Prenatal Environmental Exposure:
Toxoplasmosis

Nelson B Isada MD FACOG FACP FACMG
Providence Maternal-Fetal Medicine
Toxoplasmosis is a clinical illness caused by the protozoan parasite *Toxoplasma gondii*. Domestic cats and wild cats of the family Felidae are the only known definitive hosts. Large numbers of oocysts are excreted transiently from infected animals, which sporulate in the environment and are ingested by intermediate hosts.
Toxoplasma gondii
Ctenodactylus gundi
Fig. 1. Postulated life cycle of *Toxoplasma*. Cats and some other felines are shown as final hosts, and other animals and humans as intermediate hosts. Flies and cockroaches can serve as transport hosts. Infection with oocysts is shown at the right. Transmission by ingestion of meat is indicated at the left. Below, the transplacental route of transmission is indicated. Slightly modified from and reprinted by permission from Frenkel, J. K.: Toxoplasmosis. In: *Pathology of Protozoal and Helminthic Diseases*, Marcial-Rojas, R. A. editor. Baltimore, Williams & Wilkins, 1971, pp. 254-90.
Toxoplasma life-cycle

- Oocysts mature to tachyzoites in the intermediate host, migrate to neural and muscle tissue, and form tissue cysts bradyzoites.
- These cysts are then consumed by felids, completing the life cycle.
Toxoplasma acquisition

- Consumption of undercooked meats containing tissue cysts
- Ingestion of sporulated oocysts in food, soil or water or after changing pet cat litter-boxes
- Transplacentally after primary infection in pregnant women resulting in congenital disease
- Following organ transplantation or blood transfusion
Toxoplasma – epidemiology

• World-wide infection; variable (UK 6%, Brazil 76%)
• 30-63% of primary exposure during pregnancy tissue cysts in undercooked meat (Europe)
• 50% of toxoplasmosis cases may be from ingestion of contaminated meat (US)
• 78% of infections during pregnancy are due to oocyst ingestion with no risk factors such as cat ownership or changing of cat litter boxes (US)
Toxoplasma – other clinical

- HIV co-infection
- Schizophrenia (?)
- Obsessive-compulsive disorder (?)
- Neuroticism (?)
- Behavioral gender differences (?)
- Male fetuses
• Raw oysters, mussels, clams
• Three or more kittens
• Unpasteurized goat milk

In our case-control study, we identified eating raw oysters, clams, or mussels as a new risk factor for recent *T. gondii* infection. Oysters, clams, and mussels are filter feeders that concentrate *T. gondii*, as has been shown under experimental conditions [29]. Sea otters in California have been found to be infected with *T. gondii* [30], and it is likely that they are often infected by eating mollusks, which filter *T. gondii* from seawater. The seawater in California is thought to be contaminated by *T. gondii* oocysts that originate from cat feces, survive or bypass sewage treatment, and travel to the coast through river systems [30, 31]. *T. gondii* has been identified in a California mussel by polymerase chain reaction and DNA sequencing [32]. In light of the potential presence of *T. gondii*, pregnant women and immunosuppressed persons should be aware of this potential risk associated with eating raw oysters, muscles, and clams.
Toxoplasma – obstetric aspects

- *Toxoplasma* infection may be a serious complication when contracted during pregnancy.
- Severity of symptoms associated with congenital toxoplasmosis is dependent on the gestational age at the time of exposure, as well on the timely recognition and treatment of the condition in the mother and fetus.
Toxoplasma – obstetric aspects

• Congenital disease may result in hydrocephalus, brain or liver calcifications, enlarged spleen, cardiac arrhythmia, chorioretinitis, fetal growth restriction (FGR), erythroblastosis, hydrops fetalis, and/or ascites.

• Some of these conditions may be identified sonographically prior to delivery.

• Non-invasive and invasive testing can identify infection.
Prenatal testing

• Non-invasive serologic testing (toxoplasma IgG, toxoplasma IgM)
• Toxoplasma IgM generally indicates a recent, primary infection
• Invasive testing includes amniocentesis and cordocentesis
Amniocentesis

Image from www.pregmed.org/amniocentesis.htm
Cordocentesis
Congenital toxoplasmosis presenting with fetal atrial flutter after maternal ingestion of infected moose meat

Sarah M Colosimo MSCGC¹, Jose G Montoya MD²,³, Benjamin P Westley MD⁴, Jack Jacob, MD⁵ and Nelson B Isada, MD¹

¹Providence Maternal-Fetal Medicine (Anchorage, AK), ²Palo Alto Medical Foundation Toxoplasma Serology Laboratory, National Reference Laboratory for the Diagnosis and Management of Toxoplasmosis (Palo Alto, CA), ³Stanford University School of Medicine (Stanford, CA), ⁴Private practice, Infectious Disease (Anchorage, AK), ⁵Alaska Neonatology Associates/Pediatrix Medical Group (Anchorage, AK)

Alaska Medicine Volume 54, September 2013
Case report

• 25 year-old Gravida 2 Para 1 Caucasian at 34 weeks, 0-days with a singleton male fetus, presented for urgent perinatology consultation because of new-onset fetal tachycardia (205 beats per minute, normal 120-160 bpm) during office Doppler examination and confirmed with a non-stress test.
Case report – findings

- Sustained regular tachycardia with atrial flutter and 2:1 block.
- Cardiomegaly, tricuspid regurgitation, echogenic bowel wall, decreased pulmonary artery flow, enlarged pulmonary outflow tract and splenomegaly.
- Large for gestational age (93rd %tile).
- No serous cavity effusions, hydramnios or placentomegaly
Sonographic findings

Enlarged pulmonary artery

Splenomegaly
Sonographic findings

Enlarged heart

Atrial flutter
Case report – hospital course

- Persistent fetal atrial flutter and 2:1 block.
- New findings of intermittent premature atrial contractions (PACs) and perisplenic rim of peritoneal fluid (up to 2.9 mm)
- Primary C-section (breech, hydrops) – live male infant (“Bennett”), weight 3010 gm (3lb 10oz), Apgar 8/9
Case report – maternal history (retrospective)

After serology results were obtained, mother disclosed that her husband was an avid hunter and that the family ate Alaskan game meat almost exclusively. Specifically, she ate moose, Dall sheep, and Sitka black-tail deer during her pregnancy.
Case report – maternal history (retrospective)

These animals were all killed by the patient’s husband, and generally the meat was frozen prior to consumption. She reported that in one instance, moose meat was “fresh” rather than frozen. This meat was consumed two days after the moose was killed by her husband at JBER around 26 weeks gestation.

In hindsight, the mother recalled that at 28 weeks gestation she developed a flu-like illness characterized by mildly-tender, cervical lymphadenopathy that spontaneously resolved over 1 to 2 weeks.
Case report – neonatal course

• The infant developed mild respiratory distress, poor perfusion and was still in atrial flutter.

• DC cardioversion and IV propranolol converted the arrhythmia and reversed the respiratory distress.
Case report – neonatal course

Abdominal ultrasonography: hepatosplenomegaly and minimal ascites.

Hearing screen (ALGO®) at 30 dB thresholds was normal.

Initiation of three-drug oral therapy with pyrimethamine (2 mg/kg/day on day #1 and #2, then 1 mg/kg daily), sulfadiazine (100 mg/kg/day divided twice daily), and leucovorin (10 mg on Monday, Wednesday, and Friday) was begun on day of life 19.
Case report – neonatal course

CT scanning of the brain without contrast revealed punctate calcifications in the right centrum semiovale and right caudate head.

Fundoscopic exam revealed right greater than left peripheral retinal lesions consistent with retinitis attributed to toxoplasmosis.

CSF evaluation revealed an elevated WBC count of 44 (nl < 30/ml³), predominantly lymphocytes, and a normal CSF glucose and protein.
Case report – neonatal course

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Case report – neonatal course

• The child completed 12 months of therapy without significant toxicity.
• Neurodevelopmental assessment at 1 year of age was normal.
• His retinitis has resolved and he is meeting all growth and developmental milestones to date.
• It is anticipated that the child will continue to develop normally.
Case report – neonatal imaging
Case report – neonatal imaging

Right centrum semiovale

Right caudate
Case report – toxoplasma PCR

Frozen meat samples remaining from each of the five animals consumed during the pregnancy were obtained from the family, and PCR testing for *Toxoplasma gondii* was performed on these samples by the Palo Alto Medical Foundation *Toxoplasma* Serology Laboratory.
# Case report – lab results

## Table 1: Results of maternal and neonatal evaluation

<table>
<thead>
<tr>
<th>Assay</th>
<th>Source</th>
<th>Value</th>
<th>Range &amp; Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMV IgG</td>
<td>Serum</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>CMV IgM</td>
<td>Serum</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>CMV PCR</td>
<td>Serum</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Parvovirus B19 IgG</td>
<td>Serum</td>
<td>4.47</td>
<td>&lt;0.90 index</td>
</tr>
<tr>
<td>Parvovirus B19 IgM</td>
<td>Serum</td>
<td>0.04</td>
<td>&lt;0.90 index</td>
</tr>
<tr>
<td>Toxoplasma lgG</td>
<td>Serum</td>
<td>&gt;500 IU/mL</td>
<td>&lt;6.0 IU/mL</td>
</tr>
<tr>
<td>Toxoplasma lgG (Dye test)</td>
<td>Serum</td>
<td>1:16,000</td>
<td>Negative</td>
</tr>
<tr>
<td>Toxoplasma lgM ELISA</td>
<td>Serum</td>
<td>8.1</td>
<td>0.0–1.6</td>
</tr>
</tbody>
</table>

## Table 2: Results of meat sample evaluation

<table>
<thead>
<tr>
<th>Meat</th>
<th>Aliquot</th>
<th>Result</th>
<th>Positive Reactions (of 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deer</td>
<td>1</td>
<td>Indeterminate</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Negative</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Negative</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Negative</td>
<td>0</td>
</tr>
<tr>
<td>Moose</td>
<td>1</td>
<td>Negative</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Indeterminate</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Positive</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Negative</td>
<td>0</td>
</tr>
<tr>
<td>Sheep</td>
<td>1</td>
<td>Negative</td>
<td>0</td>
</tr>
</tbody>
</table>

A positive result is defined as one or more reactions for each target having a Ct (crossing threshold) ≤ 38 cycles.

A negative result is defined as all reactions having Cts ≥ 40 cycles.

An indeterminate result comprises any other combination of results.
Joint Base Elmendorf-Richardson
Link found between moose meat and unborn baby's infection

Benjamin S. Brasch | October 10, 2013

Lauren Hamm’s 34-week prenatal checkup was only supposed to be 10 minutes.

She didn’t know then, she didn’t even know she was pregnant.
Domestic cats in Alaska are unable to survive in the wild because of extreme winter temperatures, and therefore are uncommon wild reservoirs in this region.

The lynx is the only wild felid in Alaska and thought to be the lone, natural definitive host of *Toxoplasma* in the state. The prevalence of *Toxoplasma* antibodies in lynx throughout Alaska’s interior is ~15%.

Prevalence also varied by lynx age. Almost no kittens carried *Toxoplasma*, while its prevalence was nearly 100% in adult lynx over the age of 10 years.
Toxoplasma - Alaska

- Studies of *Toxoplasma* in Alaska Native populations have found that individuals in regions avoided by lynx are still infected.
- In 1974, prevalence of *Toxoplasma* antibodies among individuals living in different regions of Alaska was studied, including the northern and western coastal regions, which are rarely inhabited by lynx.
Toxoplasma - Alaska

• Unexpectedly, all villages tested were found to carry *Toxoplasma gondii* antibodies. It was postulated that other animals, such as herbivores, enter the infection cycle by becoming exposed to oocysts through the soil that they feed on.

• Marine animals may also be possible hosts of *Toxoplasma gondii*; individuals who ate raw oysters, clams and mussels were at increased risk of infection, presumably as a result of filter feeders inhabiting contaminated water.
Toxoplasma - Alaska

- A 1986 study found 23% (25/110) of free-ranging moose from the Susitna River, Alaskan Peninsula and the Kenai Peninsula-Anchorage areas of Alaska to be seropositive for *Toxoplasma* by IHA. This rate is similar to that reported for moose from Sweden (20%) and Nova Scotia (15%).
- A 2000 study found 43% of black bears, 9% of wolves, 7% of Dall sheep, and 6% of caribou were seropositive for *Toxoplasma gondii*. 
No toxoplasma in Alaska?

- A more recent 2000 study of blood sampling from 1976 to 1996 in Alaskan animals found that only 1% (3/240) of tested moose had antibody evidence of prior *Toxoplasma* infection.
- Similarly, a 2010 study failed to identify *Toxoplasma gondii* antibodies in 202 Alaskan moose.
No toxoplasma in Alaska?

- The low rates of *Toxoplasma* found in Alaskan moose may be due to their eating habits as well as to freezing temperatures.
- Moose are herbivores and primarily graze on tall plants thought to pose limited risk of oocyst exposure.
- Oocysts of *Toxoplasma gondii* are killed by extremely low temperatures and are poorly capable of surviving in the Alaskan climate for lengthy periods of time.
- Because oocysts require 1 to 5 days in the environment to sporulate and become infectious, the cold climate should minimize transmission to intermediate hosts in non-summer months.
Toxoplasma in Anchorage?

- The Municipality of Anchorage (MOA) is poorly represented in seroprevalence studies cited above.
- The MOA is heavily populated by lynx.
- Approximately 1,500 moose live within the MOA.
- Relatively few moose are consumed from the MOA.
- Hunting on JBER is limited by permit drawing and requires use of either a bow and arrow or muzzleloader, minimizing the number of animals taken each season.
Lynx
Why is meat red?
Myoglobin

- Myoglobin (MB) transports oxygen from the cell membrane to the mitochondria and stores oxygen inside the cytoplasm of myocytes.
- MB reversibly binds molecular oxygen and enhances the rate of oxygen diffusion through the muscle cell.
- MB is a small globular protein composed of a single polypeptide chain of 153 amino acids and an iron-containing heme prosthetic group identical to that of hemoglobin.
- Most of what we enjoy as meat juice is primarily water and MB, not blood.
Why is cooked meat brown?

- H_2O (Fe^{2+}, blue/purple (raw, no air))
- O_2 (Fe^{2+}, red (raw, air))
- H_2O (Fe^{3+}, brown (cooked or not fresh))
- NO (Fe^{2+}, pink (cured or smoked))
Meat preparation
Recommendations

• While early recognition of congenital toxoplasma and initiation of antimicrobial therapy can minimize the sequelae in infected neonates, prevention of primary infection during pregnancy should be the goal.

• Women in the United States are not routinely screened for toxoplasmosis during pregnancy, and detection instead relies on the identification of symptoms through prenatal evaluation.
Recommendations

- Women preparing or consuming undercooked game meats should be considered at heightened risk of primary toxoplasmosis during pregnancy and encouraged to notify their obstetric provider for any illness associated with flu-like symptoms and/or lymphadenopathy.
- Obstetric providers should be aware of sonographic findings suggesting toxoplasmosis.
- Samples can be sent to Palo Alto if further evaluation is necessary.