Pathology of Lung tumours

Dr Gayana Mahendra
Department of Pathology

Lung tumours

- At the end of this lecture the students should be able to
- Describe the epidemiology of lung cancer
- Understand the aetiology and carcinogenetic mechanisms of lung cancer
- Understand the basis of classification of lung cancer into
  - peripheral and central
  - small cell and non-small cell
- Describe the morphology of different types of lung cancer
- Explain the pathological basis of clinical features of lung cancer
- List the other common types of lung tumours
- Briefly describe the aetiology and morphology of pleural tumours.

Lung tumours

– Primary lung tumours
  - Malignant
  - Benign

- Secondary/ metastatic deposits in lung

- 90-95% of primary lung tumours are carcinomas
- Metastatic tumours in the lung are common as it receives the entire cardiac output

Primary lung cancers

- Most frequently diagnosed cancer and the leading cause of cancer mortality worldwide.
- In Sri Lanka , second commonest cancer diagnosed in males.
  - Males : oral cavity-lung-oesophagus-colorectum-lymphomas
  - Females : breast-cervix-thyroid-ovary-oeophagus
- Largely due to the effects of cigarette smoke.
- A tumour with a bad overall prognosis.
- Only 10% are operable at the time of diagnosis.

Aetiology of primary lung cancers

1. Tobacco Smoking

- Cigarettes, pipes, cigars and bidis
- A major risk factor
- Progressive change in lung epithelium from metaplasia → dysplasia → malignancy
- Significant association with
  - Amount of daily smoking
  - Tendency to inhale
  - Duration of the smoking habit
- Women have a higher susceptibility carcinogenic effect of smoke

- Cessation of smoking for **10 years** – will reduce the risk , but never to control level!!!
- Only 11% of all heavy smokers will develop lung cancers in their lifetime!!
- Never-smokers also develop lung cancers!!!
  - Secondhand/passive smoking
- Clearly there are other factors that are involved in lung cancer carcinogenesis

Aetiology of primary lung cancers

2. Occupational exposure to carcinogens

- Asbestos
  - Long term exposure
  - Long latent period
  - Smoking has an additive effect
  - Results in adenocarcinoma
- Industries involved with Ni, Cr, Cd, As
- High dose ionizing radiation- Uranium miners
- Air pollution- indoor exposure to Radon
- Radioactive gases

Aetiology of primary lung cancers

3. Lung fibrosis

- Some peripheral lung cancers arise in fibrous scars
  - Old TB foci, infarcts and wounds
- Cryptogenic fibrosing alveolitis

4. Genetic predisposition

Read further on carcinogenesis in lung tumours

Molecular genetics of lung cancer

- Nearly 10-20 genetic mutations have occurred by the time the cancer is clinically detected
- Oncogenes involved
  - C-MYC, KRAS, EGFR, C-KIT, C-MET
- Tumour suppressor genes that are inactivated
  - P53, RB1, p16

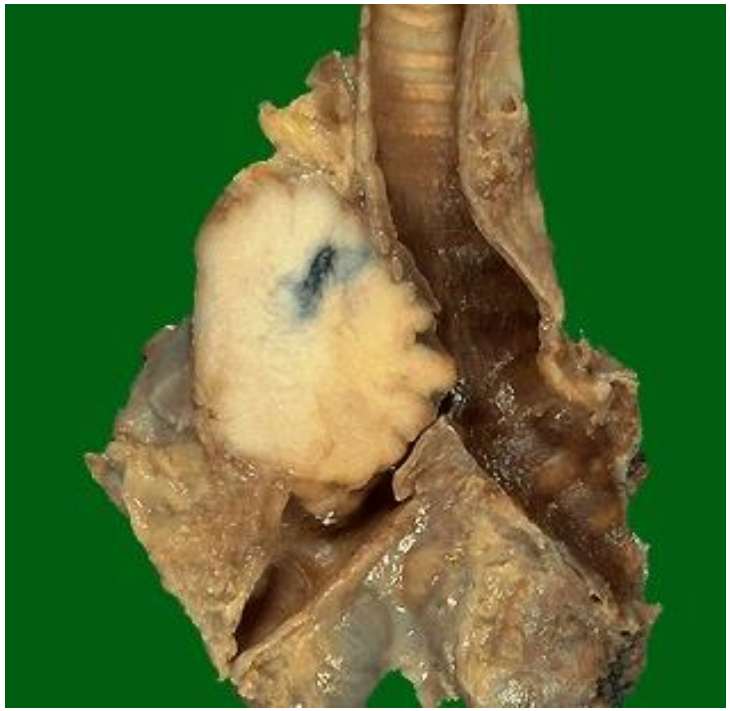
Classification of lung cancers

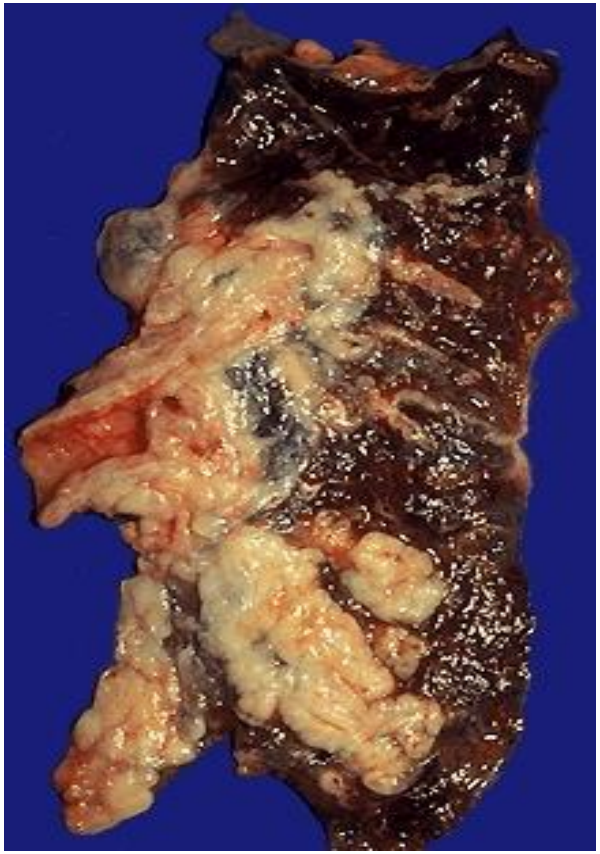
- Major histological categories include
  - Squamous cell carcinoma
  - Adenocarcinoma
  - Small cell carcinoma
  - Large cell carcinoma
- For common clinical use these types of lung cancers are divided into two groups
  - Small cell carcinoma
    - almost always metastatic and with poor prognosis
    - High initial response to chemotherapy
  - Non-small cell carcinoma
    - Less often metastatic
    - Less responsive to chemotherapy

Morphology of lung cancers

- Tumours arising from the main bronchi close to the hilum of lung
  - Central lung tumour
    - squamous carcinomas
    - small cell carcinomas.
- Tumours arising from alveolar septal cells or terminal bronchioles
    - Peripheral lung tumours
    - Mostly adenocarcinomas

Central lung tumours





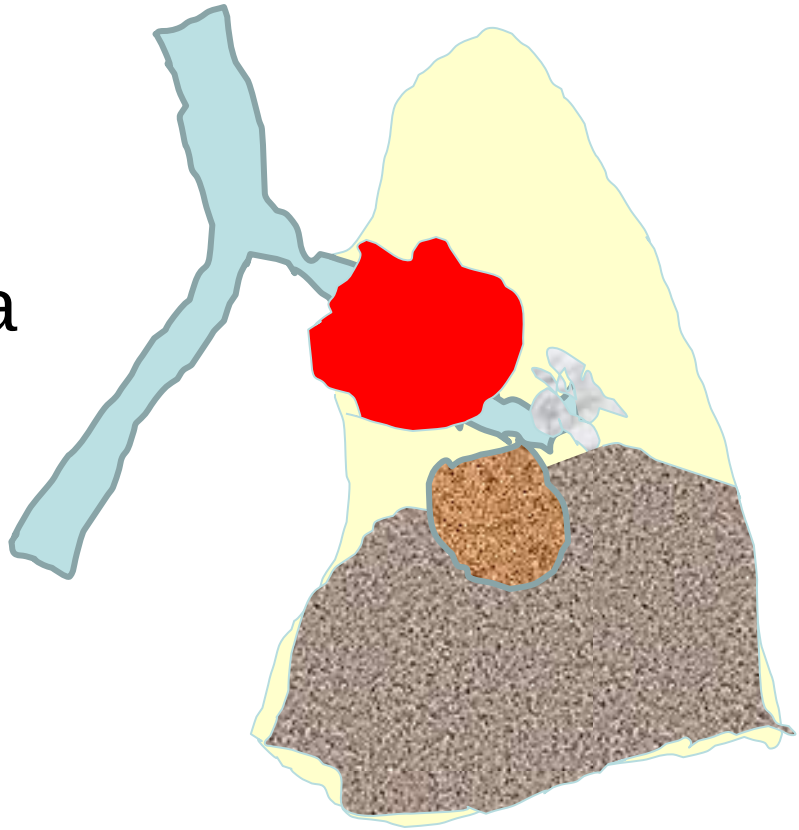
- Solid,haemorrhagic and necrotic tumours.
- Ulceration of the tumour leads to blood stained sputum which can contain malignant cell.
  - **Identified on sputum cytology**

Peripheral lung tumours

What are the causes for a radiologically identified peripheral lung lesion?

Morphology of lung cancers

- Distal to the tumour
  - Features of bronchial obstruction
    - Partial-emphysema
    - Complete -atelectasis
  - Accumulation of mucus
  - Consolidation of parenchyma
  - abscess formation



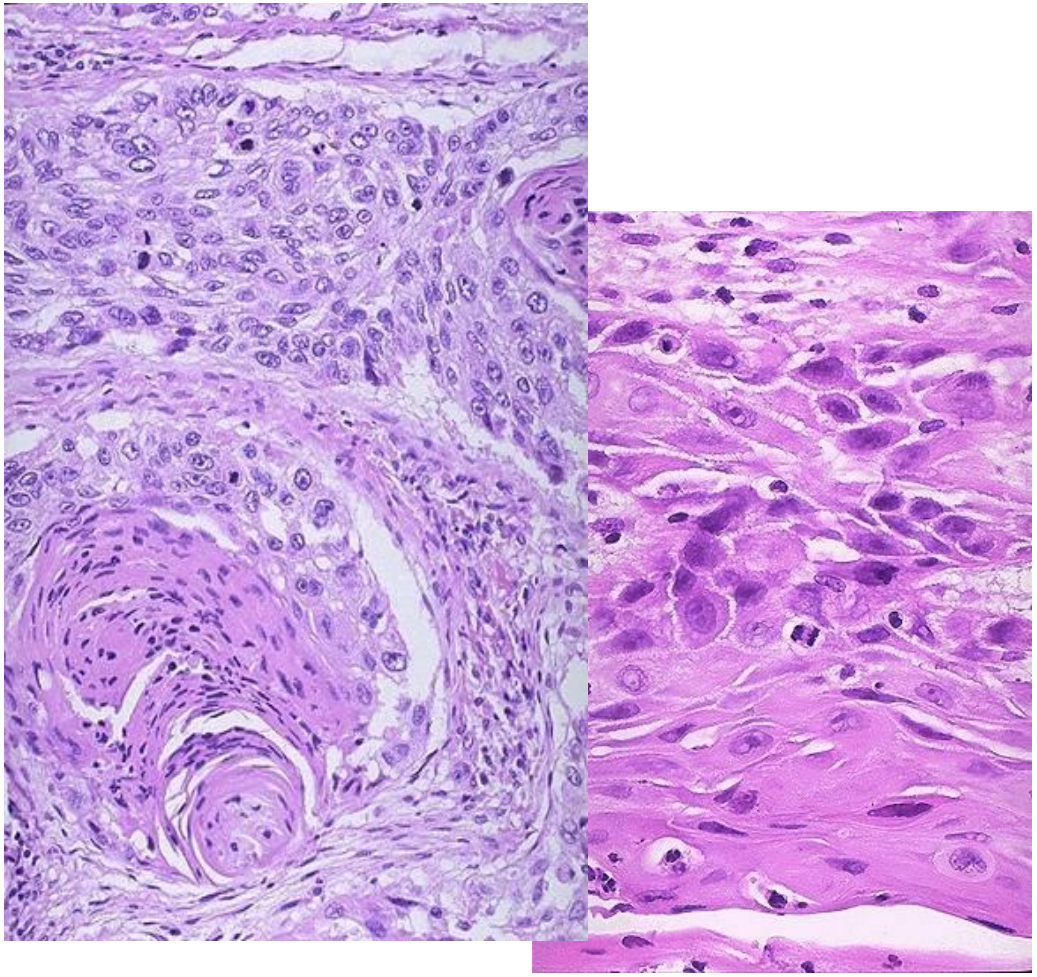
Non small cell carcinomas

- Squamous cell carcinoma (SqCC)
- Adenocarcinoma (AC)
- Large cell undifferentiated carcinoma (LCUC)

Squamous cell carcinoma (SqCC)

- Closely associated with smoking
- Central/ hilar tumours
- Haemorrhagic and necrotic mass
- Preceded by squamous metaplasia –dysplasia and CA-in situ
- Histologically
  - well- poorly differentiated squamous cell carcinoma.

SqCC



Adenocarcimoma

- Usually peripheral tumours
- Associated with pulmonary fibrosis
- Now known to be associated with cigarette smoking
- The incidence has increased over the last 2 decades
- Most common form of lung cancer in women
- Presentation could be late because bronchial obstruction is uncommon as the tumours are peripheral.
- May present with extremely extensive systemic disease

Adenocarcinoma

- Thought to be arising from a precursor lesion

Atypical adenomatous hyperplasia

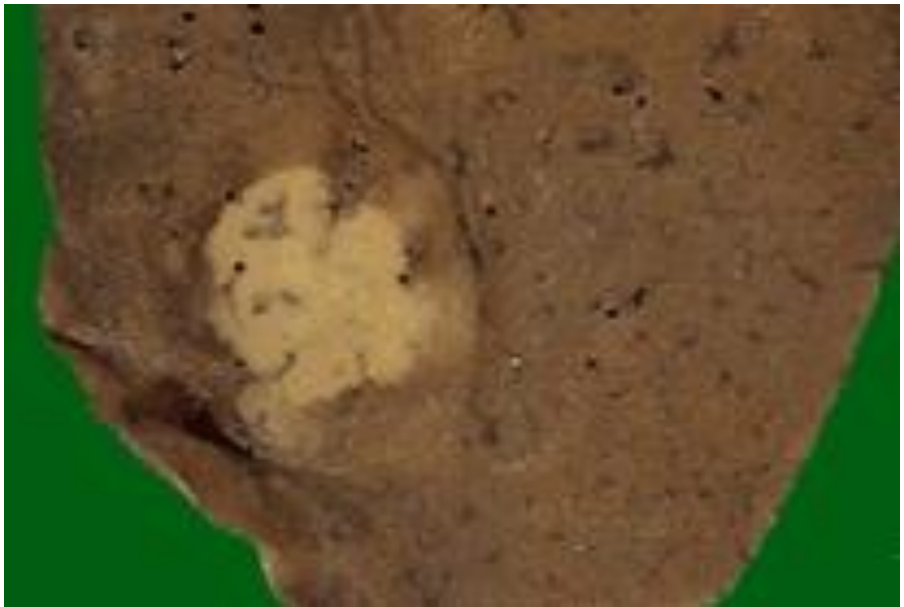
Adenocarcinoma in-situ

Invasive adenocarcinoma

Adenocarcinoma- macroscopy

- Commonly a single peripheral nodule
- Could be multiple – mimic metastatic deposits
- Could be central tumours

- Can contain carbon pigments
- Marked scaring due to desmoplasia

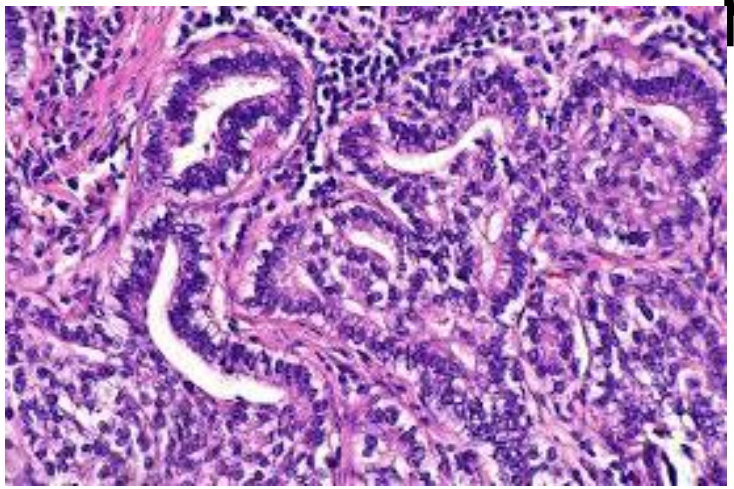


Adenocarcinoma

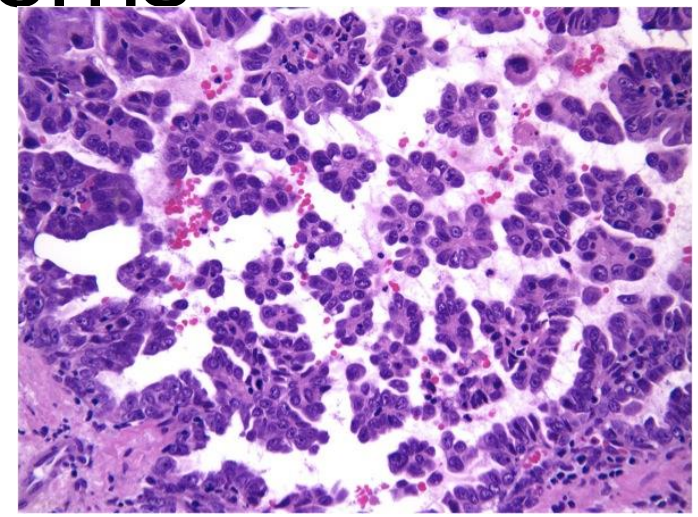
- Arises from glandular cells of pulmonary epithelium
- A heterogeneous group with different growth patterns
  - Tubular, papillary acinar and signet ring cell patterns
  - lepidic growth pattern
- Difficult to differentiate from metastatic deposits of an adenocarcinoma

eg :stomach, colon, ovary

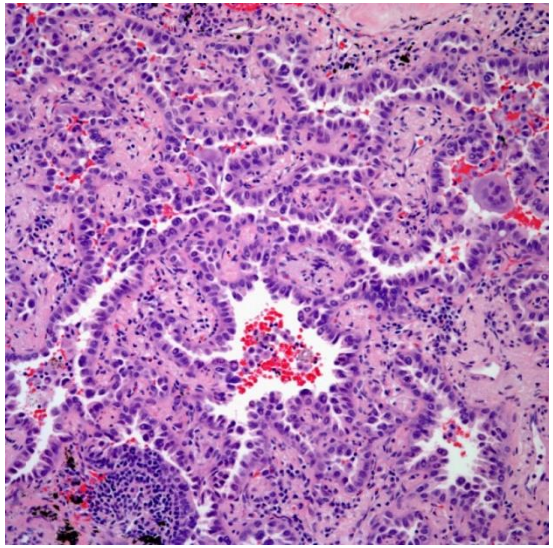
Adenocarcinoma different growth patterns



Acinar pattern

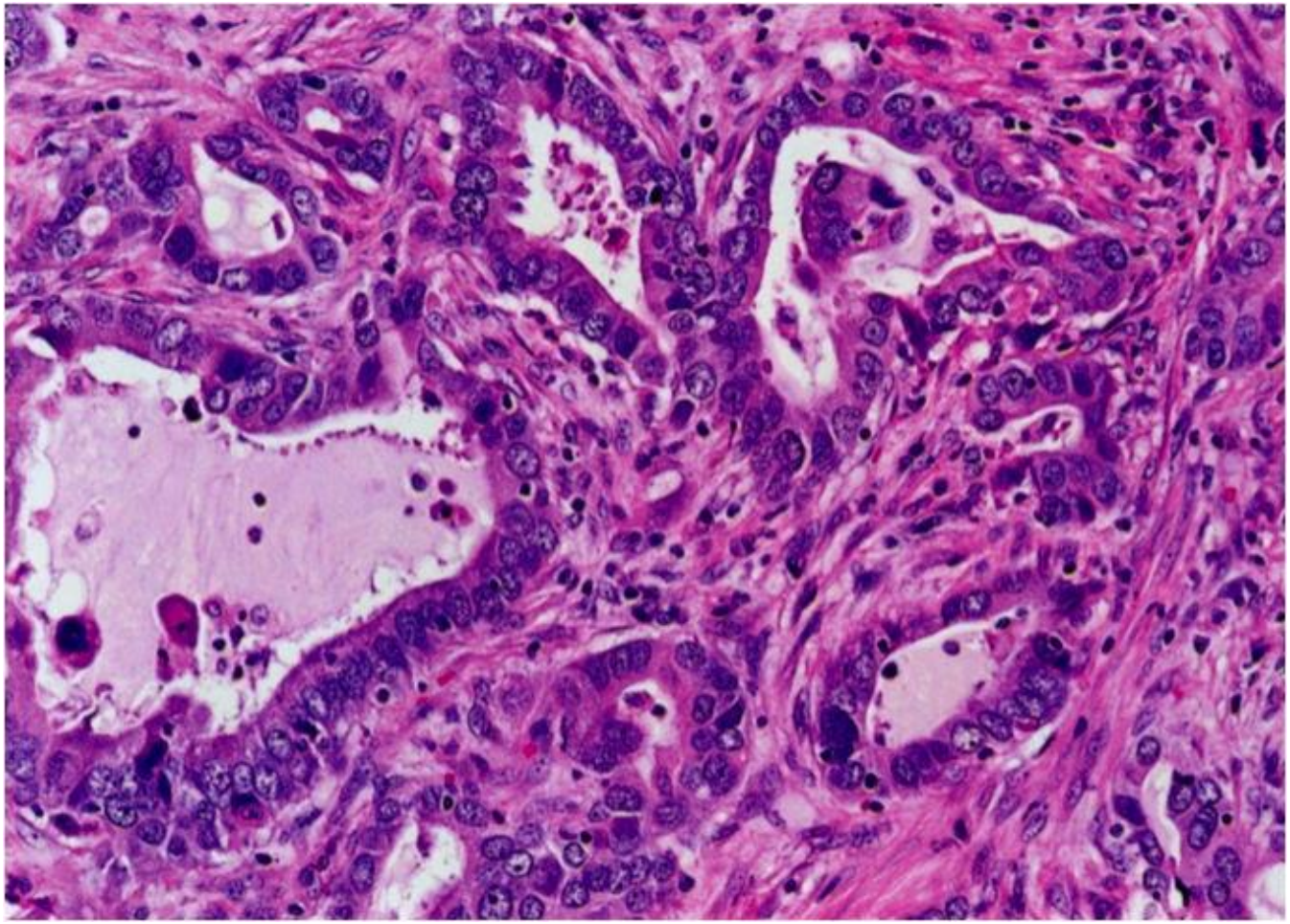


Micropapillary pattern



papillary pattern

Adenocarcinoma –cellular features

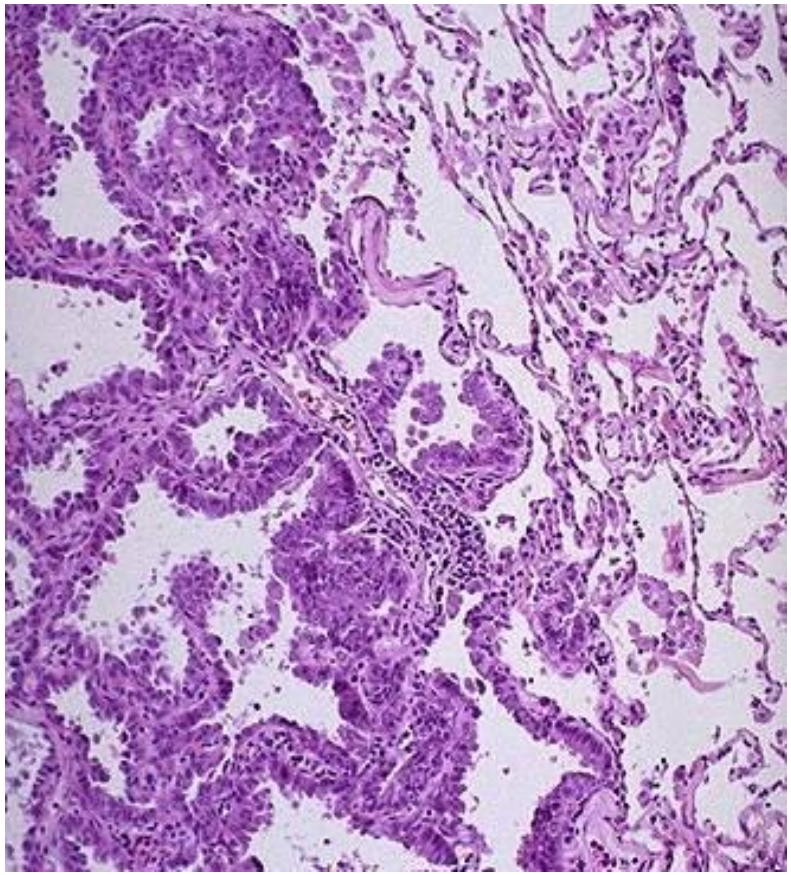


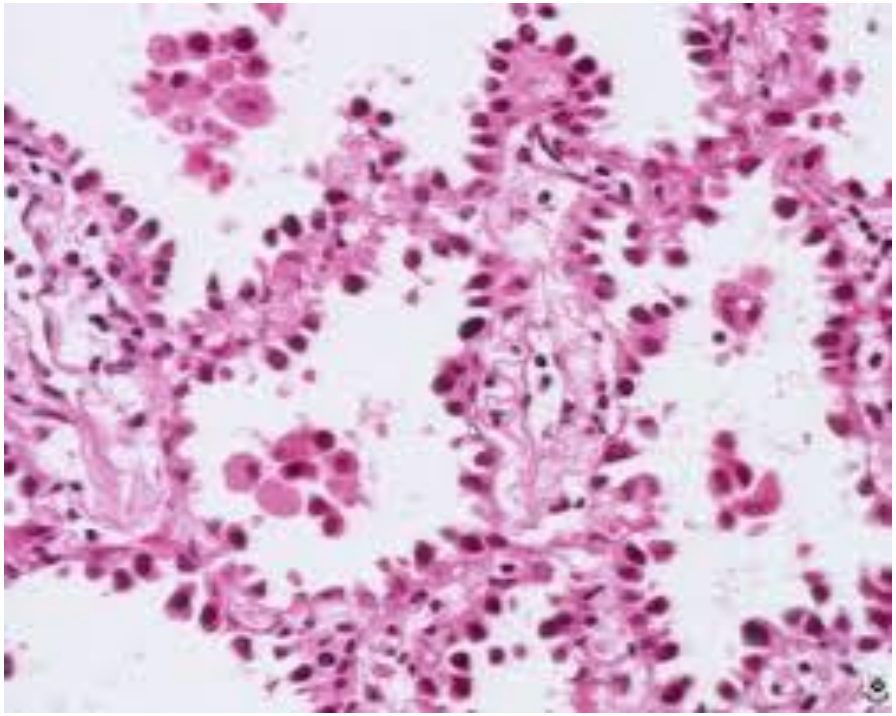
Lepidic adenocacinoma

- A variant of adenocarcinoma
- Previously known as bronchioloalveolar carcinoma-

  Now an obsolete term
- The tumour cells line up along preserved alveolar septa, forming papillary projections within the spaces.
- The basic alveolar architecture is preserved.
- Invasive foci at least one

Lepidic adenocarcinoma





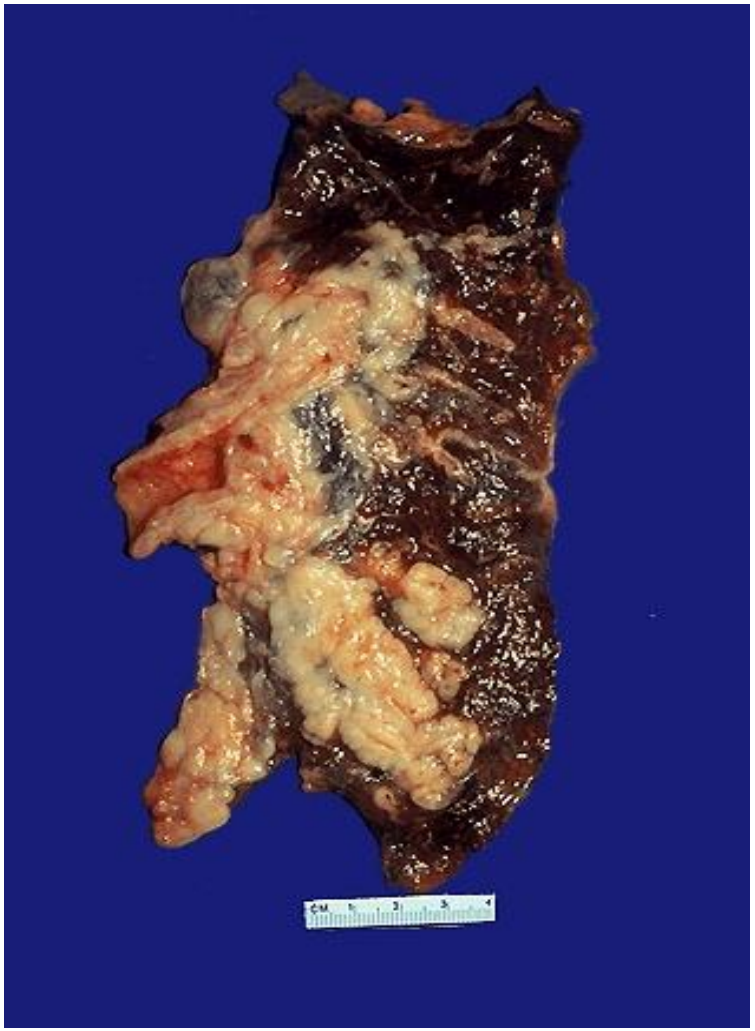
Large cell undifferentiated carcinoma

- Highly aggressive and destructive lesion with haemorrhage and necrosis
- Usually central tumours, can be peripheral as well.
- Necrotic and haemorrhagic masses
- Widely disseminated at the time of diagnosis.
- Histology-
  - gross nuclear pleomorphism with numerous bizarre mitosis.
  - No squamous or glandular differentiation

Small cell carcinoma (SCC)

- Highly malignant
- Central/ Hilar tumours
- Primary tumour can be small but metastases early
- bulky secondary deposits
- Therefore bad prognosis
- Often associated with ectopic hormone production -

Small cell carcinoma (SCC)



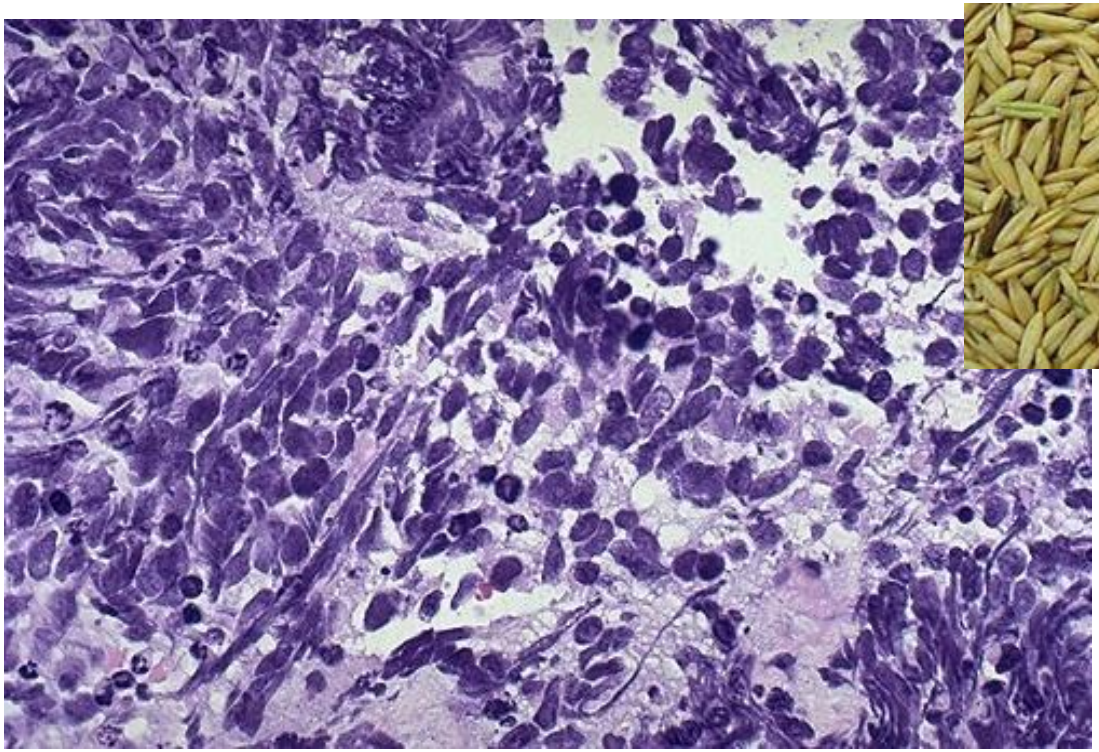
Extensive tumour spread

Small cell carcinoma (SCC) microscopy

- Derived from neuroendocrine cells of lung epithelium
- Highly cellular
- small cells with hyperchromatic nuclei
- Scanty cytoplasm

  “oat cell carcinoma”
- Cells have a neuroendocrine differentiation.

Small cell carcinoma (SCC) /Oat cell cancer

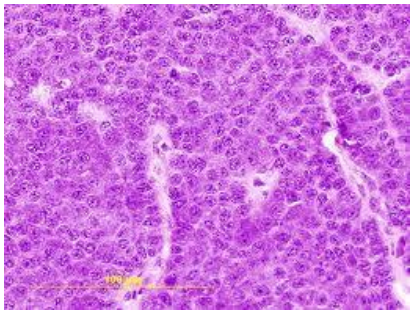


Small dark blue cells with minimal cytoplasm are packed together in sheets.

Small cell carcinoma (SCC)

A spectrum of differentiation of neuroendocrine cells

Bronchial carcinoids

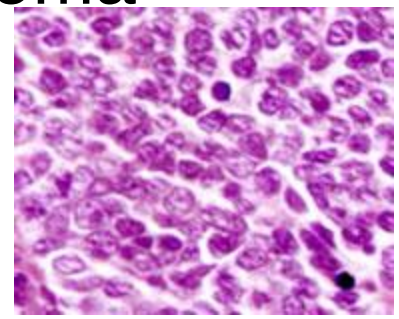


Slow growing tumours

Intermediate type

Atypical carcinoids

Small cell carcinoma



Highly malignant

Symptoms of lung cancer

Manifestations of locally advanced disease

- Cough-infection distal to airway block
- Haemoptysis-Ulceration of tumour in bronchus
- Dyspnoea-local extension of tumour
- Chest pain- pleural or chest wall involvement
- Wheeze-narrowing of airways
- Dyaphagia-oesophageal invasion
- Horner syndrome –sympathetic ganglia involvement

»Read More

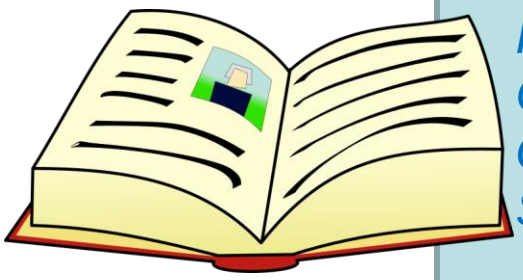
Symptoms of lung cancer

- Due to metastatic spread
- Bloodstream spread-
  - Bone
    - pathological fractures
    - Leucoerythroblastic anaemia
  - Brain
    - Neurological signs
  - Liver
    - Jaundice and hepatomegaly
- Lymphatic spread
  - Cervical sympathetic chain- Horner’s syndrome
  - Paratrachial nodes- SVC obstruction
  - Paratracheal nodes- recurrent laryngeal nerve palsy

Non metastatic extra pulmonary complications

Paraneoplastic syndromes

- May be the presenting symptoms of lung cancer
- Endocrine symptoms(ADH, ACTH, PTHrP)
- Neurological symptoms
- Hypertrophic pulmonary osteoarthropathy



Paraneoplastic syndrome :refer and read more

• *ADH*	*-SIADH*
• *ACTH*	*-Cushing syndrome*
PTH, PTH rP,PGE	*- hypercalcaemia*
Calcitonin	*-hypocalcaemia*
Gonadotrophins	*-gynaecomastia*
Serotinin	*- carcinoid syndrome*

Other primary lung tumours

- Primary tumours other than carcinomas are rare in lung.

Benign

- Bronchial adenomas
- mesenchymal lesions-Neurofibromas, lipomas, chondroma etc
- Bronchial harmartoma/ mesenchymoma
  - A neoplastic lesion
  - Hard, whitish, nodular lesion
  - “coin lesion’ on Xray
  - Consist of cartilage, fat , bone and glandular tissue

Bronchial adenomas

Polypoidal/ sessile growth in the bronchus
Can cause obstruction
Arises from bronchial mucus glands

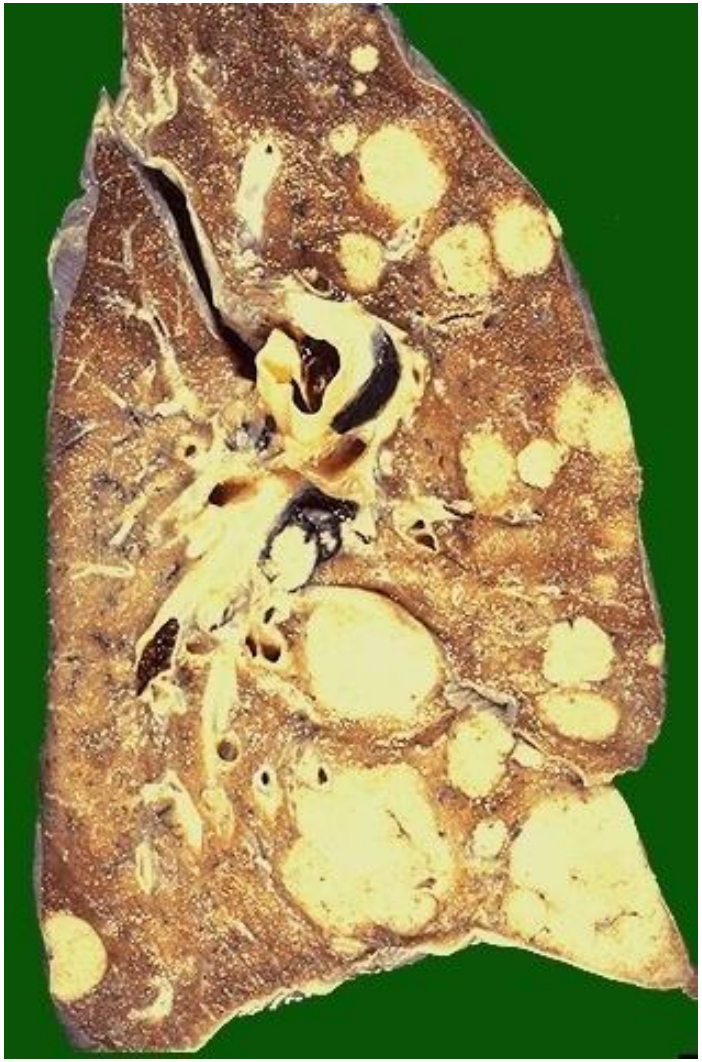
Other primary lung tumours

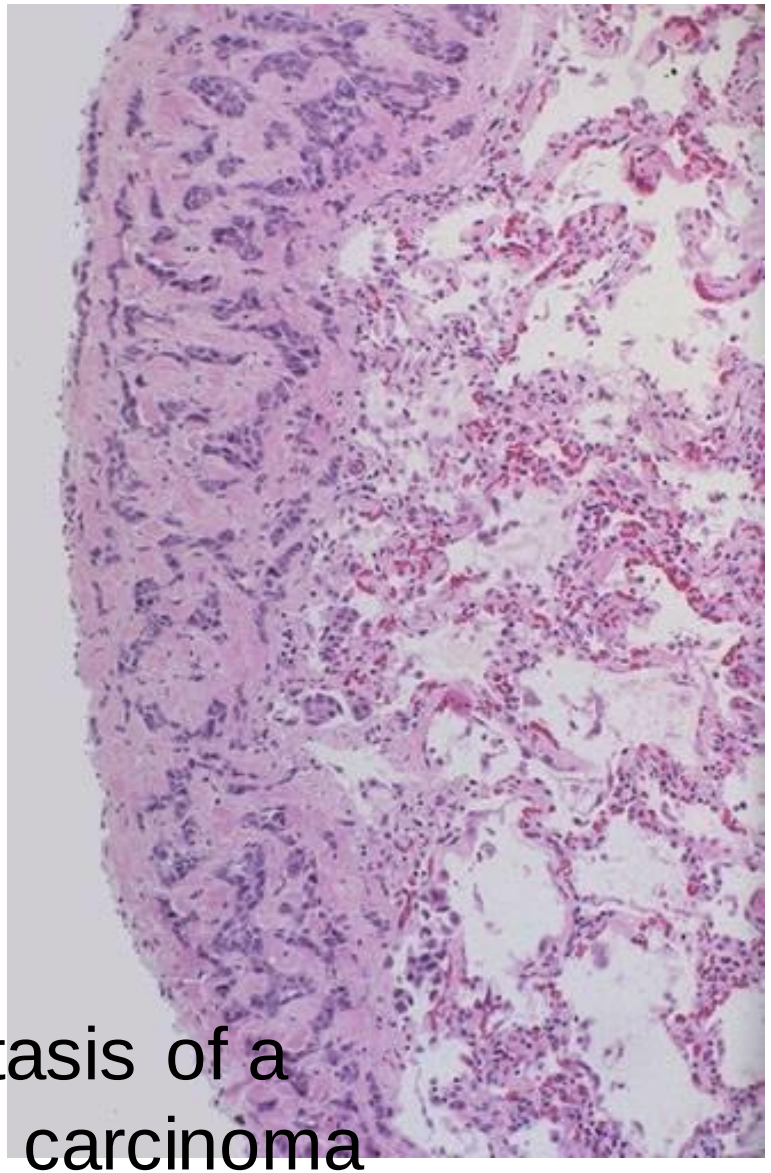
- Malignant tumours
  - Rare
  - Sarcomas – rare
  - Lymphoma
    - Rare
    - Increased incidence in HIV/AIDS patients
    - B cell lymphoma arising from bronchiole associated lymphoid cell population.

Secondary/metastatic lung tumours

- More commoner than primary tumours
- Arises via
  - Blood borne spread
  - Lymphatic spread
- Discrete multiple nodules scattered throughout both lungs
- “cannon ball’ deposits
- Diffuse involvement of lymphatics
  - **Lymphangitis carcinomatosis –** presents with breathlessness

Secondary/ metastatic lung tumours





Metastasis of a
Breast carcinoma

Secondary/ metastatic lung tumours

Secondaries of

- Carcinomas –commonest

  Common primary sites include

  – breast

  – Kidney

  – GI tract

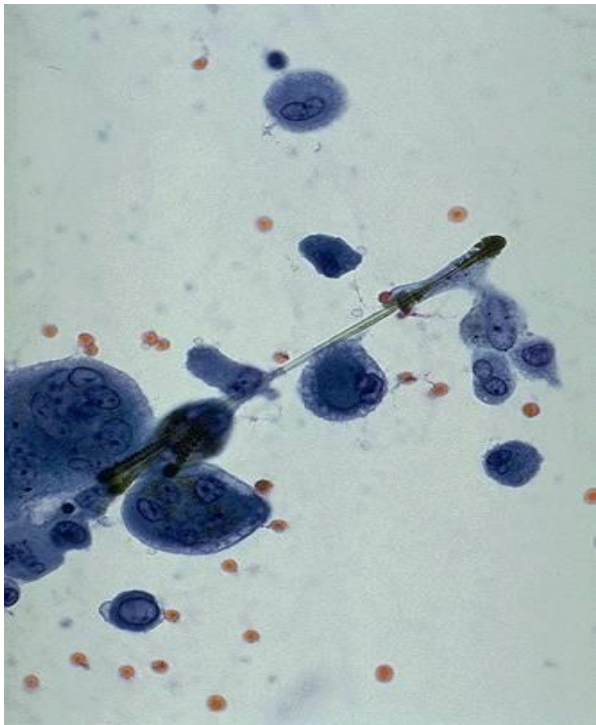
- Sarcomas
- lymphomas

Pleural tumours

- Malignant tumours are commoner than benign tumours
- Metastatic deposits are the most common tumours of pleura
  - Primary lung tumours
  - Breast tumours
  - Ovarian tumours
- Associated with an exudative effusion in pleura.

Mesothelioma

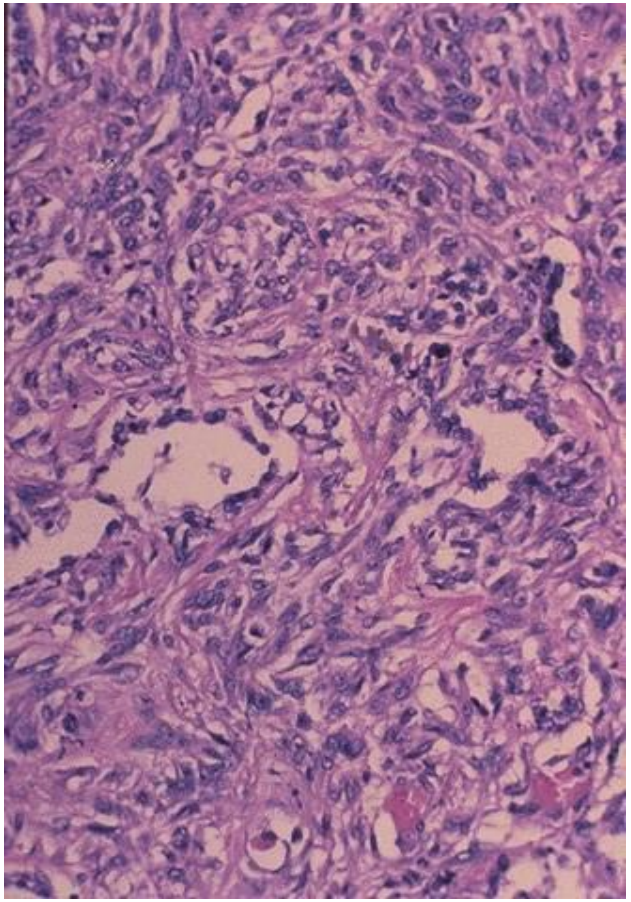
- Primary malignant tumour of pleura
- Strongly associated with
- Exposure to asbestos
  - Fibre types- Crocidolite and amosite
- A long latent period



Mesothelioma

- Starts as nodules over the pleura
- Spreads as a confluent sheet around lung ensheathing the lung
- Histologically spindle cells and glandular pattern- “biphasic”
- Highly malignant tumours
- Spreads around pleural cavity and pericardium

Mesothelioma



Summary

- Metastatic deposits are the commonest tumour in the lung
- Carcinomas are the commonest primary lung tumour
- Broadly SCC and NSCC
- SCC has a poor overall prognosis
- Smoking is the most significant association
- Clinical presentation is variable depending on the site and type of tumour.