SHORT RAPID COMMUNICATION

High prevalence of potentially virulent strains of *Helicobacter pylori* in the general male British population

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Abstract

Background—Strains of *Helicobacter pylori* that express the cytotoxin associated gene product A (CagA) may be more strongly associated with serious gastric diseases, such as gastric cancer and peptic ulceration, than other strains. Data, however, are sparse on the prevalence, risk factors, and other correlates of these strains in the general population.

Aim—To characterise aspects of the sero-epidemiology of CagA⁺ strains of *H pylori* in the general British population.

Methods—We measured serum IgG antibodies to mixed *H pylori* antigens and separately to CagA in 1025 men aged 40–59 years who were randomly selected from a larger group of participants in a community based survey conducted in 18 different British towns.

Results—Overall, 44% (95% confidence interval 41–47%) of the men were seropositive to CagA antibodies, representing about 61% (57–65%) of the men seropositive to mixed antigen *H pylori*. The risk factors for seropositivity to CagA antibodies were similar to those for seropositivity to mixed antigen *H pylori*, apart from an increased prevalence of reported bedroom sharing in childhood ($p < 0.01$).

Conclusion—In a nationwide study of potentially virulent *H pylori* strains, there was a high prevalence of the infection, with some evidence that acquisition of such strains might occur earlier in life than other strains.

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Keywords: *Helicobacter pylori*; cytotoxin associated gene A

Despite suggestions that potentially virulent strains of *Helicobacter pylori* infection produce greater risks of gastric inflammation, peptic ulceration, and gastric cancer than other strains, little is known about the characteristics of these organisms in the general population, such as their prevalence, geographical variation, risk factors, and any relationship

with markers of systemic inflammation.^{1–8} Here we report a nationwide investigation of cytotoxin associated gene product A (cagA⁺) strains of *H pylori* in 1025 middle aged British men.

Methods

During 1978–1980, 7735 males, aged 40–59 years (response rate 78%), were randomly selected from general practice registers in 24 British towns where nurses administered questionnaires and performed physical measurements. In 5661 men from 18 of the towns, non-fasting venous blood samples were collected and stored at -20°C for subsequent analysis.⁹ Additional questionnaires on car ownership and childhood social circumstances were posted at five years (98% response among survivors) and at 12 years after entry (90% response among survivors), respectively. Among the 5016 men who remained free of incident coronary heart disease by 1996, 1025 were randomly selected for measurements of *Helicobacter pylori* specific IgG titres using an ELISA kit (Premier, Meridian Diagnostics, Cincinnati, Ohio, USA) and anti-CagA serum antibodies using recombinant CagA antigen orv220.² Our CagA assay had 92% (34/37) sensitivity and 96% (24/25) specificity in 62 patients in another study in whom CagA status was directly assessed by western blot in gastric biopsy specimens (Helicoblot, 2.0, Genelabs Diagnostics, Singapore). This level of accuracy is comparable with that described for the original serological assay² and is confirmed by the fact that only two individuals seronegative to mixed antigen *H pylori* in the present study tested CagA seropositive.

Results

A total of 448 (44% (95% confidence interval 41–47%)) of the 1025 men were seropositive to CagA antibodies, representing about 61% (57–65%) of the men seropositive to mixed antigen *H pylori* (table 1). Seropositivity to CagA antibodies was more common in men

Abbreviations used in this paper: CagA, cytotoxin associated gene product A.

Table 1 Levels of risk factors and other characteristics by *Helicobacter pylori* seropositivity and CagA serostatus in 1025 British men aged 40–59 years (mean (SD) or number (%))

	<i>H. pylori</i> seronegative (n=285)	<i>H. pylori</i> seropositive		
		All Hp+ (n=740)	CagA- (n=292)	CagA+ (n=448)
Age (y)	51 (3)	53 (4)*	52 (5)	53 (5)
Current smoker	93 (33%)	343 (46%)	135 (46%)	208 (46%)
>2 drinks alcohol/day	58 (20%)	173 (23%)	75 (26%)	98 (22%)
Adult socioeconomic factors				
Occupation in social class I or II	121 (42%)	158 (21%)****	66 (23%)	92 (21%)
Homeowner	230 (83%)	437 (64%)**	178 (66%)	129 (62%)
Married	252 (82%)	652 (88%)	251 (86%)	401 (90%)
Car owner	246 (89%)	493 (72%)**	202 (75%)	291 (70%)
Childhood socioeconomic factors				
Father with non-manual job	78 (32%)	113 (21%)	49 (23%)	64 (20%)
Family owned a car	52 (21%)	64 (11%)	28 (13%)	36 (10%)
Bathroom in house	146 (58%)	253 (44%)*	110 (49%)	143 (42%)
Hot water tap in house	137 (55%)	274 (48%)	116 (52%)	158 (46%)
Bedroom shared	124 (49%)	409 (72%)***	148 (66%)	261 (76%)*
Physical measurements				
Body mass index (kg/m ²)	25.3 (1.7)	25.4 (2.6)	25.3 (3.3)	25.4 (3.5)
Systolic blood pressure (mm Hg)	144 (12)	147 (16)	148 (21)	147 (21)
Diastolic blood pressure (mm Hg)	82 (8)	83 (10)	82 (13)	84 (13)
Blood markers of infection or inflammation				
<i>Chlamydia pneumoniae</i> titres (FC×10 ⁶)	163 (40)	188 (43)****	186 (57)	189 (58)
Log ₁₀ C-reactive protein (mg/l)	0.05 (0.31)	0.19 (0.38)	0.19 (0.51)	0.19 (0.55)
Log ₁₀ serum amyloid A protein (mg/l)	0.83 (0.16)	0.84 (0.24)	0.83 (0.31)	0.85 (0.31)
Albumin (g/l)	45.1 (1.4)	44.3 (1.8)	44.3 (2.4)	44.3 (2.3)
White cell count (× 10 ⁹ /l)	6.9 (1.1)	7.3 (1.3)	7.2 (1.5)	7.3 (1.8)

The comparisons in the table involve columns 1 v 2 (all *H. pylori* seronegative v all *H. pylori* seropositive) and columns 3 v 4 (among those *H. pylori* seropositive: CagA seronegatives v CagA seropositives). Information on some factors was available in only a subset of participants. Car ownership: 964; father's occupation: 783; family car: 818; bathroom in house: 820; hot water supply: 818; bed sharing: 819. FC, fluorescent count.

p values are shown only after adjustment for age, cigarette smoking status, and indicators of socioeconomic status and are denoted by: *p<0.01, **p<0.001, ***p<0.0001, ****p<0.00001. Adjustments for social class were omitted in the regressions involving markers of socioeconomic status. Emphasis was given to results more extreme than 2.6 standard deviations (p=0.01) to make some allowance for multiple comparisons.

resident in northern England and Scotland than in southern England (49% v 28%, p<0.00001), with a similar geographical pattern for seropositivity to mixed antigen *H. pylori* (79% v 53%; p<0.00001). Reported bedroom sharing in childhood was more frequent in CagA seropositive men compared with *H. pylori* infected CagA seronegative men (76% v 66%; p<0.01). The strong correlation between *H. pylori* seropositivity and *Chlamydia pneumoniae* IgG titres (p<0.0001) did not change much after adjustment for age, cigarette smoking, and markers of socioeconomic status (suggesting that these two infective agents may share as yet unrecognised risk factors).¹⁰ Associations between *H. pylori* seropositivity and low FEV₁ and short stature, however, weakened substantially after adjustments. The data were too sparse to subdivide reliably by town of residence and racial origin (the large majority of men were Caucasian).

Discussion

Previous studies have reported great variation in the prevalence of potentially virulent *H. pylori* strains with much higher prevalences generally reported in developing countries than in North America and western Europe.^{4 6 11 12} Most, however, have been small studies conducted in selected populations or in selected regions within certain countries. By contrast, we conducted a nationwide community based study of cagA⁺ *H. pylori* strains, including detailed information on a number of possible risk factors and other characteristics in more than 1000 individuals. We found that about 45% of middle aged British men resident in 18 different towns in 1980 were infected with potentially more virulent strains of *H. pylori*. Moreover, we found a greater prevalence of

these organisms in the less affluent regions of Scotland and northern England than in southern England. It may be that some of the individuals seropositive for CagA antibodies in this study were also coinfecting with other *H. pylori* strains, but this would not alter the interpretation of the present findings.

As *H. pylori* is believed to be transmitted mainly by person-to-person contact, our observation that men infected with CagA positive strains of *H. pylori* reported bedroom sharing during childhood more frequently than men infected with other strains is consistent with suggestions that potentially virulent strains may be acquired earlier in life than other strains.¹³ More direct evidence is needed, however, to determine reliably both the timing and mode of transmission of various strains of the infection. We observed no strong associations between CagA seropositivity and blood markers of systemic inflammation, despite previous suggestions of increased intragastric inflammation in CagA positive individuals.³ We also observed no important differences between men infected and those not infected with CagA positive strains for a number of other characteristics listed in table 1, suggesting that these characteristics cannot explain differences in the strengths of association reported between different *H. pylori* subtypes and gastric diseases.

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