Parasitic Infections Affecting CNS and Special senses

Case Scenario

Patient presented with enlarged cervical lymph nodes, **hepato-splenomegaly**, fever and generalized weakness. The condition started when he went for a trip in **Africa**, where he was exposed to numerous **insect bites**. He had a history of having indurated painful **swelling** on his face before his complaints. Then, he suffered fever, chills, aches, night sweats, and nausea. After that he developed cognitive deterioration, ataxic gait and **sleepiness**.

What is the most likely parasitic diagnosis?

➢Parasitic Infections Affecting CNS :

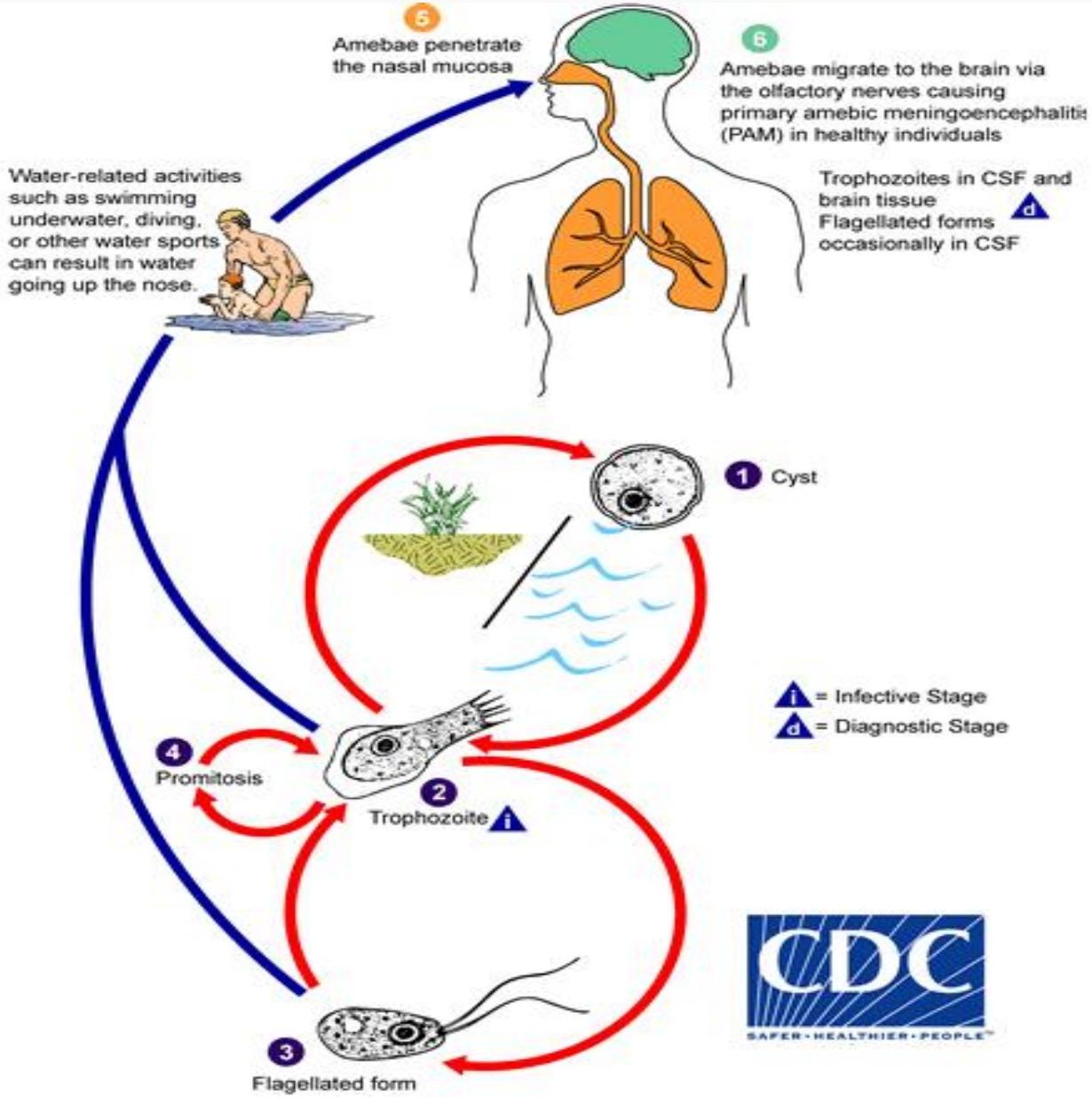
Free living amoeba:	• Primary Amoebic Meningoencephalitis • Granulomatous Amoebic Meningoencephalitis
***Trypanosoma bruci* :**	• Sleeping Sickness
Entamoebae histolytica	• Secondary Amoebic Cerebral Abscess
Taenia solium:	• NeuroCysticercosis

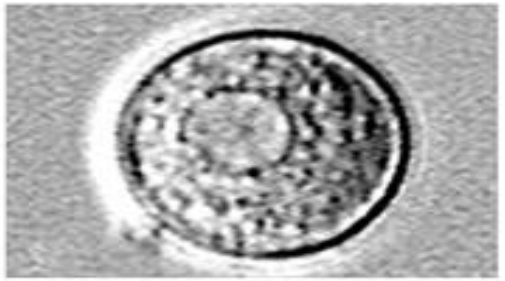
1) Pathogenic Free-Living Amoebae

1) *Naegleria fowleri*

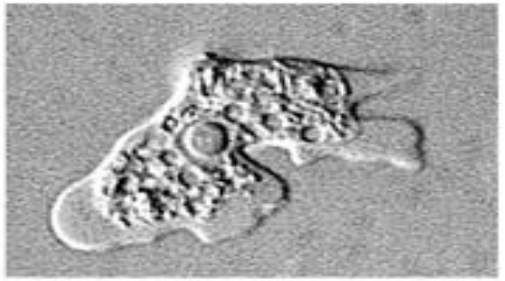
2) *Acanthamoeba castellani*

Naegleria fowleri Life cycle:

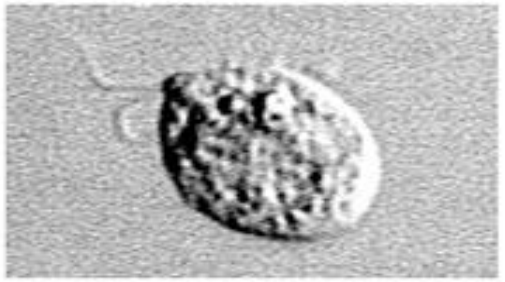




Cyst stage



Trophozoite stage



Flagellated stage

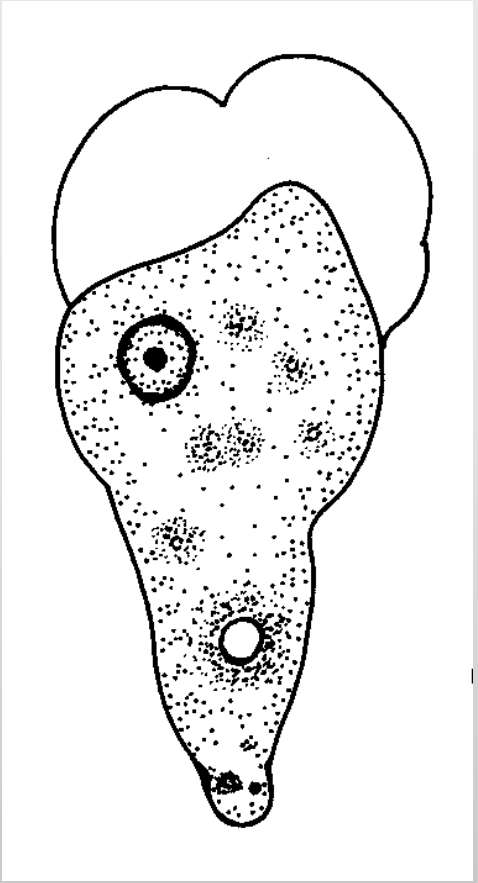
Naegleria fowleri Life cycle:

- Habitat:
- Free living in soil and fresh- stagnant water
- In man it attack CNS
- Infective stage: Amoeboid trophozoite
- Mode of infection: through Nasal route.

1- Swimming in /or sniffing contaminated water.

2- Inhalation of contaminated air.

➢ *Naegleria fowleri* morphological stage:



Amoeboid Trophozoite:

- (in tissues and CSF)
- Elongate with broad anterior end, tapering posterior end.
- with single pseudopodium.
- 15µ

Flagellate Trophozoite

- (when contact with water)
- Pear shaped
- two long equal flagellae

Cyst:

- Occurs in soil (never in tissues):
- Rounded
- 10 µm.

Pathogenesis of *Naegleria fowleri*

➢ Primary Amoebic Meningoencephalitis

- Amoeboid trophozoite is **neurotropic**, where it feeds on nerve tissue, by means of an **amoebostome**, resulting in significant necrosis and bleeding; causing **acute meningoencephalitis**.
- In the subarachnoid space, an inflammatory exudate of neutrophils and monocytes is seen.
- In **the white matter** of the brain and spinal cord, there is **demyelination** due to the production of **phospholytic enzyme** or enzyme-like substance by the growing amoebae

Clinical picture of *Naegleria fowleri*

➢ Acute meningoencephalitis:

- The course of PAM is dramatic and death usually occur after 3-6 days.

Prodromal symptoms (Stage I):

- severe frontal headache, fever, blocked nose. Then nausea and vomiting.

2- **Rapidly developing Signs of meningeal irritation (Stage II)**

- as stiffness of neck (Kering's sign).
- Fever, photophobia, seizures, altered mental status.

3- The patient become **irritable then lapse in coma** before dying.

Diagnosis of *Naegleria fowleri*

1-Clinical diagnosis: **History of swimming in lakes, few days before the disease.**

2- Laboratory diagnosis:

a- C.S.F. examination by lumbar puncture →

-- Amoeba (trophozoite) forms

-- CSF pressure is raised – Purulent. CSF protein is above 1gm/L.

-- marked raised cell count, mainly polymorph-nuclear cells

b- Culture of C.S.F. on non nutrient agar (with E. coli)

c- Intracerebral inoculation of mice

d- Molecular diagnosis

Treatment of *Naegleria fowleri*:

❑**Treatment:**

1- Hospitalization

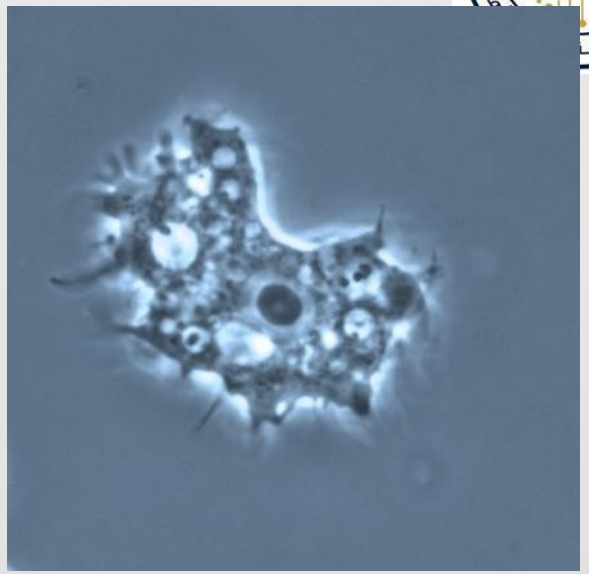
2- I.V. Amphotericin-B, Fluconazole and Rifampicin.

❑**Prevention and control:**

-Public education.

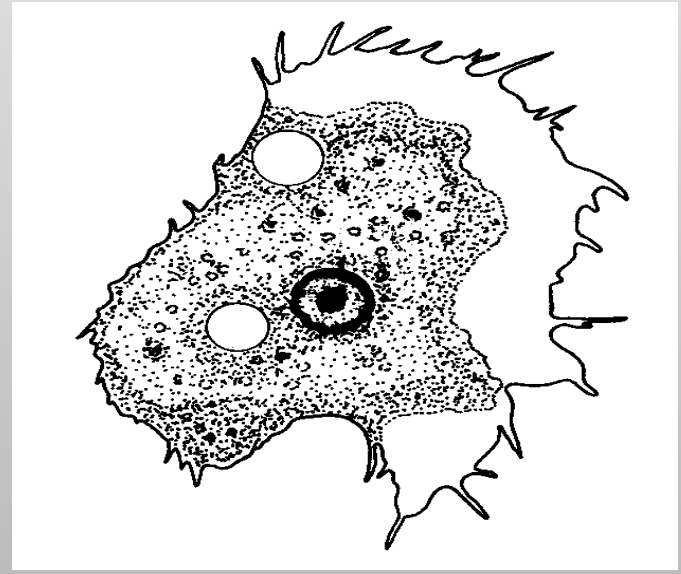
-Adequate chlorination of swimming pools and water supplies.

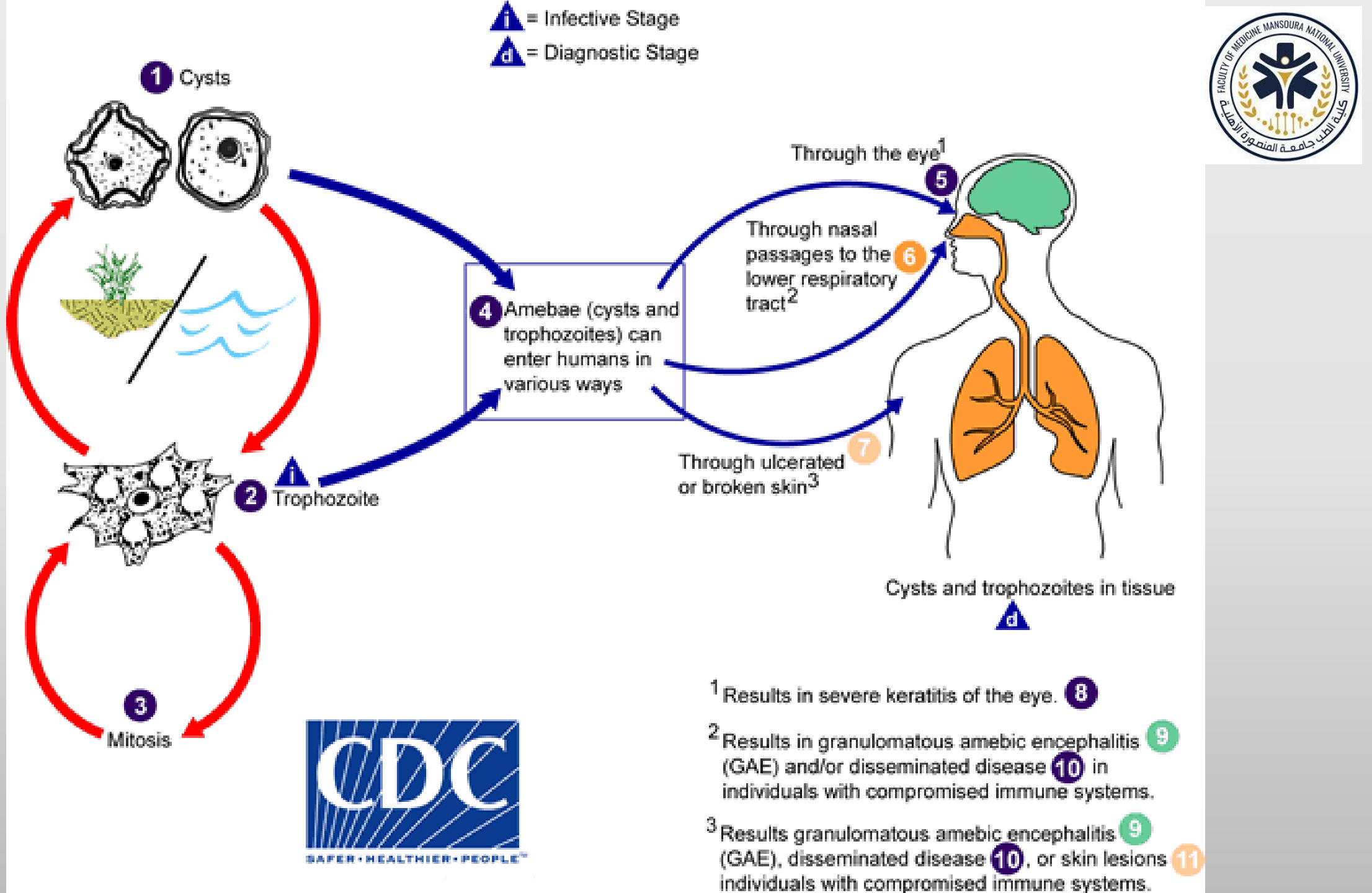
Acanthamoeba castellani



<u>Free-living trophozoite and cyst stages may exist in environment and in tissues</u>

- **Present in soil, dust, stagnant water and contact lens fluid.**
- **<u>in man it affect CNS, eye, skin and lungs.</u>**




i = Infective Stage
d = Diagnostic Stage
1 Cysts
2 Trophozoite
3 Mitosis
4 Amebae (cysts and trophozoites) can enter humans in various ways
Through the eye[1]
5
Through nasal passages to the lower respiratory tract[2]
6
Through ulcerated or broken skin[3]
7
Cysts and trophozoites in tissue
d
CDC
SAFER • HEALTHIER • PEOPLE™
[1] Results in severe keratitis of the eye. 8
[2] Results in granulomatous amebic encephalitis (GAE) and/or disseminated disease 10 in individuals with compromised immune systems. 9
[3] Results granulomatous amebic encephalitis (GAE), disseminated disease 10, or skin lesions 11 individuals with compromised immune systems. 9

Life Cycle of *Acanthamoeba castellani*

- **Habitat: free living in soil, stagnant water and dust.**

Or infect Human host (Brain, eye, skin)

- **Infective stage: Trophozoite & Cyst**
- **Source of infection: dust, stagnant water and contact lens fluid.**
- **Portal of entry (Mode of infection):**

  -Through skin and mucosal ulcers,

  -Inhalation into the lungs,

  -Through cornea (contaminated contact lenses)

Pathology & Clinical picture of *Acanthamoeba castellani*

(1)CNS: Granulomatous amoebic meningoencephalitis

- Haematogenous spread from the lungs or skin abrasions → focal granulomas as tumours (**space occupying lesions**).

- Infected tissues contain trophozoites, cysts and multinucleated giant cells.

- **The patient complains of headache, seizers, stiff neck, nausea and vomiting.**

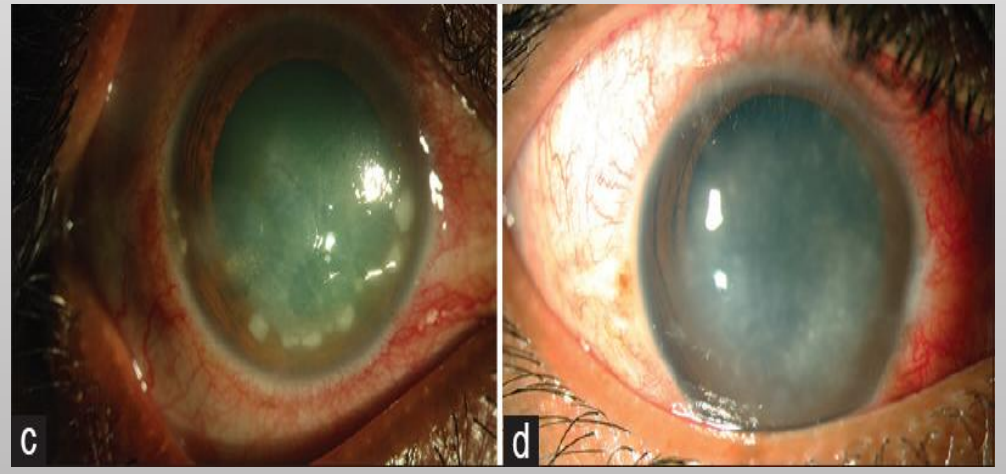
- Chronic course. Usually immunocompromised patient (opportunistic).

Clinical picture of Primary Amoebic Meningoencephalitis:

2) Eye: Amoebic keratitis. Infection occurs by direct contact of the cornea with contaminated water or contact lens.

-The disease is a chronic progressive ulcerative keratitis, characterized by severe unilateral ocular pain, photophobia, annular corneal infiltration, congested conjunctiva and loss of vision or even eye perforation may occur.

3) Chronic granulomatous skin lesions.



Diagnosis of *Acanthamoeba castellani*

a-CSF examination: Identification of trophozoites and cysts in brain tissues or CSF.

b- ***Culture of CSF*** on non-nutrient agar seeded with Escherichia coli.

c. ***CT scan*** of brain.

2. Amoebic keratitis: Corneal scrapings or histologic sections for detection of the organism by direct microscopy or after staining and culture

Treatment of *Acanthamoeba castellani:*

➢ **Treatment:**

CNS: Sulfamethoxazole/Trimethoprim+ Fluconazole and Rifampin.

➢ **Prevention and control:**

1) Health education.

2) Avoid swimming in stagnant water.

3) The use of proper contact lens solution.

4) Secondary Amoebic Cerebral Abscess

- Invasion of brain tissue by *Entamoeba histolytica* trophozoite (**Never cyst detected in tissue).**
- *E. histolytica* trophozoite inhabit large intestine then invasion of submucosal blood vessels may lead to spread of amoebae causing extra intestinal amoebiasis e.g. liver, lung, brain.
- It results in **secondary amoebic meningoencephalitis**, with severe destruction of brain tissue.
- It manifests as a brain tumor (Space-occupying lesion

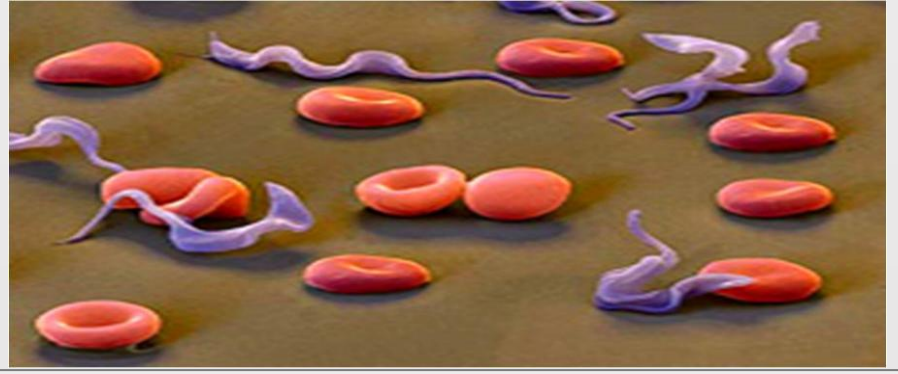
Mode of infection:

- Ingestion of mature quadrinucleated *E. histolytica* cysts (**infective stage**), in contaminated food or drink. Mechanical transmission by flies and cockroaches. Autoinfection: feco-oral route (hand to mouth contact)

4) Neurocysticercosis

- Invasion of CNS by the larval stage of *Taenia solium* (Cysticercus cellulosa).
- In this case man acts as an intermediate host.
- Mode of infection:
- Ingestion of food or water contaminated by the **eggs (Infective stage) of *Taenia solium***.
- Autoinfection either:
- a- External autoinfection: Feco-oral.
- b- Internal autoinfection: antiperistaltic movements of intestine leads to regurgitation of the gravid segments from small intestine to the stomach.

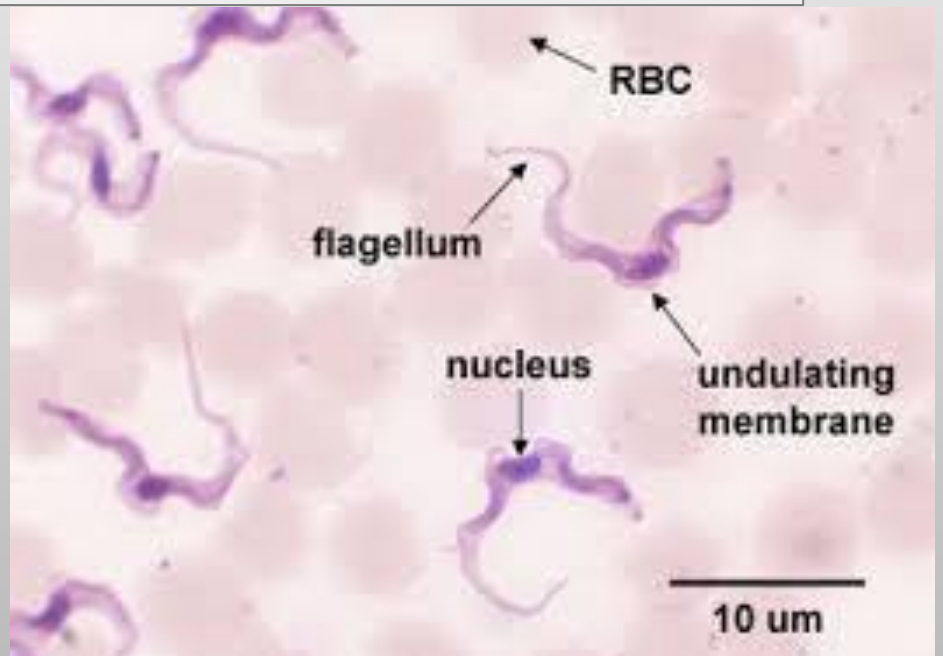
4) African Trypanosomiasis
Sleeping sickness



Parasitic diseases caused by *Trypanosoma brucei*. There are 2 main forms:

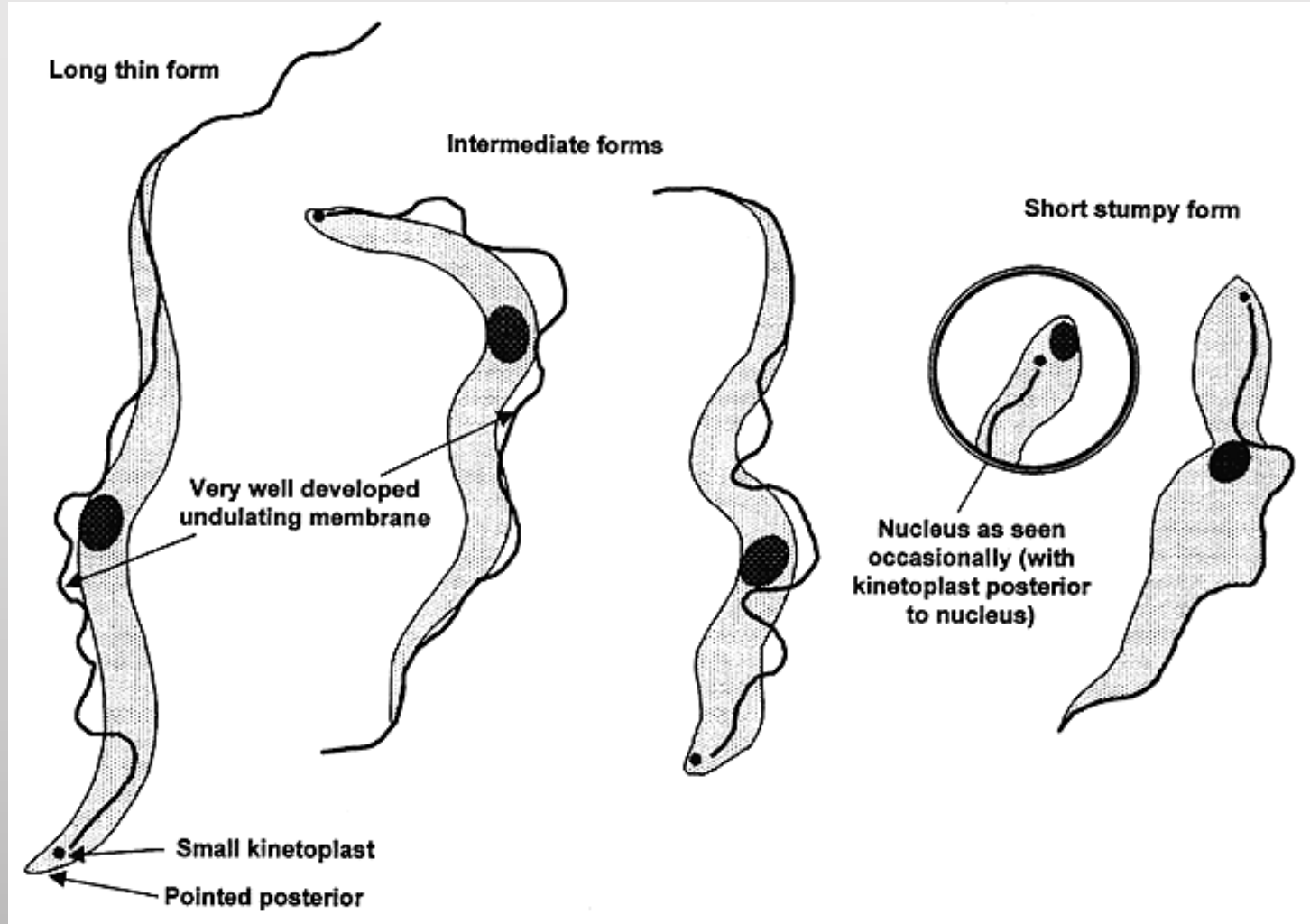
- **Chronic Sleeping sickness: caused by *Trypanosoma brucei gambiense***
- **Acute Sleeping sickness: caused by *Trypanosoma brucei rhodesiense***

Trypomasitogtes (flagellated form): Motile (with anterior flagellum & undulating membrane).



- **In Vector (Glossina fly)→ Metacyclic trypomastigote**

(infective stage) in salivary gland.



Life Cycle:

- **Habitat**
- During the early stages of the disease; *Trypanosomes* are found extracellular in the peripheral blood. Then, RECs (Liver, Spleen, Lymph nodes, Bone marrow).
- In the terminal stages; in CNS

D.H. (**man**)

R.H. (**animals**) **as, antelopes, pigs, goats, dogs.**

I.H. (Vector) **Glossina fly.**

Mode of transmission:

1-Bite of the fly, infective stages in the Saliva of infected vector.

2-Blood transfusion

3-Organ transplantation

4- Congenital

Clinical picture of African Trypanosomiasis :

1- *Trypanosoma* chancre [skin] It is a local inflammatory response at the site of tsetse bite with intense cellular infiltration, oedema and divided trypomastigotes.

2- Haemolymphatic stage [Blood & Lymph nodes]:

- **Toxic manifestations:** irregular fever, headache, joint & muscle pain and rash.
- Lymphadenopathy especially in posterior triangle of neck >>> "**Winterbottom's sign**"
- **Hepatosplenomegally,**
- **Bone marrow affection:** Anaemia, leukopenia and thrombocytopenia.

3- Meningoencephalitis stage [CNS] (Sleeping Sickness)

- Patient suffers of: Severe headache, mental apathy, slow speech, tremors, involuntary movements & convulsions.
- **Sleeping stage** >> Coma & death [from disease or infections as pneumonia].

Acute sleeping sickness (*Trypanosoma rhodesiense*)

Clinical features of Rhodesian disease are similar to Gambian but they cause severe fatal disease in short duration. Acute course; patients usually die rapidly.

Diagnosis of African Trypanosomiasis :

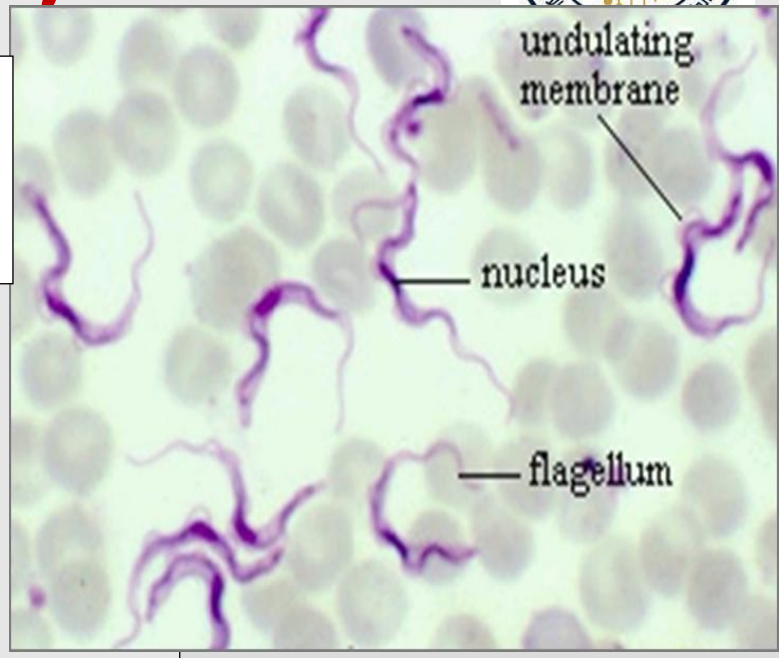
Laboratory Diagnosis

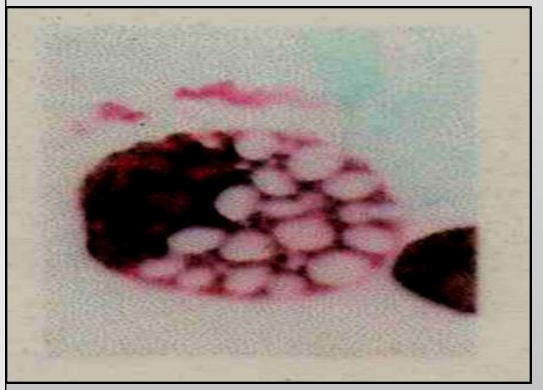
- 1- Direct Microscopic Examination of fresh or Giemsa stained films :

To demonstrate the **parasite** in **blood**, **aspirate** (chancre, lymph node, bone marrow) & lumber puncture for **CSF** : >>> **polymorphic trypomastigote**

- CSF examination: Trypomastigotes, and Morula cells of Mott.

Polymorphic Trypanosomes in blood film





Morula cells

- 2- Culture (NNN media)
- 3- Animal inoculation
- 4. Antibodies or Antigen detection by ELISA.
- 5. Blood examination: Anaemia, thrombocytopenia. ↑immunogobulins (IgM).
- 7. Molecular diagnosis.
- 8. Imaging: CT scan & MRI of the brain show cerebral oedema.

Treatment of African Trypanosomiasis :

Treatment:

- Early

Suramin & Pentamidine

- Late (Drugs that pass CNS barrier)

Melarsoprol

- Treatment of anaemia, dehydration and concurrent infections.

Melarsoprol

➢ Parasitic Infections Affecting special sense :

***Acanthamoeba castellani*:**	• Keratitis & corneal ulcers
Taenia solium:	• NeuroCysticercosis
Onchocerca volvulus	• Onchocerciasis

Onchocerciasis

- Infection of human skin and subcutaneous tissue by ***Onchocerca volvulus*** adult and microfilaria (Nematode).

- **Mode of infection**: through inoculation of the **infective filariform larva** (**Infective stage**) present in the mouth of intermediate host (*Simulium* fly) into skin bite.

- Adult worms live in fibrous subcutaneous nodules from the host reaction (not tender).

Onchocerca volvulus
Pathogenicity and clinical picture:

Skin manifestations:

- Onchocerca nodule (onchocercoma): Smooth firm, painless fibrous nodule in the subcutaneous tissue surrounding one to several adults
- Severe dermatitis: Oedema and inflammatory cellular infiltration of against microfilaria with subsequent fibrosis.
- Disturbed pigmentation: dermatitis with pruritus, pigmentation, atrophy and fibrosis

Onchocerca volvulus
Pathogenicity and clinical picture:

River blindness (or Sudan blindness)

- This is a serious complication of onchocerciasis resulting in blindness.
- Common when the nodules are in the scalp, neck and shoulders.
- The microfilariae have great affinity to the eye tissues.
- It is characterized by keratitis, iritis, uveitis, choroiditis, retinitis and optical atrophy which end in blindness. **The most common early finding is conjunctivitis with photophobia**
- ***Causes:***

-Hypersensitivity to toxins liberated from living and dead microfilariae.

-Mechanical action of the moving microfilariae in the eye tissues.

➢ Diagnosis

➢ Clinical diagnosis.

➢ Laboratory diagnosis:

- Detection of **microfilaria** (**Diagnostic stage**) or adult in Skin-snip biopsy or aspiration from the nodules or tissue biopsy.
- **In patients with ocular manifestations**, microfilariae may be found in conjunctival biopsies.
- **PCR** of skin snips.
- **Patch skin test:** 10% of Hetrazan in lanolin cream is applied to an area of skin. In positive cases; papular eruption develop after 8-24 hours.

➢ Treatment:

1 - Ivermectin against microfilaria.

2- Doxycycline against adult worm.

3- Surgical removal of the nodules.

Discussion & Feedback

10 minutes