



Cancer and the Environment Lecture Series

Alan Abelsohn MD FCFP
Riina Bray MD CFPC

Ontario College of Family Physicians
Supported by the
Saunders-Matthew Cancer Prevention Coalition



Outline

- Incidence
- Causes
- Prevention overview
- Carcinogenesis
- Environmental carcinogens and exposure
- 2 Cases
- Primary prevention of environmental cancer

Objectives

- To review cancer incidence, morbidity and mortality
- To understand how environmental exposures can lead to the development of cancer
- To become familiar with one of the most prevalent types of cancer and how it relates to the environment
- To understand what is being done with regards to cancer prevention



Cancer Incidence

International Cancer Incidence

- Lung cancer is most common cancer worldwide - 1.2 million new cases annually
- Next most common is cancer of the breast - just over 1 million cases
- Colorectal - 940,000
- Stomach - 870,000
- Liver - 560,000
- Cervical - 470,000
- Esophageal - 410,000
- Head and neck - 390,000
- Bladder - 330,000

WHO, 2003

International Cancer Incidence (cont'd)

- Malignant non-Hodgkin lymphomas - 290,000
- Leukemia - 250,000
- Prostate and testicular - 250,000
- Pancreatic - 216,000
- Ovarian - 190,000
- Kidney - 190,000
- Endometrial - 188,000
- Nervous System - 175,000
- Melanoma - 133,000
- Thyroid - 123,000
- Pharynx - 65,000
- Hodgkin disease - 62,000

WHO, 2003



Worldwide Cancer Mortality Rates (cont'd)

- Three leading cancer killers are:
 - Lung cancer – 17.8% of all cancer deaths
 - Stomach – 10.4%
 - Liver – 8.8%

WHO, 2003



Geographic Distribution

- Patterns of high & low mortality may reflect exposure to varying levels of particular carcinogens for
 - cultural, dietary, occupational or environmental reasons
- Might illustrate regionalization for
 - racial reasons,
 - a specific genetic predisposition,
 - resistance to particular cancers.
- Might also display geographical variations in the quality of health



Geographic Distribution

- There are significant differences in the geographic patterns of death resulting from cancer
 - i.e. colon & rectal cancer in both males and females – high mortality rate in NE & urban centers along the Great Lake
 - i.e. USA → East has more cancers; Idaho & New Mexico lowest total cancer mortality; Rhode Island Peak



Numbers of Cancer Deaths and New Cases in the World as Estimated for 2000 and Predicted for 2020¹

Year	Region	New cases (millions)	Deaths (millions)
2000	More developed countries	4.7	2.6
	Less developed countries	5.4	3.6
	All countries	10.1	6.2
2020	More developed countries	6.0	3.5
	Less developed countries	9.3	6.3
	All countries	15.3	9.8

¹Ferlay et al, 2001

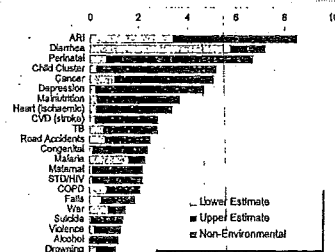
Asian Pacific Journal of Cancer Prevention (H. Vainio, 2002)

- Internationally in 2000 there were
 - 10 million new cancer cases
 - 6 million deaths
 - 22 million people living with cancer
- more in developing countries than developed

(Parkin, 2001, Table 1)



Percent of Total Lost DALYs



International Statistics

- Population attributable risk for
 - Tobacco-induced cancers is 30% in Western populations vs 20 over the world as whole
 - Dietary-associated cancers is 30% vs for cancers associated with infection 15%
(Pisani et al., 1997; WHO, 2002)
 - Occupational & environmental carcinogens is 3-9%, depending on prevalence and intensity of exposure
 - Asian Pacific Journal of Cancer Prevention, Vol 3, 2002.

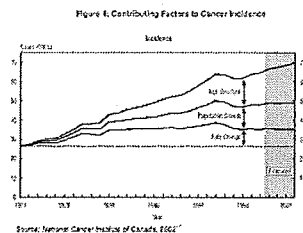
What is Meant by "Attributable?"

- "Attributable environmental risk"
 - Percentage of a particular disease category that would be eliminated if environmental risk factors were reduced to their lowest feasible values
- "Attributable risk percent (population)"
 - Considers both the prevalence of the exposures and strength of the risks

Smith, Corvalan, Kjellstrom, 1999

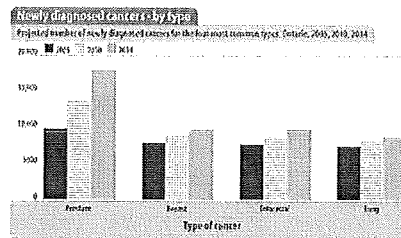
Cancer Epidemic

A slow epidemic



Cancer Epidemic

A slow epidemic



What causes cancer?

Causes of Cancer

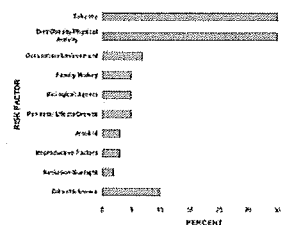


Figure 2: Causes of Cancer Deaths in Developed Countries
Source: Adapted from ACSM et al., 2001 and Cohen et al., 1995

From: Targeting Cancer. An action plan for cancer prevention and detection. Cancer 2000. Cancer Care Ontario. May, 2001



Cancer prevention



Cancer Prevention

- Primary Prevention
- Secondary Prevention
- **At least 50% of cancer can be prevented.**
Primary prevention efforts have the greatest potential to reduce the burden of cancer and other diseases through healthy living, public policies and systemic changes that protect the health of Canadians. (Canadian Strategy for Cancer Control)



Primary Prevention

- **Removing the cause of cancer**
- Screening
- Medical or nutritional treatment that prevents the development of cancer



Primary Prevention:

Removing the cause of cancer

- Reducing personal exposure to carcinogens in the environment
 - Voluntary exposures
 - Involuntary exposures
- Reducing or eliminating the release of carcinogens into the environment



Cancer Prevention

- **Personal health behaviours (Voluntary exposures)**
 - Tobacco
 - Diet
 - Physical activity
 - Obesity
 - Alcohol consumption
 - Sun exposure
- **The Healthy Living Strategy**

Centre for Chronic Disease Prevention and Control, Public Health Agency of Canada, 2004.
Progress Report on Cancer Control in Canada. (<http://www.phac-aspc.gc.ca/publicat/prcccrclcc/index.html>)



Carcinogenesis

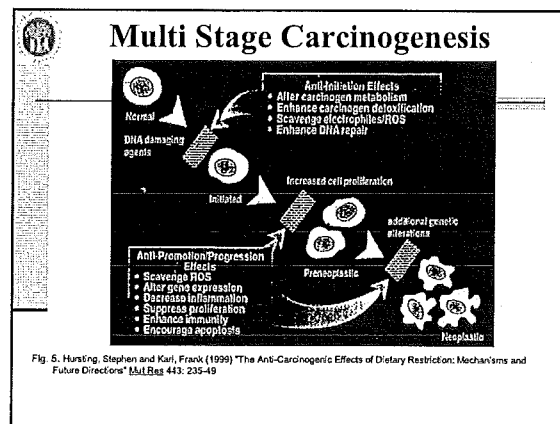
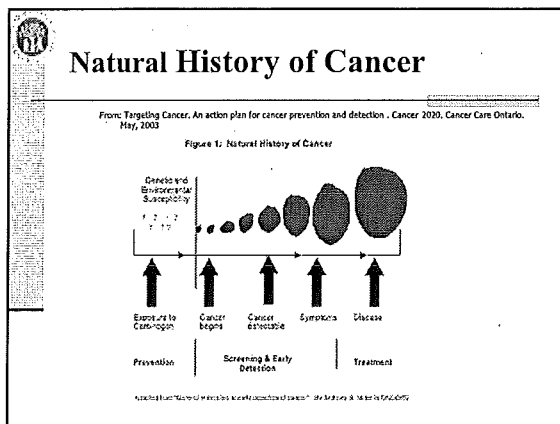
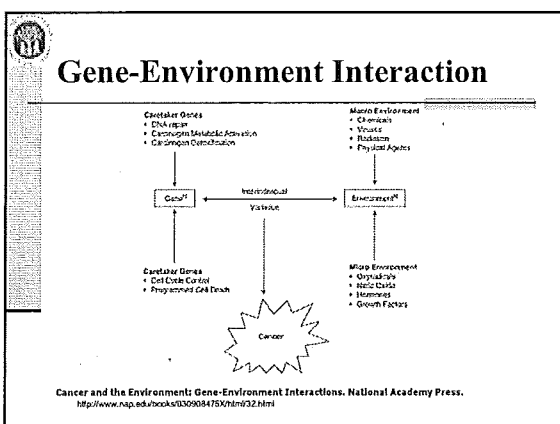


Fig. 5. Hurling, Stephen and Karl, Frank (1999) "The Anti-Carcinogenic Effects of Dietary Restriction: Mechanisms and Future Directions" *Mol. Cell. Biochem.* 443: 235-49



- ## Gene-Environment Interaction
- Risk of childhood acute lymphoblastic leukemia (ALL)
 - associated with drinking water disinfection by-products (THMs)
 - modified in the presence of variants in genes involved in the metabolism of trihalomethanes (THMs).
 - Infante-Rivad C. GSTT1 and CYP2E1 Polymorphisms and Trihalomethanes in Drinking Water: Effect on Childhood Leukemia. *Environ Health Perspect* (2002) 110:591-593

Carcinogens

Endocrine disruptors

Exposure

- ## Carcinogens
- IARC International Agency for Research on Cancer
 - CEPA Canadian Environmental Protection Act
 - NTP National Toxicology Program
 - CAREX Carcinogen Exposure database
 - Endocrine Disruptors



Carcinogens: IARC

Group 1: The agent (mixture) is carcinogenic to humans. Exposures that are carcinogenic to humans.(95)

Group 2A: The agent (mixture) probably carcinogenic.(66)

Group 2B: The agent (mixture) possibly carcinogenic (241)

Group 3: The agent (mixture or exposure circumstance) is not classifiable as to its carcinogenicity to humans.(497)

Group 4: The agent (mixture) probably not carcinogenic (1)

<http://www.iarc.fr/>



CEPA

■ CEPA Toxic

- Enters the environment in a such a quantity as to pose risk to the environment or to human health

■ Priority Substances List (PSL)

- 70 substances listed
- Any carcinogen is listed, even if exposure is small, as it is assumed that there is no "safe" exposure to a carcinogen



Endocrine Disruptors

- Hormonally active chemicals
 - cancer promotion
 - effecting on mammary gland development
 - responsiveness to other carcinogens.
- Mechanism of action
 - mimic hormones at binding sites,
 - turn on the receptor,
 - or block the receptor.
 - estrogenic, anti-estrogenic or androgenic



Endocrine Disruptors

- PCBs
- Dioxins
- Some pesticides, such as DDT, now banned
- Phthalates
- Bisphenol A
- The flame retardants, PBDEs.



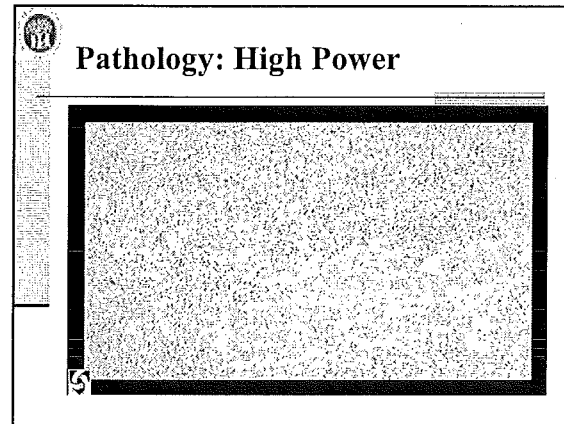
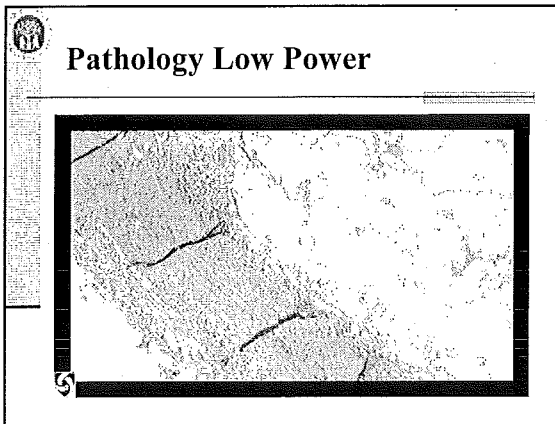
Human Exposure

- Limited surveillance
- Limited data
- Carcinogen releases
 - Ontario 2003: **7,625,732 kg** carcinogens
(Pollution Watch: <http://www.pollutionwatch.org/>)



Body Burdens

- Environmental Defence Study 2005
- www.ToxicNation.ca
- 11 Canadians
- Blood and urine for
 - PBDEs
 - Perfluorinated chemicals PFOs
 - VOCs
 - PCBs
 - Organochlorine pesticides
 - Organophosphate pesticide metabolites
 - Heavy Metals

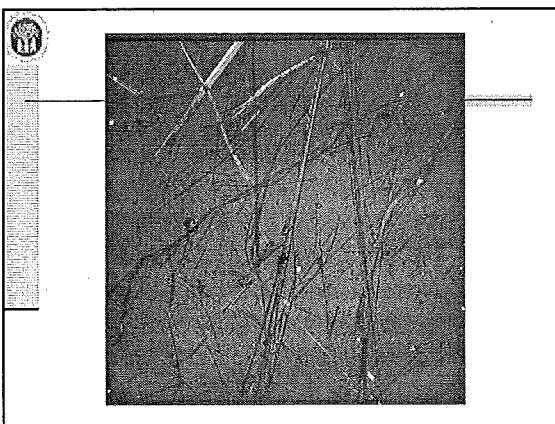


Mesothelioma and Asbestos

- The only cancer with a unique and clear link to a single exposure

Mesothelioma: Epidemiology

- Pathognomonic of asbestos exposure
- 20-40 year latency
- Males:Females 3-4:1



Mesothelioma: Natural History

- Locally invasive
- At autopsy, found in heart, liver, spleen, adrenals, GI tract, bone, pancreas and kidneys
- 10% survival at 2 years
- Surgery and chemotherapy do not improve survival



Mesothelioma

- Asbestos exposure
 - Occupational
 - In the home



Asbestos: Occupations at Risk

- Plumbers, pipefitters, steamfitters
- Insulation workers
- Managers and administrators
- Electricians, carpenters, laborers
- Welders and cutters
- Janitors and cleaners
- Production supervisors
- Machinists



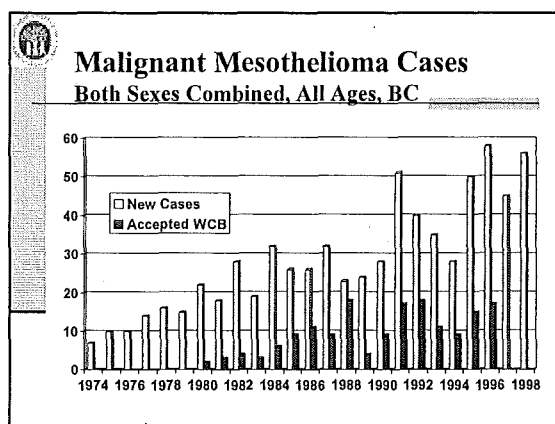
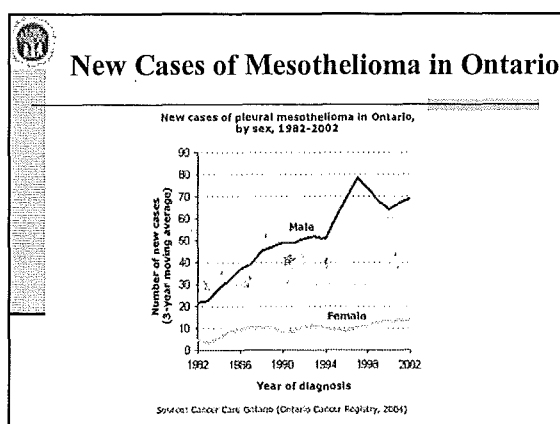
Home Exposures: Vermiculite Insulation





Asbestos-Related Diseases

- Pleural fibrosis, pleural effusion
- Asbestosis (fibrotic disease)
- Malignant mesothelioma
- Lung Cancer (bronchogenic cancer)



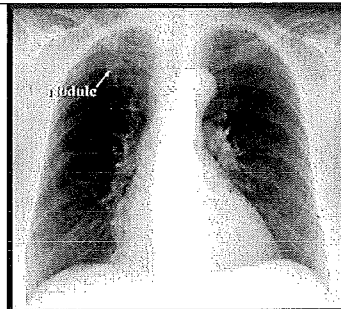


Asbestos Politics

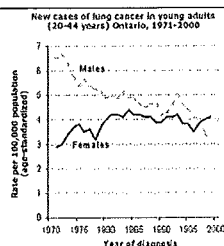
- 2000: EU Ban on asbestos use
- 2003: UN proposal to ban importation of chrysotile asbestos
- Canada blocked proposal because of strong asbestos lobby



Case 2: Non-smoker with chronic cough



Lung Cancer



Cancer Care Ontario

http://www.cancercare.on.ca/index_statisticsLung.htm



Lung Cancer Exposure History

- 60 year old with Ca Lung
- What exposures might be related?
 - CH2OPD2



Exposure History CH2OPD2

- C Community
 - Air
 - Food
 - Soil
 - Water
- H2 Home, Hobbies
- O Occupation
 - Latency period up to 30 years
- P Personal
- D2 Diet, Drugs



Exposure History: Ca Lung

- C- Community
 - Diesel exhaust
 - Air Pollution PM2
 - Second hand smoke
- H- Home
 - Radon
 - Asbestos insulation
- H- Hobbies ?
- O- Occupation
 - Asbestos
 - Second hand smoke
- P- Personal
 - Smoking
- D2- Diet and Drugs

Cigarette Smoke and Asbestos	
Group	Mortality Ratio
Nonsmokers not exposed	1.00
Nonsmokers exposed	5.17
Smokers not exposed	10.85
Smokers exposed	53.24

Hammond et al, 1979

- ### Lung Cancer and Asbestos
- All cell types seen
 - 5X increase in Lung Ca from asbestos exposure
 - Dose-response seen
 - Risk multiplicative with cigarettes
 - All fibers cause

Lung Cancer and Air Pollution

Particulate Matter PM 2.5

8% increase lung cancer mortality risk for males for each 10 µg/m3 increase in PM2.5 concentration

Pope CA, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K & Thurston GD (2002). Lung cancer, cardiopulmonary mortality and long-term exposure to fine particulate air pollution. JAMA, 287: 1132-1141.

Lung Cancer and Diesel Exhaust

Attributable cancers

LA	16,250
NYC	10,360
GTA	2,410

Cancer Risk from Diesel Particulate:
National and Metropolitan Area Estimates for the United States
Prepared by the State and Territorial Air Pollution Program Administrators
and the Association of Local Air Pollution Control Officials

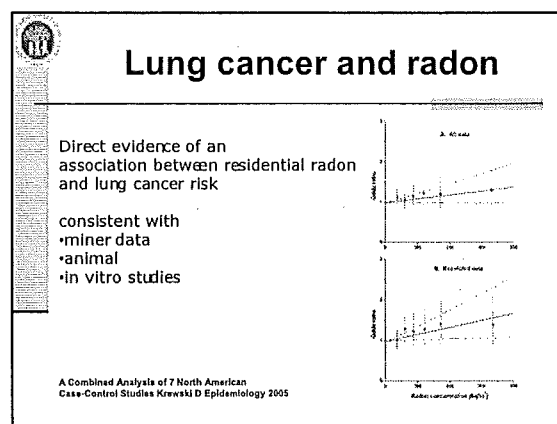
<http://www.4cleanair.org/comments/CancerRiskreport.PDF>

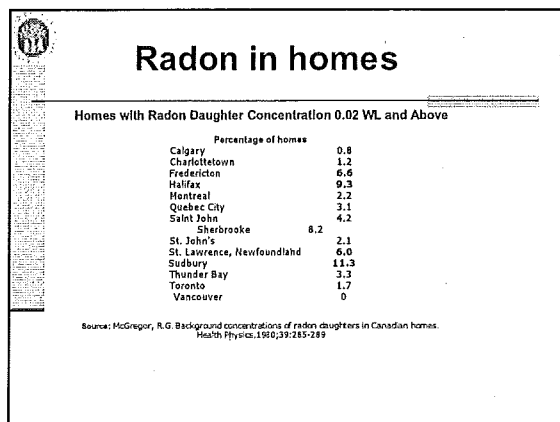
Gene-Environment Interaction

Table 3. Lung cancer ORs and 95% CIs for the CYP1A1 polymorphism by cell type and sex

No. of cases N (%)	All lung cancers		Epithelial cell carcinomas		Adenocarcinomas	
	n	OR (95% CI)	n	OR (95% CI)	n	OR (95% CI)
ALL	1566/2177	1.00	241/3177	1.00	111/1779	1.00
1	336/441	1.15 (0.91-1.39)	121/144	1.31 (0.79-1.30)	122/116	1.11 (0.55-1.89)
2	24/48	1.14 (0.39-2.49)	25/36	1.81 (1.03-3.62)	14/36	1.09 (0.37-2.19)
		<i>p</i> = 0.60		<i>p</i> = 0.16		<i>p</i> = 0.16

Le Marchand L, Guo C et al. Pooled analysis of the CYP1A1 exon 7 polymorphism and lung cancer (United States). (2003). Cancer Causes and Control; 14: 339-346.

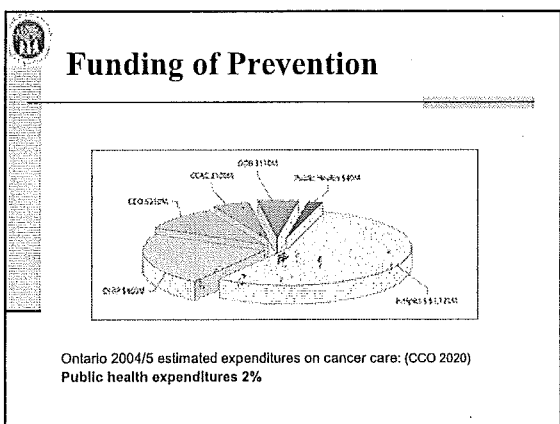




Primary Prevention of Cancer

- ## Primary Prevention of Cancer
- Research is difficult
 - Funding (Under-funding)
 - Principles
 - Precautionary Principle
 - Pollution Prevention
 - Just Transition
 - Community Right to Know

- ## Primary Prevention Research
- Funding
 - Toxicology
 - Animal models
 - Low dose long term exposures
 - Epidemiology:
 - Observational vs Experimental (RCT)
 - Latent period
 - Association vs Causation
 - Multiple exposures
 - Timing of exposure: critical periods



Precautionary Principle

When an activity raises threats of harm to human health, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically.

Canadian Cancer Society



Pollution Prevention

- It is **less expensive** and **more effective** to prevent environmental and human health damage, than to manage or cure it.
- Example:
 - Toxic Use Reduction in Mass.



Just Transition

- Allows workers and communities to choose both **economic security** and a healthy environment

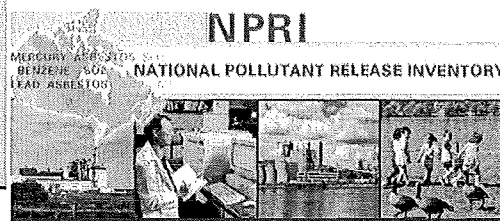


Community Right to Know

- About environmental risks and exposures
- Participate in decisions affecting health



National Pollutant Release Inventory



http://www.ec.gc.ca/pdb/npri/npri_home_e.cfm



NPRI On-Line Data Search

- **Substance - based**
 - Substance
 - Facility, type of industries and location
 - Year
- **Location - based search**
 - National Pollutant Release Inventory (NPRI) and
 - Criteria Air Contaminant (CAC) emissions data
 - in your community using a geographic search



Pollution Watch

- Get Answers about Pollution in your Community
- Search for facilities in your area using your postal code.
- <http://www.pollutionwatch.org/>



References

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 - Ontario College of Family Physicians
<http://www.ocfp.on.ca/local/files/EHC/Exposure%20Hx%20Forms%2010Feb2004.pdf>
 - Marshall L, Weir E, Abelsohn A, Sanborn MD Identifying and managing adverse environmental health effects: 1. Taking an exposure history. CMAJ. 2002 Apr 16;166(8):1049-55.
■ <http://www.cma.ca/cql/content/full/166/8/1049>
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Canadian Cancer Society, Cancer Care Ontario. Vol 4, June 2005.
<http://www.cancercare.on.ca/documents/InsightOnCancer-Environmental05.pdf>