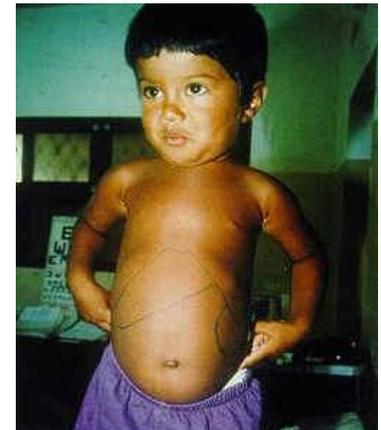
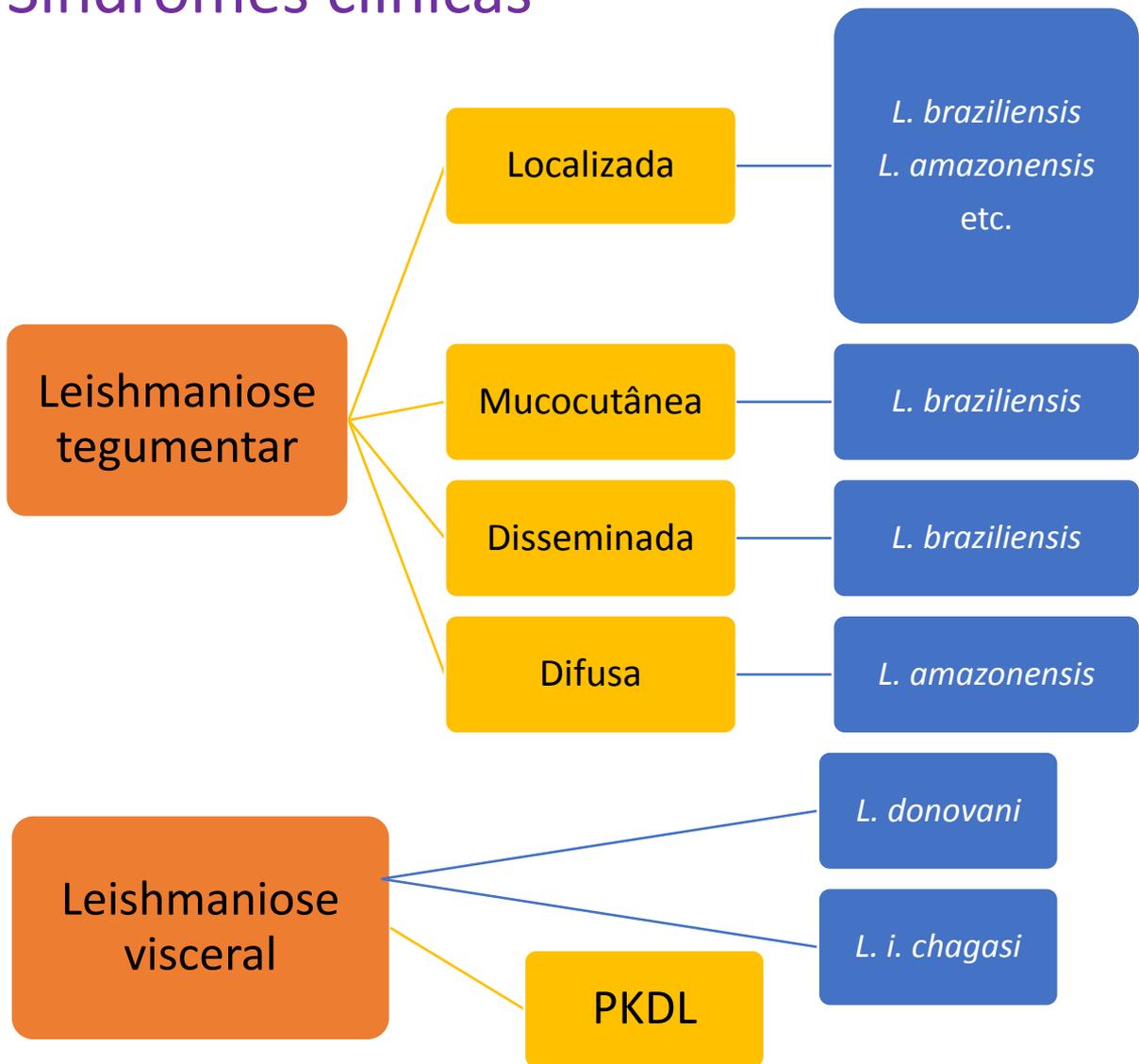


Leishmanioses

Silvia Reni B. Uliana – ICB - USP



Síndromes clínicas



Leishmania

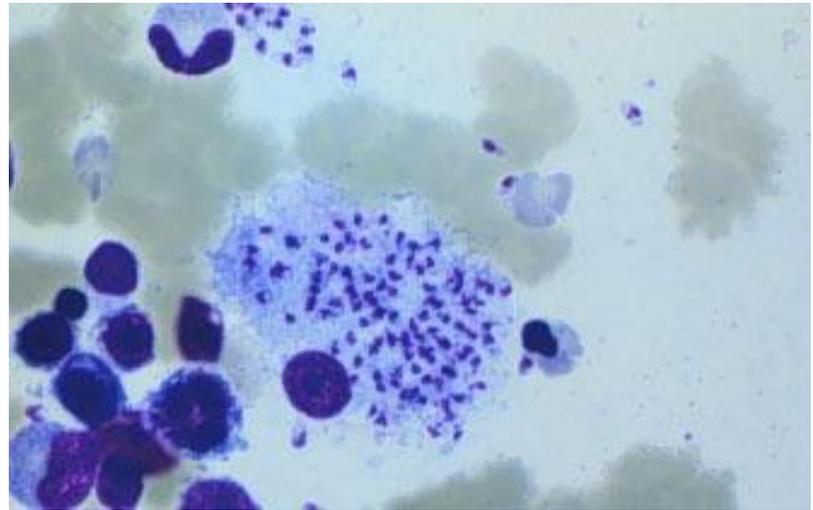
Família **Trypanosomatidae**

Gênero *Leishmania*

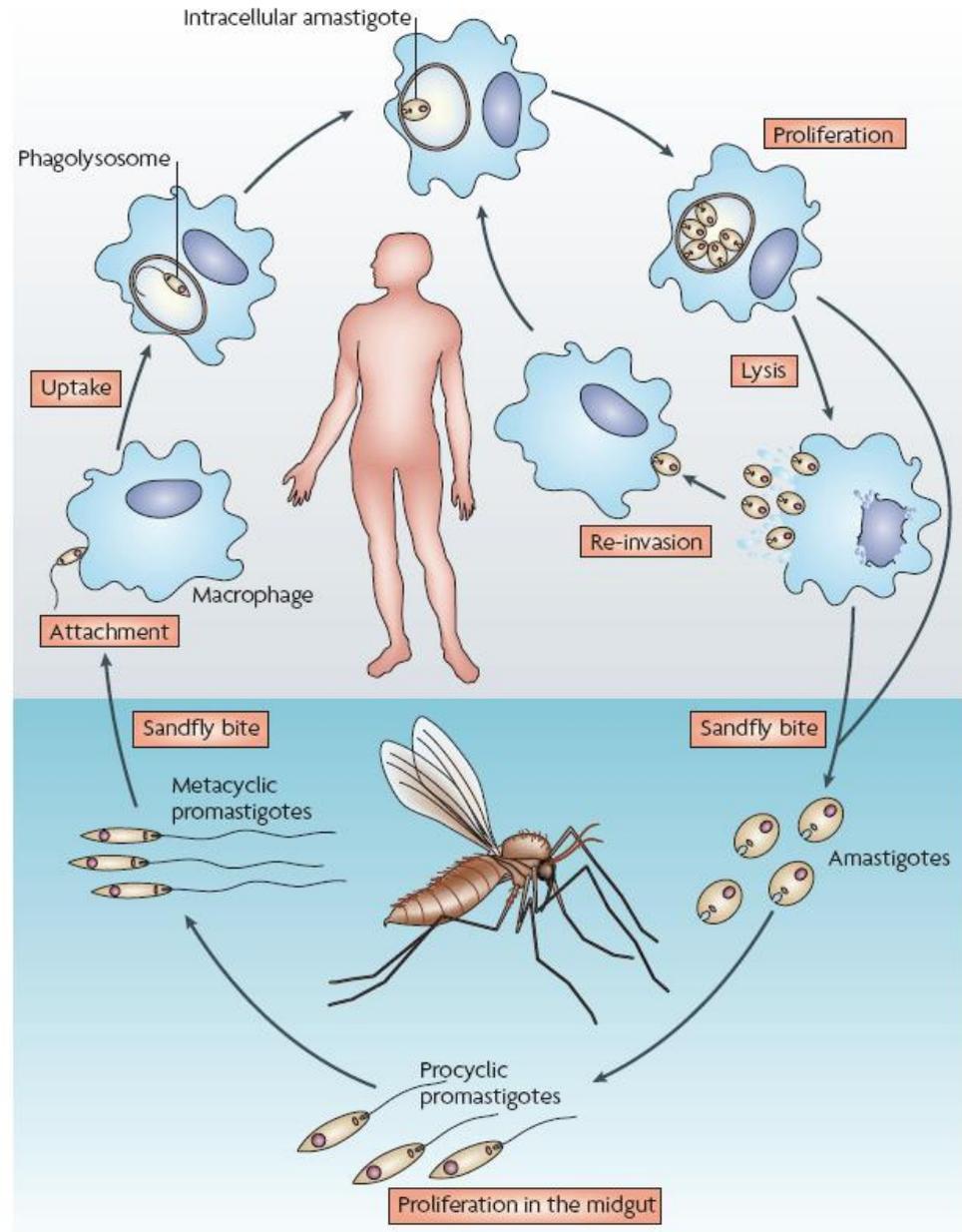
Sub-gêneros *Leishmania*
Viannia

Mais de 30 espécies descritas





Ciclo de vida



Vetor - flebotomíneos



Lutzomyia longipalpis



Lutzomyia longipalpis

***Phlebotomus* spp.**

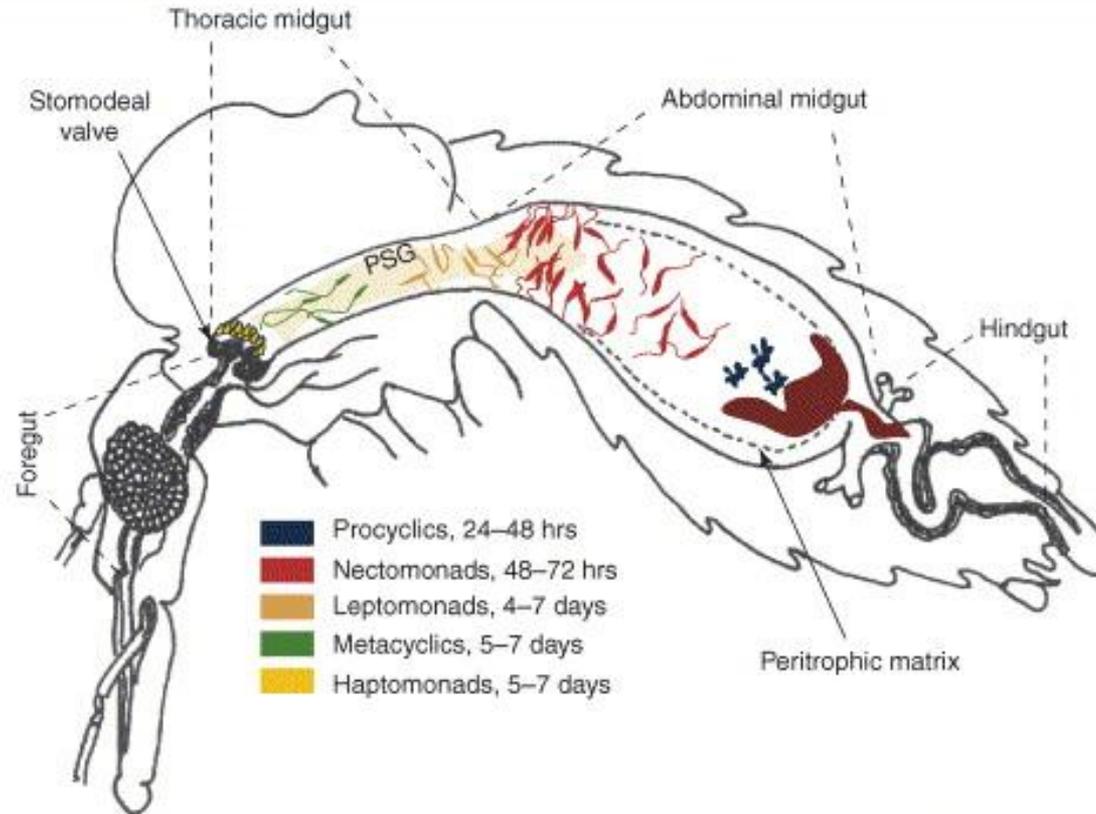
***Lutzomyia* spp.**

“Mosquito palha”



Phlebotomus papatasi

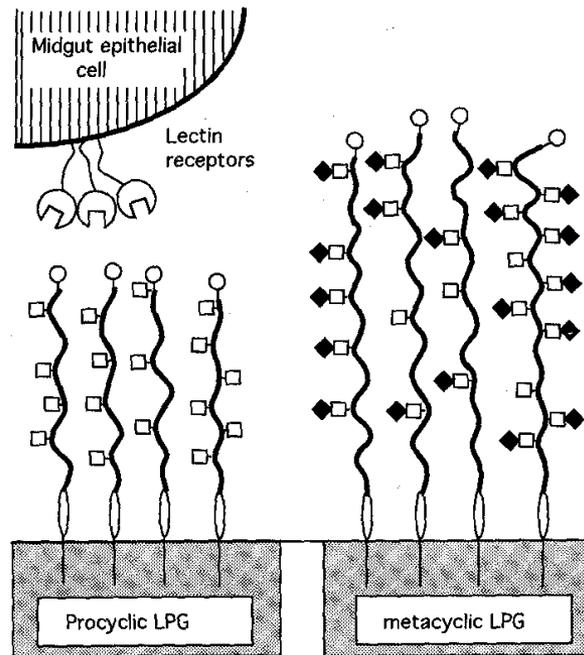
Desenvolvimento no intestino do vetor



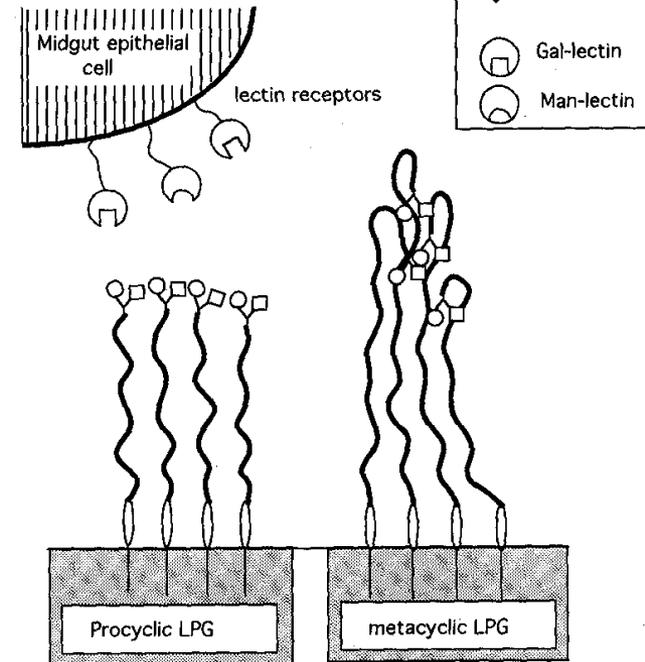
TRENDS in Parasitology

Mecanismos de evasão

A *Leishmania - Phlebotomus papatasi*
major



B *Leishmania - Phlebotomus donovani*
argentinae

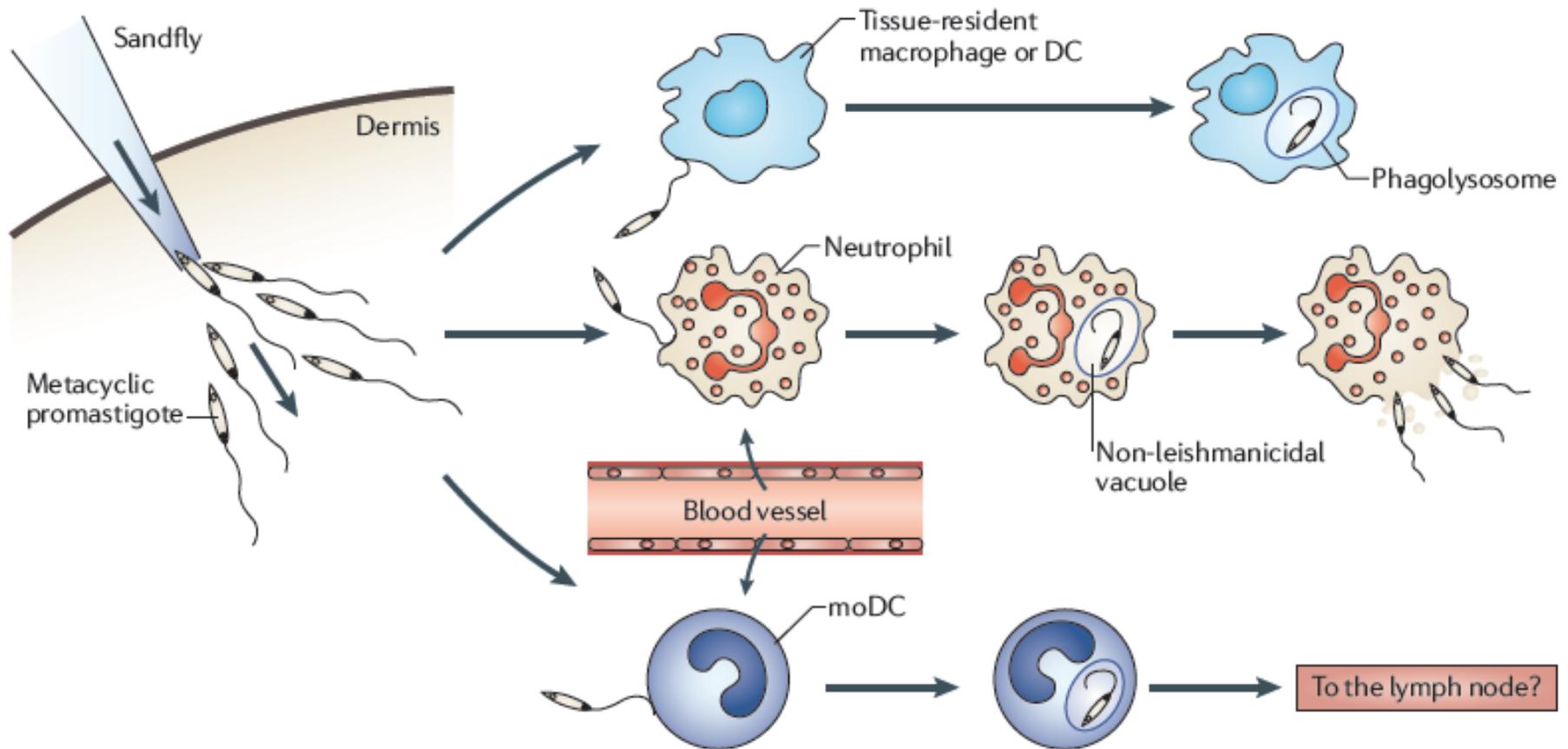


multiplicação no intestino – aderência - procíclico



“livre” para o próximo hospedeiro - metacíclico

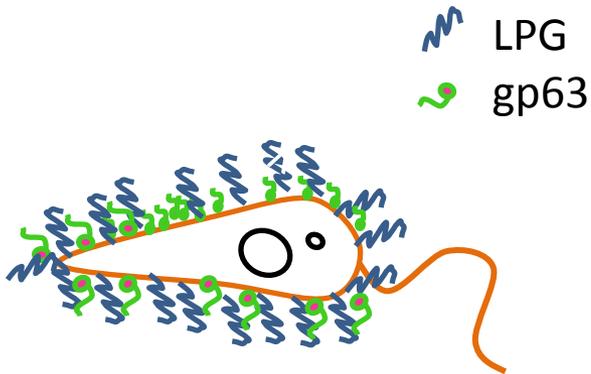
Inoculação de promastigotas + saliva do inseto



“chegando em casa...” - o macrófago!

Promastigota **metacíclico**: ativação do complemento

Interação com receptores do macrófago



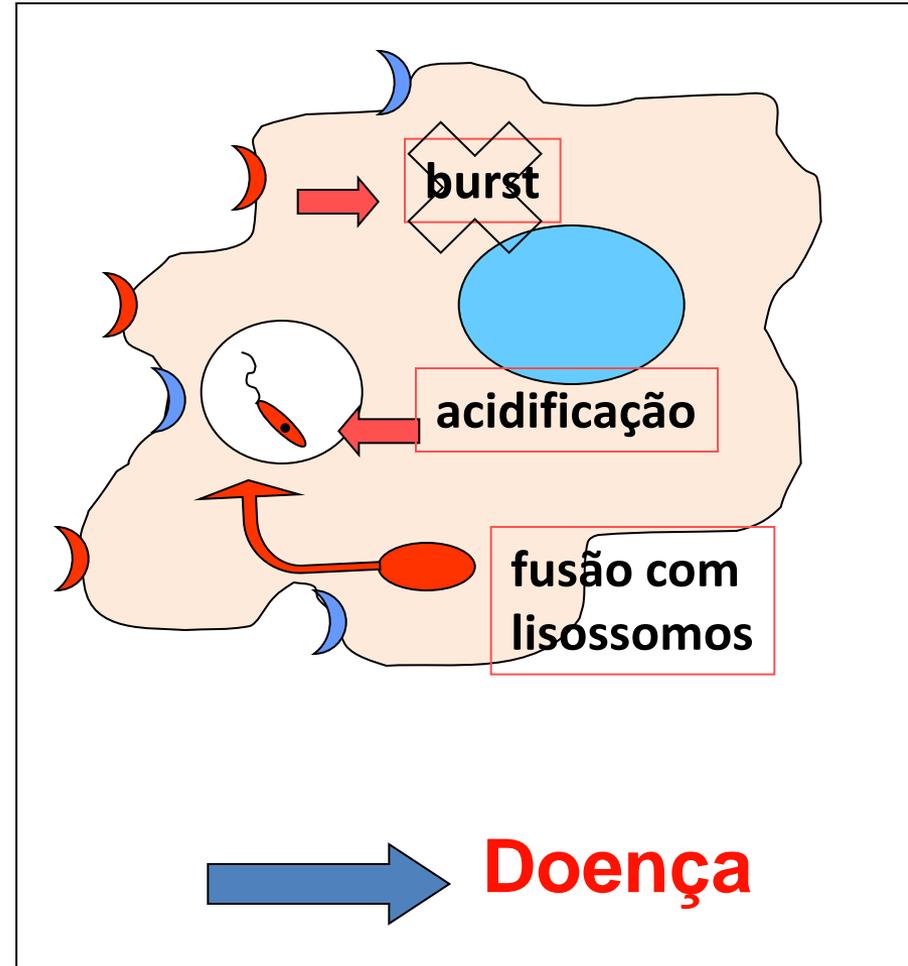
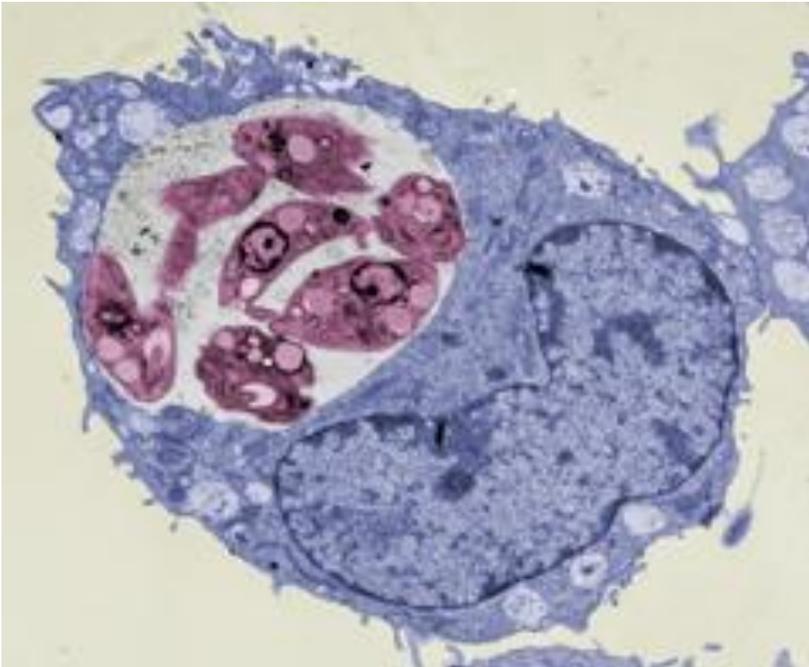
Opsonização: facilitação da fagocitose

inibição do **burst respiratório**

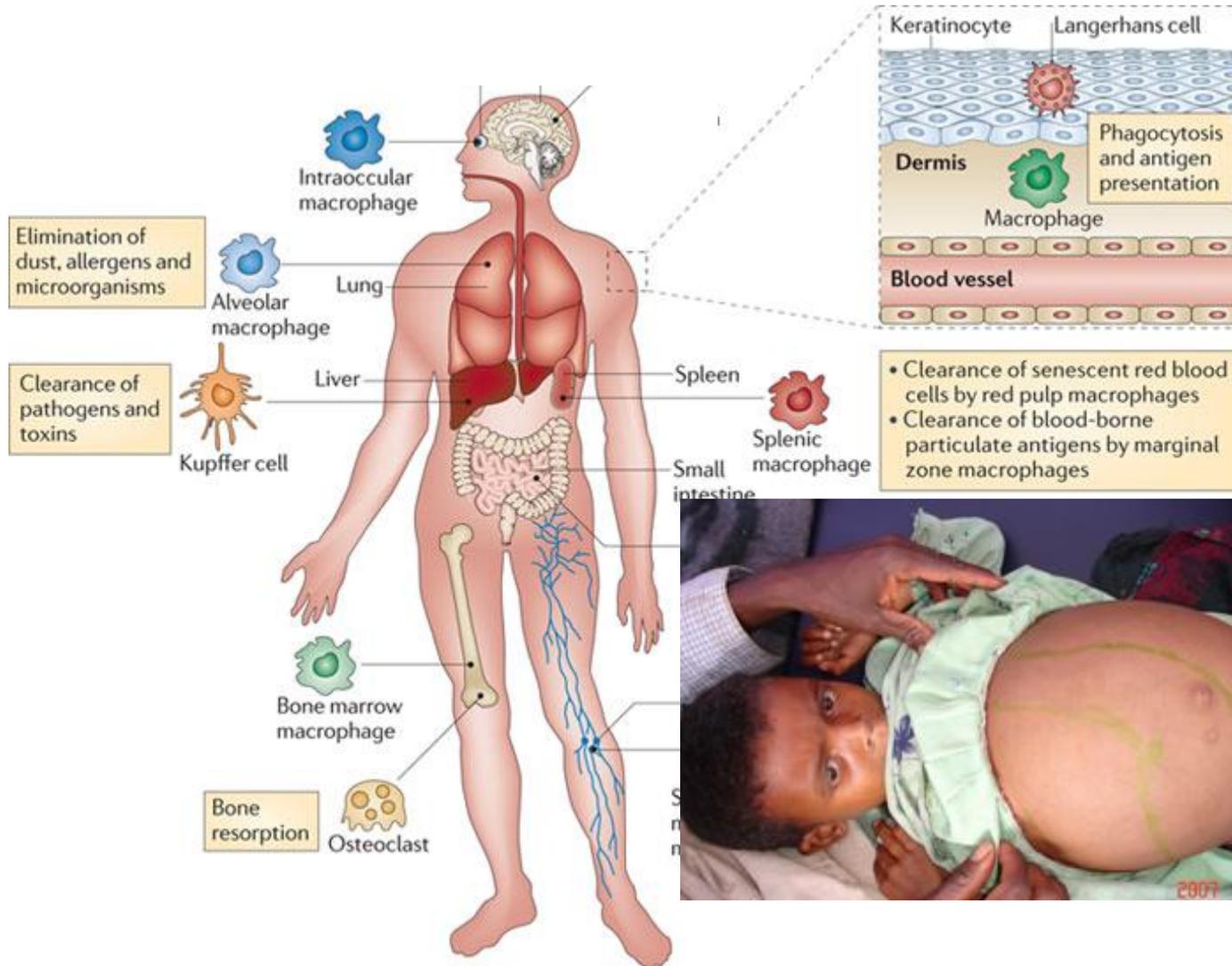
“arrumando a casa”... o vacúolo parasitóforo

Acidificação: pH ótimo para os amastigotas

Fusão com lisossomos: gp63 é uma protease



Formas clínicas: tegumentar e visceral



Formas clínicas

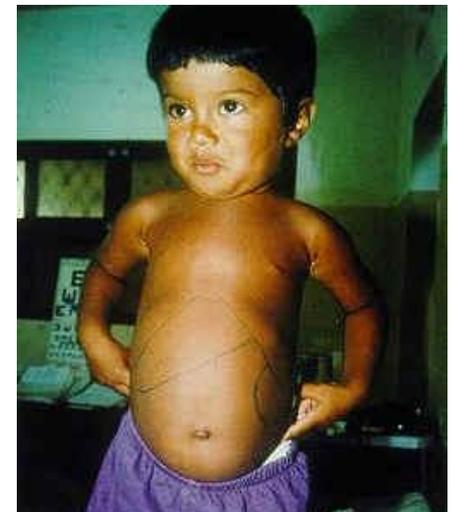
Leishmaniose cutânea

Leishmaniose difusa

Leishmaniose mucocutânea

Leishmaniose disseminada

Leishmaniose visceral



Quadro clínico - forma cutânea localizada

L. (L.) amazonensis

L. (V.) guyanensis

L. (V.) braziliensis

Outras espécies do
subgênero *Viannia*



Reservatórios: roedores silvestres,
marsupiais (gambá), preguiça, tamanduá



Figura 3- Lesão ulcerada típica em membro superior direito de criança de 3 anos.



Figura 4- Duas pequenas lesões pápulo-ulceradas em membro inferior direito, com 8 dias de evolução e que ao exame histopatológico apresentavam índice parasitário 3 (100 parasitas X 100 campos).



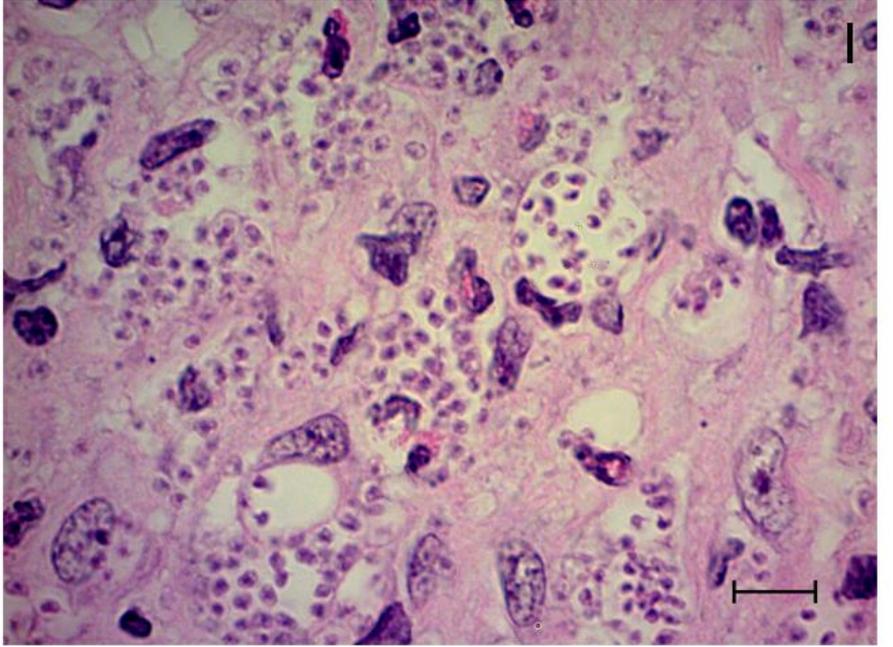
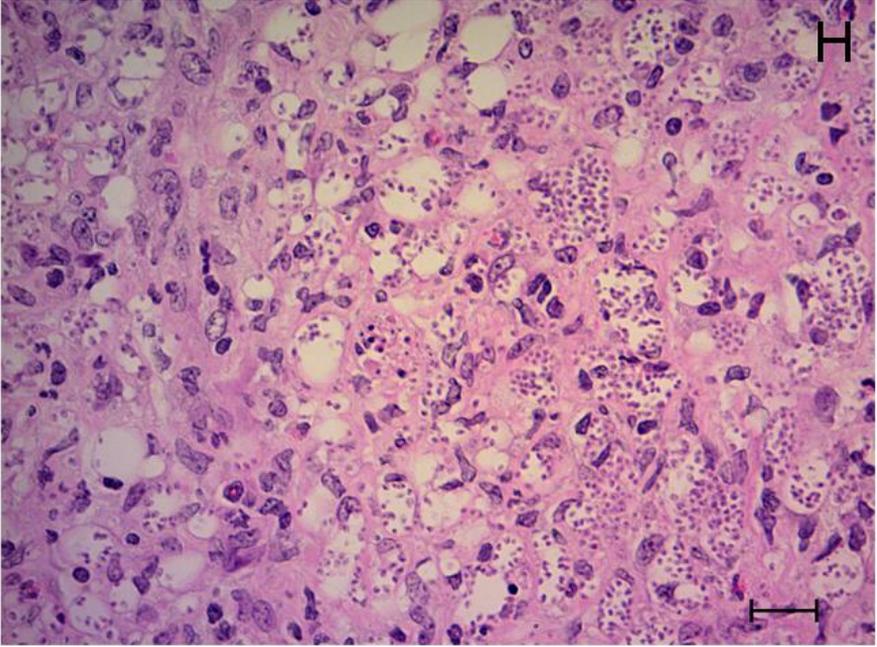
Figura 3 - Paciente do grupo experimental: NAF, masculino, 19 anos, com duas lesões ulceradas no cotovelo e com 3 meses de evolução. Isolado identificado como L(V)b. Foi tratado com pentamidina na dose de 4mg/kg/dia por 3 dias. Dose total = 720mg. A: pré-tratamento. B: apresenta resolução completa, 6 meses após uso de pentamidina.

Quadro clínico - forma difusa

L. (L.) amazonensis



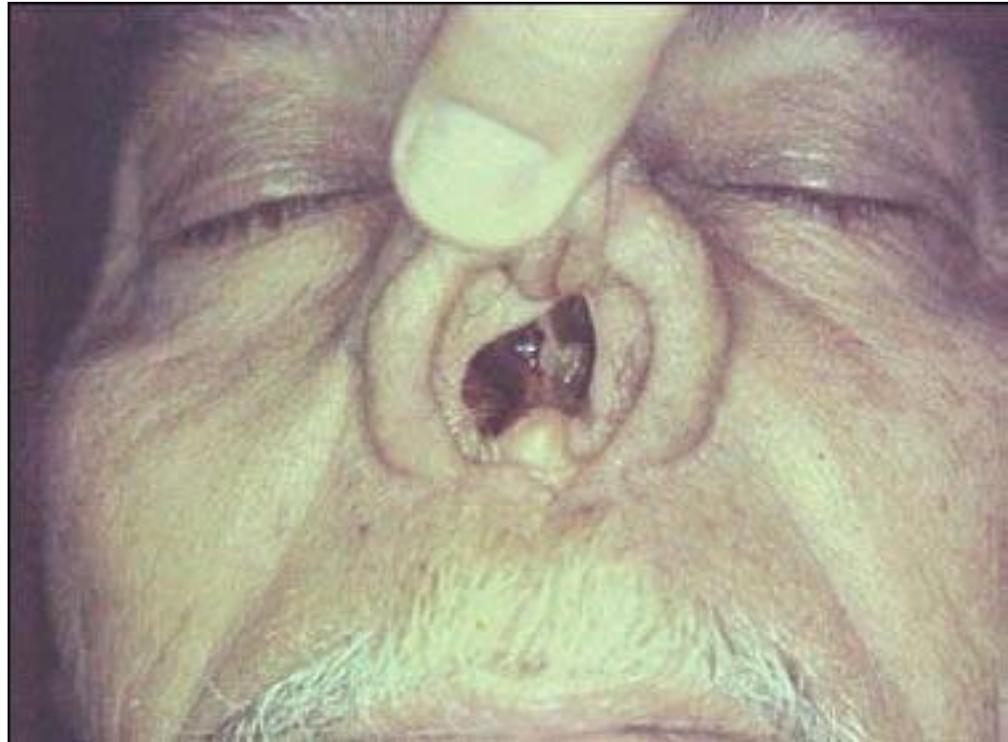
Reservatório: roedores silvestres

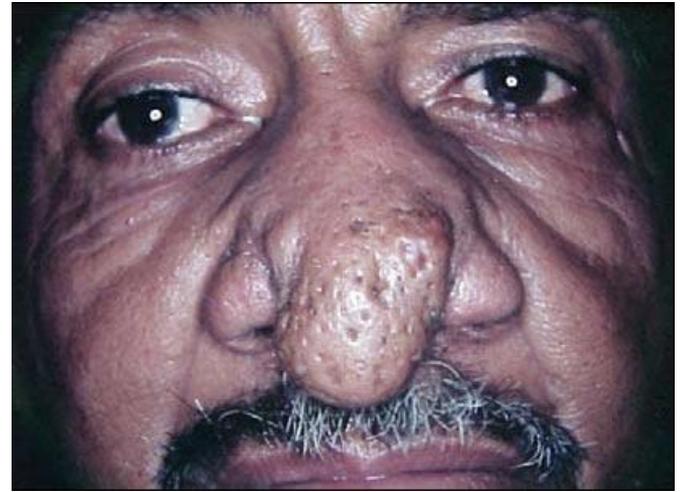


Quadro clínico - forma muco-cutânea

L. (V.) braziliensis

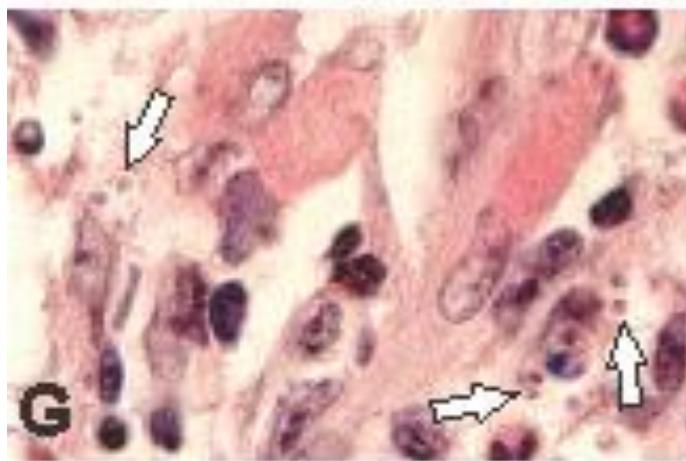
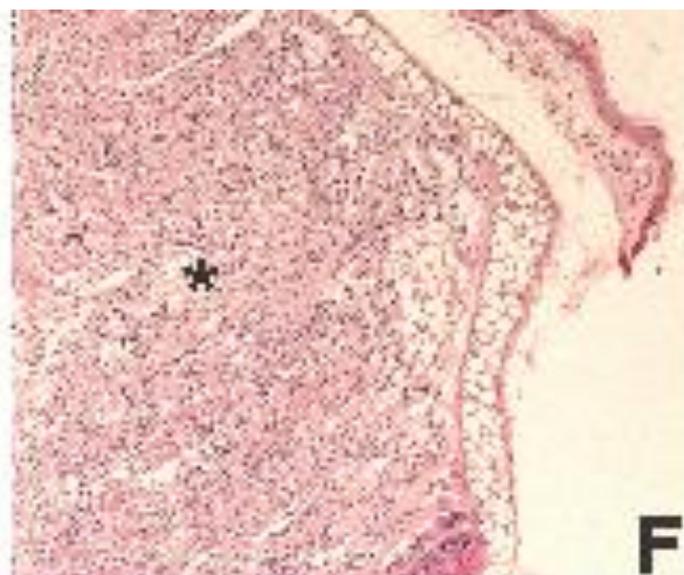
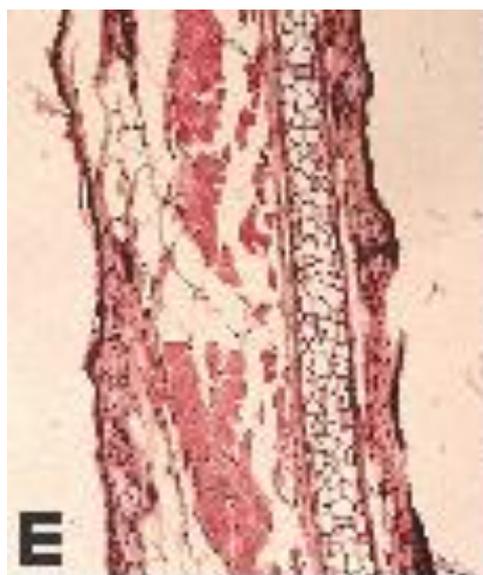
Reservatório:
roedores silvestres







Velozo et al., An. Bras. Dermatol. vol.81 no.3, 2006
Fatal mucosal leishmaniasis in a child

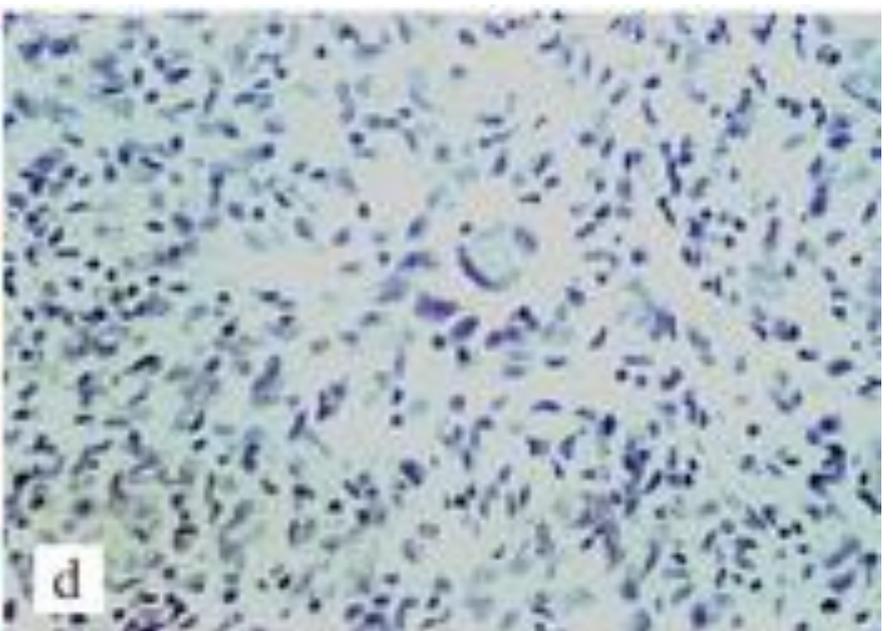
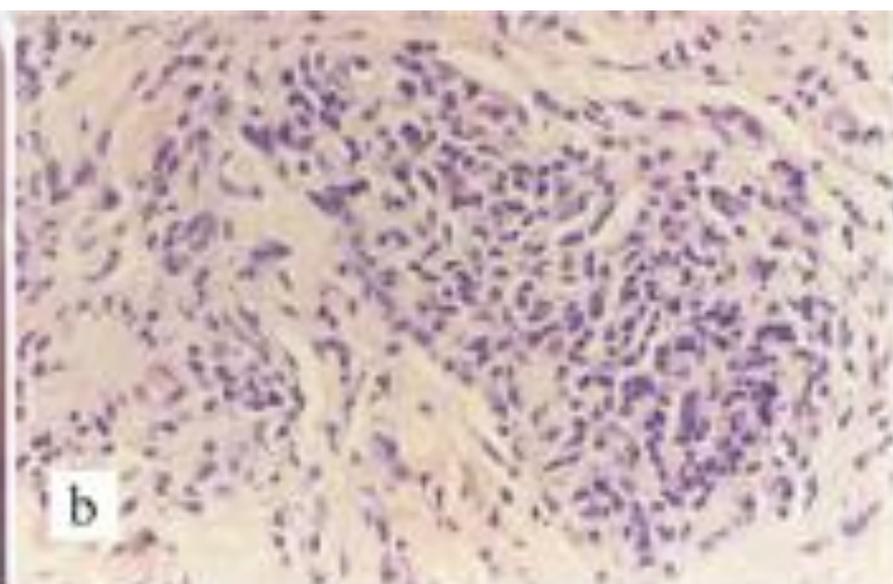
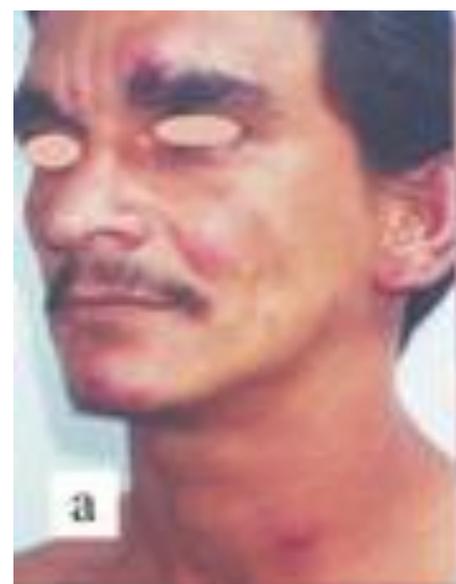


Quadro clínico - forma disseminada

L. (V.) braziliensis

Disseminated Cutaneous Leishmaniasis: A Patient with 749 Lesions





Quadro clínico - forma visceral

- L. (L.) infantum chagasi*
- L. (L.) donovani*
- L. (L.) infantum*

**Reservatório: canídeos,
marsupiais**



Forma visceral

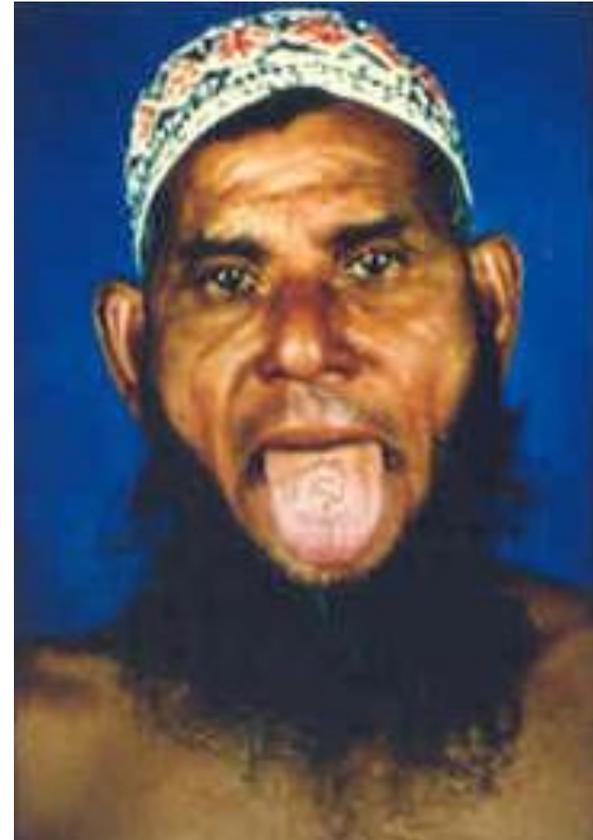
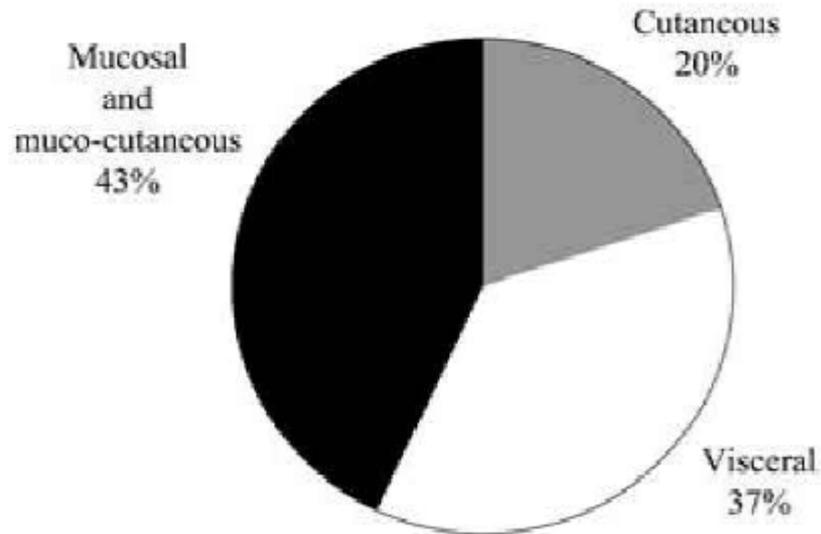
L. (L.) infantum chagasi

L. (L.) infantum



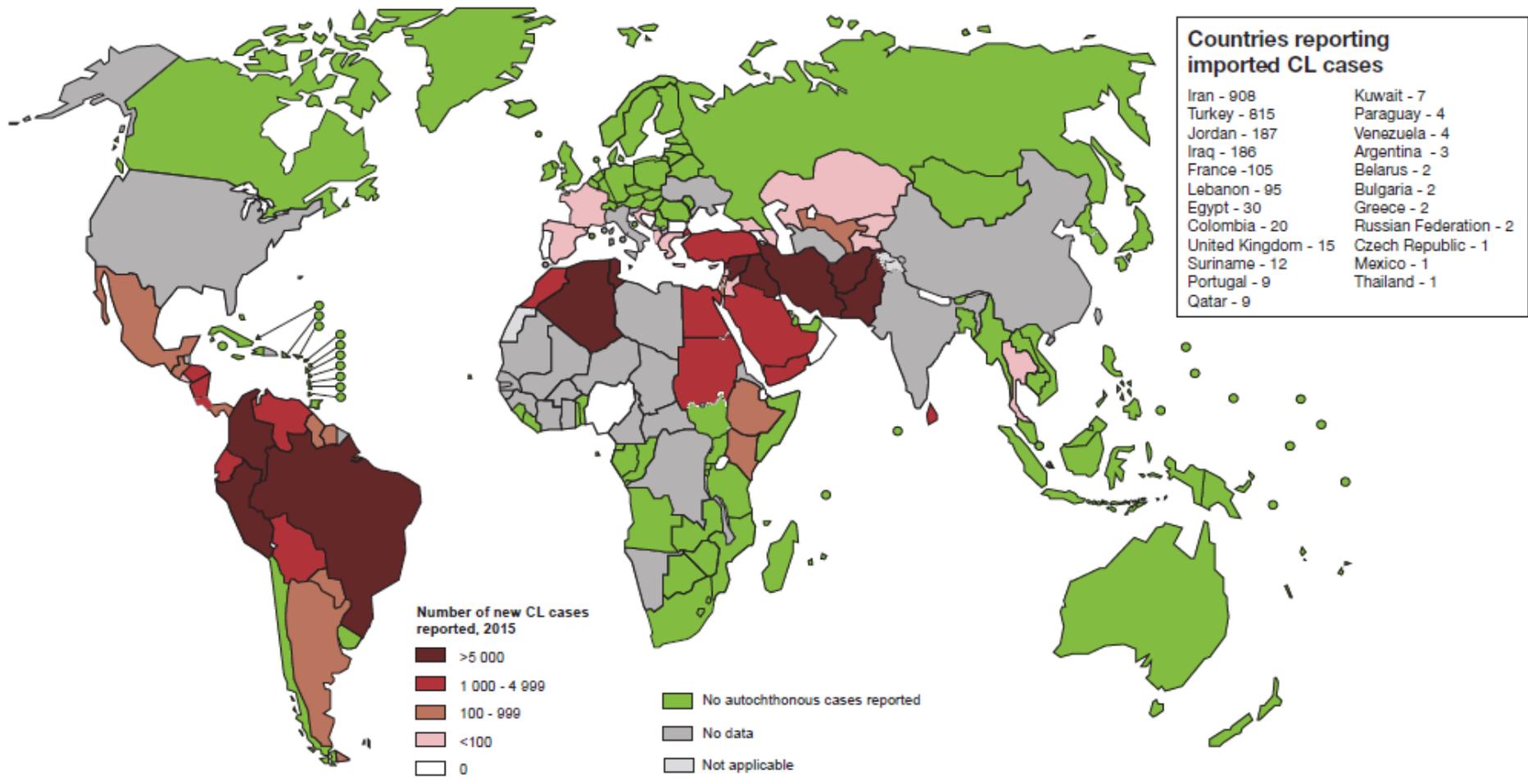
Reservatório: canídeos

Quadro clínico – leishmaniose/AIDS



**Frequentemente atípico
e pouco responsivo ao tratamento**

Status of endemicity of cutaneous leishmaniasis worldwide, 2015



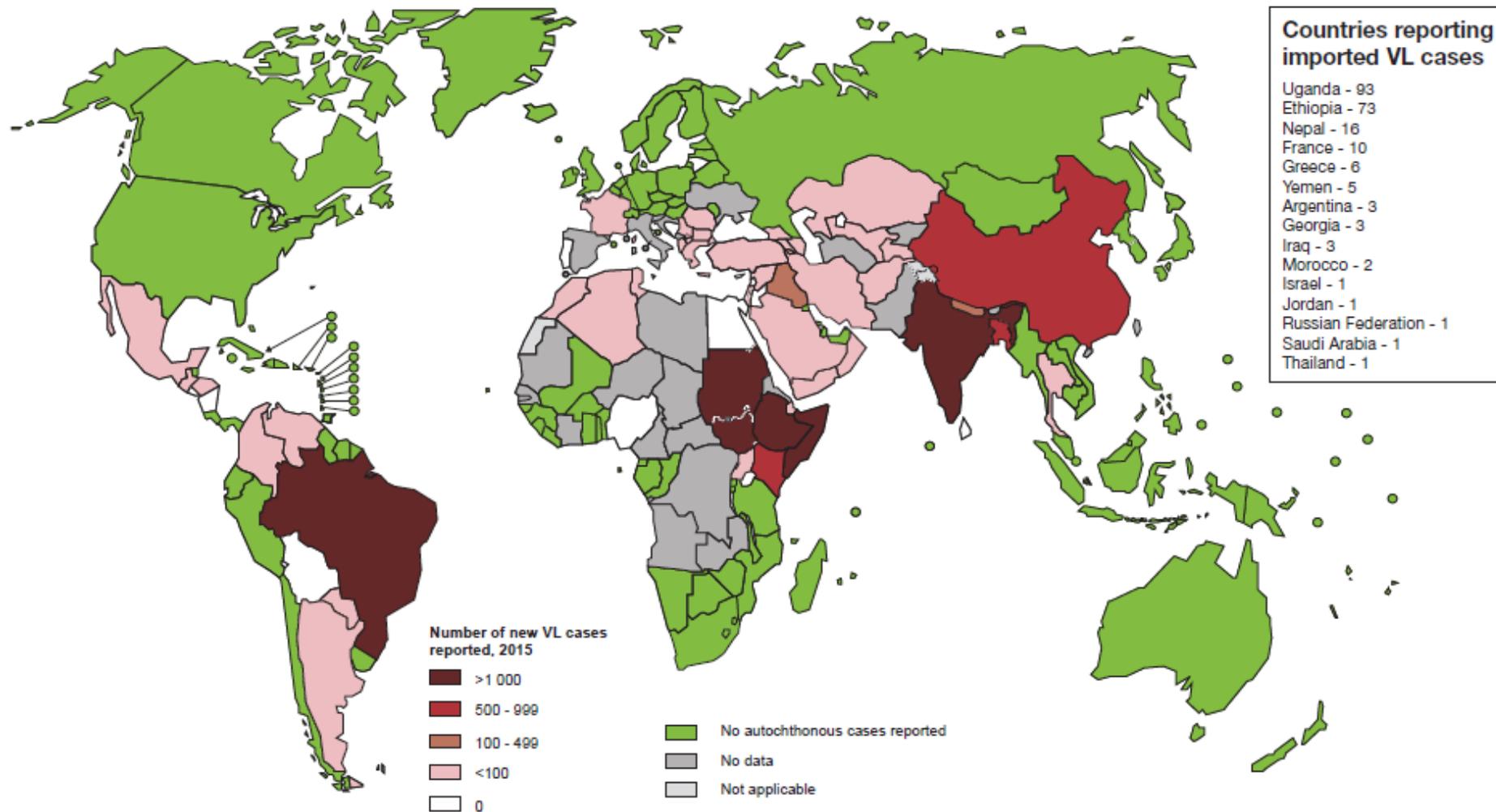
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2017. All rights reserved

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



0.7 to 1.2 million new CL cases occur each year worldwide

Status of endemicity of visceral leishmaniasis worldwide, 2015



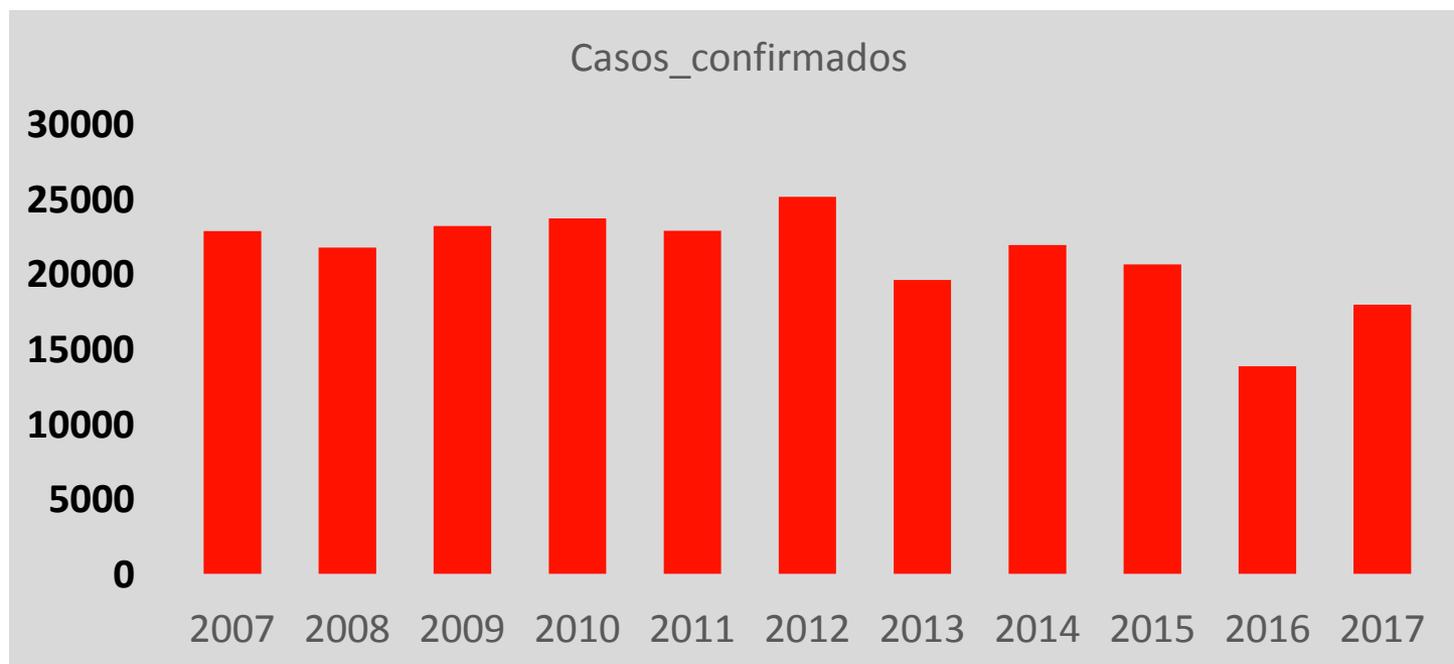
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2017. All rights reserved

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



0.2 to 0.4 million new VL cases occur each year worldwide

Leishmaniose Tegumentar no Brasil

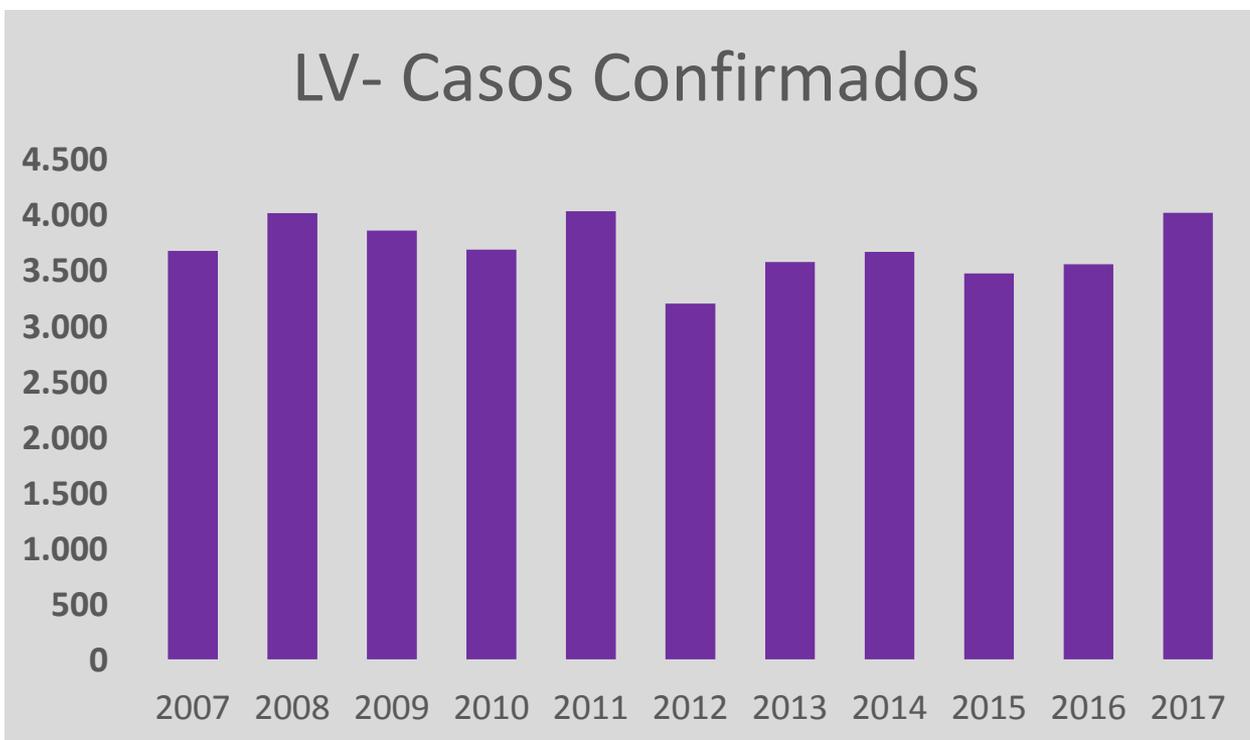


33000 casos em 2000
21000 casos em 2010
18000 casos em 2017

Ministério da Saúde – Portal da Saúde TabNet

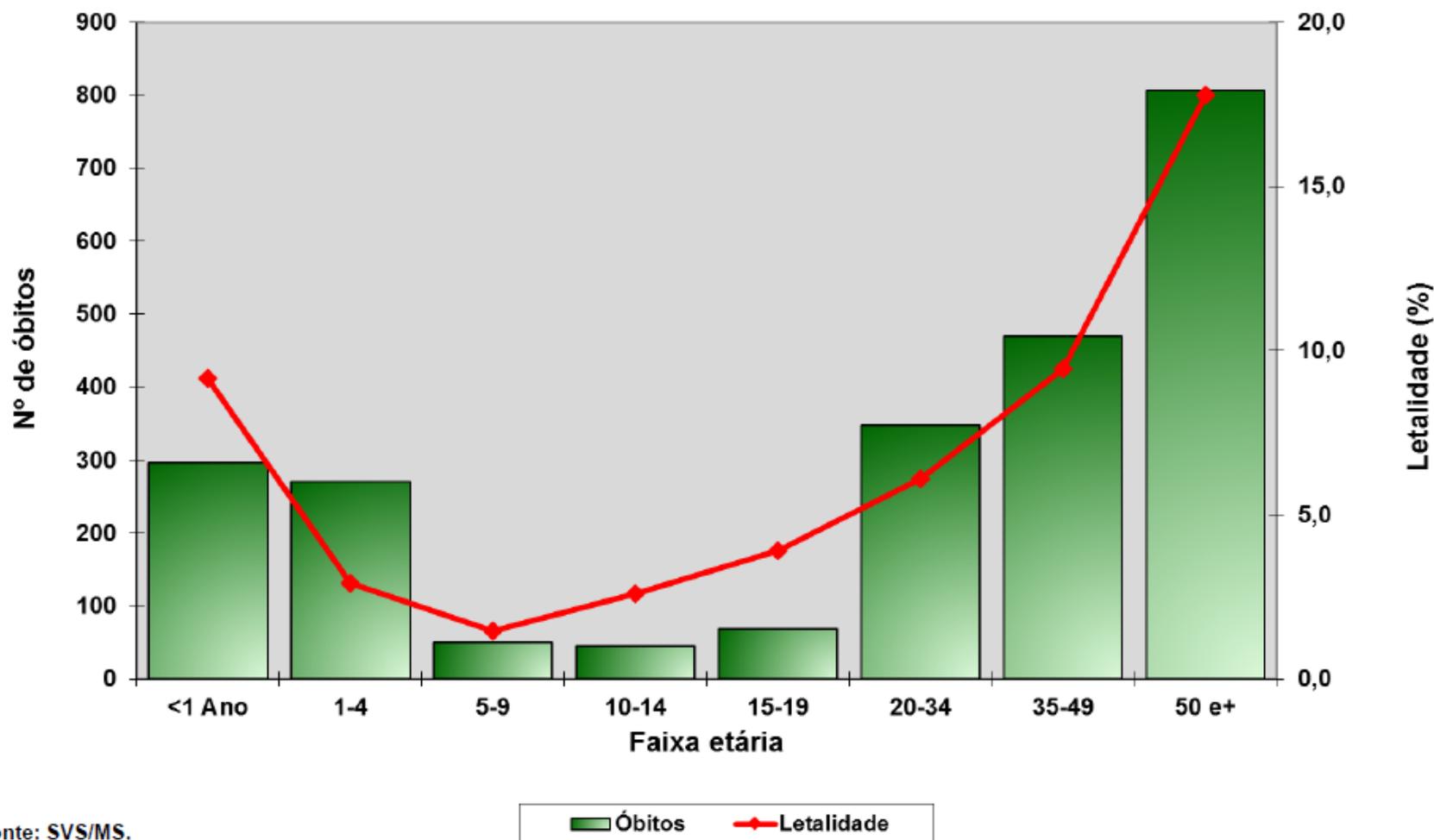
<http://tabnet.datasus.gov.br/cgi/tabcgi.exe?sinannet/cnv/ltabr.def> em 11/10/2018

Leishmaniose Visceral - Brasil



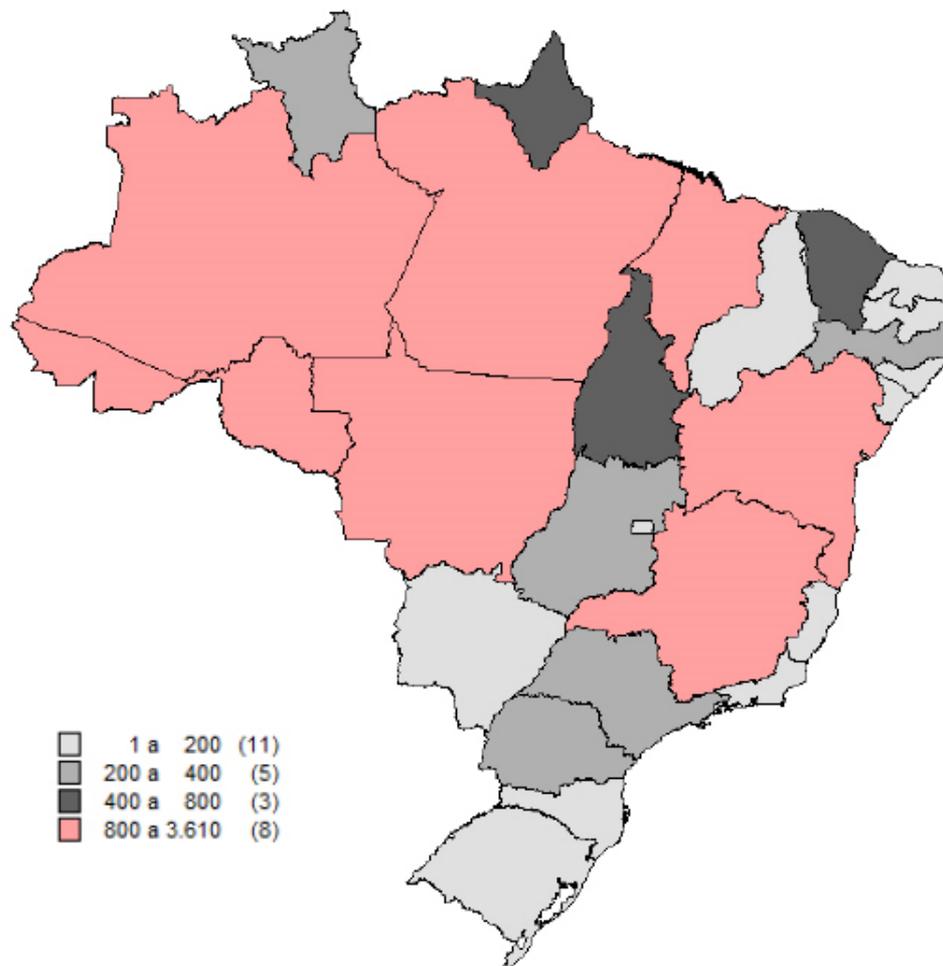
Óbitos por LV: 5 a 8%

Óbitos e letalidade por faixa etária, Brasil, 2007 a 2016

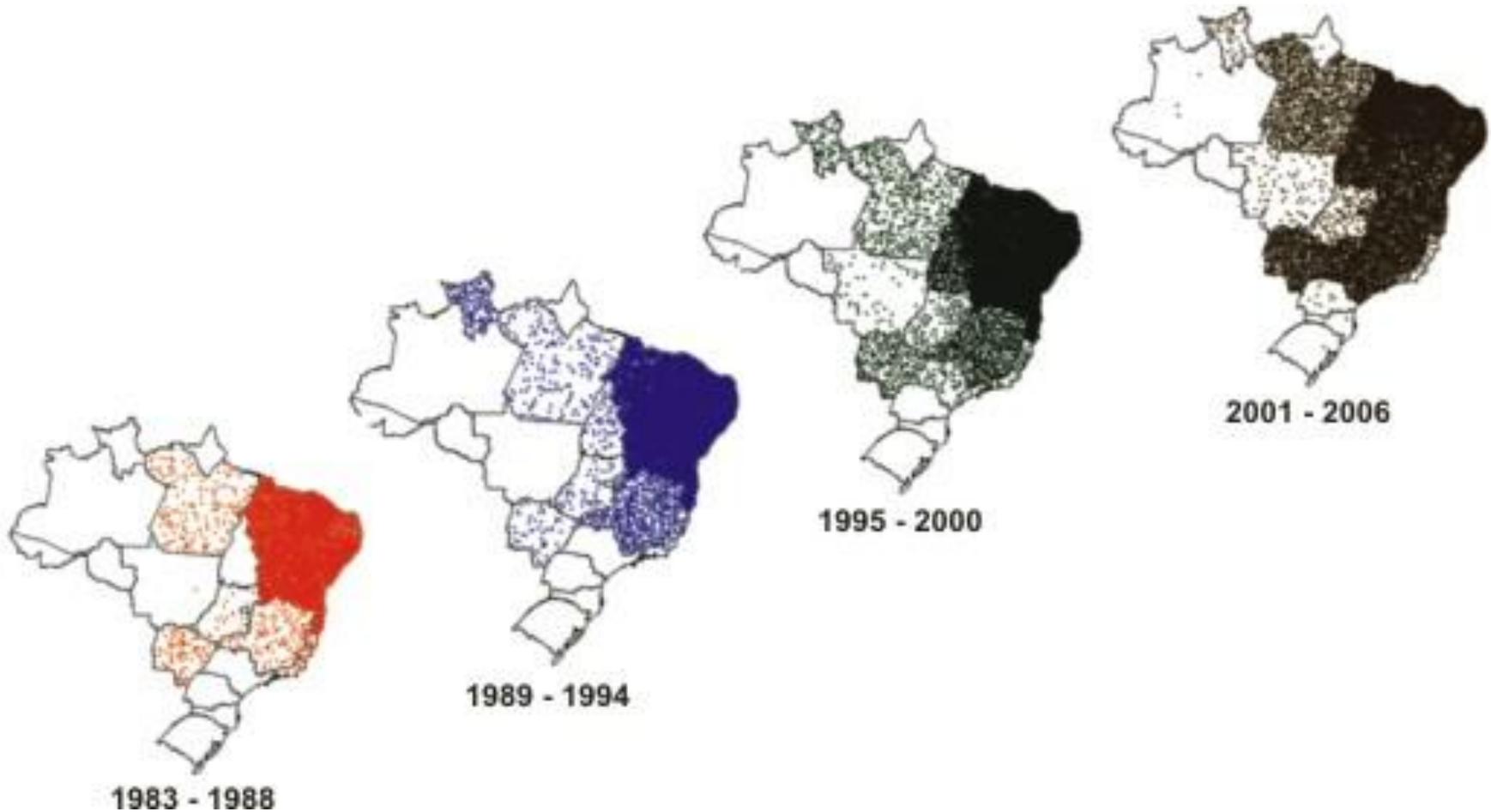


Fonte: SVS/MS.

Casos de leishmaniose tegumentar por UF - Brasil, 2015



Incidência de LV no Brasil

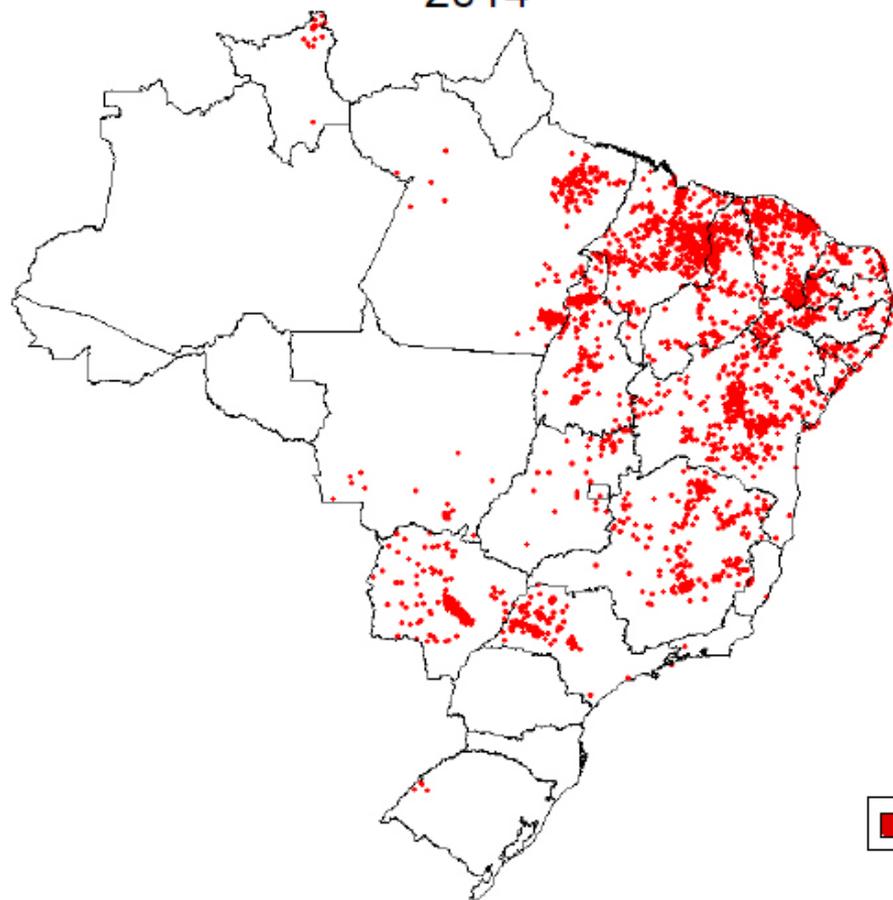


Waneska Alexandra Alves

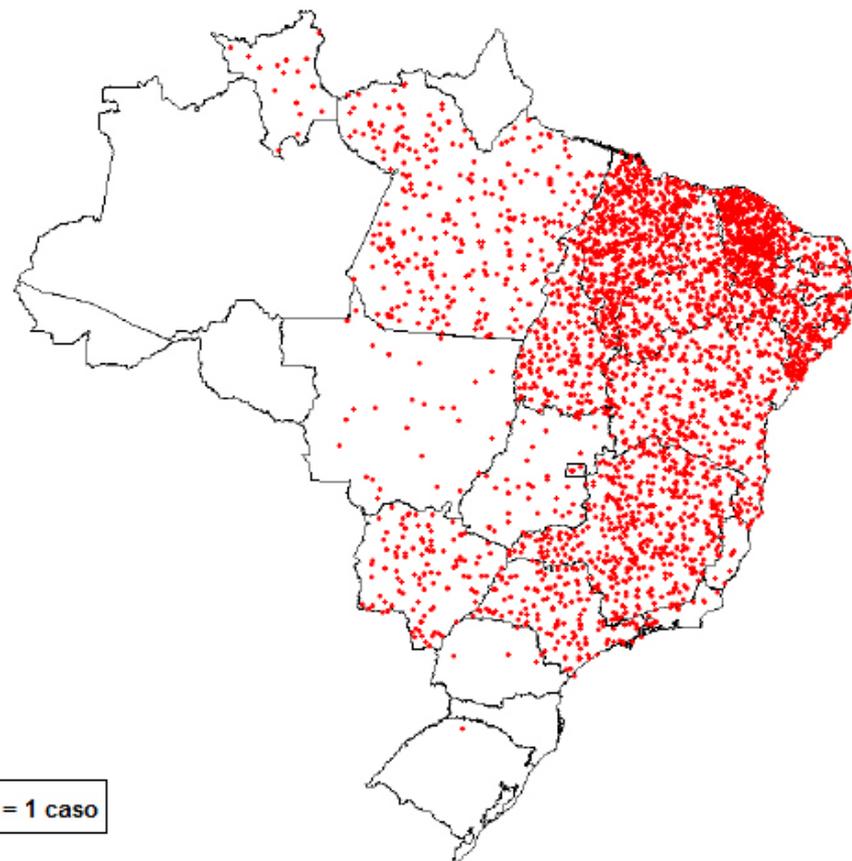
http://www.cve.saude.sp.gov.br/agencia/bepa71_lva.htm

Casos de LV por Município de infecção, Brasil, 2014 e 2015

2014



2015



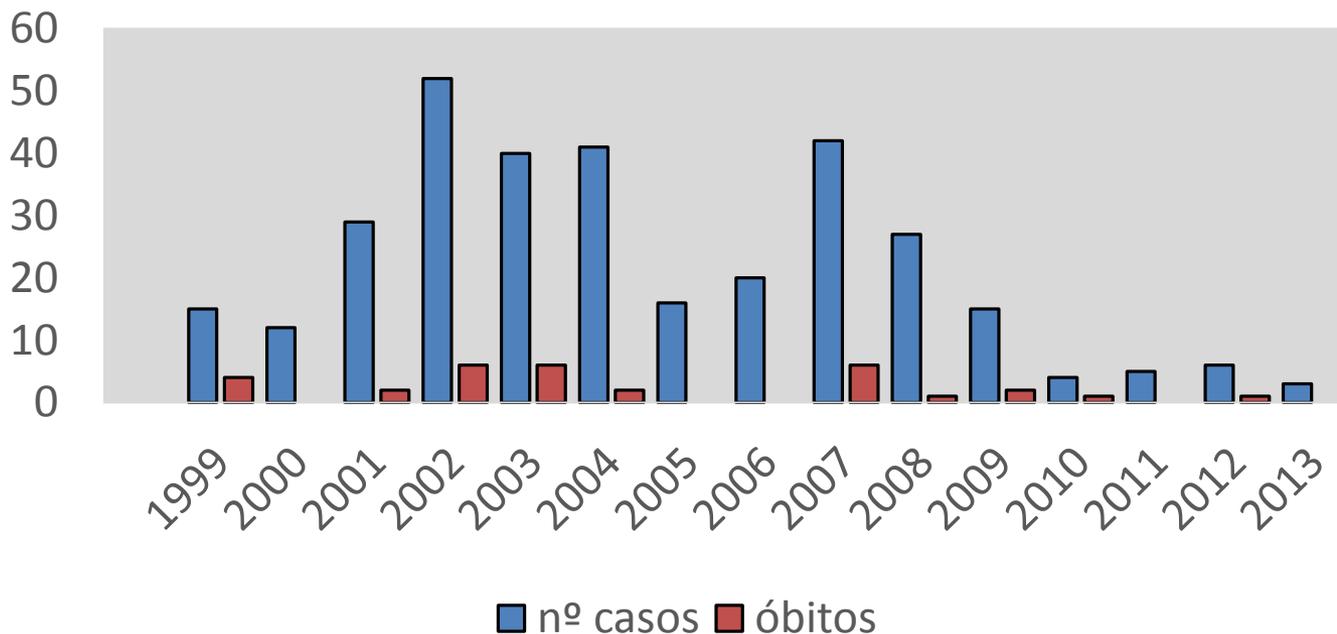
1 ponto = 1 caso

**Quarta-feira,
7 de abril de 1999**

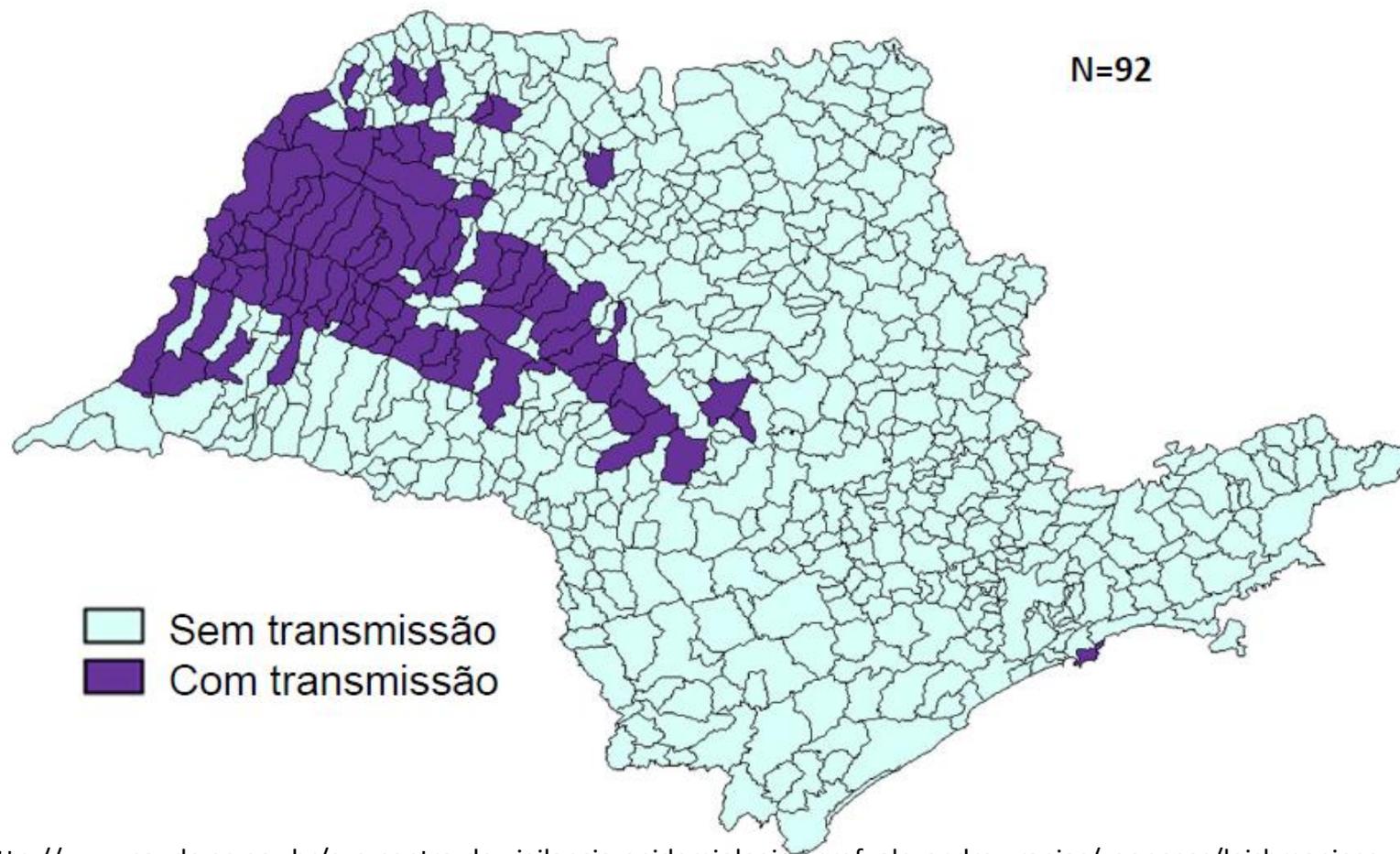
Araçatuba registra 1º caso de leishmaniose

ARAÇATUBA - A Secretaria Estadual da Saúde registrou o primeiro caso de leishmaniose em um ser humano na cidade de Araçatuba, a 540 quilômetros da capital.

LV - Araçatuba

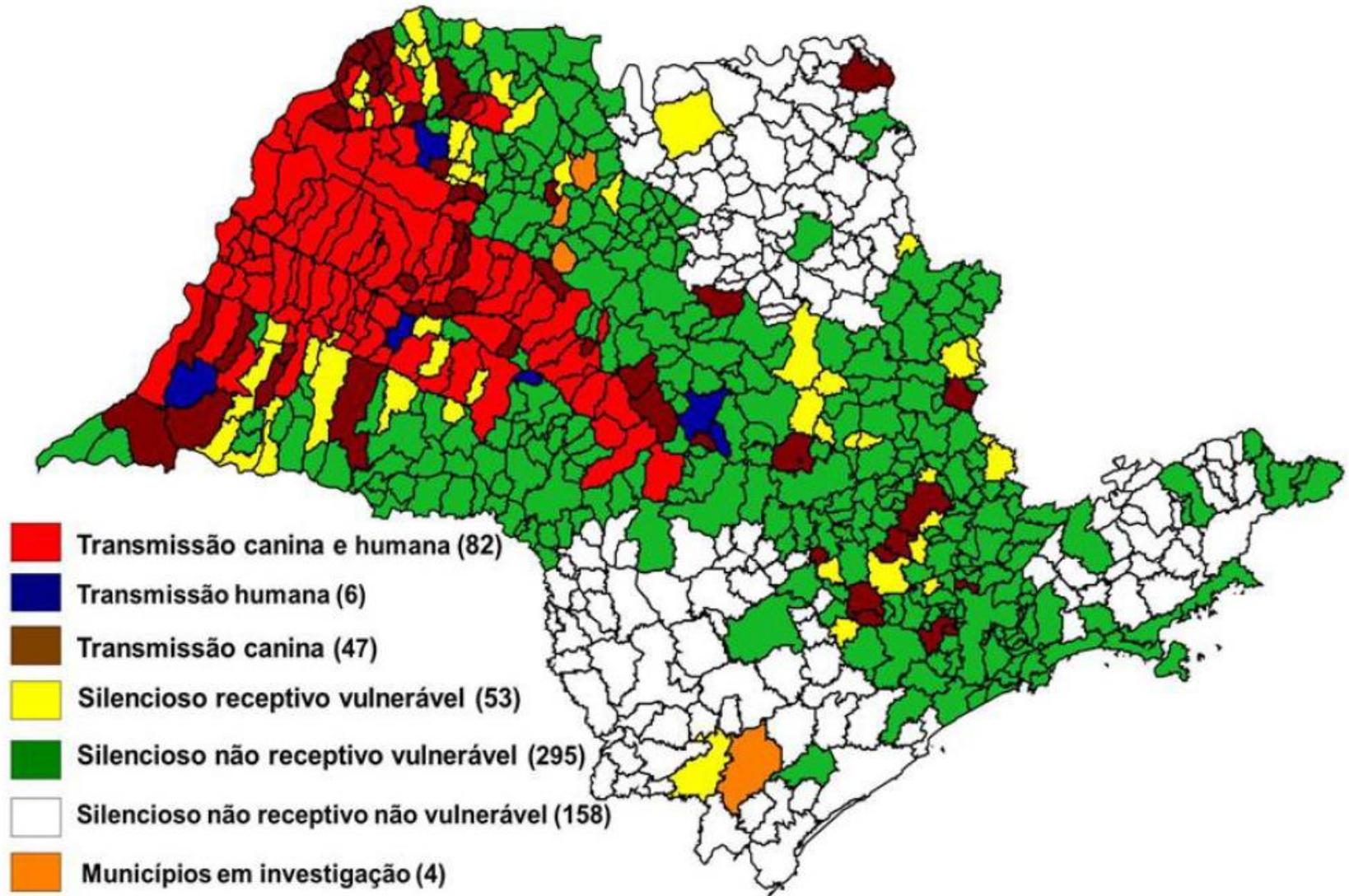


Municípios com casos humanos autóctones de LV no Estado de São Paulo, 1999 a 2016



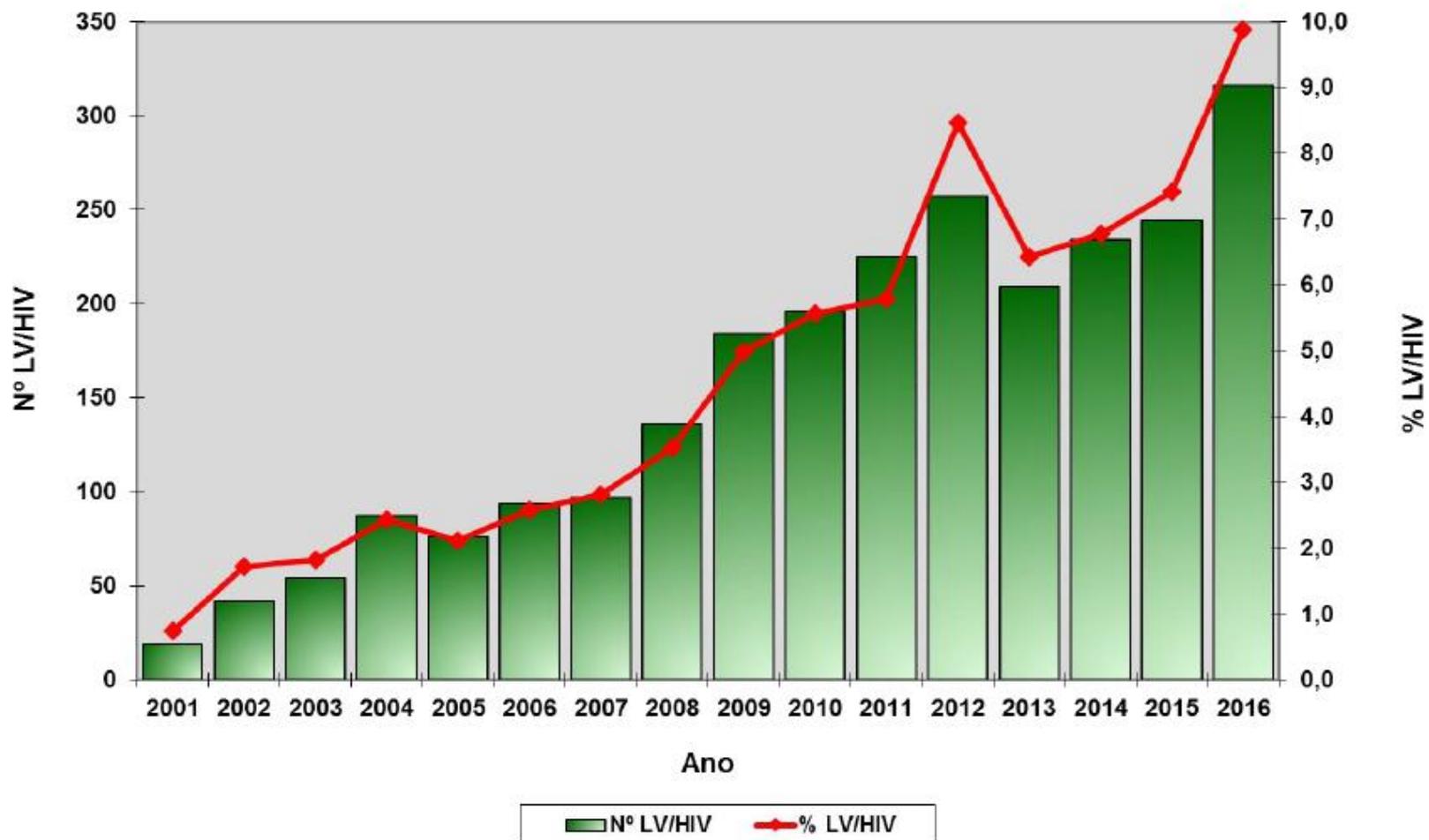
<http://www.saude.sp.gov.br/cve-centro-de-vigilancia-epidemiologica-prof.-alexandre-vranjac/zoonoses/leishmaniose-visceral/dados-estatisticos>

Classificação epidemiológica para Leishmaniose Visceral dos municípios do Estado de São Paulo, 1999 a 2015.



Fonte: Div. Zoonoses/CVE; Núcleo de Parasitose Sistêmicas/IAL, SUCEN

Casos e percentual de coinfeção LV e HIV, Brasil, 2001 a 2016



Diagnóstico

1- Procura do parasita

- VL- aspirado de medula óssea/baço/fígado
- CL – biópsia ou raspado de lesão

Pesquisa direta (imprint/esfregaço ou histopatológico)

Cultura em meio que imita as condições do intestino do inseto: crescimento de promastigotas

Diagnóstico

2- VL - Immunodiagnóstico: pesquisa de anticorpos específicos contra o parasita

- Teste imunocromatográfico (baseado no antígeno k39) (teste rápido IT-Leish[®])
- Imunofluorescência, ELISA
- Imunohistoquímica

3- CL – Immunodiagnóstico

- Teste de hipersensibilidade tardia (Teste de Montenegro)
- Pesquisa de anticorpos circulantes (????)

Teste imunocromatográfico (teste rápido IT-Leish[®]);



sensibilidade 93%
especificidade 97%



[Vídeo produzido pela Fundação Ezequiel Dias sobre a realização do teste rápido It leish para o diagnóstico da leishmaniose visceral humana](https://www.youtube.com/watch?v=ezN8ed-qEXE)

<https://www.youtube.com/watch?v=ezN8ed-qEXE>

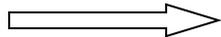
Tratamento

- antimoniais pentavalentes - Glucantime, Pentostam
- pentamidina
- anfotericina B (desoxicolato/liposomal)

TOXICIDADE ↑

DURAÇÃO DO TRATAMENTO ↑

RESISTÊNCIA



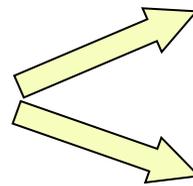
Miltefosine (VO)

Profilaxia



Controle do vetor

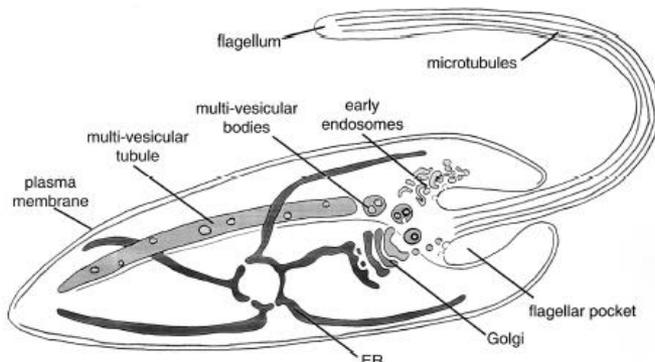
**Controle do hospedeiro
mamífero**



RESERVATÓRIOS

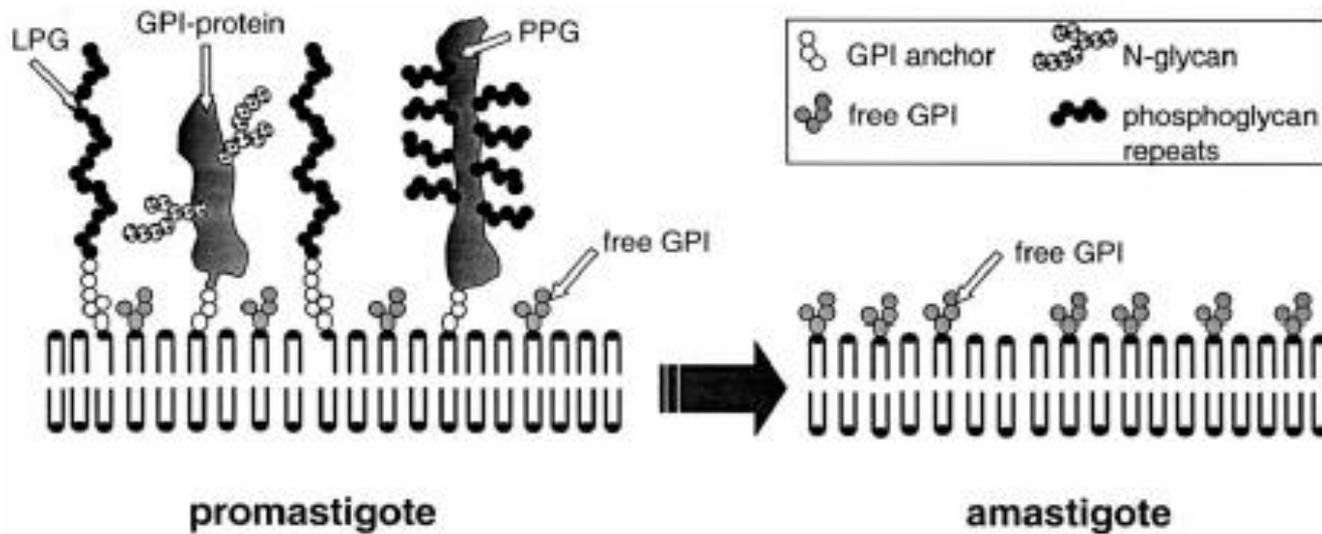
PACIENTES

Mecanismos de evasão



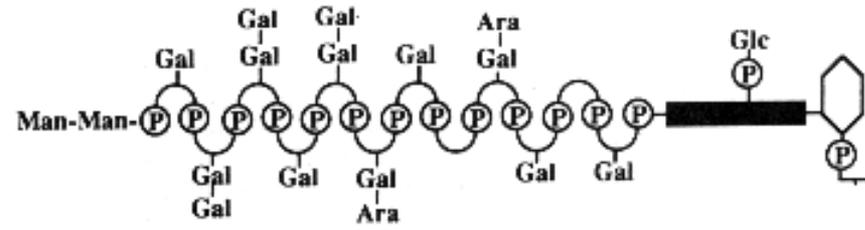
900

S.C. Ilgouz, M.J. McCoville / International Journal for Parasitology 31 (2001) 899-908

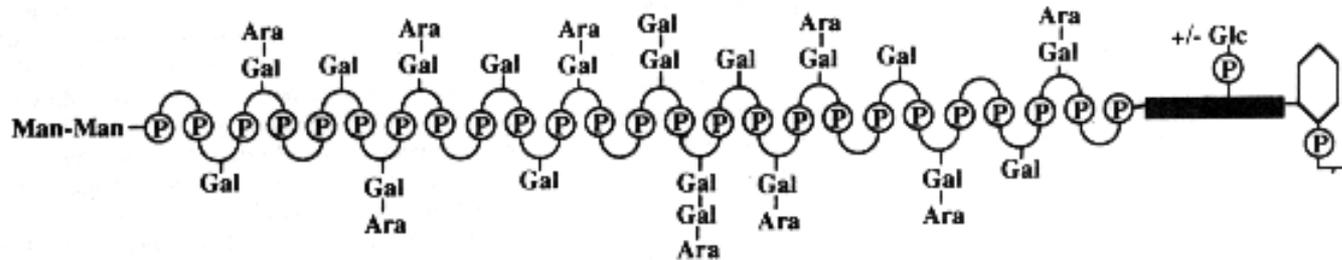


Mecanismos de evasão- LPG

P-LPG



M-LPG



= phosphorylated disaccharide backbone, PO₄-6Galβ1-4Man



= Hexasaccharide core, Galα1-6Galα1-3Galβ1-3Manα1-3Manα1-4GlcN