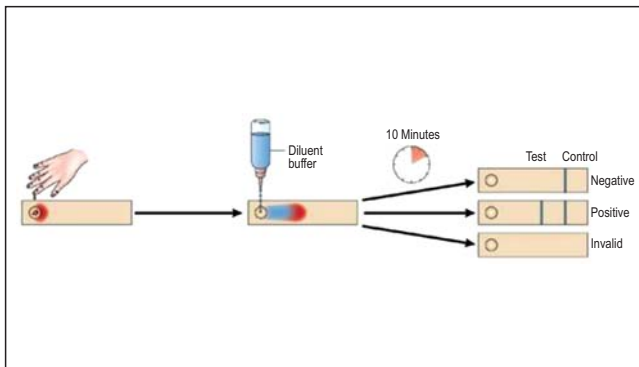


Government of Nepal
Ministry of Health and Population

National Guideline on Kala-azar Elimination Program (Updated) 2019



Department of Health Services
Epidemiology and Disease Control Division
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**Government of Nepal
Ministry of Health and Population**

**National Guideline on
Kala-azar
Elimination Program (Updated)
2019**



Government of Nepal
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Foreword

Kala-azar is a chronic febrile illness which is fatal if it is not detected and diagnosed timely and is not treated properly. Delayed diagnosis is associated with increased complication of the disease, devastating economic consequences on the patients' family. Thus, kala-azar cases must be searched for, diagnosed and managed actively.

Recent advances in kala-azar diagnosis and treatment has made possible to confirm the diagnosis and treat the patient at health institutions efficiently by a trained health worker. Rapid diagnostic test has made the active case detection of kala-azar and post kala-azar dermal leishmaniasis cases feasible in the kala-azar endemic areas.

It gives me an immense pleasure to inform that "National Guideline on Kala-azar Elimination Program" has been revised after thoroughly analyzing the national program and current developments in disease diagnosis, treatment, case detection and vector management. This guideline will be a reference to national, regional and district level managers to guide the program to achieve elimination of kala-azar in Nepal.

Finally, I would like to acknowledge the effort made by the team involved in revising the guideline.

Dr Guna Raj Lohani
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Foreword

Nepal government is intensifying the implementation of activities with an aim to eliminate kala-azar by the end of the year 2020. For this, different strategies and objectives have been formulated and active case detection and vector control activities have been intensified in the program during the attack phase of elimination. There is timely revision and adaption of strategies such as use of rapid diagnostic test and new short course therapy. The program has identified the focus area and population to control kala-azar.

It gives me immense pleasure to express that the “National Guideline on Kala-azar Elimination Program” has been revised according to current developments in case detection, diagnosis, treatment, vector control, disease surveillance and recording and reporting of the kala-azar. The guideline was revised after a wide consultation with national experts of kala-azar, Post-kala-azar dermal leishmaniasis, cutaneous and mucocutaneous leishmaniasis, district program managers, academic institutions, WHO experts, communication experts, and members of the civil society.

I hope the guideline will assist program managers and health workers to practice recommended approaches and ensure uniformity of the program.

Finally, I would like to thank the members of the core team and my colleagues who have been actively involved during the revision and finalization of the guideline, and to WHO for providing technical support in bringing this guideline to this shape.

Dr Bibek Kumar Lal
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Abbreviations and Acronyms

ACD	active case detection
ADR	adverse drug reaction
AIDS	acquired immunodeficiency syndrome
ANM	auxiliary nurse midwife
ART	antiretroviral therapy
BCC	behaviour change communication
BPKIHS	BP Koirala Institute of Health Sciences
CBC	complete blood count
COMBI	communication for behavior impact
CL	cutaneous leishmaniasis
CKD	chronic kidney disease
DA	dextrose
DAT	direct agglutination test
DDT	dichlorodiphenyltrichloroethane
DHIS	district health information system
DNA	deoxyribonucleic acid
DPHO	district public health officer
EDCD	Epidemiology and disease control division
ECG	electrocardiogram
ELISA	enzyme linked immunosorbent assay
FCHV	female community health volunteer
FCHW	female community health worker
HF	Health facility
HIV	human immunodeficiency virus
HMIS	health management information system
HP	Health post
ICBA	index case-based approach
IEC	information, education and communication
IFAT	immunofluorescence antibody test
IM	intra-muscular
IPC	interpersonal communication
IRS	indoor residual spray
ISC	Indian subcontinent
IVM	integrated vector management
KA	kala-azar
KOIRC	kala-azar outbreak investigation and response committee
LD bodies	Leishmania Donovan bodies
L-AmB	liposomal amphotericin B
LFT	liver function test
LLIN	long-lasting insecticidal treated net

LMP	last menstrual period
MCL	Mucocutaneous leishmaniasis
MTB/RIF	mycobacterium tuberculosis/resistance to rifampicin
MCHW	maternal and child health worker
MWRA	married women of reproductive age
NGO	Non-governmental organization
NNN	Novy-MacNeal-Nicolle
OPD	Outpatient department
ORS	Oral rehydration solution
PCD	passive case detection
PCR	polymerase chain reaction
PHC	primary health care
PHCC	primary health care centres
PKDL	post-kala-azar dermal leishmaniasis
PLHIV	people living with HIV
PSI	pound-force per square inch
RDT	rapid diagnostic test
RFT	renal function test
RHD	regional health directorate
RTAG	regional technical advisory group
SAE	serious adverse event
SEAR	south-east Asia region
SGPT	serum glutamic pyruvic transaminase
SOP	standard operating procedure
STIDH	Sukraraj Tropical and Infectious Disease Hospital
TB	Tuberculosis
TLC	total leucocyte count
TNF	tumour necrosis factor
VDC	village development committee
VHW	village health worker
VL	visceral leishmaniasis
WHO	World Health Organization
WHOPES	WHO Pesticide Evaluation Scheme

1.1 Introduction

Leishmaniasis is a group of vector-borne diseases caused by *Leishmania* protozoan parasite which are transmitted to humans by the bite of infected female phlebotomine sandflies. There are 3 main forms of the disease: Visceral leishmaniasis (VL) or kala-azar; cutaneous leishmaniasis (CL); and mucocutaneous leishmaniasis (MCL). Post-kala-azar, a sequelae of VL which is a potential reservoir of the disease is also seen in Nepal. VL remains a public health problem in Nepal. Post-kala-azar derman keusgnabuasus (PKDL) and CL cases have also been reported in the country. CL is seeing an increasing trend in more districts especially in hilly districts of western Nepal.

Kala-azar (KA) is slated for elimination as a public health problem in the South-East Asia Region (SEAR). Elimination of KA is defined as achieving annual incidence of less than 1 case of kala-azar in 10,000 population at the implementation unit i.e. **district** level in Nepal, **sub-district (block)** in India and **(upazila)** in Bangladesh. It is a public health milestone towards realizing the vision of kala-azar free communities as new kala-azar cases are expected to occur for a foreseeable future.

The factors favorable for elimination of this disease in this region are: 1) human beings are the only reservoir; 2) *P. argentipes* is the only vector; 3) vector is sensitive to insecticides; 4) there is high political commitment in all the endemic countries and elimination strategy is in place; 5) rapid diagnostic test and new efficacious drugs and short regimens are available.

Government of Nepal is committed to the WHO regional strategy to eliminate kala-azar and is signatory to the MOU on strengthening collaboration in the regional elimination efforts along with Bangladesh and India that was formalized during the side meeting on the occasion of World Health Assembly held in May 2005 and renewed in 2014 with inclusion of Bhutan and Thailand.

The SEARO regional strategic plan has outlined four phases in the kala-azar elimination initiative in the region. These are:

- i. **The preparatory phase:** starts with the development or review of national policies for kala-azar, development of strategic, advocacy and operational plans, formulation of technical guidelines and reporting formats

- ii. **The attack phase:** includes implementation of activities such as early diagnosis and complete treatment, vector control activities in the form of indoor residual spray and monitoring of the strategies. It continues till elimination is achieved in all implementation units.
- iii. **The consolidation phase:** begins at the end of the attack phase. During this period active surveillance continues with focal indoor residual spray activities in limited areas. It ends after three years of active surveillance has shown no increase in the incidence rate at **district**/sub district/upazila levels in the endemic countries.
- iv. **The maintenance phase:** the case incidence at the **district**/sub district or upazila level should be less than 1 per 10 000 population and surveillance against re-emergence of kala-azar will be continued.

In 2005, the Epidemiology and Disease Control Division (EDCD), Department of Health Services, formulated a National Plan for the Elimination of Kala-azar (KA) in Nepal which was revised in 2010 as National Strategic Guideline on Kala-azar Elimination in Nepal and then updated in 2014 to introduce liposomal amphotericin B (L-AmB) and combination therapy in the national treatment protocol. This updated national guideline on kala-azar elimination program includes all the WHO recommendations.

In alignment with the regional plan, the national plan is divided into three phases: Preparatory Phase; Attack Phase and Consolidation Phase. The maintenance phase will start once elimination is sustained in all areas reporting kala-azar cases. The overall goal of the plan is “to contribute to improving the health status of vulnerable groups and at-risk populations living in kala-azar endemic areas of Nepal through the elimination of kala-azar so that it no longer remains a public health problem”. The programme targeted to achieve KA elimination as a public health problem by reducing the annual incidence to less than 1 case per 10,000 population at district level by 2015. This target was achieved in 2013 in endemic districts and has been sustained since then in programme districts. However, cases have also been reported from other districts in significant numbers. Endemicity status in these districts is being ascertained.

1.2 Epidemiology of Leishmaniasis

The epidemiology of leishmaniasis depends on the type of the parasite species endemic, the local ecological characteristics of the transmission areas, the current and past exposure of the human population to the parasite and widely varying human behavior such as movement, sleeping habits etc. Leishmaniasis manifest mainly in three forms: cutaneous leishmaniasis (the most common) which produces ulcer on the exposed parts of the body such as the face, arms and legs; mucocutaneous leishmaniasis in which lesions affect and cause destruction of mucous membranes of the nose, mouth and throat resulting into severe disabilities and Visceral leishmaniasis or kala-azar (the most severe form), which is characterized by prolonged irregular fever, splenomegaly, anemia, and progressive weight loss and sometimes darkening of the skin. In endemic areas, children and young adults are mainly affected. The disease is fatal if not treated or treatment given very late. It affects the poorest and most marginalized people and is commonly associated with malnutrition, poor housing and a weak immune system.

Out of the 194 countries and six regions reporting to the WHO, 75 (38%) are considered endemic for VL and 87 (44%) for CL. A total of 65 (69%) are endemic for both VL and CL. Globally, an estimated 700,000 to 10,00,000 new cases of leishmaniasis and 20,000 to 30,000 deaths occur annually. Of these an estimated of 50, 000 to 90,000 cases of VL occur worldwide with 90% of these cases occurring in seven countries, namely Brazil, Ethiopia, India, Kenya, Somalia, South Sudan and Sudan. In the countries of South-East Asia region, kala-azar occurs mainly in three countries- India, Bangladesh and Nepal. A small focus has also been reported from Bhutan and Thailand and Sri Lanka. In the three major endemic countries of the region about 189 million people in 109 districts are at risk. However, new cases are being reported from newer districts as well.

1.2.1 Epidemiology

Kala-azar is a major public health problem in Nepal. The first cases of kala-azar were reported in Nepal as early as 1960s. The programme initially identified 12 districts of central and eastern Terai region as KA endemic. However, 6 new districts were added to that list in 2016, including hilly districts, because sporadic cases have been consistently reported from other parts of the country including hilly and Kathmandu valley districts and local transmission was verified by epidemiological and entomological studies. Cases have been reported from other 27 districts and disease transmission in these districts is under verification. Irrespective of the endemicity status, new kala-azar cases have been reported from 50 (out of 77) districts in the country. Despite this geographical expansion of the disease, the programme has seen a steady decline in incident cases and mortality since 2003. Over 8.6 million people living in these 18 endemic districts are at risk of kala-azar. The highest numbers of kala-azar cases were reported in 2003 and since then the cases are in decreasing trend. In 2017, only **271** cases were reported. Since cases are being reported from newer areas, the country decided **NOT** to use terminology of '**programmatically**' and '**non-programmatic**' districts anymore and instead follow the standard international definitions for endemicity status as below:

Endemicity status

Endemic:

Full cycle of transmission has been demonstrated at any given time (maintained population of competent vector + parasite reservoir + locally-acquired cases) AND at least 1 locally-acquired case in the last 10 years.

Endemicity doubtful:

- Full cycle of transmission has **never** been demonstrated BUT at least 1 locally-acquired case in the last 10 years
- OR**
- Full cycle of transmission has been demonstrated at any given time, BUT no case has been reported in the last 10 years (0 case or no data)

Non-endemic:

- **Previously reported cases:** Full cycle of transmission has **not** been demonstrated AND no locally-acquired case has been reported in the last 10 years, BUT locally-acquired case has been reported earlier
- **At risk:** No locally-acquired case has **ever** been reported but epidemiological risk factors are present (a competent vector population, a reservoir, and appropriate environmental conditions).
- **No autochthonous cases reported** = No locally-acquired case has **ever** been reported

Endemicity status can be applied to any defined and circumscribed geographical area or implementation unit: countries, regions, districts, villages, community. It is advised to use the smallest geographical or administrative sub-national resolution available.

1.2.2 Transmission

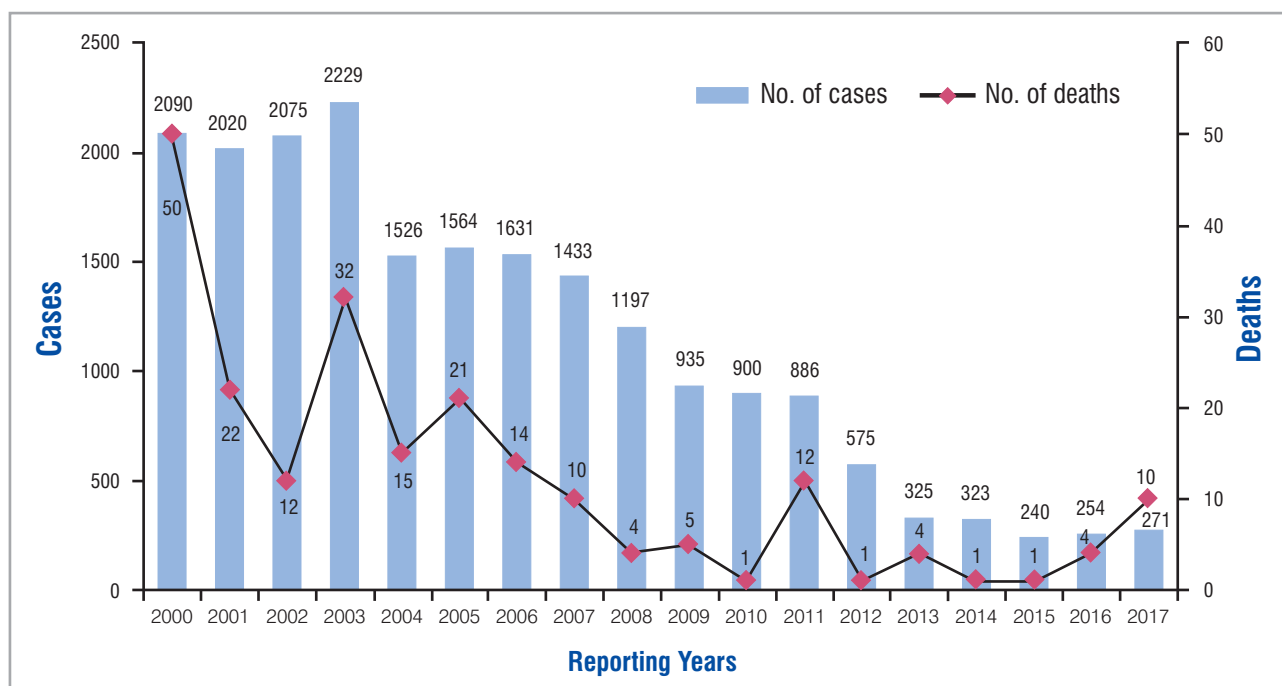
Infection is transmitted with the bite of an infected female sand-fly into a susceptible host. The transmission is ‘anthroponotic’ – human to human transmission by the vector without other animals in between. The average incubation period ranges from 2 to 6 months. Risk factors for transmission are generally rural areas at less than 600 m above sea level, a heavy annual rainfall, a mean humidity above 70%, a maximum temperature of 38 °C and a minimum temperature of 15 °C, with a diurnal variation of less than 7 °C, abundant vegetation, subsoil water and alluvial soil¹. The disease occurs in agricultural villages where houses are frequently constructed with mud walls and earthen floors, and cattle and other livestock are kept close to human dwellings. The highest case reporting season for Nepal is seen in the months from June to October.

Risk factors of developing disease include: young age, malnutrition, immunosuppressive conditions such as HIV and poverty. Kala-azar is fatal if left untreated in almost all cases.

In Nepal, the parasite species is *Leishmania donovani* and the main vector is *P. argentipes*. Since kala-azar is a disease of poverty affecting people from the lowest socio-economic strata and living in rural areas where access to health care services is a major challenge. Households with damp earthen floors are ideal breeding sites for sandflies; poor families will be more affected by malnutrition thus more vulnerable to the disease and will be less likely to seek for health care in a timely manner if sick.

¹Control of the leishmaniasis, Report of a meeting of the WHO expert committee on the control of leishmaniasis, WHO Technical Report Series 949 http://apps.who.int/iris/bitstream/handle/10665/44412/WHO_TRS_949_eng.pdf;jsessionid=9EDE4BD9061452C83542E688F28498DA?sequence=1.

Figure 1: **Trend of kala-azar cases and deaths in Nepal, (2000 – 2017)**

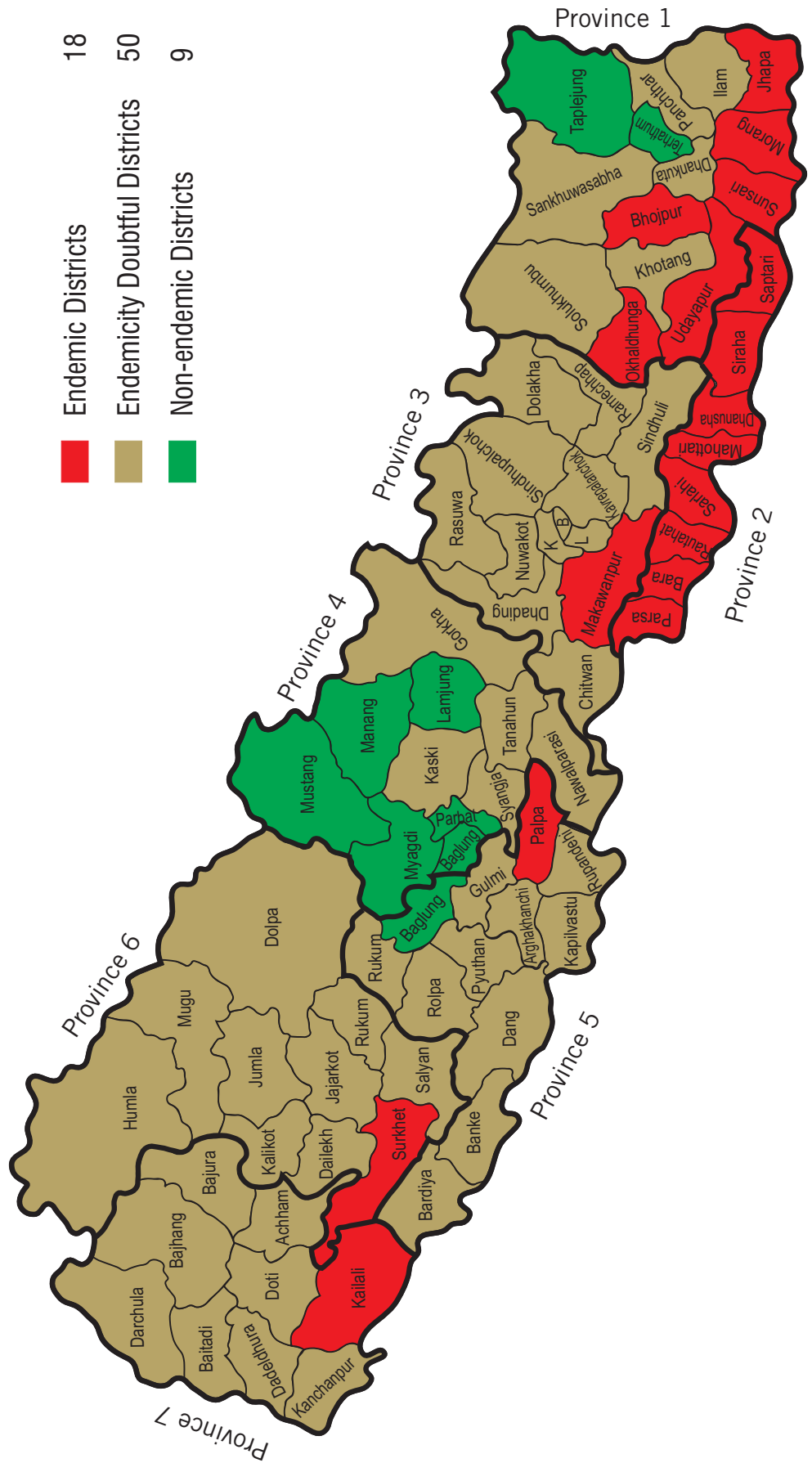


1.2.3 Changing Epidemiology of kala-azar in Nepal

Since 2000, kala-azar cases have been reported in increasing numbers from the areas/districts hitherto considered as non-endemic districts of Nepal. Kala-azar cases are now being also reported from hills, Kathmandu valley and some mountainous districts. In 2017, 65% (107 out of 271 cases) of all reported cases were from 31 districts which are considered as non-endemic, some of which are in immediate geographical proximity to endemic districts. This shift in occurrence of cases in earlier called non-program districts has prompted to verify the travel history of patients, existence of vector and other evidences to establish endemicity status of these districts reporting new cases. In several of these cases, no obvious non-vector route could be established.

The elimination program added six new districts namely Bhojpur, Okhaldhunga, Makwanpur, Palpa, Surkhet and Kailali to that list of kala-azar endemicity in 2016; presently a total of 18 districts are considered kala-azar endemic in Nepal. In recently added six new districts, the evidences of local transmission of *Leishmania donovani* has been verified by an epidemiological and entomological evidences. Disease is observing unique features that not only new cases have been reported from non-endemic districts there has also been reporting of cutaneous and mucocutaneous leishmaniasis in western districts of Nepal.

Figure 2: Spatial distribution of kala-azar cases in Nepal, 2017



1.2.4 Goal and Elimination Target

The goal of kala-azar elimination program is to contribute to mitigation of poverty in kala-azar endemic districts of Nepal by reducing the morbidity and mortality of the disease and assisting in the development of equitable health systems.

1.2.5 Target

The renewed MoU signed by Bangladesh, Bhutan, India, Nepal and Thailand during the Regional Committee meeting in 2014, has revised the elimination time line by the end of 2017 or before.

1.2.6 Objectives

The **overall objectives** are to:

- Reduce incidence of kala-azar in endemic communities with special emphasis on poor, vulnerable and unreached populations.
- Reduce case fatality rates from primary kala-azar to **ZERO**;
- Detect and treat Post-kala-azar Dermal Leishmaniasis (PKDL) to reduce the parasite reservoir;
- Prevent and manage kala-azar-HIV-TB co-infections.

1.2.7 Strategies

Based on the regional strategy and the adjustments proposed by the Nepal expert group, Government of Nepal, Ministry of Health has adopted the following strategies in the implementation of the kala-azar elimination program in Nepal:

- Early diagnosis and complete treatment
- Integrated vector management
- Effective disease and vector surveillance
- Social mobilization and partnerships
- Improve program management.
- Clinical, implementation and operational research

2.1 Clinical description and case definitions

Kala-azar (Visceral Leishmaniasis) in Nepal mainly affects underprivileged rural communities with majority of cases found in children and young adults. The incubation period is typically **2-6 months**. The onset of the disease is usually gradual.

Kala-azar should be suspected in a patient from an endemic locality who presents with prolonged irregular fever, splenomegaly and weight loss as its main manifestations.

In VL endemic areas where malaria is also prevalent kala-azar should be suspected when fever lasts for more than 2 weeks. Malarial patients are likely to have acute fever and will most of the time respond with standard anti-malarial treatment recommended by national guideline. Technical Working Group noted that among 1250 VL cases treated over past years at B.P. Koirala Institute of Health Sciences Dharan Nepal, fever, splenomegaly and weight loss was found in more than 97% of cases.

A typical patient presents with several of the following symptoms and signs:	Some patients have other uncommon manifestations:
Fever of 2 weeks or more	Oedema
Moderate to severe splenomegaly (abdominal distension as experienced by patients)	Jaundice
Weight loss (wasting) in the form of low Body mass index (BMI)	Vomiting
Loss of appetite (seen invariably among all patients)	Abdominal pains
Hepatomegaly	Lymphadenopathy
Early satiety	Cough
Anaemia	Diarrhea
Epistaxis	

Since chronic fever with constitutional symptoms and splenomegaly are non-specific there is a need for additional specific laboratory test to confirm a case of kala-azar. Using a standard case definition (sensitivity of 97%) along with a specific laboratory test (specificity of more than 95%) increases the post- test probability of correct diagnosis.

2.2 Common physical examination findings in VL

- Fever- high-grade for prolonged duration (more than 2 weeks), present in almost all cases
- Splenomegaly- the most specific sign which is non-tender with smooth surface. Regression after cure is a rule which may take months.
- Usually moderate to severe pallor
 - ▶ Tachycardia usually in severe anemic cases
 - ▶ Signs of heart failure in severe anemia cases
- Malnutrition in form of wasting with low BMI (moderate or severe)
- Hepatomegaly- less common than splenomegaly, measured below right costal margin along the mid clavicular line. Regression after cure is a rule and it may present other signs like edema, jaundice, etc.
- Lymphadenopathy (especially in cases of teenage population)
- Icterus (in some patients presenting with jaundice) usually in severe cases
- Signs of secondary infections like respiratory, gastrointestinal.

2.3 Case Definitions

Probable VL (KA) case:

A person living in or having travelled to kala-azar endemic areas showing clinical signs and symptoms of kala-azar (mainly irregular fever lasting more than two weeks and splenomegaly and/or weight loss), after ruling out malaria in endemic areas.

Confirmed VL case:

Laboratory-confirmed VL case:

A probable VL case with laboratory confirmation, either serological (RDT, DAT, ELISA, IFAT) and/or parasitological (smear, culture) and/or positive by PCR or related techniques.

OR

Clinically-confirmed VL case:

A probable VL case that has not been confirmed by any laboratory test (i.e. test(s) not done or negative) but is assessed by a clinician to be a confirmed VL case based on clinical grounds.

All confirmed VL cases, either clinically or laboratory; should be treated according to the protocol and must be reported.

2.4 Differential diagnosis

Several diseases may mimic VL in endemic areas the close differential diagnosis are:

- ▶ If symptoms are of more than 2-4 weeks
 - Tuberculosis: usually not massive spleen as VL
 - Brucellosis: usually associated with bone and joint symptoms and signs
 - Malnutrition: usually not massive spleen as VL
 - AIDS: usually not massive spleen as VL
 - Chronic hepatitis: usually features of liver failure
 - Liver cirrhosis: usually features of portal hypertension
 - Lymphomas and Leukemias: usually rK39 negative

- ▶ **If symptoms and signs are of 2 weeks**
 - Malaria (usually clinically very sick, hemodynamically unstable and Antigen detection test for malaria is highly sensitive and specific followed by very good response to standard antimalarial drugs)
 - Typhoid fever usually clinically very sick, hemodynamically unstable and not massive spleen as VL and rK39 negative
 - Leptospirosis usually clinically very sick, hemodynamically unstable and not massive spleen as VL and rK39 negative

Table 1: Summary of clinical manifestations (% among 1250 VL cohort of BPKIHS)

Symptoms	Signs	Lab findings
Fever (97%)	Pallor (100%)	Low hemoglobin (100%)
Weight loss (99%)	Emaciation (99%)	Low white blood cell count (92%)
Abdominal swelling (97%)	Splenomegaly (90%)	Low platelet count (95%)
Epistaxis	Hepatomegaly (49%)	Hypo-albuminemia (96%)
Easy bleeding	Petechie	Hypergammaglobulinemia (91%)
Leg swelling	Edema, ascites	Elevated transaminases, bilirubin and creatinine

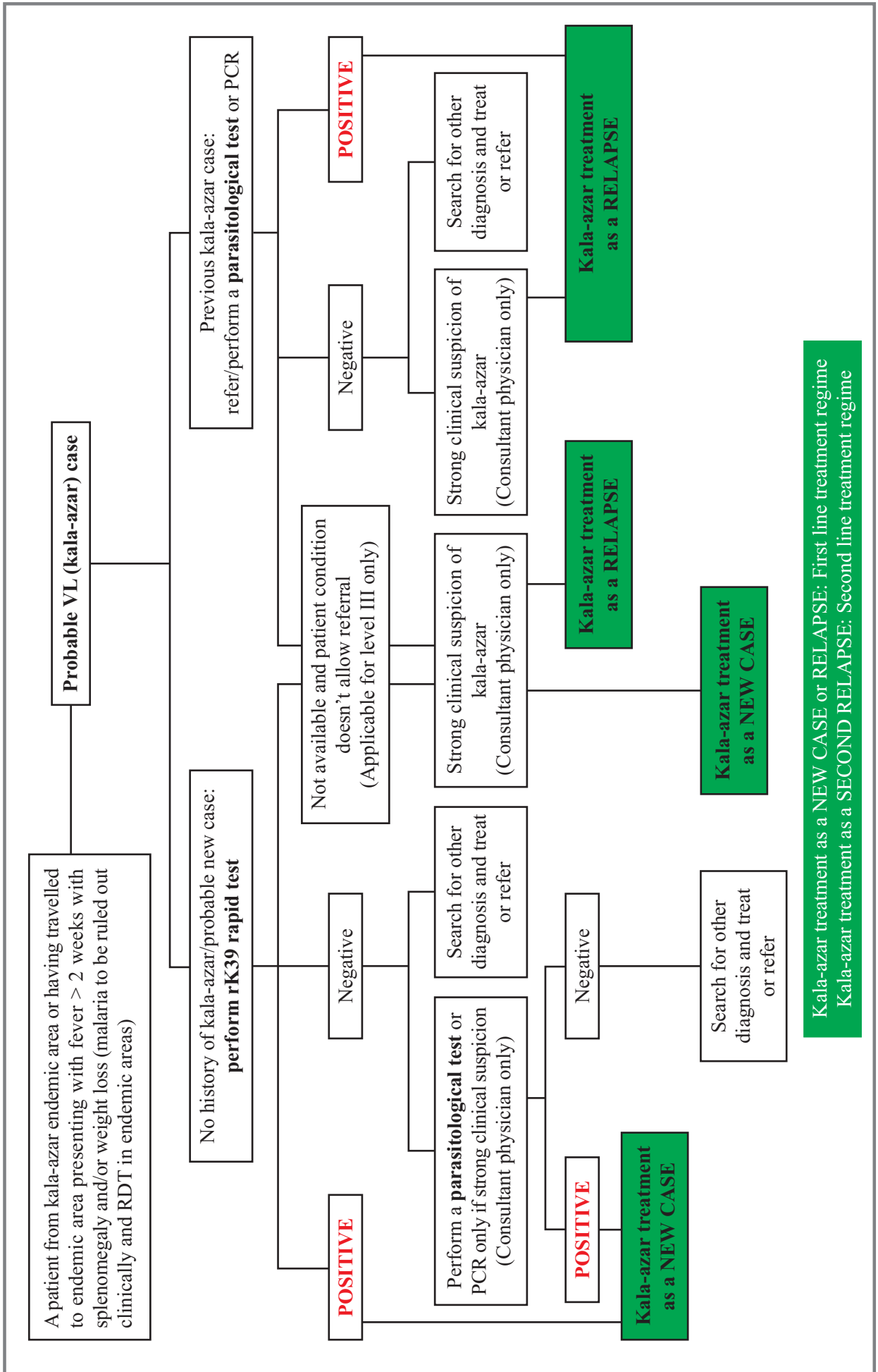


Wasting with decreased middle upper arm circumference (MUAC)

Distended abdomen with massive splenomegaly mark

(PC: Dr. V. Kattel)

Figure 3: Kala-azar Diagnostic Algorithm



2.5 Post-kala-azar dermal leishmaniasis (PKDL)

2.5.1 Epidemiology:

PKDL is sequelae of VL that usually occurs after a few years of treatment of VL. PKDL occurs in all areas endemic for *L. donovani*. It is common in East Africa and in the Indian subcontinent. The frequency is low in other endemic countries. Chronic PKDL patients are generally assumed to act as potential reservoirs for the parasites during interepidemic periods of visceral leishmaniasis. Hence in VL elimination settings PKDL diagnosis and treatment may likely be an important issue.

The global information on prevalence of PKDL are largely based on estimates due to poor availability of data. The factors that increase the risk for PKDL within an endemic area are not fully understood but appear to be associated with young age at the time of developing visceral leishmaniasis and an inadequate course of treatment especially due to poor compliance with prolonged course treatment. PKDL has been reported frequently after treatment for visceral leishmaniasis with sodium stibogluconate, but also after treatment with Miltefosine, amphotericin B (deoxycholate and liposomal) and paromomycin. Of all the medicines, sodium stibogluconate has been used since long and thus most extensively used in the treatment.

The prevalence of PKDL in Nepal has been estimated to be 2.3% of patients treated for visceral leishmaniasis, based on screening of cases treated by the B. P. Koirala Institute of Health Science in Dharan and by district hospitals. Data on the number of PKDL cases are limited because of the surveillance and reporting gaps. As per WHO consultative meeting on PKDL report, in 2010, a survey in Nepal found that the median onset of PKDL after visceral leishmaniasis was 23 months. Patients who received only partial treatment (<20 injections of sodium stibogluconate) were 11 times more likely to develop PKDL than those who received the complete treatment series.

It is difficult to predict who will develop PKDL. Inadequate treatment for visceral leishmaniasis (inadequate dose or an inadequate duration treatment), young age (generally, 5–17 years), malnutrition, HIV infection and antiretroviral treatment, may play a part.

Biopsy samples have shown a picture of diffuse dermal infiltrate of macrophages, lymphocytes and plasma cells. The inflammatory cells are mainly CD3+ cells; IL-10 is prominent in the lesions; interferon-gamma and tumour necrosis factor (TNF) alpha are found uniformly; and IL-4 is present in varying amounts. Diminished expression of interferon-gamma receptor 1 and TNF-R1 receptors during PKDL may interfere with an effective host response. Favorable outcomes for patients with PKDL are predicted by a positive leishmanin skin test or when levels of interferon-gamma are higher than levels of IL-10².

²Post kala-azar dermal leishmaniasis: A manual for case management and control. Report of a WHO consultative meeting, Kolkata, India, 2012

2.5.2 Clinical manifestations of PKDL

Most patients on the Indian subcontinent have mixed presentations comprising macules, papules, plaques or nodules mainly on or around the chin and mouth or face³. These lesions are: Non-ulcerative like the bacterial or viral infections; Non-itchy like the fungal infection or atopic lesions and, Non-anesthetic like the leprosy lesions. The lesions are of prolonged duration, persistent and progressive. Macules may progress over weeks to months into papule and plaque then progress to nodules.

This presentation can be seen in different forms:

- Monomorphic (macular and nodular)
- Polymorphic or mixed (both macules and indurated lesions such as papules are present)
- Rare presentations (e.g. erythrodermic)

There is no standard system for grading the severity of PKDL on the Indian subcontinent. The severity may be described as:

- Mild (very few lesions, usually on the face)
- Moderate (lesions easily visible and generalized)
- Severe (dense coverage with lesions and little normal skin remains)



(PC: Dr. V. Kattel)

PKDL-severe and polymorphic lesion in a patient treated with SSG 6 years back for VL.

³Post kala-azar dermal leishmaniasis: A manual for case management and control. Report of a WHO consultative meeting, Kolkata, India, 2012.

Table 2: **Differential diagnosis: following diseases should be considered**

■ Leprosy	■ Chronic arsenic poisoning
■ Pityriasis alba	■ Pityriasis versicolor
■ Vitiligo	■ Nutritional deficiencies
■ Measles	■ Malaria rubra
■ Neurofibromatosis	■ Acne
■ Secondary syphilis	■ Lupus vulgaris
■ Chronic arsenic poisoning	■ Discoid lupus erythematosus

2.5.3 PKDL operational case definition

Probable PKDL case:

A patient living in or having travelled to visceral leishmaniasis (kala-azar) endemic areas presenting with a typically symmetrical multiple hypopigmented macules, papules, plaques, or nodules without loss of sensation.

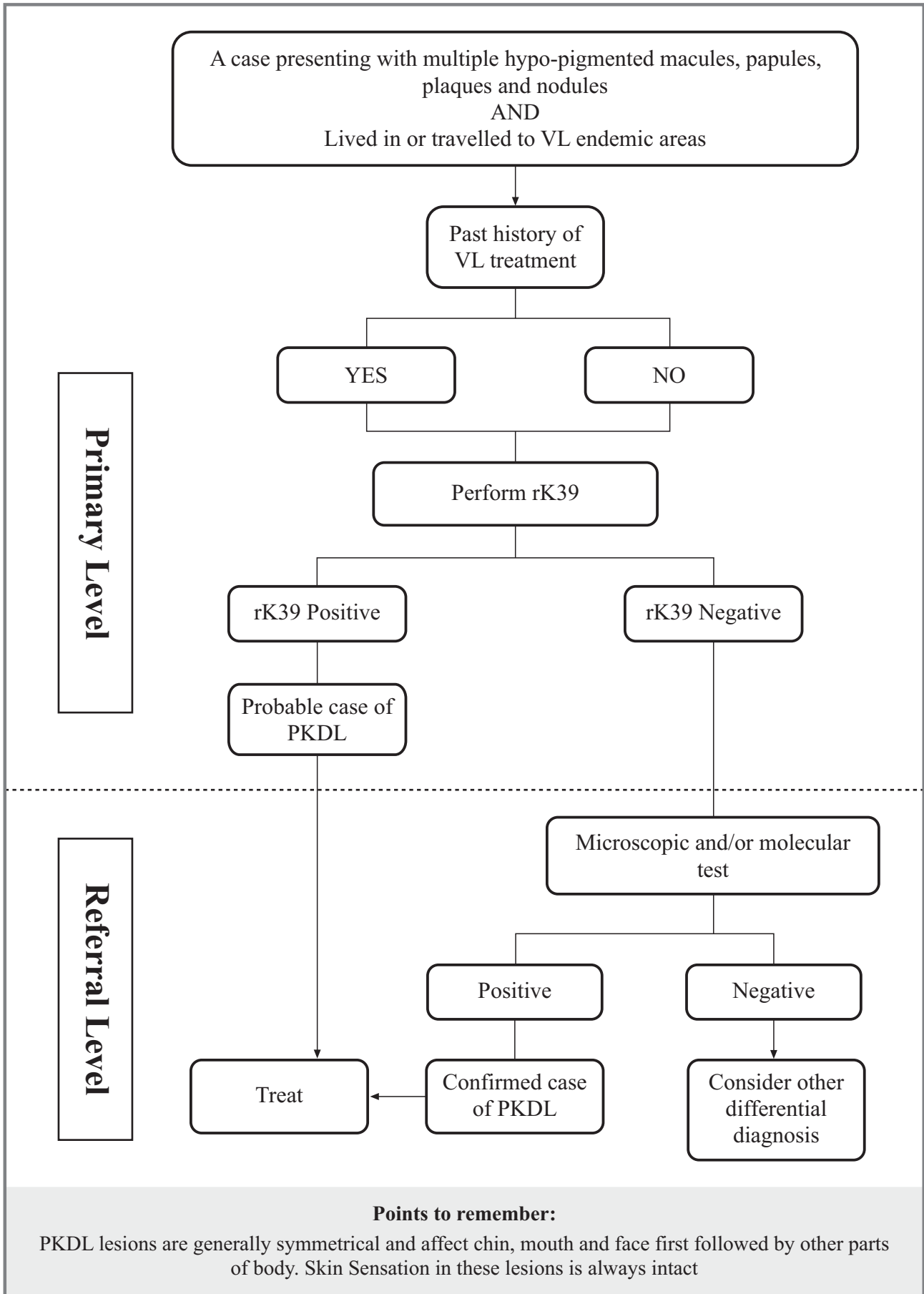
PKDL can occur in patients with previous or concomitant visceral leishmaniasis (kala-azar). In some cases, it occurs without the history of VL. Serological test such as rK39 rapid diagnostic test positivity acts as a strong evidence when other diseases (for example, leprosy) are considered in the differential diagnosis, or if a history of VL is uncertain.

In elimination settings, all probable PKDL cases are recommended for treatment and must be reported.

Confirmed PKDL:

A probable PKDL case with *Leishmania* infection confirmed parasitologically, by PCR or a slit-skin smear or biopsy.

Figure 4: **Algorithm for diagnosing and treating post-kala-azar dermal leishmaniasis (PKDL)**



2.6 Cutaneous and mucocutaneous leishmaniasis

2.6.1 Cutaneous leishmaniasis

Cutaneous leishmaniasis presents with a wide clinical spectrum that may mimic other skin conditions. The species are usually other than *donovani*. The disease is more common in Mediterranean basin, Central Asia and Americas. Recently there has been case series reports from western Nepal especially tropics and hills.

Probable CL case:

A person living in or having travelled to endemic areas showing typical CL skin lesions (macule, plaque, nodule, ulcer)

Confirmed CL case:

Laboratory-confirmed CL case:

A probable CL case with parasitological confirmation, by positive smear, culture or PCR.

OR

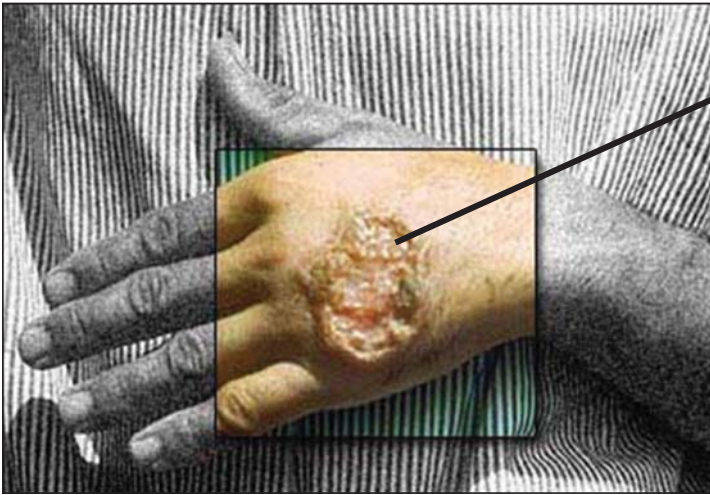
Clinically-confirmed CL case:

A probable CL case that has not been confirmed by any laboratory test (i.e. test(s) not done or negative) but is assessed by a **consultant physician** to be a confirmed CL case based on clinical grounds.

Diagnosis of CL is either demonstration of parasite microscopically or parasite antigen by PCR on probable case or diagnosis of exclusion with response to treatment.

Clinical features to identify skin lesions suggestive of cutaneous leishmaniasis

- Cutaneous leishmaniasis is characterized by the appearance of one or more lesions, typically on uncovered parts of the body. In localized cutaneous leishmaniasis, a typical lesion starts as a raised papule at the site of inoculation. It grows over several weeks to reach a final size of a nodule or a plaque. A crust develops centrally, covering an ulcer with a raised edge and variable surrounding induration
- The face, neck, arms and legs are the commonest sites.
- If left without therapy, lesions usually heal gradually over months or years, usually leaving a depressed scar.



Ulcer with rolled borders
irregular margin central
crusting and base with
granulation tissue

Skin lesion from a person with cutaneous leishmaniasis (CDC/Dr. D.S. Martin).

The infecting species of the parasite can influence the lesion aspect:

- Cutaneous leishmaniasis caused by **L. tropica** (previously known as anthroponotic or urban anthroponotic cutaneous leishmaniasis) frequently appears as dry ulcers of the skin, which usually heal spontaneously within about 1 year or longer, often leading to disfiguring scars. The incubation period is usually 2–8 months.
- Cutaneous leishmaniasis caused by **L. major** (previously known as zoonotic or rural zoonotic cutaneous leishmaniasis) frequently appears as severely inflamed and ulcerated skin, which usually heals spontaneously within 2–8 months. There may be multiple lesions, especially in non-immune patients, which can lead to disfiguring scars. The incubation period is often less than 4 months.
- Cutaneous leishmaniasis caused by **L. infantum** typically causes a single nodular lesion of the face (i.e. there is no crust or ulcer and except for the induration and colour, the skin on the lesion looks almost normal). Although *L. infantum* also causes visceral leishmaniasis, cutaneous lesions most often develop without any visceral involvement.

Table 3: **Differential diagnosis of CL is either:**

■ Staphylococcal or streptococcal infection	■ Mycobacterial ulcer
■ Leprosy	■ Fungal infections
■ Cancer	■ Sarcoidosis
■ Tropical ulcer	

2.6.2 Mucosal/mucocutaneous leishmaniasis

The involvement of mucosa primarily or as an extension of cutaneous leishmania gives mucosal/mucocutaneous leishmaniasis (ML/MCL). The common site are mucosal tissues of the mouth and upper respiratory tract (by lymphatic or blood route). The mucocutaneous lesions are associated to the New World disease caused by *L. braziliensis*, *L. panamensis* and, rarely, other species and are mostly reported in Bolivia and Peru.

Malnourished young adult male migrants are more at risk. Other risk factors include delayed healing of cutaneous leishmaniasis, the site of the primary lesion above the waist, multiple or large primary lesions.

Clinical presentation

Involvement of nose is always present with nodules and infiltration of the anterior cartilaginous nasal septum. This presents with obstruction of the nostril and in late cases perforation of the septum, collapse and broadening of the nose. The skin of the nose is thickened in some cases, swollen and red. In about 30% of cases other sites are involved (in decreasing order of frequency): the pharynx, palate, larynx, trachea and upper lip.

Local lymphadenopathy is common. In the final stages, there is severe mutilation of the tissue, obstruction and destruction of the nose, pharynx and larynx. This condition never heals spontaneously and results in secondary bacterial infections and other complications- pneumonia being the commonest cause of death.

Probable ML/MCL case:

A person living in or having travelled to CL endemic areas showing mucosal/mucocutaneous lesions (including nodules, infiltration, obstruction, mutilation)

Confirmed ML/MCL case:

Lab-confirmed:

A probable case with parasitological confirmation of the diagnosis (positive smear or culture), PCR and/or, for mucocutaneous leishmaniasis only, serological diagnosis.

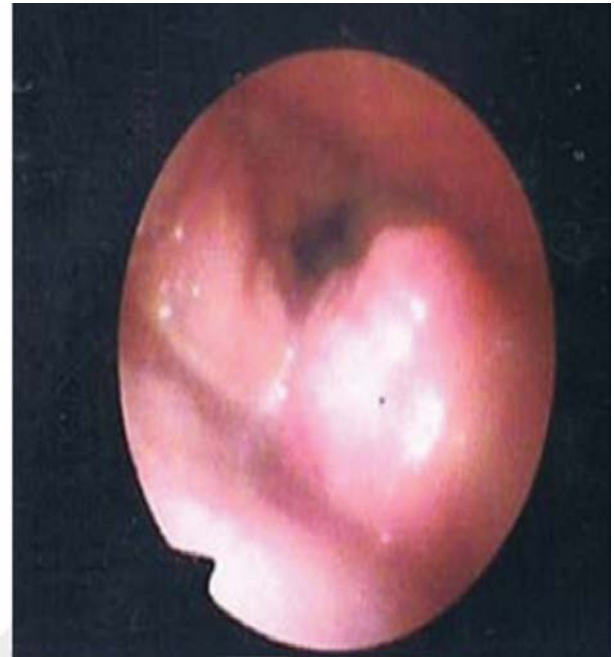
OR

Clinically-confirmed:

A probable ML/MCL case that has not been confirmed by any laboratory test (i.e. test(s) not done or negative), but is assessed by a **consultant physician** to be a confirmed ML/MCL case based on clinical grounds



55 years male presented with non healing ulcerated lesion of 3*2 cm² with crust formation over upper lip. Punch biopsy showed **Leishmania species**
(Photo Courtesy Dr. Vivek Kattel)



46 years male with history of hoarseness of voice with Swelling of right aryepiglottic and aryepiglottic fold on flexible naso-endoscopy. Punch biopsy showed **Leishmania species**
(Photo Courtesy Dr. Dipak Poudel)

Differential diagnosis

Table 4: **Following conditions may mimic early or advanced mucocutaneous leishmaniasis**

<ul style="list-style-type: none"> ■ Allergic rhinitis 	<ul style="list-style-type: none"> ■ Paracoccidioidomycosis
<ul style="list-style-type: none"> ■ Other deep mycoses 	<ul style="list-style-type: none"> ■ Cancrum oris
<ul style="list-style-type: none"> ■ Lymphoma and other neoplasia 	<ul style="list-style-type: none"> ■ Leprosy
<ul style="list-style-type: none"> ■ Sarcoidosis 	

2.7 Laboratory diagnosis

2.7.1 Rapid test (rK39 test)

A RDT is a simple test which can be used at all levels of the health care services. Results can be read easily and within 30 minutes. It does not need highly skilled laboratory staff and test results expedite the initiation of treatment provided standard case definitions are followed.



They are currently the best available diagnostic tool for VL for use in remote areas, and their use in field setting should be promoted. Apart from use in routine services, use of rK39 in campaigns and active case search is highly recommended.

rK39 could be false negative in immuno-compromised status like HIV/kala-azar co-infection, patients on immunosuppressant therapy and severe acute malnutrition. Such cases should be confirmed using the PCR test or parasitological test whichever is appropriate and available.

rK39 is available at kala-azar endemic districts from level II and above health institutions. There is provision of supply on demand to any health facility in high degree of clinical suspicion. These health facilities will also receive supplies of the drugs used for the treatment of kala-azar. Laboratory technician perform and report the test. Each batch of the rK39 RDT should be checked for its performance in the referral level hospitals to assure the quality (See annex-1).

Table 5: **The following table advantages and disadvantages of rK39.**

Advantages	Disadvantages
<ul style="list-style-type: none"> ■ Can be used in field settings ■ Enables individual patients be tested at the bedside/field e.g. camps ■ Tests are individually packed and easy to store and transport ■ Simple to perform with minimal training ■ Results are reproducible ■ Does not require a laboratory set up ■ Test can be performed using finger prick whole blood, serum or plasma. ■ Kits can be transported and stored at ambient temperature (up to 30°C). ■ Results are easy to read and interpret and are available within 10 – 30 minutes. 	<ul style="list-style-type: none"> ■ Remains positive after the successful treatment of VL patients (past infection) ■ Cannot distinguish between active cases (current infection)-NEW CASES and RELASPES cases ■ The rK39 antibodies can also be present in healthy persons from endemic areas who were exposed to Leishmania but have not developed clinical disease, therefore, interpretation must always be done in combination with clinical case definition ■ In patients with advanced HIV infection a negative result cannot rule out the diagnosis of VL

Table 6: **The following table explains indication of the test, its false positive and false negative conditions**

<p>To whom rK39 test should be used?</p> <ul style="list-style-type: none"> ■ <i>Probable new cases of VL,</i> <p>Which scenario rK39 is not useful for diagnosis of persons with history of VL?</p> <ul style="list-style-type: none"> ■ <i>Patients under current VL treatment or treated</i> ■ <i>PKDL with past history of VL. However, in PKDL cases treated for past VL, positive rK39 makes such patients as probable PKDL.</i> <p>Which conditions it works less well (False negative)?</p> <ul style="list-style-type: none"> ■ <i>HIV-VL co-infected persons with CD4 less than 200 or those with other immune disorders or severely malnourished</i>
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2.7.2 Parasitological

Definitive diagnosis of VL can be done by microscopic confirmation of the amastigote form of the parasite in tissue aspirates from spleen followed by bone marrow followed by lymph nodes or culture (usually only in tertiary care laboratory set up).

Indications for parasitological examinations for diagnosis of kala-azar are as follows:

- (i) The rK39 test is negative but the suspicion of kala-azar is still high in normal individual.
- (ii) The rK39 test is negative but the suspicion of kala-azar is high in cases like PLHIV with low CD4 count, severe malnutrition, and severe immune suppression.
- (iii) A patient treated for VL in the past presenting again with symptoms suggestive of VL (high degree of suspicion of relapse),
- (iv) In settings where studies are done for monitoring of drug resistance.



Figure 1: Bone marrow showing intracellular and extracellular amastigotes

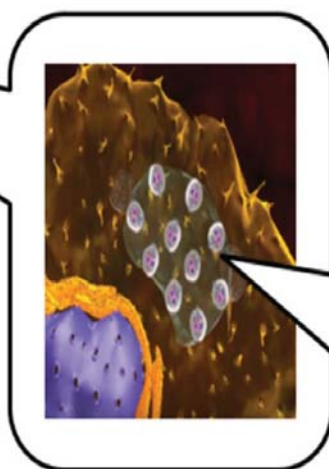


Figure 2: Schematic representation of vacuole and amastigotes

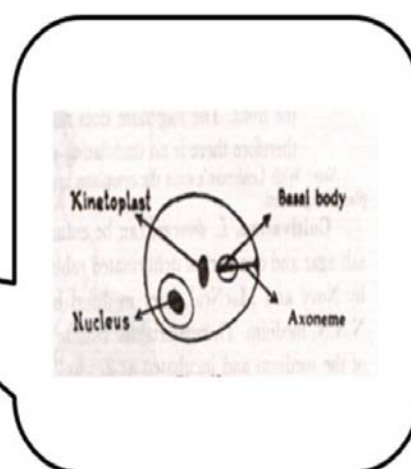


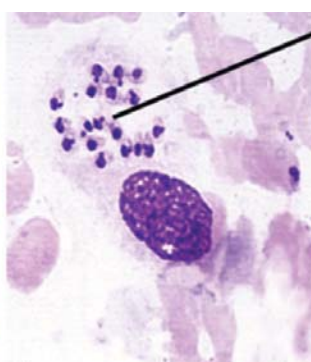
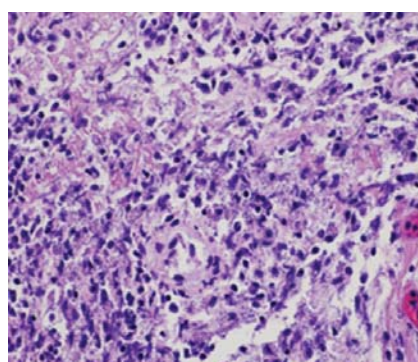
Figure 3: Diagrammatic representation of amastigotes

Picture Courtesy: Dr. Vivek Kattel

Table 7: **Comparative features of different clinical specimen for parasitological diagnosis of VL**

Features	Splenic	Bone marrow	Lymph node
Sensitivity	<ul style="list-style-type: none"> ■ 95% ■ Sensitivity highest among the three methods ■ Considered reference standard 	<ul style="list-style-type: none"> ■ 53-86% 	<ul style="list-style-type: none"> ■ Low (52-58%)
Availability	<ul style="list-style-type: none"> ■ Not recommended for field settings ■ Only in district hospitals or higher (referral) centre ■ Where surgical services are available ■ Where blood transfusion services are available ■ Where nursing surveillance is present 	<ul style="list-style-type: none"> ■ Not recommended for field settings ■ District hospitals or higher (referral) centre 	<ul style="list-style-type: none"> ■ proper tissue preparation is needed
Procedure	<ul style="list-style-type: none"> ■ Expertise required for the procedure 	<ul style="list-style-type: none"> ■ Painful 	<ul style="list-style-type: none"> ■ Need experience
Risk	<ul style="list-style-type: none"> ■ Risk of fatal bleeding (0.1%) 	<ul style="list-style-type: none"> ■ Sterilization is required 	
Important general considerations	<ul style="list-style-type: none"> ■ demonstration of parasites in aspirates is proof of VL ■ sensitivity of the test depends on the expertise and quality of reagents ■ identification of amastigotes under the microscope requires experience and skill ■ examine at least 1000 microscope fields for amastigotes using x100 oil immersion lens ■ inability of find amastigotes in an aspirate cannot be a reason to exclude VL in a patient having a strong suspicion of the disease. 		

Details of the procedures are given in the annexures.



Higher magnification of 40x revealed: Intra cytoplasmic small oval shaped structure with spherical nucleus and dot like structure i.e. kinetoplast

Photo Courtesy: Dr. Yamuna Agrawal

2.7.3 Polymerase chain reaction (PCR)

PCR has higher sensitivity than parasitological examination however this is not available in all referral hospitals of Nepal. PCR has been the choice among doubtful cases of primary VL, VL relapse, PKDL, CL and MCL cases. However, it is not available in public health field settings at district level. The test is available only in few higher centers.

2.7.4. Culture

Culture of parasite needs special media named NNN media. This has been replaced by PCR technique as culture is time consuming process.

2.7.5 Other recommended laboratory test

In order to monitor the side effects of drugs and progress of treatment, the following lab tests would be made available at different levels of health institutions:

Table 8: **List of laboratory tests available at different levels of health institutions of Nepal**

S. No	Test	Level II	Level III and above
1.	CBC	Hb %, TLC, Platelet count	Hb %, TLC, Platelet count
2.	Prothrombin time	No	Yes
3.	Renal function test	No	Urea, Creatinine
4.	Liver function test	No	Bilirubin, SGPT
5.	Pregnancy test	Yes	Yes
6.	Malaria parasite	Yes	Yes
7.	HIV	No	Yes
8.	Urine dipstick test for protein	Yes	Yes

Since tuberculosis is endemic in Nepal and there have been case reports of VL-TB co-infections. Therefore, it is recommended to **screen all kala-azar cases for TB** as per national protocol (Sputum, GeneXpert MTB/RIF and chest x-ray).

Presence of VL in HIV is AIDS defining criteria and presence of HIV in VL has more adverse impact on treatment course and outcome of VL. Hence **HIV status should be checked in all VL cases and all HIV positives should be clinically assessed for VL signs and symptoms in endemic areas.**

2.7.6 Diagnosis of Relapse

A relapse of kala-azar means that a kala-azar patient was successfully treated in the past but has presented again with clinical manifestations of kala-azar with parasitological confirmation at any point after cure. In many cases relapses usually occur **within 6 months** after treatment.

Diagnosis in relapse cases should be based on parasitological diagnosis. rK39 test cannot differentiate between recent (new) and past infection (relapse) because it can still be positive for months to years after a case is successfully treated even if a person is feeling well.

Sometimes especially in children during or post treatment there may be worsening of symptoms in the form of high grade fever, pancytopenia, mild to moderate icterus, progression of hepatosplenomegaly, generalized lymphadenopathy and rashes. This is rare case scenario however serum ferritin, triglyceride level and fibrinogen level may help to differentiate hemophagocytic syndrome a close differential of relapse. Bone marrow biopsy will reveal hemo-phagocytosis. Thus, role of microscopy plays vital in such scenario.

Relapse CL cases: a patient who experiences recurrence of CL symptoms with parasitological confirmation at any time point after initial cure.

2.7.7 Diagnosis of PKDL

Microscopy or PCR

High degree of clinical suspicion on typical skin lesion without features of VL should be referred for diagnostic test.

Confirmation of diagnosis is usually done by skin slit smear (SSS) microscopy or histopathology. (Sensitivity of SSS microscopy is, 40–60% from patients with nodular lesions). The advantage of microscopy is the acknowledged high specificity, which leads to low numbers of patients unnecessarily treated with anti-leishmanial drugs.

PCR has higher sensitivity than microscopy however it is not available due to cost factor in resource limited set up.

Hence in absence of diagnostic test clinical judgment and treatment response plays a significant role.

2.7.8 Diagnosis of cutaneous leishmaniasis

Microscopy or PCR

Parasitological diagnosis remains a reference standard because of high specificity. However, it depends on geographical location, type of species and the stage of the lesion. Multiple parasitological diagnosis should be performed in each patient.

Hence in absence of diagnostic test clinical judgment and treatment response plays a significant role. Serological diagnosis is of limited use in CL due to low sensitivity and variable specificity

2.7.9 Diagnosis of mucocutaneous leishmaniasis

Microscopy or PCR

A diagnosis can be strongly suspected in patients with typical mucosal lesions and a history of cutaneous leishmaniasis with one or more visible scars, sometimes with concomitant cutaneous leishmaniasis in rare cases.

Due to strong local immune reaction, parasites are scarce in mucosal lesions. Looking for parasites in mucosal samples (obtained by brushing or biopsy) by microscopic examination or by culture lacks sensitivity. The demonstration of parasite DNA by PCR has proved to be the most sensitive approach to confirm mucosal leishmaniasis.

2.8 Fate of untreated cases

VL is exclusively fatal. Almost all untreated cases will die, and the most common cause of death is complication like secondary infection due to delay in diagnosis and treatment. Hence, early diagnosis and treatment is strongly advocated by national health policy in all VL cases. The rK39 antibodies can also be present in healthy persons from endemic areas who were exposed to *Leishmania* but have not developed clinical disease. National guideline **does not advocate** for treatment of subclinical cases, but they must be under observation for development of symptoms or signs.

PKDL cases in Indian subcontinent rarely heal spontaneously without treatment. In elimination settings, all probable PKDL cases are recommended for treatment.

CL may resolve or progress if untreated however the associated factor for these two spectra are not clearly defined. Unless severe form it can be closely followed up.

MCL if not treated is likely to progress with permanent damage of function/organ hence are recommended for treatment as early as possible.

3.1 Treatment of kala-azar, PKDL, CL and MCL

Kala-azar affects underprivileged populations primarily in rural communities. Patients belong to poor socio-economic strata. In many reporting districts geographical terrain poses challenge to patients in accessing health services on permanent basis. Several factors e.g. poor health seeking behavior, long distance travels etc result in both case detection and treatment delays resulting into poor treatment outcomes and continued transmission.

To overcome these challenges, Ministry of Health and Population recommends Liposomal Amphotericin B (L-AmB) as the first option regimen unless situations warrants use of other drugs.

Liposomal Amphotericin B has the highest therapeutic index among all the available anti-leishmanial medicines.

The effectiveness of VL treatment throughout the globe is more than 95% however the treatment outcome is determined by severity of the disease and patient factors. Some of the poor prognostic factors of VL treatment are

- Jaundice
- Severe wasting
- Severe anemia
- HIV co-infections
- Extreme of ages
- Pregnancy
- Hemodynamically unstable
- Hemophagocytic Syndrome
- Comorbidities
- Biochemical markers (Neopterin)

**All kala-azar patients must be admitted for treatment with
Liposomal Amphotericin B**

3.2 General principles and objectives

The main objectives of the treatment are:

1. Clinical cure of the patient
2. Minimize drug toxicities and side effects, if any
3. Prevent and/or identify and treat complications
4. Support patient's nutritional and hydration status
5. Manage other medical conditions
6. Reduce the risk of relapse and PKDL
7. Report to national system.

Treatment outcomes are directly linked with management of a patient as a whole than giving anti kala-azar drugs alone.

3.3 Supportive management

3.3.1 Nutritional support

All patients should be clinically assessed for their general condition and nutritional status. Most of the patients are malnourished and require adequate nutrition and vitamin supplements wherever required. In some patients therapeutic feeding may also be needed.

3.3.2 Treatment of inter-current infections

Inter-current infections are very common in kala-azar patients and should be looked for. Most of the patients die due to secondary bacterial infections.

- Treat pneumonia and other infections with appropriate antibiotics
- Treat other bacterial infections of intestine causing dysentery (in kala-azar diarrhoea occurs due to parasitic enteritis)
- Maintain oral hygiene to prevent mouth infections (cancrum oris). If it occurs, then treat with appropriate antibiotics
- Maintain hydration with right fluids and doses
- Treat skin infections and maintain skin hygiene
- Treat other parasitic infections (if present) like malaria or other infections like tuberculosis etc

3.3.3 Anaemia

Most of the patients suffer from anaemia and may occasionally require blood transfusion to correct severe anaemia or bleeding due to thrombocytopenia.

3.3.4 Other situations

Manage other conditions as and when present e.g. nose bleed etc

3.4 Drug treatment

3.4.1 Primary kala-azar

3.4.1.1 First line regimen- Liposomal Amphotericin B

WHO Expert Committee on Leishmaniasis in 2010 and Regional Technical Advisory Group (RTAG) for the kala-azar elimination programme meeting in 2011 recommended Liposomal Amphotericin B (L-AmB) as the first option regimen, during the attack phase, for the Indian sub-continent (ISC).

Liposomal amphotericin B at the dose of 10mg/kg single dose over 2 hours. Single dose treatment ensures 100% treatment compliance.

Liposomal amphotericin B is safe in pregnant women, severely ill patients, children less than 2 years old and old aged patients and HIV co-infected patients.

Successful therapy improves the general condition, resolves fever in most of the cases by end of week and causes regression of splenomegaly in most of the cases and recovery of blood counts towards normal in most of the cases by end of weeks. Complete regression of splenomegaly may take several months however most cases it completely regresses by 6 months. A good indicator of definitive cure is the absence of clinical relapse at 6 months.

Most clinical trials have been conducted with a reference liposomal amphotericin B formulation. Therefore, all other lipid formulations should be evaluated for toxicity, bioequivalence and efficacy before they are used clinically. Currently the national programme is receiving AmBisome (Liposomal Amphotericin B) donation through WHO. Therefore, details about the indications, preparations, storage and other aspects of L-AmB in this guideline has been made with reference to as AmBisome.

Things to remember for L-AmB treatment

- Do not use underweight dose
- Give test dose before starting L-AmB infusion
- Do not freeze
- Always prepare in Dextrose solutions

- L-AmB is not compatible with saline and other fluids
- Prevent foam formation while constituting drug

Preparations, mode of administration, dose calculations are given in the annexure III

Adverse events due to Liposomal amphotericin B (in order of frequency of occurrence)

Reported side effects of AmBisome in order of frequency of occurrence include infusion related fever and rigor, chills, nausea/vomiting, headache, backache, chest pain, hypokalemia, dyspnoea, bronchospasm, tachycardia, hypotension, nephrotoxicity, and hepatobiliary disorders. Side effects like feverish feeling, nausea, backache are more common. Life threatening ADR (adverse drug reaction) are very rare. In case of infusion related reactions, infusion can be slowed down and/or physician may give medicines to prevent or treat infusion related reactions, such as diphenhydramine (antihistamine), paracetamol and or hydrocortisone to reduce immune system response.

Indications for stopping L-AmB treatment

Patients who develop hypersensitivity reactions require cessation of L-AmB and switching to an alternative treatment. If a severe anaphylactic reaction occurs, the infusion should be immediately discontinued, and the patient should not receive any further infusions.

Storage conditions

Before use, medicine should be stored at 2–25 °C and should not be frozen. It should also be protected from exposure to light. Once reconstituted, the product must be used immediately.

3.4.1.2 Second line treatment

Other than liposomal amphotericin B, mono drug therapy is not recommended. Combined regime reduces the dose requirement of individual drugs and its consequences without compromising the cure rate. Ministry of Health and Population, Nepal has endorsed following treatments for kala-azar ranked in order of preference as per WHO recommendations⁴.

Combination regimens

Three separate combinations showed 95.06–99.78% cure rates. These include co-administration of

1. Liposomal amphotericin B (5 mg/kg, single infusion) plus 7 days Miltefosine 50 mg BID in adult or 2.5mg/kg/day
- OR**
2. Liposomal amphotericin B (5 mg/kg, single infusion) plus 10 days' Paromomycin (11 mg/kg base),
- OR**
3. Miltefosine plus Paromomycin for 10 days

⁴Control of the leishmaniasis, Report of a meeting of the WHO Expert Committee on the Control of Leishmaniases, Geneva, 22–26 March 2010, http://apps.who.int/iris/bitstream/handle/10665/44412/WHO_TRS_949_eng.pdf;jsessionid=E636D979AE734A8800D17380232A6304?sequence=1

No safety issues were recorded with above regimens. Combination regimens have the potential advantages of reducing the probability of selection of drug-resistant parasites, thereby prolonging the effective life of the available medicines. Regional Technical Advisory Group (RTAG) recommends use of combination regimen once the attack phase is over.

The implementation of combination regimens will be used in patients where the first line treatment is either not indicated or not available. It will be made available as a second line regimen for patients who cannot be given Liposomal Amphotericin B monotherapy.

3.4.1.3 Third line treatment

In case of lack of the first and the second line drugs, third line can be accepted however national guideline strongly recommend first line treatment.

Amphotericin B deoxycholate: 0.75–1.0 mg/kg per day by infusion, daily or on alternate days for 15–20 doses.

Amphotericin B deoxycholate

Amphotericin B deoxycholate has been used in the past for treatment of visceral leishmaniasis.

However, due to its side-effects, it has been replaced by safer liposomal formulations, however, it is still a rescue medicine in non-responsive patients to anti-leishmanial medicines.

Dosage: The drug is given at 0.75-1mg/kg daily as IV infusion in 5% dextrose over 4 hours for 14days. If there is poor response to the treatment, the drug has to be continued for a period of 21-28 days. A test dose of 1 mg, given by infusion is recommended followed by a full dose 4-6 hours later.

The cure rate of this drug is very high, exceeding 90%. The patient must be admitted at level III health institution or special referral centers for administering Amphotericin B as it requires monitoring of renal parameters.

Indications: Amphotericin B deoxycholate is generally recommended in the following conditions:

- ▶ This is the third line regimen used when first and second line treatment regimen are not available
- ▶ Kala-azar treatment failure i.e. unresponsive to first and second line regimen or in cases of relapse.
- ▶ Kala-azar patients whose first and second line therapy is discontinued due to severe side effects.

Table 11: **Side effects**

Renal impairment	Hypokalaemia and hypomagnesaemia
Headache	Nausea
Vomiting	Chills
Fever	Malaise
Muscle and joint pain	Diarrhoea, gastrointestinal cramps
Hypertension/hypotension	Cardiac arrhythmias including ventricular fibrillation
Skin rashes	Anaphylactoid reactions
Blurred vision	Vertigo
Hearing loss	Tinnitus
Liver disorders,	Peripheral neuropathy
Convulsions	Thrombophlebitis at the injection site and anaemia.

Renal function should preferably be monitored weekly during treatment. Renal impairment can be reduced by pre-hydrating the patient with an infusion of normal saline. If a rise in urea and creatinine occur, the interval between doses should be lengthened.

3.4.1.4 Forth line treatment

In very uncommon instances when first, second and third line treatment are not available, the fourth line can be considered.

Miltefosine

Miltefosine is the only available oral anti kala-azar drug. It is available in two doses: as 10mg and 50mg capsule. It is to be noted that Miltefosine monotherapy has observed higher relapse rates in Nepal therefore it is preferred as part of the combination therapy. However, the monotherapy course for the treatment of kala-azar is 28 days if at all used as fourth line in absence of first, second and third line treatment as already mentioned under treatment section.

Recommended doses of Miltefosine according to body weight

Drug category	Morning	Evening	Duration
More than 12 years of age and more than 50 kg body weight): 150mg/day	100 mg	50 mg	28 days
More than 12 years of age and more than 25-50 Kg body weight) at a dose of 100mg/day	50 mg	50 mg	28 days
≥12 years of age and less than 25 Kg body weight) at a dose of 50mg /day.	50 mg	0	28 days
Children aged (2-11 years age) at (2.5mg/kg body weight 10mg formulation in divided doses)			28 days

Note:

- a) The drug should not be taken on an empty stomach, i.e. should be taken after meals.
- b) In case of its use as a monotherapy in the treatment of kala-azar, any missed doses, the 28-day course can be completed by 35 days without exceeding the maximum recommended daily dose.

Source: WHO TRS http://apps.who.int/iris/bitstream/10665/44412/1/WHO_TRS_949_eng.pdf. Page no. 58.

Table 9: **Contraindications of Miltefosine and methods of verification**

Contraindication	Method of verification
Pregnancy	History of last menstrual period (LMP) and Pregnancy test
MWRA not using contraceptives	History
Lactating mother	History
Less than 2 years	History
Severe illness, bed bound	History and Physical examination
Malnutrition	< 10 percentile weight for age
Severe anemia (Hb% < 5 gm)	Level of Hb
Patients with known kidney disease	Edema, decreased urine output, Proteinuria
Patients with known liver disease	Jaundice
Chronic alcoholism	History

Table 10: **Recommended laboratory tests that are to perform for baseline and monitoring purposes**

Test	Frequency	Timing	Indication
Hematology: Hb %, WCC	2	Baseline, End of therapy	Exclude contra-indications Monitoring of clinical response
Pregnancy test	1	Pre-treatment	Women of child bearing age
Urine for albumin (dipstick)	2	Pretreatment, End of 1st week	To exclude contraindications To monitor for complication

Note: *Frequency of the tests and additional tests can also be recommended as per the discretion of the treating physician.*

Side effects and its management

- a) The common side effects of Miltefosine are vomiting, diarrhea and abdominal pain. Rarely, there may be liver or kidney related side effects.
- b) Usually the drug may produce vomiting and diarrhea during the first week of treatment in some patients. The symptoms are generally mild, of short duration and reversible.
Patients having diarrhea should be advised to take oral re-hydration solution frequently and they should be reassured that the diarrhea and vomiting will stop after a few days.
- c) If vomiting is severe and does not stop, the patient should be referred to level III health institution for further treatment.
- d) Puffiness of face, jaundice, or decreased urine output may be liver or kidney related side effects. The patients, family members, FCHVs should be advised to monitor these symptoms. If these symptoms are reported, the patient should be referred to level III health institution for further investigation and treatment.
- e) If fever persists in spite of taking Miltefosine for two weeks, then the patient may have other infections along with kala-azar. Such patients should be referred to level III health institution for further investigation and treatment.
- f) Do pregnancy test/rule out pregnancy

Indications for stopping Miltefosine treatment

If any of the following conditions is observed, stop the Miltefosine and immediately refer the patient to level III health institution.

- ▶ Pregnancy during the treatment
- ▶ Development of any of the following signs and symptoms:
 - Jaundice
 - Puffiness of face
 - Decreased urine output
 - Breathlessness
 - Severe vomiting
 - Severe diarrhea

OR

Paromomycin: 15 mg (11 mg base) per kg body weight per day intramuscularly for 21 days.

Paromomycin

Paromomycin is an aminoglycoside antibiotic and promising new effective drug for the treatment of kala-azar. The recommended dose is 15mg/kg/day to be given by intramuscular (IM) injections for 21 days. Paromomycin is absorbed quickly after intramuscular injection, reaching peak plasma levels within 1 hour.

Paromomycin dosage and administration

- The recommended dose is 15 mg/kg sulfate (equivalent to 11 mg/kg base); no maximum dose
- Patients must remain well hydrated. Tell patients to drink enough
- If patients have severe vomiting and diarrhoea, do not give the injections.
- This medicine **cannot** be given intravenously
- Weigh the patient weekly and recalculate the dose.
- Not recommended during pregnancy.

Common side-effects

The medicine is safe with minimal ototoxicity or nephrotoxicity. In the recommended dose, the ototoxicity is reversible. Pain in injection site is common. Paromomycin can be administered intramuscularly according to body weight to patients with visceral leishmaniasis who have normal renal function including children without the need for therapeutic monitoring or dose adjustment.

These effects are usually mild to moderate and transient or reversible at the end of treatment. There is increase in liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT), pyrexia, abnormal audiogram, and vomiting.

The drug is particularly useful for child bearing age women and children since safety and efficacy are not affected by gender and age. Monitoring of aspartate amino-transferase or alanine aminotransferase levels, or both, will be important for patients with pre-existing liver disease.

In pregnant women, Paromomycin crosses the placenta and can cause renal and auditory damage in the fetus. Therefore, it is not recommended in pregnancy. Paromomycin is excreted in breast milk and adverse effects in the breastfed infant cannot be excluded.

Things to be remembered for treatment

- a) Paromomycin is administered intramuscularly **(IM) only**
- b) Do not use during pregnancy
- c) Paromomycin should be avoided in patients with severe anaemia with hemoglobin <5g/dl
- d) Do not use in patients with hypersensitivity to paromomycin or to other aminoglycoside antibiotics. Discontinue use if an allergic reaction occurs.
- e) Paromomycin is contraindicated in patients with renal insufficiency
- f) In cases where Paromomycin or the combination therapy using Paromomycin do not lead to a VL cure at or before 6 months, do not repeat therapy. Instead, switch to another anti-leishmanial drug
- g) The medicine may have minimal ototoxicity or nephrotoxicity. Other factors that may increase patient risk of toxicity are dehydration and advanced age.
- h) It should be stored below 30°C but do not freeze. It should also be protected from light.

3.5 Complete Treatment

Cure from kala-azar can be achieved only after completion of treatment regimen. The following measures are recommended to complete the treatment:

A. Counseling

After confirming the diagnosis of kala-azar the following needs to be explained to the patient and family:

- Explain the importance of the need to treat kala-azar, and inform that early diagnosis and treatment is crucial.
- Inform that the drug is provided free of cost.
- Explain the need to complete the full course of the treatment.
- In case of treatment with L-AmB, patients should be counselled that the current symptoms will decrease in severity, frequency and then gradually disappear in next few days.
- Patient should be informed to report back to the health facility if symptoms persist beyond two weeks or recur during any period after discharge/cure
- Explain the need to start and continue treatment under supervision/observation.
- Inform that the patient will begin to start feeling better after a few days of treatment, but this does not mean cure. The symptoms will reappear if the treatment is not taken as advised and cure would occur only when full treatment has been taken.
- Explain the side effects of the treatment and advised them to contact the health worker if such events occur.

Key points

1. Fever and other signs and symptoms will reduce in frequency and will finally disappear in few days period after the successful treatment
2. Appetite will be regained and there will be well-being after the treatment
3. Patient must return to the health facility if signs and symptoms still persist beyond 14 days and/or recur any time after the treatment
4. If patient comes across any person with similar symptoms and signs in the household, neighbourhood or in the community, s/he should refer such persons to health facilities

3.6 Treatment outcomes in kala-azar

3.6.1 Treatment completion

Treatment completion is the assessment of whether the full-course of treatment has been received by the patient, as per the national protocol. Treatment completion should be assessed and recorded at the end of the treatment course or at the time the patient stops the treatment. In case of single dose Liposomal amphotericin B regimen, initial assessment after treatment completion done at 15 days.

- ▶ **Treatment completed:** The patient has completed the full-course of the treatment as per the national protocol, and the clinician's prescription. Length of treatment depends on drug regimen.
- ▶ **Treatment stopped for medical reasons:** the treatment was stopped by decision of the clinician (e.g. patient suffering from side effects, treatment failure) or after the death.
- ▶ **Default:** The patient does not complete the full-course treatment
- ▶ **Treatment completion unknown:** the patient completion of treatment is unknown (unrecorded). This is different from default, where the clinician knows that the patient has not completed the treatment.

3.6.2 Treatment outcome

Treatment outcomes for leishmaniasis patients have to be assessed twice:

- At the end of treatment, or **15 days** after treatment starts for short- course regimen = initial assessment
- and**
- **Six months** after the last drug was taken (final outcome) = Final assessment.

At initial assessment, 15 days after treatment start

- ▶ **Initial cure:** a full course of drugs has been completed AND the patient has clinically improved. Clinical criteria for initial cure defined as “*no fever + regression of splenomegaly + return of appetite and/or gain in body weight*”.
- ▶ **Failure (non-response):** signs and symptoms persist or recur during treatment or up to initial treatment outcome assessment.
- ▶ **Lost-to-Follow-up/Unknown:** the patient does not present for initial assessment 15 days after completion of treatment, or the patient status was not recorded.
- ▶ **Death:** death of any person having been diagnosed of VL regardless of the treatment status and the cause of death within the standard post-treatment follow-up period.

Any death should be notified with specification of the cause of death, as follows:

- Death due to VL
- Death due to HIV
- Death due to other disease or medical condition(s)
- Death due to SAE (iatrogenic)
- Death due to non-medical condition (accident)
- Death due to unknown cause

At final assessment, six months after the last drug was taken

- ▶ **Final cure:** a patient who after initial cure remains symptom-free at six months after the end of treatment.
- ▶ **Relapse:** a patient who experiences recurrence of VL/KA symptoms with parasitological confirmation at any time point after initial cure.
- ▶ **Loss to follow-up:** patient does not present for assessment at six months.
- ▶ **Death:** death of any person having been diagnosed of VL regardless of the treatment status and the cause of death within the standard post-treatment follow-up period

Any death should be notified with specification of the cause of death, as follows:

- Death due to VL
- Death due to HIV
- Death due to other disease or medical condition(s)
- Death due to SAE (iatrogenic)
- Death due to non-medical condition (accident)

Criteria for cure:

The cure of kala-azar is confirmed by absence of parasite from splenic and bone marrow smears. Such provision is available in specialized institutions only. However, for program purpose a case completing treatment is considered clinically cured when there are no sign and symptoms of kala-azar. Complete clinical criteria of cure of kala-azar are as follows:

- The full course of treatment has been taken.
- Fever is absent.
- Regression of spleen has occurred.
- Return of normal appetite is reported.
- Increase in body weight has been reported.
- Improvement in anemia and a rise in hemoglobin have been demonstrated.

3.7 Treatment of PKDL

Cases of PKDL usually do not have any signs of kala-azar like fever, splenomegaly, or anemia. Although 85-90% of them appear after the cure of kala-azar, it is important to note that 10-15% of cases of PKDL occur without the preceding history of kala-azar. They present with skin lesions that may be macular, popular, nodular, or mixed. In PKDL cases sensation over the lesions is preserved in contrast to leprosy where similar lesions lose sensations. Sometimes the lesions of PKDL are extensive. Following complete treatment of PKDL case, all skin lesions tend to disappear.

The patients do not have any other problem other than the skin lesions. If PKDL cases need to be actively looked for as they act as a potential reservoir of kala-azar and contribute to continued transmission at community level, so counseling of PKDL cases is very important for completing treatment.

It is advised to refer all the PKDL cases to level III health institution or special referral center for treatment. The following recommendations are considered for the treatment of PKDL:

The WHO recommended dose for the treatment of Post –kala-azar dermal leishmaniasis in Bangladesh, India and Nepal

1. Amphotericin B deoxycholate: 1 mg/kg per day by infusion, up to 60–80 doses over 4 months
2. Miltefosine orally for 12 weeks at dosage as below

Table 12. **Dose and treatment schedule for PKDL**

Drug	Dose	Schedule
Miltefosine*	Daily doses of 100 mg for patients weighing > 25 kg and 50 mg for those <25 kg.	Daily for 12 weeks
Amphotericin B	1 mg/kg IV infusion	60–80 doses over 4-5 months with (20 doses on followed by 20 days interval)

**As the safety of courses of Miltefosine longer than 4 weeks has not been evaluated, all patients should be closely monitored for any unexpected side effects. (All patients should be admitted for first 4-7days).*

3.7.1 Treatment outcomes in PKDL

Treatment outcomes in PKDL should be clinically assessed at district hospital. A significant improvement can mean, for example, at least 80% resolution in the number of macules and/or a decrease in erythema and flattening of lesions.

Initial cure: clinical improvement at the end of treatment—defined as a considerable reduction in the number and size of skin lesions.

Final cure: clinical cure **12 months** after the end of treatment—defined as a complete resolution of macules, papules, plaques and nodules, no new lesion, and near total re-pigmentation of maculae.

3.8 Treatment of cutaneous leishmaniasis^{5,6}

General principles:

Cutaneous leishmaniasis is not a life-threatening condition, and severe complications are not very common. Various therapeutic interventions like local, systemic and physical treatments (e.g. cryotherapy, thermotherapy) have been used and tested in the management of cutaneous leishmaniasis.

The infecting species, geographical region and the immune status of the patient affect the efficacy of treatments and therefore treatment recommendations.

In cutaneous leishmaniasis due to *L. tropica* (anthroponotic cutaneous leishmaniasis), prompt treatment is important to improve the patient's health and also to reduce transmission of the parasite. Because of a predominant human-to-human transmission of *L. tropica*, there appears to be a higher risk for selection and spread of drug-resistant parasites of this species.

Superficial secondary infections may complicate ulcerated cutaneous leishmaniasis, therefore it is important to clean lesions. Cutaneous leishmaniasis due to *L. major* is associated with a self-cure rate above 50%–75% at 4–6 months.

The recommended drug or treatment approach in cutaneous leishmaniasis should not induce life threatening complications; however, in severe cases, the risk–benefit ratio is different.

The treatment decision is based first on the risk–benefit ratio of the intervention for each patient. To determine which treatment is the most appropriate, it is important to collect the clinical information on the following five aspects:

- Size of lesion: papule (<1 cm), nodule (<4 cm) or plaque (≥4 cm)
- Number of lesions
- Location of lesions on the body
- Evolution of the lesions: duration, aggravation (active lesion), improvement (self-curing);
- Immunological and general health status of the patient

⁵Adopted from Manual for case management of cutaneous leishmaniasis in the WHO Eastern Mediterranean Region, http://apps.who.int/iris/bitstream/handle/10665/120002/EMROPUB_2013_EN_1590.pdf?sequence=1&isAllowed=y

⁶Control of the leishmaniasis, Report of a meeting of the WHO Expert Committee on the Control of Leishmaniases, Geneva, 22–26 March 2010, http://apps.who.int/iris/bitstream/handle/10665/44412/WHO_TRS_949_eng.pdf;jsessionid=E636D979AE734A8800D17380232A6304?sequence=1

Step-wise treatment decision in cutaneous leishmaniasis due to *L. major* or *L. tropica* or *L. infantum*

Lesion(s) less than 4 cm (papule, nodule or ulcerated nodule)

Active lesion 4 cm or more (plaque)

Situation 1

L major or self-curing lesion (1)
No potentially disfiguring or disabling lesion (face, fingers, toes,...)
No immunocompromise or diabetes
Patient adheres to this option

All criteria above are present?

YES

Specialized facility

Wash lesion, dress wound
Assure follow-up (2)

Peripheral facility

Cure? → NO

YES

Situation 2

<4 lesions for which the patient asks for treatment (3)
No immunocompromise*
Lesion site compatible with method (4)

All criteria above are present?

YES

Cryotherapy + intralesional SB (5) if available
Topical paromomycin (L major)

IL Sb alone or thermotherapy if available
Topical paromomycin (L major)

Cure? → NO

YES

Situation 3

No cardiac or other major diseases (liver, kidney)
No pregnancy (6)

All criteria above are present?

YES

Systemic Sb with appropriate follow-up (7)

Referral to specialized facility or use topical or oral treatment (8)

Cure? → NO

YES

Specialized advice (9)

Situation 1	Situation 2	Situation 3
<ul style="list-style-type: none"> ■ The patient has lesions that are limited in size (papules, nodules or ulcerated nodules all <4 cm); ■ Less than four lesions; ■ Lesions that are not potentially disfiguring or disabling (i.e. not on face, fingers or toes); and ■ Patient is not immunocompromised and does not suffer unbalanced diabetes 	<p>Patients of situation 1 don't improve or have:</p> <ul style="list-style-type: none"> ■ Lesions <4 cm; and ■ Less than four lesions for which he or she asks for treatment; and ■ Lesion(s) located in sites compatible with local treatment; and ■ One or more active lesion due to <i>L. tropica</i>; and ■ Patient is not immunocompromised and does not suffer unbalanced diabetes. 	<p>Patients of situation 1 and 2 don't improve or have:</p> <ul style="list-style-type: none"> ■ Lesion =4 cm (plaque); or ■ Four or more lesions requiring immediate therapy; or ■ Lesion(s) located in sites not compatible with local treatment; or ■ Patient is immunocompromised or suffers unbalanced diabetes.
TREATMENT		
<p>The recommendation is to wash lesions and put a dressing on the lesion without specific anti-leishmanial therapy. It is important to make sure that the patient adheres to this option</p>	<ul style="list-style-type: none"> ■ Topical paromomycin ointment twice daily for 20 days (if <i>L. major</i>) ■ Cryotherapy (liquid nitrogen -195°C) plus intralesional pentavalent antimonials ■ Thermotherapy (one or two applications of localized heat-500 C for 30 seconds) ■ Intralesional antimonials alone: 0.5–5 ml, twice weekly for 3–4 weeks until complete cure 	<ul style="list-style-type: none"> ■ Fluconazole, orally 200–600 mg/day for 4–6 weeks, has been proposed to treat <i>L. major</i> cutaneous leishmaniasis but the efficacy is variable. ■ Itraconazole has been tested in cutaneous leishmaniasis due to <i>L. tropica</i> in adults. ■ Topical paromomycin 1–2 applications per day for 20–28 days, where available, can be used simultaneously on a large number of lesions. ■ Pentavalent antimonials 15–20 mg/kg per day IM/IV for 10–20 days

Patients with pre-existing cardiac, hepatic, renal, pancreatic or haematological morbidity or advanced age are at high risk for toxicity-related mortality and should not be treated with systemic antimonials.

Standard operating procedures for diagnosis and local treatment is given in annexure II

3.8.1 Treatment outcomes in cutaneous leishmaniasis

Treatment outcomes for CL cases have to be assessed twice:

- (i) Between 2 to 4 weeks after initiating the treatment
- (ii) Between 45 and 90 days after initiating treatment, or longer depending on the parasite

Initial assessment: 2-4 weeks after starting the treatment

- **Initial cure (Improvement):** Decrease in the size of the lesion or signs of reepithelization
- **Failure:** Increase in the size of a nodule or a plaque or an ulceration
- **Death with specification of the cause of death :**
 - o Death due to CL
 - o Death due to HIV
 - o Death due to other disease or medical condition (s)
 - o Death due to SAE (iatrogenic)
 - o Death due to non-medical condition (accident)
 - o Death due to unknown cause
- **Unknown:** patient does not present for assessment or the outcome was not recorded

Final outcome: Day 45-90, or longer depending on the parasite

- **Final cure** = Total re-epithelization
- **Failure** = Lack of complete re-epithelization
- **Death with specification of the cause of death :**
 - o Death due to CL
 - o Death due to HIV
 - o Death due to other disease or medical condition (s)
 - o Death due to SAE (iatrogenic)
 - o Death due to non-medical condition (accident)
 - o Death due to unknown cause
- **LTFU/Unknown:** patient does not present for assessment or the outcome was not recorded

3.9 Treatment of Kala-azar in Special Situations

Following conditions are considered as special situations for kala-azar, and the national program recommends treatment of such cases at level III health institution or special referral centers.

- (i) Pregnancy
- (ii) Married women of reproductive age who are not using contraceptives regularly
- (iii) Absolutely breast-feeding mother
- (iv) Children less than two year of age
- (v) Kala-azar and severe anemia (hemoglobin less than 5mg/dl)
- (vi) Kala-azar and TB co-infections
- (vii) Kala-azar with HIV co-infections
- (viii) Kala-azar patient suffering from any other serious disease(s) especially CKD.

The treatment of choice in these situations is L-AmB

3.9.1 Relapse:

Relapse: a patient who experiences recurrence of VL symptoms with parasitological confirmation at any time point after initial cure. VL relapses are usually observed within 6 months of completion therapy.

The treatment of choice is higher doses of L-AmB or Amphotericin B deoxycholate

Rescue treatment in case of non-response and relapse

Non-responder or relapses are recommended for liposomal amphotericin B at higher cumulative doses up to 30mg/kg

OR

Conventional Amphotericin B deoxycholate

OR

Combination regime of two drugs.

Table 13: **Recommended doses of L-AmB according to body weight**

Drug category	Day 1	Day 2	Day 3	Duration
Liposomal Amphotericin B	5mg/Kg body weight	5mg/Kg body weight	5mg/Kg body weight	3 days

3.9.2 Leishmania with HIV co-infection

Visceral leishmaniasis is an AIDS-defining condition and a valid entry point for starting antiretroviral treatment, irrespective of CD4+ count. The baseline CD4+ count is lower in Leishmania–HIV co-infected patients, as visceral leishmaniasis itself causes a reduction in CD4+ cells. The impact of antiretroviral treatment on visceral leishmaniasis in co-infected patients observed in the Mediterranean area can be summarized as: a reduction of incidence by 50–65%, higher survival rates, a reduction in relapse rate and possible immune reconstitution inflammatory syndrome.

HIV and Leishmania infection reinforce each other. HIV patients are more likely to develop visceral leishmaniasis (due to reactivation of a dormant infection or clinical manifestation after primary infection). Patients characteristically have high disseminated parasite loads. Visceral leishmaniasis negatively affects the response to antiretroviral treatment and is difficult to cure in coinfecting patients, especially those with CD4+ counts < 200 cells/ mm³, who typically relapse.

The prognosis of coinfecting patients is characterized by a high mortality rate during the first episode, increased antileishmanial drug toxicity (predominantly with antimonials), poor long-term clinical response, parasitological cure and a high relapse rate over a lifetime. The risk factors for relapse are: no antiretroviral treatment, low CD4+ cell count, previous visceral leishmaniasis episode, failure to achieve clinical or parasitological cure during the first episode and no secondary prophylaxis.

- Visceral leishmaniasis in a HIV patient is an AIDS defining illness
- All VL patients should be offered Provider Initiated Testing and Counselling for HIV screening
- All HIV patients should be clinically assessed for signs and symptoms of visceral leishmaniasis
- In VL-HIV con-infected patients, ART should be started without delay

3.9.3 Few issues are important with HIV-co-infections:

A. Higher dose regimen

L-AmB at a dose of 5mg/kg/day (D1, 2, 3, 5, 9, 13, 17, 21) total up to 40mg/kg body weight.

B. Relapse in HIV-VL co-infected patients:

Relapse is inevitable with VL-HIV co-infection, so it has recommended starting ART as early as possible in such scenario.

Relapse has to be treated with combination therapy- L-AmB +Paromomycin

- L-AmB at a dose of 5mg/kg/day; total 30-40mg/kg/ on (D1,2,3,5,9,13,17,21)
- Paromomycin at a dose of 15mg/kg/day for 21 days). Secondary prophylaxis can be initiated if logistic supply of the L-AMB is available.

C. Immune Reconstitution Inflammatory Syndrome (IRIS)

Usually it is recommended to have a gap of 2 weeks between VL treatment and ART if CD4 count is very low due to IRIS. However, in a tertiary care centers both treatments can be initiated simultaneously, and IRIS can be managed if it occurred. Symptomatic therapy and/or steroid are recommended in mild to moderate IRIS. In life threatening IRIS it is better to hold ART. While prescribing ART concern should be made on ART and VL drug interactions.

D. Secondary prophylaxis:

All HIV-VL co-infection are strongly recommended for secondary prophylaxis with L-AmB at a dose of 5mg/kg/month.

E. Other conditions:

Non-Communicable Disease, L-AmB has demonstrated safe in kala-azar with Diabetes mellitus, Hypertension, and stable heart disease patients. L-AmB is also safe for elevated liver enzymes.

Note:

- All level II health institutions are not equipped to diagnose HIV. So, every kala-azar case with high risk behavior for HIV/STDs should be referred to a health facility where HIV testing and counseling services are available, and all HIV positive cases should be referred to health facilities where ART services are available. It is important to note that rK39 test has lower sensitivity in HIV positive or AIDS cases; and parasitological diagnosis is required to confirm kala-azar infection among all rK39 negative cases.
- The treatment and care of KA patients with HIV or TB co-infection is advised in the special referral centers.

3.10 Kala-azar focused Pharmacovigilance

Pharmacovigilance (PV) is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems. The core purpose of pharmacovigilance is to enhance patient care, patient safety and generate the evidence-based information on safety of medicines; and to support control programme by providing reliable, balanced information for the effective assessment of the risk-benefit profile of drugs.

The drugs recommended for the treatment of kala-azar or PKDL has some side effects. These may be looked for in the form of signs and symptoms. Laboratory tests like hematological tests, liver function tests, kidney function tests, electrolytes and ECG are recommended to monitor the side effects (wherever available). Such laboratory tests can help recognize the occurrence of the side effects at early stage. The program should initiate clinical and laboratory monitoring of side effects and this information can be complemented by regular reporting of major and minor side effects by the local health institution.

Definitions

Adverse event: any untoward medical occurrence that may occur during treatment with a pharmaceutical product that is not necessarily causally associated with the treatment⁷.

Adverse drug reaction (ADR): a response to a drug that is noxious and unintended and that occurs at doses normally used in humans for prophylaxis, diagnosis or therapy of disease or for modifying physiological function

Serious adverse event or reaction: any untoward medical occurrence that, at any dose results in following:

- Results in death,
- Is life threatening,
- Requires hospitalization or prolongation of hospitalization,
- Results in persistent of significant disability or incapacity or
- Results in congenital abnormality or birth defect^{8,9}

The term “severe” is not synonymous with serious. Seriousness of an event is based on patient/event outcome or action criteria which serves as guide for defining regulatory reporting obligations. SAEs should be recorded in the patient form and the case register and reported.

Pharmacovigilance for kala-azar treatment

Kala-azar elimination programme has introduced kala-azar focused pharmacovigilance programme in Nepal with the joint effort of Epidemiology & Disease Control Division, Department of Health Services, Ministry of Health & Population and B. P. Koirala Institute of Health Sciences, Dharan, Nepal with support from PATH India have initiated VL focused pharmacovigilance programme in Nepal.

Process of reporting adverse events for kala-azar drugs

Detection and documentation of adverse drug reaction: At PV monitoring sites nurses, paramedics and doctors who play the major role in detection and documentation of possible ADRs because these are the persons who notice the potential ADRs and fill an adverse event reporting form. These person hands over the completed ADR reporting form to the nodal contact person of the respective monitoring sites. The treating physician should sign on the form at the end, before sending to EDCD nodal centre. The serious adverse event reporting form found in *Annex VII*.

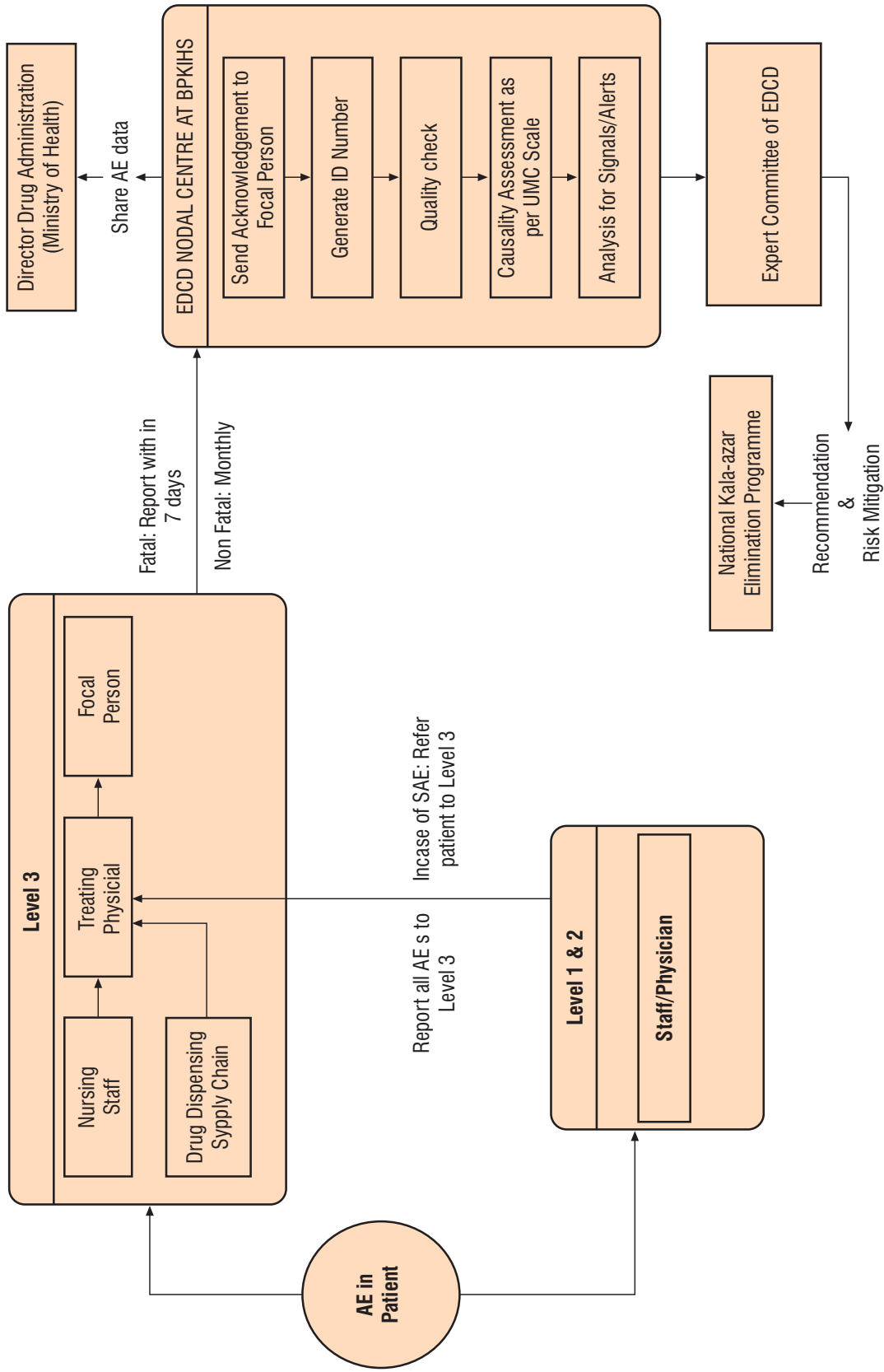
⁷The importance of pharmacovigilance – safety monitoring of medicinal products. Geneva: World Health Organization; 2002 (<http://apps.who.int/medicinedocs/en/d/Js4893e/>)

⁸Assuring safety of preventive chemotherapy interventions for the control of neglected tropical diseases. Practical advice for national programme managers on the prevention, detection and management of serious adverse events. Geneva: World Health Organization; 2011 (http://apps.who.int/iris/bitstream/10665/44683/1/9789241502191_eng.pdf)

⁹SAE handbook (A handbook for managing adverse events following mass drug administration and serious adverse events). Washington DC: Envision; 2014.

The process of reporting ADRs is given below and all the forms are given at the annexures.

Flow Chart for Operational plan for Pharmacovigilance Activities for Visceral Leishmaniasis



4.1 Integrated vector management

Integrated Vector Management (IVM) is “a rationale decision-making process for the optimal use of resources for vector control”. Through evidence-based decision making, IVM rationalizes the use of human and financial resources and organizational structures for the control of vector-borne diseases and emphasizes the involvement of communities to ensure sustainability. It encourages multi-disease control approaches, and integration with other disease control measures for synergistic effect.

There are 5 building blocks of an IVM framework¹⁰ :

1. Advocacy, social mobilization, regulatory control
2. Collaboration within the health sector and with other sectors
3. Integration of non-chemical and chemical vector control methods, and integration with other disease control measures.
4. Evidence-based decision making guided by operational research and entomological and epidemiological surveillance and evaluation.
5. Development of adequate human resources, training to local level to promote capacity building and manage IVM programmes

Key characteristics of IVM include the following:

1. Utilization of methods based on an evidence base (in which there has been recorded impact against local vector populations), disease transmission, and morbidity.
2. Use of a range of interventions, often used in combination for their synergistic effect.
3. Collaboration within the health sector and with other public and private sectors that work on cross-cutting issues associated with disease vectors.
4. Involvement of local communities and other stakeholders.
5. A public health regulatory and legislative frame work.

Prevention of kala-azar through vector control is one of the major strategies in the elimination of the disease. Country guidelines and standard operating procedures for the prevention of kala-azar through IVM strategies require standardized application of the right mix of interventions based on local vector species and vector bionomics. Vector control options for the elimination of kala-azar in Nepal comprises of indoor residual spraying (IRS), personal protective measures, and environmental modification/manipulation techniques.

¹⁰http://www.who.int/neglected_diseases/vector_ecology/ivm_concept/en/

4.1.1 Indoor Residual Spraying (IRS)

4.1.1.1 Objectives of IRS:

Indoor residual spray is the application of a long-lasting insecticide with residual efficacy to potential vector resting surfaces such as internal walls and structures (including domestic animal shelters) where such vector might come into contact with the insecticide.

IRS is a powerful intervention to rapidly reduce adult vector density and longevity and therefore, reduce transmission of infection (parasites).

4.1.1.2 How IRS works:

When sandfly enters into human habitations or animal shelters in search of blood meal, they rest on the walls and other interior surfaces before and/or after feeding on the inhabitants. When a sandfly comes into contact with a sprayed surface, it adsorbs lethal dose of insecticide and thereby reducing its lifespan- this results in a progressive decline in vector density and longevity, especially among older females, reduces overall vectorial capacity and contributes to a reduction in transmission.

IRS is most effective against indoor feeding (endophagic) and indoor resting (endophillic) vectors which applies well to sandflies. The greatest impact of IRS intervention takes place when after feeding vector is more likely to rest on a sprayed surface and picks up a lethal dose of insecticide. After blood meal vector becomes heavier than its weight and prefers to rest on lower surfaces. This means that for IRS to be effective there must be high coverage of all structures in order to obtain the mass effect on the vector population.

High coverage means over 85%, of the structures in a targeted area has been sprayed. If vector doesn't die even after sitting in an insecticide treated/sprayed surfaces for 30 minutes, this could be an indication of resistance.

In order to maximize the impact of the elimination programme, IRS and active case surveillance should be synchronized.

The success of IRS operations depends on effective planning, training, and implementation of the plan especially at the district level to maximize household coverage in targeted areas to achieve a “mass-effect” on local vector populations. The plans for IRS operations should be developed in advance so that there is timely delivery of the programme during the “window of opportunity” (usually just prior to the on-set of the monsoon season when disease transmission is predominantly seasonal). The plan should include the following key stages:

4.1.1.3 Identification of areas for IRS

Targeted areas to be sprayed should be selected according to local vector behavior and spatial distribution. The program should aim IRS coverage on the programmes capacity to achieve complete

and uniform coverage. If there are resource/logistical constraints, it is preferable to limit the size of the operation in preference to achieve maximized coverage, rather than to have patchy household coverage over a larger area in which impact may not be sufficient to reduce infective vectors and thus reduce disease transmission. The number of houses to be sprayed in the villages should be identified according to the VDC or Municipality selected for IRS. The entire village should be covered if selected for IRS. The areas to be sprayed can be identified best by mapping (of the areas) based on the following criteria:

- All villages that reported a case of kala-azar during the last three years.
- All villages that report a case of kala-azar during the current year.
- Villages that have cases on active surveillance during the current year.

4.1.1.4 Timing of IRS

Timing of IRS is critical; it should be decided based on vector behavior, density, and spatial distribution from longitudinal vector surveillance and the disease transmission season. Two rounds of IRS should be considered in a year. The objective of the first round should be to obtain maximized coverage in targeted areas. When the WHOPES approved insecticide is used, the residual effect of IRS should last for a period of approximately 3 months. The second round of spraying should not be considered a “mop-up” round but is to be done to sustain the effects of the first round and maintain a “mass-effect” against local vectors, and thus curtail the transmission of kala-azar.

The first round of spraying should be completed when the vector population is building up but prior to when the transmission season starts. A seasonal density curve should be prepared by vector surveillance in order to decide the optimum timing for spraying. As an illustrative example, the build-up of the vector occurs in the month of March and peak densities can be found between July to October. The maximum effect of insecticide lasts for a period of about 10-12 weeks and the transmission season lasts from June until October. Therefore, the first round should be undertaken in the months of May-June. The second round of spraying should commence approximately 3 months after the first round but may have to be scheduled according to meteorological forecasting during the height of the monsoon season. In the case of targeted areas which are endemic for malaria, scheduling of IRS delivery may have to also take into consideration the seasonal transmission of malaria, so as to combine efforts and resources for each round of spraying to target both diseases.

4.1.1.5 Insecticide selection and quantity estimation for IRS

The choice of insecticide for IRS is based on several considerations that include national policy, formulations that have WHOPES approval, cost of insecticide and efficacy of the insecticide.

Insecticide will be selected on the basis of following criteria:

- Should have a long-lasting effect on a given surface to prevent necessity of repeated application
- Highly toxic to the target insect
- Least repellency to the insect

- Safe to humans and domestic animals
- Acceptable to the community
- Stable during storage and transportation
- High grade suspension so that it mixes well with water and does not clog equipments
- Cost effective

Efficacy of insecticide depends upon following factors:

- Resting behavior of vector (endophilic, endophagic)
- Vector susceptibility to insecticide
- Suitability of wall of surfaces for spraying
 - ▶ Mud surfaces absorb spray (some walls have high pH which break down the active ingredient of insecticide)
 - ▶ Best surfaces are which are non-absorbent
- Suitability of insecticides
- Cooperation of community

Based on the above criteria in combination with national policy and legislation, insecticides belonging to the pyrethroid group will be selected for use in the IRS programme. Large-scale use of pyrethroids both within the public health and agricultural sector may increase the selection pressure for “knock down (kdr)” resistance mechanisms to evolve in local vector populations, and so routine insecticide susceptibility testing should be completed on operational insecticides as well as those selected as future alternatives.

Table 14: Guideline for using synthetic pyrethroids for indoor residual spraying in Nepal

Insecticide	Recommended dosage (gm/m ²)	Required quantity	Effectiveness (months)
Alphacypermethrin 5% WP	0.03	100 gm /8 liters	2-3
Cyfluthrin	0.025		3-5
Cypermethrin	0.5		4 or more
Deltamethrin 5% WP	0.05	160 gm /8 liters	2-3 or more
Lambda cyhalothrin 10 % WP	0.05	50 gm /8 liters	2-3
Permethrin	0.5		2-3

(Note: Insecticidal action is contact)

Table 15: **WHO recommended insecticides for indoor residual spraying against malaria vectors**

Insecticide compounds and formulations ¹	Class group ²	Dosages (g.a.i. m ²)	Mode of action	Duration of effective action (months)
<i>DDT WP</i>	OC	1-2	contact	>6
<i>Malathion WP</i>	OP	2	contact	2-3
<i>Fenitrothion WP</i>	OP	2	contact and airborne	3-6
<i>Pirimiphos-methyl WP, EC</i>	OP	1-2	contact and airborne	2-3
<i>Pirimiphos-methyl CS</i>	OP	1	contact and airborne	4-6
<i>Bendiocarb WP, WP-SB</i>	C	0.1-0.4	contact and airborne	2-6
<i>Propoxur WP</i>	C	1-2	contact and airborne	3-6
<i>Alpha-cypermethrin WP, SC</i>	PY	0.02-0.03	contact	4-6
<i>Alpha-cypermethrin WG-SB</i>	PY	0.02-0.03	contact	up to 4
<i>Bifenthrin WP</i>	PY	0.025-0.05	contact	3-6
<i>Cyfluthrin WP</i>	PY	0.02-0.05	contact	3-6
<i>Deltamethrin SC-PE</i>	PY	0.02-0.025	contact	6
<i>Deltamethrin WP, WG, WG-SB</i>	PY	0.02-0.025	contact	3-6
<i>Etofenprox WP</i>	PY	0.1-0.3	contact	3-6
<i>Lambda-cyhalothrin WP, CS</i>	PY	0.02-0.03	contact	3-6
<i>Clothianidin WG</i>	NN	0.3	contact	3-8

Chlorfenapyr 240 SC: The current assessments of Chlorfenapyr SC (class group: pyrrole) are available in the report of the 16th WHOPES Working Group meeting, 22–30 July 2013 and the report of the 17th WHOPES Working Group meeting, 15–19 September 2014 (both reports are available on the WHO website at: http://www.who.int/neglected_diseases/resources/WHOPES/en/).

Note: WHO recommendations on the use of pesticides in public health are valid ONLY if linked to WHO specifications for their quality control. WHO specifications for public health pesticides are available at the WHO website at: <http://www.who.int/pqvector-control/en/>.

¹ CS = capsule suspension; EC = emulsifiable concentrate; SC = suspension concentrate; SC-PE = polymer enhanced suspension concentrate; WG = water dispersible granules; WG-SB = water dispersible granules in sealed water soluble bags; WP = wettable powder; WP-SB = wettable powder in sealed water soluble bags.

² OC = organochlorines; OP = organophosphates; C = carbamates; PY = pyrethroids; NN = neonicotinoids.

4.1.1.6 Equipment requirements for IRS

The equipment requirements for IRS are determined on the basis of the national strategy, timelines for implementation, human resource capacity, and areas to be targeted. Hand operated compression pumps can be considered since the use of this equipment requires one operator and spraying of better quality can be achieved.

Each spray team would need the following equipment:

- Hand compression pumps:4
- Spray nozzle tips for spray pumps:4
- Control flow valves (red) emitting 1.5 bar pressure
- Bucket 8 liters:1
- Asbestos thread:3meters
- Measuring mug:1
- Straining cloth:1meter
- Pump washers:4
- Plastic sheet 3x3meters:1
- Register for records:1
- Writing material to identify households covered by IRS
- Tools for minor repairs
- Personal protection equipment for each member of the team

4.1.1.7 Dose calculation of insecticides

The dosage of insecticide application for prevention of kala-azar is the same as for Malaria. The dose varies with the type of insecticide selected for IRS as shown below. For example, if Alphacypermethrin 5% WP is used 100 gm of Alphacypermethrin 5% when dissolved in 8 liters of solvent, the dose will be 0.03gm/m². When the spraying is done for kala-azar, the requirement is only half of that for malaria since the walls are to be sprayed up to a height of 6 feet only and the cattle sheds are to be covered. The average area to be sprayed per house is about 75 square meters. In areas where malaria is common, the calculation of insecticide should be done for malaria which would also cover kala-azar. The requirements can be calculated based on the recommendations summarized in the table above. Based on previous experience of IRS programming for malaria prevention, an 8-liter suspension of the insecticide can conveniently be prepared and carried from house to house.

Calculation of amount of insecticide needed for one round of spraying

The total amount of insecticide (T) needed depends on

N: the number of houses to be sprayed

S: the average sprayable surface per house (m²)

Y: the target dosage of insecticide (g/m²)

C: the concentration of active ingredient in the formulation (%)

T: $N \times S \times Y / C$

For example: if a village has 100 houses. The average surface that can be sprayed per house is 75m². The recommended dose of Alphacypermethrin 0.03gm/m². The Alphacypermethrin is available as a 5% water dispersible powder.

Amount of insecticide needed for one round of spraying would be

$$T = \frac{100 \times 75 \times 0.03}{5} \times 100 = 4.5 \text{ kg of alphacypermethrin (5\% water dispersible powder)}$$

Plus 10% buffer should be added to the total quantities.

4.1.1.8 Human resource requirements for IRS

The operation of IRS should be completed in a maximum of 45-60 days but may vary depending on targeted areas in any given year and the human resources and equipment that may be available. Prolonging the duration of the first round of IRS would make operations difficult since there would be problems in timely undertaking of the second round of spraying in a timely manner. Usually labor on a daily wage is employed to undertake the job which includes time for training. The spray teams should be supervised adequately to ensure the quality of household coverage of insecticide, i.e. correct dose, uniformity and completeness of wall spraying, and continued maintenance of equipment.

The supervisor of the spray teams should be a regular staff member of the spray team. The average number of persons for “spraying team” should comprise of 4 field workers and one supervisor (experienced field worker who can provide spot checks and provide continual technical assistance). Four such teams form a “spraying group”. The group is headed by group leader, who must be a government employee and a health worker. Additionally, an “insecticide distributor” (I.D) supports the group to prepare and distribute insecticide. The number of houses to be sprayed is determined by the terrain in which the team is operating.

District planning is needed to identify the number of houses to be sprayed in target areas based on the criteria outlined previously on disease transmission risk. The number of houses to be covered in a village would vary according to density of population in a particular target VDC or municipality. The population to be covered should be divided by 5 since each household has an average of about 5 members. The district plan should include a plan for IRS operations based on the criteria identified above. The plan should include identification of dates when the selected villages are proposed to be sprayed. Each supervisor should then develop a plan for each spray team. This plan should be used to calculate and forecast insecticide quantities, which should be supplied and safely stored at least one week before spraying commences.

The number of spray teams that would be required in each district can then be ascertained by calculating the number of households to be targeted and how many can be sprayed per day by a given person and therefore how many sprayers would be then needed to provide optimal coverage in a given period of time. Each spray team should be adjoined by a trained health worker either from the local health institution or from the district health office to provide national representation and support. This individual is different from the spray team supervisor who monitors technical aspects with regards to spraying.

4.1.1.9 Training of the spraying team

Training of IRS team is essential for quality of IRS within a geographic area. The team comprises of the health workers who are responsible for supervising the overall IRS operation within a given target area and training of the spray teams; and training of the spray team supervisor who monitors coverage rates and day to day technical issues and machine maintenance. The district focal point for kala-azar and/or malaria is responsible for organizing the training.

The training agenda for spraying team should include the following areas:

- Informing target communities and obtaining cooperation from them
- Preparation of insecticide suspensions/solutions
- Correct use of IRS equipment
- Importance of uniform and complete spraying
- Regulation off low from nozzle tip
- Regulation of speed of application, including movements of the lance and spray persons
- Safe storage of the insecticide
- Safety precautions and personal protection measures during the spraying operation
- Care and maintenance of IRS equipment
- Safe disposal of insecticide and waste
- Preparation of daily consumption reports

Additionally, supervisors should be trained in:

- Enumeration of houses
- Marking of houses
- Mapping
- Cleaning procedures
- Raising community awareness/provision of advance information
- Record keeping and reporting
- Safety and precautionary measures.

Practical sessions are required during the training which focuses on the correct use of spray equipment and the steps required for preparation of the insecticide suspension, effective dispersal and coverage, and safe disposal of any unused insecticide. In addition, during field-based training of the spray team, allowances should be made to include active involvement of the community to ensure household compliance during the spraying campaign. The training of the spray team supervisors should also include practical aspects such as equipment troubleshooting, maintenance checklists, safety precautions and first-aid assistance.

Such training should be completed at least one week before the first round of spraying operations in targeted areas. However, a long interval between the spray operations and the training is not beneficial, as trained personnel may not clearly remember all aspects of the training modules. Training should be an integral part of the district work plan for the kala-azar elimination program. The district health office should prepare a report on training of the supervisors and the spraying teams and send it to regional and national departments.

4.1.1.10 Transportation, storage, safe handling of the insecticides

The containers in which the insecticide is transported should be well sealed and properly labeled. The transport of insecticide should not be done along with transportation of food items. In consultation with the community, the insecticide should be stored in a safe place where the chances of contact with humans/animals are minimal. The insecticide should be properly labeled with the name of the insecticide, the name of the manufacturer, date of manufacture, the date of expiry, and appropriate visible labeling that hazardous chemicals are contained within. There should be written guidelines with each container/sac on what to do in case there is exposure to the insecticide. The insecticide should be stored in a well-ventilated room, not exposed directly to sunlight, and away from the walls. The place where the insecticide is stored should be away from the reach of children and animals. It is important to be sure that no food items are stored in the vicinity of the place where the insecticide is stored. During the storage process insecticides should be moved carefully so that there is no spillage. The stocks that arrive first are to be used first and make sure that the expiry date has not been exceeded prior to its use.

Stock registers should be carefully maintained to keep a track of insecticide dispatch to targeted areas. No unauthorized person should have access to the insecticides. The room where the insecticide is stored should be kept locked and a large label indicating that “hazardous materials” are being stored should be highly visible. Eating, drinking and smoking is not permitted in the place where the insecticide is stored, nor such habits are allowed during the spraying operation.

4.1.1.11 Informing and involving the community

The spray team supervisors should inform the community leaders and key persons in targeted villages about the plans and time lines for the spraying operation, at least a week before the spraying is done. The spray team members should re-visit targeted areas to remind them about spraying activities at least one day before the operation is to commence. During the first visit to targeted areas the following issues/tasks should be discussed with the involvement of community leaders and key persons in the community:

- Distribute brochures or leaflets (in local language) explaining the purpose of the spraying and including the common dos and don'ts (Annex10) before and during the spraying operation. If possible, simple illustrations should be included in the sensitization materials to facilitate easy understanding amongst those who may not be literate. This sub-activity forms part of a behavior change communication (BCC) strategy.
- Explain to the community leaders/key persons that it is their responsibility to share the contents of the brochure or leaflet to the people in the community.

- Explain about what is proposed to be done, why this is an effective way of preventing kala-azar and contributes to the control of malaria and that why community compliance is key to the success of the programme.
- Inform the community leader of the propose and date for spraying in their village.
- Discuss what specific role the community leaders and key persons can play to ensure that the spraying is complete and thorough. This would require that no household is missed and the spraying in each household and animal shelter must be complete.
- Explain that if surfaces are not sprayed adequately the sand fly may rest on unsprayed surfaces and the desired effect of spraying will not be obtained.
- Make community leaders aware that the insecticide can harm people if contaminated food items are ingested. Therefore, it is very important that food items must not be exposed to the insecticides.
- Explain that each house hold must not mud plaster the walls and other sprayed surfaces for 6-10 weeks after the completion of spraying. Therefore, it is important that any building maintenance should be conducted prior to spraying.
- Inform the community people one day prior to the spraying operation through loudspeaker micro phone messaging.

4.1.1.12 Supervision and monitoring of IRS activities

Supervision is an essential and integral part of IRS to ensure its efficacy and safety. This should be thorough to produce programme impact and ensure that there is no compromise to safety. There should be a written plan for supervision and supervisory checklists are to be developed and used. Supervision will be effective if problems are identified and they are solved by the supervisors as soon as they are detected. Any unsolved problems should be referred to district authorities for resolution. All supervisory reports should be sent to the district to facilitate any follow up actions. The supervisory reports should be kept safely in the district and where possible an electronic copy be made.

Daily Summary Report

		Health Institution (Name & address):						VDC/Municipality:		
		Date:								
Ward No	Date	Village	Target			Sprayed			Remarks	
			Houses	Rooms	Animal shelters	Houses	Rooms	Locked/Refused		Animal shelters

Daily consumption record of insecticide

Spray operations on (day/month/year):		Ward No:	Village:	Number of buckets (8 liters)	
VDC/Municipality:				Prepared	Consumed
Insecticide issued (Qty: WP)	Balance (insecticide available from previous day)				

The following points should be taken into consideration in supervision and monitoring of IRS activities:

- Check the availability of plan with the spray team.
- Review the plan and monitor activities to ensure that the plan is being followed.
- Ensure that all members of the spray team are present and are conducting activities to agreed specifications under the time line for employment.
- Check that the spraying is being done correctly according to standard operating procedures.
- Examine the spray equipment daily to ensure that it is in good working condition and is being properly maintained.
- Ensure that spare parts for maintenance are in stock and deployed to the spray teams in advance so as not to affect daily coverage targets.
- Visit the households with the spray team if there is a household refusal or reluctance for spraying.
- Check the records of the spray teams.
- Discuss about the plans for “mopping up” activities to cover any households in which initially there was refusal, or the house was vacant.
- Assess the consumption of insecticides and make arrangements for additional supplies if required.
- Prepare a daily summary report and send the consolidate report to the DPHO once a week.
- Review the spraying schedule for the following week.

The supervisor should undertake the following activities whilst on a supervision mission:

- *Visit randomly selected households and ask whether the house was sprayed or not.*
- *If the house was sprayed, then check for grey white deposits as evidence for spraying and check on different parts of different walls to ensure there is overall coverage.*
- *Check whether the deposits are uniform or not. Uniform deposits indicate that the spraying was satisfactory*
- *Check to see if any portions of the dwelling or the cattle shed were skipped.*
- *Check whether the walls have been plastered with mud. If the walls have been plastered then determine when this was done to determine the time interval between the IRS and the plastering.*
- *Visit the households that were not covered and find out the reasons for non-coverage. Try to express the importance for household members to get their houses sprayed as a part of special “mop-up” drive.*
- *Prepare a written report along with recommendations and share with the spray teams to ensure that any mistakes are corrected as soon as possible.*

Good and poor IRS practices

Bad practice is not uncommon during spray activities. The following highlight the most common issues and what should be done:

- External walls should not be sprayed;
- Spray solution should not be carried in damaged buckets;
- Hanging objects/pictures/photos etc. should be removed and stored elsewhere before walls are sprayed;
- Leaking nozzle tips and lances waste large amounts of insecticide and should be replaced;
- Food grains should be covered with plastic sheets before spraying;
- Spray persons should mix formulations well away from any source of drinking water;
- Ideally, a van with a banner should visit villages to provide advance intimation of the next day's spraying;
- Supervisors should visit spray squads to ensure work is carried out properly and efficiently.
- Use of personal protective equipment by all the spray workers

4.1.1.13 Proper disposal of insecticides and containers after use

The unused insecticides or contaminated residues from washed equipment and protective clothing should be disposed off safely, to ensure that it does not mix with water or food. Prepare only the required quantity of insecticide suspension, which is likely to be consumed in one day and ensure that there is no carry over of any unused insecticide the next day. Never put any leftover insecticide into a river, pond, well or source of drinking water where it can persist in the ecological chain causing pollution and/or poisoning. Any spilled insecticide in solid or liquid form, and residues from washed equipment and protective clothing should all be emptied in to a pit which is dug away from the source of drinking water and covered with mud. Empty sacs or containers in which the insecticide was stored should not be used for any other purpose. These must be buried safely away from the drinking water source. As a rule, all equipment should be washed at the end of the day of operation. All empty containers/sacs should be returned to the supervisor. The supervisor must check carefully that all empty sacs/containers have been received.

4.1.1.14 Personal Protective Measures

The use of insecticide treated bed nets (ITNs) or long-lasting insecticide treated bed nets (LLINs) can be an effective, relatively cheap, and sustainable method of vector control. The synthetic pyrethroids used for the treatment of bed nets contain chemicals of low to moderate mammalian toxicity, low volatility and high insecticidal activity. Untreated, locally available bed nets are also associated with a decrease in kala-azar risk and can offer a degree of barrier protection. The protective efficacy of bed nets has been observed in both Bangladesh and Nepal and intervention trials of ITNs in Afghanistan demonstrated strong protective efficacy against leishmaniasis transmission. The efficacy of bed nets is increased when there is a demand by the community as use will be high, for this often a complimentary

BCC campaign needs to be conducted prior to net distribution. It is often argued that the small size of sand flies means that the mesh size used in standard bed nets for malaria control would allow sand flies to still obtain a blood meal. However, field experience indicates that even with larger mesh size, insecticide treated nets can cause a reduction in sand fly populations, or the insecticide incorporated into the netting can serve as a deterrent.

Individual protective measures in outdoor areas include application of repellents, such as diethyl toluamide (DEET) or natural based chemicals that are known to repel vectors, to the skin or clothing to reduce man-vector contact. Portable mosquito coils could be effective but have not been evaluated for the use against sandflies. Indoor protection from sand-fly bites can be obtained by the use of fine-mesh screens on windows and doors, insecticide treated curtains, mosquito coils, electrically heated fumigation mats and fumigant canisters.

4.1.2 Environmental Management

The following environmental measures can be considered as a part of the integrated vector management strategy for the prevention of kala-azar in Nepal:

4.1.2.1 Household modification and relocation

Kala-azar affects primarily poverty-stricken groups in rural communities, who are either marginal farmers or landless laborers. Their houses usually consist of mud huts with thatched roofs which invariably do not meet the requirements of low income housing and pre-dispose residents to pest infestation and increased vector-contact which in turn contributes to higher rates of illness in such groups. Such poor dwellings are characterized by the absence of secure foundations, imposing limits to the height of walls that can be supported resulting in low houses with inadequate ventilation and dark interiors. Rainfall damage concentrated at the base of the walls opens up crevices and cracks and uneven earth floors provide refuge for insect larvae among the debris in the cracks.

Sandflies like all arthropods require shade, and an undisturbed resting site within the houses for part of their lives. They generally rest during this in active phase in the dark crevices near the floor, walls or even eaves of low roof's and also in the moist corners of such houses. Such moist corners with loose soil are also suitable breeding sites for the sand fly vector. Because of the propensity of resting and breeding in particular household, where human blood meals are readily available; where applicable community-based interventions should focus on simple structural modifications that prevent entry of host-locating sand flies. In more extreme cases re-housing to suitable buildings with adequate space and ventilation, and which are not liable to cracking is an important, additional input in to the kala-azar elimination program.

4.1.2.2 Environmental manipulation in peri domestic areas

Cleanliness of households and cattle sheds is a measure potentially useful but has never been scientifically evaluated. This approach needs to be pilot tested in a sufficient sample and range of villages to measure impact on sandflies in Nepal.

5.1 Disease Surveillance

Communicable disease surveillance is the continuous, systematic collection, analysis and interpretation of disease-related data needed for the planning, implementation, and evaluation of disease control and elimination. Recording, regular reporting and exchange of information should be done upwards, downwards and laterally in the system to develop a common understanding of the problems.

It comprises the people, procedures, tools and structures required to generate information for planning and targeting interventions and monitoring and evaluating leishmaniasis programme:

- The **people** include decision-makers both inside and outside the health service who use data from surveillance systems, the health staff who gather and/or use the data and the patients and communities whose details are registered.
- The **procedures** include case definitions, reporting frequency, pathways of information flow, data quality checks, incentive schemes, data analysis, mechanisms for reviewing performance, methods for and frequency of disseminating results, using data for making decisions about appropriate responses, supervision and planning.
- The **tools** include report forms, registers, patient cards, dashboards, computer hardware and software, documentation and training materials.
- The **structures** include the ways in which staff are organized to manage, develop and use the system.

I. Objectives

A. Objectives of kala-azar and PKDL surveillance

Kala-azar is targeted for « elimination as a public health problem » in Nepal, which is defined as an incidence below 1 KA case per 10,000 population, at district level.

The main objectives of kala-azar surveillance, in this elimination context, are as follows:

- To monitor incidence trends over time and progress towards elimination
- To determine the distribution and potential extension of KA
- To identify and treat PKDL cases in order to decrease leishmaniasis reservoir
- To detect outbreaks in order to respond in a timely manner
- To evaluate elimination activities
- To identify and prioritize at-risk population
- To monitor vectors distribution and density in country (entomological surveillance): see dedicated section

B. Objectives of cutaneous leishmaniasis surveillance

Cutaneous leishmaniasis cases have been reported only very recently in Nepal, with no travel history. It is therefore not yet a public health issue, but it should be closely monitored in order to:

- To estimate CL and MCL burden
- To monitor incidence trends over time
- To determine the distribution and potential extension of CL
- To inform appropriate and effective control activities
- To identify and prioritize population at-risk
- To evaluate control measures
- To monitor vectors distribution and density in country (entomological surveillance): see Leishmaniasis Vector Guideline

II. Case definitions

All health facilities, either in endemic and non-endemic areas, should be trained on case definitions in order to increase kala-azar awareness among health workers in Nepal.

Kala-azar Case definition

There is no definition for a suspected case of VL, given the low specificity of the symptoms.

Probable VL case: A person living in or having travelled to VL endemic areas showing clinical signs and symptoms of VL (mainly irregular fever lasting more than two weeks and splenomegaly and/or weight loss).

Confirmed VL case:

- **Laboratory-confirmed VL case:** A probable VL case with laboratory confirmation, either serological (RDT, DAT, ELISA, IFAT) and/or parasitological (smear, culture) and/or positive by PCR or related techniques.

OR

- **Clinically-confirmed VL case:** A probable VL case that has not been confirmed by any laboratory test (i.e. test(s) not done or negative) but is assessed by a clinician to be a confirmed VL case based on clinical grounds.

All confirmed VL cases, either clinically or laboratory; should be treated according to the protocol and reported.

Post-Kala azar dermal leishmaniasis (PKDL)

Probable PKDL case: A patient living in or having travelled to visceral leishmaniasis endemic areas presenting with a typically symmetrical multiple hypopigmented macules, papules, plaques, or nodules without loss of sensation.

PKDL can occur in patients with previous or concomitant VL. In some cases it occurs without the past history of VL. Serological test such as rK39 rapid diagnostic test positivity acts as a strong evidence when other diseases (for example, leprosy) are considered in the differential diagnosis, or if a history of VL is uncertain.

Confirmed PKDL: A probable PKDL case with *Leishmania* infection confirmed parasitologically by PCR or a slit-skin smear or biopsy.

Cutaneous leishmaniasis (CL)

Probable CL case: a person living in or having travelled to endemic areas showing typical CL skin lesions (macule, plaque, nodule, ulcer)

Confirmed CL case:

- **Laboratory-confirmed CL case:** A probable CL case with parasitological confirmation, by positive smear, culture or PCR.
- OR**
- **Clinically-confirmed CL case:** A probable CL case that has not been confirmed by any laboratory test (i.e. test(s) not done or negative), but is assessed by a clinician to be a confirmed CL case based on clinical grounds

Mucosal/mucocutaneous leishmaniasis (ML/MCL)

Probable CL case: a person living in or having travelled to endemic areas showing typical CL skin lesions (macule, plaque, nodule, ulcer)

Confirmed CL case:

- **Laboratory-confirmed CL case:** A probable CL case with parasitological confirmation, by positive smear, culture or PCR.
- OR**
- **Clinically-confirmed CL case:** A probable CL case that has not been confirmed by any laboratory test (i.e. test(s) not done or negative), but is assessed by a clinician to be a confirmed CL case based on clinical grounds

KA-HIV co-infection:

A case of coinfection is an HIV-positive person meeting the definition of probable leishmaniasis case with serological and/or parasitological confirmation of the *Leishmania* parasite. Coinfection is more common with VL (i.e. VL-HIV) than the other forms of leishmaniasis.

Other patient definition:

Patient type: new/relapse

- Origin of the infection:
 - **Imported:** infection acquired outside the country of reporting
 - Autochthonous : infection acquired within the country of reporting
 - **Locally-imported:** infection acquired within the country but outside the implementation/administrative unit of reporting

Locally-infected: infection acquired inside the implementation/administrative unit of reporting.

All confirmed VL/PKDL and CL/MCL cases should be treated according to the national protocol and should be clearly recorded as either a “laboratory” or “clinically” confirmed case in the information system to allow proper data analysis on the quality of the health services and the implications in post-treatment follow-up.

III. Surveillance strategy

A. Characteristics of leishmaniasis surveillance

Leishmaniasis surveillance in Nepal should be:

- **Permanent:** even when the target of elimination as a public health problem will be reached, the surveillance efforts should be sustained in order to prevent an increase / resurgence of leishmaniasis
- **Continuous:** surveillance should be sustained throughout the year. Due to the seasonality pattern, particular efforts should be made during the peak season.
- **Exhaustive:** the KA surveillance should aim at capturing all KA cases in order to ensure the reliability of the figures used to calculate KA incidence at district level.
 - Surveillance through sentinel sites would not enable to capture the full burden of the disease and will not enable to validate the achievement of the elimination target.
 - KA should be a **notifiable disease** in order to ensure mandatory and exhaustive case reporting

B. Case detection strategy

Case detection is a core function of the surveillance system. Case detection can be active (when the program reaches out to the community to actively screen and find the cases) or passive (when patients seek care at health facilities at their own initiative)

1. Kala-azar as notifiable disease

Timely reporting of all KA cases to public health authorities is essential to achieve the elimination target. Surveillance data should be collected from all public health facilities able to diagnose leishmaniasis, but also from the private sector and non-governmental organizations. When disease notification is made compulsory in a country, and robust reporting systems are in place, the system is likely to be far more complete than when reporting is voluntary.

2. Passive Case Detection (PCD)

Passive case detection (PCD) is the timely, regular and accurate reporting of the leishmaniasis cases who seek diagnosis and treatment from a health facility:

- It covers both endemic and non-endemic areas
- It includes all level of health institution from public sector, but an effort should be made to cover private medical services and services delivered by non-governmental organizations.

PCD is an important component of the KA elimination program and is key for all forms of leishmaniasis. It is useful and sensitive for the areas where the community awareness about leishmaniasis is high and the health services are actively involved in KA control.

This method does not require additional efforts and resources as it is currently part of the existing health system.

3. Active Case Detection

Active case detection or active case search means that health staff reaches out to the community and systematically screens the population to find cases of leishmaniasis KA is mainly a disease of the poor, their poor health seeking behaviour is a complex of many factors. Most of the people living in KA endemic areas are daily wage earners or small farmers, and one day visit to seek care means absence from work, loss of wage or both. Due to chronic nature of the illness, a KA case consults local level care providers multiple times. The recurrent cost of treatment depletes their health care resources. They are unaware that the illness is fatal and getting rid of the disease in fact improves their income. Thus, other aspects of livelihood become priority to them rather than seeking health care. Interventions at community level are thus essential to identify hidden cases and thus justify the need for active case search. A recent study conducted in Nepal, Bangladesh, and India suggests that the chance of case detection by active case detection (ACD) is significantly higher than PCD.

ACD is an essential additional component of the KA elimination strategy on the Indian subcontinent. It helps to reduce disease transmission by shortening the infectious period of cases and earlier diagnosis and treatment improves treatment outcomes.

Currently four approaches of active case detection (ACD) have been validated for their utility in KA and PKDL case detection in the Indian subcontinent.

1. The **blanket approach** is conducting house to house visit by trained public/private health workers in the endemic areas for detection of KA, PKDL, CL and MCL cases.
 - The blanket approach is considered the “gold standard”
 - Due to the high cost incurred with this method, it is only recommended in outbreak situations.
 - It can also be conducted if integrated with other health activities, such as family planning activities.
2. The **camp approach** is done by organizing health camps in defined KA endemic communities where screening of KA and PKDL is done by mobile teams of medical officers, nurses, laboratory technicians, health workers/health volunteers. The community people are pre-informed about the visit of the team, its purpose; and the time, date and place of the team’s activities.
 - The camp approach is a sensitive tool for the detection of new kala-azar and PKDL cases

- It has been shown that when conducting the camp approach twice in a year is sufficient to capture a substantial number of new KA and PKDL cases in a given area.
3. The **index case-based approach** includes the search of new KA and PKDL cases among the household members through house-to-house visits around the house (radius of 100 meters or 50 households) of a recently diagnosed (usually in the previous 6 months) KA case.
 - The index approach is the preferred method for ACD for endemic and non-endemic areas and in those areas where households are scattered.
 4. In the **incentive-based approach** the search for new KA and PKDL cases is done through Female Community health volunteers (FCHW) who receive an incentive for each newly detected, if it is confirmed.
 - Incentive based ACD can be a useful method, particularly in low KA endemic areas or in combination with the above-mentioned methods.
 - It may induct the snow ball technique for new KA and PKDL case finding.
 - However, this method needs meticulous supervision and monitoring to prevent misuse of funds.

Standard Operating Procedures (SOPs) for the different ACD methods are available in **Annexure VIII**.

C. Data collection – Case registration

1. Case registration

For leishmaniasis surveillance purpose, all the health facilities, from public and private sectors, which are able to diagnose and/or treat confirmed leishmaniasis cases should make sure the “**KA treatment register**” (**Annexure VII**) is available for leishmaniasis case registration.

Health facilities may implement other tools for detailed clinical information recording while managing the case. But the “KA treatment register” consists of the minimum information to be recorded and reported to the KA elimination programme. The “KA treatment register” should therefore comprise complete data **for all confirmed leishmaniasis cases**, either laboratory or clinically-confirmed, that has been diagnosed and/or treated at the health facility.

If the register is not available due to some reason, record should be maintained in a separate register by including all information required and transferred to the register as soon as it becomes available.

Each case (each episode) should be uniquely identified in the system.

Individual data collection –KA treatment register

The information recorded for each patient is detailed in the KA treatment register (**Annexure VII**). It comprises:

- **Identification of the reporting health facility**
- **Identification of the patient**
 - Unique identification code
 - First name and last name
 - Family head's name
 - Place of residence/address (district, municipality, ward number and village/tole)
 - Contact number
- **Socio-demographics information**
 - Gender (female/male)
 - Age
 - Caste code
- **Clinical information**
 - Date of admission (or registration in case of outpatient)
 - **Date of onset of symptoms**
 - *This detailed information, if difficult to collect, could be replaced by "Time elapsed since onset of symptoms, in days"*
 - Type of disease (new KA/relapse/PKDL)
 - Mode of detection (active case detection / passive case detection)
 - Travel history in endemic area in the last 2 years (yes / no / unknown)
 - Pregnancy status
- **Diagnosis**
 - Type of diagnostic test and date it was performed
 - Laboratory result (positive/negative/not done)
 - Diagnostic centre
 - HIV test result (reaction / non-reactive / not done)
- **Treatment**
 - Treatment regimen
 - Treatment start and end dates
 - Side effect
- **Treatment outcome**
 - Treatment completion
 - Initial treatment outcome, 15 days after treatment start (date and outcome)
 - Final treatment outcome, 6 months after treatment end (date and outcome)

It is crucial all of these variables and related indicators are well-defined for all the actors of the KA surveillance system. It should be largely disseminated and used for any training on leishmaniasis.

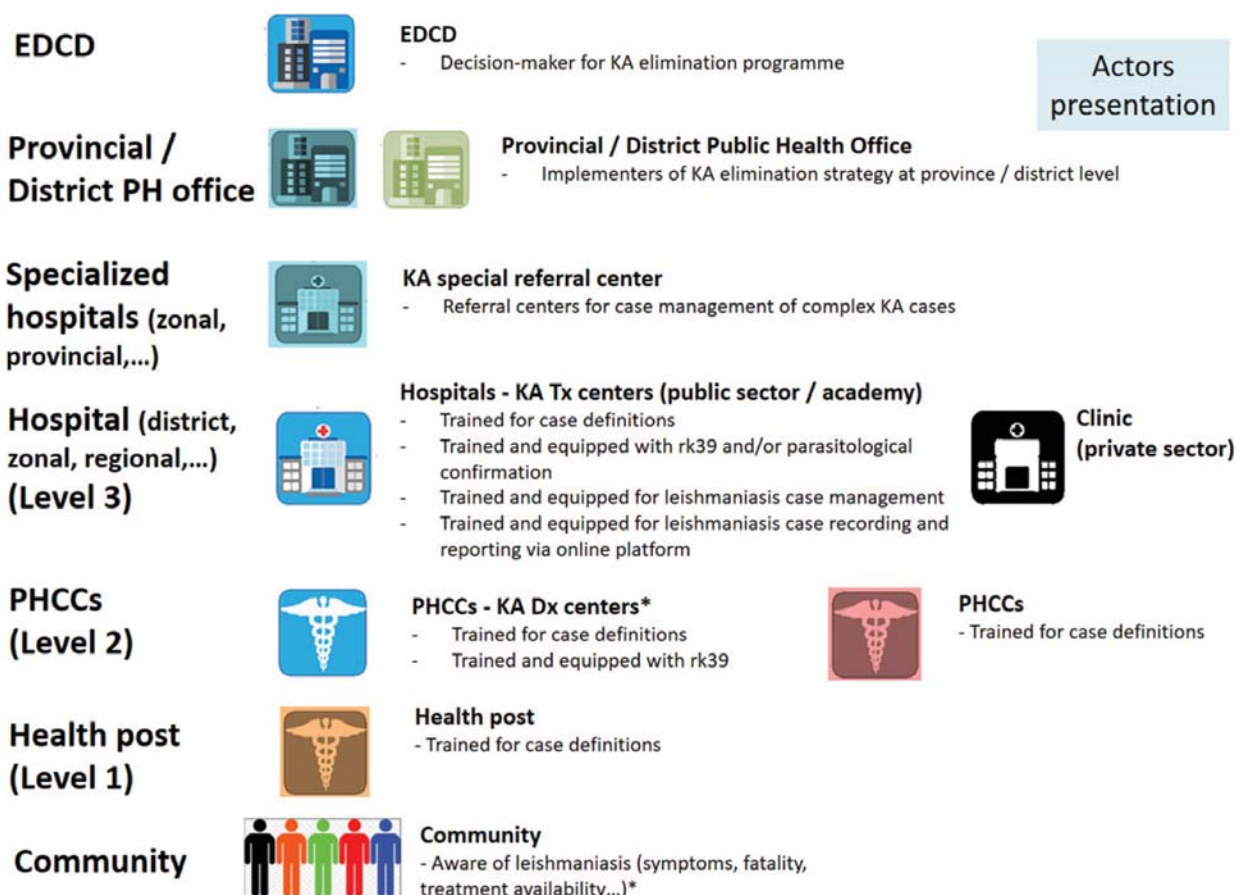
D. Data flow

1. Actors of leishmaniasis surveillance

The **actors** of the leishmaniasis surveillance system include the **EDCD** who is coordinating the national KA elimination programme who uses data from surveillance systems in order to take decision and adjust KA strategy and elimination activities, the **public health officers** at provincial and district levels who are implementing KA elimination strategy and use data from the surveillance systems to monitor the performance of the KA elimination programme in their area, the **health staff** who detect, diagnose and treat leishmaniasis cases, gather and/or use the data both for case management and to improve the knowledge about population at risk in their catchment area and the patients and the affected **communities** who are suffering from leishmaniasis and whose details are registered (**Figure 5**).

Figure 5: **Presentation of the actors of the leishmaniasis surveillance system**

PH: Public Health; KA: Kala-azar; Tx: treatment; Dx: Diagnostic; PHCCs: Primary Health Care Centers;



** In endemic districts and ditrict having reported new indigeneous KA cases in the last 10 years*

2. Actors responsibilities

The existing network of national health care delivery system (**Annexure IX**) should clearly understand their roles and responsibilities on kala-azar elimination program.

All health care providers at any level of the health systems are trained for the case definitions. Their responsibility is to detect probable leishmaniasis cases, i.e. cases who meet the case definition. For health facilities who are neither diagnostic nor treatment centers, and therefore not trained and equipped to diagnose and treat leishmaniasis cases, their responsibility is also to refer the probable cases to upper level for laboratory confirmation and treatment (Figure 5).

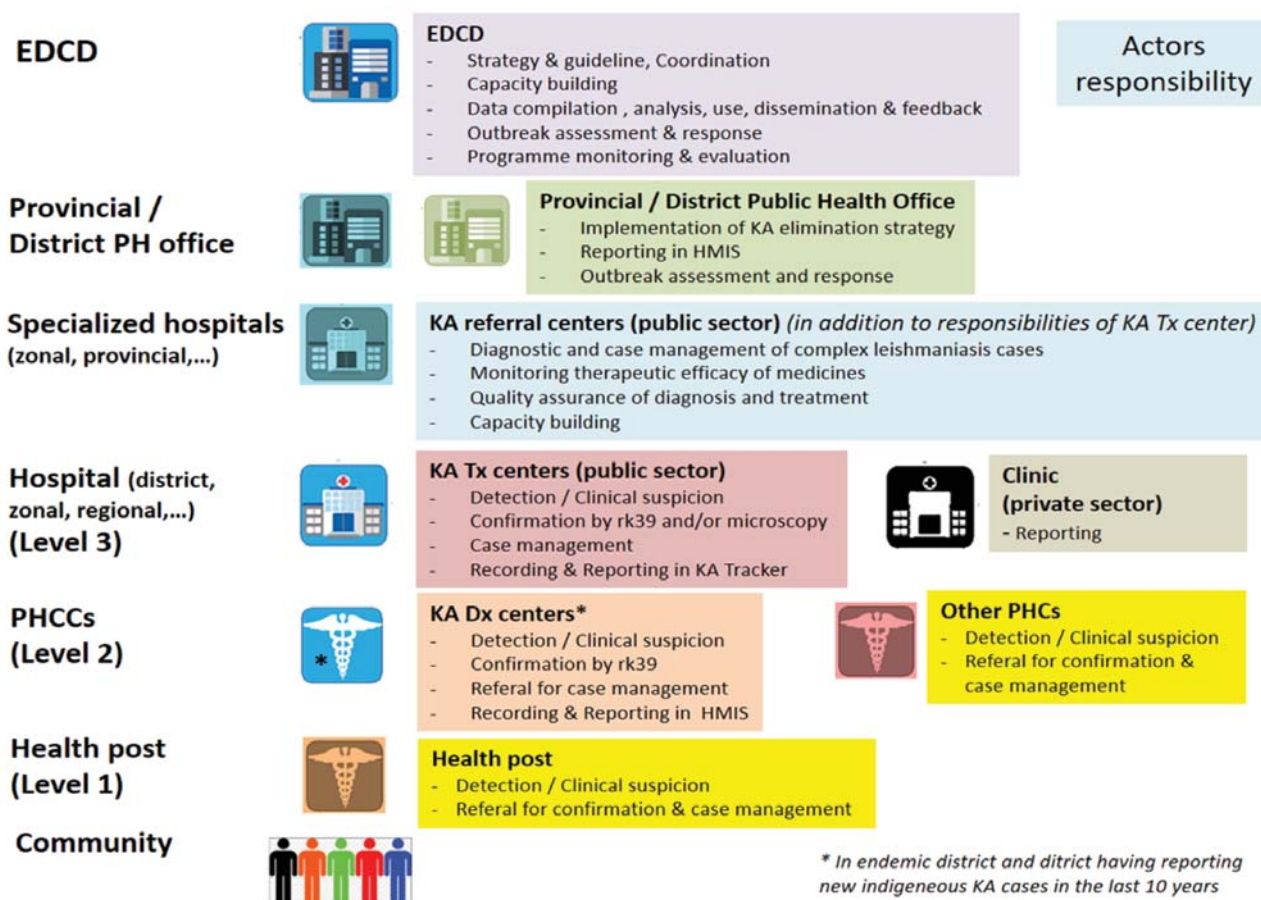
In districts considered as endemic and districts having reported new indigenous KA cases in the last 10 years, the Primary health care centers (PHCC) are considered **KA diagnostic centers**: health staff is trained and equipped to confirm new KA cases with rk39 test. They will have to refer the confirmed cases to KA upper level for case management. The physician in these diagnostic centers is also responsible to register all confirmed leishmaniasis cases on the “*KA treatment register*”. Due to the current logistical constraints, they are not expected to report these cases in the **KA Tracker**. However, they are responsible for reporting in HMIS.

In each district, at least one hospital from the public sector is designated as **KA treatment center**: health staff is trained and equipped to confirm new KA cases with rk39 test and/or parasitological confirmation. They are also trained and supplied and therefore responsible for KA case management, as per national treatment protocol. The physician in these treatment centers is also responsible to register all confirmed leishmaniasis cases on the “*KA treatment register*” while the medical recorder is responsible to report all confirmed leishmaniasis cases in the “*KA Tracker*”. If supplied by the EDCD with diagnostic tests and treatment, hospitals from private sectors which are able to diagnose and treat leishmaniasis cases are also responsible for data reporting in the “*KA Tracker*”.

At upper level, some health facilities are identified as **KA referral centers**. In addition to the roles and responsibilities of KA treatment centers, KA referral centers are responsible for: difficult diagnosis and complicated case management (including management of HIV-VL co-infections); monitoring therapeutic efficacy of medicines according to national treatment protocol; quality assurance of diagnosis and treatment; PCR testing of samples in selected cases as a part of quality assurance and capacity building of staff at all level health institutions

Provincial and/or district public health office is responsible of the implementation of KA elimination strategy in their area. They are also accountable for the reporting in the HMIS. They are responsible for outbreak assessment response, along with EDCD team. Finally, at central level, the **EDCD** is responsible for guiding the strategy and coordination the effort in eliminating KA. Its team is responsible for leishmaniasis trainings, data compilation, analysis, use, dissemination and feedback, outbreak assessment and response and programme monitoring and evaluation.

Figure 6: Role and responsibilities of actors in leishmaniasis surveillance



3. Recording and Reporting Units

Recording in the KA treatment register

The hospitals providing diagnostic and treatment service (**KA Treatment centers** and **KA Referral centers**) and the PHCs in districts considered as endemic and district having reported new indigenous KA cases in the last 10 years (**KA diagnostic centers**) are identified as the reporting units for KA elimination program.

All these centers must record every confirmed leishmaniasis case in the paper-based KA treatment register. This task is under the responsibility of the physician who has diagnosed the case. Delays between confirmation of the case and recording the individual data in the KA treatment register should be minimized in order to increase data quality.

Health posts are also identified as sub-unit for reporting about KA elimination activities and they should report the district about their performance of KA elimination related activities. However, as they are not trained and equipped to diagnose and/or treat leishmaniasis cases, they are not expected to report any confirmed leishmaniasis case.

Reporting individual data in the KA Tracker

The **KA treatment and the referral centers** must report individually every confirmed leishmaniasis cases in the KA Tracker. This is under the responsibility of the medical recorder or equivalent.

Delays between confirmation of the case and reporting the individual data in the KA Tracker should be minimized in order to increase data quality. The reporting of all cases diagnosed during a month must be completed before the 10th of the following month.

Reporting aggregated data in the HMIS

The **KA diagnostic centers** should report every month aggregated data related to the confirmed cases they have diagnosed to HMIS through the monthly form *HMIS 9.3*. If there are no cases then it should be a **zero report**. A zero report is as important as a report which enumerates the cases seen. In most of the case, a hard-copy of the form *HMIS 9.3* is sent from the PHCs to the DPHO who is responsible for entering the data in the HMIS. The reporting of all cases diagnosed during a month must be completed before the 10th of the following month.

The **KA treatment and referral centers** do not have to fill out the KA aggregated data in the monthly form *HMIS 9.3* in the HMIS, because data will be aggregated automatically from the *KA Tracker*. However, in order to ensure the quality of the zero reporting, the **KA treatment and referral centers** will have to validate the aggregated data pushed to HMIS from KA Tracker.

Reporting spraying activities

The recording of spraying should be done in monthly reporting and annual reporting format.

District public health office

The district (public) health offices should also establish a functional system of collecting such reports from the non-government/private sectors.

4. Data flow

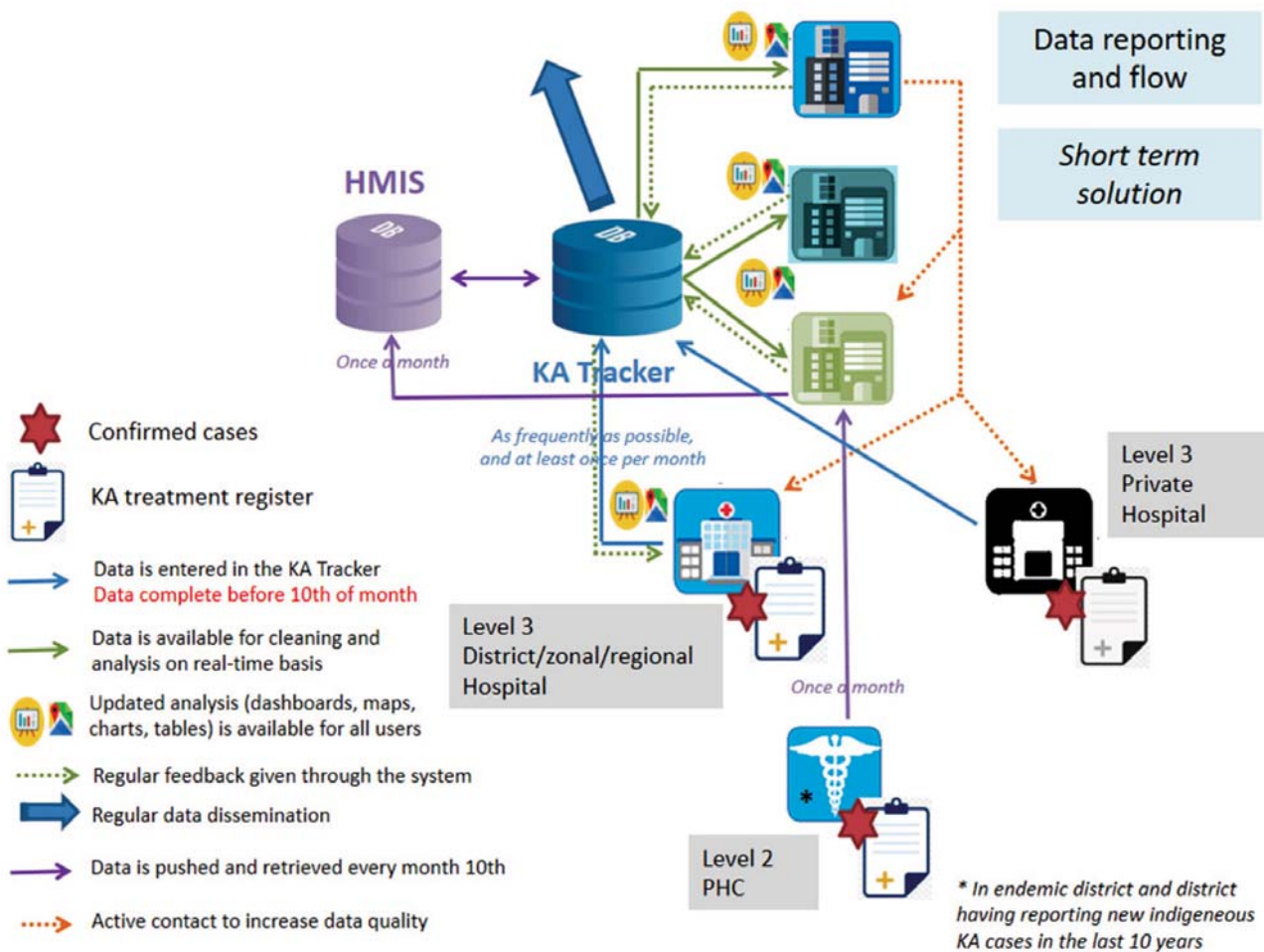
Once entered in the KA Tracker, data will be available for upper level users (**Figure 7**).

Moreover, all existing data visualization (tables, chart, maps, dashboard, etc) will be automatically updated when new cases will be reported. Processed data will be used and regularly disseminated.

Users at upper levels of the surveillance system will be able to give feedback and share interpretations with other users of the online platform directly through the tracker system.

It is important to keep in mind that regular contacts from the EDCD, provincial and district public health offices with reporting units will still be instrumental in order to ensure good quality of the data entered in the KA Tracker.

Figure 7: **Data flow chart for the leishmaniasis surveillance system**



5. Reporting System

The individual data will be entered in an online platform called KA Tracker. This online platform is based on the DHIS2 software, which is also used for the HMIS platform. The KA Tracker uses the web-application “Tracker capture” of the DHIS2 which enables to track patient from diagnostic to final outcome and to capture individual data.

The KA Tracker offers pre-defined visualization (tables, charts, maps and dashboard) in order to stimulate data interpretation and use. Additional analysis of the data can be performed in the online platform or after extracting the anonymized data.

The KA Tracker is hosted in secured servers. The visibility of individual data is controlled by username and password and the fine control of users’ authorities.

An ad hoc application will enable the monthly aggregation of leishmaniasis data which will be shared with the HMIS platform.

6. Data analysis

▶ Data quality

Good evidence-based decision for KA elimination can be taken only if the quality of the data reported through the surveillance system is good. The quality of the data should be regularly checked and ensured:

- **Duplication / double counting** of cases: some patients may seek care from different health facilities from public and private sector and could therefore be reported several times through the surveillance system. The potential duplication of cases will have to be checked on monthly basis by comparing key identification information

Note that when registering a new patient in the online system, the potential duplication of an existing case in the platform will be performed.

- **Completeness:** good quality data should be complete, i.e. all cases should be reported, and all data should be recorded for each case

- ***Completeness of reporting from public and private health facilities***

The completeness is defined as the number of report received over the total number of report expected for the considered month. KA being a notifiable disease, the national elimination programme will have to ensure that at least all health facilities able to diagnose and/or treat KA cases have been reporting.

- ***Completeness of recording***

The variables that are requested on the KA treatment registers have been chosen because of their importance in monitoring KA elimination in Nepal. They should all be recorded for each KA case.

The completeness of variable recording can be measured as:

- the proportion of information recorded in the form over the total number of variables expected on the KA register
- for each variable, the proportion of cases for whom the variable is recorded, over the total number of cases

- **Timeliness** is defined as the percentage of reports that are submitted before the deadline (10th of the month). In the KA tracker (online platform) where cases can be reported all through out the month, it is important to monitor the delay in recording (time between date of admission and date when the case is entered in the system).

- **Accuracy:** the data recorded should measure what they are intended to measure and minimize errors (e.g. male being pregnant).

- Note that internal validation rules in the KA Tracker online platform will aim at minimizing data entry errors and increase data accuracy.

- **Consistency:** The consistency of the data has to be checked at least once a year before data review: Consistency has to be checked over time (recent data compared to historical data) and between indicators which have a predicted relationship. The consistency of data reported, and original records should also be assessed annually during supervision mission.
- **Representativeness:** Confirmed cases diagnosed during active case detection or by KA diagnostic centers will be referred to KA treatment centers for case management. As only data from the KA treatment centers will be entered in the KA Tracker, this represent a risk of losing some confirmed cases who will have been diagnosed but may never reached the treatment center. The representativeness of the data captured in the KA Tracker will have to be assessed at least once per year by selecting diagnostic centers which have reported confirmed KA cases through the HMIS and assessing, based on their KA treatment register, the proportion of cases which have been reported in the KA Tracker.

► **Data analysis**

The surveillance data should be analysed based on the objectives of the surveillance as above, and interpreted taking into consideration data quality, context and potential modifications of surveillance activities or elimination strategy.

Good epidemiological descriptive analysis covers time, place and person aspects.

- **Time:** Looking at the trend in the number of cases will help assessing the progress towards elimination or detect outbreaks
- **Place:** Mapping the number of new cases and/or the incidence rate of the disease at the finest level possible will help identifying population at-risk and clusters of the disease
 - a map of the KA incidence at district level will help identifying easily, districts which are above the threshold of 1 case / 10,000 population

- **Person:**

Age and gender distribution helps understanding who the cases are. It is also recommended to look at the recommended indicators (**Annex VI**) and do some comparison, over time and between treatment centers and/or district, in order to assess the performance of the KA elimination programme in terms of diagnosis and case management, and to identify treatment centers which may require supervision.

The KA tracker offers tools to produce tables, charts and maps based on the individual data that will be captured by the KA treatment centers. Predefined dashboard which will be automatically updated when cases will be registered in the platform will be available in order to increase data use and encourage data interpretation and evidence-based action, at all levels of the surveillance system.

7. Data dissemination / feedback

Regular feedback will motivate the data producers and improve data quality and use at all levels of the surveillance system.

► Dissemination

Dissemination is the process of communicating information through defined channels and media in order to reach various target groups (e.g., national policymakers, researchers, health professionals, or consumers). In the elimination context, dissemination is important in order to elicit immediate action, solicit support or participation, document progress towards elimination and justify program activities. It also participates to behaviour change promotion. Dissemination is efficient only if well prepared. It is important to establish communications message, define the audience, select the communication channel and market the message. Afterwards, it is good practice to evaluate the impact of data dissemination.

► Feedback

The program focal person of the district in coordination with statistical assistant should provide a regular feedback to reporting units and sub-units based on review of the reports. Review and feedback are important at all level of health institution.

Feedback can be provided through the online platform by commenting certain visualization or sending messages to users or groups or users. They can also be provided outside of the online platform, through supervision visits, regular meetings or personal communication.

All reviews and the supervisory visit reports should be summarized, and the reports submitted to the respective higher level along with the monthly report.

5.2 Vector surveillance

Sandflies are small (that bite and take blood meal) insects, light or dark-brown in color belonging to the Psychodidae family. They are smaller than mosquitoes, measuring 1.5 to 2.5 mm in length with their bodies and wings densely clothed with hair. Some 30 species of sandflies have been recorded in Indian sub-continent (Sub family: Phlebotominae, Genus: Phlebotomus). Important species (because of their role as a confirmed or suspected vector of kala-azar) are: *Phlebotomus argentipes*, *P. papatasi*, *P. sergenti*, and *P. punjabensis*, the former being confirmed as the vector responsible for kala-azar transmission in Nepal.

The life cycle of the sandfly is characterized by complete metamorphosis, comprising of egg, larval, pupal, and adult stages. The eggs are laid in damp dark places in the vicinity of cattle sheds and poultry enclosures. The eggs are comparatively large, and torpedo-shaped with longitudinal wavy lines on the outside. The eggs hatch within 7 days. The larvae are hairy maggots with a distinct head, thorax and abdomen. The last abdominal segment carries two pairs of long stout hairs, one pair is remarkably

long. The larva feeds on decaying organic matter and becomes a pupa in about two weeks. The pupal stage lasts for about one week. The average life of an adult sandfly is about two weeks.

5.2.1. Vector Bionomics

Phlebotomus argentipes thrives best in alluvial soil, in areas with relatively controlled temperatures, high humidity, and presence of large cattle populations. Eggs and larvae of the sandfly can withstand immersion in water for a period of 5 days and the larvae of the fourth stage can withstand the immersion for a period of 14 days. Thus, they can survive even flooding. Breeding places can be found within a radius of about 20-50 meters from a dwelling in dark, humid soil protected from the sunlight, however they are notoriously difficult to find and hence why vector control is not really targeted towards larval stages of the life cycle. In the cattle sheds, the favorite breeding place is underneath cattle troughs while in households, adults and flies are usually collected from cracks and crevices within walls.

Sand flies are troublesome nocturnal pests. Their bite is irritating and painful while their presence is scarcely observed. They infest dwellings during the night time and take shelter during the day in holes and crevices in walls, holes in trees, caves, stables and store rooms. The females alone bite as they need a blood meal every third or fourth day for ovi positioning.

They have tendency and preference to feed on cattle blood than human blood. Transmission can occur after a heavy build-up of the sandfly population because the sandfly shifts from cattle to humans only after it has exhausted the option of a blood meal from cattle. Sandflies can hop short distances but cannot fly, although slow wind movement could assist flight and help identify an odour plume, therefore increasing the chances of obtaining a blood meal. Sandflies seldom reach a height of more than 6 feet and are generally confined to within 150 feet of their emergence site.

The highest risk of disease transmission for Nepal is in the months of June to October when the humidity is high and densities peak. Currently *P. argentipes* in Nepal are susceptible to pyrethroid insecticides that are used in IRS.

If concerted vector control efforts are introduced as part of the kala-azar elimination programme then interruption of kala-azar is achievable based on the following factors associated with vector bionomics of sandflies in Nepal:

- *Phlebotomus argentipes* is the only vector to be associated in the transmission of kala-azar in Nepal to date.
- The vector is so far susceptible to all pyrethroid insecticides that are used or have been used for IRS operations in Nepal.
- There is historical evidence which highlighted the interruption of transmission as a collateral benefit of malaria eradication program when kala-azar was virtually eliminated from the subcontinent as a result of IRS.

- Cross border collaboration for the implementation and operation of IRS in in KA affected villages from both Nepal-India side can interrupt the transmission of the disease. For this, simultaneous IRS operations can be mounted since the areas under the South-East Asia Regional Kala-azar elimination programme have similar seasonal factors.

Vector surveillance is a critical component of the kala-azar elimination program since it helps to target IRS operations more effectively, based on updated knowledge on vector abundance and behavior. It is an important part of the elimination strategy because it is also useful in determining the impact of IRS if it is conducted on a regular basis. There are no easy methods for estimating the size of local sandfly populations reliably, however most sampling methods should focus on sandfly adults as immature phlebotomines occupy obscure terrestrial habits.

All levels of the IRS programme have to ensure that it reaches its goal of reducing vector densities to low levels during the transmission seasons. This can be assessed by:

- Monitoring vector densities
- Bio-efficacy of insecticides
- Vector susceptibility to insecticides

Table 16: M&E of IRS impact on vector densities, bio-efficacy and insecticide susceptibility

Topic area	Indicator	Information source	Measurement frequency	Information collector
Vector density	Number of vectors per light trap per night	Documentation of light trapping	2–4 weeks before IRS; 2–4 weeks and 3–4 months after IRS	Entomologist of the public health service or subcontracted academic/research institution
Bio-efficacy of insecticides	% mortality in bioassays >80%	Documentation of bioassays (WHO cone method)	1 month and 3–4 months after IRS	Entomologist of the public health service or subcontracted academic/research institution
Insecticide susceptibility	Vector mortality above 80%	WHO tube method with impregnated papers	Once per year before IRS	Entomologist of the public health service or subcontracted academic/research institution

The national program for Kala-azar elimination is currently focused on increasing the awareness about the program to general population. The information gap does not only occur at the community level but there are issues that need to be cleared and consulted with the policy level decision makers. A strong political commitment, appropriate strategies, development of a strong program network, community involvement and empowering the community with information are key to achieving elimination of Kala-azar at national and district level.

The current BCC strategy aims to bridge this gap by devising methods and messages that are pre-tested, specific, simple, and culturally sensitive that reaches and is understood amongst wide geographical areas and communities.

The program considers that increase in knowledge and awareness does not necessarily bring about a change in behavior. For behavior to change, it is important to make sure that as a first step people are informed about the problem and solutions. An enabling environment is needed to encourage the people to take healthy actions. Finally, it is necessary that the action is sustained to have an impact.

Objectives of BCC strategy

To bring about behavior change at individual, household and community level at high risk areas by building communication skills of front line workers such as female community health volunteers (FCHVs) and community health workers through capacity building activities such as training and orientation in order to achieve Kala-azar elimination goals is the overall objective.

- To increase awareness in the communities about disease, prevention, diagnosis and complete treatment of Kala-azar
- To generate greater demand for IRS at risk areas, involve communities and motivate service providers in improving IRS administration.
- To provide enabling environment which facilitates and provides quality services - sensitizing private care providers and traditional healers about correct diagnosis and treatment and for referral.
- Advocacy for resources and services with programme managers and administration
- Motivating people and care providers about surveillance and reporting of PKDL cases - reservoir of infection which increases case load within the family.
- Building capacities of frontline workers in effective use of communication tools and IPC skill building

6.1 BCC Strategy within the context of Kala-azar elimination

Many of the issues explored and identified are service delivery. However, the vital issues to be addressed is that there is a lack of awareness about the disease, cause, signs & symptoms, prevention, vector control, diagnosis, availability of free service available for kala-azar treatment at public health system and vector control activities in support of kala-azar elimination programme in Nepal.

Behavioral change communication strategy is needed for the following reasons:

- To influence planners, policy makers, other stakeholders for intersectoral collaboration
- To mobilize additional resources and optimally use the existing resources
- To use ‘influencers’ in the community for the empowerment of the community
- To empower and motivate community with information for appropriate behavior
- To get maximum output vis-à-vis the inputs
- To get behavior impact and monitor and measure the impact

Target audiences

Primary Audience: *Primary audience* is the one who will be doing the desired action. Primary audiences for kala-azar in KA endemic areas are:

- Patients; their families;
- Community in general living in pockets or clusters around damp areas/ humid, agriculture land or areas which are prone to sand fly breeding;
- Vulnerable sections such as workers living in and around cowsheds, pregnant women and families that have children in those localities.

Primary audience from kala-azar endemic areas (especially in *Terai* region) will be the prime target for BCC interventions.

Secondary Audience: The *secondary audience* is equally important as he/she is responsible for either facilitating or inhibiting the desired action. So the nature of messages that addresses the primary and the secondary audience are clearly different but together they facilitate the onward march to successful behavior change. School teachers, key leaders, private care providers/traditional healers/*Dhamis* are important for kala-azar, as research shows that more than 50% of the people prefer to seek treatment for them at their first visit. They need to know the importance of timely, correct diagnosis and complete treatment and preventive measures as well as identification and treatment of PKDL cases.

Private providers’ non-government service providers and private sectors would need to be targeted in endemic districts. Programme managers and policy makers are an important part of this category of audiences as their actions have bearing on the health care services and resources. These groups are very important for advocacy and allocation of resources for elimination of kala-azar.

Tertiary Audience: The *tertiary audience* not only needs to know the existence of these audience categories but also needs to have some communication qualities, skills and competencies that motivate people to take, accept and adopt desired behavioral action. His/her behavioral action or attitude, if not appropriate, can be de-motivating and one can lose confidence in the health care provided at the government health facilities. The research also reveals that reasons for not seeking diagnosis and treatment from the government health facilities relate to the attitude of care providers, lack of confidence in the services and lack of medicines, delay besides distance and cost involved in seeking treatment. Care providers, kala-azar workers and front-line workers are the target audiences in this category. Training of FCHVs, CHWs, ANMs, teachers, in giving uniform messages regarding IRS in the endemic districts in Nepal would need attention.

Table 17: **Description of activities according to target groups for kala-azar control**

Target Groups	Communication objectives	Description of BCC activity	BCC materials/tools
A. Primary audiences			
1. Patients and families in the endemic areas	Awareness about prevention and vector control	Training cum orientation to front line healthcare providers.	<ul style="list-style-type: none"> • Posters at health facilities • Display posters on rickshaws, rural vehicles
2. Communities/ clusters in damp humid areas and near the vegetation	<ul style="list-style-type: none"> • Getting all places sprayed in the house including cowsheds • Filling up of all cracks in the walls • Proper ventilation • Avoiding sleeping on floor • Staying away from cowsheds 		
3. Workers in agricultural fields and in cowsheds	Awareness about services	Group communication session with the use of video CDs	<ul style="list-style-type: none"> • Display poster (flex and vinyl) • Flipbooks • Leaflets • Wall paintings • Miking • Video CDs
4. Pregnant women and families with children in the endemic areas	<ul style="list-style-type: none"> • Where (accessibility) - PHC/ district hospitals • Symptoms and mode of transmission • Lack of awareness that delay treatment increases chances of transmission and family case load • Side effects- what has to be done at the individual level and at health system level • Lack of awareness about provision of incentives and food during treatment at hospital 		

B. Secondary audiences

1. Key leaders and religious organization	<p>Awareness about their role in Vector control and promoting-</p> <ul style="list-style-type: none"> • Ensuring IRS of the whole areas • Filling up of the cracks • Knowledge of signs and symptoms and mode of spread 	<ul style="list-style-type: none"> • Inter personal communication • Sensitization meeting 	<ul style="list-style-type: none"> • Poster (vinyl) • Panel (flex) • Video CD for group session • Leaflets
2. Political leaders	<p>For elimination programme, the political commitment of elected members (Health Minister/Health Secretary) are essential.</p>	<ul style="list-style-type: none"> • Organizing advocacy meeting of key stakeholders of endemic districts under the chairmanship of public health manager • Subsequently, the public health manager can regularly monitor the programme and take appropriate steps 	<p>An advocacy package for politicians</p>
3. Media	<p>It is important to provide the appropriate messages and orient the media to support the elimination program.</p>	<p>One day workshop for press/media to sensitize them about the elimination programme</p>	<p>Press release</p>
4. Private practioners/traditional healers	<p>Early diagnosis and complete treatment</p> <ul style="list-style-type: none"> • Referral for diagnosis and treatment • Standardized drug schedules • Proper recording and reporting 	<p>Sensitization meetings</p>	<ul style="list-style-type: none"> • Poster for display in the clinics • Mass media-radio/TV/Print
5. School teachers	<p>Awareness about disease, prevention and treatment</p> <ul style="list-style-type: none"> • Mode of transmission • Prevention and vector control • Early reporting of fever and PKDL cases 	<p>Group interaction with school teachers</p>	<p>Leaflet Poster</p>
6. Programme managers	<ul style="list-style-type: none"> • Ensuring supply of diagnostics & medicines • Need for coordinated efforts with other departments 	<p>Capacity building session</p>	<p>Advocacy materials</p>

C. Tertiary audiences

1. Healthcare providers	<ul style="list-style-type: none"> • Early diagnosis and treatment • Identification of PKDL cases • Kala-azar fortnight for identification of cases • Information about incentives to the patients 	District level capacity building workshop	Display materials for health facilities
2. Frontline health workers (FCHVs, CHWs)	<ul style="list-style-type: none"> • Early diagnosis and treatment • Identification of PKDL/CL/MCL cases • Motivating patients and their families for seeking early treatment for fever & PKDL/CL/MCL • Information about the incentives for the patients 	Capacity building sessions	<ul style="list-style-type: none"> • FCHVs flip chart/module • FAQ book • Flip book
3. NGOs & other civil society	<ul style="list-style-type: none"> • Early diagnosis & treatment • Identification of PKDL cases • Motivating patients & their families for reporting fever over two weeks and PKDL cases 	Capacity building session	<ul style="list-style-type: none"> • FAQ booklet • Flip book

Programme strategy for reducing incidence	Identified Behavioral Barrier	BCC strategy
1. Case management	Not able to identify signs & symptoms of kala-azar	Awareness about the signs & symptoms Free treatment
1.1 Early diagnosis	Delay in identifying signs & symptoms lead and delay in timely diagnosis and treatment	Place for diagnosis & treatment Awareness among private care providers & traditional healers
1.2 Complete treatment	Side effects of anti-VL drugs Costs to family of losing work	Motivating families to complete treatment
1.3 Reducing case fatality	Not able to identify cases of kala-azar	Capacity building
1.4 Surveillance of PKDL	Not recognized a case of PKDL	Capacity building for identifying PKDL symptoms and treat PKDL

1.5 Prevent resurgence	Can't identify PKDL	Identifying PKDL & strengthening surveillance
2. Vector control		
2.1 Indoor Residual Spraying	Not identify by the IRS team or provider Not accepted by the community	Preparing communities Proper spraying including cowsheds No mud plastering after IRS
2.2. Prevention of vector breeding	Unaware of vector breeding places	Closing cracks and cervices
2.3. Prevention of man-vector contact	Don't use any protection measures	Use mosquito nets

Key messages for dissemination and airing for kala-azar prevention and control

The following messages are identified as key messages and recommended to use while developing IEC materials for kala-azar elimination program:

Table 18: **Key messages for kala-azar elimination program**

Focus area	Key messages	Target audience
Early diagnosis and complete treatment	<ul style="list-style-type: none"> • Kala-azar is a curable disease. • Early diagnosis and treatment of kala-azar can save the life • You might have suffered with kala-azar if you have fever for equal or more than 2 weeks. • Go to nearby health institution for checkup if you have above symptoms. • Should take full course of medicine if diagnosed as kala-azar. • Diagnosis of KA and treatment is made available at free of cost. 	<ul style="list-style-type: none"> • Kala-azar patients • Patients' family • Community people • Community leaders • FCHVs • School teachers • School students
Ensure uniform and complete coverage with IRS	<ul style="list-style-type: none"> • IRS is very effective in the prevention of many vector borne diseases including kala- azar, malaria and encephalitis. • It should be done two times per year. • Spraying should be done within the households, animal shelters and places where animal wastes are present. 	<ul style="list-style-type: none"> • Family members • Community leaders • School teachers • FCHVs

	<ul style="list-style-type: none"> • Each household should cooperate and help the spray team to identify above mentioned areas. • All the surfaces to be sprayed should be cleared. • Keep foods and food products covered and make sure that these are not sprayed with insecticides. • To ensure maximum effect of the insecticides, do not wash or mud plaster the sprayed surface for a period of 8-10 weeks after the spray. 	
Personal protective measures	<ul style="list-style-type: none"> • Kala-azar is caused by the bite of sandflies. • The sandflies bite most often between dusk and dawn. • Protect yourself from a bite especially between dusk and dawn. • Wear long sleeves clothes to prevent the sandfly from biting. • Use mosquito repellants to keep the sandfly away. • Sleep under bed nets to prevent the sandflies from entering the nets. 	<ul style="list-style-type: none"> • Individuals • Community leaders • FCHVs • School teachers
Environmental Management	<ul style="list-style-type: none"> • Keep household and surroundings clean and reduce the breeding sites. 	<ul style="list-style-type: none"> • Family members • Community people

Note: *During the active case finding period, the key messages should be disseminated targeting the affected community through the means of miking, FM radios, interpersonal communication and mass meeting*

Monitoring is the collection and use of data on implementation of the programme. Its aim is to ensure that programme is working in the right direction and any mid-course corrections are done. Monitoring includes use of administrative data to track inputs, processes and outputs; programme outcomes and impacts may also be included. Monitoring is an ongoing continuous activity. Whereas “Evaluation” involves a more comprehensive assessment of a programme. It is normally undertaken at a fixed time and addresses the longer-term outcomes and impacts.

The goal of monitoring and evaluation is to improve the effectiveness, the efficiency and equity of programmes.

7.1 Functions of monitoring and evaluation

Monitoring and evaluation can accelerate progress towards sustained kala-azar elimination, if used to:

- Regularly assess whether plans are progressing as expected or whether adjustments are required to the scale up of the intervention or combination of interventions
- Allocate resources in order to achieve the greatest possible public health impact
- Evaluate whether the programme objectives have been met and to learn what has worked and what has not, so that more efficient, effective programmes can be designed
- Advocate for investment in kala-azar programmes in accordance with the disease burden in a subnational area; and
- Track progress toward elimination in all implementation units

The health workers working at health post and at community level (FCHVs) should be aware of the case definition of kala-azar, availability of diagnostic tests at the nearest PHC or hospital including other lab investigations required for monitoring the side effects. They should be aware of side effects of drugs including its management. So, the district health office and PHC should monitor the following activities that are supposed to be carried out by the health posts:

- Kala-azar cases referred to PHC or hospital on the basis of given case definition.
- Recording and reporting of kala-azar related activities.
- Follow up of treated patients for treatment outcomes
- Participation in case search activities particularly index-based approach

Designated PHCs have the responsibility of diagnosis of every suspected case of kala-azar by using rK39 test kit and initiate the treatment as per the treatment protocol for positive cases.

They should monitor the treatment, follow-up of treatment compliance; treatment completion and side effects. They are also responsible for doing or referring the cases for lab tests required for monitoring any side effects of drugs. In addition, PHC has the responsibility of monitoring the KA related activities carried out by HP under their jurisdiction.

Since level III health institution has more responsibility on kala-azar elimination program, the district, region or center should monitor their following activities:

- Diagnostic tests
- Other laboratory tests, i.e. electrolytes, RFT, LFT and complete blood counts
- Treatment with first line and second line drug and follow up of treatment
- Management of adverse effects of drugs
- Referral of PKDL/CL/MCL cases to special referral center
- Disease surveillance and recording and reporting
- Line listing of kala-azar patients in prescribed format and reporting on the KA tracker

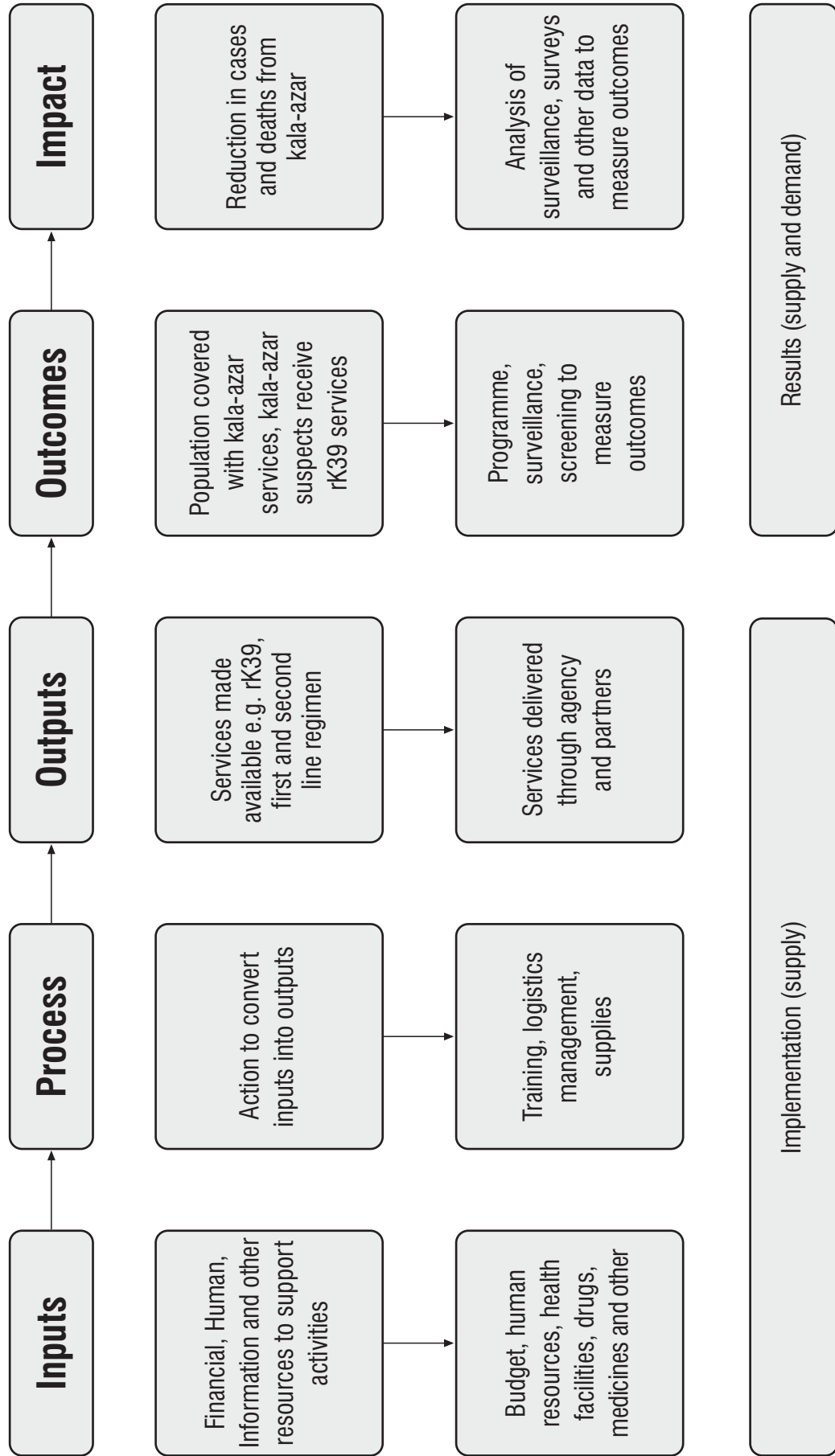
7.2 Review and Evaluation

The performance review of kala-azar elimination program should be planned at each level of health system. At the treatment centre level, a monthly review meeting should be organized together with the review of other public health programs. DHO/ DPHO chief and program focal person should attend and facilitate this meeting. Suspected case referral, contact identification and referral, follow up of patients for treatment outcomes and overall progress on KA elimination should be discussed during the monthly review of performances at health post level.

The district should organize quarterly review meeting at district level with participation from community level health facilities. The issues, challenges, constraints and operational problems should be discussed during the meeting. Problems that can be solved without further assistance from the district or center at local level should be identified. These problems and improvement plan should be communicated at the same meeting. District level and national level issues should be further discussed at program managers meeting organized in every quarter and appropriate solutions should be implemented as early as possible.

The national coordination committee evaluates the achievement once a year whereas an international review committee would verify the achievement of the program once the country claims of achieving the elimination goal.

Monitoring and evaluation framework



Above framework can be understood from an example of monitoring and evaluation of surveillance system as below:

Structure of surveillance system:

- What are surveillance strategies
- How it is implemented
- Partnerships and networking for strengthening surveillance

Core functions of surveillance:

- Case detection
- Case registration
- Case confirmation
- Reporting
- Data analysis and interpretation
- Epidemic preparedness
- Response and control
- Feedback

Quality of surveillance:

- Completeness
- Timeliness of reporting
- Usefulness of data and surveillance system
- Simplicity of system
- Acceptability of system
- Flexibility of system
- Sensitivity in surveillance
- Specificity in surveillance
- Positive predictive value
- Representativeness of system

Support functions of surveillance system

- Standards and guidelines
- Training
- Supervision
- Communication facilities
- Resources
- Monitoring and evaluation
- Coordination

Programme management is an inbuilt component of any national programme. It includes several components like allocation of resources essential to perform activities, procurement and uninterrupted supplies of drugs and diagnostics, capacity building of all levels of health personnel, intra-and-inter-sectoral coordination within the health department, line departments and outside of it, advocacy and social mobilization activities, etc.

Table 19: **Stakeholders in the programme and their roles and responsibilities in kala-azar programme**

Level I	Level II	Level III
<p><u>Public Sector</u></p> <ul style="list-style-type: none"> • Health post • Female Community Health Volunteers (FCHV) 	<p><u>Public Sector</u></p> <ul style="list-style-type: none"> • Primary Health Care Centers (PHCC) 	<ul style="list-style-type: none"> • National hospitals • Regional hospitals • Zonal hospitals • Provincial hospitals • District hospitals • Medical College
<p><u>Private Sector</u></p> <ul style="list-style-type: none"> • Unqualified practitioners • Qualified practitioners • Medicine shops 	<p><u>Private Sector</u></p> <ul style="list-style-type: none"> • Nursing homes • Private laboratories • NGOs 	<p><u>Private Sector</u></p> <ul style="list-style-type: none"> • Large hospitals • Medical colleges

Note: (i) BP Koirala Institute of Health Science, Dharan and (ii) Sukraraj Tropical and Infectious Diseases Hospital, Teku, Kathmandu are identified as national referral centers.

Level I	Level II	Level III
<p><u>Public Sector</u></p> <ul style="list-style-type: none"> • Aware of key essential messages related to kala-azar and PKDL • To have the capacity to suspect a case of kala-azar and PKDL • To be aware of the health centres where such suspects can be referred for diagnosis and then treatment • To be aware of all kala-azar and PKDL cases (new and old) in his/her area • To follow up confirmed cases for full treatment and its outcome 	<p><u>Public Sector</u></p> <ul style="list-style-type: none"> • Aware of key signs and symptoms of kala-azar and PKDL • To have the capacity to diagnose cases of kala-azar and PKDL (probable cases) • To be aware of the health centres where such confirmed cases can be referred for treatment • To be aware of all kala-azar and PKDL cases (new and old) in his/her area • To be aware of all essential variables which are important for patient recording and reporting 	<p><u>Public Sector</u></p> <ul style="list-style-type: none"> • To have the capacity to diagnose of kala-azar and PKDL • To have the capacity to admit kala-azar cases and manage them • To have the capacity to identify complications, adverse drug effects and their management and report them • To be aware of the referral centres where complicated cases can be referred for further treatment e.g. HIV-VL • To have the capacity to record and report detailed information of kala-azar and PKDL cases • To have information on the follow up of confirmed cases and outcome
<p><u>Private sector</u> (wherever possible)</p> <ul style="list-style-type: none"> • Have heard about kala-azar • Aware of key information about kala-azar • Aware that kala-azar is a fatal disease and can save lives of patients by referring them • Aware of the centres where diagnostic and treatment services are available 	<p><u>Private sector</u> (wherever possible)</p> <ul style="list-style-type: none"> • Aware of key signs and symptoms of kala-azar and PKDL • To have the capacity to refer such cases • Aware of the health centres where such confirmed cases can be referred for treatment 	<p><u>Private sector</u> (wherever possible)</p> <ul style="list-style-type: none"> • Aware of key essential messages related to kala-azar and PKDL • To have the capacity to diagnose case of kala-azar and PKDL • To be aware of the referral centres where complicated cases can be referred for further treatment e.g. HIV-VL • To have the capacity to record and report detailed information of kala-azar and PKDL cases

Drug and diagnostic procurement plans and supply chain:

National programme will take all measures to avoid ad-hoc mechanisms to manage drug and logistic procurements and supply chain for rapid diagnostic tests, treatment regimens, essential supplies for treatment e.g. sterile water for injection, dextrose solution, syringes etc., insecticide and other commodities.

Capacity building:

Based on the presence of various stakeholders (health personnel, private sector, line ministries, etc), advocacy and capacity building plans should be developed and implemented. It is essential to train all the three levels of workers in the national programme as per their roles and responsibilities.

Above table for roles and responsibilities and relevant messages mentioned in behavior change communication chapter are important for organizing capacity building plan for the health workers and physicians.

Inter-sectoral coordination: Kala-azar is a climatic disease and occurs in rural areas therefore ministries responsible for rural development, housing, safe water, sanitation and hygiene and agriculture should be appropriately engaged in the dialogue for ‘one health policy’ which encompasses collateral benefits for reducing the disease burden by addressing socio-economic issues in those at-risk areas.

For example- decision to change the insecticide should be taken in consultation with the agriculture ministry on the use of a particular insecticide and relevant supportive data on it.

Cross-border coordination: Kala-azar and PKDL are endemic across border and following activities can be synchronized and shared for achieving a common goal of kala-azar elimination in the South-East Asia Region-

- Information on the imported cases
- Information on resident cases being treated across the border
- Information on the timing of IRS and type of insecticides used
- Information on the timing of active case detection drives

9 Chapter

Outbreak assessment and response

Kala-azar is an outbreak prone disease and many outbreaks have been reported in many endemic areas including in South-East Asia region.

WHO defines “A disease outbreak is the occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area or season. An outbreak may occur in a restricted geographical area or may extend over several countries. It may last for a few days or weeks, or for several years.”

There is no strict definition of VL outbreak as it depends on the context and epidemiology.

In Nepal, several outbreaks have been reported in the past (table below).

Table 20: **Areas with kala-azar outbreaks reported in recent years in Nepal**

Year of KA outbreaks reported	Place	Districts	No of KA cases reported
2017 (April)	Bhaktipur Ward no. 2	Sarlahi	13
2014 (January)	Majhare 1 & 7	Morang	37
2013 (May/June)	Taiwan Bastie, Ward no. 6	Sarlahi	27
2013 (April/May)	BelhiChapena Ward no. 3	Saptari	17
2012 (Nov/Dec)	Majhare Ward no. 7	Morang	21
2011	No information		
2010	No information		
2009 (April / May)	Baijnaathpur VDC Ward no. 6 & 7	Morang	19
2008 (Feb, March, April)	Taiwan Basti, Hariwan VDC ward no. 6	Sarlahi	21
2007/2008 (Dec / Jan)	Panchkanya VDC ward no. 5	Sunsari	23
2007 (March / April)	Bathanaha VDC ward no. 4	Saptari	32
2007 (April/ May)	Anarmani VDC ward no.7	Jhapa	42
2004	Pindeshwori Slum area, Dharan Municipality- 14/17	Sunsari	49

Objectives

The main objective of a kala azar outbreak investigation is:

- a) To confirm that there is indeed an outbreak of VL (i.e. temporally and epidemiologically linked, local transmission confirmed), and
- b) To determine the most effective and practical means of controlling the outbreak (= adaptation of the outbreak response to the actual, local situation) and avoid spreading to neighboring VDCs.

The outbreak investigation needs to answer the following questions:

A. Epidemiological data collection

1. Is there actually an outbreak?

- a) are all reported cases indeed VL?
- b) if yes, are they epidemiologically/temporarily linked? (e.g. all occurring within the same household or neighborhood, or common occupation etc.) suggesting that the infection by sand fly bite indeed occurred in this location. – or is there another explanation for this number of VL cases than local transmission?)
- c) Are there **more cases** than the number reported so far (underreporting)?

2. What are the characteristics of outbreak?

- a) What is the potential area where outbreak reported?
- b) Who is affected, men/women, children/adults?
- c) Is a particular population group affected (migratory population etc)
- d) Are the cases clustered or spread throughout the VDC/district?
- e) In a previously not affected community?
- f) Rural vs urban outbreak?
- g) Total number of cases reported and any mortality?

3. More specific questions for an outbreak in VL program districts (known VL endemicity):

- a) What seems to have caused the outbreak?
(= focusing on the local conditions: changes in vector population, changes in environment, changes in the host/reservoir population (malnutrition, migration, ...))
- b) What is history of VL incidence and of IRS spraying in this community? Have there been VL in the past, has the village been sprayed, since when spraying has not been done (since no more cases)

4. More specific questions for an outbreak in non-program districts (no previous history of VL incidence).

a) is there a local transmission of VL ?

In non-program districts, this is the key question, since outbreak response includes (apart from diagnosis and treatment) the implementation of vector control measures which may be difficult to implement in remote non-program locations (training, mobilization of human, logistic and financial resources)

Therefore, evidence of local transmission required, should include:

- **Travel history of the cases:** If **all** cases have a history of travel to known endemic areas in India or Nepal, then development of VL can be the result of earlier infection elsewhere, without local transmission. However, presence of **one or more cases** without travel history (such as young children), should always be considered as a sign of local transmission (secondary infection, vector-borne)
- **Leishmanin skin test (LST):** LST is done to determine acquired immunity in a population. It assesses the exposure status of the population to the infection. In general, in populations in which substantial levels of transmission have been sustained over a period of time, exposed population has acquired immunity to the parasite. This is indicated by a high prevalence of leishmanin skin test results which rises with increasing age.

Since infection is not evenly distributed in a population group, it is better to sample all the people in a village or sample close contacts of recent cases to detect micro-foci.

A positive leishmanin skin test (> 5mm diameter) is considered to be indicative of cell-mediated immunity. LST is negative during active visceral leishmaniasis and becomes positive after cure, generally after months to 1 year. A positive response is also seen after asymptomatic infection. Generally, a positive response is there for lifelong, but it can revert to negative over a period of time.

In endemic areas, the positivity rate is higher in adults than in children and it increases with age. This pattern takes long time to develop after substantial levels of transmission has been sustained and is not seen when leishmaniasis has recently been introduced in a nonimmune population.

- **Tests to detect asymptomatic infection**
 - **Direct agglutination test (IFAT and ELISA):** These are more sensitive tests to detect antibodies in asymptomatic people with visceral leishmaniasis infection at low cut-off titres. In epidemiological surveys, a combination of direct agglutination test along with more specific test like PCR, is the most practical way in detecting asymptomatic infections in the community.
 - **rK39 positivity in healthy household and village contacts:** This is a very less sensitive test to detect asymptomatics particularly when transmission is

low or in new foci. However, in areas with no previous records of VL, if healthy household contacts are found to be rK39 positive, then it can indicate a presence of local transmission, even if at the time of the investigation, no sand flies can be observed)

b) has there been any IRS spraying in the village/area (for other vector-borne diseases than VL such as malaria)?

B. Entomological data collection

In VL endemic districts in the terai lowlands, *P. argentipes*, the vector of Kala azar, is omnipresent, and local transmission after re-introduction of the *Leishmania donovani* parasite in the community (be it from a new or from a relapse VL case, a PKDL case or an asymptomatic carrier) is more than likely to reappear.

In these conditions, local transmission does not need to be proven, and entomological investigations are not necessary to launch the standard outbreak response including responsive case-based IRS spraying (see below).

However, it is recommended that the Vector Control Officer in charge of outbreak response and IRS, makes the effort to collect a limited amount of sand flies for identification and storage (for details on sand fly collection methods and preservation, see below and in annex)

Specific entomological investigations such as sand fly density studies, studies on sand fly infection rate, microbiological (genomic) sand fly identification, insecticide resistance testing etc. are not required in the investigation phase, as these are time-consuming and would delay the implementation of the immediate outbreak response imposed.

In non-VL endemic districts, the collection and identification of locally captured sand flies is a strong additional argument for local transmission. However, sand fly density may be low or zero at the time of the outbreak investigation visit, so absence of sand flies is no argument against local transmission, and epidemiological evidence as explained above (4.a) should be sufficient to launch an outbreak response.

Again, it is recommended that a short sand fly collection exercise is done by the investigation team during the visit (mouth aspiration method). As the non VL-program districts (57/75 of all districts in Nepal) do not have staff that is trained and experienced in VL and VL response, an investigation team will be identified and sent by EDCD, upon demand of the DPHO.

Capacity training in basic entomology and in VL response will be organized under KalaCORE, whereby trainees will be selected geographically, in order to have teams in each of the five Nepalese regions. Experts from BPKIHS will organize this training, and monitor outbreak

investigation and response efforts by sending a supervisor along to help and advise the regional teams on the ground (KalaCORE BPKIHS project)

Considerations in kala-azar outbreak:

Kala-azar outbreak can occur both in stable endemic areas and in new areas. In non-endemic areas, children and adults are more equally affected than in endemic areas. In stable endemic areas, infections are commoner in children or displaced persons.

While declaring outbreak following points should be considered:

- Confirm the outbreak by comparing current and previous (ideally for the previous 5 years) incidence of the disease,
- Allow for seasonal variation,
- Past epidemics
- Potential changes in completeness of reporting due to alterations in local conditions e.g. access to health- care facilities)
- Clinical skills which may overly inflate outbreak or underreport an outbreak if clinical skills are poor movement of patients
- Using a standard case definition for suspect, probable and confirmed cases

9.1 Criteria for initiation of an assessment of a possible kala-azar outbreak

Need for a criterion: following points are important considerations for the rationale of having a criterion for an outbreak:

- To identify, confirm and declare an outbreak
- To fast track detection and control measures
- To prevent mortalities by early diagnosis and treatment
- To allocate additional resources to improve medical and social services
- To contain and prevent spread to other areas
- To document, analyze and apply learnings to other areas as part of preparedness

Criteria:

In kala-azar endemic districts:

Five or more (*) laboratory-confirmed local kala-azar cases reported in a given area such as cluster/hamlet/villages or among a specific group of people within six months of occurrence of index case

In Grey districts: (there have been cases reported but it is not clear whether transmission occurs in that district or not):

Two or more (*) laboratory-confirmed local kala-azar cases reported in a given areas such as clusters/hamlet/villages or among a specific group of people, within six months of occurrence of index case should be considered as an outbreak.

(*) thresholds as proposed by the working group. Note that there is no denominator, but threshold refers to a clustering of cases in time and place. New surveillance tools such as DHIS2 should facilitate the early detection of such clustering, which in the reporting by line-listing is not easily identified (e.g. geographically clustered cases but separated by an administrative border, will be reported separately and possibly skip the attention of data managers).

Criteria to decide for additional support for an outbreak investigation:

Central level kala-azar outbreak investigation and response team may decide for additional support for an outbreak investigation if required the following information/evidences about kala-azar outbreak for planning and control measures.

1. Epidemiological related information: case validation, disease frequency, spatial distribution of cases, risk factors associated with kala-azar and others.
2. Entomological related information: sand fly vector density, species, sandfly infection rate and others
3. immunological related information: Leishmania donovani infection in healthy population of the outbreak place,

BPKIHS Dharan is a centre of excellence in tropical and infectious disease and has expertise for the outbreak investigation in the country.

9.2 Role of Surveillance System in identifying an Outbreak

Kala-azar surveillance should be capable of early detection and subsequent investigation of any suspected case of kala-azar and subsequently predicting of outbreaks in a timely manner. At present, disease surveillance is mostly passive and private sector is not covered by the surveillance system. Surveillance will be extended to non-program districts since increasing number of kala-azar cases have been reported from the districts which are not program districts. Kala-azar should be made a notifiable disease in the affected areas to improve reporting. Detection of cases of PKDL is important since they are responsible for continued transmission of the disease.

Networking with dermatologists is necessary for confirmation of PKDL cases since variable presentation of these cases requires expertise on diagnosis

Nepal has Health Management Information System (HMIS) and Early Warning and Reporting System (EWARS) for surveillance of kala-azar. Early warning about outbreaks through surveillance systems allows prompt initiation of response and control measures to prevent further spread of kala-azar. The case-based surveillance ensures detection, investigation and confirmation of every suspected kala-azar case in the community and ensures availability of information for monitoring progress. Well-defined standard operating procedures should be followed, integrating routine surveillance and detection and reporting of outbreaks. Surveillance information should be used in developing preparedness and outbreak response plans for kala-azar.

9.3 Detection and reporting of outbreaks

The definitions of a KA outbreak, as proposed above, require that health staff and district health office staff be very attentive and critical towards the collected data regarding VL. The index of 5 cases over a period of 6 months is a cumulative index, requiring that monthly reports and caseloads be interpreted taking into account the previous months. It is not defined as an incidence, as no denominator is given, but focuses on the geographical clustering, suggestive for local transmission. Therefore, it is the DHO, with its knowledge of geography and boundaries that is best placed to identify an outbreak.

The Early Warning and Reporting System at the Epidemiology & Disease Control Division, has the role to check the data at central level, and should alert the DHO when cumulative incidences appear to increase.

It is correct that the definitions lack sensitivity and specificity: 5 cases “in a given area” may be scattered around the area without any geographical linking, or the clustering of cases on both sides of an administrative border may lead to a delay in recognizing an existing geographical linking. On the other hand, unlike highly contagious infections such as meningitis, VL spreads relatively slow, giving time to prepare and implement a response.

It should also be noted that even in the event of one single isolated case of VL, a standard response is defined and should be implemented (active case finding and local spraying in the index household and surrounding households) as described in the *National Strategic Guideline on KA Elimination Program in Nepal*, EDCD 2014

Information channels:

Person(s) capable of identifying or alerting for a “possible VL outbreak”

- Vector control officer/supervisor of the respective district/public health office
- Focal person of Early Warning & Reporting System at EDCD and
- Monitoring & Evaluation Officer placed at EDCD through WHO Nepal

Whom to report a “possible VL outbreak”

- Program manager of respective District/Public Health Offices should inform EDCD of a possible or confirmed outbreak in his district (outbreak report)
- Disease control section, Epidemiology & Disease Control Division should alert the DHO in case of observed increase of VL incidence in the district (or surrounding districts).
- If increase in VL incidence observed through DHIS2, EDCD should be informed

Kala-azar Outbreak Assessment

Given the limitations of the proposed KA outbreak definition, and outbreak cannot simply be declared on the basis of an absolute number of cases, without information about population size, clustering, epidemiological linkage between cases, previous VL history in the area, sand fly presence and density, etc. which strongly influence the probability or improbability of an outbreak which implies local transmission.

Therefore, each KA outbreak based on numbers should be followed by a assessment process, that might vary from very basic and rapid, to quite specialized and resource-intensive, according to the setting.

9.4 Roles and responsibilities in the Outbreak Assessment and Response Process

9.4.1. In VL endemic districts:

In the VL program districts (currently 18 in Nepal), DPHOs and VCOs should be/have been trained in the management of VL and VL outbreaks (Surveillance, Diagnosis and treatment, active case finding, available tools for IEC/BCC, Indoor Residual Spraying campaigns – see below). As they are already familiar with VL, both the investigation of and the response to an outbreak will be their responsibility, whereby the central level Outbreak Task Force at EDCD has a merely monitoring role.

This implies that DHOs should have assigned roles for outbreak investigation (and response) and dispose of **supplies and equipment** to implement an outbreak investigation.

Step one - Verification process:

1. **The DPHO** (the Vector Control Officer or another assigned DHO team member) verifies or double-checks the data (e.g. by **contacting the public health facility** covering the area (VDC, ward) where the cases have been reported, in order to collect further data on:
 - Number of cases, age, location, past VL and travel history and epidemiological linking between cases (same household, same hamlet, etc.)
 - How and where the diagnosis was made (RDT in the PHC, or diagnosis in referral hospital?)

This may also include contacting the **private health practitioners** if applicable/relevant.

2. The DPHO consults the VL data of bordering VDCs and VDC wards, in order to determine the extension of the outbreak: Cases in bordering wards may be included as part of the outbreak due to their short distance.
3. In function of the VL history of the area affected, the **DPHO decides** whether cases need to be confirmed parasitological or whether an RDT is sufficient to diagnose active VL. *Rule of thumb: if there have been no cases of VL in the area for more than 5 years (post-elimination phase), then a parasitological confirmation is required for the first 5 cases.*
4. In absence of arguments of epidemiological linking between the reported cases (e.g. scattered randomly around the area, clearly proven import cases, cases of VL relapse after treatment) the DPHO may decide to not declare an outbreak, provided that all standard measures are put in place to avoid further transmission around the individual cases (active case finding around the index case, and focal IRS).

In the latter case, the DHO reports to EDCD to justify its decision.

Step two – Preparation for field investigation

a. Preparatory work at DPHO level

- Compilation of the collected data so far: line listing of recent cases reported, diagnostic method used, epidemiologic curve, data on previous VL incidences and the response (IRS campaigns)
- Define objectives of the outbreak investigation visit (which questions remain unanswered and how to collect this information)
- Identify investigation team in function of the objectives
- Manage supplies and equipment necessary for field work
- Administrative procedures e.g. travel documents, cash advances
- Coordination & consultation: task descriptions of team members, **identify and inform local contact persons** (administrative authorities and health staff) of the upcoming visit and its objectives

b. Supplies and equipment include:

- rK39 rapid tests, gloves, lancets (for finger prick) *or* venous blood sampling tools
- materials for sand fly collection
- forms and formats: referral forms, data collection forms, questionnaires
- leaflets & pamphlets for awareness activities to start immediately

Step three – Field work

A. Field activities in outbreak investigation

- Meeting with local authorities and local health staff to:
 - Inquire on local VL history in the area (incidence in the past, IRS efforts in the past)
- Home visit to the reported cases to:
 - Collect supplementary clinical and epidemiological data (standard questionnaire) i.e. regarding previous individual and family history of VL, travel history, concomitant diseases, exposure
 - Inquire on recent mortality in the family or surroundings (possibly VL related?)
 - Inquire on latest IRS spraying (if any) in the house and surroundings
 - In case of finding of additional clinically suspect VL cases, perform an rK39 rapid test, and refer for treatment if the test is positive.

B. Evaluate hypothesis of possible local transmission from first “index” case to the other “secondary” cases - and perform additional sampling if necessary/relevant:

- a. Search for sand flies
- b. Search for asymptomatically infected persons in household contacts and neighbors.

In areas where there has been continued VL incidence over the past years, local transmission is evident, and no additional studies are necessary. If the visit takes place during the sand fly season, sand flies can be collected for storage and later analysis.

In areas where there have been no VL reports for 5 years or more (post-elimination phase), it might be worthwhile to screen the population with rK39 rapid test of the hamlet with rK39 rapid test to see whether, in the young age groups, there has been exposure to *L. donovani* infection (shown by positive testing in persons with no history of clinical VL. Obviously, such screening will require justification and acceptance from the local community.

C. Formulate conclusions & communicate findings with local administrative authorities and health staff. This includes:

- a. Confirm that reported cases are indeed VL- (or not)
- b. Confirm that there is an outbreak with local transmission - (or not)
- c. Identify the affected area – this might include contacting also neighboring VDCs and wards.

D. Plan for outbreak response with the local administration and health staff.

This includes:

- a) Enforce active surveillance, in the affected ward **and** surrounding wards/VDCs
- b) Identify available human resources for case management + refreshment training

- c) Rapid refreshment training on active case finding for/by FCHV,
- d) Evaluate needs in terms of diagnosis and treatment (supplies)
- e) Evaluate needs and strategies for IEC/BCC to the population
- f) Evaluate needs in terms of IRS (number of houses to spray)

Step four - reporting

At return, findings, conclusions and planning must be summarized in a report to EDCD.

In the report, additional resources for investigation and/or response can be requested, e.g.

- If available outbreak response emergency stocks at DHO level are insufficient
- If doubts about vector presence, behavior, or sensitivity to the available pyrethroids (entomological support)
- Additional training needs
- Budget

9.4.2. In districts that are not included in the VL endemic districts:

In the non-VL program districts (currently 57 districts in Nepal, of which 38 reported one or more VL cases in 2015/2016), DPHOs and VCOs have not been trained in the management of VL and VL outbreaks (Surveillance, Diagnosis and treatment, active case finding, available tools for IEC/BCC, Indoor Residual Spraying campaigns – see below), and may have no clinical and management experience with VL. As they are not familiar with VL, both the investigation of and the response to an outbreak will be organized and managed from the central level, by the central level Kala-azar Outbreak Investigation and Response Committee, at EDCD.

This requires from EDCD a preparedness plan to respond to new or suspected outbreaks (in non-program districts defined as *two or more cases of VL in an area over 6 months*) by sending in an outbreak investigation team composed of trained and experienced health staff. EDCD should therefore identify and train persons **at provincial level**, who can be mobilized in relatively short time and can lead the outbreak investigation and the response with the support of the local DPHO team.

Step one - Verification process:

1. The central level kala-azar Outbreak Investigation and Response Committee (**KOIRC**) at EDCD verifies or double-checks the data by contacting the District Public Health Office covering the area (VDC, ward) where the cases have been reported, in order (for the PHO) to collect further data on:
 - Number of cases, age, location, past VL history, travel history and epidemiological linking between cases (same household, same hamlet, etc

- How and where the diagnosis was made (RDT in the PHC, or diagnosis in referral hospital?)

DPHO can collect missing or additional data from the local health staff (public and private) in the affected area, and to report back.

2. Since there have never been any cases of VL in the area, **a parasitological confirmation is required for each case**, *and this until a local outbreak is officially confirmed by KOIRC/EDCD*. Only from that moment onwards, new cases epidemiologically and spatio temporarily linked to this outbreak area, can be diagnosed on the basis of an RDT.
3. The KOIRC also consults the VL data of bordering VDCs and VDC wards, in order to determine the extension of the outbreak: Cases in bordering wards may be included as part of the outbreak due to their short distance.
4. Based on the information and data collected, the KOIRC will decide if a team must be send to the reporting district/VDC to further investigate the possible outbreak. Such outbreak investigation is only justified if there is (a strong suspicion of) epidemiological linking between two or more reported and confirmed cases. In case of doubt KOIRC can also consult national experts for advice or additional support (e.g. BPKIHS, Dharan)

Step two – Preparation for field investigation

- a. Preparatory work at EDCD KOIRC level
 - Compilation of the collected data so far: line listing of recent cases reported, epidemiologic curve, data on previous VL incidences and the response (IRS campaigns)
 - Define objectives of the outbreak investigation visit (which questions remain unanswered and how to collect this information)
 - Inform DPHO of the district about the planned visit
 - Identify investigation team in function of the objectives amongst the regionally trained staff, and inform BPKIHS' TIDC (who may delegate extra staff if possible for supervision/research purposes)
 - Manage supplies and equipment necessary for field work
 - Administrative procedures e.g. travel documents, cash advances
 - Coordination & consultation with the DPHO: task descriptions of team members, **identify and inform local contact persons** (administrative authorities and health staff) of the upcoming visit and its objectives
- b. Supplies and equipment include:
 - rK39 rapid tests, gloves, lancets (for finger prick) *or* venous blood sampling tools
 - forms and formats: referral forms, data collection forms, questionnaires

- materials for sand fly collection
- Supplies and materials for immediate response action such as insecticide impregnated bed nets (LLIN); IEC/BCC materials (leaflets& pamphlets) for awareness activities, etc.

Step three – Joint Field work with the DPHO

The central level outbreak investigation team will join the District Health Office of the affected area. Meetings will be held to summarize findings so far and work out further steps of the investigation process. With assigned staff from the DPHO, the outbreak investigation team will visit the affected VDC/wards and implement the investigation

A. Field activities in outbreak investigation

- Meeting with local authorities and local health staff to:
 - Inquire on local VL history in the area (incidence in the past, IRS efforts in the past) - *if any*.
 - Inquire on increased morbidity and mortality of unknown origin that might indicate unrecognized and unreported VL
- Home visit to the reported cases to:
 - Collect supplementary clinical and epidemiological data (standard questionnaire) i.e. regarding contacts between the reported VL cases, travel history, concomitant diseases, etc.
 - Inquire on recent unexplained mortality in the family, suggestive for VL (“Verbal autopsy questionnaire” see annex
 - In case of finding of additional clinically suspect VL cases, perform an rK39 rapid test, and refer for treatment if the test is positive.

B. Evaluate hypothesis of possible local transmission from first “index” case to the other “secondary” cases: perform additional sampling:

- a. Search for sand flies through aspiration method (see annex)
- b. Search for asymptotically infected persons in household contacts and neighbors, by population screening with RDT (see annex).

In areas where there has never been any known VL incidence, local transmission must be proven before starting an outbreak response which, by its content and by the local road conditions, will be very labor-intensive. As said earlier, a positive rK39 rapid test in healthy (= non-VL affected) family or village members (especially without travel history) is strong evidence for local transmission, even if at the time of the investigation, no sand flies can be observed)

- C. Conclusions - Communicate findings to the local administrative authorities and health staff
 - a. Confirm that reported cases are indeed VL- or not
 - b. Confirm that there is an outbreak with local transmission - or not
 - c. If indeed there is sufficient evidence for an outbreak with local transmission, Identify the affected area
 - d. Contact and inform also neighboring VDCs and wards.

- D. Plan for outbreak response with the DPHO, the local administration and local health staff. This includes:
 - a) Identify the human resources that need to be trained on diagnosis, referral or case management
 - b) Enforce active surveillance in the affected ward and surrounding wards
 - c) Rapid training on active case finding for/by FCHV, and other health workers
 - d) Evaluate needs in terms of supplies for diagnosis and treatment
 - e) Evaluate needs and strategies for IEC/BCC to the population
 - f) Define area to cover (radius or number of households around the index cases) for future Active Case Detection activities
 - g) Evaluate needs in terms of IRS (number of houses to spray), and best timing to organize such campaign (in function of road access)
 - h) Already start distribution of LLINs and IEC/BCC materials if available

Step four - reporting

At return at the DPHO, findings, conclusions and planning will be exchanged with the DPHO staff and summarized in a report. **In the report, the necessary resources for further investigation and response will be listed, e.g.**

- If available outbreak response emergency stocks at DHO level are insufficient
- If doubts about vector presence, behavior, or sensitivity to the available pyrethroids (entomological support)
- Additional training needs
- Budget

9.5 Kala-azar outbreak response and management

Key principles of the Kala-azar outbreak response

Once the Kala azar outbreak confirmed, the outbreak response is primarily the responsibility of the concerned District Public/Health Office. This is definitely the case for outbreaks in VL-Program Districts, where case management and control activities are part of the “routine” practices of the DPHO. Nevertheless, the DPHO may seek the supplementary technical support from Epidemiology and Disease Control Division (EDCD), if required.

Technical support from EDCD will be required especially in the 57 non-program districts, where VL cases are rarely reported, and therefore have no supplies or trainings to implement a state-of-the-art outbreak investigation and response. In those regions, the kala azar Outbreak Investigation and Response Committee (KOIRC) will have to take the leading role in the outbreak response, by sending in an experienced team.

In order for EDCD to be able to respond quickly and appropriately to outbreaks in non-program districts, capacity building at provincial level should be organized, so that in the future, DPHOs can rely on these experienced teams or individuals in case of outbreak on their territory.

The response to kala-azar outbreaks includes:

1. the treatment of the confirmed kala-azar cases, as well as the confirmation of diagnosis of suspected KA and PKDL cases identified during active case detection
2. active case detection of other kala-azar and PKDL cases through index case-based approach,
3. vector control activities following national guideline and vector survey,
4. advocacy and communication to ensure effective community involvement and public awareness.

These activities are described below.

Appropriate diagnostic confirmation

In case of a confirmed outbreak (i.e. with local transmission, see previous chapter) in an area where KA was not known to be endemic, or where for five consecutive years, no endemic VL cases have been reported, it is recommended that the first five new VL cases be diagnosed and confirmed by direct microscopy (on bone marrow or spleen biopsy). Once this is done, further diagnosis on epidemiologically-linked suspected VL cases in the same outbreak area, can be done on the basis of a positive rK39 RDT.

The diagnostic confirmation of suspected PKDL should be done on the basis of a Slit Skin Smear (SSS), by a trained dermatologist.

Appropriate treatment

All confirmed KA cases are to be treated following the national kala-azar treatment protocol

Active Case Detection

Index case-based approach (ICBA) should be rapidly implemented in kala-azar outbreak areas with newly detected kala-azar cases. The *index case-based approach* includes the search of new Kala azar cases as well as PKDL cases¹¹ among the households members through house-to-house visits around a house (radius of 50 meters or 100 households) of a recently diagnosed (usually in the previous 6 months) kala-azar case.

The District Public/Health Officer is responsible for implementing the kala-azar case search activities around index case in kala-azar outbreak villages through active case detection. This should be implemented as soon as possible after the declaration of the outbreak, and therefore emergency supplies for outbreaks should be present at DPHO (program districts) or easily and rapidly dispatched (non-program districts).

Step one: Preparatory activities at district level

(=immediately after confirmation of the outbreak)

1. Identify villages of kala-azar outbreak where the index case approach will be applied.
2. Make for each village, a list of the all (index) cases identified so far – with name, age, sex and detailed address of patient, and name of health post responsible for index case search.
3. If available, print out or photocopy list of all inhabitants of the hamlet/village/ward.
4. Identify and orient public health workers, VCA, VCO, laboratory technician/health volunteers in identification and referral of chronic fever cases.
5. Identify the nearest health facility (zonal hospital, provincial hospital) where VL patients can be diagnosed and treated, contact and inform this health facility about the outbreak and the ACD activities organized, assure that capacity and supplies for diagnosis and treatment are available, and define communication channels
6. Ensure availability of the necessary supplies of rk39 test kits, IEC material, referral slips, treatment cards etc. for the ACD field activities
7. Communicate planning, need for extra supplies in case of insufficient stocks at district level, and required funding to EDCD.
8. Communicate planning (date and time) of the ACD activity to the village authorities and the executing staff
9. Prepare plan for supervision and M&E of index case-based approach in an outbreak area– identify supervision team for supervision activities.
10. Define reporting system from village/community to district public/health office.

¹¹PKDL cases are suspected to be a source of persistent transmission risk in a community and therefore must be identified and treated. For diagnosis and treatment of PKDL, please see the *National Strategic Guideline for Kala-azar Elimination program in Nepal* (EDCD 2014)

Step two: Preparatory activities at health post level

(= just prior to the ACD activity, when all necessary supplies are ready)

1. Identify and orient health workers/health volunteers from HP/PHCC in supporting for identification and referral of chronic fever cases and skin lesion cases from the community.
2. Identify staff/health volunteers responsible for supporting index case-based search of neighbourhood by the district team.
3. Confirm date and time of ACD to the village/community

Step 3: Index case-based search activities

1. Review of all kala-azar cases reported by zonal/district hospital from the district, identify outbreak areas.
2. List kala-azar patients – name, age, sex and detailed address of patient, name of health post responsible for index case search. This list may need to be extended, with the new cases **identified during the ACD campaign**, around whom once again an index case-based search activity will have to be organized
3. Under the leadership of the assigned team leader of the outbreak team, D(P)HO staff visits the community of the index case, traces the home, confirms identity of the patient and alerts other health worker of HP/PHCC and FCHV.
4. Team leader of the DPHO outbreak team decides, in function of the geography and village organisation on the size of the area to cover during the ACD activity (with a radius of 50 meters or 100 households as a minimum)
5. House-to-house search around index case using screening forms or format or register.
6. Screen all individuals for fever = 2 weeks in neighbouring households in the village/hamlet around the house of index case; using rK39 RDT
7. Fill patient referral form and refer patients to district/zonal hospital for (confirmation and) treatment.
8. Maintain a list of patients referred for confirmation of KA diagnosis and treatment.
9. Inform district/zonal hospital staff of patients referred for KA diagnosis.
10. Maintain records and report to district on index case finding activities conducted.

Post index case-based search activities at district/Zonal hospitals

1. Ascertain diagnosis of all patients referred by health workers from villages with kala-azar outbreak after index case-based search.
2. Ensure that all kala-azar patients are started on treatment.
3. Monitor treatment compliance and side effects.
4. Ensure timely payment of wage-loss money to kala-azar/PKDL patients.

5. Ensure timely payment of incentives to FCHV for patient follow up.
6. Ensure availability of drugs and diagnostics at hospitals based on number of kala-azar cases.

Post index case-based search activities at district level

1. Assess monthly reports on number of kala-azar cases, drug distribution.
2. Ensure supply of drugs and diagnostics based on number of kala-azar cases reported.
3. Evaluate index case finding activities based on supervision/monitoring reports.

Post index case-based search activities at health post level

1. Inform public health workers of patients diagnosed and started with KA/PKDL treatment to ensure treatment compliance or for any side effects.

9.6 Vector Control

Outbreaks as those discussed in this guideline, obviously are not included in the yearly action plans, and therefore require supplementary resources. An emergency stock of insecticide for such events should be considered in the yearly planning if possible.

Timing of the IRS campaign in the context of an outbreak:

Depending on the time in the year when the outbreak is identified and confirmed, the DPHO and EDCD will decide if and how to include the affected area into the existing planning: i.e. into the next round of IRS already planned (be-it in round one - in April, or in round two - in July-October. If opportune, e.g. if

- an outbreak is declared just after round one (with round two still far off),
- local sand fly densities are at their peak,
- and/or road access and weather conditions leave only a small window of opportunity to organize a IRS campaign,

it is recommended to organize an emergency IRS campaign as soon as logistically possible in order to interrupt the ongoing transmission.

Targets of the IRS campaign in the context of an outbreak:

In an immediate response to the newly identified outbreak, the minimum activity should be to spray the immediate surroundings of the index case i.e. focal spraying in and around all houses of the hamlet, or at least all houses in a perimeter of 50 m around the index case house. The inside walls of huts and cattle sheds should be treated with insecticide to a height of 1.8 m.

In a second time, the hamlet/full ward should be included in next year's macro action plan of the district, and this for at least two consecutive years without new VL cases.

D(P)HO and VCA/VCO of the D(P)HO will be responsible for planning and implementation of spraying program in outbreak reported villages. HP/PHCC of the outbreak village should co-operate to ensure quality of spray and complete coverage of the households in the villages.

For further details on IRS, please check "Monitoring and evaluation **tool kit** for indoor residual spraying", WHO-TDR, August 2010

Distribution of Insecticide treated bednets (LLIN *or* long-lasting insecticide treated nets)

In addition to spraying of the households, bed nets distribution can also be conducted as part of the VL Elimination Program Strategy. In certain conditions (e.g. confirmed outbreak in remote village with difficult access, this might be the fastest way to prevent further local transmission as IRS might be difficult to organize. Household members of the outbreak villages should be provided health education on kala-azar vector, transmission of kala-azar and made aware to use personal protection measures.

9.7 Community Awareness

Advocacy and communication are outreach activities that should be part of the kala-azar outbreak response from an early stage. Outreach to affected community or population groups helps to ensure effective community involvement and public awareness, to address public concern, and to encourage cooperation with D(P)HO and EDCD. Outreach should be focused on communities or settings identified as most affected or at high risk of transmission of kala-azar. It is most effective when D(P)HO form partnerships with local community groups, health post/PHC, or nongovernmental organizations. It is important to identify persons in the community who can serve as liaisons between D(P)HO and the local population. Liaisons should be informed about characteristics of the current kala-azar outbreak and clinical symptoms of kala-azar, as well as about recommended response measures. Public health officials should work with liaisons to develop targeted education messages and materials that address community members' knowledge, attitudes, practice and beliefs regarding health care. Messages and materials should be distributed where community members who are at risk are likely to have access to them.

Various means of communication can be used to transmit messages to the community, taking into consideration characteristics of the targeted population. Involvement of health care workers from HP/PHCC in advocacy- and communication-related outreach activities is crucial for ensuring successful implementation of outbreak response measures. Messages conveyed through the outreach should be clear and concise, tailored to targeted populations, and cover the following:

- inform about the existence of kala-azar outbreak;
- explain the seriousness of kala-azar;
- describe signs and symptoms of the kala-azar;
- encourage persons with symptoms and signs of kala-azar to seek medical advice as soon as possible;
- inform about the benefits of treatment against kala-azar;
- explain vector control and personal protection.

Roles and Responsibilities – a summary

Kala-azar outbreak investigation and response will be the joint efforts of EDCD, the D(P)HO of the affected district, the HP/PHCC of the affected villages, Female Community Health Volunteers (FCHVs) of the villages and the community. There is also specific roles for the third level reference centers (STIDH, BPKIHS) in diagnosis and treatment and in research. The responsible organizations and communities will have the following specific roles and responsibilities for kala-azar outbreak investigations and responses:

Role of EDCD

- a) EDCD will be the central level authority to liaise with D(P)HO and community level health facilities for initiation of outbreak investigation and response activities. Director of EDCD along with Disease Control Section of EDCD based on previously mentioned definitions will suggest D(P)HO to conduct outbreak investigations.
- b) Disease Control Section of EDCD will co-ordinate with D(P)HO to manage logistics including rK39 test kits, drugs for treatment and other necessary supplies for outbreak investigation and response.
- c) If special survey of outbreak including tracking of transmission dynamics, genotyping of parasites and xenomonitoring of collected sandflies, then Epidemiology and Disease Control Division (EDCD) appoints additional team of Epidemiologist, Microbiologist and Entomologist to support the district outbreak investigation team.
- d) Central level kala-azar investigation and response committee at EDCD will provide technical support to the district team.

In districts that are not considered as endemic, i.e. that are no “program districts”, and therefore do not have the necessary experience, training and supplies to launch an outbreak investigation and to set up an outbreak response, EDCD will identify a provincial outbreak investigation and response team, composed of persons who have been selected and trained for this. This investigation team will take the leading role on the ground in collaboration with the local D(P)HO.

Role of D(P)HO

- a) District Public/Health Office will be the primary responsible authority to conduct kala-azar investigation and response in VL program districts. In non-program districts, this role will be shared with or delegated to the KA outbreak investigation and response team sent by the EDCD.
- b) Co-ordination with EDCD at the central level and HP/PHCC at the peripheral level will be the responsibility of D(P)HO.
- c) D(P)HO will identify potential outbreak villages based on kala-azar case reports from the district. Focal person of kala-azar control program under D(P)HO will collect monthly reports from hospitals and will prepare VDC wise line lists of kala-azar cases.
- d) If case definition of kala-azar outbreak is met, VCA/VCO will inform District Public/Health Officer and start planning for outbreak investigation and response.
- e) An outbreak investigation team will be formed and required logistics will be secured.
- f) The kala-azar outbreak investigation team will verify the outbreak through conducting case investigation and case verification. The team doctor will clinically examine the kala-azar suspected cases as well as skin lesions suggestive for PKDL around the index cases and the laboratory technologist will collect blood samples and perform rK39 test.
- g) The entomology team including VCA/VCO will be in charge of collecting sand flies (aspiration method).
- h) Contact tracing of suspected kala-azar cases with index cases will be conducted by the investigation team.
- i) Outbreak investigation team will refer kala-azar and PKDL positive cases from outbreak villages to the District/Zonal/BPKIHS/STIDH hospitals for the confirmatory diagnosis and treatment.
- j) IRS, distribution of bed nets and community awareness activities will be conducted by D(P)HO.
- k) D(P)HO will submit report to EDCD within one month of completion of investigation and response activities in prescribed format as given in this guideline.
- l) Further, D(P)HO should report daily activities conducted in outbreak village on weekly basis to EDCD.

Role of HP/PHC

- a) HP/PHCC will help the district outbreak investigation and response team to identify the villages with kala-azar outbreak.
- b) HP/PHCC will support in active case detection of kala-azar and PKDL cases based on index cases-based approach.
- c) HP/PHCC will support in vector control activities and awareness rising among community people.

Role of FCHVs

- a) FCHVs will support in identifying villages and households for active case detection.
- b) FCHVs will inform households of their respective wards to participate in active case detection.
- c) FCHVs will support in spraying, bed nets distribution and awareness activities.

Role of community people

Community people will support in kala-azar outbreak investigation and response team for implementation of activities.

Role of level III health institutions and special referral centers (e.g. STIDH, BPKIHS)

Referral hospitals with VL experience have a specific role of confirming the diagnosis of VL by direct microscopy (demonstration of *Leishmania donovani* (LD) bodies by microscopy, on spleen or bone marrow aspirate, and if negative, culture and or PCR. Confirmation with direct methods is necessary in suspected VL cases from an area with no former known endemicity for VL, or if cases haven't been reported for more than three years (post-elimination phase). Referral hospitals also have the expertise in diagnosing PKDL.

9.8 Report of the Outbreak

Analysis of outbreaks can provide useful information regarding factors that may have facilitated kala-azar outbreak occurrence. The investigation may help to identify risk factors for infection and provide information that can be used to refine and improve programmatic aspects of the elimination program. In addition to ongoing analysis during the outbreak, final analysis should be performed at the end of the outbreak to prepare the report. Forms of report include verbal reports to the outbreak coordination team, verbal and written progress reports to EDCD, information briefings for the media/public, and the final report. The information briefing for the media/public should be done by EDCD. The final report of the outbreak should be prepared within one month of outbreak investigation.

The findings, including recommendations on strategies for improving preparedness, surveillance, specific high-risk areas and populations, should be disseminated as a written report to all stakeholders and partners, in order to prevent future outbreaks. Lessons learnt from an outbreak response can provide valuable information for updating and improving kala-azar outbreak response plans.

Structure of Outbreak Investigation Report

1. Summary
2. Background
3. Investigation Methods
4. Results
5. Control Measures

6. Conclusion/Discussion
7. Recommendations
8. References
9. Appendices

The **summary** of the report should include date and place of kala-azar outbreak, number of risk population residing in the VDC, numbers of suspect, probable and confirmed cases, number hospitalized, number of deaths (if any), key statistics, control measures applied, and recommendations.

The **background** part of the report should describe the context of the outbreak including the size and composition of population affected (WHO), any recent demographic changes, location/place/setting (WHERE), a map of the community, time of onset (WHEN), description of clinical findings (WHAT), and suspected or known risk factors (WHY). It should also include primary objective(s) of the kala-azar outbreak investigation.

The **investigation methods** of the report should include the following:

- Epidemiologic investigations
 - Case definition
 - Diagnostic/laboratory criteria
 - Time and place of kala-azar outbreak
 - Case finding or investigation process
 - Epidemiological studies
 - Hypothesis generation
 - Descriptive study
 - Analytical case control study
 - What population was considered to be at risk?
 - What and how much data was collected?
 - From whom and from how many people were data collected?
 - By whom were data collected?
 - How were case definition(s) developed and used?
 - How was the well comparison group selected, and how many people were in it?
- How were data collected and analyzed?
 - Records reviewed
 - People interviewed

- Questionnaires developed and distributed
- Questionnaire reliability and validity
- Microbiological investigations for parasite
 - Laboratories involved
 - Type of specimens and source (blood samples and biopsies)
 - Type of tests and laboratory methods (rK39 test and biopsy)
 - What laboratory standards were used?
- Entomological investigations
 - Sandfly density monitored, distribution and insecticide resistance of vectors
- Environmental investigations
 - Where, by whom and how were environmental inspections done?

The **results** section of the report should include:

- Epidemiological
 - Descriptive epidemiology results including:
 - ▶ Study population
 - Cases
 - Demographic data
 - Clinical data (symptoms, signs, duration of illness, incubation period, travel history)
 - Outcome of illness (hospitalization, death, chronic effects)
 - ▶ Location of cases (facility, VDC, ward, etc.)
 - ▶ Epidemic curve with histograms and other graphs
 - ▶ Compare characteristics of cases and controls, if applicable
 - ▶ Describe VDC population, if applicable
 - ▶ Describe the results of analytical studies
- Microbiological
 - Number and nature of specimens submitted for testing
 - Results of laboratory testing
- Environmental
 - Describe observations and pertinent findings from environmental investigation(s)
 - Describe the results of trace-back investigations.

Key statistics that should be used in outbreak data analysis:

- Attack rate (if available)
- Hospitalization rate
- Death rate
- Frequency distribution of symptoms
- Median date of exposure
- Median date of onset
- Average incubation period
- Average duration of illness
- Average duration of hospitalization
- Results of statistical probability testing

The report should include the **control measures** adopted for outbreak response. This section of the report should answer what methods were used for outbreak control, how were they implemented, where, when and by whom were they implemented, how was their effectiveness measured, and how effective were they.

Conclusion and discussion section of the report should include analysis and interpretation of the investigation results and any conclusions drawn as a result of the investigation, discussion on main hypothesis, description of the likely causative agent and mode of transmission, the risk factors, what was done to control the outbreak, and the lessons learned.

The **recommendations** should be related to controlling disease and/or preventing/mitigating exposure, measures to control the outbreak, suggestions to improve investigation and management of such outbreaks in the future, measures to prevent such outbreaks in the future, and educational message to the public, public health professionals and policy makers.

General instructions:

- Outbreak report should be completed within one month of closing the outbreak investigation and response.
- Personal identifying information need not be mentioned.
- No attribute of any specific information to a specific individual/facility.

In **appendices**, outbreak investigation team, questionnaire and laboratory format should be kept as extra information.

10 Chapter

Assessment of districts where endemicity is not confirmed and associated actions

Current situation

a) Endemic Districts

« program » districts = endemic districts prioritized by the national KA elimination programme.

There are 18 endemic districts, in 5 different regions.

Table 21: **List of the 18 KA endemic districts, Nepal, 2018**

GID_3	Country	Province	District	HASC_3	KA cases 2017
NPL.1.2.1_1	Nepal	PR2	Dhanusa	NP.MM.DN	5
NPL.1.2.3_1	Nepal	PR2	Mahottari	NP.MM.MH	11
NPL.1.2.5_1	Nepal	PR2	Sarlahi	NP.MM.SA	24
NPL.1.3.1_1	Nepal	PR2	Bara	NP.MM.BA	1
NPL.1.3.3_1	Nepal	PR2	Makwanpur	NP.MM.MK	6
NPL.1.3.4_1	Nepal	PR2	Parsa	NP.MM.PR	
NPL.1.3.5_1	Nepal	PR2	Rautahat	NP.MM.RT	1
NPL.2.1.1_1	Nepal	PR1	Bhojpur	NP.PW.BJ	7
NPL.2.1.3_1	Nepal	PR1	Morang	NP.PW.MO	20
NPL.2.1.5_1	Nepal	PR1	Sunsari	NP.PW.SN	11
NPL.2.2.2_1	Nepal	PR1	Jhapa	NP.PW.JH	5
NPL.2.3.2_1	Nepal	PR1	Okhaldhunga	NP.PW.OK	3
NPL.2.3.3_1	Nepal	PR2	Saptari	NP.PW.ST	6
NPL.2.3.4_1	Nepal	PR2	Siraha	NP.PW.SR	15
NPL.2.3.6_1	Nepal	PR1	Udayapur	NP.PW.UD	3
NPL.3.2.5_1	Nepal	PR7	Kailali	NP.SP.KL	3
NPL.4.1.5_1	Nepal	PR6	Surkhet	NP.MP.SU	17
NPL.5.3.5_1	Nepal	PR5	Palpa	NP.PM.PL	17

b) **Endemicity concept**

An area is considered as endemic if at least 1 new indigenous confirmed KA case has been reported and the whole cycle of transmission has been demonstrated.

The “demonstration” of the existence of the whole cycle of transmission may be challenging and costly as it requires to confirm the presence of the vector (entomological survey), the parasite, both in humans (at least 1 confirmed case) and in the vector (competent vector and infected vector), and the seropositivity of non-sick people, which shows that the parasite has been circulating. Ideally, the endemicity assessment should be conducted in all the non-endemic and endemicity doubtful districts which have been reporting new indigenous KA cases, in order to prove the endemicity of the disease.

c) **Definitions of endemicity:**

However, while waiting for the endemicity assessment following standard definitions are used to describe endemicity:

Endemicity status

▶ **Endemic:**

Full cycle of transmission has been demonstrated at any given time (maintained population of competent vector + parasite reservoir + locally-acquired cases) AND at least 1 locally-acquired case in the last 10 years.

▶ **Endemicity doubtful:**

Full cycle of transmission has never been demonstrated BUT at least 1 locally-acquired case in the last 10 years

OR

Full cycle of transmission has been demonstrated at any given time, BUT no case has been reported in the last 10 years (0 case or no data)

▶ **Non-endemic:**

- Previously reported cases: Full cycle of transmission has not been demonstrated AND no locally-acquired case has been reported in the last 10 years BUT locally-acquired case has been reported earlier
- At risk: No locally-acquired case has ever been reported but epidemiological risk factors are present (a competent vector population, a reservoir, and appropriate environmental conditions).
- No autochthonous cases reported = No locally-acquired case has ever been reported

Endemicity status can be applied to any defined and circumscribed geographical area or implementation unit: countries, regions, districts, villages, community. It is advised to use the smallest geographical or administrative sub-national resolution available.

- ▶ **A focus:** is defined as any circumscribed geographical endemic area. Bear in mind that leishmaniasis cases can be infected in a given focus but can be reported in another location because of travel or access to health care.
- ▶ **New focus:** a focus (see definition above) where leishmaniasis transmission had not been reported for at least the last 10 years.
- ▶ **Outbreak:** As per WHO “a disease outbreak as the occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area or season. An outbreak may occur in a restricted geographical area or may extend over several countries. It may last for a few days or weeks, or for several years.”

ANNEXURE

ANNEXURE

A. Procedure for Testing, Interpretation of the Result and Storage of Test Kits (rK39)

Points to remember:

- The test should be performed as per the manufacturer's instructions.
- It is preferred that the tests should be performed in serum as opposed to whole blood.
- The vial or the pouch of the test kits should be checked for expiry date to ensure that the test strips have not expired.
- The strip should be taken out from the vial or the pouch only at the time of performing the test.
- If the strip has not been used within one hour of taking out from the vial or the pouch, it should be discarded.

Procedure:

- Remove the test strip from the pouch or the vial.
- With a new lancet, prick the finger tip of the patient suspected to be suffering from kala-azar. Lancets should not be re-used because of the risk of transmitting HIV and Hepatitis B and C.
- Let the blood come out on its own. Do not use pressure or squeezing for obtaining blood.
- Place one drop of blood or serum (as indicated in the manufacturer information sheet) on the absorbent pad of the strip bottom.
- Place the test strip into a test tube so that the end of the strip is facing downwards. This would encourage the blood to migrate upwards by capillary action. Follow the recommendations made by the manufacturer to obtain the best results.
- Add 2-3 drops of buffer solution provided with the kit to the pad.
- Read the results in 10 minutes. Do not read the results before or after 10 minutes. If the time period of 10 minutes is not adhered to there are chances of mistake being made.
- Use universal precaution for infection prevention



Interpretation of the results:

The rK39 test stays positive in the patients who had KA infection for a long time after the treatment. The dipstick test can be positive in healthy persons from endemi careas who are infected with leishmania but not sick. Therefore, the test should be performed only in a clinically suspected case of KA, who has a first-time episode.

Positive result:

The test is positive if both the control and test lines appear. A faint red line is to be considered as a positive result.

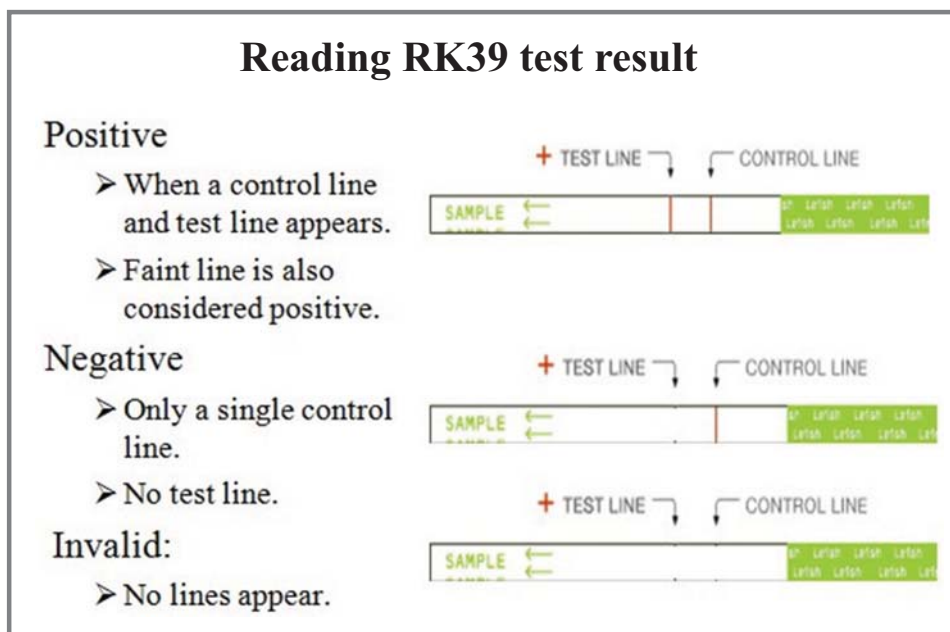
A red line appears in the control line where the blood/serum was placed, and another red line appears where the blood has migrated through capillary action. The red line appears in the control line a little distance away from where the blood\serum was placed. Thus, there should be two red lines for the test to be positive.

Negative result:

The test is considered as negative if there is a red line where the drop of blood was placed but there is no red line where the blood has migrated by capillary action at the end of 10 minutes.

Invalid result:

The test is considered as invalid if no control line appears whether the test line appears or not. There is no red line at the place where the drop of blood was placed or in the test area where the blood is to migrate by capillary action. The test is also invalid if there is a red line in the test are a but no red line in the control area where the blood was initially placed. If the test is invalid, a fresh sample with a new strip is recommended for retesting for which the correct procedures should be strictly followed.



Storage of rK39 test Strips:

- The test strips and the buffer should be stored safely at room temperature between 20 and 30 degrees Celsius since the temperature in excess of 30 degrees can reduce the quality of the test.
- The test strips and the buffer should not be frozen since freezing deteriorates the quality of the reagent.

Note:

It is not advisable to store large quantities of ‘rK39’ test kits in the peripheral locations since it is difficult to maintain appropriate temperature. However, the test kits can be stored for a long time in identified central locations in the districts where the temperature can be properly maintained as required in the specifications. These locations should serve as the supply points for the peripheral units. The supplies can be made once in a month or when health workers come for a review meeting.

B. Bone Marrow Aspiration

The bone marrow aspiration is done by a bone marrow puncture. The sites for bone marrow aspiration are manubrium sterni, iliac crest or tibia. The most common site is sternum. Before doing the procedure, blood should be checked to make sure that there is no bleeding or clotting disorder. This can be done by the estimation of platelet count and determination of prothrombin time. If these are abnormal then bone marrow aspiration should not be done until the tests are within safe limits. The test should be avoided in severely anemic patients.



Procedure:

- ▶ Ask the patient to lie down on the back.
- ▶ As a part of the preparation of the site, shave the hair and clean the part thoroughly with savlon.
- ▶ Give an injection of local anesthetic 2 percent solution at the aspiration site as the injection is made prior to the procedure.
- ▶ Check to make sure that the sensations are blunted.

- ▶ The aspiration is done with a sterilized sternal puncture needle which is short and stout with a well-fitting style to make sure that the needle does not pierce too deep.
- ▶ Once the needle has pierced the periosteum, there is a feeling of loss of resistance needed to push the needle. At this point a negative suction should be done to suck the bone marrow out.
- ▶ The needle is then withdrawn carefully and the material sucked put in to a sterile tube.
- ▶ In contrast to the splenic aspirate, the bone marrow has blood mixed with the bone marrow. One drop of the material aspirated should be placed on a glass slide about 1 cm from the edge of the slide.
- ▶ With a micro pipette or by a filter paper, the blood should be sucked out by the filter paper. This is because the presence of blood can interfere with identification of LD bodies.
- ▶ Use the edge of another slide as a spreader to make a thin smear of the bone marrow. While making a thin slide, make sure to prepare a trail of marrow cells.

C. Splenic Aspiration

Before doing the splenic aspiration, it is important to make sure that the patient does not have a bleeding or clotting disorder. This can be ensured by doing platelet and prothrombin time estimations and assessments of bleeding time and clotting time. If these are abnormal then the splenic aspiration should not be done. If the patient has a local infection at the site where the aspiration is planned, the test should not be done until the infection has been treated. Do not perform a splenic puncture if the patient is severely anaemic.

Procedure

- ▶ Clean the skin at aspiration site thoroughly the same way as for a surgical procedure. It should be dry when the aspiration is done.
- ▶ Use a 5 ml syringe and 21- gauge needle for the procedure.
- ▶ Withdraw the plunger of the syringe about 1ml to create negative suction.
- ▶ Pierce the skin and puncture the spleen by pushing the needle deep. Maintain the suction all the way while injecting and withdrawing so as to maintain a negative suction.
- ▶ Coordinate the procedure such that the diaphragm does not move while the procedure is being carried out. The procedure becomes difficult in young children who may not keep still during the procedure.
- ▶ Expel part of the material sucked on the side of a sterile culture tube, label the culture tube and transport it to the microbiology laboratory for examination.
- ▶ The other part of the material sucked should be placed on a clean slide about 1 cm from the edge and a thin smear made of the aspirate.
- ▶ After the procedure, keep the patient under close observation.

- ▶ Observe the pulse, respiratory rate and measure the blood pressure every half an hour for any complications.
- ▶ The patient should be kept under observation for a period of 12 hours after the procedure.

D. Microscopy of Tissue Aspirates for *Leishmania donovani*

The slides collected should be labeled to facilitate the identification of the patient. Write the patient's name, identification number and the date on which the slide was prepared. Each slide should be fixed before staining. This can be done by dipping the slide in methyl alcohol for 20 minutes. The slides can be stained by using Leishman's stain or Geimsa's stain. These stains are available commercially but can also be prepared locally. It is preferable to use commercially available stains since there can be variations in quality if each laboratory prepares its own stains.

The air-dried slides or properly fixed slides should be transferred to a jar containing Geimsa's stain diluted with 15-20 volumes of buffer. The slides then should be kept upright to dry and allow the stain to dry out. If Leishman's stain is used, the slide should be kept horizontally on a slide rack or on a tray with the help of two glass rods using them as a support. After placement, the slide is flooded with the stain for about 30-60 seconds and then by adding double the volume of water. After this, the slide should be allowed to stain for a period of about 5-7 minutes. The slide should then be washed in a stream of buffered water until it acquires a pinkish tinge. After this, the slide should be kept vertically to dry out. The stained slides should be examined for LD bodies under a good quality microscope with 10 x eye piece and 100 x oil immersion lenses.

Table 22: **Grading of parasite density:**

Grade	Average parasite density
6 plus	More than 100 parasites/field
5 plus	10-100 parasites/field
4 plus	1-10 parasites /field
3 plus	1-10 parasites/10 fields
2 plus	1-10 parasites/100 fields
1 plus	1-10 parasites/1000 fields
0	0 parasites/1000 fields

Standard operating procedure for parasitological diagnosis (adopted from WHO manual for case management of cutaneous leishmaniasis in the Eastern Mediterranean Region¹²)

Skin sampling

1. Prepare the part/lesion and clean the whole lesion and its border using 70% alcohol at least 3 minutes before injecting the anaesthetic.
2. Inject 0.1–0.5 ml of lidocaine with adrenaline, using a short 23-gauge needle thereby creating a blanching area. It is not necessary to anaesthetize the whole lesion. For lesions on fingers or toes use lidocaine without adrenaline (due to risk of necrosis).
3. Pinch strongly the lesion to further prevent bleeding.
4. Remove the crust, remove blood with a gauze, scratch firmly (using a sterile scalpel with a short-angle curved blade) the border and the centre of the lesion until tissue material is visible on the blade.
5. Gently move the blade on the surface of a slide to deposit a thin layer of the scraped material. Repeat the procedure on different parts of the anaesthetized zone until at least half of the surface of each of three slides is covered with material.
6. Dry the three slides at room temperature (>3 minutes).
7. Fix the slides and stain them with Giemsa according to validated procedures.

Giemsa staining

Materials

- Reagents:
 - Giemsa stain
 - Giemsa buffer
- Supplies:
 - Glass slides, alcohol washed
 - Glass marker

¹²Manual for case management of cutaneous leishmaniasis in the WHO Eastern Mediterranean Region
http://applications.emro.who.int/dsaf/EMROPUB_2013_EN_1590.pdf

- Equipment:
 - Microscope, binocular with mechanical stage; low (10×), high dry (40×) and oil immersion (100×) lens.
 - Procedure
 1. Fix air-dried slides in methanol by dipping the slides briefly (two dips) in a jar containing methanol.
 2. Remove and let air dry.
 3. Stain with diluted Giemsa stain (1:20 vol/vol) for 20 minutes. For a 1:20 dilution, add 2 ml of stock Giemsa to 40 ml of buffered water in a jar.
 4. Wash by briefly dipping the slides in a jar of buffered water (one or two dips).
 5. Let air dry.
 6. Examine the slides under the microscope (100× oil immersion lens).
 7. Read smears for at least 20 minutes (1000 fields) at 400× or 1000× magnification.
 8. A smear can be reported positive when at least two amastigotes are observed.
 9. For valid identification, an amastigote form must show a nucleus, a kinetoplast and a plasma membrane.

Standard operating procedure for cryotherapy and intralesional injection of antimony

Swab the lesion with antiseptics several minutes before starting the procedure. Repeat the procedure once a week, until complete healing of lesions. Generally, three to five sessions are sufficient to cure most lesions.

Cryotherapy

Apply the liquid nitrogen (-195°C) on the lesion and up to 2 mm outside the lesion margin, ideally with a sprayer, alternatively with a cotton-tipped applicator, until a 10-second blanching is obtained.

When cryotherapy is applied before an intralesional injection of antimony, one 10-second blanching is enough. When cryotherapy is applied alone, the procedure is repeated two or three times at short intervals, resulting in a total time of 30 seconds.

Intralesional injection

- Withdraw aseptically the product directly from the ampule of antimony as formulated for parenteral administration by the manufacturer.
- Inject the antimony (immediately after liquid nitrogen application) into the lesion and induce blanching of the borders, until the lesion is entirely swollen.

Standard operating procedure for thermotherapy

Thermotherapy is an available technique for the treatment of cutaneous leishmaniasis patients by application of local heat at the site of lesion with a portable, battery operated, localized current field radiofrequency generator (Thermo Med 1.8; Thermo-surgery Technologies).

Indication

- Papule, nodule or ulcer <4 cm
- Number of lesions < 4
- Location of the lesion should not be close to the eyes, nose or lips.

Method

A single thermotherapy treatment (one or more applications of localized heat of 50°C for 30 seconds, depending on lesion size). The area between the electrodes covers 49–73 mm². Therefore, several thermotherapy applications may be required to cover a lesion.

Procedure

- Disinfect the lesion and 2 cm border of healthy skin around the lesion with antiseptic (e.g. 0.1% chlorine dioxide solution).
- Anaesthetize the lesion with 1% lidocaine HCl.
- Moisturize the lesion with sterile saline solution.
- Apply the heat locally for 30 seconds.
- Apply chlorine dioxide gel to the lesions and then cover them after treatment.

Patient follow-up

To evaluate the outcome of thermotherapy, follow-up after completion of treatment should be scheduled at 14, 30, 45 and 180 days. It will be important to explain to patients that in case the lesion does not improve they should return to the health facility at any time.

SOP for reconstitution and dilution of Liposomal Amphotericin B (AmBisome™) (Single dose of AmBisome @10 mg/kg)

Objective of SOP: To prepare AmBisome for infusion accurately and with proper aseptic precaution.

Scope and applicability:

1. To administer AmBisome by infusion in a visceral leishmaniasis patient
2. Hypersensitivity test to AmBisome

Logistics required:

1. An aseptic area in which medicine is reconstituted (there is no preservative or bacteriostatic agent present in AmBisome)
2. Disposable syringe (1 ml & 20 ml) with sterile needle (19G)
3. Distilled/ Sterile water for injections
4. Disposable infusion set (Paediatric & adult)
5. 70% isopropyl alcohol/ spirit
6. 5% DA (500 ml) bottle/ pouch
7. Disposable hand gloves
8. AmBisome vial
9. A 5 micron syringe filter (comes with AmBisome pack)
10. Permanent marker
11. Infusion stand
12. Emergency medicine kit

Dose calculation: An example for a patient of 47 kilogram

- ▶ Dose given: 10 mg/kg single dose
- ▶ AmBisome needed: $47 \times 10 = 470$ mg

Each AmBisome vial contains 50 mg of amphotericin

- ▶ Vials needed: $470 \text{ divided by } 50 = 9.4$; thus 10 vials needed

Each vial after constitution with sterile water contains 4 mg/ml concentration of the reconstituted AmBisome

- ▶ The volume of reconstituted AmBisome to be withdrawn for further dilution in 5% dextrose: is calculated by dividing 470 mg by 4 = 117.5 ml
- ▶ Total volume (5% dextrose plus AmBisome) of fluid needed to obtain minimum concentration of 0.2 mg/ml:
 - Divide 4 mg/ml (reconstituted concentration) by 0.2 mg/ml (concentration needed) = 20
 - 117.5 ml (volume of amphotericin) x 20 = 2350 ml total volume
 - Thus: 117.5 ml of AmBisome solution needs to be added to 2232.5 ml of 5% dextrose will result in a 0.2 mg/ml concentration
- ▶ Same calculation method is adopted for maximum concentration of 2 mg/ml
- ▶ 1 ml = 0.05 drops; infuse the fluid over 120 minutes

Preparations:

1. Choose a sterile area for preparation of AmBisome
2. Wash your hands with soap and water vigorously before preparation. Take proper aseptic precaution. Wear a pair of gloves.
3. Take 12 ml of sterile water/distilled water in a 20 ml disposable syringe (marked up to 12ml)
4. Remove the rubber cap of the AmBisome containing vial
5. Push the distilled water into one 50 mg AmBisome vial gently
6. Shake the vial immediately and vigorously for 30 seconds to completely disperse the AmBisome
7. Inspect the vial visually for particulate matter and continue shaking until complete dispersion is obtained
8. Avoid forming foams and allow bubbles to dissipate before use
9. Follow the same instruction for the next vial to be reconstituted using the same syringe; calculate the total number of vials based on body weight according to the Table given below.
10. Take 0.25ml of reconstituted AmBisome in another 1 ml disposable syringe and dilute it up to 10 ml with 5% DA for hypersensitivity test
11. Calculate the volume of 5% DA to dilute the whole dose of AmBisome according to the patient's body weight using the table given below
12. Now hang the 500ml pack of 5% DA on an infusion stand
13. Fix an infusion set with the 5% DA bottle/pouch. Keep the required volume of 5% DA in the bottle/ pouch and discard the excess amount of 5% DA
14. Take another syringe to pull the reconstituted AmBisome from the vial and set a syringe filter on it

15. Wash the pack/bottle surface with a ball of cotton soaked with chlorohexidine at the site of injecting the reconstituted AmBisome
16. Inject the drug into that 5% DA solution
17. Use one syringe filter for one vial of AmBisome
18. Inject the total volume of reconstituted AmBisome in that 5% DA solution in the same manner
19. Mark the bottle/pouch with important details by a permanent marker
20. Follow strict aseptic precaution from preparation site to infusion to the patient

Procedure:

1. Explain the procedure to the patient
2. Wash your hands with soap, take proper aseptic precaution and wear gloves
3. Bind the tourniquet in the arm of the patient, take cotton soaked with chlorohexidine, rub the site of injection and wait until it is dried up
4. Take the IV cannula, prick the vein ensuring it is well placed. Fix the cannula with micro-pore filter.
5. Take the syringe loaded with the test dose of AmBisome (prepared according to the ‘SOP guideline for Preparation of AmBisome’) just prior to use in a patient
6. Start pushing the plunger very slowly and give the whole 10ml of test dose AmBisome in 10 min using the cannula. At the end of administration, seal the open end of the cannula by putting the white cap on it. Do not close the iv channel or infuse 5% DA slowly.
7. While administering the test dose of AmBisome look for any hypersensitivity reaction.
8. After finishing the test dose wait for 30 min and observe the patient for adverse drug reaction
9. If any hypersensitivity reaction occurs the patient should not receive AmBisome infusion, give:
 - a. Tab. chlorpheniramine (4mg) in adult or 1-2mg/kg body weight in children orally.
 - b. Tab. paracetamol (500mg) in adult or 15-20mg/kg body weight in children orally
10. If the symptoms don't disappear, measure/record vital signs of the patient and call the physician
11. If there are no symptoms or signs of hypersensitivity reaction after 30 min, take a disposable infusion set, fix it with the bottle/pack containing Measured Total dose of AmBisome diluted in 5% DA (refer to the ‘SOP for AmBisome Preparation’ to measure the dose of AmBisome and dilution in 5% DA)
12. Label the bottle/pouch with name of the patient, dose of AmBisome, time of starting and drops per min to be infused. Calculate drops/min to give the whole volume in 2 hours

13. Start the IV channel very slowly initially and observe the patient closely for any adverse drug reaction for first 30 min and continue observing the condition of the patient every 30 min
14. Discard all the sharp and soft instruments in appropriate waste disposal containers
15. At the end of the administration seal the open end of the cannula with the white cap and remove the infusion set and the dextrose pouch/bottle
16. The physician will check/record the vital signs of the patient at the end of administration
17. Continue checking the vital parameters of the patient every 30min
18. Inform the physician if patient has any complaints; s/he will examine/record/manage the condition accordingly in compliance with the protocol
19. Report any adverse event to appropriate authority using the appropriate form

Reference: Leaflet provided with the AmBisome vial

Table 23: **Volume of reconstituted AmBisome and 5% DA according to body weight**

Dosage chart for single dose AmBisome 10 mg/Kg

Weight of the patient in Kg	AmBisome needed (@dose 10 mg/Kg)	No of vials (each AmBisome vial contains 50 mg amphotericin B)	Concentration of the reconstituted AmBisome with sterile water (=AmBisome needed/4 mg)	To make up minimum concentration 0.2 mg/ml [divide 4 mg/ml reconstituted concentration by 0.2mg/ml = 20]		To make up maximum concentration 2 mg/ml [divide 4 mg/ml reconstituted concentration by 2mg/ml = 2]	
				Volume of 5% dextrose needed (ml)	Total volume (ml) (AmBisome plus 5% dextrose)	Volume of 5% dextrose needed (ml)	Total volume (ml) (AmBisome plus 5% dextrose)
5	50	1	12.5	237.5	250	12.5	25
6	60	2	15	285	300	45	60
7	70	2	17.5	332.5	350	52.5	70
8	80	2	20	380	400	60	80
9	90	2	22.5	427.5	450	67.5	90
10	100	2	25	475	500	75	100
11	110	3	27.5	522.5	550	82.5	110
12	120	3	30	570	600	90	120
13	130	3	32.5	617.5	650	97.5	130
14	140	3	35	665	700	105	140
15	150	3	37.5	712.5	750	112.5	150
16	160	4	40	760	800	120	160
17	170	4	42.5	807.5	850	127.5	170
18	180	4	45	855	900	135	180
19	190	4	47.5	902.5	950	142.5	190
20	200	4	50	950	1000	150	200
21	210	5	52.5	997.5	1050	157.5	210
22	220	5	55	1045	1100	165	220
23	230	5	57.5	1092.5	1150	172.5	230
24	240	5	60	1140	1200	180	240
25	250	5	62.5	1187.5	1250	187.5	250
26	260	6	65	1235	1300	195	260
27	270	6	67.5	1282.5	1350	202.5	270
28	280	6	70	1330	1400	210	280
29	290	6	72.5	1377.5	1450	217.5	290
30	300	6	75	1425	1500	225	300

31	310	7	77.5	1472.5	1550	232.5	310
32	320	7	80	1520	1600	80	160
33	330	7	82.5	1567.5	1650	82.5	165
34	340	7	85	1615	1700	85	170
35	350	7	87.5	1662.5	1750	87.5	175
36	360	8	90	1710	1800	90	180
37	370	8	92.5	1757.5	1850	92.5	185
38	380	8	95	1805	1900	95	190
39	390	8	97.5	1852.5	1950	97.5	195
40	400	8	100	1900	2000	100	200
41	410	9	102.5	1947.5	2050	102.5	205
42	420	9	105	1995	2100	105	210
43	430	9	107.5	2042.5	2150	107.5	215
44	440	9	110	2090	2200	110	220
45	450	9	112.5	2137.5	2250	112.5	225
46	460	10	115	2185	2300	115	230
47	470	10	117.5	2232.5	2350	117.5	235
48	480	10	120	2280	2400	120	240
49	490	10	122.5	2327.5	2450	122.5	245
50	500	10	125	2375	2500	125	250
51	510	11	127.5	2422.5	2550	127.5	255
52	520	11	130	2470	2600	130	260
53	530	11	132.5	2517.5	2650	132.5	265
54	540	11	135	2565	2700	135	270
55	550	11	137.5	2612.5	2750	137.5	275
56	560	12	140	2660	2800	140	280
57	570	12	142.5	2707.5	2850	142.5	285
58	580	12	145	2755	2900	145	290
59	590	12	147.5	2802.5	2950	147.5	295
60	600	12	150	2850	3000	150	300
61	610	13	152.5	2897.5	3050	152.5	305
62	620	13	155	2945	3100	155	310
63	630	13	157.5	2992.5	3150	157.5	315
64	640	13	160	3040	3200	160	320

65	650	13	162.5	3087.5	3250	162.5	325
66	660	14	165	3135	3300	165	330
67	670	14	167.5	3182.5	3350	167.5	335
68	680	14	170	3230	3400	510	680
69	690	14	172.5	3277.5	3450	517.5	690
70	700	15	175	3325	3500	525	700
71	710	15	177.5	3372.5	3550	532.5	710
72	720	15	180	3420	3600	540	720
73	730	15	182.5	3467.5	3650	547.5	730
74	740	15	185	3515	3700	555	740
75	750	15	187.5	3562.5	3750	562.5	750
76	760	16	190	3610	3800	570	760
77	770	16	192.5	3657.5	3850	577.5	770
78	780	16	195	3705	3900	585	780
79	790	16	197.5	3752.5	3950	592.5	790
80	800	16	200	3800	4000	600	800
81	810	17	202.5	3847.5	4050	607.5	810
82	820	17	205	3895	4100	615	820
83	830	17	207.5	3942.5	4150	622.5	830
84	840	17	210	3990	4200	630	840
85	850	17	212.5	4037.5	4250	637.5	850
86	860	18	215	4085	4300	645	860
87	870	18	217.5	4132.5	4350	652.5	870
88	880	18	220	4180	4400	660	880
89	890	18	222.5	4227.5	4450	667.5	890
90	900	19	225	4275	4500	675	900
91	910	19	227.5	4322.5	4550	682.5	910
92	920	19	230	4370	4600	690	920
93	930	19	232.5	4417.5	4650	697.5	930
94	940	19	235	4465	4700	235	470
95	950	19	237.5	4512.5	4750	237.5	475
96	960	20	240	4560	4800	240	480
97	970	20	242.5	4607.5	4850	242.5	485

The following methods are recommended to be integrated into routine vector surveillance:

A. Monitoring of Vector Density

Vector density is measured in six interventions and six sentinel/control houses in each village two to four weeks before spraying as well as two to four weeks and three to four months after spraying, using Centers for Disease Control and Prevention (CDC) light traps for one night. The density in sprayed houses is compared to sentinel and/or control HHs. Sentinel houses are houses in IRS villages in which families are requested not to spray their houses for a short period but in the interim are provided with non-impregnated mosquito nets for personal protection (WHO, 2006). Given the ethical concerns of not spraying, locked houses or those for which the owners themselves have refused permission to spray insecticide may be used as sentinel houses. The monitoring of vector densities in sentinel houses shows the mass effect of IRS on the vector population. Control houses are the houses in neighboring villages which have not been sprayed. Comparison of vector densities in intervention houses and control houses over time allows identification of seasonal or social effects (e.g. lime plastering) on sandfly densities which interfere with the spray effect.

CDC light trap set-up and collection is carried out by trained insect collectors supervised by the entomologist. The CDC light traps are setup 15cm away from the wall and 5cm above the ground in one corner of the main bedroom of a household. The same room and position is used for subsequent surveys. Sandflies are collected from sunset to sunrise on one night. On the collection night, HH members can use the room as usual but should be requested not to use electric light bulbs, mosquito repellants or mosquito coils.

Sandflies collected in light traps are transferred to the laboratory. Sandflies are separated from other insects and according to species. A binocular microscope is used to identify the species; number and gender of all sandflies as well as the physical status of female *P. argentipes* are preserved separately in 80% alcohol or mounted on Berlese media.

Morphological identification uses the criteria listed below.

1. Species:
 - a. *P. argentipes* (Pa): black thorax, silvery shine on tarsal tip of the leg, 3 mm long;
 - b. *P. papatasi* (Pp): brown body, 3 mm long;
 - c. *Sergentomyia* spp (Sr): colour varies from dark brown to dark grey, 1–2 mm long.

2. Sex and physiological status:
 - a. males: external genitalia with claspers
 - b. females: without claspers
 - c. unfed, blood fed, gravid (non-digested blood).

Man landing catches

For this method, trained persons should work in pairs and catch the sandflies that come to humans to bite over a certain period (shift) during the night time. The numbers caught per hour per person is the man-landing rate. Because of the risk of contracting leishmaniasis skilled personnel should be utilized for this collection technique and sandflies should not be allowed to actually bite. In addition, collectors should wear protective clothing. Owing to human variation; some collectors will always be more efficient and/or more attractive than others. Such factors should be taken into account when measuring patterns of sandfly biting activity overtime

Endophilic resting collections

Trained vector collectors can search for indoor resting sandflies in households on a regular basis and in a systematic way ensuring that all walls and crevices on each wall are searched. Alternatively, indoor resting collections can be conducted by means of a “Knock down catch” when a fast acting pyrethroid insecticide can be sprayed into a room after covering the floor with a clean white sheet. This method allows the number of sandflies knocked down per room or house to be assessed. Regular monitoring in such a way can monitor the impact of IRS on resting densities in targeted areas. This method ensures larger catches than use of sticky traps; however, there may be some residual effects from the pyrethroid spray, and this needs to be allowed to dissipate before repeat collections can be made, to avoid confounding with regards to future monitoring of sandfly resting densities.

Trapping by interception and attraction

In principle, interception traps sample active sand flies in a given habitat/ecotype, without bias, during a set time period. Use of sticky traps is one low tech method of sampling sandflies by interception. Standardized paper or cards 25x20cm' are soaked in castor oil and placed in places where sandflies are likely to be active at night. Rows of traps hung at floor or ceiling level can be used to sample intradomestic activity of sandflies. Collected sand flies can be removed with a brush, washed with saline with a little bit of soap solution and then counted. The results can be expressed as number of sandflies caught per square meter per night.

CDC Light traps can be used as a way of attracting sand flies. This is a non-labor-intensive method of collecting active sandflies over a whole night. The distance at which these traps are attractive to sand flies is relatively small and therefore numerous light traps may be required in any one given sampling foci.

Table 25: **WHO recommended methods for sandfly surveillance**

Vector control method	Entomological parameter	Collection type	Monitoring type
Indoor Residual spray	Day time indoor resting	Endophilic Resting Collections, Knock, Down Catches	Regular
	Human biting rate	Man Landing Collections	Trend
	Parous rate	Endophilic Resting Collections, Knock down Catches, Man Landing Collections	Trend
	Insecticide susceptibility testing	WHO Susceptibility Test-Kits	Regular
	Adult sand fly density	Man Landing Collections, CDC Light Trap Collections, Sticky Trap Collections	Trend
Insecticide treated nets	Biting in relation to sleeping habits	Man Landing Collections	Specific purpose
	Adult mosquito density	As Above	Trend

B. Bio-efficacy of Insecticide on Sprayed Surfaces (Bioassay)

Bioassays are performed to measure the efficacy of IRS two to four weeks and again five months after spraying in the houses in which light traps are fixed. These are carried out independently by insect collectors / entomologists not involved in spraying operations, supervised by an entomologist. Six HHs in each of six villages (wards) in each district are selected for residual activity measurement by bioassay (WHO 2006). Bioassay tests are performed by exposing non-fed susceptible female sandflies for a period of 30 minutes. Ten sandflies (collected by aspirators or originating from insectariums) are introduced in to each WHO plastic cone fixed on the insecticide- treated surfaces. There are four replications of the test on treated walls (four sides of the room) in each of the six selected houses and one test on an untreated wall, to act as a control. After exposure, the females are placed in 150 ml plastic cups (10 individuals per cup) with sucrose solution provided and maintain in a climatic chamber for 24 hours at $27^{\circ}\text{C} \pm 2^{\circ}\text{C}$ and $80\% \pm 10\%$ relative humidity (RH). Percentage of knock down after 60 minutes and percentage mortality after 24 hours are recorded. Results are pooled for analysis.

C. Monitoring of Insecticides Resistance

Vector resistance to insecticides results from the repeated use of the same insecticide or insecticides that form part of the same chemical group (e.g. pyrethroids). This provides increased selection pressure in wild populations, to adopt physiological / biochemical changes after contact exposure

with the insecticide so it is no longer affected by it. It is therefore imperative to introduce regular insecticide susceptibility testing of *Phelbotomus argentipes*, following WHO standardized protocols so as to monitor insecticide resistance patterns in Kala-azar endemic areas where IRS is deployed but also in areas where insecticides are also used for agricultural use. Monitoring of insecticide resistance will allow an evidence base in which to appropriately select insecticides in combination with national policy, cost and availability. To date, few tests on the susceptibility of *Phelbotomus argentipes* to insecticides have been carried out in the South-East Asia Region. What little work has been done indicates that this species is susceptible to the insecticide DDT, with a slight increase in tolerance over many years of use.

Insecticide susceptibility (WHO standard chamber method)

The WHO standard chamber method is used to test insecticide susceptibility to the insecticide used by the country concerned. Wild caught, non-blood-fed non-gravid female *P. argentipes* are introduced into WHO susceptibility chambers (lined with the insecticide impregnated paper) for a period of one hour. Batches of no more than 20 sandflies are introduced into each chamber in order to minimize the chances of disturbing each other during the exposure. For each insecticide/concentration, 5 replicates and 1 control of 20 *P. argentipes* are tested.

Results are pooled for analysis. After exposure, females are taken out and placed in 150 ml paper cups (20 individuals per cup), with sucrose solution provided, and maintained in a climatic chamber for 24 hours at $27 \pm 2^{\circ}$ C and $80\% \pm 10\%$ RH. Percentage of knock-down after 60 minutes and mortality after 24 hours are recorded.

Correction of mortality in bioassay and susceptibility tests

Test series with control mortality of over 20% are cancelled. Those with control mortality between 5% and 20% test mortality are corrected by Abbott's formula (1925) as follows:

$$P = \frac{P1-C}{100-C} \times 100$$

Where, P = corrected mortality
P1 = % observed mortality
C = % mortality in control

D. Spraying Technique

The suspension should be prepared correctly so that sufficient quantities of the insecticide are sprayed to be effective. Prepare 8 liters of the suspension at a time. This will be sufficient for 6-8 households for kala-azar and 3-4 households for Malaria. If the village is high endemic for malaria it is advised that the norms for Malaria should be followed. This will also be effective against kala-azar.

Place the required quantities of wettable powder of insecticide in a 15-liter bucket as per instructions. Add volume of water with a mug that is considered adequate to make a paste. Do not put too much water at this stage. Once the paste is made, then pour water on the paste and keep mixing vigorously to make a uniform suspension. Add measured volume of water. After this procedure, filter the solution through a clean cloth to remove any particulate matter. Any particulate matter will block the nozzle of the spray pump. This will cause difficulty in spraying the surface with the insecticide.

The barrel of the spray pump is placed in the bucket containing the spray suspension. One person operates the pump and the other is responsible for the spray. If a compression pump is used, it can be operated by one person. The spray lance should be kept 45 cm away from the surface to be sprayed. The swath should be parallel. It is applied in a vertical swath about 53 cm wide. There should be an overlap of about 7.5 cm between two swaths. Spraying should be done from the top down wards. The top should be about 6 feet from the ground. The spray should not drip on to the floor.

The deposits on the wall should be uniform and no areas should be skipped. This is an indication of good spray. The supervisor should check the quality of the spray. It takes about 3 minutes to spray about 150 sq meters area. This is the average size of a dwelling in rural areas. There are always some households that are not covered in the first round. These should be covered under subsequent mopping up round on the same day or on a pre-decided different day.

The spray man should spray a 2 meter (6ft) high wall with 0.75 m swathe in 5 seconds, i.e. speed equals to 24 m/minute. The discharge rate: (i) if hand compression pump with control flow valve (CFV) is used 550mL liquid per minute, (ii) if hand compression pump without CFV is used- 650-750mL liquid per minute (average 700mL), (iii) If stirrup pump with CFV is used -550mL liquid per minute, (iv) if stirrup pump without CFV is used -650-750 mL liquid per minute (average 700mL)

The person who is responsible for pumping them at aerial should give 20-26 strokes per minute with 10-15 cm plunger movement at a pressure of 10 pounds per square inch. Spraying into a bucket for one minute and measuring the discharge rate per minute helps to ensure that the discharge rate is satisfactory. This is done three times and measured and then average of it is taken to see the discharge rate. If it is more than the recommended one, then appropriate measures are taken. If the discharge rate exceeds 850 ml minute, then the nozzle should be rejected.

A blockage in the nozzle is a frequent problem. The nozzle cap should be removed by unscrewing it and replaced by a new nozzle, which is patent. The blocked Nozzle tips should be dipped in water container overnight and in majority of cases debris is removed automatically. If it is not then a used old toothbrush is used to clean the debris which has choked the nozzle.

The unused insecticide should be disposed off safely as per the guideline provided. The buckets that were used should be cleaned properly ensuring safe disposal of the waste to ensure that it does not contaminate the environment.

E. Use of Hand Compression Pump

This hand operated compression pump is mainly used for residual spraying of wall surfaces and for larviciding.

The sprayer shall consist of a tank, usually cylindrical, equipped with a hand-operated air pump with a two handed handle (if required) and locking device, separate from the tank lid, pressure-release safety device, hose attached at the top of the tank to a dip-tube, trigger valve with locking-off device, lance, control flow valve and nozzle, with other accessories as specified by the user agency. The sprayer should have a system for parking the lance when not in use to protect the nozzle. The sprayer with fittings assembled shall have no sharp edges or projections that might injure workers during normal operation.

The materials of construction, including filler cover, shall be declared and shall be corrosion, pressure and UV resistant. No broken or leaking welds or cracks should result when subjected to the tank fatigue test. No solder containing lead and/or tin as major components shall be used in the construction of sprayers or component parts, except on joints between the lance, the cut-off valve, the nozzle body and the dip-tube, provided that all tests pertaining to this item are satisfactory. No wooden parts shall be used in the construction of any part of the sprayer.

The weight of the complete sprayer, when filled to the manufacturer's maximum recommended capacity for operation, shall be declared and shall not exceed 25 kg. The filler opening shall be declared and shall be not less than 90 mm in minor axis.

Following actions may be ensured by the operators/supervisors:

- The compression sprayer is pressurized before commencing spraying but it is not continuously pumped.
 - The pump is filled to levels usually at about $\frac{3}{4}$ liquid to $\frac{1}{4}$ air. A smaller air volume in relation to liquid volume would not retain sufficient pressure for long periods.
- When the tank is not in use, the spray lance is held in a bracket and nozzle cup, which protects the nozzle from damage.
 - The nozzle tip is the most important part of the sprayer. It should deliver a precise amount of spray suspension per minute (*740-850 ml*) at a certain pressure (*40 PSI or 2.8 kg/cm²*) in the tank and maintain a uniform spray pattern and swath width (*53cm or 21"*).
 - The type of the nozzle tip and the flow rate shall be declared and comply with international standards. Tolerance limits of the discharge rate shall not exceed +5% when tested.
- The flat-fan spray nozzle delivers a fan-shaped spray and is used for residual wall spraying.
- The flat-fan spray nozzle of 8002 E is used for indoor residual spraying which produces a spray with an angle of 80. per minute output at a standard tank pressure of 40 PSI

(2.8kg/m). It is usually made of especially hardened stainless steel. The nozzle tip is designed with flat surfaces on either side of the orifice so that it can be removed easily. The pressure at nozzle tip is calibrated at 10 PSI (0.7kg/cm).

- The inside tank should be thoroughly cleaned.
- The distribution hose and accessories should be securely attached to the delivery outlet. The cut- off valve should be tightly closed.
- Full strokes to be pumped till the pressure gauge register 2.8 kg/ cm (40PSI).
- The sprayer must be suspended on the shoulder or carried in hands.

F. Routine Maintenance of the Equipment and Minor Repair Work

The spray equipment is subject to normal wear and tear since the insecticides are corrosive. To reduce the deterioration the following actions should be undertaken at the end of each day:

- The discharge line should be disconnected at the delivery outlet at the end of spraying.
- The bucket and the discharge line should be emptied.
- The spray pump should be thoroughly rinsed with clean water.
- The filter assembly should be rinsed and cleaned.
- Filter should be removed from the valve by grasping it at its screen and slightly twisted on pulling it out.
- Reassemble all the clean parts except the nozzle.
- Put clean water in the tank, seal the tank and pump air in to it.
- Open the control valve and let the water flow from the lance to flush the hose, filters, control valve and lance.
- Remove the tank cover and dry the inside of the tank.
- Clean the nozzle tip by washing thoroughly with water.
- Remove any dirt from the orifice with a fine bristle/a brush.
- Never use a wire or nails to clean the nozzle.

Minor Repair of the spraying equipment

- Cleaning the nozzle
- Cleaning of the discharge line
- Tightening of the hose clamp
- Tightening of the gasket
- Tightening of the nut and compression of the cut off valve
- Replacement of the nozzle.

G. Instructions for the Spray Team Members (Do's and Don'ts)

- A simple leaflet should be provided to each member of the spray team. This should be in simple local language with appropriate illustrations.
- Wash your hands thoroughly with soap and water after preparing the insecticide spray. This is to be repeated every time the spray operation is stopped.
- Washing of hands thoroughly with soap and water is advised when the team takes a lunch or tea break.
- The personal protection comprising of apron, gloves, mask and goggles should be worn during the insecticide spray.
- Avoid direct contact of the insecticides with eyes or skin. If this happens wash the skin coming in contact and adjacent skin thoroughly with soap and water. Eyes should be flushed repeatedly with clean water for a period of at least 5 minutes or 10 times to protect yourself against any harmful effects of the insecticides.
- If irritation persists even after thorough washing, seek medical advice.
- If any member of the spray team suffers from any symptoms while the spraying operations are ongoing, medical attention should be sought without any delay.

Table 25: Data Collection Form after the End of the Spraying Cycle at the District Level

Supplies	To be Entered	Indicator calculated automatically	Auto generated
#pumps available		%functional pumps available	
#functional pumps			
#PPE for how many squads?		% of squads with protective clothing	
Insecticide available (tons, kg or sachets)		% quantity of insecticide received that was requested	
Insecticide needed/requested (tons, kg or sachets)			
Human resources & training			
#squads hired		% of needed squads actually hired	
#squads needed/requested			
#squads trained before start of cycle		% of squads trained before start of cycle	
#villages supervised for IRS		% IRS villages supervised	
#villages sprayed			
#squads with quality score*		% squads with acceptable quality	
#squads observed			
Achievement of targets			
#PHCS targeted for IRS		% of targeted PHCs sprayed	
#PHCS sprayed			
#villages with KA in last 3 years [§]		% KA villages targeted for IRS	
#villages targeted for IRS		% KA targeted villages sprayed	
#Villages sprayed			
#HHs targeted for IRS		% of target HHs sprayed	
#HHs sprayed			
HOUSEHOLD SURVEY+			
#households interviewed			
#HH who received adequate information		% HH with adequate information	
#HH reporting to have been sprayed		% HH covered by IRS	
#HH satisfied		% HH satisfied	

Sandfly Collection Record Sheet

Name of VDC: _____ Name of village: _____

Name of Cluster: _____

Code: --**S**-

village (1,2,3,4) - collection method (C = CDC Light Trap) - number of the survey (S0, S1, S2, S3) - house number (01-35)

Date: / / dd/mm/yy Signature:

Sandfly	Males	Females			Total
		Unfed	Fed	Gravid	
<i>P.argentipes</i>					
<i>P.papatasi</i>					
<i>Sergentomyia</i>					

.....
Name of Insect collector

.....
Entomologist

Bioassay Test Record Sheet

Code the collector: _____ Code of team leader: _____
 Name of VDC _____ Name of cluster/Village: _____
 Name of the insecticide used: _____

Concentration of the insecticide per m²

Test performed in – Lab/ field _____
 Species of the sand fly exposed – *P. argentipes*/*P. papatasi* _____
 Temperature 24 hour: Max: _____ /Min: _____ /Exposure time: _____
 minutes

Batch Code: - - - **T**

Hamlet / VDC (1,2,3,4) - arm-number of the test (T1, T2) _____

Household Code no.	Surface	Cone No.	Exposure period		24 hours		% Mortality rate	Species of Sand fly exposed	Remarks
			No. Hold	KD	Dead	Alive			
		1							
		2							
		3							
		4							
		5							

Percent control mortality: _____
 Percent test mortality: _____
 Percent corrected mortality: _____

Signature: _____

Sandfly Collection Sheet

One sheet per building/construction (e.g. sleeping quarter, upper floor, cattle shed)

Date: / / (dd/mm/yy)

Name of VDC: _____ Ward number: _____

Name of village:

Household number/name of head of household:

Place and type of construction where these sandflies were collected:

<input type="checkbox"/> inside	<input type="checkbox"/> outside
<input type="checkbox"/> house: <div style="margin-left: 40px;"> <input type="checkbox"/> kitchen/living room <input type="checkbox"/> sleeping room <input type="checkbox"/> other: </div>	<input type="checkbox"/> cattle shed: type of animals kept:

Collection method: mouth aspiration method
 other - specify:

Sand fly identification:

Sand fly identification method:

Sandfly	Males	Females			Total
		Unfed	Fed	Gravid	
<i>P.argentipes</i>					
<i>P.papatasi</i>					
<i>Sergentomyia</i>					

.....
 Name of Insect collector

.....
 Name of Entomologist-Supervisor

Case definitions

All health facilities, either in endemic and non-endemic areas, should be trained on case definitions in order to increase kala-azar awareness among health workers in Nepal.

Kala-azar Case definition

There is no definition for a suspected case of VL, given the low specificity of the symptoms.

Probable VL case: A person living in or having travelled to VL endemic areas showing clinical signs and symptoms of VL (mainly irregular fever lasting more than two weeks and splenomegaly and/or weight loss).

Confirmed VL case:

- **Laboratory-confirmed VL case:** A probable VL case with laboratory confirmation, either serological (RDT, DAT, ELISA, IFAT) and/or parasitological (smear, culture) and/or positive by PCR or related techniques.
- OR**
- **Clinically-confirmed VL case:** A probable VL case that has not been confirmed by any laboratory test (i.e. test(s) not done or negative) but is assessed by a clinician to be a confirmed VL case based on clinical grounds.

All confirmed VL cases, either clinically or laboratory; should be treated according to the protocol and reported

Post-Kala azar dermal leishmaniasis (PKDL)

Probable PKDL case: A patient living in or having travelled to visceral leishmaniasis endemic areas presenting with a typically symmetrical multiple hypopigmented macules, papules, plaques, or nodules without loss of sensation.

PKDL can occur in patients with previous or concomitant VL. In some cases it occurs without the past history of VL. Serological test such as rK39 rapid diagnostic test positivity acts as a strong evidence when other diseases (for example, leprosy) are considered in the differential diagnosis, or if a history of VL is uncertain.

Confirmed PKDL: A probable PKDL case with *Leishmania* infection confirmed parasitologically by PCR or a slit-skin smear or biopsy.

Cutaneous leishmaniasis (CL)

Probable CL case: a person living in or having travelled to endemic areas showing typical CL skin lesions (macule, plaque, nodule, ulcer)

Confirmed CL case:

- **Laboratory-confirmed CL case:** A probable CL case with parasitological confirmation, by positive smear, culture or PCR.

OR

- **Clinically-confirmed CL case:** A probable CL case that has not been confirmed by any laboratory test (i.e. test(s) not done or negative), but is assessed by a clinician to be a confirmed CL case based on clinical grounds

Mucosal/mucocutaneous leishmaniasis (ML/MCL)

Probable CL case: a person living in or having travelled to endemic areas showing typical CL skin lesions (macule, plaque, nodule, ulcer)

Confirmed CL case:

- **Laboratory-confirmed CL case:** A probable CL case with parasitological confirmation, by positive smear, culture or PCR.

OR

- **Clinically-confirmed CL case:** A probable CL case that has not been confirmed by any laboratory test (i.e. test(s) not done or negative), but is assessed by a clinician to be a confirmed CL case based on clinical grounds

KA-HIV co-infection:

A case of coinfection is an HIV-positive person meeting the definition of probable leishmaniasis case with serological and/or parasitological confirmation of the *Leishmania* parasite. Coinfection is more common with VL (i.e. VL-HIV) than the other forms of leishmaniasis.

Other patient definition:

Patient type: new/relapse

- Origin of the infection:
 - **Imported:** infection acquired outside the country of reporting
 - Autochthonous : infection acquired within the country of reporting
 - **Locally-imported:** infection acquired within the country but outside the implementation/administrative unit of reporting

Locally-infected: infection acquired inside the implementation/administrative unit of reporting.

Treatment-related definition

Treatment completion

Treatment completion is the assessment of whether the full-course of treatment has been received by the patient, as per the national protocol.

- ▶ **Treatment completed:** The patient has completed the full-course of the treatment as per the national protocol, and the clinician's prescription.
 - Length of treatment depends on drug regimen, e.g. Sodium Stibogluconate (SSG) plus Paromomycin: 17 days; SSG: 30 days; AmBisome®: 1 or 6-10 days...
- ▶ **Treatment stopped for medical reason:** the treatment was stopped by decision of the clinician (e.g. patient suffering from side effects, treatment failure) or after the death.
- ▶ **Defaulter:** The patient does not complete the full-course treatment
- ▶ **Treatment completion unknown:** the patient completion of treatment is unknown (unrecorded). This is different from default, where the clinician knows that the patient has not completed the treatment.

Treatment outcome definitions

Treatment outcomes for VL cases have to be assessed twice:

- (i) At the end of the treatment, or 15 days after treatment starts for short-course regimen (less than 5 days) = initial assessment; and
- (ii) Six months after the last drug was taken (final outcome) = Final assessment

At initial assessment,

- **Initial cure:** a full course of drugs has been completed AND the patient has clinically improved. Clinical criteria for initial cure defined as “*no fever + regression of splenomegaly (even partial) + return of appetite and/or gain in body weight*”.
- **Failure (non response):** signs and symptoms persist or recur during treatment or up to initial treatment outcome assessment
- **Lost-to-Follow-up/Unknown:** the patient does not present for initial assessment after completion of treatment, or the patient status was not recorded.
- **Death:** death of any person having been diagnosed of VL regardless of the treatment status and the cause of death within the standard post-treatment follow-up period

Any death should be notified with specification of the cause of death, as follows:

- Death due to VL
- Death due to HIV
- Death due to other disease or medical condition(s)
- Death due to SAE (iatrogenic)
- Death due to non-medical condition (accident)
- Death due to unknown cause

At final assessment,

- **Final cure:** a patient who after initial cure remains symptom-free at six months after the end of treatment.
- **Relapse:** a patient who experiences recurrence of VL symptoms with parasitological confirmation at any time point after initial cure.
- **Death:** death of any person having been diagnosed of VL regardless of the treatment status and the cause of death within the standard post-treatment follow-up period

Any death should be notified with specification of the cause of death, as follows:

- Death due to VL
- Death due to HIV
- Death due to other disease or medical condition(s)
- Death due to SAE (iatrogenic)
- Death due to non-medical condition (accident)
- **Loss to follow-up:** patient does not present for assessment at six months.

Cure of PKDL:

Initial cure: clinical improvement at the end of treatment – defined as a considerable reduction in the number and size of skin lesions

Final cure: clinical cure 12 months after the end of treatment – defined as a complete resolution of macules, papules, plaques and nodules, no new lesion, and near total depigmentation of maculae.

Cutaneous leishmaniasis (CL):

Treatment outcomes for CL cases have to be assessed twice:

- (i) Between 2 to 4 weeks after initiating the treatment
- (ii) Between 45 and 90 days after initiating treatment, or longer depending on the parasite

Initial assessment: 2-4 weeks after starting the treatment

- **Initial cure (Improvement):** Decrease in the size of the lesion or signs of reepithelization
- **Failure:** Increase in the size of a nodule or a plaque or an ulceration
- **Death with specification of the cause of death:**
 - Death due to CL
 - Death due to HIV
 - Death due to other disease or medical condition (s)
 - Death due to SAE (iatrogenic)
 - Death due to non-medical condition (accident)

- Death due to unknown cause
- **Unknown:** patient does not present for assessment or the outcome was not recorded

Final outcome: D45-90 days, or longer depending on the parasite

- **Final cure** = Total re-epithelialization
- **Failure** = Lack of complete re-epithelialization
- **Death with specification of the cause of death:**
 - Death due to CL
 - Death due to HIV
 - Death due to other disease or medical condition (s)
 - Death due to SAE (iatrogenic)
 - Death due to non-medical condition (accident)
 - Death due to unknown cause
- **LTFU-Unknown:** patient does not present for assessment or the outcome was not recorded

Serious adverse event (SAE)

It is defined as any untoward medical occurrence that at any dose results in following:

- Results in death;
- Requires inpatient hospitalization or prolongation of existing hospitalization;
- Results in persistent or significant disability or incapacity;
- Is life threatening;
- Results in a congenital anomaly or birth defect.

The term “severe” is not synonymous with serious. Seriousness of an event is based on patient/event outcome or action criteria which serves as guide for defining regulatory reporting obligations. SAEs should be recorded in the patient form and the case register.

Countries are expected to monitor the pharmacovigilance of antileishmanial drugs. SAEs should also be notified to the national pharmacovigilance system.

SAEs consecutive to treatment with antileishmanial drugs should be reported to WHO through the standardized pharmacovigilance form available in Annex 11.

Minor adverse events are not included in serious adverse events reporting. More definitions can be seen in Safety Monitoring of Medical Products, Reporting system for the general public, World Health Organization, 2012.

Other key epidemiological definitions

In addition to these operational definitions for the surveillance system, there are other terms that are frequently used in the forms and reports.

Locally acquired case: Case infected at a defined and specific local level (region, district, sub-district, village)

Endemicity status

- ▶ **Endemic:** full cycle of transmission has been demonstrated at any given time (maintained population of competent vector + parasite reservoir + locally-acquired cases) AND at least 1 locally-acquired case in the last 10 years
- ▶ **Endemicity doubtful:**
 - Full cycle of transmission has **never** been demonstrated BUT at least 1 locally-acquired case in the last 10 years
 - OR**
 - Full cycle of transmission has been demonstrated at any given time BUT no case has been reported in the last 10 years (0 case or no data)
- ▶ **Non endemic:**
 - **Previously reported cases:** Full cycle of transmission has **not** been demonstrated AND no locally-acquired case has been reported in the last 10 years BUT locally-acquired case has been reported earlier
 - **At risk:** No locally-acquired case has **ever** been reported but epidemiological risk factors are present (a competent vector population, a reservoir, and appropriate environmental conditions).
 - **No autochthonous cases reported** = No locally-acquired case has **ever** been reported

Endemicity status can be applied to any defined and circumscribed geographical area or implementation unit: countries, regions, districts, villages, community. It is advised to use the smallest geographical or administrative sub-national resolution available.

Locally acquired case: Case infected at a defined and specific local level (region, district, sub-district, village)

A focus:

is defined as any circumscribed geographical endemic area. Bear in mind that leishmaniasis cases can be **infected** in a given focus but can be **reported in another location** because of travel or access to health care.

New focus:

a focus (see definition above) where leishmaniasis transmission had **not been** reported for at least the last 10 years.

Outbreak:

WHO defines “a disease outbreak as **the occurrence of cases of disease in excess of what would normally be expected** in a defined community, geographical area or season. An outbreak may occur in a restricted geographical area or may extend over several countries. It may last for a few days or weeks, or for several years.”

Table 26: **Indicators recommended for leishmaniasis surveillance Visceral leishmaniasis indicators, as per WHO recommendations**

Core Indicators	Definition	Dis-aggregations	Comment
EPIDEMIOLOGY			
Number of VL cases	Number of confirmed (either laboratory or clinically) VL cases.	<ul style="list-style-type: none"> By type of patient (new/relapse) By origin (autochthonous/imported) 	<ul style="list-style-type: none"> Number of VL cases disaggregated by type of patient is part of core morbidity data. This indicator is part of the SDG indicators for NTDs
VL incidence ¹³	Number of <u>new autochthonous</u> VL cases per 10,000 population	<ul style="list-style-type: none"> At finest administrative level available Eventually by age and gender, if population data are available. 	<ul style="list-style-type: none"> VL incidence is part of the core morbidity module, based on number of new autochthonous VL cases reported. Population data at finest administrative level are required
Endemic areas	Number of endemic areas, i.e. areas where at least 1 <u>new autochthonous</u> VL cases has been reported during the last 3 years	<ul style="list-style-type: none"> At finest administrative level available 	<ul style="list-style-type: none"> Endemic areas for VL is part of the core morbidity module, based on number of new autochthonous VL cases reported.
	Number of endemic areas with a VL incidence above 1/10,000 population	<ul style="list-style-type: none"> At finest administrative level available 	
Population at risk of VL	Number of people living in an endemic area, i.e. an area where at least 1 <u>new autochthonous</u> VL case has been reported during the last 3 years	<ul style="list-style-type: none"> At finest administrative level available Eventually by category of risk (<1/10,000 / [1-2.5 / 10,000[/ [2.5-10 / 10,000 [, ≤10/10,000) 	<ul style="list-style-type: none"> Population at risk of VL is part of the core morbidity module, based on number of new autochthonous VL cases reported. Population data at finest administrative level are required
Number of VL outbreak	Number of VL outbreak reported during the year		
Gender distribution of VL cases	% of female among VL cases = number of female among VL cases / total number of VL cases * 100	<ul style="list-style-type: none"> By type of patient (new/relapse) 	
Age distribution of VL cases	% of children under 5 years among VL cases = number of children under 5 years among VL cases / total number of VL cases * 100	<ul style="list-style-type: none"> By type of patient (new/relapse) 	
	% of children 5 to 14 years among VL cases = number of children 5 to 14 years among VL cases / total number of VL cases * 100	<ul style="list-style-type: none"> By type of patient (new/relapse) 	
	% of VL cases over 15 years of age = number of VL cases over 15 years of age / total number of VL cases * 100	<ul style="list-style-type: none"> By type of patient (new/relapse) 	

¹³In countries where VL is targeted for elimination as a public health problem, VL incidence should be maintained below the threshold of 1 new autochthonous VL case / 10,000 population, at the implementation unit level.

DIAGNOSIS			
Confirmation by rapid diagnostic tests (RDTs)	% of VL cases confirmed by RDTs = Number of VL cases with positive result to RDT / Total number of confirmed (either laboratory or clinically) VL cases * 100	• Applies only to new VL cases	• Data from laboratory register
	% of positive RDTs = Number of positive RDTs / Total number of probable VL cases tested with RDTs * 100	• Applies only to new VL cases	
Confirmation by parasitology	% of VL cases confirmed by parasitology = Number of VL cases with positive slide / Total number of confirmed (either laboratory or clinically) VL cases * 100	• By type of patient (new/relapse)	• Data from laboratory register
	% of positive slides = Number of positive slides / Total number of probable VL cases tested for parasitology * 100	• By type of patient (new/relapse)	
Clinical confirmation only	% of VL cases clinically confirmed = Number of VL cases confirmed based on clinical presentation / Total number of confirmed (either laboratory or clinically) VL cases * 100	• By type of patient (new/relapse)	
VL-HIV co-infection	% of VL-HIV co-infection = Number of VL cases co-infected with HIV (either oral reporting or laboratory testing) / Number of VL cases assessed for HIV (either oral reporting or laboratory testing) * 100	• By type of patient (new/relapse)	
	Coverage of HIV screening = Number of VL cases assessed for HIV (either oral reporting or laboratory testing) / Total number of VL cases * 100	• By type of patient (new/relapse)	
VL and malnutrition	% of patients with VL and acute or severe malnutrition/Total number of VL cases *100	• By type of patient (new/relapse)	
TREATMENT			
VL cases treated (%)	Number of VL cases who started treatment/VL cases*100	• By type of patient (new/relapse)	
Treatment delay	Mean time elapsed between onset of symptoms and treatment, in days	• By type of patient (new/relapse)	
Treatment regimen distribution	% of VL cases treated, by treatment regimen = Number of VL cases treated, by treatment regimen / Total number of VL cases treated * 100	• By type of patient (new/relapse) • By treatment regimen	
Serious adverse events	Number of severe or life-threatening adverse events among VL cases who have received treatment	• By type of patient (new/relapse)	
Severe adverse events	Number of severe or life-threatening adverse events among VL cases who have received treatment	• By type of patient (new/relapse)	• To be reported also to the national pharmacovigilance system

Defaulter rate (%)	Number of defaulters / Total number of VL cases treated * 100	<ul style="list-style-type: none"> • By type of patient (new/relapse) • By treatment regimen 	
Completion rate (%)	Number of VL treatments completed/Number of VL treatments started	<ul style="list-style-type: none"> • By type of patient (new/relapse) • By treatment regimen 	
INITIAL TREATMENT OUTCOME			
Failure rate	Number of failure as initial treatment outcome / Total number of VL cases treated * 100	<ul style="list-style-type: none"> • By type of patient (new/relapse) • By treatment regimen 	
Case-fatality ratio	Number of death as initial treatment outcome (related or not to VL) / Total number of VL cases * 100	<ul style="list-style-type: none"> • By type of patient (new/relapse) • By treatment regimen 	
FINAL TREATMENT OUTCOME			
Relapse rate	Number of relapse between initial and final treatment outcome / Number of VL cases treated * 100		<ul style="list-style-type: none"> • This is the ideal indicator in case there is a cohort follow-up or individual data are computerized for VL cases.
	Number of relapse between initial and final treatment outcome / Number of VL cases followed-up at 6 months* 100		<ul style="list-style-type: none"> • In case there is no cohort follow-up and only aggregated data are computerized.
CASE SCREENING			
Number of people screened actively for VL	Number of people clinically screened for VL, either clinically or with rapid diagnostic tests, outside the health facility, during active screening activities.		<ul style="list-style-type: none"> • Active case detection register
Number of people tested passively for VL	Number of people tested with RDTs at the health facility		<ul style="list-style-type: none"> • Laboratory register
MANAGEMENT OF DRUG STOCKS			
VL drug availability	Number of days with a stock out of VL drugs	<ul style="list-style-type: none"> • By drug 	<ul style="list-style-type: none"> • Monthly leishmaniasis stock form
Coverage rate of vector control (%)	No. of HH protected/All HH at Risk		<ul style="list-style-type: none"> • Annual

Table 27: Definitions of Recommended Minimum Aggregated variables for Post Kala-Azar Dermal Leishmaniasis

These indicators need to be included in the routine monthly reporting done from each health centre treating PKDL cases (see annex 4). A recommended form for further adaptation in each country is in Annex 5.

PKDL cases	<p>Probable PKDL: A patient from a <i>L. donovani</i>-endemic area who has a typically symmetrical macular, papular, nodular or mixed rash often starting on the face with further spread to other parts of the body without loss of sensation and with positive rk39 RDT-that may occasionally present even in the absence of a previous history of visceral leishmaniasis.</p> <p>Confirmed PKDL: A probable PKDL case with <i>Leishmania</i> infection confirmed by PCR or a slit-skin smear or biopsy.</p>
PKDL cases by gender	<p>The number of PKDL cases, disaggregated by Gender (Male/Female)</p> <p>The sum of the number of cases in each category should be equal to the total number of PKDL cases.</p>
PKDL cases by age	<p>The number of PKDL cases disaggregated by age group (<5 years/ 5-14 years / 15 years and older)</p> <p>The sum of the number of cases in each category should be equal to the total number of PKDL cases.</p>
PKDL HIV coinfection	<p>A case of coinfection is a HIV-positive person showing clinical signs of PKDL with serological and/or parasitological confirmation of the diagnosis. All confirmed cases should be tested for HIV. The sum of the number of cases in each category should be equal to the total sum of VL cases.</p>

Table 28: Recommended Minimum CL patient variables

No.	Name of Variable	Options
1	Orgunit Code	-
2	Admission date	-
3	ID number	-
4	Date of birth	-
5	Age (at Diagnosis)	-
6	Gender	Male
		Female
		Unknown
7	Type of patient / Patient category	New
		Relapse
		Unknown
8	Time elapsed between onset of symptoms and presentation to a health centre (patient delay, in days)	-
9	Is the patient pregnant?	Yes
		No
		Unknown
10	Country of residence	-
11	Place of residence	-
12	Village of residence (coordinates)	-
13	Village of residence (free text)	-
14	Landmark (if available)	-
15	Country of infection	-
16	Infection imported from another country	Yes
		No
		Unknown
17	Probable place of infection	-
18	Probable village of infection (coordinates)	-
19	Probable village of infection (free text)	-
20	Travel in the last 6 months to endemic areas	-
21	Localization of lesions	Head/face/neck
		Torso/abdomen
		Arms/hands
		Legs/feet
22	Number of lesions	-
23	Larger diameter of biggest lesion	-
24	Smaller diameter of biggest lesion	-

25	Clinical form of CL	Cutaneous
		Muco-cutaneous
		Unknown
26	Classification/Situation	Situation 1
		Situation 2
		Situation 3
		Situation unknown
27	Biopsy done	Yes
		No
28	Date of Biopsy	-
29	Culture done	Yes
		No
30	Culture result	Positive
		Negative
		Not done
		Unknown
31	Direct exam (parasitology)	Yes
		No
32	Direct exam (parasitology) Result	Positive
		Negative
		Not done
		Unknown
33	PCR done	Yes
		No
34	Date of initial PCR testing	-
35	PCR result	Positive
		Negative
		Inconclusive
		Borderline
		Not done
		Not applicable
		Unknown
36	Parasite	<i>L. infantum</i>
		<i>L. tropica</i>
		<i>L. major</i>
		<i>L. aethiopica</i>
		<i>L. donovani</i>
		<i>L. mexicana</i>
		<i>L. braziliensis</i>

		L. panamensis
		L. guyanensis
		L. peruviana
		L. amazonensis
		Other
37	ACL / ZCL	-
		-
38	Date of diagnosis/confirmation	-
39	CL confirmation type	Parasitology
		Clinically only
		Confirmation unknown
40	CL Treatment start date	-
41	CL Treatment route or other therapies	Wash/Dressing only
		Cryotherapy only
		Thermotherapy only
		Pentavalent antimonials intralesional only
		Cryotherapy + pentavalent antimonials
		Pentavalent antimonials intramuscular or systemic only
		Other treatment route (CL)
		Treatment route unknown (CL)
		Not applicable
42	Pentavalent antimonial regimen used	Antileishmanial treatment not started
		Meglumine antimoniate (glucantime)
		Sodium stibogluconate (SSG)
		Treatment regimen unknown (CL)
43	Was the CL treatment completed?	Treatment completed
		Treatment stopped for medical reasons
		Defaulter
		Treatment completion unknown
44	If failure of treatment, please specify	-

45	Serious adverse events?	Yes
		No
		Unknown
46	If yes, please specify which severe adverse events	-
47	Date of initial outcome	-
48	Initial treatment outcome	Initial cure
		Failure
		Death
		Lost-to-follow-up
49	Cause of initial death (if applicable)	CL/MCL
		HIV
		Other disease
		SAE (iatrogenic)
		Non-medical condition
		Unknown cause
50	Date of final treatment outcome assessment	-
51	Final treatment outcome	Final Cure
		Relapse
		Death
		Lost-to-follow-up
52	Cause of final death (if applicable)	CL/MCL
		HIV
		Other disease
		SAE (iatrogenic)
		Non-medical condition
		Unknown cause

Table 29: **Cutaneous leishmaniasis indicators, as per WHO recommendations**

Core Indicators	Definition	Dis-aggregations	Comment
EPIDEMIOLOGY			
Number of CL cases	Number of confirmed (either laboratory or clinically) CL cases.	<ul style="list-style-type: none"> By type of patient (new/relapse) By origin (autochthonous/imported) 	<ul style="list-style-type: none"> Number of CL cases disaggregated by type of patient is part of core morbidity data. This indicator is part of the SDG indicators for NTDs
CL incidence	Number of <u>new autochthonous</u> CL cases per 10,000 population	<ul style="list-style-type: none"> At finest administrative level available Eventually by age and gender, if population data are available. 	<ul style="list-style-type: none"> CL incidence is part of the core morbidity module, based on number of new autochthonous CL cases reported. Population data at finest administrative level are required
Endemic areas	Number of endemic areas, i.e. areas where at least 1 <u>new autochthonous</u> CL cases has been reported during the last 3 years	<ul style="list-style-type: none"> At finest administrative level available 	<ul style="list-style-type: none"> Endemic areas for CL is part of the core morbidity module, based on number of new autochthonous CL cases reported.
Population at risk of CL	Number of people living in an endemic area, i.e. an area where at least 1 <u>new autochthonous</u> CL case has been reported during the last 3 years	<ul style="list-style-type: none"> At finest administrative level available 	<ul style="list-style-type: none"> Population at risk of CL is part of the core morbidity module, based on number of new autochthonous CL cases reported. Population data at finest administrative level are required
Gender distribution of CL cases	$\% \text{ of female among CL cases} = \frac{\text{number of female among CL cases}}{\text{total number of CL cases}} * 100$	<ul style="list-style-type: none"> By type of patient (new/relapse) 	
Age distribution of CL cases	$\% \text{ of children under 5 years among CL cases} = \frac{\text{number of children under 5 years among CL cases}}{\text{total number of CL cases}} * 100$	<ul style="list-style-type: none"> By type of patient (new/relapse) 	
	$\% \text{ of children 5 to 14 years among CL cases} = \frac{\text{number of children 5 to 14 years among CL cases}}{\text{total number of CL cases}} * 100$	<ul style="list-style-type: none"> By type of patient (new/relapse) 	
	$\% \text{ of CL cases over 15 years of age} = \frac{\text{number of CL cases over 15 years of age}}{\text{total number of CL cases}} * 100$	<ul style="list-style-type: none"> By type of patient (new/relapse) 	
DIAGNOSIS			
Patient delay	Mean time elapsed between onset of symptoms and presentation at the health facility, in days	<ul style="list-style-type: none"> By type of patient (new/relapse) 	<ul style="list-style-type: none"> Data from laboratory register
Confirmation by parasitology	$\% \text{ of CL cases confirmed by parasitology} = \frac{\text{Number of CL cases with positive slide}}{\text{Total number of confirmed (either laboratory or clinically) CL cases}} * 100$	<ul style="list-style-type: none"> By type of patient (new/relapse) 	<ul style="list-style-type: none"> Data from laboratory register
	$\% \text{ of positive slides} = \frac{\text{Number of positive slides}}{\text{Total number of probable CL cases tested for parasitology}} * 100$	<ul style="list-style-type: none"> By type of patient (new/relapse) 	

Clinical confirmation only	% of CL cases clinically confirmed = Number of CL cases confirmed based on clinical presentation / Total number of confirmed (either laboratory of clinically) CL cases * 100	<ul style="list-style-type: none"> By type of patient (new/relapse) 	
TREATMENT			
CL cases treated	Number of CL cases who started the treatment	<ul style="list-style-type: none"> By type of patient (new/relapse) 	
Treatment regimen route	% of CL cases treated, by treatment route = Number of CL cases treated, by treatment route / Total number of CL cases * 100	<ul style="list-style-type: none"> By type of patient (new/relapse) By treatment route 	
Treatment regimen	% of CL cases treated, by treatment regimen = Number of CL cases treated, by treatment regimen / Total number of CL cases * 100	<ul style="list-style-type: none"> By type of patient (new/relapse) By treatment route 	
Severe adverse events	Number of severe or life-threatening adverse events among CL cases who have received treatment	<ul style="list-style-type: none"> By type of patient (new/relapse) 	<ul style="list-style-type: none"> To be reported also to the national pharmacovigilance system
Defaulter rate	Number of defaulters / Total number of CL cases * 100	<ul style="list-style-type: none"> By type of patient (new/relapse) By treatment regimen By treatment route 	
INITIAL TREATMENT OUTCOME			
Failure rate	Number of failure as initial treatment outcome / Total number of CL cases * 100	<ul style="list-style-type: none"> By type of patient (new/relapse) By treatment regimen (antimonials/+paramomycin / Other) 	
FINAL TREATMENT OUTCOME			
Relapse rate	Number of relapse between initial and final treatment outcome / Number of CL cases treated * 100		<ul style="list-style-type: none"> This is the ideal indicator in case there is a cohort follow-up or individual data are computerized for CL cases.
	Number of relapse between initial and final treatment outcome / Number of CL cases followed-up at 6 months* 100		<ul style="list-style-type: none"> In case there is no cohort follow-up and only aggregated data are computerized.

Household Screening Register

District: _____ VDC/Municipality: _____

Ward No. _____ Village _____ Date: _____

Name of head of household _____ Contact Number: _____

S. No.	Name	Contact Number (if)	Age (years)	Sex (1=male, 2=female)	Suffered from KA during past 1 year or presently		Currently with fever = 2weeks	Skin lesion like PKDL (1=yes, 2=no)	Examination of suspected VL patient	
					(1=yes, 2=no)	If yes, date of diagnosis (mm/yyyy)			Spleen enlarged (1=yes; 2=no; 9=not done)	rK39 test result (1=pos; 2=neg; 9=not done)

Name of health worker: _____

Date: _____

Camp Attendance Register

District: _____ VDC/Municipality: _____ Village: _____

Date: _____

S.No.	Name	Ward	Village	Contact Number (if)	Age (years)	Sex (1=male, 2=female)	Suffered from KA in the past / currently		Currently with fever > 2weeks (1=yes, 2=no)	Skin lesion like PKDL (1=yes, 2=no)	Examination of probable VL patient	
							(1=yes, 2=no)	If yes, date of diagnosis (mm/yyyy)			Spleen enlarged (1=yes; 2=no; 9=not done)	rK39 test result (1=pos; 2=neg; 9=not done)

Case referral form

*Only for the patient with fever+splenomegaly+rk39 positive OR
patient with past history of KA+Skin lesion+rK39 positive)*

Referred from: 1=camp; 2=house to house search; 3=incentive approach

- Name of patient: _____
- Name of head of household: _____
- District: _____ VDC/Municipality: _____ Ward# _____ Village: _____
- House hold No:..... (to be copied from HH screening form)
- Patient ID: _____ (recorded as 001,002,..)
- Patient Age (in years): /____ / (record as 0 if less than 1-year age)
- Patient Sex: /____ / (1-male, 2-female)
- Date: _____

- Splenomegaly: 1= yes / no / not examined
- rK39 test result: positive / negative / not done
- Suspected case of VL? Yes / no
- Suspected case of PKDL? Yes / no

- Referred to: (name of doctor/hospital/ PHC)
- Reason for referral: For confirmation of suspected diagnosis of VL/PKDL
 - For rk39 test
 - For treatment
 - Any other reason

Name of referring doctor/health worker/FRA: _____

Signature: _____

Date: _____

► one copy to be retained by referring health worker

Government of Nepal
Department of Health Services
Epidemiology and Disease Control Division
Teku, Kathmandu, Nepal
Patient card

District: _____

Health facility name: _____

Health facility Code: _____

Unique patient ID code:

NPL-VL- 20 Date of admission:..... (DD/MM/YYYY)

Registration number:

Patient's Name: Sex: Female Male Age: (years)

Caste: Dalit/Janjati/Madheshi/Muslim/Brahman/Chhetri/others; Patient contact no.

Father/Husband's/family head's name:

Address:

Household Identification: Village: Ward no.:

VDC/Municipality: Metropolitan city/sub-metropolitan city/rural municipality/ urban municipality

District: Province: Country:

Patient's Information:

Date of onset of symptoms:

Time elapsed between onset of symptoms and admission, in days:

Does the patient live or work in a VL endemic area Yes No Unknown

Has the patient travelled to VL endemic areas in last 2 years Yes No Unknown

Probable place of infection: Same as place of residence Same as place of residence

Country: _____ Province: _____

District: _____ Ward: _____ Village/town: _____

Infection acquired outside the country : imported case Yes No Unknown

Source of detection: active case detection/passive case detection

Laboratory examination

Rapid diagnostic test : Yes No

Date of test (dd/mm/yyyy) ___/___/___ Result positive/ neg/ inconclusive/ unknown

DAT: Yes No

Date of test (dd/mm/yyyy) ___/___/___ Result positive/ neg/ Borderline/ unknown

Microscopy (Spleen/BM/Lymph node aspirate): Yes/ No

Date of test (dd/mm/yyyy) ___/___/___ Result positive/ negative/ inconclusive/ unknown

How was the VL case confirmed: RDT DAT Parasitology Clinically Only Unknown

Name of the diagnostic centre (if diagnosis was made in other centre):

Diagnosis: 1. Primary KA 2. Relapse-KA 3. PKDL 4. CL/MCL

Pregnant: Yes/No **Breast feeding:** Yes/No

HIV status: Reactive/Non-reactive/Not done (unknown)

Any other disease diagnosed:

.....

Date of treatment started: Treatment end date:

Treatment given:

No treatment given

Liposomal Amphotericin B (AmBisome®) Dosage _____

Liposomal Amphotericin B (AmBisome®)+ Paromomycin Dosage _____

Liposomal Amphotericin B (AmBisome®) + Miltefosine Dosage _____

Amphotericin B deoxycholate Dosage _____

Miltefosine Dosage _____

Other (specify _____) Dosage _____

Unknown

Was the treatment completed? Yes No

If No, give reason(s):

No, **Stopped for medical reason**

No, **Defaulter**

Unknown

Signature of MO:

Name: Date:

Seal of the health institution:

Patient's follow up

Initial Treatment Outcome (15 days after start of treatment)

Date of initial follow-up appointment ____/____/____

Clinical Assessment

Initial Outcome:

- Initial cure
- Failure/non-response
- Death: specify the cause of death:
 - Death due to VL Death due to HIV Death due to other disease
 - Death due to SAE (Iatrogenic) Death due to non-medical condition (accident)
 - Death due to unknown cause
- Referred
- Unknown/Lost-to-follow-up

Final Treatment Outcome (6 months after treatment completion)

Date of final follow-up appointment: ____/____/____

Clinical Assessment

Laboratory test _____ Result positive/ neg/ inconclusive/ not done

Final Outcome:

- Final cure
- Relapse
- Death :
 - Death due to VL Death due to HIV Death due to other disease
 - Death due to SAE (Iatrogenic) Death due to non-medical condition (accident)
 - Death due to unknown cause
- Unknown/Lost-to-follow-up

Examination and laboratory findings before and after treatment

Date of Visit (Before Treatment)	Date of Visit (after Treatment):
Temp: °F	Temp: °F
Weight: kg	Weight: kg
Pulse: /min	Pulse: /min
BP:	BP:
Spleen size:	Spleen size:
Hb%:	Hb%:
Creatinine:	
Malaria parasite:	
ALT (SGPT)	
AST (SGOT)	
Potassium (K ⁺)	

Treatment

No treatment given

Date of administration:				Dose of the drug:			
Duration of treatment:				Date of 1st treatment received:			
Treatment Given at- daily/ alternative day				(in case of relapse)			
Drug received	Batch No/expiry date	Drug dose & unit	Frequency	Route	Start Date	End Date	Was drug stopped for ADR (Yes/no)
L-AmB							
L-AmB+							
Miltefosine							
L-AmB+							
Paromomycin							
Amphotericin B deoxycholate							
Miltefosine							
Paromomycin							
Other							

Concomitant drugs							
Name	Indications	Batch No/expiry date	Drug dose & unit (if I.V) infusion rate in ml/hour	Frequency	Route	Start Date	Stop Date

HMIS Reporting Form 9.3

१२. कालाजार नियन्त्रण कार्यक्रम (Kala-azar Control Programme)															
Patient Type		Age/Sex				Method of Diagnosis				Treated With		No. of Deaths			
		<5 Years		≥5 Years		RK-39		BM		SP		Other		L,A/M*	Other
1		2	3	4	5	6	7	8	9	10	11	12	13		
Indi- genous	Within District														
	Outside District														
Foreigner															

* Liposomal Amphotericin B/Miltefosine

HMIS 5.3 Kala-Azar Treatment Register

Registration																		Admission and Diagnosis												Treatment										Treatment Outcome																																									
S.N	Unique Pt Identification Code	Service Registration Number	Date of Admission			Patient's												Mode of detection		Pregnant (Y/N)	Days between symptoms and presentation				Type of Disease				Method and date of diagnosis				Diagnostic center	Type of confirmation clinically	RDT microscopy	Treatment		Treatment regimen						Any side effects, specify if any				Treatment completion				Initial outcome				Final outcome				Remarks																					
			D	M	Y	First Name	Last Name	Caste code	Age (in Years)	Gender (F/M)	Province	District	Local Level	Ward No.	Village/Tole	Contact No.	Family Head's Name	ACD (Active case detection)	PCD (Passive case detection)		New KA	Relapse	PKDL	CL/MCL	Has the patient traveled to VL endemic region in last 2 yrs? If yes place to visit	Origin of the infection (autochthonous/imported from another endemic region or from another country?)	HIV Status	D	M	Y	RK39 result	D				M	Y	D	M	Y	D	M	Y	Microscopy result	D	M	Y	D	M	Y	Not started	Monotherapy	1. Miltefosine	2. Miltefosine	3. Paromomycin	4. Amphotericin B	Combination	1. L-AmB + Miltefosine	2. L-AmB + Paromomycin		3. Miltefosine + Paromomycin	Other (specify)	Unknown	1. Completed	2. Stopped for medical reasons	3. Discontinued	4. Unknown	D	M	Y	D	M	Y	D	M	Y	D	M	Y	Outcome	1. Initial Cure
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69													

Column 9: Caste/Ethnicity code: 1 Dalit, 2 Janajati, 3 Madheshi, 4 Muslim, 5 Brahman/Chhetri, 6 others

Column 24: Relapse -Reappearance of KA (VL) signs and symptoms within a period of 6 months after the end of the treatment

Column 25, 26: Post Kala-azar Dermal Leishmaniasis, Cutaneous leishmaniasis, mucocutaneous leishmaniasis

Column 29: HIV status- Reactive(1), Non reactive(2), Not done (3)

Column 63, 68: Cause of death- due to VL, due to HIV, due to other medical conditions, due to SAE, due to non medical condition, unknown cause

Adverse Event Reporting Form

A. Patient and Health Facility Information			
Patient ID number:		Treatment Centre:	
Date of Birth (or Age):		Province:	
Sex:	<input type="checkbox"/> Male	<input type="checkbox"/> Female	<input type="checkbox"/> Other
HIV status:	<input type="checkbox"/> Non-reactive	<input type="checkbox"/> Reactive	<input type="checkbox"/>
Pregnancy:	<input type="checkbox"/> No	<input type="checkbox"/> Yes	<input type="checkbox"/> Trimester:
Weight (kg):			

B. Adverse events experienced by patient					
Adverse event	Onset date	End date	Severity grade	Seriousness*	Outcome [§]
*Please select: <i>D</i> died <i>LT</i> life threatening <i>HA</i> caused or prolonged hospital admission <i>PD</i> permanent disability					
<i>OS</i> other medically serious <i>CA</i> congenital abnormality <i>NS</i> not serious					
§Please select: <i>A</i> recovered <i>B</i> recovering <i>C</i> recovered with residual effects <i>D</i> died <i>E</i> not recovered <i>F</i> unknown					

Detailed description of adverse event (s):

Was treatment of adverse event required? No Yes (please specify):

C. Laboratory assessment: Results of tests if any				
Test performed	Test date	Result	Unit	Reference range

D. Medicines: List all medicines used for the treatment as well as other commitment medications if any								
<input checked="" type="checkbox"/> Tick if medicine suspected of causing adverse event								
Medicine	Dose	Frequency	Route	Start date	Stop date	Reason for use	Action taken [†]	Response [‡]
<input type="checkbox"/>								
<input type="checkbox"/>								
<input type="checkbox"/>								
<input type="checkbox"/>								
<input type="checkbox"/>								
<input type="checkbox"/>								
†Action taken in response to AE: <i>DW</i> drug withdrawn <i>DR</i> dose reduced <i>DI</i> dose increased <i>DNC</i> dose not changed <i>UK</i> unknown <i>NA</i> not applicable								
‡Response to action taken: <i>RA</i> recovered <i>NE</i> no effect on AE <i>FA</i> fatal AE <i>UN</i> unknown <i>NA</i> not applicable								

E. Other relevant information

Name and Brand name of the Drug used:

Batch number:

Expiration date:

Any other information on the drug:

F. Reporter Information

Name:

Phone Number:

Email:

Occupation: Doctor Nurse Paramedics Other (please specify):

Signature:

Date

Submit form to:

EDCD, Teku: edcd@gmail.com

EDCD Use Only:

Date received:

Causality assessment: Likely Unlikely

Comment:

To accelerate the elimination program in the district, success of active case detection is important. This approach will help facilitate early detection and prompt treatment. The district health/public health office in coordination with the health institutions from where passive cases are reported should be responsible for planning and implementation of active case detection. The standard protocol for active case detection of KA and PKDL cases is given below:

A. Index Case Based Approach

Policy/scope: This approach is to be implemented in low KA endemic areas (to be defined in each country) on an ongoing basis throughout the year in communities with newly detected KA cases.

General responsibilities: The District Public/Health Officer is responsible for implementing the activity.

Materials required: 1) Work diary; 2) Patient register; 3) Patient Referral slips; 4) Training manual; 5) Household screening register; 6) Kala azar treatment card; 7) Drug distribution register

Procedures

Preparatory activities at district level

1. Identify villages where the index case approach will be applied.
2. Identify and train public health workers / health volunteers in identification and referral of chronic fever cases.
3. Identify staff at DPHO / DHO responsible for conducting index case search of neighborhood.
4. Define information sources of index cases—e.g. monthly review meetings at district etc.
5. Ensure availability of drugs, rk39 test kits, fund requirements, IEC material, treatment cards etc. at the district.
6. Prepare plan for supervision and M & E of index case-based approach –identify supervision team for supervision activities on a sample basis.
7. Define reporting system from health facility to district.

Preparatory activities at health post level

8. Identify and train health workers / health volunteers in identification and referral of chronic fever cases, skin lesion cases (suspected PKDL/CL/MCL).
9. Identify staff / health volunteers responsible for conducting index case-based search of neighborhood.

Index case-based search activities

1. Monthly review of all KA cases reported by zonal / district hospital from the district.
2. List KA patients – name, age, sex and detailed address of patient, name of health post responsible for index case search.
3. Health post staff visits the community of the index case, traces the home, confirms identity of the patient and alerts the health worker/health volunteer.
4. Organize house to house search around index case in the same month of reporting of index case using screening forms or format or register.
5. Screen all individuals for fever =2 weeks in neighboring households in the village/hamlet around the house of index case done by HP staff and health worker / health volunteer.
6. Fill patient referral form and refer cases to district / zonal hospital for confirmation of kala-azar.
7. Maintain a list of cases referred for confirmation of KA diagnosis.
8. Inform district / zonal hospital staff of cases referred for KA diagnosis.

Maintain records and report to district on index case finding activities conducted.

Post index case-based search activities at district/zonal hospitals

1. Ascertain diagnosis of all cases referred by health workers after index case-based search.
2. Ensure that all kala-azar cases are started on treatment.
3. Monitor treatment compliance and side effects.
4. Ensure timely payment of wage-loss to kala-azar/PKDL patients.
5. Ensure timely payment of incentives to Female Community Health Volunteer for case follow-up.
6. Ensure availability of drugs and diagnostics at hospitals based on number of kala-azar cases.

Post index case-based search activities at district level

1. Assess monthly reports on number of kala-azar cases, drug distribution.
2. Supply of drugs and diagnostics based on number of kala-azar cases reported.
3. Evaluate index case finding activities based on supervision / monitoring reports.

Post index case-based search activities at health post level

1. Inform public health workers of cases diagnosed and started with KA/PKDL treatment to ensure treatment compliance or for any side effects/adverse events.

B. Camp Approach

Policy/scope: The camp approach is to be implemented in kala-azar high endemic districts. The camp approach ideally is to be implemented twice a year.

General responsibilities: The District Public/Health Officer is responsible for implementing the camp approach strategies.

Materials required: 1) rK39 kits in a cool box for transport; 2) Lancet & Lancet disposal box; 3) Cotton; 4) Spirit; 5) Gloves; 6) General medicines – anti-pyretics, antibiotics, anti-diarrheal, anti-malarial drugs etc.; 7) Rapid diagnostic kits for malaria (optional in malaria endemic areas) and other diseases, if available; 8) Patient referral form; 9) Lab investigation form; 10) Camp register (Register book); 11) Photo album of PKDL; 12) VL/PKDL patient registration form; 13) IEC materials, banners, posters, pamphlets (local language), pictures of PKDL skin lesions; 14) Mikes; 15) BP apparatus; 16) Thermometer; 17) Stethoscope; 18) Disposable syringes, IV infusion sets etc. (optional); 19) Transport box for drugs, supplies etc.; 20) Emergency drugs – cortisone, anti-histamines, IV fluids, adrenaline; 21) Bio-waste disposal containers; 22) Equipment for starting treatment (optional in areas where treatment will be started in the camp)

Procedures

Pre-camp preparatory activities at district level

1. List the villages with high kala-azar incidence (new cases reported).
2. Conduct a meeting with DP/HO to prepare a micro-action plan at least 1 month before initiation of camps.
3. Prepare a time schedule for camps—decide number of camps, timings, duration of each camp, list name of villages where camps are to be held etc.
4. Prepare logistics plan—estimate requirement of drugs, rk39 test kits, lancets, gloves, fund requirements, IEC material etc.
5. Prepare supervision and monitoring plan for camps— identify supervision team, supervision schedule etc (on a sample basis).

Pre-camp preparatory activities at village level

1. DPHO/DHO staff meeting to plan camp activities at least 2 weeks before initiation of camps.
2. Identify the DPHO/ DHO team (medical officer, nurse, lab technician, health inspector, etc) which will conduct/ coordinate camp activities.
3. Define duration of camp (usually one day camp).
4. Prepare plan for camp logistics—drugs, diagnostics etc.
5. Arrange/provide refreshments for camp team on the day of camp.
6. Vehicle requirement.
7. Identify and coordinate with village level functionaries/leaders.

Pre-camp preparatory activities (village level)

1. One HP staff (nurse, lab technician, health inspectors or other) conducts coordination meeting at least 1 week before camp with community leaders/members and others to inform and solicit community involvement in publicity and conduct of camp activities.
2. Identify venue for camp and determine its suitability for conducting camp.
3. Identify, train and assign roles to village functionaries/volunteers / religious leaders/school teachers for camp publicity activities.
4. Publicity activities to include miking, public announcement, distribution of pamphlets, putting up of banners/posters in public places, announcement on local FM radio, interpersonal communication by health workers etc.
5. Publicity activities to be conducted at least one day prior to camp and on the day of camp.
6. List and manage locally camp furniture (tables, chairs, bench, examination table, bedside screens), drinking water provision etc.
7. Set up camp one day prior or early morning of the camp day (e.g. Through local volunteers).

Camp day activities

1. Camp Team: one MO, one lab technician, one nurse, NGO/ community volunteers/school teachers etc.
2. Organize flow of camp activities.
3. Patient registration (name, address, age and sex).
4. Examination of patient for fever = 2 weeks by MO, past history of kala-azar, spleen examination, general examination, examination for skin lesions.
5. rk39 test to be done by lab technician at camp if fever =2 weeks and splenomegaly.
6. If rk39 test positive, Case Referral form to be filled and given to patient. Case referral register to be completed.
7. Kala-azar treatment card filled for rk39 positive patients. One copy of treatment card given to patient. Office copy of treatment card archived in district hospital.
8. For probable PKDL patients (PKDL-like skin lesions with rk39 test positive and past history of kala azar treatment) will be referred to district/appropriate level hospital for confirmation of diagnosis and treatment start.
9. Drug distribution register maintained.
10. If rk39 test negative or for all other patients, MO advises appropriate treatment / refers for further diagnostic tests. Particular emphasis may be given to suspected leprosy patients.
11. All patients with severe kala-azar and or other co-infections to be referred to appropriate level hospital.
12. Proper disposal of bio-was treat the end of the camp.

Post camp activities at district level

1. Maintain camp records - camp registers, treatment cards, referral register, drug distribution register.
2. Manage patient specific drug box for kala-azar patients.
3. Ensure that patients referred from camp or patients started on KA treatment follow up regularly for further treatment.
4. Ensure timely payment of wage-loss monies to kala-azar patients
5. Assessment of camps- Number of attendees, number of chronic fever cases, number of rk39 tests done, number of rk39 test positives, number of patients started treatment for kala-azar/PKDL, number of patients referred for KA/PKDL treatment and follow up, drug distribution.
6. Assessment of constraints, difficulties of conducting camp.
7. Submit camp activity reports to district.
8. Supply of drugs and diagnostics based on number of VL/PKDL cases reported.
9. Evaluate camp activities based on supervision/monitoring reports.

Post camp activities at village level

1. Inform health workers of patients diagnosed and started with KA/ PKDL treatment to ensure treatment compliance or for any side effects/adverse events.

Note: As PKDL is one of the differential diagnoses of leprosy, all suspected PKDL cases should be ruled out for leprosy. During camp activities health workers who can screen leprosy should be mobilized. Leprosy programme people should be informed of this activity and at district level, district TB and leprosy officer (DTLO) is the appropriate person to coordinate leprosy screening in these camps.

C. Incentive Based Approach

Policy/scope: The incentive approach is to be implemented in low kala-azar endemic areas (to be defined in each country) and is implemented on an ongoing basis throughout the year in communities with newly detected kala-azar/PKDL cases.

General responsibilities: The District Public/Health Officer is responsible for implementing the incentive-based case detection strategies.

Materials required: 1) Work diary; 2) Patient register; 3) Patient Referral slips; 4) Training manual, Pictures of PKDL skin lesions

Procedures:

Preparatory activities at district level

1. Identify villages where the incentive approach will be applied based on endemicity.
2. Identify and train health workers / health volunteers in identification and referral of chronic fever cases.
3. Ensure availability of drugs, rk39 test kits, fund requirements, IEC material, treatment cards etc. at the district.
4. Prepare plan for supervision and M&E of incentive approach - identify supervision team for supervision activities on a sample basis and based on the report of the cases in the district hospital.
5. Define reporting system from health post to the DPHO/DHO.
6. Manage fund for providing incentive.

Preparatory activities at health post level

1. Identify and train health workers/health volunteers in identification and referral of chronic fever cases, skin lesions.

Incentive based search activities

1. Screen individuals for fever =2 weeks in the village / hamlet.
2. Fill patient referral form and refer patients to nearest PHC /district/zonal hospital for confirmation of kala-azar.
3. Maintain a list of patients referred for confirmation of KA diagnosis.
4. Inform PHC/ health post staff of patients referred for KA diagnosis.

Post incentive-based search activities at health post level

1. Ascertain diagnosis of all patients at the district hospital referred by health workers.
2. Ensure that all kala-azar patients are put on treatment.
3. Monitor treatment compliance and side effects.
4. Maintain records and report to district about case finding.
5. Ensure availability of drugs and diagnostics at District Hospital based on number of kala-azar/ PKDL cases.

Post incentive-based search activities at district level

1. Assess monthly reports from health facility –Number of kala-azar / PKDL cases, drug distribution.
2. Supply of drugs and diagnostics based on number of kala-azar/PKDL cases.
3. Evaluate incentive-based case search activities based on passively reported cases in the district hospital.

Post incentive-based search activities at health post level

1. Inform health workers/health volunteers about the patients diagnosed and started with kala- azar/PKDL treatment to ensure treatment compliance or for any side effects/adverse events.

Table 30: **Classification of different levels of health facilities in Nepal**

Level I	Level II	Level III
<p><u>Public Sector</u></p> <ul style="list-style-type: none"> • Health post • Female Community Health Volunteers (FCHV) 	<p><u>Public Sector</u></p> <ul style="list-style-type: none"> • Primary Health Care Centers (PHCC) 	<ul style="list-style-type: none"> • National hospitals • Regional hospitals • Zonal hospitals • Provincial hospitals • District hospitals • Medical College
<p><u>Private Sector</u></p> <ul style="list-style-type: none"> • Unqualified practitioners • Qualified practitioners • Medicine shops 	<p><u>Private Sector</u></p> <ul style="list-style-type: none"> • Nursing homes • Private laboratories • NGOs 	<p><u>Private Sector</u></p> <ul style="list-style-type: none"> • Large hospitals • Medical colleges

Note: (i) BP Koirala Institute of Health Science, Dharan and (ii) Sukraraj Tropical and Infectious Diseases Hospital, Teku, Kathmandu are identified as national referral centers.

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