Heredity? Behaviors? Other Factors?

Colon Cancer
(Number of new cases per 100,000 people)

Stomach Cancer
(Number of new cases per 100,000 people)
Tobacco Use and Cancer

Some Cancer-Causing Chemicals in Tobacco Smoke

- aminostilbene
- arsenic
- benz[a]anthracene
- benz[a]pyrene
- benzene
- benzo[b]fluoranthene
- benzo[c]phenanthrene
- cadmium
- chrysene
- dibenz[a,c]anthracene
- dibenzo[a,e]fluoranthene
- dibenz[a,h]acridine
- dibenz[a,j]acridine
- dibenzo[c,g]carbazone
- N-dibutylnitrosamine
- 2,3-dimethylchrysene
- indeno[1,2,3-c,d]pyrene
- S-methylchrysene
- S-methylfluoranthene
- alpha-naphthylamine
- nickel compounds
- N-nitrosodimethylamine
- N-nitrosomethyleneimine
- N-nitrosodiethylamine
- N-nitrosonornicotine
- N-nitrosoanabasine
- N-nitrosopiperidine
- polonium-210
High-Strength Radiation

Leukemia Incidence

X-ray Dose (atomic radiation)

High

Low

Least

Most

National Cancer Institute
Lag Time

20-Year Lag Time Between Smoking and Lung Cancer

Cigarette consumption (men)

Cigarettes smoked per person per year

Lung cancer (men)

Lung Cancer Deaths (per 100,000 people)

Year

1900 1920 1940 1960 1980
Viruses

Cancer-linked virus

Virus inserts and changes genes for cell growth
**Examples of Human Cancer Viruses**

<table>
<thead>
<tr>
<th>Virus</th>
<th>Type of Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epstein-Barr virus</td>
<td>Burkitt’s lymphoma</td>
</tr>
<tr>
<td>Human papillomavirus</td>
<td>Cervical cancer</td>
</tr>
<tr>
<td>Hepatitis B virus</td>
<td>Liver cancer</td>
</tr>
<tr>
<td>Human T-cell lymphotrophic virus</td>
<td>Adult T-cell leukemia</td>
</tr>
<tr>
<td>Kaposi’s sarcoma-associated herpesvirus</td>
<td>Kaposi’s sarcoma</td>
</tr>
</tbody>
</table>
AIDS and Kaposi’s Sarcoma

Without disease

HIV infection

Depressed immune system

KSHV infection

Kaposi’s sarcoma
Bacteria and Stomach Cancer

Patient's tissue sample

H. pylori
Heredity and Cancer

All Breast Cancer Patients

- Inherited factor(s)
- Other factor(s)
### Heredity Can Affect Many Types of Cancer

**Inherited Conditions That Increase Risk for Cancer**

<table>
<thead>
<tr>
<th>Name of Condition</th>
<th>Type of Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hereditary retinoblastoma</td>
<td>Retinoblastoma</td>
</tr>
<tr>
<td>Xeroderma pigmentosum</td>
<td>Skin</td>
</tr>
<tr>
<td>Wilms’ tumor</td>
<td>Kidney</td>
</tr>
<tr>
<td>Li-Fraumeni syndrome</td>
<td>Sarcomas, brain, breast, leukemia</td>
</tr>
<tr>
<td>Familial adenomatous polyposis</td>
<td>Colon, rectum</td>
</tr>
<tr>
<td>Paget’s disease of bone</td>
<td>Bone</td>
</tr>
<tr>
<td>Fanconi’s aplastic anemia</td>
<td>Leukemia, liver, skin</td>
</tr>
</tbody>
</table>
Genetic Testing
Cancer Risk and Aging

Number of Cancer Cases (per 100,000 people)

Age of Person (in years)

Cancer Risk and Aging

Colon

Breast

National Cancer Institute
Genes and Cancer

- Viruses
- Chemicals
- Radiation

Chromosomes are DNA molecules

Heredit
DNA Mutation

DNA

CAAGCTAACT
Normal gene

CAAGCACACT
Single base change

CAAGGCTACCT
Additions

CAAGAACT
Deletions

[Image: DNA structure showing different types of mutations]
Proto-Oncogenes and Normal Cell Growth

Normal Growth-Control Pathway

- Growth factor
- Receptor
- Signaling enzymes
- Transcription factors
- DNA
- Cell nucleus
- Cell proliferation

Source: National Cancer Institute
Oncogenes are Mutant Forms of Proto-Oncogenes

Inactive growth factor receptor

Inactive intracellular signaling protein

Signaling protein from active oncogene

Activated gene regulatory protein

Transcription

Cell proliferation driven by internal oncogene signaling
Go to http://www.hhmi.org/biointeractive/, then at the top of the screen under the Topic tab, choose cancer with the drop down menu at the top, and scroll down to:

**Cancer as a Genetic Disease**, lecture.

The first half (segments 1-12) is about how cancer is defined as a genetic disease and shows the difference between proto-oncogenes and oncogenes using the Rous sarcoma virus example. Tumor suppressor genes are revisited in terms of dominant and recessive mutations in cancer. (22 minutes, 10 seconds).

The second half (segments 18-26) is about using drug therapy (Gleevec) to treat Chronic Myeloid Leukemia (CML) and how to treat patients with Gleevec-resistant CML (21 minutes, 27 seconds).
Cause of Chronic Myeloid Leukemia (CML)

Example: Translocation of \textit{Bcr-Abl} Genes

http://www.cancer.gov/cancertopics/understandingcancer/cancergenomics/AllPages
Tumor Suppressor Genes

Normal cell

Remove or inactivate tumor suppressor genes

Cancer cell

Mutated/inactivated tumor suppressor genes

Normal genes prevent cancer

Damage to both genes leads to cancer

National Cancer Institute
Tumor Suppressor Protein Complexed with DNA

Tumor Suppressor Genes Act Like a Brake Pedal

Growth factor

Receptor

Signaling enzymes

Transcription factors

DNA

Cell nucleus

Cell proliferation

Tumor Suppressor Gene Proteins

INHIBIT

INHIBIT

INHIBIT

INHIBIT
p53 Tumor Suppressor Protein Triggers Cell Suicide

Normal cell → Excessive DNA damage → Cell suicide (Apoptosis)
Cancer Tends to Involve Multiple Mutations

Benign tumor cells grow only locally and cannot spread by invasion or metastasis.

Malignant cells invade neighboring tissues, enter blood vessels, and metastasize to different sites.

Time
- Mutation inactivates suppressor gene
- Cells proliferate
- Mutations inactivate DNA repair genes
- Proto-oncogenes mutate to oncogenes
- More mutations, more genetic instability, metastatic disease
### Mutations and Cancer

#### Genes Implicated in Cancer

<table>
<thead>
<tr>
<th>The prime suspects</th>
<th>But</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mutations in:</td>
<td>Other mutations also occur in:</td>
</tr>
<tr>
<td>Oncogenes</td>
<td>Cell death genes</td>
</tr>
<tr>
<td>Tumor suppressor genes</td>
<td>Cell signaling genes</td>
</tr>
<tr>
<td>DNA repair genes</td>
<td>Cell cycle checkpoint genes</td>
</tr>
<tr>
<td></td>
<td>Cellular senescence genes</td>
</tr>
<tr>
<td></td>
<td>Cellular differentiation genes</td>
</tr>
<tr>
<td></td>
<td>Metastasis/invasion genes</td>
</tr>
</tbody>
</table>
|                    | Carcinogen  
|                    | – activating genes  
|                    | – deactivating genes |

*Image courtesy of [National Cancer Institute](https://www.cancer.gov)*
Cancer Tends to Corrupt Surrounding Environment

Growth factors = proliferation

Invasive

Matrix

Fibroblasts, adipocytes

Proteases

Blood vessel

Cytokines

Cytokines, proteases = migration & invasion
The Immune System and the Nervous System

Brain

Thymus

Neuroendocrine and autonomic pathways

Immunotransmitters (feedback, regulation and modulation)

Bone marrow

Thymosins

T cell

Lymphokines

Monokines

Macrophage

B cell
Cancer Prevention

- Carcinogenic chemicals
- Carcinogenic radiation
- Cancer viruses or bacteria
Avoid Tobacco

Lung Cancer Risk Increases with Cigarette Consumption

- Lung Cancer Risk
- 15x
- 10x
- 5x
- Non-smoker

Cigarettes Smoked per Day
- 0
- 15
- 30

National Cancer Institute
Protect Yourself From Excessive Sunlight
Limit Alcohol and Tobacco

Combination of Alcohol and Cigarettes Increases Risk for Cancer of the Esophagus

Risk Increase

- 40x
- 30x
- 20x
- 10x

Alcoholic Drinks Consumed per Day
- 0
- 4+
- 0
- 4+

Packs of Cigarettes Consumed per Day
- 0
- 0
- 2+
- 2+

AND
Diet: Limit Fats and Calories

Correlation Between Meat Consumption and Colon Cancer Rates in Different Countries

Number of Cases (per 100,000 people)

Grams (per person per day)

Countries: USA, U.S.A., G.B., CAN, CAN, DEN, N.Z., NETH, GERMANY, ICE, SWE, NOR, ISR, FIN, PR., POL, HUNG, YUG, JAPAN, CHILE, ROM, NIG, COL, JAM, NIG.
Diet: Consume Fruits and Vegetables
Avoid Cancer Viruses

HPV Infection Increases Risk for Cervical Cancer

Cervical Cancer Risk

High

Low

Noninfected women

Women infected with HPV
## Avoid Carcinogens at Work

### Some Carcinogens in the Workplace

<table>
<thead>
<tr>
<th>Carcinogen</th>
<th>Occupation</th>
<th>Type of Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic</td>
<td>Mining, pesticide workers</td>
<td>Lung, skin, liver</td>
</tr>
<tr>
<td>Asbestos</td>
<td>Construction workers</td>
<td>Lung, mesothelioma</td>
</tr>
<tr>
<td>Benzene</td>
<td>Petroleum, rubber, chemical workers</td>
<td>Leukemia</td>
</tr>
<tr>
<td>Chromium</td>
<td>Metal workers, electroplaters</td>
<td>Lung</td>
</tr>
<tr>
<td>Leather dust</td>
<td>Shoe manufacturing</td>
<td>Nasal, bladder</td>
</tr>
<tr>
<td>Naphthylamine</td>
<td>Chemical, dye, rubber workers</td>
<td>Bladder</td>
</tr>
<tr>
<td>Radon</td>
<td>Underground mining</td>
<td>Lung</td>
</tr>
<tr>
<td>Soots, tars, oils</td>
<td>Coal, gas, petroleum workers</td>
<td>Lung, skin, liver</td>
</tr>
<tr>
<td>Vinyl chloride</td>
<td>Rubber workers, polyvinyl chloride manufacturing</td>
<td>Liver</td>
</tr>
<tr>
<td>Wood dust</td>
<td>Furniture manufacturing</td>
<td>Nasal</td>
</tr>
</tbody>
</table>

Artwork by Jeanne Kelly © 2004

National Cancer Institute
Is There a Cancer "Epidemic"?

**MYTH**

The Daily News 5¢

Cancer Rates Reach Epidemic Proportions

**FACT**

Colon Cancer Deaths (per 100,000 men, age adjusted)

<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Rate</td>
<td>40</td>
<td>30</td>
<td>20</td>
<td>10</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>

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National Cancer Institute