LUNG TUMORS

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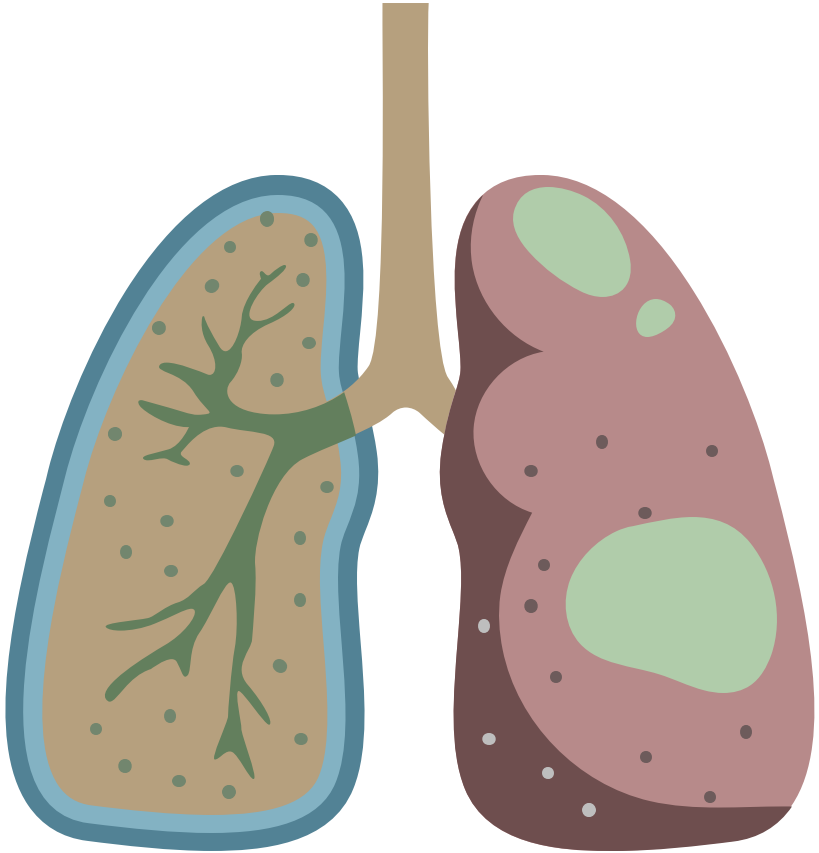
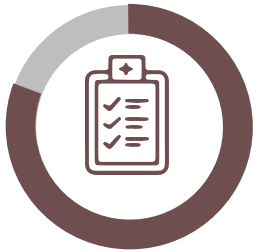
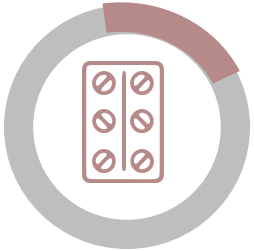


Lung Tumors



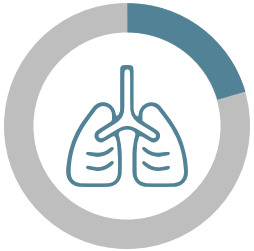
95%

95% of primary lung tumors are carcinomas



5%

Is a miscellaneous group, includes carcinoids, mesenchymal malignancies (e.g., fibrosarcomas, leiomyomas), lymphomas, and a few benign lesions



12.4%

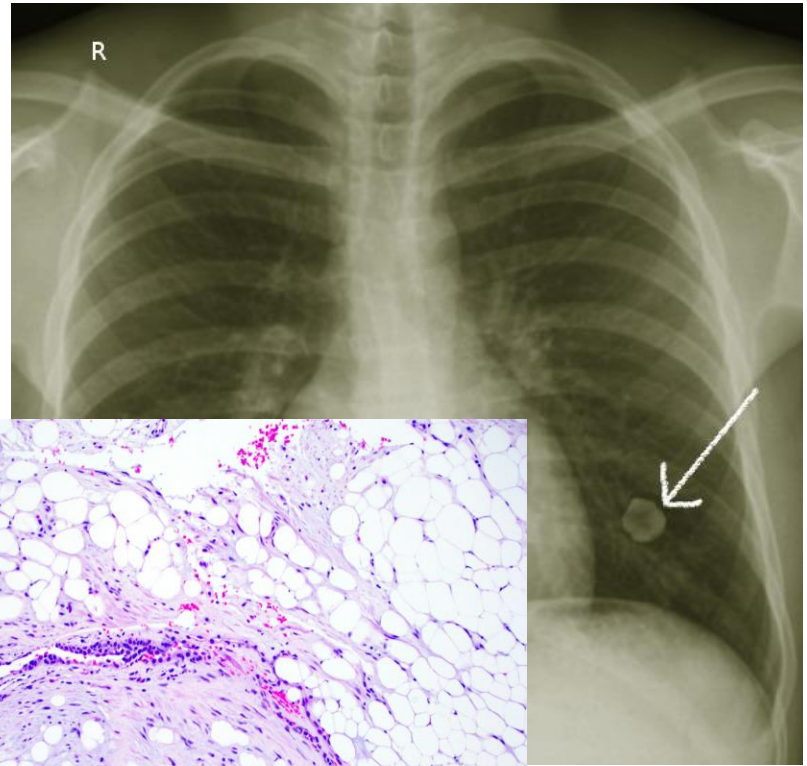
Lung cancer is the most commonly diagnosed cancer worldwide. Globocan 2022

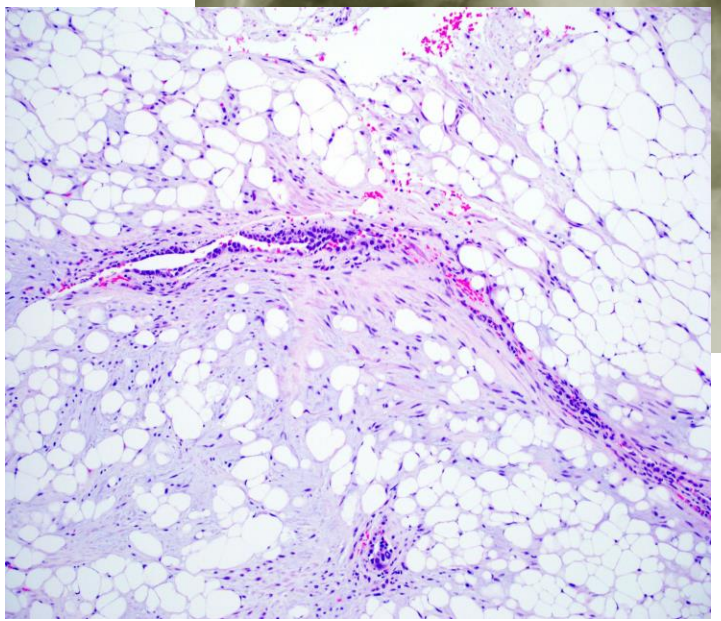
18.7 %

Lung cancer is the leading cause of cancer death worldwide. Globocan 2022

Hamartoma

- The most common benign tumor.
- A spherical, small (1-4 cm), discrete lesion often shows up as a so-called “coin lesion” on chest imaging.
- It consists mainly of mature cartilage admixed with fat, fibrous tissue, and blood vessels in various proportions.





https://www.ncbi.nlm.nih.gov/books/NBK539806/figure/article-22508.image.f1/

Carcinomas

- Peak incidence 50s and 60s.
- At diagnosis, > 50% of patients already have distant metastases.
- The prognosis remains dismal: the 5-year survival rate for all stages of lung cancer combined is about 16% (not changed much over the last 35 years)
- If disease localized to the lung, the 5-year survival rate is 45%

The four major histologic types of carcinomas of the lung are:

- Adenocarcinoma
- Squamous cell carcinoma
- Small cell carcinoma
- Large cell carcinoma

Etiology and Pathogenesis

- Like other cancers, smoking-related carcinomas of the lung arise by a stepwise accumulation of driver mutations that result in transformation of benign progenitor cells in the lung into neoplastic cells possessing all of the hallmarks of cancer.
- For instant;

✓ Early event: inactivation of the tumor suppressor genes located on the short arm of chromosome 3 (3p) is a very common. Found in benign bronchial epithelium of smokers without lung cancer.

* Represent a fertile soil→ those cells that accumulate additional mutations ultimately develop into cancer.

"**field effect**": large areas of the respiratory mucosa are mutagenized by exposure to carcinogens.

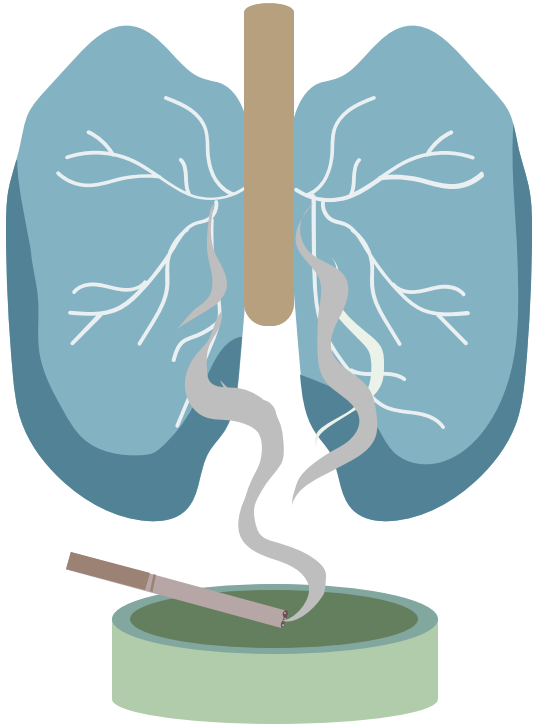
✓ Late event: mutations in the *TP53* tumor suppressor gene and the *KRAS* oncogene

Etiology and Pathogenesis

- A subset of adenocarcinomas (10% in whites & 30% in Asians), particularly those arising in nonsmoking women, harbor mutations that activate the *epidermal growth factor receptor (EGFR).*
- *EGFR:* a receptor tyrosine kinase that stimulates downstream pro-growth pathways involving RAS, PI3K, and other signaling molecules.
- These tumors are sensitive to drugs that inhibit EGFR signaling, often short-lived ☹
- EGFR and KRAS mutations (in 30% of adenocarcinomas) are mutually exclusive → KRAS lies downstream of EGFR.
- Other "targetable" mutations have been described in a low frequency of adenocarcinomas (4- 6%), including mutations that activate other tyrosine kinases, (ALK, ROS1, HER2, or c-MET.)
- Each one is optimally targeted by a different drug → spurred a new era of "personalized" lung cancer treatment; the genetics of the tumor guide therapy

Etiology and Pathogenesis

- **Cigarette smoking** and, to a much lesser extent, other environmental carcinogens are the main **culprits responsible for the mutations that give rise to lung cancers.**
- About 90% of lung cancers occur in active smokers or those who stopped recently.
- Passive smoking (proximity to cigarette smokers) also increases the risk for developing lung cancer, as does smoking of pipes and cigars. (less than cigarettes)



Etiology and Pathogenesis

- Occupational exposures act with smoking and may be responsible for lung cancer all by themselves:

work in uranium mines, with asbestos, and inhalation of dusts containing arsenic, chromium, nickel, or vinyl chloride.

- A synergistic interaction between two carcinogens: asbestos and tobacco smoking;

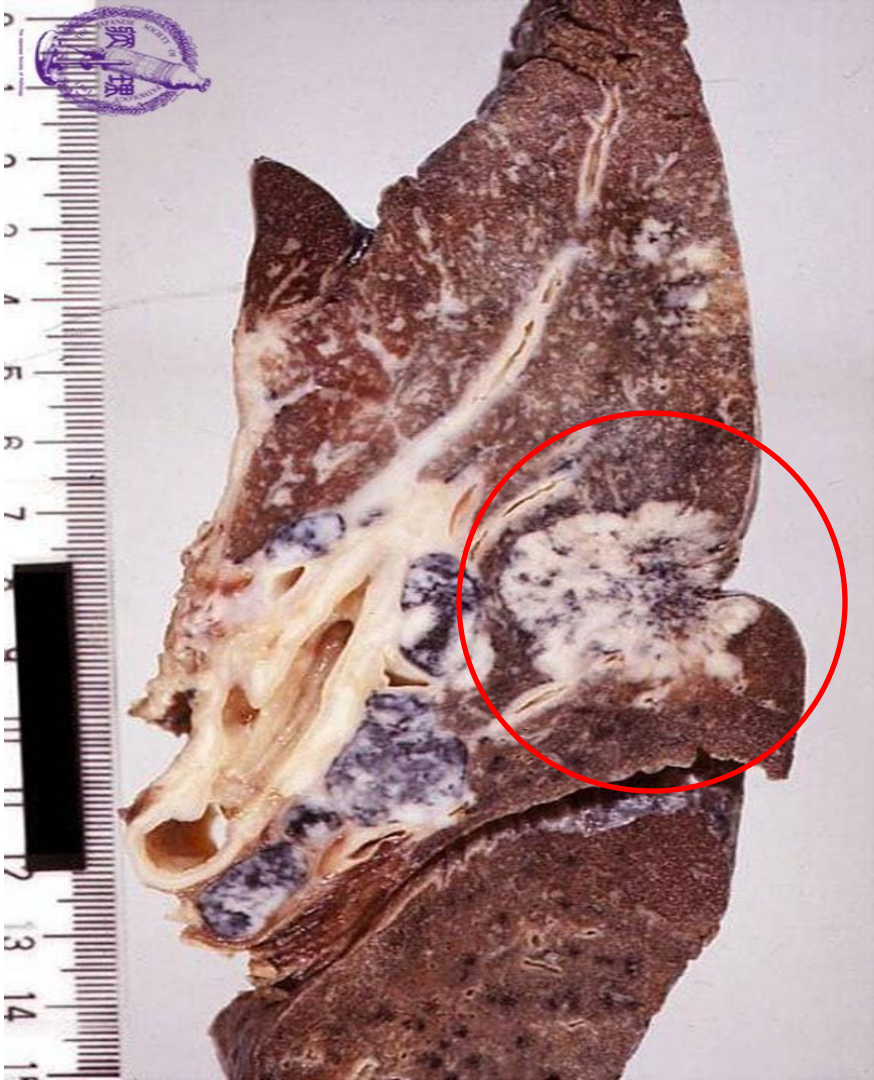
✓ Exposure to asbestos in nonsmokers increases risk for lung cancer 5-fold.

✓ Heavy smokers exposed to asbestos risk is elevated approximately 55-fold.

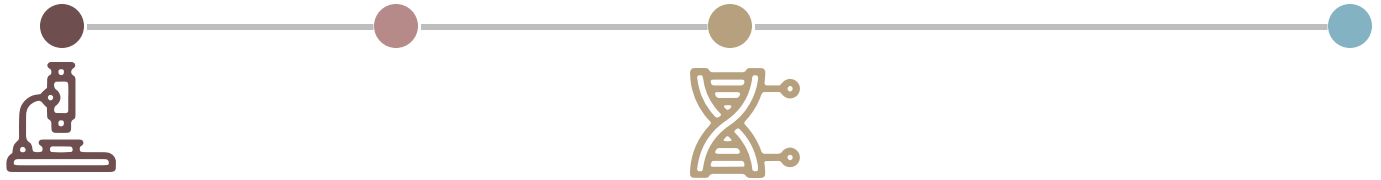
- Not all individuals exposed to tobacco smoke develop cancer (~ 11% of heavy smokers) → mutagenic effect of carcinogens is modified by hereditary (genetic) factors.

Morphology - Adenocarcinomas

- usually **peripherally located,** but also may occur closer to the hilum.
- In general, it grow slowly and form smaller masses than do the other subtypes, but they tend to metastasize widely



Adenocarcinoma and precursors:



Atypical adenomatous hyperplasia (AAH)

5mm or less atypical cells

Adenocarcinoma in situ

3cm or less preservation of alveolar architecture

Minimally invasive adenocarcinoma

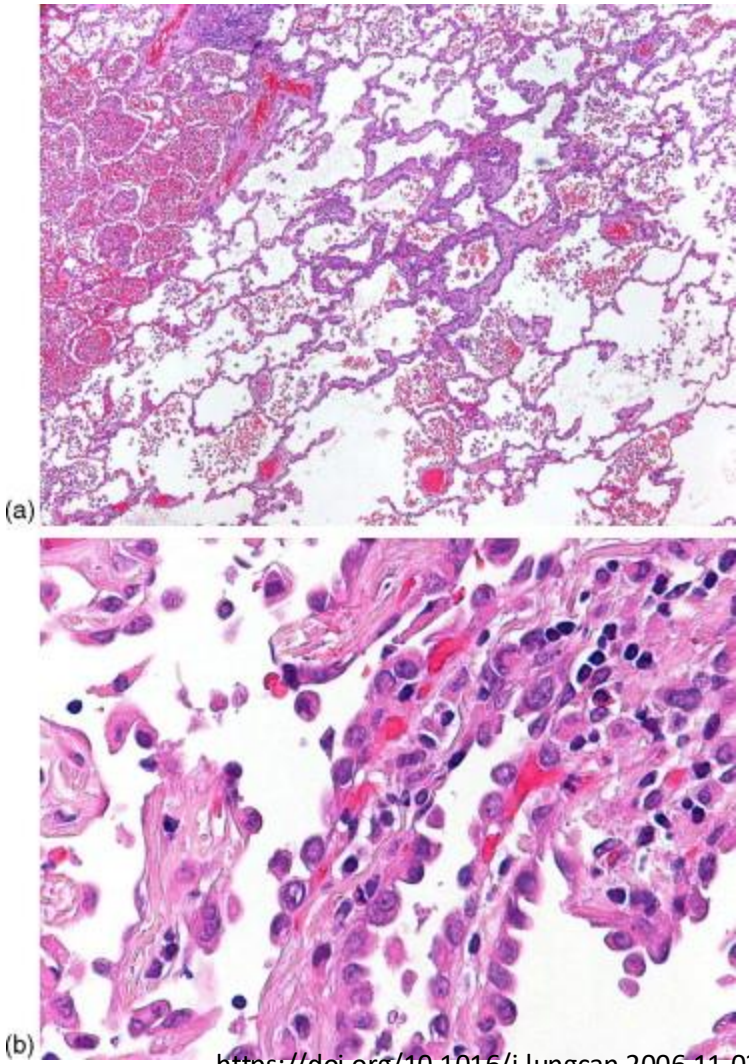
<3 cm in diameter with an invasive component of <5 mm

Invasive adenocarcinoma

A tumor of any size with an area of invasion >5 mm

Atypical adenomatous hyperplasia (AAH)

- The putative precursor of adenocarcinoma that progress in a stepwise fashion.
- A well-demarcated focus of epithelial proliferation (diameter: <= 5 mm) composed of cuboidal to low-columnar cells that demonstrate nuclear hyperchromasia, pleomorphism, and prominent nucleoli.
- Genetic: AAH is monoclonal and shares many molecular aberrations with adenocarcinomas (e.g., *KRAS* mutations).



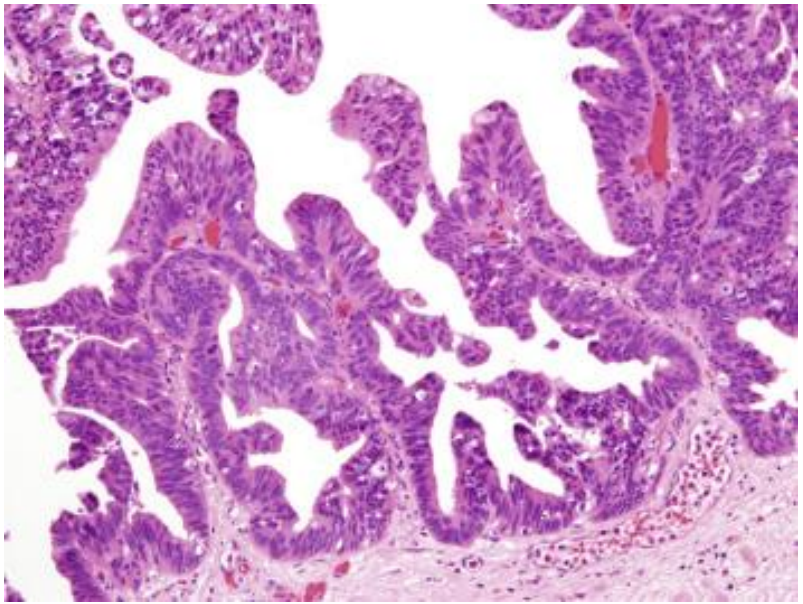
https://doi.org/10.1016/j.lungcan.2006.11.022

Adenocarcinoma in situ (AIS)

- Involves peripheral parts of the lung as a single nodule
- diameter of 3 cm or less, growth along preexisting structures, and preservation of alveolar architecture
- The tumor cells, which

may be nonmucinous, mucinous, or mixed, grow in a monolayer along the alveolar septa.

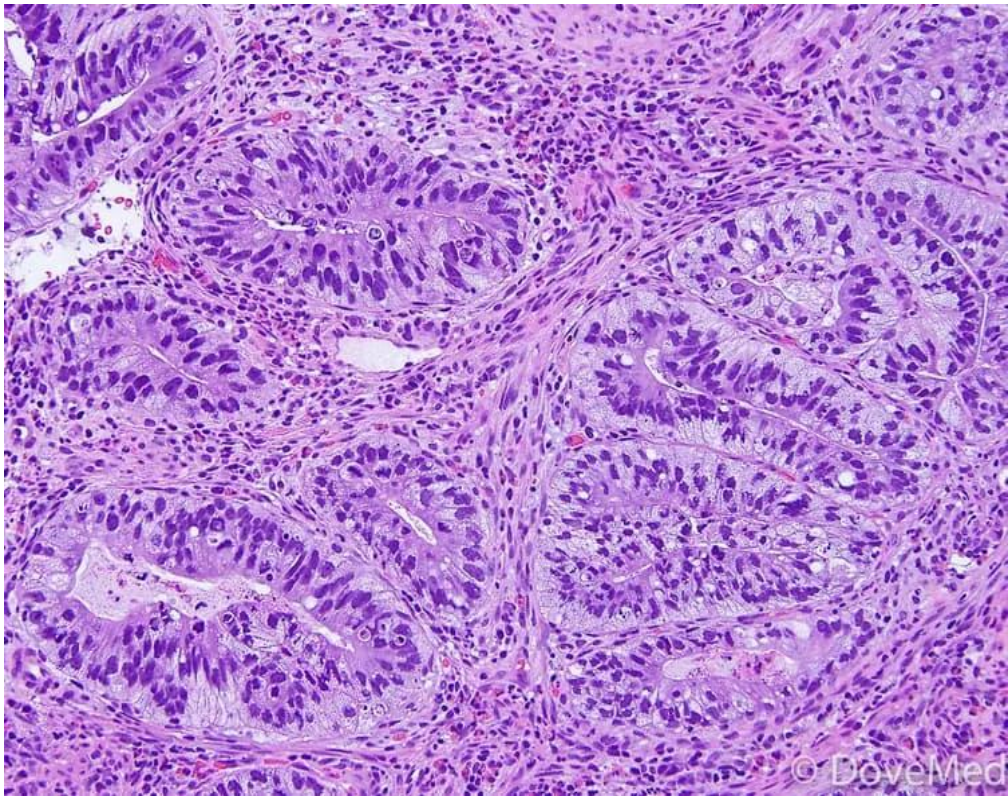
- By definition, no destruction of alveolar architecture or stromal invasion with desmoplasia.



https://doi.org/10.1016/S0272-2712(03)00057-X

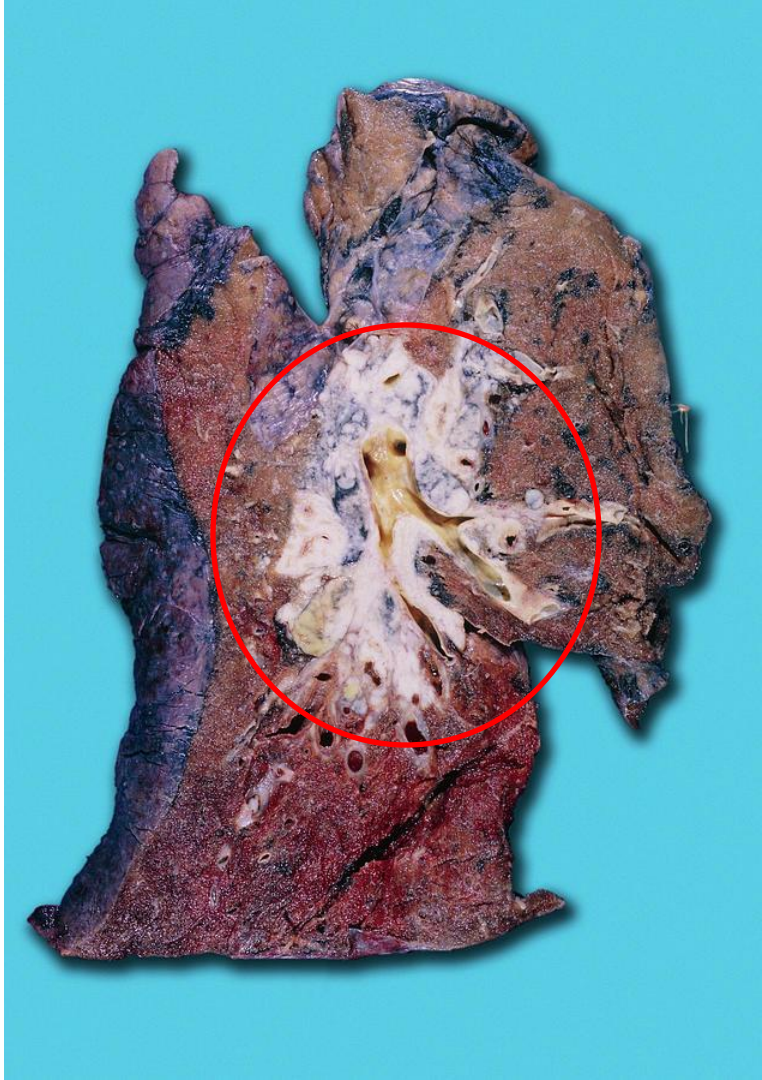
Invasive adenocarcinoma

- A tumor of any size with an area of invasion >5 mm.
- Destruction of alveolar architecture
- or Stromal invasion with desmoplasia



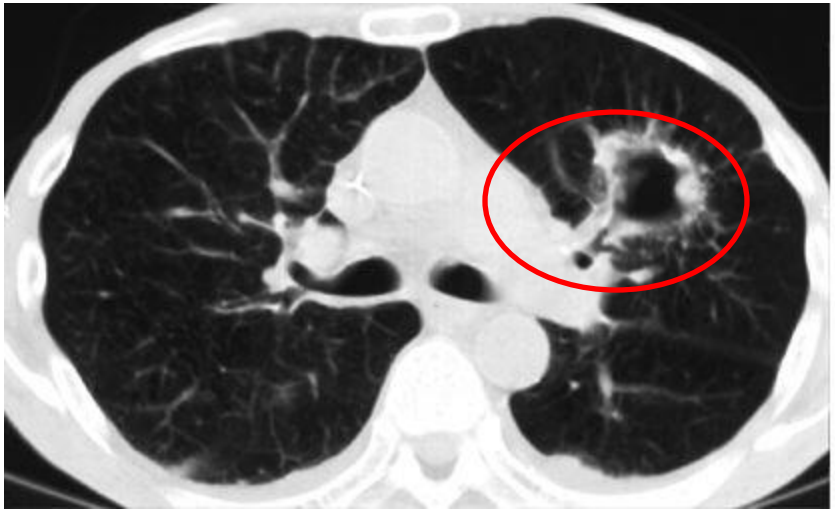
Morphology - Squamous cell carcinomas

- tend to **arise centrally in major bronchi** and eventually
- spread to local hilar nodes, but they disseminate outside the thorax later than do other histologic types.



Morphology - Squamous cell carcinomas

- Large lesions may undergo central necrosis, giving rise to **cavitation**



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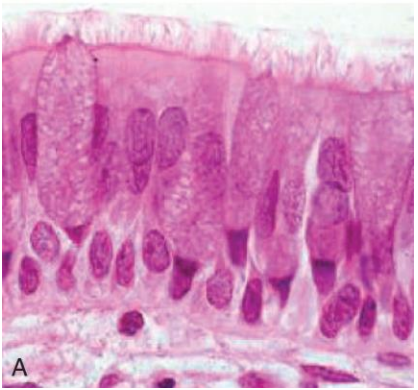
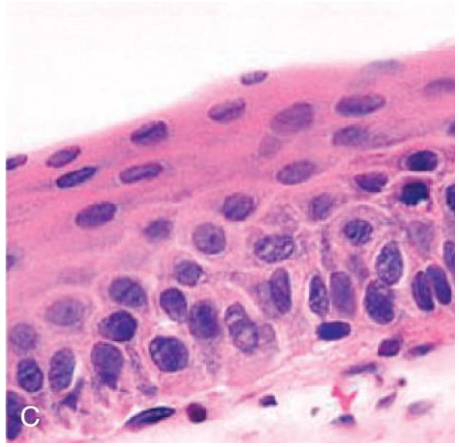
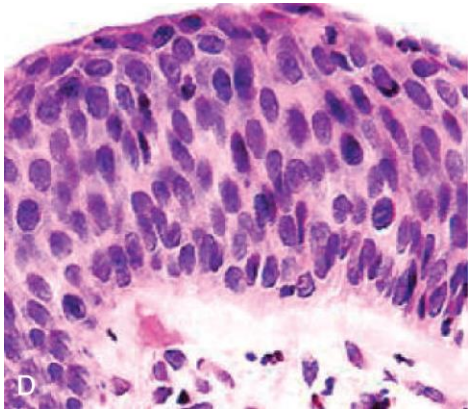
Adenocarcinoma and precursors:



Reactive respiratory epithelium

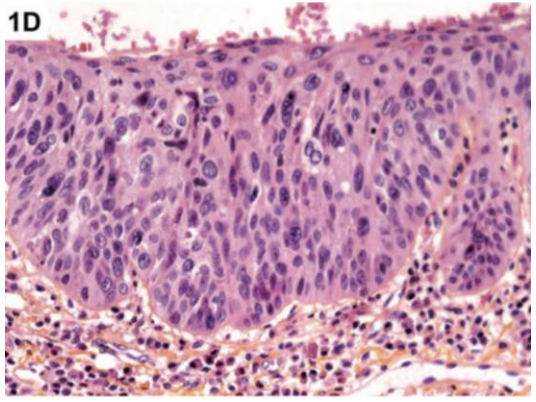
Squamous metaplasia





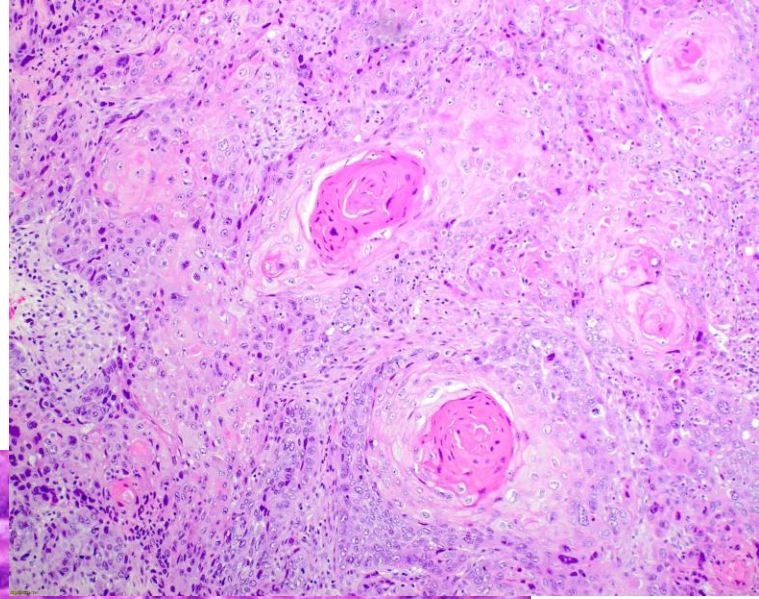
Squamous dysplasia

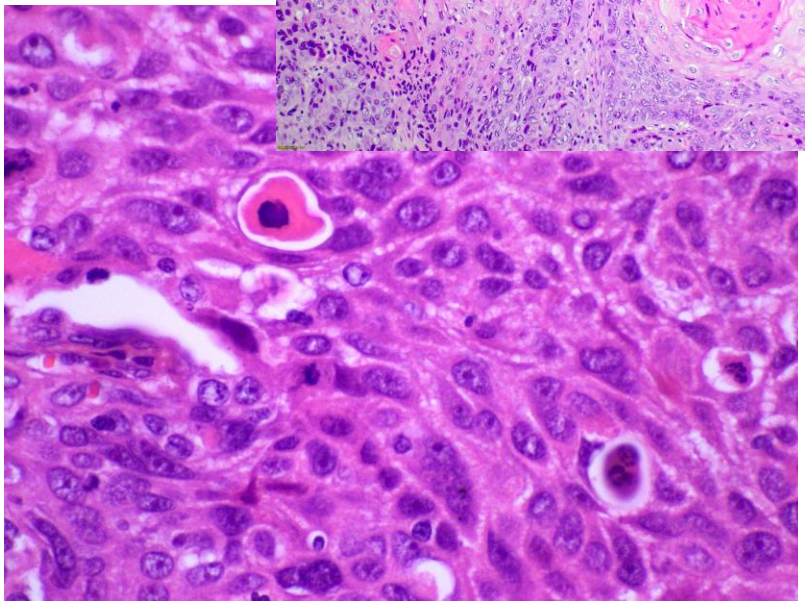
Carcinoma in situ



Morphology - Squamous cell carcinomas

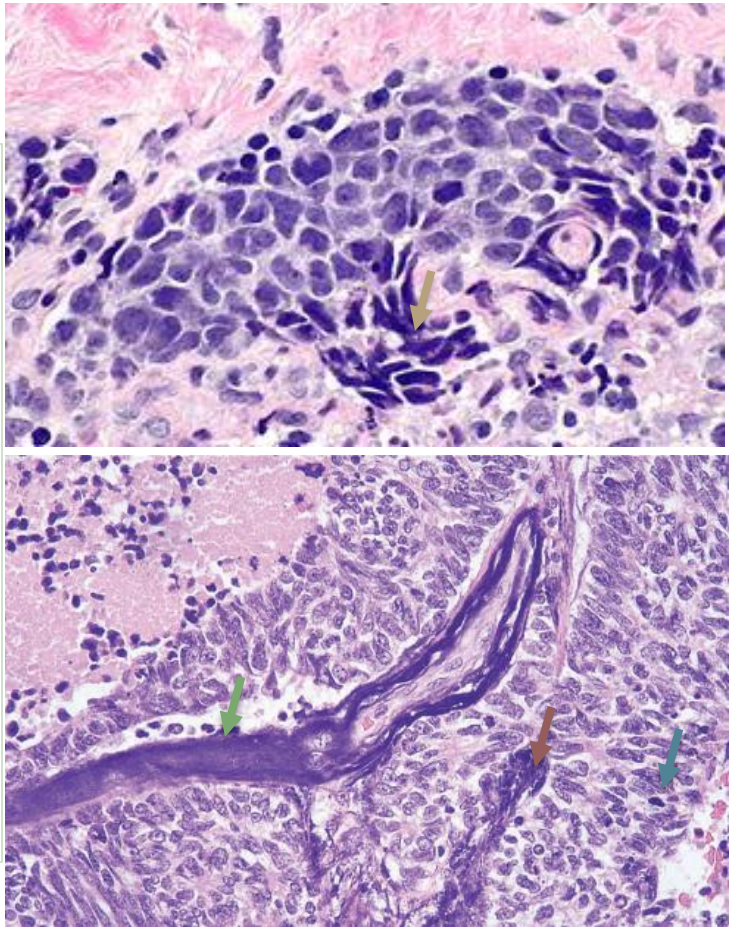
- tumors range from well differentiated SCC with keratin pearls & intercellular bridges to poorly differentiated neoplasms exhibiting only minimal squamous cell features.
- when a well-defined tumor mass begins to obstruct the lumen of a major bronchus, often producing distal atelectasis and infection.





Morphology - Small cell lung carcinomas (SCLCs)

- A pale gray, **centrally located masses** that extend to lung parenchyma.
- Small tumor cells with a round shape, scant cytoplasm, and finely granular chromatin with a salt and pepper appearance. Numerous **mitotic** figures.
- Necrosis is invariably present
- The tumor cells are fragile and often show fragmentation and "**crush artifact**"
- **Nuclear molding** resulting from close apposition of tumor cells that have scant cytoplasm
- Basophilic staining of vascular walls due to encrustation by DNA from necrotic tumor cells **(Azzopardi effect).**

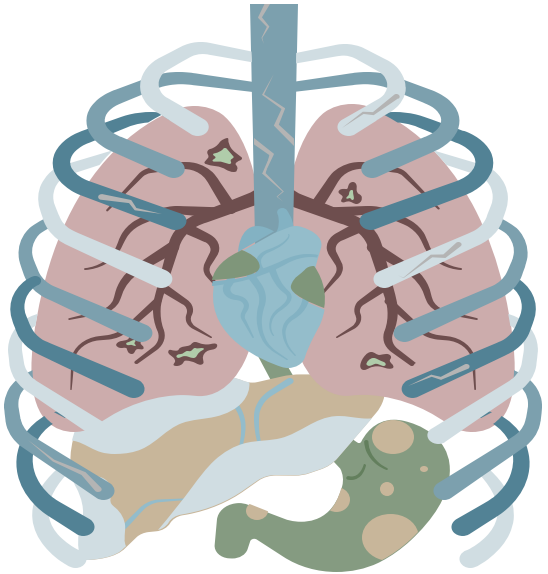


Morphology - Large cell carcinomas

- Undifferentiated malignant epithelial tumors that lack the cytologic features of neuroendocrine carcinoma and show no evidence of glandular or squamous differentiation.
- The cells typically have large nuclei, prominent nucleoli,
  and moderate amounts of cytoplasm.

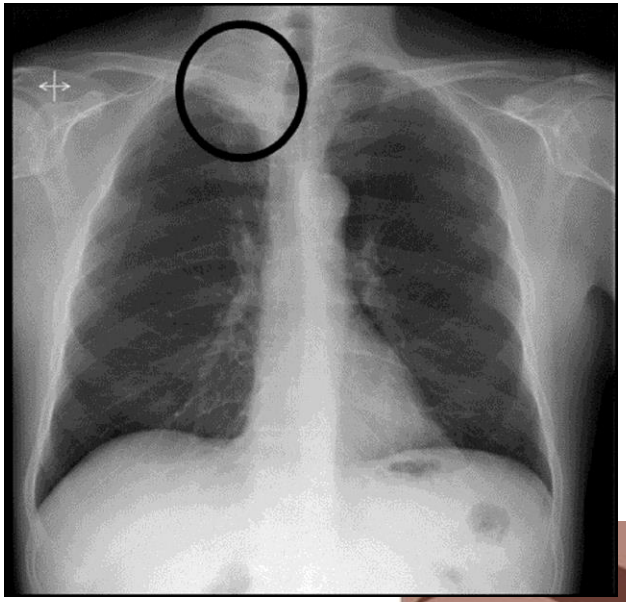
Tumor spread

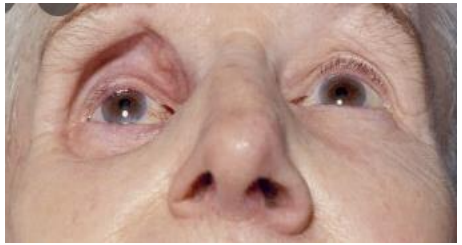
- All lung cancer subtypes tends to spread to lymph nodes; (carina, mediastinum, the neck (scalene nodes) and clavicular regions, and, sooner or later, to distant sites.
- Involvement of the left supraclavicular node (Virchow node).
- extend into pleural or pericardial space (inflammation & effusions).
- They may compress or infiltrate the superior vena cava to cause venous congestion or the vena caval syndrome.

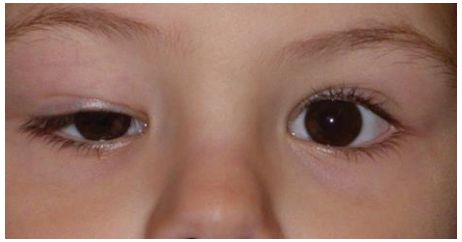


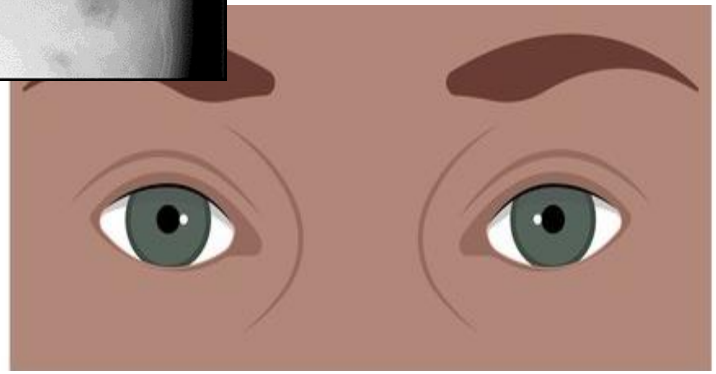
Pancoast tumors

- Apical neoplasms may invade the brachial or cervical sympathetic plexus, causing severe pain in the distribution of the ulnar nerve or Horner syndrome (ipsilateral enophthalmos, ptosis, miosis, and anhidrosis).
- The combination of clinical findings is known as **Pancoast syndrome.**
- Pancoast tumor is often accompanied by destruction of the first and second ribs and sometimes the thoracic vertebra



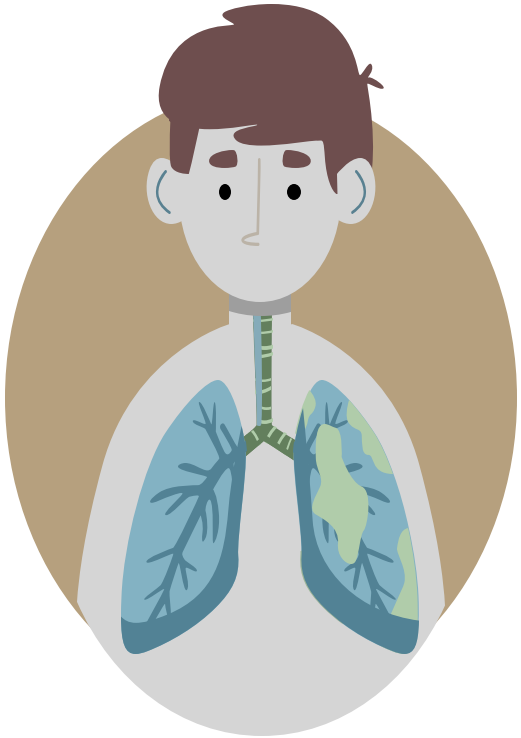






Clinical - presentation

- Carcinomas of the lung are insidious lesions; in many cases have spread to be unresectable before they produce symptoms.
- In some instances, chronic cough and expectoration call attention to localized, resectable disease.



- Other symptoms have poor prognosis when the patient presents with them → advanced disease: hoarseness, chest pain, superior vena cava syndrome, pericardial or pleural effusion, or persistent segmental atelectasis or pneumonitis

SCC and AdenoCa. - Prognosis

- More favorable prognosis than SCLC.
- When detected before metastasis or local spread (as in high-risk patients undergoing surveillance imaging), cure is possible by lobectomy or pneumonectomy.
- Unresectable adenoCa. Ass/w targetable mutations in tyrosine kinases such as EGFR → may show remarkable responses to specific inhibitors.
- Much effort is currently being devoted to understanding the mechanisms of targeted drug resistance in order to develop strategies that prevent it from occurring.

SCLCs - Prognosis

- Invariably spread by the time they are detected, even if the primary tumor appears to be small and localized → surgical resection is not a viable option.
- SCLCs are very sensitive to chemotherapy but invariably recur.
- No targeted therapies are unavailable.
- Median survival even with treatment remains only 1 year, and only 5% are alive at 10 years.

Paraneoplastic syndromes

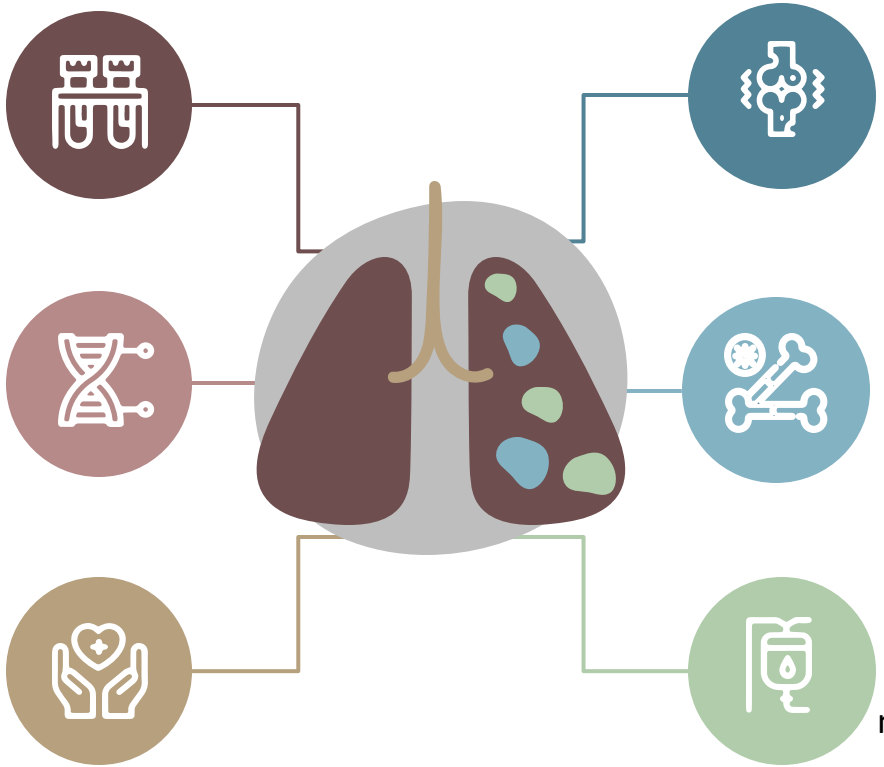
Hypercalcemia

Secretion of a parathyroid hormone–related peptide

Cushing syndrome

Increased production of adrenocorticotropic hormone

Syndrome of inappropriate secretion of anti-diuretic hormone



Neuromuscular syndromes

a myasthenic syndrome, peripheral neuropathy, and polymyositis

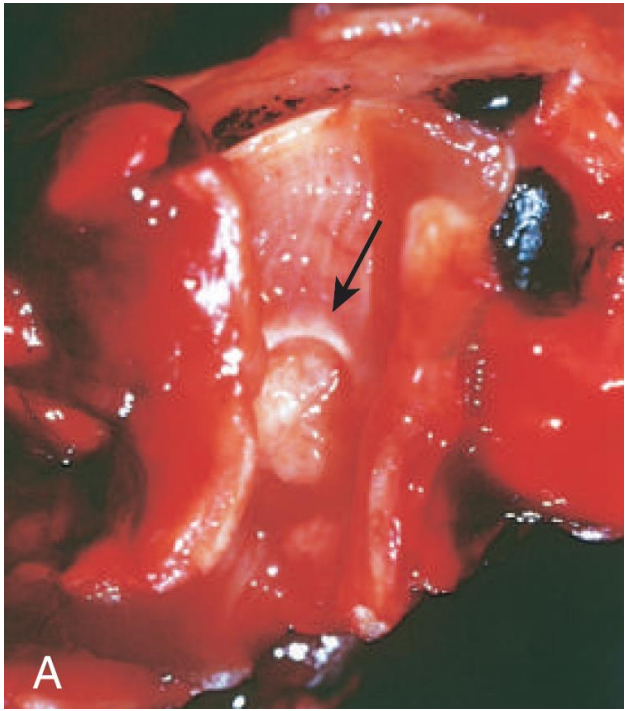
fingers Clubbing & hypertrophic pulmonary osteoarthropathy

Coagulation abnormalities

migratory thrombophlebitis, nonbacterial endocarditis, & DIC

Carcinoid tumors

- A malignant tumors composed of cells that contain dense-core neurosecretory granules in their cytoplasm and, rarely, may secrete hormonally active polypeptides.
- a low-grade neuroendocrine carcinomas; subclassified as typical or atypical
- Often resectable and curable.
- Can occur as part of the multiple endocrine neoplasia syndrome (MEN)
- Young adults (mean 40 years).
- 5% of all pulmonary neoplasms.



Carcinoid tumors

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

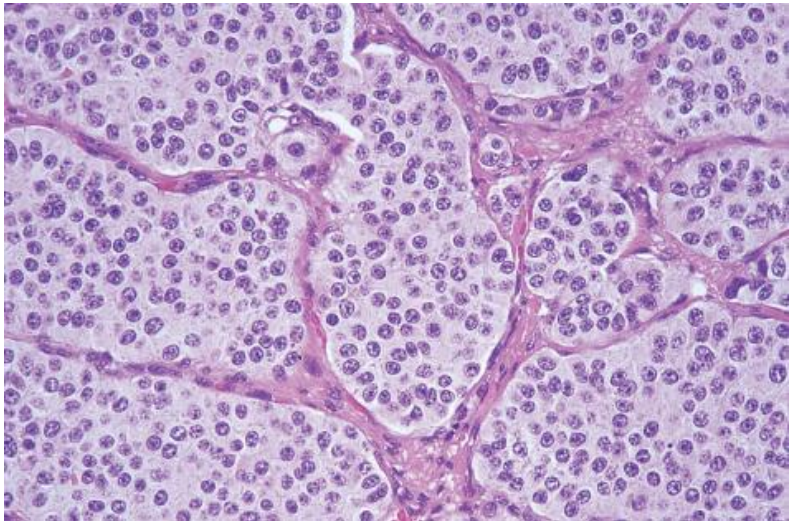
(1) an obstructing polypoid, spherical, intraluminal mass
(2) a mucosal plaque penetrating the bronchial wall to fan out in the peribronchial tissue **collar-button lesion.**

- Both are well demarcated.
- Peripheral carcinoids are less common.
- 5-15% metastasized to the hilar nodes at presentation, distant metastases are rare.

Carcinoid tumors - histologic

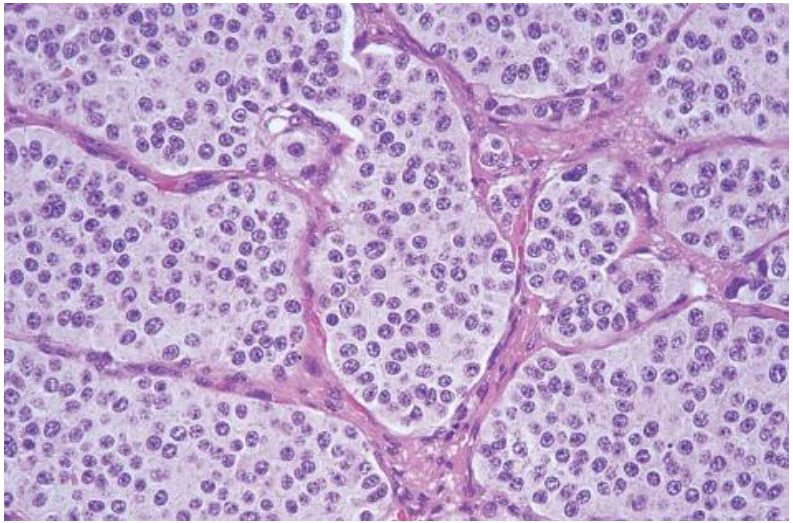
- **Typical carcinoids,** like their counterparts in the intestinal tract, are composed of nests of uniform cells that have regular round nuclei with “salt-and-pepper” chromatin, absent or rare mitoses and little pleomorphism
- **Atypical carcinoids** display a higher mitotic rate and small foci of necrosis.

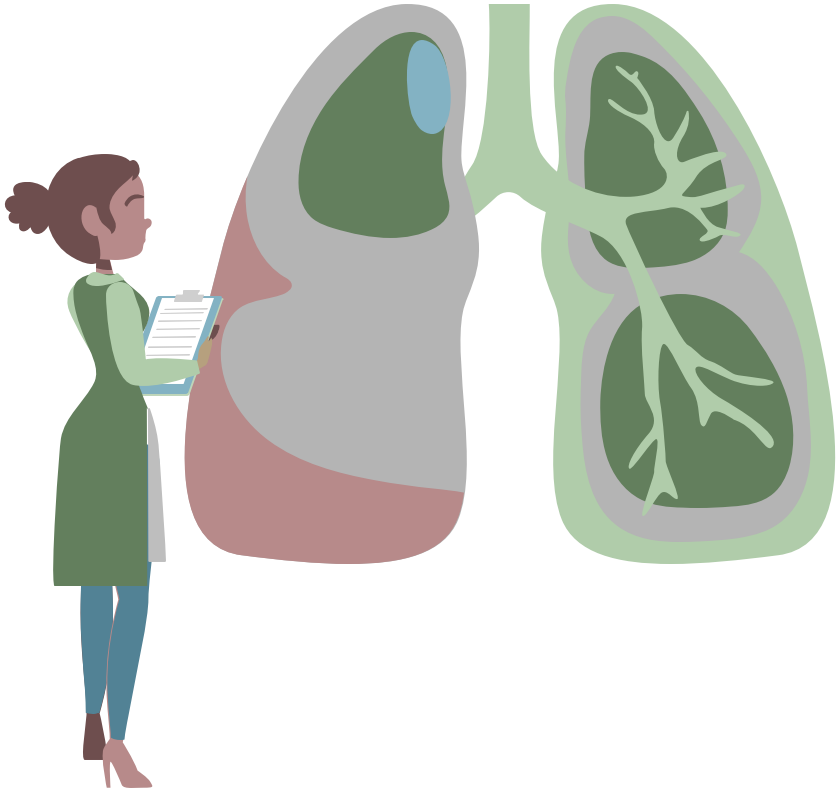
+have a higher incidence of lymph node and distant metastasis than typical carcinoids
+have *TP53* mutations in 20% to 40% of cases.



Carcinoid tumors - clinical

- Manifest with signs and symptoms related to their intraluminal growth: cough, hemoptysis, & recurrent bronchial & pulmonary infections.
- Peripheral tumors often asymptomatic & discovered incidentally on chest radiographs.
- Only rarely do pulmonary carcinoids induce the *carcinoid syndrome,* characterized by intermittent attacks of diarrhea, flushing, & cyanosis.
- 5- & 10-year survival rates for typical carcinoids are > 85%, while rates drop to 56% & 35%, respectively, for atypical carcinoids.





Thank you!
Take care of your lungs.