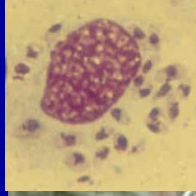
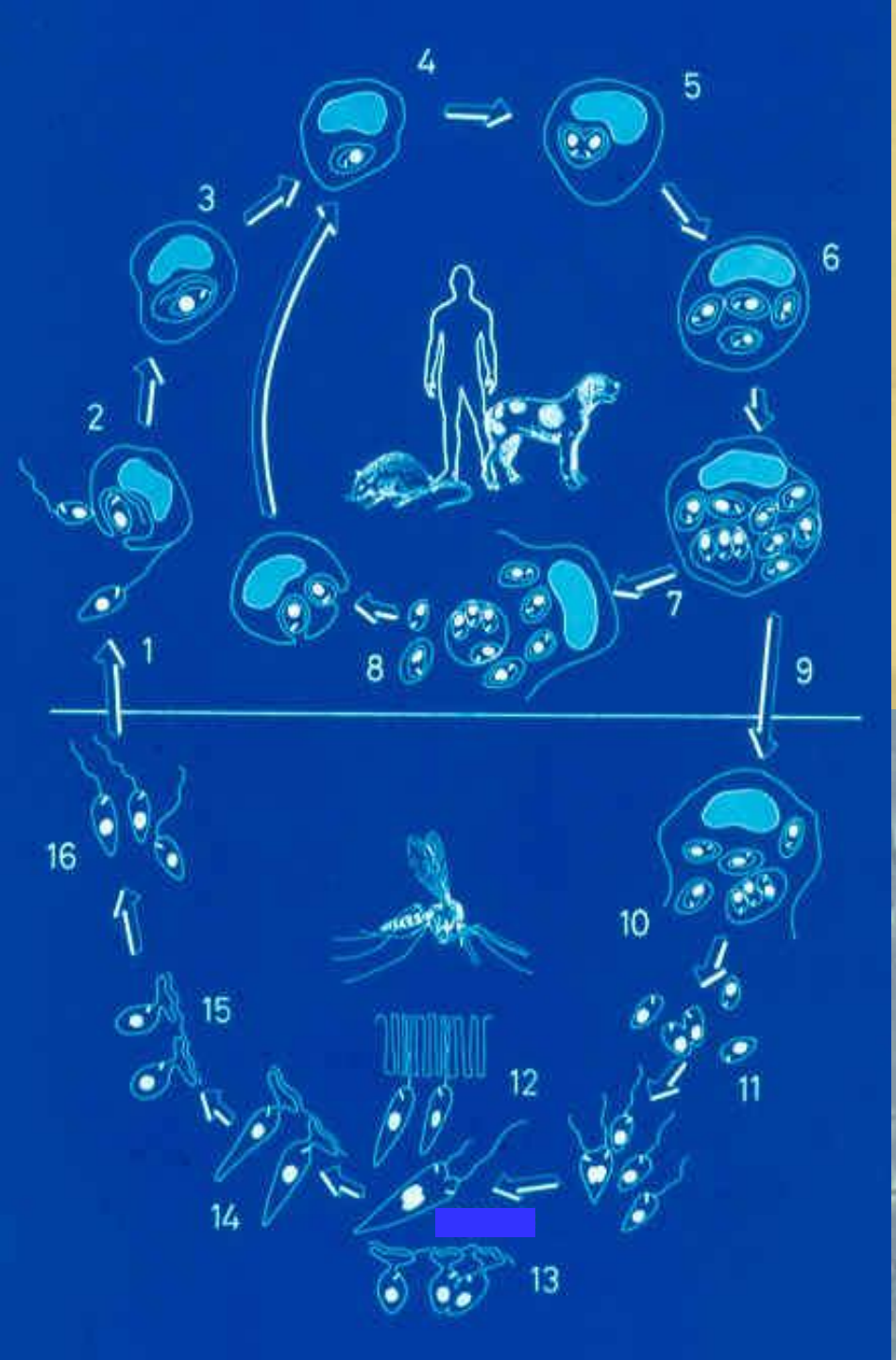
Public Health impact of Leishmaniasis in Mediterranean Europe



Luigi Gradoni

Unit of Vector-borne diseases & International health
Istituto Superiore di Sanità, Rome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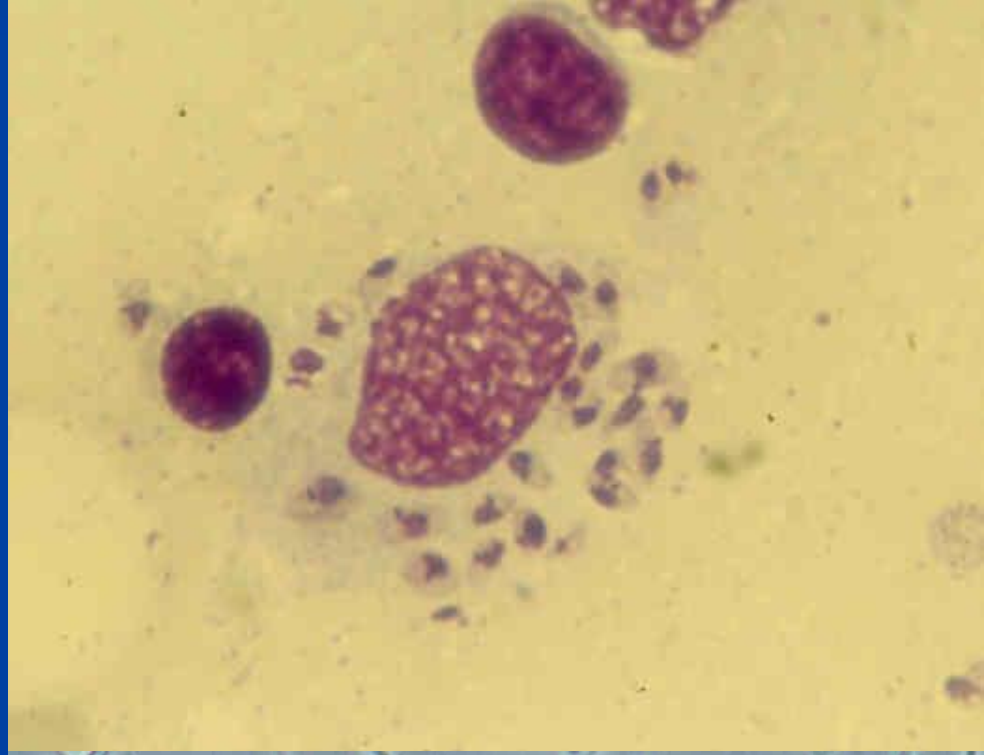
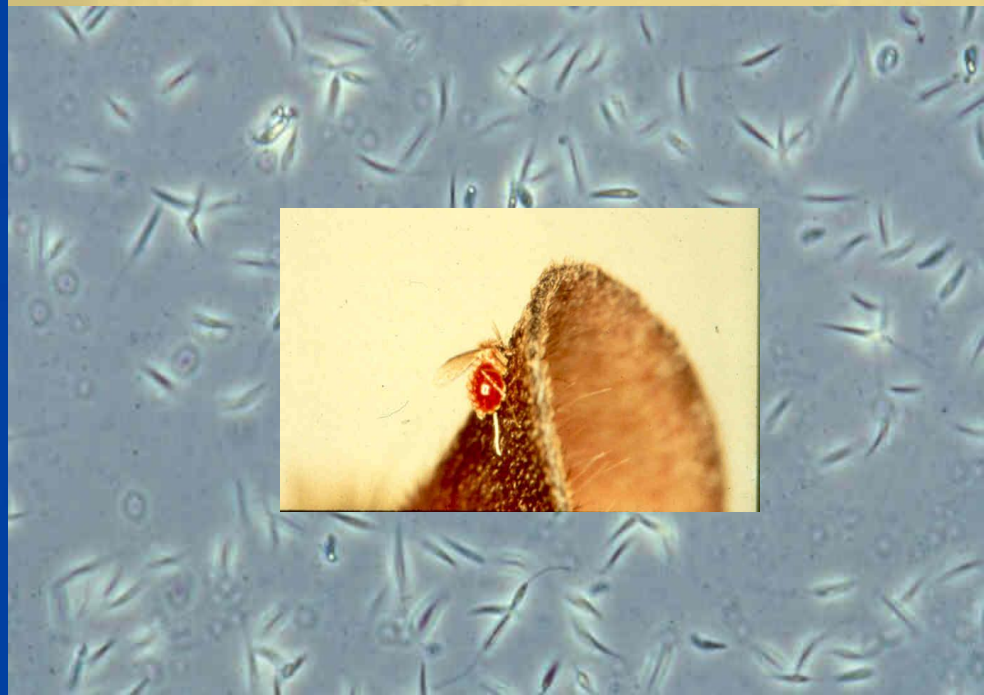
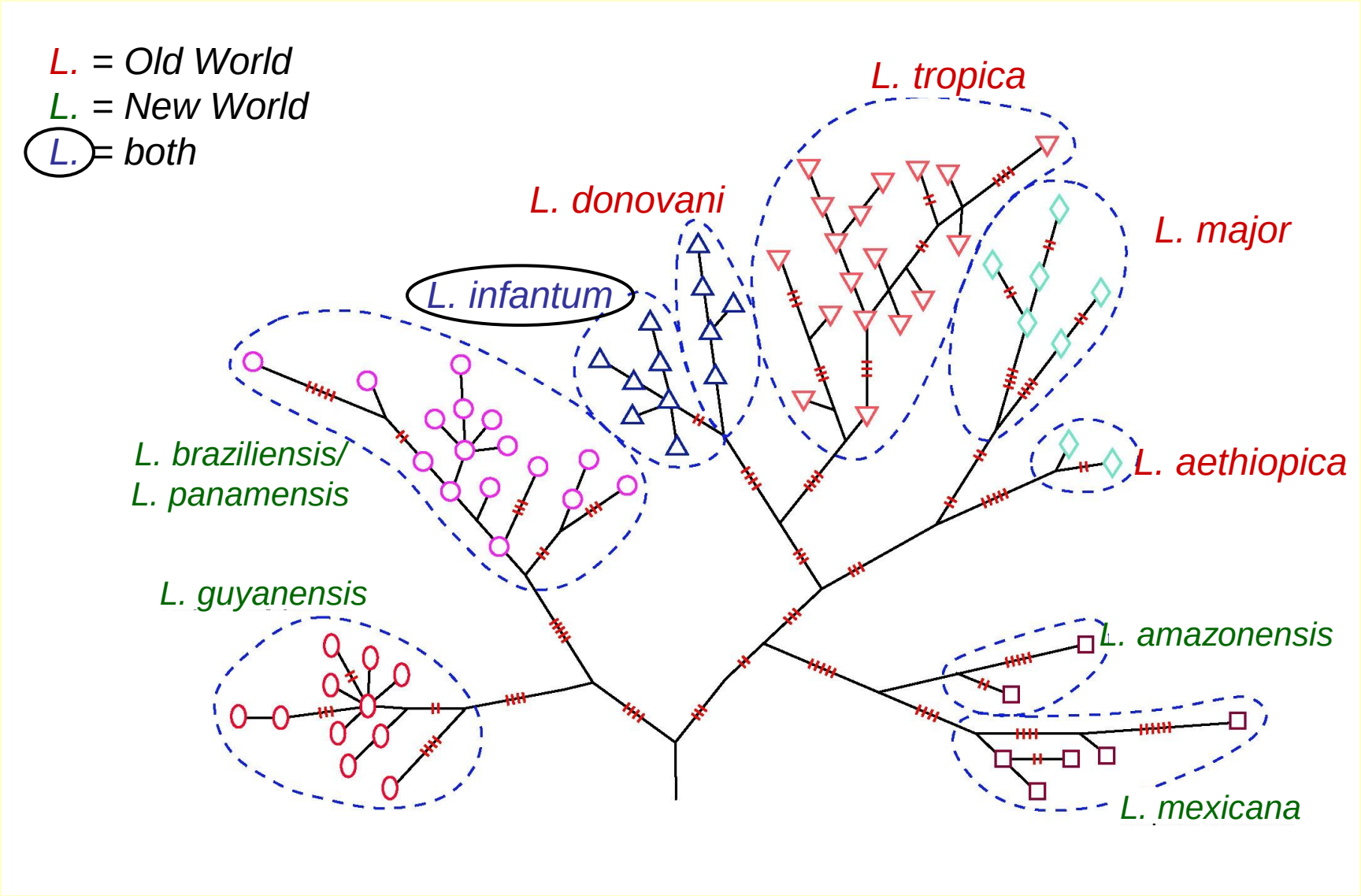




World distribution of leishmaniases

Phylogenetic tree of *Leishmania* genus based on zymodeme polymorphism



The specific association

✓ PARASITE-RESERVOIR-VECTOR

and the respective

✓ DISEASE IN MAN

distributed in a given

✓ TERRITORY

contribute to the

NOSOGEOGRAPHICAL ENTITY OF LEISHMANIASIS

Zoonotic Visceral Leishmaniasis (ZVL) by viscerotropic *Leishmania infantum*

Sporadic Cutaneous Leishmaniasis (SCL) by dermotropic *Leishmania infantum*

The canine reservoir of ZVL and SCL

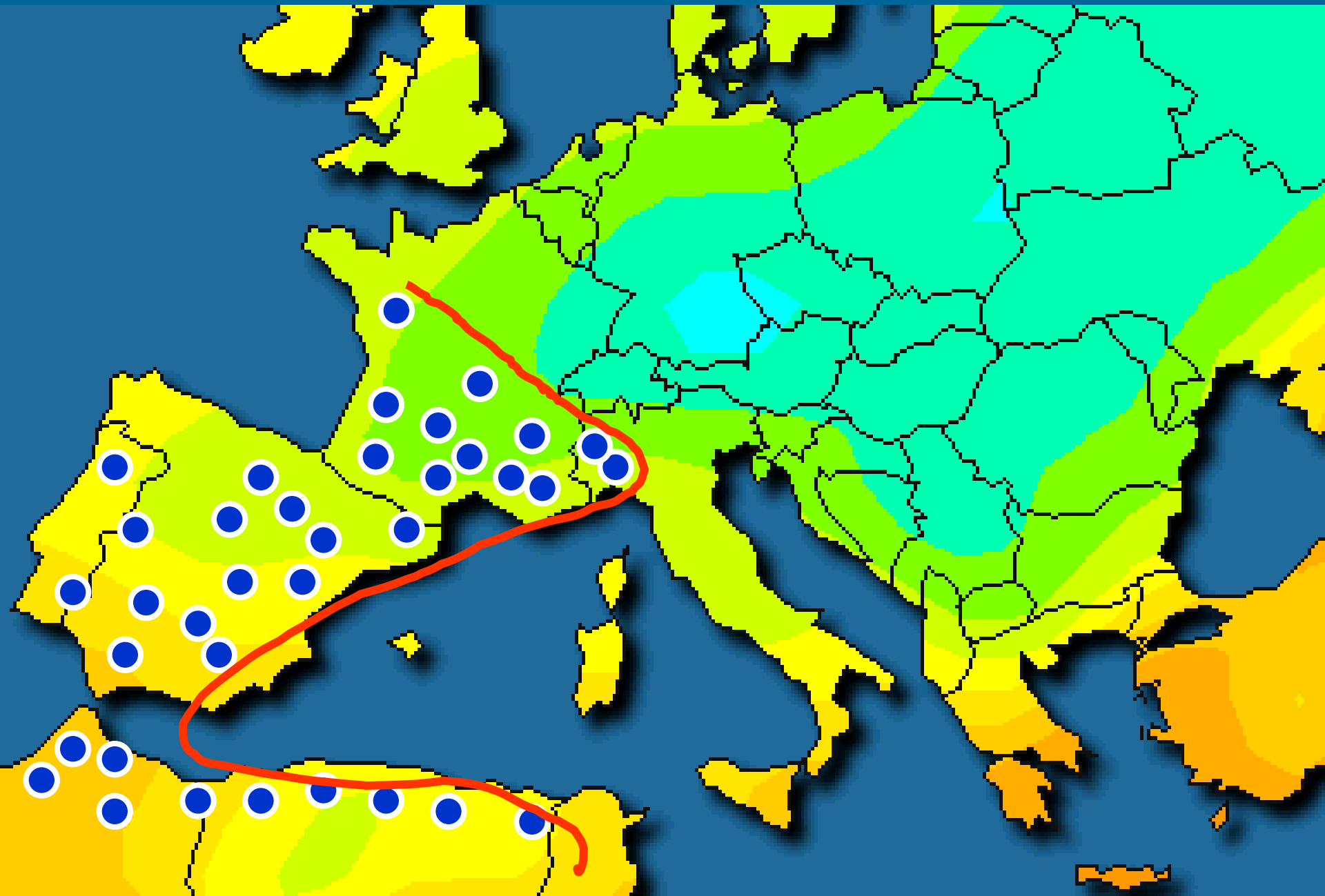
2-45% seroprevalence in stable foci of ZVL and SCL

Clinical disease in less than 50% of seropositive dogs

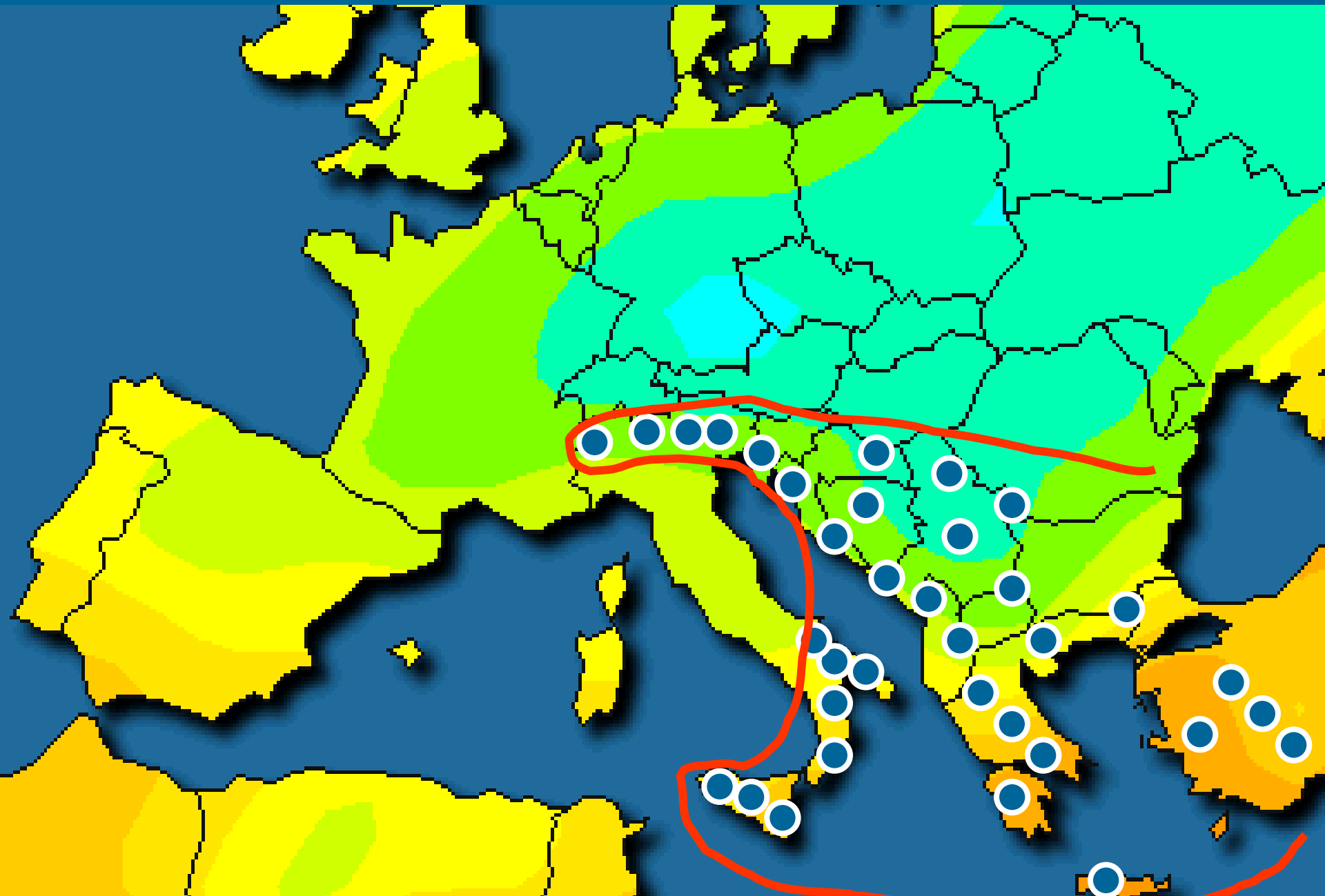
The coevolution of *Leishmania infantum* and the subgenus *Phlebotomus (Larroussius)*

P.ariasi *P.perniciosus* *P.neglectus* *P.tobbi* *P.major* *P.kandelakii*

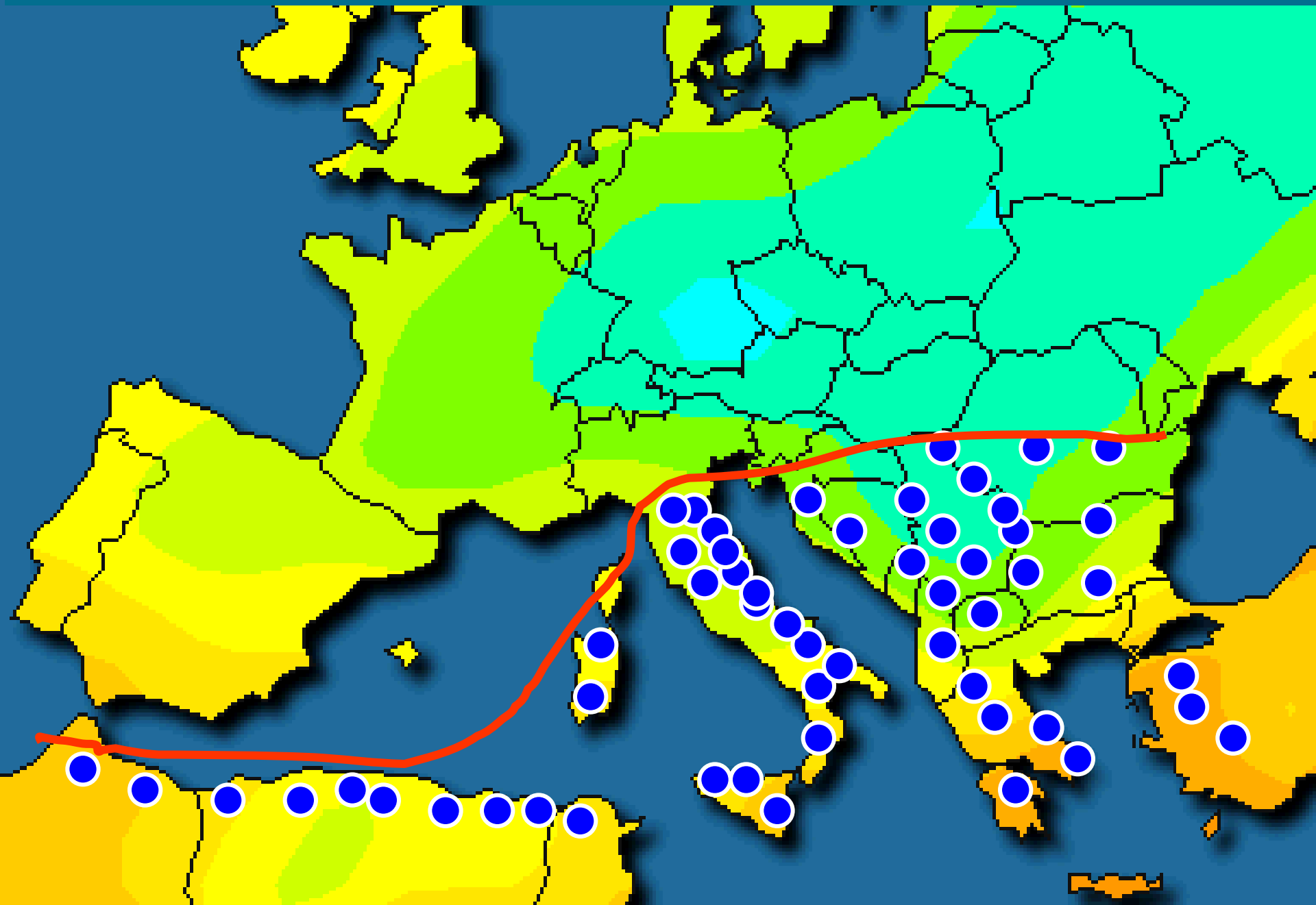
Phlebotomus ariasi



Phlebotomus neglectus



Phlebotomus perfiliewi



Phlebotomus perniciosus

INCIDENCE OF HUMAN LEISHMANIASES IN MEDITERRANEAN EUROPE:

INFORMATION SOURCES

Centralized information system for infectious diseases (CISID)

Passive notification of any clinical leishmaniasis case

[no distinction for VL vs CL, first episodes vs relapses, endemic vs imported, HIV- vs HIV+ coinfections]

Country/Year	96	97	98	99	00	01	02	03	04	05	06	07
Albania	80	88	156	105	107	162	140	129	111	70	nr	66
Croatia	nr	1	1	0	1	1	3	1	1	2	1	5
Cyprus	nr	nr	nr	nr	nr	nr	nr	nr	0	2	4	1
France	nr	nr	nr	nr	nr	nr	nr	81	15	102	115	213
Greece	6	46	25	36	52	46	53	28	48	50	nr	54
Italy	178	159	133	158	213	199	218	173	158	88	109	126
Malta	16	8	32	22	18	13	nr	4	4	4	3	13
Portugal	17	15	11	19	7	13	13	9	nr	13	10	23
Spain	72	93	92	74	82	105	93	109	115	110	93	128

Leish Med

Yearly incidence of VISCERAL LEISHMANIASIS [regardless HIV condition; includes first episodes only]: Information from Leishmaniasis Reference Centres

Country	Average 2000-2006	
	Autochthonous	Imported
Cyprus	5	?
France	24	65
Greece	21	?
Italy	200	8
Portugal	22	2
Spain	100	5

Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 14, No. 7, July 2008

Current drug therapy of VISCERAL LEISHMANIASIS: Information from Leishmaniasis Reference Centres

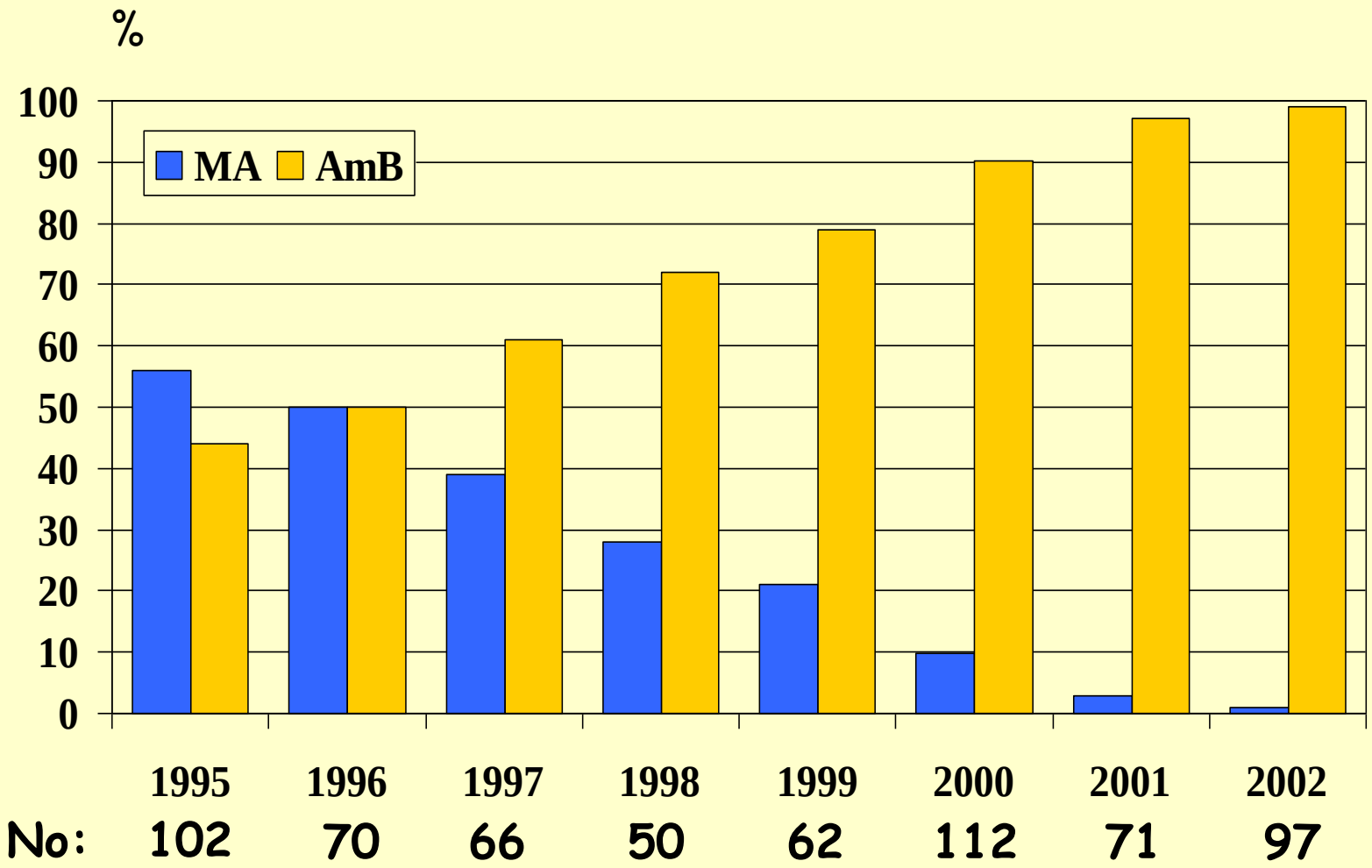
BACKGROUND

In the early 1990s*, information on drug efficacy and tolerability of first-line treatment regimens employed for Mediterranean VL, was collected from nine endemic countries of Southern Europe and Northern Africa.

MEGLUMINE ANTIMONIATE was the only drug employed in the Region

*Gradoni et al, 1995. Bull WHO 73, 191-197

Analysis of the shift from MEGLUMINE ANTIMONIATE to L-AMPHOTERICIN B for the treatment of VL in Italy



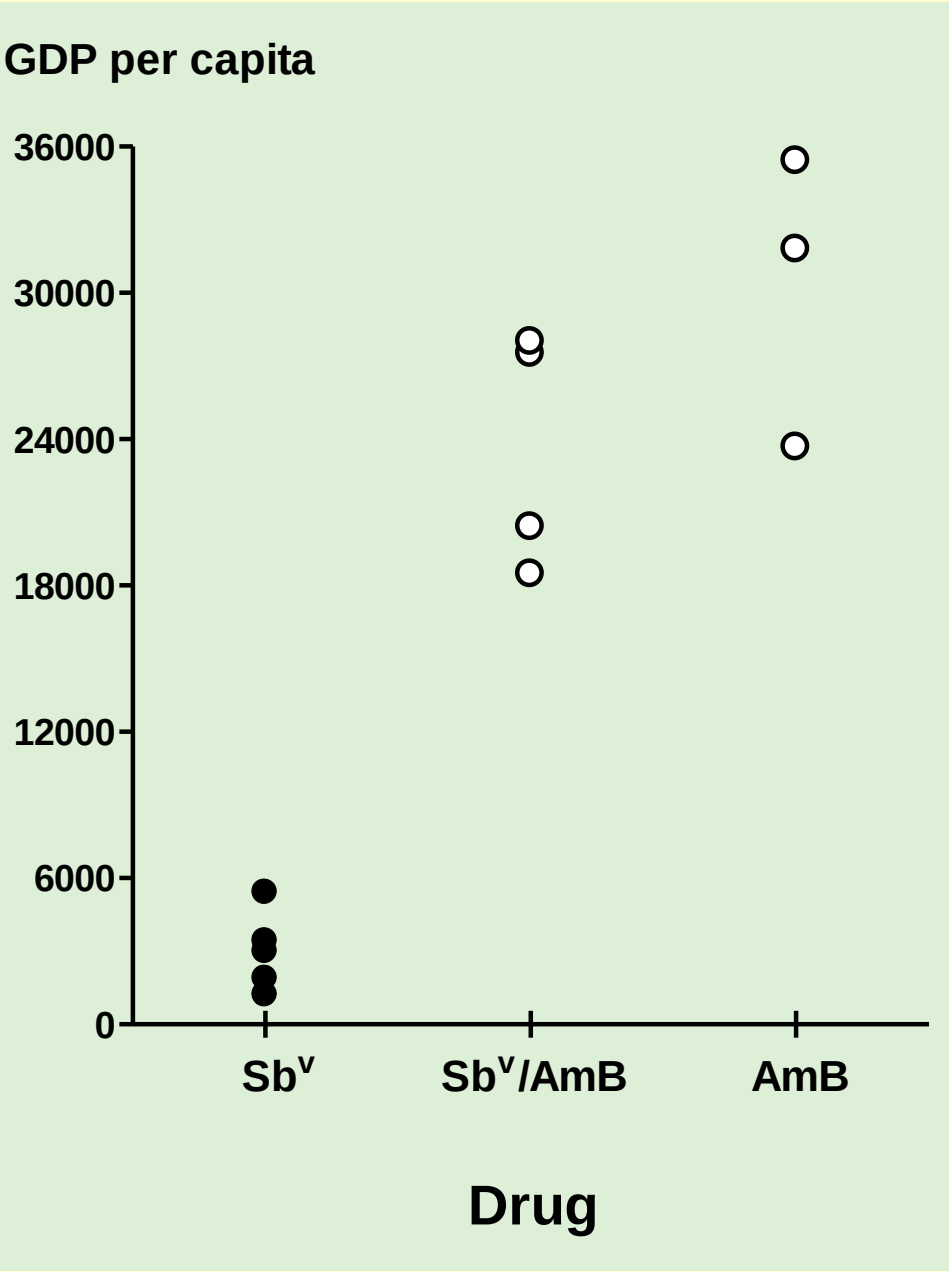
Relationship between gross domestic product (GDP) per capita and first-line VL treatment options in Mediterranean countries

Sb^v: exclusive use of pentavalent antimony drugs
Sb^v/AmB: both pentavalent antimony and lipid-associated amphotericin B-based drugs are employed but in different patients' categories
AmB: predominant use of liposomal amphotericin B

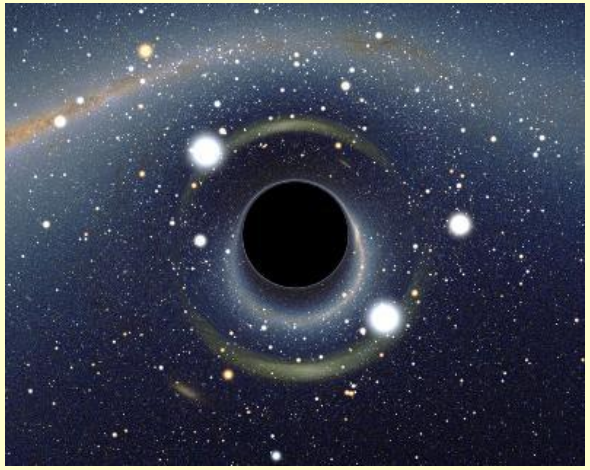
● Northern African and Middle East countries, excluding Israel

○ Southern European countries and Israel

(*Gradoni et al, TM&IH 2008*)



Yearly incidence of CUTANEOUS LEISHMANIASIS



A BLACK HOLE !!!

- **Benign nature**
- **Misdiagnosed**
- **Cases seen at private dermatologists (only complicated forms hospitalized)**
- **Unreported**

CUTANEOUS LEISHMANIASIS by dermotropic *L.infantum*: HIGHLY POLYMORPHIC





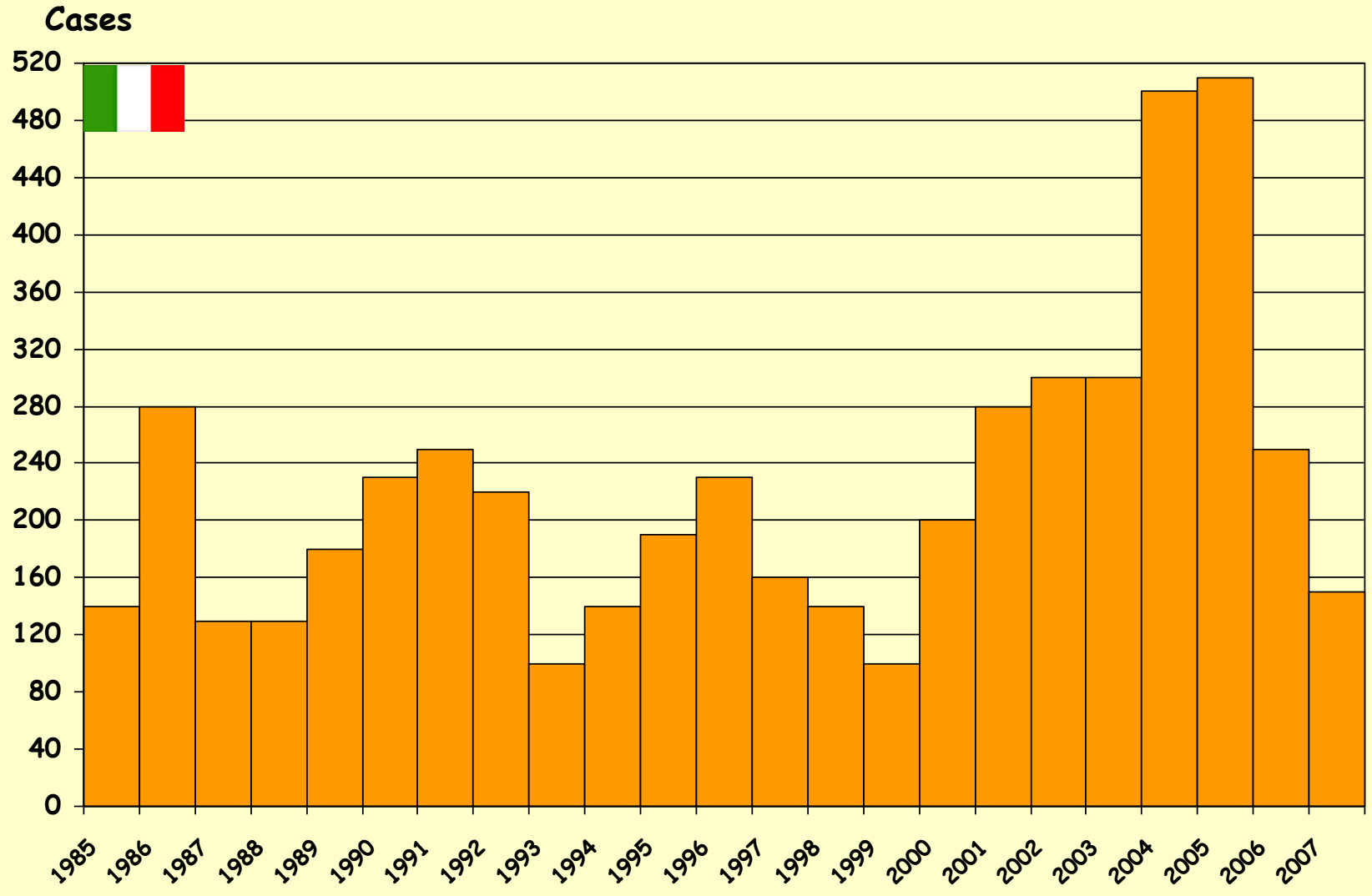


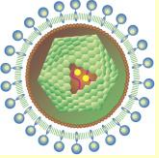


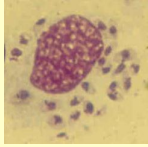





ISS estimates of CUTANEOUS LEISHMANIASIS incidence





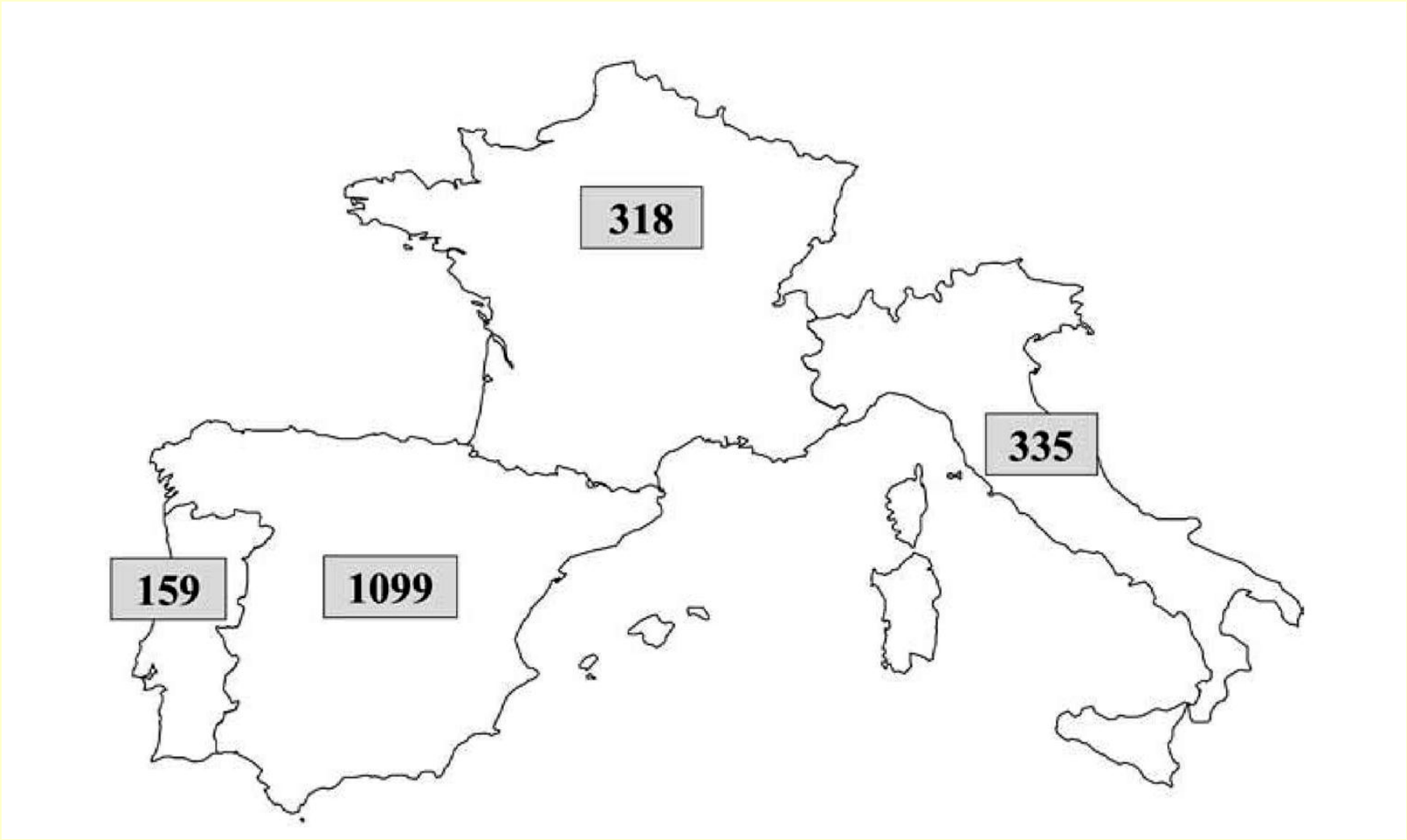


HIV-*LEISHMANIA* COINFECTIONS IN SOUTH EUROPE: AN UPDATE

***For the 2001-2005/6 period*:**

- WHO Collaborating Centre for Leishmaniasis, Servicio de Parasitologia, Centro Nacional de Microbiologia, Instituto de Salud Carlos III, Majadahonda-Madrid, **Spain**
- Centre Nationale de Référence des *Leishmania*, Laboratoire de Parasitologie, Montpellier, **France**
- Leishmanioses Unit, Instituto de Higiene e Medicina Tropical, Lisboa, **Portugal**
- Unit of Vector-borne Diseases & International Health, Istituto Superiore di Sanità, Roma, **Italy**

Distribution by country of the 1911 *Leishmania*/HIV co-infection cases in south western Europe by early 2001



For the incidence analysis of the 2001-2005/6 period, only new cases ('primary infections') were considered

 Spain: from late 2001 through 2006 → 95

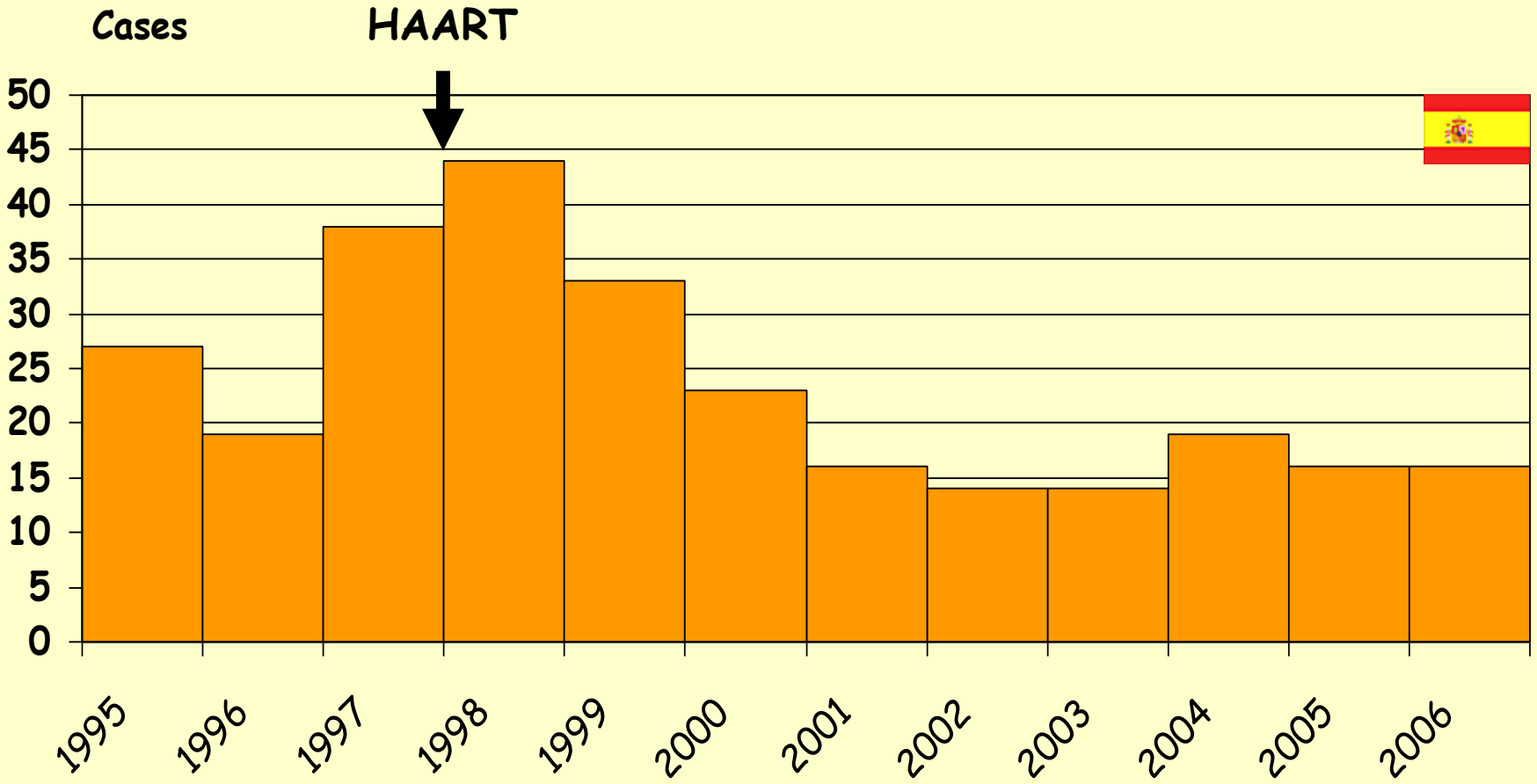
 Portugal: from 2001 through 2006 → 64

 Italy: from 2001 through 2006 → 52

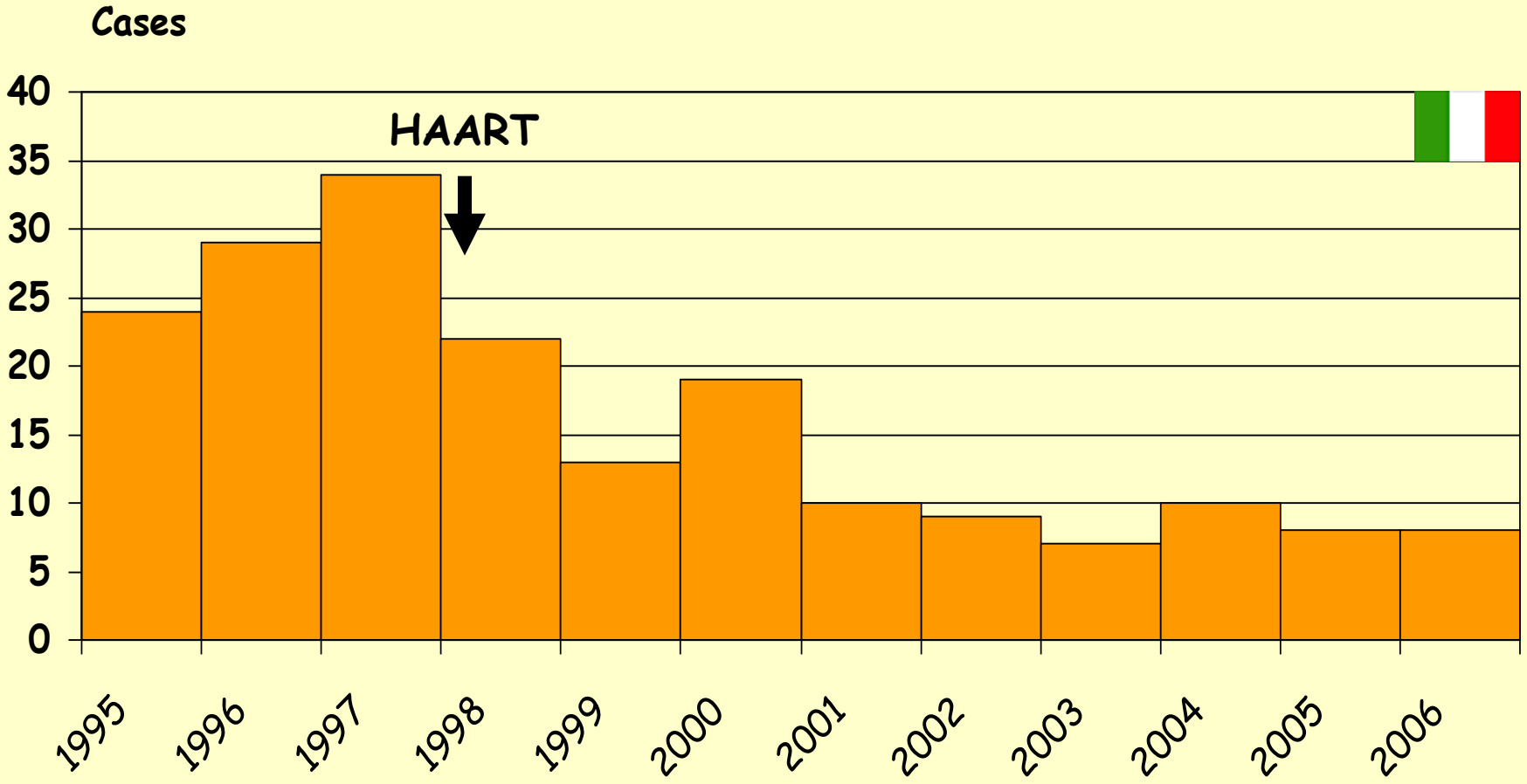
 France: from late 2001 through 2005 → 30

… for a total of 241 new HIV/VL cases

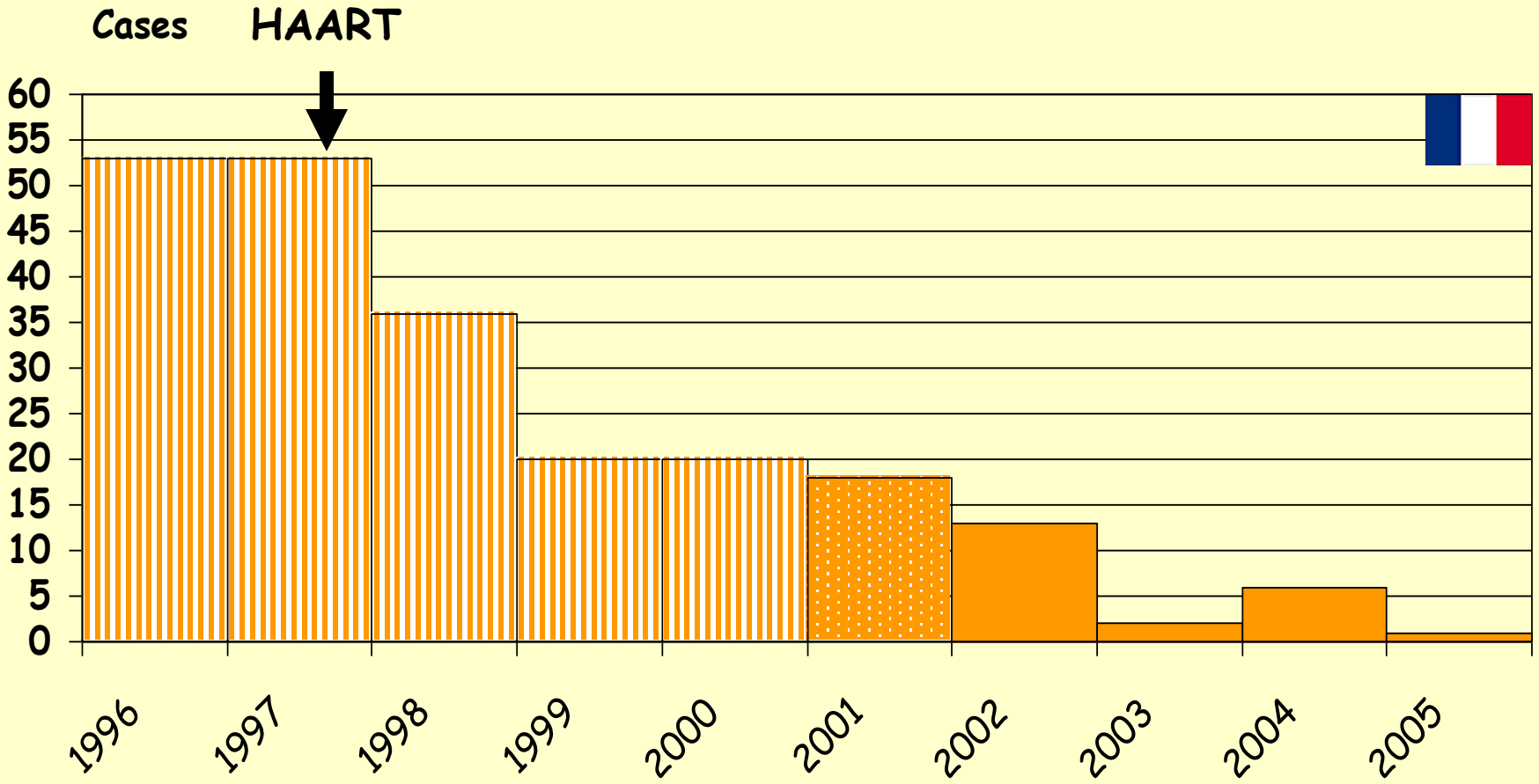
Incidence trend of HIV/*Leishmania* co-infections diagnosed at the WHO CC for Leishmaniasis, Madrid, Spain



Incidence trend of HIV/*Leishmania* co-infections diagnosed and recorded at Istituto Superiore di Sanità, Rome, Italy



Incidence trend of HIV/*Leishmania* co-infections diagnosed and recorded in the Montpellier Reference centre, France (1996-early 2001: estimated means)



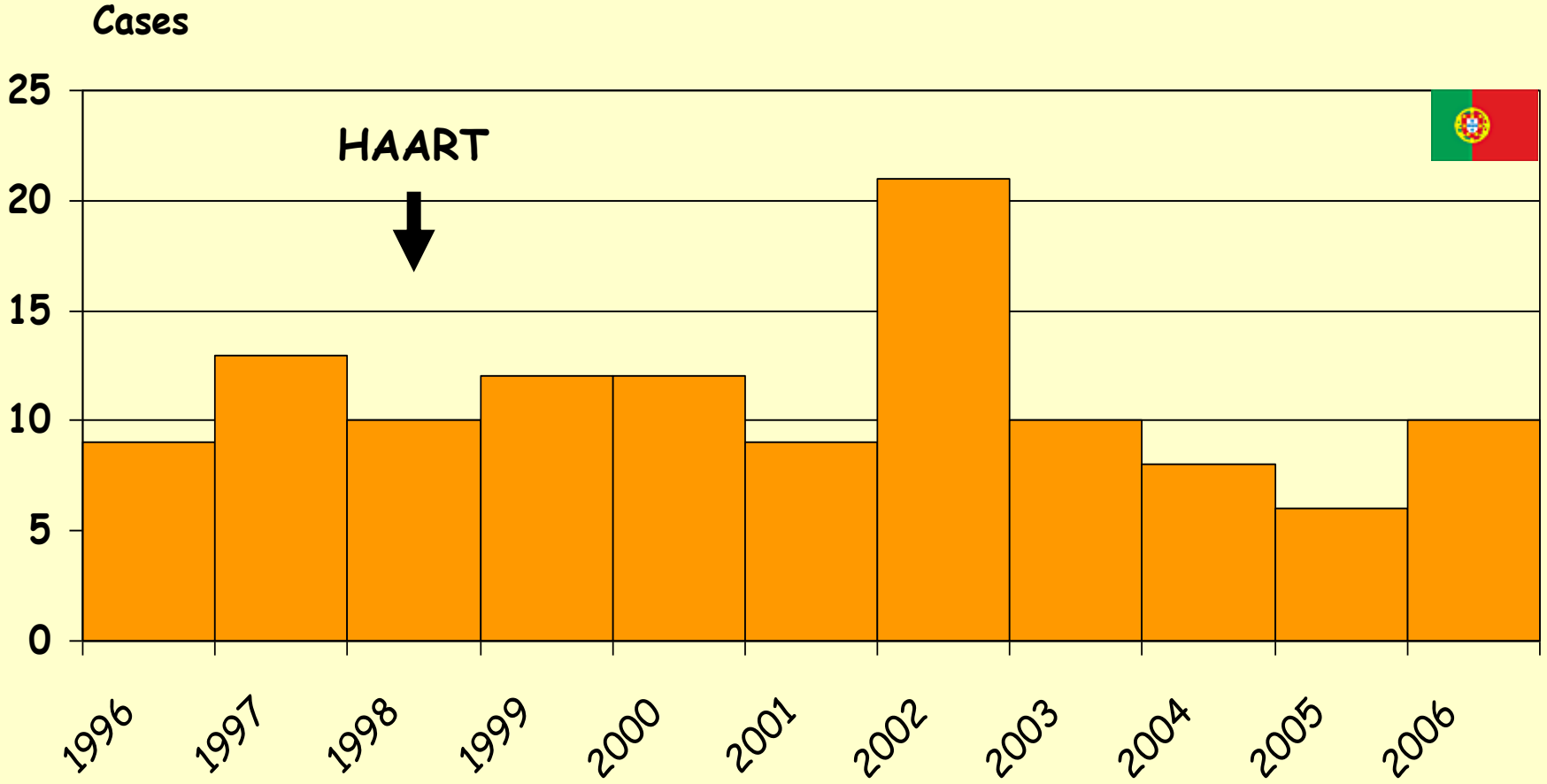
These 3 countries presented a similar trend

Incidence peak period

Steady low incidence period

One country showed a different trend

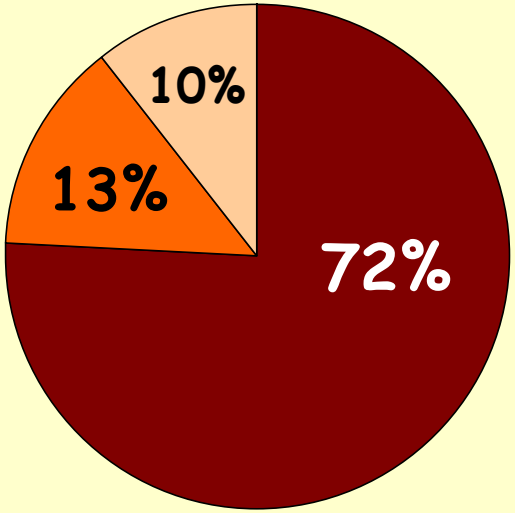
Incidence trend of HIV/*Leishmania* co-infections diagnosed and recorded at the Leishmaniasis Unit, Lisbon, Portugal



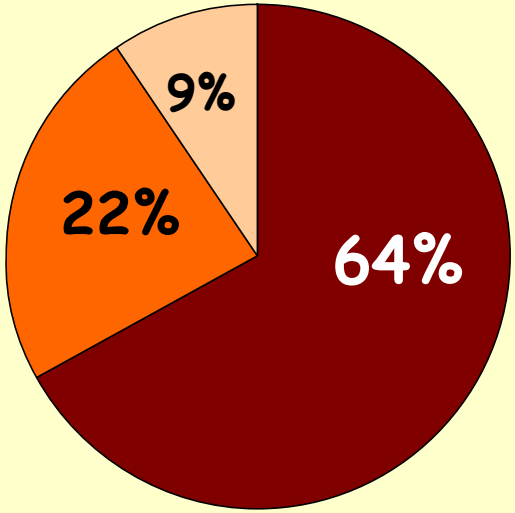
HIV risk groups: a comparison with previous data

Note: 3 main risk groups account for **95% of cases** in both periods

1990-early 2001
1124 HIV/L



2001-2006
101 HIV/L



Intravenous-drug use Heterosexual Homosexual

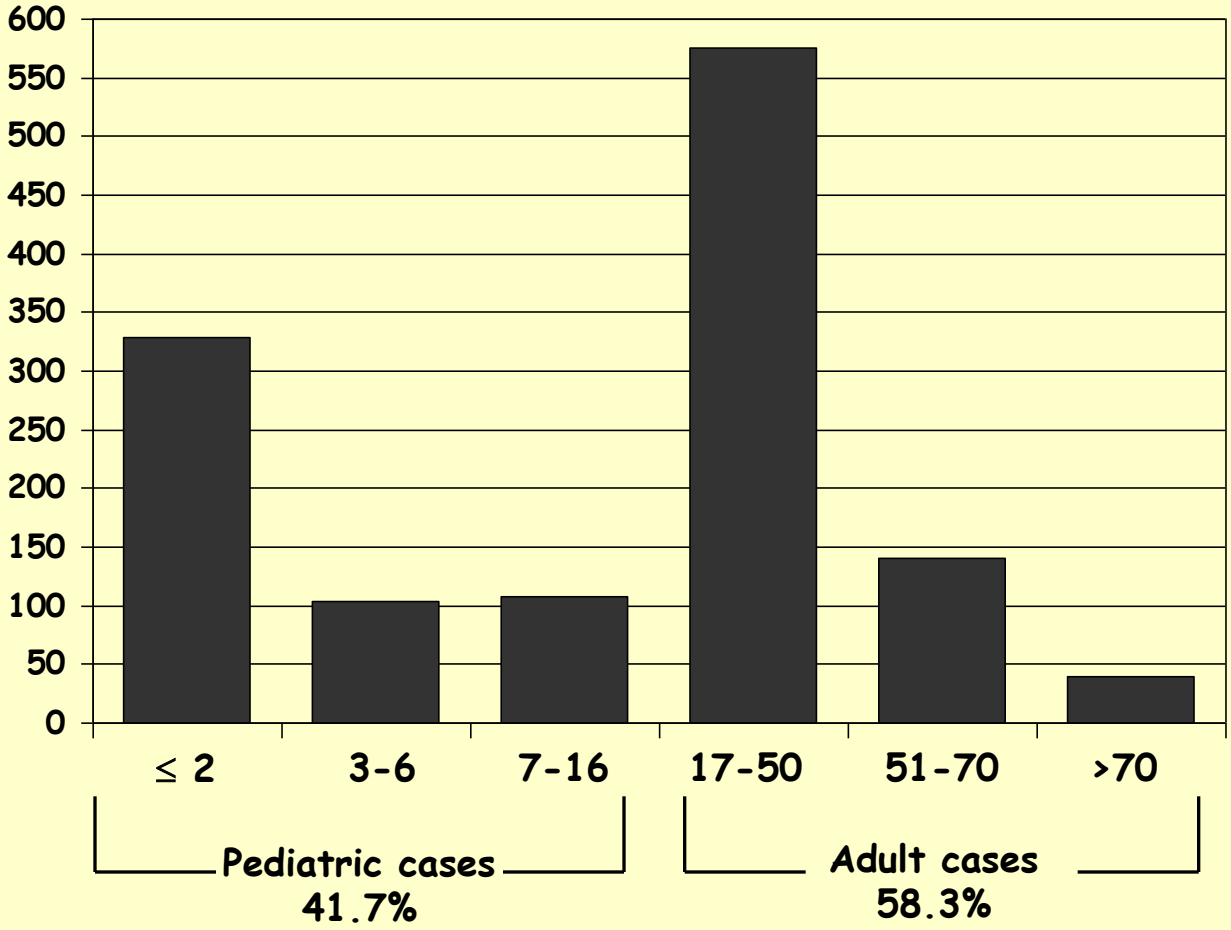
Concomitant/underlying clinical conditions other than HIV infection in

VISCERAL LEISHMANIASIS

Retrospective analysis from a Southern European Reference Centre (ISS, Italy)

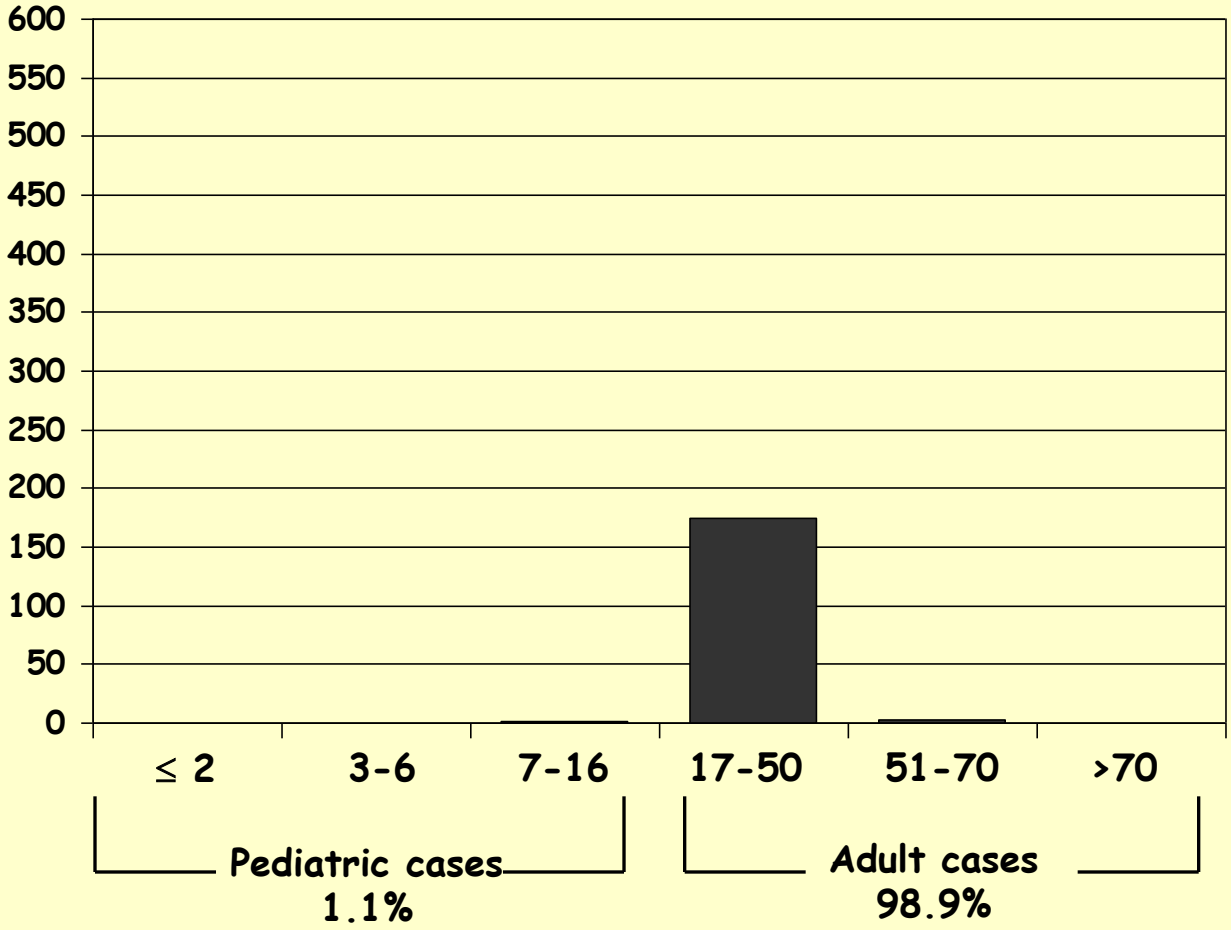
All VL cases from 1987 to 2005

No: 1296

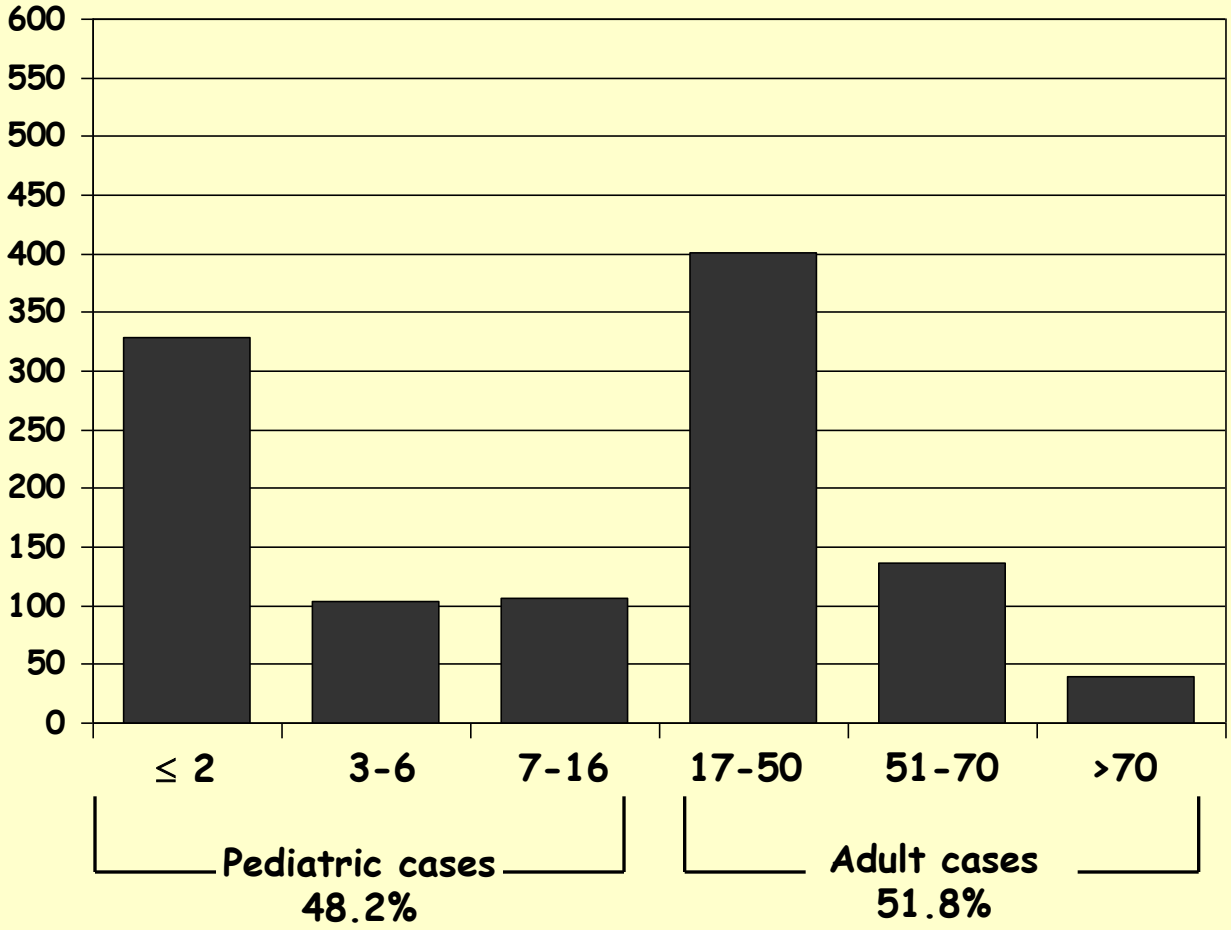


HIV positives

No: 179 = 14% of total VL cases,31% among young adults

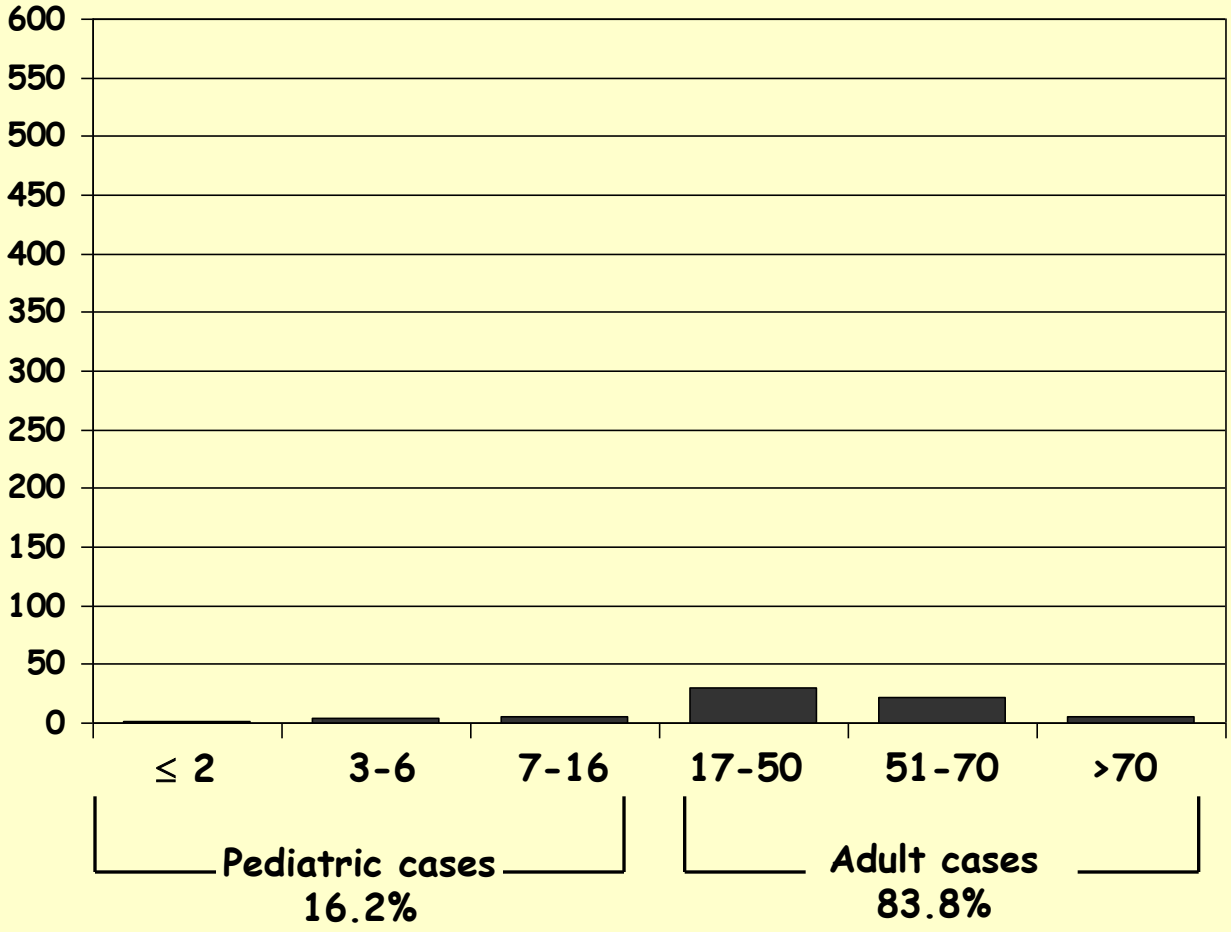


HIV negatives
No: 1117



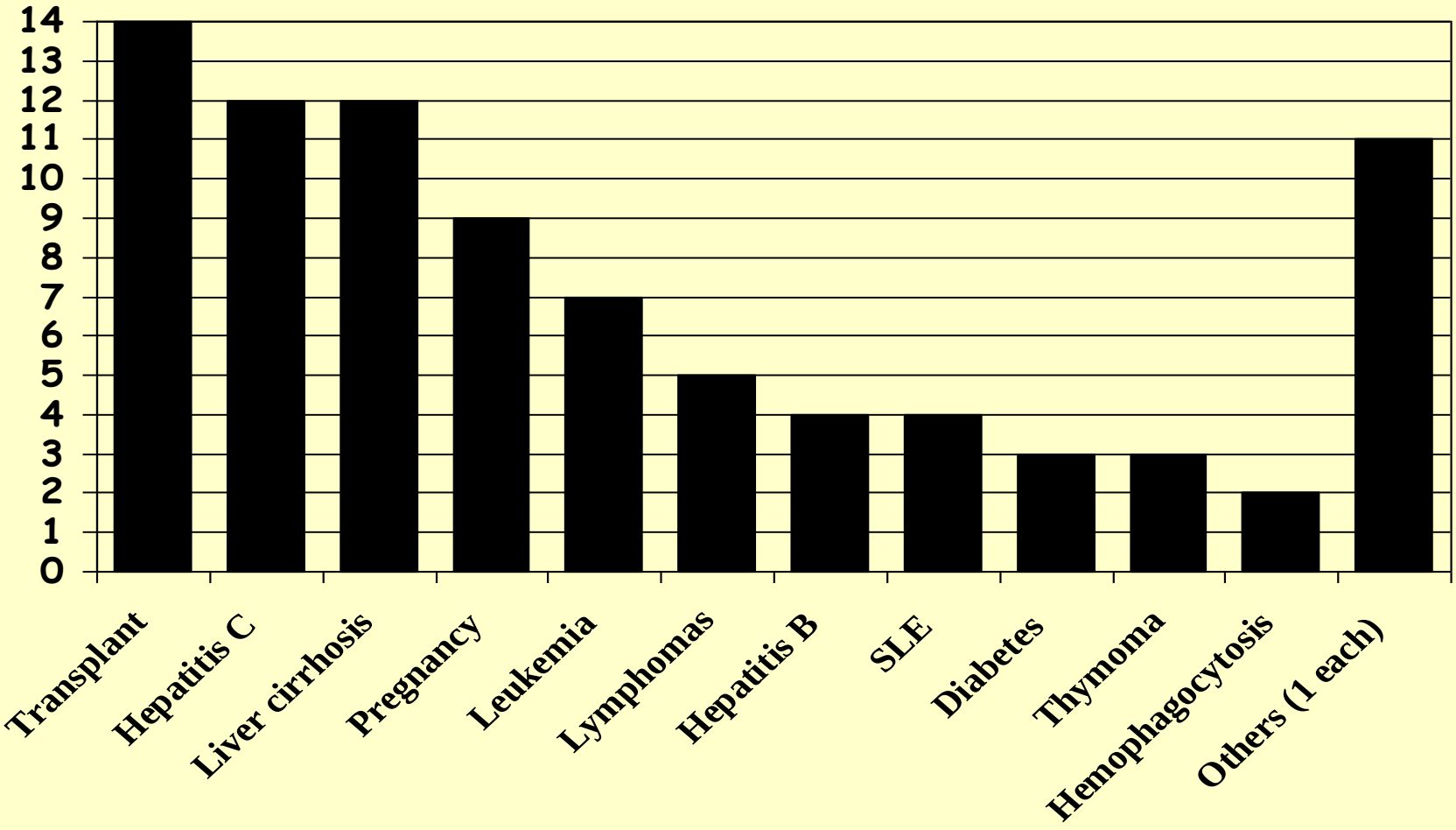
Patients with concomitant/underlying clinical conditions other than HIV

No: 68 = 5% of total VL cases, 12% among adults



Concomitant/underlying conditions (no: 23)

Single in 54 patients, double in 14 patients

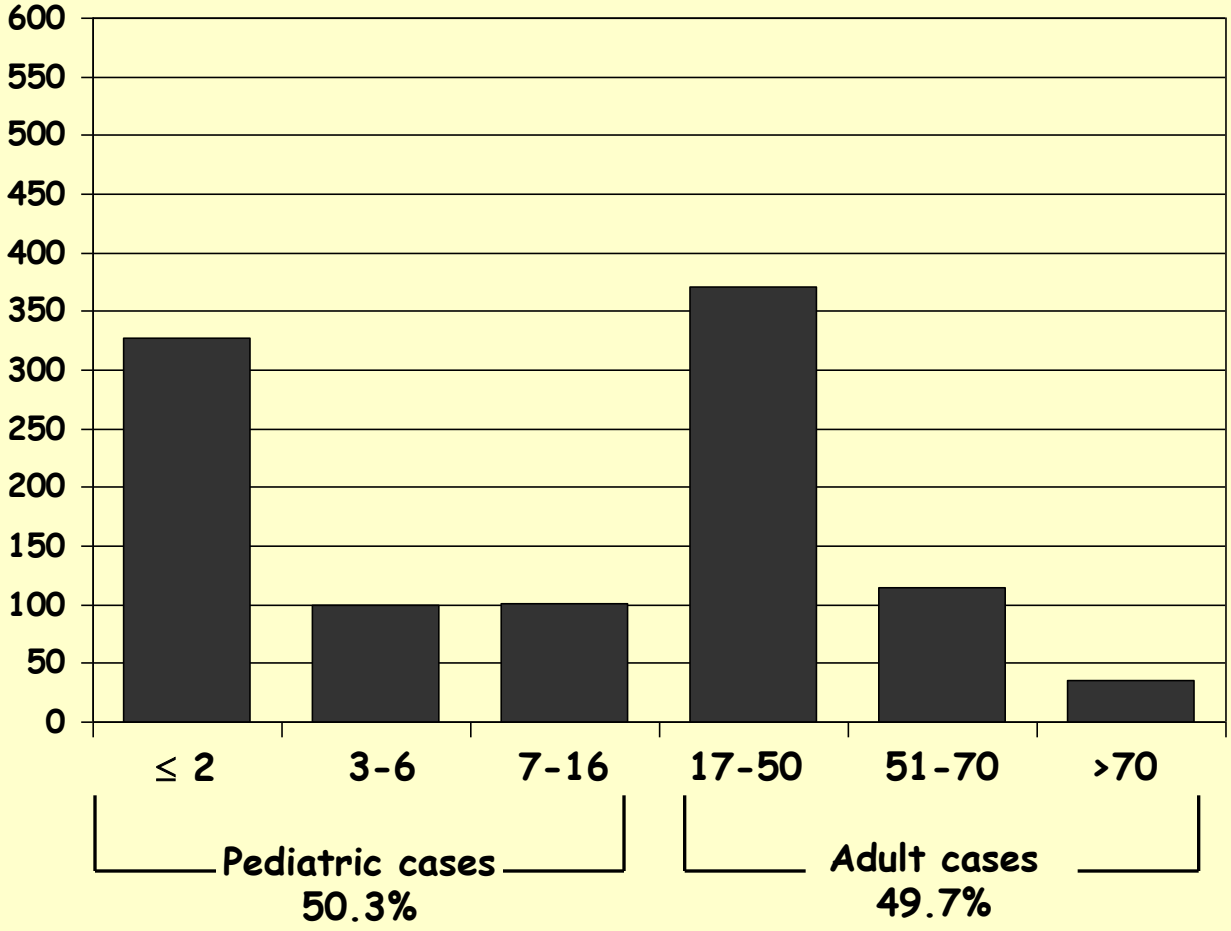


Others (1 each)

- ✓ Chronic glomerulonephritis
- ✓ Multiple sclerosis
- ✓ Pneumonia
- ✓ Primitive immunosuppression
- ✓ Cytomegalovirus
- ✓ Wegener's granulomatosis
- ✓ Rheumatoid arthritis
- ✓ Thalassemia
- ✓ Splenectomy
- ✓ Pericarditis
- ✓ Chronic renal failure

Patients <u>without</u> concomitant/underlying clinical conditions

No: 1049 = 81% of total VL cases



PREVALENCE OF ASYMPTOMATIC LEISHMANIASIS IN MEDITERRANEAN EUROPE

1974	First description of asymptomatic cases of VL in Southern Europe (Pampiglione et al., 1974. Trans R Soc Trop Med Hyg 68:447-53)
1975 – 2010	Several reports from Italy, France, Spain and Greece
Methods	Leishmanin skin test (LST) Serology (Western blot, ELISA, IFAT) Blood culture Blood PCR
Prevalence range (%)	All age groups: 9.7 – 46.8 (LST)

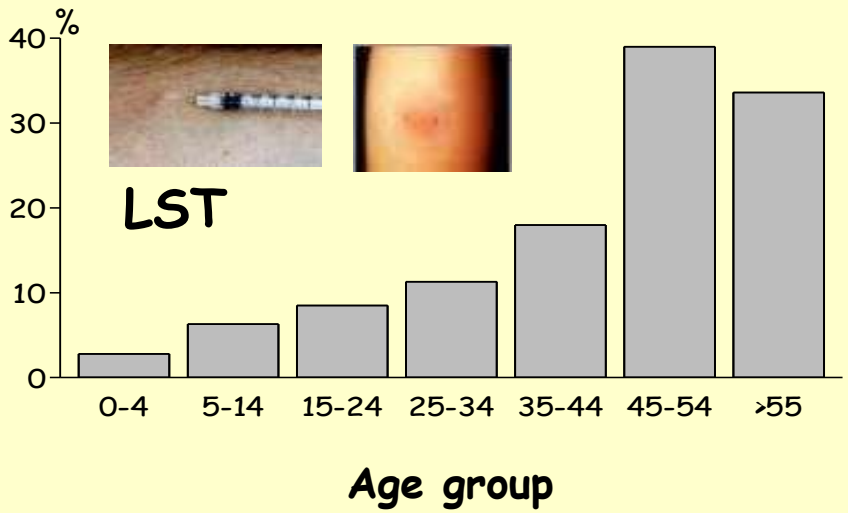
First demonstration of viable cultured parasites

JOURNAL OF CLINICAL MICROBIOLOGY, June 1999, p. 1953–1957 Vol. 37, No. 6
0095-1137/99/$04.00+0

Occurrence of *Leishmania infantum* Parasitemia in Asymptomatic Blood Donors Living in an Area of Endemicity in Southern France

YVES LE FICHOUX,[1] JEAN-FRANÇOIS QUARANTA,[1,2] JEAN-PIERRE AUFEUVRE,[3] ALAIN LELIEVRE,[1] PIERRE MARTY,[1] ISABELLE SUFFIA,[1] DEBORAH ROUSSEAU,[1] AND JOANNA KUBAR[1]*

Groupe de Recherche en Immunopathologie de la Leishmaniose, Laboratoire de Parasitologie, Faculté de Médecine de Nice, Nice,[1] and Cellule d'Hémovigilance, Hôpital Pasteur, CHU Nice,[2] France, and Centre de Transfusion Sanguine, Hôpital Princesse Grace, Monaco[3]



1981

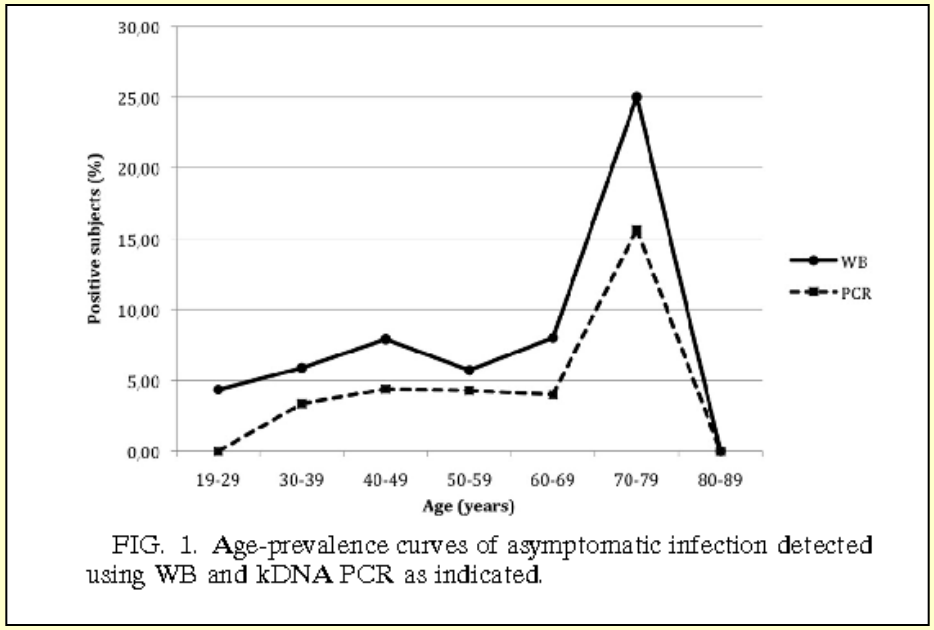
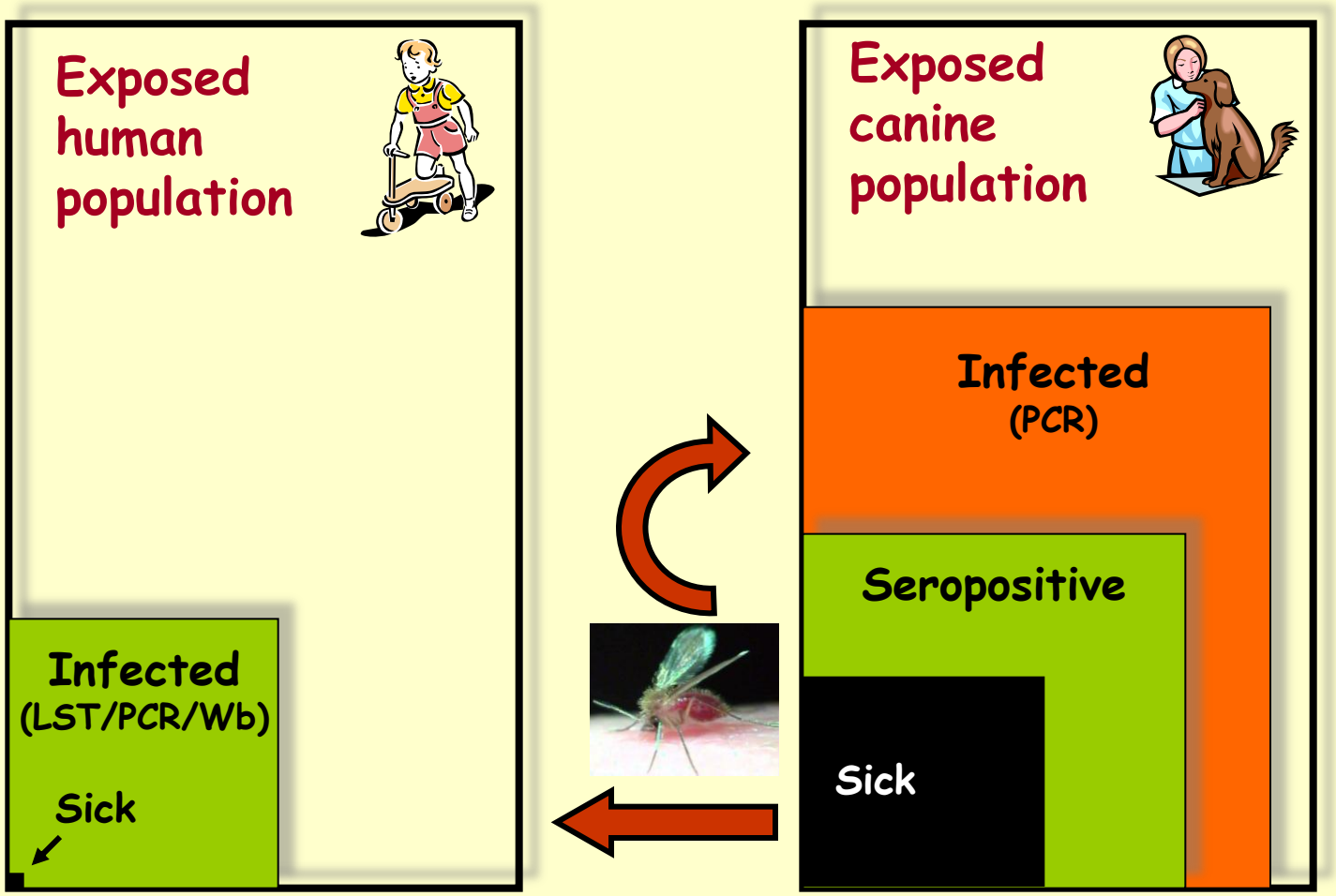


FIG. 1. Age-prevalence curves of asymptomatic infection detected using WB and kDNA PCR as indicated.

2005

Quantitative relationship between human and canine leishmaniasis in a typical ZVL focus



Importation and risk for introduction of

"EXOTIC" *LEISHMANIA*

Report from a Southern European Reference Centre (ISS, Italy)

Great Britain

Sand flies: NO; Risk for introduction: NO

Period	Human leishmaniases		Canine leishmaniasis
	VL	CL and MCL	
1985-2004	39		
1995-2003		79	
2005-2007			275

QJM, 2004; EID, 2006; Vet Parasitol, 2009

HOLLAND

San flies: NO; Risk for introduction: NO

Period	Human leishmaniases		Canine leishmaniasis
	VL	CL and MCL	
1996-2007	32	47	
1989-1993			145

Int Health, 2010; Acta Vet Scand, 2002

GERMANY

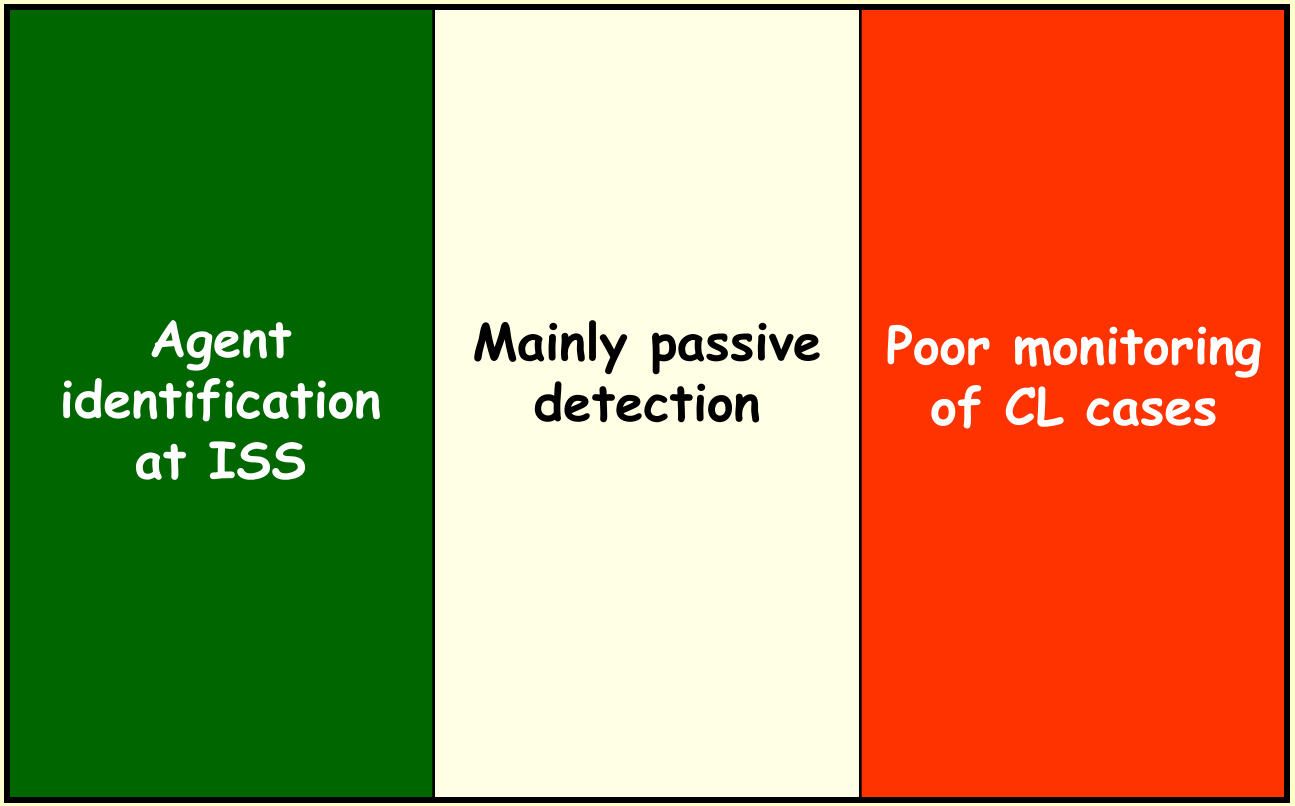
Sand flies: YES (*P.perniciosus*, 1 site); Risk of introduction:?

Period	Human leishmaniases		Canine leishmaniasis
	VL	CL and MCL	
2000-2002	27	43	
1993-1995			236

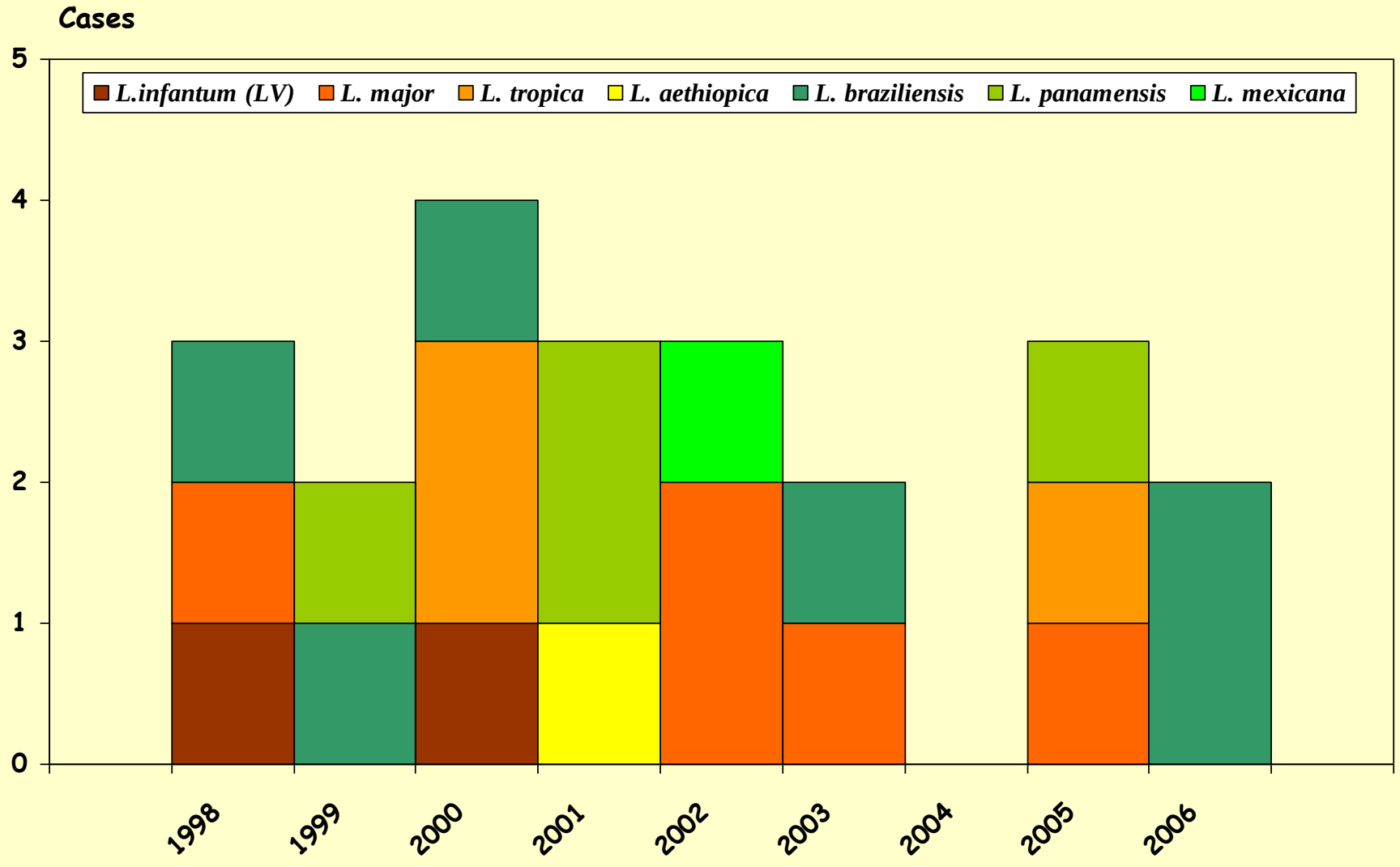
Tierarztl Prax 1997; EID, 2003; Parasitol Res 2008

ITALY

Sand flies: 6 vector species; Risk for introduction: YES



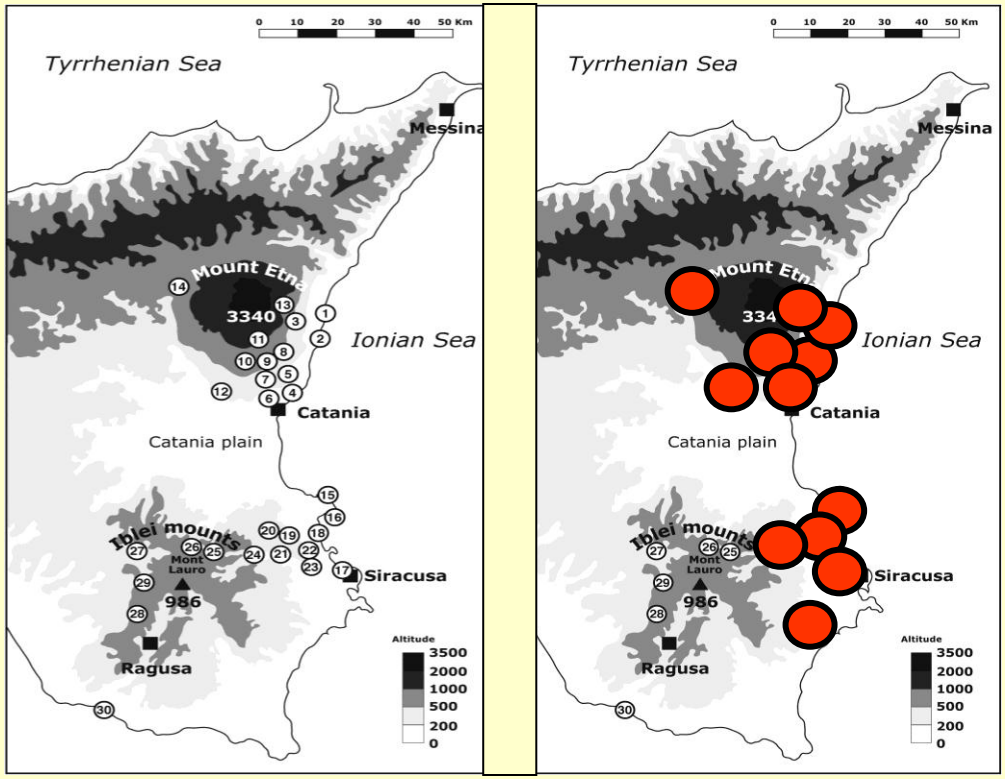
Imported cases of exotic *Leishmania* in Italy
Identified at ISS by MLEE and/or PCR-RFLP



Competent sand fly species other than *L.infantum*
Larroussius vectors found endemic in Italy

Species	Specificity
P.papatasi	*L.major*
P.sergenti	*L.tropica*

The main concern:
risk for the introduction of *Leishmania tropica* in Sicily



Phlebotomus sergenti

The Sicilian population of *P. sergenti* is genetically very similar to the Northern African populations competent for *L. tropica* transmission

THE NORTHWARD SPREAD OF LEISHMANIASIS

Report from a Southern European Reference Centre (ISS, Italy)


Major climatic zones in Italy
AUSTRIA
SWITZERLAND
SLOVENIA
FRANCE
CONTINENTAL
MEDITERRANEAN-TYPE


Boundaries of endemic leishmaniasis in Italy through late 1980s
AUSTRIA
SWITZERLAND
SLOVENIA
FRANCE

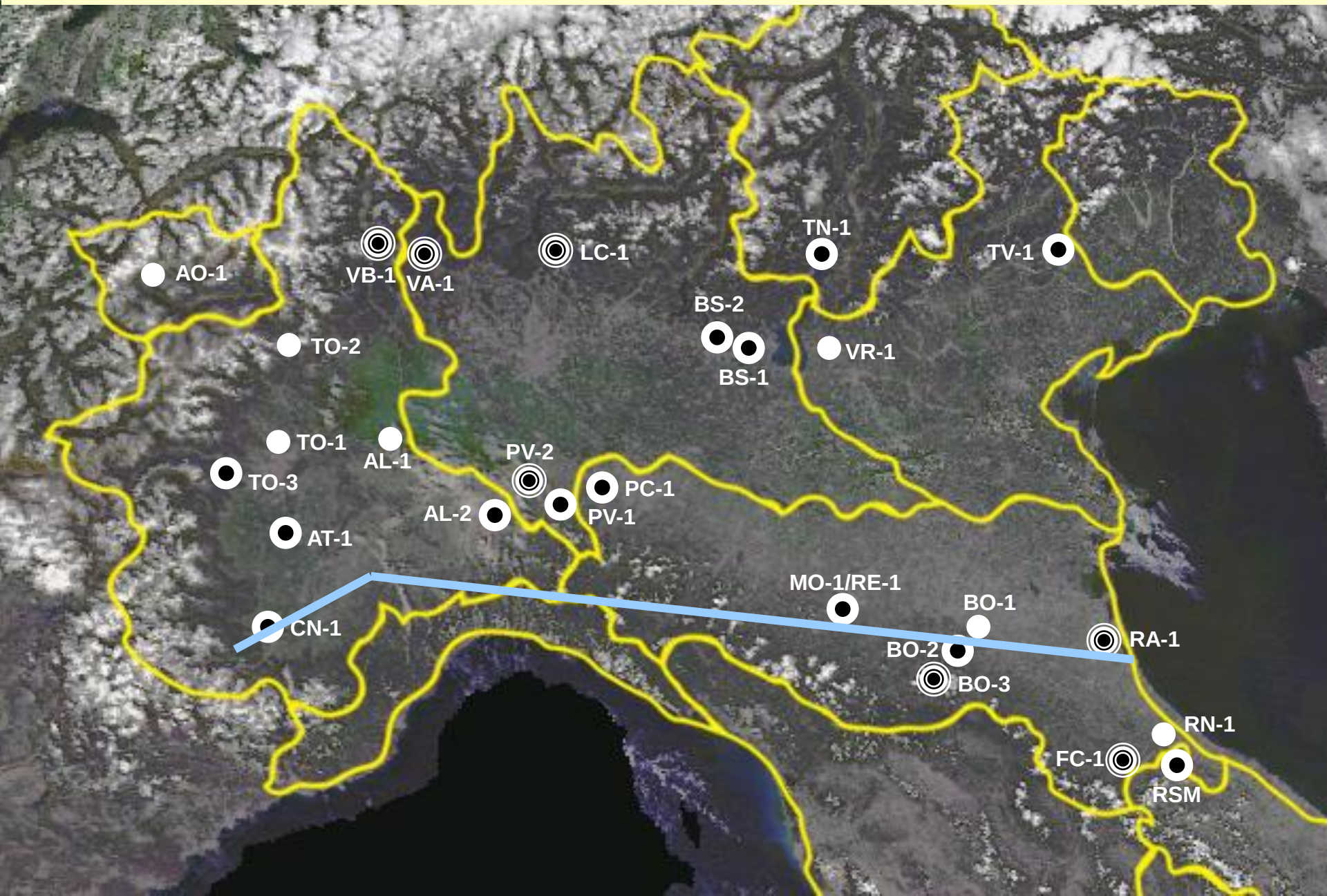
CanL in continental Italy: analysis of literature before 1993

Canine leishmaniasis

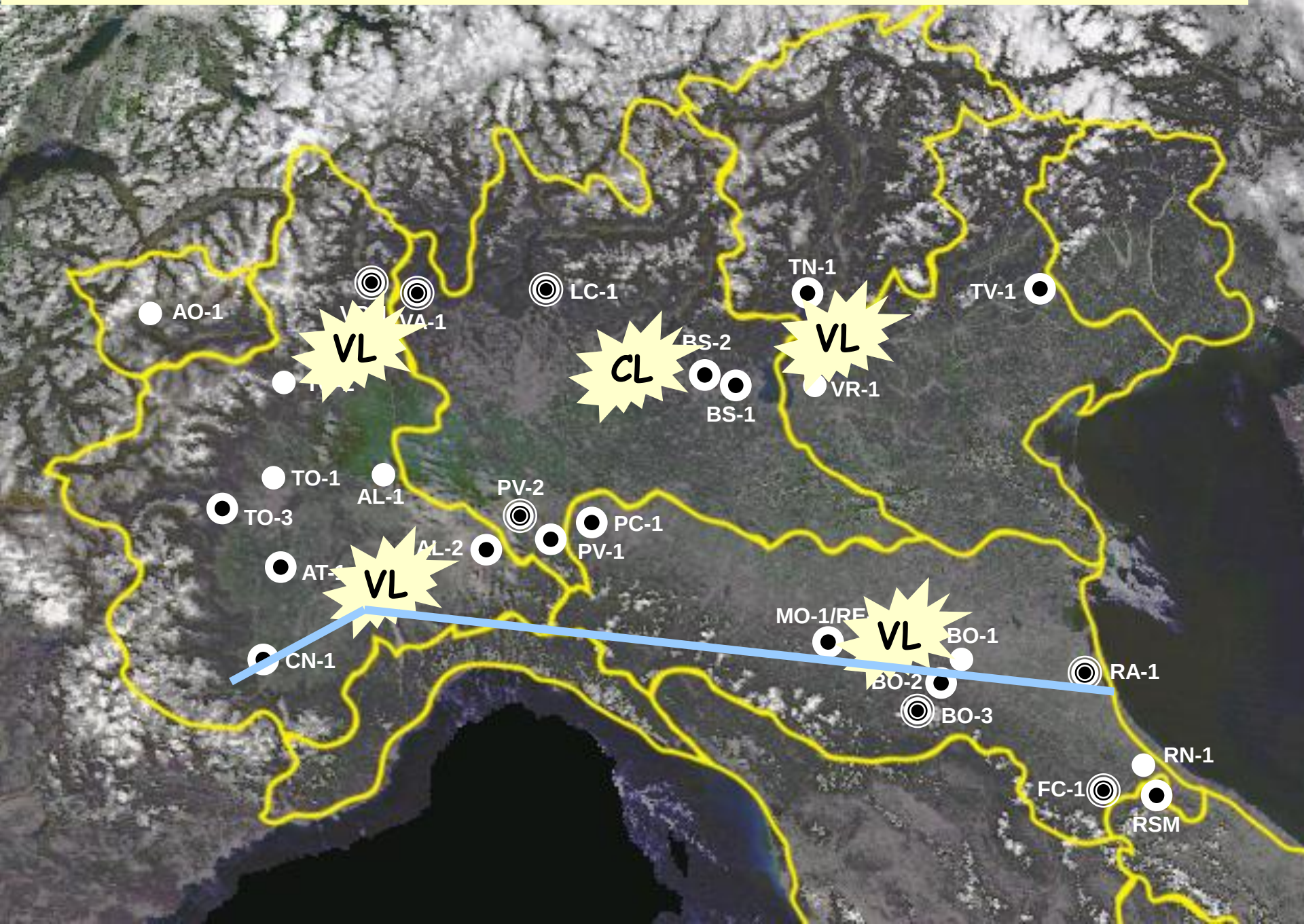
no autochthonous cases recorded

CanL: 2003-2005 prospective survey.

47 clinical index cases; 106 seropositives/5442 asymptomatic (2%)



Autochthonous human cases recorded (passive detection)



The burden of CANINE LEISHMANIASIS in Southern Europe

Risk map of canine leishmaniasis prevalence
(EDEN analysis of canine serosurveys – Submitted for publication)