



WORLD
HEALTH
SUMMIT

REGIONAL MEETING
LATIN AMERICA
SÃO PAULO
APRIL 6-8, 2014

Centro de Convenções de Reboças
08.04.2014
Red Room
17: 00h

Recommendations for Coping with Leishmaniasis: A Review of Control Strategies

Ministério
da Saúde



Leishmaniasis - a Global Problem

Visceral 2012

300 000 cases

20,000 deaths (6.7%)

310 million at risk



Southern Ethiopia

Cutaneous

in last 5 years

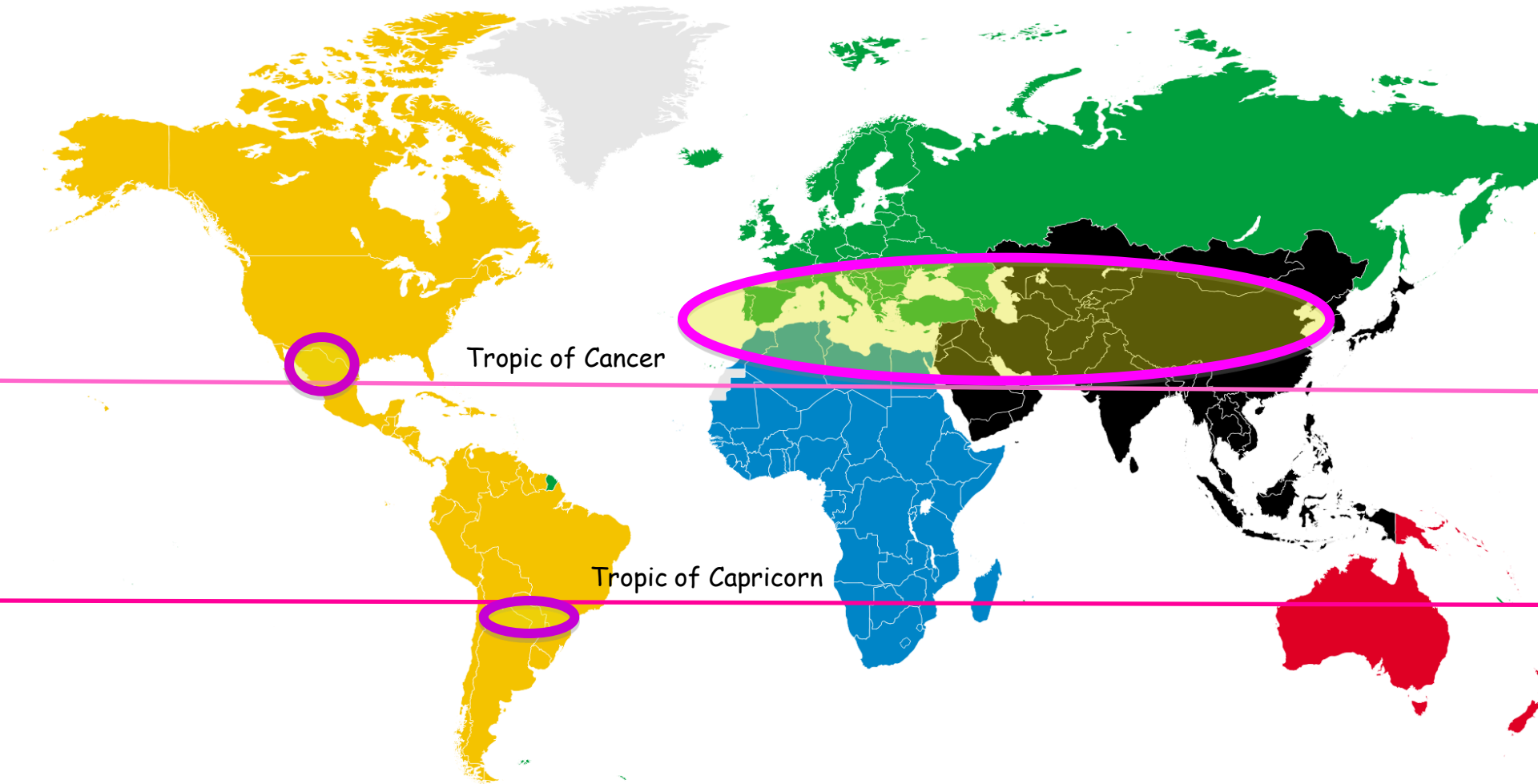
1 million cases



Syria/Turkey

A Neglected Tropical Disease Is it?

Neglected **Yes** but **not only** Tropical



Leishmaniasis - a serious health problem in the Americas and control strategies are precarious



Estimates* of CL cases per year:
187,200 to 307,800



Estimates* of VL cases per year:
3,668 to 4,500



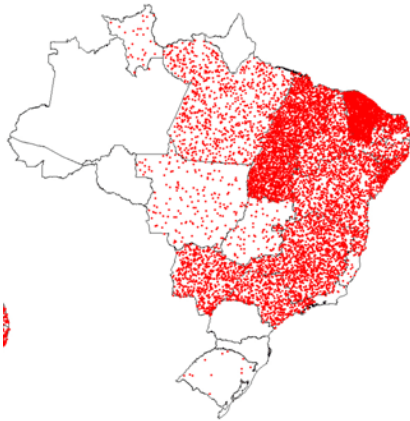
+ Alvar J, Vélez ID, Bern C, Herrero M, et al. (2012) Leishmaniasis Worldwide and Global Estimates of Its Incidence. PLoS ONE 7(5): e35671. doi:10.1371/journal.pone.0035671

<http://www.plosone.org/article/info:doi/10.1371/journal.pone.0035671>

VL in Brazil

From 1995 to 2011 - 53,633 (X 3,352)

2009-2011



In São Paulo State
from 1999 to 2012

2,146 cases with 169 deaths (7.9%)



1992 India 77,102 cases 1,049 deaths (1.4%)

Brazil - Addressing the challenge

- In February 2014 a 3 day forum was convened by the **Brazilian Ministry of Health** to discuss 3 questions on the strategies of the **surveillance and control of visceral leishmaniasis**.
- The result was a 7 page document with specific recommendations as well as suggestions for support of 12 research areas.

Ministério
da Saúde



So why is the control of the
leishmaniases so difficult?



John Snow
The Principal is Simple
Cholera in Soho
London



1854

Find and treat the source

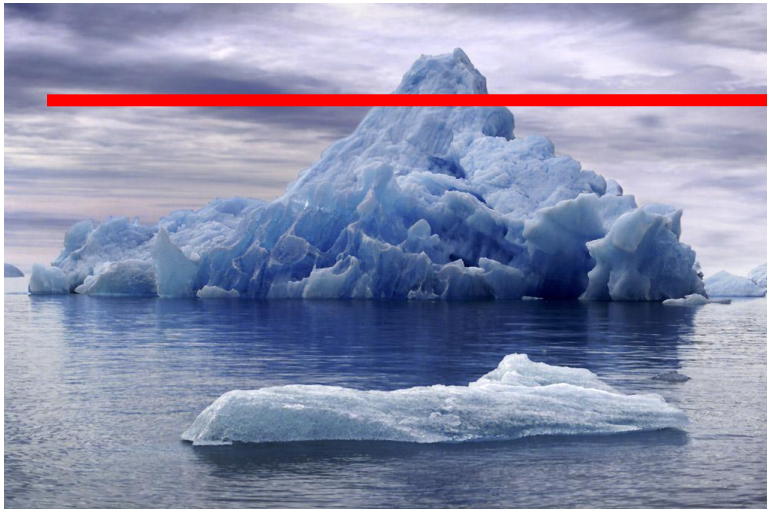
Can this be done for American
Visceral and Cutaneous leishmaniasis?

The American Leishmaniases are Zoonoses

Man - tip of the iceberg

Not a reservoir host

15 *Leishmania*
species recorded in man



There are 20 named neotropical *Leishmania* species



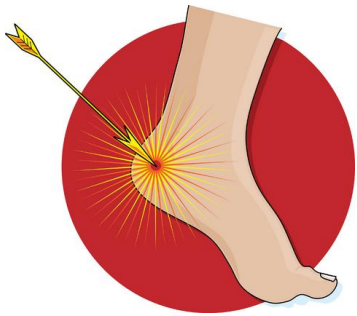
The 3 Control Frontiers

Reservoirs

Vectors

(Leishmania's Achilles' heel)

Man



Reservoirs

Cutaneous leishmaniasis

Principally small sylvatic mammals but in some foci dogs are considered as sources.



Feasible Control actions
Habitat management



Visceral Leishmaniasis

principal reservoir is the dog but cats, as well as other small mammals may increase the basic reproductive rate (R_0)

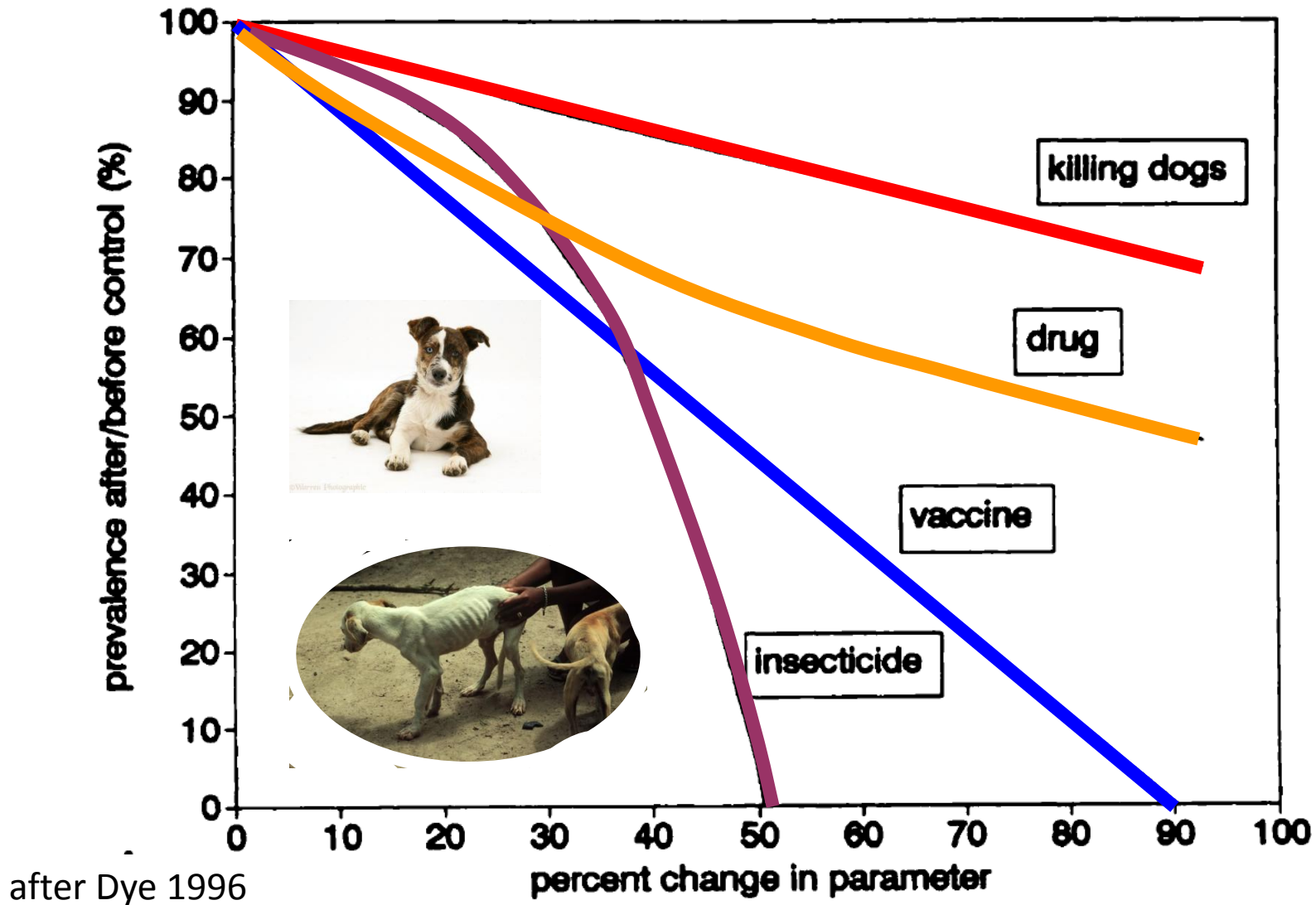


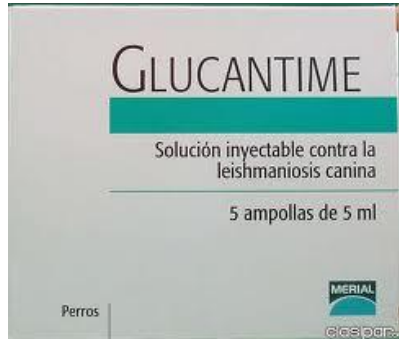
Control of canine infection is feasible

But what method?



The impact of different control methods on canine visceral leishmaniasis





Should we treat dogs?

Meglumine antimoniate

Miltefosine

Allopurinol

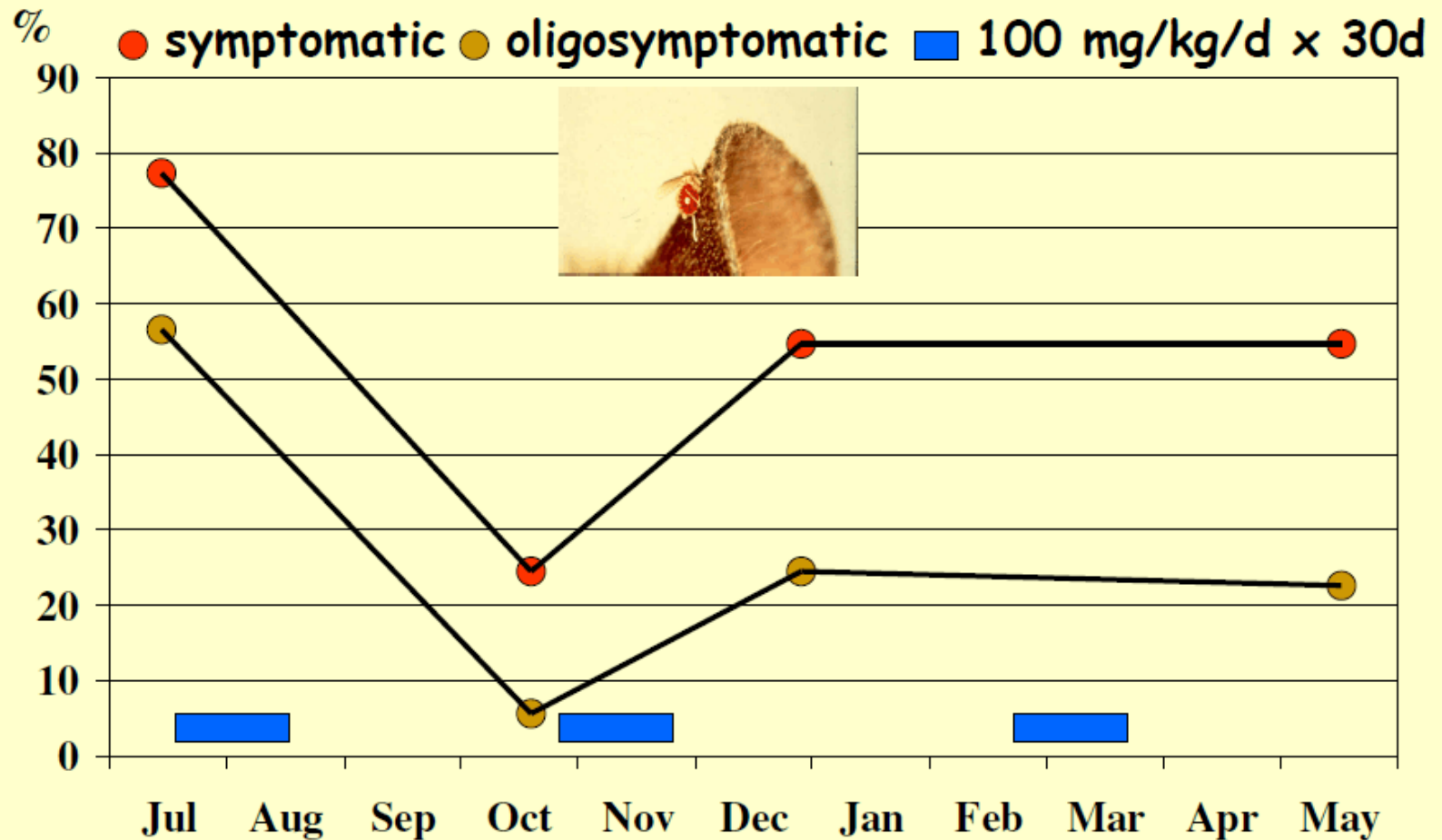


Danger - Resistance



In Europe this is not considered important as patients are treated with Liposomal amphotericin B (Ambisome®)

Infection rates in *Phlebotomus perniciosus* fed on dogs under meglumine antimoniate treatment (Gradoni et al 1987)



Available Vaccines for canine visceral leishmaniasis

LEISHMUNE® (FML)



LEISH-TEC®



CANILEISH®
(LiESP/QA-21)



The levels of protection in the field are presently controversial

CANILEISH® (LiESP/QA-21)



Experimental results in Beagles



Reduction but not elimination of
infectiousness to sand flies

A significant reduction in the number
of animals that developed acute
infections



A major problem with laboratory vaccination experiments

Concussively shown that needle challenge is immunologically different from sand fly challenge

Conclusion: The level of protection can only be assessed using infected sand flies as the source of infection



Vectors



Many different species

Strategies will depend on knowing the habits of the different species



Sand fly biology

Based on a vector's biology
Avoid contact

Rarely used
It can be very efficient

Control of leisure habits

Construction Company - Amapá State, Brazil



High incidence of cutaneous leishmaniasis in work force resulting in loss of production

Common factor - the majority were hunting at night

Solution - prohibit hunting and entering forest at night

Result - number of infections fell dramatically to nearly zero

Limitations - only possible in controlled communities but local communities can be notified of the danger via **educational programs** and advised to avoid forest as much as is possible



Time of year

Serra dos Carajás, Pará State Endemic for *L. (V.) braziliensis*



The vector
Psychodopygus
wellcomei hibernates
in the dry season

Seasonal transmission - No cases in dry season



Environmental management

Potentially one of the most important control methods



Why?



Community based - long term sustainability. Less dependant on the availability of governmental funds (NGOs)

Requirements: knowledge of vector ecology and education of population in endemic area

Effectiveness: Shown to reduce the density of visceral and cutaneous leishmaniasis vectors

Danger of inadequate sustainability of vector control

Vector population reduced

Transmission rate lowered

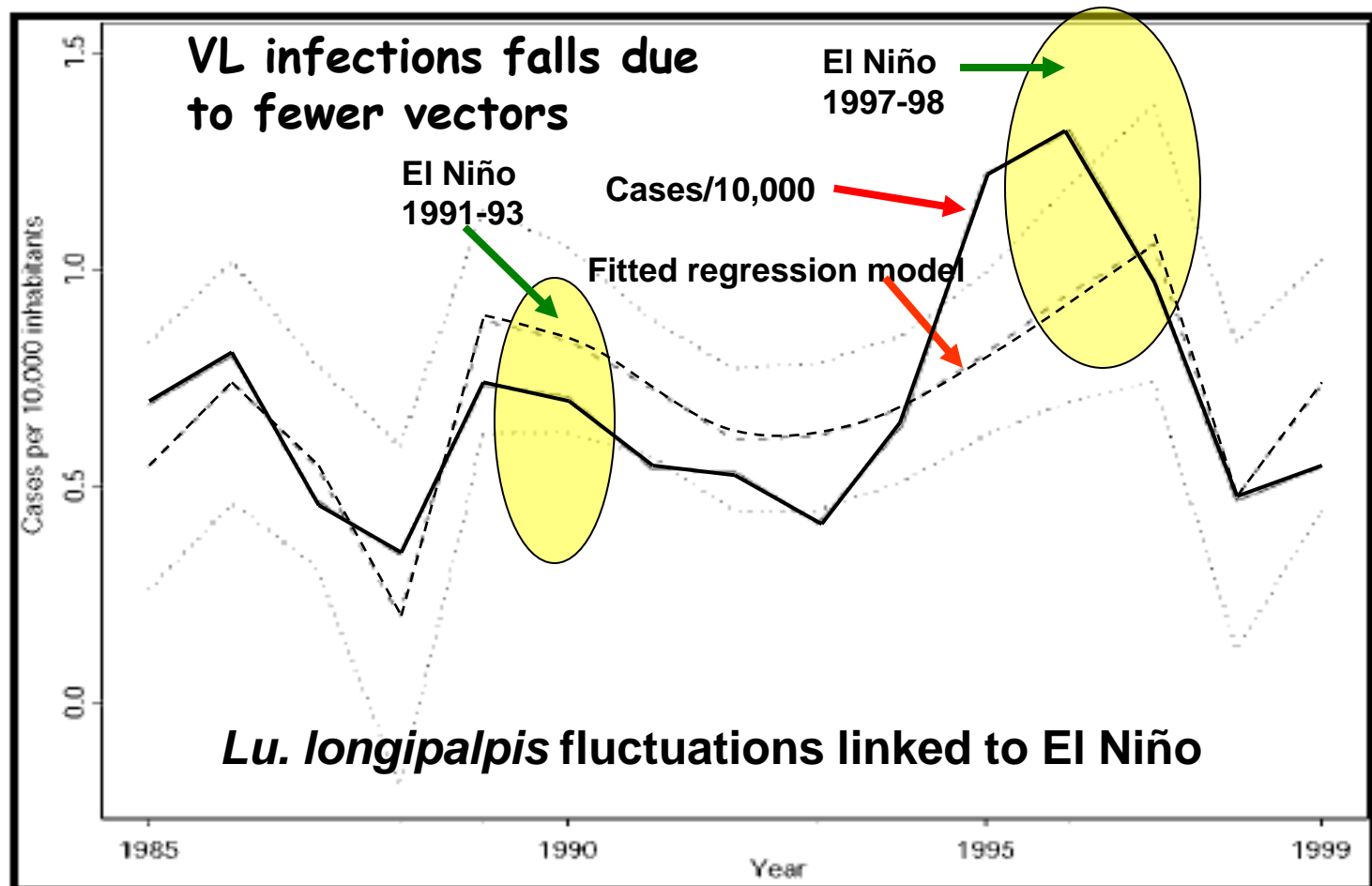
Host population's acquired immune status altered

Control interrupted or stopped

Return of increased transmission levels that lead to an epidemic

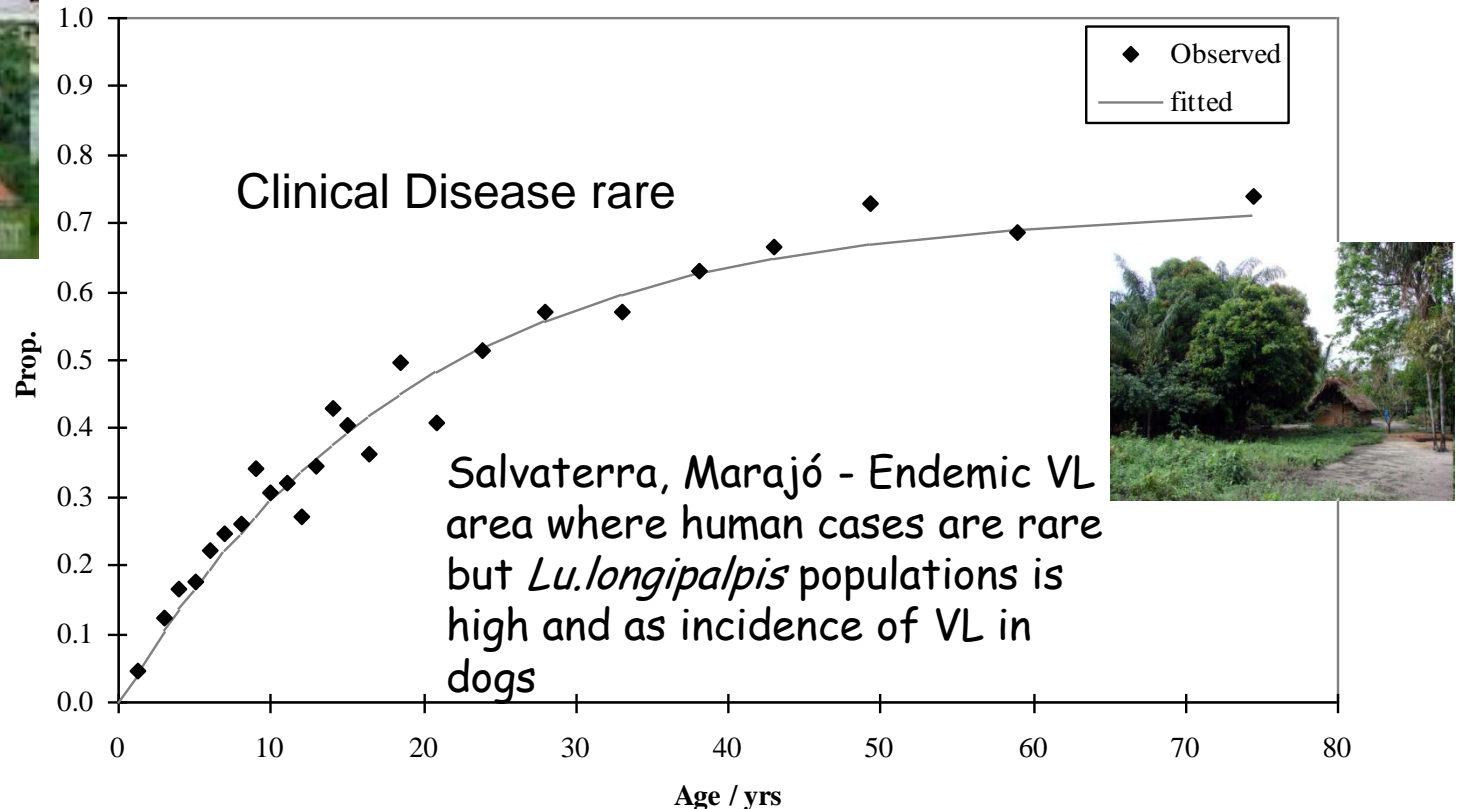
El Niño & La Nina 3 -7 years

Lasts for 6-18 months



An Ethical consideration

If you reduce the sand fly population could you be reducing protection against clinical disease?



+ve skin tests are evidence of recovery from infection ¹
and are associated with sand fly saliva antibodies ²

¹ Skin test +ve/age Courtenay et al unpublished observations; ² Barral et al 2000

Canine visceral leishmaniasis

Reduce or eliminate contact with the vector *L. longipalpis*



Inseticida impregnated collars

Difficulties: Loss of collar

What is the minimum coverage that will cut transmission levels efficiently to dogs and man?



Deltamethrin dipping/baths

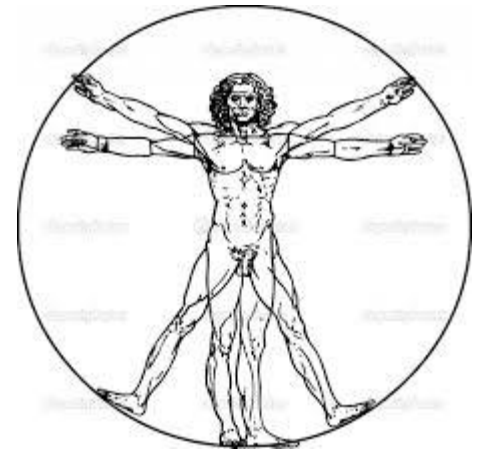
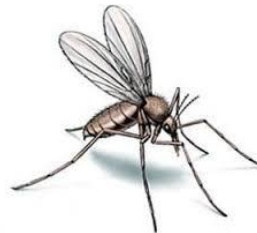
Improve formulation

Application of residual insecticide in the domestic environment

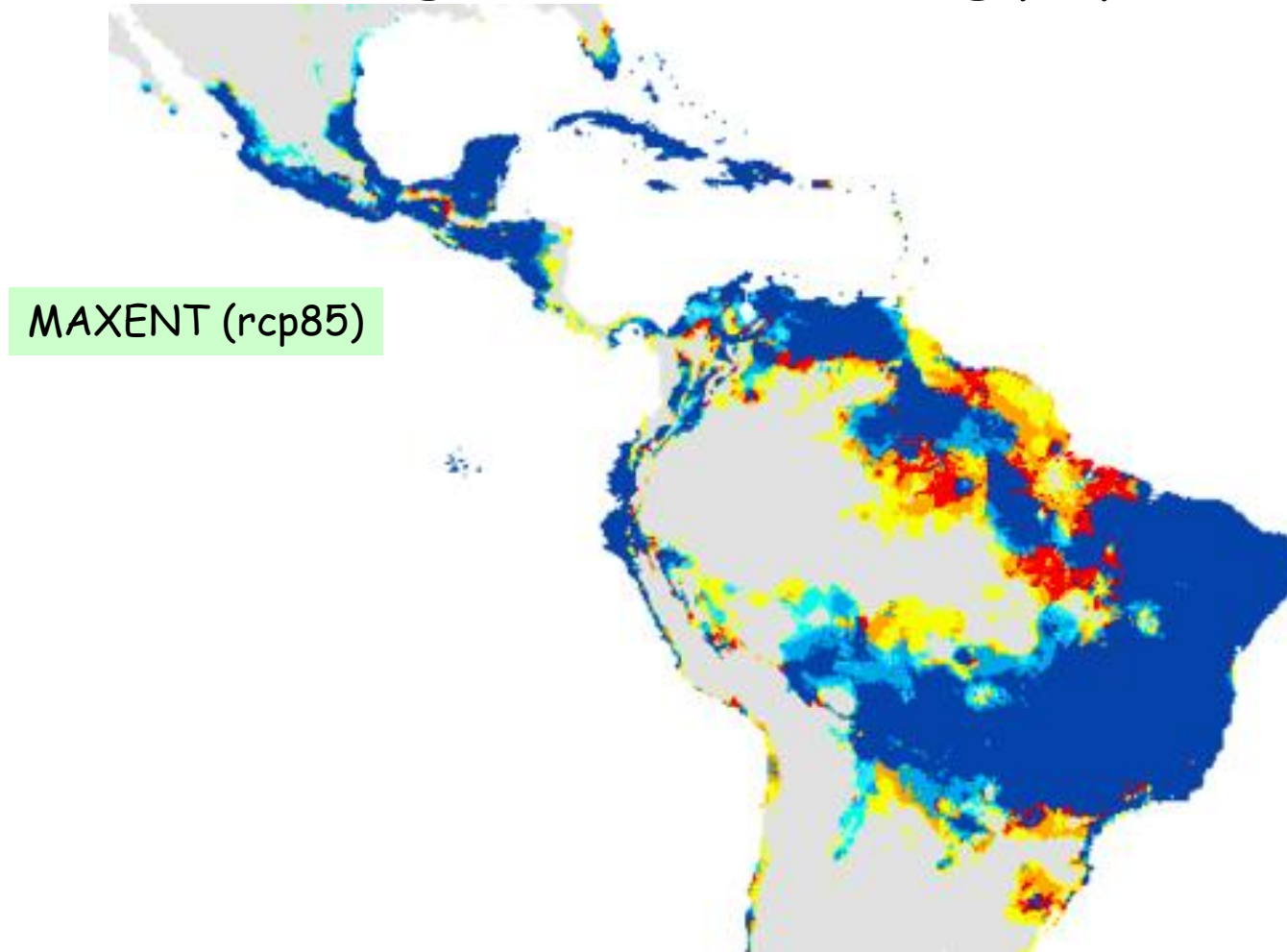
Models have shown that ineffective control may provoke changes in vector feeding preferences

Such as

Dog  Man

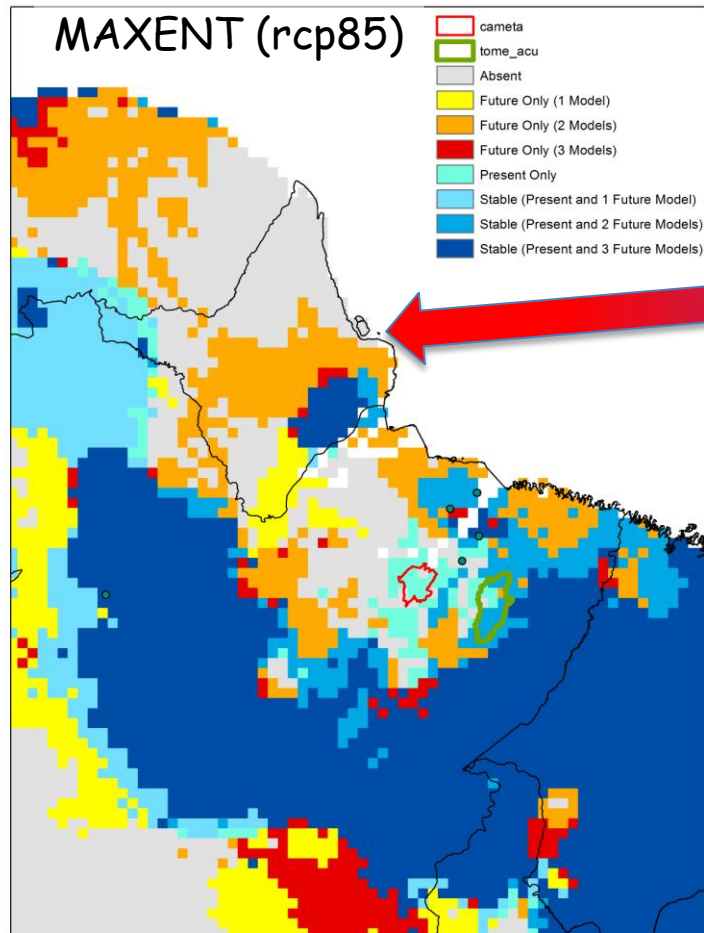


An early warning system
Predicting the distribution of vector
ecological niches - *Lu.longipalpis**



* Shaw et al unpublished projections

An early warning system Predicting the distribution of vector ecological niches - *Lu.longipalpis**



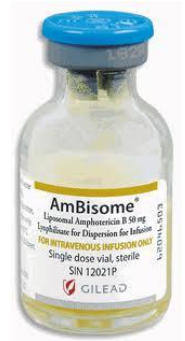
Predicted but first record
only in 2013

* Shaw et al unpublished projections

Visceral leishmaniasis chemotherapy

New Drugs - Expensive

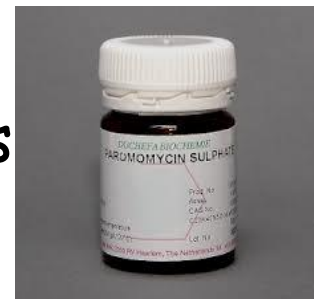
1. Liposomal amphotericin B (Ambisome®)
VL



2. Miltefosine
VL/CL? Needs further evaluation



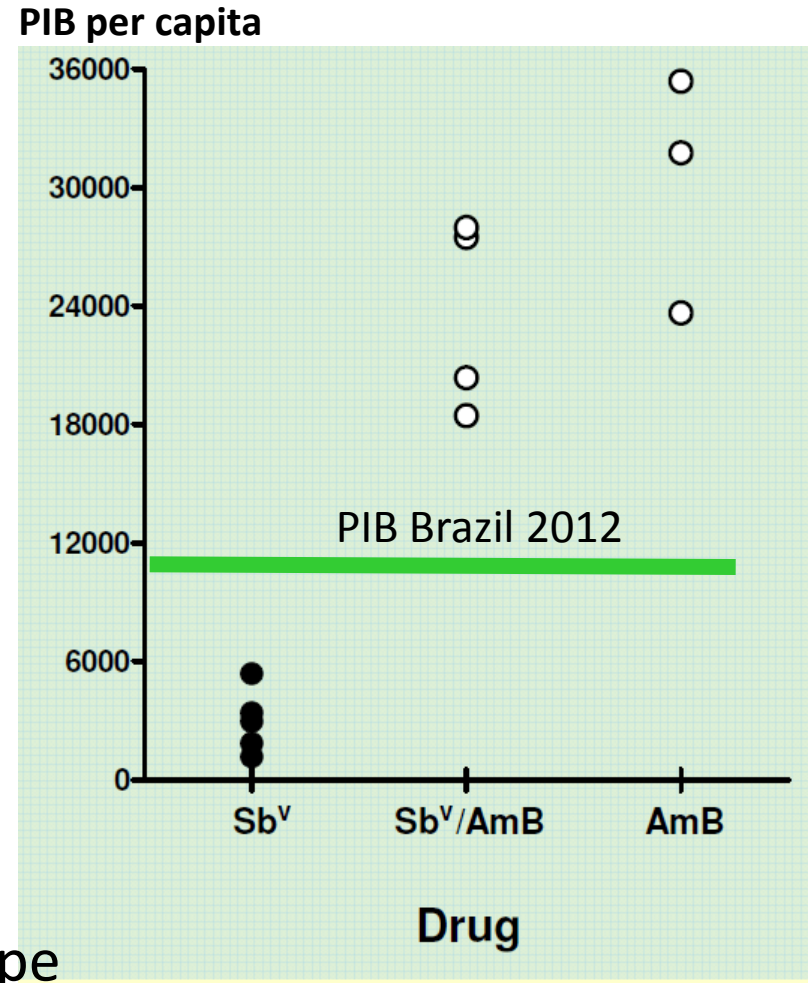
3. Paromomycin
VL oral India
Only available if purchased in large quantities



Global changes in the treatment regime of human visceral leishmaniasis

Clear relationship
to the national
PIB*

- Africa e Asia
- Southern Europe



*Gradoni et al, TM&IH 2008

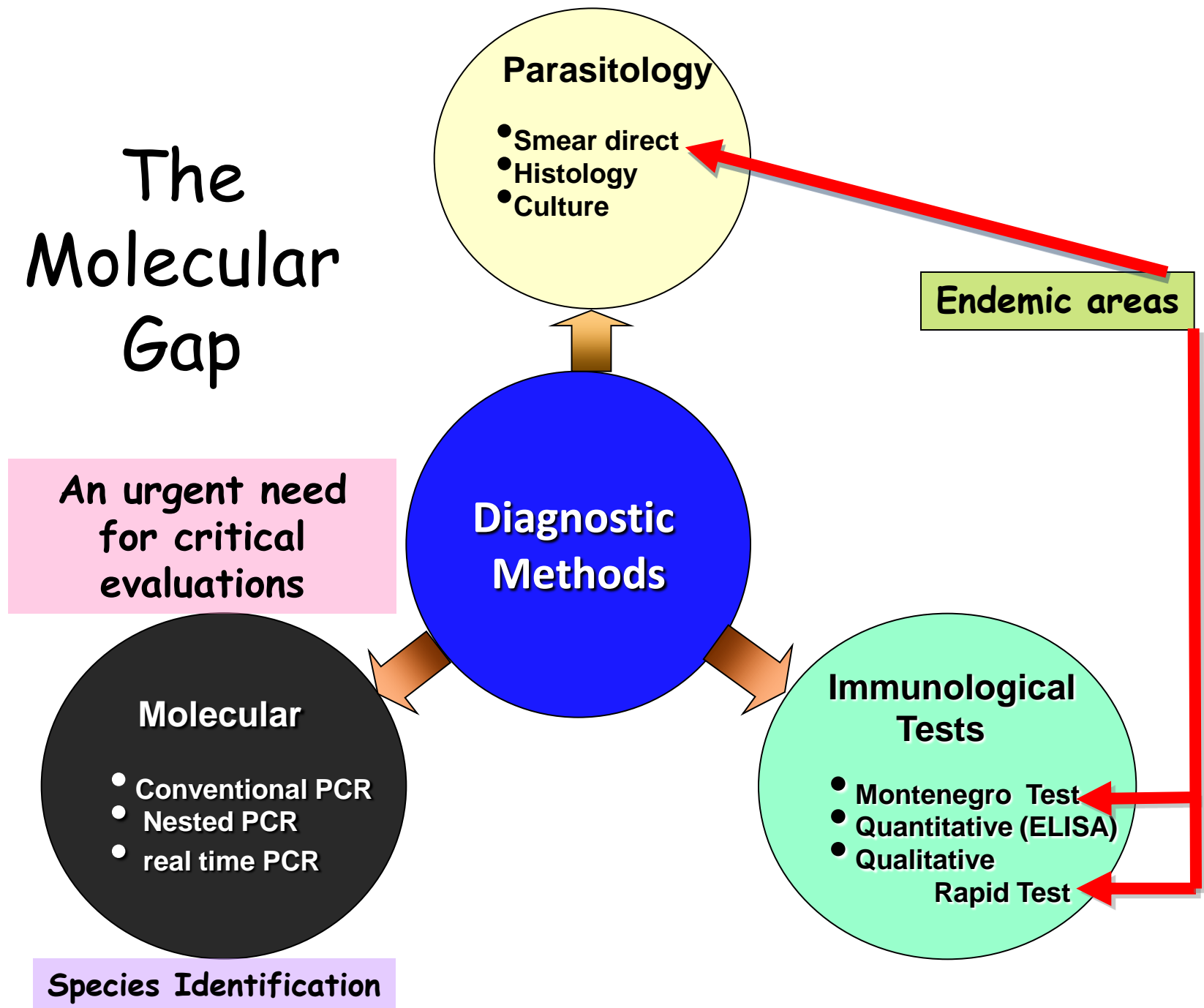
Leishmaniasis - Diagnosis

The Corner Stone of Control

The methods used for man and reservoirs, such as dogs, are basically the same

Accurate diagnosis is crucial for
successful control

The Molecular Gap



An Excellent Example of Test Evaluation

MAJOR ARTICLE

Clinical infectious diseases

A Global Comparative Evaluation of Commercial Immunochromatographic Rapid Diagnostic Tests for Visceral Leishmaniasis

Jane Cunningham,^{1,a} Epco Hasker,^{2,a} Pradeep Das,³ Sayda El Safi,⁴ Hiro Goto,⁵ Dinesh Mondal,⁶ Margaret Mbuchi,⁷ Maowia Mukhtar,⁸ Ana Rabello,⁹ Suman Rijal,¹⁰ Shyam Sundar,¹¹ Monique Wasunna,⁷ Emily Adams,¹² Joris Menten,² Rosanna Peeling,¹³ and Marleen Boelaert² for the WHO/TDR Visceral Leishmaniasis Laboratory Network^b

1312 • CID 2012:55 (15 November) • Cunningham et al

In Brazil the sensitivity of 5 kits varied from 61,5% to 92,0% but the specificity of all was high

Education & Participation

Community centers and schools

Present Simple Facts



The life cycle

How to stop being
bitten

Boost individual
responsibility

Your house and pets

Finally how to evaluate control
measures?

Independent assessment

Development of models related to
intervention

Conclusions

A control method must be based on irrefutable scientific evidence of its efficacy.

A control method must be tested independently and planned in collaboration with experts in statistical and epidemiological modeling and analysis.

Prior to any trial or campaign the method of execution must be explained in detail to the local population to guarantee its acceptability, taking into account different fractions of that population.

The viability of long term financial support must be guaranteed. If this is not available it is questionable if the campaign should be installed.