Respiratory System
RS

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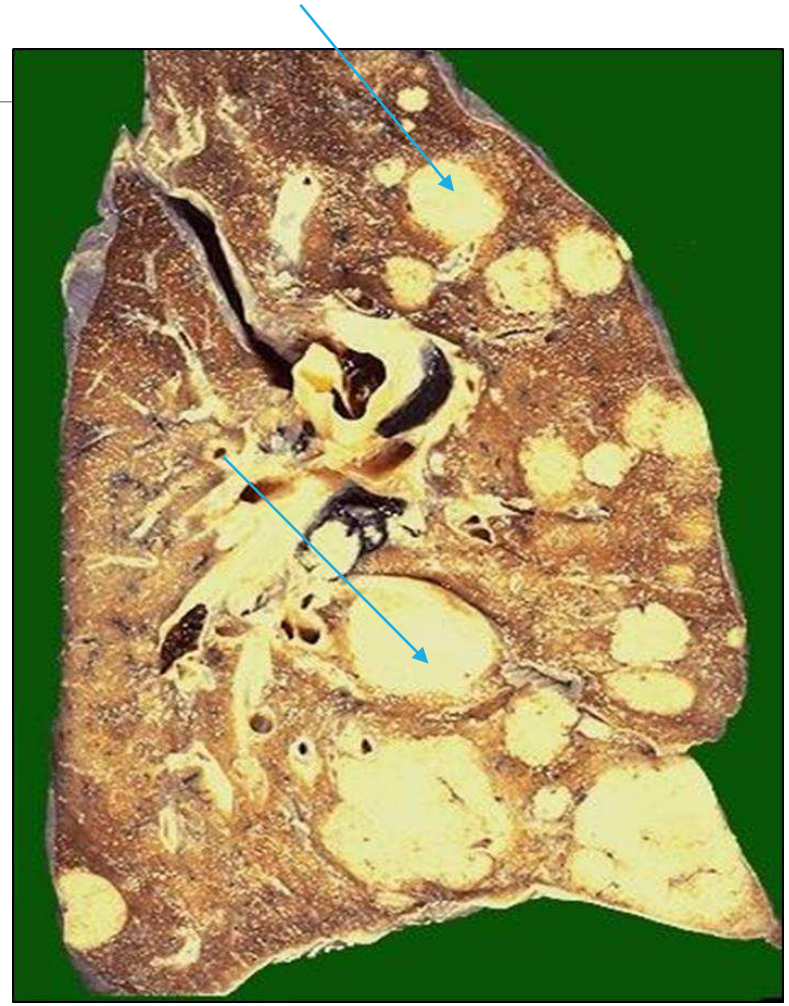
Metastatic tumors in lung

- All types of cancer can metastasize to the lung.
- Reach the lung by lymphatic or hematogenous route & may show :
  - Multiple discrete nodules (Cannon Ball)
  - Single nodule.
  - Endobronchial, pleural
  - Pneumonic consolidation
  - Diffuse lymphatic dissemination called ***Lymphangitis Carcinomatosa.***



Neuroendocrine proliferation and tumors

-The normal lung contains neuroendocrine cells within the epithelium as single cells or as clusters, the neuroepithelial bodies.

✶ Neoplasms of neuroendocrine cells in the lung:

1. Tumourlets:

- Nodular proliferation of neuroendocrine cells that invade beyond the bronchiolar wall and measure <5 mm.

-Inconsequential, hyperplastic nests of neuroendocrine cells seen in areas of scarring or chronic inflammation.

2. Carcinoid tumors (≥ 5 mm)

3. Large cell neuroendocrine carcinoma

4. Small cell carcinoma

Carcinoid Tumors

- Are **malignant** tumors composed of cells that contain dense-core neurosecretory granules in the cytoplasm and, rarely, may secrete hormonally active polypeptides.

- They are best thought of as **low-grade neuroendocrine carcinomas.**

- Are subclassified as **typical or Atypical**.

- Both are often resectable and curable.

- Occur in young adults (mean 40 years), M=F.

- ~ 20-40% of the patients are **non**smokers.

Clinically

The clinical manifestations may arise from: 1. intraluminal growth, 2. capacity to metastasize and 3. ability of some to elaborate some vasoactive amines.

- Can be central or peripheral (less common).

- Most present with signs and symptoms related to their intraluminal growth, including cough, hemoptysis, and recurrent bronchial and pulmonary infections.

-Peripheral tumors are often asymptomatic and are discovered incidentally on chest radiographs.

Morphology

-Most originate in main bronchi and grow in one of two patterns:

(1) an obstructing polypoid mass, or (2) a mucosal plaque penetrating the bronchial wall to fan out in the peribronchial tissue.

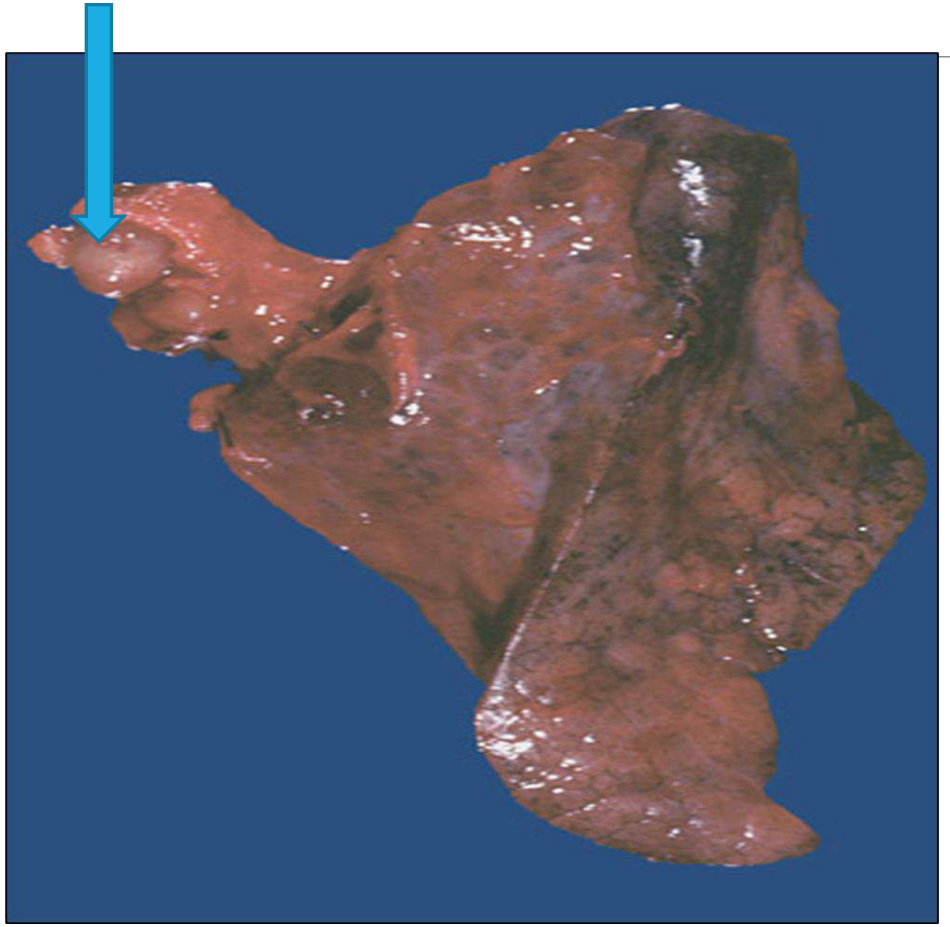
Histologically:

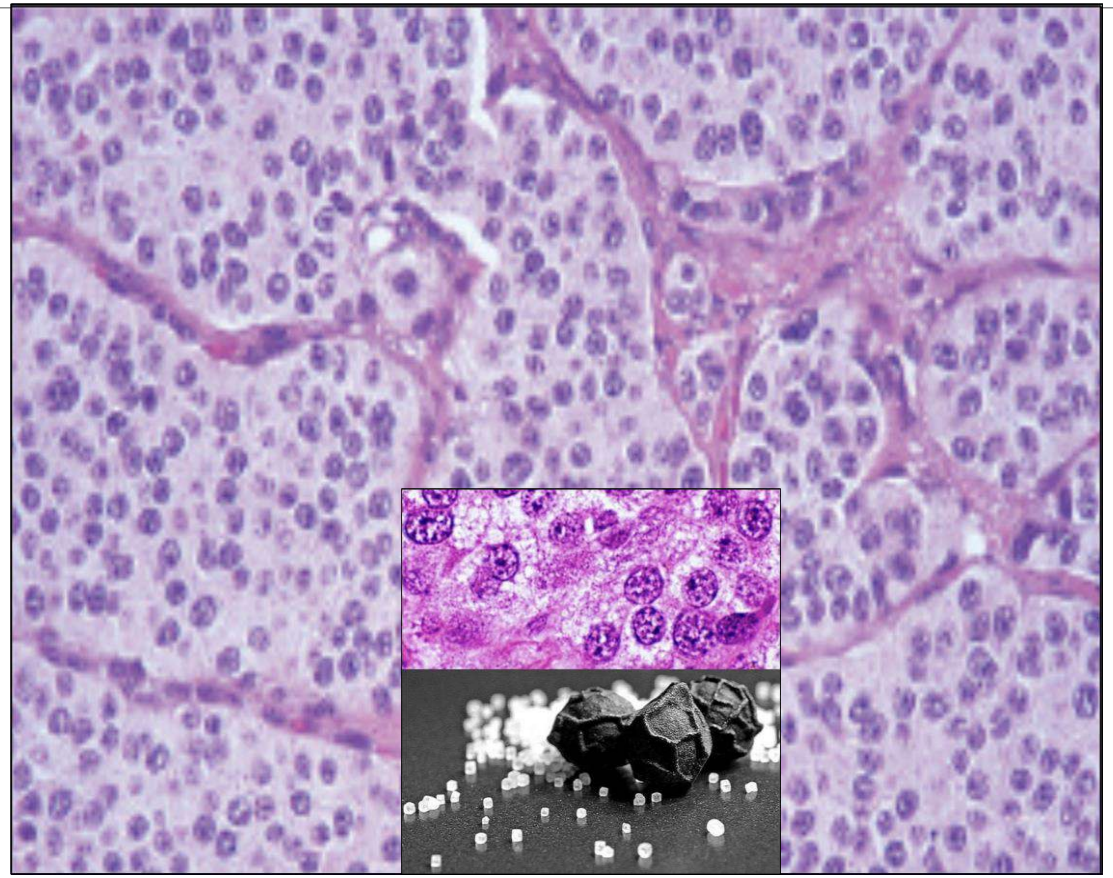
Typical carcinoid:

- Composed of nests or trabeculae of uniform cells with regular round nuclei with **“salt-and-pepper”** chromatin, absent or rare mitoses, and little pleomorphism.

<2 mitoses/2 mm^2 and NO necrosis

Bronchial carcinoid grows as a spherical, pale mass (arrow) protruding into the lumen of the bronchus. Histologic appearance demonstrating small, rounded, uniform nuclei and moderate cytoplasm.





Atypical carcinoid

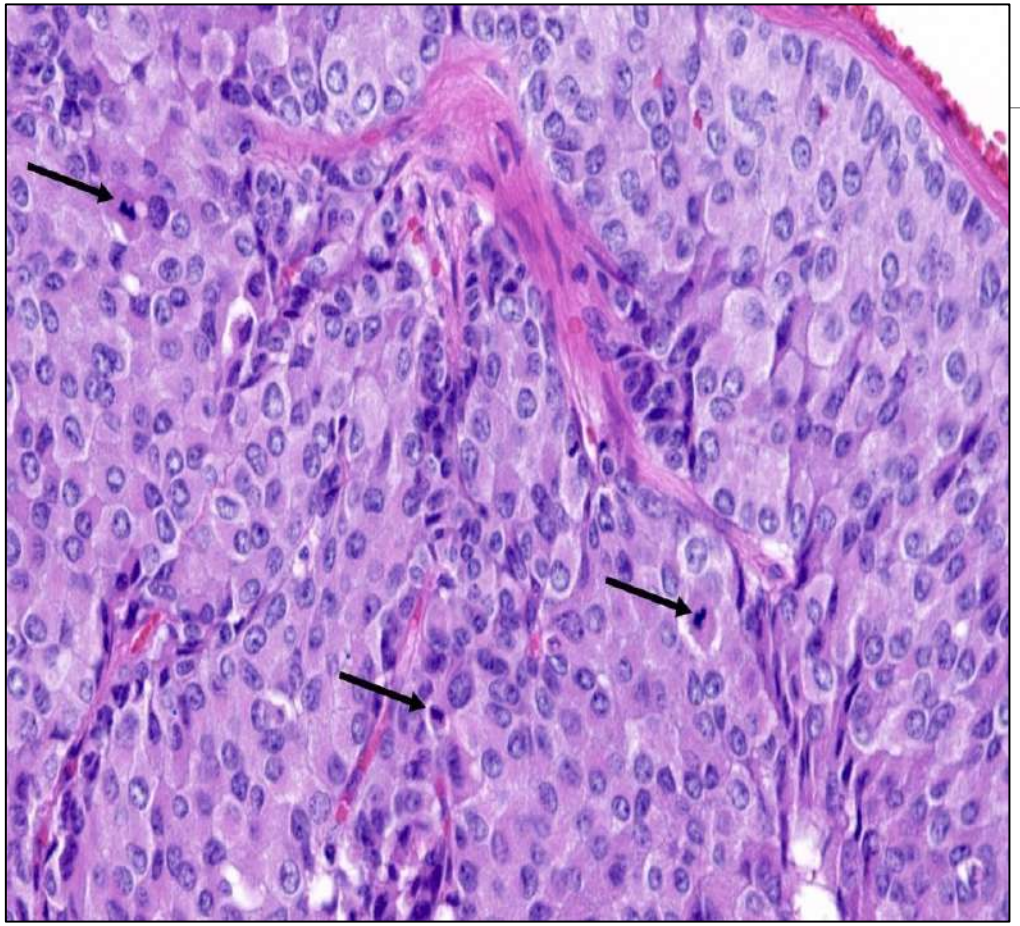
- Display a higher mitotic rate and small foci of necrosis.

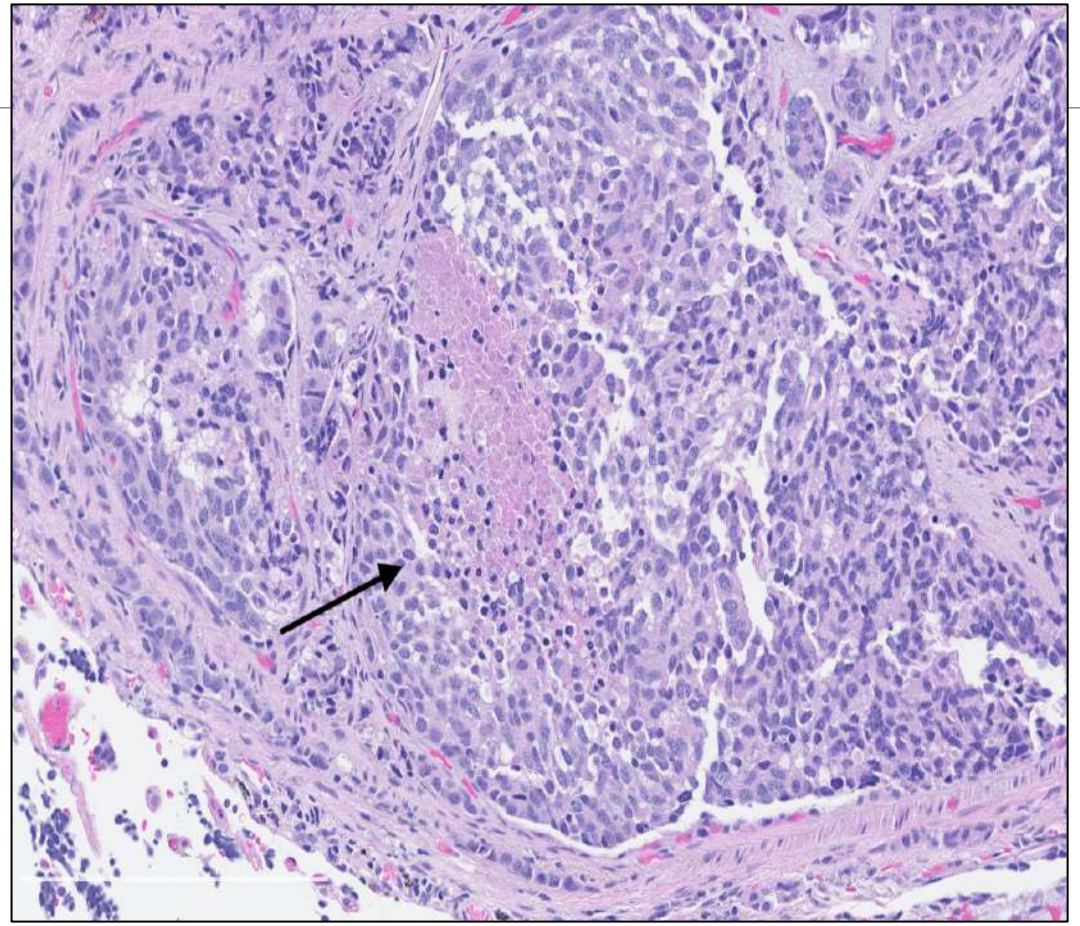
- Have a higher incidence of lymph node and distant metastasis than typical carcinoids.

2-10 mitoses/ 2mm^2 and/or foci of necrosis, usually punctate and focal

❖Unlike typical carcinoids, atypical tumors have *TP53* mutations in 20% to 40% of cases.

Atypical Carcinoid





Benign Tumors of the lung :

Pulmonary Hamartoma : (most common benign tumor)

- Usually discovered as an incidental, rounded radio-opacity (coin lesion) on a routine chest film.
- Most are solitary, peripheral, small, and well-circumscribed.
- May simulate tumor radiologically

The traditional term hamartoma is retained for this lesion, but it is in fact a **clonal neoplasm**

Histologically:

- Consists of nodules of **cartilage,**
- **cellular fibrous tissue and fat intersected by epithelial clefts**.

- The epithelial clefts are lined by ciliated columnar epithelium or non-ciliated epithelium and probably represent entrapment of respiratory epithelium

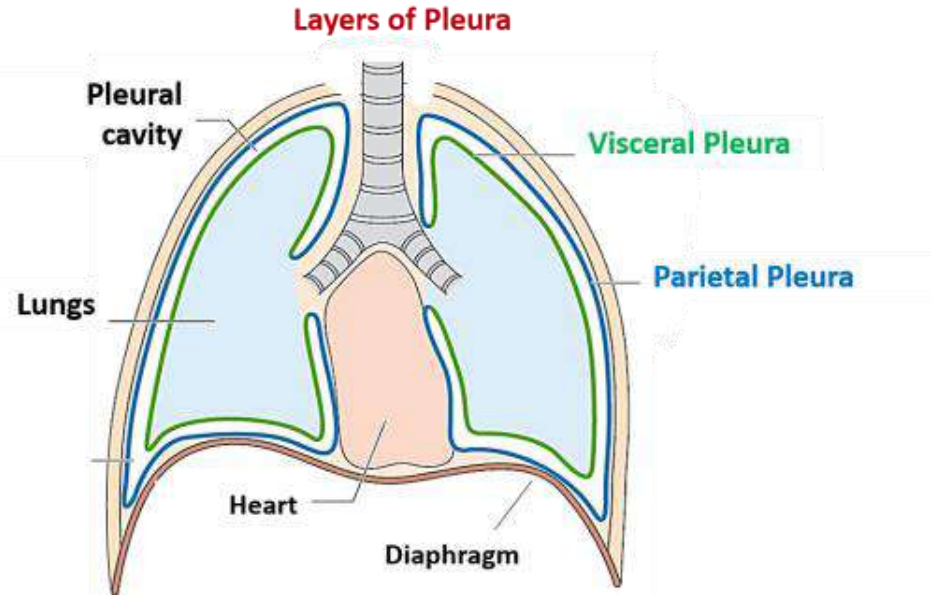
Pathology of the Pleura :

- Disease of the pleura usually is a complication of an underlying pulmonary disease.
- Secondary infections and pleural adhesions are common findings at autopsy.

<u>Important primary disorders:</u>

(1) Primary intrapleural bacterial infections

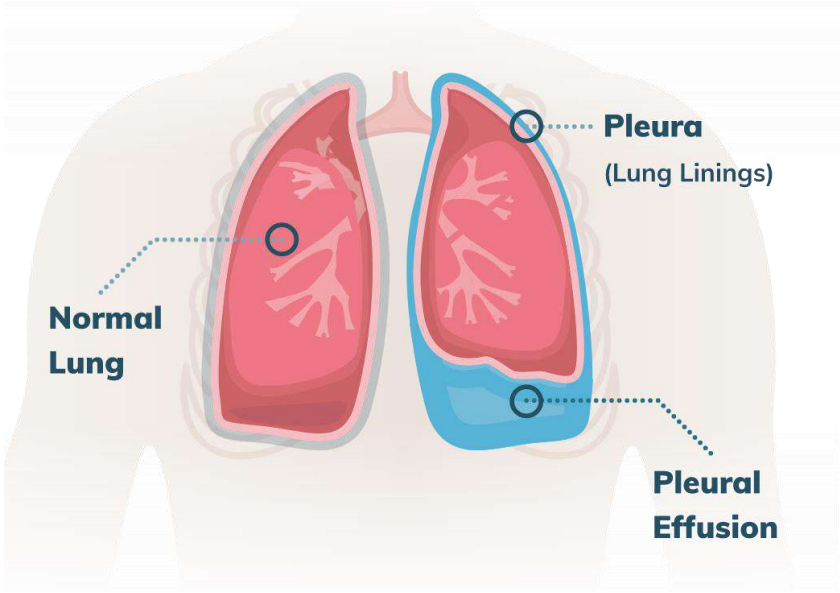
(2) Malignant mesothelioma.



❑ Pleural Effusion And Pleuritis

Pleural effusion: Accumulation of **fluids** in the pleural space

- It is a common manifestation of both primary and secondary pleural diseases and may be **inflammatory or noninflammatory.**



- ❑ Hydrothorax: When the effusion is a transudate, e.g. Congestive heart failure.
- ❑ Exudates: Characterized by protein content greater than 30 g/L and, often, inflammatory cells, suggests pleuritis, e.g. infection, cancer or systemic diseases
- ❑ Hemorrhagic (bloody): Malignant effusions, TB, infarcts

❑ Pneumothorax, Hemothorax, And Chylothorax

Pneumothorax: Presence of air or other gas in the pleural sac.

- Simple or spontaneous pneumothorax: It may occur in young, apparently healthy adults, usually men without any known pulmonary disease.
- Secondary pneumothorax: as a result of some thoracic or lung disorder

Hemothorax:

- Collection of whole blood (in contrast with bloody effusion) in the pleural cavity.

✓ A complication of a ruptured intrathoracic aortic aneurysm

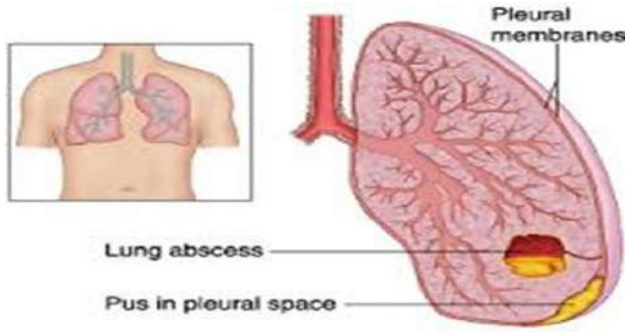
✓Vascular trauma.

Chylothorax

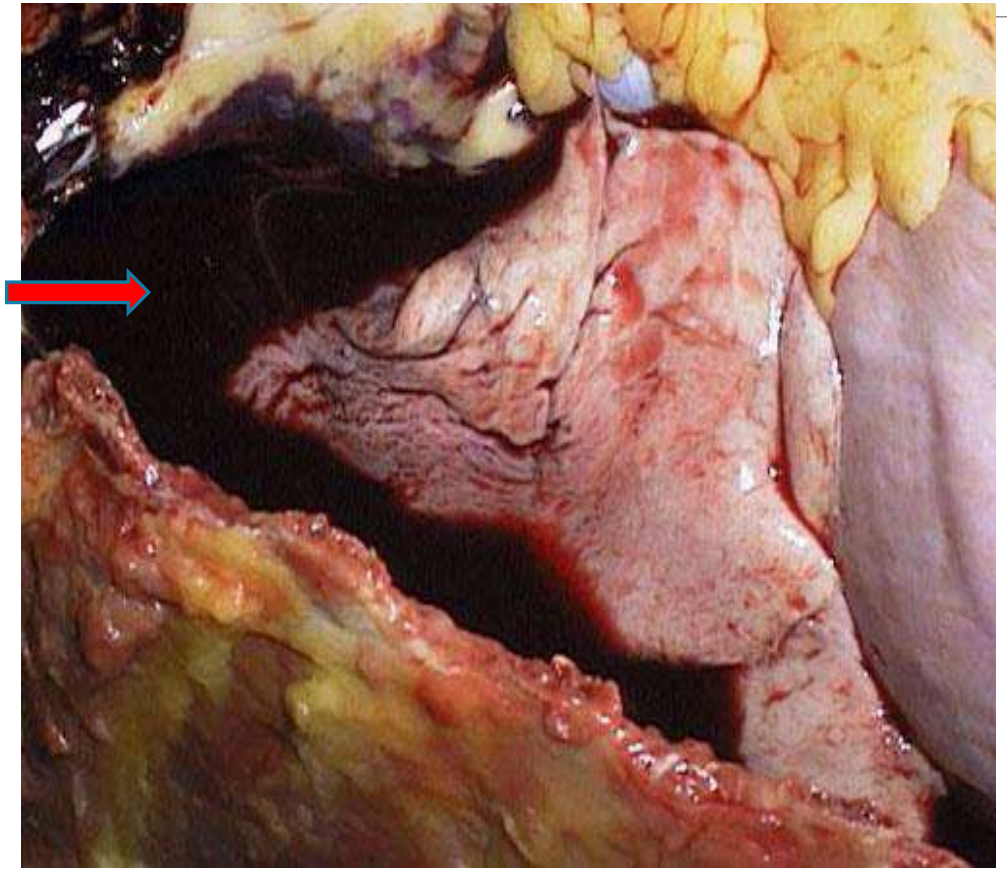
- A pleural collection of a milky lymphatic fluid containing microglobules of lipid.

Pyothorax/Empyema :

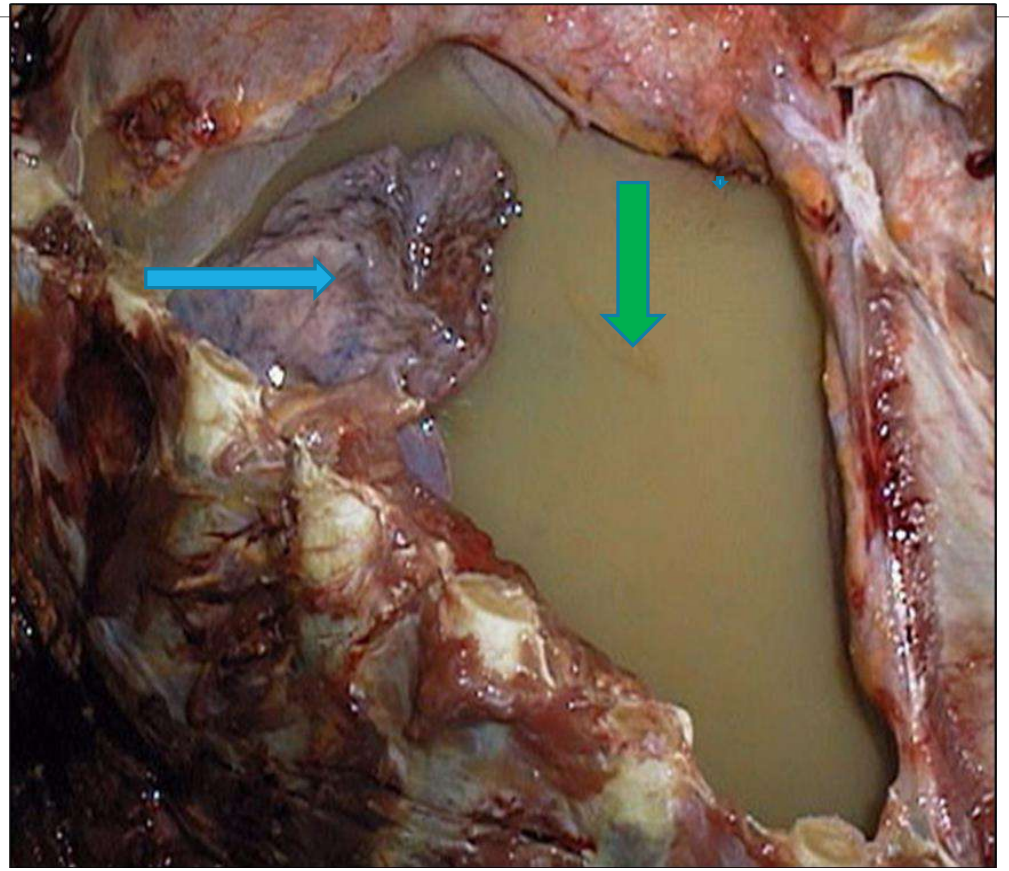
- Pus in the pleural cavity



The lung is atelectatic and floating in bloody fluid filling the chest cavity because of trauma. This is a hemothorax.



The pleural cavity is filled with a cloudy milky yellowish-tan fluid, characteristic for a chylothorax. The lung is markedly atelectatic.



❖ Pleural Tumors

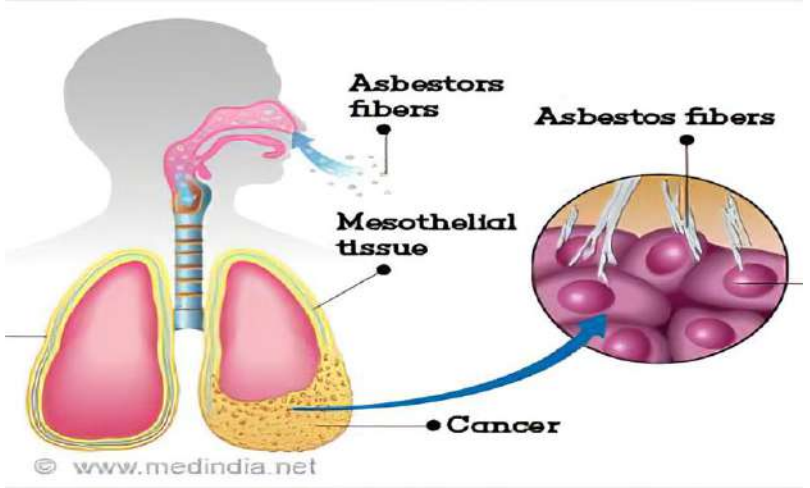
-The pleura may be involved by primary or secondary tumors.

-Secondary **metastatic involvement is far more common** than primary tumors.

-The most frequent metastatic malignancies arise from primary neoplasms of the lung and breast.

Malignant Mesothelioma

- ❖ A **rare cancer** of mesothelial cells.
- ❖ Usually arises in the **parietal or visceral** pleura
- ❖ Approximately 80% to 90% of individuals have a history of exposure to Asbestos.



- Those who work directly with asbestos (shipyard workers, insulators) are at the greatest risk.

- The latent period for developing malignant mesothelioma after the initial exposure is 25 to 40 years long.

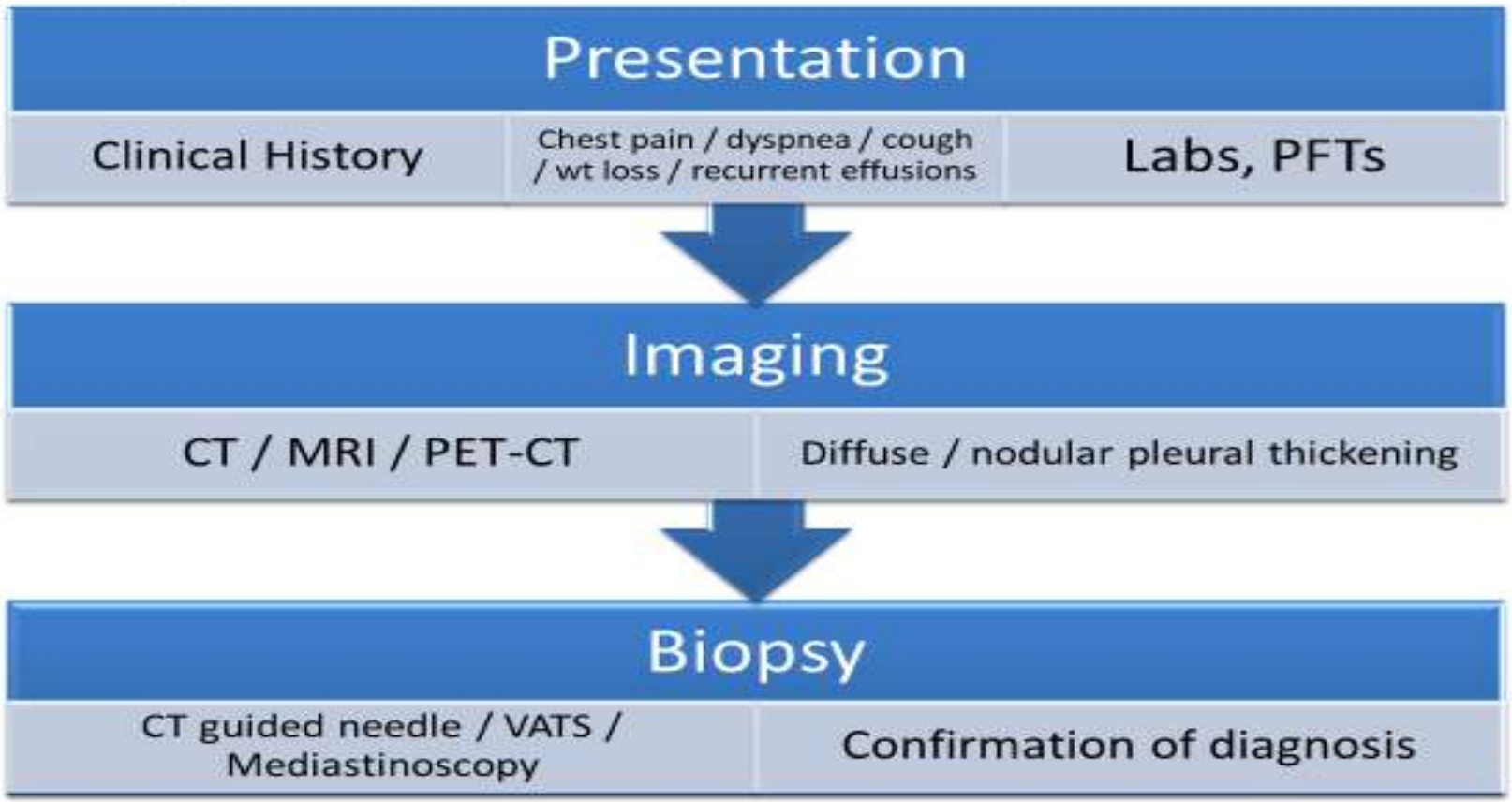
- Once inhaled, asbestos fibers remain in the body for life. Thus, the lifetime risk after exposure does not diminish over time

- The combination of cigarette smoking and asbestos exposure greatly increases the risk of developing lung carcinoma but not developing malignant mesothelioma.

Sequencing of mesothelioma genomes has revealed multiple driver mutations.

- The commonest genetic change in malignant mesothelioma is the homozygous deletion of P16.
- The most frequently mutated genes are BAP1 (**lost on IHC**), NF2 and TP53.

Typical presentation & work up



Morphology:

- Begin in a localized area and, over time, spread widely. At autopsy, the affected lung typically is ensheathed by a layer of yellow-white, firm tumor that obliterates the pleural space

Histologically:

- Three morphologic appearances:

(1) **Epithelioid:** cuboidal cells with small papillary buds, line tubular and microcystic spaces

(2) **Sarcomatoid:** spindled grow in sheets

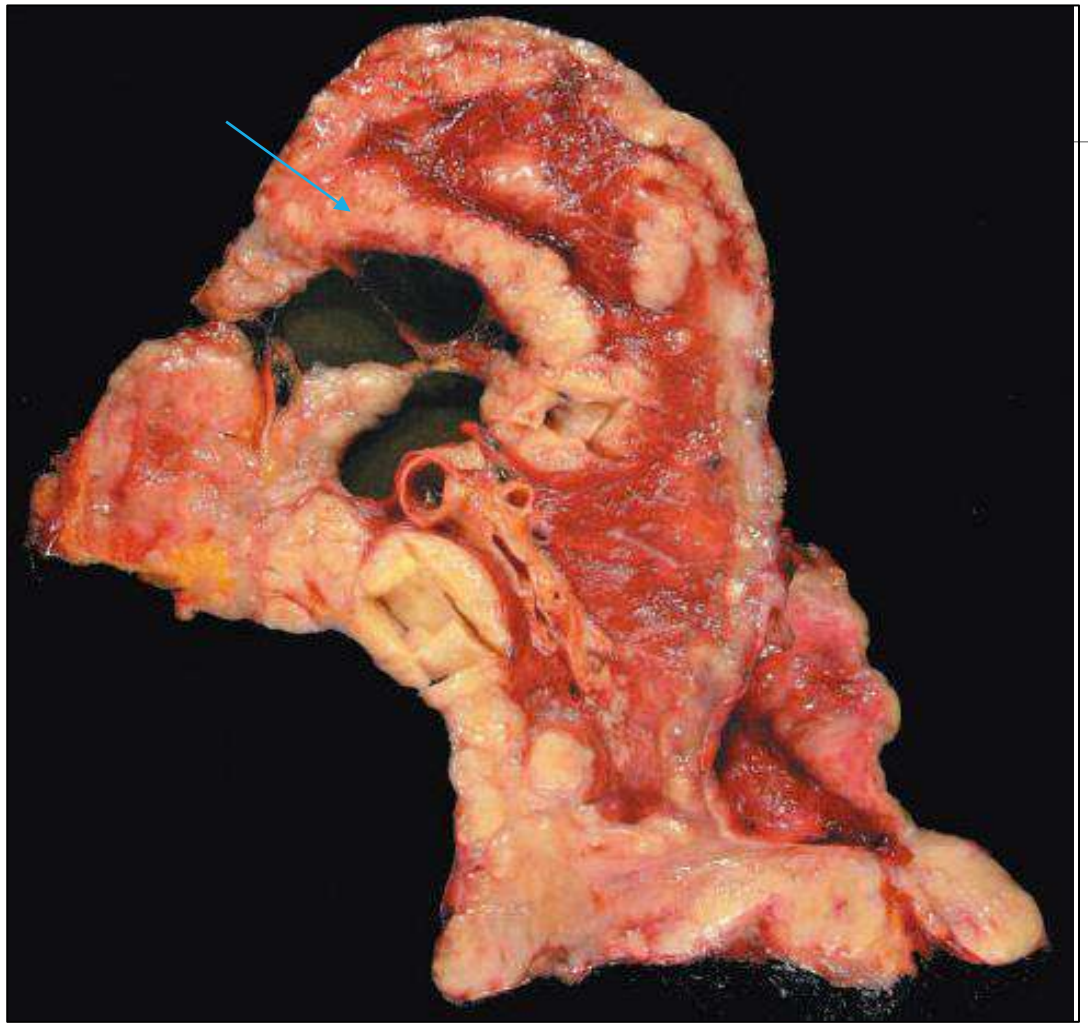
(3) **Biphasic:** both sarcomatous and epithelial areas.

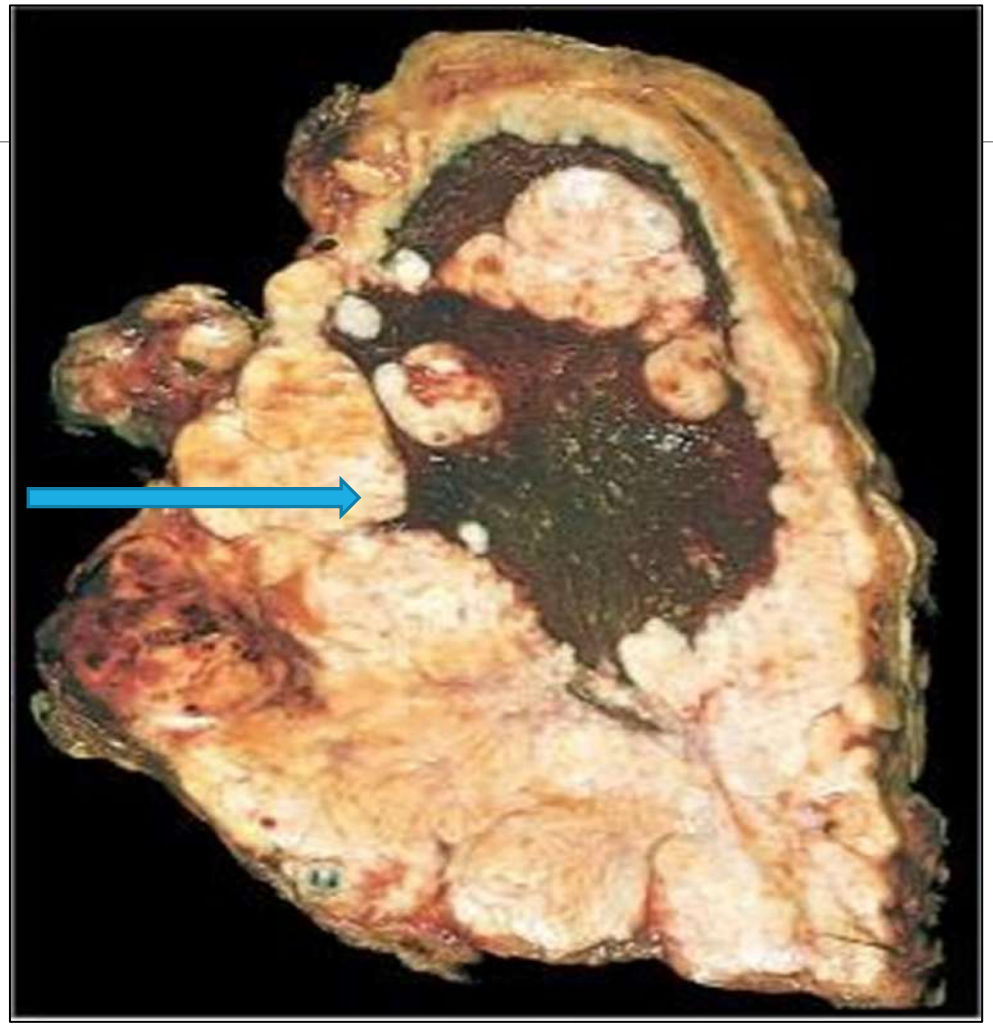
Confirmation of Diagnosis:

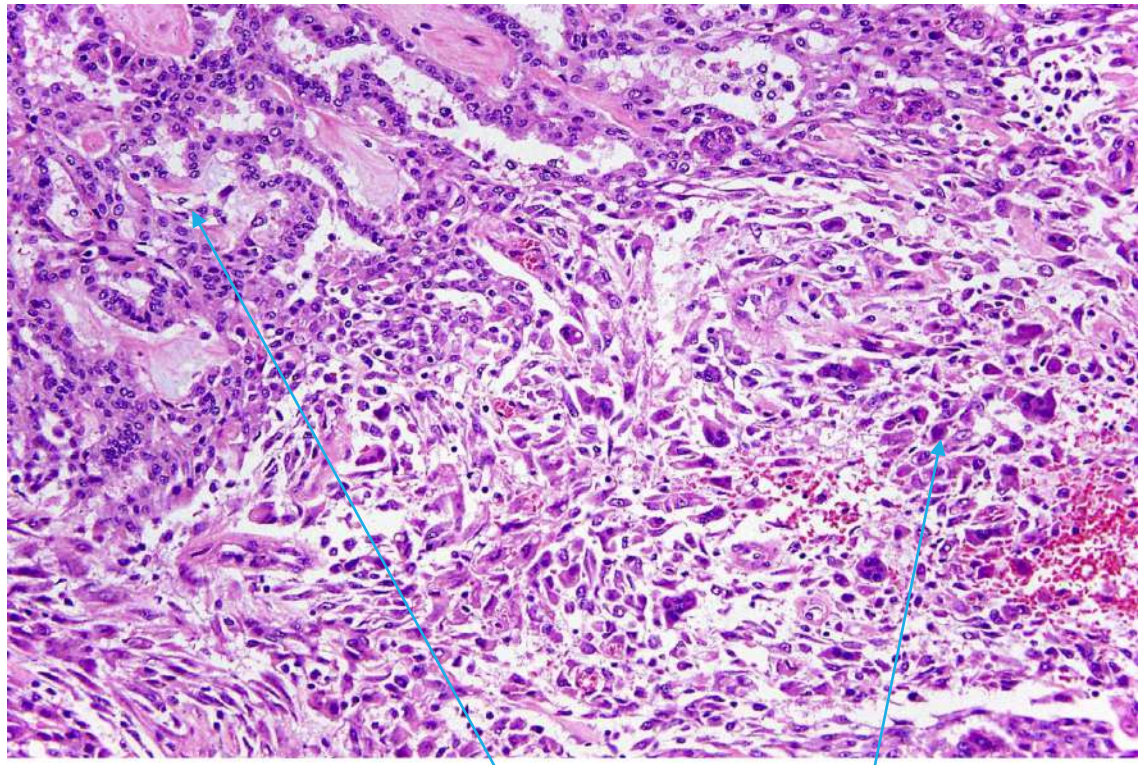
Mesothelioma markers (positive):

Calretinin, WT-1, D2-40

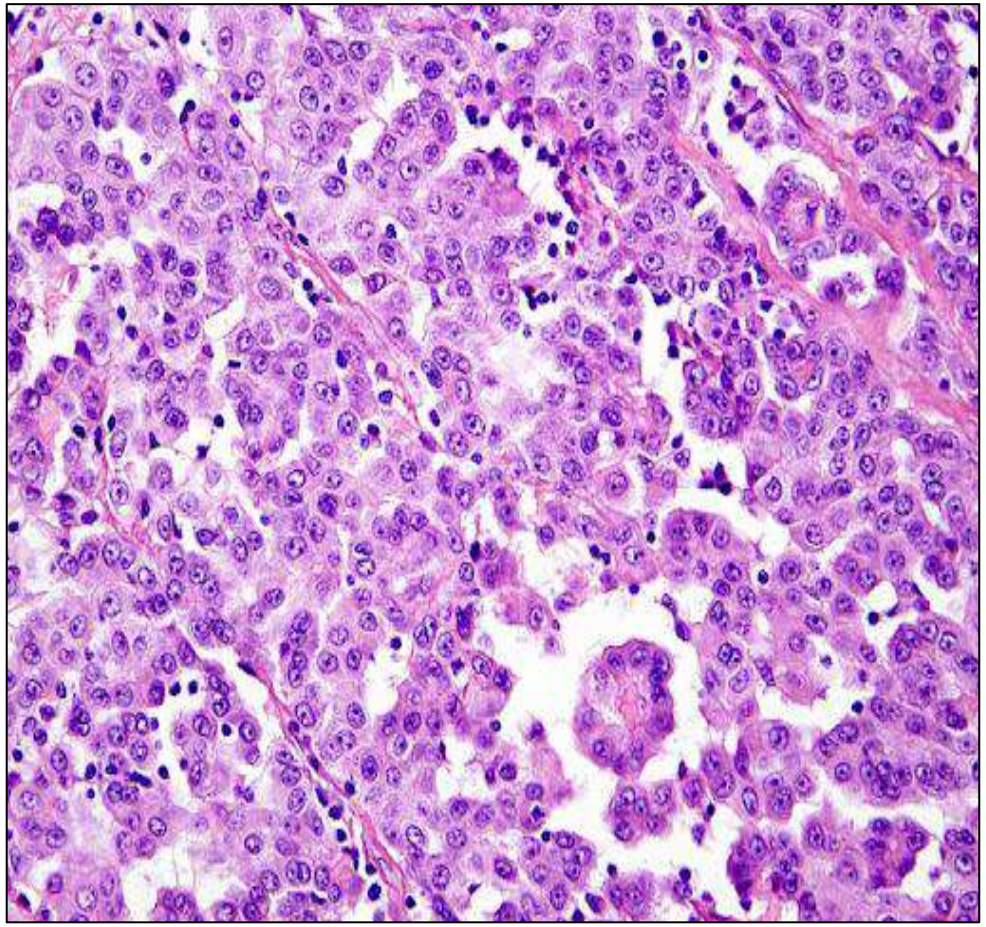
A thick, firm, white pleural tumor that is ensheathing this bisected lung.



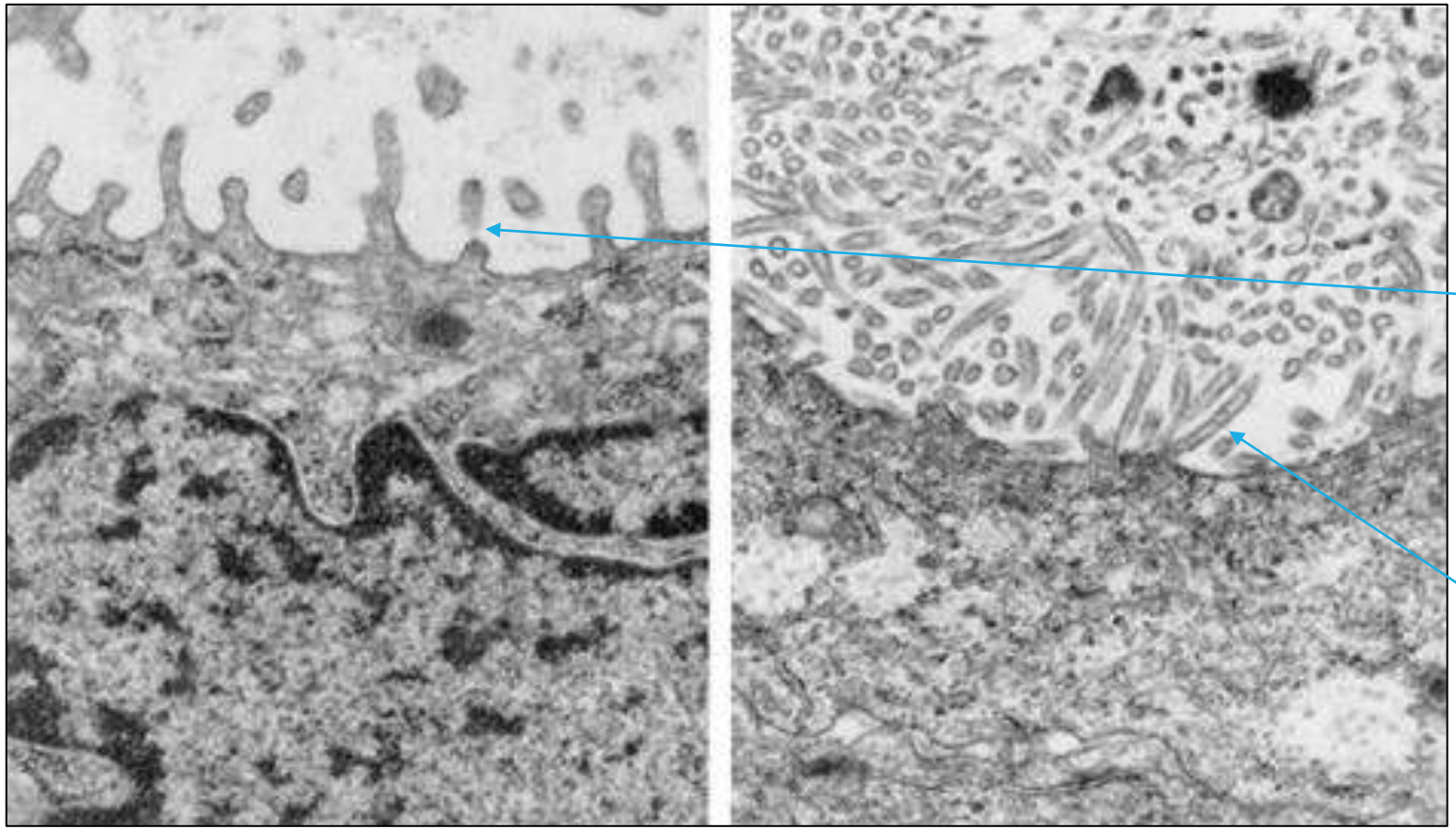




Biphasic mesothelioma is characterized by the presence of both epithelioid component (upper left; tubulopapillary pattern) and sarcomatoid component (lower right) (H&E 200×).



❖ On electron microscopy, MM characterized by the presence of long microvilli.



Ultrastructural features of pulmonary adenocarcinoma: Characterized by short, plump microvilli, contrasted with those of **mesothelioma**: in which microvilli are **numerous, long, and slender.**

Prognosis

- Has poor prognosis
- The lung is invaded directly, and there is often metastatic spread to the hilar lymph nodes and, eventually, to the liver and other distant organs.
- 50% of patients die within 12 months of diagnosis

- Concurrent pulmonary asbestosis (fibrosis) is present in only 20% of individuals with pleural mesothelioma.

Thank you

Good Luck