The first great advance in our knowledge of yellow fever came at the turn of the present century, when Reed and his associates demonstrated that it is an insect-borne disease. Since that time a long and impressive list of observations have been made in the field and in the laboratory, and it is upon these that our conception of the epidemiology of the disease is based. Detailed results of the numerous investigations which have been carried out are to be found in the literature and it will suffice here to recall, briefly, some of the more outstanding findings, and particularly those which have a bearing on the problem confronting the health officer in Africa.

For a period of about thirty years following Reed's discovery, the epidemiology of yellow fever was based on the belief that man was the only susceptible vertebrate host, and that the mosquito, *Aedes aegypti*, was the sole vector. Many urban epidemics were eliminated by the control of the vector, and, in due course, a plan was formulated which, it was believed, would result in the complete eradication of the disease. However, the results were disappointing, and the infection continued to manifest itself despite successful and persistent vector control. The first indication that there were epidemiological factors which had not previously been known came, in 1952, when Soper and his colleagues reported an epidemic of yellow fever in an area in Brazil in which there were no *Aedes aegypti*. Following this, many outbreaks were observed in *A. aegypti*-free areas in South America. They were always associated with forested areas and in many cases they occurred in places where the human population was scanty. In due course, it became evident that yellow fever can persist indefinitely in certain sparsely populated,
or even uninhabited forest areas, and that animals other than man are involved in maintaining the infection. Furthermore, it was found that various species of forest mosquitos play an important role as vectors of the disease. Unlike the classic urban yellow fever, this was a disease of the jungle. It was, in fact, yellow fever in an entirely different environment, and this epidemiological type of the disease became known, in the Western Hemisphere, as jungle yellow fever.

While workers in South America were making valuable contributions to our knowledge of yellow fever, events of outstanding importance were taking place in Africa. In 1927, members of the West African Yellow Fever Commission of the Rockefeller Foundation demonstrated that the rhesus monkey is highly susceptible to yellow fever infection when they succeeded in isolating the first strain of yellow fever virus. A fertile period of study followed the finding of a satisfactory experimental animal, and a wealth of new knowledge gained in the laboratory became a valuable aid in the solution of the problems encountered by the observer in the field. For example, the properties of the causative agent could now be fully studied for the first time; it was shown that many species of mosquitos, in addition to Aedes aegypti, were capable of transmitting the virus from animal to animal under laboratory conditions; a highly specific test, known as the protection test, was elaborated, and it became possible to demonstrate, experimentally, the life-long immunity possessed by the individual who has recovered from an attack of yellow fever; and an effective vaccine was developed which has since been used to immunize many millions of persons.

As work progressed, in Africa, it was soon realized that reported cases of yellow fever give no indication of the actual incidence of the disease, and the protection that was used to provide information on the extent to which selected areas had been involved in the recent past. In the early immunity surveys in West Africa, the tests were made in rhesus monkeys, and were, necessarily, limited in extent. However, this difficulty was overcome when a similar test was devised in which the white mouse became the experimental animal. Large-scale studies now became possible and the immunity survey has been extended to include practically all parts of Africa. As a result of this work, some of which, with World Health Organization assistance, has only recently been completed, we can now delineate, with reasonable accuracy,
the boundaries of the area in Africa in which the disease has occurred in recent years.

The results of the survey in Africa revealed that the belt of immunity extended far beyond the area where clinical yellow fever had been observed. It indicated that the infection had been present in a vast area in Central and East Africa where cases had never been recognized. This somewhat unexpected finding was not, at first, universally accepted, since many of the local medical authorities found it difficult to believe that cases of yellow fever, in the numbers indicated by the survey, could have passed unnoticed. The solution of this and other problems raised by the immunity survey became the objective of the Yellow Fever Institute which was opened in Uganda in 1936.

Early in the work of this Institute attention was directed to an area in western Uganda, known as Bwamba County, because of the high incidence of immunity found in persons resident there. Many years of intensive study followed in this area, the results of which have made a significant contribution to our knowledge of the epidemiology of yellow fever in Africa. Meanwhile, an extensive epidemic of the disease occurred in the Nuba Mountains district of the Anglo-Egyptian Sudan during the course of which two strains of virus were isolated, and clinical and pathological investigations were carried out. It was found that the disease and its causative agent were in every respect the same as that observed in West Africa and in South America.

The results of the work in Bwamba County have provided the fundamental facts upon which our conception of the epidemiology of yellow fever in Africa is based. Briefly, they revealed evidence of the existence in the inhabited portion of the county, of a man-to-man cycle of infection with *Aedes simpsoni* as vector; and, in the uninhabited forest area, of a monkey-to-monkey cycle transmitted by *Aedes africanus*. Furthermore, the findings indicated that yellow fever is enzootic in the monkeys of the forest, and that it is essentially a disease of animals which does not depend, in any way, on the presence of human infection, but which is introduced from time to time into areas inhabited by man. This forest disease is basically the same as the jungle yellow fever of the Western Hemisphere.
It is apparent, then, that in Africa as in America, there are two distinct types of epidemiology, occurring in two entirely different environments. One is a disease of man which occurs in urban centres and is transmitted by the domestic mosquito, *Aedes aegypti*. The other is primarily a disease of animals which occurs in association with forest, and which is transmitted by forest-dwelling vectors. It should be stressed, however, that the difference between these two types is strictly epidemiological, and that the disease itself is the same, regardless of the environment in which it is found. It is now believed that sylvan yellow fever is the original epidemiological type, and that it is from this source that urban centres are invaded from time to time. We have, then, the explanation of the earlier attempts to eradicate the infection by controlling the vector in urban communities. Although this procedure was highly successful in eliminating the disease in those centres, it did not in any way influence the permanent reservoir of virus which exists in the animals of the forest, and which is the source of the urban disease.

This brief review will serve to illustrate the lines along which our knowledge of the epidemiology of yellow fever has advanced during recent years. It should be pointed out, however, that this knowledge is by no means complete. Conditions differ markedly in different sections of the country and there are indications that, in certain localities, the vertebrate host as well as the vector responsible for the maintenance of the sylvan disease are quite different from those incriminated in Bwamba County. Many gaps in our knowledge still remain to be filled and this can only be accomplished through persistent effort by experienced investigators.

The first concern of all of us is, of course, the effective control of the disease, including measures designed to prevent its spread from infected to non-infected areas. It is essential that those responsible for this control should have a clear understanding of the two epidemiological types of yellow fever which are now known to exist. The method of control of the urban disease has not changed since Reed first recommended that it can best be achieved by the destruction of the vector, *Aedes aegypti*. This mosquito is the only known urban vector of importance, and it has repeatedly been demonstrated that its elimination rapidly results in the disappearance of the disease. Although the method is the same, new and improved means for the control of *Aedes aegypti* have become available in recent
years, and these will be described later in our discussions. Suffice it to say here that there is convincing evidence that complete eradication of this insect from urban centres is now both possible and practical. Since this is an established fact, it is obvious that the aim of those responsible for the control of yellow fever in Africa should be the elimination of Aedes aegypti from all urban communities in the endemic area. A successful eradication programme of this nature carries with it results of such profound importance, not only to Africa, but to infectible territories outside Africa, that it is impossible to over-emphasize the necessity for its initiation at the earliest possible moment.

In the case of sylvan yellow fever, other methods must be employed. Thorough and widespread control of forest vectors is not at present possible, nor can the animal hosts be eliminated. This source of infection remains, therefore, a constant threat to any urban community with which it is in communication, and in which the urban vector has not been suppressed. Although the forest infection cannot be controlled effectively, human populations who are exposed to it can now be protected. A highly satisfactory vaccine is available in quantity and its use provides us with a means of protecting communities which are exposed to the sylvan disease. It is now officially recognized that a single inoculation with yellow fever vaccine protects the recipient for a period of six years, but evidence is accumulating which indicates that this period can be extended. It is, perhaps, not too much to hope that it will eventually be found that the immunity following vaccination is life-long, just as is that following a non-fatal attack of the disease, even in its mildest form. The immunization of the population against yellow fever infection can now be accomplished as readily as in the case of smallpox and, in fact, the two inoculations have been successfully combined on a large scale in Africa. The advantages of the mass immunization of the population in yellow fever endemic areas are obvious and, although great strides towards this end have been made in some parts of Africa, much remains to be done.

Prior to the time when it became known that yellow fever was an insect-borne disease, quarantine played a dominant role in its control. With the advance in our knowledge of the disease other, and more effective, measures have been developed. However, these newer and better methods have not been universally applied, with the
result that the formulation of quarantine regulations is still considered a necessity by those concerned with international control. It should be stressed, however, that, under conditions existing in Africa, quarantine, as a method of control, is inadequate. As already mentioned, reported cases of yellow fever in Africa give no indication of the incidence of the disease. Only a small percentage of the cases actually occurring, in Africa, are seen or recognized, and it is only when an immunity survey is carried out that the extent and distribution of the disease is realized. Studies undertaken recently in at least two large cities in West Africa revealed a significant degree of immunity in children under five years of age, although no cases were reported from either place for many years. It is apparent that yellow fever can be, and is, widespread, in Africa, unknown to anyone, including those whose responsibility it is to control it. Under these circumstances it is reasonable to suggest that an important port in the endemic area might be less dangerous, from the point of view of spread of the infection, when the disease is known to be present, than when it is believed to be absent. When cases are known to exist, quarantine regulations and vector control can be rigidly applied; when it is present but unrecognized rigid control is less likely. It is difficult, if not impossible, to enforce quarantine regulations against a disease which apparently does not exist. The solution of the problem lies, not in quarantine, but in the vigorous application of the more effective control measures.

Briefly stated, the practical answer to the yellow fever problem, in Africa, is to be found in the eradication of the urban vector, and in the mass immunization of the population. To reach these objectives will require time, and with directed and persistent effort, but the reward lies in the knowledge that, with their attainment, the problem will have been solved.