Constituents of Tobacco Smoke

- The list of ingredients in tobacco smoke includes over 4,000 chemical compounds

- About half are found naturally in the tobacco leaf and half are created by chemical reactions when tobacco is burned

- Some are introduced during the curing process; others are added by manufacturers to impart a distinctive flavor or quality to their product
Health Effects of Active Smoking: Jon Samet, MD, MS

Constituents of Tobacco Smoke

Some Compounds Found in Smokers’ Blood

- Carbon monoxide
- Benzene
- Nicotine
- Cyanide (thiocyanate)
- Toluene
- N-hexane
- Ethylbenzene
- Xylenes
- Elevated concentrations of PAH and DNA adducts
Early Health Warnings

- 1938: Dr. Raymond Pearl reports smokers do not live as long as nonsmokers
- 1939: Franz Hermann Muller of Germany finds strong dose-response between smoking and lung cancer

1950: Three Key Case-Control Studies

- Morton Levin publishes a study linking smoking and lung cancer in *JAMA*
- Ernst L. Wynder and Evarts A. Graham publish study in *JAMA* in which 96.5% of lung cancer patients interviewed were smokers
- Richard Doll and Bradford Hill publish study in *BMJ* finding that heavy smokers are 50 times more likely to get lung cancer; follow-up in 1954
Surgeon General’s First Report on Smoking and Health

- Advisory committee concluded that cigarette smoking is:
  - A cause of lung and laryngeal cancer in men
  - A probable cause of lung cancer in women
  - The most important cause of chronic bronchitis
  - “A health hazard of sufficient importance to warrant appropriate remedial action”


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Tobacco smoking and tobacco smoke are carcinogenic to humans (Group 1)


Most Recent Scientific Evidence: Active Smoking

**Mortality in Current Smokers and Never Smokers**

Relative Risks for Mortality in Current Smokers vs. Never Smokers: CPS I and II

<table>
<thead>
<tr>
<th>Underlying cause of death</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CPS-I</td>
<td>CPS-II</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>11.9</td>
<td>23.2</td>
</tr>
<tr>
<td>COPD</td>
<td>9.3</td>
<td>11.7</td>
</tr>
<tr>
<td>CHD</td>
<td>1.7</td>
<td>1.9</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.3</td>
<td>1.9</td>
</tr>
<tr>
<td>Total mortality</td>
<td>1.7</td>
<td>2.3</td>
</tr>
</tbody>
</table>

CPS-I Cancer Prevention Study (1959-1965); CPS-II Cancer Prevention Study (1982-1986)
CHD = coronary heart disease; COPD = chronic obstructive pulmonary disease

Source: adapted by CTLT from Thun et al. (1997).

**Global Number of Deaths**

Number of Deaths: Developed and Developing Countries

- Arises from airways and alveoli
- Often asymptomatic but symptoms may include the following: chronic cough, hemoptysis, fever, pain
- Treated by surgery, radiation, and chemotherapy
- Some occupational agents are synergistic
- One-year U.S. survival rate: 40.5%
- Five-year U.S. survival rate: 14.2%

Causes of Lung Cancer

- Smoking
- Occupational exposures
  - Radon
  - Asbestos
  - Chloromethyl ethers
- Radiation
- Air pollution
- Diet and nutrition

Male Lung Cancer Mortality Rate per 100,000

Source: adapted by CTLT from GLOBOCAN (2002). IARC.
Health Effects of Active Smoking: Jon Samet, MD, MS

Female Lung Cancer Mortality Rate per 100,000

Source: adapted by CTLT from GLOBOCAN (2002). IARC.

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Relative Risk of Lung Cancer by Cigarettes per Day

Image source: adapted by CTLT from Trial Exhibit 30,092, State of Minnesota and Blue Cross and Blue Shield of Minnesota against the U.S. tobacco industry.

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Risks Vary with Smoking Patterns

- Duration of smoking—age of starting
- Inhaling
- Number of cigarettes smoked
- Number of years since stopping
- Types of cigarettes smoked
- Other exposures

Laryngeal Cancer

- Arises from vocal cords
- Symptoms: hoarseness, cough, pain, hemoptysis
- Treated by surgery and radiation
- Alcohol and cigarettes are synergistic in increasing risk
- One-year U.S. survival rate: 88.1%*
- Five-year U.S. survival rate: 65.5%*

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Laryngeal Cancer: Relative Risk in U.S. White Males


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Laryngeal Cancer: Turkey

Source: adapted by CTLT from Dosemeci et al. (1997).

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Oral Cancer

- Squamous cell cancer that arises in the mouth and throat
- Pre-cancerous lesions are called leukoplakia
- Symptoms—lumps, pain, bleeding, dysphagia
- Surgical removal can cure with “high aesthetic cost”
- One-year U.S. survival rate: 81.5%*
- Five-year U.S. survival rate: 53.2%*


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Oropharyngeal Cancer: A U.S. Case-Control Study

Source: adapted by CTLT from Blot et al. (1992).

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Esophageal Cancer

- Most are squamous cell cancers, but adenocarcinoma is increasing
- Symptoms—dysphagia, pain
- One-year U.S. survival rate: 43.3%*
- Five-year U.S. survival rate: 14.8%*

*Source: U.S. National Cancer Institute.

Esophageal Cancer: Case-Control Study in South Africa

Source: adapted by CTLT from Castellsague et al. (1999).
Cancer of the Pancreas

- Adenocarcinoma is the principal type
- Late detection because of location and symptoms
- Symptoms include jaundice, pain, and weight loss
- One-year U.S. survival rate: 19.9%*
- Five-year U.S. survival rate: 4.6%*

*Source: Ries et al. (2000).

Source: adapted by CTLT from Silverman et al. (1994).

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Liver Cancer Mortality Rate per 100,000 Men

Source: adapted by CTLT from GLOBOCAN. (2002). IARC.

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Liver Cancer Mortality Rate per 100,000 Women

Source: adapted by CTLT from GLOBOCAN. (2002). IARC.

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Liver Cancer

- Liver cirrhosis, chronic hepatitis, aflatoxins, and smoking are some of the risk factors.
- Symptoms include—pain on the right side of the stomach, breast swelling in men, weight loss, jaundice, and feeling very full after eating a meal.
- Treatment includes surgery, chemotherapy, and/or radiation therapy.
- Mortality increases with age, especially for males.
- Five-year U.S. survival rate: 10.5%*


Liver Cancer: Taiwan

Renal Cancer

- Renal cancer
  - Adenocarcinoma tends to spread early while cancer of the renal pelvis results in blockage of urine and bleeding
  - One-year U.S. survival rate: 77.3%*
  - Five-year U.S. survival rate: 60.8%*

- Cancer of the urinary bladder
  - Symptom—bleeding can be fatal if metastasis occurs
  - Urine of smokers contains tobacco-specific carcinogens and has a higher level of mutagenic activity
  - One-year U.S. survival rate: 90%*
  - Five-year U.S. survival rate: 80.4%*


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Chronic Obstructive Pulmonary Disease (COPD)

- COPD is a diagnostic label that refers to the permanent loss of lung function that occurs in some smokers
  - Results in shortness of breath, impaired exercise capacity, and the frequent need for oxygen

- Emphysema refers to permanent dilation and destruction of the alveoli

- Chronic bronchitis refers to chronic mucus hypersecretion

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Cardiovascular Diseases

- Includes the following:
  - Cerebral vascular disease (stroke)
  - Coronary heart disease (myocardial infarction, angina pectoris, and sudden cardiac death)
  - Arteriosclerotic peripheral vascular disease (including abdominal aortic aneurysm)

Cerebrovascular Disease

- Two major types
  - Cerebral infarction
  - Cerebral hemorrhage (subarachnoid, parenchymal)
Atherosclerotic Peripheral Vascular Disease

- Smoking affects the blood vessels, making them narrower and decreasing blood flow
- Consequences include:
  - Intermittent claudication
  - Abdominal aortic aneurysm

Peptic Ulcer Disease

- Ulcers of the lining of the stomach and the duodenum
- *H. pylori* is the main cause— but smoking contributes
- Symptoms: pain and bleeding, high morbidity
- Smoking increases risk and may delay healing
- Morbidity and mortality declining
Health Effects of Active Smoking: Jon Samet, MD, MS

Smoking and Tuberculosis

<table>
<thead>
<tr>
<th>Induration size</th>
<th>Pooled RR*</th>
<th>OR† (95% CI‡)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5mm</td>
<td>2.08</td>
<td>1.53-2.83</td>
</tr>
<tr>
<td>10 mm</td>
<td>1.83</td>
<td>1.49-2.23</td>
</tr>
</tbody>
</table>

* Studies conducted in five countries: the U.S., Spain, South Africa, Pakistan, and Vietnam
† RR: relative risk
‡ OR: odds ratio
CI: confidence interval

Source: adapted by CTLT from Lin et al. (2006).

Cervical Cancer

- 2004 Surgeon General’s Report conclusions:
  - “The evidence is sufficient to infer a causal relationship between smoking and cervical cancer”

- Higher risk for women who smoke and have human papillomavirus (HPV):
  - Smoking was associated with risk for incident low-grade squamous intraepithelial lesion development
    - Relative hazard = 1.67 (95% CI, 1.12-2.48) in a prospective study of HPV-infected women (Moscicki et al. [2001])
  - Risk increases with amount of cigarettes smoked

### Cervical Cancer Risk by Amount of Cigarettes Smoked

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Number of cases</th>
<th>OR† (95% CI‡)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>23</td>
<td>1.0 (referent)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>17</td>
<td>3.3 (1.6 to 6.7)</td>
</tr>
<tr>
<td>Current smoker, &lt;1 pack per day</td>
<td>15</td>
<td>2.9 (1.4 to 6.1)</td>
</tr>
<tr>
<td>Current smoker, ≥1 pack per day</td>
<td>13</td>
<td>4.3 (2.0 to 9.3)</td>
</tr>
</tbody>
</table>

*CIN3*: cervical intraepithelial neoplasia grade 3  
† OR: odds ratio  
‡ CI: confidence interval

Source: adapted by CTLT from Castle et al. (2002).

### Most Recent Scientific Evidence: Active Smoking

**Cancer**
- Leukemia, 2002
- Nasal & oral pharynx, 1982
- Larynx, 1980
- Esophagus, 1982
- Lung, 1964
- Liver, 2002
- Stomach, 2002
- Pancreas, 1990
- Kidney, 1982
- Cervix (women), 2002
- Ureter, 1990
- Bladder, 1990

**Other diseases**
- Stroke, 1983
- Cataract, 2004
- Diminished health, 2004
- Coronary heart disease, 1979
- Atherosclerotic peripheral vascular disease, 1983
- Aortic aneurysm, 1983
- Chronic obstructive pulmonary disease (COPD), 1964

“That so many diseases—major and minor—should be related to smoking is one of the most astonishing findings of medical research in this century; less astonishing perhaps than the fact that so many people have ignored it.”

— Sir Richard Doll, 1912-2005