Toxoplasmosi:

EPIDEMIOLOGIA, PREVENZIONE E DIAGNOSI

Meroni V

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Toxoplasma gondii

- The most successful parasite
- worldwide distribution,
- capable to infect all warm-blooded animals,
- highly transmissible,
- ¼ of the human population is chronically infected

Low prevalence (10-30%): North America, nel Suth East Asia, North Europe, Sahelian country of Africa

Moderate prevalence (30-50%): Central and Southern Europe

High prevalence (>50%): Latin America, Tropical African countries
## Anti-Toxoplasma antibodies in 3047 pregnant women (2005-2007)

<table>
<thead>
<tr>
<th>Anti-Toxoplasma antibodies</th>
<th>Italian women (2465)</th>
<th>Foreign women (609)</th>
<th>P</th>
<th>Total women (3074)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG neg IgM neg</td>
<td>80.6 %</td>
<td>65.0 %</td>
<td>&lt;0.01</td>
<td>77.5 %</td>
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<tr>
<td>IgG POS IgM neg</td>
<td>17.7 %</td>
<td>33.2 %</td>
<td>&lt;0.01</td>
<td>20.8 %</td>
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<tr>
<td>IgM POS (or border line)</td>
<td>1.7 %</td>
<td>1.8 %</td>
<td>NS</td>
<td>1.7 %</td>
</tr>
</tbody>
</table>

De Paschale et al Microbiologia medica 2008
Anti *Toxoplasma gondii* antibodies in 1584 solid organ donors and recipients in Pavia (1997-2007)

540 Donors  285 (53%) seropositive
8 (1,5%) IgM positive

1084 Recipients 611 (56%) seropositive
Toxoplasmosis involves parasite and host factors

**THE PARASITE**
- Inoculum +++
- Infective stage (cysts vs. oocysts)
- Genetic background

**THE HOST**

Photo: Luc Viatour
• Interviews with a standard questionnaire
• Europe: Naples, Lausanne, Copenhagen, Oslo, Brussels, and Milan
• Main risk factor of infection with *T. gondii* = undercooked meat (+++cyst) in all centers
• The type of meat varies among countries
• The authors were not able to explain 14-49% of the risk for *T. gondii* infection, depending on the center
Prevalence and risk factors for *Toxoplasma gondii* infection among pregnant and postpartum women attended at public healthcare facilities in the City of Niterói, State of Rio de Janeiro, Brazil

Fernanda Loureiro de Moura[1], Maria Regina Reis Amendoeira[2], Otílio Machado Pereira Bastos[1], Danuza Pinheiro Bastos Garcia de Mattos[1], Ana Beatriz Monteiro Fonseca[3], José Leonardo Nicolau[2], Leandro Baptista das Neves[2] and Patricia Riddell Millar[1],[2]


Prevalence and Risk Factors of Toxoplasmosis among Pregnant Women in Fortaleza, Northeastern Brazil

Susann Sroka, Nina Bartelheimer, Andreas Winter, Jörg Heukelbach, Liana Ariza, Heliane Ribeiro, Fabiola Araújo Oliveira, Ajax Jose Nogueira Queiroz, Carlos Alencar Jr., and Oliver Liesenfeld

Factors associated to infection by *Toxoplasma gondii* in pregnant women attended in basic health units in the city of Rolândia, Paraná, Brazil


Renata Cristina Ferreira Dias(1), Fabiana Maria Rutz LOPES-MORI(2), Regina MITSEA-KA-BREGANÔ(2), Rafael André Ferreira Dias(3), Deise Vieira TOKANO(3), Edna Maria Visoci REICHE(4), Roberta Lemos FREIRE(5) & Italmar Teodoro NAVARRO(5)

Serological screening and toxoplasmosis exposure factors among pregnant women in South of Brazil

Triagem sorológica e fatores de risco para toxoplasmosose em gestantes no Sul do Brasil


Silvia Maria Spalding[1,4], Maria Regina Reis Amendoeira[1], Carlos Henrique Klein[1,4] and Luis Carlos Ribeiro[5]

- Questionnaire
- Contact with soil and cats
- Low educational level
- Home-made water ice
- Residence in rural areas
- Vegetables washed with untreated water

- Main risk factor = via oocysts in Brazil
Low genetic diversity of *T. gondii* strains in Europe and North America

3 major genotypes:

- type I: 19%
- type II: 54%
- type III: 27%

*Toxoplasma gondii* comprises three clonal lineages: correlation of parasite genotype with human disease.

**Howe** DK, **Sibley** LD. J Infect Dis. 1995 Dec;172(6):1561-6.
Strains from Europe in 2013 (+++ France)

- **Type II:**
  - 99% of strains from wild and domestic animals
  - 94% in congenital toxoplasmosis

- **Type III <5%; no type I**

- Atypical strains = imported

An innovative survey underlining the significant level of contamination by *Toxoplasma gondii* of ovine meat consumed in France

Lénaïg Halos a,*, Anne Thébault b, Dominique Aubert c,d, Myriam Thomas d, Catherine Perret a, Régine Geers c,d, Annie Alliot a, Sandie Escotte-Binet c,d, Daniel Ajzenberg f,g, Marie-Laure Dardé Benoit Durand e, Pascal Boireau d, Isabelle Villena c,d


Genotype of 86 *Toxoplasma gondii* Isolates Associated with Human Congenital Toxoplasmosis, and Correlation with Clinical Findings

Daniel Ajzenberg,1 Nadine Cogné,1 Luc Paris,2 Marie-Hélène Bessières,3 Philippe Thulliez,3 Denis Filisetti,1 Hervé Pelloux,6 Pierre Marty,7 and Marie-Laure Dardé1

1Service de Parasitologie-Mycologie, EA 3174, Faculté de Médecine, Limoges, 2Service de Parasitologie, Hôpital Pitié-Salpêtrière, and 3Institut de Périiculture, Paris, 4Service de Parasitologie-Mycologie, Hôpital de Rangueil, Toulouse, 5Institut de Parasitologie et de Pathologie Tropicale, INSERM U392, Strasbourg, 6Service de Parasitologie-Mycologie, Hôpital A. Michallon, Grenoble, and 7Service de Parasitologie-Mycologie, Hôpital de l’Archet, Nice, France

Strains from South America (+++ Brazil)

- almost exclusively from animals
- genetically different from type I, II, and III strains
- high genetic diversity: countless diverse genotypes
- = atypical strains
Ocular lesions in congenital toxoplasmosis in Brazil are:

• more frequent,
• more recurrent,
• more multiple,
• larger,
• more likely to impair vision than in Europe.

"We suggest that the increased frequency and severity of ocular disease in Brazil compared with Europe is due to exposure to more virulent strains of *T. gondii* in Brazil."
Clinical case 2

- Strain genotyping:
  - atypical strain
  - genotype close to 1 strain from Uruguay and 1 strain from Nigeria...

- Imported food linked to the infection:
  - raw horsemeat consumption in pregnancy (May and June)
  - origin of the horsemeat: unknown

Congenital Toxoplasmosis and Reinfecion during Pregnancy: Case Report, Strain Characterization, Experimental Model of Reinfecion, and Review

Annie Elbez-Rubinstein,1 Daniel Ajzenberg,3,4 Marie-Laure Dardé,3,4 Robert Cohen,2 Aurélien Dumètre,4 Hélène Yera,5 Emmanuelle Gondon,1 Jean-Claude Janaud,1 and Philippe Thulliez5

Virulence in human?
Host factor (immune status)

• Type II : chronic infection in healthy adults
• Life threatening in immunocompromised
Virulence in human?
Congenital toxoplasmosis

• Age of gestation at maternal infection
Prevention of Congenital toxoplasmosis

**PRIMARY**

Prevention of infection in pregnancy (hygienic prophylactic measures)

**SECONDARY**

Prevention of vertical transmission and severity of fetal damages reduction (prenatal diagnosis, therapy)

**TERTIARY**

Sequelae reduction (early diagnosis and therapy in newborns)

Decrease in severity and incidence of congenital toxoplasmosis
“Lo screening prenatale della toxoplasmosi e raccomandato e consiste in una sierologia al primo controllo prenatale, ripetuta ogni 4-6 settimane se il primo esame risulta negativo, fino al termine della gravidanza. Le donne devono essere informate delle misure igieniche che possono evitare l’infezione in gravidanza”

La sua esecuzione in epoca preconcezionale e durante la gravidanza (preferibilmente entro le prime 13 settimane di gestazione e ogni 30-40 giorni in caso di sieronegatività) è esentata dal pagamento del ticket ai sensi del DPR 245 del 10/09/1998.
Congenital *Toxoplasma* Infection: Monthly Prenatal Screening Decreases Transmission Rate and Improves Clinical Outcome at Age 3 Years


**Background.** *Toxoplasma* infection during pregnancy exposes the fetus to risks of congenital infection and sequelae that depend heavily on gestational age (GA) at time of infection. Accurate risk estimates by GA are necessary to counsel parents and improve clinical decisions.

**Methods.** We analyzed data from pregnant women diagnosed with acute *Toxoplasma* infection in Lyon (France) from 1987 to 2008 and assessed how the risks of congenital toxoplasmosis and of clinical signs at age 3 years vary depending on GA at the time of maternal infection.

**Results.** Among 2048 mother-infant pairs, 93.2% of mothers received prenatal treatment and 513 (24.7%) fetuses were infected. Because of a significant reduction in risk since 1992 when monthly screening was introduced (59.4% vs 46.6% at 26 GA weeks; *P = .038*), probabilities of infection were estimated on the basis of maternal infections diagnosed after mid-1992 (n = 1624). Probabilities of congenital maternal infections before 12 weeks of gestation, rose to 20.0% at 19 weeks, and then continued increasing to 52.3% and almost 70% at 28 and 39 GA weeks, respectively. Because of a significant reduction in risk of clinical signs of congenital toxoplasmosis in infected children born from mothers diagnosed after 1995 when polymerase chain reaction testing on amniotic fluid was initiated (87/794 vs 46/1150; *P = .012*), probabilities of clinical signs at 3 years were estimated based on 1015 maternal infections diagnosed after 1995 including 207 infected children, with symptoms in 46 (22.2%).

**Conclusions.** These analyses demonstrated that introduction of monthly prenatal screening and improvement in antenatal diagnosis were associated with a significant reduction in the rate of congenital infection and a better outcome at 3 years of age in infected children. Our updated estimates will improve individual management and counseling in areas where genotype II *Toxoplasma* is predominant.
Gruppo multidisciplinare

"Malattie infettive in ostetricia-ginecologia e neonatologia"

AMCLI (Associazione Microbiologi Clinici Italiani), SIGO (Società Italiana di Ginecologia e Ostetricia), SIMaST (Società Interdisciplinare delle Malattie Sessualmente Trasmissibili), SIMIT (Società Italiana di Malattie Infettive e Tropicali), SIN (Società Italiana di Neonatologia), SIP (Società Italiana di Pediatrica).

Percorsi diagnostico-assistenziali in Ostetricia-Ginecologia e Neonatologia

TOXOPLASMA GONDII

APRILE 2012
Diagnosis of Toxoplasmosis in pregnancy

Negative screening:
- **IgG- IgM-**
  - Hygienic prophylactic measures
  - Monthly control
  - No seroconversion
  - No Immunity
    - Counselling for further pregnancies

Positive screening:
- **IgG- IgM+**
  - WB IgG/IgM
    - IgG Neg*
    - No therapy
  - WB IgG/IgM
    - IgG Pos*
    - Seroconversion

- **IgG+ IgM+**
  - Low/Intermediate IgG Avidity
  - High**
    - **In the first trimester**

- **IgG+ IgM-**
  - Previous Immunity
    - Serology one month later
    - Keep the report for further pregnancies

* One month later no therapy
** In the first trimester
Norme igienico alimentari per la gestante recettiva alla toxoplasmosi

- cuocere sempre molto bene le carni prima del consumo;
- evitare il consumo di carni crude o poco cotte, salumi crudi, frutti mare crudi, latte non pastorizzato, uova crude;
- lavare accuratamente frutta e verdure prima del consumo;
- lavare sempre le mani prima di mangiare e dopo aver toccato carni crude, frutta e verdure non lavate, terra o altri materiali potenzialmente contaminati con le feci del gatto;
- pulire accuratamente le superfici della cucina e gli utensili venuti a contatto con carni crude, frutta e verdure non lavate;
- usare sempre guanti di gomma in tutte le attività che possono comportare il contatto con materiali potenzialmente contaminati con le feci del gatto (giardinaggio, orticoltura, pulizia lettiera del gatto, ecc.);
- evitare il contatto con il gatto e soprattutto con le sue feci; in caso di presenza di un gatto in casa adottare le seguenti precauzioni: alimentare l’animale con cibi cotti o in scatola evitando che esca di casa, affidare ad altri la pulizia della sua cassetta, facendo sostituire frequentemente (meglio se quotidianamente) la lettiera e igienizzando il contenitore per almeno 5’ con acqua bollente;
- evitare viaggi al di fuori dell’Europa e del Nord America
- eliminare dalla propria abitazione veicoli animali (mosche, scarafaggi, ecc.)
Diagnosis of Toxoplasmosis in pregnancy

**Serological screening**

- **Negative**
  - IgG- IgM-
    - Hygienic prophylactic measures
    - Monthly control
    - No seroconversion
    - No Immunity
      - Counselling for further pregnancies

- **Positive**
  - IgG- IgM+
    - WB IgG/IgM
      - IgG Neg*
      - WB IgG/IgM
        - IgG Pos*
        - Low/Intermediate IgG Avidity
        - High** IgG Avidity
  - IgG+ IgM+
    - Low/Intermediate IgG Avidity
    - In the first trimester
  - IgG+ IgM-
    - High** IgG Avidity
    - Previous Immunity
      - Serology one month later
      - Keep the report for further pregnancies

**ACUTE INFECTION**

* One month later no therapy
** In the first trimester
Effectiveness of prenatal treatment for congenital toxoplasmosis: a meta-analysis of individual patients’ data

The SYROCO (Systematic Review of Congenital Toxoplasmosis) study group

Summary

Background Despite three decades of prenatal screening for congenital toxoplasmosis in some European countries, uncertainty remains about the effectiveness of prenatal treatment.

Methods We did a systematic review of cohort studies based on universal screening for congenital toxoplasmosis. We did a meta-analysis using individual patients’ data to assess the effect of timing and type of prenatal treatment on mother-to-child transmission of infection and clinical manifestations before age 1 year. Analyses were adjusted for gestational age at maternal seroconversion and other covariates.

Findings We included 26 cohorts in the review. In 1438 treated mothers identified by prenatal screening, we found weak evidence that treatment started within 3 weeks of seroconversion reduced mother-to-child transmission compared with treatment started after 8 or more weeks (adjusted odds ratio [OR] 0.48, 95% CI 0.28–0.80; p=0.05). In 959 infected liveborn infants identified by prenatal or neonatal screening, we found no evidence that prenatal treatment significantly reduced the risk of clinical manifestations (adjusted OR for treated vs not treated 1.11, 95% CI 0.61–2.02). Increasing gestational age at seroconversion was strongly associated with increased risk of mother-to-child transmission (OR 1.15, 95% CI 1.12–1.17) and decreased risk of intracranial lesions (0.91, 0.87–0.95), but not with eye lesions (0.97, 0.93–1.00).

Interpretation We found weak evidence for an association between early treatment and reduced risk of congenital toxoplasmosis. Further evidence from observational studies is unlikely to change these results and would not distinguish whether the association is due to treatment or to biases caused by confounding. Only a large randomised controlled clinical trial would provide clinicians and patients with valid evidence of the potential benefit of prenatal treatment.

Prenatal Treatment for Serious Neurological Sequelae of Congenital Toxoplasmosis: An Observational Prospective Cohort Study

Mario Cortina-Borja1, Hooi Kuan Tan1, Martine Wallon2, Malgorzata Paul3, Andrea Prusa4, Wilma Buffolano5, Gunilla Malm6, Alison Salt7, Katherine Freeman8, Eskild Petersen9, Ruth E. Gilbert1*

1 Centre for Pediatric Epidemiology and Biostatistics, UCL Institute of Child Health, London, United Kingdom. 2 Hospices Civils de Lyon, Service de Parasitologie, Hôpital de la Croix-Rousse, Lyon, France. 3 Department and Clinic of Tropical and Parasitic Diseases, University of Medical Sciences, Poznan, Poland. 4 Medical University of Vienna, Department of Paediatrics and Adolescent Medicine, Division of Paediatric Neonatology, Intensive Care and Neuropaediatrics, Vienna, Austria. 5 Perinatal Infection Unit, Department of Paediatrics, University of Naples Federico II, Naples, Italy. 6 Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Division of Paediatrics, Karolinska University Hospital, Huddinge, Sweden. 7 Wolfson Centre, UCL Institute of Child Health, London, United Kingdom. 8 Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, New York, United States of America. 9 Department of Infectious Diseases, Aarhus University Hospital, Skejby, Aarhus N, Denmark.

PLOS MEDICINE

OPEN ACCESS Freely available online

Abstract

Background The effectiveness of prenatal treatment to prevent serious neurological sequelae (SNDS) of congenital toxoplasmosis is not known.

Methods and Findings: Congenital toxoplasmosis was prospectively identified by universal prenatal or neonatal screening in 14 European centres and children were followed for a median of 4 years. We evaluated determinants of postnatal death or SNDS defined by one or more of functional neurological abnormalities, severe visual impairment, or pregnancy termination for confirmed congenital toxoplasmosis. Two-thirds of the cohort received prenatal treatment (189/293; 65%). The odds ratio for SNDS of 23/293 (8%) fetuses developed SNDS of which nine were pregnancy terminations. Prenatal treatment reduced the risk of SNDS. The odds ratio for prenatal treatment, adjusted for gestational age at maternal seroconversion, was 0.24 (95% Bayesian credible intervals 0.07–0.71). This effect was robust to most sensitivity analyses. The number of infected fetuses needed to be treated to prevent one case of SNDS was three (95% Bayesian credible intervals 2–15) after maternal seroconversion at 10 weeks, and 18 (9–75) at 30 weeks of gestation. Pyrimethamine-sulphonamide treatment did not reduce complications compared with spiramycin alone (adjusted odds ratio 0.78, 0.21–2.95). The proportion of live-born infants with intracranial lesions detected postnatally who developed SNDS was 31.0% (17.0%–38.1%).

Conclusion: The finding that prenatal treatment reduced the risk of SNDS in infected fetuses should be interpreted with caution because of the low number of SNDS cases and uncertainty about the timing of maternal seroconversion. As these are observational data, policy decisions about screening require further evidence from a randomized trial of prenatal screening and from cost-effectiveness analyses that take into account the incidence and prevalence of maternal infection.

Please see later in the article for the Editors’ Summary.
Antibodies kinetics in early treated pregnant woman
Antibodies kinetics in treated pregnant woman

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG CLIA</td>
<td>NEG</td>
<td>NEG</td>
<td>8</td>
<td>NEG</td>
<td>25</td>
</tr>
<tr>
<td>IgG ELFA</td>
<td>NEG</td>
<td>NEG</td>
<td>ND</td>
<td>4</td>
<td>24</td>
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<tr>
<td>IgM CLIA</td>
<td>POS</td>
<td>POS</td>
<td>POS</td>
<td>POS</td>
<td>POS</td>
</tr>
<tr>
<td>IgM ISAGA</td>
<td>12+</td>
<td>12+</td>
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<td>IgA ELISA</td>
<td>200</td>
<td>250</td>
<td>200</td>
<td>150</td>
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<tr>
<td>WB IgG/IgM</td>
<td>NEG/POS</td>
<td>POS/POS</td>
<td>POS/POS</td>
<td>POS/POS</td>
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<tr>
<td>IgG AVIDITY</td>
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<td></td>
<td></td>
<td></td>
<td>0.114</td>
</tr>
</tbody>
</table>

Spyramicin 10/11 till 15/12 2010
LDBIOTOXO II

- (immunoblot)
- ready to use
- standardized (60’- 60’- 30’)
- positive control For IgG included

5 specific band:
30 – 31 – 33 – 40 – 45 kDa

IgG positive: 3 specific bands
IgM positive: 2 specific bands including
30 kDa band
41 IgG-/IgM+ spiramycin treated pregnant women

<table>
<thead>
<tr>
<th>No.</th>
<th>IgM ISAGA</th>
<th>IgG WB</th>
<th>IgM WB</th>
<th>Seroconversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>NEG</td>
<td>NEG</td>
<td>NEG</td>
<td>No seroconversion</td>
</tr>
<tr>
<td>14</td>
<td>POS</td>
<td>NEG</td>
<td>NEG</td>
<td>No seroconversion</td>
</tr>
<tr>
<td>13</td>
<td>POS</td>
<td>POS</td>
<td>POS</td>
<td>Seroconversion</td>
</tr>
<tr>
<td>4</td>
<td>POS</td>
<td>NEG</td>
<td>POS</td>
<td>No seroconversion</td>
</tr>
</tbody>
</table>
Serological screening

**Positive**

- IgG+ IgM+
  - Low/Intermediate IgG Avidity
  - High** IgG Avidity

**IgG+ IgM-**

- Hygienic profilactic measures
  - Monthly control

**Negative**

- IgG- IgM-

No seroconversion

No Immunity
Counselling for further pregnancies

**IgG- IgM+**

- WB IgG/IgM IgG Neg*
- WB IgG/IgM IgG Pos*

Seroconversion

ACUTE INFECTION

Previous Immunity
Serology one month later
Keep the report for further pregnancies

* One month later no therapy
** In the first trimester
Maturazione dell’ Indice di Avidità in 28 gravide trattate (122 campioni) e in 16 linfoadeniti non trattate (51 campioni)
## Cohen’s Kappa

<table>
<thead>
<tr>
<th>AVIDITY TEST</th>
<th>k</th>
<th>SE</th>
<th>%agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.89</td>
<td>0.0468</td>
<td>93%</td>
</tr>
<tr>
<td>2</td>
<td>0.55</td>
<td>0.0481</td>
<td>70%</td>
</tr>
<tr>
<td>3</td>
<td>0.57</td>
<td>0.0553</td>
<td>72%</td>
</tr>
<tr>
<td>4</td>
<td>0.51</td>
<td>0.0509</td>
<td>68%</td>
</tr>
<tr>
<td>5</td>
<td>0.58</td>
<td>0.0489</td>
<td>73%</td>
</tr>
<tr>
<td>6</td>
<td>0.20</td>
<td>0.0355</td>
<td>47%</td>
</tr>
<tr>
<td>7</td>
<td>0.57</td>
<td>0.0485</td>
<td>72%</td>
</tr>
</tbody>
</table>

**Kappa evaluation**
- <0 no correlation
- 0.00-0.2 slight
- 0.21-0.40 fair
- 0.41-0.60 moderate
- 0.61-0.80 good
- 0.81-1.00 very good
CLIA

y = 0.0328x + 0.1087

R² = 0.7557

VIDAS

y = 0.0208x + 0.0511

R² = 0.6619
CONCLUSIONS

• Great individual variability, slow maturation, persistence of intermediate avidity

• Test characteristics and limits

• Therapy effects

• In the diagnosis of toxoplasmosis, the IgG avidity test must still be considered as an exclusion test: High avidity Index clearly excludes infections in the previous 3-4 months, but low or intermediate avidity index can persist longer than expected.
Diagnosis of toxoplasmosis
Italian Consensus  April 2012

Acute infection

Spiramycin
Ultrasound controls

> 23a wks

Prenatal diagnosis
PRC on AF >18wks
4-6 weeks after seroconversion

Pirimethamine + sulfadiazine

At delivery
mother-newborn blood samples
IgG, IgM, IgA IgG IgM WB
Immunological tests
Clinical examination

Positive

Normal U.S

Abnormal US
TOP

Negative (spiramycin)
<table>
<thead>
<tr>
<th>Seroconversion Trimester</th>
<th>N°</th>
<th>CT+ PCR</th>
<th>CT- PCR</th>
<th>Sensibility</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>I</td>
<td>357</td>
<td>3</td>
<td>6</td>
<td>1</td>
<td>347</td>
</tr>
<tr>
<td>II</td>
<td>200</td>
<td>37</td>
<td>9</td>
<td>5</td>
<td>149</td>
</tr>
<tr>
<td>III</td>
<td>36</td>
<td>17</td>
<td>8</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Tot</td>
<td>593</td>
<td>57</td>
<td>23</td>
<td>7</td>
<td>506</td>
</tr>
</tbody>
</table>

L. Thalib et al, BJOG, May 2005
Performance of state-of-art Toxoplasmosis PCR on amniotic fluid

Wallon et al, Obstet Gynecol. April 2010 - N=377

<table>
<thead>
<tr>
<th></th>
<th>First Trimester</th>
<th>Second Trimester</th>
<th>Third Trimester</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>75 (19–99)</td>
<td>97 (83–99.9)</td>
<td>88 (67–98.5)</td>
<td>92.2 (81–98)</td>
</tr>
<tr>
<td>Specificity</td>
<td>100 (97–100)</td>
<td>100 (95.4–100)</td>
<td>100 (66.4–100)</td>
<td>100 (98–100)</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>100 (29.2–100)</td>
<td>100 (88.1–100)</td>
<td>100 (78.2–100)</td>
<td>100 (92.5–100)</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>99 (96–99.9)</td>
<td>99 (93–99.9)</td>
<td>82 (48–98)</td>
<td>98.1 (95–99.5)</td>
</tr>
</tbody>
</table>

Table 2. Characteristics of the Four Infected Children With Negative Polymerase Chain Reaction Results

<table>
<thead>
<tr>
<th>Case</th>
<th>Seroconversion</th>
<th>Spiramycin</th>
<th>Amniocentesis</th>
<th>IgM at Birth</th>
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<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>15.5</td>
<td>18</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>26</td>
<td>29</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>28</td>
<td>30.5</td>
<td>34</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>32</td>
<td>36</td>
<td>40</td>
<td>+</td>
</tr>
</tbody>
</table>

No false +
Rare false -
Probability of congenital infection (---) and severity of clinical signs (—)
According to gestational age at maternal seroconversion
Congenital toxoplasmosis

Clinical presentation:

Severe malformations

Sub clinical forms ;
Late onset of ocular lesions
At birth

• Is the new born contaminated?
  Yes if: PCR on amiotic fluid was positive
  Yes if:

Extremely rare usually detected by Ultra sound
Is he infected?

- Yes if: IgM or IgA in peripheral blood

Sensitivity: $\approx 76\%$

Specificity: $\sim 99.7\%$

depends on age of pregnancy at maternal infection
Do not stop follow-up before a negative serology

- Post natal serological trough
The only way to rule out a congenital infection:

Negative serology within the first year

Regular blood sampling:
  - painful
  - not well accepted by parents
VAL Pia, Toxo -

AxSYM IgG

OD Salivary IgG

Brussels january 2014
IgG IgM WB
Uninfected newborn

<table>
<thead>
<tr>
<th></th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>72</td>
<td>54</td>
</tr>
<tr>
<td>IgM</td>
<td>NEG</td>
<td>NEG</td>
</tr>
<tr>
<td>IgM ISAGA</td>
<td>12+</td>
<td>NEG</td>
</tr>
<tr>
<td>IgA</td>
<td>100</td>
<td>NEG</td>
</tr>
<tr>
<td>Isolamento</td>
<td>NEG</td>
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</table>
Mother Day of Birth

Infected newborn

<table>
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<tr>
<th></th>
<th>17</th>
<th>18</th>
<th>38</th>
<th>12+</th>
<th>NEG</th>
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</thead>
<tbody>
<tr>
<td>IgG</td>
<td>NEG</td>
<td>NEG</td>
<td>38</td>
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<tr>
<td>IgM</td>
<td>NEG</td>
<td>NEG</td>
<td>18</td>
<td></td>
<td>NEG</td>
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<tr>
<td>IgM ISAGA</td>
<td>NEG</td>
<td>NEG</td>
<td>12+</td>
<td></td>
<td>NEG</td>
</tr>
<tr>
<td>IgA</td>
<td>NEG</td>
<td>NEG</td>
<td>NEG</td>
<td></td>
<td>NEG</td>
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</table>
### IgG / IgM WB at birth

**Infected newborn**

<table>
<thead>
<tr>
<th></th>
<th>5</th>
<th>6</th>
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<tbody>
<tr>
<td>IgG</td>
<td>&gt; 300</td>
<td>&gt; 300</td>
</tr>
<tr>
<td>IgM</td>
<td>100</td>
<td>800</td>
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<tr>
<td>IgM ISAGA</td>
<td>12+</td>
<td>12+</td>
</tr>
<tr>
<td>IgA</td>
<td>&gt; 400</td>
<td>200</td>
</tr>
<tr>
<td>Avidity</td>
<td>0.065</td>
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</table>

- madre
- figlio alla nascita
### IgG-IgM WESTERN BLOT

<table>
<thead>
<tr>
<th></th>
<th>POS</th>
<th>NEG</th>
<th>TOT</th>
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<tbody>
<tr>
<td>POS</td>
<td>38</td>
<td>6</td>
<td>44</td>
</tr>
<tr>
<td>NEG</td>
<td>2</td>
<td>178</td>
<td>180</td>
</tr>
<tr>
<td>TOT</td>
<td>40</td>
<td>184</td>
<td>224</td>
</tr>
</tbody>
</table>

Sens 95,0 (IC 95%: 83,1-99,4)*  
Spec 96,7 (IC 95%: 93,0-98,8)

---

### IgM ISAGA + IgA ELISA

<table>
<thead>
<tr>
<th></th>
<th>POS</th>
<th>NEG</th>
<th>TOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>POS</td>
<td>30</td>
<td>2</td>
<td>32</td>
</tr>
<tr>
<td>NEG</td>
<td>10</td>
<td>182</td>
<td>192</td>
</tr>
<tr>
<td>TOT</td>
<td>40</td>
<td>184</td>
<td>224</td>
</tr>
</tbody>
</table>

Sens 75,0 (IC 95%: 58,8-87,3)*  
Spec 98,9 (IC 95%: 96,1-99,3)
IGRA TEST

QuantiFERON Cellestis® (ADA)

1 ml heparinized blood

Spin 10 min

Replace plasma with the same amount of RPMI

24 hours 37°C + CO₂

Raccogliere il surnatante di ogni pozzetto

Keep plasma frozen -80° until γ-IFN determination by ELISA

NIL, Ag, MIT

PLASMAFOR SEROLOGY

Replace plasma with the same amount of RPMI
Sensitivity, Specificity, Cut-Off

Sensitivity
S: 81,58% (IC 95%)
R: 93% (IC95%)

SPECIFICITY
S: 83,48% (IC 95%)
R: 89,7% (IC95%)

CUT OFF
S: 0,151 (IC 95%)
R: 0,156 (IC95%)

P=0.076
132 newborns from January to December 2011

<table>
<thead>
<tr>
<th>Newborn</th>
<th>IgM/IgA POS</th>
<th>IgM/IgA NEG</th>
<th>WB IgG/IgM POS</th>
<th>WB IgG/IgM NEG</th>
<th>IGRA POS</th>
<th>IGRA NEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>INFECTED (10)</td>
<td>4</td>
<td>6</td>
<td>9</td>
<td>1</td>
<td>10</td>
<td>0</td>
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<tr>
<td>NOT INFECTED (122)</td>
<td>0</td>
<td>122</td>
<td>0</td>
<td>122</td>
<td>0</td>
<td>65</td>
</tr>
<tr>
<td>TESTED</td>
<td>132</td>
<td>132</td>
<td>75</td>
<td></td>
<td></td>
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</table>
41 IgG-/IgM+ spiramycin treated pregnant women

<table>
<thead>
<tr>
<th></th>
<th>IgM ISAGA</th>
<th>IgG WB</th>
<th>IgM WB</th>
<th>IFN-γ</th>
<th>Seroconversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>NEG</td>
<td>NEG</td>
<td>NEG</td>
<td>NEG</td>
<td>No seroconversion</td>
</tr>
<tr>
<td>14</td>
<td>POS</td>
<td>NEG</td>
<td>NEG</td>
<td>NEG</td>
<td>No seroconversion</td>
</tr>
<tr>
<td>13</td>
<td>POS</td>
<td>POS</td>
<td>POS</td>
<td>POS</td>
<td>Seroconversion</td>
</tr>
<tr>
<td>4</td>
<td>POS</td>
<td>NEG</td>
<td>POS</td>
<td>NEG</td>
<td>No seroconversion</td>
</tr>
</tbody>
</table>