

# Lung tumors

# Lung cancer pathogenesis

1. **tobacco smoking** is the most important etiologic factor in the development of lung cancer
  - P450 monooxygenase enzyme metabolize procarcinogens derived from cigarette smoke
  - persons with specific genetic polymorphism for P450 gen have increased capacity to metabolize procarcinogens derived from cigarette smoke and increase the risk of carcinoma

# Lung cancer pathogenesis

## Other etiologic factors:

- 2. radiation
- 3. asbestos (5x) especially combined with smoking (55x)
- 4. air pollution (radon)
- 5. miscellaneous occupational inhaled substances (nickel)

# Lung cancer pathogenesis

## 6. Genetic mechanism, mutation

### **small cell cancer:**

mutation of p53, Rb1 tumor suppressor genes

### **squamous cell carcinoma:**

highest frequency of p53 mutations

inactivation of p16

### **adenocarcinoma:**

highest frequency of K-RAS mutation

*Mutations important from the point of therapy:*

mutation and amplification of EGFR gene

EML4-ALK tyrosin kinase fusion gene

c-MET tyrosin kinase gene

# General features, gross pattern

- 95% of primary lung tumors arise from bronchial epithelium (bronchogenic carcinoma)
- tumor starts as small mucosal lesions, firm, grey-white
- forms intraluminal masses
- invades the mucosa and the adjacent lung
- invade the pleura, pleural cavity and chest wall

# Squamous cell carcinoma

Grey-white tumor of the main bronchus invades the mucosa and the adjacent lung.



# Bronchogenic carcinoma, consequence of local spread

1. **vena caval syndrome:** the tumor may compress or infiltrate the superior vena cava
2. **Pancoast tumors:** apical tumors  
**Pancoast syndrome:** + combination of clinical findings

# Bronchogenic carcinoma, consequence of local spread

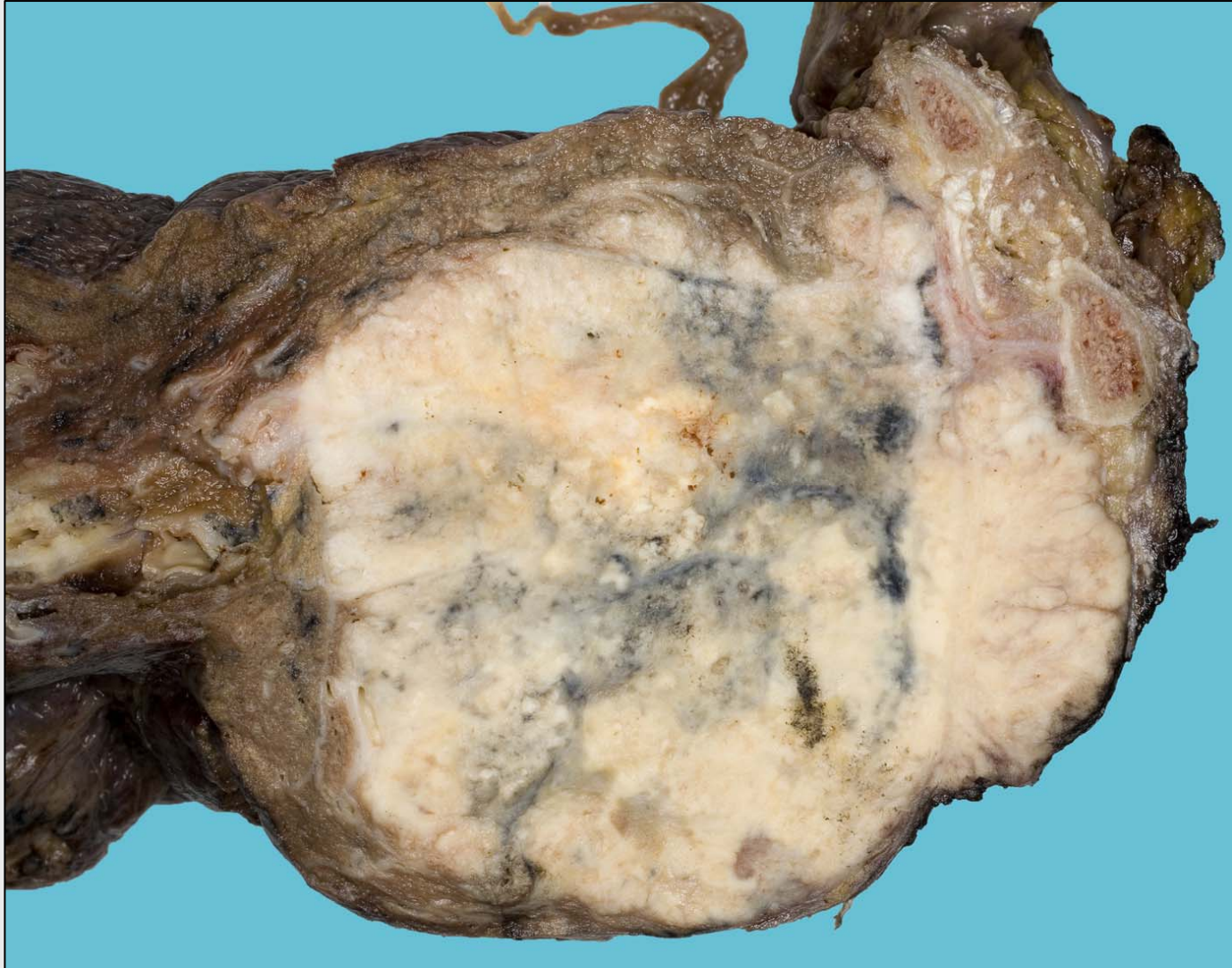
**Pancoast syndrome:** + combination of clinical findings

- may invade the brachial or cervical sympathetic plexus to cause severe pain in the distribution of the ulnar nerve
- **Horner-triad:** ipsilateral enophthalmos, ptosis, miosis and anhidrosis
- is often accompanied by destruction of the first and second ribs, thoracic vertebrae



# Pancoast tumour

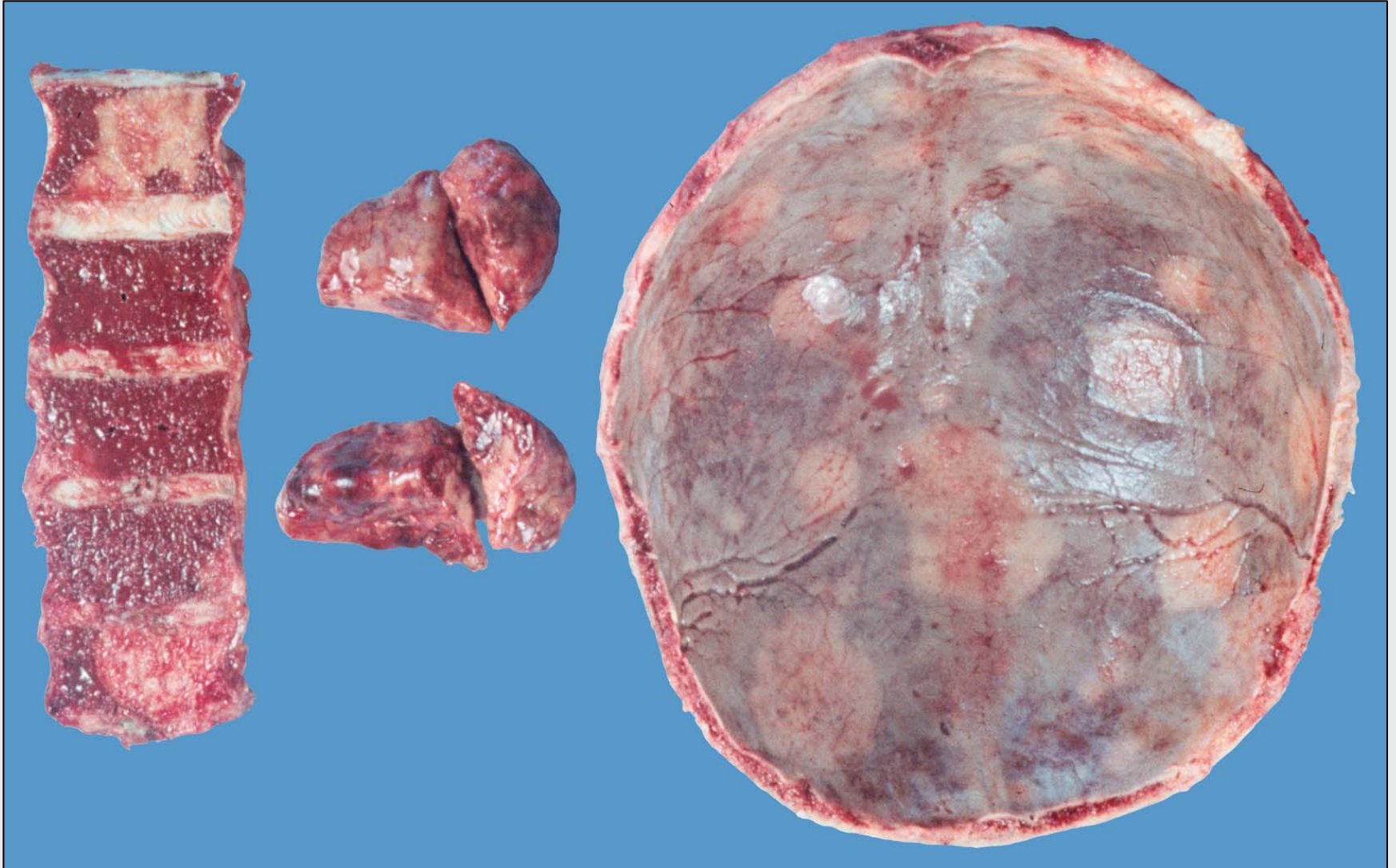
Apical tumour, the tumor infiltrates the first and second ribs.



# Spread of bronchogenic carcinoma

- **lymph node metastasis:** regional peribronchial, hilar, mediastinal, Virchow node: supraclavicular node. Lymphangitis carcinomatosa
- **distant metastasis:** *bone, brain, suprarenal glands, liver*
- **dg:** cytology of bronchial lavage fluid or brushings, biopsy

# Metastasis of bronchogenic carcinoma vertebrae, suprarenal glands and calvaria





# Lung carcinoma, brain metastasis



# Bronchogen carcinoma

## precursor lesions:

- 1. squamous dysplasia, carcinoma in situ
- 2. atypical adenomatous hyperplasia
- 3. diffuse idiopathic pulmonary neuroendocrine cell hyperplasia

# Bronchogenic carcinoma, histological types

- 1. small cell lung carcinoma
- 2. non-small cell carcinomas
  - 2.1 squamous cell carcinoma
  - 2.2 adenocarcinoma
    - A. adenocarcinoma in situ
    - B. minimally invasive adenocarcinoma
    - C. invasive adenocarcinoma
  - 2.3 large cell carcinoma
- 3. *combined patterns*
  - squamous cell cc + adenocarcinoma
  - squamous cell cc + small cell carcinoma

# Bronchogenic carcinoma

## Bases of distinction:

### 1. small cell lung carcinoma

- most often have metastasized by the time of dg, hence not amenable to curative surgery
- best treated with chemotherapy with or without irradiation

### 2. non-small cell carcinomas

- less often metastatic, respond poorly to chemotherapy
- best treated with surgery

# 1. Small cell lung cancer (neuroendocrine cells)

- more common in men
- strongly associated with smoking
- centrally located
- they tend to give metastasis early
- radiosensitive
- high initial response to chemotherapy
- worse prognosis

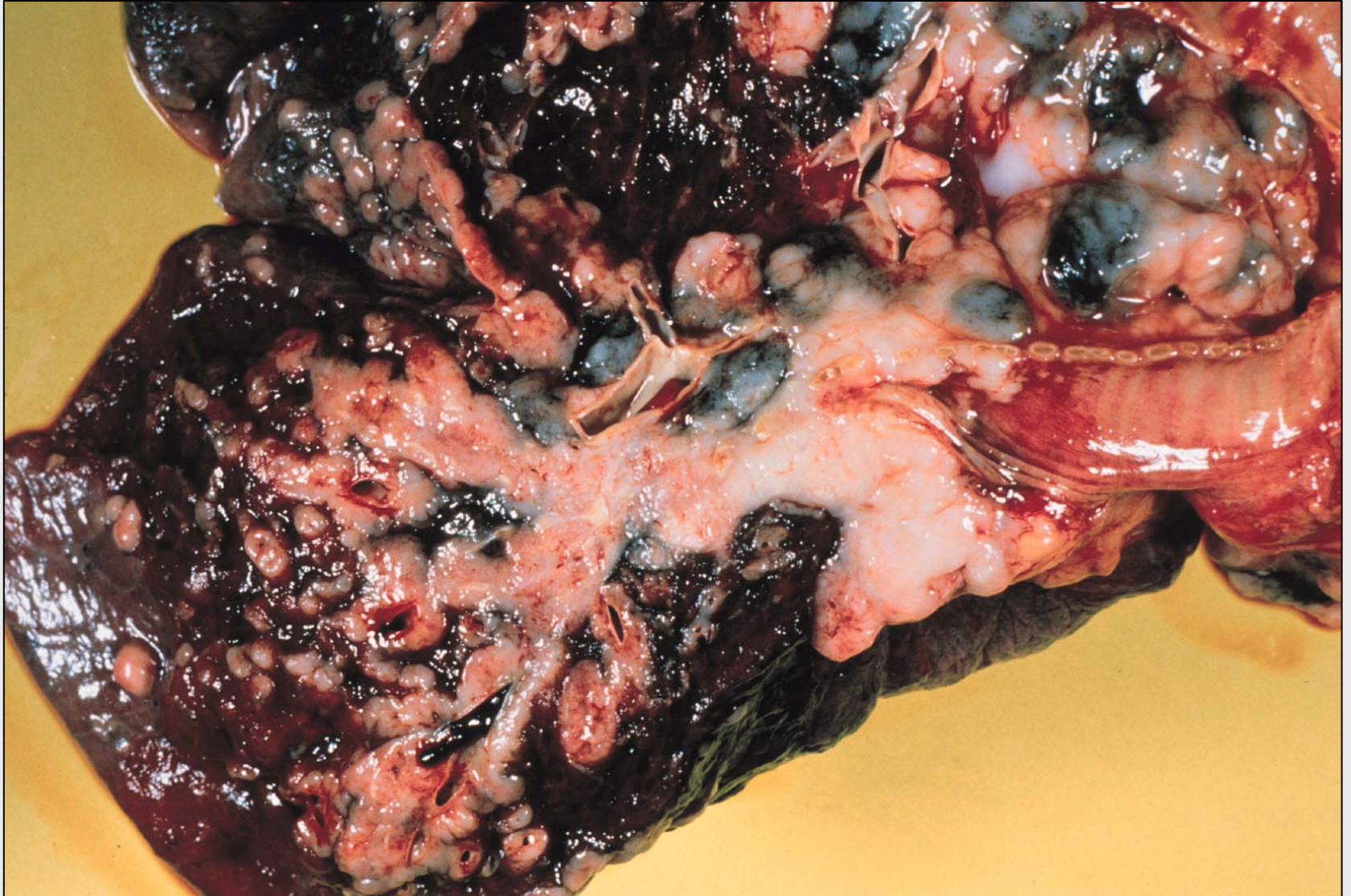


# 1. Small cell lung cancer

- **histology:** small dark round to oval cells, mitosis is frequent
- **specific feature:** presence of neurosecretory granules in the cytoplasm **chromogranine +**
- secrete polypeptide hormones and cause **paraneoplastic syndrome**

# 1.Small cell carcinoma

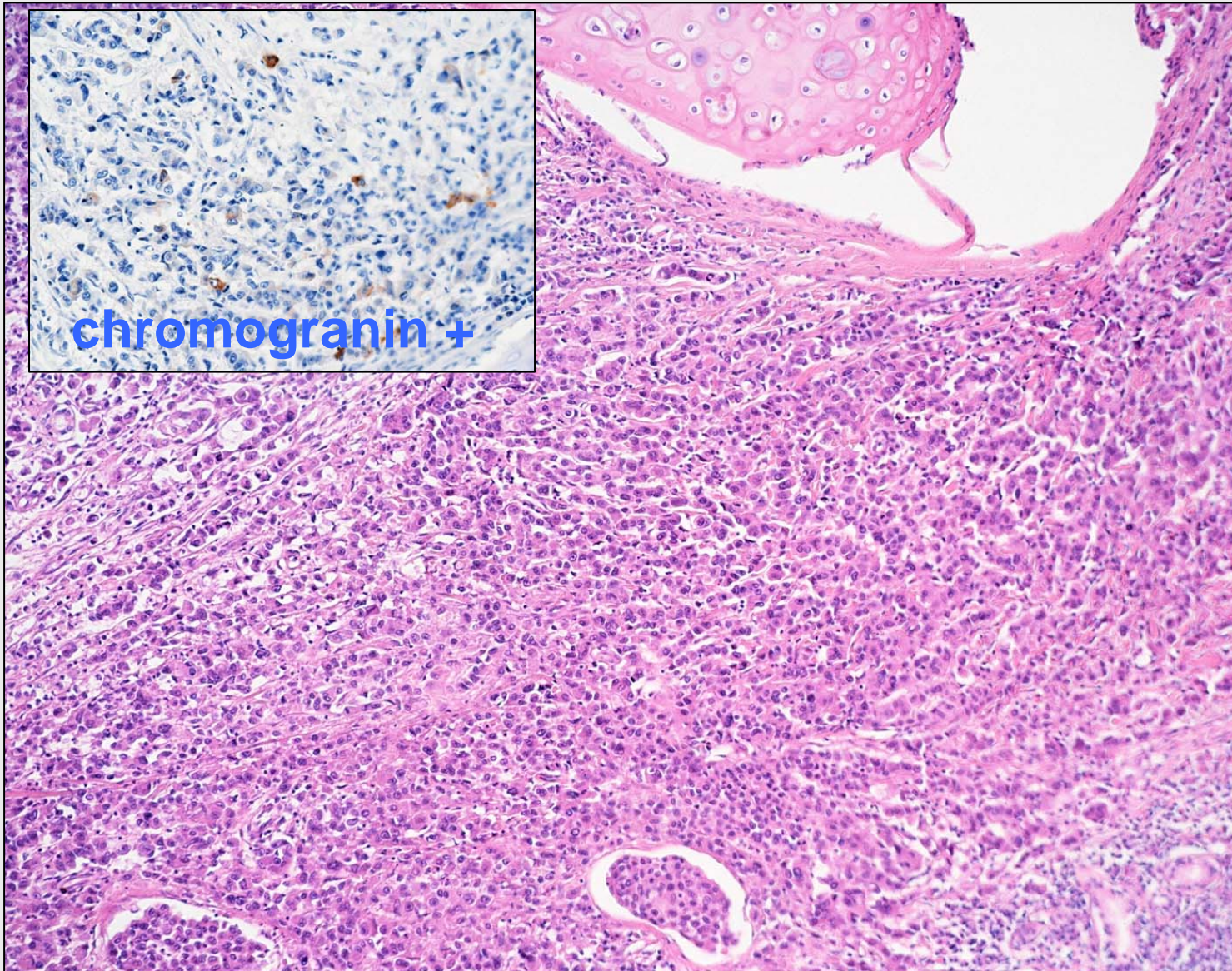
The tumor invades the main bronchus and the lung parenchyme.





# 1.Small cell carcinoma: chromogranin +

The tumor destructs the bronchus wall and shows lymphatic spread



## 2.1 Squamous cell carcinoma (bronchial epithelium)

- has the closest **correlation with smoking**
- **more common in men**
- **symptoms late**, when the tumor is causing bronchus obstruction (atelectasis, infection)

## 2.1 Squamous cell carcinoma

- most arise in the central bronchi, invades the adjacent lung parenchyma, gives metastasis to the regional lymph nodes
- preceded by squamous cell metaplasia, dysplasia or cc in situ in the bronchial epithelium

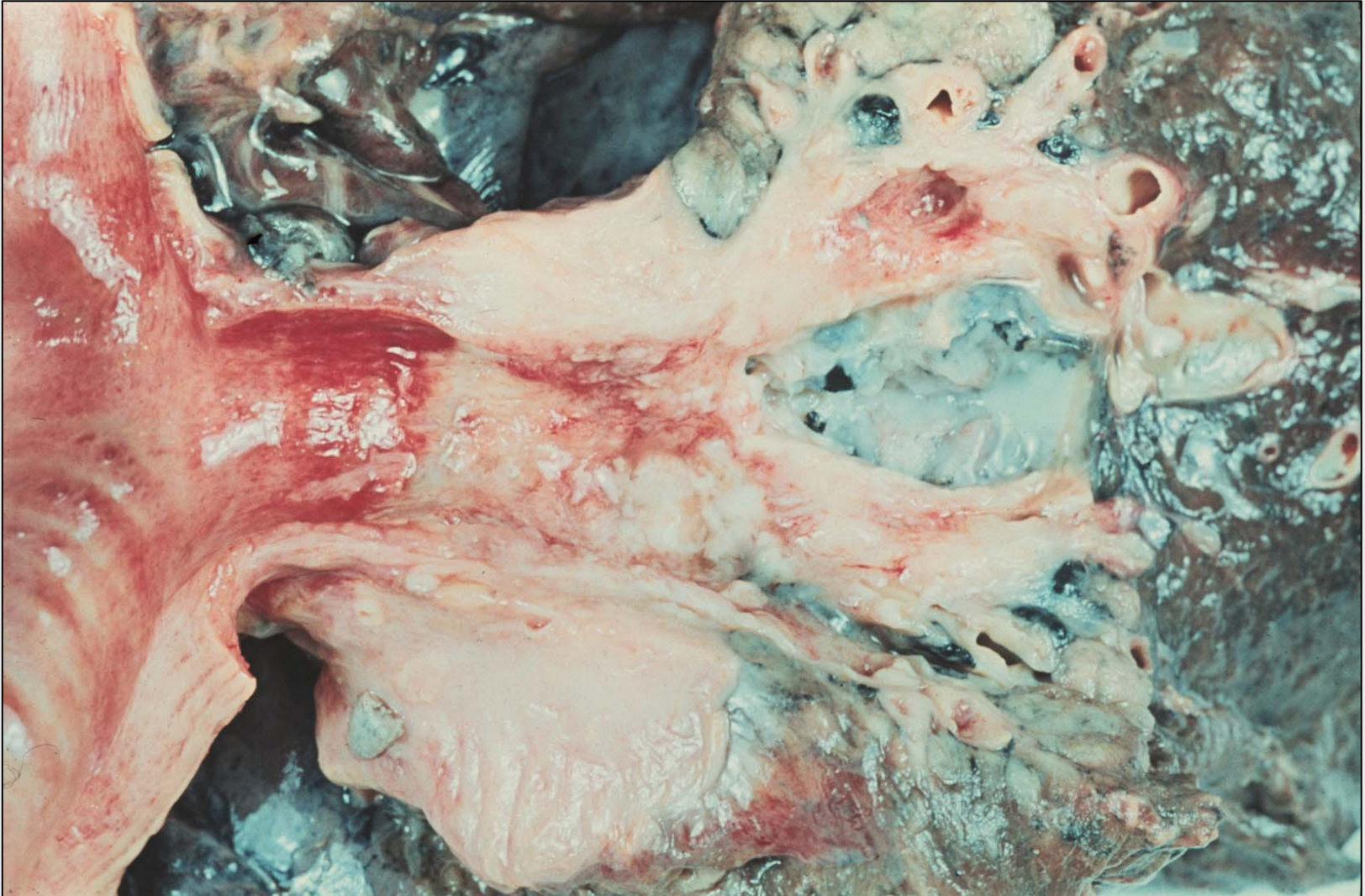
## 2.1 Squamous cell carcinoma

- dissemination outside the thorax occurs later than other histologic types
- histology: well to poorly differentiated, CK17+



## 2.1 Squamous cell carcinoma

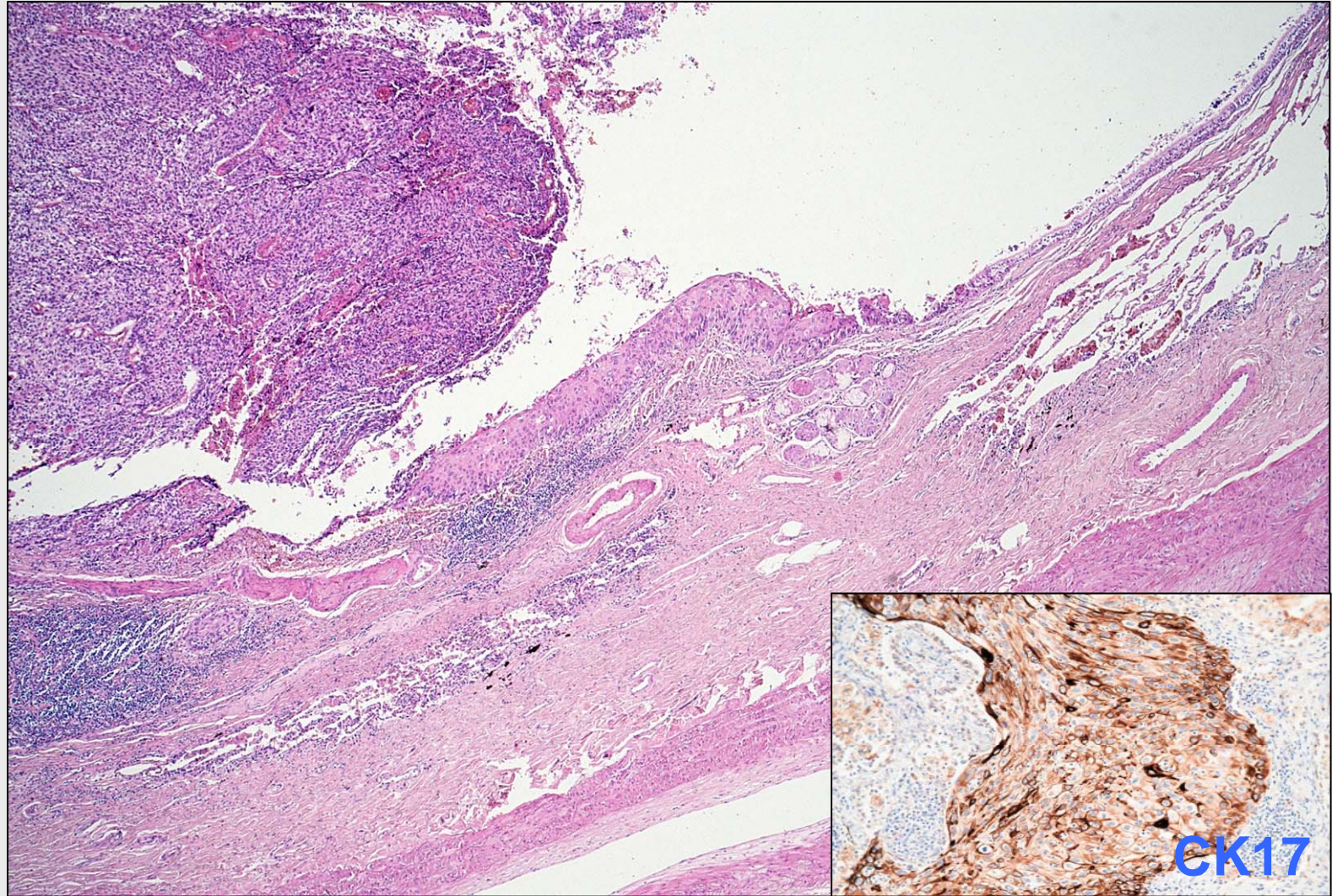
Grey-white tumor of the main bronchus invades the mucosa and the adjacent lung.





## 2.1 Squamous cell carcinoma

Squamous cell carcinoma arising in the bronchus, next to the tumor squamous cell metaplasia and dysplasia in the bronchial epithelium.





# AAH: atypical adenomatous hyperplasia

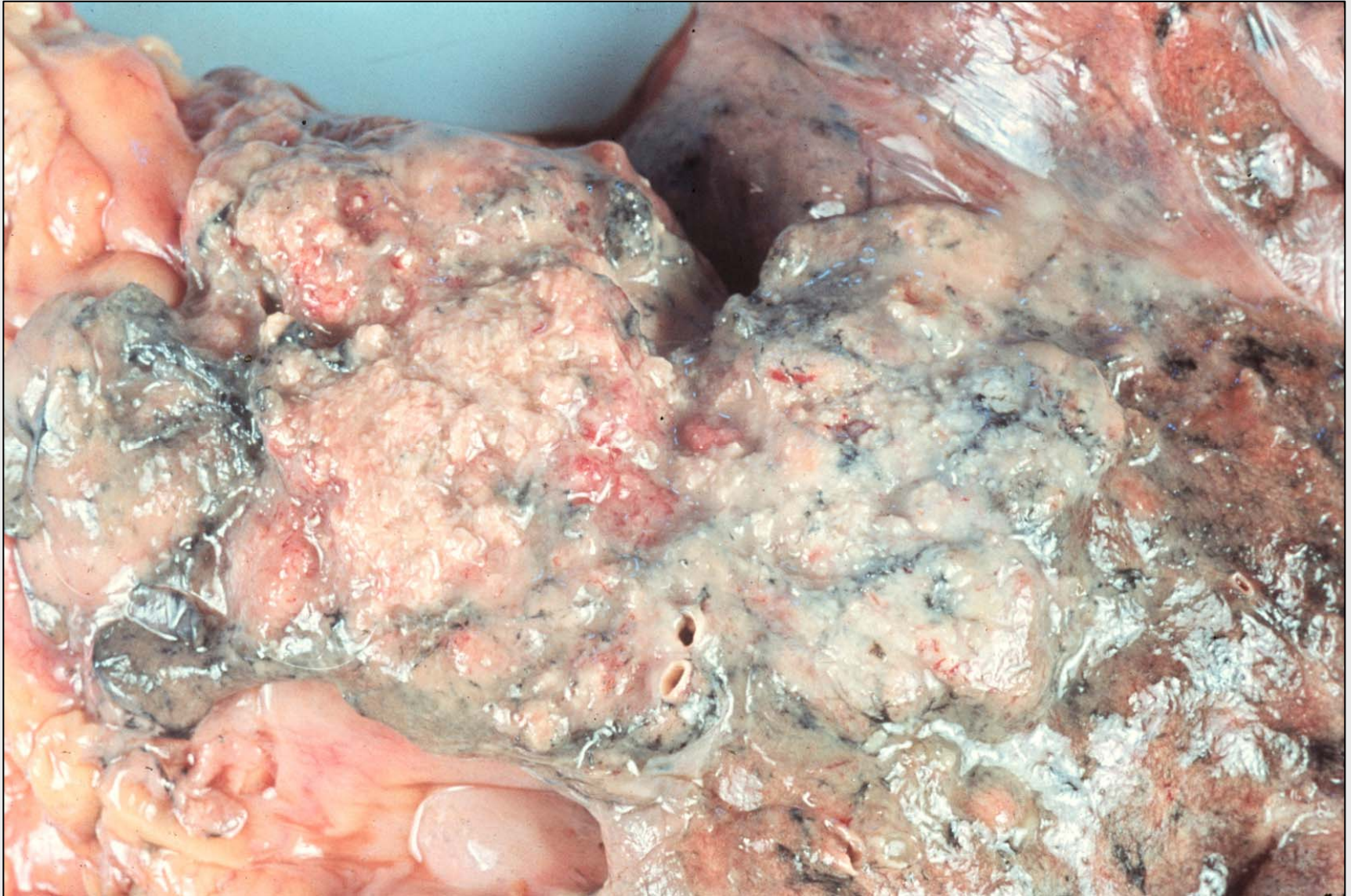
- precursor lesion of adenocarcinoma
- proliferation of type 2 pneumocytes with atypia
- can be multifocal, and is found in the lung of patients with existing adenocarcinoma

## 2.2A Adenocarcinoma

- man and women are equally involved
- smokers and nonsmokers are equally involved
- **localization:**
  1. frequently periferally located
  2. may occur as central lesion

## 2.2 Adenocarcinoma, peripheral

The peripheral tumor invades the pleura.



## 2.2 Adenocarcinoma

- **gross:** grow slowly and form smaller masses than do other subtypes
- **histologic type:**
  - A. adenocarcinoma in situ  
lepidic tumor  $\leq 3\text{cm}$
  - B. minimally invasive adenocarcinoma  
lepidic tumor  $\leq 3\text{cm}$ , invasion  $\leq 5\text{ mm}$
  - C. invasive adenocarcinoma  
invasion  $>5\text{ mm}$

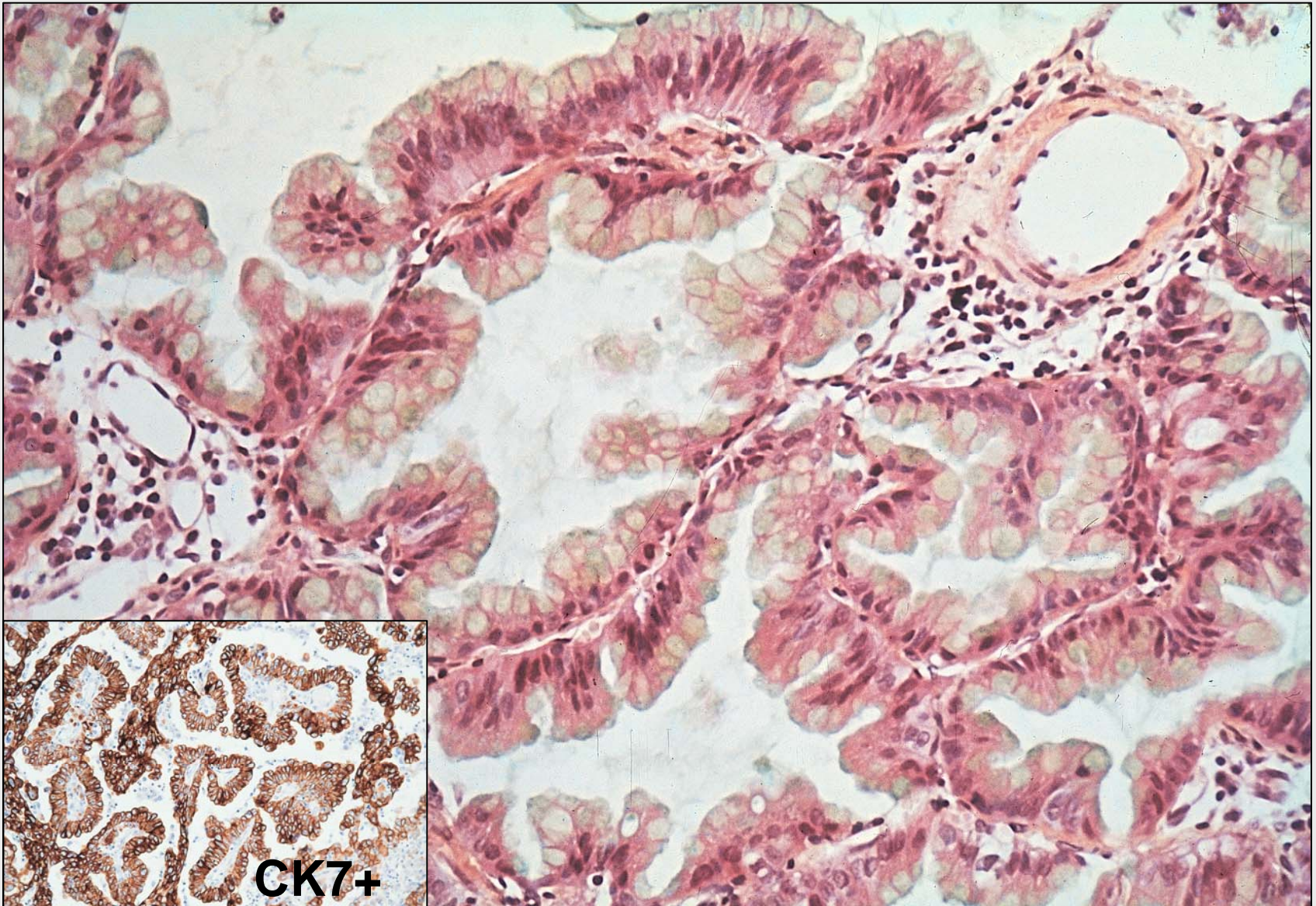
## 2.2. A. Adenocarcinoma in situ.

- **histology:** the tumor cells grow along preexisting structures such as bronchioli and alveoli, **structure is preserved (lepidic tumor)!**
- **prognosis** is relatively good
- **immunohistochemistry:**
  - CK7+
  - thyroid transcription factor **TTF1+**



## 2.2. A. Adenocarcinoma in situ.

**Lepidic tumour: the tumor cells grow along the wall of alveoli, CK7+.**



# Bronchogenic carcinoma

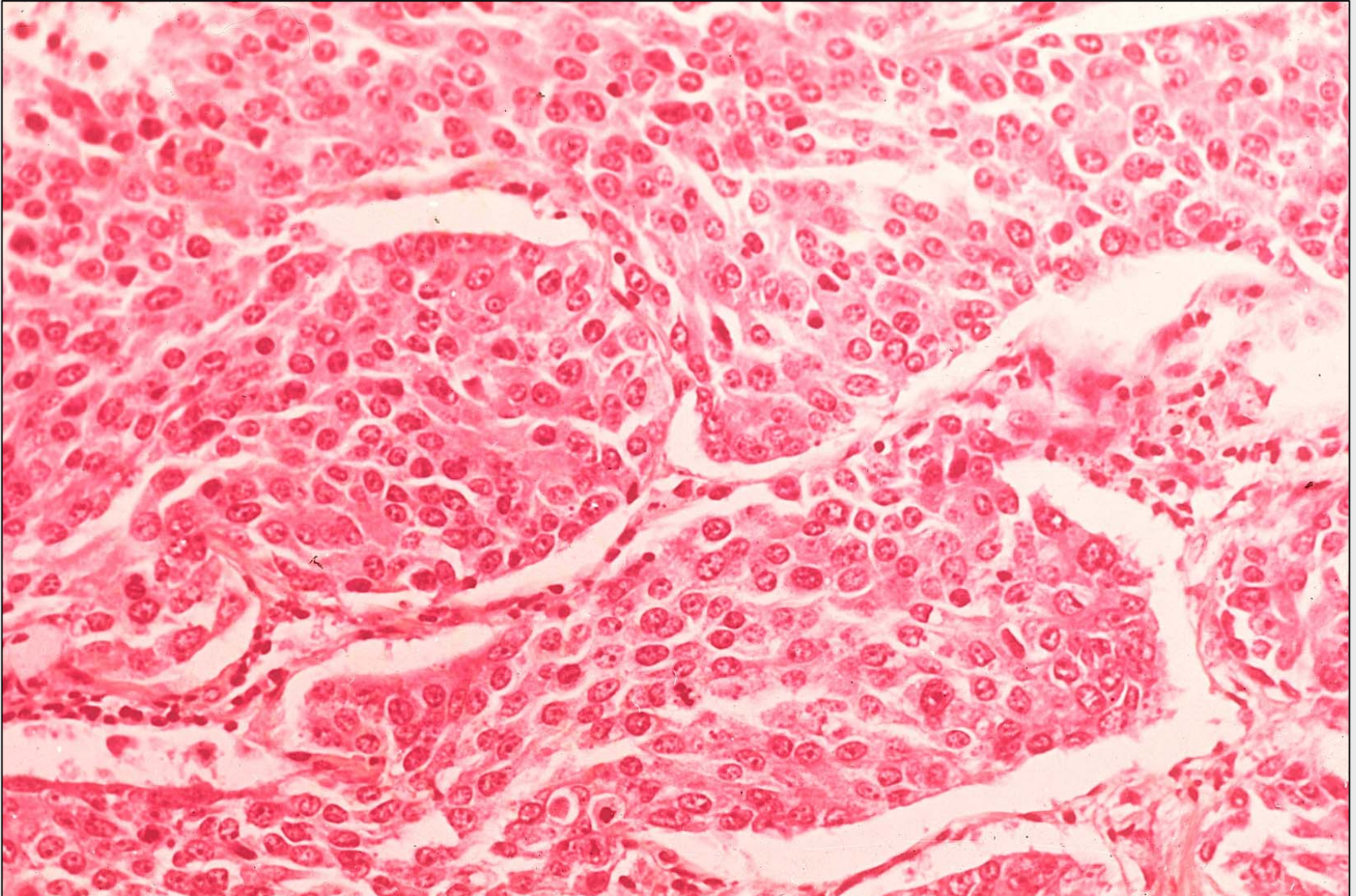
**2.3 large cell carcinoma:** lack of cytological differentiation, poor prognosis, tendency to spread to distant sites early in their course  
*special histological variant:* large cell neuroendocrine carcinoma

**3. combined patterns:** squamous cell carcinoma and adenocarcinoma or small cell carcinoma



## 2.3 Large cell carcinoma

Poorly differentiated tumor.





# Bronchogenic carcinoma

## **TNM, factors determining stage:**

- size of tumor
- involvement of main bronchus
- location to distal carina
- involvement of pleura
- spreading to chest wall, diaphragm, mediastinum, heart, large vessels

# Bronchogenic carcinoma

**clinical:** silent, insidious lesions

- cough, weight loss, chest pain, dyspnoea, hemoptoe
- death: respiratory insufficiency, infection, metastasis

# Bronchogenic carcinoma

## **prognosis:**

- combined overall 5 year survival rate is 14%
- small surgically resectable tumors 45% 5 year survival
- small cell cc almost always metastasize by the time of diagnosis

## Other primary lesions:

### 1. bronchial carcinoid

- < 5% of all lung tumors, thus rare
- characterized by **neuroendocrine** differentiation
- surgical resection is curable in more than 90% of cases.

## Other primary lesions:

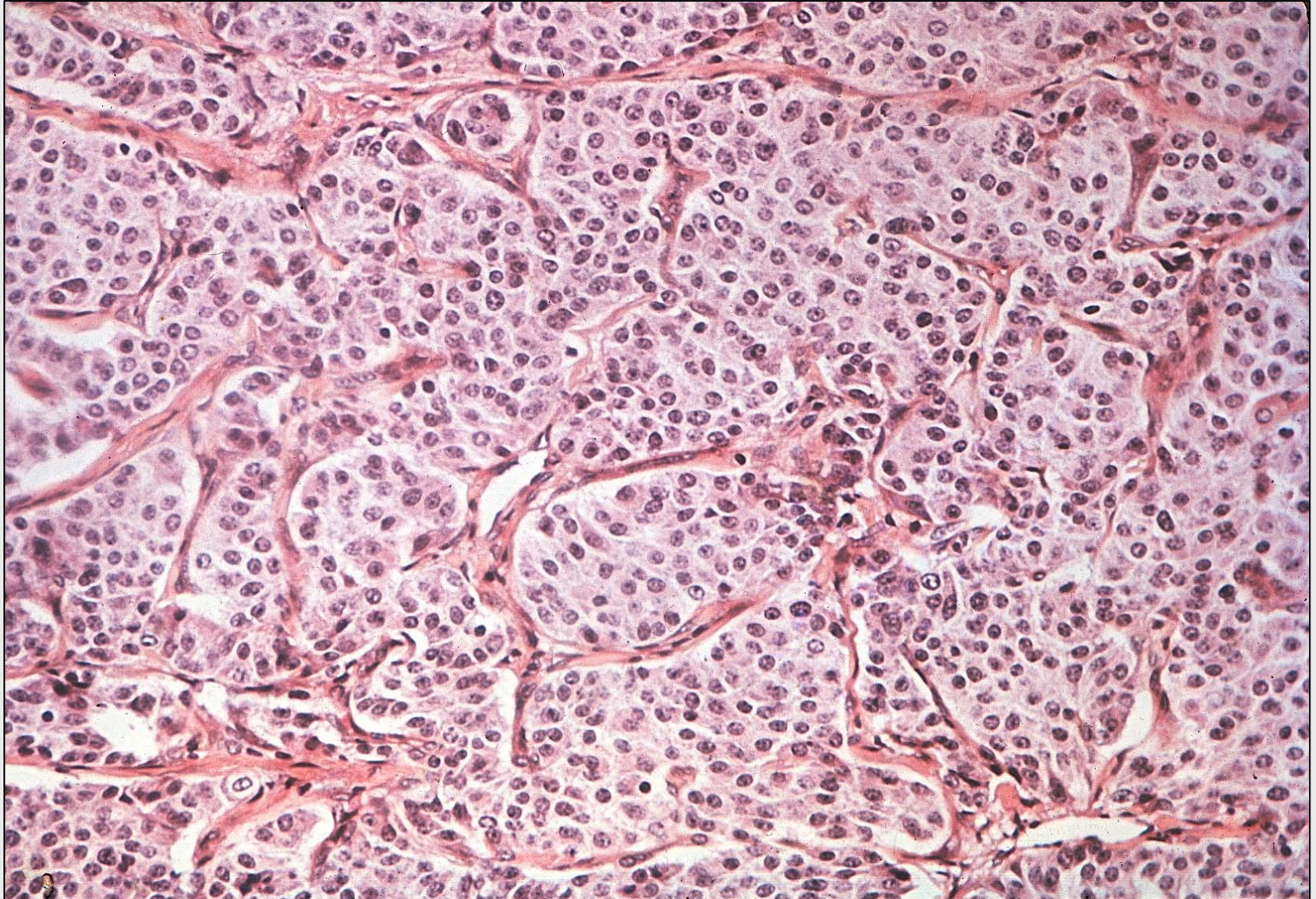
### 1. bronchial carcinoid

- **atypical carcinoid: minority**  
**more aggressive, local invasion distant metastasis**



# 1. Bronchial carcinoid

Tumor composed of uniform small, round cells



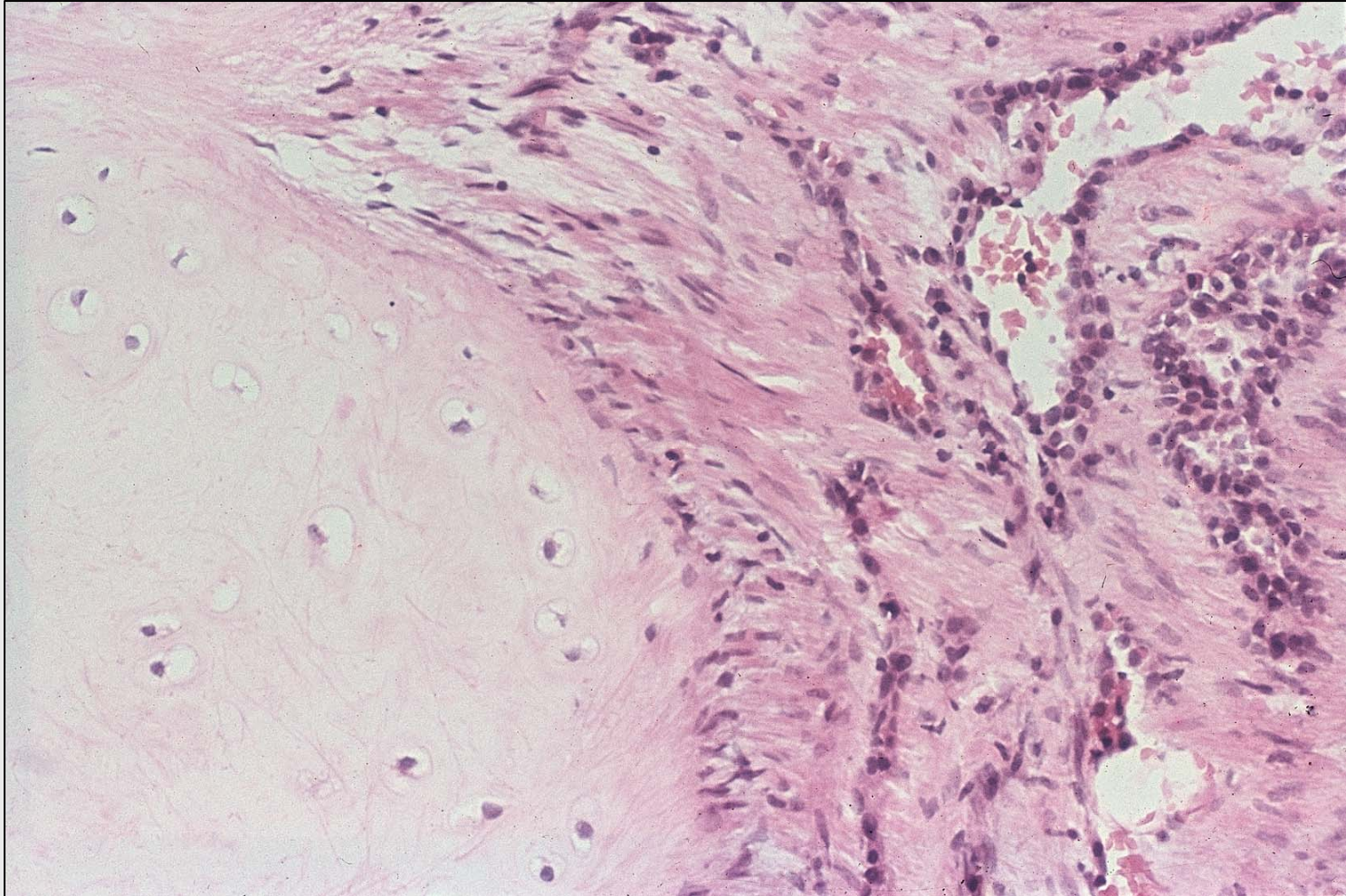
# 1. Bronchial carcinoid

## typical carcinoid:

- **gross:** intrabronchial polypoid masses < 4 cm=d
- **histology:** composed of uniform small, round cells with neurosecretory granules
- **immunohistochemistry: chromogranin+**
- only rarely induce carcinoid syndrome



**2. Hamartoma:** benign nodular tumorlike lesion composed of matured hyaline cartilage, and other mesenchymal tissue



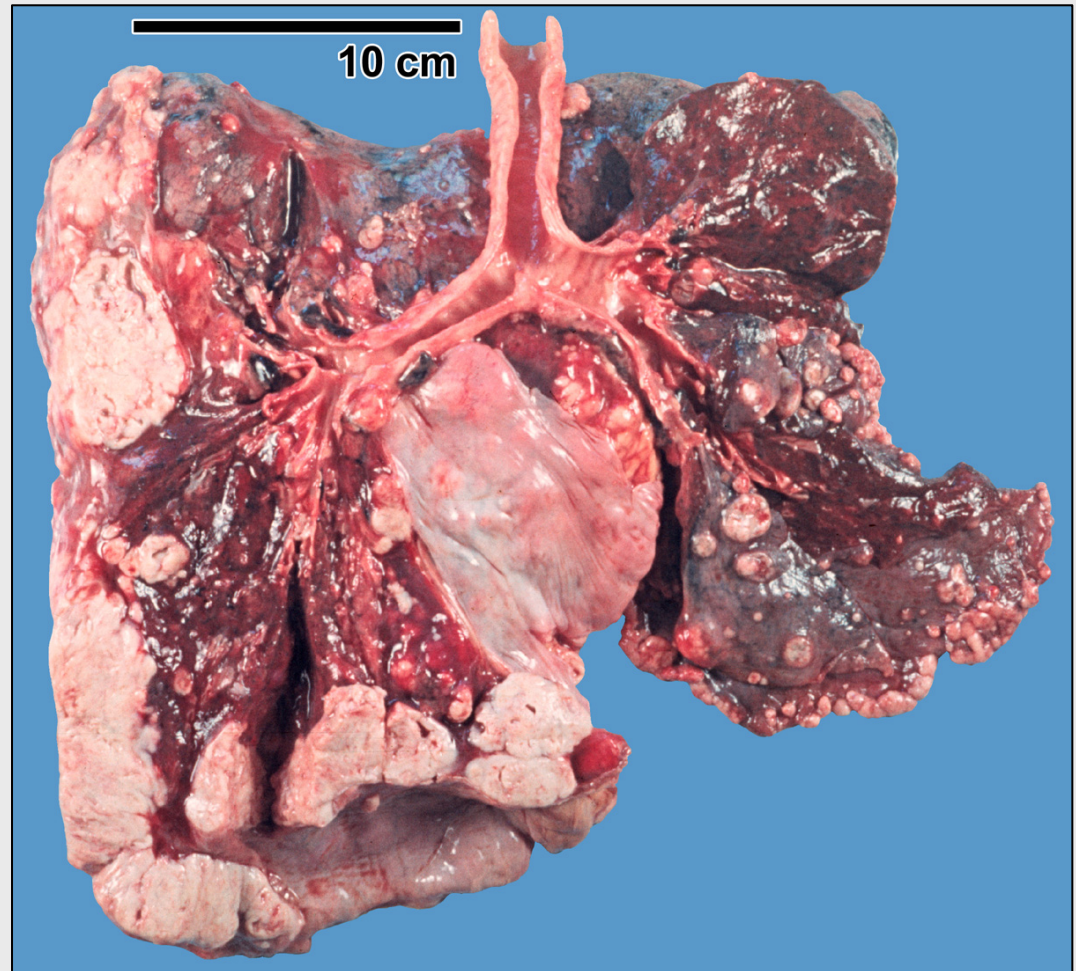


# Metastatic tumours in the lung

Multiple gray-white metastatic tumors in the lung and on the pleura.

## primary sites:

tumours drained  
by caval system  
liver  
kidneys  
etc



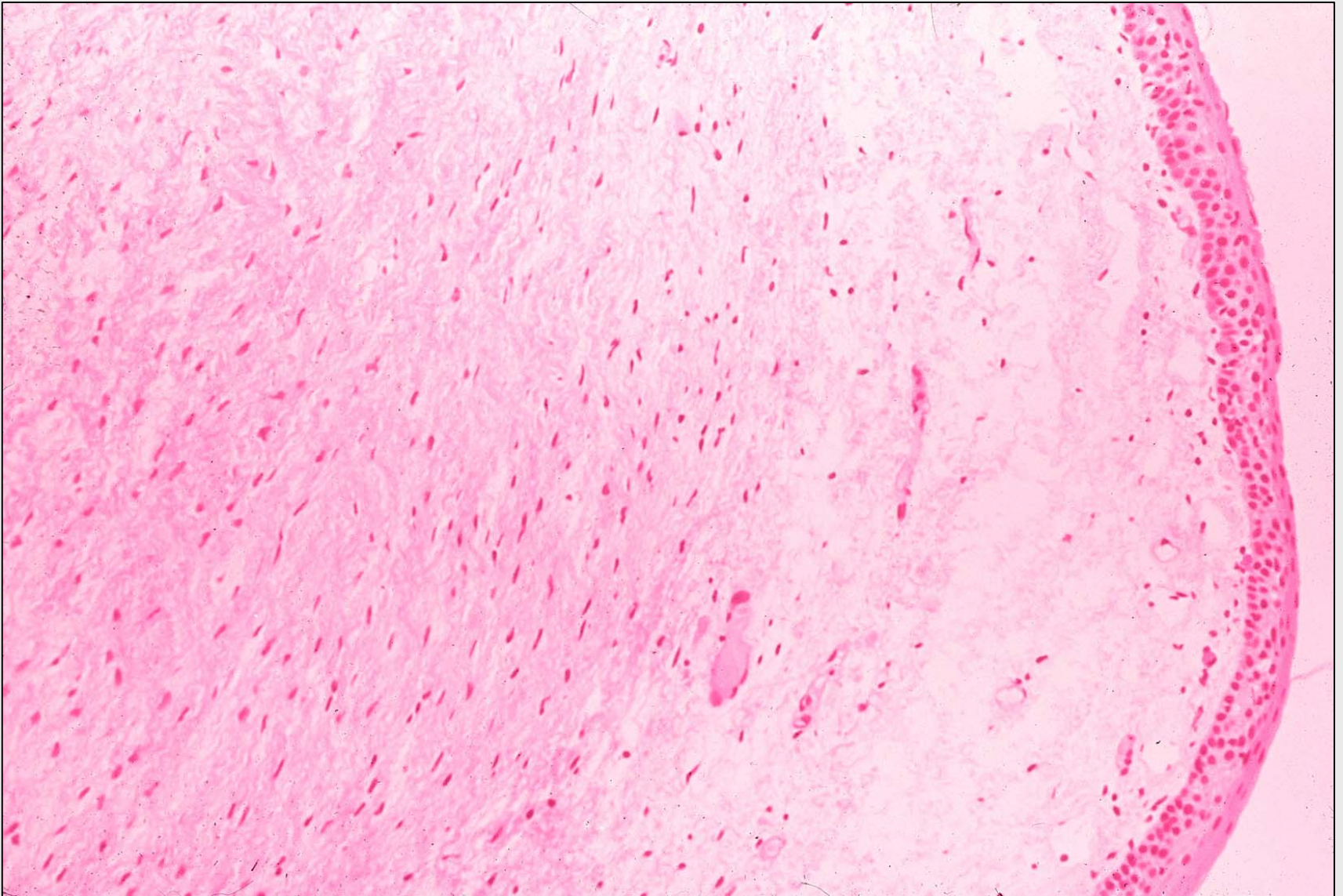
# LARYNGEAL TUMORS

# Vocal cord nodules (polyp)

- singers nodules
- inflammatory in origin
- often on true vocal cords
- fibrous tissue covered by stratified squamous epithelium

# Vocal cord nodule

fibrous tissue covered by stratified squamous epithelium





# Laryngeal papilloma

- benign tumor
- true vocal cords
- soft raspberry-like tumor less than 1 cm
- multiple fingerlike projections supported by a fibrovascular core covered by stratified squamous epithelium
- trauma may cause hemoptysis
- single in adults
- multiple: juvenile laryngeal papillomatosis, HPV 6 and 11, spontaneously regress

# Laryngeal papilloma

multiple fingerlike projections supported by a fibrovascular core  
covered by stratified squamous epithelium



# Carcinoma of Larynx

- after the age of 40.
- male:female, 7:1
- smoking, alcohol, asbestos exposure

- **clinical:**

persistent hoarseness

pain, dysphagia

hemoptysis

**cause of death** in one third of cases:  
infection, metastasis, cachexia

# Carcinoma of Larynx

- **localization:**
  - **vocal cord** carcinoma (75%)
  - **supraglottic** carcinoma (25-40%)
  - **subglottic** carcinoma (5%).

types:

- 1. **intrinsic:** confined to the larynx
- 2. **extrinsic:** arise or extends outside larynx



# Carcinoma of Larynx

## gross:

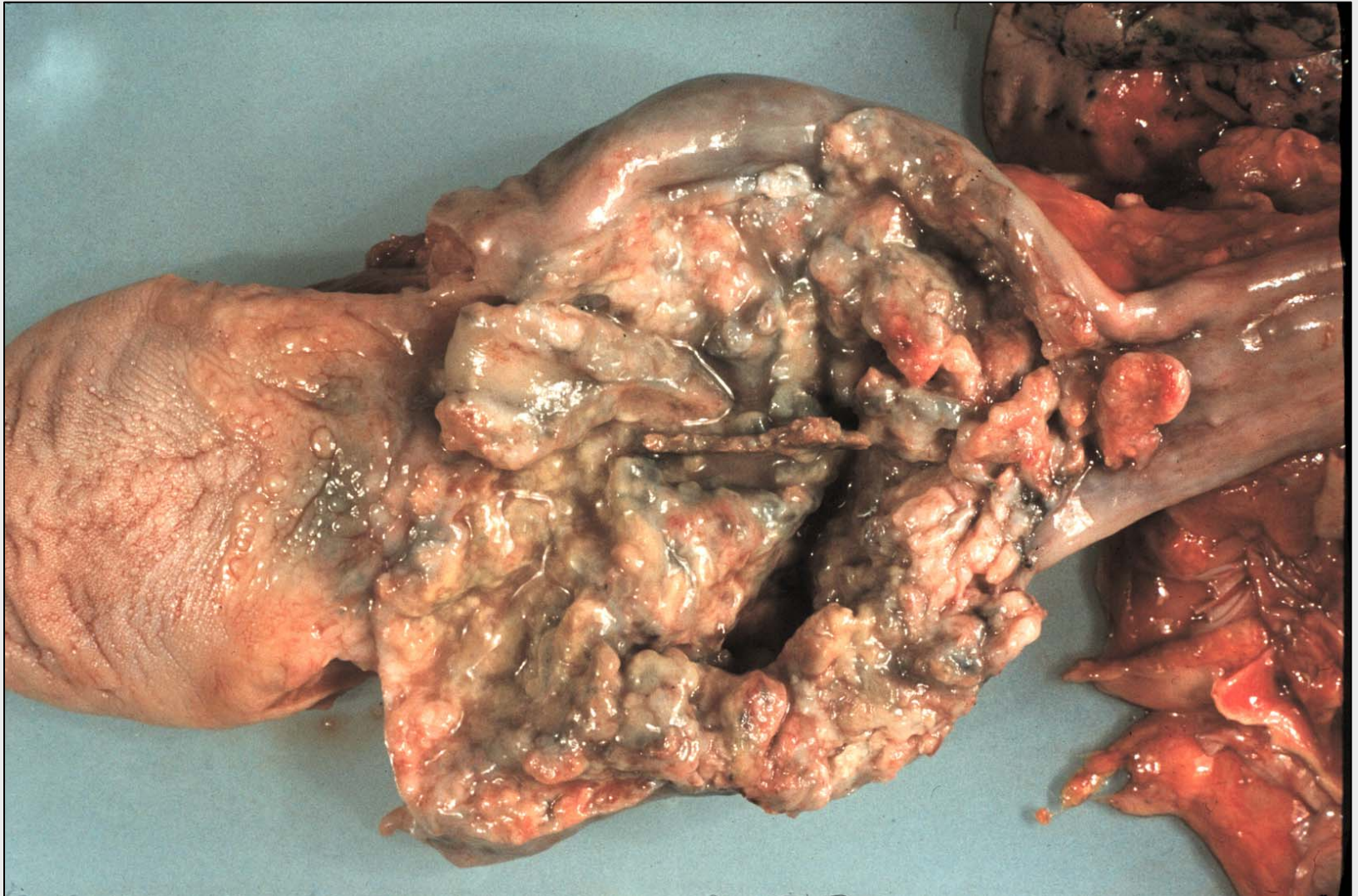
- early lesion cc in situ, later pearly gray, wrinkled plaque on the mucosal surface,
- with progression ulceration and fungation follows

## histology:

- 95% squamous cell cc, rarely adenocarcinoma
- the surrounding epithelium may show dysplasia or cc in situ

# Carcinoma of larynx

Advanced stage. The tumor shows ulceration, destroys the larynx.



# Carcinoma of Larynx

**prognosis** depends on location:

- *vocal cord*: **better**
  - immobility, symptoms early
  - sparse lymphatic supply
  - spread beyond the larynx is rare
- *supraglottic*: **bad**
  - rich in lymphatics
  - 1/3 already regional cervical lymph node metastasis at the time of diagnosis
- *subglottic*: **worse**, silent for longer period of time, presents as advanced disease