

Kinetoplastids Handout

Kinetoplastids

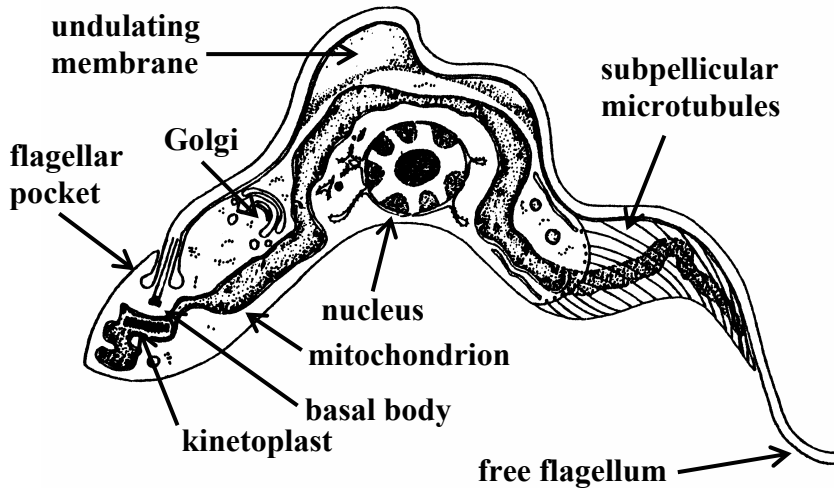
- widespread group of flagellated protozoa
- parasitize virtually all animal groups as well as plants and insects
- 3 distinct kinetoplastid species cause human disease (see box)
- distinguishing feature is **kinetoplast**:
 - a staining body distinct from and smaller than the nucleus
 - found near the base of the flagellum
 - previously believed to be associated with the flagella and cell movement
 - (basal body can also be seen sometimes near the kinetoplast)
 - actually a distinct region of the mitochondria and staining is due to mitochondrial DNA
 - existence of extranuclear DNA (ie, organellar DNA) was first demonstrated in the kinetoplastids.

Disease Causing Kinetoplastids

- *Trypanosoma brucei* complex
African sleeping sickness
- *Trypanosoma cruzi*
Chagas' disease
- *Leishmania* species
leishmaniasis

Kinetoplastid DNA

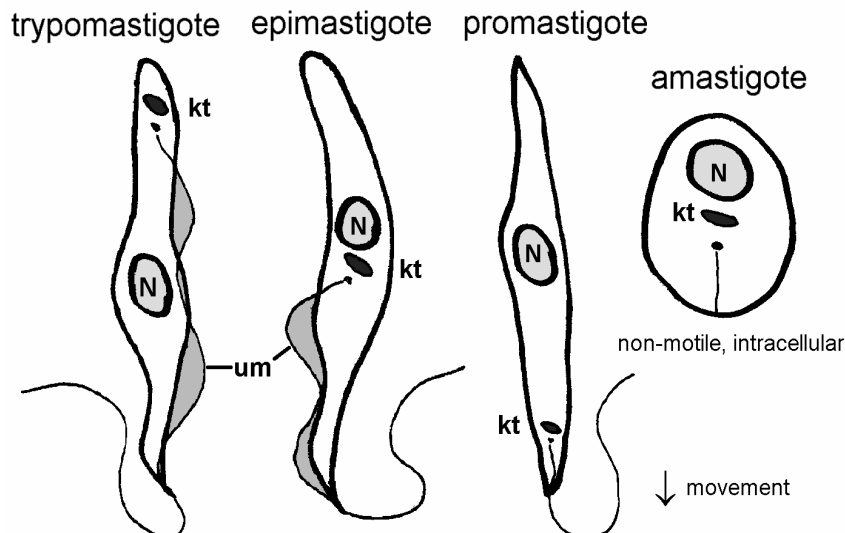
- relatively abundant
- concatenated mass of mini-circles and maxi-circles
- maxi-circles = mitochondrial DNA
 - few copies
 - encode several mitochondrial genes
- mini-circles
 - many copies
 - heterogeneous and rapidly evolving
 - function is less clear
- both encode guide RNA genes
 - some genes on the maxi-circles have 'errors'
 - guide RNAs are important for RNA editing
 - extent of editing seems to correlate with different parasite life cycle stages and the changes that occur in mitochondrial respiration associated with the different life cycle stages
- mini-circle DNA is also used for parasite detection and typing



Morphological Forms

- the various kinetoplastid species exhibit different morphological forms
- the different forms are distinguished by the position of the kinetoplastid in relation to the nucleus and the presence or absence of an undulating membrane
- four major forms found in kinetoplasts causing human disease are:

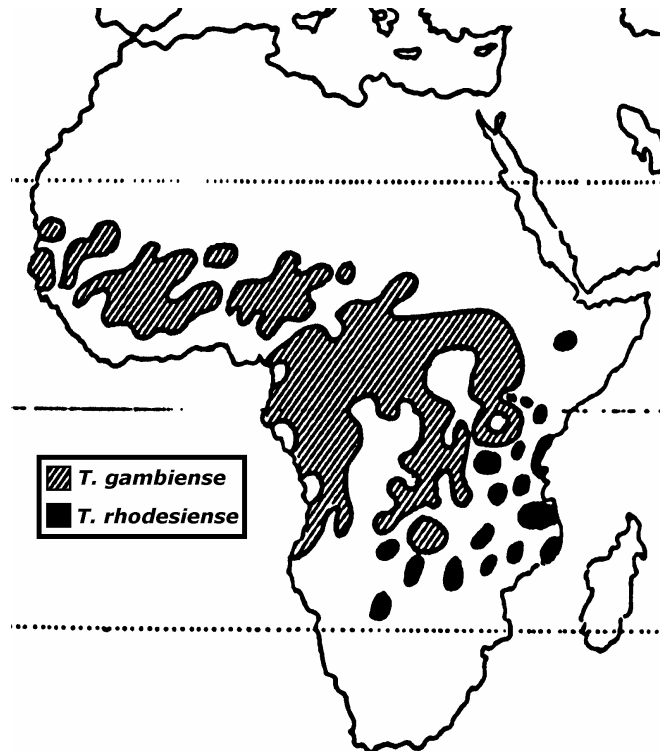
trypomastigote	The kinetoplastid is located posterior to the nucleus, usually on the most posterior end. The flagella folds back along the body of the parasite forming an undulating membrane which runs the entire length of the organism.
epimastigote	The kinetoplastid is more centrally located, usually just anterior to nucleus. This results in a shorter undulating membrane.
promastigote	The kinetoplastid is between the nucleus and the anterior end and no undulating membrane is formed.
amastigote	This form is found as an intracellular stage. The parasite is more rounded and has no flagella. The kinetoplast is still detectable.



African Trypanosomes

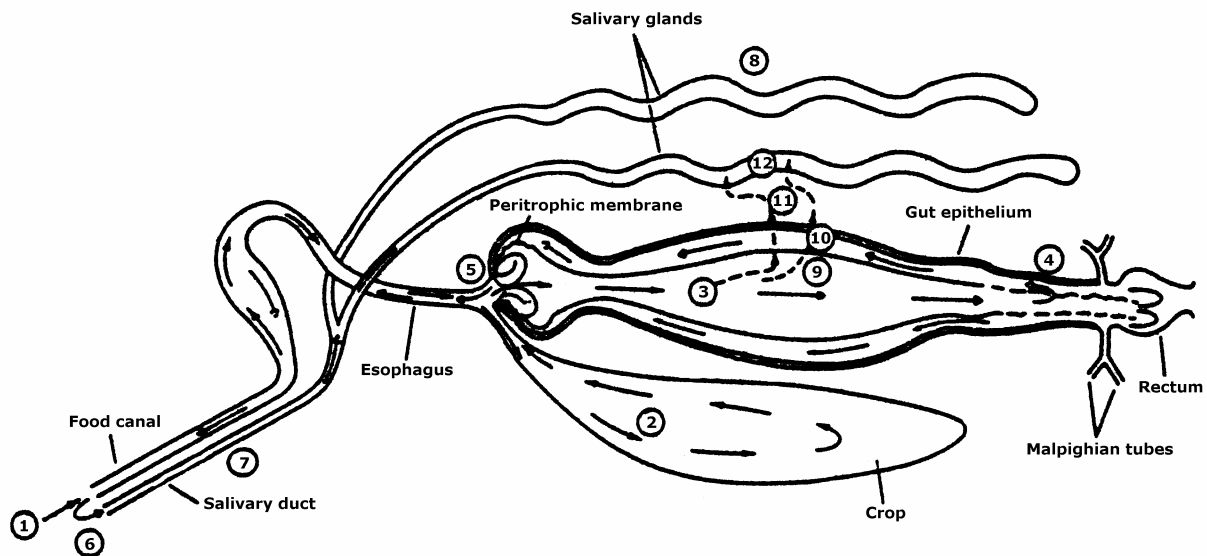
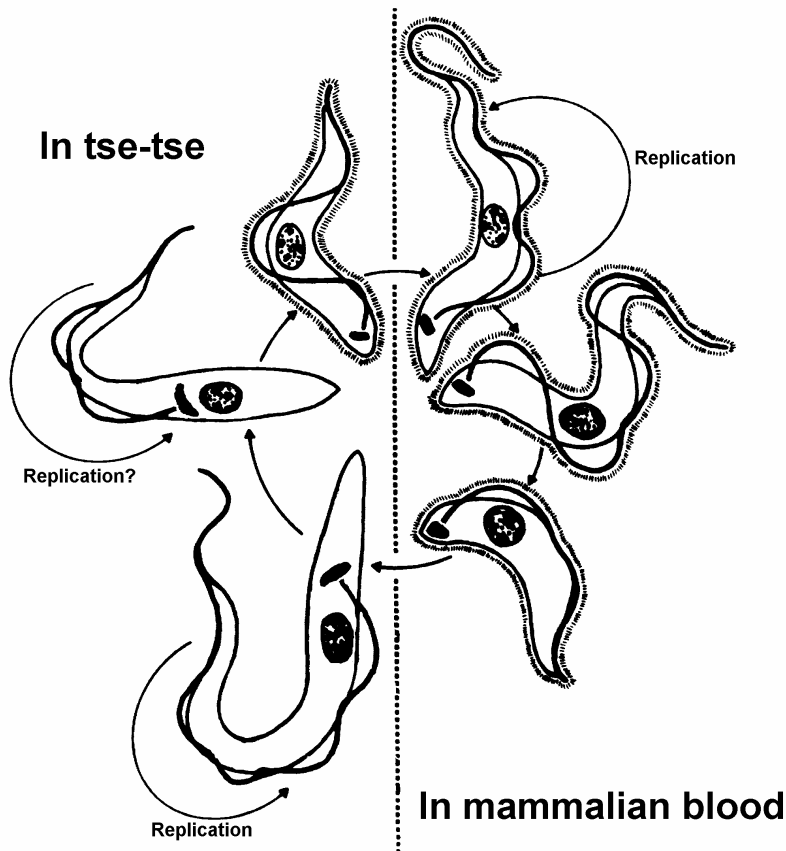
Trypanosoma brucei Species Complex

Subspecies	Disease
<i>Trypanosoma brucei brucei</i>	game animals/livestock (nagana)
<i>Trypanosoma brucei rhodesiense</i>	East African trypanosomiasis
<i>Trypanosoma brucei gambiense</i>	West and Central African sleeping sickness



Comparison of *T. brucei* Subspecies

	<i>rhodesiense</i>	<i>gambiense</i>
tse-tse vector	<i>G. morsitans</i> group	<i>G. palpalis</i> group
ecology	dry bush or woodland	rainforest, riverine, lakes
transmission cycle	ungulate-fly-human	human-fly-human
non-human reservoir	wild animals	domestic animals
epidemiology	sporadic, safaris	endemic, some epidemics
disease progression	rapid, often fatal	slow (~1 yr) acute → chronic
parasitemia	high	low
asymptomatic carriers	rare	common



Blood-stream forms of African trypanosomes are taken up during tse-tse feeding. Trypanosomes pass through the food canal (1) and crop (2) in route to the midgut (3). The blood meal is surrounded by the peritrophic membrane. To complete the life cycle the trypanosomes must migrate to the salivary glands. One possible route is to escape from the peritrophic membrane at its posterior extremity (4) and move forward through the proventricular valve (5) and esophagus. Upon leaving the food canal (6) the trypanosome could migrate up the salivary duct (7) to the salivary gland (8). An alternative and more direct route would be to penetrate the peritrophic membrane (9) and the midgut epithelium (10) and escape into the hemocoel (11). The trypanosomes would then directly penetrate the salivary glands (12). It is not clear which of these routes (or both) is used.

AFRICAN TRYPANOSOMIASIS SUMMARY

I. Disease course and symptoms

- A. A local inflammatory nodule known as a trypanosomal chancre is sometimes at formed at the site of the tse-tse bite.
- B. The typical incubation period is 1-2 weeks.
- C. The acute disease is characterized by trypanosomes in the blood and irregular fever and headache. *T. rhodesiense* can develop into a fulminating and often fatal infection, whereas *T. gambiense* exhibits a variety of manifestations including self-limiting, slowly progressing or fulminating.
- D. Disease progression is often characterized by invasion of lymphatics. Lymphatic stage symptoms can include: enlarged lymph nodes (particularly post-cervical group), weight loss, weakness, rash, itching, edema, and continued intermittent febrile attacks.
- E. Parasites crossing the blood-brain barrier result in CNS involvement and nervous impairment. Described as a progressive meningoencephalitis. Indications of nervous impairment include: apathy, fatigue, confusion, somnolence, and motor changes such as tics, slurred speech, and incoordination.
- F. Continued CNS impairment results in convulsions or coma leading to death.

II. Diagnosis

- A. Travel or residence in endemic area
- B. History or scar of 'trypanosomal chancre'
- C. Fever and enlarged lymph nodes (particularly posterior cervical)
- D. Behavioral changes/mental symptoms
- E. Serological tests
- F. Demonstration of trypanosomes in blood, lymph node aspiration, or spinal fluid especially during fever.

III. Treatment

- A. Suramin or pentamidine is recommended during early acute stage without CNS involvement. Prognosis is excellent.
(Eflornithine, an ornithine decarboxylase inhibitor, is an effective anti-trypanosomal drug. However, it is expensive and the standard treatment is 14 consecutive daily injections. Phase III clinical trials with an oral formulation are currently underway.)
- B. Melarsoprol or tryparsamide is recommended during chronic stage with CNS involvement.

IV. Prophylaxis and control

- A. Prophylactic drugs are contraindicated (mask infections and toxicity).
- B. Insect repellents and vector avoidance.
- C. Control activities include: surveillance and treatment, traps, insecticides, and habitat alteration.

ANTIGENIC VARIATION

