Epidemiol. Infect. (1994), **113**, 121–128

Prevalence of hepatitis A virus infection among sewage workers in Singapore

B. H. HENG[1], K. T. GOH[1], S. DORAISINGHAM[2] AND G. H. QUEK[1]

[1] *Institute of Environmental Epidemiology, Ministry of the Environment, Environment Building #22-00, 40 Scotts Road, Singapore 0922*

[2] *Department of Pathology, Singapore General Hospital, Outram Road, Singapore 0316*

(*Accepted 22 February 1994*)

SUMMARY

To determine whether or not occupational exposure to sewage is associated with a higher seroprevalence of hepatitis A virus (HAV) infection, 600 sewage workers in Singapore were tested for total (IgG and IgM) antibody to HAV by enzyme immunoassay. Using logistic regression with stepwise procedure, the adjusted seroprevalence of sewage workers was 2·2 times higher than that of another non-occupationally exposed population group. Seroprevalence was significantly correlated with age and educational levels, the association being independent of the occupational association. The epidemiological data in the study show that sewage workers have an increased occupational risk of acquiring HAV infection and should be protected by active immunization.

INTRODUCTION

With the great improvements in environmental hygiene in Singapore during the last two decades, the transmission of hepatitis A virus (HAV) infection has declined sharply [1]. It is no longer an infection of children and adolescents because < 1% of the population below 20 years of age possess IgG antibody to HAV (anti-HAV) [2]. About 40% of the reported hepatitis A cases were imported, mainly from Southeast Asia and the Indian sub-continent [3]. Both endemic and epidemic transmission have been associated with the ingestion of imported bivalve shellfish [4, 5].

With declining transmission of HAV infection and accompanying delay of infection until adult life, some workers recommend active immunization of children and young adults [6] while others recommend immunization for selected populations at risk [7]. Until a policy is made on the mass immunization of susceptible children, identification and immunization of high-risk groups provide a practical option. One such group is sewage workers [8–14].

Here we report our findings on the seroprevalence of HAV infection of sewage workers in Singapore and provide epidemiological evidence that occupational exposure to sewage is significantly associated with a higher infection rate.

MATERIALS AND METHODS

Study population

All categories of unimmunized sewage workers who could have had contact with sewage at any stage of its treatment from the raw form to the final effluent and sludge, were encouraged to participate in the survey. Relevant epidemiological information obtained at the time of blood collection included demographic data (age, sex, ethnic group), employment history (previous employment, duration of current job), terms of employment (i.e. whether daily-rated for manual workers, or monthly-rated for technical/professional staff), food history (frequency and types of bivalve shellfish consumed raw or partly cooked in the previous 3 months), medical history (history of hepatitis or other illness), and the highest educational level attained (none, primary, secondary, pre-university or university).

To compare the seroprevalence of sewage workers with that of a control group not occupationally exposed to sewage, 453 unimmunized healthy adults attending government out-patient clinics for routine health checks during the period February–July 1993 were screened after consent had been obtained. Information on demography and educational level of respondents was also obtained.

Test method

Blood was despatched at the end of each day's collection to the Department of Pathology, Singapore General Hospital. The sera were separated, transferred to polypropylene tubes, and stored in the freezer at −20 °C before being tested in batches. Specimens were tested by enzyme immunoassay (EIA) for the qualitative detection of total (IgG and IgM) antibody to HAV. The Abbott Laboratories assay was used and carried out according to the manufacturer's instructions, using the Abbott COMMANDER Parallel Processing Center (PPC). In this procedure, beads coated with HAV were incubated with the samples (undiluted test sera, and positive and negative control sera) and anti-HAV conjugated with horseradish peroxidase (HRPO). Anti-HAV present in test or positive control sera competed with the conjugated anti-HAV for the limited number of binding sites on the beads. Unbound material was removed by washing the beads, which were then incubated with *o*-phenylenediamine (OPD) substrate solution containing hydrogen peroxide. The intensity of colour resulting from the reaction between OPD and HRPO was inversely proportional to the amount of anti-HAV present in the sample. The enzyme reaction was stopped by adding 1N sulphuric acid and the intensity of colour read by a spectrophotometer in the PPC, set at 492 nm. The presence (positive) or absence (negative) of anti-HAV in the test sera was determined by comparing the absorbance value of the test sample to a cut-off value, calculated automatically by the PPC from the negative and positive control absorbance values.

Statistical analysis

For statistical tests, differences in proportions observed were initially compared by χ^2 test using Yates continuity correction and probability (P) values less than 0·05 were considered significant. To test for significance in differences in age-

Table 1. *Demographic characteristics and frequency distribution of antibody to hepatitis A virus in sewage workers and control group*

Demographic characteristic	Sewage workers*			Control group*		
	+ve	−ve	No.	+ve	−ve	No.
All	436	164	600	230	223	453
Sex						
Male	416	154	570	77	76	153
Female	20	10	30	153	147	300
Age group						
20–29	20	63	83	14	87	101
30–39	150	77	227	59	77	136
40–49	98	18	116	76	42	118
⩾ 50	168	6	174	81	17	98
Ethnic group						
Chinese	138	80	218	215	203	418
Malay	143	54	197	4	12	16
Indian	148	29	177	10	6	16
Others	7	1	8	1	2	3
Educational level						
None	57	5	62	22	8	30
Primary	222	39	261	61	23	84
Secondary	96	56	152	92	100	192
Pre-university	21	14	35	39	41	80
University	40	50	90	16	51	67

* +ve, anti-HAV present; −ve, anti-HAV absent.

specific prevalence rates between sewage workers and the control population after controlling for educational levels, the Mantel–Haenszel χ^2 test was used. To determine whether or not the adjusted seroprevalence of sewage workers was significantly raised, a logistic regression analysis was performed on the combined sample of sewage workers and control population with the former as one of the independent covariates. Other potentially confounding covariates included in the regression model were age, sex, ethnic group, past medical history, and educational level. Stepwise procedure (forward and backward) by adding categories of variables one by one to the model and selecting those that maximize the fit was carried out. Similarly, to identify factors associated with increased seroprevalence, the same procedure was carried out on the subsample of sewage workers with inclusion of additional independent covariates such as terms of employment and duration of employment of current job into the model. Statistical analyses were performed using the microcomputer-based Statistical Analysis System (SAS) software.

RESULTS

Descriptive data

A total of 600 individuals, 77 % of the sewage workers deployed in all the sewage treatment plants in Singapore, was surveyed between November 1992 and January 1993. Of the sewage workers tested, 436 (72·7 %) were positive for anti-

Table 2. *Age-specific prevalence of antibody to hepatitis A virus among sewage workers and control population, Singapore*

Age-group	Number positive/number tested (%)		(a) *vs.* (b)*		
	Sewage workers (a) $n = 600$	Control population (b) $n = 453$	Odds ratio	(95% CI†)	*P* value
20–29	20/83 (24·1)	14/101 (13·9)	1·5	(0·6–3·4)	ns‡
30–39	150/227 (66·1)	59/136 (43·4)	2·4	(1·5–3·9)	< 0·01
40–49	98/116 (84·5)	76/118 (64·4)	2·3	(1·1–4·6)	0·02
⩾ 50	168/174 (96·6)	81/98 (82·7)	6·1	(2·3–16·2)	< 0·01

* Mantel–Haenszel χ^2 test after controlling for educational level.
† Confidence intervals.
‡ ns $P \geqslant 0{\cdot}05$.

Table 3. *Univariate analysis* of seroprevalence of antibody to hepatitis A virus in 600 sewage workers*

Variable	No. positive/ no. tested (%)	*P* value	Odds ratio	(95% CI†)
Sex				
Male	416/570 (73·0)	ns‡	1·4	(0·6–3·1)
Female	20/30 (66·7)	—	1	—
Age				
< 40 years	170/310 (54·8)	—	1	—
⩾ 40 years	266/290 (91·7)	< 0·0001	9·1	(5·6–15·1)
Ethnic group				
Chinese	138/218 (63·3)	—	1	—
Malay	143/197 (72·6)	ns	1·5	(1·0–2·4)
Indian	148/177 (83·6)	< 0·0001	3·0	(1·8–4·9)
Educational level				
None	57/62 (91·9)	< 0·0001	14·3	(4·9–44·8)
Primary	222/261 (85·1)	< 0·0001	7·1	(4·0–12·6)
Secondary	96/152 (63·2)	0·007	2·1	(1·2–3·8)
Pre-university	21/35 (60·0)	ns	1·9	(0·8–4·5)
University	40/90 (44·4)	—	1	—
Medical history				
Yes	106/117 (90·6)	< 0·0001	4·5	(2·3–9·1)
No	330/483 (68·3)	—	1	—
Duration on current job				
< 10 years	79/161 (49·1)	—	1	—
10–19 years	187/258 (72·5)	< 0·0001	2·7	(1·8–4·2)
⩾ 20 years	170/181 (93·9)	< 0·0001	16·0	(7·8–33·8)
Terms of employment				
Daily-rated	272/322 (84·5)	< 0·0001	3·8	(2·5–5·7)
Monthly-rated	164/278 (59·0)	—	1	—
Shellfish consumption§				
Yes	32/55 (58·2)	– not applicable –		
No	404/545 (74·1)			

* χ^2 test using Yates continuity correction.
† Confidence intervals.
‡ ns $P \geqslant 0{\cdot}05$.
§ History of consumption of raw or partly cooked shellfish in the previous three months.

Table 4. *Variables significantly associated* with the presence of antibody to hepatitis A virus among sewage workers and control population in Singapore*

Variable	Regression coefficient	Odds ratio	(95% CI†)	*P* value
Age group				
30–39	1·73	5·7	(3·6–8·9)	< 0·0001
40–49	2·60	13·4	(8·1–22·3)	< 0·0001
⩾ 50	3·54	34·6	(18·9–63·1)	< 0·0001
[20–29]‡				
Ethnic group				
Indian	0·62	1·9	(1·1–3·1)	0·02
[Chinese]‡				
Highest educational level attained				
None and primary	1·31	3·7	(2·3–6·0)	< 0·0001
Secondary and pre-university	0·64	1·9	(1·2–2·9)	0·004
[University]‡				
Occupational group				
Sewage workers	0·79	2·2	(1·6–3·1)	< 0·0001
[Control population]‡				

* $P < 0·05$ by logistic regression using stepwise procedure.
† Confidence intervals.
‡ [ ] reference category (see Tables 2, 3).

HAV, compared with 230 (50·8%) of the control population. The demographic profile and frequency distribution of anti-HAV in the two groups are shown in Table 1. Three sewage workers were admitted to hospital for acute hepatitis A after they had worked in the sewage treatment plants for between 5 and 22 years.

Univariate analysis

As expected, the antibody prevalence increased progressively from 24·1% in persons aged 20–29 years, to 66·1, 84·5 and 96·6% in those aged 30–39, 40–49 and 50+ years, respectively. Compared with the control population, the rates were significantly higher in those aged 30–39, 40–49 and 50+ years after controlling for educational levels (Table 2). Table 3 shows that among sewage workers, anti-HAV prevalence rates were significantly higher in Indians compared with Malays or Chinese; those with either no or primary education compared with those with higher education; those with positive medical history of illness compared with those without; those who worked for more than 10 years compared with those less than 10 years; and those who were daily rated compared with those who were monthly rated. However, seroprevalence was not associated with consumption of raw or partly cooked shellfish in the previous 3 months.

Logistic regression analysis

Results of logistic regression using stepwise procedure showed that the adjusted seroprevalence of sewage workers was 2·2 times higher than that of the control population (95% CI, 1·6–3·1) (Table 4). Among the sewage workers, two variables, i.e. increasing age and lower educational levels, were significantly associated with elevated seroprevalence (Table 5). However, age seemed to be a more important

Table 5. *Variables significantly associated* with the presence of antibody to hepatitis A virus among 600 sewage workers in Singapore*

Variable	Regression coefficient	Odds ratio	(95% CI†)	*P* value
Age group				
30–39	1·86	6·4	(3·5–11·6)	< 0·0001
40–49	2·80	16·4	(7·8–34·3)	< 0·0001
⩾ 50	4·11	61·0	(23·0–161·9)	< 0·0001
[20–29]‡				
Highest educational level attained				
None and primary	1·63	5·1	(2·8–9·2)	< 0·0001
Secondary and pre-university	0·88	2·4	(1·4–4·3)	0·003
[University]‡				

* $P < 0·05$ by logistic regression using stepwise procedure.
† Confidence intervals.
‡ [ ] reference category.

determinant than educational level as the regression coefficient for the former was higher (1·86–4·11) than the latter (0·88–1·63).

DISCUSSION

In view of the nature of the work, sewage workers are thought to be at risk of HAV infection and were recommended for active immunization when hepatitis A vaccine became commercially available [8, 11]. However, the recommendation was made based on theoretical considerations without sound supporting epidemiological data [15–17]. Only one published study by Poole and Shakespeare [8] reported a higher seroprevalence among sewage workers. However it was based on a population of only 40 individuals and the effect of confounders such as age [18–26] and socio-economic status [19, 24, 27, 28] was not considered when compared with the control population. Others have doubted the significance of data presented [16].

We have overcome the problems of such a small cross-sectional study by using a larger study population and logistic regression analyses to eliminate the confounding effect of extraneous factors. To our knowledge, our study is the first extensive survey carried out. We need not resort to prospective study to demonstrate conclusively whether or not sewage workers have a higher occupational risk of acquiring HAV infection. Based on univariate analysis, a number of factors were found to be significantly associated with higher seroprevalence; viz. age, educational level, ethnic group, past medical history of illness, duration of employment and terms of employment. In our series, sewage workers of Indian ethnic group were observed to be older, daily-rated, had been in the service for more than 10 years, of lower educational level and had a higher frequency of medical illness. By controlling for educational level alone, the age-specific prevalence of sewage workers over 30 years of age was significantly higher than that of the control population. After controlling for a series of potential confounders by logistic regression using stepwise procedure, the adjusted seroprevalence of sewage workers was still more than twice that of the control population. Only two variables were significantly associated with the presence of

anti-HAV among sewage workers independent of the occupational association; i.e. age, reflecting a cohort effect, and educational level. The inverse 'dose–response' association with educational levels, used here as a measure of socioeconomic status, relates to lower standards of hygiene among those with lower educational levels. These are the very individuals employed in manual jobs with accompanying greater exposure to sewage than the higher educated employees who were more likely to do office jobs.

Unlike childhood HAV infection, which is often asymptomatic or subclinical [29–34], adult infection is more severe with case-fatality rates of 0·02–1·5% [35]. More than three-quarters of our sewage workers < 30 years of age were not immune and are at risk of HAV infection. Our study showed that 0·5% of the workers contracted acute hepatitis A during the course of their work and had to be hospitalized. The true incidence may well be higher, as infected workers could have presented with non-specific clinical signs and symptoms or misdiagnosed for other diseases, because serological tests for the confirmation of acute hepatitis A was not routinely available prior to 1984.

Sewage workers are required to work in harsh and dirty conditions. As such, they are educated on the risk of transmission of HAV infection and advised to take appropriate precautionary measures. In practice, however, it is extremely difficult to maintain absolute hygienic working practices and avoid accidental ingestion of sewage. The key to prevention of occupationally acquired HAV infection and outbreaks [36] among sewage workers is active immunization. The HAV vaccine is safe and protective for at least 10 years, if not for life [37]. Based on our epidemiological data, we have decided to immunize all seronegative sewage workers against HAV. All new recruits will also be routinely serologically tested for HAV infection and those found to be non-immune are advised to be immunized.

ACKNOWLEDGEMENTS

The authors are grateful to Mr Yeo Seow Eng, Head, Sewerage Department, Ministry of the Environment for his permission to carry out the survey, and to the nursing and public health inspectorate staff, Quarantine and Epidemiology Department, Ministry of the Environment for their excellent assistance in organizing and implementing the survey.

REFERENCES

1. Goh KT, Wong LYM, Oon CJ, Kumarapathy S. The prevalence of antibody to hepatitis A virus in Singapore. Asia-Pacific J Pub Hlth 1987; **1**: 9–11.
2. Yap I, Guan R. Hepatitis A sero-prevalence in Singapore: a changing pattern. Trans Roy Soc Trop Med Hyg 1983; **87**: 22–3.
3. Committee on Epidemic Diseases. Epidemiology of hepatitis A virus infection in Singapore. Epidemiol News Bull 1992; **18**: 63–4.
4. Goh KT, Chan L, Ding DL, Oon CJ. An epidemic of cockles-associated hepatitis A in Singapore. Bull W H O 1984; **62**: 893–7.
5. Goh KT, Doraisingham S, Monteiro EH, Ling AE. Acute hepatitis A in Singapore: importance of shellfish ingestion in a non-epidemic period. Ann Acad Med Singapore 1987; **16**: 591–4.
6. Bancroft WH. Hepatitis A vaccine. New Engl J Med 1992; **327**: 488–90.
7. Zuckerman JN, Cockcroft A, Griffiths P. Hepatitis A vaccination. B M J 1991; **303**: 247.

8. Poole CJM, Shakespeare AT. Should sewage workers and carers for people with learning disabilities be vaccinated for hepatitis A? B M J 1993; **306**: 1102.
9. Jilg W. Adult use of hepatitis A vaccine in developed countries. Vaccine 1993; **11** (Suppl 1): S6–8.
10. Hoffmann F, Wehrle G, Berthold H, Koster D. Hepatitis A as an occupational hazard. Vaccine 1992; **10** (Suppl 1): S82–4.
11. Tilzey AJ, Palmer SJ, Barrow S, et al. Clinical trial with inactivated hepatitis A vaccine and recommendations for its use. B M J 1992; **304**: 1272–6.
12. Anonymous. Hepatitis A: a vaccine at last. Lancet 1992; **339**: 1198–9.
13. PHLS Working Group. The present state of hepatitis A infection in England and Wales. PHLS Microbiol Dig 1991; **8**: 122–6.
14. Banatvala JE, Tilzey AJ. Recommendations for use of hepatitis A vaccine. B M J 1992; **304**: 1570.
15. Longson PJ. Hepatitis A vaccine. B M J 1992; **305**: 888.
16. Maguire H. Hepatitis A infection: risk to sewage workers unproved. B M J 1993; **307**: 561.
17. Anand JK. Hepatitis A vaccine for sewage workers. B M J 1992; **305**: 477.
18. Noguchi A, Hayashi J, Nakashima K, Ikematsu H, Hirata M, Kashiwagi S. Decrease of hepatitis A and B virus infections in the populations of Okinawa, Japan. J Infect 1991; **23**: 255–62.
19. Kilpatrick ME, Escamilla J. Hepatitis A in Peru: the role of children. Am J Epidemiol 1986; **14**: 111–13.
20. Gust ID, Lehmann NI, Lucas CR. Relationship between prevalence of antibody to hepatitis antigen and age: a cohort effect? J Infect Dis 1978; **138**: 425–6.
21. Green MS, Zaaide Y. Sibship size as a risk factor for hepatitis A infection. Am J Epidemiol 1989; **129**: 800–5.
22. Ikematsu H, Kashiwagi S, Hayashi J, et al. A seroepidemiological study of hepatitis A virus infections: statistical analysis of two independent cross-sectional surveys in Okinawa, Japan. Am J Epidemiol 1987; **126**: 50–4.
23. Briem H. Declining prevalence of antibodies to hepatitis A virus infection in Iceland. Scand J Infect Dis 1991; **23**: 135–8.
24. Green MS, Tsu S, Lepon R. Sociodemographic factors and the declining prevalence of anti-hepatitis A antibodies in young adults in Israel: implications for new hepatitis A vaccines. Internat J Epidemiol 1992; **21**: 136–41.
25. Lim WL, Yeoh EK. Hepatitis A vaccination. Lancet 1992; **339**: 304.
26. Anonymous. Prevalence of hepatitis A virus infection in Spain. Scand J Infect Dis 1988; **20**: 113–14.
27. Joussemet M, Bourin Ph, Lebot O, Fabre G, Deloince R. Evolution of hepatitis A antibodies: prevalence in young French military recruits. Eur J Epidemiol 1992; **8**: 289–91.
28. Stroffolini T, De Crescenzo L, Giammanco A, et al. Changing patterns of hepatitis A virus infection in children in Palermo, Italy. Eur J Epidemiol 1990; **6**: 84–7.
29. Hadler SC, MacFarland L. Hepatitis in day care centers: epidemiology and prevention. Rev Infect Dis 1985; **8**: 548–57.
30. De Filippis P, Divizia M, Mele A, Adamo B, Pana A. Detection of hepatitis A virus in the stools of healthy people from endemic areas. Eur J Epidemiol 1987; **3**: 172–5.
31. Prakazchikov SA, Balayan MS. Shifts in the rates and levels and antibody to hepatitis A virus associated with hepatitis A infection in children's communities. Eur J Epidemiol 1987; **3**: 370–6.
32. Rooney PJ, Coyle PV. The role of herd immunity in an epidemic cycle of hepatitis A. J Infect 1992; **24**: 327–31.
33. Gingrich GA, Hadler SC, Elder HA, Owen AK. Serological investigation of an outbreak of hepatitis A in a rural day care centre. Am J Epidemiol 1983; **73**: 1190–3.
34. Lemon SM. Type A viral hepatitis. New developments in an old disease. New Engl J Med 1985; **313**: 1059–67.
35. Polakoff S. Clinical hepatitis A: Laboratory reports years 1980–8. Commun Dis Report 1989; 89/46: 3–6.
36. Timothy E, Mephan P. Outbreak of infective hepatitis amongst sewage sludge spreaders. Commun Dis Report 1984; 84/03: 3.
37. World Health Organisation. Weekly epidemiological record 1992; **67**: 261–3.