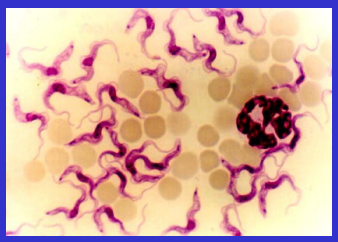
BioMedical Parasitology

Blood flagellates



Prof Peter O'Donoghue

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PROTOZOA

65,000 species

(31,250 extant + 33,750 extinct)

flagellates	amoebae	sporozoa	ciliates
6,900 species	**11,550 species**	**5,600 species**	**7,200 species**
5,100 free-living 1,800 parasitic	11,300 free-living 250 parasitic	all parasitic	4,700 free-living 2,500 parasitic

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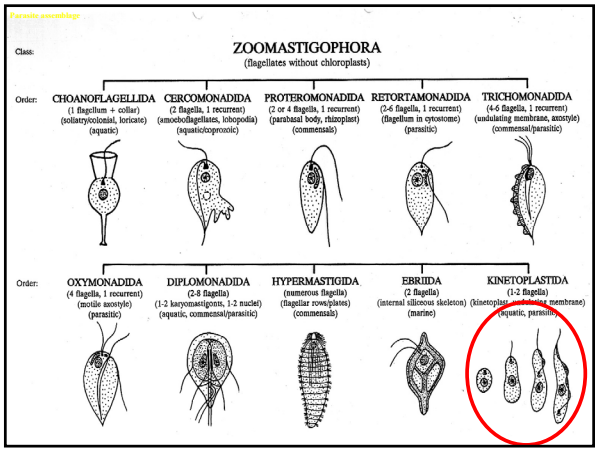

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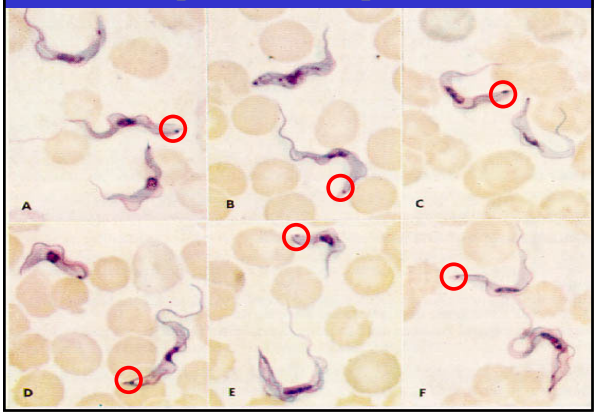
Kinetoplastids = trypanosomes



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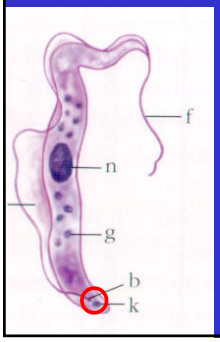
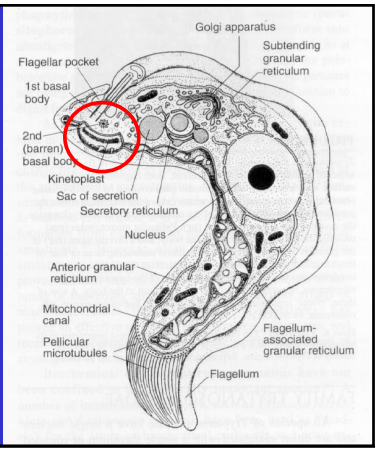
Parasite morphology

Kinetoplastids extranuclear DNA





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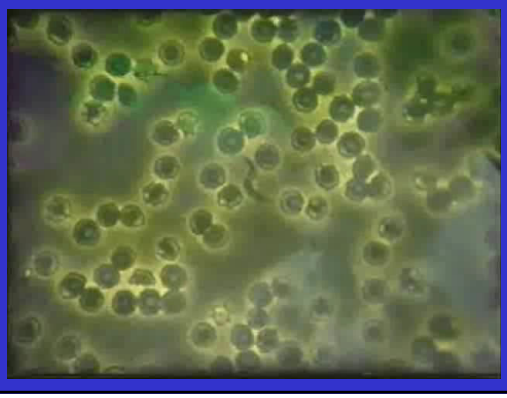
Trypanosomes



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Parasite morphology

Mastigotes

invertebrate gut	vertebrate host: tissue	vertebrate host: blood	invertebrate gut
			
P	A	T	E
promastigote	amastigote	trypomastigote	epimastigote
Leishmania/sandfly/kala azar		*T. brucei*/tsetse fly/sleeping	
		T. cruzi/reduviid bug/Chagas	

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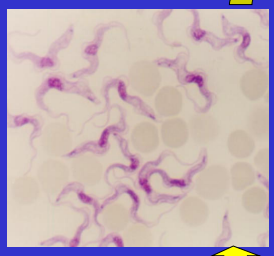
Parasite problem

Trypanosoma brucei

Old World/African trypanosomiasis



trypomastigotes — salivarian transmission — tsetse fly

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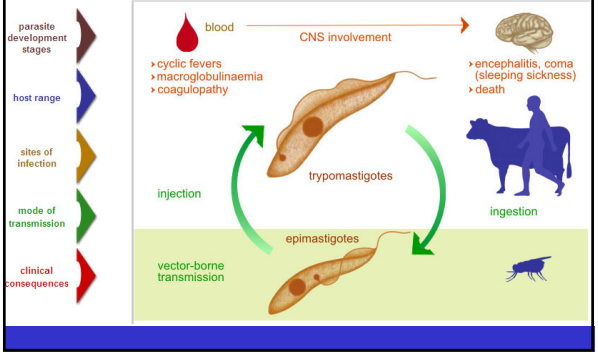
Parasite life-cycle

Trypanosoma brucei (Protozoa: Kinetoplastida)



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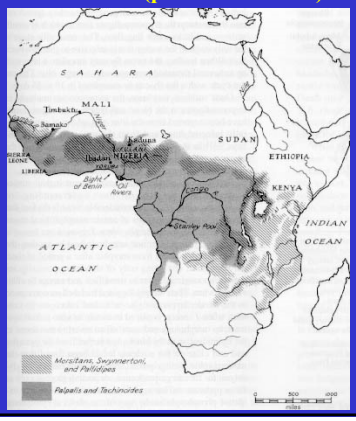
Parasite biodiversity

Distribution (parasite + vector)



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Parasite pathogenesis

Sleeping sickness

- trypanosomes multiply in plasma and interstitial fluid
- cyclic fevers due to parasite destruction
- antigenic variation results in macroglubulinaemia
- microvascular damage
- coagulopathy
- perivascular inflammation
- penetrate blood-brain barrier
- encephalitis
- coma

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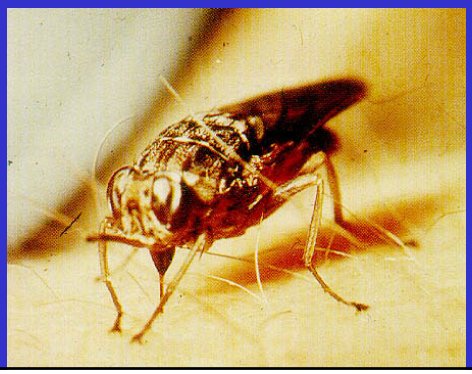
Tsetse fly

salivarian transmission



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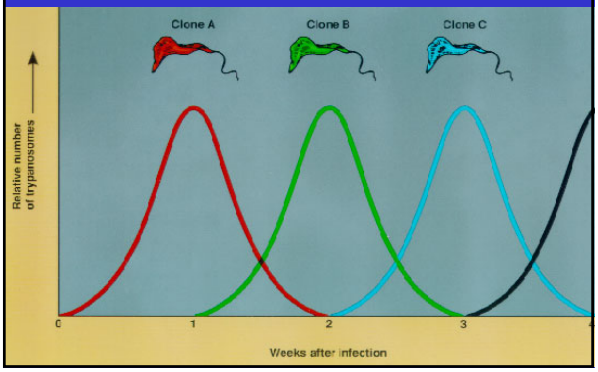
Parasite pathogenesis

Recurrent parasitaemia



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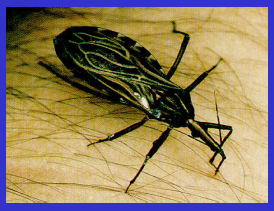
Parasite problem

Trypanosoma cruzi
New World/American trypanosomiasis



amastigotes — stercorarian transmission — reduviid bug

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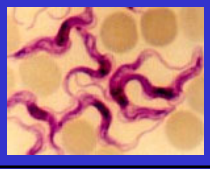
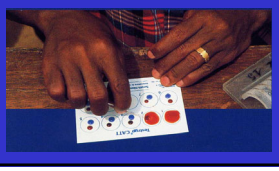
Parasite diagnosis

Diagnosis

- symptomatology (nonspecific symptoms/signs)
- direct detection (blood, bone marrow, CSF)
- *in vitro* cultivation (variable success)
- *in vivo* inoculation (variable success)
- indirect indication
  - immunoserology (antibody tests)
  - molecular characterization (PCR amplification)





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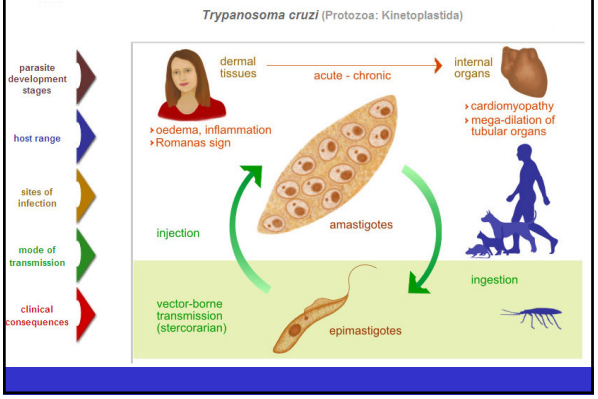
Parasite life-cycle



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Parasite management

Treatment

<u>acute</u>

- suramin (anionic urea)
- pentamidine (aromatic diamine)

<u>chronic</u> (CNS signs)

- melarsoprol (arsenical)
- trypursamide (arsenical)
- eflornithine (sub. amino-acid)

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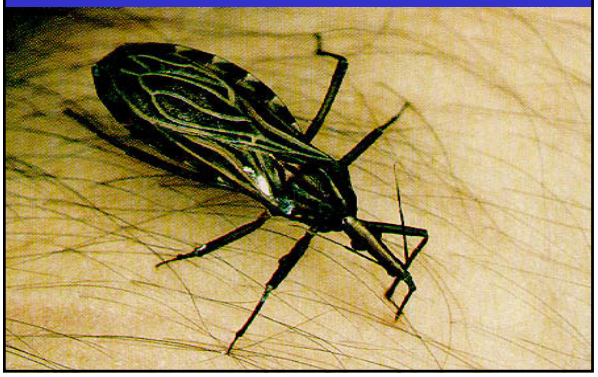
Reduviid bug (assassin bugs)
stercorarian transmission



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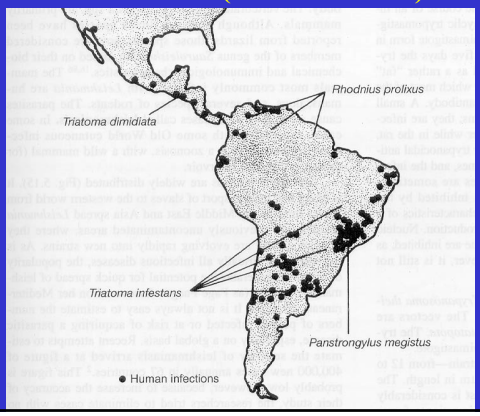
Parasite biodiversity

Distribution (mirrors vector)



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Parasite pathogenesis

Chagas disease

chronic infections
amastigotes throughout tissues

- cardiomyopathy
- myositis
- 'megasyndrome' dilation of tubular organs (esp. oesophagus and colon)

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Parasite pathogenesis

Chagas disease

acute clinical signs
amastigotes multiply in tissues

- Romana's sign (unilateral orbital oedema)
- inflammation
- fever
- hepatosplenomegaly
- lymphadenopathy
- cardiac arrhythmia

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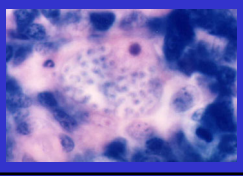
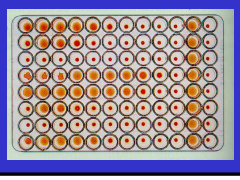
Parasite diagnosis

Diagnosis

- symptomatology (nonspecific symptoms/signs)
- direct detection (blood, lymph, CSF, biopsy)
- *in vitro* cultivation (nutrient agar-blood)
- *in vivo* inoculation (lab. mice)
- indirect indication
  - immunoserology (antibody tests)
  - molecular characterization (PCR amplification)





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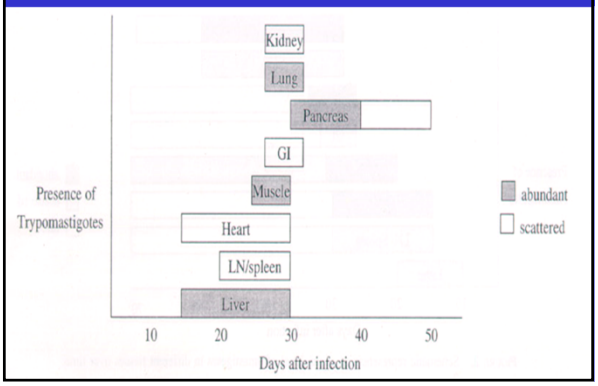
Tissue trophism



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Parasite management

Treatment

few drugs effective (parasites hidden)

acute infections

- nifurtimox (nitrofuran derivative)
- benznidazole (2-nitroimidazole)
- allopurinol (purine analog)

(all with adverse side-effects)

chronic infections

- surgical repair?

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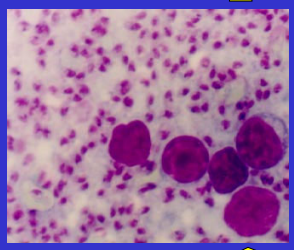
Parasite problem

Leishmania spp.
cutaneous/visceral leishmaniasis



amastigotes — vector transmission — sand flies

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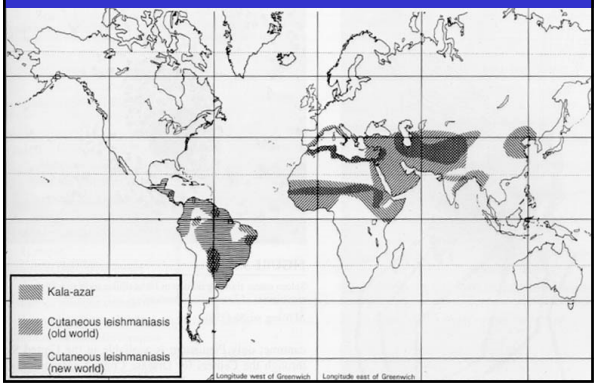
Parasite biodiversity

Leishmania spp. distribution



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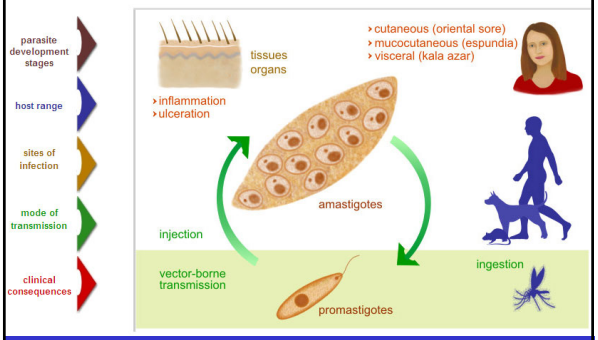
Parasite life-cycle

Leishmania spp. (Protozoa: Kinetoplastida)



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Parasite pathogenesis

Leishmaniasis

Three types of clinical disease

- cutaneous/oriental sore (*L. tropica/mexicana*)
  skin lesions, sores, ulceration
- mucocutaneous/espundia (*L. braziliensis*)
  destructive nasopharyngeal lesions
- visceral/kala azar (*L. donovani*)
  hepatosplenomegaly, oedema, anaemia

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Sandflies
Phlebotomus/Lutzomyia Old/New World

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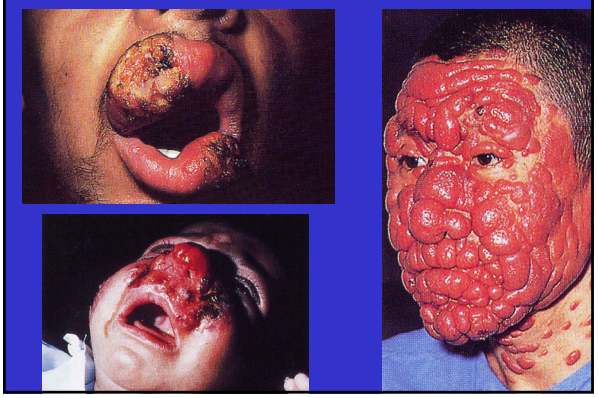
Parasite pathogenesis

Leishmaniasis



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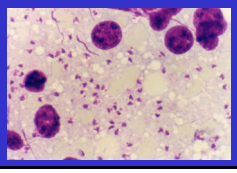
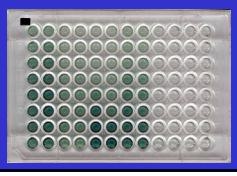
Parasite diagnosis

Diagnosis

- symptomatology (nonspecific symptoms/signs)
- direct detection (biopsy tissues/smears/secretions)
- *in vitro* cultivation (nutrient agar-blood)
- *in vivo* inoculation (variable success)
- indirect indication
  - immunoserology (antibody tests)
  - molecular characterization (PCR amplification)





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Parasite management

Treatment

Cutaneous lesions exhibit 'self-cure'

Vaccination through 'leishmanization'

Visceral/mucocutaneous lesions require systemic therapy

- pentavalent antimonials
- macrolide antibiotics
- aminoglycoxide antibiotics
- aromatic diamidine

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Summary - trypanosome diseases

T. brucei	*T. cruzi*	*Leishmania*
sleeping sickness	Chagas disease	kala azar
tsetse fly	reduviid bug	sandfly
salivarian transmission	stercorarian transmission	salivarian transmission

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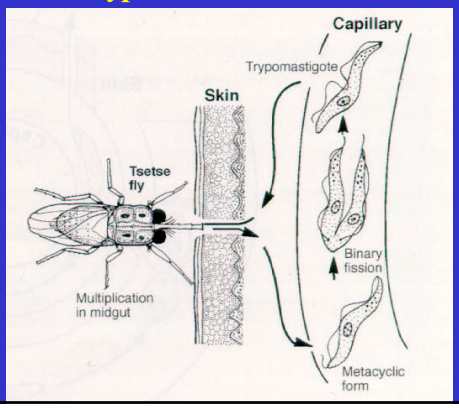
Trypanosoma brucei



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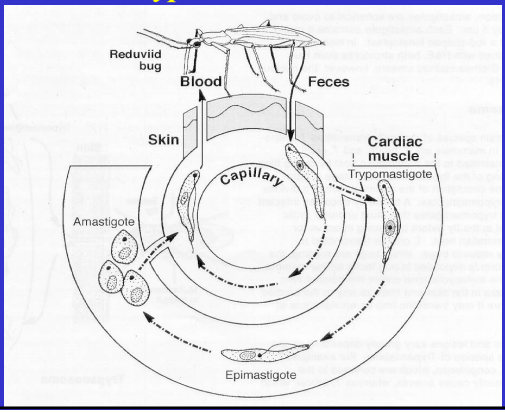
Trypanosoma cruzi



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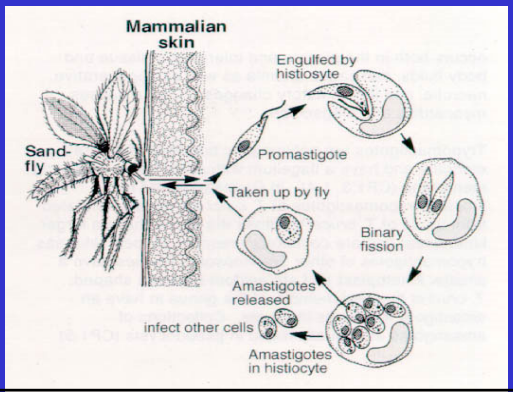
Leishmania spp.



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