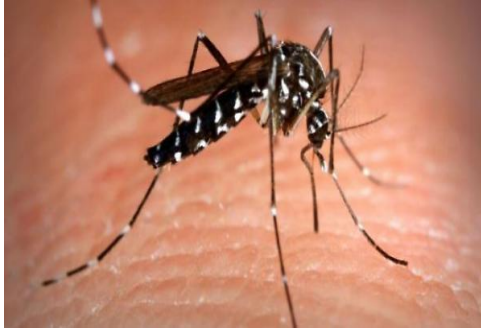
Novità in Infettivologia
Autumn 2018
Bologna, 23 Novembre 2018



Le Infezioni trasmesse da artropodi

Dott. Filippo Trapani

Outline

- **Introduction**
- **Arthropods of medical importance**
- **Epidemiological and clinical aspects of most important arthropod-borne infection in Italy (West Nile Virus, Leishmaniasis)**

Introduction

- **The phylum Arthropoda is the largest phylum of the animal kingdom** and includes the subphylum Crustacea and the classes Insecta and Arachnida.

- **All the medically important ectoparasites, including mosquitoes, fleas, flies, lice, mites, and ticks, are members of the phylum Arthropoda.**

Principali Artropodi vettori e patologie associate

Nome Comune	Malattie
Phylum Arthopoda, Classe Insetti	
Zanzara	Malaria, West Nyle Virus, Arbovirosis (ZikaV, Dengue, Chikungunya), Filariasis
Mosca, pappatacio	Leishmaniasis, Loiasis, Onchocerciasis, Tripanosomiasi africana, myiasis
Cimice	Chagas' Disease
Pidocchio	Pediculosis, trench fever (Bartonella quintana), epidemic Borrelliosis and Rickettsiosis
pulce	mechanical vectors of dog and rat tapeworms, tungiasis, vector of plague
Phylum Arthropoda, Class Arachnida	
Acaro, zecca	Scabies, Anaplasmosis, Babesiosis, Lyme, TBE, Rickettsiosis, Endemic Borrelliosis, Q fever

Mechanisms of Ectoparasite-Borne Diseases and Injuries

- **Directly** by burrowing into, feeding, dwelling, and reproducing in human skin and orifices (mites, fleas, and flies) or
- **by blood or tissue juice sucking** (fleas, lice, mites, and ticks).
- **The arthropod ectoparasites can also threaten human health indirectly by infectious disease transmission** (fleas, mosquitoes, mites, and ticks).
- **Ticks are the most versatile ectoparasitic arthropods and can transmit a variety of infectious diseases (viral, bacterial, and protozoan) and even inject paralytic toxins** (tick paralysis) during their prolonged blood meals.
- **Unlike other ectoparasites, ticks can be infective as males and females at birth** (by transovarial pathogen transmission) and throughout all stages of their development (by trans-stadial pathogen transmission).

Table 1 | *Most relevant vector borne diseases endemic in Italy and their own characteristics. * indicates the emergent VBD recently experienced in the country*

Disease	Present status	Vector(s)	Pathogen(s)	Kind of disease and reservoirs(s)
Visceral leishmaniasis	Endemic, mainly in central and southern Italy (about 200 cases/year). Moving northward. Rising trend	Sand flies Genus *Phlebotomus:* *P. pernicious* (main), *P. ariasi, P. neglectus,* *P. perfiliewi*	*Leishmania infantum*	Zoonosis (domestic dogs)
Cutaneous leishmaniasis	Endemic, mainly on the regions of the East Coast and islands. Probably some hundred undiagnosed cases per year	Sand Flies *P. perfiliewi* (main), *P. pernicious*		
Toscana virus meningitis	Endemic, mainly in central regions (Toscana and Marche). Scattered rare cases in other regions. Less than 10 cases/year reported, but rising trend	Sand flies *Plhebotomus* spp.	Phlebovirus Toscana v.	Zoo-anthroponosis Bats, wild rodent, foxes
Chykungunya fever*	2007. Outbreak of Chyk fever in Emilia-Romagna region. About 250 cases	Culicine mosquitoes *Aedes albopictus*	Alphavirus CHYK virus	Anthroponosis Humans
West Nile encephalitis*	1998: first epidemics of equine encephalitis in Toscana region. 2008-2010 outbreaks of equine disease mainly in Emilia-Romagna, Veneto, Lombardia and scattered foci in other regions. About 30 human cases in total	*Culicinae* mosquitoes *Culex pipiens* Cx. spp	Flavivirus WN virus	Zoonosis Birds
Dirofilariasis	Endemic. Rare cases in rural areas, mainly in northern and central regions	Anopheline and Culicine. mosquitoes	*Dirofilariae* *D. immitis* *D. repens*	Zoonosis. Dogs and small wild mammals
Lime disease	Endemic since the 1980's. Mainly present in northern/eastern regions with isolated foci elsewhere. Relatively few cases/year reported. Rising trend	Ixodides ticks *Ixodes ricinus*	Borreliosis *B. burgdorferi* s.l. *(B. afzelii)*	Zoo-anthroponosis Small/large wild mammals
Tick-borne encephalitis	Endemic, More affecting North-Eastern regions, with respect to Lime disease. Cases and trend presumably as above		Flavivirus TBE	Zoo-anthroponosis Wild and domestic rodents
Botonneuse fever (MSF)	Endemic, mainly in central/southern regions with minor cases elsewhere. Moving Northward. Apparently rising trend regions. About 1000 cases/year. Stable trend	*Ripicephalus sanguineus*	Rickettiosis *R. conorii*	Zoo-anthroponosis (dogs)

Table 2 | *Arthropod borne diseases endemic and emerging in Italy, and evaluation of the future events that could make possible the increase of their incidence and the possibility of introduction of other ABD in our country*

Disease	Cause of the event	Probability level
Visceral leishmaniasis (zoonosis)	Increase of temperature	**High:** risk of a further spreading northward **Moderate:** for increasing of incidence in the original endemic foci
Other leishmaniasis present in the Mediterranean basin	Increasing temperature and introduction of *L. tropica* and *L. major* and of their vectors	**None:** for *L. major* because of the lack of specific natural reservoir hosts (Gerbillidae rodents) **Very low:** for *L. tropica* (anthroponotic) because of limited distribution of the vector *(P. sergenti)*
Malaria	Introduction of gametocyte carrier (mainly of *P. vivax*) from endemic areas and introduction of alloctonous anopheline vectors	**Low:** nevertheless the occurrence of isolated cases of *P. vivax* in rural areas cannot be excluded **None:** for the establishment of tropical Anophelines because of their peculiar ecology
Sand flies fever	Climatic and environmental changes	**Low:** risk of expanding the area of endemy and increasing incidence
Chykungunya fever (anthroponosis)	Introduction of virus carriers from endemic areas	**Very high:** particularly in urban areas where the vector density is high and a late diagnosis of secondary autochtonous cases may occurs
West Nile encephalitis (zoonosis)	New introduction of infected reservoirs (migratory birds) and spreading of the virus by indigenous vectors	**Very high:** at risk all humid areas of the country, extensible to urban areas: the WNV is probably already going to become endemic
Dengue (anthroponosis)	Increasing of temperature Importation of both main vector and virus carriers	**High:** for the introduction of the main vector **Moderate:** for epidemics. Urban areas at major risk
Japanese encephalitis (zoonosis)	Introduction of the most competent vector *(Ae. japonicus)* and of the virus	**Moderate:** for he Introduction of the vector **Low to very low:** for virus introduction as well as for animal reservoirs
Rift Valley fever (zoonosis)	Increasing rainfall. Introduction of infected reservoirs (sheeps, domestic and wild mammals)	**Very, very low:** for the introduction, of the virus by human or animal reservoirs **Nevertheless:** it should be stressed that potential competent vectors are already part of our indigenous mosquito fauna
Dirofilariasis	Introduction of *Ae. albopictus* in the epidemiological cycle of the disease	**Moderate:** risk of diffusion in urban areas
Lime disease TBE	Heavy increasing of rainfall and of the mean temperature	**Very low:** risk of spreading southward **High:** increasing incidence in the existing foci
Rickettiosis	Increasing temperature	**High:** risk of moving northward and of increasing incidence in the existing foci

Zika Virus

Ann Ist Super Sanità 2010 | Vol. 46, No. 4: 436-443

Diagnosi differenziale

Features	Zika	Dengue	Chikungunya
Fever	++	+++	+++
Rash	+++	+	++
Conjunctivitis	++	-	-
Arthralgia	++	+	+++
Myalgia	+	++	+
Headache	+	++	++
Hemorrhage	-	++	-
Shock	-	+	-
Blood cell count	~or↓ plt/WBC	↓↓ plt/WBC (neutropenia)	↓ or ~ plt/WBC (lynphopenia)
Transaminases	~	↑	~

Courtesy Dr. Zammarchi

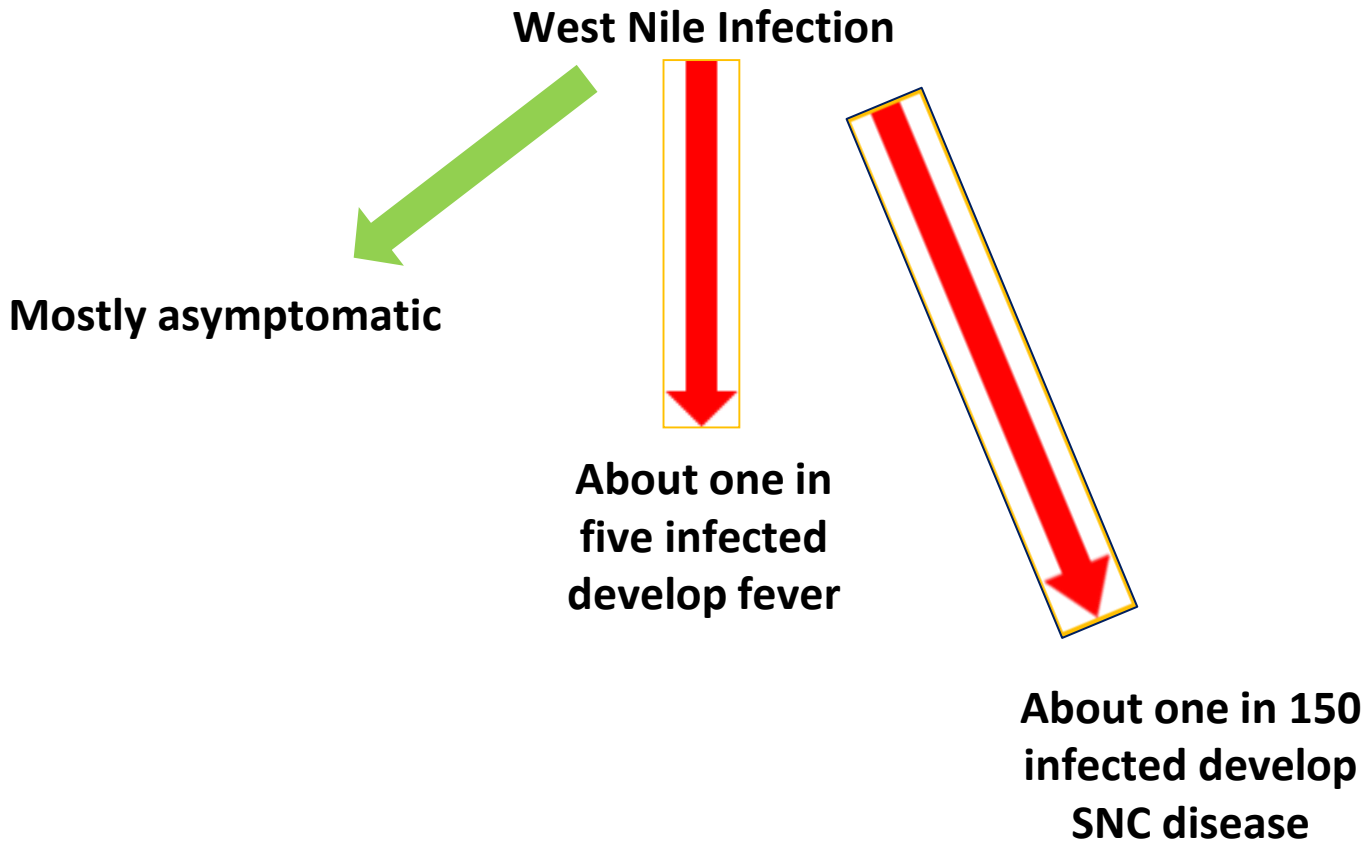
West Nile Virus

- WNV is transmitted in an enzootic cycle between birds by mosquitoes.
- Recent studies in the United States have demonstrated infection in at least 300 different bird species and 62 mosquito species.
- The family Corvidae (crow and blue jays) is particularly susceptible.

- Of the many mosquito species from which WNV has been isolated, Culex spp. appears to be important in the enzootic cycle, although the species varies by geographic location.
- In addition, at least 30 vertebrate species are infected, but they have insufficient viremia to infect a feeding mosquito and are considered "dead-end" hosts.

- Some, however, may have clinical infection (e.g., in humans).

- Viral transmission could occur by transplantation of infected organs, from infected blood products, transplacentally, and, possibly, through breast milk.



In New York, Romania, and Israel, the risk for neurologic disease increased with age, which may explain, in part, the different epidemiologic patterns seen in parts of Africa.

In Egypt and South Africa neurologic disease is rare.

Although immunosenescence affecting innate and/or adaptive immune responses is a likely scenario, other observations indicate roles for functional or structural CNS changes that facilitate neuroinvasion.

WNV- Clinical manifestation

- **Neurologic disease** occurs in less than 1% of infected individuals. Patients **typically have a febrile prodrome of 1 to 7 days**, which may be biphasic, before developing neurologic symptoms.
- In recent outbreaks, approximately two thirds of hospitalized patients had encephalitis and one third had meningitis.
- **Acute flaccid paralysis** caused by virus infection of the anterior horn of the spinal cord (myelitis) has been recognized in recent outbreaks.
- The clinical picture **suggests poliomyelitis**; paralysis is frequently asymmetrical and may or may not be associated with meningoencephalitis.

WNV- Clinical manifestation

- Other neurologic features include
- cranial neuropathies,
- optic neuritis,
- ataxia.
- Stiffness, rigidity, spasms, bradykinesia, and tremors, **associated with basal ganglia damage**, have also recently been recognized in WNE

WNV- Clinical manifestation

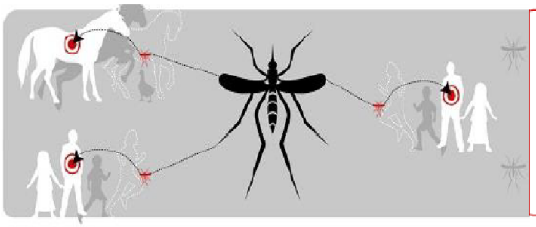
- In recent outbreaks, **overall case-fatality rates for hospitalized patients ranged from 4% to 14% but were higher in older patients.**
- Other risk factors for death include
- the presence of profound weakness,
- deep coma,
- failure to produce IgM antibody,
- impaired immunity,
- coexisting illness such as hypertension or diabetes mellitus.
- Neurologic sequelae are common among survivors. **In one study, half of hospitalized patients still had a functional deficit at discharge and only one third had recovered fully by 1 year.**
- ***IgG is the predominant antibody most likely confering long-term immunity against WNV re-infection. Although not enough data exists, immunity against WNV in convalescent patients is presumed to be life-long.***

WNV- Diagnosis

- **PCR in serum, CSF, urine**
- **Serology in serum and CSF**
- **(Serum IgM in some WNV patients persist for longer than 16 months, potentially limiting the specificity of tests,**

  CROSS REACTIVITY among flaviviruses and

  recent vaccination against Yellow Fever and Japanese Encephalitis virus).
- **Culture**



Sorveglianza integrata del West Nile e Usutu virus

Bollettino N. 18 del 15 novembre 2018
RISULTATI NAZIONALI

577 CASI

68 casi in donazioni di sangue

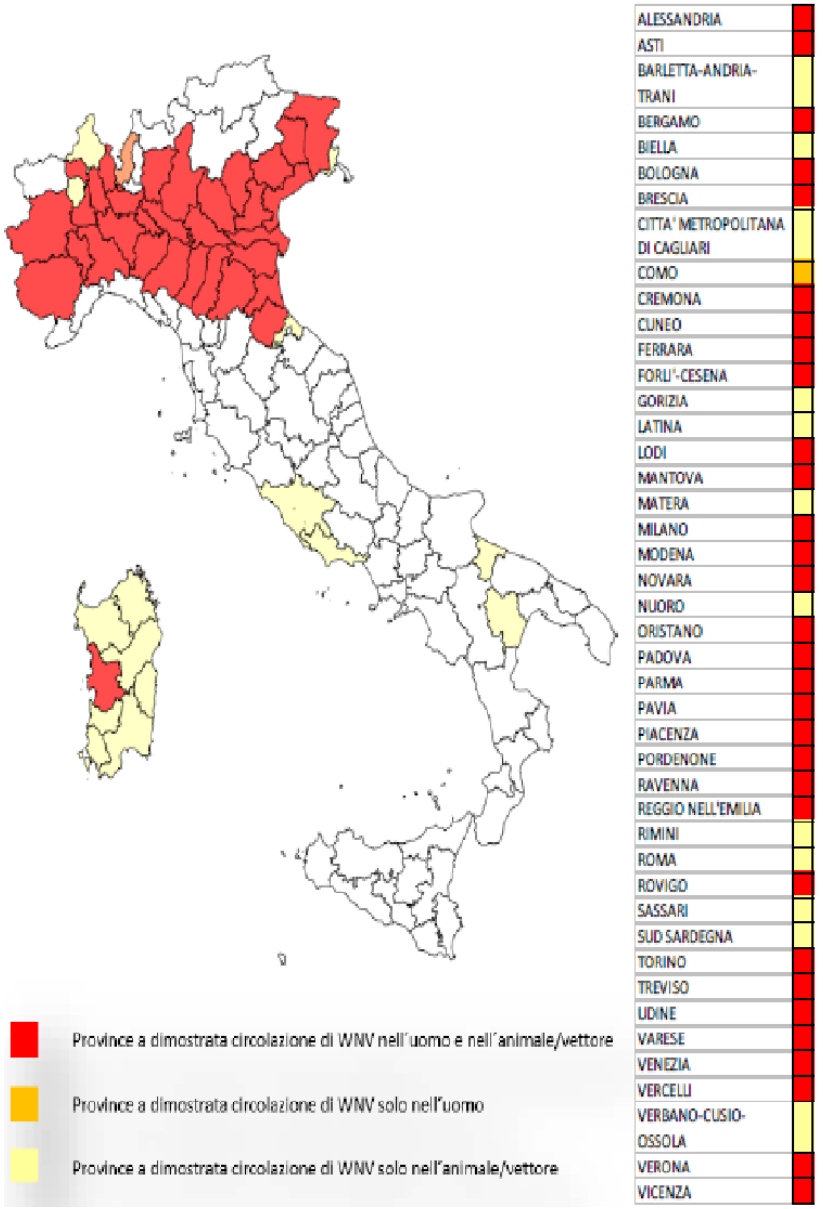
230 forme neuroinvasive, 100 in E-R

42 decessi

Verosimili cause:

- Primavera calda e piovosa
- Maggiore quantità di zanzara Culex
- Proporzione maggiore di zanzare infette per WNV
- Proporzione maggiore di uccelli morti positivi per WNV

Figura 1. *Province con dimostrata circolazione di WNV in vettori, animali e uomo (donatori asintomatici, febbri e casi neuroinvasivi confermati)*



Increase of West Nile virus cases in Europe for 2018

Burki T. *Lancet* 2018 Sep 22;392(10152):1000

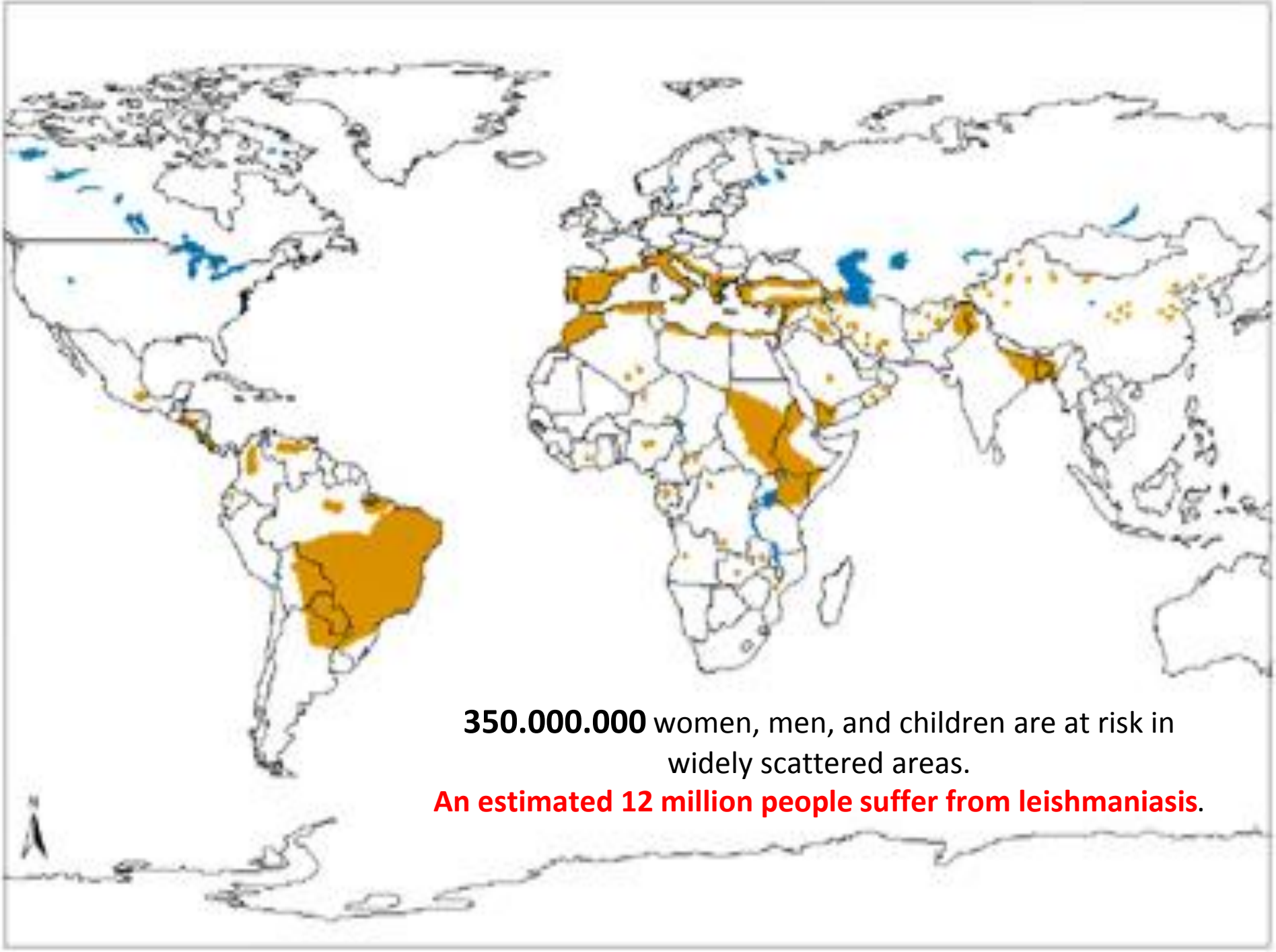
This year's spike in European cases could be down to the unusually hot summer.

- **Mosquitoes breed more rapidly** in higher temperatures and they tend to be more energetic.
- Warm weather also **speeds up the replication of the virus.**
- People spend more time outsider
- This year, **West Nile virus was found to be circulating** among mosquitoes and birds **in Italy several weeks earlier than in previous seasons**.
- **The possibility of a more pathogenic virus cannot yet be ruled out.**

Visceral Leishmaniasis

- The leishmaniases are widely distributed across the tropical, subtropical, and temperate regions in 88 countries, 72 of which are in developing areas of the world.

- In 2014, more than 90% of new cases reported to WHO occurred in six countries: Brazil, India, Ethiopia, Somalia, South Sudan and Sudan.



350.000.000 women, men, and children are at risk in widely scattered areas.

An estimated 12 million people suffer from leishmaniasis.

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- **In the WHO South-East Asia Region, the kala-azar elimination programme is progressing satisfactorily**, and countries such as Bangladesh that reported more than 9000 cases in 2006 reported an average of some 600 news cases in 2014–2015.

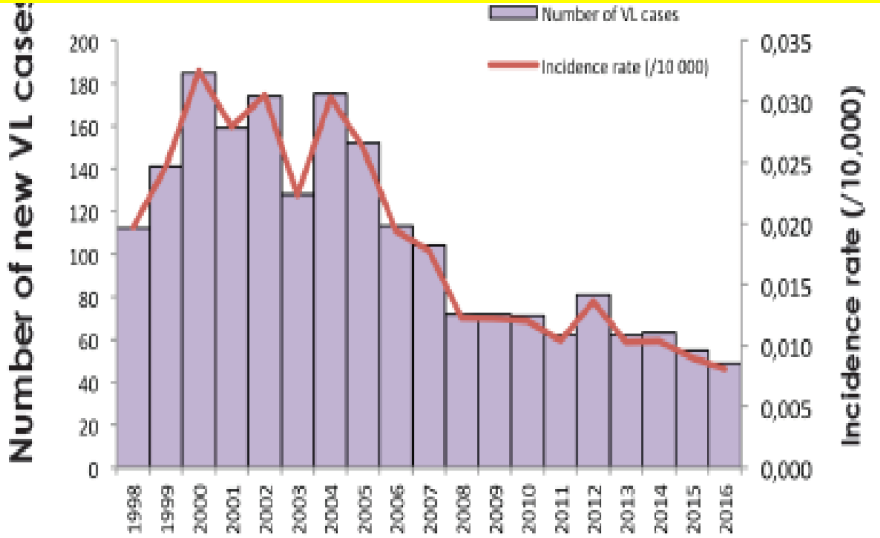
Visceral Leishmaniasis in Italy

- Italy is **endemic** for **visceral leishmaniasis** and **cutaneous leishmaniasis**.
- Transmission occurs by *L. infantum*.
- VL focus is zoonotic in nature and domestic dogs and wild canines serve as reservoir hosts, bringing the infection close to humans.
- Between 1998 and 2016, about 2030 VL cases have been reported.

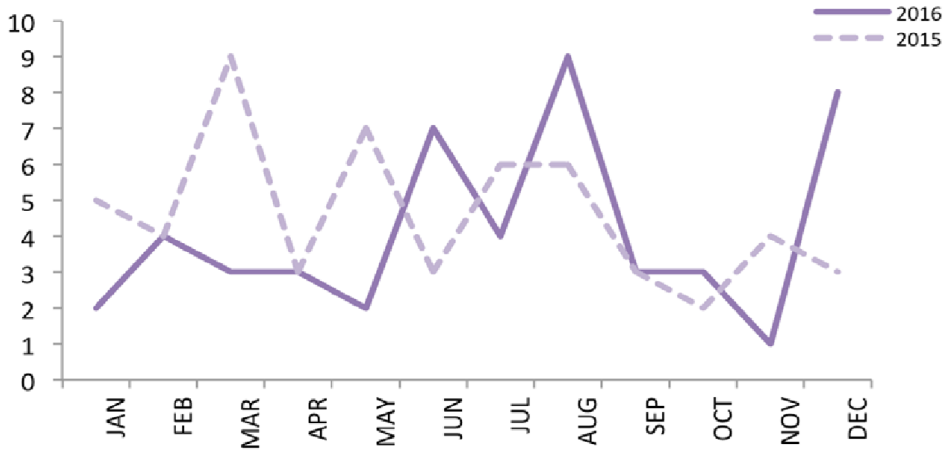
- About 807 CL cases were reported during the same period.

Visceral Leishmaniasis in Italy

Incidence rate/10,000 (at the national level) and number of new cases from 1998 to 2016



Monthly distribution of new cases (January-December)



Disease distribution of new VL cases at province level per 10,000 population (2016)

Visceral Leishmaniasis

is a spectrum of symptoms and findings

At the other end are those with classic VL (kala-azar), who present with a characteristic pentad of prolonged fever, weight loss, hepatosplenomegaly, pancytopenia, and hypergammaglobulinemia

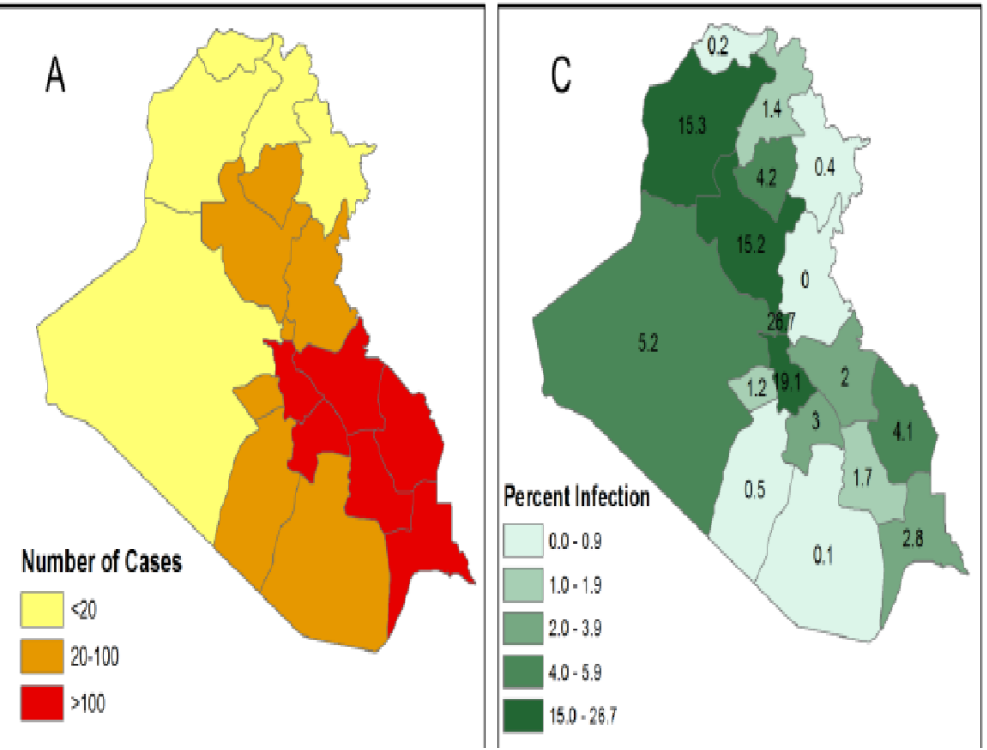
high positive rate of asymptomatic carrier (20% to 25% in India and 14% in Brazil).

At one extreme are persons with asymptomatic, inapparent, or self-resolving infections

Asymptomatic Visceral Leishmania infantum Infection in U.S. Soldiers Deployed to Iraq

Rupal M. Mody, et al. *Clin Infect Dis*. 2018 Sep 20. [Epub ahead of print]

Methods: Healthy soldiers exposed to VL endemic areas in Iraq and 50 controls who never traveled to endemic regions were recruited through military healthcare facilities (2015-17). Blood samples were obtained.
Leishmania research diagnostics utilized included ELISA, rk39 test strips, quantitative PCR, and interferon gamma release (IGRA) assays.



Results: 200 deployed subjects were enrolled.
Vector exposure was high, 64%.
Prevalence of AVL (any positive test result) was 39/200 (19.5%, 95% CI 14.4%-25.8%).
No subjects had positive rK39 test results.
Two (1.0%) PCR, ten (5%) ELISA, and **28 (14%) IGRA samples were positive**.
Travel to Ninewa governorate increased risk for AVL (p=0.01).

Visceral Leishmaniasis

- **VL has also emerged as an important opportunistic** disease in persons with
- **AIDS**
- **persons who have had organ transplants**,
- **impairment of cell-mediated immunity.**

- **Immunocompromised are at increased risk of asymptomatic parasitemia and developing progressive disease**.
- **Malnutrition has long been recognized as a risk factor for progression of infection to disease**.

- Persons with self-**resolving infection** with *L. donovani* or *L. infantum/L. chagasi* and those who have undergone successful chemotherapy **develop protective immune responses, but**
- **VL disease can develop years later if the infected person becomes immunocompromised**

Risk factors, clinical features and outcomes of visceral leishmaniasis in solid-organ transplant recipients: a retrospective multicenter case–control study

W. Clemente, et al. *Clin Microbiol Infect* 2015; 21: 89–95

This multicenter, matched case–control study (1:2 ratio) was designed to determine the risk factors, clinical features and outcomes of VL among this population. Control and case subjects were matched by center, transplant type and timing.

TABLE I. Frequency of VL in solid-organ transplant recipients at ten Spanish and two Brazilian hospitals

	Total		Spain		Brazil		
Transplant	Cases per total transplants	% (95% CI)	Cases per total transplants	% (95% CI)	Cases per total transplants	% (95% CI)	RR (95% CI)[a], p
Kidney	25/12 895	0.2% (0.2–0.3)	15/11 819	0.1% (0.1–0.2)	10/1076	0.9% (0.5–1.6)	7.4 (3.1–17.4), <0.001
Liver	4/8681	0.05% (0.01–0.1)	1/7360	0.01% (0.0–0.1)	3/1321	0.2% (0.1–0.6)	16.1 (1.57–99.9), 0.01
Heart	6/2669	0.2% (0.1–0.5)	5/2535	0.2% (0.1–0.4)	1/134	0.7 (0.04–3.6)	0.3 (0.03–6.0), 0.27
Lung	1/894	0.1% (0.00–0.5)	1/877	0.1% (0.0–0.6)	0/17	—	—
All	36/25 139	0.1% (0.1–0.2)	22/22 591	0.1% (0.1–0.2)	14/2548	0.5% (0.3–0.9)	5.7 (2.7–11.6), <0.001

Relapses occurred in 25.7% of cases, and the crude mortality rate was 2.8%.

Single-Dose Liposomal Amphotericin B for Visceral Leishmaniasis in India

Shyam Sundar, Jaya Chakravarty, Dipti Agarwal, Madhukar Rain and Henry W. Murray *N Engl J Med* 2010;362:504-12.

Methods. In this open-label study, we randomly assigned 412 patients in a 3:1 ratio to receive either liposomal amphotericin B or amphotericin B deoxycholate.
L-AMB at a dose of 10 mg per kilogram of body weight was given once, and patients were discharged home 24 hours later.
Amphotericin B deoxycholate, which was administered in 15 infusions of 1 mg per kilogram, was given every other day during a 29-day hospitalization.
Cure rate 6 months after treatment was determined.

Variable	Liposomal Amphotericin B (N=304)	Amphotericin B Deoxycholate (N=108)
Removed from study — no.	0	2
Completed treatment — no.	304	106
Apparent cure at day 30 — no.	304	106
Relapse — no. (%)*	13 (4.3)	2 (1.9)
Lost to follow-up — no.	0	0
Definitive cure at 6 mo†		
Intention-to-treat population		
No. of patients	291	104
Percent (95% CI)	95.7 (93.4–97.9)	96.3 (92.6–99.9)
Per-protocol population‡		
No. of patients	291	104
Percent (95% CI)	95.7 (93.4–97.9)	98.1 (95.5–100.0)

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Table 4. Adverse Events.*

Event	Liposomal Amphotericin B (N=304)		Amphotericin B Deoxycholate (N=108)		P Value†
	Day 1–2	Day 30	During Treatment	Day 30‡	
	no. of patients (%)				
Infusion-related fever or rigors	121 (40)	0	69 (64)	0	<0.001
Increased anemia	6 (2)	4 (1)	21 (19)	18 (17)	<0.001
Increased thrombocytopenia	5 (2)	0	2 (2)	0	NS
Nephrotoxicity	2 (1)	0	1 (1)	0	NS
Hypokalemia	0	0	2 (2)	0	0.02
Hepatotoxicity	2 (1)	1 (<1)	0	1 (1)	NS

Single-Dose Indigenous Liposomal Amphotericin B in the Treatment of Indian Visceral Leishmaniasis: A Phase 2 Study

Shyam Sundar, Anup Singh, Madhukar Rai, and Jaya Chakravarty ***Am. J. Trop. Med. Hyg.*, 92(3), 2015, pp. 513–517**

A higher-dose regimen of an indigenously manufactured liposomal amphotericin B was intended to improve the efficacy in terms of long-lasting cure rate. 60 patients were enrolled. Subjects in cohort I were administered one dose (10 mg/kg body weight) of L-AmBL. Subjects in cohort II received one infusion of an escalated dose (15 mg/kg body weight). The **safety** of these two doses was evaluated over a period of 30 days, and **efficacy** was assessed for initial cure **at day 30** and **definitive cure at 6 months**.

Hematological and biochemical parameters of two treatment groups

	Group I ($N = 15$)			Group II ($N = 15$)		
	Baseline test mean (SD)	At 30 days test mean (SD)	*P* value	Baseline test mean (SD)	At 30 days test mean (SD)	*P* value
Age (years)	26.1 (10.52)			29 (11.14)		
Male sex *n* (%)	7 (46.7)			8 (53.3)		
Weight (kg)	38.9 (6.69)	42.1 (6.45)	0.002	38.9 (6.69)	42.1 (6.45)	< 0.001
Spleen (cm below costal margin)	4.1 (2.09)	0.2 (0.41)	< 0.001	4.3 (2.89)	0.5 (0.99)	< 0.001
Hemoglobin (g/dL)	7.88 (1.119)	9.65 (0.988)	< 0.001	8.43 (1.796)	9.47 (1.124)	0.020
Platelets (/μL)	112,266.7 (45,857.65)	247,133.3 (56,496.35)	< 0.001	130,466.7 (46,321.65)	226,666.7 (71,454.95)	0.001
White blood cells (/μL)	3,213.3 (1,247.78)	7,726.7 (2,528.54)	< 0.001	3,053.3 (1,779.19)	6,406.7 (1,211.53)	< 0.001
Alanine aminotransferase (ALT; IU/mL)	27.1 (10.26)	32.2 (10.99)	0.258	43.8 (28.75)	30.1 (12.97)	0.070
Aspartate aminotransferase (AST; IU/mL)	62.5 (26.44)	52.3 (15.34)	0.383	70.5 (26.95)	44.6 (15.1)	0.004
BUN (mg/dL)	8.97 (2.399)	10.53 (2.801)	0.038	9.49 (3.157)	12.26 (4.179)	0.079
Creatinine (mg/dL)	0.742 (0.1147)	0.704 (0.1541)	0.423	0.776 (0.1418)	0.784 (0.1504)	0.842

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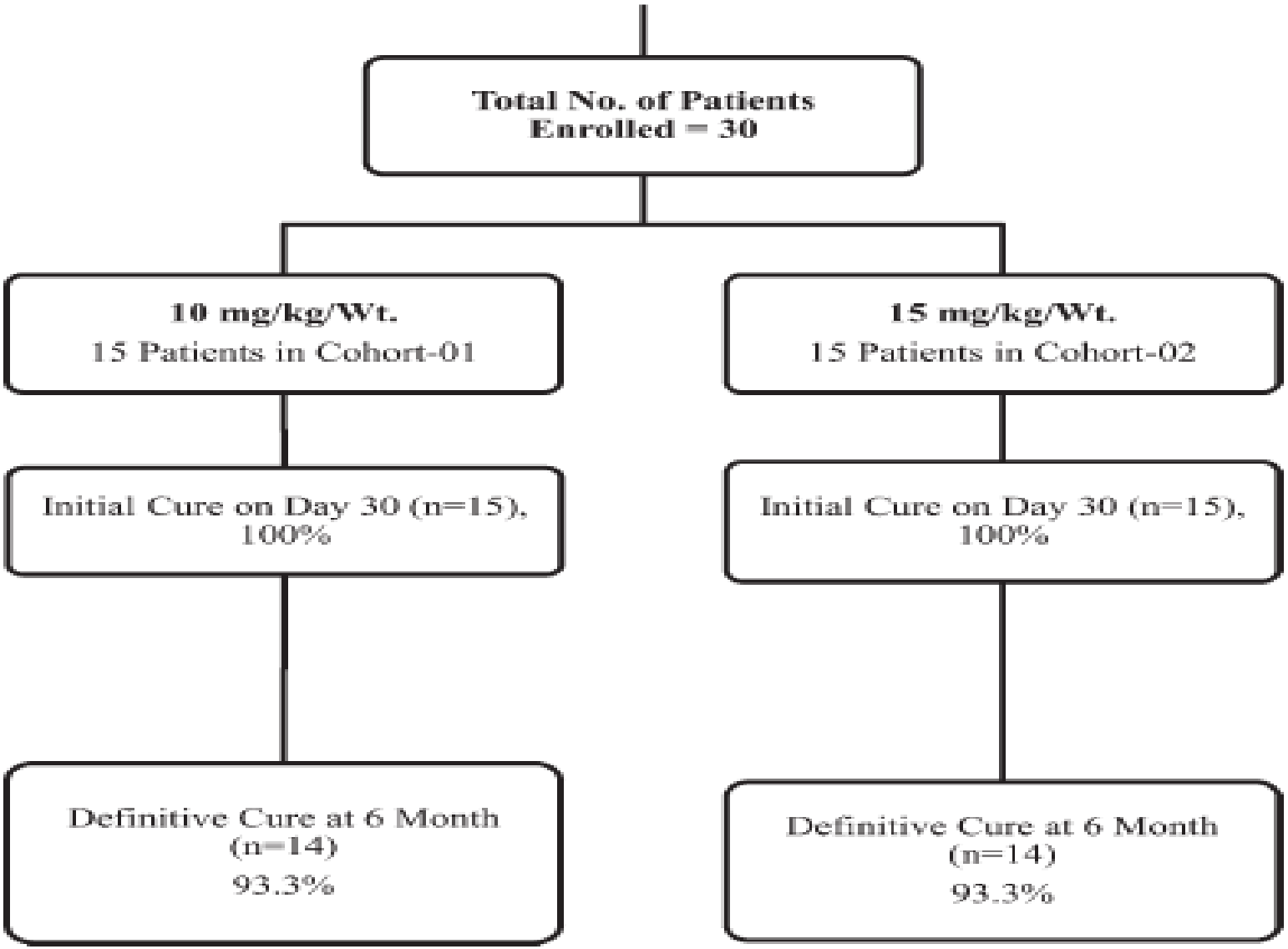
Shyam Sundar, Anup Singh, Madhukar Rai, and Jaya Chakravarty ***Am. J. Trop. Med. Hyg.*, 92(3), 2015, pp. 513–517**



Efficacy and Safety of Liposomal Amphotericin B for Visceral Leishmaniasis in Children and Adolescents at a Tertiary Care Center in Bihar, India

Krishna Pandey, et al. *Am. J. Trop. Med. Hyg.*, 97(5), 2017, pp. 1498–1502

A total of 100 parasitologically confirmed visceral leishmaniasis patients aged < 15 years were included in this study. They were administered one dose intravenous infusion of liposomal amphptericin B at 10 mg/kg body weight. Efficacy was assessed as initial and final cure at 1 and 6 months, respectively, and safety of all participants who were recruited in the study.

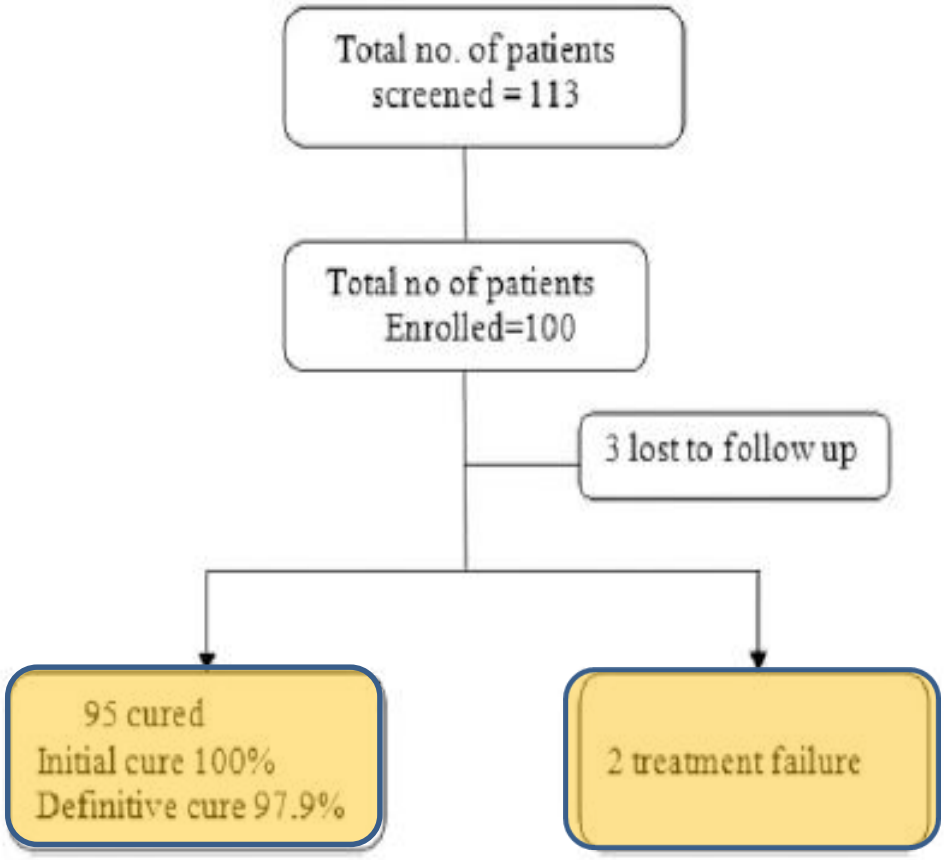


TABLE 3
Summary of adverse events (AEs)

Adverse events (N = 40)	Frequency (%)	CTC Grade
Gastrointestinal		
Abdominal distension	2 (5)	1
Abdominal pain	4 (10)	1
Vomiting	3 (7.5)	1
Elevation of hepatic enzymes (ALT/AST)	8 (20)	1
Blood		
Eosinophilia	2 (5)	2
Infusion related reaction		
Chills and Rigor	18 (45)	1
Muscle-skeletal system		
Back pain	2 (5)	1
Others		
Swelling of face	1 (2.5)	1

ALT = alanine aminotransferase; AST = aspartate aminotransferase.

None of the patients experienced any serious AEs.

No patients developed nephrotoxicity

Quaderni della Società Italiana di
MEDICINA TROPICALE e SALUTE GLOBALE

TERAPIA

Leishmaniosi viscerale

A) Trattamento di prima scelta

1) Amfotericina B liposomiale (L-AmB, AmBisome®): è consigliata un'infusione di soluzione salina prima della somministrazione del farmaco

- pazienti immunocompetenti: 3 mg/Kg/die, ev (giorni 1-5, 14 e 21; tot max 21 mg/kg). E' risultato efficace l'utilizzo di 10 mg/kg in dose unica per il trattamento di VL da *L. donovani*
- pazienti immunocompromessi: 4-5 mg/Kg/die, ev (giorni 1-10, 17, 24, 31, 38; tot max 40 mg/kg)

2) *Miltefosina* (Impavido®, cp da 50 mg, non in commercio in Italia): 2.5 mg/Kg/die (max 150 mg/die) per os per 28 giorni. Unico farmaco attualmente disponibile per os, si è dimostrato efficace in forme di LV da *L. donovani* (Indiana) anche resistenti agli antimoniali. Gravato da una tossicità limitata (vomito, diarrea, epato- e nefrotossicità), presenta tuttavia una potenziale teratogenicità (classe X), per cui sono da evitare gravidanze durante il trattamento e per i 2 mesi successivi. La lunga emivita lo pone a rischio di ingenerare resistenze, quando usato in monoterapia.

Diagnosis and Treatment of Leishmaniasis: Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA) and the American Society of Tropical Medicine and Hygiene (ASTMH)

Naomi Aronson, et al. *Clinical Infectious Diseases* 2016;63(12):e202–64

Treatment of visceral leishmaniasis

Tipologia paziente	Molecola	Dosaggio	Grado
Immunocompetente in Nord America, India (*L. donovani, L. infantum-chagasi*)	L-AMB	3 mg/kg/die, day 1-5, 14, 21 (tot 21 mg/kg)	*Strong, high*
Immunocompetente in East Africa	L-AMB	(tot 40 mg/kg or more)	
Immunocompetente in India (*L. donovani*)	Miltefosina (**alternativa a L-AMB)**	2,5 mg/kg/die for 28 days	*Strong, moderate*
Immunocompetente, recidiva	Incrementare dosaggi e durata L-AMB		

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Tipologia paziente	Molecola	Dosaggio	Grado
VL in immunodepressi, compresi HIV	L-AMB	4 mg/kg/die, day 1-5, 10, 17, 24, 31, 38 (tot 40 mg/kg)	*Strong, low*
Immunodepresso, recidiva	L-AMB + Miltefosina	Efficacia e durata ottimale non note	*Weak, very low*
HIV (CD4+ < 200/mmc)	Profilassi secondaria		*Strong, moderate*

Routine serologic screening of organ donors from leishmaniasis- endemic areas is not recommended.

If an available **donor** is known to be **seropositive,** it is advisable to perform **clinical and laboratory monitoring of the recipien**t in the posttransplant period rather than to reject the organ for transplant (strong, low).

We suggest that **clinicians not routinely perform diagnostic testing to assess persons for evidence of asymptomatic visceral infection*, including persons at epidemiological risk and are considering organ transplantation or initiation of therapy with biologic immunomodulating agents***. **Neither preemptive treatment nor primary prophylaxis for VL in asymptomatically infected persons is suggested (weak, very low).**