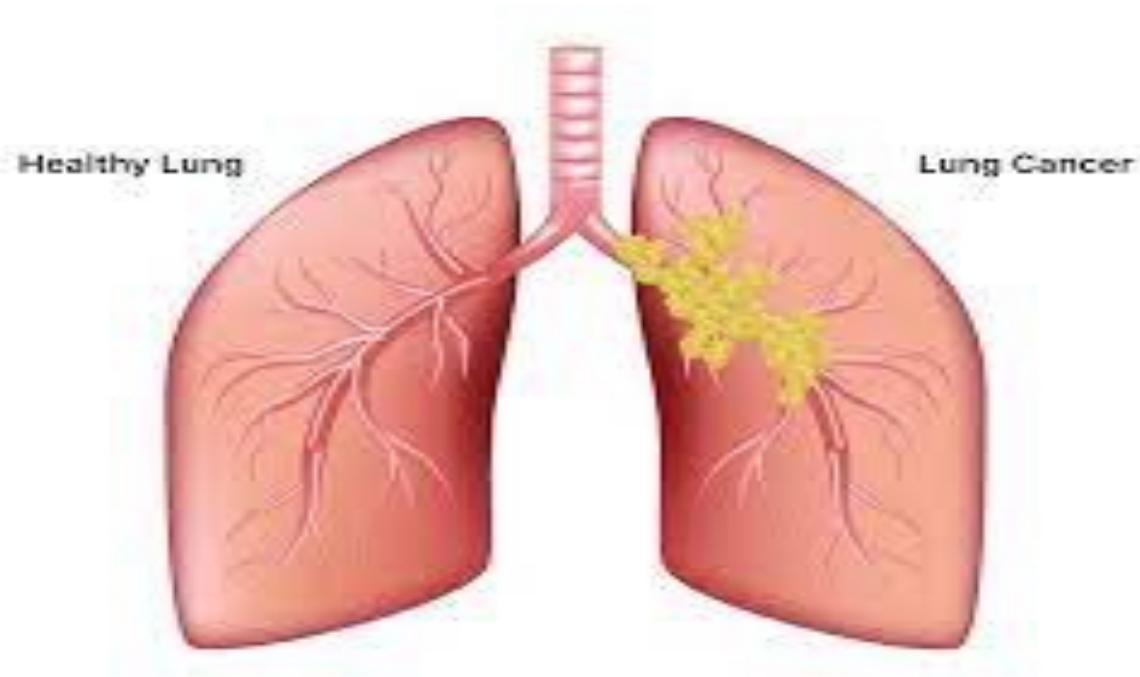


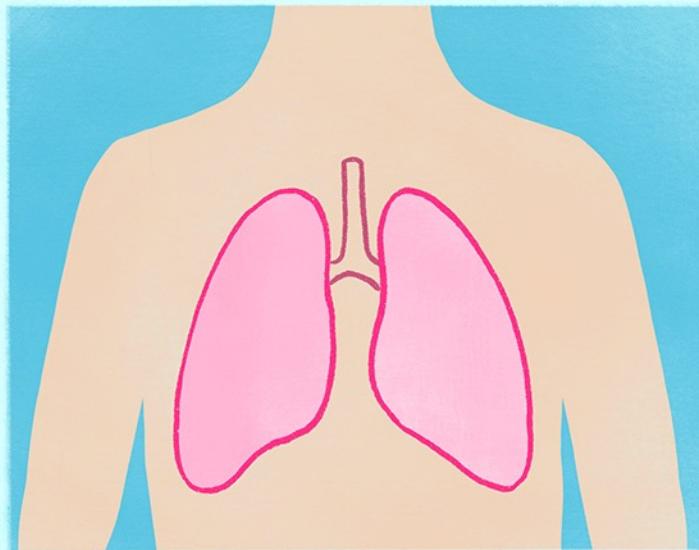
# LUNG TUMORS



**MARAM ABDALJALEEL, MD**

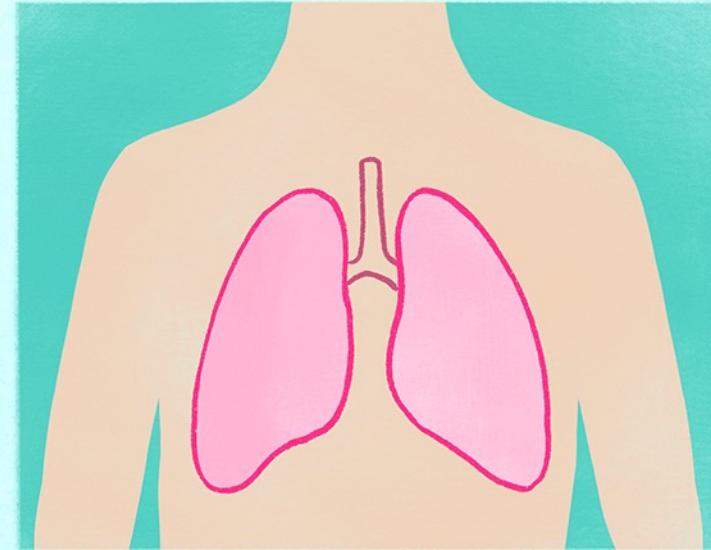
**DERMATOPATHOLOGIST & NEUROPATHOLOGIST**

# Metastatic vs. Primary Lung Cancer



## Metastatic Lung Cancer

originated from a different part of the body and spread to the lungs



## Primary Lung Cancer

originated in the lungs

**95% of primary lung tumors are carcinomas**

# HAMARTOMA

- The most common benign tumor
- It's clonal, so the name hamartoma is a misnomer
- Gross: spherical, small (1 to 4 cm), discrete
- CXR: coin lesion.
- Microscopic: mature cartilage, fat, fibrous tissue, and blood vessels.

# **CARCINOMA OF THE LUNG**

- The most important cause of cancer-related deaths in industrialized countries
- The **incidence** among males is gradually decreasing, but it continues to increase among females **BECAUSE** the incidence of smoking in women increased markedly over the past half century.

- peak incidence at **50s & 60s.**
- **At diagnosis:**
  - >50% of pts have distant metastases
  - $\frac{1}{4}$  have disease in the regional LNs.
- **The prognosis is dismal:**
  - the 5-year survival rate for all stages of lung cancer combined is about **16%**
  - Prognosis has not changed over the last 35 yrs; even with disease localized to the lung, the 5-year survival rate is only **45%**.

# **THE FOUR MAJOR HISTOLOGIC TYPES OF CARCINOMAS OF THE LUNG**

- 1. adenocarcinoma**
- 2. squamous cell carcinoma**
- 3. small cell carcinoma (a subtype of neuroendocrine carcinoma)**
- 4. large cell carcinoma**

**Table 13.6 Histologic Classification of Malignant Epithelial Lung Tumors (2015 WHO Classification, Simplified Version)**

Adenocarcinoma

Acinar, papillary, micropapillary, solid, lepidic predominant, mucinous subtypes

Squamous cell carcinoma

Large cell carcinoma

Neuroendocrine carcinoma

Small cell carcinoma

Large cell neuroendocrine carcinoma

Carcinoid tumor

Mixed carcinomas

Adenosquamous carcinoma

Combined small cell carcinoma

Other unusual morphologic variants

Sarcomatoid carcinoma

Spindle cell carcinoma

Giant cell carcinoma

- **Squamous cell and small cell carcinomas have the strongest association with smoking**
- **adenocarcinoma** has replaced squamous cell carcinoma as **the most common primary lung tumor** in recent yrs, because of changes in smoking patterns in US.
- **Adenocarcinomas is the most common primary tumors arising in women, in never-smokers, and in individuals younger than 45 years of age.**

- Old designation to small cell lung cancer (**SCLC**) and non–small cell lung cancer (**NSCLC**)
- **NSCLC** includes adenocarcinoma, squamous and large cell carcinoma, and large cell neuroendocrine carcinomas

- **SCLCs:**

- virtually all cases have metastasized by the time of diagnosis
- not curable by surgery.
- best treated by chemotherapy, +/- radiation therapy.

- **NSCLCS:**

- more likely to be Resectable
- Respond poorly to chemotherapy
- targeted therapy nowadays for adenocarcinoma and SqCC.

# **ETIOLOGY AND PATHOGENESIS**

# **PATHOGENESIS:**

Accumulation of **genetic abnormalities** after exposure to **carcinogens** resulting in a stepwise accumulation of driver mutations → transformation of benign progenitor cells in the lung into neoplastic cells possessing all of the hallmarks of cancer

**Genetic abnormalities**

**carcinogens**

# GENETIC ABNORMALITIES:

- Inactivation of tumor suppressor genes located on chromosome 3 (3p) as an early event
- mutations in ***TP53*** tumor suppressor gene and ***KRAS*** oncogene as a late event
- mutations that activate the *epidermal growth factor receptor (EGFR)*

# **CARCINOGENS:**

- cigarette smoking
- environmental carcinogens

# CIGARETTE SMOKING

- **90%** in active smokers or those who stopped recently.
- linear correlation between the frequency of lung cancer and pack-years of cigarette smoking.
- **habitual heavy smokers** (two packs a day for 20 years) have **60X** more risk than among nonsmokers.
- For unclear reasons, **women are more susceptible to carcinogens** in tobacco smoke than men.

- Although smoking cessation **decreases** the risk over time, it **never** returns to baseline levels
- **smoking of pipes, cigars and passive** smoking increases the risk.
- 11% of heavy smokers develop lung cancer
- Not all individuals exposed to tobacco smoke develop cancer because **the mutagenic effect of carcinogens is modified by hereditary (genetic) factors**

# **ENVIRONMENTAL CARCINOGENS:**

- **Occupational exposures** to some environmental carcinogens may sometimes be responsible for lung cancer **all by themselves**, e.g:
  - **uranium mines**
  - work with **asbestos**
  - inhalation of dusts containing **arsenic, chromium, nickel, or vinyl chloride.**

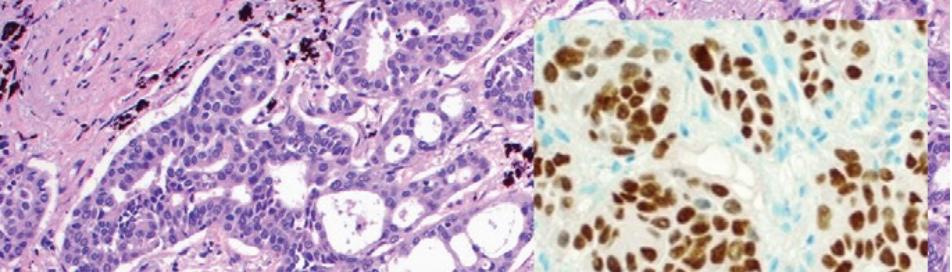
# **ASBESTOS AND TOBACCO SMOKING**

- **SYNERGISTIC INTERACTION:**
  - Exposure to asbestos in nonsmokers increases the risk for developing lung cancer 5-fold
  - heavy smokers exposed to asbestos the risk is elevated approximately 55-fold.

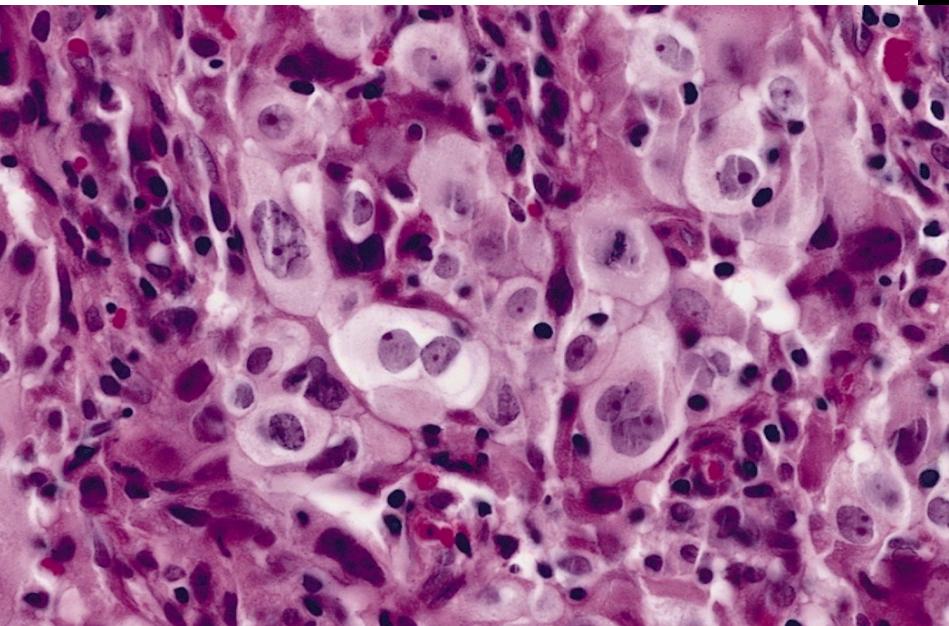
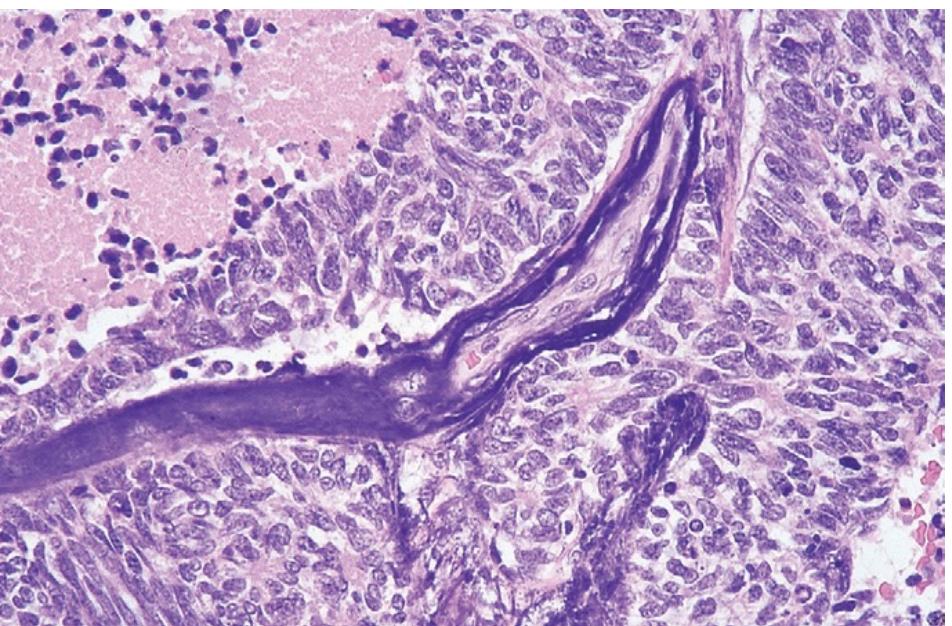
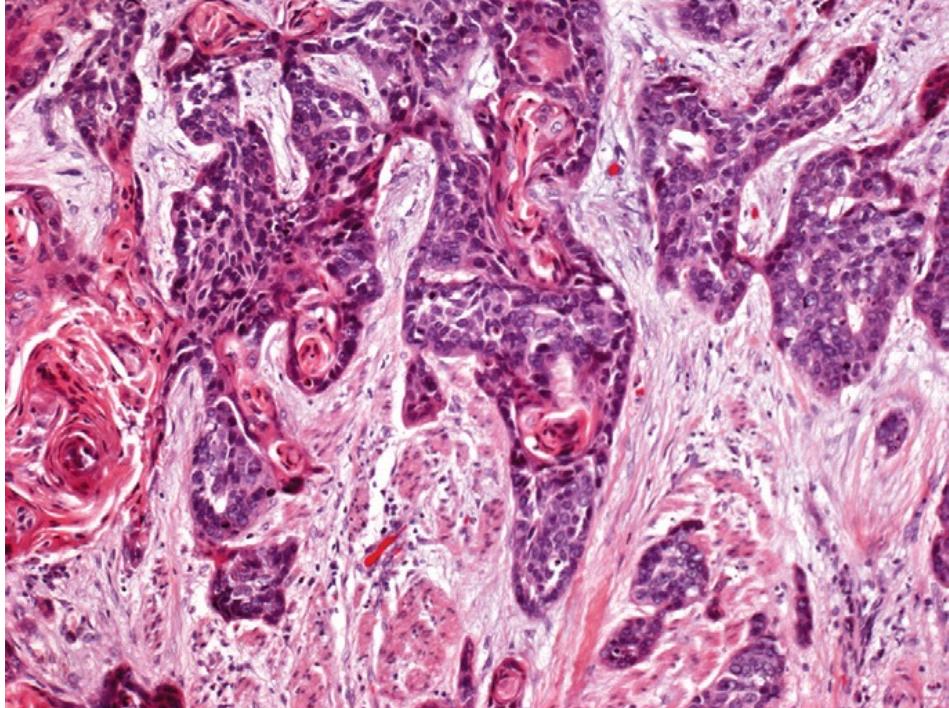
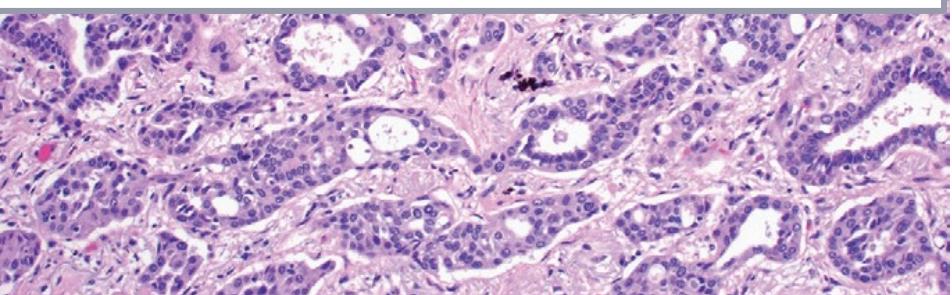
Some invasive adenocarcinomas of the lung arise through an **atypical adenomatous hyperplasia–adenocarcinoma in situ–invasive adenocarcinoma** sequence.

# **THE FOUR MAJOR HISTOLOGIC TYPES OF CARCINOMAS OF THE LUNG**

- 1. Adenocarcinoma**
- 2. Squamous Cell Carcinoma**
- 3. Small Cell Carcinoma (a subtype of neuroendocrine carcinoma)**
- 4. Large Cell Carcinoma**



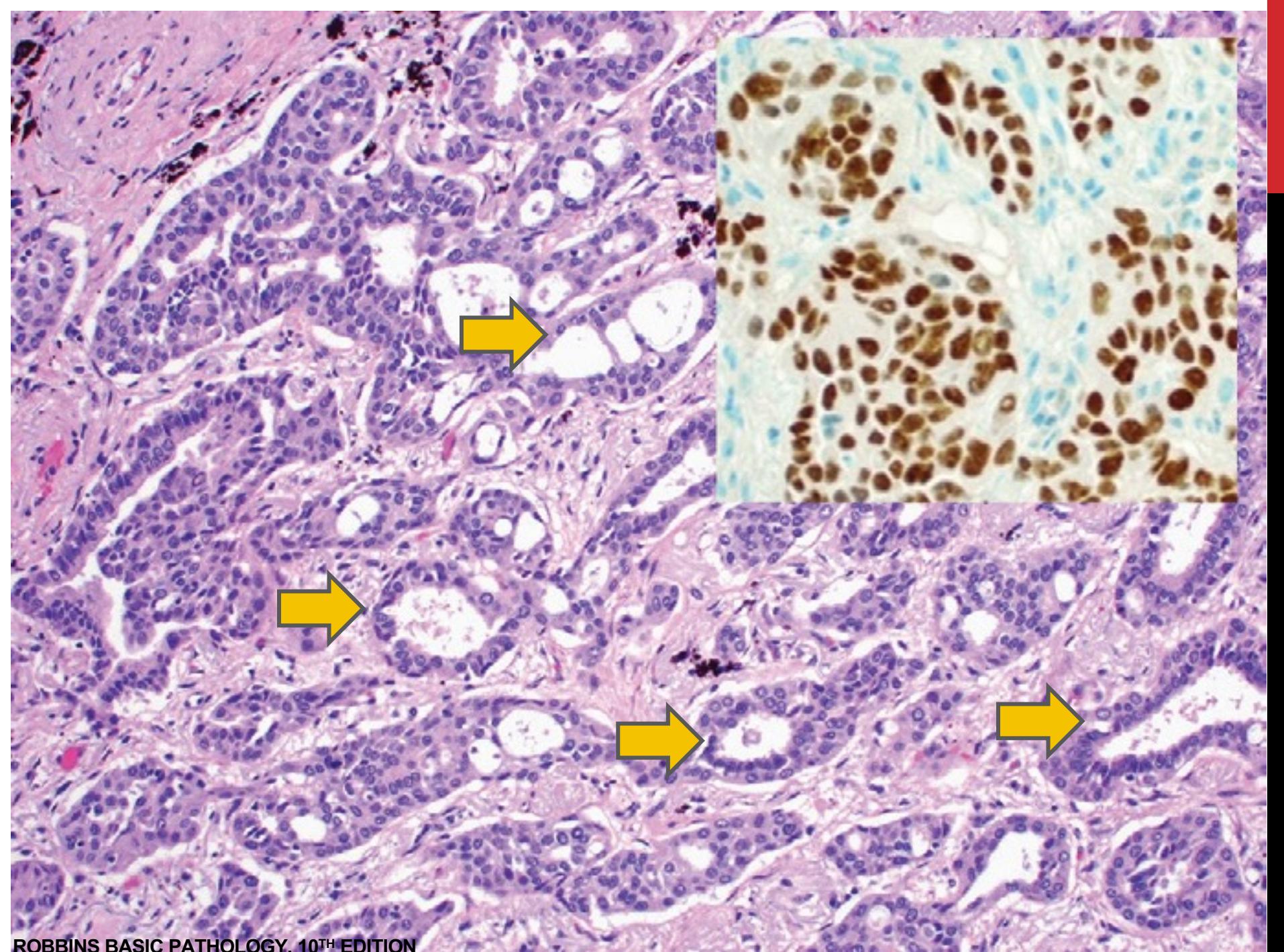
# Adenocarcinoma

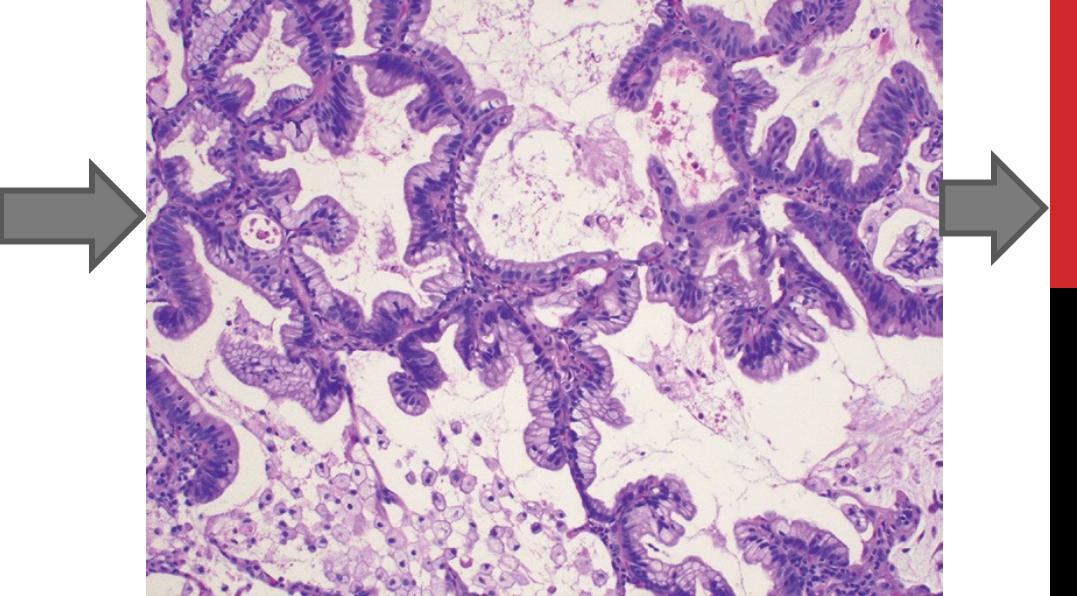
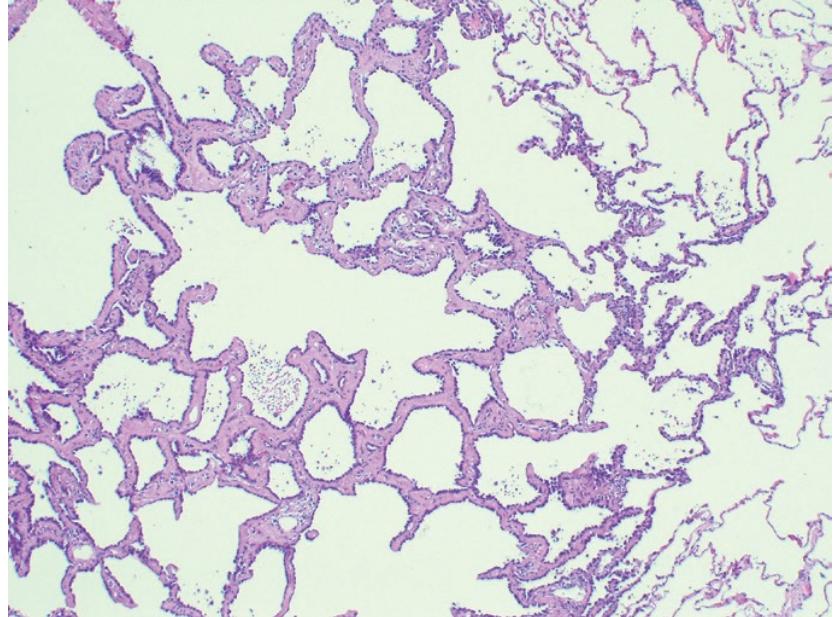


<https://www.verywellhealth.com/large-cell-carcinoma-of-the-lungs-2249356>

# **ADENOCARCINOMA:**

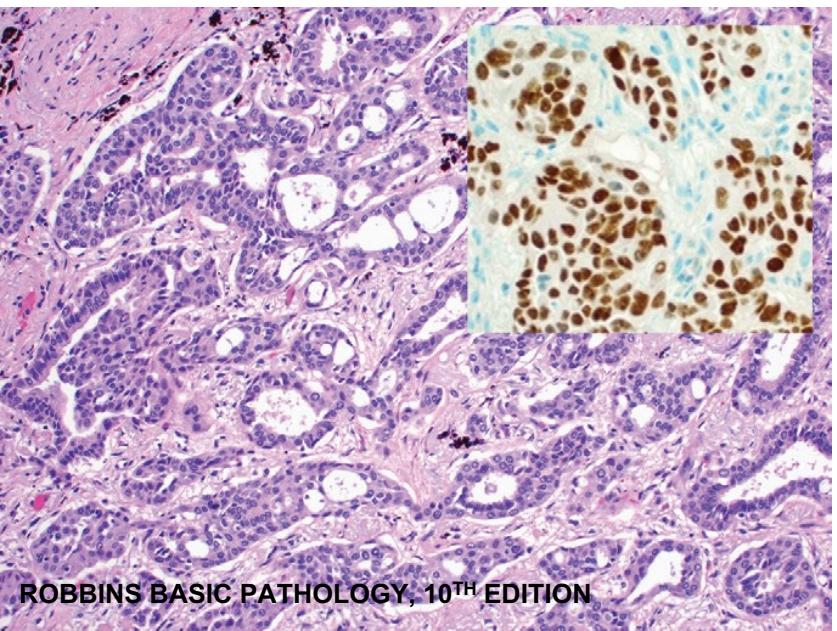
- usually **peripherally located**, but also may occur closer to the hilum.
- grow slowly
- form smaller masses
- tend to metastasize widely at an early stage





**atypical adenomatous  
hyperplasia (AAH)**

**adenocarcinoma in situ (AIS)**

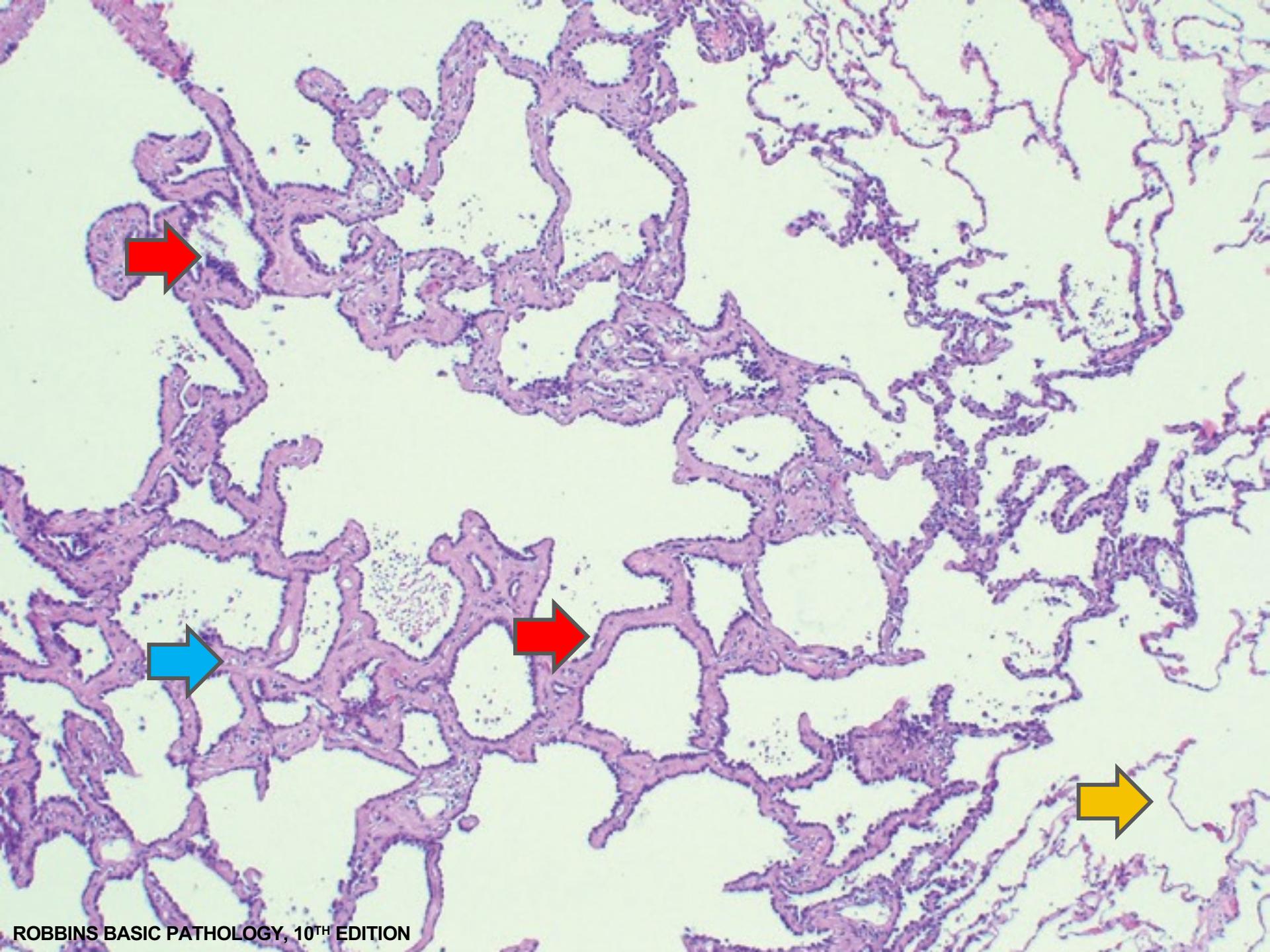


**Adenocarcinoma,  
minimally invasive or invasive**

# **Atypical adenomatous hyperplasia:**

well-demarcated focus of epithelial proliferation

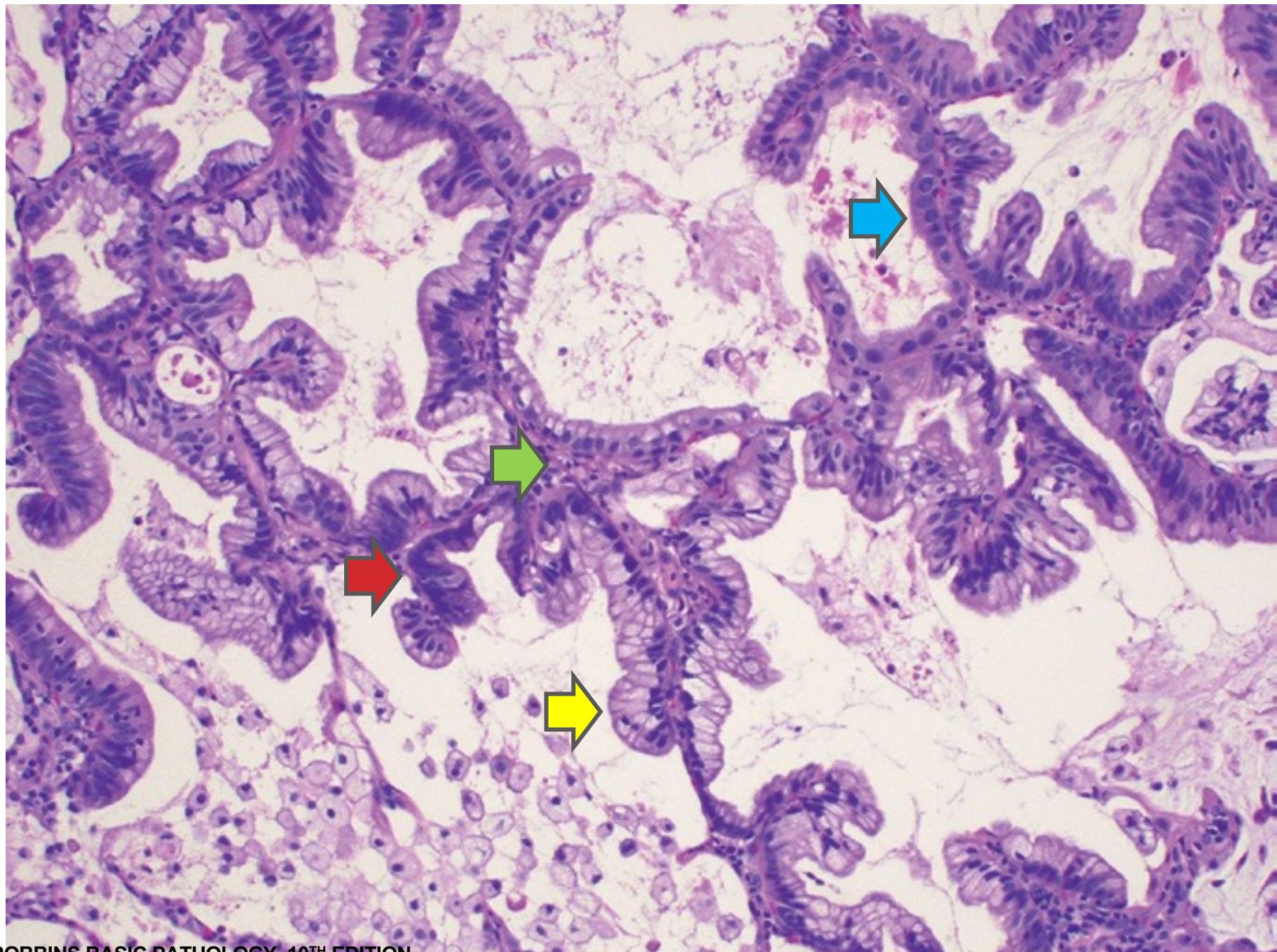
- diameter of ≤5 mm
- composed of cuboidal to low-columnar cells
- demonstrating nuclear hyperchromasia, pleomorphism, and prominent nucleoli.
- **monoclonal** and shares many molecular aberrations with adenocarcinomas (e.g., *KRAS* mutations).



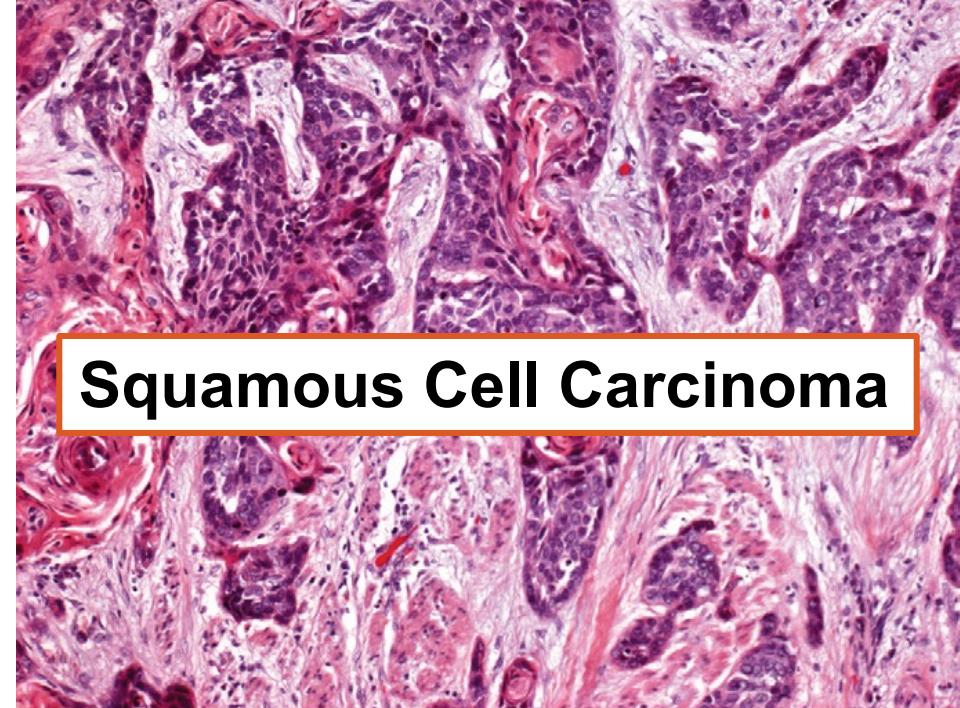
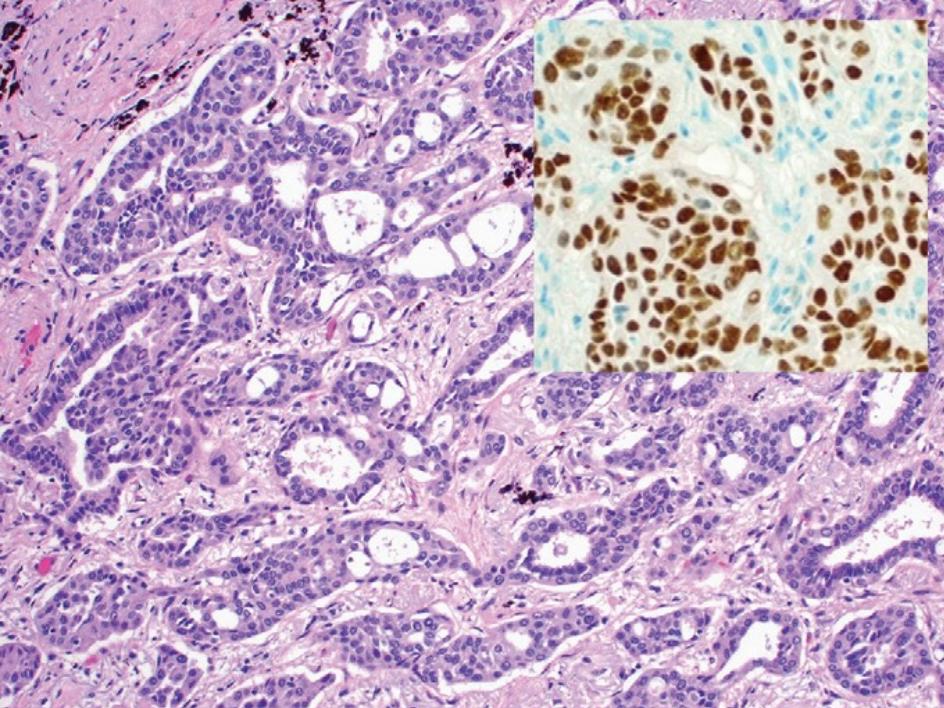
# **Adenocarcinoma in situ (AIS):**

- formerly **bronchioloalveolar carcinoma**
- often involves **peripheral parts** of the lung as a single nodule.
- diameter of **<3 cm**
- **growth along preexisting structures, and preservation of alveolar architecture.**

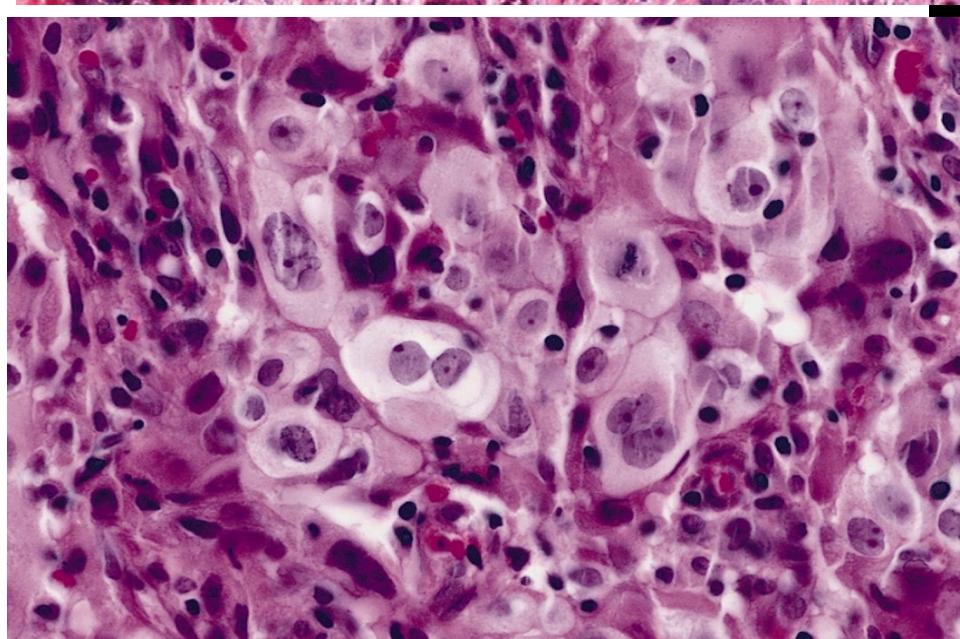
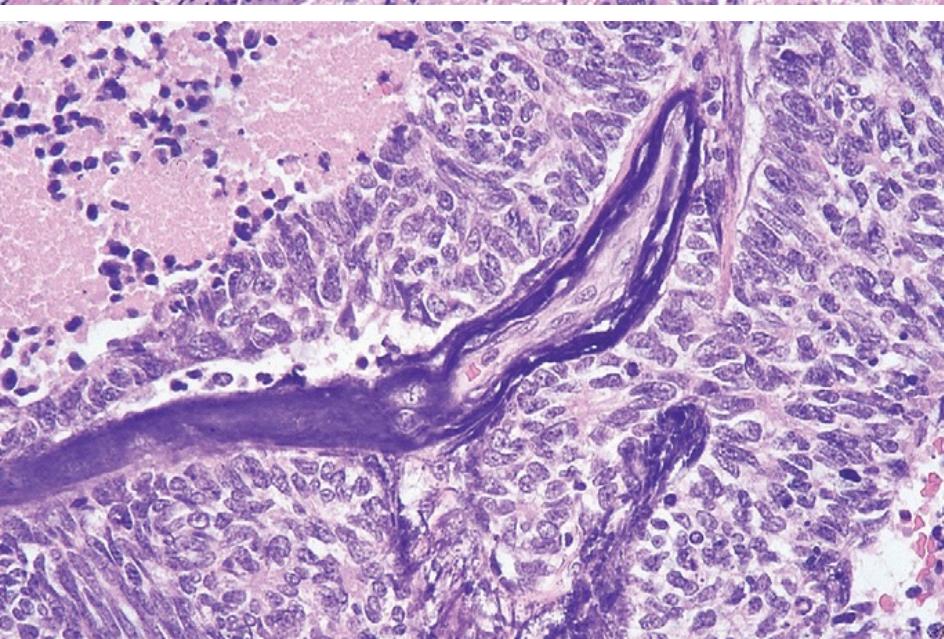
- The tumor cells, which may be nonmucinous, mucinous, or mixed
- grow in a monolayer along the alveolar septa, which serve as a **scaffold**.



- **Minimally invasive adenocarcinoma:** <3 cm in diameter with an invasive component of <5 mm
- **Invasive adenocarcinoma** a tumor of any size with an area of invasion >5 mm.



## Squamous Cell Carcinoma



# SQUAMOUS CELL CARCINOMAS

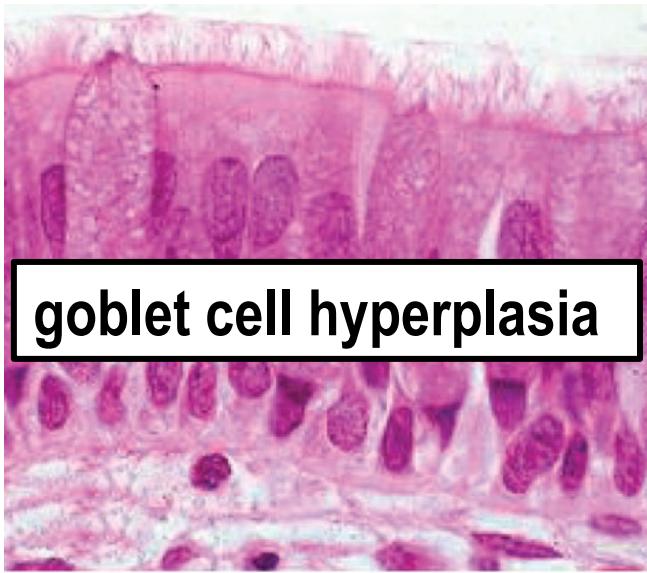
- More common in men
- Closely correlated with **smoking history**
- Arise **Centrally in major bronchi** and eventually spread to local hilar nodes and outside the thorax
- Large lesions may undergo **central necrosis**, giving rise to **cavitation**.

- **Preneoplastic lesions:**

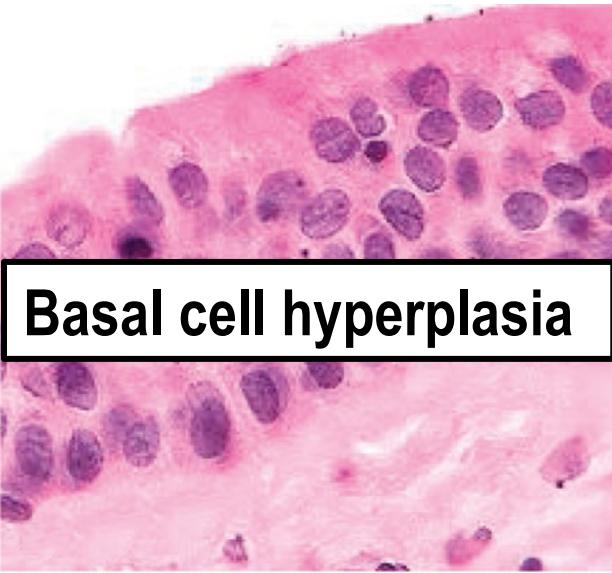
- **squamous metaplasia or dysplasia** in the bronchial epithelium → **carcinoma in situ** → **Squamous cell carcinoma**
- the lesion is asymptomatic until reaches a symptomatic stage when it begins to obstruct the lumen of a major bronchus, +/- atelectasis and infection.

# **MORPHOLOGY:**

Ranges from **Well differentiated squamous cell neoplasms** showing keratin pearls and intercellular bridges to **Poorly differentiated neoplasms** with only minimal residual squamous cell features.



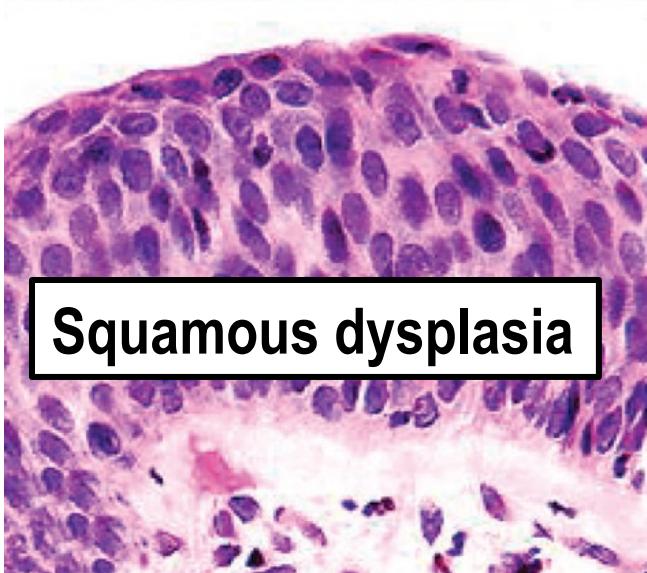
**goblet cell hyperplasia**



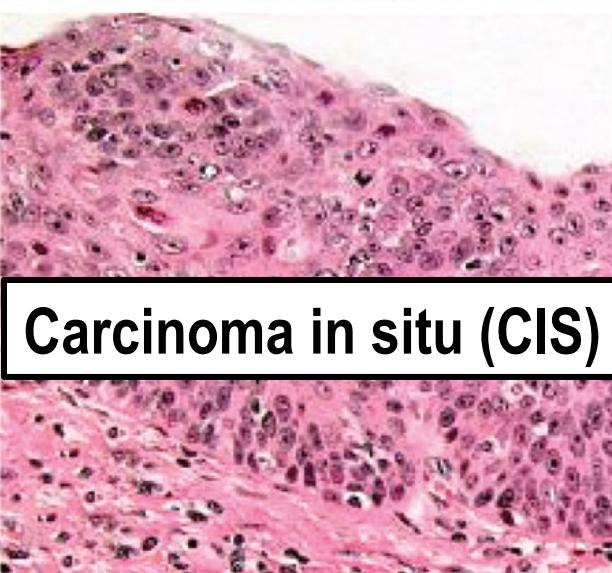
**Basal cell hyperplasia**



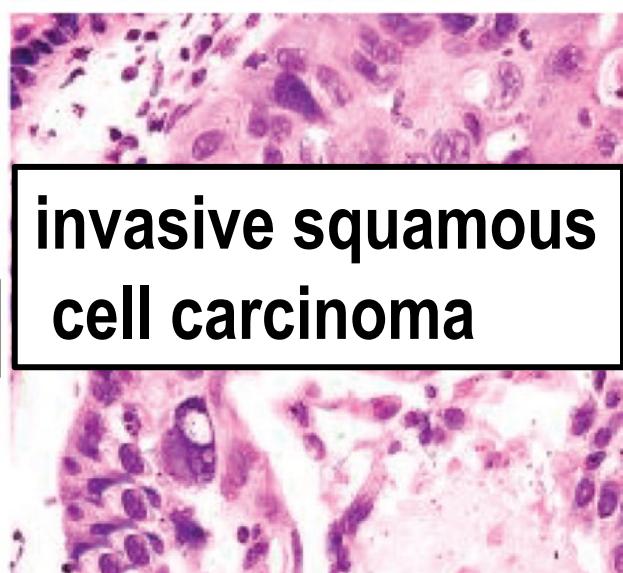
**Squamous metaplasia**



**Squamous dysplasia**



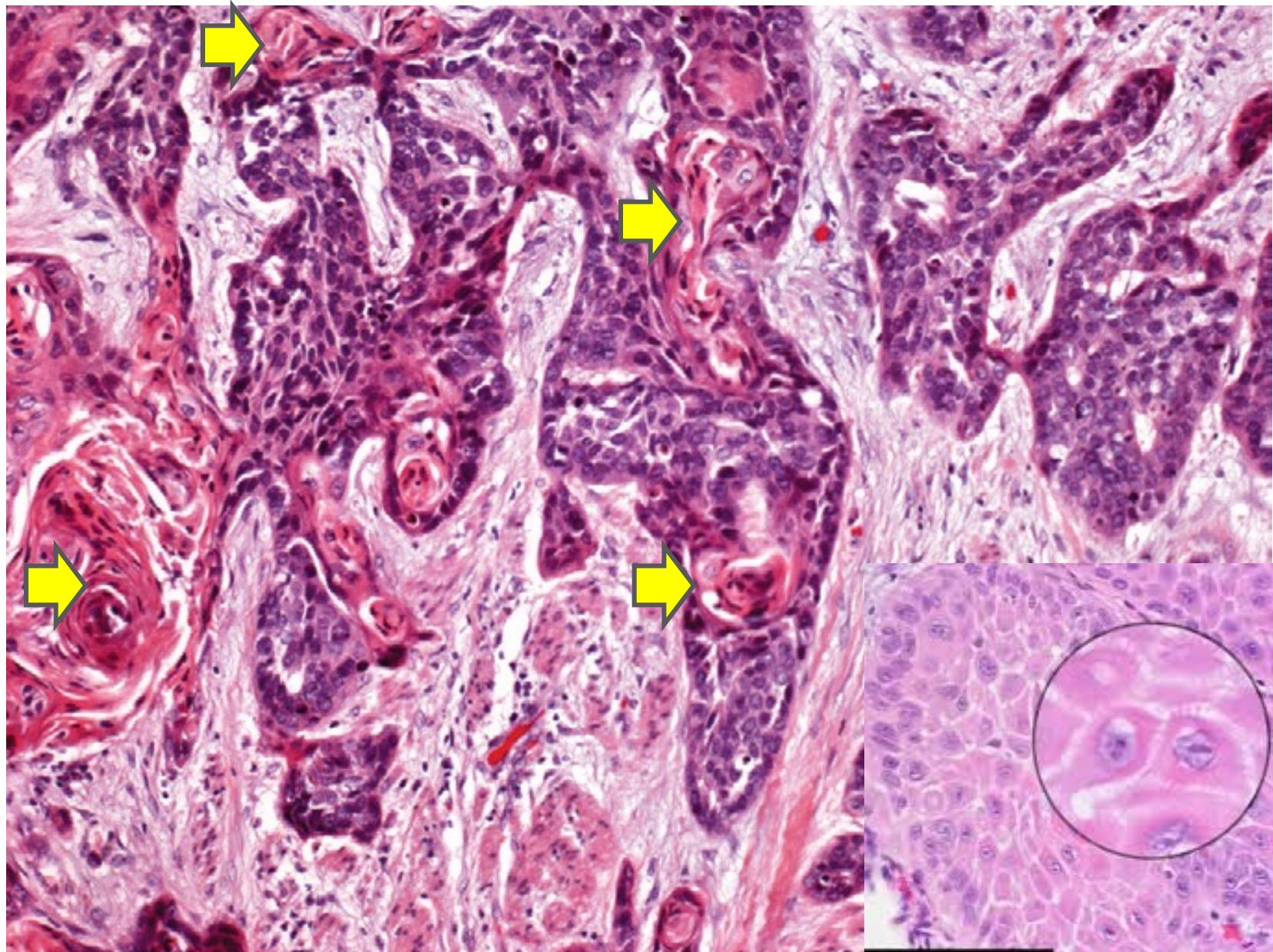
**Carcinoma in situ (CIS)**



**invasive squamous  
cell carcinoma**



# **WELL-DIFFERENTIATED SQUAMOUS CELL CARCINOMA SHOWING KERATINIZATION AND PEARLS.**



**UNSOLVED**

A large, bold, red stamp with the word "UNSOLVED" in capital letters is superimposed diagonally across the center of the image. The background consists of a collage of various newspaper clippings and black and white photographs. Some visible text from the clippings includes "unsolved", "murder", "two dead", "Upcoming", "Hand murder case", and "leaves 2 dead". There are also several small photographs, one of which appears to be a portrait of a young man.

69 year old gentleman, smoker, presented with cough and a 7 kg weight loss over the past 4 months. Physical examination shows finger clubbing. He is afebrile. CXR shows no hilar adenopathy, but there is cavitation within a 3-cm lesion near the right hilum. Labs show elevated serum calcium. Bronchoscopy shows a lesion occluding the right main bronchus. A surgical procedure with curative intent is attempted. Which of the following neoplasms is most likely to be present in this patient?

- A Adenocarcinoma in situ
- B Squamous cell carcinoma
- C Metastatic renal cell carcinoma
- D Small cell anaplastic carcinoma

**UNSOLVED**

A large, bold, red stamp with the word "UNSOLVED" in a thick, sans-serif font is overlaid diagonally across a collage of newspaper clippings and photographs. The background consists of various news snippets and images, including a house, a man, and a woman's face. The stamp is partially obscured by the underlying images.

A 57 year old lady presented with chronic nonproductive cough for 4 months along with loss of appetite and a 7 kg weight loss. She does not smoke. On physical examination, no remarkable findings. Her CXR shows a right peripheral subpleural mass. A fine-needle aspiration biopsy is performed, and she undergoes a right lower lobectomy. Microscopically the proliferating cells show glandular differentiation. Which of the following neoplasms did she most likely have?

- A) Adenocarcinoma
- B) Bronchial carcinoid
- C) Hamartoma
- D) Squamous cell carcinoma

**FOR YOUR QUESTIONS:**

**M.ABDALJALEEL@JU.EDU.JO, M. Teams**

**Or E-learning**



# **THANK YOU!**