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TOXOPLASMOSIS AND MENTAL RETARDATION – REPORT OF A CASE-CONTROL STUDY

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A case-control study evaluating the association between mental retardation and toxoplasmosis was conducted among 845 school children in Belo Horizonte, MG, Brazil. Cases (450) were mentally retarded children attending a public school for special education. Controls (395) were children from the regular public school system. Clinical and anthropometric examinations and interviews were carried out to determine risk factors for toxoplasmosis and mental retardation. Diagnosis of Toxoplasma gondii *infection was based upon an indirect immunofluorescent test (IFA); 55% of cases and 29% of controls were positive. The Relative Odds of mental retardation in children with positive serology was 3.0 (95% CI 2.2-4.0). Maternal exposure to cats and contact with soil were associated with an increased risk of mental retardation. Retinochoroiditis was fourfold more prevalent among cases than controls and was only diagnosed in* T. gondii *IFA positive participants. Congenital toxoplasmosis, in its subclinical form, appears to be an important component in the etiology of mental retardation, especially in high risk (lower socio-economic) groups. The population attributable risk was estimated as 6.0 - 9.0%, suggesting the amount of mental retardation associated with this infection.*

Key words: toxoplasmosis – *Toxoplasma gondii* infection – mental retardation – case-control study

Although the multifactorial etiology of mental retardation is well recognized, the etiology of mental retardation in a large proportion of these individuals is unexplained (Crome, 1960; Drillien et al., 1966; Classification of Mental Retardation, 1972; Smith & Simons, 1975; Ajuriaguerra, 1977; Hagberg et al., 1981). The association of mental retardation with symptomatic congenital toxoplasmosis is well known (Sabin, 1942). However, in subclinical toxoplasmosis, infected children are partially or totally free of symptoms during early life, but often become symptomatic with brain and eye lesions during their early school years (Miller et al., 1967; Stagno, 1980; Wilson et al., 1980; Koskiniemi et al., 1989).

Toxoplasma gondii infection has a world-wide distribution and varies markedly among different populations. It ranges from 10% among Navajo Indians and Australians to 50% in the United States and Brazil and 90% in Paris (Feldman, 1982; McCabe & Remington, 1988). Frequencies as high as 1 per 750 livebirths have been reported in United States (Alford et al., 1975). In areas where seroconversion rates range from 3-5% during pregnancy, the prevalence of congenital infection has been estimated to occur in 4.0 to 6.4/1,000 livebirths (Frenkel, 1985; Papoz et al., 1986).

Prevalence rates of mental retardation have varied according to the classification system used. For mild mental retardation (intelligence quotient between 50 and 70), rates of 5.6 to 30.5/1,000 have been described. Higher rates in children by school age, adolescents, and young adults are reported (Kiely, 1987).

Previous investigations of the prevalence of *T. gondii* infection among children with cerebral damage reported Relative Risk estimates of 3.5 when comparing neuropsychiatric

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patients and healthy children (Elias et al., 1960), of 7.4 when comparing children with congenital cerebral defects and controls without central nervous system diseases (Thalhammer, 1961, 1962), and of 2.3 when comparing mentally retarded children with those from the general population (Al-Saffar & Najim, 1965). However, none of these studies attempted to identify risk factors for toxoplasmosis infection.

In São Paulo, Brazil, a survey of postpartum women age 15-44 years showed a prevalence rate of 747 per 1000 women (Sabin-Feldman). Congenital toxoplasmosis rates were estimated as 16 per 1000 live births regardless of clinical disease and 5 per 1000 live births for symptomatic congenital toxoplasmosis based on these results (Castilho, 1976). A study of 1032 blood samples of neonates (2-5 days) conducted in Rio de Janeiro, Brazil, revealed 15 (1.4%) to be IgM positive (indirect immunofluorescence) and were considered as being potential risk for congenital toxoplasmosis (Coutinho et al., 1983).

The present case-control study was carried out to investigate the association of toxoplasmosis with mental retardation in an area with a high prevalence of *T. gondii* infection. Risk factors associated with toxoplasmosis infection, either acquired or congenital, and their possible relationship with other risk factors for mental deficiency were studied.

MATERIALS AND METHODS

Cases consisted of mentally retarded students attending the Instituto Pestalozzi, a public school for children with learning disabilities in Belo Horizonte, Minas Gerais, Brazil, in 1985. They were referred by public or private schools or the community for special education. All of the 450 students attending class were identified from a list provided by the school. None of them had a previous diagnosis of congenital toxoplasmosis in their medical records.

Controls were students without learning problems attending an elementary/middle public school (1st through the 9th grade) located in the neighborhood (same city block) of the Instituto Pestalozzi during the same time period. They comprised a total of 395 students chosen by simple random sampling from each classroom.

Maternal interviews were conducted by trained interviewers using a pretested, standardized questionnaire designed to obtain information about several risk factors for mental retardation. Questions addressing risk factors for *T. gondii* infection in both mother and child included residence in rural areas, contact with soil or animals, and ingestion of raw milk and meat. The questions were designed to differentiate a possible congenital from an acquired infection. Information on socioeconomic status consisted of annual income per capita: US$ 400 or less and over US$ 400. Educational level defined as four years or less of schooling and occupation of the household head was used in a three grade score to validate the information about income.

Assessment of the nutritional status included weight, height, triceps skinfold thickness, arm, thorax and head circumference, and clinical signs of malnutrition according to standardized criteria (Jellife, 1966). The diagnosis of *T. gondii* infection was made using the indirect immunofluorescent antibody test (IFA) for both IgG and IgM (Camargo, 1966) using the criterion of a positive titer as ≥ 1:16 (Camargo, 1966; Feldman, 1982; Frenckel, 1986). All sera were tested in a masked fashion. An indirect ophthalmoscopic examination was conducted in a subsample of 230 cases and 173 controls who were chosen by simple random sampling. The severity of mental retardation was based on intelligence quotient (IQ) and the etiological diagnosis of the mental deficiency. Data were collected from the psychological service records of the Instituto Pestalozzi. The IQ test was previously conducted as a psychological screening admittance to the Institute. All interviews, clinical exams, and blood sample drawings were performed during the same visit for each participant, and the examiners were not aware of the results of *T. gondii* IFA test.

Data analysis was performed using Statistical Package for Social Sciences (SPSS, 1990) and GLIM (Healy, 1988). Anthropometry was analyzed comparing the variables among the two groups and with a standard population (Marcondes et al., 1982). Relative Odds and 95% confidence intervals were calculated (Lilienfeld & Lilienfeld, 1980; Kleinbaum et al., 1982; Schlesselman, 1982; Rothman, 1986) to determine the association between selected potential risk factors and *T. gondii* infection or mental retardation. Stratified analysis and logistic regression techniques were employed as

the approaches to identify confounders (Kleinbaum et al., 1982; Rothman, 1986; Greenland, 1989). In the logistic regression techniques (Hosmer & Lemeshow, 1989) the mental retardation was the outcome variable and the Relative Odds for *T. gondii* infection alone was calculated. For each potential confounder, a model was constructed and the Relative Odds of being mentally retarded was determined. Each model consisted of *T. gondii* infection and the potential risk factor as independent variables. The variable was considered a confounder if the magnitude of the Relative Odds change with and without control of the potentially confounding variable (Greenland, 1989).

Evaluation of effect modification was performed using either stratified or logistic regression approaches. For the additive risk model, stratified analysis was adopted. For the multiplicative risk model, both approaches were used. In the logistic regression, the Wald test was obtained to determine whether the independent variables or interaction terms were significantly related to the outcome. The likelihood ratio test was used to assess the goodness of fit of the model.

RESULTS

Complete data were collected for over 95% of the sample, and there were no significant differences in completion between cases and controls. The refusal rate was less than 0.5%. The severity of mental deficiency among cases revealed that 55% had moderate to mild mental retardation (IQ 50 to 90) and 45% were markedly mentally retarded (IQ below 50).

Demographic characteristics of cases and controls are shown in Table I. The mean age was similar but cases were more often male and nonwhite ($p < 0.01$). There was a significant difference in socioeconomic status between cases and controls ($p < 0.01$); the majority of both groups were of low socioeconomic status (less than U.S. $ 400.00 per capita per year). No significant differences were found for other variables related to general living conditions. Thirty-seven percent of cases compared to 76% of controls lived in the school neighborhood area ($p < 0.01$). Cases were moderately stunted as assessed by anthropometric criteria and had a higher proportion of clinical signs related to malnutrition.

TABLE I

Demographic characteristics of cases of mental retardation and controls (Belo Horizonte, MG, Brazil, 1985)

Characteristics[a]	Cases		Controls	
	n = 450		n = 395	
Mean age (years)	450	(13.7)	395	(13.3)
Proportions (%)				
Sex[d]				
Males	302	(68.3)	188	(48.3)
Females	140	(31.7)	201	(51.7)
Ethnic group[d]				
White	204	(46.4)	315	(81.4)
Black	72	(16.4)	19	(4.9)
Mulatto	164	(37.3)	53	(13.7)
Socioeconomic status[d]				
Lower educational level[b]	435	(98.9)	340	(88.5)
Lower income[c]	388	(98.7)	265	(84.1)

a: actual n may vary because of missing information.
b: defined as equal or less than four years of schooling and occupation of the head of household.
c: defined as equal or less than US$ 400.00 annual income per capita.
d: significant at .05 level: X^2 heterogeneity.

Fifty five percent of cases and 29% of controls had a positive IFA-IgG test for *T. gondii*. The crude Relative Odds was 3.0 (95% CI 2.2-4.0). The majority (99%) of those testing positive from both groups had titers ≤1:1024, with the geometric mean titer being 1:64 for cases and 1:46 for controls. All IFA-IgM tests were negative. Infection rates did not vary markedly by age among cases (the difference observed for the group ≥ 20 years was not statistically significant), being similar to the average rates reported for adults in Brazil. In the control group, an increasing trend was observed from 15 years on (the difference observed between 5-9 and 10-14 age groups was not statistically significant); one could expected rates similar to the cases for older controls if they were available (Table II).

The frequency of *T. gondii* infection was equally distributed among the cases despite known etiological diagnoses. It was slightly but not significantly greater in those classified as having mild to moderate mental retardation compared to severe cases. Only one of the mentally retarded students (0.2%) could be identified as having signs of congenital toxoplasmosis based on serological (IFA-IgG equal 1:256) and clinical findings (microcephaly, retinochoroiditis, and mental deficiency).

TABLE II

Age-specific seropositivity of *Toxoplasma gondii* infection in cases of mental retardation and controls (Belo Horizonte, MG, Brazil, 1985)

Age (years)	Percent with *T. gondii* infection[a] Cases (+/n)	%	Controls (+/n)	%
5 - 9	(36/ 69)	52.2	(25/ 88)	28.4
10 - 14	(123/217)	56.7	(44/179)	24.6
15 - 19	(69/122)	56.6	(42/112)	37.5
⩾ 20	(16/ 37)	43.2	(0)	–
Total	(244/445)	54.8	(111/379)	29.3

a: defined as IFA-IgG ⩾ 1:16

The crude and adjusted Relative Odds for selected risk factors for mental retardation are listed on Table III. Significant risks consisted of maternal age > 30 years, race (non-white), low socioeconomic status, and gender. Medical risks during pregnancy included maternal history of infection being misdiagnosed, threatened abortion, and hypertension. Absent or inadequate prenatal care represented a high health care risk. Mentally retarded children were more likely to have a history of labor and delivery exceeding 6 hr, prematurity, low birthweight, and birth outside of a hospital. According to maternal reports, they were more likely to have suffered from anoxia, jaundice and transitional neonatal problems related to respiratory distress, and to have had seizures and meningitis. A history of either maternal or paternal alcohol abuse and a family history of epilepsy were also risk variables.

Potential risk factors for congenital or acquired *T. gondii* infection are presented in Table IV. The mothers of mentally retarded children appeared to have an increased risk for factors related to maternal exposure such as the presence of cats in a household during the pregnancy, and higher exposure to soil or gardens. Mentally retarded children did not appear to be at increased risk from contact with

TABLE III

Health related risk factors for mental retardation among cases and controls. Crude and adjusted relative odds (RO) for *Toxoplasma gondii* infection (Belo Horizonte, MG, Brazil, 1985)

Risk factors[a]	Crude RO (95% CI)	Adjusted RO (95% CI)[b]
Prenatal		
Maternal age ⩾ 30 years	1.8 (1.3 - 2.4)	1.7 (1.3 - 2.4)
Race (non white)	5.1 (3.6 - 7.0)	4.8 (3.4 - 6.7)
Gender (male)	2.3 (1.7 - 3.1)	2.3 (1.7 - 3.1)
Low socioeconomic status[c]	20.1 (8.1 - 64.5)	18.1 (7.0 - 54.0)
Misdiagnosed infection during pregnancy	3.6 (1.9 - 6.7)	3.3 (1.8 - 6.5)
Threatened abortion[d]	3.1 (1.2 - 5.7)	3.1 (1.7 - 5.8)
Hypertension during pregnancy	1.5 (1.1 - 2.2)	1.4 (1.0 - 2.1)
Absent or inadequate prenatal care	2.7 (1.8 - 3.9)	2.0 (1.4 - 2.9)
Family history of epilepsy	3.0 (1.9 - 4.7)	2.5 (1.6 - 3.9)
Maternal smoking (⩾ 5 cigarettes/day)	0.7 (0.5 - 1.1)	0.7 (0.5 - 1.2)
Maternal alcohol abuse[e]	2.2 (1.2 - 4.3)	2.0 (1.2 - 4.0)
Paternal alcohol abuse[e]	2.6 (1.9 - 3.5)	2.5 (1.8 - 3.5)
Perinatal		
Duration of labor > 6 hours	2.5 (1.7 - 3.5)	2.8 (1.9 - 4.1)
Birth outside hospital	3.2 (2.0 - 4.9)	2.7 (1.7 - 4.2)
Low birthweight (< 2500g)	4.3 (2.7 - 6.9)	4.6 (2.7 - 7.6)
Short gestational interval	5.6 (2.1 - 18.0)	4.9 (1.8 - 15.0)
Asphyxia/hypoxia	10.6 (5.1 - 23.1)	10.7 (4.9 - 22.8)
Jaundice	5.7 (2.3 - 16.7)	7.0 (2.5 - 20.2)
Transitional neonatal problems[f]	4.4 (2.6 - 7.7)	5.4 (2.8 - 9.3)
Postnatal		
History of seizures	3.7 (2.6 - 5.3)	4.0 (2.7 - 5.8)
History of meningoencephalitis	4.6 (1.8 - 15.9)	4.2 (1.5 - 12.6)

a: according to timing of exposure.
b: adjusted RO by *T. gondii* infection (Weighted Mantel-Haenszel).
c: annual income per capita equal or less than US$ 400.00.
d: defined as the first or second trimester bleeding.
e: defined as at least two alcoholic "binges" per week.
f: related to respiratory distress or prolonged mechanical problems.

TABLE IV

Risk factors related to maternal and child exposure to *Toxoplasma gondii* Infection among cases and controls (Belo Horizonte, MG, 1985)

Characteristics[a]	Cases (n = 450)	%	Controls (n = 395)	%	Relative Odds (95% CI)
Maternal exposure during current pregnancy					
Cats in household	82	18.2	40	10.1	1.9 (1.2 - 2.9)
Contact with cats	60	14.7	34	9.8	1.5 (1.0 - 2.4)
Eating raw or uncooked meat	132	32.8	89	25.8	1.4 (1.0 - 2.0)
Drinking goat's milk	20	4.9	26	7.7	0.6 (0.3 - 1.7)
Contact with garden or soil	235	55.7	164	44.6	1.6 (1.2 - 2.1)
Child exposure					
Contact with cats in household	60	18.2	33	9.2	1.1 (0.8 - 1.6)
Eating raw or uncooked meat	120	27.9	98	25.6	1.1 (0.8 - 1.5)
Drinking goat's milk	13	2.9	8	2.0	1.4 (0.5 - 3.5)
Pica[b]	46	11.0	21	6.4	1.8 (1.0 - 3.2)

a: actual n may vary slight because of missing value.
b: defined as the habit of eating dirt.

TABLE V

Effect modification between *Toxoplasma gondii* and selected risk factors for mental retardation. Distribution of cases of mental retardation and controls within subgroups of socioeconomic status and toxoplasmosis infection (Belo Horizonte, MG, Brazil, 1985)

Socioeconomic status[a]	Toxoplasmosis infection[b]	Cases n	Controls n	Relative Odds
High	No	3	50	1.0[c]
High	Yes	2	16	2.1
Low	No	174	178	16.3
Low	Yes	208	76	45.6[d]

a: defined as high $>$ US$ 400.00 and low $\leqslant$ US$ 400.00 annual income per capita.
b: defined as IFA-IgG $\geqslant$ 1:16.
c: reference group.
d: risk model based in the joint effect of the two risk factors with an approximate X^2 test of significance
Additive risk model: expected Relative Odds = 17.4 (p = 0.00017)
Multiplicative risk model: expected Relative Odds = 34.2.(p = 0.76)

cats or ingestion of oocysts from dirt (pica).

According to the two approaches proposed to identify confounders, all variables of Table III and IV were examined as potential confounders. The Relative Odds of being mentally retarded for each variable was compared to the Relative Odds of mental retardation adjusted by *T. gondii* infection. For all variables the adjusted Relative Odds did not differ from the crude Relative Odds, and the Relative Odds of mental retardation given infection with *T. gondii* was 2.9 (95% CI 2.0-4.5) either in the bivariate or logistic regression analysis. The same variables above were analysed for effect modification. There was a significant positive interaction between infection and low socioeconomic status ($p < 0.001$) according to the additive risk model (Table V) and a negative interaction between toxoplasmosis and threatened abortion ($p = 0.0383$) according to the multiplicative risk model, confirmed by stratified and multiple logistic regression (Table VI, Table VII, respectively).

The ophthalmoscopic examinations showed significantly higher proportions of retinochoroiditis (4.9%) and optic nerve atrophy (6.2%) in mentally retarded cases than in controls (1.2 and 0.6% respectively). The Relative Odds were 4.3 (95% CI 1.0-40.3) and 11.2 (95% CI 1.7-474.1), respectively. Retinochoroiditis and optic nerve atrophy were only diagnosed in children with positive serology for *T. gondii* infection. A more detailed de-

TABLE VI

Effect modification between *Toxoplasma gondii* and selected risk factors for mental retardation. Distribution of cases of mental retardation and controls within subgroups of reported threatened abortion and toxoplasmosis infection (Belo Horizonte, MG, Brazil, 1985)

Threatened abortion[a]	Toxoplasmosis infection[b]	Cases n	Controls n	Relative Odds
No	No	161	225	1.0[c]
No	Yes	91	89	3.0
Yes	No	29	8	5.1
Yes	Yes	24	8	4.2[d]

a: defined as the first or second trimester bleeding.
b: defined as IFA-IgG $\geqslant$ 1:16.
c: reference group.
d: risk model based in the joint effect of the two risk factors with an approximate X^2 test of significance.
Additive risk model: expected Relative Odds = 7.1 (p = 0.3).
Multiplicative risk model: expected Relative Odds = 15.3 (p = 0.03).

TABLE VII

Effect modification between *Toxoplasma gondii* and selected risk factors for mental retardation. Multiple regression coefficients (standard errors) and relative odds (95% confidence interval) of mental retardation for toxoplasmosis infection (TOXO) and threatened abortion group (ABORT) (Belo Horizonte, MG, Brazil, 1985)

Factor	Mental Retardation Estimated coefficient (SE)	p value	Relative Odds (95% CI)
TOXO (yes)[a]	1.098 (0.1647)	0.0000	2.9 (2.2 - 4.1)
ABORT (yes)[b]	1.623 (0.4125)	0.0000	5.1 (2.3 - 11.4)
TOXO effect ABORT	-1.288 (0.5944)	0.0307	4.2 (1.9 - 9.6)

a: toxoplasmosis infection (IFA-IgG $\geqslant$ 1:16)
b: defined as first or second trimester bleeding

scription is published elsewhere (Figueiredo et al., 1989).

Assuming that the seroconversion rate of negative adult females is between 3 and 5% in the reproductive age years in Brazil (Frenkel, 1985; Papoz et al., 1986) and using this study crude Relative Odds (3.0) for toxoplasmosis, the population attributable risk or etiological fraction (Rothman, 1986) was estimated to range from 6.0 to 9.0%, suggesting the amount of mental retardation possibly associated with *T. gondii* infection.

DISCUSSION

The present study indicates that there is an important association between mental retardation and *T. gondii* infection with a threefold increased Odds of toxoplasmosis in mentally retarded students compared to controls. This association was not modified by selected variables which are considered risk factors for mental deficiency, but interacted negatively with threatened abortion and positively with low socioeconomic level.

Since the Instituto Pestalozzi was the public referral center for students with learning disabilities, and the control group was selected from a public school in which the main admission criteria was residence in the school neighborhood, the observed large difference in place of residence was consistent with the fact that approximately 60% of cases were referred from different schools located in several parts of the city of Belo Horizonte after approximately two years of regular education.

The findings of a larger proportion of males and students belonging to a lower socioeconomic status among cases are consistent with previous reports (Papoz et al., 1986). A considerable proportion of non-whites among the mentally retarded participants may be due to a relationship between skin color and socioeco-

nomic status, which has already been described in Brazil (Alvim, 1958). The majority of risk factors for mental deficiency related to the time of exposure are consistent with the literature regarding different risks at various stages of development (Smith & Simons, 1975; Hagberg et al., 1981; Kiely, 1987).

Several sources of potential bias exist. Psychological records were available for cases assuring an accurate classification for the cases. Although mentally retarded students could have been included in the control group, this misclassification, if present, would affect the risk in the opposite direction, lowering the estimates.

Recall bias is classically described in case-control studies, especially in the field of maternity outcome (Raphael, 1987; Coughin, 1987). In an attempt to reduce recall bias, several approaches were adopted during the design of the questionnaire, training of interviewers, and collection of data. Both the interviewer and respondent were masked to the research hypothesis and irrelevant exposures were included in the protocol to reduce the likelihood of hypothesis guessing by either interviewer or the respondent. The inclusion of the specific questions concerning the knowledge of disease and risk factors for infection revealed that almost 90% of the respondents had no prior information about toxoplasmosis. The majority (60%) of the mothers of cases were unawere of their child's mental retardation, suggesting that recall bias was less likely to happen. However, this finding raises concern about the quality of maternal history. During the analysis step, the differential of misclassification of exposure between cases and controls was similar despite the severity of mental retardation, suggesting again, that there was not an overestimation of exposure.

The ascertainment of exposure has already elicited a long discussion in the literature. According to some authors the only way to identify patients with congenital toxoplasmosis is to perform reliable antibody screening during pregnancy (Koskiniemi et al., 1989). However others have stated that reasonably applied serologic tests are usually diagnostic (Frenkel, 1990). They focused on children and regions where there is no evidence of infection from the environment. The IgG test is useful for general serologic diagnosis, especially in a high risk population and the IFA test is considered simpler and more readily available than the dye test, with titers in good qualitative agreement with those obtained in the reference test (Freij & Sever, 1991). The IFA-IgG seropositivity has assumed to be lifelong, and a positive test is generally interpreted that the person has acquired a *Toxoplasma* infection in the past. Furthermore, the risk for acquired infection before adolescence is expected to be lower than thereafter (Druten et al., 1990). Failure to demonstrate IgM antibodies using the IgM-IFA test can occur in sera from patients with the acute acquired infection due to an inhibitory effect of high titers of IgG antibodies to *Toxoplasma* in these sera. This situation has been found mostly in infected newborn, due to a high concentration of maternal IgG (Remington & Desmonts, 1990). Since in this study, 99.2% of all students had IgG-IFA titers less than 1:1024, which is considered low titers and suggestive of chronic infection, as discussed above, the likelihood of false-negative seems to be very low.

Although the certainty of diagnosis of congenital toxoplasmosis cannot be absolutely established by this study, there are several associations which suggest transplacental transmission. The encounter of potential risk factors for maternal *T. gondii* infection previously reported in the literature (Sturchler et al., 1987), could represent subsequent steps in the risk cycle of maternal infection with toxoplasmosis. The close contact with soil and gardens contaminated with feline feces due to the presence of cats during pregnancy could increase the likelihood of maternal infection. Furthermore, the lack of differences in characteristics related to acquired infection between cases and controls, including behavior, environmental and age exposure contributes to this hypothesis. The consistently higher age-specific *T. gondii* infection rates among cases versus controls with no aging trend, the presence of low IgG titer (Frenckel, 1986) and no detection of recently acquired infection preceding the date of testing evaluated by IgM tests suggests chronic infection. The higher proportion of mothers of cases reporting misdiagnosed infections during pregnancy and the consistent findings of retinochoroiditis and optic nerve atrophy only in subjects with *T. gondii* infection and more often in mentally retarded students additionally leads support to this hypothesis.

The argument that mental retardation itself may be a risk factor for acquiring toxoplas-

mosis seems less probable in this study due to an absence of association between *T. gondii* infection and all variables constructed for the acquired model.

No confounding factors were identified in this study. The results of both bivariate and multivariate analysis did not show a change in the risk of *T. gondii* infection between different ethnic or socioeconomic groups. Residual confounding related to the use of broad categories in the income level, increasing the danger that confounding could take place within categories (Greenland, 1989) seemed have not occurred since the risk ratio was the same when considering even five strata in the income level.

The consequence of threatened abortion super-imposed upon *T. gondii* infection shows a probable negative interaction (Lilienfeld & Lilienfeld, 1980; Rothman, 1986) resulting in a decrease in the expected risk of mental deficiency, among those who were exposed to both characteristics. Biologically, this may be suggestive of an effect of a selective survival: a large proportion of infected fetuses may have been aborted, resulting in the lack of association between the infection and mental retardation in the stratum reporting threatened abortion during pregnancy.

In view of these considerations, the present investigation provides a plausible argument for an association of transplacental *T. gondii* infection in the development of mental retardation. It also suggests that children from a high risk population, identified in this investigation as children from lower socioeconomic status, given transplacental *T. gondii* infection, would more likely present with subclinical congenital toxoplasmosis, resulting in learning disabilities by school age.

The importance of the proposed model can be appraised by the attributable risk estimated from the data. This may also be helpful in explaining in part, the proportion of mental deficiency presently considered as having an unexplained cause.

The control of toxoplasmosis through prevention has been discussed in the recent literature (McCabe & Remington, 1988). There is a need to predict the effects of the infection, particularly in countries where the incidence or prevalence are high and the risk factors for mental deficiency are intertwined. The study suggests that the control of toxoplasmosis may reduce the incidence or the severity of mental retardation, and future prospective studies may confirm this findings.

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