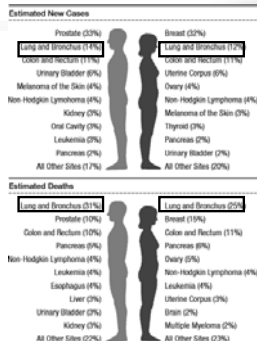


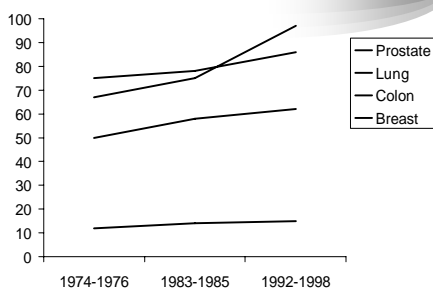
Cancer in the United States, 2004



Lung Cancer Risks

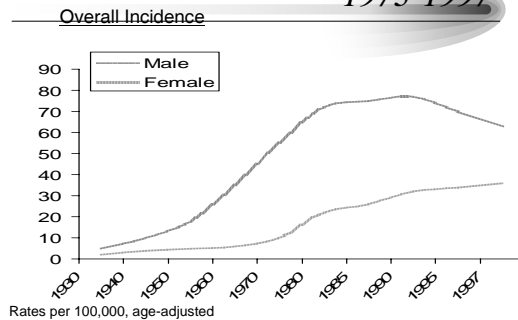
- Cigarette Smoking
 - Environmental Tobacco Smoke
- Other Carcinogens
 - Asbestos, Arsenic, Radon,
 - Bis(chloromethyl) ether, Chromium, Foundry fumes, nickel, mustard gas, coke oven emissions
- Air Pollution (foundries, diesel exhaust)
- Family History
- Diet (Vitamins A,C, E and selenium “protective”)

Five-year Cancer Survival Rates (%) US 1974-1998



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

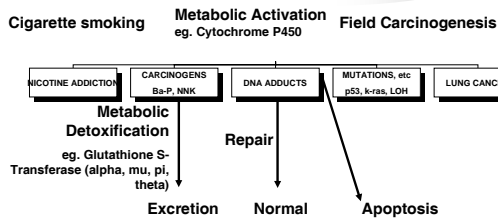
Cancer Death Rates, US 1973-1997



Rates per 100,000, age-adjusted

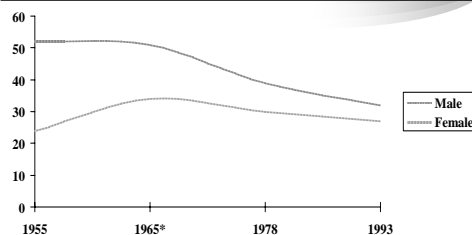
Source: SEER

The Scheme: From Nicotine Addiction to Lung Cancer



Modified from Hecht JNCI; 1999

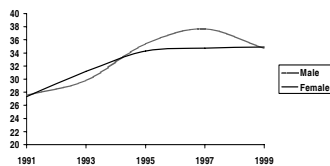
Smoking Prevalence Rates, US



*Surgeon General's Report

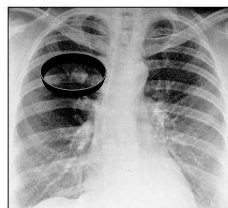
Garfinkel, Prev Med 26:447

Percentage of High School Students Who Reported Current Cigarette Smoking



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

| Pack-years | MALES | FEMALES |
|------------|-----------------|------------------|
| 0 | 1.0 | 1.0 |
| 1-19 | 2.4 (1.4-4.1) | 6.8 (4.1-11.4) |
| 20-39 | 5.6 (3.6-8.7) | 11.2 (7.5-16.8) |
| 40-49 | 11.6 (7.7-17.6) | 21.4 (14.3-32.3) |
| >50 | 13.8 (9.2-20.9) | 32.7 (19.0-56.2) |

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

Zang, JNCI 88:183, 1996

Pathologic diagnosis: specimen types

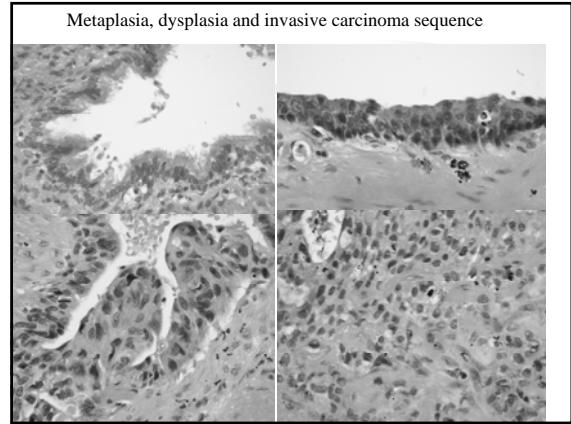
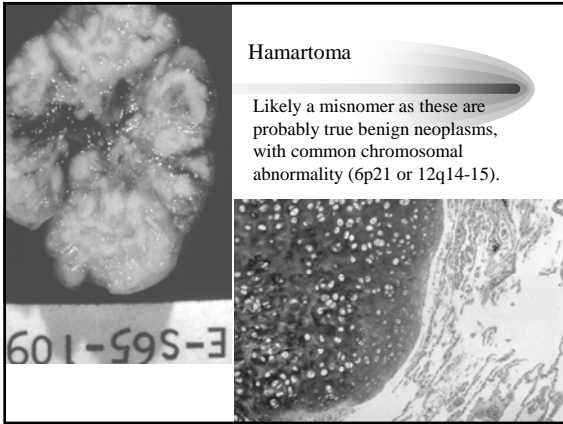
- Transbronchial biopsy
- Transthoracic needle biopsy
- Cytology
 - Bronchial brushing
 - Lavage
 - Aspiration (transthoracic or transbronchial)
- Thoracotomy/VATS

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
 - Horners 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)

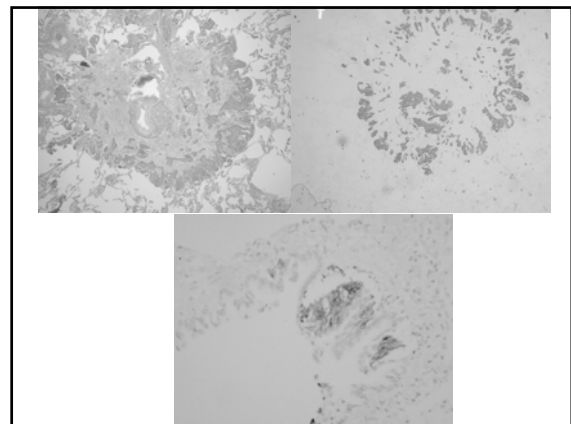
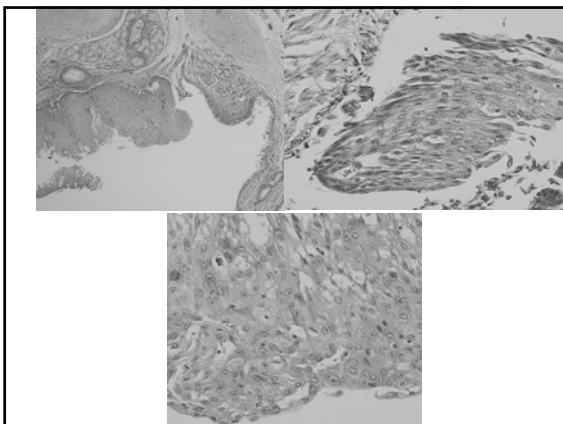


Squamous precursors

- 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)

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)

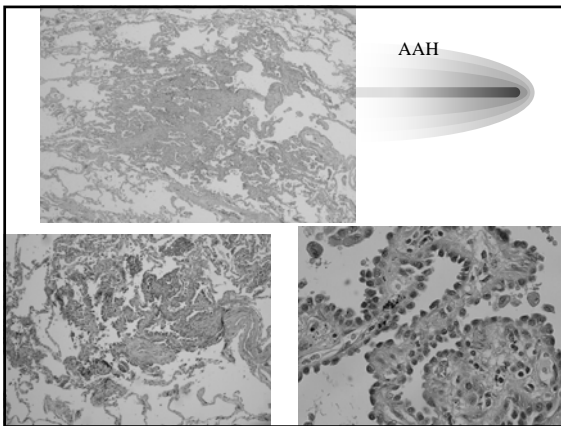


Atypical adenomatous hyperplasia

- 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

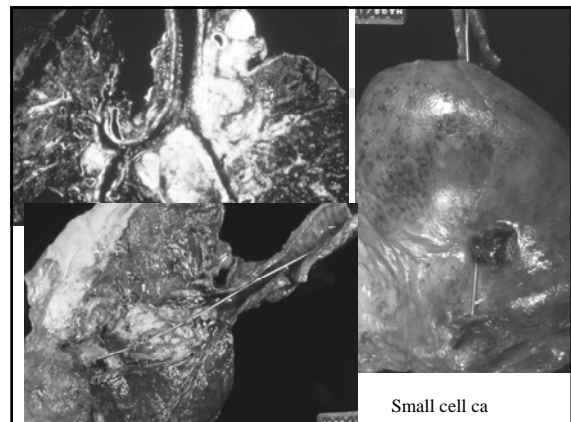
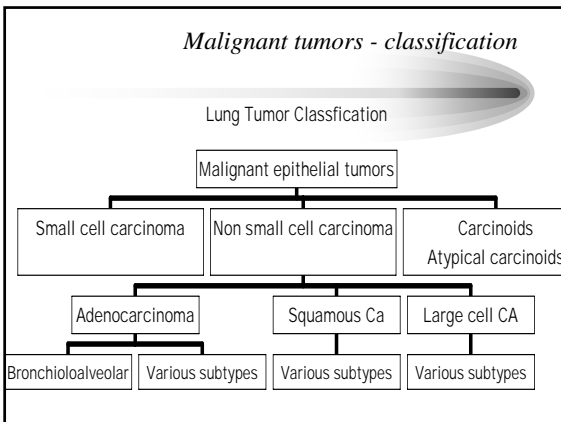
- Usually hilar/ central tumor
- The majority have extrapulmonary spread at time of presentation.
- Only 5% present as early stage disease.



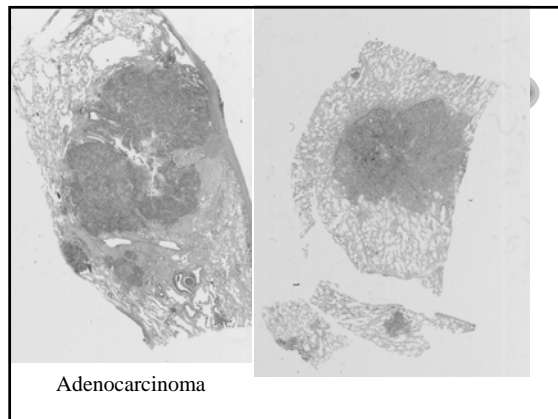
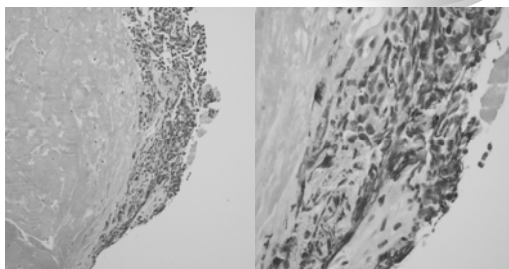
Small cell carcinoma

- 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)

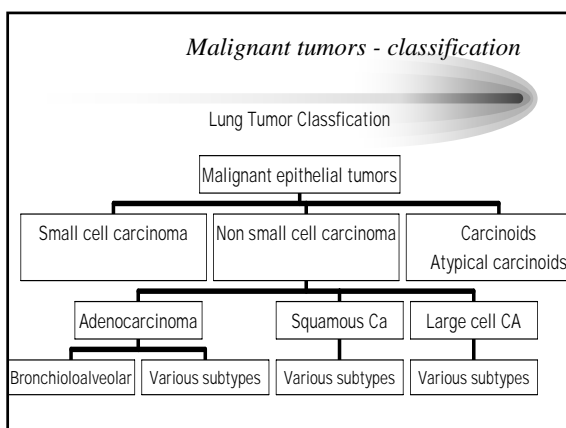
Malignant tumors - classification



Small Cell



Malignant tumors - classification

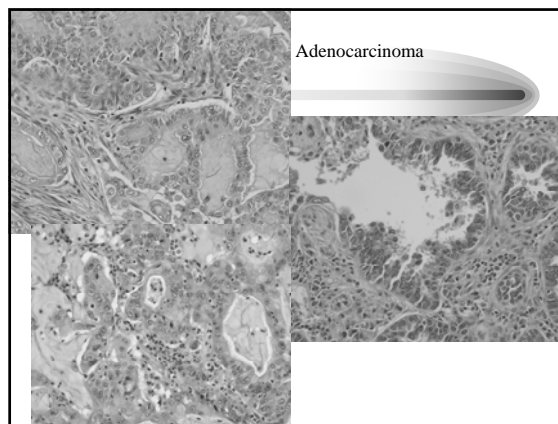


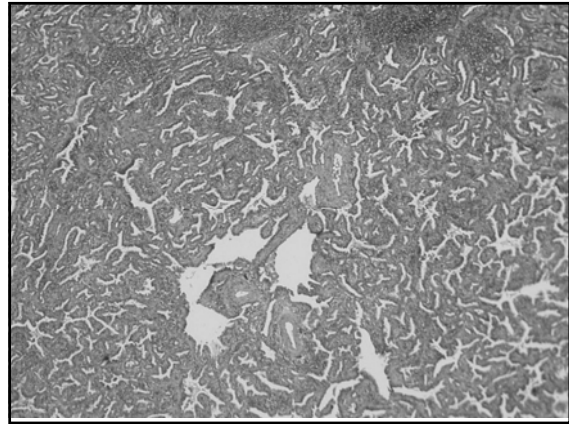
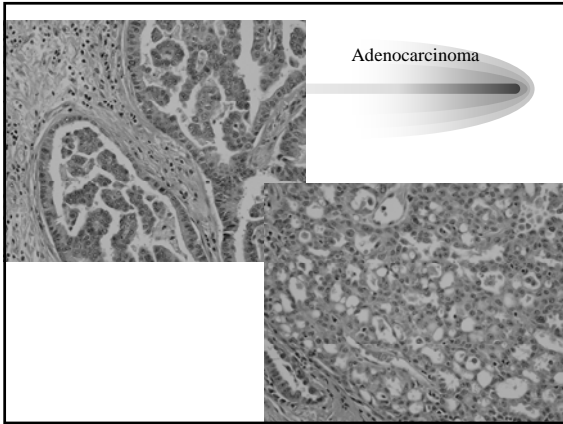
Adenocarcinoma

- 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

- 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.



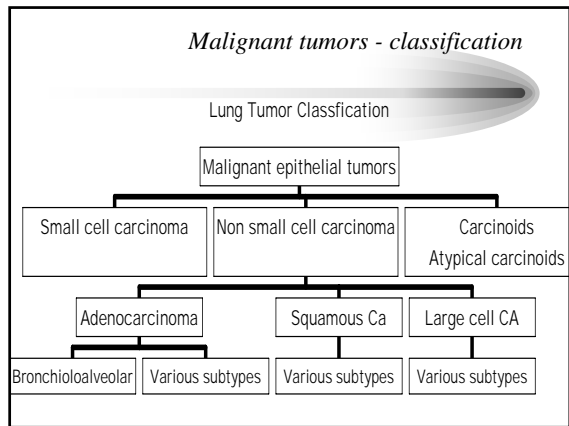
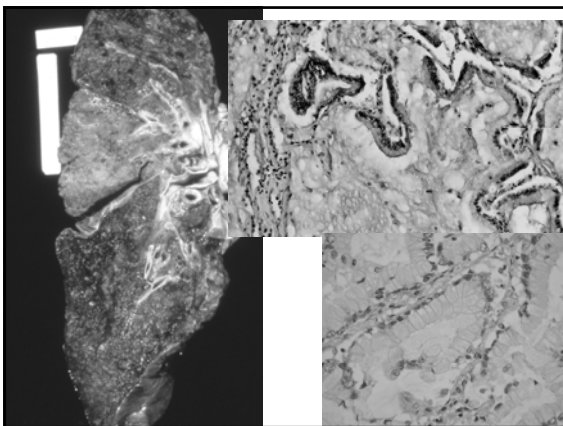


Adenocarcinoma - Bronchioloalveolar

- 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

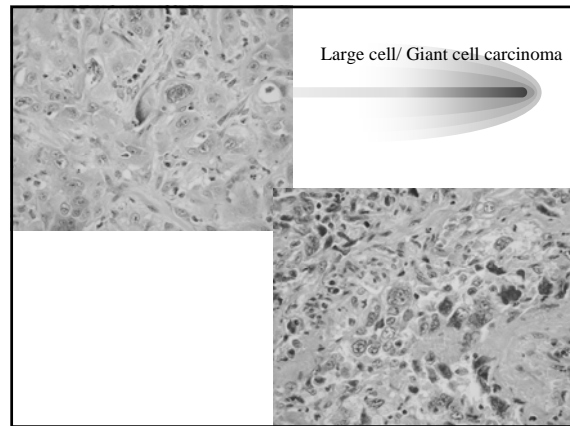
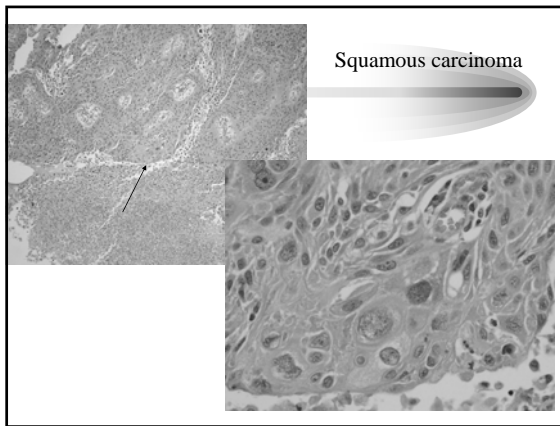
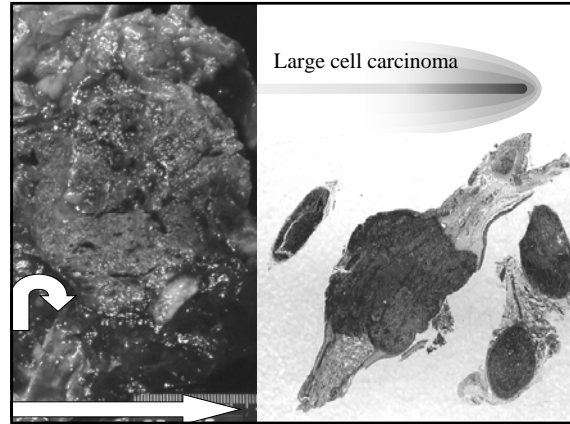
Adenocarcinoma/"BAC features"

Combined in situ and invasive carcinoma



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

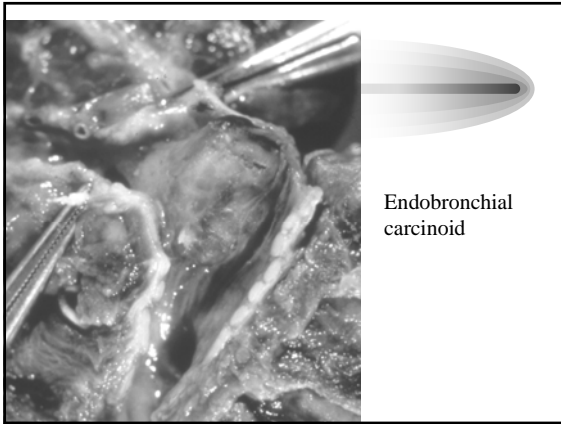


Large cell carcinoma

- 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

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

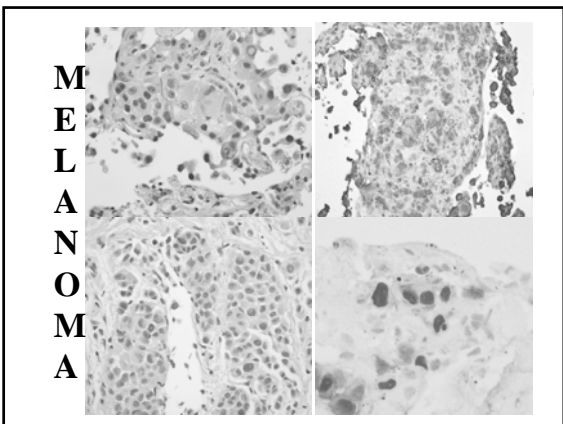
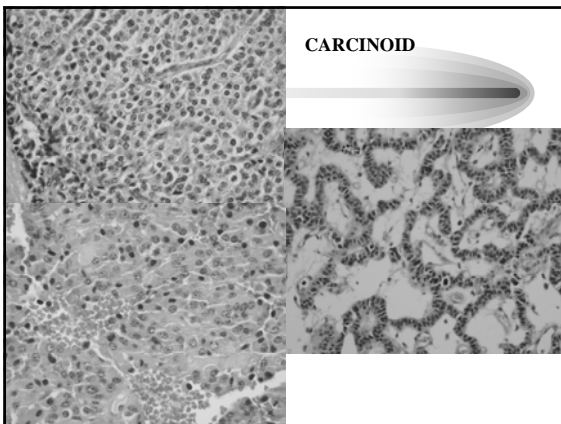
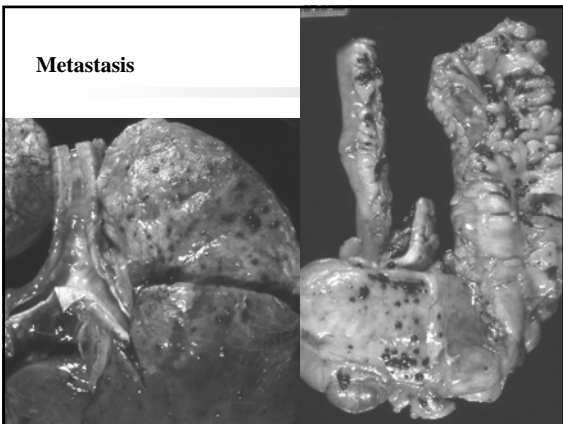


Metastatic Carcinoma

- 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

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)



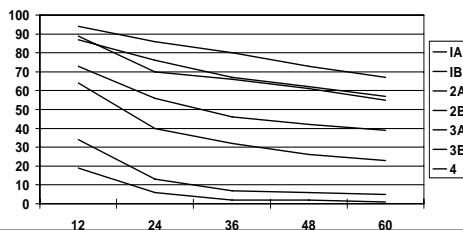
Lung Cancer Staging

- Small Cell Carcinoma
 - Limited- confined to hemithorax
 - Extensive
- Non-small Cell Carcinoma
 - T, N, M- Clinical Stage 1-4

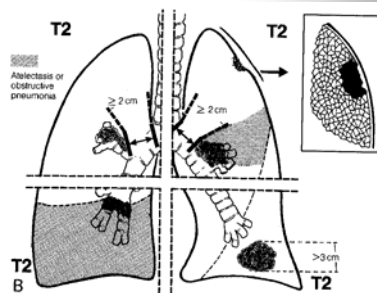
International Staging System, Revised 1997

| | |
|------------|------------------|
| Stage IA | T1, N0, M0 |
| Stage IB | T2, N0, M0 |
| Stage IIA | T1, N1, M0 |
| Stage IIB | T2, N1, M0 |
| | T3, N0, M0 |
| Stage IIIA | T1-3, N2, M0 |
| | T3, N1, M0 |
| Stage IIIB | T4, any N, M0 |
| | Any T, N3, M0 |
| Stage IV | Any T, Any N, M1 |

Chest 111:1710-17



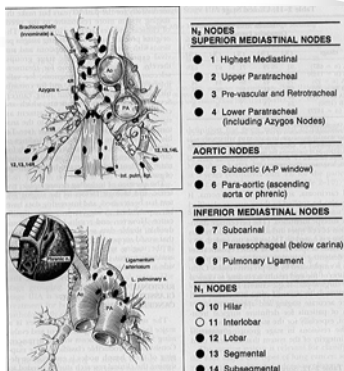
TNM Staging - T2



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?

