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Prevalence of Toxoplasmic Retinochoroiditis in an Australian Adult Population

A Community-Based Study

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Purpose: Toxoplasmic retinochoroiditis is the most common clinical manifestation of an infection with the protozoan parasite, *Toxoplasma gondii*. Up to 50% of the human population is estimated to be infected with *T. gondii*; however, the epidemiology of toxoplasmic retinochoroiditis has not been widely reported. We sought to estimate the prevalence of toxoplasmic retinochoroiditis in Australia using data that were collected as part of the Busselton Healthy Ageing Study.

Design: Cross-sectional, community-based, prospective cohort study.

Participants: 5020 Australian adults (2264 men and 2756 women; age range, 45–69 years, and median age, 58 years).

Methods: Retinal color photographs, centered on the optic disc and macula, were captured using a digital retinal camera after the dilation of the pupils. Three uveitis-subspecialized ophthalmologists assessed each pigmented retinal lesion, and complete concordance of opinion was required to assign a toxoplasmic etiology. Serum *T. gondii* immunoglobulin (Ig)G levels were measured for those participants with retinal lesions judged to be toxoplasmic retinochoroiditis.

Main Outcome Measures: Prevalence of toxoplasmic retinochoroiditis.

Results: Eight participants (0.16%) had retinal lesions that were considered to have the characteristic appearance of toxoplasmic retinochoroiditis, plus detectable serum *T. gondii* IgG, consistent with the diagnosis of toxoplasmic retinochoroiditis. On the assumption that 23.81% of retinal lesions occur at the posterior pole, as reported in a community-based survey conducted in Brazil (*Sci Rep*. 2021;11:3420), the prevalence of toxoplasmic retinochoroiditis was estimated to be 0.67% or 1 per 149 persons.

Conclusions: Toxoplasmic retinochoroiditis is common in Australian adults. Efforts to quantify and address risk factors for human infection with *T. gondii* are justified. *Ophthalmology Retina 2022;6:963-968 © 2022 by the American Academy of Ophthalmology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).*

Toxoplasma gondii is an Apicomplexan protozoan parasite that causes the infectious disease known as toxoplasmosis.[1] Globally, a wide spectrum of mammals and birds are infected with *T. gondii*, which is contracted in environments soiled by primary feline hosts or by consuming the carcasses of other infected animals.[2] Humans, in particular, develop toxoplasmosis most commonly after eating undercooked meat sourced from infected livestock.[3] Manifestations of the disease depend on the age, health, and genetics of the infected individual and the parasite strain, load, and form, as well as environmental factors.[4] The most common clinical manifestation is a recurrent, unilateral, inflammatory retinal disease—or posterior uveitis—termed ocular toxoplasmosis or, more specifically, toxoplasmic retinochoroiditis.[5,6] Cohort studies have demonstrated that approximately 60% of inflamed eyes develop reduced vision, and up to 25% become irreversibly blind.[7–9] On resolution of an attack of inflammation, the individual is left with a pigmented retinal scar that has a highly typical clinical appearance.[10]

It has been widely stated that between 30% and 50% of the human population is infected with *T. gondii*.[11] This estimate is based on the prevalence of anti–*T. gondii* immunoglobulin (Ig) in the serum, and studies from around the world have provided seroprevalence rates that range widely from 0.5% to 87.7%, with regional differences.[12] Arguably, the more important statistic is the prevalence of the clinical disease, but there have been no national population-based and few community-based observational studies of toxoplasmic retinochoroiditis with serologic confirmation of *T. gondii* infection.[1] A major

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challenge in studying the epidemiology of this condition is that, unless an individual experiences an attack of inflammation, they are unlikely to present for medical care. Moreover, screening for the disease requires pharmacologic dilation of the pupils and examination of the retina, which are not routine procedures outside an ophthalmology clinic.

In the study reported here, we sought to address the epidemiologic knowledge gap in toxoplasmic retinochoroiditis by using data that were collected as part of the Busselton Healthy Ageing Study.[13] Retinal color photographs from approximately 5000 individuals living in urban Western Australia were obtained during this project to evaluate the prevalence of glaucoma and age-related macular degeneration. Three uveitis-subspecialized ophthalmologists reviewed these photographs, and serum was tested for *T. gondii* IgG to provide an estimate of the prevalence of toxoplasmic retinochoroiditis in an Australian cohort.

Methods

This study made use of clinical data that were collected in the course of the Busselton Healthy Ageing Study. The design and methods of this study have been previously described in detail.[13] In summary, this is a community-based, prospective cohort study involving 5107 "baby boomers" (ie, individuals born between 1946 and 1964) who resided within the local government electoral boundary of the City of Busselton in Western Australia. All persons listed on the compulsory Western Australian Electoral Commission Electoral Roll were eligible to participate; 82% of those on the electoral register were contacted and confirmed eligible, and 76% of those contacted were recruited between May 2010 and December 2015. The overall goal of the project is "to identify the cumulative effects of disparate illnesses that constitute the burden of disease that impacts on healthy ageing."[13] Baseline data collection included a health- and lifestyle-focused questionnaire, blood sampling, anthropometric measurements and body imaging, cardiovascular and respiratory monitoring, tests of physical function and balance, cognitive assessment, sleep studies, and auditory and ophthalmic examinations.

The ophthalmic assessment included retinal color photography, with the stated purpose of assessment for glaucoma and age-related macular degeneration. Unless they declined, the participants had dilation of the pupil of each eye with 1% tropicamide eye drops. Between 15 and 20 minutes later, retinal photographs were taken using a digital retinal camera (Canon CR-1). Two images were obtained, one centered on the optic disc and the other centered on the macula. These images were saved in JPG format with 300 pixels/inch resolution of a 15.84×10.56 inch^2 photograph. Retinal images were available for 5020 participants. These images were screened to identify the participants with pigmented retinal lesions in 1 or both eyes.

The diagnosis of toxoplasmic retinochoroiditis was based primarily on the clinical appearance of the retinal lesion, which is standard practice.[14,15] Three uveitis-subspecialized ophthalmologists (L.B.F., J.M.F., J.R.S.) assessed each pigmented retinal lesion during a virtual conference chaired by a fourth ophthalmologist (D.M.) (Zoom Video Conferencing).[16] As noted by Stanford et al,[16] the intraclass correlation coefficient for diagnosis of toxoplasmic retinochoroiditis from retinal photographs by experts is moderate to good, and complete concordance of opinion was required to establish the diagnosis. Given the high infection rate with *T. gondii* in the human population, a negative *T. gondii* serologic test is used to exclude the diagnosis.[14,15] Thus, for participants who had retinal lesions that were judged to be toxoplasmic retinochoroiditis, serum *T. gondii* IgG levels were measured at PathWest Laboratory Medicine WA (Nedlands, Australia), using the Alinity i Toxo IgG Reagent Kit, which is a chemiluminescent microparticle immunoassay (Abbott Laboratories).

The Busselton Healthy Ageing Study is approved by the University of Western Australia Human Research Ethics Committee (approval number RA/4/1/2203). The study adheres to the Declaration of Helsinki, and all study participants have provided written informed consent. The use of retinal photographs from the Busselton Healthy Ageing Study for the purpose of this work specifically was approved by the Busselton Population Medical Research Institute Scientific Committee (approval number BSN20/02). A literature search conducted using the National Library of Medicine, National Center for Biotechnology Information PubMed database with multiple search terms (ie, population AND ocular toxoplasmosis; population AND toxoplasmic retinochoroiditis; community AND ocular toxoplasmosis; community AND toxoplasmic retinochoroiditis; epidemiology AND toxoplasmic retinochoroiditis; epidemiology AND ocular toxoplasmosis, last updated on April 11, 2022) identified no national population-based studies of the epidemiology of serologically confirmed ocular toxoplasmosis.

Results

A total of 5020 participants in the Busselton Healthy Ageing Study (2264 men and 2756 women, aged 45 to 69 years, with a median age of 58 years) provided retinal color photographs. Among this group of adults, 4909 (97.8%) were meat eaters, including 4808 (95.8%) who ate red meat, and 963 (19.2%) were cat owners. Overall, 306 participants had pigmented retinal lesions around the macula or optic nerve. Twelve participants (0.24%) had retinal lesions that were judged by all 3 uveitis-subspecialized ophthalmologists to have the characteristic appearance of toxoplasmic retinochoroiditis. Serum tested from 8 of these 12 participants (0.16%) returned a positive result for *T. gondii* IgG, indicating the diagnosis of toxoplasmic retinochoroiditis. Retinal photographs from these 8 participants are presented in Figure 1; given that the retinal photographs were obtained for the purpose of visualizing the macula or optic nerve, in several of the images, the lesions are located at the edge of the field of photography.

Toxoplasmic retinochoroiditis may occur at any location across the retina, although there is a tendency for the lesions to occur in the central retina (ie, in the region of the macula and optic disc). A recent community-based survey conducted in Cássia dos Coqueiros, São Paulo, Brazil (721 adult participants), used our definition of toxoplasmic retinochoroiditis and described the disease by location across the retina, distinguishing "central" and "peripheral" lesions located within and outside the posterior pole, respectively; the work showed that toxoplasmic retinal lesions were located in the central retina in 23.81% of affected individuals.[17] By applying this figure to our findings from the photographs centered on the macula and on the optic disc, the prevalence of toxoplasmic retinochoroiditis at any location across the retina may be estimated at 0.67% of the Busselton Healthy Ageing Study population or 1 per 149 persons.

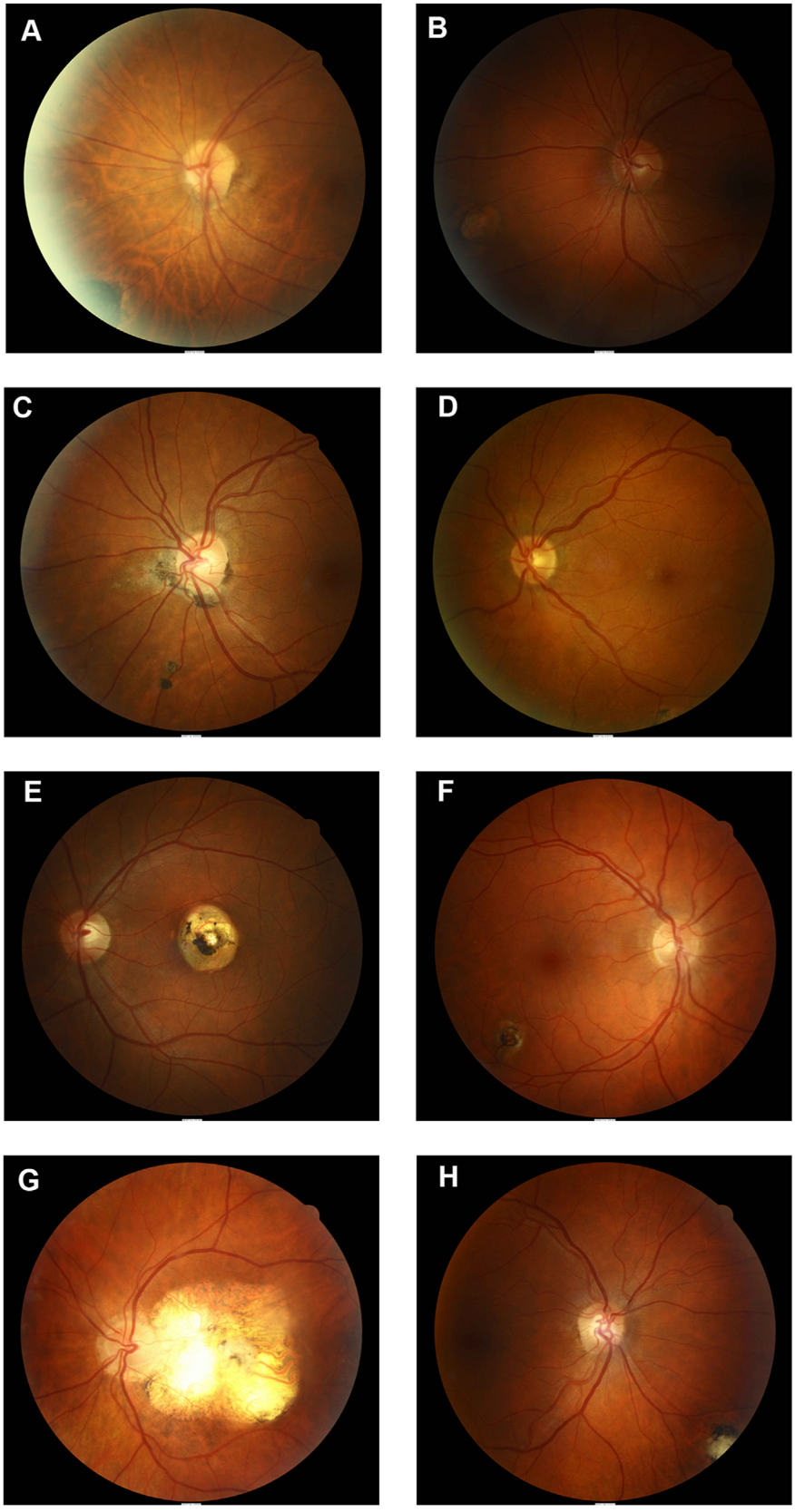

Figure 1. Color photographs of the retina from participants of the Busselton Health Ageing Study, who were diagnosed with toxoplasmic retinochoroiditis on the basis of clinical appearance and serum *Toxoplasma gondii* immunoglobulin G. Images were centered on the optic disc (**A–C, H**) or macula (**D–G**), and for some images (**A, D, H**), the lesions are located at the edge of the photographic field.

Discussion

Despite the high rates of *T. gondii* infection in human and diverse animal populations across the world, the prevalence of the clinical disease remains poorly described. The most common manifestation of the infection is toxoplasmic retinochoroiditis, but because toxoplasmosis is a neglected disease, it is difficult to gain traction for dedicated studies to describe its epidemiology. To estimate the prevalence of toxoplasmic retinochoroiditis, we applied standard diagnostic methods to retinal photographs based at the macula and at the optic disc that were collected as part of an Australian community-based health survey with independent goals. We drew from a smaller community-based study conducted in Brazil that involved retinal examinations, with assessments of both the posterior pole and periphery[17]; although parasite strains differ between these countries, this factor is not known to influence the location of lesions. We found that toxoplasmic retinochoroiditis was common in Australian adults—approximately 1 in 150 adults suffers from this condition—based on a population of baby boomers aged 45 to 69 years at the time of the retinal photography. The rate of *T. gondii* infection increases with age,[18] and thus, the prevalence is expected to be lower than this figure in children and younger adults and higher than this figure in older adults.

There have been no national population-based studies of the epidemiology of serologically confirmed ocular toxoplasmosis, but community-based surveys have been conducted in the Americas and Africa. An early survey, undertaken in Erechim, Rio Grande do Sul, alerted the field to a potentially high prevalence of the disease in Brazil,[19] and several surveys have been conducted in different regions of the country over the past 2 decades. Applying the same criteria that we employed to identify toxoplasmic retinochoroiditis, De Amorim Garcia et al[20] described a prevalence of 0.94% in 959 students studying in Natal, Rio Grande do Norte, in 2001; Aleixo et al[21] reported a prevalence of 3.8% in 1071 residents of Santa Rita de Cássia, Rio de Janeiro, in 2004; and De Angelis et al[17] measured a prevalence of 5.8% in 721 adults living in Cássia dos Coqueiros, São Paulo, in 2016 and 2017. Surveys in 2005 of 200 staff and students at the University of Quindío, Colombia, and in 2013 of 390 children and adults across households in the Central Region, Ghana, indicated a prevalence of toxoplasmic retinochoroiditis by clinical and serologic markers of 4.5% and 2.6%, respectively.[22,23]

This work represents the first effort to quantify the rate of ocular toxoplasmosis in the Western Pacific Region of the world. The prevalence of toxoplasmic retinochoroiditis that we have estimated is lower than those reported in the South American and West African surveys. Although it may be relevant that our study included a considerably higher number of participants than any of the other surveys, regional environmental factors are likely to influence the prevalence of the condition. Interestingly, in 2003, Holland[24] predicted the prevalence of toxoplasmic retinochoroiditis in the United States to be 2% of the infected population, which most recently was measured at 11.14% of persons aged over 5 years[18]; his prediction suggests a prevalence that is also lower than the previously reported figures and, indeed, is lower than our result in the Busselton community cohort.

A summary of serologic studies conducted at antenatal clinics and blood banks across Australia, published in 1979, suggested that 24% to 44% of the population was infected with *T. gondii*.[25] The treatment of drinking water by filtration and regulated farming and food processing in Australia are likely to reduce the risk of contamination of food with *T. gondii*. On the other hand, Australia has substantial feral cat populations that are highly infected,[26] which, together with the high levels of free-range and organic livestock farming, may promote infection with the parasite. We recently detected frequent contamination of Australian lamb with *T. gondii*.[3] There is a vogue for eating a wide range of meats undercooked or raw, which overall is considered the most common route for becoming infected,[27] and over 95% of the study group were meat eaters. Parasite genetics may also affect the likelihood of developing ocular toxoplasmosis, although review of 19 parasite genotyping studies in patients with ocular toxoplasmosis shows that strains across all genotypes may cause toxoplasmic retinochoroiditis.[1] There have been several reports of *T. gondii* genotypes in Australia, each involving the study of a small number of animals, including 12 kangaroos and bettongs, 16 kangaroos and wallaroos, 8 wombats, and 8 domestic cats.[28–31] The study of macropods was conducted in the state of Western Australia, approximately 450 miles from Busselton.[29] These studies showed marked genotypic diversity across the strains, with a majority having nonarchetypal clonal or atypical genetics.

As applies to all clinical research on toxoplasmic retinochoroiditis, not only epidemiologic studies, one limitation of our work relates to diagnostic accuracy. It is not possible to recover an organism to confirm the diagnosis, given that *T. gondii* resides in the retina and retinal biopsy is inherently damaging to the intraocular tissues. Polymerase chain reaction amplification of parasite DNA in ocular fluid is used clinically,[32] but only in ambiguous cases because there is risk to the sampling procedure,[33] and not in epidemiologic studies. Thus, the diagnostic standard is the clinical appearance—which was judged by 3 uveitis-subspecialized ophthalmologists in this study—along with positive *T. gondii* serology.[15] Negative serology is possible in patients with ocular toxoplasmosis, specifically in immunocompromised or aged persons.[34,35] Like other investigators, we observed lesions that were typical of toxoplasmic retinochoroiditis but had to be discounted because serology was negative. Recently reported diagnostic criteria apply to active disease only[14] and must be modified for epidemiologic surveys, in which most or all toxoplasmic lesions are expected to be inactive. Another limitation of our work relates to the ocular imaging; with the advent of wide-field photography and nonmydriatic cameras,[36] there exists the opportunity for a broader retinal coverage and increased participation in future studies in this area.

In summary, this work represents the first effort to estimate the prevalence of toxoplasmic retinochoroiditis in an Australian population. Our findings indicate that this condition is common. Furthermore, these results imply that efforts to quantify and address risk factors are justified, including infections in domesticated and feral cats, contamination of meat, and preparation of meat and meat products for human consumption.

Footnotes and Disclosures

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HUMAN SUBJECTS: Human subjects were included in this study. The Busselton Healthy Ageing Study is approved by the University of Western Australia Human Research Ethics Committee (approval number: RA/4/1/2203). The study adheres to the Declaration of Helsinki, and all study participants provided written informed consent. The use of retinal photographs from the Busselton Healthy Ageing Study, specifically for the purpose of this work, was approved by the Busselton Population Medical Research Institute Scientific Committee (approval number BSN20/02).

No animal subjects were used in this study.

Author Contributions:

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Ig = immunoglobulin.

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