Epidemiol. Infect. (1998), **120**, 297–303. Printed in the United Kingdom © 1998 Cambridge University Press

Active infection with *Helicobacter pylori* in an asymptomatic population of middle aged to elderly people

D. ROTHENBACHER[1]*, G. BODE[2], F. PESCHKE[1], G. BERG[1], G. ADLER[2] AND H. BRENNER[1]

[1] *Department of Epidemiology, University of Ulm, D-89069 Ulm/Germany*
[2] *Department of Internal Medicine I, University of Ulm, D-89070 Ulm/Germany*

(*Accepted 26 January 1998*)

SUMMARY

The study objective was to investigate prevalence and determinants of current *Helicobacter pylori* infection in an asymptomatic population of middle-aged to elderly people. A cross-sectional study was conducted among 337 participants of a general education programme of the University of Ulm aged 50–85 years. Prevalence of infection as determined by means of the [^{13}C]urea breath test was 34·8% (95% CI 29·6–40·3%); overall, 33·8% (95% CI 23·0–46·0) in the age group 50–59 years, 32·4% (95% CI 25·4–39·9) in the age group 60–69 years and 41·0% (95% CI 30·0–52·7) in the age group 70–85 years. Duration of school education of the father, sharing a bed with parents or siblings during childhood, and the area in which participants had grown up were independent determinants of current infection status in a multivariable analysis. We conclude that the prevalence of current *H. pylori* infection in healthy elderly subjects may not be as high as seroprevalence studies have suggested. Socioeconomic characteristics of childhood living conditions appear to be important determinants of infection status even at older age.

INTRODUCTION

Infection with *Helicobacter pylori* almost always causes a chronic inflammation of the gastric mucosa. It is associated with considerable morbidity such as peptid ulcer [1, 2] and gastric malignancy [3–6]. The prevalence of infection within populations increases with age [7]. For example, seropositivity in the EUROGAST study, a population-based study of 17 geographically defined populations, was shown to vary between 29% in the age group 25–34 years and 69% in the age group 55–64 years in three selected regions of the southern part of Germany [8]. Infection is assumed to be acquired mainly in early childhood. Differences between age categories within populations seem to reflect primarily a birth cohort effect associated with lower rates of infection in more recent birth cohorts due to improved childhood living conditions over time [9].

In most previous epidemiological studies *H. pylori* infection status has been determined by serological testing. Yet this method does not allow a safe distinction between current and past infection. This may lead to a falsely high prevalence in subjects who may have had contact with the agent in the past and then lost active infection due to the development of atrophic gastritis [10]. This problem affects especially older persons among whom development of atrophic gastritis is common [11]. In contrast to serology, the [^{13}C]urea breath test only indicates active infection with *H. pylori* [12]. In addition, because it is a non-invasive method with no risks and no side effects, it is applicable to large populations outside the medical setting.

The objectives of this study were to determine the

* Author for correspondence.

https://doi.org/10.1017/S0950268898008644 Published online by Cambridge University Press

Table 1. *Sociodemographic characteristics of the study population by sex*

Characteristic	Male	(%)	Female	(%)	All	(%)
Number	111	(34·8)	208	(65·2)	319	
Age (years)						
Mean	65·3	(S.D. 6·1)	64·8	(S.D. 7·8)	65·0	(S.D. 7·2)
Range	53–83		50–85		50–85	
School education						
⩽ 9 years	14	(12·6)	34	(16·3)	48	(15·0)
10–11 years	32	(28·8)	95	(45·7)	127	(39·8)
⩾ 12 years	65	(58·6)	79	(38·0)	144	(45·1)
Occupation (current or if retired, former)						
Housekeeping	0	(0)	83	(40·7)	83	(26·4)
Blue-collar worker	2	(1·8)	2	(1·0)	4	(1·3)
White-collar worker	96	(87·3)	103	(50·5)	199	(63·4)
Independent businessman	9	(8·2)	14	(6·9)	23	(7·3)
Other	3	(2·7)	2	(1·0)	5	(1·6)
Family situation						
Single	2	(1·8)	28	(13·5)	30	(9·4)
Married	100	(90·1)	113	(54·3)	213	(66·8)
Divorced/widowed	9	(8·1)	67	(32·2)	76	(23·8)

prevalence of, and determinants for *H. pylori* infection in an asymptomatic population of subjects aged 50 or over in Southern Germany by means of [^{13}C]urea breath test.

METHODS

Study population and study design

All participants of the continuing education week at the University of Ulm in September 1996 were invited to participate. The continuing education programme is a seasons' academy, which is held twice a year. It is targeted at older people and is open to the public. The programme consists of a series of lectures and workshops. The study was approved by the Ethics Board of the University of Ulm. Informed consent of the participants was obtained in each case.

Data collection

[^{13}C]*urea breath test*

H. pylori infection status was determined during the education week by [^{13}C]urea breath test. An initial breath sample and, after administration of 75 mg non-radioactive labelled ^{13}C urea (Mass Trace, Woburn, MA, USA) in 200 ml of apple juice (pH 2·2–2·4), a 30 min breath sample was collected. Breath samples were analysed with an isotope selective non-dispersive infrared spectrometer (NDIRS; Wagner Analytical Systems, Worpswede, Germany). A change of the $^{13}CO_2/^{12}CO_2$ ratio over baseline of more than 5‰ was considered positive.

The accuracy of the [^{13}C] urea breath test in adults is well documented [12]. Sensitivities close to 100% have been reported consistently. Recently, it has been demonstrated that this test shows a perfect concordance with culture and rapid urease test and is therefore ideal for the diagnosis of active infection with *H. pylori* [13].

Self-administered questionnaire

Participants were asked to fill out a standardized questionnaire which was sent in advance. Information was sought regarding demographic and socioeconomic factors, medical history, including family history and history of medication as well as housing and living conditions during childhood. Questionnaire data were checked for completeness and plausibility by trained research assistants.

Statistical analysis

The proportions of infected patients and 95% confidence intervals (CIs) were calculated for various age categories. The bivariate association of variables concerning family demographics, socioeconomic status, housing and living conditions with infection

https://doi.org/10.1017/S0950268898008644 Published online by Cambridge University Press

Table 2. *Age-stratified prevalence of* H. pylori *infection measured by means of* [^{13}C]*urea breath test*

Age (years)	Birth cohort	No.	*H. pylori* positive No.	(%)	95% CI†
50–59	1937–1946	71	24	(33·8)*	23·0–46·0
60–69	1927–1936	170	55	(32·4)*	25·4–39·9
70–85	1911–1926	78	32	(41·0)*	30·0–52·7
Total		319	111	34·8	29·6–40·3

* $P = 0{\cdot}404$ for differences between the three age categories.
† 95% CI for proportion *H. pylori* positive.

Table 3. *Association of* H. pylori *infection with sociodemographic and personal factors*

Factor	No.	*H. pylori* positive No.	(%)	*P* value
Sex				
Male	111	40	(36·0)	
Female	208	71	(34·1)	0·734
Marital status				
Single	30	8	(26·7)	
Married	213	76	(35·7)	
Widowed/separated	76	27	(35·5)	0·617
Occupation				
Housekeeping	83	22	(26·5)	
Blue collar/else	9	4	(44·4)	
White collar	199	74	(37·2)	
Business man	23	11	(47·8)	0·170
Working in the health service sector				
No	258	90	(34·9)	
Yes	61	21	(34·4)	0·946
Occupational handling of animals				
No	303	105	(34·7)	
Yes	15	6	(40·0)	0·672
School education				
⩽ 9 years	48	25	(52·1)	
10–11 years	127	44	(34·6)	
⩾ 12 years	144	42	(29·2)	0·015
School education of mother				
⩽ 9 years	211	87	(41·2)	
10–11 years	87	20	(23·0)	
⩾ 12 years	20	4	(20·0)	0·004
School education of father				
⩽ 9 years	150	66	(44·0)	
10–11 years	74	26	(33·8)	
⩾ 12 years	92	18	(19·6)	< 0·001
History of antibiotic treatment within the last 5 years				
No	121	39	(32·2)	
Yes	166	60	(36·1)	0·491

status was assessed. In addition we assessed the independent effects of various determinants of current *H. pylori* infection by means of multivariable statistical modelling (unconditional logistic regression). The following covariates which had been identified as risk factors for infection in previous studies or which were associated with infection status in our bivariate analyses were included in the initial model: sex, occupation (white collar, housekeeping, else), number of years of school education of participants and their parents (⩽ 9 years, 10–11 years, ⩾ 12 years), number of siblings (0, 1 or 2, ⩾ 3), sharing a bed with parents or siblings over a prolonged time period during childhood (yes/no), area where participants had grown up (countryside, city), cat in the household during childhood (yes/no). Covariates that did not contribute to the prediction of infection status at a significance level of 0·05 were removed from the model by means of a stepwise backward elimination strategy. All statistical procedures were carried out with the SAS statistical software package [14].

RESULTS

Of 486 subjects aged 50–85 years who registered for the academy's programme via mail, 337 (69%) participated in the study. However, we were unable to check whether all subjects who registered in advance attended the lectures and workshops. Therefore, the participation rate may have been higher among the subjects present. In order to exclude the possibility of false negative test results, 13 participants who had reported *H. pylori* infection in the past and whose infection had been successfully eradicated were excluded from the analysis, as were five participants who reported taking antibiotics while the examination was performed, leading to a final sample size of 319. Table 1 shows the sociodemographic characteristics of the study population. As most of the participants were pensioners, their former occupational status has been given.

Table 2 shows age-stratified prevalence of *H. pylori* infection as measured by ^{13}C[urea] breath test. Table 3 shows the association of *H. pylori* infection with

https://doi.org/10.1017/S0950268898008644 Published online by Cambridge University Press

Table 4. *Association of* H. pylori *infection with childhood living conditions*

Factor	No.	*H. pylori* positive No.	(%)	*P* value
Age at menarche				
11–12	31	15	(48·4)	
13–14	112	35	(31·3)	
⩾ 15	58	18	(31·0)	0·176
Number of siblings during childhood				
0	44	13	(29·5)	
1 or 2	182	60	(33·0)	
> 2	93	38	(40·9)	0·315
Sharing a bed with siblings or parents during childhood				
No	291	94	(32·3)	
Yes	27	17	(63·0)	< 0·001
Area of upbringing				
Countryside	100	48	(48·0)	
City (up to 100000)	163	49	(30·1)	
City (> 100000)	56	14	(25·0)	0·003
Geographical region in childhood				
Germany	278	92	(33·1)	
Elsewhere	41	19	(46·3)	0·096
Pet in the household during childhood				
No	137	45	(32·8)	
Yes	182	66	(36·3)	0·526
Dog in the household during childhood				
No	216	75	(34·7)	
Yes	103	36	(35·0)	0·968
Cat in the household during childhood				
No	225	69	(30·7)	
Yes	94	42	(44·7)	0·017

sociodemographic and personal factors. Table 4 shows the association of factors and conditions during childhood with current *H. pylori* prevalence. Though keeping a pet in the household during childhood was not associated with infection status, keeping a cat in the household was strongly associated with an increased prevalence of infection in the bivariate analysis (44·7 *vs.* 30·7%, $P = 0·017$). No association with current *H. pylori* prevalence was found for specific living conditions during or since World War II. Factors investigated were periods of starving, serving in the army, spending time in captivity or in a refugee camp. Spending more than 3 months abroad was also not associated with current infection status (data not shown).

Table 5. *Adjusted odds ratios* (OR) for significant predictors of* H. pylori *infection*

Factor	Adjusted OR (95% CI)
School education of father	
⩽ 9 years	1†
10–11 years	0·8 (0·5–1·5)
⩾ 12 years	0·4 (0·2–0·7)
Sharing a bed with siblings or parents during childhood	
No	1†
Yes	2·6 (1·1–6·1)
Area of upbringing	
City	1†
Countryside	1·9 (1·1–3·1)

* Adjusted for all variables listed in the table by multiple logistic regression.
† 1, reference category.

Table 5 shows the results of the multivariable analysis. All variables which had been identified as risk factors for infection in previous studies or which were associated with infection status in the bivariate analyses were included in the initial model. However, only school education of father, sharing a bed with parents or siblings during childhood, and the area in which subjects had grown up (countryside versus city) made a statistically significant contribution to the prediction of *H. pylori* infection.

DISCUSSION

In this study we describe the prevalence of current *H. pylori* infection as determined by [^{13}C]urea breath test in a sample of participants aged 50 years or over in a public education programme at the University of Ulm in Southern Germany. Overall, the prevalence of *H. pylori* infection was about one third. There was no clear difference regarding prevalence of infection in this age range from 50 to 85 years. However, shorter school education of the father, having grown up in the countryside and having shared a bed with siblings or parents in childhood were independent determinants of infection, confirming the importance of living conditions in childhood relative to the influence of more recent living circumstances.

In contrast to the findings in this study, a higher overall prevalence of seropositivity from 57 to 76% was seen in three regional samples of the German

https://doi.org/10.1017/S0950268898008644 Published online by Cambridge University Press

population in the age stratum 55–64 years in the EUROGAST study [8, 15], as in some other studies from European countries [16–19]. Some of the differences may be explained by regional variation of infection and sociodemographic differences because, as a comparison with national survey data demonstrates, our population consists of a large proportion with a high school education (44·5% had 12 years or more of school education). In comparison, the distribution of duration of school education in a representative population-based sample from Germany was 9·3, 26·7 and 64·0%, for equal to more than 12 years, 10–11 years, or less than or equal to 9 years of school education [20]. Nevertheless, the prevalence of infection among participants in the lowest category of school education in our study population was still low compared with other studies estimating seroprevalence. Furthermore, age-specific prevalence was similar to prevalence in a sample of 505 consecutive outpatients attending a general practitioner in the same region [21]. Prevalence of infection in this patient population as determined also by means of [^{13}C]urea breath test was 28·2 and 30·8% in 50–59 and 60–79 year age cohorts, respectively. Therefore we suggest that the lower prevalence of active infection with *H. pylori* in our study population compared to seroprevalence data from Germany [8, 15] is not totally attributable to the higher socioeconomic status of our study population.

The fact that *H. pylori* status was measured by [^{13}C]urea breath test rather than serologically may be an important factor. Meyer and colleagues determined infection status in 100 volunteers aged 20–92 years by means of [^{13}C]urea breath test and serologically [22]. They found that only half of those with positive serology also had a positive breath test. Another study showed that 3 of 18 asymptomatic elderly subjects (16%) had a negative breath test when serology was positive [23]. In a study of asymptomatic volunteers, serology was positive in 33·7% whereas a positive culture was obtained in only 19·4% [10]. All these results imply that serostatus indicates past as well as present exposure to *H. pylori* and is not sufficiently specific to indicate active infection, especially in elderly subjects.

Apart from age, *H. pylori* is a risk factor for the development of atrophic gastritis [11]. Once this has developed, the intensity of infection may lessen because of the resulting inhospitable condition of the gastric mucosa [24]. It may well be that a certain proportion of particularly elderly subjects may have lost active infection already due to the development of atrophic gastritis. Prevalence of chronic gastritis with severe atrophy as determined by pepsinogen levels was shown to be up to 11% in 55 to 64-year-old subjects from Southern Germany [15].

We found a clear relationship between living conditions in childhood and infection status in accordance with previous studies; above all, residential crowding may play a key role for transmission within families [25]. Close physical contact in early childhood (e.g. by sharing a bed with parents or siblings) may promote spread of infection [26]. Further determinants are a low level of socioeconomic status and poor living and housing conditions [27, 28]. In the bivariate analyses educational level of participants themselves and of their parents were strongly associated with prevalence of infection. However, only the fathers' education, which may best reflect socioeconomic conditions during childhood, showed an independent effect on *H. pylori* prevalence in multivariable analysis.

Factors characterizing present living conditions, as well as marital status or history of recent antibiotic treatment were not related with infection status in this study. This was also the case for occupational history, e.g. working in the health-care sector in general, although other studies have suggested an increased risk for certain health-care professionals such as nurses and gastroenterologists [29, 30].

People who were raised in the countryside showed a higher prevalence of infection, even after controlling for other variables in the multivariable analysis. Keeping a cat during childhood was only associated with current *H. pylori* infection status in the bivariate analysis. After controlling for other variables the association disappeared. This is consistent with current knowledge as humans are the only identified source of infection at present [31].

This study is one of the first to report the prevalence of current *H. pylori* infection in an asymptomatic healthy population aged 50 years and over. The strengths of the study include the use of the [^{13}C]urea breath test to determine infection status. The high sensitivity and specificity of this test allow estimation of the prevalence of current *H. pylori* infection with high accuracy. Although the sample is population based and the academy's programme is open to the public, participants are self selected and thus may not be representative of the general population. Nevertheless, the living conditions during childhood of this high socioeconomic group in our study population

https://doi.org/10.1017/S0950268898008644 Published online by Cambridge University Press

may be similar to those of lower socioeconomic groups born later and may therefore, be used to predict the future *H. pylori* prevalence of the general population.

Despite its limitations, the study indicates that prevalence of current *H. pylori* infection in middle aged or elderly people may not be as high as seroprevalence studies suggest. Another important finding is that socioeconomic characteristics of parents, especially the fathers' school eduction, which may best characterize childhood living conditions, are important determinants of infection even in elderly subjects. This gives further support to the evidence that early childhood is the major period for acquisition of the infection.

ACKNOWLEDGEMENT

We would like to thank the Centre for General Science-Oriented Continuing Education at the University of Ulm for help in conduct of the study and appreciate the participation of the mature students.

REFERENCES

1. Peterson WL. *Helicobacter pylori* and peptic ulcer disease. N Engl J Med 1991; **324**: 1043–8.
2. Graham DY. *Helicobacter pylori*: its epidemiology and its role in duodenal ulcer disease. J Gastroenterol Hepatol 1991; **6**: 105–13.
3. Nomura A, Stammermann GN, Chyon PH, Kato J, Perez-Perez GI, Blaser MJ. *Helicobacter pylori* infection and gastric carcinoma among Japanese Americans in Hawaii. N Engl J Med 1991; **325**: 1132–6.
4. Parsonnet J, Friedmann GD, Vandersteen DP, Orentreich N, Sibley RK. *Helicobacter pylori* infection and the risk of gastric carcinoma. N Engl J Med 1991; **325**: 1127–31.
5. Forman D, Newell DG, Fullerton F, et al. Association between infection with *Helicobacter pylori* and risk of gastric cancer: evidence from a prospective investigation. BMJ 1991; **302**: 1302–5.
6. Parsonnet J, Hansen S, Rodriguez L, et al. *Helicobacter pylori* infection and gastric lymphoma. N Engl J Med 1994; **330**: 1267–71.
7. Goodman KJ, Correa P. The transmission of *Helicobacter pylori*. A critical review of the evidence. Int J Epidemiol 1995; **24**: 875–87.
8. The EUROGAST Study Group. Epidemiology of, and risk factors for *Helicobacter pylori* infection among 3194 asymptomatic subjects in 17 populations. Gut 1993; **34**: 1672–6.
9. Banatvala N, Mayo K, Mégraud F, Jennings R, Deeks JJ, Feldman RA. The cohort effect and *Helicobacter pylori*. J Infect Dis 1993; **168**: 219–21.
10. Karnes WE, Samloff IM, Siurala M, et al. Positive serum antibody and negative tissue staining for *Helicobacter pylori* in subjects with atrophic body gastritis. Gastroenterol 1991; **101**: 167–74.
11. Kawaguchi H, Harum K, Komoto K, Yoshihara M, Sumii K, Kajiyama G. *Helicobacter pylori* infection is the major risk factor for atrophic gastritis. Am J Gastroenterol 1996; **91**: 959–62.
12. Braden B, Schäfer F, Caspary WF, Lembcke B. Nondispersive isotope-selective infrared spectroscopy. A new analytical method for the ^{13}C-urea breath test. Scand J Gastroenterol 1996; **31**: 442–5.
13. Thijs JC, van Zwet AA, Thijs WJ, et al. Diagnostic tests for *Helicobacter pylori*: a prospective evaluation of their accuracy, without selecting a single test as the gold standard. Am J Gastroenterol 1996; **91**: 2125–9.
14. SAS Institute Inc. SAS Language: Reference. Version 6, 1st ed. Cary, North Carolina: SAS Institute, Inc., 1990.
15. Haubrich T, Boeing H, Göres W, Hengels KJ, Scheuermann W, Wahrendorf J. Prevalence of *Helicobacter pylori* and gastritis in the South of Germany. (Results of a representative cross-sectional study.) Z Gastroenterol 1993; **31**: 432–43.
16. Andersen LP, Rosenstock SJ, Bonnevie O, Jørgensen T. Seroprevalence of immunoglobulin G, M, and A antibodies to *Helicobacter pylori* in an unselected Danish population. Am J Epidemiol 1996; **143**: 1157–64.
17. Bergenzaun P, Kristinsson KG, Thjodleifsson B, et al. Seroprevalence of *Helicobacter pylori* in South Sweden and Iceland. Scand J Gastroenterol 1996; **31**: 1157–61.
18. Sitas F, Forman D, Yarnell JWG, Burr ML, Elwood PC, Pedley S, Marks KJ. *Helicobacter pylori* infection rates in relation to age and social class in a population of Welsh men. Gut 1991; **32**: 25–8.
19. Mégraud F, Brassens-Rabbe MP, Denis F, Belbouri A, Hoa DQ. Seroepidemiology of *Campylobacter pylori* infection in various populations. J Clin Microbiol 1989; **27**: 1870–3.
20. Moch KJ. Public use file NVS und Vera. Ernährungsumschau 1994; **41**: 394.
21. Rothenbacher D, Bode G, Winz T, Berg G, Adler G, Brenner H. *Helicobacter pylori* in out-patients of a general practitioner: prevalence and determinants of current infection. Epidemiol Infect 1997; **119**: 151–7.
22. Meyer B, Werth B, Beglinger C, et al. *Helicobacter pylori* infection in healthy people: a dynamic process? Gut 1991; **32**: 347–50.
23. Newell DG, Hawtin PR, Stacey AR, MacDougall MH, Ruddle AC. Estimation of prevalence of *Helicobacter pylori* infection in an asymptomatic elderly population comparing [^{14}C]urea breath test and serology. J Clin Pathol 1991; **44**: 385–7.
24. Faisal MA, Russel RM, Samloff IM, Holt PR. *Helicobacter pylori* infection and atrophic gastritis in the elderly. Gastroenterol 1990; **99**: 1543–4.
25. McCallion WA, Murray LJ, Bailie AG, Dalzell AM, O'Reilly DPJ, Bamford KB. *Helicobacter pylori* infection in children: relation with current household living conditions. Gut 1996; **39**: 18–21.
26. Mendall MA, Goggin PM, Molineaux N, et al.

https://doi.org/10.1017/S0950268898008644 Published online by Cambridge University Press

Childhood living conditions and *Helicobacter pylori* seropositivity in adult life. Lancet 1992; **339**: 896–7.
27. Webb PM, Knight T, Greaves S, et al. Relationship between infection with *Helicobacter pylori* and living conditions in childhood: evidence for person to person transmission in early life. BMJ 1994; **308**: 750–3.
28. Whitaker CJ, Dubiel AJ, Galpin OP. Social and geographical risk factors in *Helicobacter pylori* infection. Epidemiol Infect 1993; **111**: 63–70.
29. Mitchell HM, Lee A, Carrick J. Increased incidence of *Campylobacter pylori* infection in gastroenterologists: further evidence to support person-to-person transmission of *C. pylori*. Scand J Gastroenterol 1989; **24**: 396–400.
30. Wilhoite SL, Ferguson DA Jr, Soike DR, Kalbfleisch JH, Thomas E. Increased prevalence of *Helicobacter pylori* antibodies among nurses. Arch Intern Med 1993; **153**: 708–12.
31. Mendall MA; Northfield TC. Transmission of *Helicobacter pylori* infection. Gut 1995; **37**: 1–3.

https://doi.org/10.1017/S0950268898008644 Published online by Cambridge University Press