

# INDUSTRIAL CARCINOGENS: A NEED FOR ACTION

Richard Clapp, D.Sc, MPH  
 B.U. School of Public Health  
 Boston, MA  
 Sept. 18, 2008

## Harming workers and the public alike

Beginning with Percival Pott's 1775 observation of an excess of scrotal cancer among young chimney sweeps in London, specific agents and processes in the industrial environment are some of the most well-studied and well-recognized causes of human cancer. Of the 935 agents and exposure circumstances evaluated by the International Agency for Research on Cancer (IARC), over 400 are now listed as carcinogenic, probably carcinogenic, or possibly carcinogenic<sup>[1]</sup> and 40% of these are considered industrial/occupational carcinogens.<sup>[2]</sup>

The National Institute for Occupational Health and Safety estimates that millions of U.S. workers are currently exposed to substances considered carcinogenic in animal studies and millions more may be exposed to carcinogens not yet defined because only 2% of chemicals in commerce have undergone carcinogenicity testing.<sup>[3]</sup> The full burden of industrial agents that can contribute to cancer becomes even more striking when considering that these agents extend beyond the factory walls and into the materials and products used in daily life. These carcinogens enter the environment as contaminants in the air, water, food, and soil that people come in contact with in their communities.

Strength of the Evidence linking Industrial Agents with Cancer		
Cancer Type	Causal Evidence Regarding Involuntary Environmental or Occupational Exposures	
	Strong	Suspected
Bladder	Aromatic amines; Arsenic; Coal tars; Metalworking fluids and mineral oils	Ionizing radiation; PAHs; Tetrachloroethylene
Brain and other Central Nervous System	Ionizing radiation	Arsenic; Benzene; Lead; Mercury; Methylene chloride; Non-ionizing radiation (extremely low electro-magnetic frequency, microwaves and radiowaves); N-nitroso compounds; Pesticides; Toluene; Xylene
Breast	Ionizing radiation	Bisphenol A; Dioxin; Ethylene oxide; Non-ionizing radiation; PAHs; Phthalates; PCBs; DDT/DDE; Hexachlorobenzene; Lindane; Heptachlor; Triazine herbicides; Solvents
Cervical		Non-specified solvents; Tetrachloroethylene; Trichloroethylene
Colon		Ionizing radiation; Toluene; Xylene
Esophageal		Metalworking fluids; Tetrachloroethylene; Soot
Hodgkin's disease		Chlorophenols; Phenoxy acid herbicides; Trichloroethylene
Kidney		Arsenic; Benzene; Cadmium; Lead; Trichloroethylene; Tetrachloroethylene; Unspecified Pesticides

Source: Clapp RW, Jacobs MM, Loechler EL. Environmental & Occupational Causes of Cancer: New Evidence 2005-2007, Reviews on Environmental Health. 2008; 23(1):136.

From industrial/municipal waste incineration dioxin emissions, to formaldehyde in pressed wood, methylene chloride in paint strippers, and crystalline silica in construction debris, the public has many ways of being exposed to industrial carcinogens. Moreover, many of us

live, work and play near polluting industrial facilities and hazardous waste sites exposing us to a mixture of industrial carcinogens through various routes. According to the most recent data from the Toxics Release Inventory, 820 million pounds of known or suspected carcinogens were released or disposed of by reporting industries in 2006 alone.<sup>[4]</sup> One reliable source estimates suggest that 1 in every 50 children live within one mile of a Superfund site while approximately 1 in 6 people live within four miles of these sites.<sup>[5]</sup> Preventing cancer associated with industrial carcinogens must consider all components of a material's lifecycle, including manufacturing, product use and disposal.

### Flawed methods, flawed estimates, flawed policy

Given ubiquitous exposures to industrial carcinogens across the production-consumption lifespan, several researchers have tried to estimate the numbers of cancer cases due to occupational and environmental exposures. Yet current estimates are a significant underestimation of the true burden. In 1981, Sir Richard Doll and Sir Richard Peto<sup>[6]</sup> estimated the percentage of cancer deaths that would be avoided if certain individual factors were addressed—an approach repeated in 1996 by the Harvard Center for Cancer Prevention<sup>[7]</sup> and again by Doll in 1998.<sup>[8]</sup> These well-cited sources estimated that ~4% of cancer deaths are due to occupation and ~2% to the broader environment while the largest percentage of cancer deaths are attributable to smoking and diet – results which are reflected in the focus of our current cancer prevention programs and policies. Yet attributing the population burden of cancer to single factors is seriously flawed given our current understanding of the mechanisms of cancer, which suggests all cancers arise from a complex multi-factorial, multi-stage process.<sup>[9]</sup>

<b>Strength of the Evidence linking Industrial Agents with Cancer</b>		
<b>Cancer Type</b>	<b>Causal Evidence Regarding Involuntary Environmental or Occupational Exposures</b>	
	<b>Strong</b>	<b>Suspected</b>
Laryngeal cancer	Asbestos; Metal working fluids; Mineral oils; Sulfuric acid	Mustard gas; Nickel; "Strong acid process" for manufacturing isopropyl alcohol; diethyl sulfate in ethanol production; Wood dust
Leukemia	Benzene; Ionizing radiation	Carbon disulfide; Carbon tetrachloride; Butadiene; DDT; Ethylene oxide; Non-ionizing radiation (including electro-magnetic frequencies and radio frequencies); Methyl bromide; Phosphine; Trichloroethylene; Unspecified pesticides
Liver and Biliary	Ionizing radiation; Trichloroethylene; PCBs; Vinyl chloride	Arsenic; Methylene chloride; Unspecified organic solvents
Lung Cancer	Air pollution (indoor and outdoor); Arsenic; Asbestos; Beryllium; Cadmium, Chromium; Chloromethyl ethers; Coal tar and pitches; Diesel exhaust; Ionizing radiation (including radon); Nickel; Mustard gas; PAHs; Silica; Soot; Wood dust	Benzene; Lead; Pesticides (e.g. dieldrin, diazinon, carbofuran, metachlor); Sulfuric acid; Toluene
Mesothelioma	Asbestos	
Multiple Myeloma	Benzene; Ionizing radiation	Dioxin; Hair dyes; Phenoxy acid herbicides and unspecified pesticides, Trichloroethane
Nasal and Nasopharynx	Chromium; Formaldehyde; Mineral oils; Nickel; Wood dust	Benzene; Ionizing radiation

*Source: Clapp RW, Jacobs MM, Loechler EL. Environmental & Occupational Causes of Cancer: New Evidence 2005-2007, Reviews on Environmental Health. 2008; 23(1):136.*

Professor Luc Montagnier from the Institut Pasteur said in *The War on Cancer*, "And what my colleagues often don't understand is that there's an accumulation of these doses - they all add up. A little dose of radiation here, and exposure to some chemical there, a bit of something in your food, and so on. . . All of this adds up to create an oxidant field and it's the

totality of this field which does all the damage and may bring about a cancer."<sup>[10]</sup> Cancer researchers have identified at least six essential alterations that unfold over time and overwhelm the natural defenses built into human cells and tissues to produce a tumor.<sup>[9]</sup>

The problem of calculating “attributable fractions” isn’t just a methodological issue; it’s become a programmatic and policy issue as well. Some cancer control proponents have created a causal hierarchy from these calculations and issued statements such as, “Public concern about environmental carcinogens is out of proportion with the true risk.”<sup>[7]</sup> Within the context of a multi-causal model of cancer, there is no such thing as a strong or weak risk factor for an individual’s cancer.<sup>[11]</sup> However, on a population level, it is true that some risk factors such as smoking tobacco or exposure to asbestos more strongly increase cancer risk than others. There are dozens of industrial agents that when examined one at a time may only modestly increase risk. Yet, when all such agents are considered together, a national commitment to mitigate these exposures will protect hundreds of thousands from a cancer diagnosis. Our past under-emphasis of occupational and environmental factors in our cancer control programs means we have missed many important opportunities for primary prevention. To drastically reduce cancer incidence in the U.S. and throughout the world, we need to move beyond current programmatic priorities based on dubious attributable fractions and commit to comprehensive cancer prevention.

Evidence linking Industrial Agents with Cancer		
Cancer Type	Causal Evidence Regarding Involuntary Environmental or Occupational Exposures	
	Strong	Suspected
Non-Hodgkin's Lymphoma	Benzene; Dioxin	Carbon disulfide; Chlorophenols; Ethylene dibromide; Hair dyes; Organophosphorous insecticides; Methyl bromide; PCBs; Phenoxy acid herbicides; Phosphine; Styrene; Trichloroethylene; Tetrachloroethylene
Ovarian		Atrazine; Ionizing radiation; Talc powder
Pancreatic	Acrylamide; Metal working fluids; Mineral oils	DDT/DDE and unspecified pesticides; Cadmium, Nickel; Unspecified solvents
Prostate		Aromatic amines; Arsenic; Cadmium; Dioxin; Bisphenol A); Metal working fluids; PAHs; Chlorinated, organophosphorous insecticides and unspecified pesticides
Rectal	Metal working fluids and mineral oils	Chlorination by-products; Toluene; Xylene
Soft tissue sarcoma	Dioxin; Ionizing radiation; Vinyl chloride	Arsenic; Chlorophenols; DDT; Phenoxy acid herbicides and unspecified pesticides
Skin	Arsenic; Coal Tars; Creosotes; Ionizing radiation; Metal working fluids and mineral oils; PAHs	
Stomach	Asbestos; Metal working fluids and mineral oils	Coal dust; Ionizing radiation; Lead; Nickel; Unspecified solvents; Unspecified pesticides
Testicular		Chlorinated insecticides
Thyroid	Ionizing radiation	

*Source: Clapp RW, Jacobs MM, Loechler EL. Environmental & Occupational Causes of Cancer: New Evidence 2005-2007, Reviews on Environmental Health 2008; 23(1):136*

## Dose doesn't tell the whole story: critical windows of susceptibility and effects across multiple generations

We recommend designing studies to examine cancer risks not only associated with low levels of exposure, but also exposures that occur during critical windows of susceptibility. Prior research has repeatedly documented examples of differential cancer risk with age at exposure. Evidence from studies of nuclear workers reveals that cancer risk is greater

among older workers than younger workers when first exposed to the same dose of radiation.<sup>[12-14]</sup> Evidence from atomic-bomb survivors and medical irradiation studies clearly indicates an increased risk of leukemia among children exposed while in utero<sup>[15, 16]</sup> or post-natally<sup>[15]</sup> and evidence is emerging that fathers exposed to radiation prior to conception increases the risk of leukemia among their children.<sup>[17]</sup> Strong evidence also indicates an increased risk of childhood leukemia from parental exposure to benzene and possibly to other solvents.<sup>[18]</sup> More recently, a study by Cohn and colleagues demonstrated that girls first exposed to elevated levels of DDT before puberty – when mammary cells are more susceptible to the carcinogenic effects of hormones, chemicals and radiation – are five times more likely to develop breast cancer when they reach middle age.<sup>[19]</sup> Continued funding for large prospective studies such as the National Children’s Study will undoubtedly produce new knowledge regarding the timing of exposures that increase cancer risk later in life. But current evidence should compel action on what we already know to protect vulnerable populations.

## Filling knowledge gaps and acting on what we already know

Although there are laws and regulations in place, evidence to date suggests we have too often failed to uncover and act on knowledge necessary to protect public and worker health. The most direct way to achieve primary prevention of cancer is to avoid the introduction of carcinogenic agents into the environment and our workplaces in the first place. There needs to be greater emphasis on the pre-market testing of new chemicals and post-market testing of those chemicals in use in order to prevent future cases of cancer.

A second priority strategy for the primary prevention of cancer is to eliminate or drastically reduce exposure to known and suspected carcinogenic agents. As Dr. Harold Freeman put it, “To win the war against cancer, we must apply what we know at any given time to all people.”<sup>[20]</sup> Recent studies have shown that people of color, recent immigrants and the poor are far more likely to work with carcinogens, have less access to institutions that protect them and suffer disproportionately from exposure to environmental contaminants where they live.<sup>[21,22]</sup> It is essential that these disparities be eliminated if we expect to reduce the cancer burden overall. Cancer prevention programs too often rely on individuals to protect themselves even from exposures at their workplace. However, individual action alone is not enough to prevent exposure to industrial carcinogens and we need to identify safer technologies, stronger regulations and enforcement, and the adoption of safer chemical alternatives.

The current state of the evidence based on IARC’s evaluations of industrial carcinogens would lead one to believe that certain cancers, such as breast cancer, prostate cancer, brain cancer and cancers of the digestive system, are unrelated to such exposures. Yet research has produced abundant evidence that these cancers are associated with exposure to a range of industrial agents. Some of this evidence comes from animal studies. However, our current carcinogen ranking schemes demand consistent and sufficient evidence from human studies before an agent is considered “carcinogenic in humans.” In reality, virtually all human carcinogens were first identified in studies of laboratory animals. If our goal is to protect the public and prevent harm, more weight needs to be given to early warnings from animal studies and emerging high throughput testing procedures.

## How committed are we to preventing cancer?

The more we learn about cancer causation, the more it becomes evident that a cancer prevention program based simply on exposure reduction just isn't protective enough. Future exposure reduction programs likely need to be replaced by chemicals policies that promote green chemistry, alternatives assessment and "sunsetting" of current carcinogenic chemicals.

We need a comprehensive U.S. cancer prevention agenda that promotes health, prevents cancer and protects the most vulnerable members of society. This agenda must attend to all modifiable risk factors and no longer trivialize the contributions of industrial carcinogens to our current cancer burden. This prevention agenda must inform people as to what they can do as individuals to reduce their exposures to cancer causing agents or activities and provide them with the information and tools required to act collectively to reduce their exposure to carcinogens in their workplace and their environment. And furthermore, the agenda needs to promote the adoption of bolder policies to eliminate exposures to industrial carcinogens wherever feasible.

## REFERENCES

1. International Agency for Research on Cancer. Complete List of Agents evaluated and their classification, Accessed June 9, 2008 at: <http://monographs.iarc.fr/ENG/Classification/index.php>
2. Siemiatycki J, Richardson L, Straif K, et al. Listing Occupational Carcinogens, Environ Health Perspect. 2004; 112(15): 1447-1459.
3. National Institute of Occupational Safety and Health. NIOSH Safety and Health Topic: Occupational Cancer. Accessed June 29, 2008 at <http://www.cdc.gov/niosh/topics/cancer/>
4. Environmental Protection Agency. 2006 Toxics Release Inventory (TRI) Public Data Release Brochure. Accessed June 9, 2008 at [www.epa.gov/tri/tridata/tri06/brochure/brochure.htm](http://www.epa.gov/tri/tridata/tri06/brochure/brochure.htm).
5. Johnson B. *Impact of Hazardous Waste on Human Health*. Boca Raton, FL: CRC Press, 1999.
6. Doll R and R Peto. The Causes of Cancer: Quantitative estimates of Avoidable Risks of Cancer in the United States Today, J Nat Cancer Inst. 1981; 66: 1191-1308.
7. Harvard Reports on Cancer Prevention, Vol 1: Human Causes of Cancer. Cancer Causes & Control, November 7, 1996. Accessed June 9, 2008 at: [www.hsph.harvard.edu/cancer/resources\\_materials/reports.index.htm](http://www.hsph.harvard.edu/cancer/resources_materials/reports.index.htm)
8. Doll R. Epidemiological Evidence of the Effects of Behavior and the Environment on the Risk of Human Cancer, Rec Results Cancer Res. 1998; 154: 3-21.
9. Weinberg RA. *The Biology of Cancer*. New York, NY: Garland Science, 2007.
10. Montagnier L. *The War on Cancer: Part 2*. Les Productions Virage, 2006.
11. Rothman KJ. *Epidemiology, an Introduction*. Oxford: Oxford University Press, 2002.
12. Kneale GW, Stewart AM. Reanalysis of Hanford data: 1944-1986, Am J Ind Med. 1993; 23(2):371-389.

13. Wing S, Richardson D, Wolf S, et al. A case-control study of multiple myeloma at four nuclear facilities, *Ann Epidemiol.* 2000 Apr;10(3):144-53.
14. Richardson DB, Wing S. Greater sensitivity to ionizing radiation at older age: follow-up of workers at Oak Ridge National Laboratory through 1990, *Int J Epidemiol.* 1999; 28:428-436.
15. Gilman EA, Kneale, GW, Knox EG, et al. Pregnancy x-rays and childhood cancers: effects of exposure age and radiation dose, *J Rad Protect.* 1988; 8(1):2-8.
16. Doll R and Wakeford R. Risk of childhood cancer from fetal irradiation, *Br J Radiol.* 1997; 70:130-139
17. Smulevich VB, Solionova LG, Belyakova SV. Parental occupation and other factors and cancer risk in children: II. Occupational factors, *Int J Cancer.* 1999; 83:718-722.
18. Colt JS and Blair A. Parental occupational exposures and risk of childhood cancer. *Environ Health Persp.* 1998; 106(S3): 909-925.
19. Cohn, BA, Wolfe MS, Cirillo PM, et al. DDT and breast cancer in young women: new data on the significance of age at exposure, *Environ Health Perspect.* 2007;115:1406-1414.
20. Freeman HP. Poverty, culture, and social injustice determinants of cancer disparities, *CA A Cancer Journal for Clinicians.* 2004; 54:72-77.
21. Morello-Frosch R, Pastor M, Porras C, Sadd J. Environmental justice and regional inequality in Southern California: implications for future research, *Environ Health Perspect.* 2002; 110(2):149-154.
22. Brulle RJ and Pellow DN. Environmental Justice: Human Health and Environmental Inequalities, *Ann Rev Public Health.* 2006; 27:103-124.