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Hepatitis E, Helicobacter pylori, and gastrointestinal symptoms in workers exposed to waste water

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Abstract: **BACKGROUND:** Workers exposed to sewage may have an increased risk of infection by *Helicobacter pylori* and hepatitis E virus (HEV). **AIMS:** To assess the prevalence of clinical hepatitis E (HE) and peptic ulcer disease as well as the seroprevalence of antibodies to *H pylori* and HEV in workers with and without sewage exposure and to look for symptoms due to exposure to endotoxin. **METHODS:** In the first year of a prospective cohort study 349 sewage exposed workers and 429 municipal manual workers (participation: 61%) underwent a complete medical examination. Travelling to endemic areas, socioeconomic level, age, country in which childhood was spent, and number of siblings were considered as the main confounding factors. **RESULTS:** Peptic ulcer disease and clinical HE did not occur more often in workers exposed to sewage. Prevalence of antibodies to HEV was 3.3% and overall prevalence of IgG antibodies to *H pylori* was 42% with large differences between subgroups. Logistic regression did not show an increased risk of seropositivity or antibodies to parietal cells in sewage exposed workers, but disentangling the effect of exposure from that of confounders was extremely difficult. No increase of symptoms due to exposure to endotoxin was found in sewage workers, with the exception of diarrhoea. **CONCLUSIONS:** No clear increased risk of infection by *H pylori* or by HEV in workers exposed to sewage was found in this cross-sectional study, but these results need to be confirmed by follow up.

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Hepatitis E, *Helicobacter pylori*, and gastrointestinal symptoms in workers exposed to waste water

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Background: Workers exposed to sewage may have an increased risk of infection by *Helicobacter pylori* and hepatitis E virus (HEV).

Aims: To assess the prevalence of clinical hepatitis E (HE) and peptic ulcer disease as well as the seroprevalence of antibodies to *H pylori* and HEV in workers with and without sewage exposure and to look for symptoms due to exposure to endotoxin.

Methods: In the first year of a prospective cohort study 349 sewage exposed workers and 429 municipal manual workers (participation: 61%) underwent a complete medical examination. Travelling to endemic areas, socioeconomic level, age, country in which childhood was spent, and number of siblings were considered as the main confounding factors.

Results: Peptic ulcer disease and clinical HE did not occur more often in workers exposed to sewage. Prevalence of antibodies to HEV was 3.3% and overall prevalence of IgG antibodies to *H pylori* was 42% with large differences between subgroups. Logistic regression did not show an increased risk of seropositivity or antibodies to parietal cells in sewage exposed workers, but disentangling the effect of exposure from that of confounders was extremely difficult. No increase of symptoms due to exposure to endotoxin was found in sewage workers, with the exception of diarrhoea.

Conclusions: No clear increased risk of infection by *H pylori* or by HEV in workers exposed to sewage was found in this cross-sectional study, but these results need to be confirmed by follow up.

Hepatitis E (HE) is a viral hepatitis with mostly benign course and low case fatality rate (0.5–3%), except in pregnant women (15–25%). Sewage plays a role in transmission because the virus of HE (HEV) is shed into faeces and transmitted principally by faecally contaminated water.^{1–4} HE occurs primarily in countries with inadequate sanitation.^{1–4} Although in industrialised countries HE is generally restricted to travellers from endemic areas or to immigrants, sporadic cases of HE in patients without known risk factors have been described repeatedly,^{5–8} and one case of presumably occupationally acquired HE has been reported in a waste water worker.⁹ The mode of transmission in these sporadic cases is presently unclear. This raises important issues relating to compensation and prevention of HE, especially in pregnant workers exposed to sewage. Indeed, workers in waste water plants are no longer exclusively males.

Helicobacter pylori is a bacterium associated with peptic ulcer disease, gastric cancer, and mucosa associated lymphoid tissue (MALT) lymphoma.^{10–11} Faeces and waste water are possible routes of transmission.^{11–13} The occupational risk for sewage exposed workers has received little attention. Friis and colleagues^{14–15} have not found an increased prevalence of peptic ulcer and immunoglobulin G to *H pylori* in sewage workers. However, results from some historical prospective studies suggest an increased risk of stomach cancer,^{16–19} which suggests a higher rate of infection by *H pylori*.

Besides HE and peptic disease gastrointestinal symptoms in sewage workers may be due to endotoxin exposure.^{20–21} However, no data regarding endotoxin exposure are available for the local sewage plants, making the planning of preventive measures difficult.

Since 1996 a global assessment of the risks of the workplace, which has to be regularly updated, has been required by the Swiss law for all occupations. Owing to the lack of definite data about the risk of HE and *H pylori*

infection in sewage workers, a risk assessment was planned to gain information on these diseases. Furthermore, as Rylander²¹ reported a high prevalence of diarrhoea (about 43%) and general symptoms, presumably due to occupational endotoxin exposure of sewage workers, such symptoms were looked for as well. This report presents the results of the risk assessment relative to HE, *H pylori*, and endotoxin induced symptoms in sewage workers. The main purposes of the study were to compare both the prevalence of clinical HE, peptic ulcer disease, and symptoms of endotoxin exposure, and the seroprevalence of HE and *H pylori* in sewage workers with those of occupational groups participating in a risk assessment at the same time.

SUBJECTS AND METHODS

Subjects

The selected design was that of a prospective cohort study. The power could be only crudely assessed owing to large differences between published study results, considerable differences in immunological methods, and the paucity of incidence data in comparable populations. Several hypotheses based primarily on *H pylori* seroprevalence were considered, suggesting that detecting a difference of 10–20% with a power of 80–90% and a significance level of 5% would require a total population of 500–1000 subjects. Therefore, it was attempted to constitute two groups of at least 300 subjects.

Eligible subjects were municipal manual workers from the Canton of Zurich. All workers exposed to sewage in the Canton of Zurich had the opportunity to participate, whereas the groups of control subjects were approached one by one and asked for participation until enough control subjects had entered the study. At the end of the study it was found that the list of municipal sewage workers contained erroneously seven workers from three non-municipal plants treating waste water from industry (vegetable or paper production).

Main messages

- The prevalence of clinical hepatitis E and peptic ulcer disease is not clearly increased in sewage exposed workers.

Five of them had no contact with urine or faeces and were included as control subjects, one was exposed to sewage, and one did not participate. All other plants treat only household waste water.

Workers from sewage plants (n = 355; participation: 90%) were compared to control persons from several occupational groups: garbage collectors (n = 86; participation: 28%), gardeners (n = 197; participation: 76%), workers maintaining waterways (n = 52; participation: 79%), public transport workers (n = 25; participation: 15%), and forestry workers (n = 63; participation: 93%). Workers maintaining waterways have jobs like gardeners in summer and forestry workers in winter. Public transport workers maintain tramways, buses, and railways (welding, painting, metalworking, etc). Overall, 778 subjects participated in the study (participation: 61%). A total of 423 entered as workers from control plants (participation: 49%) and 355 as sewage plant workers (participation: 90%). The individual occupational history disclosed some misclassifications. Therefore, the final group sizes are 429 control workers and 349 subjects exposed to waste water.

The results of this report are limited to the first annual examination. Some preliminary results regarding HE have already been reported.²²

Methods

All examinations were conducted in the Canton of Zurich between June 2000 and July 2002. They took place in the frame of an obligatory assessment of occupational risks which is now required by Swiss law. All workers were informed about the purposes of the risk assessment. They were included in the study only after they had given written consent. The study protocol was approved by the Swiss National Accident Insurance Fund, the major insurance fund for accidents and occupational diseases in Switzerland.

To minimise a recall bias it was attempted not to draw specifically the attention of the participants to gastrointestinal symptoms but rather to stress that a complete health examination was conducted. An extensive clinical history was taken by physicians according to a check list and written rules. Each physician examined both exposed and unexposed subjects and the coding of the answers was reviewed during the whole study by the same occupational health practitioner. Divergences were resolved by consensus.

Current symptoms were defined as those having occurred during the four weeks prior to clinical examination and work related symptoms as brought about by a specific task, occurring during a specific task in co-workers as well as without other cause. Fever, chills, fatigue, arthralgias, and headache were defined a priori as general symptoms possibly due to an endotoxin induced inflammatory reaction.^{21–23} The socioeconomic level was defined by the highest education level attained at age 20 with three levels (no apprenticeship, apprenticeship, university). Number of siblings was defined according to the results of Woodward and colleagues²⁴ (0–1, 2–3, ≥4). “Country of childhood” is the country in which the subject spent the first 10 years of life. Up to two countries could be reported. Alcohol consumption was recorded according to Rollason and colleagues,²⁵ and smoking by using questions from the questionnaire of the European

Policy implications

- For a population comparable to that examined in this study no specific measures seem necessary to protect workers exposed to sewage from hepatitis E virus or the bacterium *H pylori*.

Community of Steel and Coal (revision 1967). Travel to endemic areas was defined as at least a one week stay in the Indian subcontinent, Asia, Central America/Mexico, or South America. Subjects having never been at least one week in any of these regions were the reference group.

Exposure to sewage during the whole working life was assessed for each job separately according to Brugha and colleagues.²⁶ Work as a farmer was defined by the occupations with the codes 111.01 and 111.02²⁷ in the occupational history. Height and weight were measured with shoes and jacket removed.

Blood was taken without fasting (Vacutainer, Ref. 368441), kept at 4°C and centrifuged within seven hours. Serum was kept at –20°C. Analyses were done in batches and the laboratory did not know the exposure status. γ -Glutamyltransferase (GGT) activity was determined at 37°C with a Technicon RA 1000 (Technicon RA systems, 1989/1994) within two months. Results are given as percentages of the upper limit of the reference range (male: 86, female 47 U/l). Immunoglobulin G antibodies to *H pylori* (*H pylori* IgG), antibodies to parietal cells, and immunoglobulin A antibodies to *H pylori* (*H pylori* IgA) were determined with enzyme linked immunosorbent assays (ELISA) (Synelisa *H pylori* (IgG) Abs and Synelisa parietal cells, respectively, Pharmacia and Upjohn, Germany; Quanta Lite *H pylori* IgA ELISA, Inova Diagnostics Inc., California, USA). The target of the antibodies to parietal cells is a protein in the tubulovesicular membrane which contains large quantities of H,K-ATPase, the proton pump of parietal cells. Test results below 10 and 20 U/ml for *H pylori* IgG and IgA, respectively, were considered negative and the upper limit of the reference range for parietal cell antibodies was less than 10 U/ml. Antibodies (IgG/IgM) to HEV were determined with an ELISA using rDNA as an antigen (ORF3 and part of ORF2) (Abbott Laboratories, Abbott Park, IL 60064, USA). Every positive result for antibodies to HEV is based on a duplicate determination. Three cases with borderline results were classified as positive for statistical analyses. Immunological tests were performed as instructed by the manufacturers.

Data analyses

The normality of the distribution was tested and logarithmic transformations done if necessary or non-parametric tests used. Logistic and linear multiple regression models were laid down before the beginning of the study, taking into account confounders reported in the literature.^{4 11 24 28–30} Odds ratios (OR) are indicated with 95% confidence interval (95% CI). In the regression models the variables were coded as follows: male = 0, female = 1; age groups from 0 (<20 years) to 5 (60–69 years). As only 18 (2%) subjects had achieved a university level, this socioeconomic category was either collapsed with the group “apprenticeship” or excluded from the analyses. Alcohol consumption was coded 0 for no and social drinking and 1 for daily drinking; smoking as 0, 1, and 2 for never, ex-, and current smokers, respectively. Owing to the large number of countries of childhood, two subgroups were selected (*H pylori* IgG seroprevalence in parentheses): Greece (71), Turkey (77), Serbia and Montenegro (75), Italy (84), Spain (88), and Portugal (78) on the one hand and

Switzerland (35) and Germany (44) on the other hand. A third subgroup (*H pylori* seroprevalence: 63%) encompasses 27 subjects having spent their childhood in 19 countries. As this subgroup was very heterogeneous it was excluded from analyses, including the factor country of childhood. Because of collinearity between country of childhood and nationality, only the former was used in the regression equations. Goodness of fit was examined according to the Hosmer and Lemeshow goodness-of-fit test. All calculations were done with SAS statistical software (version 6.12; SAS Institute Inc., Cary, NC, USA).

With regard to exposure, exposure duration is calculated for all consecutive exposed jobs over the whole life. Occurrence of splashes was categorised as never exposed to sewage, never more than 20 splashes of raw sewage in any job, or at least one job with more than 20 splashes (codes 0, 1, and 2, respectively). With regard to exposure to raw sewage, categories were never exposed, exposure 1–5 times monthly, or more than 5 times monthly in at least one job (codes 0, 1, and 2, respectively). Both groupings were done without knowing the results. Year of first contact with sewage was dichotomised according to the observed distribution (before 1990 and 1990 and later) to have two approximately equal subgroups. In analyses with exposure status, never and ever exposed occupationally to sewage were coded 0 and 1, respectively.

RESULTS

Table 1 presents the characteristics of the study population. Year of birth ranged from 1933 to 1986 (median 1956). As only 25 subjects (3%) had spent the first 10 years of life in more than one country the second country of childhood, if any, was ignored. "Other countries" encompasses more than 20 countries but most subjects came from Italy, Spain, Portugal, Turkey, and Kosovo. A total of 333 subjects (42.8%) came from plants with less than 10 people.

Twenty four workers from sewage plants were actually not exposed to sewage, whereas an exposure was found in 18 control persons, leaving 429 control and 349 sewage exposed workers. Seventeen male subjects formerly exposed to sewage but without current exposure at the time of the study are included in the exposed group. Time elapsed since

their last exposure was 0.5–31 years (median 10). In the whole group of sewage exposed workers year of first exposure ranged from 1957 to 2002 (median 1989). In workers currently exposed to sewage, 195 (59%) and 44 (13%) were sewage plant or sewer workers, respectively. Ninety three had other occupations (electricians, fitters, etc). Table 2 presents further work characteristics. Overall, 109 (14%) workers had an occupational history as farmers.

Non-participation was mostly due to refusals (96%). Non-participating workers were more often foreigners (52.5 v 33.8%) and slightly older (median 47 v 44 years). Gender was not associated with participation (p > 0.4; χ^2 test).

Table 3 presents the main results with respect to clinical history and prevalence of workers with antibodies to HEV, *H pylori*, and parietal cells.

Overall prevalence of subjects with antibodies to HEV was 3.3% (n = 25). There was a slight association with age. No relevant clusters were found according to gender, education, nationality, country of childhood, number of siblings, travelling to endemic areas, farming,^{31 32} and exposure to sewage (p = 0.7; Fisher's exact test). However, all statistical analyses were very imprecise because of the small number of cases. Regarding liver diseases the clinical history was negative in 21 seropositive workers. The four other cases were all sewage exposed workers. One of them had never left Europe and the other had never left Switzerland, suggesting that sewage workers travel less frequently to endemic areas than control workers. Indeed, six of the 14 control workers but only one of the nine HEV positive sewage exposed subjects had ever been in an endemic area.

Twenty six (3.3%) and 22 (2.8%) workers had a previous history of stomach or duodenal ulcer or histologically verified gastritis, respectively, and 16 and 10 subjects reported an eradication of *H pylori* for any disease or because of peptic ulcer disease, respectively. None of these endpoints were associated with exposure to sewage (p > 0.6; Fisher's exact test). Peptic ulcer disease was diagnosed before every exposure in five of the 11 workers exposed to sewage. In two further cases the diagnosis and the beginning of sewage exposure occurred in the same year. In the logistic regression the OR of the factor "ever exposed to sewage" adjusted for age, smoking, and alcohol consumption was 0.72 (95% CI 0.32 to 1.61).

Overall prevalence of subjects with *H pylori* IgG was 43% (n = 318) but univariate analyses show large and statistically significant differences according to country of childhood (35–88%), nationality, education (37–66%), number of siblings (28–54%), alcohol consumption (39–67%), exposure (34% and 50% with and without exposure to sewage, respectively), and subgroups of control workers (35% in waterway maintenance workers to 60% in garbage collectors). Owing to the numerous associations between these variables, logistic regression was necessary (table 4). In accordance with the univariable analysis a slight but statistically significant reduced OR in sewage workers was found.

Table 1 Characteristics of the study population

	Exposure to waste water	
	No (n = 429)	Yes (n = 349)
Age (years)	41 (22–58)	46 (30–60)
Female sex	29 (7)	1 (0.3)
Education level		
Low	104 (25)	39 (11)
Middle	307 (72)	306 (88)
High	14 (3)	4 (1)
Childhood		
Switzerland	316 (74)	315 (90)
Other countries	113 (26)	34 (10)
Smoking		
Never	172 (40)	105 (30)
Former	101 (24)	104 (30)
Current	154 (36)	140 (40)
Pack-years	16.5 (1.0–62.5)	20.0 (1.3–64.0)
Alcohol		
No/only socially	286 (67)	229 (66)
Daily	141 (33)	119 (34)
GGT activity (%)	24.4 (12.8–73.3)	29.1 (12.8–93.0)
Exposure to sewage (years)	0	10 (1–27)

Figures are median (5th–95th centile) or number (percentage). GGT activity expressed as percentage of the upper limit of the reference range according to sex (see methods). Pack-years: median and centiles calculated in the subgroup of cigarette smokers only.

Table 2 Exposure in currently exposed sewage workers (n = 332)

	No	1–5 times	>5 times
Going down into sewers	174 (54)	111 (34)	39 (12)
Working with raw sewage	17 (5)	60 (19)	246 (76)
Raw sewage splashed on skin, face, eyes, or mouth	27 (8)	102 (32)	193 (60)

Figures are numbers (%). "Going down into sewers" and "working with raw sewage": no, 1–5 times, and >5 times are monthly averages in the present job. The number of splashes is assessed for the whole duration of the present job.

Table 3 Clinical history and prevalence of workers with antibodies to HEV, *H pylori*, and parietal cells

	Exposure to waste water	
	No	Yes
Clinical history		
History of peptic ulcer	15/429 (4)	11/349 (3)
History of histologically verified gastritis	12/429 (3)	10/349 (3)
Positive antibodies		
HEV IgG	15/414 (4)	10/338 (3)
<i>H pylori</i> IgG	205/413 (50)	113/336 (34)
<i>H pylori</i> IgA	87/413 (21)	76/337 (23)
Parietal cells	102/412 (25)	92/337 (27)

Figures are number with positive response or antibodies/total number of exposed or non-exposed workers (%). The percentages are crude percentages without any adjustment. A total of 26, 29, 28, 29 determinations are missing for HEV IgG, *H pylori* IgG, *H pylori* IgA, and parietal cells, respectively, because of blood sampling refusals or technical reasons.

Using GGT activity and number of pack-years instead of drinking and smoking category, excluding the small subgroup (n = 46) comprising women and workers in the highest education category, excluding this small subgroup and the occupational subgroups with the highest (forestry) or lowest participation rate (garbage and public transport) did not change the results. Restricting analyses to a homogeneous population of subjects, who had spent their childhood in Switzerland or who had both spent their childhood in Switzerland and belonged to the intermediate education level, did not change the results.

An analysis of the association between *H pylori* IgG and each occupational subgroup in turn (garbage workers, gardeners, waterways and forestry workers) unexpectedly disclosed one statistically significant association between prevalence of IgG and forestry work (OR = 2.0; 95% CI 1.14 to 3.52). No significant association was found with farming (p > 0.5). The statistical analyses were then restricted to workers exposed to sewage (after excluding the small group made of the single woman exposed to sewage and all workers belonging to the highest education category). No significant association with exposure duration, having been mostly exposed to raw sewage, and year of first contact with sewage was found. Having had a job with more than 20 splashes had a protective effect (OR = 0.45; 95% CI 0.26 to 0.79).

Overall prevalence of IgA was 22% (n = 163). Both *H pylori* IgA and IgG were positive or negative in 63% of the workers, whereas a positive IgG test result but a negative IgA test result were found in 29% of the cases. The main logistic

Table 5 Work related symptoms

	Control subjects (n = 429)	Current sewage exposure (n = 332)
Fatigue	13 (3.0)	11 (3.3)
Fever, chills	1 (0.2)	1 (0.3)
Headache	5 (1.1)	3 (0.9)
Diarrhoea	1 (0.2)	6 (1.8)
Epigastric pain	1 (0.2)	3 (0.9)
Abdominal cramps	0 (0)	2 (0.6)

Definition of work related symptoms: see Methods. Figures are numbers (%). Seventeen workers with only previous sewage exposure excluded. Epigastric pain: cases with pain relieved by food not included.

regression equations were run again with IgA instead of IgG as the dependent variable. The OR for “ever exposed to sewage” was 1.29 (95% CI 0.86 to 1.91). In workers exposed to sewage (after excluding the single woman and the workers in the highest education category) no statistically significant OR between seropositivity and exposure duration, exposure to raw sewage, exposure to splashes, or year of first exposure to sewage appeared.

The overall prevalence of increased concentration of antibodies to parietal cells was 26%. No association with exposure to sewage was found (p = 0.45, Fisher’s exact test).

After excluding formerly exposed sewage workers, 17 sewage workers but no control subject reported a previous history of diarrhoea induced by specific occupational tasks. In many cases the symptom had subsided after some time. Indeed, only six sewage workers and one control person reported work related diarrhoea during the four weeks before the medical examination. The prevalence of work related epigastric pain and/or abdominal cramps in the past four weeks was always low (table 5). General symptoms were not more frequent in sewage exposed workers (table 5). Work related arthralgias were more frequent in the control group but this could be due to differences in physical load. Work related irritative symptoms (conjunctiva, airways) did not cluster in sewage workers.

DISCUSSION

To the best of our knowledge, this study is the first study on HE in sewage workers. Furthermore, it extends the findings of Friis and colleagues¹⁴ in a large population with higher overall *H pylori* seroprevalence (43 v 29%).

This selection of manual and municipal workers aimed at establishing a homogeneous study population with regard to socioeconomic background which is considered as one major determinant of *H pylori* seropositivity. Therefore, only 18

Table 4 Multiple logistic regression

Sex	Age	Education	Country of childhood	Sibling	Alcohol	Smoking	Eradication	Exposure
<i>H pylori</i> IgG								
2.07	1.03	0.30						
(0.94–4.56)	(0.90–1.18)	(0.21–0.45)						
2.63	1.05	0.64	5.73					
(1.17–5.94)	(0.91–1.21)	(0.39–1.04)	(3.26–10.06)					
2.53	1.02	0.65	5.27	1.28				
(1.12–5.72)	(0.88–1.18)	(0.40–1.07)	(2.98–9.30)	(1.02–1.61)				
2.14	1.03	0.72	4.97	1.29	1.28	1.09	0.98	0.65
(0.93–4.90)	(0.88–1.20)	(0.44–1.19)	(2.79–8.86)	(1.03–1.63)	(0.90–1.81)	(0.91–1.32)	(0.30–3.26)	(0.47–0.91)
<i>H pylori</i> IgA								
1.08	1.21	0.65	3.29	1.02	0.99	1.11	1.31	1.29
(0.35–3.32)	(1.0–1.46)	(0.38–1.01)	(1.88–5.74)	(0.78–1.34)	(0.66–1.48)	(0.89–1.39)	(0.38–4.54)	(0.86–1.91)

With country of childhood alone the OR is 7.14 (95% CI 4.34–11.73). Definition of categories: see Methods.

people belong to the highest socioeconomic level. This reflects the actual situation and should not have distorted the results. Workers from private companies that clean sewers, or people who work by the hour in very small plants were non-eligible or very difficult to identify. However, part time workers were included if they were known, and the sewer workers of the cities of Zurich and Winterthur participated, which makes a large bias unlikely.

Participation amounted to 90% in the sewage workers, whereas it was low in two control plants, but exclusion of subgroups according to participation rate did not affect the results. Therefore, a bias due to different participation rates is unlikely. However, as older and foreign workers participated somewhat less often than younger Swiss workers, the overall prevalence of *H pylori* was probably underestimated in this population.

Very few women are presently working as garbage collector or sewage or forestry workers. This small subgroup had to be excluded from several analyses because the ORs are very imprecise. No generalisation to the general population can therefore be made.

Regarding *H pylori* the results of this study are consistent with those of Friis and colleagues^{14 15} in Sweden. However, precautions to protect the health of workers may even differ between European countries (Sweden, Switzerland, and others). Furthermore, epidemiology of HEV differs considerably between Europe or North America and endemic regions. Before these findings may be generalised, they should be explored in further studies.

Regarding HE the results do not support the hypothesis of an increased risk of HE in workers exposed to sewage. Indeed, the seroprevalence in sewage workers was the same as found in control subjects and as reported by Lavanchy and colleagues³³ in a group of 94 Swiss blood donors. Moreover, most cases were subclinical and the symptoms of the four symptomatic HE positive sewage workers were unspecific and possibly due to causes other than HE. However, whether the main route of infection is the same in control subjects and sewage exposed workers remains an open question. The study results might be interpreted as suggesting that sewage is a risk factor which was masked by control workers travelling more often to endemic areas. However, it must be stressed that this hypothesis was suggested by the examination of the clinical records and has to be tested with the results of the follow up of this cohort. Working as a farmer was considered as a possible confounder because many workers had previously been farmers, which could increase their risk.^{31 32} However, farming did not increase HE seroprevalence.

With respect to *H pylori*, clinical history of peptic ulcer disease and of eradication of *H pylori* did not occur more often in sewage exposed workers than in the control group. Moreover, the latent period did not support a causal relation. These results are in line with those of Friis and colleagues,¹⁵ who suggested that the increased number of peptic ulcers in the sewage workers they studied might be a chance finding.

With respect to *H pylori* IgG the prevalence of seropositive sewage workers (but not of control subjects) was comparable to that reported by Friis and colleagues¹⁴ (34% versus 29% and 50% versus 29%, respectively). In the logistic regression country of childhood had the largest effect and made the effect of socioeconomic level non-significant, a finding partly in agreement with the recent observation by Heuberger and colleagues³⁴ in Swiss adolescents. However, both socioeconomic level and country of childhood may be surrogates for hygienic conditions during childhood and should, therefore, not be viewed as causal factors. No clear increase of seroprevalence with age was found despite a broad range of age. Although year of birth may be a better indicator of

hygienic conditions during childhood than age because of a birth cohort effect,³⁵ the inclusion of year of birth instead of age in the regression model would not have been meaningful in this study. Indeed, all subjects had been recruited between June 2000 and July 2002. Therefore, age and year of birth were very tightly correlated. Further statistical analyses with restriction and stratification were not helpful and the reason for age being without effect in this population remains presently elusive. Unexpectedly, occupational exposure to sewage defined as a dichotomous category or by the frequency of splashes had a protective effect when *H pylori* IgG was used as an endpoint. Regular use of personal protection devices might explain this finding. However, a reconstruction of the use of protective devices over the whole work life was deemed unreliable and this hypothesis was, therefore, not tested. A chance finding is possible too, but the most probable explanation is unknown or residual confounding. Indeed, owing to the lack of accurate information about the routes of infection, the independent variables included in the logistic model are somewhat arbitrary and they may represent only crude surrogates.^{24 29 34} Therefore, our regression model might not describe adequately the epidemiology of *H pylori*. In fact, the uncertainty regarding the hidden biases or confounders is one important limitation of this cross-sectional examination.

Overall, the logistic model was very little or not improved by the inclusion of various exposure indicators ("having ever been exposed to sewage", "frequency of splashes", duration of exposure, "having been mostly exposed to raw sewage", year of first contact with sewage). Moreover, hidden biases and unknown confounders are quite possible. Hence, the decreased OR in waste water workers may be due to some unknown factor associated with work in sewage plants rather than to a causal association. The follow up of the cohort should cast some light on this question.

Using *H pylori* IgA instead of IgG removed the effect of exposure to sewage. Otherwise, it did not affect the main results. The limited agreement between IgG and IgA was expected.^{36 37}

The gastric H,K-ATPase represents a major autoantigen in atrophic *H pylori* gastritis.³⁸ However, autoantibodies to this antigen did not occur more frequently in subjects exposed to sewage, a finding in line with the hypothesis of a similar risk of *H pylori* infection in control and exposed workers.

Rylander²¹ reported a prevalence of diarrhoea in sewage exposed workers of nearly 45% (prevalence in controls of about 3%) and assumed that endotoxins cause diarrhoea. Although the OR was definitely increased in our study as well, the prevalence of work related diarrhoea in currently exposed workers was less than 2% and fell to 0% in several sewage plants. This may be explained, at least partly, by a tolerance to endotoxins. Indeed, several workers reported that diarrhoea had disappeared with time. However, a recall bias may also explain part of the difference between Swedish and Swiss sewage plant workers. Indeed, several studies have been published on Swedish sewage workers,^{14 15 20 21 39-41} which may have promoted a recall bias. The distribution of epigastric pain, abdominal cramps, fatigue, fever, and headache in the past four weeks did not differ clearly between groups although it would also be a consequence of endotoxin exposure. This suggests that some other factors are playing a role as well. Measurements are currently being carried out to confirm the excessive exposure to endotoxin during the tasks that cause diarrhoea, and to plan preventive measures.

In conclusion, this study disclosed an increased prevalence of diarrhoea in workers exposed to sewage in some waste water treatment plants, but the prevalence of symptoms was considerably lower than reported in Sweden. This may have been due to endotoxin, but other components of organic

dusts are possible agents too. Household waste water cannot definitively be excluded as a source of infection by *H pylori* or HEV but the risk, if any, seems to be low. Owing to the numerous potential confounding factors these results have to be confirmed by the follow up of these workers.

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REFERENCES

- Smith JL. A review of hepatitis E virus. *J Food Prot* 2001;**64**:572-86.
- Aggarwal R, Krawczynski K. Hepatitis E: an overview and recent advances in clinical and laboratory research. *J Gastroenterol Hepatol* 2000;**15**:9-20.
- Pina S, Jofre J, Emerson SU, et al. Characterization of a strain of infectious hepatitis E virus isolated from sewage in an area where hepatitis E is not endemic. *Appl Environ Microbiol* 1998;**64**:4485-8.
- Labrique AB, Thomas DL, Stoszek SK, et al. Hepatitis E: an emerging infectious disease. *Epidemiol Rev* 1999;**21**:162-79.
- Suzuki K, Aikawa T, Okamoto H. Fulminant hepatitis E in Japan. *N Engl J Med* 2002;**347**:1456.
- Levine DF, Bendall RP, Teo CG. Hepatitis E acquired in the UK. *Gut* 2000;**47**:740.
- Tsang THF, Denison EK, Williams HV et al. Acute hepatitis E infection acquired in California. *Clin Infect Dis* 2000;**30**:618-19.
- Zanetti AR, Schlauder GG, Romano L, et al. Identification of a novel variant of hepatitis E virus in Italy. *J Med Virol* 1999;**57**:356-60.
- Tumerelle E, Domart M. Hepatite E autochtone presumee professionnelle. A propos d'un cas. *Arch Mal Prof* 2000;**61**:318-23.
- Suerbaum S, Michetti P. Medical progress: *Helicobacter pylori* infection. *N Engl J Med* 2002;**347**:1175-86.
- Brown LM. *Helicobacter pylori*: epidemiology and routes of transmission. *Epidemiol Rev* 2000;**22**:283-97.
- Parsonnet J, Shmueli H, Haggerty T. Fecal and oral shedding of *Helicobacter pylori* from healthy infected adults. *JAMA* 1999;**282**:2240-5.
- Hulten K, Enroth H, Nyström T, et al. Presence of *Helicobacter* species DNA in Swedish water. *J Appl Microbiol* 1998;**85**:282-6.
- Friis L, Engstrand L, Edling C. Prevalence of *Helicobacter pylori* infection among sewage workers. *Scand J Work Environ Health* 1996;**22**:364-8.
- Friis L, Agreus L, Edling C. Abdominal symptoms among sewage workers. *Occup Med (Oxf)* 1998;**48**:251-3.
- Hansen ES, Hilden J, Klausen H, et al. Wastewater exposure and health—a comparative study of two occupational groups. *Occup Environ Med* 2003;**60**:595-8.
- Friis L, Mikoczy Z, Hagmar L, et al. Cancer incidence in a cohort of Swedish sewage workers: extended follow up. *Occup Environ Med* 1999;**56**:672-3.
- Betemps EJ, Buncher CR, Clark CS. Proportional mortality analysis of wastewater treatment system workers by birthplace with comments on amyotrophic lateral sclerosis. *J Occup Med* 1994;**36**:31-5.
- Lafleur J, Vena JE. Retrospective cohort mortality study of cancer among sewage plant workers. *Am J Ind Med* 1991;**19**:75-86.
- Thorn J, Beijer L, Rylander R. Work related symptoms among sewage workers: a nationwide survey in Sweden. *Occup Environ Med* 2002;**59**:562-6.
- Rylander R. Health effects among workers in sewage treatment plants. *Occup Environ Med* 1999;**56**:354-7.
- Jeggli S, Steiner D, Joller H, et al. Hepatitis E und Abwasserkontakt. *Schweiz Rundsch Med Prax* 2003;**92**:433-5.
- Rylander R. Endotoxin in the environment—exposure and effects. *J Endotoxin Res* 2002;**8**:241-52.
- Woodward M, Morrison C, McCall K. An investigation into factors associated with *Helicobacter pylori* infection. *J Clin Epidemiol* 2000;**53**:175-81.
- Rollason JG, Pincherle G, Robinson D. Serum gamma glutamyl transpeptidase in relation to alcohol consumption. *Clin Chim Acta* 1972;**39**:75-80.
- Brugha R, Heptonstall J, Farrington P, et al. Risk of hepatitis A infection in sewage workers. *Occup Environ Med* 1998;**55**:567-9.
- Meier U, Bundesamt für Statistik. *Verzeichnis der persönlichen Berufe*. Bern: Bundesamt für Statistik, 1996:1-385.
- Luzza F, Imeneo M, Maletta M, et al. Seroepidemiology of *Helicobacter pylori* infection and hepatitis A in a rural area: evidence against a common mode of transmission. *Gut* 1997;**41**:164-8.
- Murray LJ, McCrum EE, Evans AE, et al. Epidemiology of *Helicobacter pylori* infection among 4742 randomly selected subjects from Northern Ireland. *Int J Epidemiol* 1997;**26**:880-7.
- Pretolani S, Stroffolini T, Rapicetta M, et al. Seroprevalence of hepatitis A virus and *Helicobacter pylori* infections in the general population of a developed European country (the San Marino study): evidence for similar pattern of spread. *Eur J Gastroenterol Hepatol* 1997;**9**:1081-4.
- Pina S, Buti M, Cotrina M, et al. HEV identified in serum from humans with acute hepatitis and in sewage of animal origin in Spain. *J Hepatol* 2000;**33**:826-33.
- Meng XJ, Dea S, Engle RE, et al. Prevalence of antibodies to the hepatitis E virus in pigs from countries where hepatitis E is common or is rare in the human population. *J Med Virol* 1999;**59**:297-302.
- Lavanchy D, Morel B, Frei PC. Seroprevalence of hepatitis E virus in Switzerland. *Lancet* 1994;**344**:747-8.
- Heuberger F, Pantoflickova D, Gassner M, et al. *Helicobacter pylori* infection in Swiss adolescents: prevalence and risk factors. *Eur J Gastroenterol Hepatol* 2003;**15**:179-83.
- Harvey RF, Spence RW, Lane JA, et al. Relationship between the birth cohort pattern of *Helicobacter pylori* infection and the epidemiology of duodenal ulcer. *Q J Med* 2002;**95**:519-25.
- Ho B, Marshall BJ. Accurate diagnosis of *Helicobacter pylori*. Serologic testing. *Gastroenterol Clin North Am* 2000;**29**:853-62.
- Cutler AF, Havstad S, Ma CK, et al. Accuracy of invasive and noninvasive tests to diagnose *Helicobacter pylori* infection. *Gastroenterology* 1995;**109**:136-41.
- Faller G, Kirchner T. Role of antigastric autoantibodies in chronic *Helicobacter pylori* infection. *Microsc Res Tech* 2000;**48**:321-6.
- Lundholm M, Rylander R. Work related symptoms among sewage workers. *Br J Ind Med* 1983;**40**:325-9.
- Rylander R, Andersson K, Belin L, et al. Studies on humans exposed to airborne sewage sludge. *Schweiz Med Wochenschr* 1977;**107**:182-4.
- Rylander R, Andersson K, Belin L, et al. Sewage worker's syndrome. *Lancet* 1976;**2**:478-9.