Toxoplasmosis

Objective:

Describe the Life cycle
Mention the Infective stages
Define Congenital Toxoplasmosis

List the Lab. Diagnosis

Illustrate the Immunity to Toxoplasmosis

Show the relationship between Toxoplasmosis & Pregnancy
Human Toxoplasmosis

Toxoplasmosis is a zoonotic disease
Caused by Coccidian protozoan Toxoplasma gondii
Infectes a wide range of animals, birds but does not appear to cause disease in them
Toxoplasmosis

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**
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.
Definitive host (Cat)

Unsporulated oocysts passed in feces

Cysts ingested by cat

Cysts in tissues of intermediate host

Ingested cysts in infective meat (raw or undercooked)

Tachyzoites transmitted through placenta

Contaminated food and water

Infected fetus

Intermediate hosts

Oocysts in feed, water, or soil

Sporulated oocysts

Ingested by intermediate host

Definitive host (Cat)
Spread from Rats – Cats to Humans

Definitive host

Unsporulated oocyst (in feces)

Sporulated oocyst

Rodent

Raw pork, lamb, chicken

Intermediate hosts

Litter box

LIFE CYCLE OF TOXOPLASMOsis
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 where in 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, eye or brain.
The tissue cysts are infective when ingested by cats or eaten by other animals. In man it is a dead end of disease or change to acute stage (tachyzoites) when the Immunity is Low.
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.
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 host resistance and causes the chronic infection becomes fulminating acute toxoplasmosis.
Premunition: a host may recover clinically & be resistant to specific challenge but some parasites may remain and reproduce slowly
Immunity to T. gondii

- 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 immuno-compromised 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.
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)
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
Summery of Clinical presentations:
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
  Lymphnodes
  Tonsil tissues
  Striated muscle biopsy
Diagnosis

Suspected toxoplasmosis can be confirmed by finding the organism from tonsil or lymph gland biopsy.

Pseudocyst seen in the acute stage
Microscopic Examination of Tissues

Smears and sections stained with Giemsa’s stain
Periodic acid Schiff method preferred

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
ELISA Principle

Substrate + chromogen

Anti-human antibodies conjugated with enzyme

Serum antibodies

Solid phase antigens
Specific antigen is incubated

serum from patient is added.

anti-human IgG conjugated with HRP enzyme-

the chromogen and its substrate added.

Reading under 450 nm → OD

serum from patient is added.

Specific antigen is incubated

Solid support
Reading under 405 nm $\rightarrow$ OD

anti-human IgG conjugated with HRP enzyme-

serum from patient is added

Specific antigen is incubated for overnight

Solid support
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.

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
  - 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.
Avoid eating raw or undercooked meat. Freezing < \(-20^\circ c\) Heating at \(50^\circ c\) for 4-6 minutes destroys the cysts and sterilizes the meat.
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)
Toxoplasmosis  TTT

• 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
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.
Under research

• developing vaccines against Toxoplasma gondii.
Thank You