CNS II
Microbiology Lecture V

DR. JUMANA ABBADI

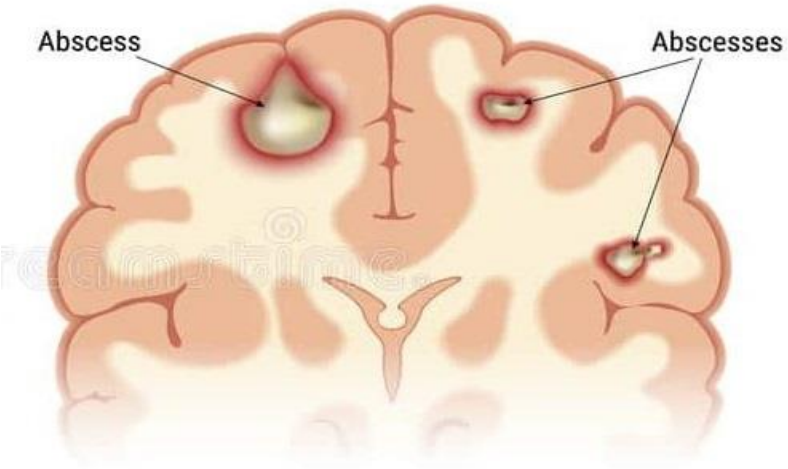
THIRD YEAR MEDICAL STUDENTS, HASHEMITE UNIVERSITY

Other CNS infections

- Brain abscess
- Parameningeal infections
- Toxoplasmosis
- African trypanosomiasis
- Cerebral malaria
- Miscellaneous viruses that affect the CNS

Brain Abscess

- Brain abscess is considered as one of the most serious diseases of the Central Nervous System (CNS). This is more common among men and the morbidity rate is highest in the fourth decade of life.
- It is associated with high morbidity and includes seizures, persistent alteration in the mental status and also focal motor deficits.



- Brain abscess acquired by:
  - Spread from a nearby focus of infection:
    - Sinusitis, otitis media or mastoiditis
    - Dental sepsis
    - Penetrating injury or neurosurgery.
  - Hematogenous spread from a distant site of infection:
    - Congenital heart disease with a right-to-left shunt
    - Hereditary hemorrhagic telangiectasia with AV fistulas.
    - Suppurative pulmonary infection.
    - Endocarditis.
    - Opportunistic infections arising in patients who are immunocompromised.

Etiology

- Streptococci, both aerobic and anaerobic.
- Other aerobic bacteria such as *Staphylococci* or Gram-negative rods.
- Anaerobic bacteria are often present.
- Unusual microorganisms such as fungi and *Toxoplasma gondii* cause brain abscess mainly in the severely immunocompromised.

Presentation

- The presenting symptoms often evolve slowly and are non-specific. Symptoms and signs of the predisposing disease such as sinusitis, otitis media, dental sepsis, or pulmonary disease are often but not always present
- Symptoms:
  - Headache is the most common symptom (70% of patients) and can be localized or generalized.
  - Fever is present in slightly less than one-half of adults.
  - Seizures, nuchal rigidity, and papilledema
  - Altered mental status and hemiparesis are the most common focal neurologic signs.

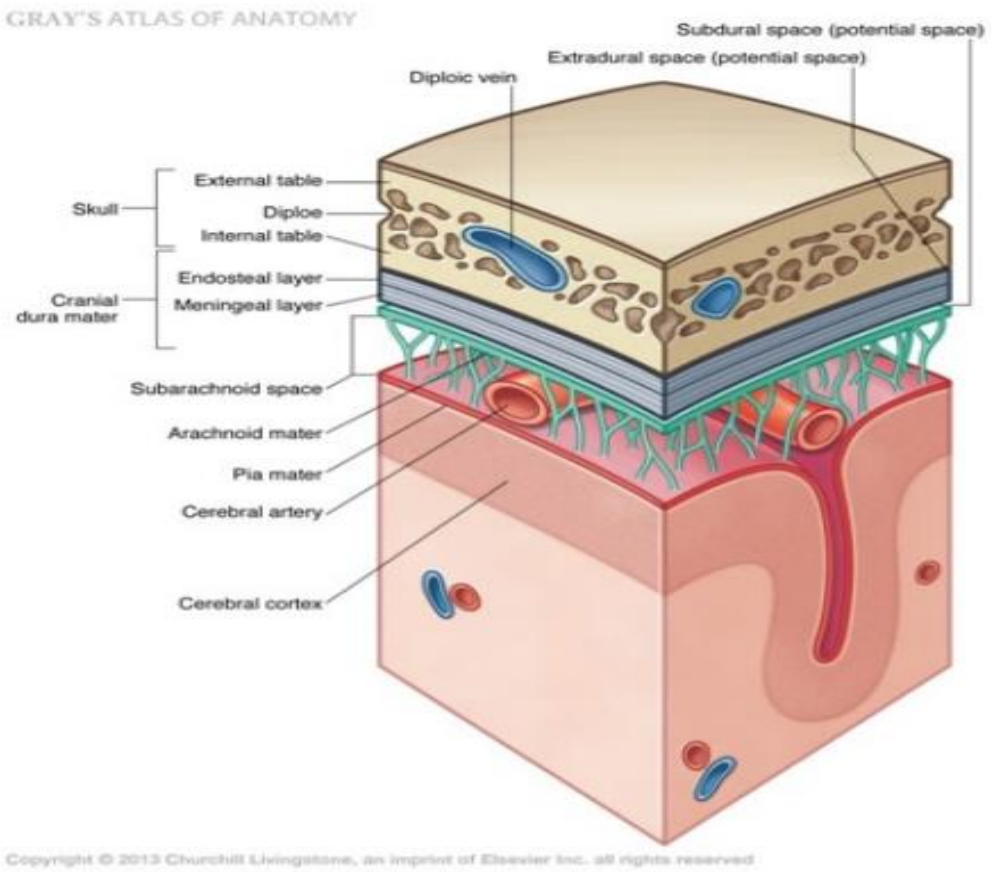
- Neurologic signs frequently predict the site of disease:
  - Bizarre behavior with frontal lobe abscess
  - Speech abnormalities with temporal lobe abscess
  - Ataxia, nausea, and nystagmus with cerebellar abscess
  - Visual field cuts with temporal, parietal, or occipital lobe abscess.
- Despite of this, mortality has decreased from 50-20% as a result of introduction of CT scanning. CT scanning resulted in earlier diagnosis and accurate localization of the abscess.

Diagnosis and management

- Neurodiagnostic imaging, high-resolution CT scan with enhancement or MRI scan with enhancement, are now the diagnostic procedure of choice for brain abscess.
- Management of these infections requires a multidisciplinary approach, consisting of a combination of neurosurgical intervention and appropriate long-term antibiotic therapy.

Parameningeal infections

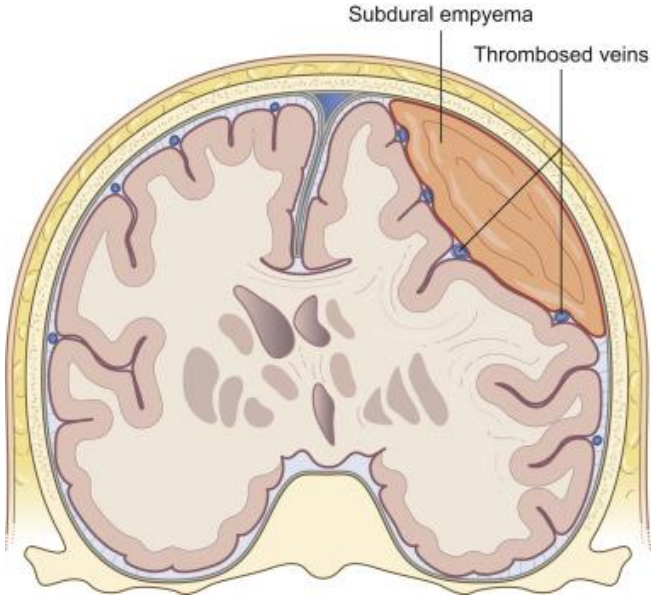
- Subdural empyema.
- Intracranial epidural abscess
- Spinal epidural abscess
- Septic thrombosis of the dural sinuses.



Subdural Empyema

- Subdural empyema is a localized collection of pus contained between the dura and arachnoid.
- Arises most often (60% to 70%) as an extension from sinusitis, especially frontal sinusitis. Otitis media with or without mastoiditis is the other major cause. Cases also result from trauma or surgery.
- Streptococci and especially anaerobic streptococci are again the most common isolates, but staphylococci (notably, *S. aureus*) and aerobic gram-negative rods are also encountered.
- Subdural empyema usually evolves **more rapidly** than does brain abscess.

- Typically, symptoms suggestive of sinusitis or of otitis media are followed within days to several weeks by fever, severe headache, neck pain and then by altered mental status and focal neurologic signs, sometimes with seizures.
- The mortality for subdural empyema from 6% to 20%. Many patients, and especially those with subdural empyema, are often left with a neurologic deficit.



Intracranial epidural abscess

- Intracranial epidural abscess is a collection of pus between the dura mater and the skull
- Intracranial epidural abscess, which is rare, has similar predisposing causes and a similar microbiology to subdural empyema.
- Intracranial epidural abscess usually develops slowly over weeks or even months.
- Nonspecific symptoms give way to symptoms of increased intracranial pressure (nausea, vomiting, headache, altered mental status) and focal neurologic signs.

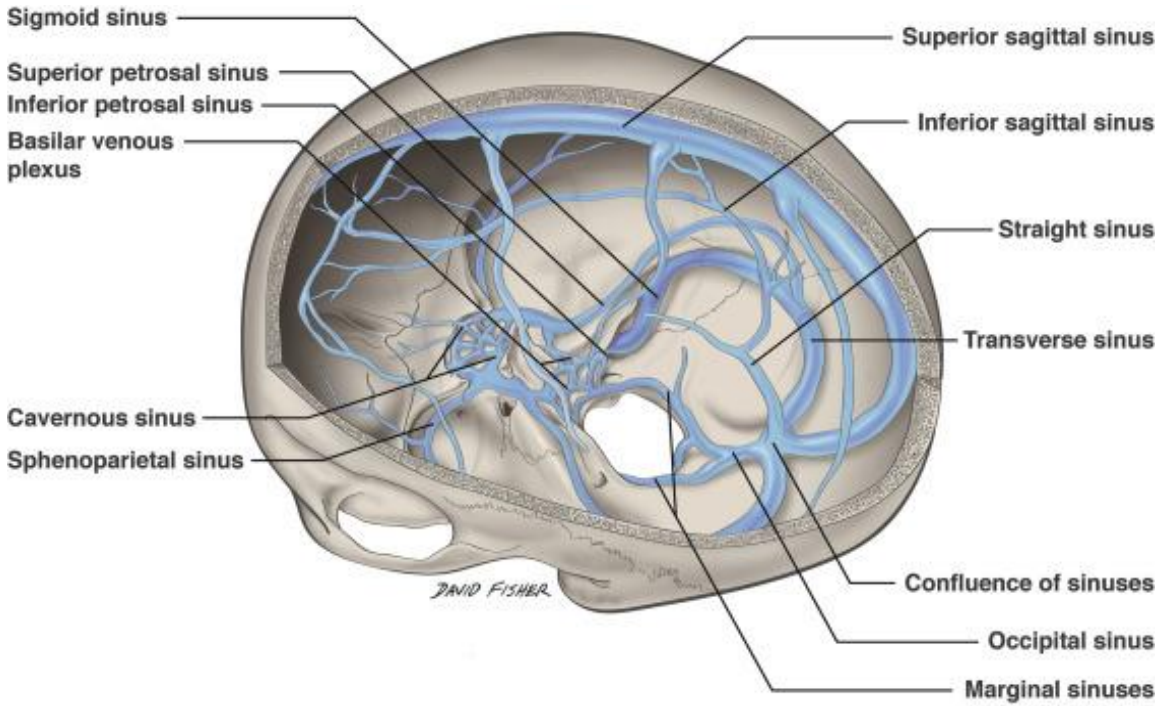
Spinal epidural abscess

- Spinal epidural abscess classically presents initially with fever and back pain and progresses to weakness of the lower extremities with impaired bowel or bladder function and then to paralysis. The correct diagnosis is seldom made at the first patient encounter.
- Spinal epidural abscess is acquired through:
  - a complication of vertebral osteomyelitis or diskitis.
  - Hematogenous dissemination.
  - a complication of spinal surgery, trauma, drug use, or spinal anesthesia
- *S. aureus* is the most common microorganism, being found in more than 60% of cases, but aerobic gram-negative rods, streptococci and *M. tuberculosis* are also major causes of the disease.
- Untreated, spinal epidural abscess progresses to complete compression of the spinal cord with permanent paralysis

Cavernous sinus thrombosis

- Septic thrombosis of the large dural sinuses that provide venous drainage to the brain is a rare but life-threatening cause of severe headache. Diagnosis is usually delayed.

- There are 3 major syndromes:
  1. **Cavernous sinus thrombosis.**
  2. Lateral (transverse) sinus thrombosis.
  3. Superior sagittal sinus thrombosis.



- Causes:
  - Facial infections, most often nasal furuncles, precede about 50% of cases
  - Sphenoid sinusitis accounts for about 30% of cases
  - Dental infections about 10% of cases
  - Otitis media, mastoiditis, or other nearby localized infections.
- *Staphylococcus aureus* is the most common etiologic agent. *S. pneumoniae* and other streptococci explain some cases, and anaerobic bacteria sometimes cause the condition especially when it is due to dental infection or other forms of sinusitis.
- Diabetes mellitus is possibly a risk factor

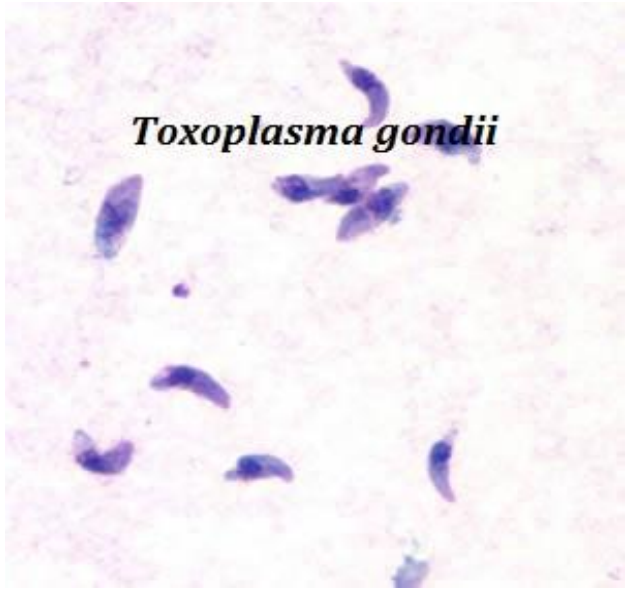
- Most patients with cavernous sinus thrombosis present with severe, progressive, unilateral, retroorbital and frontal headache. Migraine is a common misdiagnosis.
- Subsequent symptoms include unilateral swelling of the orbit, diplopia, and drowsiness. Rapid progression of the disease leads to proptosis, chemosis, papilledema, and ophthalmoplegia (inability to move the eyeball).
- Untreated, septic cavernous sinus thrombosis is nearly uniformly fatal.

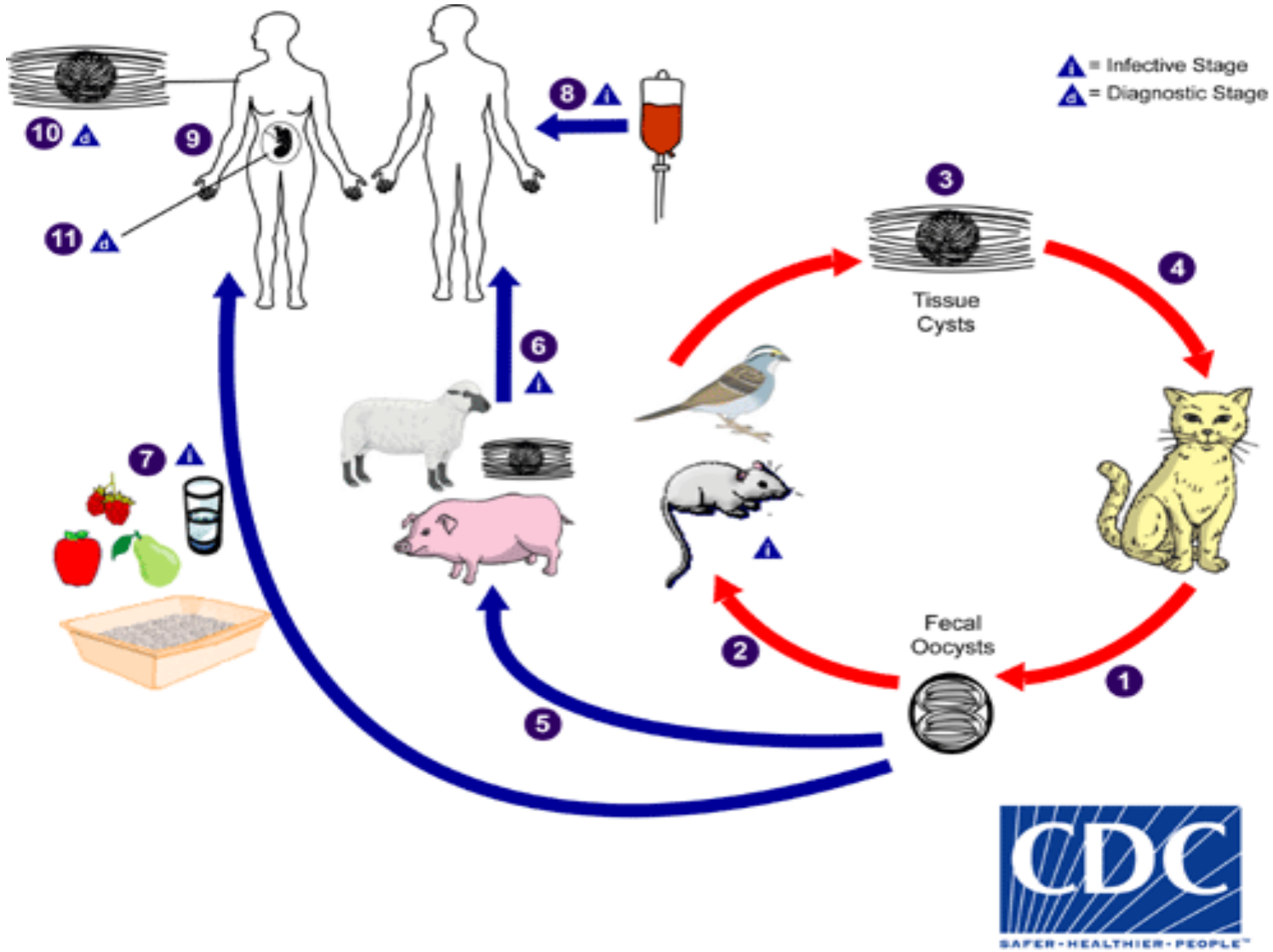
Diagnosis and management

- The diagnostic evaluation of parameningeal infections requires advanced imaging technology. Magnetic resonance imaging (MRI) is preferred in most instances.
- Management of these infections requires a multidisciplinary approach, consisting of a combination of neurosurgical intervention and appropriate long-term antibiotic therapy.

Toxoplasmosis

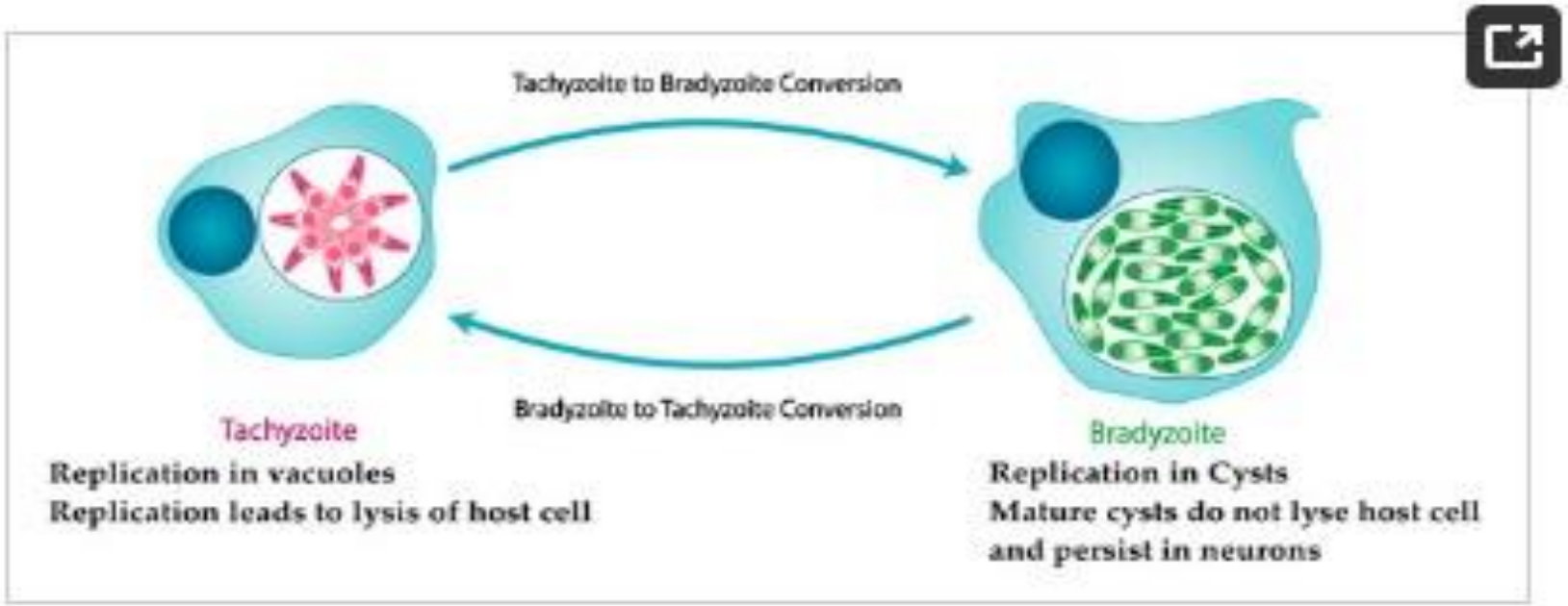
- Toxoplasmosis is caused by infection with the protozoan *Toxoplasma gondii,* an obligate intracellular parasite.
- In most immunocompetent individuals, primary or chronic (latent) *T gondii* infection is asymptomatic.
- Neurological symptoms associated with toxoplasmosis:
  - Infection in immunosuppressed individuals.
  - Congenital toxoplasmosis.




= Infective Stage
= Diagnostic Stage
Tissue Cysts
Fecal Oocysts
1
2
3
4
5
6
7
8
9
10
11
CDC
SAFER·HEALTHIER·PEOPLE™

Pathogenesis

- In individuals chronically infected with *T. gondii*, the parasite resides in tissue cysts in neurons in the brain.
- *T. gondii* consists of two stages in the brain, the rapidly replicating tachyzoite stage and the slowly replicating bradyzoite stage in cysts.
- Tachyzoites enter the brain shortly after infection and initially replicate in neurons as well as astrocytes and microglia, but convert to the bradyzoite stage, producing cysts located in neurons.
- Intraneural cysts last for the lifetime of the chronically infected host. The chronic infection in immunocompetent individuals has been considered to be asymptomatic. However, under certain circumstances the cyst may rupture and bradyzoite to tachyzoite conversion occurs.


Tachyzoite to Bradyzoite Conversion
Bradyzoite to Tachyzoite Conversion
Tachyzoite
Replication in vacuoles
Replication leads to lysis of host cell
Bradyzoite
Replication in Cysts
Mature cysts do not lyse host cell
and persist in neurons

- Immunocompromise is one of the major reasons for intraneural cyst rupture. Among immunodeficient individuals, toxoplasmosis most often occurs in those with defects of T-cell mediated immunity:
  - Patients with hematologic malignancies
  - Bone marrow and solid organ transplants
  - Acquired immunodeficiency syndrome (AIDS)
- **AIDS:** as the host adaptive immune response weakens, parasite tissue cysts rupture and release bradyzoites. Then they convert to the rapidly-dividing tachyzoite stage and produce significant morbidity, including *Toxoplasma* encephalitis.
- Toxoplasmosis is considered as an AIDS defining illness (CD4 count <200).

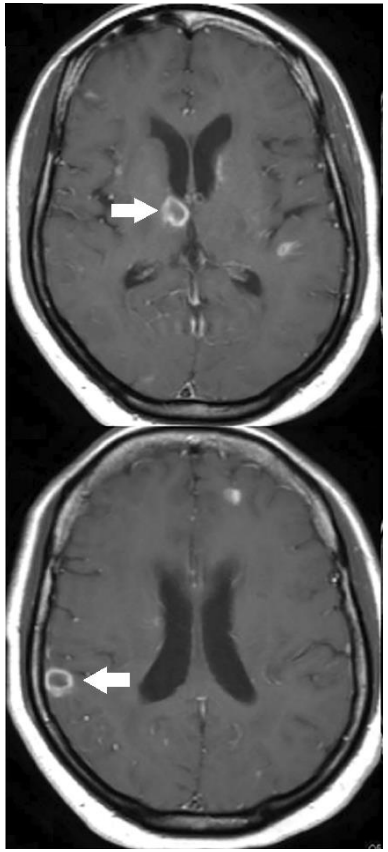
Presentation

- *Toxoplasma* encephalitis and brain abscess present most commonly as headache, but focal neurologic deficits and seizures are as common. With significant disease, patients may also demonstrate the signs and symptoms of elevated intracranial pressure.
- Recent investigations have suggested that chronic toxoplasmosis may play several roles in the etiology of different mental disorders such as schizophrenia and psychosis.

Congenital Toxoplasmosis

- When a mother is infected with *T gondii* during gestation, the parasite may be transmitted to the fetus transplacentally or during vaginal delivery.
- If the mother acquires the infection in the first trimester and it goes untreated, the risk of infection to the fetus is approximately 14-17%, and toxoplasmosis in the infant is usually **severe**.
- Manifestation of toxoplasmosis in the fetus:
  - Encephalomyelitis (inflammation of the brain and spinal cord)
  - Retinochoroiditis (15% of patients)
  - Intracranial calcifications (in about 10%)
  - Microcephaly.
  - Affected survivors may have mental retardation, seizures, visual defects, spasticity, hearing loss or other severe neurologic sequelae. The prevalence of sensorineural hearing loss is as high as 28% in children who do not receive treatment.

Diagnosis



- Cerebral toxoplasmosis is generally identified on computed tomography (CT) scan as multiple **ring-enhancing** lesions; however, solitary lesions may be seen.

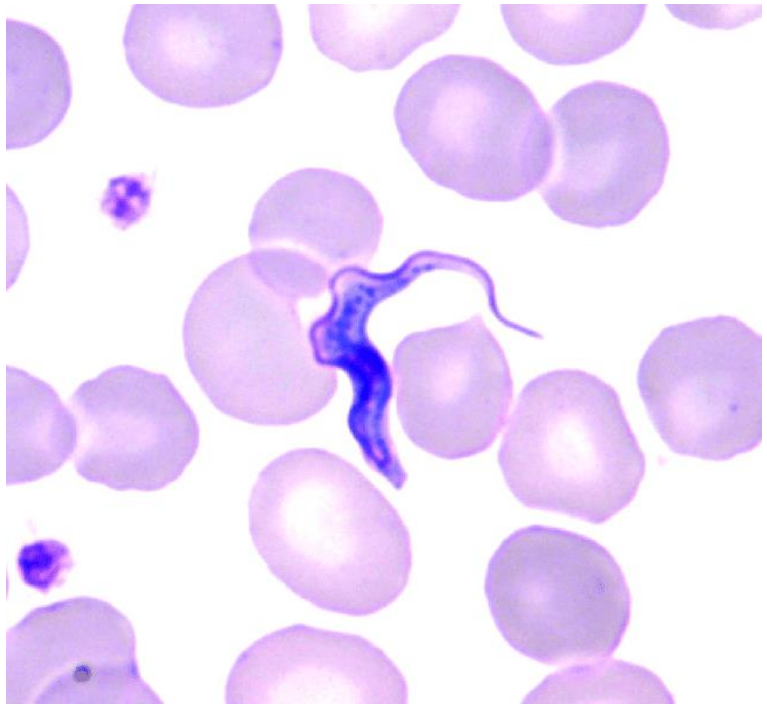
- The incidence of toxoplasmosis (including CNS disease) in patients with AIDS has declined dramatically, likely due to the evolution of highly active antiretroviral therapy (HAART) and the routine use of prophylaxis against *P. jiroveci* and *T. gondii*.

Management and prevention

- Toxoplasmosis is treated with Sulfadiazine and pyrimethamine combination.
- Prophylaxis for prevention of toxoplasmosis in HIV patients is trimethoprim and sulfamethoxazole given daily until patient's immune system is reestablished (CD4 count is more than 200).

African trypanosomiasis

- African trypanosomiasis (sleeping sickness) is an illness endemic to sub-Saharan Africa.
- It is caused by the flagellate protozoan *Trypanosoma brucei*, which is transmitted to human hosts by bites of infected **tsetse flies.**
- There are 2 stages of the disease:
  - Stage 1: early hemolymphatic stage
  - Stage 2: late neurologic stage



Presentation

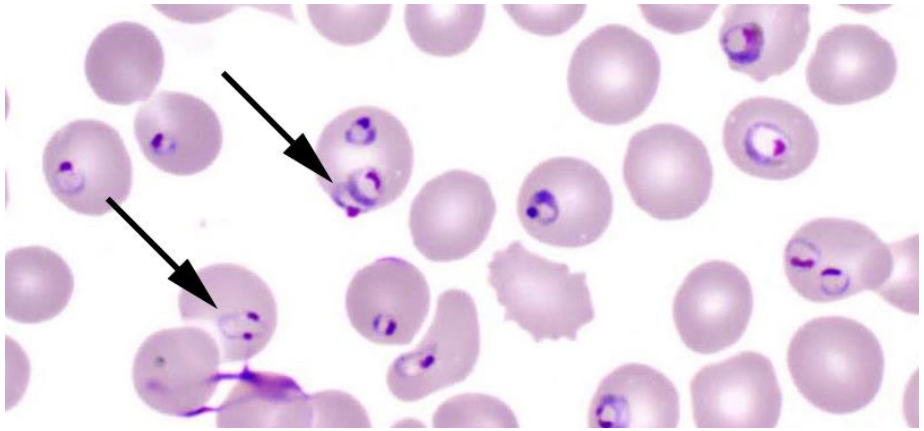
- Symptoms of stage 2 of African trypanosomiasis include the following:
  - Persistent headaches (refractory to analgesics)
  - Daytime somnolence followed by nighttime insomnia
  - Behavioral changes, mood swings, and, in some patients, depression.
  - Weight loss.
  - Seizures in children (rarely in adults)

Treatment

- Complications if untreated include meningoencephalitis and seizures, coma (sleeping sickness) and eventually death.
- The type of drug treatment used depends on the stage of African trypanosomiasis (sleeping sickness)—that is, whether it is stage 1 (early/hemolymphatic) or stage 2 (late/neurologic).
- Management of stage 2: Melarsoprol
- Prevention (CDC):
  - Wear long-sleeved shirts and pants of medium-weight material in neutral colors that blend with the background environment. Tsetse flies are attracted to bright or dark colors, and they can bite through lightweight clothing.
  - Inspect vehicles before entering.
  - Avoid bushes.
  - Use insect repellent.

Cerebral Malaria

- Cerebral malaria is the most severe neurological complication of infection with *Plasmodium falciparum* malaria. It is a clinical syndrome characterized by coma and asexual forms of the parasite on peripheral blood smears.
- Mortality is high and some surviving patients sustain brain injury which manifest as long-term neuro-cognitive impairments.
- The clinical hallmark of cerebral malaria is impaired consciousness, with coma as the most severe manifestation.



Presentation

- Most transmission occurs in Africa where children under the age of 5 years are most affected. In South-East Asia, malaria occurs more commonly in adults.
- In African children, coma develops suddenly with seizure onset often, following 1-3 days of fever. A few children develop coma following progressive weakness. Brain swelling, intracranial hypertension, retinal changes and brainstem signs (abnormalities in posture, ocular movements or abnormal respiratory patterns) among other non-neurological symptoms are commonly observed. The prognosis is grave in deeply comatose patients with severe metabolic acidosis, shock, hypoglycemia and repeated seizures.
- In adults, cerebral malaria is part of a multi-organ disease. Patients develop fever, headache, body ache and progressively, delirium and coma. Compared to African children, seizures, papilledema and retinal changes are less common.

Treatment and complications

- Without treatment, cerebral malaria is invariably **fatal**.
- In children, parenteral antimalarials are indicated, but even with this treatment, 15-20% die.
- In adults, mortality was lower if patients were treated with intravenous antimalarials.
- Surviving patients fully recover but over the past 20 years, it became clear that many children sustain significant brain injury. Although some gross deficits, particularly blindness, ataxia and central hypotonia improve with time, 25% have long-term impairments especially cognition, motor function or behavior impairments and epilepsy develops in 10%.

Miscellaneous viruses

- Epstein Barr virus (EBV): Primary CNS Lymphoma, myelitis.
- HHV-6, HHV-7: Encephalitis.
- HTLV: Myelitis.
- Nipah and Hendra virus: Meningitis and/or encephalitis.

Thank you ☺