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Respiratory disease in relation to patient residence near to hazardous waste sites

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Abstract

We have examined rates of hospitalization for respiratory diseases in relation to residences in zip codes with hazardous waste sites, as well as socio-economic status. Chronic bronchitis and chronic airway obstruction were elevated in persons who live in zip codes containing persistent organic pollutants (POPs) (PCBs and persistent pesticides) as compared to "clean" zip codes without hazardous waste sites or zip codes with hazardous waste sites containing other kinds of wastes, but the differences could be due to socio-economic status and behavioral risk factors since these are also important risk factors for respiratory diseases. Therefore, we investigated rates of hospitalization for individuals living in zip codes along the Hudson River, because here the average per capita income is higher than in the rest of the state, and there is less smoking, better diet and more exercise. We found a similar elevation of chronic bronchitis and chronic airway obstruction along the Hudson. These observations are consistent with the possibility that living near a POPs-contaminated site poses a risk of exposure and increased risk of chronic respiratory disease, probably secondary to suppression of the immune system.

Keywords: Chronic bronchitis; Respiratory infections; Allergic diseases; Socio-economic status

1. Introduction

Persistent organic pollutants (POPs) are halogenated compounds, most man-made, that are resistant to degradation in the environment and in living organisms. A short list of POPs (the "dirty dozen") has been the focus of an United Nations Environment Programme (Proffitt, 2004) effort to reduce or eliminate their use, culminating in the Stockholm Convention, which was adopted and opened for signature on 22 May 2001 and ratified by 59 nations in 2004 (Kaiser and Enserink, 2000; Proffitt, 2004). This Convention commits countries to stop using polychlorinated biphenyls (PCBs), hexachlorbenzene, several chlorinated pesticides (aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, mirex and toxaphene) and to reduce unintended production of dioxins and furans. PCBs are industrial chemicals manufactured and widely used for a variety of purposes before they were banned in the US in 1977 because of their environmental persistence and adverse effects on animal and human health (ATSDR, 2000). PCBs are a class of 209 chemical compounds (known as congeners) defined by the number and position of the chlorine atoms attached to the biphenyl rings. Some congeners are planar and have actions similar to those of dioxin. Though most of the chlorinated pesticides have not been manufactured in the US for many years, they remain in the environment due to their environmental persistence (Sinkkonen and Paasivirta, 2000) and are carried long distances through atmospheric transport (Lohmann et al., 2001). Dioxins and furans are products of combustion, and remain as unwanted byproducts of industrialization.

POPs are widely distributed in the environment and throughout the food chain (Kalantzi et al., 2001; Lohmann et al., 2001). There is almost certainly no person living that does not have some body burden of dioxin-like compounds, PCBs and persistent organochlorine pesticides in their body fat. In

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the past, high exposure has resulted from occupational exposures (ATSDR, 2000) or consumption of POPs-contaminated fish (Schwartz et al., 1983). However, POPs are now widely distributed throughout the food supply at low levels, being concentrated in animal fats (IOM, 2003). While POPs are widely distributed, there are many sites of particularly high contamination or localized point source areas (Bobovnikova et al., 2000; Hermanson and Hites, 1990; Hsu et al., 2003).

There have been a number of studies that have demonstrated an elevation in incidence of particular diseases in individuals who live near hazardous waste sites, many of which contain POPs. Several have investigated the incidence of birth defects in relation to residence near hazardous waste sites, and have reported that such residence increased risk of several different types of birth defects (Geschwind et al., 1992). Others have found that serum PCB levels are elevated in individuals living near chemical plants that manufactured PCBs (Hansen et al., 2002), and that these elevated levels were not due to ingestion of locally caught fish or employment at the plant (Carpenter et al., 2002a). These observations raise the possibility that simply living near a POP-contaminated site poses a risk of exposure and of disease. If this is the case, at least one major route of exposure must be atmospheric transport of POPs, either in the vapor or particulate phase.

In 1998, Health Canada released a series of 17 reports on diseases diagnosed at hospitalization in Areas of Concern in Ontario (see Elliott et al., 2001b). At the request of the International Joint Commission (IJC) we instituted a similar study in New York. New York has an excellent database of diagnoses of all in-patients in hospitals that are regulated by the state, which includes all but federal hospitals, such as those operated by the Veterans' Administration. For each hospitalized patient the hospital must report all diagnoses (primary diagnosis and up to 15 others) for the patient, plus age, sex, race and zip code of residence. We have used this database for the years 1993–2000, where each year contains approximately 2.5 million hospitalizations. New York also has a large number of identified hazardous waste sites. There are 89 National Priority List (NPL) sites identified by the Environmental Protection Agency (EPA), plus 864 state Superfund sites identified by the New York Department of Environmental Conservation (DEC). In addition the IJC, the US–Canadian body that advises the two governments on issues relating to the boundary waters, has identified six bodies of water in New York as Areas of Concern (the Niagara River, the Buffalo River, 18 Mile Creek, the Rochester Embayment, the Oswego River and the St. Lawrence River near Massena, NY) because of excessive contamination with organochlorines and other contaminants (ATSDR, 2004). Thus, we have examined information on each of these sites and created a dataset that lists the contaminants identified by EPA, DEC or the IJC at each site, plus the zip code(s) of each site. This then allows us to investigate the rates of hospitalization for specific diseases for individuals living in zip codes containing or abutting POPs-contaminated sites to those living either in zip codes with no hazardous waste sites, or zip codes with a hazardous waste site but not one containing POPs.

Planar PCBs, dioxins and furans are well known to be immunosuppressive substances (ATSDR 1998, 2000), and suppression of the immune system is known to be one of the most sensitive indicators of exposure. Ortho-substituted PCBs have also been shown to have effects on immune cells (Jeon et al., 2002; Tan et al., 2003). A number of chlorinated pesticides are also persistent, and have adverse effects on the immune system (Repetto and Baliga, 1997; Vine et al., 2000). In the present study we have focused on respiratory diseases, comparing those with an infectious etiology to those with an allergic etiology. There are many confounders for respiratory disease, and we have attempted to determine the contribution of these confounders through information on average per capita income from the US Census and through use of the Behavioral Risk Factors Surveillance System (BRFSS). The hypothesis behind these studies is that residential proximity to a POPs-contaminated hazardous waste site increases risk of exposure, perhaps via air transport, and that such exposure will be reflected in an increased incidence of respiratory diseases of an infectious origin.

2. Materials and methods

Because of significant differences in population density and demographics we excluded New York City from this analysis. All of the hazardous waste sites in New York identified by EPA (http://www.epa.gov/superfund/sites/rodsites/0202609.htm), DEC (Registry of Inactive Hazardous Waste Disposal Sites in New York State) and the IJC (http://www.epa.gov/glnpo/aoc/index.html) were reviewed and the contaminants listed as being the major contaminants were identified, along with the zip code or codes containing or abutting the sites. We identified 213 zip codes, with a population in the 2000 Census of 2,816,653, as containing or abutting a POPs-contaminated site containing one or more of the "dirty dozen". The great majority of these sites contained PCBs, sometimes with the added presence of persistent pesticides. Relatively few sites report dioxins or furans. Of the POPs sites, 78 abut the PCB-contaminated portion of the Hudson River, which is all of the river south of Hudson Falls, New York. There were 244 zip codes, with a population of 3,464,571 that contained or abutted a hazardous waste site, but not one containing POPs. Most of these sites contain metals or volatile organics. In addition there were 1382 zip codes, with a population of 4,742,193, that did not contain any identified hazardous waste site.

Average per capita income was obtained from the 1990 Census, and was US$ 14,616.38 in the POPs-contaminated zip codes, US$ 16,594.53 in the "other waste" zip codes and US$ 19,311.93 in the "clean" zip codes.

The Statewide Planning and Research Cooperative System (SPARCS) is a dataset maintained by the New York State Department of Health. Under New York law every hospital

which falls under Article 26 (all hospitals in the state other than federal hospitals) must report all diseases diagnosed for in-patients to the Department upon discharge of the patient. The report includes the primary diagnosis plus up to 15 other diseases, based on the International Classification of Disease, Ninth Revision (ICD-9) codes, and the name, age, sex, race and street address of the patient. We obtained these data without personal identifiers (name and street address) but with zip codes of patient residences for the years 1993–2000.

There are some limitations to this dataset above and beyond possible errors in data entry at hospitals. Without personal identifiers we cannot distinguish a particular disease diagnosis of multiple hospitalizations of one individual from those of different people. However, since there are about 2,500,000 recorded diagnoses per year, the number of entries over the 8-year period for which we have data is large. Another major limitation is that we have no information from SPARCS on socio-economic status nor behaviors which might pose risks for a particular disease. This is a particular problem in the study of respiratory disease, where behaviors such as smoking are major risk factors. We have used the BRFSS in some situations in an effort to control for behaviors. Unfortunately, at present, the BRFSS contains information only at the county level, and therefore its usefulness is limited. However, even county level information is valuable for demonstrating regional trends. In this study we have utilized the BRFSS only for those counties that abut the Hudson River.

Data analysis was done as previously detailed (Carpenter et al., 2001) following the methods used in the Health Canada studies. Age-standardized morbidity rates (ASMR) were determined and significance was evaluated by use of the Z-test (Breslow and Day, 1987). In this report we analyzed hospitalization for several forms of respiratory disease as follows:

ICD 460–466 Acute respiratory infections;
ICD 480–487 Pneumonia and influenza;
ICD 490 Bronchitis, not specified as acute or chronic;
ICD 491 Chronic bronchitis;
ICD 492 Emphysema;
ICD 494 Bronchiectasis;
ICD 495 Extrinsic allergic alveolitis;
ICD 496 Chronic airway obstruction, not elsewhere classified.

The goal of these investigations is to determine whether various forms of respiratory disease are more frequent among individuals living near hazardous waste sites and, if so, to attempt to determine whether this is secondary to exposure to contaminants and consequent alteration of immune function or to socio-economic factors.

3. Results

Table 1 shows a summary of significant differences among the three residential areas for the respiratory diseases that were investigated. For three ICD-9 groups there were no significant differences. These included bronchitis (not specified as acute or chronic), emphysema and bronchiectasis. There was a significant excess of diagnosis of acute respiratory infections when comparing the POPs zip codes to the clean zip codes, and a non-significant excess when comparing the POPs zip codes to the other waste zip codes (Fig. 1). A similar pattern, but somewhat less striking, was seen with pneumonia and influenza. While these patterns might reflect suppression of the immune system in residents living near to POPs-

Table 1
Z-test values for hospitalization for respiratory diseases in pops zip codes as compared to clean and other waste zip codes

Pathology	Gender	Clean sites				Other waste sites			
		0–24	25–44	45–74	75+	0–24	25–44	45–74	75+
ARI; ICD 460–466	F	+	+	+	0	0	0	0	0
	M	+	+	0	0	0	0	0	0
Pneumonia and influenza; ICD 480–487	F	0	0	+	0	0	0	0	0
	M	0	0	+	0	0	0	0	0
Bronchitis, not specified; ICD 490	F	0	0	0	0	0	0	0	0
	M	0	0	0	0	0	0	0	0
Chronic bronchitis; ICD 491	F	0	0	+	0	0	0	+	0
	M	0	0	+	0	0	0	+	0
Emphysema; ICD 492	F	0	0	0	0	0	0	0	0
	M	0	0	0	0	0	0	0	0
Bronchiectasis; ICD 494	F	0	0	0	0	0	0	0	0
	M	0	0	0	0	0	0	0	0
Estrinsic allergic alveolitis; ICD 495	F	0	0	0	0	0	0	0	0
	M	0	0	0	–	0	0	0	0
Chronic airway obstruction not classified; ICD 496	F	0	0	+	+	0	0	+	0
	M	0	0	+	+	0	0	+	0

Positive significance is marked by (+); Negative significance is marked by (−); no significance is 0.

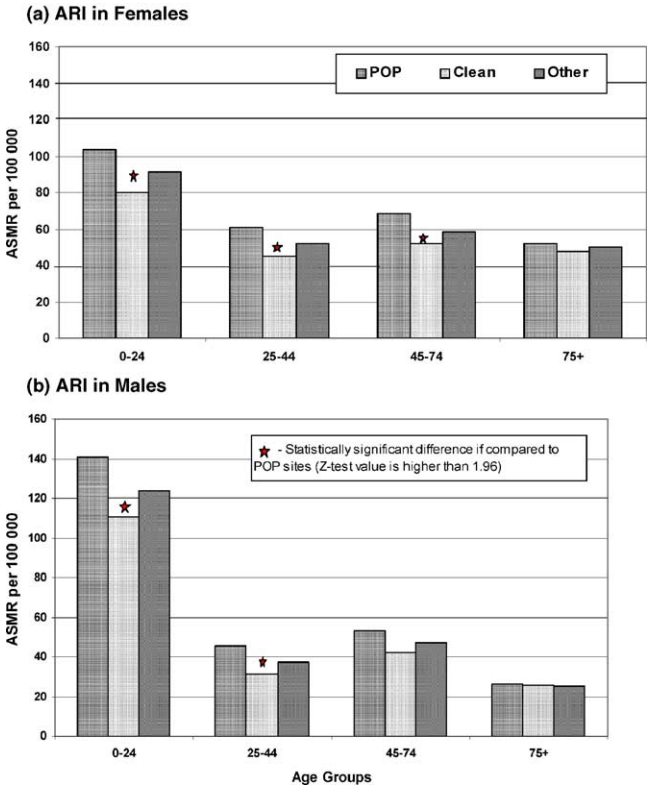

Fig. 1. Diagnosis of acute respiratory infections (ICD-9460-466), presented as age-standardized morbidity rates per 100,000 population, in New York residents (other than New York City) hospitalized in state-regulated hospitals between 1993 and 2000. The bars show the ASMRs on the basis of whether the persons have residence in a zip code that contains or abuts a hazardous waste site containing persistent organic pollutants (POP), has no federally or state-designated hazardous waste site (clean) or has a hazardous waste site which contains primarily toxic substances other than POPs. Data are presented for four age ranges for women (a) and men (b). The stars indicate results significantly different from the POPs value on the basis of the Z-test value is higher than 1.96.

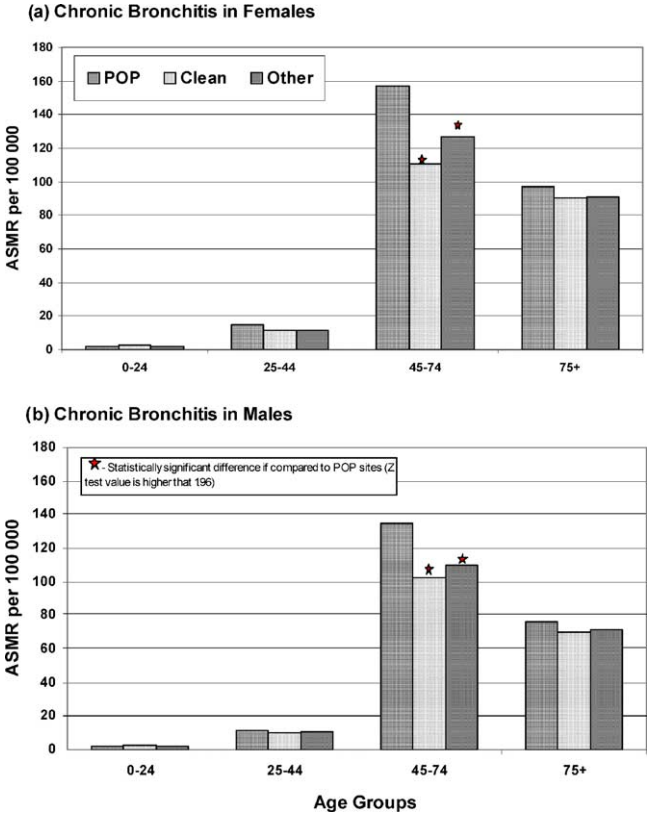

Fig. 2. ASMRs as in Fig. 1 but for hospitalization with chronic bronchitis (ICD-9491).

contaminated sites, they also may be a reflection primarily of socio-economic status.

Fig. 2 shows the rates of hospitalization diagnosis for chronic bronchitis in women (a) and men (b). Fig. 3 shows similar data for chronic airway obstruction not otherwise classified. For both diseases there is a significantly elevated rate of hospitalization in residents of POPs zip codes as compared to both comparison populations in the 45–74 years age group. Both of these diseases have an infectious component, but incidence is also altered by behavioral risk factors, such as smoking.

We next examined diseases associated with elevated immune responses. Fig. 4 shows results for allergic alveolitis. While fewer age groups show statistically significant differences (due to the lower frequency of diagnosis of this disease, and therefore the smaller numbers), it is clear that the trend is for allergic alveolitis to occur more frequently among residents of zip codes that do not contain any hazardous waste sites.

Because it is almost impossible to distinguish effects of socio-economic status from exposure to contaminants in the above results, we have examined a subset of zip codes that abut the Hudson River. Table 2 shows than the zip codes along the Hudson are characterized by having higher incomes than in the rest of the state. Table 3 shows the frequency of smoking, degree of physical activity and relative consumption of fruits and vegetables in counties abutting the Hudson River as compared to other counties in New York outside of New York City, taken from BRFSS. Of those who provided information (some reported they did not know or refused to answer) the residents near the Hudson River smoke less, have more exercise and a more healthy diet than the rest of upstate New Yorkers. Therefore, we compared morbidity rates in this population, where we have at least some information on behavioral risk factors.

Table 2
Income distribution (% of population)

Income level (US$ per year)	Hudson	Rest of NYS
<10,000	2.0	3.6
10,000–14,999	2.6	4.3
15,000–19,999	6.7	5.9
20,000–24,999	3.6	7.8
25,000–34,999	9.5	13.0
35,000–49,999	13.3	15.9
50,000–74,999	17.4	13.9
75,000+	26.3	17.4

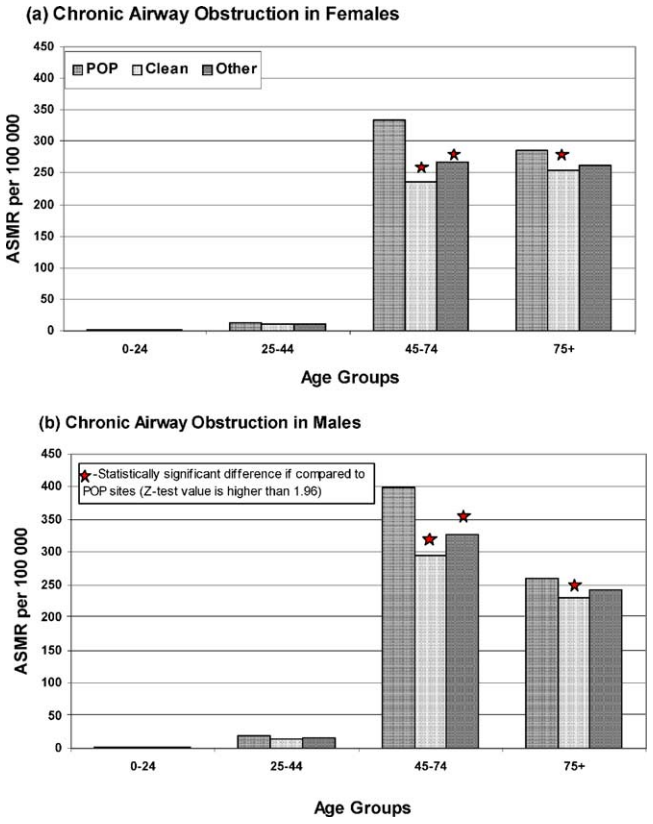

Fig. 3. ASMRs as in Fig. 1 but for hospitalization for chronic airway obstruction, not otherwise classified (ICD-9496).

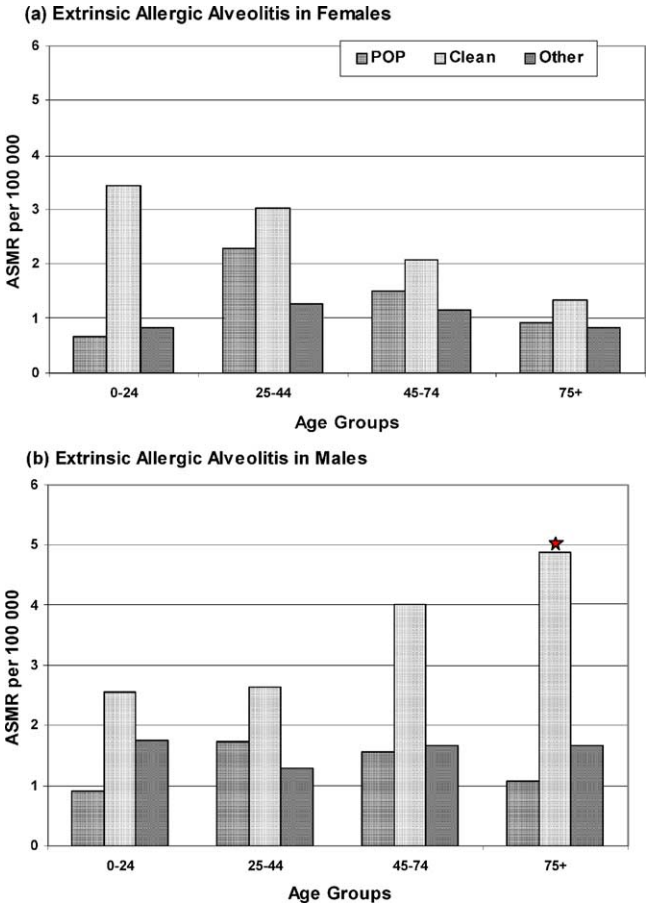

Fig. 4. ASMRs as in Fig. 1 but for extrinsic allergic alveolitis (ICD-9495).

Fig. 5 shows the rate of hospitalization for chronic bronchitis and Fig. 6 for chronic obstructive pulmonary disease among residents in PCB-contaminated zip codes abutting the Hudson River, as compared to those in clean zip codes and zip codes with other wastes for all of New York except New York City. The results obtained from this population are almost identical to those from all POPs-contaminated zip codes in New York. This evidence provides at least some support for the conclusion that socio-economic status and rates of smoking, exercise and diet do not explain the elevated incidence of infectious respiratory diseases in POPs-contaminated zip codes.

Table 3
Frequency of smoking, degree of physical activity and relative consumption of fruits and vegetables (% of population)

Frequency	Hudson	Rest of NYS
Smoking status		
Current smoker (every day)	15.05	18.42
Current smoker (some days)	2.77	5.56
Former smoker	25.54	27.37
Never smoked	56.04	48.13
Physical activity		
Physically inactive	14.06	14.91
Irregular activity	21.39	15.37
Regular activity	17.82	16.14
Regular and vigorous activity	10.50	8.07
Fruit and vegetable consumption		
Less than once a day or never	1.39	1.63
One to less than three times a day	18.61	16.20
Three to less than five times a day	24.75	22.38
Five or more times a day	19.01	14.34

4. Discussion

There is evidence that human exposure to POPs constitutes a significant threat to health, and leads to increased risk of many different diseases, including cancer, endocrine disruption, neurobehavioral abnormalities and immunosuppression (ATSDR, 2000; Carpenter et al., 2002b; Johnson et al., 1998). The hypothesis being tested in these studies is that living in a zip code containing or abutting a POP-contaminated zip code poses a risk of exposure, and that such exposure increases the risk of hospitalization for both acute and chronic respiratory disease of an infectious origin. The results obtained are consistent with the hypothesis, although they do not constitute proof. The most serious limitation of these studies is the exposure assessment. Living in a zip code that contains or abuts a POPs-contaminated site is a very crude way to assess exposure, since zip codes are large and irregular in shape. In the present study we have no other exposure matrix. Nonetheless, this hypothesis is not without support from some other

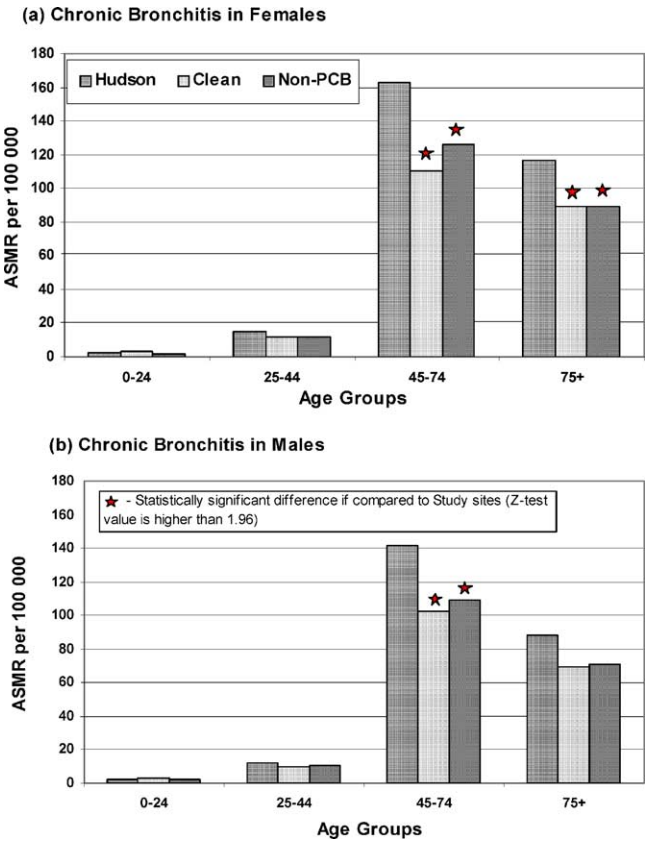

Fig. 5. ASMRs for chronic airway obstruction, not otherwise classified, as in Fig. 3 but considering only those persons who reside in a zip code that abuts the PCB-contaminated Hudson River, as compared to the persons living in clean and other waste site zip codes.

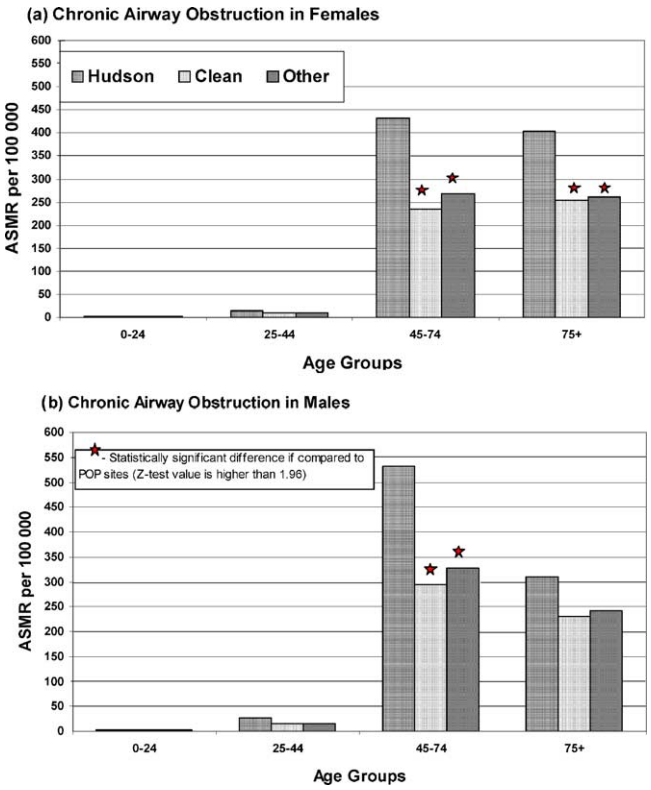

Fig. 6. ASMRs for chronic bronchitis as in Fig. 2 but considering only those persons who reside in a zip code that abuts the PCB-contaminated Hudson River.

studies. Residence in relationship to proximity to a hazardous waste site has been shown to be a risk factor for several cancers (Ozonoff et al., 1994) and congenital malformations in some (Gerschwind et al., 1992) but not all studies (Marshall et al., 1997). Residence near landfill sites has also been shown to correlate with risk of giving birth to a low birth weight infant (Baibergenova et al., 2003; Berry and Bove, 1997; Elliott et al., 2001a; Vianna and Polan, 1984). Health Canada has recently released reports on hospitalizations, cancer and birth defects in 17 Areas of Concern in Ontario. These results are summarized by Elliott et al. (2001b) and Gilbertson and Brophy (2001), and demonstrate reasonably consistent patterns of elevations of certain diseases. Carpenter et al. (2001) showed that residence near three Areas of Concern in New York was associated with significant elevations in rates of hospitalization for thyroid and genital disease in women. The report by Baibergenova et al. (2003) is particularly important in relation to the present results because that study was based on use of the same exposure assessment methods used in the present study, but used data from an entirely different dataset, the New York State birth registry. This study showed that after accounting for other confounders, such as smoking, age, race and weight of the mother, there was still an excess risk of giving birth to a low birth weight infant if the zip code of residence of the mother contained a POPs hazardous waste site.

Use of hospitalization data alone does not allow one to control for socio-economic status nor behavioral risk factors for respiratory disease. There is a smaller difference in per capita income when one compares residents of POPs-contaminated zip codes to those in zip codes with other wastes, but the POPs zip codes still have a lower income.

Lower income has been shown to be a predictor of ill health (Jha et al., 2002; Lochner et al., 2001), and socio-economic status may explain some of the differences we have found. There are also other sources of error, such as misclassification of ICD codes and possible differences in access to and/or standards of care in different parts of the state. Nevertheless, hospitalization data obtained from over a number of years, because of the large numbers involved, has considerable potential for generation of and testing of hypotheses regarding the causes of disease.

There is evidence from both laboratory animal (Harper et al., 1993; Segre et al., 2002; Tryphonas et al., 1991) and wild polar bear (Bernhoft et al., 2000) and porpoise (Jepson et al., 1999) populations that POPs are immunosuppressive, often leading to infectious diseases. It was shown as early as 1978 that PCB or hexachlorobenzene exposed mice showed impaired resistance and decreased survival to malaria and bacterial endotoxin (Loose et al., 1978). Human studies also

show that dioxin-like PCBs, dioxins and furans are immunosuppressive. In humans Nakanishi et al. (1985) reported that Yusho patients showed marked elevations in respiratory diseases that correlated well with the concentrations of PCBs in blood, and that the elevations in respiratory disease remained 14 years after the exposure. The pathology seen in Yushu patients was primarily small airway disease in bronchioles with associated infection. In a 6-year follow up of YuCheng children they were found to consistently have higher frequencies of bronchitis, influenza and otitis media (Ju et al., 1992), although this elevation had disappeared with longer time (Yu et al., 1998).

In an earlier report, Carpenter et al. (2000b) showed that hospitalization for five infectious diseases of childhood was 30% greater in POPs as compared to clean zip codes, in children in the first year of life, with the elevated risk decreasing somewhat with age up to 9 years. Svensson et al. (1994) demonstrated that men who ate fatty fish from the Baltic Sea had lower proportions and numbers of natural killer cells in peripheral blood than non-consumers.

More recent studies have demonstrated the Dutch infants exposed to dioxins and PCBs have elevated incidence of recurrent middle-ear infections and chicken pox, and a lower prevalence of allergic reactions (Weisglas-Kuperus et al., 2000). These children also showed abnormalities in lymphocyte numbers, and a lowered antibody response to mumps and measles vaccinations. An elevated incidence of otitis media was found in Inuit infants exposed to high levels of organochlorines (Dewailly et al., 2000). Van Den Heuvel et al. (2002) studied Flemish adolescents in relation to exposure to dioxin-like compounds using the CALUX TEQ assay, and found a negative relationship between exposure and allergies of the upper airways. They also found that there was a negative relationship between total TEQ and IgG, but a positive relationship with IgA. Baccarelli et al. (2002) also reported a negative relationship between IgG and dioxin levels in Seveso residents more than 20 years after exposure.

There have not been many studies on the effects of pesticides on the immune system. Repetto and Baliga (1997) have reported immune suppression in individuals exposed to organochlorine and other pesticides in developing countries. Vine et al. (2000) have demonstrated that residents living closer to a pesticide dump site and having higher serum levels of DDE showed significantly lower mitogen-induced lymphoproliferative activity than residents living further away.

The results obtained in this investigation show patterns of disease that implicate socio-economic status as a major predictor of respiratory ill health, but are also consistent with the hypothesis that simply living near to a POP-contaminated site poses an elevated risk of exposure, a reduction in immune competence and an increased incidence of respiratory disease. The similarity of data for chronic bronchitis and chronic obstructive pulmonary disease when considering all of New York as compared with the results obtained from residents living along the Hudson River, where we have at least some control over confounders such as smoking, diet and exercise, and where per capita income is higher than in the rest of the state, adds support to this hypothesis. The differences seen with the acute infectious diseases cannot be attributed to POPs with any confidence, since there are differences in per capita income, but they also are consistent with the hypothesis. The results with allergic alveolitis suggest that this diagnosis is more common in individuals living in clean zip codes. This is consistent with the previous reports of reduced incidence of allergic disease in individuals exposed to POPs (Van Den Heuvel et al., 2002; Weisglas-Kuperus et al., 2000). However, allergic alveolitis is an uncommon diagnosis, so the numbers are relatively small even in this large dataset.

The conventional wisdom is that ingestion is the major source of exposure to POPs, especially from contaminated fish. However, those individuals who eat fish from contaminated waters are not defined by the zip code in which they live. The most logical way that living near to a POP-contaminated site could lead to widespread exposure of the population in adjacent zip codes is via air transport of contaminants, either particulates containing POPs that get into homes and are ingested or inhaled, or vapor phase POPs that are inhaled. There is some evidence from both human (Hansen et al., 2002) and animal (Casey et al., 1999) studies that inhalation of PCBs may be an important route of exposure, but to date there has been relatively little attention to diseases caused by POPs inhalation. In the specific case of PCBs, the major contaminant at most of the POPs sites, the more volatile congeners are those with fewer chlorines. These are less persistent in the human body. This does not mean, however, that these lower chlorinated congeners are without biological effects upon chronic exposure, such as will occur at a residence near a PCB site. Further studies testing the possible role of inhalation of POPs as a mediator of human disease are needed.

Acknowledgments

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