LEISHMANIASIS

Dr. Feiszt Zsófia
Department of Infectious Diseases

Neglected tropical diseases (NTDs) are a diverse group of communicable diseases that prevail in tropical and subtropical conditions in 149 countries and affect more than one billion people, costing developing economies billions of dollars every year. They mainly affect populations living in poverty, without adequate sanitation and in close contact with infectious vectors and domestic animals and livestock.

Neglected tropical diseases

- Buruli ulcer
- Chaga's disease, African trypanosomiasis
- Cysticercosis
- Dengue
- Dracunculiasis
- Echinococcosis
- Fascioliasis
- Leishmaniasis
- Leprosy
- Rabies
- Schistosomiasis
- Trachoma
- Yaws

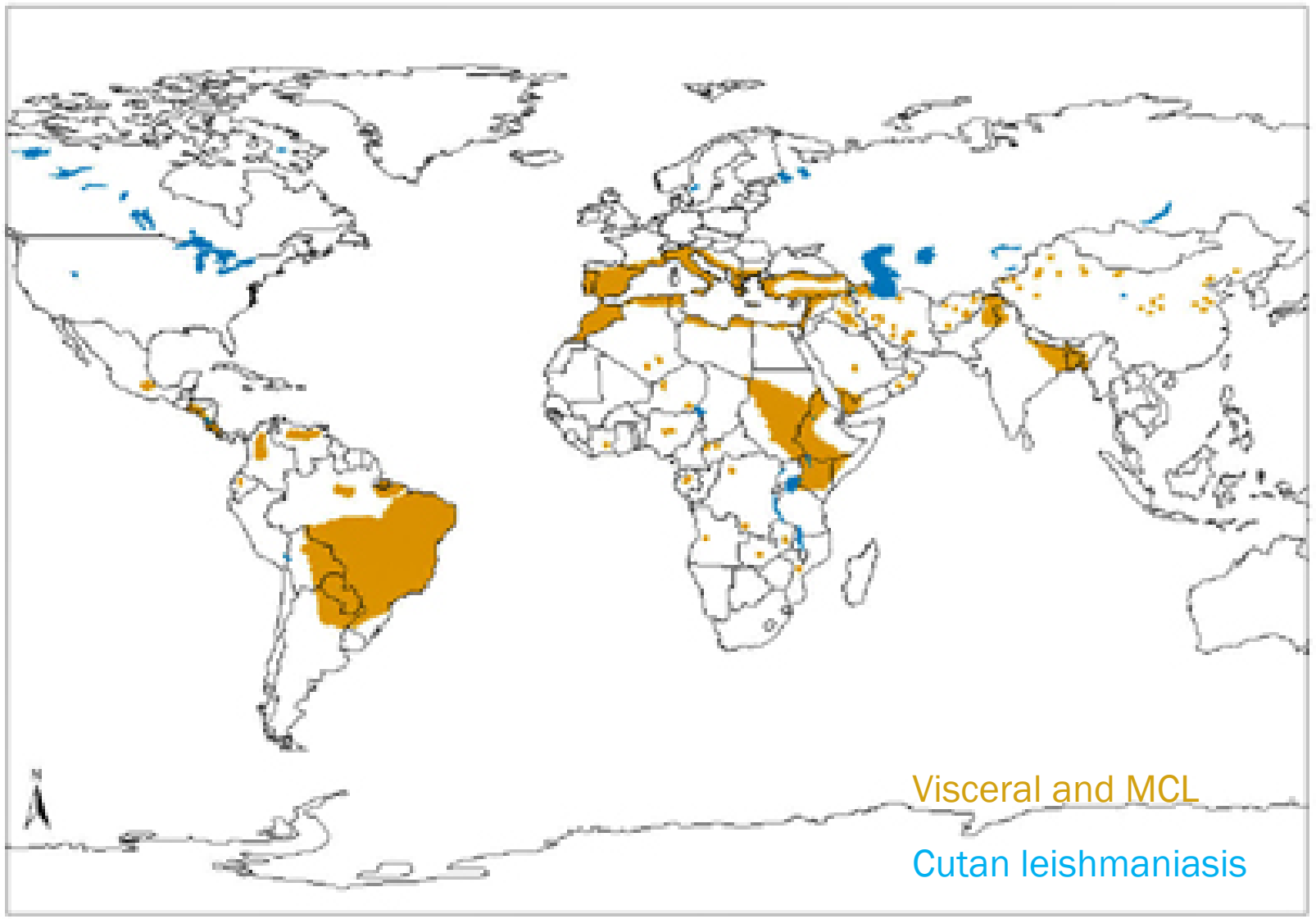
Leishmaniasis

The Leishmaniasis threaten 350 millions people in 88 countries of four continents. The annual incidence of new cases is estimated between 1.5 and 2 million.

The genus Leishmania includes around 30 different taxa, the majority of which commonly infects humans and couse various types of disease: visceral, cutaneous (of localised and diffuse type) and mucocutaneous leishmaniasis.

Leishmania are protozoa belonging to Trypanosomiadae

Geographical aspects of leishmaniasis



Reservoir

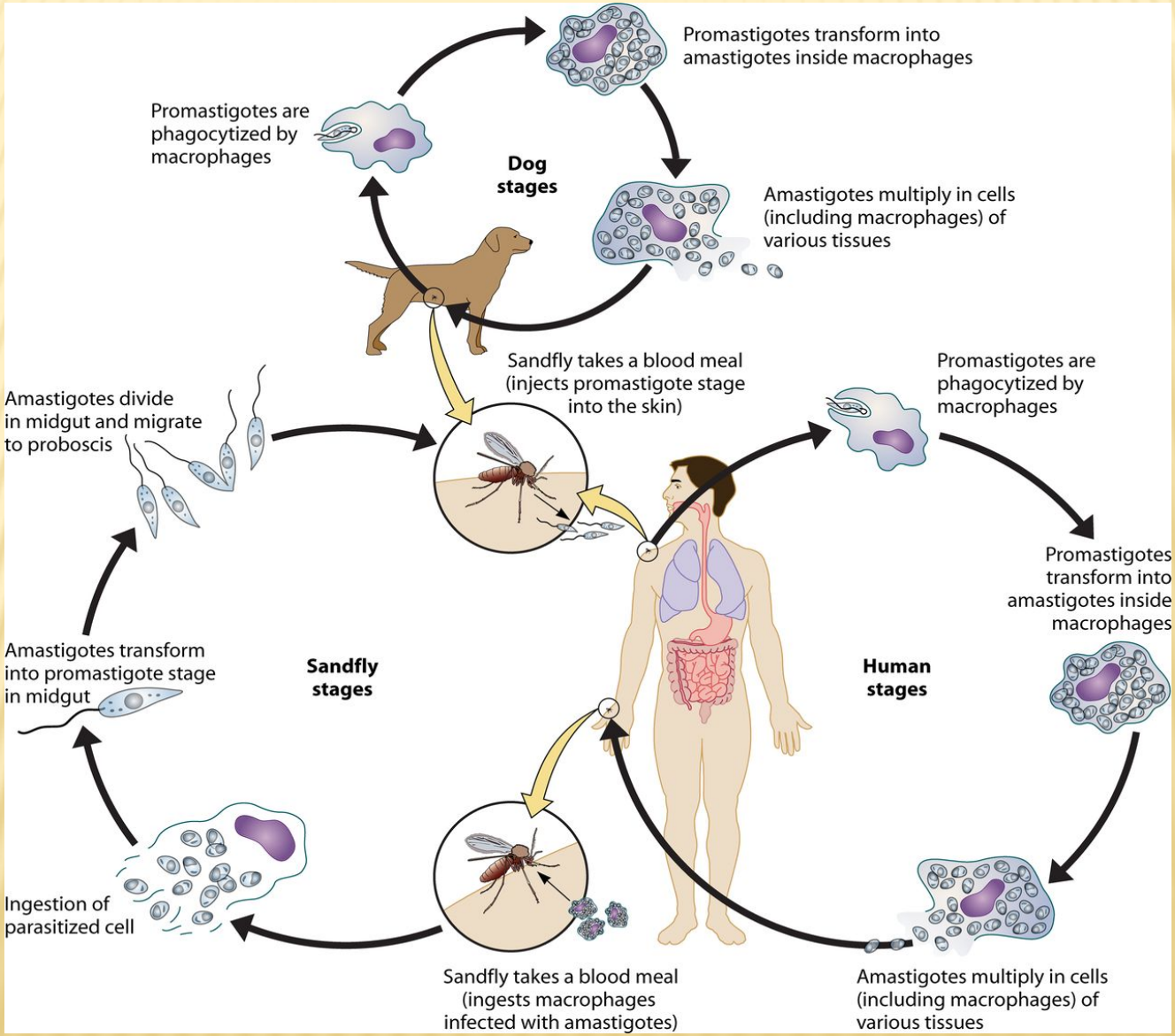
Most leishmaniasis are zoonoses and the reservoir hosts are various species of mammals which are responsible for the longterm maintenance of Leishmania in nature. Most reservoir hosts are well adapted to Leishmania and develop only mild infections which may persist for many years, an important exception being the dog, which commonly develops a generalised and fatal disease.

Life cycle

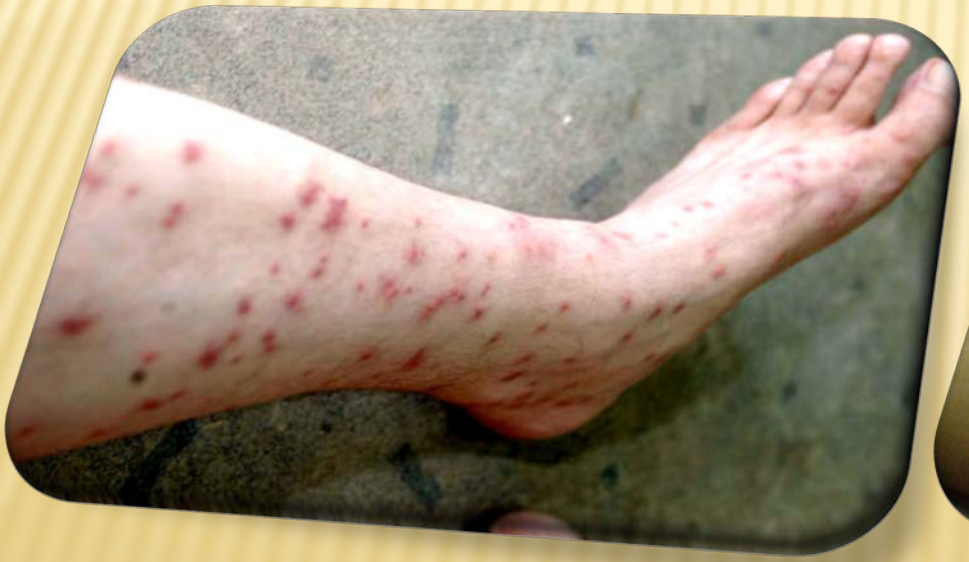
Leishmania are alternatively hosted by the insect (flagellated promastigote) and by mammals (intracellular amastigote stage). When a female sandfly (Phlebotomus mosquito) takes a bloodmeal from a Leishmania-infected mammal, intracellular amastigotes are ingested by the insect. Inside the blood meal, amastigotes transform into motile promastigotes. The promastigotes multiply intensively inside the intestinal tract of the sandfly, then transform to infective metacyclic promastigotes.

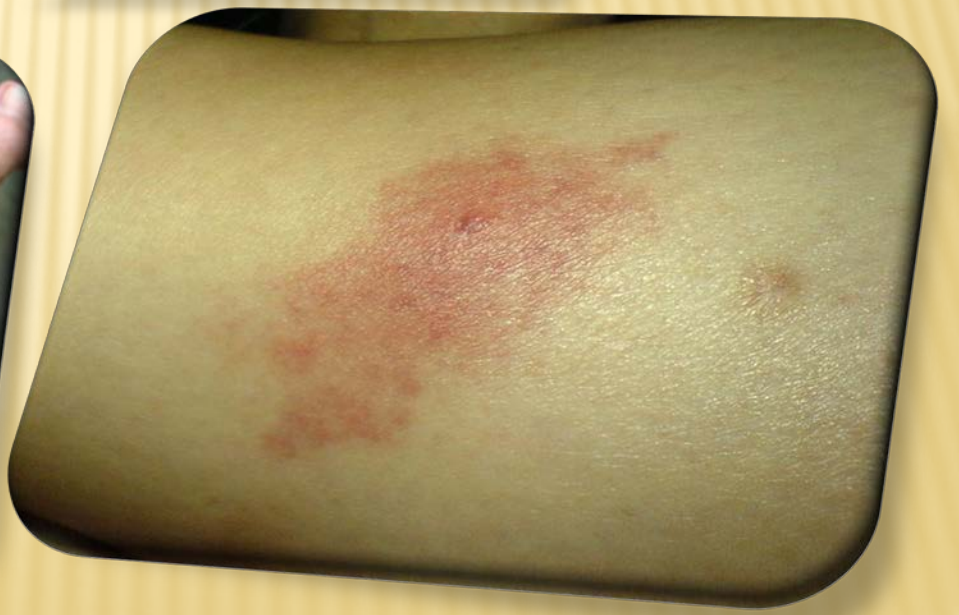
The bite of an infected sandfly deposits infective metacyclic promastiotes in the mammal's skin, which are rapidly phagocytosed by cell of the mononuclear phagocyte system. The intracellular parasites changes into amastigotes, which multiply by mitosis.

Life cycle

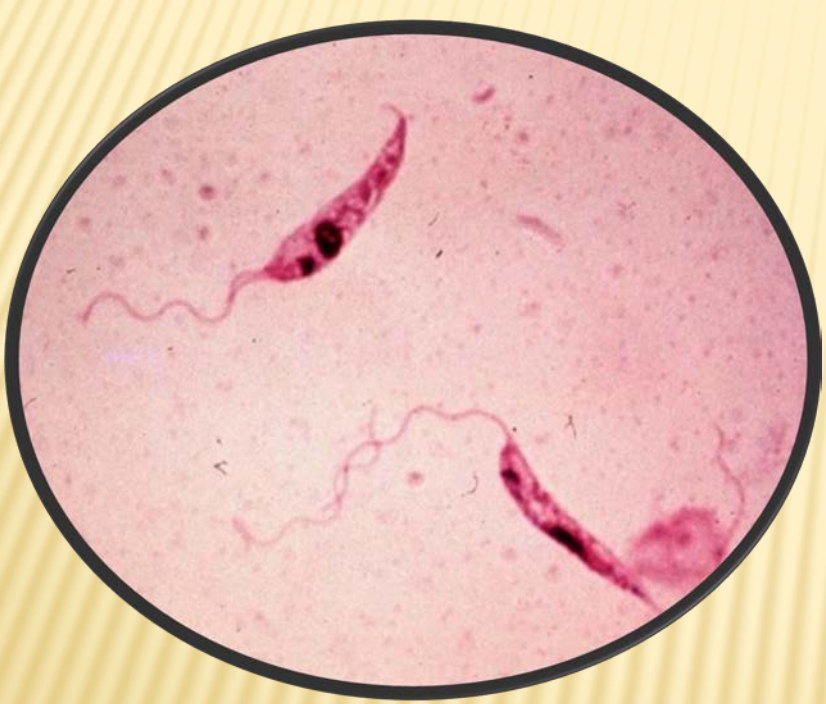

Promastigotes transform into amastigotes inside macrophages
Promastigotes are phagocytized by macrophages
Dog stages
Amastigotes multiply in cells (including macrophages) of various tissues
Sandfly takes a blood meal (injects promastigote stage into the skin)
Promastigotes are phagocytized by macrophages
Amastigotes divide in midgut and migrate to proboscis
Promastigotes transform into amastigotes inside macrophages
Amastigotes transform into promastigote stage in midgut
Sandfly stages
Human stages
Ingestion of parasitized cell
Sandfly takes a blood meal (ingests macrophages infected with amastigotes)
Amastigotes multiply in cells (including macrophages) of various tissues

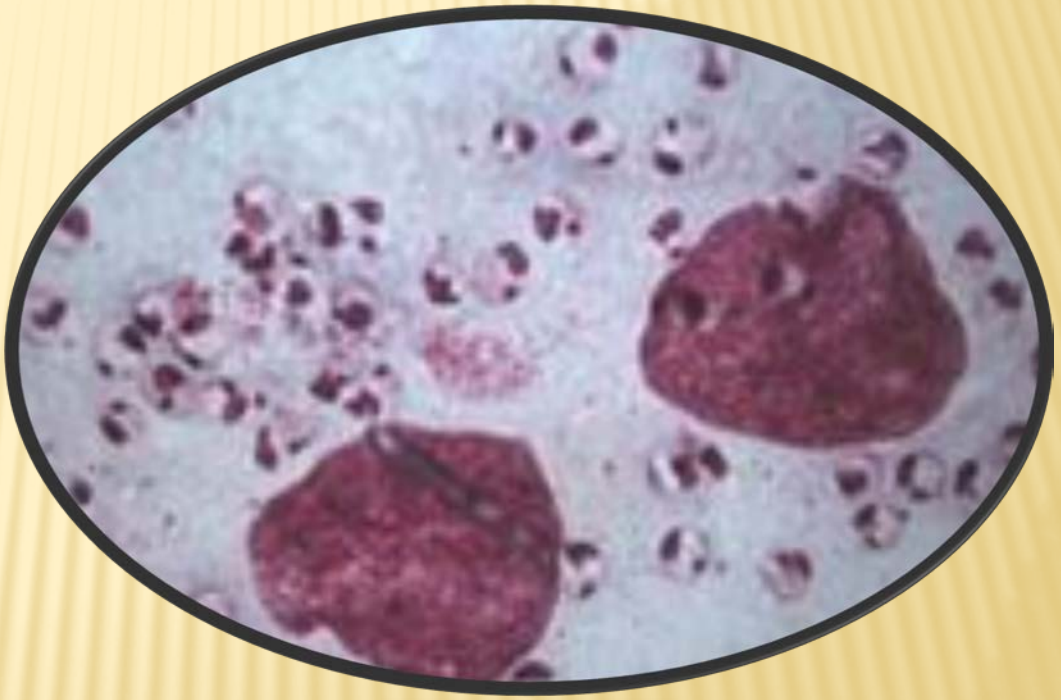
Phlebotomus mosquito (sandfly) and it's bite





Leishmania promastigots and amastigots





Pathology

When the intracellular development of the amastigotes remains localized at the inoculation site, various cytokines are released and cell reactions are generated, resulting in the development of localized lesion of CL. In other instances the parasites spreads to the organ of the mononuclear phagocytic system, giving rise th VL. Amastigotes may also spread to other cutaneus sites, as in diffuse cutaneous leishmaniasis (DCL), or to muvosae in the case of mucocutaneous leishmaniasis (MCL). The localisation of the parasite is directly related to the tropism of the parasite species.

In spite of general tropism of the species, some exceptions occur, which are independent of the clinical status of the patient harbourin the parasite.

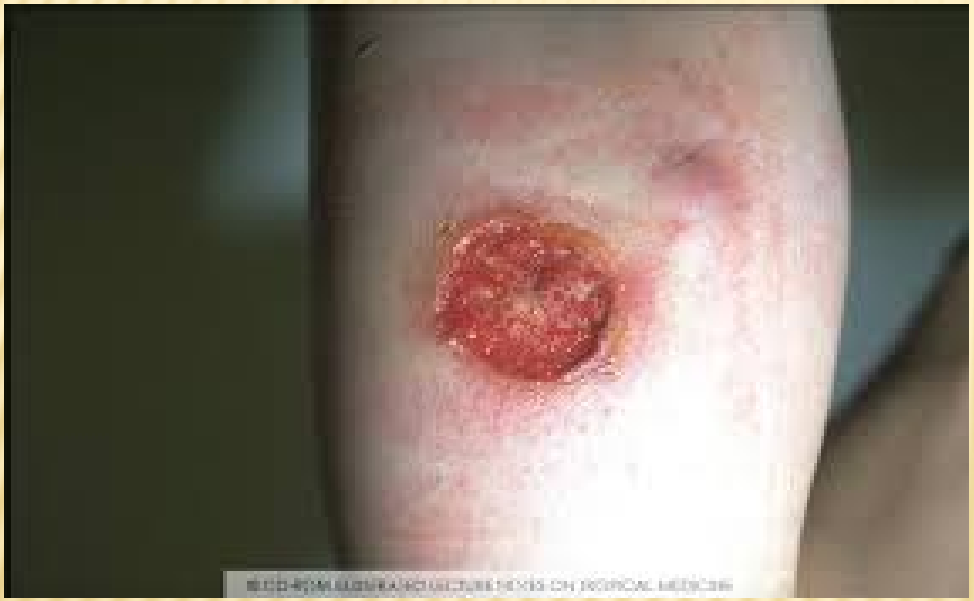
Clinical expression

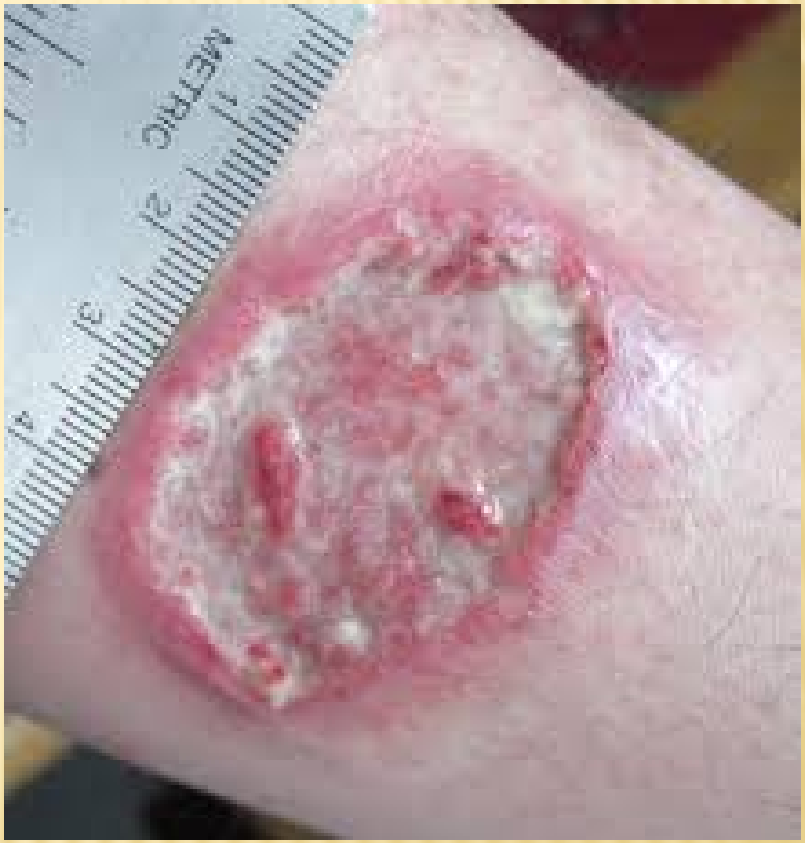
Tropism	Species	Usual localisation	Exceptional
Viscerotrop sp.	L. donovani L. infantum	VL VL	LCL LCL, DCLi
Dermotrop sp.	L. aethiopica	LCL	DCL
	L. major	LCL	DCLi
	L. tropica	LCL	VL
	L. amasonensis	LCL	DCL, VL
	L. colombiensis	LCL	
	L. guyanensis	LCL	MCL
	L. mexicana	LCL	DCL
	L. peruviana	LCL	
	L. venesuelensis	LCL	
	L. lainsoni	LCL	
Dermo-mucotrop sp.	L. brasiliensis	LCL, MCL	DCLi, VLi
	L. panamensis	LCL	MCL, DCLi

Cutaneous leishmaniasis
Localised cutaneous leishmaniasis

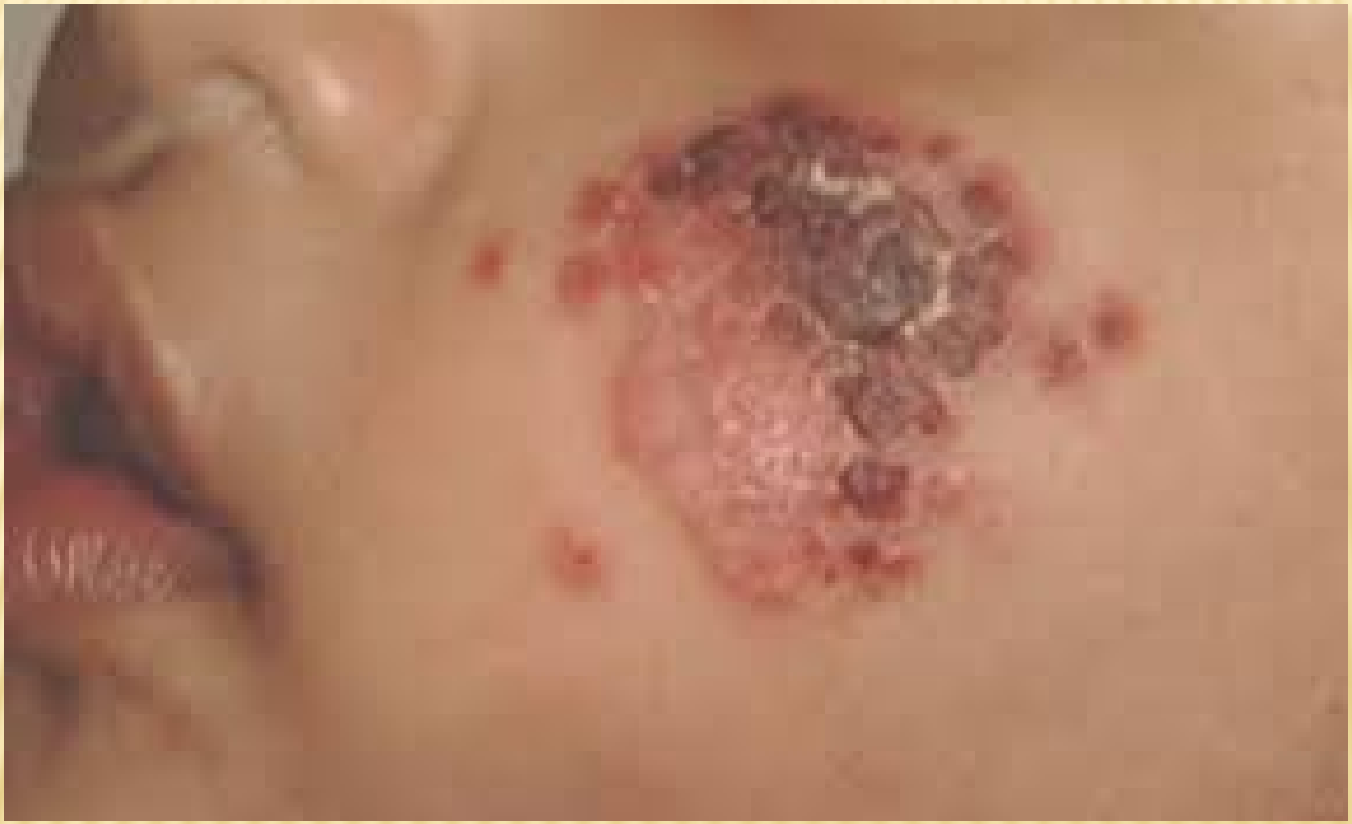
- the incubation period depends on the infecting species and the size of the inoculum, the mean duration is around 1 month
- Starts as an erythematous papule, similar to an insect bite
- regularly enlarges, reaching the definitive size in a few weeks, usually in the range of 0.5-10 cm in diameter
- The lesions are painless unless secondarily infected
- the most common clinical feature of LCL is the ulcerative lesion
- The dry type is a papulo-nodular lesion, covered by superficial scales. It can enlarge to form a plaque

Localised cutaneous leishmaniasis



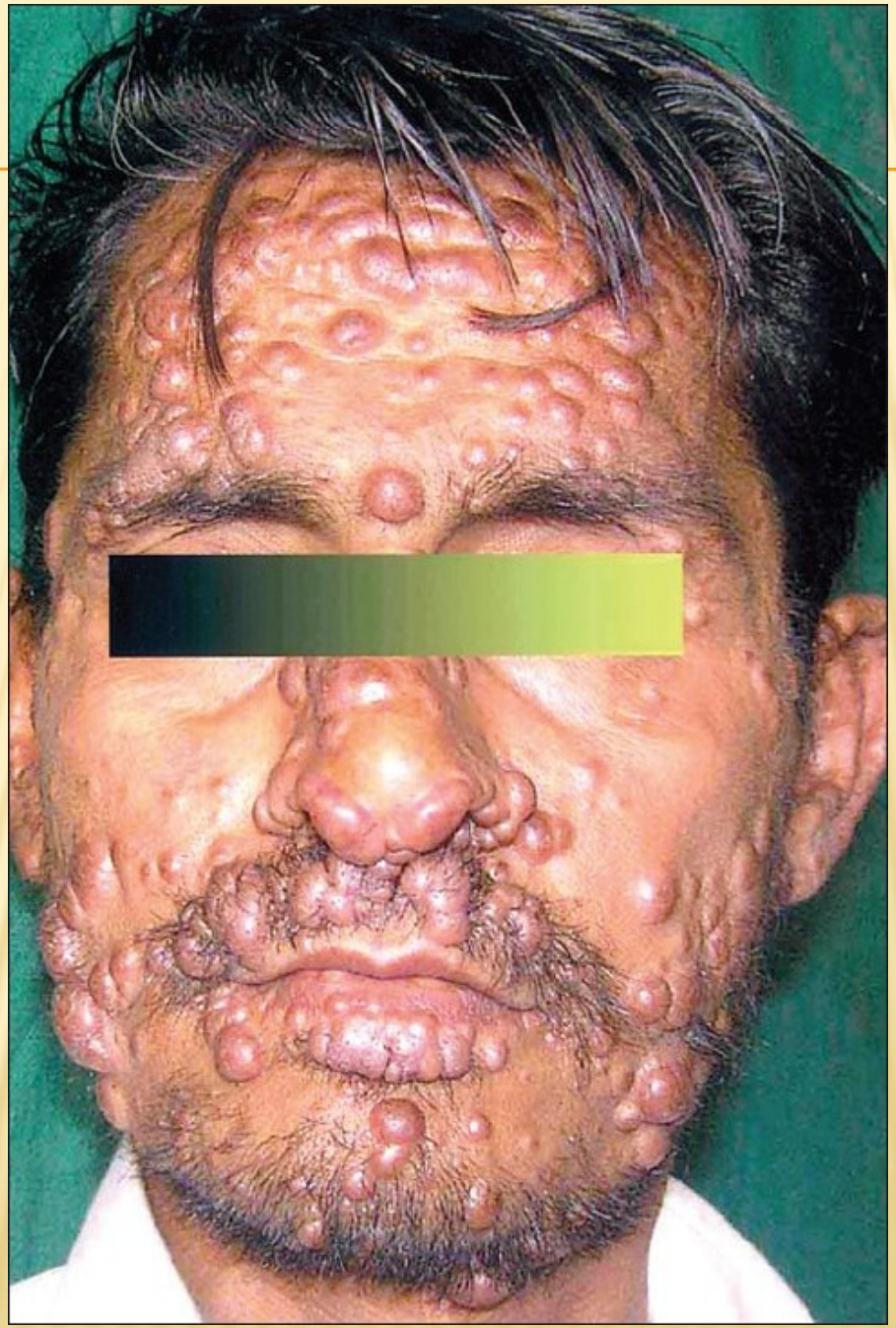


Localised cutaneous leishmaniasis



Cutaneous leishmaniasis
Diffuse cutan leishmaniasis (DCL)

- This particularly sever form of CL is resulting from the parasitsm of particular Leishmania species, L. amazonensis and L. mexicana in the New World, and L. aetiopica in the Old World, in patients with antileishmanial specific defect of cell-mediated immunity.
- Since HIV infection has spread to Leishmania endemic countries, DCL cases have been ocasionally reported due to unusual species, such as L. braziliensis, L. infantum and L. major
- A non-ulcerated nodule rich in parasites represent the basic lesion of this form. The nodules are numerous, at first isolated, then joining to form large patches, disseminated to the whole body (ddg. Facies leonine). There is no ulceration, nor mucosal or visceral involvement
- This form is resistant to the classical antileishmanial drugs



Cutaneous leishmaniasis
Leshmaniasis recidivans

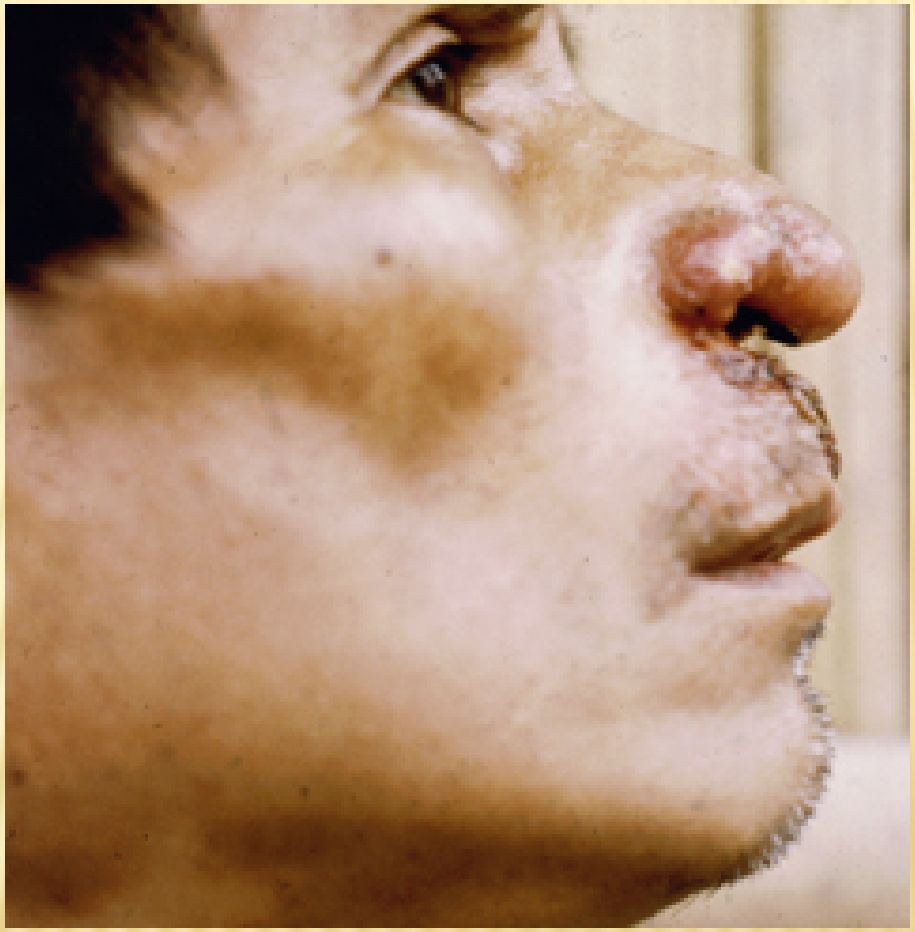
- L. tropica, L. braziliensis
- The lesion is located on the face and follows an acute lesion, after numerous month of evoluation. The lesion shows a periferal active zone, constantly enlarging, around a central healing part.

Mucocutaneous Leishmaniasis

- L. braziliensis, occasionally L. panamensis
- This form of leishmaniasis involve of two stages: a primary cutanous lesion, followed after a variable time of latency by a secundary mucosal lesion
- The primary lesion does not fundamentally differ from the localised lesion occurring during infections by other dermatotropic species
- Cure spontaneously
- The period of time between cutaneous and the secondary mucosal involvement extends from several weeks to many years

Mucocutaneous Lesihmaniasis

- the mucosal involvment starts on the nasal mucosa. The patients suffer with nasal congestion, which causes nocturnal discomfort
- The initial nasal lesion occurs on the anterios cartilaginous part of the nasal septum. It seems as a small-sized hyperaemic, inflammatory granuloma, rapidly evolving to an ulcer
- The septum is rapidly invade and destroyed, which leads to the perforation of the nasal septum in it's anterior part
- 'tapir nose'



Mucocutaneous Lesihmaniasis

- The buccal mucosa is commonly affected at a later stage, with or without of the contaguous spread from the nasal lesions
- The musosae of the palate and the interior lips are the most frequently involves, while the tongue generally remains uninjured
- The lip lesios are inflamed and ulcerated, sometimes extending to the external part, with frequent tissue destruction
- Laryngeal extension follows the rhino-buccal-pharyngeal localisation of the parasite. Cause dysphonia and mettalic cough

Mucocutaneous Lesihmaniasis

- Tissue necrosis and disfigurement appear in the advanced stage of the condition and can be extremly severe.
- The nose and lips can totally disapear, at which time the mouth and nasal acinty become connected by a single hole
- Socio-psychologycal consequenses are considerable for patients, often leading to suicide

KENYA

- 39 millióan élnek az országban, 43% 15 év alatti, 4% 60 év felett
- Orvosok száma: 1/10,000
- A költségvetés 9,7%-át fordítják az egészségügyre
- Leismaniasis endémiás: Rift Vally, Keleti- és Észak-keleti tartomány
- P. martini- *L. donovani*
- A CL megjelenése a VL-hoz képest ritka
- A betegek 66%-a férfi, 50%-a 5-14 év közötti


MINISTRY OF HEALTH
HARAMBEE
KIMALEL HEALTH CENTRE
P.O.Box.139, MARIGAT.
DNDi / KEMRI
KENYA MEDICAL RESEARCH INSTITUTE
KEMRI
Drugs for Neglected Diseases initiative.
Kenya Medical Research Institute.
Kala-azar Research & Treatment Centre.


ADMINISTRATION/OUT-PATIENT/BLOCK.
VISION
OTA
KAW 092Z

Symptomes:

- Reoccuring fever
- Hepatosplenomegaly
- Lymphadenopathy
- Anaemia
- Weighloss
- Weakness

DIAGNOSIS

- Prove the presence of parazites from spleen, bone marrow or lymphnode aspiration with microscopy (spleen aspiration is the most sensitive)
- rK39 quicktest (you can use anywhere)
- Direkc agglutinin test (well prepared stuff and laboratory are needed

THERAPY

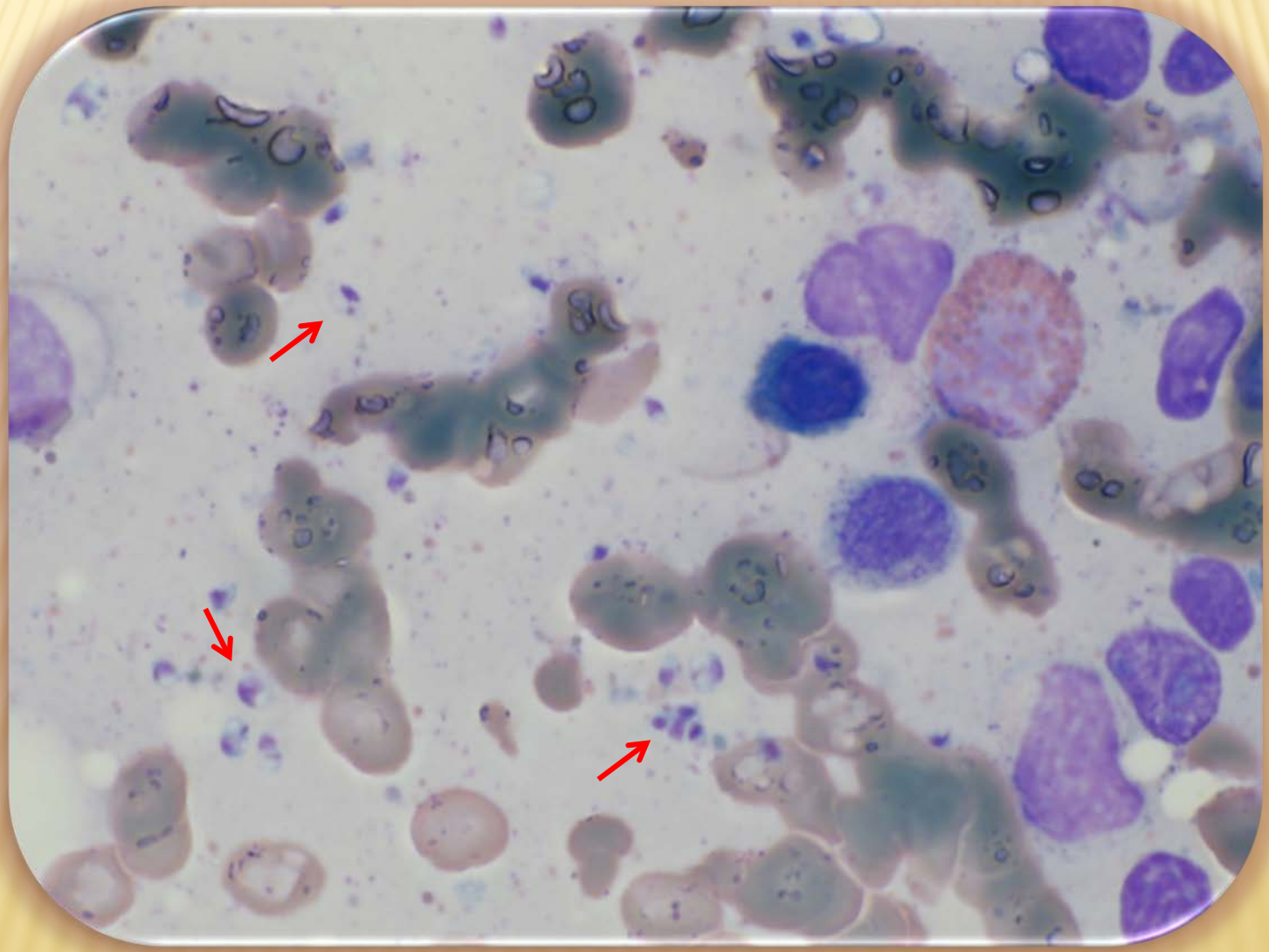
- Natrium-stibogluconate (SSG)
- liposomal amphotericin B
- paramomycin
- Miltefosine

Case presentation

Anamnesis

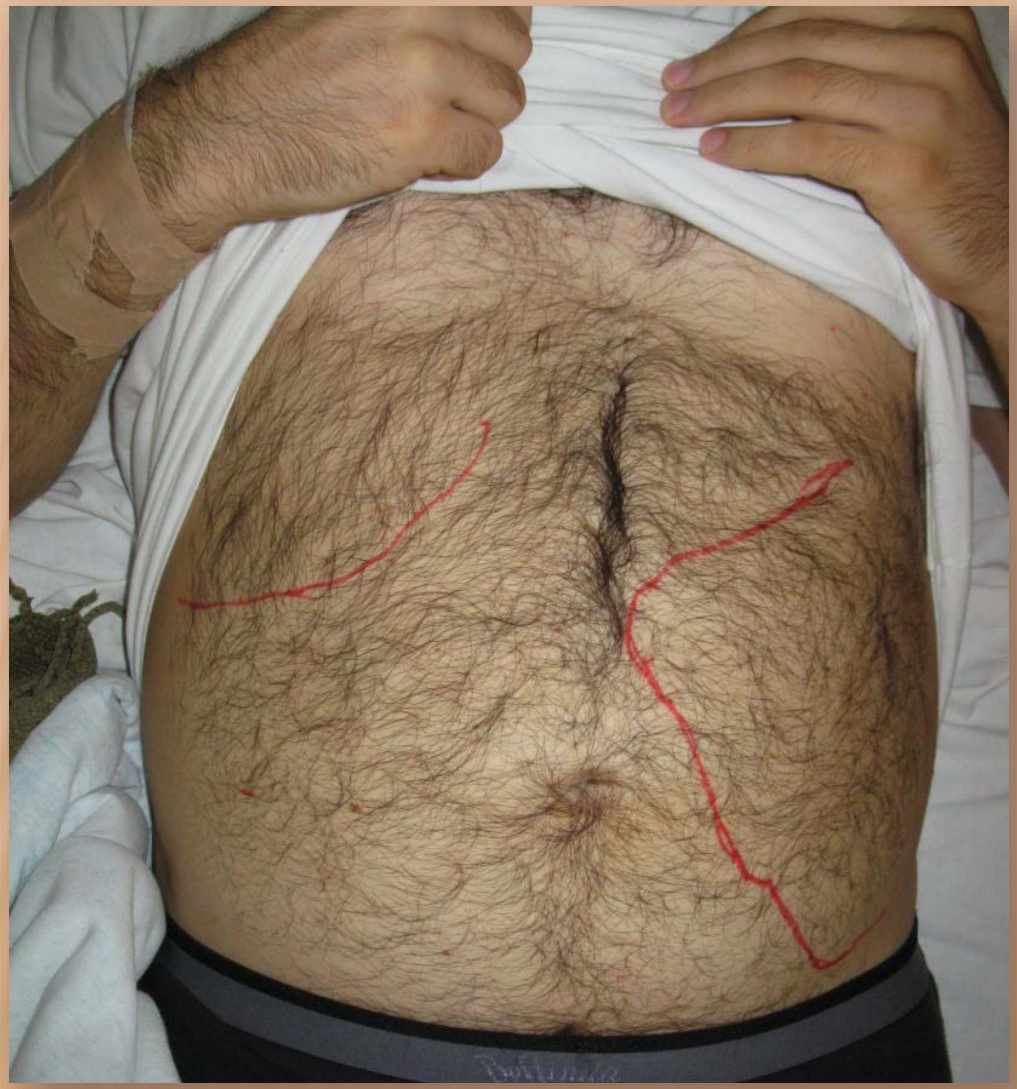
- 32 éves ffi.
- komolyabb belgyógyászati megbetegedése nem volt
- utazás (2009.aug.):Trogir, Makarska, Dubrovnik
- 2009. szeptemberében jelentkeztek panaszai lázzal (39-40C), hidegrázással, profuz éjszakai verítékezéssel. Majd átmeneti panaszmentesség után szept. végén panaszai gyakoribbá váltak
- PTE II. sz. Bel. Klin.: leucopenia, thrombocytopenia, kenetében 15% aktivált monocyta, magas CRP, emelkedett LDH és se. összfehérje; hasi UH-on splenomegalia, flowcytometria során aktivált monocytákat láttak. Immunszerológia:negatív
- 2009.11.04.: PTE I. sz. Bel. Klin. Haematológia: fokozódó microcyter anaemiát, haemolysist, Coombs pozitivitást, thrombocytopaeniát igazoltak. Echocardiographia fiziológiás viszonyokat ábrázolt. Cristabiopsia történt, malignitas, aplasticus csontvelői kép nem igazolódott.

Crista-biopsia kenete



- fvs 0,85 G/L, hgb 86 g/L, htc 27%, TCT 50 G/L
- GOT 59 IU, GPT 10 IU, ALP 119 IU, GGT 42 IU, LDH 705 IU
- Na 138 mmol/L, K 3,54 mmol/L, CN 2 mmol/L, kreat. 59 mmol/L
- CRP 135,8 mg/L, We 50 mm/h
- albumin 28 g/L, IgG >40, IgM 0,84 g/L, IgA norm. C3, C4 norm,
- A/G 0,4
- EBV, CMV, HBsAg, HCV, HIV, Toxoplasma, Mycoplasma, Chlamydia, Legionella neg.
- Parvovírus B19 IgM kétes
- Brucella, Coxiella szerológia negatív

Physical examination at admitance



Diagnostic of Leishmania

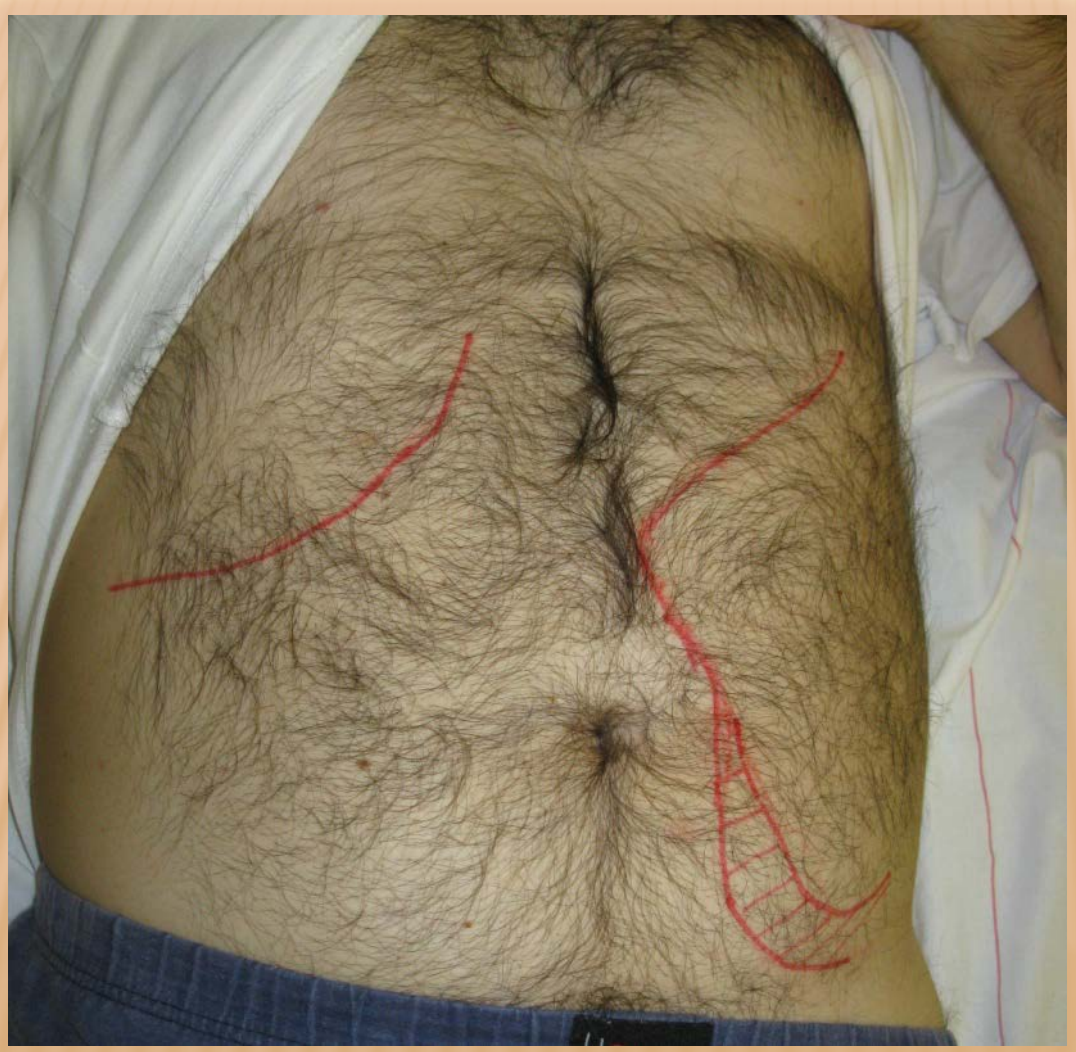
- Leishmania IgG Western blot: pozitív

THERAPY

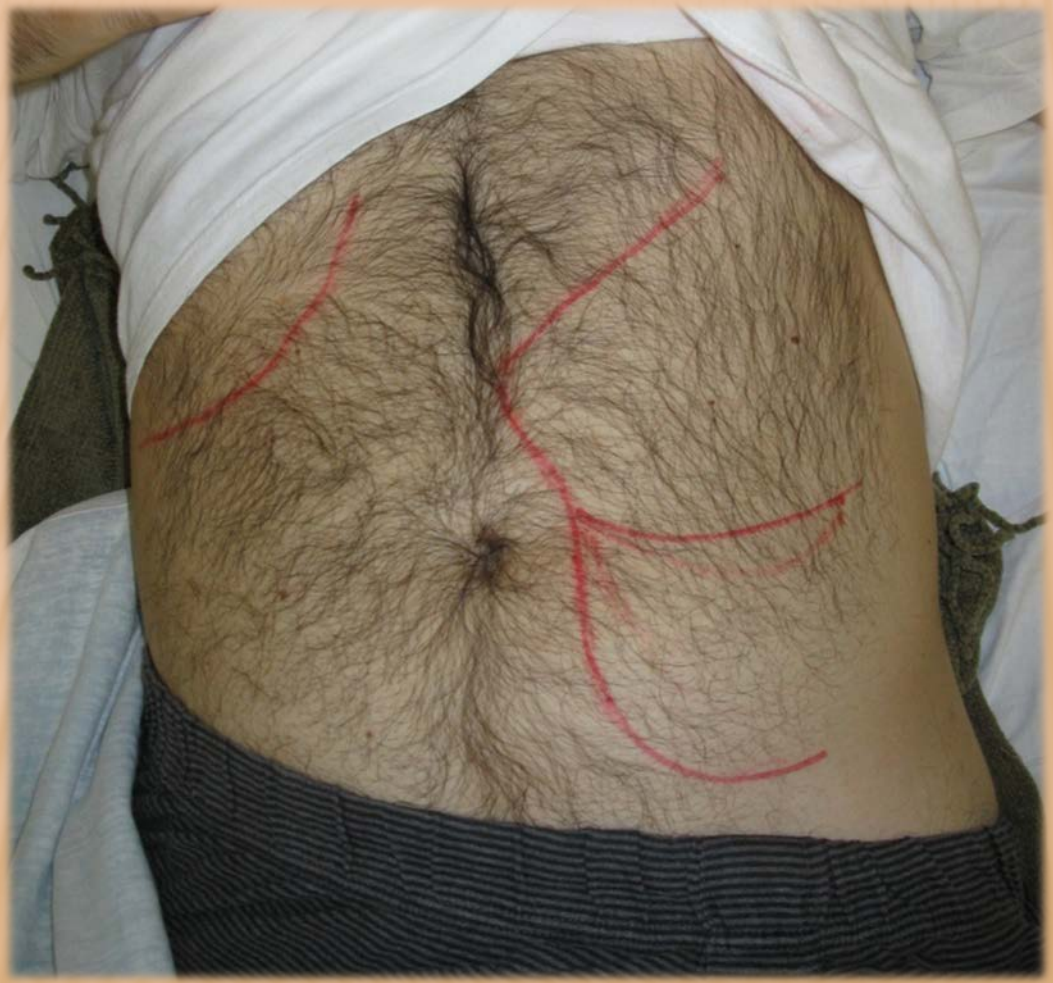
- Amphotericin B (20 mg/kg total dose)
- Thiogamma

	At admittance 0. week	During therapy 2. week	Emission 4. week
Fvs	0,85	3,63	3,97
Hgb	86	85	102
Htc	27	28	30,8
Tct	50	130	152
CRP	135	82	5,7
LDH	705	228	382
Albumin	28	32	39
IgG	>40	38,25	32
A/g	0,4	0,6	0,8
CN	2	10,9	6,6
Kreatinin	59	156	108

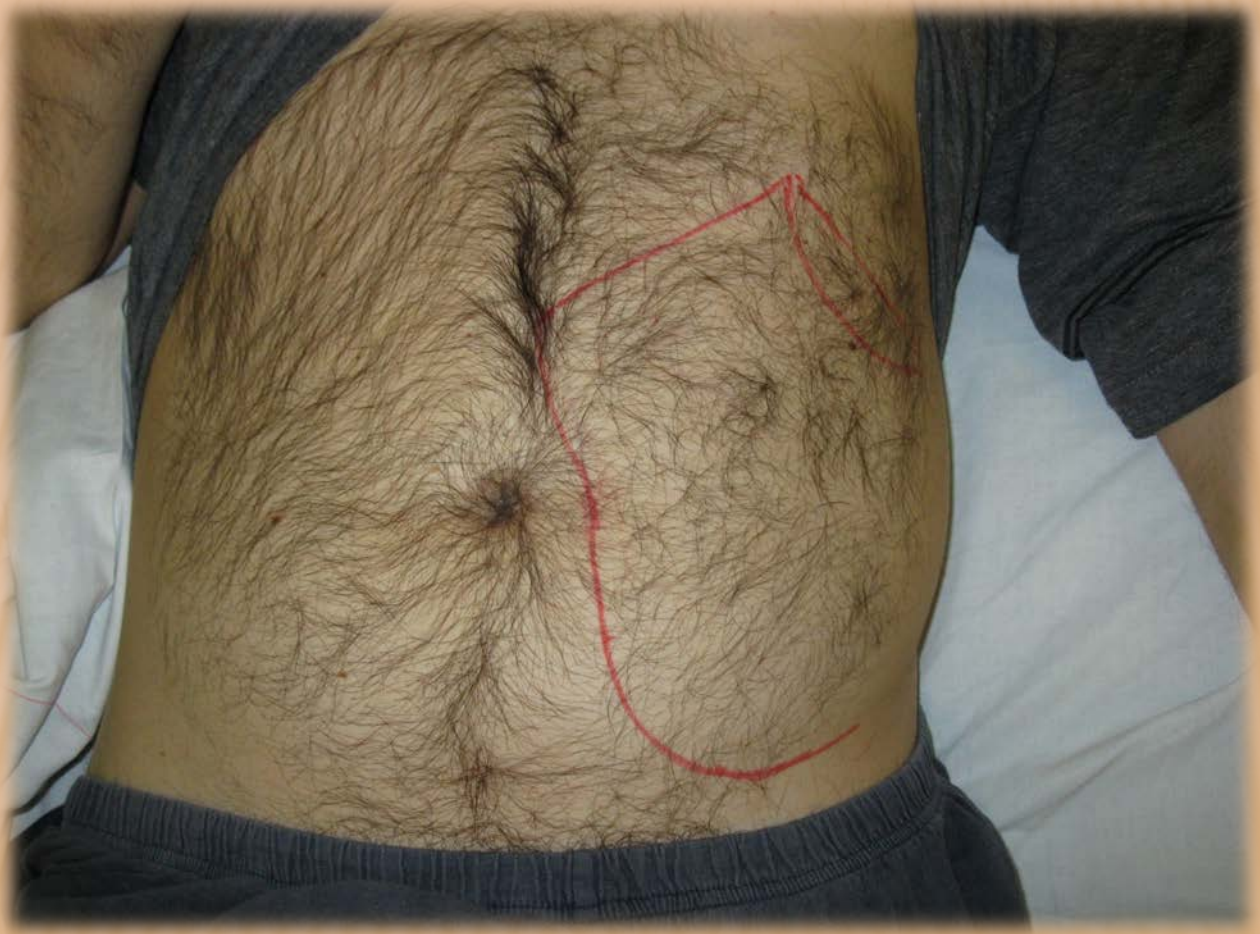
AFTER FOUR DAYS OF TREATMENT



AFTER TWO WEEKS OF TREATMENT



AFTER FOUR WEEKS OF TREATMENT




Tank you for your attention!