**African Trypanosomiasis**

Synonyms include: *African/Gambian/Rhodesian sleeping sickness, human African trypanosomiasis (HAT)*

Human African trypanosomiasis is endemic in sub-Saharan Africa. The disease is caused by infection with the gambiense and rhodesiense subspecies of the extracellular parasite *Trypanosoma brucei*, and is transmitted to humans by bites of infected tsetse flies.\(^1\)

The disease evolves in two stages, the haemolymphatic and meningo-encephalitic stages, the latter being defined by central nervous system infection after trypanosomal traversal of the blood-brain barrier. African trypanosomiasis leads to severe neuro-inflammation and is fatal without treatment.\(^1\)

- *Trypanosoma brucei rhodesiense* (East African or Rhodesian African sleeping sickness). This is more virulent, with deaths often occurring within months. It is a zoonotic infection with animal vectors, primarily game animals (waterbuck, hartebeest, reedbuck, duiker and antelope).
- *Trypanosoma brucei gambiense* (West African or Gambian African sleeping sickness). Man is the main reservoir, through its chronic form with long latency period, although animals can act as reservoirs but evidence is scanty. Only small numbers of tsetse flies have been shown as necessary to maintain endemic transmission cycles at relatively high levels.

African trypanosomiasis is almost invariably spread by bites from infected tsetse flies, but it is rarely transmitted by blood transfusion, or across the placenta. The latter is rare because the disease causes infertiltiy and abortion in women of child-bearing age. The rhodesiense form is a zoonosis, with occasional infection of humans. In the gambiense form, humans are regarded as the main reservoir that plays a key role in the transmission cycle of the disease.\(^2\)

- The tsetse fly is found only in Africa and comprises three groups of species, *Glossin fusca* (or forest tsetse) is of little significance to man, *G. palpalis* (or riverine tsetse) is responsible for the transmission of *T. gambiense*, and *G. morsitans* (or savannah tsetse) is predominantly a vector of *T. rhodesiense*.
- Tsetse flies are fastidious in terms of conditions and satellite imaging techniques can be used to map potential transmission foci. They are not infected easily, but infection is lifelong (one to six months) and they produce only six to eight larvae in a lifetime.
- Both male and female flies feed by cutting through the skin, rupturing small blood vessels and feeding on the pool of blood formed, intermittently ejecting saliva, with metacyclic trypanosomes if infected.
- The trypanosomes display antigenic variation in successive generations during host infection. This enables persistence of infection, immune exhaustion, penetration of the central nervous system (CNS) and eventual death.

**South American sleeping sickness (or Chagas’ disease)** is a totally different disease with a different pathogen and different treatment.

**Epidemiology**

- Over the period of a decade, increased public health control efforts in the major endemic countries in sub-Saharan Africa have resulted in the reduction of cases from 300,000-500,000 cases to approximately 50,000-70,000 cases. However, 17,000 new cases still occur annually.\(^3\)
- East African sleeping sickness occurs in most countries in East Africa, including Kenya, Tanzania, Malawi, Zambia and Mozambique. They usually report fewer than 200 cases each per year but Uganda may have 1,000 or more. The World Health Organization (WHO) says that infection covers a total of 36 countries in sub-Saharan Africa.\(^4\)
West African sleeping sickness is endemic around waterholes and river areas in Western and Central Africa. The Democratic Republic of Congo reports about 20,000 cases a year, Angola about 2,000 and north western Sudan around 1,500 cases. Senegal, Gambia, Guinea Bissau, Sierra Leone and Ghana do not report any cases, but about 200 to 300 cases are recorded annually in the Ivory Coast, Guinea, Nigeria and Uganda.

In recent decades, those infected from non-endemic countries are older, and more likely to be tourists who acquired the disease while visiting game parks in East and Southeast Africa.\[6\]

Sleeping sickness claims comparatively few lives annually, but the risk of major epidemics means that surveillance and ongoing control measures must be maintained.\[6\]

Presentation

Stage 1
This is the early or haemolymphatic stage. It occurs about three weeks after the bite.

Symptoms tend to be nonspecific, including:

- General malaise.
- Intermittent fever.
- Myalgia.
- Headache.
- Pruritus, urticaria and facial oedema which sometimes occur.

Signs include:

- A painless, indurated chancre on the skin appears 5 to 15 days after the bite (although this may be absent if the fly has fed from a large enough blood vessel without needing a ‘pool’, the organism going straight into the circulation).
- Lymphadenopathy: axillary and inguinal lymphadenopathy are more prominent in patients with the East African disease whilst cervical lymphadenopathy is more usual in the West African type. The classical Winterbottom’s sign is a clearly visible, enlarged, firm and rubbery, mobile, non-tender gland of the posterior cervical triangle.
- Fevers, tachycardia, irregular rash, oedema and weight loss.
- Multiple organs, including spleen, liver, skin, cardiovascular, endocrine and eyes may be affected.

Stage 2
This is late or CNS stage and is of insidious onset.

Symptoms include:

- Continuous headaches with a poor response to analgesics.
- Daytime somnolence then nocturnal insomnia with upset of the circadian rhythm.\[7\]
- Behavioural changes with mood swings and sometimes depression.

Signs include:

- In East African sleeping sickness, CNS signs appear early, presenting in weeks to a month with the two stages merging, whereas West African sleeping sickness has a more gradual onset with CNS symptoms taking months to a year.
- Anorexia, wasting and weight loss.
- Irritability, tremors, and increased muscle tone are usual signs; sometimes ataxia or hemiparesis occurs, but rarely meningism.
- Kerandel’s sign is deep hyperaesthesia, often delayed, after a slight blow on a bony projection of the body (the tibia is often quoted).
- Behavioural changes such as mania or psychosis with speech disorders and seizures. Seizures occur in children but rarely in adults.
- Stupor and coma (hence the name sleeping sickness).
Differential diagnosis

- **Malaria**: where inappropriate antimalarial treatment reduces the fever of sleeping sickness and where the two diseases may co-exist.
- **HIV infection**.
- **Borrellosis**.
- **Brucellosis**.
- **Leishmaniasis**.
- **Toxoplasmosis**.
- **Typhoid fever** and other enteric fevers.
- Other causes of lymphadenopathy, such as tuberculosis, cancer and other causes of acute confusional state (eg, meningitis).

Investigations

Blood tests may show:

- Anaemia and thrombocytopenia. There is no eosinophilia.
- Hypergammaglobulinaemia and a raised ESR.
- Hypoalbuminaemia.

A wet smear of unstained blood or, if more sensitivity is required, a Giemsa-stained thick smear of blood will look for mobile trypanosomes.

More sensitive tests are now available. The haematocrit centrifugation technique for buffy coat examination and the miniature anion-exchange centrifugation technique filter out the red cells but not the trypanosomes.

The standard serological test for West African trypanosomiasis is the card agglutination test for trypanosomiasis (CATT). The CATT can be performed in the field. [8]

Other tests include:

- Lymph node aspirate is often used in a rapid test for parasites.
- Lumbar puncture should be performed. [9] CNS disease can present early in East African trypanosomiasis.
- CSF is examined for trypanosomes, elevated WBC count, elevated IgM and elevated total protein levels. CSF examination by PCR for trypanosome DNA has been used.
- Classically, diagnosis requires detection of trypanosomes in lymph nodes but they can be found in blood, CSF, skin chancre aspirates, or bone marrow.
- In rural Africa, giving chemotherapy to produce symptomatic improvement is often used to confirm the diagnosis.

Management

- Care before hospital admission involves management of the acute symptoms of fever and malaise while closely monitoring the neurological condition.
- Control of the airway may be required to prevent aspiration.
- In severe disease where CNS complications and coma occur, intensive care is needed while treatment is administered.
- Potential adverse effects from drugs require monitoring of haematological, renal and hepatic function.

Drugs [10, 11, 12]

The four current anti-trypanosomiasis drugs have major disadvantages that limit their use:

- Pentamidine and suramin are limited by their effectiveness against the only first stage of *Trypanosoma brucei gambiense* and *Trypanosoma brucei rhodesiense*, respectively.
- Melarsoprol and eflornithine (two second-stage drugs) each have disadvantages:
  - Melarsoprol is toxic and has increasing treatment failures.
- Eflornithine is expensive, difficult to administer and lacks efficacy against *Trypanosoma brucei rhodesiense*.

- Melarsoprol's toxicity and decreasing efficacy mean phasing out the drug as a frontline treatment against *Trypanosoma brucei gambiense* is now possible with the emergence of effective, safe combination chemotherapies such as nifurtimox-eflornithine combination treatment (NECT).

Drug resistance is an increasing problem. However, new drugs are in the pipeline for treatment of CNS human African trypanosomiasis, giving rise to cautious optimism.

### Follow-up

- Following recovery from stage 2 disease, a lumbar puncture is required every three months for the first year in patients with East African disease and every six months for two years in patients with West African disease.
- Relapse has occurred if symptoms return, CSF pleocytosis appears, or if trypanosomes are still present in blood or CSF. A persistently elevated CSF white cell count can be found in recovering patients, so a change in white cell count is more helpful as an indicator of relapse.
- If relapse occurs, treatment with melarsoprol or eflornithine should be repeated.

### Complications

- Anaemia and fatigue.
- Wasting syndrome.
- Meningoencephalitis with seizures.
- Stupor or coma (sleeping sickness).
- Death occurs in untreated disease.

### Prognosis

- African trypanosomiasis is fatal if not treated.
- In early or stage 1 disease, most patients recover fully with treatment.
- In late or stage 2 disease, the CNS disease will be fatal if untreated but the cure rate approaches 95% with drugs that cross the blood/brain barrier, such as melarsoprol.
- Treatment usually resolves symptoms and clears parasites on repeat blood smears.
- Previous infection does not grant future immunity.

### Prevention

Elimination will not be achieved without vast improvements in field diagnosis for both forms of sleeping sickness, especially if there is a hidden reservoir of 'chronic carriers'.

- Treatment of asymptomatic carriers is possible and infection can be detected by CATT or node aspirate and confirmed with smears.
- There is no vaccine.
- There is no effective prophylaxis.
- Wear protective clothing of dull colours and use bed nets in areas with tsetse flies.
- Insect repellent is less effective than with other insect-borne diseases.
- Avoid areas where African trypanosomiasis is endemic.

### Further reading & references

- Parasites A-Z; Centers for Disease Control and Prevention

4. African Trypanosomiasis Fact Sheet; World Health Organization
6. African Trypanosomiasis. Strategic direction. Overview and strategy for research; World Health Organization

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Author: Dr Colin Tidy
Peer Reviewer: Dr Adrian Bonsall

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