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Risk Factors for *Toxoplasma gondii* Infection in Pregnancy

Results of a Prospective Case-Control Study in Norway

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From 1992 to 1994, a prospective case-control study designed to identify preventable risk factors for *Toxoplasma gondii* infection in pregnancy was conducted in Norway. Case-patients were identified through a serologic screening program encompassing 37,000 pregnant women and through sporadic antenatal testing for *Toxoplasma* infection. A total of 63 pregnant women with serologic evidence of recent primary *T. gondii* infection and 128 seronegative control women matched by age, stage of pregnancy, expected date of delivery, and geographic area were enrolled. The following factors were found to be independently associated with an increased risk of maternal infection in conditional logistic regression analysis (in order of decreasing attributable fractions): 1) eating raw or undercooked minced meat products (odds ratio (OR) = 4.1, $p = 0.007$); 2) eating unwashed raw vegetables or fruits (OR = 2.4, $p = 0.03$); 3) eating raw or undercooked mutton (OR = 11.4, $p = 0.005$); 4) eating raw or undercooked pork (OR = 3.4, $p = 0.03$); 5) cleaning the cat litter box (OR = 5.5, $p = 0.02$); and 6) washing the kitchen knives infrequently after preparation of raw meat, prior to handling another food item (OR = 7.3, $p = 0.04$). In univariate analysis, travelling to countries outside of Scandinavia was identified as a significant risk factor, but this variable was not independently associated with infection after data were controlled for factors more directly related to the modes of infection. *Am J Epidemiol* 1996;144: 405–12.

case-control studies; pregnancy; risk factors; *Toxoplasma;* toxoplasmosis

The two primary ways in which humans acquire toxoplasmosis are consumption of raw or undercooked meat containing tissue cysts of *Toxoplasma gondii* and contact with cats (*Toxoplasma*'s definite host), which shed oocysts in their feces during acute infection (1–3). In addition, a number of risk factors that are indirectly related to contact with cat feces and raw meat are currently mentioned in the literature. Such factors include handling raw meat, even without consuming it; exposure to soil or sand contaminated with cat feces (e.g., during gardening); and eating unwashed raw vegetables or unpeeled fruits (1–3). Although these mechanisms are biologically plausible, epidemiologic and parasitologic evidence supporting the importance of these factors is sparse.

More information is also needed to clarify the significance of cultural habits and behavioral risk factors such as personal hygiene, kitchen hygiene, food handling practices, cooking preferences, and cat contact patterns. A better understanding of the relative importance of various risk factors is essential to the development of a specific control strategy.

Health education on avoidance of maternal infection is an important aspect of any program for prevention of congenital toxoplasmosis, although the efficiency of antenatal education in modifying the behavior of pregnant women needs further evaluation (4–9). In the absence of information on the relative contributions of the various risk factors, women are usually advised to avoid all potential sources of infection. Such broad-based advice reduces the likelihood of compliance and limits the efficiency of health education.

In Norway, the seroprevalence of *T. gondii* infection among women of childbearing age is low in comparison with that in many other European countries. Consequently, the percentage of women at risk of acquiring the infection during gestation is high. In 1992, a case-control study designed to identify risk factors for

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Abbreviation: OR, odds ratio.

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Toxoplasma infection in pregnancy was launched in Norway. The study was an integral part of a research program that assessed the costs and benefits of serologic screening for detection and treatment of acute *Toxoplasma* infection in pregnant women (10). The purposes of the study were to 1) identify potentially preventable risk factors most likely to have the greatest impact on the incidence of *Toxoplasma* infection in pregnancy, 2) determine the relative importance of these risk factors, and 3) provide a scientific basis for a specific control and prevention strategy, in terms of adequate health education and measures needed to reduce the levels of *Toxoplasma* in food and animals.

MATERIALS AND METHODS

Serologic screening program

During the period June 1992–June 1994, a serologic screening program was conducted in 11 of Norway's 19 counties—an area with a combined population (1993 census) of 2,537,500, or 59 percent of Norway's population (11). All pregnant women inhabiting the study area were examined for antibodies to *T. gondii* at their first prenatal care visit, in approximately the 10th week of their pregnancy. In all, 11.0 percent of the pregnant women were seropositive. Seronegative women were retested at about weeks 22 and 38 of pregnancy. If any of the samples showed evidence of recent infection, a follow-up sample was collected as soon as possible to confirm the diagnosis. All serologic investigations were carried out at the National Institute of Public Health (Oslo, Norway). Details concerning the sampling protocol and the serologic methods employed are presented elsewhere (P. A. Jenum et al., National Institute of Public Health, unpublished manuscript). A total of 37,000 women participated in the screening program. At their first prenatal care visit, all participants received an information folder containing a general description of the project and advice on specific precautions to take to prevent *Toxoplasma* infection.

Definition and identification of cases

We defined a case as a pregnant woman with serologic evidence of recent primary *Toxoplasma* infection according to one of the following criteria: 1) seroconversion during pregnancy (Platelia Toxo immunoglobulin G; Sanofi Diagnostics Pasteur, Marnes la Coquette, France) or 2) a dye-test value greater than 300 IU/ml in addition to the presence of specific immunoglobulin M measured by enzyme immunoassay (Platelia Toxo immunoglobulin M; Sanofi Diagnostics Pasteur) in the first serum sample tested (12). Forty-seven case-patients were identified through the screening program (incidence = 0.18 percent of susceptible pregnancies). During the same time period, an additional 22 cases were identified among women not included in the program, on the basis of sporadic antenatal testing for primary maternal *Toxoplasma* infection throughout the country. All cases were verified by the *Toxoplasma* Reference Laboratory at the National Institute of Public Health. Whenever a case was identified, a letter was mailed to the patient's health care unit to request written informed consent from the patient for participation in the study.

Definition and identification of controls

Once enrolled, each case was matched with two control women selected from participants in the screening program. Criteria for selection of a control were that she be 1) a pregnant woman who was seronegative for *Toxoplasma* (tested within 2 weeks of the case) and 2) matched with the case on age (±2 years), stage of pregnancy (±2 weeks), expected date of delivery (±2 weeks), and geographic area (resident of the same or a neighboring municipality). Informed consent was obtained through the woman's health care unit. If a person declined to be interviewed, additional controls were identified and contacted until at least two agreed to participate.

Interviews

Whenever a case or control consented to participate in the study, she was mailed a structured questionnaire along with a standard letter in which she was encouraged to answer all of the questions. About 1 week later, she was telephoned by a trained interviewer who went over the answers to the questionnaire on the telephone or made an appointment to do so on a later date. With few exceptions, each case and her matched controls were interviewed by the same person. The interviewers were not blinded to the case/control status of the study subjects. Cases were interviewed about exposures during the 4-month period before the first sample indicating recent infection had been collected; the median interval between the date of sampling and the date of interview was 68 days (range, 5–242). Controls were queried about the same time period as that of the case to whom they were matched; a median of 97 days elapsed between the date of sampling and the control interview (range, 24–455 days). The interviewers were periodically monitored to ensure that the questionnaire text was being followed.

The questionnaire covered personal and demographic data and exposures to potential risk factors, including travel abroad or within Norway; contact with cats or cat feces; eating raw or undercooked meat

in Norway or abroad; eating outside of the home; eating unwashed raw vegetables, unpeeled fruits, or berries; drinking untreated water; and kitchen hygiene, food handling practices, and cooking preferences. Exposure frequencies were recorded for each risk factor variable (e.g., number of days or times exposed or number of meals consumed). Precise information on drinking water quality was obtained from local food control authorities.

Statistical analyses

All risk factor variables were analyzed in dichotomous as well as continuous format; ordinal scaling was used when appropriate. Univariate analysis of dichotomous and ordinal variables was performed using the procedure for matched data sets in the Epi Info computer program (Epi 5.01a; Centers for Disease Control and Prevention, Atlanta, Georgia). Conditional logistic regression was implemented for univariate analysis of continuous variables and for multivariate analysis using the EGRET program (version 0.26.04; Statistics and Epidemiology Research Corporation, Seattle, Washington). Variables were included in the multivariate analysis if they had a p value of 0.25 or less in the univariate analysis, were potential confounders, or were of theoretical interest regardless of statistical significance. The results are reported as matched odds ratios with 95 percent confidence intervals and two-tailed p values. Adjusted estimates of population attributable fractions based on the logistic regression model were calculated as suggested by Coughlin et al. (13), using the multivariable adjustment procedure for matched data provided by Bruzzi et al. (14).

Some variables that were statistically significant in univariate analysis were not entered into the multivariate model because the number of persons exposed was too low for evaluation. Such variables were aggregated into broader categories in the final analysis. For example, consumption of tartar and undercooked hamburgers and tasting of raw minced meat during food preparation were first analyzed individually. They were then combined, along with other items referring to raw or undercooked minced meat, into an aggregate variable. An analogous approach was followed for other food categories and exposures.

RESULTS

Enrollees

Of 47 eligible case-patients identified through the serologic screening program, 43 (91 percent) consented to participate in the study. In addition, 20 (91 percent) of 22 case-patients diagnosed among women not included in the program were enrolled. Two matched controls were enrolled for each case-patient, except for seven cases who were matched with three controls and five cases for whom only one eligible control could be found. Consequently, 63 cases and 128 controls were included in the final data set. The median age of the case-patients was 28 years (range, 18–41 years). Forty-one of the cases (65 percent) showed evidence of recent *Toxoplasma* infection in the first serum sample collected, while the remaining 22 cases (35 percent) seroconverted during pregnancy (three seroconverted in the first trimester, six in the second, and 13 in the third).

Contact with cats or cat feces

Neither daily contact with cats nor living in a neighborhood with cats was identified as a risk factor for *Toxoplasma* infection (table 1). However, cases were more likely than their matched controls to report daily contact with a kitten less than 1 year of age (odds ratio (OR) = 3.6, $p = 0.04$). Cases and controls did not differ in terms of their ownership of indoor cats or cats that caught mice or birds. Feeding a cat raw meat scraps was identified as a strong risk factor (OR = 9.3, $p = 0.04$), but only five cases and two controls reported this practice. Having a cat with diarrhea was associated with an increased risk of infection, but the relation was not statistically significant (OR = 3.9, $p = 0.11$). Living in a household with a cat that used a litter box was strongly associated with infection (OR = 6.7, $p = 0.003$). Cleaning the cat litter box was also associated with increased risk (OR = 5.9, $p = 0.007$). However, since almost everyone who had a cat litter box also cleaned it, we were unable to determine whether these factors were independently related to infection. More cases than controls reported other contacts with cat feces (OR = 2.4, $p = 0.08$). The respondents were asked to specify how frequently they washed their hands after petting the cat and after having contact with the litter box or cat feces. No association with *Toxoplasma* infection was detected. It is notable, however, that all but two respondents said they always washed their hands after having contact with the litter box or cat feces.

Cooking preferences and meat consumption

Cases were more likely than controls to report a general preference for beef to be prepared raw or rare (OR = 3.5, $p = 0.03$). The numbers of persons who preferred undercooked mutton, pork, or minced meat products were too low to permit meaningful analysis. When respondents were asked whether they had actually eaten undercooked meat during the relevant

TABLE 1. Univariate analysis of selected risk factors for *Toxoplasma* infection during pregnancy, Norway, 1992–1994

Risk factor	Cases		Controls		Matched odds ratio	95% confidence interval	*p* value
	No. exposed	Total no. of respondents*	No. exposed	Total no. of respondents*			
Contact with cats or cat feces							
Living in a neighborhood with a cat	44	57	89	116	0.9	0.4–1.9	0.71
Living in a household with a cat	16	63	22	128	1.9	0.8–4.5	0.13
Living in a household with a kitten (<1 year of age)	8	63	5	128	3.6	1.1–12.2	0.04
Living in a household with a cat which:							
Was kept indoors	5	63	6	128	1.6	0.5–5.4	0.43
Caught mice or birds	10	62	13	125	1.6	0.6–4.0	0.31
Was fed raw meat scraps	5	63	2	128	9.3	1.1–82.0	0.04
Had diarrhea	6	60	5	120	3.9	0.8–20.0	0.11
Used a cat litter box	14	63	9	128	6.7	1.9–24.3	0.003
Cleaning the cat litter box	12	63	7	128	5.9	1.6–21.3	0.007
Other contacts with cat feces	10	58	8	120	2.4	0.9–6.3	0.08
Washing hands infrequently† after:							
Petting the cat	26	62	45	128	1.3	0.7–2.4	0.42
Having contact with the litter box or cat feces	1	62	1	127	1.4	0.08–23.6	0.81
Cooking preferences and meat consumption							
Preferring beef raw or rare	9	62	8	128	3.5	1.1–10.7	0.03
Eating raw or undercooked beef	45	62	80	128	1.7	0.8–3.5	0.14
Eating raw or undercooked mutton	15	62	10	128	7.1	2.0–25.7	0.003
Eating raw or undercooked pork	16	63	10	128	4.7	1.8–12.3	0.001
Eating raw or undercooked minced meat	24	63	22	128	3.2	1.5–6.6	0.002
Eating raw or undercooked poultry	9	61	2	126	8.9	1.9–41.5	0.005
Tasting raw meat while preparing food	25	61	17	126	5.6	2.4–13.1	<0.001
Eating meat at a barbecue	36	63	72	127	1.1	0.4–2.6	0.88
Eating meat prepared in a microwave oven	5	63	5	127	2.0	0.6–6.9	0.27
Eating tartar	10	63	6	127	4.6	1.4–15.1	0.01
Eating roast beef	26	62	66	127	0.7	0.4–1.2	0.19
Eating "gravet" meat‡	4	62	1	126	8.0	0.9–71.6	0.06
Frequency of meat consumption§	18	63	28	128	1.5	0.7–3.0	0.30
Kitchen hygiene and food handling practices							
Washing hands/kitchen utensils infrequently‖							
Hands	7	62	5	127	3.0	0.9–10.4	0.09
Knives	8	62	4	127	4.6	1.2–17.6	0.03
Cutting boards, chopping blocks	7	62	4	127	4.0	1.0–15.6	0.05
Countertops	7	62	4	127	3.7	0.9–14.6	0.06
Eating unwashed vegetables/fruits/berries							
Raw vegetables	16	63	9	128	5.7	2.0–15.7	<0.001
Unpeeled fruits	28	63	33	128	2.4	1.2–4.8	0.01
Raw vegetables or unpeeled fruits	30	63	38	128	2.3	1.2–4.5	0.02
Berries	26	63	44	127	1.6	0.7–3.4	0.23
Miscellaneous factors							
Travelling within Scandinavia	3	63	13	128	0.4	0.1–1.4	0.14
Travelling outside of Scandinavia	23	63	25	128	2.6	1.2–5.3	0.01
Eating outside of the home¶	55	62	120	128	0.4	0.1–1.4	0.18
Contact with soil (gardening, farming)	27	61	58	126	0.9	0.4–1.9	0.83
Playing with children in a sandbox	13	58	54	127	0.5	0.2–0.9	0.03
Drinking water from a private well	1	63	11	128	0.1	0.02–1.1	0.07
Drinking untreated surface water	30	58	78	114	0.5	0.2–1.0	0.04
Educational level#	29	62	42	127	1.8	0.9–3.6	0.08
Eating raw eggs	16	60	24	125	1.8	0.8–3.9	0.17
Drinking unpasteurized milk	3	63	10	127	0.6	0.2–2.5	0.52
Having previous children	28	63	65	123	0.7	0.4–1.3	0.28

* Excludes missing values.
† Always or usually versus less frequently.
‡ A Scandinavian delicacy made of spiced raw meat.
§ Several times per week versus less frequently.
‖ Washing hands/utensils never or rarely after contact with raw meat, prior to handling another food item.
¶ Eating at hotels, restaurants, hamburger bars, hot-dog stands, canteens, etc.
# ≥3 years after high school versus less.

4-month period, more cases than controls reported consuming raw or undercooked mutton, pork, poultry, or minced meat. These exposures were all associated with a significantly increased risk of *Toxoplasma* infection in univariate analysis (table 1). However, undercooked poultry was not an independent risk factor after the effect attributable to the other meat items was controlled for by logistic regression. Ingestion of raw or undercooked beef was not significantly associated with infection (OR = 1.7, $p = 0.14$), even when exposure frequency (number of meals eaten) was considered. Of the 50 cases who had eaten undercooked meat, 25 had tasted or nibbled raw meat while preparing food (OR = 5.6, $p < 0.001$).

In contrast to the case in many other European countries, more than 95 percent of the meat products sold at retail outlets in Norway are domestically produced (15). In this study, persons who had eaten raw or undercooked mutton, pork, poultry, or minced meat purchased in Norway were at significantly increased risk of infection (data not shown). Except for beef, few respondents reported having eaten undercooked meat in foreign countries. Although an elevated odds ratio was noted for several meat items consumed abroad, statistical significance was not achieved.

Eating meat at a barbecue was not associated with increased risk of infection, regardless of the type of meat or number of meals consumed (table 1). Likewise, eating meat prepared in a microwave oven was not identified as a risk factor. A significant difference between cases and controls was detected for consumption of tartar, but not for roast beef. Eating "gravet" meat, a Scandinavian delicacy made of spiced raw meat, was marginally associated with infection. Frequency of meat consumption was not found to be associated with *Toxoplasma* infection.

Kitchen hygiene and food handling practices

More cases than controls reported that they never or seldom washed their hands or kitchen utensils after preparation of raw meat prior to handling another food item. Washing kitchen knives infrequently was significantly associated with an increased risk of infection (OR = 4.6, $p = 0.03$). Although they were not statistically significant, increased odds ratios were also detected for infrequent cleaning of hands, cutting boards, and countertops (table 1). Cases and matched controls did not differ significantly with regard to consumption of raw vegetables, unpeeled fruits, strawberries, or other berries, whether in Norway or abroad (data not shown). However, the cases were more likely to report ingestion of raw vegetables or fruits that had not been washed (OR = 2.3, $p = 0.02$). Eating strawberries or other types of berries unwashed was not associated with infection (table 1).

Miscellaneous factors

Persons who had been travelling abroad outside of Scandinavia were at increased risk of infection, while travellers within Scandinavia were not (table 1). Eating outside of the home, whether in Norway or abroad, was not identified as a risk factor even when the number of meals consumed was taken into account. Persons who had visited a hamburger bar, fast-food restaurant, or hot-dog stand were not at increased risk. Contact with soil (e.g., through gardening or farming) was not associated with infection (OR = 0.9, $p = 0.83$). However, all but three respondents always washed their hands after such activities, or used gloves. Playing with children in a sandbox was associated with a decreased risk of infection (OR = 0.5, $p = 0.03$). Drinking water from a private well or drinking untreated surface water was also protective. Educational level (having at least 3 years of education after high school) was marginally associated with infection (OR = 1.8, $p = 0.08$). Cases and controls did not differ with regard to any of the following factors: eating raw eggs, drinking unpasteurized milk, living on a farm, having contact with sheep, having previous children, or travelling within Norway.

Stratified analyses

The serologic screening program showed that the incidence of *Toxoplasma* infection during pregnancy was substantially higher among residents of Oslo City, the most urbanized area in Norway, than in the remaining study areas (P. A. Jenum et al., National Institute of Public Health, unpublished manuscript). To ascertain whether the individual risk estimates varied geographically, we performed a stratified analysis of all factors that were significant in the univariate analysis. No significant differences in odds ratios were detected between Oslo and the remainder of the study area. However, the stratification led to considerable loss of precision of risk estimates, and thus limited our ability to detect relevant differences. It is notable that among our study enrollees, those residing in Oslo were more likely than residents of other areas to report consumption of undercooked meat (68/85 vs. 67/105, $p = 0.01$) and foreign travel (29/85 vs. 19/106, $p = 0.01$).

The seroconvertants and their matched controls, unlike the remaining enrollees, received specific information on putative *Toxoplasma* risk factors prior to the 4-month period on which they were interviewed, and thus had had the opportunity to modify their behavior accordingly. In a stratified analysis, the seroconvertants and their controls were less likely than the remaining study subjects to report foreign travel (11/69 vs. 37/121, $p = 0.03$); no differences were detected for exposure to other risk factors.

Logistic regression model

The following variables were found to be independently associated with an increased risk of *Toxoplasma* infection in conditional logistic regression analysis (in order of decreasing attributable fractions) (table 2): 1) eating raw or undercooked minced meat products (OR = 4.1, $p = 0.007$); 2) eating unwashed raw vegetables or fruits (OR = 2.4, $p = 0.03$); 3) eat-

TABLE 2. Multivariate analysis of risk factors for *Toxoplasma* infection during pregnancy, Norway, 1992–1994*

Risk factor	Cases		Controls		Matched odds ratio	95% confidence interval	*p* value	Attributable fraction
	No. exposed	Total no. of respondents†	No. exposed	Total no. of respondents†				
Eating raw or undercooked minced meat	24	63	22	128	4.1	1.5–11.2	0.007	0.288
Eating unwashed raw vegetables or fruits	30	63	38	128	2.4	1.1–5.6	0.03	0.278
Eating raw or undercooked mutton	15	62	10	128	11.4	2.1–63.1	0.005	0.221
Eating raw or undercooked pork	16	63	10	128	3.4	1.1–10.4	0.03	0.179
Cleaning the cat litter box	12	63	7	128	5.5	1.3–22.7	0.02	0.155
Washing the kitchen knives infrequently‡	8	62	4	127	7.3	1.1–50.2	0.04	0.111

* Conditional logistic regression analysis.
† Excludes missing values.
‡ Washing the kitchen knives never or rarely after contact with raw meat, prior to handling another food item.

ing raw or undercooked mutton (OR = 11.4, p = 0.005); 4) eating raw or undercooked pork (OR = 3.4, p = 0.03); 5) cleaning the cat litter box (OR = 5.5, p = 0.02); and 6) washing kitchen knives infrequently after preparation of raw meat, prior to handling other food items (OR = 7.3, p = 0.04). No significant interactions were detected among the variables included in the analysis.

DISCUSSION

To our knowledge, this study is the first published investigation to have determined specific risk factors for *Toxoplasma* infection during pregnancy using a case-control design. The epidemiologic approach employed permitted identification of several biologically plausible risk factors and allowed assessment of their relative importance. In addition to the more commonly recognized means of transmission—having contact with cat feces and eating undercooked meat—the findings of this study support the possibility of transmission through contaminated unwashed kitchen utensils and unwashed vegetables and fruits. Therefore, the results appear to both support and extend current recommendations for prevention of congenital toxoplasmosis. The information gained from the multivariate analysis and the attributable risk estimates may contribute to the planning of control and prevention efforts to reduce maternal infection, including health education campaigns. However, since perception and avoidance of risk factors are based on subjective assessments, practical and psychological considerations should also be taken into account when formulating prevention messages.

The present results were obtained in a country with a cold climate and a comparatively low prevalence of toxoplasmosis. The pattern of risk factors and their relative importance are likely to vary appreciably across national boundaries in accordance with cultural patterns and climatic factors affecting the survival of oocysts.

Consumption of raw or undercooked meat

The findings of the present study complement the results of veterinary investigations of the seroprevalence of *Toxoplasma* infection among meat-producing animals in Norway. A recent serologic survey found the highest prevalence of *Toxoplasma*-specific antibodies in sheep (18.0 percent), followed by cattle (5.1 percent) and pigs (2.5 percent) (E. Skjerve et al., Norwegian College of Veterinary Medicine, unpublished manuscript). In our study, consumption of undercooked mutton and pork was found to be associated with an increased risk of infection, whereas ingestion of undercooked beef was not. This apparent discrepancy may be explained by the fact that cattle are less likely than sheep or pigs to develop long-term latent infection with tissue cysts after the acute phase of infection (2, 16). With few exceptions, attempts to isolate the parasite from cattle have been unsuccessful, although a high prevalence of antibodies has been reported in several countries (2). Interestingly, consumption of raw or undercooked minced meat, which usually contains beef, pork, or both, was identified as an independent risk factor in this study. Since the mincing process provides ample opportunity for cross-contamination between beef and pork, our results do not warrant the conclusion that undercooked beef is completely safe. Pregnant women should be advised not to eat raw or undercooked meat regardless of type. Attempts to make a distinction between beef and pork or mutton will only complicate the recommendations and reduce their efficiency.

Kitchen hygiene and food handling practices

Our study revealed that 25 of 50 patients who reported consuming undercooked meat had tasted raw meat while preparing food. A majority had nibbled raw minced meat, a factor contributing to the comparatively high attributable fraction associated with minced meat consumption. Therefore, pregnant

women in Norway should be advised not only to cook their meat thoroughly but also to refrain from tasting raw meat during food preparation. Because patients were more likely to report kitchen hygiene practices that might facilitate cross-contamination of *Toxoplasma* to other food items, increased attention to the proper handling of raw meat, including the use of soap and water to clean hands and utensils afterward, would also be a useful prevention measure.

Consumption of unwashed vegetables and fruits

Our study's results strengthen the evidence that *Toxoplasma* infection may result from consumption of unwashed raw vegetables and fruits, and indicate that this is a major factor contributing to maternal infection in Norway. Even though the percentage of vegetables and fruits contaminated with *Toxoplasma* may be small, the frequency with which these foods are consumed may result in appreciable exposure. This argument applies to undercooked meat as well.

Contact with cats or cat feces

Cats bury their feces in soil or sand, where the oocysts sporulate and remain infectious for periods ranging from several months to more than a year (1). The buoyancy of the oocyst allows it to float to the top layer of the soil after rain (3). Any food items or other objects which come into contact with soil may potentially become contaminated with the parasite in its infectious stage (6, 8, 9).

Pregnant women are commonly advised to refrain from gardening or to wear gloves when so engaged (1, 9, 17). The apparent lack of association between *Toxoplasma* infection and soil contact in this study may be explained by the fact that almost all of our study subjects had used gloves or washed their hands after such exposures.

It has been debated whether pet cats should be banished from the household for the duration of pregnancy (3, 18). Our study reinforces the suggestion that living in a household with a cat, per se, is not an important risk factor for *Toxoplasma* infection. On the other hand, cleaning the cat litter box and having other contacts with cat feces were associated with increased risk. The results indicate that washing one's hands after such exposures may not be sufficient to prevent infection, since almost all of our study enrollees did so. Pregnant women should therefore be persuaded to avoid contact with cat feces altogether, and to arrange for another member of the household to clean the cat litter box. We were not able to determine whether the mere presence of a litter box in the household was independently associated with increased risk of infection. However, the finding that hand-washing was not effective in preventing infection indicates that the cat litter box might serve as a potent source of infection irrespective of who cleans it, possibly through dissemination of oocysts in the home environment. Further investigation is needed to clarify this point.

Travelling abroad and eating outside of the home

It would appear that several of our patients acquired *Toxoplasma* infection while travelling abroad in countries with a higher seroprevalence than is seen in Scandinavia. However, although travelling outside of Scandinavia was identified as an appreciable risk factor in univariate analysis, this factor was not independently associated with infection after we controlled for factors more directly related to modes of infection. This implies that the risk associated with foreign travel can be explained by the factors included in the regression model or by unidentified factors correlated with them (table 2). Nevertheless, Norwegian women should be advised not to travel outside of Scandinavia when pregnant, since preventive measures to avoid *Toxoplasma* infection may be difficult to apply conscientiously abroad. Although attempts to avoid undercooked meat and unwashed raw vegetables and fruits would reduce the risk of infection, most meals taken while travelling are usually eaten in hotels or restaurants, where the traveller has no influence on kitchen hygiene and food handling practices.

Limitations of this study

Although relations between *Toxoplasma* infection and the risk factors identified in this study are highly plausible, some caution is needed in interpreting these results. The majority of our study subjects were identified through a screening program that encompassed all pregnant women within a geographically defined study area; this approach ensures that all true cases have an equal probability of being enrolled. However, the inclusion of sporadic cases already tested may have introduced selection bias, because the factors that influence the decision to be tested may often be associated with the exposures of concern, leading to overestimation of odds ratios (19, 20). The serologic screening program led to considerable publicity about toxoplasmosis and its risk factors, even in counties not covered by the program. Moreover, most cases and controls were aware of the study hypotheses by the time of the interview, since they had received an information brochure about special precautions to take against *Toxoplasma* prior to entering the screening program. The 22 seroconvertants and their controls, unlike the remaining enrollees, received this informa-

tion prior to the time period covered by the interview. Although the present study does not justify conclusions regarding the effectiveness of health education in modifying the behavior of the study subjects, the pattern of risk factors identified, as well as their relative importance, may differ in a situation where no information is provided beforehand. Furthermore, it is conceivable that the cases were more likely than controls to remember their own exposures, since they were sensitized to their recall of suspected risk factors (19, 20). While it seems unlikely that subjects would falsely report an exposure that did not occur, differential recall of actual exposures may have introduced a bias resulting in spuriously high odds ratios (21).

An additional type of bias may have been introduced by the fact that the interviewers were aware of the case/control status of the enrollees. It is interesting to note, however, that ingestion of undercooked mutton and pork was associated with increased risk, while eating undercooked beef was not. Neither the study subjects nor the interviewers knew that beef is less likely than other types of meat to harbor *Toxoplasma*. Likewise, the possibility of transmission through unwashed kitchen utensils was not disclosed. On the other hand, contact with soil or sand and handwashing practices were not found to be associated with infection, even though these potential risk factors were explicitly mentioned in the information brochure. These observations support the reliability of our results.

Conclusion

The consequences of congenital toxoplasmosis may be severe (3, 22). These consequences make toxoplasmosis a public health problem of greater magnitude than the actual number of cases would suggest. Our findings indicate that modification of kitchen hygiene, food handling practices, cat contact patterns, and travel habits during gestation offer the potential for substantial reduction of the burden of congenital toxoplasmosis in Norway. Such measures would help to prevent not only toxoplasmosis but also a range of other infections (17).

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