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Helicobacter pylori Infection in the Colombian Andes: A Population-based Study of Transmission Pathways

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In 1992, the authors studied *Helicobacter pylori* infection and exposures relevant to person-to-person, waterborne, foodborne, and zoonotic transmission in a census sample of 684 2–9-year-old children in Aldana, Nariño, a rural community in the Colombian Andes. *H. pylori* prevalence, as determined by the ^{13}C-urea breath test, was 69%, and prevalence increased from 53% in 2 year-olds to 87% in 9 year-olds. Beginning at 3 years of age, a higher percentage of males compared with females were infected. Odds ratios were estimated by multivariate logistic regression to control for mutual confounding by transmission-pathway proxy variables and socioeconomic indicators. Among transmission-pathway proxies, the strongest predictor of *H. pylori* status was the number of persons who lived in the home, with the number of children apparently being of greater importance than the number of adults. Swimming in rivers, streams, or pools increased the odds of infection, as did using streams as a drinking water source. Children who frequently consumed raw vegetables were more likely to have the infection, and children who had contact with sheep also had increased prevalence odds. Because the results did not implicate a single mode of transmission, the possibility of multiple pathways is indicated. *Am J Epidemiol* 1996;144:290–9.

child; diet; *Helicobacter pylori*; hygiene; infection; socioeconomic status; transmission

Since its identification in 1982 (1), overwhelming evidence has implicated *Helicobacter pylori* as an etiologic component of chronic gastritis, peptic ulcer, and gastric cancer (2–8). Successful control of this chronic infection would reduce the occurrence of gastritis and peptic ulcer, and it might substantially lower the rates of one of the world's deadliest neoplasms. Given the public health impact of *H. pylori* infection, attention must be given to identification of preventive measures. Contrary to their success in developed countries, anti-*H. pylori* therapies have proven much less successful in populations where this infection is most prevalent (9, 10), presumably in part due to reinfection (11, 12). The means of preventing reinfection have not been identified, because the mode of transmission remains unknown (13).

Knowledge regarding the epidemiology of *H. pylori* stems largely from seroprevalence studies. Studies designed to observe the incidence of *H. pylori* infection have been limited due to difficulties in identifying incident cases (10). Symptoms of acute infection comprise common forms of gastric discomfort (14); infection is thought generally to lead to chronic gastritis, which is frequently asymptomatic. Furthermore, the inadequate sensitivity of available techniques for detecting *H. pylori* in material other than gastric tissue has presented obstacles to pinpointing portals of entry and exit, and to identifying or ruling out environmental reservoirs. Most researchers believe that infection occurs through person-to-person transmission (15, 16). Evidence to support both fecal-oral and oral-oral routes has been reported (17–21), while other findings support the possibility of waterborne transmission (22–26).

When we were considering an *H. pylori* transmission intervention designed to discriminate between person-to-person and waterborne routes, our review of the literature revealed a lack of solid evidence to rule

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Abbreviations: CI, confidence interval; *H. pylori*, *Helicobacter pylori*; OR, prevalence odds ratio.

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out other modes of transmission (13). We therefore decided to conduct a population-based study of *H. pylori* prevalence and exposures related to a range of infectious disease transmission routes for the purpose of refining hypotheses in regard to *H. pylori* transmission.

MATERIALS AND METHODS

Population

We conducted this study in 1992 in the rural municipality of Aldana, Nariño, in the southern Colombian Andes, a region with gastric cancer rates that rank among the highest in the world (27, 28) and an estimated *H. pylori* prevalence of 93 percent in asymptomatic adults (2). At an altitude of 3,010 m, Aldana has an average temperature of 10°C. The 1992 population comprised 844 households with 4,447 inhabitants, 35 percent of whom were under 15 years of age. Nineteen percent of the population lived in close quarters in an urban nucleus. The Nariño Health Department supports a health care center in Aldana with a physician, a nurse, a dentist, an auxiliary nurse, and a dental hygienist, who each commute from Ipiales, a neighboring city on the Colombia-Ecuador border, as well as a sanitary engineer, five health promoters, a receptionist, and an ambulance driver, who each reside in Aldana. This team collected the data for this study.

Design

This investigation employed a cross-sectional design based on a census sample of 2–9-year-old children. Because nearly all adults in this population are infected, we selected the youngest children that could feasibly be studied (children under age 2 years generally require special techniques for collection of breath samples). The data were collected during 1992 in three phases: 1) a household survey of observable transmission-related exposures, conducted in all Aldana homes as part of the annual health department census in February and March; 2) an interview of the mothers or primary caretakers of participating children carried out in April to July; and 3) screening of the children for *H. pylori* infection by the ^{13}C-urea breath test in June to September.

Study population

The children targeted for inclusion were all residents of Aldana born between February 1, 1983 and August 1, 1990, and aged 2.0–9.5 years at the time of *H. pylori* testing. Subsequent verification of the annual census yielded the age and sex for 4,447 inhabitants of all 844 Aldana households. In this way, we determined that 6 percent of the households had not been detected by the census. Birth documents of all 1–9 year-olds identified by the census were examined to determine eligibility. Of the 892 children in this age group, 40 were not identified by the census and thus were not screened for eligibility.

A total of 746 children were born within the cutoff dates (including 32 whose ages were unverified). Of these, 685 (92 percent) completed participation in the study, 29 (4 percent) migrated from Aldana before participation was completed, and 32 (4 percent) were not identified in time to participate. No family refused participation. The resulting study population included 95 percent of eligible urban children and 91 percent of eligible rural children. One child's breath test was destroyed in processing, leaving a total of 684 children in the analysis.

Definition of *H. pylori* status

H. pylori status was determined by the ^{13}C-urea breath test (29, 30). The following protocol was observed: a baseline breath sample was obtained in a breath collection bag (younger children) or a syringe (older children) and then injected into a 20 ml vacutainer; consumption of bread and butter was followed by a 2.5 mg/kg oral dose of ^{13}C-urea diluted in a glucose polymer solution; and two additional breath samples were taken 20 and 40 minutes later. Breath samples were shipped to Louisiana, where the urea-derived $^{13}CO_2$ was measured by gas-isotope-ratio mass spectrometry. A positive result was defined by an increase in the $^{13}C/^{12}C$ isotope ratio value of 6/1,000 over baseline, as recommended by Graham and Klein (30), on either of the subsequent breath samples. Care was taken not to test any child within a week of ingesting oral antibiotics. Repeat samples using an alternate collection method (bag or syringe) were obtained from 33 children to assess the reliability of collection and transport; identical results were obtained for 32 of 33 children (97 percent).

Reported sensitivities and specificities for this test range from 94–100 percent and 93–100 percent, respectively, in persons not recently treated with antibiotics (29, 31–33). Validation of this test in Andean children has not been reported. The ^{13}C-urea dose varies across studies, because it has been shown over time that smaller doses produce valid results (30). A dose of 2 mg/kg of ^{13}C-urea in 95 Belgian children produced a sensitivity of 96 percent and a specificity of 93 percent with culture as the gold standard (31).

Transmission-pathway proxy variables

Person-to-person, waterborne, foodborne, and zoonotic transmission hypotheses were evaluated by estimating the effects on *H. pylori* prevalence of proxy variables that would be expected to increase the probability of infection given a particular mode of transmission. Aldana's drinking water comes from three primary sources: 1) private ground wells or pumps; 2) an aqueduct that carries local spring water to tanks, where it is treated with aluminum sulfate and calcium hypochlorite, and then to taps in the urban center and proximal sectors; and 3) local streams. Some children swim on occasional warm afternoons in the local river or streams. Nearby towns have commercially operated swimming pools. Raw vegetables are a potential vehicle of waterborne transmission, because they may be contaminated by irrigation water or unpurified water used for washing. Homes in the urban nucleus have toilets that drain into local sewage pipes. Most homes in the rural sectors have private latrines; families with no disposal facility use the fields behind their homes.

Background covariates

H. pylori infection has been linked to poor socioeconomic conditions and in particular to residential crowding (13). Beyond this, little information on specific risk factors exists. Correlates of transmission-pathway proxy variables that could conceivably influence *H. pylori* infection were evaluated as potential confounders: socioeconomic indicators, including household income, parents' occupation, parents' education, livestock ownership, and source of cooking fuel; health indicators, including anthropometric measures, recent history of illness, aspirin intake, and selected components of diet, such as consumption of coffee, herbal tea, milk, fruits, and vegetables.

Analysis

All study factors were examined initially using stratified analysis to observe dose-response patterns. Maximum likelihood logistic regression was used to estimate prevalence odds ratios adjusted by selected covariates. Product terms were added to the models to obtain age- and sex-specific estimates. Because the study population included sets of siblings and the outcome is contagious, the data were presumed to violate the standard logistic regression assumption of independent response probabilities across observations. To avoid potential underestimation of standard errors (34), odds ratios were estimated using the logistic-binomial random effects model for distinguishable data from the EGRET software package (35). This model includes a random effects parameter, based on the variability of average outcome probabilities across households, which measures a residual household effect on the probability of having *H. pylori* infection. Odds ratios produced by this model were adjusted for the effect of household.

Each of the transmission-pathway proxies and background covariates correlate with several others. Therefore, we constructed a model that included variables with odds ratios outside the 0.7–1.5 range or p values less than 0.2 to control for mutual confounding. In the case of highly colinear or redundant factors, those that appeared to have the strongest independent effects were retained in the full model. Variables that showed dose-response trends were retained even if p values became large. Because the aim of this investigation was to detect factors of potential consequence to *H. pylori* infection in order to inform subsequent investigations, we chose not to perform a traditional adjustment for multiple comparisons, because this would increase the probability that we would overlook a potentially important variable (36).

RESULTS

Table 1 lists the factors included in the model used to adjust the reported odds ratios.

Household effect

The effect of household can be viewed as the degree to which the probability of being infected depends on the *H. pylori* status of the cohabitating children who participated in the study. The random effects parame-

TABLE 1. Full model of exposure effects on *Helicobacter pylori* prevalence in 2–9-year-old children in Aldana, Nariño, Colombia, 1992

Person-to-person exposures
No. of children in home
No. of adults in home
Presence of ≥50 year-olds in home
Shares drinking cups
Mother's handwashing habits after cleaning child's feces
Location of latrine relative to handwashing facility
Waterborne exposures
Raw vegetable consumption
Lifetime drinking water source
Swims in rivers
Swims in swimming pools
Zoonotic exposure
Cares for or plays with sheep
Background covariates
Age
Sex
Principal household occupation
Mother's occupation
Rabbit ownership
Height-for-age percentiles (international growth curve)
Fruit and vegetable intake
Milk intake
History of amebiasis
Random effects
Residual effect of household membership

ter reflects the residual effect of household beyond that accounted for by the variables in the regression model. Table 2 presents coefficients of the household random effects parameter for five models. Comparison of the likelihood ratio statistics for this parameter across these models showed that the background covariates accounted for a large part of the overall household effect and the transmission-pathway exposures accounted for much of the remaining household effect. The full model, nevertheless, revealed a substantial residual effect of household beyond that accounted for by all of the modeled transmission pathway proxies and background covariates.

Background covariates

Sixty-nine percent of the children had positive breath tests, increasing from 53 percent of 2 year-olds to 87 percent of 9 year-olds (table 3). By age 3 years, the increase became greater in males compared with females. This sex difference persisted when adjusted for factors included in the full model (table 4), however, the summary odds ratio masks the effect of sex across age levels: odds ratios for males compared with females were 1.0, 1.7, 2.7, and 4.7 among children aged 2–3, 4–5, 6–7, and 8–9 years, respectively; the likelihood ratio statistic p value for entering the product term for age (in continuous form) and sex in the full model was 0.015.

Of the socioeconomic indicators examined, those that predicted *H. pylori* status were parents' occupation and rabbit ownership (table 4). Principal household occupations (the highest status occupation among adult household members) included farmers/cattle ranchers (51 percent), field workers (22 percent), non-agricultural laborers (19 percent), merchants (3 percent), paraprofessionals/professionals (2 percent), and unemployed (3 percent). In relation to *H. pylori* prevalence, these groups collapsed into a dichotomy of agricultural and non-agricultural trades, and children of non-farming households had higher odds of infection. Children whose mothers were gainfully employed had lower odds of infection compared with children whose mothers had no earnings, particularly if the mothers were health promoters or government-supported child care providers. Livestock, which may provide a source of supplemental income, tended to reflect protective effects, particularly for rabbits (raised as food). Consumption of two or more daily servings of fruit and vegetables showed a 10-fold decrease in prevalence odds. Other background covariates that appeared to be protective were consumption of milk, tall stature compared with peers of the same age, and a history of amebiasis in the preceding year.

TABLE 2. Multiple logistic regression models for residual effect of household on *Helicobacter pylori* prevalence in 2–9-year-old children in Aldana, Nariño, Colombia, 1992

Model*	Household random effects parameter		
	β ± SE†	Likelihood ratio statistic	*p* value
1. Age and sex	1.731 ± 0.295	32.49	<0.001
2. Background covariates	1.370 ± 0.291	15.53	<0.001
3. Background covariates + waterborne exposures	1.343 ± 0.297	13.99	<0.001
4. Background covariates + person-to-person exposures	1.169 ± 0.283	9.69	<0.001
5. Full model	1.065 ± 0.291	7.04	0.004

* Variable groups as defined in table 1.
† SE, standard error.

TABLE 3. *Helicobacter pylori* prevalence by age and sex in 2–9-year-old children in Aldana, Nariño, Colombia, 1992

Age (years)	Females		Males		Prevalence in both sexes
	No.	Prevalence	No.	Prevalence	
2	37	0.57	40	0.50	0.53
3	50	0.56	47	0.60	0.58
4	47	0.57	54	0.65	0.61
5	55	0.64	43	0.79	0.70
6	56	0.73	43	0.84	0.78
7	46	0.72	36	0.81	0.76
8	54	0.74	38	0.90	0.80
9	20	0.75	18	1.00	0.87
2–9	365	0.66	319	0.73	0.69

Person-to-person transmission

Family composition attributes. Attributes of family composition revealed striking effects on *H. pylori* prevalence (table 5); most notably, the total number of persons who lived in the home showed a positive dose-response gradient. Given that all but nine of the children lived in homes with at least two adults, the number of children appeared to be a stronger determinant of infection than did the number of adults. Birth order (among all children who lived in the home) showed a moderate effect independent of the number of children, with which it correlated highly. When birth order was not adjusted for the number of children, compared with firstborn, the odds ratios were 1.9 (95 percent confidence interval (CI) 1.0–3.4) for second children and 2.3 (95 percent CI 1.2–4.4) for third through ninth children. The number of children in the home appeared to be a stronger predictor of *H. pylori* status than birth order; adjustment for the latter yielded odds ratios of 2.2 (95 percent CI 0.9–5.2) for 1–2 siblings compared with none and 2.7 (95 percent CI

TABLE 4. Effects of background covariates on *Helicobacter pylori* prevalence in 2–9-year-old children in Aldana, Nariño, Colombia, 1992

Covariate	No.	Unadjusted		Adjusted by full model†	
		OR*	95% CI*	OR	95% CI
Age 2–9 years	684	1.3	1.2–1.4	1.3	1.2–1.5
Sex					
Female	365	1.0		1.0	
Male	319	1.4	1.0–2.0	1.9	1.2–3.0
Principal household occupation					
Farming	500	1.0		1.0	
Nonfarming	184	1.5	1.0–2.2	2.6	1.4–4.7
Mother's occupation					
Not employed outside home	605	1.0		1.0	
Employed, other occupations	63	0.5	0.3–0.9	0.4	
Employed, health/child care	16	0.2	0.1–0.5	0.1	0.0–0.7
Rabbit ownership					
Household does not have rabbits	617	1.0		1.0	
Household has rabbits	67	0.5	0.3–0.8	0.3	0.1–0.6
Milk					
<½ cup/day	112	1.0		1.0	
½–4 cups/day	572	0.6	0.4–1.0	0.5	0.3–1.1
Fruits & vegetables					
½–1½ servings/day	47	1.0		1.0	
2–12 servings/day	637	0.1	0.0–0.5‡	0.1	0.0–0.3‡
Height-for-age percentile					
<1st percentile	139	1.0		1.0	
1st–9th percentile	266	0.9	0.6–1.5	1.0	0.5–1.9
10th–25th percentile	140	0.7	0.4–1.2	0.6	0.3–1.4
26th–99th percentile	139	0.6	0.3–0.9	0.5	0.2–1.1
Amebiasis					
No history in preceding year	658	1.0		1.0	
History in preceding year	29	0.3	0.1–0.7	0.2	0.1–0.8

* OR, prevalence odds ratio; CI, confidence interval.
† As listed in table 1.
‡ Estimates rounded to two decimal places: unadjusted OR = 0.14, 95% CI 0.04–0.46; adjusted OR = 0.09, 95% CI 0.03–0.33.

0.8–9.2) for 3–8 siblings compared with none. Presence of household members 50 years of age or older revealed a protective effect; an increasing number of generations weakly increased the odds of infection, however.

Oral-oral transmission. Drinking from unwashed cups previously used by another person increased the odds of *H. pylori* infection (table 6). Nearly all children were reported to use toothbrushes, and toothbrushes were observed in nearly all homes; however, there was no clear association between toothbrush use and *H. pylori* infection. Almost no sharing of toothbrushes was reported to occur. The frequency of vomiting in the home was not clearly related to *H. pylori* positivity.

Fecal-oral transmission. Children whose mothers rarely used soap to wash their hands after cleaning their children's feces had increased odds of *H. pylori* infection (table 6). Compared with children who lived in homes where the latrine was less than 25 m from the nearest handwashing facility, those whose latrine was further away had moderately increased prevalence odds; those whose homes had no latrine were also more likely to be infected.

Person-to-person proxy variables that did not show clear associations with *H. pylori* infection included school or group care attendance, sanitary condition of the home, household cleaning tasks, availability of soap, use of soap or hot water to clean dishes, and child's handwashing habits.

Waterborne transmission

Children who swam in rivers, streams, or swimming pools a few times a year or more had greater than three times the odds of *H. pylori* infection compared with children who swam less often (table 6). The number of raw vegetables eaten per day showed a positive dose-response effect that became even stronger when adjusted for the protective effect of total fruit and vegetable consumption. In particular, frequent consumption of lettuce increased the odds of infection. In terms of drinking water source, children whose families had always used private pumps or ground wells

TABLE 5. Effects of family composition attributes on *Helicobacter pylori* prevalence in 2–9-year-old children in Aldana, Nariño, Colombia, 1992

Variable	No.	Unadjusted		Adjusted by family composition attributes† and household effect		Adjusted by full model‡	
		OR*	95% CI*	OR	95% CI	OR	95% CI
No. of persons							
3§	30	1.0		1.0		1.0	
4–5	212	1.9	0.9–4.0	2.8	0.9–9.2	3.7	1.2–11.4
6–8	287	2.5	1.2–5.4	6.4	1.9–21.9	6.3	1.9–20.5
9–15	155	2.9	1.3–6.4	9.2	2.4–36.2	8.0	2.2–28.9
No. of children							
1	64	1.0		1.0		1.0	
2–3	341	1.8	1.0–3.0	2.5	1.1–5.7	2.4	1.1–5.4
4–9	279	2.8	1.6–5.0	4.4	1.8–10.9	3.5	1.5–8.4
No. of adults							
1–2‖	300	1.0		1.0		1.0	
3	109	1.0	0.6–1.6	1.3	0.6–3.0	1.6	0.7–3.5
4–11	275	1.1	0.8–1.6	2.5	1.2–5.4	2.7	1.3–5.6
≥50 year-olds							
0	424	1.0		1.0		1.0	
1–3	260	0.6	0.5–0.9	0.3	0.2–0.7	0.3	0.1–0.6
Birth order							
1	175	1.0		1.0		1.0	
2	204	1.5	1.0–2.3	1.2	0.6–2.3	1.5	0.7–2.9
3–9	305	1.8	1.2–2.7	1.0	0.5–2.2	1.6	0.7–3.6

* OR, prevalence odds ratio; CI, confidence interval.

† Number of children, number of adults, presence of ≥50 year-olds; number of persons is not adjusted for number of children or adults since it is a linear combination of the two.

‡ As defined in table 1.

§ No households had fewer than three members.

‖ Only nine children lived in homes with one adult.

had the lowest *H. pylori* prevalence. Children whose families had used tap water during their lifetime appeared similar to well or pump users when factors in the full model were controlled. Children whose families had obtained their drinking water from local streams at some time during the child's life had increased prevalence odds.

Most Aldana families (84 percent) indicated that they boiled their drinking water, the only water purification method used in this community; 32 percent of the families reported that they initiated this practice during the preceding 3 years. (The Nariño Health Department has promoted this practice as part of its cholera prevention campaign.) No clear associations were observed between *H. pylori* prevalence and current or past water purification practices.

Foodborne factors

Aside from the effect of eating raw vegetables, no other evidence of foodborne transmission was encountered. Milk, eggs, and a small number of vegetables were the only raw foods reported. Refrigerator ownership did not appear to be protective in this population; however, only 43 children lived in homes that had a working refrigerator during their lifetime and most of these children resided in the urban center, where the *H. pylori* prevalence was high relative to other sectors.

Zoonotic exposures

Most Aldana families had dogs, chickens, pigs, and guinea pigs (raised as food) that lived in or around their homes. The families of nearly one-third of the children possessed cows, while 23 percent had cats, 11 percent had sheep, and 10 percent raised rabbits. Five percent or fewer had horses, turkeys, geese, ducks, pigeons, or parrots. Animals that were likely to live inside the homes included cats, dogs, chickens, and guinea pigs, although animals that lived indoors revealed no distinctive patterns of association with *H. pylori* infection relative to outdoor animals.

Odds ratios adjusted by the full model for ownership of individual animal types were in the 0.8–1.3 range, except for sheep (odds ratio (OR) = 0.6, 95 percent CI 0.3–1.3) and rabbits, as reported above (table 4). Direct contact with animals among children in Aldana were of two types—caring for them or playing with them, or both. Except for dogs, a small fraction of children had direct contact with other animal types. Odds ratios adjusted by the full model for contact with individual animal types were in the 0.9–1.3 range, except for contact with pigs, rabbits, and sheep. Con-

TABLE 6. Estimated effects of transmission-pathway proxy variables on *Helicobacter pylori* prevalence in 2–9-year-old children in Aldana, Nariño, Colombia, 1992

Variable	No.	Unadjusted		Covariates included in model: *Model 1*†: Transmission proxy variables		*Model 2*†: Model 1 + background variables		*Full model*†: Model 2 + household effect	
		OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Person-to-person exposures									
Shares cups									
Never	447	1.0		1.0		1.0		1.0	
Sometimes/often	237	1.5	1.0–2.1	1.4	1.0–2.1	1.7	1.1–2.6	1.8	1.1–3.1
Mother's handwashing‡									
Sometimes/always uses soap	260	1.0		1.0		1.0		1.0	
Rarely uses soap	88	2.4	1.4–4.4	2.5	1.3–4.8	2.3	1.1–4.6	2.7	1.1–6.6
Location of latrine relative to handwashing facility									
<25 meters distance	460	1.0		1.0		1.0		1.0	
≥25 meters distance	154	1.2	0.8–1.9	1.4	0.9–2.1	1.5	0.9–2.4	1.6	0.8–2.9
Household has no latrine	70	1.5	0.8–2.7	1.7	0.9–3.3	1.7	0.8–3.4	2.2	0.9–5.3
Waterborne exposures									
Raw vegetables									
0–1 servings/day	464	1.0		1.0		1.0		1.0	
2 servings/day	135	0.9	0.6–1.3	1.0	0.7–1.6	1.4	0.8–2.3	1.5	0.8–2.9
3–4 servings/day	84	1.3	0.8–2.3	1.3	0.7–2.3	1.8	0.9–3.4	2.0	0.9–4.6
Raw lettuce									
A few servings/year or less	212	1.0		1.0		1.0		1.0	
A few servings/month	299	1.2	0.8–1.7	1.0	0.7–1.6	1.0	0.7–1.6	1.1	0.8–2.0
Several servings/week	172	1.3	0.8–2.0	1.2	0.8–2.0	1.6	0.9–2.7	1.8	0.9–3.6
Swims in rivers/streams									
<Once/year	617	1.0		1.0		1.0		1.0	
A few times/year or more	67	3.1	1.5–6.4	2.9	1.4–6.2	2.8	1.2–6.3	3.3	1.2–9.4
Swims in swimming pools									
<Once/year	594	1.0		1.0		1.0		1.0	
A few times/year or more	90	1.9	1.1–3.3	2.4	1.3–4.3	2.8	1.4–5.6	3.6	1.5–8.5
Lifetime drinking water source									
Well/pump only	432	1.0		1.0		1.0		1.0	
Tap (at some time)§	185	1.3	0.9–1.8	1.4	0.9–2.2	1.1	0.6–1.9	1.0	0.5–2.0
Stream (at some time)	67	1.7	0.9–3.2	2.1	1.1–4.0	2.5	1.2–5.0	2.8	1.2–6.8
Zoonotic exposure									
Contact with sheep									
No contact with sheep	664	1.0		1.0		1.0		1.0	
Plays with/cares for sheep	20	4.1	0.9–17.9	3.2	0.7–14.5	3.9	0.8–18.8	4.5	0.7–30.5

* OR, prevalence odds ratio; CI, confidence interval.

† Model 1, person-to-person and waterborne exposures listed in table 1; Model 2, Model 1 + background covariates listed in table 1; Full model, as described in table 1.

‡ After cleaning children's feces among children whose mothers who report cleaning feces.

§ Children who have had tap and stream sources are classified as stream.

tacts with pigs (OR = 0.6, 95 percent CI 0.2–1.4) and rabbits (OR = 0.6, 95 percent CI 0.2–1.8) were linked to reduced prevalence odds. The 20 children who had contact with sheep revealed an excess *H. pylori* prevalence (table 6); this difference became even greater when the protective effect of sheep ownership was controlled (OR = 5.4, 95 percent CI 0.8–36.2).

Effect modification by age and sex

In general, these data provide insufficient power to detect statistically significant differences in age- or sex-specific odds ratios; however, consideration of stratum-specific effects may shed light on transmission. Factors that showed stronger effects in younger children included number of children in the home, birth order, mother's handwashing habits, absence of a latrine, lettuce consumption, and exposure to river or stream water. The factors that showed stronger effects in older children were the number of adults in the home, the presence of family members 50 years or older, the sharing of cups, the distance from the latrine to the handwashing facility, and swimming in pools.

Exposures that revealed stronger effects in girls included number of children in the home, the presence of family members 50 years or older, birth order, mother's handwashing habits, lettuce consumption, and swimming in pools. The exposures that appeared to be strongest for males were the number of adults in the home, the absence of a latrine, and exposure to river or stream water.

DISCUSSION

The strong effects of family composition attributes support the person-to-person transmission hypothesis, as does the residual household effect, which indicates that cohabitating children are likely to be concordant on infection status independently of the covariates examined in this analysis. The finding of waterborne exposures related to increased *H. pylori* prevalence odds, however, suggests the possibility of waterborne transmission.

Other investigations in Latin America have confirmed associations of water-related factors with *H. pylori* prevalence (25, 26). A study conducted in China, on the other hand, found a similar *H. pylori* prevalence in rural residents who drank river water compared with those who drank well water, although most respondents practiced the custom of boiling drinking water and storing it in a vacuum flask (37). *H. pylori* survives in aquatic conditions in the laboratory (23, 24, 38), and recent preliminary reports have documented its detection by polymerase chain reaction in water samples from Aldana (39) and Lima (40). Innovative detection techniques will permit more sensitive examination of additional environmental sources; however, it remains to be shown whether organisms detected in the environment are infective.

The effects noted for contact with sheep lack precision and the literature lacks evidence relevant to this observation. An elevated *H. pylori* seroprevalence has been observed in asymptomatic Sardinian shepherds (118/120; 98 percent) compared with dyspeptic patients (497/710; 70 percent), although relevant covariates were not considered (41). In relation to animal exposures, it must be noted that nonhuman *Helicobacter* species occasionally infect humans and the urea breath test cannot discriminate between urease-producing *Helicobacter* species that colonize the stomach. It has been estimated, however, that nonhuman *Helicobacter* species account for no more than one percent of human gastritis cases (42). In more than 3,000 gastric biopsy specimens we have examined from Colombian adults, including rural Nariño residents, we have observed only one infection (resembling *Helicobacter heilmani*) to be morphologically inconsistent with *H. pylori*; all strains recovered by culture from the Colombian specimens have been consistent with *H. pylori*.

An apparent disadvantage of this population is its sociocultural homogeneity, which reduces the variation in exposure status, thereby decreasing the power for detecting effects. This disadvantage may be offset to some degree by a reduction in the number of confounders that must be considered when comparing diverse groups. What this population does provide are clues to understanding why some children are infected sooner than others, as highlighted by the modifying effect of age observed for several study factors. The sex-specific effects suggest that boys may be more likely than girls to be infected outside the home; this may explain the higher prevalence in boys.

This study examined behaviors that are difficult to measure accurately and are therefore subject to nondifferential misclassification, an error that would tend to underestimate the magnitude of exposure effects. Exposures such as occupation, family composition attributes, drinking water source, location of latrine, and animal ownership that were observed directly or are common knowledge within the community should contain minimal misclassification. Another potential source of misclassification is respondents' concern for social appropriateness. Differential misclassification is a possibility because the mother's knowledge of health-promoting behaviors may influence responses, and knowledgeable mothers may employ behaviors that protect against *H. pylori*. For example, the protective effect of recent amebiasis may reflect a greater probability of *H. pylori*-negative children to have amebiasis diagnosed or to have mothers who recall this diagnosis, though some part of this effect may be due to antibiotic therapy used to treat amebiasis.

Although spontaneous elimination of *H. pylori* infection has been observed rarely in follow-up of prevalent cases among adults, follow-up of infants suggests that it may not be uncommon in young children (43). If spontaneous elimination occurs to an important degree among children, the general limitations of prevalence data apply to the reported findings; in particular, it is not possible to know whether an exposure influences the acquisition of infection or its chronicity. It is not likely, however, that infection status has influenced exposure to study factors given that a similar proportion of positive (16.2 percent) and negative (16.7 percent) children were reported to have experienced one or more gastritis symptoms for 3 months or longer; furthermore, an equal proportion (11 percent) of both positive and negative children were reported to have changed their diet as a result of stomach complaints.

Given the multiple correlations among the factors studied, it is difficult to determine whether the observed effect of an exposure reflects a role as an independent risk factor or is the result of residual confounding by inadequately measured determinants of infection. In light of this limitation, it is of interest to note that two waterborne factors linked to higher socioeconomic status, frequent consumption of raw vegetables and swimming in swimming pools, are associated with increased *H. pylori* prevalence odds, contrary to what one would expect if these results were due to confounding by factors linked to socioeconomic status.

The findings from this population-based study do not discriminate between person-to-person and waterborne transmission, the two pathways most supported by the *H. pylori* literature. The evidence presented favors both routes, confirming the inconsistencies of previous reports that failed to identify a singular mode of transmission. A potential explanation of these inconsistencies is that *H. pylori* is spread through multiple pathways. It must be recognized, however, that, in general, studies on *H. pylori* risk factors that have been reported to date have not adequately controlled for likely confounders, including hygienic practices, diet, antibiotic use, family composition, and population density. Investigations that control for such factors are needed to clarify further the mode of transmission of *H. pylori*.

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