

## HUMAN CYSTIC ECHINOCOCCOSIS IN A URUGUAYAN COMMUNITY: A SONOGRAPHIC, SEROLOGIC, AND EPIDEMIOLOGIC STUDY

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**Abstract.** A prevalence and transmission study of human cystic echinococcosis (CE), due to infection with the dog tapeworm *Echinococcus granulosus*, was undertaken in the village of La Paloma in central Uruguay. The human population was registered and screened for CE by abdominal ultrasound scan as well as a number of serologic tests. Dogs were screened for *E. granulosus* infection by arecoline purgation as well as specific coproantigen testing. The total prevalence of human CE (new cases and those with a previous history) was 5.6% (64 of 1,149); 3.6% (40) of the cases were new ultrasound detected asymptomatic cases (mean age = 45 years). Age prevalence increased from 1.1% in the 4–6-year-old group to > 11% in the > 60-year-old group; the 20–29-year-old group had a significantly higher CE rate of 7.4%, compared with younger and older age groups, and there was no difference between sexes. A CE rate of 3.9% (20 of 514) was also recorded by ultrasound for new cases in the population residing outside the village. Most of the hydatid cysts were located in the liver presenting as either univesicular cysts or a solid mass, and of those 71% and 63%, respectively, with such cyst presentations were seropositive against *E. granulosus* cyst fluid antigens. Two of eight individuals who were filter paper blood spot seropositive, but ultrasound scan negative, were subsequently diagnosed respectively with pulmonary hydatidosis after radiography, and hepatic hydatidosis after computed tomography scan. Of 36 households with a CE patient, 32 were single cases while four households each harbored two CE cases. This did not represent a clustered distribution within families (23 of 117). Almost 20% of the dogs from La Paloma were found infected with *E. granulosus* after purge examination, with a mean worm number of 67 (range = 1–1,020). An additional eight dogs that were purge negative were *Echinococcus* coproantigen positive. The study showed that human CE is highly endemic in Uruguay, with one of the highest local prevalence rates in the world. Transmission appears to occur readily within well-developed towns, as well as on rural sheep ranches. Mass screening by ultrasound scanning with confirmatory serologic testing is an effective approach to case detection at the community level.

Echinococcosis (CE) is a chronic zoonotic parasitic helminthic disease due to infection with the larval stage (hydatid) of the small dog tapeworm *Echinococcus granulosus*. The parasite has a global distribution but is particularly prevalent in rural areas where it is transmitted in a cycle between the dog, the definitive host, and the sheep, the intermediate host.<sup>1</sup> In South America, *E. granulosus* is endemic and a significant public health problem in several countries including Brazil, Peru, Bolivia, Chile, Argentina, and Uruguay.<sup>2–12</sup>

Human CE is one of the most important endemic infectious diseases in Uruguay.<sup>6,12</sup> However, recent data on surgical series are unfortunately lacking. A detailed assessment of hospital records between 1962 and 1971 revealed a total of 1,503 surgical interventions for hydatid disease. This would correspond to a national incidence of 17.7 per 100,000. In 1973, the mortality rate of CE was estimated to be between 25 and 42 per year.<sup>12</sup> A more recent ultrasound survey for abdominal CE performed in 6,035 people in a rural community in Uruguay reported a CE prevalence of 1.4%.<sup>13</sup> Similarly, seroprevalence studies in rural communities, using an ELISA with crude sheep hydatid cyst fluid antigen to detect antibodies (total immunoglobulin) revealed an overall seropositive rate of 1.2% (17 of 420).<sup>14</sup> Ovine hydatidosis has been reported in all of the 19 Departments of Uruguay with an overall prevalence rate of 34% at slaughter; a prevalence rate of 10.7% was also recorded in 5,500

dogs subjected to arecoline purgation (Orlando D, unpublished data).

Perhaps not surprisingly the natural history of human CE, the relative risk factors, and the infection pressure to humans in endemic areas are very poorly known.<sup>15,16</sup> One problem for community studies is quantification of infection in both humans and dogs.<sup>17–19</sup> The ability to undertake mass screening programs for human CE has been greatly advanced by the advent of portable ultrasound, which has proved highly effective in the diagnosis of asymptomatic cases.<sup>13,20,21</sup> In addition, serologic tests based on *Echinococcus* antibody detection have also been effectively used in some endemic regions, such as Argentina, to identify asymptomatic seroreactors.<sup>22,23</sup> However, the combination of ultrasound and serology is likely to be most effective for detection of asymptomatic CE cases.<sup>24</sup> The use of pre-mortem diagnosis of canine echinococcosis in communities was in the past usually associated with surveillance of control programs based on mass arecoline purge treatment of dogs.<sup>25</sup> Immunodiagnostic tests for canine echinococcosis based on serum antibody detection<sup>26</sup> or, more reliably, coproantigen detection<sup>27,28</sup> now provide a more effective methodology for screening and identification of dogs currently infected with *E. granulosus* tapeworms.

The current collaborative study was undertaken during 1991 and 1992 in a small rural town in the Department of

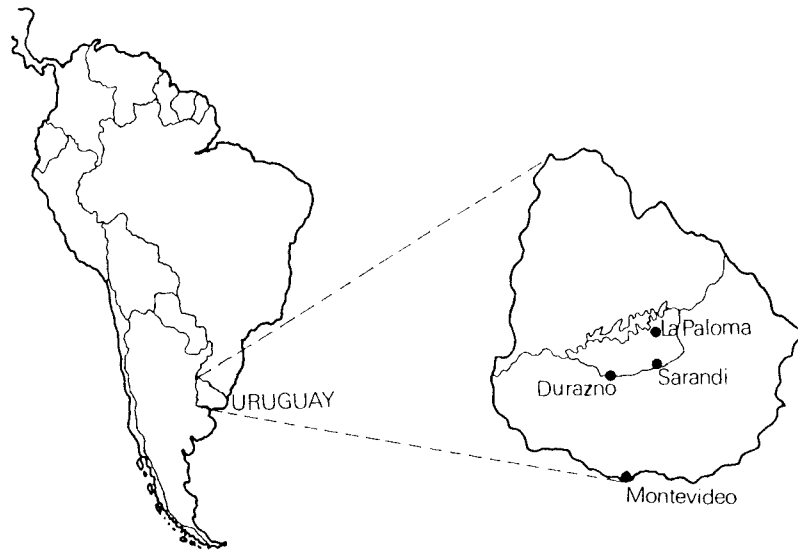


FIGURE 1. Location of Uruguay in South America with the location of La Paloma town.

Durazno in central Uruguay, a Department with known high endemicity of CE.<sup>3,6,12</sup> The study sought to both quantify human CE and canine echinococcosis within a well defined community and to evaluate epidemiologic factors associated with transmission within and around the town. Furthermore, the study permitted a detailed comparative assessment of the relative effectiveness of ultrasound and various serologic tests in the diagnosis of CE within an endemic community.

#### MATERIALS AND METHODS

**Study area and community.** The village of La Paloma with a population of 1,388 persons, is located 70 km from the administrative town of Sarandi del Yi (Figure 1). All households had electricity and the majority had a flushing latrine and piped water. While approximately 50% of the households in La Paloma kept a few sheep, a small number of large ranches (*estancias*) located in the surrounding countryside were responsible for managing 95% of the sheep population in the area. These *estancias* employed a number of male workers from La Paloma; these individuals usually lived on the *estancias* for most of the time but made frequent visits to their families living in La Paloma. The population in La Paloma lived in 397 houses that were divided between 39 household blocks (*manzanas*) containing between three and 23 houses (average = 2–10), and between six and 161 people per block. Average household size was four (range = 1–10). The population of La Paloma owned a total of 170 dogs. In addition to the La Paloma villagers, a significant number of individuals (n = 514) from the rural area surrounding the village (but who did not reside in the village) presented for hydatid screening.

Ethical approval for the study was given by Ethical Committees of the Fundacion San Antonio de Padua and the Liverpool School of Tropical Medicine. Informed consent was obtained in writing by participants completing a form detailing the reasons for and procedures used in the proposed community study.

#### Human CE screening—ultrasound and serologic testing.

Families without any age limit and any exclusion factor and living in La Paloma village were assigned a registration number and asked to attend the local medical clinic on a particular day within a scheduled period of eight days. Individuals were registered by name, age, and sex and directed to a room where three drops of blood (each at least 5 mm in diameter) were obtained by a fingerprick using an automatic lancing device (Autolet; Owen Mumford, Ltd., Oxford, United Kingdom) and collected onto a pre-labeled strip (6 cm × 1 cm) of Whatman No. 1 filter paper (Whatman International Ltd., Maidstone, United Kingdom). Strips were air-dried, placed in plastic bags, stored initially at 4°C and then at –20°C, and transported to Montevideo and the United Kingdom for antibody testing. After the fingerprick test, each individual was directed to a second room for abdominal ultrasound scanning in the horizontal position. Two portable ultrasound scanners with a thermal printout facility (SAL 32-B; Toshiba, Tokyo, Japan) were operated simultaneously by skilled medical ultrasonographers (HC and BB). Liver, kidneys, spleen, and the upper abdominal area were scanned in each person. Individuals with an ultrasonographic image suggestive of CE or who exhibited any cystic images were asked to donate 5 ml of venous blood for serologic testing. Serum was removed after blood was allowed to clot and separate overnight at 4°C. Serum samples were stored at –10°C or –20°C before testing. Cystic images obtained from ultrasound scans of the liver or other sites were graded according to the classification described originally by Gharbi and others,<sup>29</sup> but modified to include an extra category for multiple cysts, i.e., Type VI. These categories were Type I, univesicular cysts; Type II, cysts showing evidence of either a laminated or detached membrane; Type III, cysts showing evidence of daughter cysts; Type IV, solid cystic masses; Type V, calcified or partially calcified cysts; Type VI multiple cysts present within the liver or in the liver and other organs (may appear as Types I to V).

Individuals finally diagnosed as having CE were counseled by the local physician (RT) and offered treatment that was essentially surgery for patients with viable, noncalcified

cysts who were considered operable. Individuals who were seropositive, but who had a negative ultrasound result, were followed-up with a chest radiograph to check for pulmonary cysts, and by abdominal computed tomography (CT) in one case.

**Serologic tests for antibodies to *Echinococcus* in human sera.** Serum samples from those individuals who demonstrated a cyst on ultrasound were tested for total immunoglobulin antibodies by micro-ELISA using crude hydatid cyst fluid antigens as previously described,<sup>14</sup> and for total IgG, IgG1, and IgG4 antibodies using purified antigen B from hydatid cyst fluid.<sup>30,31</sup> In addition, a Western blot test using crude sheep hydatid cyst fluid was used to check for specific antibody (IgG) binding to the low molecular weight (between 8 and 20 kD) hydatid cyst fluid antigen B subunits.<sup>32,33</sup> Dried blood spots on filter papers (i.e., from all individuals) were tested using a micro-ELISA after elution of serum according to the method described previously.<sup>34</sup>

**Coproantigen detection.** *Echinococcus*-specific fecal antigens were detected in dog stools by a capture ELISA using an IgG fraction of a rabbit polyclonal anti-serum against *E. granulosus* adult worm extract, as described by Craig and others.<sup>28</sup> Fecal samples were collected per rectum using a plastic rectal loop (Jorgensen Butler Co., Dublin, OH) or from the solid feces passed following arecoline treatment. Fecal supernatants were stored at  $-20^{\circ}\text{C}$  until tested.

**Arecoline purgation of dogs.** Dogs were registered by their owners and dosed orally with 2mg/kg of arecoline hydrobromide in suspension using a drench gun. The duodenal purge was collected from the ground into 5% formalin, boiled, and examined immediately for presence of *Echinococcus* tapeworms and within 24 hr in the laboratory under a dissecting microscope.<sup>7</sup> For each positive purge, total worm numbers were counted. Dogs were treated and examined in a restricted area according to standard operating and safety procedures defined by the Uruguayan Dog Commission.

**Statistical analysis.** Data were entered into and most analysis was carried out using the Epi Info 6 program (Centers for Disease Control and Prevention, Atlanta, GA). Relative risks were calculated with corresponding 95% confidence intervals and *P* values to identify risk factors associated with infection. Either the chi-square or Fisher's exact test were used to compute two-tailed *P* values for independent variables. Chi-square tests for linear trend were used in the determination of linear trends in stratified data. A test for binomial variability was used to analyze the distribution of infections with respect to households.<sup>35</sup>

## RESULTS

**Mass screening of the human population.** A total of 1,149 of 1,388 residents (82.8%) of La Paloma (urban population) had an abdominal ultrasound scan and a fingerprick blood test (sampling was proportionately similar in each age group). This included 562 males, with a mean age of 29 years and a median age of 23 years (range = 2–91 years) and 584 females with a mean age of 30 years and a median age of 26 years (range = 1–91 years). Of the 1,149 residents, 135 (11.8%) exhibited a pathologic lesion (not necessarily a cystic lesion) on the abdominal ultrasound scan. Forty of

TABLE 1

Age prevalence of human cystic echinococcosis in La Paloma, Uruguay\*

Age group (years)	Ultrasound screening		Total	% Prevalence	Difference from 20–29-year-old group $P^{\dagger}$
	+	–			
0–3	0	53	53	0	<0.05
4–6	1	86	87	1.1	<0.05
6–9	1	97	98	1.0	<0.05
10–19	2	241	243	0.8	<0.05
20–29	12	151	163	7.4	NA
30–39	3	157	160	1.9	<0.05
40–49	2	90	92	2.2	NS
50–59	3	87	90	3.3	NS
60–69	8	64	72	11.1	NS
>70	8	61	69	11.6	NS
Total	40	1,087	1,127	3.6	

\* Overall  $\chi^2$  test for linear trend = 43.641,  $P < 10^{-4}$ . Not all positive persons had age data because 22 ages were missing; thus the difference in % total and % by age.

$\dagger$  NA = not applicable; NS = not significant.

these persons (3.6%) were finally diagnosed (ultrasonographically and/or serologically) as having CE (mean age = 45 years, median age = 45, range 6–83). All but one case were located in the liver; one pulmonary case of CE was identified by filter paper blood serology and a follow-up radiograph.

Of the 40 cases with CE detected (22 males and 18 females), three had a history of previous operative removal of a hydatid cyst and therefore were considered recurrences. An additional 24 individuals had a history of confirmed hydatid infection (mean age at the time of the current study was 45 years, median age = 45, range = 2–79), but had a normal ultrasound scan in the current study. Therefore, taking both new and previous CE cases into account, 5.6% (64 of 1,149) of individuals of La Paloma were currently infected or had been infected with *E. granulosus*.

A total of 514 individuals who were not residents of La Paloma but came from the surrounding area also voluntarily agreed to ultrasonographic examination. Twenty new cases of CE were diagnosed in this population (3.9%). This gave a total ultrasound based point prevalence of CE from the current study of 3.6% (60 of 1,663) for the two populations (urban and rural) combined.

The age-specific prevalence of newly diagnosed infections within the urban population showed a generally upward trend with age ( $\chi^2$  test for linear trend = 43.64,  $P < 10^{-4}$ ). Age prevalence increased from 0% in the 0–3-year-old age group to > 11% in the > 60-year-old group. There was, however, a striking peak in prevalence in the 20–29-year-old age group and again in the those more than 60 years of age (Table 1). No individual risk factors such as ownership of dogs, gender, etc., could be determined. There were no statistically significant clustering of cases in households or any relationship between the presence of infected dogs in households and human CE.

**Hydatid cyst classification.** The distribution of ultrasound images, following essentially the classification of Gharbi and others,<sup>29</sup> for newly diagnosed cysts in both the urban and the rural population samples is shown in Table 2. Cystic images classified as Types II, III, and VI were considered characteristic of human CE. On this basis, 10 pa-

TABLE 2

Ultrasound image classification and frequency of hepatic hydatid cysts in the La Paloma and rural population samples

Ultrasound image classification	La Paloma	Rural	Total (%)
Hepatic I (Univesicular)	11	6	17 (28.3)
II (Membrane)	0	2	2 (3.3)
III (Daughter)	2	3	5 (8.3)
IV (Solid)	14	6	20 (33.3)
V (Calcified)	5	2	7 (11.7)
VI (Multiple)	8	1	9 (15)
Total	40	20	60

tients from the La Paloma sample were designated as having CE. When combined with the rural sample, a total of 16 of the 60 (26.7%) individuals had an ultrasonographic image highly pathognomonic of CE (Table 2). Thirty newly diagnosed CE patients from La Paloma and 14 from the rural population were classified by ultrasound as Types I, IV, or V. Although suggestive of CE in an endemic region, these could not be regarded as strictly pathognomonic for *E. granulosus* based on ultrasound image alone.

**Serology.** Table 3 summarizes the serologic data broken down by ultrasound image classification for those 57 individuals (three people had no serology performed) considered to have CE by ultrasound. Overall 73.7% (42 of 57) were seroreactive on one or more tests. For 15 persons with ultrasound images regarded as characteristic for CE, 14 (93.3%) were seropositive on one or more of the tests. For hydatid cysts classified on ultrasonographic images as Types I (simple), IV (solid mass), or V (calcified or partially calcified), 70.6%, 63.2%, and 66.7%, respectively, were seropositive in one or more tests, for an overall rate of 66.7% (28 of 42). The ELISAs using either crude hydatid cyst fluid antigen or purified antigen B to detect total Ig or IgG antibodies were significantly more sensitive (59.7% and 63.2%, respectively) than the 8–12-kD Western blot test (39.6%). Interestingly however, six (12.5%) of the 48 cases positive by Western blot were seronegative by ELISA. On the other hand, 12 cases (25%) were seropositive by ELISA (using either antigen preparation) but seronegative in the Western blot test for the 8–20-kD antigens. The *Echinococcus* IgG subclass antibody response detected by ELISA using antigen B was slightly higher for the IgG1 subclass (28.1%) compared with IgG4 (21.1%) ( $P < 0.01$ ). However, for diagnos-

tic sensitivity, total IgG antibody detection was more sensitive (63.2%) than detection of either IgG1 or IgG4 antibodies (or IgG1 and IgG4 combined).

**Filter paper seroreactors.** During the community study (La Paloma and environs), eight individuals (0.5%) with no history of CE and a normal ultrasound scan were strongly seropositive when their filter paper blood eluates were tested by ELISA using both crude hydatid fluid and purified antigen B. All eight were also seropositive on the arc 5—agar gel diffusion test performed as described previously.<sup>23</sup> These eight cases were followed-up by chest radiograph and in one patient a single pulmonary cyst (6 cm × 8 cm) was identified and subsequently confirmed as CE after surgical treatment. In one of the other seven cases, a CT scan was performed and two hepatic cysts (one 3-cm calcified cyst and one 4-cm cyst) were identified on the edge of the liver that had been missed by ultrasonography. None of the other six seroreactors volunteered for the CT scan. This latter case confirmed by CT was included among the 60 cases of abdominal CE.

**Surgical follow-up of hepatic CE.** By early 1994, 32 of the 60 hepatic CE cases diagnosed (mean age = 29.6 years, range = 6–67, 19 males and 13 females) had been treated surgically. All cysts were confirmed to be due to *E. granulosus*. All of these patients were seropositive, except for four of 12 patients with Type I hepatic cysts. The overall serologic sensitivity for this operated CE group was therefore 84.4%. Clinically, a hepatic cyst presenting on ultrasound as a solid mass (Type IV) presents the most difficult diagnostic challenge. Of the 32 CE cases that underwent surgery, eight, were Type IV and all were seropositive; therefore, serologic confirmation in these patients was important in recommending treatment.

**Prevalence of *E. granulosus* in dogs.** A total of 155 of 170 dogs registered in La Paloma were dosed with arecoline. A total of 117 (75.5%) purged successfully and 23 (19.7%) passed purges containing *Echinococcus* worms. Purge worm counts ranged from one to 1,020 (mean = 67, median = 8). An additional 82 dogs for whom no location was registered (composed of dogs of unknown ownership and dogs from the surrounding rural community) were also dosed with arecoline. Of these, 53 purged successfully and 21 (40%) were positive for *E. granulosus* (range = 1–4,331 worms, mean = 389, median = 10). Another eight dogs that were purge-

TABLE 3

Ultrasound image classification of hydatid cysts and seroreactivity in La Paloma and rural cystic echinococcosis cases\*

Hepatic cyst classification	Total number of patients†	Serology							
		EgCF-ELISA		EgB-ELISA (%)			Western blot %		Total seropositive
		Total Ig (%)	IgG	IgG1	IgG4	8–12 kD	16–24 kD		
Type I (univesicular)	17	8 (47)	10 (58.8)	4 (23.5)	4 (23.5)	6/15 (40)	5/15 (33.3)	12 (70.6)	
Type II (laminated membrane)	2	1	1	1	1	1/1	0/1	2 (100)	
Type III (daughter cysts)	5	4 (80)	5 (100)	2 (40)	2 (40)	3/5 (60)	1/5 (20)	5 (100)	
Type IV (solid mass)	19	13 (68.4)	11 (57.9)	5 (26.3)	0 (0)	4/16 (25)	3/16 (18.8)	12 (63.2)	
Type V (calcifications)	6	3 (50)	3 (50)	1 (16.7)	2 (33.3)	2/6 (33.3)	2/6 (33.3)	4 (66.7)	
Type VI (multiple cysts)	8‡	5 (62.5)	6 (75)	3 (37.5)	3 (37.5)	3/5 (60)	2/5 (40)	7 (87.5)	
Total	57§	34 (59.7)	36 (63.2)	16 (28.1)	12 (21.1)	19/48 (39.6)	13/48 (27.1)	42 (73.7)	

\* EgCF = *Echinococcus granulosus* cyst fluid; EgB = *E. granulosus* B antigen.

† La Paloma and rural cases.

‡ Includes one case missed on the initial ultrasound examination but detected by filter paper blood serology.

§ Excluding three cases (type IV, V, and VI) where serology was not done.



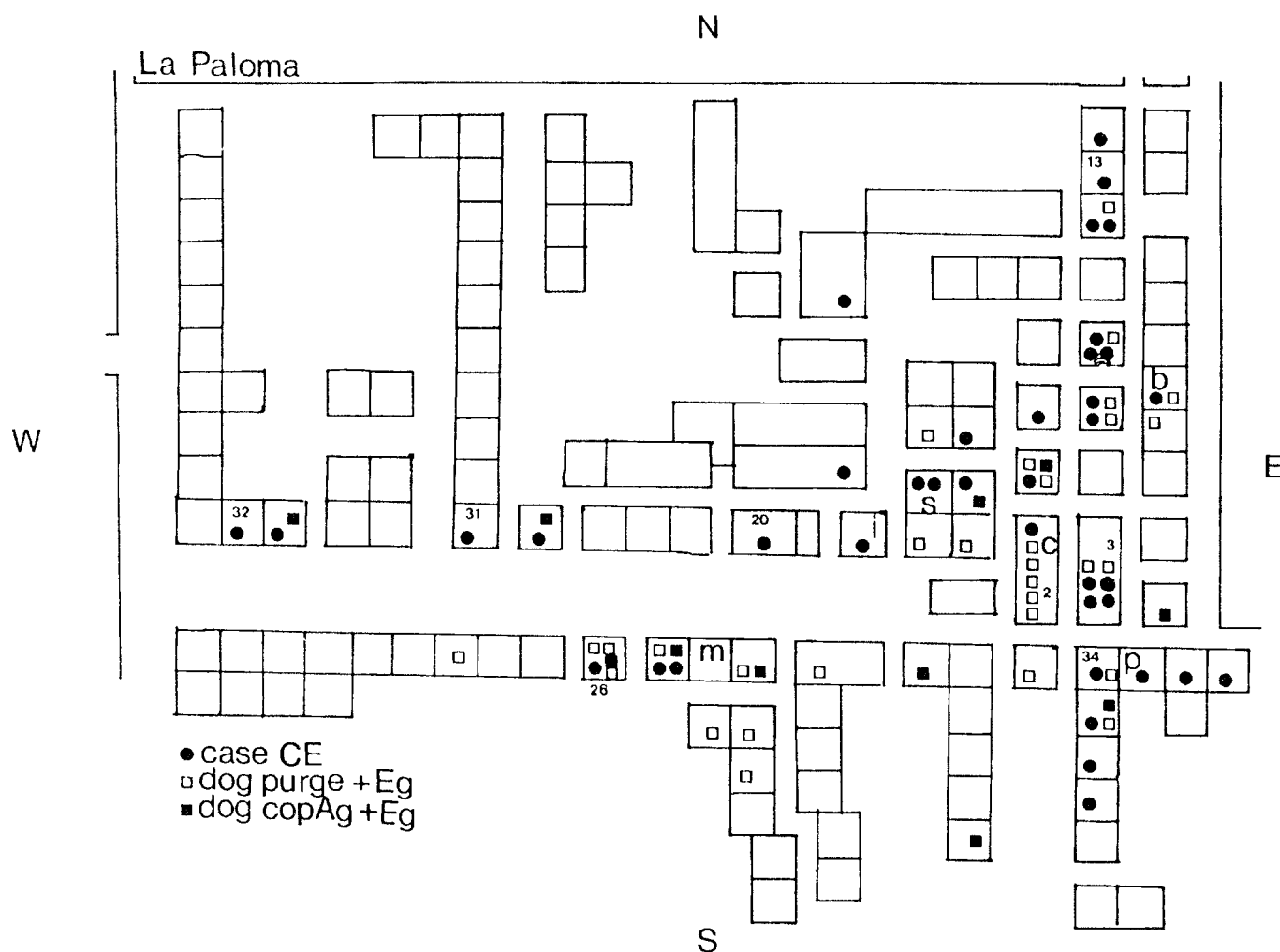


FIGURE 2. Map of La Paloma town by house block (*manzana*), some of which are numbered. Location of human cystic echinococcosis (CE) cases (●) and infected dogs (□, ■) are marked. B = butchers; c = cantina (restaurant); p = police station; s = school; i = information office; m = market. Dog purge +Eg = positive for *Echinococcus granulosus* worms after arecoline treatment. Dog copAg +Eg = positive in ELISA for *Echinococcus* coproantigens. The distance from east (E) to west (W) is approximately 2 km.

negative were positive for *Echinococcus* coproantigen. The coproantigen ELISA was found to be 100% sensitive in detecting dogs in La Paloma when purge worm numbers were >20.<sup>28</sup> Therefore, the total prevalence of canine echinococcosis in La Paloma dogs was considered to be 24.8% (31 of 125).

**Distribution of human and canine echinococcosis in La Paloma.** Twenty-one (52.5%) of the human CE cases detected occurred in just five of the 39 *manzanas* or house blocks (i.e., *manzana* 1, 3, 9, 13, and 34), which collectively owned 41 dogs of which nine (22%) were infected (purge and/or coproantigen positive), and also included 18 dogs seropositive for *Echinococcus* antibodies. In addition eight of the human CE cases (20%) resided in five *manzanas* that owned at least one heavily infected dog, i.e., with individual purge worm counts >100.

Figure 2 shows the basic plan of La Paloma with location (by *manzana*) of human CE cases and positive dogs (purge, coproantigen, or arecoline positive). A significantly larger number of CE cases ( $n = 28$ ) occurred in the east side of the town compared with the west side (12 CE cases). The

east and west sides had respective populations of 624 and 728. At the *manzana* level, there was a weak but statistically nonsignificant positive correlation ( $r = 0.68$ ) between the percentage CE cases and of currently infected dogs. At the household level, only single family members were diagnosed with CE in the majority of them (32 cases in 32 households). Four separate households each harbored two family members with CE. None of the four households with two CE cases owned dogs that were currently positive for *E. granulosus* (arecoline or coproantigen) at the time of survey; however, all four households were situated in house blocks (*manzanas* 3, 8, 9, and 34 containing a total of 257 people, 30 dogs, and 15 CE cases) in which *E. granulosus*-infected dogs were found (i.e., a total of seven dogs in three *manzanas* with two parasitologically positive dogs, and one *manzana* with one positive dog). *Manzana* 34, in addition to having two currently infected dogs, contained an additional seven seropositive dogs. These four households were also situated in the same general locality within the east part of the town and, interestingly, in the vicinity of the butcher's shop. Despite these observations, statistical analysis showed

that there was no increased risk of newly diagnosed CE in families with currently infected dogs. Furthermore, there was no statistically significant clustering of CE cases within families or manzanas.

#### DISCUSSION

Despite the fact that CE caused by infection with the tapeworm *E. granulosus* is one of the most serious and geographically widespread of the parasitic zoonoses, very little is known about its public health importance and epidemiology within defined endemic communities. Cyclical transmission of the parasite between domestic dogs and sheep in pastoral areas, usually associated with home slaughter, is responsible for maintaining the infection in most endemic regions.<sup>1</sup> Human CE is often considered an occupational public health problem for sheep farmers, ranchers, or shepherds in endemic regions.<sup>36</sup> It is probable, however, that there is a risk of infection from dog contact, dog feces, or food contaminated with *E. granulosus* eggs for any individual residing in an endemic area. To date, few studies have sought to quantify both human and dog infection rates<sup>17</sup> as well as distribution within a single community. This was the purpose of the current study in the town of La Paloma, in the Department of Durazno (central Uruguay), which is an area of known high endemicity.<sup>3,6</sup>

The finding of an overall total prevalence of human CE in a single rural Uruguayan town (La Paloma), of 5.6% (64 of 1,149), is one of the highest in the world, and confirms older surgical records that CE is still a serious public health problem in the Department of Durazno.<sup>12</sup> Forty of these CE cases in the town were new diagnoses (3.5%) and most were totally asymptomatic. The age prevalence rate increased from 0% in the 0–3-year-old age group to nearly 12% in the group > 70 years of age. This age prevalence distribution appears to be characteristic of human CE in the majority of endemic areas and probably reflects slow growth of cysts, continued exposure, and poor immunity against an established hydatid cyst.<sup>24</sup> The La Paloma population sample, however, showed a significant peak in the 20–29-year-old age group. The reason for this is not clear and it could be just an artifact; however, this age group might have more contact with dogs both within the town and possibly on the surrounding sheep ranches (*estancias*). The prevalence of ultrasound-detected CE among the 514 people who resided in the rural area around La Paloma was 3.9%, which was similar to that for La Paloma residents (3.6%). It would appear, therefore, that the risk of CE is the same for both town residents and those in rural homesteads.

Portable ultrasound was very effective in abdominal scanning for CE as has previously been described by others in community based mass screening projects in regions of Kenya, Uruguay, and Tunisia.<sup>13,20,21</sup> In the current study, the majority of all types of cysts detected were univesicular. The differential diagnosis between Type I CE and nonhydatid (simple) cysts is difficult. Serology is useful in this differential diagnosis. The majority of the cystic images were univesicular (Type I) (28.3%) or solid cystic masses (Type IV) (33.3%), which is not necessarily characteristic for CE. A significant proportion of them, however, were seropositive against hydatid fluid antigen(s), i.e., 71% and 63%, respec-

tively. Twenty of the 37 Type I and Type IV cases were surgically treated by 1994 and antibody positivity (by ELISA) was important in confirmation of hydatidosis prior to surgery in 16 (80%). In a known endemic country such as Uruguay, multiple cystic masses (Type VI) in the liver and/or other organs are highly likely to be CE and tend to be highly seroreactive. In the current study, 88% of such cases were seropositive. However, persons with multiple cysts made up only 15% (9 of 60) of detected CE cases. The most characteristic ultrasound image presentation for CE are Types II and III but comprised only seven (11.7%) of 60, although all were seropositive. All but one of the 15 Type II, III, and IV CE patients from La Paloma who underwent surgery in 1994 were seropositive by ELISA. Although the natural history of human CE is poorly characterized, a number of asymptomatic cases may be expected to spontaneously regress and present as a calcified or a partially calcified image on ultrasound (Type V). Seven such cases (11.7%) were identified in the current study and four (67%) of the six Type V cases serologically tested were antibody positive.

Serologically, ELISAs were more sensitive (60–63%) than the immunoblot test. In the latter, the low molecular weight antigen B subunits (i.e., 8 of 12, 16, 24 kD) were detected, which gives a sensitivity of 40%. Other groups have commented on the low sensitivity of antigen B subunit recognition in immunoblotting;<sup>16,33,37</sup> however, the advantage of the immunoblot test lies in its high specificity.<sup>16,32</sup> The serologic confirmation by immunoblot of 12.5% (6 of 48) of the case sera that were seronegative by ELISA indicates the usefulness of the test. The IgG subclass analysis in human CE has indicated significantly elevated levels of both IgG1 and IgG4 antibodies.<sup>30</sup> Furthermore, IgG4 appears to be indicative of advanced/active CE while IgG1 levels are more likely to be elevated in asymptomatic cases.<sup>38</sup> The IgG subclass analysis in the current study also supported these observations with significantly more new asymptomatic CE cases seropositive for IgG1 compared with IgG4 (28% versus 21%). The numbers of CE cases in each pathologic group defined by ultrasonography (i.e., Types I–VI) were not large enough to accurately analyze IgG1/IgG4 reactivity related to cyst pathology, or for age-specific pathology, but this may be important in describing the natural history of human CE.

It is surprising that the relationship between infected dogs and human CE cases has never been seriously investigated in any endemic settled pastoral community. In La Paloma village, the total parasitologic prevalence of canine echinococcosis in 117 dogs was 19.7%. The inclusion of eight coproantigen-positive but arecoline purge-negative dogs would indicate a total prevalence of 24.8%. The coproantigen ELISA for *Echinococcus* has been shown to be highly specific (> 95%) and very sensitive (100%) when purge worm counts were > 20.<sup>27,28</sup> Previous arecoline purge studies for pre-mortem diagnosis of canine echinococcosis throughout Uruguay have indicated a canine *Echinococcus* prevalence of approximately 10%.<sup>7</sup> Analysis of dog infection rates and respective human CE rates by house block (*manzana*) did not show a significant positive correlation. Dogs have a significantly reduced longevity compared with humans and the adult tapeworm is considered to have a maximum life span of only two years, while human hydatid cysts probably de-

velop over several years. Dogs are also mobile and may wander significantly within a community. Close human contact with infected dogs over a relatively long period is probably important in transmission of *E. granulosus* as was indicated by a detailed observational study in the Turkana District of Kenya.<sup>39,40</sup> In that study, females were significantly more at risk of infection than males. This was not observed in the La Paloma community where CE cases were evenly divided between sexes. Overall, >50% of the human CE cases were distributed in only 13% of *manzanas*, or house blocks, where more heavily infected dogs were also recorded. This suggests that a subpopulation of dogs may have greater access currently (and historically) to infected sheep offal due either to habitual feeding by owners or to active scavenging around butchers' slaughter areas. Finally, the distribution of CE within households appeared to be random, with the vast majority of affected households containing only one CE case. This is consistent with a finding in Tunisia in which the family members of surgically confirmed CE cases were no more likely to be serologically positive for CE than individuals from families that did not have surgically confirmed CE.<sup>41</sup> There are relatively few reports in the literature of CE within extended families.<sup>42</sup> Host genetic or immunologic factors could be involved in susceptibility to infection with *Echinococcus*, and/or the nature of human-dog contact. Recent evidence in human alveolar echinococcosis (due to *E. multilocularis*) suggests a possible HLA association for disease expression.<sup>43</sup> It is also known that significant protective anti-oncosphere immune responses occur in sheep against *E. granulosus* infection,<sup>44</sup> and a role for resistance based on antibody-mediated complement-dependent killing of *E. granulosus* in humans has been suggested to occur in endemic areas.<sup>45</sup>

In conclusion, human CE is an important endemic disease in rural communities in Uruguay and probably in other endemic regions of South America. Even within relatively well-developed rural towns, transmission of *E. granulosus* clearly occurs, as well as on sheep farms or ranches. Therefore, humans are at risk of infection in both types of communities. A combination of mass abdominal scanning by ultrasound with serologic testing is currently the most effective approach to identify asymptomatic patients. Additional inclusion of microfilm chest radiographs in CE surveys would enable detection of pulmonary cases.<sup>19</sup> It is also suggested that pathologic characterization of hydatid cysts using ultrasound in community-diagnosed patients will help in the description of the natural history of human CE.

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