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Agenda item 9

MINIMUM LABORATORY REQUIREMENTS FOR THE CONDUCT OF A LEPROSY CONTROL PROGRAMME INCLUDING TRAINING NEEDS AND LABORATORY FACILITIES

by

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1. Drug Sensitivity Testing

There is an increasing interest in many developing countries for the building and maintenance of mouse foot pad laboratories (MFPL) to perform dapsone sensitivity tests for M. leprae. Before embarking on such relatively expensive programmes, all the aspects should be considered, the objectives clearly formulated and the value of the information expected should be judged.

The MFP Laboratory

Buildings and Equipment

This entails proper laboratory space, with tables, drawers, a hood, an autoclave (may be a table model), small equipment, possibly air conditioning, an office with furniture. Equipment amounts to about US $ 25 000.

An animal house, air conditioned, rat- and mosquito-proof, equipped with racks and cages, a "kitchen" for cleaning and steaming or autoclave sterilization of cages and drinking bottles.

The animal house will in most instances have two rooms : one for keeping inoculated animals and one for breeding, since only in exceptional circumstances will laboratory mice be commercially available. A third rat-and mosquito-proof room is necessary for keeping the mouse food and litter reserve. This is in practice the most difficult item, since mouse food pellets will be unavailable in most countries and the mixture of ingredients will have to be made fresh from locally-available resources. An important laboratory could envisage the acquisition of a pelletting machine; this is however very expensive.

Litter may be locally obtained wood dust or sawing, but will have to be sterilized to kill insects, preferably in a dry air oven, which should also be available.

For actual dapsone sensitivity testing, a blending machine to incorporate the drug in the mouse diet is necessary.

Personnel

One person trained in the mouse foot pad technique should be helped by an animal caretaker/breeder, having had a minimum of appropriate training. Lastly, cleaning personnel is necessary.

Objectives

Most drug sensitivity testing of M. leprae has up to now been done for dapsone

After the period of anecdotal or case reports of secondary resistance, continuous studies of particular patient groups and formal surveys among populations have been performed. These have revealed that secondary dapsone resistance occurs worldwide, at the earliest eight years after start of therapy up to 20 years and longer.

Therefore, and because of the time necessary to obtain a result - at least six months and possibly as long as nine to twelve months - dapsone sensitivity testing for the benefit of the individual patient is useless. In our own chemotherapeutic studies, for example, we apply the rule of thumb that any patient previously treated for five years or more with dapsone monotherapy is at risk of dapsone resistance and the therapeutic regimens are adapted in consequence. Another possible strategy is as in the regimen for multibacillary patients, as proposed by the WHO Study Group on Chemotherapy of Leprosy in Control Programmes, which are active on dapsone-sensitive and dapsone-resistant strains as well.

Another application of DDS sensitivity testing could be to convince clinicians of the reality of the problem, but this cannot justify the heavy investment.

Again, the problem of primary dapsone resistance is a subject for particular studies and should not be part of a long-lasting effort, justifying heavy investments and long time recurrent expenses.

In most countries other drugs such as clofazimine or rifampicin have not been used or were only introduced too recently for resistance to occur.

In conclusion, there is no need at present, in leprosy control programmes, for provisions of drug sensitivity testing. However, there will be a need for some MFP facilities in the future, for two particular applications :

a) Investigation of suspected cases of relapse after stopping combined therapy in multibacillary patients. Suspected relapse may be real relapse or reversal reactions; it will be useful to document these cases by MFP inoculations, although a sole histopathological examination may be very informative.

b) To determine the drug sensitivity of M. leprae responsible for relapses. Although on theoretical grounds, any relapse after combined therapy should be with fully sensitive organisms, it will be important to document this in mice, at least in a number of cases.

It is clear that for these applications, MFP laboratories are not necessary in every region or even every country, but that collaboration should be established with existing laboratories even at a distance.

2. Histopathology

As mentioned before, histopathology is useful for the distinction between relapses and reversal reactions. Fixed tissue specimens lend themselves quite well to transportation over long distances, and here again, collaboration with specialized histopathology laboraties should be sought.

3. Monitoring of Drug Intake

In all cases, some monitoring of drug intake is extremely important, either to verify patient compliance for the drugs that are taken unsupervised, or to have a control on the drug providers.

Urine can be checked for the presence of rifampicin by simple visual inspection or after chloroform extraction.

There are several test procedures to detect DDS in the urine from DDS/creatinine ratio determination to ELISA or haemagglutination tests. Some drugs may be mixed with a small amount of isoniazid, allowing the detection of isonicotinic acid in the urine, by simple colorimetry.

Each of these techniques requires relatively simple equipment and some laboratory space.

4. Drug Quality Control

We are sometimes asked to control the quality of drugs available in some countries, particularly in the absence of a national control laboratory. This occurs most frequently with rifampicin transported and distributed in hot climates. Again, for such accidental requests, collaboration with existing national control laboratories

in other countries is the most practical solution at present. (This however does not solve the general problem of quality of imported drugs in such countries, for which appropriate laboratories are mandatory, eventually on an international agreement basis.)

SUMMARY

There is no need for mouse foot pad facilities for drug sensitivity testing to start leprosy control programmes, since the size of the problem is known.

There will however be a need for some mouse foot pad work in later stages, to document relapse cases and test relapse strains for drug sensitivity. Arrangements should be made to ship such specimens to existing laboratories.

There is more need however for facilities for monitoring drug intake. Finally there may be incidentally some need for quality control - where non-existent - of imported drugs, which can be solved through collaboration with existing facilities in other countries.