

# Growth in infancy, infant feeding, childhood living conditions, and *Helicobacter pylori* infection at age 70

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## Abstract

**Aim**—To examine childhood correlates of *Helicobacter pylori* infection in adults.

**Design**—Follow up study of men and women whose birth weight, weight at age 1 year, and feeding in infancy were recorded by health visitors. Data on childhood housing conditions were obtained by recall.

**Subjects**—631 men and 389 women born in Hertfordshire during 1920–30 and still living in the east or northwest districts of the county.

**Main outcome measures**—Serum *H pylori* IgG antibodies measured by enzyme linked immunosorbent assay.

**Results**—Independent of their current social class, subjects were more likely to be *H pylori* seropositive if they had large numbers of siblings ( $p < 0.0001$ ), and if they had lived in a crowded house ( $p = 0.001$ ), or shared a bedroom or bed in childhood ( $p = 0.02$ ). Low weight at 1 year was associated with increased seropositivity rates in men ( $p = 0.0002$ ), but not women ( $p = 0.8$ ). Men and women who were breast fed in infancy were less likely to be seropositive than those who were bottle fed ( $p = 0.08$ ).

**Conclusions**—The findings support the current view that *H pylori* infection is often acquired in childhood by close person to person contact, and persists into adult life. *H pylori* infection may be a cause of failure to thrive in infancy, especially in boys. Alternatively, small infants may be more susceptible to infection. Breast feeding may prevent early infection.

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tions in childhood,<sup>10–14</sup> and the relatively low rate of infection in young people in developed countries is thought to be due largely to improved housing conditions during this century.

The importance of *H pylori* infection in childhood is controversial. It has been suggested that adult morbidity increases with duration of infection, and that people infected in early life are at greater risk of gastric cancer.<sup>15</sup> In childhood itself, *H pylori* is known to cause gastritis, and may cause recurrent abdominal pain.<sup>16</sup> Weight loss and short stature have been reported in infected children.<sup>14 17 18</sup> Early infection, during infancy, is common in developing countries,<sup>7 19</sup> and although overall rates of childhood infection in developed countries are lower, infancy is still the time when most of the infections are acquired.<sup>20</sup> Data on the influence of infant feeding are sparse, but breast feeding has been shown to protect against early *H pylori* infection in a developing country.<sup>21</sup>

Measurement of serum IgG antibodies to *H pylori* by enzyme linked immunosorbent assay (ELISA) is a sensitive and specific method for diagnosis of current infection.<sup>22 23</sup> We have studied serology in 1020 men and women aged 65–75 years who were born in the county of Hertfordshire, where health visitors routinely recorded birth weight, infant weight gain, and method of feeding in infancy for all babies. In addition, we asked the subjects about their household living conditions up to the age of 10 years, including size and type of housing, and availability of domestic sanitary amenities. We aimed to determine whether poor early growth and bottle feeding in infancy are associated with higher rates of *H pylori* infection, and to confirm previously reported associations between *H pylori* infection and adverse living conditions in childhood, especially household crowding.

## Methods

In Hertfordshire, from 1911 onwards, all births were notified by the attending midwife, and the birth weight recorded.<sup>24</sup> A health visitor saw each infant regularly during the first year of life, and recorded whether it was breast fed, bottle fed, or breast+bottle fed (breast fed initially but changed to bottle feeds during the first year). She also recorded whether the infant used a dummy (comforter). At the age of 1 year she recorded the infant's weight. From 1923, childhood infections, for example 'bronchitis' and 'measles', were recorded. These were listed

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*Helicobacter pylori* is a Gram negative organism which colonises the stomach. It has recently been recognised as a major cause of chronic gastritis, peptic ulcer disease,<sup>1</sup> and gastric cancer<sup>2</sup> in adults. Infection is thought usually to be acquired in childhood, and persists for life unless treated with specific antibiotics.<sup>3–6</sup> New infection in adult life is unusual in developed countries. The mode of transmission is unknown, but is probably by oral-oral or faeco-oral person to person spread.<sup>7–9</sup> Infection is strongly associated with crowded living condi-

Table 1 Odds ratios for *H pylori* seropositivity according to sex, family size, birth weight, weight at 1 year, and social class

	No of subjects	% <i>H pylori</i> positive	OR (95% CI)	<i>p</i> for trend*	<i>p</i> for trend†
Sex					
Men	631	49	1.5 (1.1 to 1.9)		
Women	389	40	1.0	0.003	0.002
No of siblings					
0	97	28	1.0		
1/2	371	41	1.8 (1.1 to 3.0)		
3/4	269	50	2.6 (1.6 to 4.3)		
≥ 5	281	54	3.1 (1.9 to 5.1)	< 0.0001	0.0009
Birth order					
1st	319	41	1.0		
2nd/3rd	407	43	1.1 (0.8 to 1.4)		
4th/5th	164	53	1.6 (1.1 to 2.4)		
> 5th	127	56	1.8 (1.2 to 2.7)	0.0005	1.0
Birth weight, pounds (kg)					
≤ 5.5 (2.50)	44	34	1.0		
- 6.5 (2.95)	151	48	1.7 (0.9 to 3.5)		
- 7.5 (3.41)	317	41	1.3 (0.7 to 2.5)		
- 8.5 (3.86)	326	46	1.5 (0.8 to 3.0)		
- 9.5 (4.32)	127	54	2.1 (1.0 to 4.4)		
> 9.5 (4.32)	55	56	2.2 (1.0 to 5.0)	0.03	0.002
Weight at 1 year, pounds (kg)					
≤ 18 (8.18)	75	51	2.6 (1.2 to 5.6)		
- 20 (9.09)	207	46	2.0 (1.0 to 4.0)		
- 22 (10.00)	330	48	2.0 (1.1 to 3.8)		
- 24 (10.91)	251	44	1.7 (0.9 to 3.2)		
- 26 (11.82)	109	43	1.5 (0.7 to 3.1)		
> 26 (11.82)	48	33	1.0	0.002	0.0008
Social class at birth					
Manual	147	46	1.1 (0.7 to 1.5)		
Non-manual	815	45	1.0	0.5	0.7
Current social class					
Manual	367	50	1.5 (1.1 to 1.9)		
Non-manual	643	39	1.0	0.005	0.1

Social class at birth was unclassifiable for 58 subjects, and current social class for 10 subjects.

\* By logistic regression, allowing for sex, † allowing for all other variables in the table.

OR = odds ratio; CI = confidence interval.

separately for infancy (0–12 months) and early childhood (1–5 years). As described previously,<sup>24–28</sup> we have traced men and women born in Hertfordshire between 1920 and 1930 and still living there, using the NHS Central Register, Southport.

Our study sample were 631 men and 389 women who had taken part in earlier studies of cardiovascular risk factors.<sup>26–28</sup> They comprised 5% of all men and women born in east and northwest Hertfordshire during 1920–30, and 42% of those known to be still living there. During previous studies (1992–4), the men and women were visited at home by a nurse who obtained the following information by questionnaire: marital status, birth order and number of siblings, occupation of their father at birth, their own most recent full time occupation (and in the case of housewives, that of their husbands), lifetime history of smoking, and current alcohol intake. The father's occupation was used to define social class at birth, and current social class was derived from the subject's occupation (or the husband's occupation for married women).<sup>29</sup> The men and women were then invited to a local clinic for investigations. Their weight and height were measured. Blood samples were taken, separated in the clinic, and the serum stored at -80°C.

In 1995 the stored sera were analysed for anti-*H pylori* IgG antibodies using an ELISA method (HELICO-G; Shield Diagnostics). The sensitivity and specificity of this assay are 93–94% and 88–93% respectively. The concentration of specific antibody was derived from a standard curve of IgG mass against optical density at 450 nm, and subjects were

classified as positive if concentrations exceeded 12 U/ml.

The men and women were also reinterviewed at home by a nurse, to obtain information on childhood household living conditions. Thirty four people had died, and 23 had moved away. Of the remaining 963 subjects, 838 (87%) agreed to contribute further data. They were asked for details of the houses in which they had lived as children and their age when they lived in each house. For each house they were asked whether it was a farm; how many rooms it had; whether they regularly shared a bedroom or bed; and whether the house had an inside water tap, an inside flush lavatory, mains drainage, its own hot water supply, and a separate bathroom. Subjects were omitted from the analysis of household living conditions if they were unable to recall this information.

Our analysis relates to all 1020 men and women from whom serum samples were collected. The relation of *H pylori* seropositivity to factors in early life was examined using multiple logistic regression analysis, both with and without inclusion of potential confounding factors. Since birth weights and weights at 1 year were recorded in pounds, and often rounded to the nearest quarter or half pound, we have retained these units for the analysis.

## Results

### SEX, FAMILY SIZE, AND BIRTH ORDER

The 1020 men and women were aged 65 to 75 (mean 68) years; 463 (46%) were seropositive for *H pylori*. A greater proportion of men than women were seropositive (table 1). Of all the factors examined, the strongest predictor of

Table 2 Percentages of men and women seropositive for *H pylori* according to birth weight and weight at 1 year. Numbers of subjects in parentheses

Birth weight, pounds (kg)	Weight at 1 year, pounds (kg)			All
	≤ 21 (9.55)	– 23 (10.45)	> 23 (10.45)	
<b>Men</b>				
≤ 7.25 (3.30)	52 (83)	48 (67)	27 (48)	44 (n=198)
– 8.25 (3.75)	65 (55)	44 (80)	39 (83)	47 (218)
> 8.25 (3.75)	55 (42)	62 (69)	52 (104)	56 (215)
All	57 (180)	51 (216)	42 (235)	49 (631)
<b>Women</b>				
≤ 7.25 (3.30)	42 (102)	36 (45)	46 (13)	41 (160)
– 8.25 (3.75)	38 (66)	29 (38)	35 (26)	35 (130)
> 8.25 (3.75)	37 (27)	53 (43)	38 (29)	44 (99)
All	40 (195)	40 (126)	38 (68)	40 (389)

Table 3 Percentages of men and women seropositive for *H pylori* according to method of feeding in infancy and weight at 1 year. Numbers of subjects in parentheses

Weight at 1 year, pounds (kg)	Method of feeding in infancy		
	Breast	Bottle	Breast + bottle
<b>Men</b>			
≤ 21 (9.55)	53 (122)	60 (10)	65 (48)
– 23 (10.45)	51 (160)	100 (4)	48 (52)
> 23 (10.45)	47 (148)	47 (17)	30 (70)
All	50 (430)	58 (31)	45 (170)
p for trend	0.08	0.2	0.0008
<b>Women</b>			
≤ 21 (9.55)	41 (155)	80 (5)	31 (35)
– 23 (10.45)	44 (80)	0 (5)	37 (41)
> 23 (10.45)	33 (51)	100 (3)	43 (14)
All	40 (286)	54 (13)	36 (90)
p for trend	0.5	0.6	0.5

seropositivity was family size in childhood. The prevalence of seropositivity rose with increasing number of siblings, and with birth order (table 1). Of these two variables, total number of siblings was more strongly related to seropositivity than birth order, and was the only variable remaining statistically significant in a simultaneous analysis.

#### BIRTH WEIGHT AND WEIGHT AT 1 YEAR

The prevalence of *H pylori* seropositivity rose with increasing birth weight (table 1). Males are heavier than females at birth, however, and birth weight rises with increasing parity. The relation of seropositivity to higher birth weight was no longer significant after allowing for sex and birth order. Higher seropositivity rates were associated with low weight at the age of 1 year (table 1). This association was independent of birth order, and was in the same direction in both sexes, but stronger in men ( $p = 0.0002$ ) and not significant in women ( $p = 0.8$ ). Although there was no relation of seropositivity with birth weight alone after allowing for birth order, a simultaneous regression analysis with birth weight and weight at 1 year showed that seropositivity in men was related to higher birth weight ( $p = 0.0004$ ) and lower weight at 1 year ( $p = 0.0001$ ). The highest prevalence rates were in men who had a low weight at 1 year relative to their birth weight (table 2). The trend with weight at 1 year was least strong in those with high birth weights (table 2). There was no similar pattern in women (table 2).

#### METHOD OF FEEDING IN INFANCY

There were only small numbers of men and women who had been exclusively bottle fed from birth (table 3). They were more likely to

be seropositive for *H pylori* than those who had been breast fed (table 3;  $p$  for difference, both sexes together = 0.08). There was no difference between those exclusively breast fed throughout infancy compared with the breast+bottle fed group. The trend of seropositivity in men with weight at 1 year was stronger in those who were breast+bottle fed than in those who were exclusively breast fed (table 3). There was no difference between people who had a dummy during infancy (48%) and those who did not (44%).

#### CHILDHOOD INFECTIONS

Nine hundred and thirty four subjects were born on or after 1 January 1923, and their records contained information about childhood infectious diseases. The numbers recorded as having infections under the age of 1 year were as follows: measles 25, whooping cough 31, bronchitis or pneumonia 78, diphtheria 0, chicken pox 21, mumps 0, impetigo 6, scarlet fever 1. Seropositivity rates for *H pylori* rose from 43% in subjects who had no infections recorded in infancy to 51% in those with at least one infection recorded, and 59% in those with two or more ( $p$  for trend = 0.03). The findings were similar in men and women. The numbers recorded as having infections between 1 and 5 years were: measles 182, whooping cough 177, bronchitis or pneumonia 70, diphtheria 7, chicken pox 70, mumps 29, impetigo 32, scarlet fever 16. Subjects who had mumps between 1 and 5 years were more likely to be seropositive than those who did not (69% compared with 43%), but otherwise seropositivity was not related to infections during 1–5 years of age.

#### CHILDHOOD LIVING CONDITIONS

Men and women were more likely to be *H pylori* seropositive if their childhood home was crowded, or if they had regularly shared a bedroom or bed (table 4). Living on a farm in childhood was not associated with a higher risk of seropositivity. People who did not have a bathroom in childhood were more likely to be seropositive than those who did. None of the other features of household sanitation, however, was related to seropositivity (table 4).

Household crowding and bedroom or bed sharing were associated with lower social class, currently and at birth. These factors remained significantly related to seropositivity after allowing for social class. Numbers of siblings in a household, degree of crowding, and bedroom or bed sharing were all closely correlated, and collinearity made it difficult to separate the relation of these factors to *H pylori* infection. Cross tabulations of the data suggested, however, that they had cumulative effects. Household crowding was associated with lower weight at the age of 1 year ( $p = 0.0001$ ). The association of seropositivity with low weight at 1 year in boys remained statistically significant ( $p = 0.02$ ) after allowing for household crowding.

#### FACTORS IN ADULT LIFE

*H pylori* seropositivity was not related to social class at birth, but higher percentages of

Table 4 Odds ratios for *H pylori* seropositivity according to living conditions in childhood

	No of subjects	% <i>H pylori</i> positive	OR (95% CI)	<i>p</i> for trend*
No of people per room				
≤ 0.5	72	35	1.0	
- 0.7	132	30	0.8 (0.4 to 1.5)	
- 0.8	141	43	1.4 (0.7 to 2.4)	
- 1.0	145	50	1.9 (1.1 to 3.4)	
- 1.5	137	53	2.0 (1.1 to 3.7)	
> 1.5	102	53	2.1 (1.1 to 3.8)	0.001
Bedroom and bed sharing				
Shared neither	256	35	1.0	
Shared bedroom	133	41	1.3 (0.9 to 2.0)	
Shared bed	426	53	2.1 (1.5 to 2.9)	0.02
Inside water tap				
Yes	553	43	1.0	
No	184	47	1.1 (0.8 to 1.6)	0.5
Inside flush lavatory				
Yes	191	41	1.0	
No	516	47	1.2 (0.9 to 1.7)	0.2
Mains drainage				
Yes	496	43	1.0	
No	197	49	1.2 (0.8 to 1.7)	0.3
Hot water supply				
Yes	86	44	1.0	
No	610	45	1.0 (0.6 to 1.6)	1.0
Separate bathroom				
Yes	160	37	1.0	
No	536	47	1.5 (1.0 to 2.1)	0.03

The living conditions variables are calculated for age 0-10. Number of people per room is the maximum number of people per room at any time during 0-10 years. Bedroom and bed sharing refers to sharing a bedroom or bed regularly at any time during 0-10 years. For the remaining variables: 'Yes' means the amenity was present throughout 0-10 years. Subjects were omitted if unable to recall the information.

\* By logistic regression, allowing for sex.

OR = odds ratio; CI = confidence interval.

subjects in the lower social classes currently were positive (table 1). This relation was not statistically significant after allowing for other factors (table 1). After allowing for sex and social class, there was no relation between seropositivity and smoking or alcohol consumption. Seropositivity was not related to adult height or weight: mean height was 1.72 m and 1.60 m in seropositive men and women, compared with 1.73 m and 1.60 m in those who were seronegative.

## Discussion

As in other studies,<sup>10-14</sup> we found that family size and degree of household crowding in childhood were strongly related to seropositivity for *H pylori* at the age of 65-75 years, independent of current social class. This provides additional support for a role of person to person transmission of *H pylori* in childhood, and persistence of infection into adult life.

The relation of *H pylori* seropositivity to low weight at 1 year was a new finding. The association was confined to men, and was independent of social class and family size. The highest rates of infection were in men who had failed to thrive in infancy, being lighter at 1 year than would be expected from their birth weight. One interpretation of this finding is that *H pylori* infection is a cause of infant growth failure. Theoretically, *H pylori* infection might impair growth by several mechanisms, including malabsorption, chronic inflammation, or diminished food intake caused by dyspeptic symptoms. Although a causal link has not been established, *H pylori* infection in older children is associated with weight loss and reduced height.<sup>14 17 18</sup> Reduced infant growth may be the result of other infections. By producing achlorhydria, *H pylori* encourages infection with other

enteric pathogens.<sup>16 21</sup> The conditions in which *H pylori* is acquired may also favour non-enteric infections. A further possible explanation for the link between low weight at 1 year and increased rates of *H pylori* infection is that smaller infants may have lower immunity to infection. Nutritional factors may influence susceptibility to *H pylori* infection in children.<sup>30</sup> We are unable to explain why *H pylori* seropositivity was related to low infant weight in men and not women. It is unlikely that there was any difference in exposure to infection between the sexes. Possible explanations are that boys are more susceptible to *H pylori* infection in infancy than girls or that infection during infancy has a greater impact on the growth of boys, which is more rapid in infancy than that of girls.

The feeding data contained in the Hertfordshire health visitor records allowed us to examine the influence of infant feeding on *H pylori* seropositivity. Bottle feeding from birth was unusual, and many mothers continued to breast feed throughout infancy. Studies in the Gambia have shown that breast feeding protect infants against *H pylori* infection, by passage of IgA antibodies.<sup>21</sup> Protection is probably only transient, for the duration of the breast feeding.<sup>21</sup> This may explain our finding that, although men and women who had been breast fed from birth were less likely to be *H pylori* seropositive than those who had been bottle fed, the effect was weak and not statistically significant. The data show, however, that the association of *H pylori* seropositivity with lower weight at 1 year in men was most marked in those who were breast+bottle fed. Exclusive breast feeding may have prevented *H pylori* infection in infancy, and protected the breast fed male babies from growth failure.

The mode of transmission of *H pylori* is not known; there is debate as to whether it is oral-oral or faeco-oral, or both.<sup>7-9</sup> The association with crowding and bed or bedroom sharing in childhood is compatible with either mode of transmission. Faeco-oral spread of disease is reduced by the introduction of household sanitary amenities in two ways. Flush toilets, mains drainage, and a protected water supply prevent faecal contamination of drinking water. Hot water and bathrooms mean that people wash, reducing faecal contamination of the skin and hands. Although data recalled in old age must not be overinterpreted, the association of *H pylori* infection in our study with absence of a bathroom in childhood, but the lack of correlation with absence of a flush toilet, mains drainage, or separate water supply, supports other evidence<sup>8 9</sup> that transmission of *H pylori* through skin contamination may be important, but that transmission from a contaminated water supply is not, at least in this rural English setting.

In contrast to a recent study in Stoke on Trent,<sup>12</sup> seropositivity in the Hertfordshire men and women was not related to social class at birth. Hertfordshire was a rural and relatively affluent area in the 1920s. Father's occupation may not be such a good proxy for the living conditions which favour *H pylori* infection as in

urban populations. The association of seropositivity with other infections in infancy is likely to reflect living conditions which favoured transmission of infections. The stronger association with infant infections than with infections from 1–5 years may be because infections in infancy are more likely to be acquired in the home, as is *H pylori* infection, whereas in the older child many infections are community acquired.

The men and women in our study were born in one English county, were traced, and still lived in their county of birth. They were therefore not a true population sample. Their mean birth weight and weight at 1 year were similar, however, to those of all babies born in Hertfordshire at the same time. The recalled data on household living conditions may be inaccurate, and some subjects were unable to provide all the data. The ELISA test for *H pylori* is thought to be less reliable in the elderly than in young adults, with higher false negative rates, perhaps due to a decline in immune function with age.<sup>31</sup> Although we believe that specific treatment for *H pylori* would have been unusual in this group of men and women, some people may have become seronegative after treatment.<sup>32–35</sup> All these factors would tend to obscure, not accentuate, relations between *H pylori* and factors in early life.

Our findings raise the possibility that *H pylori* infection has significant effects on infant growth, especially in boys. Further studies are needed to determine whether *H pylori* is a major cause of infant growth failure, whether there are true differences between the sexes, and whether breast feeding prevents early infection. These questions are particularly important for developing countries where rates of infection in infancy remain high, and for high risk, poor families in developed countries. The current debate about community level screening for *H pylori*, and the quest for better methods of treatment and prevention of infection, should certainly excite the interest of paediatricians.

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