



EXPERT COMMITTEE ON YELLOW FEVER

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FURTHER RESEARCH AND INVESTIGATION

by

M. Cornet, W. G. Downs, J. Hamon and H. Saenz

This document enumerates some of the points which would justify further research and investigation. It has been conceived as a provisional guide and is expected to be modified to reflect the opinions of the Committee.

1. EPIDEMIOLOGY AND ECOLOGY

1.1 Vectors

It is extremely important to compile an accurate list of the blood-sucking arthropods liable to harbour yellow fever virus and transmit it by their bite, giving priority to species in natural foci with considerable longevity or which retain a normal rhythm of activity in the dry season. In particular the vector role of ticks should be reassessed. It should be noted furthermore that the ability to transmit pathogens seems to be genetically determined. Consequently, most of the older negative experiments should be repeated and extended, working with a larger range of both virus and vector strains.

In regard to already known potential vectors, many studies and investigations are necessary.

1.1.1 Distribution

The distribution and relative abundance of Aedes aegypti are only very imperfectly known in some yellow fever endemic areas. They should be investigated wherever recent data are not available. As concerns Africa, these studies should deal in particular with the countries of Central and East Africa, the English-speaking countries of West Africa (excluding North Ghana) and territories under Portuguese rule. Similar studies might be envisaged in countries where yellow fever could be introduced accidentally, such as the Comoro Islands and Madagascar.

As concerns the Americas, the situation as regards eradication operations and recent re-infestations should be followed up.

The distribution and relevant abundance of other yellow fever vector mosquitos are generally extremely little known, except in a few limited areas. It would be advisable, both in Africa and the Americas, to obtain additional data on distribution and to organize studies on relevant abundance in the different bioclimatic zones. Priority could be given to species liable to cause epidemics.

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1.1.2 Ecology

So far, little is known concerning the ecology of the vectors, even of Ae. aegypti. Research should cover all points bearing a relationship to the epidemiology and control of yellow fever.

The localization of resting places, average longevity and the spreading powers of adults from their pre-imaginal breeding places and from sites where they feed should be known in order to organize effective imagocidal campaigns in the event of an epidemic. Moreover, flight ranges higher than those usually accepted might explain the rapid dissemination of yellow fever virus from one separate wooded area to another.

The nature and productive capacity of the different larval breeding places, the length of the pre-imaginal life-cycle and the extent of seasonal variations in density are important data in any preventive campaign whose aim is to eradicate or greatly reduce the numbers of potential vectors.

A good knowledge of maximum longevity, possibilities of survival in the dry season and feeding preferences constitutes, together with the factors already mentioned, an essential element in any epidemiological research programme.

Determination of absolute densities would be desirable, both for quantitative epidemiology and with a view to biological control.

1.2 Vertebrate hosts other than man

Though the role of monkeys as disseminators and amplifiers is well established, it would be necessary to follow up frequently their immunological status in order to detect circulation of the virus in wild life. Isolation of the virus would be more significant, and should be tried, although it is difficult to achieve, as the viraemia lasts only for a short period. The use of sentinel animals in studies should be extended.

A large variety of vertebrates other than primates have been found to give positive serological tests for yellow fever. A limited number of wild and domestic vertebrates have been experimentally infected. Whereas the primates are almost all receptive, the response of other vertebrates varies from species to species. Such studies should be intensified by looking for vertebrate hosts with a longer period of viraemia, or a transient immunity, or able to spread the virus over long distances. Susceptibility to yellow fever infection must always be taken into consideration; vertebrates which die from yellow fever may be good "amplifiers" of the disease, but they have little chance of playing a part in maintaining the virus in circulation in natural foci. The practical importance of very slight degrees of viraemia might be reassessed.

1.2.1 Distribution and abundance

The distribution of vertebrate hosts is still often only very partially known, particularly in the case of small species. Studies on this point should be extended. Generally, even less is known regarding the abundance of individuals although, together with population dynamics, it governs the real epidemiological significance of the different species of vertebrate host.

In an initial stage, priority could be given to vertebrates which amplify the circulation of the virus during enzootics and in the pre-epidemic phase.

1.2.2 Ecology

Infection of vertebrates and spread of the virus by them depend on their ecology. The chief aspects to be considered are the resting places, feeding places, usual range of activity and the possibility of long distance dispersion or migration.

1.3 Transmission cycles

It is possible that the cycles at present known are only amplifying cycles which exist merely during the epizootic and pre-epidemic phases and that the permanent cycle in natural foci is of a different type, involving neither primates nor mosquitos.

Research along these lines can only be successfully undertaken if permanent yellow fever foci are accurately located. A major effort should be placed on the detection and full study of such foci and also on the way in which the virus spreads out of those areas.

2. VIROLOGY AND IMMUNOLOGY

The minimal antigenic differences observed between the strains seem to have no practical implications and so far no special adaptation has been reported of a given strain to a given vector, but this aspect might be studied.

Study of cross immunity with other group B arboviruses has been commenced in monkeys. The importance of immunity involved by infections with other group B arboviruses in either blocking the propagation of the virus in populations or in ameliorating the severity of the disease in individuals requires further study. These investigations should be continued in order to determine the extent of the protection afforded individuals and communities by previous infection with these arboviruses.

All research which can lead to increased accuracy of the immunological methods employed for identifying virus strains and for characterizing and assaying specific antibodies should be strongly encouraged since it could greatly facilitate epidemiological studies.

Administration of immunodepressants to wild animals captured in natural foci would perhaps make it possible to detect yellow fever virus in species whose viraemia level is too low for detection by the usual methods.

3. VACCINATION

The use of 17D yellow fever vaccine in mass campaigns in tropical areas directs the attention to the need for improvement of its thermostability. There are already indications that yellow fever may be used in association with other vaccines and research on these lines should be continued. Ways of administration of the vaccine other than subcutaneous inoculation should be explored.

The possibility that yellow fever vaccine (and natural infection with yellow fever) results in protracted persistence of the virus in a masked or thus far undetected form or focus in the host calls for further study. As a corollary of this, the duration of immunity invoked by vaccination requires continuing study.

4. VECTOR CONTROL

Research should be carried out simultaneously in five different directions:

- selection and evaluation of insecticides other than Abate which can be added without risk to drinking-water,

- selection and evaluation of insecticides which can be applied by fogging against larvae and adult vectors,
- improvement and evaluation of equipment and methods for application of insecticides in a very small volume in the different bioclimatic and plant regions of yellow fever endemic areas, both from the ground and from the air,
- determination of the distribution and characteristics of insecticide-resistant vector populations,
- development and evaluation of biological or genetic vector control methods.

5. SURVEILLANCE METHODS

The improvement of surveillance methods as concern's vertebrate hosts depends firstly on the results of immunological research. Progress could also definitely be made in regard to the sampling of wild vertebrate populations.

With respect to the surveillance of vectors, one of the biggest advances would be the development of simple and effective traps giving reproducible results.