## "Toxoplasmosis in 2010: What the Infectious Diseases Specialist Needs to Know"

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33 yo woman who is 14 weeks pregnant has been diagnosed with reactivation of her previously diagnosed ocular toxoplasmosis. Her ophthalmologist insists that her macular active lesions require immediate anti-toxoplasma therapy. She has positive Toxoplasma IgG and negative IgM. Without anti-toxoplasma treatment, what is the risk of transmission of the parasite to her fetus?

A. 100%
B. 75%
C. 50%
D. 25%
E. Essentially zero

### Palo Alto Medical Foundation Toxoplasma Serology Laboratory (PAMF-TSL)

- Jack S. Remington
- Jose G. Montoya
- Cindy Press
- Jeanne Talucod
- Ian Selsky
- Raymund Ramirez
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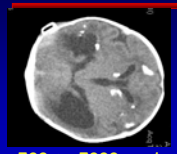
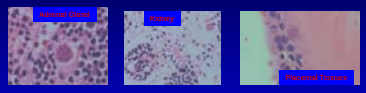
## *Toxoplasma gondii* infects over one billion people worldwide

- disease burden due to toxoplasmosis
- epidemiology update
- is there a correlation between parasite strain and clinical manifestations?
- during pregnancy
- ocular disease
- immunocompromised patients

Kovacs J, Boothroyd J, Montoya JG. "*Toxoplasma gondii*". In: Mandell G, Dolin A, Bennett J, eds. 2009 7th Edition Principles and Practice of Infectious Diseases

## Congenital Toxoplasmosis (CT) in the United States





~500 to 5000 newborns with CT/~4.2 million live births per year

ocular disease in 12%–30% of CT children. New lesions in up to 31% o referred children who followed up to a mean age of 10.8 years

intracranial calcifications in 9.5% of infants identified by prenatal screening programs and in 21.7% of infants identified by postnatal programs

hydrocephaly, microcephaly, and psychomotor and mental retardation

~89% of women of childbearing age are susceptible

## Ocular Sequelae of Congenital Toxoplasmosis in Brazil Compared with Europe

Ruth E. Gilbert[1*], Katherine Freeman[2], Eleonor G. Lago[3], Lilian M. G. Bahia-Oliveira[4], Hooi Kuan Tan[1], Martine Wallon[5], Wilma Buffolano[6], Miles R. Stanford[7], Eskild Petersen[8], for The European Multicentre Study on Congenital Toxoplasmosis (EMSCOT)

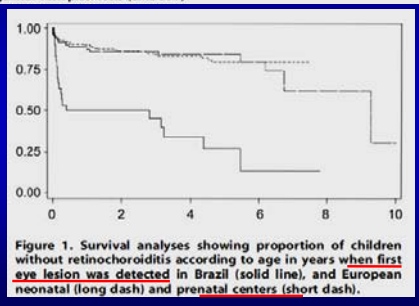
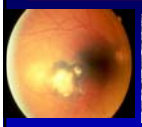
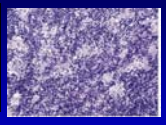
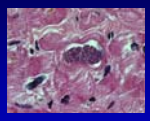



Figure 1. Survival analyses showing proportion of children without retinochoroiditis according to age in years when first eye lesion was detected in Brazil (solid line), and European neonatal (long dash) and prenatal centers (short dash).

Gilbert RE,etal. PLoS Negl Trop Dis 2008; 2(8): e277

## Toxoplasmosis in immunocompetent patients

ocular toxoplasmosis affects an estimated 1.26 million persons in the United States alone. Post-natally acquired ocular disease is more common than it was once thougth

*T. gondii* can also cause lymphadenopathy, myocarditis, myositis, hepatitis

in addition, pneumonia, fever, brain abscesses, and death have been reported in certain geographical areas

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Fatal Outbreak of Human Toxoplasmosis along the Maroni River: Epidemiological, Clinical, and Parasitological Aspects


**Community outbreak of acute toxoplasmosis in immunocompetent patients**

- Unusually severe clinical presentation 11 otherwise normal individuals
- 8 had severe disseminated disease (including pneumonia and hepatitis) that resulted in three deaths -one adult, one newborn and one fetus
- genotype analysis with 8 microsatellite markers revealed that only one strain was responsible for at least 5 of the 11 cases

**Demar M et al. Clin Infect Dis 2007;45: e88-95**

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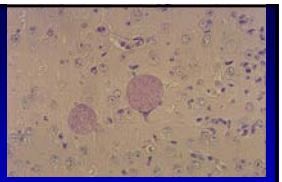
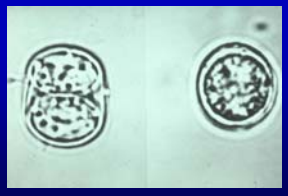
Tachyzoites



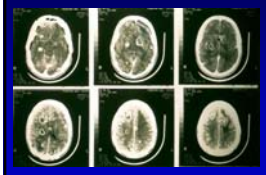
Tissue cysts



Oocysts

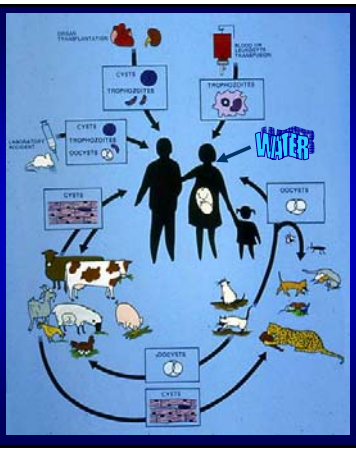
*T. gondii* strains
Type I
Type II
Type III

## Toxoplasmosis in immunocompromised patients



patients with organ transplants, AIDS, cancer, or those taking immunosuppressive drugs, reactivated and untreated toxoplasmosis has 100% mortality rate

brain abscesses, diffuse encephalitis without brain-occupying lesions, pneumonia, fever of unknown origin, myocarditis, hepatospenomegaly, lymphadenopathy and skin lesions




Bowie WR et al. Lancet 1997;350:173-177

Bahia-Oliveira L et al. Emerg Infect Dis 2003; 9:55-62.

Miller MA et al. Int J Parasitol 2002; 32:997-1006.

Lopez -Castillo CA et al. Rev Salud Publica 2005; 7(2):180-90

MAJOR ARTICLE

### Risk Factors for *Toxoplasma gondii* Infection in the United States

**Jeffrey L. Jones,[1] Valerie Dargelas,[2] Jacquelin Roberts,[1] Cindy Press,[2] Jack S. Remington,[2,3] and Jose G. Montoya[2,3]**

[1]Division of Parasitic Diseases, National Center for Zoonotic, Vectorborne, and Enteric Diseases, Coordinating Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; [2]Palo Alto Medical Foundation, Toxoplasma Serology Laboratory, Palo Alto, and [3]Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University School of Medicine, Stanford, California

***Background.*** Toxoplasmosis can cause severe ocular and neurological disease. We sought to determine risk factors for *Toxoplasma gondii* infection in the United States.

***Methods.*** We conducted a case-control study of adults recently infected with *T. gondii*. Case patients were selected from the Palo Alto Medical Foundation Toxoplasma Serology Laboratory from August 2002 through May 2007; control patients were randomly selected from among *T. gondii*–seronegative persons. Data were obtained from serological testing and patient questionnaires.

***Results.*** We evaluated 148 case patients with recent *T. gondii* infection and 413 control patients. In multivariate analysis, an elevated risk of recent *T. gondii* infection was associated with the following factors: eating raw ground beef (adjusted odds ratio [aOR], 6.67; 95% confidence limits [CLs], 2.09, 21.24; attributable risk [AR], 7%); eating rare lamb (aOR, 8.39; 95% CLs, 3.68, 19.16; AR, 20%); eating locally produced cured, dried, or smoked meat (aOR, 1.97; 95% CLs, 1.18, 3.28; AR, 22%); working with meat (aOR, 3.15; 95% CLs, 1.09, 9.10; AR, 5%); drinking unpasteurized goat's milk (aOR, 5.09; 95% CLs, 1.45, 17.80; AR, 4%); and having 3 or more kittens (aOR, 27.89; 95% CLs, 5.72, 135.86; AR, 10%). Eating raw oysters, clams, or mussels (aOR, 2.22; 95% CLs, 1.07, 4.61; AR, 16%) was significant in a separate model among persons asked this question. Subgroup results are also provided for women and for pregnant women.

***Conclusions.*** In the United States, exposure to certain raw or undercooked foods and exposure to kittens are risk factors for *T. gondii* infection. Knowledge of these risk factors will help to target prevention efforts.

Jones JL et al. Clinical Infectious Diseases 2009; 49:878-84

## Risk factors associated with acute *T.gondii* infection in the United States

| | aOR | CL | AR |
|---|---|---|---|
| • Eating raw ground beef | 6.67 | 2.09-21.24 | 7% |
| • Eating rare lamb | 8.39 | 3.68-19.16 | 20% |
| • Eating locally produced cured, dried, or smoked meat | 1.97 | 1.18-3.28 | 22% |
| • Working with meat | 3.15 | 1.09-9.10 | 5% |

Jones JL et al. Clinical Infectious Diseases 2009; 49:878-84

## Risk factors associated with acute *T.gondii* infection in the United States

| | aOR | CL | AR |
|---|---|---|---|
| • Drinking unpasteurized goat's milk | 5.09 | 1.45-17.80 | 4% |
| • Having 3 or more kittens | 27.89 | 5.72-135.86 | 10% |
| • Eating raw oysters, clams, or mussels | 2.22 | 1.07-4.61 | 16% |

Jones JL et al. Clinical Infectious Diseases 2009; 49:878-84

## Risk Factors for Acute *T. gondii* Infection in the United States

Drinking untreated water elevated the risk [aOR= 3.11 (0.92- 10.51)]

Eating frozen ground pork was associated with an increased risk of recent *T.gondii* infection in pregnant women [aOR= 2.30 (1.12- 4.74); AR= 22 (6-33)]

Not able to explain the risk for 48% of the infections (14 to 49% in Europe)

Jones JL et al. Clinical Infectious Diseases 2009; 49:878-84

## Risk factors for *T. gondii* infection in 131 mothers of infants with congenital toxoplasmosis

**Summary epidemiologic factors of maternal exposure and illness history**

| Factor | % |
|---|---|
| Any exposure to cats | 65 |
| Any exposure to undercooked or uncooked meat | 50 |
| Any exposure to cats or undercooked or uncooked meat | 75 |
| Specific exposure to cat litter or uncooked meat | 39 |
| Unexplained febrile illness or lymphadenopathy during pregnancy | 48 |
| Exposure to cat litter, uncooked meat, or toxoplasmosis-like illness during pregnancy | 48 |

Boyer K et al. Am J Obstet Gynecol. 2005 Feb;192(2): 564-71

# Toxoplasmosis during pregnancy

## Clinical Presentation of Congenital Toxoplasmosis during Pregnancy

- asymptomatic
- abnormal ultrasound
  - hydrocephalus
  - calcifications (brain or hepatic)
  - splenomegaly
  - ascites
- death of the fetus

## Clinical Presentation of Congenital Toxoplasmosis in the Newborn and Children

(1) sub-clinical infection

(2) disease (mild or severe) occurring in the first months of life

(3) overt neonatal disease

(4) sequelae or relapse of a previously undiagnosed infection manifested during infancy, childhood or adolescence

## Clinical Dictum:

Only those women who acquire toxoplasma infection during pregnancy are at risk for giving birth to a congenitally infected infant

## In Women with Prior History of Toxoplasmic Chorioretinitis, What is the Risk of delivering a Congenitally Infected Child?

Garweg JG. Reactivation of ocular toxoplasmosis during pregnancy BJOG 2005;112:241-2

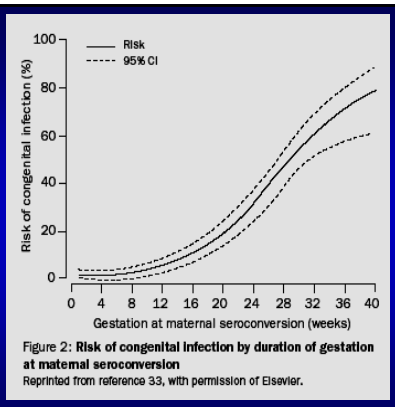



Figure 2: **Risk of congenital infection by duration of gestation at maternal seroconversion**
Reprinted from reference 33, with permission of Elsevier.

Dunn D, et al. Mother-to-child transmission of toxoplasmosis: risk estimates for clinical counselling. *Lancet* 1999; **353**: 1829–33.

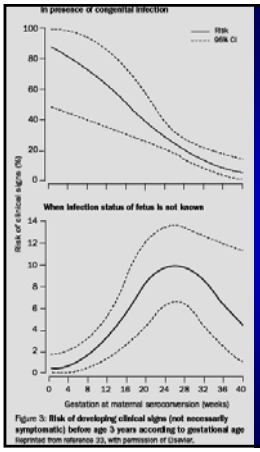



Figure 3: **Risk of developing clinical signs (not necessarily symptomatic) before age 3 years according to gestational age**
Reprinted from reference 33, with permission of Elsevier.

Dunn D, et al. Mother-to-child transmission of toxoplasmosis: risk estimates for clinical counselling. *Lancet* 1999; **353**: 1829–33.

## Demonstration of antibodies in serum

IgG,*IgM, *IgA, IgE

Differential agglutination (AC/HS)

IgG avidity

*Antibody may persist for months or a year or more

## IgM antibody response during acute and chronic infection

- In patients with recently acquired primary infection, *T. gondii*-specific IgM antibodies are detected initially and in most cases these titers become negative within a few months
- However, *T. gondii*-specific IgM titers may be observed for a year or more after initial infection

## IgM antibody response during acute and chronic infection

- Prolonged persistence of IgM antibodies does not appear to have clinical relevance and these patients should not be considered to have recently acquired infection
- Several kits for detection of IgM may yield relatively high frequency of false positive results (JCM 1997;35:174-8)

## Interpretation of a Positive *T. gondii*-Specific IgM antibody

- True positive result in the setting of a recently acquired infection
- True positive result in the setting of an infection acquired in the distant past
- False positive result in the setting of an infection acquired in the distant past

## Confirmatory Serological Testing for Toxoplasmosis and Abortion in the United States

- ~20% of pregnant women will choose abortion when told they have IgM antibody
- ~60% of positive IgM tests reported by outside laboratories are falsely positive; thus, 6 of every 10 aborted fetuses are not infected

Liesenfeld O. et al. Am J Obstet Gynecol 2001 Jan;184(2):140-5

## Initial Serological Screening at Commercial or non-Reference Labs

| IgG | IgM | |
|---|---|---|
| Negative | Negative | No evidence of prior exposure |
| Positive | Negative | Infected prior to pregnancy* |
| Negative | Positive or equivocal | Confirmatory testing at a Reference Lab |
| Positive | Positive or equivocal | Confirmatory testing at a Reference Lab |

*Except duing third trimester

A + IgM test alone can never be used to diagnose the acute infection (value of toxoplasma serologic profile in pregnancy)

| Date | IgG | IgM | IgA | IgE | AC/HS |
|---|---|---|---|---|---|
| 1/10* | + | + | | | |
| 1/10 | 8,000 | 6.9 | 20 | 5.0 | ≥1600/≥3200 |

**Acute Pattern**

Final Interpretation: most consistent with a recently acquired infection. Can not exclude possibility of having acquired the infection during this pregnancy

AC/HS = differential agglutination
*YB, 32.5 weeks pregnant on 1/10

## Confirmatory Serological Testing during Pregnancy at PAMF-TSL

| Date | IgG | IgM | IgA | IgE | AC/HS | AVT |
|---|---|---|---|---|---|---|
| 11/28 | + | + | | | | |
| 12/23* | 256 | 4.0 | – | – | 50/400 | 0.631 |
| | | | | | Equivocal | High |

Final Interpretation: most consistent with a chronic infection acquired prior to this pregnancy

AC/HS = differential agglutination; AVT = avidity
*AP, 10 weeks pregnant on 12/23

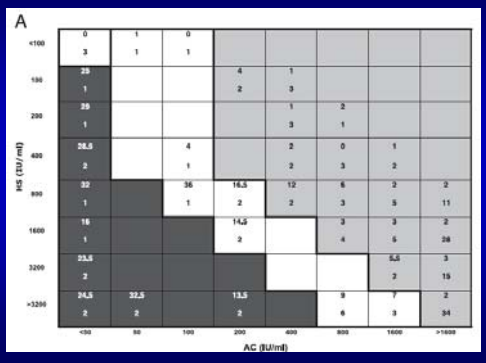
## Confirmatory Serological Testing during Pregnancy at PAMF-TSL

| Date | IgG | IgM | IgA | IgE | AC/HS |
|---|---|---|---|---|---|
| 1/31* | + | + | | | |
| 1/31 | 4096 | – | – | – | 400/>3200 NA Pattern |

Final interpretation: most consistent with a chronic infection acquired prior to this pregnancy

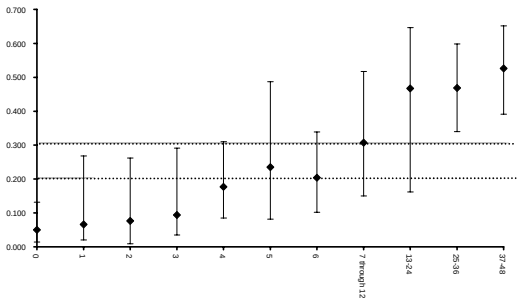
AC/HS = differential agglutination; NA = Non-Acute
*DT, 18 weeks pregnant on 1/31

## The Differential Agglutination Test as a Diagnostic Aid in Cases of Toxoplasmic Lymphadenitis




Montoya JG. et al. . J Clin Microbiol. 2007; 45: 1463-68

MEAN AND RANGE OF TOXOPLASMA IgG AVIDITY TITERS FOLLOWING ONSET OF TOXOPLASMIC LYMPHADENOPATHY




Time from onset of lymphadenopathy to sampling of sera (months)

Montoya JG., Huffman HB, Remington JS. J Clin Microbiol. 2004 Oct;42(10):4627-31

## IgG avidity interpretation during gestation

High avidity in the first 16 weeks essentially rules out that acute infection occurred during the first 4 months of pregnancy

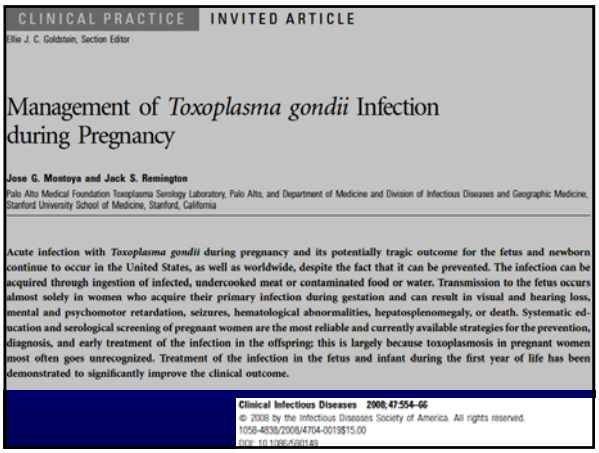
Low or equivocal avidity *does not* mean the patient has a recently acquired infection; *low avidity antibodies may persist for more than five months or even one year*

## Can we prevent fetal infection by treatment of a mother who acquires infection during pregnancy?

- Spiramycin* (*attempt* to prevent transmission - *controversial*)
- Pyrimethamine/Sulfadiazine (after 18-21 weeks gestation)
  - Also treats the fetus
  - Potentially teratogenic

*? 60% effective if given in early gestation

Montoya JG. And Remington JS Clinical Infectious Diseases 2008; 47: 554–66



CLINICAL PRACTICE INVITED ARTICLE

Ellie J. C. Goldstein, Section Editor

# Management of *Toxoplasma gondii* Infection during Pregnancy

**Jose G. Montoya and Jack S. Remington**

Palo Alto Medical Foundation Toxoplasma Serology Laboratory, Palo Alto, and Department of Medicine and Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, Stanford, California

**Acute infection with *Toxoplasma gondii* during pregnancy and its potentially tragic outcome for the fetus and newborn continue to occur in the United States, as well as worldwide, despite the fact that it can be prevented. The infection can be acquired through ingestion of infected, undercooked meat or contaminated food or water. Transmission to the fetus occurs almost solely in women who acquire their primary infection during gestation and can result in visual and hearing loss, mental and psychomotor retardation, seizures, hematological abnormalities, hepatosplenomegaly, or death. Systematic education and serological screening of pregnant women are the most reliable and currently available strategies for the prevention, diagnosis, and early treatment of the infection in the offspring; this is largely because toxoplasmosis in pregnant women most often goes unrecognized. Treatment of the infection in the fetus and infant during the first year of life has been demonstrated to significantly improve the clinical outcome.**

**Clinical Infectious Diseases 2008; 47:554–66**



1058-4838/2008/4704-0019$15.00

DOI: 10.1086/590149

## Prenatal diagnosis

- PCR in amniotic fluid (18 weeks)
- Ultrasonography

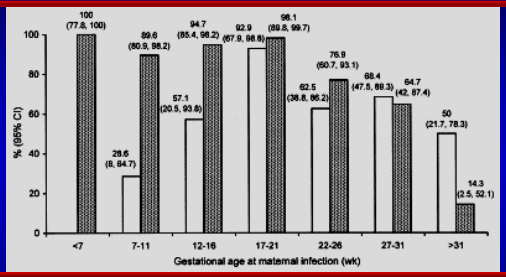
## Diagnostic Value of PCR in Amniotic Fluid

- At a major reference laboratory in France

| | |
|---|---|
| • SPECIFICITY: | 100% |
| • PPV: | 100% |
| • SENSITIVITY | 64% |
| • NPV: | 88% |

Romand S, Wallon M, Franck J, Thulliez P, Peyron F, Dumon, H. Obstet Gynecol 2001; 97: 296-300

## Prenatal diagnosis using PCR on amniotic fluid according to gestational age at maternal infection




*unshaded bars* = sensitivity
*shaded bars* = negative predictive value
CI = confidence interval

Romand et al. Obstet Gynecol. 2001 Feb;97(2):296-300

# Ocular Toxoplasmosis

## Toxoplasmosis of the Eye in Humans

Symptomatic or active

1. discovered at birth in a newborn with CT
2. reactivation of CT
3. in association with acute post-natally acquired infection
4. reactivation of a previous post-natally acquired infection

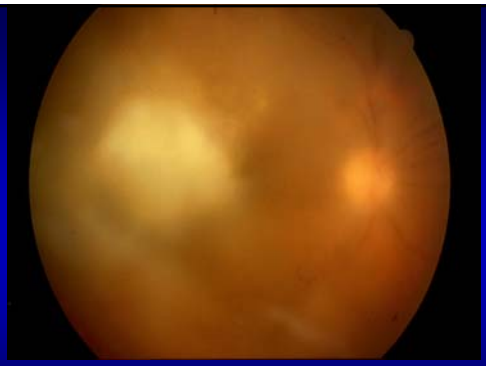
Asymptomatic scar

## Ocular Toxoplasmosis Typical Retinal Lesions

- In the setting of typical appearing lesions and serological test results consistent with toxoplasma infection, invasive procedures are usually not indicated

## Ocular Toxoplasmosis Atypical Retinal Lesions

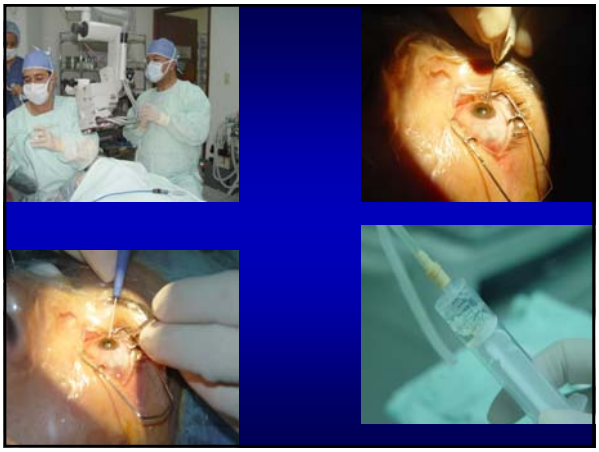
- In a number of patients, the retinal lesion morphology may be non-diagnostic and/or the response to treatment is suboptimal



Fundus photography of right eye at initial presentation. There is vitreous opacity and intraretinal whitening in posterior pole.
HSV, VZV, CMV, Toxoplasma, Toxocara, Syphilis

## Ocular Toxoplasmosis
## Atypical Retinal Lesions

- abnormal Toxoplasma antibody response in ocular fluids (immune load)
- demonstration of the parasite by isolation, histopathology or PCR



## "Use Of The Polymerase Chain Reaction for Diagnosis of Ocular Toxoplasmosis"

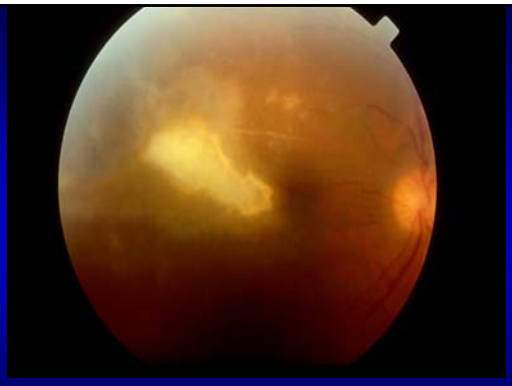
Ophthalmology *Volume 106, Number 8, August 1999*

Table 1. Clinical Findings, Treatment, and Outcome in Seven Patients in Whom Vitreous Fluid Examination by Polymerase Chain Reaction (PCR) Was Positive for *T. gondii* DNA

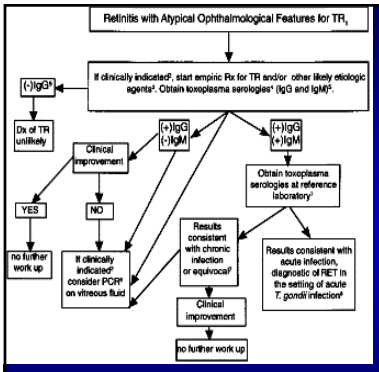
| Patient No. | Age (yrs)/Sex | Host Status | Eye(s) Involved | Eye Findings | Treatment Agents | Degree of Clinical Improvement | PCR Result Influenced Treatment |
|---|---|---|---|---|---|---|---|
| 1 | 34/M | No RF | R | Retinitis | Pyr/Sdz/Cm Atov | Partial | Yes |
| 2 | 78/M | No RF | R | Acute retinal necrosis | Pyr/Sdz/Cm | Partial | Yes |
| 3 | 81/M | No RF | R | Retinitis | TMP-SMZ Cater | Total | No |
| 4 | 59/M | HIV negative | R | Retinitis, detached retina | Pyr/Sdz | Total | Yes |
| 5 | 40/M | HIV positive | R | Retinitis | Pyr/Sdz/Cm | Total | Yes |
| 6 | 60/F | BMT | R | Retinitis involving macula | Pyr/Cm | Died | Yes |
| 7 | 70/F | SLE (Cster) | R | Acute retinal necrosis, detached retina | Pyr/Sdz | Partial | Yes |

Atov = atovaquone; BMT = bone marrow transplant; Cm = clindamycin; Cster = corticosteroids; Pyr = pyrimethamine; R = right; RF = risk factors or HIV infection; Sdz = sulfadiazine; SLE = systemic lupus erythematosus; TMP-SMZ = trimethoprim-sulfamethoxazole.

Montoya JG, Parmley S, Liesenfeld O, Jaffe GJ, Remington JS Ophthalmology 1999; 106:1554-1563



Appearance of right eye 3½ weeks after initiation of anti-Toxoplasma Rx. Macular lesion is more circumscribed, and there is now surrounding chorioretinal atrophy




atypical-appearing lesions: multiple foci of active retinitis, retinitis resembling virally induced retinal necrosis syndrome (vitreitis, peripheral retinitis, retinal vasculitis), significant intraretinal hemorrhage, absence of ophthalmoscopically visible chorioretinal scarring

Montoya JG, Parmley S, Liesenfeld O, Jaffe GJ, Remington JS
Use of the polymerase chain reaction for diagnosis of ocular toxoplasmosis.
Ophthalmology. 1999 Aug;106(8):1554-63

**Immunocompetent 10 yo girl with unilateral retinitis (right eye)**
**District of Columbia**

| Date | IgG | IgM | IgA | IgE | AC/HS* | Avidity |
|---|---|---|---|---|---|---|
| 1/15/08 | 8,000 | >10.0 | 0.0 | 2.8 | 800/800 acute pattern | 3.9 low |

**Final Interpretation**:
Consistent with a recently acquired infection.
If eye lesion(s) is consistent with toxoplasmic chorioretinitis, these serologic test results support an acute infection rather than reactivation of a congenital infection as the mechanism for this patient's eye disease.
Treatment with anti-toxoplasmic drugs may be indicated.

*AC/HS = differential agglutination

**57 yo man with unilateral diffuse retinitis (HIV negative) Connecticut**

| Date | IgG | IgM | IgA | IgE | AC/HS* |
|---|---|---|---|---|---|
| 2/09 | 512 | 0.0 | 0.0 | 0.0 | <50/800 non acute pattern |

PCR on vitreous fluid positive

**Final Interpretation**:
Consistent with an infection acquired in the distant past, thus eye disease is most likely the result of reactivation of a latent infection rather than of a recently acquired infection.
We recommend that, unless there is a contraindication, the patient be treated with anti-toxoplasma medications.

*AC/HS = differential agglutination

**HIV + 49 yo man with diffuse white exudates on the retina. History of travel to South America. Ophthalmologist suspected VZV. Lesion involves the macula North Carolina**

| Date | IgG | IgM |
|---|---|---|
| 3/08 | 1,024 | 0.0 |

PCR on vitreous fluid positive

**Final Interpretation**:
The positive PCR result from the vitreous fluid suggests that T. gondii is the etiologic agent.
Anti-toxoplasmic therapy is indicated.

**8 yo girl with unilateral lesion, morphology suggestive of toxo chorioretinitis California**

| | Date | IgG | IgM | IgA | IgE | AC/HS* |
|---|---|---|---|---|---|---|
| Mother | 1/11/08 | 64 | 0.3 | 0.0 | 0.0 | <50/200 Non acute pattern |
| Child | 1/22/08 | 512 | 0.0 | | | |

**Final Interpretation**:
These serologic test results consistent with a chronic infection suggesting eye disease is the result of reactivation of latent infection rather than of an acute infection, most likely congenital.

*AC/HS = differential agglutination

# Toxoplasmosis in Immunocompromised Patients

**Immunocompromised patients can develop toxoplasmosis as a result of their acute/primary infection…**

although primary infection tends to be asymptomatic, it may in some patients result in the following clinical manifestations (alone or in combination):

- lymphadenopathy
- chorioretinitis
- fever
- headache
- general malaise
- hepatitis
- myositis
- myocarditis

**…or reactivation of their latent infection if they have already been exposed to the parasite**

- brain abscesses
- diffuse encephalitis without brain-occupying lesions
- pneumonia
- fever of unknown origin
- myocarditis
- hepatospenomegaly
- lymphadenopathy
- skin lesions

## Laboratory Diagnosis of Toxoplasmosis in the Immunocompromised Patient

serologies

PCR

histological examination with hematoxylin and eosin (H&E) or Wright Giemsa stains, immunohistochemistry with *T. gondii*-specific immunoperoxidase

isolation of the parasite

**Table 1. Drugs used in transplant patients with toxoplasmosis in the setting of acute infection or reactivation* (primary therapy)**

| | **Immunocompromised Patients*** with toxoplasmosis including clinicallly active, toxoplasmic encephalitis, pneumonia, fever of unknown origin, ocular disease, myocarditis, myositis, hepatitis or in the setting of acute infection** |
|---|---|
| Pyrimethamine (PO): | 200 mg loading dose followed by 50 mg (<60kg) to 75 mg (>60 kg)/day |
| Folinic acid** (PO): | 10 to 20 mg daily (up to 50 mg/day) (during and 1 week after therapy with pyrimethamine) |
| *plus* | |
| Sulfadiazine (PO): | 1000 (<60 kg) to 1500 mg (> 60 kg) every 6 hour |
| *or* | |
| Clindamycin (PO or IV) | 600 mg every 6 hours (up to 1200 mg every 6 hours) |
| *or* | |
| Atovaquone (PO) | 1500 mg orally twice daily |
| Trimethoprim/ Sulfamethoxazole (PO or IV) | 10 mg/kg/day (trimethoprim component) divided in two to three doses (doses as high as 15 - 20 mg/kg/day have been used) |
| Pyrimethamine/folinic acid | Same doses as above |
| *plus* | |
| Clarithromycin (PO) | 500 mg every 12 hours |
| *or* | |
| Dapsone (PO) | 100 mg/d |
| *or* | |
| Azithromycin (PO) | 900 to 1200 mg/day |

**Prefered regimens: pyrimethamine/sulfadiazine/folinic acid or trimethoprim/sulfamethoxazole**

*Assistance is available for the diagnosis and management of patients with toxoplasmosis at the Palo Alto Medical Foundation Toxoplasma Serology Laboratory, telephone number Palo Alto, CA; http://www.pamf.org/serology/ ; 1-650-853-4828; e-mail: toxolab@pamf.org

** Folinic acid = leucovorin; folic acid should not be used as a substittue for folinic acid .

***After the successful use of a combination regimen during the acute/primary therapy phase, same agents at half-does are usually used for maintenance or secondary prophylaxis

33 yo woman who is 14 weeks pregnant has been diagnosed with reactivation of her previously diagnosed ocular toxoplasmosis. Her ophthalmologist insists that her macular active lesions require immediate anti-toxoplasma therapy. She has positive Toxoplasma IgG and negative IgM. Without anti-toxoplasma treatment, what is the risk of transmission of the parasite to her fetus?

A. 100%

B. 75%

C. 50%

D. 25%

E. Essentially zero