Ocular Toxoplasmosis
Uveitis course – Antalya 2013

Miles Stanford
Medical Eye Unit
St Thomas’ Hospital
London
Toxoplasma gondii

- Obligate, intracellular, apicomplexan protozoan
- Infects > 1/3 world population
- Predilection for tropical countries – Brazil, W. Africa
- Usually asymptomatic but may cause retinochoroiditis (nb 10-15% affected eyes become blind)
Stages of Toxoplasma

• Tachyzoites are responsible for active infection
• Bradyzoites are found in tissue cysts
• Sporozoites are found in environmentally resistant oocysts
The lifecycle of Toxoplasma
Toxoplasmosis
Clinical Syndromes

• Asymptomatic
• Acute febrile illness
• Lymphadenopathy
• Encephalitis
• Neonatal jaundice/epilepsy
• Retinochoroiditis
Ocular toxoplasmosis presents with a granulomatous uveitis, often with raised intraocular pressure.
Macular scar in a four year old presenting with a squint
Severe vitreous haze – “headlight in the fog” sign
Classical phenotype – new retinitis adjacent to old scar
Kyrieleis phenomenon affecting retinal arteries
Kyrieleis phenomenon affecting retinal veins
Toxoplasmosis may cause retinal venous occlusion
Extensive retinal venous sheathing away from the focus of infection
Extensive pre-retinal fibrosis before (left) and after (right) vitrectomy
Opacified posterior hyaloid face after vitrectomy
Toxoplasmosis is a rare cause of secondary choroidal neovascularisation.
Toxoplasma optic neuritis in a HIV positive patient
Acquired toxoplasmosis in immunodeficient
Acquisition of infection

- Ingestion of oocysts (soil, water)
- Ingestion of tissue cysts (undercooked meat)
- Vertical transmission (congenital disease)
- Tissue transplantation
- Laboratory accident
Acquisition of infection
Ingestion of oocysts

• Outbreak studies
  - Vancouver study
  - South Brazil
  - Miscellaneous
Ocular toxoplasmosis from acquired disease – Vancouver outbreak

Lancet 1997;350:173-7

• Contaminated reservoir
• 100 serologically positive cases
• 20 ocular cases – 1 bilateral
• 2,894 – 7,718 presumed infected
• 0.5% (0.26-0.69) of those presumed infected presented with retinitis
Ocular toxoplasmosis from acquired disease – Vancouver outbreak

Ophthalmological findings

- Mean age 54 years
- Male=female
- 40% systemically unwell
- Large lesions
- 4 (20%) had recurrences over a 2 year period

Burnett et al Ophthalmology 1998;105:1032-7
Acquisition of infection (oocysts)  
Brazilian studies 1

- Population based serological survey
- Sero-prevalence varied with socio-economic group
  - 84% lower
  - 62% middle
  - 23% upper

Drinking unfiltered water the greatest risk factor
(OR 3.0 for lower; 1.7 for middle, 0.4 for upper)

Oliviera et al Emerging Infect Dis 2003;9:55-62
Prevalence of toxoplasma infection according to age and socio-economic status
Bahia-Oliveira et al Emerging Inf Dis 2003;9(1):55-62
Acquisition of infection
Ingestion of tissue cysts

• European case control study of screened women: 252 infected v. 858 control
• 30-63% of infection due to consumption of undercooked or cured meat
• 6-17% from soil contact
• No relation to contact with cats

Cook A et al BMJ 2000 321 142-7
## Risk factors for acquisition of toxoplasmosis in the USA

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Adjusted OR</th>
<th>Attributable risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raw beef</td>
<td>6.67</td>
<td>7%</td>
</tr>
<tr>
<td>Rare lamb</td>
<td>8.39</td>
<td>20%</td>
</tr>
<tr>
<td>Cured meat</td>
<td>1.97</td>
<td>22%</td>
</tr>
<tr>
<td>Working with meat</td>
<td>3.15</td>
<td>5%</td>
</tr>
<tr>
<td>&gt; 2 kittens</td>
<td>28</td>
<td>10%</td>
</tr>
<tr>
<td>Raw seafood</td>
<td>2.22</td>
<td>16%</td>
</tr>
</tbody>
</table>

Clint Infect Dis 2009
When do we acquire infection?

- In utero
- In childhood?
- In adulthood?
Challenges in the control of toxoplasmosis

- Control of parasite
- Control of acquisition
- Control of infection
Control of parasite/acquisition

- Clean water supplies
- Adequate animal husbandry
- Freezing meat (< -12 C)
- Adequate cooking of raw meats (> +67 C)
- Avoidance during pregnancy
Control of infection

Antibiotic treatment
Antibiotics used in the treatment of TR:

- atovaquone
- minocycline
- azithromycin
- septrin
- sulphadiazine
- trimethoprim
- pyrimethamine
- rifabutin
- spiramycin
- clarithromycin
- dapsone
- piritrexin
- sulphamethoxazole
- sulphadoxine
- clindamycin
- tetracycline
Antibiotics against Toxoplasma
General requirements

- Effective
- Parasiticidal
- Kills tachys and bradys
- Penetrates cysts
- Distributed in main site of infection
Antibiotics against Toxoplasma Folate inhibitors

- Toxoplasma synthesises folate de novo
- Drugs inhibit either
  - Dihydrofolate reductase eg, pyrimethamine, trimethoprim
  - Dihydropterate synthase eg, sulphonamides
- Most cause folate deficiency
Antibiotics against Toxoplasma
Macrolides

- Parasitostatic
- Action unclear
- Includes spiramycin, azithromycin, clindamycin
- Combinations may be useful
Indications for treatment

• Lesions within the macular arcade
• Lesions within 1 DD of disc
• Poor VA (<6/18) in an only eye
• Immunosuppressed patient
• NB consider vitrectomy if media do not clear by 4-6 months
Therapy for ocular toxoplasmosis

Rothova et al  Am J Ophthalmol 1993
115;317-23
Therapy for ocular toxoplasmosis

• Group 1
  - Pyrimethamine, sulphadiazine, steroids
• Group 2
  - Clindamycin, sulphadiazine, steroids
• Group 3
  - Trimethoprim, sulphamethoxazole, steroids
• Group 4
  - Nothing
Medical treatment for ocular toxoplasmosis

- Treatment does not reduce the length of an attack
- Duration of attack depends on the size of the retinitis
- Delay of treatment by 1 week from onset of symptoms does not alter disease course
- Treatment is no more effective in recurrent disease
Medical treatment for ocular toxoplasmosis

- Treatment does not alter visual prognosis
- 50% recurrence at 3 years despite treatment
The Treatment of Toxoplasma Retinochoroiditis – What do I do?

- Topical treatment as necessary
- Azithromycin 500mg od for 3/52
- Consider treatment with steroids if profound visual loss
- **NEVER** treat with steroids alone or peri- or intraocular injections of steroids
- Consider vitrectomy if VA <6/60 at 4-6 months
Toxoplasma retinochoroiditis
What we don’t know

• The true incidence of acquired disease
• The explanation for the age distribution of presentation with symptoms
• The effect of treatment on pre- or postnatal infection with respect to ocular disease
• Relevance of ante- and neonatal screening
Toxoplasma
Controlling infection – the future

• Improving sanitation to prevent contamination of ground water
• Control of cats on farms
• Freezing foodstuffs