Severe Congenital Toxoplasmosis in the United States

Clinical and Serologic Findings in Untreated Infants

Tudor Rares Olariu, MD, PhD.†† Jack S. Remington, MD, †† Rima McLeod, MD, ‡‡ Ambereen Alam, MD, §§ and Jose G. Montoya, MD††

Background: Congenital toxoplasmosis can cause significant neurologic manifestations and other untoward sequelae.

Methods: The Palo Alto Medical Foundation Toxoplasma Serology Laboratory database was searched for data on infants 0 to 180 days old, in whom congenital toxoplasmosis had been confirmed and who had been tested for Toxoplasma gondii-specific immunoglobulin G (IgG), IgM, and IgA antibodies, between 1991 and 2005. Their clinical findings were confirmed at the National Collaborative Chicago-based Congenital Toxoplasmosis Study Center. We reviewed available clinical data and laboratory profiles of 164 infants with congenital toxoplasmosis whose mothers had not been treated for the parasite during gestation.

Results: One or more severe clinical manifestations of congenital toxoplasmosis were reported in 84% of the infants and included eye disease (92.2%), brain calcifications (79.6%), and hydrocephalus (67.7%). In 61.6% of the infants, eye disease, brain calcifications, and hydrocephalus were present concurrently. T. gondii-specific IgM, IgA, and IgE antibodies were demonstrable in 86.6%, 77.4%, and 40.2% of the infants, respectively. Testing for IgM and IgA antibodies increased the sensitivity of making the diagnosis of congenital toxoplasmosis to 93% compared with testing for IgM or IgA individually. IgM and IgA antibodies were still present in 43.9% of infants diagnosed between 1 and 6 months of life.

Conclusions: Our study reveals that severe clinical signs of congenital toxoplasmosis including hydrocephalus, eye disease, or intracranial calcifications occurred in 85% infants whose sera were referred to our reference Toxoplasma Serology Laboratory during a period of 15 years. Laboratory tests, including serologic and polymerase chain reaction tests, were critical for diagnosis in the infants. Our results contrast remarkably with those of European investigators who rarely observe severe clinical signs in infants with congenital toxoplasmosis.

Key Words: toxoplasmosis, congenital, toxoplasma, infants, laboratory diagnosis, serologic findings, clinical findings

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From the †Toxoplasma Serology Laboratory, Palo Alto Medical Foundation, Palo Alto, CA; †Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University School of Medicine, Stanford, CA; ‡Department of Medicine, University of Chicago School of Medicine, Chicago, IL; §Toxoplasmosis Center, University of Chicago Medical Center, Chicago, IL; and ‡Department of Pediatrics, University of Chicago School of Medicine, Chicago, IL.

The congenital toxoplasmosis database of PAMF-TSL was examined the long-term sequelae of congenital toxoplasmosis.

C ongenital toxoplasmosis can cause a wide spectrum of clinical manifestations. Infected infants might appear normal at birth or can be born severely damaged. The most severe clinical findings observed in affected infants include chorioretinitis, cerebral calcifications, hydrocephalus, pneumonia, and disseminated disease. Early studies revealed that the congenital infection essentially occurred only in infants born to women who acquired their primary infection during gestation. Women infected before gestation were not at risk to transmit the parasite to their fetus, unless they were severely immunocompromised. It also became obvious that the primary infection in pregnant women often occurs without clinical manifestations and without a history of the most common epidemiologic risk factors (eg, ingestion of undercooked or raw meat, or unrecognized ingestion of material contaminated with oocysts). In contrast to Western Europe, national screening programs at the prenatal or postnatal level have not been implemented in the United States. There are approximately 4 million infants born each year in the United States. Only rarely is routine screening for toxoplasmosis performed in these infants. The same is true for their mothers during gestation. Neither the current disease burden nor the actual incidence of congenital toxoplasmosis in the United States is known. Congenital toxoplasmosis is not a notifiable disease (available at: http://www.cdc.gov/nchhi/dsss/mdns/mdnshis.htm). However, it is estimated that 500 to 5000 infants are born each year with congenital toxoplasmosis in the United States.

The present study was initially begun to determine the usefulness of Toxoplasma gondii-specific IgM and IgA antibody testing in untreated infants in the United States with suspect or proven congenital toxoplasmosis. Physicians had suspected or diagnosed congenital disease in their patients and contacted the Palo Alto Medical Foundation Toxoplasma Serology Laboratory (PAMF-TSL; Palo Alto, CA; available at: www.pamf.org/serology/; +1-650-853-4828; toxolab@pamf.org) or the National Collaborative Chicago-based Congenital Toxoplasmosis Study ([NCCCTS], Chicago, IL; available at: http://www.uchospitals.edu/specialties/infectious-diseases/toxoplasmosis/; +1-773-834-4131; rmcleod@midway.uchicago.edu). On examining the charts of the infants, we were again dismayed to learn how many of them were severely damaged by the time their first serum was submitted to our laboratory for testing. This led us to attempt to correlate the available data on clinical manifestations in the infants along with their initial serologic test results. Our study was not designed to examine the long-term sequelae of congenital toxoplasmosis.

MATERIALS AND METHODS

The congenital toxoplasmosis database of PAMF-TSL was retrospectively searched for data on infants (from birth to 180 days of age), in whom congenital toxoplasmosis was suspected or confirmed and who had been tested for both T. gondii-specific IgM and IgA antibodies, between January 1991 and December 2005. PAMF-TSL is a non-for-profit reference laboratory solely for the diagnosis of toxoplasmosis.
The primary reason why health care providers send specimens to PAMF-TSL is for laboratory confirmation or diagnosis of toxoplasmosis during pregnancy and in the infant. In most cases, because of clinical signs, pediatricians in the United States first suspect a congenital infection, not necessarily toxoplasmosis. It is important to emphasize that, in contrast to Europe, most of pediatricians in the United States do not know a priori whether the mother has been infected with *T. gondii* during gestation. Thus, initially their differential diagnosis is broad and includes many other infections of the fetus and newborn. When laboratory confirmation is required for the diagnosis of congenital toxoplasmosis, clinicians in the United States send their specimens to PAMF-TSL. It is also clear that most pediatricians in the United States only include these infectious agents in their differential diagnosis, including *T. gondii*, when clinical signs are present in their infants.

The criteria for diagnosis of congenital toxoplasmosis for this study were infants who were IgG antibody positive in the Sabin-Feldman dye test (DT) and who met at least 1 of the following: (1) presence of IgM and or IgA *T. gondii* antibodies after day 10 of life; (2) persistence of IgG antibodies in the DT by 12 months of age; (3) presence of IgM antibodies in cerebrospinal fluid (CSF); (4) positive polymerase chain reaction (PCR) results or isolation of *T. gondii* from amniotic fluid (AF), CSF or blood, or positive PCR results in urine. In addition, congenital toxoplasmosis was also diagnosed in 4 infants who had a positive DT result, were born to mothers whose serologic test results were consistent with their having acquired *T. gondii* infection during gestation, and who had clinical signs of congenital toxoplasmosis (eg, eye findings cerebral calcifications and/or hydrocephalus).

A total of 430 such infants with suspected or diagnosed congenital toxoplasmosis were identified and tested for *T. gondii*-specific IgG (DT), IgM, and IgA. Of these 430 infants, 241 (56%) were excluded from the study because they did not meet any of the previously mentioned inclusion criteria, and 25 (6%) were excluded because of the potential effect of antitoxoplasma treatment of their mothers during gestation on their serologic test results. In these 25 infants, sera were submitted because the prenatal diagnosis of the acute acquired infection had been suspected in the mother by the primary care provider and had been confirmed at PAMF-TSL. However, information regarding gestational age of maternal infection, timing, and doses of the antitoxoplasma drugs used during gestation (eg, spiramycin, pyrimethamine/sulfadiazine/zolinic acid, or spiramycin followed by pyrimethamine/sulfadiazine/zolinic acid), in an attempt to prevent or treat infection in the fetus, was not available. In the remaining 164 infants, prenatal treatment had not been administered, and they were included in this study. Most of the 164 infants had not received postnatal treatment either at the time when their serum had been obtained. Clinical information obtained at PAMF-TSL was carefully checked against the information available at NCCCTS in those infants who had been referred to NCCCTS. This information was corroborated by the data recorded at the NCCCTS database. In the NCCCTS, all available medical records and serologic tests of mother and infant were reviewed (R.M.); every infant was examined in person in Chicago by the same study group to confirm any reported positive finding. The evaluations confirmed the validity of each positive clinical finding reported herein for the infants evaluated by the NCCCTS. In only 1 baby with hydrocephalus, this information had not been recorded at PAMF-TSL but was available at NCCCTS. To increase the accuracy of our clinical findings, we did not assume that absence of information in a given disease category (eg, eye disease, cerebral calcifications, or hydrocephalus) meant absence of that disease. Thus, infants in whom clinical information was not available for a given disease category were excluded from the analysis of that category.

Of the 164 infants, 155 were from the United States (from 32 states), and 9 from Canada (2 provinces). The infants were born to 158 mothers. Six pairs were twins. The age given for each infant is the age when the first serum sample was drawn for testing at PAMF-TSL. Infants were grouped into the following 3 categories by age: 0 to 30 days (neonates), 31 to 90 days, and 91 to 180 days.

Serologic test results are solely those obtained in the first serum submitted for testing to PAMF-TSL. If maternal serum was available and was drawn at approximately the same time as birth of the infant, the infant’s serum was tested in parallel with that of their mother. The gestational age at which maternal infection was acquired was not available.

All serologic and PCR tests, and attempts to isolate the parasite, were performed at PAMF-TSL. Serologic tests included the DT, immunosorbent agglutination assay (IgM ISAGA), IgM enzyme-linked immunosorbent assay (ELISA) only performed in CSF, IgA ELISA, and IgE ELISA. The tests were performed as previously described. The following titers were considered positive: IgM ISAGA, 3 to 12; IgA ELISA, ≥1.0; IgE ELISA, ≥1.9. A positive IgM ISAGA antibody titer in the CSF was considered diagnostic of congenital toxoplasmosis. As stated earlier in the text, all infants (n = 164) enrolled in our study were tested for IgG, IgM, and IgA antibodies (this was a prespecified inclusion criteria). Of the 164 untreated infants, IgE ELISA was ordered and performed in 102, CSF PCR in 58, urine PCR in 10, peripheral blood PCR in 7, attempts at isolation of the parasite from blood in 26, and attempts of CSF isolation in 8. Ordering of IgE, PCR, and isolation was driven by choices of the referring physicians according to the various clinical scenarios in their infants. However, when the data were analyzed for IgE, PCR, and isolation tests, the number of infants in the denominator was always corrected to account for the number of infants in whom the test was performed. The Toxoplasma Serologic Profile was performed on and avidity determined (data not shown) in their mothers after birth if serologic testing was required to confirm the diagnosis of toxoplasmosis during their gestation.

PCR was performed using 2 target sequences from the 35-fold repetitive B1 gene. In 2002, the PCR method was modified to use real-time technology on the Applied BioSystems Sequence Detection System (ABI PRISM 7700 and 7000; Carlsbad, CA) and was performed according to the manufacturer’s recommendations. The probes consisted of an oligonucleotide with a 5’-reporter dye (FAM) and a downstream, 3’-quencher dye (TAMRA). Fluorescence was measured during PCR and is a direct consequence of target amplification. Each sample was tested in duplicate, with primers and probes targeting different sequences in the B1 gene. When samples were available, PCR was performed in CSF, whole blood, or urine. Isolation of the parasite was attempted by inoculating body fluids and/or tissue into mice as previously described.

### Statistical Methods

Data were analyzed using EPI INFO statistical package (version 3.3.2; CDC, Atlanta, GA). Mantel-Haenszel χ² and the 2-tailed Fisher test were used to compare proportions between groups.

### RESULTS

#### Clinical Findings

The 164 infants ranged in age from 0 to 180 days (average, 44 days), 95 (57.9%) were males. Ninety-two (56.1%) were diagnosed with congenital toxoplasmosis from 0 to 30 days, 46 (28%) from 31...
Antibodies were demonstrated in 127 (77.4%) of the 164 infants. Positive IgA test results were more commonly detected in neonates, and their rate of detection slightly decreased with increasing age of the infants. Both IgM and IgA antibodies were more commonly detected in neonates than in those whose sera were submitted between 91 and 180 days of age ($P = 0.036$). Neither IgM nor IgA antibodies were demonstrated in 11 (6.7%) of the 164 infants (Table 2). In these 11, the diagnosis was made by the presence of clinical findings consistent with congenital toxoplasmosis (4 infants whose mothers’ serum at birth had serologic test results consistent with their having acquired Toxoplasma gondii infection during gestation), persistence of IgG antibodies at 1 year of age (1 infant), positive PCR results in CSF (3 infants) and blood (1 infant), and isolation of the parasite from blood (1 infant) and AF (1 infant). In the baby in whom the diagnosis was made by isolation in AF, the amniocentesis was performed right before delivery and the isolation became positive 6 weeks after. For this reason, this baby was not treated during gestation.

Of the 102 infants tested for IgE antibodies, 41 (40.2%) showed positive results. IgE antibodies were not found in infants aged > 5 months of age. One infant at day 5 of life had detectable IgE but not IgM or IgA antibodies; PCR result was also positive in the CSF of this infant at 9 days of age.

### PCR Findings

PCR results were positive in CSF of 27 (46%) of the 58 infants in whom it was performed, in urine of 5 (50%) of the 10 infants, and in whole blood of 2 (29%) of 7 infants in whom it was performed. PCR in CSF was the sole basis for the diagnosis of congenital toxoplasmosis in 3 (5%) of 58 infants in whom it was attempted.

### Attempts to Isolate the Parasite

The parasite was isolated from CSF of 1 (12.5%) of 8 infants and from blood of 8 (31%) of 26 infants in whom it was attempted. Isolation of the parasite from blood or AF was the sole basis for diagnosis of congenital toxoplasmosis in 2 (7.5%) of the 27 infants in whom it was attempted.

### Correlation of Serologic Test Results With Clinical Findings

Overall, presence or absence of IgM and IgA antibodies did not correlate significantly with the presence of severe clinical manifestations (Table 3). However, there were significantly more neonates with eye disease who had positive IgA test results (86.9%) than those without eye findings (55.5%) ($P = 0.04$) (data not shown).

### TABLE 1. Eye Disease and Central Nervous System Findings in Infants With Untreated Congenital Toxoplasmosis in the United States

<table>
<thead>
<tr>
<th>Age*</th>
<th>No. Infants With Clinical Signs/ No. Infants Evaluated (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E C H</td>
</tr>
<tr>
<td>0–30</td>
<td>61/70 (87.1)</td>
</tr>
<tr>
<td>31–90</td>
<td>35/36 (97.2)</td>
</tr>
<tr>
<td>91–180</td>
<td>23/23 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>119/129 (92.2)</td>
</tr>
</tbody>
</table>

*Age in days when first serum was drawn for testing. E indicates eye disease; C, calcifications; H, hydrocephalus.

### TABLE 2. IgM and IgA Toxoplasma Antibody Test Results in Infants With Untreated Congenital Toxoplasmosis in the United States

<table>
<thead>
<tr>
<th>Age*</th>
<th>IgM</th>
<th>IgA</th>
<th>IgM or IgA</th>
<th>IgM (−) or IgA (−)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. Infants Tested</td>
<td>(%)</td>
<td>(%)</td>
<td>(%)</td>
</tr>
<tr>
<td>0–30</td>
<td>92</td>
<td>85 (92.4)</td>
<td>74 (80.4)</td>
<td>87 (94.5)</td>
</tr>
<tr>
<td>31–90</td>
<td>46</td>
<td>37 (80.4)</td>
<td>34 (73.9)</td>
<td>42 (91.3)</td>
</tr>
<tr>
<td>91–180</td>
<td>26</td>
<td>20 (76.9)</td>
<td>19 (73.1)</td>
<td>24 (92.3)</td>
</tr>
<tr>
<td>Total</td>
<td>164</td>
<td>142 (86.6)</td>
<td>127 (77.4)</td>
<td>153 (93.3)</td>
</tr>
</tbody>
</table>

*Age in days when first serum was drawn for testing.

### TABLE 3. Correlation Between IgM/IgA Antibody Test Results and Clinical Manifestations in Infants With Untreated Congenital Toxoplasmosis in Whom Clinical History Was Available

<table>
<thead>
<tr>
<th>Results of Examination (n)</th>
<th>IgM Antibody (%)</th>
<th>IgA Antibody (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye disease (119)</td>
<td>102 (85.7%)</td>
<td>95 (79.8%)*</td>
</tr>
<tr>
<td>No eye disease (10)</td>
<td>9 (90.0%)</td>
<td>6 (60.0%)*</td>
</tr>
<tr>
<td>Calcifications (94)</td>
<td>81 (86.2%)</td>
<td>77 (81.9%)</td>
</tr>
<tr>
<td>No calcifications (24)</td>
<td>20 (83.3%)</td>
<td>17 (70.8%)</td>
</tr>
<tr>
<td>Hydrocephalus (67)</td>
<td>58 (86.6%)</td>
<td>53 (79.1%)</td>
</tr>
<tr>
<td>No hydrocephalus (32)</td>
<td>25 (78.1)</td>
<td>24 (75.0%)</td>
</tr>
</tbody>
</table>

*The difference in frequency of IgA antibodies observed between infants with and without eye disease primarily reflects differences in neonates and not in infants older than 30 days.

n indicates number of infants.
The results described previously in the text reveal that 85% of infants clinically suspected of having congenital toxoplasmosis and who had laboratory confirmation of the disease in a reference laboratory in the United States were severely damaged due to the infection. This is in marked contrast with what workers in this field have observed during essentially the same period in Europe.

Few studies have analyzed and correlated both the clinical and serologic profiles of untreated, congenitally infected infants born to mothers who were not treated during gestation, as was the case in the present study. In an early study of congenital toxoplasmosis performed in 1947 by Eichenwald, eye disease, intracranial calcifications, and hydrocephalus were reported in 94.4%, 50%, and 27.8%, respectively, of the infected infants. Another study was that by McAuley et al, published in 1994, that described severe clinical signs at presentation during the first months of life in the infants referred to them. In all, 73% of the 41 infected infants had eye disease; cerebral calcifications were noted in 58.5%, hydrocephalus in 41.4%, and microcephalus in 17.1%. Findings present in newborns detected in the New England screening program have also been described. In contrast to the findings in the present study and those of the NCCCTS investigators are recent reports from Europe, which reveal a much lower prevalence of severe clinical signs in the infected newborn.

Nations in Western Europe with systematic prenatal screening programs and prophylaxis for those pregnant women identified as having acquired the infection during gestation have recently reported lower frequency of eye findings (15%) and intracranial calcifications (6%) (Table 4). It appears that hydrocephalus and other systemic signs such as pneumonia and splenomegaly are of rare occurrence and have not been the subject of reports from Western European nations for several decades. Of note, those European studies were prospective, and the mothers were treated during gestation. The low frequency of clinical findings observed in these recent European cohorts contrasts with the greater frequency of symptomatic children observed in their earlier reports at times before systematic serologic screening of pregnant women and treatment during gestation were implemented.

This high prevalence of severe clinical findings in infants with congenital toxoplasmosis referred to PAMF-TSL may reflect a number of different factors related to both the host and the parasite. Among the former are referral bias; lack of treatment of the mother during gestation to attempt to prevent or decrease transmission of the parasite to the fetus; maternal infection acquired early in gestation, which is known to result in the highest percentage of severely affected infants, genetics of the host, or combinations of these factors. Because PAMF-TSL is a reference laboratory specialized in the diagnosis of toxoplasmosis, it is possible that referral bias may partially explain why our cohort of infected infants has such high prevalence of clinical signs. However, we believe that it is unlikely that referral bias alone could account for such a high magnitude in the difference in prevalence of clinical signs observed between our cohort (eg, 90% ocular and 80% intracranial lesions) and those reported from Europe (eg, 15% for ocular and 6% for intracranial lesions). Regardless of how much referral bias can explain the high frequency of clinical signs in infected infants in the United States, we believe that such high absolute numbers of damaged infants due to the parasite is unacceptable and should be addressed by public health authorities and academic centers in North America.

Parasite load or strain virulence and antigenic factors (of the parasite) are additional factors that may have played an important role in the clinical outcome of such infants. The higher prevalence of calcifications in the infants in the present study (79%) when compared with other studies may also reflect in part the use since 1981 of computerized tomography to evaluate each of these children. One of the major limitations in interpretation of the high prevalence of clinical manifestations in our study is that the gestational age at which maternal infection was acquired was not known; gestational age at time of maternal infection is known to have a marked impact on the rate of clinical findings in infected infants.

Serological results in the infants in the present study reveal that a high percentage of these previously untreated infants had a high prevalence of IgM and IgA antibodies when first tested. The sensitivity of the IgM ISAGA in the present study was similar to that previously reported in untreated, infected neonates by Naessens et al (85%). Of note, approximately 14% of congenitally infected infants in our study were negative in the IgM ISAGA. Detection of IgA antibodies has also been found useful for the diagnosis of congenital toxoplasmosis. The sensitivity of the IgA ELISA in our neonates was also similar to that reported by Naessens et al in their untreated infants. A negative IgA antibody test result was observed in 22% of our infants.

Performing both IgM and IgA antibody tests increased the sensitivity of antibody testing for diagnosis of congenital toxoplasmosis when compared with the use of either test alone. Other investigators have also underscored the importance of performing both tests. Wallon et al reported a lower prevalence of either IgM (67%) or IgA (59%) antibodies when used alone for the diagnosis of congenital toxoplasmosis versus when both tests were used (73%). Of note, the infants in the Wallon et al study had received prenatal treatment during the gestational period. Although only 7% of our study patients were negative for both IgM and IgA antibodies, it is apparent that negative results in these 2 tests do not rule out the possibility of congenital toxoplasmosis.

IgE antibodies were demonstrable in our infants less frequently than IgM and IgA antibodies. In fact, only 1 serum sample that was negative for both IgM and IgA antibodies had detectable IgE antibodies; in that case, the IgE antibody was not the sole determinant of disease.

**TABLE 4.** Ocular and Intracranial Lesions in Treated Infants With Congenital Toxoplasmosis in European Countries With Systematic Prenatal Screening and Treatment Programs for Toxoplasmosis During Gestation

<table>
<thead>
<tr>
<th>Cohort Region</th>
<th>Recruitment Period</th>
<th>Infected Live-born Children</th>
<th>Clinical Manifestations</th>
<th>Any</th>
<th>Ocular Lesions</th>
<th>Intracranial Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nice</td>
<td>1996–2000</td>
<td>15</td>
<td>1</td>
<td>0</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Grenoble</td>
<td>1996–2000</td>
<td>6</td>
<td>2</td>
<td>1</td>
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<td>1</td>
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<tr>
<td>Lyon</td>
<td>1996–2000</td>
<td>43</td>
<td>10</td>
<td>9</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Marseille</td>
<td>1996–2000</td>
<td>20</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Nice</td>
<td>1996–2000</td>
<td>8</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Paris</td>
<td>1996–2000</td>
<td>65</td>
<td>8</td>
<td>8</td>
<td>1</td>
<td></td>
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<tr>
<td>Reims</td>
<td>1996–2000</td>
<td>8</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td></td>
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<tr>
<td>Toulouse</td>
<td>1996–2000</td>
<td>22</td>
<td>3</td>
<td>3</td>
<td>2</td>
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<tr>
<td>Austria</td>
<td>1992–1995</td>
<td>33</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td></td>
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<tr>
<td>1996–2000</td>
<td>24</td>
<td>5</td>
<td>5</td>
<td>2</td>
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<tr>
<td>Italy</td>
<td></td>
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<td></td>
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<tr>
<td>Naples</td>
<td>1996–2000</td>
<td>11</td>
<td>3</td>
<td>3</td>
<td>3</td>
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<tr>
<td>Milan</td>
<td>1996–2000</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>Slovenia</td>
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<tr>
<td>Ljubljana</td>
<td>1996</td>
<td>3</td>
<td>0</td>
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laboratory marker for congenital toxoplasmosis; this infant also had a positive PCR in CSF. Thus, according to our findings and those of other investigators, testing for IgE antibodies appears to add little value for diagnosis of congenital toxoplasmosis. Of interest is that there was a higher proportion of positive IgA antibody tests in neonates with eye findings \((P = 0.04)\). Other investigators working with adult cases noted a correlation between the presence of serum IgA antibodies and toxoplasmic chorioretinitis. For instance, Portela et al reported that the size of the ocular lesion in patients with ocular disease correlated positively with the serum level of IgA antibodies.

As stated previously in the text, gestational age is known to have an impact on the rate of both clinical and serological findings in infected infants. Our infants had an unexpected high prevalence of both these findings. It is clear that infection acquired by the mother early in gestation is associated with more severe outcome in the child.

In addition to serology, attempts at isolation of the parasite, histopathologic examination, and PCR have been used successfully for the diagnosis of congenital toxoplasmosis. From our data and those of other investigators, PCR should be performed in all infants suspected of having congenital toxoplasmosis in whom the diagnosis cannot be promptly made by serological methods. Attempts at isolation of the parasite are uncommonly performed because of the lack of an animal or tissue culture facility.

Congenital toxoplasmosis continues to be a tragedy for parents and children in the United States. Decades ago some countries responded to the challenge by implementing national programs for systematic serologic screening of all pregnant women. Others did so by performing routine serologic screening in all newborns. Yet, despite the fact that all studies performed in the United States continue to reveal that congenitally infected children are born severely affected each year, a national program or policy to address the threat of this disease is currently lacking.

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REFERENCES


