

# Kala-azar: Can Visceral Leishmaniasis Ever Be Controlled?

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# The Burden of the Leishmaniases

## **All forms:**

**Global prevalence: ~12 million cases**

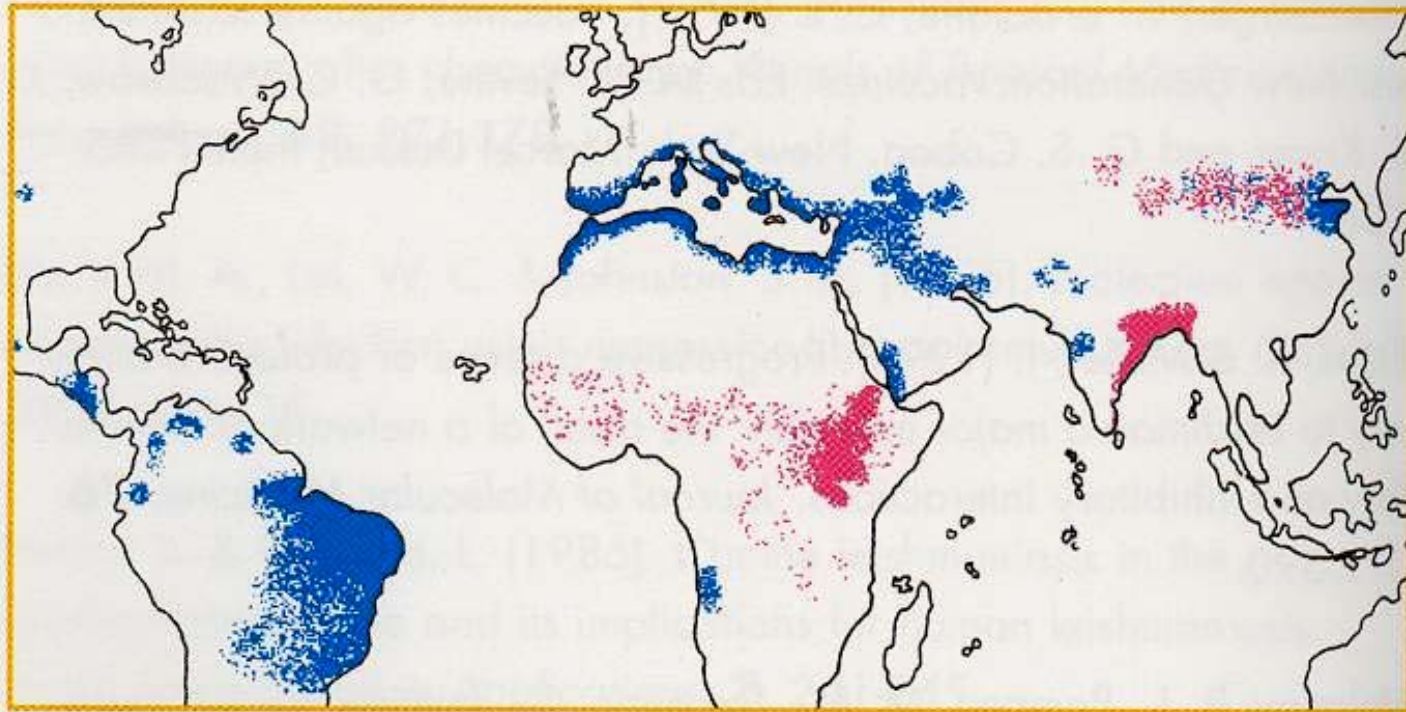
**Annual incidence: 1.5 - 2.0 million**



**Countries affected : 88**

**People at risk : 350 million**

## Visceral Leishmaniasis alone

- Estimated Disability Adjusted Life Years:  
2 million
- Estimated new symptomatic cases annually:  
500,000  
(90% in East Africa, Brazil  
and the Indian subcontinent)



-  *L. chagasi/L. infantum*
-  *L. donovani*

## Distribution of the Visceral Leishmaniasis

# East Africa

# Patient with visceral leishmaniasis in a Médecins sans Frontières clinic in East Africa.



T. Burki (2009). *Lancet*, 374: 371-372.



*Photo: Ed Rowton, Walter Reed Army Institute of Research*



Photo: R. Killick-Kendrick

*Acacia seyal* woodland in Eastern Sudan, the habitat  
of the Sudanese vector of visceral leishmaniasis  
(*Phlebotomus orientalis*)

“Should an extensive outbreak of kala-azar occur in any village, the whole village should be burnt and a new village built on a fresh site, after the patients and contacts have been isolated.”

Thomson, D.S.B. (1910). Kala-azar Commission to investigate the prevalence and cause of the disease in Eastern Sudan; (1) General report.

No control programme has so far been implemented in Sudan. Important questions concerning epidemiology, entomology and animal and/or human reservoir must first be answered.'

(Zijlstra and El Hassan, 2001)

In 1999 – 2001, Médecins sans Frontières distributed 35,700 insecticide-impregnated bednets in 155 villages in a highly active VL focus in Eastern Sudan.

Seventeen to twenty months later, clinical cases had fallen by 59%

It was estimated that the intervention prevented 1,060 new cases ---

and the mean protection effect was 27%.

*(Ritmeijer et al. 2007)*

In March, 2009, aid agencies were expelled from northern Sudan.

Médecins sans Frontières was obliged to cancel plans to control visceral leishmaniasis in the east of the country.

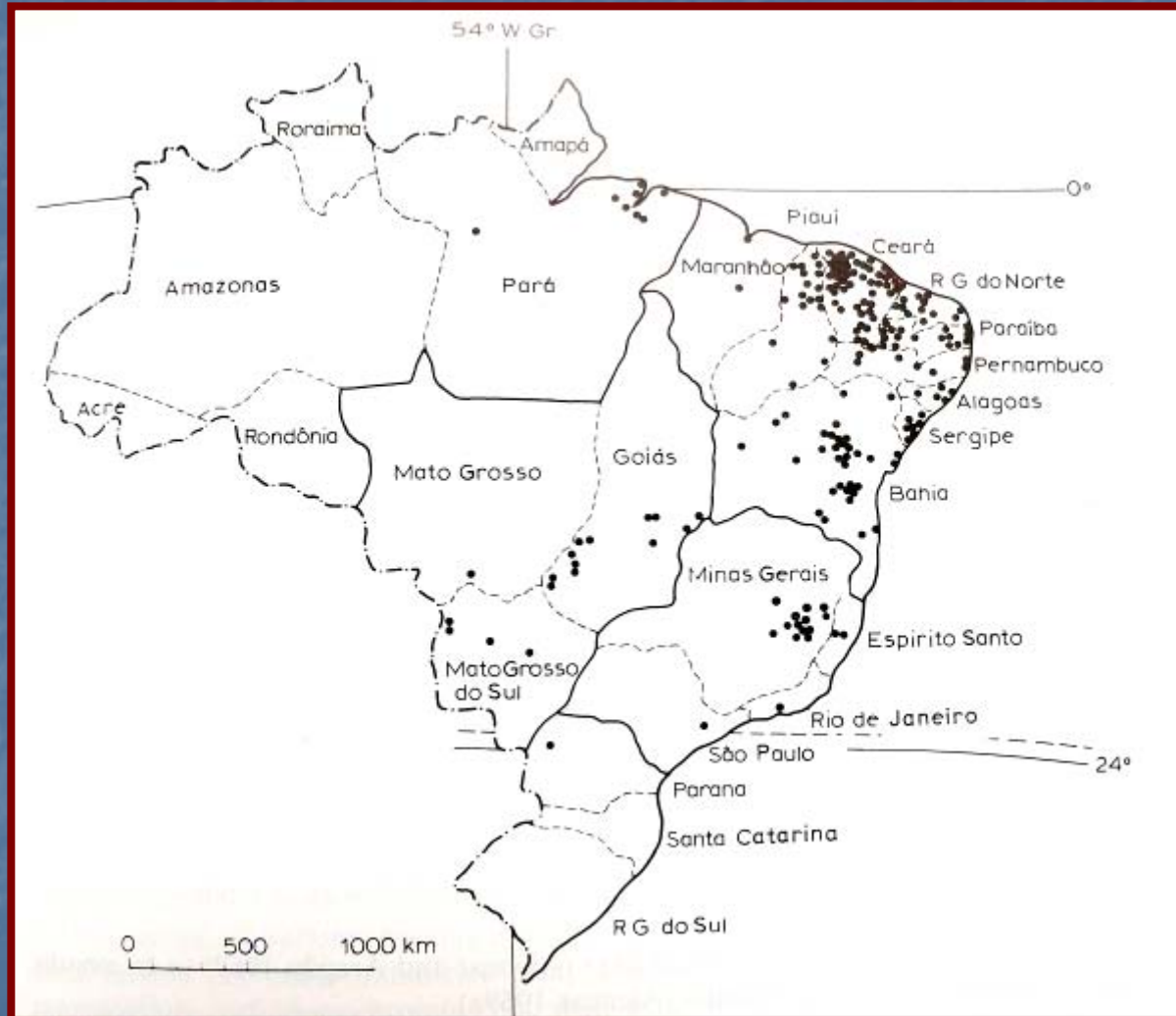
Brazil

Visceral leishmaniasis caused by *Leishmania infantum* with a canine reservoir (Brazil).  
(L = liver; S= spleen)

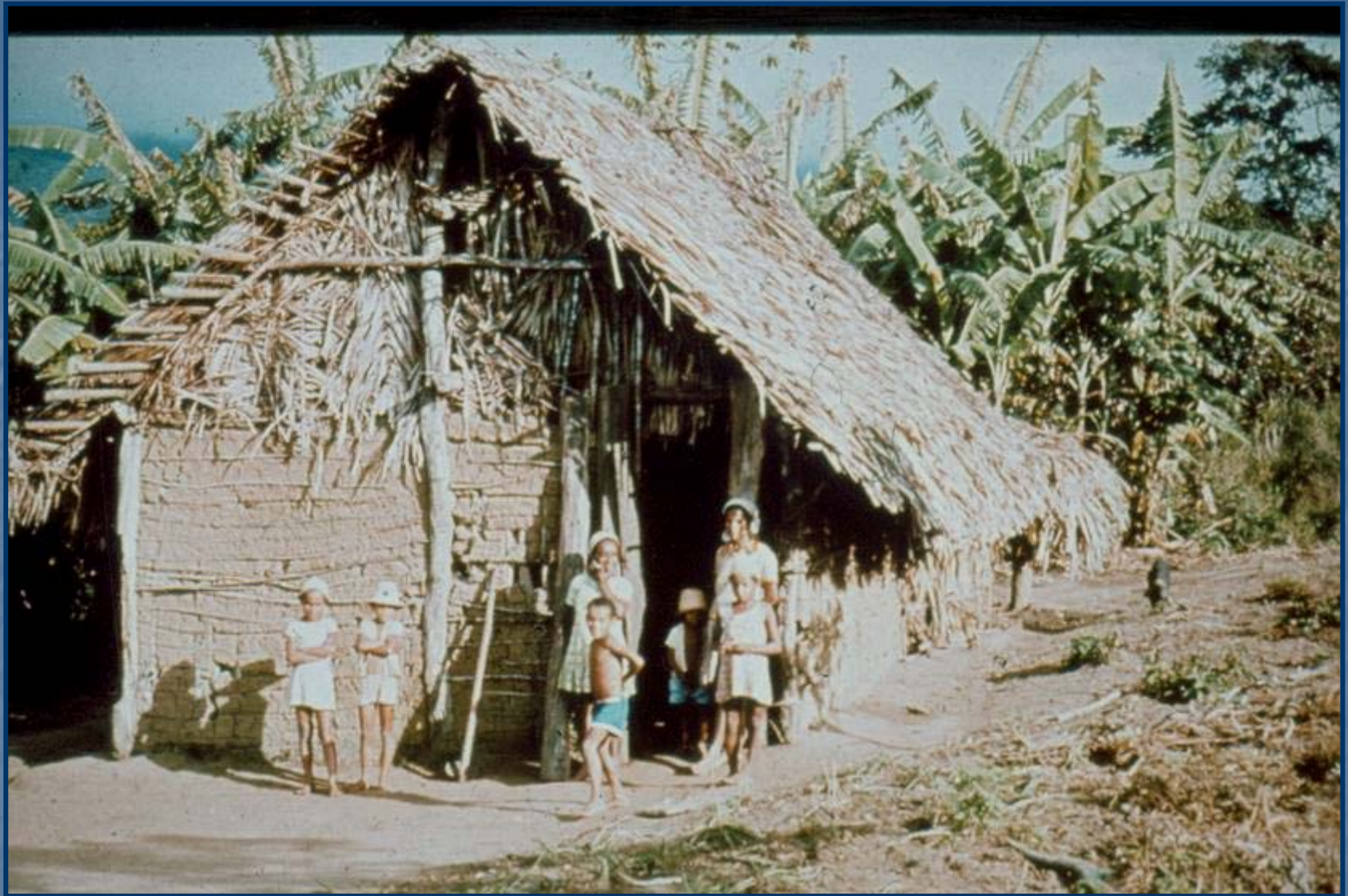


Photo: W. Peters

# Distribution of visceral leishmaniasis in Brazil, 1984



Deane & Grimaldi, 1985



Poor rural housing in north east Brazil



*Photo: P.D. Ready*

An urban focus of visceral leishmaniasis  
in north-east Brazil

# Last stages of canine leishmaniasis with severe emaciation and depilation



*Photo: R. Killick-Kendrick*

# Control by culling seropositive dogs (1)

## *Brazil Control Programme 1984-1996*

- Sera of 6.5 million dogs tested
- 153,819 seropositive dogs destroyed
- One million houses sprayed with insecticide
  - Cost >US\$ 96 million

# Serologically positive dogs culled to control visceral leishmaniasis

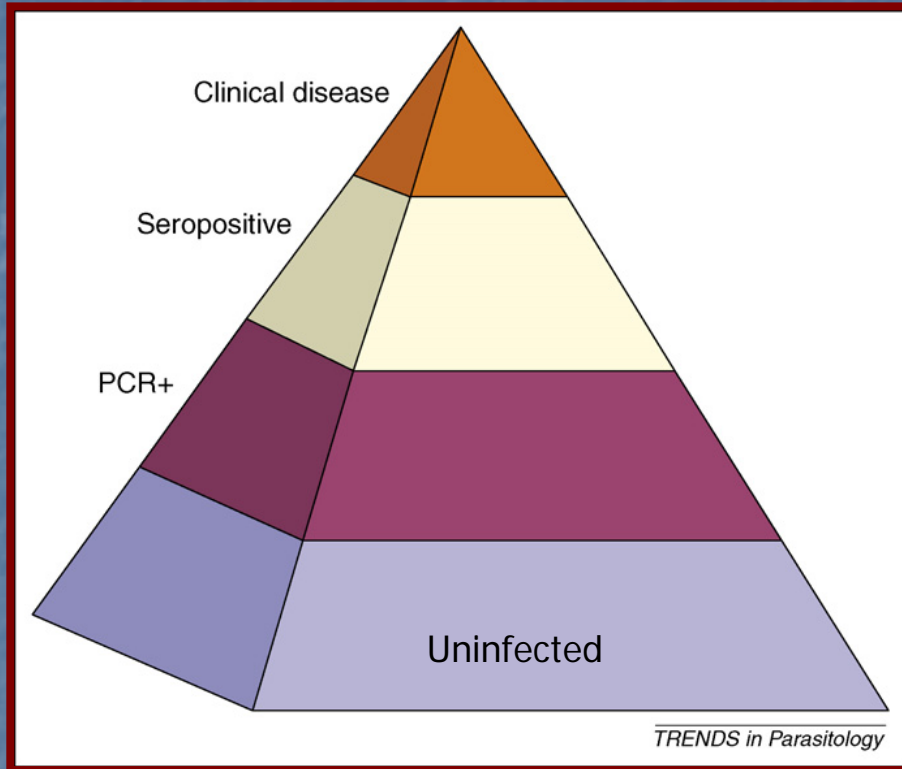


*Photo: R. Killick-Kendrick*

# Culling serologically positive dogs as a means of control: reasons for failure

- Resentment by dog owners,
- Inability of the tests to reveal all dogs that are infectious to sand flies,
- Delay between testing and culling,
- And, in some places, the possible presence of other reservoir hosts.

(Oliveira *et al.*, 2008).



Baneth, G. *et al.*, (2008)  
*Trends in Parasitology*, **24**: 324-330

Clinical signs reveal only a small proportion of dogs with CanL: serology and/or PCR reveal many more without clinical signs (but able to infect sand flies).

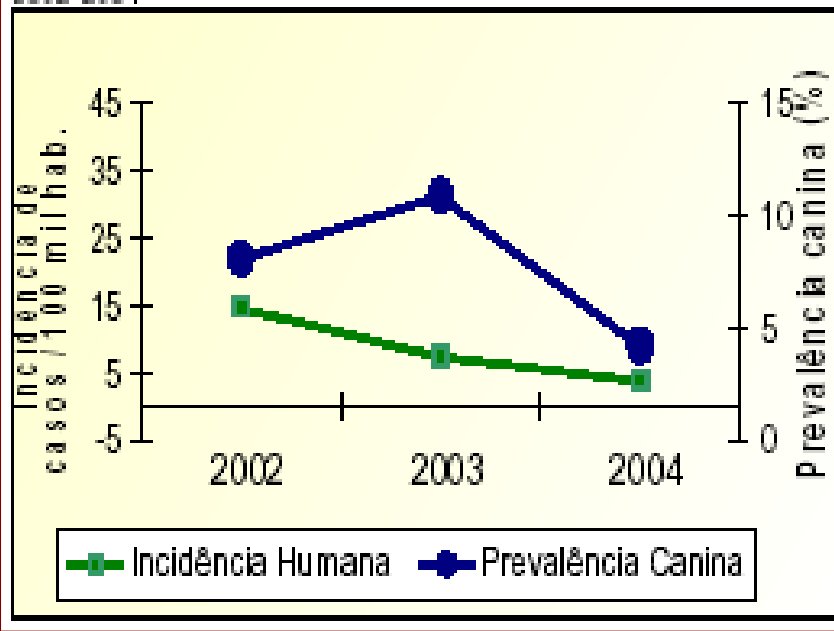
# Field trial to reduce risk of infection with VL in São Paulo State, 2002-2005

- All seropositive dogs in a chosen cohort were killed
  - 22,260 seronegative dogs were fitted with deltamethrin-impregnated collars, changed annually
  - From 2002 to 2005, the prevalence of canine infections fell from 12.5% to 3.9%
- During the same period, the incidence of human cases fell from 34.1/100,000 to 5.4/ 100,000

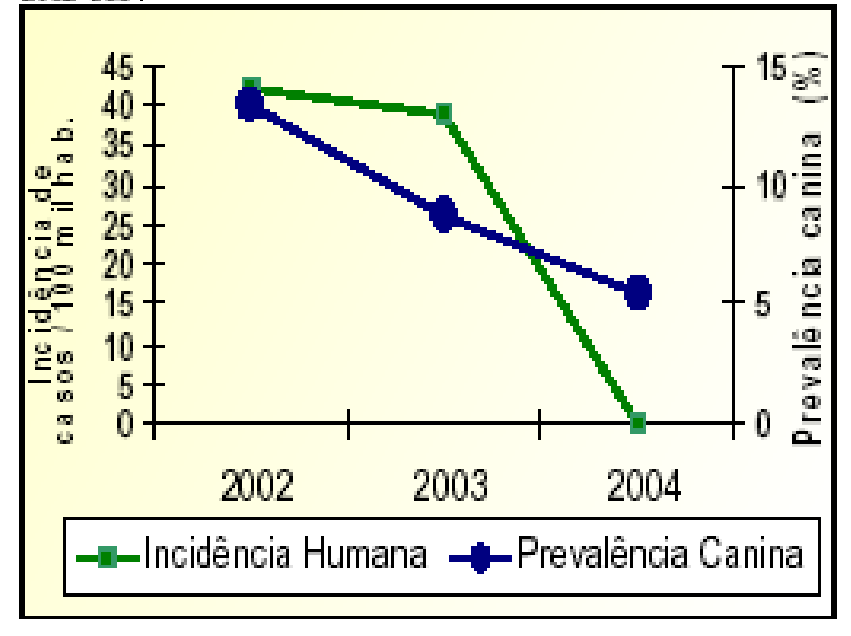
(Camargo-Neves *et al.*, 2004, 2009)

# Changes in the prevalence of CanL and the incidence of human VL in two study sites in Brazil after collaring all seronegative dogs in April 2002

Taxa de prevalência canina e coeficiente de incidência de leishmaniose visceral americana por ano. Área 1, Andradina SP, 2002-2004



Taxa de prevalência canina e coeficiente de incidência de leishmaniose visceral americana por ano. Área 2, Andradina SP, 2002-2004



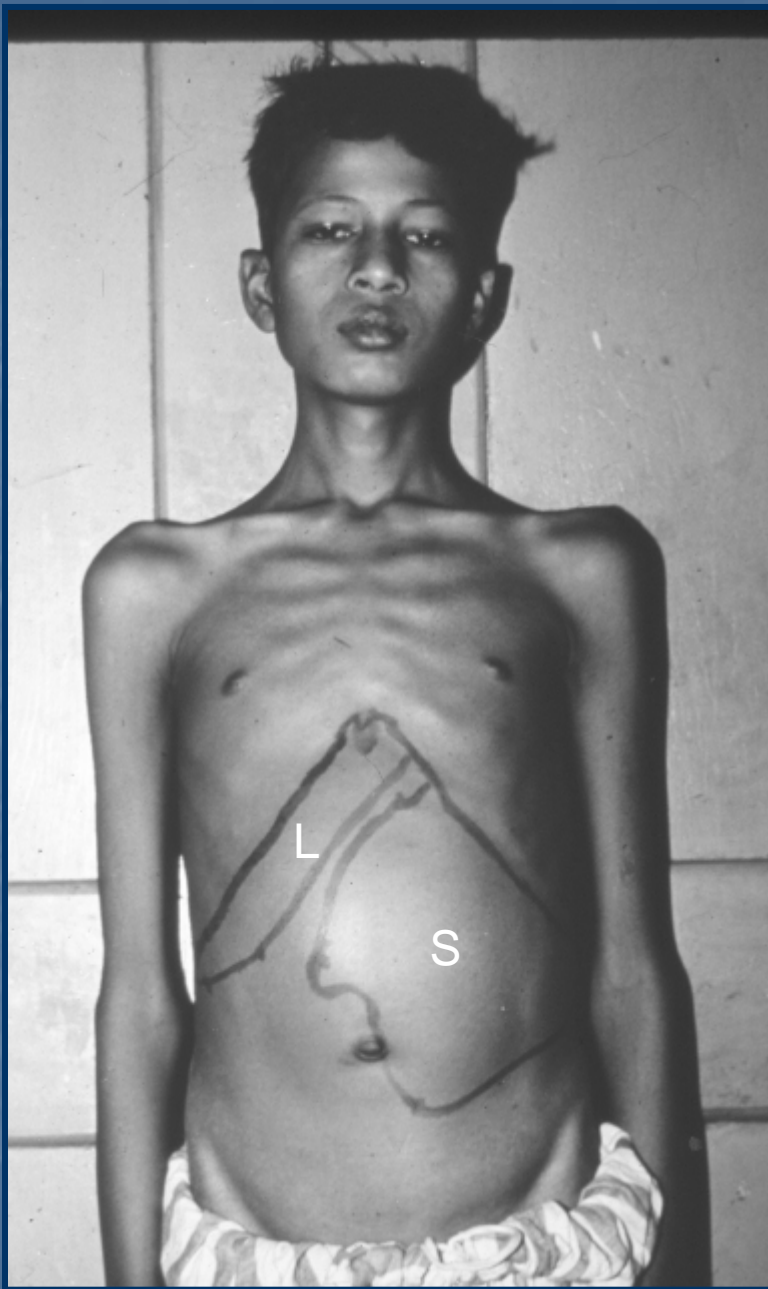
From: Camargo-Neves, V.L.F., et al. (2004). *Boletim Epidemiológica Paulista*, No12, 7-14.

India



*Photo: R. Killick-Kendrick*

The habitat of *P. argentipes* in a focus of anthroponotic visceral leishmaniasis in Bihar State, India.



Anthroponotic  
visceral  
leishmaniasis;  
Bihar State,  
India; the spleen  
(S) and the liver  
(L) are greatly  
enlarged.



*Photo: R. Killick-Kendrick*

Post kala-azar dermal leishmaniasis of the thigh showing depigmentation and a skin rash; the skin is heavily infected: these patients are reservoirs of infection. Bihar State, India.

# Treatment of kala-azar in India (1)

Urea stibamine introduced in 1922

Many thousands of cases successfully treated

Survival much improved

But little measurable effect on prevalence of infection

(H.E. Shortt, 1932)

## Treatment of kala-azar in India (2)

‘In hyperendemic areas of India, no more than 9% of those affected with VL seek medical advice for diagnosis and/or treatment.’

‘Owing to lack of resources and health education, compliance with treatment is extremely low.’

# Treatment of kala-azar in India (3)

Pentostam: resistance widespread

Ambisome: intravenous infusion, average cost for two injections: US\$ 250: one injection treatment, under investigation, average cost: US\$ 125

Paramomycin: intramuscular injections for 21 days, average cost of drug: US\$ 15-20

# Treatment of kala-azar in India (4)

**Miltefosine**: oral twice daily for 28 days; contraindicated in pregnancy; long half life and therefore fears for resistance of parasite; not yet known if it cures PKDL

Guidelines on use of Miltefosine, Govt. of India

# Treatment of kala-azar in India (5)

Mean household expenditure for one case of VL in Bihar is estimated at US\$ 59.8.

[Vinod B. Annigeri (unpublished) *In: Rijal et al.(2005).TRSTMH, 100: 838-841.*]

'In Bihar State, 75% of VL patients have a daily income of <US\$ 1.'

(Desjeux, P. 2001)

# Limitations in house spraying with DDT (1)

## Environmental damage

'DDT is cheap, but its harmful and long-lasting environmental effects require proper evaluation; it may not in the end be the insecticide of choice for long-term control.'

(Thakur, 2000)

# Limitations in house spraying with DDT (2)

## Operational deficiencies

'--- despite the supposed 5 DDT spray-rounds between 1992 and 1994, 57% of houses had not, in fact, been sprayed.'

(Thakur, 2000)

# Limitations in house spraying with DDT (3)

## Insecticide Resistance

In Bihar, *Phlebotomus argentipes* developed resistance to DDT during house spraying in the epidemic in the 1970s

(Singh *et al.*, 2001)

## Limitations in house spraying with DDT (4)

### Danger of post-spraying epidemics.

When house spraying is abandoned prematurely, the population of sand flies recovers quickly and an epidemic is highly probable.

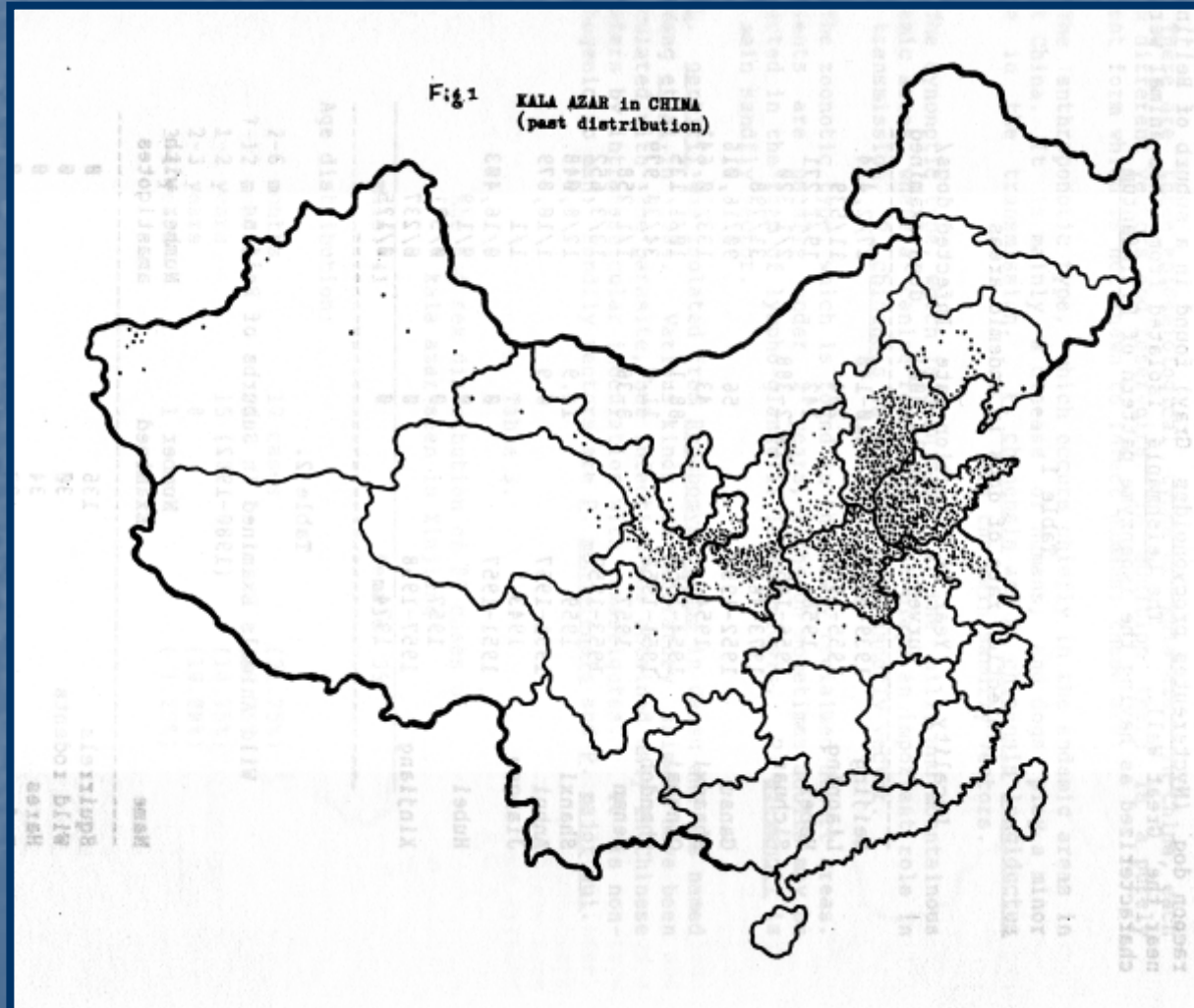
This happened in India in the 1970s after the campaign to eradicate malaria worldwide was abandoned 1969

(Sen Gupta, 1975, Makhopadhyay *et al.*, 1987).

# Can Visceral Leishmaniasis Ever Be Controlled?

YES

# Distribution of visceral leishmaniasis in China in 1958 before the control campaign



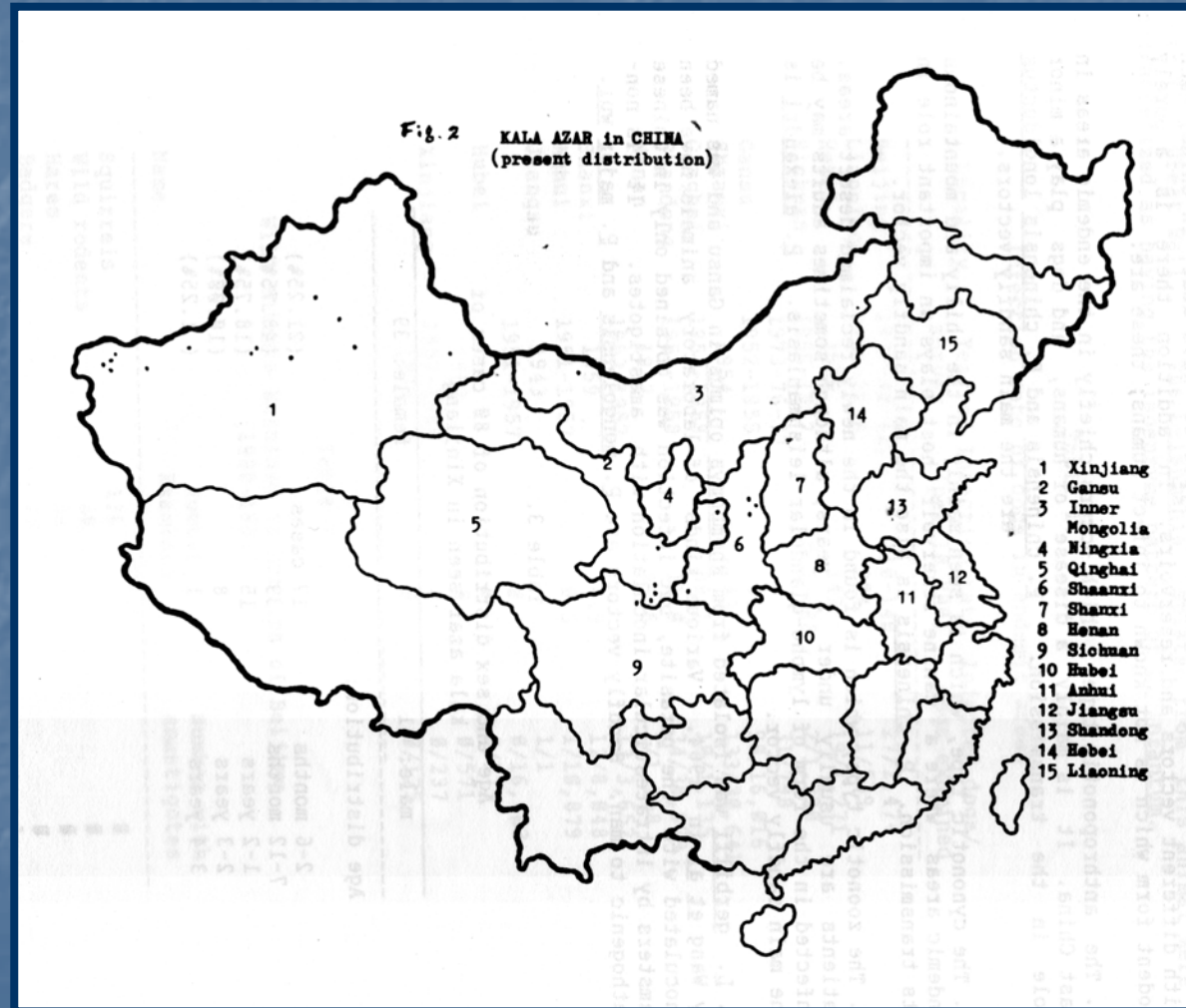
Xu Zhi-biao (1988)

All dogs were destroyed

All houses sprayed with either DDT or  
Gammexane annually for 30 years

Annual active case detection  
and treatment

# Distribution of visceral leishmaniasis in China in 1988 after the control campaign



Xu Zhi-biao (1988)

# Lessons (1)

## ESSENTIALS

Peace

Political Commitment

Long-term Funding

Feasible Strategies

Public Education

# Lessons (2)

## Structure of the Focus

Distribution and Incidence

Population dynamics and behaviour  
of vector(s)

Identification and behaviour of animal  
reservoir(s) (if appropriate)

# Lessons (3)

## Action against the source of infection

Destroy stray dogs: protect all other dogs from sand fly bites with insecticide-impregnated collars or by dipping in insecticide

Active case detection and treatment including PKDL patients (How?)

Asymptomatic cases?

# Lessons (4)

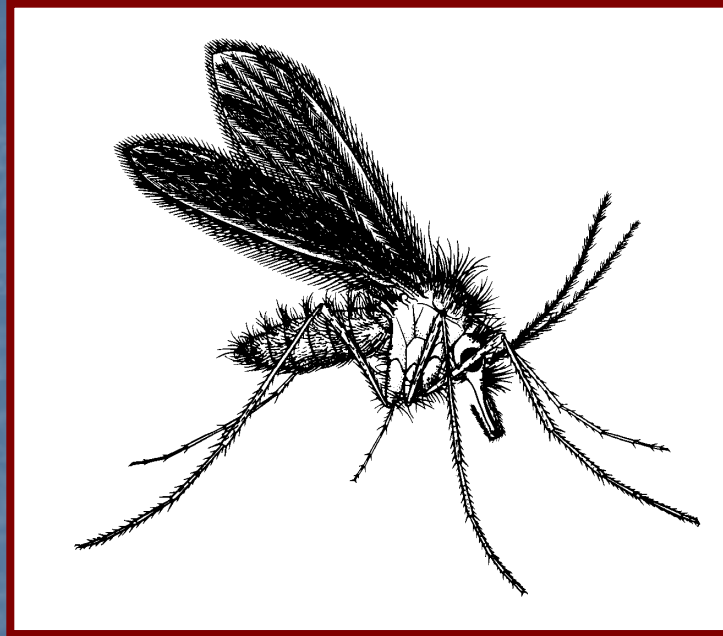
## Action against the vector

Efficient and supervised house spraying

With more than one insecticide

Regular tests for insecticide resistance

Insecticide-impregnated bed-nets



© American Mosquito Control Association

Del: Hilda Munoz

Thank you