Toxoplasmosis

Life cycle
Infective stages
Congenital Toxoplasmosis
Lab. Diagnosis
Immunity to Toxoplasmosis
Toxoplasmosis & Pregnancy
Toxoplasmosis is a zoonotic disease caused by the Coccidian protozoan Toxoplasma gondii. It infects a wide range of animals and birds but does not appear to cause disease in them.
Toxoplasmosis
(TOX-o-plaz-MO-sis)

A disease of the blood and lymphatic system. Cats are a critical part of the life cycle. It is usually acquired by eating undercooked meats but can also be acquired by contact with cat feces.

Primary problem is a congenital infection of fetus, resulting in either a stillbirth or a child with severe brain damage or vision problems.
Toxoplasmosis

The normal final host is cat and relatives in the family Felidae, only hosts in which the Oocyst is produced & the sexual stage of Toxoplasma can be developed.
Introduction

Toxoplasma gondii has very low host specificity, and it will probably infect almost any mammal. Non species Specific & Non organ specific), and has been found in virtually every country of the world.

Like most of the Apicomplexa, Toxoplasma is an obligate intracellular parasite. Its life cycle includes two phases called the intestinal (or enteroepithelial) and extraintestinal phases.
• The intestinal phase occurs in cats only (wild as well as domesticated cats) and produces "oocysts."

• The extraintestinal phase occurs in all infected animals (including cats) and produces "tachyzoites" and, eventually, "bradyzoites" or "zoitocysts."

• The disease toxoplasmosis can be transmitted by ingestion of oocysts (in cat feces) or bradyzoites (in raw or undercooked meat). **Tachyzoites are less resistant to stomach secretions so less important sources of infection than the other stages**
DEFINITIVE HOSTS:
Domestic and wild cats

INTERMEDIATE HOSTS:
Humans, wild animals, domestic animals

Humans:
Can be infected by eating meat with zoitocysts or by ingesting oocysts

Direct transmission to fetus

Congenital neurological defects in infant

Bradyzoites released in intestine

Fertilization

Immature oocyst

Mature oocyst (contains 2 sporocysts with 4 sporozoites)

Passed in feces

Bradyzoites in zoitocyst located in brain tissue
Many Humans at risk with Toxoplasmosis
Cats

• Cats are the only animal species to **shed** the infectious stage in their feces.

• All animals however, can disseminate Toxoplasmosis if their **infected meat** is eaten.

• cats get it by eating rodents, **raw meat**, cockroaches, **flies**, or by contacting infected cats, infected cat feces, or contaminated soil.
Events on Development in man

When man ingests Oocysts with eight Sporozoites excreted in Cats feces, can establish an infection in humans. Oocysts open in duodenum and releases eight Sporozoites which pass through the gut wall Circulate in body and invade various cells.

In most humans infected with *Toxoplasma*, the disease is **asymptomatic**. However, under some conditions, toxoplasmosis can cause serious pathology, including hepatitis, pneumonia, blindness, and severe neurological disorders. This is especially true in individuals whose immune systems are compromised (e.g., AIDS patients).
Toxoplasmosis can also be transmitted transplacentally resulting in a spontaneous abortion, a still born, or a child that is severely handicapped mentally and/or physically.
Morphology

Acute stage:
The intracellular parasites (tachyzoite) are 3x6μ, crescent shaped organisms that are enclosed in the host cells as Macrophages to form the Pseudocyst
*Toxoplasma gondii* tachyzoites.

**Acute stage**
- Asymptomatic or
- Flu like symptoms

(by P.W. Pappas and S.M. Wardrop)
Intracellular tachyzoites of *Toxoplasma gondii*.
In the pseudocyst
As macrophages
Reproduction is by

**Endodyogeny**, a process of division wherein 2 daughter zoites are formed within the parent parasite, which is destroyed when the young zoites are released.
Invade Organs

In further development they penetrate new cells especially Eye and Brain. Further development slows down in these organs called ad Bradyzoites to form a quiescent tissue cysts.

The event lead to chronic stage of disease.

Brain involvement carries higher Morbidity and Mortality if the immunity is low.
A zoitocyst of *Toxoplasma gondii* filled with bradyzoites; this zoitocyst (true cyst) is in the muscle.
Fate of Tissue Cysts

The tissue cysts are infective when ingested by cats or eaten by other animals, where tissue cysts are formed.

In man, it can be the dead end of disease or change to an acute stage (tachyzoites) when the immunity is low.
Spread from Rats – Cats to Humans
Both oocysts and tissue cysts transform into tachyzoites shortly after ingestion. Tachyzoites localize in neural and muscle tissue and develop into tissue cyst bradyzoites. If a pregnant woman becomes infected, tachyzoites can infect the fetus via the bloodstream.
Sources of infection

• Source of all oocytes ...
  – Domestic (cats) and wild (zoo) cats
    (Cats are the only known full-life-cycle host of the protozoan) parasite Complete host

• Persist in environment (soil) if moist > one year
  – reservoir of infective oocytes

• Many intermediate hosts
  – reservoir of infective tissue cysts (farm animals—cattle, sheep, rabbit)

• Cycle in humans (an accidental host)
  – Infected
    • by ingesting infective oocytes (in >4 day old cat feces)
    • by ingesting tachyzoites or bradyzoites in raw meat
    • by receiving blood or tissues with “-zoites”
    • CONGENITALLY by transplacental tachyzoites
  – Proliferative stages in humans
    • tachyzoites result from all infective stages
    • bradyzoites predominate within cysts
Humans become infected in several ways:
- ingestion of oocysts through contamination of food, water, hands, etc. with cat feces.
- ingestion of bradyzoites in uncooked meat, e.g. lamb, pork, beef, caribou.
- transplacental when mother develops acute infection during pregnancy.
- blood transfusion, organ transplant.
In immunocompetent adults, toxoplasmosis, may produce flu-like symptoms, sometimes associated with lymphadenopathy. In immunocompromised individuals, infection results in generalized parasitemia involvement of brain, liver lung and other organs, and often death.
Other Human Infections
Early detection reduce Morbidity

Toxoplasmosis • produces severe Human infections in patient with AIDS
The chronic infection is altered to Acute manifestations
Toxoplasmosis – Immunosuppressed patients

Varying degrees of disease may occur in Immunosuppressed individuals results in Retinitis Chorioretinitis Pneumonias severe neurological disorders Other non specific manifestations
Immunology

Both humoral and cell mediated immune responses are stimulated in normal individuals. Cell Mediated Immunity is protective and humoral response is of diagnostic value.
Acquired immunity in women is particularly protective to the fetus. In immunosuppressed and AIDS patients, changes in the host resistance can cause the chronic infection to become fulminating acute Toxoplasmosis.

Premunition: a host may recover clinically and be resistant to specific challenge, but some parasites may remain and reproduce slowly.
Toxoplasmosis in Pregnancy

In 1st Trimester
may lead to still birth
major central nervous system anomalies

In 2nd Trimester
Less severe complications

Transmission to the fetus is more frequent if the maternal infection occurs in the 3rd trimester
Congenital Toxoplasmosis

Congenital infection develop in fetus only when non immune mothers are infected during pregnancy.

Post natal Toxoplasmosis is less severe.
Congenital infections occur in about 1-5 per 1000 pregnancies of which 5-10% result in miscarriage, 8-10% result in serious brain and eye damage to the fetus, 10-13% of the babies will have visual handicaps. Although 58-70% of infected women will give a normal birth, a small proportion of babies will develop active retino-chorditis or mental retardation in childhood or young adulthood.

(Post natal Toxoplasmosis is less severe)
Babies infected with congenital Toxoplasmosis manifest with:

- brain damage
- enlarged spleen and liver
- eye damage
- jaundice
- poor motor coordination
- unusually small head
- rash
Congenital Infection

Prenatal toxoplasmosis Lead to
Still Birth
Or Sabin`s tetrad:
Chorioretinitis
Intracellular calcification
Psychomotor disturbances
Hydrocephaly
or
Microcephaly
Prenatal toxoplasmosis may manifest with blindness apart from congenital defects
Clinical:
1. majority are asymptomatic
2. **acute toxoplasmosis**: fever, lymphadenopathy (much like infectious mononucleosis - EBV); can rarely cause specific organ inflammation, e.g. encephalitis, myocarditis.
3. **reactivation toxoplasmosis**: occurs in immunosuppressed such as AIDS, transplant and cancer patients: presents with specific organ involvement e.g. encephalitis, pneumonitis.
4. **choreoretinitis**: occurs later in life in individuals who acquired toxoplasmosis congenitally **Post natal toxoplasmosis**; focal lesion in retina presenting as decreased visual acuity; rarely occurs during acute toxoplasmosis.
5. **congenital toxoplasmosis**: transmission from mother to fetus when mother has developed acute toxoplasmosis during pregnancy - increased transmission rate in third trimester, but increased severity of fetal disease in first trimester. Presents as hydrocephalus, hepatomegaly, cerebral calcifications, mental retardation with death at one end of spectrum and mental retardation or just later choreoretinitis at the other end of spectrum.
Diagnosis of Toxoplasmosis

Desired specimens,
- Blood (serum)
- Sputum
- CSF
- Exudates
- Lymphnodes
- Tonsil tissues
- Striated muscle biopsy
- Ventricular fluid in Neonates
Diagnosis

Suspected toxoplasmosis can be confirmed by isolation of organism from tonsil or lymph gland biopsy.
Microscopic Examination of Tissues

Smears and sections stained with Giemsa’s stain
Periodic acid Schiff method preferred
Pseudocyst seen in the acute stage.
The densely packed cysts seen in the brain or other parts of nervous system suggest chronic infection
Immunological tests:

Tests which employ whole parasites include

• the dye test (Sabin-Feldman Dye Test (DT), direct agglutination and the fluorescent antibody test,

• whilst tests that use disrupted parasites as an antigen source include ELISA, latex agglutination, indirect haemagglutination and complement fixation.
Serology

Sabin Feldman dye test

based on principle that Antibodies to Toxoplasma appear in 2-3 weeks that will render the membrane of the laboratory cultured living *T.gondii* impermeable to Alkaline methylene blue. So the organism are unstained in the presence of serum with antibodies
Newer Methods in Diagnosis

- Immuno florescent assay method.
- ELISA for IgM and IgG detection
- PCR

Frankel’s intracutaneous test (Toxoplasmin skin test) useful for epidemiological purpose
fluorescent antibody test,
ELISA Test
Test serum for presence of *Toxoplasma*-specific IgG antibodies

IgG Negative: Not Infected

IgG Positive: Infected

To determine approximate time of infection, test serum for presence of *Toxoplasma*-specific IgM antibodies

IgG Positive
IgM Negative: Infected for more than 1 year.

IgG Positive
IgM Positive: Acute infection

Obtain 2nd sample 2 weeks after 1st; send both samples to a *Toxoplasma* Reference Laboratory for confirmation before any intervention.
Detectable levels of IgM antibody appear immediately before or soon after the onset of symptoms. IgM levels normally decline within 4 to 6 months, but may persist at low levels for up to a year.

IgG levels begin to rise 1 or 2 weeks after infection. Peak levels are reached in 6 to 8 weeks, then gradually decline over a period of months or even years. Low levels of IgG are generally detectable for life.

Immunocompromised individuals may not produce any IgM. Antibody levels do not correlate with severity of illness.
Serologic Diagnosis of Toxo

• unreliable in immunodeficient (AIDS) pts
• normally IgM and IgG rise simultaneously
  – IgG - persists for years
  – IgM - undetectable after “cure”
• elevated IgM titer is diagnostic of recent infection in persons with normal immunity

• A negative IgG or IgM test excludes Diagnosis
  – both should be + if acutely infected
• If IgG screening is + then do IgM test
  – a + IgM test confirms acute toxoplasmosis or current Toxoplasma infection (measure IgM antibodies, have low specificity )
• in the United States, most pregnant women are not screened routinely for toxoplasmosis. Only those with a high risk.
Polymerase Chain Reaction (PCR)

- PCR amplification is used to detect *T. gondii* DNA in body fluids and tissues.
- It has been successfully used to diagnose congenital, ocular, cerebral and disseminated toxoplasmosis.
- PCR performed on amniotic fluid has revolutionized the diagnosis of fetal *T. gondii* infection by enabling an early diagnosis to be made,
- PCR has allowed detection of *T. gondii* DNA in brain tissue, cerebrospinal fluid (CSF), vitreous and aqueous fluid, bronchoalveolar lavage (BAL) fluid, urine, amniotic fluid and peripheral blood.
Incidence

- Seroconversion rate ---- 7.5% in Egypt
- 30% in Canada
- 50% in USA
- > 60% in France

Very common throughout the world; up to 50+% in other developed or developing countries.
Care of the Meat

Avoid eating raw or undercooked meat.
Freezing $< -20^\circ\text{C}$
Heating at $50^\circ\text{C}$ for 4-6 minutes destroys the cysts and sterilizes the meat.
Immunity to TG

- Active infection normally occurs **only once** in a lifetime.
- Although the parasite remains in the body indefinitely, latent infections usually persist for life (the immune system reacts against the parasite, causing the parasite to hide in an inactive form (cyst) in tissues throughout the body (usually the skeletal muscles and the brain). . .
- True cyst generally is harmless and inactive **unless** the immune system is not functioning properly in immunocompromised host -- the parasite can reactivate and cause serious illness, characterized by inflammation of the brain
- If a woman develops immunity to the infection at least six to nine months before pregnancy, there is a very **rarely** any danger of passing it on to her baby because immunity is developed to it
Widespread phobia

Toxoplasmosis is a part of TORCH syndrome

It is not a cause of habitual abortion

Only pregnant with primary active infection with toxoplasmosis during pregnancy leads to congenital tox and after primary infection there is persistence of cysts of tox BUT development of active immunity protect subsequent pregnancy

Very rarely reactivation of previously latent T. gondii infection induced by severe decrease of immunity (People on chemotherapy, People with congenital immune deficiencies, People with AIDS/HIV, long administration of corticosteroid drugs in the case of transplant patients)

Many doctors believe that is the case which has created a widespread phobia among pregnant women and has given some sort of satisfaction among some doctors by treatment their pregnant women by chemotherapy which is in fact unnecessary
Toxoplasmosis

- Drugs of choice for pregnant women or immunocompromised persons:
  - Spiramycin or Pyrimethamine plus Sulfadiazine

- Prophylaxis – in the primary prevention of toxoplasmosis in persons with HIV who have dormant or latent infection
  - trimethoprim-sulfamethoxazole
  - pyrimethamine plus folinic acid
  - dapsone + pyrimethamine
Treatment of Infected Newborns

• Infected babies should be treated as soon as possible after birth with pyrimethamine and sulfadiazine which, as mentioned earlier, can help prevent or reduce the disabilities associated with toxoplasmosis.
Figure-5- Girl with hydrocephalus due to congenital toxoplasmosis.
Under research

• developing vaccines against Toxoplasma gondii by using surface plasmon resonance.
Thank You