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Brown, Bruce L.; Berrett, Andrew N.; Erickson, Lance D.; Gale, Shawn D.; Stone, Allison; and Hedges, Dawson W., "Toxocara Seroprevalence and Associated Risk Factors in the United States" (2017). Faculty Publications. 5992.
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Toxocara Seroprevalence and Associated Risk Factors in the United States

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Abstract. Caused by the parasitic nematodes Toxocara canis and cati, toxocariasis in humans can result in covert toxocariasis, ocular toxocariasis, visceral larval migrans, and neurotoxocariasis. A common infection, toxocariasis exposure varies widely within and between countries, with a previous estimate of Toxocara seroprevalence using data from 1988 to 1994 in the United States of approximately 13%. Age, poverty, sex, educational attainment, ethnicity, and region have been associated with Toxocara seroprevalence. In this study, we sought to determine the seroprevalence and factors associated with Toxocara seropositivity in the United States using data from the National Health and Nutrition Examination Survey from 2011 to 2014 to provide a more recent estimate of Toxocara seroprevalence in the United States. We found an overall Toxocara seroprevalence of 5.1%. Increasing age, male sex, low educational attainment, low income, and immigration status each was associated with Toxocara seropositivity. Mexican Americans had reduced odds of exposure. These findings show that toxocariasis continues in the United States and that several demographic factors influence the risk of exposure.

INTRODUCTION

Toxocara canis and Toxocara cati are parasitic nematodes responsible for human toxocariasis, a common and likely underrecognized zoonotic helminth infection. Among the nematodes found in the genus Toxocara, T. canis and T. cati are the only Toxocara species known to cause human disease. Toxocara infects humans via embryonated eggs in the environment, particularly in soil or in raw vegetables or other foods, contaminated water, and possibly contact with dog hair. Although routine veterinary care for household pets may increase detection of the parasite and thereby decrease risk for human exposure, infection is still prevalent throughout the world. The major clinical conditions of human toxocariasis are covert toxocariasis, ocular toxocariasis, visceral larval migrans, and neurotoxocariasis. In the United States, children and adults seropositive for toxocariasis had worse cognitive function than did seronegative controls. In fact, in mice, Toxocara infection has been associated with biomarkers of Alzheimer’s disease.

Despite the clinical significance of human toxocariasis, the epidemiology of toxocariasis remains insufficiently known. The prevalence of human toxocariasis appears to vary both between and within countries. Regardless, toxocariasis appears to be one of the most common helminth infections in humans worldwide. Previous estimates based on data from the US Centers for Disease Control and Prevention’s (CDC) third National Health and Nutrition Examination Survey (NHANES III) suggest that approximately 14% of the population older than the age of 6 years in the United States in 1988–1994 was seropositive for Toxocara species. Using the same dataset that Won et al. used but with a different statistical approach, Congdon and Lloyd found an overall US seroprevalence of 12.6% for females and 14.6% for males. A systematic review of Toxocara seroprevalence in North America suggested a prevalence ranging from less than 1% in an indigenous group in Canada to approximately 31% in a sample of children with asthma in Mexico. However, the current estimates for this infection in the United States come from data collected between 1988 and 1994. In Denmark, one study found a Toxocara seroprevalence of 2.4%, and Holland et al. found a seroprevalence of 31% in school children in Ireland. In a particular area of Nigeria, toxocariasis may have a seroprevalence of 86%. There are identified risk factors for Toxocara infection in humans, although many of the findings have been inconsistent. Sociodemographic factors such as age, poverty, ethnicity, sex, and geographical region appear to be associated with Toxocara seropositivity. For example, Toxocara seroprevalence may exceed 20% in males in some US counties, particularly in the South and Northeast. In addition, other factors associated with infection include pet ownership, climate because Toxocara has optimal temperatures for breeding, and rurality with higher seroprevalence in rural as compared with urban areas. Toxocara seroprevalence also differs across ethnic groups, suggesting that cultural and genetic factors might affect seroprevalence. Furthermore, Won et al. found associations between Toxocara seropositivity and blood lead concentration, educational attainment, and socioeconomic status.

The US CDC periodically tests serum samples from the NHANES for anti-Toxocara IgG antibodies and recently released data collected from 2011 to 2014 that contained anti-Toxocara IgG antibodies. Accordingly, our study objectives were 2-fold: first, to update seroprevalence estimates of Toxocara in the United States because prior work used NHANES data collected from 1988 to 1994 and second, to investigate sociodemographic characteristics associated with Toxocara seropositivity in the United States. In the previous report by Congdon and Lloyd, Toxocara seroprevalence was disaggregated by US counties and general geographical regions. However, geographical or other location data in the NHANES data sets are restricted and require funding to obtain. Therefore, we chose to report only findings for the United States as a whole.

MATERIALS AND METHODS

The National Center for Health Statistics (NCHS), a division of the CDC, conducts the NHANES, a cross-sectional survey. The NHANES uses a stratified, multistage cluster design to

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recruit a sample representative of the noninstitutionalized US population and collects an extensive amount of sociodemographic, laboratory, examination, and other data from a large number of individuals residing in various locations in the United States. Before 1999, the CDC conducted the NHANES irregularly, and the survey generally spanned multiple years, resulting in very large sample sizes. In 1999, the CDC converted the NHANES to a continuous, 2-year cycle format with approximately 10,000 participants in each cycle. Although the NHANES collects much of the same data for each NHANES cycle, some of the cycles, including the NHANES III (1988–1994), contain data for variables that the NHANES irregularly surveys, such as anti-Toxocara IgG antibodies. Until recently, data for Toxocara seropositivity was available only for the NHANES III dataset. However, the availability of surplus sera from the 2011–2012 and 2013–2014 NHANES cycles enabled the CDC to assess again serum samples for anti-Toxocara IgG antibodies, allowing a current exploration of Toxocara seroprevalence and factors associated with Toxocara seropositivity.

In the 2011–2012 and 2013–2014 cycles, the NHANES assessed 13,509 participants aged 6 years and older for anti-Toxocara IgG antibodies and collected sociodemographic data for all participants including age, sex, race-ethnicity, education, poverty-to-income ratio (PIR), and immigrant status. Whereas for all participants including age, sex, race-ethnicity, education, poverty-to-income ratio (PIR), and immigrant status. Whereas for all participants including age, sex, race-ethnicity, education, poverty-to-income ratio (PIR), and immigrant status. Whereas for all participants including age, sex, race-ethnicity, education, poverty-to-income ratio (PIR), and immigrant status. Whereas for all participants including age, sex, race-ethnicity, education, poverty-to-income ratio (PIR), and immigrant status.

Laboratory testing. CDC laboratory technicians tested serum samples for Toxocara-specific IgG antibodies using a Luminex assay. A full description of the laboratory methods used is on the NHANES website (https://www.cdc.gov/Nchs/Nhanes/2011-2012/SSTOCA_G.htm). The CDC considered results from the assay to be Toxocara seropositive if the mean fluorescence intensity was greater than 23.1 and negative if the value was equal to or less than 23.1.

Statistical analyses. We used Stata version 14.2 for all statistical analyses and used the svy prefix for all relevant commands to account for the NHANES sampling design. Before analyses, we treated missing data using multiple imputation with chained equations. The chained equations approach allows for distribution-specific imputation equations (e.g., ordinary least squares regression for continuous data and logistic regression for dichotomous data). We used twenty imputed datasets. Two-hundred iterations separated each imputed dataset. The graphical diagnostics indicated that the imputation model converged well before that point. We computed means or proportions, minimums, and maximums for each of the sociodemographic variables we used in this study. We then used logistic regression to estimate the relationship between Toxocara seropositivity and each of the sociodemographic variables while controlling for all other variables. For example, we used logistic regression to test for an association between Toxocara seropositivity and sex while controlling for age, race-ethnicity, education (we used head-of-household education for respondents younger than 20 years old), PIR, and immigrant status.

RESULTS

The study sample consisted primarily of young to middle-aged adults (mean (standard deviation [SD]) = 38.6 (24.5)) and included nearly equal numbers of males (48.8%) and females (51.2%). The majority were non-Hispanic White (65.3%) and had attained at least some post-high school education (62.7%). The sample was relatively evenly distributed across income levels, and approximately 15% were immigrants (Table 1). The overall seroprevalence of Toxocara for respondents ages 6 years and over sampled in the 2011–2014 NHANES data cycles was 5.1% (95% confidence interval [CI]: 4.3, 5.9). Seroprevalence by age group varied from 2.6% in the group aged 6–9 years to 7.0% in the group aged 80 years and older. In females, the overall seroprevalence was 3.9%, and in males, the overall seroprevalence was 6.4%. For subjects with no high-school diploma, the Toxocara seroprevalence was 10.1% but 3.2% for those with more than a high-school education. For a PIR of 0–0.999, the seroprevalence was 9.4%, dropping to 2.2% for those with a PIR of five or higher. In immigrants, the seroprevalence was 12.4%, compared with 7.7% for nonimmigrants (Table 2). Table 3 reports odds ratios.

### Table 1

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<tr>
<th>Age</th>
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<tr>
<td>6–9</td>
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<td>20s</td>
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<td>40s</td>
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<td>0.53</td>
</tr>
<tr>
<td>50s</td>
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<td>60s</td>
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<tr>
<td>Female</td>
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<td>0.38</td>
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<th>Race-ethnicity</th>
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</thead>
<tbody>
<tr>
<td>Non-Hispanic white</td>
<td>65.3</td>
<td>2.6</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>10.9</td>
<td>1.4</td>
</tr>
<tr>
<td>Mexican American</td>
<td>9.8</td>
<td>1.4</td>
</tr>
<tr>
<td>Other</td>
<td>14.0</td>
<td>0.99</td>
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<td>No high school diploma</td>
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<tr>
<td>High school diploma</td>
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<td>0.83</td>
</tr>
<tr>
<td>More than high school</td>
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<td>1.6</td>
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<th>Poverty-to-income</th>
<th>Proportion</th>
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</thead>
<tbody>
<tr>
<td>0–0.999</td>
<td>18.7</td>
<td>1.2</td>
</tr>
<tr>
<td>1–1.999</td>
<td>21.7</td>
<td>0.83</td>
</tr>
<tr>
<td>2–2.999</td>
<td>15.1</td>
<td>0.55</td>
</tr>
<tr>
<td>3–3.999</td>
<td>12.9</td>
<td>0.77</td>
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<td>4–4.999</td>
<td>9.3</td>
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<td>5+</td>
<td>22.4</td>
<td>1.5</td>
</tr>
<tr>
<td>Immigrant</td>
<td>15.6</td>
<td>1.2</td>
</tr>
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</table>

corrected for all the other sociodemographic variables we used from logistic regression for variables that represent risk factors for Toxocara. Compared with subjects aged 6–9 years, subjects aged 40 years or older were nearly twice as likely to be seropositive for Toxocara. Females were about half as likely to be seropositive as males (odds ratio [OR] = 0.54, 95% CI: 0.45, 0.65). Compared with subjects who self-identified as non-Hispanic White, Mexican American subjects were also about half as likely as being seropositive for Toxocara (OR = 0.52, 95% CI: 0.35, 0.79). Subjects who had attained education beyond high school were less likely to be seropositive compared with subjects with less than a high-school education (OR = 0.49, 95% CI: 0.38, 0.64). Finally, immigrants were more than three times as likely to be seropositive for Toxocara as were nonimmigrants (OR = 3.3, 95% CI: 2.4, 4.7).

**DISCUSSION**

In this population-based study representative of 13,509 noninstitutionalized subjects weighted to represent the US population, the overall weighted seroprevalence of Toxocara in subjects aged 6 years and older was 5.1%. However, Toxocara seroprevalence varied according to sociodemographic factors. In general, males were nearly twice as likely to be seropositive for Toxocara than were females, seropositivity tended to increase with age, and both education and socioeconomic status were inversely associated with seroprevalence. These general trends are consistent with previous findings with infectious diseases, including parasitic infections. In terms of race-ethnicity, subjects self-reported as Mexican American had reduced odds of infection (OR = 0.52), while all other race-ethnicity categories had similar seroprevalence rates. Finally, immigrants, regardless of race-ethnicity, were more than three times as likely as to be seropositive than were nonimmigrants in these US samples.

The weighted Toxocara seroprevalence of 5.1% that we found in the combined 2011–2012 and 2013–2014 NHANES datasets is lower than the 14% seroprevalence Won et al. reported and lower than the 12.6% seroprevalence in females and 14.6% in males Congdon and Lloyd reported based on the 1988–1994 NHANES dataset. This change in Toxocara seroprevalence suggests a possible decrease in the seroprevalence of Toxocara in the United States since 1994. However, differences in the assays used to detect Toxocara and their cutoff points for seropositivity between the earlier and later NHANES datasets preclude direct comparison of Toxocara seroprevalence between the two NHANES datasets. Based on these datasets, therefore, we cannot definitively determine whether Toxocara seroprevalence in the United States has changed since 1994. Nonetheless, the data we used from the 2011–2012 and 2013–2014 datasets provide the most up-to-date estimates of Toxocara seroprevalence in the United States and indicate that Toxocara exposure remains present in the United States.

Despite the difficulty in making direct comparisons of Toxocara seropositivity between the earlier and later NHANES datasets, we found that, similar to Congdon and Lloyd, male sex, race-ethnicity, and socioeconomic status were associated
with Toxocara seroprevalence. Although we found that males were approximately twice as likely as females to be Toxocara seropositive and that there were clear gradients with increasing educational attainment and PIR and lower odds ratios of Toxocara seropositivity, Toxocara seroprevalence odds ratios did not differ between non-Hispanic Blacks and non-Hispanic Whites in adjusted models, although they both had higher odds ratios than did Mexican Americans. These results suggest that based on these models controlling for PIR and educational attainment, Toxocara seroprevalence may differ less between race-ethnicity groups in the US in 2011–2014 than it did in 1988–1994.

Consistent with prior work, we found that Toxocara seroprevalence is higher in people with less educational attainment and lower income. Similar to Won et al., we found odd ratios for Toxocara seropositivity among people in their 20s and 30s of 1.5. However, in contrast to Won et al., we found that seroprevalence increased with age with the highest odds ratios for Toxocara seropositivity occurring in people in their 50s (odds ratio: 2.4) and 70s (odds ratio: 2.3) and in those older than age 80 years (odds ratio: 2.6), suggesting that exposure to Toxocara may increase with age in the United States. In regard to Toxocara seropositivity and age, however, not all studies have found an association between Toxocara seroprevalence and increasing age. In La Plata, Argentina, for instance, Toxocara seropositivity was higher in subjects under age 15 years than in subjects older than 16 years. Won et al. also found higher seroprevalence in subjects in their 20s and 30s compared with older subjects and speculated that this may be due to increased soil exposure in children. In a Jordanian sample aged 5–24 years, by contrast, Toxocara seroprevalence was highest in females ages 5–9 years and in males ages 15–19 years, pointing out that factors such as sex might influence the association between age and seropositivity. The increased seroprevalence with age that we found could reflect cohort effects or even changes in veterinary practices in detecting and treating animals with toxocariasis, as treatment guidelines for animals are now readily available. Indeed, improved veterinary and household care for pets could have led to higher detection rates in more recent years thereby reducing the risk of infection in pets and, subsequently, in humans. The increasing seropositivity with age we found also might suggest that other sources of Toxocara exposure besides soil may be relevant in the United States.

Several considerations affect the interpretation of these findings. Enzyme-linked immunosorbent assay used to identify exposure to Toxocara can cross-react with antibodies to other parasites, potentially inflating estimates of Toxocara seroprevalence. In addition, we based our analyses on cross-sectional data and so do not know the timing of the initial exposure to Toxocara and whether subjects had additional exposures. Although we corrected for age, race-ethnicity, education, PIR, and immigrant status, we might well have missed other covariates related to Toxocara exposure, potentially resulting in residual confounding.

In conclusion, based on the most recently available NHANES datasets containing information about the seroprevalence of Toxocara, we found a seroprevalence of 5.1% in the United States, indicating that Toxocara exposure continues in the United States. However, the risk of Toxocara exposure is not evenly distributed through the US population but rather relates to a variety of sociodemographic factors. Male sex, increasing age, low educational attainment, and low PIR were associated with Toxocara seropositivity. Subjects self-reported as Mexican American had reduced odds of infection, whereas all other race-ethnicity categories had similar seroprevalences. Immigrants were more likely than nonimmigrants to be Toxocara seropositive.

Received July 7, 2017. Accepted for publication August 12, 2017.

Published online September 25, 2017.

Disclosure: Dawson Hedges and Bruce L. Brown have a patent pending for an Eigenvector-based method of EEG analysis.

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REFERENCES


