

# Community Health Profile of Windsor, Ontario, Canada: Anatomy of a Great Lakes Area of Concern

Michael Gilbertson<sup>1</sup> and James Brophy<sup>2,\*</sup>

<sup>1</sup>International Joint Commission, Windsor, Ontario, Canada; <sup>2</sup>Occupational Health Clinics for Ontario Workers, Sarnia-Lambton, Point Edward, Ontario, Canada

The rates of mortality, morbidity as hospitalizations, and congenital anomalies in the Windsor Area of Concern ranked among the highest of the 17 Areas of Concern on the Canadian side of the Great Lakes for selected end points that might be related to pollution in this relatively highly industrialized city. Mortality and morbidity rates from all causes were higher than in the rest of the province. Anomalously high rates of diseases included various cancers; endocrine, nutritional, metabolic, and immunity disorders; diseases of the blood and blood-forming organs, nervous system and sense organs, circulatory and respiratory systems, digestive system, genitourinary system, skin and subcutaneous tissue, musculoskeletal system and connective tissues; congenital anomalies, and infant mortality. Of particular concern was the early onset of the elevated rates of many of these diseases and conditions. Comparison of these incident rates with those in Hamilton, another industrial municipality in southern Ontario, suggested that in addition to a variety of local sources of industrial pollution from automobile manufacturing and use, transboundary air and water pollution from Detroit, Michigan, should be investigated as potentially important causes of these health outcomes in the Windsor Area of Concern. Some of the institutional and political trends of the past decade may need to be reversed before effective remedial programs are implemented for cleaning up contaminated sediments and for containment of leaking hazardous waste sites. This pilot project would seem to be a useful preliminary method of integrating human health concerns and of priority setting for the administration of the Great Lakes Water Quality Agreement and the Canada–United States Air Quality Agreement. *Key words:* injury to health, methodology, transboundary pollution. — *Environ Health Perspect* 109(suppl 6):827–843 (2001). <http://ehpnet1.niehs.nih.gov/docs/2001/suppl-6/827-843gilbertson/abstract.html>

The Canadian and United States governments have been involved since 1972 in the implementation of the Great Lakes Water Quality Agreement (1), pursuant to the 1909 Boundary Waters Treaty (2). Water quality in the Great Lakes basin had deteriorated throughout the 19<sup>th</sup> century with the growth of cities and industries, and particularly through the first half of the 20<sup>th</sup> century with the growth of chemical manufacturing. The signing of the Great Lakes Water Quality Agreement was not only a diplomatic acknowledgment that pollution of the boundary waters between the two nations had caused injury to health and property on the respective other sides but also represented a scientific and regulatory response to this injury. Similarly, in 1991 the two governments signed the Canada–United States Air Quality Agreement (3) to address issues of transboundary air pollution, with particular reference to human health. The International Joint Commission, which was established under the Boundary Waters Treaty of 1909, has responsibilities for assisting the parties in implementing these agreements through evaluation of progress and through public consultation and information programs.

In recent years there has been substantial progress in integrating the science concerning the pollutant-induced injury to Great Lakes populations of humans (4,5) from exposures

to persistent toxic substances, particularly polychlorinated biphenyls (PCBs) and dioxins. Many of the original observations of injury were concerned with reproductive and developmental effects reported in Great Lakes wildlife (6), particularly in colonial fish-eating birds. These wildlife served as useful models of the structural and functional effects that might have been occurring in human populations exposed to teratogenic substances. These observations of effects in Great Lakes populations of wildlife and of humans were particularly influential in the original formulation of the hypothesis on endocrine disruptors (7,8). Since the late 1980s and early 1990s, this progress has been achieved not only through extensive funding of toxicology and epidemiologic research and monitoring by both governments (9,10) but also through application of epidemiologic criteria (11) to the various case histories to attain a higher level of certainty in the causal statements relating the chemically induced epizootics and epidemics to exposures to specific persistent toxic substances. Much of this research undertaken by the governments has been to identify critical subpopulations and to determine the exposures to and effects of persistent toxic substances, particularly in relation to human consumption of contaminated fish from the Great Lakes and from the St. Lawrence River (12).

## Health Canada Studies of the Designated Areas of Concern

In the mid-1980s, the two governments had designated 42 Areas of Concern, under the Great Lakes Water Quality Agreement, that represented locations where water quality conditions routinely exceeded the established objectives. In the mid-1990s, Health Canada, as part of the Canadian government's responsibilities for implementing the Great Lakes Water Quality Agreement, collated health data and statistics for the populations in the 17 Areas of Concern on the Canadian side of the Great Lakes. Some of these locations were on interconnecting channels and therefore potentially susceptible to proximate sources of transboundary pollutants. The interconnecting channels include the St. Lawrence River, Niagara River, Detroit River, St. Clair River, and St. Mary's River. Canada has a national health service, and health data are collected from the provinces and territories and stored on a national basis by Statistics Canada. Within each of these 17 communities, the data were selected by Health Canada (13) related to the cases of mortality and morbidity as hospitalization for selected health outcomes, including cancers, that might be related to pollution. In addition,

This article is based on a presentation at the Workshop on Methodologies for Community Health Assessment in Areas of Concern held 4–5 October 2000 in Windsor, Ontario, Canada.

Address correspondence to M. Gilbertson, International Joint Commission, 8th Floor, 100 Quellette Ave., Windsor, Ontario, Canada N8X 6T3. Telephone: (519) 257-6706. Fax: (519) 257-6740. E-mail: gilbertsonm@windsor.ijc.org

\*Present address: School of Social Work, University of Windsor, Windsor, Ontario, Canada.

This article is based primarily on the 17 Health Canada reports compiled by staff members of the former Great Lakes Health Effects Program and by their contractors. R. Whitehurst of the Windsor Cancer Prevention Coalition tabulated the cancer data, and many of the additional references were supplied by J. Hummel and by the staff of the Windsor Occupational Health Information Service.

This report was initially prepared as a technical background paper. The information in this document is based on the methodology, health data, statistics, and references compiled by Health Canada, but the interpretation is that of the authors in their personal and professional capacities and should not be construed to represent either the views of Health Canada, the International Joint Commission, the Occupational Health Clinics for Ontario Workers, or of any parts of their organizations.

Received 11 January 2001; accepted 26 June 2001.

data were accessed concerning the incidence of congenital anomalies and low birth weights.

The 17 reports were prepared by Health Canada to provide quantitative data as a resource to professionals to begin to investigate the health status of populations within and around the Areas of Concern and to compare rates of human disease with the rates in the population in the rest of the Province of Ontario. No attempt was made to explain causal relationships between exposures to contaminants or other risk factors and any specific health outcome. The objective was to provide a basis for forming hypotheses that could be further investigated about whether the rates of human diseases and conditions might be linked to exposures to pollutants that were being or had been discharged or emitted to the Canadian Areas of Concern. Previous research in the United States on the distribution of cancer had demonstrated a "lake effect" of increased incidences of stomach and esophageal cancers in counties on the Great Lakes shoreline (14).

Though the reports were published in November 1998, they were not released until November 1999 after a news reporter with the Canadian Broadcasting Corporation on camera produced a copy of the report for the Detroit River Area of Concern during an interview with a Health Canada official. This reluctance to release the reports was because of the responses from environmental agencies concerned about costs of cleanup, the reactions of the medical officers of health to the widespread public dissemination of uninterpreted data and statistics, and the potential liabilities of governments for exposures of communities to pollutants and for any remedial actions. The medical authorities are learning how to collaborate in responding to these kinds of evidence of diseases suspected to be induced by pollutants. For example, responsibilities for health in Ontario are divided among the following three ministries: the Ontario Ministry of Health is responsible for healthcare delivery and for the local health units, headed by the medical officers of health; occupational aspects of human health are the responsibility of the Ontario Ministry of Labour; and environmental aspects of human health are the responsibility of the Ontario Ministry of Environment. The recurrent challenges of these kinds of epidemiologic data are the estimation of the contribution of occupational and environmental exposures of communities to chemicals, and the separation of these factors from genetic, lifestyle, nutritional, and other factors, particularly when there are split jurisdictions. The Health Canada reports were focused on diseases that might be linked to pollutants and were therefore outside the direct jurisdiction of the local health units.

### Selection of Windsor for Intensive Study

One of these 42 Areas of Concern is the Detroit River, which is a severely polluted interconnecting channel between Lake St. Clair and Lake Erie and forms part of the boundary waters between Canada and the United States. Windsor was selected by the Great Lakes Science Advisory Board of the International Joint Commission as a model community for a detailed study of the efficacy of the use of health data in the Remedial Action Plan process at the local level for the following reasons:

- It is located beside the Detroit River, which is a large interconnecting channel and has been the subject of investigations of transboundary air and water pollution for several decades.
- Windsor is one of several Canadian cities in southwestern Ontario (including Toronto, Hamilton, and London) on a major transportation corridor, resulting in poor air quality.
- The community is large enough to provide a population size that can potentially yield statistical significance for all except the rarest of diseases but is not so large that all variations from the provincial rates of disease become statistically significant.
- There has been a community-based movement, including an occupational health clinic and information service, since the discovery in the late 1970s of a mesothelioma epidemic among auto workers (15).
- There are previous reports and studies of the cancer risks from air pollutants (16), of the geographic distribution of cancers (17), and of mandated community health profiles (18,19).
- The Great Lakes Regional Office of the International Joint Commission is located in Windsor, enabling the development of a level of familiarity with the study area including the city, the medical establishments, the unions, the university, and various industries.

Health Canada (13) prepared the report on the Canadian part of this Area of Concern using the selected health data and statistics for the 7-year period from 1986 to 1992 for the Ontario municipalities close to Windsor. For the purposes of this article, these conterminous municipalities are referred to as the "Windsor Area of Concern" or "Windsor," though it is only part of the Detroit Area of Concern, and includes more than just the municipality of Windsor.

### Sources of Contaminants and of Population Exposures

Until recently, residents in the Windsor Area of Concern thought they were being exposed to a variety of pollutants from a

variety of well-known sources. In addition to well-characterized occupational exposures of the workforce to a variety of products during automobile manufacturing, residents believed they knew the major sources of water and air pollutants to which they were exposed not only in Windsor but also in Detroit. For example, the major industries in Windsor include three car assembly plants (General Motors and two Daimler-Chrysler plants), a Ford engine plant and a foundry, and the Zalev scrap-metal recycling plant. Similarly, Windsor is immediately downwind of the Rouge Steel and National Steel Corporation steel mills with associated coking operations in Detroit; the wastewater treatment plant of the city of Detroit and associated sludge incineration facilities; the Greater Detroit Resource Recovery Authority municipal waste incinerator; and the Conners Creek Power Plant, which until recently was coal fired (16). Detroit is a large, mature metropolitan area largely dependent economically on car manufacturing and associated industries, such as chrome-plating plants. These have left an appreciable legacy of environmental contamination and toxic waste dump sites, some of which are being addressed through the Superfund program.

In previous studies, using air sampling and analysis, emission inventories, and cancer risk assessment modeling, the major air pollutants of concern for carcinogenesis in the Windsor community were ranked as follows: chromium (VI), benzene, 1,3-butadiene, chloroform, carbon tetrachloride, polycyclic aromatic hydrocarbons (PAHs), acetaldehyde, perchloroethylene, ethylene dichloride, formaldehyde, methylene chloride, cadmium, and 1,4-dichlorobenzene (16). Ingestion was identified as a major route of exposure for formaldehyde, cadmium, chromium (VI), dioxins, furans, and mercury. Subsequently, mapping techniques were used to investigate the possible relationships between the distribution of cancer rates for breast, lymphoma, lung, oral, prostate, colorectal, stomach, ovary, brain, uterine, and leukemia in the population in the city of Windsor and exposures to several of the above environmental contaminants (17). A recent review of air quality studies for toxic substances undertaken in the Detroit–Windsor region (20) concluded that "modeling and health assessment studies continue to predict concentrations in the region that exceed the 1:10<sup>6</sup> risk ratio for air toxics."

More recently, significant new databases have become available in Canada and in the United States (21), respectively, using data on the National Pollutant Release Inventory and the Toxic Release Inventory. In Windsor the top three sources of releases of toxic chemicals

were from a little-known plant called Maple Roll Leaf (616,091 kg of pollutants); the city of Windsor (562,747 kg); and ADM Agri-Industries Ltd. (473,500 kg). Similarly, the three largest releases of toxic substances on the Detroit side were from Wayne Disposal in Belleville (8,267,660 lb); Detroit Edison (2,029,702 lb at the River Rouge Power Plant, and 1,772,349 lb at the Trenton Channel Power Plant); and from the General Motors assembly plant at Hamtramck (1,105,809 lb).

The purposes of this article are

- to demonstrate how the Health Canada health data and statistics can be used by lay public involved in remedial action plans at the local level to describe the health of their communities in relation to sources of a variety of chemical pollutants;
- to compare community health in Windsor with that in Hamilton and with some other Canadian Areas of Concern, such as Sarnia; and
- to generate hypotheses about potential pollutant-induced health effects in Great Lakes communities as a template for further research, particularly in Windsor.

## Methods

Health Canada (13) detailed the methods used in the study under the following headings: assigning standard geographic codes; selecting health outcomes; gathering data; and analyzing the data.

### Assigning Standard Geographic Codes

Briefly, each of the 17 Areas of Concern was described using standard geographic codes, which not only contain provincial, census division, and census subdivision information, but also coincide with the Canadian process for collection of human health data. Each of the 17 reports contained detailed background information on the study area and its population, methods used in the study for assigning standard geographic codes, and gathering associated health data. In the specific case of preparing the report on the Windsor Area of Concern, the following municipalities with associated standard geographic codes were selected: Windsor (3537039); Amherstburg (3537029); Tecumseh (3537044); Sandwich West (3537034); Essex (3537054); Belle River (3537059); St. Clair Beach (3537052); Anderdon (3537031); Malden (3537026); Colchester North (3537018); Sandwich South (3537046); Rochester (3537058), and Maidstone (3537051). The population in this area in 1991 was 274,145, which represented 2.71% of the Ontario provincial population of 10,104,317. Data for the rates for diseases and disorders for the populations for all the Areas of Concern were age standardized by gender, and comparisons were made with the

rates for the rest of Ontario. Comparisons are made throughout this account with the health data and statistics for the Hamilton Harbour Area of Concern, which is another industrial municipality in southern Ontario comprising the following municipalities with standard geographic codes: the cities of Hamilton (3525014), Burlington (3524002), and Stoney Creek (3525003); the towns of Ancaster (3525014), Dundas (3525026), Flamborough (3525030), and Milton (3524003); and the township of Glanbrook (3525009). All represented a population of 613,315 or 6.07% of the provincial population.

Though the population in the Hamilton Harbour Area of Concern is more than twice the population included by Health Canada in the Detroit River Area of Concern, the populations were similar in terms of many demographic and socioeconomic measures, including the percentage of the population who were 15 years of age and older; basic education, families and dwellings, and average income; these were similar to the rest of the Province of Ontario (22). Health Canada did not include detailed consideration of demographic and socioeconomic risk factors. These have been shown to be important, together with other risk factors, in relation to the geographic distribution of the incidence of cancer in the province (23,24), though there still remains a need to investigate these and other possible risk factors in relation to the incidence of other diseases.

### Selecting Health Outcomes

Health Canada (13) selected about 70 categories of health end points, using the *International Classification of Diseases, Ninth Edition (ICD-9)* (25). Because this project was undertaken by the former Great Lakes Health Effects Program (13) under the mandate of the Great Lakes Water Quality Agreement, there was an orientation toward selecting diseases and disorders, based on references in the published literature, that might plausibly be linked to exposures to contaminants in the Great Lakes environment. Although the Health Canada documents included a consideration of a wide variety of physical, chemical, and biologic agents that could cause selected diseases and disorders, this community health profile for Windsor, Ontario focused particularly on the possible environmental and occupational agents. A second consideration in selecting the health outcomes was that data would be available for these diseases and disorders.

There is a possible discrepancy between different interpretations of “pollutants” and “contaminants.” Several of the categories of selected outcomes included microbiologic agents such as bacterial infections and viruses and other agents such as helminths. For the

purposes of this paper, diseases and disorders caused by these biologic agents are omitted. Table 1 contains the selected health outcomes used in this article and based on those of the *ICD-9* (25).

## Gathering and Analyzing the Data

Population census data for the years 1986 and 1991 were accessed from the Demography Division of Statistics Canada to calculate mortality and morbidity rates on an age-specific and gender-specific basis. Mortality data were provided by Statistics Canada to Health Canada’s Laboratory Centre for Disease Control and included information on the cause of death, reported by ICD code, the last location of residence based on the census subdivision, and the sex and age of the deceased (13). Hospital separations data were supplied by the Canadian Institutes for Health Information, and included data on sex, age, and residence, and the ICD code for the diagnosis for the main cause in cases of hospitalization. Health Canada (13) warned about some of the pitfalls of using hospital separations data, and these concerns included multiple visits or transfers between or within hospitals. They also exclude visits to clinics, doctors’ offices, and outpatient departments. Similarly, there may have been difficulties in transforming residence information based on a postal code or an Ontario residence code into a census subdivision. Further, these data for Ontario Province do not include Ontario residents who were hospitalized in another province. These pitfalls were addressed in the Health Canada reports in analyzing the data and statistics. For example, in using the hospital separations data, Health Canada referred to morbidity rates rather than incidence rates. One potentially significant pitfall not mentioned in the reports relates to the possible differences between large metropolitan areas and small municipalities in local policies concerning hospital admittance; the latter may be more inclined to admit a patient than the former.

The age-standardized rates were calculated based on 19 age groups, and the report presented the rates for the following five age ranges: all ages, 0–24 years, 25–44 years, 45–74 years, and over 75 years. The age-adjusted mortality and morbidity rates were compared with the rates for the rest of the Province of Ontario, and ratios were calculated comparing the local rates with the provincial rates. Appreciable sampling variation may arise from considering small numbers of deaths, cases, or incidences within some of the age groups and the Poisson test was applied to overcome these possible inaccuracies. In the following account of community health in Windsor and its

comparison with some other Areas of Concern, only those rates of disease outcomes that are statistically significantly elevated at or above the 95% level are generally commented on. Health Canada also occasionally included a flag to warn that though a rate or ratio, compared with the rest of the province, was not statistically

significant, the limited sample size could undermine the accuracy of such a statistical determination of nonsignificance. In interpreting the data and statistics for the Windsor Area of Concern, there has been considerable reliance on the references in several Health Canada reports (13,26,27), as well as other reference sources.

## Results

### Mortality and Morbidity Rates Based on Hospitalization Records, 1986–1992

The rate at which people die or go to the hospital can be taken as an indication of the overall health of the community. During the 7-year period between 1986 and 1992,

**Table 1.** Health outcomes that might be linked to pollution.<sup>a,b</sup>

ICD-9 category	ICD-9 number	Disease or condition	ICD-9 category	ICD-9 number	Disease or condition	
Category II		All malignant neoplasms	Category VIII	460–466	Acute respiratory infections	
	140–149	Malignant neoplasm of lip, oral cavity, and pharynx		470–478	Other diseases of the upper respiratory tract	
	146–148	<i>Malignant neoplasm of the pharynx</i>		470–487	Pneumonia and influenza	
	150–159	Malignant neoplasm of digestive organs and peritoneum		490–496	Chronic obstructive pulmonary disease and allied conditions	
	150	<i>Malignant neoplasm of oesophagus</i>		491	<i>Chronic bronchitis</i>	
	151	<i>Malignant neoplasm of stomach</i>		492	<i>Emphysema</i>	
	153–154	<i>Malignant neoplasm of colon and rectum</i>		493	<i>Asthma</i>	
	155	<i>Malignant neoplasm of liver and intrahepatic bile ducts</i>		500–537	Pneumoconioses and other lung diseases due to external agents	
	156	<i>Malignant neoplasm of gallbladder and extrahepatic bile ducts</i>		Category IX	530–537	Diseases of esophagus, stomach, and duodenum
	157	<i>Malignant neoplasm of the pancreas</i>			555–558	Noninfective enteritis and colitis
	160–165	Malignant neoplasm of respiratory and intrathoracic organs			560–569	Other diseases of intestines and peritoneum
	162	<i>Malignant neoplasm of the trachea, bronchus, and lung</i>		570–579	Other diseases of digestive system	
	170–175	Malignant neoplasm of bone, connective tissue, skin, and breast		Category X	580–589	Nephritis, nephrotic syndrome, and nephrosis
	172	<i>Malignant melanoma of skin</i>			590–599	Other diseases of urinary system
	174	<i>Malignant neoplasm of female breast</i>			600–608	Diseases of male genital organs
	179–189	Malignant neoplasm of genitourinary organs			606	<i>Infertility, male</i>
	183	<i>Malignant neoplasm of ovary and other uterine adnexa</i>			610–611	Disorders of the breast
	185	<i>Malignant neoplasm of the prostate</i>			617–629	Other disorders of female genital tract
	186	<i>Malignant neoplasm of testis</i>		617	<i>Endometriosis</i>	
	188	<i>Malignant neoplasm of the bladder</i>		628	<i>Infertility, female</i>	
189	<i>Malignant neoplasm of kidney, other, and unspecified urinary organs</i>	Category XI	630–639	Pregnancy with abortive outcome		
190–199	Malignant neoplasm of other and unspecified sites		634	<i>Spontaneous abortion</i>		
193	<i>Malignant neoplasm of thyroid gland</i>		640–648	Complications mainly related to pregnancy		
200–208	Malignant neoplasm of lymphatic and haematopoietic tissue		642	<i>Hypertension complicating pregnancy, childbirth, and the puerperium</i>		
200,202	<i>Non-Hodgkin lymphoma</i>		644	<i>Early or threatened labor</i>		
201	<i>Hodgkin disease</i>		680–686	Infections of skin and subcutaneous tissue		
204–208	<i>Leukaemia</i>	690–698	Other inflammatory conditions of skin and subcutaneous tissue			
Category III	240–246	Disorders of thyroid gland	700–709	Other diseases of skin and subcutaneous tissue		
	250–259	Diseases of other endocrine glands	Category XII	710–719	Arthropathies and related disorders	
	250	<i>Diabetes mellitus</i>		720–724	Dorsopathies	
	255	<i>Ovarian dysfunction</i>		725–729	Rheumatism, excluding the back	
	257	<i>Testicular dysfunction</i>		730–739	Osteopathies, chondropathies, and acquired musculoskeletal deformities	
270–279	Other metabolic disorders and immunity disorders	Category XII		All anomalies		
Category IV	280–289		Diseases of blood and blood-forming organs	740.0–742.9	Central nervous system anomalies	
	Category VI		330–337	Hereditary and degenerative diseases of the central nervous system	740.0–740.2	<i>Anencephalus and similar anomalies</i>
332			<i>Parkinson disease</i>	741.0–741.9	<i>Spina bifida</i>	
340–349			Other disorders of the central nervous system	742.1–742.2	<i>Microcephalus and brain reduction</i>	
340			<i>Multiple sclerosis</i>	742.3	<i>Congenital hydrocephalus</i>	
343	<i>Infantile cerebral palsy</i>		743.0–743.9	Eye anomalies		
350–359	Disorders of the peripheral nervous system		745.0–746.9	Congenital heart defects		
359	<i>Muscular dystrophies and other myopathies</i>		745.4	<i>Ventricular septal defect</i>		
360–379	Disorders of the eye and adnexa		745.5	<i>Atrial septal defect</i>		
369	<i>Blindness and low vision</i>	747.1–747.9	Circulatory system anomalies			
380–389	Diseases of the ear and mastoid process	747.3	<i>Pulmonary artery anomalies</i>			
Category VII	401–405	Hypertensive disease	748.0–748.9	Respiratory system anomalies		
	410–414	Ischemic heart disease	749.0–749.2	Cleft lip and/or palate		
	415–417	Diseases of pulmonary circulation	750.1–751.9	Digestive system anomalies		
	420–429	Other forms of heart disease	752.6	<i>Hypospadias, epispadias</i>		
	440–448	Diseases of arteries, arterioles, and capillaries	753.0–753.9	Urinary system anomalies		
	440	<i>Atherosclerosis</i>	753	<i>Renal agenesis and dysgenesis</i>		
			754.5–754.7	Clubfoot		
		755.0–755.1	Polydactyly, syndactyly			
		755.2–755.3	Limb reduction anomalies			
		758	Down syndrome			
		Category XIV	760–779	Certain conditions originating in the perinatal period		

<sup>a</sup>Based on the *International Classification of Diseases, Ninth Edition* (25). <sup>b</sup>Adapted from Health Canada (13).



people in the Windsor Area of Concern died at significantly higher rates (males: 8% higher, 613 excess deaths; females: 5% higher, 366 excess deaths) than in the rest of Ontario Province. This increased mortality occurred significantly among people 45–74 years of age for both males (14% higher, 496 excess deaths) and females (10% higher, 232 excess deaths). In contrast, the mortality rates in both males and females in Hamilton, Ontario, were the same as those in the rest of Ontario, but were about 10% lower for males up to 44 years of age and 14% lower for females up to 24 years of age. The rates of mortality from all causes for both Windsor men and women ranked sixth out of 25 Canadian census metropolitan areas in a recent analysis of 1994–1996 data and were significantly elevated above the rates for Canada (28).

The number of cases of people in the Windsor Area of Concern being hospitalized for all causes during the 7-year period between 1986 and 1992 was 122,776 cases, or 21% higher in males (20,987 excess cases of morbidity), and 165,344 cases, or 15% higher for females (21,567 excess cases of morbidity). All age categories had significantly elevated morbidity as hospitalization rates: among those between birth and 24 years of age, the rate was 12% higher for males (2,809 excess) and 9% higher for females (2,866 excess) but rose to 32% higher in males (5,610 excess) who were between 25 and 44 years of age compared with 10% higher for females (5,729 excess). For those 45–74 years of age, the rate was about 25% higher (10,955 excess for males and 9,819 excess for females); for those over 75 years of age, the morbidity was 14% higher for males (2,290 excess) and 20% higher for females (4,649 excess). In contrast, rates of morbidity as hospitalization in Hamilton are about 15% lower than those for the rest of the province, and significantly lower rates are apparent throughout all age categories. It would seem that, despite the apparent similarities in latitudes, locations in southern Ontario, degree of industrialization, and several demographic and socioeconomic measures, the community in Windsor has much higher rates of morbidity and mortality than Hamilton, suggesting that there are serious public health issues that might possibly be related to exposures to pollutants.

Of 11 Canadian cities studied (29) in relation to mortality and air pollution, Windsor had the highest daily mortality, followed by Hamilton (2.09 vs 2.02 deaths/day/10<sup>5</sup> population). This mortality in Windsor did not seem to be explained by concentrations of carbon monoxide, nitrogen dioxide, sulfur dioxide, or ozone, or by consideration of these pollutants in aggregate, but these pollutants were associated with

hospital admissions (30). These results pose the question of whether there were other factors in Windsor that might have accounted for the high mortality rate.

### **ICD-9 Category II: Cancer Mortality and Morbidity**

The following is a description of the cancer mortality and incidence based on the health data and statistics from 1986 to 1992. Among the 17 Canadian Areas of Concern, the Windsor Area of Concern was the only location that had a cancer incidence rate for the aggregated age groups in either males or females that was statistically significantly elevated. Cancer incidence in the population in the Windsor Area of Concern was 4,275 cases for males and 3,941 for females. The incidence rate for males for the aggregated age groups was 7% above the rate for the rest of the province, resulting in about 280 extra cases. The elevated cancer incidence rates occurred particularly among males and females 45–74 years of age, and were 10% (254 excess) and 5% (115 excess) higher, respectively, than the provincial rates.

In contrast, the incidence of cancers in the population in Hamilton was 3% lower than the provincial rate for both males and females, and no age category was significantly elevated. These results are not inconsistent with the predictions of the carcinogenesis risk assessment for the Windsor population (16) and indicate that the population in the Windsor Area of Concern is being exposed to carcinogenic compounds at concentrations that are probably injurious. The following classes of cancers that might be related to exposures to pollutants were significantly elevated in the Windsor Area of Concern.

### **Cancers of the Lip, Oral Cavity, and Pharynx (ICD-9: 140–149)**

Health Canada (13) noted the possible involvement of air pollution as a potential factor in the development of cancer of the pharynx, but based on the review by Björklund and Wennersberg (31), also referenced the associations with several other potential risk factors including tobacco, marijuana, alcohol, diet, occupational factors, virus infections, genetic instability, and compounds that induce aryl hydrocarbon hydroxylase. The mortality rate from cancers of the lip, oral cavity, and pharynx among Windsor residents 45–75 years of age was 54% higher for males (about 32 extra deaths) and more than 2-fold (2.11 times) higher for females (about 15 extra deaths) than in the rest of the province. The cancer mortality and incidence rates in the Hamilton population were generally not statistically significantly lower than the provincial rates. The exception was in Hamilton males 45–74 years of age,

for whom the cancer incidence rate was significantly 12% below the provincial rate.

Thomas (32), in reviewing the epidemiologic evidence in relation to alcohol consumption as a risk factor for these cancers, remarked on the role of alcohol in potentiating the carcinogenic effect of cigarette smoke on the increased risk of oral and pharyngeal cancer. The feasibility of investigating the attributable role of carcinogenic air pollutants in causing these reported excess cancers in the Windsor population might be evaluated in relation to other recognized risk factors.

### **Cancers of Digestive Organs and Peritoneum (ICD-9:150–159)**

This aggregated class of cancers included malignant neoplasms of the esophagus, stomach, colon and rectum, liver and intrahepatic bile ducts, gall bladder and extrahepatic bile ducts, and pancreas. Health Canada (13) relied heavily on the review of Ahlgren and Macdonald (33) in selecting these various cancers of the digestive organs and the peritoneum for inclusion in its study of diseases that might be related to pollution in the Areas of Concern. Major risk factors include various genetic, lifestyle, and socioeconomic factors. But Health Canada (13) also noted studies relating exposures to radiation as a risk factor in colon and rectal cancer (34), and long-term consumption of chlorinated drinking water as risk factors in colon cancer (26). More recently, Paulu et al. (35) demonstrated an increased risk of colon and rectal cancer from contamination of a water supply with tetrachloroethylene.

Among this class of cancers, there was a 10% higher mortality rate among Windsor males than the rest of Ontario, particularly among those males 45–74 years of age. Much of this increased rate of mortality from cancer in males was attributable to cancer of the colon and rectum, resulting in about 48 excess deaths. The comparable mortality rate for Hamilton males 45–74 years of age is 12% below the provincial rate. The feasibility of further investigations of the factors associated with the elevated mortality rate from colorectal cancer in the population in the Windsor Area of Concern should be evaluated. There are, for example, several occupational and environmental risk factors associated with colorectal cancer, including exposures to soot, asbestos, cutting fluids and oils, and combustion gases from coal, coke, and wood (36). Trends could be monitored prospectively over the long term to track whether recent changes in drinking water treatment from a chlorination process to an ozonation process have an effect on the incidence of this cancer.

Of particular concern was the increased rate of mortality from pancreatic cancer among both Windsor males (44% higher, 42

extra deaths) and females (37% higher, 36 extra deaths), particularly for those 45–74 years of age. This significantly elevated mortality from pancreatic cancer among this age group was reflected in increased incidence rates in males (33% higher, 21 excess cases) and females (40% higher, 21 excess cases). An increased incidence rate from pancreatic cancer (43% higher, 20 excess cases) even persisted for those women over 75 years of age in the Windsor Area of Concern.

The Health Canada study (13) cited the review of Ahlgren and Macdonald (33) in identifying associations of pancreatic cancer not only with cigarette smoking, but also with occupational exposures to solvents, petroleum compounds, and  $\beta$ -naphthylamine in chemical and coke plant workers, sawmill workers, miners, and metal workers. A more recent review (37) indicated that the causes of pancreatic cancer are still obscure, but that higher rates seem to occur in more industrialized nations, though no single chemical agent has been consistently identified. Of particular interest in this latter study was the association of pancreatic cancer with pancreatitis and with non-insulin-dependent diabetes mellitus. Windsor is the largest Canadian manufacturing center for automobiles, and there are many workers involved in a variety of industries involving metal manufacturing. In addition, Windsor residents are downwind of several large coking operations in Detroit associated with steel production. The feasibility of investigating the factors associated with these elevated rates of pancreatic cancer incidence and mortality should be evaluated to determine whether they warrant special epidemiologic investigations on a priority basis, not only because a significant proportion of these cancers are likely preventable but also because the survival rate for this cancer is so low.

### Cancers of the Respiratory and Intrathoracic Organs (ICD-9:160–165)

There were increased incidence rates and mortality from cancers of the respiratory and intrathoracic organs for both males and females in the Windsor Area of Concern (13). The mortality rate for males was 17% higher than the provincial rate, yielding 115 excess deaths and associated mostly with those 45–74 years of age. Of particular concern was the more than 2-fold rate (2.23 times, 14 excess deaths) for Windsor males 25–44 years of age from these cancers. The mortality rate for Windsor females was 12% higher than the provincial rate and was associated with 39 excess deaths. Whereas Hamilton males had a mortality rate for this cancer 6% higher (92 excess deaths) than the provincial rate, there was, in contrast to Windsor, a total of 2 deaths among males 25–44 years of age. The mortality rate was

statistically indistinguishable from the provincial rate for both Hamilton males and females 45–74 years of age. Only among those Hamilton males who were over 75 years of age was there a statistically significantly higher rate (13% and 53 excess deaths) from cancer of the respiratory and intrathoracic organs. Windsor men and women both ranked fourth out of 25 Canadian census metropolitan areas for mortality for lung cancer (28).

These elevated mortality rates in the Windsor Area of Concern were reflected in increased incidence rates in males (19% higher and nearly 165 excess cases) and in females (16% higher and 70 excess cases). Among males 25–45 years of age, the incidence rate was 77% higher than the provincial rate, and elevated incidence rates were evident for males (20%) and females (17%) 45–74 years of age. In contrast, the incidence rates for respiratory and intrathoracic cancer in Hamilton males and females were indistinguishable from the provincial rates, even among Hamilton males 45–74 years of age and among those over 75 years of age.

Health Canada (13) cited the work of Motta (38) in listing the following factors associated with lung cancer: mainstream and secondary-stream tobacco smoke, radon, asbestos, formaldehyde, end products of uncontrolled combustion, air pollution, and occupational exposures to a variety of substances. The following compounds were identified by the Windsor Air Quality Committee (16) in the inhalation cancer risk assessment for the Windsor population as having concentrations above the  $10^{-5}$  risk level: 1,3-butadiene, benzene, chromium (VI), chloroform, carbon tetrachloride, PAHs, acetaldehyde, perchloroethylene, ethylene dichloride, formaldehyde, methylene chloride, cadmium, and 1,4-dichlorobenzene. The health data and statistics for the elevated rates of mortality and incidence of respiratory and intrathoracic cancer in the population in the Windsor Area of Concern, the contrast in these rates with the rates for Hamilton, and the elevated risk levels from the identified substances of concern indicate that there are atmospheric sources of carcinogens to the Windsor–Detroit airshed that are injurious to the health of the Windsor community. The feasibility of undertaking investigations of these specific sources should be assessed on a priority basis, and controls that could lead to significant reductions in the incidences of these preventable cancers should be undertaken.

### Cancers of the Genitourinary Organs (ICD-9:179–189)

Health Canada (13) selected the following cancers of the genitourinary organs as potentially linked to pollutants: ovary, prostate,

testis, bladder, kidney, and other urinary organs. A statistically significant increase in bladder cancer incidence was evident for Windsor males (19% higher, 29 excess cases) 45–74 years of age. Health Canada noted that the risk factors for this category of cancers (ICD-9:189) are as yet unknown but may include tobacco use, obesity, and a rich diet of animal fats and cholesterol (39).

### Cancers of the Lymphatic and Hematopoietic Tissues (ICD-9:200–208)

The following three kinds of cancers of the lymphatic and hematopoietic system were selected by Health Canada (13) as potentially associated with exposures to pollutants: non-Hodgkin's lymphoma, Hodgkin's lymphoma, and leukemia. The incidence rate for this category of cancers in Windsor females 45–74 years of age was 23% higher (37 excess cases) than in the rest of the province. In Hamilton males over 75 years of age, there was a 17% higher (32 excess cases) incidence for this category of cancers.

Of particular concern was the incidence rate from leukemia in Windsor males of all ages, with a 21% higher rate (29 excess cases). The incidence rate from leukemia was elevated in both males (33% higher, 24 extra cases) and females (44% higher, 21 extra cases) 45–74 years of age compared with the rest of the province. The Hamilton mortality and incidence rates and ratios from leukemia in males and females were comparable with those for the rest of the province.

Health Canada (13) noted the association of the leukemias with heritable factors, viruses, radiation, electromagnetic fields, pesticides, chemicals such as benzene, and other occupational exposures, and drugs (34,39,40). In the risk assessment undertaken by the Windsor Air Quality Committee (16), benzene was ranked second only to hexavalent chromium as the leading chemical of concern for cancer, with an upper risk factor between  $10^{-4}$  and  $10^{-3}$ . At that time, 3,611,000 kg benzene was emitted to the atmosphere in the Detroit area, representing 96.3% of the emissions in the airshed, and 139,201 kg (3.7%) was emitted from Windsor and vicinity.

The six females over 75 years of age who had Hodgkin's disease represented more than a 2-fold (2.75 times) increase in the incidence rate compared with the rest of the province. There were 12 deaths attributable to Hodgkin's disease in females, representing more than a 2-fold (2.26 times) rate compared with the rest of the province. Though the numbers of deaths in females in each age category were too small to attain statistical significance, the more than 2-fold elevated mortality rates occurred consistently in all age categories. In Hamilton females 25–44 years of age, there was a 63% higher incidence (13

excess cases) of Hodgkin's disease compared with the rest of the province. The deaths of five Hamilton males who died from Hodgkin's disease between birth and 24 years of age represent a mortality rate more than 3-fold the rate in the rest of the province. Health Canada (13), in addition to the associations of Hodgkin's disease with heritable factors, surgical procedures including tonsillectomy and appendectomy, and infectious diseases such as mononucleosis, mentioned exposures to pesticides, electromagnetic fields, benzene, and radiation (39,40).

A recent review of the epidemiology of Vietnam veterans has reaffirmed earlier reports of associations between exposures to the chlorophenoxy herbicide mixture Agent Orange and Hodgkin's and non-Hodgkin's lymphoma as well as an increased risk of a rare childhood leukemia, acute myelogenous leukemia (41). A possible interactive effect between Epstein-Barr virus and higher concentrations of organochlorine chemicals, particularly hexachlorobenzene, has been associated with the risk of hairy cell leukemia, one of the group of non-Hodgkin's lymphoma malignancies (42). The feasibility of investigating the excess incidence and mortality from cancers of the lymphatic and hematopoietic systems in the community in the Windsor Area of Concern should be assessed, as these cancers may be preventable through controls on the releases of known and previously unsuspected carcinogenic compounds.

### **ICD-9 Category III: Endocrine, Nutritional and Metabolic, and Immunity Disorders**

In recent years there has been a growing appreciation of the effects of environmental contaminants on the functioning of the endocrine systems (7), and thereby concerns about the development and functioning of the immune (43) and neurologic systems (44).

#### **Disorders of the Thyroid Gland (ICD-9:240–246)**

There were 314 cases of morbidity as hospitalization for disorders of the thyroid gland in females in the Windsor Area of Concern, representing a 24% increase over the provincial rate. In contrast to all the other 16 Areas of Concern, the onset of the increased rate of thyroid disease in females occurred in the Windsor Area of Concern between birth and 24 years of age, and this increase was more than 2-fold (208%) the provincial rate. Further, there were elevated rates for thyroid disease in Windsor women occurring in all age categories. These findings contrast with the rates of thyroid morbidity in the Hamilton population that had a 30% lower rate in males and 28% lower rate in females compared with the rest of the province, suggesting the possible

presence of thyroid-active agents in the Detroit/Windsor environment.

The Detroit/Windsor area has had endemic goiter since early times, but this has been successfully counteracted through the use of iodized salt. Despite this endemic goiter, observations of Great Lakes fish and wildlife have demonstrated that the most severe thyroid hyperplasia, unrelated to iodine status, occurs in the region of the Detroit River and Western Lake Erie and implicates environmental goitrogens (45,46). There are a variety of compounds that can affect the thyroid gland, including naturally occurring goitrogens such as flavonoids in legumes; drugs such as phenytoin and lithium; pesticides such as DDT, thiocarbamates, and aminotriazole; and industrial chemicals such as polyhalogenated aromatic compounds, phenol derivatives, and phthalates (47). Interference with thyroid function has recently been implicated in the abnormal structural and functional development of the fetal and infant brain, with consequences for learning and behavior (48). The feasibility of undertaking epidemiologic investigations, possibly including mapping of the distribution of prescriptions for thyroid supplement, should be evaluated to investigate the possible presence, identity, and sources of thyroid-active agents in the Windsor Area of Concern, with the intention of bringing in strict controls, including prohibitions of releases.

#### **Diseases of Other Endocrine Glands (ICD-9:250–259)**

There are increased rates of morbidity for diseases of other endocrine glands in both males (41% higher, 625 excess cases) and females (41% higher, 735 excess cases) in the Windsor Area of Concern.

#### **Diabetes Mellitus (ICD-9:250)**

In contrast to Hamilton and Toronto, which had rates of morbidity from diabetes 30–40% lower than the provincial rates, the rates in the Windsor Area of Concern were 44% higher for males (604 excess cases) and 41% higher for females (637 excess cases). Of particular concern is the early onset of diabetes. In common with other relatively polluted locations such as Thunder Bay, Sault Ste. Marie, Spanish River, and Niagara Falls, the onset of the increase in the rates of diabetes in the Windsor Area of Concern occurred between birth and 24 years of age (58% for males or 112 excess cases, and 41% for females or 94 excess cases). For Windsor males 25–44 years of age, the rate of hospitalization for diabetes was 51% higher than the rest of the province and 59% higher for females, and the respective rates for those 45–74 years of age were 49 and 40% higher. These data indicate that there is a much

higher rate of morbidity as hospitalization for diabetes in the Windsor community for all age groups up to 75 years of age. Diabetes was practically an unknown disease among First Nations and Inuit people 50 years ago, but Health Canada has acknowledged there is an epidemic of type 2 diabetes in some First Nations communities and among Aboriginal children as young as 5 years of age, and has responded with an Aboriginal Diabetes Initiative.

Health Canada (13) reviewed the factors associated with diabetes (49,50). In addition to hereditary and immune-mediated factors, it can be related to a variety of viruses such as mumps, rubella, cytomegalovirus, Coxsackie viruses, retroviruses, and reoviruses, or linked to encephalomyocarditis caused by a group of small RNA picornaviruses. There are several substances, such as nitroso compounds, that are toxic to beta cells located in the pancreatic islets of Langerhans. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin has been shown to decrease blood sugar and insulin levels in treated rats and to result in hypersensitivity to insulin (51). Vietnam veterans exposed to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in Agent Orange have an increased incidence of diabetes, and those without diabetes had a higher incidence of hyperinsulinemia (52). The association between exposure to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and diabetes has been recently affirmed (41,53). An association has been demonstrated between elevated PCB levels in serum and diabetes in pregnant women (54). Associations between exposures to arsenic and the incidence of diabetes have been published (55,56), and more recently, a mechanism has been proposed through interference with the action of glucocorticoids (57). The feasibility should be assessed of undertaking epidemiologic investigations into the causes of the markedly elevated rates for diabetes in all age categories in the Windsor Area of Concern, including consideration of the possibility that pollutants released to the environment are interfering with the normal functioning of the pancreas.

#### **Ovarian Dysfunction (ICD-9:256)**

Similarly, in contrast to Hamilton and Toronto, which had morbidity as hospitalization rates of ovarian dysfunction related to diseases of the endocrine system well below the provincial rate, the rate in the Windsor Area of Concern was more than twice (2.12 times, 30 excess morbidity cases) the provincial rate. This rate was comparable with the rates at Thunder Bay (2.19 times) and Sault Ste. Marie (2.34 times), though not as high as at Spanish River (5.84 times). There was an early onset of the significantly elevated rates of hospitalization of women for ovarian dysfunction in the Windsor Area of Concern;



the increased rates began in the group under 25 years of age with a rate that was 96% higher than the provincial rate and increased to over 2-fold (2.18 and 22 excess cases) in females 25–44 years of age.

Health Canada (13) included the following in this category of disease: hyperestrogenism, hyperandrogenism, ovarian failure, premature menopause, and polycystic ovaries. Risk factors associated with ovarian dysfunction including obesity, heredity, enzymatic defects, autoimmune disorders, congenital anomalies, radiation, chemotherapy, viruses, cigarette smoking, surgery, and other idiopathic conditions (13,58). There are several experiments in animals that demonstrate that exposures to reproductive toxicants such as benzo[*a*]pyrene (59) and hexachlorobenzene (60), affect ovarian follicle development. Exposure of monkeys to lead resulted in suppression of circulating luteinizing hormone, follicle stimulating hormone, and estrogen levels (61). The feasibility of investigating the risk factors associated with the high morbidity rates of ovarian dysfunction in the Windsor Area of Concern should be evaluated.

#### **Other Metabolic and Immunity Disorders (ICD-9:270–279)**

This category of disorders, selected by Health Canada (13), includes not only metabolism and/or transport of amino acids, carbohydrates, lipids, plasma proteins, minerals, and fluid, electrolyte and acid-base balance, but also disorders of immune development and function. Health Canada (13) noted the wide array of substances, including halogenated aromatic hydrocarbons, asbestos, benzene, and heavy metals, that have been associated with immunosuppression and immunodeficiencies in humans (40,62). Of specific interest is the relationship between prenatal exposures to PCBs and dioxins and changes in immune function [reviewed in Weisglas-Kuperus (63)].

In terms of morbidity as hospitalization from disorders of the metabolic and immune systems, Windsor males had rates that were 42% (196 excess cases) and females were 49% higher (413 excess cases) than the rest of the province. There was an early onset of this excess morbidity (30% higher) in Windsor males under 25 years of age. In males and females over 45 years of age, the morbidity rate as hospitalization was 47% higher and 61% higher, respectively, and rose for those over 75 years of age to 60 and 94% higher, respectively.

The 46 females who died of these disorders yielded a rate that was 33% (11 excess deaths) higher than the rest of the province. Most of this increased rate of mortality (86% higher than the rest of the province) occurred among females 45–74 years of age.

There is a need to disaggregate these data to determine whether the increased rates are mostly associated with changes in metabolic or in immune functioning. This determination should be used to determine the feasibility of undertaking an epidemiologic investigation of the factors associated with this increased morbidity and mortality.

#### **ICD-9 Category IV: Diseases of the Blood and Blood-Forming Organs (ICD-9:280–289)**

Health Canada (13) described the various anemias, coagulation defects, hemorrhagic conditions, and diseases of white blood cells included in this category and their variety of risk factors. Of particular interest for this study on possible health effects of pollutants are the references (40,64) used by Health Canada to various associations of certain anemias, platelet disorders, haemolytic conditions, effects on heme-containing enzymes, and vascular disorders, with environmental exposures to organic or inorganic contaminants or low-level radiation.

The population in the Windsor Area of Concern tended to have higher morbidity rates for diseases of the blood and blood-forming organs compared with the rest of Ontario. Males had a 29% higher rate (229 excess cases) and the corresponding figure for females was 13% higher (138 excess cases). As with the previous category, there was an early onset of the increased rates (68% higher, 210 excess cases) among males between birth and 24 years of age, but females in this age category also had elevated rates (19% higher, 46 excess cases). Males over 45 years of age had rates 15% higher, and among females over 75 years of age the rate was 10% higher than the corresponding provincial rates.

There was a contrast between the Windsor and Hamilton Areas of Concern in terms of the morbidity rates for diseases of the blood and blood-forming organs. Females in Hamilton had rates 12% lower and particularly in the age group from birth to 24 years of age had rates that were 27% lower than the provincial rates. In contrast to the Hamilton females and to the Windsor males, Hamilton males under 25 years of age were not significantly different from the rest of the province, but those 25–44 years of age were 25% higher.

#### **ICD-9 Category VI: Diseases of the Nervous System and Sense Organs (ICD-9:330–337)**

Health Canada (13) selected several diseases of the central and peripheral nervous systems and of the sense organs that might be affected by exposures to pollutants. For the central nervous system, these included Parkinson's disease, multiple sclerosis, and infantile cerebral palsy. Muscular dystrophies and

other myopathies were included relative to the peripheral nervous system, together with disorders of the eyes and ears.

There were several disorders of the central nervous system and sense organs that exhibited significantly higher rates in the Windsor Area of Concern than in the rest of the province. The rate of hereditary and degenerative diseases of the central nervous system in males was 14% higher (52 excess cases) and 16% in females (64 excess cases) than the rate for the rest of Ontario. For both males and females 25–44 years of age, the rate rose to 44 and 54%, respectively, above the provincial rate, but continued higher than the provincial rate up to 75 years of age. These excess cases of morbidity from hereditary and degenerative diseases of the central nervous system did not seem to be related to increased rates of Parkinson's disease. They also contrast strongly with the 25% lower rate in Hamilton males and 30% lower rate in Hamilton females. There is a priority need to investigate whether some significant proportion of these excess cases might be related to autoimmune disorders, central nervous system infections, metabolic disorders, drug intoxications, other diseases, or brain tumors, as some pollutants are suspected to be involved in neurodegenerative disorders such as Parkinson's disease, dementia, and amyotrophic lateral sclerosis (Lou Gehrig's disease) (65,66).

Similarly, for other disorders of the central nervous system, the morbidity rate for Windsor males was 31% higher (217 excess cases) and for females was 21% higher (188 excess cases). Of particular concern, in addition to the elevated rates for all age categories, was the early onset for both males (50 excess cases) and females (35 excess cases) between birth and 24 years of age. The mortality rate for males 25–44 years of age for disorders of the central nervous system was more than 2-fold (2.31 times) the provincial rate and resulted in 8 excess deaths that did not seem to be related to an increased rate of multiple sclerosis or infantile cerebral palsy. In contrast, Hamilton had rates for morbidity as hospitalization for other diseases of the central nervous system in males and females that were generally nearly 30% below the rates for the rest of the province. The notable exception for Hamilton was the number of morbidity as hospitalization cases for infantile cerebral palsy. There were 60 males and 58 females yielding a rate of 2.9 cases per 100,000 population, and anomalously, this was statistically significant only for the females. Further work is under way to analyze the morbidity data on infantile cerebral palsy, which were included by Health Canada because of the association with prenatal exposures to methylmercury (67), for all the 17 Canadian Areas of Concern. Meanwhile, there is a need to better



define the specific disorders that contribute to these elevated rates of morbidity in the Windsor population and to determine whether they might be demyelination disorders possibly linked to organophosphorous insecticides or other neurotoxic chemicals (68).

Disorders of the peripheral nervous system were 46% higher in males (153 excess cases) and 43% higher for females (183 excess cases) than the provincial rates. Among those 25–44 years of age, the rates rose to 99% higher for males (86 excess cases) and to 81% for females (87 excess cases) above the provincial rate and continued high to 74 years of age, and even for females over 75 years old (37 excess cases). Hamilton had an increased rate of diseases of the peripheral nervous system in females, particularly among the age group 25–44 years of age (93 excess cases). There is a need to better define the parts of the peripheral nervous system that have significantly elevated rates of disorders within the population in the Windsor and Hamilton Areas of Concern. Health Canada (13) noted that disorders of the peripheral nervous system are most often caused by metabolic disorders, predominantly diabetes mellitus, and these have already been shown to be elevated in this population. In addition to several risk factors for disorders of the peripheral nervous system, including infections, Hodgkin's disease, recent surgery, pregnancy, vaccination, and pharmacologic immunosuppression, Health Canada (13) cited various industrial and environmental neurotoxic agents such as triorthocresyl phosphate, hexacarbons, acrylamide, dimethylaminopropionitrile, organophosphorous compounds (especially insecticides), lead, arsenic, and thallium salts. Of particular concern are the changes in the central and peripheral nervous system from exposures to polychlorinated dibenzo-*p*-dioxins (69).

The rate of disorders of the eye and adnexa was 21% higher among males (213 excess cases) and 11% higher for females (144 excess cases) than the provincial rate among those in the Windsor Area of Concern 45–74 years of age, and the excess cases continued for males over 75 years of age (81 cases). These increased rates were not associated with morbidity as hospitalization from increased blindness. In addition to the hereditary and congenital factors, penetrating wounds, ulcers, infections, and ultraviolet radiation that cause eye disorders, Health Canada (13) listed chemicals, ischemic and immunogenic factors, drugs, and allergies. Health Canada (13) noted that *a*) air pollution causes eye irritation; *b*) methylmercury (70) and organochlorine compounds can result in deficits in the visual field; and *c*) alcohol, lead, arsenic, and carbon dioxide cause toxic polyneuritis (71). There is a need to investigate whether significant proportions of these elevated rates of

disorders of the eyes and adnexa are caused by occupational or environmental exposures to chemicals and pollutants.

### **ICD-9 Category VII: Diseases of the Circulatory System (ICD-9:401–440)**

There are several diseases of the circulatory system for which the population in the Windsor Area of Concern had significantly higher rates of mortality and morbidity than the rest of the province (13). The mortality rate for heart disease for Windsor women ranked fourth behind those for Sudbury, Thunder Bay, and St. Catharines–Niagara in the analysis of 1994–1996 data for 25 Canadian metropolitan census areas, and seventh for Windsor men (28). Of particular concern was the rate of mortality for hypertensive disease in males, which was 56% higher (20 excess deaths), and ischemic heart disease in both males (21% higher, 427 excess deaths) and females (25% higher, 453 excess deaths). Mortality from diseases of the arteries was 65% higher for males, associated with an excess of 142 deaths, and 92% higher for females, with 244 excess deaths. Atherosclerosis was more than 2 times the rate in the rest of the province for males (2.23 times, 99 excess deaths) and for females (2.45 times, 248 excess deaths).

This elevated mortality from diseases of the circulatory system was reflected in the high morbidity as hospital separations from these diseases. There were 1,390 excess hospitalization cases of ischemic heart disease in males (18% higher than the rest of the province) and 1,736 excess cases in females (36% higher). Similarly, there were 624 excess cases of diseases of the pulmonary circulation and other forms of heart disease in males and 945 excess cases in females. Diseases of the arteries, arterioles, and capillaries were elevated more than 25%, resulting in 392 excess cases in males and 217 excess cases in females. Of particular concern was the early onset of an elevated morbidity rate from heart disease (37% higher) in females from birth to 24 years of age and from 25 to 44 years of age. Similarly, there was an early onset of a higher rate (38% higher) in males 25–44 years of age for ischemic heart disease, resulting in 214 excess cases.

There is a sharp contrast between Windsor and Hamilton in terms of mortality from circulatory diseases. Whereas Windsor had a 56% higher mortality rate for hypertension in males, Hamilton was nonsignificantly different from the rest of the province. Similarly, the percentage spread between Windsor and Hamilton females was 39%. Similarly, for diseases of the arteries, arterioles, and capillaries, there was a 76 percentage point spread for males and a 116 percentage point spread for females between Windsor and Hamilton. The

only disease of the circulatory system that had elevated mortality in the Hamilton population was ischemic heart disease, which was 6% higher for males and 11% higher for females than the provincial rates compared to the 21% higher rate for Windsor males and 25% higher rate for Windsor females.

These contrasts were reflected in the morbidity rates for circulatory diseases between Windsor and Hamilton. There was a 69% spread between the morbidity rate for hypertensive disease in Windsor males (41% higher than the provincial rate) compared to Hamilton (28% lower than the provincial rate). Ischemic heart disease was 17 percentage points higher in Windsor males than in Hamilton males, and Windsor females were 33 percentage points higher than Hamilton females. There were similar contrasts for other forms of heart disease and for diseases of the arteries, arterioles, and capillaries, but both Hamilton and Windsor males and females had significantly elevated morbidity from atherosclerosis: Hamilton males were 91 percentage points above the provincial rate; Windsor females were 66 percentage points above; Hamilton females 63 percentage points; and Windsor males 23 percentage points. Atherosclerosis is the only circulatory disease for which there was an early onset of morbidity as hospitalization in Hamilton, though this is not associated, as in Windsor, with an elevated mortality rate. Hamilton males 25–44 years of age had an 81% higher morbidity than the rest of the province with 13 excess cases; Hamilton males 45–74 years of age had more than twice (2.13 times) the provincial rate with 500 excess cases; and Hamilton females had 95% higher than the provincial rate with 220 excess cases.

The patterns of circulatory disease in Windsor and Hamilton seem to be distinctly different and there would seem to be a need for further investigation as to whether these differences might be attributable to occupational or environmental factors in the Windsor community and thereby be preventable. Health Canada (13) noted that there was very little information on the effects of environmental contaminants on cardiovascular diseases. Apart from the many genetic, nutritional, metabolic, and lifestyle factors that have been implicated, Health Canada (13) included mention of the following references: hypertension is a known outcome of lead poisoning (72) and exposures to cadmium (73); ischemic heart disease may be caused by atherosclerosis, which may be associated with some contaminants (74); diseases of pulmonary circulation may be caused by radiation and exposure to contaminants through air pollution; diseases of the arteries, arterioles, and capillaries may be affected by certain chemicals; there are unsubstantiated

studies of the relationship of atherosclerosis with mineral content in drinking water, trace elements, blood groups, coffee, climate, noise, air pollution, the urban environment, a low socioeconomic status, and education (74). Burnett et al. (75) showed a relationship between the daily number of hospitalizations for congestive heart failure (*ICD-9:427*) in the elderly in 10 Canadian cities, including Windsor and Hamilton, and levels of carbon monoxide, primarily from common transportation sources. In other research on 16 Canadian cities including Hamilton and Windsor, Burnett et al. (30) demonstrated associations between hospital admissions for all ages and concentrations of ambient air pollutants, including ozone, carbon monoxide, and particulate matter.

Because diseases of the circulatory system account for a high proportion of the excess mortality and morbidity in the Windsor Area of Concern, and because the pattern of disease is so different from, and the rates more severe than, the equivalents in the Hamilton Harbour Area of Concern, there is a priority need to determine whether epidemiologic investigations of the possible contributory role of occupational and environmental exposures to chemicals and pollutants are feasible.

#### **ICD-9 Category VIII: Diseases of the Respiratory System (*ICD-9:460–508*)**

Health Canada (13) included the following diseases of the respiratory system in its survey of health data and statistics for the 17 Canadian Areas of Concern: acute respiratory infections; other diseases of the upper respiratory tract; pneumonia and influenza; chronic obstructive pulmonary disease and allied conditions, including chronic bronchitis, emphysema, and asthma; and pneumoconioses and other lung diseases due to external agents. Though many of these diseases are microbiologic in etiology, they are included because they may not only reflect the general infectivity of the local environment, but also indicate the effects of pollution on the general functioning of the immune system. Health Canada (13) noted that *a*) other airborne pollutants such as sulfur dioxide and nitrogen dioxide, and trace metals such as vanadium and cadmium can result in acute bronchitis; *b*) high levels of ozone and other atmospheric contaminants cause histopathologic changes in the nasal mucosa; *c*) sinusitis and laryngitis may be promoted by certain toxic agents; and *d*) atmospheric sulfur dioxide and organic solvents may affect the sense of smell (76–78). Atmospheric sulfur dioxide and particulate matter are directly implicated in chronic obstructive pulmonary disease (79). The pollutants associated with the various pneumoconioses and other lung diseases due to external agents have been well established

and include coal dust, silica and silicates, inorganic dust, chemical fumes and vapors, solids, and liquids. Asbestos has become a ubiquitous air pollutant and causes asbestosis and mesothelioma.

In terms of the rates of diseases of the respiratory system, mortality from pneumonia and influenza was lower than in the rest of the province, but chronic obstructive pulmonary disease and allied conditions among Windsor males 45–74 years of age was 30% higher than the rest of the province, resulting in 38 excess deaths. Similarly, the rate for Windsor females of the same age category was 32% higher, resulting in 25 excess deaths. Of particular concern was the mortality from chronic bronchitis in males that was more than 2-fold higher (19 excess deaths) than the rest of the province, with 8 of these deaths occurring among those over 45 years of age. Two females under 25 years of age died of chronic bronchitis, yielding a rate 14.32 times the provincial rate.

Elevated rates of morbidity for other disorders of the respiratory system included acute respiratory infections (682 excess cases in males and 456 in females); other diseases of the respiratory tract (210 excess cases in males and 270 excess cases in females); pneumonia and influenza (230 excess cases in males and 233 excess cases in females); chronic obstructive pulmonary disease (549 excess cases in males and 694 excess cases in females), particularly chronic bronchitis (30% higher in males, 45 excess cases, and 77% higher in females, 100 excess cases); and asthma in females (9% higher, 198 excess cases). Much of this increased morbidity as hospitalization for acute respiratory infections in males and females, for other diseases of the upper respiratory tract in males and females, and for pneumonia and influenza in males, was in those under 25 years of age. Of particular concern was the number of cases of hospitalization for asthma between birth and 24 years of age between 1986 and 1992, which was 1,637 for males (490 per 100,000 population) and 1,239 for females (380 per 100,000 population).

There was a marked contrast between the morbidity rates for Hamilton versus those for Windsor for the respiratory systems in both males and females. Rates in Hamilton for acute respiratory infections and other diseases of the upper respiratory tract, pneumonia, and influenza, and for chronic obstructive pulmonary diseases including chronic bronchitis, emphysema, and asthma, were markedly below the provincial rates in contrast to those in Windsor, which were significantly elevated. For example, the morbidity rates for acute respiratory infections were separated by more than 70 percentage points, and by about 60 percentage points for chronic obstructive pulmonary diseases. The

feasibility of investigating the much higher rates of respiratory disease in the population in the Windsor Area of Concern should be evaluated, and existing clean air regulations should be enforced.

#### **ICD-9 Category IX: Diseases of the Digestive System (*ICD-9:530–579*)**

Health Canada (13), in selecting the following four categories, noted that the digestive system may be exposed to environmental pollutants through the consumption of contaminated drinking water and food: diseases of the esophagus, stomach, and duodenum; non-infective enteritis and colitis; other diseases of intestines and peritoneum; and other diseases of the digestive system. Significant increases in mortality for diseases of the digestive system occurred in males 45–74 years of age, accounting for 11 excess deaths. A significant increase in diseases of the esophagus, stomach, and duodenum occurred in females over 75 years of age, accounting for 12 excess deaths. Mortality from these diseases tended to be only slightly higher in Windsor than in Hamilton. For example, for those 45–74 years of age, there were only 2 or 3 percentage points between the mortality rates for diseases of the esophagus, stomach, and duodenum in Windsor and Hamilton males (67% vs 65% higher) and females (57% vs 54% higher). There were, however, for those 45–74 years of age, large parallel differences between males and females for noninfective enteritis and colitis in Windsor (99 percentage points) and Hamilton (86 percentage points), with males in both locations having the higher rates. But this situation was reversed for mortality from other diseases of the intestines and peritoneum, with females tending to have the higher rates.

Significantly elevated rates of morbidity as hospitalization separations over the provincial rates were evident for all four categories and resulted in 3,665 excess cases in males and 5,059 excess cases in females as follows: diseases of the esophagus, stomach, and duodenum (39% higher for males, 685 excess cases, and 58% higher for females, 934 excess cases); noninfective enteritis and colitis (67% higher for males, 930 excess cases, and 46% for females, 829 excess cases); and other diseases of the intestines, peritoneum (23% higher for males, 456 excess cases, and 33% for females, 872 excess cases), and digestive system (16% for males, 516 excess cases, and 20% for females, 1,012 excess cases). Of particular concern were the increased rates compared with the rest of the province for these diseases among young males and females between birth and 24 years of age, with rates about 70% higher than in the rest of the province for diseases of the esophagus, stomach, and duodenum,

about 80% higher for noninfective enteritis and colitis, 20% higher for other diseases of intestines and peritoneum in young males, and 14% higher in young females. Higher rates occurred in all age categories for both sexes compared with the rest of the province.

The rates of morbidity as hospitalization separations in Hamilton for these four categories of diseases of the digestive system were all significantly lower than the provincial rates and none were significantly elevated in any of the age categories. For diseases of the esophagus, stomach, and duodenum, there was a spread of 60 percentage points for males and 87 percentage points for females between Windsor and Hamilton. For noninfective enteritis and colitis, there was a spread of 90 percentage points for males and 74 percentage points for females. For diseases of the intestines and peritoneum, there was a difference of 32 percentage points for males and 50 percentage points for females. For other diseases of the digestive system, there was a 24 percentage point spread for males and a 27 percentage point difference for females.

These substantial differences between rates of morbidity for diseases of the digestive system in the communities in Windsor and Hamilton and the high rates for all age categories and for both sexes indicate the need for epidemiologic studies to investigate the causes and whether these diseases are preventable in the Windsor Area of Concern.

### **ICD-9 Category X: Diseases of the Genitourinary System (ICD-9:580–628)**

Health Canada (13) chose the following diseases of the genitourinary system as being potentially related to exposures to pollutants: nephritis, nephrotic syndrome, and nephrosis; other diseases of the urinary system; diseases of the male genital organs, including male infertility; disorders of the breast; and other disorders of the female genital tract, including endometriosis and female infertility.

Several of the rates of morbidity from diseases of the genitourinary system in the population of the Windsor Area of Concern were elevated, and these increased rates occurred in several age classes. For females 25–44 years of age, there was a 33% increased morbidity from nephritis, nephrotic syndrome, and nephrosis, resulting in 19 excess cases. However, for other diseases of the urinary system and for all ages, there was a 60% increase in males, resulting in 1,798 excess cases, and in females the rate was 64% higher, yielding 1,583 excess cases. Of particular concern was the early onset of elevated morbidity rates in males under 25 years of age (23% higher than the rest of the province, with 70 excess cases).

For diseases of the male genital organs, there was a 40% higher rate than in the rest

of the province, leading to 1,582 excess cases, with 58 excess cases (13% higher) occurring in those males under 25 years of age. Forty-one males were hospitalized for infertility at a rate 55% above the provincial rate, and the seven males under 25 years of age who were hospitalized for male infertility represented a morbidity rate nearly 7 times (6.90 times) the provincial rate. Similarly, there was an excess of 50 males with disorders of the breast, representing a rate 44% above the provincial rate. Among those 25–44 years of age, this rose to 60% higher than the provincial rate, to 96% higher than the provincial rate for those 45–74 years of age, and finally, to 2.5 times the provincial rate for those over 75 years of age. For females there was a 30% higher rate of disorders of the breast than the rate in the rest of the province, resulting in 302 excess cases, and although the 14% rate (29 excess cases) in those under 25 years of age was not statistically significantly different from the rate for the rest of the province, the rate rose to 34% higher for females 25–44 years of age (130 excess cases) and continued at 37% higher than the provincial rate for those 45–74 years of age (141 excess cases).

The 22% higher rate of other disorders of the female genital tract resulted in 733 excess cases for those 25–44 years of age, and even the 5% higher rate for those 44–74 years of age yielded 119 excess cases. Part of this excess morbidity as hospitalization is attributable to the 48 excess cases of endometriosis and part to the 43 excess cases of female infertility among the group 25–44 years of age.

These markedly elevated rates of morbidity for diseases of the genitourinary systems are in contrast to the corresponding data and statistics for the Hamilton Harbour Area of Concern in which nearly all the health end points were 10 or 20 percentage points below the provincial rates. For example, there was a spread of 42 percentage points for Windsor males 45–74 years of age for nephritis, nephrotic syndrome, and nephrosis compared to equivalent-age Hamilton males. For other diseases of the urinary system, there was a spread of 74 percentage points for males and 86 percentage points for females. There was a difference of 47 percentage points for the rates of diseases of the male genital organs and 100 percentage points for male infertility. The contrasts between the rates of disorders of the female genital tract in Windsor females compared with the rates in Hamilton females were less marked than in the males but were still separated by 31 percentage points for the group 25–44 years of age, specifically by 21 percentage points for endometriosis, and by 27 percentage points for female infertility. Interestingly, these elevated rates of diseases of the male and female genitourinary systems in the population in the Windsor Area of

Concern were not associated with elevated rates of complications of pregnancy, childbirth, and the puerperium. All these measures were significantly lower in the Windsor Area of Concern than in the rest of the province.

Although there are many factors known to affect the health of the genitourinary system, Health Canada (13) referenced effects of toxic substances such as lead (80), cadmium (81), and 1,1-dichloroethylene (82) on the kidney. The effects of pesticides on diseases of the male genital organs, particularly male infertility, have been linked to pesticide manufacturing plants (83), occupational exposure to lead (84), and organochlorine compounds (85). References to disorders of the female genital tract included *in utero* exposure to diethylstilbestrol, and exposure to hexachlorobenzene and to pesticides (58). Endometriosis has been associated with exposure of monkeys to organochlorine compounds (86). Hormonal disorders through exposure to organochlorine compounds and heavy metals are suspected to cause female infertility through interfering with ovulation.

The marked increase in the rates of morbidity as hospitalization for diseases of the male and female genitourinary system among the population in the Windsor Area of Concern indicate priority needs for evaluating the feasibility of investigation of the specific causes, implementation of existing regulatory controls, and development of new controls for sources of compounds causing these elevated rates for diseases of the genitourinary system.

### **ICD-9 Category XII: Diseases of the Skin and Subcutaneous Tissue (ICD-9:680–709)**

There were significantly elevated morbidity rates from inflammatory conditions and other diseases of the skin and subcutaneous tissues in both males (235 excess cases) and females (401 excess cases), and elevated rates occurred in all age classes. The rates in males and females between birth and 24 years of age were, respectively, about 60% and 30% higher than those for the rest of the province, rose to about twice the provincial rate in the group 25–44 years, and continued high compared to the rest of the province through to those over 75 years of age. This morbidity was not related to infections of the skin and subcutaneous tissues.

Health Canada (13) referenced a wide variety of physical, chemical, and biologic agents and conditions associated with atopic and contact dermatitis (87). Of particular interest are the reports in the literature of associations of chloracne, hyperpigmentation, hyperkeratosis, and conjunctivitis with exposures to high levels of PCBs, dioxins, and furans. The feasibility of investigating the specific causes of the elevated rates of diseases of the skin and subcutaneous tissues needs to



be evaluated and controls placed on sources and pathways of exposure.

### **ICD-9 Category XIII: Diseases of the Musculoskeletal System and Connective Tissues (ICD-9:710–739)**

The rates of morbidity as hospitalization cases for diseases of the musculoskeletal system and connective tissues in the population of the Windsor Area of Concern were significantly elevated for the following: arthropathies and related diseases (12% for males, 11% for females); dorsopathies (26% for males, 21% for females); rheumatism, excluding the back (2-fold for males, 88% increase for females); and osteopathies, chondropathies, and acquired musculoskeletal deformities (27% for males, 30% for females). These elevated rates tended to occur in all age classes up to 75 years of age. Five females 45–74 years of age died of diseases classified as osteopathies, chondropathies, and acquired musculoskeletal deformities, resulting in rates more than 3-fold (3.61 times) the provincial rate.

This category of diseases was included because exposures to cadmium are associated with skeletal diseases, possibly linked to kidney damage (82). Among the wide variety of agents associated with diseases of the musculoskeletal system and connective tissues, Health Canada (13) mentioned the relationship between arthropathies and metabolic disorders and changes in the endocrine system, such as diabetes mellitus and hypothyroidism. The feasibility of investigating whether environmental pollution is contributing to the elevated rates of morbidity for diseases of the musculoskeletal system and connective tissues in the Windsor population needs to be evaluated.

### **ICD-9 Category XIV: Congenital Anomalies and Infant Mortality (ICD-9:740–758)**

The Windsor Area of Concern had 13,196 females born in the 7-year period between 1986 and 1992. Of these girls, 779 had some kind of anomaly diagnosed within the first year. This was 25% higher (156 excess cases) than the rate in the rest of Ontario and included 13 females born without brains (anencephaly) at a rate 3 times that in the rest of Ontario; 149 girls born with heart defects (56% higher, 53 excess cases); 95 with clubfoot (69% higher), and 10 with reductions in the length of their limbs (2.24 times the provincial rate). Ninety-three girls died within the first year at a rate that was 24% higher than the provincial rate.

Similarly, there were 13,950 boys born between 1986 and 1992, and 885 had anomalies (13% higher than the provincial rate, 101 excess cases). Twenty-four had water on the brain (congenital hydrocephaly) at a rate that was 88% higher than that of the rest of

the province; 172 had congenital heart defects (65% higher, 68 excess cases), and 89 had clubfoot (36% higher); 97 boys died within the first year at a rate comparable to that of the rest of Ontario.

From a statistical standpoint it is impossible to determine whether the infants who died had significantly elevated rates of anomalies, but the table in the Health Canada report flags several conditions, including anomalies of the nervous system and heart, renal and urinary systems, circulatory and respiratory systems, and Down syndrome. Only further analysis of the existing databases in Statistics Canada for a greater number of years would provide a sufficient number of cases to determine whether the apparently elevated rates of these anomalies had arisen by chance.

Recent data on the rates of congenital anomalies for 1998 (19) confirm continuing elevated rates in females (27% higher) and in males (13% higher) born in Windsor and Essex County; the rate of congenital heart defects remains at 56% higher than the provincial rate. By contrast, the overall rates of congenital anomalies in the Hamilton population were 20–30% lower than the Ontario provincial rates, thus the rates for males in Hamilton were 35% lower than those in the Windsor area and 53% lower for females.

In reviewing the possible teratogenic agents to which the Windsor population is exposed, it is necessary to distinguish between increased abnormality rates caused by exposures to alcohol (88) and those associated with exposures to environmental teratogens. Health Canada (13) noted the reproductive and teratogenic effects of organochlorine compounds such as PCBs and dioxins and heavy metals such as lead, cadmium, and mercury on laboratory animals and wildlife but remarked on the uncertainty about whether existing levels in the Great Lakes basin could have affected people. The contrasts between the rates in Windsor and Hamilton could indicate the presence of teratogenic contaminants in the Windsor environment that might be increasing the rates of congenital anomalies.

The literature on the teratogenic actions of chemicals has recently been reviewed (89). Occupational exposures of males to solvents have been related to anencephaly (90), and exposures to benzene have been related to a greater probability of hydrocephaly in their offspring (91). Defects of the fetal heart from occupational exposure during pregnancy have been associated with benzene (92) and organic solvents (93). In a survey of the contamination of drinking water for 75 New Jersey towns, those with higher levels of benzene were associated with a higher rate of major heart defects (94). Similarly, exposures to groundwater contaminated with trichlorethylene, and trace

amounts of dichloroethylene and chromium in a neighborhood near Tucson, Arizona, have been associated with congenital heart defects (95). Another location where studies have shown an association of heart deformities with exposures to solvents is Santa Clara County, California (96). These findings are consistent with the findings of congenital heart defects in animal studies (97,98). The findings of an elevated rate of clubfoot in the Windsor population is of concern. A high rate of clubfoot has been a characteristic among a population on a small island off Australia with rich manganese deposits (99). There is a priority need to investigate the cause of the elevated rates of clubfoot in the Windsor population, particularly because of the recent introduction of methylcyclopentadienyl manganese by Ethyl Corporation as a gasoline additive, and because there is evidence of synergistic effects of mixtures of metals, including manganese with chromium and lead, on prenatal development at very low doses (100).

The apparent stability of the elevated rates of congenital anomalies over more than a decade, particularly for heart defects, indicates a priority need for epidemiologic investigations to determine the causal agent(s). If the increased rate is from the consumption of alcohol during pregnancy, public health interventions can be devised and implemented at the local level to prevent these abnormalities. If the increase is from exposures to teratogens that are being released to the environment, an effective public health program would first require identification of the source(s) and subsequent control, surveillance, and monitoring.

## **Discussion**

The mandate for this project derived from the United States–Canada Great Lakes Water Quality Agreement, based on Article IV of the 1909 Boundary Waters Treaty, which states that the boundary waters shall not be polluted on either side to the injury of health or property on the other side. Since the mid-1980s the International Joint Commission has assisted the parties to the agreement by developing a list of 42 Areas of Concern that did not meet the water quality objectives developed in common by the parties and for which Remedial Action Plans have been developed. The former Great Lakes Health Effects Program was originally developed in the late 1980s by Health Canada as part of the implementation of the agreement by the government of Canada. The project on health data and statistics was part of that program to generate hypotheses on whether pollution was affecting the health of the communities in the 17 Canadian Areas of Concern. Previous work undertaken on the United States side of the Great Lakes basin using similar tech-

niques (14) suggested an association between the rates of mortality for stomach and esophageal cancers and living in the border counties close to the Great Lakes. Other research on the significant regional patterning of the incidence of cancer in Ontario (23) has reconciled this geographic variation with several risk factors, suggesting that these diseases are not associated with variations in air and water quality at the regional scale (24). This still, however, leaves the possibility of associations between certain health end points and variations in air and water quality at the local scale. It would seem that the consistently elevated rates of mortality, morbidity as hospitalization, and congenital anomalies in the community in the Windsor Area of Concern for health end points that may be linked to pollution indicate that this population in this location is an example of health effects occurring at a local scale.

### Methodologic Limitations

From a methodologic standpoint, these ecologic analyses of the health of circumscribed populations are in contrast to the cohort studies that have heretofore been carried out to study the effects of pollution on human health. The cohort studies have focused on critical subpopulations known to be highly exposed or susceptible to pollutants from the Great Lakes. For example, cohorts were established in 1980, in western Michigan (101), and in 1990, at Oswego, New York (102), particularly to investigate the effects of maternal consumption of contaminated Great Lakes fish, prior to or during pregnancy, particularly on child behavior and neurologic development.

The statistical analyses undertaken so far have compared the rates of mortality, morbidity as hospitalization separations, and congenital anomalies in each of the 17 Areas of Concern with the rates in the rest of the Province of Ontario, and these have provided opportunities to describe the profile of diseases that might be related to pollution within the communities. There are, however, several limitations to this approach. First, there are limitations in terms of the selection of the end points based on published associations with exposures to pollutants. For example, although the broad list of selected end points is fairly comprehensive, there are other end points such as malignant neoplasms of the brain (103–105) that are suspected to be affected by pollutants, particularly pesticides (106,107), and that might have been valuable in assessment of the community health profiles had they been included.

Similarly, although data on morbidity, mortality, and congenital anomalies are useful in describing gross differences between communities that might be related to

pollution, there are other more subtle end points derived from the endocrine disruptor hypothesis, such as neurologic and immunologic functioning, that need to be investigated and compared on a community basis. For example, recent data for the year 1998 (19) indicate that the morbidity rates as hospitalization separations for mental disorders (*ICD-9:290–319*) are 44% higher for females and 60% higher for males compared with the rates for the rest of the province. Similarly, the rate of hospitalization for suicide (*ICD-9:e950–e959*) is 20% higher in females and 54% higher in males. A recent survey by the Ontario Ministry of Community and Social Services found that Windsor and Essex County are the areas of southwestern Ontario with the highest rate of usage of these child protection and residential services. There is a list of about 700 children waiting for mental health services, and over half the children who receive services in Essex County have disabilities in addition to their mental health disorders. Although Windsor and Essex County are underserved in terms of medical practitioners in general and psychologists in particular, the possible contributory involvement of pollution to these excess rates of hospitalization for mental disorders and suicides needs to be investigated so that preventive approaches can be formulated. Similarly, there is reliable information from pediatricians of an increased rate of autism, and from teachers of an increased rate of attention deficit and hyperactivity disorder in classes in certain parts of Windsor and Essex County. The number of school-aged children with the highest level of special needs has significantly outpaced the provision of provincial funding made available for this purpose. These concerns have recently resulted in the formation of a Mental Health Task Force by the Windsor–Essex Health Unit. One of the orders of business will be to investigate whether these concerns portend a local manifestation of the epidemic of learning, behavioral, and developmental disorders from preventable exposures to neurotoxicants (108).

A second limitation is the use of the rates in the rest of Ontario as the standard by which to judge statistical significance. The first concern is that there are several diseases, such as prostate cancer and breast cancer, that are increasing on a provincial, national, and international basis. Comparison of health data and statistics for the community in an Area of Concern with the provincial rate can only indicate whether the rate in the community is the same as the changing provincial rate. The second concern is that the provincial rate for a particular health end point may be elevated relative to those in other countries or to a previous period of time. Thus, there is a need for communities not only to analyze the long-term trends in particular diseases

within their community, but also to compare their rates of diseases with those of other communities, other jurisdictions, and other countries. For example, there is a need to establish whether the elevated rates of thyroid disease in Windsor females, particularly the early onset, are a recent phenomenon, and to investigate whether comparable epidemics are occurring in other parts of Ontario, elsewhere in Canada, the United States, or other parts of the world.

A third limitation is the use of narrative associations for generating hypotheses about the relationship between statistically significant differences in the rates of selected health end points and the plausibility of an association with pollution. The Health Canada (13) study listed a wide array of potential factors and agents associated with the selected health end points, and this account for Windsor, in the interests of brevity, has been oriented toward those related to pollution. However, any inference of a causal relationship between the increased rates of disease within a community and exposures to pollutants will require more than this narrative association if effective regulatory action is to be undertaken based on scientifically defensible evidence of injury, though there is a growing sentiment that preventive public health action should not require this level of proof when a causal factor is suspected.

A fourth limitation in this approach is the failure to detect known epidemics. For example, in Windsor and Sarnia there have been serious outbreaks of asbestosis in the past 20 years related to the industrial use of asbestos in foundries in these two communities, but these were undetected using these techniques to collect data on pneumoconioses and other lung diseases due to external agents (*ICD-9:500–508*). The epidemics of asbestosis are associated with epidemics of mesothelioma, and it is possible that the cases of mesothelioma were included in the cases on malignant neoplasms of respiratory and intrathoracic organs (*ICD-9:160–165*) that were seriously elevated in the two communities. This may exemplify the loss of some of the sensitivity of the analysis through the aggregation of data and the masking of specific epidemics in larger categories of diseases. Similarly, there are concerns that the rates of scleroderma, which has been associated with exposures to silica and various solvents (109), may be elevated in this community but that this specific condition is subsumed within the larger categories of inflammatory conditions and diseases of skin and subcutaneous tissues (*ICD-9:690–698;700–709*).

There is much more information that could be gleaned from these databases; the feasibility of using further statistical techniques such as principal component and

cluster analyses on the databases for the 17 Areas of Concern is being carefully evaluated.

### Institutional Capabilities and Constraints

Modern epidemiology is seeking new methods of analysis and synthesis, and an ecopidemiologic approach has been proposed over the past decade (12,110–112), including tying individual and population epidemiology to molecular epidemiology, reconnecting these to public health, and placing these in social, economic, and political institutional contexts. Windsor, Ontario, is a useful location in which to study the institutional constraints to implementing the Great Lakes Water Quality Agreement and the Canada–United States Air Quality Agreement. This project of the former Great Lakes Health Effects Program and the process for preparation of the Detroit River Remedial Action Plan were undertaken not only within a scientific context involving toxicologists, epidemiologists, chemists, and ecologists, but also within social, economic, and political contexts at the local, provincial, and federal levels.

Windsor is known as “The Automobile Capital of Canada” and as such has a long history of union activism dating back to the 1930s. In the late 1970s, union health and safety activists in Windsor began the modern occupational health movement when it was revealed that workers at the Bendix Automotive Plant were dying of asbestos-related cancers. When a brief was being presented to the former Ontario Worker’s Compensation Board on behalf of three widows whose husbands had died of laryngeal cancer, officials of the board gave the union representatives copies of government orders that had been issued in 1966 and again in 1970 to control asbestos exposures (15). These orders were never enforced even at the time that the union representatives were meeting with the compensation officials. Several occupations are now recognized by the workers’ compensation authorities to be associated with injury (113), including metalworker exposures to metalworking fluids and other toxicants in the workplace; auto industry workers with elevated mortality from laryngeal, stomach, and colorectal cancer; steel industry workers with increased rates of lung cancer; electrical workers and increased rates of brain cancer and leukemia; dry cleaners with elevated rates of digestive tract cancers; firefighters with brain and blood-related cancers at many times the expected levels and miners with rates of respiratory cancer many times higher than expected; and women in the plastics and rubber industry with greater risks of uterine cancer and possibly breast cancer.

In response to the specific knowledge about the cancer mortality in their Windsor

membership and the general information about cancer and exposures to carcinogens, the Canadian Auto Workers (CAW) supported a cancer prevention campaign to activate workers to learn about cancer, to rid the workplace of carcinogens, and thereby prevent exposures to agents that cause cancer. This local initiative eventually became a national CAW campaign. At the local level there is a Windsor Cancer Prevention Coalition with groups working on research, communications, and political action.

Windsor also became the scene for grassroots activists working on environmental issues. Through the CAW, the Clean Water Alliance was formed. However, there is often tension between the blue-collar workers in the trade unions and the environmentalists because of concerns among workers about jobs. Windsor is unusual in that it has generated leaders, particularly through the union movement, in both the areas of occupational and environmental health. In addition, in the early 1980s, community groups and the unions, against some strong local opposition (15), organized the Windsor Occupational Health Information Service as the first community-based health and safety information service in Canada. In the late 1980s these same groups in Windsor successfully lobbied for the establishment of a clinic on behalf of the Occupational Health Clinic for Ontario Workers to diagnose diseases and disorders related to employment and to help injured workers with their claims for compensation from the Ontario Worker’s Compensation Board. Though Ontario law, as in the United States, requires employers to disclose health studies relevant to their employees, local auto manufacturers did not bring the existence of more than 120 health and hygiene studies undertaken on U.S. auto workers to the attention of Ontario workers, even though they were undertaking the same occupational operations. The Windsor Occupational Health Information Service and the Occupational Health Clinic for Ontario Workers have become important conduits for information on the dangers of particular jobs posed by specific substances.

In the same way that Windsor is the “Automotive Capital of Canada,” Sarnia is the “Chemical Capital of Canada,” where more than 40% of the Canadian bulk chemicals are manufactured mainly through branch plant subsidiaries of United States corporations. In the late 1990s, based on the discovery of a large cluster of occupational disease in Sarnia, Ontario, senior management from the Windsor Occupational Health Information Service and from the Windsor Occupational Health Clinic for Ontario Workers set up a new clinic and information service in Sarnia, against some continuing local and provincial

opposition. The immediate concern was that Sarnia has the highest rates of mesothelioma in Canada. Since opening the clinic, over 2,000 people have registered with a variety of cancers and respiratory and neurologic diseases, and 500 new registrations are expected in 2001. The rates of these diseases were known for a long time to be elevated but seemed to be tolerated within the community. “Sarnia men die young” were the words of the daughter of a Sarnia worker who died of lung disease related to asbestos exposure, and they reflect an implicit sense of fatalism within the community (114). In turn, the Sarnia clinic, in addition to the diagnostic work and claims for injured Sarnia workers, has become a resource center for helping a nearby rural community investigate its suspicions about the apparently high rates of various cancers.

Recently, the community of Sarnia has undergone a profound psychosocial change. In the past year there has been a series of accidental releases of pollution to the air, to industrial land, and to the St. Clair River from different industrial facilities. One recent release to the atmosphere engulfed the police station, resulting in several officers being taken to the hospital. The media are reporting that spokespersons for the industries are acknowledging that the trust of the public within this community has been lost. There is a pressing need for social and political scientists and anthropologists to document the community, institutional, and political processes that are occurring and perhaps to help with the predictable psychosocial changes.

Through a unique partnership between the Windsor Occupational Health Clinic for Ontario Workers and the Windsor Cancer Treatment Centre, oncologists are collecting occupational histories of cancer patients. Expansion of the partnership to include the university has resulted in a grant from the Ontario Worker’s Compensation Board for a case–control study of breast cancer and for a second study involving men with laryngeal cancer. The intent is that, eventually, occupational histories will be collected for every cancer patient in the province of Ontario (113).

If some or all of these increased rates of mortality, morbidity, and congenital abnormalities in the Windsor Area of Concern are partly or completely attributable to exposures to pollutants in the environment, this would place these issues in a series of complex political circumstances. Environment tends to be perceived as an issue of the political left, along with occupational health. Gordon Durnil, the former U.S. co-chairman of the International Joint Commission urged his Republican colleagues to embrace conservation, environment, and health as right-wing issues and has expressed his disappointment



that they have, in his opinion, so far declined (115,116). The specifics of the situation in Windsor need to be seen in the context of a much broader politics, expressed by some Canadian liberal politicians, of globalization and corporatism and reflected in a growing body of political writings (117–119) exploring these issues, and in a world movement opposing these economic trends. In Ontario an inquiry into the deaths and hospitalizations from an outbreak of *Escherichia coli* in the community of Walkerton, Ontario, has requested testimony from the Conservative Premier Mike Harris to ascertain whether the cuts in staffing and budgets of the Ministry of Environment during the first mandate contributed to the tragedy. At the federal level, there has been a general shift of power away from the social and environmental toward the industrial and economic portfolios, and this has fueled the writings of several social, economic, and political commentators (117–119). In Windsor the fear produced by the recurrent experiences of long-term cyclical unemployment in the automotive industry has produced an implicit multilateral understanding between industry, labor and the unions, and the municipality. There is, however, also an implicit ambivalence about occupational health and environment in case these might somehow threaten jobs.

John Ralston Saul (118) has explored the consequences of the prevailing motif in Western governments of corporatism and the power of the multinational companies in influencing the affairs of states based only on interests. The affairs of Windsor, of Ontario, and of Canada are no less influenced by these political forces than are the affairs of other municipalities, jurisdictions, and nations. A second motif that has developed in the past 20 years has been the general fiscal restraints within national governments, the specific reductions in government staff and funding for research and monitoring in environmental toxicology and public health, and the devolution of these responsibilities from national to regional governments and from regional to local governments. For example, fiscal restraints within Health Canada led to the closure of the Great Lakes Health Effects Program on 31 March 2000, at the end of the Canadian fiscal year, bringing to an end further work on this community-based epidemiology, though there is a stated intention to reconstitute a federal program in the Ontario region.

The concerns raised by corporatism and the devolution of responsibilities were exemplified at the local level in the attempts to prepare the Remedial Action Plans for the Detroit River Area of Concern. The Remedial Action Plan process is part of the Great Lakes Water Quality Agreement,

which is an agreement between the United States and Canada as national governments. The process for the Detroit River was originally undertaken on a bilateral basis, with representatives from all levels of governments, from industries, and from nongovernment organizations. The bilateral process failed about 4 years ago because these groups could not come to a consensus about the specific concerns that required remedial actions. At that time there was no objective consideration of human health using epidemiologic data and statistics as a scientifically defensible basis for costly remedial actions on contaminated sediments and hazardous waste sites. Federal funds for remedial actions are made available to the local conservation authorities rather than to health and environmental protection authorities and are used for habitat improvements, such as tree planting, and for improvements to amenities, such as access to and pathways beside the river. The public health issues inferred from the health data and statistics in the Health Canada (13) document on the Windsor Area of Concern suggests that there is a priority requirement for the Canadian federal government to remain involved at this local level and to reallocate the funds specifically to the investigation and control of sources of pollution and to remedial action on contaminated sediments and hazardous waste sites. Because some of the pollutants that are likely contributing to these public health issues are from transboundary sources from the United States, and specifically from Detroit in the state of Michigan, the Canadian federal government must remain involved, as it has sole jurisdiction in Canada to undertake international consultations and negotiations. In addition, the financial resources needed to implement Remedial Action Plans relevant to protection of public health, particularly for the interconnecting channels, are on a scale that neither a Canadian municipality nor probably the province of Ontario acting alone could underwrite. The International Joint Commission (119) has recently commented on the relative lack of progress in Canada in addressing contaminated sediments.

At the local level, there seems to be a ubiquitous reluctance to acknowledge these public health issues. This is not only at the level of local governments, but also in relation to industries, the unions, and the academic and medical establishments. Local activist organizations have been effectively sidelined into projects on preservation of wetland and woodland habitats rather than focused on issues of injury to health and property from air and water pollution. The scale and significance of these public health issues are known by many individuals, but the technical skills to research and monitor aspects of the epidemics

tend to be fragmented. Recently, there is evidence of a nascent institutional vision and leadership that is a prerequisite to galvanizing the local community and authorities into coalescing these individuals and their skills into a coherent environmental and occupational research program on which sound regulatory and remedial actions can be based.

The Health Canada reports of health data and statistics for the 17 Canadian Areas of Concern in the Great Lakes basin have potentially provided radical challenges, not only to environmental managers responsible for implementing the Great Lakes Water Quality Agreement and the Canada–United States Air Quality Agreement, but also to those authorities responsible for enforcing provincial control orders and municipal bylaws. If Windsor, Ontario, is a representative model of the institutional constraints in other Areas of Concern, not only in Canada but also in the U.S. portion of the Great Lakes basin, is it likely that further interpretations of the Health Canada health data and statistics for the other Areas of Concern will be both necessary and sufficient to lead to significant decreases in levels of pollution that may be linked to human health? Will the public health concerns raised by the Health Canada data and statistics for Windsor be sufficient to galvanize renewed political actions to implement these bilateral agreements on local and transboundary pollution of the Great Lakes ecosystem? Or will the political processes of corporatism and devolution of responsibilities need to be reversed before significant progress can be made in terms of remedial actions to clean up the existing sources, the legacy of contaminants in the sediments and the leakages from hazardous waste sites?

#### REFERENCES AND NOTES

1. Revised Great Lakes Water Quality Agreement of 1978 between the United States and Canada as amended by Protocol signed November 18, 1987: Office Consolidation. International Joint Commission, United States and Canada. September 1989.
2. Treaty Between the United States and Great Britain Relating to Boundary Waters, and Questions Arising Between the United States and Canada. International Joint Commission, United States and Canada. Rules of Procedure and Text of Treaty. Ottawa, Canada—Washington, DC, 1909.
3. Canada–United States Air Quality Agreement. Environment Canada, Ottawa, Ontario, and U.S. Environmental Protection Agency, Washington, DC, 1991.
4. Johnson BL, Hicks HE, Jones DE, Cibulas W, DeRosa CT. Public health implications of persistent toxic substances in the Great Lakes and St Lawrence Basins. *J Great Lakes Res* 24:698–722 (1998).
5. Johnson BL, Hicks HE, De Rosa CT. Key environmental human health issues in the Great Lakes and St. Lawrence River basins. *Environ Res Sect A* 80:S2–S12 (1999).
6. Ewins PJ, Weseloh DV, Fox GA, Bishop CA, Boughen T. Using wildlife to monitor contaminants and their effects in the North American Great Lakes ecosystem. In: *Great Lakes of the World (GLOW): Food-web, Health and Integrity* (Munawar M, Hecky RE, eds). Leiden:Backhuys, 2001;341–362.
7. Colborn T, Clement C, eds. *Chemically-Induced Alterations in Sexual and Functional Development: the Wildlife/Human Connection. Advances in Modern Environmental Toxicology*. Princeton, NJ:Princeton Scientific, 1992.

8. Colborn T, Dumanoski D, Myers JP. Our Stolen Future. New York:Dutton, 1996.
9. Tremblay NW, Gilman AP. Human health, the Great Lakes, and environmental pollution: a 1994 perspective. *Environ Health Perspect* 103(suppl 9):3-5 (1995).
10. DeRosa C, Johnson BL. Strategic elements of ATSDR's Great Lakes Human Health Effects Research Program. *Toxicol Ind Health* 12:315-325 (1996).
11. Fox GA. Practical causal inference for ecotoxicologists. *J Toxicol Environ Health* 33:359-373 (1991).
12. Johnson BL, Hicks HE, Cibulas W, Farron O, Ashizawa AE, DeRosa CT, Cogliano VJ, Clark M. Public Health Implications of Exposure to Polychlorinated Biphenyls. Available: <http://www.atsdr.cdc.gov/DT/pcb007.html> [cited 7 May 2001].
13. Health Canada. Detroit River Area of Concern: Health Data and Statistics for the Population of Windsor and Region (1986-1992). Great Lakes Health Effects Program. Technical Report for the RAP Community, 1998. Available: <http://www.hc-sc.gc.ca/ehp/ehd/bch/bioregional/healthdata.htm> [cited 19 May 2000].
14. U.S. EPA. Evaluation of the Methods Used to Determine Potential Health Risks Associated with Organic Contaminants in the Great Lakes Basin. EPA-600/3-84-002. Duluth, MN:U.S. Environmental Protection Agency, 1984.
15. Keith M, Brophy J. Your health is not for sale. In: *The New Rank and File* (Lynd S, Lynd A, eds). Ithaca, NY: Cornell University Press, 2000:187-198.
16. Windsor Air Quality Committee. Windsor Air Quality Study: Executive Summary Report. Windsor, Canada: Ministry of Environment and Energy, 1994.
17. Rizkallah J, Mustac DS. An Investigation of Possible Relationships between Environmental Pollutants and Cancer Rates in Windsor, Ontario. Windsor, Canada: University of Windsor, 1995.
18. Windsor-Essex County Health Unit. A Picture of Health: The 1995 Health Profile of Windsor-Essex County Residents. Windsor, Ontario, Windsor-Essex County Health Unit, 1995.
19. Windsor-Essex County Health Unit. Health Profile: Windsor-Essex County. Windsor, Ontario, Windsor-Essex County Health Unit, 2000.
20. Kummier RH. A Critical Review of Air Quality Studies of Air Toxics in the Detroit-Windsor Region: a Decade Later. A Report to the International Joint Commission, contract 50176100 0561. 2001.
21. Canadian Institute for Environmental Law and Policy, Canadian Environmental Law Association, Canadian Environmental Defense Fund and Environmental Defense. Available: <http://www.scorecard.org/pollutionwatch/> and <http://www.scorecard.org/> [cited 14 May 2001].
22. Statistics Canada. 1991 Census. Statistical Profile Highlights. Available: <http://www.statcan.ca> [cited 6 June 2001].
23. Walter SD, Birnie SE, Marrett LD, Taylor SM, Reynolds D, Davies J, Drake JJ, Hayes M. The geographic variation of cancer incidence in Ontario. *Am J Public Health* 84:367-376 (1994).
24. Walter SD, Marrett LD, Taylor SM. An analysis of the geographic variation in cancer incidence and its determinants in Ontario. *Can J Public Health* 90:104-108 (1999).
25. International Classification of Diseases. Clinical Modifications, Vols 1 and 2. Ninth Revision, 4th ed. Los Angeles: Practice Management Information Corporation, 1992.
26. Health Canada. Great Lakes Water and Your Health. A Summary of Great Lakes Cancer Risk Assessment: A Case-Control Study of Cancers of the Bladder, Colon and Rectum. Ottawa, Canada: Great Lakes Health Effects Program, 1995.
27. Health Canada. State of Knowledge Report on Environmental Contaminants and Human Health in the Great Lakes Basin. Ottawa, Canada: Great Lakes Health Effects Program, 1997.
28. Gilmour H, Gentleman JF. Mortality in metropolitan areas. *Health Reports* 11:9-19 (1999). Available: <http://www.statcan.ca/english/ads/82-003-XIB/06-99.htm> [cited 6 June 2001].
29. Burnett R, Cakmak S, Brook JR. The effect of the urban ambient air pollution mix on daily mortality rates in 11 Canadian cities. *Can J Public Health* 89:152-156 (1998).
30. Burnett RT, Brook JR, Yung WT, Dales RE, Krewski D. Association between ozone and hospitalization for respiratory disease in 16 Canadian cities. *Environ Res* 72:24-31 (1997).
31. Björklund A, Wennersberg J. Epidemiology of cancer of the oral cavity and oropharynx. In: *Carcinoma of the Oral Cavity and Oropharynx* (Pape H-D, Ganzer U, Schmitt G, eds). Berlin: Springer-Verlag, 1994:1-8.
32. Thomas DB. Alcohol as a cause of cancer. *Environ Health Perspect* 103(suppl 8):153-160 (1995).
33. Ahlgren J, Macdonald J. *Gastrointestinal Oncology*. Philadelphia: Lippincott, 1992.
34. Black RJ, Sharp L, Finlayson AR. Cancer incidence in a population potentially exposed to radium-226 at Dalgety Bay, Scotland. *Br J Cancer* 69:140-143 (1994).
35. Paulu C, Aschengrau A, Ozonoff D. Tetrachloroethylene-contaminated drinking water in Massachusetts and the risk of colon-rectum, lung, and other cancers. *Environ Health Perspect* 107:265-271 (1999).
36. Gerhardsson de Verdier M, Plato N, Steineck G, Peters JM. Occupational exposures and cancer of the colon and rectum. *Am J Ind Med* 22:291-303 (1992).
37. Weiderpass E, Partanen T, Kaaks R, Vainio H, Porta M, Kauppinen T, Ojajarvi A, Boffetta P, Malats N. Occurrence, trends and environmental etiology of pancreatic cancer. *Scand J Work Environ Health* 24:165-174 (1998).
38. Motta G. Lung Cancer: Frontiers in Science and Treatment. Genoa: Grafica LP, 1994.
39. Calabresi P, Schein PS. *Medical Oncology*, 2nd Edition. New York: McGraw-Hill, 1993.
40. Lisiewicz J. Immunotoxic and hematotoxic effects of occupational exposures. *Folia Med Craiova* 34(1-4):29-47 (1993).
41. Institute of Medicine. *Veterans and Agent Orange: Update 2000*. Washington, DC: National Academy Press, 2001.
42. Nordström M, Hadell L, Lindström G, Wingfors H, Hardell K, Linde A. Concentrations of organochlorines related to titers to Epstein-Barr virus early antigen IgG as risk factors for hairy cell leukemia. *Environ Health Perspect* 108:441-445 (2000).
43. Colborn T. Chemically-induced alterations in the developing immune system: the wildlife/human connection. *Environ Health Perspect* 104(suppl 4):807-842 (1995).
44. Brouwer A, Longnecker MP, Birnbaum LS, Cogliano J, Kostyniak P, Moore J, Schantz S, Winneke G. Characterization of potential endocrine-related health effects at low-dose levels of exposure to PCBs. *Environ Health Perspect* 107(suppl 4):639-649 (1999).
45. Moccia RD, Fox GA, Britton A. A quantitative assessment of thyroid histopathology of herring gulls (*Larus argentatus*) from the Great Lakes and a hypothesis on the causal role of environmental contaminants. *J Wildl Dis* 22:60-70 (1986).
46. Leatherland JF. Changes in thyroid hormone economy following consumption of environmentally contaminated Great Lakes fish. In: *Environmental Endocrine-Disrupting Chemicals: Neural, Endocrine, and Behavioral Effects* (Colborn T, vom Saal F, Short P, eds). Princeton, NJ: Princeton Scientific, 1998:49-68.
47. Brucker-Davis F. Effects of environmental synthetic chemicals on thyroid function. *Thyroid* 8:827-856 (1998).
48. Colborn T, vom Saal F, Short P, eds. *Environmental Endocrine-Disrupting Chemicals: Neural, Endocrine, and Behavioral Effects*. Princeton, NJ: Princeton Scientific, 1998.
49. Becker KL, ed. *Principles and Practice of Endocrinology and Metabolism*, 2nd ed. Philadelphia: Lippincott, 1995.
50. Wilson ID, Foster DW, eds. *Williams Textbook of Endocrinology*, 8th ed. Philadelphia: Saunders, 1992.
51. Gorski JL, Rozman K. Dose-response and time course of hypothyroidism and hypoinsulinemia and characterization of insulin hypersensitivity in 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-treated rats. *Toxicology* 44:297-307 (1987).
52. Cranmer M, Louie S, Kennedy RH, Kern PA, Fonseca VA. Exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is associated with hyperinsulinemia and insulin resistance. *Toxicol Sci* 56:431-436 (2000).
53. Longnecker MP, Michalek JE. Serum dioxin level in relation to diabetes mellitus among Air Force veterans with background levels of exposure. *Epidemiology* 11:44-48 (2000).
54. Longnecker MP, Klebanoff MA, Brock JW, Zhou H. Polychlorinated biphenyl serum levels in pregnant subjects with diabetes. *Diabetes Care* 24:1099-1101 (2001).
55. Lai MS, Hsueh YM, Chen CJ, Shyu MP, Chen SY, Kuo TL, Wu MM, Tai TY. Ingested inorganic arsenic and prevalence of diabetes mellitus. *Am J Epidemiol* 139:484-492 (1994).
56. Rahman M, Axelson O. Diabetes mellitus and arsenic exposure: a second look at case-control data from a Swedish copper smelter. *Occup Environ Med* 52:773-774 (1995).
57. Kaltreider RC, Davis AM, Lariviere JP, Hamilton JW. Arsenic alters the function of the glucocorticoid receptor as a transcriptional factor. *Environ Health Perspect* 109:245-251 (2001).
58. Copeland LJ. *Textbook of Gynecology*. Philadelphia: Saunders, 1993.
59. Miller MM, Plowchalk DR, Weitzman GA, London SN, Mattison DR. The effect of benzo(a)pyrene on murine ovarian and corpora lutea volumes. *Am J Obstet Gynecol* 166:1535-1541 (1992).
60. Jarrell JF, McMahon A, Villeneuve D, Franklin C, Singh A, Valli VE, Bartlett S. Ovarian germ cell destruction in the monkey with hexachlorobenzene in the absence of induced porphyria. *Reprod Toxicol* 7:41-47 (1993).
61. Foster WG. Reproductive toxicity of chronic lead exposure in the female cynomolgus monkey. *Reprod Toxicol* 6:123-131 (1992).
62. Luster MI, Rosenthal GJ. Immunotoxic and hematotoxic effects of occupational exposures. *Environ Health Perspect* 100:219-226 (1993).
63. Weisglas-Kuperus N, Patandin S, Berbers GAM, Sas TCJ, Mulder PGH, Sauer PJJ, Hooijkaas H. Immunological effects of background exposure to polychlorinated biphenyls and dioxins in Dutch preschool children. *Environ Health Perspect* 108:1203-1207 (2000).
64. Beutler E. *Williams Hematology*, 5th Edition. New York: McGraw-Hill, 1995.
65. Rosenberg RN, ed. *Comprehensive Neurology*. New York: Raven Press, 1991.
66. Spence PS, Ludolph AC, Kisby GE. Are human neurodegenerative disorders linked to environmental chemicals with excitotoxic properties? *Annals N Y Acad Sci* 648:154-160 (1992).
67. Mandelbaum D, Paneth N. Cerebral Palsy. *Continuum. Lifelong Learning in Neurology* 6:8-30 (2000).
68. Verity MA. Environmental neurotoxicity of chemicals and radiation. *Curr Opin Neurol Neurosurg* 6:437-442 (1993).
69. ATSDR. *Toxicological Profile for Chlorinated Dibenzo-p-Dioxins*. Atlanta, GA: Agency for Toxic Substances and Disease Registry, 1998.
70. Harada M. Minamata disease: methylmercury poisoning in Japan caused by environmental pollution. *Crit Rev Toxicol* 25:1-24 (1995).
71. Newell FW. *Ophthalmology: Principles and Concepts*, 7th ed. St Louis, MO: Mosby Year Book, 1992.
72. Goyer RA, Epstein S, Bhattacharyya M, Korach KS, Pounds J. Environmental risk factors for osteoporosis. *Environ Health Perspect* 102:390-394 (1994).
73. Luoma PV, Nayha S, Pyy L, Hassi J. Association of blood cadmium to the area of residence and hypertensive disease in Arctic Finland. *Sci Total Environ* 160-161:571-575 (1995).
74. Hurst JW, Schlant RC, Rackley CE, Sonnenblinck EH, Wenger NK. *The Heart, Arteries and Veins*, 7th ed. New York: McGraw-Hill, 1990.
75. Burnett RA, Dales RE, Brook JR, Raizenne ME, Krewski D. Association between ambient carbon monoxide levels and hospitalizations for congestive heart failure in the elderly in 10 Canadian cities. *Epidemiology* 8:162-167 (1997).
76. Holt GR. Toxicology of upper aerodigestive tract pollutants. *Otolaryngol Head Neck Surg* 106:655-659 (1992).
77. Calderon-Garciduenas L, Osorno-Velazquez A, Bravo-Alvarez H, Delgado-Chavez R, Barrios-Marquez R. Histopathologic changes of the nasal mucosa in southwest Metropolitan Mexico City inhabitants. *Am J Pathol* 140:225-232 (1992).
78. Ballenger JJ. *Diseases of the Nose, Throat, Ear, Head, and Neck*, 14th ed. Philadelphia: Lea and Febiger, 1991.
79. Baum G, Wolinsky E. *Textbook of Pulmonary Disease*, 5th Edition, Vols 1 and 2. Boston: Little, Brown, 1994.
80. Tanagho EA, McAninch. *Smith's General Urology*, 14th Edition. Norwalk, CT: Appleton and Lange, 1995.
81. Cikrt M, Tichy M, Blaha K, Bittnerova D, Hardova J, Lepsi P, Sperlingova I, Nemecek R, Roth Z, Vit M, et al. The study of exposure to cadmium in the general population. II: Morbidity studies. *Pol J Occup Med Environ Health* 5:345-356 (1992).
82. Elinder CG. Cadmium as an environmental hazard. *IARC Sci Publ* 118:123-132 (1992).
83. Whorton D, Krauss RM, Marshall S, Milby TH. Infertility in male pesticide workers. *Lancet* 197:1259-1261 (1977).
84. Jockenhovel F, Bals-Pratsch M, Bertram HP, Nieschlag E. Seminal lead and copper in fertile and infertile men. *Andrologia* 22:503-511 (1990).
85. Lamb EJ, Bennett S. Epidemiological studies of male factors in fertility. *Annals N Y Acad Sci* 709:165-178 (1994).
86. Reir SE, Martin DC, Bowman RE, Mowski WP, Becker JL. Endometriosis in rhesus monkeys (*Macaca mulatta*) following chronic exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Fundam Appl Toxicol* 21:433-441 (1993).
87. Fitzpatrick TB, Johnson RA, Polano MK, Suurmond D, Johnson RA, Wolff K. *Color Atlas and Synopsis of Clinical Dermatology: Common and Serious Diseases*, 2nd ed. New York: McGraw-Hill, 1992.
88. Shepard TH. *Catalog of Teratogenic Agents*, 5th ed. Baltimore, MD: Johns Hopkins University Press, 1986.
89. Schettler T, Solomon G, Valenti M, Huddle A. *Generations at Risk*. Cambridge, MA: Massachusetts Institute of Technology Press, 1999.
90. Brender JD, Suarez L. Paternal occupation and anencephaly. *Am J Epidemiol* 131:517-521 (1990).
91. Louik C, Mitchell AA. *Occupational Exposures and Birth Defects: Final Performance Report*. Cincinnati, OH: National Institute for Occupational Safety and Health, 1992.

92. Holmberg PC, Nurminen M. Congenital defects of the central nervous system and occupational factors during pregnancy. *Am J Ind Med* 1:167–176 (1980).
93. Sever LE. Congenital malformations related to occupational reproductive hazards. *Occup Med* 9:471–494 (1994).
94. Bove FJ, Fulcomer MC, Klotz JB, Esmart J, Dufficy EM, Savrin JE. Public drinking water contamination and birth outcomes. *Am J Epidemiol* 41:850–862 (1995).
95. Goldberg SJ, Lebowitz MD, Graver EJ, Hicks S. An association of human congenital cardiac malformations and drinking water contaminants. *J Am Coll Cardiol* 16:155–164 (1990).
96. Swan SH, Shaw G, Harris JA, Neutra RR. Congenital cardiac anomalies in relation to water contamination, Santa Clara County, California, 1981–1983. *Am J Epidemiol* 129:885–893 (1989).
97. Dawson BV, Johnson PD, Goldberg SJ, Ulreich JB. Cardiac teratogenesis of trichloroethylene and dichloroethylene in a mammalian model. *J Am Coll Cardiol* 16:1304–1309 (1990).
98. Dawson BV, Johnson PD, Goldberg SJ, Ulreich JB. Cardiac teratogenesis of halogenated hydrocarbon-contaminated drinking water. *J Am Coll Cardiol* 21:1466–1472 (1993).
99. Kilburn CJ. Manganese, malformations and motor disorders: findings in a manganese-exposed populations. *Neurotoxicology* 8:421–429 (1987).
100. Tsuchiya H, Shima S, Kurita H, Ito T, Kato Y, Kato Y, Tachikawa S. Effects of maternal exposure to six heavy metals on fetal development. *Bull Environ Contam Toxicol* 38:580–587 (1987).
101. Jacobson JL, Jacobson SV. Intellectual impairment in children exposed to polychlorinated biphenyls in utero. *N Engl J Med* 335:783–789 (1996).
102. Lonky E, Reihman J, Darvill T, Mather JH Sr, Daly H. Neonatal behavioral assessment scale performance in humans influenced by maternal consumption of environmentally contaminated Lake Ontario fish. *J Gt Lakes Res* 22:198–212 (1996).
103. Thomas TL, Fonham ETH, Norman SA, Stenhagen A, Hoover RN. Occupational risk factors for brain tumors. *Scand J Work Environ Health* 12:121–127 (1986).
104. Park RM, Silverstein MA, Green MA, Mirer FE. Brain cancer mortality at a manufacturer of aerospace electrical systems. *Am J Ind Med* 17:537–552 (1990).
105. Hadfield MG, Adera T, Smith B, Fortner-Burton CA, Gibb RD, Mumaw V. Human brain tumors and exposure to metal and non-metal elements: a case-control study. *J Environ Pathol Toxicol Oncol* 17:1–9 (1998).
106. Daniels JL, Olshan AF, Savitz DA. Pesticides and childhood cancers. *Environ Health Perspect* 105:1068–1077 (1997).
107. Davis JR, Brownson RC, Garcia RB, Bentz BJ, Turner A. Family pesticide use and childhood brain cancer. *Arch Environ Contam Toxicol* 24:87–92 (1993).
108. Schettler T, Stein J, Reich F, Valenti M. In Harm's Way: Toxic Threats to Child Development. Boston: Greater Boston Physicians for Social Responsibility, 2000.
109. Silman AJ, Hochberg MC. Occupational and environmental influences on scleroderma. *Scleroderma* 22:737–749 (1996).
110. Susser M, Susser E. Choosing a future for epidemiology: from black box to chinese boxes and eco-epidemiology. *Am J Public Health* 86:674–677 (1996).
111. Pearce N. Traditional epidemiology, modern epidemiology, and public health. *Am J Public Health* 86:678–683 (1996).
112. Pekkanen J, Pearce N. Environmental epidemiology: challenges and opportunities. *Environ Health Perspect* 109:1–5 (2001).
113. Firth M, Brophy J, Keith M. *Workplace Roulette: Gambling With Cancer*. Toronto, Canada: Between The Lines, 1997.
114. Durnil G. *The Making of a Conservative Environmentalist*. Bloomington, IN: Indiana University Press, 1995.
115. Durnil G. *Is America Beyond Reform? Or Do Some Things in Our Society No Longer Fit?* Bloomington, IN: Indiana University Press, 1997.
116. Jacobs J. *Systems of Survival*. New York: Random House, 1992.
117. Brophy J, Parent M. Documenting the asbestos story in Sarnia. *New Solutions* 9:297–315 (1999).
118. Barlow M, May E. *Frederick Street: Life and Death on Canada's Love Canal*. Toronto, Canada: HarperCollins, 2000.
119. International Joint Commission. *Tenth Biennial Report on Great Lakes Water Quality*. Windsor, Ontario: International Joint Commission, 2000.