Seroprevalence of Toxoplasma gondii

in Sweden, Estonia and Iceland

Running headline: Prevalence of T. Gondii in the Nordic Baltic Region

Alda Birgisdóttir¹, Hulda Asbjörnsdottir¹, Elisabet Cook³, David Gislason², Christer Jansson⁴, Isleifur Olafsson³, Thorarinn Gislason², Rain Jogi⁵, Bjarni Thjodleifsson²

University of Iceland, Faculty of Medicine.¹, Medical Department, Landspitali University Hospital, Iceland². Department of Clinical Chemistry Landspitali University Hospital, Iceland³. Respiratory Medicine and Allergology. Akademiska sjukhuset Uppsala, Sweden⁴. Tartu University Lung Clinic, Estonia⁵.

Correspondence:
Bjarni Thjodleifsson MD. Ph D. FRCP.
Professor and Head of Gastroenterology
Landspitali University Hospital
Hringbraut
101 Reykjavík
Iceland
Tel. +354-543-6105
Fax +354-543-4834
Mobile +354-896-6629
e-mail bjarnit@landspitali.is
Abstract

Background: Toxoplasmosis is a disease caused by the intracellular protozoan parasite, Toxoplasma gondii which infects up to one third of the world human population. Toxoplasmosis in neonates and immunocompromised patients can lead to severe disease and death.

Objective: 1) To investigate the prevalence and risk factors for T. gondii infection in Iceland, Sweden and Estonia. 2) To test the hypothesis that the encysted state of T. gondii infection causes systemic inflammation.

Material and methods: Blood samples were collected from 1277 randomly selected subjects. The presence of T. gondii IgG antibodies was determined by an ELISA method and levels of Hs-CRP by immunoturbidimetric assay.

Results: The prevalence of T. gondii antibodies was 54.9% in Tartu, 23% in Uppsala and 9.8% in Reykjavik (p<0.0001). The risk of positive T. gondii antibodies increased with the number of siblings and with age in Sweden. T. gondii infection was associated with asthma related symptoms and increased Hs-CRP (p=0.02). No association was found with IgE-sensitisation and lung function.

Conclusion: The risk factors for T. gondii infection suggested that soil exposure was one of the mechanisms in all three countries and meat associated infection route is a risk in Sweden. Hs-CRP indicates a role of T. gondii in systemic inflammation and asthma.
Key words
Toxoplasma gondii/epidemiology
Toxoplasma gondii /Asthma
Toxoplasma gondii /C reactive protein
High sensitivity C-Reactive Protein (HsCRP)
Hygiene
Risk Factors

Cats
Cookery
Humans
Meat
Pregnancy
**Introduction.**

Toxoplasmosis is a disease caused by the intracellular protozoan parasite, Toxoplasma gondii. Toxoplasmosis is one of the more common parasitic zoonoses world-wide and it has been estimated that up to one third of the world human population has been exposed to the parasite (1). Eighty to 90 percent of acute T. gondii infections in immunocompetent hosts are asymptomatic (2) but latent asymptomatic infection can persist for the life of the host. In immunosuppressed patients, especially patients with the acquired immunodeficiency syndrome (AIDS) the parasite can reactivate and cause disease. Toxoplasmosis was found to be the most frequent and severe neurologic infection among persons with AIDS in the United States (3). Newly acquired T. gondii infection in a pregnant woman can be transmitted to the fetus and may cause mental retardation, blindness, epilepsy, and death. Over the past 3 decades, the incidence of prenatal infection with T. gondii has been estimated to vary from 1 to 100 per 10,000 births in different countries (1).

Felines of all types are the only animals in which T. gondii can complete its reproductive cycle (1, 2). Following feline ingestion of any of the forms of T. gondii, the parasite infects the gut epithelial cells and reproduces. The feline then excretes infectious oocysts in feces for about two weeks (4). Oocysts become infective one to five days after excretion, are spread by surface water, and can survive for more than a year (4). If non-felines, including humans, ingest T. gondii oocysts, the organisms invade intestinal epithelium and disseminate throughout the body. They then encyst and can lie dormant in any nucleated cells within tissues for the life of the host.

Seroprevalence estimates vary greatly among different countries, among different geographical areas within one country, and among different ethnic groups living in the same area. Over the past 3 decades antibodies to T. gondii have been detected in from 0 to 100% of individuals in various adult human populations (1). A prevalence of 100% has been reported.
from Saudi Arabia (5), 71% in French women (6), 22.5% in United States (7), 11% in Norway (8) and decreasing prevalence has been reported in Swedish women, 34% in 1969 and 18% in 1987 (9). Regional variations have been attributed to climate (8) cultural differences in the amount and type of raw meat consumed and the variable consumption of meat from animals farmed indoors and frozen meat.

Ingestion of undercooked meats is responsible for the majority of toxoplasmosis cases in France (10) and in United States undercooked meats accounts for half of the cases (11). In six European countries eating undercooked, raw or cured meat contributed to between 30% and 63% of infections, with soil contact contributing to up to 17% of infections (12). However, in most underdeveloped countries infection is more likely due to environmental exposure since meats are usually not eaten undercooked. *T. gondii* is also of importance in veterinary disease were it is a common cause of abortion and mortality in sheep and goats throughout the world (1).

New aspects of possible health consequences of *T. gondii* infection have been suggested in recent years. The hygiene hypothesis proposes that changes in the environment due to improved hygiene and fewer childhood infections has modulated immune responses away from the Th1 cellular responses and toward Th2 responses that favor atopy and allergies (13) (14). *T. gondii* and other food born infections have been part of the human biota throughout human developement and its disappearance may have contributed towards modulated immune responses. Furthermore, little attention has been paid to possible effects of encysted state of *T. gondii* infection on general health such as lung function or systemic inflammation. C-reactive protein (CRP) is an inflammatory marker known to be a risk factor for cardiovascular disease (15). Measurement of CRP could give an indication of possible interaction of *T.*
gondii with the immune/complement system with potential cardiovascular or systemic implications.

The present study is based on data that were accumulated in The European Community Respiratory Health Survey (ECRHS) (16) and contains extensive information on atopy, asthma and allergy related pulmonary symptoms and lung function. Serum samples are also available. The present study works with data from Sweden, Estonia and Iceland. The ECRHS database makes it possible to test several hypothesis about the interaction of infectious agents, atopy and lung related allergic symptoms and the effect on inflammatory parameters. The main objectives of the present study were as follows. 1) To document the present serological prevalence of T. gondii in Sweden, Estonia and Iceland and attempt to elucidate the risk factors for infection. 2) To explore the hypothesis of involvement of T. gondii with atopy and allergy related lung symptoms. 3) To assess possible effects of T. gondii infection on lung function and systemic inflammation.

Material and Methods:

Study sites and population

The European Community Respiratory Health Survey I (ECRHS I) was a project which was embarked on to study geographical difference in the incidence of asthma and atopy and their risk factors in a young adult population. Individuals aged 20-44 years were randomly selected during the period 1990-94, from the population of 22 nations and 48 study sites. Each participant was sent a brief questionnaire (Stage 1) and from those who responded, a random sample was selected to undergo a more detailed clinical examination (Stage 2). In addition a “symptomatic sample”, reporting symptoms of waking with shortness of breath, asthma attacks or using asthma medication in stage 1 were also studied.(17)
Our study populations comprises all those living in Reykjavik, Uppsala and Tartu who participated in ECRHS I (n=2033) and where invited for a repeated study in the years 1999-2001 (ECRHS II) (18). The median length of follow up was 8.4 years. Blood samples for determination of T. gondii status was collected from 1277 subjects (Reykjavik 503, Uppsala 492, Tartu 282), 606 men and 657 women. Of these 1016 subjects (440 in Reykjavik, 361 in Uppsala and 215 in Tartu) were from the random sample and 261 from the symptomatic sample.

The appropriate Ethics Committees approval was obtained in all countries.

Serologic methods

The presence of T. gondii IgG antibodies was determined by an ELISA method using microtitre plates coated with inactivated T. gondii antigens. For calibration we used T. gondii IgG standards calibrated in accordance with the 3rd International Standard of the WHO. All reagents were obtained from Novatec Immundiagnostica GmbH, Dietzenbach, Germany. Serum samples with titers >35 IU/ml were classified as positive while equivocal samples with titers between 030 – 35 IU/ml and samples with titers 30 IU/ml were classified as negative. The diagnostic sensitivity and the specificity of the T. gondii IgG ELISA method has been shown to be 96,8% and 100%, respectively (17).

Questionnaire

The subjects underwent a structured interview, which included detailed information on respiratory symptoms and diagnoses, smoking history, occupation and early life exposure. “Asthma” was defined as having physician-diagnosed asthma and having had asthma-related symptoms or attacks of asthma in the preceding 12 months (19) From the questionnaire the subjects were divided into three smoking history categories: never-smokers, ex-smokers and current smokers. The following early life exposure variables were included: hospitalizations
before the age of five for lung disease, age when attending day care, bedroom sharing with other children before the age of five, pets during childhood and rural versus urban living as a child when under the age of five (Table 4).

Socio-economic status was defined from information on the subjects occupation provided during ECRHS I according to the United Kingdom social classification. Using this classification the subjects were divided into: (a) professional and semi-professionals, (b) skilled non-manual worker, (c) skilled manual worker and (d) unskilled manual workers (e) un-defined.

**Body mass index**

Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters.

**Allergy testing**

Total and specific serum IgE was determined using the Pharmacia CAP System (Pharmacia Diagnostics, Uppsala, Sweden). In all centres specific IgE was measured against Dermatophagoides pteronyssinus, timothy grass, cat and Cladosporium herbarum. Detection of specific IgE (≥0·35 kU/L) was used as the definition of sensitisation. Atopy was defined as being sensitised to any of the above allergens.

**Systemic inflammation**

High sensitivity C-Reactive Protein (HsCRP) concentrations were measured on a Hitachi 911 analyzer using a commercially available latex-enhanced immunoturbidimetric assay from Roche. The lower detection limit of the assay is 0.1 mg/l. The between-day coefficient of variation was 1.1% at a concentration of 3.73 mg/l and 1.9 % at a concentration of 0.68 mg/l.

**Spirometry**
The maximum forced expiratory volume in one second (FEV₁) and maximum forced vital capacity (FVC) of up to five technically acceptable blows were determined, and also whether FEV₁ and FVC each met the American Thoracic Society (ATS) criterion for reproducibility.

**Description of socio-economic development**

The United Nations Human Development Report (20) classifies 178 nations into human development categories based on composite Human Development Index (HDI) which ranges from 0 to 1. All countries included in the HDI are classified into three clusters by achievement in human development: high human development (with an HDI of 0.800 or above), medium human development (HDI of 0.500–0.799) and low human development (HDI of less than 0.500). In the year 2003 Iceland was in 2nd world rank, Sweden 6th and Estonia 38th with HDI index of 0.956, 0.949 and 0.853 respectively, all countries in the high development category. In the year 1975 Iceland and Sweden had a HDI of 0.863 and 0.864 respectively but the first report for Estonia is from 1990 when HDI was 0.814 but in 1995 the HDI was 0.795 or in the medium category.

**Statistics**

The statistical analysis was performed using Stata 8.0 (Stata Corporation, College Station, Texas). Chi squared test and test for trend using unadjusted logistic regression was used when comparing differences in T. gondii status between centres, gender and age groups. Multiple logistic regression was used to calculate adjusted odds ratios (OR) for the different determinants for T. gondii status. Multiple linear regression was used to study associations between T. gondii status, lung function and HsCRP. In these analyses adjustments were made for age, sex, smoking, BMI and centre and for the spirometric values also for height. The adjusted OR was analysed on pooled data from all three centres adjusting for centre. Analyses of association between T. gondii status and respiratory health and allergy were performed.
using both the random and symptomatic sample (n=1277). All other analyses were performed on the random sample (n=1016).

**Results**

The data is from 1016 subjects (random sample) (488 men and 528 women), mean age 41.9±7.3 (range 28-54) years randomly sampled from the population of Reykjavik (n=440), Uppsala (n=361) and Tartu (n=215). The original sample was 1046 but serum samples were not available from 30 subjects.

The number of subjects with a positive serology for T. gondii was 244 (24.0%). The prevalence of T. gondii antibodies was highest in Tartu and lowest in Reykjavik (Table 1). The prevalence of T. gondii increased significantly by age in Uppsala (p=0.004) but no significant age trend was found in the other two centres. The prevalence of T. gondii was significantly higher in women than in men in Tartu (68.6 vs. 48.4%, p=0.003) while no significant sex difference was found in the other centres.

<table>
<thead>
<tr>
<th>Age</th>
<th>T. gondii IgG antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reykjavik</td>
</tr>
<tr>
<td>&lt;35</td>
<td>9.3</td>
</tr>
<tr>
<td>35-39</td>
<td>9.3</td>
</tr>
<tr>
<td>40-44</td>
<td>5.6</td>
</tr>
<tr>
<td>45-49</td>
<td>18.3</td>
</tr>
<tr>
<td>≥50</td>
<td>7.8</td>
</tr>
<tr>
<td>28-54</td>
<td>9.8</td>
</tr>
</tbody>
</table>

**Table 1** The prevalence of IgG antibodies to T. gondii by age and centre (%).

No significant associations were found between BMI, socio-economic status or smoking history and the prevalence of T. gondii in any centre. T. gondii was not significantly
associated with age, female gender and ever-smoking when combining data from all centres (Table 2). No association was found between having IgG antibodies against T. gondii and height.

**Early life exposure and the prevalence of T. gondii**

The following early life variables were assessed: dog, cat and birds during childhood, day care before the age of 3 years, hospitalisation because a respiratory infection before the age of 5 years, mothers age, educational level (age when completing full time education), number of siblings and rural vs. urban upbringing. The risk of T. gondii increased with the age of the mothers when born in Tartu and in participants that had been in day care before the age of 3 years in Reykjavik. In the combined model the risk of T. gondii increased with the number of siblings.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Reykjavik OR (95% CI)*</th>
<th>Uppsala OR (95% CI)*</th>
<th>Tartu OR (95% CI)*</th>
<th>All centre OR (95% CI)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (10 years)</td>
<td>1.06 (0.64-1.76)</td>
<td>1.67 (1.14-2.48)</td>
<td>0.91 (0.57-1.45)</td>
<td>1.23 (0.96-1.57)</td>
</tr>
<tr>
<td>Women</td>
<td>1.28 (0.65-2.51)</td>
<td>1.12 (0.67-1.88)</td>
<td>2.14 (1.14-4.00)</td>
<td>1.38 (0.995-1.92)</td>
</tr>
<tr>
<td>Ever smoker</td>
<td>1.25 (0.62-2.52)</td>
<td>1.28 (0.76-2.16)</td>
<td>1.15 (0.63-2.12)</td>
<td>1.13 (0.81-1.57)</td>
</tr>
<tr>
<td>One sibling</td>
<td>1.98 (0.79-4.98)</td>
<td>1.23 (0.68-2.22)</td>
<td>1.31 (0.70-2.45)</td>
<td>1.37 (0.94-2.00)</td>
</tr>
<tr>
<td>Two or more siblings</td>
<td>2.46 (0.91-6.68)</td>
<td>2.12 (1.03-4.38)</td>
<td>2.31 (0.90-5.93)</td>
<td>2.18 (1.37-3.47)</td>
</tr>
<tr>
<td>Rural upbringing</td>
<td>1.01 (0.42-2.43)</td>
<td>0.87 (0.50-1.51)</td>
<td>1.09 (0.56-2.12)</td>
<td>0.99 (0.68-1.42)</td>
</tr>
<tr>
<td>Day care</td>
<td>3.72 (1.02-13.4)</td>
<td>1.63 (0.27-9.98)</td>
<td>0.67 (0.33-1.36)</td>
<td>0.99 (0.55-1.80)</td>
</tr>
<tr>
<td>Mothers age</td>
<td>0.95 (0.90-1.01)</td>
<td>0.98 (0.94-1.02)</td>
<td>1.07 (1.02-1.12)</td>
<td>1.00 (0.98-1.03)</td>
</tr>
<tr>
<td>Age when completing education</td>
<td>1.03 (0.99-1.08)</td>
<td>0.99 (0.98-1.01)</td>
<td>1.00 (0.98-1.03)</td>
<td>1.00 (0.99-1.01)</td>
</tr>
<tr>
<td>Living in Uppsala</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3.16 (2.06-4.86)</td>
</tr>
<tr>
<td>Living in Tartu</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>14.1 (8.79-22.5)</td>
</tr>
</tbody>
</table>

* Adjusted for all the variables in the table

** Adjusted for centre and all the variables in the table

Table 2. Age, sex, smoking and early life exposure variables and the risk of Toxoplasma gondi
**Cat exposure and the prevalence of T. gondii**

No significant association was found between cat keeping in childhood or at present and IgG antibodies against T. gondii (Table 4).

<table>
<thead>
<tr>
<th></th>
<th>Reykjavik OR (95% CI)*</th>
<th>Uppsala OR (95% CI)*</th>
<th>Tartu OR (95% CI)*</th>
<th>All centre OR (95% CI)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat 1 year</td>
<td>0.51 (0.14-1.81)</td>
<td>1.59 (0.80-3.14)</td>
<td>1.40 (0.63-3.12)</td>
<td>1.22 (0.79-1.89)</td>
</tr>
<tr>
<td>Cat age 1-4 years</td>
<td>0.81 (0.38-1.74)</td>
<td>1.45 (0.80-2.63)</td>
<td>1.40 (0.72-2.72)</td>
<td>1.21 (0.85-1.73)</td>
</tr>
<tr>
<td>Cat age 5-15 years</td>
<td>0.79 (0.39-1.58)</td>
<td>0.99 (0.56-1.74)</td>
<td>1.53 (0.83-2.81)</td>
<td>1.13 (0.80-1.58)</td>
</tr>
<tr>
<td>Cat now</td>
<td>2.09 (0.87-5.05)</td>
<td>1.01 (0.57-1.79)</td>
<td>1.21 (0.62-2.37)</td>
<td>1.17 (0.80-1.72)</td>
</tr>
</tbody>
</table>

* Adjusted for age, sex, smoking and early life exposure variable (table 2)

** Adjusted for centre and all the variables above

**Table 3.** Cat ownership at different ages and the risk of T. gondi

**Association between T. gondii and respiratory symptoms, asthma and IgE-sensitisation**

T. gondii was significantly associated with nocturnal chest tightness and an increased risk of having at least two asthma related symptoms and was borderline significantly associated with decreased IgE-sensitisation (p=0.097) (Table 4).

**Association between T. gondii, lung function and systemic inflammation**

A week but statically significant association was found between T. gondii and HsCRP (r=0.07, p=0.02). No significant associations were found between T. gondii and FEV1 or FVC.
Table 4. Association between T. gondii and respiratory symptoms, asthma and IgE-sensitisation

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Reykjavik</th>
<th>Uppsala</th>
<th>Tartu</th>
<th>Whole population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>Yes</td>
<td>p-value</td>
<td>No</td>
</tr>
<tr>
<td>Wheeze</td>
<td>24.1</td>
<td>17.4</td>
<td>0.31</td>
<td>30.2</td>
</tr>
<tr>
<td>Wheeze and breathlessness</td>
<td>10.2</td>
<td>6.5</td>
<td>0.43</td>
<td>20.2</td>
</tr>
<tr>
<td>Wheeze without a cold</td>
<td>16.4</td>
<td>13.0</td>
<td>0.56</td>
<td>20.4</td>
</tr>
<tr>
<td>Nocturnal chest tightness</td>
<td>11.7</td>
<td>6.5</td>
<td>0.29</td>
<td>19.3</td>
</tr>
<tr>
<td>Breathlessness at rest</td>
<td>6.4</td>
<td>2.2</td>
<td>0.25</td>
<td>8.7</td>
</tr>
<tr>
<td>Breathlessness after effort</td>
<td>22.7</td>
<td>21.7</td>
<td>0.88</td>
<td>14.5</td>
</tr>
<tr>
<td>Nocturnal breathlessness</td>
<td>2.2</td>
<td>0</td>
<td>0.31</td>
<td>12.6</td>
</tr>
<tr>
<td>At least two asthma symptoms</td>
<td>24.4</td>
<td>21.7</td>
<td>0.68</td>
<td>31.2</td>
</tr>
<tr>
<td>Nocturnal cough</td>
<td>22.3</td>
<td>15.2</td>
<td>0.27</td>
<td>38.9</td>
</tr>
<tr>
<td>Morning cough</td>
<td>11.5</td>
<td>17.4</td>
<td>0.24</td>
<td>9.5</td>
</tr>
<tr>
<td>Daytime cough</td>
<td>12.2</td>
<td>10.9</td>
<td>0.80</td>
<td>24.2</td>
</tr>
<tr>
<td>Morning phlegm</td>
<td>16.2</td>
<td>19.6</td>
<td>0.56</td>
<td>15.1</td>
</tr>
<tr>
<td>Daytime phlegm</td>
<td>9.5</td>
<td>10.9</td>
<td>0.76</td>
<td>14.8</td>
</tr>
<tr>
<td></td>
<td>Asthma</td>
<td>IgE-sensitisation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------------------</td>
<td>--------------</td>
<td>-------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>14.8 15.2 0.94</td>
<td>17.0 17.4 0.95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>21.0 22.3 0.77</td>
<td>40.2 28.3 0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum</td>
<td>4.2 4.4 0.92</td>
<td>25.0 21.7 0.51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>1.01 (0.66-1.55)</td>
<td>0.75 (0.54-1.05)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Adjusted for centre, age, sex, smoking and BMI
Discussion

All analyses in our study were performed on a representative sample from the populations of the three countries in the age range 28-42 years. The samples were collected in the period 1999-2001. The diagnostic sensitivity and the specificity of the T. gondii IgG ELISA method has been shown to be 96.8% and 100%, respectively (17). IgG antibodies appear within one to two weeks of infection with T. gondii, peak in six to eight weeks and then decline over the next two years but IgG antibodies remain detectable for life. Our methods should give an accurate estimate of the prevalence of T. gondii in the three populations.

The main finding in our study is a striking difference in prevalence of T. gondii between the three countries, 9.8%, 23% and 54.9% respectively for Iceland, Sweden and Estonia. The risk of T. gondii infection was increased in participants that had been in day care before the age of 3 years in Reykjavik. In the combined model for all countries the risk of T. gondii increased with the number of siblings. This suggests that soil exposure, which is greatest during the childhood years, may be one of the mechanisms by which persons are exposed to T. gondii in the Nordic Baltic region. The higher incidence in females than men in Estonia may also be related to soil exposure since women are more involved with child rearing than men.

The risk of T. gondii infection increased with age in Sweden and this finding is compatible with cohort effect, with a higher risk for T. gondii infection in the past. This suggests a transmission of T. gondii infection by meat since freezing of meat was formerly less common but freezing below 12 Cº kills T gondii cysts. Livestock rearing practices have also improved and have probably contributed to a decline in toxoplasmosis. Previous studies on T. gondii prevalence in Swedish women showed a declining prevalence from 34% in 1969 to 30% in 1979 and 18% in 1987 (9) and this conforms to the age related increase in the present study. No significant associations were found in our study for having a cat in childhood or later in life, dog or rural or urban upbringing. Previous studies on the risk of T. gondii infection
associated with keeping cats have shown no association (21), negative association in Mexicans in USA (21) and no association in HIV infected adults (22). Cats excrete up to 10 million oocysts per day but for only two weeks of their life, when they first acquire infection. Cats kept in urban environments should pose minimal risk of promoting T. gondii infection. The most likely explanation of the different prevalence between the countries is environmental exposure by ingesting infectious oocysts from contaminated soil or water. This route of infection is associated with socioeconomic development and availability of clean running water which is a precondition of good personal and household hygiene. Cooking practice and kitchen hygiene can be an important factor for transmission of T. gondii particularly the contamination of cooked food with contaminated kitchen appliances. The high rating of Iceland and Sweden on the HDI scale is an indication of good standing in this respect. Estonia however is considerably lower on the HDI scale and was most likely in the medium HDI category before 1970 and with inferior hygienic sanitary standard compared to Iceland and Sweden.

Another indirect indicator of hygienic standard is the prevalence of hepatitis A. The prevalence of anti-HAV IgG antibodies in Sweden was only 4% among a cohort born between 1948 and 1952 (23) which indicates a fairly high hygienic standard already during this period. In Iceland the prevalence of anti-HAV IgG antibodies was 6% in a cohort born 1950-59 (24) which also indicates a good hygienic standard. Nevertheless the prevalence of T. gondii infection in Sweden is 2.4 times higher than in Iceland and this raises the possibility of other infectious routes in Sweden unrelated to hygiene. However, the prevalence of anti-HAV IgG antibodies in Estonia in a cohort born around 1950 is ≈ 70% (unpublished measurements).

Previous study in Iceland on T. gondii IgG antibodies in 139 women aged 17-32 years showed a prevalence of 4.7% (25). The blood samples were collected in 1979-80 for rubella
antibody measurements and an ELISA method was used for T. gondii IgG antibody measurements. This shows that the prevalence of T. gondii infection in Iceland has remained low for two decades. There are some climatic differences between the countries related to different latitudes which are 59, 62 and 65 North for Estonia, Sweden and Iceland respectively. Warmer climate promotes T. gondii soil exposure (8) but the difference in temperature between the countries is however minimal due to the North Atlantic Current around Iceland.

The hypothesis, that disappearance of T. gondii from the study populations would decrease the prevalence of atopy and lung related allergy symptoms, is not supported by our study. On the contrary T. gondii antibodies were significantly associated with an increased risk of having at least two asthma related symptoms. The hypothesis may depend more on the infectious burden from several pathogens rather than on single pathogens (14). Our study did not reveal any effect of T. gondii on respiratory function. A weak but statistically significant association was found between T. gondii and elevated HsCRP indicating that T. gondii may to some extent be related to systemic inflammation. The association of T. gondii with an inflammatory parameter like Hs-CRP and asthma related symptoms may be connected but the precise mechanism is not clear.

**Acknowledgements**

The study was supported financially by the Icelandic Research Council grant no 050405011, The Landspitali University Hospital Research Fund, the Swedish Heart and Lung Foundation, the Vårdal Foundation for Health Care Science and Allergy Research, the Swedish Association Against Asthma and Allergy, and the Estonian Science Foundation grant no 4350. There is no conflict of interest for any of the authors.
References:


