

Cutaneous Leishmaniasis in Suspected Afghan Refugees and Local Population in NWFP Pakistan



Dr. Akram Shah & Arif Shah

Department of Zoology

University of Peshawar, Pakistan

Cutaneous Leishmaniasis

- Leishmaniasis caused by *Leishmania* transmitted by infected female sand fly.
- Affects people in 88 countries of the old and new world
- Has a global prevalence of 12 million
- Causes 1.5—2million new cases each year

- According to Akilove *et al.* (2007) about 100 promastigotes are needed for induction of a lesion, while Less than 50 promastigotes results in cryptic (silent) disease, a natural vaccine in endemic area.

- Lesions may occur anywhere on the body but the most likely sites are exposed parts.
- Cutaneous lesions are usually single and often self-healing, but a presentation with multiple ulcers resulting from multiple bites from the sandfly is not rare in Pakistan.

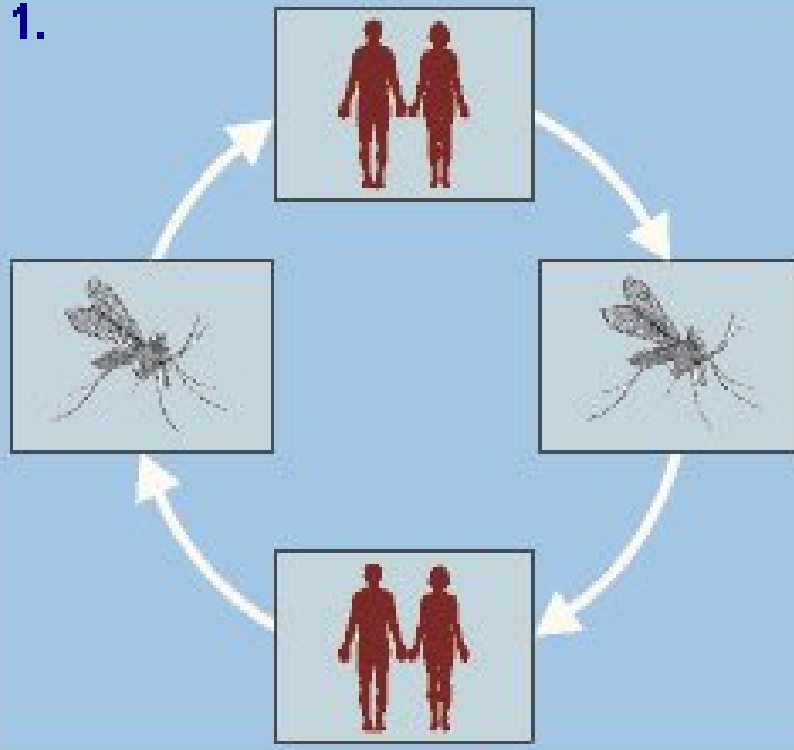
- Migratory trends during last decade (urbanization, political conflicts, etc.), increase incidence of Old World cutaneous leishmaniasis (CL).
- infection may be restricted to primary cutaneous lesions, may involve metastasis of the micro-organisms to the mucous membranes, or may spread throughout the reticulo-endothelial system, as in visceral leishmaniasis.
- In Pakistan and Afghanistan there is two types of cutaneous leishmaniasis:
 1. Anthroponotic CL
 2. Zoonotic CL

Cutaneous leishmaniasis has been given various names in different civilizations such as "Delhi boil" in India, "Baghdad boil" in Iraq, "Aleppo boil" in Syria and "saldana" in Afghanistan.

Anthroponotic and zoonotic infections

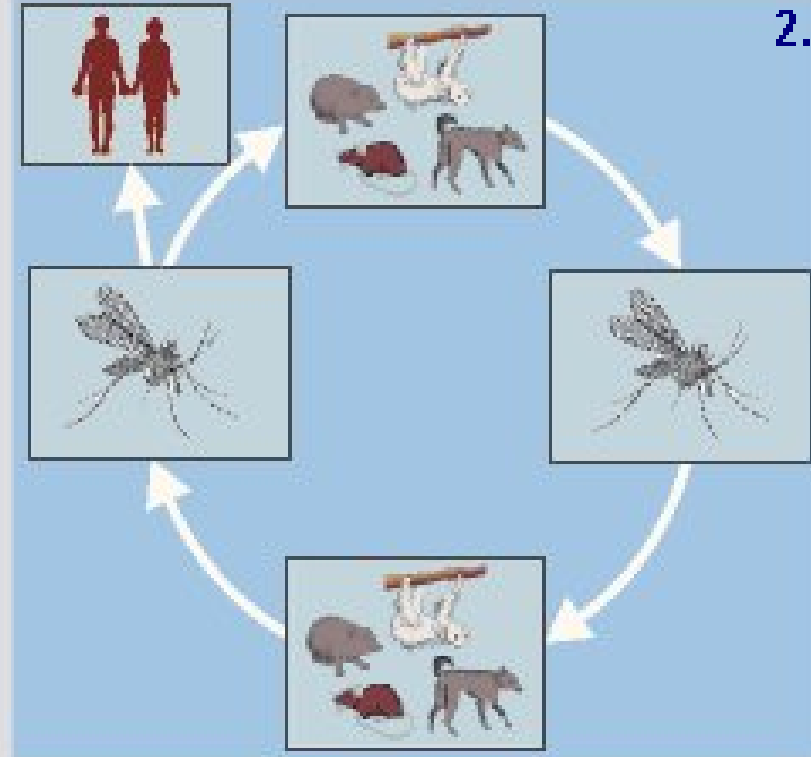


1.



1. An anthroponotic infection is passed from human to human, eg. CL due to *L. tropica* in Kabul, Afghanistan is transmitted by *P. sergenti*.

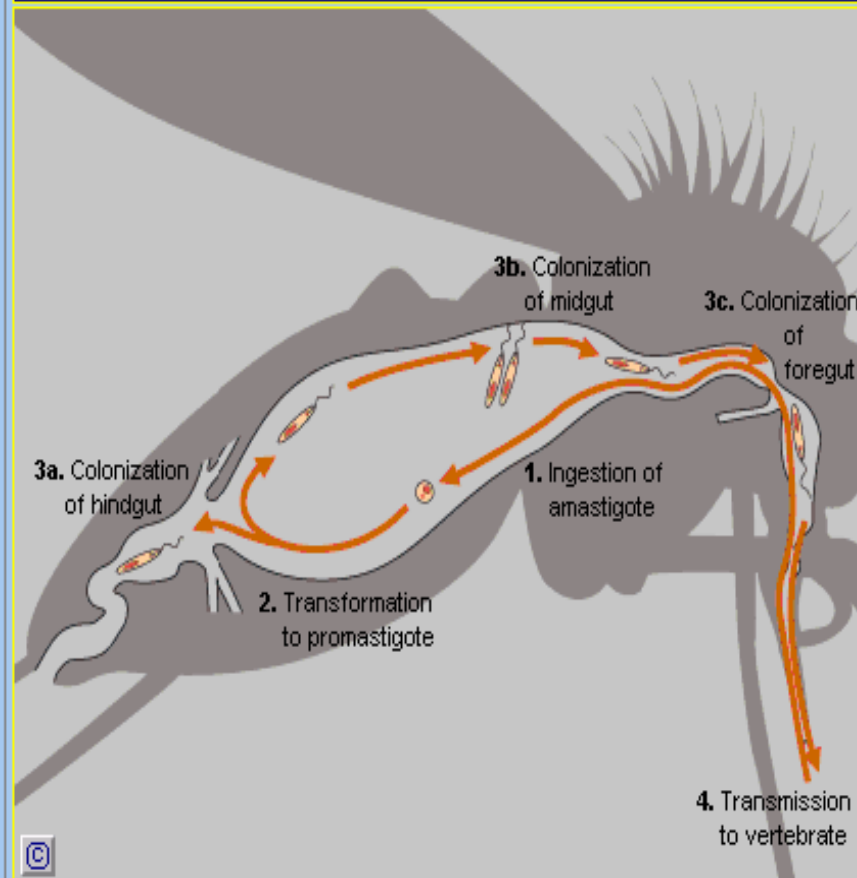
2.



2. A zoonotic infection is caused by a parasite whose host range includes mammals and humans. In Iran, CL due to *L. major* is an infection of the great gerbil which is transmitted by sand flies to humans who intrude into the natural cycle of infection.

Life cycle within fly

Sand Fly Stages of the Life Cycle - 2



Parasite stages in the sand fly

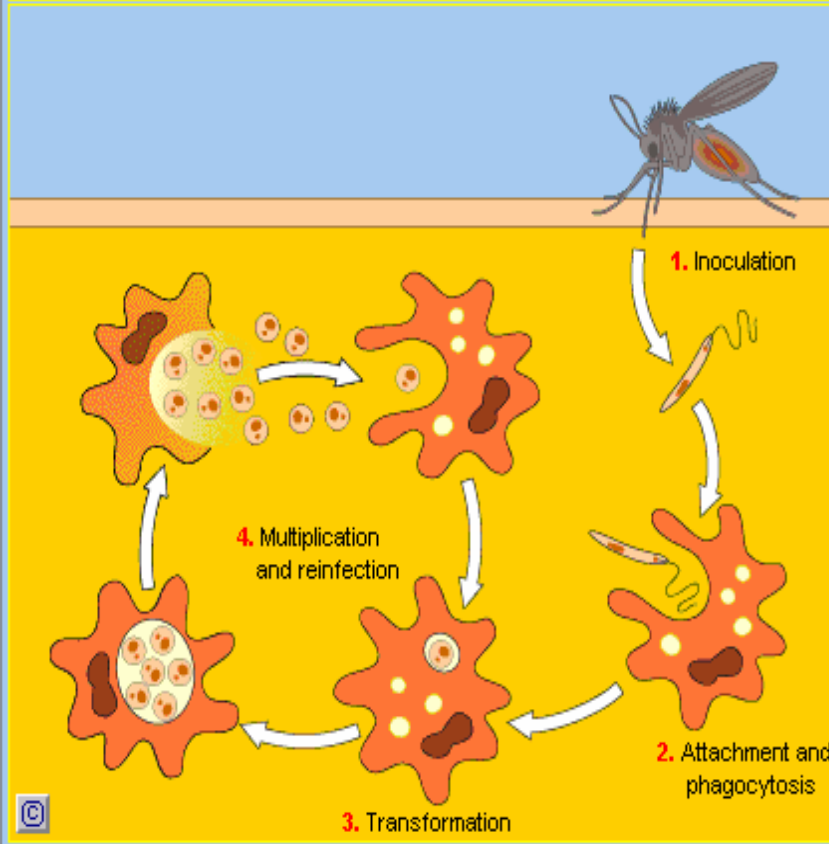
The parasite life cycle in the sand fly can be divided into four stages:

1. ingestion
2. transformation
3. colonization
4. transmission

Parasite multiplication is an important feature of many of these stages (see screen 27).

Picture: Parasite stages in the sand fly gut.

Vertebrate Host Stages of the Life Cycle - 1



Stages in the vertebrate host

The parasite life cycle in the vertebrate host can be divided into four stages:

1. inoculation
2. attachment and phagocytosis
3. transformation
4. multiplication and reinfection

Picture: *Leishmania* stages in the vertebrate host.

Sand fly

- Sand flies are small (1.5-4mm) delicate, pale and hairy insects with almost erect hairy wings
- occur in a wide range of habitat, from sea level to the altitude of 2800m or more and from hot dry deserts to dense tropical rain forests
- They are weak fliers, usually have a short hopping (Jumping) flight. Although can fly up to 2.2km over a period few days in open
- Sand flies are classified into 700 species with five genera
- only 19 of them have so far been incriminated to be the vector of *Leishmania*
- Sand fly can breed in cracks in walls or among rocks, animals burrows, caves, damp leaf litter in forests, holes in ground, stable floor, poultry houses and termite hills
- Main requirements for breeding sites are moisture and organic matter, on which the larvae feed
- Oviposition usually takes place 5-10 days after a blood meal

- Both male and female feeds on sugar and plants juices but only females suck blood
- Feeding takes place on the exposed parts of the body
- Blood is taken directly into the mid gut while other liquid (sugar) are directed first to the crop for sterilization and then to mid gut
- Almost all the *Leishmania* vector species of sand fly belong to the genus *Phlebotomus* in Old World and genus *Lutzomyia* in New World
- *P. sergenti* is considered to be the vector of *L. tropica* while *P. papatasi* transmits *L. major*



Vector Identification:

to identify a sandfly, and differentiate male from female – Characteristic “V” shape wings. Males have a fan-like external genitalia



Ideal sand fly breeding site in AR camp





Cracks in a house wall and wooden roof Ideal for sand fly breeding in AR camp



Anthroponotic cutaneous Leishmaniasis (ACL)

- ACL is spread by the sand fly *Phlebotomus sergenti* and is basically a human disease (so called anthroponotic). Occasionally dogs may also be infected.
- ACL is also called Urban or dry leishmaniasis
- Causative agent of ACL is *Leishmania tropica*

Clinical view of ACL

- Ulcer with a diameter of 1-4cm
- Commonly develop satellite papules
- Are described as dry sores as they have :
 - A central crust
 - No exudates
- Heal slowly usually within two years
- Incubation period of ACL is 1-3 months

Papular Stage

- The parasites stay dormant for several months, inside a macrophage in the dermis i.e., incubation period, and lasts between 3-12 months (1-2 months for ZCL)
- At the end of the incubation period the parasites actively multiply, filling the infected cell with amastigotes until the cell bursts, the released amastigotes then infect new cells
- As this happens a small red spot or papule will develop

Papular stage



Nodular stage:
The papule enlarge it develop a smooth lump
in the skin called a nodule



ULCER:the nodule eventually breaking down to form an ulcer the margin of the ulcer are shaped like the edges of a volcano. the edges are raised containing infected cells and immune cells which are trying to remove the infection. Thus the margins and base of the lesion are swollen and red.

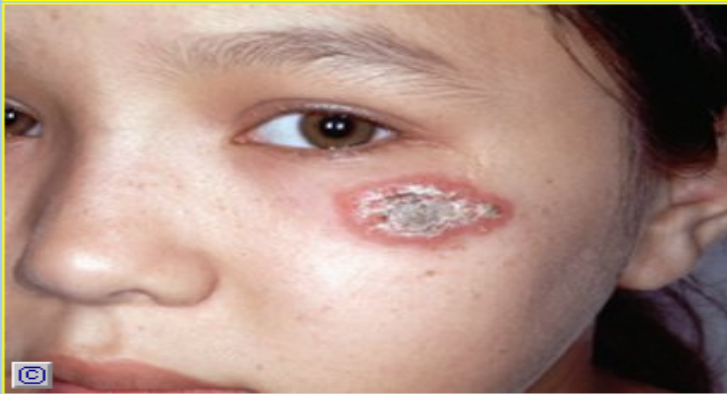






ACL Ulcers

Simple Cutaneous Leishmaniasis - 3



Picture: This is a raised, crusted ulcer due to *L. tropica*.







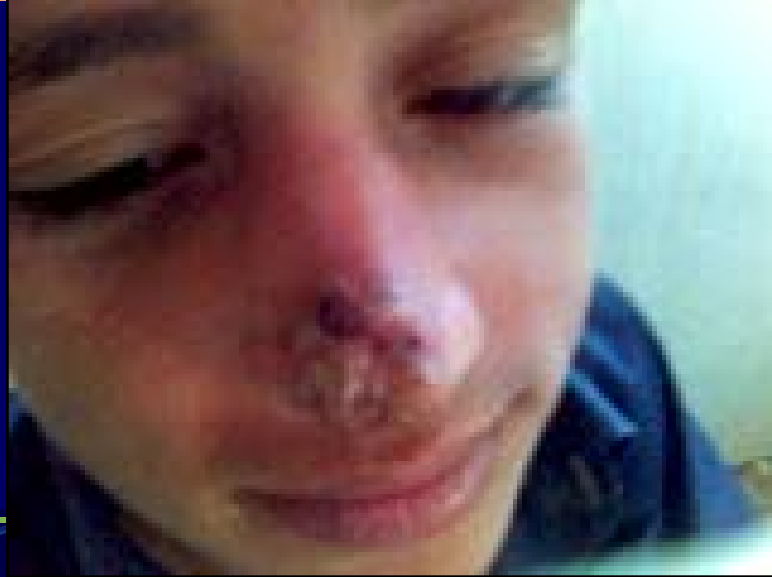
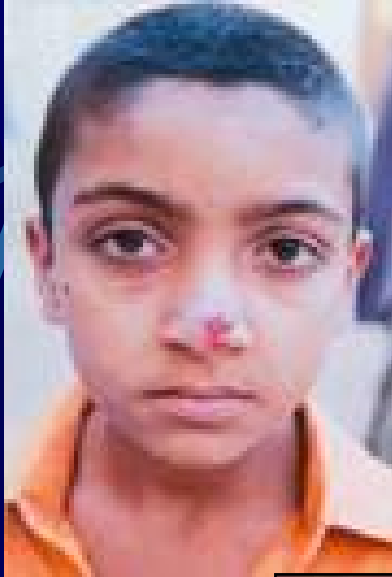
Zoonotic CL

Old World simple CL due to *L. major*

Simple CL lesions due to *L. major*:

- have an incubation period of 1 - 10 weeks
- have a diameter of 2 - 6 cm
- often present as multiple lesions
- are described as 'wet' sores as they are:
 - ulcerated
 - often severely inflamed
 - covered with a seropurulent exudate
- are fast-healing (usually within 2 - 8 months)

Zoonotic CL



CL: obtaining samples

Ideally several samples should be obtained:

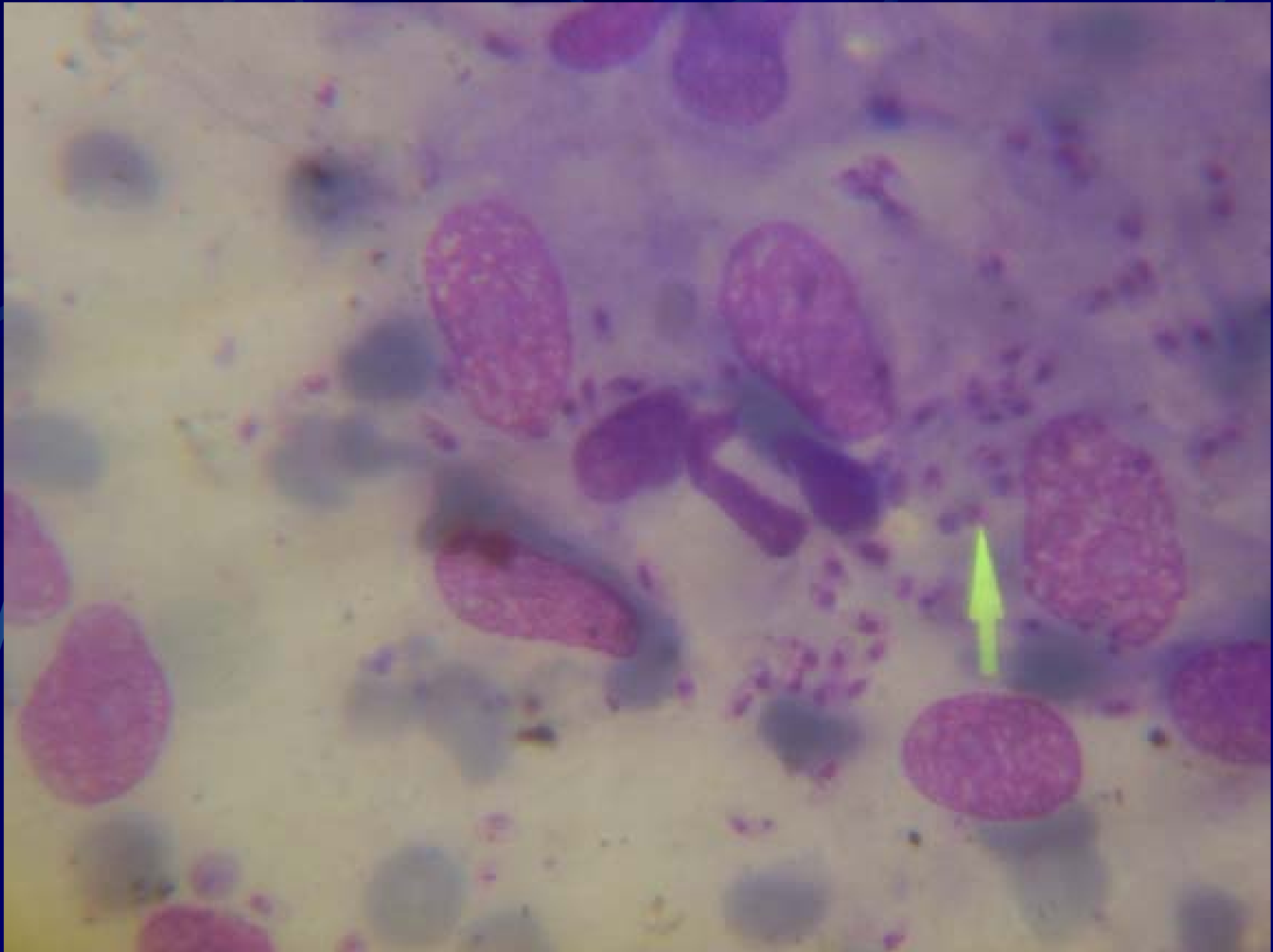
- from active lesions
- from the:
 - inflamed edge of a lesion
 - raised edge of an ulcer
 - centre of a nodule
- using several techniques
- by taking several samples per technique

Material for parasitological diagnosis can be obtained by:

- dermal scraping
- needle aspiration
- full thickness biopsy

Smear Preparation





Lesions on foot pads after sub-dermal inoculation into Balb/C Mice



Typical cutaneous lesion on foot pad



Table 1. CL in Local population and A. Refugees

<u>POPULATION</u>	<u>SUBJECTS EXAMINED</u>	<u>POSITIVE FOR CL</u>	<u>PERCENTAGE</u>
Local	320	210	65.62
Afghan	195	71	36.41
Total	515	281	54.56

($\chi^2 = 40.543$, $P > 0.05$)

Table 2. Age-wise prevalence of CL in Local population and A. Refugees

Age groups	Positive cases (%)
0-9	20
10-19	18
20-29	10
30-39	10
40-49	14
50-59	14
60 and above	14

Table 3. Sex-wise prevalence of CL in Local population and A. Refugees

Male	63 %
Female	37%

$(\chi^2=28.34, d.f=1, P>0.05).$

Table 4. Sites of active lesions

Site	%
Face	45
Legs	22
Hands	17
Mixed	16

Table 5. Number of active lesions

No. of lesions	%
1	46
2-3	30
4-5	15
>6	9

Table 6. Dry and wet types of the lesions

Dry Lesions	80%
Wet lesions	20%

Table 7. Impact of construction type and domestic animals on the prevalence of Leishmaniasis

Construction type	% Prevalence
Kacha (Mud)	64
Pacca (Cemented bricks)	36
Domestic animals	
Present	60
Absent	40





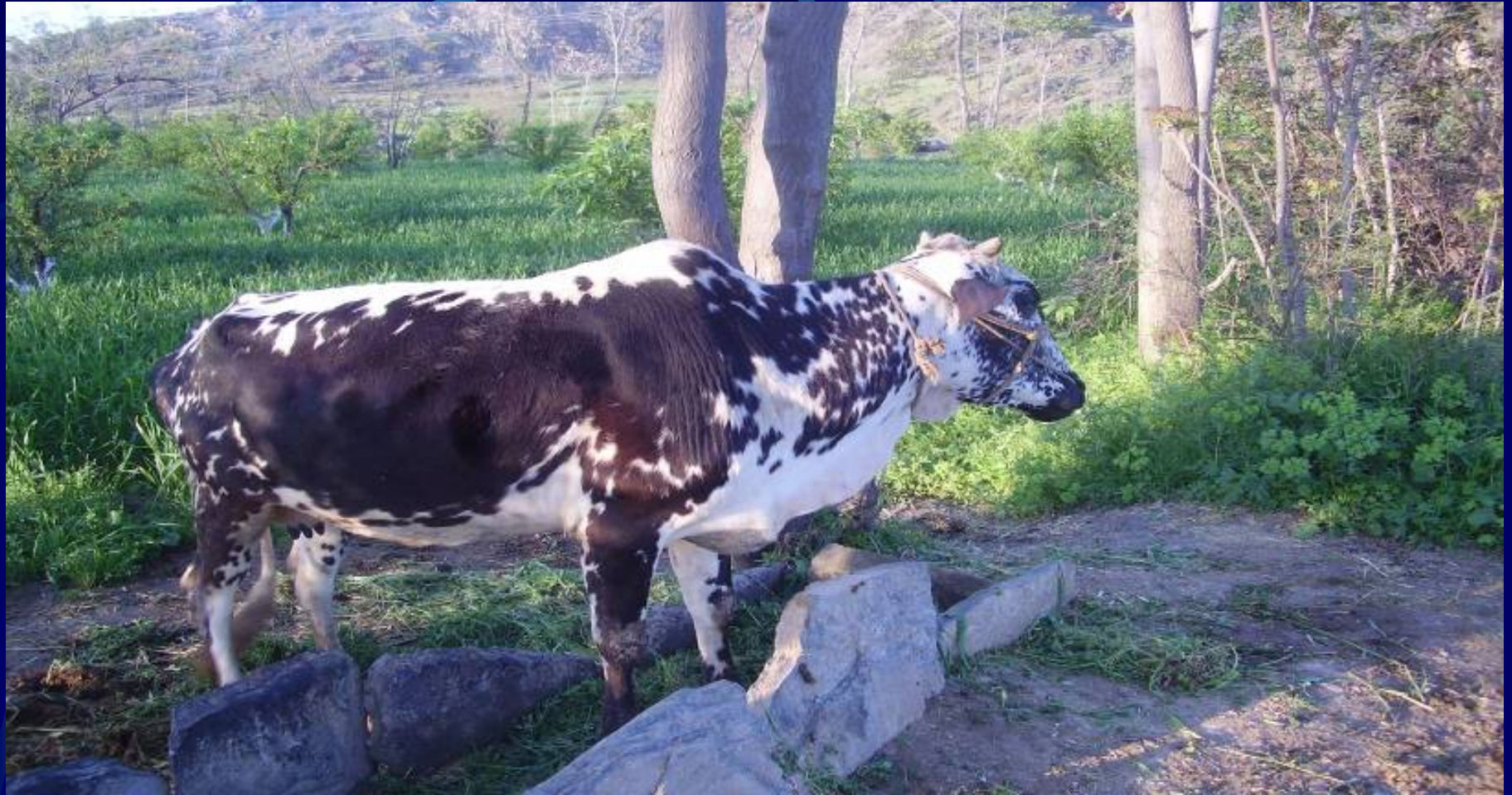






Table 8. District wise distribution of CL in Afghan refugees in NWFP Pakistan during 2006

District	Prevalence %
Hangu	29
Dir	25
Peshawar	11
D.I.Khan	9
Malakand	9
Mianwali	6
Kohat	4
Nowshera	3
Mansehra	2
Haripur	1
Mardan	1

Table 9. CL incidence rate/1000 AR population in Pakistan 2001-2006

Year	Incidence /1000
2001	5.6
2002	13.2
2003	14.8
2004	10.6
2005	6.6
2006	3.3

The parenteral administration of pentavalent antimonials has been the mainstay of treatment for all forms of leishmaniasis since the 1940s.

However, other drugs and modes of treatment are now available or are being assessed, including:

- intralesional injection with pentavalent antimonials
- antifungal agents, eg. amphotericin B
- topical agents, eg. paromomycin sulphate ointment
- oral agents, eg. miltefosine

Cutaneous Leishmaniasis - 3



Picture: Intralesional injection of sodium stibogluconate for treatment of a dry, single lesion due to *L. tropica* (Iran).



Thank you