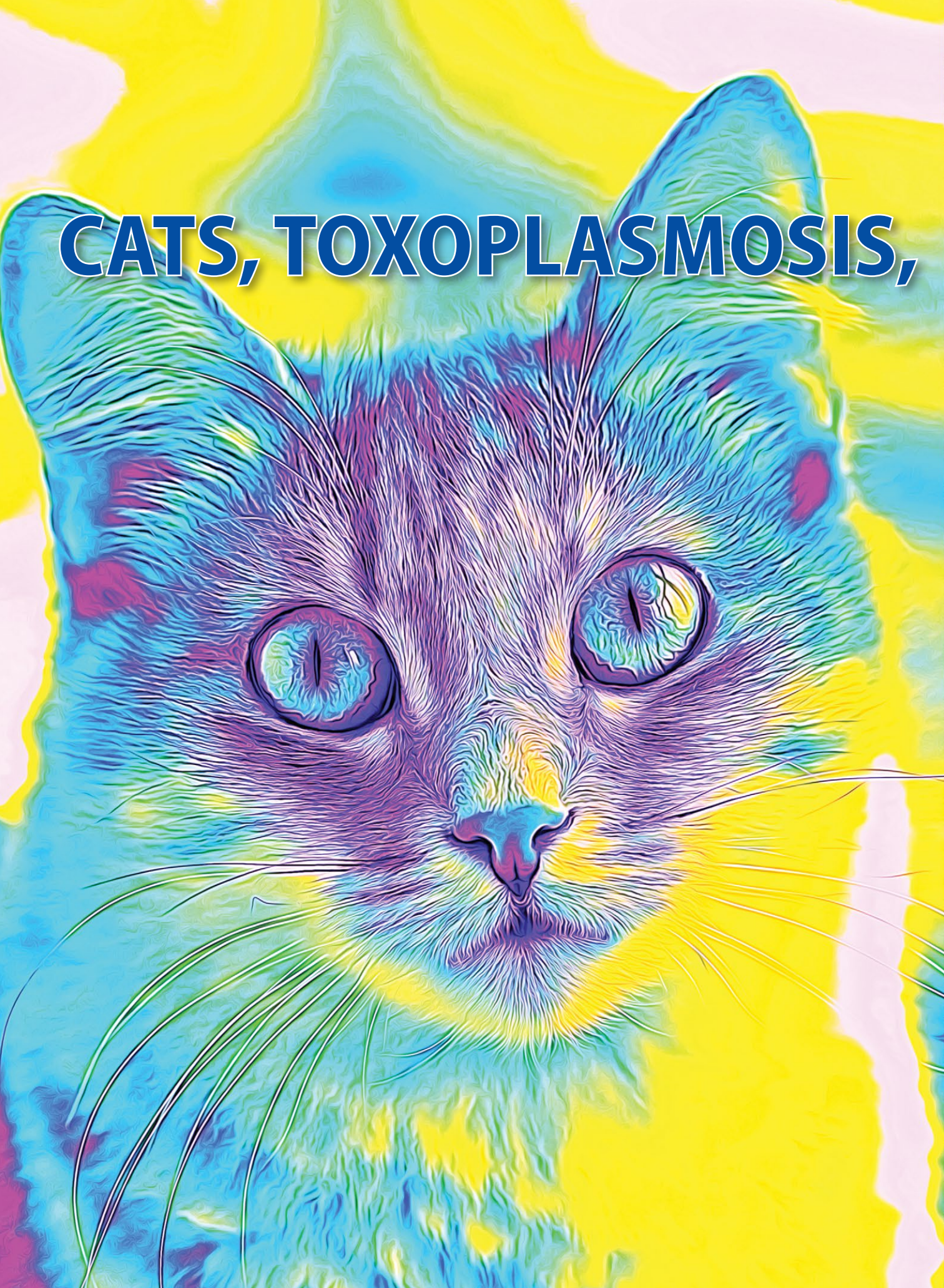


CATS, TOXOPLASMOSIS,



AND PSYCHOSIS: Understanding the risks

Accumulating evidence has linked *Toxoplasma gondii* infection with schizophrenia

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It has been clearly established that most human infectious diseases are caused by infectious agents that have been transmitted from animals to humans.¹ Based on published estimates from the 2000s, 60% to 76% of emerging infectious disease events are transmitted from animals to humans.²

When we consider animals that cause human diseases, we usually think of rats and bats. We rarely think of the 90 million cats owned as pets in the United States, or the approximately 30 to 80 million feral cats. Many consider cats as family members, and three-fourths of cats owned in the United States are allowed to sleep on the beds of their owners.¹ These cats may be a substantial source of human disease. Researchers at the University of Liverpool have identified 273 infectious agents carried by cats, of which 151 are known to be shared with humans.¹ The most widely known of these agents are *Lyssavirus*, the virus that causes rabies; *Bartonella henselae*, the bacteria that causes cat scratch disease; and *Toxoplasma gondii* (*T. gondii*), the parasite that causes toxoplasmosis.

In my new open-access book *Parasites, Pussycats and Psychosis* (available at <https://link.springer.com/book/10.1007/978-3-030-86811-6>), I describe the relationship between cats, *T. gondii*, and toxoplasmosis, and detail the evidence linking *T. gondii* to some cases of schizophrenia, bipolar disorder, and other diseases.¹ Though human *T. gondii* infection is typically asymptomatic or produces minor, flu-like symptoms, there are a few important exceptions. This article outlines those exceptions, and investigates evidence that implicates a link between *T. gondii* and psychosis.

continued



Cats and psychosis

Clinical Point

Most human cases of *T. gondii* infection are benign, but there are 3 exceptions that can result in severe outcomes



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Box

Toxoplasma gondii and nonpsychiatric conditions

As interest in *Toxoplasma gondii* (*T. gondii*) has increased, researchers have looked for associations between this parasite with other diseases and conditions. Based on the literature, the following are of most interest:

Epilepsy. Since 1995, 16 studies¹ have explored the relationship between *T. gondii* and epilepsy. A recent meta-analysis reported a statistically significant association between *T. gondii* and epilepsy.¹⁶

Brain cancer. Authors in 2 of 3 studies of meningiomas and 4 of 5 studies of gliomas reported statistically significant associations between these brain tumors and infection with *T. gondii*.^{1,17}

Rheumatoid arthritis. Eight studies reported an increased prevalence of *T. gondii* antibodies in individuals with rheumatoid arthritis.^{1,18}

Motor vehicle accidents. Infection with *T. gondii* is known to decrease motor reaction times in humans. At least 11 studies¹ have examined whether infected individuals are more likely to have been involved in motor vehicle accidents. The results are mixed; the largest study reported a weak but statistically significant association.¹⁹

How *T. gondii* can be transmitted

T. gondii has been called “one of the most successful parasites on earth.”³ Globally, approximately one-third of the human population is infected with *T. gondii*, though this varies widely by country and is dependent on dietary habits and exposure to cats. A 2014 survey reported that 11% of Americans—approximately 40 million people—have been infected, as evidenced by the presence of antibodies in their blood.¹

T. gondii begins its life cycle when a cat becomes infected, usually as a kitten. Most infected cats are asymptomatic, but for approximately 8 days they excrete up to 50 million infectious oocysts in their feces daily. Depending on the temperature, these oocysts can live for 2 years or longer. It is thought that a single oocyst can cause human infection.¹ Since cats like loose soil for defecation, the infective oocysts commonly end up in gardens, uncovered sandboxes, or animal feed piles in barns. After 24 hours, the oocysts dry out and may become aerosolized. For this reason, cat

owners are advised to change their cat’s litter daily.

The number of ways *T. gondii* can be transmitted to humans is extensive. Farm animals can become infected from contaminated feed; this causes *T. gondii* oocysts in animals’ muscles, which later may cause human infection if eaten as undercooked meat. Many such family outbreaks of toxoplasmosis have been described.¹

If infective oocysts get into the water supply, they may also cause outbreaks of disease. More than 200 such outbreaks have been described, including an instance in Victoria, British Columbia, in which 100 people became clinically infected.⁴

Family outbreaks have also been described that involve multiple children who played in an infected sandbox or dirt pile.⁵ Similarly, an outbreak has been reported in a riding stable that was home to infected cats. Infective oocysts were thought to have become aerosolized and breathed in by the patrons.⁶ Multiple other possible modes of transmission are being investigated, including sexual transmission among humans.⁷

Human infections are not always benign

In most human *T. gondii* cases, the infected individual experiences mild, flu-like symptoms, often with enlarged lymph nodes, or has no symptoms.¹ Thus, most people who have been infected with *T. gondii* are unaware because clinicians do not routinely test for it.

There are 3 exceptions to this otherwise benign clinical picture. The first is cerebral toxoplasmosis, which occurs in individuals who are immunosuppressed because they have AIDS or are receiving treatment for cancer or organ transplantation. Cerebral toxoplasmosis can be severe and was a common cause of death in patients with AIDS before the development of effective AIDS treatments.

The second exception is congenital toxoplasmosis, when an infection occurs in a pregnant woman. Such infections can cause severe damage to the developing fetus, including abortion, stillbirth, and

brain damage. Congenital toxoplasmosis infections occur in approximately 1 of every 10,000 births in the United States, or approximately 3,800 each year.⁸ As a result, pregnant women are advised not to change their cat's litter and to be tested for evidence of *T. gondii* infection.

The third exception is eye disease. Toxoplasmosis is one of the most common causes of eye disease, especially of the retina. Each year in the United States, approximately 4,800 individuals develop systematic ocular toxoplasmosis.⁹

Toxoplasmosis and psychosis: What evidence supports a link?

Until recently, cerebral infections, congenital infections, and eye disease were thought to be the main clinical problems associated with toxoplasmosis. However, accumulating evidence suggests that psychosis should be added to this list. Five lines of evidence support this.

1. *T. gondii* can cause psychotic symptoms. It has been known for decades that *T. gondii* can cause delusions, auditory hallucinations, and other psychotic symptoms.¹ In one of the earliest publications (1966), Ladee¹⁰ concluded "The literature not infrequently focuses attention on psychosis with schizophrenia or schizophreniform features that accompany chronic toxoplasmosis." Among the cases Ladee¹⁰ described was a laboratory worker who became infected with *T. gondii* and developed delusions and hallucinations.¹⁰

2. Patients with schizophrenia who are infected with *T. gondii* have more severe psychotic symptoms. This finding has been reported in at least 7 studies.¹ Holub et al¹¹ evaluated 251 patients with schizophrenia who were treated in Prague Psychiatric Centre between 2000 and 2010. Overall, 57 participants were infected with *T. gondii* and 194 were not infected. Compared to those who were not infected, the infected group:

- had significantly more severe symptoms ($P = .032$) as measured on the Positive and Negative Symptom Scale
- were prescribed higher doses of anti-psychotic medications
- had been hospitalized longer.¹¹

3. Compared with controls, patients with psychosis are significantly more likely to have antibodies against *T. gondii*, indicating previous infection. To date there have been approximately 100 such studies, of which at least three-fourths reported a positive association. In a 2012 meta-analysis of 38 such studies, Torrey et al¹² reported an odds ratio (OR) of 2.7—compared to persons who have not been infected, those who have been infected with *T. gondii* were 2.7 times more likely to have schizophrenia.¹² This study replicated the findings of a previous meta-analysis of 23 antibody studies, which also found an OR of 2.7.¹³

4. Compared with controls, individuals with schizophrenia or bipolar disorder are significantly more likely as a child to have lived in a home with a cat. Since 1995, 10 such studies have been published; 7 were positive, 2 were negative, and 1 was inconclusive.¹ Torrey et al¹⁴ reviewed 2,025 individuals with schizophrenia or bipolar disorder and 4,847 controls and found that 51% of the cases and 43% of the controls had owned a cat before age 13; this difference was highly significant ($P < .001$). In fact, it is surprising that any study can find a statistically significant association between cat ownership and childhood psychosis. This is because a child who did not own a cat could become infected in many locations where cats have been present, including sandboxes at school, a babysitter's or friend's house, or a public park. And even if a child became infected at home, they would not necessarily have owned a cat, since the neighbor's cat could have been responsible for the oocyst contamination.

5. Epidemiologically, there is a close temporal correlation between the rise of cats as pets and the rise of psychosis. This can be illustrated most clearly in England, where the rise of cat ownership has been documented by writers and where there is data on the rise of psychosis, especially in the 18th and 19th centuries.¹

How many cases of psychosis might be caused by *T. gondii*?

In 2014, using data from the antibody studies discussed above,^{12,13} Smith¹⁵ sought to

Clinical Point

Patients with schizophrenia who were infected with *T. gondii* had more severe psychotic symptoms



Cats and psychosis

Clinical Point

Toxoplasmosis is typically treated with pyrimethamine, but this medication is ineffective when *T. gondii* infects the brain

Related Resources

• Torrey EF. *Parasites, Pussycats, and Psychosis: The Unknown Dangers of Human Toxoplasmosis*. Springer Nature; 2022. <https://link.springer.com/book/10.1007/978-3-030-86811-6>

Drug Brand Names

Pyrimethamine • Daraprim

discover how many cases of psychosis might be caused by *T. gondii*. He concluded that 21% of cases of schizophrenia might have been caused by *T. gondii*. Based on the annual incidence of schizophrenia in the United States, this would mean an estimated >10,000 new cases of schizophrenia each year are attributable to this parasite.

Some researchers have found links between *T. gondii* and several nonpsychiatric diseases and conditions, including epilepsy and brain cancer (*Box*,^{1,16-19} page 16).

Clinical implications: What to tell patients about cats

What do these studies of toxoplasmosis imply for psychiatric care? As mental health professionals, part of our job is to educate our patients. Anything that appears to be a risk factor for the development of psychosis is thus of interest. Consider discussing the following with your patients.

Are cats safe? Cats that are kept exclusively indoors are safe pets because they are unlikely to become infected with *T. gondii*. However, cats that are allowed to go outdoors may not be safe, especially for children and young adults. What is needed is an effective vaccine that could be given

to newborn kittens to prevent infection, but development of this type of vaccine has never been prioritized. At the community level, programs to decrease the number of stray and feral cats would also decrease the risk of infection.

How to decrease risk. On a personal level, we can decrease *T. gondii* infections by not eating undercooked meat. Pregnant women and individuals who are immunocompromised should not change cat litter. When gardening, we should wear gloves because cats favor loose soil for depositing their feces. We should also protect children by covering sandboxes when not in use and by not allowing children to play in uncovered public sandboxes.

Treatment. Toxoplasmosis typically is treated with pyrimethamine, usually in combination with a sulfa drug. However, pyrimethamine does not cross the blood brain barrier and thus is ineffective when *T. gondii* infects the brain. The development of a drug that will effectively treat *T. gondii* in the brain should be a high priority.

For additional details on the studies discussed in this article as well as more resources on the impact *T. gondii* can have if proper precautions are not taken, see my open-access book at <https://link.springer.com/book/10.1007/978-3-030-86811-6>.

References

1. Torrey EF. *Parasites, Pussycats, and Psychosis: The Unknown Dangers of Human Toxoplasmosis*. Springer Nature; 2022. <https://link.springer.com/book/10.1007/978-3-030-86811-6>
2. Rohr JR, Barrett CB, Civitello DJ, et al. Emerging human infectious diseases and the links to global food production. *Nat Sustain*. 2019;2(6):445-456.
3. Joynson DHM. Preface. In: Joynson DHM, Wreghitt TC, eds. *Toxoplasmosis: A Comprehensive Clinical Guide*. Cambridge University Press; 2001:xi.
4. Bowie WR, King AS, Werker DH, et al. Outbreak of toxoplasmosis associated with municipal drinking water. *Lancet*. 1997;350(9072):173-177.

Bottom Line

Some evidence suggests that infection with *Toxoplasma gondii* (*T. gondii*) may cause psychotic symptoms, may increase an individual's risk of developing psychosis, and may result in more severe psychotic symptoms. Cats can transmit *T. gondii* to humans. Educate patients that they can reduce their risk by keeping their cats inside, avoiding exposure to cat feces, particularly while pregnant or if immunocompromised, and not eating undercooked meat.

5. Stagno S, Dykes AC, Amos CS, et al. An outbreak of toxoplasmosis linked to cats. *Pediatrics*. 1980;65(4):706-712.
6. Teutsch SM, Juranek DD, Sulzer A, et al. Epidemic toxoplasmosis associated with infected cats. *N Engl J Med*. 1979;300(13):695-699.
7. Kaňková Š, Hlaváčová J, Flegr J. Oral sex: a new, and possibly the most dangerous, route of toxoplasmosis transmission. *Med Hypotheses*. 2020;141:109725.
8. Guerina NG, Hsu HW, Meissner HC, et al. Neonatal serologic screening and early treatment for congenital *T. gondii* infection. *N Engl J Med*. 1994;330(26):1858-1863.
9. Jones JL, Holland GN. Annual burden of ocular toxoplasmosis in the US. *Am J Trop Med Hyg*. 2010;82(3):464-465.
10. Ladee GA. Diagnostic problems in psychiatry with regard to acquired toxoplasmosis. *Psychiatr Neurol Neurochir*. 1966;69(1):65-82.
11. Holub D, Flegr J, Dragomirecká E, et al. Differences in onset of disease and severity of psychopathology between toxoplasmosis-related and toxoplasmosis-unrelated schizophrenia. *Acta Psychiatr Scand*. 2013;127(3):227-238.
12. Torrey EF, Bartko JJ, Yolken RH. *T. gondii* and other risk factors for schizophrenia: an update. *Schizophr Bull*. 2012;38(3):642-647.
13. Torrey EF, Bartko JJ, Lun ZR, et al. Antibodies to *Toxoplasma gondii* in patients with schizophrenia: a meta-analysis. *Schizophr Bull*. 2007;33:729-736.
14. Torrey EF, Simmons W, Yolken RH. Is childhood cat ownership a risk factor for schizophrenia later in life? *Schizophr Res*. 2015;165(1):1-2.
15. Smith G. Estimating the population attributable fraction for schizophrenia when *T. gondii* is assumed absent in human populations. *Prev Vet Med*. 2014;117(3-4):425-435.
16. Sadeghi M, Riahi SM, Mohammadi M, et al. An updated meta-analysis of the association between *T. gondii* infection and risk of epilepsy. *Trans R Soc Trop Med Hyg*. 2019;113(8):453-462.
17. Hodge JM, Coghill AE, Kim Y, et al. *T. gondii* infection and the risk of adult glioma in two prospective studies. *Int J Cancer*. 2021;148(10):2449-2456.
18. Hosseini Z, Sharif M, Sarvi S, et al. Toxoplasmosis seroprevalence in rheumatoid arthritis patients: a systematic review and meta-analysis. *PLoS Negl Trop Dis*. 2018;12(6):e0006545.
19. Burgdorf KS, Trabjerg BB, Pedersen MG, et al. Large-scale study of *Toxoplasma* and Cytomegalovirus shows an association between infection and serious psychiatric disorders. *Brain Behav Immun*. 2019;79:152-158.

Clinical Point

Tell patients that they can reduce their risk of *T. gondii* infection by keeping their cats inside