DISPERSIÓN RECENTE DE LA LV URBANA EN ÁREA DE FRONTERA
PROYECTO IDRC:
ADDRESSING THE EMERGENCE AND SPREAD OF LEISHMANIASIS
IN THE BORDERS OF ARGENTINA, BRAZIL AND PARAGUAY +
URUGUAY + BOLIVIA

Salomon OD, Thomaz-Soccol V, Gonzalez-Britez N, Willat G, Garcia L,
Yadon Z & Project Team IDRC#107577-000

23 e 24 de abril de 2018
Faculdade de Medicina da Universidade de São Paulo – SP - Brasil

SIMPÓSIO INTERNACIONAL
LEISHMANIOSE VISCERAL:
DESAFIOS PARA O CONTROLE
NO CONTEXTO DA DIVERSIDADE DE CENÁRIOS
VL epidemiological context

First reports of rural hVL in the country

PY 1911 railway SP-Corumba construction - Migone
AR 1923 Catania, Italia/ 1926 Salta - Mazza
   8 cases Pará, Ceará, Chagas E et al.
AR 1923-1989 16 hVL cases ou of border
   1951 & 2000 *Lu longipalpis* NE border (forest)
Py 2005-2010 cVL foci (central Py) 20,9%-38,7%-69%

‘80s BR Corumba hVL, 8,7% urban cVL, *Lu cruizi, Lu forattinii*
Spread to south
Urban epidemic transmission*
Parasite dispersion /reservoir migration-vector spread

Source:
COVEV/DEVEP/SVs
Mato Grosso do Sul State, Brazil: VL expansion route west-east:
1) Federal highway/rail-road since early XXth century from SP State
2) Bolivia - Brazil gas pipeline since 1998, migration thousands of workers.

Salles Abreu Passos MF
http://ecen.com/eee10/gas.htm

hVL cases Paraguay, 1994 - 2017
hVL cases Argentina, 2000 – 2017

182 Cases (147- 80,8% NE), lethality 15 (8,2%)
VLc foci 18,33% (8,5-26,2%)
SPREAD BY CONTIGUITY
First report of hVL by second sub-national administrative level and year, ARGENTINA 2006-2014
**Lutzomyia longipalpis modelling distribution**

- **AUC = 0.998**
- **Training 75% Validation 25%**
- **Variables**
  - Annual Rainfall
  - Ppt drier quarter (corr)
  - Av T° coldest quarter
- **Test Jackniffe - Model**
- **Annual rainfall**

**Quintana MG, 2012**
**VL epidemiological context**

**BR - PR 1973/74 & 1980 autochtonous hVL in SEast**
- 2012 Foz Iguacu *Lu. longipalpis* (2010 AR Pto Iguazu)

**BR- SC 2003 no *Lu longipalpis*, no hVL**
- 2011 29/2124 cVL Florianópolis
- 2014 Border Argentina 48/252 cVL 7:3 rural:urban

**BR – RS 1985 Santa María rural-central 5 cVL, 2003 no cVL, no *Lu. longipalpis***
- 2008 São Borja cVL, hVL, 2009 *Lu. longipalpis*
- 2009 Uruguaiana cVL, 1 hVL
- 2016-2017 Porto Alegre 3hVL deaths

**UY 2009 *Lu. longipalpis* in border Salto y Bella Unión (AR Concordia)**

**BO – 2013 (AR Tartagal) no records of hVL, cVL, *Lu. Longipalpis***

PY - 2008 first case hVL Ciudad del Este (away from border) 2014 No Lu. longipalpis

PY - 2008 - 2016 Leishmaniasis Cases in the border area (IDRC Project Area)

Source: Programa Nacional de Leishmaniasis SENEPA
ADDRESSING THE EMERGENCE AND SPREAD OF LEISHMANIASES IN THE BORDERS OF ARGENTINA, BRAZIL AND PARAGUAY 2014-2017

Salomon OD, Thomaz-Soccol V, Gonzalez-Britez N, Yadon Z
Urban grid 400x400 census or stratified + ecotone transects ≈ 750 sites

Sampling

Transversal Seasonal (10%)

Environmental variables
Micro-scale: site
Meso-scale: area
Macro-scale: land use

Domestic reservoir/Biol Mol
5 dogs around each trap

Medical anthropology

Collectives
Key informants
Community

Entomology/Mol Biol ‘Critical Site’
REDILA light trap X 3 nights

Synanthropic rodent activity traps / Transects

ODS - INMET
ARGENTINA Macro-Scale Land Use

Vulnerable Population - Puerto Iguazu Department 2001-2014, Association with land use and land cover
ARGENTINA Environment Stratification and Sampling
84 ‘critical areas and sites’ (meso-scale and micro-scale)

Puerto Iguazú 400 x 400 m

29 environmental variables

Border transect
Barrio Pescadores e100m

Border Ecotone
Barrio Cooperativa e50m

Puerto Libertad 400 x 400 m
ARGENTINA Phlebotominae

'HOT SPOTS', 'COLD SPOTS' & ENVIRONMENT

**Phlebotomine 10 spp**
- **Lu. longipalpis** 47%,
- **Ny. whitmani** 45%,
- **L. infantum** DNA
  - **Lu. longipalpis** 13.3%,
  - **Ny. whitmani** 3.76%

**Krigging**: range 400m, sill 20, nugget 0

**Spatial auto-correlation 400 m**

**Distance to forest**

**Krigging**: range 400m, sill 1.8, nugget 0

ODS - INMET
Six landcover classes was estimated for surface areas between 0.27 and 20.25 hectares. Adjusted GLM. Zero-inflated negative binomial regression model.

Lu. longipalpis abundance better explained by land cover characteristics of 20.25ha.

Significant variables:
Presence - chicks (micro scale) and NDWI (meso scale),
Abundance - availability of different blood sources (hens, dogs or both) (micro scale); drinking water network, garbage collection, sewer (meso scale).
Lu. longipalpis autocorrelated up to 700-1000 m
Lu. longipalpis kept 76.4% of 2011 distribution in 2015
‘Hot spots’ consistent with other modeling approaches

Distribution of Abundance *Lu. Longipalpis* and Rk39+ Dogs

Puerto Iguazu dogs rK39+ 21,2%

> Abundance *Lu. longipalpis* > dogs rK39+
Dog distribution rK39+ explained by dog associated-social networks
> Abundance < distance Phlebotomine trap- human sleeping area
> *Lu. longipalpis* peridomestic than indoors (> autumn)
**RODENT ACTIVITY**

11.7%+ sites (n 773)
None spatial auto-correlation
Urban > forest > rural

**AR- SOCIAL COMPONENT**

- Border territory – environment - urbanization
  Social history – construction – porosity
- Land use – urban ‘green patches’
  ‘low cost areas’ CL - labour regulation

**Actor map – actor KAPP***:
- Focused in cVL.
- KAPP disparate, fragmentated, opposites
- Human-dog interspecific distance
- Gender bias domestic issues
  *family health, environment ‘cleanliness’*
- Dog uses - stray dogs
- State de-legitimization but accountability

**SOCIAL INEQUITIES – PROGRAM INEFFECTIVENES**


**Inter-sectoral POLICY**

Master Plan dog management- P.Iguazu
Public-Private cVL management Workshop & Agreement Act
Discourses-practices participative and actor oriented

**ODS - INMET**
Area where CDC traps were installed for sand fly fauna studies: Foz do Iguaçu city; T1 and T2 transects areas (between Foz do Iguaçu and Santa Terezinha de Itaipu); Santa Terezinha de Itaipu city.

http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0006336
Phlebotominae sand fly distribution in the three survey areas (Foz do Iguaçu, Santa Terezinha de Itaipu and transects).

http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0006336
Abundance and spatial *Lutzomyia longipalpis* distribution showing the number of collected specimens: (A) hydrographic network, (B) forest remnant, (C) hypsometry in m, (D) normalized vegetation index—winter period, (E) normalized vegetation index summer period, (F) normalized vegetation index—spring period, (G) winter temperatures, (H) summer temperature, (I) average temperature over the last 30 years in Foz of Iguacu (FI) and transects areas (T1 + T2) October/November 2014 and Santa Terezinha de Itaipu (STI) October 2015.
Loadings of the variables public services, temperature and humidity, food supply, site, mesoscale, microscale analyzed in each group.

Network of influence of the public services, temperature and humidity, food supply, site, mesoscale, microscale on the abundance of *Nyssomyia whitmani* and *Lutzomyia longipalpis*.


http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0006336
In the 196 sites (pointed in the maps) from three areas of the extreme west of the Southern of Brasil (Foz do Iguaçu, Santa Terezinha de Itaipu and transect between the two cities) dogs were sampled to determine the seroprevalence to leishmaniasis.


http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0189182
Path analysis with extrinsic (environmental) characteristics that affect the infection rate in dogs from western region of the Paraná State, Brazil.

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0189182
### ASPECTO CLÍNICO EM CÃES

<table>
<thead>
<tr>
<th>SINAIS DERMICOS</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>TOTAL</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcera em bolsa escrotal</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0,0</td>
</tr>
<tr>
<td>Descamação furfurácea</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0,3</td>
</tr>
<tr>
<td>Ulcera em outro local (Descrição)</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0,3</td>
</tr>
<tr>
<td>Seborrhea Úmida</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>0,4</td>
</tr>
<tr>
<td>Nódulos (Dérmicos)</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>4</td>
<td>0,6</td>
</tr>
<tr>
<td>Ulcera em membros</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>5</td>
<td>0,7</td>
</tr>
<tr>
<td>Ulcera em nariz</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>9</td>
<td>1,3</td>
</tr>
<tr>
<td>Eritema</td>
<td>4</td>
<td>5</td>
<td>0</td>
<td>1</td>
<td>10</td>
<td>1,5</td>
</tr>
<tr>
<td>Alopecia em Região abdominal</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>4</td>
<td>11</td>
<td>1,6</td>
</tr>
<tr>
<td>Alopecia em Membro Anterior</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>5</td>
<td>13</td>
<td>1,9</td>
</tr>
<tr>
<td>Alopecia em Outro Local</td>
<td>10</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>13</td>
<td>1,9</td>
</tr>
<tr>
<td>Seborrhea Seca</td>
<td>7</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>14</td>
<td>2,1</td>
</tr>
<tr>
<td>Alopecia em Focinho</td>
<td>4</td>
<td>2</td>
<td>3</td>
<td>9</td>
<td>18</td>
<td>2,6</td>
</tr>
<tr>
<td>Ulcera em ponta de orelhas</td>
<td>3</td>
<td>7</td>
<td>4</td>
<td>4</td>
<td>18</td>
<td>2,6</td>
</tr>
<tr>
<td>Alopecia em Região Dorsal</td>
<td>1</td>
<td>5</td>
<td>4</td>
<td>9</td>
<td>19</td>
<td>2,8</td>
</tr>
<tr>
<td>Prurido</td>
<td>8</td>
<td>7</td>
<td>3</td>
<td>1</td>
<td>19</td>
<td>2,8</td>
</tr>
<tr>
<td>Alopecia em Membro Posterior</td>
<td>9</td>
<td>1</td>
<td>4</td>
<td>6</td>
<td>20</td>
<td>2,9</td>
</tr>
<tr>
<td>Hiperqueratose</td>
<td>3</td>
<td>9</td>
<td>8</td>
<td>1</td>
<td>21</td>
<td>3,1</td>
</tr>
<tr>
<td>Alopecia Generalizada</td>
<td>10</td>
<td>3</td>
<td>5</td>
<td>6</td>
<td>24</td>
<td>3,5</td>
</tr>
<tr>
<td>Onicogrifose</td>
<td>8</td>
<td>9</td>
<td>15</td>
<td>1</td>
<td>33</td>
<td>4,8</td>
</tr>
<tr>
<td>Alopecia em Orelhas</td>
<td>26</td>
<td>5</td>
<td>5</td>
<td>11</td>
<td>47</td>
<td>6,9</td>
</tr>
<tr>
<td>Adenomegalia</td>
<td>11</td>
<td>23</td>
<td>22</td>
<td>6</td>
<td>62</td>
<td>9,1</td>
</tr>
</tbody>
</table>

---

Path analysis with intrinsic characteristics of the dogs that affect their probability of infection in the western region of the Paraná State, Brazil.

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0189182
Patches sampled and spatial distribution of Leishmania spp. in the extreme west of Parana state, Southern Brasil.

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0189182
Figura 5. Área de estudio dividida en zonas correspondientes a los distritos de Ciudad del Este y Presidente Franco.

Study Area

Phlebotominae abundance

cVL
We also asked respondents what they thought about the feelings perceived by animals, mainly dogs, and most of them stated that animals have rights (95.2%), morality (74.2%), and feelings (98.4%), and that they need to be respected.
PHLEBOTOMINE DISTRIBUTION

*Lutzomyia longipalpis*

*Nyssomyia whitmani*

NDVI

Land cover

‘Hot spots’

Metapopulation dynamics

Source populations
Visceral Leishmaniasis settled

Urban distribution of *Lutzomyia longipalpis* in ‘hot spots’, Canine VL prevalence rates 22-26% increasing along time.
Ar- Puerto Iguazu, Br- Foz do Iguacu

Visceral Leishmaniasis incipient

*Lu. longipalpis* and canine VL restricted to small clusters, Canine VL general prevalence up to 4%.
Br- Santa Terezinha do Itaiupu, Pr- Presidente Franco, Ur- Salto, Bo – Pocitos.

Cutaneous Leishmaniasis steady

*Nyssomyia whitmani* in ecotones, Without *Lu. longipalpis*, canine VL imported cases.
Ar – Puerto Iguazu urban periphery, Ar, Br, Py - transects

*Uy-Paysandu No risk* 32º19’S, 58º04’W
Consistent S-T Models

Lu longipalpis ~ 400 sampling sintews

POSADAS ARGENTINA 2007

POSADAS ARGENTINA 2009

Abundancia Interpolada enero 2009

Interpolación Abundancia febrero-marzo 2007
Consistent S-T Models

Santini MS et al., PLOS NTD 2015
Santo Tome Corrientes

Berrozpe P. et al. MIOC 2017 Corrientes City

Gomez-Bravo A et al. Parasites & Vectors. 2017 Clorinda Formosa
MODEL of MODELS

Surveillance-Control
Cost-effective strategy

Remote sensing
Secondary sources

Probable Risk
Critical area

Critical site

Weighthed environmental, biological, social risk drivers

Potential risk

Few ‘hot spots’ monitoring
Few source populations interventions

Validation – transference- evaluation

Secondary sources
Primary sources
Social Unfeasibility of cVL culling

Inefficiency – stray dogs

Public-Private cVL management- Workshop & Agreement Act
Puerto Iguazu, 8/2015

ODS - INMET
Progamas Nacionales: Leishmaniasis; Control Enfermedades Zoonóticas; Tenencia Responsable y Sanidad de Perros y Gatos; SENASA

Zoonosis Provinciales: Misiones, Corrientes, Formosa, Chaco, Santa Fe, Entre Ríos, Santiago del Estero (no concurre Salta)

Zoonosis Municipales: Posadas, Iguazú, Santo Tomé, Oberá, Instituto Pasteur BsAs

Federación Veterinaria Argentina
Consejo Veterinarios Provincia: Misiones, Corrientes, Chaco, Formosa, Entre Ríos (no concurre Santiago del Estero, Salta)

Discussion of evidences and roles
Intersectoral Technical Advisory Group - CITAG
coordinated by the National Leishmaniasis Program

Public-Private cVL management - Workshop & Agreement Act

National Leishmaniasis Program
+ Standardized integrated interventions by risk stratification
+ Natl lab network: cVL diagnoses QC and lab certification (publ & private)
+ Validation of new techniques, experimental designs, health cards.
+ Dog culling just another possible complementary measure:
  Risk stratification and cVL prevalence, individual reservoir capacity, psycho-social context, vector/environment management, dog replacement, stray dogs

Private MVs National Federation
+ Dog owner: right to be informed about actual risk
+ Infected dog conditions that allow the culling refusal
+ Co-responsibility form signed by owner, MV, NLP local agent
+ NLP accepted treatments / preventive measures:
  Castration, restriction of transit, traceability, follow up.

Public-Private cVL management - Workshop & Agreement Act
Posadas/Misiones:
- Pheromone (S)-9-methylgermacrene-B *(spreading type)*
- *per* gene: Fst values ranging from 0.17-0.43, might be a different sibling species from those found in NE and SE Brazil

Salomón OD, Araki AS, Hamilton GC, Acardi SA, Peixoto AA., MIOC 2010

Argentina populations: Haplotype diversity motochondrial markers ND4, cytb.
- Two K populations
- Three clusters (lineages): Ar1, Ar2 (six populations), Ar-Bra grouped with Jacobina and Lapinha, Brazil

Pech-May A Thesis unpublished

Dispersion routes hypothesis
A: Argentina, Bo: Bolivia, Br: Brasil, P: Paraguay, U: Uruguay, IDRC-CDRI y OPS-PAHO

Fila superior: Jorge Miret (P), Javier Liotta (A), Oscar Daniel Salomón (A), Luis Calegari (U), André Luiz Gonçalves (Br), Luciana Chiyo (Br), Mónica Ruoti (Br), Gabriela Willat (U), Mílsa Britez (P), Esteban Couto (A), Mario Sergio Michaliszyn (Br), Alceu Bissetto Junior (Br)

Fila medio: Pablo Berrozpe (A), Sofial Moya (A), Soledad Santini (A), Roberto Bazzani (IDRC-CRDI), Ivana Belmonte (Br), Magali Giuliani

Photo Credit: Dr. Salomón