

# Layışmanyoz Gözden kaçıyor mu? Tanısı ve tedavisi zor mu?

Dr.A.Seza İnal  
Çukurova Üniversitesi Tıp Fakültesi  
Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji  
A B D

# Layışmanyoz

Alem : Protista

Altalem : Protozoa

Filum : Sarcomastigophora

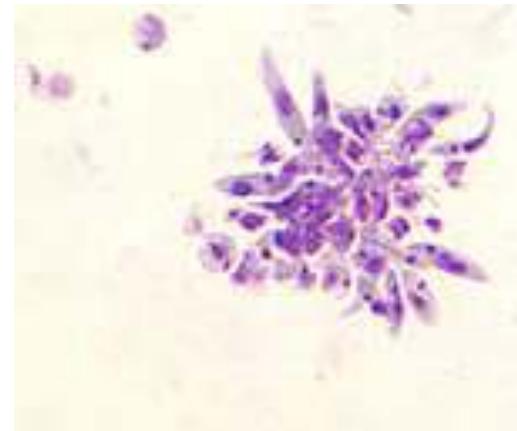
Sınıf : Zoomastigophora

Takım : Kinetoplastida

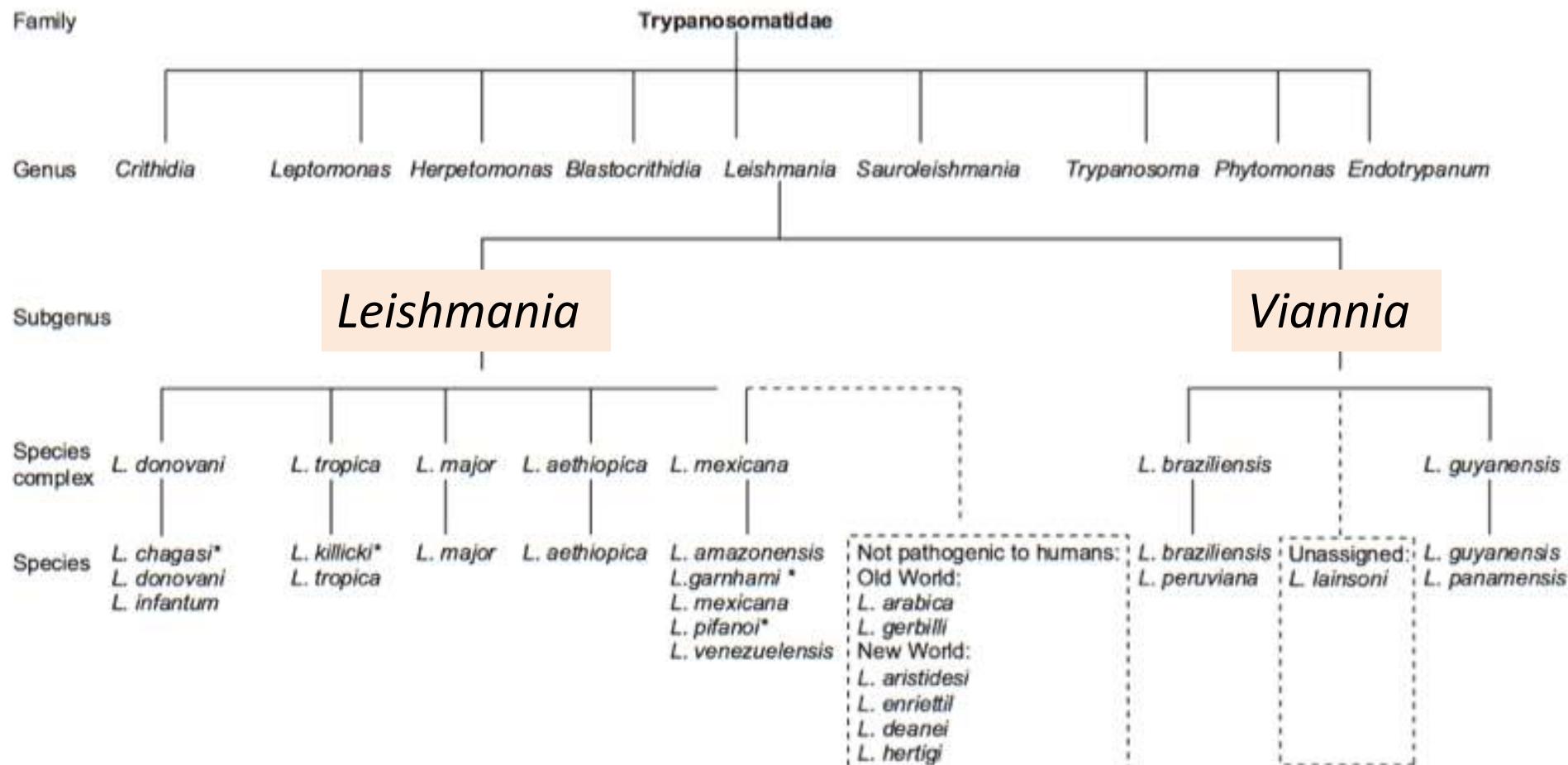
Familya : Trypanosomatidae

Genus : *Leishmania*

Türler : *donovani, tropica, mexicana, brasiliensis*



# Leishmania Taksonomisi



\*Species status is under discussion. *L. chagasi* in the New World is the same species than *L. infantum*

WHO Leishmaniases 2010

# *Leishmania spp*

- İnsanlarda hastalık yapan > 21 tür

## Vektörleri

- *Phlebotomus*
- *Lutzomyia*



Subgenus	<i>L. (Leishmania)</i>	<i>L. (Leishmania)</i>	<i>L. (Viannia)</i>	<i>L. (Viannia)</i>
Old World	<i>L. donovani</i> <i>L. infantum</i>	<i>L. major</i> <i>L. tropica</i> <i>L. killicki</i> <i>L. aethiopica</i> <i>L. infantum</i>		
New World	<i>L. infantum</i>	<i>L. infantum</i> <i>L. mexicana</i> <i>L. pifanoi</i> <i>L. venezuelensis</i> <i>L. garnhami</i> <sup>b</sup> <i>L. amazonensis</i>	<i>L. braziliensis</i> <i>L. guyanensis</i> <i>L. panamensis</i> <i>L. shawi</i> <i>L. naiffi</i> <i>L. lainsoni</i> <i>L. lindenbergi</i> <i>L. peruviana</i> <i>L. colombiensis</i> <sup>a</sup>	<i>L. braziliensis</i> <i>L. panamensis</i>
Principal tropism	Viscerotrophic	Dermotropic	Dermotropic	Mucotropic

<sup>a</sup> Species status is under discussion

<sup>b</sup> Taxonomic position is under discussion

# Layışmanyoz

- Visseral
- Kutanöz
- Mukokutanöz
- Postkalaazar dermal



# Layşmanyoz Endemik



# Layışmanyoz Epidemiyoloji

- 5 kıtada
- 102 ülke bildirmiş- 88 endemik
  - 65 → VL + KL
- 2007-2011

	KL Olgı/yıl	VL Olgı/yıl
	220.000	58.000
Tahmin	700.000-1.200.000	200.000-400.000

20.000-40.000 ölüm /yıl

Alvar PLoS ONE 2012

Salam PLoS Neglected Trop Dis 2014

# Layışmanyoz Epidemiyoloji

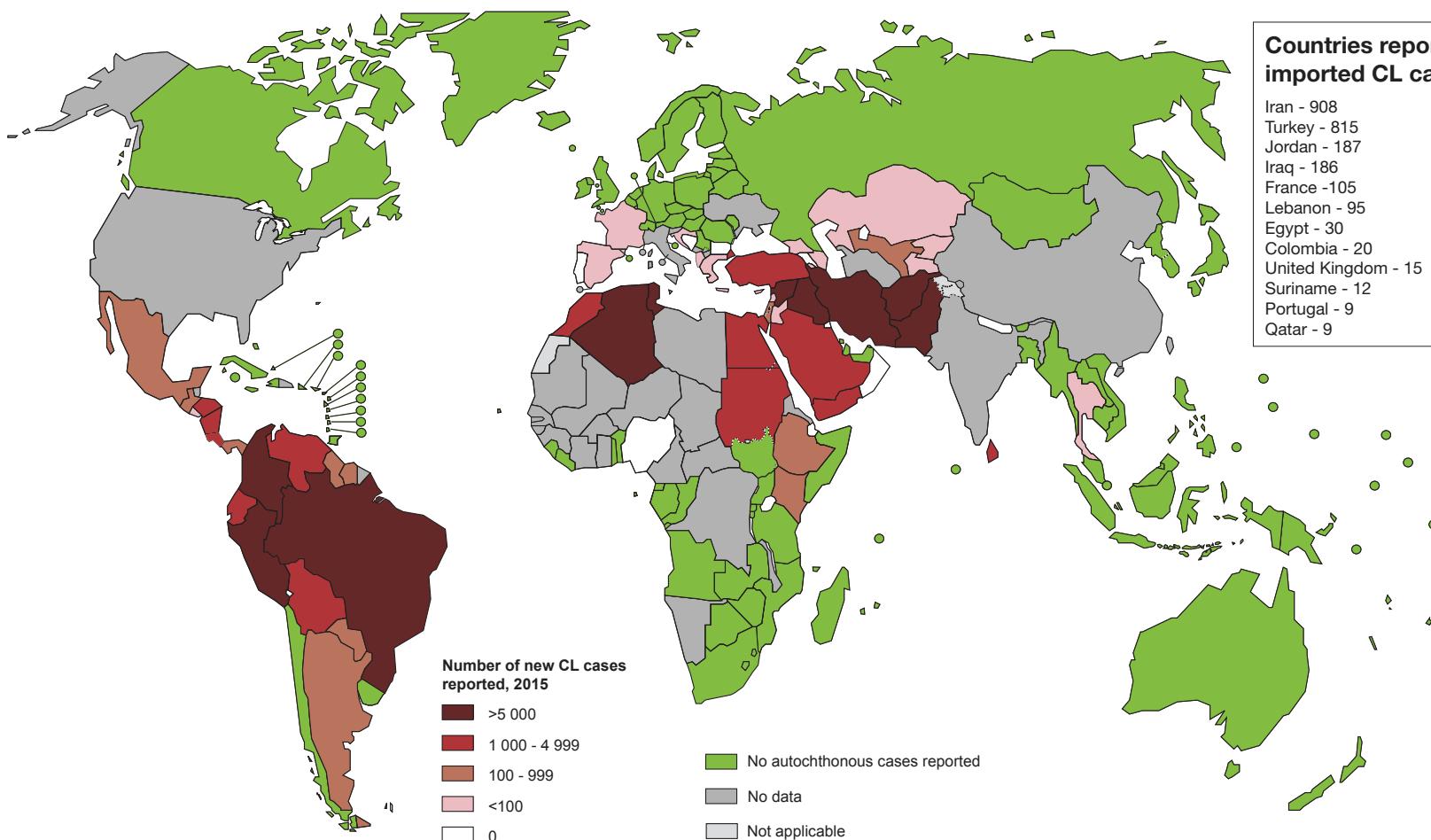
VL

- Olgularının %90'ı 6 ülke
  - Bangladeş
  - Brezilya
  - Etiyopya
  - Hindistan
  - Güney Sudan
  - Sudan

KL

- Olguların %70'i 10 ülke
  - Afganistan
  - Etiyopya
  - Suriye Halk Cumhuriyeti
  - İran İslam Cumhuriyeti
  - Cezayir
  - Sudan
  - Brezilya
  - Kolombiya
  - Kosta Rika
  - Peru

# Kutanöz Layışmanyoz Epidemiyoloji



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2017. All rights reserved

Data Source: World Health Organization  
Map Production: Control of Neglected  
Tropical Diseases (NTD)  
World Health Organization



## Countries reporting imported CL cases

Iran - 908	Kuwait - 7
Turkey - 815	Paraguay - 4
Jordan - 187	Venezuela - 4
Iraq - 186	Argentina - 3
France - 105	Belarus - 2
Lebanon - 95	Bulgaria - 2
Egypt - 30	Greece - 2
Colombia - 20	Russian Federation - 2
United Kingdom - 15	Czech Republic - 1
Suriname - 12	Mexico - 1
Portugal - 9	Thailand - 1
Qatar - 9	

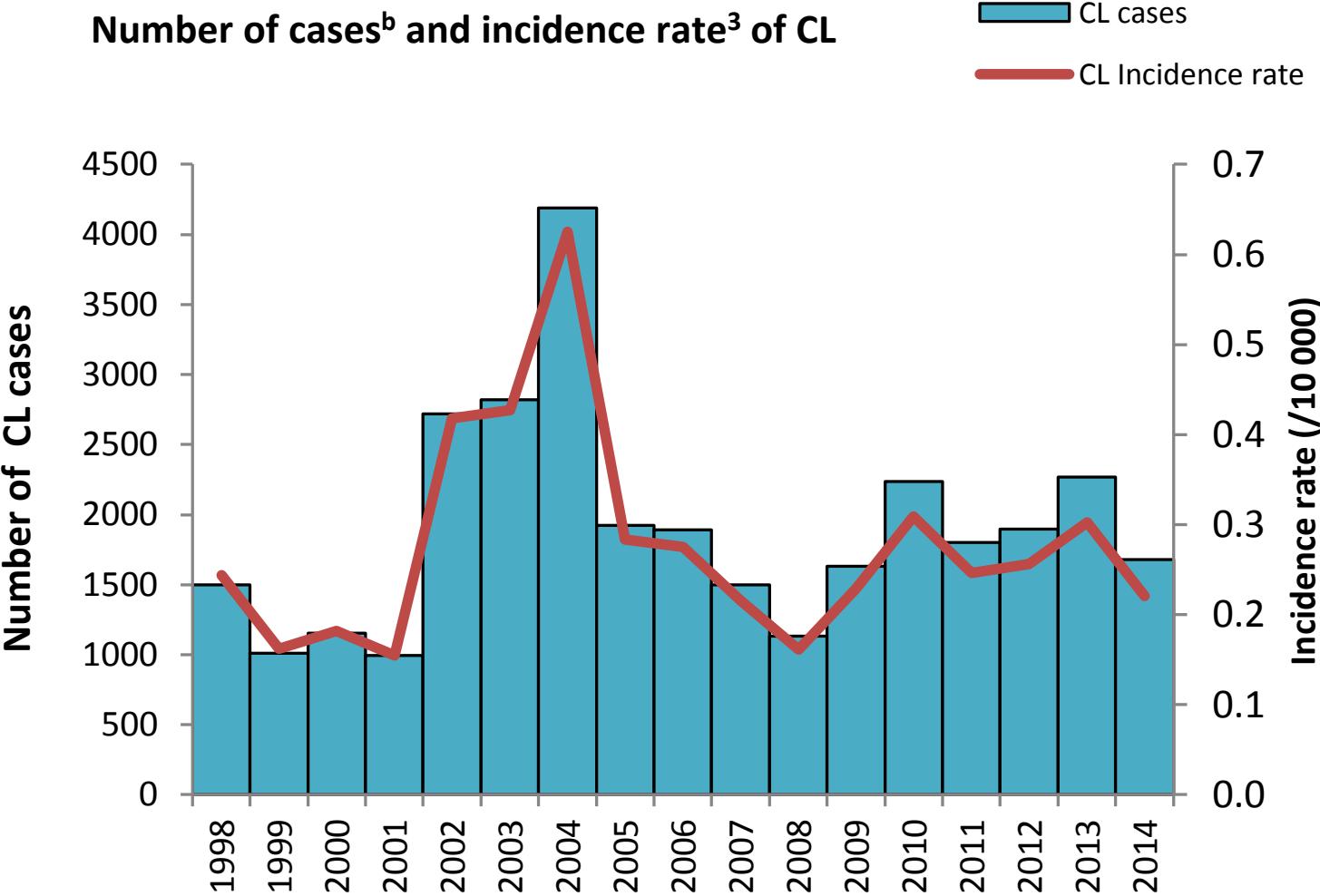
## Leishmaniasis

## TURKEY

2014

*Published in July 2016*

Country General Information (WHO, 2013)



Leishmaniasis

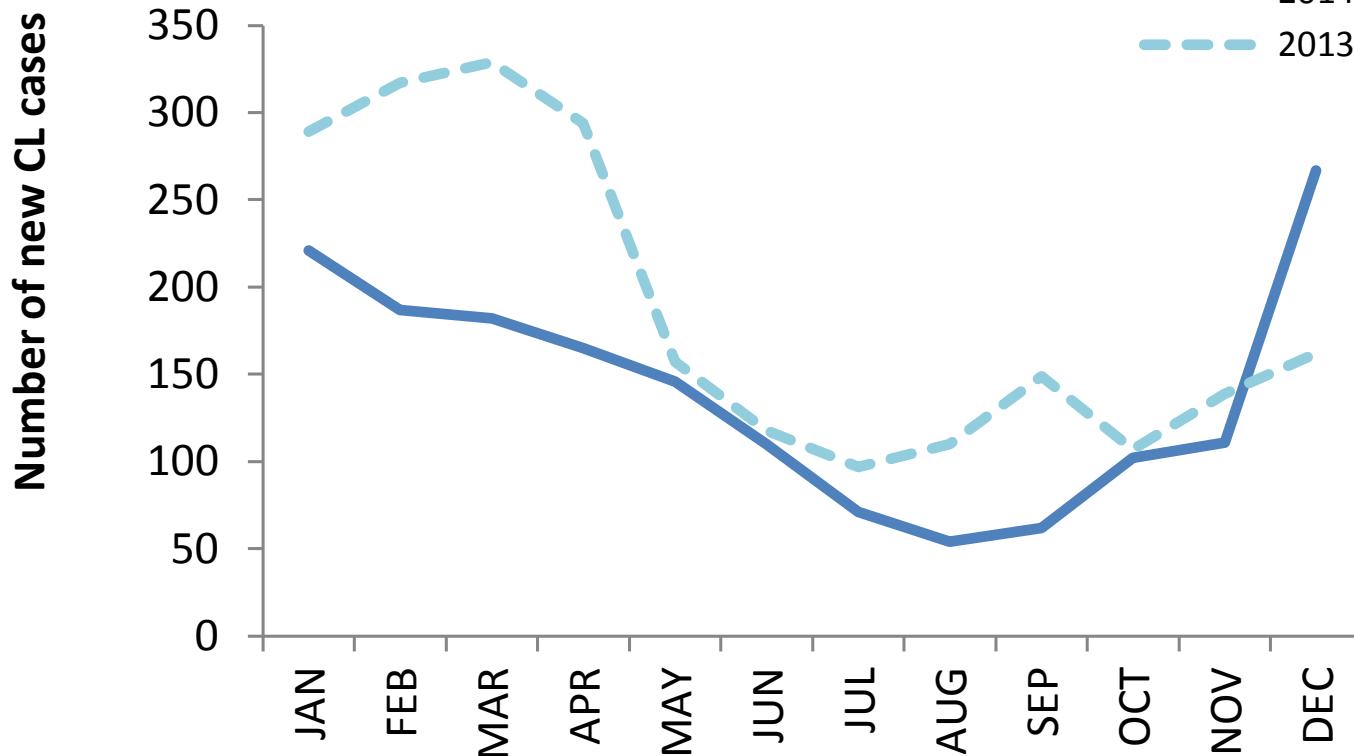
TURKEY

2014

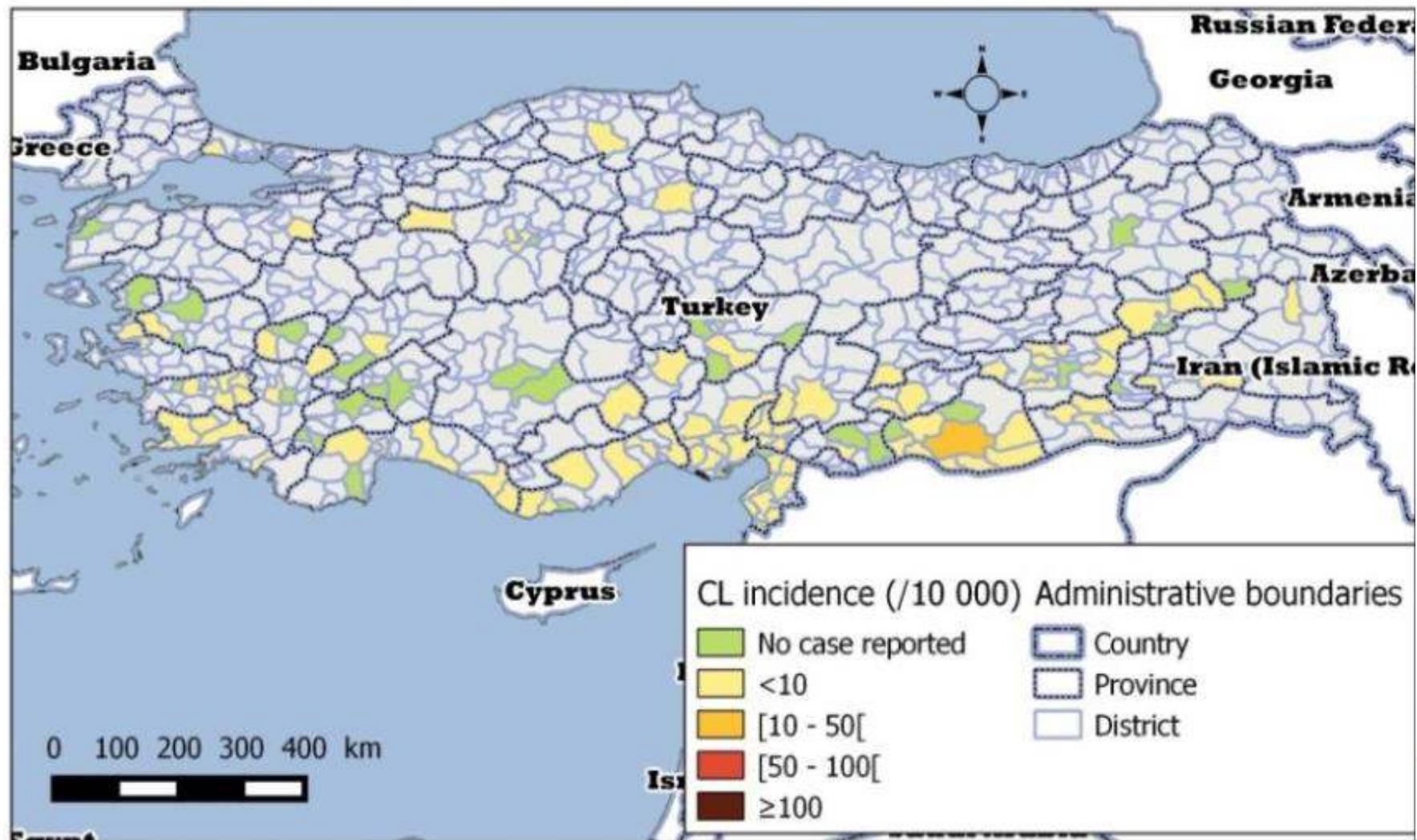
Published in July 2016

Country General Information (WHO, 2013)

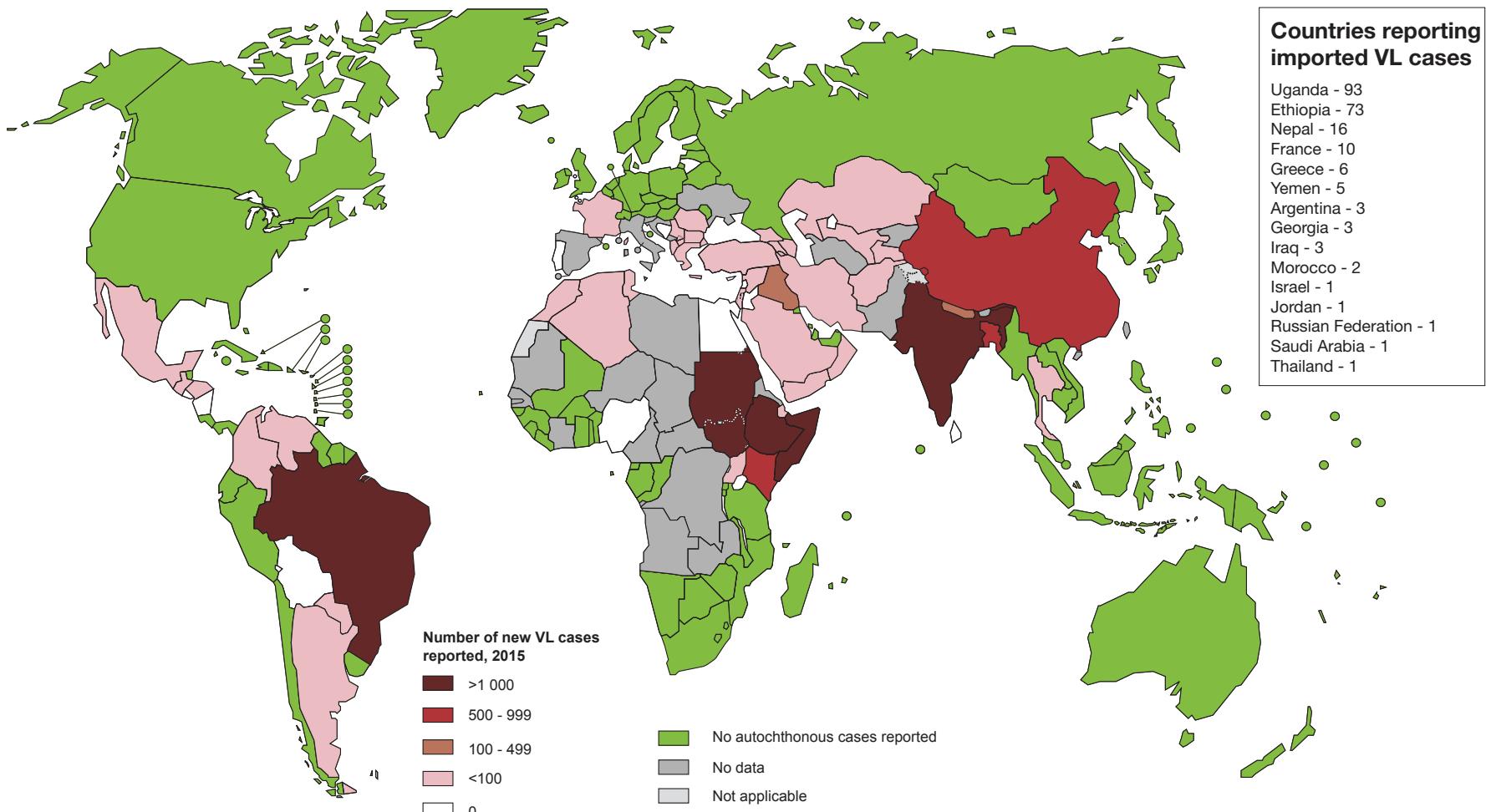
## Number of new CL cases reported by month in 2013 and 2014



## Incidence of CL in Turkey in 2014 at district level per 10 000 population



# Visseral Layışmanyoz Epidemiyoloji



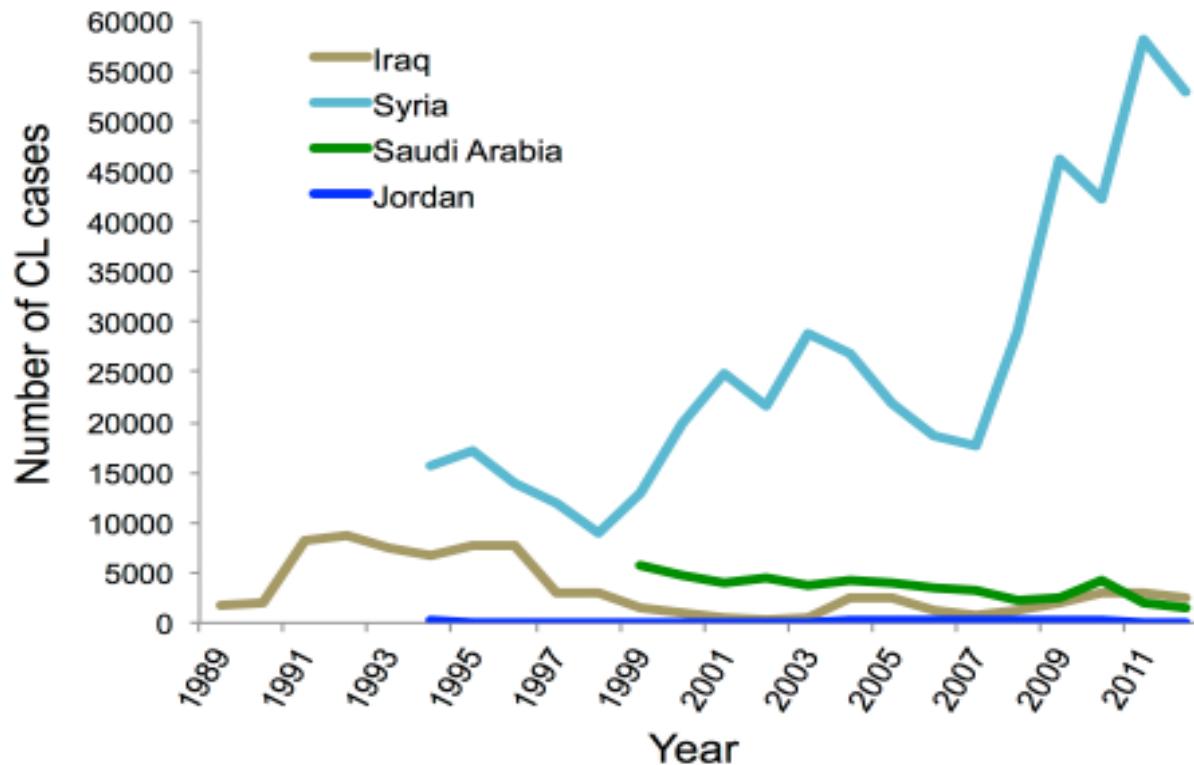
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2017. All rights reserved.

Data Source: World Health Organization  
Map Production: Control of Neglected Tropical Diseases (NTD)  
World Health Organization



## Review

# Leishmaniasis in the Middle East: Incidence and Epidemiology



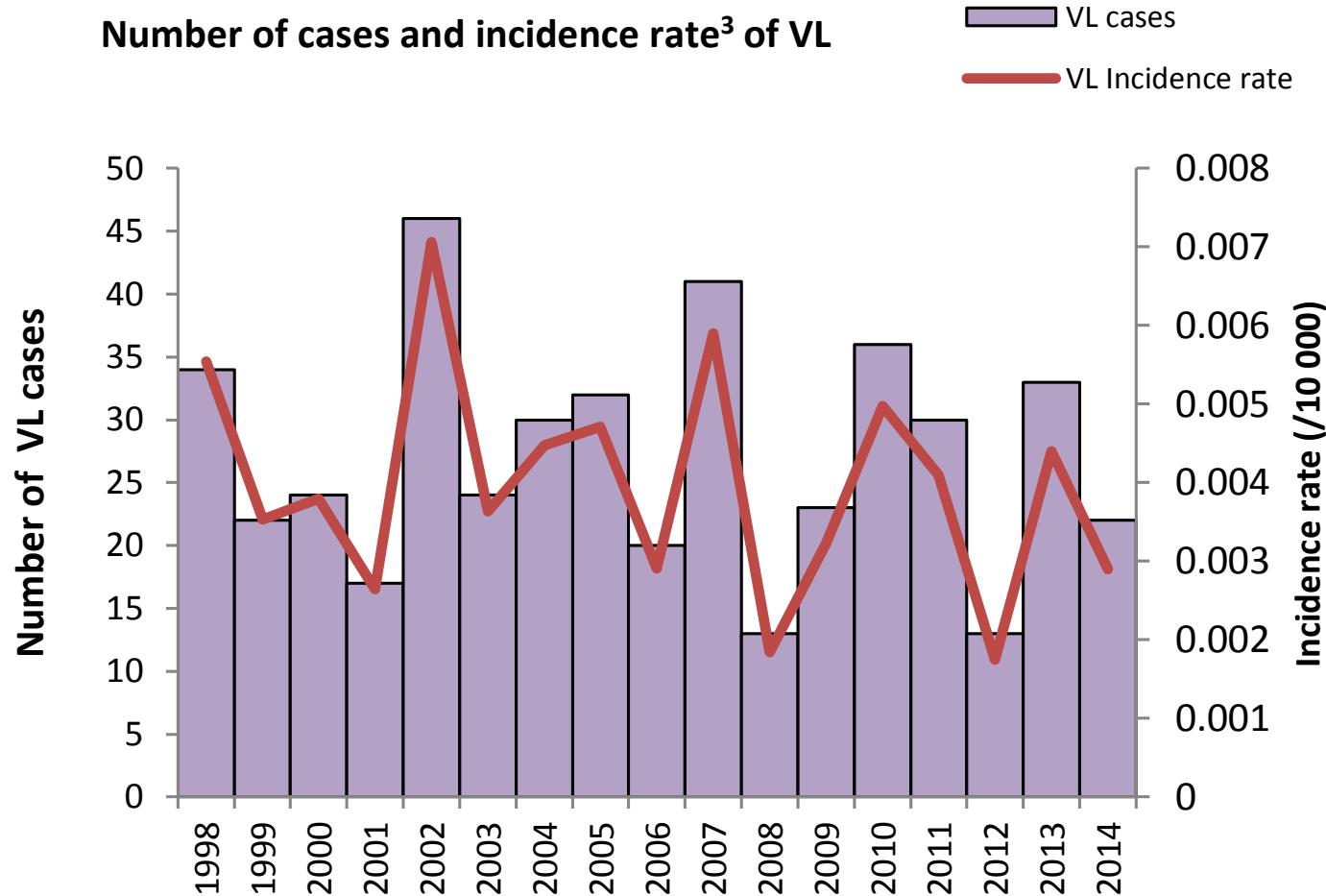
## Leishmaniasis

## TURKEY

**2014**

*Published in July 2016*

Country General Information (WHO, 2013)



Leishmaniasis

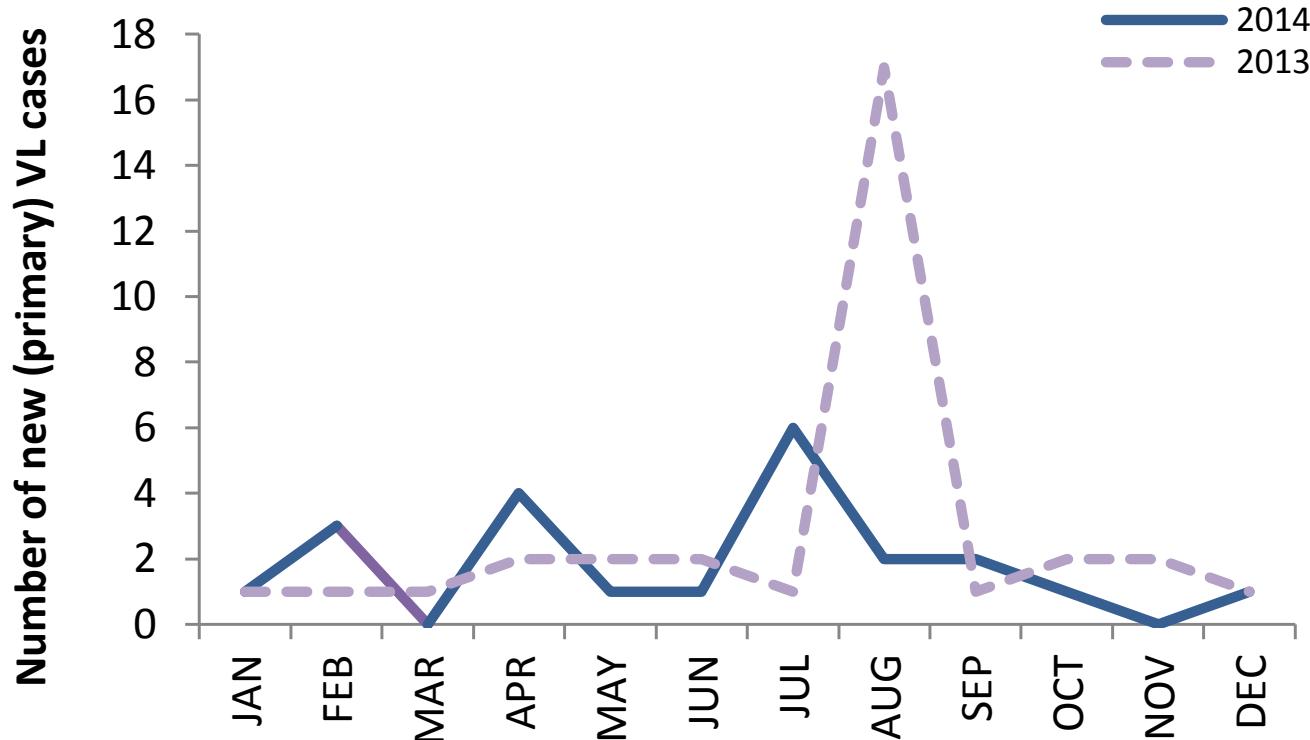
TURKEY

2014

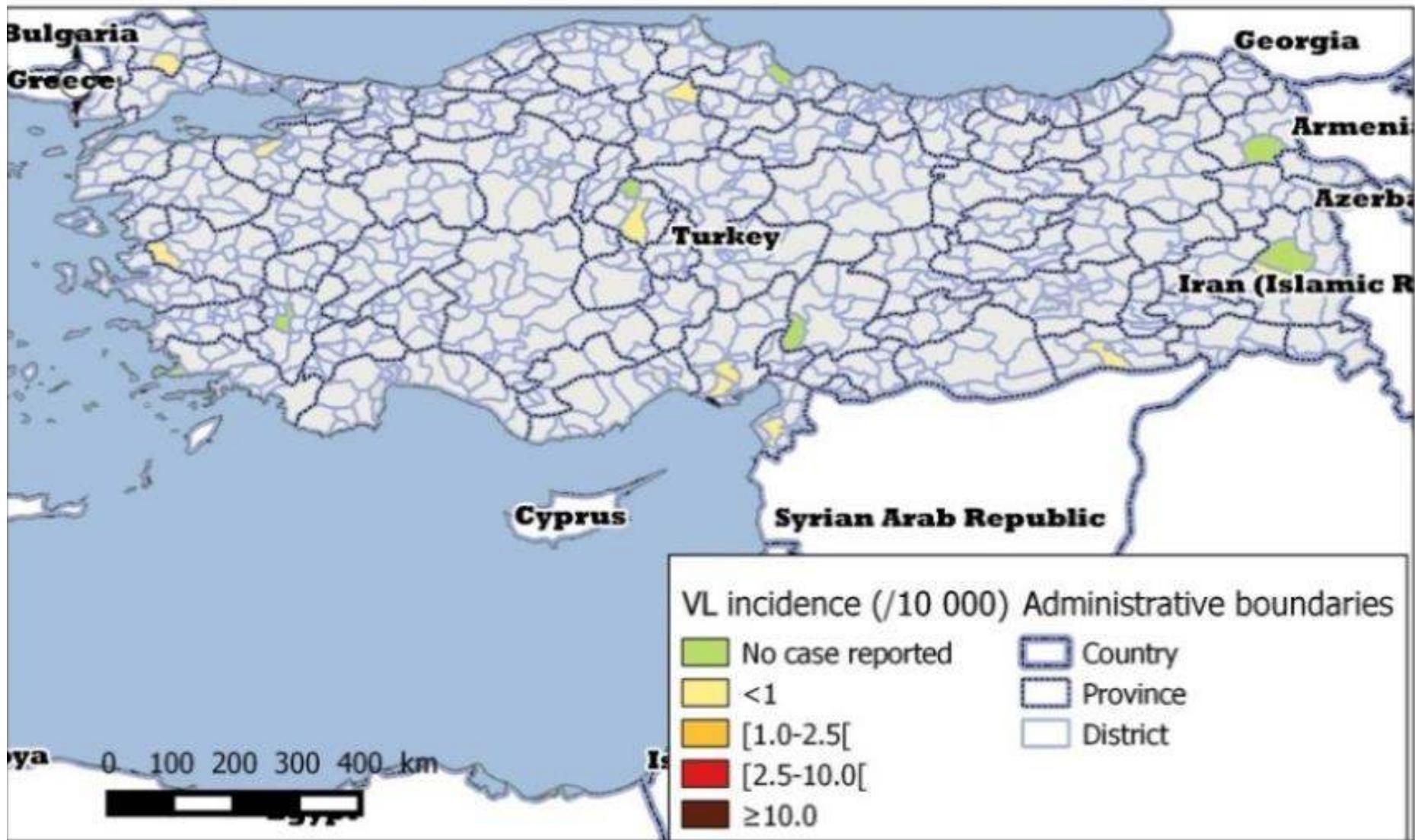
Published in July 2016

Country General Information (WHO, 2013)

## Number of new (primary) VL cases reported by month in 2013 and 2014



## Incidence of VL in Turkey in 2014 at district level per 10 000 population



## On Dört Erişkin Viseral Leyişmanyoz Olgusunun Değerlendirilmesi

Evaluation of Fourteen Adult Cases with Visceral Leishmaniasis

Ebru KURŞUN<sup>1</sup>, Tuba TURUNC<sup>1</sup>, Yusuf Ziya DEMİROĞLU<sup>1</sup>, Soner SOLMAZ<sup>2</sup>,  
Hande ARSLAN<sup>3</sup>

## Erişkin Viseral Leyşmanyaz Olgularının Klinik ve Laboratuvar Bulgularının Değerlendirilmesi

Evaluation of Clinical and Laboratory Findings of Adult  
Visceral Leishmaniasis Cases

Serap URAL<sup>1</sup>, Figen KAPTAN<sup>1</sup>, Nurbanu SEZAK<sup>1</sup>, Sibel EL<sup>1</sup>, Bahar ÖRMEN<sup>1</sup>, Nesrin TÜRKER<sup>1</sup>,  
Tuna DEMİRDAL<sup>1</sup>, İlknur VARDAR<sup>1</sup>, Pınar ÖZKAN ÇAYIRÖZ<sup>1</sup>, Fulya ÇAKALAĞAOĞLU<sup>2</sup>

# Layışmanyoz Epidemiyoloji

KL

VL

- *L. infantum*
- *L. tropica*

- *L. infantum*

Antroponotik

RESEARCH ARTICLE

# Pediatric Cutaneous Leishmaniasis in an Endemic Region in Turkey: A Retrospective Analysis of 8786 Cases during 1998-2014

Mustafa Aksoy<sup>1</sup>, Nebiye Doni<sup>2</sup>, Hatice Uce Ozkul<sup>3</sup>, Yavuz Yesilova<sup>4\*</sup>, Nurittin Ardic<sup>5</sup>, Abdullah Yesilova<sup>6</sup>, Jennifer Ahn-Jarvis<sup>7</sup>, Steve Oghumu<sup>8</sup>, Cesar Terrazas<sup>9</sup>, Abhay R. Satoskar<sup>9\*</sup>

**1** Department of Dermatology, Harran University School of Medicine, Sanliurfa, Turkey, **2** Department of Microbiology, Harran University School of Medicine, Sanliurfa, Turkey, **3** Department of Dermatology, Yuzuncu Yıl University School of Medicine, Van, Turkey, **4** Ministry of Health, Health Sciences University, Van Training and Research Hospital, Dermatology Clinic, Van, Turkey, **5** Department of Microbiology, Gulhane Military Medical Academy, Ankara, Turkey, **6** Department of Biostatistics, Yuzuncu Yıl University School of Medicine, Van, Turkey, **7** Biosciences, College of Dentistry, Ohio State University, Columbus, Ohio, United States of America, **8** Environmental Health Sciences, College of Public Health, Ohio State University, Columbus, Ohio, United States of America, **9** Department of Pathology, Ohio State University Medical Center, Columbus, Ohio, United States of America

\* [yavuzyesilova@gmail.com](mailto:yavuzyesilova@gmail.com) (YY); [abhay.satoskar@osumc.edu](mailto:abhay.satoskar@osumc.edu) (ARS)



CrossMark  
click for updates

RESEARCH ARTICLE

# Pediatric Cutaneous Leishmaniasis in an Endemic Region in Turkey: A Retrospective Analysis of 8786 Cases during 1998-2014

Mustafa Aksoy<sup>1</sup>, Nebiye Doni<sup>2</sup>, Hatice Uce Ozkul<sup>3</sup>, Yavuz Yesilova<sup>4\*</sup>, Nurittin Ardic<sup>5</sup>, Abdullah Yesilova<sup>6</sup>, Jennifer Ahn-Jarvis<sup>7</sup>, Steve Oghumu<sup>8</sup>, Cesar Terrazas<sup>9</sup>, Abhay R. Satoskar<sup>9\*</sup>

**1** Department of Dermatology, Harran University School of Medicine, Sanliurfa, Turkey, **2** Department of Microbiology, Harran University School of Medicine, Sanliurfa, Turkey, **3** Department of Dermatology, Yuzuncu Yıl University School of Medicine, Van, Turkey, **4** Ministry of Health, Health Sciences University, Van Training and Research Hospital, Dermatology Clinic, Van, Turkey, **5** Department of Microbiology, Gulhane Military Medical Academy, Ankara, Turkey, **6** Department of Biostatistics, Yuzuncu Yıl University School of Medicine, Van, Turkey, **7** Biosciences, College of Dentistry, Ohio State University, Columbus, Ohio, United States of America, **8** Environmental Health Sciences, College of Public Health, Ohio State University, Columbus, Ohio, United States of America, **9** Department of Pathology, Ohio State University Medical Center, Columbus, Ohio, United States of America

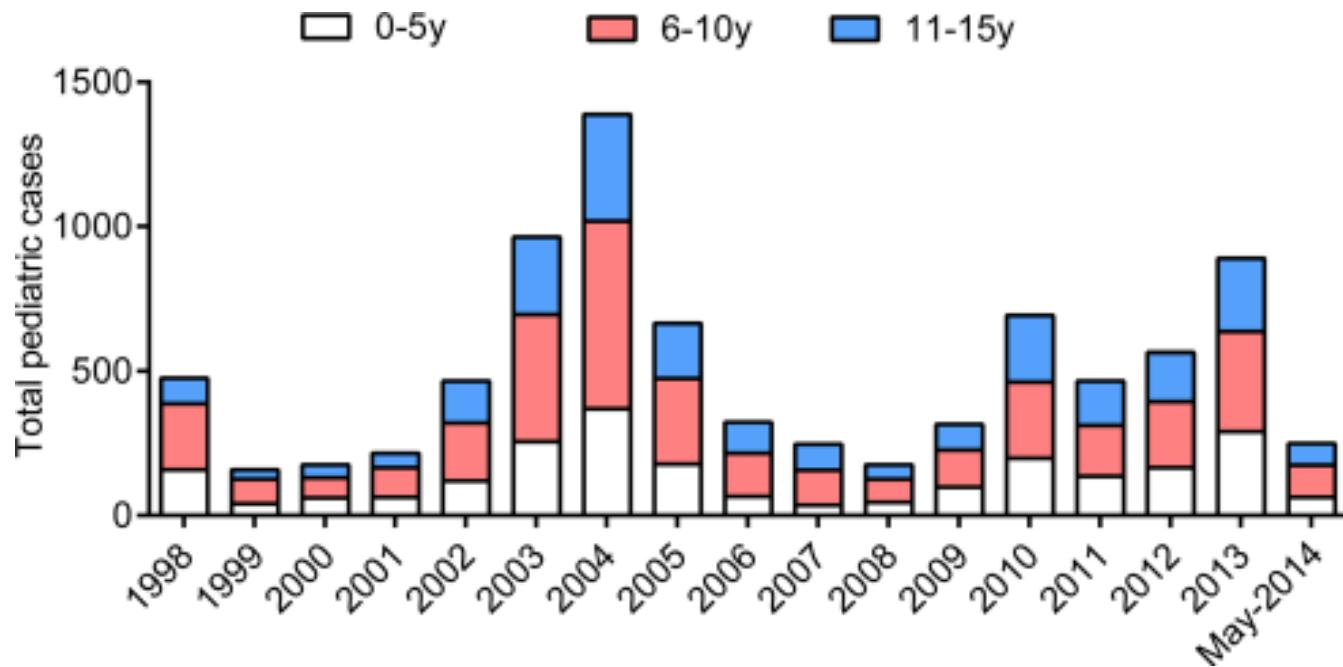
\* [yavuzyesilova@gmail.com](mailto:yavuzyesilova@gmail.com) (YY); [abhay.satoskar@osumc.edu](mailto:abhay.satoskar@osumc.edu) (ARS)



CrossMark  
click for updates

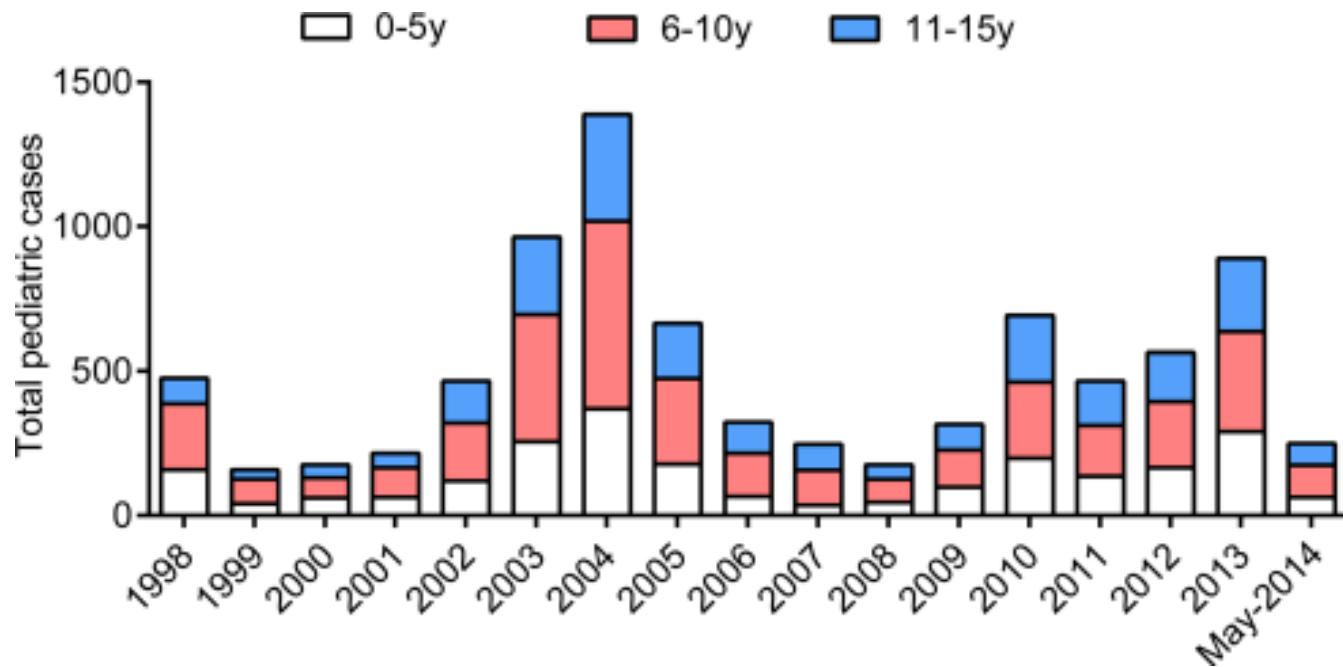
## Cutaneous Leishmaniasis in Pediatric Patients from 1998 to May 2014 in Sanliurfa

The last few years have reported increasing cases of CL in Turkey [7]. We determined whether pediatric patients also showed increased numbers of CL cases (Fig 4). Of 8786 pediatric patients, 3098 (35.26%), 3464 (39.43%), and 224 (25.31%) were 0–5, 6–10–11–15 age groups, respectively. We found that total CL cases in pediatric patients peaked in 1998, 2002–2005 and 2010–2013. In all the years considered in this report, the frequency of 6–10 years old patients was higher than the other groups.



## Cutaneous Leishmaniasis in Pediatric Patients from 1998 to May 2014 in Sanliurfa

The last few years have reported increasing cases of CL in Turkey [7]. We determined whether pediatric patients also showed increased numbers of CL cases (Fig 4). Of 8786 pediatric patients, 3098 (35.26%), 3464 (39.43%), and 224 (25.31%) were 0–5, 6–10–11–15 age groups, respectively. We found that total CL cases in pediatric patients peaked in 1998, 2002–2005 and 2010–2013. In all the years considered in this report, the frequency of 6–10 years old patients was higher than the other groups.



Received: 2015.01.03

Accepted: 2015.03.23

Published: 2015.07.20

## Effect of the Syrian Civil War on Prevalence of Cutaneous Leishmaniasis in Southeastern Anatolia, Turkey

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

ABCDEF 1 **Rahime Inci**  
ABCD 2 **Perihan Ozturk**  
ABE 2 **Mehmet Kamil Mulayim**  
ABC 3 **Kemal Ozyurt**  
ACDF 4 **Emine Tugba Alatas**  
CF 5 **Mehmet Fatih Inci**

1 Department of Dermatology, Izmir Katip Celebi University, Atatürk Training and Research Hospital, Izmir, Turkey

2 Department of Dermatology, Sütçü Imam University, School of Medicine, Kahramanmaraş, Turkey

3 Department of Dermatology, Kayseri Training and Research Hospital, Kayseri, Turkey

4 Department of Dermatology, Mugla Sitki Kocman University, School of Medicine, Mugla, Turkey

5 Department of Radiology, Izmir Katip Celebi University, School of Medicine, Izmir, Turkey

**Corresponding Author:** Rahime Inci, e-mail: [drrahimeinci@gmail.com](mailto:drrahimeinci@gmail.com)

**Source of support:** Departmental sources

**Background:** Cutaneous leishmaniasis (CL) is a vector-mediated skin disease, characterized by chronic wounds on the skin and caused by macrophages in protozoan parasites. It is an endemic disease in the southern and southeastern Anatolia region and is still an important public health problem in Turkey. Because of the civil war in Syria, immigrants to this region in the last 3 years have begun to more frequently present with this disease. The aim of this study was to draw attention to the dramatic increase in new cases with CL after the beginning of the civil war in Syria.

**Material/Methods:** In this retrospective study, we evaluated demographic, epidemiological, and clinical features of 110 patients diagnosed with cutaneous leishmaniasis who were admitted to the Department of Dermatology at Kahramanmaraş Sutcu Imam University Faculty of Medicine between January 2011 and June 2014.

**Results:** A total of 110 patients included in the study; 50 (45%) were males, and 60 (55%) were females. The age range of the study group was 1–78 years, and the infection was more prevalent in the 0–20 year age group. Of these patients, 76 (69%) were Syrian refugees living in tent camps and 34 (31%) were Turkish citizens. The majority of the cases were diagnosed between October and December.

**Conclusions:** Immigrations to endemic regions of Turkey from neighbouring countries where CL incidence is higher may lead to large increases in case numbers. In order to decrease the risk of exposure, housing conditions of the refugees must be improved, routine health controls must be performed, effective measures must be set in place for vector control, and infected individuals must be diagnosed and treated to prevent spread of the infection.



**Figure 1.** Multiple papulonodular lesions in the right cheek of a 11-year-old Syrian boy diagnosed with cutaneous leishmaniasis.



# Layışmanyoz Epidemiyoloji

KL

Zoonotik

Ana Rezervuar: Köpek

- *L. infantum*
- *L. tropica*
- *L. infantum*

Antroponotik

# Layışmanyoz Epidemiyoloji

KL

VL

- *L. infantum*
- *L. tropica*

- *L. infantum*
- *Leishmania major*

## Multi-Site DNA Polymorphism Analyses of *Leishmania* Isolates Define their Genotypes Predicting Clinical Epidemiology of Leishmaniasis in a Specific Region

LEYLA AKMAN,<sup>1</sup> H. S. Z. AKSU,<sup>2</sup> R.-Q. WANG,<sup>3</sup> S. OZENSOY,<sup>4</sup> Y. OZBEL,<sup>5</sup> Z. ALKAN,<sup>6</sup> M. A. OZCEL,<sup>2</sup> G. CULHA,<sup>2</sup> K. OZCAN,<sup>2</sup> S. UZUN,<sup>2</sup> H. R. MEMISOGLU<sup>2</sup> and KWANG-POO CHANG<sup>2</sup>

<sup>1</sup>Department of Microbiology and Immunology, University of Health Sciences, Chicago Medical School, North Chicago, Illinois, 60064 USA, and

<sup>2</sup>Department of Infectious Diseases, <sup>3</sup>Department of Parasitology <sup>4</sup>Department of Dermatology,

Cukurova University Faculty of Medicine, Adana, Turkey, and

<sup>5</sup>Department of Parasitology, Ege University Faculty of Medicine, Izmir, Turkey

**ABSTRACT.** *Leishmania* isolates from 57 cases of human cutaneous (CL), human visceral (VL), and canine visceral (CVL) leishmaniasis in Turkey were grouped by multi-site DNA polymorphism analyses into five genotypes. The initial grouping was based on DNA heterogeneity of the faster-evolving mitochondrion (kinetoplast) minicircles and the intergenic regions of two nuclear repetitive genes. Taxonomic affiliation and phylogenetic relationships of the five genotypes were inferred by comparing them with reference species for sequence heterogeneity in a ~1.4 kb conserved single-copy gene, encoding *N*-acetylglucosamine-1-phosphate transferase (*NAGT*). Alignment of the available sequences revealed no gap, but up to 7% scattered base substitutions, suggesting that this functionally important gene is a suitable marker. Three genotypes are completely identical to the *NAGTs* of the reference species, identifying them as *L. infantum*, *L. tropica*, and *L. major*, respectively. The remaining two are recognized as *L. major* *NAGT* variants with one and four base substitutions, respectively. As expected, Maximum Likelihood analysis of the *NAGT* sequences separates them into three clades, corresponding to the three species. The majority of the isolates obtained are *L. infantum* and *L. tropica*, which have been known to cause infantile VL and anthroponotic CL in western and southeastern Turkey, respectively. Unexpected is the finding of *Leishmania major* variants and their dispersal, possibly as previously unrecognized clinico-epidemiologic entities of CL and VL.

**Key Words.** Clinical epidemiology, kinetoplast DNA, *Leishmania*, nuclear DNA, *N*-acetylglucosamine-1-transferase, phylogeny, sequence polymorphism.

## Şanlıurfa'da Şark Çıbanı Etkeni Değişiyor mu? İlk *Leishmania major* Vakaları

Is the agent of Cutaneous Leishmaniasis in Sanliurfa changing? First cases of *Leishmania major*

Fadile Yıldız Zeyrek<sup>1</sup>, Gülcen Gürses<sup>2</sup>, Nermin Uluca<sup>1</sup>, Nebiye Yentür Donı<sup>2</sup>, Şahin Toprak<sup>3</sup>,  
Yavuz Yeşilova<sup>4</sup>, Gülnaz Çulha<sup>5</sup>

<sup>1</sup>Harran Üniversitesi Tıp Fakültesi, Tıbbi Mikrobiyoloji Anabilim Dalı, Şanlıurfa, Türkiye

<sup>2</sup>Harran Üniversitesi Sağlık Hizmetleri Meslek Yüksekokulu, Tıbbi Mikrobiyoloji Anabilim Dalı, Şanlıurfa, Türkiye

<sup>3</sup>Harran Üniversitesi Fen Fakültesi, Biyoloji Bölümü, Şanlıurfa, Türkiye

<sup>4</sup>Harran Üniversitesi Tıp Fakültesi, Dermatoloji Anabilim Dalı, Şanlıurfa, Türkiye

<sup>5</sup>Mustafa Kemal Üniversitesi, Tıbbi Parazitoloji Anabilim Dalı, Hatay, Türkiye



## The emergence of *Leishmania major* and *Leishmania donovani* in southern Turkey

Ismail S. Koltas<sup>a,\*</sup>, Fadime Eroglu<sup>a</sup>, Derya Alabaz<sup>b</sup> and Soner Uzun<sup>c</sup>

<sup>a</sup>Department of Parasitology, Faculty of Medicine, University of Cukurova, 01330 Balcali, Saricam, Adana, Turkey; <sup>b</sup>Department of Pediatrics, Faculty of Medicine, University of Cukurova, 01330 Balcali, Saricam, Adana, Turkey; <sup>c</sup>Department of Dermatology, Faculty of Medicine, University of Akdeniz, 07070 Konyaalti, Antalya, Turkey

\*Corresponding author: Tel: +90 535 3059393; E-mail: koltas@cu.edu.tr

ORIGINAL ARTICLE

DOI:

Tropical Medicine and International Health

doi:10.1111/tmi.12698

VOLUME 21 NO 6 PP 783–791 JUNE 2016

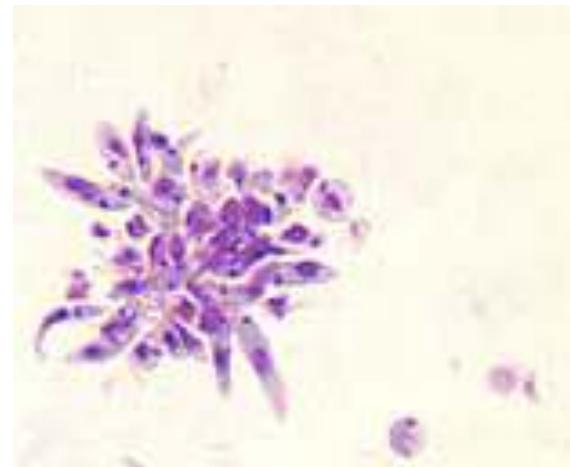
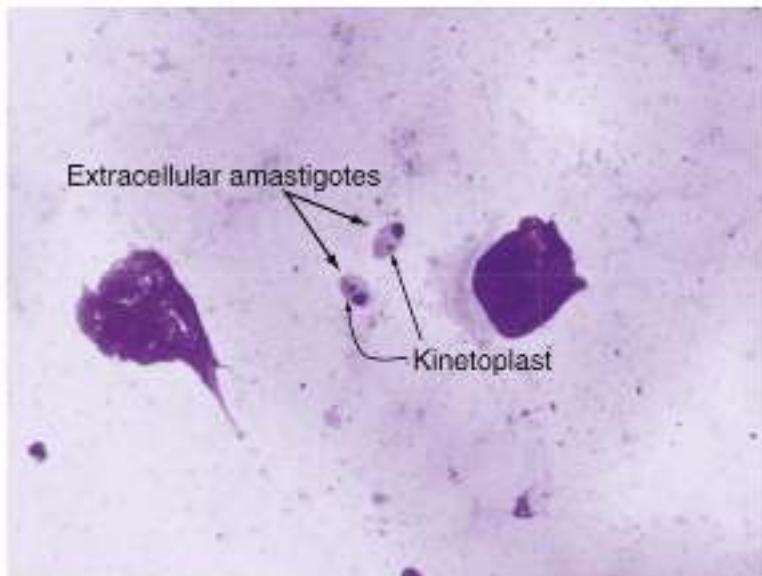
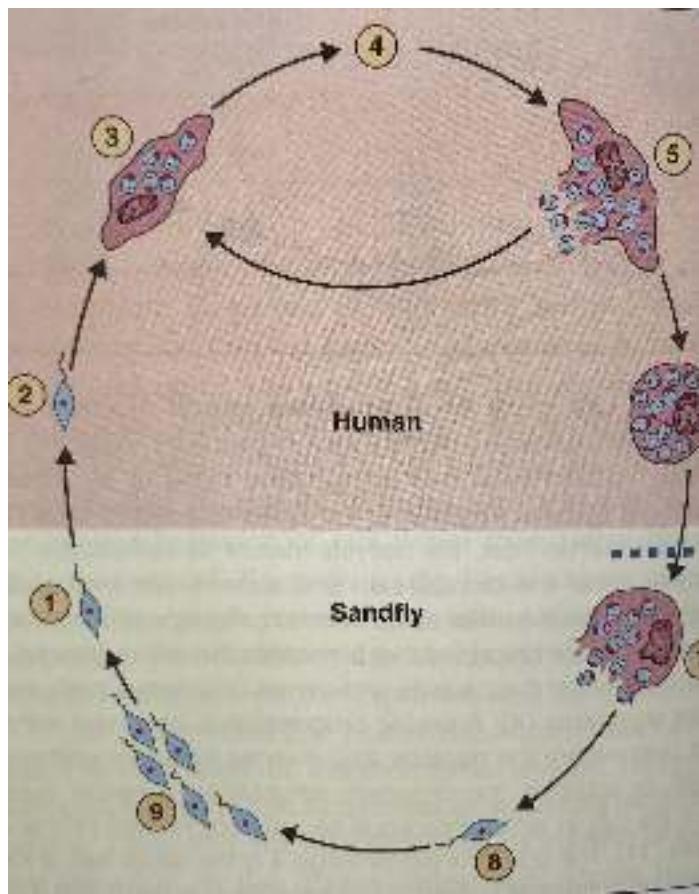
## Leishmaniasis in Turkey: first clinical isolation of *Leishmania major* from 18 autochthonous cases of cutaneous leishmaniasis in four geographical regions

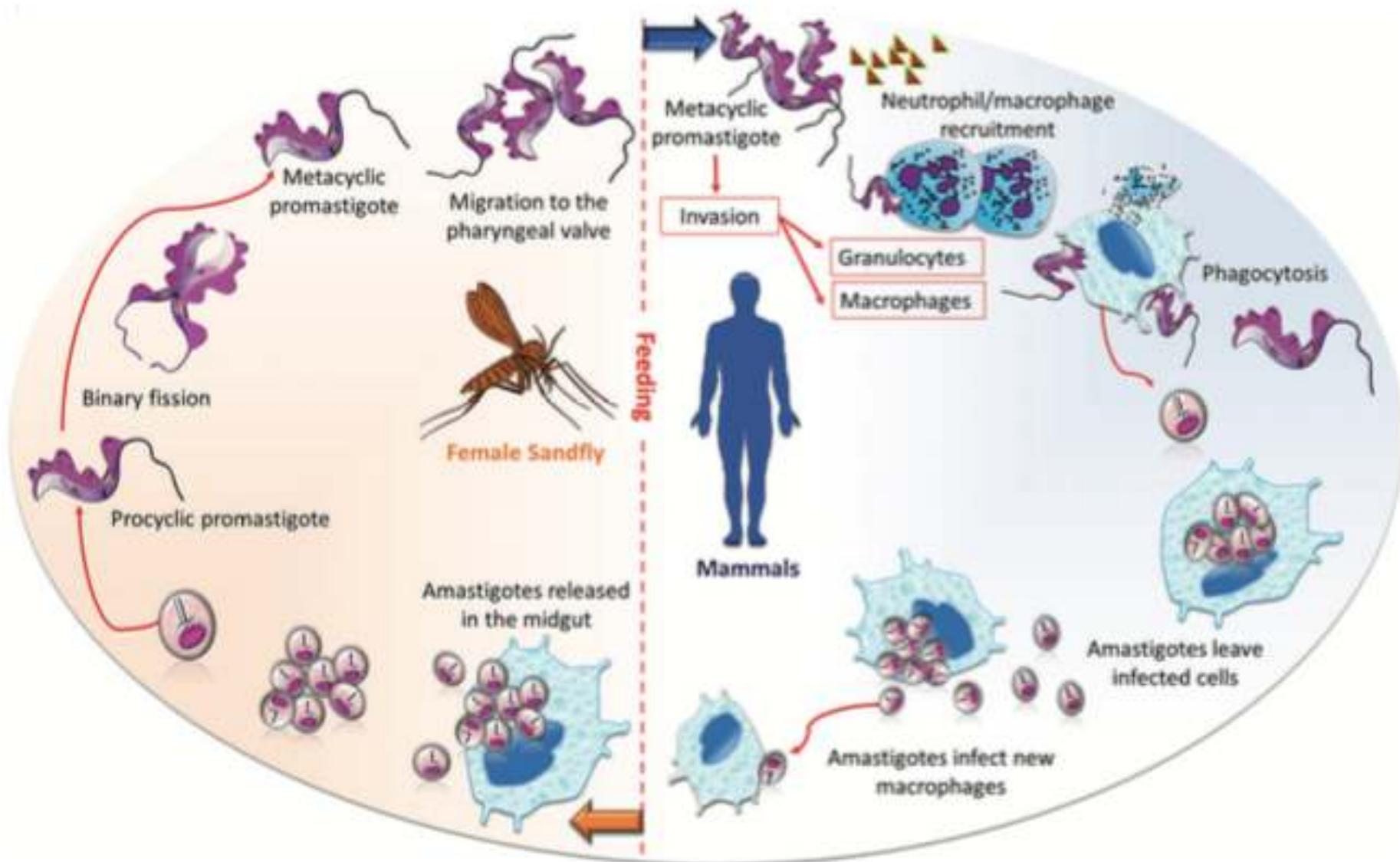
Ahmet Özbilgin<sup>1</sup>, Gülnaz Çulha<sup>2</sup>, Soner Uzun<sup>3</sup>, Mehmet Harman<sup>4</sup>, Suhan Gunaşçı Topal<sup>5</sup>, Fulya Okudan<sup>6</sup>, Fadile Zeyrek<sup>7</sup>, Cumhur Gunduz<sup>8</sup>, İpek Ostan<sup>9</sup>, Mehmet Karakuş<sup>10</sup>, Seray Toz<sup>10</sup>, Ozgür Kurt<sup>11</sup>, İşin Akyar<sup>11</sup>, Ayşegül Erat<sup>3</sup>, Dilek Güngör<sup>5</sup>, Çağla Kayabaşı<sup>8</sup>, İbrahim Çavuş<sup>1</sup>, Patrick Bastien<sup>12</sup>, Francine Pratlong<sup>12</sup>, Tanıl Kocagoz<sup>11</sup> and Yusuf Ozbel<sup>10</sup>

# Layışmanyoz Tarihçe

- 1900 Leishman dalakta etkeni gösterdi
- 1903 Donovan; hastalık bulgularını tanımladı
- 1916 Trabzon'da ilk olgu
- 1918 İzmir'de ikinci olgu
- 1954-1965 55 olgu
- 1974-1980 74 olgu
- 2003-2007 120 olgu

# Etken: *Leishmania* spp





# *Leishmania* spp: Patogenez

## Promastigot

- Memelide : PMNL/makrofaj
  - İlk karşılaştıkları hücre

## Amastigot

- Konağın immün yanıtından kaçar
  - LPG (lipofosfoglikan) ; fagositoya direnç
  - Mononükleer lökositlerden  $H_2O_2$  salımını azaltır
  - Süperoksit dismutaz üretir
  - Lenforetiküler h invazyonu
  - Çoğalma
  - Hücreyi parçalayarak yayılma

# *Leishmania* spp: Patogenez

## Promastigot

- Memelide : PMNL/makrofaj  
– İlk karşılaştıkları hücre

## İmmunsupresyon

- Hücresel immün yanıt yetersiz
- Ig G çok artar: işe yaramaz

## Amastigot

- Konağın immün yanıtından kaçar
  - LPG (lipofosfoglikan) ; fagosoza direnç
  - Mononükleer lökositlerden  $H_2O_2$  salımını azaltır
  - Süperoksit dismutaz üretir
  - Lenforetiküler h invazyonu
  - Çoğalma
  - Hücreyi parçalayarak yayılma

# Patogenez

- Makrofajlar → Kan dolasımı
  - Dalak
  - Karaciğer
  - Kemik iliği
  - Lenf nodları
  - İntestinal lenfatik dokular
  - Submukoza
  - RES

Mononükleer fagositer hücre artar

- Dalak
- Karaciğer
- Hepatosplenomegali → Hipersplenizm

# VL Klinik

- İnkübasyon süresi 2-8 ay
  - 14 gün-10 yıl
- Ateş
- Kilo kaybı
- Hepatosplenomegali
- Pansitopeni
- Hasta immünsupresif olana kadar belirtisiz

# VL Klinik

- Çocuk
- İmmünsupresyon
  - HIV
  - Metotreksat
  - Steroid
  - TNF  $\alpha$  inhibitörleri
  - Organ nakli
  - Subklinik olgular (serolojik tanı)

# VL Klinik

- Akut
- Subakut
- Kronik

# VL Klinik

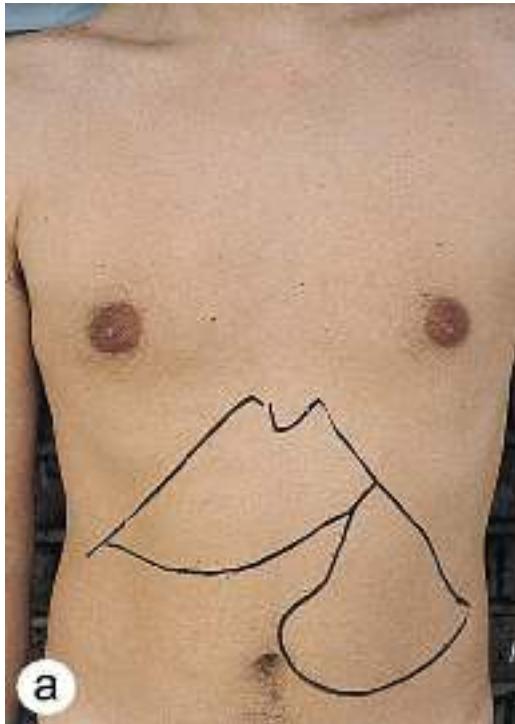
- Akut
  - Ateş
  - Üşüme –titreme
    - Periyodik tekrar-Sıtma?
  - Dalak genellikle yumuşak
  - Deride kepekleşme
  - Diskolorizasyon
    - “Kala-azar”
  - Periferik ödem
  - Hematüri, proteinüri
  - Hemoraji
    - Dişeti, bağırsak, ekimoz
  - Pansitopeni
- Subakut
- Kronik

# VL Klinik

- Akut

EN SIK

- Subakut



- Ateş
  - Günde 2 kez
  - Dalgalı ateş
- Hasta daha iyi hisseder
- Kanama yok
- Dalak
  - önce yumuşak
  - Ateşlendikçe sertleşir
- İshal
- Sarılık
- Asit, ödem
- Jinjivit, purpura
- %10 iyileşir
- Süperenfeksiyon-Ölüm

# VL Klinik

- Akut
  - Zayıflama
  - Hepatosplenomegalı
  - Anemi
- Subakut
  - Daha hafif
- Kronik

# VL Klinik

- Laboratuvar
  - Anemi : Normokrom normositer
  - Lökopeni- bazen nötropeni
    - Eozinopeni
  - Trombositopeni
  - Hipergamaglobulinemi
  - Globulin/albumin oranı yüksek
  - RF (+)
  - ABY, nefrotik sendrom, proteinüri

# VL Klinik

- Tedavisiz %90 mortal
- Sekonder bakteriyel enfeksiyon
  - Pnömoni
  - Sepsis
  - Tüberküloz
  - Dizanteri
  - Kızamık
  - Malnütrisyon
  - Kanama
- Tedavi ile %95 iyileşme

# VL Klinik

- Visserotropik Layışmanyoz
  - Körfez Savaşı- ABD askerleri
    - Brezilya ve İtalya'da da
  - *L. tropica*
  - Hafif ateş
  - Halsızlık, yorgunluk
  - İshal
  - Hafif splenomegali
  - VL veya kala-azar yok!

# VL Klinik

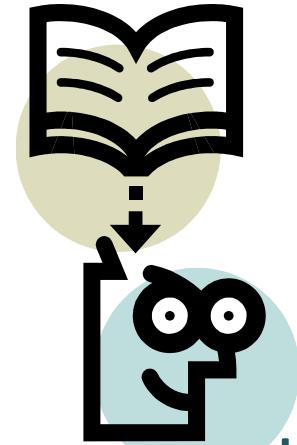
- Post Kala-Azar Dermal Layışmanyoz
  - VL komplikasyonu: iyileşen hastalarda
    - *L. donovani*
  - Döküntüler
    - Maküler
    - Makülopapüler
    - Nodüler
  - Erken dönemde immünsupresyon nedeniyle IFN- $\gamma$  üretilemez
  - Tedavi sonrasında üretebilme → Deride kalan parazitler
  - VL olgularında IL-10 artışı → prediktif

# VL ve HIV

- Kuluçka süresi daha kısa
  - CD4<sup>+</sup> T hücreler < 200 /mm<sup>3</sup> %77-99
  - AIDS tanımlayıcı %42-72
  - Bulgular atipik olabilir
  - Klasik triad %75
    - Ateş, pansitopeni, hepato/splenomegalı
  - Amastigotlar intestinal tutulum: İshal %50  
Kronik ishalde akla gelmeli!
  - Eşlik eden enfeksiyonlar olabilir: CMV

# VL - Tanı

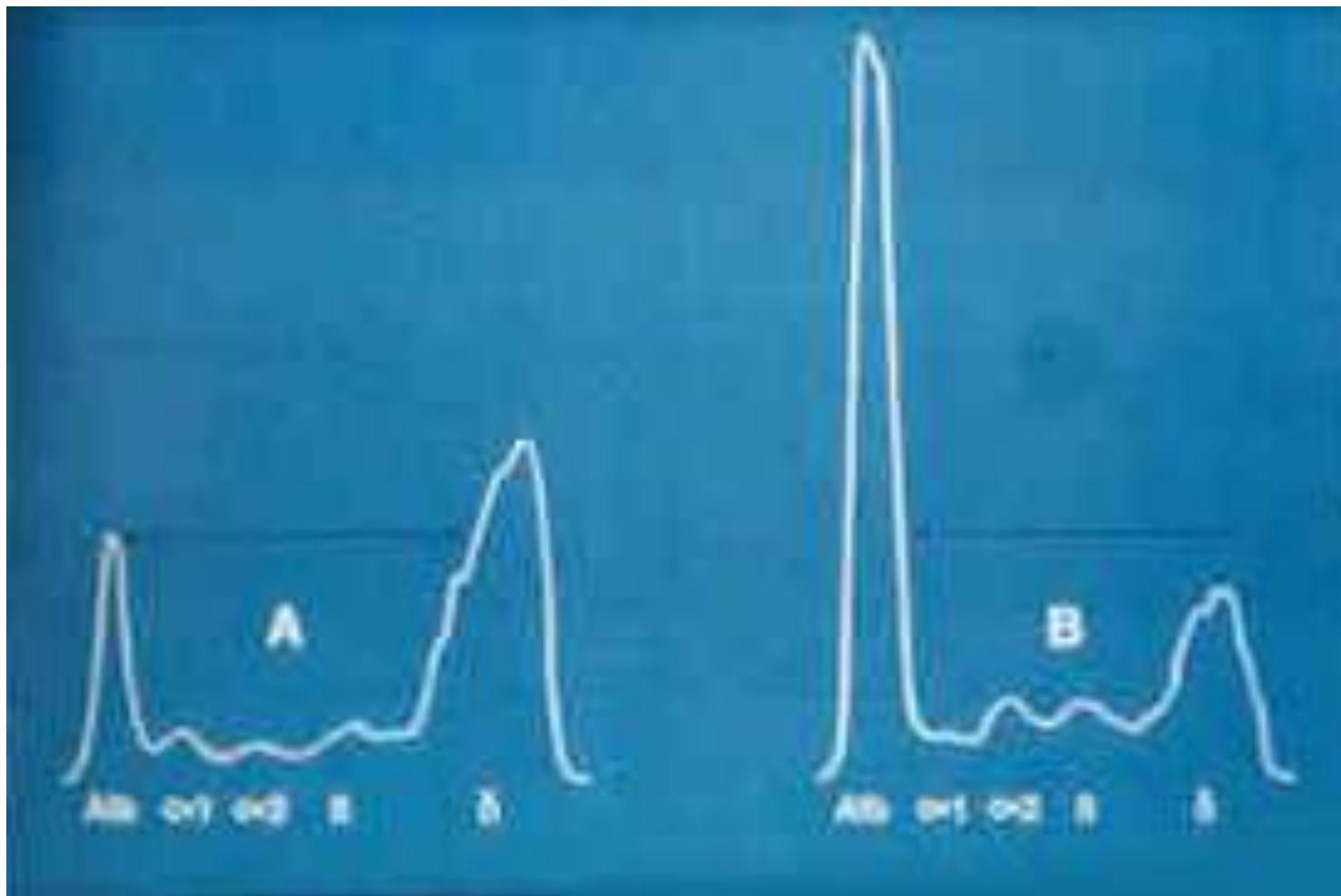
- Uzamış ateş
- İlerleyici kilo kaybı
  - Kuvvet kaybı
- İleri derecede splenomegali, hepatomegali
- Sitopeni
  - Anemi, Lökopeni, trombositopeni
- Hipergamaglobulinemi



PENTAT

Endemik bölgede PPD yüksek

# VL - Tanı



# VL - Tanı

## GÜÇLÜKLER:

- Ateşi olmayanlar
- Splenomegalisi olmayanlar
- Endemik bölge dışında semptom gelişenler
- HIV/AIDS
  - Semptomlar atipik

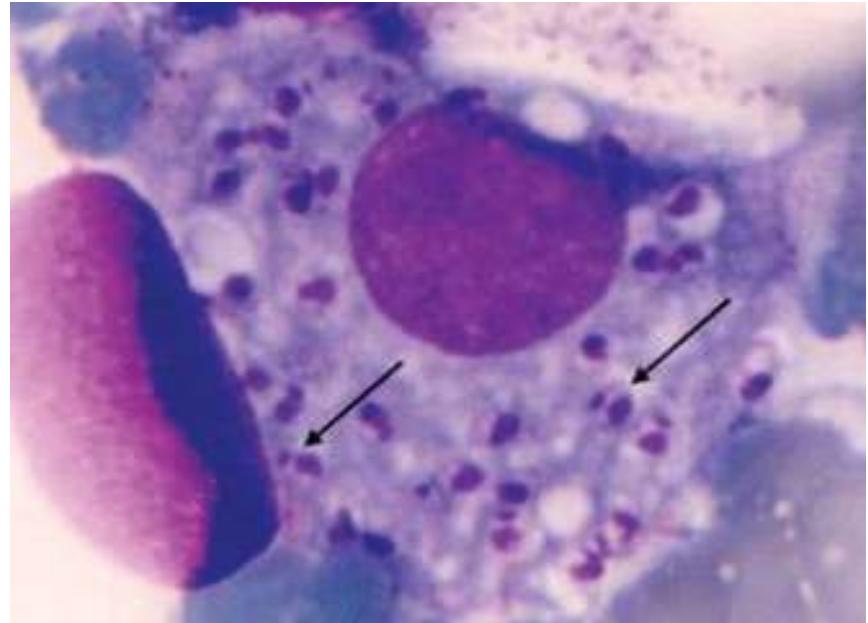
# VL - Tanı

1. Amastigotların tespiti
  - a) Mikroskopik
  - b) Kültürde
  - c) Hayvan deneyi
2. Etkenin DNA'sının gösterilmesi
3. İmmünodiagnoz
  - Antikor tespiti
4. Ksenodiagnoz

# VL - Tanı

## Amastigotların tespiti

- Kemik İliği
  - Güvenli
  - Giemsa, Wright
  - İlk enfeksiyon %94
  - Relaps %64
- Dalak aspirasyonu
  - Komplikasyon: Rüptür riski
- Karaciğer biyopsisi
  - Duyarlılığı düşük



# VL - Tanı

- Dalak aspirasyonu

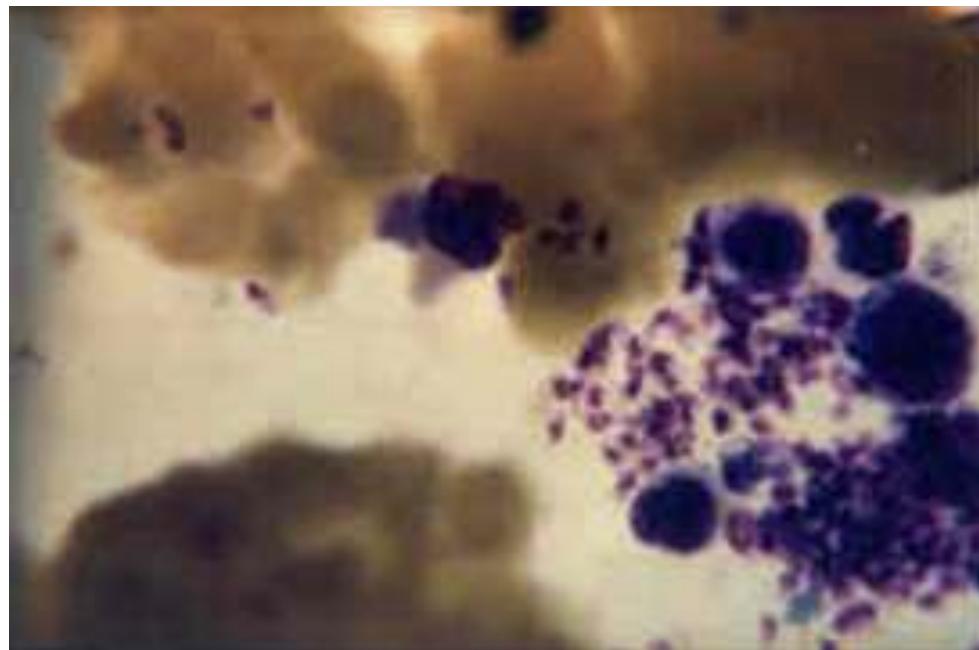
Kontrendike:

- Platelet  $\leq 40\ 000/\text{mm}^3$
- PT uzun  $\geq 5 \text{ sn}$  (Hasta-Kontrol)
- Dalak kostofrenik açıdan itibaren 4 cm palpabl
- Hekim işlem hakkında tecrübeli değilse



## VL - Tanı

- Dalak aspirasyonu
- Tedavinin etkinliğinin değerlendirilmesinde en üstün



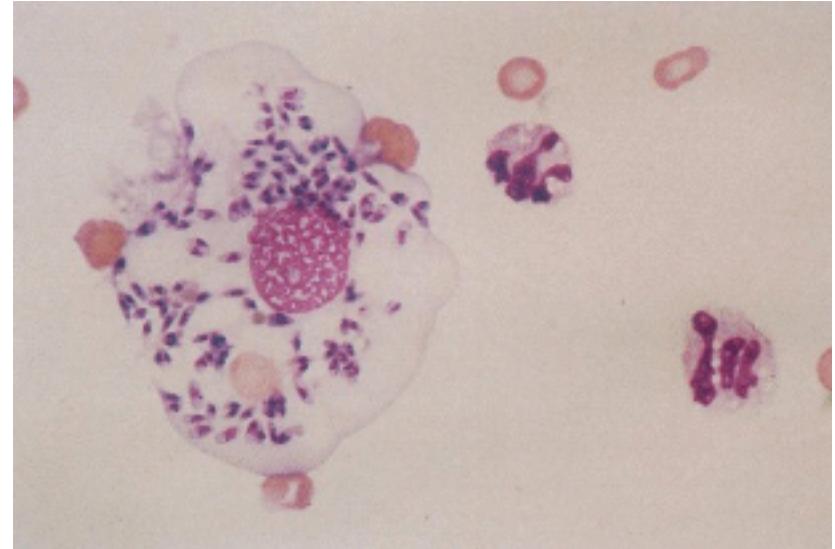
# VL - Tanı

## Tanışal örnekler

- Lenf bezi
- Buffy coat yayması
- BOS

## HIV/AIDS

- PY da makrofaj içinde
- BAL
- Plevral effüzyon
- Biyopsi
  - Oropharynx
  - Mide
  - Barsak



# VL - Tanı

## Kültür

- 22-26°C
  - Oda sıcaklığı
- Kontaminasyonu önlemek
  - Penisilin
  - Streptomisin
  - 5-flusitozin
- Haftada bir pasaj

- Monofazik
  - Schneider besiyeri
  - Hockmeyer (ticari)
- Difazik
  - Novy-MacNeal-Nicolle besiyeri
  - Tobie



# VL - Tanı

## Serolojik tanı

- IFAT
- ELISA
- Rekombinan *L. donovani major* gen B proteini
  - rGBP
  - Duyarlılık VL %92, PKDL %93
- rK39
  - *L. donovani*, *L. infantum (chagasi)* iyi
  - Kutanöz ve mukokutanöz olgularda yararsız
  - Tedaviden sonra da yüksek

# VL - Tanı

- İdrar Antijen Testi
  - KAtex
  - Özgül, ama duyarlılık <%70
  - Tedaviden sonra hızla negatifleşir
- Montenegro Testi
  - Leishmanin Deri testi
  - Aktif VL da negatif
  - İyileşenlerde pozitif
  - Epidemiyolojik yararı var

# VL - Tanı

- Polimeraz Zincir Reaksiyonu (PZR)
- Kan, doku ve diğer sıvılarda
  - Duyarlılık: %70-96
  - Hindistan'da KL: %93,8
  - Tedavinin etkinliğini değerlendirmede
  - Tiplendirmede: Epidemiyolojik
- Kinetoplast DNA'sı
  - KDNA halkacıkları

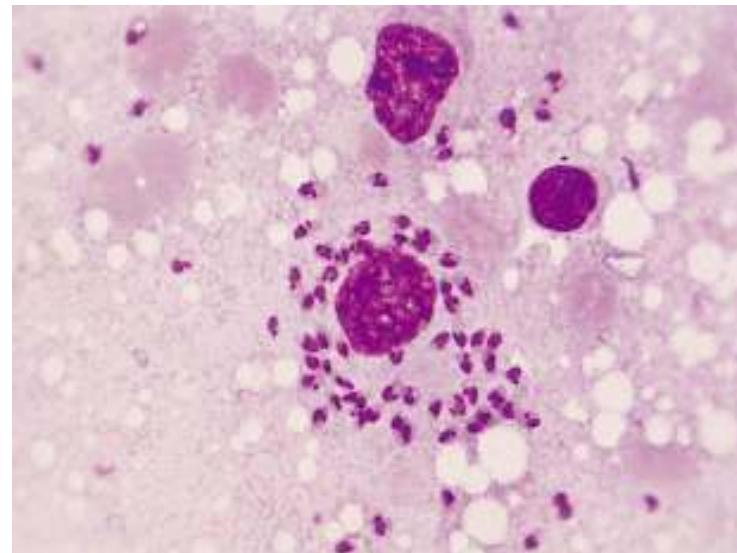
# KL - Klinik

- Türkiye'de *L. tropica*
- En çok Güney Doğu Anadolu Bölgesi
  - %70 20 yaş altı
- 1-12 hf inkübasyon süresi
- Papül → Sivilce
- 6 ay civarlı genişler
- Ülser



# KL - Tanı

- Klinik
- Parazitolojik
  - Lezyon kenarından, sağlam deriyle birleşim yeri
  - Biyopsi



# KL - Tedavi

- Sistemik tedavi
  - 5 değerli antimon
  - Lipozomal amfoterisin B
- İntralezyoner
- Kriyoterapi
- Lokal eksizyon
- Küretaj



# VL - Tedavi

- Amfoterisin B
- 5 değerli antimon bileşikleri
- Paromomisin
- Miltefosin

# VL - Tedavi

- Amfoterisin B
  - Lipozomal
- 5 değerli antimon bileşikleri
  - İlk seçenek **Lipozomal**
  - İmmünkompetan
    - 3 mg/kg
    - 21 mg/kg total
    - 1-5, 14, 21. gün
- Paromomisin
- Miltefosin
  - Gebelerde de verilir
  - Konvansiyonel
    - 0,75-1 mg /kg /gün
    - Her gün 15-20 gün
    - Günaşırı 30-40 gün

# VL - Tedavi

- Amfoterisin B
  - Lipozomal
- 5 değerli antimon bileşikleri
  - Steroid kullanımı
  - İmmunsupresif tedavi (Mtx vb)
- Paromomisin
- Miltefosin
- HIV araştırılmalı!
- Transplantasyon
- İmmünsupresyonda relaps yüksek

# VL - Tedavi

- Amfoterisin B
  - Lipozomal
- 5 değerli antimon bileşikleri
  - Immunsupresif tedavi (Mtx vb)
  - Lenfoma, lösemi
  - Kr. hepatit-
- Paromomisin
- Miltefosin
  - İmmünyetmezlikli
  - 4 mg/kg
  - 40 mg/kg total
  - 1-5, 10, 17, 24, 31, 38
- HIV araştırılmalı!
  - Transplantasyon
  - Steroid kullanımı

# VL - Tedavi

- Amfoterisin B
- 5 değerli antimon bileşikleri
- Paromomisin
- Miltefosin
- Meglümin antimonat
  - Glukantim
- Sodyum stiboglukonat
  - Pentostam
  - 20 mg/kg/gün im/iv
  - En az 28 gün
  - Direnç: Hindistan yarımadası, Nepal

# VL - Tedavi

- Amfoterisin B
  - 30S ribozomal altbirim
  - 12-20 mg/kg/gün im iv
- 5 değerli antimon bileşikleri
  - Hindistan
  - 15 mg/kg/gün 21 gün
- Paromomisin
- Miltefosin

# VL - Tedavi

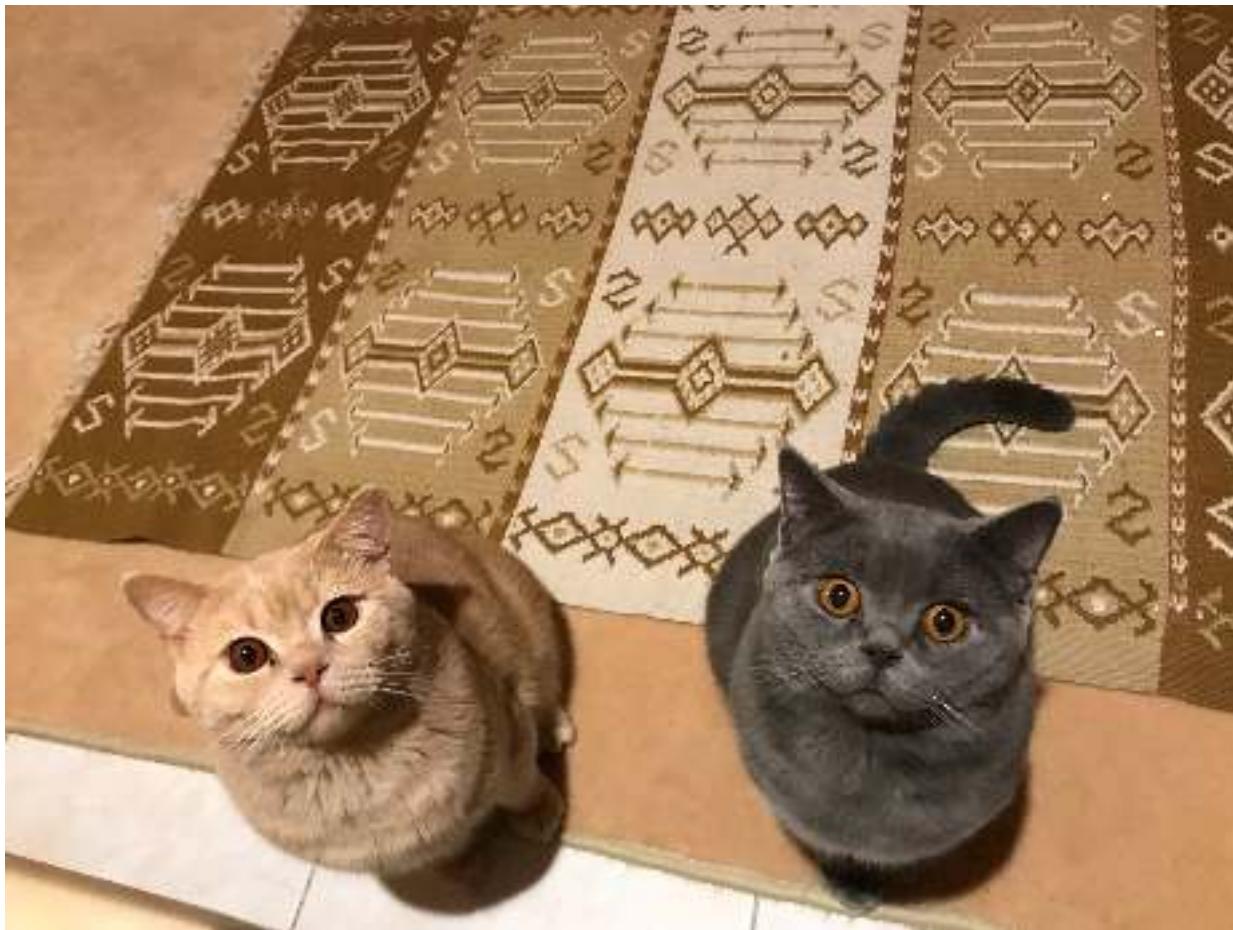
- Amfoterisin B
  - Oral
  - > 30 kg hastalarda
- 5 değerli antimon bileşikleri
  - 30-44 kg 2 x 50 mg
  - 45- 3 x 50 mg
  - 28 gün
- Paromomisin
- Miltefosin
  - Relaps %3-11

# VL - Takip

- Tedavi Etkinliğini Değerlendirme
  - Klinik!
  - Ateşin düşmesi
  - Dalağın küçülmesi
  - Kilo alma
- 12 ay takip
- Relapslar 6-12 ay içinde
  - Nadiren 18 ay
- İmmünkompromize hasta en az 12 ay takip!

# Layışmanyoz - Korunma

- Rezervuar
  - Hasta insan ve hayvanların tedavisi
  - Ev hayvanlarının gece kapalı ortamda ve uzaklaştırıcı tasma ile korunması
  - Barınaklarda tellere insektisit uygulama
- Vektör
  - Kovucu losyonlar
  - Cibinlik
  - Cibinliklerin kovucularla muamelesi
- Etkili aşısı yok



*Teşekkürler*