

# Cutaneous Leishmaniasis Management Guide

Ministry of Health, Public Health Deputyship, Saudi Arabia

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## Foreword

Leishmaniasis, a neglected tropical disease, is endemic in Saudi Arabia. Despite the significant breakthroughs in reducing the disease burden, Leishmaniasis remains a significant public health challenge.

The predominant form in Saudi Arabia is the Cutaneous Leishmaniasis (CL), while the more severe visceralizing leishmaniasis (VL) is scarce; only a few cases occur every year.

Saudi Arabia hosts different species of the Leishmania parasites and several sand fly species. Massive internal and external population movements make the control of leishmaniasis very laborious.

The Leishmaniasis Control Program (LCP), established 20 years ago, succeeded to reduce the disease burden dramatically. With time and through gaining of experience, the control program has amended its targets, objectives, and goals, and has set-up comprehensive plans and strategies to achieve its mission. Regular updates of the objectives and strategies are carried out based on the integration of the available data, new scientific discoveries, and the available resources. This manual reflects the current view of the leishmaniasis control program and the most recent updates in handling of CL patients.

## Introduction

Leishmaniasis is characterized by a broad spectrum of clinical manifestations, ranging from mild localized disease to a lethal form. Generally, the disease occurs in three main forms: cutaneous leishmaniasis (CL), mucocutaneous leishmaniasis (MCL) and visceral leishmaniasis (VL).

CL is the most common form of leishmaniasis, and it is a potentially disfiguring disease that can lead to social stigmatization. Currently, it is endemic in 87 countries worldwide, mainly in the Mediterranean region and the Americas (Fig.1). However, new cases are reported from areas which were previously known as free zones. The actual incidence is estimated to be much higher since not all cases seek medical advice, and not all diagnosed cases are reported to the official records of health authorities. Due to the clinical multi-faceted of CL, and incrimination of different parasite species, management of cases pose a major challenge facing guidelines development.

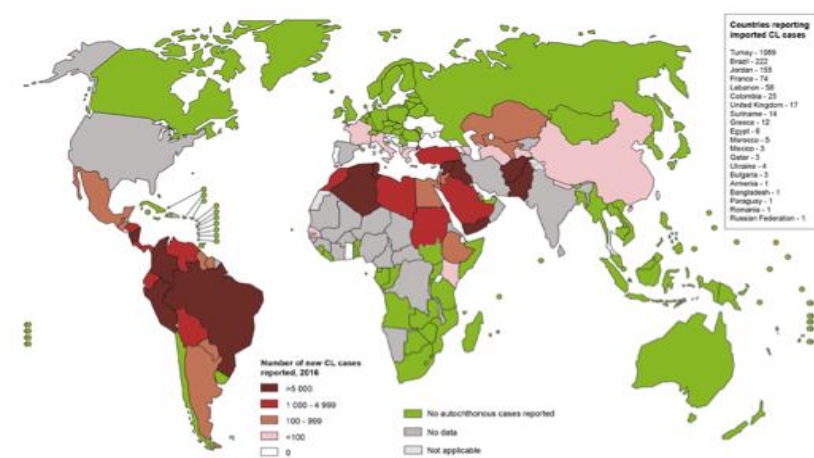


Fig. 1 Status of endemicity of CL worldwide, 2016

## Epidemiology is Saudi Arabia

Two decades ago, KSA was among the top ten endemic countries concerning the incidence of CL. In the year of 1983, 18,318 new cases of CL were reported. The incidence dropped dramatically in the subsequent years following the establishment of the Leishmania Control Program (LCP) at the

ministry of health. In 2017, 1007 new cases in Saudi Arabia have been reported to LCP (Fig 2).

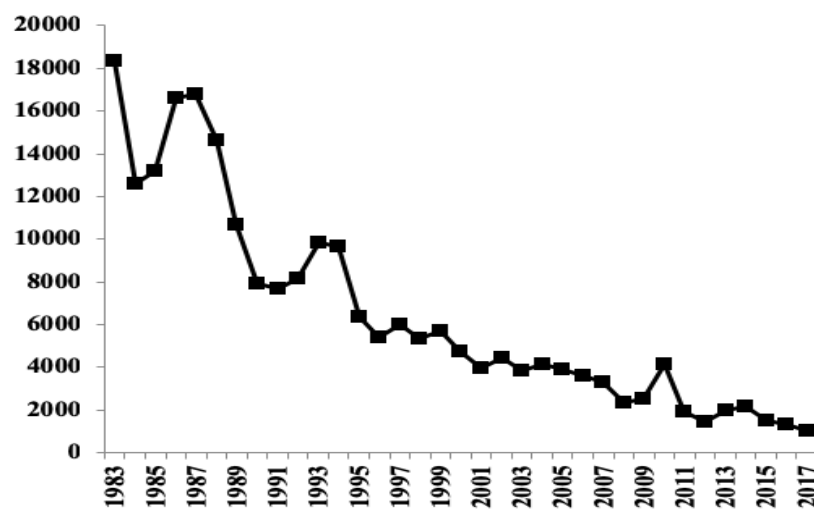


Fig. 2 Total number of CL cases reported from 1983 -to 2017

With the exception of three regions, Makkah, Qurayyat and Qunfudah, CL is reported from most parts of the country with regional hot foci. The vast majorities of cases are reported from Qaseem and Riyadh (Central), Al-Ahsa (East), Aseer (South West), Ha'il and Madina (North West).

The rapid urbanization process, the development of agricultural schemes and the changing climatic pattern, in Saudi Arabia, is modifying the spatial-temporal distribution of sand flies and animal reservoir of parasites. This is reflected in the huge variation seen in the number of reported cases from the same region over different years. Another major challenge facing the disease containment effort is the increasing number of religious visitors and job seeker entering the country from Leishmania endemic countries.

The highest numbers of cases occur during winter. The number of cases usually start to increase during August, peaks in January and February, then decline and reach the lowest number between April and July (Fig. 3).

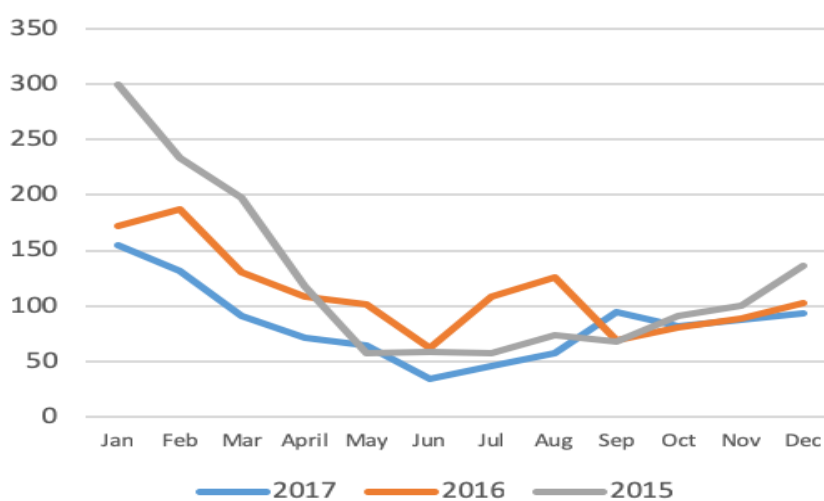


Fig. 3 Number of new cases reported by month, 2015 - 2017

## Etiology

### Parasites

Two leishmania species are incriminated in causation of CL in Saudi Arabia: *L. major* and *L. tropica*.

*L. major* (Zoonotic cutaneous leishmaniasis - ZCL) is widely distributed but is found mainly in the central and eastern regions of Saudi Arabia. On the other hand, *L. tropica* (Anthroponotic cutaneous leishmaniasis - ACL), was mainly reported from the south-western regions of the country, but recent studies showed that it does exist in many other regions. The two species co-exist in Qaseem, Madina, Ta'if and Al-Baha (Fig. 4).

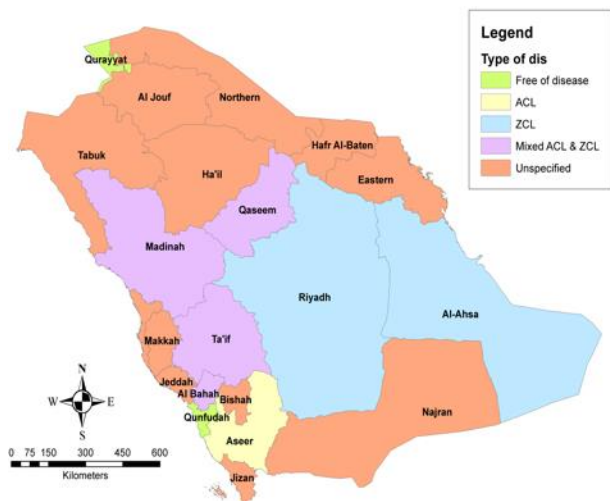


Fig. 4 Regional distribution of ACL & ZCL

## Vectors

Leishmania parasites are transmitted from host to another through the bite of female sand-fly. Many sand-fly species have been described in Saudi Arabia, but only two species are thought to be transmitting CL; *P. papatasi* (the vector for *L. major*) and *P. sergenti* (the vector for *L. tropica*) (Fig. 5a and 5b).

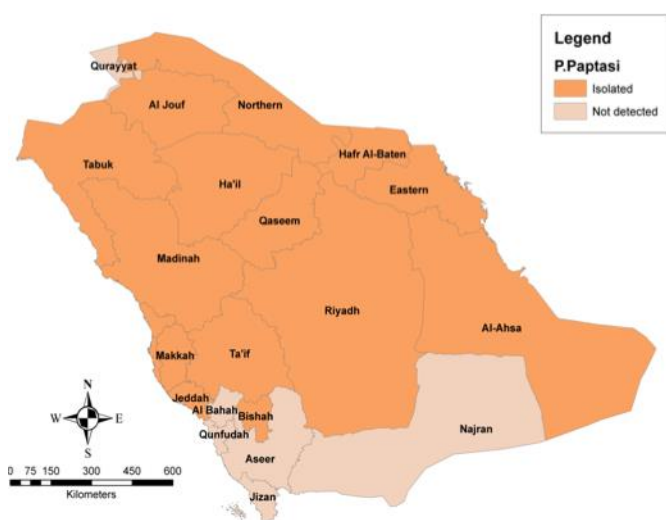


Fig. 5a Geographical distribution of sandflies *P. papatasi*

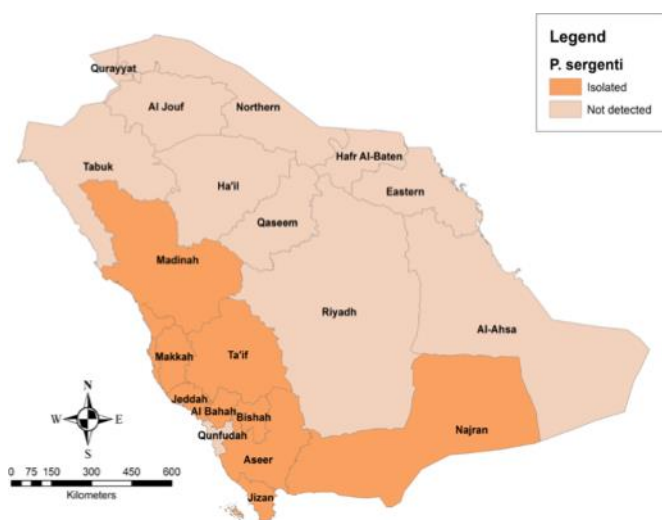


Fig. 5b Geographical distribution of sandflies *P. sergenti*

## Reservoirs

Rodents have been identified as the principal reservoir of *L. major* (ZCL) in Saudi Arabia. Two types of rodents were defined as reservoir hosts; *Psammomys obesus* and *Meriones libicus*. Zoonotic mode of transmission has also been documented for *L. tropica* (ACL).

## Transmission cycle

Sand-flies transmit Leishmania parasites from human-to-human, animal-to-human, and human-to-animal.

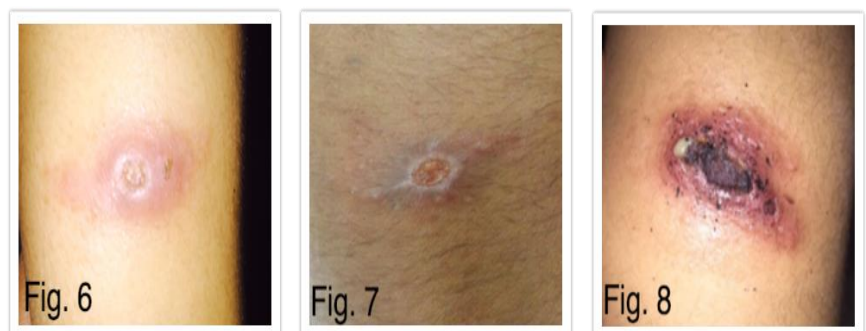
When a sand-fly bites an infected skin, it scratches the tissue of the dermis and suck the blood which contains *amastigotes* filled macrophages. In the midgut of the sand-fly, *amastigotes* change to *promastigotes* (infective stage), which migrate to the anterior part of the gut. At this stage, the sand-

fly is infective, and during the next meal, it injects *promastigotes* into the dermis of the new host. The *promastigotes* change to *amastigotes*, which are engulfed again by macrophages in the dermis where they multiply.

## Clinical presentation

### Clinical description

Appearance of one or more lesions, typically on uncovered parts of the body. At the site of inoculation, a papule appears which may enlarge to become an indolent ulcerated nodule or plaque. The sore remains in this stage for a variable time before healing and typically leave a depressed scar (Fig 6). Sometimes, small papules appear at the edge of the original lesion (Fig. 7). Bacterial superinfection of lesion might occur (Fig. 8).



The most common presentations are:

- A single ulcerative lesion in the face, neck or extremity.
- Nodular and nodulo-ulcerative type of lesions are less common.
- The incubation period of *L. tropica* is 2 to 8 months and usually present with dry ulcerative lesions.
- The incubation period of *L. major* is less than 4 months and tend to cause multiple inflamed and ulcerated lesions. Lesions may become confluent and secondarily infected especially in non-immune individuals.

### Case classification (WHO)

1. *Probable case*: A person showing clinical signs of CL (skin lesions) without parasitological confirmation of the diagnosis.
2. *Confirmed case*: A person showing clinical signs (skin lesions) with parasitological confirmation of the diagnosis.
3. *Cured case*: Complete re-epithelialization before Day 45.
4. *Relapse case*: Reappearance of a nodule, plaque or ulceration after cure. Parasitological confirmation only in complex cases.
5. *Treatment failure*: Increase of a nodule, plaque or ulceration within 14 days of treatment, or lack of complete re-epithelialization within 45 days of treatment starting.

### Demographic features of CL in Saudi Arabia

The disease affects both citizens and expatriates. Males between 14 and 45 years are the most affected. Most affected expatriates are field worker e.g. farmers.

## Diagnosis

As many skin conditions can display similar features to CL, parasitological confirmation of CL is needed. In addition, systemic anti-leishmanials are generally toxic and costly, so it is morally unacceptable to expose individuals to such medicines without solid diagnosis. Laboratory criteria for diagnosis require positive parasitology (Geimsa stained smear, culture from the lesion or by Polymerase Chain Reaction-PCR).

Sampling procedures include scrapping, fine needle aspiration and punch biopsy.

### Parasites determination

Currently, iso-enzyme electrophoresis is the main tool used for precise species determination. However, molecular techniques provide rapid determination of species and their use is increasing.

## Treatment

In general, CL is a self-limiting disease. *L. major* lesions tend to heal spontaneously within 2 - 8 months, while *L. tropica* lesions spontaneous healing usually takes a year or longer.

The use of specific Anti-Leishmania therapy may help accelerate the healing process and shorten the infectivity period. Treatment of CL is determined by disease severity:

- Mild Disease: 4 or fewer lesions (1 cm or more), none  $\geq$  to 5 cm in diameter; no lesions in cosmetically sensitive areas, no lesions over joints or genitalia; may observe.
- Complex Disease: >4 lesions and/or one over 4 cm in diameter and/or lesion(s) over joints or in cosmetically sensitive area(s), or failure of previous treatment, or substantial local or lymphatic nodules, or large regional lymphadenopathy.

For all patients, lesions should be derided, cleaned, and covered by a clean dressing.

Treatment of CL can be divided into three approaches:

- Wait & see policy: involves local wound care only
- Local therapies: consist of topical, physical and/or intralesional interventions
- Systemic treatments: consist of parenteral and oral medicines.

Treatment options

*Guidelines don't specify treatment of choice for cutaneous disease, all listed options must be individualized.*

#### **Mild Disease:**

Observation only for spontaneous healing is preferred in most cases and particularly when *L. major* is incriminated.

A plan of follow-up should be established (day 14, 30, 45, and 180). Lesion(s) should be >50% healed by 4-6 weeks. If not healing, or if *L. tropica* is suspected, local therapy should be considered:

- Debride necrotic tissue before any local therapy instituted.
- *Paromomycin* ointment bid x 20 days.
- Heat therapy one or two applications (painful).
- Intralesional antimony; *Sodium Stibogluconate* 100-500 mg (1-5 mL) per session every week for 1-5 sessions.
- Cryotherapy: freeze up to 6 times per week with liquid nitrogen (alone or together with intralesional antimony)
- Laser therapy

#### **Complex Disease**

- *Sodium Stibogluconate* or *Meglumine antimoniate* 20 mg/kg/day IV/IM x 20 days
- *Liposomal Amphotericin B* 3 mg/kg IV once daily for 7 days
- *Fluconazole* 200 mg po daily x 6 weeks. Data for *L. major* only
- *Ketoconazole* 600 mg po daily for 30 days. Data for *L. major* only.
- *Amphotericin B* 0.5-1 mg/kg IV daily or qod to total dose of 15-30 mg/kg

#### **References**

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