The changing prevalence of *Helicobacter pylori* infection in Canadian children: Should screening be performed in high-risk children?

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While several studies have demonstrated a decline in the overall prevalence of *Helicobacter pylori* infection in developed countries, there is variability in the burden of infection linked to socioeconomic status and living conditions. Improved socioeconomic status, living conditions and the availability of *H pylori*-eradication therapy have been associated with a lower prevalence of infection in First World populations, yet immigrants and indigenous people continue to have a high burden of *H pylori* infection and disease. Although the changing prevalence of *H pylori* infection in children has been recognized in a few reports, further studies are required to determine the impact of *H pylori* infection in this population. Moreover, additional studies are required for those populations at risk.

Key Words: *Children; Epidemiology;* Helicobacter pylori

L'évolution de la prévalence de l'infection à *Helicobacter pylori* chez les enfants canadiens : Un dépistage devrait-il être exécuté chez les enfants très vulnérables?

Tandis que plusieurs études ont démontré une diminution de la prévalence globale d'infection à *Helicobacter pylori* dans les pays industrialisés, on remarque une variabilité du fardeau de la maladie selon le statut socio-économique et les conditions d'existence. Un meilleur statut socio-économique, de meilleures conditions d'existence et la disponibilité d'un traitement d'éradication de l'*H pylori* s'associent à une réduction de la prévalence d'infection dans les populations des pays industrialisés, mais les immigrants et les populations autochtones continuent d'afficher un fardeau élevé d'infection et de maladie à *H pylori*. Bien que l'évolution de la prévalence de l'infection à *H pylori* chez les enfants aient été soulignée dans quelques rapports, des études supplémentaires s'imposent pour déterminer les répercussions de l'infection à *H pylori* au sein de cette population. De plus, d'autres études sont nécessaires auprès des populations vulnérables.

PREVALENCE OF *HELICOBACTER PYLORI*

Helicobacter pylori infection, frequently acquired during childhood and adolescence, is linked to socioeconomic status and living conditions (1-3). While the prevalence of *H pylori* is decreasing in developed countries (4), it remains high in developing countries, in populations of low socioeconomic status and in immigrant populations within developed countries (5-7).

Seroepidemiological studies of *H pylori*-infected children in western Europe (8-10), the United States (11-13) and, to a limited degree, in Canada, have demonstrated variability in *H pylori* seropositivity (5,6). While these data are useful and convenient for the evaluation of large populations, they must also be considered in the context of geographical location, population studied, lack of appropriate symptom assessment instruments, lack of clearly defined controls, accuracy of the serological assay (13) and lack of confirmation of *H pylori* infection with the urease breath test (UBT) or endoscopy with biopsy. The latter is important because a positive serology indicates either a past or present *H pylori* infection.

In a recent, multisite, cross-sectional prospective study (13) involving 992 children from 12 children's hospitals or medical centres predominantly in the eastern and southeastern regions of the United States, the overall prevalence of *H pylori* antibodies was 17.2%. A wide geographical variation in seropositive rates was observed, with rates ranging from 8.3% (one of 12) to 38.6% (39 of 101) at different centres. Among symptomatic children referred to pediatric gastrointestinal (GI) clinics with abdominal pain (n=182), abdominal pain and vomiting (n=168), or vomiting alone (n=12), the seropositivity rate was 22.5%. In contrast, among children (n=619) seen in non-GI outpatient clinics (who had no GI complaints and who required blood drawing as part of standard clinical management) during the same period, the seropositivity rate was 14.1%. Although the seropositive rates were significantly different between the two groups, the GI referral patients were older than the non-GI patients (mean age 10.1 years [range one to 18 years] versus mean age 7.7 years [range two months to 18 years], respectively). In keeping with previous studies (9,11,14), *H pylori* seropositivity was strongly associated with increasing age, being non-white, living in poverty, crowded household conditions, an annual household income less than US$36,000 and the mother's education being grade 12 or less (Table 1).

Similarly, in Canada, *H pylori* infection rates vary considerably. Low prevalence rates of 5.28% (13 of 246) have been observed in children aged five to 18 years in an ongoing study (prevalence, symptomatology and investigation of pediatric *H pylori* infection [PSI-PHI] study [unpublished data]) involving four Canadian academic centres where upper GI endoscopy is

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TABLE 1
Demographic and household characteristics of gastrointestinal (GI) and non-GI referral children in the United States

	GI referral			Non-GI referral		
	Seropositive rate (%)	RR	CI	Seropositive rate (%)	RR	CI
Age (years)						
<13	19.1	–	–	11.2	–	–
13–18	29.5	1.54	(1.06–2.24)	27.3	2.43	(1.64–3.59)
Ethnicity						
White	15.4	–	–	9.7	–	–
Nonwhite	32.6	2.13	(1.44–3.13)	17.7	1.83	(1.20–2.80)
Income (US$)						
<36,000	29.6	2.79	(1.68–4.66)	16.6	1.78	(1.03–3.06)
≥36,000	10.6	–	–	9.3	–	–
Mother's education						
≤Grade 12	29.0	2.06	(1.32–3.20)	16.9	1.64	(1.06–2.54)
>Grade 12	14.1	–	–	10.2	–	–

Comparisons were made within each referral group. Adapted from reference 13

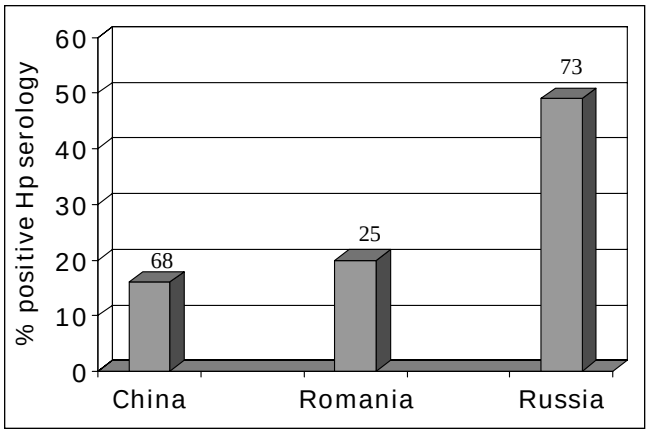

Figure 1) Helicobacter pylori *(Hp) seropositive rates in adopted children from China (11 of 68), Romania (five of 25) and Russia (36 of 73). Adapted from reference 7*

performed for upper GI symptoms. In contrast, high seroprevalence rates have been observed in indigenous people, with rates ranging from 51% in children from the Arctic communities of Chesterfield Inlet and Repulse Bay, Nunavut (5) to 95% in First Nation's children of the subarctic community Wasagamack, Manitoba (6). In keeping with American studies, in communities with widespread *H pylori* infection, overcrowding and poor living conditions, including primitive toileting (Arctic community households had flush toilets versus only 0.3% in the Wasagamack community), there was increased likelihood of *H pylori* infection. In the Arctic communities, antibodies to *H pylori* were identified in 32% (nine of 28) of children by 15 years of age and 58.9% (63 of 107) of individuals by 29 years of age. However, in the children in Wasagamack, using an enzyme immunoassay for detection of stool antigen, approximately 70% (16 of 23) of the seven- to nine-year-old children were positive. Moreover, approximately 20% of children (five of 23) younger than one year of age were stool antigen-positive. The number of children studied was small and the stool antigen test was not validated with UBT or endoscopy with biopsy. However, these results provide valuable data regarding acquisition of *H pylori* and experience with stool testing in a population where UBT might be challenging, particularly in younger children, and where endoscopy is not always possible.

Immigrants to Canada provide a further burden of *H pylori* infection. The immigrant population comprises approximately 200,000 individuals per year with approximately 80% to 90% of immigrants settling in Montreal, Quebec; Toronto, Ontario; or Vancouver, British Columbia. Approximately 70% of immigrants belong to minority groups that contribute to higher prevalence rates and variability of *H pylori* infection across the country. In a recent study in the United States (7), 226 children adopted from 18 countries (mean age 24±2.05 months, range four months to 16 years) demonstrated a seroprevalence rate of 31%. *H pylori*-positive children were older at arrival in the United States than their *H pylori*-negative counterparts (40±11 versus 15±1 months for Chinese children; 61±28 versus 24±9 months for Romanian children; and 48±5 versus 22±3 months for Russian children) and were more likely to have resided in orphanages rather than foster care. Sixty-six per cent of children who resided entirely in orphanages, or other institutional settings such as hospitals, were *H pylori* antibody-positive compared with 22% who lived in institutions and family settings, and 12% who lived only in family settings. That study (7) also demonstrated variability in seropositivity, with higher rates of *H pylori* antibodies observed in Russian children (49%) compared with Romanian (20%) and Chinese children (16%) (Figure 1).

CHANGING PREVALENCE OF *H PYLORI*

With improved socioeconomic status and *H pylori* eradication therapy (whether intentional or the result of another treatment, ie, when proton pump inhibitors are used to treat gastroesophageal reflux disease or antibiotics to treat infectious illness), studies have begun to demonstrate a change in *H pylori* prevalence. Recently, in a study from Greece (4), *H pylori* seroprevalance was compared in banked serum from 200 consecutive adult outpatients collected in 1987, from serum samples from 201 similarly selected outpatients from the same unit, and from 120 consecutive blood donors from the same hospital collected in 1997. An overall 10.75% decrease in seroprevalence was demonstrated (from 59.5% to 48.75%). In particular, the decrease in seroprevalence was most marked in the 15 to 24 year old age group. Presently, no published data are available in Canada and the United States; however, if one extrapolates from available data, the decline appears evident.

A 1991 study from Arkansas (14) demonstrated a seroprevalence of 45% in children aged three to 20 years. While this rate is higher than the seropositivity rate of 17.2% recently reported by Chong et al (13) (suggesting a decline in seroprevalence), this may simply reflect geographical variability and a different population studied. Moreover, older patients were included in the study by Fiedorek et al (14), adding to the higher prevalence rate.

Children referred to the gastroenterology department of the Hospital for Sick Children, Toronto, Ontario, for upper GI symptoms in the early 1990s were found to have *H pylori* infection rates of 26% to 43% (15,16) (Table 2); whereas elsewhere, infection rates appear to be decreasing, with lower infection rates of approximately 5% recently observed in Canadian children referred to tertiary care institutions in the ongoing PSI-PHI study (unpublished data). Although these

TABLE 2
Prevalence of *Helicobacter pylori* (Hp) infection in Canadian children undergoing upper gastrointestinal (GI) endoscopy for upper GI symptoms from 1990 to 1994

Site (year)	n	Male (%)	Mean age (years)	Prevalence of Hp
Toronto, Ontario (1990)	93	60.8	12.8±3.7	(24/93) 26%
Toronto, Ontario (1994)	56	–	12.6	(24/56) 43%
Total (1990–1994)	149	–	–	(48/149) 34.5%

All children had upper GI endoscopy with biopsy-proven Hp infection

studies (15,16) were not specifically designed for comparison of trends, and the populations are from different centres, the data nevertheless agree with current trends. The variability in infection rates are likely also influenced by the proportions of subjects who belong to immigrant and First Nations populations.

COMPLICATIONS ASSOCIATED WITH *H PYLORI* INFECTION

Because *H pylori* infection contributes to the development of peptic ulcer disease and gastric cancer, the burden of these diseases in the Western world may fall primarily on the high-risk minority groups. While the complications associated with *H pylori* infection have not been systematically studied in Canada, Bernstein et al (17) have demonstrated a higher average annual age-adjusted incidence of hospitalizations between 1989 and 1993 associated with the diagnosis of peptic ulcer disease for the subarctic treaty-status Aboriginal community of Wasagamack, Manitoba (394.3 of 100,000) than for the non-Aboriginal Manitoban population (203.8 of 100,000). Interestingly, the average annual age-adjusted incidence of hospitalizations for treaty-status Aboriginals aged zero to nine years and 10 to 19 years was not different from other age-matched Manitobans (1.15 versus 1.19 and 18.7 versus 19.5, respectively). However, it is possible that fewer patients received medical attention and that different diagnostic and therapeutic medical practices were followed, leading to a potential underestimation of the severity of the disease in the Wasagamack community. In contrast, the mean annual age-adjusted gastric cancer incidence rates were statistically similar for treaty-status Aboriginals (11.2 of 100,000) and non-Aboriginals (11.6 of 100,000). Low rates of gastric cancer have also been observed in specific Chinese and African populations associated with a high prevalence of childhood *H pylori* infection (18,19). While these data require further study, it is possible that the Wasagamack community is infected with strains of *H pylori*, and has a host genetic profile that is associated with a diminished susceptibility to gastric cancer.

Clearly, studies should be performed on populations at risk. However, the declining prevalence of *H pylori* infection in the Western world suggests changing patterns of transmission. Therefore, studies should be performed on children in both low- and high-risk geographical areas, and with diverse socioeconomic and ethnic backgrounds. In Canada, studies need to be undertaken to identify populations at risk and to determine whether the high prevalence rates of *H pylori* infection are associated with high complication rates. Moreover, improving the socioeconomic status and living conditions of populations at risk will reduce the burden of infection and, thus, the burden of disease.

To ensure the validity of such population-based studies, one needs to ensure that the screening tools are both validated and safe. Moreover, we need to determine whether there are indeed consequences to *H pylori* infection in childhood, whether eradication is associated with reduced *H pylori*-related consequences, and whether the eradication regimens are safe and if eradication of *H pylori* infection in childhood produces a significant benefit in adulthood. Finally, testing also requires that we consider an intent-to-treat approach for *H pylori*-infected individuals.

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