Epidemiol. Infect. (1993), **111**, 63–70

Social and geographical risk factors in *Helicobacter pylori* infection

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(*Accepted 24 January 1993*)

SUMMARY

A correlation between childhood crowding and the later development of gastric cancer has been demonstrated by Barker and colleagues, who proposed that the relationship was the consequence of infection by an organism such as *Helicobacter pylori*. In order to test this hypothesis the presence of IgG antibodies to *H. pylori* in sera from blood donors in North Wales has been investigated. During donation sessions, donors answered questions relating to social conditions and domicile in childhood (at age 10 years) and adult life (the preceding 2 years).

A stepwise logistic regression analysis of the data demonstrated significant independent relationships between seropositivity and the following factors: sharing a bed in childhood, housing density, locality of birth, adult social class and age.

INTRODUCTION

Helicobacter pylori, a spiral, microaerophilic, Gram-negative bacterium first isolated in 1983 [1], is considered to be largely a human pathogen predominantly present in the stomach [2] where it is found beneath the mucous layer in close association with the surface epithelium of gastric pits [3]. The organism can be acquired by mouth, by contact with inanimate objects [4], and under some circumstances maybe transmitted through the water supply [5]. Epidemiological studies have shown the infection to be more prevalent in those of lower social class [6], in developing compared to developed nations, and to vary among different racial groups within the same country [7, 8].

It is generally accepted that *H. pylori*, though possibly some strains only [9], plays a role in the aetiology of chronic atrophic (Type B) gastritis. The organism is also thought to contribute to the development and persistance of duodenal ulcer and to have a role in the aetiology of gastric cancer [10–12]. Although several mechanisms of pathogenesis have been suggested [13], the precise means by which the organism causes mucosal injury is at present unknown and it is possible that a combination of mechanisms is involved.

The association of gastric cancer with low social class is well documented [14]. In an investigation of aetiological processes which might explain this association, overcrowding in the home during childhood was considered to be a major factor and it was suggested that crowding might promote the transmission of a causative

organism such as *H. pylori* [15]. The present study investigates the relationship between *H. pylori* infection and childhood and adult living conditions in North West Wales, an area of relatively high mortality from gastric cancer [16].

MATERIALS AND METHODS

The study population comprised blood donors taken sequentially from those attending sessions at 26 sites throughout Gwynedd and North West Clwyd. Subjects gave informed consent to their participation in the study and were questioned about their living conditions as an adult over the preceding 2 years, and during childhood at around 10 years of age. The questions are specified in the appendix and are summarized in Table 1.

Apart from personal data they were designed to define circumstances of domicile, inter-personal contact and hygiene arrangements available. As a study has suggested an association between gastric cancer and contact with bracken during childhood, enquiries were made of possible exposure.

Sera were separated and stored at −5 °C prior to despatch to the Public Health Laboratory, Preston, for examination. A urease-rich antigen preparation was used and serum IgG antibodies measured using the enzyme-linked immunosorbent assay (ELISA) with a cut-off titre of 1000, as previously described [18]. A sensitivity of 97% and specificity of 90% has been reported for this method.

A stepwise logistic regression analysis [19] retaining age and sex in the model was used to assess whether seropositivity is related to the measured variables. A logistic regression analysis is necessary to allow the dependent, dichotomous variable of seropositivity to be predicted from the risk factors. A stepwise analysis determines which risk factor is most related to seropositivity, then which risk factor in combination with the one already chosen is most related to seropositivity. Further risk factors are included in the model until no more are significantly related with seropositivity ($P > 0{\cdot}05$). Subsequent analysis was restricted to individuals who did not have missing values for the variables in the final model.

RESULTS

A total of 1000 persons was surveyed. The model for the data was developed using the 961 people who gave full information for the risk factors in Table 1, with the exception of childhood social class (missing data for 46 people), drinking untreated milk as a child (missing for 102 people) and bracken exposure (missing for 45 people). The largest number of people who did not answer any of the remaining questions was 8. The data presented here is for the 985 people who gave full information for the risk factors in the final model. The effect of the relatively small amount of missing data was observed to be minor.

Of the 985 persons studied 41% were positive for *H. pylori* IgG antibody. The proportions infected by age group, sex and social class are shown in Table 2.

There were a number of significant risk factors when added one at a time to the model consisting of age and sex. These were, in order of significance: adult social class, sharing a bed in childhood, number of people in the bedroom in childhood, area of domicile, number of older siblings, childhood house density, number of

Table 1. *Questions asked concerning childhood and adult conditions*

		Childhood	Adult
	Social class	✓	✓
	District of domicile	✓	✓
*	Housing density	✓	
†	Housing type	✓	✓
	No. of bedrooms	✓	✓
	No. of other rooms	✓	
	No. of people in house	✓	✓
	No. of people in bedroom	✓	
	Sharing a bed	✓	
	No. of siblings	✓	
	Mains water supply	✓	
	Mains drainage	✓	
	Indoor toilet	✓	
	Hot running water	✓	✓
	Untreated milk	✓	✓
‡	Exposure to bracken	✓	

* Classified as: sole (isolated residence), edge (residence with adjacent fields but not isolated), village, town (small conurbation), city (large conurbation).

† Classified as: detached, semi-detached, terraced, flat, hotel, other.

‡ Within 200 m of home or persistently playing amongst bracken.

Table 2. *The percentage seropositive in each category of age group, sex and adult social class*

			Age group (yrs)											
		Adult social class	< 20		21–30		31–40		41–50		51–60		> 61	
			n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Sex	Male	N*	14	21	40	38	47	28	36	31	26	62	5	40
		M	14	50	99	44	101	43	77	53	34	56	5	60
	Female	N	29	28	97	31	100	38	95	35	39	46	8	50
		M	5	60	39	51	30	50	31	29	9	67	5	40

* N, non-manual; M, manual.

The numbers in the table are derived from the 985 blood donors who had no missing values for seropositivity, age, sex, adult social class, sharing a bed in childhood, childhood house density and the residential area variables.

younger siblings, number of people in the house in childhood, and type of house in childhood. None of the other risk factors listed in Table 1 was significant ($P > 0{\cdot}05$). It was recognized that a number of the above factors are essentially measuring overcrowding in the house in childhood. However, of these, only the number of people in the bedroom in childhood is a significant addition to a model containing sex, age and sharing a bed in childhood.

When the stepwise logistic regression with age and sex already in the model is performed then the variables which best predicted seropositivity were adult social class, sharing a bed during childhood, childhood house density and area of domicile. After adjustment for age, sex, adult social class, sharing a bed, housing density and area, none of the other childhood or adulthood factors was

Table 3. *The number, odds ratio and 95% confidence interval for each risk factor in the model*

	n	Odds ratio	95% C I
Sex			
Female	487	0·98	0·73 1·32
Male	489	1	(P = ns)
Age			
Each additional year		1·02	1·00 1·03 ($P < 0·01$)
Adult social class			
Manual	449	1·53	1·14 2·05
Non manual	536	1	($P < 0·01$)
Sharing a bed during childhood			
Sharing	277	1·50	1·12 2·02
Not sharing	708	1	($P < 0·001$)
Childhood house density			
Sole	127	0·80	0·46 1·38
Village	332	0·67	0·42 1·06
Edge	48	0·60	0·29 1·24
Town	347	1·13	0·73 1·76
City	131	1	($P < 0·05$)
Area			
Living in and born in Gwynedd	373	1·46	1·04 2·04
Living in but not born in Gwynedd	316	0·95	0·67 1·35
Not living or born in Gwynedd	296	1	($P < 0·05$)

Table 4. *The predicted probability of seropositivity for each risk factor in the model*

Variables	Predicted probability of seropositivity
Sex	
Male	0·41
Female	0·41
Age	
20	0·35
30	0·38
40	0·42
50	0·46
60	0·49
Adult Social Class	
Non-manual	0·36
Manual	0·46
Sharing a bed during childhood	
Sharing	0·48
Not sharing	0·38
Childhood House Density	
Sole	0·39
Village	0·35
Edge	0·32
Town	0·47
City	0·44
Area	
Living in and born in Gwynedd	0·47
Living in but not born in Gwynedd	0·37
Not living in or born in Gwynedd	0·38

significantly associated with seropositivity. Odds ratios and 95% confidence intervals for the risk factors in the model are shown in Table 3. Interactions between these terms were not related to seropositivity ($P > 0{\cdot}05$). The probability that an individual is seropositive for each category predicted using the model, after accounting for the other risk factors, is shown in Table 4.

DISCUSSION

The study population was drawn from those attending routine donor sessions. Blood donors represent the age range 18–70 years, they are drawn from both sexes and all social classes but not necessarily in the proportion found in the population. As a group they cannot be regarded as being wholly representative of the population of this age range in Gwynedd and North West Clwyd community at large. Owing to the different populations and methods of recruitment in other surveys, with consequent effects upon the sex, age, race and social class structure, the overall infection rate of 41% in this survey is difficult to compare. However, in common with a study of South Wales men [6], this finding would seem to represent a higher prevalence of the infection than those reported in other serological surveys of non-symptomatic individuals in the UK [20].

Our findings are consistent with previous studies in that seropositivity increased with age and was associated with lower social class [6]. In common with some other studies we find seroprevalence is independent of sex [8]. Both communal and personal crowding were found to have an association with seropositivity, the strongest effect from personal crowding.

The association between lower social class and increased risk of *H. pylori* infection is well established but has remained unexplained. A simple explanation of the social class differences could have been the effect of personal crowding. Were this to be true then an interaction between social class and childhood crowding should be observed. We failed to demonstrate any such relationship. This result was not due to the relatively small numbers analysed as very similar proportions of the non-manual and manual classes shared beds in childhood (26 *v.* 31%). A more detailed examination of socio-economic structure might shed more light on this relationship.

The finding relating to communal crowding is equally puzzling. Although this feature was significantly related to seropositivity none of the individual categories showed a significant association nor did the expected trend with increasing housing density develop. The odds ratios suggest it may be more meaningful to define communal crowding as rural (edge, village, sole) or urban (town, city). If close physical contact is, as seems likely, the important factor promoting transmission of the organism, there is clearly more opportunity for contact to occur in streets, public transport and in the larger schools of cites and towns.

That seropositivity amongst those born in Gwynedd contrasted sharply with those born elsewhere although living in Gwynedd supports the view that childhood is the time that many of those born in the county acquire the infection. This conclusion is supported by Mendall and colleagues [21] who suggest that most British adults acquired their infection from household contact in childhood.

Other factors – absence of provision of mains water supplies, mains drainage, hot water supply and an indoor toilet – were not found to increase chances of being

infected. In contrast Mendall and colleagues reported an association between lack of a hot water tap in the childhood home and seropositivity in adult life.

Close physical contact in childhood results in a cohort of people infected early in life. Natural remission of the infection is rare [22] and even if acquisition of infection continues with increasing age, then the cohort will at any one time show a higher rate of seropositivity than those from a less crowded childhood environment.

Recent studies have shown that infection with *H. pylori* leads to an increased risk of developing gastric cancer [12, 23]. The higher prevalence of the infection in the general population, however, shows clearly that additional agents are involved. In previous work [17] we reported a significant relationship between childhood exposure to bracken and the later development of gastric cancer. We pointed out that 'The possibility exists that bracken exposure is a proxy variable for something not studied here.' *H. pylori* infection could have been the underlying risk factor but the finding here of no relationship between the two negates this and suggests that bracken exposure has an independent role in the aetiology of gastric cancer.

In conclusion, our results indicate a connection between childhood overcrowding and *H. pylori* infection and therefore give support to the views of Barker and colleagues [15] who showed a relation between domestic crowding and geographical variation in gastric cancer mortality, suggesting the involvement of a transmissible organism. Our results appear to indicate the importance of close personal contact in the transmission of this infection, the causative organism of which has recently been isolated from human faeces [24]. Finally our finding that Gwynedd-born individuals have a higher prevalence of *H. pylori* infection than those born elsewhere may explain the observations of Coggon and colleagues [16] who demonstrated that the area of birth in England and Wales rather than that of death is important in determining risk from gastric cancer.

ACKNOWLEDGEMENTS

We are indebted to Dr D. N. Hutchinson, Preston, for the serological analysis, to Professor D. Barker and Dr D. Coggon, Southampton and to Dr A. Howard, Bangor for valuable advice. The funding of this study was provided by the Gwynedd Research Committee. The study was made possible by the essential help and cooperation of Dr V. J. Martlew, Blood Transfusion Service, Liverpool, B. Brailsford and all the staff of the Blood Transfusion Service, Caernarfon, and M. Pool and K. Davies, Ysbyty Gwynedd Hospital. We are grateful to Miss J. Thistlethwaite and Mrs B. Evans for secratarial services.

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APPENDIX

The questions asked were classified using the following criteria.

1. *Date of birth*

Used to calculate age at last birthday.

2. *Residence in Gwynedd*

Total number of years spent in Gwynedd exclusive to any periods away.

3. *Social class (childhood and adulthood)*

Subjects were categorized into Manual and Non-manual classes according to the standard OPCS classification (Classification of Occupations, OPCS, 1980). Childhood social class was derived from the father's occupation during the subject's childhood.

4. *Place of birth*

The area where the subject's family lived at the time of their birth which was classified as: (1) Gwynedd, (2) Wales – area of Wales other than Gwynedd, (3) England, (4) Scotland, (5) Other.

5. *Place of residence*

Classified into the five districts of Gwynedd:
(1) Môn, (2) Arfon, (3) Aberconwy, (4) Dwyfor, (5) Merionydd and (6) Clwyd, (7) Wales – areas of Wales not included elsewhere, (8) England, (9) Scotland, (10) Other.

6. *Housing density (childhood)*

(1) Sole – isolated residence, (2) Village – rural residence but not isolated, (3) edge – residence is in village or town but with adjacent fields, (4) Town – small town or city, (5) City – large town or city.

7. *House type (childhood and adulthood)*

(1) Detached, (2) Semi-detached, (3) Terraced, (4) Flat – bedsit or flat in part of house, (5) Hotel – hotel, hostel, highrise flats or other multi-resident accommodation, (6) Other – including caravans.

8. *Number of bedrooms (childhood and adulthood)*

Total number of bedrooms.

9. *Number of other rooms (childhood)*

Total number of rooms excluding bedrooms, bathrooms and kitchens.

10. *Number of people in the house (childhood and adulthood)*

Total number of people in house including the subject.

11. *Number in the bedroom (childhood)*

The number of people in the bedroom at around the age of 10.

12. *Sharing a bed (childhood)*

Whether the subject shared a bed at any time up to the age of 10 years:
(1) Never of occasionally but not regularly and (2) Usually.

13. *Number of older and younger siblings (childhood)*

Only siblings living in the childhood home were included.

14. *Mains water, mains drainage, indoor toilet (childhood)*

Whether or not the childhood home had these facilities.

15. *Hot water (childhood and adulthood)*

Whether or not the house had running hot water.

16. *Untreated milk (childhood and adulthood)*

Whether unpasteurized milk was drunk: (1) Regularly (at least once a week), (2) Sometimes (at least once a month), (3) Occasionally (less than once a month), (4) Never.

17. *Bracken*

Whether there was bracken in the vicinity (up to 200 m) of the childhood home. Also included were subjects who had a vivid recollection of persistently playing amongst bracken as a child.