

# *Manual on the Integrated Management of Five Neglected Tropical Diseases*

(For peripheral-level health workers)

*Leprosy*

*Buruli ulcer*

*Endemic Treponematoses*

*Leishmaniasis*

*Human African Trypanosomiasis*

## Abbreviations

FNA	Fine needle aspiration
AARB	Acid-alcohol resistant bacillus
ENL	Erythema nodosum leprosum
IEC	Information, education and communication
LABO	Laboratory
CL	Cutaneous leishmaniasis
ACL	Urban anthroponotic cutaneous leishmaniasis
DCL	Disseminated cutaneous leishmaniasis
LCL	Localized cutaneous leishmaniasis
MCL	Mucocutaneous leishmaniasis
CSF	Cerebrospinal fluid
ZCL	Rural zoonotic cutaneous leishmaniasis
PKDL	Post-kala-azar dermal leishmaniasis
LEISH	Leishmaniasis
LEP	Leprosy
LV	Visceral leishmaniasis
MB	Multibacillary leprosy
MDT	Multiple Drug Therapy
LLIN	Long-lasting insecticide-treated bed net
NTD	Neglected Tropical Disease
CM-NTD	Case management Neglected Tropical Disease
NECT	Nifurtimox-eflornithine combination therapy
WHO	World Health Organization
PB	Paucibacillary leprosy
PCR	Polymerase chain reaction
R°/LEP	Leprosy reaction
PHC	Primary health care
LST	Leishmanin skin test
ET	Endemic treponematoses
HAT	Human African Trypanosomiasis
BU	Buruli ulcer
HIV	Human immunodeficiency virus

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## SUMMARY

Neglected Tropical Diseases (NTDs) are 17 infections that proliferate in the tropical regions of the world. For several decades, the programmes designed to combat these diseases have received neither special attention nor substantial funding from affected countries and the international community. In the WHO African Region, five neglected tropical diseases, which require individual case management (CM-NTDs), have been identified as priority diseases. These are leprosy, Buruli ulcer, endemic treponematoses (yaws and bejel), cutaneous and visceral leishmaniasis and Human African Trypanosomiasis (HAT) or sleeping sickness.

The management of CM-NTDs involves screening and treatment of patients and of contacts in the case of endemic treponematoses. This requires responsibilities at various levels of the health system. Accordingly, the peripheral level of the health system is involved in case suspicion, screening and/or diagnosis and prevention of complications and disabilities resulting from these diseases. As regards endemic treponematoses, there is also need to search for and monitor contacts within the community, to detect and treat other cases and contacts with a view to combating these diseases effectively. The district level is responsible for confirming diagnoses through more specialized clinical examination and laboratory tests, as well as management of serious cases, including hospitalization for high-risk treatments. Lastly, the intermediate and central levels are referral centres for diagnosis and treatment of cases that exceed the expertise and capacity of the lower levels.

The integrated CM-NTD control strategy, developed by a working group in December 2014, recommends capacity building for health workers at all levels so that they can perform their assigned responsibilities well. That is the objective of this handbook designed for peripheral level health workers to enable them to:

- detect CM-NTDs and contribute to their diagnosis through clinical tests and collection of specimens for additional tests (bacteriological, parasitological, serological and molecular biology);
- treat simple cases and refer for treatment all serious or complicated cases, as well as those requiring hospitalization and/or specialized monitoring;
- monitor cases of endemic treponematoses within the community to detect and treat other cases and contacts;
- provide advice and preventive care for disabilities, complications or sequelae resulting from CM-NTDs.

This manual is also aimed at guiding health workers on social mobilization to combat CM-NTDs and mainstream CM-NTD control activities into general health services, thus ensuring that they contribute to the implementation of the integrated CM-NTD control strategy.

## INTRODUCTION

Neglected tropical diseases (NTDs) are approximately 15 infections that proliferate in the tropical regions of the world. For several decades, these diseases have received neither special attention nor substantial funding from countries and from the international community. The serious disabilities and sequelae resulting from these diseases contribute in maintaining the poorest communities within the vicious cycle of “poverty-disease-poverty”. In 2006, WHO prepared an integrated global NTD control plan, which classifies these diseases under two categories, namely: preventive chemotherapy NTD and those that require diagnosis and treatment of cases - commonly referred to as “case management NTDs or CM-NTDs”.

In the WHO African Region, five of them are identified as priority diseases because of the number of affected countries, their complications and their negative socio-economic consequences. Of these five, leprosy, Buruli ulcer and endemic treponematoses (yaws and bejel) are bacterial infections, while cutaneous and visceral leishmaniasis and Human African Trypanosomiasis (HAT) or sleeping sickness are parasitic infections.

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae*, which mainly affects the skin and the nerves. It is especially rampant in underprivileged communities or in areas that are inaccessible to health services, as well as in marginalized communities, especially the poorest. The bacillus is transmitted through the upper respiratory tract, during close and frequent contacts with an infected and untreated person. It affects both men and women, and both adults and children. It takes three to five years to manifest itself and can be easily cured with multidrug therapy (MDT) that interrupts transmission and prevents complications when administered at the first signs of the disease. This treatment is (or should be) available in all health centres and a programme has been developed to eliminate the disease. The programme requires all health workers to be able to diagnose, treat and monitor cases of CM-NTD in all health centres, and to integrate such services with the other primary health care (PHC) services.

Buruli ulcer is a skin disease caused by *Mycobacterium ulcerans*, a microorganism belonging to the same family as the bacteria that causes tuberculosis and leprosy. The exact mode of transmission to humans remains unknown. It mostly attacks children from rural communities located in hot and humid tropical areas, near marshes or plains located along slow-flowing rivers or streams. Patients who do not receive early and proper treatment can develop large progressive ulcers, which produce severe disfigurement and deformities, including disabling contractures and even amputation of the limbs. The goal of the Buruli ulcer control programme is to reduce morbidity and disabilities resulting from the disease in endemic countries. The strategies implemented are based on early detection, proper case management, an integrated surveillance system and research to improve knowledge about the disease with a view to developing simpler diagnostic tests and oral treatment.

Endemic treponematoses are a group of chronic infections such as yaws, endemic syphilis (or bejel) and pinta. The first two are endemic in Africa, while pinta is found in Latin America. All of these infections are manifested by skin lesions. Yaws, a chronic infection of the skin, bones and cartilage, is the most common of them. It is caused by a bacterium called *Treponema pallidum*, sub-species *pertenue*. Syphilis also, caused by *Treponema pallidum*, sub-species *pallidum*, is a venereal disease, while yaws is not. Yaws is found primarily in poor communities located in the warm and humid tropical environments of Africa, Asia and

Latin America. Nearly 75% of those affected are children under 15 years, with a peak incidence within the 6-10 years age group. Yaws is transmitted mainly through physical contact with an infected person. Bejel, caused by *Treponema pallidum*, sub-species *endemicus*, is prevalent in dry and arid climates, especially in the Sahelo-Saharan areas, and affects mostly children. A yaws eradication programme is being developed and could lead to integration of yaws control activities with those of diseases eligible for preventive chemotherapy.

Leishmaniasis are parasitic diseases of the monocyte-macrophage system caused by a flagellate protozoan of the genus *leishmania*. It is often a zoonosis, transmitted from vertebrate to vertebrate by the female of a hematophagous gnat, the sand fly. Leishmaniasis include visceral (VL) or Kala-azar leishmaniasis, which can be fatal if left untreated, localized cutaneous leishmaniasis (LCL) disseminated cutaneous leishmaniasis (DCL) and mucocutaneous leishmaniasis (MCL). Furthermore, there is a cutaneous form that is secondary to the visceral form, called post-kala-azar dermal Leishmaniasis (PKDL). This multiplicity of clinical profiles stems from the wide range of species and variations in the immune response of the infected host. This disease, which affects the poorest communities in the world, is associated with malnutrition, population displacement, poor housing conditions, weakened immune systems and poverty. It is linked to environmental changes such as deforestation, the construction of dams, irrigation systems and urbanization. Effective monitoring of the disease is important. Early detection and treatment of cases help to reduce transmission and to monitor the spread and burden of the disease.

Human African Trypanosomiasis (HAT), also known as "sleeping sickness", is a vector-borne parasitic disease. It is the only vector-borne parasitic disease whose geographical distribution is limited to the African continent. The parasite pathogenic to man is transmitted through the bite of an infected tsetse fly. The communities most exposed to this disease are those engaged in activities, which are likely to bring them into contact with tsetse flies, such as fishing, gathering wild honey, fetching water from streams, rearing livestock, and collecting fuel wood or sheanuts from forest and woodland areas. HAT appears in two strains, depending on the parasite, namely: the *gambiense* strain in West and Central Africa, and the *rhodesiense* strain in East and Southern Africa. Sleeping sickness, which is fatal if left untreated, saps the energy to work and reduces the cultivable surface area, thus undermining socio-economic development. The strategies developed are aimed at strengthening the operational capacities of national programmes, surveillance systems, and monitoring/evaluation of interventions; supporting operational research to improve treatment and diagnostic tools; and encouraging inter-sectoral collaboration and coordination in vector control. The objective is to eliminate HAT as a public health problem in 100% of households by 2020.

These five diseases are generally chronic mutilating infections and, apart from endemic treponematoses, two of them (visceral leishmaniasis and HAT) are fatal if they are not subjected to often-protracted treatments. Treatment sometimes requires increased monitoring due to the serious complications that may arise. In the absence of pathognomonic signs and given the possible collateral effects of treatments, some of these diseases require biological confirmation and treatment in appropriate centres. Nevertheless, all these infections produce skin manifestations, although such manifestations are rare in the case of HAT.

This manual is intended to guide health workers to make a diagnosis based on the above-mentioned skin lesions and their accompanying signs. It is also intended to train health workers to administer treatment and organize integrated CM-NTD control in the WHO

African Region. It will familiarize health workers with the essential elements of diagnosis and treatment and acquaint them with the salient information and activities under programmes developed for the integrated control, elimination or eradication of these diseases.

After studying this manual, which should serve as the desk book of health workers in peripheral health centres located in CM-NTD endemic areas, the health worker should be able to:

- Detect CM-NTDs and contribute to their diagnosis through clinical examination and collection of specimens for additional tests (bacteriological, parasitological, serological and molecular biology);
- Treat simple cases or refer for treatment the cases which are serious or complicated, as well as those that require hospitalization and/or specialized monitoring;
- Monitor cases of endemic treponematoses within the community to detect and treat other cases and contacts;
- Provide advice and preventive care for the disabilities and complications or sequelae resulting from CM-NTDs.



## 1. Examination of a patient with a skin condition

A skin or dermatological examination is conducted in three stages.

### 1.1. Stage One: Questioning

Question the patient on the following six points:

- Identifying information: age, sex, profession, place of residence or origin;
- Reason for consultation: skin lesions, other symptoms;
- Contact with a case of the disease having skin lesions;
- History of the disease: trauma or bite; early lesion; duration; slow and progressive evolution; presence of similar cases in the family or place of residence; treatment already started;
- Associated signs: absence or presence of signs of inflammation (pain, heat, redness, swelling) or other general signs (fever, anaemia, oedema, jaundice); presence or absence of itching and scaling;
- Characteristics of the living environment (hot and humid environments near a stream or marshland; residence at or visit to an endemic environment; presence of vectors - tsetse flies or sand flies).

### 1.2. Stage Two: Clinical examination of the skin

- Examine the entire body under good lighting, from a distance and then up close;
- Look for suspect CM-NTD lesions, namely: macule or spot, papule, papilloma, nodule, plaque, oedema, ulcer or ulcerative wound, osteitis with fistulation;
- Carefully examine suspicious lesions and describe them:
  - ✓ Size (large or small), appearance, painless or painful when touched, induration or softness of non-ulcerative lesions, sensitivity of the damaged skin;
  - ✓ Characteristics of ulcers: wounds with detached borders and a yellowish necrotic aspect, which are relatively less painful, and have no satellite lymph nodes;
  - ✓ Location and number of lesions.

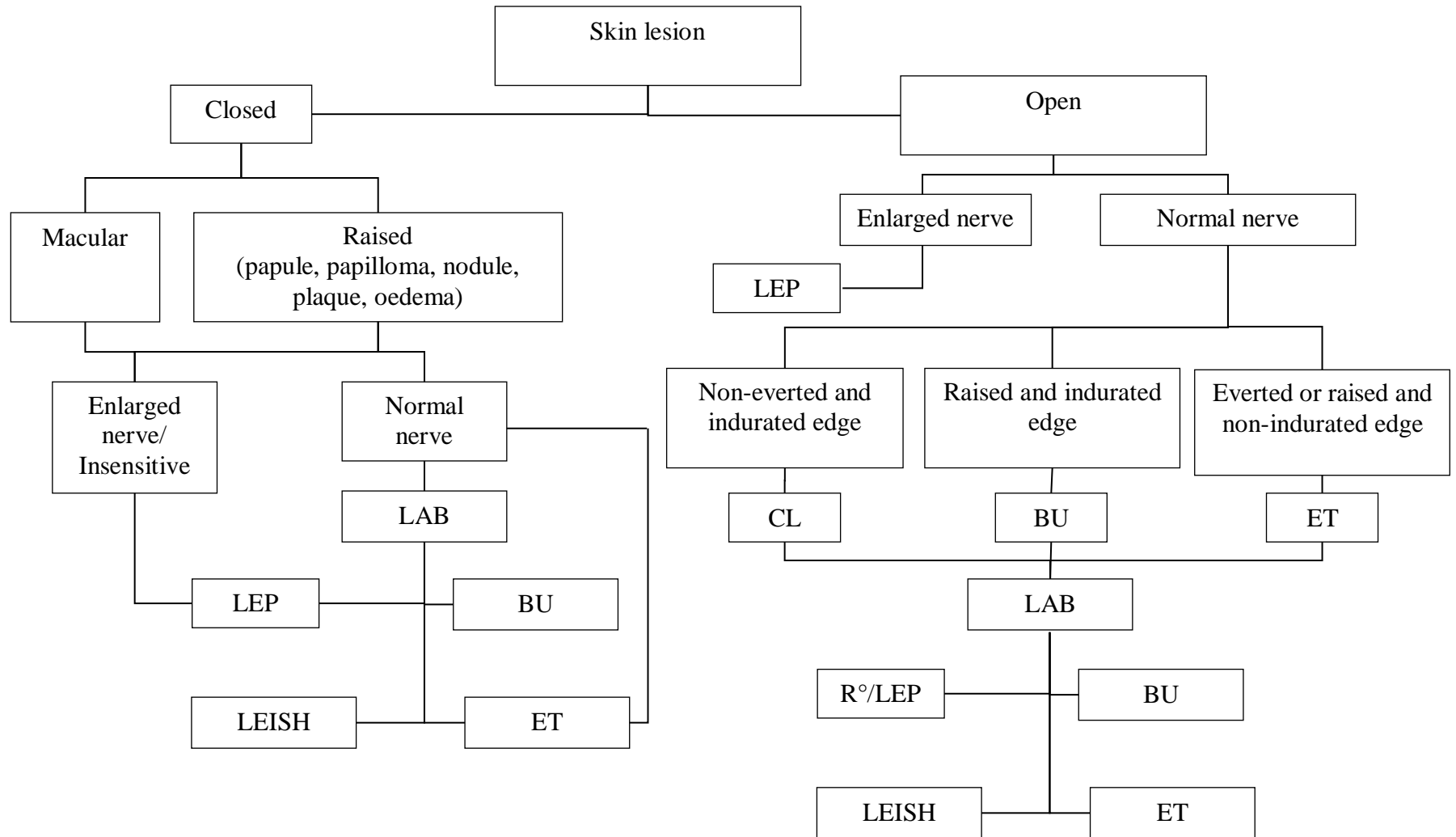
### 1.3. Stage Three: General clinical examination

- Assess the patient's general condition and anaemic state. Check the temperature, blood pressure and weight.
- Check for limitation of movement in the joints, and loss of sensitivity in the limbs (hands and feet).

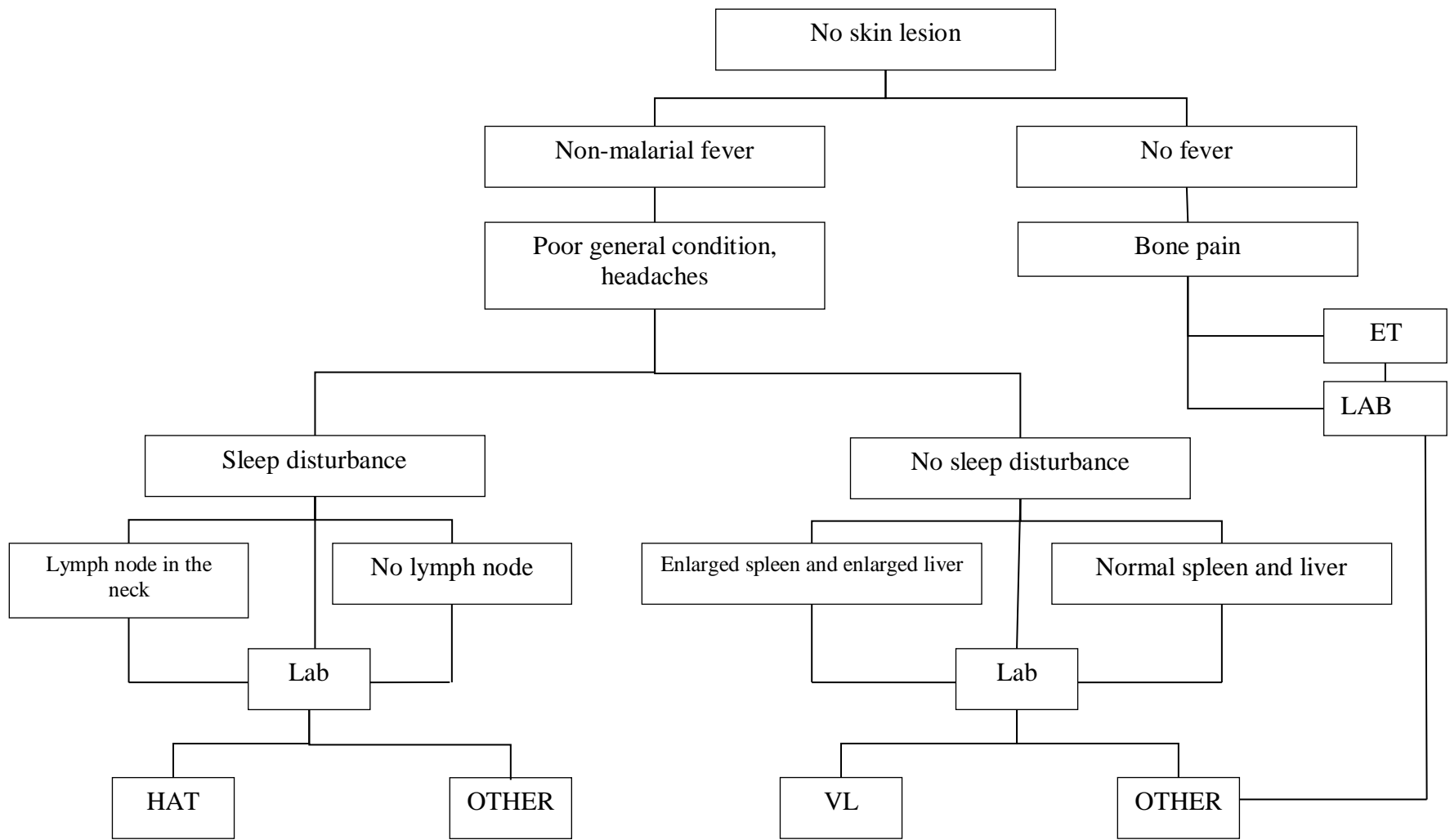
At the end of this examination, consolidate all the observations made and use the decision trees below to make a diagnosis or suspect an infection.

## 2. Decision trees

### 2.1. Decision tree when there is a skin lesion



**2.2. Decision tree when there is no skin lesion**



## 3. Leprosy

### 3.1. Clinical examination

- Non-pruritic light-coloured spot or isolated nodule on the skin which develops gradually and slowly, with reduced or no sensitivity on the site;
- Family history of leprosy or leprosy contact in the family;
- “Typical” leprosy patch: “Clear-coloured or coppery red patch with net loss of sensitivity when touched with cotton wool”;
- Neurological examination in search of hypertrophic (enlarged) nerves, conducted through palpation of the auricular branch of the facial nerve, in the neck and below the ear; of the ulnar nerve, at the level of the elbow and above the epitrochleo-olecranal canal; and of the external popliteal sciatic nerve, in the hollow of the knee, behind the upper extremity of the fibula;
- Search for complications through sensitivity and motricity tests:
  - ✓ In the eyes: red eye, reduced blink rate;
  - ✓ On the hands and feet: complications associated with muscle wasting, ankyloses and paralysis with wrist drop;
  - ✓ On the feet: complications associated with perforating ulcers on the soles of the foot, amputations, resorption and foot-drop when walking.
- Classification of the patient based on the number of spots on the skin:
  - ✓ Paucibacillary leprosy (PB): 1 to 5 skin lesions;
  - ✓ Multibacillary leprosy (MB): 6 or more skin lesions, or nodules caused by leprosy.
- Scale of the disabilities observed in the eyes, hands and feet in (three) degrees
  - ✓ 0 degree: normal neurological test, as regards sensitivity and motricity
  - ✓ 1st degree: insensitivity without visible lesions;
  - ✓ 2nd degree: insensitivity with visible lesions (muscle wasting, wounds, amputation, lagophtalmos, decreased visual acuity and blindness).
- Leprosy reaction (there are two types):
  - ✓ Type 1 leprosy reaction or reversal reaction: inflammation of cutaneous spots which become red, warm, swollen and sensitive (redness, sensitivity, tumour and pain), in which case there is a risk of neuritis characterized by the sudden onset of sharp pain in the nerve trunks, associated with motor disorders (paralysis) or sensory disorders (insensitivity);
  - ✓ Type II leprosy reaction or erythema nodosum leprosum (ENL): sudden appearance of new lesions in the form of hard, painful, warm, sub-cutaneous nodules (called lumps), associated with hypersensitivity of the skin, even to light touch; poor general health condition with fever, sometimes accompanied by a drop in blood pressure and swelling of the lower limbs.

### 3.2. Laboratory tests

The diagnosis and therapeutic classification of leprosy patients are essentially based on clinical observations. It is recommended to take a bloodless specimen from the edges of the suspected spots or at the centre of the nodules (lepromas) to search for acid-alcohol resistant bacilli (AARB) in the laboratory. However, a negative result does not necessarily signal the absence of leprosy.

### 3.3. Treatment

Any patient recognized as a leprosy case must receive the multidrug therapy (MDT) recommended by WHO. In this context, a leprosy case is anyone exhibiting clinical signs of leprosy and who has not received any adequate MDT treatment since the onset of clinical signs.

- Treatment of PB leprosy:

Six months of MDT, combining rifampicin and dapsone, as follows:

Rifampicin: Single monthly dose of rifampicin - 600 mg for adults and 450 mg for children.

Dapsone: Single daily dose - 100 mg for adults and 50 mg for children.

These medicines are packaged in monthly blister packs. The PB blister pack for adults is green in colour. The PB blister pack for children is blue (see the MDT blister packs after the photographs). Six PB blister packs are needed and the duration of PB treatment is six months. The patient is declared healed after completion of the sixth MDT blister pack.

- Treatment of MB leprosy:

Twelve months of MDT, combining rifampicin, Clofazimin and dapsone, as follows:

Rifampicin: Single monthly dose - 600 mg for adults and 450 mg for children.

Clofazimin: Single monthly dose - 300 mg for adults and 150 mg for children.

Single daily dose - 50 mg/day for adults and 25 mg for children.

Dapsone: Single daily dose - 100 mg for adults and 50 mg for children.

These medicines are packaged in monthly blister packs. The MB blister pack for adults is red in colour. The MB blister pack for children is orange (see the MDT blister packs after the photographs). 12 MB blister packs are needed and the duration of MB treatment is 12 months. The patient is declared healed after completion of the 12th MDT blister pack.

- Treatment of leprosy reactions and neuritis:
  - ✓ Minor reactions: acetylsalicylic acid or non-steroidal anti-inflammatory drugs;

- ✓ Serious reactions: begin with non-steroidal anti-inflammatory drugs and refer; a reaction is said to be serious when the general signs are severe, with the onset of motor disorders, or lesions on the face.
- Advice to patients:
  - ✓ Eyes: Protection of the eyes with eyeglasses, artificial tears, voluntary blinking exercises;
  - ✓ Hands: Protection of the hands by wearing gloves for manual work; use of handles for kitchen utensils; wrapping of the handles of kitchen tools and utensils with cloth, etc.
  - ✓ Feet: Protection of the feet by wearing shoes with soft soles; frequent resting when walking long distances (more than a kilometre).

### **3.4. Monitoring of patients**

- Monitoring activities for patients who are on treatment:
  - ✓ Correctly fill out the card and booklet or treatment log for each patient;
  - ✓ Verify appointment dates to ensure supervised drug administration;
  - ✓ Check the clinical evolution of each patient during each visit to the treatment centre;
  - ✓ Carry out personalized health education to reassure each patient;
  - ✓ Adapt the type of MDT to the situation of each patient (flexible MDT, supervised MDT, community-based MDT);
  - ✓ Look for patients who are irregular in their MDT treatment (criteria being 2/3 of the MDT dose for the time period considered).
- Neurological monitoring:
  - ✓ Conduct periodic neurological assessments to detect neuritis and other complications;
  - ✓ Undertake the health education of patients to prevent possible anomalies that may occur in the eyes, feet and hands, and which may require the patient to return to the health centre;
  - ✓ Take adequate measures to treat leprosy reactions and all other complications.

### **3.5. Prevention of leprosy**

There is no specific primary prevention measure, because there is no vaccine against leprosy. However, poor socio-economic conditions are believed to have a certain impact on the epidemiology of the disease. Indeed, leprosy disappeared from countries of the North following improvements in drinking water supply and in individual and community hygiene and sanitation.

Secondary prevention essentially entails early detection and treatment of all cases with MDT based on WHO recommendations, as well as improvements in socio-economic conditions and in hygiene and sanitation.

Patients with sequelae should be referred to specialized centres for enrolment into a rehabilitation programme.

### 3.6. Photographs



Multibacillary leprosy

**Figure 1: Types of clinical lesions of leprosy**

# MDT regimes

Each blister pack contains treatment for 4 weeks.

It is crucial that patients understand which drugs they have to take once a month and which every day.



PB adult blister pack

**PB adult treatment:**

- Once a month:** Day 1
  - 2 capsules of rifampicin (300 mg X 2)
  - 1 tablet of dapsone (100 mg)
- Once a day:** Days 2–28
  - 1 tablet of dapsone (100 mg)
- Full course:** 6 blister packs



PB child blister pack

**PB child treatment (10–14 years):**

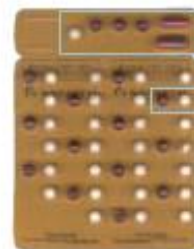
- Once a month:** Day 1
    - 2 capsules of rifampicin (300 mg+150 mg)
    - 1 tablet of dapsone (50 mg)
  - Once a day:** Days 2–28
    - 1 tablet of dapsone (50 mg)
  - Full course:** 6 blister packs
- For children younger than 10, the dose must be adjusted according to body weight.



MB adult blister pack

**MB adult treatment:**

- Once a month:** Day 1
  - 2 capsules of rifampicin (300 mg X 2)
  - 3 capsules of clofazimine (100mg X 3)
  - 1 tablet of dapsone (100 mg)
- Once a day:** Days 2–28
  - 1 capsule of clofazimine (50 mg)
  - 1 tablet of dapsone (100 mg)
- Full course:** 12 blister packs



MB child blister pack

**MB child treatment (10–14 years):**

- Once a month:** Day 1
    - 2 capsules of rifampicin (300 mg+150 mg)
    - 3 capsules of clofazimine (50 mg X 3)
    - 1 tablet of dapsone (50 mg)
  - Once a day:** Days 2–28
    - 1 capsule of clofazimine every other day (50 mg)
    - 1 tablet of dapsone (50 mg)
  - Full course:** 12 blister packs
- For children younger than 10, the dose must be adjusted according to body weight.

Figure 2: Types of MDT leprosy treatment blister-packs.



## 4. Buruli Ulcer

### 4.1. Clinical examination

The following elements facilitate the clinical diagnosis of Buruli ulcer

- Origin: the patient comes from a known endemic area (or has visited such an area);
- Age of the patient: children under 15 years of age are the most affected;
- Location of lesions: frequent on the limbs, especially the lower limbs;
- Non-ulcerative lesions are virtually painless or less painful, and any pain, fever, or lymphadenopathy is indicative of a secondary bacterial infection caused by common germs or a co-infection.

The clinical diagnosis requires a biological confirmation. When presented with the above elements, the health worker at the peripheral level should be able to take specimens to confirm the diagnosis at the district laboratory or reference laboratory.

When operating in a recognized endemic area, the health worker can start the treatment without waiting for the result of the biological confirmation. Elsewhere (uncertain endemic area), the health worker should wait for the results before starting treatment.

### 4.2. Laboratory tests

The biological confirmation of Buruli ulcer should be systematic.

- Collection of specimens  
Three sampling techniques can be used:
  - ✓ **Non-ulcerative lesions (nodules, plaques and oedema)**  
Fine needle aspiration (FNA);  
Punch biopsy at the centre of the lesion (using a punch).
  - ✓ **Ulcers**  
Swabs used to collect specimens from the undermined edges of wounds;  
Fine needle aspiration (FNA) used to collect specimens from the undermined edges of ulcers and from the necrotic yellowish core of the ulcer;  
Biopsy on the necrotic debris from the core of the ulcer.

Only swabs and fine needle aspiration can be done at the peripheral health centre. It is recommended to take two samples for each lesion, regardless of the sampling technique. Biopsy is not recommended in routine practice.

- Packaging and transmission of specimens
  - ✓ Search for AARB, cellular biology (PCR) or thin-layer chromatography (being validated): the various specimens are placed in tubes and transported using the most appropriate and adapted means;
  - ✓ Biopsy specimens for histopathological test can be kept in bottles or containers filled with formalin diluted to 10%.

### 4.3. Treatment

- Classification of patients

Prior to initiating treatment, patients are classified under the following four categories:

- ✓ **Category I:** single lesion with diameter < 5 cm;
- ✓ **Category II:** single lesion measuring 5 to 15 cm in diameter;
- ✓ **Category III:** single lesion with diameter > 15 cm; multiple lesions; lesion(s) located in critical areas (eye, breast, genital organs) and osteomyelitis:
  - **IIIa:** single lesion diameter > 15 cm or osteomyelitis;
  - **IIIb:** lesions in critical locations;
  - **IIIc:** multiple small lesions.

- Treatment components

The treatment components are the following:

- ✓ Antibiotic treatment;
- ✓ Dressing
- ✓ Prevention of joint movement limitation;
- ✓ Surgery, sometimes necessary for some lesions;
- ✓ Rehabilitation when there is sequelae.

- Conduct of the treatment

- ✓ Category 1
  - Antibiotic treatment;
  - Maintain joint mobility in case of joint damage;
  - Dressing, if the lesion is ulcerative;
  - Refer, if the evolution is not satisfactory at the end of antibiotic therapy.
- ✓ Category 2
  - Antibiotic treatment;
  - Physiotherapy;
  - Dressing, if the lesion is ulcerative
  - Refer, if the evolution is not satisfactory at the end of antibiotic therapy.
- ✓ Category 3
  - Refer immediately to the referral hospital;
  - Initiate antibiotic treatment prior to referral, if immediate transfer is not possible;
  - Physiotherapy.
  - Dressing, if the lesion is ulcerative.

- Antibiotic treatment protocol

A combination of rifampicin and streptomycin or rifampicin and clarithromycin is recommended.

- ✓ Prescription conditions
  - Clinical diagnosis of BU;
  - Collection of the specimens needed for laboratory confirmation (swabs, fine needle aspiration);
  - Classify BU cases according to categories;
  - Weigh the patient, especially children;
  - Eliminate potential contraindications;
  - Prescribe treatment based on the patient's weight.

- ✓ Duration of treatment and dosage.  
The duration of treatment is 56 days. The recommended dosages are as follows:
  - Rifampicin:
    - 300 mg (or 150 mg) tablets
    - Dosage: 10 mg/kg of body weight
    - Taken daily by oral route
  - Streptomycin:
    - Injectable vial of 1g, or 2 ml
    - Dosage: 15mg/kg of body weight
    - Daily intramuscular injection (change injection site each day)
  - Clarithromycin
    - 500 mg tablets and 250 mg syrup
    - Dosage: 7.5 mg/kg of body weight
    - To be taken twice daily by oral route
- ✓ Main contraindications of the antibiotic treatment
  - Pregnancy (primarily for the streptomycin);
  - Allergy to rifampicin, streptomycin or clarithromycin;
  - Renal or hepatic impairment;
  - Persons previously treated with streptomycin (the total dose that can be administered to an adult during his entire life must remain below 90 g, or 90 one gram injections);
  - Taking of other medicines that are nephro-toxic (kidneys) or oto-toxic (hearing and dizziness).

#### 4.4. Monitoring of patients

- Monitoring during treatment
  - ✓ Ensure compliance with and completion of the treatment
    - Daily administration of antibiotics;
    - Regular dressing of the wound;
    - Regular photographs of the lesion;
    - Mobilization and regular use of the affected body part;
    - Monitoring of side effects;
    - Assessment of the improvement or worsening of the clinical condition (superinfection, limitation of movement).
  - ✓ Fill out the data sheets:
    - Patient's clinical and treatment form (Form BU 01);
    - Notification form (Form BU 02);
    - Form BU 03 for the laboratory.
  - ✓ Search for irregular patients and those who have stopped coming for treatment
- Follow-up after healing
  - ✓ Advise the patient on the proper management of scars, joint mobilization;
  - ✓ See the patient periodically: The regularity of follow-up visits will be determined with the patient, based on how far the patient's place of residence is; in general, it

is recommended that follow-up be conducted 1 month after discharge, and subsequently 3 months, 6 months and 12 months later.

#### **4.5. Prevention of Buruli ulcer**

- **Primary prevention**  
There is no vaccine against Buruli ulcer. Primary prevention activities are essentially awareness raising on protective measures and on personal and community hygiene.
- **Secondary prevention**  
The purpose of secondary prevention is early detection of BU before the emergence of complicated forms (category 3). To that end, the nurse will have to:
  - ✓ Organize awareness-raising sessions on the signs of Buruli ulcer;
  - ✓ Organize early screening within the community.
- **Disability prevention and rehabilitation**
  - ✓ Conduct joint mobilization for each patient;
  - ✓ Provide advice to the patient or his/her guardian on active and passive joint mobilization;
  - ✓ In case of sequelae, direct the patient to a specialized centre so that he/she can be admitted into a rehabilitation programme.

**4.6. Some photographs**



**Figure 3: Types of Buruli ulcer lesions**

## 5. Endemic Treponematoses

Apart from venereal syphilis, treponematoses also include non-venereal forms of the disease or endemic treponematoses: yaws, bejel or endemic syphilis and pinta, rare cases of which have been reported in Latin America. Treponematoses are a group of chronic infections caused by bacteria of the *Treponemaceae* family, genus *Treponema*. Yaws, endemic syphilis and pinta are respectively caused by *T. pallidum*, sub-species *pertenue*; *T. pallidum*, sub-species *endemicus*; and *T. carateum*. Man is their only natural host.

### 5.1. Clinical examination

#### 5.1.1. Yaws

- Early yaws lesions
  - Papilloma: yellowish in colour, indurated, having the form of a boil, painless and slightly pruritic; it may be moist or dry and often occurs on the legs;
  - Ulcer: raised edges, non-indurated and painless; the base may be crusty and/or pruritic;
  - Papules: small lesion <1 cm, painless, pale-coloured and indurated; they may be pruritic and coalesce to form a plaque;
  - Macules: flat, pale-coloured and often squamous lesions; they can be discreet or coalesce to form a large patch and may be pruritic;
  - Circular lesions: micro nodules that coalesce to form a circular lesion and may be pruritic;
  - Palmar and plantar lesions: often painful lesions that occur on the palms of the hands or the soles of the feet; they can occur in the form of erosions, cracks, hyperkeratosis (thickenings), papilloma or macules;
  - Mixed forms: occurrence of different types of yaws lesions in the same individual at the same time.
- Late yaws lesions
  - Osteoperiostitis;
  - Juxta-articular nodules;
  - Sabre tibia;
  - Gangosa.
- Definition of yaws cases.
  - **Suspected case:** Person with (past or present) residence in an endemic area, who has clinically-active (visible) yaws;
  - **Confirmed case:** Suspected case diagnosed as seropositive (through a rapid treponemal test or rapid plasma reagin qualitative and quantitative tests);
  - **Imported Case:** Person found in an area which is not known to be yaws-endemic and who has clinically-active and serologically-confirmed yaws;
  - **Princeps case:** First case of yaws observed in a given geographical area;
  - **Contact** of a person with clinically-active yaws: person who has close and frequent contact with an infected subject; for the purposes of yaws

eradication, contacts are considered to be the members of the same household, classmates or playmates as identified by the case.

### 5.1.2. Clinical characteristics of treponematoses

**Table 1: Clinical description of the treponematoses**

	<b>Venereal syphilis</b>	<b>Yaws</b>	<b>Bejel</b>
Initial lesion	Common in the genital area	Common in the limbs	Rare, in the oral mucosa
Disseminated lesions	80% to 100% of cases, generalized and widespread	90% to 100% of cases, widespread on the skin and bones	90% to 100% of cases, limited to skinfolds
General symptoms	Common	Rare	Rare
Regional	Common	Common	Common
Relapse	25% of cases	75% to 90% of cases	Unknown

### 5.2. Laboratory Tests

- A rapid serological diagnostic test is available and is used to diagnose active treponemal infections. However, it does not make a distinction between yaws and other treponematoses.
- PCR diagnostic test

### 5.3. Treatment

- Azithromycin

The recommended treatment for yaws and bejel is 30 mg/kg (2 g maximum) of azithromycin, taken as a single dose. The syrup form is preferable for children under the age of six years. However, if this form is not available, the tablet can be crushed and mixed with a bit of water. Azithromycin is contraindicated for children below the age of six months.

**Table 2: Recommended dosage by age group**

<b>Age (years)</b>	<b>Total dose (mg)</b>	<b>Number of tablets</b>	<b>Syrup (ml)</b>
< 6	500	1	12.5
6 - 9	1000	2	
10 - 15	1500	3	
> 15	2000	4	

- Benzathine benzylpenicillin (extencillin)

Benzathine benzylpenicillin remains effective and relevant in the treatment and eradication of yaws. Considering the operational and logistical problems encountered in its administration, it is reserved as backup for patients who do not tolerate azithromycin or for use in situations where there is shortage of azithromycin. The standard dosage is 0.6 million international units for children below the age of 10 years, and 1.2 million international units for persons above the age of 10 years.

#### **5.4. Monitoring of patients**

All patients treated should be reviewed after four weeks to assess the therapeutic outcome. There are two possibilities:

- **Therapeutic success (cure)**

This refers to a person with clinically active yaws, who receives a single dose of azithromycin by oral route (or an injection of benzathine benzylpenicillin) and whose lesion(s) is (are) completely healed four weeks after the treatment.

- **Therapeutic failure (yaws resistant to treatment)**

This refers to a person with clinically active yaws, who receives a single dose of azithromycin by oral route (or an injection of benzathine benzylpenicillin) and whose lesion(s) is (are) not completely healed four weeks after the treatment. In such cases, it is important to request for a serological test to confirm the presence or absence of yaws. If the result is positive, specimens have to be taken from the active lesion so that PCR can detect any resistance. If the result is negative, another diagnosis should be considered and the appropriate treatment administered.

#### **5.5. Prevention of treponematoses**

- Personal hygiene: bath with soap and water at least once a day;
- Improve access to drinking water, hygiene and sanitation;
- Treat all yaws cases and their contacts with specific antibiotics (azithromycin or benzathine benzylpenicillin).



## 5.6. Some photographs



Ulcerative wound



Papillomas



Maculo-papular Crusted lesion



Papilloma and ulcer



Papillomas and macule



Plantar lesions



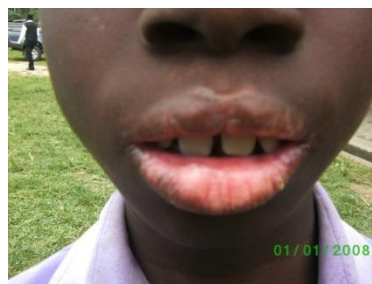
Palmar lesions (finger)



Crusted papilloma of the scalp



Diseased bone  
(Sabre shin)



Lip lesions

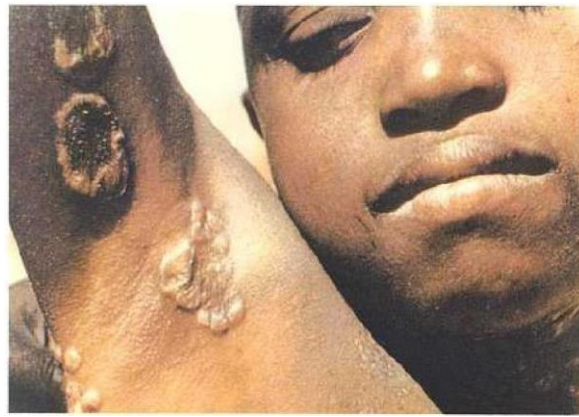


Plantar lesion

**Figure 4: Overview of the clinical forms of early yaws**



Commissurale stomatitis of bejel



Maculo papules

**Figure 5: Overview of bejel lesions**

## 6. Cutaneous and muco-cutaneous leishmaniasis

### 6.1. Clinical examination

#### ▪ Typical lesions

A clinical history suggestive of cutaneous leishmaniasis is characterized by the appearance of one or more lesions, typically on the uncovered parts of the body. The face, neck, arms and legs are the most common sites.

As regards localized cutaneous leishmaniasis, a typical lesion starts as a raised papule on the infected site. Over several weeks, it grows into a painless ulcerative nodule or plaque. A crust develops at the centre, covering an ulcer with a raised edge and variable surrounding induration.

If left untreated, the lesion gradually heals over months or years, usually leaving a depressed scar. Localized superficial dissemination of satellite papules at the edge of the lesion is common in certain species (*L. major*).

- The species of the infecting parasite may determine the appearance of the lesion
  - ✓ Cutaneous leishmaniasis caused by *L. tropica* (previously known as anthroponotic or urban anthroponotic cutaneous leishmaniasis - ACL) usually appears as dry and painless skin ulcers which usually heal spontaneously within a year or more, often leaving unsightly scars. The incubation period is usually two to eight months.
  - ✓ Cutaneous leishmaniasis caused by *L. Major* (previously known as zoonotic or rural zoonotic cutaneous leishmaniasis - ZCL) often appears as severely inflamed and ulcerative skin, which usually heals spontaneously within a period of two to eight months. The lesions are generally painless, without any complications. There may be multiple lesions, especially in non-immune patients, which can produce unsightly scars. The incubation period is often less than four months.
  - ✓ Cutaneous leishmaniasis caused by *L. infantum* generally produces a single nodular lesion on the face (i.e. there is no crust or ulceration and apart from its induration and colour, the skin on the lesion appears to be almost normal). Although *L. infantum* also causes visceral leishmaniasis, skin lesions most often develop without any visceral affection.
  - ✓ Cutaneous leishmaniasis caused by *L. aethiopica* typically leads to localized cutaneous leishmaniasis (LCL). LCL begins as a small red papule, which gradually enlarges to a diameter of 2 cm, forming nodules or plaques. The surface forms a crust at the centre, and the lesions may be single or multiple. The distribution of initial lesions corresponds to the sites bitten by the sand fly. Hence, the lesions occur on the exposed parts of the body such as the face (over 90%) and the limbs. The clinical incubation period ranges from a few weeks to several months. LCL lesions vary according to size, clinical appearance and the time needed for spontaneous healing. Usually, the lesions heal spontaneously over a period of two to five years, leaving a flat atrophic scar. Spontaneous healing usually leaves lifelong immunity against reinfection by *L. aethiopica*.

- **Variable characteristics and unusual forms**

- ✓ Skin lesions resulting from other causes may have characteristics similar to those of cutaneous leishmaniasis. Furthermore, there are unusual forms of cutaneous leishmaniasis. Several characteristics of cutaneous leishmaniasis are highly variable; for example, the number and location of lesions, their basic appearance (i.e. ulcer, nodule or plate) and size.
- ✓ In some cases, often but not exclusively in patients with immunosuppression, cutaneous leishmaniasis is characterized by the presence of over 10 lesions. These multilesional forms are often difficult to treat and require specific or appropriate care.
- ✓ Cutaneous leishmaniasis with nodular lymphangiitis is a rare form of the disease. Subcutaneous nodules are usually discrete, painless and close to primary skin lesions. When there are several of them, they often appear in linear formation.
- ✓ *L. aethiopica* can cause disseminated cutaneous leishmaniasis (DCL) and mucocutaneous leishmaniasis (MCL).
- ✓ Disseminated cutaneous leishmaniasis is a rare form of LC caused by *L. aethiopica*, which occurs in areas where LCL is common, and arises from a deficit of specific cell-mediated immunity. DCL begins with some papular or nodular lesions, followed by gradual dissemination of the infection, leading to multiple nodular and papular lesions as well as plaques on extensive areas of the skin. Local dissemination begins at the same time in 30% of cases. New metastatic lesions appear on remote sites on the skin, most likely initiating the spread of the disease through the bloodstream. The face, ears, limbs, buttocks, the penile skin and scrotum may be affected. The LCD is chronic and progressive. It does not heal spontaneously. It is difficult to treat, thus requiring long-term treatment.
- ✓ Mucocutaneous leishmaniasis (MCL) may develop if the bite of the sandfly is very close to the mucosa of the nose or mouth, with the disease spreading to the mucosa and causing a swelling of the lips or nose, which lasts for several years. It may also result from prolongation to a nearby skin lesion. In Ethiopia, MCL is more frequently confined to the area around the nose and mouth, but it may also spread deeply into the nose, mouth or pharynx, where it can cause large destructive and disfiguring lesions. MCL does not heal spontaneously and therefore needs to be treated.

- **Post-kala-azar dermal leishmaniasis (PKDL)**

VL caused by *L. donovani* occurs with a post-treatment complication called PKDL. PKDL is characterized by the appearance of painless skin lesions, which are relatively common towards the end of treatment or shortly after treatment. Sometimes, PKDL occurs before or concomitantly with active VL. PKDL is relatively common in co-infections with HIV. Patients with a PKDL harbour the *Leishmania* parasite in skin lesions of the skin and can be potential sources of infection.

PKDL diagnosis is essentially clinical, since the skin smear test has very low sensitivity. Clinical diagnosis is conducted by evaluating a typical rash and its distribution in a patient with a history of visceral leishmaniasis. PKDL may be concomitant with VL or even occur without any antecedents of leishmaniasis. Patients with PDKL must be treated in a centre of reference, depending on the severity of the disease, and advised to use long-lasting insecticide-treated bed nets.

PKDL may be classified according to the gravity of the skin lesion. PDKL classification will facilitate treatment decisions. Severe cases of PDKL, grades 2 and 3, require treatment and must be transferred to VL treatment centres.

✓ Classification of PDKL lesions

- Grade 1: Scattered eruption of macules, papules or nodules on the skin, mainly on the face and around the mouth, with or without some lesions on the chest and the upper limbs;
- Grade 2: Dense skin eruptions of macules, papules or nodules covering most of the face and extending to the chest, back, arms and legs; if the lesions are extensive or have a darker shade, then we talk of severe Grade 2 PDKL;
- Grade 3: Eruption of dense macules, papules or nodules covering most of the body, including the hands and feet; in Grade 3, there are crusts, ulcers, bedsores, squama, a darkening of the skin and a dissemination of lesions to the mucosa of the lips and mouth.

Skin lesions must be differentiated from other skin pathologies, including leprosy (which leads to loss of sensitivity), bacterial and fungal skin infections (where laboratory tests for the specimens are positive for bacteria or fungi).

▪ Case classification based on the operational definition of WHO

- ✓ *Probable case*: A probable case of cutaneous leishmaniasis is a person with clinical signs (skin or mucosal lesions), without any parasitological confirmation of the diagnosis;
- ✓ *Confirmed case*: A confirmed case of cutaneous leishmaniasis is a person with clinical signs (skin or mucosal membranes), with parasitological confirmation of the diagnosis (pap smear or culture positive) and/or serological diagnosis in the case of mucocutaneous leishmaniasis only;
- ✓ *Cured cases*: Total re-epithelialization before day 45;
- ✓ *Relapsed case*: Reappearance of a nodule, plaque or ulceration after healing; parasitological confirmation only in complex cases;
- ✓ *Therapeutic failure*: enlargement of a nodule, a plaque or ulceration within the 14 days of treatment; or no complete re-epithelialization within 45 days after the beginning of treatment.

To confirm a probable case of cutaneous or mucosal leishmaniasis, it is necessary to examine the skin or mucosa (pap smear of lesions), mainly through the microscope. Unfortunately, the laboratory tests generally available in endemic areas are not 100% sensitive or the laboratories are inaccessible to the patient, such that the clinician may have to take a decision based on clinical and epidemiologic criteria, after having ruled out other conditions.

## 6.2. Laboratory tests

Clinical suspicion of cutaneous leishmaniasis should be confirmed through a parasitological test. Specimens from suspected lesions are collected through aspiration, scraping and tissue biopsy on active lesions and not on scar lesions. The Giemsa stained skin smear is the simplest test that can be conducted in a health centre that has a parasitology laboratory.

Three specimen-taking techniques are possible, namely: aspiration, scraping and biopsy. The simplest test at the health centre level is aspiration conducted on the raised edges of lesions or on the central part of nodules.

The leishmanin skin test (LST) is used in surveys for disease prevalence evaluation.

## 6.3. Treatment

In some cases, cutaneous leishmaniasis does not need to be treated with specific antileishmanial drugs (see Situation 1 below). In that case, what is needed is washing and dressing of the wounds.

Cutaneous leishmaniasis is not a life-threatening illness, and serious complications are rare. However, since superficial secondary infections may complicate ulcerative cutaneous leishmaniasis, it is important to clean the lesions. Cutaneous leishmaniasis, caused by *L. Major*, has a self-healing rate of over 50% to 75% within four to six months.

The recommended drug or treatment for cutaneous leishmaniasis should not induce potentially fatal complications. However, in serious cases, the risk-benefit ratio is different. The treatment decision is based primarily on the risk-benefit ratio of the intervention for each patient. To determine the treatment that is most appropriate, it is important to collect clinical information on the following five aspects:

- ✓ Size of the lesion: papule (<1 cm), nodule (<4 cm) or plaque ( $\geq 4$  cm);
- ✓ number of lesions;
- ✓ location of lesions on the body;
- ✓ evolution of lesions: duration, worsening (active lesion), improvement (self-healing);
- ✓ general health and immunological status of the patient: immunocompromised or not, diabetes, heart, liver or kidney problems.

In all patients, the lesions should be washed with clean water and soap, and then covered with a dressing (gauze and tape) which must be changed three or four times per week. This facilitates the healing and prevents the formation of a sticky crust.

Bacterial superinfection is a rare complication of cutaneous leishmaniasis. However, if the lesions show obvious signs of clinically significant bacterial superinfection - i.e. a red, swollen and tender zone extending beyond the cold infiltrated borders of the leishmanial

lesion itself (a complication rarely associated with fever) - then it would be appropriate to initiate oral antibiotic treatment that is effective against common streptococci and staphylococci, such as cloxacillin, pristinamycin or amoxicillin, with clavulanic acid.

If the bacterial superinfection appears in cases treated with intralesional antimonials, the injection must be postponed and systemic antibiotics should be prescribed. When superinfection is managed, intralesional antimonials can be resumed.

If the bacterial superinfection appears in cases treated with systemic antimonials, then treatment should be continued and systemic antibiotic added.

The treatment of cutaneous leishmaniasis is organized as a step-by-step process.

▪ Situation 1

The patient has less than four lesions that are limited in size (papules, nodules or ulcerative nodules all < 4 cm) and not potentially disfiguring or disabling (i.e. not on the face, fingers or toes). He/She is infected with *L. major* (or the lesion is already self-curing), is not immunocompromised, and does not suffer from uncontrolled diabetes.

- ✓ In this situation, it is recommended to wash and dress the lesions without resorting to any specific antileishmanial therapy. It is important to ensure that the patient agrees with this option; otherwise he/she will probably look for other interventions and lose confidence.
- ✓ It is also important to provide a clear explanation of the benefits and safety of this approach:
  - cutaneous leishmaniasis harbours no risk of general disease and there is no risk of transmission to family members;
  - there is a reasonably high probability that it will be cured within the next few months;
  - this avoids the discomfort resulting from specific antileishmanial treatment.
- ✓ A follow-up schedule is established and communicated to the patient at 14, 30 and 45 days, with a final visit at 180 days. It is important to clearly mention the possibility that the patient will come back to receive specific antileishmanial therapy if the evolution is not satisfactory.

▪ Situation 2:

The patient has all the features defined in Situation 1 but does not heal despite previous care as provided in Situation 1, or has less than four lesions < 4cm located in sites that can be handled with local treatment. He/she may have one or more active lesions caused by *L. tropica* or *L. infantum*, is not immunocompromised and does not suffer from uncontrolled diabetes.

In this situation, one of the following therapeutic options can be adopted:

- ✓ topical paromomycin ointment twice daily for 20 days (if *L. major*);
- ✓ cryotherapy (liquid nitrogen -195°C) plus intralesional pentavalent antimonials;
- ✓ thermotherapy;
- ✓ intralesional antimonials alone: 1–5 ml, twice weekly for 3–4 weeks until complete cure.

The same follow-up schedule as in Situation 1 is proposed.

- Situation 3:

The patient has all the features defined in Situation 1 or 2 but is not cured despite previous care provided in those situations; has a lesion  $\geq 4$  cm (plaque); or has four or more lesions requiring immediate treatment and located in sites not compatible with local treatment and is immunocompromised or suffers from uncontrolled diabetes.

In this situation, the recommended treatment is systemic pentavalent antimonials with appropriate elimination of contraindications.

In complex situations (different from Situations 1–3 above), the decision must be discussed on a patient-by-patient basis.

It is also important to bear in mind that allergic reactions may emerge when using any of the different medicines or materials for treatment of cutaneous leishmaniasis (especially when used systemically). Here are the allergies resulting from pentavalent antimonial and how to address them:

- Treatment of allergic reactions

Treatment depends on the severity of the allergy and the resulting inflammatory response:

- ✓ Mild to moderate symptoms

If the symptoms are mild to moderate (erythema, oedema, blisters that may be haemorrhagic, marked pruritus, etc.), anti-allergic drugs should be added systemically. Antimonials should be stopped temporarily until the allergic symptoms disappear, after which they can be cautiously resumed (the patient should be under direct medical supervision). Meanwhile, the anti-allergic medicines should be administered as long as the treatment lasts.

- ✓ Severe Symptoms

If the symptoms are severe (hives, general eruption covering the body, shock, etc.), antimonial therapy should be stopped completely and alternative medications should be administered with caution after the allergy has been cured.

#### **6.4. Monitoring of patients**

A monitoring schedule is established and communicated to the patient, with respective visits after 14, 30 and 45 days, and a final visit after 180 days. It is important to clearly state the possibility of the patient returning for specific antileishmanial therapy if the evolution is not satisfactory.

ZCL: The main control measures are based on the reduction and/or elimination of the reservoir host (mainly rodents) and are implemented by the National Control Program. In-depth epidemiological and entomological studies must be conducted to obtain the baseline data needed to properly define control methods and strategy.

ACL: It is important to provide patients and their relatives with long-lasting insecticide-treated bed nets (LLIN) or encourage them to effectively use such nets. It is also important to cover the lesion so as to interrupt the transmission cycle by reducing the possibility of the vector reaching the parasite.



Active screening to ensure diagnosis and rapid treatment is also essential to reduce the human reservoir.

### 6.5. Some photographs



**Oriental Button - ulcerative and crusty in appearance**



**PKDL**

**Figure 6: Types of clinical lesions of cutaneous leishmaniasis**

## 7. Visceral leishmaniasis

### 7.1. Clinical examination

- Clinical suspicion

The clinical signs and symptoms associated with VL include fever for more than two weeks, fatigue, weight loss, anaemia, splenomegaly, hepatomegaly and lymphadenopathy.

Some of these clinical signs and symptoms are similar to those of other diseases rampant in areas where VL is endemic.

Patients may also have gastrointestinal and respiratory symptoms, with or without concomitant infections (diarrhoea, pneumonia, malaria, skin infections, etc.).

Visceral leishmaniasis must be suspected in any person who has a fever for more than two weeks, hypertrophy of the spleen and/or lymph nodes, weight loss, anaemia or leukopenia, while living in or visiting an identified VL endemic area.

- Case definition of VL

A case of visceral leishmaniasis is someone who has the clinical signs (mainly prolonged and irregular fever, splenomegaly, and weight loss) and whose disease is **confirmed by parasitological and/or serological tests**.

Since clinical signs and symptoms are not specific to VL, laboratory tests are crucial to confirm the diagnosis.

### 7.2. Laboratory tests

- Laboratory diagnosis of VL at the peripheral level

Serological diagnosis, with rK39 rapid diagnostic tests, is widely used to diagnose VL in endemic countries, because it is relatively simple and has proper sensitivity and specificity. The rK39 immunochromatographic test yields results in 15 minutes. This test can be conducted using serum or total blood specimens from the fingertip.

- Limitations of the test

The test cannot distinguish between past and present infections because the level of serum antibodies remains high, even after successful treatment. Consequently, VL relapse should not be diagnosed with a serological test, including rK39. Suspected cases of VL relapse should be referred to a centre where parasitological tests can be conducted.

The test cannot differentiate between symptomatic and asymptomatic infections, and must be conducted only for those who fit the clinical suspect case definition.

### 7.3. Treatment

Visceral leishmaniasis treatment is very long and requires hospitalization. Furthermore, the disease is often severe and complicated by other co-morbidities. Most of the drugs currently available for the treatment of visceral leishmaniasis are toxic; hence, there is need for regular monitoring. Therefore, patients should be reoriented to a hospital or a specialized treatment centre.

#### **7.4. Follow-up of patients**

During treatment, follow-up will be done at the specialized treatment centre. If the patient leaves the treatment centre with an improvement of his/her signs and symptoms (initial healing), he/she should return for a follow-up consultation six months later (or earlier in case of any discomfort) to ascertain that there is no relapse. Relapses may also occur later and require specialized assessment in treatment centres.

#### **7.5. Photograph**



**Figure 7: Visceral leishmaniasis: patient with splenomegaly**

## 8. Prevention of leishmaniasis

Leishmaniasis is a disease which can be epidemic and which requires rapid case detection and appropriate support. Health workers in endemic areas must be trained and have a high index of suspicion of visceral leishmaniasis for cases with a prolonged fever. The main element in visceral leishmaniasis control is early detection of cases and rapid treatment, although the integrated management of anti-vector control can greatly contribute to disease control. Health workers at the peripheral level have a major role to play in the prevention and control of leishmaniasis, and especially visceral leishmaniasis.

### 8.1. Early detection of cases and transfer

Health workers in peripheral health centres can greatly contribute to leishmaniasis prevention and control. Early detection and treatment of cases is the main thrust of visceral leishmaniasis control. Consequently, referring patients for confirmation of the diagnosis or for treatment helps to save their lives and reduce disease transmission. At the peripheral-level health centre, suspected cases of VL or those tested positive through rK39 can be sent to hospital for better management. Furthermore, patients who develop PKDL skin lesions after VL treatment should be monitored and advised to use treated mosquito nets, and then transferred for treatment.

### 8.2. Health education

This is aimed at promoting behaviour change for personal protection, early recognition of signs and symptoms and demand for healthcare. Health education is an integral part of the leishmaniasis control programme and the central component of health interventions at the peripheral health centre. It can be conducted in the health establishment or during campaigns for various health programmes. Health education should target disease transmission and prevention, disease symptoms and signs, the importance of early treatment and the fate of untreated persons. Furthermore, patients who develop PKDL skin lesions after VL treatment should be advised to use treated mosquito nets consistently to avoid transmission of the disease.

### 8.3. Monitoring, registration and reporting of leishmaniasis

The documentation and reporting of suspected cases and/or transferred VL/PKDL cases are crucial to the control programme, since they improve programme planning and quantification of leishmaniasis diagnosis and treatment needs. Apart from the self-presentation of cases, active surveillance of visceral leishmaniasis can be conducted in hotspot areas during the high-transmission season.

Health workers in peripheral health units can train and supervise community health agents on leishmaniasis transmission and prevention. Emphasis should be placed on the integrated management of vector control, which is the most effective method of combating sand flies using a combination of several control methods determined by local conditions, as well as the behaviour and ecology of the vector. Activities for leishmaniasis vector control can be integrated with those of other diseases that are co-endemic in the region such as malaria, lymphatic filariasis, etc.

## 9. Human African trypanosomiasis

### 9.1. Clinical examination

The diagnosis of human African trypanosomiasis, caused by *T.b. gambiense*, is essentially para-clinical; conducted through the detection of trypanosomes in the lymph, blood or cerebrospinal fluid (CSF). The confirmation of trypanosomes is guided by clinical and serological suspicion. The presence of the vector (tsetse fly or *Glossina palpalis*) in the area of origin or residence of the suspect case is one element that should be factored into the diagnosis.

#### ▪ Clinical suspicion

- ✓ Stay or residence in an HAT-endemic area;
- ✓ The individual or his/her family has a history of HAT
- ✓ General signs or symptoms considered to be suggestive of HAT such as fever that is resistant to the usual treatments, protracted headaches, lymph nodes in the neck, behaviour change, neurological disorders, sleep disorders, significant weight loss and general weakness;
- ✓ Presence of (cervical) ganglia felt through palpation of the cervical collar; the lymph nodes in the cervical region may become enlarged to the point of being visible to the naked eye; in some cases, they are more difficult to distinguish, and in that case the lymph nodes can be felt through palpation of the cervical region with the fingers;
- ✓ Rare skin signs, bite site lesions or trypanomes and trypanides.

#### ▪ Serological suspicion

Presence of the parasite generates the production of antibodies that circulate in the blood, three to four weeks after the infection. These antibodies can be detected with serological tests, which make it possible to suspect the disease, without confirming it.

#### ✓ Collection of specimens

- Open the test sachet, remove the test and write down the patient's name;
- Firmly take the 4<sup>th</sup> finger on the patient's left hand;
- Disinfect the finger with cotton wool moistened with alcohol. Leave the finger to dry before pricking;
- Remove the lancet from its sachet;
- Prick the patient's finger to obtain a drop of blood; dispose of the lancet in a sharps waste container immediately after pricking the finger;
- Gently press the base of the disposable pipette and touch its end to the drop of blood; slowly release the pressure on the pipette in order to collect the blood up to the black line.

#### ✓ Reading of the test

##### Wait 15 minutes before reading the test result

- **Positive result:** The control line as well as one or two other lines are visible in the reading window. Even if the lines are only faintly visible, the test is positive. This means that the test has detected the presence of antibodies against *T.b. gambiense*.
- **Negative result:** The control line is visible in the reading window, and there are no other lines. This means that the test has not detected the presence of antibodies against *T.b. gambiense*.

- **Invalid result:** The control line is not visible meaning the specimen failed to perform the migration.

#### ✓ **Confirmation of the parasite**

- Clinical symptoms and serological tests facilitate suspicion of the infection. Meanwhile, HAT confirmation diagnosis is based on detection of the parasite under a microscope. The diagnosis is difficult because of the low number of parasites in body fluids. Consequently, parasite concentration methods are used to detect trypanosomes in the blood and cerebrospinal fluid.
- Methods that do not involve concentration, such as blood smear or thick smear, which are sometimes helpful in detecting trypanosomes are, however, not sufficiently reliable because of their low sensitivity.
- Due to low parasitemia and fluctuations in the number of parasites in body fluids, it is often recommended to repeat negative parasitological tests that may later be positive.
- Included on the list of confirmation parasitological tests are the thick smear and lymph node fluid aspiration test, which can be conducted by peripheral-level health workers.

## 9.2. Laboratory tests

### ▪ **Lymph node fluid aspiration test**

#### ✓ **Equipment**

- Disinfectant & cotton;
- 5 ml syringe & needle (25G);
- Slides;
- 24x24 mm coverslips;
- Microscope with 40x objective lens and 10x ocular eyepiece lens;
- Gloves;
- Contaminated waste containers.

#### ✓ **Lymph node palpation**

- Ask the patient to uncover his/her neck and shoulders, and stand behind the patient;
- Hold out your hand in the form of pliers, with the thumb placed against the other four fingers; the area to palpate extends from the base of the neck up to the ear;
- Palpate the neck region to the left and to the right with both hands, starting from the bottom near the shoulder and moving up slowly, so as palpate the entire area. The affected nodes are enlarged and form a small round mass. They are elastic and slide under the skin, with little resistance to pressure. They are generally not indurated and are painless.

#### ✓ **Lymph node puncture**

- Prepare the syringe and pull the plunger completely. Wash your hands and put on gloves.

- Sit the patient down and disinfect the puncture site (where the node is located).
- With your left hand, grab the node between your thumb and forefinger such that it protrudes clearly. Keep your hand steady. With your other hand, hold the needle between the thumb and ring finger, and insert it perpendicularly into the centre of the node, in two stages: first penetrate beneath the skin and then penetrate the lymph node. Be careful not to touch the jugular veins or the carotid arteries. Lightly massage the node to facilitate entry of the lymph node fluid into the needle and rotate the needle.
- Cover the base of the needle with your forefinger and pull out the needle in quick motion. Next, place a disinfectant pad on the puncture site (never place the disinfectant pad before removing the needle, else some of the disinfectant might wet the needle, penetrate into the specimen and immobilize the trypanosomes). Connect the needle to the syringe and push the plunger to flush the lymph node fluid onto the slide.
- Cover the preparation with a coverslip for immediate examination under a microscope.

(See the continuation of the microscopic test in the annex).

### 9.3. Treatment

#### ▪ Determination of the stage of the disease

Drug prescriptions are based on the stage of the disease, and on whether the blood-brain barrier (BBB) is crossed or not. Hence, it is necessary to determine the stage of the disease before prescribing drugs. The disease stage is determined through counting of the white blood cells in the cerebrospinal fluid (CSF) using the Fuchs-Rosenthal or Nageotte counting chambers.

Stage 1 of the disease: 0 -5 GB per mm<sup>3</sup>;

Stage 2 of the disease: > 5 GB per mm<sup>3</sup>.

#### ▪ Therapeutic decision:

- ✓ Stage 1 of the disease: *Pentamidine*® (4 mg/kg of body weight per day for seven days through deep intramuscular administration);
- ✓ Stage 2 of the disease: (NECT) nifurtimox-eflornithine combination therapy:
  - Nifurtimox: 15 mg/kg of body weight per day, taken three times daily for 10 days and by oral route;
  - Eflornithine: 400 mg per kg per day, taken in two intravenous drips of two hours each for seven days; the doses are diluted in 250 ml of water for injection.

NECT is available as a kit, composed of the two products and accessories.

### 9.4. Follow-up of patients

- After treatment, the patient is seen again every six months for two years for the conduct of a clinical parasitological test and a control lumbar puncture;

- Since the cerebrospinal fluid mirrors the evolution of sleeping sickness, it is equally important that during diagnosis and in the two years following treatment a lumbar puncture be carried out regularly in patients;
- The lumbar puncture is considered normal when the cerebrospinal fluid (CSF) has 0 to 5 elements (lymphocytes) per mm<sup>3</sup>.

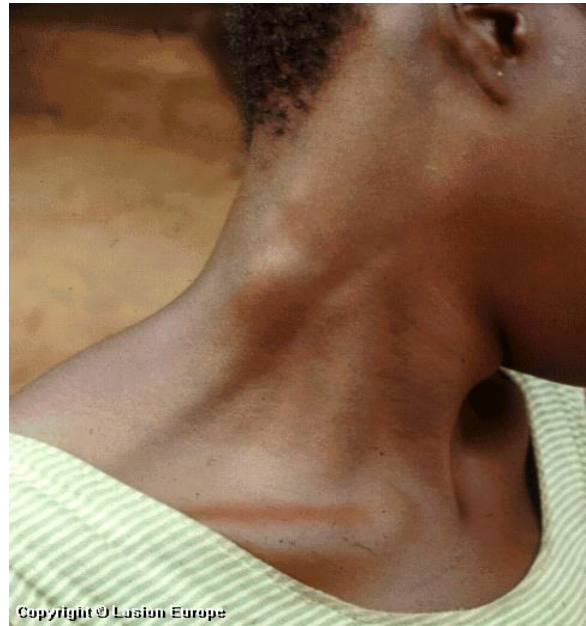
### 9.5. Prevention of Human African Trypanosomiasis

For the people living in endemic areas, there are no specific measures and no vaccine. The primary and secondary prevention measures are the detection of cases and reservoirs, treatment and vector control.

- **Role of the first-line nurse in HAT-endemic areas**
  - ✓ Clinically suspect HAT in patients during external consultations;
  - ✓ Carry out HAT serological tests in clinical suspects;
  - ✓ Confirm/invalidate the existence of the disease through a parasitological test, especially the lymph node fluid test or the thick smear;
  - ✓ Refer confirmed HAT patients to a competent level for determination of the disease stage;
  - ✓ Refer unconfirmed (clinical and serological) suspects for more sensitive parasitological tests;
  - ✓ Collect the specimens of serologically unconfirmed suspects on filter paper for trypanolysis;
  - ✓ Manage un-referred stage 1 patients through proper treatment;
  - ✓ Disseminate the message on the extension of HAT control;
  - ✓ Join the mobile team in conducting community awareness/mobilization to promote massive participation in active screening activities;
  - ✓ Participate in active screening activities with the mobile team;
  - ✓ Provide proper treatment to all stage 1 patients diagnosed by the mobile team during active screening;
- **Vector control: The first-line nurse is expected to:**
  - ✓ Raise community awareness on their involvement in the activity
  - ✓ Participate in training the community on vector trapping
  - ✓ Supervise the community on maintenance of the trapping device



## 9.6. Some photographs



**Figure 7: Human African trypanosomiasis - cervical lymphadenopathy**



**Figure 8: Human African Trypanosomiasis, trypanosomal ulcer or chancre at the bite site**

## 10. Social mobilization in favour of NTDs

The scope and severity of neglected tropical diseases have become the focus of attention for all our communities and policy makers. Reducing the magnitude and negative economic impact of these diseases in communities is the focus, with screening and treatment as the main tool. Screening can be passive – i.e. conducted during daily consultations in health institutions. It must also be active if we wish to attain our objectives within the prescribed time period. It requires total social mobilization - the participation of all individuals and groups. To ensure the smooth coordination and perfect integration of active screening into community health activities, WHO recommends that social mobilization efforts be organized against the common NTDs in each community.

Social mobilization in favour of neglected tropical diseases is perceived not as a mere IEC (information, education and communication) programme, but especially as an approach to the management of all community-based disease control activities. It seeks to achieve:

- Better knowledge of targeted diseases;
- Increased community interest in disease control;
- Identification or early suspicion of cases, thanks to the community's greater capacity to recognize clinical signs;
- Significant reduction of prejudice and stigma surrounding these diseases;
- Skills development to ensure proper management of patients.

The centrepiece of these community-based activities is organizing good communication, through:

- ✓ The mass media: town criers, radio, television and billboards;
- ✓ Producing TV, radio and theatre sketches to combat prejudices rampant in the society and popularize appropriate information on diseases;
- ✓ Individual interviews which are more complex because they require manpower and time; it being understood, however, that these individual interviews provide appropriate feedback to ensure comprehension, as well as the credibility and impact of the messages disseminated by the mass media.

Social mobilization will be conducted by a group of villagers composed of a local leader, the health worker in charge of the centre, the community health worker, and some healed patients. This group should disseminate messages within the communities and support community efforts to ensure proper social reintegration for patients. The group will have audio-visual material such as posters, banners and stickers.

Social mobilization in favour of NTDs requires support from various hierarchical levels. Such support must be continuous over time. It involves critical activities such as:

- The dissemination of radio and television messages/spots for urban communities;
- Integrated training of nurses to prepare workers for the organization of NTD days in the communities. The training will focus on recognition of clinical signs, the organization of patient monitoring and presentation of technical material (messages, posters and posters) for social mobilization. It should result in the identification of communities recognized or suspected of being endemic for certain diseases and the development of a schedule for

organizing mobilization days. A limited number of villages (5 to 10 in maximum) will be programmed for each health worker for a period of one year.

- On the day of mobilization, a package of activities will be implemented, including:
  - ✓ An awareness meeting for the (administrative, religious and traditional) authorities of the community;
  - ✓ The organization of community awareness-raising using town criers, drums, games and popular sketches in the community;
  - ✓ The examination of suspected patients in the community on the same day;
  - ✓ The organization of treatment for detected cases.

Awareness raising, with renewal of posters will take place at some intervals while the distribution of pamphlets in communities, schools and other institutions continues more frequently.

In anticipation of these days, the national level will develop images (posters, pictures, engravings, banners and other), messages (print, audio, video, etc. ), and a national or community “cultural” theatre, depending on the resources available.

The national programme can invite artists to compose a theme song that will be popularized and used to animate the mobilization days and for the more sustained media campaigns to disseminate information and increase knowledge of the diseases at various levels.

## 11. Integration of activities

The main challenge of health services in countries of the WHO African Region is the geographical coverage of all communities and localities in the country. Apart from geographical coverage, the situation is complicated by difficulties in the proper functioning of services. The paucity of financial resources is compounded by the lack of qualified health workers in every locality, and the inaccessible or most remote localities suffer the most. It is rare to meet more than one qualified health worker in a peripheral health post. Such a worker often works alone, carrying out all tasks and is forced to meet the requirements of all health programmes. Given this context, it is important not only to provide the worker with substantial support, as recommended by the Alma Ata International Conference on Primary Health Care, but also and especially to facilitate the implementation of activities through the integration of certain interventions.

Depending on the context, integration is limited to the joint implementation of certain activities. It covers broad areas of activity, ranging from the development of a single work plan to the preparation of joint plans for supervision, monitoring and evaluation, in line with recommendations on the proper administration of primary health care.

Such integration is all the more important for tropical diseases requiring case diagnosis and treatment since the diseases targeted in the African Region of WHO generally occur in vulnerable populations; skin diseases whose endemicity is highly dependent on hygiene and living conditions. Consequently, it is recognized that the following interventions can be jointly organized to facilitate the task of the peripheral health worker:

- Capacity building;
- Disease surveillance;
- Situation analysis;
- Health promotion;
- Inter-sectorial collaboration;
- Monitoring and evaluation;
- Consolidation of partnerships;
- Advocacy and resource mobilization.

The following table indicates the priority interventions for which WHO recommends joint implementation to ensure the rational use of resources and better time management.

**Table 3: Priority interventions for CM-NTDs**

Interventions	Leprosy	Buruli ulcer	Treponematoses	Leishmaniasis	Trypanosomiasis
Active screening	+++	+++	+++	+++	+++
Passive screening	+++	+++	+++	+++	+++
Medical treatment	+++	+++	+++	+++	+++
Surgical treatment.	+++	+++			
Dressing	+++	+++	+++	+++	
Rehabilitation	+++	+++	+	+	
Vector control				+++	+++
Prevention and health education	+++	+++	+++	+++	+++

## 12. CM-NTD control strategy

Case management neglected tropical diseases undermine the economic and social situation of communities in all countries of the WHO African Region. The growing attention given by the international community to this situation has led WHO to define an integrated strategy to combat these diseases and establish a roadmap to control, eliminate or eradicate some of them. This strategy will be effectively implemented if countries take ownership and implement it efficiently in close collaboration with the communities concerned and the targeted support of all partners.

The regional strategy is aimed at scaling up the coverage of interventions, implementing results-based planning, raising resources and sustainable funding to achieve set programme objectives, increasing advocacy for these diseases and organizing follow-up, evaluation, monitoring and research on them.

The objectives of this strategy are to:

- Support the elimination of leprosy and further reduce severe disabilities from the disease;
- Control morbidity due to Buruli ulcer, Human African Trypanosomiasis (HAT) and leishmaniasis;
- Eradicate yaws.

The main interventions are:

- Complete analysis of the magnitude of Buruli ulcer, leishmaniasis and yaws;
- Active and integrated search for cases of leprosy, human African trypanosomiasis, Buruli ulcer, leishmaniasis and endemic treponematoses (yaws and bejel);
- Correct and proper treatment of cases of leprosy, HAT, Buruli ulcer, leishmaniasis and endemic treponematoses (yaws and bejel);
- Prevention and management of disabilities resulting from these diseases and their socio-economic consequences;
- Prevention and integrated surveillance of these diseases;
- Organization of inter-sectorial collaboration to enhance activities for reducing morbidity and the consequences of these diseases;
- Organization of integrated vector control against leishmaniasis and HAT.

The table below succinctly presents the roadmap established to ensure the achievement of programme objectives.

**Table 4: Milestones of the roadmap on the control, elimination and/or eradication of CM-NTDs in the WHO African region.**

Indicators	2014	2015	2016	2017	2018	2019	2020
<b>Leprosy</b>							
Percentage reduction in the rate of new leprosy cases with 2nd degree disabilities per 100,000 inhabitants at the national level, compared to end-2010 levels.	30%	35%					
Percentage of countries that have reached the threshold of less than 1 new case of leprosy with 2nd degree disabilities per 1 000 000 inhabitants	48%	65%	82%	91%	96%	98%	100%
Number of countries having completed the elimination of leprosy in all districts		50%	60%	70%	80%	90%	100%
<b>Human African Trypanosomiasis</b>							
Number of cases reported per year	5000	4500	4000	3500	3000	2500	<2000
Elimination of HAT in endemic areas		80%	83%	86%	90%	95%	100%
<b>Buruli ulcer</b>							
Proportion of endemic countries that have finalized their situation analysis		100%					
Proportion of endemic countries that have started oral treatment of Buruli ulcer			100%				
Countries that have strengthened health workers' capacity to manage Buruli ulcer cases in all endemic districts							100%
<b>Yaws and bejel</b>							
Proportion of endemic countries that have finalized their situation analysis				100%			
Proportion of endemic countries that have interrupted the transmission of endemic treponematoses							100%
<b>Leishmaniasis</b>							
Proportion of countries that have completed a situation analysis of leishmaniasis					100%		
<b>National control programme</b>							
Countries that have developed a national programme for the integrated control of CM-NTDs.			100%				

## CONCLUSION

This manual is part of a series of documents developed by the WHO Regional Office for Africa and which include: the Integrated Regional Strategy on Neglected Tropical Diseases; the revised version of the Terms of Reference and the operational conditions of the NTD Regional Programme Review Group; Guidelines for the Supervision of Peripheral Health Workers in the Management of NTDs; Guidelines on Monitoring and Evaluation of CM-NTD Programmes; and, of course, this Manual on the Integrated Management of CM-NTDs for use by health workers at the peripheral level.

The purpose of this series of guideline documents is to enhance the integration of interventions and activities for combating the five priority CM-NTDs in the African region, namely: leprosy, Buruli ulcer, endemic treponematoses, leishmaniases and HAT. The manual can be used to train peripheral-level health workers during workshops organized at the district health level. It can also be used by peripheral-level health workers for self-training and by members of the team of district health experts prior to supervision missions to health centres where patients are treated.

The manual will be distributed in all CM-NTD-endemic countries of the WHO African region to ensure its availability in all peripheral health units responsible for treating the five CM-NTDs. It is our hope that health workers at the peripheral level, members of district health teams and heads of national control programmes for the five CM-NTDs will find this manual useful for the improvement of control activities, thus helping to reduce the burden of disease and attaining the objectives of NTD control, elimination and eradication by 2020.



## **Annex: Lymph node fluid test for diagnosis of HAT**

### ✓ **Materials needed**

- Disinfectant & cotton;
- 5 ml syringe & needle (25G);
- Slides;
- 24x24 mm coverslips;
- Microscope with 40x objective lens and 10x ocular eyepiece lens;
- Gloves;
- Contaminated waste containers;

### ✓ **Palpation of the node prior to puncture**

- Ask the patient to uncover his/her neck and shoulders, and stand behind the patient;
- Hold out your hand in the form of pliers, with the thumb placed against the other four fingers; the area to palpate extends from the base of the neck up to the ear;
- Palpate the neck region to the left and to the right with both hands, starting from the bottom near the shoulder and moving up slowly so as to palpate the entire area; the affected nodes are enlarged and form a small round mass; they are elastic and slide under the skin, with little resistance to pressure; they are generally not indurated and are painless.

### ✓ **Lymph node puncture**

- Prepare the syringe and pull back the plunger completely; wash your hands and put on gloves;
- Sit the patient down and disinfect the area chosen for the puncture (where the node is located);
- With your left hand, grab the node between your thumb and forefinger such that it protrudes clearly. Keep your hand steady. With your other hand, hold the needle between the thumb and ring finger, and insert it perpendicularly into the centre of the node, in two stages: first penetrate beneath the skin and then penetrate the lymph node. Be careful not to touch the jugular veins or the carotid arteries. Lightly massage the node to facilitate entry of the lymph node fluid into the needle and rotate the needle;
- Cover the base of the needle with your forefinger and pull out the needle in quick motion. Next, place a disinfectant pad on the puncture site (never place the disinfectant pad before removing the needle, else some of the disinfectant might wet the needle, penetrate into the specimen and immobilize the trypanosomes). Connect the needle to the syringe push the plunger to flush the lymph node fluid onto the slide.

### ✓ **Examination under the microscope**

- Cover the preparation on the slide and examine it under a microscope with a magnification of x 400, adjusting the ocular eyepiece to x10 and the objective lens to x 40;
- Wait for the liquid flow to stop and examine it, starting from the edges on the borders of the coverslip towards which the trypanosomes usually tend to move;
- Next, examine the rest of the preparation. The preparation may contain erythrocytes and leucocytes. The trypanosome is approximately 20  $\mu\text{m}$  long (or thrice the size of an erythrocyte) and moves by shaking the globules with its flagellum. Trypanosomes manage to hide under the globules. The reading will be easier with the condenser of the microscope set at mid-point, and the diaphragm closed in order to get a good contrast, with enough light to examine the specimen.

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