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STUDIES AND RESEARCH TO UNDERTAKE CONCERNING YELLOW FEVER

by

J. Hamon and M. Cornet
Medical entomologists, ORSTOM

1. INTRODUCTION

It is difficult to draw up a complete list of studies and research to undertake while the viewpoints of the participants in the WHO Expert Committee on Yellow Fever are not yet known. Consequently, the following enumeration, although extensive, cannot be regarded as restrictive. The various suggestions are submitted following the order adopted in the draft agenda.

2. EPIDEMIOLOGY AND ECOLOGY

2.1 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.

2.1.1 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.

As concerns the Americas, the situation as regards eradication operations and recent re-infestations should be determined. Similar studies might be envisaged in countries where yellow fever could be introduced accidentally, such as the Comoro Islands and Madagascar.

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.

2.1.2 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.

2.2 Vertebrate hosts other than man

A large variety of vertebrates 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.

2.2.1 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 abundancy 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.

2.2.2 Ecology

Infection of vertebrates and spread of the virus by them depends 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.

2.3 Transmission cycles

It is possible that the cycles at present known are only amplifying cycles which exist

merely during the enzootic 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.

3. VIROLOGY AND IMMUNOLOGY

The minimal antigenetic 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. 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.

4. VACCINES AND VACCINATION

It would be especially valuable to have a thermostable vaccine whose pathogenicity is as low as possible, either by improving the heat stability of 17 D vaccine or by eliminating the neurotropic properties of the Dakar vaccine, or by isolating other vaccinal strains combining the advantages of both the 17 D and the Dakar strains.

5. 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.

6. SURVEILLANCE METHODS

The improvement of surveillance methods as concerns 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.