Toxoplasma gondii

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Toxoplasma gondii

Apicomplexa, Koccidia

Obligate intracellular parasite

Distribution: cosmopolite

Transmission: alimentary transplacentary
(transfusions, transplantations…)

Very low host specificity
Final host: **Felidae**

Intermediate host:

350 types of birds and mammals

Creating

discharging

Oocysts (5-20 days)

Tissue cysts

rabbit, pork, lamb
GIT: Oocyst: sporozoites

Trophozoites:
Tachyzoites: acute infection

Trophozoites:
Bradyzoites: latent infection
Tissue cyst
Toxoplasma is highly specialized for invasion of the host cell.
Contact (healthy cell; K+ ions)
Orientation
Invasion
Formation of parasitophorous vacuole
Whole process: 30 s
Toxoplasma is modifying the host cell
Tissue cyst destruction

+ 67°C
- 20°C
radiation \( \gamma \)

\[ \text{Infective stages} \]

\[ \text{Oocyst} \]

\( \text{not infectious immediately} \)

development: 2-3 days (air, sun)
remains \textit{infectious} if favourable conditions for about 1 year
Dissemination

hematogenous/lymphatic system

Immunity can control infection however is not able to eradicate it – tissue cysts
Infecting different types of cells

Preference:
- neurons (brain)
- muscles
- cells of retina
Epidemiology

USA: about 20-40% seropositive

Europe: 20-80% seropositive

HIV: 40% develop toxoplasmosis

Mortality: immunocompromised and not treated always fatal
Development of the infection depends on the **immune status** of the host.

**Immunocompetent** is usually asymptomatic.

**Symptomatic disease**

- **glandular form**: general lymphadenopathy
- **ocular form**: chorioretinitis
Toxoplasma is capable of invading through the placental barrier and infecting the fetus.

**TORCH syndrome**

Asymptomatic infection vs

Symptomatic infection:
- abortus
- brain
- retina
Congenital toxoplasmosis

- Mild disease: slightly diminished vision

- Severe disease:
  - chorioretinitis
  - hydrocephalus
  - convulsions
  - intracerebral calcifications
hydrocephalus
Sonography (frontal lamella)

Hydrocephalus  

Calcifications
Congenital chorioretinitis
Management of examinations during and after pregnancy

3 examinations during pregnancy (each trimester)

Ab IgM, IgA, IgE and IgG

Positive results

Amniotic fluid: PCR

Newborns: IgM, Western Blot IgG
Interpretation of the results – serology

Infection during or very early before pregnancy
HIGH RISK!!!!!

• **Negative** – woman in danger should undergo all three examinations during pregnancy!!!!

<table>
<thead>
<tr>
<th><strong>Acute phase</strong></th>
<th><strong>Latent phase</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Elevation of IgM, IgA, IgE</td>
<td>Elevation of IgG</td>
</tr>
</tbody>
</table>

Avidity of Ab
Therapy

Pyrimethamine + Sulfadiazine + Folate

Spiramycine
(prevents transplacentary transmission, not treatment)

Affected children (for 1 year)
Pyrimethamine + Sulfadiazine + Folate
Immunosupresion

Reactivation of latent infection

tissue cysts

Impaired immunity is unable to control infection
Immunosuppression
<table>
<thead>
<tr>
<th>Disease</th>
<th>Subacute onset</th>
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<tbody>
<tr>
<td>CD4 less than 100/ul</td>
<td>Main form of manifestation:</td>
</tr>
<tr>
<td>Toxoplasmic encephalitis</td>
<td></td>
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<tr>
<td>Focal neurological deficit (motoric, dysarthry)</td>
<td></td>
</tr>
<tr>
<td>Cefalea</td>
<td></td>
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<tr>
<td>Personality changes</td>
<td></td>
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<tr>
<td>Elevated temperature</td>
<td></td>
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<tr>
<td>Seizures</td>
<td></td>
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<tr>
<td>Cerebellum</td>
<td></td>
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<tr>
<td>Meningism</td>
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</tbody>
</table>
Toxoplasma gondii Disease
Extracerebral toxoplasmic infections (except ocular form) are extremely rare

**Ocular form**
Chorioretinitis: impairment of vision, scotomas, pain, photophobia

**Pulmonary form**
similar to *Pneumocystis* pneumonia

**Disseminated form**
high temperature, sepsis-like syndrome, DIC…
Diagnostics

Serology important in HIV+ also
Patients with elevated IgG biggest risk
Cerebral toxoplasmosis

**CSF:**
- mild pleocytosis with increased mononuclear cells
- elevated protein

Intrathecal production of anti *T. gondii* IgG:

\[
\text{CSF Sabin-Feldman dye test titer (reciprocal)} \times \frac{\text{Total serum IgG}}{\text{Total CSF IgG}} \times \frac{\text{Serum dye test titer (reciprocal)}}{\text{Serum dye test titer (reciprocal)}}
\]

Values higher than 1 – toxoplasmic encephalitis
PCR is very important method in establishment of dg

- PCR – CSF (12-70%)
  - BAL
  - vitreous a aqueous humor
  - amnious fluid

- **CAVE!** Positive PCR in CSF doesn’t always mean toxoplasmic encephalitis; tissue cysts can be present for a long period and become disrupted
CT:
ring enhancing hypodense lesions
NMR – abnormal signal, very sensitive method
PET: lesions correspond to areas with decreased interception of glucose
Dif Dg: Lymphoma – lesions with increased interception of glucose
Biopsy of affected organ (Gamma knife in the toxoplasmonic encephalitis)

- granulomatous reaction with gliosis;
- necrosis,
- presence of tachyzoites or tissue cysts
Therapy

**Pyrimethamin**
Initial dose 200 mg po; after 50-75 mg/day po in combination with

**Folic acid**
10 mg/day po; in combination with

**Sulfadiazine**
4-6 g/day po

After completion the therapy - lifelong prophylaxis
Therapy leads to improvement of the symptoms within 3 days

**Corticosteroids** are used in patients with oedema of the brain and symptoms of increased intracranial pressure

Therapy of acute phase of infection: 3-6 weeks
Prophylaxis

- **Pyrimethamine**: 50 mg/d PO
- **Sulfadiazine**: 1-1.5 g/d PO
- **Folic acid**: 10 mg/d PO
Prophylaxis

<table>
<thead>
<tr>
<th>Alternative Regimens</th>
</tr>
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<tbody>
<tr>
<td><em><em>Pyrimethamine</em> alone</em>*</td>
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<tr>
<td>50 mg q24 hours</td>
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<tr>
<td><em><em>Pyrimethamine</em> plus one of the</em>*</td>
</tr>
<tr>
<td>following:</td>
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<tr>
<td>25-50 mg q 24 hours</td>
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<tr>
<td><strong>Atovaquone</strong></td>
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<tr>
<td>1,500 mg q12 hours</td>
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<tr>
<td><strong>Clarithromycin</strong></td>
</tr>
<tr>
<td>1,000 mg q12 hours</td>
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<tr>
<td><strong>Azithromycin</strong></td>
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<tr>
<td>1,200-1,500 mg q24 hours</td>
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<tr>
<td><strong>Dapsone</strong></td>
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<tr>
<td>100 mg BIW</td>
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## Secondary prophylaxis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage (PO)</th>
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<tbody>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>1 DS tablet qd</td>
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<tr>
<td></td>
<td>2 DS tablet tiw</td>
</tr>
<tr>
<td>Pyrimethamine*/dapsone</td>
<td>50 mg qw/50 mg qd</td>
</tr>
<tr>
<td></td>
<td>50 mg BIW/100 mg BIW</td>
</tr>
<tr>
<td></td>
<td>75 mg qw/200 mg qw</td>
</tr>
<tr>
<td>Pyrimethamine*/sulfadoxine</td>
<td>3 tablet every 2 weeks</td>
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<tr>
<td></td>
<td>1 tab BIW</td>
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Follow the basic standards of hygiene

Food must be always properly cooked

CD4 under 100/ul – always prophylaxis

CD4 over 100/ul + opportunistic infection: always prophylaxis
Latent infection with toxoplasma: personality changes?

**Male**
- Low superego strength
- Protension
- Suspecting, jealous, dogmatic
- Low IQ
- High Eysenck s lie score
- Low harm avoidance
- Reserved, detached, critical

**Female**
- Warmhearted, outgoing, easygoing
- Superego
- Trustig, accepting conditions, tolerant
- Worldly, polished,
- Controlled, socially precise