النادي الطلابي
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Pathology RS

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LUNG TUMORS

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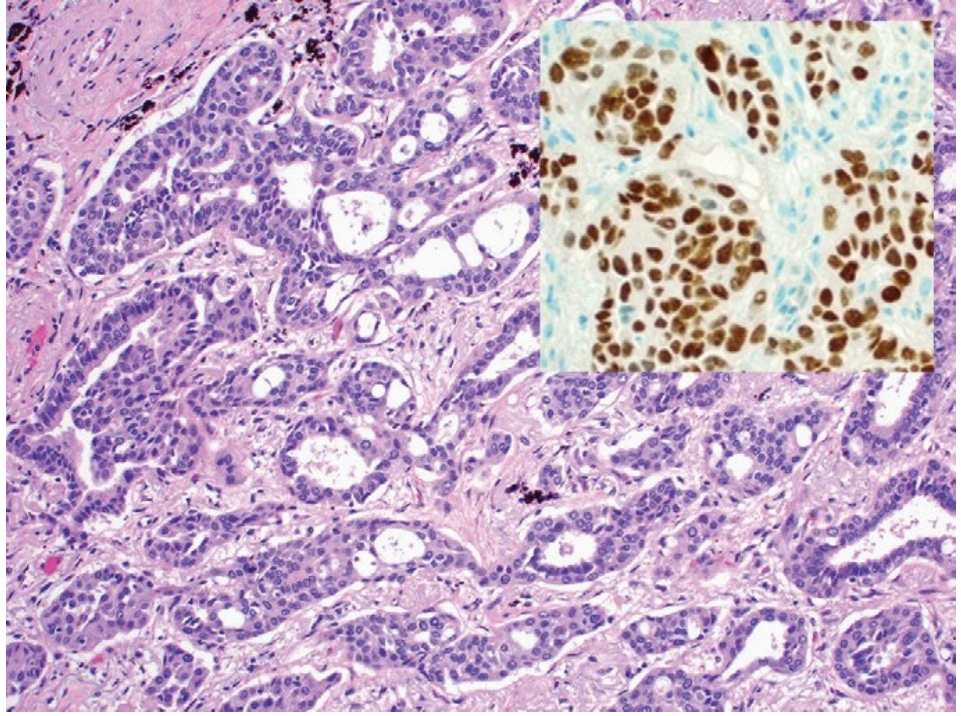
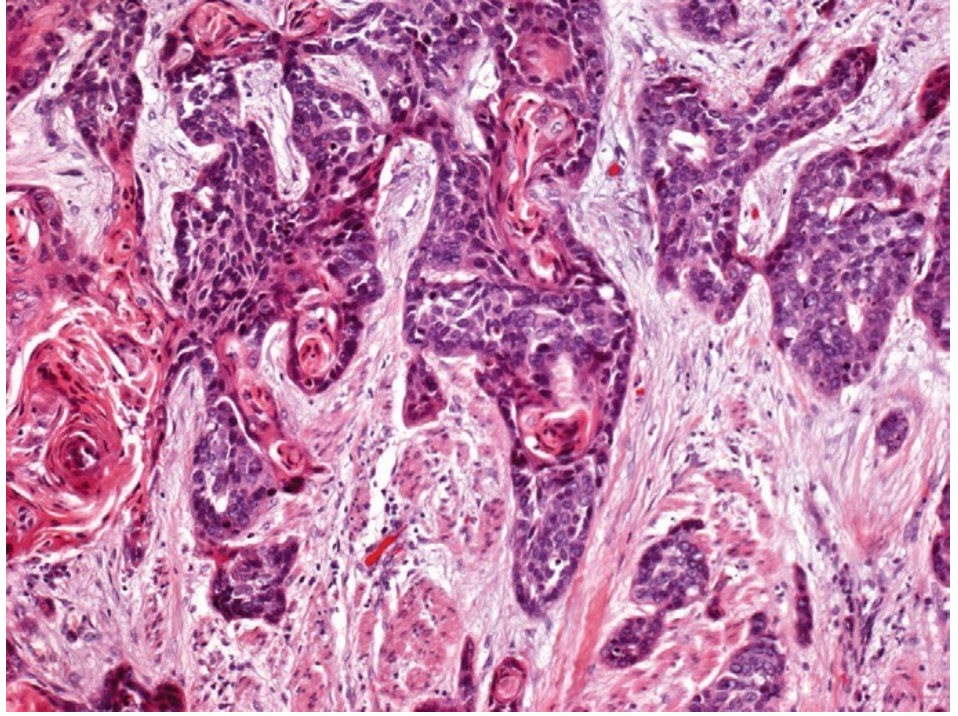
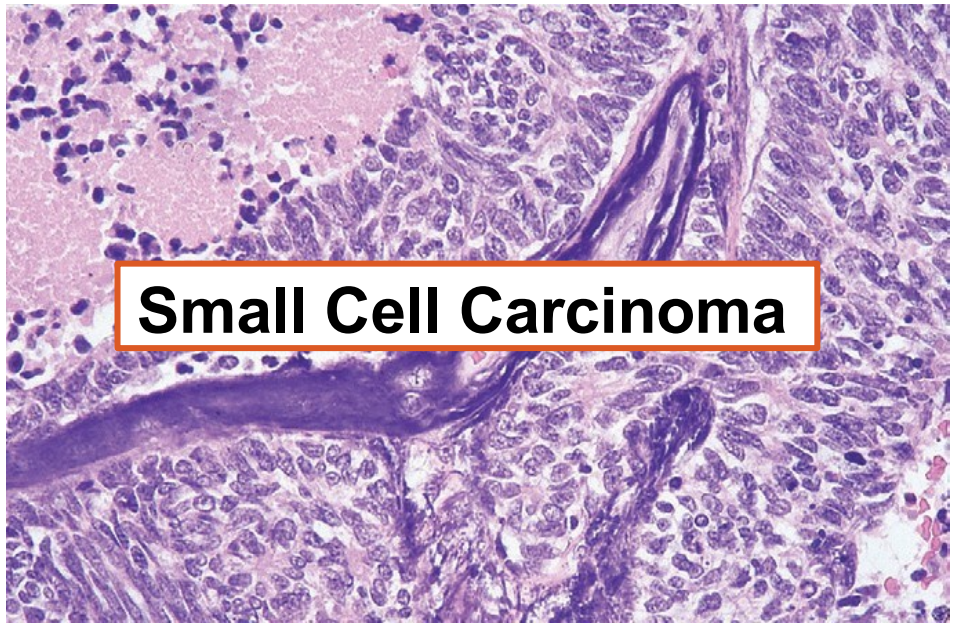
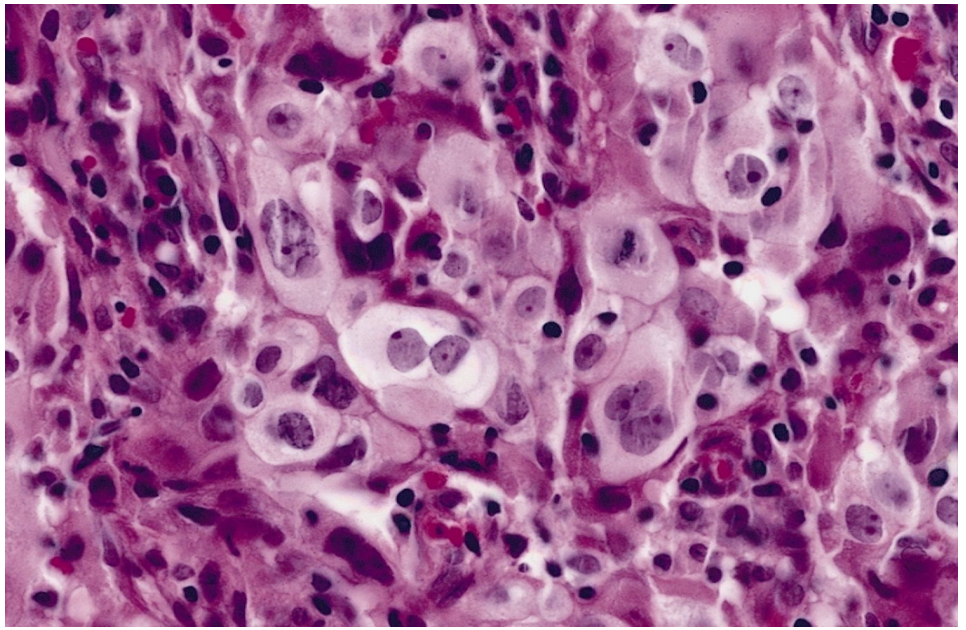








https://www.verywellhealth.com/large-cell-carcinoma-of-the-lungs-2249356

ROBBINS BASIC PATHOLOGY, 10TH EDITION

SMALL CELL LUNG CARCINOMAS (SCLC)

- Centrally located with extension into the lung paranchyma
- Early involvement of the hilar and mediastinal nodes.
- By the time of diagnosis, most will have metastasized to hilar and mediastinal lymph nodes.
- In the 2015 WHO Classification, SCLC is grouped together with large cell neuroendocrine carcinoma

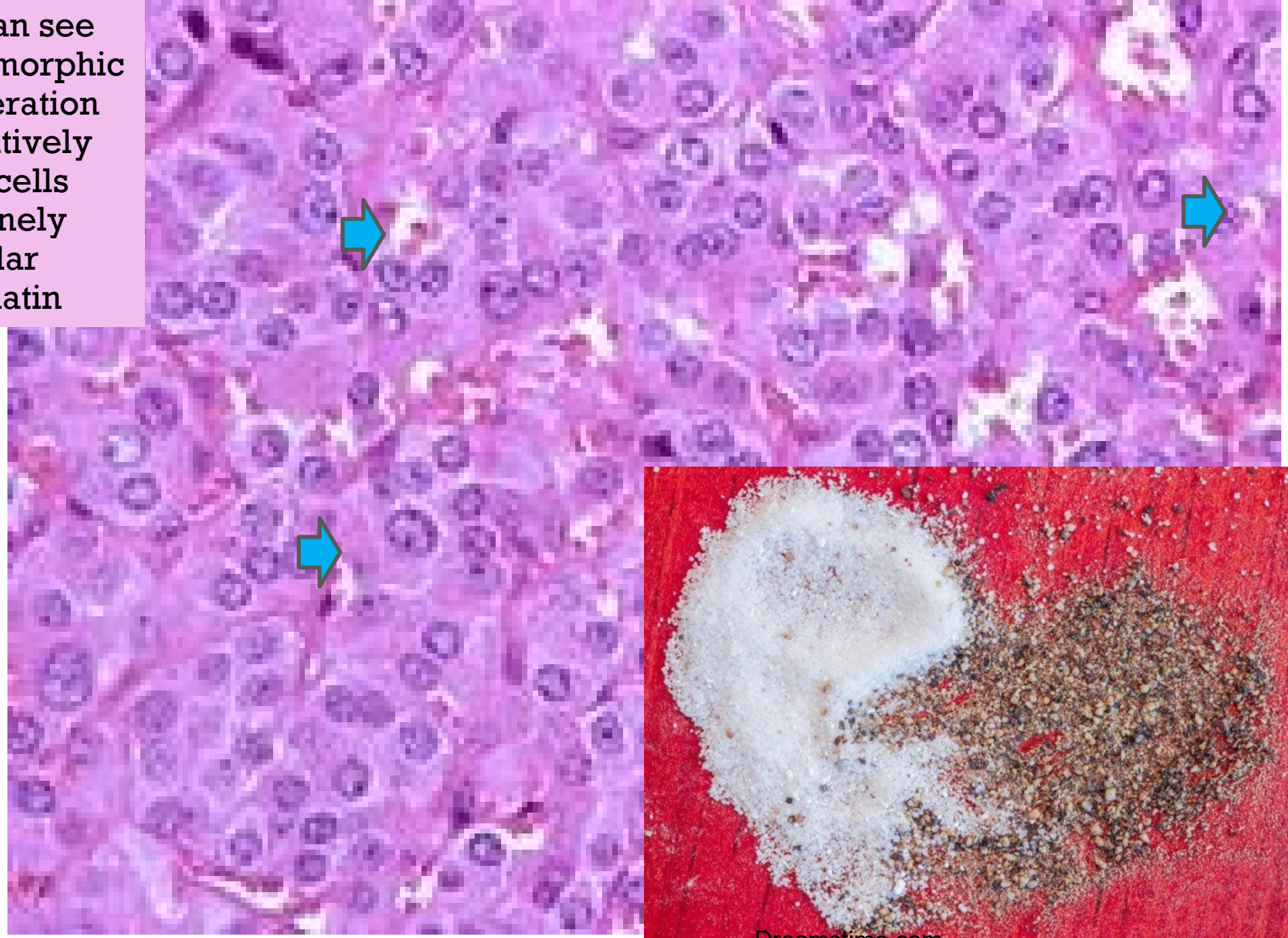
Large cell neuroendocrine carcinoma is another aggressive tumor that exhibits neuroendocrine morphology and expresses neuroendocrine markers

MORPHOLOGY:

- **Pale grey tumor** Grossly

- **Small tumor cells:** Histologically
  - Round to fusiform, scant cytoplasm, finely granular chromatin a salt and pepper appearance
  - Cells are twice the size of resting lymphocytes.

You can see monomorphic proliferation of relatively small cells with finely granular chromatin



Dreamstime.com

The appearance of the finely stabled nuclei resembles the salt and pepper mix

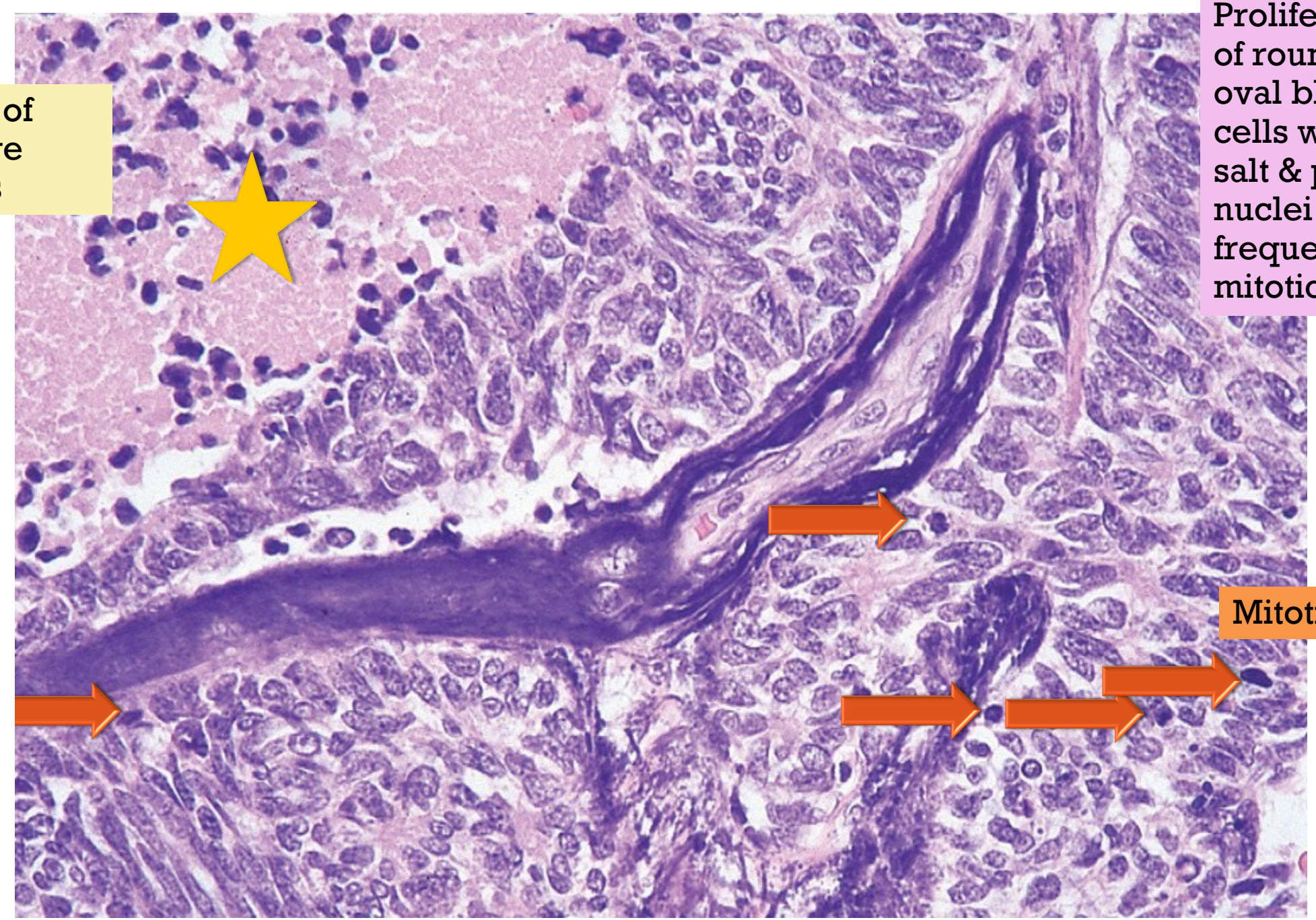
https://www.wikiwand.com/en/Salt-and-pepper_chromatin

MORPHOLOGY:

- Frequent mitotic figures
- Necrosis invariably present, can be extensive.

An area of extensive necrosis

Proliferation of round to oval blue cells with a salt & pepper nuclei and frequent mitotic figures



Mitotic figures

MORPHOLOGY:

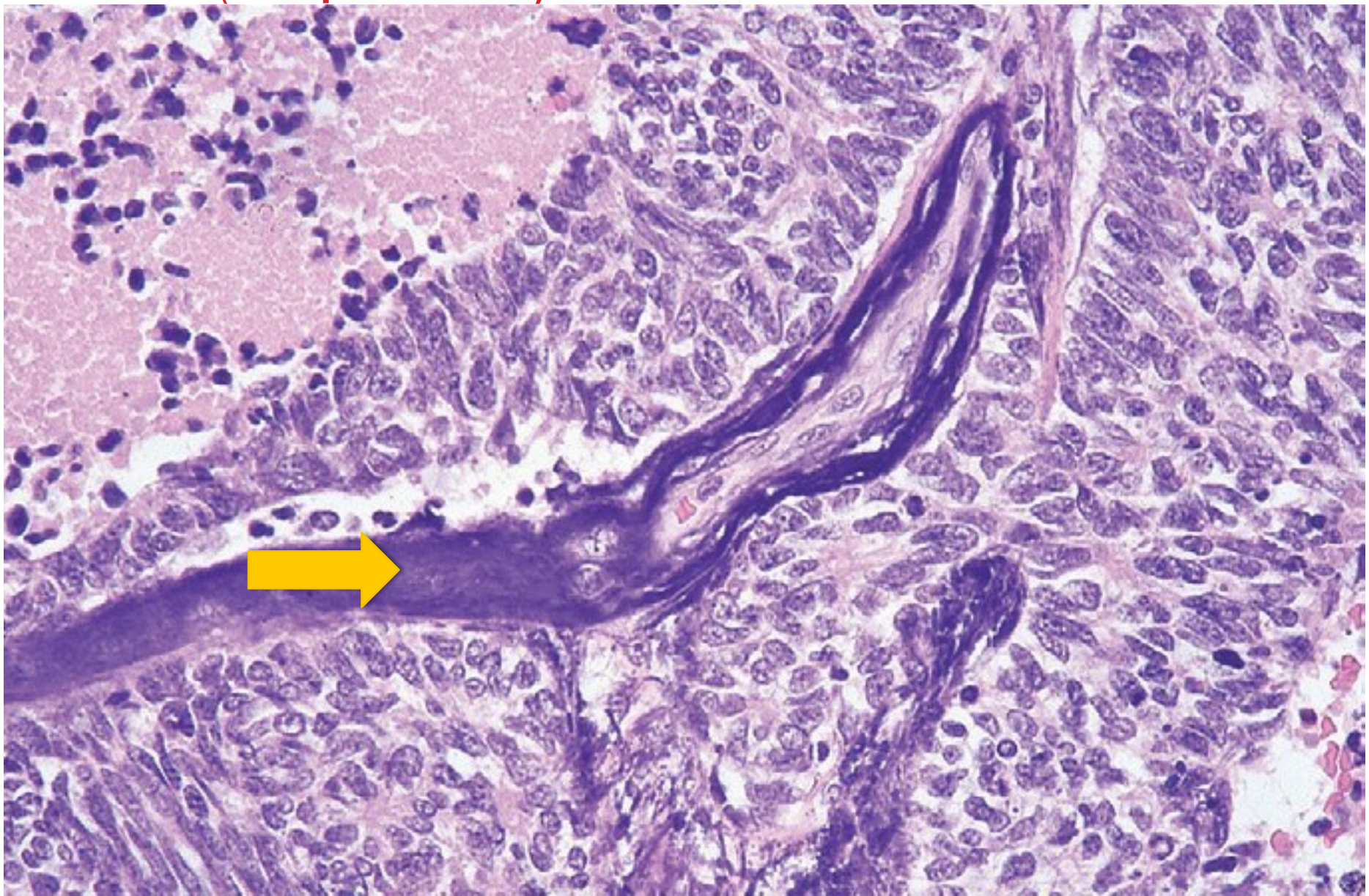
- Fragile tumor cells with **“crush artifact”** in small biopsy specimens
- **Nuclear molding** due to close apposition of tumor cells that have scant cytoplasm
- Express **neuroendocrine markers**

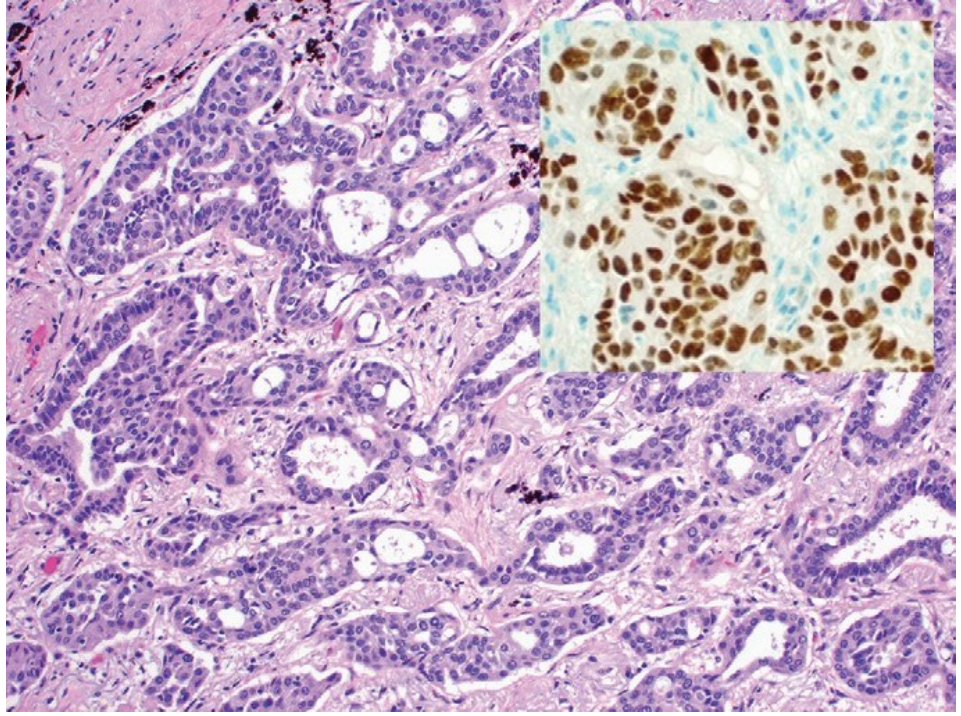
Used to highlight the neuroendocrine differentiation in the pathology lab

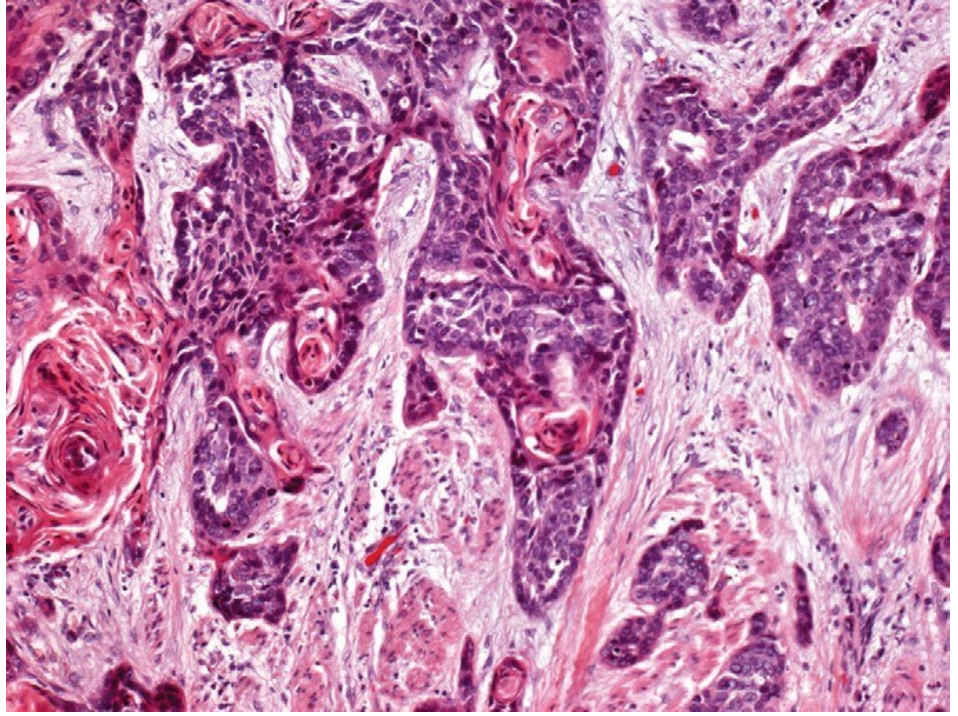
- **Secreting hormones>>paraneoplastic syndromes .**

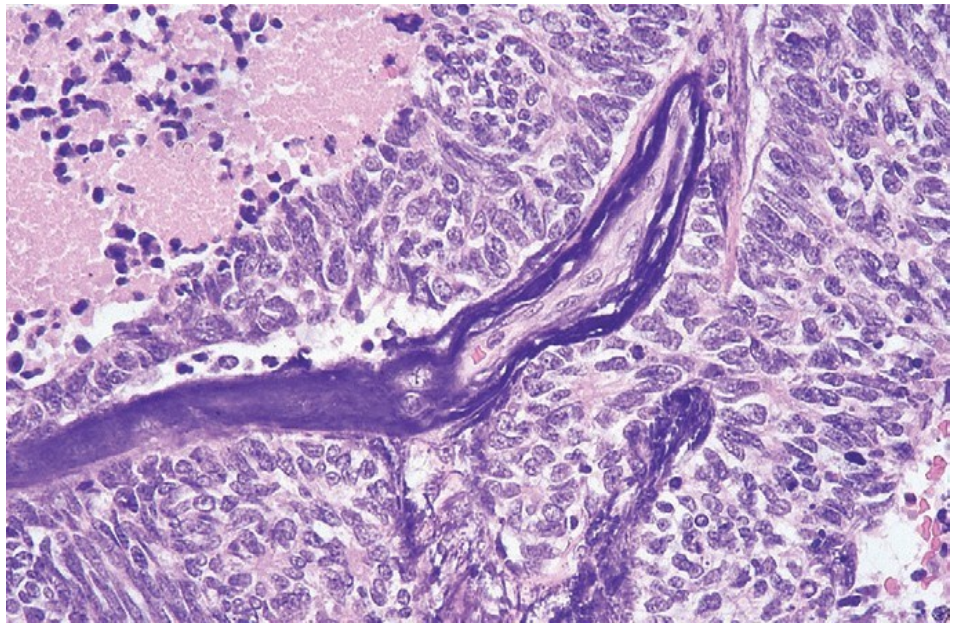
Paraneoplastic syndrome > > a syndrome that happens as a consequence of hormones & cytokines released as part of the immune response to the presence of the tumor or from the tumor cells themselves

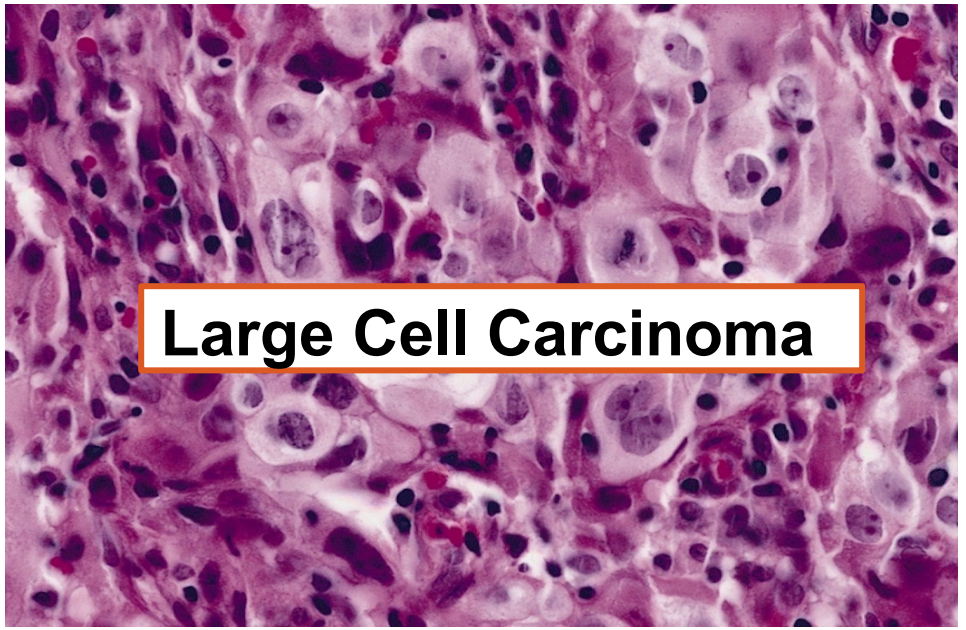
basophilic staining of vascular walls due to encrustation by and from necrotic tumor cells (**Azzopardi effect).**











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ROBBINS BASIC PATHOLOGY, 10TH EDITION

LARGE CELL CARCINOMAS

The cells don't look like the differentiated tissues > > no evidence of glandular or squamous differentiation to call them adenocarcinoma or squamous cell carcinoma

- Are undifferentiated malignant epithelial tumors.
- Lack cytologic features of small cell carcinoma and have no glandular or squamous differentiation.

Histologically

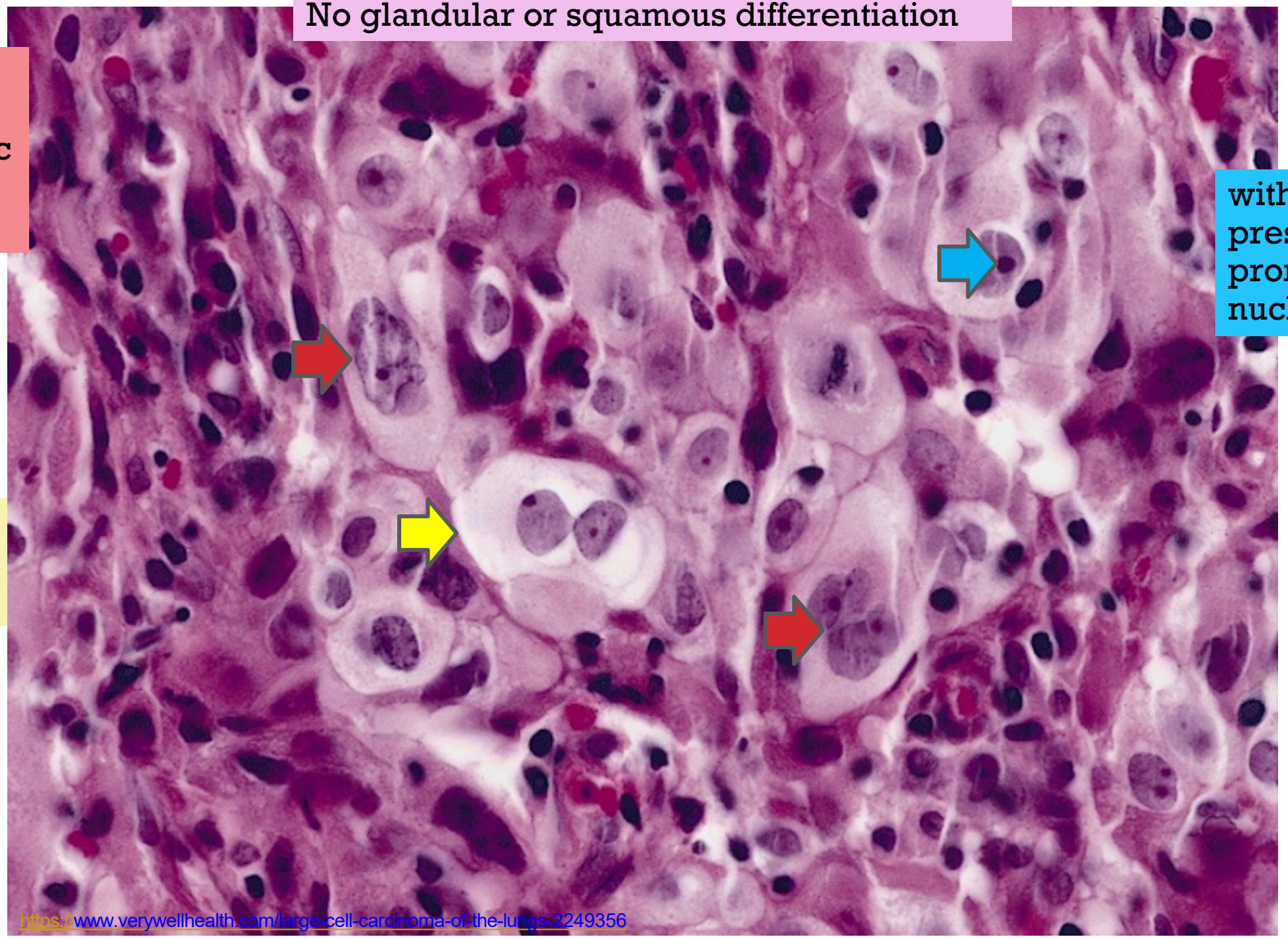
- Large nuclei, prominent nucleoli, and a moderate amount of cytoplasm.

No glandular or squamous differentiation

The nuclei are large _ pleomorphic in size & shape

with the presence of prominent nucleoli

The cells are large in size



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Mixed patterns (e.g., adenosquamous carcinoma, mixed adenocarcinoma, small cell carcinoma) are seen in 10% or less of lung carcinomas.

SPREAD AND METASTASIS

- Each of the Tumor types tends to spreads to nodes around the carina, mediastinum, and in the neck and clavicular regions

- Left supraclavicular node (**Virchow node**) involvement is particularly characteristic.

Sometimes this can be the first clue for the presence of an occult primary tumor which means that the first presentation in a patient who already has lung carcinoma is the presence of subraclavicular lymph node enlargement

- When advanced, Extend into the pleural or pericardial space, leading to inflammation and effusion or may Compress or infiltrate the SVC to cause either venous congestion or the **vena caval syndrome.**

- **Pancoast tumors (Pancoast syndrome)**:
  Apical neoplasms that may Invade the brachial or cervical sympathetic plexus to cause:
  - Severe pain in the distribution of the ulnar nerve.
  - Horner syndrome (ipsilateral enophthalmos, ptosis, miosis, and anhidrosis).
  - Destruction of the first and second ribs and sometimes thoracic vertebrae.

- **Tumor-Node-Metastasis(TNM) categories are used to indicate the size and spread of the primary neoplasm.**

TNM categories point to the anatomical extent of the lung cancer and predict the overall survival with non-small cell carcinomas & small cell carcinomas

T = tumor size (which has an important prognostic relevance) (each cm increase in size from less than 1 cm up to 5 cm yields a significantly different prognosis)

N = regional lymph node involvement (it includes the anatomical nodal involvement & the number of the involved lymph nodes , which means that there is a quantitative & qualitative assessment of the lymph node involvement)

M = distant metastasis (which includes malignant pleural effusion or malignant pericardial effusions that we talked about in the previous slide)

CLINICAL COURSE

- Mostly Silent, insidious lesions

In many cases the tumor already extended and became unresectable before producing symptoms

Sometimes the first presentation is the presence of

- Chronic cough and expectoration

Other symptoms including

- Hoarseness, chest pain, superior vena cava syndrome, pericardial or pleural effusion, or persistent segmental atelectasis or pneumonitis

Obstruction of the tumor to part of the airway resulting in resorption atelectasis

This means that by the time these symptoms are noted the prognosis is already poor because they result from the direct extension of the tumor to the adjacent structures
Ex : recurrent laryngeal nerve >> hoarseness of voice , SVC >> SVC syndrome, pleural or pericardial spaces >> malignant pleural or pericardial effusions

Indication of poor prognosis

- Symptoms from metastatic spread:
  - Brain (mental or neurologic changes)
  - Liver (hepatomegaly),
  - Bones (pain).

Although the adrenal gland may be nearly obliterated by metastatic disease, adrenal insufficiency or Addison disease is uncommon because island of the cortical cells stay functioning even if there is an extensive infiltration of the adrenal gland

PROGNOSIS, NSCLCS:

- **NSCLCs** carry a better prognosis than **SCLCs**.

Adenocarcinoma & squamous cell carcinoma carry a more favorable prognosis if compared to small cell lung carcinoma

- If **NSCLCs** detected before metastasis or local spread, **cure is possible** by lobectomy or pneumonectomy.

PROGNOSIS, SCLCS:

- **SCLCs**, invariably spread by the time they are first detected even if the primary tumor appears to be small and localized

- Surgical resection is not a viable treatment.

- Very sensitive to chemotherapy but invariably recur.

- Median survival even with treatment is 1 year. Only 5% are alive at 10 yrs

PARANEOPLASTIC SYNDROMES

Are a group of clinical disorders that are associated with malignant diseases, aren't directly related to the physical effect of the primary or metastatic tumors, so they arise from the secretions of the functional peptides or the hormones from the tumor cells themselves or inappropriate immune cross reaction between the normal host cells and the target tumor cells

More frequently associated with lung cancers

10% of patients with lung cancer are presented with paraneoplastic syndrome

(1) **Hypercalcemia** (secretion of a PTH related peptide)

Most commonly associated with squamous cell carcinoma

(2) **Cushing syndrome** (production of ACTH)

Most common associated with neuroendocrine lung tumors and can be also seen in carcinoid tumors and small cell lung carcinoma

(3) **Syndrome of inappropriate secretion of ADH**

Most commonly associated with small cell lung cancer

(4)**Acromegaly** (growth hormone-releasing hormone (GHRH) or growth hormone (GH))

Most commonly associated with bronchial carcinoid , Small cell lung carcinoma can be associated with acromegaly too

PARANEOPLASTIC SYNDROMES

(5)Neuromuscular syndromes, including a myasthenic syndrome, peripheral neuropathy, and polymyositis

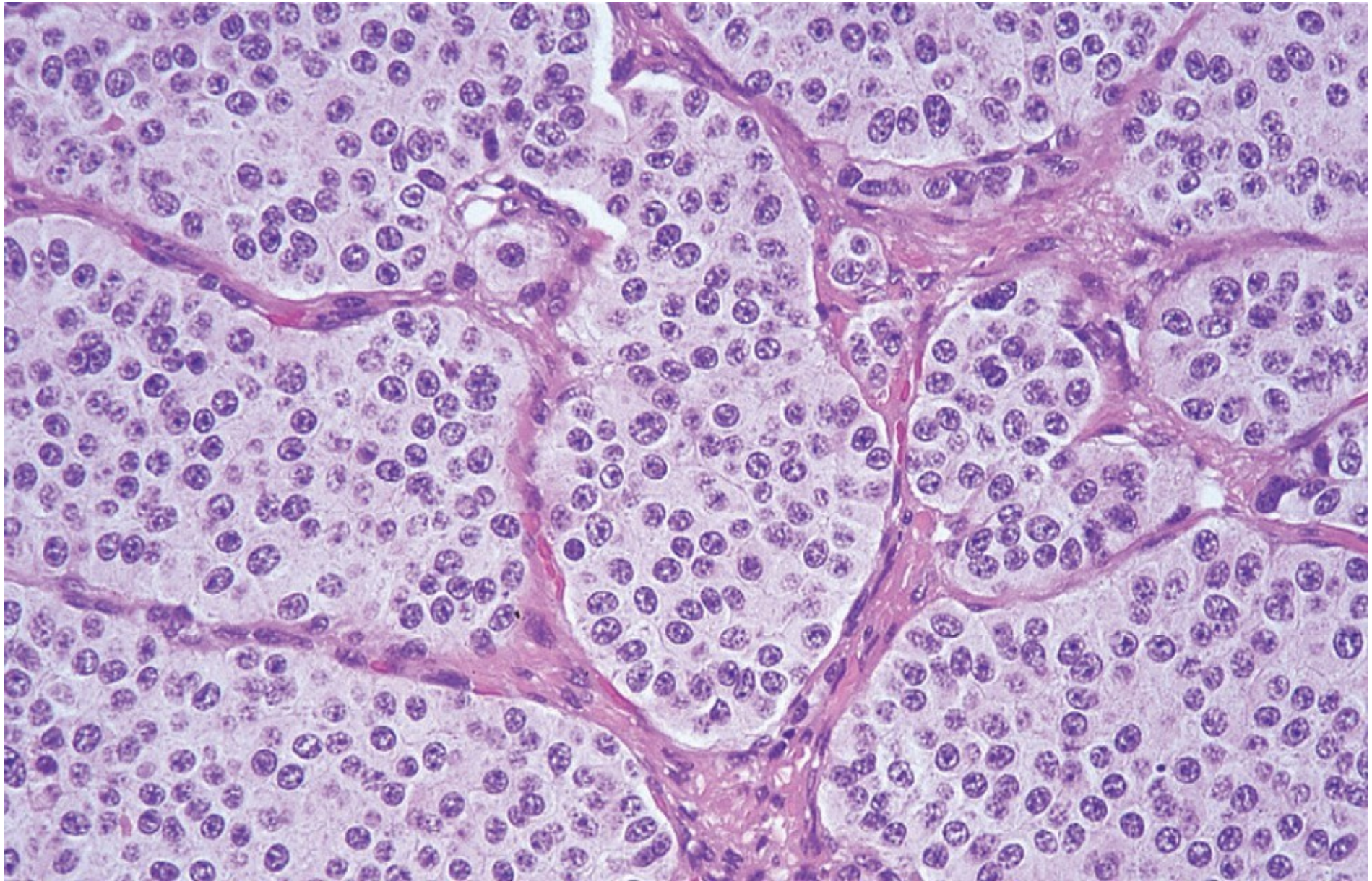
(6)Clubbing of the fingers and hypertrophic pulmonary osteoarthropathy

Most commonly associated with squamous cell carcinoma & adenocarcinoma

(7)Coagulation abnormalities, including migratory thrombophlebitis, nonbacterial endocarditis, and DIC.

CARCINOID TUMORS

Another malignant tumors involving the lung



CARCINOID TUMORS

- **5%** of all pulmonary neoplasms.
- **malignan**t tumors, **low-grade neuroendocrine carcinomas**
- composed of cells containing dense-core neurosecretory granules in their cytoplasm and, rarely, may secrete hormonally active polypeptides.

- subclassified as **typical or atypical**; both are often **resectable and curable**.

- May occur as part of the **multiple endocrine neoplasia syndrome (MEN syndrome)**

- **young adults** (mean 40 years)

- **5% to15%** of carcinoids have metastasized to the **hilar nodes at presentation**

- distant metastases are **rare**

MORPHOLOGY, MACROSCOPICALLY:

- originate in **main bronchi** mostly, Peripheral carcinoids are less common

- **well demarcated**

- grow in one **of two patterns**:

  (1) an **obstructing polypoid, spherical, intraluminal mass**

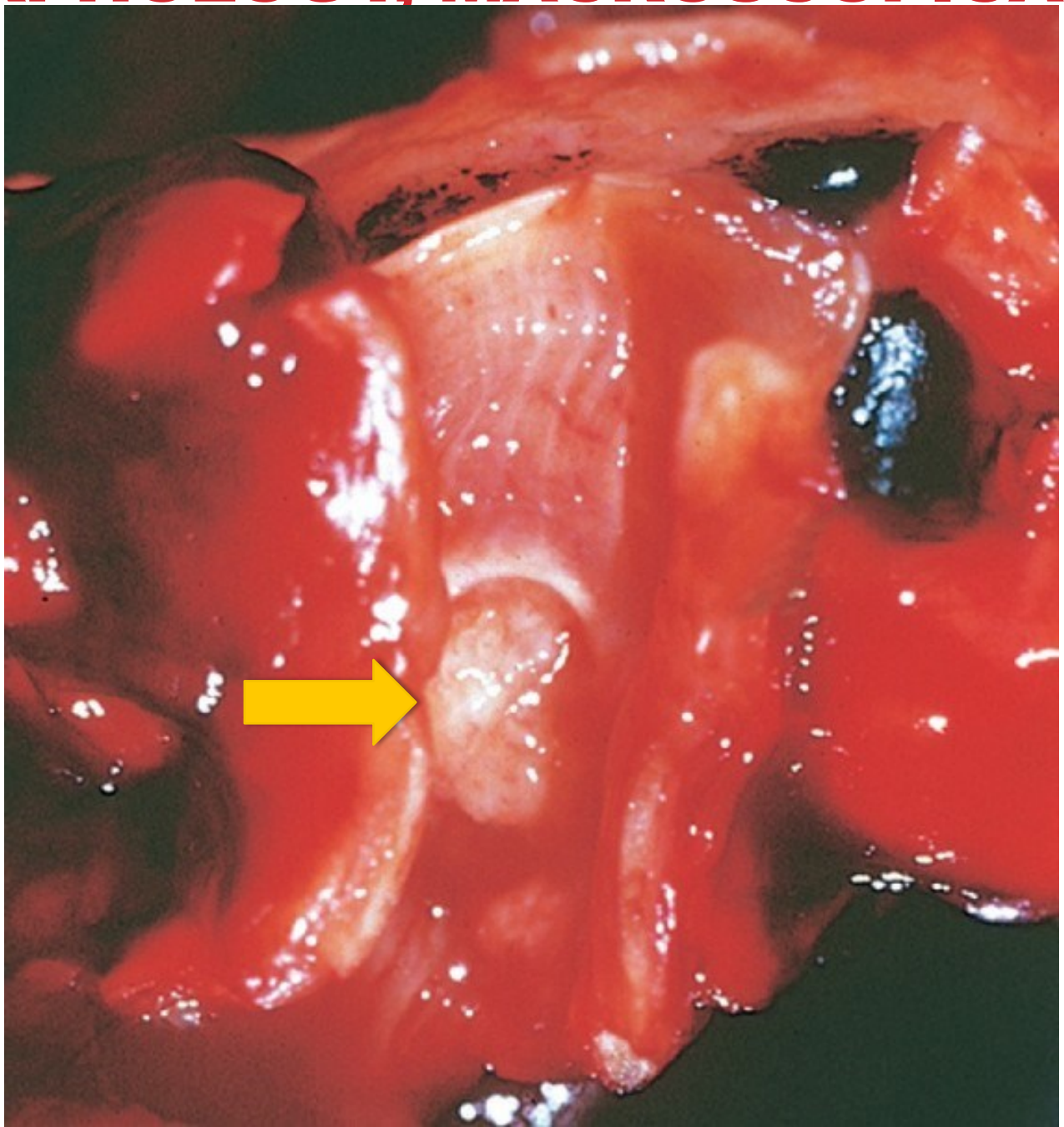
  (2) a **mucosal plaque** penetrating the bronchial wall to fan out in the peribronchial tissue—the so-called **collar-button lesion**

The figure at the top shows an obstructing polyploid tumor with a lumen of a bronchus as an example of the first growth pattern

This figure shows a collar button appearance , as you can appreciate this type of buttons has two surfaces one is wider than the other , this resembles the second growth pattern where the mucosal plaque are seen at the mucosal side and penetrates through the bronchial wall to fan out into the peri bronchial tissue

MORPHOLOGY, MACROSCOPICALLY:

Shows Carcinoid tumor growing as a spherical mass protruding into the lumen of a bronchus

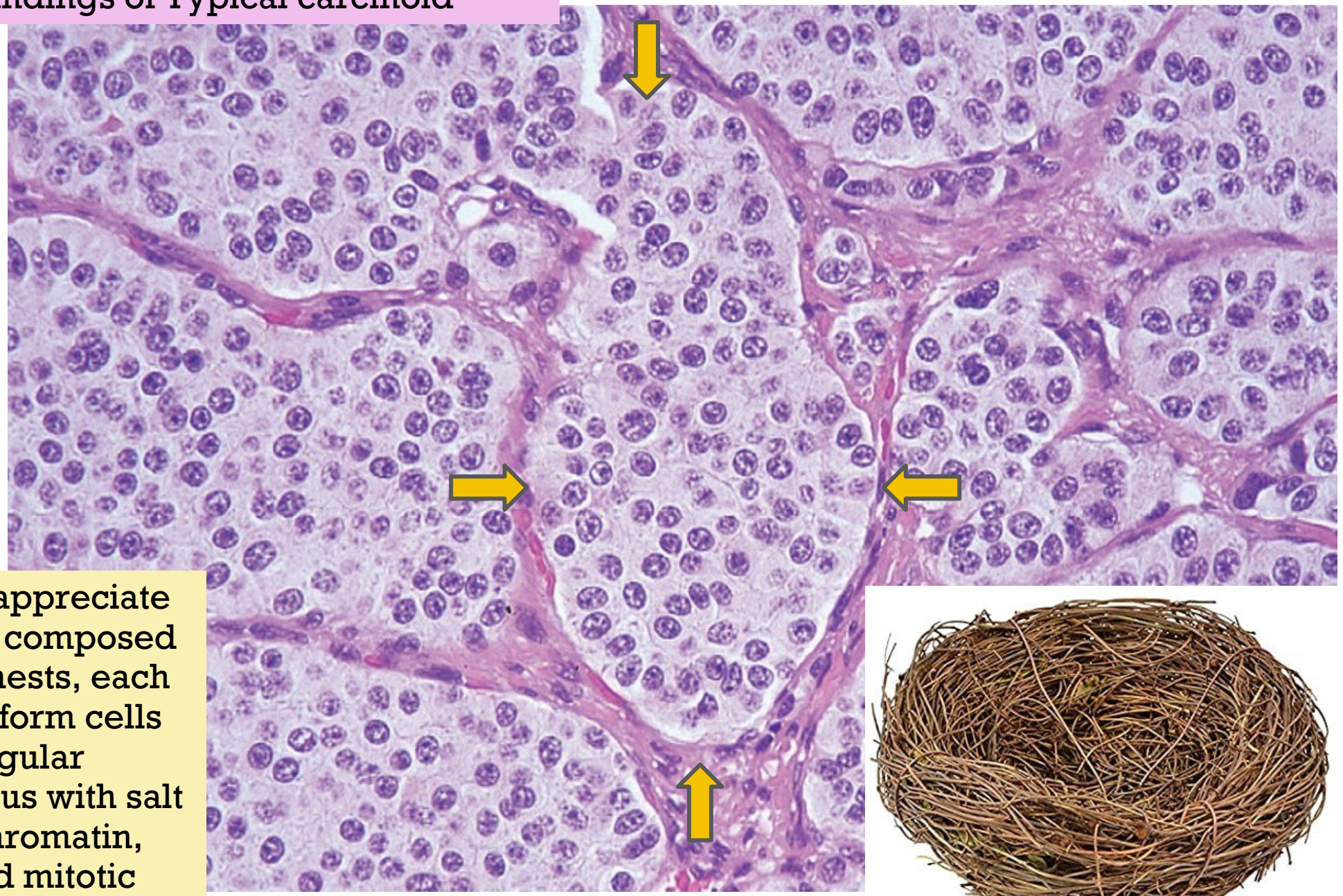


MORPHOLOGY, MICROSCOPICALLY:

- **Typical carcinoids:** composed of nests of uniform cells that have regular round nuclei with “salt-and-pepper” chromatin, absent or rare mitoses and little pleomorphism

- **Atypical carcinoid:**
  - tumors display a higher mitotic rate and small foci of necrosis. These tumors have a higher incidence of lymph node and distant metastasis than typical carcinoids
  - have *TP53* mutations in 20% to 40% of cases

Histologic findings of Typical carcinoid



As you can appreciate the tumor is composed of multiple nests, each contains uniform cells that have regular round nucleus with salt & pepper chromatin, no increased mitotic activity nor necrosis

https://www.amazon.co.uk/Props4shows-Fake-Birds-Nest-12cm/dp/B07BRDXDHX

CLINICALLY:

- Mostly manifest with signs and symptoms related to their **intraluminal growth**, including cough, hemoptysis, and recurrent bronchial and pulmonary infections.

- **Peripheral tumors** are often **asymptomatic** and discovered incidentally.

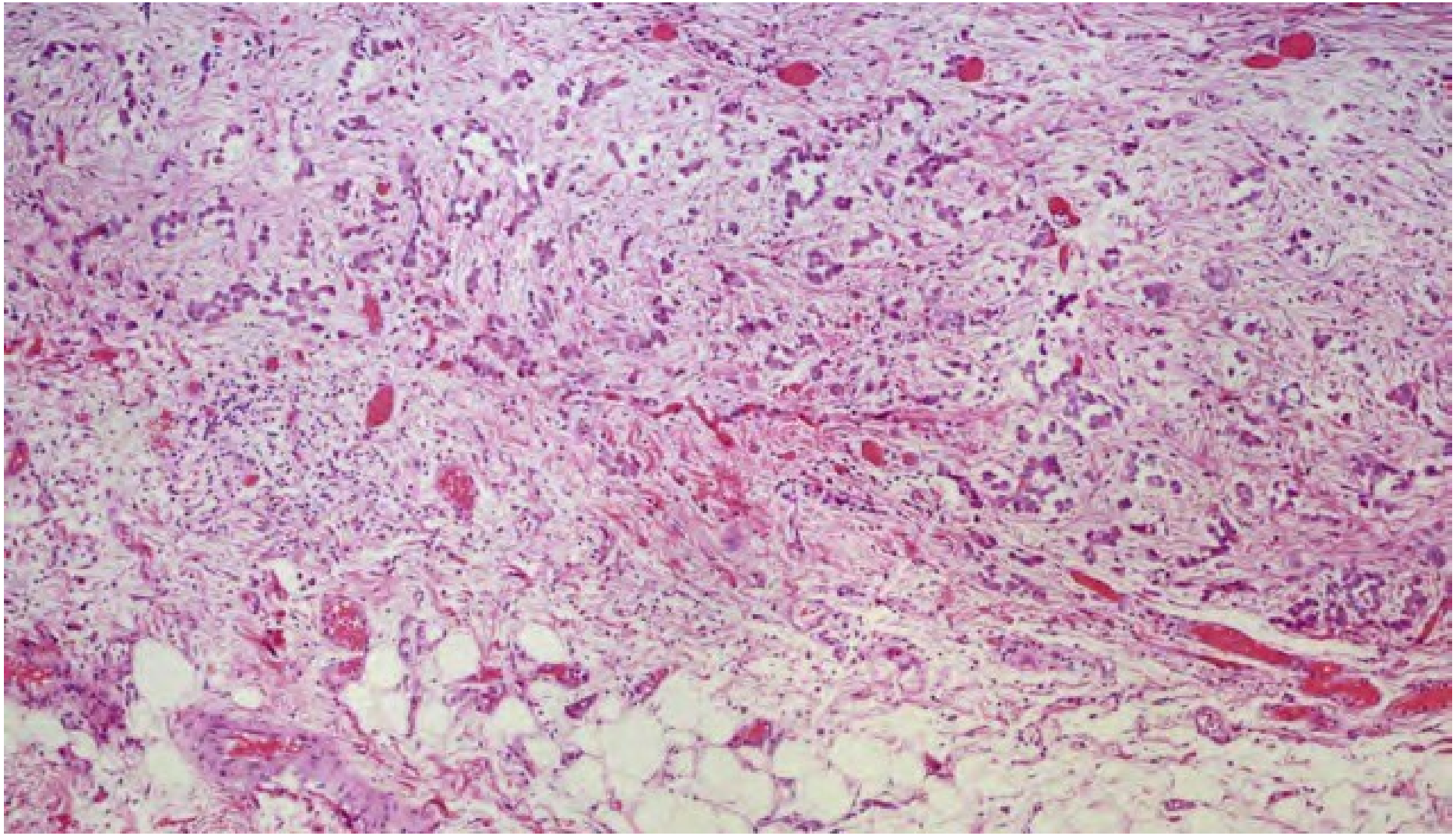
  On Chest radiographs

- Rarely induces the **carcinoid syndrome:**
  - intermittent attacks of diarrhea, flushing, and cyanosis.

PROGNOSIS:

- **5- and 10-year survival rates:**
  - for typical carcinoids are above **85%**
  - For atypical carcinoid **56% and 35%,** respectively

MALIGNANT MESOTHELIOMA



MALIGNANT MESOTHELIOMA

- Rare cancer of **mesothelial cells** lining parietal or visceral pleura

- Less commonly in the peritoneum and pericardium

- highly related to **exposure to airborne asbestos (80% to 90%** of cases):
    - Not only limit to people working with asbestos but also only exposure was living in proximity to an asbestos factory or being a relative of an asbestos worker.

- **Long latent period: 25 to 40 years** after initial asbestos exposure

- The combination of cigarette smoking and asbestos exposure **DOES NOT** increase the risk of developing malignant mesothelioma **BUT INCREASES** the risk for developing lung carcinoma

- Once inhaled, **asbestos fibers remain in the body for life**.

- the lifetime risk after exposure **DOES NOT** diminish over time (unlike with smoking, in which the risk decreases after cessation).

MORPHOLOGY, MACROSCOPIC:

- Preceded **by extensive pleural fibrosis and plaque**

Ct scans

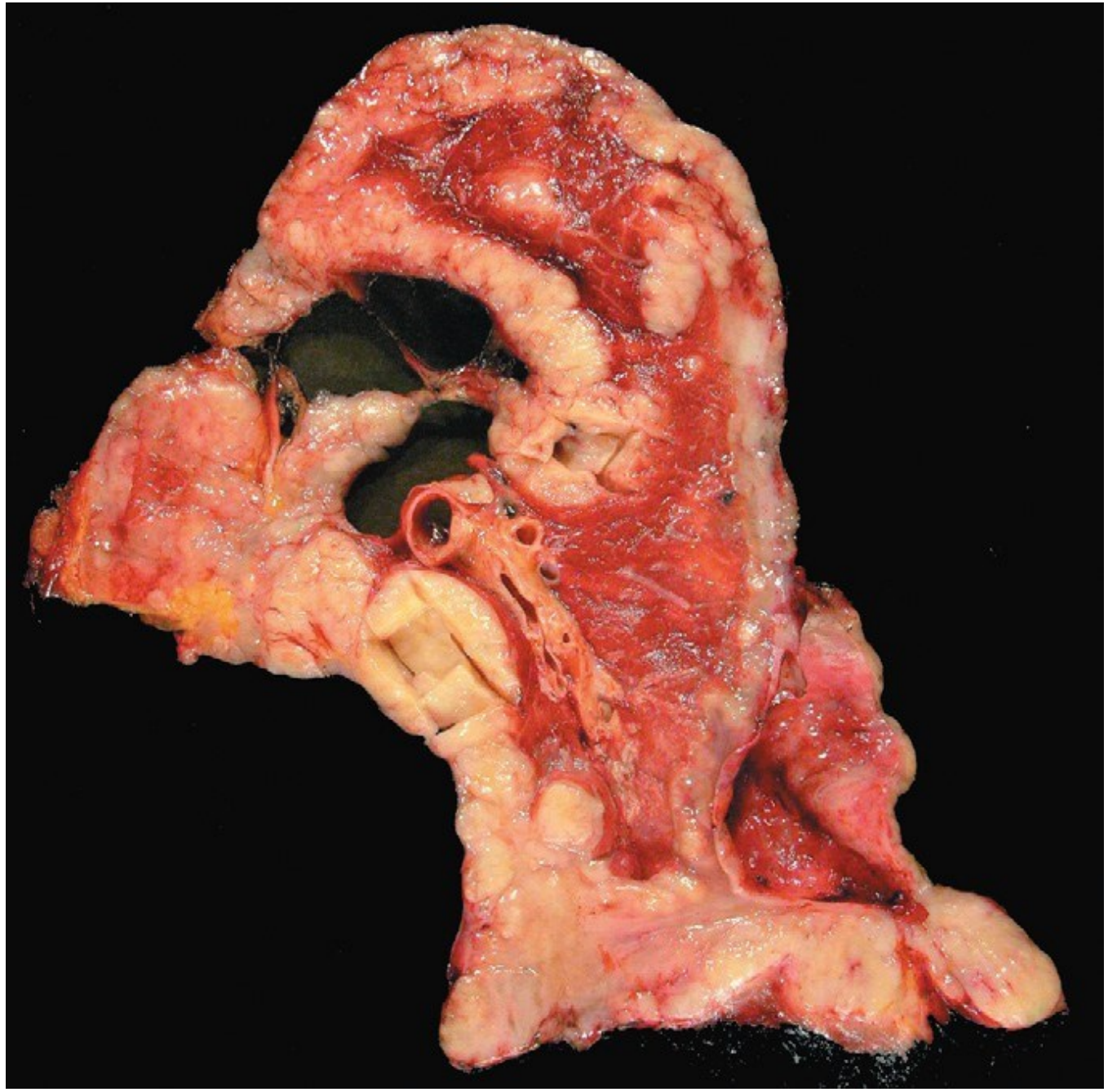
- begin in a localized area and spread widely, either by contiguous growth or by diffusely seeding the pleural surfaces.

- **Distant metastases are rare.**

May directly invade the thoracic wall or the subpleural lung tissue

At autopsy, the affected lung typically is **ensheathed by a layer of yellow-white, firm, variably gelatinous tumor that obliterates the pleural space**

In this figure the tumor appears as a thick firm white pleural tumor that ensheathes this bisected lung

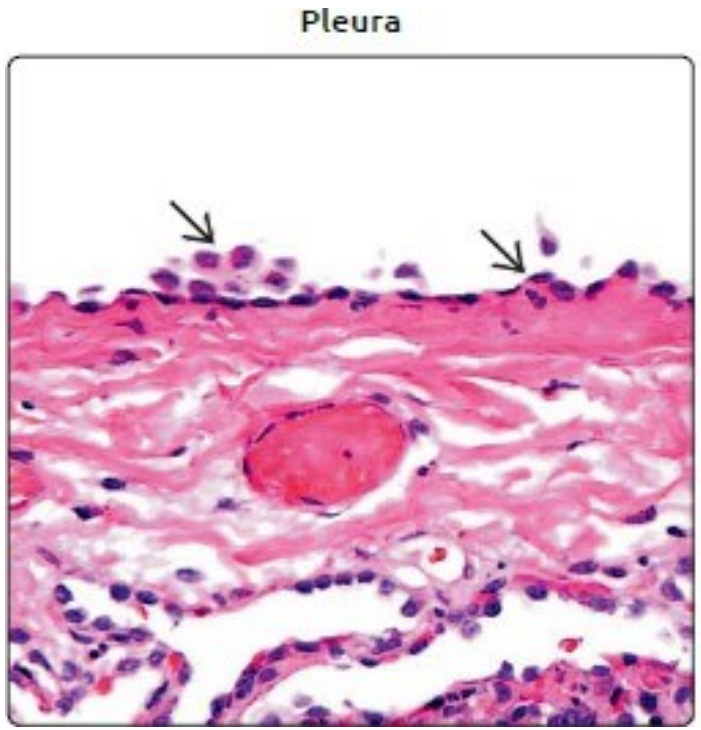


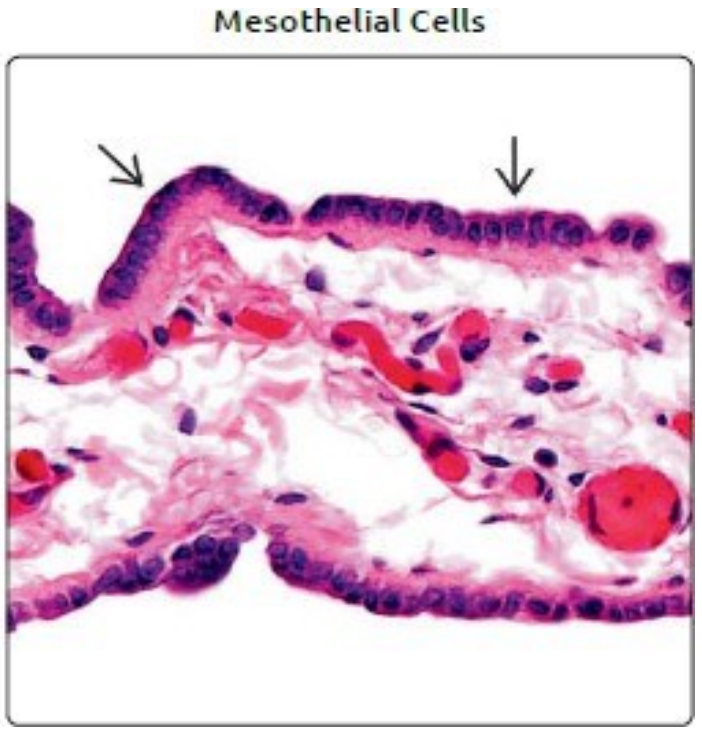
NORMAL HISTOLOGY:

- Normal mesothelial cells are biphasic, giving rise to pleural lining cells as well as the underlying fibrous tissue.

This figure shows the normal histology of benign normal mesothelial cells with aligning epithelial cells and underlying fibrous tissue

The pleura is lined by a single layer of normal mesothelial cells (flat, small cuboidal cells with eosinophilic cytoplasm & indistinct nuclear features)





Diagnostic pathology, normal histology text book

Shows the same mesothelial lining but here the cells are much more cuboidal & much easier to be identified if compared to the flat mesothelial cells in the left figure, but still in both it show the same cyto morphology

MORPHOLOGY, MICROSCOPIC:

Of mesothelioma

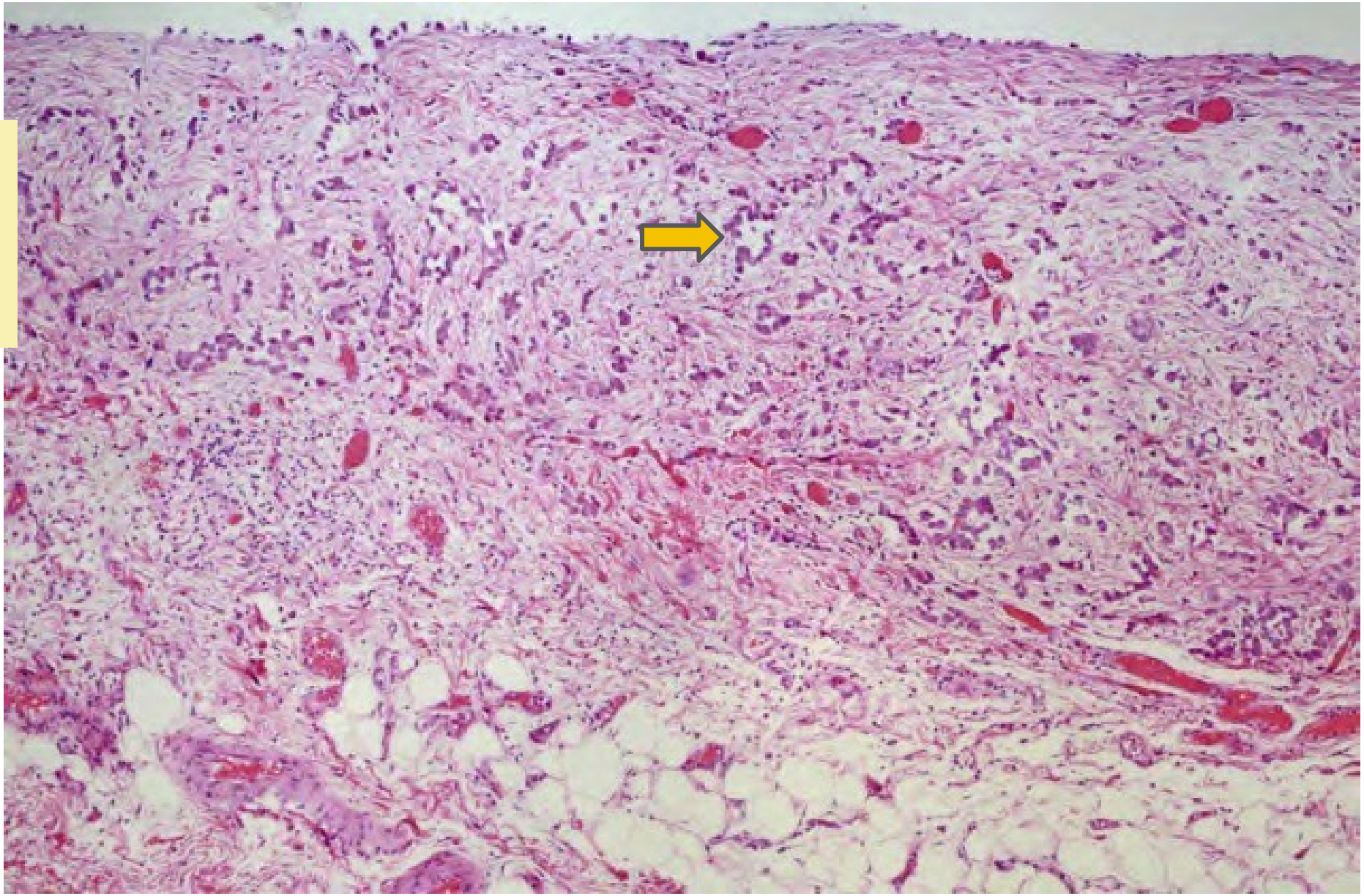
- **one of three** morphologic appearances:

(1) **Epithelial:** cuboidal cells with small papillary buds line tubular and microcystic spaces (the most common & confused with a pulmonary adenocarcinoma)

(2) **sarcomatous:** spindled cells grow in sheets

(3) **biphasic**: both sarcomatous and epithelial areas

Plumped Rounded cells forming a gland like configuration



A 48 year old gentleman developed truncal obesity, back pain, and skin that bruises easily over the past 8 months. On physical examination, he is afebrile, and his blood pressure is 160/95 mm Hg. A CXR shows an ill-defined, 5cm mass involving the left hilum of the lung. Cytologic examination of bronchial washings from bronchoscopy shows round epithelial cells that have the appearance of lymphocytes but are larger. The patient is told that, although his disease is apparently localized to one side of the chest cavity, surgical treatment is unlikely to be curative. He also is advised to stop smoking. Which of the following neoplasms is most likely to be present in this patient?

A) Adenocarcinoma

B) Bronchial carcinoid

C) Adenocarcinoma in situ (Bronchioloalveolar carcinoma)

D) Small cell carcinoma

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Indicates increased secretion of adrenocorticotropic hormone , as we said Cushing syndrome is a paraneoplastic syndrome resulting from ectopic corticotropine production which drives the adrenal cortices to produce excessive cortisol , high blood pressure is also related to Cushing syndrome

https://www.betterworldsolutions.eu/smartcirculair/challenge-energieflex/

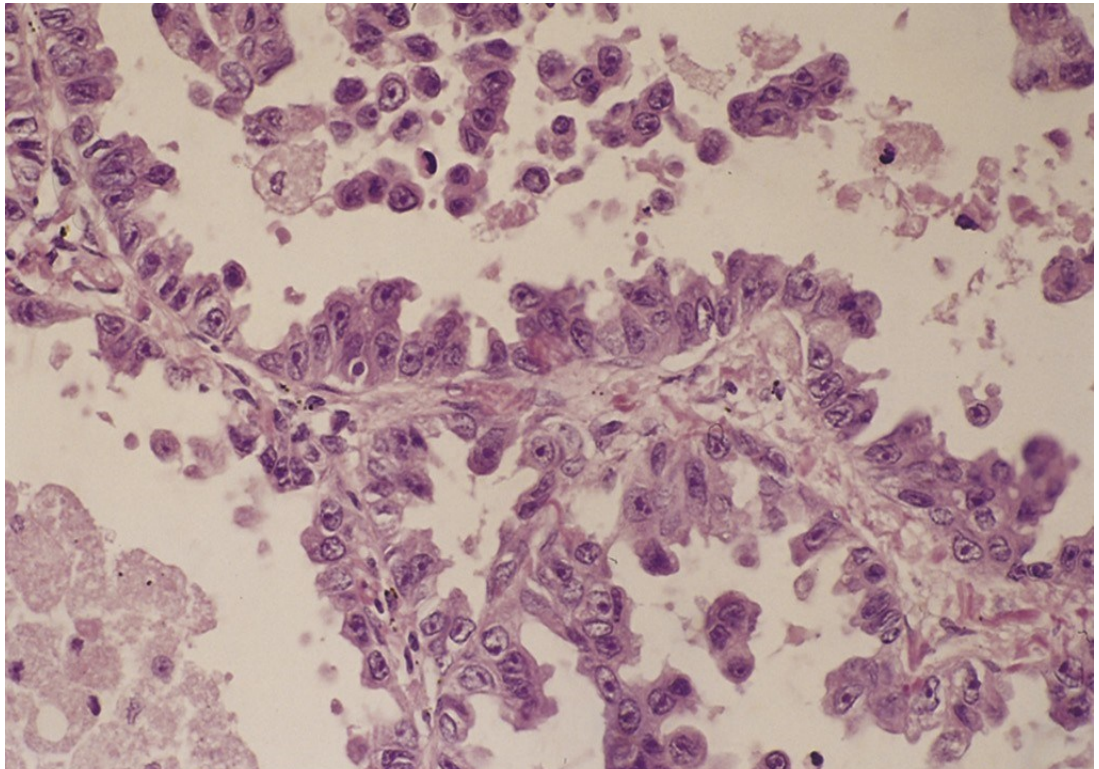
A 55 lady presented with cough and pleuritic chest pain for 3 weeks. Patient is afebrile. Some crackles are audible over the left lower lung on auscultation. A CXR shows ill-defined area of opacification in the left lower lobe. After 1 month of antibiotic therapy, her condition has not improved. CT-guided needle biopsy is performed, and the specimen is shown in the figure. Which of the following neoplasms is most likely to be present in this patient?

A)Large cell anaplastic carcinoma

B) Adenocarcinoma in situ

C) Malignant mesothelioma

D) Squamous cell carcinoma



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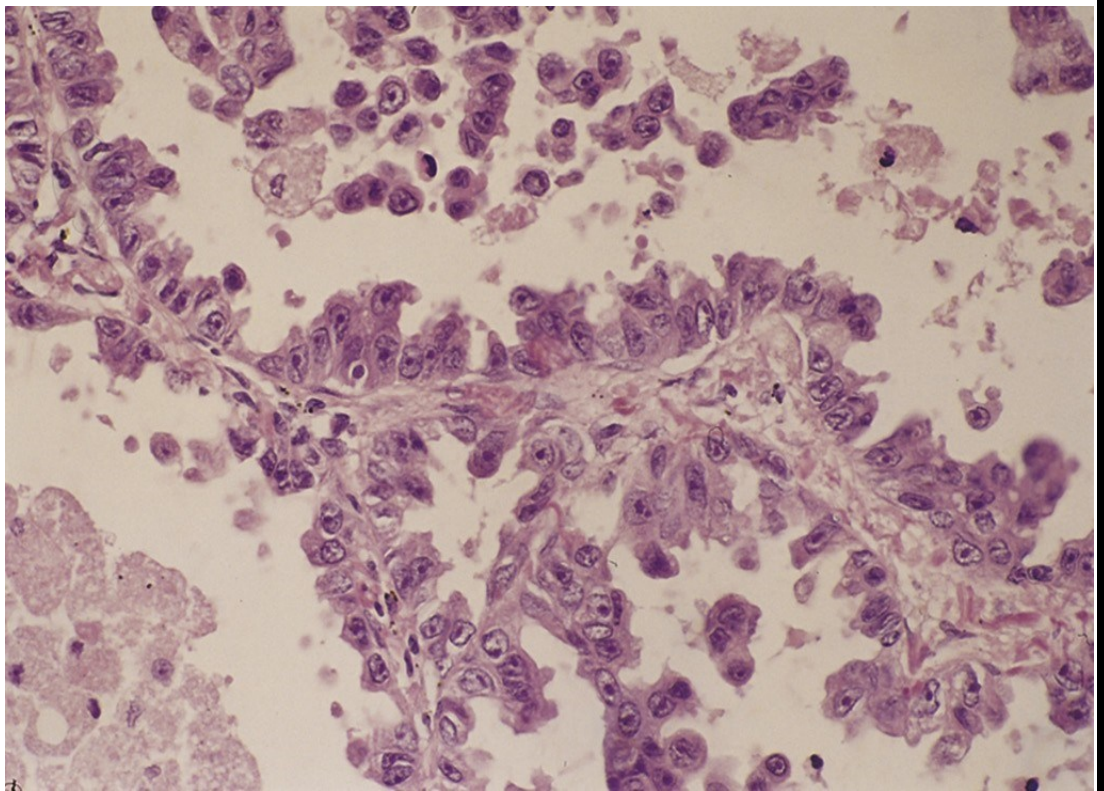
Clinical findings mimic pneumonia mostly as a peripheral tumor

A) Large cell anaplastic carcinoma

B) Adenocarcinoma in situ

C) Malignant mesothelioma

D) Squamous cell carcinoma



FOR YOUR QUESTIONS:

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Or E-learning

THANK YOU!