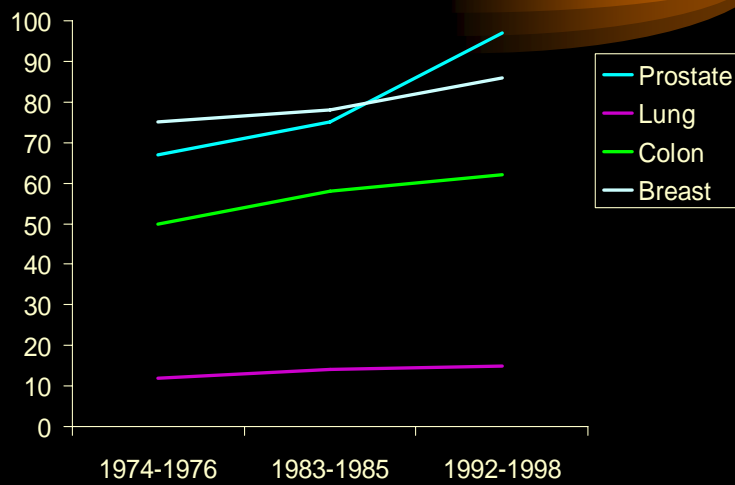


# Cancer in the United States, 2004

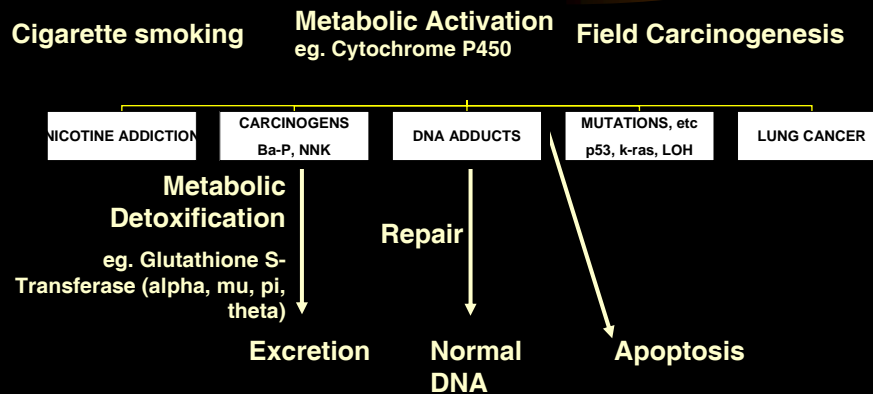


# Five-year Cancer Survival Rates (%) US 1974-1998



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

## *The Scheme: From Nicotine Addiction to Lung Cancer*



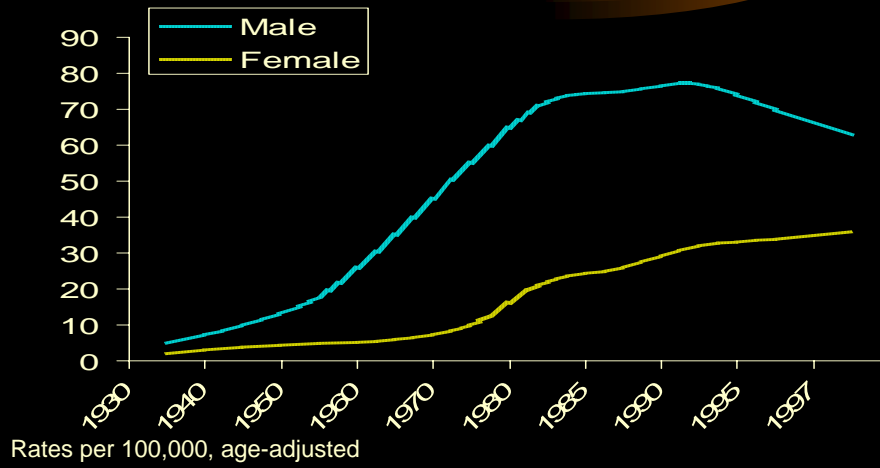
Modified from Hecht JNCI;  
1999

## *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”)

## Cancer Death Rates, US 1973-1997

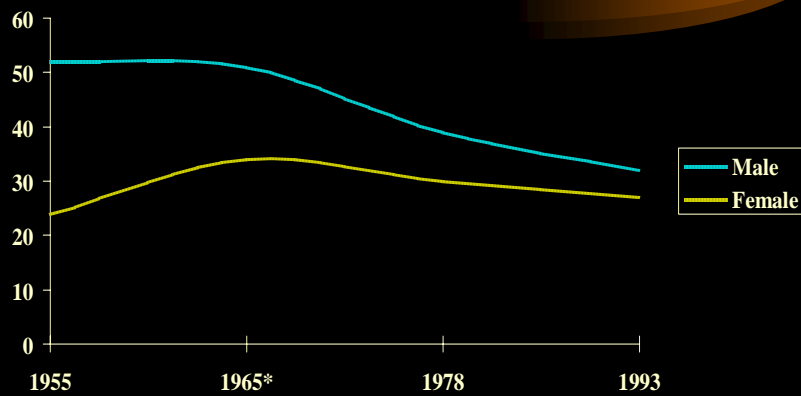
Overall Incidence



Rates per 100,000, age-adjusted

Source: SEER

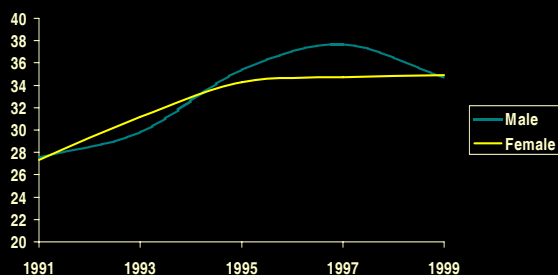
## Smoking Prevalence Rates, US



\*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

## Risk of lung cancer, men vs. women

<u>Pack-years</u>	<u>MALES</u>	<u>FEMALES</u>
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)

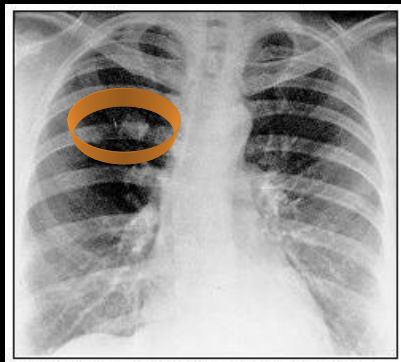
Relative risk for developing lung cancer is 1.25 for women for any "dose" of tobacco

Zang, JNCI 88:183, 1996

## *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)
    - Cushing's Syndrome (sclc)
  - Neurologic
    - Horner's Syndrome
    - Eaton-Lambert syndrome (sclc)
  - Vascular
    - Thrombophlebitis, DIC

## *Differential Diagnosis*



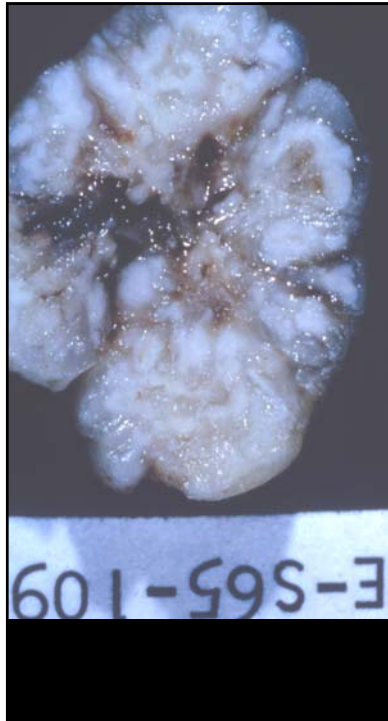
- **Benign**
  - Granuloma
  - Hamartoma
- **Malignant**
  - Metastasis
  - **Primary Lung Ca**
    - Small Cell
    - Carcinoid
    - Non-small Cell
      - Adenocarcinoma
      - Squamous
      - Large Cell

*Pathologic diagnosis:  
specimen types*

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

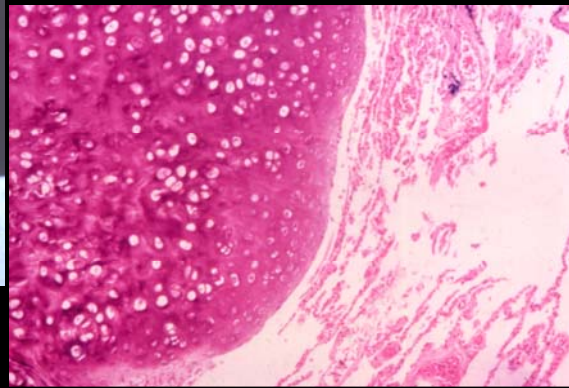
*Lung tumors - Benign*

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



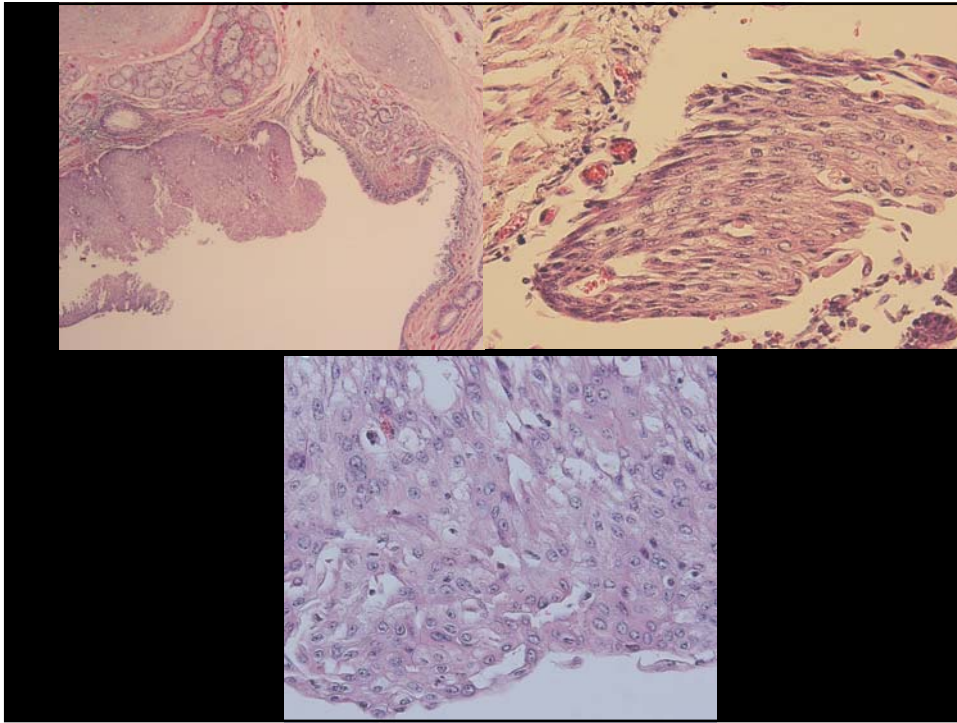
## Hamartoma

Likely a misnomer as these are probably true benign neoplasms, with common chromosomal abnormality (6p21 or 12q14-15).

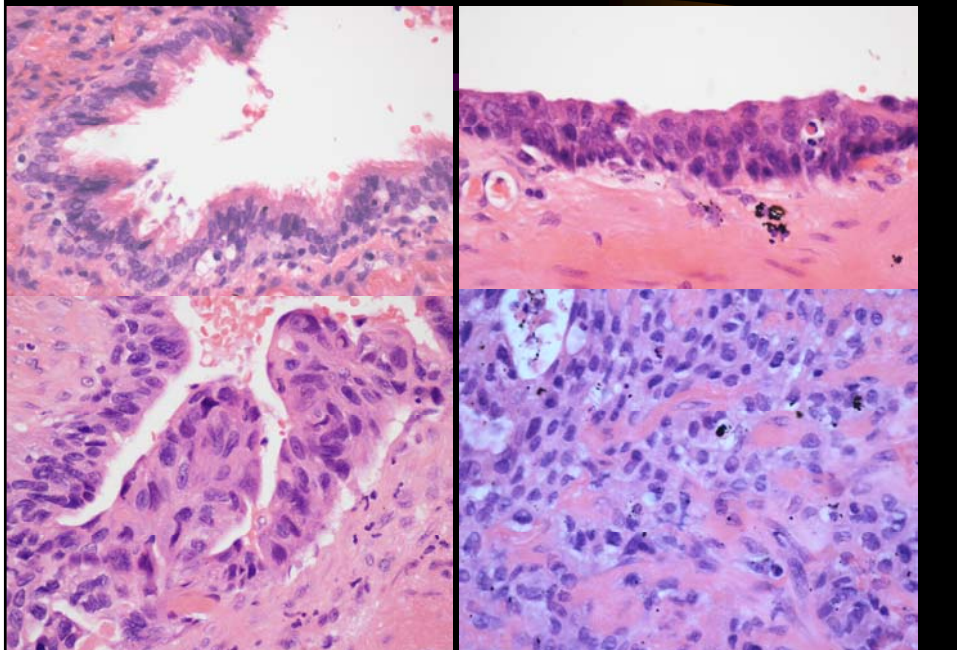


## *Squamous precursors*

- 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)



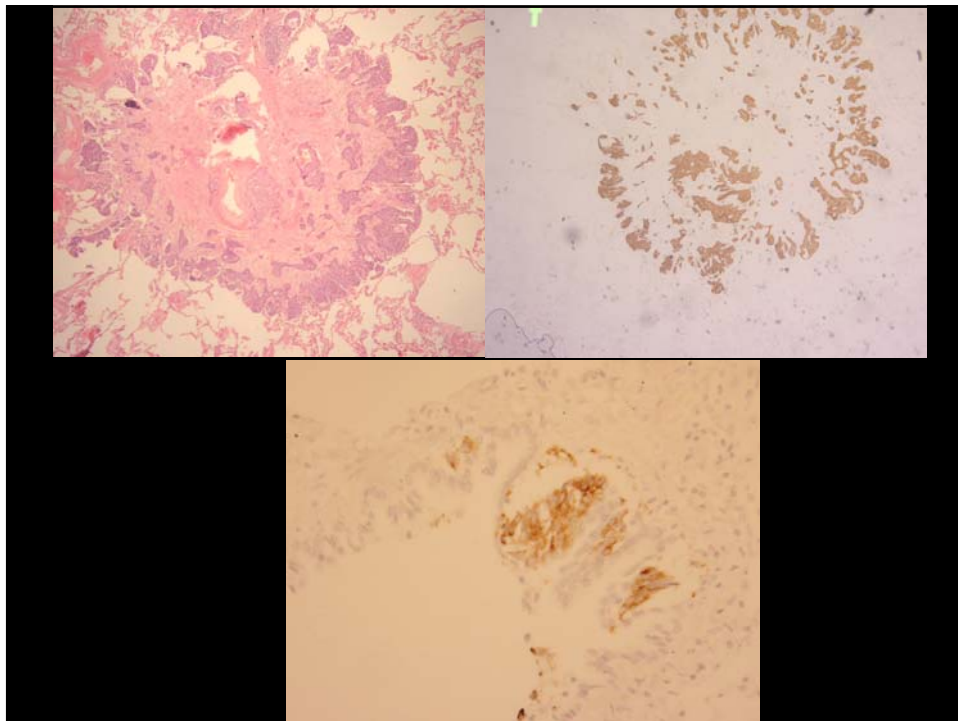
Metaplasia, dysplasia and invasive carcinoma sequence





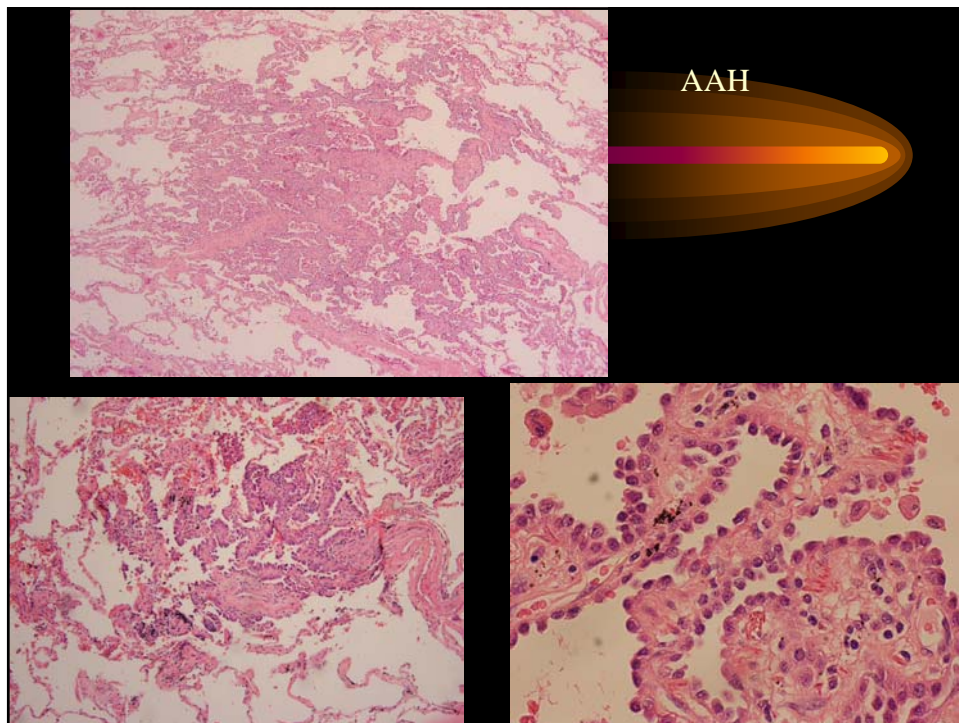
## *Diffuse Idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH)*

- 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)



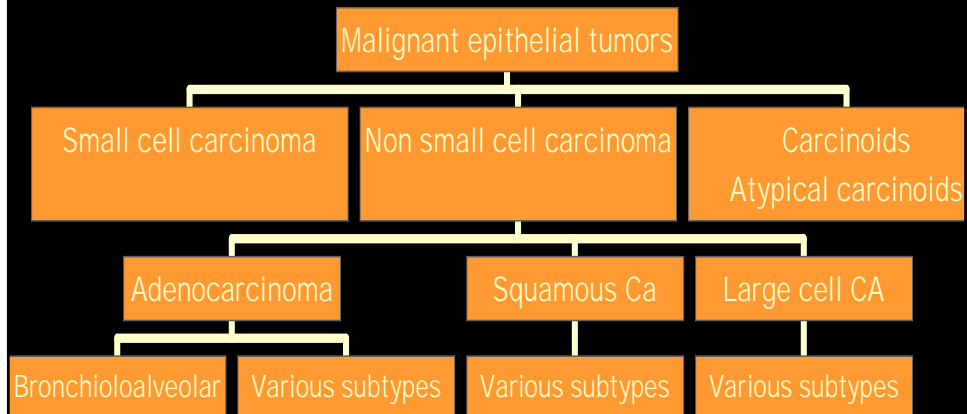
## *Atypical adenomatous hyperplasia*

- 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)



## *Malignant tumors - classification*

### Lung Tumor Classification

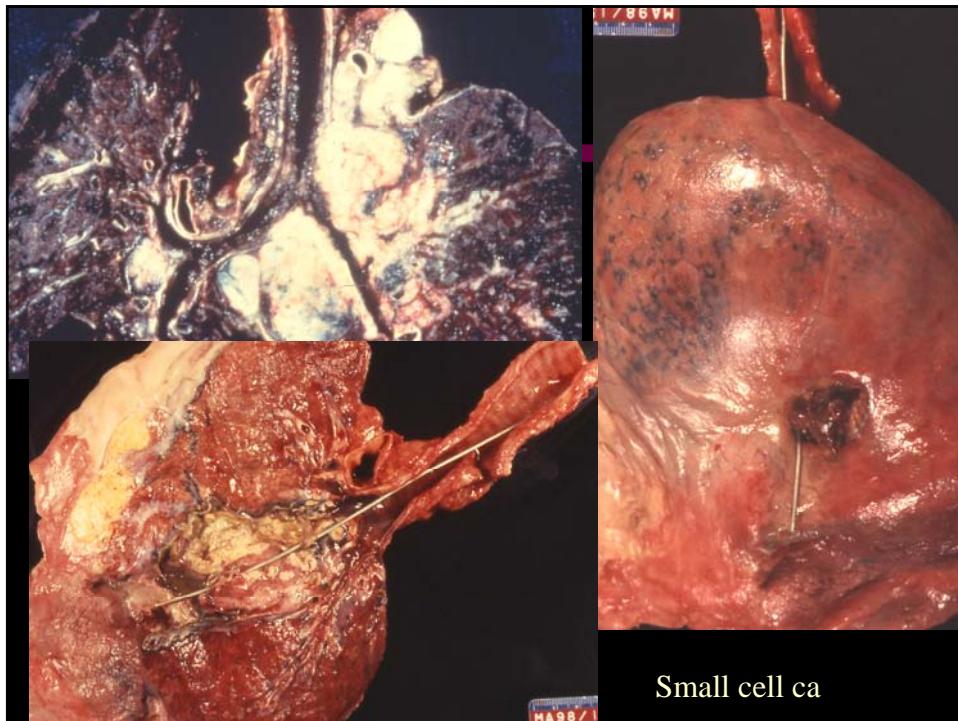


## *Small cell carcinoma*

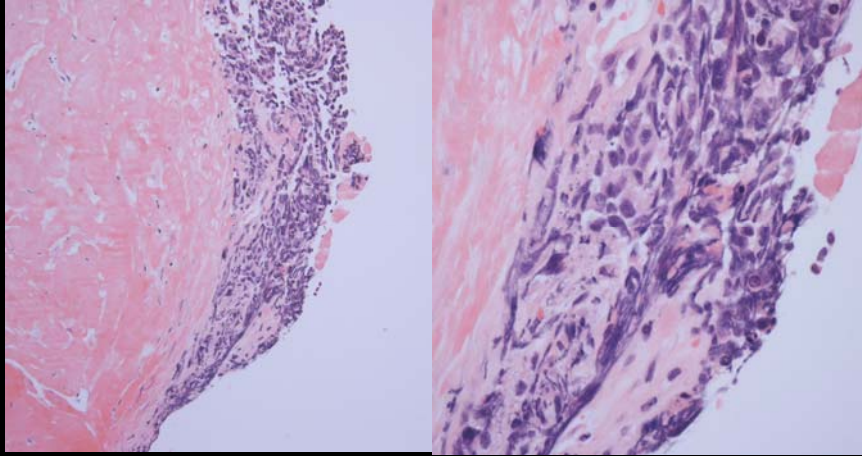
- Usually hilar/ central tumor
- The majority have extrapulmonary spread at time of presentation.
- Only 5% present as early stage disease.

## *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)

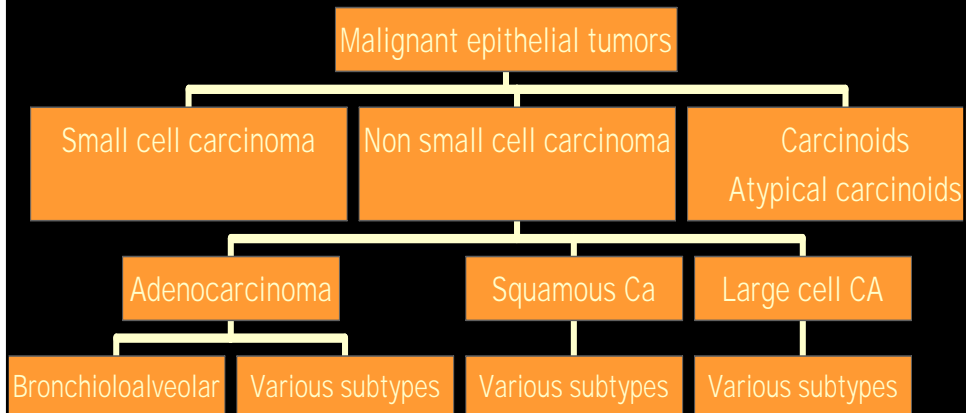


## *Small Cell*



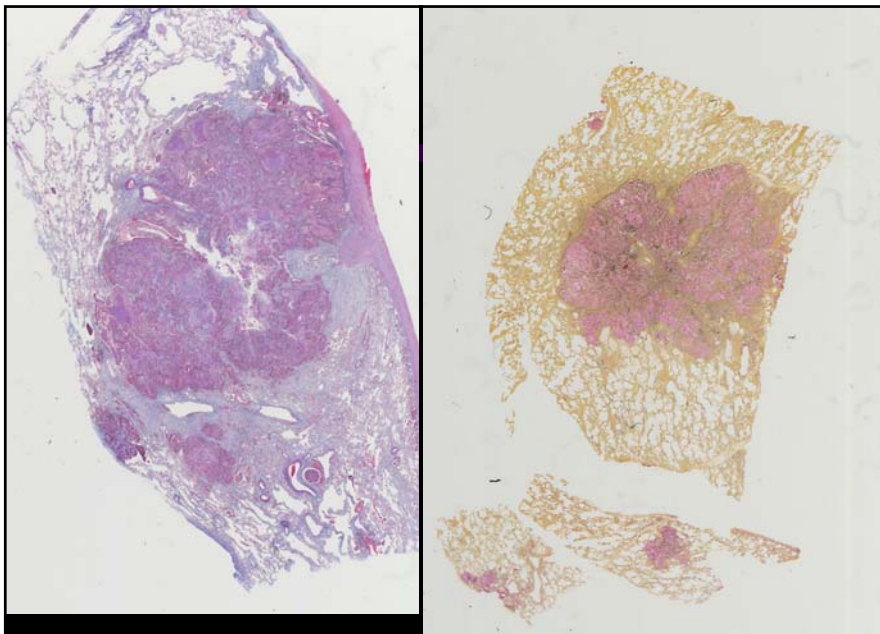
## *Malignant tumors - classification*

### Lung Tumor Classification



## *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.

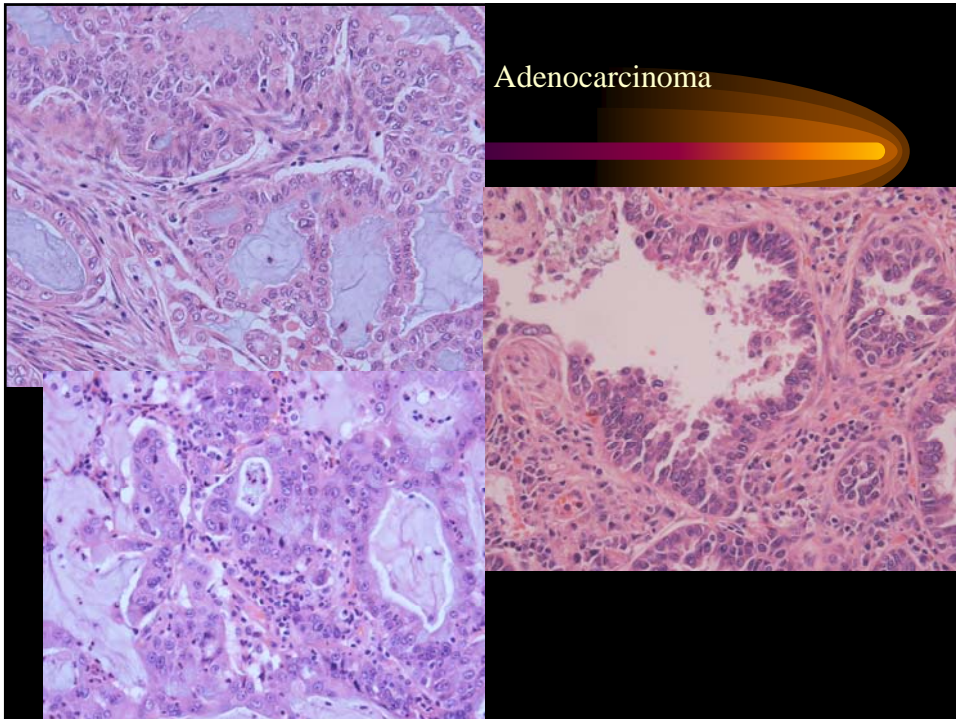


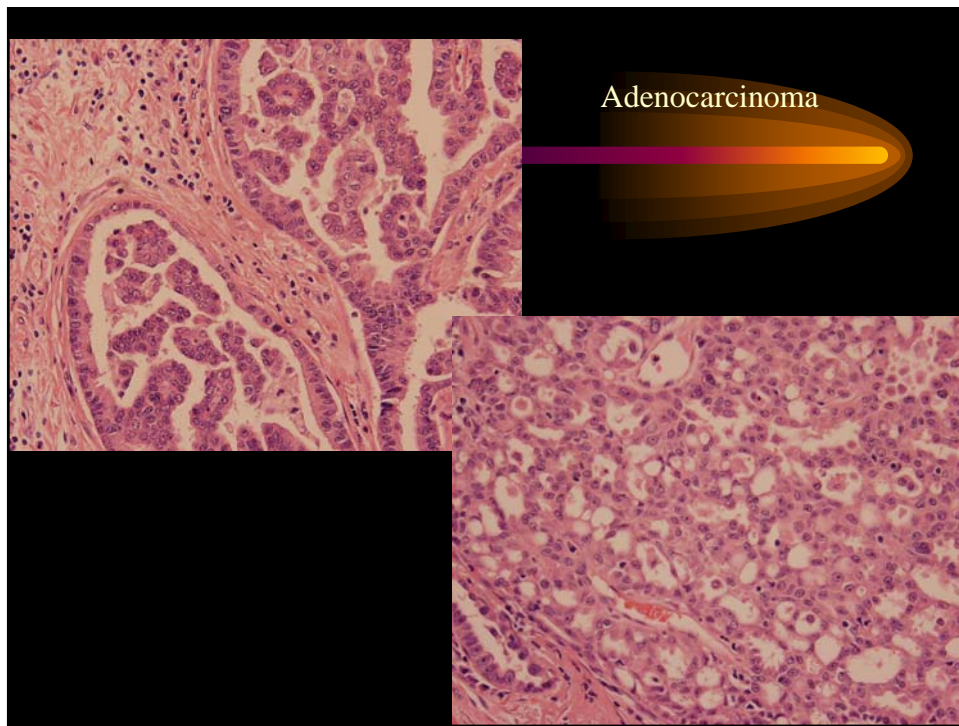
Adenocarcinoma



## *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

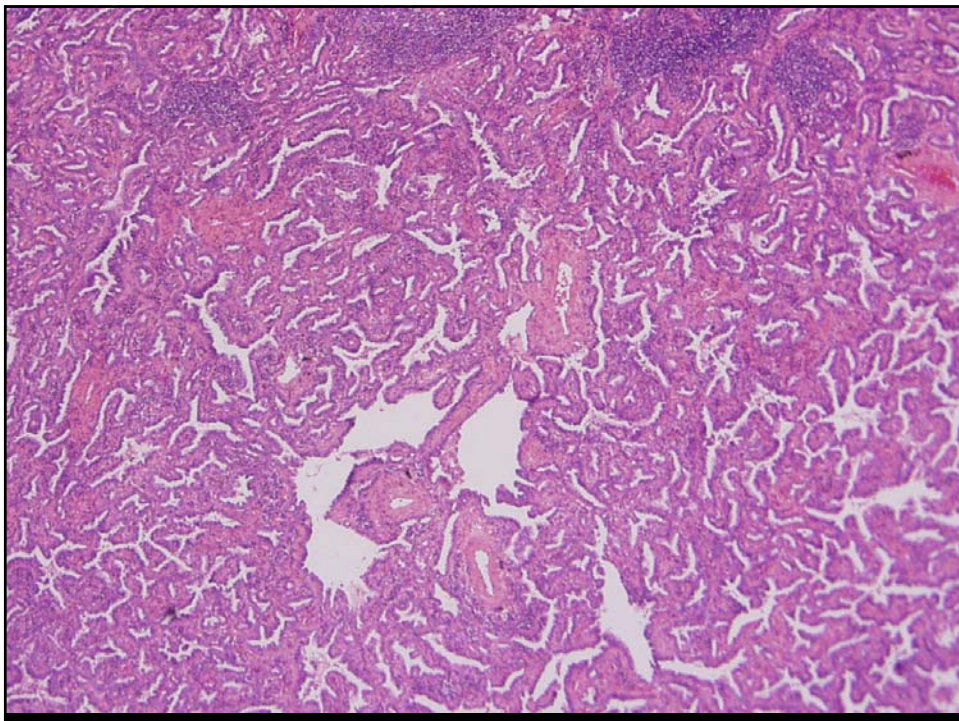
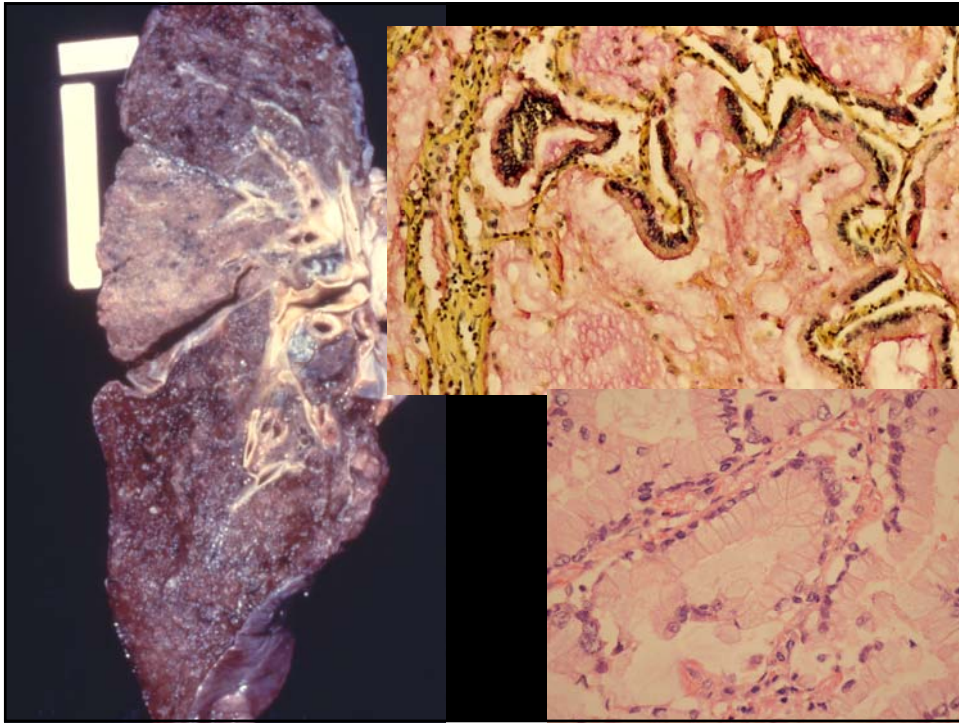


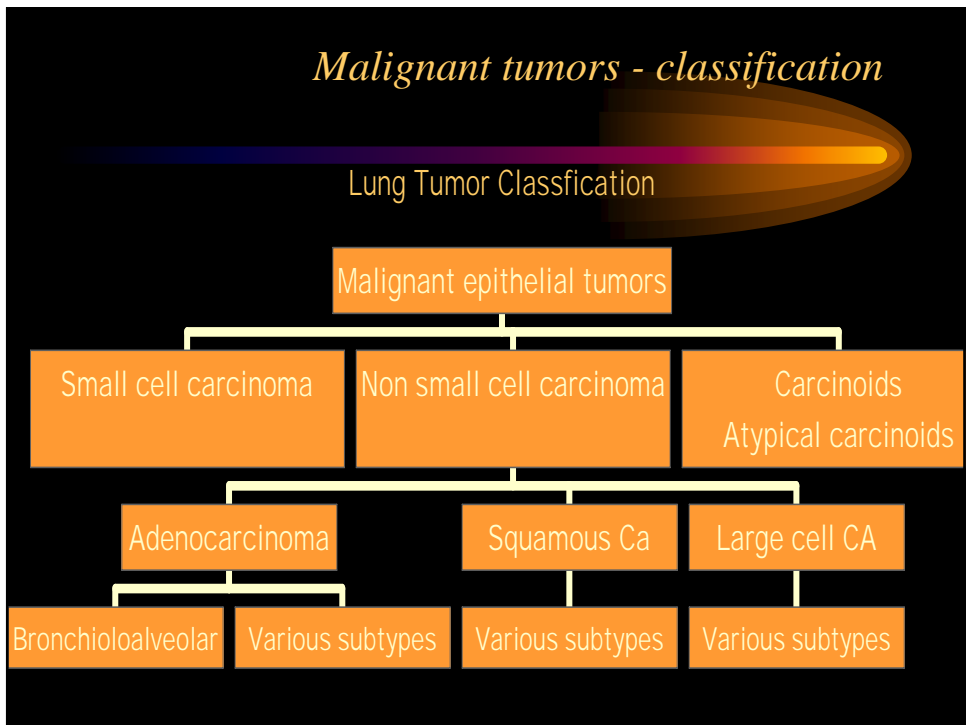
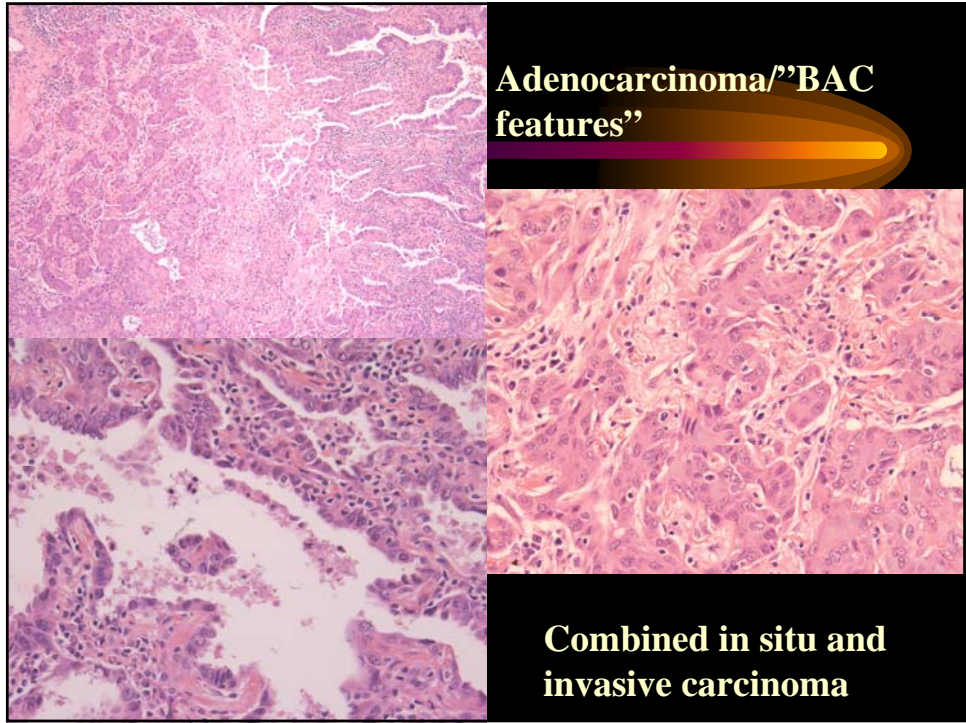


### *Adenocarcinoma - Bronchioloalveolar*

- 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

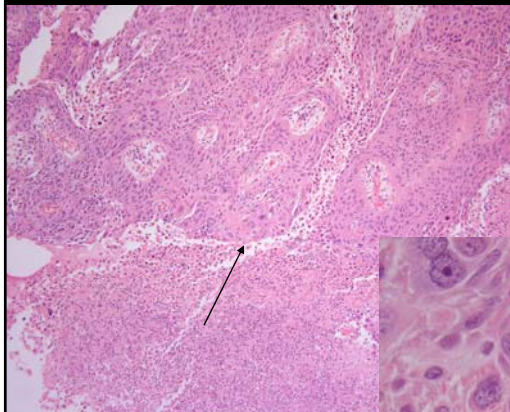




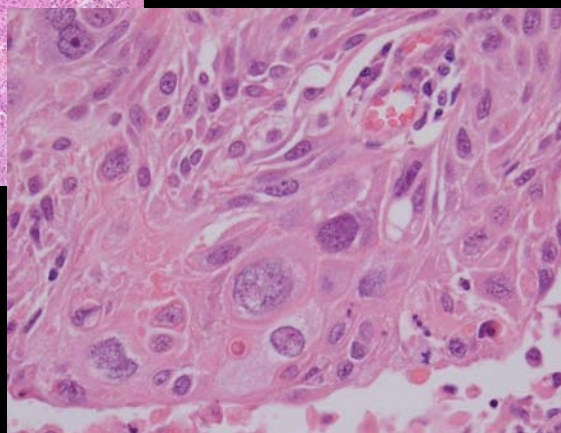


## *Squamous carcinoma*

- 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



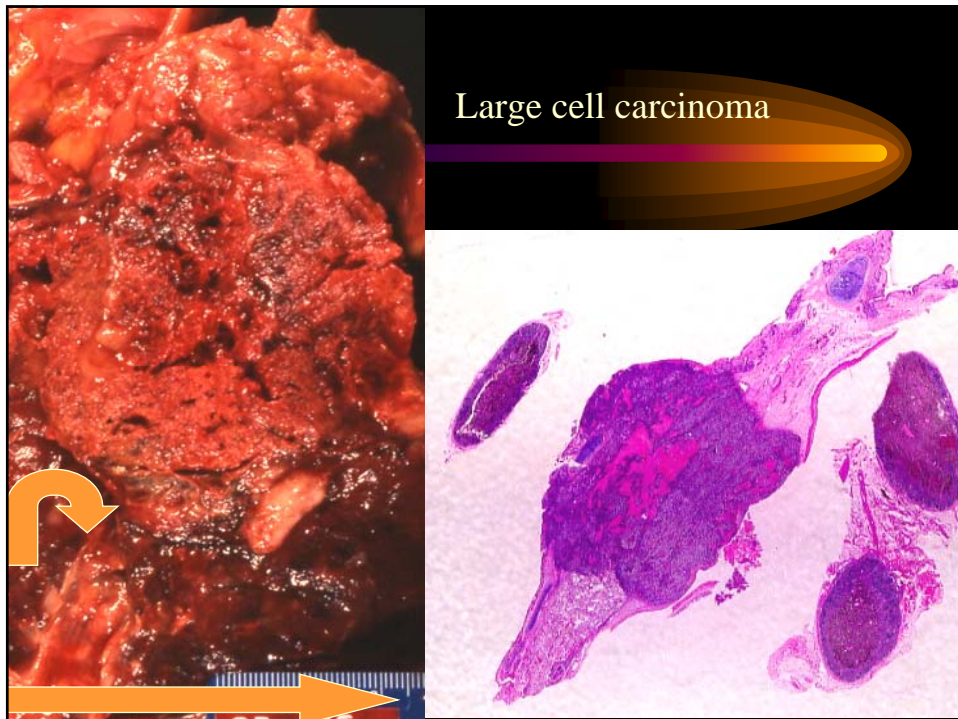
Squamous carcinoma

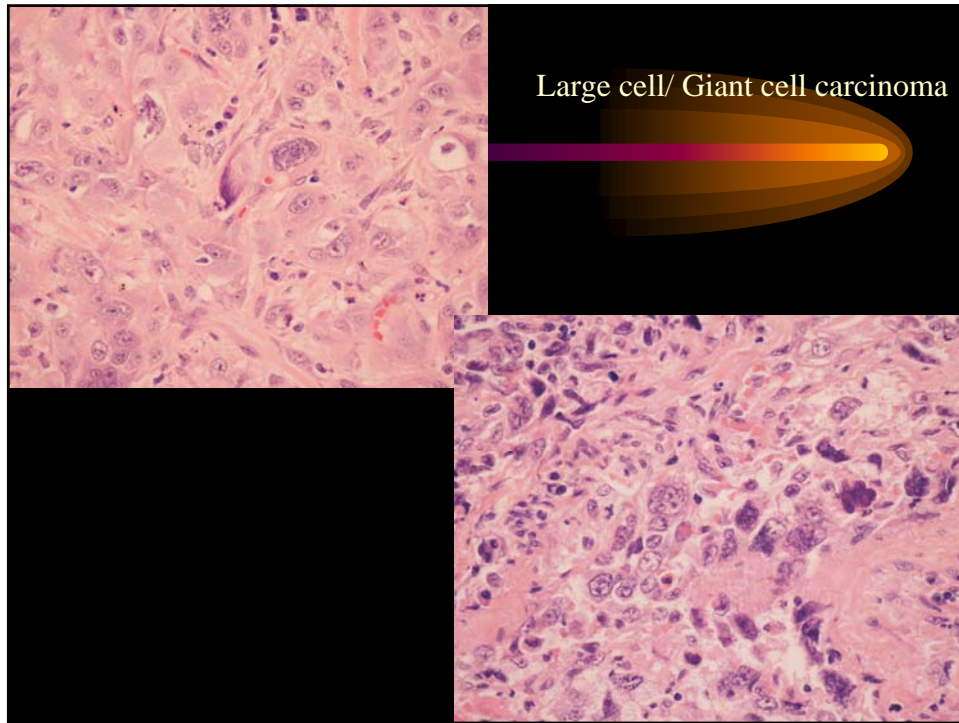




## *Large cell carcinoma*

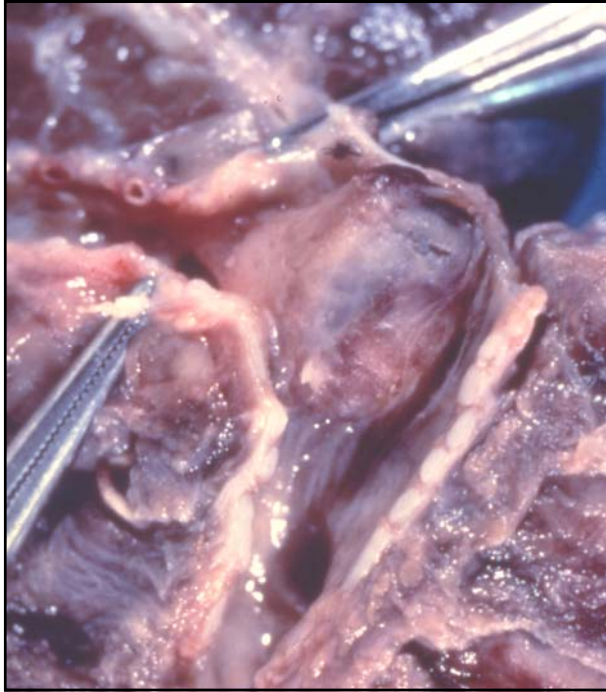
- This subtype shows no differentiation towards either squamous or adenocarcinoma
- Aggressive tumors with poor prognosis
- If subjected to ultrastructural examination, many of these tumors show either glandular or squamous differentiation.
- Nevertheless, these tumors are separated out because of their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





### *Carcinoids*

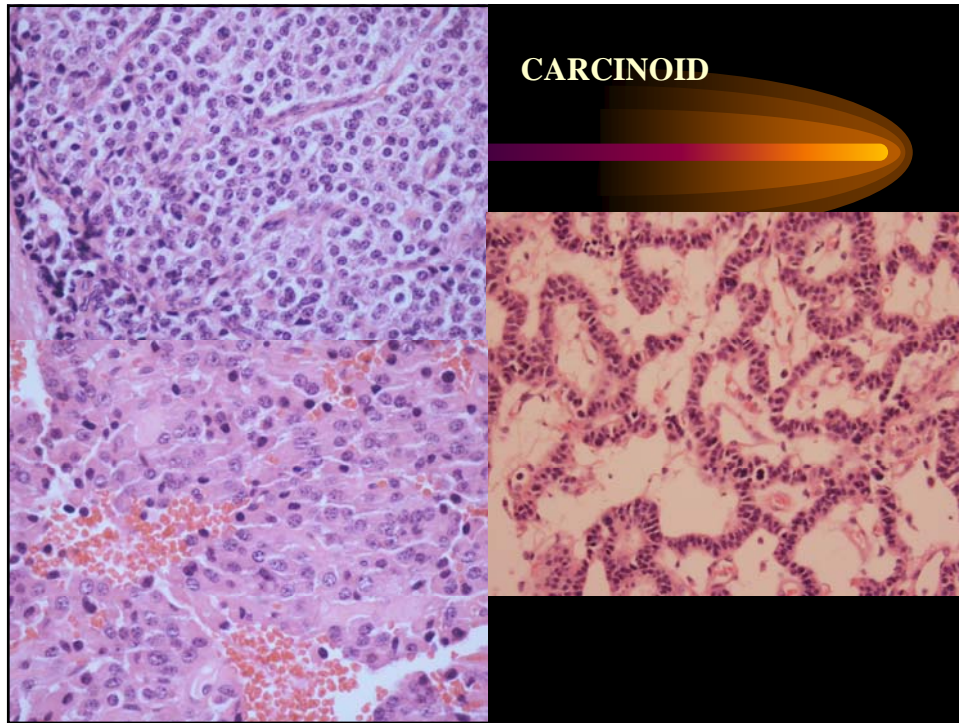
- Malignant neoplasm of neuroendocrine cell origin
- Can be central or peripheral; central lesions can cause bronchial obstruction
- Project into bronchial lumen but often have intact mucosa above them (grow under the mucosa)
- Typical carcinoids are low grade malignancies; atypical carcinoids (mitoses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



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)

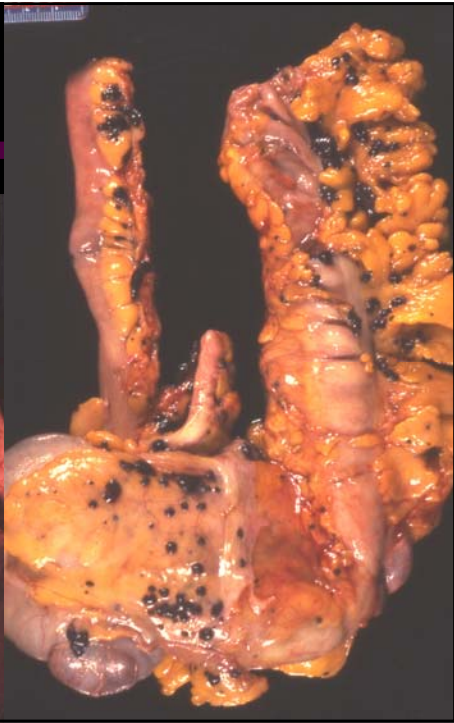
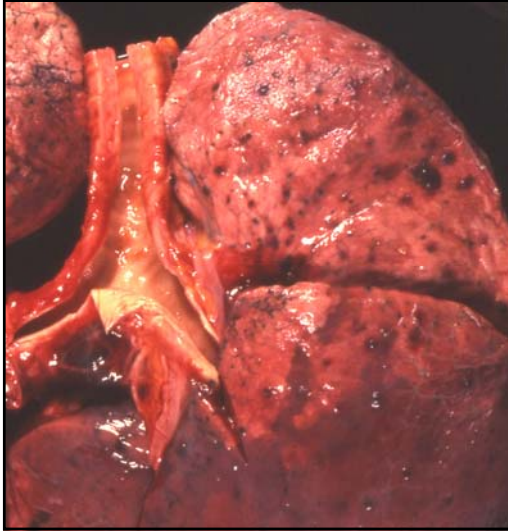


### *Metastatic Carcinoma*

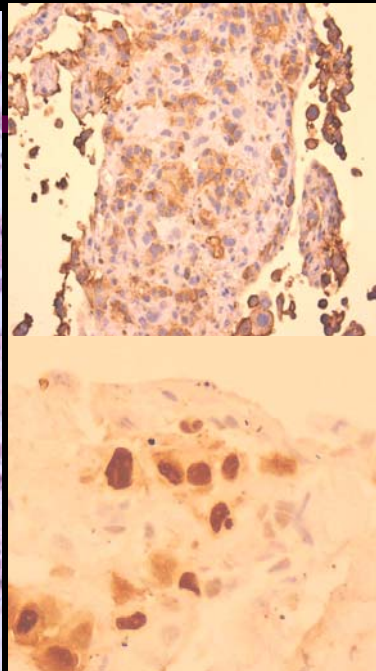
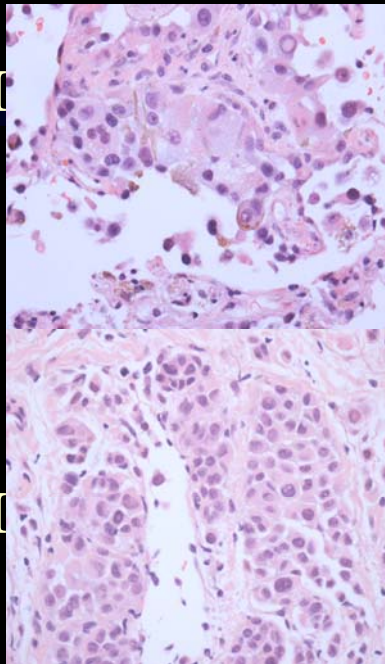
- The lung is a frequent site of metastatic tumor, both from extrapulmonary and intrapulmonary primaries.
- In autopsy series, between 20 and 50% of patients that expire from extra-pulmonary primaries have lung metastasis.
- Melanoma, sarcomas, renal cell carcinoma, germ cell tumors, breast carcinoma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



**Metastasis**



**M  
E  
L  
A  
N  
O  
M  
A**

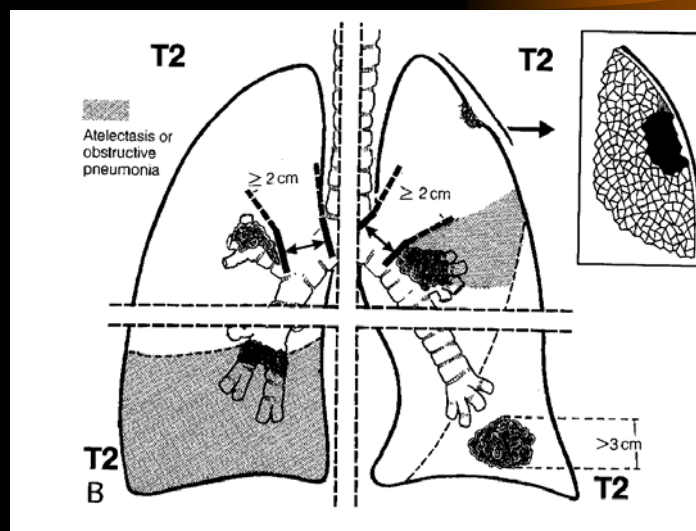




## Lung Cancer Staging

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

## TNM Staging - T2



## TNM Staging - Node Definitions

**N<sub>2</sub> NODES**

**SUPERIOR MEDIASTINAL NODES**

- 1 Highest Mediastinal
- 2 Upper Paratracheal
- 3 Pre-vascular and Retrotracheal
- 4 Lower Paratracheal (including Azygos Nodes)

**AORTIC NODES**

- 5 Subaortic (A-P window)
- 6 Para-aortic (ascending aorta or phrenic)

**INFERIOR MEDIASTINAL NODES**

- 7 Subcarinal
- 8 Paraesophageal (below carina)
- 9 Pulmonary Ligament

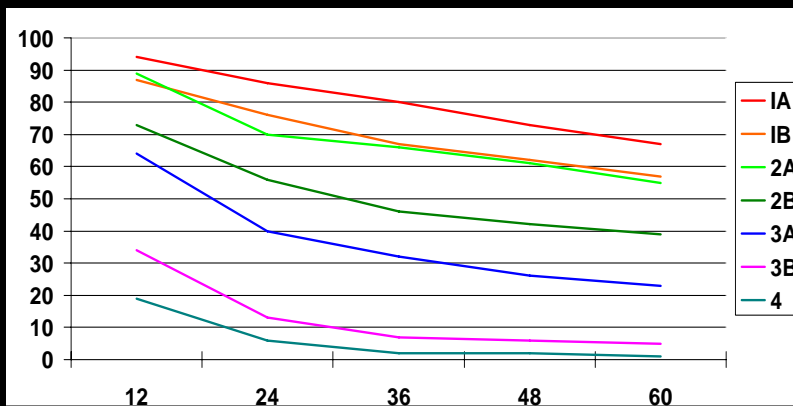
**N<sub>1</sub> NODES**

- 10 Hilar
- 11 Interlobar
- 12 Lobar
- 13 Segmental
- 14 Subsegmental

## 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
Stage IIIA	T3, N0, M0
	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



## *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

## *Therapy- small cell*

- Limited
  - Chemotherapy + Radiation
- Extensive
  - Chemotherapy

# CT Screening Assessment of Interval Growth

Benign or Malignant?

