

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

CONTROLE DAS LEISHMANIOSES O QUE FALTA FAZER?

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

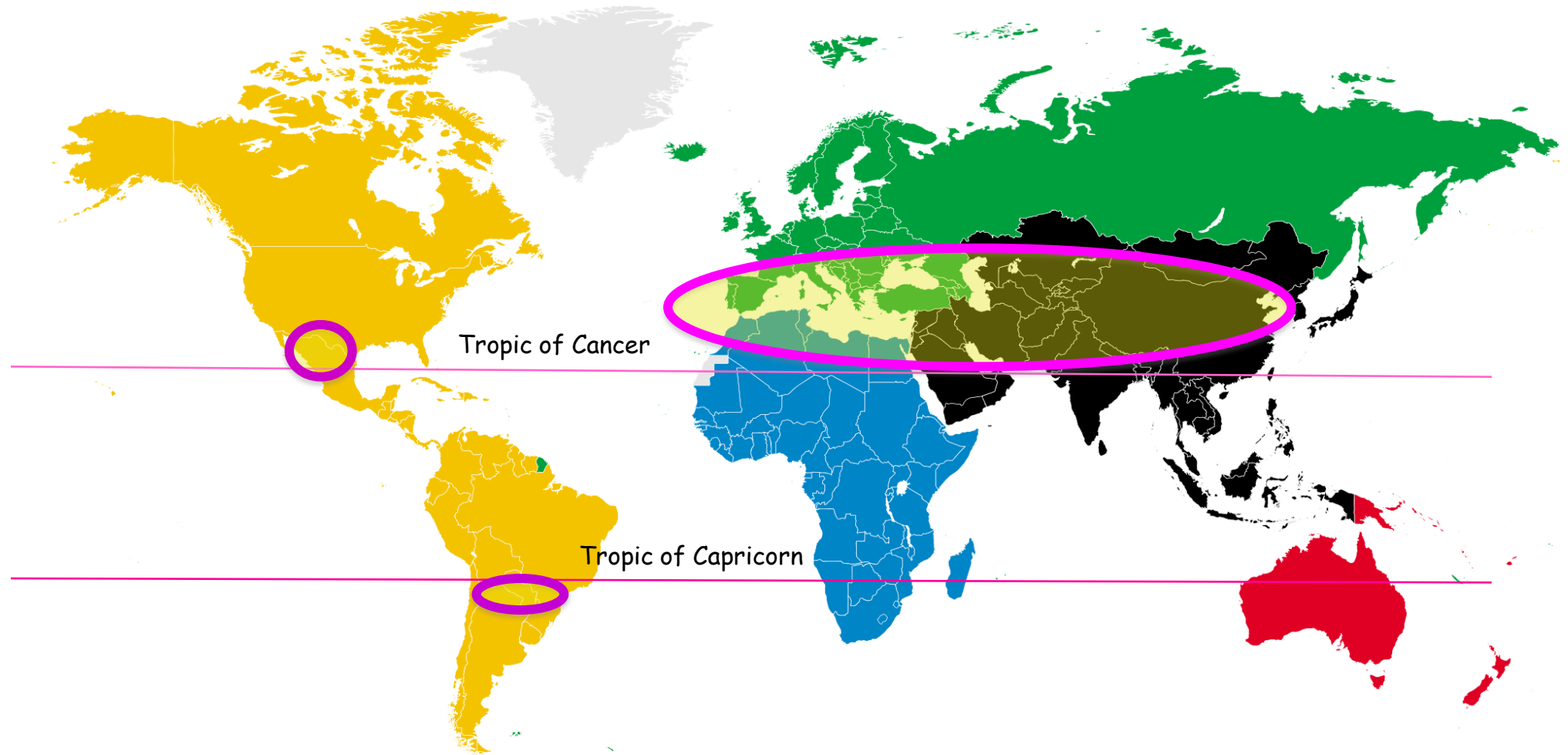
1 million cases



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>

So why is the control of the leishmaniases
so difficult?



John Snow

The Principal is Simple

Cholera in Soho
London



1854

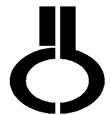
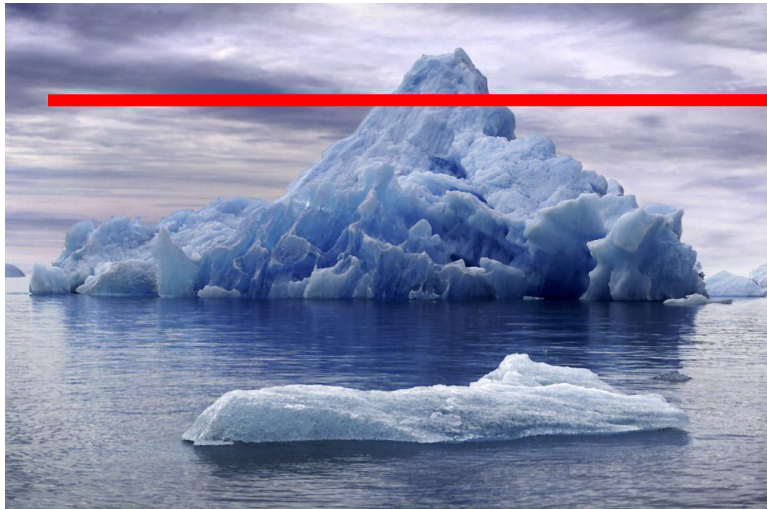
Find and treat the source

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



Jeffrey Shaw
ICB, USP

There are 20 named neotropical *Leishmania* species

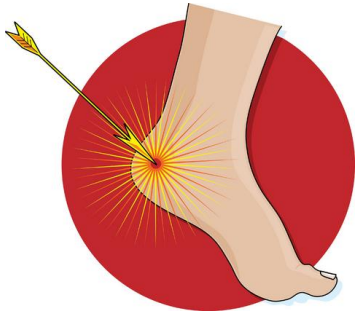
The 3 Control Frontiers

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

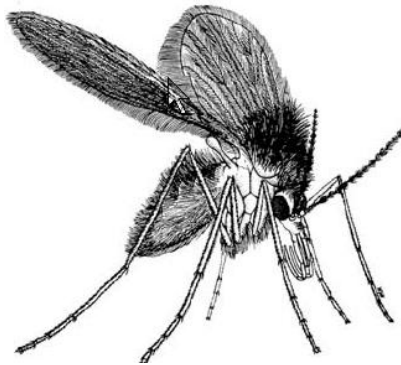
But what method?



Canine VL

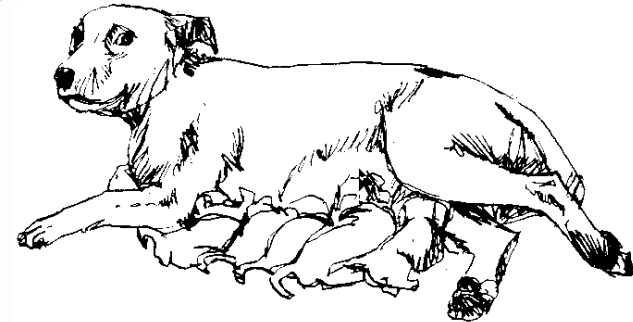
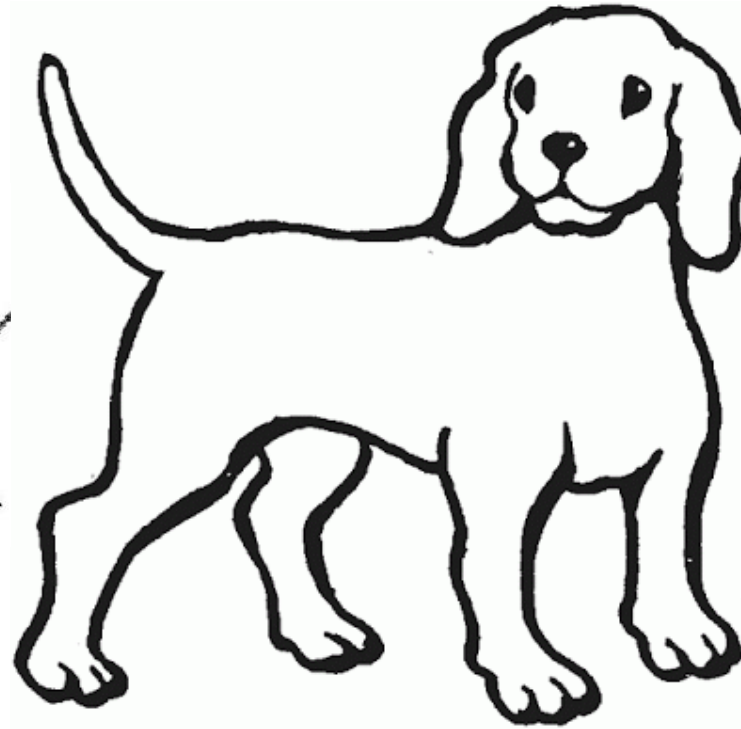


The VL Reservoir King



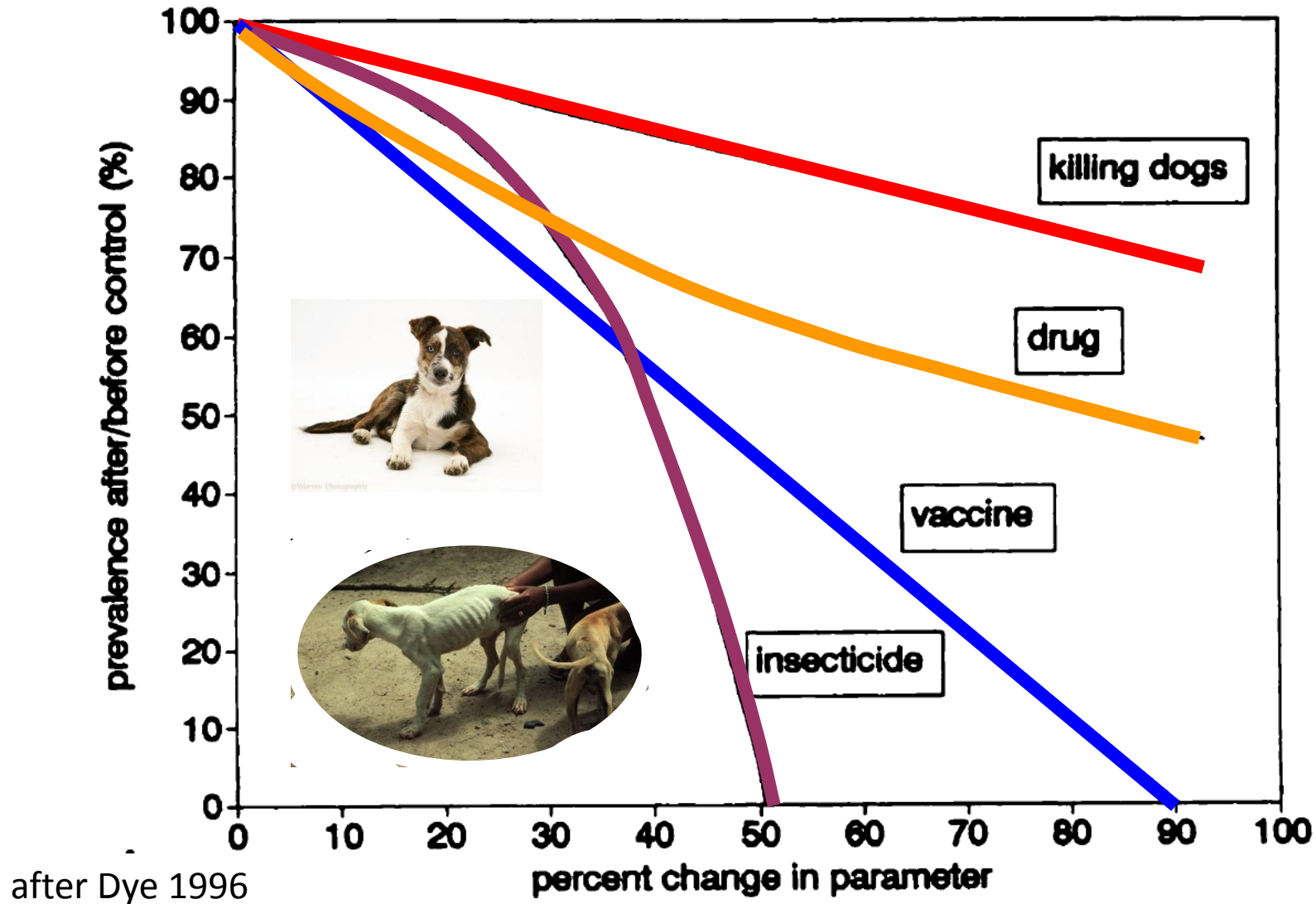
Vectorial

How many species?



Non Vectorial

The impact of different control methods on canine visceral leishmaniasis



Available Vaccines for canine visceral leishmaniasis

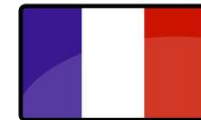
LEISHMUNE® (FML)



LEISH-TEC®



CANILEISH®
(LiESP/QA-21)



The levels of protection in the field are presently controversial

A **major problem** with laboratory vaccination experiments

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

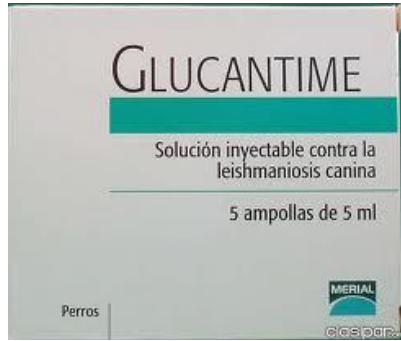
Conclusion: The level of protection can only be assessed using infected sand flies as the source of infection

Vaccine Evaluation

Two steps

Laboratory sand fly challenges

Field trials in endemic area



we treat dogs?

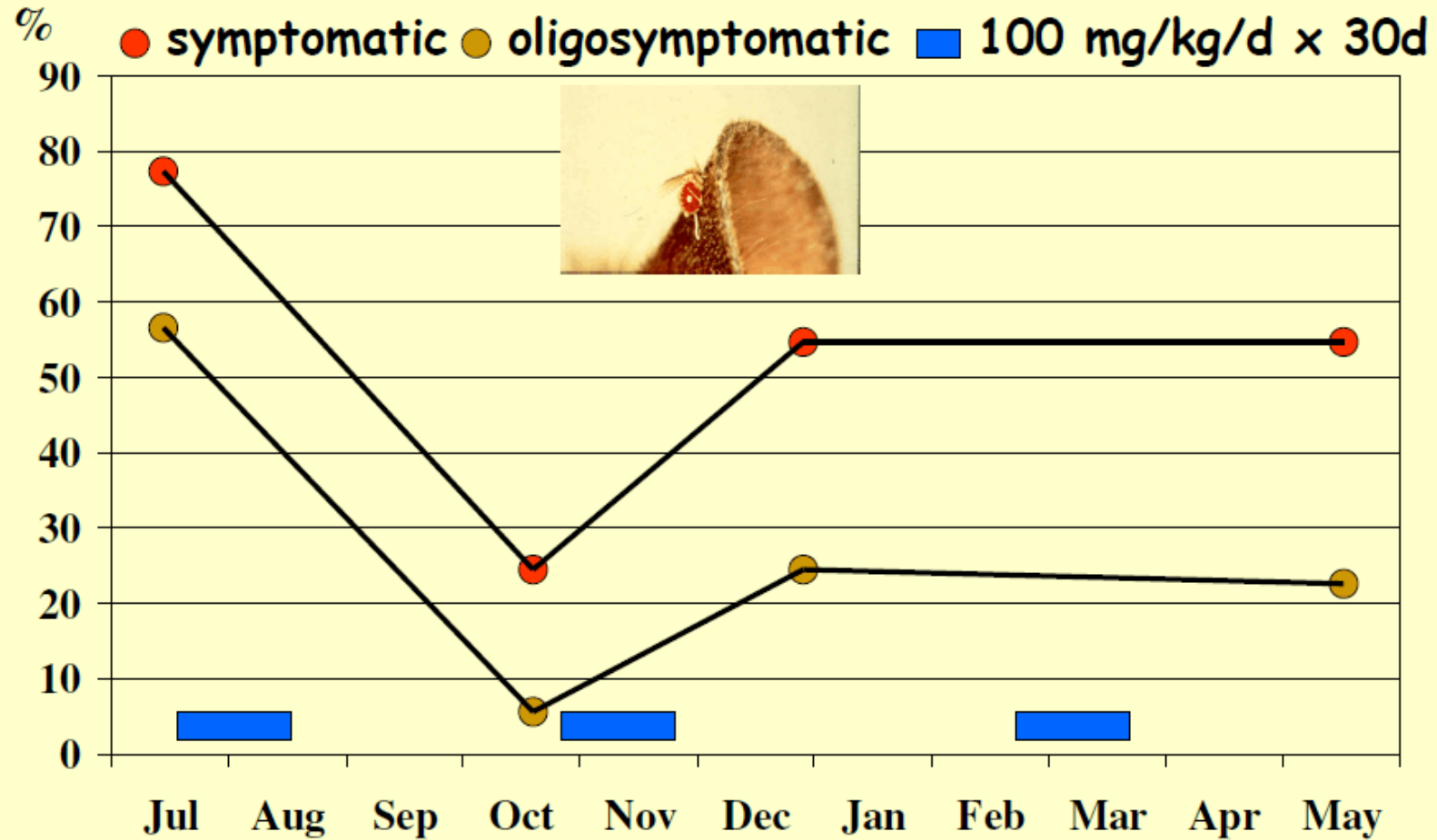
Meglumine antimoniate
Miltefosine
Allopurinol



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)



Chemotherapy Man

New Drugs – Expensive? Cost coming down

1. Liposomal amphotericin B (Ambisome®)

2007, Gilead 90% price cut (US\$18 per 50 mg vial)
for lower & middle income countries



2. Miltefosine

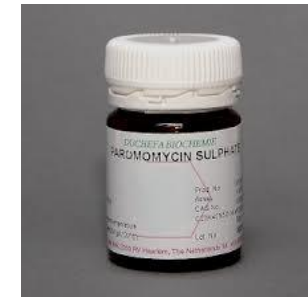
Needs further evaluation



3. Paromomycin

Oral India

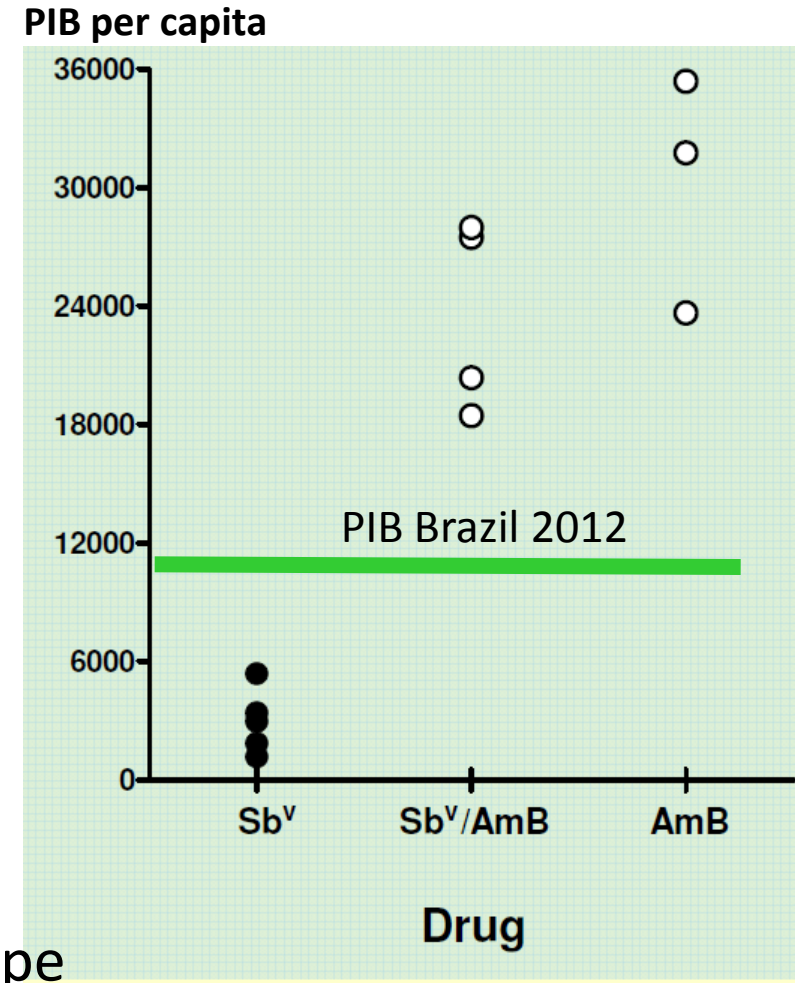
Only available in large quantities



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

Liposomal Amphotericin B

Single Dose

India

10mg per kilogram - India*

Bangladesh

500 mg for adults -

10 mg/kg for children younger than 12 years

Advantages:

Reduce administration costs (Staff, equipment,.
transport etc)

* Sundar et al 2010; ** Mondal et al 2014

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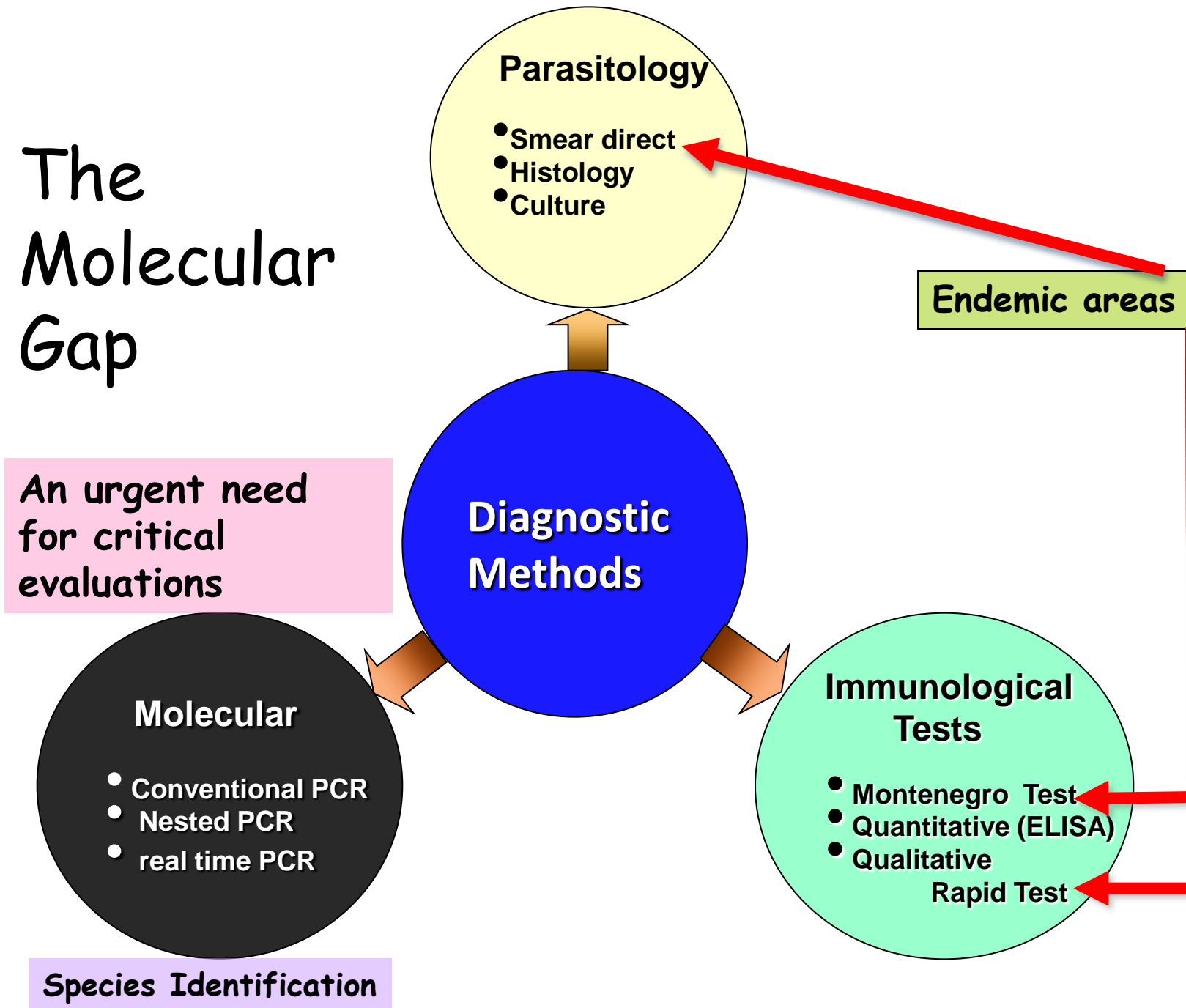
Leishmaniasis - Diagnosis

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 & evaluating 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



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

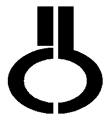


Time of year

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



The vector
Psychodopygus
wellcomei hibernates
in the dry season



Jeffrey Shaw
ICB, USP

Seasonal transmission - No cases in dry season

Danger of inadequate sustainability of vector control

Vector population reduced

Transmission rate lowered

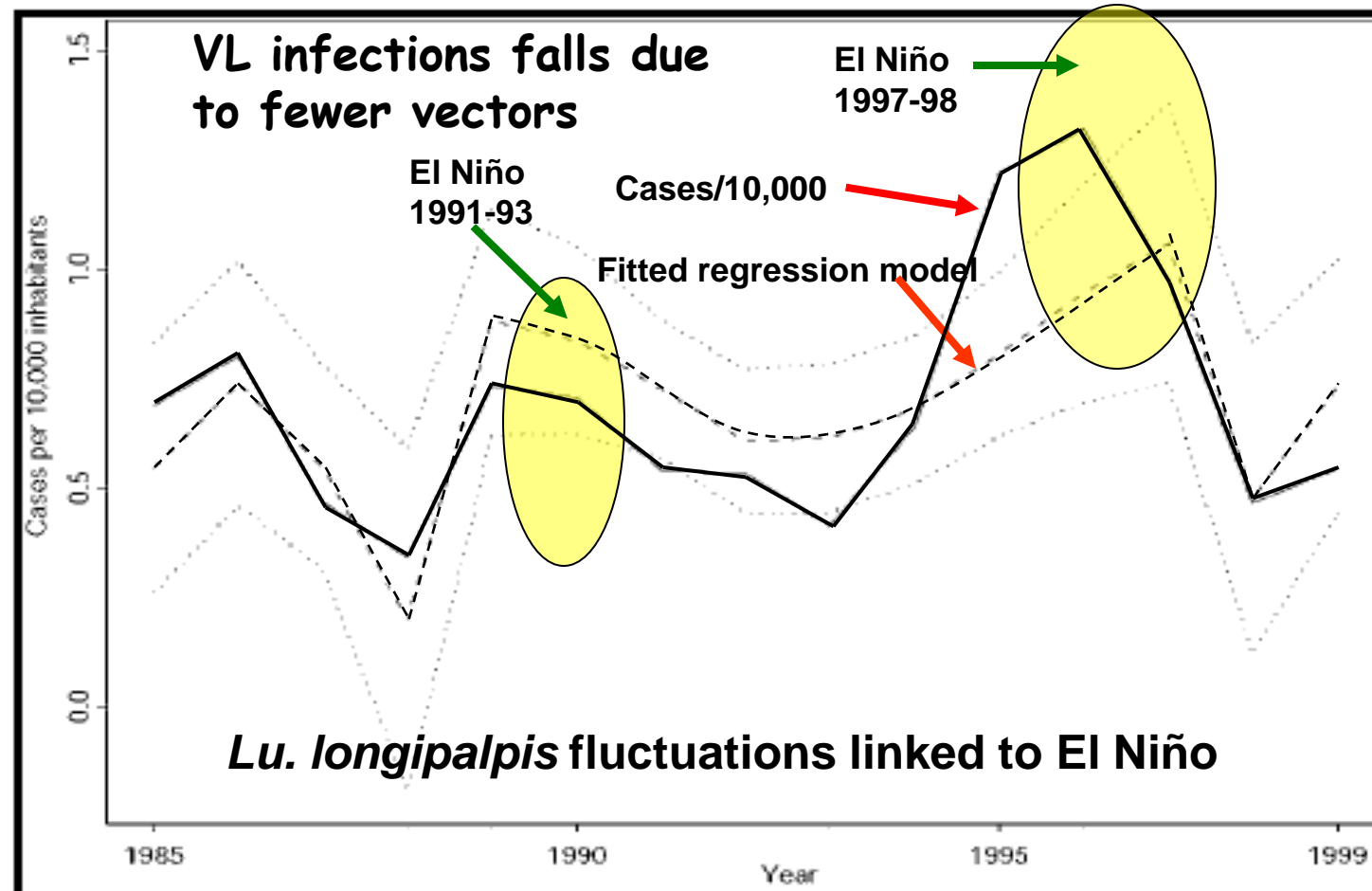
Host population's acquired immune status altered

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



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

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

Education & Participation

Community centers and schools

Present Simple Facts



The life cycle

How to stop being
bitten

Boost individual
responsibility

Your house and pets

Final Considerations

Based on irrefutable scientific evidence of its efficacy.

Tested independently - 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. If its not it is questionable if any action should be taken.

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