Lung tumors -1

Manar Hajeer, MD, FRCpath

School of medicine, university of Jordan

- Metastases to the lungs are more common than primary lung neoplasms, because so many other primary tumors can metastasize to the lungs.

- 95% of primary lung tumors are carcinomas
- 5% are other tumors:
- (Benign, carcinoids, mesenchymal and lymphoid)

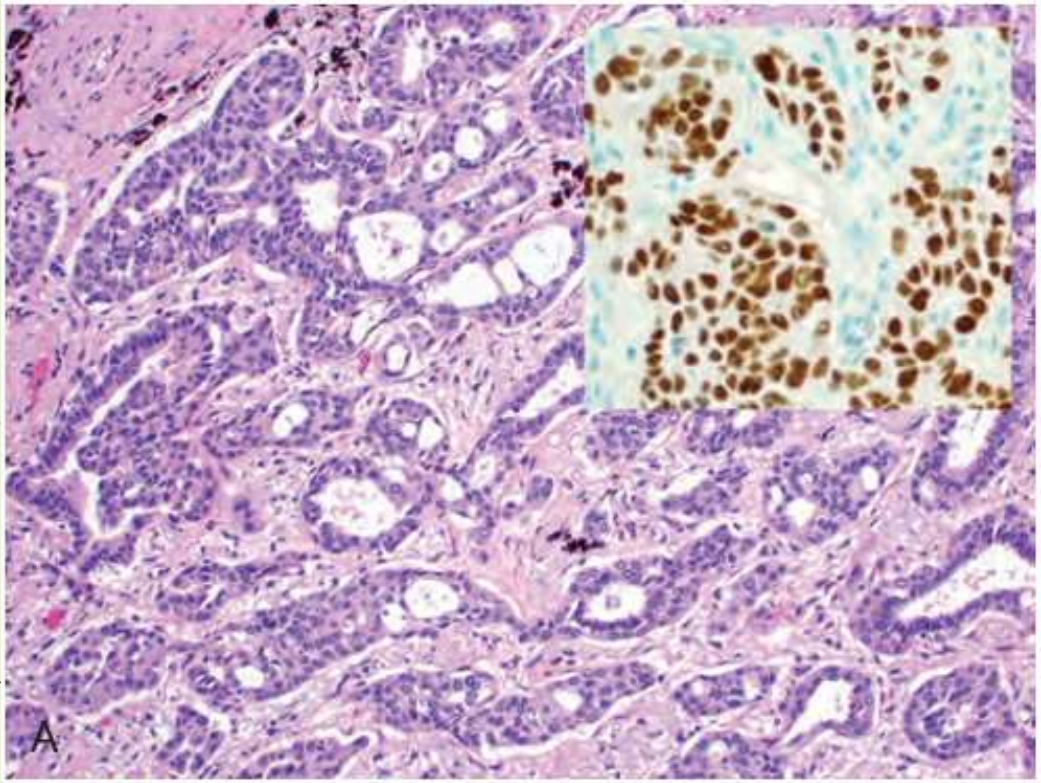
Carcinomas:

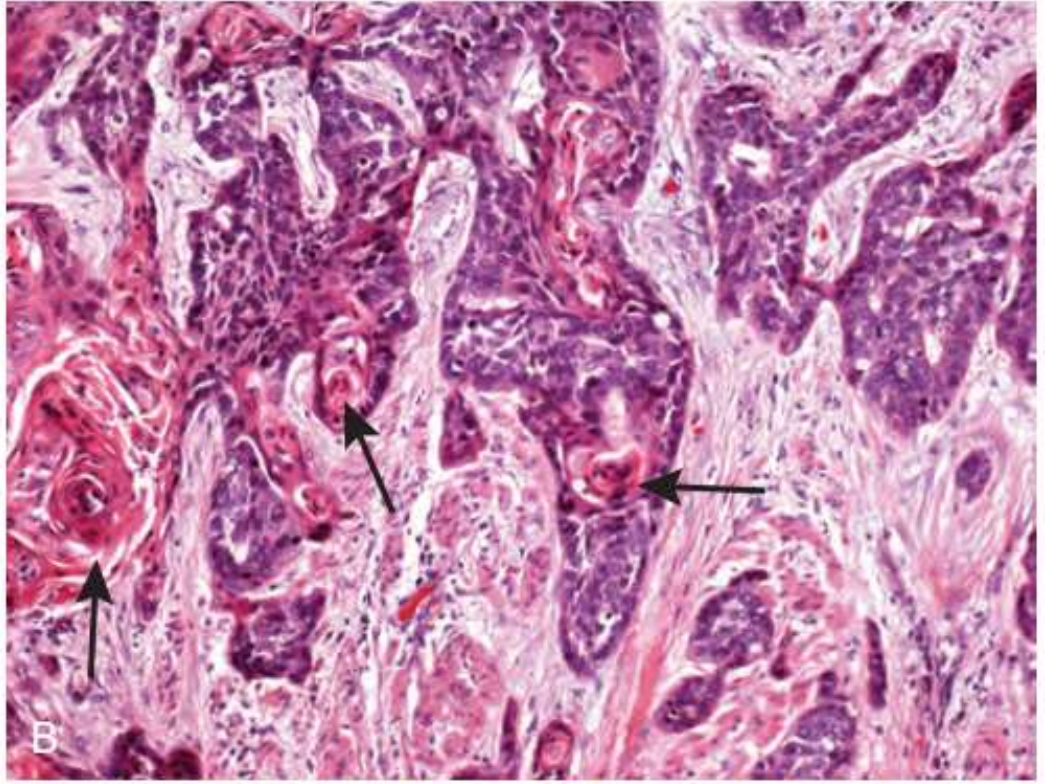
- Strongly associated with smoking.
- Leading cause of cancer related deaths in high resource countries.
- One third of cancer related deaths in men.
- Since 1987 leading cancer related deaths in women.
- Peak in 50s-60s.
- >50% have advanced disease at Dx. (Mets)

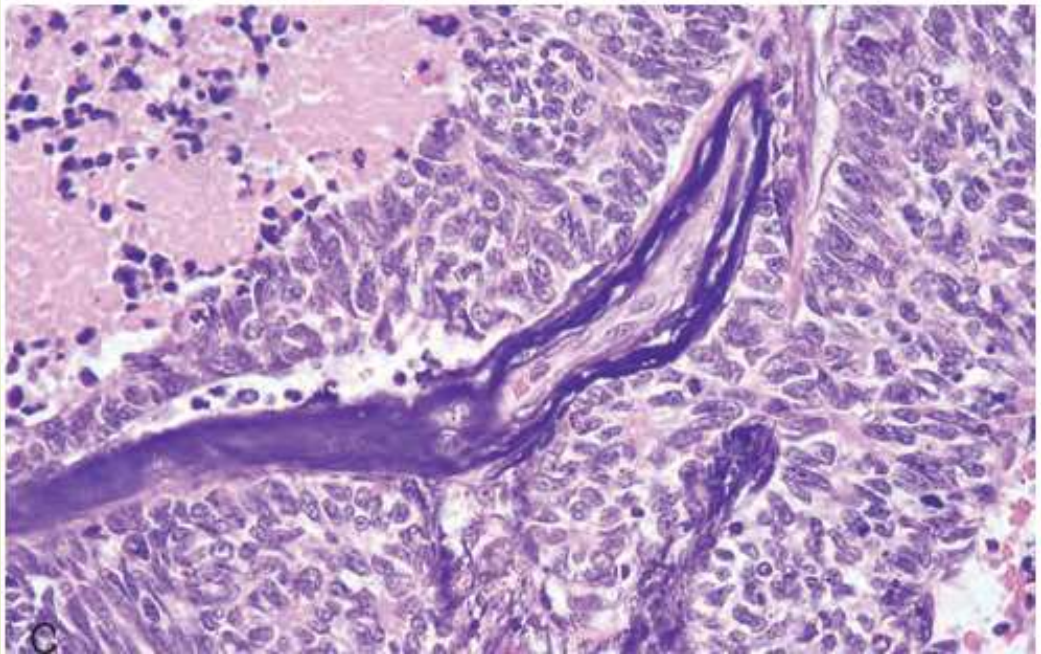
- Overall prognosis is poor.

Four major histologic types

- **A-Adenocarcinoma (most common)**
- **B-Squamous cell carcinoma**
- **C-Small cell carcinoma.**
- **D-Large cell carcinoma**


A


B


C

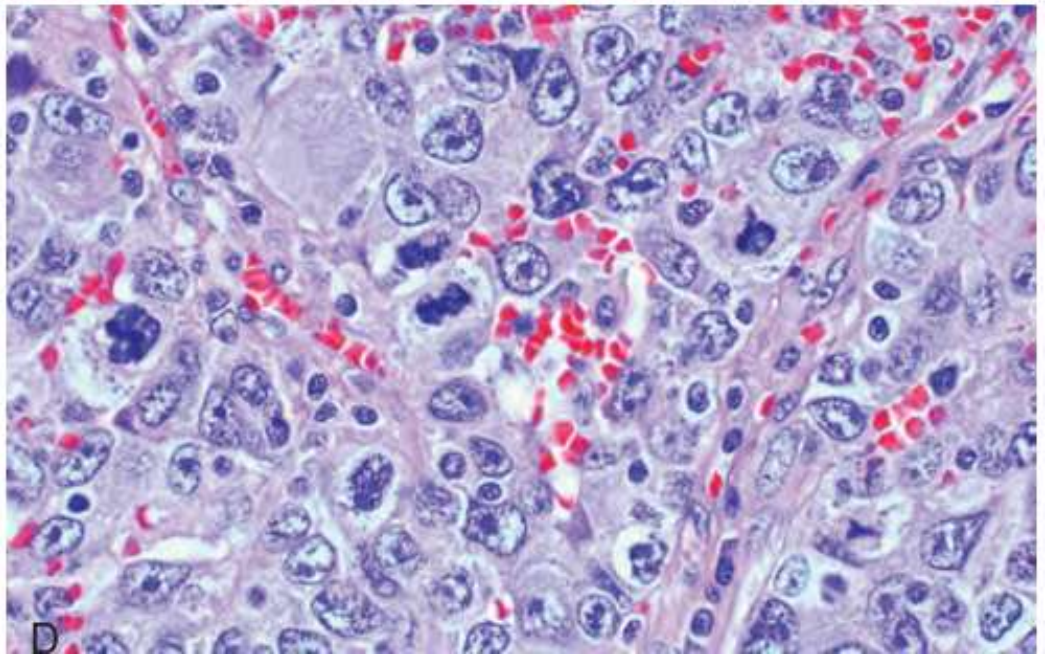

D

Table 15-9 Histologic Classification of Malignant Epithelial Lung Tumors

Tumor Classification
Squamous cell carcinoma
Papillary, clear cell, small cell, basaloid
Small-cell carcinoma
Combined small-cell carcinoma
Adenocarcinoma
Minimally invasive adenocarcinoma (nonmucinous, mucinous)
Lepidic, acinar; papillary, solid (according to predominant pattern)
Mucinous adenocarcinoma
Large-cell carcinoma
Large-cell neuroendocrine carcinoma
Adenosquamous carcinoma
Carcinomas with pleomorphic, sarcomatoid, or sarcomatous elements
Carcinoid tumor
Typical, atypical
Carcinomas of salivary gland type

- **SQUAMOUS CELL CARCINOMA and SMALL CELL CARCINOMA show STRONGEST association with SMOKING.**

- **Adenocarcinomas are the most common primary tumors arising in**
- **Women**
- **Never-smokers**
- **Persons younger than 45 years.**

- 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 have metastasized by the time of diagnosis.
- Not curable by surgery.
- Best treated by chemotherapy, with or without radiation therapy.

NSCLCs

- More likely to be resectable.
- Usually responded poorly to chemotherapy.
- Targeted therapy nowadays for adenocarcinoma and squamous cell carcinomas.

Pathogenesis:

- Carcinogenic exposure + genetic abnormalities.
- **Smoking and environmental carcinogens** >>>> stepwise accumulation of driver mutations >>> produce neoplastic cells with hallmarks of cancer.

Cigarette smoking:

- 90% of lung cancer occur in current smokers or who quit recently.
- Only 11% of heavy smokers develop lung cancer.
- Linear correlation between the frequency of lung cancer and pack- years of cigarette smoking.
- Heavy smokers (2 packs per day for 20 years): risk is 60 times higher than non-smokers.

Cigarette smoking:

- Women are more susceptible to carcinogens in tobacco 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.

Environmental carcinogens:

- Occupational exposures.
- Uranium mines, asbestos, arsenic, chromium, nickel, vinyl chloride.

- Synergistic interaction between carcinogens:
- Asbestos in non-smokers >>> 5-fold increased risk.
- Asbestos + heavy smokers >>>>> 55 folds increased risk

Pathogenesis:

- Early event: inactivation of tumor suppressor genes on chromosome 3 (3p)
- Late event: mutations in TP53 tumor suppressor gene and KRAS oncogene
- Subset of adenocarcinomas in non-smoking women: activating mutations of the epidermal growth factor receptor EGFR (receptor tyrosine kinase)
- Targeted therapy: EGFR, KRAS.

Precursor lesions:

- **Invasive adenocarcinomas:**
- **Atypical adenomatous hyperplasia ----- adenocarcinoma in situ ---- invasive adenocarcinoma sequence.**

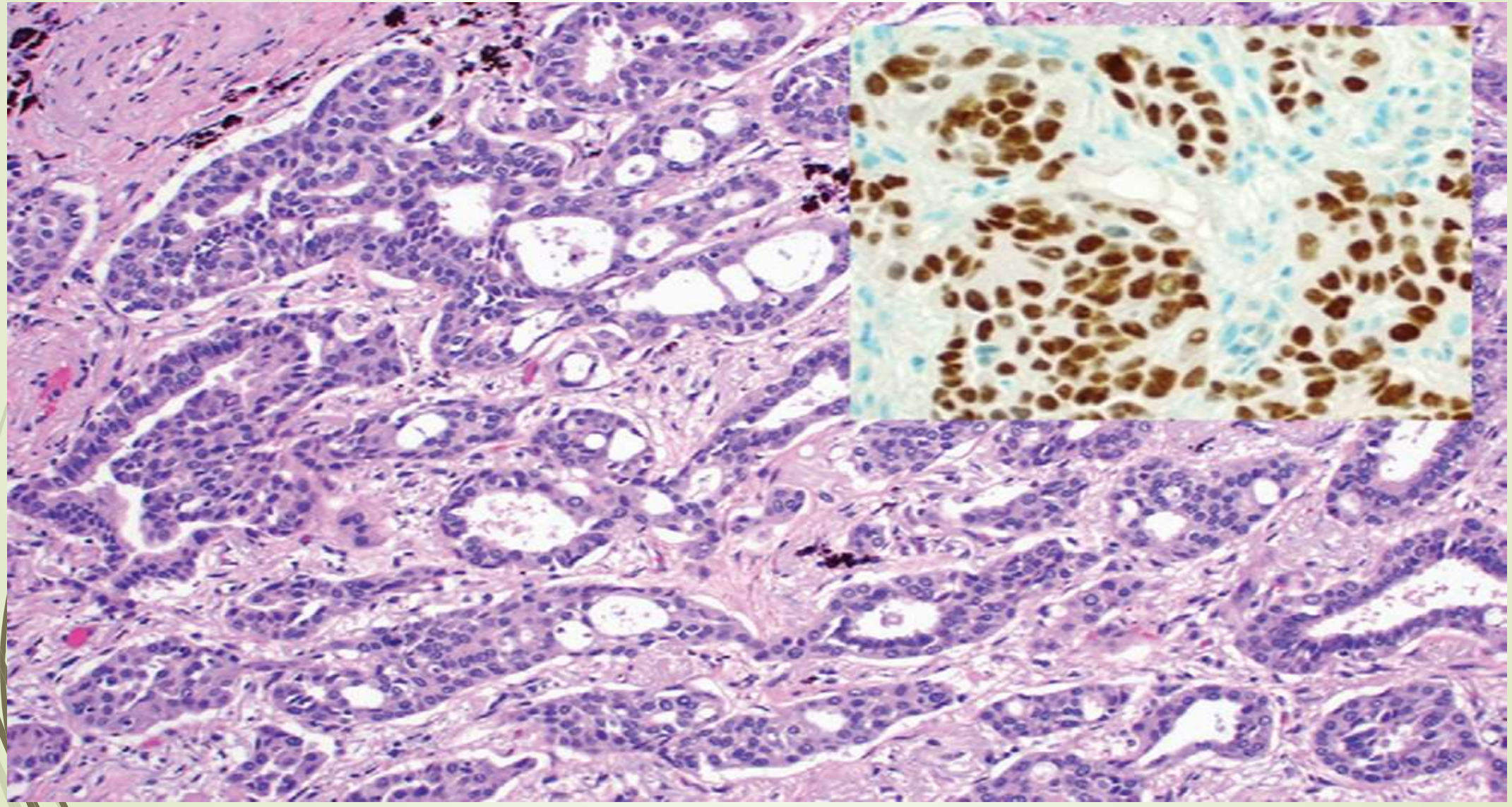
- **Squamous cell carcinoma:**
- **Basal cell hyperplasia ---- squamous metaplasia ---- squamous dysplasia ----- CIS ---- invasive SCC.**

Adenocarcinoma:

- Peripherally located.
- Slowly growing.
- Smaller than other subtypes.
- Metastasize widely at an early stage.

- Histology: Gland forming or mucin producing
- IHC: TTF-1 stain is specific.

Gland forming adenocarcinoma:

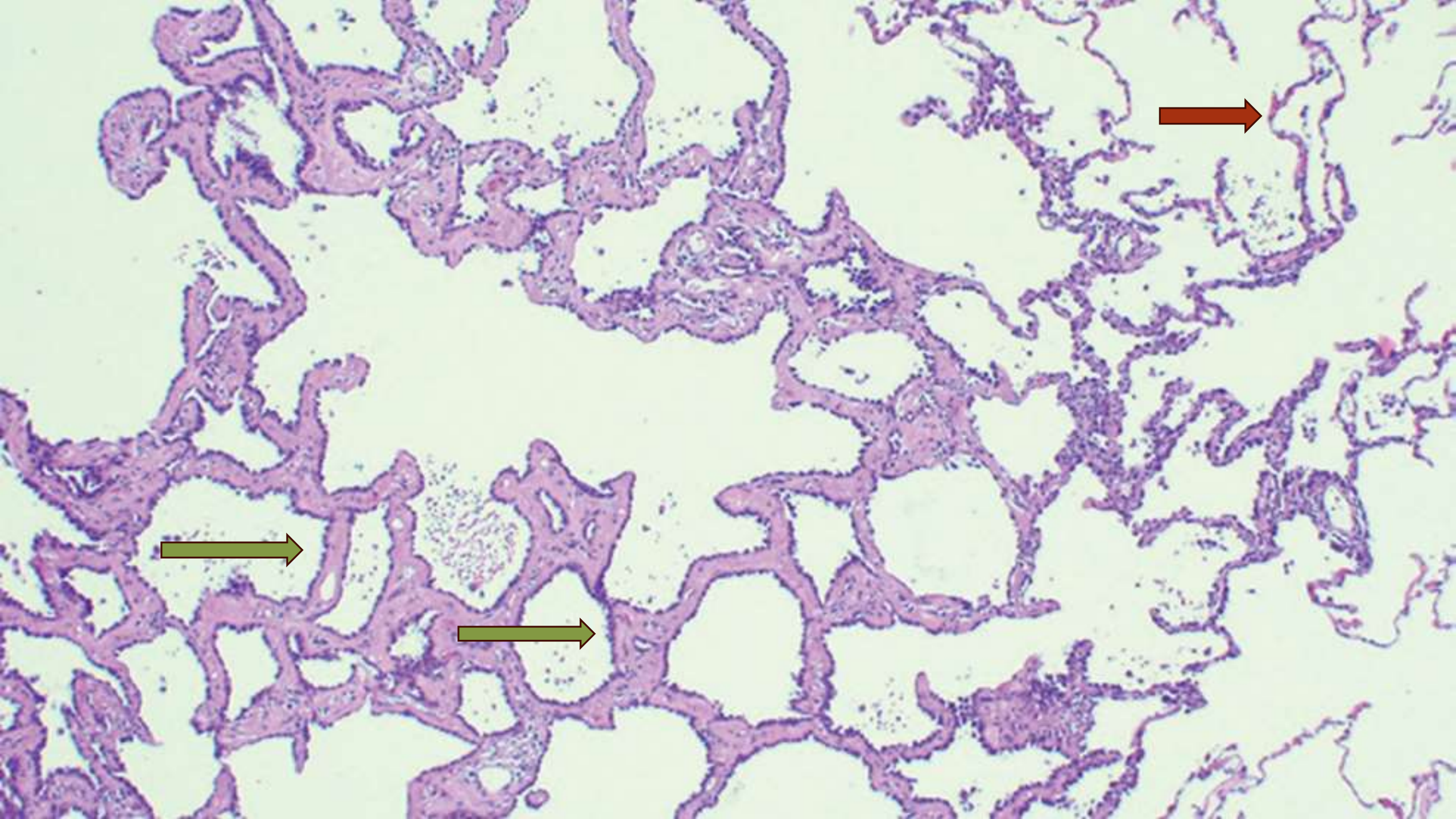


Sequence of events:

- Atypical adenomatous hyperplasia (AAH).
- Adenocarcinoma in situ (AIS).
- Minimally invasive adenocarcinoma.
- Invasive adenocarcinoma.

Atypical adenomatous hyperplasia (AAH):

- Well demarcate focus.
- 5 mm or less in diameter.
- Lined by cuboidal to low-columnar epithelial cells showing nuclear hyperchromasia, pleomorphism, and prominent nucleoli.
- KRAS mutation (monoclonal).



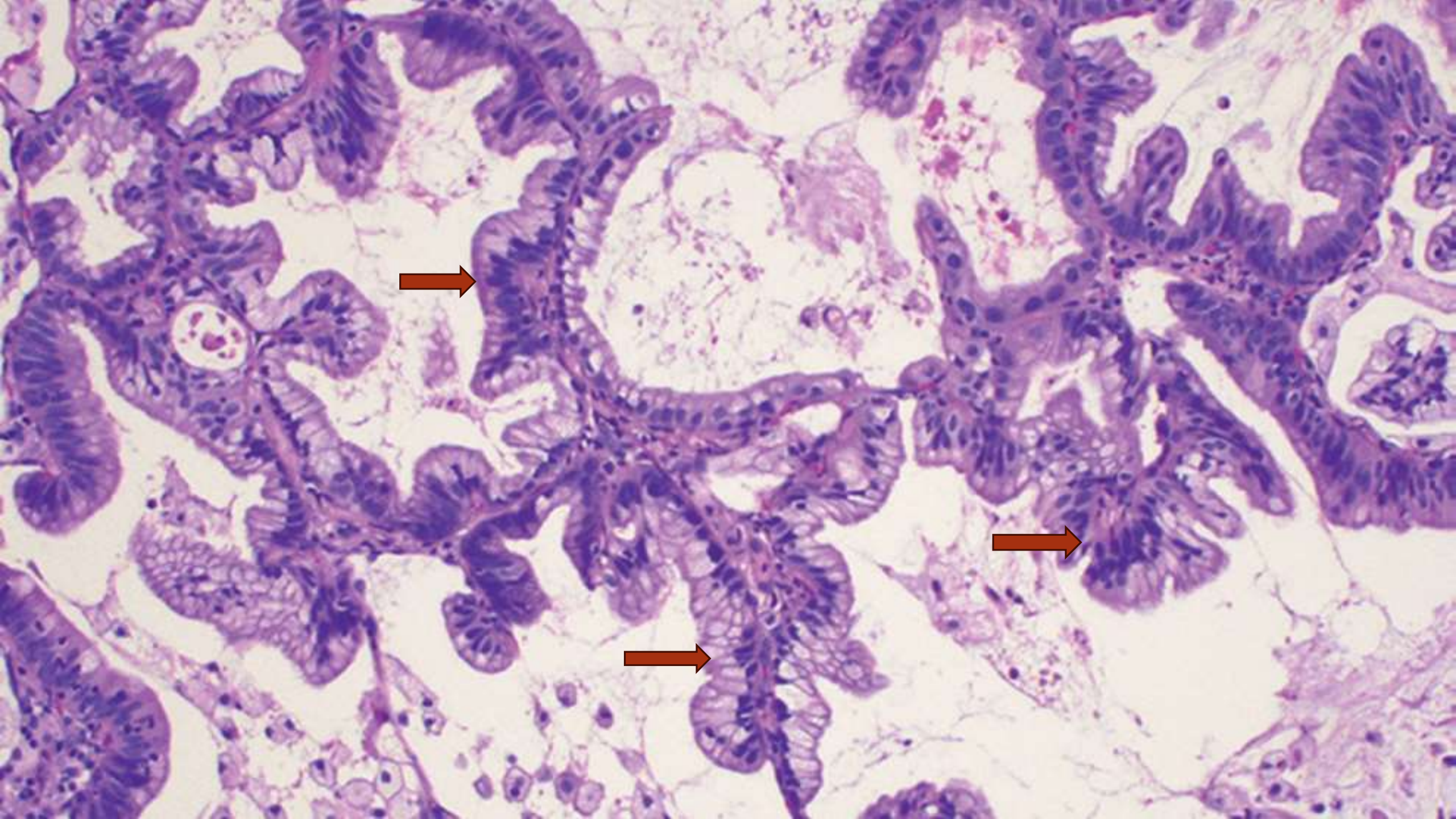
Adenocarcinoma in situ (AIS)

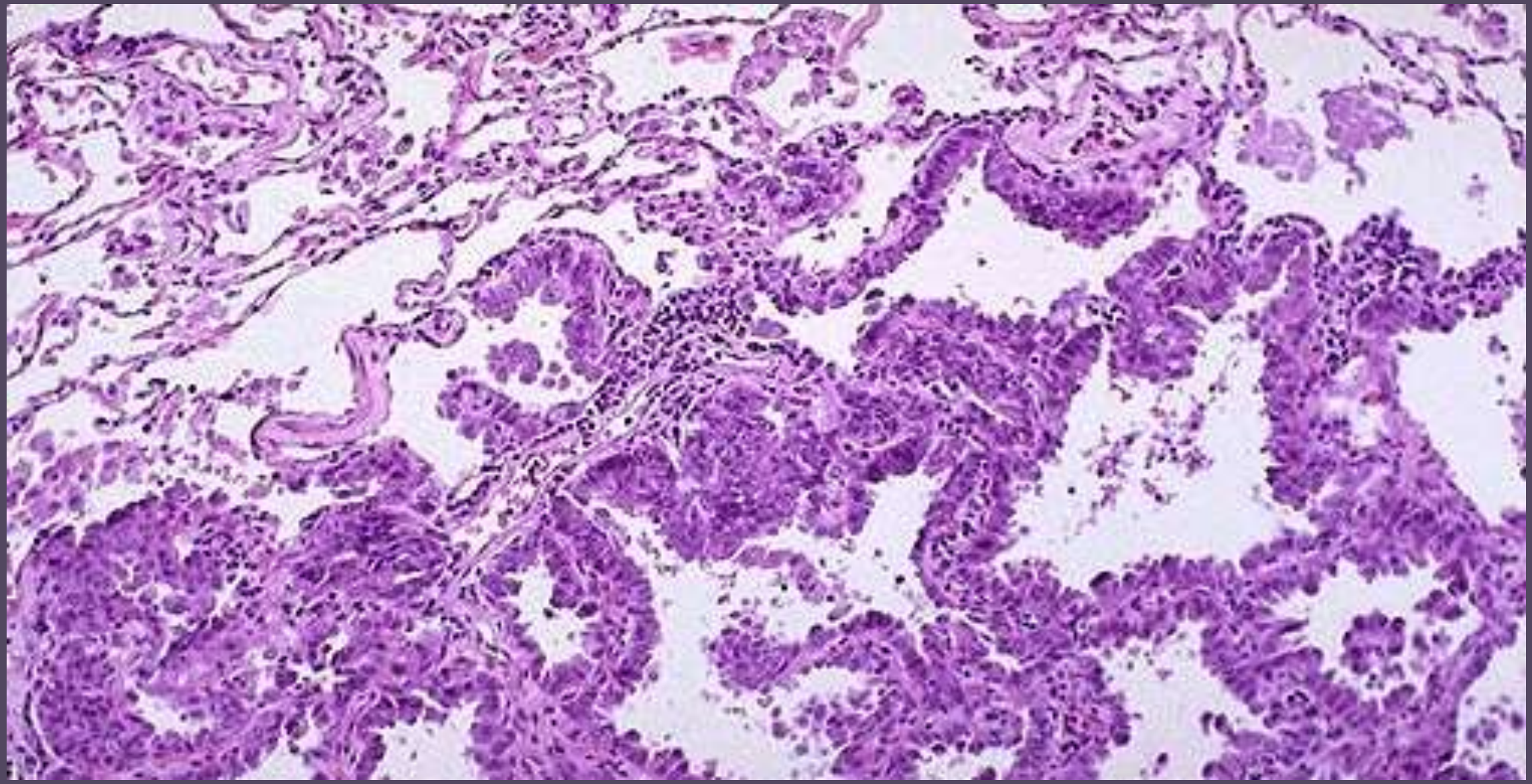
- **Bronchioalveolar carcinoma (old name)**

- **Single peripheral nodule.**
- **3 cm or less in diameter.**
- **Mucinous or non-mucinous dysplastic cells growing along pre-existing alveolar septa (scaffold) (lepidic pattern)**
- **Preservation of alveolar architecture.**

AIS by definition :

- No destruction of alveolar architecture
- No stromal invasion.
- No desmoplasia.





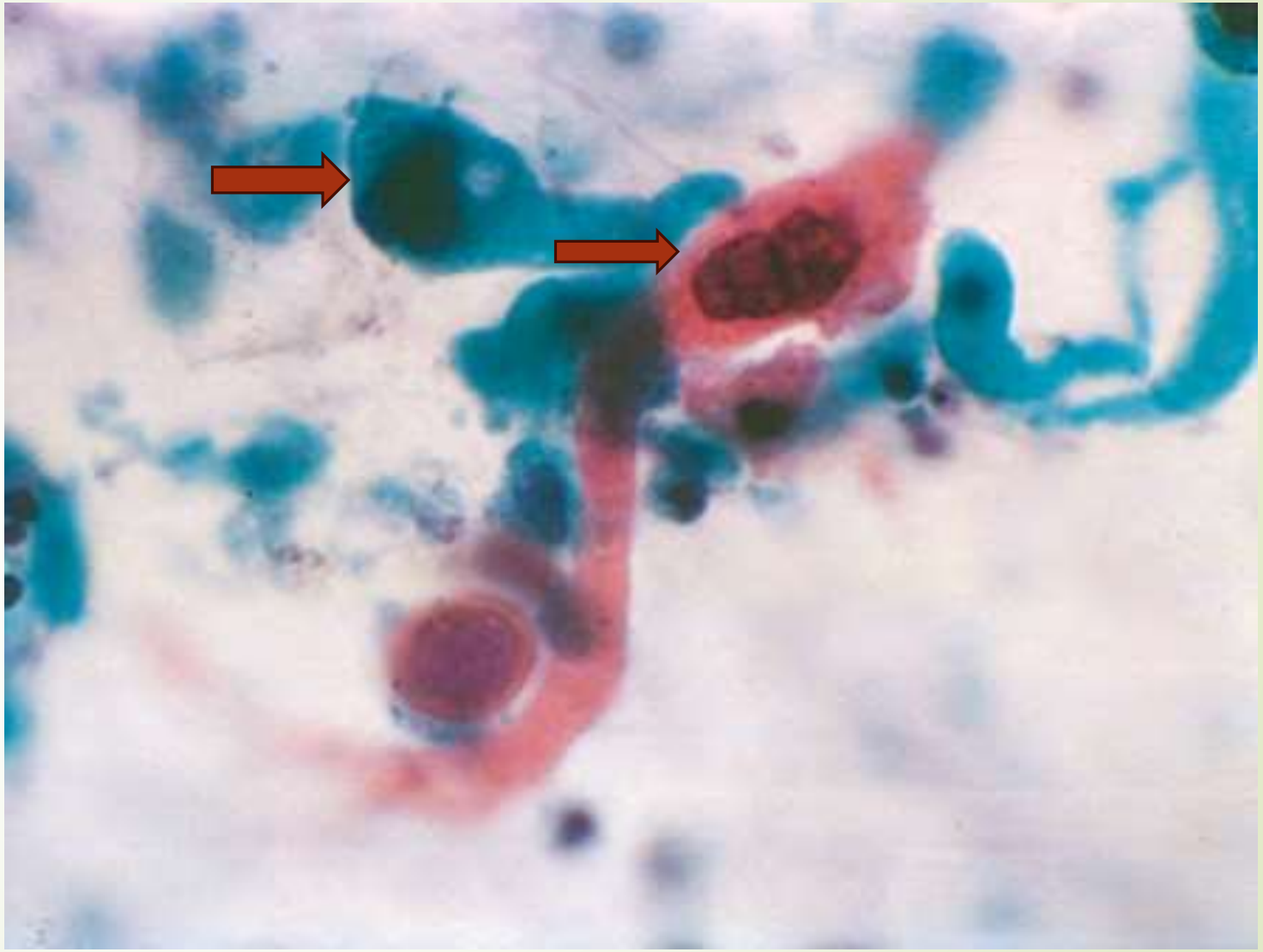
Squamous cell carcinomas

- More common in men
- Closely correlated with smoking.
- Arise centrally in major bronchi.
- Spread to local hilar nodes.
- Disseminate outside the thorax later
- Cavitation in large lesions due to central necrosis

- **Preceded by squamous metaplasia >>> dysplasia >>> carcinoma in situ.**

- **Atypical cells appear in sputum and brushing cytologic smears in asymptomatic, radiologically undetectable lesions**

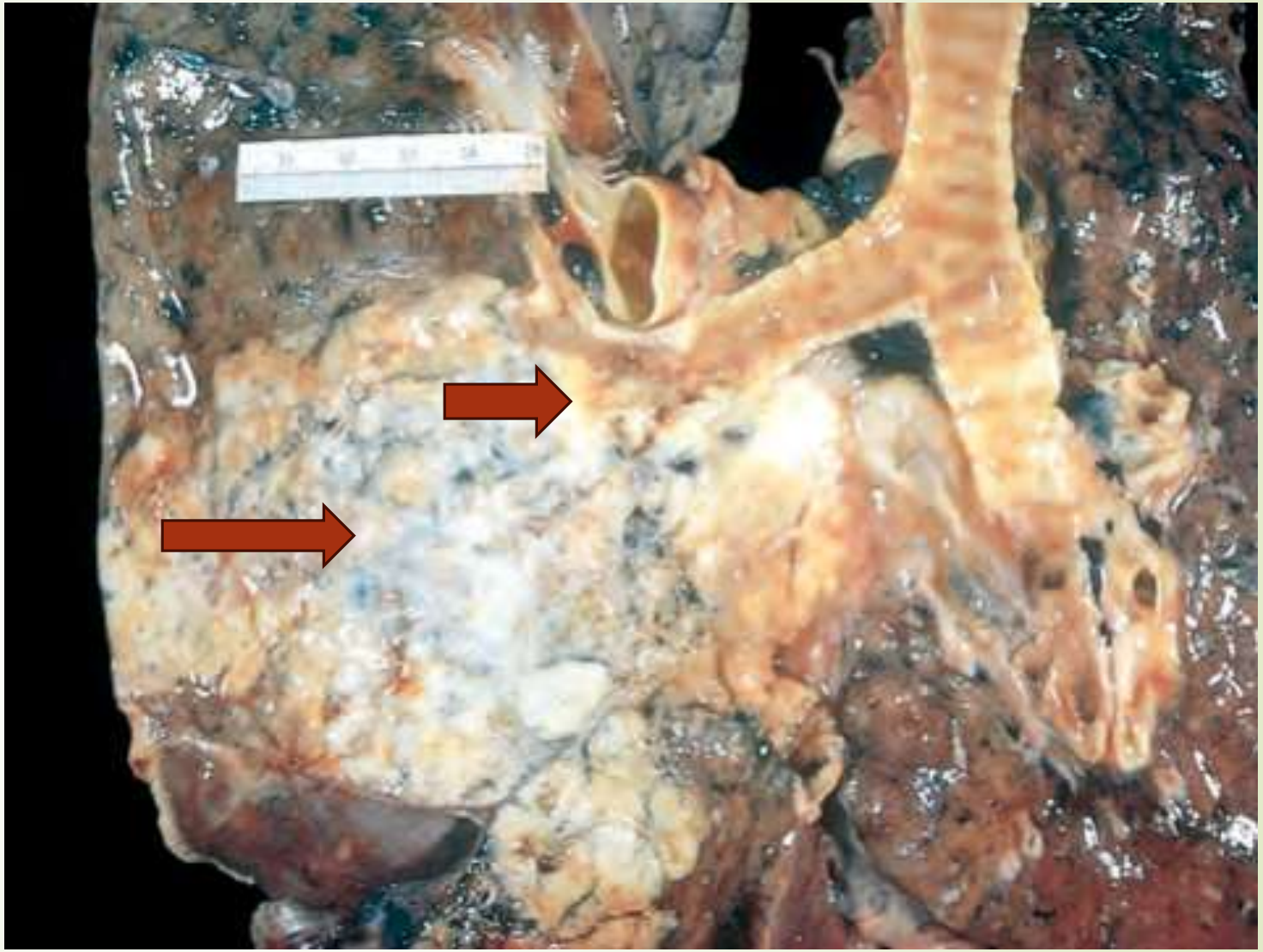
- Sputum specimen: orange-staining, keratinized squamous carcinoma cell.

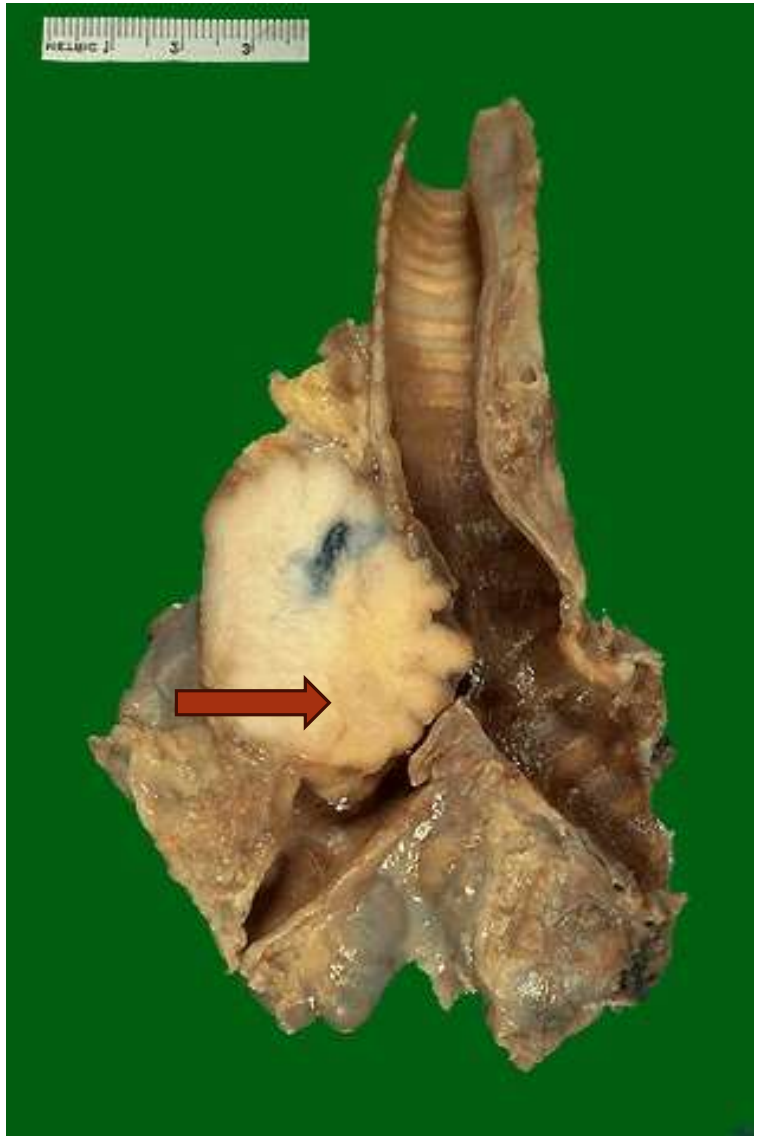


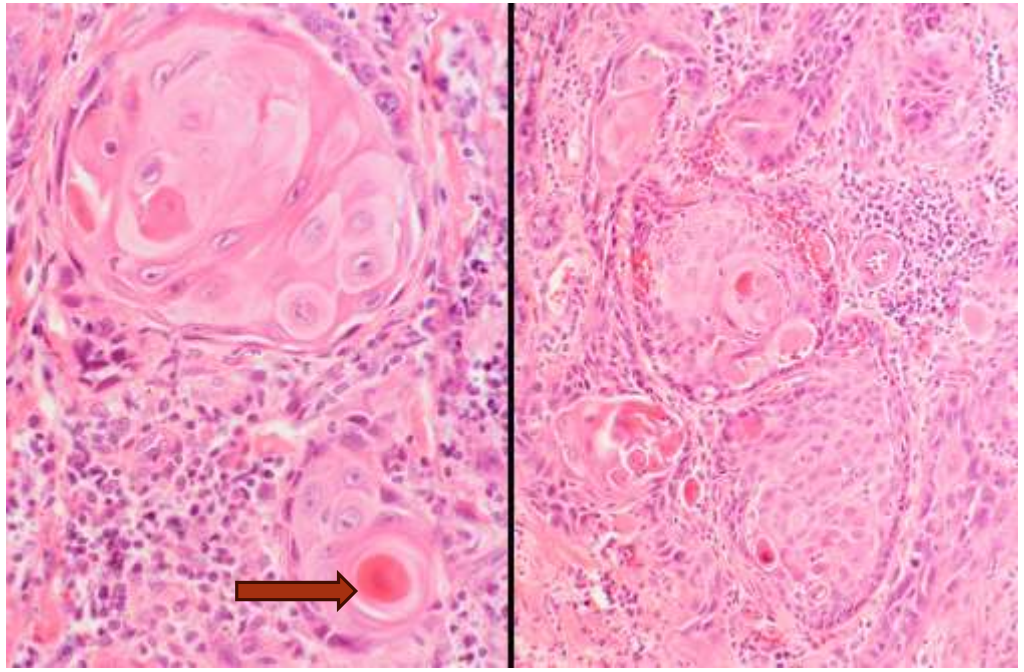
- Symptomatic stage: begins to obstruct the lumen of a major bronchus
- +/- atelectasis and infection.

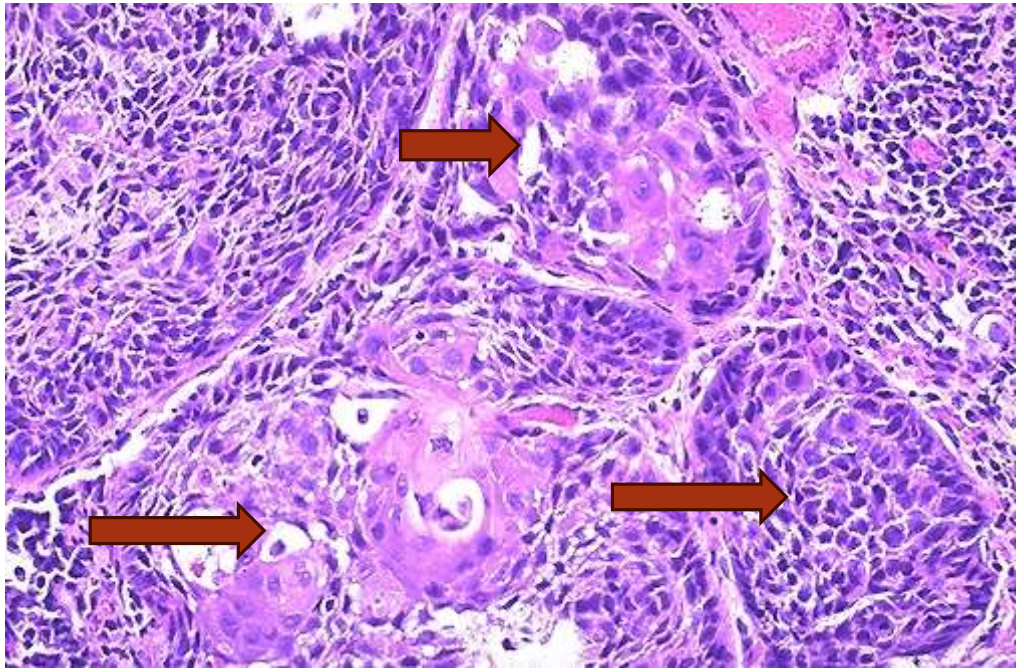
- **Histology:**
- Well differentiated SCC: keratin pearls and intercellular bridges.
- Poorly differentiated SCC: only minimal residual squamous cell features.

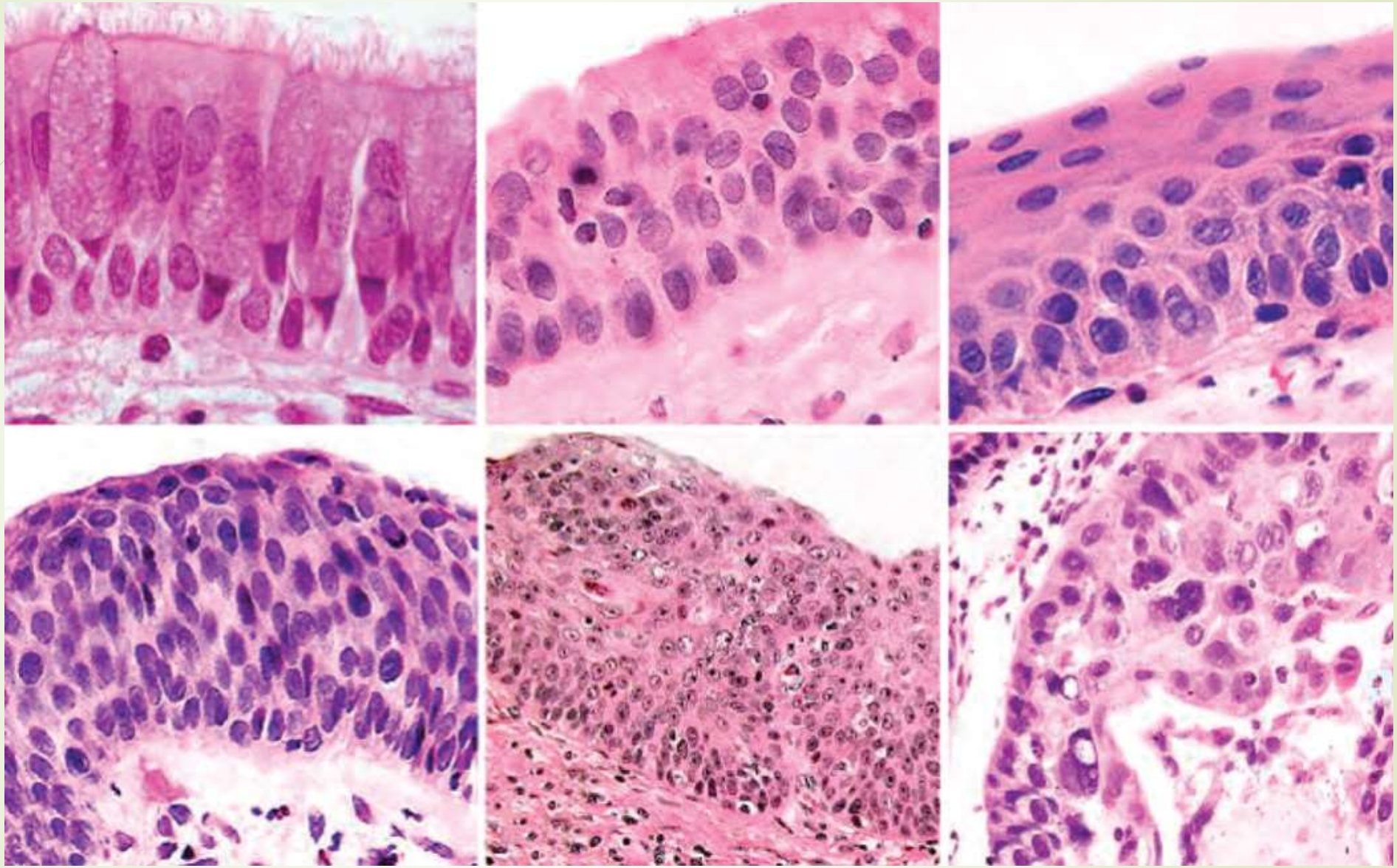
- Gray-white tumor arising from bronchus, infiltrates the lung parenchyma.





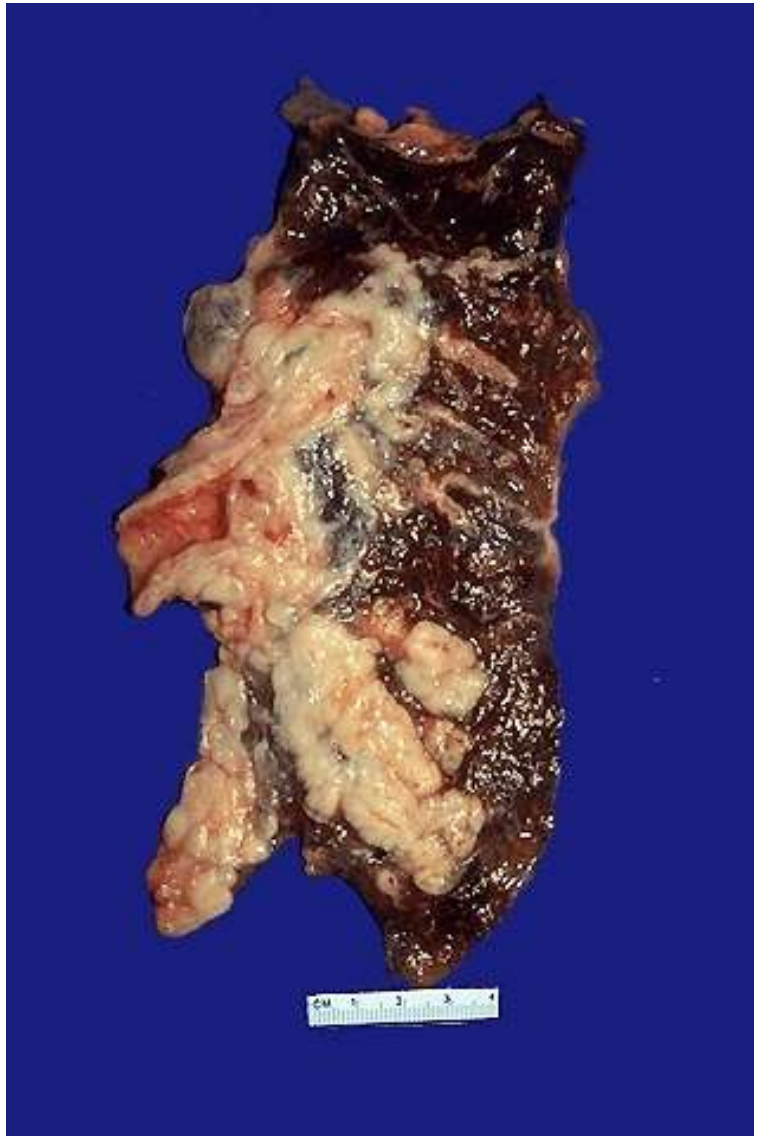






SMALL CELL LUNG CARCINOMAS (SCLC)

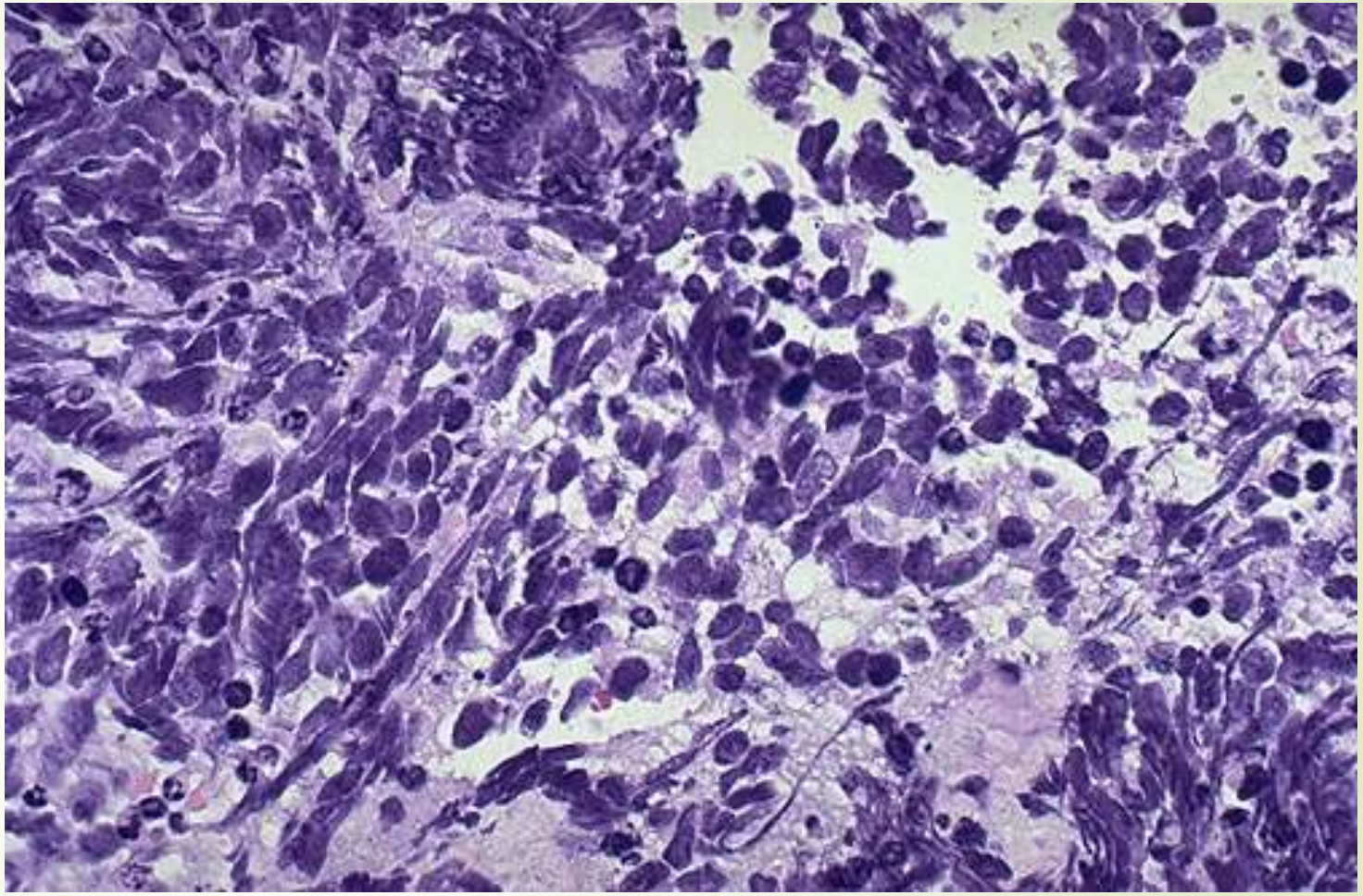
- Centrally located, may extend into the lung parenchyma.
- By the time of Dx: hilar and mediastinal LNs are involved.
- Very aggressive tumor. Grouped together with large cell neuroendocrine carcinoma.
- No known precursor lesion.



Morphology:
Microscopic:

- Small round to fusiform cells , scant cytoplasm, finely granular chromatin (salt and pepper).
- Frequent mitotic figures and necrosis.
- Fragile tumor cells with “crush artifact” in small biopsy specimens >> basophilic staining of vascular walls (Azzapardi effect)
- Express neuroendocrine markers (chromogranin, synaptophysin and CD56)
- Secrete polypeptide hormones===paraneoplastic syndromes .

Crushing of fragile tumor calls releases DNA that stains blue in biopsy specimens (Azzopardi effect).



Large cell carcinoma

- Undifferentiated malignant epithelial tumor
- Lacks cytologic features of small cell, glandular or squamous differentiation.
- Large nuclei, prominent nucleoli, and a moderate amount of cytoplasm.
- Diagnosis of exclusion.

- Histologic variant: large cell neuroendocrine carcinoma (molecular features like small cell carcinoma), but tumor cells of larger size.

Mixed patterns:

- Approximately 10% of all lung carcinomas have a combined histology, including two or more of the mentioned types.