



over 1 billion

Neglected  
tropical  
diseases

people living in  
endemic areas  
at risk of infection

# CASE SCENARIO

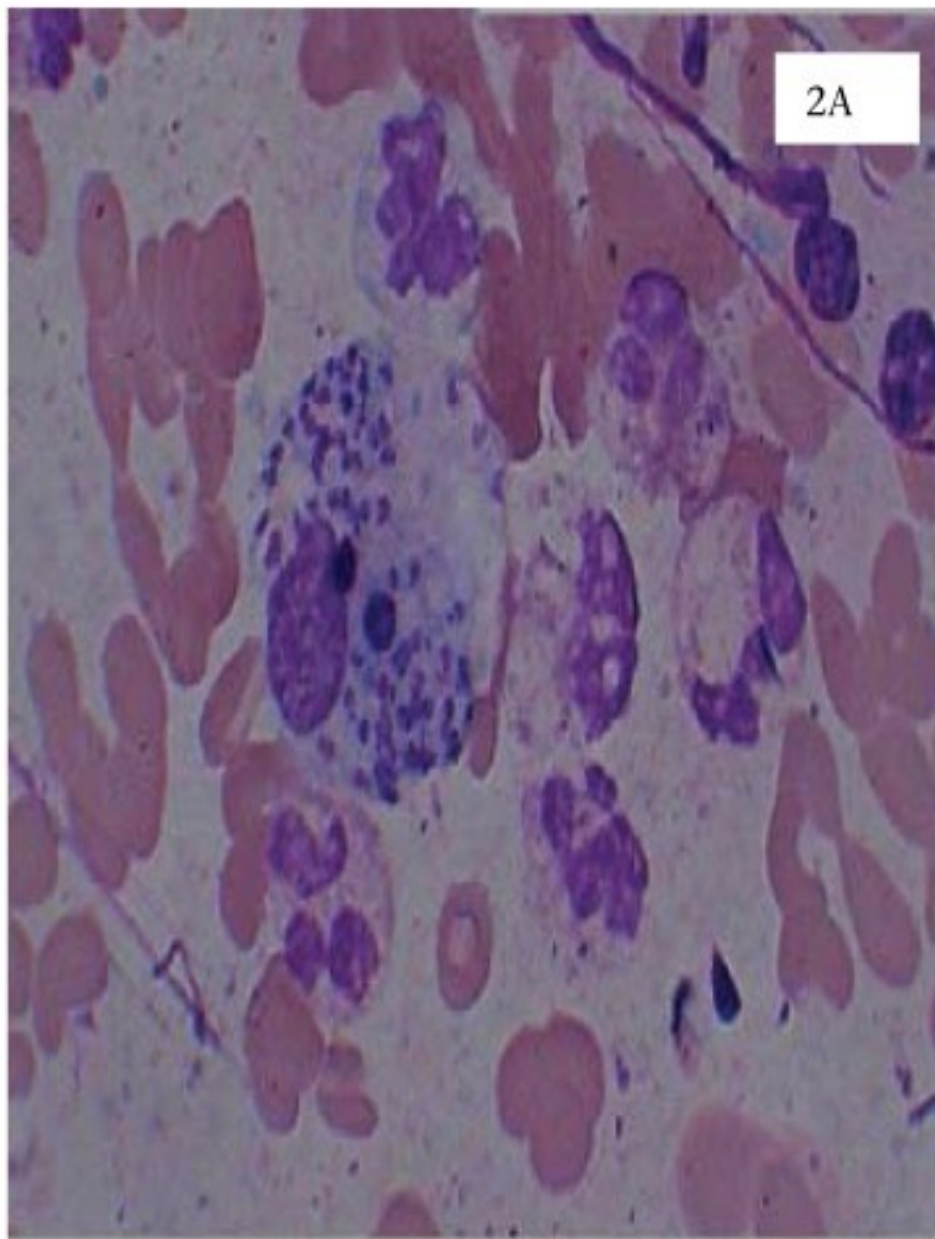
- A 37-years old man presented to the SRU of diagnostic labs for ALS test of tuberculosis advised by the physician
- 6-week history of skin lesions on his nose, ear, arm, and fingers.
- Physical examination revealed **painless erythematous papules and nodules with overlying scale and crust, some of which had central ulceration (Figure 1A and 1B)**
- The patient was from Saudi Arabia, **an area in which cutaneous leishmaniasis is endemic.**
- bitten by sandflies during his stay at Saudi Arabia.
- Following the bite, the lesion started as an itchy red papule slowly enlarged into an inflammatory papule to an ulcer.
- **THE HEALTH PERSONNEL** in the SRU suspected the case as a possible case of Cutaneous leishmaniasis.

Journal of Health, Population, and Nutrition [2014

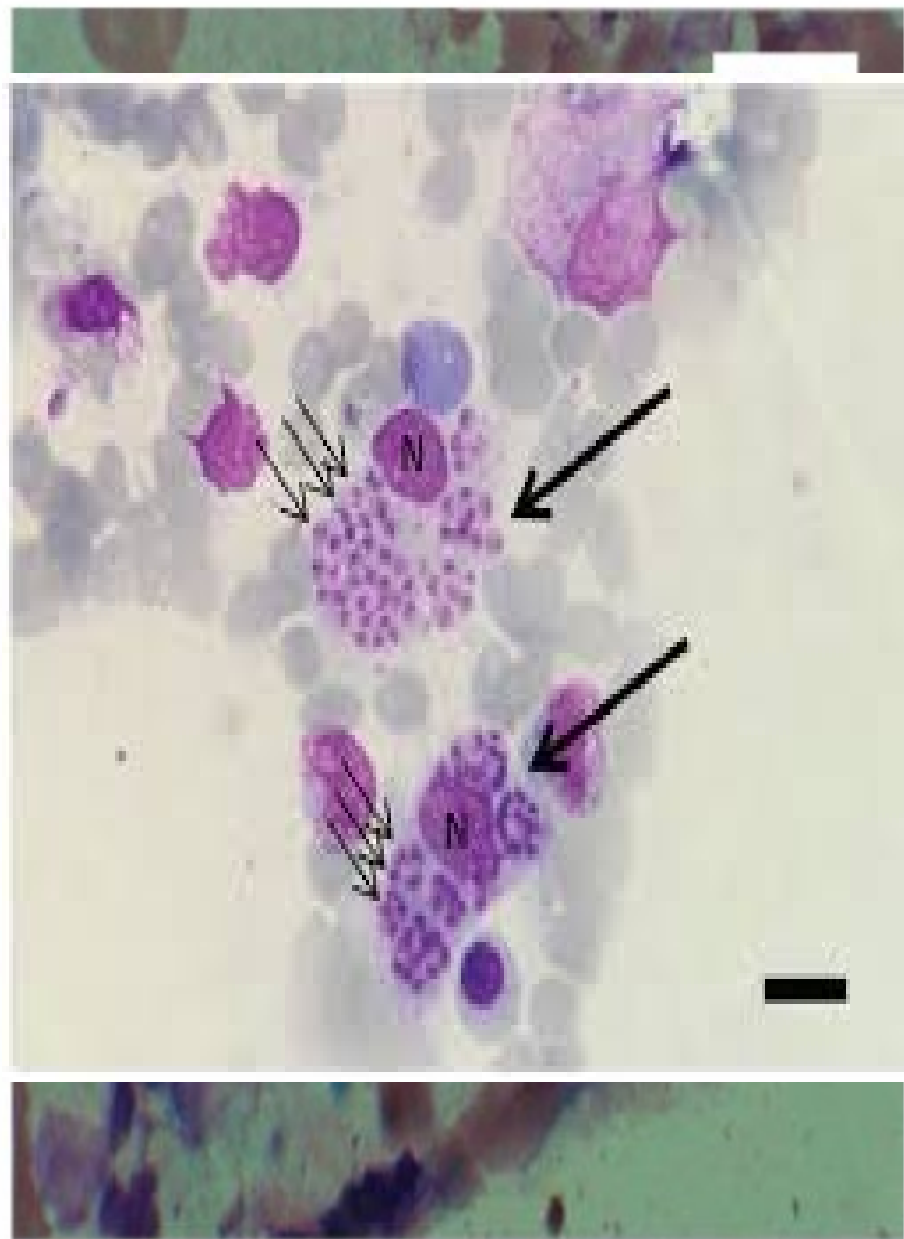
A [before treatment]

10 days after tx with sodium stilbogluconate





2A. Dermal skin scrapings Wright's stain. Plenty of LD bodies (amastigotes) within a macrophage (x100)



2B. Dermal skin scrapings Leishmann's stain. Amastigotes are seen within a macrophage (x100)



**THE MONSTER INSIDE ME**  
***THE FLESH EATER***

**LEISHMANIASIS**

# LEARNING OBJECTIVES

At the end of this lecture the students of 3<sup>rd</sup> year MBBS should be able to

- Define leishmaniasis
- Classify leishmaniasis
- Describe its epidemiology
- Describe the global burden and geographical distribution of leishmaniasis
- Describe the burden of disease in Pakistan
- Enumerate the preventive measures to reduce the risk of leishmaniasis at the primary level
- Name vaccines available against leishmaniasis
- Describe effectiveness of the vaccines available
- Enumerate headlines for rising cases of leishmaniasis in Pakistan

# INTRODUCTION

## LEISHMANIASIS

**A GLOBALLY IMPORTANT BUT NEGLECTED TROPICAL PARASITIC DISEASE**

### CAUSATIVE ORGANISM

- Protozoan parasite of **genus Leishmania**
- Obligate intracellular protozoa
- 20 out of 300 known species cause disease in humans
- most cases arise from one of three species:  
**L. donovani, L. tropica, and L. braziliensis.**

# LEISHMANIA PARASITE

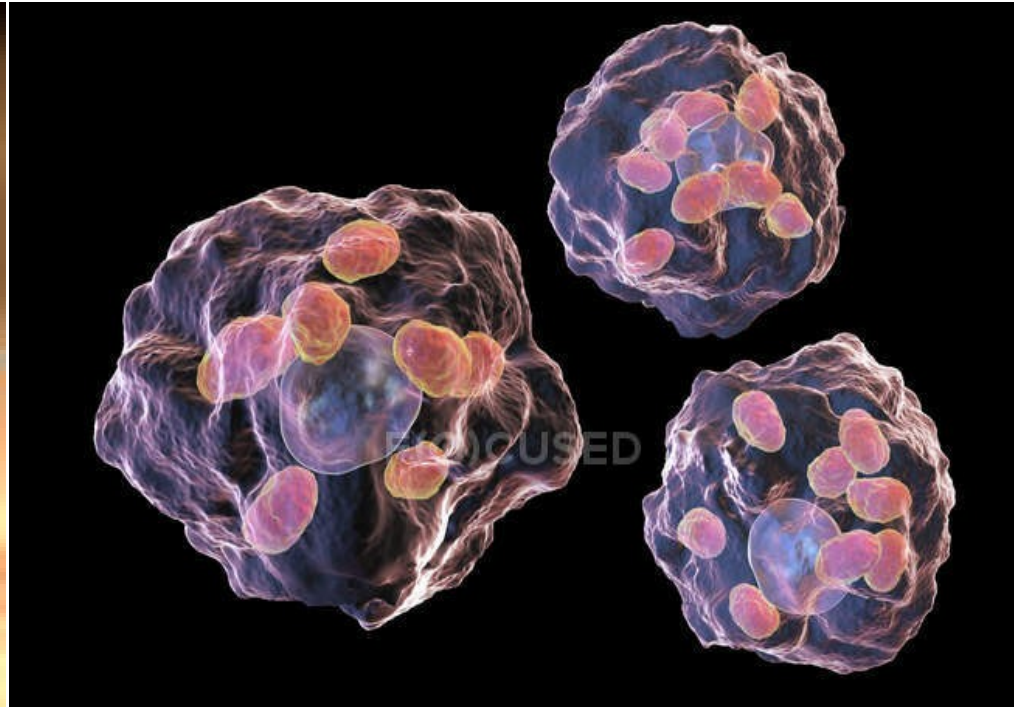
PROMASTIGOTE

Sand fly



AMASTIGOTE IN MACROPHAGE

Human





- **HOSTS**

1. humans definite host
2. domestic/wild animals  
reservoir host

# VECTORS

- *Phlebotomus* (Old World)
- *Lutzomyia* (New World)



## In Ecuador:

- Lu. trapidoi*
- Lu. hartmani*
- Lu. gomezi*
- Lu. ayacuchensis*

# RESERVOIRS



**VECTOR RESPONSIBLE** :infected female sand flies/1/3  
the size of a mosquito

1. phlebotomus [old world]
2. lutzomyia [new world]

**LUTZYMIA**

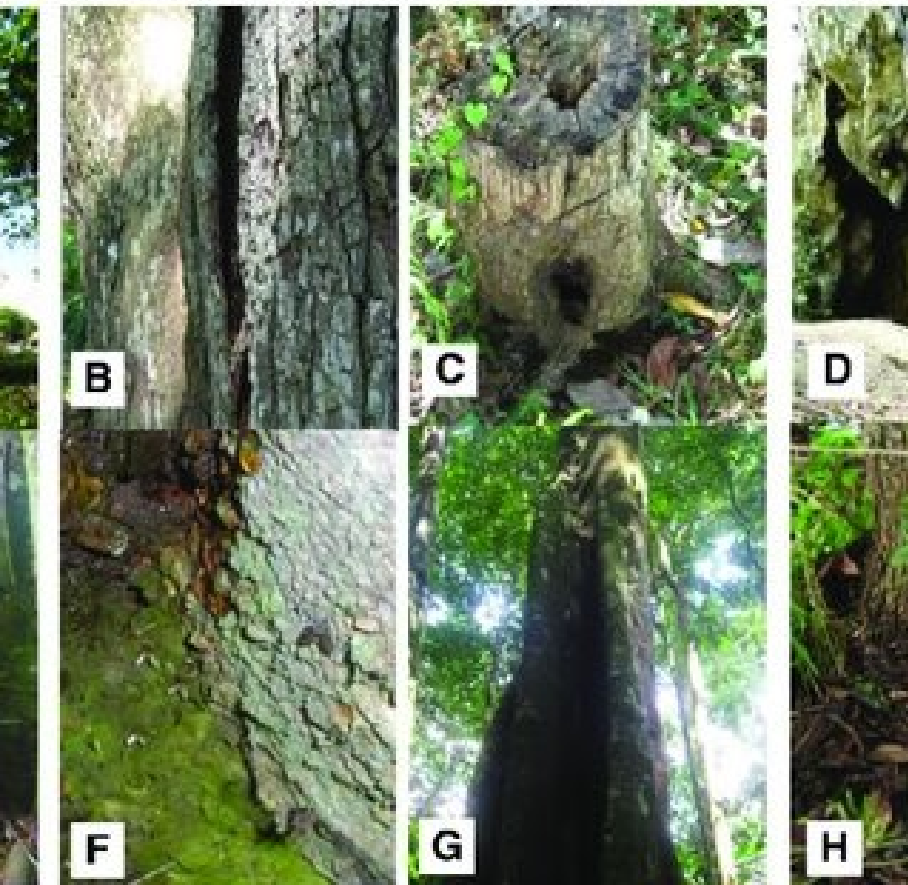


**PHLEBOTOMINE**



# They like dark and dump places

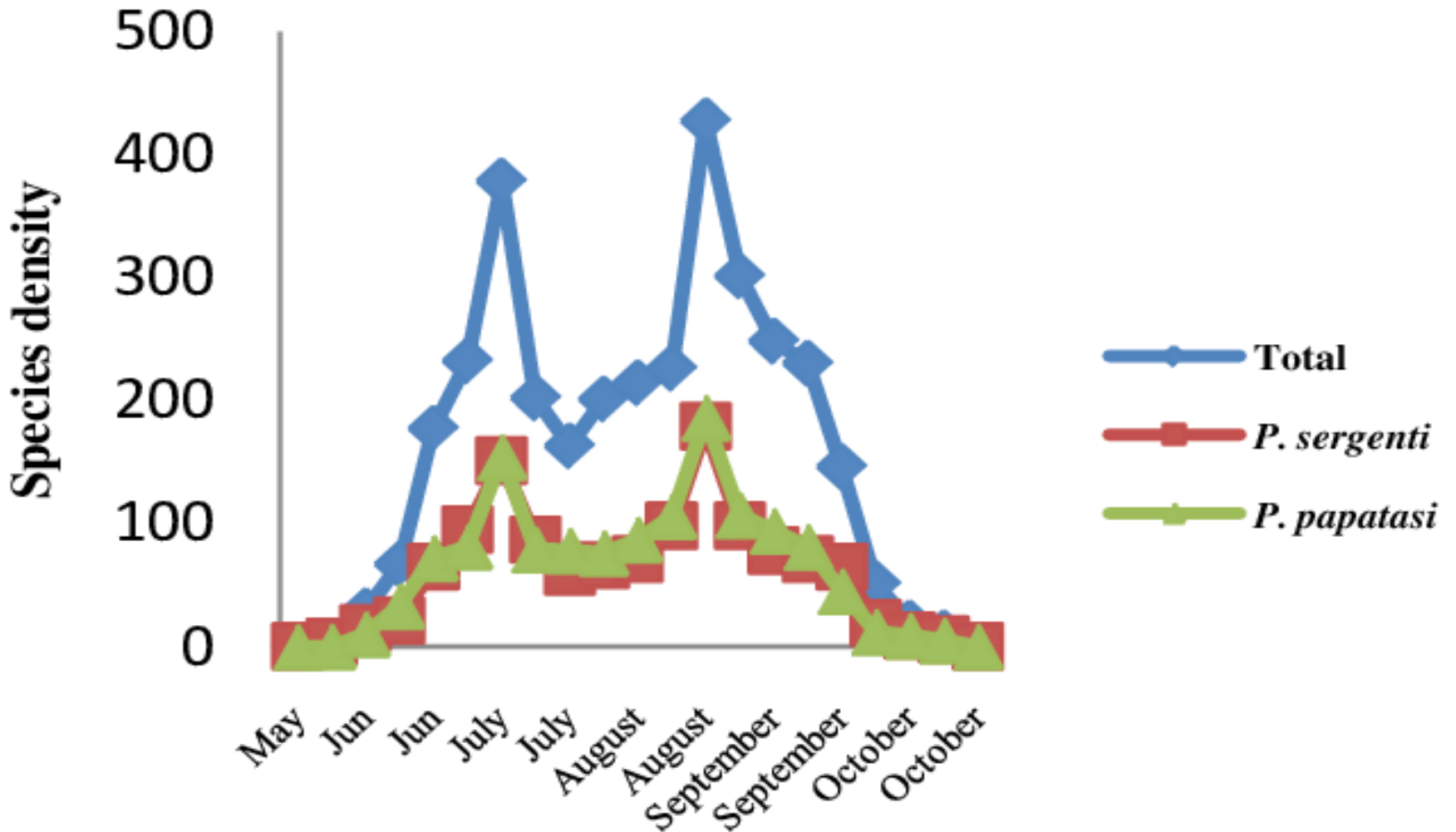
## POSSIBLE BREEDING PLACES OF VECTOR



### Sand flies resting on wall of a chicken house



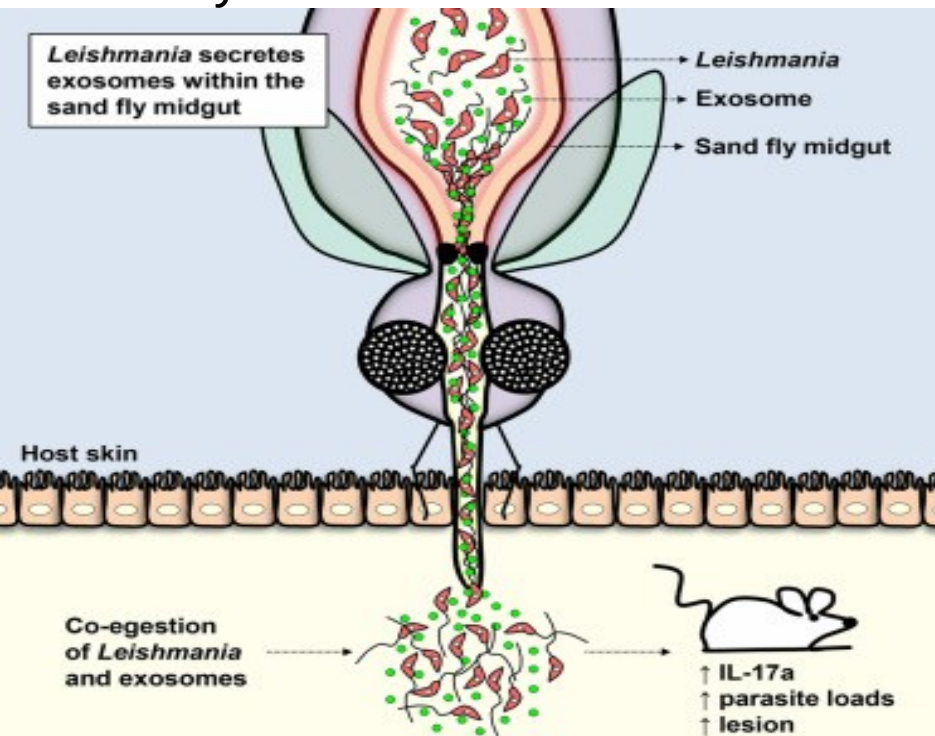
# SEASONAL ACTIVITY OF SAND FLY



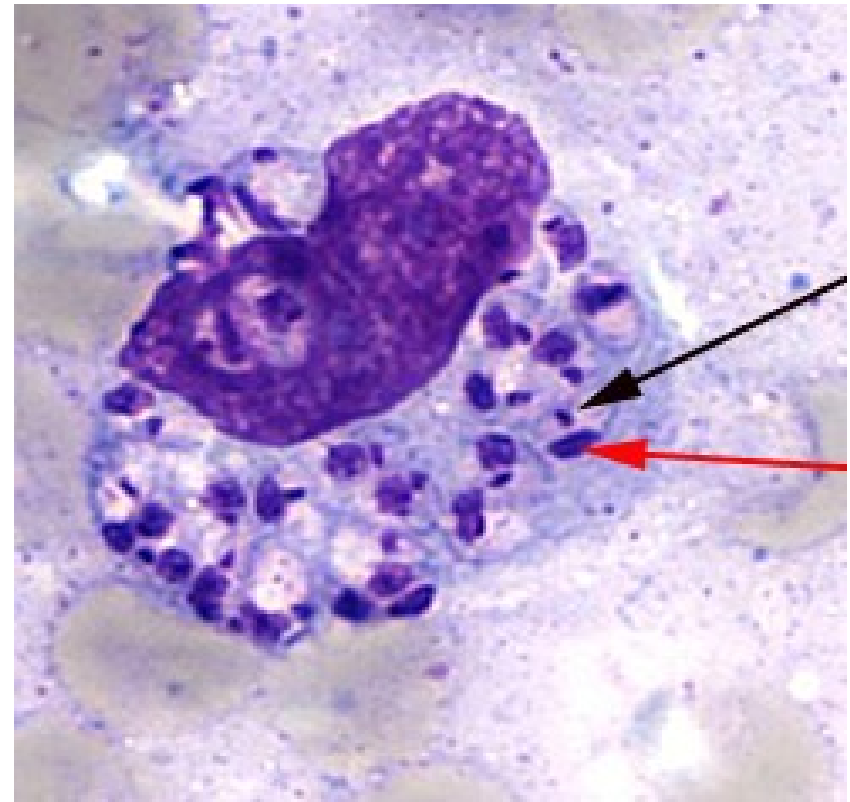
# INFECTIVE AND DIAGNOSTIC STAGES OF LEISHMANIA PARASITE

## INFECTIVE STAGE

- Promastigotes in buccal cavity and proboscis of sand fly

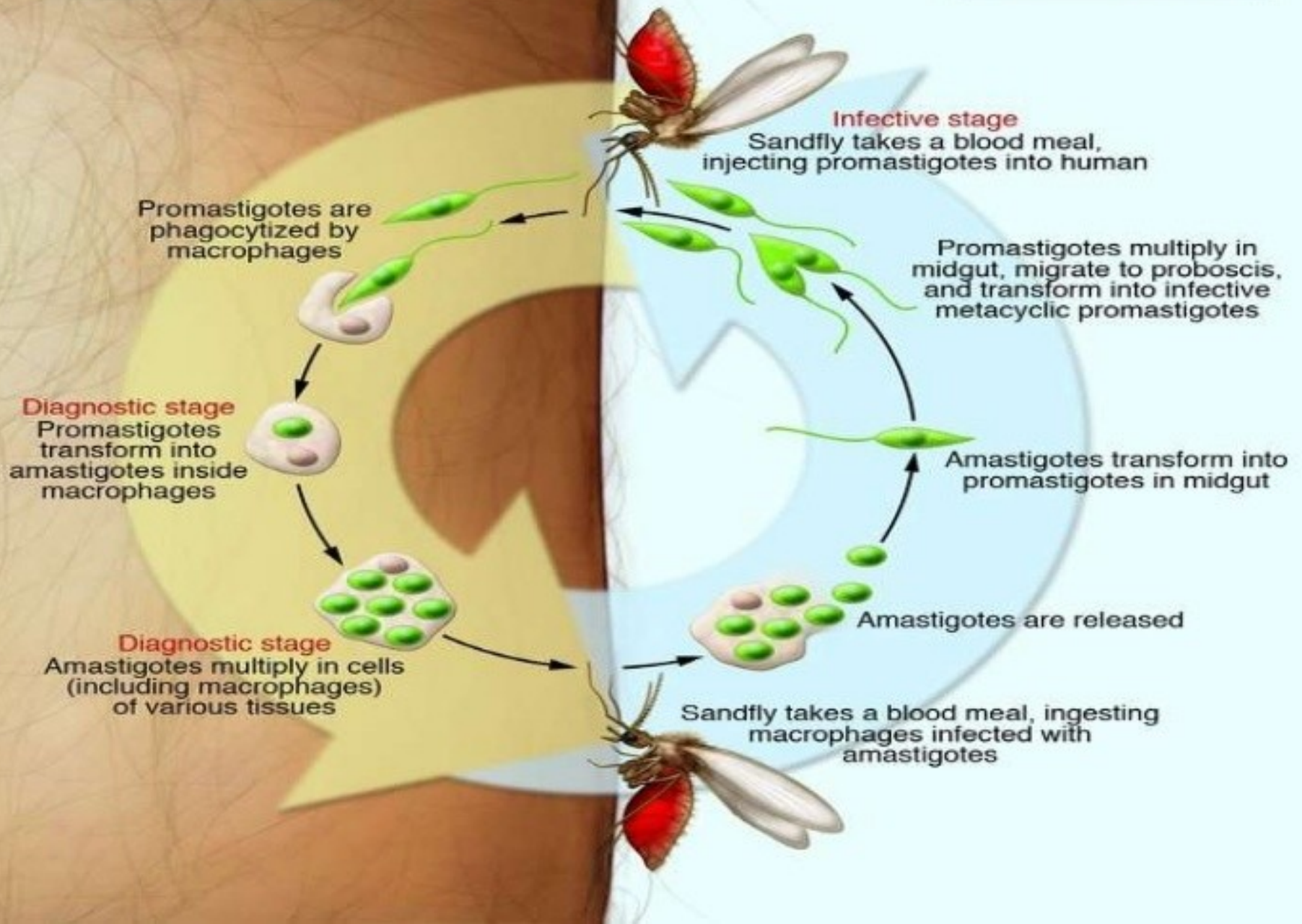


## DIAGNOSTIC STAGE



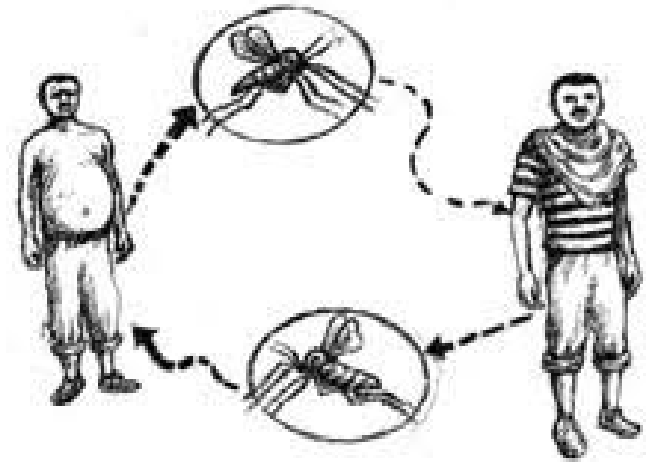
## Human stages

## Sandfly stages



# MODE OF TRANSMISSION

1. Bite of infected sand fly
2. Blood transfusion
3. Injection drug users
4. Accidental infection in laboratory
5. Congenital [from mother to fetus]
6. Organ transplant
7. Contact with active lesions of CL



# EPIDEMIOLOGY OF LEISHMANIASIS

- Currently leishmaniasis is present in **four continents**
  - Considered to be endemic **in 88 countries**
  - 72 out of these 88 countries are developing countries
1. **VL** : 90 percent in Bangladesh, Brazil, India Nepal and Sudan
  2. **MCL** : 90 percent in Bolivia, brazil and Peru
  3. **CL** : 90 PERCENT in Afghanistan, Brazil, Iran ,Peru, Saudi arabia and Syria



5. **Annual incidence** : 1 to 1.5 million cases of cutaneous leishmaniasis

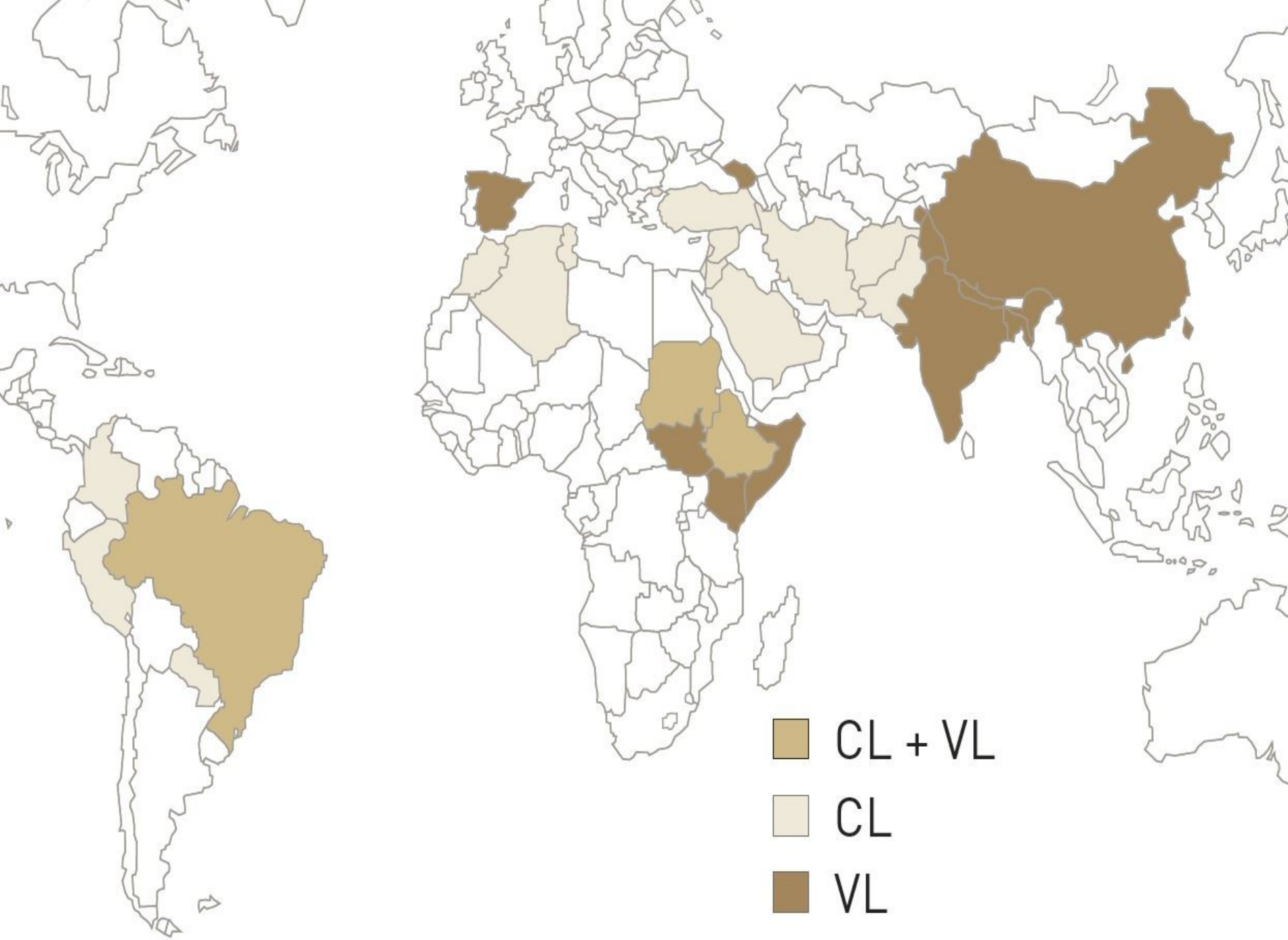
500,000 cases of visceral leishmaniasis

6. **Prevalence** : 12 million cases

7. **Population at risk** : 350 million

8. An estimated 700 000 to 1 million new cases and some

26 000 to 65 000 deaths occur annually.



- 1. WHO AFRICAN REGION :** Visceral, cutaneous or muco cutaneous leishmaniasis are endemic in Algeria and countries in East Africa
- 2. WHO REGION OF THE AMERICAS :**  
The epidemiology of cutaneous leishmaniasis in the Americas is very complex Brazil represents over 90% of the VL cases in that region.
- 3. WHO EASTERN MEDITERRANEAN REGION :**  
This region accounts for 70% of the cutaneous leishmaniasis cases worldwide

#### **4. WHO EUROPEAN REGION :**

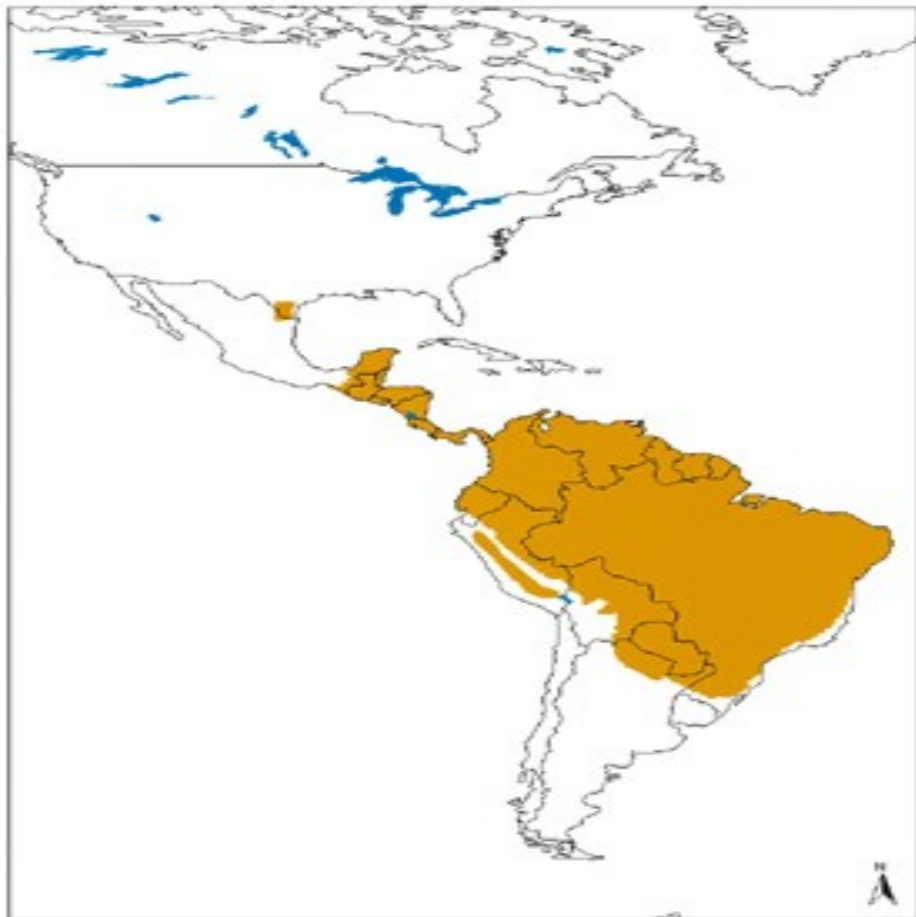
Cutaneous and visceral leishmaniasis are endemic in this region.

#### **5. WHO SOUTH-EAST ASIA REGION :**

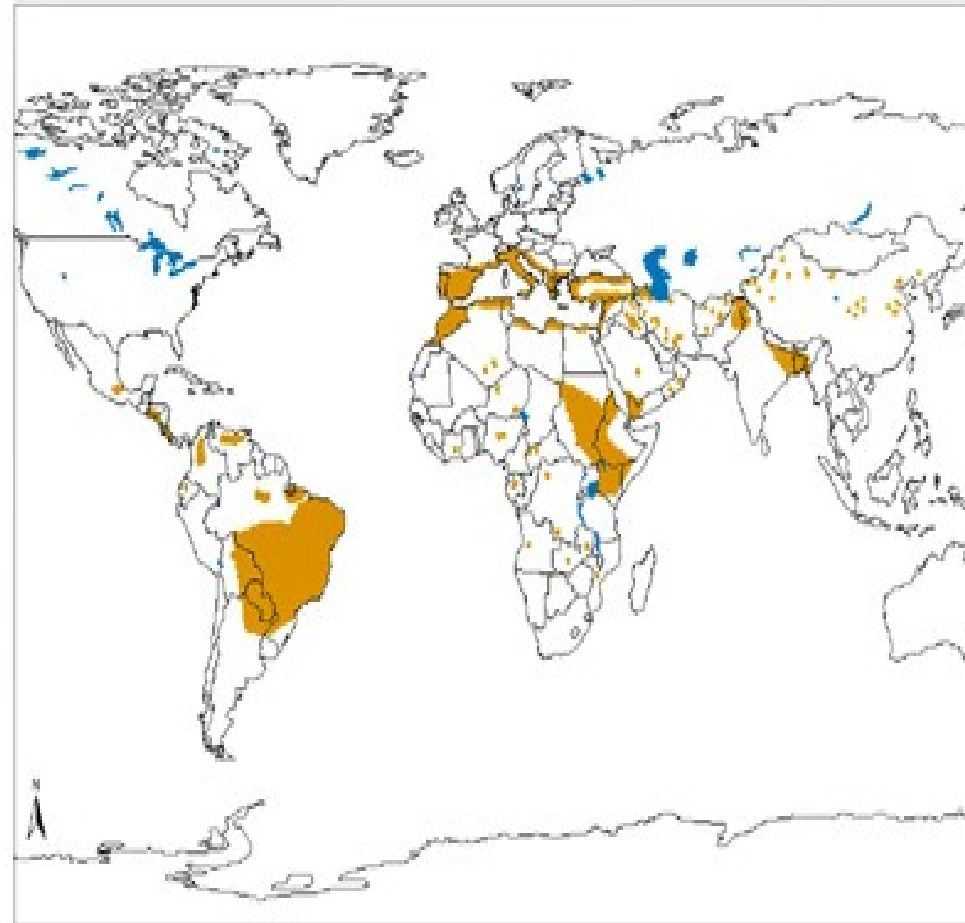
Visceral leishmaniasis is the main form of the disease in this region, also endemic for cutaneous leishmaniasis.

Regional initiative to eliminate visceral leishmaniasis as a public health problem by 2020.

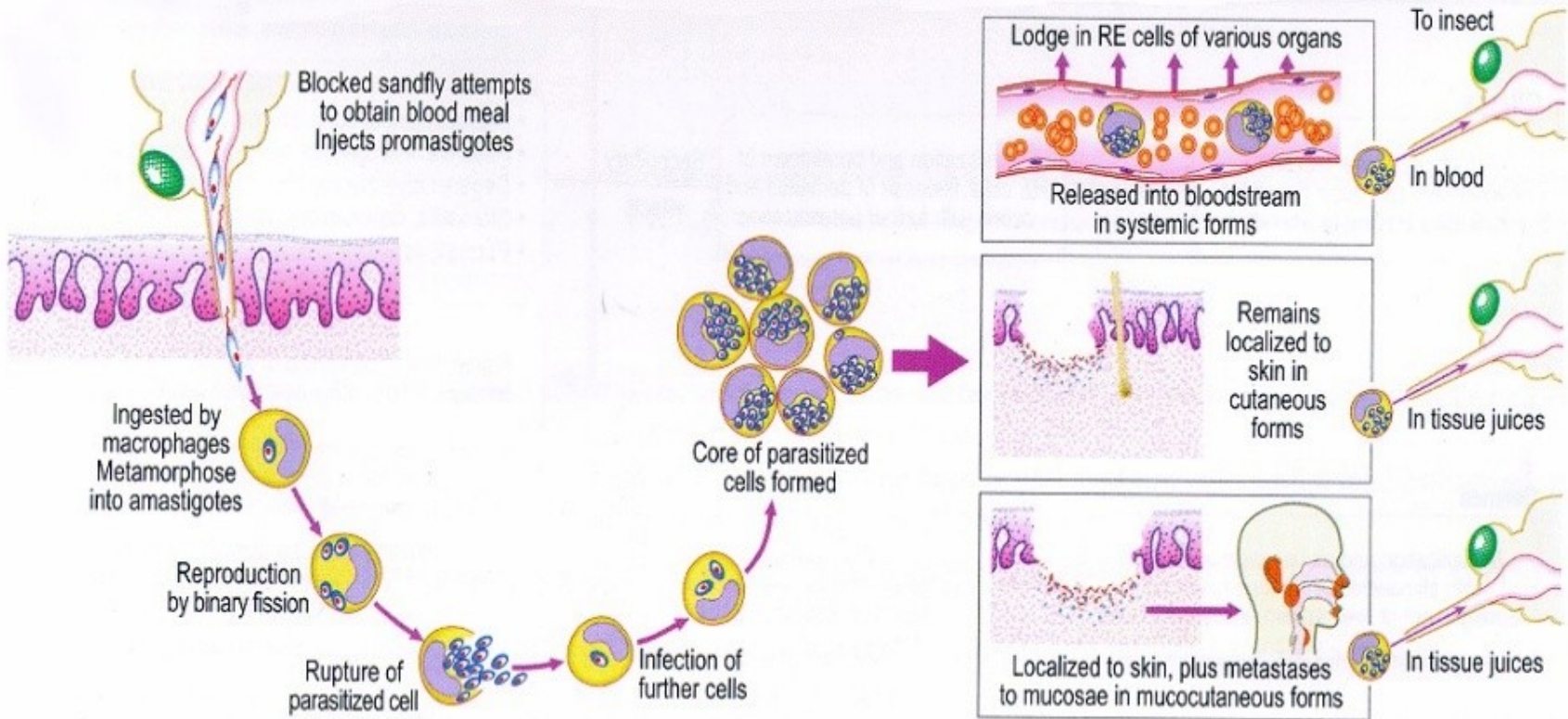
**GEOGRAPHICAL DISTRIBUTION  
OF CUTANEOUS AND MUCO  
CUTANEAOS LEISHMANIASIS IN  
NEW WORLD**



**GEOGRAPHICAL DISTRIBUTION  
OF VISCERAL LEISHMANIASIS IN  
OLD AND NEW WORLD**



# Three syndromes associated with Leishmania infection in humans



# LEISHMANIA PARASITES SPECIFIC TO TYPE OF DISEASE

- **CUTANEOUS LEISHMANIASIS**

1. L. tropica
2. L. major
3. L. mexicana
4. L. Aethiopica

- **MUCOCUTANEOUS LEISHMANIASIS**

1. L. Braziliences

- **VISCERAL LEISHMANIASIS**

1. L. Donovanii
2. L. Infantum
3. L. Chagasi

# CUTANEOUS LEISHMANIASIS

- 95% of CL cases occur in the Americas, the Mediterranean basin, the Middle East and Central Asia.
- Between 600 000 to 1 million new cases occur worldwide annually.
- Most common form of leishmaniasis and causes skin lesions and swollen glands
- Incubation period : a week to months
- The lesions is mainly a papule, nodule or ulcers, on exposed parts of the body, leaving life-long scars and serious disability



**Active cutaneous leishmaniasis** lesion with likely secondary infection in a soldier stationed in Kuwait.





**DISSEMINATED/DIFFUSE CL/  
difficult to treat**



**LOCALIZED CL**



Figure 1: Erythematous, infiltrated crusted plaque of cutaneous leishmaniasis with

Case of 75 years old Brazilian farmer with extensive ulcers **LEISHMANIASIS** for 40 years

**At time of presentation**



**After resolution**



# CUTANEOUS LEISHMANIASIS

According to the geographical distribution and vectors, leishmaniasis is classified as

## OLD WORLD CUTANEOUS LEISHMANIASIS

present in the Mediterranean basin, the Middle East, southwest and central Asia, and the tropical areas of Africa .

Old World disease is associated with multiple lesions.

Source : journal of dermatological case report 2013



## NEW WORLD CUTANEOUS LEISHMANIASIS

Source : Annual of dermatology 2016

1. Common in rural areas but can also be acquired in semi urban and urban areas.
2. New world coetaneous leishmaniasis is present in the southern USA
3. New World disease usually presents with a solitary nodule
4. **High recurrence rate**

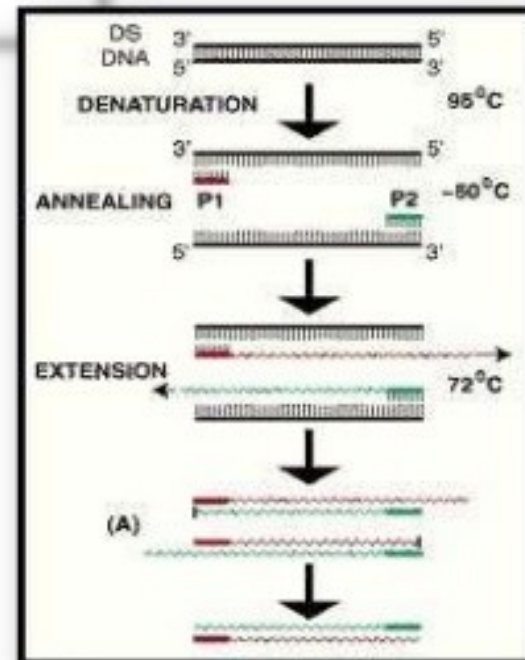
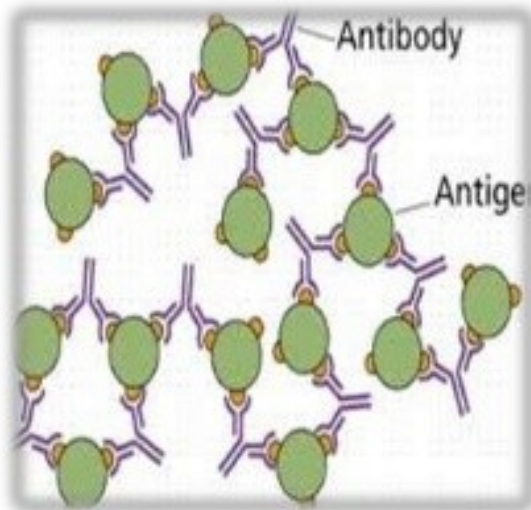


# POST LEISHMANIASIS SCARS



A Girl With Facial Scars Caused By Cutaneous Leishmaniasis, A Disfiguring And Disabling Skin Disease, Waits For Treatment At A Hospital May 8, 2016 In Kabul, Afghanistan

# DIAGNOSIS





# DIAGNOSIS

Diagnosis is achieved through an association of **clinical**, **epidemiological** and laboratory characteristics

## 1. **SMEAR**

Material obtained from scratches from the lesion margins, In non ulcerated lesions **aspirated punctures** are performed

## 2. **CULTURE**

## 3. **PCR**

- High cost
- Better understanding of leishmaniasis epidemiology.

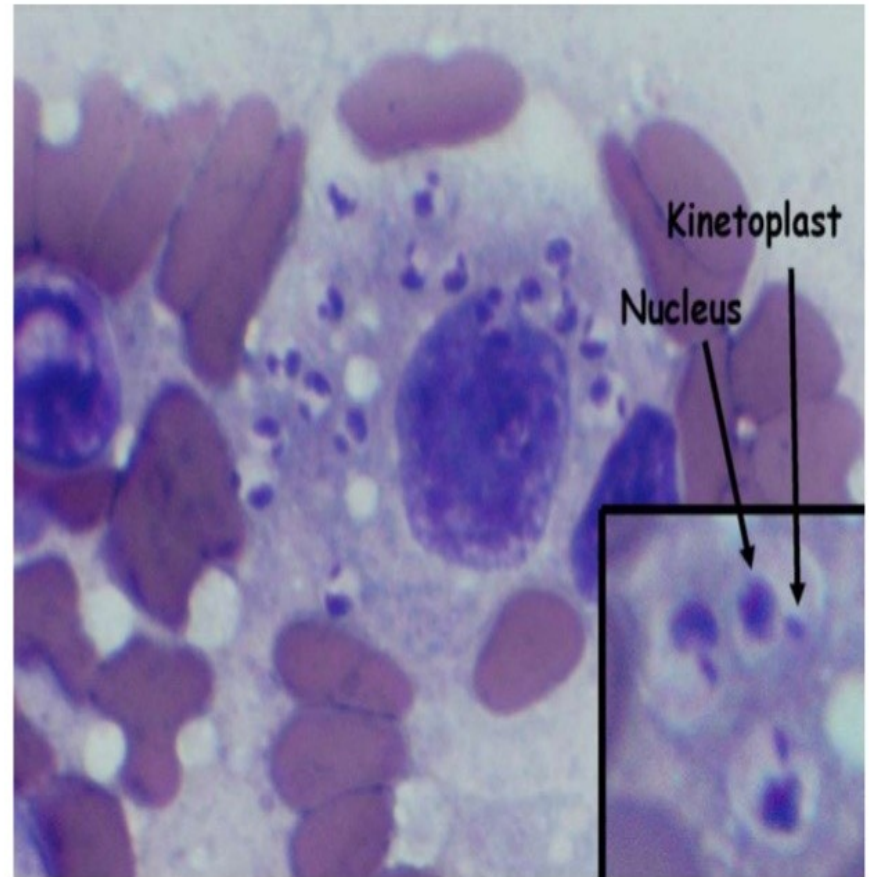
## **4. HISTOLOGY**

## **5. SKIN BIOPSIES**

should be taken from the margin of the lesion.

Making incision in active part of lesion for diagnostic purpose

**MICROSCOPY**



# TREATMENT OF CUTANEOUS LEISHMANIASIS

- **NO TREATMENT** – self-healing lesions with in one month to 3 years
- **MEDICAL:**
  - o The amino glycoside Paromomycin ointment [ local application ]
  - o Liposomal Amphotericin B [ intravenous ]
  - o Sodium stibogluconate /pentostam [ Intralesional infiltration ]
  - o Antifungal drugs



secondary ba



- **SURGICAL:**

- o Cryo therapy
- o Excision
- o Thermotherapy
- o electrotherapy

REFERENCE :WHO Control of leishmaniasis. Report of a meeting 571 of the WHO expert committee on the control of leishmaniasis.  
[http://whqlibdoc.who.int/trs/WHO\\_TRS\\_949\\_eng.pdf](http://whqlibdoc.who.int/trs/WHO_TRS_949_eng.pdf)

## **NEWLY INTRODUCED DRUGGS**

1. Miltefosine [oral therapy ]
2. Liposomal Amphotericin B (L-AmB) and Oral Miltefosine

# Source : the new England journal of medicines

## Local application of para momycin ointment



## Response to para momycin treatment



# PATIENT RECEIVING INTRALESIONAL INJ OF PENTOSTAM IN AFGHANISTAN



# MUCOCUTANEOUS LEISHMANIASIS

- Leads to partial or total destruction of mucous membranes of the nose, mouth and throat.
- Over 90% of mucocutaneous leishmaniasis cases occur in Bolivia, Brazil, Ethiopia and Peru.





# MUCOCUTANEOUS LEISHMANIASIS



## Hole in soft palate in MC leishmaniasis



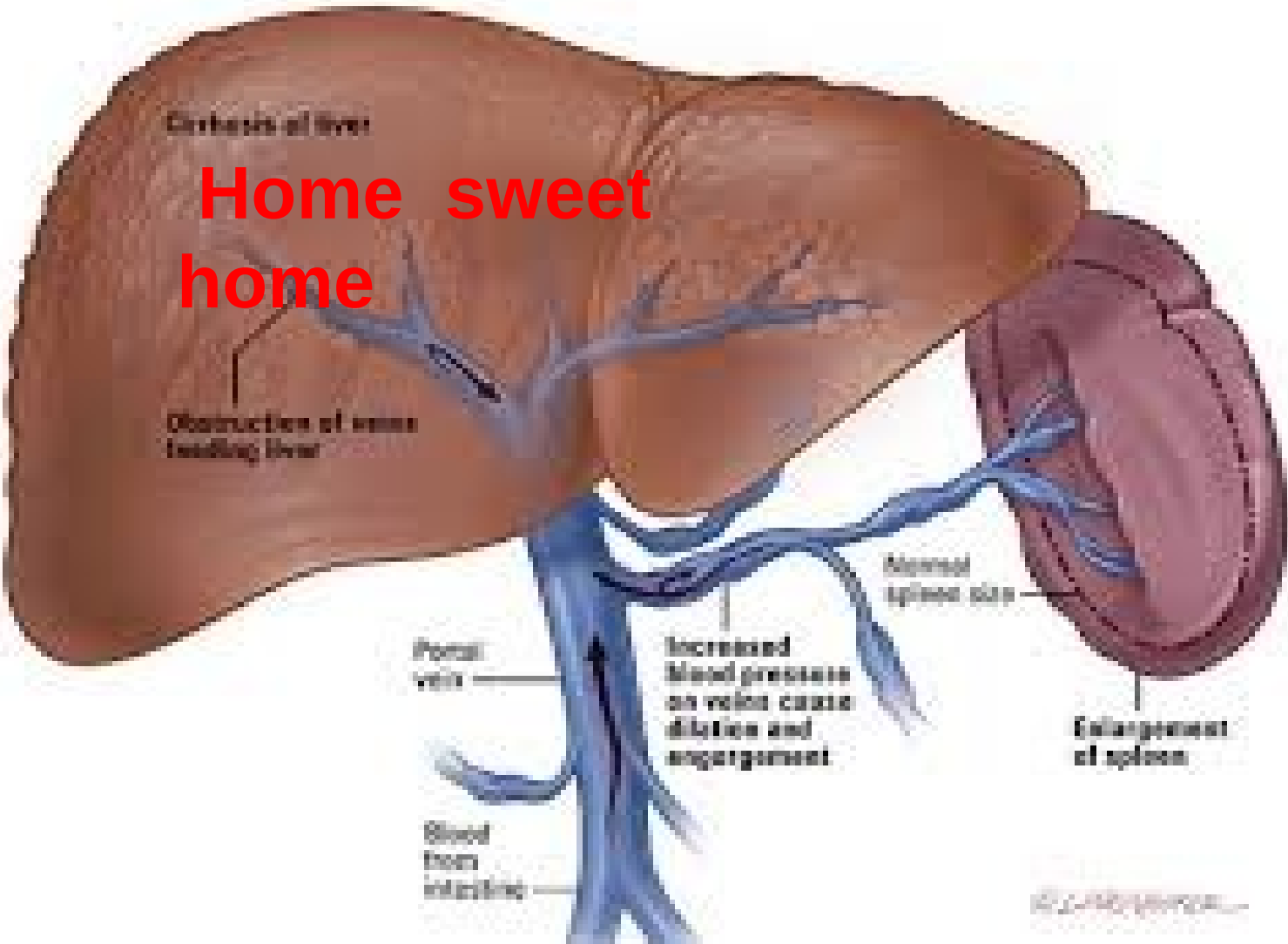
## Shabana an afghan girl with MC leishmaniasis



alamy stock photo

AMYR45  
www.alamy.com

# VISCERAL LEISHMANIASIS



# VISCERAL LEISHMANIASIS

## CAUSATIVE AGENTS :

L. donovani, L. Infantum L. chagasi.

**INCUBATION PERIOD :** days to years

## Characterized by

- Fever [irregular bouts]
- Splenomegaly, hepatomegaly hepatosplenomegaly
- Weight loss
- Anaemia
- Epistaxis
- Cough
- Diarrhoea
- bone marrow suppression

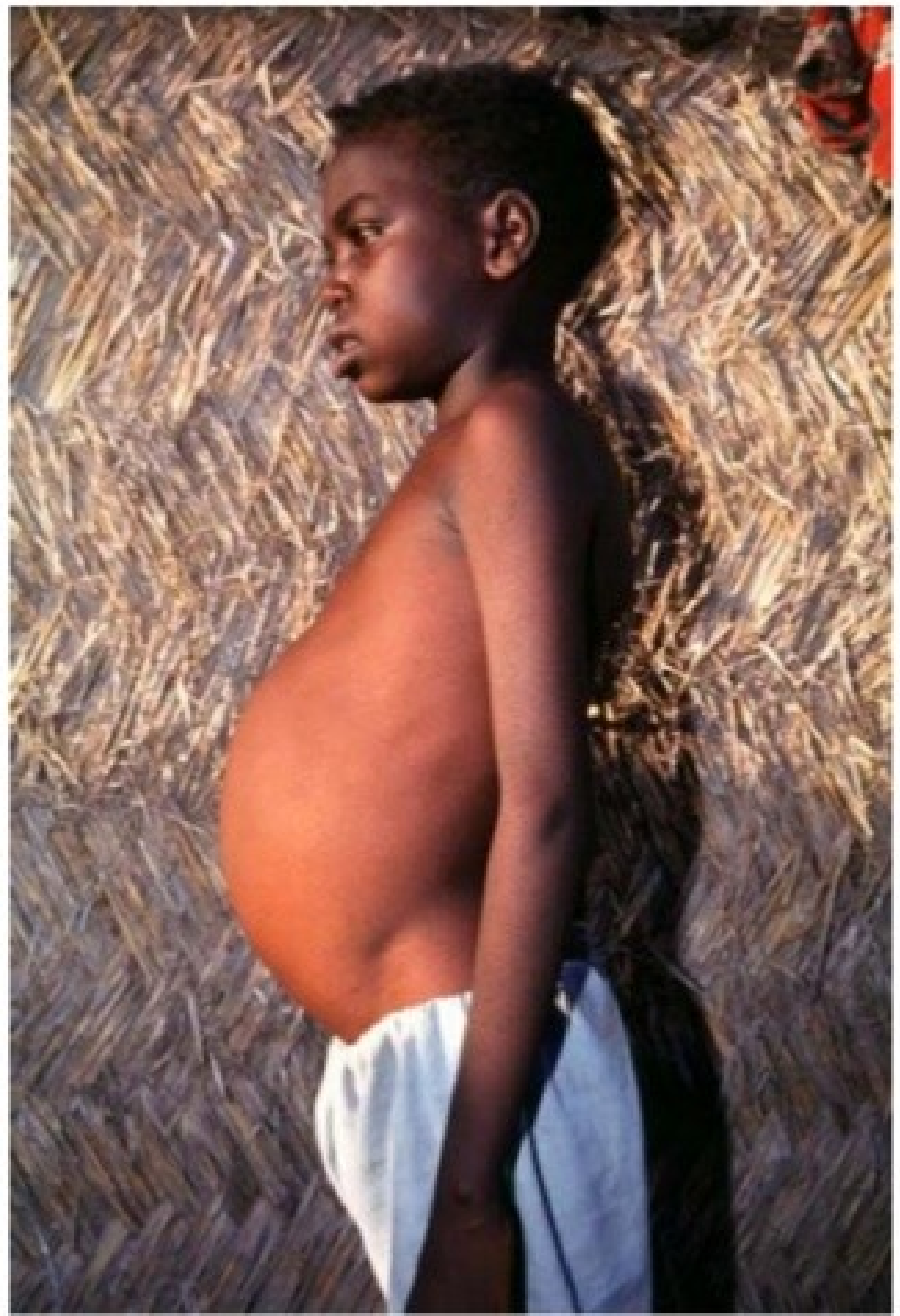
# EPIDEMIOLOGY OF VISCERAL LEISHMANIASIS

## VISCERAL LEISHMANIASIS

- Transmitted by female *P. ARGENTIPES*
- ~200 000 - 400 000 new cases/year
- Over 90% of new cases in: Brazil, Ethiopia, Sudan, South Sudan, Bangladesh, and India
- Untreated cases are fatal in 95 percent cases
- Second largest parasitic killer in the world after malaria



- Profile view of a teenage boy suffering from visceral leishmaniasis. The boy exhibits splenomegaly, distended abdomen and severe muscle wasting.

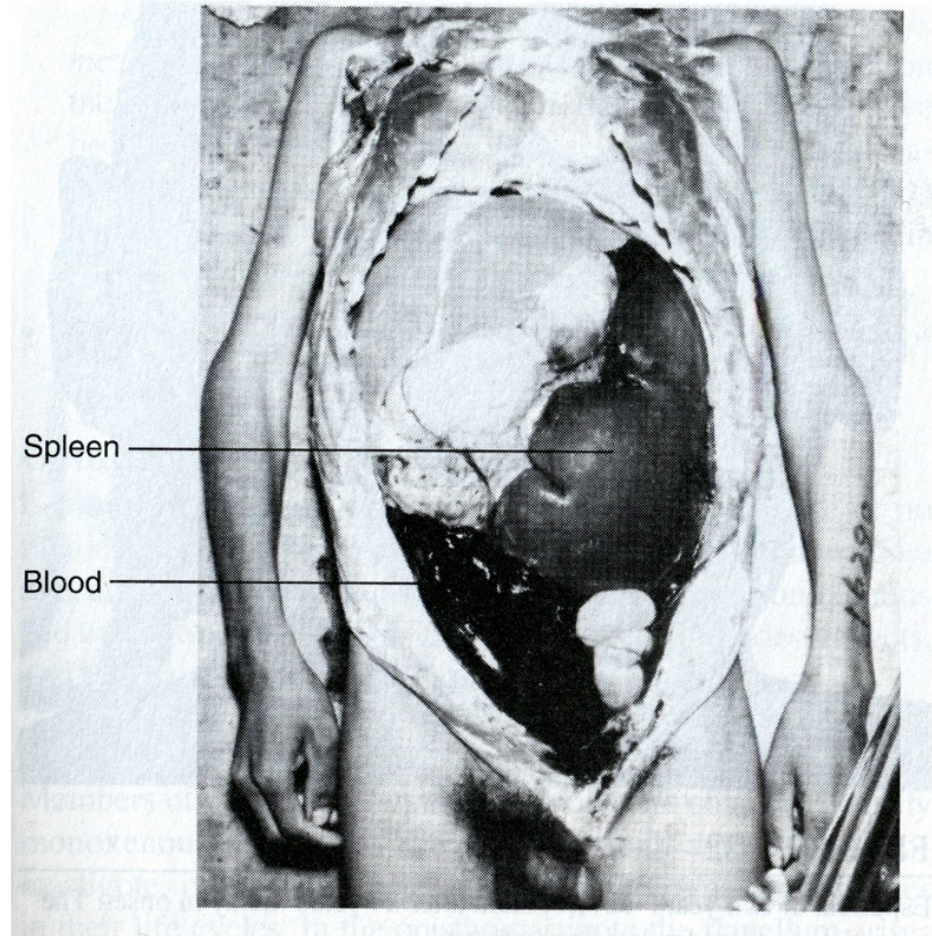
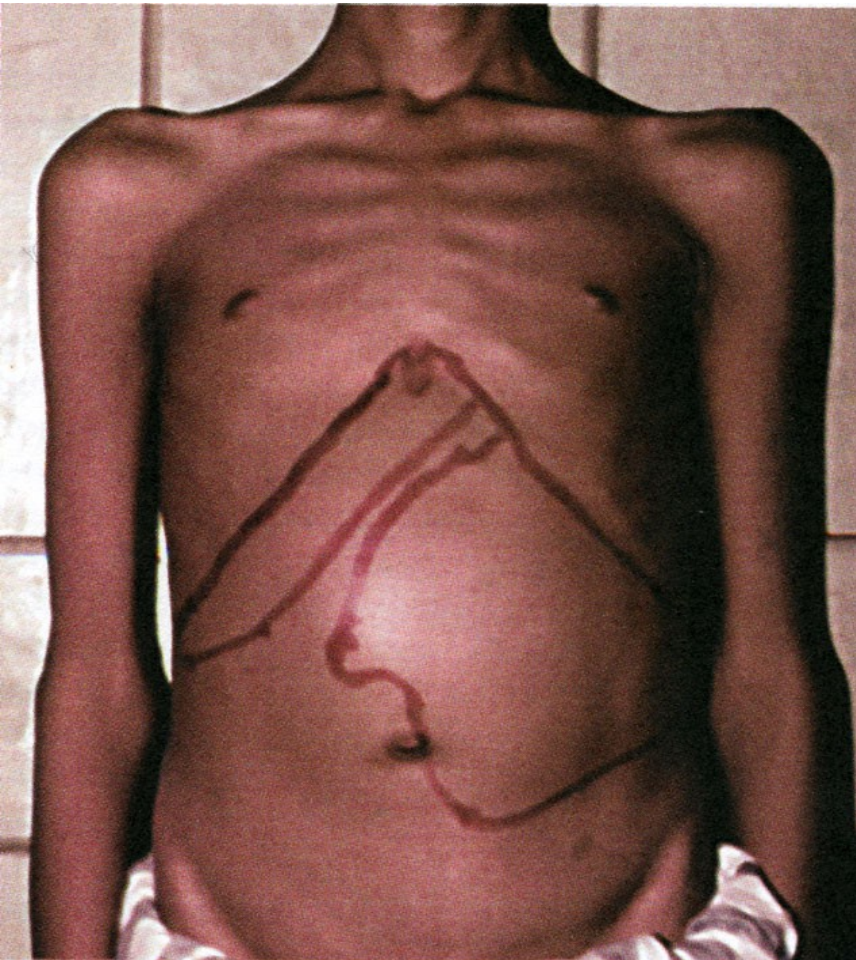


Girl suffering from visceral leishmaniasis, - with markers showing signs of liver and spleen enlargement.

Libo Kemkem district, Ethiopia.



# IMAGES FOR VISCERAL LEISHMANIASIS





A certain percentage of VL may present as **POST KALAZAR DERMAL LEISHMANIASIS (PKDL)** generally after 2-3 years following the treatment for VL People with PKDL are considered to be a *potential source of Leishmania infection*.



Child with post-kala-azar-dermal leishmaniasis in old Fangak County, South Sudan. The area suffered severe visceral leishmaniasis outbreaks from 2009 to 2012.



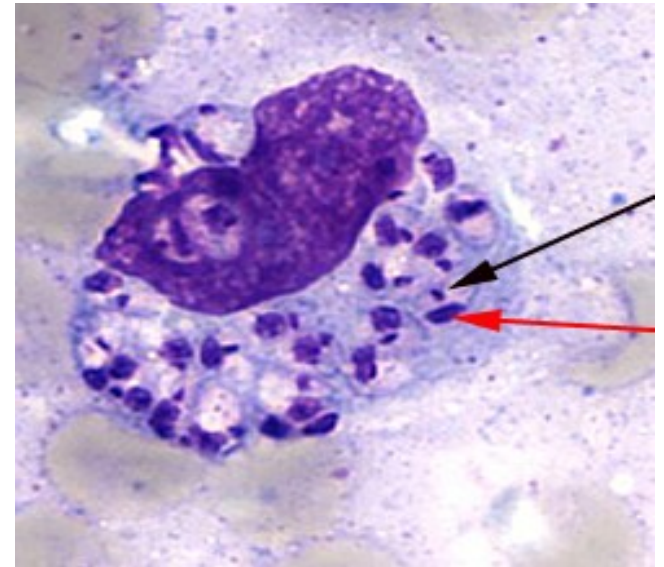
# DIAGNOSIS OF LEISHMANIASIS

Diagnosis is made by combining clinical signs with parasitological, or serological tests

# DIRECT EVIDENCE / DEMONSTRATION OF LEISHMANIA PARASITE

## SPECIMEN COLLECTED

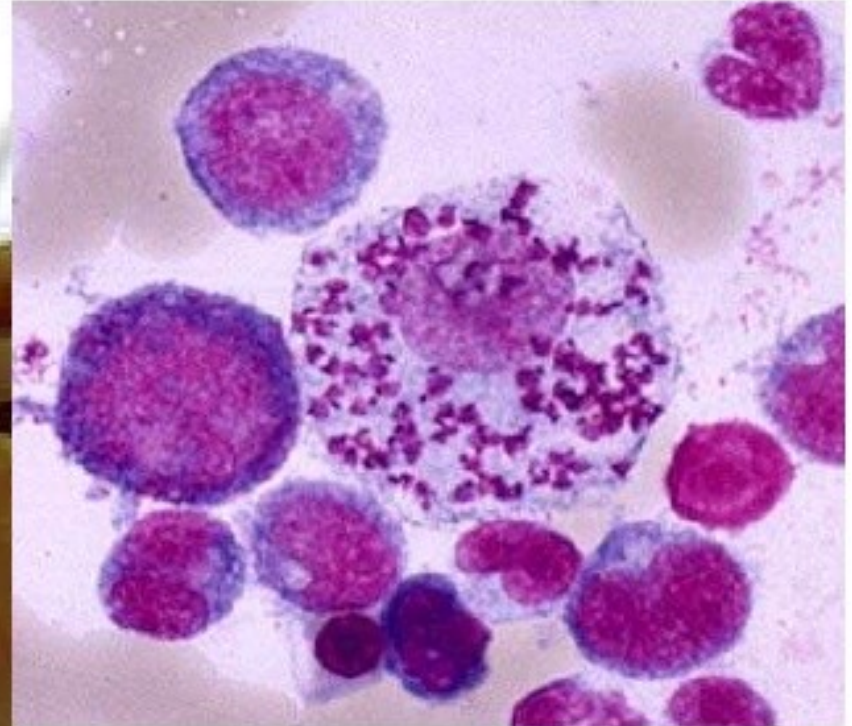
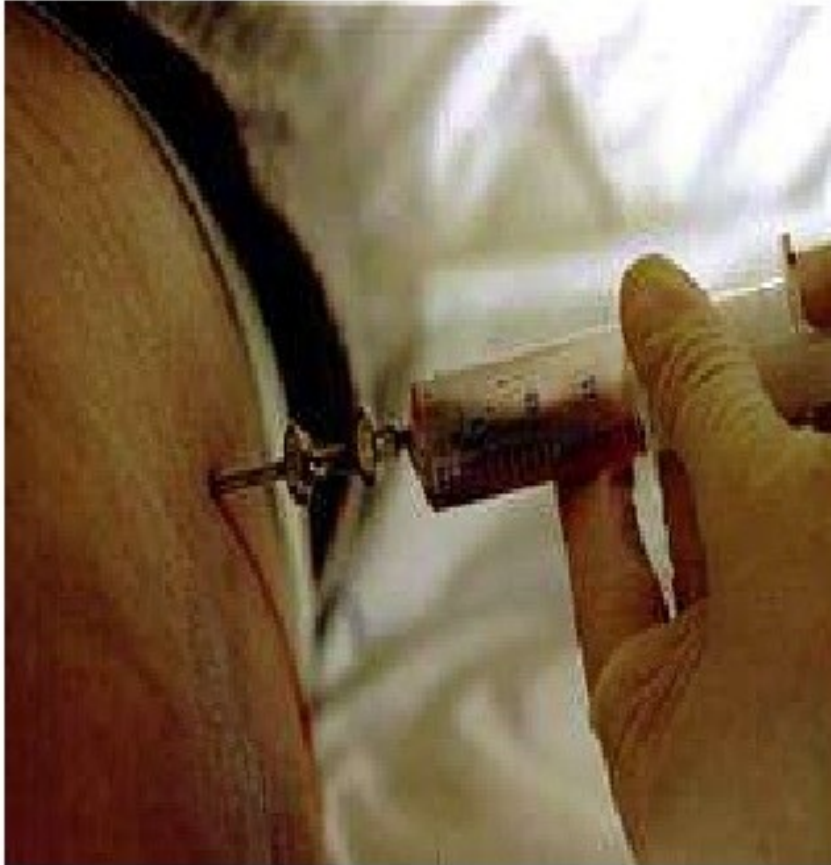
1. Splenic aspirate / biopsy
2. Liver biopsy
3. Bone marrow biopsy
4. FNAC and biopsy



## IMMUNOLOGICAL METHODS [antibodies to leishmania parasite]

5. Aldehyde test
6. Antimony test
7. Complement fixation test

# Bone marrow aspiration



Bone marrow amastigotes

**Bone aspirate from a patient with visceral leishmaniasis**

# PREVENTION OF LEISHMANIASIS

- **Suppress the reservoir** ■ dog ,rat ,gerbil, other small mammals and rodents  
Use of insecticide-impregnated dog collars and treatment or culling of infected dogs.
- **Suppress the vector** : sand fly  
Critical to prevent disease in stationary troop population
- **Prevent sand fly bites:**
  1. personal protective measures most important at night Insect repellent
  2. 20 to 30 percent DEET on exposed skin
  3. Permethrin treated dress [protective clothing]

1. Permethrin treated bed nets [ fine mesh sizes of 0.6 mm or less are required ]
2. Avoid out door activities at night
3. Sleeves down/ full sleeves

➤ **Public awareness and public health measures**

➤ **Early diagnosis and effective case management**

➤ **Effective disease surveillance**

➤ **Social mobilization and strengthening partnership**





Painting tree trunk with whitewash to make it unsuitable as a sand fly resting site

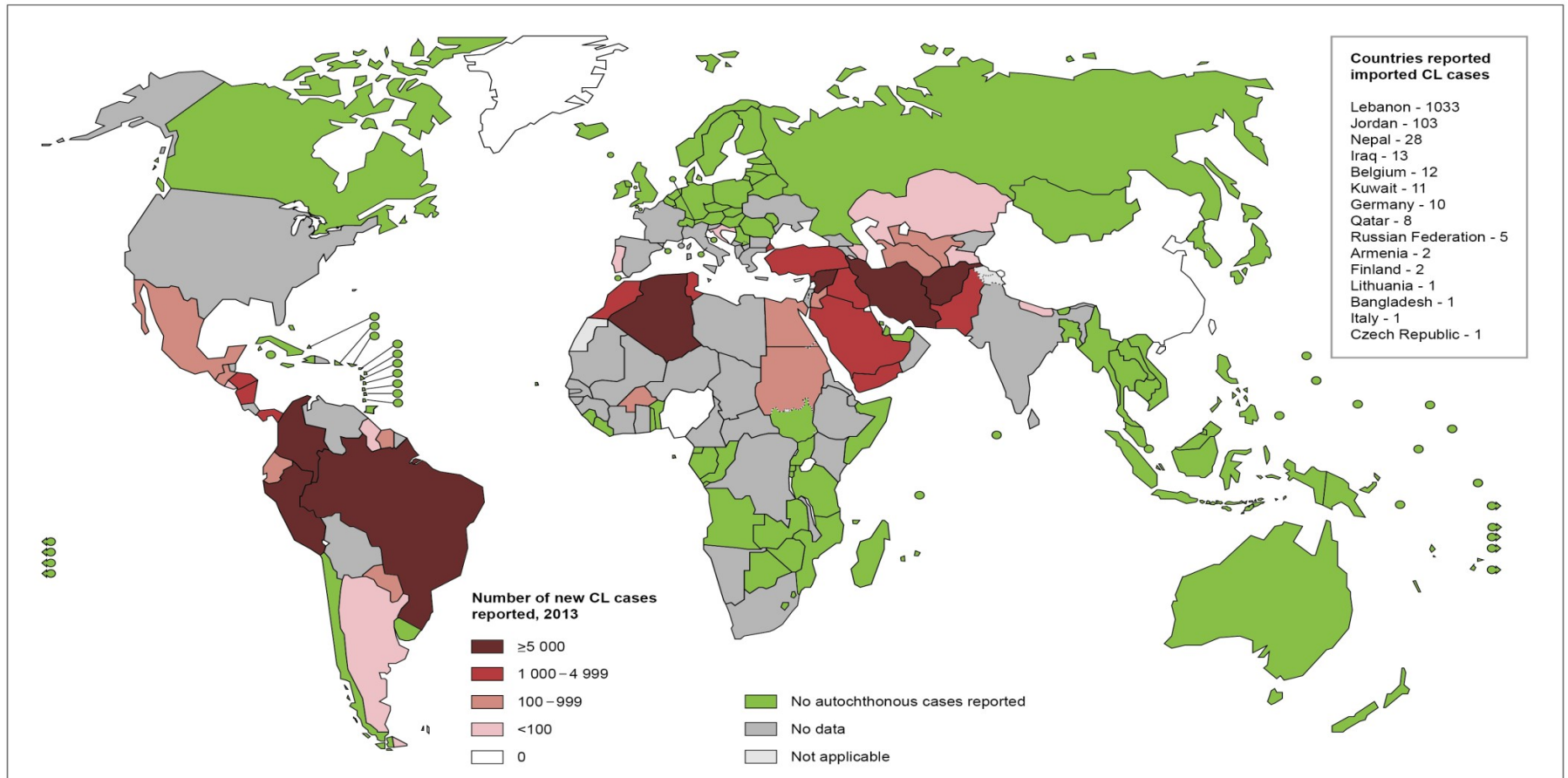


# VACCINES

- Yet no effective *vaccine*.
- Live vaccine include new genetically modified construct.
- 1st generation vaccine    Whole killed parasite
- 2<sup>nd</sup> generation vaccine    recombinant proteins

# GLOBAL BURDEN

Status of endemicity of cutaneous leishmaniasis, worldwide, 2013



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2015. All rights reserved

Data Source: World Health Organization  
 Map Production: Control of Neglected  
 Tropical Diseases (NTD)  
 World Health Organization

# LEISHMANIASIS IN PAKISTAN

- **Cutaneous Leishmaniasis** is a rising epidemic in Pakistan.
- A major public health problem especially alongside regions bordering the neighbouring Afghanistan and cities that have had the maximum influx of Afghan refugees.
- The problem is especially acute in Baluchistan and Sindh
- Pakistan has a burden of cutaneous and visceral leishmaniasis
- **The mucocutaneous** form being almost nonexistent.



# PREDISPOSING FACTORS

1. Poverty
2. Lack of financial resources
3. Associated with malnutrition
4. Population displacement
5. Poor housing
6. Weak immune system
7. Environmental changes
8. Deforestation
9. New irrigation schemes
10. Urbanization
11. Illiteracy
12. Gender discrimination
13. Building of dams
14. Migration of non-immune people to endemic areas.

- **Social mobilization** is the primary step of community development for recovery from conflicts and disasters. It allows people to think and understand their situation and to organize and initiate action for their recovery with their own initiative and creativity
- **partnerships** refer to institutionalized interactions between public and private actors jointly working towards a shared goal

# WHO RESPONSE

WHO's work on leishmaniasis control involves:

- Supporting national leishmaniasis control programmes.
- Raising awareness and advocacy on the global burden of leishmaniasis.
- Developing evidence-based policy guidelines, strategies and standards for leishmaniasis prevention and control.
- Providing technical support to Member States to build sustainable, effective surveillance system and epidemic preparedness and response systems.
- Providing diagnostic tests and antileishmanial medicines
- Promoting research on effective leishmaniasis control
- Facilitating the dissemination of research findings.



## WHO PROVIDING DRUGG TO LEISHMANIASIS IN KTH PESHAWAR

A training workshop on the diagnosis, treatment and management of leishmaniasis was held in Peshawar on 10 April 2017, organized by WHO and the Khyber Pakhtunkhwa Department of Health.



**WHAT WE ARE DOING AGAINST  
LEISHMANIASIS SPREAD IN KPK ?**

Referring to the recent outbreak of cutaneous leishmaniasis in Khyber Pakhtunkhwa that affected at least 21,000 people, an expert at an international conference continuing at Karachi University (KU) informed the audience on **Thursday** that **a local remedy scientifically proven through clinical trials existed for the skin infection**

**SOURCE: THE DAWN 01 MARCH 2019**





- **MSF** [**DOCTORS WITHOUT BOUNDARIES**] project on leishmaniasis in KPK **A HOPE FOR PATIENTS**
- In May 2018, **MSF** opened a treatment centre for cutaneous leishmaniasis in Peshawar - its fourth in Pakistan.
- Medicines for leishmaniasis are expensive and not available in markets



- Taj Bibi, along with her husband, four sons and two daughters have been infected with Cutaneous Leishmaniasis. All have been or are being treated in the **MSF treatment centre in Naseerullah Babar Memorial Hospital, Pakistan, 5 October 2018.**



- My feet hurt so much that I can't drive my taxi anymore. I can't buy food for my children anymore. My savings are almost gone. I hope I heal quickly so that I can go back to work and earn money again.”



- Nabeela, with her father and brother at MSF's cutaneous leishmaniasis treatment centre in Peshawar, 5 October 2018

# LEISHMANIASIS RISING CASES IN PAKISTAN

- Fears over disfiguring parasitic disease as cases double in northern Pakistan **DAILY TELEGRAPH UK JUNE 2018**
- Leishmaniasis: A skin disease with no vaccine is on the rise in Khyber Pakhtunkhwa **SAMAA NEWS 6 FEBRUARY 2019**
- At least 800 people had so far been infected during the last several days Bajaur tribal district
- Affected persons facing problems in availing treatment as local health centers were short of medicines. **DAWN NEWS**
- medical camp was held at the district headquarters hospital Khar aimed at providing free of cost treatment and medicines to the victims.



# OUT BREAK IN KHYBER AGENCY



# CURRENT NEWS ABOUT LEISHMANIASIS IN PAKISTAN

صرف 35 دن میں 21 ہزار مریض

خطرناک لیشمنائیسس وبا  
خیبر پختونخوا پہنچا دی گئی



خیبر پختونخوا میں لیشمنیا

کرک میں 17 سو مردان  
میں 380 کیسز رپورٹ

Health News

لیشمنیا بیماری ہے

قباٹی اضلاع میں 20 ہزار کرک  
میں ستر سو مردان میں تین سو  
اسی کیسز رپورٹ

Health News

شیر

ون



Quiz Time

Let's have  
some fun!

IDENTIFY LEISHMANIASIS ?

**A**



**B**



**C**



ANS : A carcinoma  
B carcinoma  
C Leishmaniasis

Q : How many people in the world suffer from one or more neglected tropical diseases?

1. One billion
2. 100,000
3. 100 million
4. Half a million



Q: Which cells of body does leishmania parasite infect?

1. T cells
2. Red blood cells
3. Nerve cells
4. Macrophages



Q : Name the lesions given below ?



- ANS :

My battle with leishmaniasis over a 15 weeks period

1. hole formation
2. 6<sup>th</sup> at biopsy + miltefosin tx started
3. 10 healing in progression with abscess formation due to immuno supression

# Differentiate ?

**A**



**B**





Visceral leishmaniasis is the -----  
largest parasitic killer in the world.

1. 1<sup>st</sup>
2. 2<sup>nd</sup>
3. 3<sup>rd</sup>
4. 4<sup>th</sup>

# References

- [www.pitt.edu/~super7/22011-23001/22291.pp](http://www.pitt.edu/~super7/22011-23001/22291.pp)
- <https://www.slideshare.net/DevendraNiranjana/leishmania-lecture>
- [www.who.int/mediacentre/factsheets/fs375/en/](http://www.who.int/mediacentre/factsheets/fs375/en/)
- text book by ilyas ansaari and irfan
- Front Immunol. 2012; 3:  
99<https://www.ncbi.nlm.nih.gov/pubmed/15748545>

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