Social Inequalities and Cancer
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Infection with *Helicobacter pylori* and parasites, social class and cancer

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Three genera of parasites are known or suspected risk factors for cancer in humans: Schistosoma, Opisthorchis and Clonorchis. No adequate information is available on the determinants of infections related to social class. Infection with the bacterium *Helicobacter pylori* is an important cause of stomach cancer. Studies, in particular from the United Kingdom and the United States of America, strongly suggest that social class factors, especially those acting during childhood, are determinants of the infection, with odds ratios of seroprevalence of the order of 1.5–5 for lower social class as compared with higher social class. A conservative estimate of the contribution of social class, acting through an increased prevalence of *H. pylori* infection, to the burden of stomach cancer gives a figure of over 50 000 stomach cancers per year worldwide, or 8% of all stomach cancers. In countries with both high and low prevalence of infection with *H. pylori*, it is likely that a sizeable proportion of this difference is due to social-class-related risk factors of infection.

Infection with biological agents is an important risk factor for cancer, in particular in developing countries. As the probability and severity of infection may be determined by factors related to social class, such as housing conditions, it is conceivable that at least part of the social gradient observed for cancers associated with infection is due to social class differences in infection patterns. In this chapter, I discuss the evidence linking human cancer, social class and infection with *Helicobacter pylori* and parasites. Infection by viruses is discussed elsewhere in this book (see chapter by Stuver *et al.*).

Parasites

Chronic infection with *Schistosoma haematobium* is a risk factor for bladder cancer, and infection with other schistosomes may be responsible for other cancers in humans (IARC, 1994a). It has been estimated that over 600 million people in 74 countries are exposed to the risk of schistosomal infection, and 200 million are currently infected (WHO, 1993). Contact with untreated water is the major risk factor of infection (Jordan & Webbe, 1993). Prevalence of infection seems to be highest during the second decade of life; the decline in later age is believed to be due mainly to the gradual acquisition of immunity (IARC, 1994a). Rural populations, and those with limited or no access to treated water for domestic and recreational purposes, are at increased risk of infection, in particular during childhood; in many countries, these populations are at the bottom end of the social spectrum. Direct evidence of a difference in prevalence of infection in relation to social class, however, is very limited. In a study from the state of Minas Gerais, Brazil, infection from *Schistosoma mansoni* was higher in Black children aged 6–15 than in Mulatto and in White children (91%, 84% and 73%, respectively), and this difference was interpreted by the authors as evidence of an effect of socioeconomic level (Tavares-Neto *et al.*, 1991).

Infection with liver flukes from the *Opisthorchis* and the *Clonorchis* genera has been linked with increased risk of liver cancer (IARC, 1994b). Infection takes place from ingestion of raw fish. No data on the social class pattern of infection from these agents are available in the scientific literature.

Helicobacter pylori

Infection with *Helicobacter pylori* is a risk factor for gastric cancer (IARC, 1994c). The relative risk is of the order of 2–4, and the prevalence of infection in many countries is of the order of 10–50% (IARC, 1994c) but it can be as high as 90% in areas of China (Forman *et al.*, 1990) and Japan (Tsugane *et al.*, 1993). It should be noted that a relative risk of 3 in a population with 30% of exposed individuals gives an attributable risk of the order of 46%, and that stomach cancer is the second most frequent cancer in the world (Parkin *et al.*, 1993), with approximately 750000 new cases worldwide each year.

H. pylori has been discovered and characterized only recently, and its role in the etiology of chronic gastritis, peptic ulcer disease and stomach cancer has been clarified during the last few years. It is therefore not surprising that, despite the very large public health importance infection with *H. pylori* is likely to have, relatively few studies are available on its determinants.

Epidemiological studies of H. pylori infection and social class

The association between *H. pylori* infection and social-class-related factors has been addressed by several epidemiological studies. Results on prevalence of infection according to social class are presented in Table 1.

Table 1. Prevalence of infection with *Helicobacter pylori* by social class indicators – results of selected studies

Study	Population	Social class indicator	Category	P(%)[a]
Sitas *et al.*, 1991[b]	749 adults, UK	Social class from occupation	I, II	49
			III	57
			IV, V	62
Fiedorek *et al.*, 1991	245 children, USA	Income of family	<US$ 5000/year	39
			US$ 5000–25 000/year	27
			>US$ 25 000/year	16
Mendall *et al.*, 1992	215 adults, UK	Social class from occupation	I, II	25
			III-NM	32
			III-M	46
			IV, V	34
		Persons per room in childhood	<0.70	15
			0.70–0.99	17
			1.00–1.29	43
			>1.30	54
Webb *et al.*, 1994[b]	471 adults, UK	Persons per room in childhood	<0.76	34
			0.76–1.00	29
			1.01–1.50	49
			>1.51	49
Patel *et al.*, 1994	554 children, UK	Persons per room	<0.5	10
			0.5–1.0	9
			>1.0	23
		Social class from occupation	I, II	8
			III	14
			IV, V	10
		Housing tenure	Owned	9
			Rented	16

[a]Prevalence of seropositivity to *H. pylori*.
[b]Age-adjusted prevalence.

A correlation study from 46 counties in China estimated the correlation between several causes of death, serological markers (including IgG antibody measured in a sample of the population of each county), and dietary, lifestyle and demographic variables (Junshi *et al.*, 1990). Three indicators of education were included: proportion of university graduates, proportion of junior-/middle-school graduates, and literacy. A non-significant negative correlation was found between *H. pylori* seroprevalence and each of the three indicators of education (r = −0.06, −0.05 and −0.12, respectively).

In a survey of 246 individuals from Saudi Arabia aged 21–50, those with college education had a significantly lower prevalence of infection than less-educated individuals; however, no difference was observed between illiterate individuals and people with primary or secondary education (Al-Moagel *et al.*, 1990).

A study of seroprevalence of IgG antibody in the United Kingdom included 749 adults randomly selected from the population of Caerphilly, South Wales (overall prevalence: 56.8%) (Sitas *et al.*, 1991). A trend was shown between age-adjusted prevalence of infection and social class.

In a study of factors influencing *H. pylori* infection in 245 healthy children and young adults aged 3–21 from Little Rock, Arkansas, United States of America (overall infection prevalence: 31%), the only factors significantly associated with infection besides age in a multivariate analysis were Black race and low family income (Fiedorek *et al.*, 1991).

Prevalence of *H. pylori* IgG antibody was determined in 215 healthy individuals from London, United Kingdom (overall prevalence: 33%) (Mendall *et al.*, 1992). In a mutually adjusted multivariate analysis no effect of current social class was found [odds ratios (ORs) of infection for social classes III, IV and V, as compared with I and II, were 0.74, 2.15 and 0.61, respectively], while strong associations were found for use of hot water in childhood [OR for shared or no use versus sole use was 4.34; 95% confidence interval (CI) = 1.87–10.0], persons per room in childhood [ORs were 1.00 (reference) for <0.70 persons, 1.36 for 0.70–0.99 persons, 4.04 for 1.00–1.29 persons, and 6.15 for ⩾1.30 persons] and number of children currently living in the household (ORs were 1.85 for one child and 5.53 for two or more children versus none). Age was the only other seropositivity risk factor.

In a survey of 1727 Chinese individuals from one city and three rural areas (overall infection prevalence: 44%), density of living was one of the significant factors retained in a stepwise multivariate model (Mitchell *et al.*, 1992). Other factors retained in the model were age, place of residence, antibiotic usage, smoking, and liver and ulcer disease.

In a study based on blood samples from 985 blood donors in North Wales, United Kingdom, 41% of the subjects were positive for *H. pylori* IgG antibody (Whitaker *et al.*, 1993). The OR of positivity was 1.53 (95% CI = 1.14–2.05) for manual versus non-manual social class in adulthood, and 1.50 (95% CI = 1.12–2.02) for sharing versus not sharing a bed during childhood. Other factors significantly associated with antibody positivity were age, childhood house density, and area of birth and residence. Other childhood factors such as social class, number of people in the bedroom and presence of an indoor toilet were not significantly associated with antibody positivity in a multivariate analysis.

A seroprevalence study of 471 male volunteers from Stoke on Trent, United Kingdom (overall seropositivity: 37.4%) revealed positive associations in a mutually adjusted analysis between IgG seropositivity and manual occupation of the subject (OR = 2.21; 95% CI = 1.07–4.57), manual occupation of the father (2.05; 0.85–4.93), sharing a bed (1.41; 0.83–2.40), and having more than one person per room (1.54; 0.87–2.75) (Webb *et al.*, 1994). The only additional variable associated with seropositivity in this study was age.

In a study on 554 schoolchildren from Edinburgh, United Kingdom, sampled at age 7 and followed up to age 11 (overall infection prevalence: 11%), prevalence of infection at age 11 was significantly associated with house crowding, housing tenure, and proportion of housing rented in the school catchment area. Children of social classes I and II had a lower prevalence of infection, but no trend was found among lower social classes (Patel *et al.*, 1994).

Additional evidence comes from two studies of institutionalized individuals. A study from New South Wales, Australia, found a higher prevalence of IgG antibody positivity among inmates of a residential institution for the mentally retarded than among blood donors or hospital controls, irrespective of the age group (Berkowicz & Lee, 1987). In a study from Thailand, children from an orphanage in Bangkok had a higher seroprevalence than non-institutionalized children from rural areas (Perez-Perez *et al.*, 1990).

Discussion

The evidence from the relatively few studies available strongly points towards an association between low social class and *H. pylori* infection (Veldhuyzen van Zanten, 1995). Factors linked to social class acting during childhood seem to play a particularly important role. However, it is too early to identify specific factors, like sharing a bed during childhood, as responsible for the increased risk of infection. The relatively few studies available may have tended to replicate the findings of early investigations, and the analysis of different factors linked to social class, which may act either during childhood or during early adulthood, is far from being complete.

Despite the lack of knowledge about the exact mechanism of infection and its relationship with social class, it is likely that the causal chain of social-class-related factors leading to *H. pylori* infection leading to stomach cancer represents one of the most important known explanations for social difference in cancer incidence and mortality.

In many studies, the social class difference for stomach cancer incidence and mortality is in the range of 50–400% excess risk for low social class as compared with high social class (see the chapter by Faggiano *et al.* in this book). In a conservative estimate, the proportion of *H. pylori* positivity attributable to low social class (assuming an OR of infection of 1.5 for that half of the population of lower social class) is of the order of 17%. The estimated number of new cases of stomach cancer in the world is approximately 750 000 (Parkin *et al.*, 1993) and the percentage attributable to infection with *H. pylori* is 46%. The total number of stomach cancers occurring yearly worldwide attributable to social-class-related *H. pylori* infection would therefore be 58 650 (750 000 x 0.46 x 0.17), or about 8% of all stomach cancers.

In countries with both high and low prevalence of infection to *H. pylori*, it is likely that a sizeable proportion of this difference is due to social-class-related risk factors of infection. The identification of such factors, together with a reduction in their prevalence and a general improvement of the social condition of life, would be important steps towards the prevention of stomach cancer in future generations.

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