HYPERENDEMIC HUMAN AND PORCINE *TAENIA SOLIUM* INFECTION IN PERÚ

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Abstract. The prevalence and characteristics of human taeniasis/cysticercosis and porcine cysticercosis were assessed in an endemic area of the Peruvian highlands. Individuals from 10 communities had stool examinations (N = 2,951) and serologic testing for *Taenia solium* antibodies (N = 2,583). The total porcine population present (N = 703) was also examined by serology. Cysticercosis is hyperendemic in this area and is associated with an important number of seizure cases. Human seroprevalence by village ranged from 7.1–26.9% (mean, 13.9%). Seroprevalence was higher among individuals with a history of seizures but not in those reporting a history of headache or intestinal taeniasis. Prevalence of taeniasis ranged from 0–6.7% (median, 2.5%). Coproantigen detection found 2.4 times more taeniasis cases than did microscopy (direct and after concentration). Age distribution for taeniasis showed a peak at younger ages than for seroprevalence. Porcine seroprevalence ranged from 42–75%. Random effects logistic regression models for human seropositivity demonstrated both in-house clustering of cases and a large increase in risk associated with a tapeworm carrier in the house. Besides confirming the close relationship between taeniasis and cysticercosis cases, this large-scale field study demonstrated early age of tapeworm and cysticercosis infections in humans, and short duration of taeniasis infections.

INTRODUCTION

Neurocysticercosis (NCC), the infection of the human central nervous system by *Taenia solium* larvae, is an important contributor to neurologic morbidity in developing countries and presumably is the major cause of acquired epilepsy in the world. It also is increasingly diagnosed in industrialized countries because of immigration from endemic areas, with over 1,000 cases per year in the United States. The life cycle of this zoonotic cestode includes the pig as the normal intermediate host (harboring the larval vesicles or cysticerci), and humans as the definitive host (harboring the adult form or tapeworm). Humans also can be accidental intermediate hosts and develop the larval stage of the disease by accidental ingestion of *T. solium* eggs. Porcine cysticercosis is an important cause of economic losses in developing countries.

In most developing countries, the cycle of *T. solium* between pigs and humans is sustained because of the coexistence of poor sanitary conditions and domestic pig raising without veterinary control or surveillance systems. Despite multiple field epidemiologic studies in recent years, basic data still are missing, especially regarding the interrelationship between human tapeworm infections, porcine cysticercosis, and human cysticercosis, and whether this relationship varies in different conditions of endemicity.

Although taeniasis/cysticercosis has been included in a short list of diseases considered to be eradicable in the short term, no sustainable eradication has been achieved. Whereas endemic taeniasis/cysticercosis occurs in very different scenarios (highlands, tropics, arid coast, etc.), and at different intensities of prevalence, most field studies are performed in a single selected endemic village and thus cannot be extrapolated to regional or country settings. The transmission dynamics of *T. solium* need to be better understood to design a rational control program that can be applied in various settings. As part of an interventional study on the control of *T. solium*, we used the best available diagnostic tools (enzyme-linked immunoenzyme transfer blot [EITB] assay for the detection of anti-cysticercus antibodies and coproantigen detection by enzyme-linked immunosorbent assay [ELISA] in a large-scale, comprehensive, cross-sectional survey in a wide area of the Peruvian highlands to quantify baseline infection parameters for human taeniasis and human and porcine cysticercosis.

MATERIALS AND METHODS

Study site. The central highlands area of Perú was selected because of demonstrated endemicity and accessibility by road. The area is cold and has at least two clearly defined seasons: dry from June to November, and rainy from December to May. Paved access highways are passable all year, although secondary roads may not be used during the rainy season. A preliminary trip was made to select an adequate study area on the basis of accessibility and the willingness of communities to cooperate in a longitudinal project on the control of porcine cysticercosis. In this trip, several villages less than 50 miles from Huancayo (population 300,000), the main city in the department, were inspected. Communities near Huancayo were selected because of the convenience of a city-based location for specimen-handling, centrifugation, and storage.

Nine villages of the Quilcas district, located 12 miles west from Huancayo at altitudes of 3,200–3,600 meters above the sea level, were selected for the study. They were Veintisiete de Mayo, Santa Cruz, Pampas, Llacta, Colpar, Rangra, Casacancha, Progreso, and Centro. Canchayllo, a village in an-
other district, also was included to increase sample size (Figure 1). The houses in these villages are adobe and have no sanitation facilities (10–50% have latrines). Most of the villages also lack potable water or electricity. After the study communities were chosen, a second visit was made to meet key village leaders to evaluate their interest in the project and willingness to participate. Census and mapping were initiated after the leaders consulted the communities and confirmed their consent. Before starting the project, the field personnel gave several talks to groups of villagers about the project and the disease. During these talks, villagers identified the presence of intestinal parasites as one of their principal health concerns; thus, free detection and treatment of geohelminthiasis was offered as part of the study. Human and veterinary medical attention, including animal vaccinations for porcine hog cholera, also were offered free during each field trip.

**Data collection.** The census form for villagers included identification (last name, first name, age, sex) and simple, direct questions in local terms about a history of passing tapeworm proglottids, headaches, or seizures. The questionnaire was applied to all individuals present, including children, and the head of the family gave information about members who were absent. An individual who slept two or more nights each week in a village was considered as living there. The cross-sectional sampling of humans and pigs for the study was performed from March–May 1996.

**Samples.** Approximately 5 mL of venous blood was drawn by venipuncture from all consenting villagers age 5 or older. Some samples were taken from children younger than 5 at their parents’ request. Samples were centrifuged in Huancayo the same day, coded with consecutive numbers according to the collection lists, aliquotted in two sets of 1.5-mL vials, stored at −4°C, and sent frozen to a laboratory in Lima (Laboratorio de Patologia, Universidad Peruana Cayetano Heredia) to be assayed by EITB. Stool samples were collected from all consenting individuals in disposable 500 mL plastic boxes. When the collection materials for stool samples were distributed, villagers were carefully instructed about adequate hygiene to avoid contamination, and were given toilet paper and soap.

**Pig sampling.** All pigs in the village (excluding pregnant sows to avoid the risk of miscarriage, and piglets less than 2 months old) were identified and ear-tagged with consecutive numbers. The age of the pigs was established by asking the owner and corroborated using conventional teeth-eruption indicators in young animals. At the same time, a 5-mL blood sample was taken from the pig’s cava vein using vacuum tubes. Samples were processed as described above for human serum. All pigs were vaccinated against hog cholera.

**Processing.** Serum samples were processed by EITB as originally described. In brief, this assay uses a semipurified fraction that contains seven *T. solium* glycoprotein antigens (diagnostic bands GP50, GP42-39, GP24, GP21, GP18, GP14, and GP13, the number indicating the respective molecular weight in kDa) in an immunoblot format to detect infection-specific antibodies. Reactions to at least one band are considered positive. After a macroscopic examination for worms or proglottids in the field, stool samples were sent to the reference laboratory in Lima and examined by both direct microscopy and a concentration (sedimentation) method. No further efforts at species identification were made. Individuals with a positive parasitologic examination were revisited at the end of the study and offered antiparasitic treatment. Stool samples were also examined by coproantigen detection ELISA, as originally described. This assay has a
RESULTS

Population and sampling. The total population resident in the study area at the time of the survey was 5,658 individuals, 2,696 males (47.6%), and 2,962 females. Mean age (SD) was 24.51 (20.82) years, range 0 to 99. Age distribution was typical of rural areas in developing countries, with predominance of younger age groups.

Blood sampling. Blood samples were obtained from 2,545 of 4,850 residents age 5 or older (mean sampling coverage 52.5%, Figure 2), and 38 children younger than 5.

Stool sampling. Stool samples were collected from 2,607 residents age 5 or older (53.7%) and 345 children under 5 who were not in the original sampling frame. Most people who had blood samples taken (1,749, 68%) also provided stool samples.

Unsampled individuals. Individuals who did not have a blood sample taken were more frequently male, reflecting lower presence or cooperation in male adults. (Data not shown.) Those who did not provide stool samples were older, and similar to the blood sampling, most of them were male. In general, individuals who were not sampled for blood or did not turn in stool samples were less prone to have a history of headaches, seizures, or having passed proglottids (Table 1). One-third of the population (1,873, 33.1%) was not sampled for blood and did not turn in stool samples.

Serology. Three hundred fifty-five individuals age 5 or older were seropositive to cysticercosis (13.7%). In the whole study population, seroprevalence was similar for males and females, with an early increase at age 10, a later decrease, and a rise again to a higher peak at age 40–60 (Figure 3). Children younger than 5 had lower seroprevalence (2/38, 5.3%; odds ratio [OR] 0.34; P = 0.196). The only two seropositive children in this group were 4 years old.

Human seroprevalence per village ranged from 7.1% in Canchayllo to 26.9% in 27 Víntesis de Mayo (Table 2). Seroprevalence increased with age in the two villages with lower prevalence levels, but all others showed homogeneous hyperendemicity levels across age groups. (Data not shown.) Distribution of seroprevalence by sex was extremely variable among villages. We observed a trend for higher human seroprevalence in villages farther from the main road (Spearman’s rho 0.48, P = 0.18). This trend was more evident in relation to porcine seroprevalence (Spearman’s rho 0.597, P = 0.090).

Taeniasis—parasitology. Baseline pretreatment stool samples were collected from 1,317 individuals. No proglottids were found at macroscopic examination, but eight cases had Taenia sp eggs detected by microscopy (0.6%). Post-treatment stool samples were collected from 2,471 individuals (836 individuals provided both pretreatment and post-treatment samples). Taenia proglottids were found in post-treatment samples of 13 individuals, and Taenia eggs were detected by microscopy in 21 cases (0.8%). More taeniasis cases were detected in the intervention (praziquantel-treated) than in the comparison (pyrantel-treated) areas, although the proportions were not significantly different (17/1,626 = 1.0% versus 4/845 = 0.5%; OR 2.22; P = 0.142). Prevalence of taeniasis by microscopy in the study villages ranged from 0–1.9%.

Taeniasis—coproantigen detection. Coproantigen detection ELISA was performed in post-treatment stool samples.
from 1,620 individuals, almost all of them (1,611) from the intervention areas. Forty-five (2.8%) were positive. Only 17 of 45 (37.8%) also were positive in microscopy. In general, coproantigen-positive individuals were younger than those who tested negative (mean age 19.6 [SD 20.6] and median 9 years versus mean 24.5 years [SD 20.8] and median 16 years), although the difference did not reach statistical significance ($P = 0.12$). However, most coproantigen-positive individuals were 10 years old or younger, with a significantly higher prevalence in this age group (23/595, 3.9%, versus 22/1,025, 2.1%, OR 1.83, $P = 0.042$). Prevalence of taeniasis by coproantigen detection in the study villages tested ranged from 0–6.7%.

In four cases, taeniasis was diagnosed by other means, but coproantigen testing was negative: One person was positive for *Taenia* eggs at microscopy, and proglottids were seen post-treatment; two were positive for eggs only by microscopy, and in one, proglottids were reported post-treatment, but microscopy was negative.

### Table 2

Prevalence of serum antibodies to *Taenia solium* in human and porcine populations, and human taeniasis infection. Huancayo, Perú, 1996

<table>
<thead>
<tr>
<th>Village</th>
<th>Human cysticercosis (seroprevalence)</th>
<th>Porcine cysticercosis (seroprevalence)</th>
<th>Human taeniasis (coproantigen)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canchayllo</td>
<td>33/474 (7.0%)</td>
<td>30/71 (42.3%)</td>
<td>1/217 (0.5%)</td>
</tr>
<tr>
<td>Colpar</td>
<td>13/174 (7.5%)</td>
<td>31/48 (64.6%)</td>
<td>Not done*</td>
</tr>
<tr>
<td>Centro</td>
<td>19/198 (9.6%)</td>
<td>24/52 (46.2%)</td>
<td>0/97 (0%)</td>
</tr>
<tr>
<td>Progreso</td>
<td>26/254 (10.2%)</td>
<td>21/42 (50.0%)</td>
<td>0/94 (0%)</td>
</tr>
<tr>
<td>Llacta</td>
<td>27/201 (13.4%)</td>
<td>57/78 (73.1%)</td>
<td>9/259 (3.5%)</td>
</tr>
<tr>
<td>Pampa</td>
<td>53/419 (12.6%)</td>
<td>51/102 (50.0%)</td>
<td>0/164 (0%)</td>
</tr>
<tr>
<td>Santa Cruz</td>
<td>56/372 (15.1%)</td>
<td>47/66 (71.2%)</td>
<td>10/339 (2.9%)</td>
</tr>
<tr>
<td>27 de Mayo</td>
<td>74/275 (26.9%)</td>
<td>78/104 (75.0%)</td>
<td>19/279 (6.8%)</td>
</tr>
<tr>
<td>Rangra</td>
<td>29/113 (25.7%)</td>
<td>28/43 (65.1%)</td>
<td>Not done</td>
</tr>
<tr>
<td>Casacancha</td>
<td>25/103 (24.3%)</td>
<td>72/97 (74.2%)</td>
<td>6/170 (3.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>355/2,583 (13.7%)</td>
<td>439/703 (62.4%)</td>
<td>45/1,619 (2.8%)</td>
</tr>
</tbody>
</table>

* One negative sample corresponding to a resident of Colpar is not included.

### Porcine seroprevalence

Porcine seroprevalences ranged from 42.3–75.0% (total prevalence 62.4%), and increased monotonically with age (Table 3). There were no differences in seroprevalences between male and female pigs.

### Human versus porcine seroprevalence at village level

There was a statistically significant positive correlation between human and porcine seroprevalence for each village (Spearman’s rho 0.799, $P = 0.006$) that persisted after direct standardization by age and sex. Significant positive correlations also existed between porcine seroprevalence and human taeniasis by coproantigen (Spearman’s rho 0.866, $P = 0.005$) and between human seroprevalence and taeniasis prevalence by coproantigen detection (Spearman’s rho 0.800, $P = 0.017$) (Figure 4).

### Factors related to seropositivity: Neurologic symptoms

Seroprevalence was higher among individuals with a history of seizures (16/71, 22.5% versus 339/2,512, 13.5%; OR 1.86; 95% CI = 1.01, 3.39; $P = 0.029 − \chi^2$ test, 40.1% attributable risk in exposed individuals) but not in those who had a history of headache (51/329, 15.5% versus 304/2,253, 13.5%; OR 1.18; CI = 0.84, 1.64; $P = 0.323$). Seizure complaints were more frequent in older people, particularly in seropositive individuals (Figure 5). The association between a history of seizures and a positive EITB was stronger in individuals older than 40 (8/87, 9.2% versus 15/451, 3.3%; OR 2.94; CI = 1.10, 7.70; $P = 0.021$, 63.8% attributable risk in seropositive individuals).

### Table 3

Porcine seroprevalence by age groups. Huancayo, Perú, 1996

<table>
<thead>
<tr>
<th>Age group (months)</th>
<th>Seroprevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>2–4</td>
<td>94/201 (46.8%)</td>
</tr>
<tr>
<td>5–6</td>
<td>65/114 (57.0%)</td>
</tr>
<tr>
<td>7–8</td>
<td>75/122 (61.5%)</td>
</tr>
<tr>
<td>9–10</td>
<td>52/79 (72.2%)</td>
</tr>
<tr>
<td>11–12</td>
<td>72/93 (77.4%)</td>
</tr>
<tr>
<td>&gt; 12</td>
<td>76/94 (80.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>439/703 (62.4%)</td>
</tr>
</tbody>
</table>
Seizures were reported in 4.5% (16/355) of seropositive and 2.5% (55/2,228) of seronegative individuals, corresponding to a population attributable risk of 10% of all seizures related to cysticercosis seropositivity.44

History of having passed proglottids. Seroprevalence among individuals with a history of having passed proglottids was similar to that in individuals without such antecedent (36/218 versus 319/2,364; OR 1.27; CI 0.85, 1.88; P = 0.22). This lack of association led to further analysis of this variable. We observed increased odds for seropositivity related to a history of passing proglottids in individuals younger than 25 (OR 2.76; CI 1.82, 4.08; P < 0.001) but not in older subjects (OR 0.66; CI 0.21, 2.08; P = 0.779).

Current intestinal taeniasis. There were 917 individuals who had both serum samples taken and post-treatment stool samples processed by microscopy and coproantigen detection. A comparative analysis was performed in this subgroup to evaluate the association between intestinal taeniasis and seropositivity to EITB. Most Taenia carriers in this group (23/30) were seropositive, including all seven cases with proglottids seen at macroscopical examination, 14 of 16 cases with Taenia eggs at microscopy (87.5%), and 22 of 28 cases with positive coproantigen examination (78.6%). Five of the seven seronegative taeniasis cases corresponded to coproantigen-positive individuals with negative parasitologic results (microscopy and macroscopic examination). After excluding the tapeworm carriers, the association between a positive EITB and living in a house with a Taenia carrier was exam-
ined in this same subgroup \(N = 887\). Forty percent of individuals living in a house with a tapeworm carrier were seropositive, compared with 13% of individuals in houses where no tapeworms were detected \(22/55, 40.0\%\) versus \(11/382, 3.3\%; OR 1.33; CI 1.01, 1.66; \(P = 0.043\). A similar association existed between having infected pigs and being seropositive \(190/1,224, 15.5\%\) versus \(165/1,359, 12.1\%; OR 1.33; CI 1.06, 1.66; \(P = 0.013\). Age, sex, the number of people living in the house, and having a history of passing proglottids were not associated with positive EITB in bivariate analysis. Using random effects logistic regression (RELR) models for seropositivity, raising pigs, and having seropositive pigs failed to significantly increase the explained deviance according to the likelihood-ratio test (LRT). We also tested interaction terms between the presence of tapeworm carriers and pig raising as well as having seropositive pigs, failing to observe significant effect modification. The maximum amount of deviance was explained by considering the presence of a tapeworm carrier in the house and fitting dummy variables for the seroprevalence levels, although a large amount of the variability still remained unexplained in this model.

**Household clustering of cases seropositive for cysticercosis.** Using a RELR model, we confirmed the presence of clustering at the household level both before and after considering the presence of tapeworm carriers in the house. Cluster-level effects explained highly significant amounts of the total variance in each case, 63.4 and 52.1%, respectively \(P < 0.001\) for both cases, LRT). Significant differences were observed between odds ratios estimated at the cluster level and the pooled estimates. The clustering effects remained significant when fitting individual models for groups of communities with different seroprevalence levels (high > 20%, intermediate 10–20%, and low < 10%). Less clustering was observed in communities with high seroprevalence. The percentage of the variance accounted for by clustering in those communities was only 32.5%, while it exceeded 50% in communities with intermediate and low seroprevalence.

**Clustering of seropositive cases around tapeworm carriers.** Most tapeworm carriers were seropositive \(22/28, 78.6\%\) of coproantigen-positive individuals while their household contacts had a rate 3.4 times higher than individuals living in households with no tapeworm carriers \(45/112, 40.1\%\) versus 288/2,443, 11.8%; \(P < 0.001\). RELR models showed that the presence of a tapeworm carrier was significantly associated with higher rates of seropositive cases in the house \(OR, 9.21; CI, 5.38, 15.76; P < 0.001, LRT\) after taking into account clustering of cases within the household. In all analyses by prevalence levels, clustering around carriers remained highly significant \(P < 0.005, LRT\). Communities with higher rates showed less clustering around carriers \(OR 5.43\) than communities with intermediate and lower prevalence rates \(OR 7.31 and OR 14.11, respectively\).

**DISCUSSION**

This comprehensive, large-scale study demonstrates the hyperendemicity of *Taenia solium* infection in a widespread area of the Peruvian central highlands. Most residents in 10 typical villages had either serology or stool examination performed, and an important proportion of them had both. All study villages showed human seroprevalences of antibodies to *T. solium* above 7%, reaching 25% in three of the 10 communities. Impressively, porcine seroprevalences were all above 40%, reaching 75% in two villages, and there was a strong correlation between human and porcine seroprevalence by village. As opposed to most epidemiologic studies in taeniasis/cysticercosis (performed in one or two selected villages), this study looked at all villages in a district to provide a comprehensive overview of the situation in the area.

The study also has estimated the extent of in-house clustering of cases, as well as the high risk involved for both tapeworm carriers and their household contacts. Marked clustering occurs despite the high background seroprevalence, largely in houses with tapeworm carriers. Given the ultimate goal of controlling or eradicating transmission, identifying and characterizing the sources of infection is crucial. The cumulative effect of a tapeworm carrier in in-house transmission will depend on the duration of the infection. In this series, the age-prevalence curve of intestinal taeniasis peaks at an earlier age than do human cysticercosis antibodies. This would not support the classic theories of a long tapeworm life span of 20 years and corroborates recent studies in Guatemala\(^{18,22,23}\) which suggested that the life span is much shorter than suspected, probably below 5 years in most cases. Symptomatic neurocysticercosis is known to appear years after exposure.\(^{45}\)

Recent data have shown that the frequency of taeniasis in patients with neurocysticercosis may reach 15%, and that patients with more cerebral cysticerci have a higher probability of carrying a tapeworm at the time of diagnosis.\(^{46,47}\) We postulate that many seropositive individuals, including many NCC patients, once were tapeworm carriers (i.e., that autoinfection plays a much more important role in NCC than previously suspected) or household contacts.

The coproantigen-detection test consistently detected two times more tapeworm carriers than microscopy alone did. Thus, microscopy underestimates the real prevalence of taeniasis and would be a poor monitoring tool for control purposes. Almost all tapeworm carriers in this area were EITB positive, whether they were diagnosed by microscopy or coproantigen detection. However, it is not clear whether intestinal taeniasis leads to antibody formation by itself, being a different stage of the same species, or whether the antibodies represent contamination of the carrier with *Taenia* eggs from its own source by external autoinfection. In young individuals, there was a significant association between *T. solium* antibodies and a history of having passed proglottids, but this effect disappears at older ages. This can be explained by young age of infection, short life span of the tapeworm, and later seroconversion to negative (transient seropositive cases).\(^{48}\) Short-lived intestinal tapeworm infections at younger ages can help explain the early peak in the bimodal seroprevalence curve in the human population.

It has been suggested that pigs get infected only at early ages.\(^{49}\) In this study, however, porcine seroprevalence increased monotonically with the age of the animal. This may indicate either that older animals are as susceptible as younger pigs or that some pigs are protected through the initial exposure period, perhaps via maternal transfer of antibodies, but become susceptible later. Maternal antibodies are protective for other larval cestode infections\(^{34}\) and have
been shown to slowly decrease in piglets born to cysticercosis-infected sows.29

The prevalence of individuals complaining of seizures (30/1,000) was somewhat higher than expected for developing countries.51 These individuals had almost twice the seroprevalence as individuals who did not complain of seizures. Even though the simple questionnaire that we used may have resulted in non-specific or false-positive answers, a strong association between seizures and seropositivity to *T. solium* was found in this study. The estimate of 10.2% for population-attributable risk of seizures due to cysticercosis is most likely an extremely conservative estimate. Only calcified brain cysticerci are found in over half the cases of symptomatic NCC,72–53 as in almost all asymptomatic individuals examined by neuroimaging in endemic villages.20,26,27 All these NCC cases may have become seronegative over time. Another group of cases with a single viable or degenerating parasite also may be seronegative.55 Thus, some—or many—seizures in seronegative individuals also will result from cysticercosis. The high frequency of individuals with seizures in older age strata in this population and its strong association with serum antibodies to *T. solium* probably reflect the cumulative effect of infections that occurred some time ago but only become clinically manifest years later. A history of headache was three times more frequent in women than men, as expected for general population.56 Probably because of the low specificity of the symptom, there was no association between complaining of headache and seropositivity.

Taeniasis/cysticercosis is an important public health problem in endemic areas, as demonstrated by its hyperendemic conditions in the study area and the association between seropositivity and seizures. While improvements in sanitation in poor rural zones are not to be expected in the near future, control programs are needed to deal with this endemic disease in the short and medium terms.

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