Avoidable Occupational and Environmental Causes of Cancer

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Global Cancer Incidence and Mortality

- 12.1 million new cases estimated in 2007 (5.4 million in developed countries, 6.7 million in developing countries)
  - Lung cancer is the leading site (excluding non-melanoma skin cancer), followed by breast cancer
- 7.6 million cancer deaths estimated in 2007 (2.9 million in developed countries, 4.7 million in developing countries)
  - Lung, followed by stomach and colo-rectal cancer

Incidence Percent Change between 1994 and 2003
Numbers (burden) vs Rates (risk)
All Ages

US Incidence estimates based on SEER age-specific rates applied to US population.
Burden is the change in the number of incidence cases between 1994 and 2003.
Risk is the change in the cancer incidence rates between 1994 and 2003.
*Ovary excludes borderline cases or histologies 8442, 8451, 8462, 8472, and 8473.
“Could you hurry and find a cure for cancer? That would be so much easier than prevention.”
### Table 20.—Proportions of cancer deaths attributed to various different factors

<table>
<thead>
<tr>
<th>Text section No.</th>
<th>Factor or class of factors</th>
<th>Percent of all cancer deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Best estimate</td>
</tr>
<tr>
<td>5.1</td>
<td>Tobacco</td>
<td>30</td>
</tr>
<tr>
<td>5.2</td>
<td>Alcohol</td>
<td>3</td>
</tr>
<tr>
<td>5.3</td>
<td>Diet</td>
<td>35</td>
</tr>
<tr>
<td>5.4</td>
<td>Food additives</td>
<td>&lt;1</td>
</tr>
<tr>
<td>5.5</td>
<td>Reproductive&lt;sup&gt;b&lt;/sup&gt; and sexual behav-</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>iour</td>
<td></td>
</tr>
<tr>
<td>5.6</td>
<td>Occupation</td>
<td>4</td>
</tr>
<tr>
<td>5.7</td>
<td>Pollution</td>
<td>2</td>
</tr>
<tr>
<td>5.8</td>
<td>Industrial products</td>
<td>&lt;1</td>
</tr>
<tr>
<td>5.9</td>
<td>Medicines and medical procedures</td>
<td>1</td>
</tr>
<tr>
<td>5.10</td>
<td>Geophysical factors&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3</td>
</tr>
<tr>
<td>5.11</td>
<td>Infection</td>
<td>10</td>
</tr>
<tr>
<td>5.12</td>
<td>Unknown</td>
<td>?</td>
</tr>
</tbody>
</table>

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.


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.”

International Agency for Research on Cancer (IARC)

Evaluations of agents, mixtures, and exposures (as of Jan., 2008)

Total agents evaluated over 900

- Carcinogenic to humans 102
- Probably carcinogenic to humans 69
- Possibly carcinogenic to humans 246
- Not classifiable 497
- Probably not carcinogenic to humans 1

Progress in dissecting signaling pathways has begun to lay out a circuitry that will likely mimic electronic integrated circuits in complexity and fineness, where transistors are replaced by proteins (e.g., kinases and phosphatases) and the electrons by phosphates and lipids, among others. In addition to the prototypical growth signaling circuit centered around Ras and coupled to a spectrum of extracellular cues, other reprogramming circuits transmit antigrowth and differentiation signals or mediate commands to live or die by apoptosis. As for the genetic component circuits, some known to be functionally altered are highlighted in red.
### A. Current Mechanistic Understanding

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

### B. 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 to 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.

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

<table>
<thead>
<tr>
<th>Substance or mixture</th>
<th>Occupation or industry in which the substance is founda</th>
<th>Site(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Physical agents</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 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<sup>d</sup>  
Leukemia<sup>d</sup>  
Lung<sup>d</sup>  
Liver<sup>d</sup>  
Thyroid<sup>d</sup>  
Others<sup>d</sup>  
Melanoma<sup>d</sup>  
Skin<sup>d</sup> |
| **Solar radiation**                            |                                                         |                  |
|                                               | Outdoor workers                                         |                  |
| **Respirable dusts and fibers**                |                                                         |                  |
| Asbestos                                       | Mining and milling; by-product manufacture; insulating; shipyard workers; sheet-metal workers; asbestos cement industry | Lung<sup>d</sup>  
Mesothelioma<sup>d</sup>  
Larynx<sup>e</sup>  
GI tract<sup>e</sup>  
Mesothelioma<sup>d</sup> |
| Erionite                                       | Waste treatment; sewage; agricultural waste; air pollution control systems; cement aggregates; building materials | Lung<sup>d</sup> |
| Silica, crystalline                            | Granite and stone industries; ceramics, glass, and related industries; foundries and metallurgical industries; abrasives; construction; farming | Lung<sup>d</sup> |
| Talc containing asbestiform fibers            | Manufacture of pottery, paper, paint, and cosmetics | Lung<sup>d</sup>  
Mesothelioma<sup>d</sup> |
| Talc containing asbestiform fibers            | 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 | Lung<sup>d</sup>  
Mesothelioma<sup>d</sup>  
Nasal cavities and paranasal sinuses<sup>d</sup> |

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

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
<th>Organs Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metals and metal compounds</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arsenic and arsenic compounds</td>
<td>Nonferrous metal smelting; production, packaging, and use of arsenic-containing pesticides; sheep dip manufacture; wool fiber production; mining of ores containing arsenic</td>
<td>Skin\textsuperscript{d}, Lung\textsuperscript{d}, Liver (angiosarcoma)\textsuperscript{e}</td>
</tr>
<tr>
<td>Beryllium</td>
<td>Beryllium extraction and processing; aircraft and aerospace industries; electronics and nuclear industries; jewelers</td>
<td>Lung\textsuperscript{d}</td>
</tr>
<tr>
<td>Cadmium and cadmium compounds</td>
<td>Cadmium-smelter workers; battery production workers; cadmium-copper alloy workers; dyes and pigments production; electroplating processes</td>
<td>Lung\textsuperscript{d}</td>
</tr>
<tr>
<td>Chromium compounds, hexavalent</td>
<td>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</td>
<td>Lung\textsuperscript{d}, Nasal sinuses\textsuperscript{e}</td>
</tr>
<tr>
<td>Selected nickel compounds, including combinations of nickel oxides and sulfides in the nickel refining industry</td>
<td>Nickel refining and smelting; welding</td>
<td>Lung\textsuperscript{d}, Nasal cavity and sinuses\textsuperscript{d}</td>
</tr>
<tr>
<td>Wood and fossil fuels and their by-products</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzene</td>
<td>Production; solvents in the shoe production industry; chemical, pharmaceutical, and rubber industries; printing industry (rotogravure plants, bindery departments); gasoline additive</td>
<td>Leukemia\textsuperscript{d}</td>
</tr>
<tr>
<td>Coal tars and pitches</td>
<td>Production of refined chemicals and coal tar products (patent-fuel); coke production; coal gasification; aluminum production; foundries; road paving and construction (roofers and slaters)</td>
<td>Skin\textsuperscript{d}, Lung\textsuperscript{e}, Bladder\textsuperscript{e}</td>
</tr>
</tbody>
</table>

IARC: Examples of agents classified as human carcinogens (not necessarily found in occupational settings)

- Alcohol - in alcoholic drinks
- Arsenic - in drinking water, wood preservatives, pesticides
- Benzene - in vehicle exhaust, cigarette smoke, some pesticides, around refineries
- Cadmium - as a stabilizer in PVC products, in re-chargeable batteries & phosphate fertilizers
- Dioxin - combustion of chlorinated plastics, wood preservatives
- Formaldehyde (IIA) - in resins and common household materials and products
- Radiation (ionizing) - in radioactive material, high-voltage equipment, around nuclear reactors
- Vinyl chloride - in polyvinyl resins and products
Figure XXVIII-1

SEER Delay-Adjusted Incidence and US Mortality
All Childhood Cancers, Under 20 Years of Age
Both Sexes, All Races, 1975-2003

Rate per 100,000

Delay-Adjusted Incidence

Mortality

Year of Diagnosis/Death


Source: SEER 9 areas and NCHS public use data file for the total US.
Rates are age-adjusted to the 2000 US Std Population (10 age groups - Census P25-1103).
Regression lines are calculated using the Joinpoint Regression Program Version 3.1, April 2008, National Cancer Institute.
Melanoma: Documented Links

- UV radiation [Strong]

Thyroid Cancer: Documented Links

- Ionizing radiation [Strong]
- ethylene thiourea (ETU) [Good]

Non-Hodgkin’s Lymphoma: Documented Links

- 1,3-butadiene [Strong]
- Benzene [Strong]
- Dioxins/TCDD [Strong]
- 2,4-D [Good]
- Agent Orange [Good]
- Aldrin [Good]
- Aromatic amines [Good]
- Carbon tetrachloride [Good]
- Chlorophenols [Good]
- Creosotes [Good]
- DDT/DDE [Good]
- Dicamba [Good]
- Dichlorvos [Good]
- Ionizing radiation [Good]
- MCPA [Good]
- Organochlorine pesticides [Good]
- Organophosphates [Good]
- PCBs [Good]
- Phenoxyacetic acid herbicides [Good]
- Solvents [Good]
- Tetrachloroethylene (PCE) [Good]
- Trichloroethylene (TCE) [Good]

Breast Cancer: **Documented Links**

- Active smoking [Strong]
- Estrogens/DES [Strong]
- Ethyl alcohol (ethanol) [Strong]
- Ionizing radiation [Strong]
- Secondhand smoke [Strong?]  
- Aromatic amines [Good]
- Ethylene oxide [Good]
- PAHs [Good]
- PCBs [Good]
- Progestins [Good]
- Solvents [Good]
- tetrachloroethylene (PCE) [Good]

New Endicott (New York) IBM study

- The original IBM manufacturing plant
  - Manufactured typewriters, guns, clocks, printed circuit boards
  - Exposures included asbestos, benzene, tetrachloroethylene, trichloroethylene, etc.
- Widespread community groundwater contamination with TCE
  - IBM sold the plant in 2002
Endicott mortality study results

- Melanoma PCMR=367; 95% CI: 119,856*
- Lymphoma (males) PCMR=220; 95% CI: 101,419*
- Kidney (males) PCMR=165; 95% CI: 45,421
- Brain (males) PCMR=190; 95% CI: 52,485
- Breast (females) PCMR=126; 95% CI: 34,321
  - * statistically significant (p<.05)
  - Note: These results are very similar to the pattern seen in IBM San Jose (California) workers in a study published in Environmental Health in October, 2006 (see www.ehjournal.net)
“Environmental carcinogenesis is the newest and one of the most ominous of the endproducts of our industrial environment. Though its full scope and extent are still unknown..., enough is known to make it obvious that extrinsic carcinogens present a very immediate and pressing problem in public and individual health.”

-- Wilhelm Hueper, senior scientist
U.S. National Cancer Institute
*Environmental Cancer*, 1948
"If the lessons from the tobacco control experience are applied in other areas, even greater gains can be made in cancer prevention."

-- Canadian Cancer Statistics 2005
The Need to Act on What We Know

“It is time to start pursuing alternative paths. From the right to know and the duty to inquire flows the obligation to act.”

-- Sandra Steingraber
Living Downstream, 1997
Environmental and Occupational Causes of Cancer
A Review of Recent Scientific Literature

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A Way Forward

- Blue-green alliances
- Beyond REACH
- Alternatives research and green chemistry
- Making peace with the planet as the guiding principle