**Cancer in the United States, 2004**

![Image of cancer survival rates](image)

**Five-year Cancer Survival Rates (%)**

- **US 1974-1998**

<table>
<thead>
<tr>
<th>Year</th>
<th>Prostate</th>
<th>Lung</th>
<th>Colon</th>
<th>Breast</th>
</tr>
</thead>
<tbody>
<tr>
<td>1974-1976</td>
<td>70</td>
<td>75</td>
<td>85</td>
<td>80</td>
</tr>
<tr>
<td>1983-1985</td>
<td>80</td>
<td>85</td>
<td>90</td>
<td>90</td>
</tr>
<tr>
<td>1992-1998</td>
<td>90</td>
<td>95</td>
<td>95</td>
<td>95</td>
</tr>
</tbody>
</table>

Source: CA Cancer J Clin 2000;50:7-33

**Lung Cancer Risks**

- **Cigarette Smoking**
  - Environmental Tobacco Smoke
- **Other Carcinogens**
  - Asbestos, Arsenic, Radon,
  - Bis(chloromethyl) ether, Chromium, Foundry fumes, nickel, mustard gas, coke oven emissions
- **Air Pollution** (foundries, diesel exhaust)
- **Family History**
- **Diet** (Vitamins A, C, E and selenium “protective”)

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**The Scheme:**

**From Nicotine Addiction to Lung Cancer**

- **Cigarette smoking**
- **Metabolic Activation**
  - eg. Cytochrome P450
- **Field Carcinogenesis**

![Diagram of the scheme](image)

Modified from Hacht JNCI; 1999

**Smoking Prevalence Rates, US**

![Image of smoking prevalence rates](image)

- **Male**
- **Female**

Source: Surgeon General’s Report

Garfinkel, Prev Med 26:447
### Percentage of High School Students Who Reported Current Cigarette Smoking

![Graph showing percentage of high school students who reported current cigarette smoking over time.](image)

Youth Behavior Survey, MMWR 2000; 49

### Differential Diagnosis

- **Benign**
  - Granuloma
  - Hamartoma
- **Malignant**
  - Metastasis
  - Primary Lung Ca
    - Small Cell
    - Carcinoid
    - Non-small Cell
    - Adenocarcinoma
    - Squamous
    - Large Cell

### Risk of lung cancer, men vs. women

<table>
<thead>
<tr>
<th>Pack-years</th>
<th>MALES</th>
<th>FEMALES</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>1-19</td>
<td>2.4 (1.4-4.1)</td>
<td>6.8 (4.1-11.4)</td>
</tr>
<tr>
<td>20-39</td>
<td>5.6 (3.6-8.7)</td>
<td>11.2 (7.5-16.8)</td>
</tr>
<tr>
<td>40-49</td>
<td>11.6 (7.7-17.6)</td>
<td>21.4 (14.3-32.3)</td>
</tr>
<tr>
<td>&gt;50</td>
<td>13.8 (9.2-20.9)</td>
<td>32.7 (19.0-56.2)</td>
</tr>
</tbody>
</table>

Relative risk for developing lung cancer is 1.25 for women for any "dose" of tobacco.

Zang, JNCI 88:183, 1996

### Presentation of Lung Cancer

- **Local Symptoms**
  - Cough
  - Dyspnea
  - Hemoptysis
  - Chest Pain
  - SVC Syndrome
  - Wheezing
- **Systemic Symptoms**
  - Constitutional
  - Skeletal
  - Clubbing
  - Hypertrophic Pulmonary Osteoarthropathy
  - Endocrine
    - SIADH (sclc)
    - Hypercalcemia (squamous)
    - Cushings Syndrome (sclc)
  - Neurologic
    - Horner's Syndrome
  - Eaton-Lambert syndrome (sclc)
  - Vascular
    - Thrombophlebitis, DIC

### Lung tumors - Benign

- The majority of pulmonary neoplasms are malignant
- Benign tumors/lesions
  - Hamartoma (most common)
  - Mesenchymal- leiomyoma, lipoma, chondroma (all unusual)
  - Alveolar adenoma (rare)

### Pathologic diagnosis: specimen types

- Transbronchial biopsy
- Transthoracic needle biopsy
- Cytology
  - Bronchial brushing
  - Lavage
  - Aspiration (transthoracic or transbronchial)
- Thoracotomy/VATS
Hamartoma
Likely a misnomer as these are probably true benign neoplasms, with common chromosomal abnormality (6p21 or 12q14-15).

Squamous precursors
- Squamous metaplasia, dysplasia and carcinoma in situ in lung progresses in a sequence similar to the changes described in the head and neck and cervix.
- Koilocytosis is not common; this HPV viral cytopathic change is seen in papillomatosis of larynx and trachea (HPV 6/11)

Metaplasia, dysplasia and invasive carcinoma sequence

Diffuse Idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH)
- Bronchiolar proliferation of neuroendocrine cells
- RARE as a disease that can cause severe obstruction, simulating obstructive bronchiolitis
- More common as an incidental finding
- When these cells go through airway wall, called carcinoid tumorlets (up to 0.5cm)
Atypical adenomatous hyperplasia

- Focal, 5.0 mm or less, with defined borders
- Alveoli lined by cuboidal to low columnar cells with variable atypia
- Alveolar walls may be slightly thickened
- Non-mucinous
- Clinical significance unclear (?time to progression to carcinoma)

Small cell carcinoma

- Usually hilar/central tumor
- The majority have extrapulmonary spread at time of presentation.
- Only 5% present as early stage disease.

Small cell carcinoma

- High grade tumor
- Small cells with high nuclear to cytoplasmic ratio
- Nuclear molding with stippled, salt and pepper chromatin
- Frequent mitosis and apoptosis
- “Crush” artifact - very fragile cells
- Neuroendocrine differentiation can be demonstrated by electron microscopy and immunohistochemistry (few neurosecretory granules due to poor differentiation)
Small Cell

Lung Tumor Classification

Malignant epithelial tumors

- Small cell carcinoma
- Non small cell carcinoma
- Carcinoids
  - Adenocarcinoma
  - Squamous Ca
  - Large cell CA
- Atypical carcinoids
  - Bronchioloalveolar
  - Various subtypes
  - Various subtypes
  - Various subtypes

Adenocarcinoma

- Most often a peripheral tumor
- Many are near pleura and cause pleural puckering.
- Cut surface can be mucoid or firm, depending on degree of fibrosis and mucin production
- Small tumors can be associated with lymph node and distant metastasis.

Adenocarcinoma

- Histologic varieties are multiple, including solid, acinar, papillary, mucinous types even within the same tumor
- Rarer types include signet ring morphology
- Differentiation can recapitulate goblet cell, Clara cell or type II pneumocyte differentiation
- Bronchial glands can produce a distinct subtype mimicking salivary gland type tumors
  - These unusual tumors are central and in younger patients
**Adenocarcinoma - Bronchioloalveolar**

- Distinct morphologic and clinical variant
- Grows along pre-existing alveoli and terminal bronchioles without stromal invasion
- Grossly can form a nodule, but can also produce diffuse disease mimicking pneumonia
- Can be mucinous or non-mucinous.
- Often multifocal

**Adenocarcinoma/"BAC features"**

**Combined in situ and invasive carcinoma**

**Malignant tumors - classification**

- **Lung Tumor Classification**
  - Malignant epithelial tumors
- **Small cell carcinoma**
- **Non small cell carcinoma**
- **Carcinoids**
  - Atypical carcinoids
- **Adenocarcinoma**
- **Squamous Ca**
- **Large cell CA**
- **Bronchioloalveolar**
  - Various subtypes
**Squamous carcinoma**

- Usually of bronchogenic origin; however can also arise from peripheral areas of squamous metaplasia
- Frequently have central necrosis
- Faster doubling time than adenocarcinoma; often larger at presentation
- Metastasis in relation to tumor size may occur later than adenocarcinoma

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**Large cell carcinoma**

- This subtype shows no differentiation towards either squamous or adenocarcinoma
- Aggressive tumors with poor prognosis
- If subjected to ultrastructural examination, many of these tumors show either glandular or squamous differentiation.
- Nevertheless, these tumors are separated out because of their high grade and poor prognosis

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**Carcinoids**

- Malignant neoplasm of neuroendocrine cell origin
- Can be central or peripheral; central lesions can cause bronchial obstruction
- Project into bronchial lumen but often have intact mucosa above them (grow under the mucosa)
- Typical carcinoids are low grade malignancies; atypical carcinoids (mitoses and necrosis) are intermediate grade when compared to non-small cell carcinomas
Endobronchial carcinoid

Carcinoids

- Histologic features
  - Nests and cords surrounded by delicate stroma
  - Uniform cells with salt and pepper chromatin
  - Neurosecretory granules are abundant and easily demonstrated by electron microscopy or immunohistochemistry (well differentiated tumors)

Metastatic Carcinoma

- The lung is a frequent site of metastatic tumor, both from extrapulmonary and intrapulmonary primaries.
- In autopsy series, between 20 and 50% of patients that expire from extra-pulmonary primaries have lung metastasis.
- Melanoma, sarcomas, renal cell carcinoma, germ cell tumors, breast carcinoma as well as carcinomas of bladder, larynx, thyroid and prostate

Metastasis
Lung Cancer Staging

- Small Cell Carcinoma
  Limited- confined to hemithorax
  Extensive

- Non-small Cell Carcinoma
  - T, N, M- Clinical Stage I-IV

TNM Staging - T2

Therapy- Non-small Cell Lung Cancer

- Stage I, II
  - Lobectomy + adjuvant chemotherapy
- Stage IIIa
  - Neoadjuvant chemotherapy, radiation, surgery
- Stage IIIb
  - Chemotherapy +/- radiation
- Stage IV
  - Chemotherapy

TNM Staging - Node Definitions

Therapy- small cell

- Limited
  - Chemotherapy + Radiation
- Extensive
  - Chemotherapy
CT Screening
Assessment of Interval Growth

Benign or Malignant?