Domestic Pets as Risk Factors for Alveolar Hydatid Disease in Austria

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To identify the risk of pet ownership (i.e., cats and dogs) for alveolar echinococcosis caused by Echinococcus multilocularis, the habits and activities of 21 patients (histologic confirmation or positive serology with corresponding evidence on an ultrasonogram, radiograph, or computed tomography scan) in Austria during the period 1967–1997 were compared with the habits and activities of 84 controls matched by sex, age, and residence. Cat ownership (odds ratio (OR) = 6.47, 95% confidence interval (CI) 1.54–27.29) and hunting (OR = 7.83, 95% CI 1.16–52.77) were independent risk factors associated with alveolar hydatid disease. The study is not in agreement with the hypothesis that eating mushrooms or certain wild berries which grow near the ground are the main risk factors for acquiring this disease. No other behavior patterns or activities studied were identified as risk factors. Am J Epidemiol 1998;147:978–81.

cats; dogs; echinococcosis, hepatic; Echinococcus multilocularis; risk factors

Alveolar echinococcosis is a serious illness with characteristics which resemble cancer and has a similarly high case fatality rate. It is caused by metacestodes of Echinococcus multilocularis. The adult tapeworm usually lives in the intestine of wild canines, predominantly foxes, and the usual intermediate hosts are rodents, i.e., Microtus, Arvicola, and others. Humans become infected as accidental intermediate hosts by ingesting eggs of the parasite passed in the feces of the definitive hosts (1). Alveolar echinococcosis is distributed throughout large parts of the Holarctic (Europe, northern Asia, North America) and is endemic in the mountainous regions of Tyrol and Vorarlberg, Austria, where some 153 cases have been diagnosed since the disease was first recognized in 1892 by Adolf Posselt (3). The majority of Austrian cases have been diagnosed in individuals originating from these two western provinces with a population of approximately 1 million inhabitants (2). The main organ affected is the liver. Lesions may involve a great part of the liver before patients seek help (4). Resection is not possible in up to 80 percent of patients—only complete resection has been shown to cure the disease (5, 6). The prognosis is grave because of the potential for metastases (in approximately 20 percent of patients) and invasion of vital structures such as the inferior vena cava or common bile duct (7). Foxes (Vulpes vulpes) are thought to be the major final host in Austria. Carrier rates in the Tyrol and Vorarlberg regions vary between 2.4 and 34 percent (8). In neighboring southwestern parts of Germany, a prevalence rate of 36 percent in foxes has been found (9).

The only previous case-control study of this condition was conducted in Alaska and found that domestic dogs were an important risk factor for the disease (10). We designed our study to examine the specific hypothesis that domestic cats and dogs are risk factors for the transmission of the disease in Austria. All other hypothesized risk factors were examined in the study as potential confounding variables.

MATERIALS AND METHODS

Patients were residents in the Tyrol and Vorarlberg regions of Austria who had been diagnosed in the years since 1967 as suffering from alveolar echinococcosis. In order to be eligible, each patient had to have either histologic confirmation or positive serology with corresponding evidence on an ultrasonogram, radiograph, or computed tomography scan. Cases were ascertained from a list held by the Department of Medical Parasitology at the Institute of Hygiene, University of Vienna. Although it is not mandatory to report alveolar echinococcosis in Austria, the Department of Parasitology of the Institute of Hygiene acts as
a reference laboratory and receives samples from most suspected and verified cases in Austria.

Controls were selected from the lists of residents, the so-called 'Melderegister,' of the home village of the patient. In Austria, registration with the local authority is mandatory. Four controls were selected for each case; these were individuals of the same sex and with the nearest dates of birth to that of the patient. The home village was defined as the village where the patient resided for the 20 years preceding diagnosis. For those patients who lived in more than one village during the 20 years, two controls were selected from each village in which the patient had resided.

All patients and controls were interviewed by the same person using a structured questionnaire to minimize interviewer bias since blinding to case/control status was not possible. If the patient died, a person who had been living with him/her was interviewed and a similar surrogate respondent was interviewed for the matching controls. Potential risk factors, such as frequent consumption of wild berries, hunting in the forest, and pet ownership, were recorded as well as potential confounding variables, such as years of schooling.

Controls were asked about the period of time appropriate to their matched case, i.e., the 20 years prior to diagnosis. For food items, questions were asked about the picking, sorting, and eating of the relevant food. For the purposes of analysis, these were combined so that a positive response to any question was regarded as a potential exposure. Analysis was performed by conditional logistic regression in the EGRET statistical package (Statistics and Epidemiology Research Corporation, Seattle, Washington). Univariate analysis was performed initially, and then each variable was fitted to a model including cat and dog ownership since these were the primary hypotheses. All variables that improved the fit of the model at a p value of <0.2 using the likelihood ratio statistic were then fitted to a multivariable model in which only those variables significant at a p value of <0.05 were retained to create a final estimate of association.

RESULTS

Twenty-three people fulfilled the case definition between 1967 and 1997, of which 18 were still alive. All but two cases had histologic confirmation of the diagnosis. Two subjects could not be included in the study; one declined to take part and the other had migrated out of the study area and was not traceable. Therefore, 21 cases and 84 controls were included in the study. Two patients had lived in two different villages during the period at risk of infection, and, thus, controls were selected from both villages. The mean age of cases and controls was 43 years (range 6–68 years) and the maximum age difference between any control and its matching case was 22 months. Fourteen of the cases were males.

The prevalence of exposure to each risk factor and the univariate odds ratio are shown in table 1. Whereas cat ownership showed a strong relation, dog ownership showed little evidence of an association with the disease. The number of cats among cat owners (per

<table>
<thead>
<tr>
<th>Behavioral variable</th>
<th>Cases</th>
<th>Controls</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog ownership</td>
<td>6/21</td>
<td>30/84</td>
<td>0.91</td>
<td>0.4–2.4</td>
</tr>
<tr>
<td>Cat ownership</td>
<td>17/21</td>
<td>42/84</td>
<td>6.61</td>
<td>1.8–24.5</td>
</tr>
<tr>
<td>Strawberries‡</td>
<td>11/21</td>
<td>45/84</td>
<td>0.95</td>
<td>0.4–2.6</td>
</tr>
<tr>
<td>Blueberries‡</td>
<td>16/21</td>
<td>69/84</td>
<td>0.68</td>
<td>0.2–2.3</td>
</tr>
<tr>
<td>Mushrooms‡</td>
<td>13/21</td>
<td>50/84</td>
<td>1.13</td>
<td>0.4–3.3</td>
</tr>
<tr>
<td>Cranberries‡</td>
<td>11/21</td>
<td>45/84</td>
<td>0.94</td>
<td>0.3–2.7</td>
</tr>
<tr>
<td>Parsley‡</td>
<td>16/17</td>
<td>56/72</td>
<td>4.58</td>
<td>0.5–42.8</td>
</tr>
<tr>
<td>Herbs‡</td>
<td>6/15</td>
<td>36/70</td>
<td>0.47</td>
<td>0.2–1.5</td>
</tr>
<tr>
<td>Being a farmer</td>
<td>6/21</td>
<td>13/84</td>
<td>2.71</td>
<td>0.8–9.7</td>
</tr>
<tr>
<td>Working with grass</td>
<td>17/21</td>
<td>49/82</td>
<td>3.43</td>
<td>1.0–11.9</td>
</tr>
<tr>
<td>Chewing grass/hay</td>
<td>9/18</td>
<td>24/80</td>
<td>2.33</td>
<td>0.8–6.9</td>
</tr>
<tr>
<td>Hunting in forest</td>
<td>5/21</td>
<td>4/83</td>
<td>8.10</td>
<td>1.5–43.1</td>
</tr>
<tr>
<td>Visiting alpine pastures</td>
<td>15/21</td>
<td>46/84</td>
<td>2.51</td>
<td>0.6–8.2</td>
</tr>
<tr>
<td>Leaving school &lt;17 years of age</td>
<td>1/20</td>
<td>28/79</td>
<td>0.09</td>
<td>0.01–0.7</td>
</tr>
<tr>
<td>Walking regularly in forest</td>
<td>20/21</td>
<td>69/84</td>
<td>2.59</td>
<td>0.9–7.1</td>
</tr>
</tbody>
</table>

* Univariate analysis with the reference class being absence of the behavior.
† CI, confidence interval.
‡ These items refer to picking, eating, or sorting the foods listed.
household) was one to 10 (mean 2.2; median 2.0) in the patients group and one to eight (mean 2.5; median 2.0) in the control group. Hunting, leaving school before 17 years of age, working with grass, using home-grown herbs, and walking in the forest were other variables that showed a significant association at the $p < 0.2$ level in univariate analysis and were then each added alone to both cat and dog ownership in an intermediate model. The risk of cat ownership was little affected by the addition of any of the other variables whereas the association with dog ownership became 0.52 (statistically not significant).

When all of these variables were fitted simultaneously, the only ones remaining statistically significant were cat ownership and hunting in the forest. Therefore, these variables were retained in the final model along with dog ownership. The results of fitting this model are shown in table 2. In addition to no longer being significant in a combined model, the odds ratio for leaving school at age <17 years changed from 0.16 to 0.8. There were no significant interactions between any of the three variables in the final model.

**DISCUSSION**

In this study, cat ownership was associated with a sixfold increased odds and hunting in the forest with close to an eightfold increased odds for alveolar echinococcosis. Adjustment for confounding by a wide variety of variables had little effect on the size of the association with either cat ownership or hunting in the forest, suggesting that these are true risk factors. No other behavior was statistically significant in association with alveolar echinococcosis. The study was small and of limited power—nevertheless, the point estimates for consumption or contact with wild berries were all very close to unity, suggesting that even in a small and of limited power—nevertheless, the point estimates for consumption or contact with wild berries were all very close to unity, suggesting that even in a larger study these would not be risk factors. This behavior may be less well recalled, particularly by surrogate reporters, than pet ownership and hunting and, therefore, cannot be entirely ruled out. Dog ownership had been found to be associated with the disease in the only previous case-control study of infection with *E. multilocularis* in Alaska (10). However, in that setting, dogs are kept outside the home where hunting of rodents is more likely. In Austria dogs are mainly domestic animals.

Our study was matched for neighborhood and may, therefore, have failed to detect ecologic factors related to risk of infection with this cestode. Farming, for example, has been considered a risk factor for the disease but has been taken into account by having controls from the same rural village. Nevertheless, 92 percent of farmers amongst controls (12 of 13) and all of the cases who farmed (6 of 6) owned cats. It is therefore feasible that the anecdotal association with farming (11–13) is a result of cat ownership.

The study is in disagreement with the recent hypothesis that eating wild berries growing near the ground is the main risk factor (13–15). Hunting was claimed to be a risk factor in previous publications (9, 16). Since Austria deploys programs to reduce foxes as wildlife hosts of sylvatic rabies, hunters often are exposed to fox carcasses that are sent to a reference laboratory for testing for Lyssavirus antigen. Wolves and coyotes, other possible final hosts of *E. multilocularis*, are not indigenous to Austria.

*E. multilocularis* has been described as a parasite in cats (17, 18). It seems plausible that domestic cats may excrete eggs which subsequently contaminate human food (19). Cats could also become contaminated with eggs from the soil which, sticking to their fur, are brought into the house. Information was collected on cat behavior in the home but the dataset was too sparse when restricted to cat owners to allow statistical examination. Presently, there are no data available on rates of infection with *E. multilocularis* in cats (and dogs) in Austria. The standard technique presently used is parasitologic examination of the small intestine at necropsy. Collecting and euthanizing ownerless cats and stray is opposed by animal rights groups. Eckert (9) and Deplazes and Eckert (20) recently described a "coproantigen ELISA" (enzyme-linked immunosorbent assay) and found Swiss cats and dogs to be rarely infected (mostly <1 percent). In order to further examine the biologic plausibility of cats as risk factors for alveolar hydatid disease in Austria, a study using the coproantigen ELISA is in progress to investigate the rate of infestation of domestic cats.

**REFERENCES**


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