While the object of this working paper is to try and bring out the present situation regarding yellow fever infection in East Africa, it is inevitable that we have to link the present set up intimately with investigations that have taken place before.

We recall that investigations on yellow fever infection in areas such as South America, Caribbean Islands, Central America and tropical West Africa were prompted and encouraged by the serious epidemics that used to affect many of the areas in these countries between the seventeenth and the beginning of the present century. Work in East Africa, however, was initiated as a result of the International Health Division of the Rockefeller Foundation trying to investigate the geographical distribution of yellow fever immunity in man. No outbreak or isolated cases of yellow fever had been reported from Central Africa and the principal objectives of the survey were to define the areas of the world in which yellow fever had recently been present and might still exist, and thus to contribute to the knowledge of its epidemiology. The findings of this yellow fever survey in Central Africa (including East Africa) carried out by Sawyer and Whitman have been reviewed on several occasions and need not be repeated here. It is, however, important to remember that the survey revealed a wide distribution of immunity in this area with the western and north-western parts of Uganda falling within the yellow fever-infected area while Kenya and Tanzania were outside the infected area.

It was the almost complete absence of reported cases of yellow fever disease in East Africa, despite an equivocal evidence of infection in parts of Uganda, that prompted the opening of the Virus Research Institute at Entebbe, in the hope that answers might be provided to some of the questions raised by the results of the immunity survey. It is gratifying to note that current information, together with results obtained over the past 38 years since work on yellow fever was started in East Africa, has gone a long way towards explaining why the yellow fever situation in East Africa is the way it is; i.e. there is evidence of yellow fever infection in parts of East Africa with evidence of endemicity in some parts, an abundance of known yellow fever virus vectors, and reservoirs are present in many parts, yet very few human yellow fever cases have been recorded and no yellow fever epidemic has ever been witnessed in East Africa.

The present communication tries to bring together the arguments which are being projected to explain this situation.

Vectors: Right from the beginning of yellow fever studies in East Africa the vectors incriminated for transmitting yellow fever virus were Aedes (Stegomyia) africanus, Aedes (S) simpsoni, and Aedes (S) aegypti. Yellow fever virus was isolated from one lot of sandflies.
In 1949 Garnham et al. suggested that Aedes (S) deboeri Edwards could also act as a vector for yellow fever in East Africa. Recently, Metselaar et al. (personal communication) (1970) suggested that Aedes dentatus might be the yellow fever vector in the northern frontier district of Kenya, where a high yellow fever immunity in humans was found in 1967. The coquillettidia fuscocephalata mosquito recently emerged as a candidate for yellow fever transmission when 50 of these mosquitoes yielded a strain of yellow fever virus during the 1971 yellow fever epizootic in the Zika forest (mentioned later). All yellow fever isolates from vectors have been from Uganda. No yellow fever virus has been isolated from vectors collected in either Kenya or Tanzania.

Most of the mosquitoes mentioned above have a very wide forest and/or peri-domestic distribution in East Africa. One would therefore expect that if given the opportunity of being infected by the yellow fever virus these mosquitoes would easily spread the infection to the human populations. But as far back as 1951 Aedes (S) simpsoni was observed to have two populations, the human-biting and the non-human-biting. Recently, Mukwaya (1972) observed that the non-human-biting population was also non-primatophilic and that this was genetically linked. Over much of its range in Uganda the Aedes simpsoni species appears almost wholly non-anthropophilic and hence would not play any part as a vector of yellow fever epidemics.

Combining the non-anthropophilic and non-primatophilic characters, the end-result appears to contribute considerably to the almost complete absence of human yellow fever and to the low yellow fever immunity rates in primates, such as monkeys, observed in many parts of East Africa. Aedes aegypti shows only a very slight preference for man over much of its range where it is essentially exophilic in oviposition, resting and biting activities. The non-anthropophilic population and phenomenon have in recent years been found to be more widespread than has been believed previously. Aedes africanus which is known to be essentially a monkey-to-monkey vector in the forest canopy and the forest floor may also bite man by day on the forest floor and at the forest edge. The scattered immunity in humans which occurs in areas where A. simpsoni does not attack man may be due to bites by A. africanus. But this is such an inefficient vector system that it cannot alone maintain an outbreak. The significance of Aedes deboeri and Aedes dentatus as vectors of yellow fever virus in East Africa and that of Phlebotomii has yet to be elucidated.

Reservoirs: Surveys carried out in the past have revealed that monkeys of different species are important reservoirs for yellow fever in Uganda. The reasons why immunity rates among these animals showed variations from area to area have not been clear. Present information provides us with two possible reasons. Firstly, mosquitoes are known to be strongly non-primatophilic in other places. This breaks the yellow fever cycle and the would-be reservoirs remain non-immune. Secondly, Henderson et al. (1970) showed experimentally that certain Group B arbovirus immunity (especially Wesselbron and Zika) interferes with subsequent yellow fever viraemia and immunity. Serological studies of wild mammals carried out in 1968 showed a very low yellow fever immunity rate of 3% compared with rates greater than 40% reported by Haddow et al. (1951) when it was indicated that yellow fever immunity was widespread among Uganda primates. The 1968 survey, however, showed a very high Zika virus immunity greater than 88%. It is therefore suggested from the experimental information that it is the extensive Zika immunity that may contribute heavily to the reduction of yellow fever immunity. In fact, during the yellow fever epizootic in the Zika forest during 1971, 40% of the monkey sera tested were immune to yellow fever and none had Zika antibodies, further indicating that the two infections can hardly co-exist in the same ecosystem.

In 1952 Haddow suggested that in Kenya and the drier parts of Uganda, galagos and not monekys, may be the main mammalian hosts of yellow fever. Since that time serological surveys have been carried out on galagos sera from Kenya and Karamoja (the dry area of Uganda) with negative results. In 1969 galago sera from Amani, Tanzania were tested for yellow fever neutralizing antibody and 22% were found positive. The significance of this finding has not yet been followed up. Nonetheless, one is forced to question strongly the significance of
all the yellow fever immune galagos observed over the years. Nobody has yet shown how these animals acquire their immunity; nobody knows what vector is responsible for the galago-to-galago yellow fever virus transmission. It is, therefore, impossible at present to assert any suggestion that galagos act as a source of human yellow fever infection. Other animals such as the hedgehog and the Potto which have been shown to be susceptible to yellow fever are never found in great numbers in East Africa and are not likely to be important for human infection.

**Human yellow fever immunity**

Yellow fever immune rates in the human population in East Africa have continued to remain low in most parts. The overall incidence of yellow fever immunity in 1967 was 1.3% and all were adults with exception of one child from Zaire who was found in Kigezi. Of particular interest was the total absence of yellow fever immunity in children in Bwamba. It has been known over the years as the pocket of yellow fever endemicity in East Africa. It was therefore imperative that a serological survey among the monkey population should be carried out without delay. Out of the 22 monkeys collected in the area, 48% were found to be immune; an indication that the infection was still very much present among the monkey population. Since all conditions were very favourable for yellow fever virus transmission to humans, and fearing that the infection could easily spill over into the non-immune human population, the Uganda Government was advised to repeat the mass yellow fever vaccination campaign carried out in a similar situation 33 years ago. By 1973 over 32 700 people in Toro District, including the Bwamba area, had been vaccinated.

In 1972 the yellow fever epizootic at Zika forest (mentioned later) provided an opportunity to collect as many as 2200 human sera from all age-groups in and around Entebbe. When these sera were tested for yellow fever neutralizing antibodies only six were positive despite the high virus activity that was going on in the forest. Even before the serology results were available, the Government was again advised to protect the human population around the Zika forest and neighbouring areas against any possibility of the epizootic spilling over. Over 10 000 people were vaccinated against yellow fever in a period of two weeks.

The very serious epidemic of yellow fever that affected Ethiopia (1960-1962) prompted yellow fever immunity surveys in Northern Kenya and in Karamoja (northern part of Uganda), two areas which border the part of Ethiopia affected during 1966-1967. No yellow fever immune sera were detected among the 245 sera from Karamoja sampled during the survey. Of great interest however was that yellow fever immune sera were found in the northern frontier district of Kenya with the highest rates (14.8%) ever recorded in Kenya. Some of these immune sera were from children, indicating that yellow fever infection had occurred recently, since no vaccination had ever been carried out there. These results have not yet been interpreted.

One hypothesis is that the immunity must have come into this region of Kenya as an extension of the Ethiopian yellow fever epidemic. A second hypothesis is that some of those found to be immune were infected in Ethiopia before moving into Kenya, since there is a free traffic between the two countries. Yet another possibility is that most of the yellow fever immunity was acquired in Kenya itself.

To try and elucidate the epidemiology of this high yellow fever immunity level in the northern frontier district of Kenya, intensive entomological and serological surveys were conducted in the area. None of the usually known yellow fever vectors has ever been found in these areas and no yellow fever virus has been isolated from mosquitos so far collected. The yellow fever epidemiology, therefore, still remains obscure.
Human infection: Since the study of yellow fever was started in East Africa there have been only five human cases of yellow fever disease documented. Yellow fever virus was isolated from only two of these cases. The other cases were just circumstantial.

The yellow fever epizootic in Zika forest, Uganda

The first evidence of yellow fever virus activity in this forest was in 1946 when two monkeys shot in the forest (both Cercopithecus nictitus mpange) were found to be immune to yellow fever. A year later (1947) one sentinel rhesus monkey became yellow fever immune after a subclinical infection. On both occasions intensive mosquito catches were carried out but no virus was isolated. These two observations obviously signified that yellow fever virus was active in the Zika forest and was being transmitted to monkeys.

Since 1960 routine sunset mosquito catches have been conducted in the Zika forest. It was during one of these weekly routine sunset mosquito catches that on 13 March 1972 Aedes africanus mosquitos (MP 11840) were obtained which yielded the first ever yellow fever virus from Zika forest in central Uganda. Between then and 12 June 1972, when the last isolate was obtained, 18 yellow fever virus strains were isolated from mosquitoes. All isolates were from A. africanus mosquito except one, (MP 12117) isolated from Coquillettidia fuscopennata. No human cases were detected during this period. Twenty-one monkey sera were tested for yellow fever neutralizing antibodies and 40% were positive.

In conclusion, it appears that the yellow fever situation in East Africa has not changed significantly from that observed about 40 years ago.

(i) Serological surveys both in humans and animals show that there is still evidence of yellow fever virus infection in a number of places.
(ii) Very few human cases of yellow fever disease have been recorded so far.
(iii) There has been no epidemic of yellow fever in East Africa.

It appears that the following factors have contributed to this status quo:

(a) The wide distribution of the mosquito population which is both non-anthropophilic and non-primatophilic in many parts of East Africa;
(b) cross reaction of yellow fever virus with a number of other group B arboviruses affecting its infectivity;
(c) good surveillance.
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4. 

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