Age-Specific *Helicobacter pylori* Seropositivity Rates of Children in an Impoverished Urban Area of Northeast Brazil

Anastasia Mitchell,¹ Terezinha M. J. Silva,² Leah J. Barrett,³ Aldo A. M. Lima,² and Richard L. Guerrant^{3*}

Department of Microbiology, University of Virginia,¹ and Center for Global Health, Division of Infectious Diseases and International Medicine, University of Virginia School of Medicine,³ Charlottesville, Virginia, and Federal University of Ceará, Fortaleza, Brazil²

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We determined age-specific *Helicobacter pylori* seropositivity rates of 166 children and 39 mothers in an urban shantytown in northeast Brazil. Seropositivity rates increased from 23.1% at 0 to 11 months of age to only 39.3% by 96 to 131 months of age and were 82.1% at maturity. We observed no correlation between the seropositivity of the mothers and the seropositivity of their children.

Accumulating evidence suggests that *Helicobacter pylori* is acquired in early childhood and infects more people in developing countries than in industrialized countries (1, 3, 4, 11). In impoverished areas of developing countries, the *H. pylori* seropositivity rate by 20 years of age has been shown to be more than 80%, much greater than the 30% seropositivity rate by 30 years of age in industrialized countries (3, 6, 18). Furthermore, a study of 141 adults showed no significant change in *H. pylori* infection rates from 1969 to 1990, suggesting that acquisition of

H. pylori in adulthood does not play a large role in the high seropositivity rates seen in developing countries (4).

In order to understand the transmission and health impact of *H. pylori* infection, a focus on early childhood infection is necessary (12). Our report presents new age-specific *H. pylori* seropositivity rates and suggests that neither mother-to-child nor waterborne transmission of the pathogen can account for whom is infected and when the infection occurs.

The subjects in this study live in Gonçalves Dias, a slum of

FIG. 1. Age-specific seropositivity rates of subjects living in an impoverished urban area of northeast Brazil increased to 39.3% by age 10, before reaching 82% by maturity. Most subjects in our study did not acquire *H. pylori* infection very early in childhood. n, number of samples.

* Corresponding author. Mailing address: Center for Global Health, Box 801379 HSC, University of Virginia School of Medicine, Charlottesville, VA 22908. Phone: (804) 924-5242. Fax: (804) 977-5323. E-mail: rlg9a@virginia.edu.

TABLE 1. *H. pylori* serology results for individuals with multiple samples (by age group)

Subject	Serology result with sample collected at age ^a :				
	0–11 mo	12–23 mo	24–59 mo	60–95 mo	96–131 mo
107/1	ND	–	ND	+	ND
107/2	–	ND	+	ND	ND
203/1	ND	ND	–	ND	–
204/1	ND	ND	–	ND	–
205/1	ND	ND	–	ND	+
210/1	+	+	+	+	ND
210/2	–	ND	+	ND	ND
215/1	+	+	+	+	ND
226/1	ND	–	ND	–	ND
231/1	ND	+	ND	–	–
303/2	ND	–	ND	–	ND
305/1	ND	ND	–	–	ND
307/1	ND	ND	–	ND	–
307/2	ND	ND	–	+	+
310/1	ND	ND	–	ND	–
312/1	ND	ND	–	ND	–
314/2	ND	–	ND	–	ND
317/1	ND	ND	+	ND	+
319/1	ND	–	+	ND	ND
320/1	ND	+	+	ND	ND
324/1	ND	ND	+	ND	+
325/1	ND	ND	–	ND	–
326/1	ND	ND	–	ND	–
327/1	–	–	+	ND	+
329/1	–	–	+	ND	–
331/1	ND	ND	–	ND	–
334/1	ND	ND	–	–	ND
336/1	ND	ND	–	ND	–
339/1	ND	–	+	ND	ND
343/1	ND	–	ND	–	ND
345/1	ND	–	ND	–	ND
349/1	ND	–	+	ND	ND
350/1	ND	–	–	ND	ND
403/1	–	–	+	+	+
411/1	–	+	ND	ND	ND
417/1	–	ND	+	ND	ND
432/1	ND	ND	ND	+	+
501/1	ND	ND	+	ND	–
502/1	ND	ND	–	ND	–
502/2	ND	ND	ND	+	+
507/1	ND	ND	–	ND	–
509/1	ND	ND	–	ND	–
515/1	ND	–	ND	–	ND
517/1	ND	–	ND	–	ND

^a Ages given are ranges. In the event that more than one sample per individual was available for a given age range, only the most recently collected sample was used for analysis. +, positive; –, negative.

Fortaleza, the capital city of Ceará, in northeast Brazil. Approximately 1,419 people live in this community, and all have the same impoverished socioeconomic status and lifestyle. They share a common water source and use only pit toilets for sanitation. The average household has seven people, which can include immediate and extended families as well as nonrelated individuals.

Sera from 205 people residing in Gonçalves Dias and previously enrolled in a cohort study of enteric infection(s) were available for this study (10a). In this retrospective study, sera previously collected from 166 children and 39 mothers were analyzed for immunoglobulin G antibodies against *H. pylori* by using the Premier *H. pylori* enzyme immunoassay (Meridian Diagnostics) as described by the manufacturer. In order to obtain a cross-sectional analysis of age-specific *H. pylori* seropositivity in this population, each sample was assigned to an age group according to the age of the subject at the time the sample was collected. When two samples from a subject fell into the same age range, we included only the more recent one for analysis. The number of samples per child ranged from 1 to

5, with an average of 1.39 samples per child. Due to the retrospective nature of this study, some individuals had more than one sample included in the study. Table 1 lists all of the included serology results for individuals with multiple samples analyzed.

Figure 1 presents the age-specific *H. pylori* seropositivity rates and the number of samples for each age group. Subjects 24 to 59 months old had a seropositivity rate of 37.8%, an increase from a rate of 23.1% for children 0 to 11 months old. By the time the children were 96 to 131 months of age, the *H. pylori* seropositivity rate had climbed to only 39.3%.

C. parvum infection rates in developing countries are high and are thought to be a measure of the contamination of drinking water. Both *C. parvum* and *H. pylori* have been isolated from water supplies, which potentially suggests a similar route of infection for both pathogens, i.e., contaminated drinking water (9). *H. pylori* has been detected in the stools of infected individuals by culture and PCR detection, which indicates the possibility of fecal-oral transmission and a potential source of water contamination (17; N. P. Mapstone, D. A. Lynch, F. A. Lewis, A. T. Axon, D. S. Tompkins, M. F. Dixon, and P. Quirke, Letter, Lancet **341**:447, 1993). Indeed, a study by Klein et al. demonstrated an association between the prevalence of *H. pylori* in Peruvian children and their source of drinking water (9). Most of the adults and 75% of the children living in the community in our study were infected by *C. parvum*, and most of the children acquired the infection in the first year of life (14, 19).

The high rates of *C. parvum* infection in our study population suggest that the subjects in our study were drinking unclean water. If *H. pylori* was transmitted with equal efficacy as *C. parvum* in the drinking water, the subjects would also be exposed to and, presumably, infected by *H. pylori* early in life. In contrast to their acquisition of *C. parvum* in the first year of life, most of our subjects were not infected by *H. pylori* until later in childhood. This suggests that either *H. pylori* is less efficiently transmitted by water than *C. parvum* or that water-borne transmission of *H. pylori* is not the most important route and that alternative routes of *H. pylori* acquisition, such as other environmental or personal exposures, may be important.

Low socioeconomic status has been strongly associated with the incidence of *H. pylori* infection (11). *H. pylori* infection tends to cluster in families and in people living in crowded or close conditions. For this reason, it is widely believed that impoverished children may acquire *H. pylori* through contact with their mothers (5, 10, 12, 14, 18). To test this idea, we compared the *H. pylori* serologic status of the mothers of the children enrolled in our study to that of the sera collected most recently from their children. The results for 26 women were compared to those of their 30 children, aged 5 to 114 months. The five children of the *H. pylori*-negative mothers ranged in age from 6 to 104 months, with a mean age of 50.2 months. The 25 children of the *H. pylori*-positive mothers ranged in age from 5 to 112 months, with a mean age of 36 months. We found no significantly greater incidence of *H. pylori* infection in the children of the infected mothers than in the children of the uninfected mothers. This initial result suggests that another mode of acquisition may be more important for *H. pylori* acquisition than mother-to-child transmission. However, due to the infrequency of adults without *H. pylori* infection in our

study population, more *H. pylori*-negative mothers and their children must be studied to draw any definitive conclusions. In addition, we are currently investigating the role of other familial relationships and cohabitation in *H. pylori* transmission.

In summary, children in an urban shantytown in northeast Brazil showed lower *H. pylori* seropositivity rates than have been reported in African studies but slightly higher rates than those reported from southern China (7, 8, 13, 16). The adult seropositivity rate (82.1%) was very similar to that reported in other developing areas (80%) (3, 6). As expected, the rates reported here were higher than the rates in industrialized countries (2, 15). Finally, our results indicate that transmission by routes other than waterborne or mother-to-child transmission may be important in childhood acquisition of *H. pylori*.

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REFERENCES

- Ashorn, M., M. Maki, M. Hallstrom, M. Uhari, H. K. Akerblom, J. Viikari, and A. Miettinen. 1995. *Helicobacter pylori* infection in Finnish children and adolescents. A serologic cross-sectional and follow-up study. *Scand. J. Gastroenterol.* **30**:876–879.
- Blecker, U., B. Hauser, S. Lanciers, S. Peeters, B. Suys, and Y. Vandenplas. 1993. The prevalence of *Helicobacter pylori*-positive serology in asymptomatic children. *J. Pediatr. Gastroenterol. Nutr.* **16**:252–256.
- Braga, L. L., B. J. Marshall, H. Moreno, A. A. M. Lima, D. Meneses, J. K. Roche, and R. L. Guerrant. 1995. *Helicobacter pylori*: gastritis, peptic ulcer and gastric cancer in developing countries, p. 127–147. In R. L. Guerrant (ed.), *At the edge of development: health crises in a transitional society*. Carolina Academic Press, Durham, N.C.
- Cullen, D. J., B. J. Collins, K. J. Christiansen, J. Epis, J. R. Warren, I. Surveyor, and K. J. Cullen. 1993. When is *Helicobacter pylori* infection acquired? *Gut* **34**:1681–1682.
- De Giacomo, C., L. Lisato, R. Negrini, G. Licardi, and G. Maggiore. 1991. Serum immune response to *Helicobacter pylori* in children: epidemiologic and clinical applications. *J. Pediatr.* **119**:205–210.
- Graham, D. Y., E. Adam, G. T. Reddy, J. P. Agarwal, R. Agarwal, D. J. Evans, Jr., H. M. Malaty, and D. G. Evans. 1991. Seroepidemiology of *Helicobacter pylori* infection in India. Comparison of developing and developed countries. *Dig. Dis. Sci.* **36**:1084–1088.
- Holcombe, C., B. A. Omotara, J. Eldridge, and D. M. Jones. 1992. *H. pylori*, the most common bacterial infection in Africa: a random serological study. *Am. J. Gastroenterol.* **87**:28–30.
- Holcombe, C., S. Tsimiri, J. Eldridge, and D. M. Jones. 1993. Prevalence of antibody to *Helicobacter pylori* in children in northern Nigeria. *Trans. R. Soc. Trop. Med. Hyg.* **87**:19–21.
- Klein, P. D., D. Y. Graham, A. Gaillour, A. R. Opekun, E. O. Smith, and the Gastrointestinal Physiology Working Group. 1991. Water source as risk factor for *Helicobacter pylori* infection in Peruvian children. *Lancet* **337**:1503–1506.
- Koch, K. L., D. J. Phillips, R. C. Aber, and W. L. Current. 1985. Cryptosporidiosis in hospital personnel. Evidence for person-to-person transmission. *Ann. Intern. Med.* **102**:593–596.
- Lima, A. M. M., S. R. Moore, M. S. Barbosa, A. M. Soares, M. A. Schleupner, R. D. Newman, C. L. Sears, J. P. Nataro, D. P. Fedorko, T. Wuhib, J. B. Schorling, and R. L. Guerrant. 2000. Persistent diarrhea signals a critical period of increased diarrhea burdens and nutritional shortfalls: a prospective cohort study in Northeastern Brazil. *J. Infect. Dis.* **181**:1643–1651.
- Malaty, H. M., and D. Y. Graham. 1994. Importance of childhood socioeconomic status on the current prevalence of *Helicobacter pylori* infection. *Gut* **35**:742–745.
- Malaty, H. M., J. G. Kim, S. D. Kim, and D. Y. Graham. 1996. Prevalence of *Helicobacter pylori* infection in Korean children: inverse relation to socioeconomic status despite a uniformly high prevalence in adults. *Am. J. Epidemiol.* **143**:257–262.
- Mitchell, H. M., Y. Y. Li, P. J. Hu, Q. Liu, M. Chen, G. G. Du, Z. J. Wang, A. Lee, and S. L. Hazell. 1992. Epidemiology of *Helicobacter pylori* in southern China: identification of early childhood as the critical period for acquisition. *J. Infect. Dis.* **166**:149–153.
- Newman, R. D., S. X. Zu, T. Wuhib, A. A. Lima, R. L. Guerrant, and C. L. Sears. 1994. Household epidemiology of *Cryptosporidium parvum* infection in an urban community in northeast Brazil. *Ann. Intern. Med.* **120**:500–505.
- Patel, P., M. A. Mendall, S. Khulusi, T. C. Northfield, and D. P. Strachan. 1994. *Helicobacter pylori* infection in childhood: risk factors and effect on growth. *BMJ* **309**:1119–1123.
- Sullivan, P. B., J. E. Thomas, D. G. Wight, G. Neale, E. J. Eastham, T. Corrah, N. Lloyd-Evans, and B. M. Greenwood. 1990. *Helicobacter pylori* in Gambian children with chronic diarrhoea and malnutrition. *Arch. Dis. Child.* **65**:189–191.
- Thomas, J. E., G. R. Gibson, M. K. Darboe, A. Dale, and L. T. Weaver. 1992. Isolation of *Helicobacter pylori* from human faeces. *Lancet* **340**:1194–1195.
- Webb, P. M., T. Knight, S. Greaves, A. Wilson, D. G. Newell, J. Elder, and D. Forman. 1994. Relation between infection with *Helicobacter pylori* and living conditions in childhood: evidence for person to person transmission in early life. *BMJ* **308**:750–753.
- Zu, S. X., J. F. Li, L. J. Barrett, R. Fayer, S. Y. Shu, J. F. McAuliffe, J. K. Roche, and R. L. Guerrant. 1994. Seroepidemiologic study of *Cryptosporidium* infection in children from rural communities of Anhui, China and Fortaleza, Brazil. *Am. J. Trop. Med. Hyg.* **51**:1–10.