Acute *Toxoplasma gondii* Infection among Family Members in the United States

Despina G. Contopoulos-Ioannidis, Yvonne Maldonado, and Jose G. Montoya

We investigated 32 families of persons with acute toxoplasmosis in which ≥1 other family member was tested for *Toxoplasma gondii* infection; 18 (56%) families had ≥1 additional family member with acute infection. Family members of persons with acute toxoplasmosis should be screened for infection, especially pregnant women and immunocompromised persons.

Only isolated case reports and small case series have been published on acute *Toxoplasma gondii* infections among family members (*1–6*). When a case of acute toxoplasmosis is identified in a family, additional household members might have been infected around the same time period; family members frequently share common exposures to food or environmental sources potentially contaminated with *T. gondii*. Identification of additional infections could lead to earlier implementation of appropriate interventions for persons in certain high-risk groups, such as immunocompromised persons and pregnant women.

Large-scale evaluation of the prevalence of acute*T. gondii* infections among family members in the United States has not been performed (*4*). Therefore, we investigated the prevalence of acute toxoplasmosis among household and family members of patients who had acute toxoplasmosis.

The Study

We performed a retrospective cohort study using data collected by the Palo Alto Medical Foundation Toxoplasma Serology Laboratory (PAMF-TSL; www.pamf.org), Palo Alto, California, USA, during 1991–2010. Patient blood samples were sent from diverse laboratories from throughout the United States, and testing was conducted at the PAMF-TSL. The study was approved by the Institutional Research Board at the PAMF Research Institute.

From the PAMF-TSL database, we identified families that 1) had an index case-patient with a diagnosis of acute toxoplasmosis and 2) had ≥1 additional household/family member who had been tested for *T. gondii* infection at PAMF-TSL. Details of the process used to identify additional household/family members are described in the online Technical Appendix (wwwnc.cdc.gov/EID/article/19/12/12-1892-Techapp1.pdf). All identified family/household members were categorized as acutely infected (<6 months before sample collection time); recently infected (6–12 months before sample collection time); chronically infected (>12 months before sample collection time); or never infected. The criteria used for this categorization are described in the online Technical Appendix. These criteria are routinely used in the daily clinical practice at PAMF-TSL to estimate the most likely time of the *T. gondii* infection; the accuracy of these criteria has been previously validated (*7–11*).

All identified families were categorized in 3 family groups (online Technical Appendix). Group 1 consisted of families with an index case-patient who had acute toxoplasmosis and ≥1 additionally tested family/household member who had acute or recently acquired *T. gondii* infection. Group 2 consisted of families with an index case-patient who had acute toxoplasmosis; ≥1 additionally tested family/household member who had chronic *T. gondii* infection; and no other tested household members who had evidence of acute or recently acquired *T. gondii* infection. Group 3 consisted of families with an index case-patient who had acute toxoplasmosis and in which no additionally tested family/household members showed evidence of *T. gondii* infection.

We defined as prevalence of acute *T. gondii* infection in >1 family members (prevalence of group 1 families) the number of group 1 families divided by the total number of study families over the 20-year study period (primary endpoint). As secondary endpoint, we also calculated the prevalence of group 2 families. We also tested whether the IgG-Dye test titers and IgM-ELISA titers of the index case-patients were different across the 3 family groups by using the Kruskal-Wallis test. All analyses were done in Stata/SE version 12 (StataCorp LP, College Station, TX, USA).

Among 97,279 persons serologically tested for *T. gondii* in the PAMF-TSL over the 20 year study period, we identified 107 persons who had ≥1 person from their household with a diagnosis of acute toxoplasmosis and ≥1 additional household member serologically tested for *T. gondii* infection. Those 107 persons were grouped into 32 study families (Figure). Patient demographic and clinical characteristics are shown in Table 1; serologic test results

Author affiliations: Stanford University School of Medicine, Stanford, California, USA (D.G. Contopoulos-Ioannidis, Y. Maldonado, J.G. Montoya); and Palo Alto Medical Foundation Toxoplasma Serology Laboratory, Palo Alto, California, USA (D.G. Contopoulos-Ioannidis, J.G. Montoya)

DOI: http://dx.doi.org/10.3201/eid1912.121892

for members of group 1 families are shown in Table 2, Appendix (wwwnc.cdc.gov/EID/article/19/12/12-1892-T2.htm), and for members of groups 2 and 3 families in the online Technical Appendix.

Table 1. Demographic and clinical information for persons in the 18 group 1 study families identified from data on acute toxoplasmosis cases collected during 1991–2010 by the Palo Alto Medical Foundation Toxoplasma Serology Laboratory, Palo Alto, California, USA*

IC patient no.	Clinical information for IC	No. additional household members tested	Infection status of additional household members	Clinical information for additional household members	Risk factors reported by ≥1 household member
IC-1	LN	2	Wife: acute infection	Pregnant, first trimester	Ate raw lamb
			Daughter: no infection	NA	
			(Baby girl: status not ascertained)		
IC-2	8 wks pregnant	1	Husband: acute infection	LN	NR
			(Fetus: AF PCR–)		
IC-3	8 wks pregnant	1	Husband: acute infection	Asymptomatic	Contact with cat feces, eating undercooked meat, gardening
			(Baby boy: could not R/O CT; no follow-up beyond 1 mo of age)		
IC-4	27 wks pregnant	2	Husband: acute infection	NA	NR
			Son: acute infection	NA	
			(Fetus: AF PCR–)		
IC-5	11 wks pregnant	1	Husband: acute infection	NA	None
			(Fetus: AF PCR–)		
IC-6	Infant with CT	2	(Mother: acute infection)	NA	NR
			Father: acute infection	NA	
			Brother: acute infection	NA	
IC-7	LN, fever, headache	3	Wife: acute infection	LN	Poor cleaning of cooking surfaces
			Daughter 1: acute infection	Posterior cervical LN	
			Household member: chronic infection	NA	
			Son/daughter 2: not tested		
IC-8	13 wks pregnant	1	Husband: acute infection	NA	Ate deer meat that had positive results for *T. gondii* by PCR
			(Baby Boys A and B: status not ascertained)		
IC-9	22 wks pregnant	1	Husband: acute infection	NA	NR
			(Fetus: NA)		
IC-10	Pregnant, third trimester	2	Daughter 1: Recent infection	Asymptomatic	Children played in uncovered sandbox
			Daughter 2: acute infection	Asymptomatic	
			(Baby girl A: asymptomatic; CSF PCR–, could not R/O CT; baby girl-B: CT, macular scar, ascites, AF PCR+, CSF PCR+)		
IC-11	Infant with CT†	2	(Mother: recent infection)	NA	NR
			Father: recent infection	NA	
			Sister: no infection	NA	
IC-12	LN, fever, hepatitis	3	Wife: acute infection	LN	Ate raw lamb
			Household member 1: acute infection	LN	
			Household member 2: acute infection	NA	
IC-13	21 wks pregnant	1	Husband: acute infection	LN	Ate venison tartare
			(Fetus: CT, ascites, hydrocephalus; abortion)		
IC-14	Infant with CT	1	(Mother: acute infection)	NA	Ate bear meat; ate deer meat that had positive results for *T. gondii* by PCR
			Father: acute infection	Fever, flu-like symptoms	
IC-15	9 wks pregnant	1	Husband: acute infection	NA	None
			(Baby boy: status not ascertained)		
IC-16	Febrile illness (fibromyalgia)‡	3	Daughter 1: Recent infection	NA	Ate deer meat that had positive results for *T. gondii* by PCR
			Daughter 2: no infection	NA	
			Grandson: no infection	NA	
IC-17	Eye disease	3	Son: acute infection	NA	NR
			Daughter 1: acute infection	Asymptomatic	
			Daughter 2: no infection	NA	
IC-18	LN	1	Wife: Recent infection	NA	NR

*Mother-infant pairs were counted as 1 unit/household member; infection status of these is shown in parenthesis. IC, index case-patient; LN, lymphadenopathy; NA, not available; NR, not reported; AF, amniotic fluid; R/O, rule out; CT, congenital toxoplasmosis; CSF, cerebrospinal fluid.
†Infant with CT with hydrocephalus, high bilirubin, abnormal liver function tests, low platelets, and positive PCR results on CSF.
‡Female patient taking chronic corticosteroids; patient died.

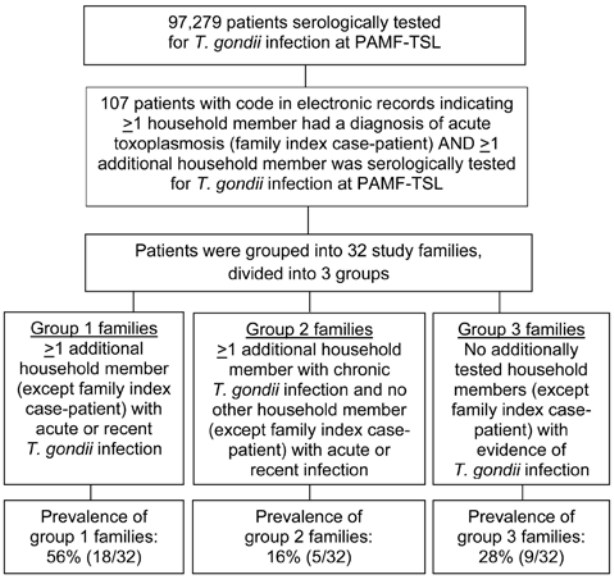

Figure. Flowchart for the identification of families with an index case-patient who had acute toxoplasmosis and ≥1 family member with acute or recent *Toxoplasma gondii* infection. Data were extracted from the database of the Palo Alto Medical Foundation Toxoplasma Serology Laboratory (PAMF-TSL; Palo Alto, CA, USA), from patient samples sent to PAMF-TSL during 1991–2010 from laboratories throughout the United States.

The prevalence of group 1 families in our study was 56% (18/32); group 2 families, 16% (5/32); and group 3 families, 28% (9/32) (Figure). The IgG-Dye test and the IgM-ELISA titers of the index case-patients were not significantly different across the 3 family groups ($p = 0.27$ for IgG and $p = 0.07$ for IgM) (Table 2, Appendix; online Technical Appendix). For group 1 families, all additional family members with acute/recently acquired infection had serologic profiles (titers of IgG, IgM, and/or IgA/IgE and avidity) that were similar to those of the index case-patients, indicating that they were infected at about the same time (Table 2, Appendix).

Conclusions

Our data provide preliminary evidence that multiple cases of acute *T. gondii* infection may occur among family/household members. These findings are particularly critical for persons at high risk from *T. gondii* infection, such as women who are or may become pregnant or immunocompromised persons. Interpretation of our study findings would have been clearer had the background prevalence of acute toxoplasmosis in the United States been known. Although no such population-level empirical data exist, we have identified at PAMF-TSL 889 patients with acute *T. gondii* infection over the 20-year study period (estimated prevalence ≈9/1,000 patients screened at PAMF-TSL; unpub. data).

A limitation of our study is that the families tested at PAMF-TSL over this study period might represent a group in whom the prevalence of acute *T. gondii* infection in ≥1 family member has been overestimated. Only 4% of persons who had acute toxoplasmosis diagnosed at PAMF-TSL during the 20-year study period had samples sent from additional household members for *T. gondii* testing (32 index case-patients with acute toxoplasmosis/889 acute infections). The collection of those additional samples depended solely on the response of the referring physicians to a 1-time written request for testing of additional family members. It is possible that the response of the primary care providers to this request would have been more likely if any of those additional family/household members had symptoms suggestive of acute toxoplasmosis. In addition, the IgG-Dye test and IgM-ELISA titers of the index case-patients did not predict which families would have additional household members with acute toxoplasmosis.

Further replication of the estimated prevalence of acute *T. gondii* infection in consecutive US families is needed. Future studies might also compare the *T. gondii* serotypes among index case-patients and family members (type II vs. non–type II) (*12*), which could help clarify whether certain serotypes are more likely to be associated with family outbreaks. Moreover, it would be useful to screen for antibodies to sporozoite-specific antigens (*13*), which can provide further insight regarding the source of *T. gondii* infection that is more likely to be associated with acute toxoplasmosis in ≥1 family member (e.g., sporozoite-specific, related to contact with cat feces, vs. bradyzoite-specific, related to ingestion of undercooked meat [*14*]).

When a case of acute toxoplasmosis is diagnosed, screening of additional family members should be considered, especially if pregnant women or immunocompromised patients live in those households, so that appropriate preventive strategies and/or therapeutic interventions are applied. These within-family clusters of cases are not easy to predict based solely on clinical or epidemiologic information, except for situations of sharing common meal (i.e., with undercooked meat), because it is unlikely that other risk factors would be different. Thus, only routine serologic screening of household members of acutely infected persons might identify such acute *T. gondii* infection infections.

Acknowledgments

We thank Catalina-Angel Malkun for help collecting hard copies of the patients' records and with data extraction.

Dr Contopoulos-Ioannidis is a clinical associate professor in the Department of Pediatrics, Division of Infectious Diseases, Stanford University School of Medicine, Stanford, CA; and Medical Consultant at the Palo Alto Medical Foundation Toxoplasma Serology Laboratory, Palo Alto, CA. Her research interests include

epidemiology of toxoplasmosis, laboratory diagnosis of congenital toxoplasmosis, pediatric infectious diseases, comparative effectiveness research, evidence-based medicine, and outcome research.

References

1. Masur H, Jones TC, Lempert JA, Cherubini TD. Outbreak of toxoplasmosis in a family and documentation of acquired retinochoroiditis. Am J Med. 1978;64:396–402. http://dx.doi.org/10.1016/0002-9343(78)90218-8
2. Stagno S, Dykes AC, Amos CS, Head RA, Juranek DD, Walls K. An outbreak of toxoplasmosis linked to cats. Pediatrics. 1980;65:706–12.
3. Sacks JJ, Roberto RR, Brooks NF. Toxoplasmosis infection associated with raw goat's milk. JAMA. 1982;248:1728–32. http://dx.doi.org/10.1001/jama.1982.03330140038029
4. Luft BJ, Remington JS. Acute *Toxoplasma* infection among family members of patients with acute lymphadenopathic toxoplasmosis. Arch Intern Med. 1984;144:53–6. http://dx.doi.org/10.1001/archinte.1984.00350130059012
5. Coutinho SG, Leite MA, Amendoeira MR, Marzochi MC. Concomitant cases of acquired toxoplasmosis in children of a single family: evidence of reinfection. J Infect Dis. 1982;146:30–3. http://dx.doi.org/10.1093/infdis/146.1.30
6. Silveira C, Belfort R Jr, Burnier M Jr, Nussenblatt R. Acquired toxoplasmic infection as the cause of toxoplasmic retinochoroiditis in families. Am J Ophthalmol. 1988;106:362–4. http://dx.doi.org/10.1016/0002-9394(88)90382-0
7. Dannemann BR, Vaughan WC, Thulliez P, Remington JS. Differential agglutination test for diagnosis of recently acquired infection with *Toxoplasma gondii*. J Clin Microbiol. 1990;28:1928–33.
8. Montoya JG, Huffman HB, Remington JS. Evaluation of the immunoglobulin G avidity test for diagnosis of toxoplasmic lymphadenopathy. J Clin Microbiol. 2004;42:4627–31. http://dx.doi.org/10.1128/JCM.42.10.4627-4631.2004
9. Montoya JG. Laboratory diagnosis of *Toxoplasma gondii* infection and toxoplasmosis. J Infect Dis. 2002;185(Suppl 1):S73–82. http://dx.doi.org/10.1086/338827
10. Montoya JG, Remington JS. Studies on the serodiagnosis of toxoplasmic lymphadenitis. Clin Infect Dis. 1995;20:781–9. http://dx.doi.org/10.1093/clinids/20.4.781
11. Montoya JG, Berry A, Rosso F, Remington JS. The differential agglutination test as a diagnostic aid in cases of toxoplasmic lymphadenitis. J Clin Microbiol. 2007;45:1463–8. http://dx.doi.org/10.1128/JCM.01781-06
12. Kong JT, Grigg ME, Uyetake L, Parmley S, Boothroyd JC. Serotyping of *Toxoplasma gondii* infections in humans using synthetic peptides. J Infect Dis. 2003;187:1484–95. http://dx.doi.org/10.1086/374647
13. Hill D, Coss C, Dubey JP, Wroblewski K, Sautter M, Hosten T, et al. Identification of a sporozoite-specific antigen from *Toxoplasma gondii*. J Parasitol. 2011;97:328–37. http://dx.doi.org/10.1645/GE-2782.1
14. Dubey JP, Rajendran C, Ferreira LR, Martins J, Kwok OC, Hill DE, et al. High prevalence and genotypes of *Toxoplasma gondii* isolated from goats, from a retail meat store, destined for human consumption in the USA. Int J Parasitol. 2011;41:827–33. http://dx.doi.org/10.1016/j.ijpara.2011.03.006

Address for correspondence: Despina G. Contopoulos-Ioannidis, Toxoplasma Serology Laboratory, Palo Alto Medical Foundation Research Institute, 795 El Camino Real, Ames Building, Palo Alto, CA 94301-2302, USA; email: dcontop@stanford.edu