas Méndez. I don't think a more splendid job of public health work was ever done than was accomplished by him and the Minister of Health, and also I have yet to see clinical studies that will equal for a long time those performed by the staff of San Juan de Dios Hospital in San José. The studies by Miranda on liver function tests, by Trejos and Romero on prothrombin levels; and by Romero and Trejos on clinical and laboratory findings on 206 cases, have recently been published in the *Revista de Biología Tropical*, 1953 and 1954, of the University of Costa Rica in San José.

THE CHAIRMAN: Thank you, Colonel Elton. Before we ask Dr. Boshell to go on with the story of the Central American wave, I should like to make one or two comments on what Colonel Elton has told us.

First, with regard to the diagnosis of the disease from the examination of the liver tissue, the difficulty that Dr. Herrera encountered is a difficulty all pathologists face in making a diagnosis of yellow fever, namely, that the diagnosis of the yellow fever liver is in part a subjective diagnosis. The diagnosis of malaria is objective in that it can be made from identification of a definite concrete parasite under the microscope—a straight objective diagnosis, based on something which can be pictured and pointed out: "Here it is." On the other hand, the yellow fever liver carries no single element that is pathognomonic of yellow fever.

Rather, significance is given to the distribution of the components of the lesion; diagnosis requires previous experience with yellow fever pathology and the ability to make a subjective decision; the diagnosis of yellow fever is made above the ears; whereas the diagnosis of malaria can be made on the basis of the slide itself. Final yellow fever diagnoses in doubtful cases should be made by those who are accustomed to seeing yellow fever livers.

One important similarity has been noted of the outbreak in Trinidad to the outbreaks in Central America in contrast with those studied previously in South America, namely, the tremendous mortality of monkeys. In Trinidad and in Central America it has been possible to follow the moving front of the epizootic wave by the observed mortality in monkeys, something that was never possible in South America. The *Cebus* monkey, the most common South American genus, is relatively unsusceptible to intoxication by the yellow fever virus so that, although the *Cebus* monkey becomes infected and becomes a source of infection for mosquitoes, it doesn't die. On the other hand, the *Alouatta* (howler) and *Ateles* (spider) monkeys, which predominate in Trinidad and in Central America, succumb readily. Therefore the movements of yellow fever virus in the forests of South America have been followed through viscerotomy of human cases, whereas the studies in both Trinidad and in Central America have been greatly facilitated by the high mortality of monkeys. The varied mortality in different genera of monkeys undoubtedly has an epidemiological consequence. Where the monkey population is largely destroyed, the development of a new susceptible population capable of supporting a later wave of infection may take many years; whereas the *Cebus* population, in which the parent monkeys are not killed, may build up through birth a susceptible population in a very few years ready to propagate another wave of infection.

Colonel Elton has properly emphasized the importance of this disease to the rural population. Jungle yellow fever represents the same threat and the same importance, as an occupational disease to the rural populations of many parts of South America, that the urban yellow fever previously represented to city populations; and it is just the most isolated population and the most difficult to vaccinate that is the most exposed to the disease.

The movement of yellow fever virus through Costa Rica was really very dramatic from the standpoint of the human disease, whereas in Nicaragua and in Honduras comparatively few human cases have occurred. Dr. Boshell, who has behind him many years of experience with jungle yellow fever in Colombia, is going to give the story of the movement of yellow fever through Nicaragua and Honduras from 1952 to 1954. Dr. Boshell.

DR. J. BOSHELL (PASB): At the time I took charge of the observation of the Central American wave, yellow fever manifestations were extremely active and intense on the border between Costa Rica and Nicaragua. This was in July, 1952. Since then—and it is very easy to follow it on the map—the yellow fever wave, both on the Pacific side and on the Atlantic side, proceeded according to schedule; that is, according to the predictions made by Colonel Elton. All through 1952

and 1953 the wave on the Atlantic side proceeded from the Rio Escondido to the Rio Grande (Matagalpa), jumped from there to the Rio Patuca and to the Rio Coco, according to schedule.

On the Pacific side, the wave proceeded on another time schedule because of the different vegetation in that area. The Atlantic side of Nicaragua is characterized by tropical rain forests and by very heavy precipitation throughout the year without a marked dry season, a fact which naturally favors the persistence throughout the year of insect vectors. The Pacific slope vegetation and climate are markedly different. The region between the Continental Divide, the lakes, and the ocean is covered by deciduous tropical forest of the type associated with the climate, which is characterized by long and severe dry seasons. Between November and the end of April practically no rain occurs. The mosquito fauna seems to disappear entirely. Exhaustive mosquito searches in April in the Rivas Isthmus yielded no mosquitoes whatever, or at most a few specimens. This emphasizes the danger of predicting in such a zone either the extension of the wave or its end point.

In April and May, 1953, I observed in the Rivas Isthmus an almost total absence of the mosquito fauna and concluded that, whereas on the Atlantic side conditions were favorable for the continuation of the epizootic wave, on the Pacific side it was bound to end because of the prolonged interruption of conditions favorable to the persistence of the virus. I was proved to be absolutely wrong, because as soon as the rains started, in spite of the apparent extinction of mosquitoes during five or six months of intense drought, monkeys suddenly began to die at the exact point reached by the epizootic when the dry season started. This shows once more the danger of inferring from observations in one place what will happen in another.

I am not satisfied yet as to the answers to these questions: what happened here? Where did the virus persist? Where did the mosquitoes go? Evidently the wave was related to the vectors. Where did they hibernate, or rather estivate? We still don't know. And this is a factor we have to keep in mind when we consider the possibilities of the wave's extension northward into Guatemala, southern Mexico, and may be farther north. Not everything is explained by the bionomics of the mosquito and the monkey (or man). The conditions in Nicaragua are extremely instructive, indicating a still unknown mechanism in the ecology of jungle yellow fever.

In December, 1953, the Guatemala Office of the Pan American Sanitary Bureau was notified of suspected cases of yellow fever in a place called Dulce Nombre situated at the head waters of the Guampu, a tributary of the Patuca River. In a survey of the Patuca and the Coco valleys we had found evidence of monkey mortality and of a few human cases. In fact, in August-September, 1953, a typical human case and monkey mortality had been reported from the junction of the Guampu and the Patuca Rivers. The Guampu Valley seems, therefore, to have been the bridge across that territory which is between Nicaragua and Honduras. And the way of penetration from Nicaragua into Honduras seems to have been that Valley. From the Catacamas-Dulce Nombre region the

epizootic wave seems to have followed the foothills, reaching the La Ceiba region from the rear and from the west through the Cangrejal and Yaruca Mountains.

In June, 1952, following a survey of Honduras made with Dr. Trapido and Mr. Galindo of the Gorgas Memorial Laboratory, it was decided to start an entomological observation station in that region, and thus, when the wave hit that special zone, they were both already well informed as to the mosquito population. It was a good preparation for the studies which were to follow through 1954 in the region of La Ceiba and Tela; and here too a very interesting problem arose, namely, the problem of the vector.

All through Panama, Costa Rica and Nicaragua, the mechanism of transmission of jungle yellow fever seems to be perfectly related to the old vector, well-known in South America, *Haemagogus spegazzinii falco*. Not so as we progress north. We cannot affirm that *Haemagogus spegazzinii falco* plays any significant role in Honduras. As we go north into the region of La Ceiba, we still find a few specimens of that mosquito, but it becomes more and more scarce—some replacement forms occur, and spread northwards. Without entering into details here, it can be said that if yellow fever progresses northward into Guatemala and Mexico, it will be transmitted by a different vector from the one we have known so far. And, naturally, that raises a new and very important unknown factor in epidemiology, which interests two countries and may be more; I mean Guatemala, Mexico, and possibly the southern part of the United States.

There are many things that we still don't know. We know that the yellow fever virus can resist through a very severe dry season and survive under adverse conditions to burst out where least expected, and where its non-recurrence has been predicted. We saw it in Nicaragua; we see it in Colombia too. We are not in possession of sufficient evidence, experience or observation to be able to say that a given type of country—even where there is no rain, even in the desert—has the conditions adverse to the persistence of virus or the transmission of virus. That is one thing we have learned in Central America, and it is one thing which should influence our predictions and our whole attitude toward the possible spread of the disease northward.

THE CHAIRMAN: Thank you, Dr. Boshell. One point that should be emphasized is that yellow fever virus has continued its march across the length of Honduras while showing itself in a very minimal way. As can be seen on Map 4, there was some evidence from dead and sick monkeys but this move from northwestern Nicaragua through Honduras to the northeastern section has been made without the occurrence of any confirmed cases, with the exception of the one case in September 1954 which came into the hospital at San Pedro Sula. And it is only because of the studies which were being carried on that the movement of the virus has been visible. Let us leave the epidemiological picture for a moment and consider yellow fever in the Americas as a threat to Asia, while at the same time answering the question on urbanization of jungle virus raised by Dr. Bayne-Jones this morning.

The threat of the movement of yellow fever virus from one part of the world to another through the movement of the human carrier or of the mosquito—and it is much more apt to go in the human than in the mosquito—is very largely dependent upon the multiplication of virus through the development of concentrated centers of dissemination of virus where *Aedes aegypti* is the vector. On Map 5, labeled "Intervals between appearance of yellow fever in specific areas," the location of Rio de Janeiro is marked and, following down the coast, the deep indentation in the outline of South America represents the River Plate, at the mouth of which we find Montevideo and Buenos Aires. Following the coastline to the northeast of Rio, and again to the northwest, the mouth of the Amazon Valley at Para is readily located. These reference points are important.

The Rockefeller Foundation began working on the control of yellow fever in Brazil in 1923; there was a period of eleven months in 1927 and 1928 during which no cases of yellow fever were diagnosed in any place in the Americas. Then in March, 1928, a single case was notified in the State of Sergipe in northeastern Brazil, some fifteen hundred miles from Rio, at a place having no direct contact, maritime or otherwise, with Rio.

In April of 1928, Dr. Clementino Fraga, Director of the National Health Service of Brazil, consulted me as the representative of the Rockefeller Foundation on the possibility of yellow fever coming back into Rio. In the face of an invasion of Rio by plague some months before, the anti-mosquito service had been disbanded in favor of an anti-rat campaign. The question raised was whether the 1929 budget should provide for the reorganization of the expensive anti-mosquito service or not. In the absence of knowledge of the existence of jungle yellow fever or any other apparent source of reinfection, there was no reason to spend money on reorganizing the *aegypti* service in Rio, and Dr. Fraga was so advised.

Just a month later, yellow fever was proven to be present in the city of Rio. At the time it was discovered, it had apparently been present for three or four months and there were at least four different foci of infection in different parts of the city. Today, this appearance of yellow fever in Rio, after an absence of 20 years, is accepted as due to an urbanization of the virus of the then unrecognized jungle yellow fever. As a result of that infection of Rio at a time when the *aegypti* index was high, yellow fever was able to maintain itself in Rio for a period of fifteen months and to spread to the interior and both south and north along the coast.

In the State of Rio de Janeiro, itself, there were some forty-two towns infected. Cases were identified, on board ship or on land, all the way from Montevideo at the mouth of the River Plate up the coast and as far inland as Manaus on the Amazon River, a total mileage distribution of something like 4,700 miles. Cases secondary to this outbreak occurred until May of 1931, a period of just three years from the time the original outbreak was identified. The fact should be stressed that previous to the entry of this virus into Rio, where *aegypti* could build up a high urban concentration of virus, a full year had passed in which only a single case had been identified in the Americas.

In 1938, ten years later, a wave of jungle yellow fever swept down to within

twenty-five miles of the city of Rio, and at that time, within a very short period, four infective cases of yellow fever came into the city. But there were no *aegypti*, there was no outbreak, and no spread of the virus from Rio to other cities and ports occurred.

The shaded area to the west, south and north of Rio, on Map 5, represents the area covered by epizootics of jungle yellow fever from 1934 to 1940. The four appearances of the virus in Rio in 1938 all occurred at the time the virus was moving very close to Rio. In 1934, jungle yellow fever was found far out on the western limb, the northwestern limb of this shaded area; and was followed year after year—1934, '35, '36, '37, '38, '39, and '40—covering all of the forested stretches in this shaded area. Yellow fever came within range of the railroad system leading to Rio in 1935. But in 1935, in '36, and in '37, as the disease was working toward Rio, no infective cases were found in the city. In 1938, when the disease had worked itself within sight of the city, I could sit in my office and point to the hills and say "There is yellow fever in them thar hills." Just at that period, the four cases mentioned were identified in Rio. Then in 1939 and 1940, as the disease was making its way off to the northeast, in an area only twelve to twenty-four hours distant by rail and much less than that by air, no infective cases were seen in the city.

If, to the experience of the last twenty-two years while jungle yellow fever has been under observation, is added that of the Rio outbreak of 1928, of the outbreaks in Venezuela and Colombia in 1939, and of one in Bolivia in 1932 which preceded the recognition of jungle yellow fever but which can only be explained by it, there are altogether twenty odd observations of the urbanization of jungle yellow fever virus.

The experience so far—and the phrase "so far" should be emphasized because of the need for very long-term observations on yellow fever before drawing final conclusions—the observations so far are to the effect that in all cases where jungle yellow fever has come into towns, such towns have been very close to jungle areas suitable for jungle yellow fever and, in most cases, when the virus was known to be nearby.

In the Americas, no *aegypti*-transmitted urban yellow fever has served, since 1934, as a source of virus for the infection of other towns. In no case has jungle yellow fever come into a town and been able to establish a secondary focus from that town. Apparently, the movement of virus through Central America between 1948 and 1954 was—and this in spite of Colonel Elton's remarks regarding the possibility of the virus having gone over the mountains in a human carrier—essentially by the movement of the jungle infection in mosquitoes and animals in the forest rather than by the human carrier.

The difficulty yellow fever virus encounters in getting into the town is, of course, largely due to the fact that a comparatively small number of people from the towns and from the cities go into the forest areas and, likewise, few forest workers come into the towns. In many areas practically all of the cases seen are in farmers or in wood cutters; and there are outbreaks in which almost all cases are in men. In a series of 108 cases in Espirito Santo, Brazil, in 1939, there were

only eight in women. However, the threat, the possibility of yellow fever virus coming into a town where *aegypti* is present, always exists. Recently—October, 1954—an infective case from eastern Venezuela came into Caracas, the first case recognized there during several decades.

The threat to Asia from yellow fever in the Americas has been exhaustively discussed at international meetings with the development of two united fronts on the subject. The American attitude, supported in the international organizations by the nations of the Americas, is based on the observation that the most dangerous factor in the spread of human yellow fever is the *aegypti*-transmitted yellow fever in urban centers, where an individual can get infected in a hotel or elsewhere while he is making his travel arrangements to leave the country. Very seldom does the individual come out of the forest with his international travel arrangements already made and everything fully prepared for immediate departure.

Aegypti eradication is the only satisfactory solution to the threat of urban yellow fever, and the elimination of urban yellow fever greatly reduces the possibility of the international spread of the disease. Vaccination certificates can never merit 100 per cent confidence. This may be illustrated by an experience during World War II. During a discussion with a colonial authority on the relative value of *aegypti* eradication and obligatory vaccination for the prevention of yellow fever, his wife spoke up and confessed that she had illegally loaned a yellow fever vaccination certificate to a fellow passenger a short time previously.

The Asiatic countries do have monkeys, they do have mosquitoes, they do have a large non-immune susceptible population; and the very thought of the possibility of yellow fever coming to that area is one which is a nightmare to the health officers. There is, then, an insistence on sanitary regulations against the possible importation of yellow fever virus, much more stringent than those acceptable to the American nations living much closer to the threat. Within a six-day incubation period a person could leave an infected yellow fever forest area, get on a plane and go almost any place in the world. The argument that "well, it never has happened," and "it hasn't happened during the twenty years that we have been watching jungle yellow fever" may satisfy us; but it isn't an acceptable argument to the Asiatic countries.

In considering the threat of jungle yellow fever to the cities, it must be remembered that there are exceptions to all of the usual situations. In Brazil, in 1937, yellow fever came to a large coffee plantation in São Paulo with some three or four hundred people living on it. However, the disease did not strike at the rural population but at a group of eight woodcutters who walked seven or eight miles out from town each morning to spend the daylight hours in the forest cutting timber. This bit of woods was probably three or four hundred meters from the population center where all the plantation people lived. All of the eight men who went to cut wood in the forest got yellow fever and three of them died; but none of the people on the plantation had yellow fever.

The question of what should be done about yellow fever in the international quarantine regulations is one of the matters that are up for discussion at the

World Health Assembly in Mexico City next May. There is a difference of opinion as to whether Brazil, which probably has jungle yellow fever constantly at one place or another in the Amazon Valley and which suffers periodic wavelike outbreaks to the south, should require travellers to be vaccinated against yellow fever ten days before leaving the country or not. The problem is not an easy one, since there are two cities of over two million people each and many lesser cities where yellow fever is no longer a threat. Vaccination necessarily represents a considerable inconvenience and difficulty for these populations.

I have covered the particular question that Dr. Bayne-Jones wanted discussed. Are there any other remarks on yellow fever in the Americas as a threat to Asia? When we say Asia, we really mean Asia and intermediate points.

We have with us Mr. Calderwood, of the State Department; Dr. Spencer, Chief of the U. S. Public Health Service Quarantine Service; Dr. Bica of the Pan American Sanitary Bureau; and Dr. Stowman, who has been following quarantine matters since the days of the League of Nations, all experts who know the answers and are ready to give them.

COLONEL NORMAN W. ELTON (MEDICAL CORPS, U. S. ARMY): This threat to Asia seems a little remote compared to the threat to the Gulf cities of the United States and Mexico in two or three years from now. According to your map on the progress of *Aedes aegypti* control and the eradication campaign as of October 30, 1954, the Gulf cities of the United States and those of Mexico are not only yellow fever receptive areas but harbor *Aedes aegypti* in densities well above the transmission level (Map 6). A natural mode of urbanization would be by the crews of fishing and shrimping boats and coastal shipping boats in general that contact the Mexican coast when it becomes involved in the epidemic and epizootic phases of the wave, who could transfer the virus to the bayou settlements of Louisiana and other coastal areas, as well as to the larger urban centers. Such human carriers might not even become noticeably sick while circulating the virus. Their crews should be vaccinated. This seems to me a more important problem than Asia, where there never has been any yellow fever.

DR. KNUD STOWMAN (U. S. PUBLIC HEALTH SERVICE): I believe that much of our trouble with international sanitary agreements stems from the fact that, being so long in preparation, they are always behind the times. The farther away we are from their effective dates the less effective become some of the measures we can take, while others become useless.

I recall how our deliberations preparatory to the International Sanitary Conventions of 1944 resulted in the setting up of the yellow fever endemic zones. I think that these zones were justified at the time. After all, only a few years had passed since Dr. Soper had first described how it happens that the jungle virus comes to town. Our knowledge of the extent and epidemiology of jungle yellow fever was scanty and, due to war conditions, case reporting was more unreliable than usual.

However, the system of the zones took root, perhaps because it was in a sense

"the lazy man's out." So comfortable was the system that not only did it become the cornerstone of yellow fever measures in the International Sanitary Regulations of 1951, but all subsequent attempts to modify the delineations to conform to the actual presence of yellow fever were wrecked on political alignments in the World Health Assembly. There was an Asiatic group, and there was also a European group, although Europe is not receptive to yellow fever. Joining forces, the two blocked such rational changes as were proposed by the WHO Committee on International Quarantine.

The United States has now formally proposed to abolish the yellow fever endemic zones and to base the quarantine measures on local areas declared infected whenever there is a human case of yellow fever, urban or jungle. The first indication of the presence of the virus in the jungle is usually the finding of a human case, and we are far better equipped in the Americas to find the human cases than we were ten years ago. The general movements of yellow fever through the jungles are now fairly well known.

North-south traffic in the Americas, especially by air, has grown immensely in volume. Our southern airports are clearing two and one-half times more aircraft in international flights than our northern airports. As far as international traffic is concerned, yellow fever is primarily an Inter-American problem. There are few active spots of yellow fever in the developed parts of Africa, and there is but little traffic from there to the Americas.

I hope, therefore, that there will be full agreement between the American Republics next year at the World Health Assembly in Mexico City. We should be able to settle this question satisfactorily between ourselves and, at the same time, give other parts of the world such guarantees as they may need.

THE CHAIRMAN: Thank you, Dr. Stowman. Before we break for luncheon, I would like to state, to stimulate discussion later, that we in the United States, have not entirely followed the international regulations during the recent Trinidad outbreak, and certain irregularities may be charged also to other countries. A Bureau representative reported, for example, observing a quarantine officer who was requiring surveillance in addition to valid vaccination certificates, yet he had *aegypti* breeding in a flower vase on his desk at the time.

(Tuesday, December 21 P.M.)

THE CHAIRMAN: We were discussing the implications of yellow fever and quarantine sanitary regulations when we broke up for lunch. I made the statement at that time that I was sure we had not finished the discussion, and I am going to ask Dr. Spencer if he would like to express what is in the background from the standpoint of the U. S. Public Health Service.

DR. CALVIN B. SPENCER (U. S. PUBLIC HEALTH SERVICE): As an introduction to my remarks, I think it is appropriate to state that quarantine officers are frequently the whipping boys on the control of introduction of epidemic diseases. I believe, in the main, we accept this rather gracefully as a part of our job.

I should like to go back and show how we have tried to anticipate what has

happened, and what we could do in the event we were confronted with a problem similar to the one currently under discussion. I recall having had a discussion with Dr. L. L. Williams in 1942 or 1943, while he was associated with Malaria Control in War Areas (now Communicable Disease Center), Public Health Service, Atlanta, in which it was mutually agreed that we should have, within the Division of Foreign Quarantine, entomologists who would actively carry out quarantine procedures in which their skills were applicable. Arrangements were made at that time for the assignment of a group of entomologists to the Miami Quarantine Station, primarily for training prior to deployment to various quarantine stations where their services could best be utilized. Miami served as an excellent training point, since the greatest number of aircraft flights from foreign countries arrived there. As a result of these early arrangements, we have given entomological coverage particularly to our southerly-located major stations, most of which receive maritime traffic in addition to air traffic. Entomological surveys are conducted periodically at the airports and seaports, and entomological inspections are made on arriving aircraft and ships. Insects found are identified by entomologists, and pertinent records are maintained.

Periodically, in discussions with the Pan American Sanitary Bureau and with others, we have highlighted the necessity of doing *Aedes aegypti* control around airports and seaports in the receptive areas. As a result, representation has been made by our division to the effect that we should have supplementation in personnel and appropriation in order that we may be able to carry on a program more completely than we are now doing.

A conference was held with representatives of the Bureau of State Services and their Communicable Disease Center, during August of this year, in an effort to arrive at an agreement as to what could be done in view of the northward progression of yellow fever in Central America, and the building up of cases in Venezuela and Colombia. There has been extensive planning on this subject and, although it has not been as productive as desired, I believe that in the near future more definite effort will be made to get some of this work done.

Now, from a quarantine standpoint, we still maintain our survey and control at the airports, using trained personnel, and require routine spraying of aircraft. In the absence of the type of problem that is immediately confronting us, aircraft coming from endemic areas are required to be sprayed while en route to the United States. We inspect these aircraft immediately following arrival to ascertain whether there are live or dead insects, particularly mosquitoes, present. In case live mosquitoes are seen, our inspectors are instructed to respray the aircraft immediately. Fortunately, most insects found are either in a knocked-down or dead state.

On June 21, immediately following notification of the first case of yellow fever in Trinidad, a telegram was sent to our major stations requiring them to step up control measures on aircraft and vessels. I will say that this first case, which was in St. Andrew county in northeast Trinidad, did not directly involve the airport and seaports from which traffic was coming to the United States. A second case of yellow fever was reported, as additional information was received.

While we stepped up our controls with respect to ships and aircraft and with regard to the requirement of vaccination of passengers, and more particularly of crew members, we still recognized that we could not take full or strict control, because Trinidad had not been declared an infected local area by its government and under the International Sanitary Regulations we had no authority to apply control measures. Following receipt of notification that a case of yellow fever had occurred in Port-of-Spain on August 7, quarantine stations were promptly advised that they could take full control measures. As evidence of that, there were wires from the consulates in Trinidad and Martinique indicating that they had been advised that control measures would be required for aircraft and ships arriving at airports and seaports in the United States. Then, as the extension of yellow fever continued, we sent out a telegram on September 10, again calling attention to the previous information and stating that full controls would be required, including, if necessary, the isolation of non-immunes as they arrived in the United States.

I give this recital of dates and other information just to indicate that, within the scope of what we could do with our personnel, the measures that could and should be taken with respect to this traffic were outlined to the responsible parties in the ports that had the personnel to handle the situation.

Now, ships coming to New Orleans, Tampa, Mobile, and certain other ports, were required to be sprayed before they were allowed to dock. Some of their crews were held up in sailing until they were immunized against yellow fever. The aircraft crews, however, were in a better position because, for a period of time, the airlines have had a program which has been carefully conducted by the medical departments in cooperation with our division which has vaccination facilities at the airports.

The shipping lines had been less completely covered in their immunizations, inasmuch as there had been objections from their crewmen to having these required vaccinations imposed on them. I wish to raise this issue for everybody's thinking because as the necessary controls were adopted, following the report of the case in Port-of-Spain and succeeding cases, many of the companies had to tie up ships until they could get their crewmen vaccinated in order that a valid certificate could be presented either on entry to Trinidad or to Venezuela. That provoked quite a problem within the shipping industry. We worked very closely with their New York offices, and created numbers of vaccination centers within their organizations in various ports of the United States; this permitted them, under our procedure of designation of yellow fever vaccination centers, to apply those immunizations locally to ships where they were tied up. Even so, we still find certain non-immunes among their complement, in which case, as they arrive back in the United States, they are required to stay on board their vessels until they complete the incubation period.

As to further controls within the United States, it would seem then that we must attempt *Aedes aegypti* eradication in the airports and seaports. A program of this nature will necessitate cooperation with State and local authorities. It will also necessitate cooperation with the Communicable Disease Center. I

believe that with the nucleus that is already operating, and with that additional assistance, we can provide adequate coverage for the airports and seaports that get the major traffic out of the troubled areas.

As to the international aspect which you touched on earlier, our opinion was, from the quarantine standpoint, that we could very well consider the first notification of a clinically recognized or suspect case in a human to be the most important notification on which to base our quarantine activity, and to begin to consider that the area was in fact an infected area, thus giving us the signal to apply strict quarantine controls. This was the central theme of our representations to the International Quarantine Committee. If we could perhaps do away with the inflexible outlining of the endemic area, we would think in terms of the notification of the first cases of yellow fever as they occurred. It seems to me that an area that has a notification of that sort is more important from an international traffic standpoint than the mere consideration of a blanket area or endemic area in which we recognize the virus to exist.

We think, also, that the various governments that are involved in this are as interested in the determination of the presence of the virus in their political confines as we are in having it determined. They are as interested in the traffic emanating from their districts as we are in that traffic as it comes to us in the receptive areas. Therefore, with their airports under control, and with the traffic under control by spraying of the aircraft and ships, I am certain they are interested in the people coming out of the jungle and in seeing that they are immune as they come to their populous areas. A great majority of those people who do come out are going to be immunized by their respective governments as they engage in international traffic or, if not immunized, I think they will agree with us that it is the prerogative, then, of the country whose receptive area receives that traffic to inquire into their status and to take appropriate control measures. That again, I think, was very briefly the central theme that was presented in the discussion in the International Quarantine Committee. In the interest of brevity, I think I shall not prolong my remarks, but if there are questions I should like to have them.

THE CHAIRMAN: Thank you very much, Dr. Spencer. I think it is only fair to say that I wasn't trying to make the quarantine service into a whipping boy when I remarked about the *aegypti* breeding on the desk of one of the quarantine officers. In that connection though, since I did mention this regarding the quarantine officer, I think it's only just to add that on my visit to Dr. Downs' office in September, with yellow fever cases in Port-of-Spain and in the presence of plenty of virus, he called my attention to the fact that the mosquito that was biting me in his office was an *Aedes aegypti*. So these things do happen, and Dr. Downs was not responsible for the control of *aegypti* in the area in which he was working.

There are one or two points in Dr. Spencer's remarks which should be emphasized. First, the question of financial interests involved; any time yellow fever invades a new area, whether *aegypti*-transmitted or not, international difficulties arise immediately. In the case of the outbreak in Panama and Central America

discussed by Colonel Elton and Dr. Boshell, after the first few days and after it was known there were no *aegypti* in Panama and in Colon—the principal ports—practically all restrictions were taken off travel out of the area. There has been some requirement of vaccination certificates in certain areas, but there has been no instance in connection with the six-years' experience of jungle yellow fever working up through Central America, in which there has been any long distance movement of the virus or its transfer to another country in infected human beings.

The financial interests involved in yellow fever are not only affected by the declaration of yellow fever infection, but they may influence the notification of the disease. Oftentimes, local authorities are under pressure not to notify yellow fever because of possible business losses. The fact should be emphasized that yellow fever is not as a rule immediately notified. In the Panama experience mentioned by Colonel Elton this morning, it should be noted that the first of the five cases died on November 11, but the first international notification was on January 14—over two months later.

If we want to be highly technical in following through my remarks of this morning on the importance of *aegypti* in the spread of yellow fever, we should pay more attention to the *aegypti* indices of cities and towns close to jungle areas than we do to the number of cases actually reported in those areas. The epidemiological bulletins of the Pan American Sanitary Bureau are beginning to carry the *aegypti* indices of the principal ports and airports throughout the Americas as part of the vital information that is necessary to the health officers as a basis for action. Previously, these results appeared from time to time in the monthly Bulletin of the PASB, but they are now a part of the epidemiologist's working document that goes directly to the particular authorities that are interested in it.

Dr. Spencer spoke of the eradication of *aegypti* in ports and airports. Our experience over a good many years with the eradication of *aegypti* is that it is not a feasible small-scale program. The attempt to eradicate *aegypti* about a port or an airport without cleaning up the surrounding area is pretty much doomed to long-term failure. Eradication of *aegypti* is one of the programs that, in order to be successful, must expand constantly at the periphery. It is very rapidly learned, in working with this problem, that it is economically much better to handle the complete problem as fast as possible than it is to continue to spend money on partial measures.

Mr. Calderwood, do you have something to add to the discussion?

MR. HOWARD B. CALDERWOOD (DEPARTMENT OF STATE): I do have one or two questions to raise. The point was made that a number of Asiatic countries have been concerned about the possible introduction of yellow fever. As a consequence of this concern their health authorities have been applying quarantine measures to persons and planes arriving from countries considered to be possible sources of infection. These measures are in excess of those permitted by the International Sanitary Regulations. These Asiatic countries, however, are permitted to take the excessive measures by virtue of their reservations to the Regulations.

The yellow fever provisions of the International Sanitary Regulations are now being studied with a view to their revision by the next Health Assembly. In order to meet the justifiable fears of the health authorities of highly receptive areas and, at the same time, to avoid the application of quarantine measures beyond those which are generally recognized to be necessary to prevent the international spread of yellow fever, it has been suggested, *inter alia*, that health administrations be required to notify areas in which no human case has been discovered, but where yellow fever virus is known or suspected to be active, as risk areas, and that persons leaving these areas be vaccinated and planes be disinfected before departing on an international voyage.

Now, the questions which I should like to raise are: (1) what criteria might be applied to determine the existence of a risk area, and (2) whether it is possible for a health administration of a country in which jungle yellow fever has been discovered to define the extent of the so-called risk area or areas.

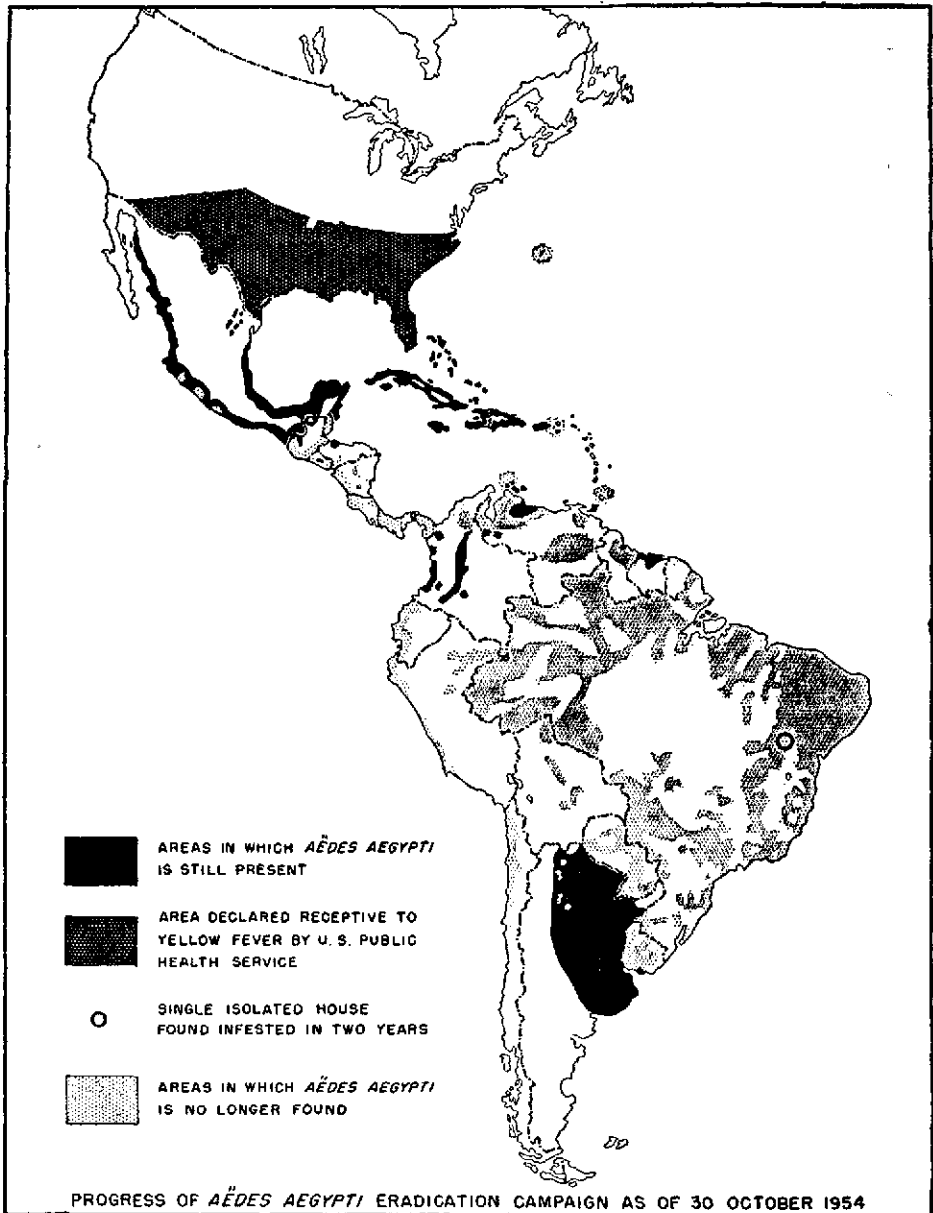
Those are questions relating to matters of a technical nature which, it seems to me, this group might consider. I have omitted any reference to other questions which have been raised here about the need for quarantine measures where human cases have been discovered and where *aegypti* are known to be present, because it is the jungle yellow fever area which appears to be the present concern of health authorities of receptive areas and which was the subject of much discussion by the Quarantine Committee at its recent meeting in Geneva. There is the Caracas case which Dr. Soper mentioned this morning. This is the sort of thing which they are afraid of: the possibility of a person getting out of the jungle area, leaving by plane and arriving at an airport in a receptive area within the incubation period. However remote, this possibility appears to exist.

THE CHAIRMAN: Thank you, Mr. Calderwood. Of course your question will be taken up later, but I suggest we do not attempt to answer it just now.

The way the discussion has taken, with the comments by Colonel Elton and some of the other points that have been raised by Dr. Spencer, I suggest we alter slightly the order of the discussion. Instead of continuing on the subject of the threat to Asia and Dr. Calderwood's question, and then passing to the unfinished business of research, our discussion leads more logically to a consideration of *aegypti* eradication possibilities.

Considering now Map 6 "The progress of the *Aedes aegypti* eradication campaign as of October 30, 1954," I shall outline for you briefly the present situation insofar as we know it because, through the piecemeal information that is distributed in epidemiological reports, most of us do not get a picture of what is happening with a given disease. I am doing this at the request of Dr. Severo, who, still a little bashful regarding his use of English, has asked me to give you this summary for him.

The possibility of eradicating *aegypti* from individual cities in the Americas was first demonstrated in 1932-1933. Those of us who were concerned with the operations at that time would very much like to be able to say that eradication was something that we had planned. It was not. *Aegypti* eradication occurred at a



MAP 6

time when the administrative controls over the anti-*aegypti* service were being intensified, but we had no idea that we were going to reach eradication, nor were we attempting to do so. It was something that occurred, and after it did occur it was discovered to be cheaper to take off part of the men from the cleaned area and put them to cleaning up the suburbs than it was to maintain a constant watch over what was happening in the city that had been cleaned. Then, once the suburbs were cleaned, it was found to be cheaper to go out and clean up the interior area than it was to maintain permanent control services in the areas cleaned.

If you take a look at the map of Brazil and the shaded areas you will see that a large part of Brazil had been infested, but that distribution of *aegypti* was not universal. It occurred very seldom in the river valleys of the Amazon area above the first waterfall, and there were certain other limiting features, but *aegypti* was present in some part of every state and the entire northeast of Brazil was infested, not only in the cities and towns, but also in the rural areas. The eradication of *aegypti* in the Americas is possible because *aegypti* is not, in this continent, a forest mosquito. In the Americas, *aegypti* is found only associated with human habitations or very close to human habitations.

The eradication of *aegypti* in Brazil began in individual cities along the eastern seacoast, and from these cities ever-expanding areas were cleaned in the interior until gradually the entire country was cleared. The eradication of *aegypti* was not easy. The use of oil—the best available larvicide—was an expensive and slow procedure. At the end of 1939 there were only six states in Brazil and the Federal Capital which were free of *aegypti*. However, the demonstration had been made and early in 1940 the Brazilian National Yellow Fever Service declared its objectives to be the complete eradication of *aegypti* from Brazil. Considerable progress had been made before the introduction of DDT, but this made *aegypti* eradication very much more rapid and much easier than before. The relative ease with which *aegypti* can be eradicated with DDT has caused some of the workers from Brazil to be overly enthusiastic in saying that *aegypti* eradication is easy. It is easy in comparison with what it was before, but eradication still requires careful administration and a hundred per cent coverage of the infested area.

By 1946 *aegypti* were so scarce in Brazil that reinfestation from other countries had become a serious problem. The Brazilian Yellow Fever Service then suggested to the Rockefeller Foundation that it would be very useful to Brazil if *aegypti* could be eradicated from Paraguay. Map 6 shows the Paraguayan infested area as contiguous to the infested areas of both Argentina and Brazil. The Brazilian Government offered to stand a large part of the expense of cleaning *aegypti* out of Paraguay, but the representative of the Rockefeller Foundation realized that cleaning Paraguay would simply change the Brazilian frontier of infestibility to the frontier of Argentina, and refused to become involved. The following year the Brazilian Representative to the Directing Council of the Pan American Sanitary Organization came forward with a proposal for eradication of the *aegypti* throughout the Americas, figuring that even though they might be able to get eradication of *aegypti* from all of the ten countries of the continent with which they had frontiers, unless the rest of the continent were cleaned, these

areas would get reinfested. The Pan American Sanitary Bureau, during the past seven years, has been collaborating with various countries in the solution of this problem, aided very greatly by the National Yellow Fever Service of Brazil, which has made available to us men and at times materials when we were in short supply of these.

Before going into the picture of the other countries, however, I should like to indicate to you something of what has happened in Brazil. Let us remember that Brazil is a larger country than the continental United States. It extends over an area of 3,300,000 square miles, which is about ten per cent more than the United States. At the end of 1950 the Director of the Yellow Fever Service reported that *aegypti* apparently had been cleared out of Brazil, none having been found during that year. Another clean year was 1951, in which nothing was found, but in 1952 a few dirty spots were discovered in the state of Rio Grande do Norte. This finding delayed the official declaration of Brazil as free of *aegypti*. In 1953 no *aegypti* were found in Brazil and it was possible to say that Brazil was clean as far as anybody knew.

In the beginning of 1954 a new Director came to the Yellow Fever Service in Brazil. I visited him early in the year, and asked whether he believed *aegypti* was no longer present in northeastern Brazil. He said he didn't know, but he was certainly going to find out. In September I saw him again and asked "Well, what have you found?" He showed me the figures, which I won't attempt to repeat from memory. A large number of men methodically had combed areas which previously had been heavily infested, and he reported "Our men have found one isolated house with *aegypti* so far this year. This house, some six hundred meters from the nearest house, had apparently been missed on previous visits, and it was the only house in the county where *aegypti* could be found in the first nine months of 1954." I understand two additional rural houses were found infested. Brazil is at a point where once infested houses are found, these are quickly condemned. It can honestly be said that nobody knows of any continuing *aegypti* infestation in Brazil.

If we look at the other countries, we find that Bolivia has not reported any *aegypti* since 1948. Paraguay is believed to be clean. Uruguay is clean, with the possible exception of a very minor infestation in Montevideo early in 1954. The most recent survey, still incomplete, has not shown any. Recent reports from Chile show that country to be cleared. Argentina is not as black as it is shown on Map 6, but information is lacking for part of the area. The Argentine Government has recently made arrangements to undertake the eradication of *aegypti* in accord with the agreements with the surrounding countries obligating each to eradicate *aegypti* within their borders (River Plate Sanitary Agreement, 1948).

In Peru there are no known foci of *aegypti* infestation. There are certain areas there which should be rechecked, but for the present Peru is considered free of *aegypti*. Ecuador has been adequately checked and is free. The anti-*aegypti* campaign in Colombia is in operation and is possibly forty to fifty per cent finished.

In Venezuela *aegypti* eradication has been very largely accomplished by the Malaria Service, with the exception of the large city of Caracas and the sur-

rounding area. The danger of this situation was obvious when an infectious case of yellow fever came into Caracas in October, 1954. Emergency measures were taken immediately, and all buildings within four hundred meters of where this case occurred were sprayed thoroughly with residual DDT. The city was sprayed with DDT from the air to kill all flying insects, and finally a systematic house by house eradication campaign has been organized. Venezuela should be free of *aegypti* in the very near future.

French Guiana is clean. British Guiana has been clean and then reinfested by ships from dirty ports. As to Central America, there are no places where *aegypti* is known to be present in Panama, Costa Rica and Nicaragua. However, there is still an *aegypti* problem in Guatemala, Honduras and El Salvador, but all three countries have well advanced programs. The eradication campaign in Mexico is being reorganized after an interruption some years ago.

In Cuba, the *Aedes aegypti* eradication campaign was organized a year ago. The work on a full scale really began in March of 1954. We have been quite fortunate with regard to Cuba, the Dominican Republic and Haiti in the timing of the agreements with the governments to get those services organized, because they had all been started and considerable work done in the capital cities of those three republics before the threat from Trinidad blossomed forth. It may interest you to know that the index of Havana was found to be twenty-two per cent, much higher than the local authorities had believed it to be.

The area blacked out in the United States on Map 6 corresponds to the area declared receptive to yellow fever by the United States Public Health Service in agreement with the international sanitary regulations. *Aegypti* is not regularly distributed throughout this area, but this is in general the area in which *aegypti* may be found. The information on the distribution and density of *aegypti* in the United States is not up-to-date and a careful survey would probably bring many surprises, with certain areas having much less and others considerably more *aegypti* than is suspected.

This, in general, is the situation throughout the Americas except for the British and Dutch colonies which have been backward, but at the present moment, as a reaction to the Trinidad outbreak, are intensifying their eradication campaigns. No serious difficulties in getting the Caribbean area cleaned are now anticipated if the United States gets rid of its *aegypti*. This will require the full collaboration of individual states under the auspices of the United States Public Health Service as the coordinating factor.

When the continental eradication of *aegypti* was proposed by Brazil late in 1947, it was estimated that the two most difficult countries to get interested in the program would be Argentina and the United States. They are the two countries which are, let us say, less exposed to immediate threat, if the *aegypti*-transmitted yellow fever of the other countries is avoided, and consequently there is a natural tendency to lag in taking expensive eradication measures. However, once Havana gets cleaned—it has a safe index at the present time, and other parts of the island will soon be worked—once Cuba gets cleaned and Mexico gets its contiguous areas cleaned, it is apparent that the United States will receive constant complaints from these countries as reinfestations of the cleaned areas occur.

This summarizes, in a way, what the situation is with regard to *aegypti*. I believe that on the whole we are facing a period in which, within a very few years, this job can be completed.

DR. FRED J. BRADY (U. S. PUBLIC HEALTH SERVICE): There are a few questions that I think should be raised at this session. I don't know whether these questions can be answered or not, but it seems to me, with the assembled group of experts we have here, it might be appropriate to pose them.

The first question concerns Trinidad. You, Dr. Soper, made reference this morning to the terrific economic losses suffered by Trinidad during this outbreak of yellow fever. All the information that we have received from official sources certainly confirms that, and in October we had the unofficial estimate that the costs were at that time \$23 million to Trinidad alone, as a result of a few cases of yellow fever. You mentioned, too, that this was the first outbreak in a maritime port for some years. Would these economic losses have been of this same magnitude in Trinidad if *Aedes aegypti* were absent? Does the presence or absence of this mosquito itself have any appreciable effect on what happens to trade and commerce in case of an outbreak? I think that is rather important to us, Mr. Chairman, when we consider this question of eradication of *aegypti*.

The second question I should like to pose has been answered in part. When we look at the Gulf of Mexico on this map we see it almost completely ringed by *Aedes aegypti*. We know at present that the nearest case of yellow fever or evidence of the presence of yellow fever virus exists in Honduras near the Yucatan Peninsula. My question is directed to those who have more information of this area than I do. Are there natural barriers that may impede the progress of the upward extension of the virus so it won't reach the Gulf area, which is apparently very vulnerable to human yellow fever from the standpoint of the presence of *aegypti*? I think Colonel Elton referred to this this morning. I would judge he thought that the virus could jump across the Motagua River and the banana plantation area on the Atlantic side of Guatemala. If it does, I would expect it could go rather fast into Yucatan. We lack information on the vector in this part of Central America. Perhaps there is someone here who could speculate on the vector and its possible extension. Furthermore, the northward limit of the monkeys, I think, has some importance to us in this problem.

So, Mr. Chairman, those are some of the questions that occur to me and the answers may be speculative but, nonetheless, I think this is the proper body to speculate on this sort of thing.

THE CHAIRMAN: Thank you, Dr. Brady. There was a time, and not too long ago, when I would have been glad to answer all of those questions. Today, I am not. I think, though, that we might call attention to the difference between what happened in Trinidad and what happened in Panama and the ports in Central America. In the case of Panama and Central America the Bureau was able, on the basis of absence of *aegypti*, to advise governments not to take measures against these countries. The notification of yellow fever in Panama came on January 14, 1949. I happened to be in Mexico City at the time, flew down to Panama the following day, and a day or two later negotiated by telephone with the Minister

of Health of Cuba the removal of restrictions on air traffic passing through Panama. Practically no difficulties with shipping have occurred as a result of the movement of virus through Central America during the past six years, since the virus has never come in contact with *aegypti*.

In general, there has been no difficulty in the Americas with regard to shipping for the past twenty years, during which yellow fever outbreaks were and could be identified clearly as jungle yellow fever. The outbreak in Trinidad is the only outbreak for many, many years which has caused any serious financial loss to the country concerned. The last previous difficulty followed a case in Asuncion, Paraguay, in 1937, which the government failed to notify officially. The Argentine Government learned of this case through a radio broadcast and hurriedly put on a three-weeks' quarantine which cost Paraguay a great deal of money.

The answer to your question probably is that, due to the present advanced stage of knowledge of the sanitary authorities throughout the Americas, a declaration from the Pan American Sanitary Bureau stating that there is no danger in a given area of *aegypti*-transmitted yellow fever will be respected, and very little loss will ensue from the declaration of jungle yellow fever.

The question regarding the barriers against the movement of the virus into Guatemala and Mexico is undoubtedly linked to the two other points you have mentioned; namely, the monkey distribution and the identity of vectors and their extension in that area. I suggest that Dr. Trapido give us a brief résumé of the vector situation in that area as he sees it and, with the aid of Dr. Boshell, give us some idea of the possibilities of yellow fever extension from its present point in Honduras on into Guatemala and Mexico.

With regard to the distribution of monkey species, Dr. Williams has here a map showing the distribution of spider monkeys in South America (Map 7) and another (Map 8) showing the distribution in Middle America, and there is no question but that there are in the properly forested areas of this region sufficient monkeys to carry the virus well into Mexico. In general, and from the information that we have, we do know that the proper monkeys do exist well up into Mexico. Let us pass these maps around and let Dr. Brady see them.

LOCALITIES SHOWN ON MAP 7

PANAMA		12. La Gloria	BRITISH GUIANA
1. Chepigana		13. Río Tarra	
2. Río Lara		14. Norosí	25. Maripá
3. Río Tuyra		15. Concordia	26. Río Supinaam
4. Cituro		16. Bolívar	
5. Tapalisa		17. Mambita	DUTCH GUIANA
6. Mount Pirre		18. Villavieencio	
7. Río Bayano		19. Gallera	27. Marowijne River
		20. Barbacoas	28. Paramaribo
COLOMBIA		VENEZUELA	
8. Cereté		21. El Llagual	FRENCH GUIANA
9. Río Atrato		22. Río Mato	29. Cayenne
10. Las Marimondas		23. Esmeralda	30. Río Lunier
11. Puerto Estrella		24. La Unión	31. Rivière Camopi

ECUADOR	PERU	
32. Cordillera de Chilluri	51. Cahuapanas	70. São Felipe [=João Pessoa]
33. Hacienda Chinipamba	52. Elvira	71. Rio Jamundá near Faro
34. Santo Domingo de los Colorados	53. Cerro Azul	72. Igarapé Anibá
35. Baeza	54. Lamas	73. Obidos
36. San José	55. West of Chayavitas	74. Santarém
37. Chimbo	56. Sarayacu	75. Aracú
38. Gualea	57. Chicosa	76. Piquiatuba
39. Mindo	58. Río Aguaytía	77. Caxiricatuba
40. Cordillera Galeras	59. Río Inuya	78. Tauary
41. Jima	60. Río Javari	79. Lago Cuipeúa
42. Tarapoto	61. Mouth of Río Urubamba	80. Cameté
43. Boca Río Curaray	62. Peruaté	81. Altamira
44. Puerto Indiana	63. Río Comerciato	82. Belterra
45. Río Santiago		83. Lago Grande
46. Río Napo	BOLIVIA	84. Río Madeira
47. Tomependa	64. Ibon [=Ivon]	85. Mouth of Río Abuña
48. Tutumberos	65. Puerto Salinas	86. Paitaná
49. Iquitos	66. Santa Helena	87. Jarú
50. Huarandosa	67. Río Yapacani	88. Barrão de Melgaço
	BRAZIL	89. Cabeceiras do Pirocoluina
	68. Serra de Cucuy	90. Rio Sararé
	69. Jaburú	91. Serra dos Parecis

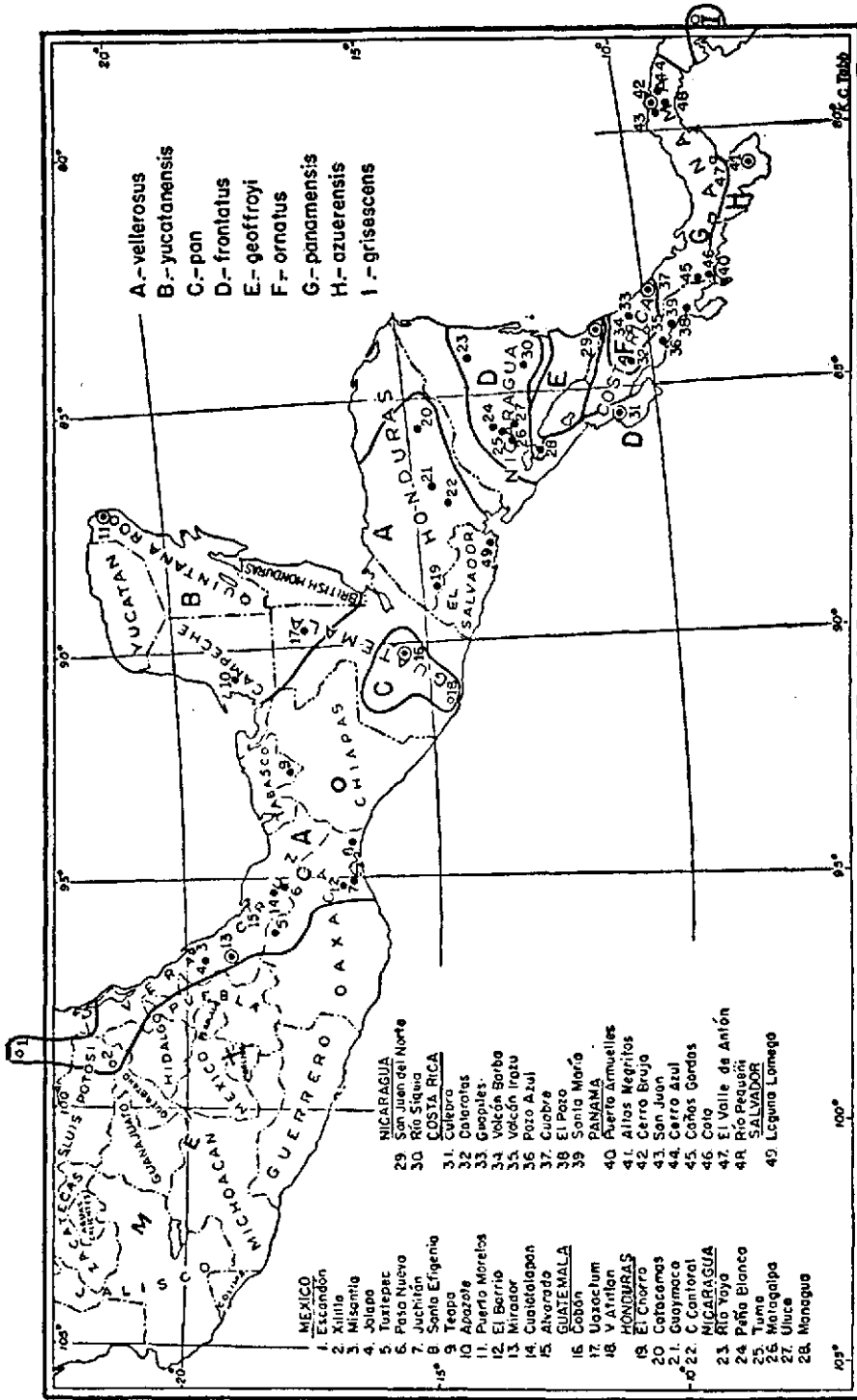
DR. HAROLD TRAPIDO (GORGAS MEMORIAL INSTITUTE): With regard to the *Cebus* monkeys, their northern distribution ends in British Honduras. In Mexico both *Ateles* (spider monkeys) and *Alouatta* (howling monkeys) are found, their northern limits coinciding very closely with the northern limit of the classical neotropical life zone at Tamazunchale in southeastern San Luis Potosí.

THE CHAIRMAN: Where is that with relation to some of the large cities?

DR. TRAPIDO: About 100 miles southwest of Tampico. That is as far north as the monkeys get.

With regard to the mosquitoes, the word "speculation" has recurred in the discussion, and I wish I were in a position to take it out of that realm, but I can perhaps provide some information on which other speculation can be carried on. In June and July of 1954 monkeys were reported dying on the north coast of Honduras between La Ceiba and Tela. When those reports were confirmed Mr. Galindo and I, of the Gorgas Memorial Laboratory, went there with several purposes in mind. One was to attempt to recover a fresh strain of virus to be used in laboratory transmission experiments we had planned, using Central American *Haemagogus* whose ability to transmit the virus was known. Another was to collect mosquitoes from where the monkeys were dying and make species pools from which we might be actually able to tell which mosquitoes were carrying the virus.

We were fortunate this time to be early enough. We arrived at Tela on July 30 and on August 6 were able to recover a dead monkey, the liver of which Dr. Carl Johnson reported to be positive. A dead monkey had been recovered pre-



Map 8. Distribution of the forms of spider monkeys (*Ateles*) in Middle America.

viously on July 16 and sent to Bogota, but due to delays in air express Dr. Gast was not able to report on it until some weeks later. It too was positive.

We started collecting mosquitoes in the canopy on the day the monkey died of histopathologically proven yellow fever, and collected 20,000 mosquitoes within a quarter-mile radius in the succeeding four weeks. First, let me say that we did not have the sort of success that Dr. Downs was able to report. No virus has been recovered from any of those mosquitoes so far, although the laboratory work on them by Dr. Rodaniche is not yet complete.

On the north coast of Honduras there is a relatively narrow coastal plain varying from five to twenty-five or thirty kilometers wide. This coastal plain between Tela and La Ceiba—two port towns—is composed of either abandoned banana land, small farms and pastures, or swampy coastal forest. Back from the coast five to twenty-five or thirty kilometers is a high mountain ridge covered with excellent primary tropical rain-forest. On hearing that the monkey died at La Masica, which is a point on the rail line between these two places, we assumed that the monkeys had been brought in from some place along this well-forested slope. They had not. The monkeys died on the coastal plain between the railroad and the sea, in the broken, rather poor swampy forest, cut up by pasture land and banana plantations; the sort of terrain in which nowhere throughout Central America have we found the known South American vectors. We were unable to get any reports of monkeys dying on the mountain slope where we were able to find the vector and where we anticipated finding it. Thus the monkeys did not die (or, at least, we were unable to get any reports of their dying) where the known vector was; but they did die where the known vector (*Haemagogus spegazzinii falco*) was not!

Now, Dr. Boshell might want to interpret these findings somewhat differently, but the fact remains that of 20,000 mosquitoes, collected within the month after the last of a series of monkeys died of yellow fever, we were unable to recover any currently known natural vector of yellow fever. *Haemagogus equinus*, known to transmit in the laboratory but never found infected in nature, was the only *Haemagogus* present. Where does that leave us, anyone may say? About twenty-five kilometers away the vector did exist but, as a biologist, I would point out that the shortness of the distance is deceptive because the ecological conditions, which are more important, are so different in the two situations; that is, one just would not expect to find *Haemagogus spegazzinii falco*, the proven natural vector, in the forest of the sort where the monkeys died.

The Lancetilla Valley, a point some thirty-five kilometers west of La Masica, is as far north as we have found *spegazzinii falco* so far. We believe northern Honduras to be at or near the northern limit of the distribution of this species. We don't know the situation in eastern Guatemala, but there is a man in the field who is now making collections there. We ran collections during a rainy season in the state of Tabasco, Mexico, and did not recover any *falco* there. So we can definitely say, or we think we can, that the proven South American vector species does not reach the north side of the Yucatan Peninsula.

However, related to this known vector group—it was, incidentally, *spegazzinii*

which was involved in Trinidad—is another *Haemagogus* on which no work has been done by way of determining its ability to transmit yellow fever virus, for the reason that the southern end of its distribution is San José, Costa Rica, and all the work on yellow fever transmission was carried on in South America. This species, which is part of a species complex with several representatives in Middle America, has never been tested. Morphologically, however, a taxonomist would say it is very closely related to *spgazzinii*. We, in the course of our field studies, have found that what had been thought of as a rare mosquito, known from a few specimens, was actually the southernmost representative of a very common species complex which extends from San José, Costa Rica, to at least San Luis Potosi, as far north as monkeys occur. We are still uncertain about the taxonomic relationships within the complex, but we are currently in the process of doing laboratory experiments on the ability of certain members of the group to transmit virus.

The one *Haemagogus* which was present out in the swampy flatland where the monkeys died in Honduras, near La Masica, was *Haemagogus equinus*. This is a species which is found in Colombia and on, north, into Mexico. Last year we recovered mosquitoes of this species in the state of Tamaulipas, Mexico, which adjoins Texas on the Gulf Coast. I think that at the proper time of year it would be possible to go into a place in Texas which I have in mind and collect it there also. I would predict that *Haemagogus* may well occur in the Chisos Mountains of Western Texas. Ecologically, the situation there is the same as that in which we took *Haemagogus* in Mexico, and physiographically the formation is also the same. But I would hesitate to imply that the numbers would be significant for the transmission of yellow fever.

While we cannot exclude the possibility that something was present which we failed to find, we can say that *equinus* was the only *Haemagogus* present among the 20,000 mosquitoes collected where the monkeys died near La Masica.

THE CHAIRMAN: Dr. Trapido, you haven't answered the question raised by Dr. Brady. Is yellow fever virus going to go from Honduras on into Guatemala and up through Mexico?

DR. TRAPIDO: Well, I prefaced my remarks by saying that I could only provide some background for speculation; that is, speculation at a slightly different level. I can provide the information on which the speculation can be carried on by persons other than myself.

THE CHAIRMAN: Do you want the definitive answer then to come from Dr. Boshell?

DR. TRAPIDO: Anyone but myself.

THE CHAIRMAN: Dr. Boshell, do you have something to say on this?

DR. BOSHELL: Well, it all depends on the vector. If *Haemagogus equinus* is a vector, which is quite a possibility, the future of the jungle yellow fever in Honduras, Guatemala and Mexico is assured, because that mosquito is almost universal under conditions which are adverse to the other *Haemagogus* as we know it.

I was present shortly after the death of the La Masica monkeys. I saw the enormous work that Dr. Trapido and others were doing to classify those mos-

quitoes and to retrieve virus from them. It is perfectly true that the monkeys were dying in a place where *Haemagogus spegazzinii* was absent. However, I wish to point out two things. One of our boys walked from where the monkeys died to where he knew *spegazzinii* was present, and came back with this mosquito in a day; so although *spegazzinii* was absent at the actual place of the death of the monkeys, this mosquito was present at a distance of a few hours walk.

The monkey concerned in this outbreak was *Alouatta palliata*. This monkey is not as sedentary as we thought for a long time. I have met, personally, groups of monkeys perambulating in grasslands long distances from their natural habitat in the trees. They do migrate, they do cross open spaces to change their feeding grounds. This must be borne in mind in connection with monkeys dying at a distance from the habitat of the known mosquito vector.

However, I must admit that the known vector is extremely scarce in the infected area of northern Honduras. We couldn't find it in numbers comparable to those found further south in Nicaragua, Panama or Colombia. Therefore, I agree with Dr. Trapido that the problem of the vector is not yet solved. This problem deserves exhaustive study, since all predictions on the spread of the wave into Guatemala, Belize or southern Mexico hinge on that factor.

The last case of jungle yellow fever in Honduras occurred in September, 1954, on the edge of the Ulúa Valley. That valley, completely deforested, is now banana land or swamp land, and should be, I think, a pretty efficient barrier, if there is such a thing as a barrier for yellow fever. But along the slopes near the headwater of the San Pedro River lies a rather narrow stretch of woodland which may afford a bridge for the virus across the valley. It is a critical point. It is possible, if not probable, that the wave may stop there. Should the wave cross that critical point, the way is clear into Belize, Guatemala, and then southern Mexico. It is a question of possibility versus probability as in every prediction.

THE CHAIRMAN: I believe, Dr. Brady, you more or less involved Colonel Elton in this discussion as to whether yellow fever is going into Guatemala and Mexico or not. Do you have any ideas, Colonel Elton, that you would care to record in the light of doubts expressed by others?

COLONEL ELTON: I should like to state that my connection with this phenomenon has been largely as a map problem, not having been endowed with funds to travel and see the terrain. I have relied much on the opinions of friends in the countries successively involved, such as Paul Allen, Oscar Vargas, Henry Kumm, Leonardo Somarriba, Alejandro Robleto Pérez, Manuel Cáceres Vijil, Mark Hoekenga and others whose advice and assistance I value most highly. It has been something like a Leavenworth problem, trying to outguess an enemy possessing many secret weapons who keeps introducing one of them from time to time.

I base the concept that the wave will continue largely on historical evidence of "xekik" contained in the Maya Chronicles and the "matlazahuatl" that wiped out the coastal settlements of Mexico in pre-Colombian times in the vicinity of Vera Cruz and Tampico and led to the forced repopulation of the coast by order

of Moctezuma. This evidence, while discounted by Carter, who based all his interpretations on the presence or absence of *Aedes aegypti* since he was quite unaware of the jungle epidemiology, was accepted by Gorgas and Carlos Finlay as evidence of yellow fever before the arrival of Columbus.

The Maya Chronicles of Chilán Balam of Chumayel and Chilán Balam of Tizimin speak very definitely of the outbreak of bloody vomiting (xekik) that ravaged Yucatan in 1484. Diego de Landa, about 1550, in writing the history of Yucatan, spoke of people within whose memory the region was so thickly populated that the whole countryside looked like a vast village, and he asked what had become of the old empire sites. I cannot prove that that was due to yellow fever in its sylvan form, but the presumptive evidence is strongly in support of it.

The current wave of yellow fever in its pure sylvan form in Central America may be a unique phenomenon, possibly one that occurs only at long intervals, with perhaps centuries between cycles. It would be difficult to determine accurately its periodicity. *Aedes aegypti* was introduced into the New World from the Old World by the early explorers and settlers, and it must have required several decades for it to become widely disseminated. When it was finally established it became difficult, if not impossible, to distinguish urban from sylvan outbreaks and the interlocking connections between the two forms epidemiologically.

This may be the first time since 1484 that a wave of yellow fever in its pure jungle form has occurred in Central America. If it had taken place since the establishment of *Aedes aegypti* we would hardly be able to identify it, because there would have been many backfires from small local outbreaks, seeded from urban and port settlements that would have arrested its progress. This condition would have obtained until 1924, when the last urban outbreaks occurred in Central America and Mexico, after which the urban vector was eradicated in Central America.

I base my prediction on a calculated risk. One might agree with Waldemar Argow that the difference between a prophet and a martyr is that whereas a martyr courts destruction, a prophet takes only a calculated risk. The death of the wave could have occurred at any time, but it has not yet happened. I would say on the basis of a calculated risk that the wave may be expected to go on into the lowlands of Mexico—the Tierra Caliente of New Spain—which history indicates has been such a fertile hunting ground for the virus in the past centuries.

Specifically, I anticipate an epidemic outbreak in the Motagua Valley of northern Guatemala about July, 1955. The epizootic phase may precede this outbreak and advance into Alta Verapaz at that time. The Gulf coast of Mexico, from Campeche to Villa Hermosa, will probably light up in 1957.

THE CHAIRMAN: Thank you, Colonel Elton. I believe, Dr. Brady, that you have heard the various opinions expressed. I might say that within our own staff there has been a varied opinion, so varied in fact, that I know of at least one future financial transaction that will be completed one way or the other according to whether yellow fever virus does go through to Guatemala and Mexico or not.

DR. TRAPIDO: The continuation of this discussion did bring to mind another point which perhaps should be made to provide more information to speculate upon, and that is that *Haemagogus* ecology changes in Mexico. Until this northern Honduras episode, the sequence of yellow fever, whether in monkey or man, in Panama and up through Central America, fitted quite well into the picture of an elevation band between 100 and 500 meters, which pretty well defines the range of elevations where *spegazzinii falco* is common. That chain of association was broken in northern Honduras, where there has been the first inconsistency. There was nothing inconsistent between the distribution of *spegazzinii* and the death of monkeys and men until the La Masica incident.

However, in Mexico something again happens with regard to what *Haemagogus* does. In the highlands of Honduras the broad-leaf tropical rain-forest is replaced by pine and *Haemagogus* is not found. The central table land would in no way be expected to be involved. *Haemagogus* is classically described as a deep tropical rain-forest mosquito. In Mexico, to our utter astonishment, we found a wholly different situation in connection with the close relative of *spegazzinii* of which I spoke. Let me illustrate.

Dr. Boshell was trying out a rifle to be used in collecting monkeys. By chance, we were at an elevation of 4,500 feet, some 1,400 meters, in open scrub, mesquite, dry limestone country above Tuxtla Gutiérrez in Chiapas. A blue mosquito bit him on his trigger finger—it was a *Haemagogus*—out in this scrub covered, dry, high altitude plateau. We followed this lead and since then have collected this *Haemagogus* within two hours drive of Mexico City at an elevation of about 5,000 feet. Of course, there are no monkeys in this sort of country. This is a species which is unnamed; incidentally, we have a manuscript name on it, but it is as yet undescribed.

If one wishes to bring into the speculation the role of marsupials, which extend out of the neotropical into the United States, as intermediate hosts, then we must consider whether in Mexico there is the possibility of a very different kind of cycle. The word "rural" perhaps would be appropriate to it. Tropical rain-forest would not be essential. We took as many of this new *Haemagogus* right out in the open among shrubs eight or ten feet high and in quite an arid situation, as we would of other species, such as *spegazzinii*, in rain forest in Panama. The key to this situation we think relates to breeding habits. The species in Mexico is associated with limestone formations and breeds in solution depressions in limestone. We were able to recover larvae in such rock holes.

This just broadens the field of speculation; it doesn't narrow it, but it should be mentioned and I neglected to do so before.

THE CHAIRMAN: Thank you, Dr. Trapido. Are there other comments on this particular thing?

DR. DOWNS: I was very interested in Colonel Elton's notes on early Mayan history, and feel another item might be mentioned in that connection. A few years ago, Kumm picked up *Anopheles darlingi* at Stann Creek, British Hondu-

ras. Since that time rather sketchy collecting has disclosed the presence of this species also along the Usamacinta River between Guatemala and Mexico, where Kumm and Bustamante made a yellow fever survey some fifteen years ago. Also it has been found as far north as Teapa, Tabasco. This discontinuous distribution, present in northern South America, then skipping a long stretch of Central America to reappear again in British Honduras, Guatemala and Mexico, is most interesting. This distribution can be fitted rather nicely over the map of the Mayan Empire. Since *A. darlingi* in South America is a most efficient vector of malaria, I began to speculate some years ago on the possibility of *darlingi* transmitted malaria being one of the unknown causes for the destruction of the Mayan Empire. The speculation will never be answered, of course, but I just introduce it as another possibility for epidemic disease in that region.

THE CHAIRMAN: A very interesting observation. I have come to a point in this program where I want to call on Dr. John Bugher. I was looking around the room to find somebody to pick on who hadn't been talking, and I must say, in connection with the choice of Dr. Bugher, that he has had an opportunity over quite a number of years to work on the problem of yellow fever, not from the standpoint of *aegypti* control and *aegypti* eradication but from the standpoint of studying the conditions under which the disease occurs. He had the opportunity to work in Colombia for some years under very favorable conditions, and then during the 1940's, part of the war period and afterwards, he was in charge of a yellow fever laboratory in West Africa. During that period in West Africa he had an opportunity to see repeatedly the conditions under which yellow fever was occurring and being studied in Central Eastern Africa.

It occurred to me that Dr. Bugher, now having been away from the problem, or let us say not working with the problem, for some years, but still with a good background in it and having had an opportunity here today to be brought up-to-date, might very well give us a somewhat more detached view of the over-all problem of what we have listed here as unfinished business, that is, further investigation of the unknown factors in the epidemiology of yellow fever. What are the things we don't know? What are the questions to which we do not know the answers? How important is further research? And what are the lines along which that research should be carried? Dr. Bugher.

DR. JOHN BUGHER (ROCKEFELLER FOUNDATION): Dr. Soper, I think my remarks have to be somewhat in the field of speculation, and therefore not nearly as fruitful as the observational things that we have been listening to today which constitute a very fascinating story. In reviewing the topics discussed I was just thinking how many times, historically, yellow fever has been classified as finished business only to be returned later to the category of unfinished business; and how many more times in the future this cycle will be repeated. So, for whatever it may be worth, these comments of mine will be directed more to some broad questions of biology than to the clinical problem.

I have been struck by the complexity of the problem in Central America, and how difficult it is to arrive at any firm pattern to which there would not be ex-

ceptions sooner or later, and most of the time the exceptions seem to occur rather soon. In this whole epidemiological complex one of the most significant things seems to be the essential fluidity of living things, both of vectors and host. In the biological complex we tend to think too much in taxonomic terms and perhaps do not fully appreciate that within what is called a species, which is quite an arbitrary thing anyway, there is not only variation geographically but there is variation in time within the same geographic area. So the biological behavior of a species unit, whether a mammal—that is, a monkey—or a mosquito, may vary from area to area at the same time and within a given area at different times.

This whole problem, which is essentially one of genetics, is being much more clearly appreciated at the present time than was true even a few years ago. I believe we see more quantitative evidence of the phenomena which we call mutations, for lack of anything better—the spontaneous modifications of the genetic complex within a species arising from whatever cause may be operating, usually not all perceived. Operating upon the genetic variation, the environmental factors which produce what we call selection pressures may result in a profound modification of the population without very much externally being visible. So we do find within the primates, for example, a great deal of difference of apparent susceptibility to the yellow fever virus, and quite commonly you find the most violently susceptible of the primates, in a clinical sense, in areas having the longest history of freedom from contact with the virus.

Other elements certainly do come into the picture quantitatively. A mosquito, which in the laboratory may be a very promising vector, transmitting without any particular difficulty, may be found to be quite inoperative at a given time in a given situation in its natural environment. One may find, as we all have found at various times, that the species actually transmitting may be the one perhaps least considered from the standpoint of some of the experimental evidence.

The ecological situation then is one which involves both space and time, and without very careful assessment of the ecology one can be led to conclusions which are entirely unfounded or even erroneous. I think we have all seen in the South American situation that transmission in the forest is largely by day-biting species and, in order for the transmission to occur, the mammalian host has to be, in point of time during the day cycle, coincident with the vector. They must share the same environment in terms of both space and time.

In the African situation we find essentially the same machinery, but the components are different. The time relationships are different. There the predominant forest vector, at least through most of Central Africa, is a nightbiting mosquito, not biting during the day at all. Transmission, both for monkeys and for man, occurs at night, which leads to a very sharp dichotomy in the epidemiology because, while the monkeys remain in the forest at night and in the leafy canopy, man not only gets out of the forest into his villages, away from the leafy canopy, but gets into the huts into which most of these mosquitoes do not enter.

So we have two quite separate epidemiological systems operating in Central

Africa, one which is sylvan, largely concerning monkeys, and a second operating in the towns and villages, almost entirely concerned with *Aedes aegypti*, but at times involving *Aedes simpsoni* which is more or less an intermediate between these extremes. The degree of crossing of the two epidemiological cycles is very difficult to determine and is not by any means as simple and intimate as one might at first think.

So it seems to me the thing that stands out here is the need for much more fundamental biologic information, not only with respect to the habits of the apparent mammalian hosts and the possibility of other cycles entering into the situation, but a great deal more needs to be known concerning the fundamental biology of all of the possible or potential vectors on the scene.

One hesitates very much to be at all dogmatic about any of the components in this whole system. I couldn't help wondering about this aspect of *Aedes aegypti* eradication. The primitive form of *aegypti* seems to be that which can be found in the forests of equatorial Africa quite widely. It does not bite man, save very reluctantly. It may bite monkeys. Usually one cannot find this primitive *aegypti* in the forest, but by following suitable tree holes, artificial or otherwise, one can usually encounter larvae and establish the fact that the mosquito is in fact present. I presume that our domesticated *aegypti* represents a selected mutant from that fundamental primitive strain. Whether this mutant could back-mutate to its more primitive form capable of forest inhabitation in the Americas has never been demonstrated and has not, as far as I know at least, been very much sought for, but it is an interesting genetic problem from the standpoint of *aegypti* eradication. Some of these phenomena may occur only once in many millions of individuals but might be significant in some instances.

So my main thought here is to reiterate the value of fundamental biological and ecological study and to attempt to anticipate possible mechanisms which might operate farther north than where they have yet been demonstrated. While it would appear that we have a dominant genus in the *Haemagogus* for the transmission within the forest in the Americas, other species certainly can transmit and probably may under particular sets of conditions. It would certainly repay us to continue to explore the cycles which do not appear to be too obvious and consider lines which might not be, in our present thinking, very likely to exist. I do think the ecological studies which Dr. Trapido and Dr. Boshell have been following are of very great value and have already shown something of the complexity of this problem. We have also seen how difficult it is to predict anything about the degree of northward extension.

THE CHAIRMAN: Thank you very much, Dr. Bugher. The differences between the yellow fever pictures of the Americas and of Africa, insofar as these are known in the two continents, are, I think, quite germane to our general discussion here. If it is possible to have two such different cycles on different continents, it is conceivably possible to have quite divergent phenomena on the same continent under different conditions.

The term "jungle yellow fever" was introduced to designate the fact that this type of yellow fever is observed only in connection with the mixed tropical forest.

The straight pine forest or the one-stand-of-wood forest was not involved in our experience with epizootics of yellow fever which always were noted in connection with the mixed type of tropical and subtropical forest. The observations of Dr. Trapido suggest the possibility of non-*aegypti*-transmitted yellow fever under conditions in Honduras somewhat different from those of previous observations.

In introducing the work of the Tropical Diseases Laboratory in Trinidad, I stated that the laboratory had been set up for the study of viruses other than the yellow fever virus. Dr. Max Theiler has taken exception to that statement. In the discussion following his declaration of my error, certain points were brought out which are important for all of us to know, and I ask Dr. Theiler to give us his views on the general problem of virus investigation, and especially on the necessity of applying back to yellow fever virus some of the things that have been learned from the study of other viruses.

DR. MAX THEILER (ROCKEFELLER FOUNDATION): As a by-product of the study of jungle yellow fever by the Rockefeller Foundation quite a number of unknown viruses were isolated from man and mosquitoes. When the Rockefeller Foundation decided to terminate its yellow fever program, an intensive study was made of these newly discovered agents. This study showed that several of these viruses, such as Ilheus from South America and West Nile, Uganda S, Ntaya and Zika from Africa, were immunologically related to well-known agents such as yellow fever, St. Louis, Japanese B encephalitis and dengue.

These observations, as well as others, led the Rockefeller Foundation to embark upon a new virus program to determine the distribution, incidence, importance and epidemiology of the arthropod-borne virus diseases of man and his domestic animals throughout the world. To achieve this objective, the work of the central laboratory in New York was to be coordinated with field laboratories established in the major zoogeographical areas in the world.

Of prime importance to such a study is the classification of the agents under investigation. Here, great advances have been made, largely due to the hemagglutination test recently developed by Drs. J. Casals and D. H. Clarke. It has been found that, from many of the agents, antigens could be prepared which have the power of agglutinating chicken red blood cells. Immune sera inhibit this hemagglutination. Extensive application of this hemagglutination inhibition test has enabled us to separate from the large number of viruses under study two clearly defined groups which we have called Group A and Group B. To Group A belong the three equine encephalomyelitis viruses (Eastern, Western and Venezuelan), Semliki Forest virus and Sindbis. An immune serum prepared against any one of these will inhibit agglutination by a homologous antigen to a high titer and to a lesser extent antigens prepared against any other member of the group.

In the second, and larger, Group B are placed yellow fever, dengue, St. Louis encephalitis, Ilheus, Japanese B encephalitis, West Nile, Uganda S, Ntaya, Zika, and Russian spring-summer encephalitis. These agents, according to the hemagglutination inhibition test, are all very closely related. An immune serum prepared against any one of this group will inhibit agglutination by an antigen

prepared from any other member of this group, but not with an antigen prepared from Group A. The two groups are quite distinct. As yellow fever belongs to Group B, I will confine my remarks entirely to this group.

While from the point of view of classification, the hemagglutination test gives the clearest group reaction, essentially similar results are obtained with the complement fixation test and the protection test in mice. Thus, by means of the latter, clear-cut evidence has been obtained that the virus of yellow fever is related to Uganda S, West Nile, dengue, and Japanese B.

Apart from the immunological evidence, these agents have many properties in common. They are all—with the possible exception of Ntaya—of approximately the same size. Infection of man and his domestic animals occurs with all as an accidental event in the course of a virus cycle in nature. The complete epidemiology of none is known. Monkeys are known to be involved in the cycle of yellow fever—and possible dengue—in nature. Birds have been shown to play a part in the epidemiology of West Nile. The mechanism by which the virus is maintained during the season when mosquitoes are scarce or absent is only known for one member of this group, namely, Russian spring-summer encephalitis. Here, the evidence is clear that the virus is maintained during the winter in ticks. We thus see that yellow fever virus is merely one of a large group of closely related agents, all of which probably evolved from a common ancestral type.

In nature, it is known that *Aedes aegypti* are able to act as efficient intermediate hosts for yellow fever and dengue. Experimentally, this species of mosquito can transmit other members of the same group. Yet, *Aedes*-borne yellow fever has, at present—as well as in the past—a very limited distribution in the world, whereas dengue has a much greater distribution. From the available knowledge of the characteristics of the viruses under study, their distribution throughout the world is illogical.

The immunological overlaps may offer a possible explanation of some of the known facts. Thus, for example, in Egypt, infection with the West Nile virus is extremely prevalent. Individuals become infected during the first few years of life. The adult population is almost 100 per cent immune. Surveys of immunity by means of the mouse protection test show that, in addition to immunity to West Nile virus, there were also some sera which protected mice against Japanese B, Ntaya and dengue viruses. The study of acute and convalescent sera from cases of West Nile infection (confirmed by virus isolation) showed that the convalescent sera not only had the power to protect mice against West Nile infection, but also, at times, against Japanese B, Ntaya, dengue and possibly yellow fever. This is very good evidence that an infection with one member of Group B will stimulate the production of antibodies which have some protective action against other members of the group. In view of the very high rate of immunity to the West Nile virus in Egypt, it is not a far-fetched hypothesis that the population is relatively resistant to infection by any other virus belonging to the same group. The implication here is that the population of Egypt is sufficiently immune so that an epidemic with dengue or yellow fever would be impossible. At present, we know that *Aedes aegypti*, the usual urban vector of yellow fever and dengue,

is relatively scarce in Egypt—hence, epidemics of these two could not take place. However, we know that in the past this species was much more prevalent, yet we have no history of any yellow fever epidemics.

A somewhat similar condition occurs in Trinidad. You have listened to the excellent account given by Dr. Downs of the epidemic of yellow fever in that island. Infection was widespread, and yet, no epidemics occurred in Port-of-Spain in spite of the prevalence of *Aedes aegypti*. Recent work has demonstrated that infections with a virus (or viruses) either identical or closely related to dengue are very prevalent in Trinidad, including Port-of-Spain. Yellow fever and dengue are closely related immunologically. In fact, during this epidemic we obtained conclusive evidence that the convalescent sera from cases of yellow fever as a rule developed antibodies which had the capacity to protect mice, not only against yellow fever, but also against dengue. The converse we know is true from experiments with sera prepared in monkeys with dengue virus.

I would like to suggest, purely as a working hypothesis, that no epidemic of yellow fever occurred in Port-of-Spain because the population is largely immune to the immunologically related dengue virus. Other explanations are, of course, possible—such as that *Aedes aegypti* is a far more efficient vector for the virus of dengue than it is for yellow fever.

If the immunological hypothesis, as outlined above, proves valid, it will go a long way in explaining the anomalous distribution of some of the arthropod-borne virus diseases throughout the world. It is questions such as this on which the present virus program of the Rockefeller Foundation hopes to shed some light.

THE CHAIRMAN: Thank you very much, Dr. Theiler. I have heard, of course, with a great deal of interest, what has been said. It is not the first time we have had the question raised as to the cross-immunity between dengue and yellow fever. It is a matter which has been discussed repeatedly in the past, and I am perfectly willing to stick my neck out to say I would certainly not feel free to inject a person with yellow fever virus just because he had had at some time in the past an attack of dengue. In this connection, we do have the repeated historical observations of the past in various countries in which significant epidemics of breakbone fever, or of Polka fever—both synonyms for dengue—occurred in one season and in the following season an outbreak of yellow fever was reported. I suffered a rather severe attack of dengue many years ago, and some years later, when my blood was tested, I was declared to be susceptible to yellow fever. Following vaccination from yellow fever, my protection test became positive. Of course, the answer to that may be that my attack of dengue may very well have been something else.

There is one very important point to be gotten from what has been said, and that is that there should be a considerable coordination of the studies in different parts of the Americas, of any activities that are going on, and of the collection and exchange of known sera for this basic fundamental testing that has been mentioned.

I want to thank Dr. Theiler for making these statements for us, for giving us the picture of the fundamental grouping of viruses that is occurring. The Rockefeller Foundation is really the only organization I know which is in a position, disinterestedly and over a long period of time, to carry out studies of this type. I want to express my admiration for the program and declare here that we, in the international organizations, feel that this work of the Foundation is invaluable.

Dr. Boshell, would you like to give us your ideas on unfinished business, on the questions to which you do not know the answers?

Before Dr. Boshell speaks, I should like to say that we literally caught Dr. Boshell in the jungle in 1934, when he established the fact that yellow fever was present on the eastern slopes of the Andes at the edge of the llanos. Then, for quite a number of years he remained in very close contact with the forest. Among the men who have worked with yellow fever in the Americas, it is he who has spent the most time actually in contact with the mosquitoes and the animals in the forest. Dr. Boshell's observations of the canopy activities of *Haemagogus*, and the importance of looking for *Haemagogus* above the surface of the ground, even though the human case gets its infected bite from this mosquito at ground level, has been very important in the study of the disease.

Dr. Boshell has had an opportunity of seeing the conditions under which yellow fever occurs, not only in Colombia but also in Brazil and some other areas, and has had a good many hours of day and night meditation over the conditions in Central America. I am calling on him as one of the individuals who should be able to answer all of our questions on this problem, and since he can't, I would like him to list for us some of the questions that he can't answer and some of the things that he believes need further study and elucidation.

DR. BOSHELL: The problems related to jungle yellow fever are really very simple and very few when the discussion boils down to programs and projects. It all hinges on the relationship of the vector and the mammalian host, and the possibility of wavelike epizootics behaving like the wave which has been passing through Central America or, under other conditions, the maintenance of continuing enzootic foci constituting a permanent threat to the neighboring towns. When I say "neighboring towns" it is in a wider sense than formerly, due to the rapidity and extension of modern transportation facilities.

The identification and study of the vector or vectors in the region where yellow fever is progressing in Central America is an urgent need. Yellow fever is emerging from known conditions, or relatively known conditions, into the unknown, coming into new geographical areas where the arthropod fauna is different, and where the conditions in which that fauna operates are different. Studies on the mechanism of yellow fever north of Honduras should concentrate on the vector problem.

The question of the animal reservoir of yellow fever is also immediately important, since the yellow fever wave is advancing towards geographical areas where the primate population dwindles and disappears. The importance of primates, which dominate the yellow fever ecology in South, Central, and North America

as far as Mexico, gives way in Mexico to other possibilities, possibilities which are not entirely theoretical, since in Colombia and Brazil we have laboratory evidence of other animal families perfectly capable of being links in the animal-mosquito-animal cycle of yellow fever infection among the marsupials and rodents.

In Colombia we concluded that the marsupials simply had to be considered in conditions where yellow fever was permanent in the absence of an adequate monkey population. This hypothesis was strengthened later by the work of Bates and Roca García in Villavicencio where marsupials were infected by the bite of mosquitoes infected from monkeys, and monkeys in turn infected through the bite of mosquitoes infected from marsupials.

The marsupials have the ideal character of very abundant and frequent littering, which facilitates the rapid replacement of the population which has become immune, with great numbers of susceptible individuals. This is a factor of obvious importance in the maintainance of a local enzootic. We have attempted under adverse conditions in Nicaragua to study the local marsupials. We found that all the marsupial genera of Colombia are found in Central America. Monkey populations do not easily become a permanent reservoir in a limited area, because either they become immune or die. The infection dies out for lack of susceptible vertebrate hosts until their numbers are replaced by breeding, which requires years and possibly decades. The study of the marsupials in Central America cannot be ignored and should be a second point of any program of exhaustive study of yellow fever there.

Those two unknowns have to be studied before any predictions on the future of yellow fever further north on the continent can be made. Is this region just the scene of a passing wave which disappears with the immunization or destruction of susceptible animals, or can it be transformed into a permanent reservoir of yellow fever such as exists in Muzo and San Vicente Chucurí in Colombia?

I am perfectly sure that certain regions of Colombia, where yellow fever occurs year after year, cannot be explained on the basis of existing monkey populations. It may seem very simple to determine whether a region can become a permanent enzootic focus or not, but in practice it proves to be difficult. To study vectors and animal reservoirs requires time, trained staff and laboratory facilities in the field. Not everybody has the luck of Dr. Downs who had yellow fever knock at the door of his laboratory. As a rule, one gets news that yellow fever has penetrated into a jungle region some time after its arrival, and rushing to the field with monkeys and mice, as I did in Rio Coco and other regions of Nicaragua and Honduras, generally proves useless because of the difficulties of transportation. One generally arrives too late and must operate under very adverse conditions. Transmission experiments cannot be done satisfactorily except in a laboratory. Attempted transportation of virus and of infected mosquitoes under field conditions are often doomed to failure from the beginning.

The ideal is to know exactly where yellow fever is going to be and when, and be there with laboratory animals and needed equipment when the epizootic wave comes. Something like that happened in Trinidad where Dr. Downs was ready

for yellow fever when it appeared. Something like that did happen where a laboratory was organized by the Rockefeller Foundation in collaboration with the Colombian Government in Villavicencio, following the first observation of yellow fever there in 1934. The laboratory was built during a silent period, which lasted for two years more before the wave came back and found us ready for it. In Central America we won't have a recurring wave at frequent intervals as we have in Colombia, which makes for great difficulty in establishing a laboratory beforehand.

THE CHAIRMAN: Thank you very much, Dr. Boshell. Possibly we have adequately discussed most of the items under unfinished business. One point which has been omitted is the failure to make additional studies on combining smallpox vaccine with the 17D vaccine in the Americas. We cannot take the time today to discuss the relationship between the 17D vaccine and the French strain of vaccine, other than to state that after the experience in Costa Rica in 1951, where a number of fatal cases of encephalitis followed vaccination with the French strain, another outbreak of encephalitis was reported with over 80 cases and with 38 deaths in Nigeria in 1952. Consequently, the Pan American Sanitary Bureau is recommending for the Americas only the use of the 17D vaccine.

In listing the available working elements for studies on yellow fever in the Americas, the Tropical Virus Laboratory of Trinidad was not included. The three laboratories mentioned: the Oswaldo Cruz Institute in Brazil, the Carlos Finlay Institute in Bogotá and the Gorgas Memorial Laboratory in Panama, are all working with yellow fever virus in one form or another. However, at the present time, not one of these three laboratories is properly equipped with the staff needed to carry on adequate coordinated field and laboratory studies of jungle yellow fever areas. The isolated laboratory staff, destitute of epidemiologists, mammalogists and entomologists, is ill-fitted to contribute to the understanding of field problems. The laboratory alone is relatively sterile. The vaccine production of the laboratory in Rio de Janeiro, and that of the Carlos Finlay Institute in Bogotá today, are on a high level of both quality and quantity. None of these institutions is able to put a complete unit in the field to get material and properly to process it when it comes back to the laboratory.

Dr. Gast, the Director of the Carlos Finlay Laboratory, is here with us and can bear witness to the present situation. The Pan American Sanitary Bureau is collaborating with the Oswaldo Cruz Laboratory and with the Carlos Finlay Laboratory, and both of them have been furnishing vaccine free of direct cost to the American countries. This is a very important contribution of these laboratories to the work in other countries, in addition to the protection test and pathological services.

It is only fair to mention here that at the Yellow Fever meeting at Kampala in September, 1953, at which Dr. Boshell and Dr. Gast were both present, the proposal was made for an international committee to establish standards for the pathological diagnosis of yellow fever. Dr. Gast protested that these standards already existed, and spent that afternoon demonstrating the application of these

standards to several series of known and unknown slides of yellow fever and suspect yellow fever cases from different parts of Africa and America. After this demonstration there was no further suggestion for an international committee on standards for the diagnosis of yellow fever.

What would you like to say, Dr. Gast, of the future possibilities of work at the Carlos Finlay Laboratory?

DR. GAST GALVIS: The Carlos Finlay Institute is at the present time engaged in the production of yellow fever vaccine and has a stock approximately of one million doses ready for use. The vaccine is produced in accordance with the UNRRA regulations and the protocols regularly sent to the Pan American Sanitary Bureau.

In the present year we have sent more than one hundred million doses to fourteen countries in America. The pathological laboratories have assured continuous service in the diagnoses of liver pathology. The mouse colony is now sufficient to take care of serum examination up to two hundred serums monthly. I wish to state that the director and the staff of the Carlos Finlay Institute will always be glad to fulfill their international commitments.

THE CHAIRMAN: Thank you, Dr. Gast. Are there any points that I have not covered regarding the availability of working elements? Are there other laboratory facilities available, other resources available, beyond those I have mentioned? The Gorgas Laboratory and the Pan American Sanitary Bureau are working together on a combined study of the yellow fever situation in Central America.

COLONEL ELTON: I should like to call attention to some work on the pathology of yellow fever in mild and "typical" cases, not "classical" cases, since the latter are not hard to diagnose clinically. A number of liver biopsies were made at San Juan de Dios Hospital in San José, Costa Rica, on patients who did not die. Dr. Marcial Fallas Díaz has told me the results were very informative, and I think efforts should be made to assist Dr. Marcial Fallas Díaz and Dr. Rodolfo Céspedes Fonseca in getting that work published. In the December, 1954, issue of the *Revista de Biología Tropical* (San José, Costa Rica), Guido Miranda has just published a very interesting paper on liver biopsy in which he includes several yellow fever cases during the acute stage and during convalescence.

THE CHAIRMAN: Thank you, Colonel Elton. I had not known of this work on biopsy material. It is important, whenever the opportunity presents itself, to get continuing studies on clinical cases. The hospital in San José is the only hospital which has had a series of cases for adequate study since the 1928-29 epidemic of Rio de Janeiro.

Both viscerotomy and routine animal studies are becoming more and more important for the location of yellow fever as a disease. As vaccination has been so widespread, with something over 20 million people vaccinated in South America, the use of the protection test is going to be of less and less value.

For an understanding of what is happening in yellow fever, routine long-term studies of both vectors and animal hosts must be undertaken.

There is one important piece of work which has not been referred to today and which I am asking Dr. Trapido to tell us about. I am referring to the five-year study which has been made on *Haemagogus spegazzinii* densities in Pacora, where the first Panamanian cases were diagnosed in 1948.

DR. TRAPIDO: One of the problems which struck us in Panama has been this. If one takes at face value what evidence there is, then one accepts the results of the surveys done in the thirties and early forties by Kumm and Crawford and Bustamante and those reported by Sawyer, in Central America, Mexico and Panama. These were all to the effect that no persons born subsequent to 1925 showed evidence of antibodies, and it was concluded that sylvan yellow fever was not endemic in Central America, Mexico or western Panama. The severe manifestations in the monkey population and the sequence of events of the past several years would tend to confirm the fact that this was indeed a nonimmune population of monkeys. Accepting these surveys at face value, we set out in 1950—that is, the year after the cases occurred at Pacora east of the Canal Zone—to show why the virus would not get west of the Canal and into Central America. We expected to be able to show that there was a zoogeographic reason; i.e., that the composition of the mosquito fauna of the forest canopy of western Panama was going to be different from that of eastern Panama, adjacent to South America. Well, it was not, and we reported the occurrence of *spegazzinii falco* in Costa Rica several months before the first cases of yellow fever showed up there.

We know from the Kumm and Crawford survey, however, that a nine-year old child from just east of Panama City had shown protection in 1941, indicating that in the thirties yellow fever had approached as close as thirty miles to the Canal and yet nothing had happened to the west. Why did the virus get across the Canal in 1950 when it had failed to do so in the thirties? Why did it pass the narrow isthmus on this occasion when we have reason to believe the virus had approached the area only a decade and a half previously and failed to cross?

We set out to do a year-long study of the forest canopy mosquito fauna and, as it worked out, it has been possible to keep this up over a period of years with the cooperation of the Army Preventive Medicine Unit, which is stationed in the Canal Zone and has necessary personnel and transportation. We have cooperatively been able to accumulate data covering five years.

From these data we can suggest an explanation; it happens that there are very large long-term cyclic fluctuations in the abundance of canopy mosquitoes. That is, *spegazzinii falco*, in a particular month of a particular year, may have a density much greater or much less than in the corresponding month of another year. We would suggest, therefore, that the central part of the Isthmus of Panama is critical for the reason that the Pacific slope, as Dr. Boshell mentioned earlier, is covered by deciduous tropical forest. This is associated with a severe dry season.

The Canal is where it is because there is a gap in the mountain system. That

gap permits the spilling of moisture from northeasterly trade winds onto the Pacific side. The rainfall in the vicinity of Panama City at the Pacific entrance to the Canal is about twice as high as it is twenty or thirty miles up or down the coast in the lee of the mountains, and this area is in fact a critical transition zone with regard to forest type. The forest is intermediate here between true tropical rain forest, which requires no month with less than five inches of rainfall, and deciduous tropical forest, which is the product of a severe dry season. In 1949 and 1950 there may have been the coincidence of two cycles, one of which is the cycle of the approach of the virus from the east, arriving at this critical area during a peak cycle for the *Haemagogus* as a consequence of particularly favorable rainfall. It would thus have been the chance intermeshing of the two cycles, if you will, the virus on the one hand and a peak mosquito population on the other, which permitted the virus to bridge this marginal area.

On the Atlantic side of western Panama there is excellent tropical rain-forest, with the ecological conditions perfectly satisfactory for maintaining the virus from there on. This might be cited as an example of the necessity for long-term continuous studies.

THE CHAIRMAN: Thank you, Dr. Trapido. That is exactly the point I wanted, namely, the need for long-term studies. Dr. Boshell, discussing the outbreak in Nicaragua, gave us the fact that the yellow fever virus had remained in the Rivas Peninsula through a very severe dry period, but failed to indicate that after the following dry period the virus had apparently died out. Between 1934 and 1940, yellow fever virus came into southern Brazil and spread throughout all of the forest areas that might be infected. Ten years later, the virus started again in exactly the same area, and the 1944 and 1945 outbreaks suggested the beginning of a second seven-year sweep. But the epizootic came to the river between Minas Gerais and São Paulo at the end of 1945 and failed to progress beyond this boundary. Five years later, 1950, another epizootic began, and this time crossed the river, went into São Paulo and Parana and, during 1952 and 1953, suggested once more a sweep through all of southern Brazil as in the 1930's. At the end of 1953, the epizootic suddenly stopped and a large part of the area covered in the first epidemic in the 1930's has now escaped two later invasions of the virus.

The point to be made is that should the virus stop in Honduras at the present time and not go on into Guatemala and Mexico, there would be no guarantee that the next wave of virus which may come through Central America might not penetrate to Mexico, since so much may depend on climatic factors which vary from year to year.

Many points have been discussed today which are worthy of considerable additional study. The emphasis this morning was on the need for studying yellow fever on a long-term basis. Dr. Theiler has suggested this is only part of the problem, and that we need to consider the entire group of virus diseases on the basis of long-term studies, both epidemiological and laboratory. And if we accept the need for long-term observations we should prepare to establish programs for

long-term studies. There should be set up in certain areas units which are prepared to follow yellow fever wherever it leads them over a considerable period of time.

In looking at the results of the work of the Rockefeller Foundation on yellow fever, we often tend to foreshorten our view of the period of the Foundation's work. The Foundation first worked on the problem of yellow fever in 1915, and as we look back on it we realize today that little definite progress had been registered during the first ten to twelve years of its activities. The range of yellow fever as an *aegypti*-transmitted disease had been reduced, but there was no increase in fundamental knowledge of the problem.

The great contribution of the Rockefeller Foundation has been possible largely because the Foundation started out to work on the problem of yellow fever and rather stuck its neck out with the declaration that it was committed to the eradication of yellow fever in the Americas. Once committed to yellow fever eradication, the Foundation continued to work with it and dedicate staff to it over a period of thirty-five years, during which some twelve or thirteen million dollars were spent. Many developments were possible only because the staff was a continuous one, not always the same individuals, but when one person dropped out for any particular reason somebody else stepped in and took up the work.

There is no doubt of the tremendous value of the Tropical Virus Laboratory, not only to the Government of Trinidad but to surrounding countries. In spite of the comments on the influence of dengue in keeping the epidemic down in Port-of-Spain, I am inclined to believe that, had the laboratory not been there and identified this infection at the time it did, the relatively high financial loss to Trinidad of this invasion would have been multiplied several times over, not only for Trinidad but probably for other areas in the region.

The program for future coordinated studies needs considerable discussion, and I suggest that a group of us meet tomorrow morning to discuss plans for the immediate future, taking advantage of the fact that Dr. Johnson is here with Dr. Trapido from the Gorgas Institute, Dr. Boshell and Dr. Gast are here from Colombia, Dr. Downs is here from Trinidad, and the Pan American Sanitary Bureau staff responsible for our activities are all here.

DR. SPENCER: I should like to take the time here—I realize this is rather an anticlimax to say it this way—to express my deep satisfaction at being able to listen to the remarks here and participate in a small way, and to say I think from what has gone on that perhaps we, each of us, have gained a concept of the magnitude of this thing which we are discussing. I would rather hope that in the future, as we view it and approach it, none of us will have a tendency to talk down or minimize any of the things that come out of researches that are to come in their application to the problem in general. Speaking for myself, and I think I voice the feeling of others, it has certainly been a stimulating, well-conceived beginning to probably more meetings to come, and certainly what has come out of it will be useful to one and all.

THE CHAIRMAN: Thank you, Dr. Spencer.

(Wednesday, December 22, A.M.)

THE CHAIRMAN: We discussed yesterday just briefly some of the elements that are available for the study of yellow fever and the production of vaccine, referring especially to the Oswaldo Cruz Institute in Brazil, the Carlos Finlay Institute in Bogotá, and the Gorgas Memorial Laboratory in Panama. We have also, of course, the Tropical Virus Laboratory in Trinidad which, with its program for the study of viruses not only in Trinidad but in the northern part of South America will, from time to time, be coming forward with information on yellow fever. We have also had an initial inquiry from the authorities in Venezuela regarding the possibility of collaboration in the organization of a virus laboratory in Caracas. The proposal for this laboratory has been, at least in part, stimulated by the recent situation with regard to yellow fever.

The situation for many years was that the Rockefeller Foundation concentrated its studies on yellow fever in South America in two laboratories: one at Bogotá in the northwest corner, the other in Rio de Janeiro, practically at the extreme southeast corner of the South American continent. In addition, the Foundation had its central base laboratory for the study of yellow fever in New York City. So there were three laboratories operating for the continent. It seemed best at the time, due to the cost of maintaining laboratory colonies of susceptible animals and to the specialized nature of the work, to concentrate the work in a limited number of laboratories. This same attitude was assumed by the Pan American Sanitary Bureau when, in 1948, it discouraged the Argentine Government from opening a yellow fever laboratory in Buenos Aires.

It is important that the diagnosis of critical cases—the diagnosis on livers at least—be made by pathologists thoroughly versed in such examinations. But I am wondering if, with the development of similar procedures for other viruses, we may not be at a point where, in spite of the cost of such operations, we should favor the development of more laboratories working with isolation of virus, identification of virus, protection tests, and so forth. This is just one of the items that come up for consideration.

We have at the present time no laboratories in the United States which are available for routine protection tests and for work in yellow fever. Dr. Theiler's laboratory does so sometimes as a matter of accommodation, but it isn't set up as it was ten or fifteen years ago for the specific purpose of handling large masses of material from the field. As most of you know, the manufacture of vaccine at the laboratory of the United States Public Health Service in Hamilton, Montana, has been turned over to commercial interests.

We should discuss the problem of coordinating the activities of the existing laboratories. What can be done in developing the work of those institutions and, specifically, the problem of planning studies in Central America; the possible extension of those studies to determine what should be done; and also the possibility of getting some work done in connection with the present outbreak in Venezuela. From Venezuela we have had a specific request for the study of mammals in the infected areas. We have not yet been able to make arrangements for a mammalogist to go into the area. Should a mammalogist be sent into an

area on a temporary appointment of a few months? How long should his appointment be? Or should somebody with over-all experience, such as Dr. Boshell, be first sent to look things over and plan long-term studies in which the mammalogist would be but a part of a team?

Another general over-all problem, which was not touched on yesterday, is the possibility of altering the size, shape and direction of such epizootic waves as may come under observation. As long ago as 1937 or 1938 the proposal was made to use airplanes and insecticides to make certain forests in Brazil safe for the workers who had to go into those particular forests. Nothing was done about it at the time. We have more recently had a suggestion from Colonel Elton regarding the possibility of blocking out an area with insecticides and making it impossible for yellow fever to proceed through that area, from Nicaragua through Honduras and into Guatemala. The proposal was made on the assumption that the virus would move through a particular area and that the date of arrival of the virus at that point would be known. The estimated costs of the project were beyond the financial possibilities of any of the agencies which might have considered undertaking it. But I am not convinced that we have any methods at the moment that are available for general application throughout the epizootic or enzootic areas. On my last visit to Trinidad, however, the Director of Medical Services came up with the proposal to undertake the eradication of the monkey population of Trinidad. I have no idea as to the feasibility of this proposal. Even though the monkey population might be eradicated, the eradication of *Aedes aegypti* in Trinidad is still necessary to prevent the spread of the mosquito to areas in other countries that had been cleaned, and in order to protect Trinidad itself against anyone with yellow fever who might come over from the nearby mainland of Venezuela. I am waiting for comments.

DR. TRAPIDO: On the question of possibly controlling *Haemagogus spegazzinii* in an area, I think there are two points on which we might contribute information. The first is that no one has ever really found the breeding place of this mosquito. It is a tree-hole breeder, but in all of our work in Panama, in an area where the adults were not particularly common but where there were quite frequent collections, we failed over a two-year period to find larvae in natural tree holes except once. By setting out over a two-year period to collect larvae from some 100 bamboos in an area where the adults were present, we collected on three occasions a total of four larvae from such bamboos up in the treetops.

The second is with regard to susceptibility to DDT. There was an interesting side observation made in setting up a field laboratory at one of our stations in Nicaragua in 1953. The Department of Public Health kindly made available to us a house which turned out to be a place where the DDT spray crews for malaria had made their headquarters. This being a wholly new area for us, we wished to use the place through which to route material to check the species determinations of forest mosquitoes we would be getting. It seemed quite hopeless; the walls were all streaked with DDT. However, we had a thin cement floor laid over the dirt floor and the walls scrubbed down and whitewashed. When we attempted to

rear larvae, *Anopheles* and *Culex* died but the *Haemagogus* larvae came through quite well.

THE CHAIRMAN: This again was the larval form?

DR. TRAPIDO: This was the larval form. I just brought this up to call attention to the fact that there is no information on DDT susceptibility of *Haemagogus* as there is for *Anopheles* and various other mosquitoes. I would point out that from this little incident I would judge that they would be less susceptible than *Anopheles* to DDT. This is a casual observation, but if *Haemagogus* control is contemplated I would suggest that there are some very simple laboratory experiments that should be performed first.

THE CHAIRMAN: Any other comments?

DR. DOWNS: In connection with the contemplated program of monkey eradication in Trinidad, this suggestion was brought forward when it was realized that the monkey areas of the island are far from including the entire island of Trinidad, which is small in itself, and that an estimated census might total no more than three to five thousand monkeys. That was about the figure I thought might be the total monkey population of the island.

The island is combed by hunters. There are no spots which can be called truly inaccessible. A great many of these hunters are very anxious to pick up money, and I was certain myself that monkey eradication could be achieved, quite rapidly, simply by the bounty method, and at a total cost not exceeding fifteen or twenty thousand British West Indian dollars, which is not a great deal of money for a program of such a nature. The local natural history societies and animal lovers, most of whom had never seen a monkey and didn't know there were any in Trinidad, had a great deal to say about this. It was drowned in a wail of tears, and I don't think it will be considered.

I am not going to argue whether or not one should contemplate eradicating the species. Certainly, at any future date they could be introduced by bringing a few over from Venezuela to repopulate the island. The question was raised as to whether we could guarantee that with the eradication of the monkeys we would really be at the nubbin of the sylvan yellow fever problem. No, we couldn't guarantee it, but for my money it would be a beautiful experiment. If the monkeys were eradicated and some form of jungle yellow fever continued, we would be that much closer to the crux of a very vital problem. Anyway, as I said, I don't see much future in the monkey eradication.

DR. SMADEL: I should like to make a few comments about the diagnostic work. One of the reasons why there is no work being done on the diagnosis of yellow fever in the United States, other than that of the Rockefeller Foundation, is because there has been no need for it. As long as the Rockefeller laboratories do it, everyone is entirely satisfied. In the absence of a laboratory which is willing to provide such facilities, it seems to me that some place in the United States there should be one capable of performing the usual procedures in a satisfactory manner. It is always well to suggest that somebody else "bell the cat." We do have

the virus laboratory in Montgomery, Alabama, that is part of the Public Health Service. It is their appointed task to do virus diagnostic work for the Departments of Health and of the State for physicians in the United States. It seems that a small extension of their normal duties, which already include diagnosis of a number of the virus agents, could be made so that that laboratory would be capable of providing those diagnostic facilities which are necessary as far as the United States is concerned.

In the Latin American areas, I would think that in general it would be feasible to organize several virus laboratories on the basis of the diagnosis of yellow fever. Certainly, in organizing virus laboratories in many areas of the United States in the last few years we have, from time to time, picked on one or another disease as the basis for starting the laboratory. Sometimes it has been influenza and sometimes poliomyelitis. At any rate, if influenza and poliomyelitis are considered adequate reasons for increasing our laboratory facilities in the United States, then yellow fever should be an adequate reason in the areas where that disease occurs.

The point that the Chairman brought up yesterday about the neutralization test is a problem that we face constantly in virus diagnostic work; the test has been a valuable diagnostic tool for many years but is becoming less so because of the prevalence of vaccination and the resultant neutralizing antibodies. Complement fixation tests for the diagnosis of yellow fever would, it seems to me, be worth reconsidering. In general, these antibodies disappear within a fairly short time; hence their presence might indicate recent infection.

The problem that bothers me most is how the base laboratory facilities are going to be provided for yellow fever, now that the Rockefeller Foundation is in the process of withdrawing from fundamental work on yellow fever virus. The laboratory that Dr. Downs has in Trinidad, while I have not seen it, would seem to me, from talking to him and from listening to his very excellent discussion yesterday, to be a good field laboratory. Such a laboratory can function beautifully if supported by a base laboratory that can do the technical things that are either too difficult, too time consuming or, for some other reason, that cannot be done in the field laboratories. Such base support has been provided by the Rockefeller Foundation, and probably will continue to be for some time, but when it stops who will provide this service in the United States? I can see no way to get this kind of essential research support from government agencies. If it is difficult to get money for yellow fever for firefighting, it will probably be impossible to get it for long-term research on this subject.

DR. BOSHELL: To come back to monkey eradication, I personally think it is perfectly feasible. We have here a very vulnerable animal species with a slow rate of multiplication, and that makes it eminently easy to wipe out. I have seen other animal families eradicated in a short time, such as wild pigs. If the local hunters could be interested in shooting monkeys for a price, I have no doubt that the monkey population could be exterminated.

As for the mosquito destruction, I am sure it is feasible in a limited area by

using a very intense spray, but unless it is done on a very large scale the mosquito free zone would very soon be reinvaded by mosquitoes, and you have to stop somewhere. It can't be done over a whole jungle, starting in Mexico and ending in Argentina, and unless it is on such a scale the effort of stopping it and of cleaning an area would be immediately lost by the reinvasion from surrounding areas. It might be possible in a place like Trinidad, which is limited and isolated, but on the mainland or in Central America I cannot see that any local, limited destruction would have permanent effects.

DR. TRAPIDO: I should perhaps add certain information we have. When the question of mosquito destruction was spoken of before, I assumed that what was meant was not eradication, but just for some brief period the elimination of the mosquitoes from some particular area, with the idea of creating a barrier. If one were speaking of actually eliminating these mosquitoes on any permanent basis, it should be pointed out that in the course of experiments we have done with *Haemagogus* we have found that the eggs of *spegazzinii* do not hatch until the third flooding, and continue hatching through the tenth flooding, after eight months. Let us assume, for the sake of discussion, one were airplane spraying the forest and let us also grant for the purpose of discussion that every adult in that forest was killed (this last is a very liberal assumption). Granting that one succeeded, it would be necessary to continue killing the adults produced from existing eggs wherever the breeding places are (which we don't know) for a minimum of eight months; and I would venture to predict that eggs will continue to hatch for a year.

DR. DOWNS: The question of plane spraying in the Island of Trinidad was brought up by some of the government people early in the Trinidad operation, and we briefly reviewed the approximate cost of plane spraying about a thousand square miles that could be considered to be involved in the affected zone. Anyone who has had any experience at all with airplane spraying knows what the cost would be of spraying adequately a thousand square miles once, and it immediately puts such a method in the realm of complete impossibility.

DR. BOSHELL: In my experience, it costs \$25 a hectare.

THE CHAIRMAN: The question has been raised as to what can be done to alter the movement of an epizootic wave of yellow fever either directly or by blocking it. The proposal made by Colonel Elton a couple of years ago was mentioned, without details. The possibility of monkey eradication in Trinidad was also mentioned.

From the experience with *aegypti* eradication we have learned that, if eradication is going to be feasible, it must be an ever-expanding program. The main difficulty with eradication is the problem of reinfestation from the periphery. This is oftentimes raised as an objection to programs of eradication. I prefer to look at it the other way. I prefer to consider this difficulty of reinfestation from the periphery as one of the blessings of the program of eradication. There are thousands and thousands of smaller communities in Brazil today which are entirely

free from the threat of urban yellow fever simply because they have been cleaned of *aegypti* for the purpose of preventing reinfestation from them of the larger centers in which the authorities were interested. We have today a number of countries either free of *aegypti* or very close to it, and free of all possible threat of urban yellow fever, because Brazil, after having cleaned up its frontiers, was getting reinfested from other countries. Whenever we begin to talk about eradication we should either specify that we mean an expanding program or local eradication such as has been mentioned in Trinidad, which is an island where it has been assumed that the monkeys would not be reintroduced. In the other areas Dr. Boshell has mentioned in South America as possible sites of eradication I think we would have to consider monkey eradication as an expanding program, if permanent benefits are to come from it.

COLONEL ELTON: As far as Trinidad is concerned, I would not be surprised if the story has ended there as far as jungle yellow fever is concerned. I note that the span of activity for the last epidemic in the southern end of the island was August to October, and that there have been no new cases since then. This is not conclusive, but the history of the pattern of epidemic episodes has shown them to be self-limited in a given locality with a duration of about two months whenever it has broken out in Central America.

I cannot comment on the possible seeding of *Aedes aegypti* in the urban centers of Trinidad, but I suspect that the jungle phase is about over. This is the saving feature of the jungle epidemiology so far as quarantines are concerned. I doubt that there has been any financial loss to the Central American countries in spite of the open publicity they have had in the scientific literature, for there has been no panic that might be induced by an urban component and the countries are cleared by the waves on schedule. Yesterday, Mr. Calderwood spoke of "risk areas", which I would definite as "zones of activity". Behind these zones there seems to be little to be concerned about.

This is perhaps contrary to the picture in Brazil, where there are many stabilized enzootic areas, for in Central America there have as yet been no stabilized enzootic areas left in the wake of the wave, or any endemic activity as far as man is concerned. This factor enables countries to clear themselves from quarantine as soon as a measurable period of time has passed, after the activity has subsided. There are, however, two phases of activity: the epizootic and the epidemic. Sometimes these two phases occur simultaneously, and sometimes the epizootic phase is a precursor of the epidemic phase, and may possibly remain active for some reason after the epidemic phase has subsided. No studies have yet been made of this continuing mortality in monkeys when it has been noted. One might surmise that two types of mosquitoes are involved in this, a species transmitting originally only to monkeys on the one hand, and another later that bring the virus down to man. Only one species may be involved, but it is a curious phenomenon and difficult to explain.

I believe a great deal of work needs to be done from the over-all biologic point of view, as John Bugher mentioned yesterday. Max Theiler's talk was also very

interesting with respect to cross immunity and indicates the need for reliability of concepts before broad conclusions are arrived at.

To me the most important thing of all is to find out how to avoid acquiring yellow fever biologically. If I were a farmer and no vaccine were available, that is what I would want to know. Suppose a person could not be vaccinated; what could he do to avoid being infected? There are measures that can be taken, as is true also with malaria, without recourse to vaccines or drugs. If one knows the bionomics of the specific vector, one can get along pretty well with self-protection and by regulating one's activities to conform with safe periods of the day or night or safe localities, and be quite successful in avoiding infection. This can be done with reference to malaria by the proper use of simple protective clothing and equipment and training. But one must understand the behavior of the vector.

The fact that we have an effective vaccine for yellow fever tends to inhibit activity in research and investigation. We should find out what is really going on in nature; instead, we smugly assume that we can control the disease and protect our civilization with vaccine or by eradicating the urban vector, *Aedes aegypti*, which is of little interest to the farmer. Civilization is protected by a man-made roof, and that roof must be maintained in constant repair. It may not remain intact indefinitely, and we should endeavor to learn how we might survive when it leaks, for we might be faced with such a problem in the not too distant future.

As for airplane spraying of forest mosquitoes or monkey eradication in man-made barrier zones, I am afraid that is no longer possible since it is now too late to do anything about La Ceiba. There is no region anywhere on the map where such a procedure would now be feasible, for the number of square miles of forest that would be involved is too great. The only place worth consideration is where the mountains approach the shore line between Vera Cruz and Tampico in Mexico, which might be attempted about 1958 if the wave maintains its past pattern of behavior. Although there is no certainty that this pattern will continue, it should be assumed nothing has yet been observed that might change it. The death of the wave could also take place. It will probably be dormant until the spring of 1955, for it has undergone many periods of quiescence since 1948. We must play for the breaks and seek all we can learn about the natural history of this phenomenon.

Dr. Soper mentioned yesterday the use of mammalogists and other scientists who might have an interest in the material available now in this great laboratory of the field. As the wave moves on through northern Guatemala and down the Usumacinta River Valley to the Gulf Coast of Mexico there will be many opportunities for study. I do not think we are going to be very successful in vaccinating the people because of the vast area and the dispersion of habitations. Not that vaccination is not effective, for it is very effective, but it is very difficult to get to the people who need it most. It is one thing to have people report to a laboratory approved by the World Health Organization, where a properly embossed certificate of vaccination can be issued. It is an entirely different matter to go out into the countryside and find people to vaccinate, or even to convince them that they need vaccination.

When the dry season sets in and activity subsides is the important time to find out what is really going on, just as in any phase of preventive medicine. When certain diseases are quiescent we should try to find out why they are quiescent and seek to determine when they may return. Cycles of this sort are not uncommon. We are prone to accept much credit for control when all is well, as if we were wholly responsible for the period of well-being. Yet that is when we should be on our guard and fully alert. When jungle yellow fever undergoes a dormant phase, we should not just go home and wait for it to flare up again further on.

I do not know much about the rains of Guatemala. I do know that jungle yellow fever is a year-round disease, sporadic during dry season, minimal during the first two months of the rainy season, and then epidemic for two to four months. That has been its pattern so far, especially in Costa Rica as determined by the observations of Arturo Romero and Alfonso Trejos. That is why I would guess that northern Guatemala will be involved about next July, probably in the vicinity of Los Amates in the Department of Izabal, where Gaitán reported a local outbreak of jungle yellow fever in 1920.

I have a map, with some explanatory notes, which I shall use to illustrate my point (Map 9). This projection, based upon the premise that the future movement of the wave of jungle yellow fever will continue to follow the pattern exhibited since 1948 at an over-all velocity of 13 miles per month between epidemic centers, is presented as a working hypothesis and tentative guide for future planning.

The last discernible epidemic center preceding the quiescence during the current dry season occurred in the vicinity of La Ceiba, Honduras, where two patients were clinically diagnosed as ill with yellow fever in August, 1954. In September, 1954, a fatality from the disease occurred in a hospital in San Pedro Sula, west of La Ceiba in the Ulúa Valley, but the circumstances surrounding this patient do not support the likelihood of contraction of the infection in or near San Pedro Sula. Since the time table cannot be based on the progress of the epizootic phase, the positive monkey livers acquired at La Masica in September would indicate only that the epidemic phase was probably east of that point at the time.

Los Amates in the Motagua Valley of the Department of Izabal, Guatemala, is selected as the center of spread because it is about 160 miles west of La Ceiba and was reported by Gaitán to have been the site of an outbreak of jungle yellow fever in 1920. For these reasons, and because of the tendency of epidemics to occur in the latter part of July and run through August and September, the next epidemic episode could develop in this vicinity in July, 1955. If this happens, then the projection bands will be properly oriented. Epizootic episodes may occur before July, and by July the epizootic precursor may be well on its way toward the headwaters of the Usumacinta River to the west through the Departments of Alta Verapaz and Baja Verapaz.

No longer canalized by the cordillera and the Gulf of Honduras, the wave may be expected to undergo a balloon-like expansion into the Peninsula of Yucatan ("12 months after Amates" band, Map 9) but the main axis should follow the

Valley of the Usumacinta to the northwest, entering the State of Chiapas in Mexico, involving the Department of Peten in Guatemala, and reaching Belize in British Honduras by July, 1956.

Early in 1957 the Gulf Coast of the State of Campeche in Mexico will probably become an epizootic region while the main axis turns westward in the State of Tabasco. Close surveillance of coastal shipping will be necessary to prevent urbanization of the virus to the Gulf settlements of Mexico and the United States wherever *Aedes aegypti* density exceeds the transmission level. How far the expansion northward into Yucatan will extend ("24 months after Amates" band, Map 9) remains to be determined.

The break in the mountain ranges in the Isthmus of Tehuantepec may slow the wave, but may also give rise to a daughter wave moving southward into eastern Oaxaca on the Pacific coast. The main axis ("36 months after Amates" band, Map 9) however, should continue westward through the State of Vera Cruz and be approaching the Papaloapan Valley by July or August, 1958.

The "48 months after Amates" band, Map 9, shows the point where the proximity of the continental mountain mass to the shore line again provides a coastal terrain funnel, through which the main axis of the wave must pass to move northward through the State of Vera Cruz toward Tampico and the Panuco Valley. The possibility of establishing a man-made barrier zone here, similar to that formerly proposed for the region of La Geiba in northern Honduras, merits consideration. Such a project should be in readiness not later than January, 1959. The wave will probably die spontaneously in the southern part of the State of Tamaulipas to the north of the Panuco Valley.

Much work needs to be done, and to me the cardinal issue is "what would I do if no vaccine was available?" I should like to be able to answer that question better than I am now able to do.

THE CHAIRMAN: I would point out that we faced that problem very definitely for several years. The first observations of jungle yellow fever were in 1932, and it was not until 1937 that mass vaccination techniques were available for protecting the exposed populations. About the only thing we were able to do was to advise people to stay out of the forests. This to many people, of course, meant the loss of their livelihood. They wanted to keep on eating, so they went into the forests. In the agricultural areas the forest is cut down at a certain time of the year in accord with a planting cycle, and it often happened that the clearing period was just the time of the year when yellow fever was most dangerous.

The picture in Central America of the moving wave is not different from that seen in southern Brazil on three different occasions. Let us consider Map 5, "Intervals between appearance of yellow fever in specific areas". In the shaded area of southeast Brazil, during the years 1934 to 1940, an epizootic wave spread from area to area, with the areas infected one year not showing in general any cases the following year. During each year there was an interval of about six months when no cases were found, followed by the summer season with yellow fever in areas not infected the previous summer. This widespread moving wave of infec-

tion observed between 1934 and 1940 was followed by lesser waves, otherwise similar, from 1944 to 1948, and again from 1950 to 1953.

If Brazil were cut up into, say, thirty or forty different independent countries, a number of these countries would lie outside any endemic area and be subject only to periodic epidemics. Likewise, the entire northeast of Brazil, in which yellow fever was previously endemic, could be declared permanently free of all threat of yellow fever. Since 1934 no yellow fever has occurred in this entire area. Then a single small state, Ilheus, could be outlined where yellow fever virus is always present. And all these could be established and classified without entering on the picture of yellow fever in the great Amazon Valley.

A point which might be made is that Costa Rica and Nicaragua, so recently infected with yellow fever but now well behind the moving front of the epizootic, are probably among the safest places in the world, insofar as danger from yellow fever is concerned.

DR. SCRUGGS: Dr. Soper, what is the per cent reduction in the animal life in the areas through which the infection has moved?

THE CHAIRMAN: There is a great difference according to the species of monkey present. I am going to ask Dr. Boshell to give us an estimate on the percentages of certain species of monkey in Central America, but in southern Brazil the predominant genus of monkey is *Cebus*, which very rarely dies as a result of yellow fever. Consequently, this genus maintains its breeding stock and after a few years there is once more a relatively high number of susceptible animals. Dr. Boshell.

DR. BOSHELL: You took the words out of my mouth. I was just going to point out a great difference between Brazil and Central America.

THE CHAIRMAN: And Colombia.

DR. BOSHELL: The predominant monkey in Brazil more than in Colombia is the *Cebus*, which survives yellow fever and builds up a new susceptible population relatively fast. In Central America the *Cebus* is relatively scarce. You see very few of them, in very small bunches. I don't know why. Besides, it is another species, *Cebus capuchinus*.

Dr. Downs mentioned that two-thirds of the population of monkeys was wiped out in Trinidad. It is my impression that in certain regions of Nicaragua, which I surveyed for several months, the extermination is practically total. On the Rio Grande and Matagalpa and on the Rio Coco, which were known to be teeming with monkeys, you can today travel by canoe or by foot for days and days without seeing a single monkey or hearing one. Not seeing monkeys is not as significant as not hearing them. This refers to the *Alouatta*, whose braying is a feature of the environment. You listen to them two or three times in the day. Farmers in Nicaragua often say "Those monkeys are our clock. We know what time it is. We know when it is going to rain, because we listen to the *Alouattas*." In those regions, in the same places, I stayed for days and covered a great amount of ground, and I never heard a single *Alouatta*. I found a few bunches of *Cebus*, the only survivors of primate life, in extensive zones. So we have had entirely different conditions than in Brazil where the intervals between successive epi-

zootic waves are relatively short. In Central America we have assumptions, we have hearsay, we have references of old people stating that 25 or 30 years ago the monkeys died, but nothing within that span. We attribute this to the fact that the predominant monkey population is virtually exterminated by each epizootic wave of yellow fever.

THE CHAIRMAN: This illustrates again the necessity of knowing the area about which we are talking. There are areas in Brazil in which similar things have occurred. In the period before we knew about the jungle yellow fever but after the susceptibility of monkeys in the laboratory was known, a doctor from Rio Grande do Sul, in the extreme southern part of Brazil where yellow fever had never been reported and which was discounted completely as a yellow fever area, told me that on his father's *fazenda* there were a great many howler monkeys when he was a boy. An epidemic had come through about twenty years before and had killed off practically all of the howlers, and for a long time they didn't hear the howlers howl. But he had recently been there, and again it was as it had been when he was a boy. They were hearing lots of howler monkeys again. Some years later, in 1939, we had an opportunity to obtain proof of the invasion of Rio Grande do Sul by jungle yellow fever, not by way of Brazil itself but through Paraguay and Argentina.

If we look at Map 5, "Intervals between appearance of yellow fever in specific areas," you will notice that we have not attempted on that map to put in any of the multiple outbreaks and occurrences of yellow fever over the years, with the exception of two specific groups: the areas where yellow fever has reappeared after a known absence of many years, and the three starred areas where there is definite proof of the more or less continuous presence of yellow fever virus for a number of years. These starred areas represent widely different conditions. The Ilheus area, on the east coast of Brazil, is a small area of heavy rainfall embracing two or three counties where the principal industry is the planting of cacao. In this area there is a heavy population of primates, with some monkeys and a considerable population of the smaller marmosets which are susceptible to yellow fever and which have a relatively short reproduction period.

The first intimation we had that yellow fever might be in the Ilheus area came in 1931, before jungle yellow fever had been identified. A Swiss cacao buyer who had gone hunting a few days previously, came up to Salvador with a typical case of yellow fever. Investigation at the time failed to show any urban outbreak in the town of Ilheus itself. Later, other cases occurred with considerable regularity until the population was thoroughly vaccinated. Ilheus is interesting in that it was the first area in the Americas from which yellow fever virus was isolated in animals, and because this isolation occurred at a time when there were no known human cases in the area. Briefly, the mechanism of the maintenance of the virus in this area is a rather constant supply of mosquitoes under rain-forest conditions, together with a heavy and rapidly renewable population of susceptible animals.

Muzo and San Vicente de Chucuri, Colombia, on the other hand—particu-

larly Muzo—have entirely different conditions, in that the primate fauna is very reduced. There are practically no monkeys in the area, with the exception of small bands of night monkeys. I am not going to take the time to discuss this more than to say that Dr. Boshell and others who have worked in this area are all convinced that there are not enough primates in Muzo to maintain the virus.

In the many years of investigation of yellow fever, the only cycle of infection found is composed of a short period of infectivity in the primate host followed by the production of immunity, alternating with the infection of the mosquito throughout its lifetime, with no transfer of the virus from one generation to the next. But there are very definite differences between the permanently infected areas in Colombia and in Brazil, and there must be factors yet unknown. Yellow fever virus is constantly present in the vast Amazon Valley, but whether essentially static or periodic has never been adequately determined. There are many points in the Amazon Valley where yellow fever does appear but where it does not maintain itself permanently in a small area.

There is, of course, the possibility—there is no evidence for it, yet there is the possibility—which must be taken into consideration, of areas in Central America or in Guatemala or in Mexico which will be able to maintain the virus over fairly long periods of time if the virus comes in. We rather doubt this possibility, since apparently the virus that was previously in the area has died out, there being no evidence of yellow fever in Mexico and in Guatemala for many years past.

The emphasis that Dr. Bugher placed on the study of general biological problems yesterday is well merited. For the proper understanding of yellow fever we need to know a great deal about the entire broad field of biology. In the old days, when the yellow fever worker had to consider only *aegypti*, man, and a domestic urban disease, it was fairly easy to cover the field, but today we must know considerably more about the vertebrates and invertebrates of the forests. We must know something about the weather. We must know about the botanical picture.

You must all have been intrigued by Dr. Trapido's statement this morning that he doesn't know where *Haemagogus spegazzinii* is really breeding. My ignorance on the subject goes back to 1935 and 1936 in Brazil. In 1935, our attention was called to the *Haemagogus* mosquito, not by the entomologists, nor by the people who were studying yellow fever, but by the people, the victims of yellow fever themselves. The first intimation that this mosquito might be involved came from the people who, when asked about mosquitoes, referred to the little blue mosquito. But the entomologists who went into the area failed to find the breeding places. I am glad to hear it still is a difficult problem.

DR. TRAPIDO: I might just mention that while it is true that we have caught a few of them, no one has ever found a male of *Haemagogus spegazzinii* in nature.

DR. BOSHELL: I found one, but it had just hatched in a bamboo stump, and was about to disappear. If I hadn't come at that precise moment, I would have missed him, and that was just one in twenty years.

THE CHAIRMAN: Where is he?

DR. BOSHELL: I wasn't able to capture him.

DR. TRAPIDO: There are plenty of males in the collections reared from eggs, but no one—well, with this exception of one just coming out of a breeding place—has ever seen one in the field in all this work.

DR. BOSHELL: We tore down one acre of brush in an area where we could catch fifty *Haemagogus* in half an hour. We tore it down tree by tree and the place was teeming with adults; we peeled the bark off the trees and put it in water. We couldn't raise a single larval specimen. In May, in the first rains, you can find all the larvae you want in every tree, but it is impossible to imagine that in December these are the same adults that were born in May.

DR. SCRUGGS: Yesterday, Dr. Boshell spoke of observing infection sometimes out in the open at a distance from the forest canopy that normally one thinks of as the natural habitat of *Haemagogus*. I wonder if in the surveys other media have been explored as possible vectors. I am thinking of something other than *Haemagogus* that might carry the virus across these barren areas where the high canopy mosquito is not indigenous.

DR. TRAPIDO: In this connection, there is a lead which we haven't followed because there is still so much to find out about mosquitoes. This is the question of *Phlebotomus*—sand flies—which are known to be vectors of another virus, Mediterranean sand fly fever, from which there has been a dubious recovery of yellow fever virus reported in Africa. In the course of the field work at one of our stations—Almirante, Panama—we made nocturnal collections and discovered an abundant arboreal species of *Phlebotomus*. We shall also consider—if we ever get through with the mosquito problem—the possibility of *Phlebotomus* being involved, if Dr. Hertig of our staff, who has spent his life studying these creatures, is interested. The feature of the biology of these insects, of interest in connection with virus survival over the dry season, is that they do not require water to breed. The larvae develop in moist soil or in moist decomposed debris in and about holes under trees, and they persist through the dry season. If they were brought into the picture, it is conceivable that they could be part of the answer as to how virus was maintained over the dry season.

DR. BOSHELL: I should like to add that during the investigation on transmission we tried to keep an open mind and not to be obsessed by the mosquito. In places where virus was recovered from the *Haemagogus* mosquito, we investigated other mosquitoes and *Phlebotomus*. We tried even grasshoppers and mites. We tried everything in places where the virus was proved to be, but it was found only in mosquitoes. That is why we carried on with mosquitoes, but I am not excluding the possibility of *Phlebotomus* or other families, which have to be kept on the agenda for virus recovery.

DR. DOWNS: In Trinidad we tested all of the mosquitoes we caught and in one of the programs we made consistent evening and night captures of mosquitoes. *Phlebotomus* were routinely injected, although we did not get them in large quantities. One thing struck me in the course of monkey collecting in Trinidad. As I mentioned yesterday, we made numerous virus isolations from *Haemagogus* collected on the forest floors at the roadside or in a clearing in the

jungle. When we would shoot monkeys in the deep forest and were getting blood specimens from them, mosquitoes would be in there biting those animals. You are working in a fog of mosquitoes. You are all in a sweat from a mad chase, your monkeys are down and you are trying to get a blood specimen before the monkey dies, and the mosquitoes are in there by the swarms biting you and the monkey. On one occasion we found *Phlebotomus* there on the job, biting the monkeys as they lay upon the ground.

Now the monkeys that catch yellow fever, when in the terminal stages of a fatal infection, are down at ground level. We were thinking that it was an interesting possibility that quite a few ground-level forest mosquitoes could get loaded up with that monkey's virus at a very critical time, right when he is fighting out his last half hour or so, down on the forest floor instead of up topside in the canopy.

THE CHAIRMAN: Once again I think we have to agree that we didn't finish yesterday all of the discussion on yellow fever.

DR. STOWMAN: Excuse me for returning to the question of quarantine while we are discussing the geographical spread of jungle yellow fever. In its recent meeting in Geneva the WHO Committee on International Quarantine proposed a new article to the International Sanitary Regulations to the effect that if a country cannot delineate the area where the yellow fever virus is present, the whole country may be declared infected without its consent. Usually, only some of the forested areas are involved. To delineate these areas accurately requires laboratory facilities, experienced field workers and budget provisions, all of which many countries do not possess in abundance. It also requires time.

I should like to hear from those who have had experience in such undertakings as to about how long they think it would take to delineate exactly the geographical extent of jungle infection such as we have recently witnessed, for example in Honduras or in eastern Venezuela. I should also like to hear opinions expressed as to the possibility of conclusively determining whether the virus may or may not still exist in a few monkeys after the yellow fever epizootic has passed. If this cannot be determined, it seems to me that the only criterion for the termination of danger from yellow fever in a given area must be the continued absence of new human cases.

THE CHAIRMAN: You have heard the question that Dr. Stowman has raised which is, just to restate it, whether the proposal that the World Health Organization might declare an entire country infected and infectible, in the absence of a suitable delineation of infected areas by the authorities of the country itself, is reasonable.

DR. STOWMAN: Let me add "without a human case." We all agree it becomes infected locally. We are supposing here there were no human cases.

COLONEL ELTON: Wouldn't that require just an arbitrary period to allow time to investigate? It wouldn't have to be permanent by any means, but a period of, say, six months or something like that, pending clarification of the situation.

DR. BOSHELL: I should like to recall what happened in Costa Rica last year,

when the wave was already in Nicaragua and everybody thought that the epidemic was over.

COLONEL ELTON: It could be renewable in six months. It really should be maintained until the following August or something like that, to make sure that the activity phases are properly considered.

THE CHAIRMAN: It is important to take the long view on yellow fever, and to remember that quarantine measures deal with the movement of yellow fever from country to country, rather than within the country itself. Now, taking the period between 1901, when the first mosquito control work was done, and 1932 when jungle yellow fever was first definitely identified, we find that as measures were taken against yellow fever in the cities, against the urban *aegypti*-transmitted yellow fever, yellow fever disappeared from the statistics, not only of the cities that were worked but of the surrounding areas, and indeed disappeared almost entirely as an international maritime threat. Only a few cases were found moving on ships after 1915, and these principally from Guayaquil towards Panama; that is, away from known infected centers. The reduction of yellow fever was so great that it gave rise to the belief that it would be possible to eradicate yellow fever completely. On the assumption that there was as much if not more jungle fever between 1902 and 1932 than there has been since, it must be admitted that jungle yellow fever has shown little aptitude to create quarantine problems.

The question that Dr. Stowman has raised, of course, brings up again the question of procedure in quarantine matters, and the procedure with all other diseases, I believe, is that the country itself has the responsibility for declaring an area infected or clean, and unless we are going to establish an official international police for policing within individual countries, I don't believe we can follow through with the proposal that the World Health Organization has the right to declare an entire country infected. The proposal to declare all of Brazil as an infected area would obviously be unacceptable to Brazil, and I am sure this proposal will not be accepted by the American nations as a whole.

COLONEL ELTON: Or should the entire United States be quarantined because New Orleans happened to be infected? As to Dr. Boshell's comment on Costa Rica, the outbreak in the Cabagra Valley, southern Puntarenas, was already active as the northern Costa Rican epidemic centers were subsiding in October 1951.

DR. BOSHELL: There was a question as to the diagnosis by the personnel in San José.

COLONEL ELTON: I understand what you mean: a problem case after the wave had cleared Costa Rica by March, 1953? Although I did not see the slide myself I can understand the difficulty, for we had a similar experience in the town of Gatun in the Canal Zone long after Panama was cleared by the wave. We finally ruled out yellow fever even on the liver slide, but if it had come up during an epidemic it might not have been so easy to dispose of. I have a collection of liver lesions simulating yellow fever which might give some trouble even to Augusto Gast Galvis. I certainly do not want Dr. Soper to know I have them. The case you refer to in Costa Rica was never officially authenticated. There are times when one must have confidence in a pathologist's opinion, although there are also

times when he needs a little clinical information. A paper on the clinical pathology of yellow fever based largely on the findings of Romero and Trejos in San José will appear in the February, 1955, issue of the American Journal of Clinical Pathology.

THE CHAIRMAN: To return to the subject of what can and should be done about yellow fever. From the standpoint of the Pan American Sanitary Bureau it is essential to have well-equipped facilities accessible for the study of yellow fever any place in the Americas. The evidence presented here of the moving picture both in time and space outlines a situation in which, repeatedly, local interest in yellow fever develops, lasts for a year or so, and then disappears. And yet the problem to be studied is not a problem of, say, Nicaragua as such. It is not a problem of Colombia as such. It is really a problem of the continent. As I indicated yesterday, the only countries in South America that are not involved are Uruguay and Chile, and the only countries which are probably not involved in North America are Canada and the United States. I am referring now to jungle yellow fever alone and not to the possibilities of *aegypti*-transmitted disease.

The Pan American Sanitary Bureau is collaborating with the yellow fever laboratory in Brazil and with the Carlos Finlay laboratory in Colombia. The collaboration is, in part, for the production of vaccine for distribution to other countries. But the basic interest is much broader than that, and the Rio laboratory and the Bogotá laboratory should have facilities and personnel for virus research, for entomological, pathological and mammalian work. Adequate technical staffs should be available over long periods of time to continue the type of studies carried out for a number of years by the Rockefeller Foundation, but with more emphasis on long-term studies in selected areas than were ever possible in the past. The Bureau and the Gorgas Memorial Institute have been collaborating on studies of the problem in Central America. So that through the Bureau we do have, let us say, coordination with, or some common tie with, the work of these three units.

One of the serious problems is that of personnel. The withdrawal of staff of the Rockefeller Foundation itself, and the natural wear and tear of time and politics and other factors on the staff which had been trained in the past, have left the field almost bare. There has not been a persisting program of developing staff for continuing studies. In Brazil the situation is rather critical as far as staff for field investigations is concerned. The situation with regard to the Carlos Finlay Laboratory has also been critical. One of the staff members of the Carlos Finlay Institute is just now finishing a year's special training in virus diseases, and one of the younger Colombians is also finishing training in entomology. We are hoping to be able to collaborate with the Government of Colombia in developing a complete unit which can undertake to continue this type of studies in Colombia and which may, from time to time, serve as a training unit for other staff or, on occasion, be used outside of the country. Dr. Boshell, we are happy to say, is going to continue or, let us say, return to the field and, we hope, on a permanent basis.

The agreements of the Pan American Sanitary Bureau with both the Oswaldo

Cruz and Carlos Finlay Laboratories provide for the use of those institutions as training centers for personnel from other countries. Adequate advantage has not been taken of that provision nor of the obvious value of having trained personnel from other countries spend periods of training in the laboratory in Rio and in the one in Bogotá. A movement of this kind would be mutually valuable. It would be practically impossible for a trained person to go to one of those laboratories without contributing as well as gaining something during the period he was there. The Bureau hopes to do more in the future than it has been possible to do in the past. Dr. Smadel has called attention to the obvious need of base laboratories for yellow fever studies, and his statement strengthens the position of the Bureau in planning more support to such programs, with more personnel, before budget committees.

One of the purposes, of course, of this meeting has been to learn what collaboration, what interest in training, what personnel might be made available; how we can get more interest, particularly from the scientific organizations and the official organizations in the United States, in this problem.

DR. BOSHELL: I agree that base laboratories are absolutely necessary, and we know that we can count on those already in existence in Bogotá, Panama and maybe Trinidad. But it is my experience that certain things simply cannot be done at a distance from the scene of activity. I should like to stress the point that a portable field laboratory, with a supply of animals, should be considered. That field laboratory should be established not behind the wave but ahead, and naturally that presupposes the ability to predict where the wave is going to spread. For instance, I would suggest in this particular case, Peten. Peten has a large network of forest and, in our experience, that type of region offers more possibilities of a certain permanence, of a certain delay in the march of the wave. The alternative is a field laboratory mounted in a helicopter. That would be the only solution. Our experience shows that trying to trail and track a wave with a load of monkeys and mice is a waste of money, sweat, and tears; but a field laboratory to diagnose or to dig into this vector of transmission probably is necessary. We made a very gallant try in Honduras, but such a form of work is necessarily limited by transportation, by refrigeration, by all kinds of factors, and the results are always delayed, are always protracted. An attempt to ship frozen mosquitoes over a long distance failed under optimal conditions.

Lots of things can be achieved in the field, on the spot, saving lots of transportation, but it naturally takes a certain equipment and personnel. It has been done before; I don't see why it couldn't be done again. The great question mark is whether the wave is going to get into Peten and southern Mexico. In this case I believe that we should keep close watch on the march of the wave and, at the first indications of its resurgence, I would suggest the establishment of a field laboratory in a chosen place in Peten in Guatemala.

MR. FRITZ (U. S. PUBLIC HEALTH SERVICE): Dr. Soper, I have some personal opinions about matters that you have touched upon in discussing training. I cannot speak officially for the Service, but we, at Communicable Disease Center,

sometimes find ourselves in the very interesting position of becoming experts in some field overnight, by receipt of official order. We often acquire responsibilities, in this manner, which require decisions in fields where we have little or no practical experience—only academic training or experience in related fields. Much of this might have been prevented by assigning us, as young officers, to work with such problems in foreign areas. Unfortunately, it appears that when we were called up to furnish personnel for overseas assignments in the past, we often sent those officers whom we thought could be spared from their assignments here. Consequently, these persons seldom came back to our organization to give it the benefit of what they might have learned overseas. I believe this attitude is now changing.

Now we are recognizing more and more the need for providing our personnel with experience in those diseases which occur so infrequently in the United States that they are unable to gain such experience here. An example of that change in attitude was the approval of my trip to Trinidad to observe the measures being undertaken there to prevent an outbreak of urban yellow fever. I can't be certain, but I believe that in the future we will be far more interested in some of our personnel taking advantage of training opportunities that exist in the Pan American Sanitary Bureau and the World Health Organization. This is my personal opinion.

THE CHAIRMAN: Thank you, Mr. Fritz, for your personal opinion, and I personally support it. There is an important point with regard to training, and that is the length of the period. We feel that an individual coming into the field to learn something about yellow fever would need a considerably longer period than you had in Trinidad.

MR. FRITZ: I admit that very definitely.

THE CHAIRMAN: And we should like to think in terms of years rather than days. The evidence is clear and definite that this problem is not one that the United States is going to cease being interested in during the lifetime of anyone here present. Adequate training requires getting out and spending enough time to really become familiar with this problem.

DR. DOWNS: Just one brief comment. You were reviewing a list of possible virus laboratories, and I thought it might be mentioned here that there is a virus laboratory in the University of Miami or University of Florida, with Dr. Murray Sanders of the Veterans Administration in charge. It is an area which allows a tapping of northern Cuba, Puerto Rico and Haiti, and I heard the other day that there is some interest awakening, possibly in the school in San Juan, Puerto Rico, about setting up a virus laboratory in Puerto Rico.

MR. FRITZ: I think there is interest in a number of places.

THE CHAIRMAN: The interest has to precede getting the money and personnel. Virus disease investigation is expensive, but it is just one of those added costs of living that should be faced.

I purposely left out a comment on the tropical virus laboratory in Trinidad, and when Dr. Downs spoke up I thought he was rushing into the breach, but he is strangely silent. However, we do know that whether his laboratory will be

actively participating in yellow fever research as such or not, we will be in touch with his findings and know that from his experience and that of Dr. Anderson will come valuable collaboration and work without its being specifically labeled as yellow fever activity.

DR. DOWNS: I might mention here that our laboratory is quite new, and we are hoping, if it becomes solidly established with the passage of time, that it will serve as a training center for individuals from the United Kingdom or from services in the United States or elsewhere who might want to get experience in one or another of the virus lines in the new world. Now, in connection with yellow fever, for example, while we might not be working directly with the program, if someone wanted to assign a person to the Trinidad Laboratory with sufficient money to cover some of the operating cost of the work that would necessarily be contingent upon his presence there, or if someone were sent there with free cash, I think we could probably find a way to fit him in where he would have working and laboratory facilities, and he could work right along in Trinidad or elsewhere on some aspect of yellow fever. We would be delighted to have him around. We would get more out of him than he would out of us.

THE CHAIRMAN: In other words, you want fellows with cash.

DR. JOHNSON: I might point out that one of the aims of the Gorgas Memorial Laboratory is the same that Dr. Downs has mentioned. We, of course, are handicapped considerably by having to operate on a budget that is determined each year by Congress, but we do have working facilities. We can offer for the investigators a base and equipment to carry on projects if they have the money when they come down. We have one man working at our place at the moment, Dr. Rosen from the United States Public Health Service, and we have space and equipment to accommodate possibly one or two others, but shortage of funds has hindered the wider participation we would have wished.

MR. FRITZ: How is Dr. Rosen financed?

DR. JOHNSON: By the National Institutes of Health.

MR. FRITZ: His salary and research funds?

DR. JOHNSON: Yes. There are certain things that we are able to furnish him; he doesn't have to depend entirely on the NIH.

THE CHAIRMAN: I think the suggestion that the individual who comes in for training under these circumstances should bring with him a certain amount of money is entirely reasonable. We think nothing of paying tuition, fairly heavy tuition these days, for students coming to the different schools of public health, and it seems to me that this should not really be a barrier. Rather, it seems to me that it is an opportunity to get something at a very low expenditure.

COLONEL ELTON: In the past, whenever I have tried to get the Surgeon General's Office interested in this problem, it has always been brushed off by saying that it was the responsibility of the Pan American Sanitary Bureau. Helicopters are an integral part of the Medical Service of the Army, and quite a few must be available. If you could interest the Surgeon General you might get medical troops to assist. They would, of course, be noncombatant troops and might be more acceptable to the Latin American Governments. However, I believe the pressure

would have to originate from a rather high level since, at the present time, due to the activities of the Rusk Committee on Medical Manpower in New York, the Medical Corps of the Armed Forces has been almost emasculated. There is a great shortage of personnel and funds. The number of medical officers in the armed forces is being reduced and a critical situation has developed. Yet this would be a source of definite assistance if it could be activated. It would take the State Department, even perhaps the President himself, to get this going and authorize the participation of the Army Medical Service. Such a move might be well worth while.

DR. BOSHELL: Referring to what was said on the opportuneness of a field laboratory, a base laboratory for the study of vector problems is an expensive proposition, but the money that is saved by field experiments may more than justify the expenses of a field laboratory.

DR. TRAPIDO: The field laboratory must depend on a base laboratory to produce the mice and for other general support. The base laboratory must depend on the field laboratory to produce the mosquitoes or the virus. There is no conflict. It is merely that there should be sufficient money for both purposes.

THE CHAIRMAN: This suggests competition for available funds. One of the purposes, quite frankly, of this meeting has been to evaluate the resources that are available, emphasize the importance of this problem and see what can be done about getting support for long-term programs.

I believe that it is entirely possible that within another few years, maybe four or five, the yellow fever in its march up through Mexico and Guatemala and so on will be terminated, and then, for actual sources of virus, the laboratory in Panama might very well be turning its attention to the south and studying the possibilities of another wave coming up through Central America. But I think that we should look at the present situation quite frankly as one in which the advancing wave in Central America towards Mexico and the Gulf, the explosion in Trinidad and the case in Caracas have all focused attention on what to us must be a permanent problem, requiring permanent study. However, I think that this is the time in which we are able to call attention to certain things that are happening, and have been happening, which emphasize this problem to the point where there should be better prospects of getting approval of long-term planning and long-term studies in this field than would have been possible even one or two years ago. Colonel Siler yesterday was obviously wanting Santa Claus to bring an insectary for the laboratory in the Gorgas Institute, and I think we should look at the problem as being much bigger than simply an additional insectary at this time. I believe those of us who are here are pretty well agreed that this is still a big, complex problem that needs considerable increase of staff devoted to it, some of which would be on a permanent basis. The problem is bigger than simply following the present wave in Central America. Plans should be made for continuing operations indefinitely, because I don't believe we will ever come to the point where we know all of the answers with regard to yellow fever.

Dr. Boshell has come forward with a rather definite program. He hasn't given

us any idea as to the size of staff that he thinks might be available or might be required. He hasn't given us an estimate of the funds, nor has he given us an idea as to the period during which a field laboratory of this type might be advantageous in a given point.

I would point out in this regard that in early 1937 the yellow fever service in Brazil, with which the Rockefeller Foundation was collaborating at that time, did make plans and established a field laboratory in southern Mato Grosso. The idea was to get into this area and establish a laboratory before the virus got there. The laboratory consisted of an epidemiological section, a virus section, an entomological section, and a mammalogical section; in other words, a fairly complete field laboratory. As a matter of fact, the laboratory and the virus got there about the same time, or the virus may actually have been ahead of the group. But they did have a very active season during that year. The following year the area was a sterile one from the standpoint of observing actual virus activity.

The planning of such studies is not simple. In the case of Villavicencio, the laboratory there was for the purpose of studying the conditions under which yellow fever had occurred, at a time when those who had seen something of the yellow fever movements in Brazil were willing to believe that the disease was no longer present. The laboratory was definitely for the purpose of studying where yellow fever had been, and we were perfectly willing to admit that it might be a number of years before the disease would come back. As a matter of fact, shortly after the laboratory was established and was operating, the disease appeared within striking distance to the south and then eventually it moved back, so that there always was something interesting in the area to study.

In your suggestion of a laboratory for the Peten, were you thinking that, once the virus had come and gone through that area, it then might be shifted into Mexico ahead of the virus?

DR. BOSHELL: I wasn't thinking of anything that couldn't be moved a certain distance if necessity should arise. It is absolutely essential for transmission and for mosquito breeding. It is really a very cheap unit, and it is not dependent on costly equipment.

MR. FRITZ: How much?

DR. BOSHELL: I wouldn't know. What we need is mice and monkeys, in the first place, in connection with a base laboratory, because I wouldn't think of establishing a mouse colony, but must have a portable freezing unit or at least congealing unit. There are now portable freezing units available. Sterilization often is essential. Traps and cages, all the glass work, syringes, tubes and so forth, tarpaulins, mosquito nets, microscopes and bacteriological stains, and all that. That's all we need. It can be packed and transported, but not every day, not running after something.

THE CHAIRMAN: I should like to make a short statement with regard to what Dr. Boshell has proposed and what he has said. It is simply this: if anybody else had proposed it, I would be skeptical; but I have seen Dr. Boshell operating in the field, and I know the experience that he has had both with mosquitoes and

with the mammals and with the laboratory phases of this problem. With the knowledge that Dr. Boshell himself would be operating a unit of this kind, I think the suggestion is a good one.

DR. DOWNS: I should like to put in a very strong vote for Dr. Boshell's suggestion of establishing a field laboratory ahead of the present epidemic front in Central America. Somebody is faced with a decision eventually involving one of two possibilities. Either that virus is going to go north or it is not. That particular point cannot be foreseen. But if it does go north and no steps have been made to find out something about it and its passage, I think that somebody is due for very heavy criticism for lack of foresight. If it should not go north, all that has been committed is a relatively small amount of money and a certain amount of somebody's time waiting for something that didn't happen. But I think the call is for action in this particular instance.

COLONEL ELTON: I should like to bring up the point of criticism of the medical profession for a lack of acuity in recognizing these cases. Such an accusation certainly cannot be directed against the physicians of Costa Rica, because although the initial fatality had to be disinterred in order to make the diagnosis, the arrival of the wave was immediately recognized and interest and diagnostic acumen were high from the onset. In Trinidad it was more insidious, as in Panama in 1948, but we should not hastily impugn the judgment of the practitioner of medicine as if we were in any way superior. If we were in his place without our special diagnostic technics we too would have the same difficulties. He needs assistance and to be alerted to the occurrence of unusual diseases. "Typical" yellow fever is hardly different clinically from malaria or influenza. Many diseases are inapparent. "Classical" yellow fever during an epidemic is, of course, unmistakable.

As for the protection of the Gulf settlements of the United States and Mexico when the wave reaches the Gulf Coast, I would recommend surveillance of the population of the coastal villages, compulsory vaccination of the crews of all fishing, shrimping and cargo vessels engaged in local coastal shipping, and as much *Aedes* control as can be accomplished. Mass vaccination of cities like New Orleans hardly seems practical, and *Aedes* control in all the scattered fishing villages of the bayous and other coastal regions again seems hardly feasible. Fortunately, there is no need for panic, for the disease seems to be approaching slowly in a predictable, albeit inexorable, advance.

THE CHAIRMAN: Just as in northeastern Brazil. When the Minister of Health protested two weeks ago that the proposed program for the eradication of *Aedes aegypti* in Argentina was going to cost a considerable amount of money, my only answer to him was that Brazil, Paraguay, Bolivia and Uruguay had already paid it.

MR. FRITZ: May I make one comment, and that is that my purpose for being here concerns these problems that Colonel Elton has just presented.

THE CHAIRMAN: We are delighted that you are here, and we are delighted that

Colonel Elton presented the problems, but I overlooked them until right at the end of the meeting.

MR. FRITZ: They are problems we have been thinking about.

THE CHAIRMAN: The experience in Brazil over the years in searching for yellow fever, was overwhelmingly in favor of routine viscerotomy rather than expecting diagnosis by local clinicians. In December, 1937, a group of five doctors went through an area in Brazil, just in front of the epizootic wave which was coming toward Rio, specifically for the purpose of talking with the doctors who were handling viscerotomy and with the practicing physicians, and warning them to be on the watch for yellow fever. On January 17 a positive liver came in to the laboratory from the visited area. After other positive livers came from undiagnosed cases, a second visit was made to the area. The doctor who had seen the first case but failed to diagnose it, was reminded of the fact that he had been visited some weeks before and that his attention had been called to the necessity of watching for yellow fever. He had, he said, been on the watch for yellow fever, but had seen no cases. He had, in fact, seen nothing that suggested to him that there might be yellow fever in the area. When told that he had viscerotomized the first case, he admitted that it was one of his patients, and that he had a series of similar cases under his care. And that afternoon, six or eight yellow fever cases were seen on a coffee *fazenda* with this doctor.

COLONEL ELTON: One cannot make a diagnosis of yellow fever on every case. I could easily be trapped.

THE CHAIRMAN: I don't believe there is anybody who can see a single case of yellow fever once at any stage in the disease and justifiably make a diagnosis without knowing the clinical history. All of the symptoms that are considered as classical symptoms of yellow fever are simply the symptoms of severe intoxication, with destruction of liver tissue. The thing that is important in yellow fever is the time schedule. What happened? When did it happen? How did the patient come to be in the condition that he is in? The individual case can be duplicated by malaria. It can be duplicated by so many things on any given day. Would you back me up in that statement, Dr. Boshell? You have seen a number of cases.

DR. BOSHELL: I remember, when we were isolating virus in Colombia, it was widely known that as soon as anybody had the slightest fever in a malaria country we would rush at any time of the day or night to try and isolate the virus. We were solicited from everywhere for the most absurd cases. The first virus isolation in Colombia was from a gentleman walking through a market place; as we met, he complained that he had a slight headache. I noticed his eyeballs, which were congested. So I said, "Come along." From him came the first yellow fever virus isolated in Colombia.

THE CHAIRMAN: I was referring to the other end of the scale—to the case with all of the typical symptoms of yellow fever.

COLONEL ELTON: The classical case.

THE CHAIRMAN: One case. If you let me see a series of cases and let me talk to the cases and find out how they happened, then I am willing to attempt a diagnosis.

COLONEL ELTON: Another thing that might be added here is that the mere finding of malarial parasites in the blood does not rule out yellow fever.

THE CHAIRMAN: How true. We learn the hard way.

COLONEL ELTON: On this Gulf business, you could declare it a coroner's disease, a medical examiner's prerogative in the presence of a public health menace, to perform autopsies as well as viscerotomies.

THE CHAIRMAN: I am going to adjourn the meeting now. Thank you all once more for coming and for contributing as you have to the discussion.