

MONITORING AND
EPIDEMIOLOGICAL
ASSESSMENT
OF THE PROGRAMME
TO ELIMINATE
LYMPHATIC FILARIASIS
AT IMPLEMENTATION
UNIT LEVEL

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World Health
Organization

LYMPHATIC FILARIASIS

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lymphatic filariasis
at implementation unit level**

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PREFACE

The Global Programme to Eliminate Lymphatic Filariasis was launched in 2000 and since then has expanded its mass drug administration coverage with the recommended two-drug co-administration from 3 million people in 12 countries in 2000 to more than 70 million people in 36 countries in 2003.

Throughout this period, the need for standardized guidelines on monitoring and epidemiological assessment of the Programme at implementation unit level has become increasingly evident because this is the level at which the core programmatic operations are conducted. These guidelines are based on current knowledge and understanding of the epidemiological aspects of the disease. However, in view of the rapid evolvement of both scientific advances and experience in implementation of national elimination programmes, adaptation of the guidelines might be required to address particular circumstances.

In light of the diverse responsibilities of the health personnel in charge of lymphatic filariasis elimination programmes, the authors have developed guidelines that are as concise as possible. Annexes have been included to provide the most relevant technical background information while avoiding too much detail in the body of the guidelines.

Similar guidelines are planned to assist health personnel at the level of the implementation unit in other areas such as drug distribution, social mobilization and disability prevention and control.

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Dr P.K. Das, Director, Vector Control Research Centre (VCRC), Pondicherry, India; Professor Dejian Sun, Institute of Parasitic Diseases, Chinese Academy of Preventive Medicine, Shanghai, China; Dr J. Gyapong, Health Research Unit, Ministry of Health, Accra, Ghana; Professor J.D.F. Habbema, Center for Decision Sciences in Tropical Disease Control, Department of Public Health, Erasmus University, Rotterdam, Netherlands; Dr R. Houston, LF Support Center, Emory University, Atlanta, GA, USA; Dr E.A. Ottesen, Director, LF Support Center, Emory University, Atlanta, GA, USA; Professor D. Molyneux, Director, LF Support Center, Liverpool School of Tropical Medicine, Liverpool, United Kingdom; Dr G. Biswas, Lymphatic Filariasis Elimination (CEE/FIL), World Health Organization, Geneva, Switzerland; Dr S. Yactayo, Lymphatic Filariasis Elimination (CEE/FIL), World Health Organization, Geneva, Switzerland.

These recommendations were endorsed by TAG-ELF during its fourth meeting held from 25 to 28 March 2003 in Veyrier-du-Lac, Annecy, France. Subsequently, the recommendations were drafted by WHO staff and the Emory LF Support Center, Atlanta, USA and approved by TAG-ELF at its fifth meeting held in Geneva, Switzerland from 3 to 6 February 2004.

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ELIMINATION OF LYMPHATIC FILARIASIS AS A PUBLIC HEALTH PROBLEM

Lymphatic filariasis (LF) is endemic in 83 countries and territories, with more than a billion people at risk of infection. Some 120 million people are affected worldwide of whom about 40 million are incapacitated and disfigured by the disease. Although LF is not fatal, it has been ranked one of the world's leading causes of permanent and long-term disability.¹

Donated (ivermectin and albendazole) or low-cost (diethylcarbamazine citrate) drugs are now available in forms that are both safe and effective. These drugs, when co-administered, reduce the number of circulating microfilariae in the blood and in so doing, prevent further transmission from occurring ultimately making elimination possible.

In 1997, the fiftieth World Health Assembly resolved that LF should be eliminated as a public health problem (resolution WHA50.29). The World Health Organization (WHO) proposed a comprehensive strategy for achieving this goal, which included interrupting transmission by drastically reducing the prevalence levels of microfilaria from communities in which LF is endemic and implementing interventions for those already infected to prevent and manage the disabilities it causes.

The Global Programme to Eliminate Lymphatic Filariasis began its first mass drug administration (MDA) campaign in 1999 in Samoa. By 2003, more than 70 million people at risk in 36 endemic countries were covered by MDA campaigns. Other countries have already started or are continuing the process of mapping at national level to ascertain in which areas LF is endemic.

At the level of the implementation unit (IU),² the responsibility for implementation of the programme generally rests with the District Officer or equivalent, either directly or through a District Management Team.

Effective surveillance can help to fulfil the aim of eliminating LF as a public health problem.

STRATEGY TO ELIMINATE LYMPHATIC FILARIASIS AS A PUBLIC HEALTH PROBLEM

Interruption of transmission

A consolidated, evidence-based strategy to interrupt transmission of filariasis in an endemic country is the administration of effective antifilarial drugs to the entire population at risk.

There are two possible kinds of MDA:

- **MDA using tablets:** this consists of an annual single-dose of a combination of two drugs administered for at least five or six consecutive years to the entire eligible population living in the endemic areas, or until the criteria for stopping MDA is reached.
- **MDA using diethylcarbamazine-citrate (DEC) fortified cooking salt:** this involves the distribution of common salt fortified with DEC to the entire population of the endemic area for one or two years.

The decision about which type of MDA to implement depends on the local situation of the country in question.

¹ *The world health report 1998 — Life in the 21st century: a vision for all.* Geneva, World Health Organization, 1998.

² Implementation unit (IU) is defined as the designated level of the administrative unit in a country, for which the decision to administer antifilarial drugs to the entire population is taken if it is identified as having indigenous transmission or endemicity.

Prevention of disability associated with lymphatic filariasis

The goal of this component of the programme to prevent disabilities associated with LF is to enable people with the disease to have a better quality of life and to ensure their full participation in community life, both socially and economically.

Prevention of LF-associated disability involves:

- **primary prevention:** directed at the at-risk population using MDA to interrupt transmission and prevent the occurrence of new infections.
- **secondary and tertiary prevention:** aimed at people who are already affected by the disease, and can be achieved through disability management as part of home-based long-term care and through changing the attitudes of communities.

THE IMPORTANCE OF MONITORING

Monitoring of implementation is a vital element in programme management that enables the success of the strategy to be assessed.

Monitoring is not just a matter of gathering data and reporting them to a higher level, but should assist programme managers at the national and subnational levels to achieve the programme objectives. Furthermore, monitoring should make it possible to assess the impact of interventions and enable the programme manager to assess the current status of the programme. It enables progress to be measured as well as providing information on which to base important decisions such as when to stop MDA.

If the results are not as foreseen, it will be necessary to establish why and to take appropriate steps to correct the situation. Effective monitoring can detect mistakes the moment they occur making it possible to rectify them and in so doing, avoid delays in achieving elimination.

What should be monitored?

Although, in principle, each step of programme implementation can be monitored (including funding, drug coverage, training of personnel in qualitative and quantitative terms, impact of drugs on microfilaraemia, interruption of transmission, etc.) this would be expensive and in many cases unnecessary. The selective monitoring of a few critical aspects of the programme is generally sufficient and cost-effective.

When assessing interruption of transmission it is most important to consider the following aspects:

- the number of people who have ingested the drugs; and
- the impact of MDA on prevalence of microfilaraemia.

Which monitoring indicators are needed?

Specific indicators for monitoring should be identified so that they can be compared over time and between different IUs or countries.

All personnel involved in collecting and using data at IU level should be familiar with the monitoring indicators and methodology used. Personnel should fully understand the significance of these indicators and should know

what bearing they have on the field activities carried out as well as an understanding of their limitations. A better understanding by health workers of the importance and significance of the monitoring process will allow them to participate more effectively in the programme.

IMPLEMENTATION UNIT (IU)

The definition of an IU is the designated level of the administrative unit in a country for which the decision has been made to administer antifilarial drugs to the entire population once the area has been identified as one in which the disease is endemic or in which indigenous transmission occurs. It must be identified before the initial assessment and mapping of designated IUs takes place. In most countries, the second administrative level – usually the district – is identified as the IU.

Most decisions on implementation and monitoring are taken at IU level.

Normally, the choice of which administrative level will constitute the IU is taken at national level in consultation with the National Task Force. However, the choice is influenced by feedback received from lower administrative units on the distribution of the disease within those units. If the filarial infection is focal, a lower administrative level is chosen as the IU, whereas if the infection is more widespread, a higher administrative level is chosen.

Preliminary information on the lymphatic filariasis status of implementation units

Before IUs are targeted for MDA, the national programme manager categorizes them into one of the three categories described below:

- **endemic (red):** IUs where the average native population, or any subunit of population (village or urban area), has an infection rate of 1% or more;
- **non-endemic (green):** IUs where either the ecological situation is not conducive to transmission, e.g. altitudes above 1600 metres, dry arid areas, or where previous surveys have indicated an infection rate of under 1%;
- **uncertain (grey):** IUs where the LF status is still undetermined and where further surveys are required to assess the infection rate.

Assessment of endemicity of lymphatic filariasis in the implementation unit

Before the initial assessment of LF endemicity is made using either immunochromatographic test (ICT) cards or a night-blood microfilaraemia survey, it is necessary first to assess how widespread the disease is in the IU(s) and to inform the authorities at national level.

This can be ascertained through reviewing:

- historical data;
- unpublished and published data on filariasis;
- reports of medical and health services at district level or its equivalent;
- hospital records on hydrocelectomy; and
- the existence and use of local names for the terms "hydrocele" and "lymphoedema".

This review should make it possible to distinguish those areas in which LF is likely to be endemic and which require further investigation.

At-risk population in the implementation unit

Once mapping has been completed using antigenaemia or microfilaraemia surveys and an IU has been declared endemic for LF (i.e. LF prevalence $\geq 1\%$), the entire population in that IU is considered at risk.

How to calculate the total population of the implementation unit

The following are possible sources of data from which to calculate the total population:

- **Census:** in many countries a nationwide census is carried out, generally at 10-year intervals, and the data obtained are available from the administrative units chosen as the IU. To estimate the total population in the years between two censuses it is necessary to multiply the base population by the population growth rate.
- **Special surveys:** in the absence of census data, surveys might be carried out under different programmes under the auspices of the Ministry of Health or other development sectors to estimate the population of the different administrative levels.
- **Enumeration of household population before MDA:** in many LF elimination programmes, household surveys are carried out to enumerate households to record the target population. These data can also be used for other health activities.

It is advisable to use official census data, if available. However, if the official census is not recent enough or is considered inaccurate, the IU concerned will have to judge which is the most accurate source to reflect its total population. It is also advisable to state the source of the data and to use the same source whenever the total population is used for calculating indicators. In case of doubt, advice should be sought from the national level.

Eligible population in the implementation unit

Certain population groups such as pregnant women, children under 2 years of age and the severely ill should be excluded from programmes of MDA that use co-administration of DEC plus albendazole.

Where co-administration of ivermectin plus albendazole is used, pregnant women, lactating women in the first week after birth, children less than 90 cm in height (approximately equivalent to a weight of 15 kg) and the severely ill should be excluded from MDA.

The *eligible population* for MDA is the population not excluded according to the above-mentioned criteria. When recording the eligible population, the source of data should be stated. As far as possible, the same data source for total population and eligible population should be used.

MONITORING FOR AN EFFECTIVE MASS DRUG ADMINISTRATION CAMPAIGN

The objective of MDA is to administer antifilarial drugs, once a year, to all eligible individuals in the endemic IU. The greater the number of people who ingest the drugs, the better the chance of successfully interrupting transmission. Correspondingly, the smaller the number of people ingesting the drugs, the lesser will be the

probability of stopping transmission and consequently more MDA rounds will be required. To measure this aspect of drug ingestion, the following indicators have been defined at IU level:

Geographical coverage indicator: is defined as the proportion of villages or urban areas covered by MDA in the targeted IU during the reported year.

$$\text{Geographical coverage of villages} = \frac{\text{number of villages covered}}{\text{total villages in IU}} \times 100$$

$$\text{Geographical coverage of urban areas} = \frac{\text{number of urban areas covered}}{\text{total urban areas in IU}} \times 100$$

The people of an IU live in rural or urban locations such as villages, hamlets, towns or cities. Once the IU has been found to be endemic for LF, the whole population is considered to be at-risk and all the eligible population is targeted for MDA and all the villages and urban areas need to be covered. This indicator helps the programme manager to assess whether the drug distributors have covered all these subunits. Sometimes certain parts of the IU are not covered, resulting in a low coverage. The geographical coverage indicator is used to explain this kind of situation.

The total number of villages and urban areas within the IU should be available as this will have been the basis for all planning exercises in it. Once the MDA has been completed, the reports of MDA coverage received from the drug distributors assigned to different villages and urban areas will provide the numerator. If the IU is a very high administrative level such as a province, it may be useful to aggregate the village data by subunits, e.g. by districts or prefectures.

Drug coverage indicator: is defined as the proportion of individuals who actually ingest the drugs. Two indicators are used to measure this: *reported coverage* and *surveyed coverage* (see also Annexes 1–5). Normally, at the time of drug administration, the responsible person (drug distributor) will record in his or her register:

- the number of individuals who swallowed the drugs;
- those who were not eligible; and
- those who were eligible but did not take the drug for various reasons.

These data on the number of people who took the drugs are compiled by the drug distributor for the area (village or urban area) he or she is responsible for and sent to the IU authorities either directly or through an intermediate level. As the IU authorities will compile data reported from all the drug distributors, this is termed as the *reported coverage* and is calculated on the basis of both the total population of the IU and the eligible population of the IU as indicated below:

$$\text{Drug coverage reported in total population by IU} = \frac{\text{number of people who were reported to have ingested the drugs}}{\text{total population in IU}} \times 100$$

$$\text{Drug coverage reported in eligible population by IU} = \frac{\text{number of people who were reported to have ingested the drugs}}{\text{total eligible population in IU}} \times 100$$

The drug coverage among the total population is a reflection of what proportion of the at-risk population is being covered by MDA and has an epidemiological value. The coverage among the eligible population is directly related to the MDA effectiveness. Both indicators are important in enabling the IU authorities to assess the status of the elimination programme.

The IU authorities should ensure that data on coverage are reported by the drug distributors or peripheral reporting units immediately after each MDA campaign for compilation and calculation for that IU. It is vital for the assessment and management of the Programme that data on reported coverage are accurate.

Whereas, in most situations, the reported drug coverage should reflect the actual drug coverage, in some instances this has not been the case. This may be because:

- The drug distributor left behind drugs for household members who were absent during his or her visit and recorded them as having been consumed presuming that the absentees would take the drugs on their return.
- In his or her enthusiasm to show a good performance, the drug distributor reported a higher than actual coverage.
- The data on total population or eligible population were outdated or incorrect resulting in an erroneous calculation of drug coverage.

As the IU authorities should be concerned to know the correct drug coverage, some of the above issues could be resolved by proper training and supervision of the drug distributors and their supervisors. It is, nevertheless, recommended that the reported coverage be verified through a *surveyed coverage*. This has the advantage of being independent of the above problems in the reported coverage.

Surveyed coverage indicator: is a measure that complements and verifies the reported coverage by using active, population-based cluster survey methods. Thirty clusters of 30 individuals per cluster are used. It is calculated as:

$$\frac{\text{Total number of individuals identified by household survey as having ingested the drugs}}{\text{Total number of individuals residing in all the surveyed households on whom information on drug ingestion could be elicited}} \times 100$$

As the surveyed coverage will require additional resources, it does not have to be done after every round of MDA, but at least once during the course of the Programme in the IU, or more frequently if possible. It may also need to be carried out following a request by the national LF programme manager when abnormalities have been detected in the Programme, such as, reported coverage rates judged to be too low or too high. The surveyed coverage should preferably be carried out by a team from outside that IU, or at least by team members who were not responsible for the implementation of MDA in that IU.

The methodology to carry out the surveyed coverage is given in detail in Annex 1 and details of interpretation and follow-up are summarized in Table 1.

Table 1 How to interpret and follow-up on reported and surveyed coverage

Finding/observation	What to look for	Corrective action
Reported coverage and surveyed coverage are both low	<p>Check the geographical coverage of areas within the IU being left uncovered.</p> <p>Check for coverage in the different age-groups (less than 2 yrs, 2–5 yrs, 6–14 yrs and >14 yrs) to determine whether any particular age-group is being left out.</p> <p>Check the reasons for the eligible population not taking the drug.</p> <p>May need a special Knowledge, Attitude and Practices (KAP) survey in the population to assess the problem.</p>	<p>Depending on the problem, may require MDA in the areas not yet covered in the IU.</p> <p>Improve social mobilization of communities.</p> <p>Improve the skill and motivation of drug distributors by better training and supervision.</p>
Reported coverage is much higher than surveyed coverage	<p>Drug distributors incorrectly reporting on ingestion of drugs.</p> <p>Figures on total population and eligible population are incorrect or outdated, or people from outside the IU are also taking the drugs from the drug distributors and are being recorded as residents of the IU.</p>	<p>Improve the skill and motivation of drug distributors by better training and supervision.</p> <p>Ask the drug distributors to record the non-resident individuals ingesting the drugs separately and not to include them in the numerator for calculating the drug coverage for the IU.</p>
Reported coverage is much lower than surveyed coverage	<p>Figures on total population and eligible population are incorrect or outdated.</p>	<p>Update and correct population data.</p>
Both reported coverage and surveyed coverage are high	<p>A good reporting system is in place. communities and drug distributors are motivated.</p> <p>All elements of the MDA programme are well in place and functional.</p>	<p>Maintain the Programme momentum for next year to maintain coverage levels.</p>

MONITORING THE IMPACT OF MASS DRUG ADMINISTRATION ON MICROFILARAEMIA

The objective of MDA campaigns is to reduce the level of microfilaraemia in infected individuals to such an extent that the potential for transmission is reduced to levels where further recrudescence is prevented after stopping MDA. In this way, transmission is interrupted.

For effective monitoring of impact, the following need to be considered:

- choice of diagnostic tool; and
- sampling and frequency of measurement.

Choice of diagnostic tool

A number of diagnostic tools are currently available for monitoring the impact of MDA including:

- night-blood films for microfilaraemia;
- *Wuchereria bancrofti* antigen detection tests that can be done any time of the day;
- filarial antibody detection tests; and
- polymerase chain reaction (PCR) techniques in humans and mosquitoes for the detection of filarial infection.

The night-blood films for microfilaraemia and the antigen detection tests have been standardized and are currently recommended for use in the Programme. The other diagnostic tests are still being standardized and assessed for their interpretation in the field.

The antigen detection test is currently available only for *W. bancrofti*. As it measures the presence of adult worm antigen, it is a useful tool for measuring the presence of infection in the community during the initial assessment phase when identifying IUs in which this organism is endemic. It can also be used to look for new infection in children born after the start of MDA. However, it is not very effective for measuring the impact of MDA on microfilaraemia as, given the presence of adult worms, the test may still be positive despite a significant reduction in levels of microfilaraemia. **The standard night-blood films examination remains the recommended diagnostic tool to assess the impact of MDA on microfilaraemia.** Techniques for night-blood film examination for microfilariae are well described and are not repeated here.³

Sampling and frequency of measurement

Ideally, when the frequency of a health event is measured, it should be representative of the geographical area. The ideal sample size for measuring microfilaraemia levels of 1% or less, with a reasonable margin of error, would require the testing of around 30 000 individuals. Moreover, a simple random sampling of individuals in the IU would be very cumbersome and cluster sampling, besides being very expensive, may not be appropriate because of the focal nature and variability of microfilaraemia rates. A practical solution for assessing trends has been recommended: that microfilaraemia be monitored in sentinel sites at appropriate intervals. Although the data from the sentinel site will not be representative of the entire IU, they will provide the IU authorities with reasonably accurate information on the trend of the infection in the sentinel sites over the course of the Programme.

However, the shortcoming of monitoring impact in sentinel sites should be recognized. Since these sites are known to the health workers responsible for implementing MDA in the area and are given special attention, it could be that a greater impact is seen in these sites than in the rest of the IU. To minimize this risk and to assess other sites in the IU, it is recommended that night-blood surveys be undertaken in an equal number of spot-check sites. Unlike the sentinel sites, which remain the same over the course of the Programme, different spot-check sites are chosen for every survey. The spot-check sites provide additional information on the prevalence of microfilaraemia in the IU.

THE CHOICE OF SENTINEL AND SPOT-CHECK SITES

Before the first round of MDA is implemented in the IU, the sentinel sites for that IU need to be identified, preferably in consultation with the national programme manager. These sites will be used to ascertain the baseline indicators (parasitological and clinical signs) and the progress indicators and will make it possible to carry out periodic evaluation of the parasitological indicators.

How many sentinel sites are needed for each implementation unit?

The greater the number of sentinel sites, the more data will be available. However, as surveys in the sentinel sites require resources, it is necessary to strike a balance between the resources available and the number of sentinel sites. It is recommended that two sentinel sites should be identified for every IU and each sentinel site should have a minimum population of 500 persons. When the IU is very large or has a population of over 1 million, more sentinel sites need to be chosen at the rate of at least two sentinel sites per million population or one for every 500 000 people.

In some countries where, because of very focal distribution, the size of the administrative unit chosen as an IU is very small (e.g. a subdistrict or village), it may not be feasible to choose two sentinel sites per IU. In such situations it is practical to choose reference sentinel sites for a group of IUs. However, it should be noted that, when grouping IUs for the common reference sentinel sites, the IUs should be in geographical proximity, share similar epidemiological characteristics and should all have implemented MDA at the same time. Decisions based on the epidemiological trend in the common reference sentinel sites would be applicable to all IUs in the group and not only to the IUs in which sentinel sites are located. As this arrangement is an exception to the usual procedure, the advice of the national programme manager and/or the national task force may be required.

Characteristics of sentinel sites

The characteristics required of a sentinel site are as follows:

- It should have a population of at least 500.
- Ideally, it should be chosen from an area of high transmission (high disease or parasite prevalence, if known) or from an area where difficulty in achieving high drug coverage is anticipated. The rationale is that these are the areas within the IU likely to require the longest period of time for interruption of transmission. However, when such information for the IU is not available, the sentinel site is chosen randomly.⁴
- It should have a stable population that is not affected by migration and should have the same demographic characteristics as the IU as a whole.
- Once chosen, the same site should act as the sentinel site throughout the course of the Programme, whereas the spot-check sites should not be fixed but changed for every survey.

Characteristics of spot-check sites

Spot-check sites have the same characteristics as sentinel sites but, unlike the sentinel sites, which remain the same over the course of the Programme, different spot-check sites are chosen for every survey. Spot-check sites provide additional information on the prevalence of microfilariemia in the IU.

Size of population of sentinel and spot-check sites

Both types of site should have a population of at least 500. In order to avoid statistical bias, as far as possible, the population should be of a similar nature to that of the IU (e.g. farmers, fishermen or city dwellers). All members of the population of the sites should be included, or, where the population of the site is too big (i.e. it exceeds 500 inhabitants), a part of it can be chosen. Children of all ages, as well as pregnant women, should be included in the survey.

⁴ Random is a statistical term indicating that the choice is made by chance following a table of random numbers. A list of villages can be drawn up, given a number and then chosen at random.

In rural areas, a county, village, hamlet or a subdistrict can be chosen whereas in cities or towns, boroughs or wards can be chosen.

Survey for baseline indicators

The measurement of the indicators in sentinel sites serve as the baseline data for tracking the impact of the Programme from start to finish. It is important to remember that these indicators will be used to measure the impact of MDA on microfilaraemia and the extent to which interruption of transmission is being achieved in the sentinel sites.

The minimum set of essential indicators required includes:

- prevalence and density of microfilariae;
- clinical signs of the disease; and
- MDA coverage (except at pre-MDA survey).

Prevalence and density of microfilariae in sentinel and spot-check sites

The prevalence and density of microfilariae, together with drug coverage, are currently the best indicators for measuring the impact of MDA. The standard method of night-blood surveys of the entire sentinel site population (around 500) is used to determine the prevalence and density of microfilariae. Because the filarial infection generally shows nocturnal periodicity, slides are made from blood obtained from finger-pricks between 22:00 and 02:00 to detect microfilariae. Thick blood smears are made and subsequently stained and examined following the standard procedure (see Annex 8).

The microfilaria prevalence (mf%) is calculated as the proportion of blood slides found positive for microfilariae, i.e:

$$\frac{\text{no. of individuals whose slides are positive for microfilariae}}{\text{total no. of individuals examined for microfilariae}} \times 100$$

The microfilarial density (mfd) is the average number of microfilariae in slides found positive for microfilariae per ml of blood⁵ (presuming 60 µl per slide) calculated as:

$$\frac{\text{total count of microfilariae in the slides found positive}}{\text{total no. of slides found positive}} \times 16.7$$

Example: You have to tally the density of microfilariae in 10 samples. All the blood samples have been collected as a 60 µl sample (Table 2).

⁵ *Bench aids for the diagnosis of filarial infections.* Geneva, World Health Organization, 1997.

Table 2 Example showing tally of density of microfilariae in 10 blood smears

Serial no. of person tested	No. of microfilariae
1	120
2	0
3	0
4	0
5	0
6	60
7	0
8	0
9	0
10	0
	Total microfilariae 180

For this exercise, take an imaginary population of 10 people, rather than 500 as would be used in reality. Only two smears are positive giving a total of 180 microfilariae.

If we apply the formula:

$180 \times 16.7/2 = 1503$ mf/ml we find that in this site the mean density is 1503 microfilariae/ml.

If a volume other than the recommended 60 μ l is used for making blood slides, an appropriate multiplication factor other than 16.7 is needed to calculate the mfd. Table 3 can be used to obtain the multiplication factor.

Table 3 Multiplication factors for different blood volumes

Volume of blood used	Multiplication factor
20 μ l	x 50
40 μ l	x 25
60 μ l	x 16.7
80 μ l	x 12.5
100 μ l	x 10

Measurement of clinical manifestations — prevalence of lymphoedema and hydrocele in sentinel sites

The presence of clinical cases of lymphoedema and hydrocele should be recorded in all sentinel sites. Apart from assessing the trend in prevalence of lymphoedema and hydrocele in the sentinel site over the period of programme implementation, this information would also give an indication of the disease burden in the IU to advise on planning for community-based activities for disability prevention and control.

Lymphoedema is defined as a hard swelling of lymphatic origin that can range from pitting oedema, spontaneously reversible on elevation, to a huge increase in volume with dermatosclerosis (hardening of the skin) and papillomatosis (development of a crop of papillomas).

Hydrocele is defined as a collection of fluid in the tunica vaginalis. On clinical examination, hydrocele is indistinguishable from chylocele (collection of chylous fluid) or haematocele (collection of blood).

Example: How to calculate the prevalence of clinical signs in a given IU (Table 4).

Table 4 Calculating the prevalence of clinical signs in a given implementation unit

IU [Name]	Sentinel site ⁶	No. of individuals of both sexes examined	No. of lymphoedema cases	Prevalence (%)	No. of males examined	No. of hydrocele cases	Prevalence (%)
[Name]	[Name]	500	6	1.2	250	39	15.6
[Name]	[Name]	510	18	3.5	245	55	22.4

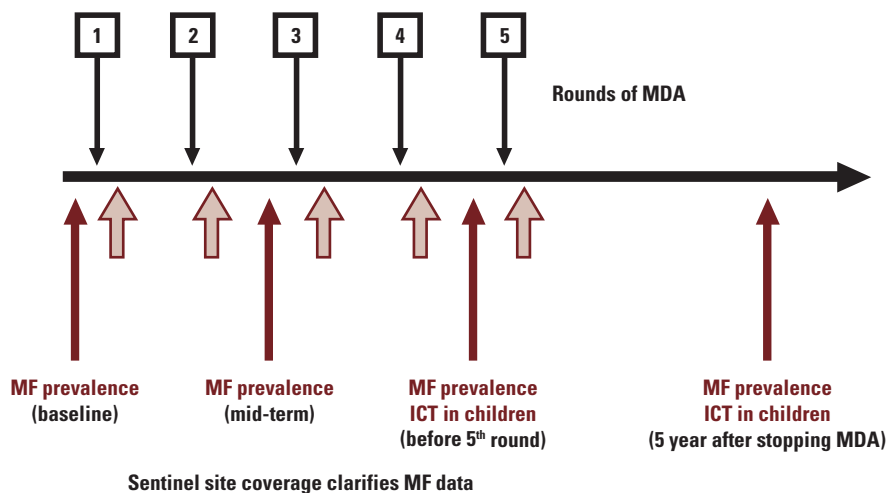
The minimum frequency for collecting these data should be before the first, third and fifth rounds of MDA then every two years up to the end of MDA when the criteria for stopping MDA have been met (Table 5; Fig. 1). Measuring these two indicators is of paramount importance in deciding whether or not MDA should be stopped. This work should be carried out in collaboration with the national authorities by using, if necessary, external laboratories for the quality control of results for mf% and mfd.

Table 5 Frequency of measuring the indicators

	MDA coverage	mf%	mfd	Clinical manifestations
Sentinel site	Following every MDA (within 1 month)	Before the 1 st , 3 rd and 5 th MDA then, if necessary, before the 7 th and 9 th rounds until criteria for stopping MDA are met	Before the 1 st , 3 rd and 5 th MDA and then, if necessary, before the 7 th and 9 th rounds until end of MDA	Before the 1 st , 3 rd and 5 th MDA and then, if necessary, before the 7 th and 9 th rounds until end of MDA
Spot-check site	No	Before the 3 rd and 5 th year then before the 7 th and 9 th rounds until end of MDA	Before the 3 rd and 5 th year and then, if necessary, before the 7 th and 9 th rounds until end of MDA	No

mf% = prevalence of microfilariae; mfd, density of microfilariae.

⁶ There is no need to estimate numbers of lymphoedema and hydrocele cases in spot-check sites.

Figure 1 Procedure for sentinel site monitoring

Mf = microfilaraemia

MEASURING THE CRITERIA FOR STOPPING MASS DRUG ADMINISTRATION

The decision about whether to stop or to continue MDA must be taken judiciously. If MDA is stopped prematurely, several years may pass before continuing transmission is discovered and re-starting MDA at that point may be extremely difficult.

Steps in deciding when to stop mass drug administration (Fig. 2)

- (a) Prior to the fifth round of *effective* MDA coverage, find <1% prevalence of microfilaraemia in the sentinel site and any spot-check sites, but add ICT testing of 2–4-year-old children⁷ (i.e. those born since transmission was likely to have stopped) and find no true positives.

In this example, four years of *effective* MDA coverage (i.e. sufficient to stop transmission) has been achieved and the testing is done shortly before the fifth round. The fifth round must already have been planned and will take place after this testing, no matter what the results.

Once the prevalence of microfilaraemia in sentinel sites and spot-check sites is less than 1%, young children in sentinel spot-check sites should be tested for antigenaemia (in areas where *W. bancrofti* is endemic). **Any** true positives for ICT or microfilaraemia in this age group should be a cause for major concern to the programme managers. In cases where there are only one or two positives or equivocal results, further investigations to confirm the judgement that transmission persists should be undertaken before deciding to continue MDA after the fifth round.

- (b) Extend the sentinel and spot-check testing to include 5–10 additional sites selected according to their estimated risk for continued LF transmission, using a risk-ranking procedure.

The information obtained from a very limited number of sentinel sites and perhaps spot-check sites as described in a. above is weak evidence on which to base assumptions on prevalence rates in an entire implementation area. Two further steps are proposed to provide confirmation of the results from the sentinel sites at modest cost. If

⁷ In determining the age group of children to select, there is a balance between having an accessible, appropriately-size cohort and risking that 4-year olds may have had a period of exposure to transmission.

the criteria of less than 1% microfilaraemia in the sentinel sites and spot-check sites and no children between the ages of 2 and 4 years being antigen-positive are met, then again prior to the fifth round of *effective* MDA coverage, repeat this procedure in 5–10 additional sites selected on the basis of their presumed high risk for continuing LF transmission and find prevalence of microfilaraemia in adults of <1% and no true ICT positives⁸ in 2–4-year-old children.

The checking of these additional 5–10 sites still provides little information on microfilaraemia and ICT positivity rates in the full implementation area. However, because these are thought to be the sites at greatest risk for continuing transmission, negative results do provide some reassurance that transmission has stopped. The proposed number of additional sites is arbitrary, but small, chosen simply to minimize costs.

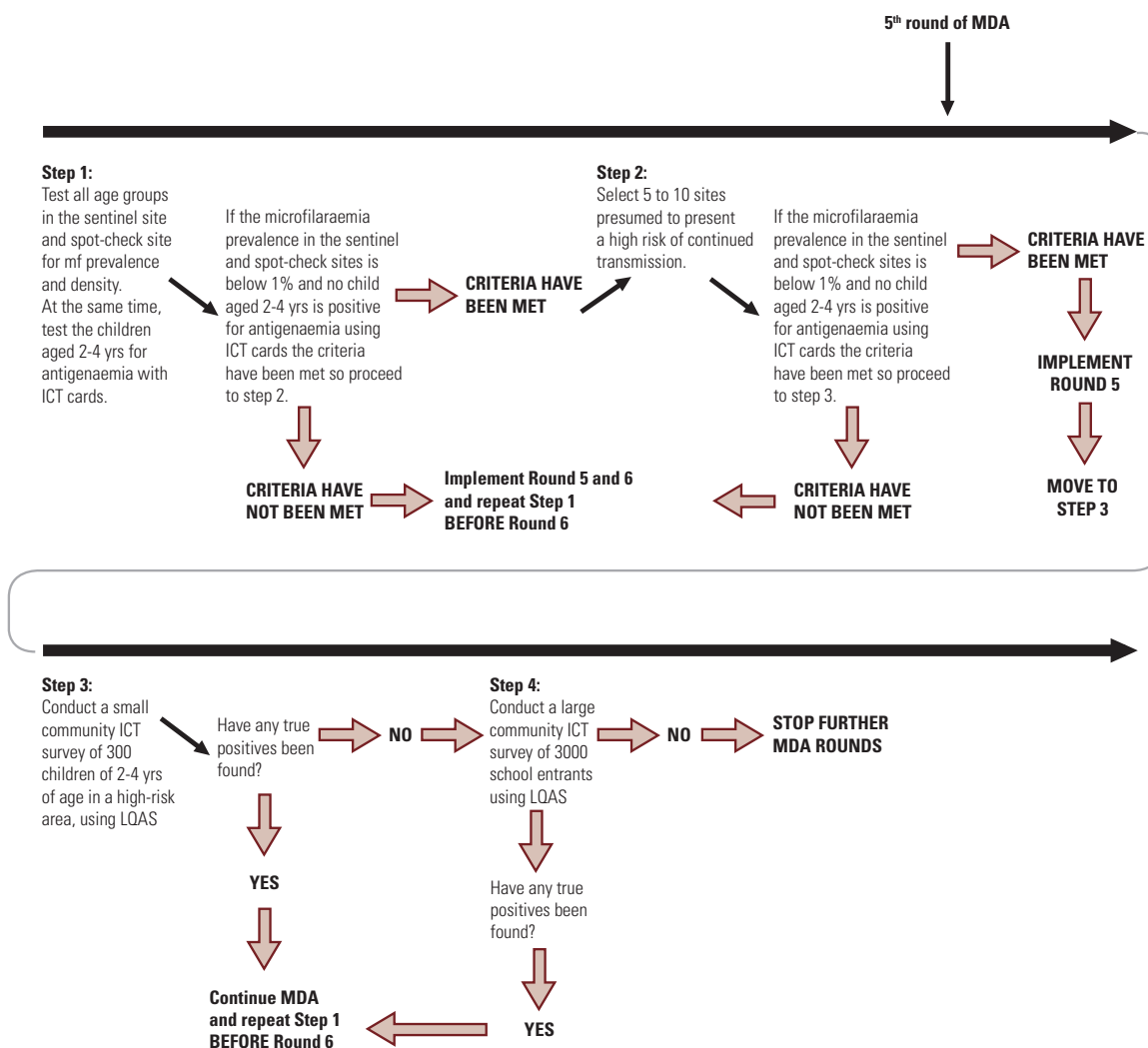
The suppressive effect of drug administration on microfilaraemia levels means that these additional sites need to be tested just before the next round of MDA, and testing should be completed before the fifth round.

- (c) Conduct the fifth round of MDA, irrespective of the results of the above surveys.
- (d) Conduct a community LQA cluster survey⁹ (see Annex 6) of ICT test positivity in 300 children aged 2–4 years (30 clusters with 10 children each) in those areas suspected to be at the highest risk for continuing LF transmission, finding no true positives.

⁸ An algorithm for ruling out false positive ICT tests is provided in Annex 2. This is a simplified version of the algorithm presented in the Memorandum on Verification of Absence of LF Transmission. Further research on this issue is required but, for the present purposes, it is assumed that this, or a similar algorithm, permits true positives, e.g. positives due to circulating filarial antigen in a local resident to be identified with a reasonable degree of confidence.

⁹ Protocol for assessing neonatal tetanus mortality in the community using a combination of cluster and lot quality assurance sampling Field test version, Stroh G, Birmingham M. Geneva, World Health Organization, 2002 (WHO/V&B/02.05).

Figure 2 Steps to be taken prior to round 5 of MDA – a flow chart



mf, microfilaraemia; MDA, mass drug administration; ICT, immunochromatographic test; LQA, lot quality assurance.

Such sampling could be conducted at any time following the testing described in steps (a) and (b) above. For the purposes of illustration here it is assumed to take place shortly after the fifth round of MDA to provide sufficient lead time to make a decision on the need for the sixth round if this and the next step show no true positives. This survey should include those children over 2 years of age (when ICT begins to become positive) who were born *after* the first round of effective MDA. In this example, they will be 2–4 years old.

This proposed LQA cluster survey of children in the community is adapted from the procedure described by Stroh and Birmingham¹⁰ for neonatal tetanus and discussed further in Annex 6.

¹⁰ Protocol for assessing neonatal tetanus mortality in the community using a combination of cluster and lot quality assurance sampling Field test version, Stroh G, Birmingham M. Geneva, World Health Organization, 2002 (WHO/V&B/02.05).

A ranking procedure is used as in step b. to identify those communities or areas at high risk for continuing LF transmission. A sample of 30 clusters of 10 children each is chosen from the highest-risk areas. In the individual cluster, one household is chosen at random, and the oldest child in the appropriate age range is selected from that household (or from the "next" household if there are no children in the first) and tested using ICT. If the selected child is absent from the household the second-oldest child is selected, but note is taken of the absentees in case the proportion of absentees becomes high enough to warrant revisiting households or necessitates some other procedure to minimize absentee bias. The "next" household, as in the WHO Expanded Programme on Immunization surveys is the "nearest" to the first, and successive households are selected until 10 children in the appropriate age range have been tested. The selection of only one child per household is proposed here to minimize the known effect of LF clustering in families. See Annex 6 for a discussion of sample size options.

- (e) Conduct an LQA survey of ICT positivity of 3000 school entrants covering the entire implementation area or areas being assessed. If no true positives are found, **stop MDA**. If true positives are found, continue with steps f. and g. (i.e. conduct the sixth round and repeat the LQA survey of school entrants).

The preceding steps are all targeted at specific sites or areas within the implementation area(s) and do not represent a statistically valid sample of the entire area. The sample of school-aged children is intended to provide this statistical validity.

In this example, step (e) is to be completed before conducting the sixth round of MDA, so that preparations for the sixth round are at an early enough stage to allow that round to be cancelled if no positives are found. A compromise is therefore proposed here: i.e. to test school entrants (presumed to be approximately 6 years old). If the results are negative, MDA can be stopped without conducting the next (sixth) round.

LQA testing in schools requires a strict adherence to random sampling principles and will require special training and close supervision of the surveyors. As further described in Annex 6, a *systematic* sample should be taken.

- (f) If true positives have been found in step e., conduct the sixth round.
- (g) Repeat the LQA school survey as described in d. If no true positives are found, **stop MDA**.

This last step (g) is intended to sample only children born *after the first round of MDA*. (In step (e), the sampled children are likely to have been born 1–2 years prior to that round.) Ensuring that only such children are included in this sample may require some screening of school entrants to exclude children born before MDA was stopped to ensure that a true positive test reflects transmission taking place after the initiation of presumed *effective* MDA.

THE PASSIVE SURVEILLANCE SYSTEM

This is a back-up system of surveillance that allows:

- detection of new foci of transmission;
- collection of data on infection trends in the general population; and
- confirmation of end of transmission.

Such surveillance is conducted regularly throughout the year.

It could be carried out in the following population groups:

- military recruits (during their medical check-up);
- university students (during their medical check-up or prenatal examination);
- blood donors; and
- hospitalized patients.

POST-OPERATIONS SURVEILLANCE

Surveillance should be carried out for at least five years after the last MDA has taken place before considering "verification of LF elimination". At the end of this period, a sample of 3000 5-year-old children should be tested by ICT. If there are no positive results then LF elimination has been achieved.

ANNEX 1: A CLUSTER-SURVEY PROTOCOL FOR ASSESSING MASS DRUG ADMINISTRATION COVERAGE FOR LYMPHATIC FILARIASIS PROGRAMMES

Introduction

This protocol is designed to assist LF programme managers in implementing population-based cluster surveys of coverage to complement the "reported coverage" obtained from tally sheet data¹¹.

Representative surveys provide a method for confirming results for reported coverage, and are especially important if there is doubt about the reported data. Additional information can economically be collected during the coverage survey by adding questions related to topics such as knowledge about LF, side-effects experienced and other aspects of the Programme.

This protocol provides a standardized sampling methodology, modelled on immunization coverage surveys, which is designed to strike a balance between statistical rigour and practical implementation. The sampling methodology is designed to provide an estimate of actual coverage accurate to within plus or minus 6.5%.

This protocol involves a series of steps, including:

- selection of the IU to be surveyed;
- selection of subunits or areas (e.g. villages, wards or localities) within the IU, using population-proportionate sampling to weight these areas according to their population size;
- random selection of a starting household followed by sampling from a cluster of contiguous households; and
- use of a simple tabular data form and questionnaire to determine whether household members participated in the MDA.

Various forms and instructions useful in carrying out a cluster survey are included in Annexes 1–5. These are:

- A draft template questionnaire (Appendix to Annex 1)
- A random number table (Annex 2)
- An example of population-proportionate sampling (Annex 3)
- Details on selection of a starting household (Annex 4)
- A table with examples of sample sizes for use under different assumptions and conditions (Annex 5).

¹¹ Alternative methods, such as LQAS have been proposed For small geographical areas where random selection of individuals is possible, LQAS may provide a means to identify areas that fail to meet a defined coverage criterion. This method is not covered in this protocol.

Overview

Purpose

The purpose of a population-based survey is to provide a coverage estimate that is statistically likely to be representative of the population sampled. The estimate does not depend on data aggregated from different distribution sites, and is thus not as subject to missing data, mathematical errors or difficulties with estimating an accurate denominator from census figures.

Sampling

Ideally, to get a representative response from individuals living in a given IU (usually a district) or a cluster of IUs, all individuals should be listed, and a sample of these individuals selected at random. Because this is impractical, the best compromise is to ensure random selection of smaller areas within the survey area, and to select individuals randomly from within these smaller areas. In order to do this, a smaller geographical area needs to be defined – this is usually a village, ward, locality or other administrative division of the district. To simplify analysis, the selection of these smaller units is made in proportion to the size of the population so that more populated areas have more chance of being included in the sample.

Once the smaller subunits have been selected, it is important to ensure that every individual within the subunit has an equal likelihood of being selected for the survey. Various methods are used to achieve this. The simplest is to randomly select a “starting household”, interview all its members and then select contiguous households until the desired number of individuals has been interviewed¹². For some subunits, it will be necessary to make further subdivisions using random selection techniques until the number of households in the subunit is small enough to be easily enumerated. Once the household has been selected, everyone in that household is interviewed.

Interpretation

This survey technique provides a representative estimate of the population coverage rate. The accuracy of this estimate depends on several factors, including the number of people included in the sample, the bias introduced by sampling people together within a subunit rather than as randomly selected individuals – the so-called design effect – and the true population coverage rate. The sample will be least accurate when the rate is 50%. Annex 5 provides a table indicating how the interactions between sample size, design effect and true coverage rate affect the accuracy of the sample estimate. In the method described here, 30 people are selected from each of the 30 subunits giving a total sample size of 900. For an assumed design effect of 4, which in most cases is probably an overestimate, and a true coverage rate of 50% – in most cases probably an underestimate – the survey result will be within 6.5% of the true coverage figure 95% of the time. The estimate from the 30 subunits applies as an average for the entire area included in the sample. The results from a single subunit are not a valid estimate of that subunit.

Methods

Selection of implementation units

The survey is done at the level of the IU, which is commonly a district. The IU, or aggregation of IUs to be surveyed, can be purposively selected, perhaps selecting those with high or low coverage, in order to include IUs where the Programme is going well and those in which there may be difficulties.

¹²In the WHO Expanded Programme on Immunization, it is the «nearest to the left when leaving the house», with other criteria used when in urban apartments on multiple floors. The issue is only to have a strict rule for selecting successive households.

The coverage estimate is representative of the IU being surveyed. A simple average of all IUs surveyed does not provide a statistically valid estimate of national coverage. Although such an estimate may hold some attraction politically, it does not identify IUs that are performing well or poorly. Although it is possible to sample individual IUs and combine results to give a national estimate, this increases costs and complexity, and should only be undertaken with expert statistical advice.

Selection of areas from which clusters of individuals will be sampled

For this protocol, within the selected survey area, 30 subunits need to be selected. From each of these, a cluster of individuals will be selected. The ideal subunit is an administrative unit for which population figures are available. The subunit may be a village, a statistical enumeration area (used for census determination), a ward or a locality.

These 30 subunits must be selected randomly from all subunits within the survey area. In addition, because different areas will have different populations, the areas need to be weighted to take these population differences into consideration. If weighting is done during selection, it is not necessary to weight the results during the analysis.

A step-by-step example of population-proportionate sampling is given in Annex 3. For this method of sampling, the following information is required:

- There must be a clear definition of the subunit (e.g. village, ward, locality) within the survey area, and the ability to define its geographical boundaries when collecting field data.
- A complete listing of all the subunits within the survey area is needed, taking care to ensure that no populated areas are excluded. If there is no listing, for example of villages for a given survey area, an alternative administrative unit may need to be chosen as the subunit, such as a ward.
- Estimated population figures for each subunit must be obtained.

Training programmes for survey workers should emphasize the importance of adhering to the principles of random selection. Once a subunit or starting household has been selected, it should be included in the sample. Substitutions invalidate random selection and easily lead to erroneous results.

Selection of households within an area or subunit

Once the 30 subunits for the survey area have been identified, enumerators will need to sample a cluster of individuals from each of those areas. For this purpose, 30 individuals will be selected from each subunit, resulting in an overall sample size for the survey of 900 individuals.

In making the selection, all individuals must have an equal chance of being included in the survey. In practical terms, this is usually done by using methods to randomly selecting a "starting household". Only households that are occupied (currently serving as a residence, even though the inhabitants may be away) are considered in the sampling.

Ideally, households should be selected at random from a list of all households in the subunit. However, this is usually not possible, because such a list is seldom available. An alternative is to map all the households within the subunit, and maps permitting numbering of individual households may be available from other programmes (e.g. polio eradication). It is costly, however, to create maps for the survey, and for LF coverage surveys, alternative methods are recommended if maps are not already available. If the subunit selected is so large that it is difficult to identify a starting household, it should be further divided. First divide the subunit into manageable areas with approximately the same number of households and select one of these at random. Then select the starting household within that area.

The most important consideration is to have a practical mechanism that allows a starting household to be selected at random, with all households in the area having an equal chance of being selected.

In order of preference, the following selection methods are recommended:

- 1) Randomly select a starting household from a list of all households in the subunit.
- 2) Use a map to enumerate all households in the subunit and randomly select one. The map should ideally be updated in collaboration with a resident of the area who knows about recent changes.
- 3) Divide the subunit into quadrants with approximately the same number of households in each. Select one quadrant at random, list the households and select one of these households at random. If the quadrant is still too large, repeat the process dividing it again into a smaller number of areas.
- 4) From the approximate centre of the subunit, randomly select a direction of travel. Count the number of households between the centre and the limit of the subunit and randomly select the starting household.

More specific details on the methods for random selection of the starting household are given in Annex 4.

Selection of individuals within the area or subunit

Once the starting household has been selected, data are collected from all individuals in that household. Once this has been done, the next nearest household is selected, and data are collected from all individuals in that household. This process continues until data have been collected from 30 individuals. If there are more individuals in the last household visited than are needed to reach the required total of 30, data on all individuals in the final household are collected, resulting in a sample of more than 30 for that particular cluster.

After completing the survey in the starting household, to select the next household, choose the one whose entrance is nearest to the starting household. Continue selecting additional households in this manner (excluding those already visited) until enough households have been visited to allow 30 individuals to have been sampled.

There are a number of definitions and criteria that apply to selection of individuals within households. The following general guidelines should be followed:

- All individuals who were living in the household during the time of the last MDA are enumerated. The list includes individuals who may not have been eligible (e.g. pregnant women), and those who may not currently reside in the household, or those not currently present. From this list, responses are tabulated.
- Ideally, each individual should answer for him or herself. Parents or caregivers can answer for young children. If a resident of the household is absent, a family member can provide information for that person if the enumerator judges that the response given by the family member is likely to be accurate.
- The questions include whether the person received a dose or not, and if not, whether it was because they were not eligible. For those who were not eligible, the reason for ineligibility is recorded (e.g. age, pregnancy or illness). For those who were eligible but did not receive the dose, the reason for not having received the dose is recorded (including refusal, not knowing about the MDA, or because of other obstacles such as knowing about MDA but being in the fields, travelling or away at work).
- Individuals enumerated, but on whom no information is available, are noted, but not included in the overall sample.
- The optional questions are asked of one respondent per household.
- The total sample should include 900 individuals on whom information is available.

The coverage survey is designed to capture data on a sample of 30 individuals for each area or subunit, rather than on a sample of a fixed number of households within each area. Thus, the total number of households visited will depend on the number of people in the households – if the average number of occupants is high, fewer households will be visited.

Analysis

Currently, the recommendation for reporting coverage is to report the total number of individuals dosed divided by the total population of the endemic areas. For coverage surveys, therefore, the coverage estimate is based on the total number of individuals who state that they were dosed during the last MDA divided by all those on whom information is available who were resident in the households sampled at the time of the last MDA.

The basic analysis for the coverage survey is simple, and can be done by hand. Data collected using the template for a data collection form in the Appendix to this Annex can be used to produce a table with basic information on each of the 30 individuals sampled from each area, and a summary table for all areas can easily be created. In this way it is possible to determine the total number of people surveyed and the total number who stated that they received a dose during the recent MDA.

In the analysis, the numerator used for coverage is the total number of people who responded that they had received the dose during the recent MDA, and the denominator is the total number of people for whom data were available; both those who did and did not receive the dose. In addition, it will be useful to report in the analysis:

- the proportion of the total sample on whom no data were available;
- the proportion of the sample on whom information was available who were deemed ineligible, and the reasons for ineligibility;
- the proportion of the sample on whom information was available who were eligible and who refused dosing; and
- the proportion of the sample on whom information was available and who were eligible for dosing, but who did not receive the dose because they were not aware of the MDA.

With this sampling method, it is not statistically valid to define coverage for any given area or subunit from which the cluster of individuals has been selected – or to compare coverage between these areas. However, it may be possible to look at coverage for different strata within the overall sample of 900 individuals to see if there are gross differences for example, between men and women, or between adults and children. Interpretation should be done with caution, however, because the smaller sample size for these strata makes the confidence interval wider, making it more difficult to determine statistically valid differences between strata.

It may be useful to enter the data into a spreadsheet or database to make sub-analyses easier, and to manage numerous coverage surveys over time. If additional questions are asked of individuals within households, for example about their knowledge, awareness, behaviour or practice, computerized records will be necessary, and this information may be valuable to review over time.

Part II: Optional questions to ask of one key respondent from each household

1) How did you know about the MDA (*tick all unprompted responses*)?

- Heard from friend or neighbour
- Heard about it on the radio
- Heard about it on the television
- Saw poster or pamphlet
- Heard about it from health worker

2) What can you tell me about lymphatic filariasis (*tick all unprompted responses*)?

- Transmitted by mosquitoes
- Causes "bigfoot"
- Causes hydrocele
- Can be prevented

3) Are there any members of this household with hydrocele (*use local terms where possible*)?

- Yes
- No

4) If yes, have they received treatment for this condition?

- Yes
- No

Describe treatment:

.....

.....

.....

.....

.....

5) Are there any members of this household with lymphoedema (*use local term where possible*)?

- Yes
- No

6) If yes, have they received treatment for this condition?

- Yes
- No

Describe treatment:

7) (*For those who participated in the MDA*) Why did you participate in the recent MDA?

- Told to by a health worker, radio or television spot
- Concerned about the disease
- Worried about transmission
- Wanted to prevent transmission to future children

8) What did you like about the MDA?

- Easy to get to distribution site
- House-to-house distribution (*if applicable*)
- Knowledgeable distributors
- No long wait for drugs
- Received other information or services

9) What didn't you like about the MDA?

- Site too far away
- Drugs ran out, or weren't available
- Unfriendly distributor
- Took too much time
- Didn't dose other members of my family
- Adverse reactions to drugs

ANNEX 2: TABLE OF RANDOM NUMBERS

	1	2	3	4	5	6	7	8	9
1	10480	15011	01536	02011	81647	91646	69179	14194	62590
2	22368	46573	25595	85393	30995	89198	27982	53402	93965
3	24130	48390	22527	97265	76393	64809	15179	24830	49340
4	42167	93093	06243	61680	07856	16376	39440	53537	71341
5	37570	39975	81837	16656	06121	91782	60468	81305	49684
6	77921	06907	11008	42751	27756	53498	18602	70659	90655
7	99562	72905	56420	69994	98872	31016	71194	18738	44013
8	96301	91977	05463	07972	18876	20922	94595	56869	69014
9	89579	14342	63661	10281	17453	18103	57740	84378	25331
10	85475	36857	53342	53988	53060	59533	38867	62300	08158
11	28918	69578	88231	33276	70997	79936	56865	05859	90106
12	63553	40961	48235	03427	49626	69445	18663	72695	52180
13	09429	93969	52636	92737	88974	33488	36320	17617	30015
14	10365	61129	87529	85689	48237	52267	67689	93394	01511
15	07119	97336	71048	08178	77233	13916	47564	81056	97735
16	51085	12765	51821	51259	77452	16308	60756	92144	49442
17	02368	21382	52404	60268	89368	19885	55322	44819	01188
18	01011	54092	33362	94904	31273	04146	18594	29852	71685
19	52162	53916	46369	58586	23216	14513	83149	98736	23495
20	07056	97628	33787	09998	42698	06691	76988	13602	51851
21	48663	91245	85828	14346	09172	30163	90229	04734	59193
22	54164	58492	22421	74103	47070	25306	76468	26384	58151
23	32639	32363	05597	24200	13363	38005	94342	28728	35806
24	29334	27001	87637	87308	58731	00256	45834	15398	46557
25	02488	33062	28834	07351	19731	92420	60952	61280	50001

ANNEX 3: **EXAMPLE OF POPULATION-PROPORTIONATE SAMPLING**

Step 1: List all subunits within the area or IU to be surveyed.

Within the selected area, make a complete list of all the subunits from which the cluster of individuals will be selected. The list does not need to be in any particular order, but must include all the subunits within the IU.

Step 2: List the population for each subunit.

In a column next to the name of the subunit, list its estimated population. The source of the population figures is not critical as long as the same source is used for each area. Usually census figures (with appropriate correction if the census is old) are used.

Step 3: Calculate the cumulative population for the list of subunits.

In a third column, successively add the population for each subunit, providing a cumulative population figure for the whole survey area. This can be done using a computer spreadsheet.

Step 4: Calculate the sampling interval.

To calculate the sampling interval, divide the total population for the IU by 30 (the total number of subunits to be selected).

Step 5: Randomly select the starting point.

Using a table of random numbers, select a number between 1 and the sampling interval, and record this in a fourth column.

Step 6: Calculate populations from which to select the subsequent subunit.

Add the sampling interval to the starting point, and record in the fourth column. Continue to add the sampling interval successively until the total population for the area is reached or exceeded.

Step 7: Select remaining subunits.

Using the figures in the fourth column, determine if a subunit is to be included in the survey as follows. If the first random number (between 1 and the sampling interval) recorded in the fourth column includes the population of the first subunit listed (in the third column), then that subunit is selected as the first of the 30 areas to be selected. If the random number is larger, then the first subunit in which the cumulative population includes this random number is selected as the first subunit.

Using the next number in the fourth column, determine the next subunit that is included in that number, and continue making selections until all 30 subunits are selected. In some instances, an area will have a large population, and it is possible that it will be selected more than once.

Table A.3.1 below shows an example of selection of areas using population-proportionate sampling methods.

Table A.3.1 Example of population-proportionate sampling

Subunit (e.g. village, ward)	Population	Cumulative population	Areas selected	Random start plus sampling interval	Sampling interval calculations
					<i>Total population = 37741 Total number of areas = 30</i>
1	480	480			
2	555	1035	1	718	
3	657	1692			<i>Sampling interval = 1258 (37741/30)</i>
4	489	2181	1	1976	
5	367	2548			
6	456	3004			
7	1299	4303	1	3234	<i>Random start = random number between 1 and 1258</i>
8	345	4648	1	4492	
9	333	4981			
10	777	5758	1	5750	<i>For this example, 718 was the randomly selected starting point</i>
11	888	6646			
12	675	7321	1	7008	
13	324	7645			
14	865	8510	1	8266	
15	567	9077			
16	756	9833	1	9524	
17	1234	11067	1	10782	
18	3465	14532	2	12040	
				13298	
19	567	15099	1	14556	
20	878	15977	1	15814	
21	898	16875			
22	909	17784	1	17072	
23	345	18129			
24	345	18474	1	18330	
25	556	19030			
26	675	19705	1	19588	
27	564	20269			
28	867	21136	1	20846	

Subunit (e.g. village, ward)	Population	Cumulative population	Areas selected	Random start plus sampling interval	Sampling interval calculations
29	933	22069			
30	967	23036	1	22104	
31	876	23912	1	23362	
32	347	24259			
33	879	25138	1	24620	
34	1266	26404	1	25878	
35	1244	27648	1	27136	
36	2134	29782	2	28394	
				29652	
37	467	30249			
38	234	30483			
39	266	30749			
40	188	30937	1	30910	
41	399	31336			
42	789	32125			
43	987	33112	1	32168	
44	867	33979	1	33426	
45	856	34835	1	34684	
46	745	35580			
47	679	36259	1	35942	
48	346	36605			
49	457	37062			
50	679	37741	1	37200	
			30		

ANNEX 4:

RANDOM SELECTION OF THE STARTING HOUSEHOLD

Randomly select a starting household from a list of all households in the subunit.

In this ideal but unlikely situation, randomly select one household from the full list by selecting a random number between 1 and the total number of households listed. This defines the "starting household". Beginning with this household, sample consecutive households as described in the text.

Randomly select a starting household from a map of all households in the subunit. The map should ideally be updated in collaboration with a resident of the area who knows about recent changes.

Maps may be available from recent demographic health surveys, national immunization days or census activities. Such a map can be used to number all households and list them. From this listing, it is possible to randomly select one household to serve as the starting household. Because consecutive households are sampled from this starting household, it will not matter if a few households are not on the list. However, if the map is grossly inaccurate, it should not be used.

Divide the subunit into smaller units such as quadrants, and following random selection of one of these, prepare a list of households within the smaller unit and randomly select the starting household.

Step 1:

Identify a central point within the subunit through consultation with a village leader.

Step 2:

Visually divide the subunit into a smaller number of units (such as quadrants), each with roughly the same number of households.

Step 3:

Randomly select one of these smaller units for household sampling.

Step 4:

Number all the households in the selected smaller unit and, by selecting a random number between 1 and the total number of households, select the starting household. If the smaller unit or quadrant proves to be too large to allow all households to be numbered, it can be divided again into smaller areas each with roughly the same number of households, repeating the process until a starting household can be randomly selected.

Randomly select a direction of travel, and after counting all households in that direction of travel, randomly select a starting household.

Step 1:

Identify a central point within the subunit through consultation with a village leader.

Step 2:

Spin a pen or bottle to randomly select a direction of travel from the central point. If there are no households in that direction, change the direction clockwise until the first house is encountered. This becomes the new direction.

Step 3:

Number all households that fall along the line of travel in this direction starting from the central point and finishing at the boundary of the area or subunit. It is important to stick as closely as possible to the actual line of the direction of travel.

Step 4:

Randomly select a number between 1 and the total number of households encountered along the direction of travel, and use this as the starting household.

ANNEX 5: SAMPLE SIZES FOR DIFFERENT ANTICIPATED COVERAGE AND DESIGN EFFECTS

Coverage	Precision	Design effect	Sample size	No. of people/ cluster
50%	0.05	1	384	13
		2	768	26
		3	1152	38
		4	1537	51
	0.1	1	96	3
		2	192	6
		3	288	10
		4	384	13
60%	0.05		369	12
			738	25
			1106	37
			1475	49
	0.1		92	3
			184	6
			277	9
			369	12
70%	0.05		323	11
			645	22
			968	32
			1291	43
	0.1		81	3
			161	5
			242	8
			323	11
50%	0.065	4	900	30
60%	0.06	4		
70%	0.06	4		

ANNEX 6: LOT QUALITY ASSURANCE SAMPLING

Community lot quality assurance cluster samples

This is a new technique developed for assessing the prevalence of neonatal tetanus. It is a hybrid that combines the power of the LQA approach in assessing whether an event exceeds some threshold of frequency with the ease of conducting a cluster survey in which individuals are selected in groups at various locations rather than each being selected randomly from the total universe being sampled. As noted in the main text, further research is needed to validate this approach for use with LF, but at present it appears to be reasonable to incorporate this method into an LF programme.

The sample size proposed for these community LQA cluster surveys represents a trade-off between the higher cost of a larger sample and the added confidence in the result that a larger sample would provide. Assuming a design effect of 1 (meaning that the selection of children in clusters is the same as having selected each child at random), a sample of some 300 children gives a 95% probability of finding at least one ICT-positive child if the true prevalence in the target population is $\geq 1\%$. At a true prevalence of 0.5%, there would be a 78% probability of finding at least one positive, and at a true prevalence of 0.25%, there would be a 53% probability of finding at least one positive¹³. So a sample of 300 children is proposed; the geographical area (or “lot”) should be “failed” if one or more positive children is found and MDA continued or further investigations pursued if the results are equivocal. The entire area would be recorded as having failed, not only the high-risk zones that had been sampled.

Systematic sampling in schools

The school LQA surveys proposed, unlike the LQA surveys of the community discussed above, require scrupulous attention to the random selection of individual children. Randomly selecting a number of schools and testing all the appropriately aged children in the selected schools, as has sometimes been done, is *not* an LQA sample, but rather a form of cluster sample.

A *systematic* sample of schoolchildren should be taken. For example, if the total population of schoolchildren in the surveyed endemic group in the area to be sampled is 180 000 and the investigators wish to select 3000 of them, a sampling interval is established by dividing the total population by the number desired in the sample: $180\,000/3000 = 60$. Each school is listed together with its population to establish a cumulative population of children. A starting point for counting is established randomly. Using the interval of 60, the number of children to be selected from any given school is calculated. A similar procedure is used to obtain the number of children required from the individual school. The procedure will result in several children being selected from the larger schools whereas few or none may be selected from the smaller schools.

Dealing with ICT-positives

The LQA sampling designs recommended here all reject the lot if only one true positive is found. Two issues require consideration. First, should the survey be terminated if a child tests positive? The problem is the time it takes to ensure that a positive ICT test really reflects a child locally exposed to LF. Depending on the availability of laboratory and other support services, this may take from weeks to months to clarify. Therefore these LQA surveys should be completed unless either a rapid method can be employed to rule out false-positives, or there is such a high positivity rate that it is clear that local transmission is still occurring. Second, the fact that the survey designs allow *no* positives means that even areas in which the true prevalence of infection is below that considered necessary to sustain transmission (say between 0.025 and 0.1%) will often be failed. If a given survey does find only one true positive, programme managers will need to consider taking additional steps before deciding that this

¹³Personal communication, George Stroh.

result warrants continuing MDA. One such step might be to do intensive screening for microfilaraemia and ICT testing in the area or areas in which the exposure presumably took place. One way of dealing with this problem is to change sample designs to allow larger numbers of positives to be identified without failing the sample. But each increase would require larger sample sizes, greater complexity and higher cost.

The double-sampling scheme proposed for neonatal tetanus by Stroh and Birmingham, is an example of how the design may be modified. Because this design permits up to three positives to be identified without failing the lot, it has less chance of failing lots that have real prevalence rates above zero, but below the designated threshold. Because of the delay which may be required to confirm ICT positives as true positives, for LF, it would probably be necessary to draw both samples at the same time. But if laboratory testing and epidemiological follow-up of positives in the first sample revealed true ICT positives, further laboratory testing could be stopped.

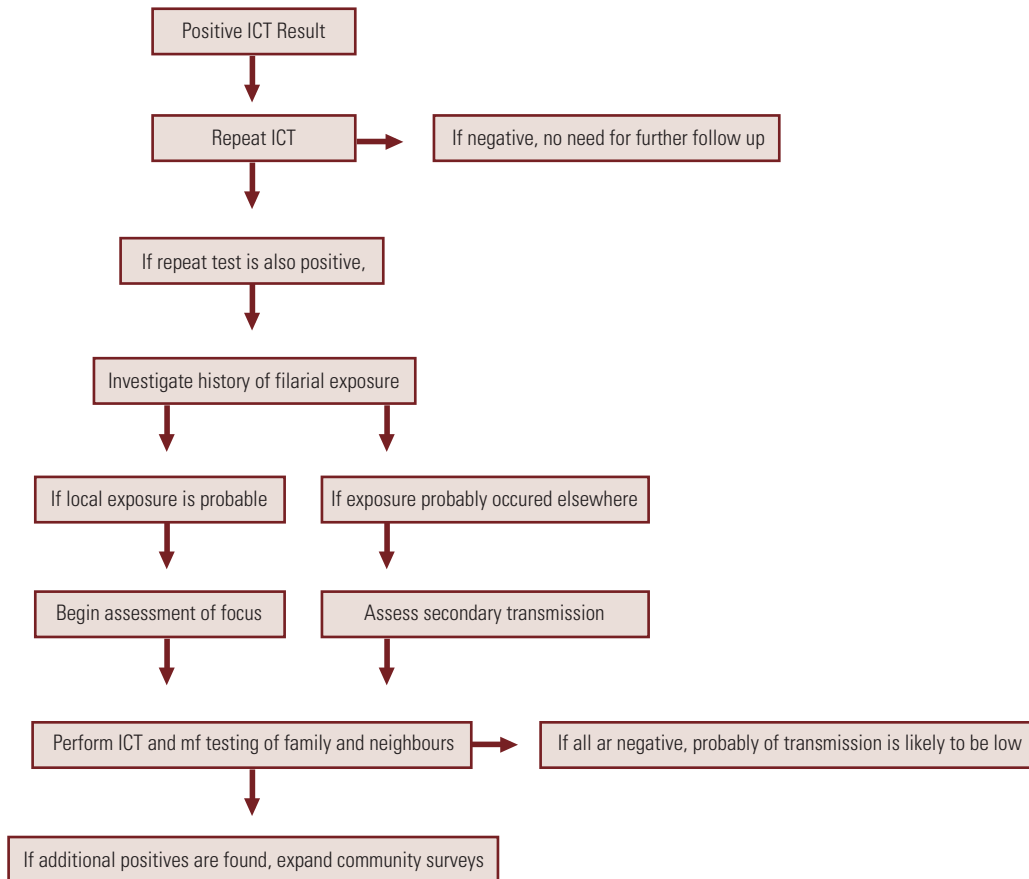
Smaller sample sizes

The number of schoolchildren to be sampled depends on how large the sample is in relation to the total number (lot) of children in the sampling frame. If a 1-year cohort of schoolchildren 6 years old is sampled, the general population from which this cohort comes will be large, because, in developing countries, such a cohort typically represents only 2–2.5% of the total population. If the children to be sampled do comprise more than 10% of the total number of schoolchildren in this age group, sample sizes can be reduced. A table showing these reductions for various proportions above 10% should be provided to programme managers¹⁴.

¹⁴If, for example, the total number of children in the “lot” were 9000, reflecting a total population of 350 000 to 450 000, an LQA sample of 2500 allowing no defectives ($n=2500$, $d=0$) would perform similarly, “failing” samples approximately 95% of the time when the actual prevalence of positives in the “lot” was $>0.1\%$. Personal communication, George Stroh.

ANNEX 7:

ALGORITHM FOR FOLLOWING UP POSITIVE IMMUNOCHROMATOGRAPHIC TEST RESULTS IN SURVEYS TO DETERMINE WHETHER OR NOT TO STOP MASS DRUG ADMINISTRATION



ICT, immunochromatographic test; mf, microfilaraemia.

ANNEX 8: RECOMMENDED PROCEDURES FOR THE DETECTION AND IDENTIFICATION OF MICROFILARIAE IN BLOOD

The microfilariae appear in the blood with a marked nocturnal periodicity in most situations. Some species and strains, however, are nocturnally subperiodic or diurnally subperiodic (Table A.8.1).

Table A.8.1 Characteristics of common human lymphatic filarial parasites

Characteristics	<i>B. malayi</i>	<i>B. timori</i>	<i>W. bancrofti</i>
Geographical distribution	South-east Asia, Indian subcontinent	Lesser Sunday Islands, Timor-Este	Tropical and subtropical countries
Vectors	Mosquitoes (Anopheles and Mansonia spp.)	Mosquitoes (Anopheles spp.)	Mosquitoes (Culex, Aedes, Anopheles and Mansonia spp.)
Habitat			
Adults	Lymphatic system	Lymphatic system	Lymphatic system
Microfilariae	Blood	Blood	Blood
Periodicity of microfilariae	Nocturnal ^a	Nocturnal	Nocturnal ^b
Morphology of microfilariae			
Sheath	Present	Present	Present
Length (µm)	175–230 in smears; 240–300 in 2% formalin	265–325 in smears; 330–385 in 2% formalin	240–300 in smears; 275–320 in 2% formalin
Width (µm)	5.0–6.0	4.4–6.8	7.5–10.0
Tail	Tapered; subterminal and terminal nuclei widely separated	Tapered; subterminal and terminal nuclei widely separated	Tapered; anucleate
Key features	Long head space, sheath stains pink in Giemsa; terminal and subterminal nuclei	Long head space; sheath unstained in Giemsa; terminal and subterminal nuclei	Short head space; sheath unstained in Giemsa; body in smooth curves; dispersed nuclei

^a Nocturnally subperiodic in Indonesia, Malaysia, parts of the Philippines and Thailand

^b Diurnally subperiodic in New Caledonia and Polynesia; nocturnally subperiodic in rural areas of Thailand.

The times for collection of blood specimens should be selected in accordance with the patient's clinical symptoms. Table A.8.2, page 42, shows the recommended times for collecting blood specimens for testing for periodic and subperiodic species of microfilariae.

Table A.8.2 Recommended times for collection of blood specimens for testing for microfilariae

Species ^a	Recommended collection time
Periodic (nocturnal)	22:00–01:00 (peak 24:00)
Periodic (diurnal)	12:00–14:00 (peak 13:00)
Subperiodic (nocturnal)	20:00–22:00 (peak 21:00)
Subperiodic (diurnal)	15:00–17:00 (peak 16:00)
Aperiodic	Any time (day or night)

^a See Table A.8.1

Note: Although microfilariae are not directly infectious to humans, all pathological specimens should be treated as potentially hazardous.

Preparation of a thick blood film for examining microfilariae

For routine filaria microscopy, a thick film is made on a glass slide.

Materials and reagents

- Microscope
- Clean glass microscope slides
- Sterile blood lancets
- Cotton wool
- Grease pencil
- 70% Ethanol.

Method

Blood to be examined for microfilariae is usually collected in the field or sometimes at a health centre.

Figure A.8.1 Cleaning the finger before collecting a capillary blood sample

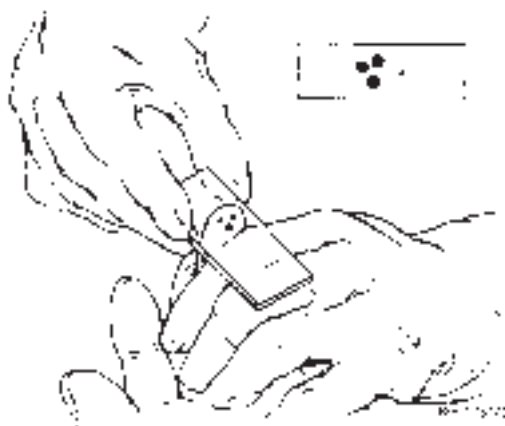
Figure A.8.2 Using a lancet to puncture the tip of the finger



1. With the patient's left hand palm upwards, select the third or fourth finger. (The big toe can be used with infants. The thumb should never be used for adults or children.) Use cotton wool lightly soaked in ethanol to clean the finger – using firm strokes to remove dirt and grease from the ball of the finger (Fig. A.8.1). Dry the finger with a clean piece of cotton wool (or lint).
2. With a sterile lancet, puncture the ball of the finger (Fig. A.8.2), using a quick rolling action. By applying gentle pressure to the finger, express the first drop of blood and wipe it away with dry cotton wool. Make sure that no strands of cotton wool remain on the finger.
3. Working quickly and handling clean slides only by the edges, collect the blood as follows:
 - Apply gentle pressure to the finger and collect drops, about this size ●, on to the slide (Fig. A.8.3).

Wipe the remaining blood away with cotton wool.

Figure A.8.3 Collecting the blood sample



4. Always handle slides by the edges, or by a corner, to make the thick film as follows:
 - Using the corner of the spreader, quickly join the larger drops of blood and spread them to make an even, thick film (Fig. A.8.4).
5. Allow the thick film to dry in a flat, level position protected from flies, dust and extreme heat. Label the dry film with a grease pencil by writing the patient's name or number and date (as shown in Fig. A.8.5).

Figure A.8.4 Preparing a thick blood film

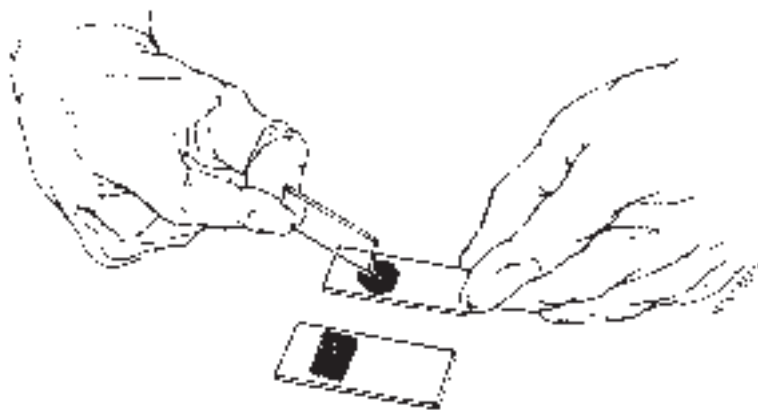
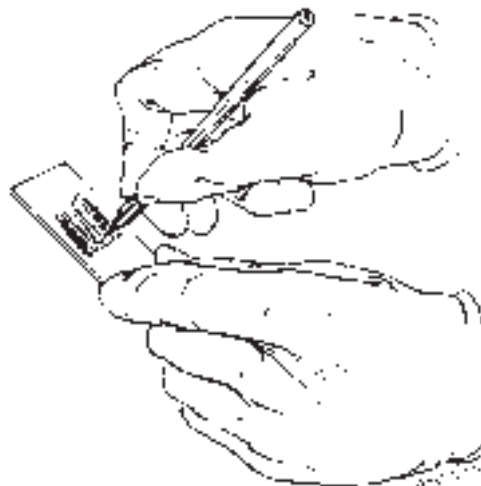


Figure A.8.5 Labelling the slide



Staining of a thick blood film for examining microfilariae

Staining is generally required to identify microfilariae in blood smears.

Technique for staining microfilariae

Materials and reagents

- Microscope
- Microscope slides
- Giemsa stain
- Methanol
- Buffered water

Method

1. Prepare a thick blood smear. Allow the smear to air-dry.
2. Stain with Giemsa stain (diluted 1 in 20 with buffered water, pH 6.8) for 30 minutes.
3. Examine the preparation under the microscope using the x 10 objective. If it is difficult to distinguish the nuclei of the microfilariae, return the slide to the Giemsa stain solution for another 5–10 seconds.
4. Examine the preparation under the microscope. Use the x 10 objective first to locate the microfilariae; then identify the filarial species using the x 40 and x 100 objectives.

Results

Under the light microscope, microfilariae appear (after appropriate staining) as primitive organisms, serpentine in shape, often enclosed in a sheath and filled with the nuclei of many cells (Fig. A.8.6).

Not all species have a sheath. In those that do, the sheath may extend a short or long distance beyond either extremity. In some species, depending on the stain used, the sheath displays a unique staining quality which aids in species identification.

Figure A.8.6 Microfilariae found in humans R1, R2, R3, R4: rectal cells.

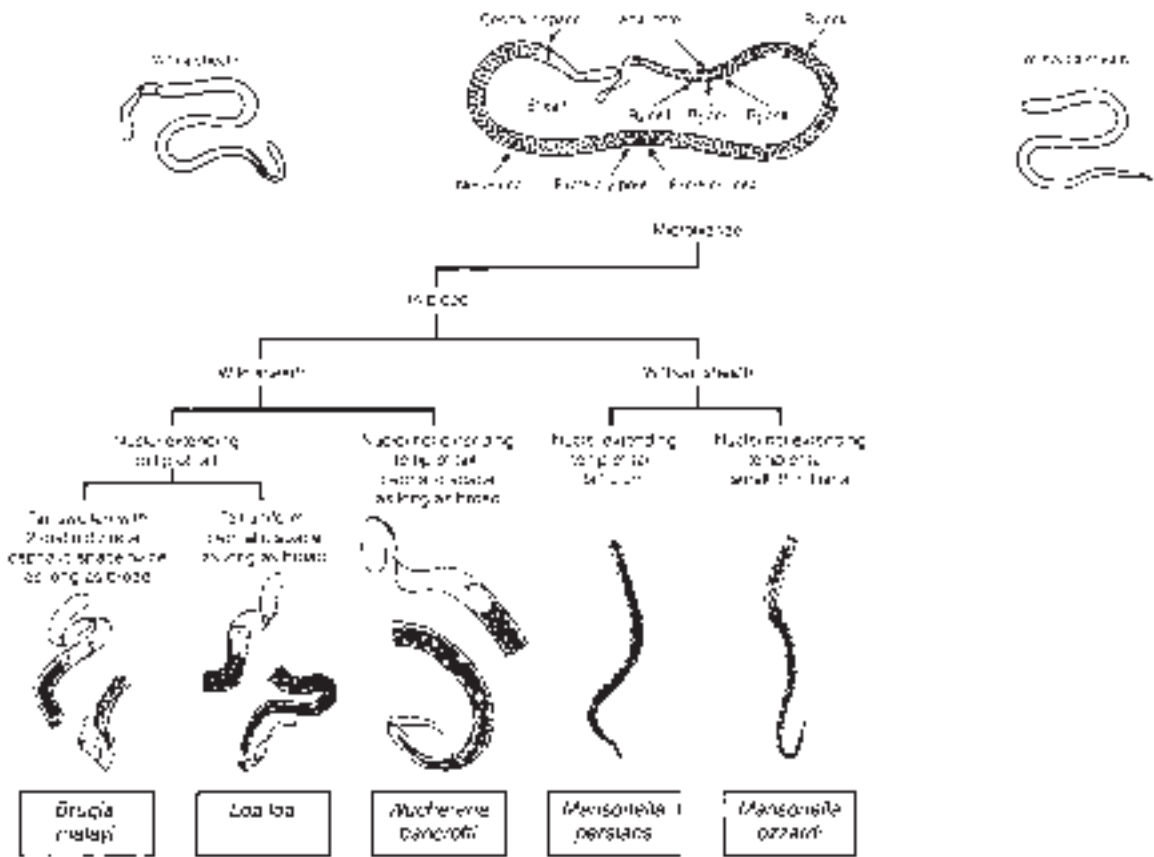
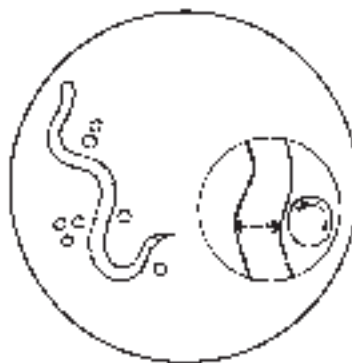


Figure A.8.7 A pathogenic microfilaria length: 250–300 μm ; thickness 6–8 μm (diameter of an erythrocyte). e.g. *W. bancrofti*, *Loa Loa*, *B. malayi*.



The nuclei of the cells which fill the body are usually darkly stained and may be crowded together or dispersed (see Fig. A.8.6). The anterior extremity is characteristically devoid of nuclei and is called the cephalic or head space; it may be short or long.

As you look from the anterior to the posterior end of the body you will see additional spaces and cells that serve as anatomical landmarks. These include the nerve ring, excretory pore, excretory cell and anal pore. In some species an amorphous mass called the inner body and four small cells (known as rectal cells) can be seen. Some of these structures and their positions are useful in identifying the species. Other useful features include the shape of the tail and the presence or absence of nuclei within it.

Table A.8.1 summarizes the features of common human filarial parasites that are used in their identification.

Note:

- Sometimes the microfilariae of the periodic strain of *B. malayi* lose their sheath.
- Identification of species can be difficult and mistakes are frequently made. The guidelines for the identification of microfilariae given above and those that appear in most textbooks make identification seem deceptively simple. Sometimes it is difficult to see the sheath. At other times, the nuclei do not appear in their characteristic position at the tip of the tail. It is good practice to examine several microfilariae carefully, before deciding on their species. If a systematic study is made of all the characteristics mentioned above, it should be possible to identify with certainty the species observed. The identification must not be based on a single characteristic, but on all the features taken together.

Possible causes of misidentification

Broken or folded tail

If the tail of *W. bancrofti* is broken or folded over (Fig. A.8.8), it appears to have nuclei extending to the tip like *L. loa*.

Torn or colourless sheath

The sheath is sometimes torn or almost colourless. In *L. loa*, for example, the sheath appears as a colourless space between the tail and the blood cells.

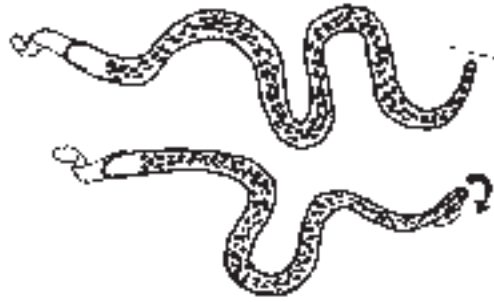
Unusually large or small microfilariae

Some *Mansonella perstans* are very long (e.g. 200 μm), and some *Wuchereria bancrofti* and *Loa loa* are small (e.g. 250 μm).

Badly made smears (or films)

If it is damaged when the smear (or film) is being made, *W. bancrofti* may appear twisted and *L. loa* may show a few curves.

Figure A.8.8 Possible cause of misidentification of *W. bancrofti*: broken or folded tail



Examination of thin films

Identification of microfilariae in stained thin films is not recommended; the microfilariae are shrunken, distorted and difficult to recognize.