Methods of Surveillance for Yellow Fever

Conduct of serological surveys in human beings (mode of sampling sera, number required, multipurpose sera, areas and groups of priority, etc)

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The conducting of serological surveys in human beings in the practice of permanent surveillance of yellow fever is usually done in better conditions than in early recognition of suspected cases, with no pressure from events. One may even say that reliability of the results will depend on the efficiency of the organization of the survey; sampling of the population and collection of the sera.

1. Sampling of the population

The sampling must fit in with the two aims of the survey: to detect the circulation of the virus and to evaluate the population at risk.

Detection of the circulation of the virus is the detection of known or unknown endemic focus in permanent or transient activity. This implies a geographical factor and a periodical follow-up. The geographical factor is dependent on the ecology of the virus, and the choice of different favourable environments will lead to procedure of the sampling by the stratification technique. Hot and humid equatorial forests are favourable to the permanence of vectors which maintain a continuous cycle of transmission of the virus. Periodically dry savanna and fluctuant populations of vectors will support episodic incursions of the virus, mostly during and soon after the rainy season. The most sensitive zone is the fringe of mosaic forest. Such studies may be coupled with advantage with animal and entomological surveys.

Contacts with the virus are dependent upon the bionomics of man. Chances of contact differ according to age, sex, habitat, occupation and length of residence. The maximum prevalence will be looked for in older age groups, but a major interest is to define the time of the infectious contact. In America, endemic yellow fever, or jungle yellow fever, occurs among adolescents or adult workers going into or close to the forest where the virus is circulating. In Africa, natural immunity may appear in very young children (Brès, 1963). Non residents or immigrants, are of exceptional interest and they may be considered as sentinels for the detection of the virus. Thus, according to the circumstances, the serological survey is based either on a representative sampling of the whole population or on a purposive sampling.

The evaluation of the population at risk considers the negative results and mainly their prevalence in different age groups. Different situations at high risk and low risk may be characterized by the survey. It has been said that the risk of epidemic transmission disappears in a population when 80 per cent are immune. In yellow fever such a figure is certainly dependent, on the density of the circulation of the virus, and on the possibilities of transmission by local vectors. No precise figure can be given for all
situations, but an epidemic outbreak occurred in Senegal (Brès 1966) where 40 per cent of the population were not protected by vaccination. Surveillance of the epidemic risk is of special interest in heavily populated areas in the endemic zone, or close to it, and this consideration would justify a priority in planning a country-wide programme of surveys.

A serological survey after a mass campaign will appreciate the effectiveness of the vaccination (% of coverage). Failures in vaccination may be relevant from different possible causes - insufficient proportion of the population being reached; defective inoculation or bad quality vaccine at the time of inoculation. The two last causes will appear in the percentage of positives among the "vaccinated" group. The prevalence of protected people may be followed up periodically or estimated in the future by extrapolation from the growth rate of the population.

Generally, a sample size of around 100 sera will provide a satisfactory degree of precision, but this number must be increased should the frequency of positive sera be very low. Practical experience indicates that 25 sera per age group (0-10; 11-20; 20-40 and above) are frequently convenient. "It is the usual experience to find that the percentage of immune persons rises with age in endemic areas, and the minimum number of tests which would give dependable negative results would therefore need to be larger in the case of children than in that of adults" (Sawyer 1936). If the rates are to be compared between two different populations, or two different intervals, the sampling must be convenient for a statistically significant comparison. Longitudinal surveys imply a good identification of donors selected for their easy collecting. Schools are a very convenient source of such sera.

Serological surveillance of yellow fever is accomplished at lower cost and less difficulties in participating to a multipurpose serological survey. These surveys usually cover a too important number of sera for the single purpose of surveillance of yellow fever and it is necessary to select subsamples. In this, one will look for a fair representation of the different strata in which the virus could circulate. Multipurpose surveys, with collaboration of WHO Serum Reference Banks will make available "posterity samples" for retrospective studies.

2. Collection of sera

In multipurpose and in longitudinal surveys, blood must be collected by venepuncture. Children under three years of age need to be punctured in the femoral vein. This procedure is sometimes badly considered by the population, but more easily accepted in epidemics. When the survey is directed to yellow fever, finger prick puncture will give 0.25 to 0.50 serum, or sometimes more, which is convenient for several reactions by microtechniques. Finger prick practice is generally well accepted by the population, even in young children. The bleeding is more important during the warmer hours of the day than early in the morning.

A surveillance survey justifies a minimum field laboratory equipment to separate sera from clots under good aseptic conditions. Good conditions must be available for the transportation of sera under refrigeration.

3. Serological tests

The choice of reactions must fit also with the two aims of the survey: detection of the circulation of the virus and evaluation of the population at risk. Three tests are currently used: haemagglutination inhibition (HI), complement fixation (CF) and neutralization (N). Other methods may prove of value for surveillance but they have not yet been assessed.
The high number of sera to deal with would suggest the use of the HI test as a screening method for negative results. One must remember that a serum may look HI negative before the apparition of antibodies or after their disparition. In the first case, the CF can be found positive and in the last the N antibodies may still persist. Specificity of the positive responses with the yellow fever antigen must be ascertained as much as possible. The introduction in the HI test of other group B antigens locally prevalent will evidence a primary type response, which is specific, from a secondary type response with a broad pattern of antibodies.

The CF test is generally considered of less value in such a survey, but in certain cases it can contribute to the distinction between homotypic and heterotypic antibodies. The N test in mice has been the most widely used, especially in 1932-1950 in an attempt to locate the American and African endemic zones. This test is more specific than the HI test, but it also leaves many secondary type responses with a doubt on their aetiology (Theiler, 1958).

A still more specific test is needed, as well as an effort in standardization of techniques and interpretations. The treatment of sera to evidence IgM antibodies has not been sufficiently assessed in serological surveys. The use of microtechniques brings a greater facility when a great number of tests are to be dealt with as in large surveys. Automation will also be an advantage.

4. Recording of information

The important number of serological surveys performed in Africa have been reviewed by Bonel et al (1954) and Brès (1970). Dispositions should be taken as soon as possible to adapt the next serological surveys to the computerized storage of data, as this is being done with multipurpose surveys.

REFERENCES

Brès, P. (1966) Méd. trop, 26, 21