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A decade of discoveries in veterinary protozoology changes our concept of "subclinical" toxoplasmosis☆

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Abstract

One of the most compelling topics to emerge from the last decade of veterinary protozoology is disease caused by a zoonotic pathogen, *Toxoplasma gondii*, in otherwise healthy people. These findings may catch the health professions by surprise, because veterinary and medical courses and textbooks typically emphasize that *T. gondii* infections are subclinical, unless acquired in utero or the patient has a serious immunosuppressive condition. Nevertheless, numerous reports in the last decade associate toxoplasmosis with lymphadenopathy, fever, weakness and debilitation, ophthalmitis, and severe multisystemic infections in people who do not have immunosuppressive conditions. Toxoplasmosis in rodents causes altered behavior, and similar mental aberrations are coming to light in humans; recent studies associate *T. gondii* infection with personality shifts and increased likelihood of reduced intelligence or schizophrenia. These conditions reduce the quality of life of individuals, and may exact a significant economic burden upon society. Of course, toxoplasmosis continues to cause serious conditions in AIDS patients and congenitally infected people, as well as abortions and encephalitis in domestic and wild animals. Environmental contamination is heavy enough to extend into marine wildlife. It is time for the health professions to amend teaching curricula regarding *T. gondii*. Veterinary parasitologists should lead the way in developing methods to reduce the prevalence of *T. gondii* in food animals. Public health policies should prohibit the practice of allowing pet cats to roam. Organizations and individuals that feed feral cats are unwittingly contributing to the dissemination of *T. gondii*, by sustaining artificially dense populations of a definitive host of this protozoal parasite.

Keywords: *Toxoplasma gondii*; Schizophrenia; Zoonosis; Mental health; Clinical disease; Prevention; Public health; Food safety; Feral cats; Marine life; Environmental contamination; Endangered species

1. Introduction

While surveying the literature for this review article, with a suggested title of "a decade of discoveries in veterinary protozoology", I was overwhelmed by the many remarkable accomplishments in this field. In the last 10 years, many thousands of articles have been published about protozoal diseases

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of domestic livestock and poultry, traditional and exotic pets, terrestrial and aquatic wildlife, and protozoal zoonoses. My attention was eventually drawn to new and diverse information about *Toxoplasma gondii*, which is of interest to all veterinary protozoologists and a great many others because it infects a wide range of domestic and wild animals, is a zoonotic pathogen, and has issues of food safety, transmission by pets, and environmental health. An overview of recent findings leads to the conclusion that toxoplasmosis has many previously unrecognized or underestimated health sequelae in the general public, in addition to the well-known consequences associated with congenital infections or immunosuppressive conditions. Consequently, recommendations are presented for more vigorous control of this pathogen; these recommendations are intended to stimulate debate and action.

2. Rodent psychology

It is well known that *T. gondii* can cause encephalitis in fetal infections and in immunosuppressed individuals (Tenter et al., 2000), as well as in certain highly susceptible species of animals (Burns et al., 2003). Even though infections in most other circumstances do not result in clinically apparent encephalitis, the organism nevertheless infects the central nervous system and forms latent tissue cysts in neurons and other permanent cells (Tenter et al., 2000). Despite this neurotropic affinity, there are only a handful of studies about the possible effects of toxoplasmosis upon behavior and mentation. Recent studies (Berdoy et al., 1995, 2000) have strengthened earlier observations (Hay et al., 1983; Arnott et al., 1990) that chronic toxoplasmosis may cause altered behavior in mice and rats. In comparison to uninfected rodents, infected rodents are more likely to investigate novel stimuli and appear less cautious when presented with signs of cats. This behavior is hypothesized to increase the susceptibility of infected rodents to predation by cats, and therefore to increase the odds of completing the *T. gondii* life cycle.

Berdoy et al. (2000) state that *T. gondii* infection specifically alters rodent behavior related to avoidance of cats, but does little else (e.g. activity levels and mate seeking behavior are unchanged). They conclude that this subtle behavioral manipulation is unlikely to be a nonspecific effect of encephalitis, and therefore it is implied that the mechanism of behavioral alteration may be controlled by the parasite as a result of evolutionary adaptation. In contrast, Hrda et al. (2000) concluded the opposite, that behavioral changes are probably nonspecific by-products of pathological symptoms of toxoplasmosis (i.e. consequences of inflammation and necrosis), rather than a result of specific manipulation by the parasite. Regardless of the mechanism, these behavioral effects appear to benefit both the parasite and the felid definitive host, but occur at the expense of rodent intermediate hosts. Could *T. gondii* exert similar effects upon other intermediate hosts?

3. Consequences of toxoplasmosis in immunologically competent people

Medical parasitology texts and articles typically emphasize the importance of toxoplasmosis in congenitally acquired infections and in immunosuppressed individuals (Jones et al., 2001). Consequences of postnatal infection of immunocompetent people usually receive little consideration, because most such cases have been thought to be subclinical (Acha and Szyfres, 1980; Hill and Dubey, 2002). Unfortunately, evidence is accumulating that toxoplasmosis in the general population may have greater consequences than previously realized.

3.1. Toxoplasmosis and the mind

Evidence is mounting to link toxoplasmosis with schizophrenia or similar psychiatric disorders. Recent studies from three countries found that schizophrenic patients had higher antibody levels to *T. gondii* than did matched control subjects (as reviewed by Torrey and Yolken, 2003). Two of those studies and a third one published later (Leweke et al., 2004) specifically investigated patients during their first episode of schizophrenia; all three studies found the association to be significant ($P < 0.01$). The above investigations included only small numbers of patients, but 13 related older studies included a total of more than 2500 psychiatric patients. Those studies were published in multiple languages, which may have mitigated widespread recognition of their collective findings until