Avoidable Causes of Cancer - the role of green chemistry

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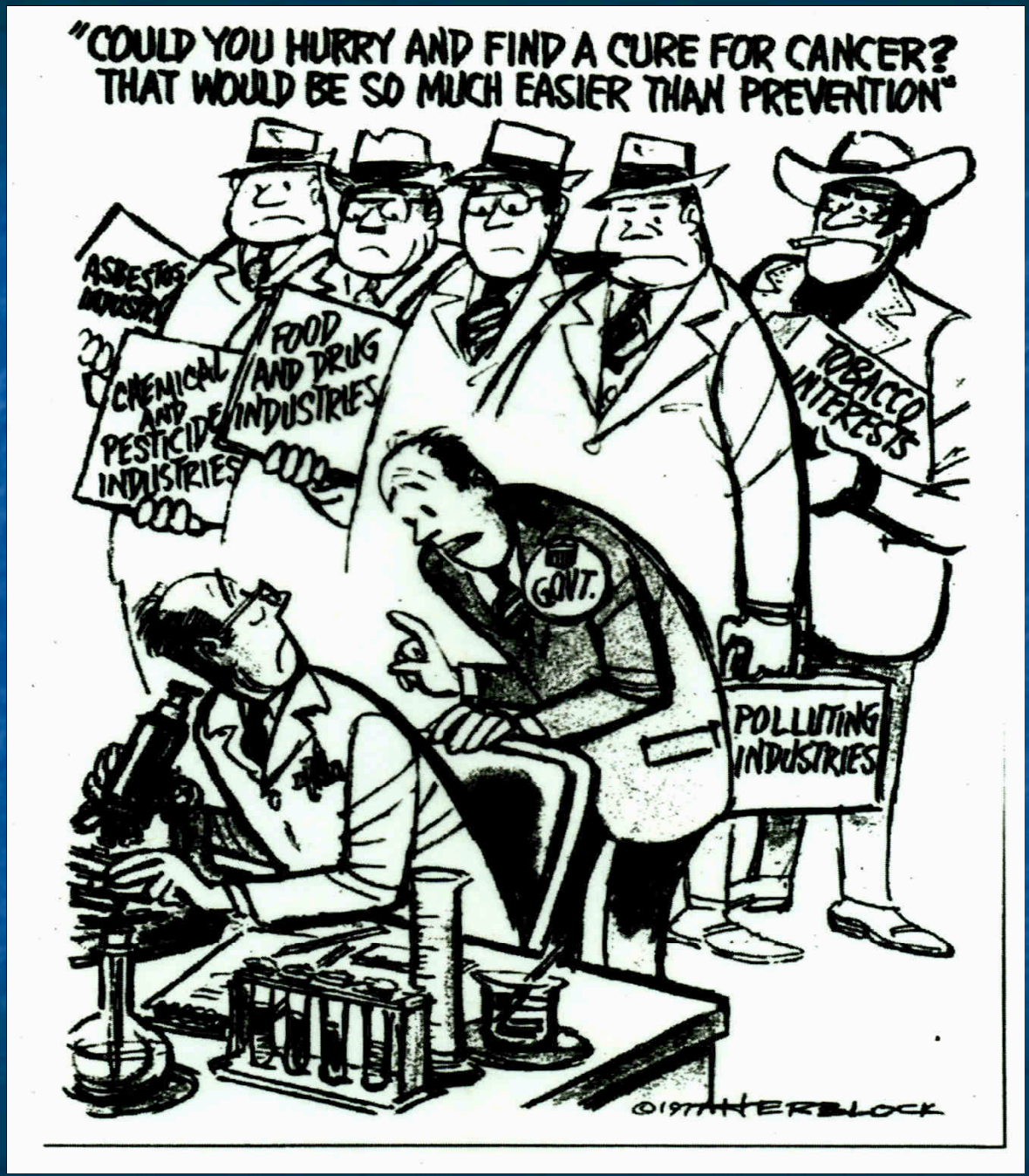
Outline

- Political context of environmental and occupational causes of cancer
- Previous estimates and knowledge base
- Current mechanistic understanding and recent epidemiologic research
- President's Cancer Panel May 2010 report
- Implications for green chemistry


"COULD YOU HURRY AND FIND A CURE FOR CANCER? THAT WOULD BE SO MUCH EASIER THAN PREVENTION"
ASBESTOS INDUSTRY
CHEMICAL AND PESTICIDE INDUSTRIES
FOOD AND DRUG INDUSTRIES
TOBACCO INTERESTS
GOVT.
POLLUTING INDUSTRIES
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Doll & Peto, 1981

TABLE 20.—*Proportions of cancer deaths attributed to various different factors*

Text section No.	Factor or class of factors	Percent of all cancer deaths	
		Best estimate	Range of acceptable estimates
5.1	Tobacco	30	25–40
5.2	Alcohol	3	2–4
5.3	Diet	35	10–70
5.4	Food additives	<1	−5[a]–2
5.5	Reproductive[b] and sexual behaviour	7	1–13
5.6	Occupation	4	2–8
5.7	Pollution	2	<1–5
5.8	Industrial products	<1	<1–2
5.9	Medicines and medical procedures	1	0.5–3
5.10	Geophysical factors[c]	3	2–4
5.11	Infection	10 ?	1–?
5.12	Unknown	?	?

Source: Doll R, Peto R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. *Journal of the National Cancer Institute*. 1981. 66(6):1191-1308.

Doll & Peto, 1981

Notable Limitations:

- Relied on epidemiologic studies of workers in large industries.
- Did not consider exposures in smaller work places.
- Did not consider exposures from indirect contact with carcinogens.
- Excluded deaths of people 65 and over

Source: Clapp R, Howe G, Jacobs M. "Environmental and Occupational Causes of Cancer," 2005.

Doll & Peto, 1981 and 1998

Acknowledged:

- Some exposures interact with each other.
- Proportions are impossible to quantify because not all avoidable causes are known.
  - When "all avoidable causes are known . . . may add up to several hundred percent."

Sources: 1) Doll R, Peto R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. *Journal of the National Cancer Institute*. 1981. 66(6):1191-1308. 2) Doll R. Epidemiological evidence of the effects of behaviour and the environment on the risk of cancer. *Recent Results in Cancer Research*. 1998. 154:3-21.

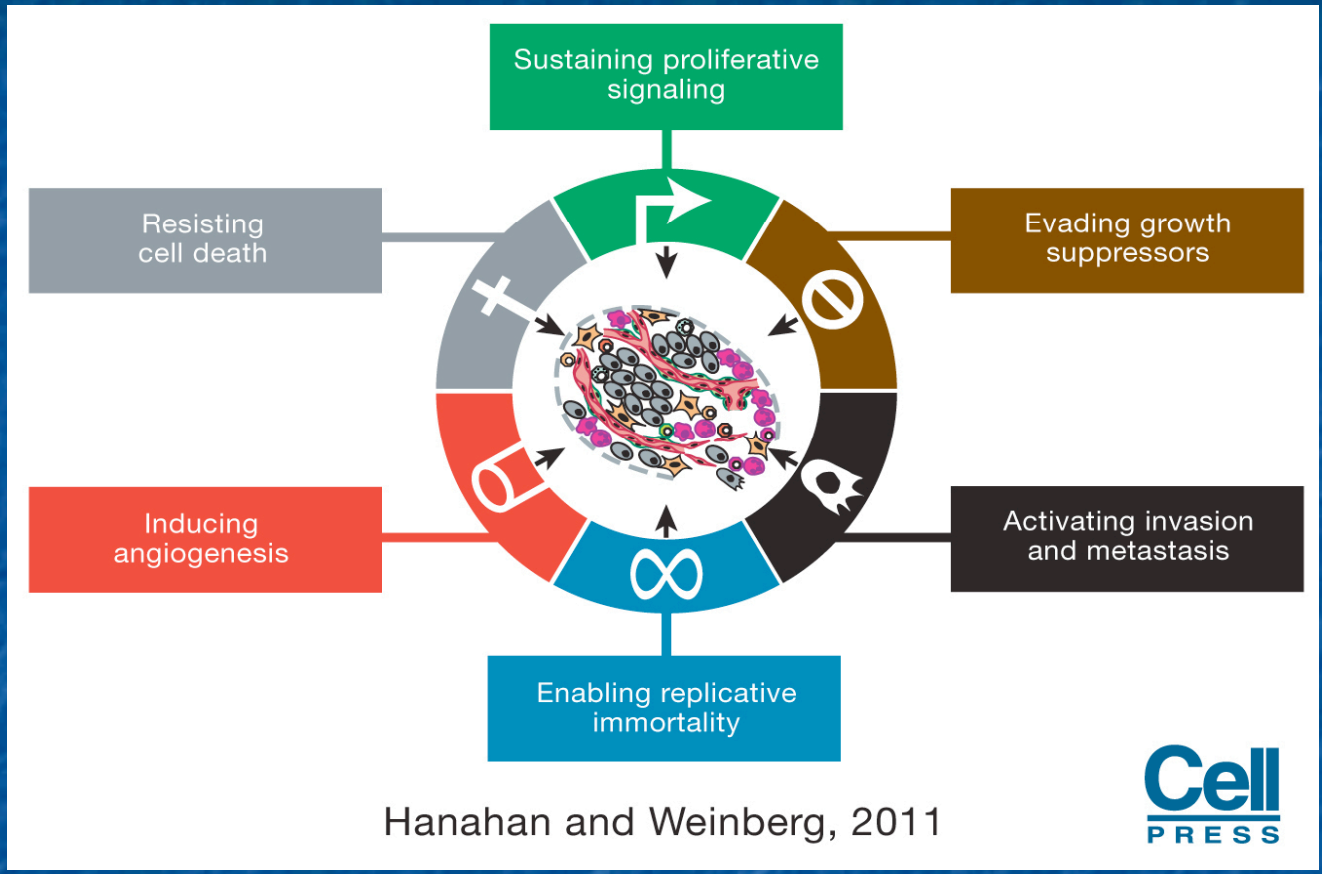
International Agency for Research on Cancer (IARC)

Evaluations of agents, mixtures, and exposures (as of April, 2011)

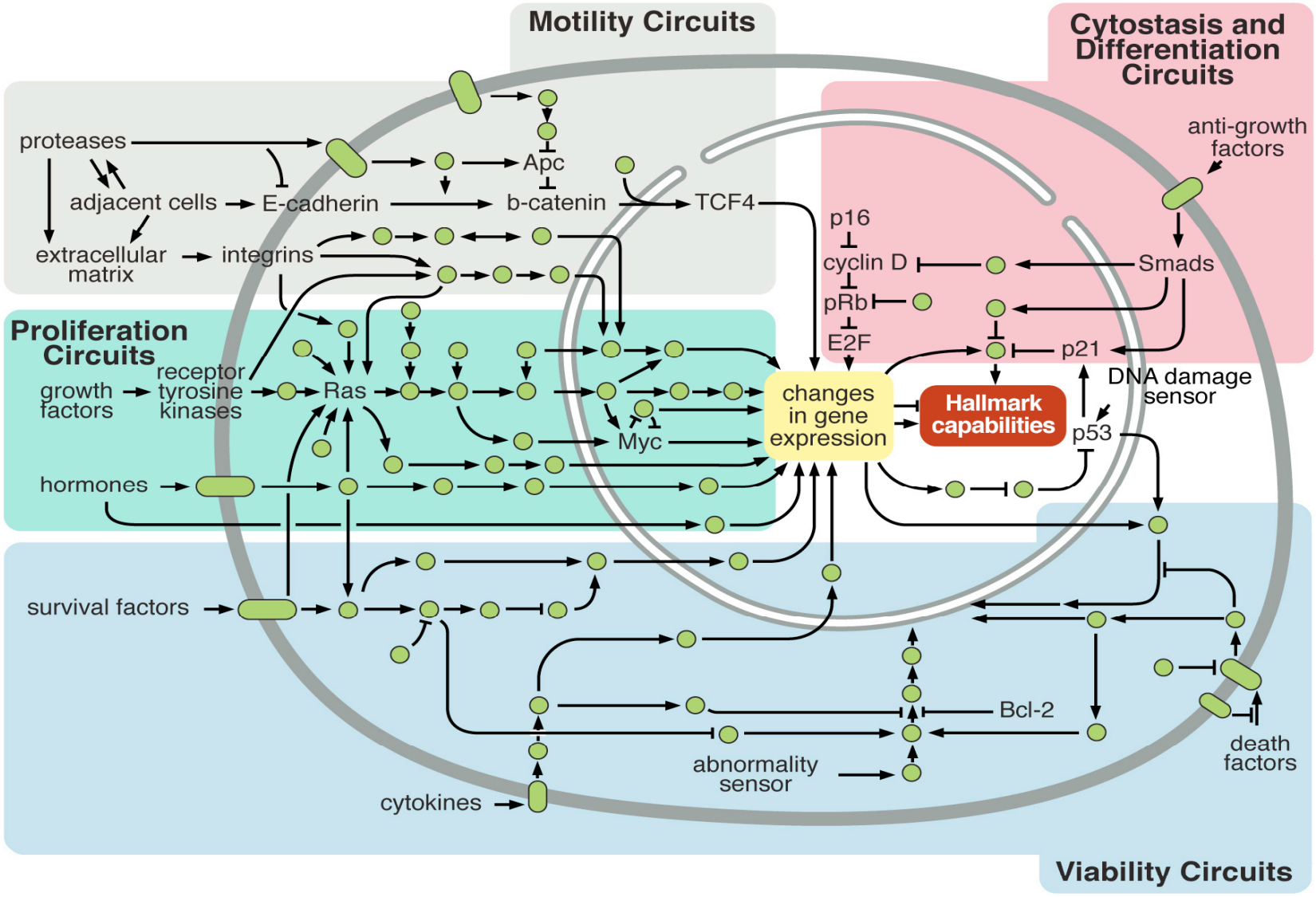
Total agents evaluated	**over 950**
• Carcinogenic to humans	107
• Probably carcinogenic to humans	69
• Possibly carcinogenic to humans	266
• Not classifiable	508
• Probably not carcinogenic to humans	1

Source: International Agency for Research on Cancer. http://www-cie.iarc.fr/

Current Mechanistic Understanding



Source: Hanahan D and Weinberg R. Hallmarks of Cancer: The Next Generation. Cell 2011;144:646-674



Hanahan and Weinberg, 2011

Cell PRESS

Current Mechanistic Understanding

A

Component	Acquired Capability	Example of Mechanism
	Self-sufficiency in growth signals	Activate H-Ras oncogene
	Insensitivity to anti-growth signals	Lose retinoblastoma suppressor
	Evading apoptosis	Produce IGF survival factors
	Limitless replicative potential	Turn on telomerase
	Sustained angiogenesis	Produce VEGF inducer
	Tissue invasion & metastasis	Inactivate E-cadherin

B

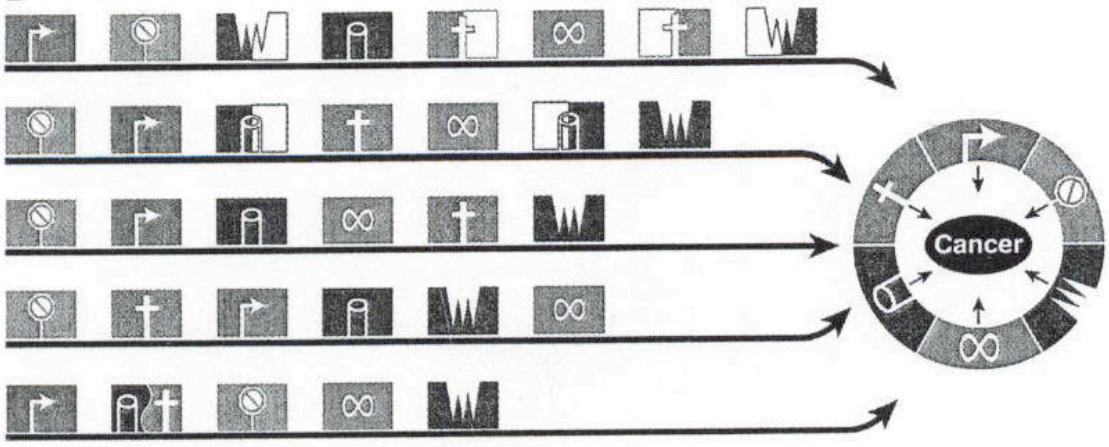


Figure 4. Parallel Pathways of Tumorigenesis

While we believe that virtually all cancers must acquire the same six hallmark capabilities (A), their means of doing so will vary significantly, both mechanistically (see text) and chronologically (B). Thus, the order in which these capabilities are acquired seems likely be quite variable across the spectrum of cancer types and subtypes. Moreover, in some tumors, a particular genetic lesion may confer several capabilities simultaneously, decreasing the number of distinct mutational steps required to complete tumorigenesis. Thus, loss of function of the p53 tumor suppressor can facilitate both angiogenesis and resistance to apoptosis (e.g., in the five-step pathway shown), as well as enabling the characteristic of genomic instability. In other tumors, a capability may only be acquired through the collaboration of two or more distinct genetic changes, thereby increasing the total number necessary for completion of tumor progression. Thus, in the eight-step pathway shown, invasion/metastasis and resistance to apoptosis are each acquired in two steps.

Source: Hanahan D and Weinberg R. The Hallmarks of Cancer. Cell 2000;100:57-70

Some substances and mixtures evaluated by IARC as definite human carcinogens and that are occupational exposures.

Substance or mixture	Occupation or industry in which the substance is found[a]	Site(s)
Physical agents		
Ionizing radiation and sources thereof, including, notably, X rays, γ rays, neutrons, and radon gas	Radiologists; technologists; nuclear workers; radium-dial painters; underground miners; plutonium workers; cleanup workers following nuclear accidents; aircraft crew	Bone[d] Leukemia[d] Lung[d] Liver[d] Thyroid[d] Others[d]
Solar radiation	Outdoor workers	Melanoma[d] Skin[d]
Respirable dusts and fibers		
Asbestos	Mining and milling; by-product manufacture; insulating; shipyard workers; sheet-metal workers; asbestos cement industry	Lung[d] Mesothelioma[d] Larynx[e] GI tract[e]
Erionite	Waste treatment; sewage; agricultural waste; air pollution control systems; cement aggregates; building materials	Mesothelioma[d]
Silica, crystalline	Granite and stone industries; ceramics, glass, and related industries; foundries and metallurgical industries; abrasives; construction; farming	Lung[d]
Talc containing asbestiform fibers	Manufacture of pottery, paper, paint, and cosmetics	Lung[d] Mesothelioma[d]
Wood dust	Logging and sawmill workers; pulp and paper and paperboard industry; woodworking trades (e.g., furniture industries, cabinetmaking, carpentry and construction); used as filler in plastic and linoleum production	Nasal cavities and paranasal sinuses[d]

Source: Siemiatycki et al. Listing occupational carcinogens. Table 3. *Environmental Health Perspectives*. 112(15):1447-57, Nov 2004. http://www.ehponline.org/.

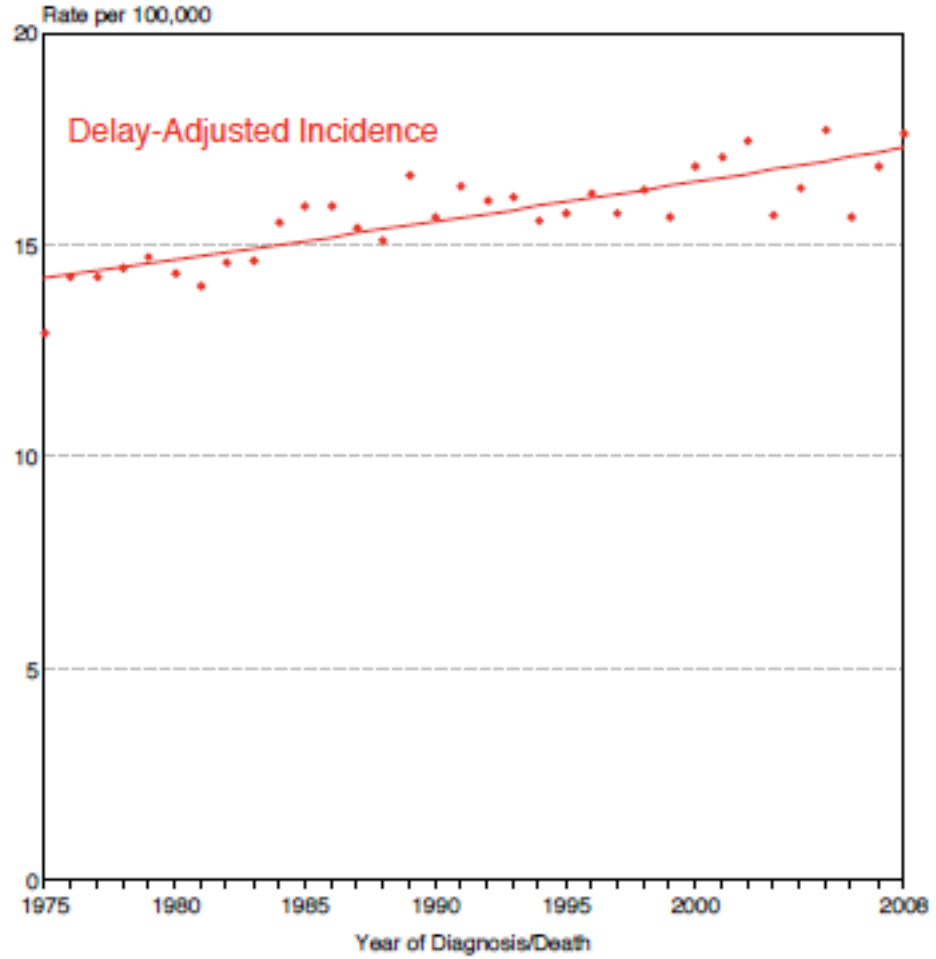
Some substances and mixtures evaluated by IARC as definite human carcinogens and that are occupational exposures, cont'd.

Metals and metal compounds		
Arsenic and arsenic compounds	Nonferrous metal smelting; production, packaging, and use of arsenic-containing pesticides; sheep dip manufacture; wool fiber production; mining of ores containing arsenic	Skin[d] Lung[d] Liver (angiosarcoma)[e]
Beryllium	Beryllium extraction and processing; aircraft and aerospace industries; electronics and nuclear industries; jewelers	Lung[d]
Cadmium and cadmium compounds	Cadmium-smelter workers; battery production workers; cadmium-copper alloy workers; dyes and pigments production; electroplating processes	Lung[d]
Chromium compounds, hexavalent	Chromate production plants; dyes and pigments; plating and engraving; chromium ferro-alloy production; stainless-steel welding; in wood preservatives; leather tanning; water treatment; inks; photography; lithography; drilling muds; synthetic perfumes; pyrotechnics; corrosion resistance	Lung[d] Nasal sinuses[e]
Selected nickel compounds, including combinations of nickel oxides and sulfides in the nickel refining industry	Nickel refining and smelting; welding	Lung[d] Nasal cavity and sinuses[d]
Wood and fossil fuels and their by-products		
Benzene	Production; solvents in the shoe production industry; chemical, pharmaceutical, and rubber industries; printing industry (rotogravure plants, bindery departments); gasoline additive	Leukemia[d]
Coal tars and pitches	Production of refined chemicals and coal tar products (patent-fuel); coke production; coal gasification; aluminum production; foundries; road paving and construction (roofers and slaters)	Skin[d] Lung[e] Bladder[e]

Source: Siemiatycki et al. Listing occupational carcinogens. Table 3. *Environmental Health Perspectives*. 112(15):1447-57, Nov 2004. http://www.ehponline.org/.

Figure 28.1

SEER Delay-Adjusted Incidence and US Mortality
All Childhood Cancers, Under 20 Years of Age
Both Sexes, All Races, 1975-2008



Source: SEER 9 areas and US Mortality Files (National Center for Health Statistics, CDC).
Rates are age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1103).
Regression lines are calculated using the Joinpoint Regression Program Version 3.5, April 2011,
National Cancer Institute.

Childhood Brain Cancer: Documented Links

- Ionizing radiation [Strong]
- Dichlorvos [Good]
- Lindane [Good]
- Pesticides [Good]
- Second-hand smoke [Good]
- Solvents [Good]

Source: Solomon G, Schettler T, Janssen S. "CHE Toxicant and Disease Database." Accessed 6-8-11: http://www.healthandenvironment.org/.

Childhood Leukemias: Documented Links

- Ionizing radiation [Strong]
- Carbon tetrachloride [Good]
- Chlorinated solvents [Good]
- Metal dusts [Good]
- Pesticides [Good]
- Secondhand smoke [Good]
- Trichloroethylene (TCE) [Good]

Source: Solomon G, Schettler T, Janssen S. "CHE Toxicant and Disease Database." Accessed 6-8-11: http://www.healthandenvironment.org/.

Non-Hodgkin's Lymphoma: Documented Links

- 1,3-butadiene [Strong]
- Benzene [Strong]
- Dioxins/TCDD [Strong]
- Formaldehyde [Good]
- Hair Dyes [Good]
- Herbicides, fungicides, insecticides [Good]
- Ionizing radiation [Good]
- PCBs [Good]
- Styrene [Good]
- Tetrachloroethylene (PCE) [Good]
- Trichloroethylene (TCE) [Good]

Source: Solomon G, Schettler T, Janssen S. "CHE Toxicant and Disease Database." Accessed 6-8-11: http://www.healthandenvironment.org/ and President's Cancer Panel, "Reducing Environmental Cancer Risk, What We Can Do Now." May, 2010.

President's Cancer Panel report

- 2008-2009 report on "Reducing Environmental Cancer Risk" released in May, 2010 (http://deainfo.nci.nih.gov/advisory/pcp/annualReports/index.htm)
- Critiqued current chemicals regulatory regime
  - Called environmental cancer burden "grossly underestimated"

Cancer Panel report con't.

- Recommended chemicals policy reform to make regulations more precautionary and prevention-oriented
- Recommended support for "Green chemistry initiatives, including process redesign . . ."
  - Urged careful study of new products to ensure short- and long-term safety

Reactions to Panel report

- Massive publicity in print and electronic media in 2010
  - Over 1 billion "impressions" in media and on-line newsletters, blogs
- Criticism by American Cancer Society, American Council on Science and Health
  - Asserted that attention would be taken off tobacco, diet and exercise

Next steps, 2011 and beyond

- Support for "Safe Chemicals Act of 2011" (S. 847), state initiatives
- Continued networking, advocacy and alternatives assessment