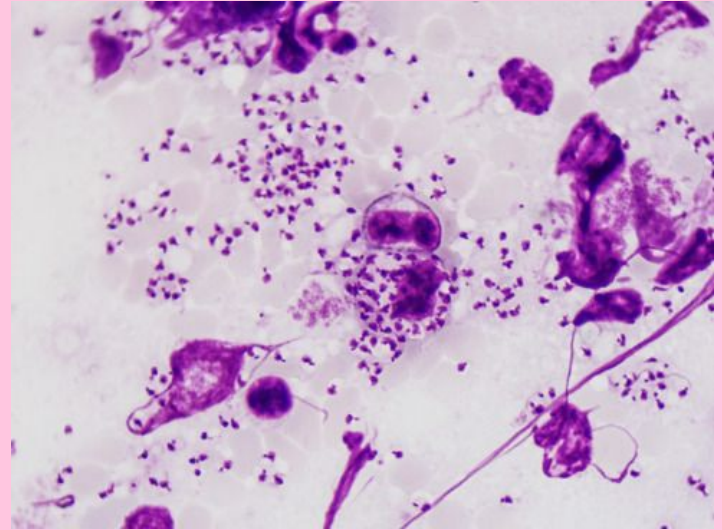


Leishmania donovani

Lillyanna Azevedo



Taxonomy

Domain: Eukaryota

Kingdom: Protista

Phylum: Euglenozoa

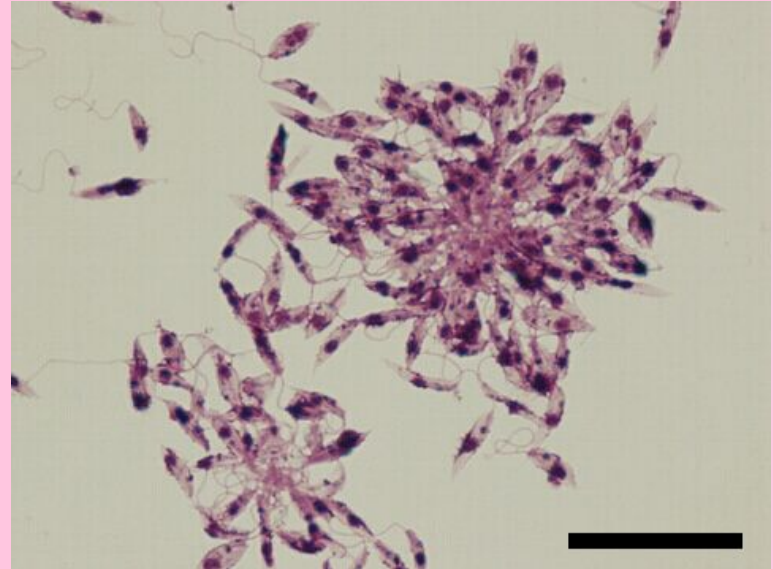
Class: Kinetoplastea

Order: Trypanosomatida

Family: Trypanosomatidae

Genus: *Leishmania*

Species: *Leishmania naiffi* species complex



History

- 1903 - discovered by William Leishman and Charles Donovan
- 1903 - Ronald Ross discovered transmission
- 1940s- less toxic pentavalent antimonials
- 1980s- rise of drug-resistant strains
- 2023- new lineages with abnormal pathologies



Morphology: Promastigote

- Found in the sand fly
(intermediate host)
- Flagellated
 - Motility and attachment
- Elongated
- Single nucleus
- Kinetoplast

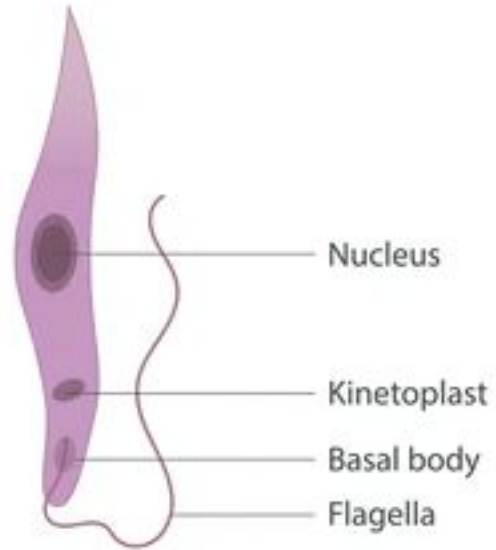


Fig: Promastigote of L.Donovani

Morphology: Amastigote

- Round/oval
- Develop in vertebrate hosts
- Single nucleus
- No flagella
- Kinetoplast
- Pellicular microtubules
- Definitive stage

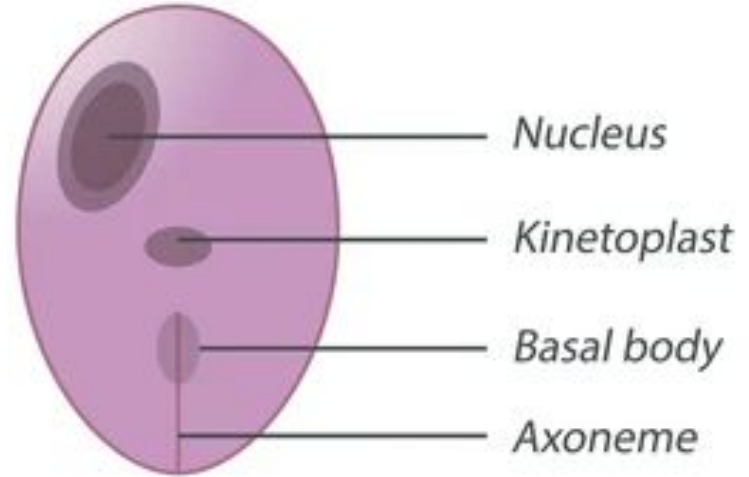
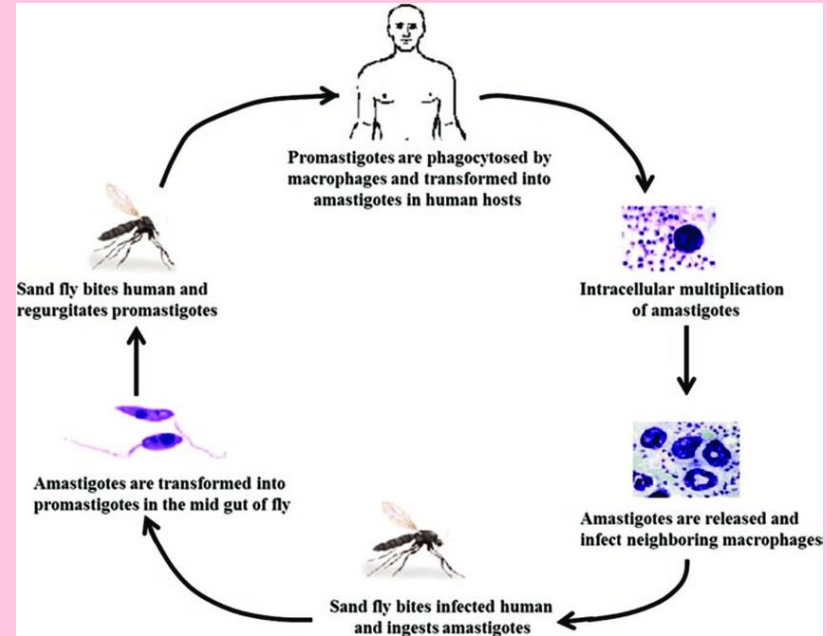


Fig: Amastigote of L.donovai

General Biology and Life Cycle

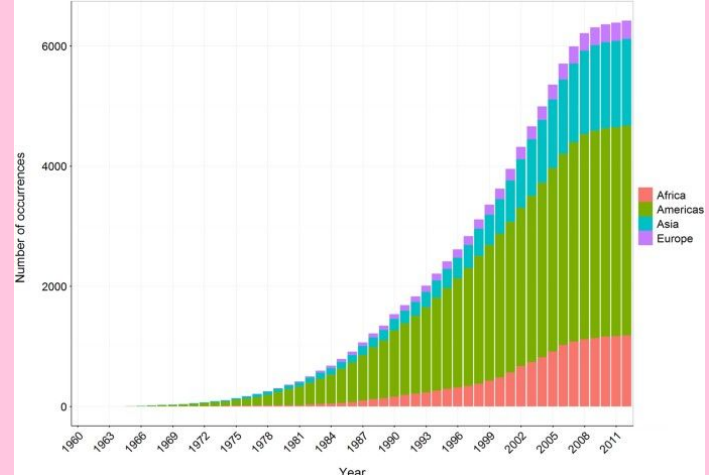
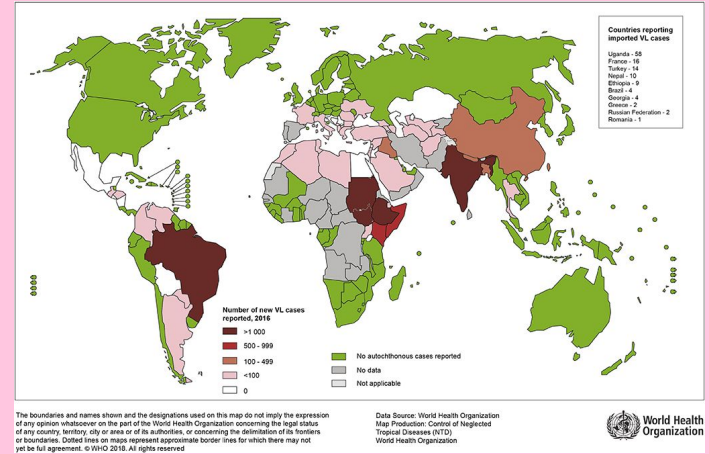
1. Sandfly takes a blood meal, infects human with promastigotes
2. Promastigotes phagocytosed by macrophage and transform into amastigotes
3. Amastigotes multiply
4. Macrophage bursts and amastigotes infect other macrophages
5. Sand fly bites and ingests amastigotes
6. Become promastigotes in the fly



Monsters Inside Me

Epidemiology

- Global distribution
- Mostly found in tropical and subtropical climates
 - India, Sudan, Bangladesh, Nepal, Brazil
- More infections:
 - In warmer months
 - Rainy season
 - Due to climate change
- Reservoir hosts



Pathogenesis

- Second deadliest parasitic disease, causes visceral leishmaniasis
- Incubation period can range from 10 days to 1 year
- Can be found in the spleen, bone marrow, liver, lymph nodes, intestine, etc.



Pathogenesis

Symptoms:

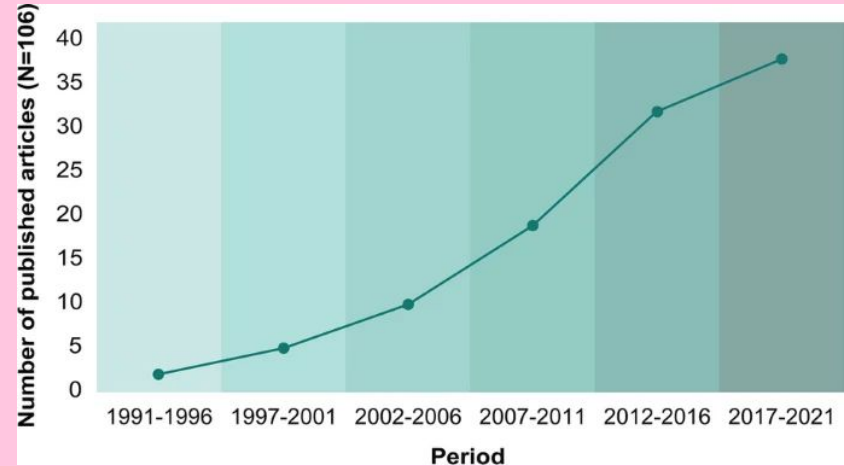
- Fever, vomiting, weakness, anemia
- Protrusion of the abdomen
 - Enlarged spleen, liver, bone marrow
- Weak inflammatory response
- Death in 1-2 years, can fluctuate



Pathogenesis

Severity of infection dependent on:

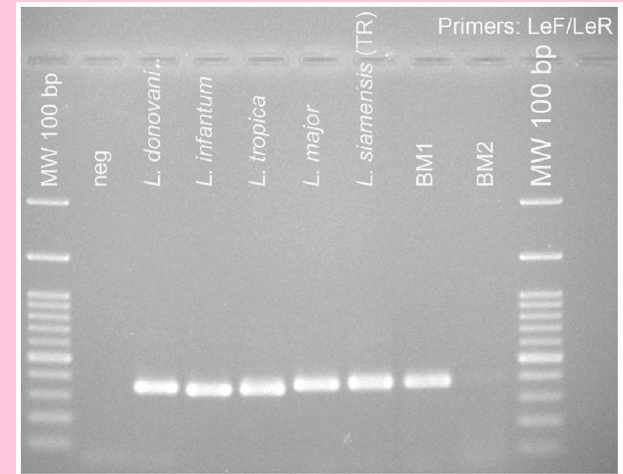
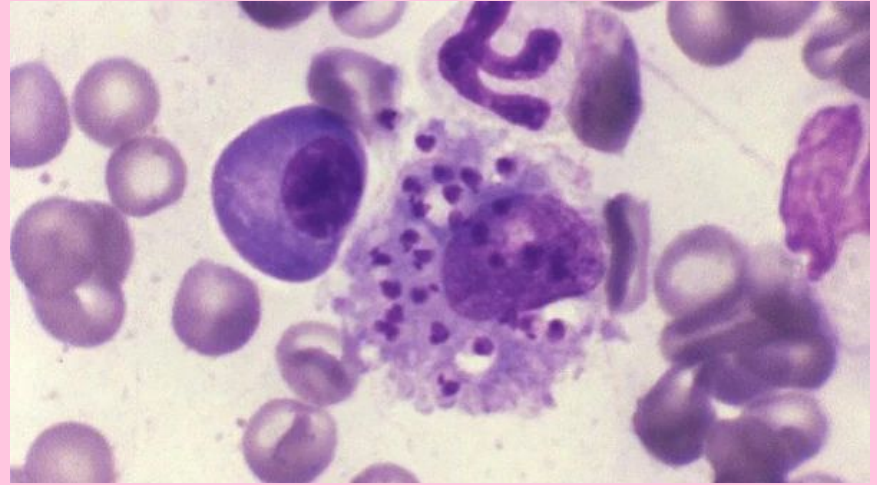
- Evading immune system
- Replication
- Temperature preference
 - $37^{\circ}\text{C} + (98.6^{\circ}\text{F} +) \rightarrow$ visceral leishmaniasis
- Asymptomatic cases are very prevalent



Country	Ratio
Sudan	1:2.4
Kenya	4:1
Ethiopia	5.6:1
Brazil	18:1
Spain	50:1
Bangladesh	4:1
India/Nepal	8.9:1

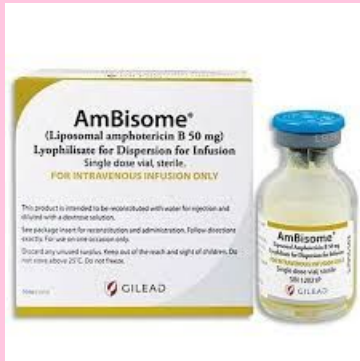
Diagnosis

- Bone marrow aspiration or biopsy is most common
 - Light microscopy of stained slides
 - Specialized culture techniques
 - Polymerase chain reaction (PCR)
 - Xenodiagnosis



Treatment

Liposomal amphotericin B vs. amphotericin B



Feature	Liposomal Amphotericin B (Ambisome)	Regular Amphotericin B (Deoxycholate)
Formulation	Encased in liposomes for better targeting	Free drug (not encapsulated)
Effectiveness	More effective , lower doses needed	Effective but requires higher doses
Toxicity	Lower toxicity , better tolerated	Higher toxicity , more damage to healthy cells
Side Effects	Milder (fever, chills possible)	More severe (strong infusion reactions)
Dosing	Lower doses , shorter treatment	Higher doses , longer treatment
Cost & Access	More expensive , limited availability	Cheaper , more widely accessible
FDA Approval for Leishmaniasis	FDA-approved	Not FDA-approved (but still used in some cases)



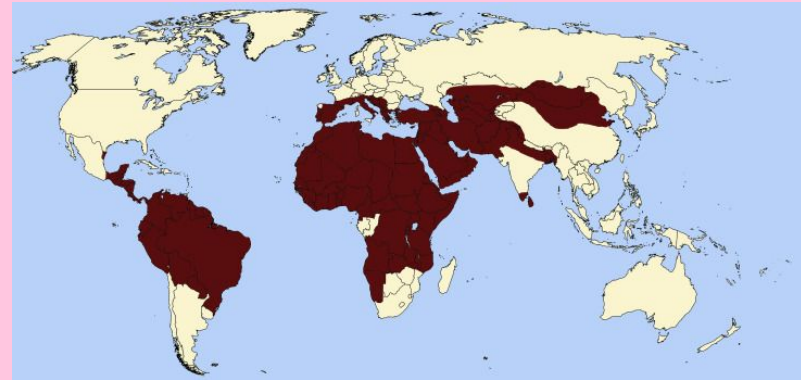
Treatment

- Miltefosine (oral)
- Pentavalent antimonials (IV, IM)
 - Decreasing usage
 - Cheaper and more accessible



Prevention

- Prevent possible exposure to sand flies:
- Stay in well screened and air conditioned areas
- Use bed nets in unprotected areas
- Wear protective clothing
- Use repellents
- Avoid nighttime outdoor exposure
- Safe traveling

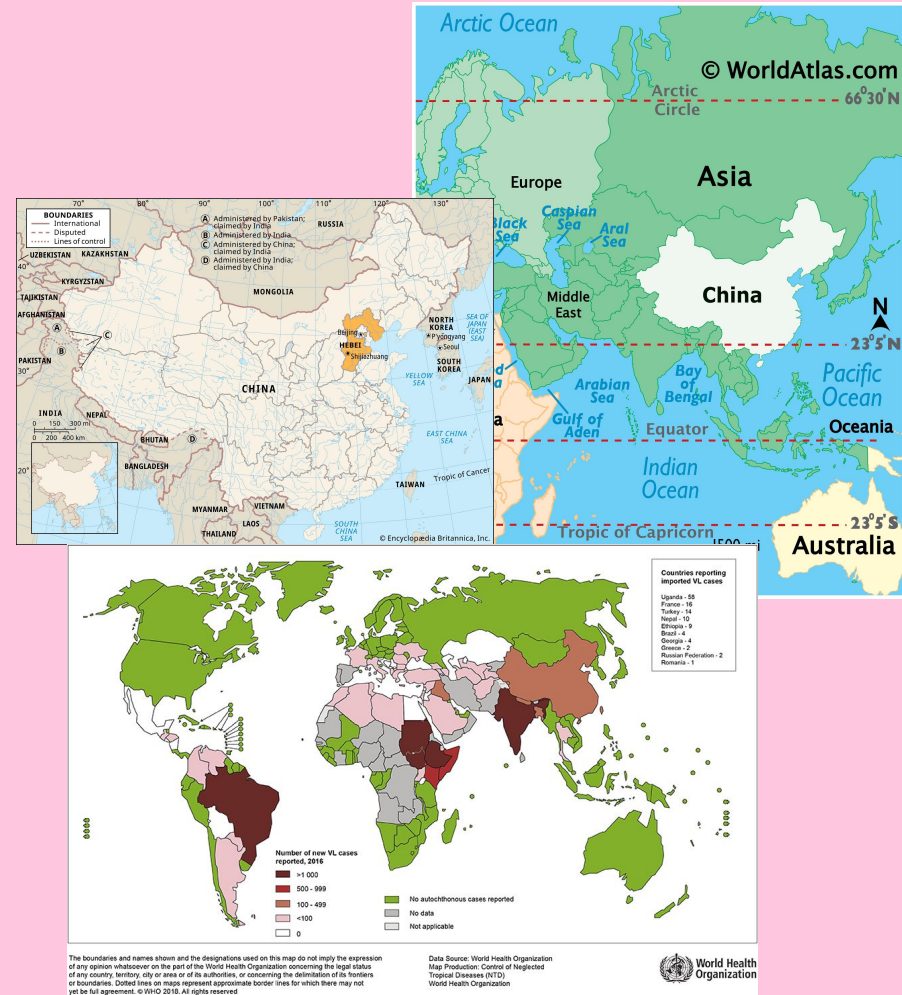


Case Study #1

- 68-year-old man from mountainous region in China

Patient presented with:

- Fever (102.2°F)
- Weight loss (about 22 pounds in 6 months)
- Sweating
- Fatigue
- Inability to walk



Case Study #1

Labs from initial visit: February 16th

Blood Component	Patient's Value	Normal Range	% Lower than Normal
Hemoglobin (Hgb)	92 g/L (9.2 g/dL)	130–177 g/L	29.2% lower
White Blood Cells (WBC)	$1.35 \times 10^9/\text{L}$	$3.5\text{--}9.5 \times 10^9/\text{L}$	61.4% lower
Platelets (PLT)	$21 \times 10^9/\text{L}$	$125\text{--}350 \times 10^9/\text{L}$	83.2% lower

Low Hgb (Anemia): weakness, fatigue

Low WBC (Leukopenia): weakened immune system

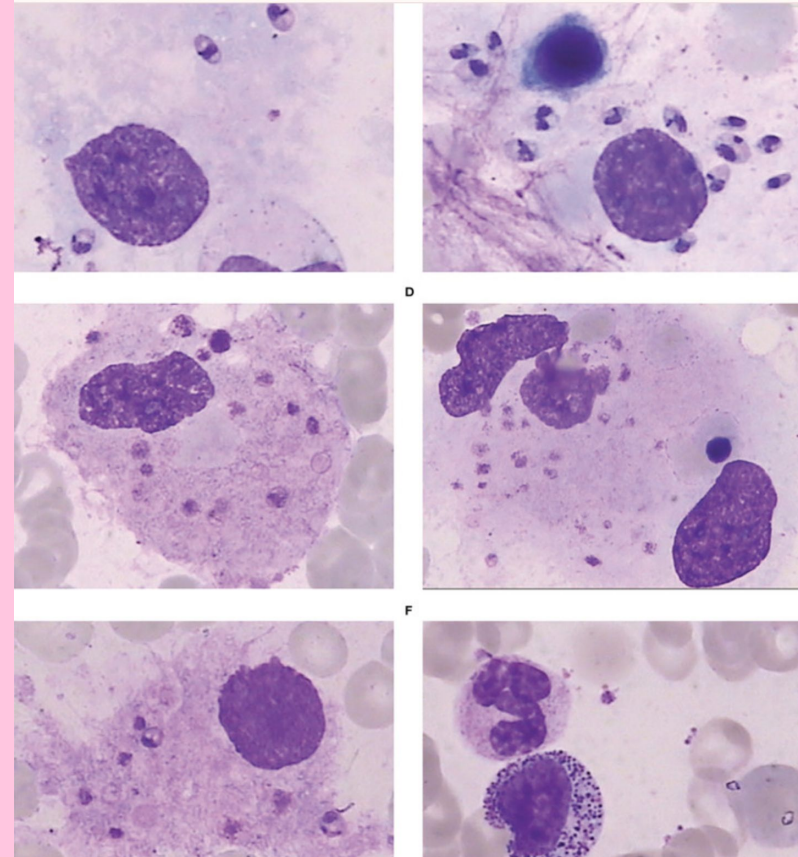
Low PLT (Thrombocytopenia) : trouble clotting if injury were to occur

Found *Leishmania donovani* in bone marrow smear

Case Study #1

Bone marrow aspiration smear:

- Revealed granulocytopenia and megakaryocyte maturation disorder
- Bone marrow dysfunction
 - Pancytopenia
 - Lack of immune cells (neutrophils)
 - Bleeding tendencies (low platelets)

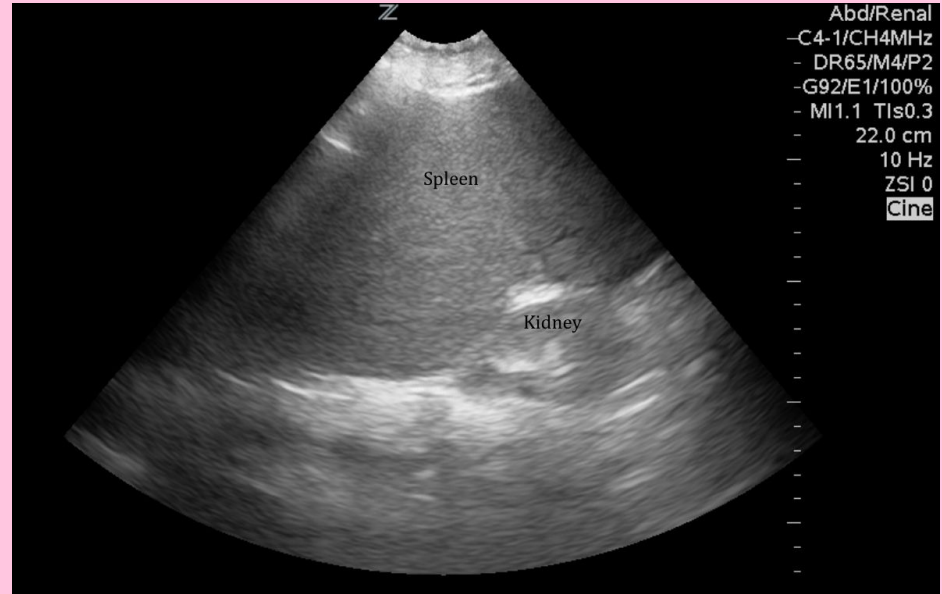


Case Study #1

Findings from an Abdominal
Ultrasound:

- Enlarged spleen (splenomegaly)
- No tumors, cysts, or masses in liver, gallbladder, or kidneys
 - Organ damage due to infection and inflammation

5 days after admission: *L. donovani*
and secondary hemophagocytic
lymphohistiocytosis (HLH)



Case Study #1

Treatment:

- Amphotericin B (5 mg/day, IV)
- Dexamethasone sodium phosphate injection (10mg/day, IV)
 - HLH

Discontinued amphotericin B:

- “6 day plan” of antimony sodium gluconate
 - 6ml/day, IM → condition improved



Case Study #1

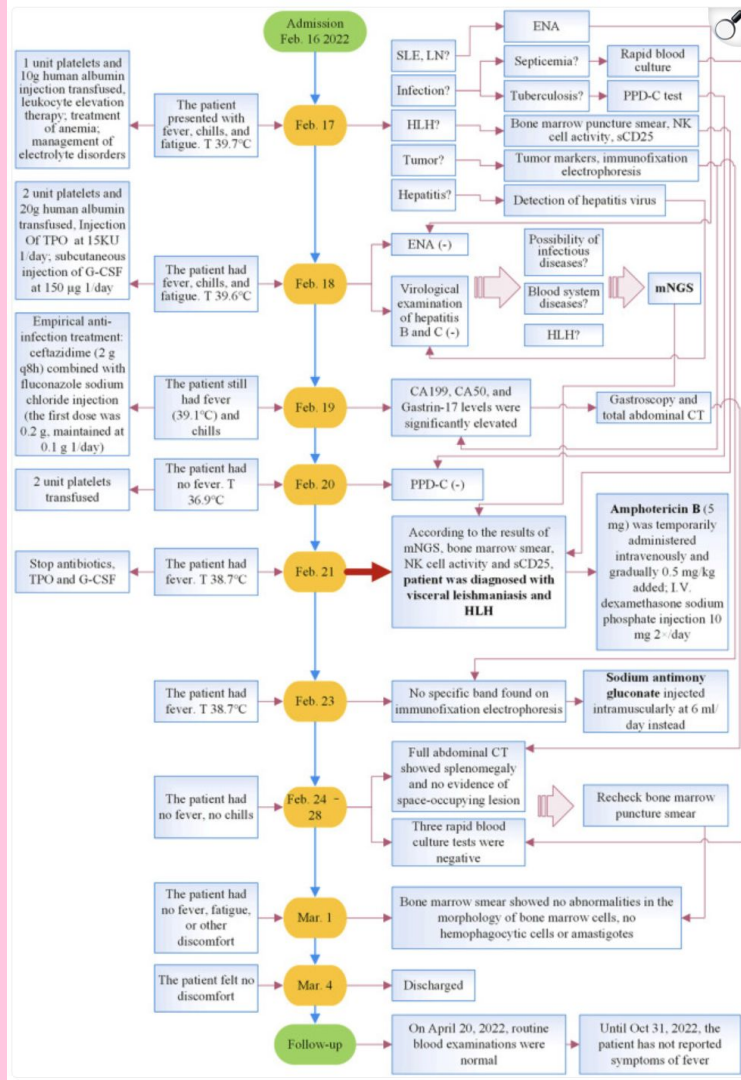
March 1, 2022: Bone marrow puncture showed no abnormalities

March 4, 2022: Patient was discharged

April 20, 2022: Follow-up visit

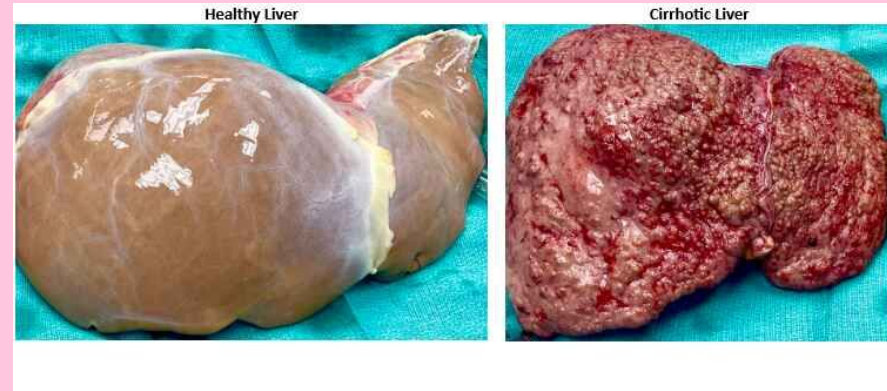
Blood Component	Patient's Value (Feb 16th)	Patient's Value (Apr 20th)	Normal Range
Hemoglobin (Hgb)	92 g/L (9.2 g/dL)	96 g/L (9.6 g/dL)	130–177 g/L
White Blood Cells (WBC)	$1.35 \times 10^9/\text{L}$	$8.3 \times 10^9/\text{L}$	$3.5\text{--}9.5 \times 10^9/\text{L}$
Platelets (PLT)	$21 \times 10^9/\text{L}$	$196 \times 10^9/\text{L}$	$125\text{--}350 \times 10^9/\text{L}$

Timeline of patient's admission to discharge



Case Study #2

- 57-year-old man that underwent a liver transplant for alcohol-related liver disease and portal hypertension, following 2 years of sobriety
- Patient was born in Wales, UK
- Has only traveled outside of the UK 15 years prior to Calais, France



Case Study #2

Transplant:

- Received transplant from brainstem death donor
- 2-day ICU stay, later he was placed on immunosuppressive therapy
- 1 month post transplant:
 - Acute cellular rejection (ACR), given pulsed steroids for three days

Case Study #2

4 months post transplant:

- Developed pancytopenia → reduced medication due to side effects
- Neutropenia worsened
 - Developed fever, chills, shivering
- Admitted to local hospital with neutropenic sepsis and an acute kidney injury → transferred to liver transplant center

Case Study #2

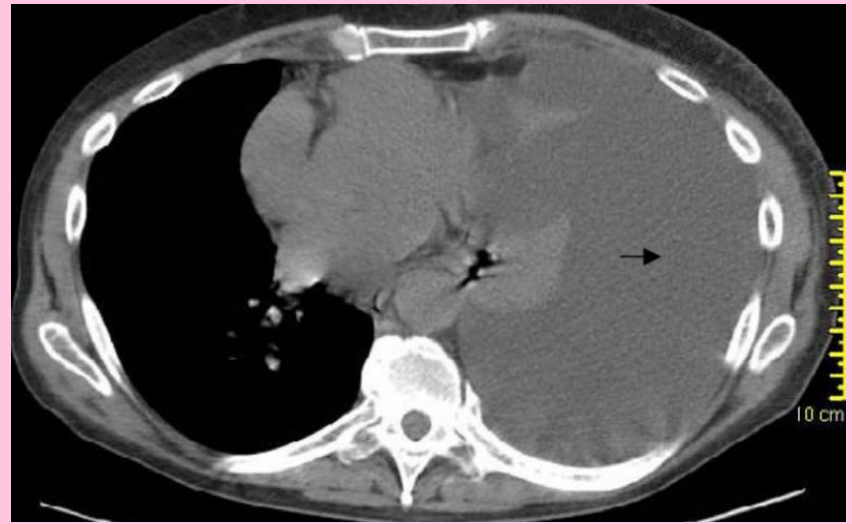
Test findings:

Blood work:

- Iron deficiency (anemia)

Computed Tomography (CT) scan results:

- Enlarged spleen, pleural effusion along right side of body
 - Inflammation → increase permeability of blood vessels
→ fluid leaks into pleural space



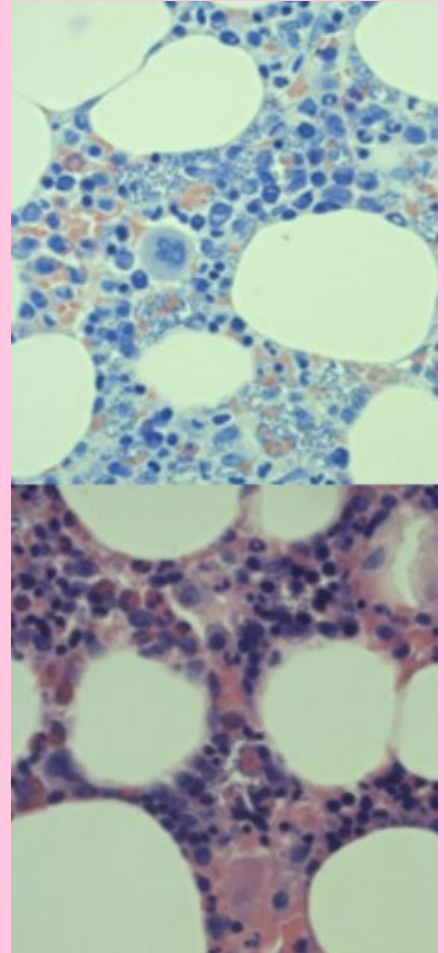
Case Study #2

Bone marrow aspirate test:

- Amastigotes present

Polymerase Chain Reaction (PCR) results:

- Bone marrow PCR was positive for *L. donovani*
- Blood PCR was negative for *L. donovani*



Case Study #2

Treatment:

- Liposomal amphotericin B (4 mg/kg) via IV for 21 days to treat VL
- After 6 days of treatment → ongoing infection, overactive immune response
- Fever settled and his pancytopenia gradually improved
- Remained on medication for immunosuppression

Case Study #2

Outcome:

- The donor had travelled to India in the year preceding his death, most likely contracted the parasite here
- Emphasizes the importance for wider differential diagnosis in post transplantation patients

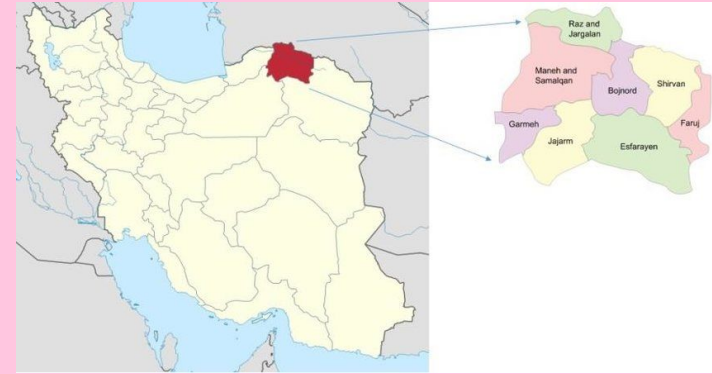


Case Study 3

- 36-year-old woman from North Khorasan Province, Bojnurd, Iran

Patient presented with:

- Fever
- Weight loss (66-88 lbs)
- Fatigue
- Abdominal pain and swelling
- No medical history, no history of immigration



Case Study #3

Blood test:

- Anemia and leukopenia

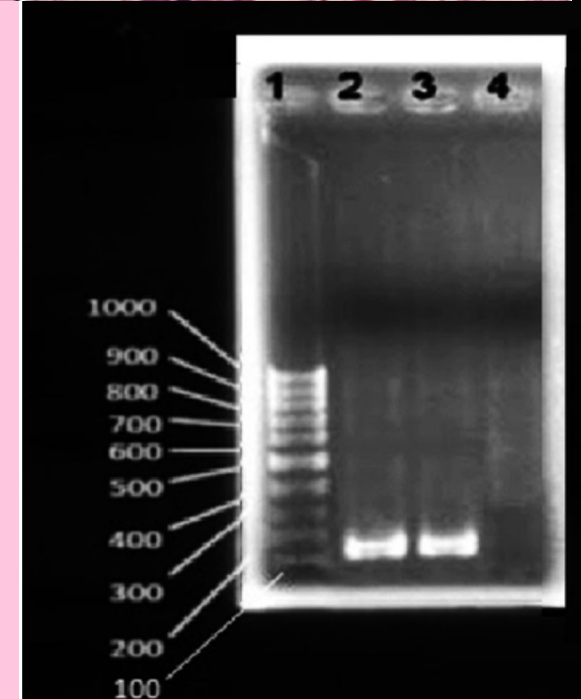
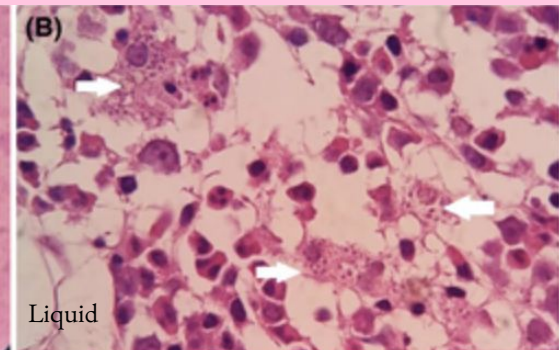
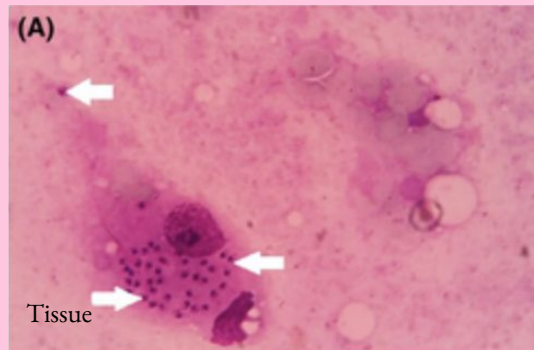
Ultrasound:

- Splenomegaly and mild hepatomegaly

Bone marrow aspiration and biopsy

- Presence of *L. donovani* amastigotes

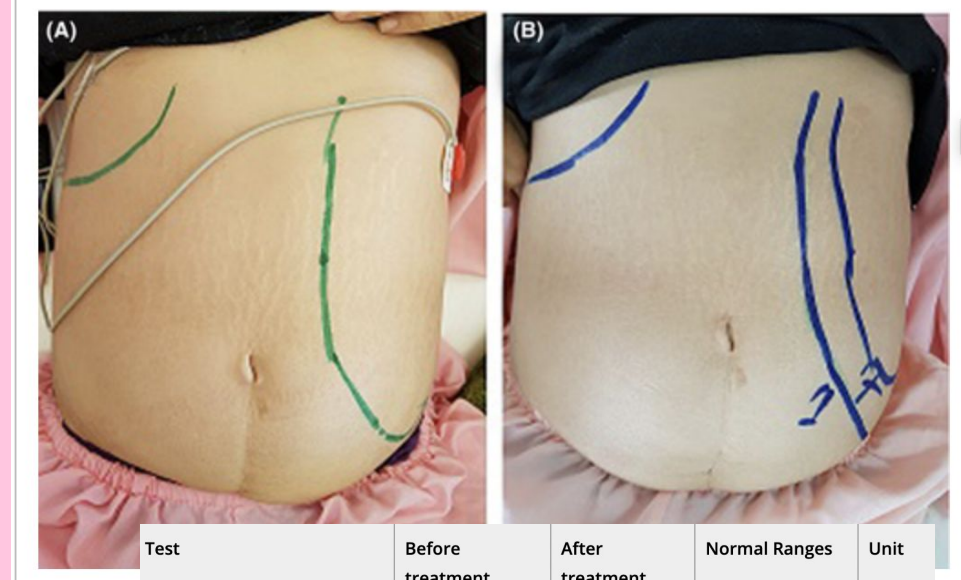
PCR testing → Confirmed *L. donovani* causing VL



Case Study #3

Treatment:

- Liposomal amphotericin B
1mg/kg for 1 month
- Symptoms gradually subsided and general condition improved



Test	Before treatment	After treatment	Normal Ranges	Unit
WBC	1.2	14.9	4-11	$10^3/\mu\text{L}$
RBC	2.35	4.50	3.8-5.1	$10^6/\mu\text{L}$
Hemoglobin	5.5	13.4	12-16	g/dL
Hematocrit	17.4	40.9	35-47	%
MCH	21.3	29.8	27-35	U/L
MCHC	28.7	32.8	31-37	U/L
neutrophil	39	79.5	35-38	%
Lymphocytes	47	14.4	18-44	%
Monocytes	19	6.1	4.7-12.5	%
Platelet count	58	228	150-440 10^3	mm

Question from Case Study #1

What two organs of the body did the parasite infect in order to cause pancytopenia?

Answer from Case Study #1

Bone marrow and spleen

Question from Case Study #2

Through PCR testing, what sample from the body was *Leishmania* found in?

Answer from Case Study #2

Bone marrow

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