PANDORA ID - 25
TIME TO WEBINAR IN INFECTIOUS DISEASES

PATOLOGIA TROPICALE DI IMPORTAZIONE E AUTOCTONA
7 luglio 2025 – Ore 16.00-19.00

16.00-19.00 **PATOLOGIA TROPICALE DI IMPORTAZIONE E AUTOCTONA**
Moderatore: *Prof. Spinello Antinori (Milano)*

16.00 **Febbre dengue autoctona: esperienza della regione Marche**
Francesco Barchiesi (Pesaro)
Discussione

16.30 **Malattia di Chagas: update epidemiologico, clinico e di terapia**
Spinello Antinori (Milano)
Discussione

17.00 **Leishmaniosi: il punto di vista One Health**
- **In Medicina umana:** *Antonio Cascio (Palermo)*
- **In Medicina veterinaria:** *Ezio Ferroglio (Torino)*

Discussione

18.00 **Review di Casistica Clinica**
Lorenzo Albertini, Riccardo Ligresti, Giada Tesfamariam, Marianna Ticozzelli
Discussione

19.00 **Conclusioni e chiusura dei lavori**

Leishmaniosi

Antonio Cascio

Università di Palermo

UNIVERSITÀ DEGLI STUDI DI PALERMO

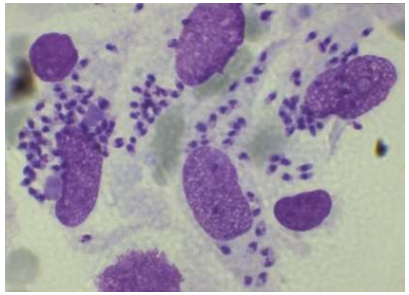
promise
Dipartimento di Promozione della Salute, Materno-Infantile, Medicina Interna e Specialistica di Eccellenza "G. D'Alessandro"

[THE BRITISH MEDICAL JOURNAL Nov. 14, 1903.]

NOTE ON THE BODIES RECENTLY DESCRIBED BY LEISHMAN AND DONOVAN.

BY MAJOR R. ROSS, F.R.S., F.R.C.S., C.B.,
Professor of Tropical Medicine, University of Liverpool.
(From the Johnston Tropical Laboratory, Liverpool.)

IN May, 1903, Major Leishman, R.A.M.C., described[1] certain small oval bodies occurring in smear preparations made *post mortem* from the spleen of a soldier suffering from low fever, chronic dysentery, and cachexia. The observation was made in London at the Military Hospital, and the patient had contracted his illness at Dum-Dum, near Calcutta. Leishman gave a very accurate description of these bodies. He said that they existed in large numbers among the spleen cells and red corpuscles; that they were round or oval, and 2 μ to 3 μ in diameter; that on staining with Romanowsky's method they were found to contain two masses of chromatin—a large circular mass or ring, and another smaller mass, "usually in the form of a short rod set perpendicularly or at a tangent to the circumference of the larger mass." The outline of the bodies containing these two masses of chromatin was faintly visible with this stain. The bodies were usually isolated, but occasionally aggregated into "clumps composed of twenty to fifty members." Regarding their nature, he thought it probable that they were the residue of trypanosomes of which the vibratile membrane had disappeared after death, leaving behind the nucleus and micronucleus shrunk together in a small mass, and quotes in support of this view the occurrence of similar *post-mortem* changes in the trypanosomes of dead rats.

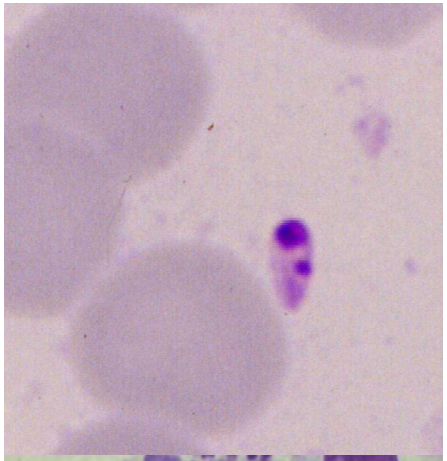


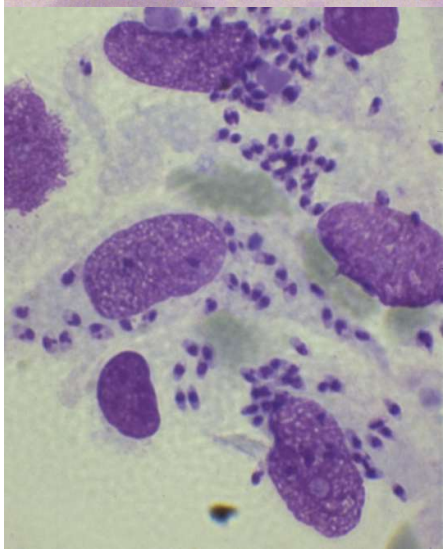
Early twentieth century – discovery of the parasite

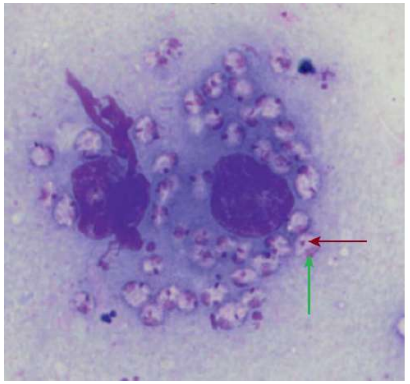
In July Captain Donovan, I.M.S., stated[2] that he had already found the same bodies on April 9th, 23rd, and 24th in *post-mortem* smears from the spleens of three consecutive cases said to have died from chronic malaria in Madras. At first he thought that the bodies represented the long-sought-for resting stage of the malaria parasite, but, after finding them in two other cases, began to think that they were *post-mortem* degenerations of spleen cells. On reading Leishman's paper he recognized their similarity to the bodies described by that observer; and next was able to recover them in blood taken *intra vitam* from the spleen of a boy suffering from irregular pyrexia (June 17th). He remarks that this case excludes the possibility of the bodies being due to *post-mortem* changes, and adds that nothing resembling trypanosomata could be found in the boy's blood.

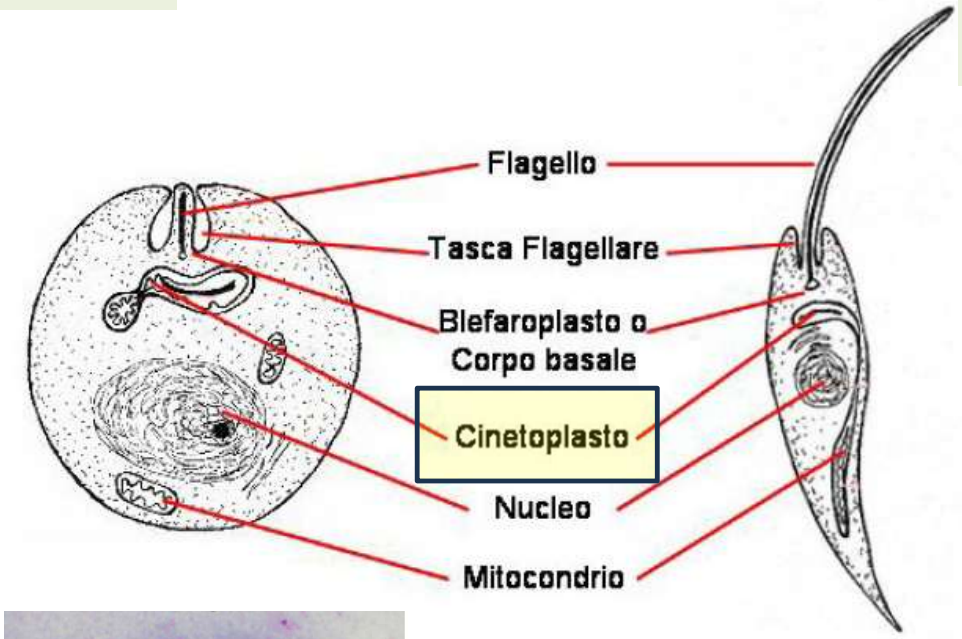
Leishmania

Amastigote (2-3 μm) , intracellulare (cellule monocito-macrofagiche)



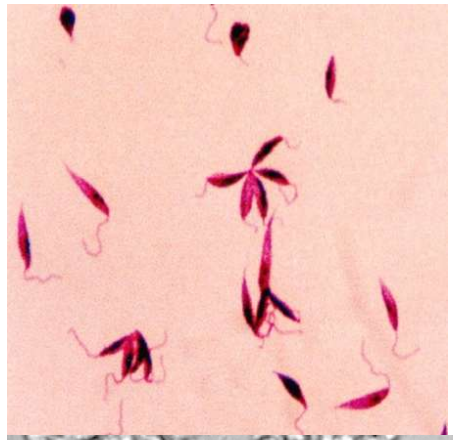


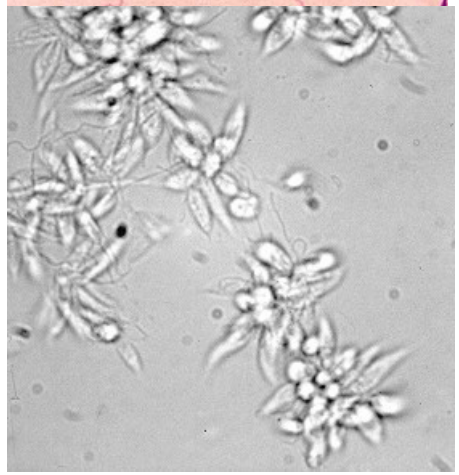


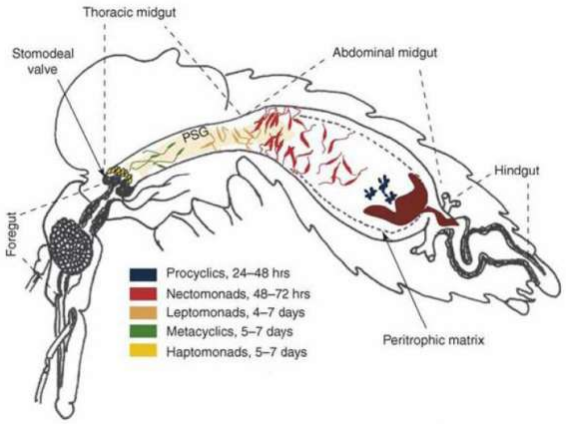


Cinetoplasto **grande mitocondrio (kinetoplasto**, kDNA extranucleare) piriforme od a bastoncino, spesso situato alla periferia del corpo parassitario ed in posizione antinucleare (spesso perpendicolare al nucleo

Promastigote (15-26 μm di lunghezza), extracellulare, mobile; flagello polo anteriore (intestino flebotomo femmina; coltura); T 22-26 °C





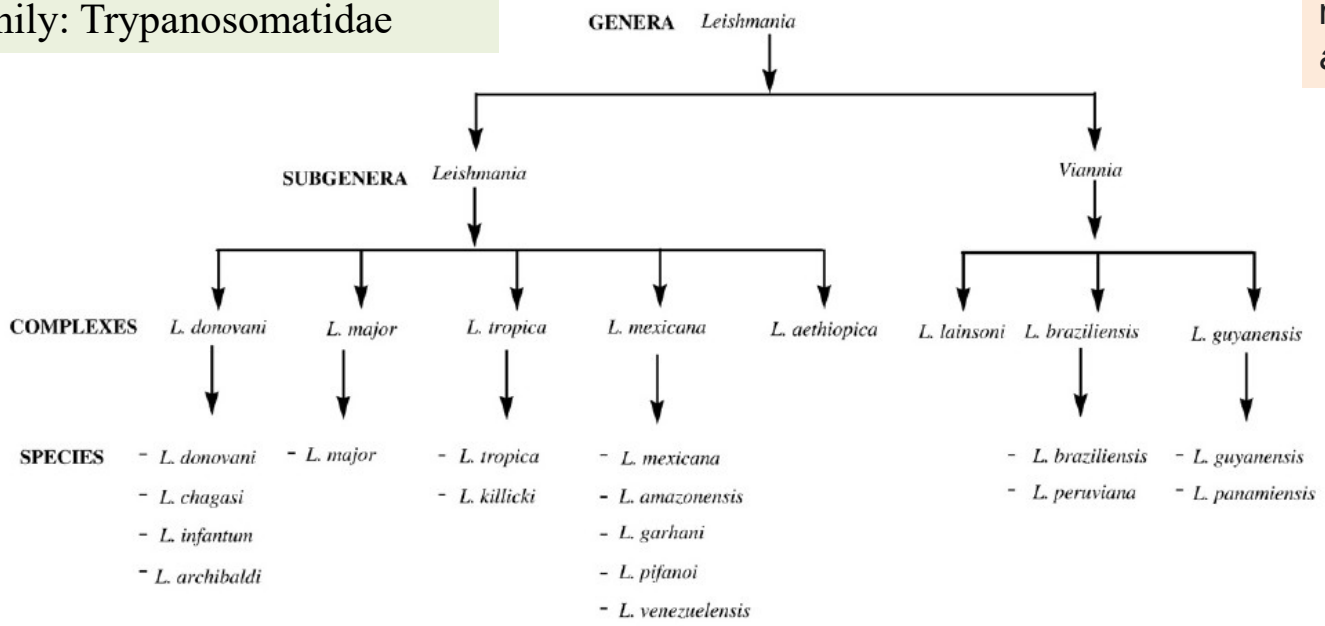


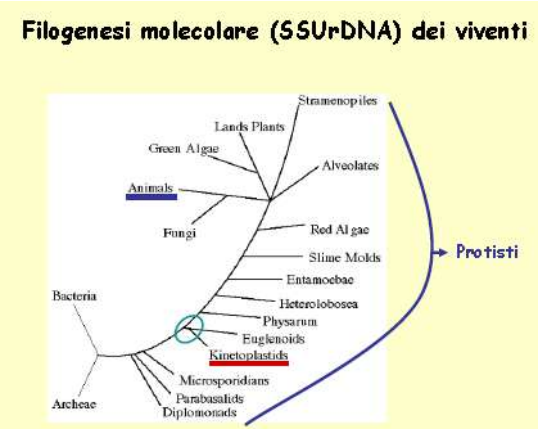
- Una volta nell'intestino il protozoo va incontro alla sua trasformazione morfologica in promastigote, caratterizzato da un corpo dalla forma allungata, che può raggiungere i 15 µm di lunghezza, e da un lungo flagello libero che fuoriesce dall'estremità anteriore dell'organismo e che ha, in genere, le stesse dimensioni del corpo.
- I promastigoti, sempre all'interno dell'intestino, si dividono per scissione binaria e, successivamente, migrano nell'intestino anteriore. A livello della faringe, i parassiti si trasformano in **promastigoti metaciclici**, più piccoli ed attivi, che migrano verso la proboscide, da cui vengono trasmessi nell'ospite definitivo all'atto della suzione (Killick-Kendrick, 1979).
- La durata del ciclo biologico del parassita nell'ospite invertebrato varia da un minimo di 4 giorni ad un massimo di 20, in relazione alle condizioni climatiche esterne.

Subkingdom: Protozoa
Order: Kinetoplastidia
Family: Trypanosomatidae

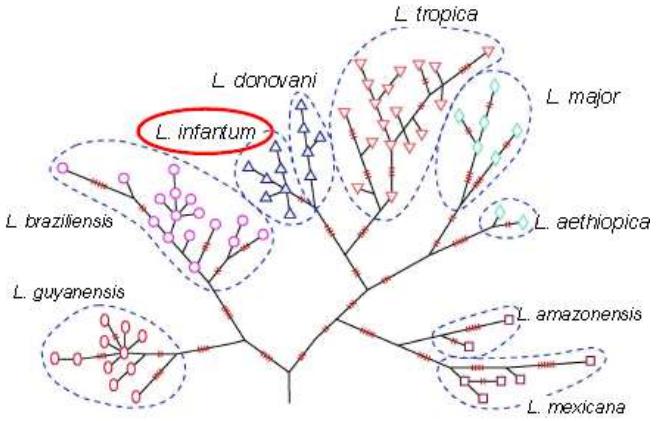
LEISHMANIOSI-tassonomia

Four subgenera of *Leishmania* are now recognised *Leishmania*, *Sauroleishmania*, *Viannia* and *Mundinia*





Evoluzione del genere in base all'analisi dei polimorfismi genetici



subgenera

	***Leishmania* (Leishmania)**	***Leishmania* (Viannia)**
Sede della replicazione nel vettore	Intestino medio e anteriore del flebotomo	Intestino posteriore e poi migrazione verso la parte anteriore
Trasmissione	Flebobotomi del genere *Phlebotomus* (Vecchio Mondo)	Flebobotomi del genere *Lutzomyia* (Nuovo Mondo)
Distribuzione geografica	Principalmente **Vecchio Mondo** (Africa, Asia, Europa)	Principalmente **Nuovo Mondo** (America Centrale e Meridionale)
Specie principali	*L. major*, *L. tropica*, *L. donovani*, *L. infantum*	*L. braziliensis*, *L. guyanensis*, *L. panamensis*
Tipo di leishmaniosi	Cutanea, viscerale, mucocutanea (più raramente)	Cutanea e **mucocutanea (più frequentemente)**
Tratti genetici e molecolari	Diverso profilo genomico; possibile distinzione con PCR-RFLP o sequenziamento	Diverso profilo genomico; alcuni geni mitocondriali e nucleari sono marcatori distintivi
Clinica associata	Le forme viscerali (come la leishmaniosi viscerale mediterranea) sono causate da *L. donovani* o *L. infantum*	*L. braziliensis* è nota per causare **forme mucocutanee gravi**

subgenera

***Leishmania* (Sauroleishmania)**
•**Ospiti**: **rettili** (principalmente lucertole)
•**Distribuzione**: Vecchio Mondo (regioni aride e calde)
•**Specie principali**: *L. tarentolae*
•**Ruolo umano**: non patogeno per l'uomo (usato anche come modello di studio)

***Leishmania* (Mundinia)**
•**Ospiti**: mammiferi (inclusi esseri umani), ma anche **moscerini chironomidi** come vettori
•**Distribuzione**: mondiale, specie emergente (Asia, Africa, America, Oceania)
•**Specie principali**: *L. martiniquensis*, *L. orientalis*
•**Particolarità**: trasmissione non sempre mediata da flebotomi; uso di vettori alternativi
•**Malattie associate**: casi di leishmaniosi cutanea e viscerale

PLOS NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

Leishmania tarentolae and *Leishmania infantum* in humans, dogs and cats in the Pelagie archipelago, southern Italy

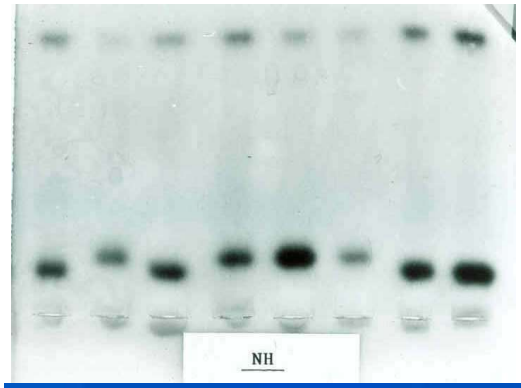
Roberta Iatta[1,2], Jairo Alfonso Mendoza-Roldan[1], Maria Stefania Latrofa[1], Antonio Cascio[3], Emanuele Brianti[4], Marco Pombi[5], Simona Gabrielli[5], Domenico Otranto[1,6]*

1 Department of Veterinary Medicine, University of Bari, Bari, Italy, **2** Department of Interdisciplinary Medicine, University of Bari, Bari, Italy, **3** Infectious and Tropical Diseases Unit, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties "G. D'Alessandro", University of Palermo, Palermo, Italy, **4** Dipartimento di Scienze Veterinarie, Università degli Studi di Messina, Messina, Italy, **5** Dipartimento di Sanità Pubblica e Malattie Infettive, "Sapienza" Università di Roma, Rome, Italy, **6** Faculty of Veterinary Sciences, Bu-Ali Sina University, Hamedan, Iran

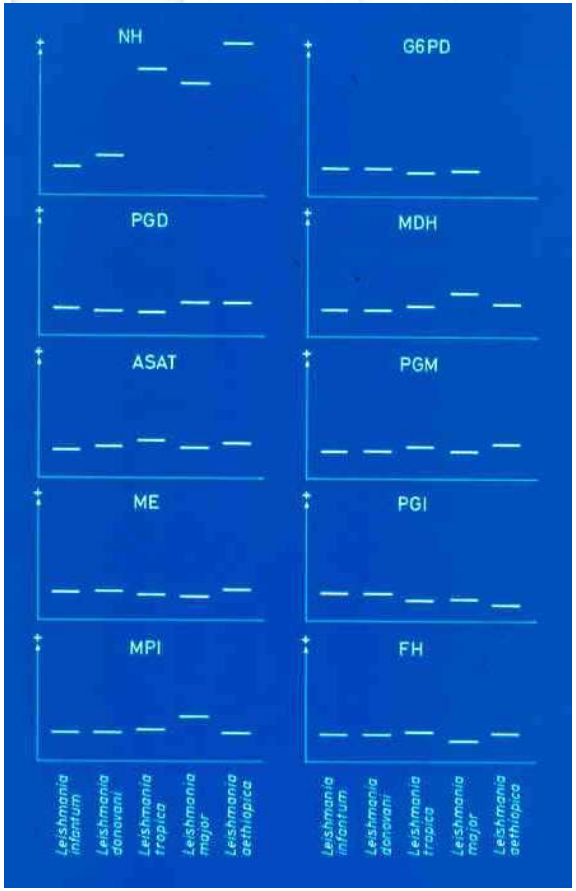
* domenico.otranto@uniba.it

- Humans, dogs, reptiles, and sand flies living in the same confined environment in small islands in the middle of the Mediterranean Sea may share *Leishmania* spp. including the non-pathogenic *L. tarentolae*.
- The presence of *L. tarentolae* in humans and dogs, undoubtedly raises many scientific questions about the potential beneficial effects this species of *Leishmania* may have in cross-protecting hosts infected by pathogenic *Leishmania* species.

Analisi elettroforetica degli isoenzimi
(⇒ **zimodema**)



- Ogni zimodema comprende leishmanie con un uguale pattern isoenzimatico; i microrganismi che presentano modeste differenze sono ritenute appartenenti allo stesso complesso di zimodemi.
- I termini di *"zimodema" e "complesso di zimodemi"* tendono a sostituire quelli che in passato erano *"specie" e "sottospecie"*. I diversi zimodemi vengono indicati con il prefisso MON (Montpelier) o LON (London) seguito da un numero arabo: MON 1, MON 2, etc.



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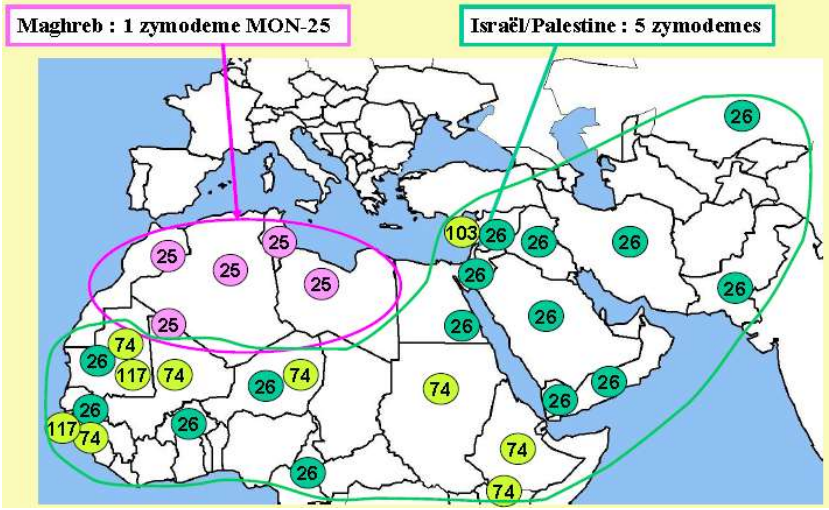
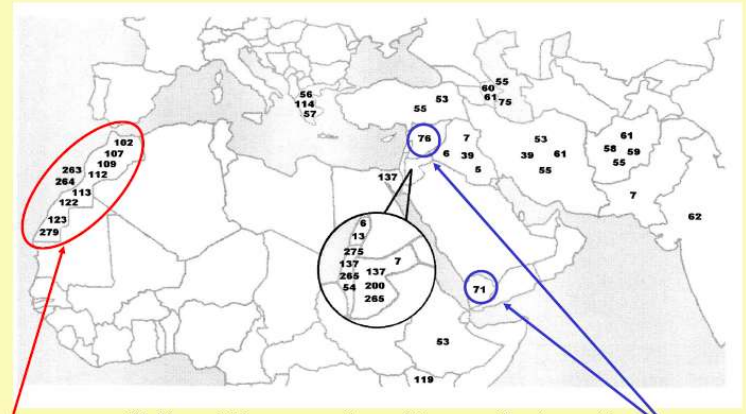
Distribution of the 12 *L. major* zymodemes



Distribution of the 35 *L. tropica* zymodemes

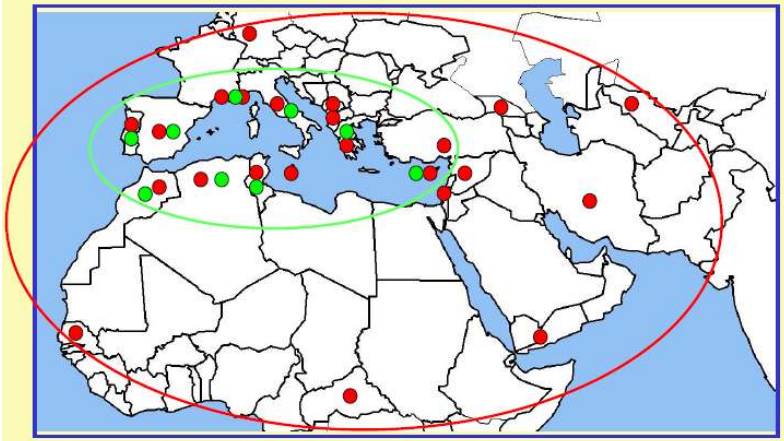
(highly diversified electromorphs)



Highly variable enzyme polymorphism according to countries

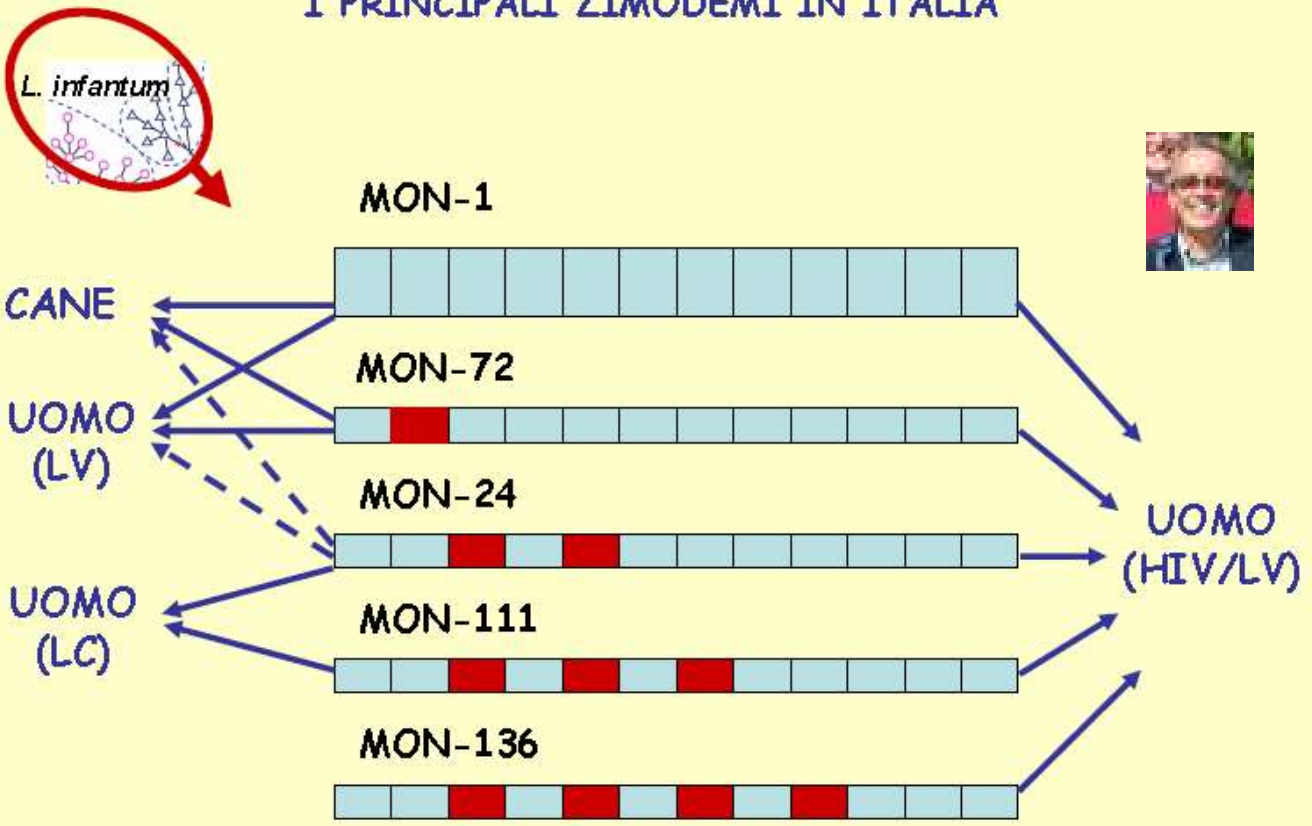
10 zymodemes — 1 zymodeme

Distribution of *L. infantum* zymodemes (n=37)



The *Leishmania* collection of Montpellier (France), a tool for studying taxonomy, phylogeography and epidemiology.

Il polimorfismo di *Leishmania infantum* e relazioni con l'ospite mammifero
I PRINCIPALI ZIMODEMI IN ITALIA

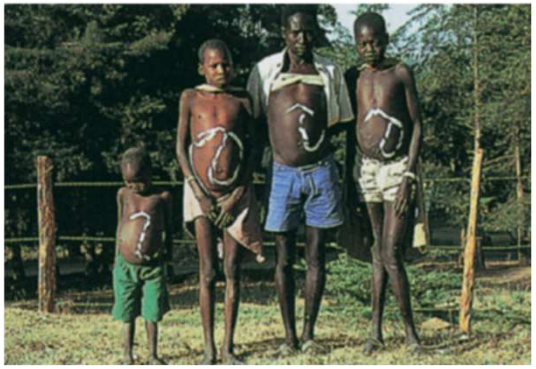


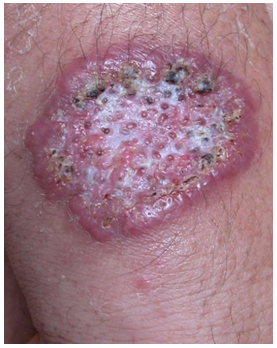
Leishmaniasis

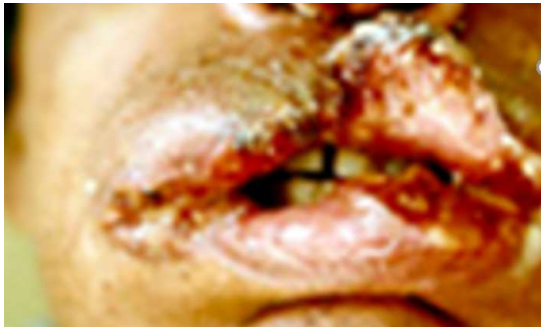
- Group of diseases caused by protozoa of the genus Leishmania, hosts of various wild and domestic animals, occasionally transmitted to humans by vector insects of the genus Phlebotomus (in America by insects of the genus Lutzomya).
- Based on the clinical picture and geographical distribution they can be classified into:
  - **Visceral leishmaniasis** (in which we distinguish the Mediterranean form (also present in China and South America), the Indian form or Kala-azar, and the African Kala-azar);
  - **Old World cutaneous Leishmaniasis** (urban eastern button, rural eastern button, diffuse cutaneous leishmaniasis);
  - **New World Cutaneous Leishmaniasis** ("uta", "ulcera de los chicleros", "pian bois", mucocutaneous form "espundia", and diffuse cutaneous leishmaniasis).

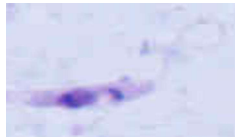
Leishmania

- **There are at least 22 species of *Leishmania*, with a wide range of geografical distributions and hosts.**
- They cause a spectrum of diseases ranging from self-healing ulcers to disseminated and often fatal infections, depending on the species involved and the host's cell-mediated immune response.



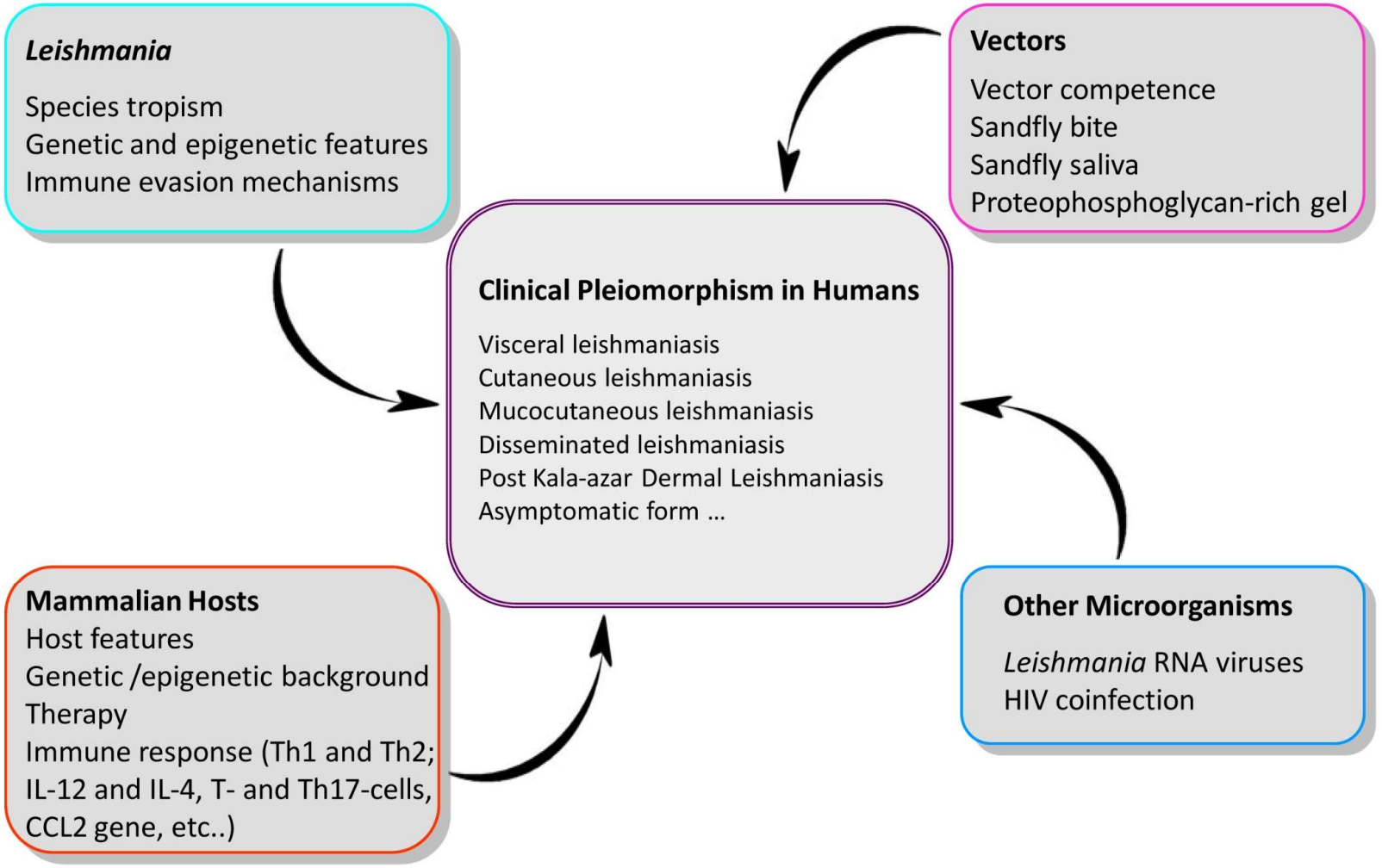






Clinical pleiomorphism in human leishmaniases, with special mention of asymptomatic infection

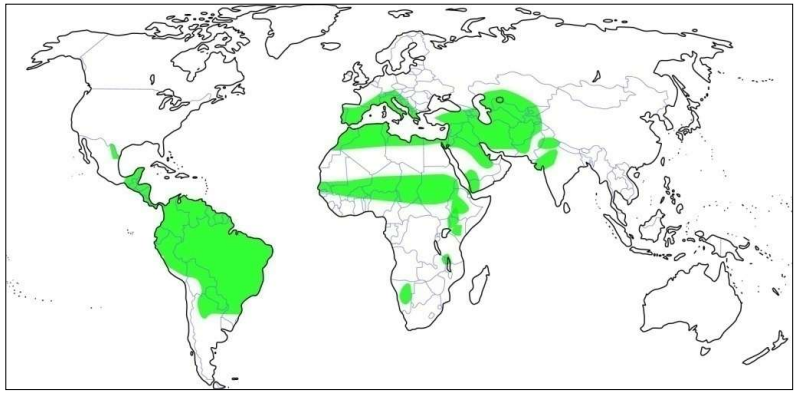
A. L. Bañuls[1*], P. Bastien[1,2*], C. Pomares[3,4], J. Arevalo[5], R. Fisa[6] ar
1) UMR MIVEGEC (IRD 224-CNRS 5290-Université Montpellier 1), 2) Université
ratoire de Parasitologie-Mycologie, National Reference Centre (CNR) for Leishmani
4) Centre Hospitalier Universitaire de Nice, Laboratoire de Parasitologie-Mycologie,
y Departamento de Bioquímica, Biología Molecular y Farmacología, Universidad Pen
Facultat de Farmàcia, Universitat de Barcelona, Barcelona, Spain



Leishmaniasis

Cutaneous leishmaniasis

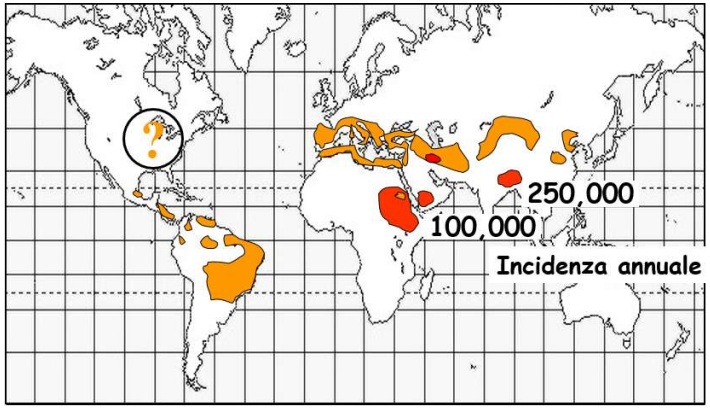
1.5-2 x 10^6 cases/y



Visceral leishmaniasis

- **Anthroponotic VL (*Leishmania donovani*)**
- **Zoonotic VL *infantum* – sin.: *L. chagasi*)**

500.000 cases/y



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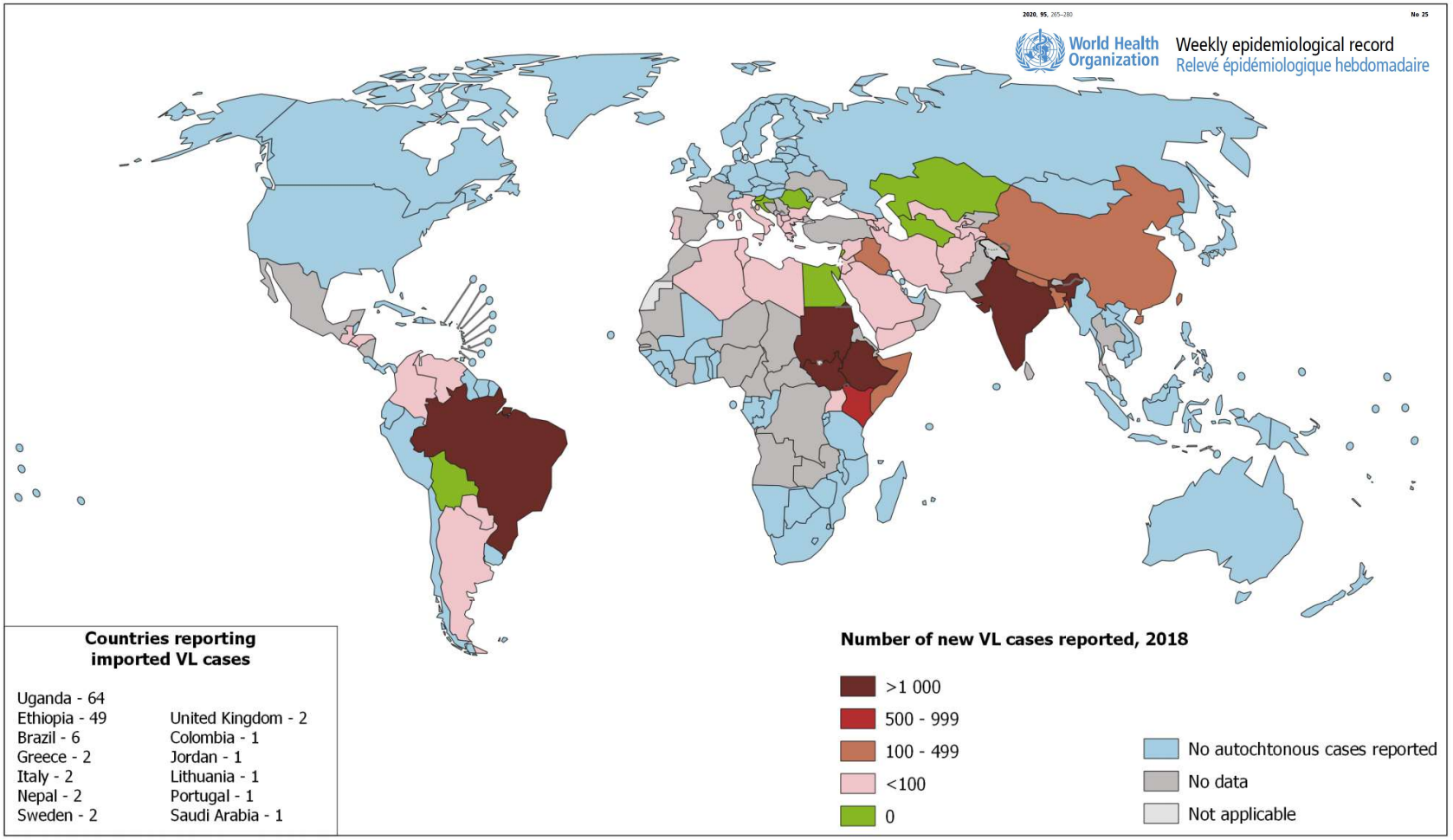
Status of endemicity of visceral leishmaniasis worldwide, 2018

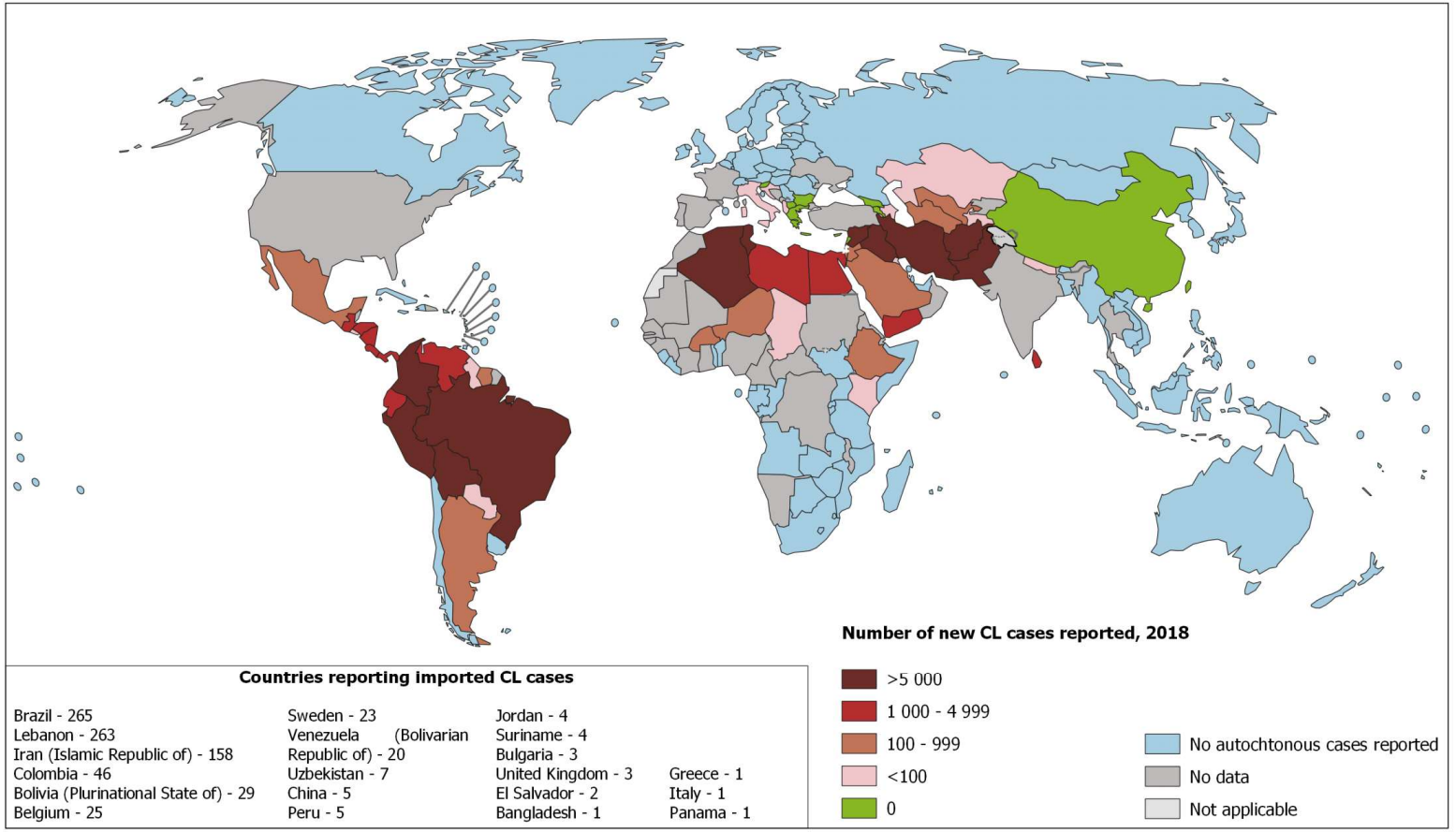


Data Source: World Health Organization
Map Production: Control of Neglected Tropical Diseases (NTD)
World Health Organization

World Health Organization

2020, 95, 265–280 No 25
World Health Organization Weekly epidemiological record
Relevé épidémiologique hebdomadaire

Status of endemicity of cutaneous leishmaniasis worldwide, 2018



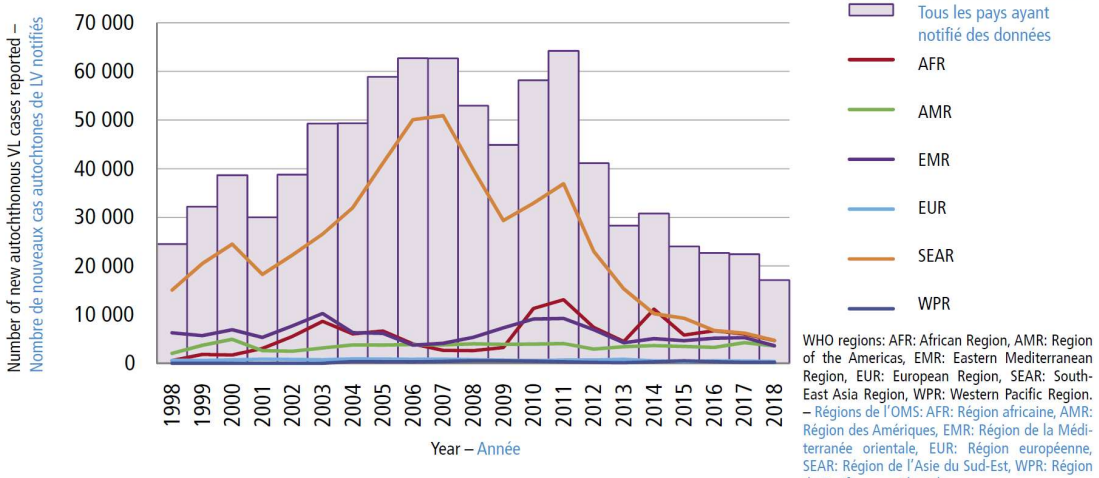
Countries reporting imported CL cases

Brazil - 265	Sweden - 23	Jordan - 4	
Lebanon - 263	Venezuela (Bolivarian Republic of) - 20	Suriname - 4	
Iran (Islamic Republic of) - 158		Bulgaria - 3	
Colombia - 46	Uzbekistan - 7	United Kingdom - 3	Greece - 1
Bolivia (Plurinational State of) - 29	China - 5	El Salvador - 2	Italy - 1
Belgium - 25	Peru - 5	Bangladesh - 1	Panama - 1

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

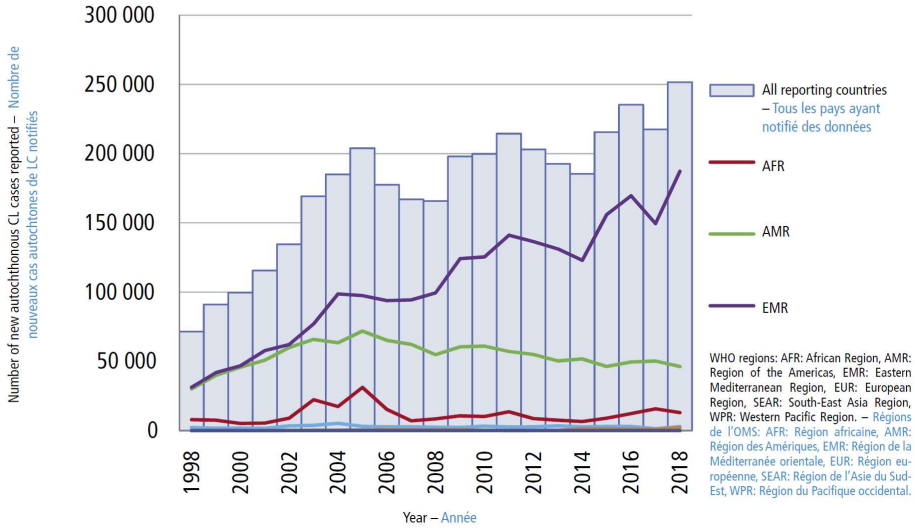
World Health Organization

Figure 1b **Evolution of numbers of visceral leishmaniasis (VL) cases, by WHO region, 1998–2018**
Figure 1b **Évolution du nombre de cas de leishmaniose viscérale (LV), par Région de l'OMS, 1998-2018**



WHO regions: AFR: African Region, AMR: Region of the Americas, EMR: Eastern Mediterranean Region, EUR: European Region, SEAR: South-East Asia Region, WPR: Western Pacific Region. – Régions de l'OMS: AFR: Région africaine, AMR: Région des Amériques, EMR: Région de la Méditerranée orientale, EUR: Région européenne, SEAR: Région de l'Asie du Sud-Est, WPR: Région du Pacifique occidental.

Figure 1a **Evolution of the numbers of cutaneous leishmaniasis (CL) cases, by WHO region, 1998–2018**
Figure 1a **Évolution du nombre de cas de leishmaniose cutanée (LC), par Région de l'OMS, 1998-2018**



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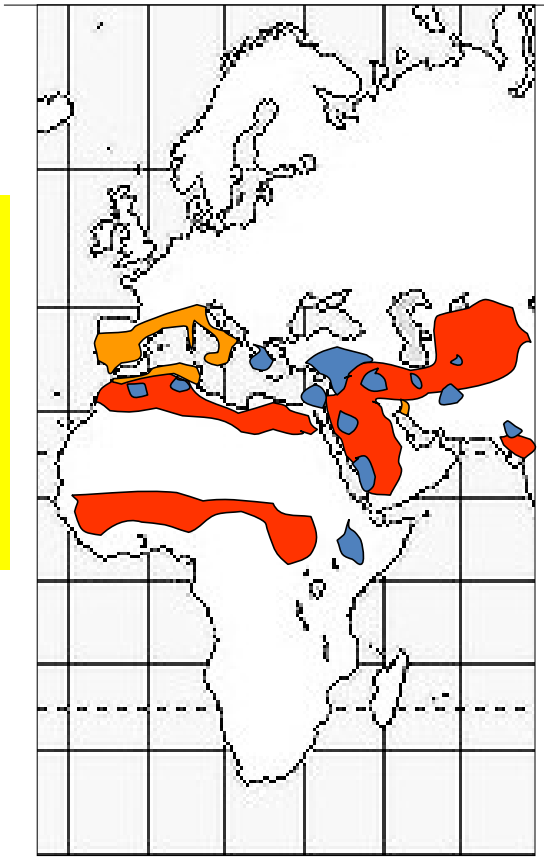
Old world cutaneous leishmaniasis

Leishmaniosi cutanea
zoonotica da *Leishmania major*

Il serbatoio: *Meriones shawi*
(Gerbillidae)

- Zoonotic LC (ZCL) (*L.major*)
- Antroponotic CL (*L.tropica*)
- Sporadic ZCL (*L.infantum*)



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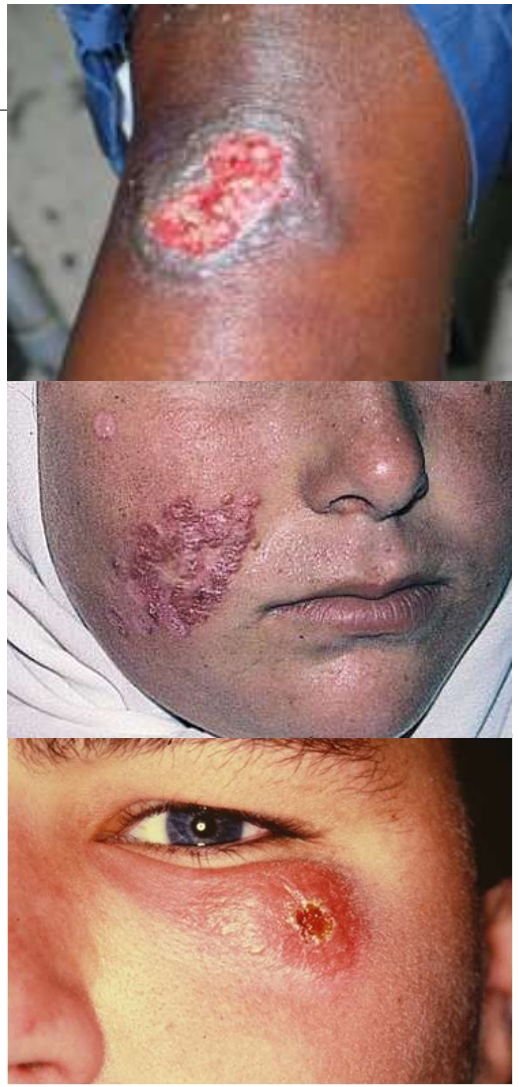
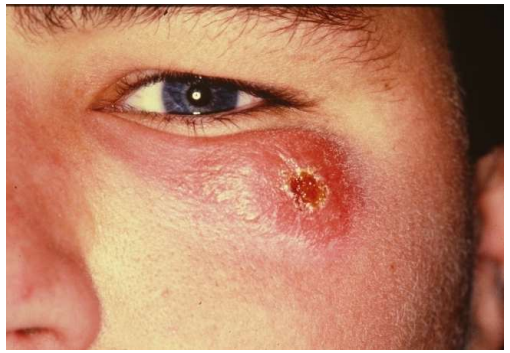
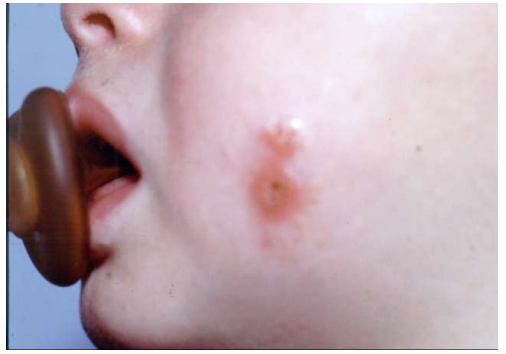


Leishmaniosi cutanea

- Lesione eritemato-papulare simile a una puntura d'insetto.
- Dopo alcune settimane: la papula diventa un nodulo duro, lucido, di colore rosso-brunastro, indolore, più o meno pruriginoso, che raggiunge lentamente le dimensioni di circa 2-3 centimetri di diametro.
- Dopo circa sei mesi: erosione superficiale ricoperta da una crosta siero-ematica grigio-marrone.



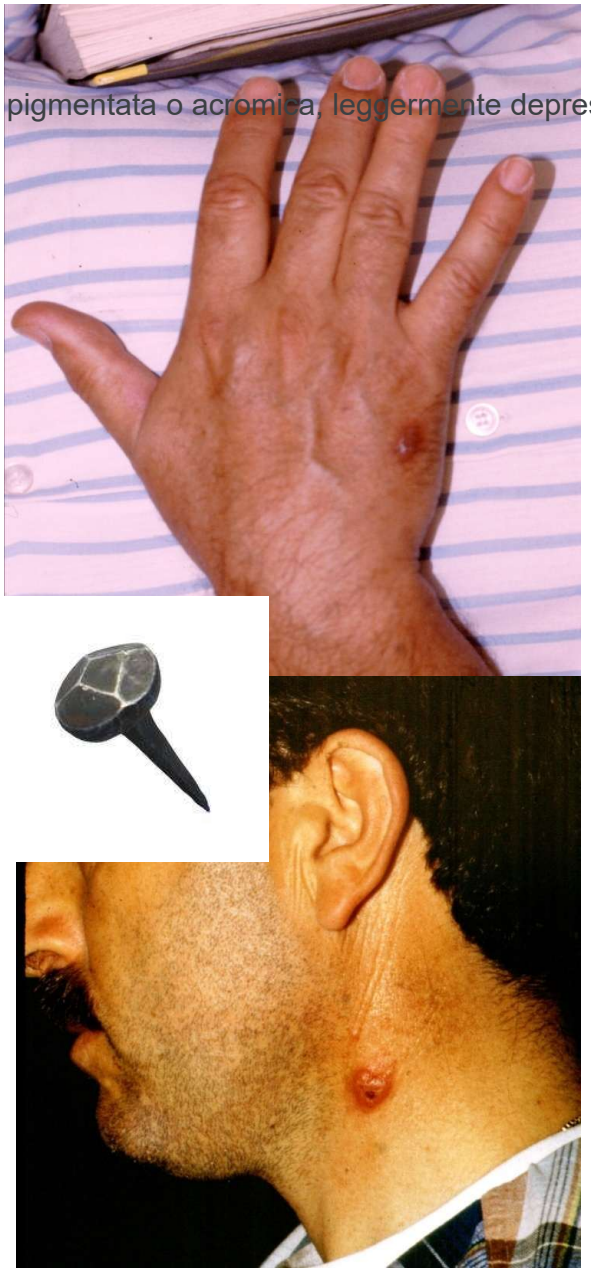


Risultati della traduzione

Risultato di traduzione

Evoluzione Molto lenta, circa un anno Tende alla guarigione spontanea Cicatrice definitiva irregolare, pigmentata o acromica, leggermente depressa.

- La crosta è strettamente aderente a causa della presenza sulla superficie inferiore di fittoni cornei (chiodi da tappezzeria) saldamente impiantati nel fondo della lesione (segno di Montpellier o del rastrello). Rimuovendo la crosta, si forma un'ulcera con bordi nettamente tagliati e fondo irregolare che secerne un liquido giallastro.

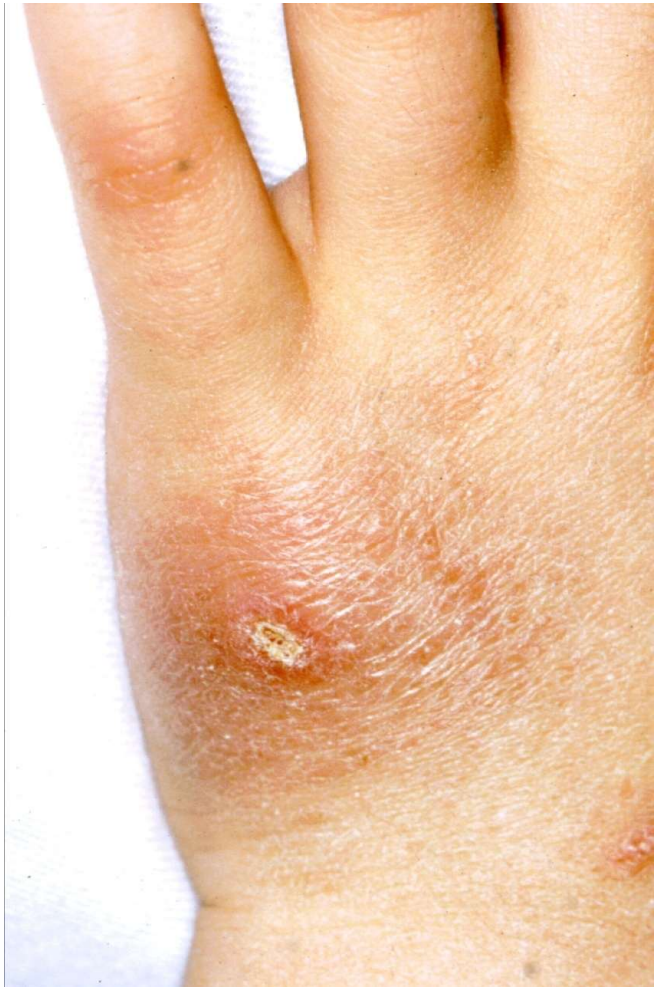


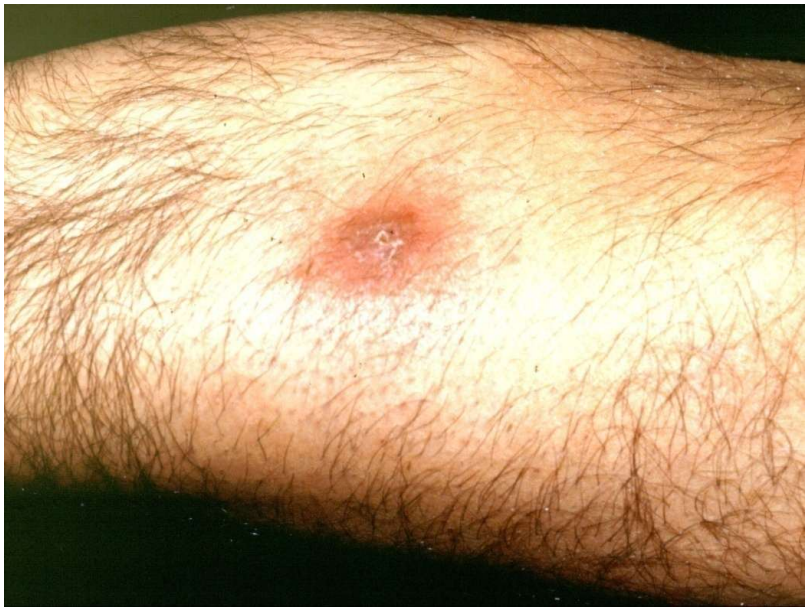
Evoluzione

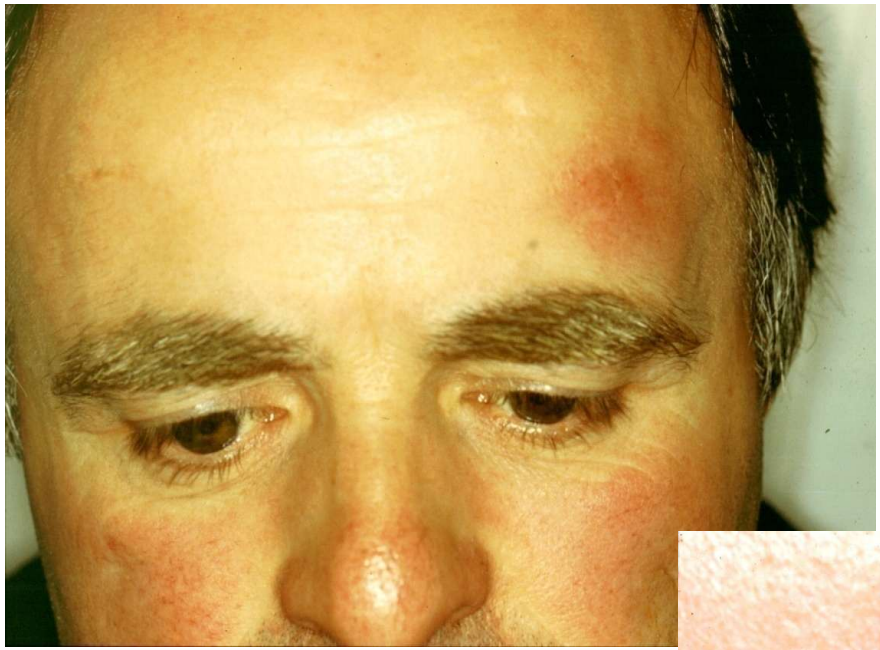
Molto lenta, circa un anno

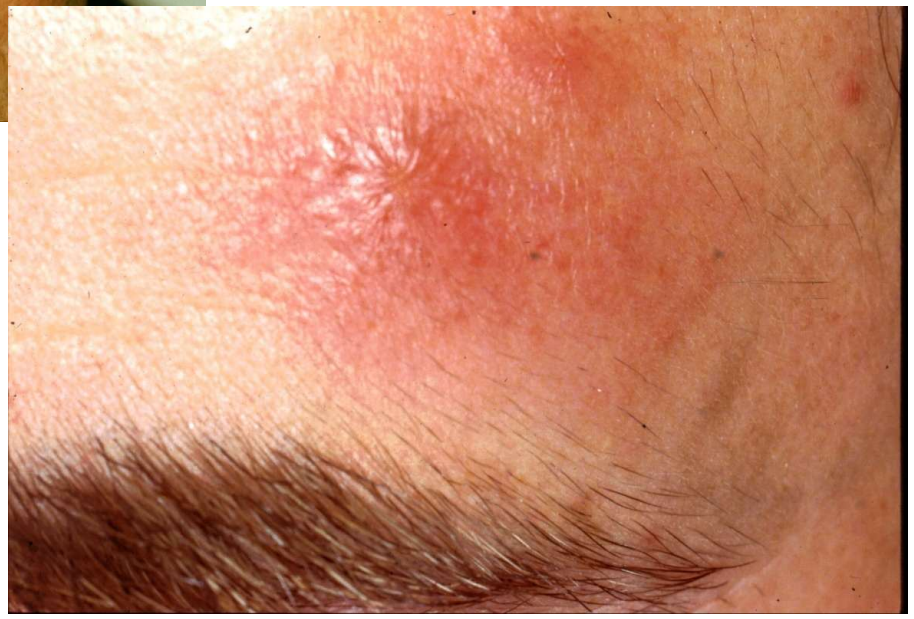
Tende alla guarigione spontanea

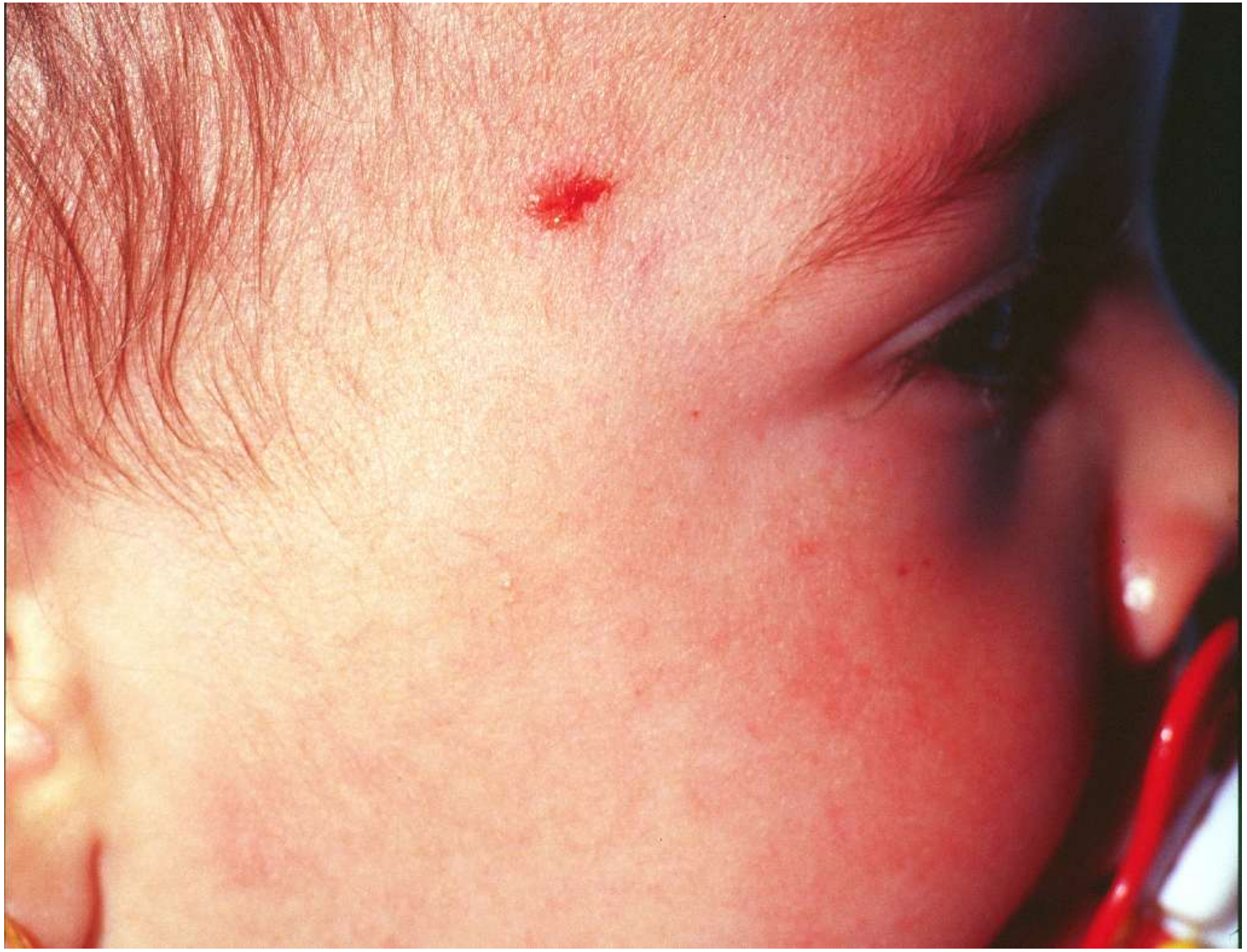
Cicatrice definitiva irregolare, pigmentata

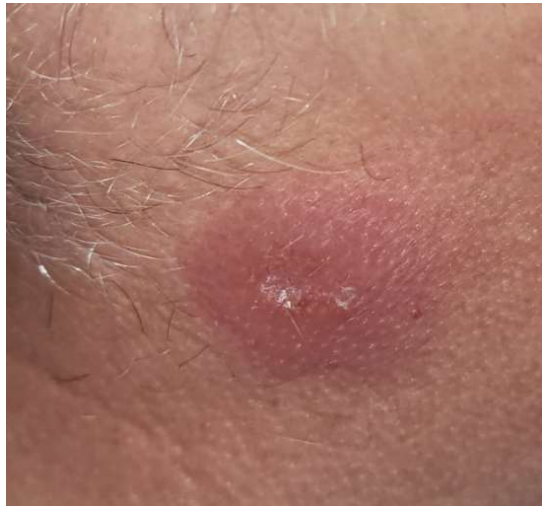


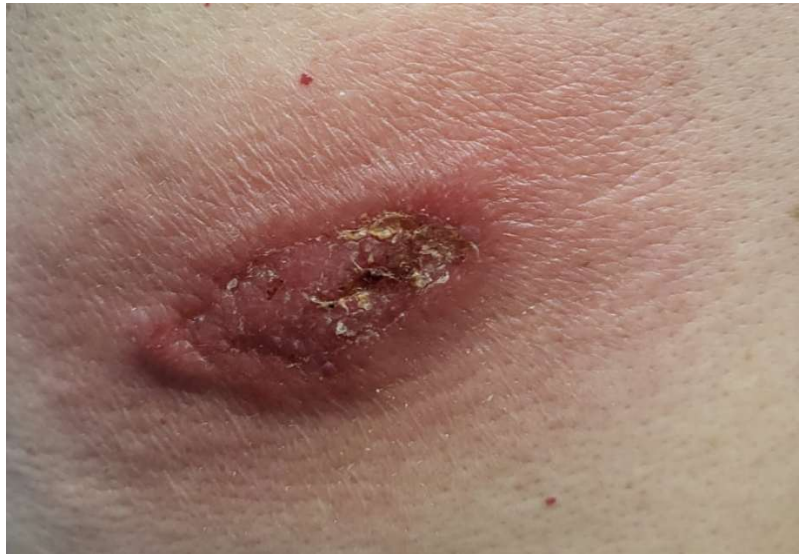


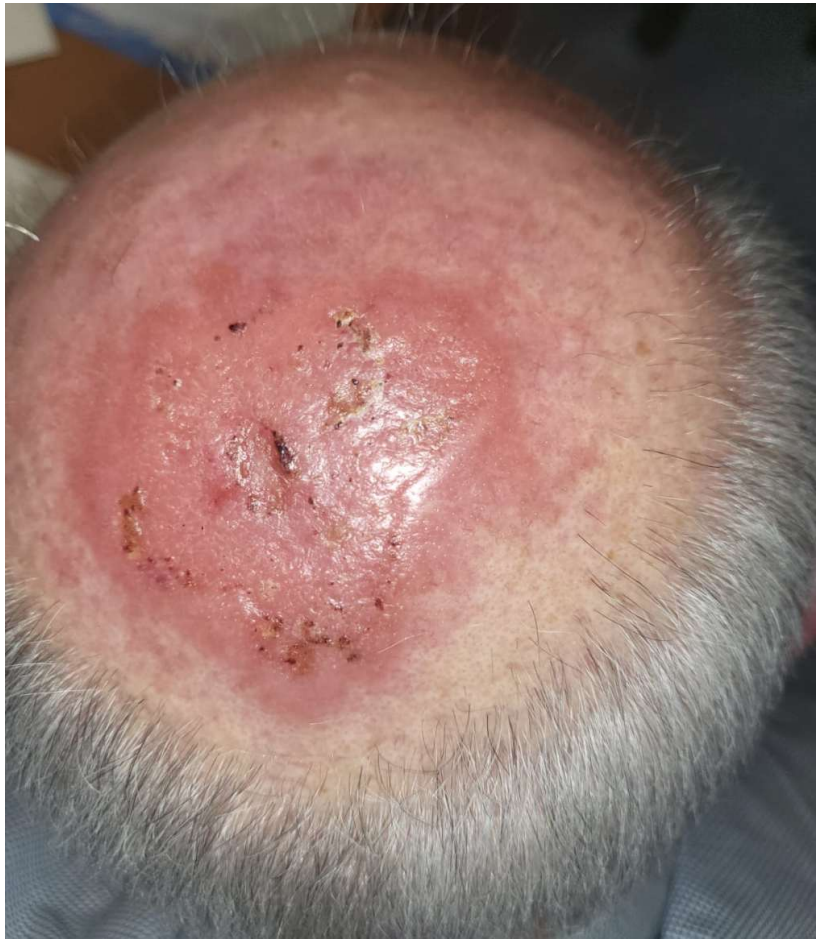


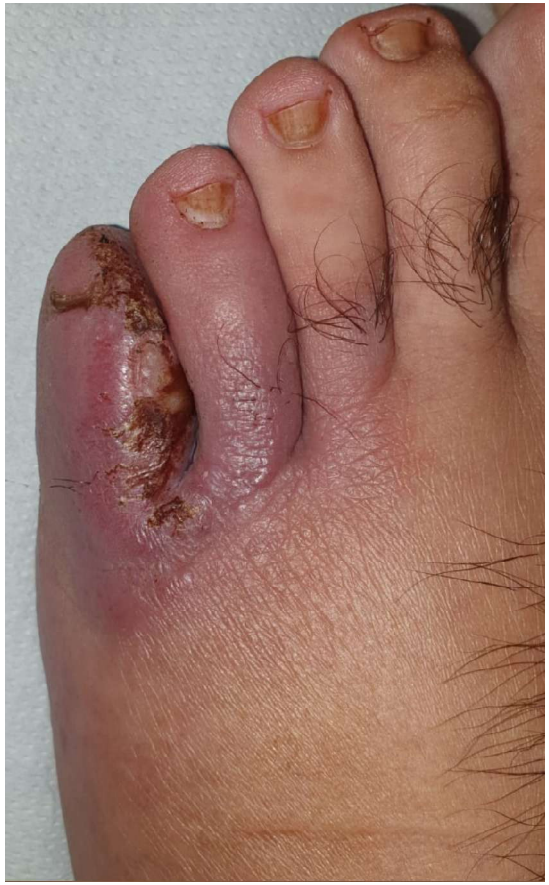


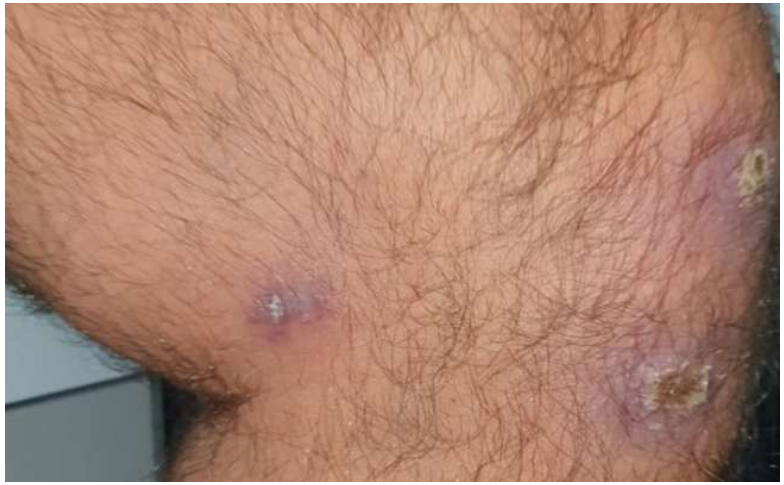


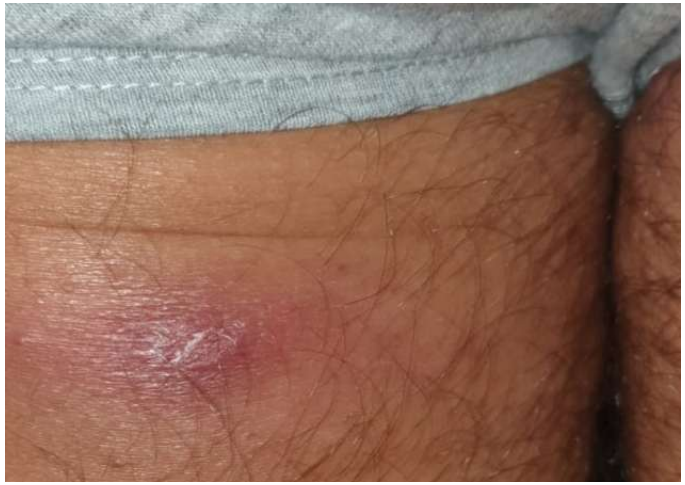


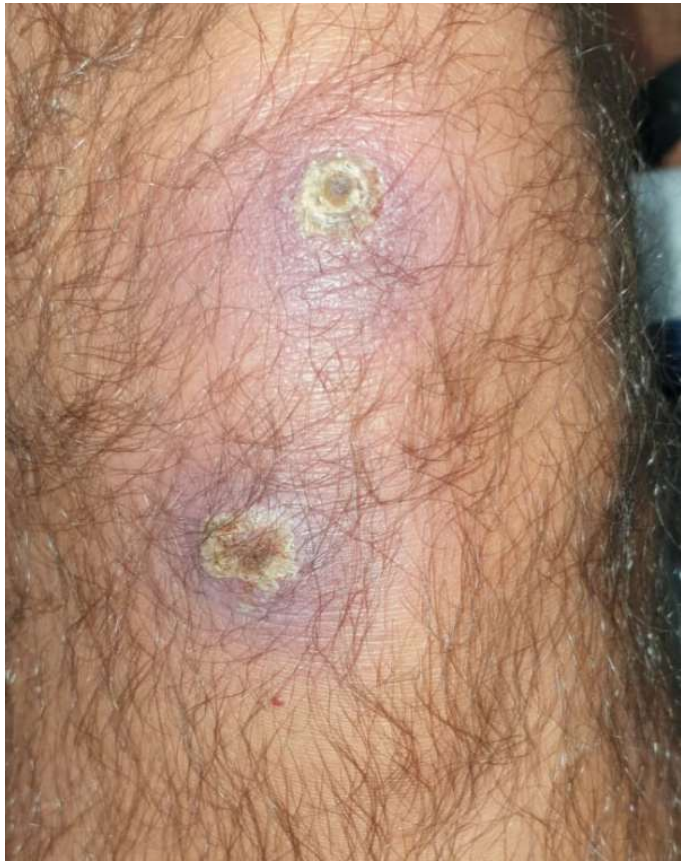


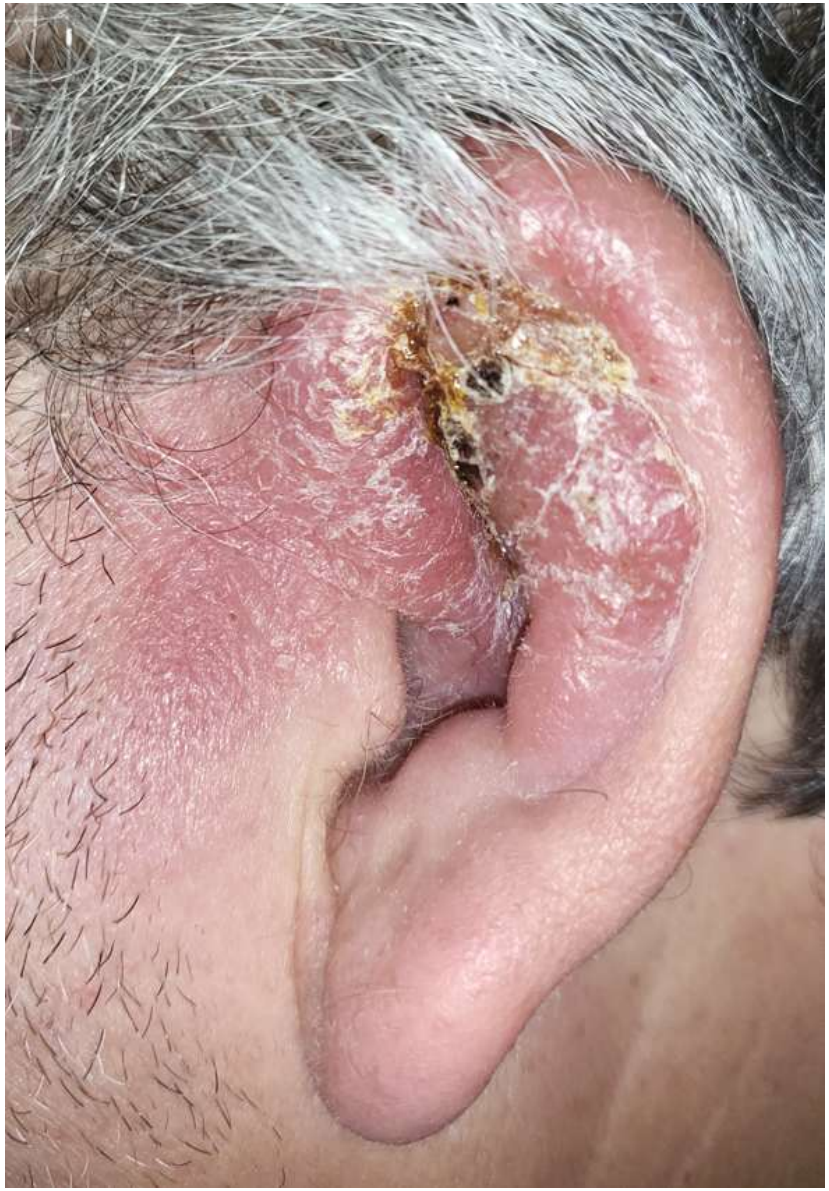


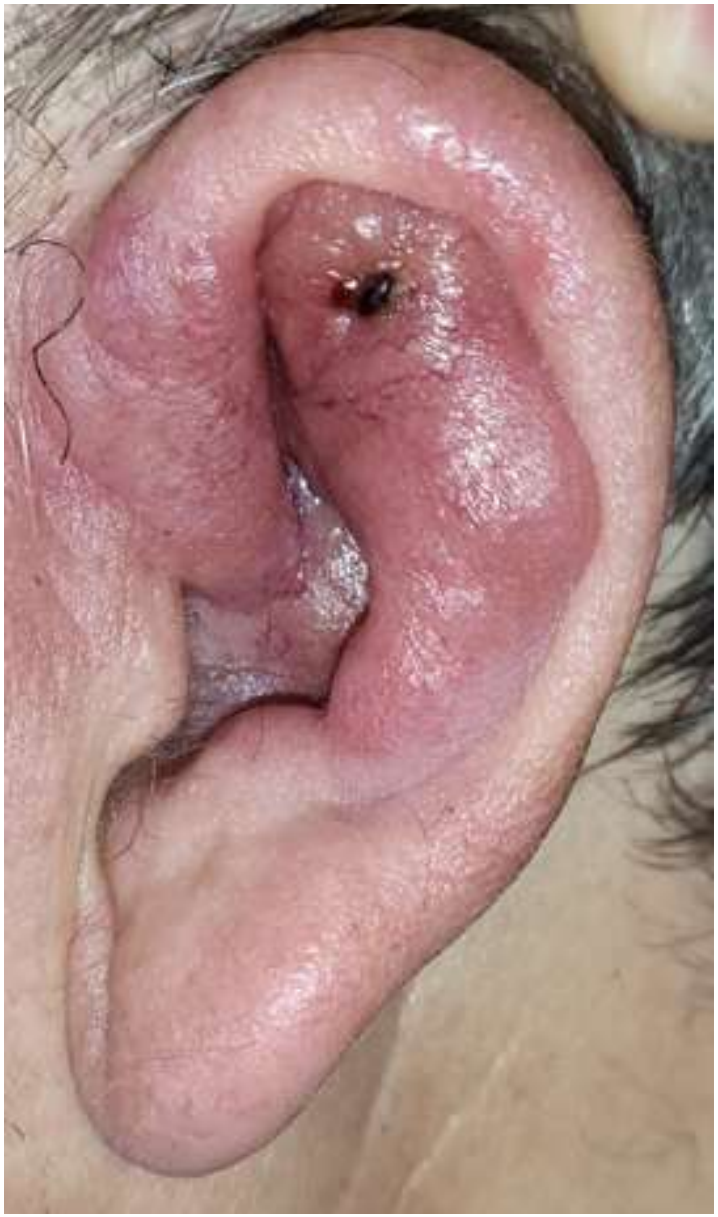


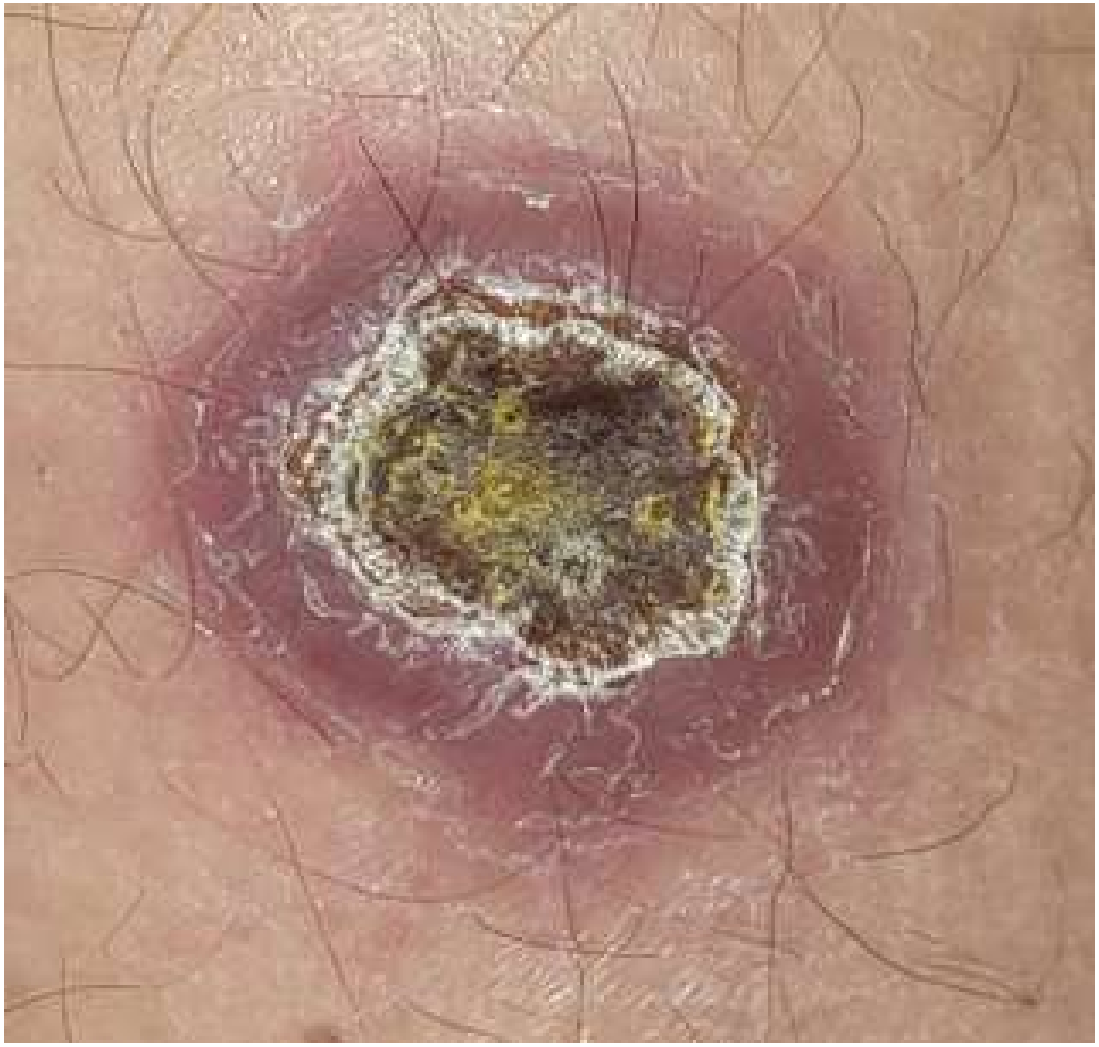


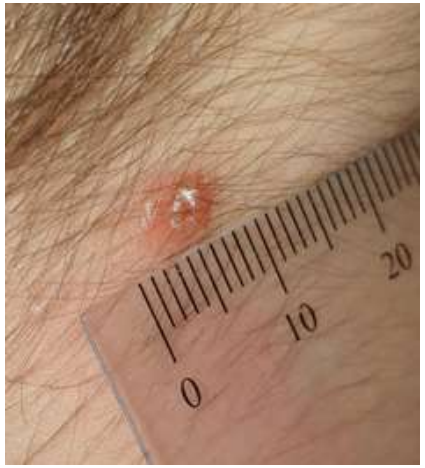








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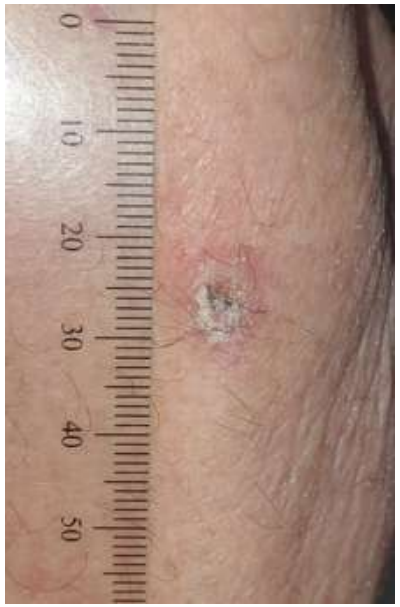
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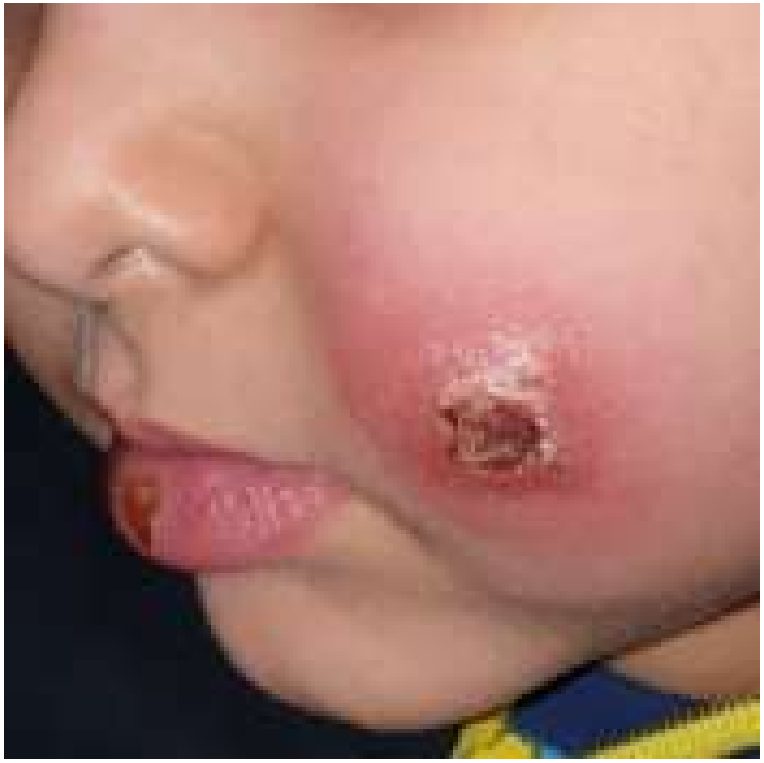
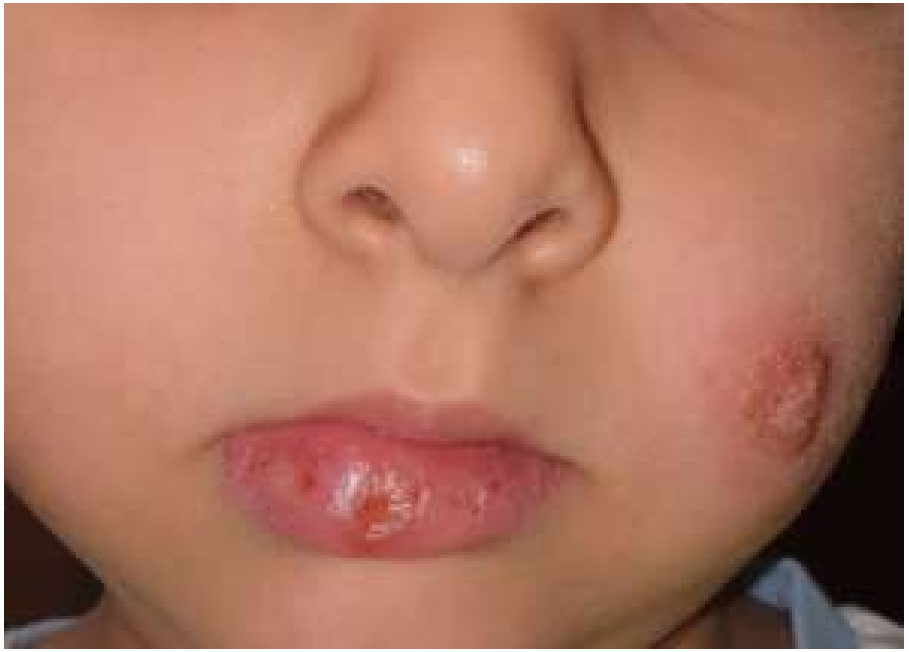
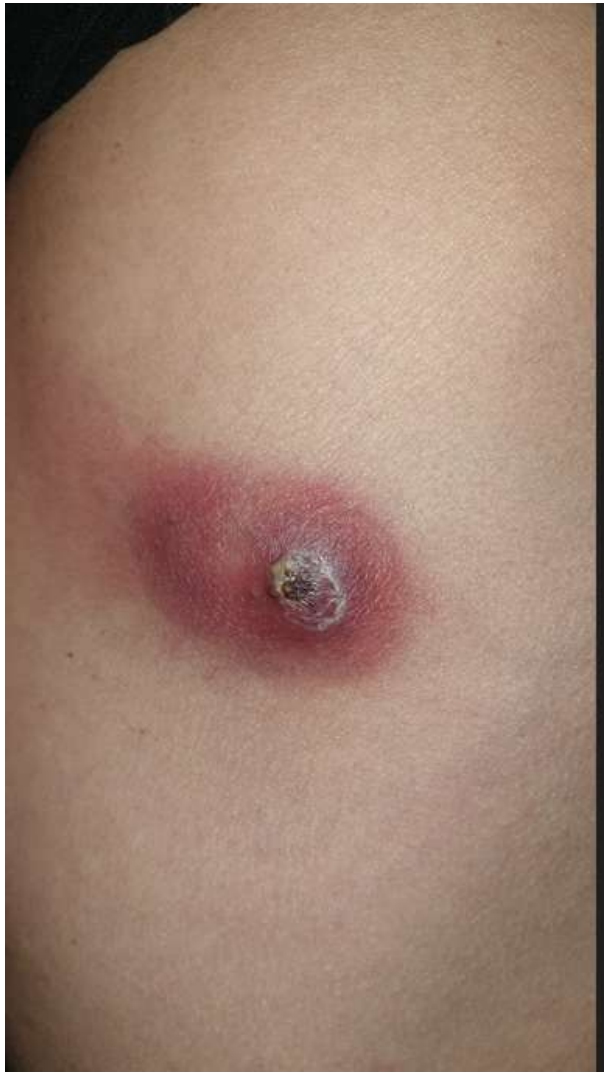
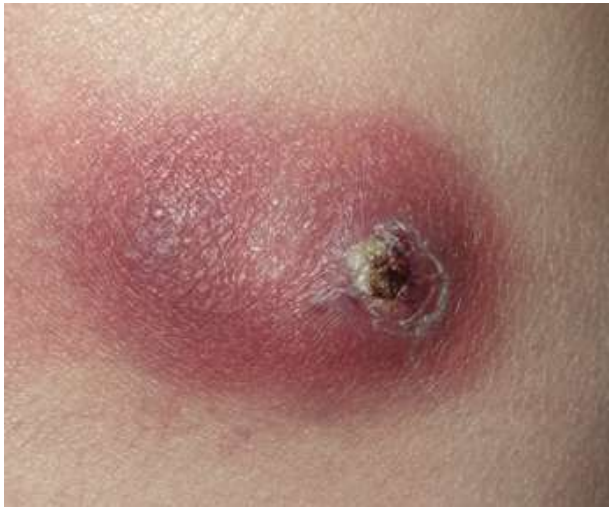
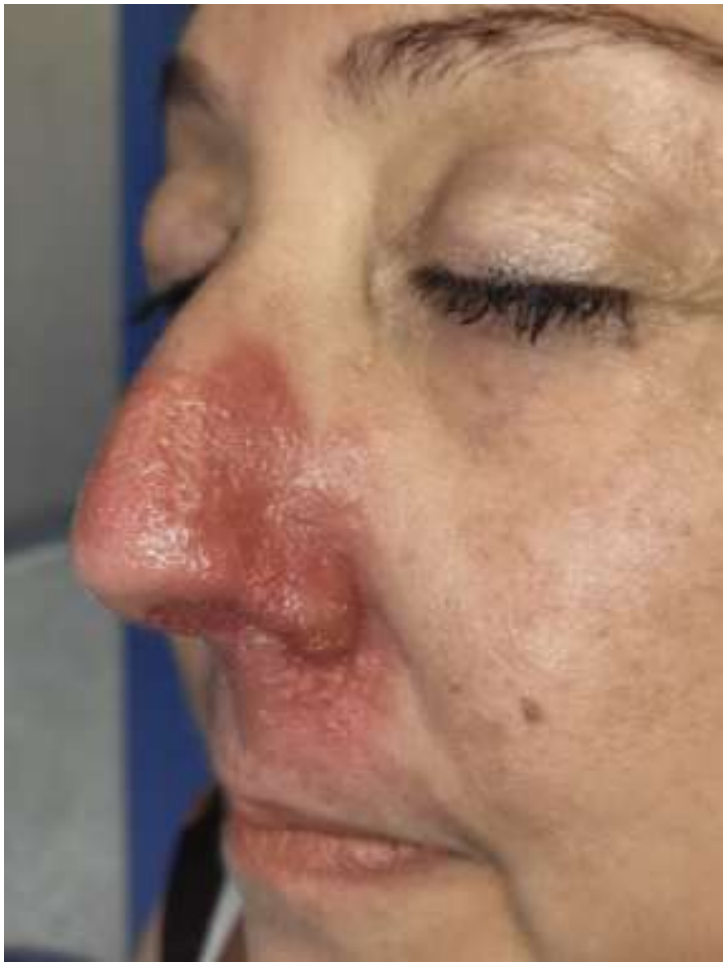


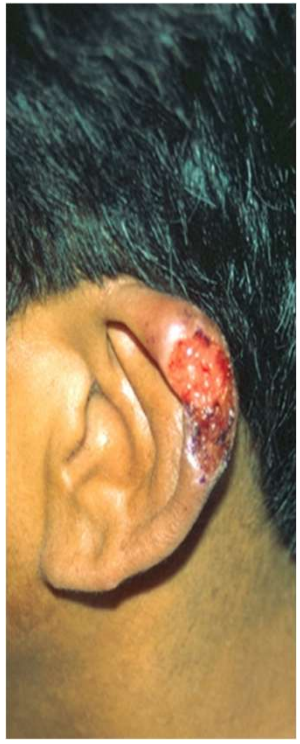


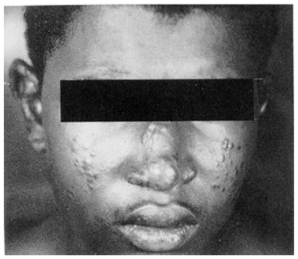




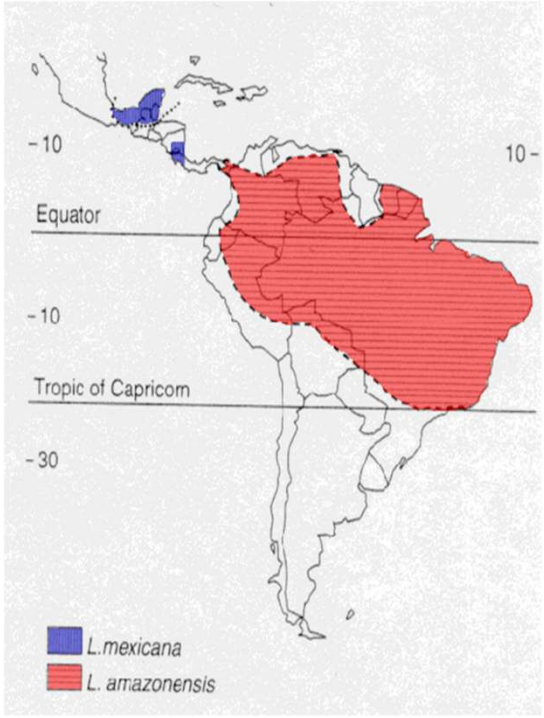


New world cutaneous and mucocutaneous leishmaniasis

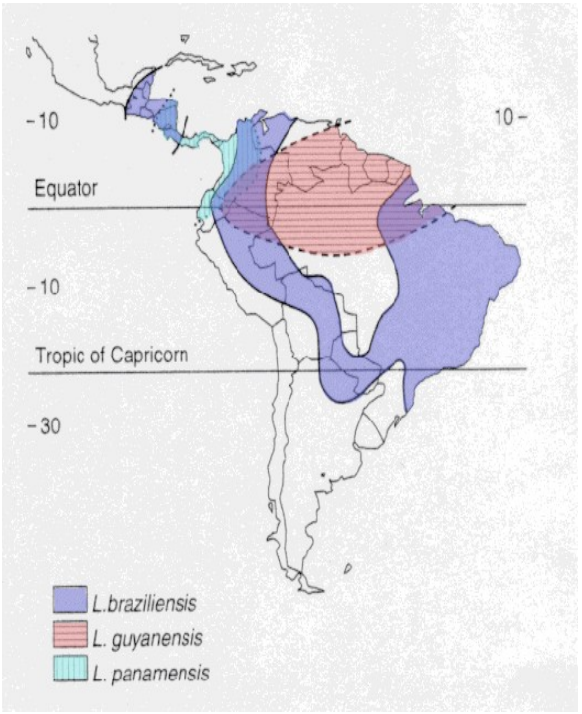


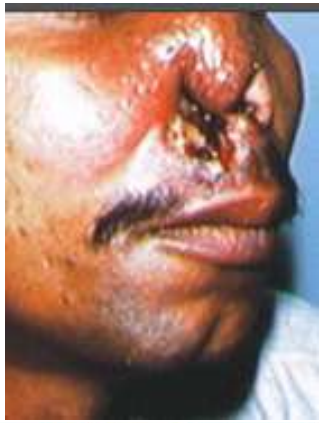


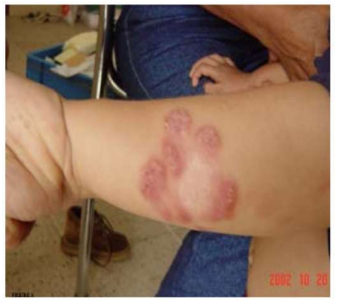
Subgenus *Leishmania*



Subgenus *Viannia*







Marina Gramiccia ISS

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REVIEW

Leishmaniasis in travelers: A literature review

Pasquale Mansueto [a,*], Aurelio Seidita [a], Giustina Vitale [a], Antonio Cascio [b]

EDITORIAL 10.1111/j.1469-0691.2004.01046.x

Cutaneous leishmaniasis: an increasing threat for travellers

S. Antinori[1], *E. Gianelli*[1], *S. Calattini*[1], *E. Longhi*[1], *M. Gramiccia*[2] *and M. Corbellino*[1]

[1]Istituto di Malattie Infettive e Tropicali, Università di Milano; [2]Reparto di Malattie Trasmesse da Vettori e Sanità Internazionale, Dipartimento di Malattie Infettive, Parassitarie e Immunomediate, Istituto Superiore di Sanità, Roma, Italy

Aissaoui et al. BMC Infect Dis (2021) 21:953
https://doi.org/10.1186/s12879-021-06631-5

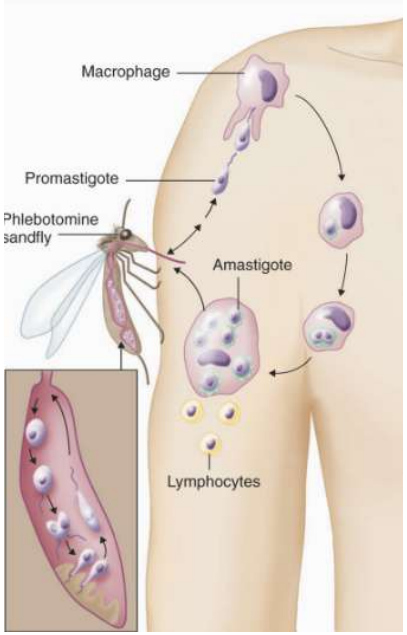
BMC Infectious Diseases

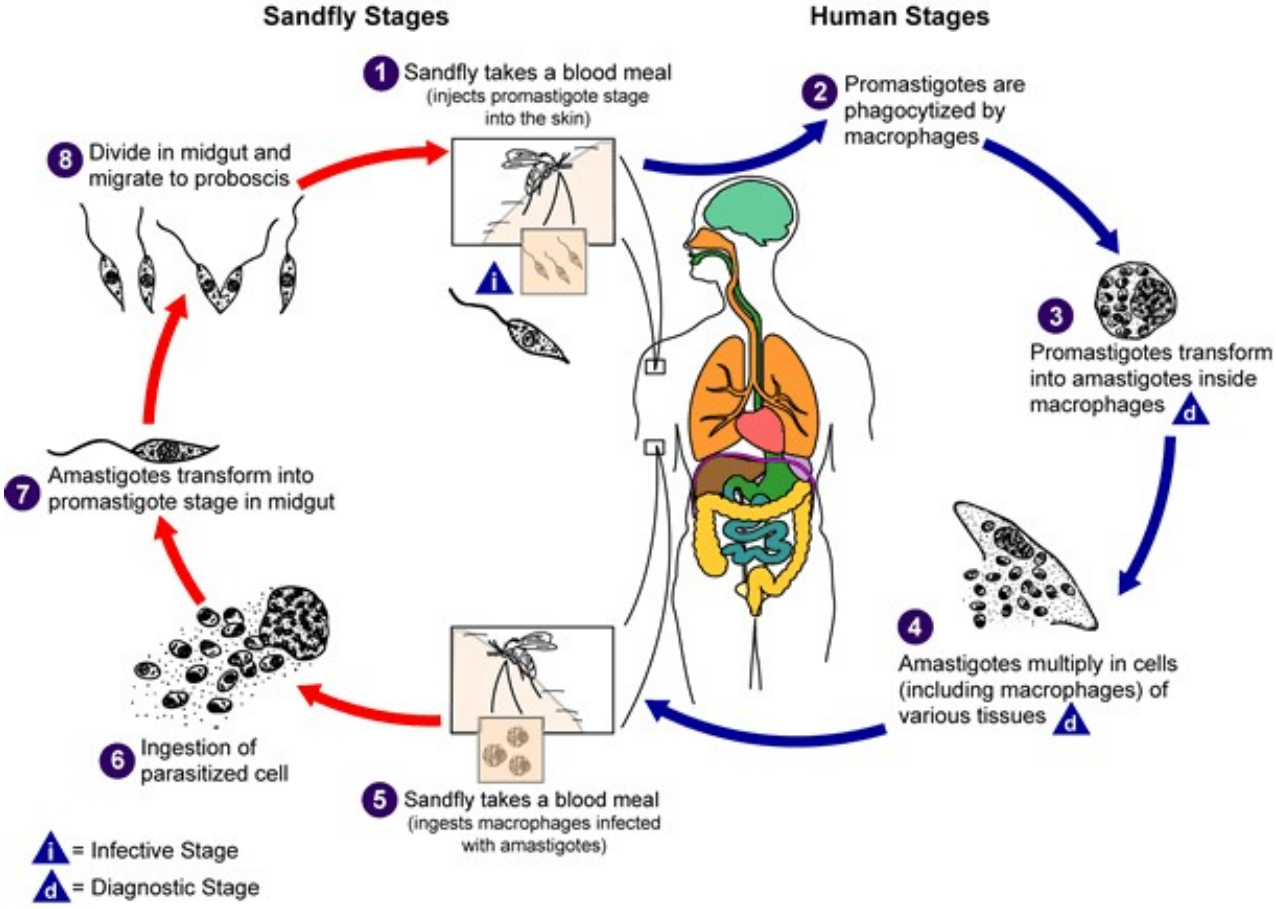
RESEARCH Open Access

Imported leishmaniasis in travelers: a 7-year retrospective from a Parisian hospital in France

Nesrine Aissaoui[1], Samia Hamane[1], Maud Gits-Muselli[1,2], Antoine Petit[3], Mazouz Benderdouche[1], Blandine Denis[4], Alexandre Alanio[1,2], Sarah Dellière[1,2], Martine Bagot[3,5] and Stéphane Bretagne[1,2*]

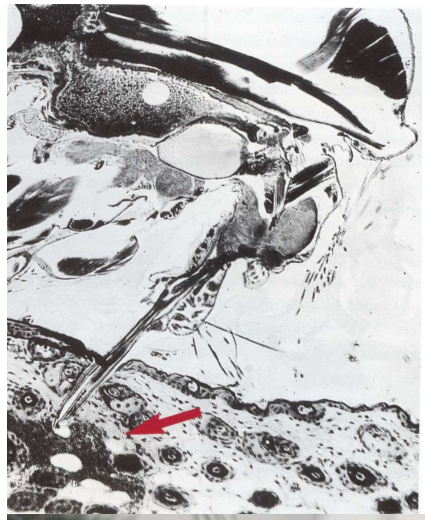
- Methods: We reviewed all consecutive leishmaniasis cases seen between September 2012 and May 2020. The diagnostic strategy included microscopy after May-Grünwald-Giemsa staining, a diagnostic quantitative PCR (qPCR) assay, and species identifcation based on sequencing of the cytochrome b gene. Results: **Eighty-nine patients had a defnitive leishmaniasis diagnosis**.
- **Nine patients had VL with Leishmania infantum**.
- **Eighty patients had CL**.
  - Twelve patients acquired CL after trips in Latin America (7 Leishmania guyanensis, 2 Leishmania braziliensis, 2 Leishmania mexicana, and 1 Leishmania panamensis).
  - Species could be identifed in 63 of the 68 CLs mainly after travel in North Africa (59%) with Leishmania major (65%), Leishmania tropica/killicki (24%), and L. infantum (11%), or in West Sub-Saharan Africa (32%), all due to L. major. The median day between appearance of the lesions and diagnosis was 90 [range 60–127].

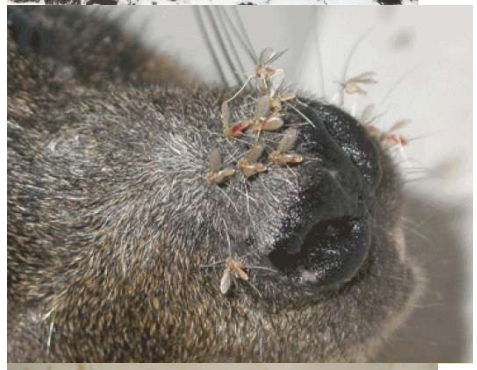

Macrophage
Promastigote
Phlebotomine sandfly
Amastigote
Lymphocytes

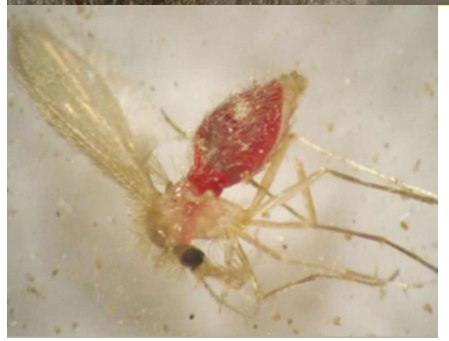

Sandfly Stages
Human Stages
1 Sandfly takes a blood meal (injects promastigote stage into the skin)
2 Promastigotes are phagocytized by macrophages
3 Promastigotes transform into amastigotes inside macrophages
4 Amastigotes multiply in cells (including macrophages) of various tissues
5 Sandfly takes a blood meal (ingests macrophages infected with amastigotes)
6 Ingestion of parasitized cell
7 Amastigotes transform into promastigote stage in midgut
8 Divide in midgut and migrate to proboscis
i = Infective Stage
d = Diagnostic Stage

Flebotomi

- Piccoli (1,5-2,5 mm) ditteri ematofagi appartenenti alla sottofamiglia Phlebotominae (Diptera: Psycodidae).
- Riconoscibili per:
  - il caratteristico movimento a “salto”,
  - per la posizione delle ali che vengono mantenute erette con una configurazione a V,
  - per il capo forma un angolo retto con il torace e
  - per la fitta peluria che ricopre addome torace ed ali
  - colorazione del corpo giallino vivace
- Meno del 10% delle specie conosciute sono coinvolte nella trasmissione di leishmanie
- Solo le femmine ematofaghe, i maschi si nutrono di pollini
- Sono in grado di trasmettere la leishmaniosi 7-10 giorni dopo essersi infettate e restano infettive per il resto della loro vita (poche settimane)
- La saliva contiene un potente vasodilatatore (maxadilan)
- L’intestino dei flebotomi infetti può essere parzialmente bloccato, il che li indurrebbe a nutrirsi ripetutamente aumentando le probabilità della trasmissione.







LEISHMANIOSI- vettori in Italia

- 97,491 flebotomi catturati (1975-1998)
- ***Phlebotomus perniciosus* (44,6%)** **P**
- ***P.perfiliewi* (37,2%)** **P**
- ***Sergentomya minuta* (17,6%)**
- ***P.neglectus* (0,2%)** **S**
- ***P.ariasi* (0,01%)** **?**
- ***P.mascittii* (0,03%)** **?**
- ***P.papatasi* (0,3%)**
- ***P.sergenti* (0,06%)** **?**

Maroli & Khoury, ISS 1998

Le larve dei flebotomi sono "terricole"

Ambienti domestici
- ✓Seminterrati e cantine
- ✓Case abbandonate
- ✓Crepe di pavimenti e muri

✓Ambienti peridomestici
- ✓Tane di animali
- ✓Rifugi di animali
- ✓Pollai
- ✓Detriti e crespe del suolo
- ✓Concimaie marcite
- ✓Terra alla base di vecchi muri
- ✓Sotto i sassi

Ambienti selvatici
- ✓Nidi di formiche
- ✓Nidi di tartarughe terrestri
- ✓Canali di scolo
- ✓Nidi di uccelli
- ✓Termitai
- ✓Tane di roditori
- ✓Grotte
- ✓Pozzi neri, asciutti
- ✓Incavi di albero
- ✓Suolo della foresta
- ✓Sotto e fra massi
- ✓Radici di grandi alberi
- ✓Suolo alla base di alberi
- ✓Suolo sotto massi sporgenti

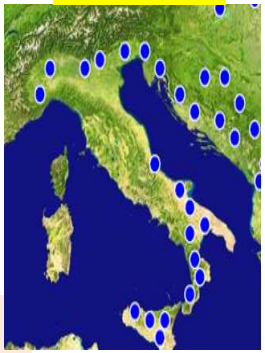
- Le uova vengono deposte nelle crepe dei muri
- Le larve richiedono un ambiente umido, le pupe un ambiente secco
- In condizioni favorevoli l'intero ciclo si completa in 2 mesi.

P. perniciosus

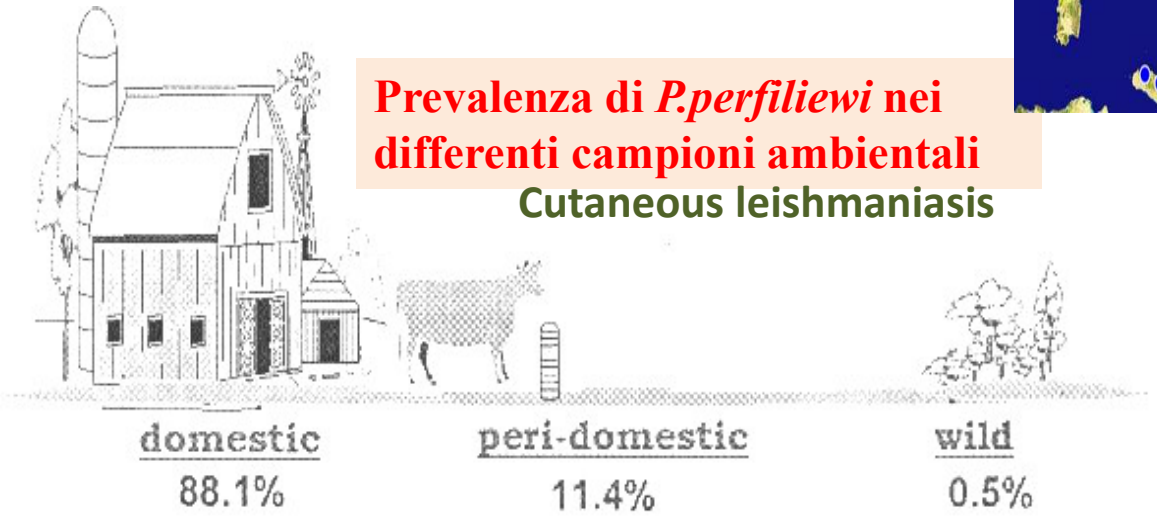
Prevalenza di *P.perniciosus* nei differenti campioni ambientali

Visceral leishmaniasis

P.neglectus

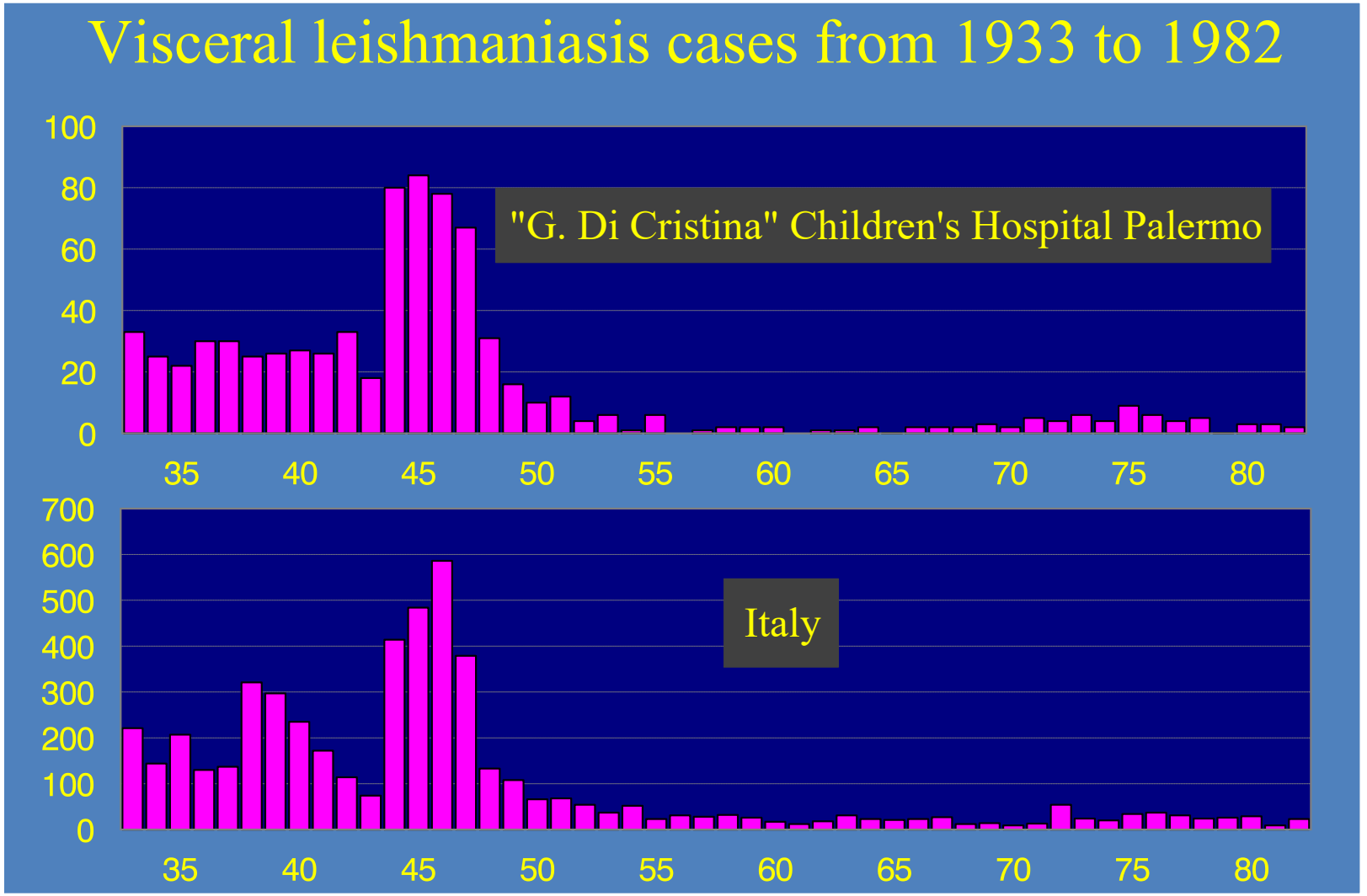


P. perfiliewi

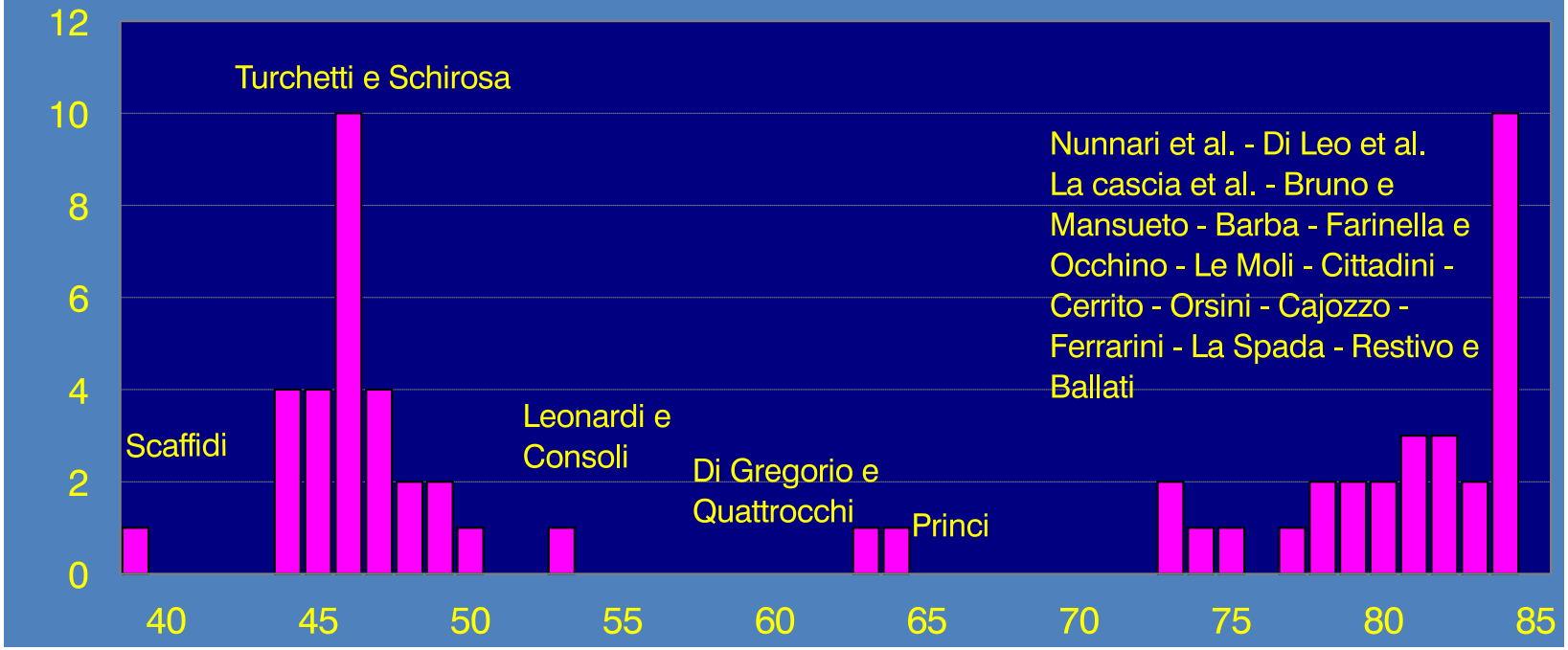


Prevalenza di *P.perfiliewi* nei differenti campioni ambientali

Cutaneous leishmaniasis


Visceral leishmaniasis cases from 1933 to 1982
"G. Di Cristina" Children's Hospital Palermo
100
80
60
40
20
0
35
40
45
50
55
60
65
70
75
80
Italy
700
600
500
400
300
200
100
0
35
40
45
50
55
60
65
70
75
80

Visceral leishmaniasis: adult cases reported in Sicily from 1939 to 1984



Am. J. Trop. Med. Hyg., 57(1), 1997, pp. 75–78

EPIDEMIOLOGIC SURVEILLANCE OF VISCERAL LEISHMANIASIS IN SICILY, ITALY

ANTONIO CASCIO, LUIGI GRADONI, FRANCESCO SCARLATA, MARINA GRAMICCIA, SALVATORE GIORDANO, ROSARIO RUSSO, ALDO SCALONE, CESARE CAMMA, AND LUCINA TITONE

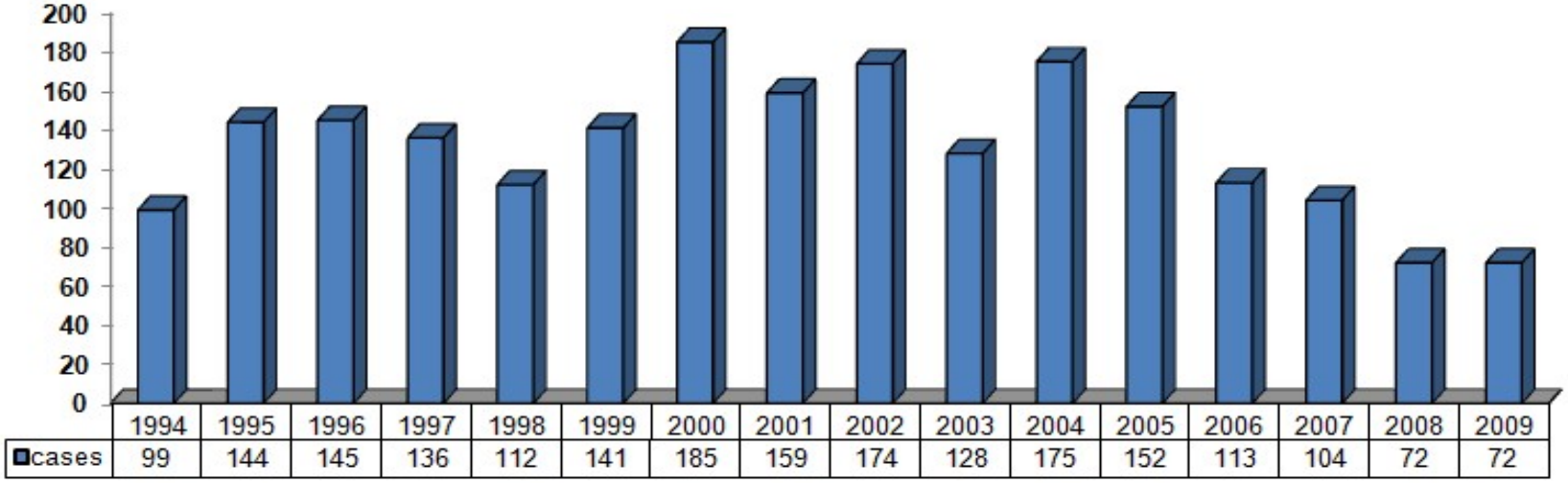
Istituto di Patologia Infettiva e Virologia, Universita di Palermo, Palermo, Italy; Laboratorio di Parassitologia, Istituto Superiore di Sanita, Rome, Italy; Istituto di Malattie Infettive, Universita di Catania, Catania, Italy; Istituto di Parassitologia Medica, Universita di Messina, Messina, Italy

Abstract. Visceral leishmaniasis (VL) is endemic in Sicily. Although it is a notifiable disease, there is evidence that the actual number of cases is higher than that reported. In 1987, a regional reference center for active surveillance of VL was established and it recorded a total of 284 cases through 1995, a mean of 31.5 cases/year and about four-fold more than previously reported. Of the 284 cases, 150 (53%) were children (≤ 14 years of age), and of the 134 adults, 39 (29%) were coinfected with human immunodeficiency virus (HIV). The commonest viscerotropic zymodeme of *Leishmania infantum,* MON 1, was identified in 40 (93%) of 43 HIV-negative and eight (57%) of 14 HIV-positive patients. Among 280 patients evaluated (i.e., all HIV-negative and 35 of 39 HIV-positive subjects), 254 (91%) were treated with meglumine antimoniate alone or in combination with other drugs; 23 (8%) received allopurinol or amphotericin B, either conventional or in liposomal form; and three terminally ill patients were not treated. Among the 245 HIV-negative patients, 236 (96%) were successfully cured, while nine (4%) (seven adults) died during the course of antimonial treatment. None of the 35 HIV-positive patients was definitively cured, although mortality was apparently associated with other opportunistic infections.

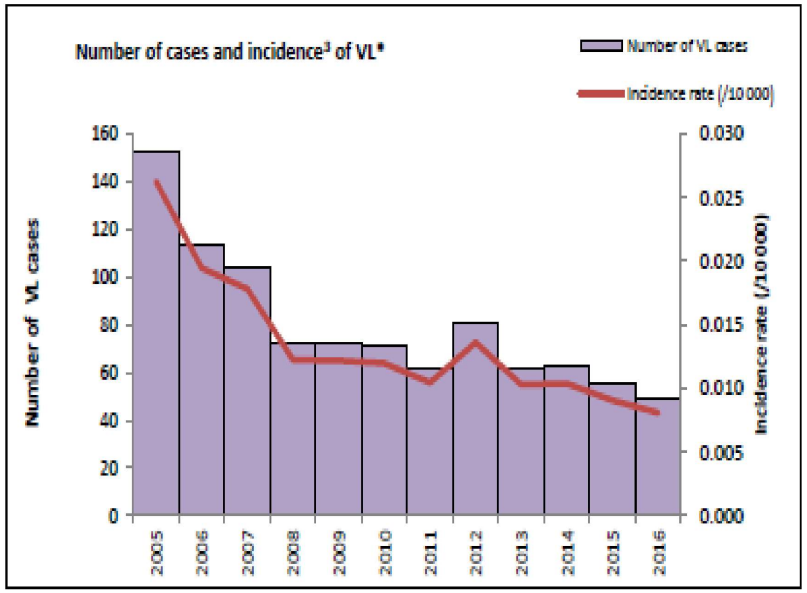
Am J Trop Med Hyg 1997; 57:75-78

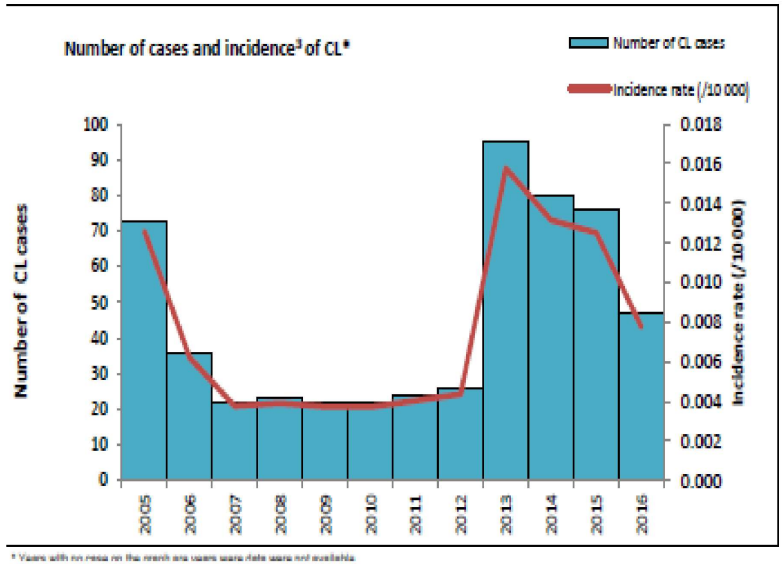
Sorveglianza della Leishmaniosi Viscerale umana in Italia

*quasi tutti casi importati



	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
cases	99	144	145	136	112	141	185	159	174	128	175	152	113	104	72	72



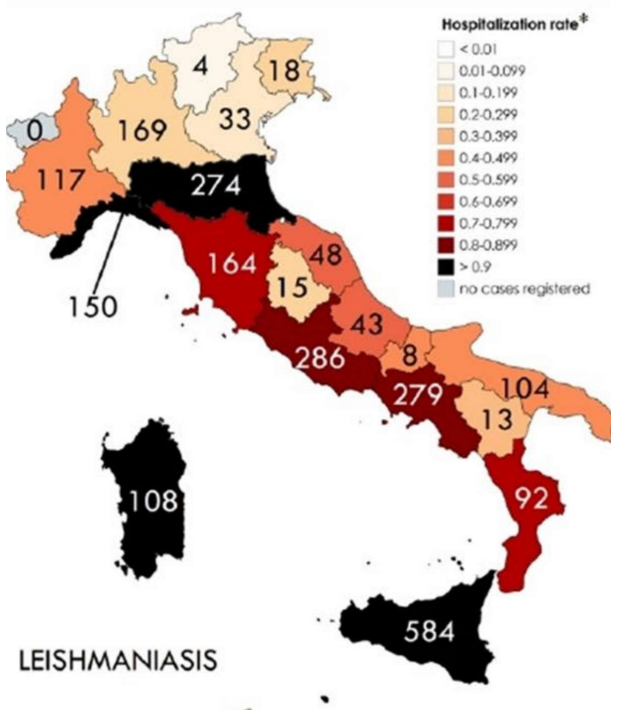


Infection (2020) 48:695–713
https://doi.org/10.1007/s15010-020-01443-2

ORIGINAL PAPER

Hospitalization for Chagas disease, dengue, filariasis, leishmaniasis, schistosomiasis, strongyloidiasis, and *Taenia solium* taeniasis/cysticercosis, Italy, 2011–2016

Marta Tilli[1] · Annarita Botta[1] · Alessandro Bartoloni[1,2,3] · Giampaolo Corti[1,2] · Lorenzo Zammarchi[1,2,3]

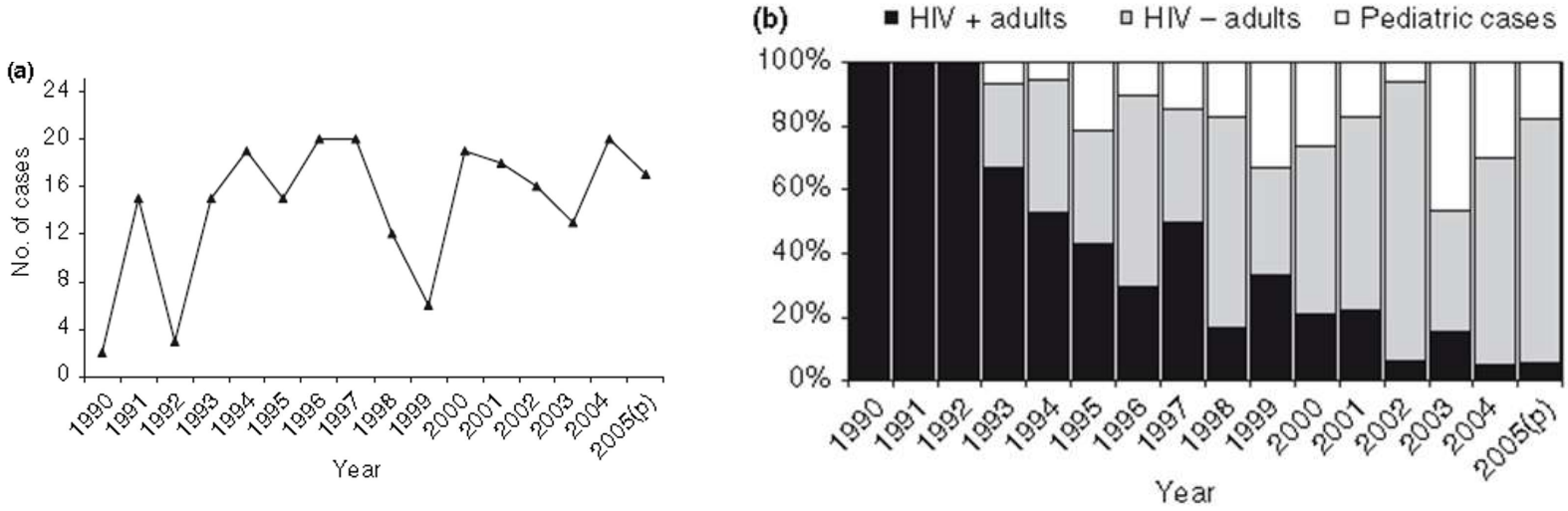


Tropical Medicine and International Health doi:10.1111/j.1365-3156.2007.01998.x

VOLUME 13 NO 2 PP 256–264 FEBRUARY 2008

The northward spread of leishmaniasis in Italy: evidence from retrospective and ongoing studies on the canine reservoir and phlebotomine vectors

Michele Maroli[1], Luca Rossi[2], Raffaella Baldelli[3], Gioia Capelli[4], Ezio Ferroglio[2], Claudio Genchi[5], Marina Gramiccia[1], Michele Mortarino[5], Mario Pietrobelli[6] and Luigi Gradoni[1]



- Annual trend of 230 visceral leishmaniasis cases recorded in in region of northern continental Italy from 1990 to 2005

RAPID COMMUNICATIONS

Ongoing outbreak of visceral leishmaniasis in Bologna Province, Italy, November 2012 to May 2013

S Varani (stefania.varani@unibo.it)[1], R Cagarelli[2], F Melchionda[3], L Attard[4], C Salvadori[4], A C Finarelli[2], G A Gentilomi[1], R Tigani[1], R Rangoni[5], R Todeschini[6], A Scalone[7], T Di Muccio[7], M Gramiccia[7], L Gradoni[7], P Viale[4], M P Landini[1]

Hindawi Publishing Corporation
BioMed Research International
Volume 2016, Article ID 6481028, 7 pages
http://dx.doi.org/10.1155/2016/6481028

Hindawi

Clinical Study

Clinical and Microbiological Characteristics of Visceral Leishmaniasis Outbreak in a Northern Italian Nonendemic Area: A Retrospective Observational Study

E. Franceschini,[1] C. Puzzolante,[1] M. Menozzi,[1] L. Rossi,[1] A. Bedini,[1] G. Orlando,[1] W. Gennari,[2] M. Meacci,[2] G. Rugna,[3] E. Carra,[3] M. Codeluppi,[1] and C. Mussini[4]

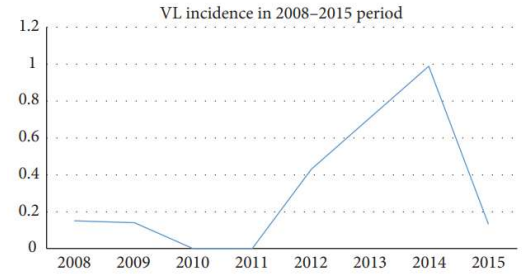


FIGURE 1: Visceral leishmaniasis incidence per 100,000 inhabitant in 2008–2015 period in the Modena province.

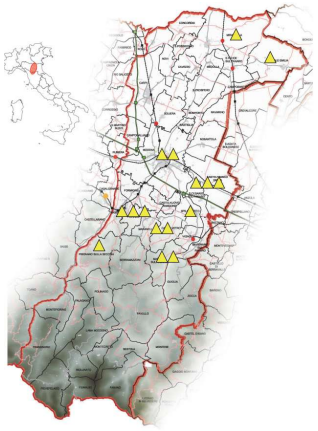
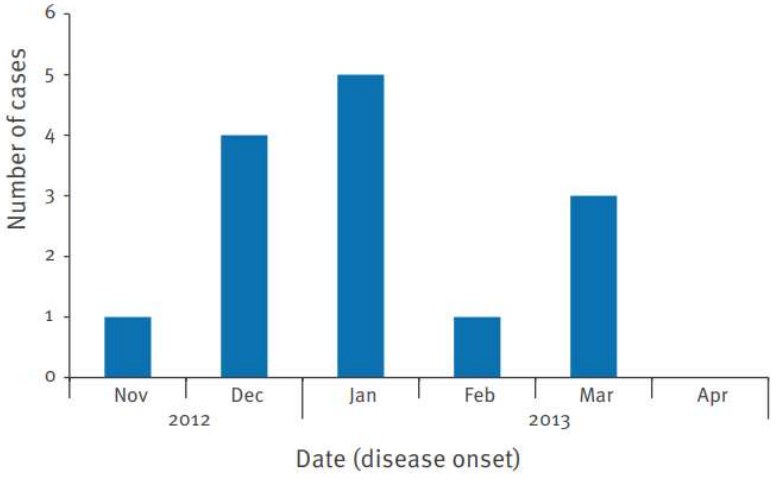


FIGURE 1

Epidemic curve of human cases of visceral leishmaniasis, Bologna Province, northern Italy, November 2012–May 2013 (n=14)



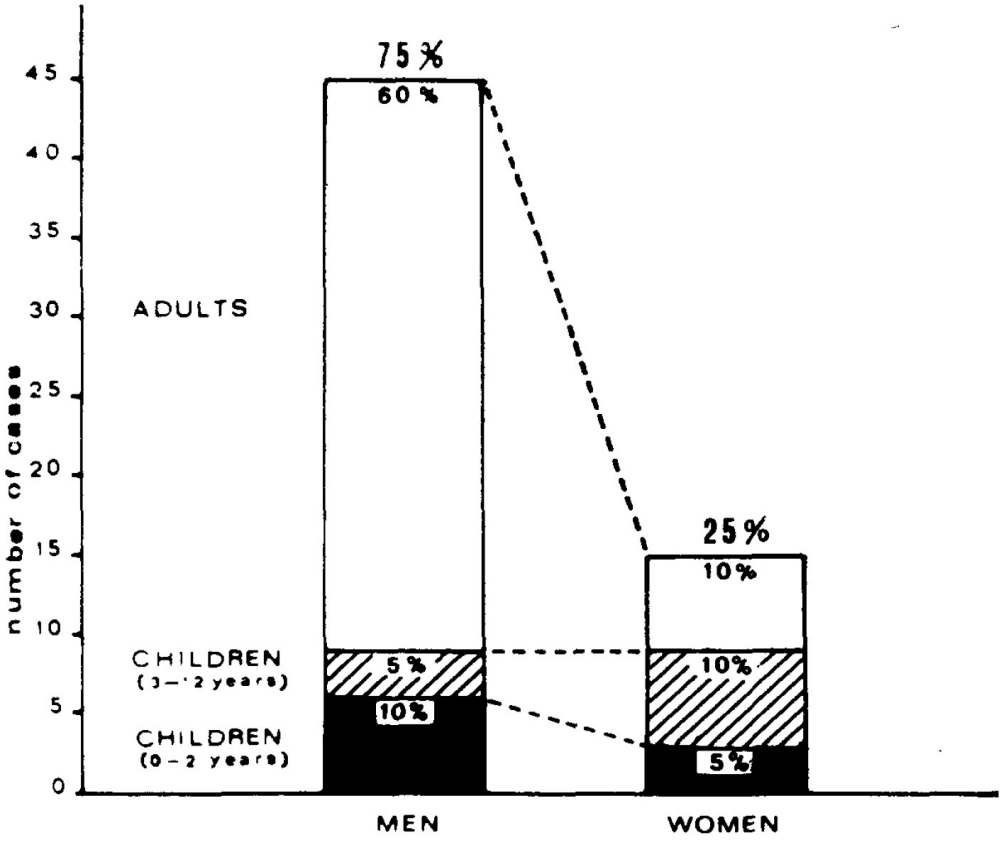
TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE. Vol. 68. No. 5. 1974.

STUDIES ON MEDITERRANEAN LEISHMANIASIS
I. AN OUTBREAK OF VISCERAL LEISHMANIASIS IN NORTHERN ITALY

S. PAMPIGLIONE
Professor of Parasitology, Facoltà di Medicina Veterinaria, Università di Bologna
M. LA PLACA
Professor of Microbiology, Facoltà di Medicina e Chirurgia, Università di Bologna
AND
G. SCHLICK
Director, Servizio di Anatomia e Istologia Patologica, Ospedale Maggiore, Bologna

Two patients displayed tonsillar hypertrophy with presence of *Leishmania* in the tonsils, and in a lateral cervical lymph node, without high rises of temperature.
The fatal cases were 13 (21,7%) all in adult males. **Most fatalities occurred before a correct diagnosis** was made and specific therapy could be used. **Death occurred in 11 patients who did not receive antimony** treatment while the remaining 2 had been partially treated

60 cases in the outbreak



Il punto di vista One health

Impact of Climate Change on Leishmaniasis

- **1. Vector Distribution and Expansion**
- **Temperature rise** allows sandflies to survive in areas previously too cold, expanding their **geographic range** (e.g., southern to northern Europe).
- **Shorter development cycles**: Higher temperatures accelerate the sandfly's life cycle and increase the rate of *Leishmania* development inside the vector, enhancing **transmission potential**.
- **Altitude shifts**: Warming allows sandflies to move to higher altitudes, where the disease was previously absent.

- **2. Changes in Vector Abundance and Activity**
- **Longer transmission seasons**: Warmer temperatures extend the activity period of sandflies beyond traditional summer months.
- **Rainfall patterns** affect breeding sites. In some cases:
  - Increased rainfall = more breeding sites (e.g., moist soil and organic matter).
  - Excessive drought = migration of humans and animals to water sources, increasing exposure.

- **3. Effects on Reservoir Hosts**
- **Population movements** of domestic animals (especially dogs) and wildlife due to environmental stress can spread the parasite to new areas.
- **Habitat changes** alter the interaction between humans, vectors, and reservoir hosts.

- **4. Human Factors Exacerbated by Climate Change**
- **Migration and displacement** due to droughts, floods, or agricultural collapse increase human exposure to endemic areas.
- **Urbanization and deforestation** alter the natural ecosystem, bringing humans closer to infected sandflies and reservoir animals.

Examples of Climate-Driven Spread

- **Southern Europe**: In recent decades, *Leishmania infantum* has been reported further north, including parts of France, Germany, and even Central Europe.
- **Latin America**: Increased incidence in peri-urban areas, linked to deforestation and climate shifts.
- **North Africa and the Middle East**: Greater sandfly activity and disease spread linked to warming and desertification.

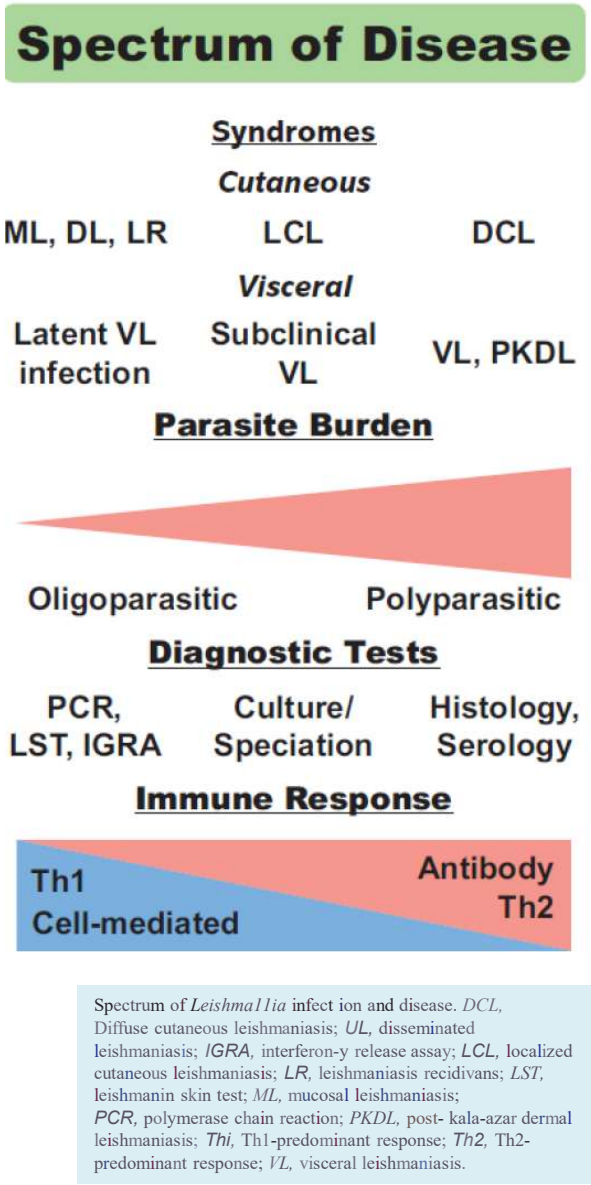
One Health Implications

- To mitigate climate-driven leishmaniasis risk, a **multisectoral approach** is essential:
- **Surveillance**: Integrated monitoring of climate data, vector populations, animal reservoirs, and human cases.
- **Vector control**: Targeted interventions in newly at-risk areas.
- **Animal health**: Screening and treating dogs, and developing effective prevention strategies (e.g., repellents, vaccines).
- **Community education**: Informing populations about preventive measures, especially in new or expanding endemic areas.
- **Climate adaptation policies**: Incorporate vector-borne disease risks into climate resilience and public health planning.

Pathogenesis and Immunology

Leishmaniasis can be considered a polar disorder similar to other intracellular infections, such as leprosy.

- On one end of the spectrum are **polyparasitic** infections (e.g., diffuse CL or VL) characterized by a predominantly Th2-type immune response with relative anergy, akin to lepromatous leprosy. Heavily parasitized macrophages are abundant, and diagnosis is readily made by smear.
- The **oligoparasitic** end of the spectrum includes ML and latent VL infection. Amastigotes are sparse, and a mononuclear cell infiltrate predominates in a Th1-type immune response, analogous to tuberculoid leprosy. In reality, the interaction between Th1 and Th2 is much more complex and includes variable modulation by Th17-type CD4 T cells, among others.



Spectrum of *Leishma1ia* infect ion and disease. *DCL,* Diffuse cutaneous leishmaniasis; *UL,* disseminated leishmaniasis; *IGRA,* interferon-y release assay; *LCL,* localized cutaneous leishmaniasis; *LR,* leishmaniasis recidivans; *LST,* leishmanin skin test; *ML,* mucosal leishmaniasis; *PCR,* polymerase chain reaction; *PKDL,* post- kala-azar dermal leishmaniasis; *Thi,* Th1-predominant response; *Th2,* Th2-predominant response; *VL,* visceral leishmaniasis.

Tissue granuloma structure-function in experimental visceral leishmaniasis

HENRY W. MURRAY
Department of Medicine, Weill College of Cornell University, New York, USA

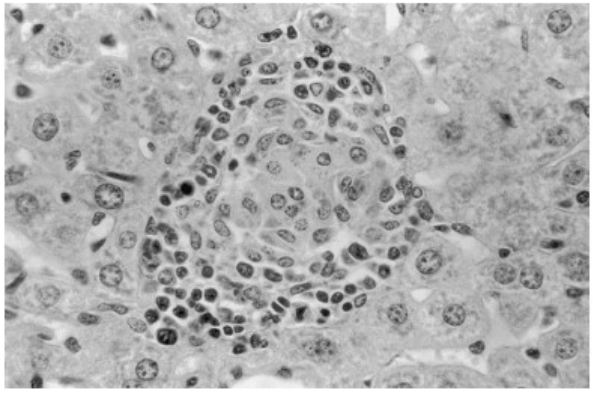


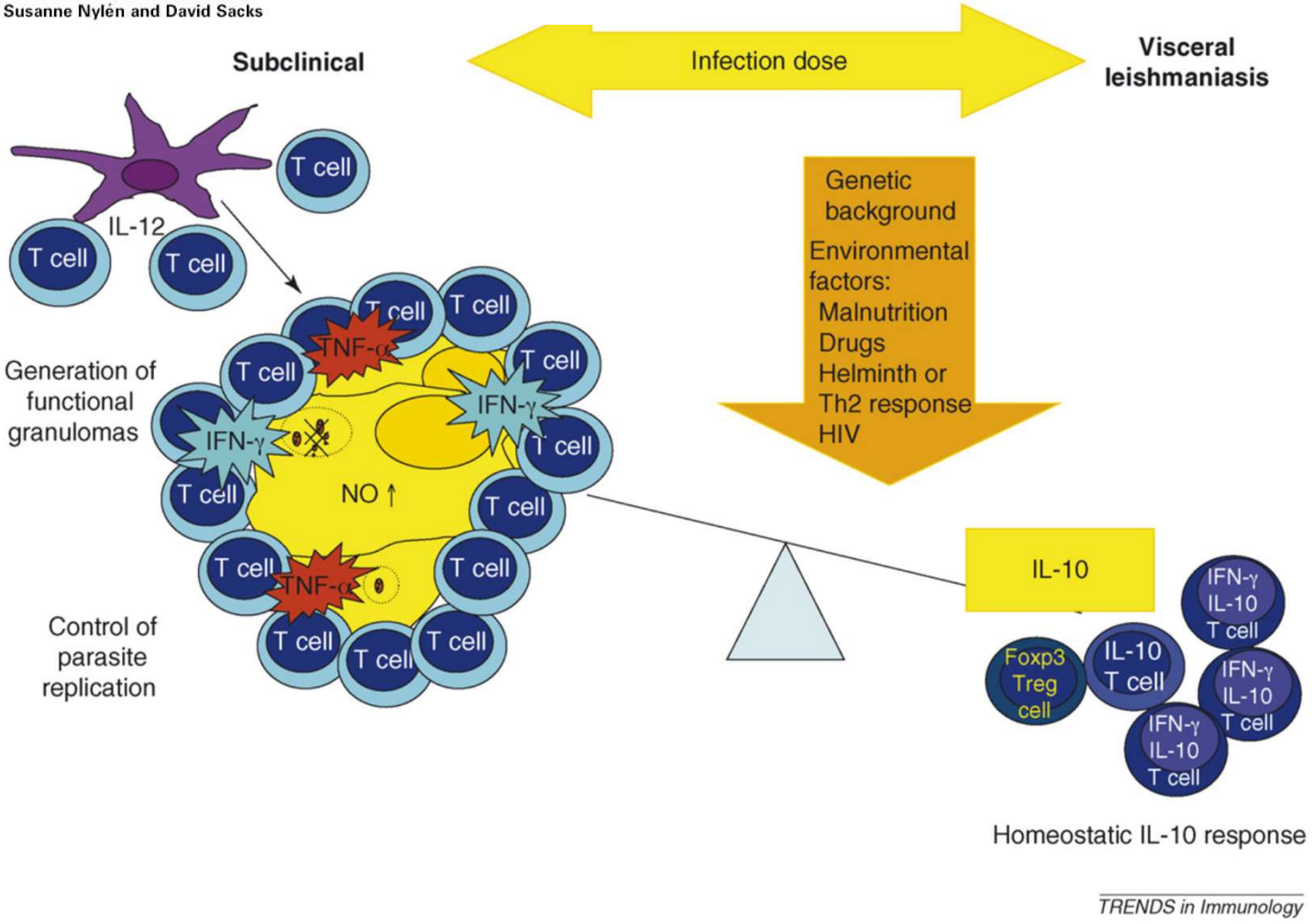
Figure 2. Mature liver granuloma 4 weeks after *L. donovani* infection in normal BALB/c mouse. Well-developed mononuclear cell mantle surrounds Kupffer cell core containing few residual amastigotes. (× 315). Reproduced with permission (Squires *et al.* 1989).

- **Leishmaniasis is a granulomatosis disease and granulomas represent the tissue expression of the successful T-cell-dependent immune response**

Review TRENDS in Immunology Vol.28 No.9

Interleukin-10 and the pathogenesis of human visceral leishmaniasis

Susanne Nylén and David Sacks



Transactions of the Royal Society of Tropical Medicine and Hygiene (2008) 102, 394–396

available at www.sciencedirect.com

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journal homepage: www.elsevierhealth.com/journals/trst

SHORT COMMUNICATION

Asymptomatic *Leishmania infantum/chagasi* infection in blood donors of western Sicily

Francesco Scarlata[a], Fabrizio Vitale[b], Laura Saporito[a,*], Stefano Reale[b], Valentina Li Vecchi[a], Salvatore G[illegible]
Francesco Occhipinti[c], Lucina Tit[illegible]

Journal of Infection 80 (2020) 116–120

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Asymptomatic *Leishmania infantum* infection in blood donors living in an endemic area, northeastern Italy

Margherita Ortalli[a], Alessandra Mistral De Pascali[a], Serena Longo[a], Nadia Pascarelli[b], Andrea Porcellini[b], Deborah Ruggeri[b], Vanda Randi[b], Anna Procopio[c], Maria Carla Re[a,d,1], Stefania Varani[a,d,1,*]

Heliyon 6 (2020) e03940

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Leishmania infantum asymptomatic infection in inflammatory bowel disease patients under anti-TNF therapy

M. Carmen Guillén [a], M. Magdalena Alcover [a], Natalia Borruel [b], Elena Sulleiro [c], Fernando Salvador [d], Diana Berenguer [a], Claudia Herrera-de Guise [b], Verónica Rodríguez [b], Zaira Moure [c], Adrián Sánchez-Montalvà [d], Israel Molina [d], Roser Fisa [a], Cristina Riera [a,*]

[a] Laboratory of Parasitology, Department of Biology, Health and Environment, Faculty of Pharmacy and Food Science, University of Barcelona, Avda Joan XXIII, 27-31, 08028, Barcelona, Spain
[b] Crohn's and Colitis Attention Unit, Vall d'Hebron University Hospital, Ps Vall d'Hebron, 119-129, 08035, Barcelona, Spain
[c] Department of Microbiology, Vall d'Hebron University Hospital, PROSICS, Ps Vall d'Hebron, 119-129, 08035, Barcelona, Spain
[d] Department of Infectious Diseases, Vall d'Hebron University Hospital, PROSICS Barcelona, Ps Vall d'Hebron, 119-129, 08035, Barcelona, Spain

Journal of Microbiology, Immunology and Infection (2020) **53**, 176–178

Available online at www.sciencedirect.com

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Short Communication

Viability of *Leishmania* in blood donors: A tangible possibility of transfusion transmission

Adriana de Oliveira França [a,*], Luiza de Oliveira Ramos Pereira [b], Tayana Serpa Ortiz Tanaka [c], Márcia Pereira de Oliveira [d], Maria Elizabeth Cavalheiros Dorval [a]

Leishmaniasis in Sardinia. 5. Leishmanin reaction in the human population of a focus of low endemicity of canine leishmaniasis

M. Gramiccia[1], S. Bettini[2], L. Gradoni[1], P. Ciarmoli[1], M. L. Verrilli[3], S. Loddo[2] and C. Cicalò[2] *[1]Laboratorio di Parassitologia, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Roma, Italy; [2]Istituto di Genetica 'Carlo Jucci', Università di Cagliari, Cagliari, Italy; [3]Medical Officer, Soleminis (CS), Italy*

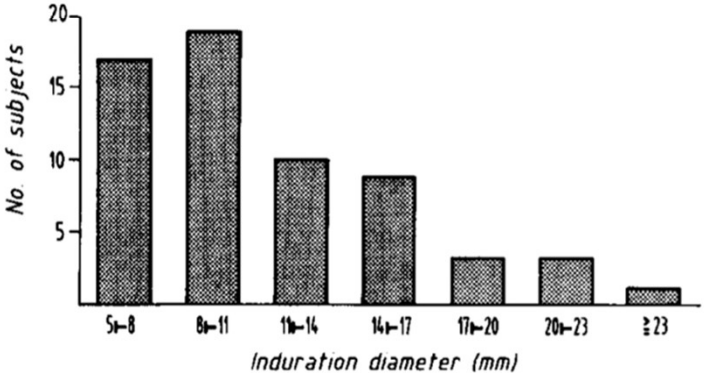
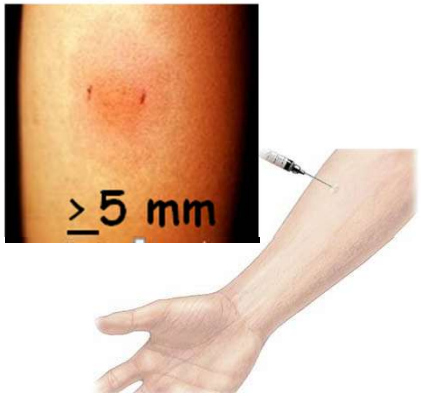


Fig. 2. Distribution of extent of reaction to leishmanin among the positive subjects in Soleminis, Sardinia.



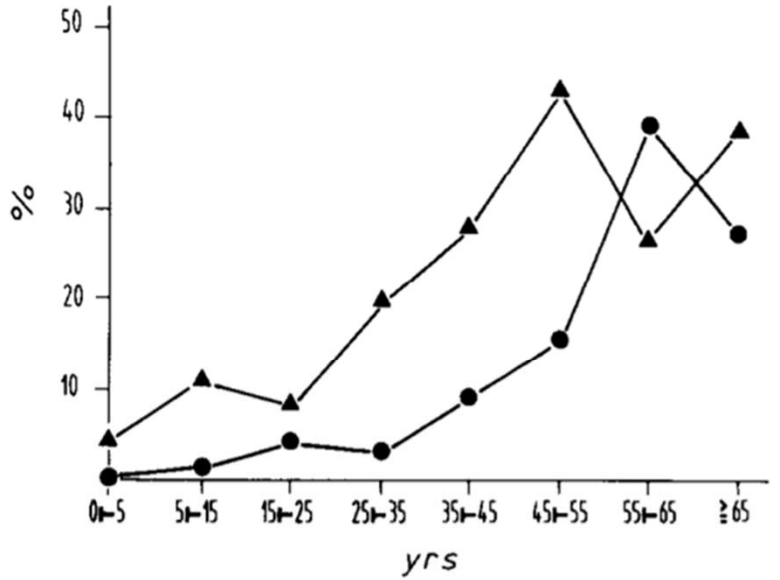


Fig. 1. Response to the leishmanin skin test according to age of 640 subjects in Soleminis, Sardinia (●) and of 1818 subjects in Monte Argentario, Tuscany (▲).

Journal of the Pediatric Infectious Diseases Society

CASE REPORT

Congenital Leishmaniasis in a Newborn Infant Whose Mother was Coinfected With Leishmaniasis and HIV

Nicolas Argy,[1,2,3,*] Sylvie Lariven,[4] Aline Rideau,[5] Anais Lemoine,[6] Agnès Bourgeois Moine,[7] Lahcene Allal,[7] Laurence Choudat,[8] Christophe Ravel,[9] Florence Michard,[4] Pierre Buffet,[10] Albert Faye,[11,12,13] Sandrine Houze,[1,2,3] and Yazdan Yazdanpanah[4,12,14]

[1]Laboratoire de Parasitologie-Mycologie, [4]Service des Maladies Infectieuses et Tropicales, [7]Service de Gynécologie-Obstétrique, and [8]Département d'Anatomopathologie, Hôpital Bichat-Claude Bernard, APHP, Paris, France; [2]Faculté de Pharmacie and [10]INSERM UMR_S 1134, Institut National de la Transfusion Sanguine, Université Paris Descartes, COMUE Paris Sorbonne, France; [3]UMR MERIT 216, Institut pour la Recherche et le Développement, Paris, France; [5]Service de Réanimation Néonatale and [11]Service de Pédiatrie Générale, Hôpital Robert Debré, APHP, Paris, France; [6]Service de Nutrition et Gastroentérologie Pédiatrique, Hôpital Armand Trousseau, APHP, Paris, France; [9]Centre National de Référence de la Leishmaniose, CHU de Montpellier, France; [12]Faculté de Médecine, Université Paris Diderot, France; [13]ECEVE, INSERM 1123, Paris, France; and [14]IAME, INSERM, Paris, France

We report here the occurrence, specific management, and monitoring of congenital leishmaniasis in a newborn infant whose mother was coinfected with leishmaniasis and human immunodeficiency virus; transplacental transmission, confirmed by overt clinical disease at birth, was documented, which provides, to our knowledge, the first evidence of hepatic and neurologic impairment in an infant with congenital visceral leishmaniasis.

Trends in Parasitology

Forum

Sexual Transmission of Visceral Leishmaniasis: A Neglected Story

Diego L. Guedes [1,2,*]
Saskia van Henten,[3]
Lieselotte Cnops,[3]
Wim Adriaensen,[3] and
Johan van Griensven[3]

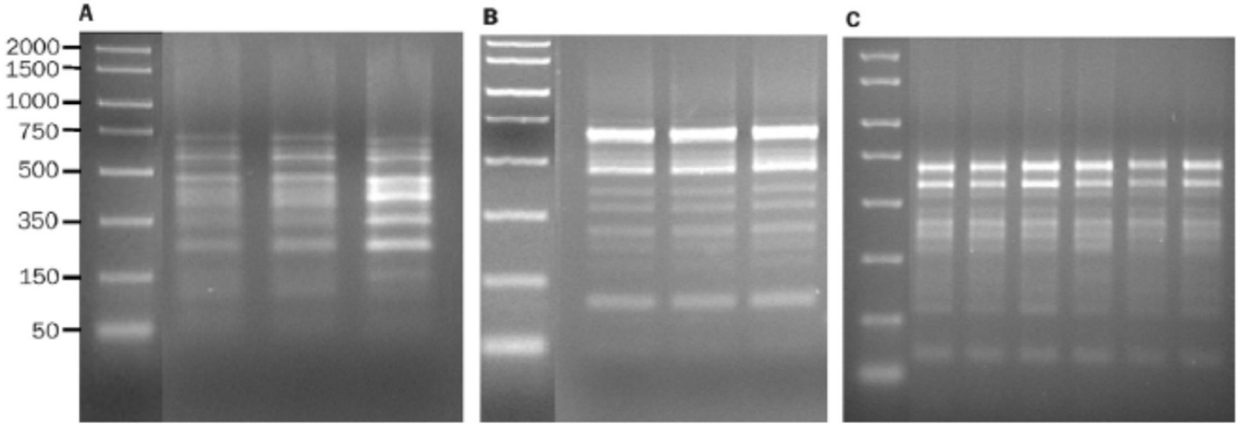
For visceral leishmaniasis (VL), a major vector-borne parasitic disease, an alternative sexual transmission route is well documented in dogs but evidence is lacking in humans. Here, we discuss the current knowledge and key questions to be answered as it may be an additional obstacle in ongoing VL elimination programs.

Leishmania in discarded syringes from intravenous drug users

I Cruz, M A Morales, I Noguer, A Rodríguez, J Alvar

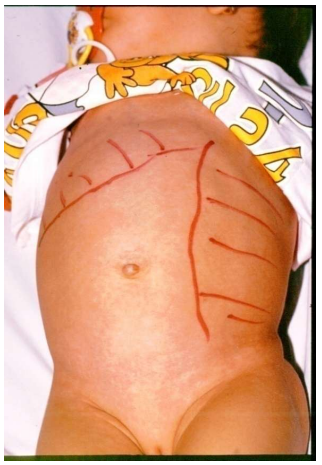
Needle sharing by intravenous drug users (IVDUs) has been proposed as providing an alternative, artificial, and anthroponotic cycle for leishmania transmission. We looked for parasites in syringes discarded by IVDUs using two different PCR techniques. *Leishmania* spp were detected in 65 (52%) of 125 syringes collected in southern Madrid, Spain, in 1998, and in 52 (34%) of 154 collected in southwestern Madrid in 2000–01. We found shared restriction fragment length polymorphisms in 12 of 65 positive samples tested, suggesting that syringe sharing can indeed promote the spread of leishmania clones among IVDUs.

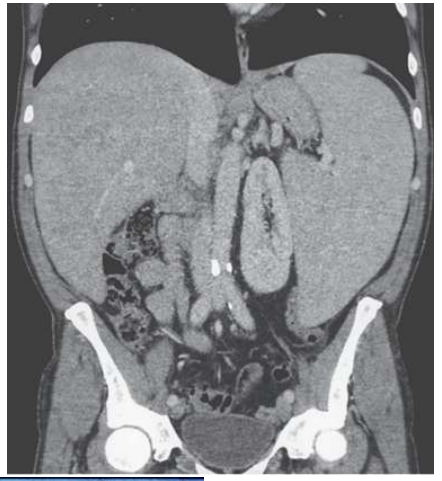
Lancet 2002; **359:** 1124–25

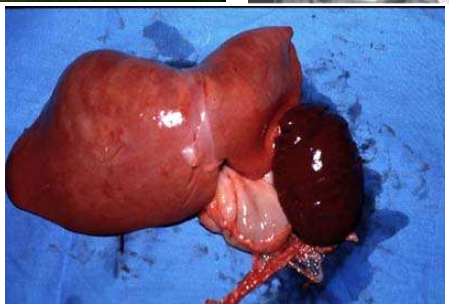


Molecular characterisation of *Leishmania* spp detected in syringes discarded by intravenous drug users
From 65 syringes positive for *Leishmania* spp, the three genotypes shown (A, B, and C) were shared by three, three, and six syringes, respectively.

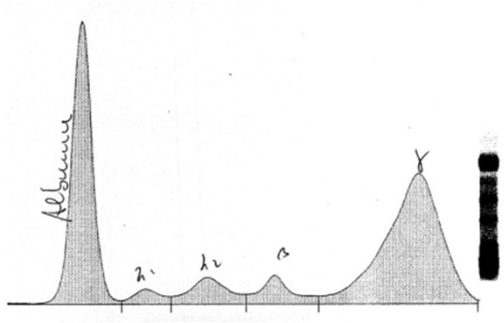
Zoonotic visceral leishmaniasis (*L.infantum*)

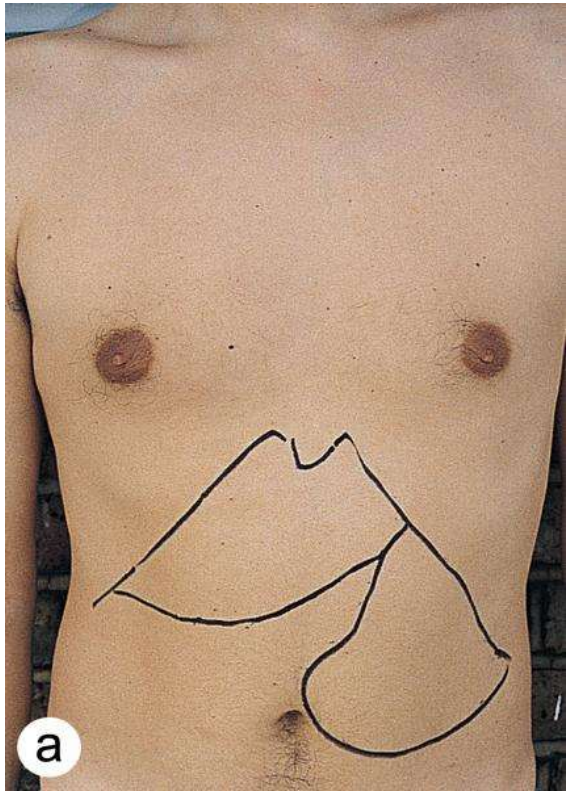


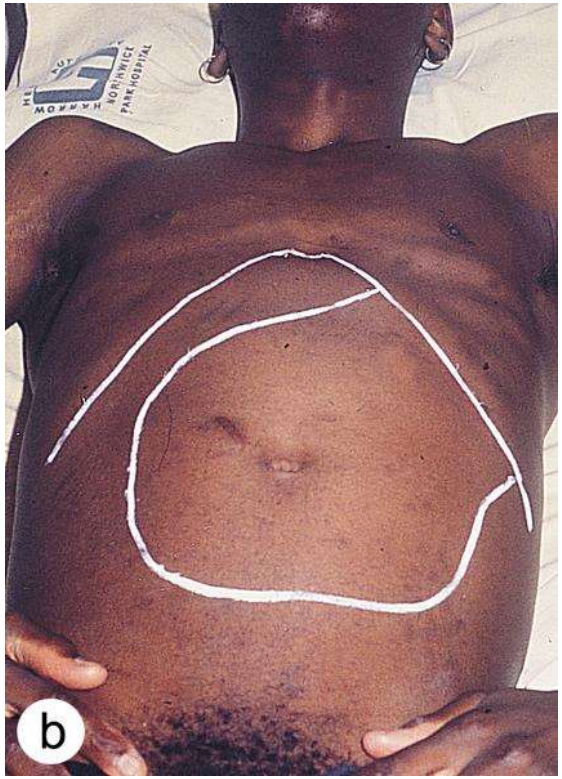




- ✓ Long incubation period (2-7 mo)
- ✓ Triad of signs and symptoms (94-100%):
  - ·Splenomegaly
  - ·Irregular fever
  - ·Pallor
- ✓ Triad of biological parameters (94-100%):
  - ·Raised immunoglobulin levels
  - ·Pancytopenia
  - ·Raised ESR







- (a) Hepatosplenomegaly and pallor in a 29-year old Italian man.
- (b) Splenomegaly and pallor in a 23-year old Angolan. Both complained of weight loss, fatigue and fever of several weeks' duration.

Eur J Clin Microbiol Infect Dis (2002) 21:277–282
DOI 10.1007/s10096-002-0707-3

ARTICLE

A. Cascio · C. Colomba · S. Antinori · M. Orobello
D. Paterson · L. Titone

Pediatric Visceral Leishmaniasis in Western Sicily, Italy: A Retrospective Analysis of 111 Cases

Table 1 Clinical features of 111 children with visceral leishmaniasis

Clinical feature	Finding
Median duration of disease before admission (range)	15 days (2 days–7 months)
Fever [no. of cases (%)]	111 (100)
Splenomegaly [no. of cases (%)]	111 (100)
Extent of spleen enlargement [median distance below left costal margin (range)]	4 cm (2–13 cm)
Hepatomegaly [no. of cases (%)]	101 (91)
Extent of liver enlargement [median distance below the right costal margin (range)]	3 cm (0–11 cm)
Skin lesions (no. of cases)	2
Lymphadenopathy (no. of cases)[a]	0

[a] Mild enlargement of the small lymph nodes in the cervical chain of 13 patients was not considered true lymphadenopathy related to visceral leishmaniasis

Eur J Clin Microbiol Infect Dis (2002) 21:277–282
DOI 10.1007/s10096-002-0707-3

ARTICLE

A. Cascio · C. Colomba · S. Antinori · M. Orobello
D. Paterson · L. Titone

Pediatric Visceral Leishmaniasis in Western Sicily, Italy: A Retrospective Analysis of 111 Cases

Table 2 Hematological and biochemical features of 111 children with visceral leishmaniasis

Variable	Median value (range)
Erythrocyte count (· 10^6 cells/∝l)	3.7 (1.9–5)
Hemoglobin (g/dl)	7.8 (3.8–12.7)
Leukocyte count (· 10^3 cells/∝l)	4.3 (1.6–10.9)
Neutrophil count (· 10^3 cells/∝l)	1 (0.2–3.7)
Platelets (· 10^3 cells/∝l)	110 (12–362)
Erythrocyte sedimentation rate (mm/h)	73 (9–138)
C-reactive protein (mg/100 ml)	2.3 (0.3–18.2)
Total protein (g/dl)	7.3 (4.5–10.4)
Albumin (g/dl)	3.3 (1.4–5.3)
Gammaglobulin (g/dl)	2.3 (0.6–6.6)
Aspartate aminotransferase (IU/l)	53 (19–847)
Alanine aminotransferase (IU/l)	33 (8–497)

Eur J Clin Microbiol Infect Dis (2002) 21:277–282
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ARTICLE

A. Cascio · C. Colomba · S. Antinori · M. Orobello
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Pediatric Visceral Leishmaniasis in Western Sicily, Italy: A Retrospective Analysis of 111 Cases

Table 3 Treatment and outcome of the 111 children with visceral leishmaniasis

Drug and dosage	Duration of therapy	No. of courses of therapy	No. of cases	Clinical response	No. of relapses
Meglumine antimoniate; median Sb^V 23.5 mg/kg/day (range, 14–30.2 mg/kg/day)	<18 days (median, 14.5; range, 2–17)	1 course, *n*=19 patients; 2 courses, *n*=2 patients	21	19/21[a]	0
	18–24 days (median, 21; range, 18–24)	1 course, *n*=50 patients; 2 courses, *n*=15 patients	65	65/65	0
	>24 days (median, 28; range, 25–30)	1 course, *n*=8 patients; 2 courses, *n*=5 patients	13	13/13	2/13
Liposomal AmB; 3 mg/kg/day	5 days (4+1 on day 10)		2	2/2	0
	6 days (5+1 on day 10)		11[b]	11/11	0
	10 days		3[c]	3/3	0

[a] Two patients were switched from meglumine antimoniate to liposomal amphotericin B: 1 on day 6 of meglumine antimoniate treatment because clinical and laboratory findings had worsened, and 1 because of adverse reaction to meglumine antimoniate (severe urticarial rash after the second dose)

[b] Includes the two cases described above in footnote "a"

[c] Includes the two cases that relapsed after antimonial therapy

GIORNALE DI SICILIA online

Nisseno muore di Leishmaniosi Forse lo ha punto una zanzara

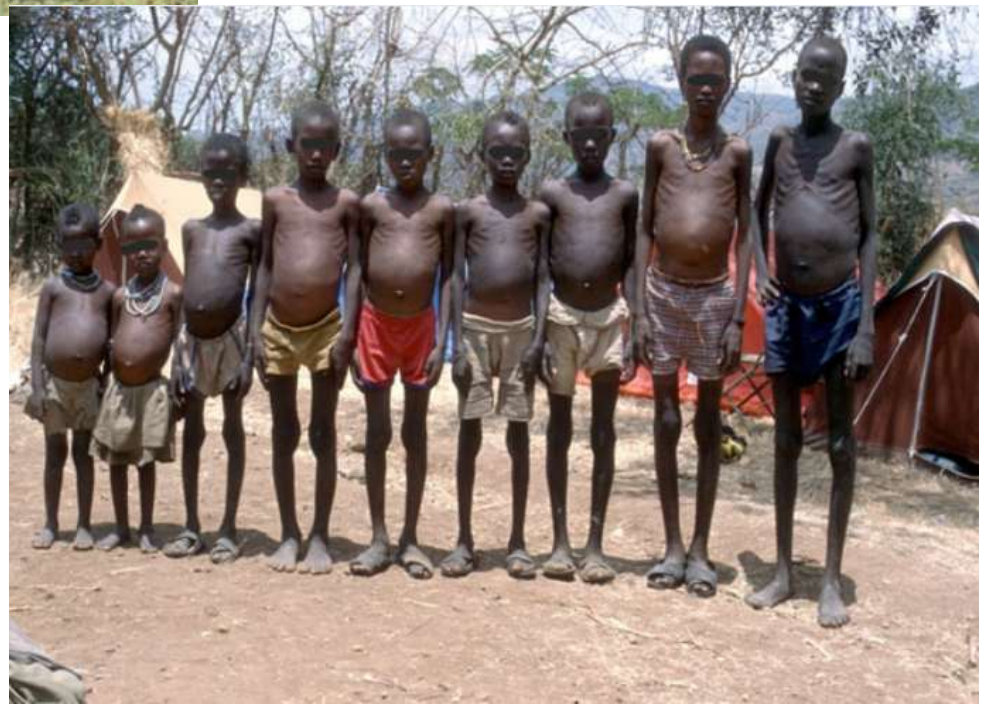
L'uomo, che è stato segretario della Dc a Serradifalco, viene ricoverato nell' ospedale Sant' Elia in day hospital, dopo che, il 29 aprile, aveva cominciato ad accusare febbre alta. Dalle analisi però non era emerso nulla. La diagnosi è arrivata solo venerdì 17 maggio, dopo ricoveri e dimissioni ospedalieri, che hanno determinato il trasferimento del paziente in elicottero a Palermo. Secondo i familiari vi sono stati ritardi nell' individuazione della malattia.

G. F., 52 anni, è morto nell' ospedale Buccheri La Ferla per leishmaniosi. L' uomo che è di Serradifalco in provincia di Caltanissetta, forse è stato punto da una zanzara.
Lunedì 13 maggio, l'uomo, che è stato segretario della Dc a Serradifalco, viene ricoverato nell' ospedale Sant' Elia in day hospital, dopo che, il 29 aprile, aveva cominciato ad accusare febbre alta. Dalle analisi però non era emerso nulla.
La diagnosi è arrivata solo venerdì 17 maggio, dopo ricoveri e dimissioni ospedalieri, che hanno determinato il trasferimento del paziente in elicottero a Palermo.
Sabato l' uomo è rimasto in rianimazione, ma a tarda sera è morto. In questo periodo G.F., che lascia una moglie e due figlie, ha avuto punte di febbre che superavano i 40 gradi.
Secondo i familiari vi sono stati ritardi nell' individuazione della malattia.

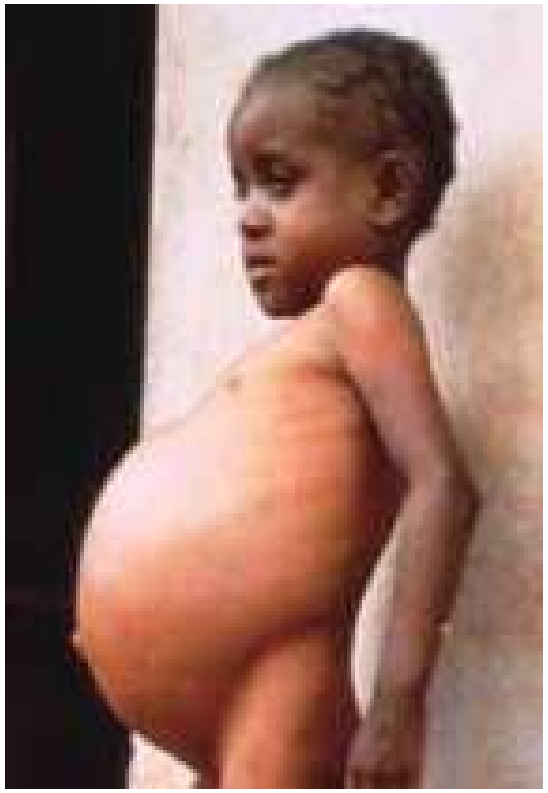
Caltanissetta 20/05/2002 h.11.36.03

Kenya

South Ethiopia



Many children suffering from visceral leishmaniasis develop a noticeable thickening, stiffening and darkening of the eyelashes and eyebrows

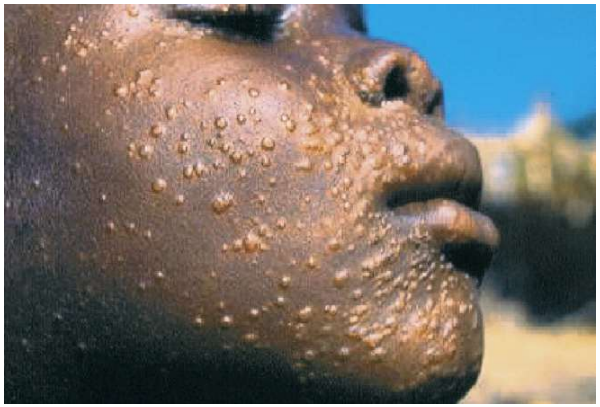


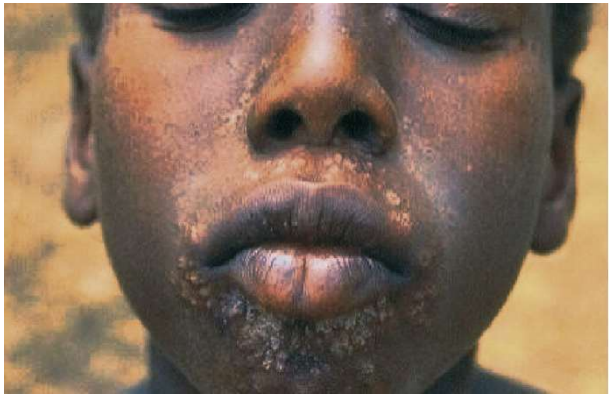
Profile view of a teenage boy suffering from visceral leishmaniasis.

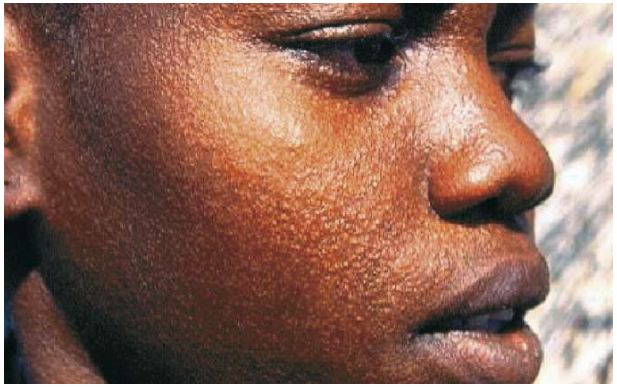
The boy exhibits splenomegaly, distended abdomen and severe muscle wasting

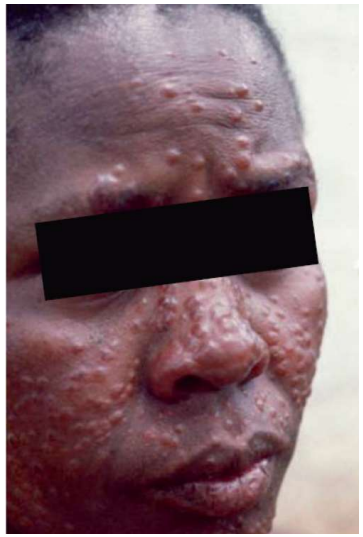
kala-azar in *sanscrito*
significa “malattia nera”

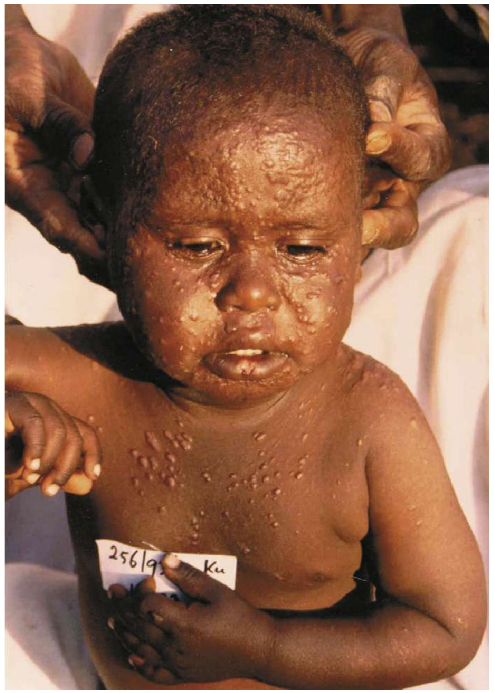
PKDL

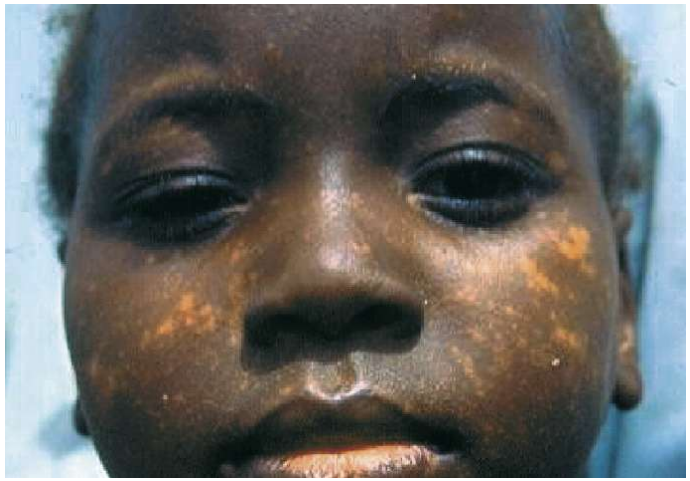




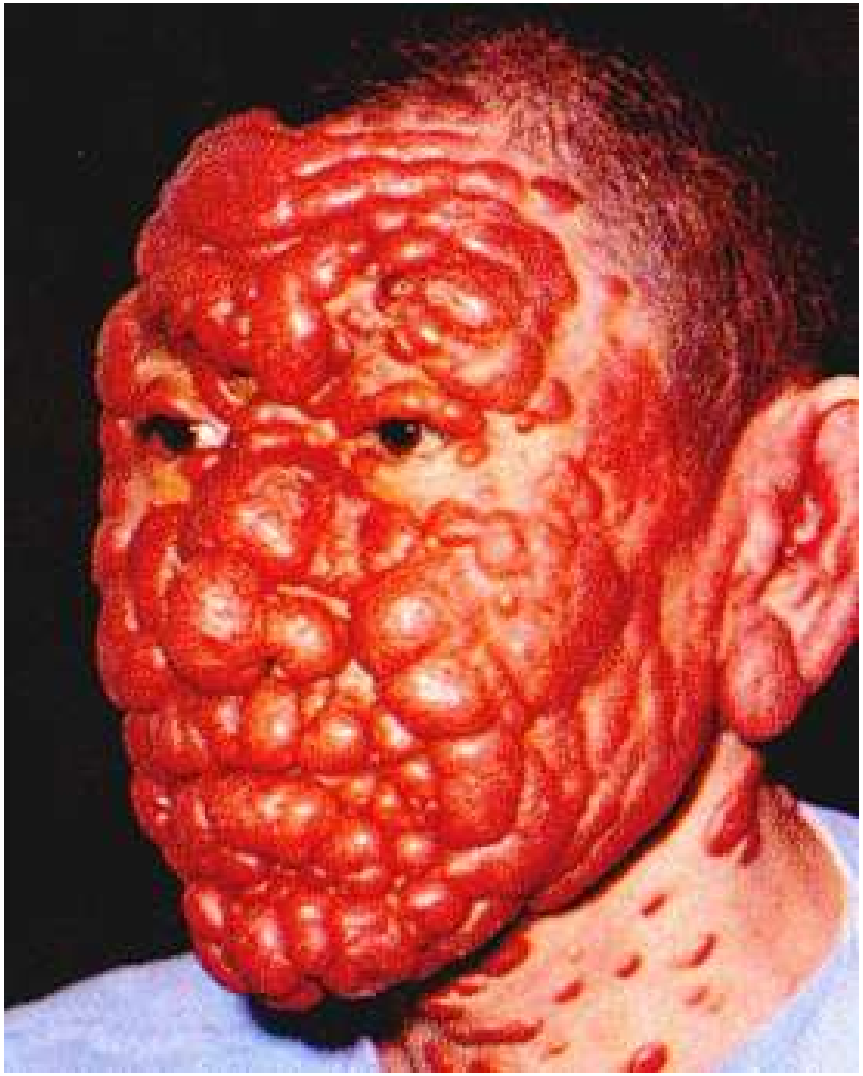








Post-Kala-Azar Dermal Leishmaniasis



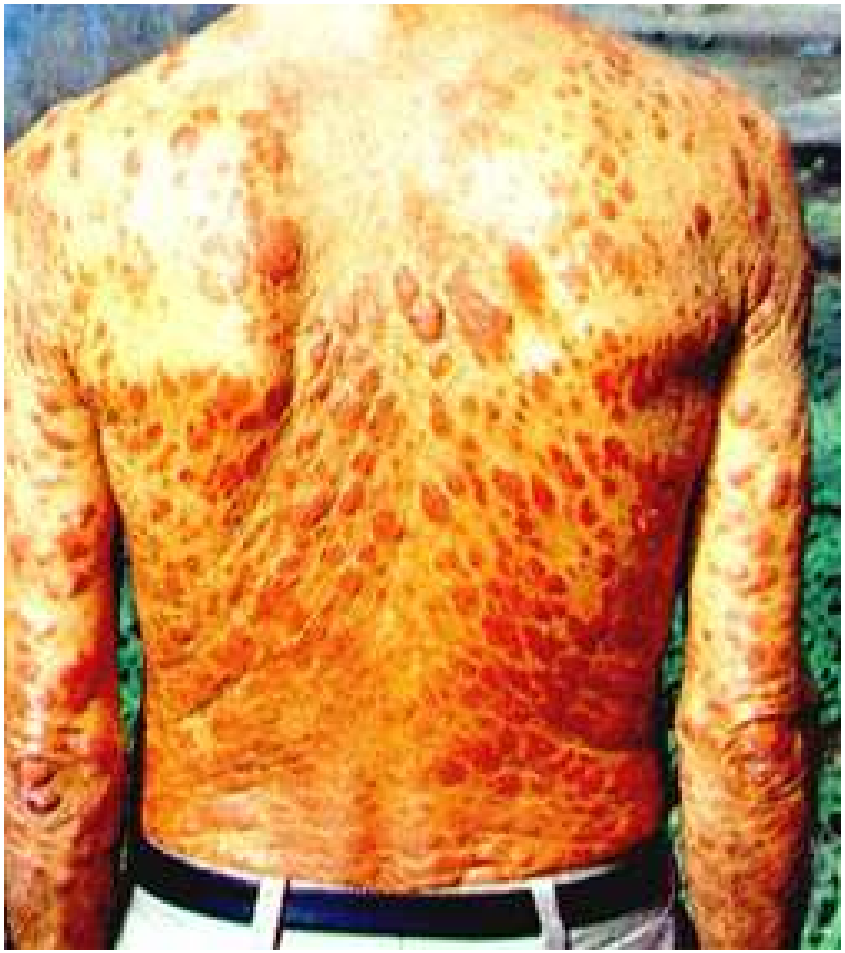
Post-kala-azar dermal leishmaniasis

THE LANCET Infectious Diseases Vol 3 February 2003 http://infection.thelancet.com

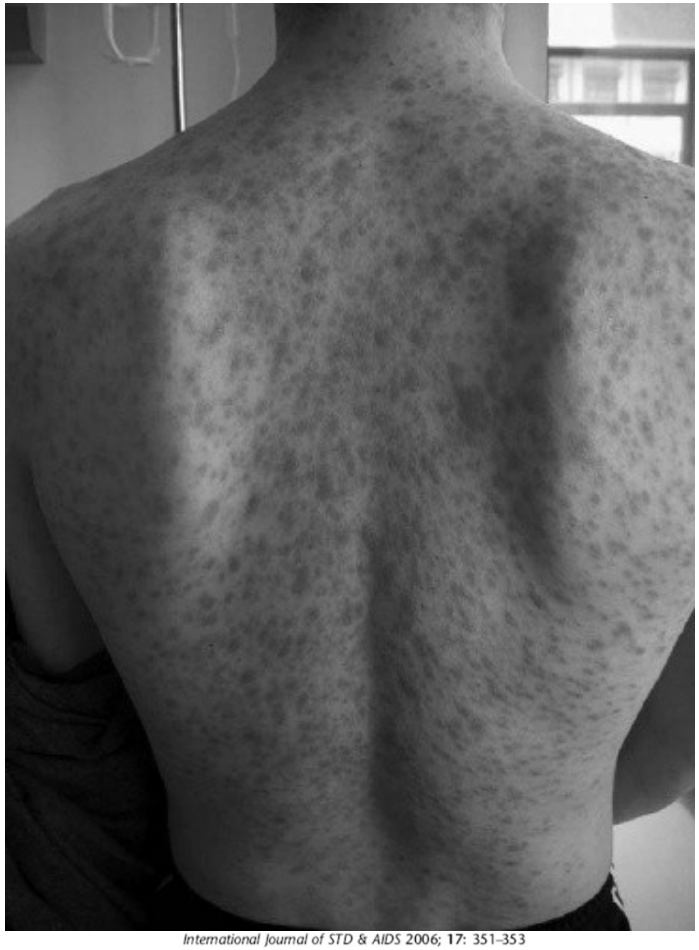
Table 1. Comparison of most important features of Sudanese and Indian PKDL

	Sudan	India
Clinical		
PKDL may occur in absence of previous VL	Yes	Yes
PKDL may occur while still on treatment for VL	Yes	No
PKDL may occur with evidence of visceralized disease (VL)	Yes	Yes
Most commonly described predilection over body	Face>trunk>arms>legs	Face>trunk>arms>legs
Type of rash	PN>MP>microP>M*	Erythema, induration M,P,N
Lymphadenopathy	Frequent	Rare
More severe disease found in	Young children, short interval after VL	Not known
Concomitant other post-kala-azar manifestations	Yes	Yes
Epidemiology		
Frequency of PKDL following VL	50–60%	5–10%
Highest prevalence reported in field study	4·8/100	4·8/1000
Interval between VL and PKDL		
most common	0–6 months	2–3 years
range	0–13 months†	6 months–32 years
Age distribution	Children, mean age 6 years	Young adults
Diagnosis		
Parasites may be demonstrated in smears	20–30%	20–40%
Parasites may be demonstrated by PCR	83%	94%
LST positive	16–65%	0–67%
Most difficult differential diagnosis	Leprosy	Leprosy
Treatment		
Treatment with stibogluconate	2–3 months	4 months
Spontaneous cure	The rule	Not reported, all cases are treated

*PN=papulo-nodular, MP=maculo-papular, MicroP=micropapular, M=macular, N=nodular. †In neighbouring Kenya, an interval of 30 years has been reported.



PKDL-India



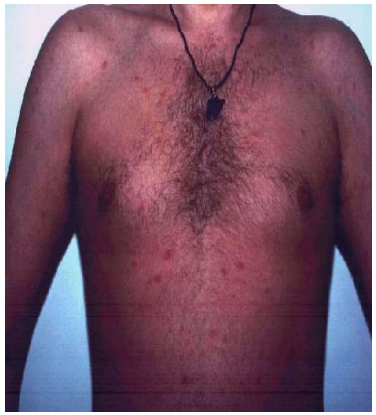
International Journal of STD & AIDS 2006; **17**: 351–353

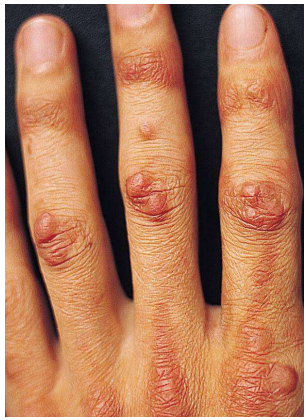
CASE REPORT

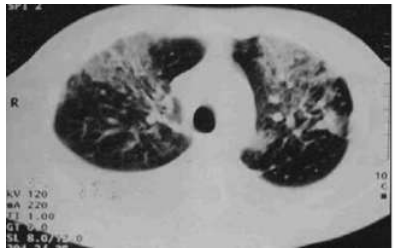
Atypical disseminated leishmaniasis resembling post-kala-azar dermal leishmaniasis in an HIV-infected patient

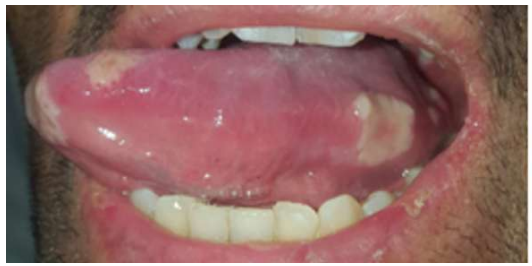
E Boumis MD[1], **P Chinello** MD[1], **C Della Rocca** MD[2], **M G Paglia** MD[1], **M F Proietti** MD[1] and **N Petrosillo** MD[1]

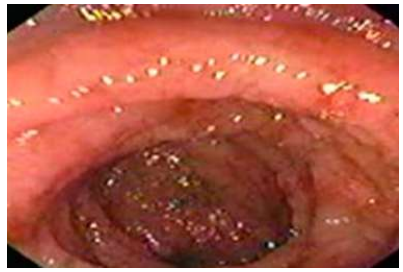
LEISHMANIASIS in HIV-Infected Patients

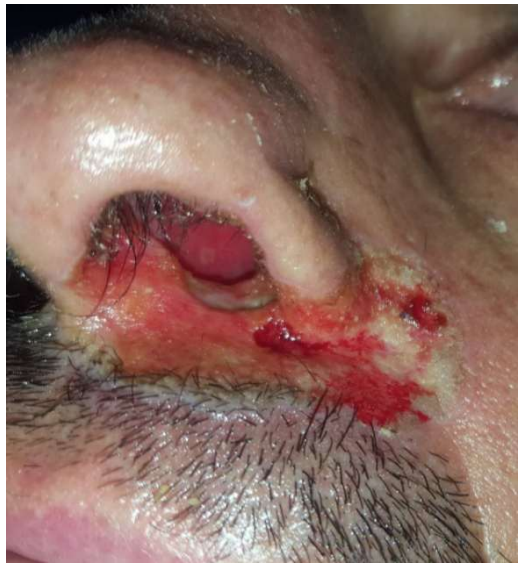


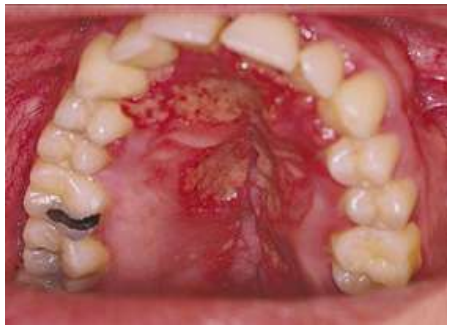












CD4	Number	Percentage
< 200/mm3	624	91.50
200 to 499/mm3	51	7.47
> 500/mm3	7	1.03
total	682	100

Clinical features	number	%
Visceral - typical	736	84.89
Visceral - atypical	82	9.46
Cutaneous	36	4.15
Others	6	0.69
Mucocutaneous	4	0.46
Mixed	3	0.35
	n = 867	

CLINICAL MICROBIOLOGY REVIEWS, Apr. 1997, p. 298–319 Vol. 10, No. 2
0893-8512/97/$04.00+0

Leishmania and Human Immunodeficiency Virus Coinfection: the First 10 Years

JORGE ALVAR,[1]* CARMEN CAÑAVATE,[1] BEATRIZ GUTIÉRREZ-SOLAR,[1] MARIBEL JIMÉNEZ,[1] FERNANDO LAGUNA,[2] ROGELIO LÓPEZ-VÉLEZ,[3] RICARDO MOLINA,[1] AND JAVIER MORENO[1]

Laboratorio de Referencia de Leishmaniasis, Servicio de Parasitología, Centro Nacional de Microbiología, Instituto de Salud Carlos III, 28220 Majadahonda, Madrid,[1] Servicio de Enfermedades Infecciosas, Centro de Investigaciones Clínicas, Instituto de Salud Carlos III, C/Sinesio Delgado s/n, 28029 Madrid,[2] and Unidad de Medicina Tropical y Parasitología Clínica, Servicio de Enfermedades Infecciosas, Hospital Ramón y Cajal, 28034 Madrid,[3] Spain

CLINICAL MICROBIOLOGY REVIEWS, Apr. 2008, p. 334–359 Vol. 21, No. 2
0893-8512/08/$08.00+0 doi:10.1128/CMR.00061-07

The Relationship between Leishmaniasis and AIDS: the Second 10 Years

Jorge Alvar,[1]* Pilar Aparicio,[1] Abraham Aseffa,[2] Margriet Den Boer,[3] Carmen Cañavate,[4] Jean-Pierre Dedet,[5] Luigi Gradoni,[6] Rachel Ter Horst,[3] Rogelio López-Vélez,[7] and Javier Moreno[8]

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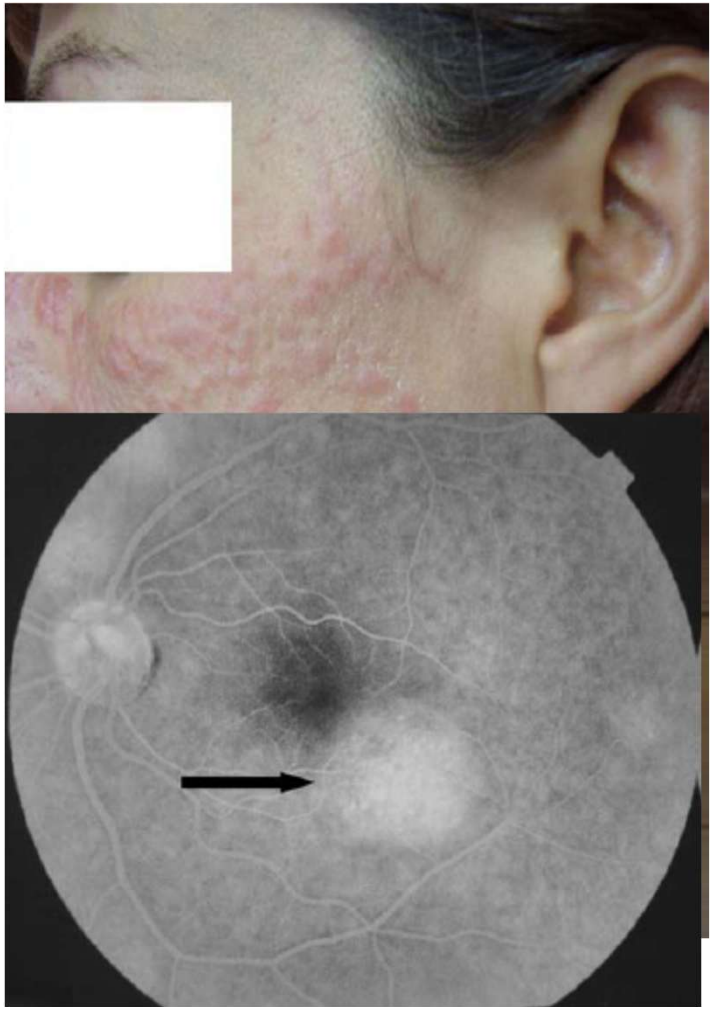
Post-kala-azar Dermal Leishmaniasis and Uveitis in an HIV-positive Patient



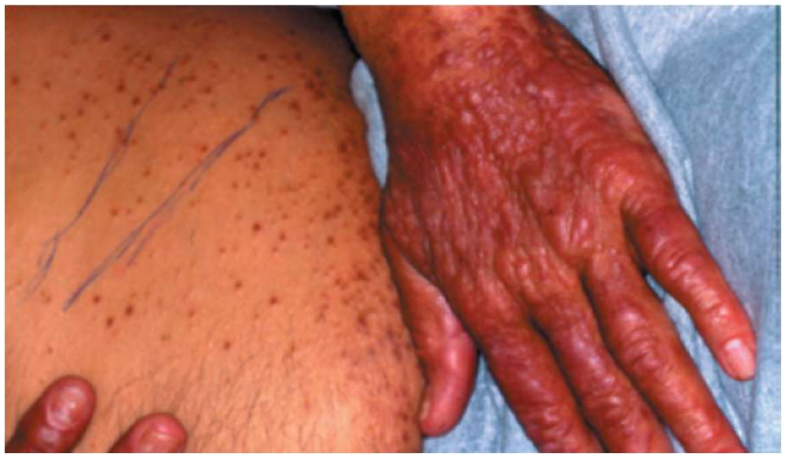
Uveitis Due to *Leishmania major* as Part of HAART-Induced Immune Restitution Syndrome in a Patient with AIDS

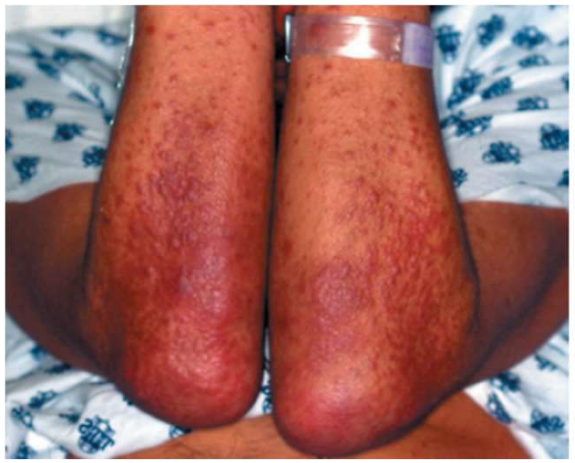
CORRESPONDENCE • CID 2002:34 (1 May) • 1279

Tropical medicine rounds

Diffuse cutaneous leishmaniasis associated with the immune reconstitution inflammatory syndrome

Smeeta Sinha, MD, Geover Fernández, MD, Rajendra Kapila, MD, W. Clark Lambert, MD, PhD, and Robert A. Schwartz, MD, MPH



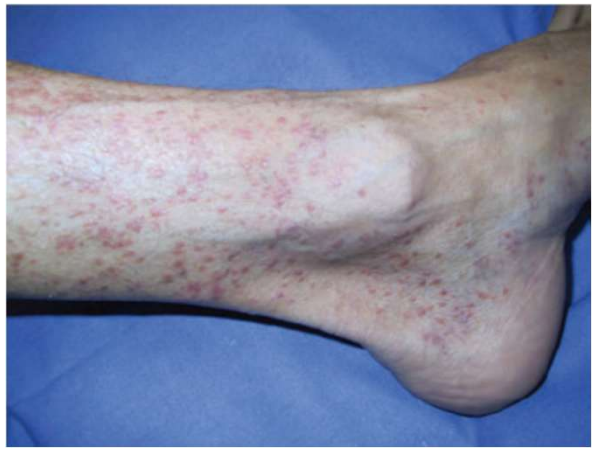


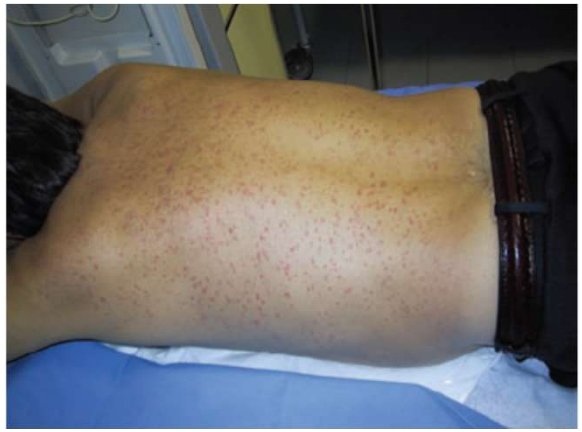
- Diffuse cutaneous leishmaniasis (DCL) is a rare anergic variant of leishmanial infection with the characteristic presentation of numerous nonulcerating nodules with an abundant parasite load, lack of visceral involvement, negative reaction to the leishmanin skin test, and a chronic course with incomplete response to treatment and frequent relapses.
- We report a case of DCL that developed in the context of the immune reconstitution inflammatory syndrome (IRIS) in a man with AIDS following initiation of antiretroviral therapy

Post-kala-azar dermal leishmaniasis as an immune reconstitution inflammatory syndrome in a patient with acquired immune deficiency syndrome

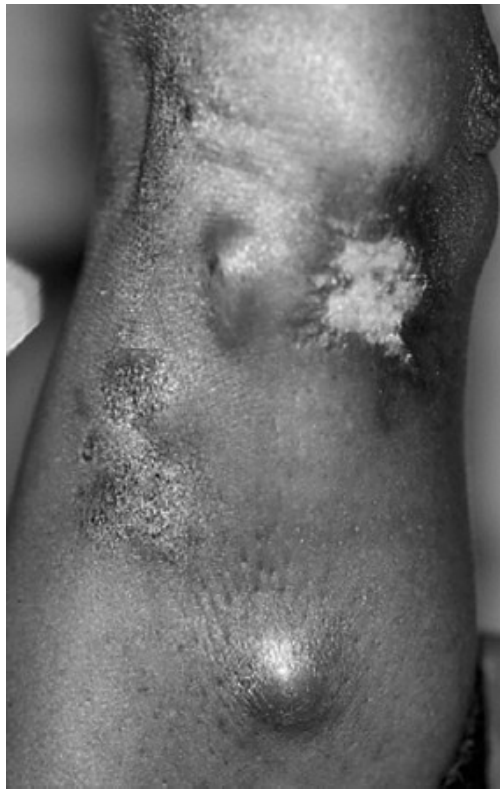
S. Antinori, E. Longhi, G. Bestetti, R. Piolini, V. Acquaviva, A. Foschi, S. Trovati, C. Parravicini, M. Corbellino and L. Meroni

- We report a 46-year-old patient with acquired immune deficiency syndrome who, 7 months after diagnosis of VL, developed PKDL and uveal leishmaniasis following HAART-induced immune recovery.
- In southern Europe PKDL seems to be an emerging clinical presentation among human immunodeficiency virus (HIV)-infected patients experiencing HAART-induced immune recovery after a previous diagnosis of VL





First Case of Cutaneous Reconstitution Inflammatory Syndrome Associated with HIV Infection and Leishmaniasis



Scand J Infect Dis 00: 1–3, 2004

Taylor & Francis healthsciences

CASE REPORT

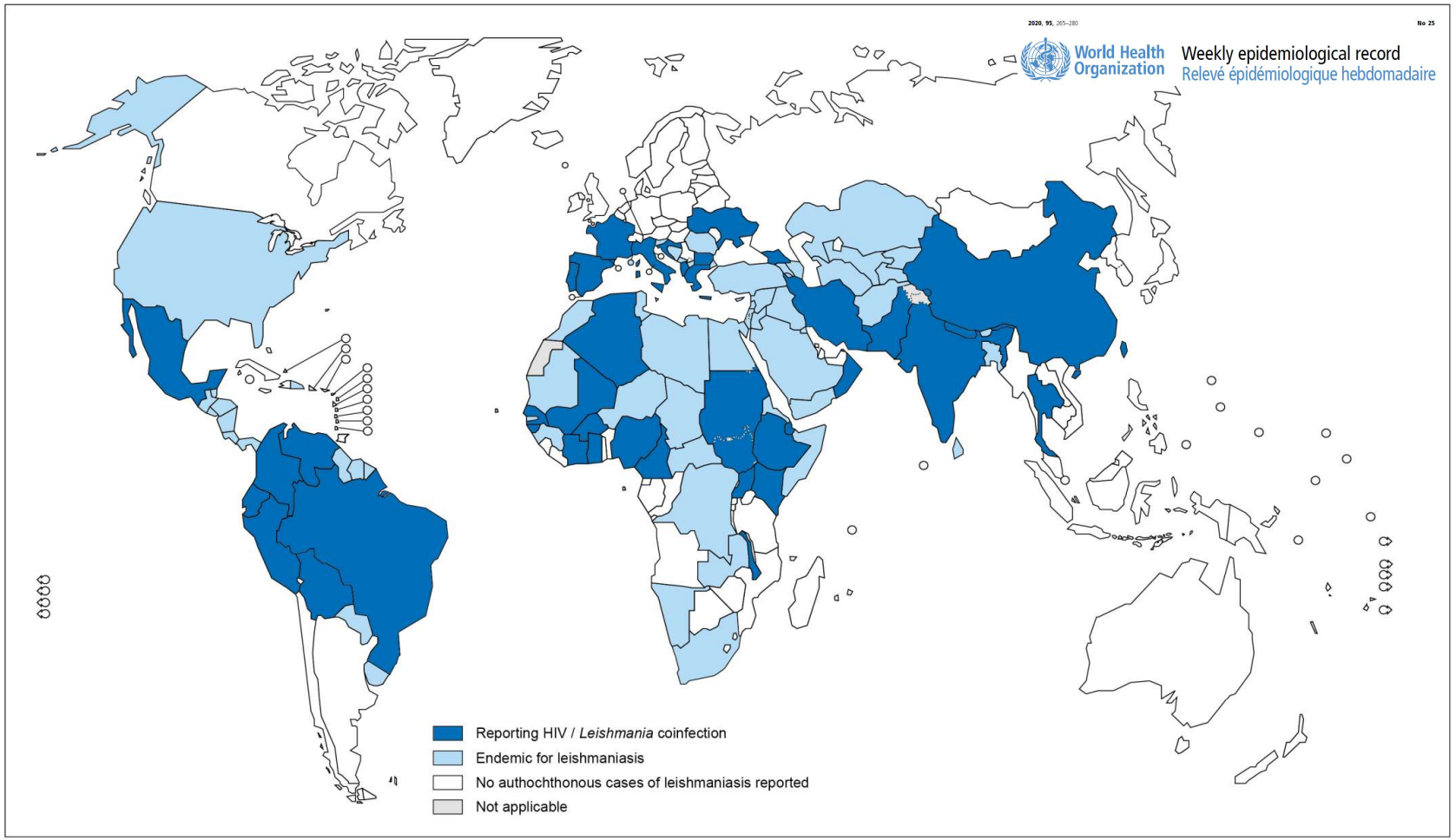
Two Case Reports of Symptomatic Visceral Leishmaniasis in AIDS Patients Concomitant with Immune Reconstitution due to Antiretroviral Therapy

ANTOINE BERRY[1], BRUNO ABRAHAM[1], JACQUES DEREURE[2], VERONIQUE PINZANI[1], PATRICK BASTIEN[2] and JACQUES REYNES[1]

Table I. *Characteristics of the patients*

	Case 1	Case 2
Gender	F	M
Age (y)	45	36
CDC classification	B	B
HIV related infections	oral candidiasis	Herpes zoster
ARV therapy	ddI/IDV/HU	D4T/ddI/LPV
Initial HIV RNA (copies/ml)	1,700,000	354,000
Clinical VL symptoms: before ARV therapy/at the onset of VL symptoms		
Fever (°C)	37.5/38.5–40	37.8/40
Splenomegaly	+/++	−/+
Hepatomegaly	−/+	−/−
Biological VL signs: before ARV therapy/ at the onset of VL symptoms		
Haemoglobin (g/dl)	13/11.9	12.5/12
Leukocyte (10^6/l)	2.5/1.8	3.5/3
Platelet (10^6/l)	95/12	180/107
Biological VL diagnostic		
Bone marrow aspirate examination	+	Not done
Blood culture	+	+
PCR L. spp. (blood)	+	+
Indirect immunofluorescence	1: 640	1: 640
Counter immuno-electrophoresis	3 bands	3 bands
Period between initiation of ARV therapy and the onset of VL symptoms (d)	10	6
CD4+ cell count (cells/ml)		
Before ARV therapy /at VL diagnosis	186/226	15/66
% increase	21%	340%
CD4+ cell count (%)		
Before ARV therapy /at VL diagnosis	15.5/25.4	2.2/10.4
% increase	64%	372%

Global distribution of leishmaniasis and countries reporting HIV/*Leishmania* coinfection



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

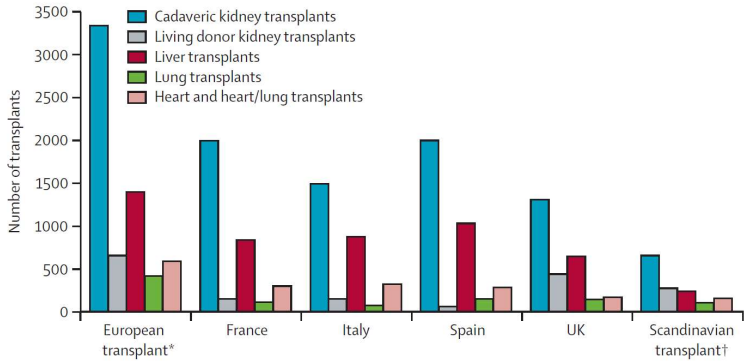
World Health Organization

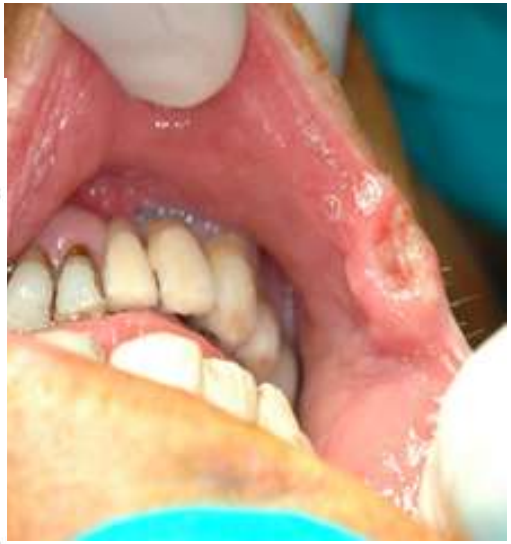
Leishmaniasis among organ transplant recipients

Spinello Antinori, Antonio Cascio, Carlo Parravicini, Roberto Bianchi, Mario Corbellino

Lancet Infect Dis 2008; 8: 191–99

Department of Clinical Sciences L Sacco, Section of Infectious Diseases and Immunopathology, University of Milan, Milan, Italy (Prof S Antinori MD, M Corbellino MD, C Parravicini MD); Department of Human Pathology, Institute of Infectious Diseases, University of Messina, Messina, Italy (A Cascio MD); and



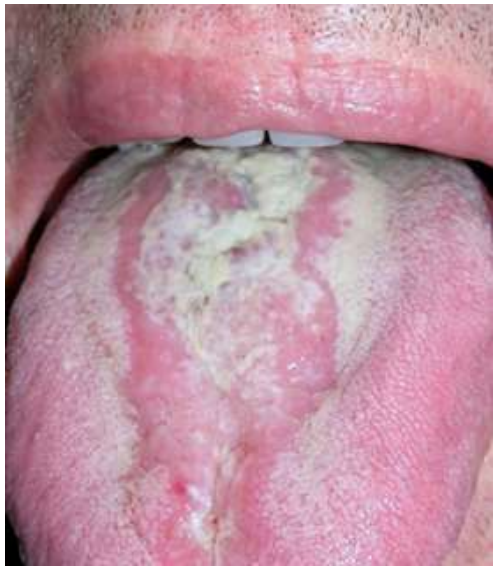


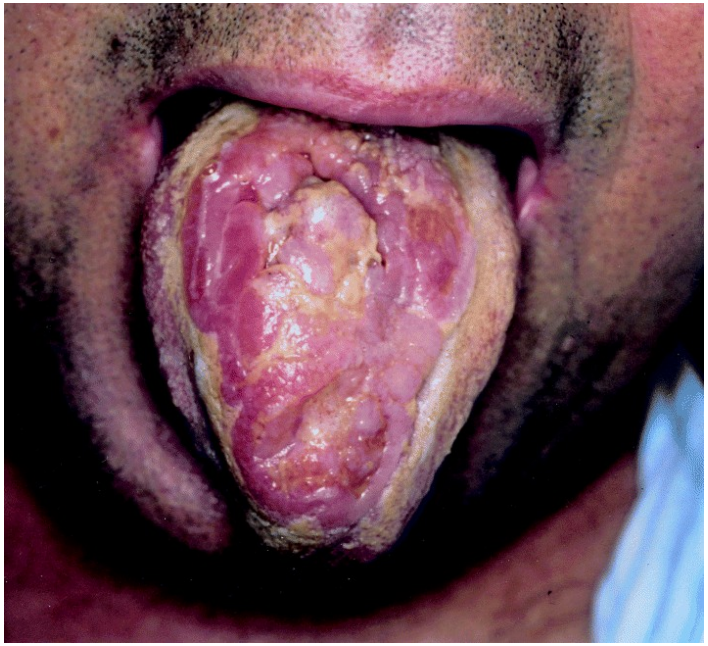
Recurrent leishmaniasis in kidney transplant recipients: report of 2 cases and systematic review of the literature

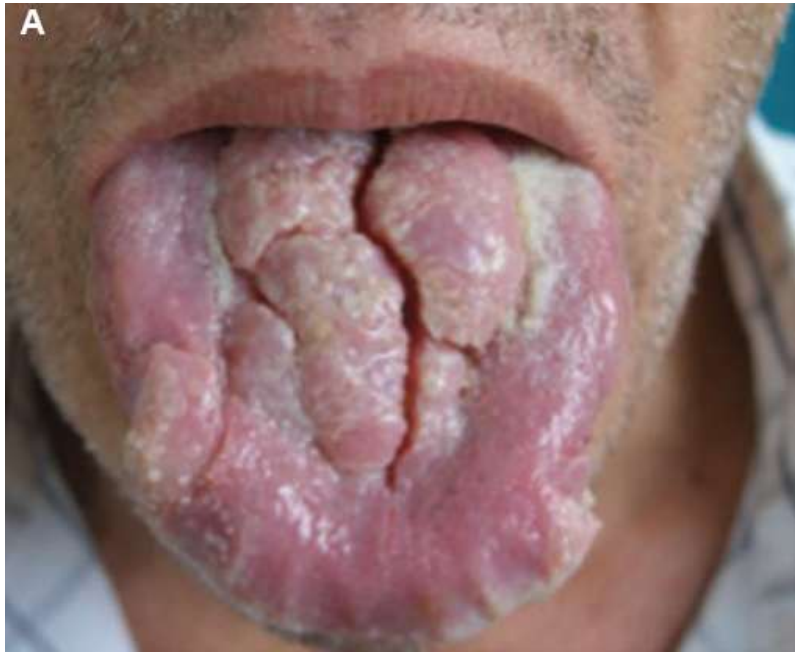
I. Simon, K.M. Wissing, V. Del Marmol, S. Antinori, M. Remmelink, E. Nilufer Broeders, J.L. Nortier, M. Corbellino, D. Abramowicz, A. Cascio. Recurrent leishmaniasis in kidney transplant recipients: report of 2 cases and systematic review of the literature. Transpl Infect Dis 2011.

I. Simon[1], K.M. Wissing[2], V. Del Marmol[3], S. Antinori[4], M. Remmelink[5], E. Nilufer Broeders[1], J.L. Nortier[1], M. Corbellino[4], D. Abramowicz[1], A. Cascio[6]

[1]Department of Nephrology, Erasme Hospital, Université



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ActaDV

Mucocutaneous Leishmaniasis due to *Leishmania infantum* Infection

Kai-Philipp LINSE[1], Christian BOGDAN[2], Holger A. HAENSSLE[1#] and Ferdinand TOBERER[1#]
[1]Department of Dermatology, University Hospital Heidelberg, Heidelberg, and [2]Mikrobiologisches Institut – Klinische Mikrobiologie, Immunologie und Hygiene, Universitätsklinikum Erlangen und Friedrich-Alexander-Universität (FAU) Erlangen, Erlangen, Germany. E-mail: kai-philipp.linse@med.uni-heidelberg.de
[#]These authors contributed equally to this work.
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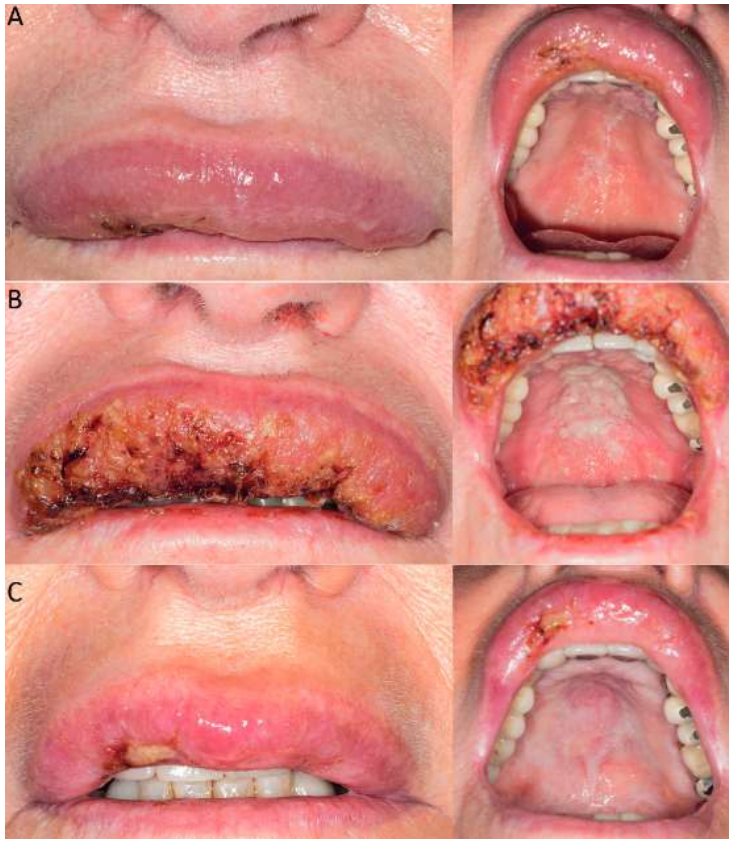


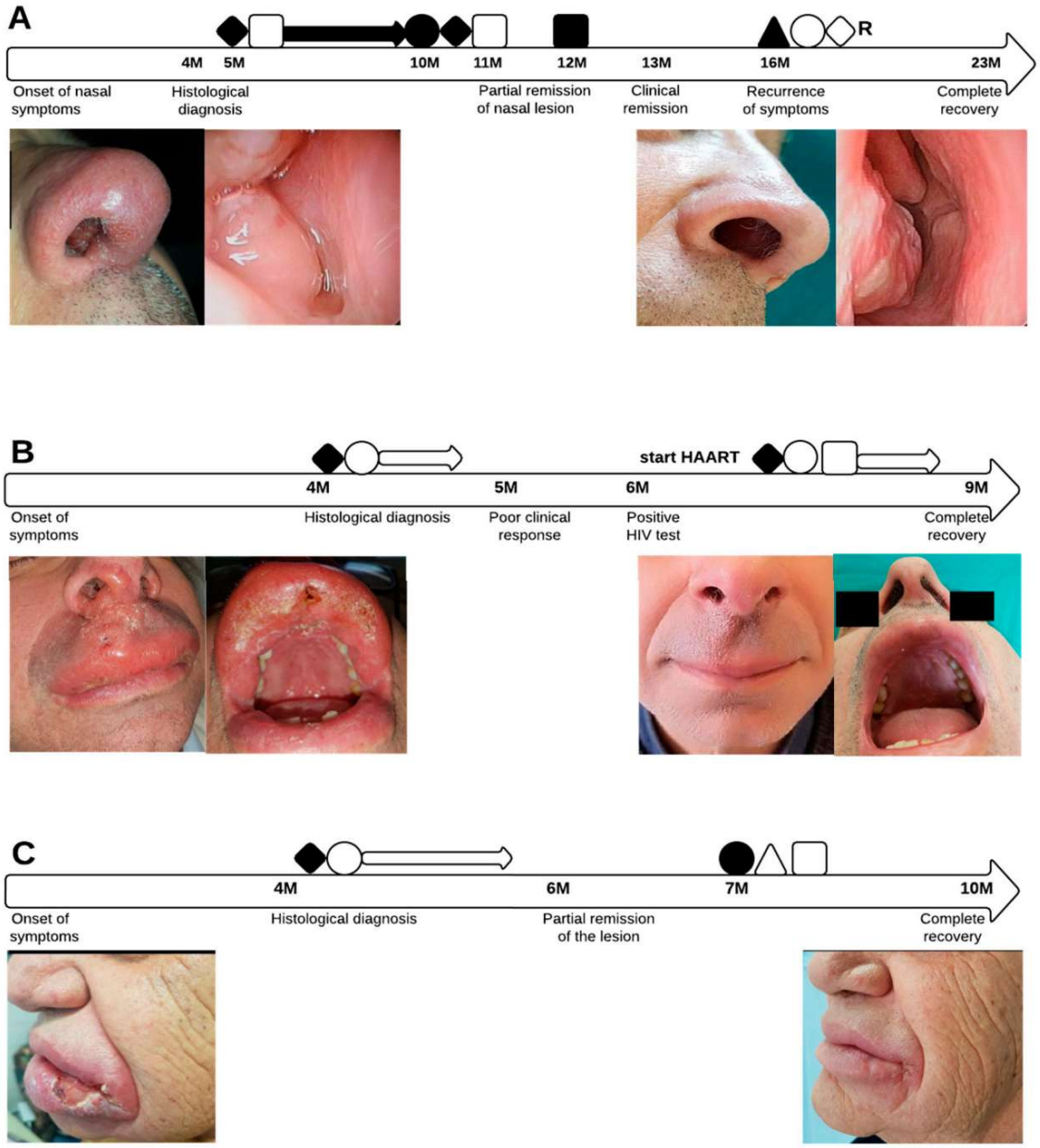
microoorganisms

MDPI

Case Report

Autochthonous Cases of Mucosal Leishmaniasis in Northeastern Italy: Clinical Management and Novel Treatment Approaches

Valeria Gaspari [1,*], Irene Zaghi [2], Giovanni Macri [3], Annalisa Patrizi [1,4], Nunzio Salfi [5], Francesca Locatelli [5], Elena Carra [6], Maria Carla Re [4,7] and Stefania Varani [4,7]



pathogens

MDPI

Brief Report

Mucosal Relapse of Visceral Leishmaniasis in a Child with SARS-CoV-2 Infection

Claudia Colomba [1,2], Giovanni Boncori [1], Chiara Albano [1,*], Valeria Garbo [1], Sara Bagarello [1], Anna Condemi [1], Salvatore Giordano [2] and Antonio Cascio [1,3]

Table 1. Table of comparisons between our case and cases identified in the literature.

Author/Country/ Year [Ref.]	Age/Sex	Pre-Existing Medical Condition	Risk Factors	VL Treatment	Time of Relapse	Location of Recurrence	Symptoms	Diagnostic Test
Jeziorski et al./ France/2009 [15]	7 y/F	JIA	Immunosuppressive therapy (anti-TNFα)	L-AmB 24 mg/kg in 6 doses	Two years after treatment of VL	Nasal mucosa	Splenomegaly, recurring nosebleeds	Pathological examination and PCR on mucosal lesion
Jeziorski et al./ France/2015 [16]	4 y/F	JIA, bilateral uveitis	Immunosuppressive therapy (anti-TNFα)	L-AmB 24 mg/kg in 6 doses	Two years after treatment of VL	Nasal mucosa	Splenomegaly, recurring nosebleeds	Pathological examination and PCR on the mucosal lesion
Our case Colomba et al./ Italy/2023	4 y/F	COVID-19	No	L-AmB 3 mg/kg/day for 5 days, other dose on 10th day	Seven months after treatment of VL	Oral mucosa	Fever, hepatosplenomegaly, gingival bleeding	PCR on the mucosal lesion

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

journal homepage: www.elsevier.com/locate/tmaid

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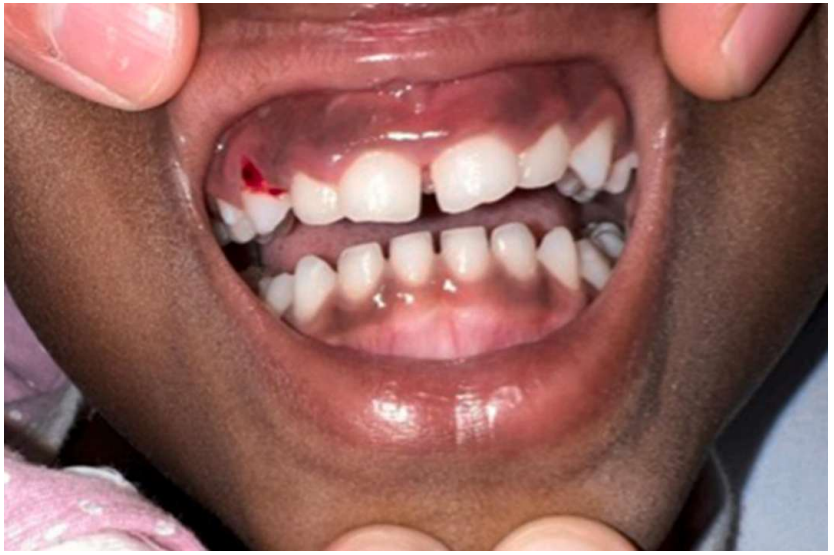
Fever with spontaneous gingival bleeding: A diagnostic challenge

Claudia Colomba [a,b], Chiara Albano [a,*], Giovanni Boncori [a], Anna Condemi [a], Antonio Cascio [a,c]

[a] Department of Health Promotion, Maternal and Child Care, Internal Medicine and Medical Specialties "G.D'Alesandro", University of Palermo, Palermo, Italy
[b] Division of Pediatric Infectious Diseases, "G. Di Cristina" Hospital, ARNAS Civico Di Cristina Benfratelli, Palermo, Italy
[c] Infectious and Tropical Diseases Unit, AOU Policlinico "P. Giaccone", Palermo, Italy



Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Case report

Good's syndrome and recurrent leishmaniasis: A case report and review of literature

Manlio Tolomeo *, Silvia Bonura, Michelle Abbott, Antonio Anastasia, Claudia Colomba, Antonio Cascio

Department of Health Promotion Sciences, Section of Infectious Diseases, University of Palermo, Via del Vespro 129, 90127, Palermo, Italy

We report the case of a 56-year-old Caucasian male affected by thymoma and myasthenia gravis that developed **recurrent visceral leishmaniasis** 11 years after thymectomy. After treatment of each relapse with liposomal amphotericin B the PCR-Leishmania was negative and the patient showed clinical improvement. An immunologic work-up was performed showing lymphopenia with an important decrease in **CD4+ T cells (52 cells/μ**) and CD4/CD8 ratio (0.2). HIV test was negative. On the basis of previous **thymoma and myasthenia gravis** and on the basis of the immunological profile a diagnosis of Good's syndrome was made.

Journal of Infection and Public Health 13 (2020) 306–308

Contents lists available at ScienceDirect

Journal of Infection and Public Health

journal homepage: http://www.elsevier.com/locate/jiph

Visceral leishmaniasis in a patient with active HBV/HDV co-infection

Tommaso Lupia*, Silvia Corcione, Lucio Boglione, Giuseppe Cariti, Francesco G. De Rosa

rsity of Turin, Italy

Antiviral Therapy 10:695–696

Correspondence

Visceral leishmaniasis during pegylated interferon therapy for chronic hepatitis C: first report

Antonio Cascio[1], Spinello Antinori[2], Filippo Ricciardi[1], Giuseppa Costantino[1] and Chiara Iaria[3]*

Visceral leishmaniasis causes fever and decompensation in patients with cirrhosis

Infections and fever due to bacterial infections are well-known complications of liver cirrhosis, and often trigger decompensation and death.[1] Visceral leishmaniasis (VL), a protozoan infection endemic in the Mediterranean area, causes a febrile disease, the clinical and laboratory features (splenomegaly, pancytopenia, reduced serum albumin and increased γ-globulin concentrations) of which largely overlap with those of cirrhosis.[2,3] Although the areas where VL is endemic coincide with areas where the prevalence of cirrhosis is high, no study has described VL in patients with cirrhosis.

During a 12-year period, all patients with cirrhosis admitted for decompensation and fever lasting more than 1 week, unresponsive to broad-spectrum antibiotics, underwent diagnostic procedures for VL. For each case diagnosed as VL, three consecutive cases of bacterial infection observed in the same period were enrolled. Cirrhosis was defined by liver histology or clinical, laboratory, ultrasonographic and endoscopic findings. VL was diagnosed by the immunofluorescent-specific antibody test (IFAT) and confirmed by the identification of *Leishmania* from Giemsa-stained smears of bone marrow or spleen

Apart from a long-lasting fever, there were no clear-cut clues to suspect VL. Some significant differences in the presentation data between VL and bacterial infections were found (table 1), but their clinical use is hampered by a substantial overlap of the laboratory values between VL and bacterial infection cases. Only white blood cell and γ-globulin data are of potential value.

IFAT serology is a sensitive and specific test for the diagnosis of VL in patients with cirrhosis; notably, IFAT was negative in all patients with bacterial infections and in 51 additional patients with cirrhosis without fever (table 1). In a series including 16 patients with

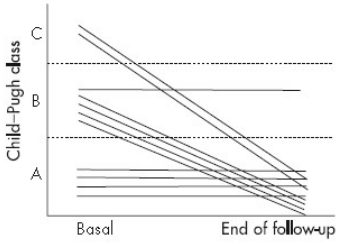


Figure 1 Child–Pugh class before and after treatment for visceral leishmaniasis.

Pasquale Pagliano
1st Division of Infectious Diseases, D Cotugno Hospital, Naples, Italy

Novella Carannante
Department of Infectious Diseases, Viral Hepatitis Unit, Second University of Naples, Naples, Italy

Marina Gramiccia
Department of Infectious, Parasitic and Immunomediated Diseases, Istituto Superiore di Sanità, Rome, Italy

Tiziana Ascione, Gianfranca Stornaiuolo
Department of Infectious Diseases, Viral Hepatitis Unit, Second University of Naples, Naples, Italy

Luigi Gradoni
Department of Infectious, Parasitic and Immunomediated Diseases, Istituto Superiore di Sanità, Rome, Italy

Francesco S Faella
1st Division of Infectious Diseases, D Cotugno Hospital, Naples, Italy

Giovanni B Gaeta
Department of Infectious Diseases, Viral Hepatitis Unit, Second University of Naples, Naples, Italy

Correspondence to: Professor G B Gaeta, Department of Infectious Diseases, Second University of Naples, Via Cotugno 1, 80135 Naples, Italy; giovannib.gaeta@unina2.it

doi: 10.1136/gut.2007.119495

Colomba *et al. BMC Infectious Diseases* (2019) 19:328
https://doi.org/10.1186/s12879-019-3947-x

BMC Infectious Diseases

CASE REPORT Open Access

Direct-acting antivirals and visceral leishmaniasis: a case report

Claudia Colomba*, Laura Saporito, Paola Di Carlo, Manlio Tolomeo, Adriana Cervo, Alberto Firenze, Marcello Trizzino and Antonio Cascio

BMC Infectious Diseases

Case report

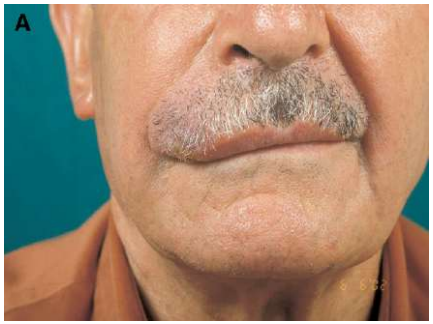
Leishmania infantum leishmaniasis in corticosteroid – treated patients

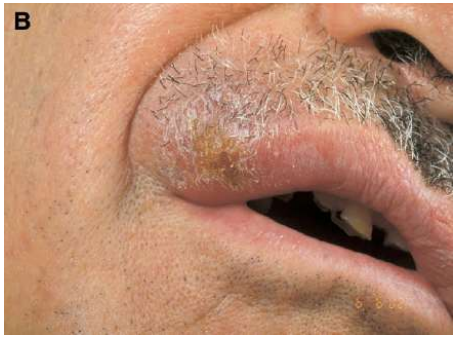
Silvia Pittalis, Emanuele Nicastri*, Francesco Spinazzola, Piero Ghirga, Michele De Marco, Maria Grazia Paglia and Pasquale Narciso

Case presentation: Three cases of *Leishmania infantum* leishmaniasis in corticosteroid (CS)-treated patients are reported: an isolated lingual leishmaniasis in a farmer treated with CS for asthma, a severe visceral leishmaniasis associated with cutaneous lesions in a woman with *myasthenia gravis*, and a visceral involvement after cutaneous leishmaniasis in a man receiving CS.

Case report: leishmaniasis of the upper lip

Stefano Veraldi, MD,[a] Silvia Bottini, MD,[b] Maria Chiara Persico, MD,[b] and Luisa Lunardon, MD,[b] Milan, Italy
INSTITUTE OF DERMATOLOGICAL SCIENCES, UNIVERSITY OF MILAN, IRCCS FOUNDATION, OSPEDALE MAGGIORE POLICLINICO, MANGIAGALLI AND REGINA ELENA

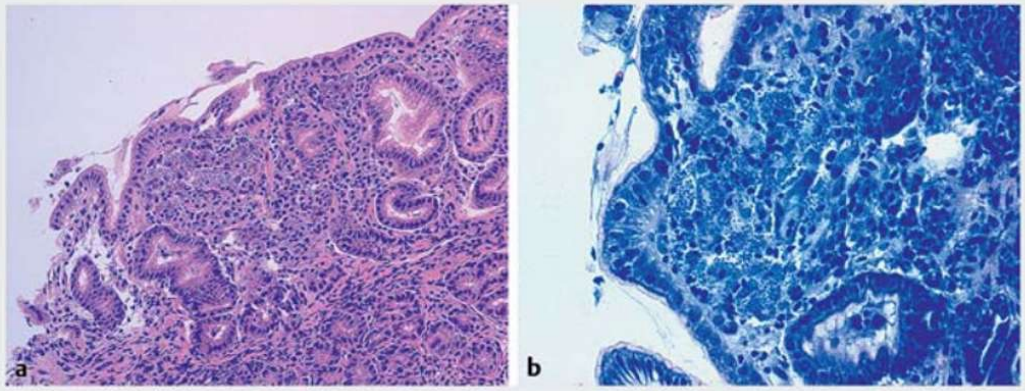




Intestinal leishmaniasis: a rare case of enteropathy

We report the case of a 34-year-old immunosuppressed woman who presented with severe malabsorption and weight loss. Her history was remarkable for systemic lupus erythematosus (SLE) complicated by antiphospholipid syndrome, lupus nephritis, and recurrent myocardial pericarditis; she had been treated with combined intensive immunosuppressive regimens. Her antitransglutaminase antibodies were negative and a flare-up of SLE was excluded.

Esophagogastroduodenoscopy revealed remarkable atrophy of the duodenal mucosa, which appeared atypical for both celiac and Whipple disease. A small-bow-



▶ **Fig. 1** Histology of the duodenal biopsy showing numerous macrophages in the lamina propria of the duodenal mucosa, with abundant intracytoplasmic *Leishmania* amastigote parasites on: **a** hematoxylin and eosin (H&E) staining (magnification × 200); **b** Giemsa staining (× 200).

Beatrice Marinoni[1], Gian E. Tontini[1,2], Marco Maggioni[3], Stefania Orlando[1], Francesca Ferretti[1,2], Maurizio Vecchi[1,2], Luca Elli[1,2]

1 Gastroenterology and Endoscopy Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
2 Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
3 Pathology Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Clinical Microbiology and Infection 26 (2020) 1345–1346

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Picture of a Microorganism

Intestinal leishmaniasis

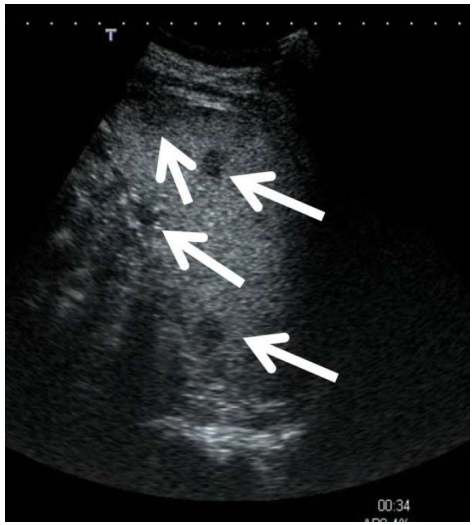
A. Chattopadhyay [1], S. Mittal [1], K. Gupta [2], V. Dhir [1], S. Jain [1, *]

[1] Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[2] Histopathology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Focal spleen lesions in visceral leishmaniasis, a neglected manifestation of a neglected disease: report of three cases and systematic review of literature

Francesca Rinaldi[1] · Susanna Giachè[1] · Michele Spinicci[1] · Paola Corsi[2] · Silvia Ambu[2] · Giacomo Gianfaldoni[3] · Luigi Rigacci[3] · Umberto Arena[1] · Alessandro Bartoloni[1,2] · Lorenzo Zammarchi[1,2]

VL may present with splenomegaly and multiple spleen focal lesions and must be added to the list of possible differential diagnosis of spleen focal lesions. The most common radiological patterns are multiple subcentimetric or centimetric lesions hypoechoic at ultrasonography and hypodense at CT scan. In these cases, PET-CT typically presents with an intense FDG spleen uptake with variable pattern (diffuse, focal or diffuse with superimposed focal uptake).



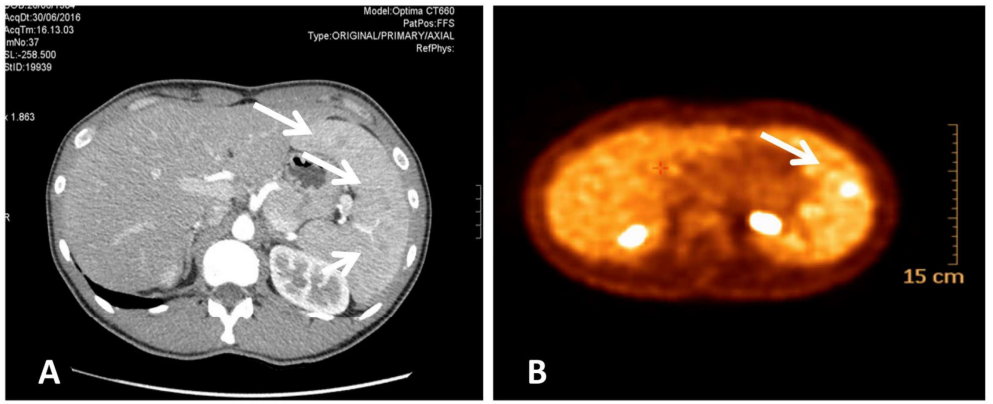


Fig. 4 Case 2: Positron emission tomography-computed tomography (PET-CT) imaging. **a** Multiple hypointense splenic lesions (arrows); **b** diffuse and superimposed multifocal splenic FDG uptake (arrow)

Annals of Nuclear Medicine
https://doi.org/10.1007/s12149-019-01381-6

ORIGINAL ARTICLE

18F-FDG PET/CT in visceral leishmaniasis: uptake patterns in the context of a multiannual outbreak in Northern Italy

Lucia Zanoni[1] · Stefania Varani[2,3] · Luciano Attard[4] · Joshua James Morigi[3,6] · Elisa Vanino[4,5] · Margherita Ortalli[3] · Cristina Fonti[1] · Pierluigi Viale[4,5] · Maria Carla Re[2,3] · Stefano Fanti[1,3] · Valentina Ambrosini[1,3]

Received: 6 April 2019 / Accepted: 18 June 2019

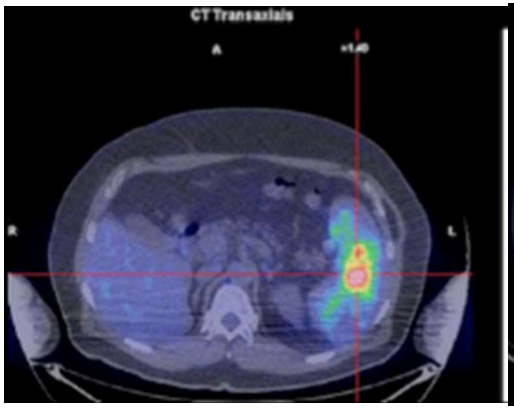


Fig. 2 FDG PET/CT showing multifocal pathological uptake within the spleen. The patient presented with chronic fever. At a diagnostic CT performed 8 days before the PET scan, unclear hypodense nodules

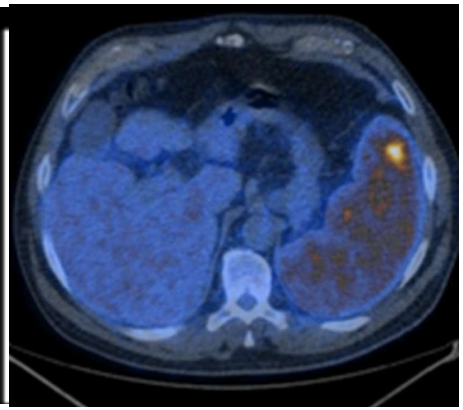


Fig. 3 FDG PET/CT showing multiple focal uptake areas within the spleen (SUVmax = 12.4 at the anterior pole; SLR = 2.9; FDR = 2.2). The images from the low-dose non-diagnostic non-contrastenhanced CT showed absence

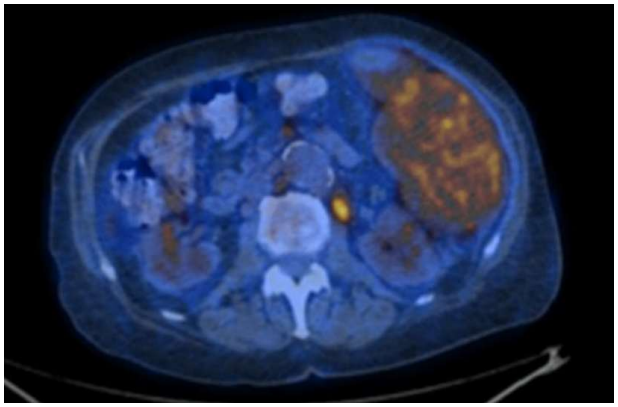


Fig. 4 The image shows diffuse FDG uptake within the enlarged spleen together with extra-splenic hypermetabolic areas in a patient diagnosed with VL after PET/CT. In particular,

Wien Med Wochenschr (2017) 167:78–82
DOI 10.1007/s10354-016-0527-1

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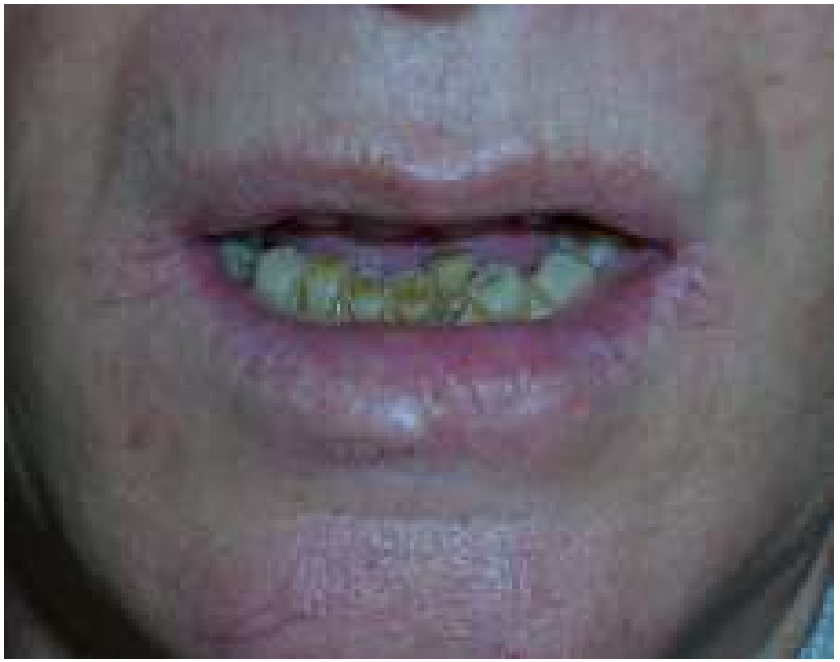
Wiener Medizinische Wochenschrift

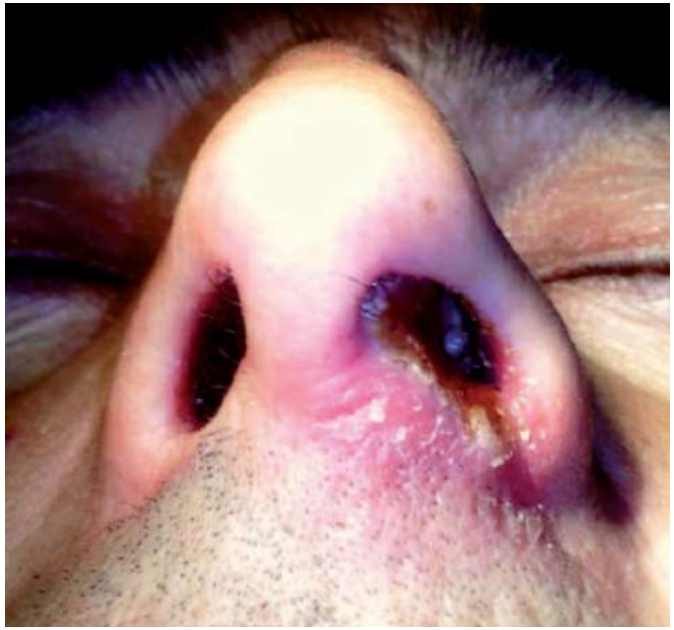
Cutaneous and visceral leishmaniasis during anti-TNFα therapy

Claudio Guarneri · Valentina Bevelacqua · James W. Patterson · Georgi Tchernev



Rheumatology 2012;51:1517–1518
doi:10.1093/rheumatology/kes030
Advance Access publication 15 March 2012

Mucocutaneous leishmaniasis in a patient treated with anti-TNF-α therapy



- 49-year-old Caucasian man, a woodsman, born in Albany and living in Tuscany (Italy) since 1999. He had been diagnosed as having AS 20 years ago.
- After the 20th infusion of adalimumab, the patient complained about rhinorrhoea, occasional epistaxis from the left nostril and nose-breathing difficulties

Adalimumab was discontinued, and he was treated succesfully with a 5-day course of intravenous (IV) liposomal amphotericin B (total dose 975 mg)

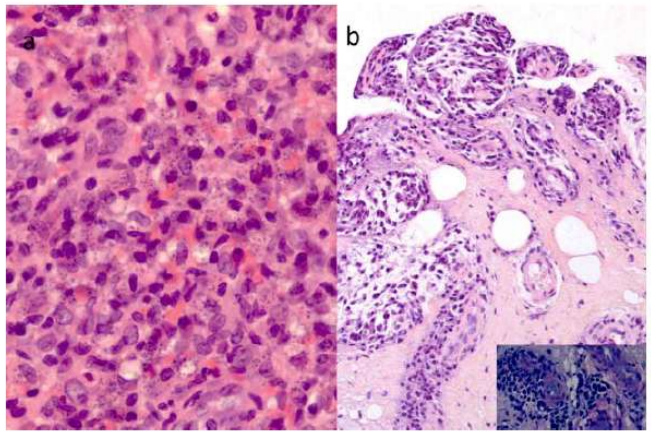
- After 3 months and a full ear, nose, and throat examination, adalimumab was reintroduced due to a florid reactivation of AS, leading to good clinical control of the disease within 1 month.
- Two years later, he returned with persistent right knee monoarthritis of 3 weeks' duration

Arthritis Rheumatol. 2016 Apr;68(4):931. doi: 10.1002/art.39541.

Synovial Leishmaniasis.

Guidelli GM[1], De Stefano R[1], Galeazzi M[1], Selvi E[1].

Clinical Images: Synovial leishmaniasis



- Adalimumab was stopped, and the patient was re-treated with IV liposomal amphotericin B (3 mg/kg/day for 5 days), with mild improvement of the knee arthritis.
- Two months later, another synovial biopsy was performed, showing complete disappearance of the intracellular parasites

Infection (2011) 39:375–378
DOI 10.1007/s15010-011-0109-5

CASE REPORT

Seronegative visceral leishmaniasis with relapsing and fatal course following rituximab treatment

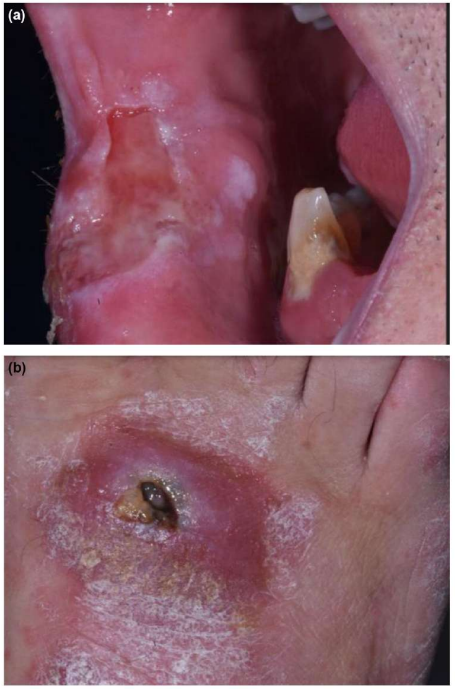
A. Casabianca · M. Marchetti · F. Zallio · E. Feyles · E. Concialdi · E. Ferroglio · A. Biglino

We describe a case of VL characterized by negative serologic testing, a relapsing course, and a fatal outcome 2 years after the patient had been successfully treated for non-Hodgkin's lymphoma with rituximab. Diagnosis of VL may be further delayed or even missed in patients treated with drugs that interfere with specific antibody production unless specific diagnostic methods, such as bone marrow examination and parasite DNA amplification/detection, are routinely employed.

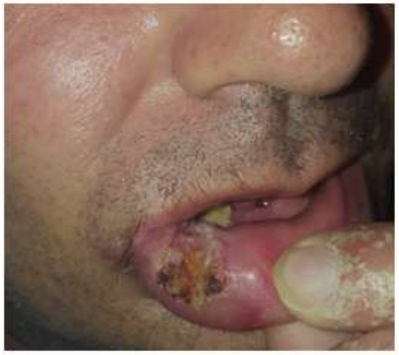
bjh images in haematology

Visceral leishmaniasis after alemtuzumab in a patient with chronic lymphocytic leukaemia

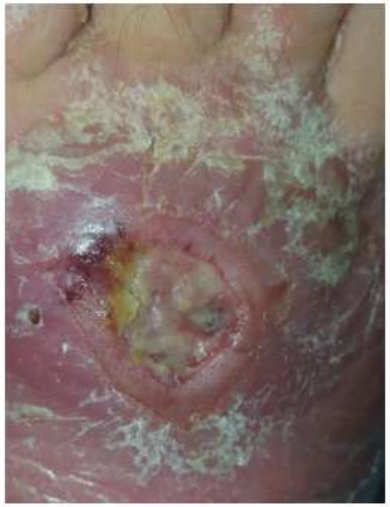
Vincenzo Pitini[1] Antonio Cascio[2] Carmela Arrigo[1] Giuseppe Altavilla[1]



Figs. 1a and b. Ulcerated lesions by Leishmania onto the oral mucosa (a) and right foot (b) in a 46-year-old patient with psoriasis.



A. Cascio 2018



Leishmania infection in psoriasis.

Colomba C, Saporito L, Bonura S, Campisi G, Di Carlo P, Panzarella V, Caputo V, Cascio A.

J Infect. 2020 May;80(5):578-606. doi: 10.1016/j.jinf.2020.01.019. Epub 2020 Feb 4.

Leishmaniasis and Biologic Therapies for Rheumatologic Diseases

Cascio A, **Iaria M**, Iaria C.

Semin Arthritis Rheum. 2010 Dec;40(3):e3-5.

Author, yr, country (ref)	Age/sex	Disease	Biological drug (dose) and duration	Immunosuppressive agents associated with biological drug	Previous immunosuppressive agents	LV symptoms	Amastigotes in bone marrow smears	IFAT	PCR	Therapy	Outcome
Romaní-Costa et al. 2004 Spain (2)	55/M	Psoriatic arthritis	Infliximab (3 mg/kg) 9 mo	NR	NR for 300 mo	Fever, asthenia, hepatosplenomegaly, pancytopenia	Pos	ND	ND	Meglumine antimoniate (840 mg/d for 28 d)	Cure
Fabre et al. 2005 France (3)	53/F	Rheumatoid arthritis	Infliximab (3 mg/kg) 9 mo	Steroids, azathioprine (100 mg/d)	NR	Fever, splenomegaly, and pancytopenia. Inflammatory markers increased	Neg; Pos a 2nd bone marrow aspirate	1:5120	Pos	Amphotericin B (0.7 mg/kg/d for 15 days, then 0.7 mg/kg every 15 d)	Cure—The patient was then treated for 1 yr with etanercept
Bassetti et al. 2006 Italy (5)	69/F	Rheumatoid arthritis	Adalimumab (40 mg every other week) 25 mo	MTX (7.5 mg weekly) and prednisone (5 mg/d) 360 mo	NR	Fluctuant fever with several peaks at 39°C, pancytopenia	Pos	1/160	Pos	L-amB (3 mg/kg/d for 5 d, and 3 mg/kg on d 10).	Cure—MTX was started again after 30 d
Bagalas et al. 2006 Greece (4)	60/F	Rheumatoid arthritis	Etanercept for 18 mo-24 mo before VL; Anakinra, for 2 to 3 weeks 6 mo before VL	NR	Steroids and cyclosporine for 7 yr	Temperature up to 39.5°C every 3 to 4 days, pancytopenia, splenomegaly	Pos	Pos	ND	L-amB (4 mg kg/d, then, due to acute renal failure, 1 mg kg/d, which was gradually increased)	Death due to severe pulmonary infection
Koné-Paut et al. 2007 France (6)	9/F	Systemic juvenile arthritis	Etanercept (to cure an episode of MAS), then anakinra (1 mg/kg/d) 6 mo	NR	Steroids, MTX, cyclosporine.	Fever, scarlet fever-like pruritic rash and hepatosplenomegaly, anemia, thrombocytopenia	Neg	NR	ND	L-amB steroids to cover the risk of MAS	Cure
Tektonidou and Skopouli 2008 Greece (7)	45/M	Psoriatic arthritis	Infliximab (3 and then 5 mg/kg) 3 yr	MTX, prednisolone for 3 yr	NR	High-grade fever, splenomegaly, acute reactive proteins, pancytopenia	Neg	Neg	Pos	L-amB (3 mg/kg/d for 5 d, and 3 mg/kg on d 20)	Cure
Balato et al. 2008 Italy (9)	42/M	Psoriasis	Efalizumab (1 mg/kg/wk) 3 mo	NR	Cyclosporine for 1 mo	Intermittent fever, hepatosplenomegaly, pancytopenia	Pos	1:640	Pos	No anti-leishmania drugs were given	Cure
Garcia-Vidal et al. 2009 Spain (8)	55/M	Rheumatoid arthritis	Infliximab (Tot 40 mg/kg) 11 mo	MTX, steroids	MTX, steroids, azathioprine, cyclosporine for 10 yr	NR	Pos	NR	ND	Meglumine antimoniate	Cure

Joint Bone Spine 77 (2010) 271–273

Available online at ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

Case report

Visceral leishmaniasis and macrophagic activation syndrome in a patient with rheumatoid arthritis under treatment with adalimumab

Anna Moltó[a,*], Lourdes Mateo[a], Natalia Lloveras[b], Alejandro Olivé[a], Sonia Minguez[a]

[a] Rheumatology Section, Hospital Universitari Germans Trias I Pujol, Ctra del Canyet s/n, 08916 Badalona, Spain
[b] Haematology Service, Hospital Universitari Germans Trias i Pujol, Ctra del Canyet s/n, 08916 Badalona, Spain

Hemophagocytic Syndrome: A Misleading Complication of Visceral Leishmaniasis in Children—A Series of 12 Cases

Marie-Helene Gagnaire, MD*; Claire Galambrun, MD‡; and Jean Louis Stéphan, MD*

J Int Assoc Physicians AIDS Care (Chic). 2009 Jul-Aug;8(4):217-20. doi: 10.1177/1545109709337902. Epub 2009 Jun 17.

Immune reconstitution visceral leishmaniasis presented as hemophagocytic syndrome in a patient with AIDS from a nonendemic area: a case report.

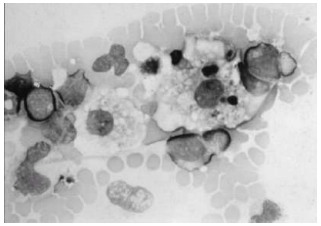
Patel KK, Patel AK, Sarda P, Shah BA, Ranjan R.

Infectious Diseases Clinic, VEDANTA Institute of Medical Sciences, Navrangpura, Ahmedabad, Gujarat, India. ketankpatel20@hotmail.com

Abstract

Visceral Leishmaniasis (VL) is endemic in the Ganges and Brahmaputra plains of India. Leishmaniasis/HIV coinfection is on the rise in India and may pose a real diagnostic and therapeutic challenge. HIV-related immunosuppression increases the risk of reactivating leishmaniasis by 100 to 1000 times and it also increases the risk of drug resistant leishmaniasis. Immune reconstitution VL is not very well reported in literature. Hemophagocytosis is known to occur with various infectious agents like viruses, bacteria, and parasites, but is rare to occur with leishmaniasis. Here the authors describe a case of VL presenting as immune reconstitution disease and hemophagocytosis in an HIV infected patient coming from a nonendemic area.

Hemophagocytic Syndrome: A Misleading Complication of Visceral Leishmaniasis in Children—A Series of 12 Cases



PEDIATRICS Vol. 106 No. 4 October 2000

- Clinico-pathologic entity characterized by **activation and uncontrolled nonmalignant proliferation of T lymphocytes and macrophages, leading to cytokine overproduction**.
- Patients usually present with an acute febrile illness, hepatosplenomegaly, pancytopenia, marked hypofibrinogenemia, and hypertriglyceridemia.
- In children it has been linked to viral, bacterial, fungal and parasitic infection (infection associated HS) and to a broad spectrum of malignancies and genetic disorders, such as Chédiak-Higashi disease, Griscelli disease, XLP syndrome, and familial erythrophagocytic lymphohistiocytosis

› Am J Trop Med Hyg. 2021 Nov 22;106(2):643-647. doi: 10.4269/ajtmh.21-0260.

Association between Hypertriglyceridemia and Disease Severity in Visceral Leishmaniasis

Mariana Garcez Varela [1 2 3], Mariana de Oliveira Bezerra [1], Felipe Vieira Santana [1], Marcos Couto Gomes [1], Pedro Ribeiro de Jesus Almeida [4], Geydson Silveira da Cruz [3 5], Enaldo Vieira de Melo [6], Paulo Roberto de Oliveira Costa [7], Fabrícia Alvisi de Oliveira [1], Amélia Ribeiro de Jesus [1 3 8], Roque Pacheco de Almeida [1 3 8]

- Severely ill patients had higher mean serum triglyceride levels than non-severely ill patients. There was a significant positive correlation between disease severity score and serum triglyceride levels, very low-density lipoprotein, international normalized ratio for prothrombin time test, total bilirubin, and age.
- An inverse correlation was detected between the disease severity score and mean platelet and neutrophil counts. Hypertriglyceridemia can be a prognostic indicator of severity in patients diagnosed with VL.

Am. J. Trop. Med. Hyg., 83(4), 2010, pp. 822–824
doi:10.4269/ajtmh.2010.09-0605

Short Report: Quantiferon-*Leishmania* as an Epidemiological Tool for Evaluating the Exposure to *Leishmania* Infection

Nevin Turgay,* I. Cuneyt Balcioglu, Seray Ozensoy Toz, Yusuf Ozbel, and Stephen L. Jones

Department of Parasitology, Ege University Medical School, Izmir, Turkey; Department of Parasitology, Celal Bayar University Medical School, Manisa, Turkey; Cellestis Limited, Carnegie, Australia

Abstract. The aim of the present preliminary study was to investigate the potential of measurement of IFN-γ secretion by T cells into blood plasma using QuantiFERON assay with leishmanial antigens to determine the presence of *Leishmania* infection. Blood samples from cured visceral (N = 18), and cutaneous (N = 20) leishmaniasis cases, and 20 healthy controls were tested. The IFN-γ responses to *Leishmania major* H2B and *Leishmania infantum* H2B antigens were detected from the majority of treated old visceral leishmaniasis cases, but not from controls. Future studies using larger gr[illegible] [illegible]demiological screening of leishmaniasis.

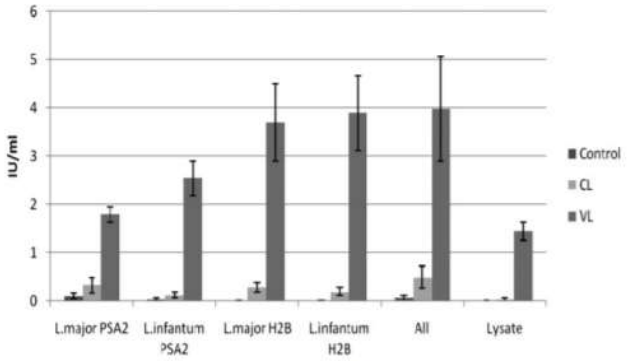


FIGURE 1. IFN-γ responses to leishmanial antigens used in the study (Mean ± SD). VL, visceral leishmaniasis; CL, cutaneous leishmaniasis; Control, healthy volunteers coming from non-endemic areas.

Immunobiology 219 (2014) 323–328

Contents lists available at ScienceDirect

Immunobiology

journal homepage: www.elsevier.com/locate/imbio

Review

Whole blood assay and visceral leishmaniasis: Challenges and promises

Om Prakash Singh, Shyam Sundar*

Infectious Disease Research Laboratory, Department of Medicine, Institute of Medical Sciences, Banaras Hindu University, India

OPEN ACCESS Freely available online

PLoS NEGLECTED TROPICAL DISEASES

Interferon-Gamma Release Assay (Modified QuantiFERON) as a Potential Marker of Infection for *Leishmania donovani*, a Proof of Concept Study

Kamlesh Gidwani[1], Stephen Jones[2], Rajiv Kumar[1], Marleen Boelaert[3], Shyam Sundar[1]*

1 Banaras Hindu University, Varanasi, India, **2** Cellestis limited, Chadstone, Victoria, Australia, **3** Institute of Tropical Medicine, Antwerp, Belgium

Clinical Microbiology and Infection 22 (2016) 739.e1–739.e4

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

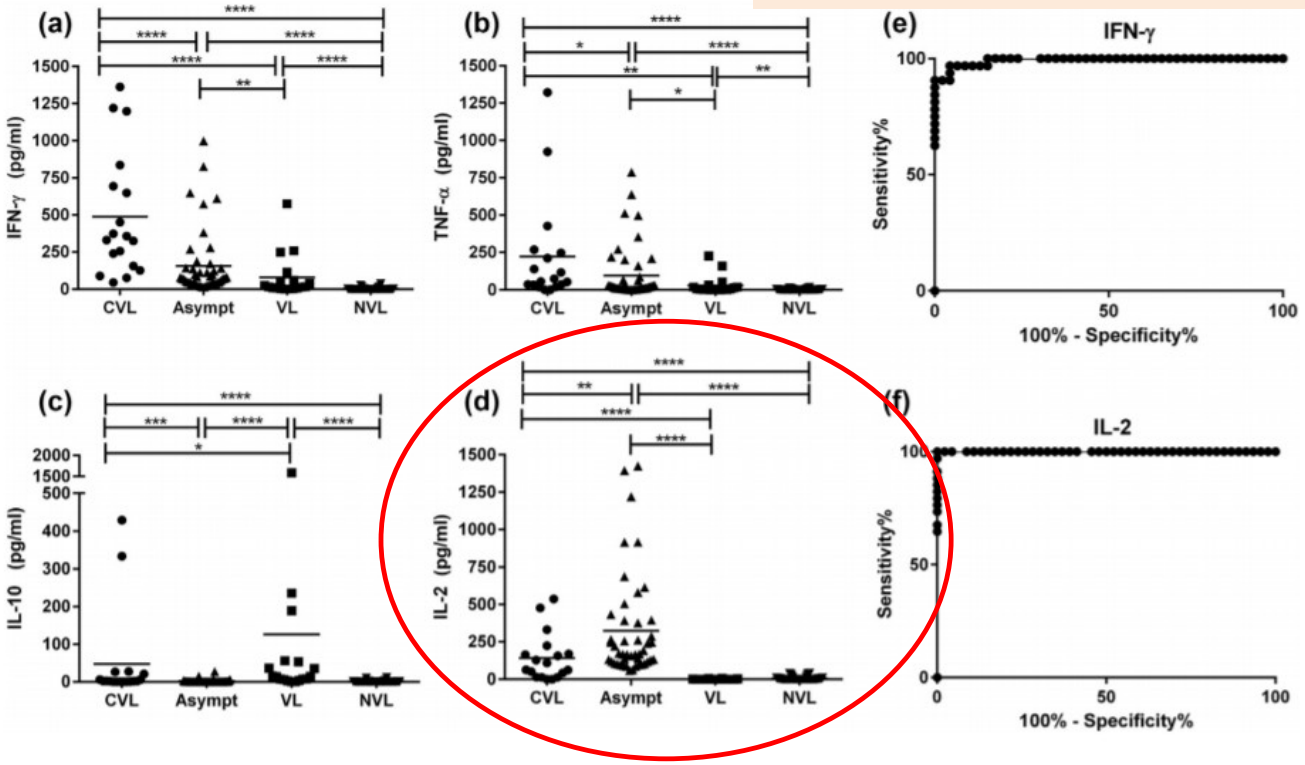
Research note

Interleukin-2 as a marker for detecting asymptomatic individuals in areas wher *Leishmania infantum* is endemic

A.V. Ibarra-Meneses [1], E. Carrillo [1,*], C. Sánchez [1], J. García-Martínez [2], D. López Lacomba [2], J.V. San Martin [3], F. Alves [4], J. Alvar [4], J. Moreno [1]

The present work investigates the soluble Leishmania antigen stimulation of whole blood from cured persons, those with active disease, and asymptomatic individuals. SLA-stimulated plasma IFN-g concentrations were recorded, as were those of tumour necrosis factor-a (TNF-a), interleukin-10 (IL-10) and IL-2.

The aim was to establish a simple method for detecting asymptomatic persons in areas where L. infantum is endemic



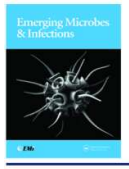
pathogens

Review

Third Case of Visceral Leishmaniasis in COVID-19: Mini Review Article

Claudia Colomba [1,2], Cristoforo Guccione [1], Raffaella Rubino [3,*], Michela Scalisi [2], Anna Condemi [1,2], Sara Bagarello [1,2], Salvatore Giordano [2] and Antonio Cascio [1,3]

Author/Year	Age	Sex	Immunocompetence	Fever and Pancytopenia	Sample for Diagnosis	Diagnosis	Therapy	Outcome
Miotti 2020	70	M	No	Yes	Blood and bone marrow	Molecular diagnosis	Amphotericin B + dexamethason	Death
Pikoulas 2021	30	F	Yes	Yes	Blood and bone marrow	Molecular diagnosis	Amphotericin B + dexamethason	Full recovery
Present case 2022	4	F	Yes	Yes	Blood	Molecular diagnosis	Amphotericin B	Full recovery



Emerging Microbes & Infections

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/temi20

Outbreak of cutaneous leishmaniasis before and during the COVID-19 pandemic in Jahrom, an endemic region in southwest of Iran

Cutaneous leishmaniasis and the COVID-19 pandemic

Samaneh Mazaherifar, Kavous Solhjoo & Amir Abdoli

To cite this article: Samaneh Mazaherifar, Kavous Solhjoo & Amir Abdoli (2022): Outbreak of cutaneous leishmaniasis before and during the COVID-19 pandemic in Jahrom, an endemic region in southwest of Iran, Emerging Microbes & Infections, DOI: 10.1080/22221751.2022.2117099

To link to this article: https://doi.org/10.1080/22221751.2022.2117099

- Before the pandemic, the annual occurrence of CL was less than 240 cases per year, while the number of cases was increased to 307 and 771 cases in the first and second years after the pandemic, respectively.
- Molecular detection of some isolates identified *Leishmania major*.
- The **rodent control program was completely interrupted during the first year of COVID-19 outbreak** in Iran (February to December, 2020), then the program restarted again as routine from the summer of 2021 till now. Interrupted rodent control program along with inadequate screening programs of CL patients were probably one of the causes of this outbreak in Jahrom.

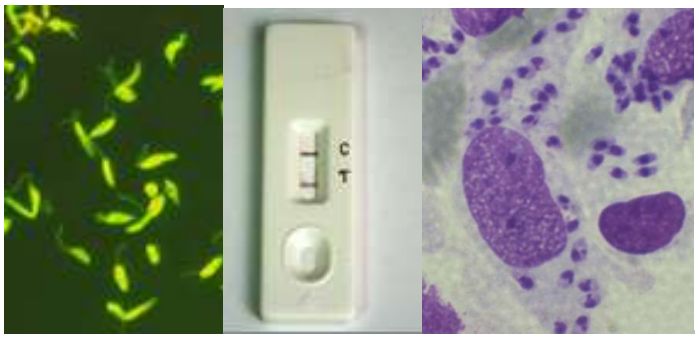
Diagnostic workup

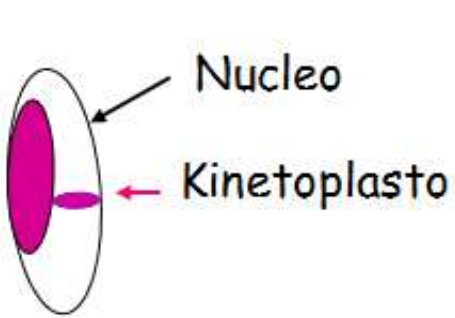
CL/MCL

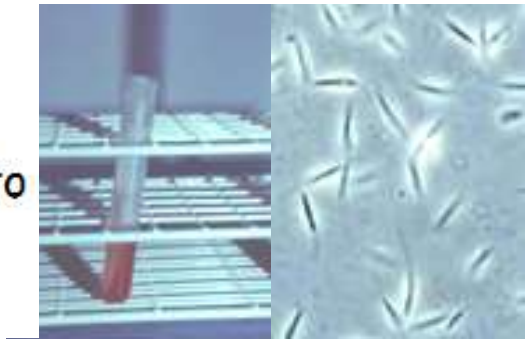
- Biopsy
- Scraping
  - Microscopy
  - Colture
  - PCR
- Serology
- PCR – blood

VL

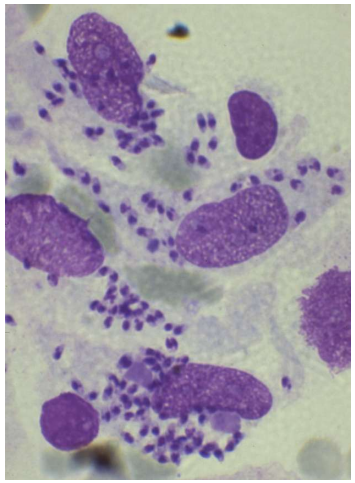
- Serology
- PCR – blood
- Bome marrow aspirate
  - Microscopy
  - Colture
  - PCR

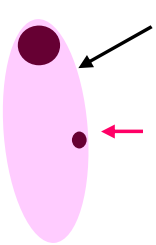


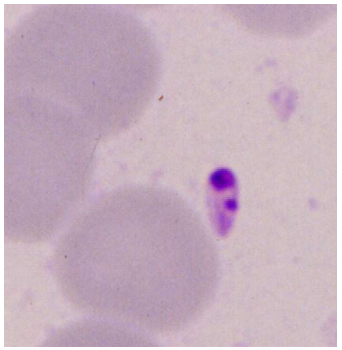


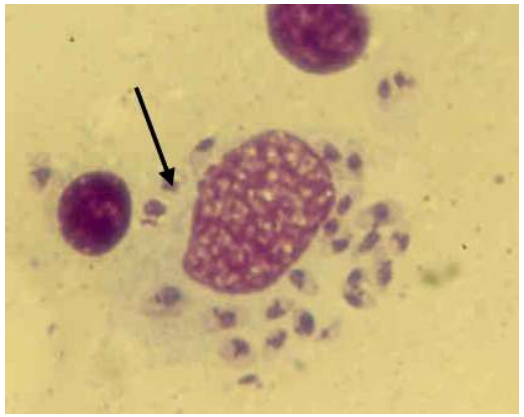


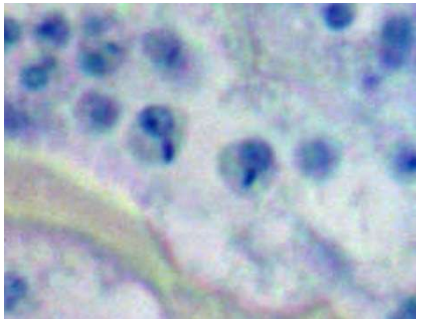
Esame microscopico del midollo osseo







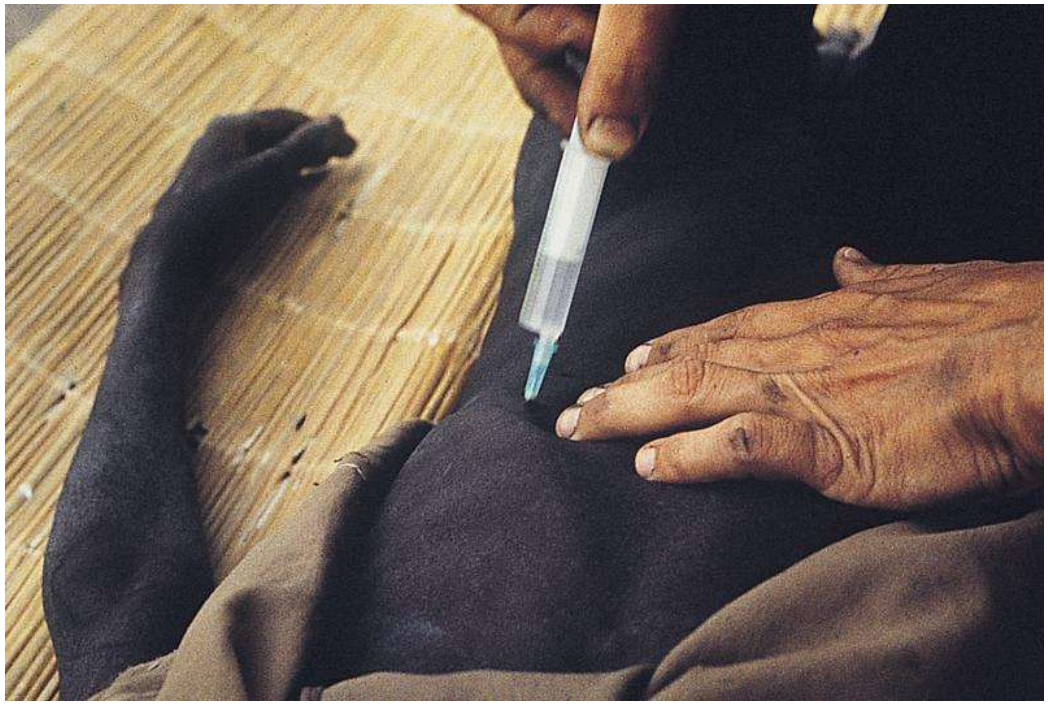




Il sangue midollare viene strisciato su vetrini che fissato in metanolo sono successivamente sottoposto alla colorazione Giemsa e osservati al microscopio (1000 X)

La sensibilità del metodo dipende dall'esperienza dell'osservatore (70-95%)

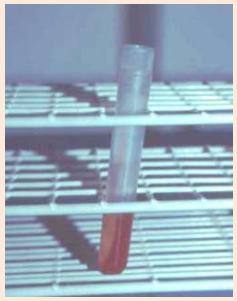
Splenic aspiration



- The procedure is simple, painless and safe if the prothrombin time is normal and the platelet count is above 40000/mm3.
- Palpate the spleen and mark its outline. Using a 1.25inch long ∞ 21-gauge needle attached to a 5ml syringe, penetrate the skin over the spleen. Withdraw the plunger 1ml and plunge the needle into the spleen upwards at an angle of 45° and withdraw immediately, maintaining suction.
- The tiny amount of material obtained is sufficient for culture and smear.

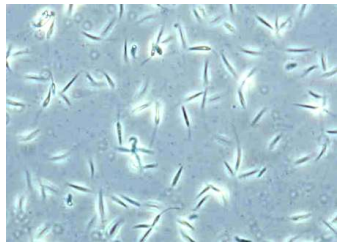
Terreni di coltura

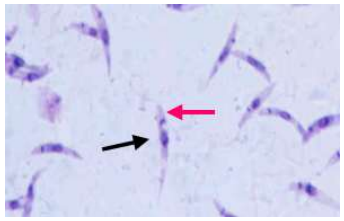
Sono tipicamente dei terreni agar sangue mono o bifasici, non disponibili in commercio:



- "EMTM" (Evans modified Tobie medium)
- "Sloppy Evans medium"
- "NNN medium" (Novy, McNeil e Nicolle)

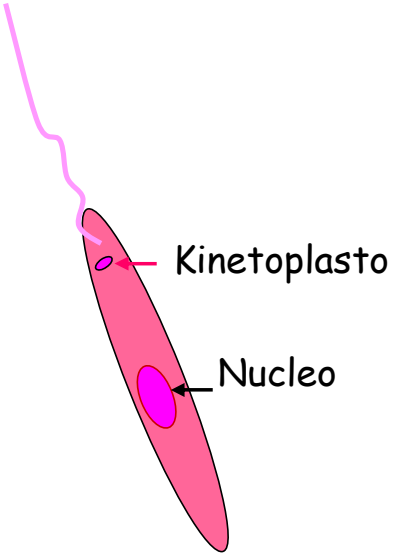
N.B. Terreni liquidi (es. Schneider e RPMI) sono disponibili per *Leishmania* in commercio ma mostrano un'efficienza inferiore ai terreni agar sangue durante l'isolamento in coltura, quindi una minore sensibilità nella diagnosi.





La sensibilità di una coltura dipende da diversi fattori:

- ✓Tipo di terreno e temperatura d'incubazione (23-24°C)
- ✓Quantità di materiale seminato



Xenodiagnosi

E' un metodo di diagnosi diretta
che permette di rilevare il parassita
attraverso l'utilizzo del suo ospite vettore

Il cane viene addormentato ed esemplari
da colonia di *Phlebotomus perniciosus*
sono lasciati liberi di pungere sulla
testa del cane

Flebotomi con pasto di sangue sono
raccolti separatamente e dissezionati
per la ricerca di promastigoti

Am. J. Trop. Med. Hyg., 60(1), 1999, pp. 51–53

INFECTION OF SAND FLIES BY HUMANS COINFECTED WITH *LEISHMANIA INFANTUM* AND HUMAN IMMUNODEFICIENCY VIRUS

RICARDO MOLINA, JEAN M. LOHSE, FEDERICO PULIDO, FERNANDO LAGUNA, ROGELIO LÓPEZ-VÉLEZ, AND JORGE ALVAR

- To determine the role that *Leishmania infantum*/human immunodeficiency virus (HIV) coinfected patients could play in the epidemiology of visceral leishmaniasis (VL), we applied direct xenodiagnosis of VL in this study to test the infectivity of six coinfected patients to colonized *Phlebotomus perniciosus.*
- All patients proved to be infective for the sand flies.
- The infectivity of patients who had still not received specific treatment for VL was inversely proportional to their absolute CD4+ T lymphocyte cell count.

Diagnosi molecolare (PCR)

Vantaggi diagnostici:

Elevata sensibilità (teorica <u>≤</u>1 parassita);

Elevata specificità: *quasi assoluta*

- Assenza di interferenze da parte di altri microorganismi;
- Automatizzazione e riproducibilità

Può essere applicata a qualsiasi tipo di campione:

- **Aspirato midollare o linfonodale**
- **Prelievo splenico**
- **Sangue periferico (Buffy Coat, PBMC)**
- **Cute**

❑**Fresco, Fissato su vetrino e/o colorato Campione istologico**

Pediatrics 2002;109(2).

Polymerase Chain Reaction in the Diagnosis and Prognosis of Mediterranean Visceral Leishmaniasis in Immunocompetent Children

Antonio Cascio, MD*; Sara Calattini, BSc‡; Claudia Colomba, MD*; Chiara Scalamogna, MD‡; Morena Galazzi, BSc‡; Massimo Pizzuto, MD‡; Romina Camilli, MD§; Marina Gramiccia, MD§; Lucina Titone, MD*; Mario Corbellino, MD‡; and Spinello Antinori, MD*

IFAT è il "gold standard" della sierologia per la leishmaniosi

Sensibilità e specificità si avvicinano al 100% nei pazienti immunocompetenti

La specificità non rappresenta un problema nell'area Mediterranea raggiungendo la soglia del 100%

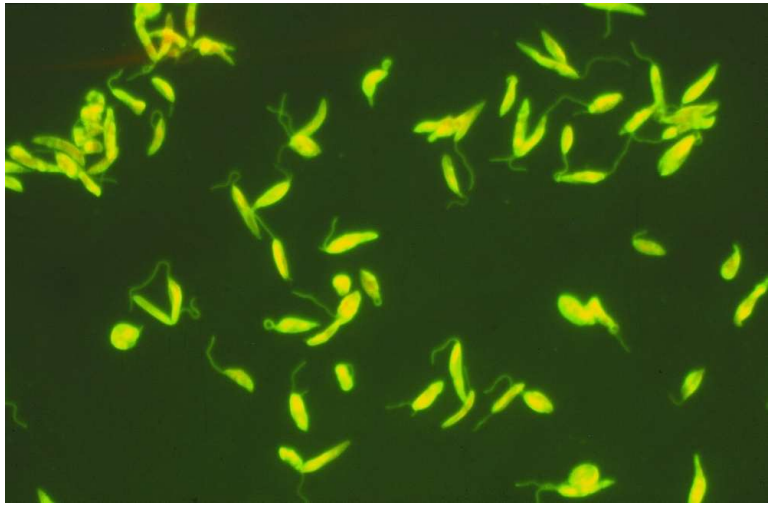
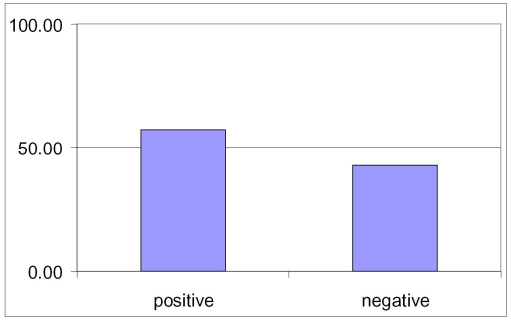


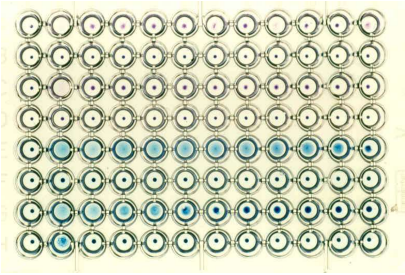
Figure 3: Sensitivity of serology, 941 patients tested, south-western Europe, 1990-1998

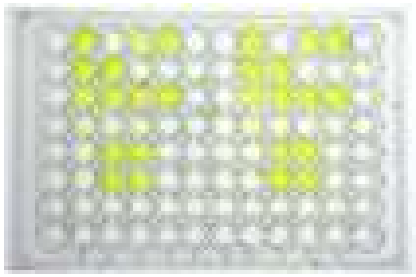


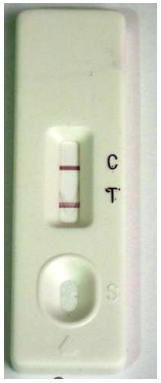
Dr.ssa Gramiccia ISS

Altre tecniche sierologiche….

- ELISA con antigene intero: diminuisce di specificità
- ELISA con antigene ricombinante: diminuisce di sensibilità
- Latex test: bassa specificità (58%)
- DAT: diminuisce di sensibilità
- Emoagglutinazione indiretta: bassa sensibilità (66%) e specificità (80%)
- Western Blot: utile come "confirmatory test" (laborioso e poco riproducibile)







Test rapido immunocromatografico

Specificità: ~100%

Sensibilità: 77-90%

Dermatologic Therapy / Volume 34, Issue 4 / e14977

ORIGINAL ARTICLE | Full Access

The role of CD1a expression in the diagnosis of cutaneous leishmaniasis, its relationship with leishmania species and clinicopathological features

Yasemin Yuyucu Karabulut, Funda Kuş Bozkurt, Ümit Türsen, Gül Bayram, Gülhan Örekeci Temel, Mehmet Emin Erdal

First published: 15 May 2021
https://doi-org.bibliosan.idm.oclc.org/10.1111/dth.14977

Transepidermal elimination in cutaneous leishmaniasis: a multiregional study

Sarah Karram, Asif Loya, Hadi Hamam, Robert H. Habib, Ibrahim Khalifeh

First published: 14 February 2012 |
https://doi-org.bibliosan.idm.oclc.org/10.1111/j.1600-0560.2012.01890.x | Citations: 33

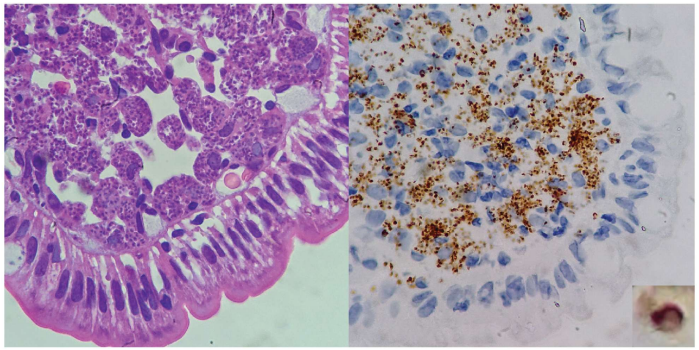
Langerhnas cell marker (CD1a)

A possible explanation for this staining overlap could be that the **amastigotes acquired the CD1a upon exiting dendritic cells expressing the marker by the process of exocytosis**.
Another less likely explanation could be that the CD1a and a leishmania surface antigen have a homologous site, resulting in cross reactivity with the CD1a antibody; however, this will need to be confirmed by further molecular analyses. Explanation aside, the highlighting of amastigotes by CD1a would be helpful especially in cases with a low parasitic index with high clinical suspicion of leishmaniasis.

http://doi.org/10.1590/S1678-9946201961025

Evaluation of the diagnostic potential of CD1a immunohistochemistry for visceral leishmaniasis

Sami de Andrade Cordeiro Gadelha[1], Maria do Perpétuo Socorro Saldanha da Cunha[2,3], Gabriela Maia Coelho[1], Tamises Melo Siqueira Marinho[1], Carlos Gustavo Hirth[1,2,3]



Therapy

- **CL**
  - Negative serology and negative blood PCR
    - **intralesional meglumine antimoniate**
  - Positive serology and/or positive blood PCR
    - **Liposomal amphotericin B**
- **MCL**
    - **Liposomal amphotericin** B (regimens vary) with total cumulative dose of 20-60 mg/kg
    - **Pentavalent antimony** (Sb) [Sodium Stibogluconate (Pentostam) or Meglumine antimoniate (Glucantime)] 20 mg/kg/day IV or IM x 28 days
- **VL**
    - Liposomal amphotericin B
      - Immunocompetent: Liposomal Amphotericin B 3 mg/kg IV once daily days 1-5 and days 14, 21 (need 21 mg/kg total dose). 40 mg/kg total dose for East African VL.
      - Immunocompromised, HIV/AIDS: Liposomal Amphotericin B: 4 mg/kg daily on days 1-5, 10, 17, 24, 31 and 38 (total of 40 mg/kg). HIV patients may need longer courses as well as maintenance therapy with liposomal amphotericin B (4 mg/kg every 2–4 weeks)

› Clin Infect Dis. 2006 Oct 1;43(7):917-24. doi: 10.1086/507530. Epub 2006 Aug 28.

Liposomal amphotericin B for the treatment of visceral leishmaniasis

Caryn Bern [1], Jill Adler-Moore, Juan Berenguer, Marleen Boelaert, Margriet den Boer, Robert N Davidson, Concepcion Figueras, Luigi Gradoni, Dimitris A Kafetzis, Koert Ritmeijer, Eric Rosenthal, Catherine Royce, Rosario Russo, Shyam Sundar, Jorge Alvar

Table 1. Efficacy and toxicity of various dosing regimens of liposomal amphotericin B (LAmB) in immunocompetent patients with visceral leishmaniasis.

Country	Reference(s)	Study design	No. of subjects		Total AmB dose, mg/kg	LAmB regimen	Percentage of cured subjects	Follow-up duration, months	Reported adverse events[a]
			Total	Per group					
Brazil	[20, 21][b]	Open-label, dose-finding	32	15	6	2 mg/kg on day 1, 5, and 10	87	6	Fever, 41%; chills, 9%; respiratory distress, 6%; cardiac arrhythmia, 9%; treatment was stopped for 2 subjects
				4	10	2 mg/kg on days 1–4 and 10	100	6	…
				13	14	1–2 mg/kg on days 1–6 and 10	62	6	…
Greece	[22]	Open-label with historical control	123[c]	41	20	10 mg/kg on days 1–2	98	6	Fever and chills, 7%; no discontinuations of treatment
				30	20	4 mg/kg on days 1–5	90	6	…
Italy	[23]	Open-label, dose-finding	31[d]	10	30	3 mg/kg on days 1–10	100	12–24	Nonsignificant increase in BUN level; no change in creatinine level; no discontinuations of treatment
				10	21	1–1.4 mg/kg on days 1–21	100	12–24	…
Italy[e]	[24]	Open-label, dose-finding	88[f]	32	15	3 mg/kg on days 1–4 and 10	91	12	Mild adverse effects; transient increase in BUN and creatinine levels; no discontinuations of treatment
				42	18	3 mg/kg on days 1–5 and 10	98	12	…
				13	24	4 mg/kg on days 1–5 and 10	100	12	…
Italy	[25]	Open-label, dose-finding	106[c]	16	15	3 mg/kg on days 1–3, 5, and 10	75	12	No adverse events, no change in levels of BUN, creatinine, electrolytes, or liver enzymes
				66	18	3 mg/kg on days 1–5 and 10	98	12	…
				11	21	1 mg/kg on days 1–21	100	12	…
				13	30	3 mg/kg on days 1–10	100	12	…

Advance Access published May 18, 2004

Journal of Antimicrobial Chemotherapy
DOI: 10.1093/jac/dkh279

JAC

A 6 day course of liposomal amphotericin B in the treatment of infantile visceral leishmaniasis: the Italian experience

Antonio Cascio[1,2]*, Lucio di Martino[3], Paolo Occorsio[3], Raffaella Giacchino[4], Salvatore Catania[5], Anna Rita Gigliotti[4], Camilla Aiassa[5], Chiara Iaria[1,2], Salvatore Giordano[6], Claudia Colomba[6], Valentina Frasca Polara[6], Lucina Titone[6], Luigi Gradoni[7], Marina Gramiccia[7] and Spinello Antinori[8]

Acute Renal Failure Due to Visceral Leishmaniasis by *Leishmania infantum* Successfully Treated With a Single High Dose of Liposomal Amphotericin B

Anna Beltrame, MD,* Alessandra Arzese, MD,*† Alessandro Camporese, MD,† Giada Rorato, MD,* Massimo Crapis, MD,* Giuseppe Tarabini-Castellani, MD,‡ Giuliano Boscutti, MD,§ Stefano Pizzolitto, MD,‖ Giuseppina Calianno, MD,¶ Alberto Matteelli, MD,# Trentina Di Muccio, MD, Marina Gramiccia, MD,** and Pierluigi Viale, MD***

*Clinic of Infectious Diseases, Department of Clinical and Morphological Research and †Institute of Microbiology, University of Udine, Udine, Italy; ‡Department of Microbiology, Santa Maria degli Angeli Hospital of Pordenone, Pordenone, Italy; §Nephrology and Dialysis Unit and ‖Division of Anatomic Pathology, General Hospital S. Maria della Misericordia of Udine, Udine, Italy; ¶Nephrology Service, Santa Maria degli Angeli Hospital of Pordenone, Pordenone, Italy; #Institute of Infectious and Tropical Diseases, University of Brescia, Brescia, Italy; **Unit of Vector-borne Diseases and International Health, MIPI Department, Istituto Superiore di Sanità of Rome, Rome, Italy

DOI: 10.1111/j.1708-8305.2008.00220.x

ELSEVIER

International Journal of Antimicrobial Agents 25 (2005) 26–30

INTERNATIONAL JOURNAL OF Antimicrobial Agents
www.ischemo.org

Discussion

Treatment of paediatric visceral leishmaniasis: amphotericin B or pentavalent antimony compounds?

D.A. Kafetzis[a,*], I.M. Velissariou[a], S. Stabouli[a], M. Mavrikou[b], D. Delis[b], G. Liapi[a]

[a] Second Department of Pediatrics, University of Athens, P. & A. Kyriakou Children's Hospital, Athens 11527, Greece

Treatment regimes, duration and cost of hospitalization in children with visceral leishmaniasis

Treatment cost regime	Number of patients	Hospitalization days	Medication cost of a 3-year-old (€)	Treatment of a 3-year-old (€)
Antimony a	6	22 [17–28]	10.6	1639
Antimony b	4	12.5 [11–16]	10.6	936
Amphotericin b1	4	6.5 [6–8]	834	1315
Amphotericin b2	6	7 [6–11]	952	1479
Amphotericin b3	6	6.5 [6–8]	834	1315
Amphotericin b4	3	7 [6–8]	834	1351

Antimony a: meglumine antimonate 20 mg/kg/day for 21 days, as an inpatient; Antimony b: meglumine antimonate 20 mg/kg/day for 21 days, as an outpatient; Amphotericin b1: liposomal amphotericin B 4 mg/kg/day for 5 days; Amphotericin b2: liposomal amphotericin B 4 mg/kg/day on days 1–5 and 9; Amphotericin b3: liposomal amphotericin B 5 mg/kg/day for 4 days; Amphotericin b4: liposomal amphotericin B 10 mg/kg/day for 2 days.

… the patients who received liposomal amphotericin B for 2 days, were hospitalized for 6–8 days (median 7 days), due to allergic reactions to the infusion

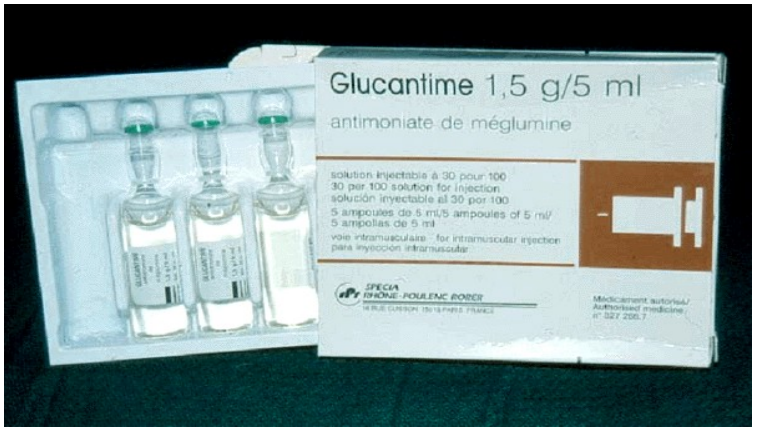
Glucantim (antimoniato di N-metil-glucamina)

- Soluzione di Sb^5 al 8,5 % (85 mg / ml)
- Venduto in fiale da 5 ml contenenti 1,5 g di farmaco equivalente a 425 mg di Sb^5

Pentostam (stibogluconato di Na)

- soluzione di Sb^5 al 10 % (100 mg/ml)
- Venduto in flaconi multidosaggio da 100 ml

Di Cristina G, Caronia G. Sulla terapia della leishmaniosi interna. Pathologica 1915; 7: 82-83



AmBisome (Liposomal ampotericin B)

- The US Food and Drug Administration lincensed AmBisome for treatment of VL and reccomended treating
  - immunocompetent patients with 3 mg/Kg daily on days 1-5, 14 and 21 (total 21 mg/Kg)
  - Immunosuppressed patients with 4 mg/Kg daily on days 1-5, 10, 14, 17, 24, 31, and 38 (total 40 mg/Kg)

Miltefosine

- Membrane-active alkyl phospholipid (phospphocholine analogue) that interferes with cell-signaling pathways
- Developed as an antineoplastic agent and now used topically in brest carcinoma skin metastates
- do not have clinical efficacy against tumors when admininistered orally
- is particularly active in animal models of visceral leishmaniasis

ORAL MILTEFOSINE FOR INDIAN VISCERAL LEISHMANIASIS

SHYAM SUNDAR, M.D., T.K. JHA, M.D., C.P. THAKUR, M.D., JUERGEN ENGEL, PH.D., HERBERT SINDERMANN, PH.D., CHRISTINA FISCHER, KLAUS JUNGE, PH.D., ANTHONY BRYCESON, M.D., AND JONATHAN BERMAN, M.D., PH.D.

NOVEMBER 28, 2002

Methods The study was a randomized, open-label comparison, in which 299 patients 12 years of age or older received orally administered miltefosine (50 or 100 mg [approximately 2.5 mg per kilogram of body weight] daily for 28 days) and 99 patients received intravenously administered amphotericin B (1 mg per kilogram every other day for a total of 15 injections).

Conclusions Oral miltefosine is an effective and safe treatment for Indian visceral leishmaniasis. Miltefosine may be particularly advantageous because it can be administered orally. It may also be helpful in regions where parasites are resistant to current agents.

J Antimicrob Chemother 2012; **67**: 2576–2597
doi:10.1093/jac/dks275 Advance Access publication 24 July 2012

Antimicrobial Chemotherapy

Miltefosine: a review of its pharmacology and therapeutic efficacy in the treatment of leishmaniasis

Thomas P. C. Dorlo[1,2]*, Manica Balasegaram[3], Jos H. Beijnen[2] and Peter J. de Vries[1]†

[1]Center for Tropical Medicine and Travel Medicine, Division of Infectious Diseases, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; [2]Department of Pharmacy and Pharmacology, Slotervaart Hospital/The Netherlands Cancer Institute, Amsterdam, The Netherlands; [3]Drugs for Neglected Diseases initiative (DNDi), Geneva, Switzerland

Am. J. Trop. Med. Hyg., 101(4), 2019, pp. 789–794
doi:10.4269/ajtmh.18-0949

Natural Resistance of *Leishmania infantum* to Miltefosine Contributes to the Low Efficacy in the Treatment of Visceral Leishmaniasis in Brazil

Juliana B. T. Carnielli,[1,2*†] Renata Monti-Rocha,[1†] Dorcas Lamounier Costa,[3] Aretha Molina Sesana,[1] Laura N. N. Pansini,[1] Marcela Segatto,[1] Jeremy C. Mottram,[2] Carlos Henrique Nery Costa,[3] Sílvio F. G. Carvalho,[4] and Reynaldo Dietze[1,5*]

[1]*Núcleo de Doenças Infecciosas, Universidade Federal do Espírito Santo, Vitória, Brazil;* [2]*York Biomedical Research Institute, Department of Biology, University of York, United Kingdom;* [3]*Instituto Natan Portella para Doenças Tropicais, Universidade Federal do Piauí, Teresina, Brazil;* [4]*Centro de Ciências Biológicas e da Saúde, Universidade Estadual de Montes Claros, Montes Claros, Brazil;* [5]*Global Health and Tropical Medicine, Instituto de Higiene e Medicina Tropical, Universidade NOVA de Lisboa, Lisbon, Portugal*

Abstract. In India, visceral leishmaniasis (VL) caused by *Leishmania donovani* has been successfully treated with miltefosine with a cure rate of > 90%. To assess the efficacy and safety of oral miltefosine against Brazilian VL, which is caused by *Leishmania infantum*, a phase II, open-label, dose-escalation study of oral miltefosine was conducted in children (aged 2–12 years) and adolescent-adults (aged 13–60 years). Definitive cure was assessed at a 6-month follow-up visit. The cure rate was only 42% (6 of 14 patients) with a recommended treatment of 28 days and 68% (19 of 28 patients) with an extended treatment of 42 days. The in vitro miltefosine susceptibility profile of intracellular amastigote stages of the pretreatment isolates, from cured and relapsed patients, showed a positive correlation with the clinical outcome. The IC_{50} mean (SEM) of eventual cures was 5.1 (0.4) μM, whereas that of eventual failures was 12.8 (1.9) μM (P = 0.0002). An IC_{50} above 8.0 μM predicts failure with 82% sensitivity and 100% specificity. The finding of *L. infantum* amastigotes resistant to miltefosine in isolates from patients who eventually failed treatment strongly suggests natural resistance to this drug, as miltefosine had never been used in Brazil before this trial was carried out.

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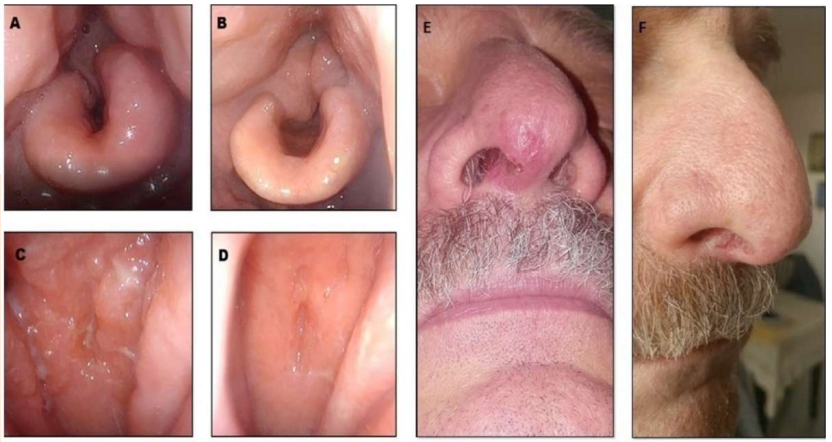
journal homepage: www.elsevier.com/locate/ijid

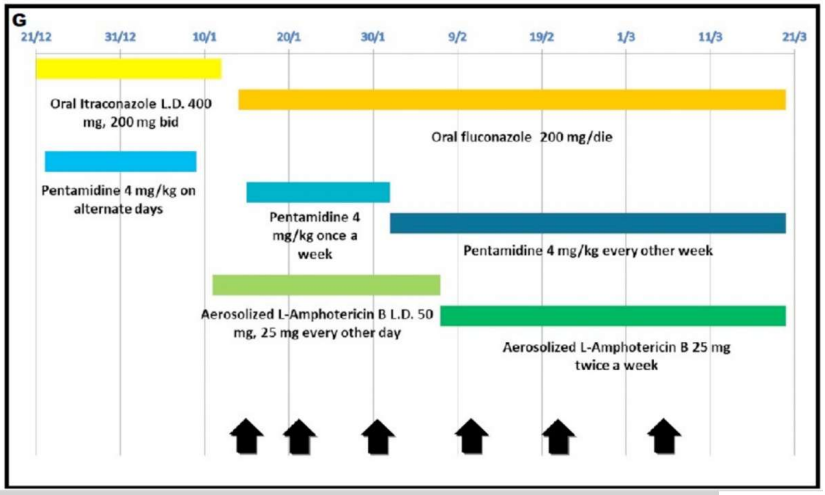
Case Report

Refractory mucocutaneous leishmaniasis resolved with combination treatment based on intravenous pentamidine, oral azole, aerosolized liposomal amphotericin B, and intralesional meglumine antimoniate

Gregorio Basile[a], Glauco Cristofaro[b], Luca Giovanni Locatello[b], Iacopo Vellere[a], Matteo Piccica[a], Silvia Bresci[c], Giandomenico Maggiore[b], Oreste Gallo[a,b], Andrea Novelli[d], Trentina Di Muccio[e], Marina Gramiccia[e], Luigi Gradoni[e], Giovanni Gaiera[f], Alessandro Bartoloni[a,c,g], Lorenzo Zammarchi[a,c,g,*]

A 65-year-old Italian male patient with chronic kidney disease, arterial hypertension, prostatic hypertrophy, and type-2 diabetes mellitus was referred for severe relapsing MCL acquired in Argentina. ENT examination showed severe diffuse pharyngolaryngeal edema and erythema, partially obstructing the airways. Despite receiving four courses of liposomal amphotericine B (L-AmB) and two courses of miltefosine over a 2-year period, the patient presented recurrence of symptoms a few months after the end of each course. After the patient was referred to us, a combined treatment was started with intravenous pentamidine 4 mg/kg on alternate days for 10 doses, followed by one dose per week for an additional seven doses, intralesional meglumine antimoniate on the nasal lesion once per week for six doses, oral azoles for three months, and aerosolized L-AmB on alternate days for three months. The treatment led to regression of mucosal lesions and respiratory symptoms. Renal function temporarily worsened, and the addition of insulin was required to maintain glycemic compensation after pentamidine discontinuation.





Prot. 35574 del 14/10/2020

0033122-14/10/2020-DGPRE-DGPRE-P

Ministero della Salute

DIREZIONE GENERALE DELLA PREVENZIONE SANITARIA
Ufficio V – Prevenzione delle malattie trasmissibili e profilassi internazionale

DIREZIONE GENERALE DELLA SANITÀ ANIMALE E DEI FARMACI VETERINARI
Ufficio III – Sanità animale e gest. oper. Centro Naz. di lotta ed emergenza contro le malattie animali e unità centrale di crisi

Allegato 5-A

SCHEDA DI NOTIFICA – LEISHMANIOSI VISCERALE

Regione _____ Provincia _____ ASL _____
Comune _____ Distretto _____

Data di compilazione: gg |_|_| mm |_|_| aa |_|_|_|_| **Data di segnalazione:** gg |_|_| mm |_|_| aa |_|_|_|_|

Dati anagrafici del paziente

Cognome _____ Nome: _____

Sesso: M □ F □ Data di nascita gg |_|_| mm |_|_| aa |_|_|_|_|

Luogo di nascita _____ _____ _____
Comune Provincia Stato

Codice Fiscale _____

Residenza: _____ _____ _____
Via/piazza e numero civico Comune Provincia

Domicilio abituale: _____ _____ _____
Via/piazza e numero civico Comune Provincia

ASL di appartenenza _____

Nazionalità _____ Cittadinanza _____

Professione _____ Recapito telefonico _____

Viaggi o soggiorni in regioni diverse dalla residenza/domicilio abituale del paziente o al di fuori dell'Italia

1. _____ _____ _____
2. _____ _____ _____
3. _____ _____ _____
4. _____ _____ _____
Paese visitato data partenza dall'Italia data rientro/arrivo in Italia

Motivo del viaggio _____

Informazioni cliniche

Data inizio sintomi gg |_|_| mm |_|_| aa |_|_|_|_| Data diagnosi gg |_|_| mm |_|_| aa |_|_|_|_|

Data ricovero gg |_|_| mm |_|_| aa |_|_|_|_| Data dimissione gg |_|_| mm |_|_| aa |_|_|_|_|

Struttura di Ricovero _____ Reparto _____

Segni e sintomi

Dimagrimento	□	Linfoadenopatia	□
Epatosplenomegalia	□	Anemia	□
Febbre	□	Trombocitopenia	□
Debolezza	□	Leucopenia	□

Altro _____
specificare

Test di laboratorio

Ricerca anticorpi specifici nel siero

Data prelievo |_|_| |_|_| |_|_|_|_| Tipo metodica usata: _____

Titolo _____ **Risultato POS** □ **NEG** □ **Dubbio** □

PCR qualitativa e/o PCR quantitativa

Data prelievo |_|_| |_|_| |_|_|_|_|

Tessuto aspirato o biopsia di:
milza □ linfonodo □ midollo osseo □ fegato □
sangue periferico □ altro (specificare) _____

Risultato POS □ NEG □

Esame microscopico

Data prelievo |_|_| |_|_| |_|_|_|_|

Tessuto aspirato o biopsia di:
milza □ linfonodo □ midollo osseo □ fegato □
altro (specificare) _____

Colorazione utilizzata: Giemsa □ Wiright-Giemsa □ Altro (specificare)_____

Risultato POS □ NEG □ Dubbio □

Densità

6+	(oltre 100 parassiti per campo)	□
5+	(10-100 parassiti per campo)	□
4+	(1-10 parassiti per campo)	□
3+	(1-10 parassiti per 10 campi)	□
2+	(1-10 parassiti per 100 campi)	□
1+	(1-10 parassiti per 1000 campi)	□
0	(nessun parassita in 1000 campi)	□

Coltura parassitaria

Data prelievo |_|_| |_|_| |_|_|_|_|

Tessuto aspirato o biopsia di:
milza □ linfonodo □ midollo osseo □ fegato □
sangue periferico □ altro (specificare) _____

Risultato POS □ NEG □

Classificazione di caso: PROBABILE □ CONFERMATO □
PRIMA INFEZIONE □ RECIDIVA/RICADUTA □

Tipo caso: IMPORTATO □ AUTOCTONO □

In caso d'importazione: Paese e località di presunto contagio_____

Note (scrivere in stampatello):

_____
_____

Operatore sanitario che ha compilato la scheda: Nome e cognome_____
Ruolo_____ Recapito telefonico_____ email _____

(timbro e firma)

ISTRUZIONI E NOTE PER LA COMPILAZIONE

La scheda va compilata per tutti i casi probabili e confermati di Leishmaniosi viscerale
Inviare a: - Ministero della Salute: via mail a malinf@sanita.it;

Allegato 5-B

SCHEDA DI NOTIFICA – LEISHMANIOSI CUTANEA

Regione _____ Provincia _____ ASL _____
Comune _____ Distretto _____

Data di compilazione: gg |_|_| mm |_|_| aa |_|_|_|_| **Data di segnalazione:** gg |_|_| mm |_|_| aa |_|_|_|_|

Dati anagrafici del paziente

Cognome _____ Nome: _____

Sesso: M □ F □ Data di nascita gg |_|_| mm |_|_| aa |_|_|_|_|

Luogo di nascita _____ _____ _____
Comune Provincia Stato

Codice Fiscale _____

Residenza: _____ _____ _____
Via/piazza e numero civico Comune Provincia

Domicilio abituale: _____ _____ _____
Via/piazza e numero civico Comune Provincia

ASL di appartenenza _____

Nazionalità _____ Cittadinanza _____

Professione _____ Recapito telefonico _____

Viaggi o soggiorni in regioni diverse dalla residenza/domicilio abituale del paziente o al di fuori dell'Italia

1. _____ _____ _____
2. _____ _____ _____
3. _____ _____ _____
4. _____ _____ _____
Paese visitato data partenza dall'Italia data rientro/arrivo in Italia

Motivo del viaggio _____

Informazioni cliniche

Data inizio sintomi gg |_|_| mm |_|_| aa |_|_|_|_| Data diagnosi gg |_|_| mm |_|_| aa |_|_|_|_|

Ricovero SI NO
se sì, Data ricovero gg |_|_| mm |_|_| aa |_|_|_|_| Data dimissione gg |_|_| mm |_|_| aa |_|_|_|_|

motivo del ricovero _____

Struttura di Ricovero _____ Reparto _____

Segni e sintomi

Lesioni cutanee □ Lesioni alle mucose □

Test di laboratorio

PCR qualitativa e/o PCR quantitativa

Data prelievo |_|_| |_|_| |_|_|_|_|
biopsia cutanea □ biopsia mucosa □

Risultato POS □ NEG □

Esame microscopico

Data prelievo |_|_| |_|_| |_|_|_|_|
biopsia cutanea □ biopsia mucosa □

Colorazione utilizzata: Giemsa □ Wiright-Giemsa □ Altro (specificare) _____

Risultato POS □ NEG □ Dubbio □

Coltura parassitaria

Data prelievo |_|_| |_|_| |_|_|_|_|
biopsia cutanea □ biopsia mucosa □

Risultato POS □ NEG □

Classificazione di caso: PROBABILE □ CONFERMATO □

Tipo caso: IMPORTATO □ AUTOCTONO □

In caso d'importazione: Paese e località di presunto contagio_____

Note (scrivere in stampatello):

_____
_____

Operatore sanitario che ha compilato la scheda: Nome e cognome_____
Ruolo_____ Recapito telefonico_____ email _____

(timbro e firma)

ISTRUZIONI E NOTE PER LA COMPILAZIONE

La scheda va compilata per tutti i casi probabili e confermati di Leishmaniosi cutanea
Inviare a: - Ministero della Salute: via mail a malinf@sanita.it;

Thank you

Giovanni Di Cristina
Palermo, 12 settembre 1875 –
Palermo, 27 febbraio 1928