

# *Helicobacter pylori* in the Canadian Arctic: Seroprevalence and Detection in Community Water Samples

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**OBJECTIVE:** Many North American arctic communities are characterized by risk markers associated with *Helicobacter pylori* (*H. pylori*) infection, including overcrowded housing and inadequate water supply and sanitation systems. Our aim was to determine the seroprevalence of *H. pylori* infection in two traditional Inuit communities in the central Canadian arctic and to test for the presence of *H. pylori*, by polymerase chain reaction (PCR), in local water supplies.

**METHODS:** Samples of venous whole blood from adults and capillary blood from children were collected and analyzed by enzyme immunoassay and Helisal Rapid Test, respectively, for IgG antibody to *H. pylori*. Antibodies to CagA were detected by enzyme immunoassay, and ABO and Lewis antigens were also determined. Demographic and clinical information were collected by questionnaire. Water samples from each community were tested for *H. pylori* by PCR.

**RESULTS:** One hundred-thirty (50.8%) of 256 subjects from the two communities were positive for *H. pylori* IgG antibodies. Seropositive subjects were more likely to be male, compared with seronegative individuals ( $p = 0.01$ ). Antibody status did not differ with respect to age, community, alcohol or cigarette use, number of persons per household, gastrointestinal complaints or previous investigations, medications, or presence of blood group O, Lewis a-b+. CagA antibodies were detected in 78 (61.9%) of 126 *H. pylori*-seropositive subjects tested; however, 41 (35.3%) of 116 *H. pylori*-seronegative subjects were also CagA positive. Water samples taken from the water delivery truck in Chesterfield Inlet and two lakes near Repulse Bay were positive for *H. pylori*.

**CONCLUSION:** The seroprevalence of *H. pylori* in the study group was higher than rates in southern Canadian populations, but lower than the seroprevalence previously docu-

mented in a Canadian subarctic Indian (First Nations) community. The detection of *H. pylori* in local water supplies may indicate a natural reservoir for the organism or possible contamination from human sewage. (Am J Gastroenterol 1999;94:1823-1829. © 1999 by Am. Coll. of Gastroenterology)

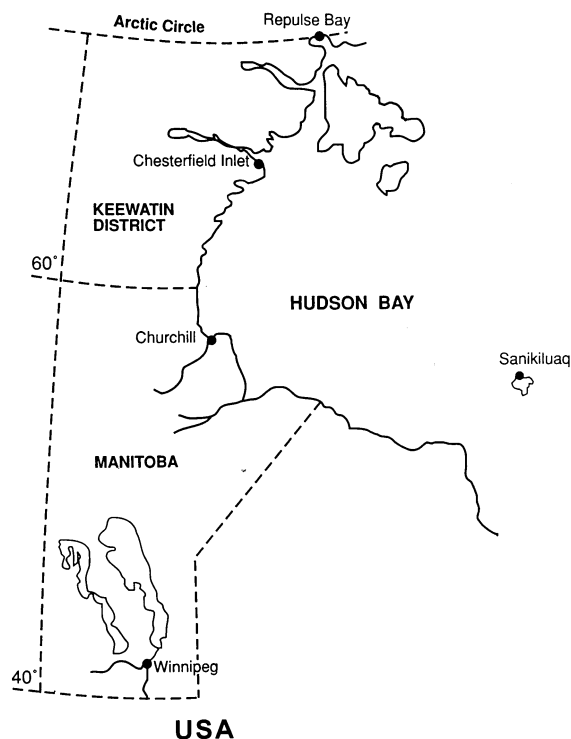
## INTRODUCTION

The prevalence of *Helicobacter pylori* (*H. pylori*) infection in northern Canadian and Alaskan populations is unknown. Many North American arctic communities are characterized by risk markers associated with *H. pylori* infection, including overcrowded housing and inadequate water supply and sanitation systems (1, 2). Yip *et al.* (3) demonstrated a high seroprevalence for *H. pylori* in an Alaskan Eskimo population, and reported a unique type of endoscopically diagnosed gastritis associated with iron deficiency anemia and heme-positive stools. In a Cree Indian (First Nations) Canadian subarctic community, 95% of tested subjects were seropositive for *H. pylori* and 85% of these individuals were positive for antibodies to the CagA antigen (4). Water samples from the local lakes in this study were negative for *H. pylori* when tested by polymerase chain reaction (PCR). Similar studies have not previously been performed in the Canadian Inuit population.

This study was undertaken to determine the seroprevalence of *H. pylori* infection in two traditional Inuit communities in the central Canadian arctic. Local water supplies were tested by PCR for the presence of *H. pylori* to investigate the possibility of an environmental reservoir for this organism.

## MATERIALS AND METHODS

In June and July 1997, subjects from the communities of Chesterfield Inlet (population: 340) and Repulse Bay (population: 560) were recruited to the study. These communi-



**Figure 1.** Chesterfield Inlet and Repulse Bay are located in the Keewatin District of the Canadian Northwest Territories.

ties are located on the western shore of Hudson Bay, in the Keewatin district of the Canadian Northwest Territories (Fig. 1). Ninety-five percent of the population in both communities are Inuit, and 43% are <15 yr of age. The people of both communities follow a traditional lifestyle of hunting and fishing.

Local health workers assisted in community education regarding the aims of the study, aiding patient recruitment, and providing language translation when required. Written informed consent was obtained from all subjects, and from parents or guardians of children who were enrolled. Subjects answered questionnaires regarding past or present medical history suggestive of gastrointestinal illness, medication, smoking of  $\geq 1$  cigarette daily, drinking any alcohol within the previous month, as well as information regarding housing, sanitation, and water supply. Subjects were asked whether they experienced heartburn or indigestion on a regular basis. Heartburn was defined as a sensation of warmth or burning located substernally, and was considered to occur regularly when experienced twice or more per week on an ongoing basis over the previous 6 months. Indigestion was defined as epigastric discomfort or upset stomach, and was considered regular if it occurred twice or more per month over the previous 6 months. Ethnic status was determined by subject self-identification.

Blood samples were collected by venipuncture for *H. pylori* antibody detection, as well as ABO and Lewis blood group antigen typing. Because venipuncture in children and

adolescents for research studies is not well accepted by the population, individuals <18 yr of age were offered *H. pylori* antibody testing through collection of capillary blood samples if they refused venipuncture.

The serum was separated, frozen, and transported by air to Winnipeg for *H. pylori* IgG antibody detection using the Pylori-Stat ELISA kit (Bio-Whittaker, Walkersville, MD; provided by Carter Wallace, Cranbury, NJ). CagA status was measured by serum ELISA using the CagA antigen (provided by Harry Kleanthous, OraVax Inc., Cambridge, MA) at a dilution of 1:100, following the method of Blaser *et al.* (5). Red cells were analyzed for ABO blood group antigens by the slanted capillary method (6) and confirmed by reverse typing sample serum against A, B, and O red cells. For Lewis antigen testing, monoclonal anti-Le<sup>a</sup> (Bio-carb AB, Carlisle, Scotland) and anti-Le<sup>b</sup> (Glasgow and West of Scotland Blood Transfusion Service) were used. For any sample typed as Le (a+b-) Le (a-b-), a fresh aliquot of cells was prepared and tested with a second anti-Le<sup>a</sup> and anti-Le<sup>b</sup> (Glasgow and West of Scotland Blood Transfusion Service). Capillary blood samples only were obtained from 14 patients  $\leq 13$  yr old. They were processed by Helisal Rapid Test (Cortecs, provided by Axcan Pharma, St. Hilaire, Que.) for IgG antibodies to *H. pylori*. This test is 95% sensitive for *H. pylori*, compared with serum ELISA (7). Blood samples for ABO and Lewis antigen testing were not available from these children.

Water samples were collected in a sterile plastic container, frozen at  $-20^{\circ}\text{C}$ , and transported to Winnipeg for DNA amplification. In Chesterfield Inlet water is pumped from a lake 4 km from town to a manmade reservoir 1 km from town, where it is chlorinated. Water is pumped from the reservoir to trucks and delivered to holding tanks in each household as needed. A second small lake in the town is used for swimming in the summer and some residents who do not like the taste of chlorinated water draw untreated drinking water directly from this lake. Three samples consisting of 4 L of water each were taken from the water delivery truck and the two lakes for *H. pylori* testing by PCR. In Repulse Bay, water is taken directly from a lake 3 km from town, chlorinated in a small pumping station adjacent to the lake, and delivered by truck to holding tanks in each household. Another lake within 1 km of the town is also used for swimming in the summer, and some residents draw untreated drinking water directly from this lake. Three samples consisting of 4 L of water each were taken from the water truck and the two lakes for *H. pylori* testing by PCR.

The water was filtered and filter sediments were gathered by immersion in 50 ml of dH<sub>2</sub>O and centrifuged at 13,000 RPM for 20 min. Sediments were combined and further centrifuged at 13,000 RPM for 20 min. The supernatant was removed and the pellet was resuspended in 500  $\mu\text{l}$  of TE buffer. A 50- $\mu\text{l}$  aliquot was boiled for 5 min and used for PCR (boiled preparation). The remaining aliquot was then centrifuged, the supernatant removed, and the final sediment was used for DNA preparations A, B, and C, as previously

**Table 1.** Demographic and Clinical Characteristics of Study Participants

	Chesterfield Inlet (n = 110)	Repulse Bay (n = 146)	Both Communities (n = 256)
Gender			
Female	69 (62.9)	76 (52.1)	145 (56.6)
Male	41 (37.3)	70 (47.9)	111 (43.4)
Age (yr)			
Mean $\pm$ SD	31.8 $\pm$ 14.2	29.8 $\pm$ 14.9	30.7 $\pm$ 14.6
Median, range	29, 2–65	28, 1–73	29, 1–73
<15 years	8 (7.2)	20 (13.7)	28 (10.9)
15–29	50 (45.5)	57 (39.0)	107 (41.8)
30–44	29 (26.4)	48 (32.9)	77 (30.1)
45–59	18 (16.4)	12 (8.2)	30 (11.7)
60–74	5 (4.5)	9 (6.2)	14 (5.5)
Upper GI complaints			
Heartburn	27 (24.5)	16 (10.9)*	43 (16.8)
Indigestion	39 (35.5)	29 (19.9)†	68 (26.6)
Medications			
H <sub>2</sub> receptor blocker	3 (2.7)	1 (0.7)	4 (1.6)
Non-Rx oral antacid	6 (5.5)	1 (0.7)‡	7 (4.8)
Proton pump inhibitor	0 (0)	2 (1.4)	2 (1.4)
NSAIDs	2 (1.8)	4 (2.7)	6 (2.3)
Daily cigarette smoking	69 (62.7)	95 (65.1)	164 (64.1)
Alcohol consumption	37 (33.6)	44 (30.1)	81 (31.6)
Blood group (ABO, Lewis)			
O, a–b+	45 (43.3)	70 (50.7)	115 (47.5)
Other	59 (56.7)	68 (49.3)	127 (52.5)
Number in dwelling			
Mean $\pm$ SD	4.6 $\pm$ 3.0	6.2 $\pm$ 1.9§	5.6 $\pm$ 2.6
Range, median	4.0, 1–20	6.0, 2–11	6.0, 1–20
$\geq$ 7 persons	12 (10.9)	70 (47.9)	82 (32.0)

When not specified, data are presented as number (%).

\*  $p = 0.003$ ; †  $p = 0.005$ ; ‡  $p = 0.044$ ; §  $p < 0.001$ .

SD = standard deviation; GI = gastrointestinal; NSAIDs = nonsteroidal antiinflammatory drugs.

described (8). In brief, 300  $\mu$ l of extraction buffer (20 mmol/L TRIS-HCL [pH, 8.0], 0.5% Tween 20) was added. The pellet was resuspended by vortexing and proteinase K was added to a final concentration of 0.5 mg/ml. After incubation for 1 h at 55°C, the proteinase K was inactivated by heating at 98°C for 10 min. Then, 50  $\mu$ l was removed into another tube for amplification (Prep A), 300  $\mu$ l of phenol-chloroform-isoamyl alcohol was added to the remainder, which was vortexed then centrifuged at 13,000 RPM for 10 min, and 30  $\mu$ l was removed from the aqueous layer for amplification (Prep B). The remainder of the aqueous layer was transferred to another tube. Seven hundred-fifty microliters of cold 100% ethanol and 30  $\mu$ l 3M sodium acetate were added (pH, 5.2), mixed, and kept at –80°C for 30 min, and then centrifuged at 13,000 RPM for 15 min at 4°C. The supernatant was then removed, and the pellet air-dried and resuspended in 30  $\mu$ l of water (Prep C). Twenty microliters of the preps were used for PCR, which was carried out using previously published primers and conditions (8); 5  $\mu$ l of the initial PCR reaction were reamplified (nested) under the same conditions. The amplified product was analyzed by electrophoresis in a 1% agarose gel. Standard procedures were used for Southern blotting of the gel. The labelled probe sequence was CTAGAGAC TATGATGTGCTG. Known *H. pylori* DNA was used as a

positive control and distilled water was used as a negative control.

The unpaired *t* test was used to compare means for continuous variables. The Kruskal-Wallis nonparametric test was used to compare means for continuous data that did not follow a normal distribution. Comparison of proportions was by  $\chi^2$ , or Fisher's exact test for small expected values.

## RESULTS

Two hundred and fifty-six subjects were enrolled in the study, 110 (43.0%) from Chesterfield Inlet and 146 (57.0%) from Repulse Bay. Of the total populations of these communities, this represented participation of 32.4% for Chesterfield Inlet and 26.1% for Repulse Bay. However, for those  $\geq$ 15 yr old the participation rates were 51.0% and 42.0%, respectively. All subjects were of Inuit ethnicity. Because of the reluctance of parents to allow venipuncture in children, the majority (89.1%) of subjects were  $\geq$ 15 yr of age (Table 1). The age distribution for study subjects in each community who were  $\geq$ 15 yr old was not significantly different from the age distribution for the general population.

Sixty-four percent of subjects smoked one or more cigarette(s) on a daily basis. However, a minority reported

**Table 2.** Antibodies to *H. pylori* and CagA Antigen in Study Participants From Chesterfield Inlet and Repulse Bay

	Chesterfield Inlet (n = 110)	Repulse Bay (n = 146)	Both Communities (n = 256)
<i>H. pylori</i> antibody			
No. +ve/no. tested (%)			
Testing method			
Helisal rapid test	1/6 (16.7)	3/8 (37.5)	4/14 (28.6)
ELISA	55/104 (52.9)	71/138 (51.4)	126/242 (52.1)
Total	56/110 (50.9)	74/146 (50.7)	130/256 (50.8)
Age group (yr)			
<15	1/8 (12.5)	8/20 (40.0)	9/28 (32.1)
15-29	26/50 (52.0)	37/57 (64.9)	63/107 (58.9)
30-44	15/29 (51.7)	19/48 (39.6)	34/77 (44.2)
45-59	11/18 (61.1)	4/12 (33.3)	15/30 (50.0)
60-74	3/5 (60.0)	6/9 (66.7)	9/14 (64.3)
CagA antibody			
No. +ve/no. tested (%)			
<i>H. pylori</i> ELISA +ve	40/55 (72.7)	38/71 (53.2)*	78/126 (61.9)
<i>H. pylori</i> ELISA -ve	11/49 (22.4)	30/67 (44.8)†	41/116 (35.3)
Total	51/104 (49.0)	68/138 (49.3)	119/242 (49.2)

\*  $p = 0.027$ ; †  $p = 0.012$ .

consuming any alcohol within the previous month (31.6%), experiencing heartburn (16.8%) twice or more per week, or indigestion (26.6%) twice or more per month over the previous 6 months. Two (0.8%) persons indicated that they had been hospitalized in the past for gastrointestinal bleeding. Previous investigations including upper gastrointestinal barium radiography and endoscopy were reported by 15 (5.9%) and eight (3.1%) subjects, respectively. One subject had undergone surgery for peptic ulcer disease. At the time of the study, use of gastrointestinal medications including histamine H<sub>2</sub> receptor antagonists (ranitidine), nonprescription oral antacids (magnesium-aluminum hydroxide), and protein pump inhibitors (omepazole) were reported by only 1.6%, 4.8%, and 1.4%, respectively. Only six (2.3%) subjects were currently taking nonsteroidal antiinflammatory medication.

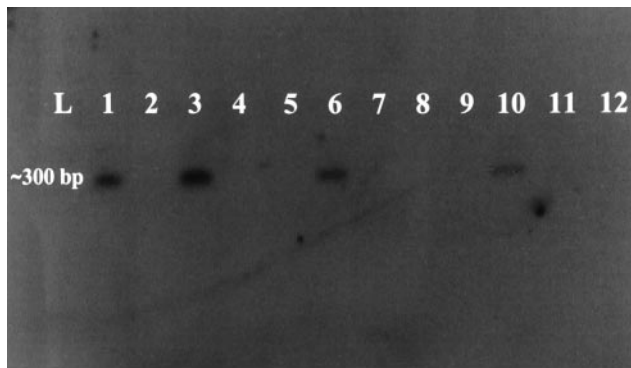
Thirty-two percent of subjects lived in houses shared by seven or more persons. Since 1980 in Chesterfield Inlet and 1969 in Repulse Bay, water has been collected from local lakes, chlorinated, and delivered by truck to tanks in each home. However, all 110 (100%) study subjects in Chesterfield Inlet and 137 (93.8%) subjects in Repulse Bay reported using ice, snow, or unchlorinated lake water as water sources when camping on the land. All houses have indoor toilets connected by utilidor sewage pipes to a household holding tank. The tanks are emptied regularly by municipal trucks, which dump the sewage into a designated disposal area 2 km from the lakes where water is collected. Bagged household garbage is trucked to disposal sites outside each community.

Subjects from the two communities were not significantly different in gender, mean age, blood group, or histories of smoking or alcohol use, gastric surgery, gastrointestinal bleeding, or endoscopy. However, heartburn ( $p = 0.003$ ) and indigestion ( $p = 0.005$ ) were noted more frequently in subjects from Chesterfield Inlet, and these individuals were

more likely ( $p = 0.01$ ) to give a history of upper gastrointestinal radiography and to use magnesium-aluminum hydroxide liquid antacid ( $p = 0.044$ ). The houses of subjects who lived in Chesterfield Inlet were significantly less crowded ( $p < 0.001$ ) than houses of subjects from Repulse Bay.

One hundred-thirty (50.8%) of the 256 study participants were positive for IgG antibodies to *H. pylori* (Table 2). Fourteen children <15 yr of age were tested by Helisal Rapid Test of capillary blood and the remaining 242 subjects were tested by serum enzyme immunoassay (ELISA). *H. pylori* antibody status did not differ with respect to age, community, alcohol or cigarette use, number of persons per household, gastrointestinal complaints, previous investigation, use of gastrointestinal or nonsteroidal antiinflammatory medication, or presence of blood group O, Lewis a-b+. However, seropositive subjects were more likely to be male than seronegative individuals (66/130 vs 45/126; 95% confidence intervals [CI], 1.09, 3.18;  $p = 0.01$ ). Four of the 14 children tested by Helisal Rapid Test were positive. This was similar to the rate of seropositivity to *H. pylori* by ELISA (five of 15) for those children <15 yr who were tested by this method.

One hundred-nineteen (49.2%) of the 242 sera tested for antibody to the CagA antigen were positive. Among 126 *H. pylori*-seropositive subjects, 78 (61.9%) were CagA antibody positive; 41 (35.3%) of 116 *H. pylori*-seronegative subjects were also CagA antibody positive. Among the subgroup of 126 participants who were *H. pylori* antibody positive, seropositivity for CagA antibodies occurred more frequently in those from Chesterfield Inlet (40/55 vs 38/71; 95% CI, 1.02, 5.29;  $p = 0.027$ ). In *H. pylori*-negative subjects, CagA antibodies were detected less frequently in subjects from Chesterfield Inlet (11/49 vs 30/67; 95% CI, 0.14, 0.88;  $p = 0.012$ ). Compared with those who were *H. pylori* or CagA negative, those who were seropositive for

**A****B**

**Figure 2.** Southern blot hybridization of nested-PCR amplified *H. pylori* from various water sources. (A) Repulse Bay lake water and Chesterfield Inlet truck water positive results. L represents 123-base pair marker on the agarose gel (not detected on the Southern blot). Lanes 1–4 are from Repulse Bay lake; Lanes 5–8 are from Repulse Bay swimming lake; Lanes 9–12 are from Chesterfield Inlet water truck. Lanes 1, 5, and 9 are from boiled prep; Lanes 2, 6, and 10 are from Prep A; lanes 3, 7, and 11 are from Prep B; Lanes 4, 8, and 12 are from Prep C. Positive results are present in Lanes 1 (Repulse Bay lake, boiled prep), 3 (Repulse Bay lake, Prep B), 6 (Repulse Bay swimming lake, Prep A), and 10 (Chesterfield Inlet water truck, Prep A). (B) Repulse Bay water truck and Chesterfield Inlet lake water negative results. L represents base pair marker on the agarose gel. Lanes 13–16 are from Repulse Bay water truck; Lanes 17–20 are from Chesterfield Inlet lake; Lane 21 is *H. pylori* positive control. Lane 22 is water contamination control. Lanes 13 and 16 are from boiled prep; Lanes 14 and 18 are from Prep A; Lanes 15 and 19 are from Prep B; Lanes 16 and 20 are from Prep C. Positive result is present only in Lane 21 (*H. pylori*-positive control).

antibodies to both *H. pylori* and CagA were not significantly different with respect to their demographic, clinical, or blood group variables analyzed.

The chlorinated water sample taken from the delivery truck in Chesterfield Inlet was positive for *H. pylori* by PCR (Fig. 2A); unchlorinated water samples from the two lakes in Chesterfield Inlet were negative (Fig. 2B). Unchlorinated water from the two lakes near Repulse Bay were positive for

*H. pylori* (Fig. 2A), whereas the chlorinated water truck sample was negative (Fig. 2B).

## DISCUSSION

*H. pylori* has been previously detected in community water supplies in Peru (9), and under experimental conditions has been shown to survive in fresh cold water, salt water, and distilled water (10). In the present study, *H. pylori* was detected by PCR in water samples taken from two lakes near Repulse Bay, and from the water delivery truck but not lake water samples in Chesterfield Inlet. Lake water may be a natural reservoir for *H. pylori* in this region, and a source of human infection. Alternatively, contamination of lake water used as the source of drinking water may have occurred through sewage runoff from disposal sites located 2 km away, particularly during the freeze-thaw cycle in Spring and Fall. The detection of *H. pylori* in water taken from the delivery truck in Chesterfield Inlet, but not from local lake water, suggests the possibility of contamination of the truck holding tank, despite monthly cleaning with ammonia.

The four DNA lysate preparations for PCR were necessary, as seen in the results. The boiling method and Preparation A yielded the highest amount of DNA from the sample. However, these preparations may also contain the highest amount of PCR inhibitors. With additional steps, such as Preparations B and C, there is loss of sample DNA. However, these DNA extraction methods, which use phenol-chloroform-isoamyl alcohol, also remove potential PCR inhibitors. Thus, a combination of the four DNA preparations increases the sensitivity of PCR detection. This technique does not allow quantification of the amount of organism present. The variable PCR results using different preparations suggests that only a small number of organisms were present. To overcome the limitation of small organism numbers, other investigators have utilized magnetic-coated beads to concentrate the organism from the water before the amplification process (9). Nonetheless, our data do not prove that the organism is growing and viable (and therefore, necessarily transmissible), as we did not culture the organism from the water, and have only proved that it has been in the water at some time.

Interpersonal spread of *H. pylori* has been postulated, supported by the identification of *H. pylori* in feces and dental plaque (11–14). Crowded living condition in arctic Canada and Alaska have been shown to facilitate interpersonal spread of other enteric organisms (15, 16).

The 50% seroprevalence of *H. pylori* infection in these two arctic communities is higher than rates seen in southern populations, particularly in the young and middle-aged (17), but lower than the 95% seroprevalence documented by the authors in the subarctic Canadian Indian (First Nations) community of Wasagamack (4). The recruitment rate for the arctic study was similar to that seen in other regional studies. One-half of the population in these communities is <16 yr of age, and acceptance of venipuncture is poor. Further-

more, during the summer months, families move back and forth from town to camping on the tundra, resulting in difficulty recruiting the rest of the adult population.

In Wasagamack, which is located 620 miles south of Chesterfield Inlet, *H. pylori* was not identified by PCR in local water supplies. Compared with Chesterfield Inlet and Repulse Bay, Wasagamack and other Canadian Indian communities are characterized by more crowded housing and inadequate sanitary conditions. Failures often occur in the chlorination of local lake water, and individuals must haul water from municipal pumps to holding tanks or barrels in their homes. Outhouses or indoor sewage pails are used, and fecal contamination of lake water occurs. The water samples were taken in Wasagamack in the late fall. To reconcile the absence of *H. pylori* by PCR in the water in a community with near-ubiquitous seropositivity, compared with the arctic communities, where water sources were PCR positive, we plan to repeat the water testing in Wasagamack during the summer. This is a time when the risk of fecal contamination is high due to recreational water use, camping in the vicinity, and runoff of ground and rain water. Nonetheless, the finding of *H. pylori* by PCR in the water does not prove that *H. pylori* in fact grows in the water or is necessarily transmissible from the water.

Association between Lewis antigen status and *H. pylori* seropositivity was not demonstrated in this study. Although some investigators (18) have suggested that *H. pylori* attachment is mediated through the Lewis b cell surface antigen, which is also expressed on gastric epithelial cells, other studies do not support a relationship between ABO blood group or Lewis antigen secretor status and *H. pylori* infection (19–21). It has recently been postulated that humans are preferentially infected with *H. pylori* organisms of the same Lewis antigen type as the host (22).

Specific data on the incidence of gastritis and peptic ulcer disease in the study population are not available. The nearest referral hospital offering secondary care, including barium radiography, is in the town of Churchill, Manitoba, 355 miles south of Chesterfield Inlet. Endoscopy, urea breath testing, and gastroenterology consultation are available 969 miles south, in Winnipeg. Because of the distances and resource issues involved, few patients are referred to southern centers for investigation, and empirical therapy for presumed dyspepsia and peptic ulcer disease is often used.

Gastric cancer accounts for 5.5% of all cancers occurring in Canadian Inuit men from 1970–1984 (23). The crude incidence rates for gastric cancer among Canadian Inuit men and women from 1984–1988 were 13.1 and 7.4 per 100,000, respectively (24). The incidence rates have increased from 2.1 and 2.3 per 100,000 during the period of 1969–1973, but this likely reflects improved cancer registration (24). The incidence of gastric cancer in the Canadian Inuit from 1969–1988 was not significantly different (23) from the incidence in the general Canadian population (age standardized incidence ratio = 1.5).

We were puzzled by our finding of CagA seropositivity

among 30% of *H. pylori*-seronegative subjects. The CagA ELISA was repeated for all *H. pylori*-negative samples, including 10 additional known *H. pylori*-negative controls, and the results were unchanged. The 41 *H. pylori*-seronegative, Cag A-seropositive subjects' sera were retested for *H. pylori* seropositivity using a different immunoassay kit (Genesys, Pheonix Biotech, Cambridgeshire, UK). Thirty-four of these samples remained negative and seven were considered low-positive (8–20 units). These data suggest either the presence of a serum antibody in these Inuit subjects that crossreacts with Cag A, or, alternatively, that these subjects make antibodies to CagA but not to the mixture of *H. pylori* antigens, at least not to the level that is indicative of seropositivity by the standard ELISA. This phenomenon of high rates of CagA seropositivity among *H. pylori*-seronegative subjects has also been seen in studies from China (Martin Blaser, M.D., personal communication) and in HIV-positive subjects (25). One explanation may be that there is heterogeneity in the humoral responses to *H. pylori*, and for some people CagA is the immunodominant antigen. If this latter explanation is true, then our *H. pylori* infection rates may be as high as 66% if all *H. pylori*-seronegative, CagA-seropositive subjects are included as being truly positive.

Further efforts to identify the reservoir(s) of *H. pylori* and the epidemiology of transmission within the Inuit population, as well as other ethnic groups and communities, are indicated to devise control programs aimed at primary and secondary prevention of infection and disease. It is unclear whether lakes represent a natural reservoir for infection in the study population, or whether they become secondarily contaminated by human waste. The possible role of person-to-person transmission also requires clarification. A prospective study to evaluate the natural history and clinical correlates of *H. pylori* infection in this population, using standardized diagnostic and treatment protocols, and controlling for other identified risk factors for gastrointestinal illness, is indicated. The remoteness of Canadian arctic communities, and limitations in local medical resources, present a challenge to the planning and implementation of such a study.

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