

# Susceptibility of Pregnant Women to Toxoplasma Infection â Potential Benefits for Newborn Screening

W Ferguson<sup>1</sup>, PD Mayne<sup>1,2,3</sup>, B Lennon<sup>1</sup>, K Butler<sup>1,2,3</sup>, M Cafferkey<sup>1,2</sup>

<sup>1</sup>The Rotunda Hospital, Parnell Street, Dublin 1

<sup>2</sup>The Childrenâ s University Hospital, Temple Street, Dublin 1

<sup>3</sup>Our Ladyâ s Childrenâ s Hospital, Crumlin, Dublin 12

## Abstract

Congenital toxoplasmosis (CT) arises as a result of new acquisition of Toxoplasma infection by a susceptible woman during pregnancy. Early detection of CT through neonatal screening programmes could optimize management and improve infant outcome. This study sought to estimate the prevalence of Toxoplasma susceptibility in pregnant women. As detection of Toxoplasma antibodies in neonatal blood reflects maternal exposure history, maternal antibody seroprevalence was determined using anonymized residual blood from newborn screening cards. A total of 20 252 cards were tested in 1 year. 4 991 (24.6%) cards tested positive for Toxoplasma antibody. Results were stratified by county. Toxoplasma antibody seroprevalence rates of 25% indicated that Toxoplasma infection is common in Ireland and that up to 75% of women remain susceptible to primary infection during pregnancy. This study aimed to a) determine the seroprevalence of Toxoplasma antibody in pregnant women, and hence b) estimate the risk for acquisition of primary toxoplasmosis in pregnancy in order to support an application to fund a pilot newborn screening programme.

## Introduction

Primary infection with Toxoplasma gondii, toxoplasmosis, in an immunocompetent individual is usually asymptomatic. However if acquired during pregnancy transmission to the foetus can occur with potentially adverse outcome.<sup>3</sup> Only 10% of infants infected in-utero are symptomatic at birth and infection often remains undetected in infancy. The most common clinical sequel of CT, chorioretinitis, eventually manifests in > 80% of those infected.<sup>2</sup> Information on the frequency and distribution of T.gondii infection in a population is a necessary prerequisite to evaluate the benefits of screening and preventative measures. The true prevalence of Toxoplasma antibody in women of childbearing age in Ireland is unknown.

## Methods

A systematic sample of blood spots was taken from cards referred to the National Newborn Screening Laboratory over a 1 year period. Sampling was anonymous and unlinked. Blood spot discs were stratified by county of maternal residence only. Blood was eluted from each spot and a modified latex agglutination test was used to detect all classes of Toxoplasma antibody.<sup>4</sup> Simulated positive and negative blood spots were used as controls. The prevalence of Toxoplasma antibody was estimated for all of Ireland and for each county. Ninety-five per cent confidence intervals were calculated for the national rate and for each county.

## Results

A total of 20 252 cards were tested which represented 40.2% of registered live births in 1 year. 4 991 (24.6%) cards tested positive for Toxoplasma antibody. The mean seroprevalence in Ireland was 25%, ranging by county from 19.9% to 41.3% indicating that a significant majority of women of child bearing age remain susceptible to Toxoplasma infection in pregnancy. Toxoplasma antibody prevalence was found to be above the mean in 6 counties and below the mean in county Dublin. Percentages of cards screened for each county were similar and average maternal age was similar throughout the country. (Data not shown).

## Discussion

Primary T. gondii infection during pregnancy exposes the foetus to the possibility of congenital infection. Transmission risk to the foetus varies with gestational age. First trimester infection is associated with 25% transmission with neurologic and ocular sequelae in 75%. Third trimester infection is associated with >60% transmission but adverse sequelae in <5%.<sup>3</sup> Most infants in the latter group will be asymptomatic at birth; some may display sub clinical disease on further evaluation. Without treatment, CT is a recurrent disease that may reactivate and progress at any time. By age 20, up to 85% of CT infants have had unilateral or bilateral chorioretinitis.<sup>2</sup> The most effective method for prevention of CT is not known. However, the importance of diagnosis and treatment of CT in the first year of life has been documented<sup>1,2</sup> and may reduce the incidence of late retinochoroiditis and progression of intracranial calcification.

**Figure 1** Counties in the Republic of Ireland with Toxoplasma seroprevalence significantly above or below the national average.

This study demonstrates that in Ireland 75% of pregnant women are Toxoplasma non-immune and potentially at risk of acute toxoplasmosis. The geographical variation in seroprevalence suggests that the risk of exposure to Toxoplasma may vary in different parts of Ireland and is in part explained by urban-rural differences. The only study in similar populations in Wales and Scotland yielded antenatal seropositivity rates comparable to this group, with anticipated rates of congenital infection of 2 per 1000. A congenital infection rate of 2 per 1000 live births has previously been demonstrated in a cohort of pregnant women attending a Dublin maternity hospital. The true rate of CT in Ireland can only be determined by nationwide newborn screening. The utility of screening programs for toxoplasmosis, either during pregnancy or postnatally remains controversial due to absence of standardized management protocols and limited long term monitoring studies of congenitally infected infants. In a metaanalysis of individual patient data, Thiebaut et al found no convincing evidence of benefit of prenatal screening programmes in preventing CT. Postnatal diagnosis and treatment has been associated with improved long term infant outcome,<sup>1</sup> and newborn CT screening programmes have been successfully employed in various countries with encouraging results.

A neonatal screening programme based on detection of Toxoplasma specific IgM antibody in serum eluted from newborn screening cards will identify 85% of cases of CT. Screen positive infants require serologic confirmation in parallel with maternal serology. Screening in the newborn period facilitates early diagnosis of both asymptomatic and symptomatic infants. The potential benefit accrued relates not only to the initiation of specific anti-toxoplasmosis treatment, but importantly identifies this vulnerable group of infants who require detailed clinical evaluation and facilitates their enrollment in early intervention services as appropriate. With 75% of the Irish pregnant population identified as at risk of acute toxoplasmosis, funding was sought and obtained from the Department of Health and Children to undertake a pilot study of newborn screening for CT to determine the incidence in Ireland and to determine the outcome to early treatment intervention.

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Correspondence: W Ferguson  
Rotunda Hospital, Parnell Street, Dublin 1  
Email: [wferguson@rotunda.ie](mailto:wferguson@rotunda.ie)

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