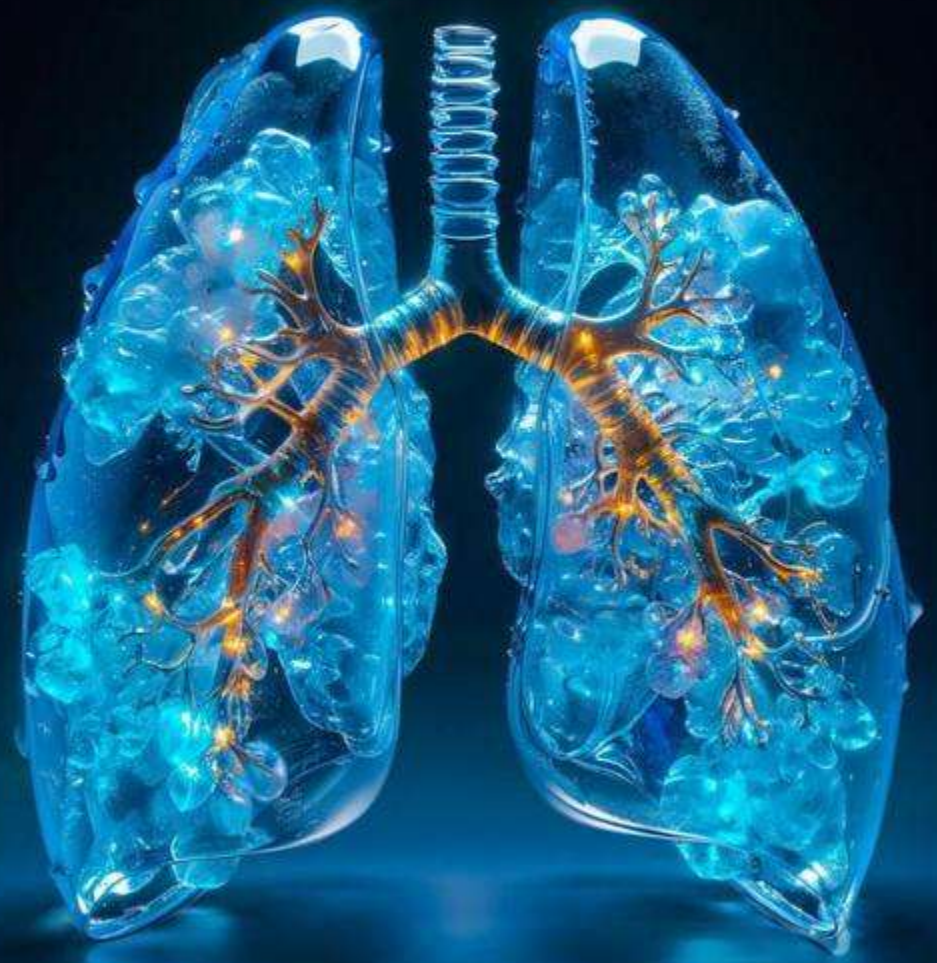

RS

PATHOLOGY

MODIFIED NO. 7

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Lung Cancer 2

Color code
Slides
Doctor
Additional info
Important

SPREAD AND METASTASIS

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

  The most common site of metastasis is the lymph nodes (sooner or later they also metastasize to distant sites).

- Left supraclavicular node (**Virchow node**) involvement is particularly characteristic.
  - Virchow node involvement is sometimes the **first clue that indicates the presence of an occult tumor**, An **occult tumor** refers to a tumor that is clinically hidden or undetectable through standard diagnostic means
  - The **most common tumors** that might involve Virchow lymph nodes are **long** cancer and **gastric** cancer
  - 'the first presentation in a patient who has lung carcinoma is its enlargement'

- When **advanced** Extend into adj structures:
  - pleural or pericardial space, leading to inflammation and effusion.
  - Large tumors might cause Compress or infiltrate the SVC to cause either venous congestion or the vena cava syndrome.

the vena cava syndrome.

Superior Vena Cava (SVC) Syndrome is a medical condition caused by infiltration or compression of the superior vena cava, a large vein responsible for returning blood from the upper body (head, neck, upper limbs, and upper chest) to the heart. This obstruction leads to impaired venous drainage, resulting in various clinical symptoms:

- Shortness of breath (dyspnea).
- Dysphagia (difficulty swallowing) due to esophageal compression.
- Congestion of the blood vessels

- **Pancoast tumors (Pancoast syndrome)**: Apical neoplasms (happens in any histological type) that may Invade and causing infiltration of 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.

Pancoast tumors : Apical neoplasms

Pancoast syndrome: Apical neoplasms that may Invade the brachial or cervical sympathetic and infiltration plexus

Horner syndrome: results from the involvement of the sympathetic plexus

Ipsilateral Enophthalmos: refers to the posterior displacement of the eye into the orbit on the same side of the body as the underlying pathology

Ptosis: is the drooping of the upper eyelid

Miosis: refers to the abnormal constriction of the pupil

Anhidrosis: loss of sweating on the same side

- **Tumor-Node-Metastasis(TNM) staging system is used to indicate the size and spread of the primary neoplasm.**

❖ Tumor-Node-Metastasis (TNM)

- We tend to stage the tumors to determine the treatment and the prognosis of your patient
- The **'T'** stands for the **size of the primary tumor**. While the **'N'** stands for **regional lymph nodes** involvement (assessing their quantitative-their **number-** and qualitative **-anatomic lymph nodes types-** involvement). And the **'M'** stands for distant metastasis.

CLINICAL COURSE

- Lung cancer is one of the **most insidious and aggressive Neoplasms (Mostly Silent)**

  Symptoms will appear when the tumor reaches certain size

- When the tumor is large enough (present respiratory symptoms), The major presenting complaints are cough (75%), weight loss (40%), chest pain (40%), and dyspnea (20%).

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

  By the time these symptoms are noted, then the result is most probably poor because they result from the direct extension of the tumor to other structures; such as **the recurrent laryngeal nerve causing hoarseness of voice**, the **SVC and the pleural and pericardial spaces causing malignant pericardial or pleural effusion**.

CLINICAL COURSE

Not infrequently, lung cancer is recognized though biopsy of tissues involved by metastatic disease

The first symptoms may not be from the lung or the lymph nodes, but from the invaded adjacent structures that give the first symptoms like:

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

    Although the adrenal glands may be nearly obliterated by metastatic disease, but adrenal insufficiency 'Addison's disease' is uncommon because the island of the cortical cells stays functional regardless of the extensive infiltration of the adrenal gland.

PROGNOSIS:

- **Prognosis is poor** for most patients, in all types of lung cancers.
- Even with thoracic surgery, radiation therapy, and chemotherapy:
  - the overall 5-year survival rate is only 18.7%.
  - The 5-year survival rate is:
    Depends on the stage of tumor if its localized, regional or distant metastases
    - 52% for cases detected when the disease is still localized,
    - 22% when there is regional metastasis,
    - only 4% with distant metastases.

PROGNOSIS:

- All are poor, but still there is a variation, the adenocarcinoma and squamous cell carcinoma carry a slightly better prognosis than SCLCs. (Small Cell Lung Carcinoma)

- **SCLCs**, invariably spread by the time they are first detected even if the primary tumor appears to be small and localized (virtually, all the patients have metastasis by the time of diagnosis)

- Surgical resection is not a viable treatment. Systemic chemotherapy and Radiotherapy is needed

- most patients present with advanced stage disease;
  - despite excellent initial responses to chemotherapy, the median survival is approximately **10 months** and the cure rate is **close to zero**
    - **SCLSs have the worst prognosis between the different histologic types of lung cancer**

PARANEOPLASTIC SYNDROMES

- Signs and symptoms resulting in clinical changes in the patient , resulting from tumor secreting hormones -that's normally are not secreted in that tissue- or peptides into the bloodstream that will results in systemic symptoms
- the **most common** tumor causing paraneoplastic syndrome is **lung cancer**
- Types:

(1)Hypercalcemia(secretion of a PTH related peptide, Parathormone, prostaglandin E) SCC

- **Most common** paraneoplastic syndrome related to lung cancer, most of the histologic types correlate with hypercalcemia, but **SCC** (squamous cell carcinoma) increases calcium the **most**.

(2) **Cushing syndrome** (excess production of ACTH) SCLC, CARCINOID

- features: truncal obesity, Buffalo Hump, hypertension, and other
- **Mostly** correlated with **carcinoid** and **small cell lung cancer**

(3) **Syndrome of inappropriate secretion of ADH**, (production of ADH), hyponatremia SCLC

- **increased ADH** increased fluid retention and dilution of sodium causing **hyponatremia**
- Mostly associated with **small cell lung cancer**

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

- **Mostly** correlated with **carcinoid** and **small cell lung cancer**
- **Remember** mostly doesn't exclude other histologic types of cancer

SCLC, CARCINOID

PARANEOPLASTIC SYNDROMES

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

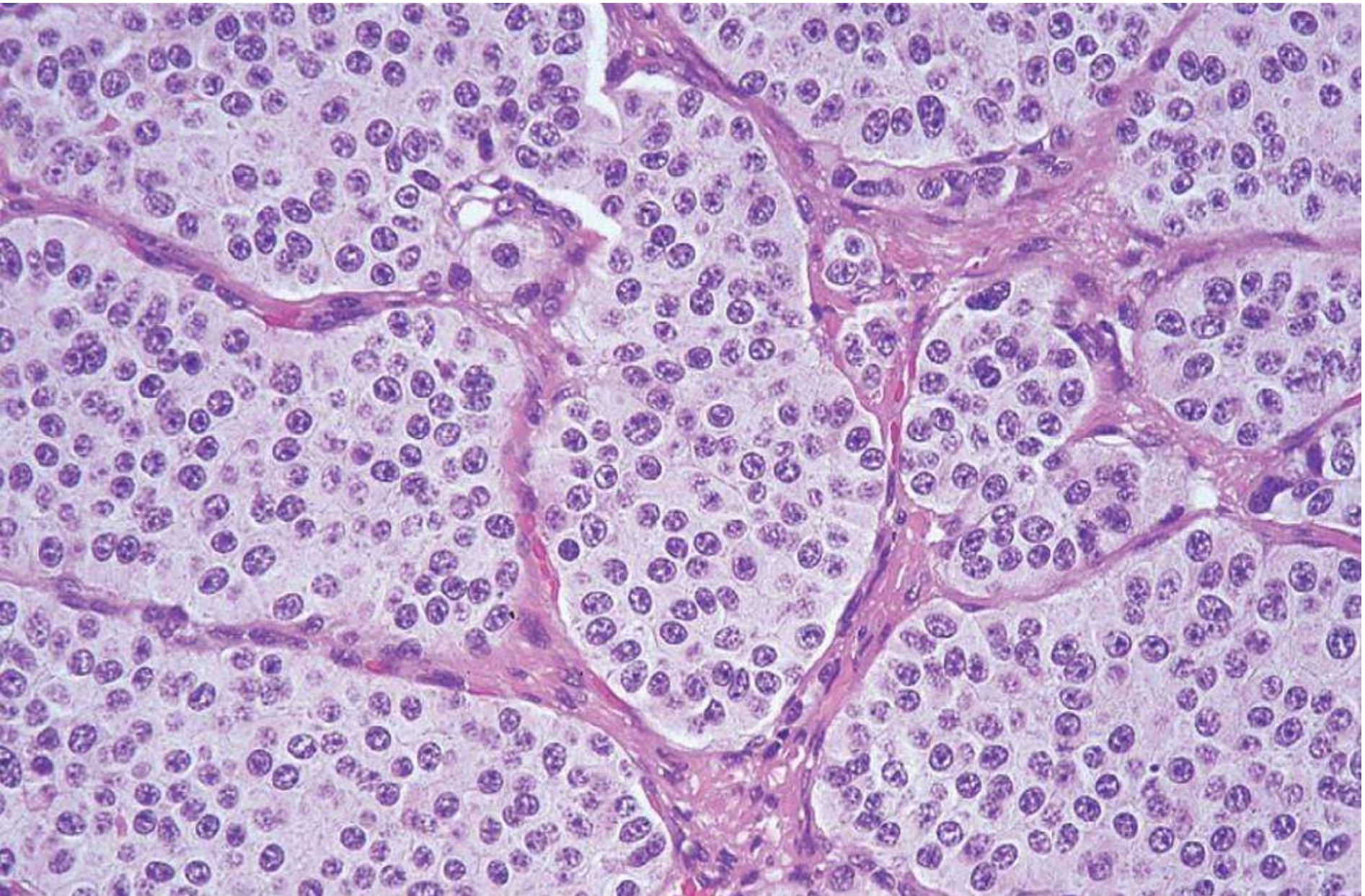
(6) hypertrophic pulmonary osteoarthropathy which is associated with fingers clubbing

- **Fingers clubbing** physical deformity of the fingers or toes characterized by the softening of the nail bed, loss of the normal angle between the nail and the nail bed, and enlargement of the distal phalanges (fingertips).
- **Fingers clubbing is not specific,** it can be seen in any pulmonary or heart disease or might be idiopathic.
- **Mostly** correlated with **Adeno** and **squamous cell carcinoma.**

Adeno, SCC

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

CARCINOID TUMORS



- The tumor is made of islands or nests of tumor cells
- The tumor cells are uniform
- Their cytoplasm is abundant with indistinct cell borders
- The nuclei look like each other
- All of them are granular and stippling.
- Neuroendocrine features
- Those tumors show low mitotic activity

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, resulting in symptoms

- subclassified as **typical or atypical,** and this will affect the risk for lymph node involvement distant metastasis both are often **resectable and curable**.
  - The prognosis here is much better than all histologic types of lung cancer.
- May occur as part of the **multiple endocrine neoplasia syndrome (MEN syndrome)** (MEN1 OR MEN2)

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

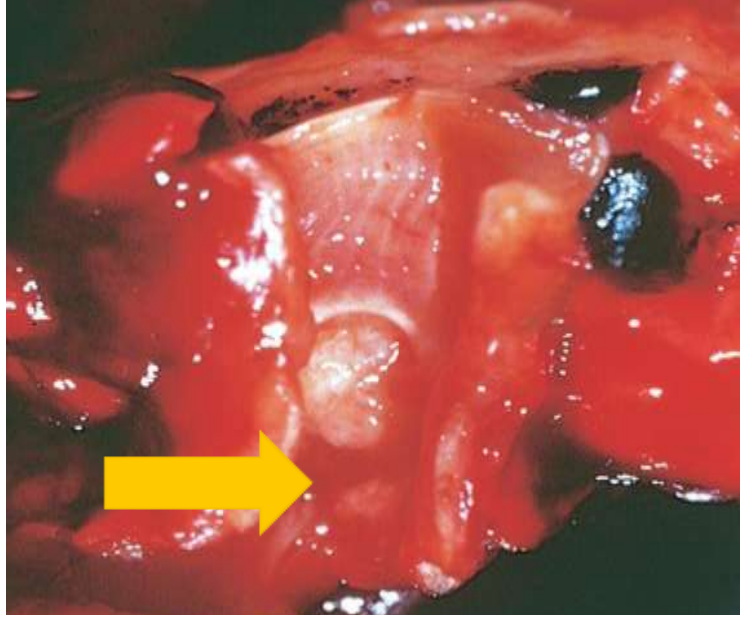
- distant metastases are **rare**

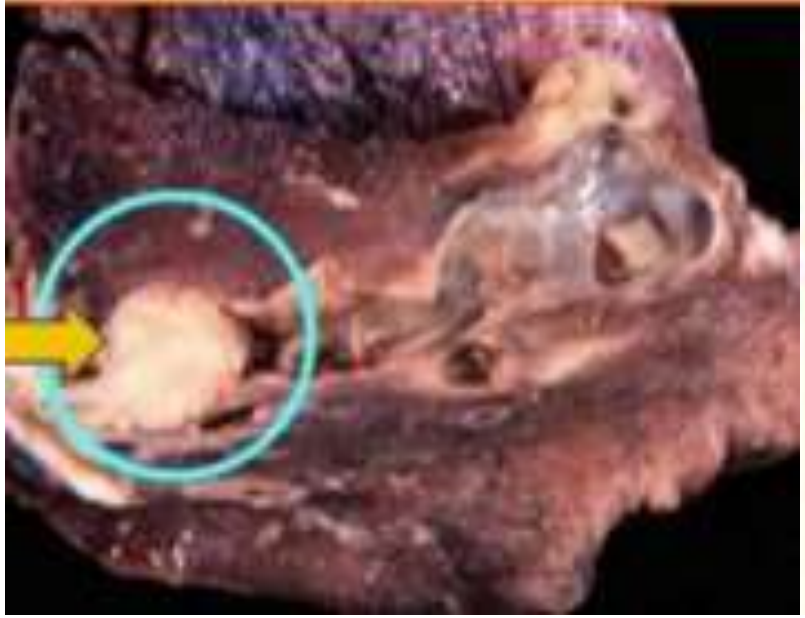
  the lesion is present centrally in the main bronchi (**mainly**)
  Peripheral carcinoid (**rare**)

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

MORPHOLOGY, MACROSCOPICALLY:

- originate in **main bronchi** mostly, Peripheral carcinoids are less common
  (mainly central, around the hilum in the main bronchi)
  Peripheral carcinoids are mainly asymptomatic; since its need a long time for the patient to be symptomatic
- **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**
  (not obstructing, instead infiltrating into the wall)





- obstructing polypoid

- collar-button

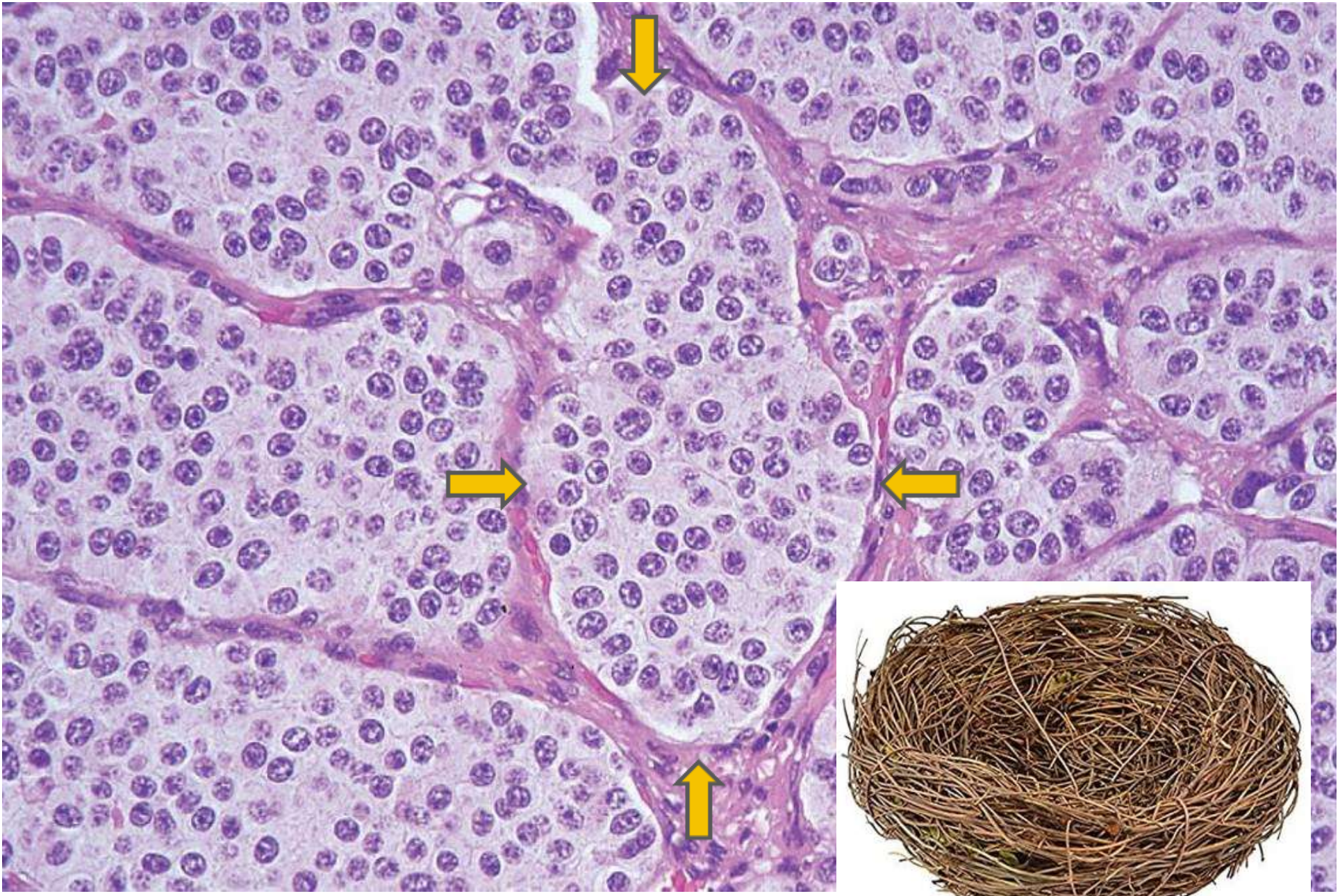
- The two figures on the left shows the gross appearance bisected bronchus, the lumen is filled by an obstructing polypoid tumor (the first pattern).

- The figure on the right show the collar-button infiltrating downward (fan out), involving the underlying structures

MORPHOLOGY, MICROSCOPICALLY:

- **Typical carcinoids:** composed of nests of uniform cells that have regular round nuclei with "salt-and-pepper" chromatin(finely granular), **absent or rare mitoses** and **little pleomorphism, no necrosis**

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



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

- The figure shows a **Typical carcinoid**
- Arranged in nestlike structure
- Without lumen in the middle
- No mitosis is seen

- In **Atypical carcinoid** scattered mitosis can be seen

CLINICALLY:

- Mostly manifest with signs and symptoms related to their **intraluminal growth**, including cough, hemoptysis (coughing blood), and recurrent bronchial and pulmonary infections.
  - The symptoms of the intraluminal growth are related to the obstruction
- **Peripheral tumors** are often **asymptomatic** and discovered incidentally. (seeing in x-ray radiopacity then taking biopsy)
- Rarely induces the **carcinoid syndrome:**
  - Rarely may produce serotonin resulting in paraneoplastic syndrome called carcinoid syndrome, the patient will present with:
    - intermittent attacks of diarrhea, flushing, and cyanosis.

PROGNOSIS:

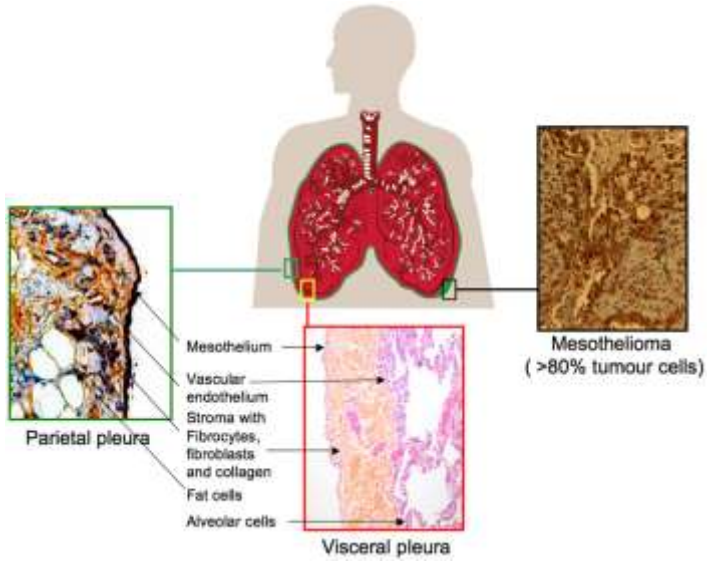
Those patients do much better than patients with lung cancer

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

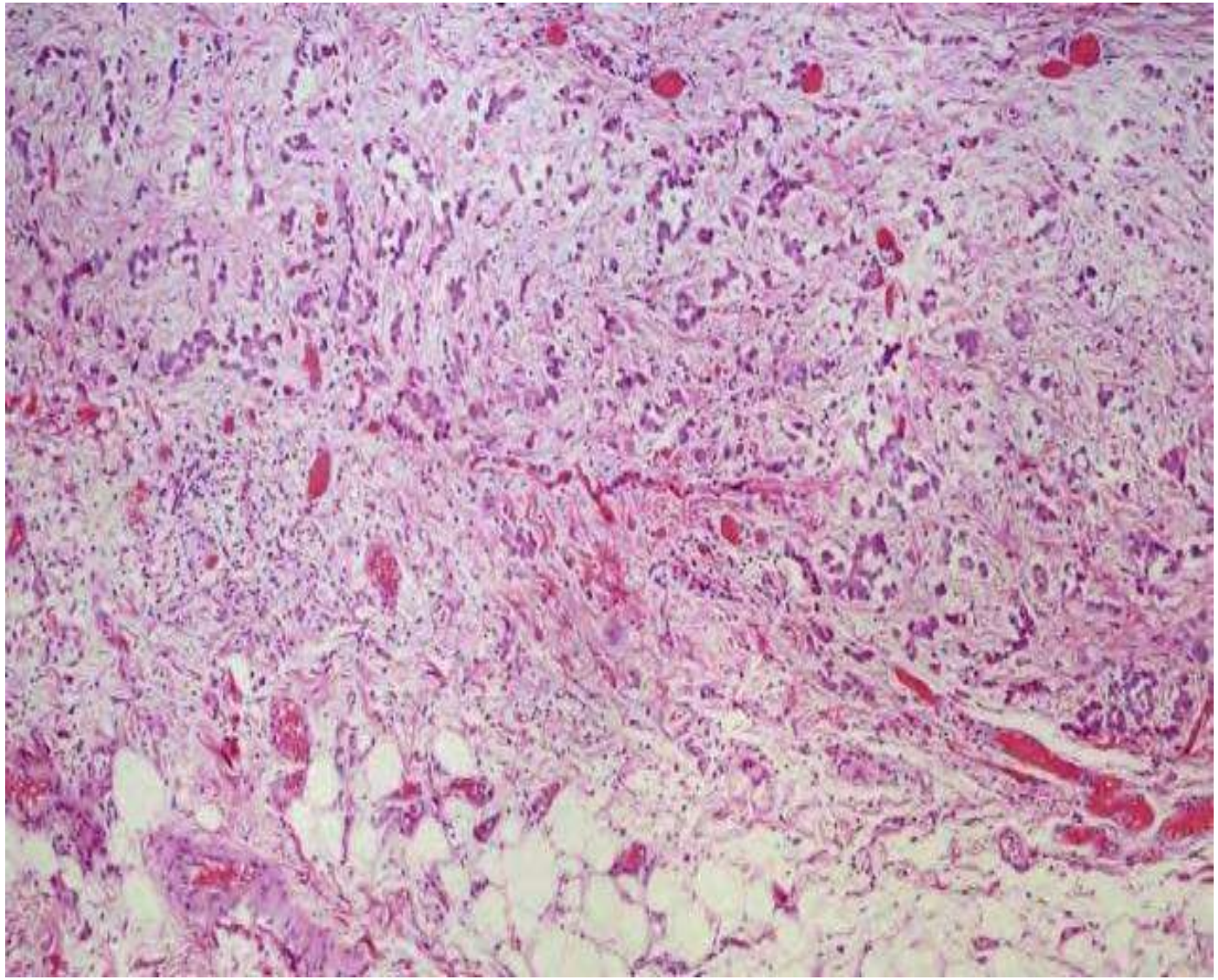
3. MALIGNANT MESOTHELIOMA

The third type of tumor in this lecture is malignant mesothelioma.

Malignant mesothelioma correlates with mesothelial cells, which line the pericardial cavity, the pleural cavity, and the peritoneal cavity.



Extra pic



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** to develop after initial asbestos exposure

- If we assume that the patient smokes, he is at an increased risk of developing lung cancer. Consequently, he may die to lung cancer before developing mesothelioma. As mentioned in the previous lecture, the synergistic effect of cigarette smoking and asbestos exposure significantly elevates the risk of lung cancer by 55-fold, whereas mesothelioma is only associated with 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.

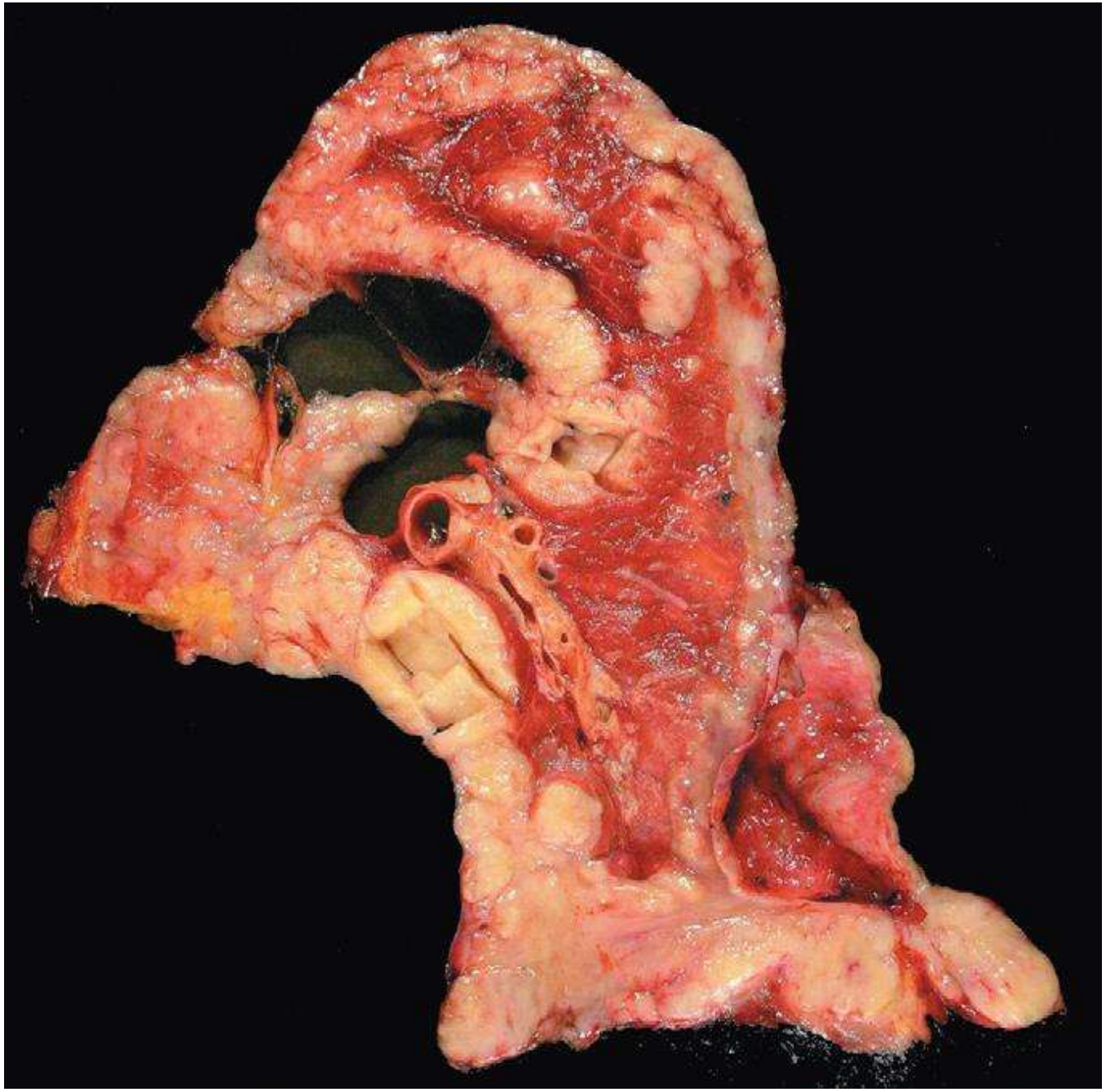
- Once inhaled, asbestos fibers remain in the body for life, inducing a reaction over time that increases the risk of developing mesothelioma. Additionally, if the patient is a smoker, the risk of developing lung cancer is further elevated.

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

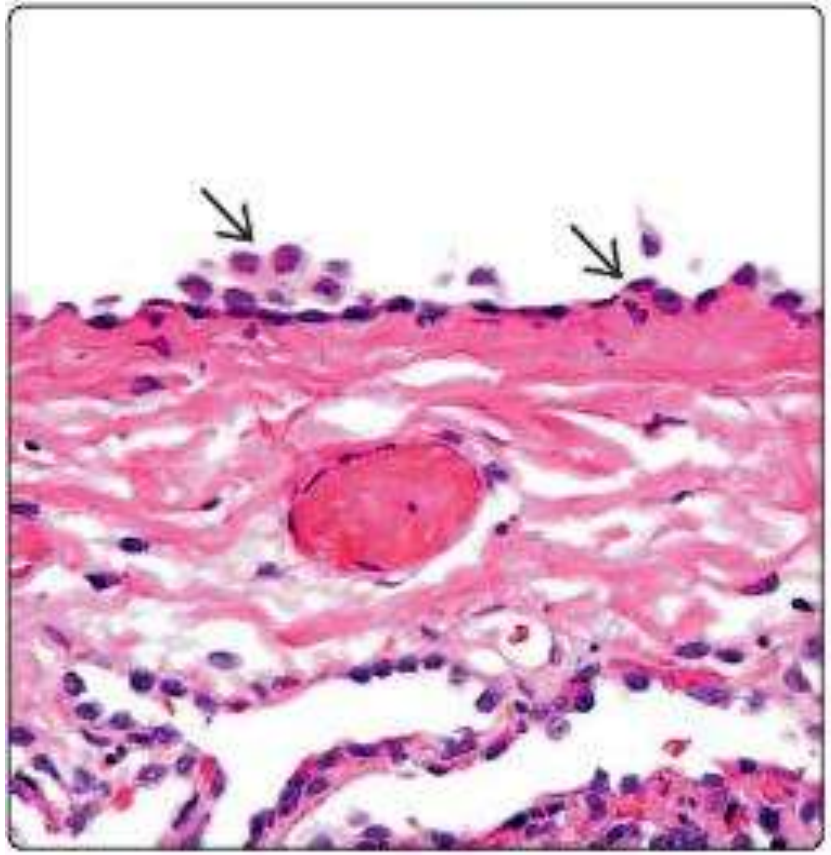
At autopsy, the affected lung typically is **ensheathed by a layer of yellow-white, firm, variably gelatinous tumor that obliterates the pleural space**



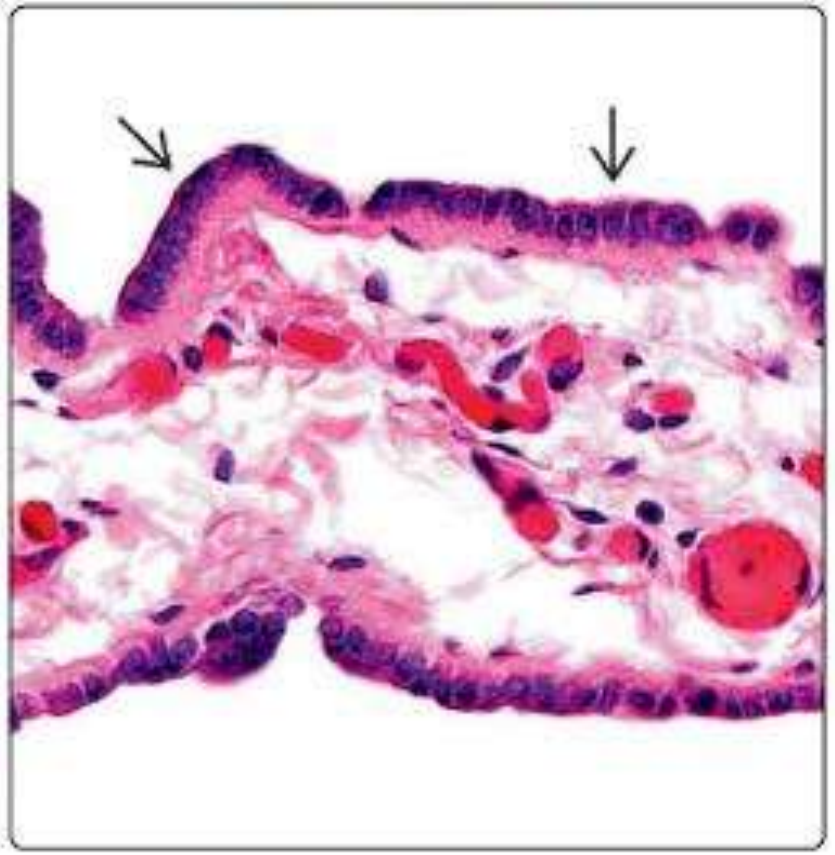
NORMAL HISTOLOGY:

To remind you of the normal histology of mesothelial cells: Mesothelial cells are **biphasic**, meaning they can present as **columnar**, **cuboidal**, or **flattened cells** lining the surfaces of the lungs, pericardium, and peritoneal cavity. Additionally, they develop a **fibrous layer** just beneath the epithelium.

Pleura



Mesothelial Cells



Diagnostic pathology, normal histology text book

MORPHOLOGY, MICROSCOPIC:

- **one of three** morphologic appearances of mesothelioma tumor:

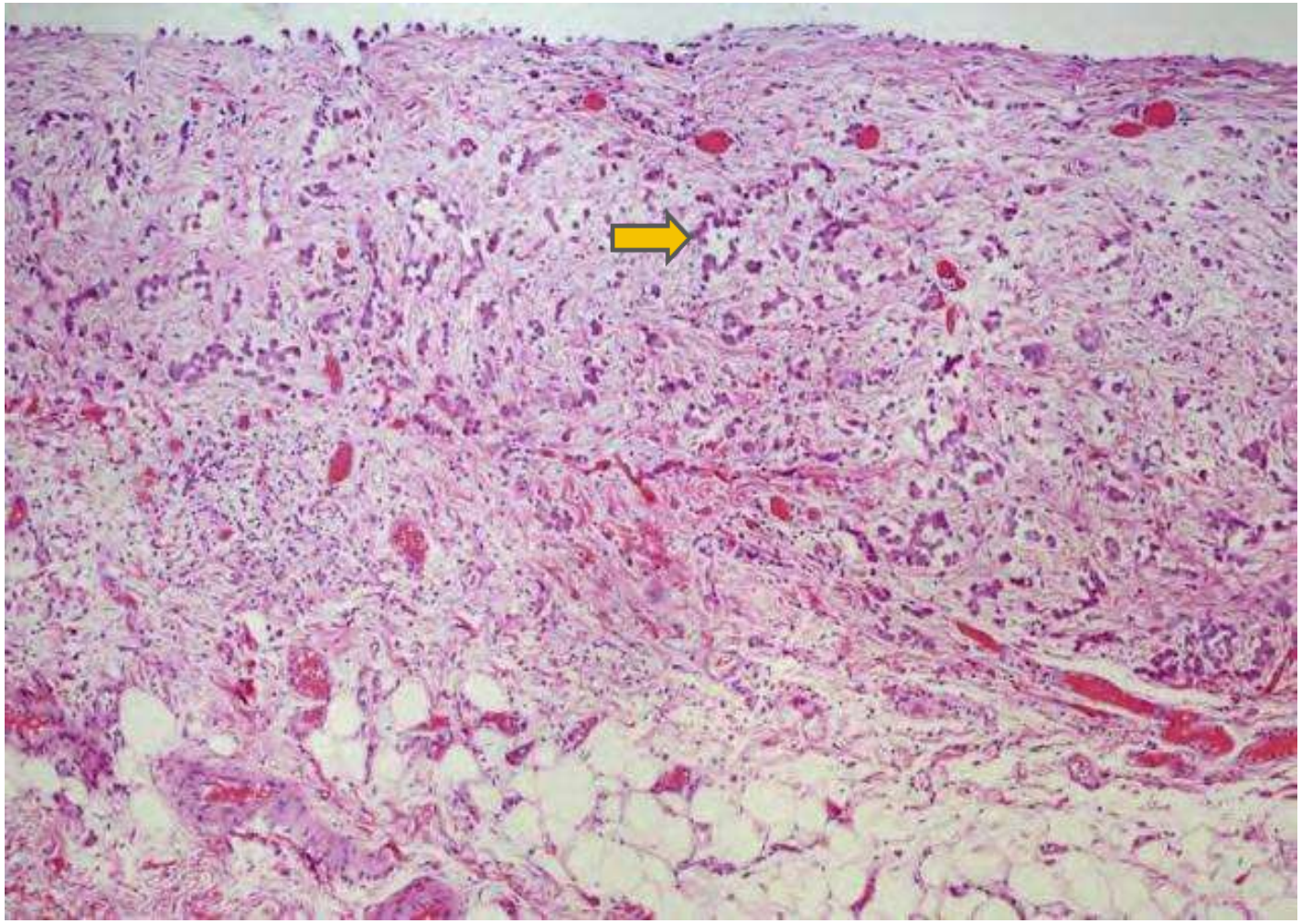
(1)Epithelial: cuboidal cells with small papillary buds line tubular and microcystic spaces **(the most common & confused with a pulmonary adenocarcinoma)**

- Epithelial pattern: This resembles cuboidal cells lining cystic-like spaces. One of the primary differential diagnoses for this pattern is pulmonary adenocarcinoma, as both tumors can exhibit gland-like growths resembling cystic spaces. To differentiate between the two, immunohistochemical staining is essential. Markers such as TTF-1 (specific for pulmonary adenocarcinoma) , WT-1 and calretinin are used to identify mesothelial differentiation.

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

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

- This figure shows invasive or malignant mesothelioma. The background tissue exhibits desmoplasia, and there is epithelial proliferation. Upon closer examination, cystic-like spaces with tubular structures can be observed, indicating an epithelial pattern of malignant mesothelioma (MM). To confirm this diagnosis, a TTF-1 test would be negative, while WT1 and calretinin would be positive, indicating that these cells are mesothelial.



Now, let's discuss some clinical cases

Case 1: A 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 carcinoma

The clues are 🤦🏻‍♂️
Old age, male , smoker.
Symptoms: cough and a 7 kg weight loss over the past 4 months --> indicates chronic process, finger clubbing (not strong clue), afebrile (ما عنده حرارة) and no hilar adenopathy --> indicate no infection, 3-cm lesion near the right hilum --> mass, elevated serum calcium --> paraneoplastic and sarcoidosis, lesion occluding the right main bronchus. A surgical procedure with **curative intent** is attempted --> indicates that this type of tumor has a better prognosis.

So, the diagnosis is Squamous cell carcinoma

Case 2: A 57-year-old lady presented with a 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 are observed. 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 atypical 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

Remember: the most common type in females is Adenocarcinoma. And the most common type in non-smokers is Adenocarcinoma.

The clues are 🤦‍♀️
Old, female , non-smoker
Symptoms: cough for 4 months along with loss of appetite and a 7 kg weight loss --> indicates chronic process, peripheral subpleural mass --> the tumor tend to be in the periphery of the lung, she undergoes a right lower lobectomy--> so they wish to cure the patient, Microscopically, the proliferating atypical cells show glandular differentiation.

So, the diagnosis is Adenocarcinoma

Case 3: 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, 5 cm 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 is also advised to stop smoking. Which of the following neoplasms is most likely to be present in this patient?

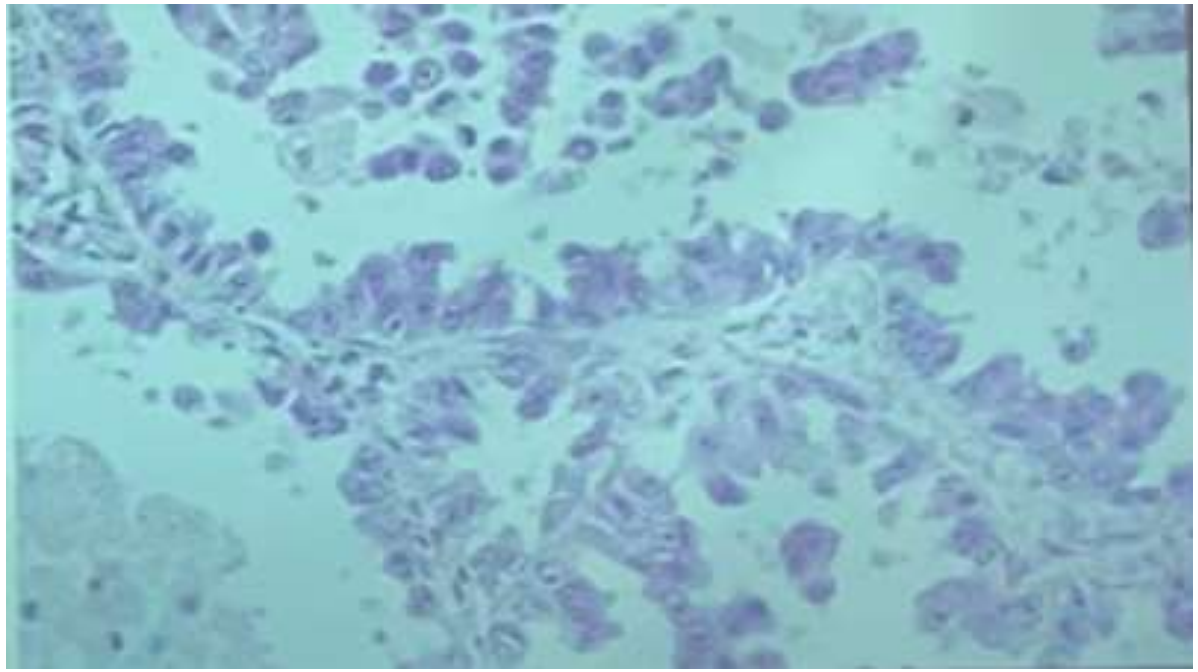
A) Adenocarcinoma
B) Bronchial carcinoid
C) Adenocarcinoma in situ (Bronchioloalveolar carcinoma)
D) Small cell carcinoma

The clues are 🕵️‍♂️
Old, male.
Symptoms: he has exhibited chronic symptoms over the past 8 months, including truncal obesity, back pain, easily bruised skin, and hypertension. These features suggest the possibility of Cushing's syndrome or a Cushing-like disease [Cushnoid features]. He is afebrile. 5 cm mass involving the left hilum of the lung. Round epithelial cells that have the appearance of lymphocytes but are larger, so we are talking about small cell neoplasm. Although his disease is apparently localized to one side of the chest cavity, surgical treatment is unlikely to be curative --> the prognosis is poor so there is a small cell carcinoma. He is also advised to stop smoking due to string association between the tumor and smoking.

So, the diagnosis is Small cell carcinoma

Case 4: A 55-year-old lady presented with cough and pleuritic chest pain for 3 weeks. The patient is afebrile. Some crackles are audible over the left lower lung on auscultation. A CXR shows an 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



The clues are 🧗‍♀️
Old, female.
Symptoms: cough and pleuritic chest pain for 3 weeks. She is afebrile. Some crackles are audible over the left lower lung on auscultation. A CXR shows an ill-defined area of opacification in the left lower lobe --> indicates an infection (pneumonia) --> 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: there is no lung infection, the epithelial cells exhibit atypia, characterized by hyperchromasia (notable dark staining of the nuclei) and pleomorphism (variation in nuclear size and shape). Some of the cells appear stratified. The alveolar wall architecture is preserved, and the basement membrane remains intact. There is no evidence of stromal invasion or desmoplasia, suggesting a form of in situ lesion with dysplasia.

So, the diagnosis is Adenocarcinoma in situ.

THANK YOU!

لحظة تفكُّرية في قوله تعالى

﴿ وَأَن لَّيْسَ لِلْإِنسَانِ إِلَّا مَا سَعَىٰ ﴾

فالإنسان لا يملك إلا سعيه ، لا سعي غيره !

اسعى ولا تفكِّر في النتيجة ، تيقّن بأن لا شيء يضيع عند ربك

﴿ وَأَنَّ سَعْيَهُ سَوْفَ يُرَىٰ ﴾

VERSIONS	SLIDE #	BEFORE CORRECTION	AFTER CORRECTION
V1→ V2			
V2→V3			

امسح الرمز و شاركنا بأفكارك لتحسين أدائنا !!