

## Maternal prevalence of toxoplasma antibody based on anonymous neonatal serosurvey: a geographical analysis

A. E. ADES<sup>1</sup>\*, S. PARKER<sup>1</sup>, R. GILBERT<sup>1</sup>, P. A. TOOKEY<sup>1</sup>, T. BERRY<sup>1</sup>,  
M. HJELM<sup>1</sup>, A. H. WILCOX<sup>2</sup>, D. CUBITT<sup>1</sup> AND C. S. PECKHAM<sup>1</sup>

<sup>1</sup>*Epidemiology and Biostatistics Unit, Department of Virology, and Department of Clinical Biochemistry, Institute of Child Health and Hospitals for Sick Children*

<sup>2</sup>*Neonatal Screening Laboratory, St Helier Hospital, Carshalton*

(Accepted 14 September 1992)

### SUMMARY

A total of 12902 neonatal samples collected on absorbent paper for routine metabolic screening were tested anonymously for antibodies to toxoplasma. Seroprevalence varied from 19.5% in inner London, to 11.6% in suburban London, and 7.6% in non-metropolitan districts. Much of this variation appeared to be associated with the proportions of livebirths in each district to women born outside the UK. However, additional geographical variation remained and seroprevalence in UK-born women was estimated to be 12.7% in inner London, 7.5% in suburban London, and 5.5% in non-metropolitan areas. These estimates are considerably lower than any previously reported in antenatal sera in the UK. The wide geographical variation highlights a need for further research to determine the relative importance of different routes of transmission.

### INTRODUCTION

*Toxoplasma gondii* is a protozoan parasite transmitted to humans either as oocysts via soil contaminated with cat faeces, or from tissue cysts in undercooked meats [1]. Infection is thought to pose few problems for the immune-competent, though a primary infection in pregnancy may lead to fetal infection. Congenital infection may result in severe disease presenting at or shortly after birth, but an unknown proportion of those without perinatal manifestations may go on to develop retinochoroiditis, sometimes leading to unilateral or bilateral visual impairment. Seroprevalence in women of childbearing age varies widely. In a 1985 survey of antenatal samples in four European cities prevalence varied from 21% in inner London to 72% in Paris, with Stuttgart 36% and Padua 56% [1]. In the United Kingdom estimates based on antenatal sera during the last 20 years have ranged from 22 to 13% [2].

The present study was undertaken initially to evaluate methods for detecting antibodies to toxoplasma in blood samples routinely collected on absorbent paper (Guthrie Cards) for neonatal metabolic screening [3]. The presence of antibody in neonatal samples reflects previous maternal exposure, and this promised to be a

\* Correspondence and reprint requests to: Dr A. E. Ades, Epidemiology and Biostatistics Unit, Institute of Child Health, 30 Guilford Street, London WC1N.

simple and inexpensive method of mass serosurvey. In the course of the study, marked differences in seroprevalence emerged between inner city, suburban, and non-metropolitan districts. These differences form the subject of this paper.

#### METHODS

After routine neonatal metabolic tests had been completed, 5.5 mm diameter dried blood spots (DBS) were punched out of Guthrie cards received at two neonatal screening laboratories serving NE, NW, and SW Thames Health Regions. The area covered in the study comprises three quarters of south eastern England, including inner London, suburban London, and non-metropolitan districts. The only information retained with each DBS was the Health District of the midwife collecting the sample, which is usually the mother's Health District. A Health District is an administrative unit of the National Health Service, and 42 were included in the study. A total of 12902 samples were collected over a 5-week period in mid 1991. Serum was eluted from the samples [3] and eluates were tested for toxoplasma-specific antibody using a modified latex-agglutination method. This test was developed using simulated DBS samples made from sera of known titre. Based on 103 negative and 170 positive samples specificity was 100% and sensitivity 98.8%, with two false negative DBS samples deriving from equivocal sera [4]. Development work established that the dilution of maternal toxoplasma-specific antibody in the 5–10 day-old neonate was slight, and that there was a clear distinction between positive and negative eluates when they were titrated to endpoints [4].

In order to interpret the geographic variation observed, we employed results from an unpublished study of toxoplasma seroprevalence. This was based on unselected, consecutive antenatal samples collected 1981–6 in an inner London clinic [5], which were tested for specific IgG by enzyme immunoassay (Captia Toxo IgG, Mercia Diagnostics). Titres greater or equal to 12 IU per ml were taken as positive, and on this criteria the test was 99.1% sensitive and 100% specific when assessed against a 'gold standard' developed for 1000 samples from tests on 5 separate commercial assays [6]. In that study, seroprevalence in UK-born women was 13.3%: differences between black and white UK-born women were negligible. Antenatal seroprevalence in women born overseas varied from 7.6% in women from India to over 40% in women born in parts of Africa. In the present study eight ethnic/country of birth groups were defined, and their antenatal seroprevalences used in the geographical analysis of District seroprevalence.

Data on the numbers of births in each district broken down by mothers' country of birth for the year 1990 were obtained from the Office of Population Censuses and Surveys (OPCS). The seroprevalence expected in each district  $i$ ,  $E_i$ , was then calculated using the proportions  $p_{ij}$  of births in district  $i$  to mothers in group  $j$ , and the group seroprevalences  $s_j$  given in Table 1:

$$E_i = \sum_j p_{ij} s_j, \quad \sum_j p_{ij} = 1. \quad (1)$$

This gives the district seroprevalence as a weighted average of the ethnic group seroprevalences, with the  $p_{ij}$  as weights, and represents the predicted district seroprevalence assuming that its ethnic/country of birth composition is the only

relevant explanatory factor. In order to examine the additional role of other demographic factors, the number of seropositives,  $r_i$ , out of the total tested,  $n_i$ , in each district was treated as the outcome variable in binomial multiple regression for risk differences [7]. The proportion  $E_i$  expected on the basis of country of birth, was included in every regression model:

$$r_i/n_i = E_i + \sum_k \beta_k z_{ik}, \quad k = 1 \dots C$$

to estimate regression coefficients  $\beta$  for  $C$  additional explanatory variables  $z$  after the district of birth composition had been taken into account. Models of this form assume a linear relation between district seroprevalence and the explanatory variables. The additional variables of interest were: the 1981 district population density, the Jarman Underprivileged Area Score, a weighted average of census variables reflecting social deprivation, and indicator variables for inner London, suburban, and non-metropolitan districts.

The goodness of fit of binomial regression models is assessed by its log-likelihood  $\chi^2$  residual deviance. The smaller the deviance the better the fit; and in a good fitting model the residual deviance should approximately equal the residual degrees of freedom.

## RESULTS

Table 1 summarises the antenatal toxoplasmosis seroprevalence from the earlier study, used to define the  $s_j$  of equation (1). There is marked variation depending on country of birth, ranging from 7.6% in women born in India and 15.3% in women from East Africa who are nearly all of Asian ethnic origin, up to 33.1% in Caribbeans and over 40% in women born in the rest of Africa. Also in Table 1 is a summary breakdown of the mothers' country of birth in 1990, based on OPCS figures. In inner London only 54.8% of deliveries are to UK-born women, compared to 90.3% in non-metropolitan districts. While Table 1 gives the percentage distribution within inner, suburban, and non-metropolitan areas, it is the percentage distribution within each of the 42 health districts that was used to define the  $p_{ij}$  used in equation (1).

The neonatal toxoplasmosis seroprevalence findings are presented in Table 2. Results from the 42 health districts have been pooled together in three classes of district. Seroprevalence in inner London is considerably higher (19.5%) than in non-metropolitan districts (7.5%), with suburban districts intermediate (11.7%). The neonatal seroprevalence expected on the basis of ethnic/country of birth composition is shown under Expected Seroprevalence model 1. The prediction for Inner London is close (19.6%). However, in suburban and non-metropolitan districts the seroprevalence is overestimated, with high  $\chi^2$  deviance evidencing a poor fit.

The seroprevalence assumed in UK-born women was 13.3% (Table 1), based on the earlier study which was set in inner London, much higher than the overall neonatal seroprevalence in suburban and non-metropolitan districts. The failure to predict seroprevalence in these areas could therefore be due to geographical variation in seroprevalence among UK-born women.

Accordingly model 2 was fitted, which took account of the ethnic/country of birth variation, and which also allowed seroprevalence in UK-born women to be

Table 1. *Toxoplasmosis seroprevalence (Captia Toxo-G, Mercia Diagnostics) in antenatal sera collected from an inner London antenatal clinic (unpublished study); and percent livebirths to women born in eight country of birth groups, based on 1990 data from the Office of Population Censuses and Surveys*

	Antenatal toxoplasmosis seroprevalence in Inner London		Percentage of 1990 deliveries in		
	%	(Number tested)	Inner London	Suburban London	Non- metropolitan
United Kingdom	13.3	(3769)	54.8	74.1	90.3
India	7.6	(317)	3.3	4.0	0.6
New Commonwealth East Africa*	15.3	(288)	2.8	3.7	1.0
Rest of Africa†	40.5	(172)	6.5	1.8	0.3
Pakistan & Bangladesh	21.7	(170)	9.6	2.7	1.7
Republic of Ireland	31.1	(412)	3.7	2.7	1.0
Caribbean	33.1	(320)	2.9	1.5	0.4
Rest of world	26.8	(959)	16.4	9.5	4.7

\* New Commonwealth (NCW) East Africa includes Kenya, Uganda, Tanzania, Zambia and Malawi. It was assumed that all women born in New Commonwealth (NCW) East Africa were Asian.

† It was assumed that 15% of those born in the rest of Africa were white [12] and that their toxoplasma seroprevalence was 10%.

Table 2. *Observed and expected neonatal seroprevalence*

	Number of districts	Observed seroprevalence		Expected* seroprevalence, % ( $\chi^2$ residual deviance)		
		Total tested	(% positive)	Model 1 42 D.F.	Model 2 39 D.F.	Model 3 37 D.F.
Inner London	10	3039	(19.5)	19.6 (7.0)	19.3 (6.8)	19.5 (4.6)
Suburban London	13	4282	(11.8)	16.2 (94.8)	11.7 (21.3)	11.8 (19.1)
Non- metropolitan	19	5581	(7.5)	14.6 (296.8)	7.6 (34.6)	7.6 (27.9)

\* Model (1): based on seroprevalence data in Table 1; Model (2): from data in Table 1 but with seroprevalence in UK-born women as shown in Table 3; Model (3): same as (2) but also accounting for population density and Jarman Area Score.

dependent on type of borough. The results are shown in Table 3. The estimates of seroprevalence in UK-born women are: 12.7% in inner London, 7.1% in suburban and 5.5% in non-metropolitan districts. These figures, together with the ethnic/country of birth distribution, can be used to generate expected district seroprevalences. Although the district seroprevalence predicted by model 2 is much closer to observed seroprevalence than model 1 (see Table 2), the overall fit of model 2 was not close ( $\chi^2 = 62.6$  on 39 D.F.  $P < 0.025$ ), particularly in non-metropolitan areas.

After accounting for ethnic/country of birth composition, and for the

Table 3. *Estimated seroprevalences in UK-born women, taking account of the ethnic/country of birth composition (Model 2)*

	Estimated seroprevalence	95% confidence interval
Inner London	12.7	10.2-15.2
Suburban London	7.1	5.9- 8.4
Non-metropolitan	5.5	4.8- 6.3

dependency of seroprevalence in UK-born women on type of district, both the Jarman area scores ( $\chi^2_1 = 10.9$ ,  $P < 0.001$ ) and the population density ( $\chi^2_1 = 4.0$ ,  $P < 0.05$ ) were independently statistically significant. In model 3, seroprevalence was higher in districts with a higher Jarman score (more underprivileged), but after controlling for Jarman score, was lower in districts with higher population density. The improvement in fit is most marked in non-metropolitan districts. The  $\chi^2$  of 51.6 on 37 D.F. is only a barely adequate fit. However, because of the relatively small study sample, the proportions of overseas-born women in each district could differ from the proportions expected on the basis of the 1990 OPCS figures. This would generate additional random variation, over and above what would be expected from the binomial error.

Models including terms for Jarman score, population density and proportions UK-born in different types of borough, but which did not take account of the ethnic/country of birth composition, fitted the data poorly ( $\chi^2_{37} = 78.9$ ). A model which allowed for overall variation between types of District, not confined to UK-born women, had residual deviance 3.8  $\chi^2$  units higher than the model allowing for variation in the UK-born alone. A model allowing for variation in non-UK-born women, but not UK-born, had a deviance 28.8 higher. Once variation in the UK-born was accounted for, variation in non-UK born was not statistically significant ( $\chi^2_3 = 2.0$ ,  $P > 0.1$ ). The assumption that the additional geographic variation resided in UK-born women, while not conclusively proven, received the most support from the data.

#### DISCUSSION

This study has demonstrated a more than twofold variation in neonatal toxoplasmosis seroprevalence between inner city and rural districts in SE England.

A limitation of using neonatal samples to conduct what is effectively a maternal seroprevalence survey is that at present only limited information is retained with each sample. A geographical analysis, explaining district seroprevalence in terms of district attributes, was therefore the only one possible. However, we were able to combine antenatal toxoplasmosis seroprevalence data for eight country of birth groups with the district distribution of mothers' country of birth. The results suggested that much of the variation between districts in neonatal seroprevalence could be explained by their ethnic/country of birth composition.

In the antenatal study, based in an inner city antenatal clinic, the seroprevalence in UK-born women was 13.3% (95%CI 12.2-14.4), and there was no dependency on ethnic status. This finding, taking into account the higher seroprevalence in

other immigrant groups, proved to be entirely compatible with the Inner London aggregate seroprevalence of 19.5%, but clearly incompatible with the much lower seroprevalence in suburban (11.6%) and non-metropolitan districts (7.6%).

One interpretation of this, supported by further analysis, was that the seroprevalence in UK-born women depended on the type of district. There were additional associations between seroprevalence and both the Jarman Area score and population density. These findings must be viewed with caution, as the methodology assumes homogeneity of seroprevalence within country of birth groups across SE England, and cannot take account of additional factors such as age-structure, or age at immigration, which could be correlated with Jarman score and population density.

Geographical analyses based on data from several sources collected at different times are inherently approximate, and the study should perhaps be regarded as generating rather than testing hypotheses. Similarly, the estimates of geographical variation in Table 3 may be less precise than the confidence intervals suggest, because it is not possible to take these additional sources of uncertainty into account. In spite of these limitations in the interpretation of the results, this survey has demonstrated in a large and unbiased population, the lowest antenatal seroprevalences ever found in the UK. Previous results based on antenatal sera ranged from 22% in London in the early 1970s [8] to 13% in Glasgow [9]. A study based on samples sent for routine virological examination in South Yorkshire between 1988 and 1990 gave an 8.2% seroprevalence in 20–30 year olds [10].

It is likely that the higher seroprevalence among immigrants largely reflects infection acquired before entry to this country, although the continuation of culinary traditions after immigration could also play a role. The differences between UK-born women in inner London and in rural districts, however, remain to be explained. Studies based on sera which have been stored for up to 30 years suggest a dramatic fall in age-specific seroprevalence both in England [10] and Sweden [11]. Some researchers suggest that this is a result of the increased use of frozen meat, but it is not clear to what extent this could account for geographical differences in SE England. An alternative explanation for the higher seroprevalence in UK-born women in inner London could be the increased contact with soil contaminated with cat faeces in parks and gardens of the inner city. The 2 to 3-fold geographical differences noted in this study highlight the need for careful research to determine the relative importance of different routes of transmission during the childbearing period.

#### ACKNOWLEDGEMENTS

This research was supported by grants from the Child Health Research Trust and the Medical Research Council.

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