APPROACH TO THE SOLITARY PULMONARY NODULE

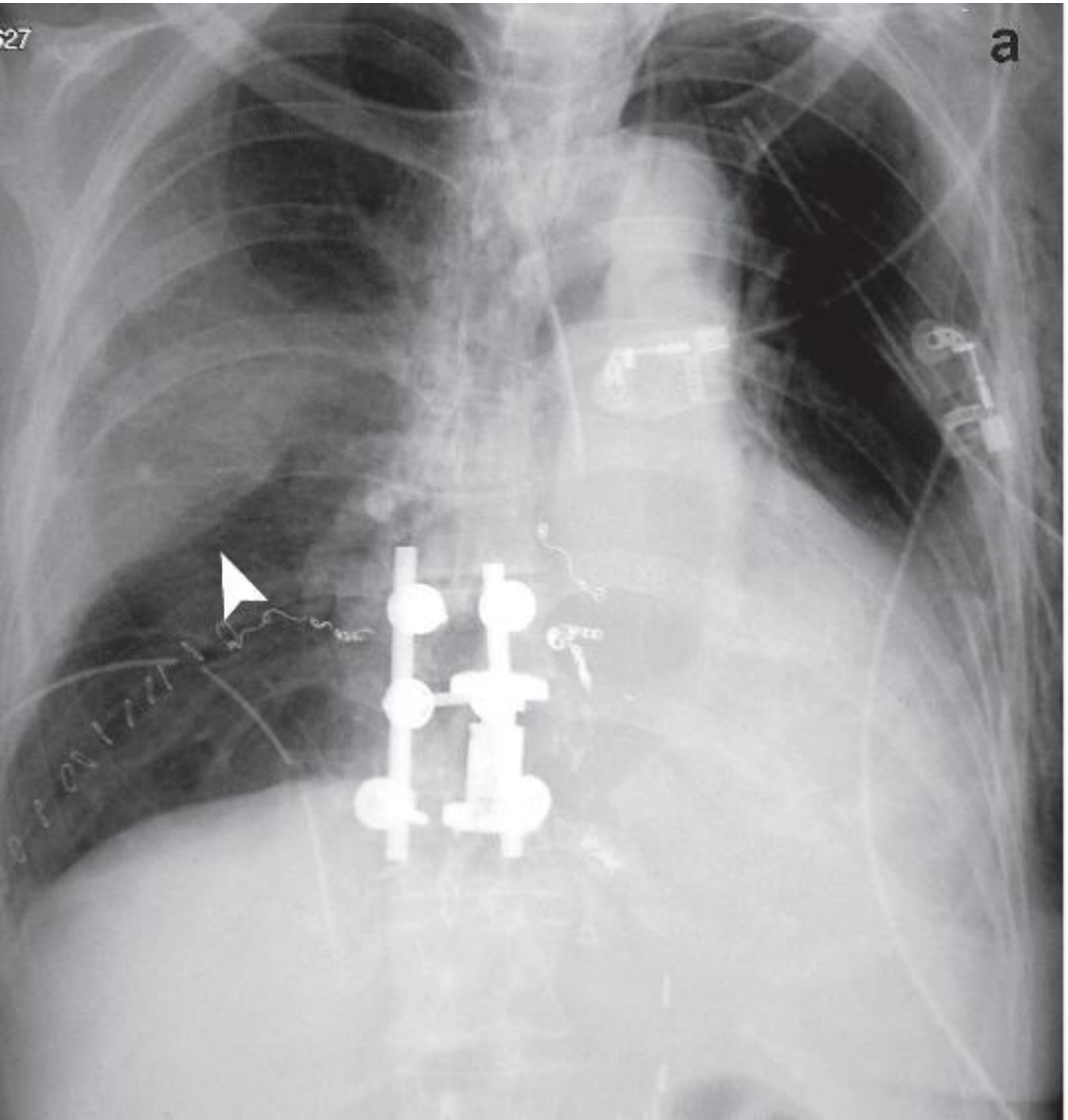
definition

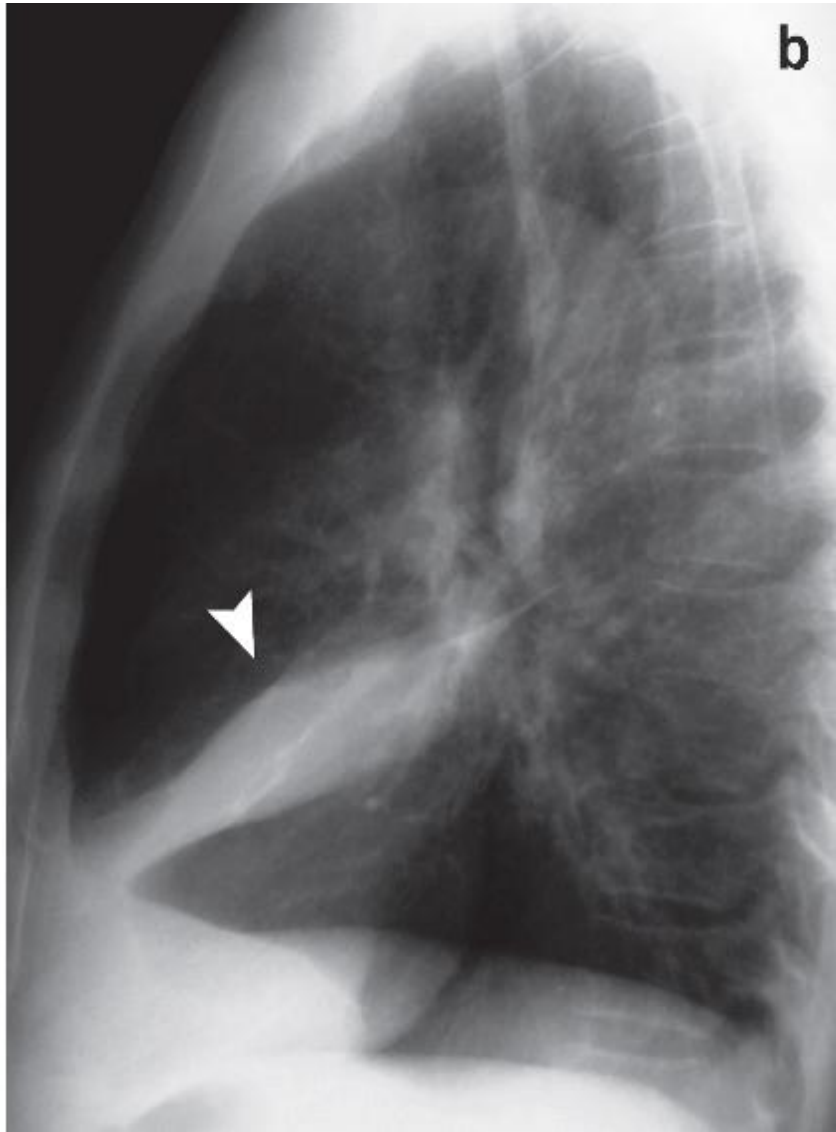
a round or oval, sharply circumscribed radiographic lesion up to 3-5 cm which may or may not contain calcium

Differential Diagnosis

- neoplasm (45%)
    - primary bronchogenic cancer (70%)
    - benign: eg. hamartoma, lipoma (15%)
    - solitary metastasis (e.g. breast, sarcoma) (10%)
- infection (53%)
    - TB, histoplasmosis, coccidiomycosis
- other (2%)
    - healed granuloma
    - vascular: A-V malformation, infarct
    - congenital: cyst
    - round pneumonia, round atelectasis, loculated effusion (=pseudotumour)

right-sided encysted pleural effusion





Causes of pulmonary nodules

Common causes

- Bronchial carcinoma
- Single metastasis
- Localised pneumonia
- Lung abscess
- Tuberculoma
- Pulmonary infarct

Uncommon causes

- Benign tumours
- Lymphoma
- Arteriovenous malformation
- Hydatid cyst (p. 375)
- Bronchogenic cyst
- Rheumatoid nodule
- Pulmonary sequestration
- Pulmonary haematoma
- Wegener's granuloma
- 'Pseudotumour'-fluid collection in a fissure
- Aspergilloma (usually surrounded by air 'halo')

investigations

- history and physical
- CXR: always check old CXR first
- CT thorax
- sputum cytology: usually poor yield
- biopsy (bronchoscopic or percutaneous):
  if sputum negative
- resection:
  if lesion is suspicious and there is no diagnosis with biopsy

Typical CXR Findings

	Benign	Malignant
Size	< 3 cm, round, regular	> 3 cm, irregular, spiculated Ill-defined or notched
Margins	Smooth margin	margin
Features	Calcified pattern: central, popcorn," calcified, pattern is eccentric or diffuse, or concentric satellite lesions usually **no cavitation**; If cavitated, wall is smooth and thin no other lung pathology	Usually **not calcified**; if calcified, pattern is **eccentric** or **speckled** ; no satellite lesions; cavitation with thick wall may have pleural effusions, lymphadenopathy
Doubling Time	Doubles in < 1 month or > 2 years	Doubles in > 1 month < 2 years

Clinical and radiographic features distinguishing benign from malignant nodules*

Risk status of patient	
Age	Increasing age increases likelihood of malignancy. Lung cancer is uncommon under the age of 40 and rare under 35
Smoking history	Risk of malignancy increases in proportion to duration and amount smoked
History of malignancy	Risk of malignancy increased by history of lung cancer in a first-degree relative, and by exposure to asbestos, silica, uranium and radon
Characteristics of nodule	
Size	Greater probability of malignancy with increasing size. Nearly all nodules > 3 cm are malignant; less than 1% of very small (< 4 mm) nodules are malignant, even in smokers; 10-20% in the 8 mm range will prove cancerous
Margin	Usually smooth in benign lesions; malignant lesions have a spiculated margin
Density	Most cancerous lesions are solid, but most solid lesions are non-cancerous. A partly solid lesion or one with air lucencies is more likely to be malignant than a solid lesion. Ground glass lesions with malignant potential grow very slowly and require longer follow-up
Calcification or fat	These favour benign disease, although CT may detect calcification in some malignant lesions. A laminated or central deposition of calcification is typical of a granuloma, while a 'popcorn' pattern is suggestive of a hamartoma. Fat content is consistent with a hamartoma or a lipoid granuloma
Location	70% of lung cancers occur in the upper lobes and the right lung is more commonly affected than the left lung. Benign lesions are equally distributed throughout upper and lower lobes
Contrast enhancement	Lack of contrast enhancement (< 15 HU) has a high negative predictive value for malignancy, but is non-specific with a poor positive predictive value. Not useful in lesions < 8 mm in diameter
Lymphadenopathy	Hilar or mediastinal adenopathy favours a malignant process and is important for staging

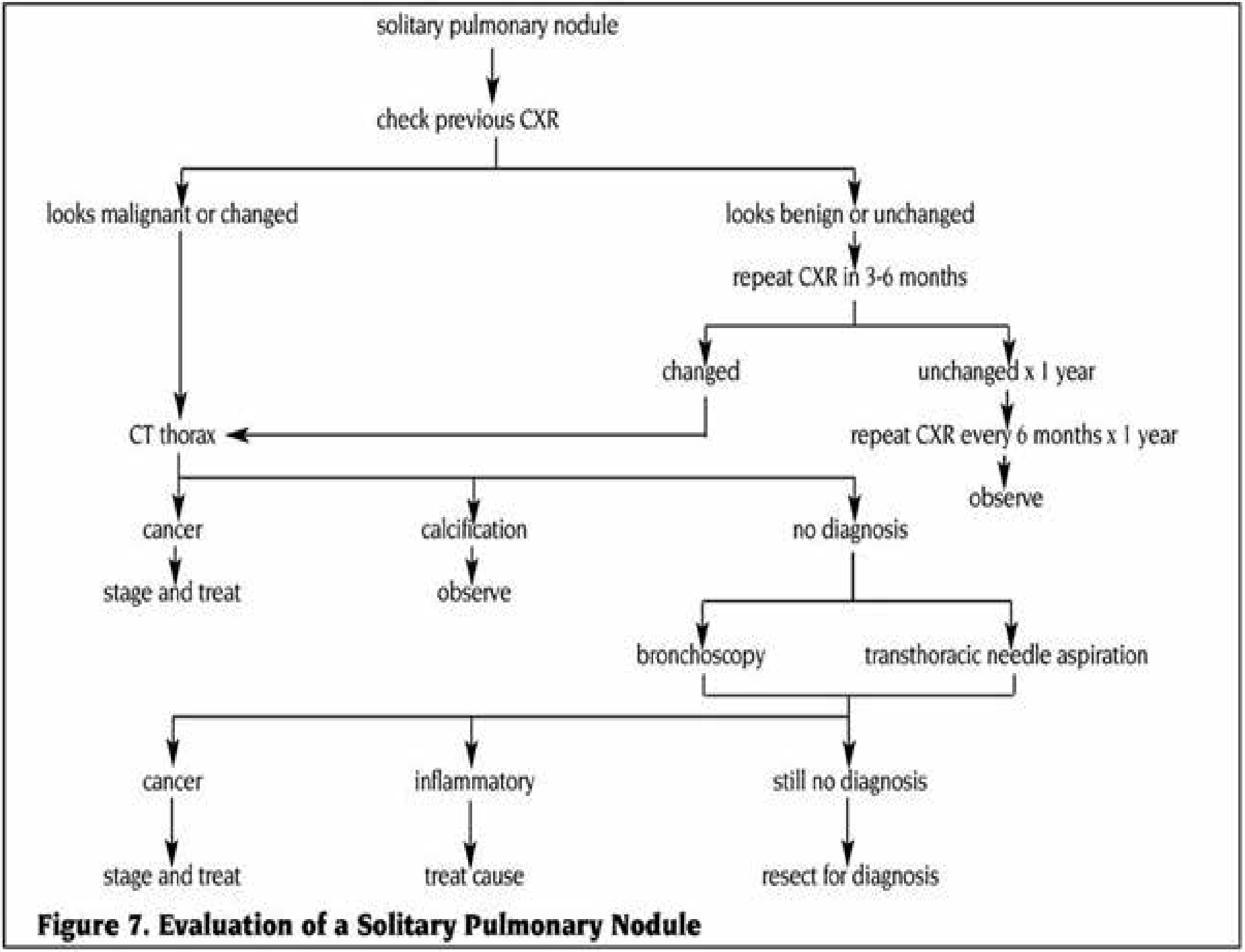


Figure 7. Evaluation of a Solitary Pulmonary Nodule

Fleischner Society 2017 Guidelines for Management of Incidentally Detected Pulmonary Nodules in Adults

A: Solid Nodules*

Nodule Type	Size			Comments
	<6 mm (<100 mm³)	6–8 mm (100–250 mm³)	>8 mm (>250 mm³)	
Single				
Low risk†	No routine follow-up	CT at 6–12 months, then consider CT at 18–24 months	Consider CT, PET/CT, or tissue sampling at 3 months	Nodules <6 mm do not require routine follow-up, but certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A).
High risk†	Optional CT at 12 months	CT at 6–12 months, then CT at 18–24 months	Consider CT, PET/CT, or tissue sampling at 3 months	Nodules <6 mm do not require routine follow-up, but certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A).
Multiple				
Low risk†	No routine follow-up	CT at 3–6 months, then consider CT at 18–24 months	CT at 3–6 months, then consider CT at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).
High risk†	Optional CT at 12 months	CT at 3–6 months, then at 18–24 months	CT at 3–6 months, then at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).

B: Subsolid Nodules*

Nodule Type	Size		Comments
	<6 mm (<100 mm³)	≥6 mm (>100 mm³)	
Single			
Ground glass	No routine follow-up	CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years	In certain suspicious nodules < 6 mm, consider follow-up at 2 and 4 years. If solid component(s) or growth develops, consider resection. (Recommendations 3A and 4A).
Part solid	No routine follow-up	CT at 3–6 months to confirm persistence. If unchanged and solid component remains <6 mm, annual CT should be performed for 5 years.	In practice, part-solid nodules cannot be defined as such until ≥6 mm, and nodules <6 mm do not usually require follow-up. Persistent part-solid nodules with solid components ≥6 mm should be considered highly suspicious (recommendations 4A-4C)
Multiple	CT at 3–6 months. If stable, consider CT at 2 and 4 years.	CT at 3–6 months. Subsequent management based on the most suspicious nodule(s).	Multiple <6 mm pure ground-glass nodules are usually benign, but consider follow-up in selected patients at high risk at 2 and 4 years (recommendation 5A).

Note.—These recommendations do not apply to lung cancer screening, patients with immunosuppression, or patients with known primary cancer.

* Dimensions are average of long and short axes, rounded to the nearest millimeter.

† Consider all relevant risk factors (see Risk Factors).

Recommendations for follow-up of incidental nodules smaller than 8 mm[1]

Nodule size (mm)[2]	Low-risk patient[3]	High-risk patient[4]
≤ 4	No follow-up needed[5]	Follow-up CT at 12 months; if unchanged, no further follow-up
4-6	Follow-up at 12 months; if unchanged, no further follow-up	Initial follow-up CT at 6-12 months, then at 18-24 months if no change
6-8	Initial follow-up CT at 6-12 months then at 18-24 months if no change	Initial follow-up CT at 3-6 months, then at 9-12 months if no change
> 8	Follow-up CT at around 3, 9 and 24 months, dynamic contrast-enhanced CT, PET and/or biopsy	As for low-risk patient

[2]Average of length and width.

[3]Minimal or absent history of smoking and of other known risk factors.

[4]History of smoking or of other known risk factors.

[5]Very low risk of malignancy (< 1%). Non-solid (ground glass) or partly solid nodules may require longer follow-up to exclude indolent adenocarcinoma.

NEOPLASMS BENIGN

- less than 5% of all primary lung neoplasms
- bronchial adenomas and hamartomas comprise 90 percent of the benign neoplasms of the lung
- uncommon benign neoplasms of the lung :

fibromas, lipomas, leiomyomas, hemangiomas, papillomas, chondromas, teratoma and endometriosis

clinical presentation

- Cough
- Hemoptysis
- recurrent pneumonia
- atelectasis
- without symptoms as a solitary pulmonary nodule

Bronchial Adenomas

- slow-growing, benign endobronchial tumours that rarely metastasizes

- may be carcinoids (90%), adenocytstic tumours, or mucoepidermoid

- symptoms

- systemic symptoms usually absent

- patients may complain of chronic cough, wheezing or give a history of recurrent pneumonia

- hemoptysis may be present

bronchial carcinoids

- atypical subtype of adenoma with a high metastasis rate (70% vs. 5%)
- often in young adults
- smoking not a risk factor

clinical presentation

- follows a slow course, metastasizes late
- can cause symptoms of carcinoid syndrome (flush, diarrhea, cardiac valvular lesions, wheezing)
- • may secrete other hormones (such as ACTH) and cause paraneoplastic syndromes

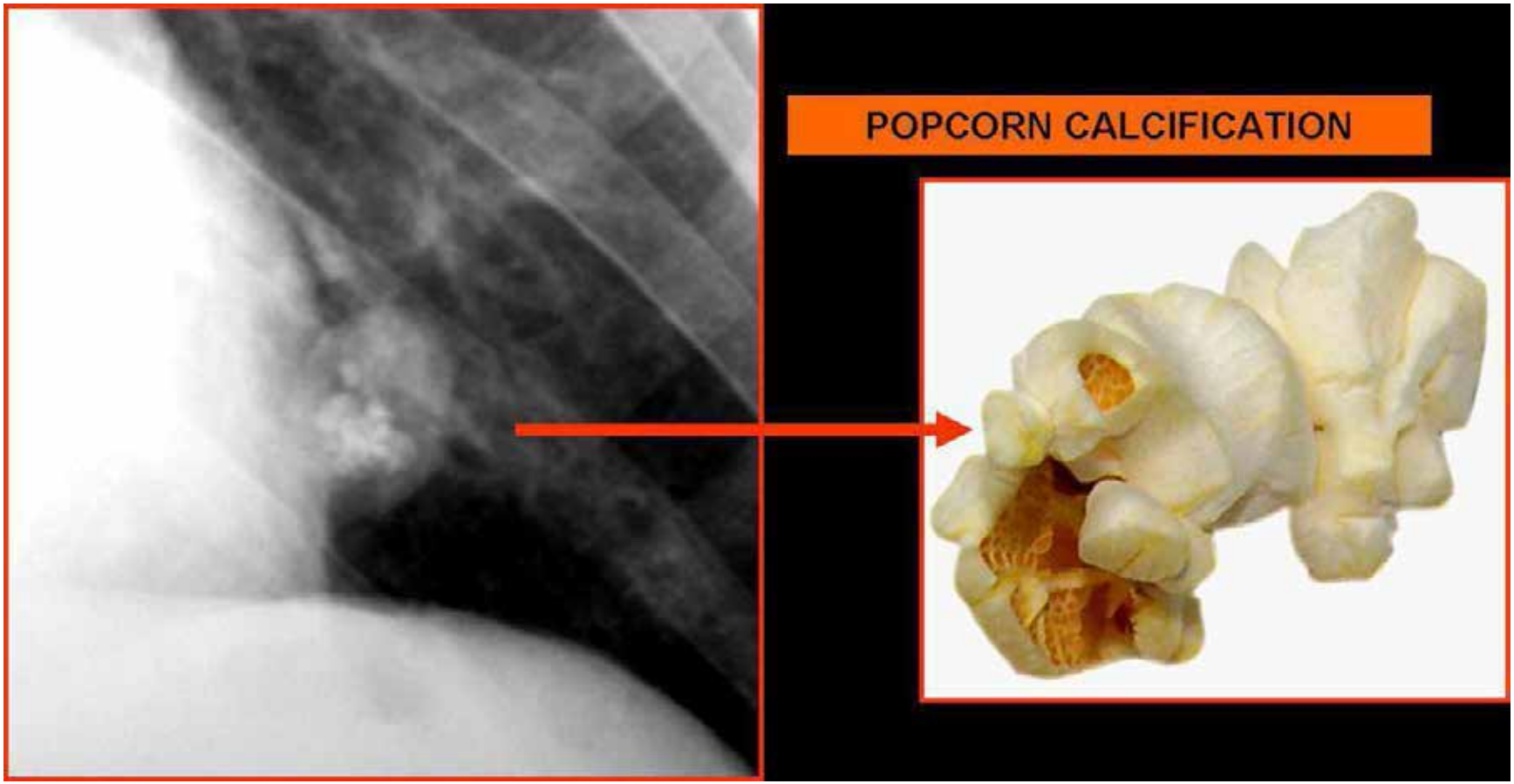
treatment and prognosis

- amenable to resection
- 5-year survival is 95%

hamartomas

- peak incidence at age 60, more common in men vs. women
- consist of normal pulmonary tissue components in a disorganized fashion
- usually peripheral, clinically silent, and benign in behaviour
- CXR:
  clustered “popcorn” pattern of calcification is pathognomonic for hamartoma

Chest radiograph demonstrates nodule with "popcorn calcification" in the right lower lobe representing hamartoma.



MALIGNANT NEOPLASMS

The burden of lung cancer

- **Strikes 900 000 men and 330 000 women each year**
- **Accounts for 18% of all cancer deaths**
- More than **a threefold increase in deaths since 1950**
- **Rates rising in women:**
  female lung cancer deaths outnumber male in some Nordic countries
- Has overtaken breast cancer in several countries, making it **the most common cause of cancer death in men and women**

Estimated Cancer Deaths in the US in 2013

Men 306,920			Women 273,430
Lung & Bronchus	28%	26%	Lung & Bronchus
Prostate	10%	14%	Breast
Colon & Rectum	9%	9%	Colon & Rectum
Pancreas	6%	7%	Pancreas
Liver	5%	5%	Ovary

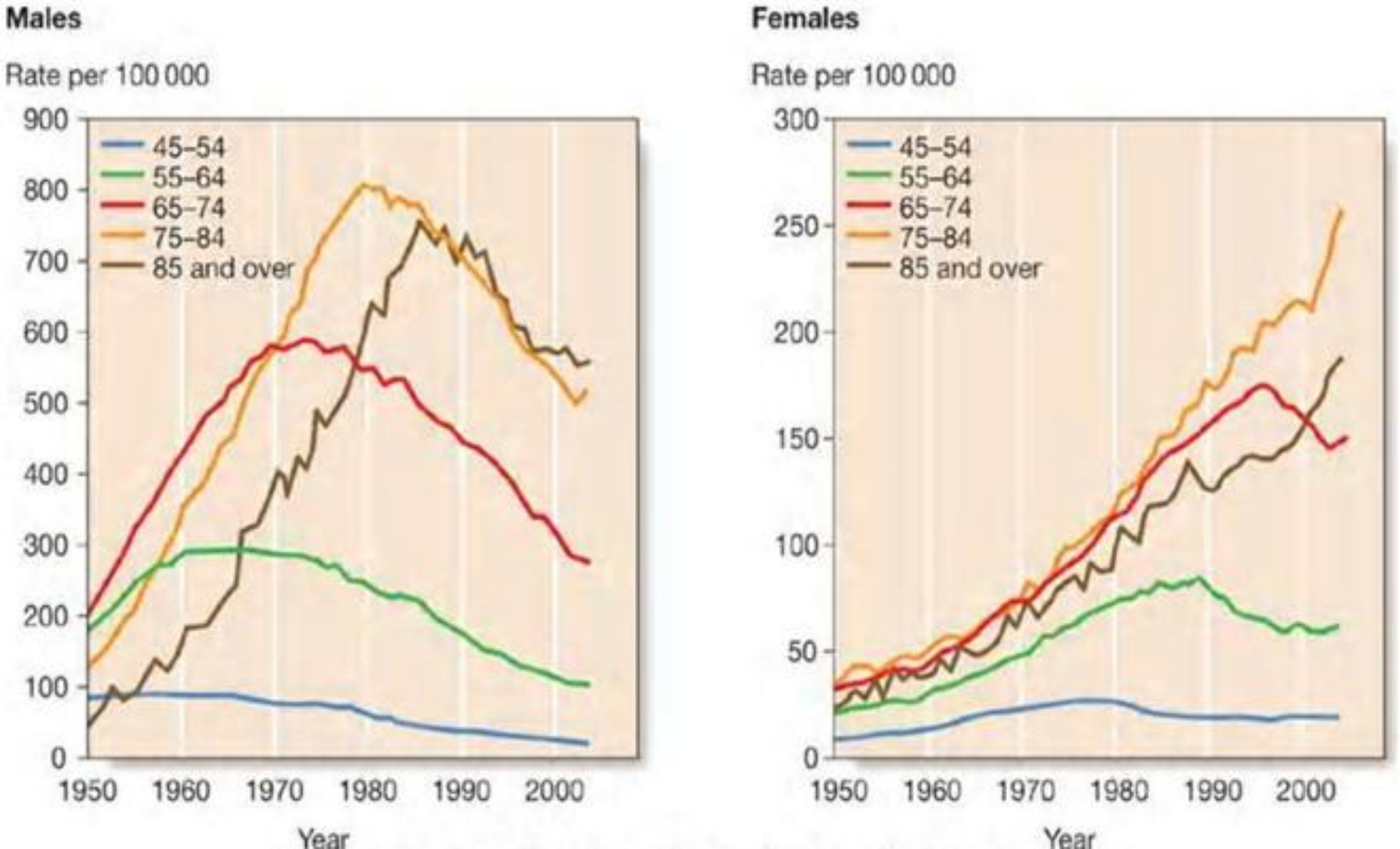
- American Cancer Society

Epidemiology

- incidence
  - most common cancer in men and women
  - most common cause of cancer death in men and women

- prognosis remains poor, with fewer than 30% of patients surviving at 1 year and 6-8 % at 5 years.

Mortality trends from lung cancer in England and Wales, 1950–2004 by age and year of death.



risk factors

- cigarette smoking:
  - 85% of lung cancer related to smoking
  - proportional to the amount smoked and to the tar content of cigarettes.
  - heavy smokers is 40 times that in non-smokers.

- asbestos (especially if smoker)

- radiation:
  radon, uranium (especially if smoker)

- arsenic, chromium, nickel

- genetic damage

- parenchymal scarring:
  granulomatous disease, fibrosis, scleroderma

- passive exposure to cigarette smoke : 5% of all lung cancer deaths.

- air pollution: exact role is uncertain

Smoking Facts

- Tobacco use is the leading cause of lung cancer
- 87% of lung cancers are related to smoking
- Risk related to:
  - age of smoking onset
  - amount smoked
  - gender
  - product smoked
  - depth of inhalation

Pathological Classification

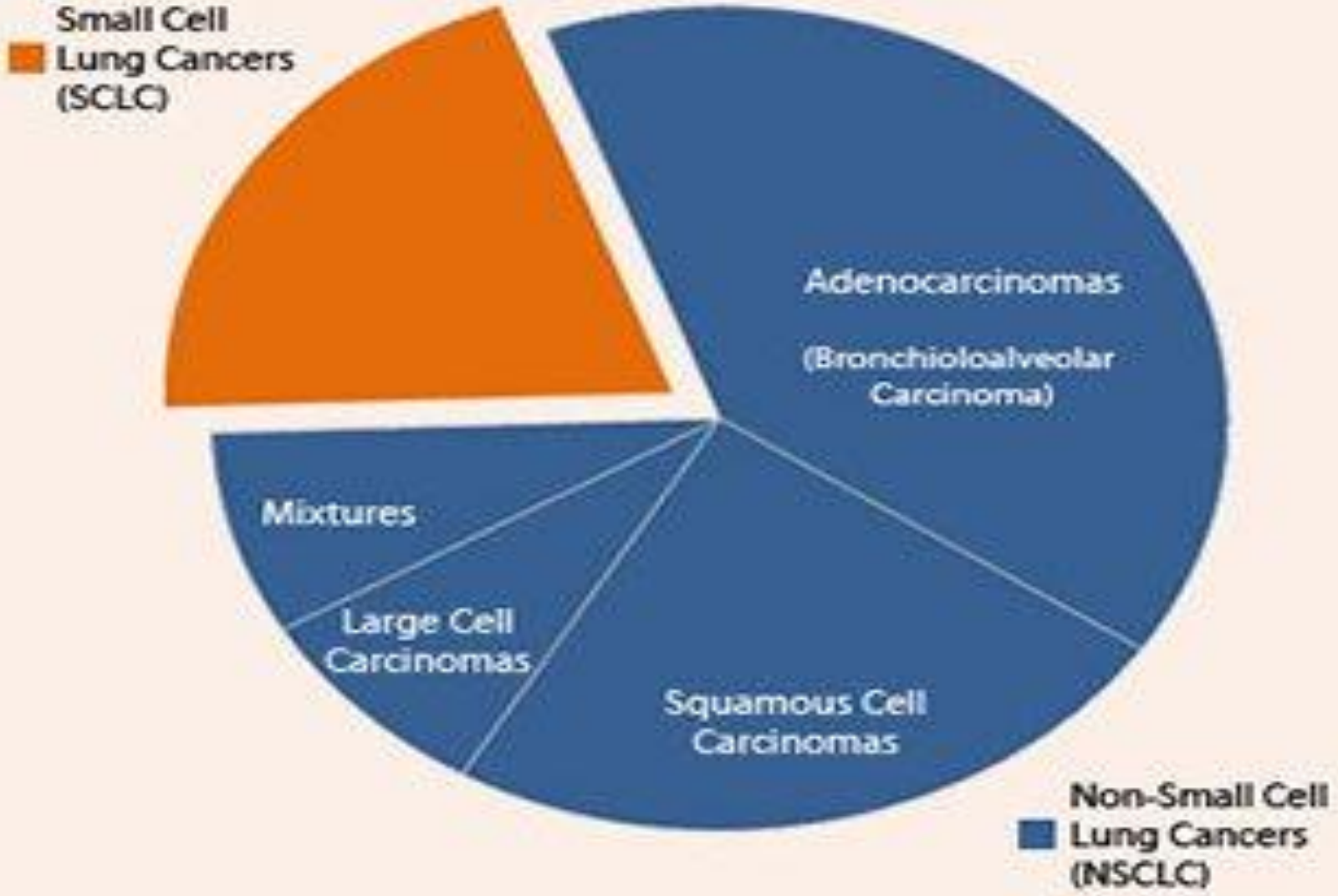
- bronchogenic cancer (90%)
  - incidence of adenocarcinoma is increasing
- bronchioloalveolar cancer (5%)
- bronchial adenoma (3%)
- lymphoma
- secondary metastases:

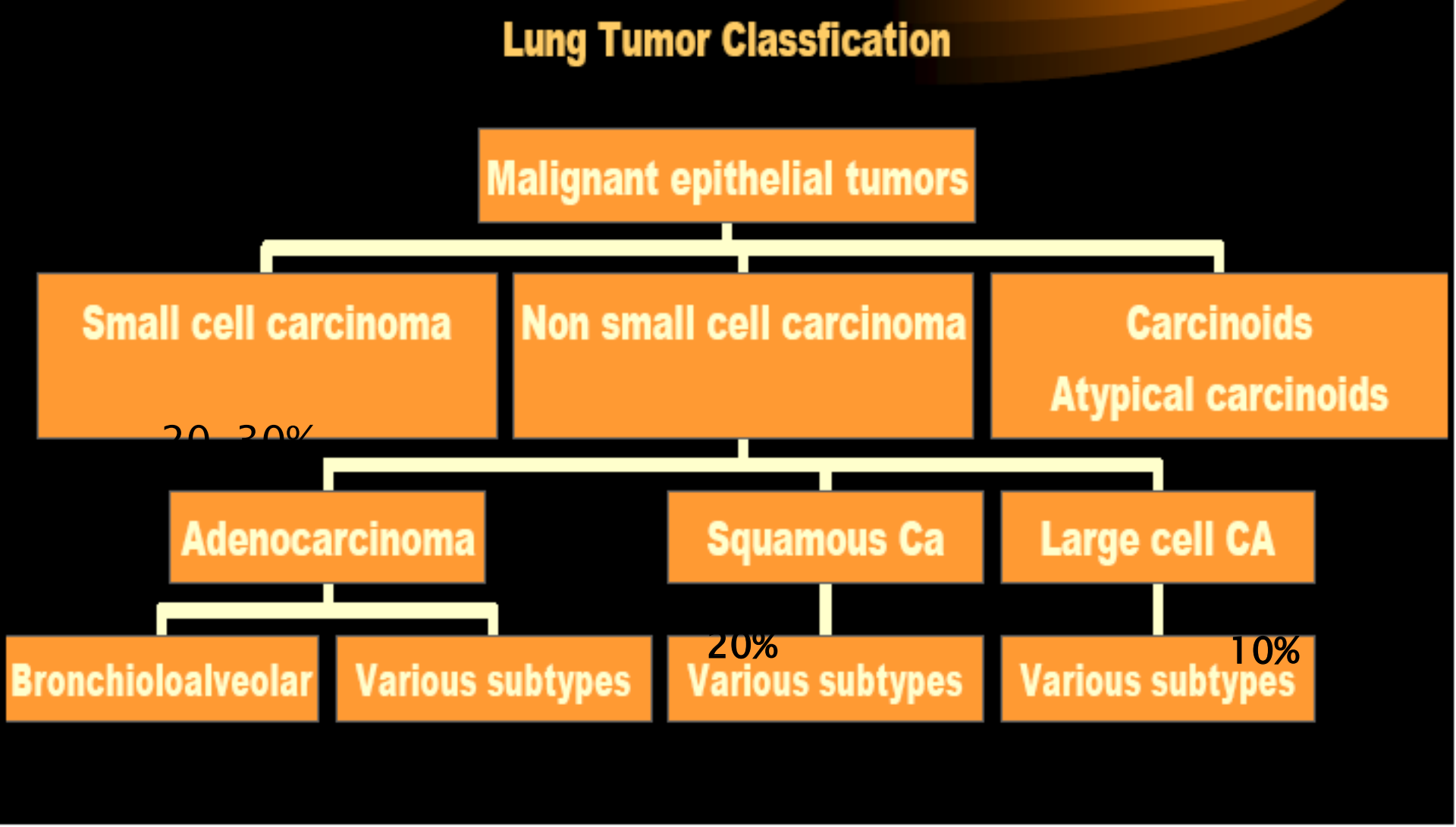
  breast, colon, prostate, kidney, thyroid, stomach, cervix, rectum, testes, bone, melanoma

Common cell types in bronchial carcinoma

Cell type	%
Squamous	35
Adenocarcinoma	30
Small-cell	20
Large-cell	15

Lung Cancer Types





- Each different type has different natural histories and responses to therapy

Characteristics of Bronchogenic Cancer

Cell Type	Frequency	Correlation with Smoking	Location	Histology	Metastasis
Adenocarcinoma	35%-M; 40%-F	Weak	Peripheral	Glandular, mucin producing	Early, distant
Squamous cell cancer (SCC) (may cavitate)	30%	Strong	Central	keratin; intercellular bridges	Slow, local invasion
SCLC	25%	Strong	Central	Oat cell, neuroendocrine origin in endobronchial (Kulchitsky) cells	Disseminated at presentation
Large cell cancer	10%	Yes	Peripheral	Anaplastic, undifferentiated	Early, distant (may cavitate)

Clinical Presentation

- tumour occurs in a large bronchus: symptoms arise early
- tumours originating in a peripheral bronchus can grow very large without producing symptoms
- Peripheral squamous tumours: central necrosis and cavitation(lung abscess)
- may involve the pleura either directly or by lymphatic spread
- extend into the chest wall
- invading the intercostal nerves or the brachial plexus and causing pain.
- Lymphatic spread to mediastinal and supraclavicular lymph nodes
- Blood-borne metastases : liver, bone, brain, adrenals and skin.
- a small primary tumour may cause widespread metastatic deposits (small-cell lung cancers)

Clinical Presentation

❑ initial symptoms and signs :

- cough (75%) :
  most common early symptom, often dry; beware of chronic cough that changes in character

- dyspnea (60%) :
  caused by collapse or pneumonia, or by a large pleural effusion or diaphragmatic paralysis.

- chest pain (45%)

- hemoptysis (35%) :
  common, especially with central bronchial tumours , massive haemoptysis

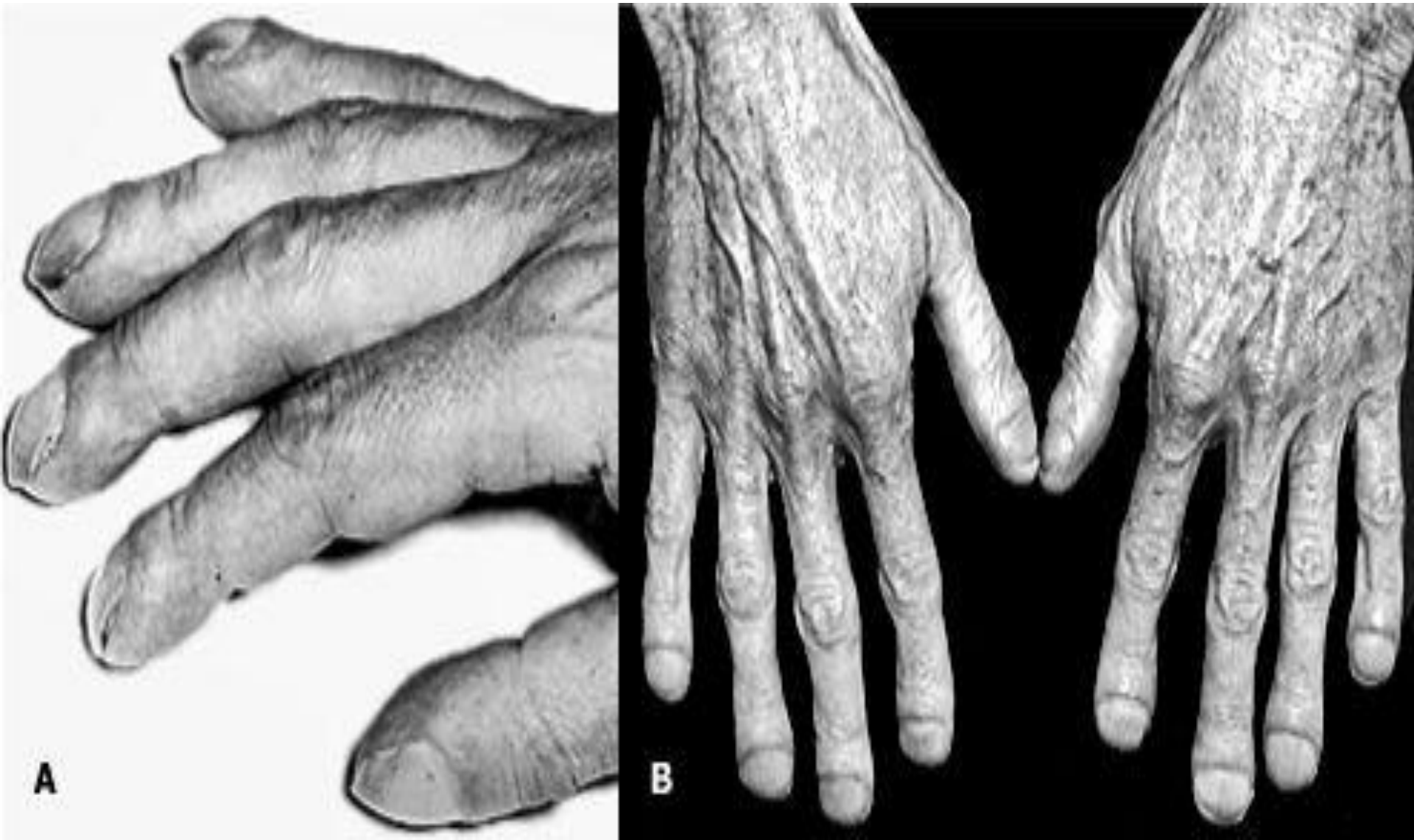
- other pain (25%) :
  Pleural pain (malignant pleural invasion) , Intercostal nerve involvement causes pain in the distribution of a thoracic dermatome.

- clubbing (21%) :
  Overgrowth of the soft tissue of the terminal phalanx leading to increased nail curvature

- hypertrophic pulmonary osteoarthropathy (HPOA), characterised by periostitis of the long bones, most commonly the distal tibia, fibula, radius and ulna.

- constitutional signs: anorexia, weight loss, fever, anemia

Clubbing :
A) Side and B) top view of nail bed hypertrophy causing a distal enlargement of the fingers in a patient with lung cancer.



Clinical Presentation

- *Bronchial obstruction :*
  - collapse of a lobe or lung, with breathlessness

  - Partial bronchial obstruction : unilateral wheeze , pneumonia or lung abscess

  - Horner's syndrome :
  (ipsilateral partial ptosis, enophthalmos, miosis and hypohidrosis of the face) due to involvement of the sympathetic chain at or above the stellate ganglion.

  - Pancoast's syndrome :
  (pain in the shoulder and inner aspect of the arm, sometimes with small muscle wasting in the hand) indicates malignant destruction of the T1 and C8 roots in lower part of the brachial plexus by an apical lung tumour.

Causes of large bronchus obstruction

Common

- Bronchial carcinoma or adenoma
- Enlarged tracheobronchial lymph nodes (malignant or tuberculous)
- Inhaled foreign bodies (especially right lung and in children)
- Bronchial casts or plugs consisting of inspissated mucus or blood clot (especially asthma, cystic fibrosis, haemoptysis, debility)
- Collections of mucus or mucopus retained in the bronchi as a result of ineffective expectoration (especially post-operative following abdominal surgery)

Rare

- Aortic aneurysm
- Giant left atrium
- Pericardial effusion
- Congenital bronchial atresia
- Fibrous bronchial stricture (e.g. following TB or bronchial surgery/lung transplant)

19.74 Non-metastatic extrapulmonary manifestations of bronchial carcinoma

Endocrine (Ch. 20)

- Inappropriate antidiuretic hormone secretion causing hyponatraemia
- Ectopic adrenocorticotrophic hormone secretion
- Hypercalcaemia due to secretion of parathyroid hormone-related peptides
- Carcinoid syndrome (p. 887)
- Gynaecomastia

Neurological (Ch. 26)

- Polyneuropathy
- Myelopathy
- Cerebellar degeneration
- Myasthenia (Lambert-Eaton syndrome, p. 1219)

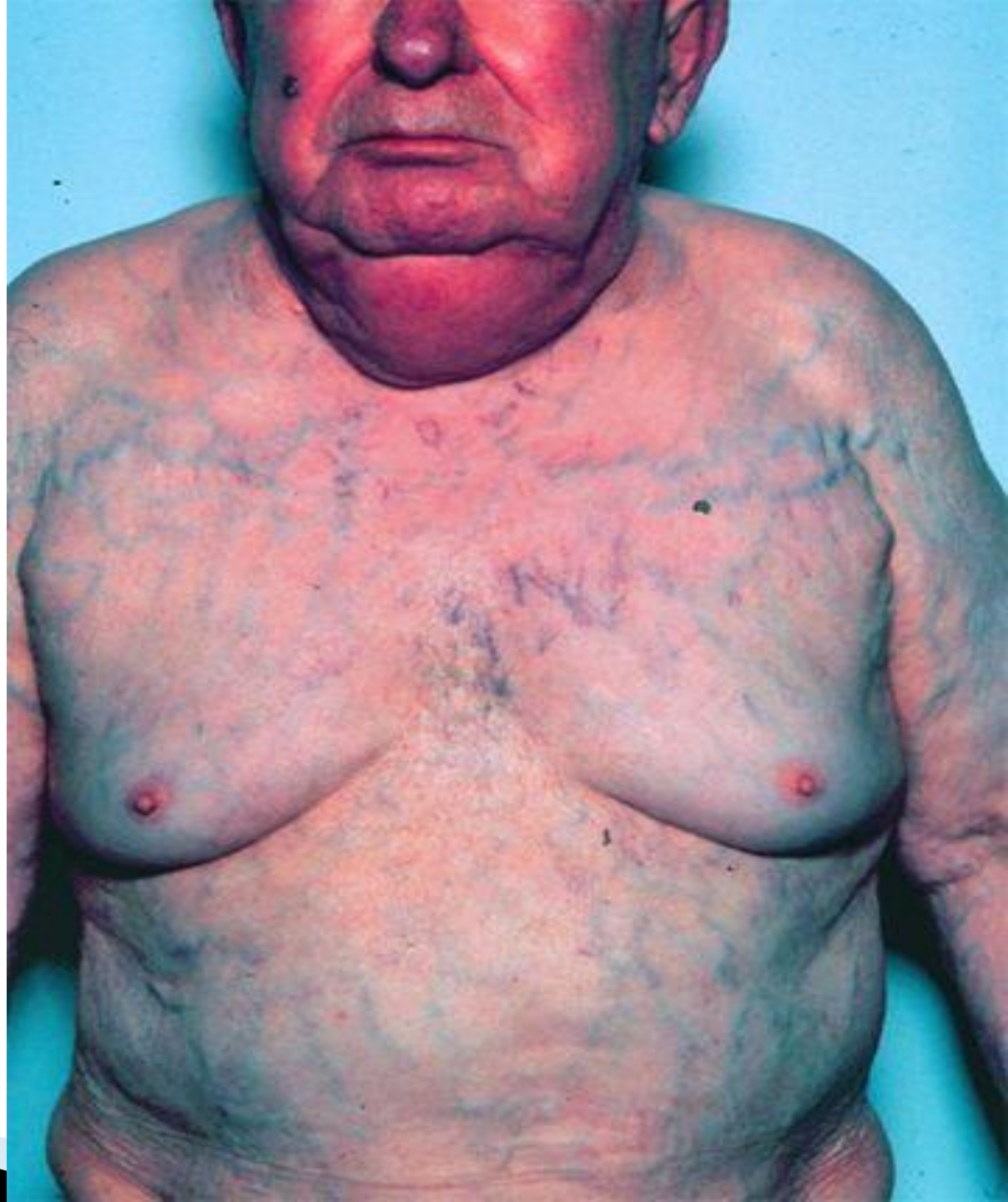
Other

- Digital clubbing
- Hypertrophic pulmonary osteoarthropathy
- Nephrotic syndrome
- Polymyositis and dermatomyositis
- Eosinophilia

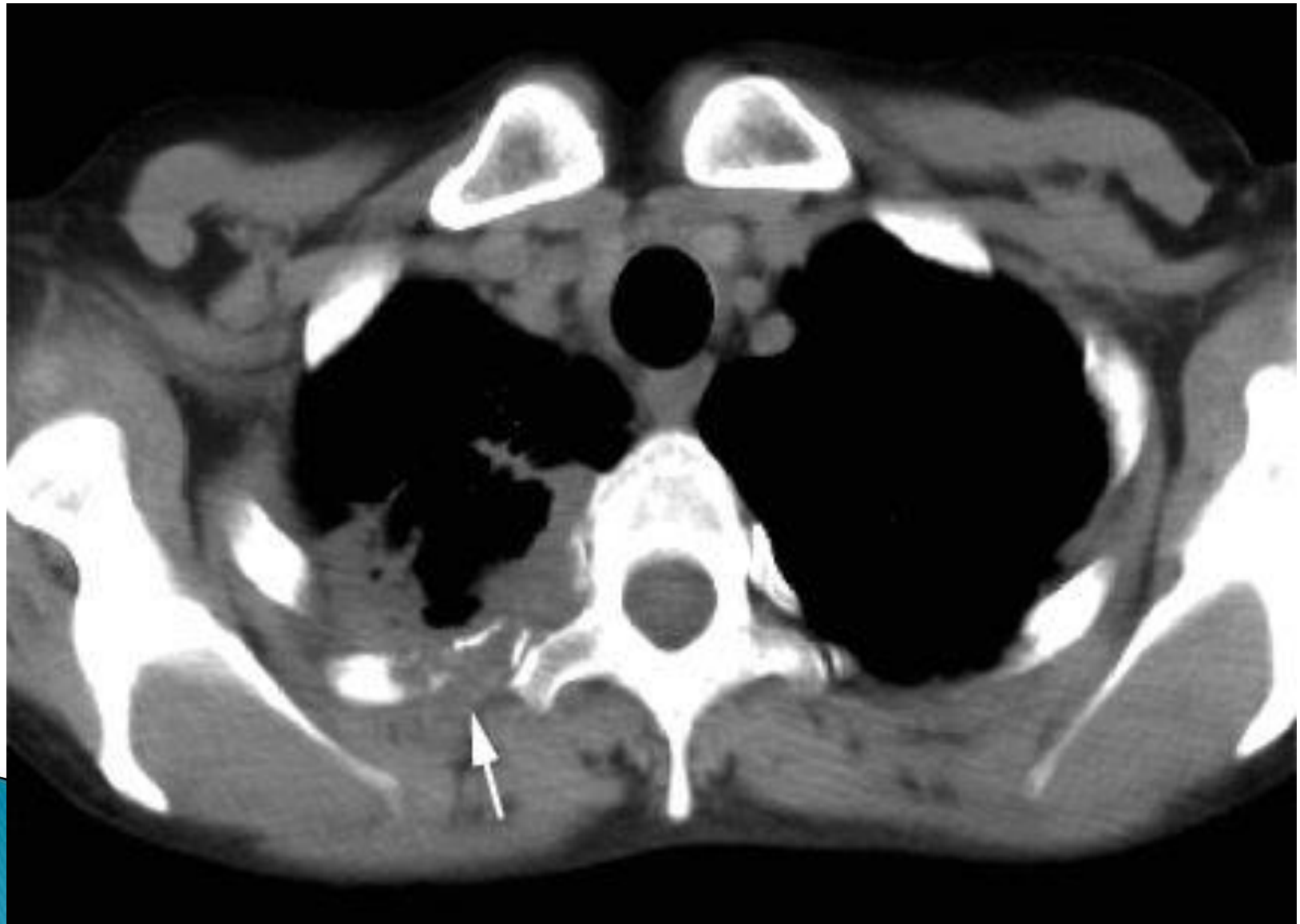
Clinical Presentation

- **local extension**
  - **lung, hilum, mediastinum, pleura** : pleural effusion, atelectasis, wheezing
  - **pericardium** : pericarditis, pericardial tamponade , arrhythmia
  - **esophageal compression**: dysphagia
  - **phrenic nerve** : paralyzed diaphragm
  - **recurrent laryngeal nerve** : hoarseness
  - **superior vena cava syndrome**:
    collateral circulation in chest and neck, facial/upper extremity edema and plethora, dyspnea, orthopnea,headache, nausea, syncope, visual changes, dizziness
  - **lung apex (Pancoast tumour)**: Horner's syndrome, brachial plexus palsy
  - **rib and vertebra** : erosion

Superior vena cava syndrome



Pancoast tumor



Clinical Presentation

- distant metastasis:

  - from lung to brain, bone, liver, adrenals
  - focal neurological defects, epileptic seizures, personality change
  - jaundice, bone pain or skin nodules.
  - Lassitude, anorexia and weight loss

- paraneoplastic syndromes :

  - inappropriate antidiuretic hormone secretion (SIADH)
  - ectopic adrenocorticotrophic hormone secretion .
    - most often associated with SCLC (small-cell lung cancer)

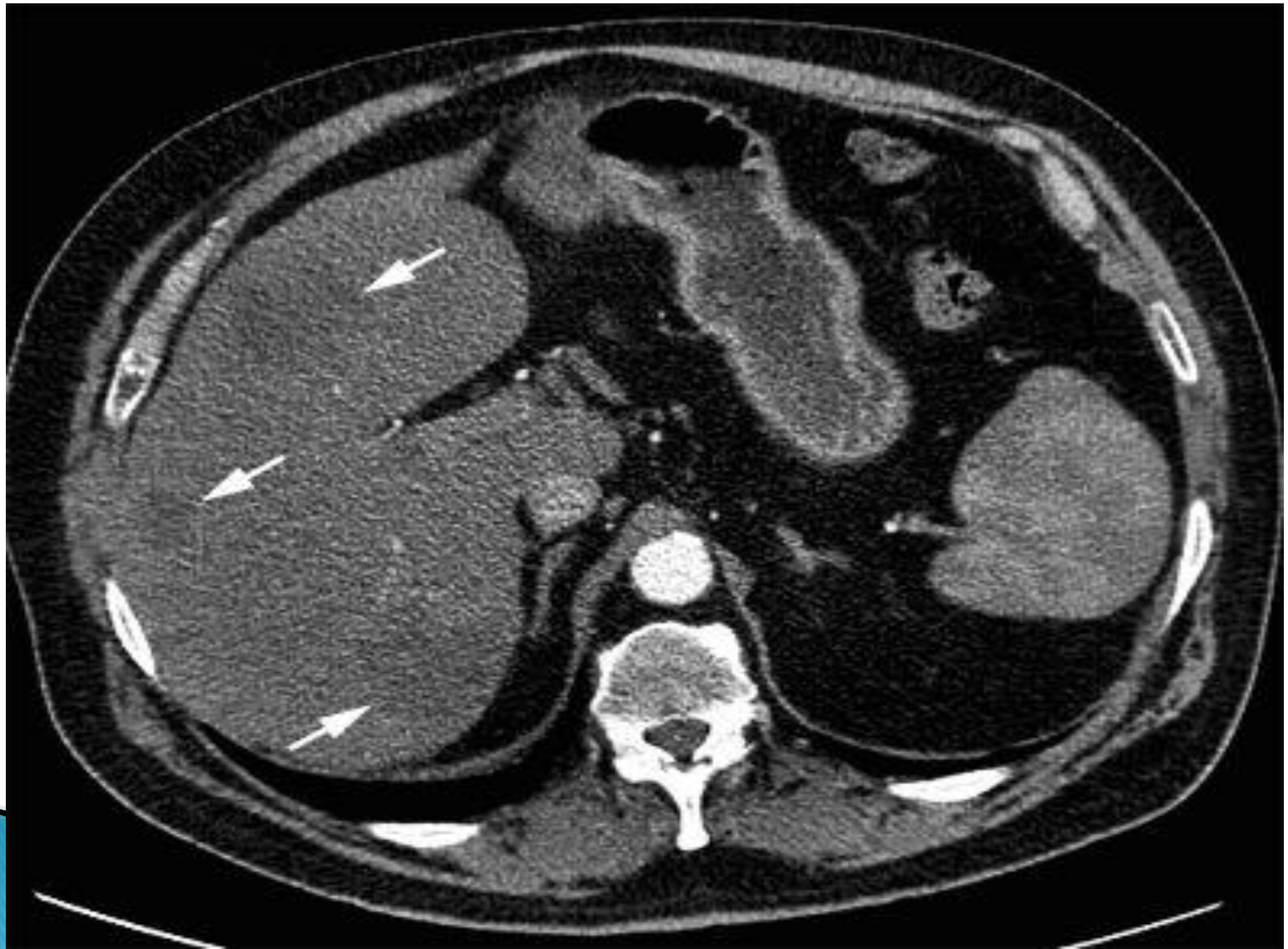
  - Hypercalcaemia is usually caused by squamous cell carcinoma.

Clinical findings suggesting metastatic disease

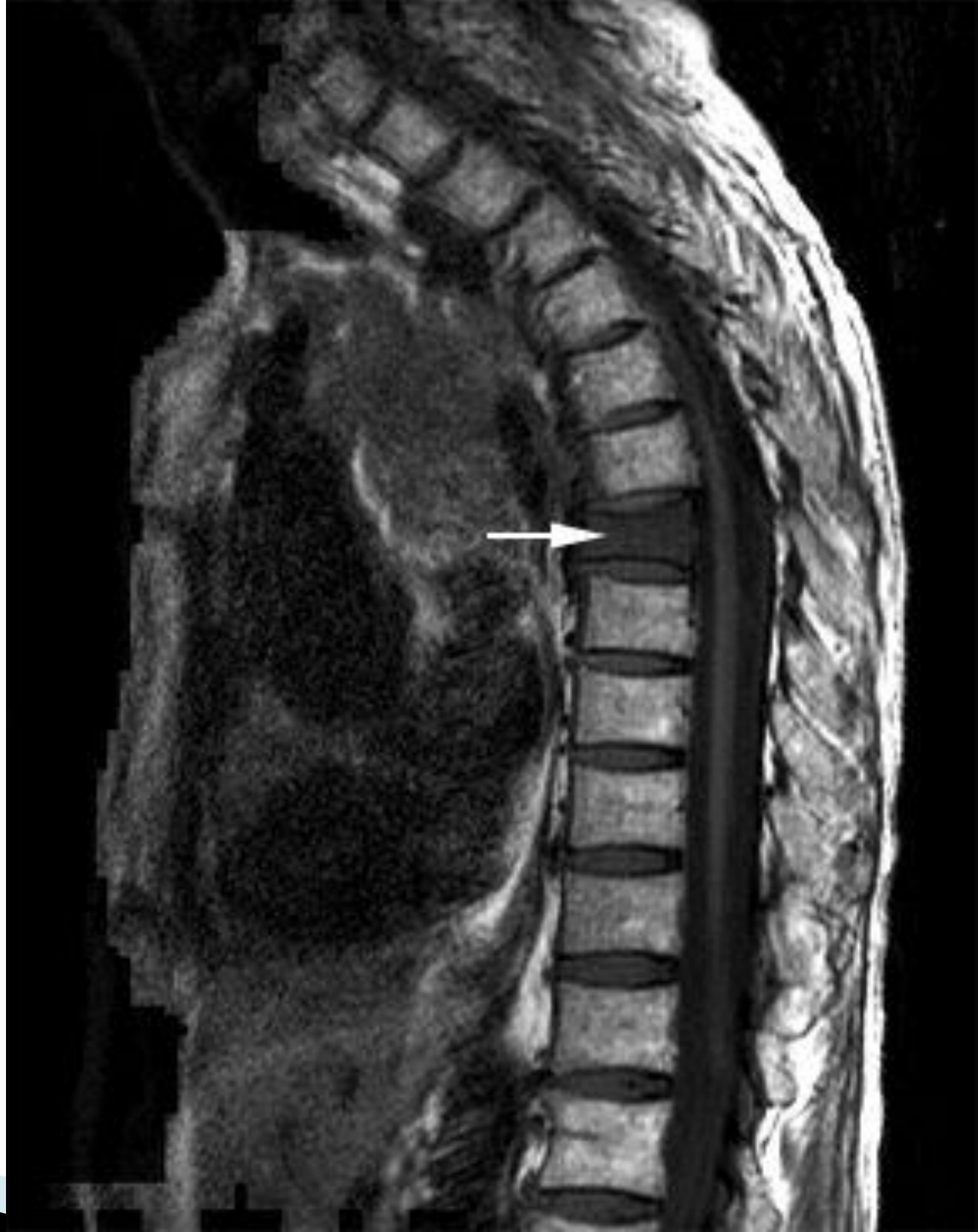
Symptoms elicited in history
Constitutional - weight loss >10 pounds
Musculoskeletal - focal skeletal pain
Neurologic - headaches, syncope, seizures, extremity weakness, recent change in mental status
Signs found on physical exam
Lymphadenopathy (>1 cm)
Hoarseness, superior vena cava syndrome
Bone tenderness
Hepatomegaly (>13 cm span)
Focal neurologic signs, papilledema
Soft tissue mass
Routine laboratory tests
Hematocrit, <40% in males
Hematocrit, <35% in females
Elevated alkaline phosphatase, GGT, SGOT

GGT: gamma-glutamyltransferase; SGOT: serum glutamicoxalonacetic transaminase.

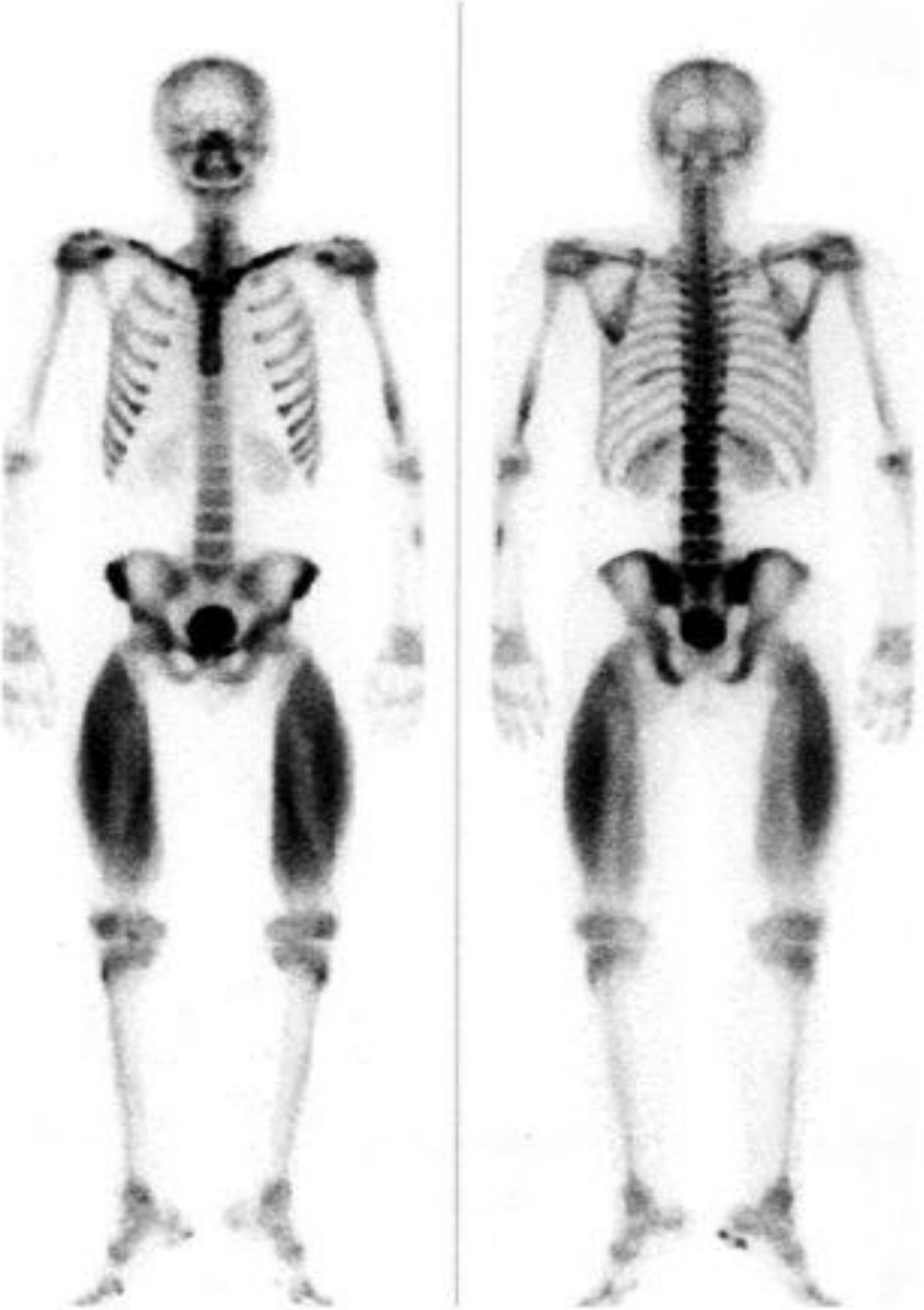
Liver metastasis-CT



MRI of a 58-year-old woman with back pain showing a hyperintense mass on T1 (shown) and T2 images involving the T8 vertebral body consistent with neoplastic involvement. Supraclavicular node biopsy confirmed small cell carcinoma.

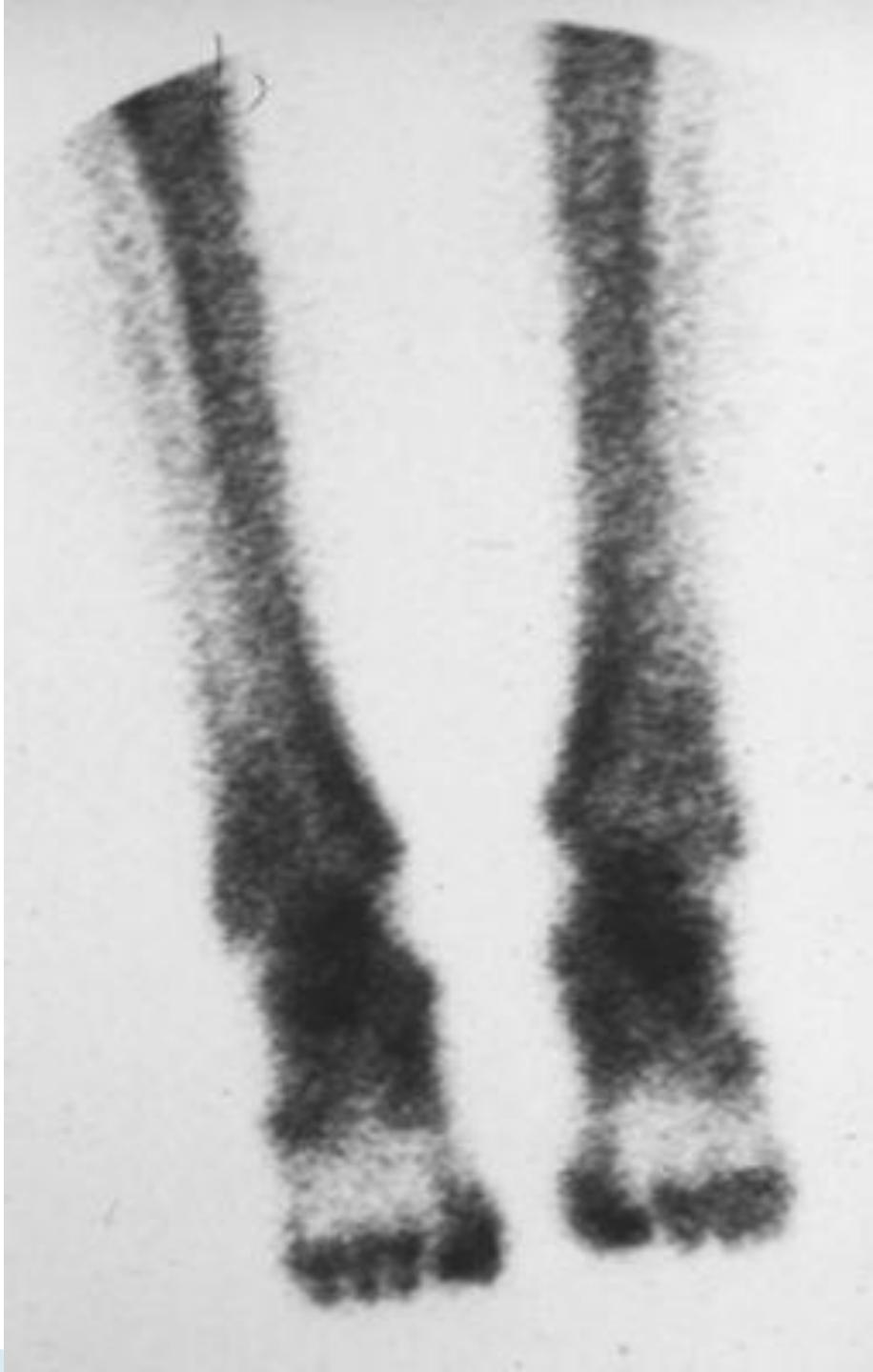


Normal bone scan for comparison.

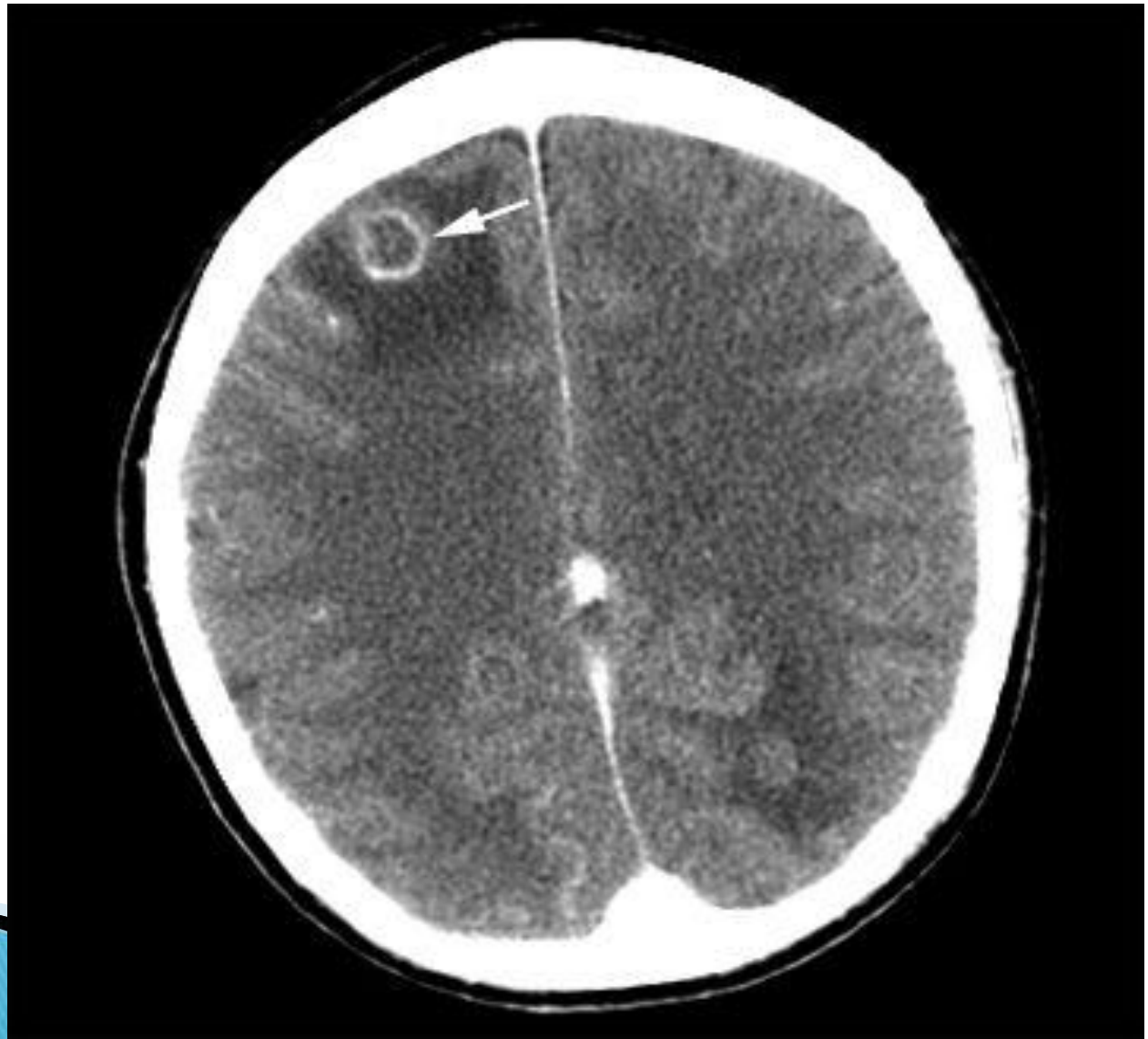


Hypertrophic pulmonary osteoarthropathy

Bone scan showing diffuse uptake by the long bones in a patient with painful arthropathy and lung cancer.



Brain metastasis



Paraneoplastic syndromes

	Clinical Presentation	Associated Malignancy
Skeletal	Hypertrophic pulmonary osteoarthropathy (clubbing)	Bronchogenic cancer (not SCLC)
Dermatologic	Acanthosis nigricans	Lung cancer
	Dermatomyositis	Bronchogenic cancer
Endocrine	Hypercalcemia (osteolysis or PTH)	Squamous cell cancer
	Hypophosphatemia	Squamous cell cancer
	Hypoglycemia	Sarcoma
	Cushing's syndrome (ACTH)	SCLC
	Somatostatinoma syndrome	Bronchial carcinoid
	SIADH	SCLC
Neuromyopathic	Eaton-Lambert syndrome	SCLC
	Polymyositis	
	Subacute cerebellar degeneration	
	Spinocerebellar degeneration	
	Peripheral neuropathy	
Vascular/Hematologic	Nonbacterial endocarditis	
	Trousseau's syndrome (migratory thrombophlebitis)	Bronchogenic cancer
	DIC	
Renal	Nephrotic syndrome	

Investigations

- initial diagnosis
  - imaging: CXR ,CT
    (direct histological sampling procedures).
  - cytology: sputum (at least three sputum samples)
  - biopsy:
    - bronchoscopy :
      (three-quarters of primary lung tumours can be visualised and sampled directly)
      blind' bronchoscopic washings and brushings
    - percutaneous needle biopsy under CT or ultrasound guidance
- staging work-up
  - blood work: LETs/LFTs, calcium, ALP
  - imaging: CXR, CT thorax and abdomen, skeletal survey, bone scan, neuroimaging
  - invasive: bronchoscopy, mediastinoscopy, mediastinotomy, thoracotomy

- 2/3 of primary lung CA is found in the upper lung;
  2/3 of metastases in the lower lung
  (hematogenous spread secondary to increased blood flow to the base of the lung).

Investigations

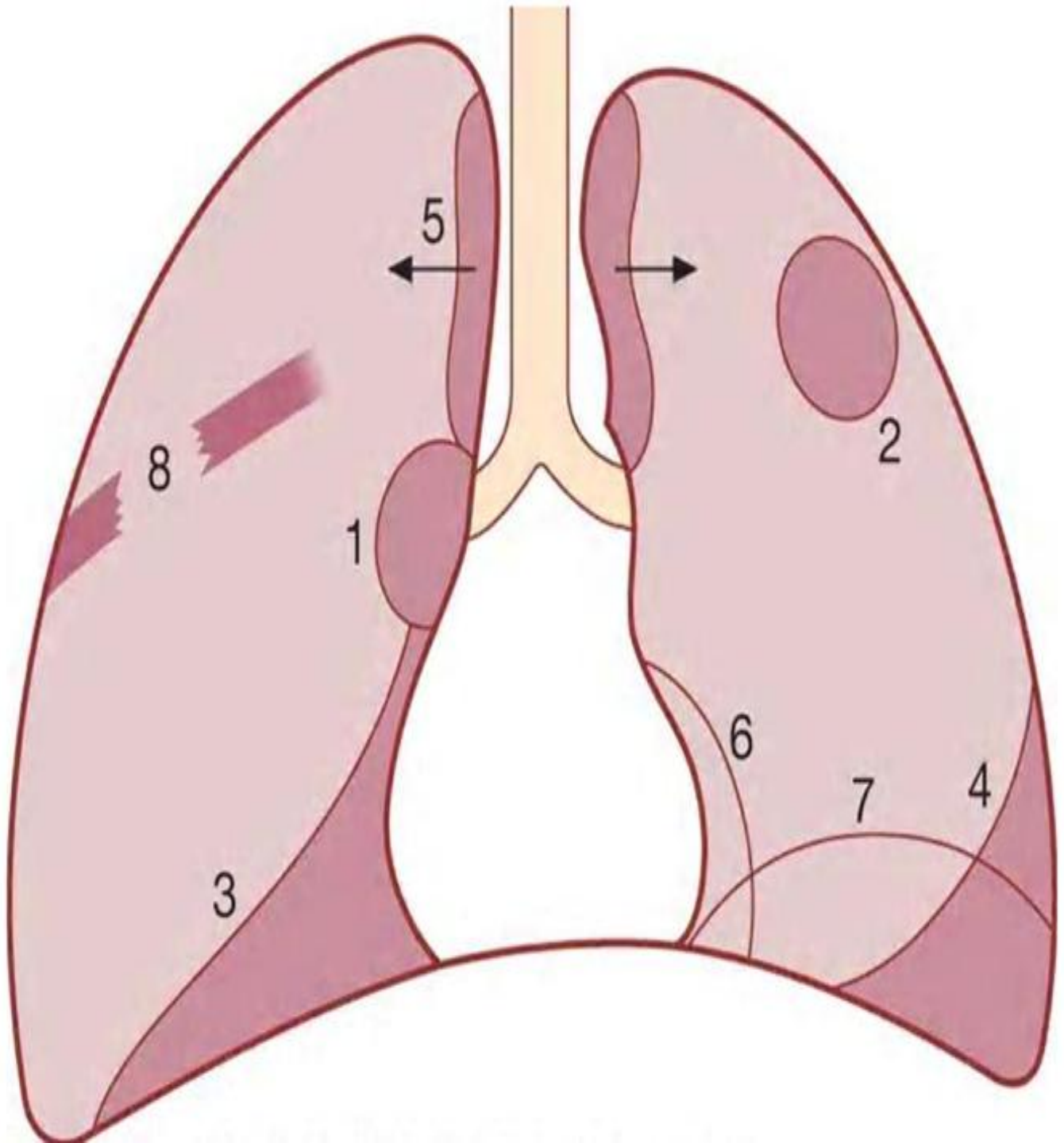
- **pleural effusions :**

  pleural aspiration and biopsy or thoracoscopy

- **metastatic disease:**

  needle aspiration or biopsy of affected lymph nodes, skin lesions, liver or bone marrow.

Common radiological presentations of bronchial carcinoma.



Common radiological presentations of bronchial carcinoma

❶ Unilateral hilar enlargement

- Central tumour. Hilar glandular involvement. However, a peripheral tumour in the apical segment of a lower lobe can look like an enlarged hilar shadow on the PA X-ray

❷ Peripheral pulmonary opacity (p. 657)

- Usually irregular but well circumscribed, and may contain irregular cavitation. Can be very large

❸ Lung, lobe or segmental collapse

- Usually caused by tumour within the bronchus leading to occlusion. Lung collapse may be due to compression of the main bronchus by enlarged lymph glands

❹ Pleural effusion

- Usually indicates tumour invasion of pleural space; very rarely, a manifestation of infection in collapsed lung tissue distal to a bronchial carcinoma

❺-❼ Broadening of mediastinum, enlarged cardiac shadow, elevation of a hemidiaphragm

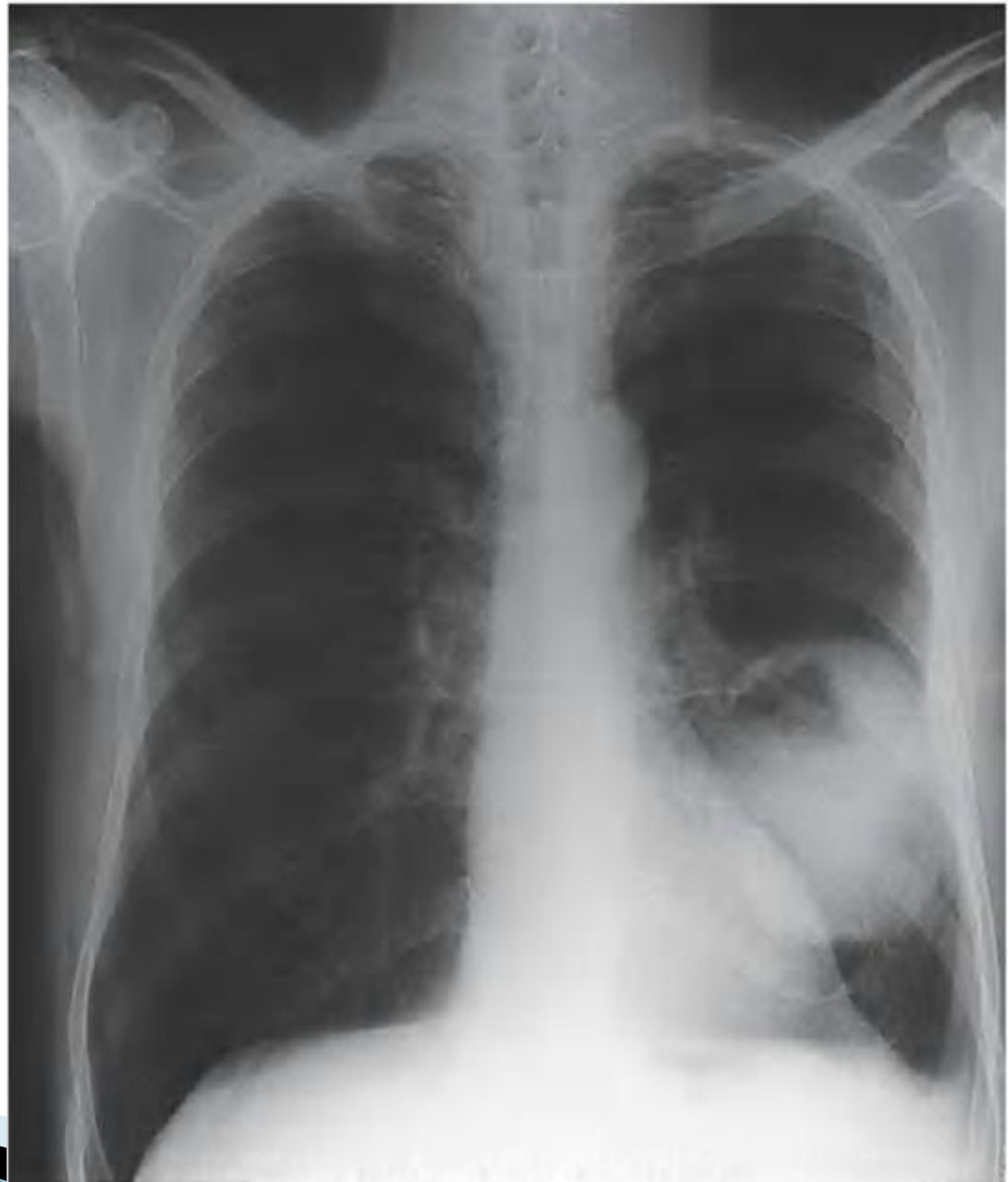
- Paratracheal lymphadenopathy may cause widening of the upper mediastinum. A malignant pericardial effusion will cause enlargement of the cardiac shadow. If a raised hemidiaphragm is caused by phrenic nerve palsy, screening will show it to move paradoxically upwards when patient sniffs

❽ Rib destruction

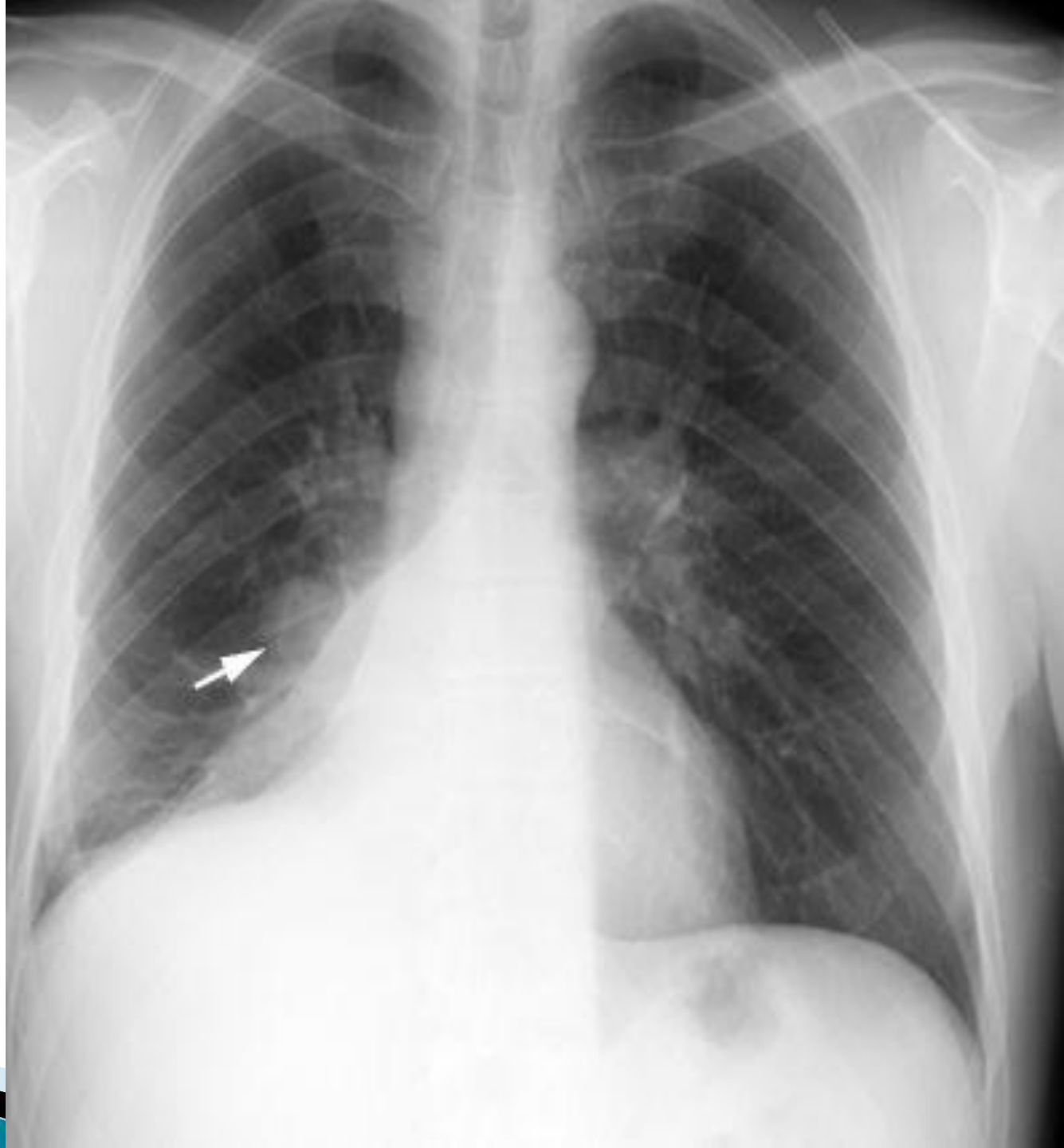
- Direct invasion of the chest wall or blood-borne metastatic spread can cause osteolytic lesions of the ribs

Large cavitated bronchial carcinoma in left lower lobe.

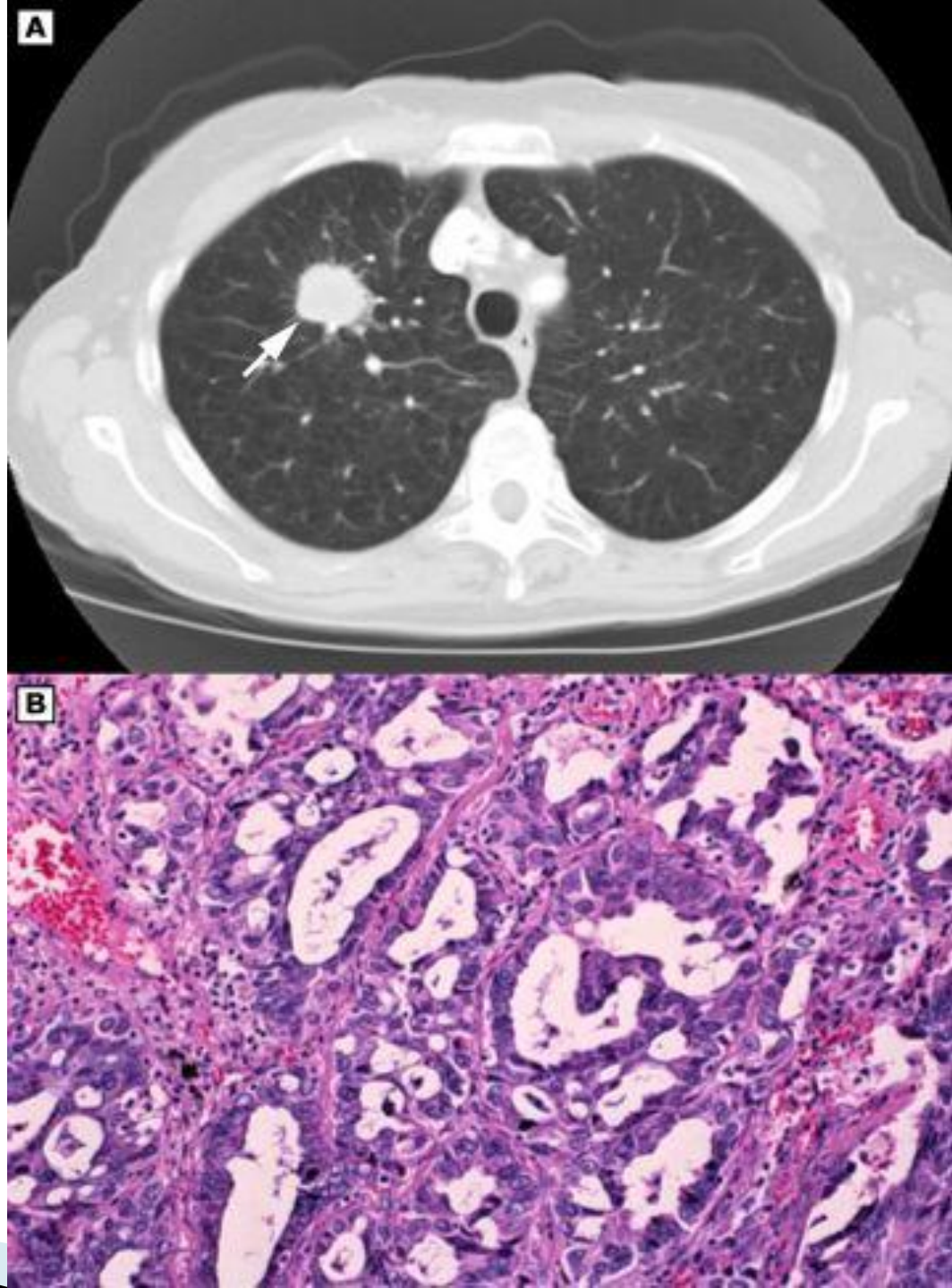
Large cavitated bronchial carcinoma in left lower lobe.



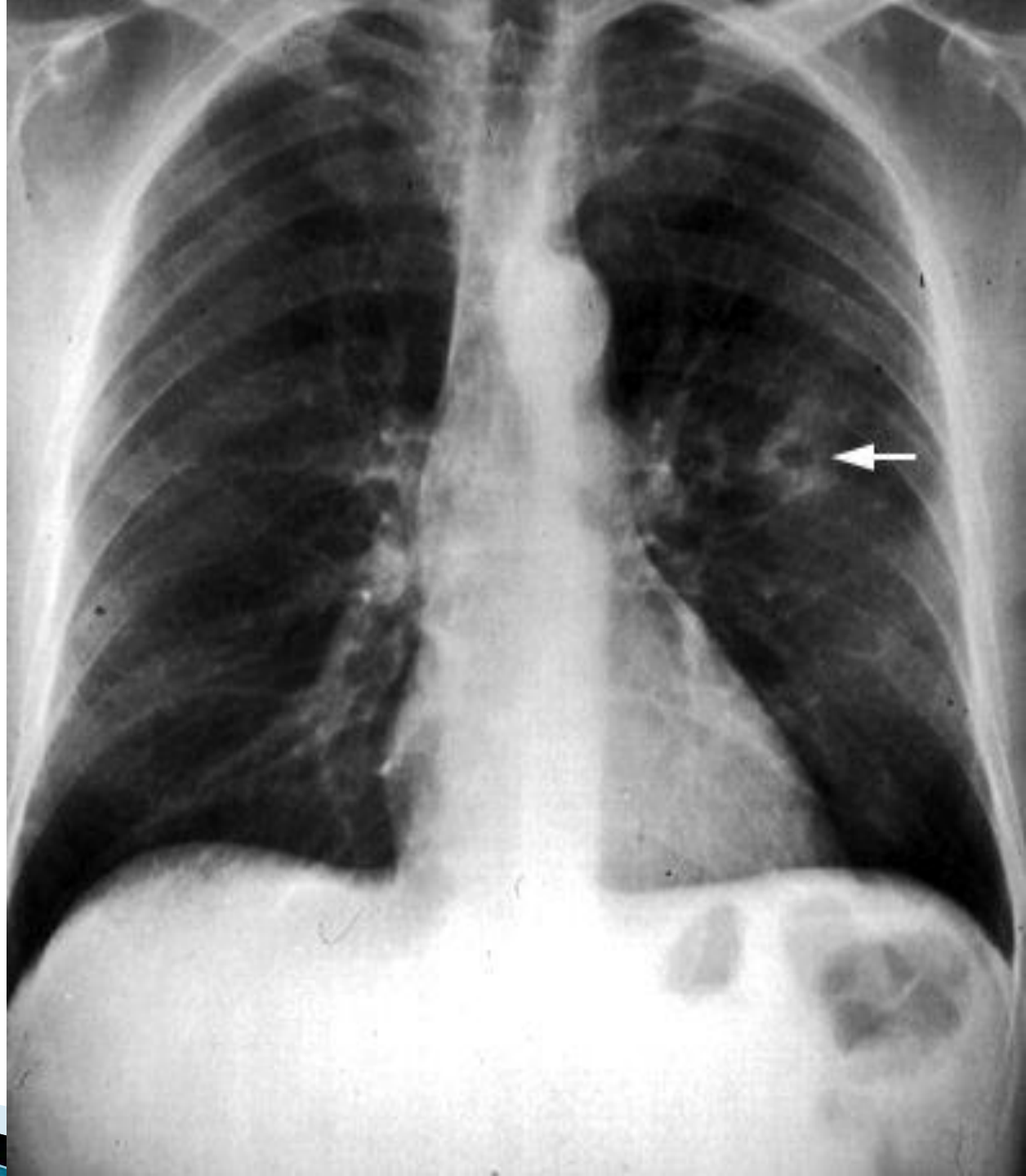
Squamous cell carcinoma
Chest radiograph in a 51-year-old man shows a right lower lobe mass and collapse of the right lower lobe.



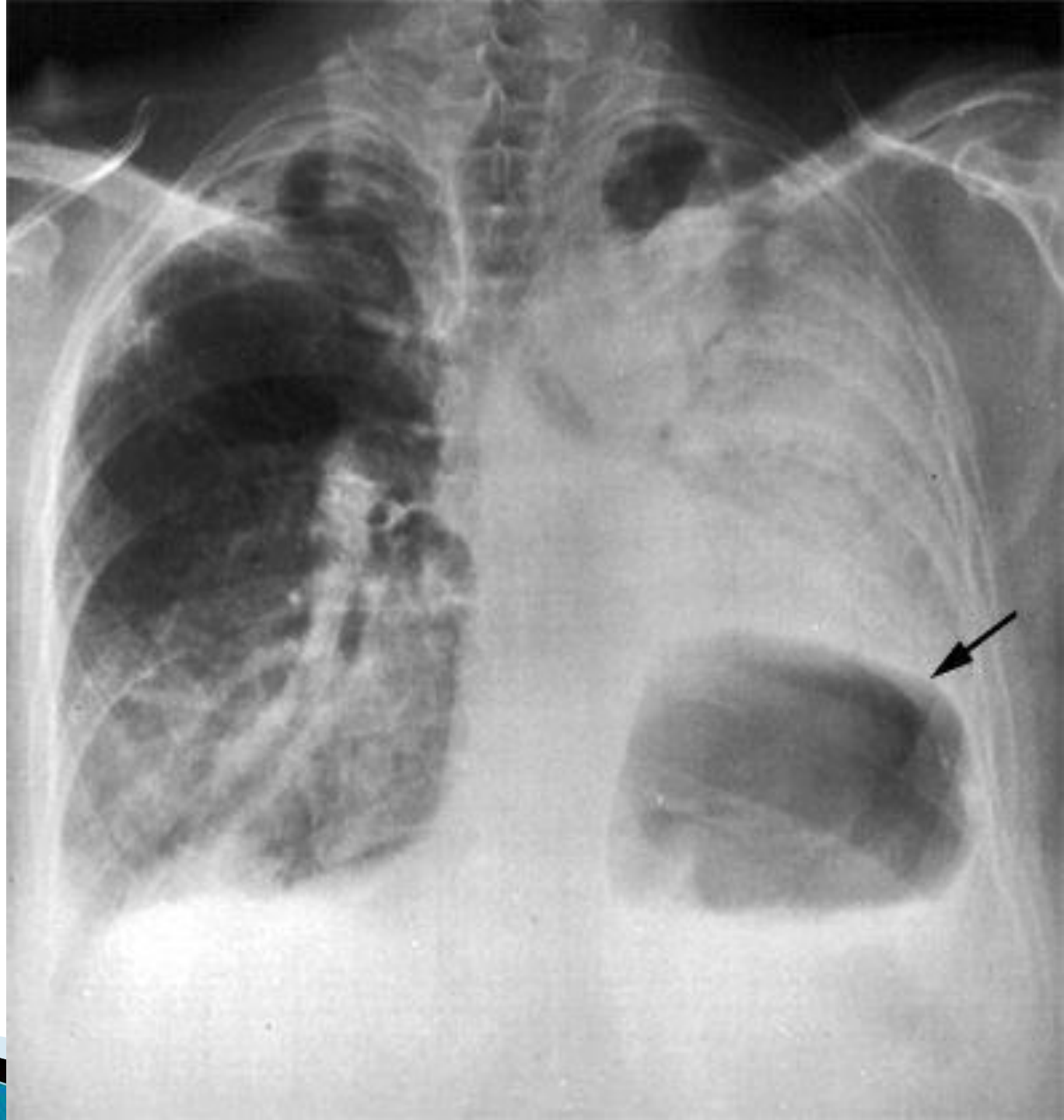
A) CT from a 63-year-old woman showing a spiculated, 2 cm right upper lobe lesion that was an adenocarcinoma at resection. B) Histology. This is an acinar type with presence of numerous irregularly shaped glands.



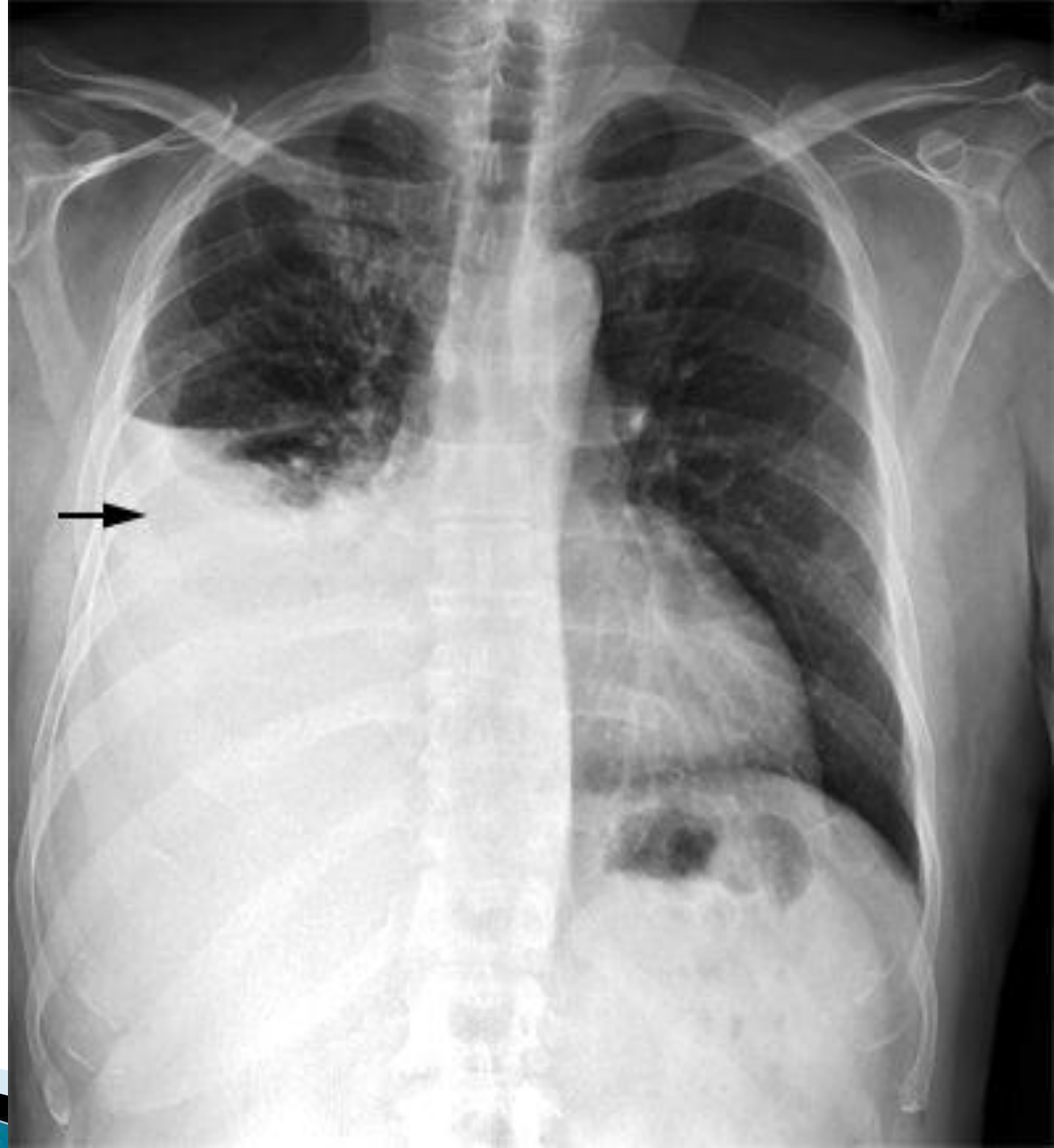
Chest radiograph in a 52-year-old man showing a cavitary nodule in the left mid-lung, which was a large cell carcinoma at resection.



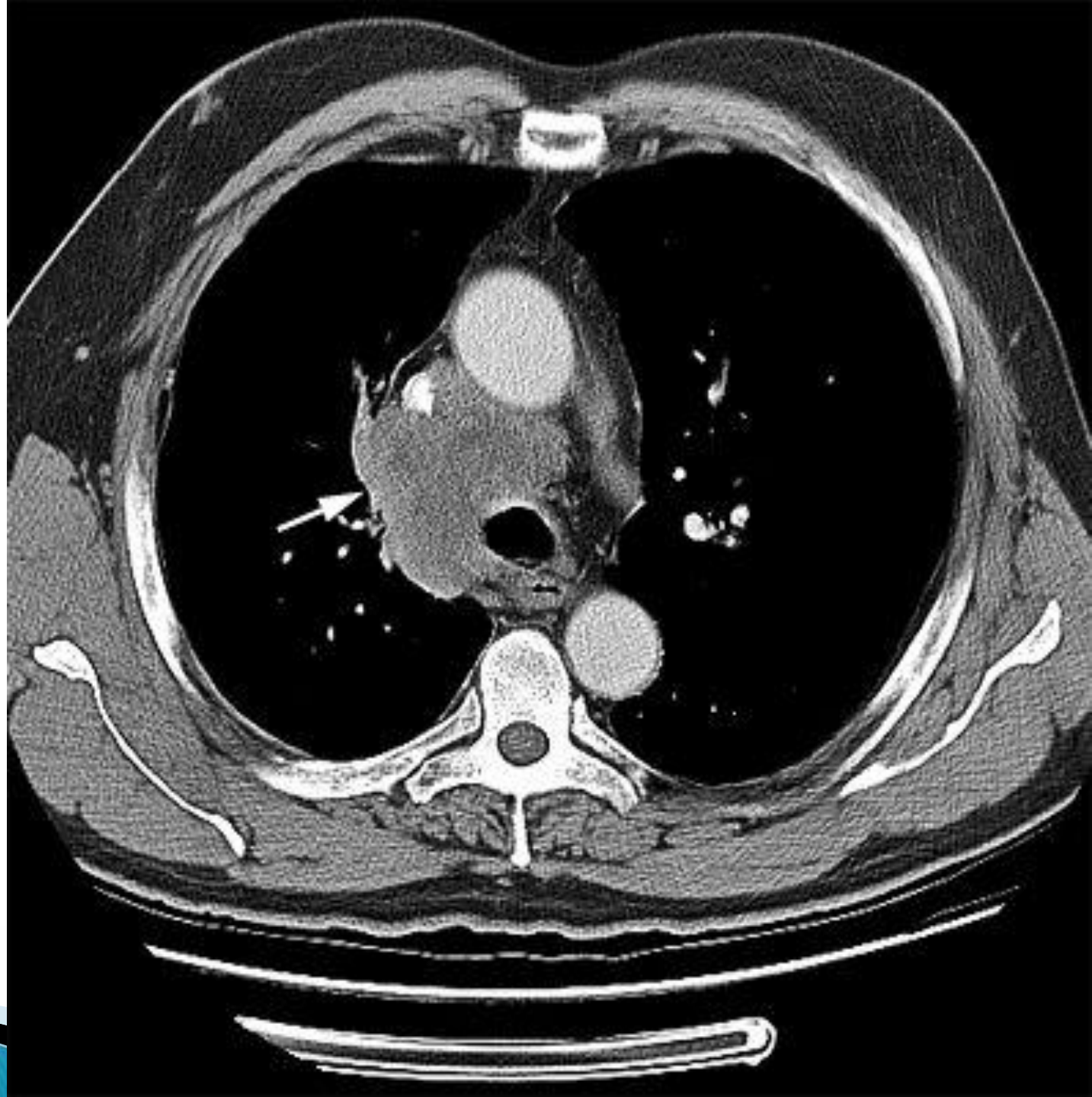
Left hemidiaphragm paralysis (confirmed by fluoroscopy) in a patient with extensive adenocarcinoma of the lung.



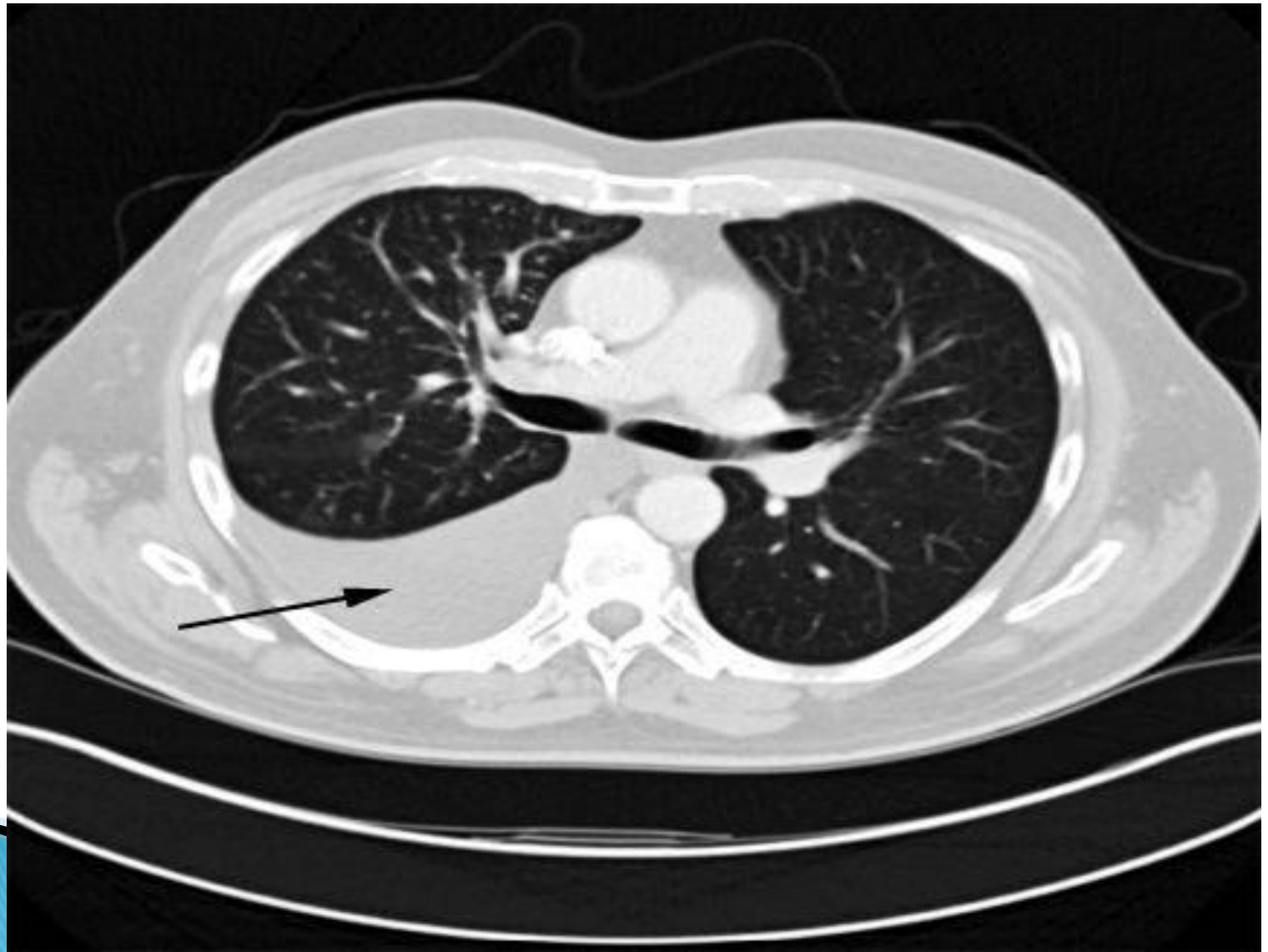
Large pleural effusion in a 60-year-old man cytologically positive for adenocarcinoma consistent with lung primary.



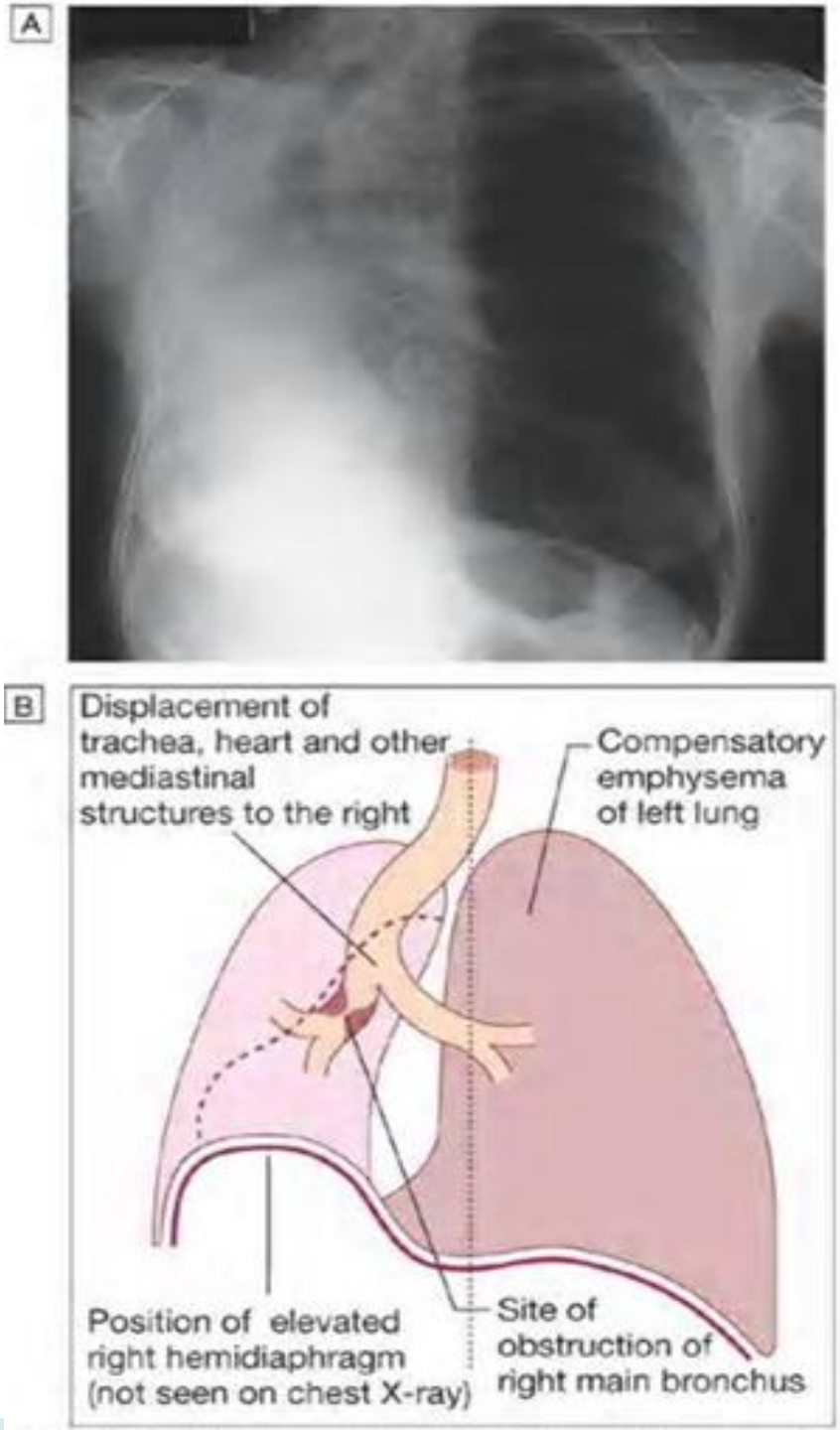
Chest CT scan from a 66-year-old man showing a bulky central mass with adenopathy confirmed by bronchoscopic needle biopsy as small cell carcinoma.



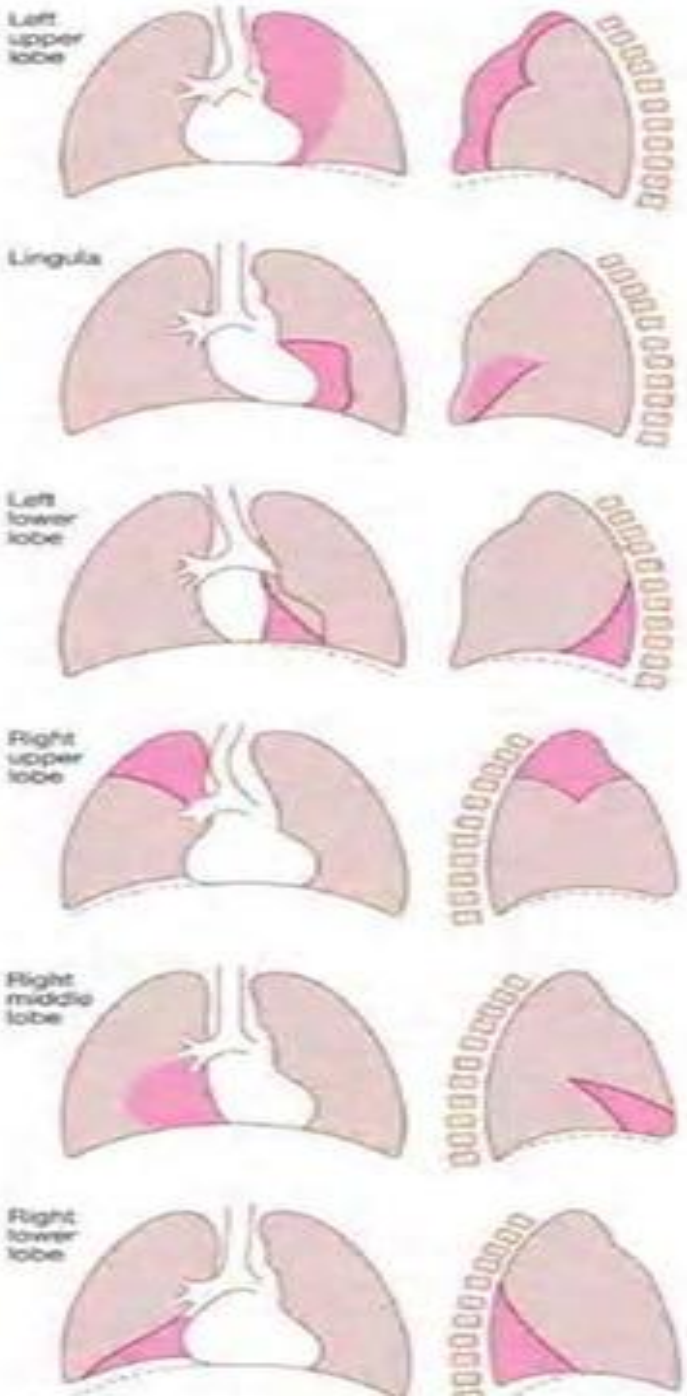
Malignant pleural effusion



Collapse of the right lung: effects on neighbouring structures.
A :Chest X-ray.
B : Abnormalities highlighted.

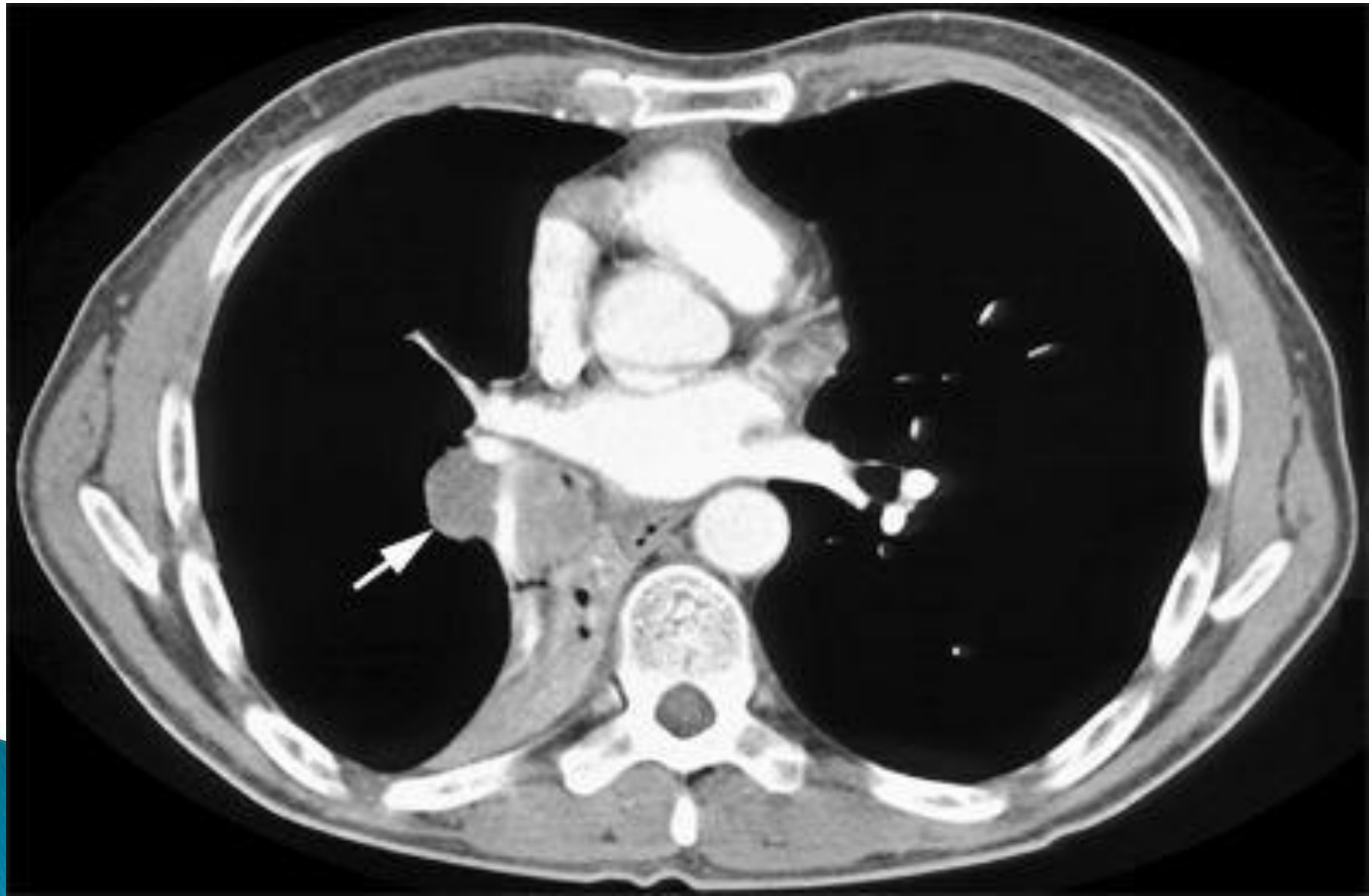


Radiological features of lobar collapse caused by bronchial obstruction.

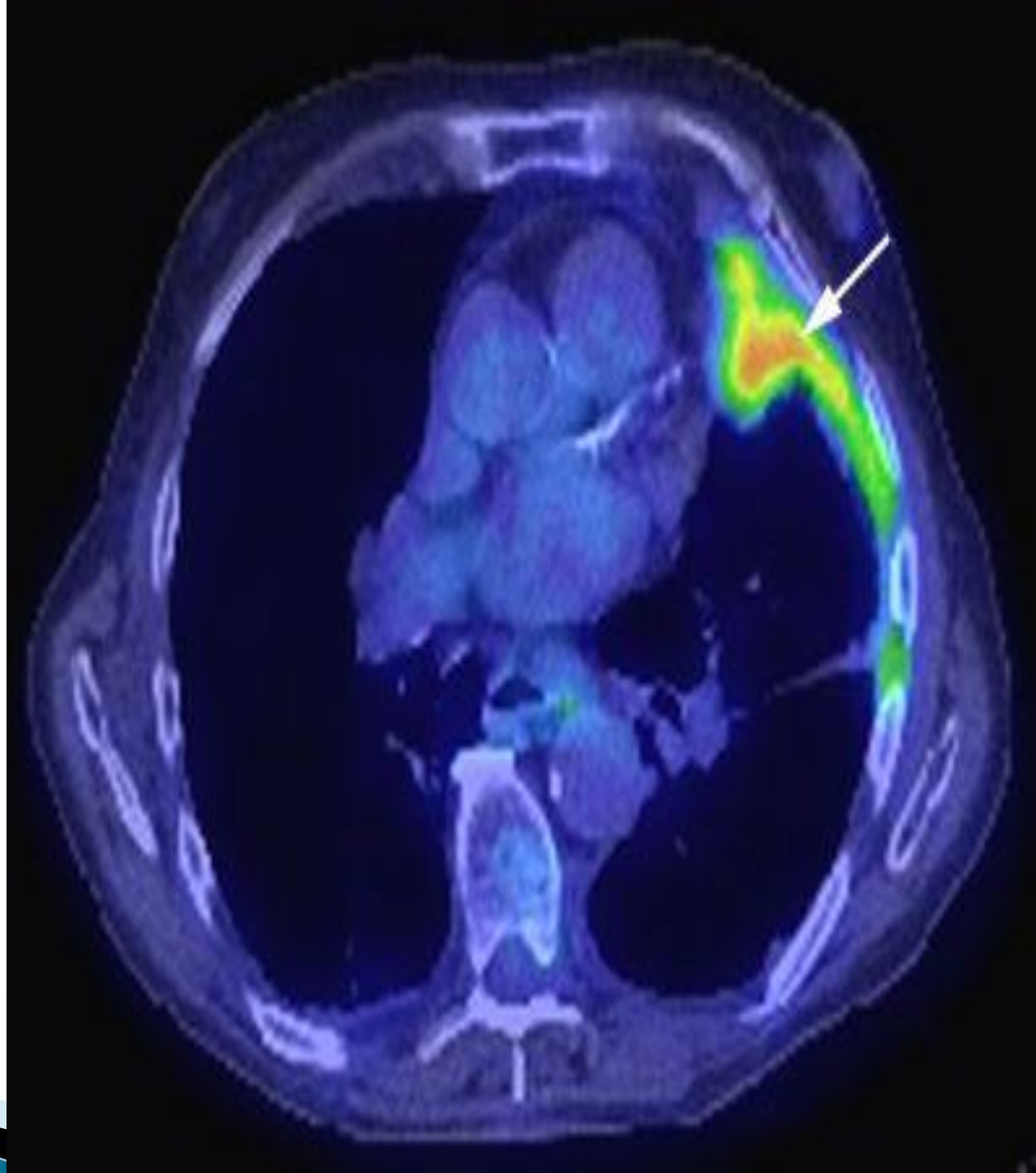


Squamous cell carcinoma

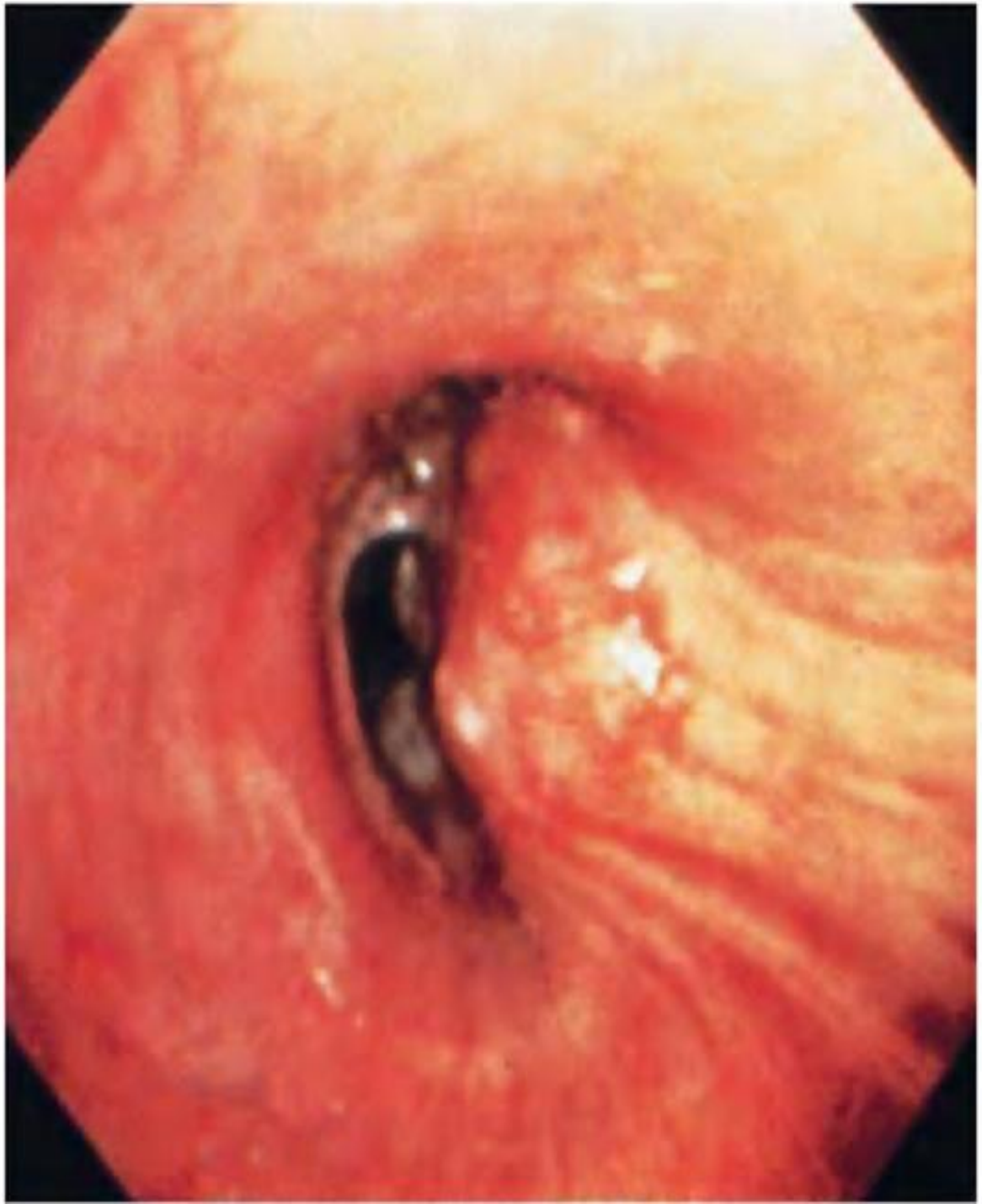
His CT shows the mass with collapse of the lower lobe.



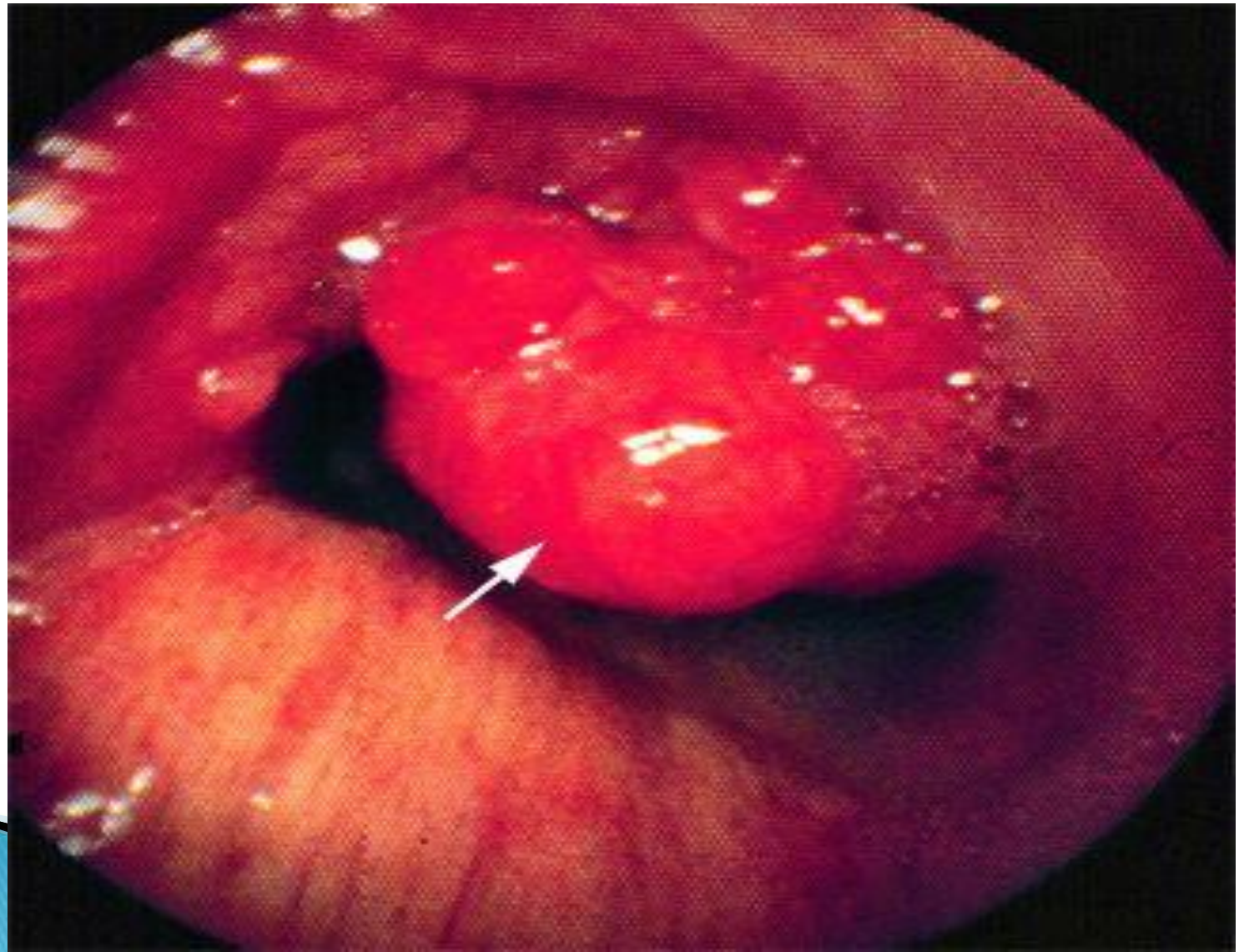
PET-CT showing a left lung mass and adjacent pleural thickening that is metabolically active. CT guided pleural biopsy showed non-small cell lung cancer.



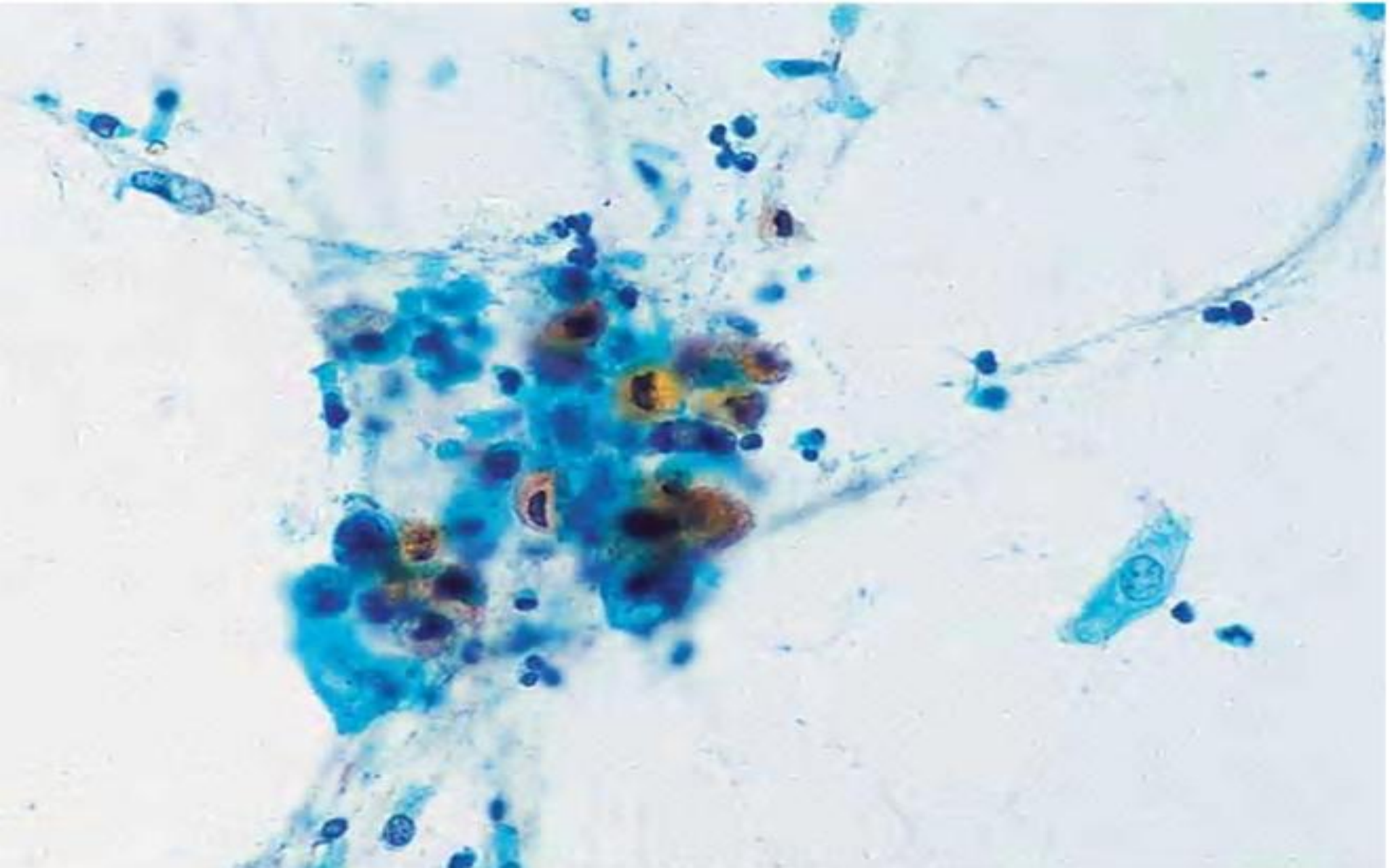
Bronchoscopic view of a bronchogenic carcinoma.
There is distortion of mucosal folds, partial occlusion of the airway lumen and abnormal tumour tissue.



Endobronchial squamous carcinoma.



Sputum sample showing a cluster of carcinoma cells. There is keratinisation, showing orangeophilia of the cytoplasm, and non-keratinised forms are also seen. The nuclei are large and 'coal-black' in density. These are the features of squamous cell bronchogenic carcinoma.



Staging to guide treatment

- CT
- Enlarged upper mediastinal nodes:
  bronchoscope equipped with endobronchial ultrasound (EBUS) or by mediastinoscopy.
- Combined CT and PET imaging:
  detect metabolically active tumour metastases.
- Head CT, radionuclide bone scanning, liver ultrasound and bone marrow biopsy :

  clinical, haematological or biochemical evidence of tumour spread to such sites.

- ensure that the patient's respiratory and cardiac function

Management

- over 75% of cases, treatment with curative intent is not possible

- Radiotherapy, and in some cases chemotherapy, can relieve distressing symptoms.

Surgical treatment

- offers 5-year survival rates of over 75% in stage I disease
- 55% in stage II disease

Management of Bronchogenic Cancer

- clinical classification as SCLC or NSCLC
- staging SCLC
  - presents as early metastasis
    (i.e. poor prognosis, surgical cure impossible)
  - limited-stage: all disease within a single radiation port in chest and supraclavicular fossa
  - extensive-stage: extends outside a single radiation port within the chest

TABLE 3] Definitions for T, N, and M Descriptors

T (Primary Tumor)		Label
T0	No primary tumor	
Tis	Carcinoma in situ (Squamous or Adenocarcinoma)	Tis
T1	Tumor ≤3 cm,	
T1a(mi)	Minimally Invasive Adenocarcinoma	T1a*(mi)*
T1a	Superficial spreading tumor in central airways[a]	T1a *SS*
T1a	Tumor ≤1 cm	T1a *≤1*
T1b	Tumor >1 but ≤2 cm	T1b *>1-2*
T1c	Tumor >2 but ≤3 cm	T1c *>2-3*
T2	Tumor >3 but ≤5 cm or tumor involving:	
	visceral pleura[b],	T2 *Visc Pl*
	main bronchus (not carina), atelectasis to hilum[b]	T2 *Centr*
T2a	Tumor >3 but ≤4 cm	T2a *>3-4*
T2b	Tumor >4 but ≤5 cm	T2b *>4-5*
T3	Tumor >5 but ≤7 cm	T3 *>5--7*
	or invading chest wall, pericardium, phrenic nerve	T3 *Inv*
	or separate tumor nodule(s) in the same lobe	T3 *Satell*
T4	Tumor >7 cm	T4 *>7*
	or tumor invading: mediastinum, diaphragm, heart, great vessels, recurrent laryngeal nerve, carina, trachea, esophagus, spine;	T4 *Inv*
	or tumor nodule(s) in a different ipsilateral lobe	T4 *Ipsi Nod*
N (Regional Lymph Nodes)		
N0	No regional node metastasis	
N1	Metastasis in ipsilateral pulmonary or hilar nodes	
N2	Metastasis in ipsilateral mediastinal/subcarinal nodes	
N3	Metastasis in contralateral mediastinal/hilar, or supraclavicular nodes	
M (Distant Metastasis)		
M0	No distant metastasis	
M1a	Malignant pleural/pericardial effusion[c] or pleural /pericardial nodules	M1a *Pl Dissem*
	or separate tumor nodule(s) in a contralateral lobe;	M1a *Contr Nod*
M1b	Single extrathoracic metastasis	M1b *Single*
M1c	Multiple extrathoracic metastases (1 or >1 organ)	M1c *Multi*

TX, NX: T or N status not able to be assessed

[a] Superficial spreading tumor of any size but confined to the tracheal or bronchial wall

[b] such tumors are classified as T2a if >3≤4 cm, T2b if >4≤5 cm.

[c] Pleural effusions are excluded that are cytologically negative, non-bloody, transudative, and clinically judged not to be due to cancer.

TABLE 5] Lung Cancer Stage Grouping (Eighth Edition)

T/M	Label	N0	N1	N2	N3
T1	T1a ≤1	IA1	IIB	IIIA	IIIB
	T1b >1-2	IA2	IIB	IIIA	IIIB
	T1c >2-3	IA3	IIB	IIIA	IIIB
T2	T2a *Cent, Visc Pl*	IB	IIB	IIIA	IIIB
	T2a >3-4	IB	IIB	IIIA	IIIB
	T2b >4-5	IIA	IIB	IIIA	IIIB
T3	T3 >5-7	IIB	IIIA	IIIB	IIIC
	T3 *Inv*	IIB	IIIA	IIIB	IIIC
	T3 *Satell*	IIB	IIIA	IIIB	IIIC
T4	T4 >7	IIIA	IIIA	IIIB	IIIC
	T4 *Inv*	IIIA	IIIA	IIIB	IIIC
	T4 *Ipsi Nod*	IIIA	IIIA	IIIB	IIIC
M1	M1a *Contr Nod*	IVA	IVA	IVA	IVA
	M1a *Pl Dissem*	IVA	IVA	IVA	IVA
	M1b *Single*	IVA	IVA	IVA	IVA
	M1c *Multi*	IVB	IVB	IVB	IVB

See Table 3 text and legend for expansion of abbreviations.

TABLE 7] 5-Year Survival (%)

Type	IA1	IA2	IA3	IB	IIA	IIB	IIIA	IIIB	IIIC	IVA	IVB
Clinical	92	83	77	68	60	53	36	26	13	10	0
Pathologic	90	85	80	73	65	56	41	24	12	-	-

Average overall survival in the International Association for the Study of Lung Cancer global database of patients receiving a diagnosis between 1999 and 2010. Data from Goldstraw et al.[21]

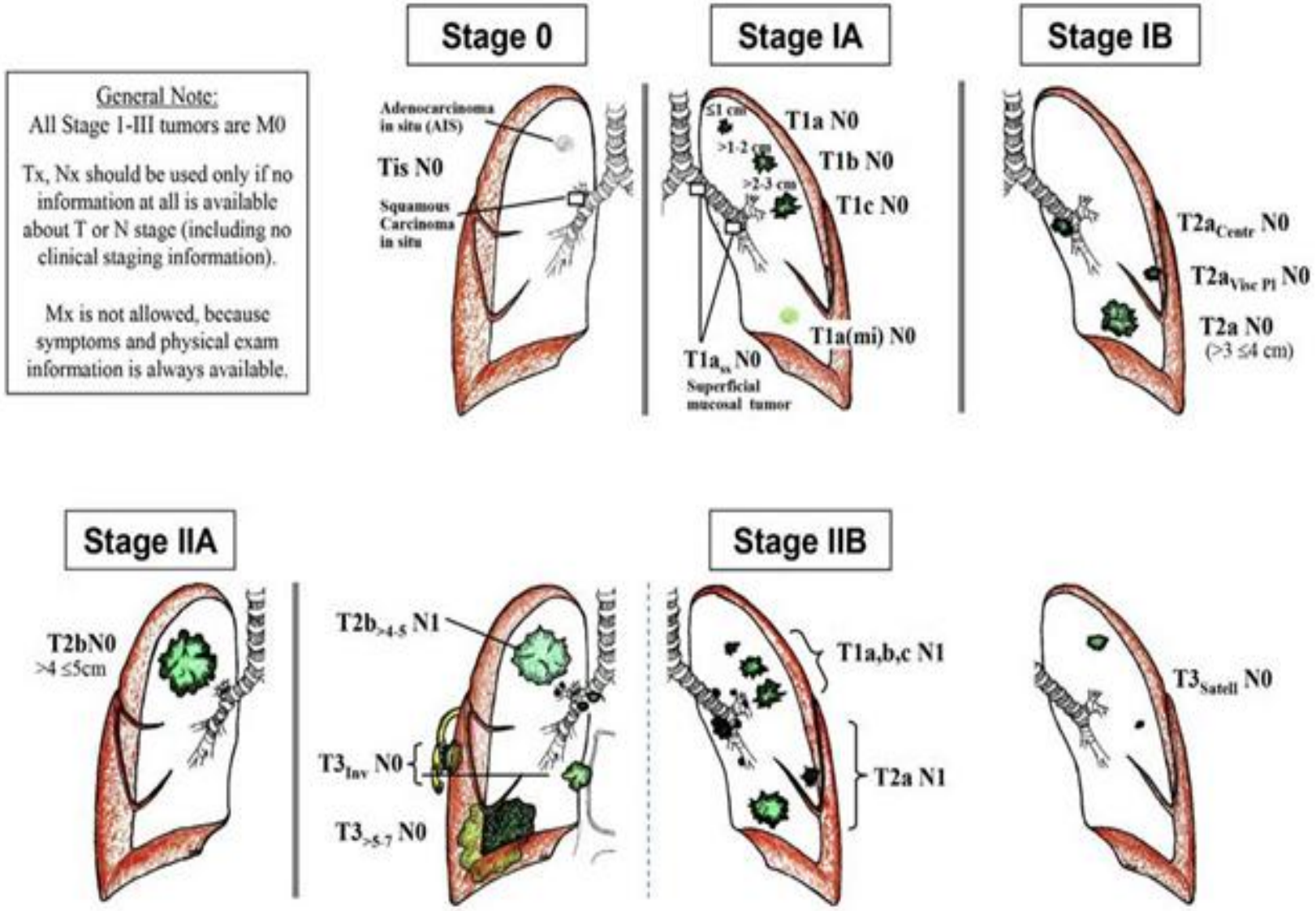
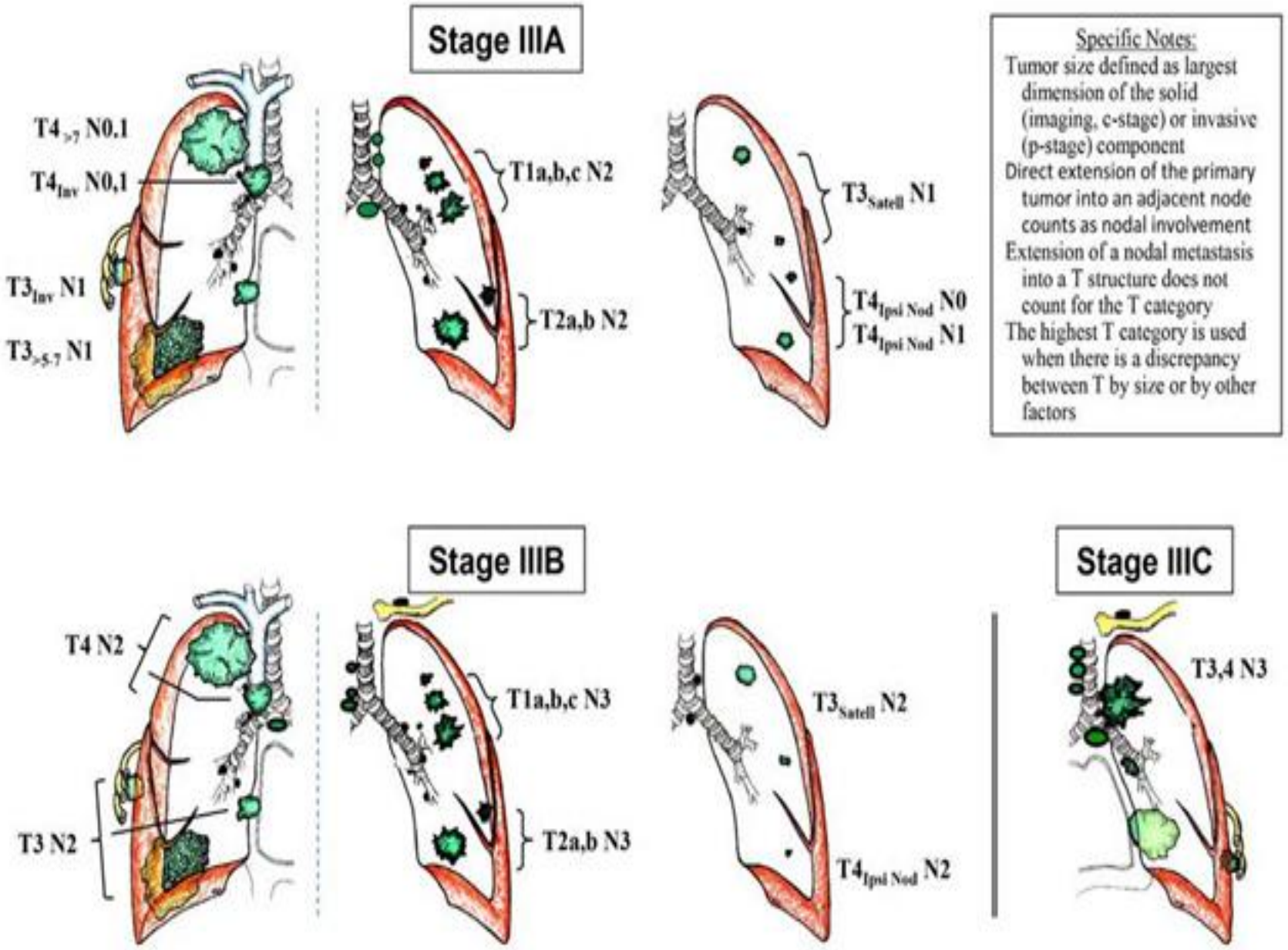


Figure 2 – *Graphic illustration of stages 0, I, and II.*


Stage IIIA
T4 >7 N0,1
T4Inv N0,1
T3Inv N1
T3>5,7 N1
T1a,b,c N2
T2a,b N2
T3Satell N1
T4Ipsi Nod N0
T4Ipsi Nod N1
Specific Notes:
Tumor size defined as largest dimension of the solid (imaging, c-stage) or invasive (p-stage) component
Direct extension of the primary tumor into an adjacent node counts as nodal involvement
Extension of a nodal metastasis into a T structure does not count for the T category
The highest T category is used when there is a discrepancy between T by size or by other factors
Stage IIIB
T4 N2
T3 N2
T1a,b,c N3
T2a,b N3
T3Satell N2
T4Ipsi Nod N2
Stage IIIC
T3,4 N3

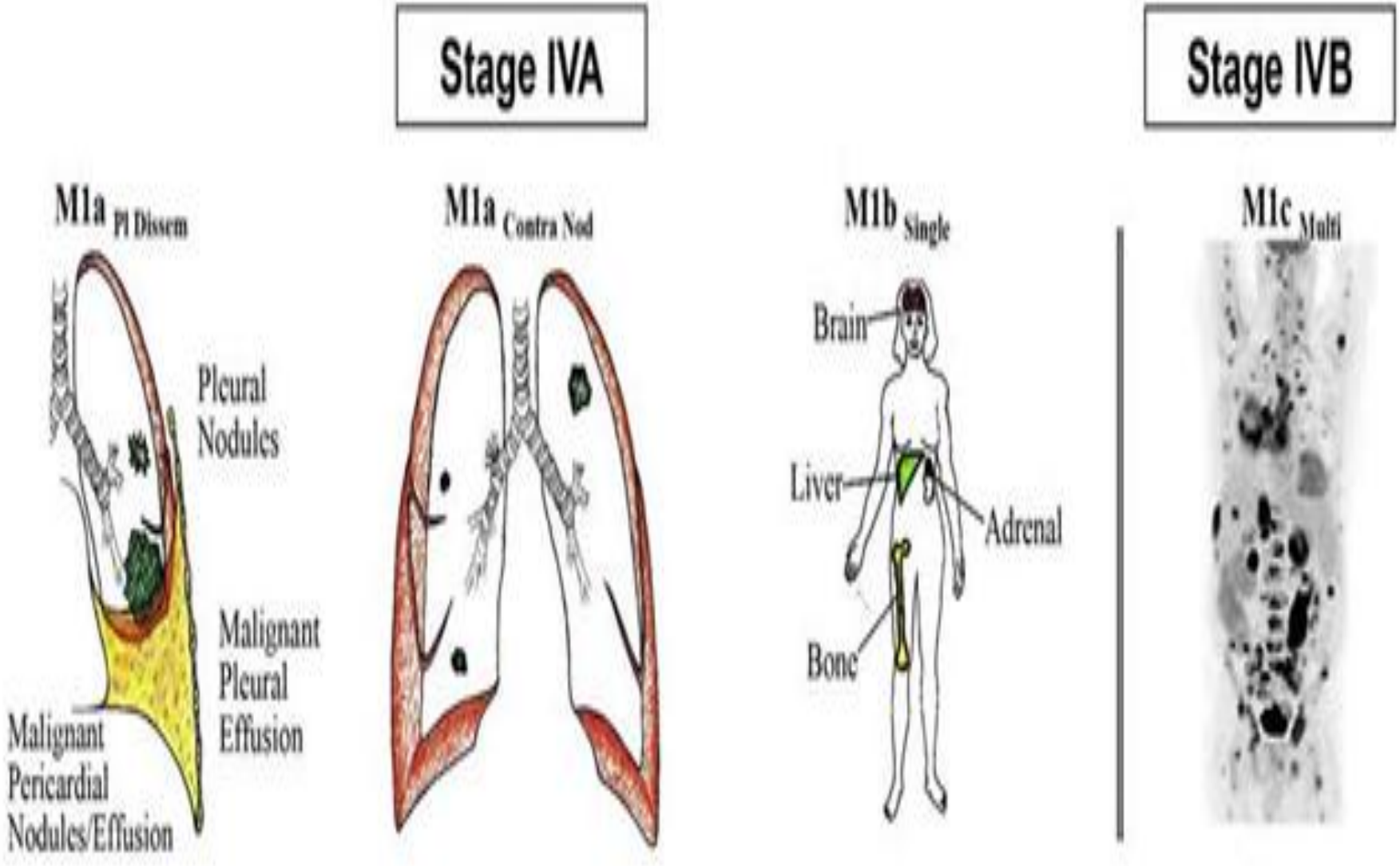


Figure 4 - *Graphic illustration of stage IV.*

TNM staging system for lung cancer (7th edition)

Primary tumor (T)	
T1	Tumor ≤3 cm diameter, surrounded by lung or visceral pleura, without invasion more proximal than lobar bronchus
T1a	Tumor ≤2 cm in diameter
T1b	Tumor >2 cm but ≤3 cm in diameter
T2	Tumor >3 cm but ≤7 cm, or tumor with any of the following features:
	Involves main bronchus, ≥2 cm distal to carina
	Invades visceral pleura
	Associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung
T2a	Tumor >3 cm but ≤5 cm
T2b	Tumor >5 cm but ≤7 cm
T3	Tumor >7 cm or any of the following:
	Directly invades any of the following: chest wall, diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium, main bronchus <2 cm from carina (without involvement of carina)
	Atelectasis or obstructive pneumonitis of the entire lung
	Separate tumor nodules in the same lobe
T4	Tumor of any size that invades the mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina, or with separate tumor nodules in a different ipsilateral lobe
Regional lymph nodes (N)	
N0	No regional lymph node metastases
N1	Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension
N2	Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)
N3	Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)
Distant metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis
M1a	Separate tumor nodule(s) in a contralateral lobe; tumor with pleural nodules or malignant pleural or pericardial effusion
M1b	Distant metastasis (in extrathoracic organs)

Stage groupings

Stage IA	T1a–T1b	N0	M0
Stage IB	T2a	N0	M0
Stage IIA	T1a,T1b,T2a	N1	M0
	T2b	N0	M0
Stage IIB	T2b	N1	M0
	T3	N0	M0
Stage IIIA	T1a,T1b,T2a,T2b	N2	M0
	T3	N1,N2	M0
	T4	N0,N1	M0
Stage IIIB	T4	N2	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1a or M1b

Disease stage

- Stage 0 — TisN0M0
- Stage IA — T1a–1bN0M0 (50%)
- Stage IB — T2aN0M0 (46%)
- Stage IIA — T1a–2aN1M0 or T2bN0M0 (36%)
- Stage IIB — T2bN1M0 or T3N0M0 (26%)
- Stage IIIA — T3N1M0 or T1a–3N2M0 or T4N0–1M0 (19%)
- Stage IIIB — T4N2M0 or T1a–4N3M0 (7%)
- Stage IV — Any T Any N M1a–1b (2%)

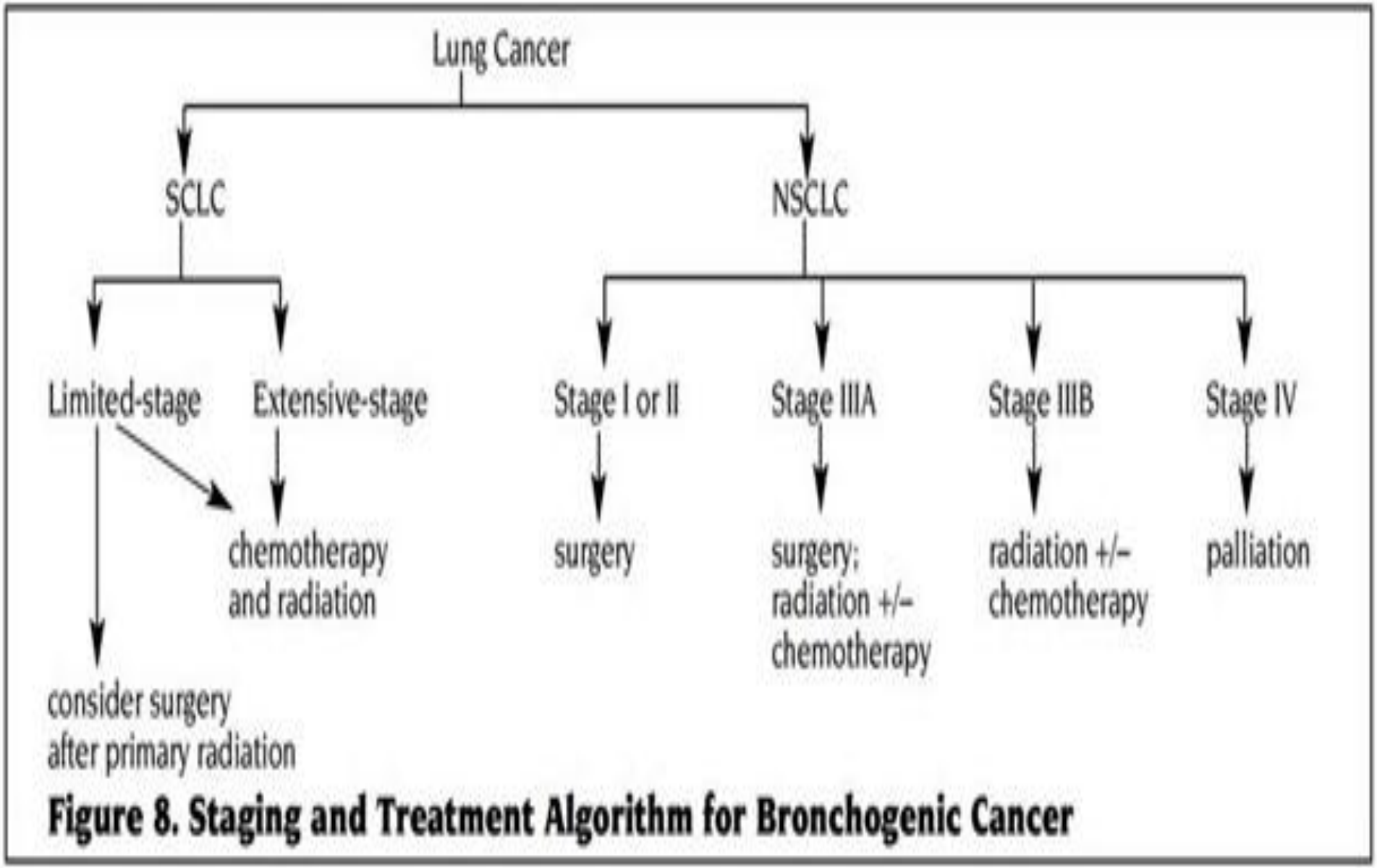


Figure 8. Staging and Treatment Algorithm for Bronchogenic Cancer

Therapy for Bronchogenic Cancer

- chemotherapy
  - cisplatin and etoposide
  - paclitaxel, vinorelbine, and gemcitabine are new NSCLC therapies
  - complications :
    - acute:
      tumour lysis syndrome, infection, bleeding, myelosuppression, hemorrhagic cystitis (cyclophosphamide), cardiotoxicity (doxorubicin), renal toxicity (cisplatin), peripheral neuropathy (vincristine)
    - chronic:
      neurologic damage, leukemia, second primary neoplasms

Chemotherapy

- small-cell carcinoma :
  combinations of cytotoxic drugs with radiotherapy can increase the median survival from 3 months to well over a year.

- less effective in non-small-cell bronchial cancers.

- non-small-cell bronchial cancers:
  platinum-based chemotherapy regimens have shown a 30% response rate associated with a small increase in survival.

Neoadjuvant and adjuvant chemotherapy

- In non-small-cell carcinoma: chemotherapy given before surgery may increase survival and can effectively 'down-stage' disease with limited nodal spread.

- Post-operative chemotherapy : improve survival rates when operative samples show nodal involvement by tumour.

Therapy for Bronchogenic Cancer

- radiotherapy
- surgery
  - only chance for cure is resection when tumour is still localized
  - contraindications
  - any evidence of local extension or metastases
  - poor pulmonary status (i.e. unable to tolerate resection of lung)
  - patients with surgically resectable disease must undergo mediastinal node sampling since CT thorax is not accurate in 20-40% of cases
- palliative care for end-stage disease

Radiotherapy

- less effective than surgery
- radical radiotherapy can offer long-term survival in selected patients with localised disease
- Continuous hyper-fractionated accelerated radiotherapy (CHART):
  - a similar total dose is given in smaller but more frequent fractions
  - may offer better survival prospects than conventional schedules.
- palliation of distressing complications :
  superior vena cava obstruction, recurrent haemoptysis, and pain caused by chest wall invasion or by skeletal metastatic deposits.
- Obstruction of the trachea and main bronchi can also be relieved
- used in conjunction with chemotherapy in the treatment of small-cell carcinoma

Contraindications to surgical resection in bronchial carcinoma

- Distant metastasis (M1)
- Invasion of central mediastinal structures including heart, great vessels, trachea and oesophagus (T4)
- Malignant pleural effusion (M1a)
- Contralateral mediastinal nodes (N3)
- $FEV_1 < 0.8$ L
- Severe or unstable cardiac or other medical condition

Laser therapy and stenting

- Palliation of symptoms caused by major airway obstruction
- clear tumour tissue and allow re-aeration of collapsed lung.
- best results are achieved in tumours of the main bronchi.
- Endobronchial stents : extrinsic compression by malignant nodes.

Management of malignant pleural effusion

- drain the pleural cavity using an intercostal drain; provided the lung fully re-expands

- pleurodesis with a sclerosing agent such as talc .

Prognosis

- Poor
- around 70% of patients dying within a year of diagnosis
- only 6-8% of patients surviving 5 years after diagnosis.
- best prognosis :
  well-differentiated squamous cell tumours that have not metastasised

Prognosis of Bronchogenic Cancer

- 5 year survival rates for different subtypes
  - squamous 25%
  - adenocarcinoma 12%
  - large cell carcinoma 13%
  - SCLC 1%
    - SCLC has the poorest prognosis
    - greatest tendency to metastasize
    - 70% present with extensive disseminated disease at initial diagnosis
    - limited-stage: 15-20% cure rate
    - extensive-stage treated: median survival of 6 months, but can live up to two years with a rare cure (1%); untreated median survival is 2-3 months
  - NSCLC
    - Stage I 50%
    - Stage II 30%
    - Stage IIIA 15%
    - Stage IIIB 5%
    - Stage IV < 2%

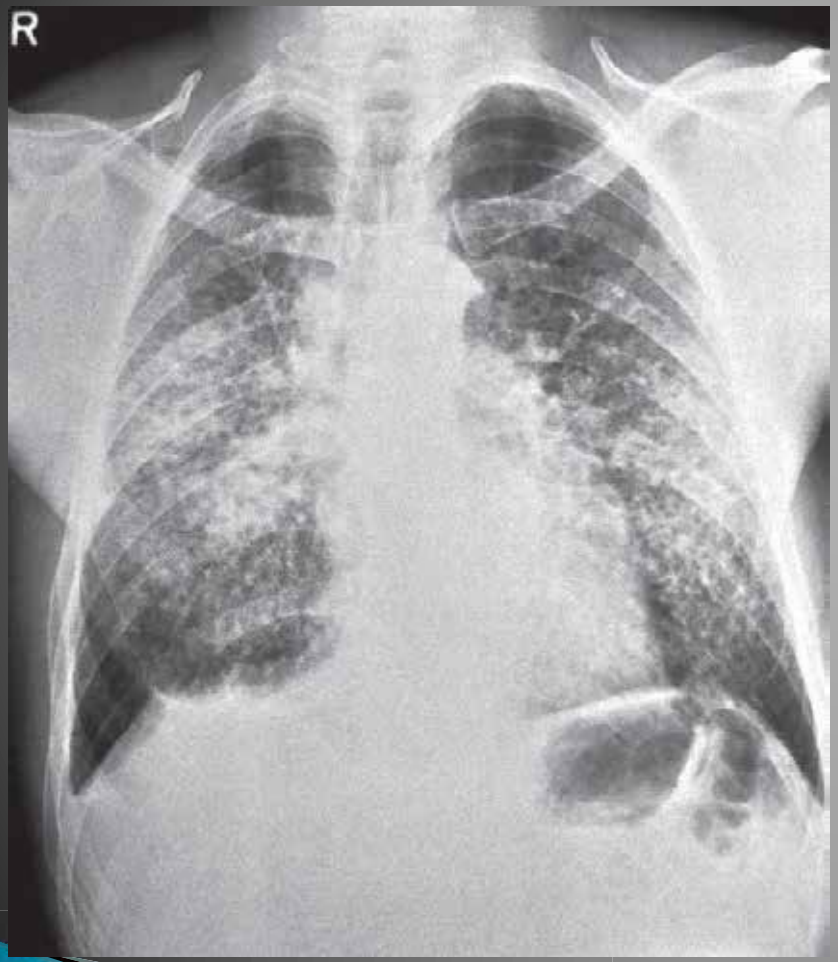
Rare types of lung tumour

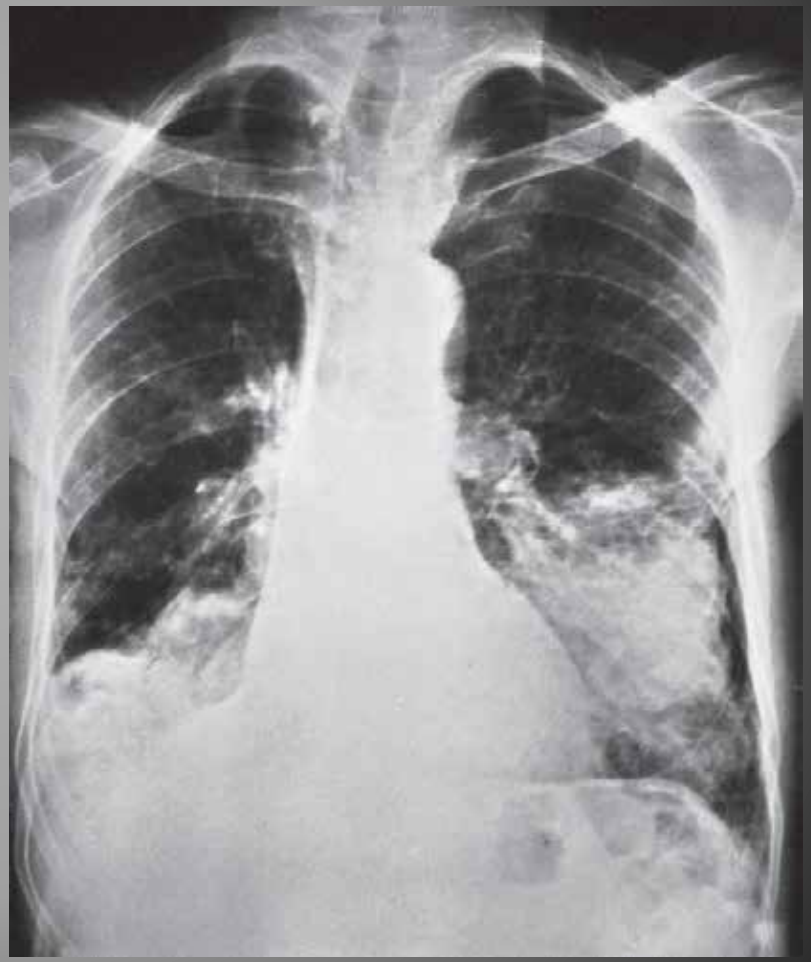
Tumour	Status	Histology	Typical presentation	Prognosis
Adenosquamous carcinoma	Malignant	Tumours with areas of unequivocal squamous and adeno-differentiation	Peripheral or central lung mass	Stage-dependent
Carcinoid tumour (p. 887)	Low-grade malignant	Neuroendocrine differentiation	Bronchial obstruction, cough	95% 5-year survival with resection
Bronchial gland adenoma	Benign	Salivary gland differentiation	Tracheobronchial irritation/obstruction	Local resection curative
Bronchial gland carcinoma	Low-grade malignant	Salivary gland differentiation	Tracheobronchial irritation/obstruction	Local recurrence occurs
Hamartoma	Benign	Mesenchymal cells, cartilage	Peripheral lung nodule	Local resection curative
Bronchoalveolar carcinoma	Malignant	Tumour cells line alveolar spaces	Alveolar shadowing, productive cough	Variable, worse if multifocal

Bronchioloalveolar Cancer

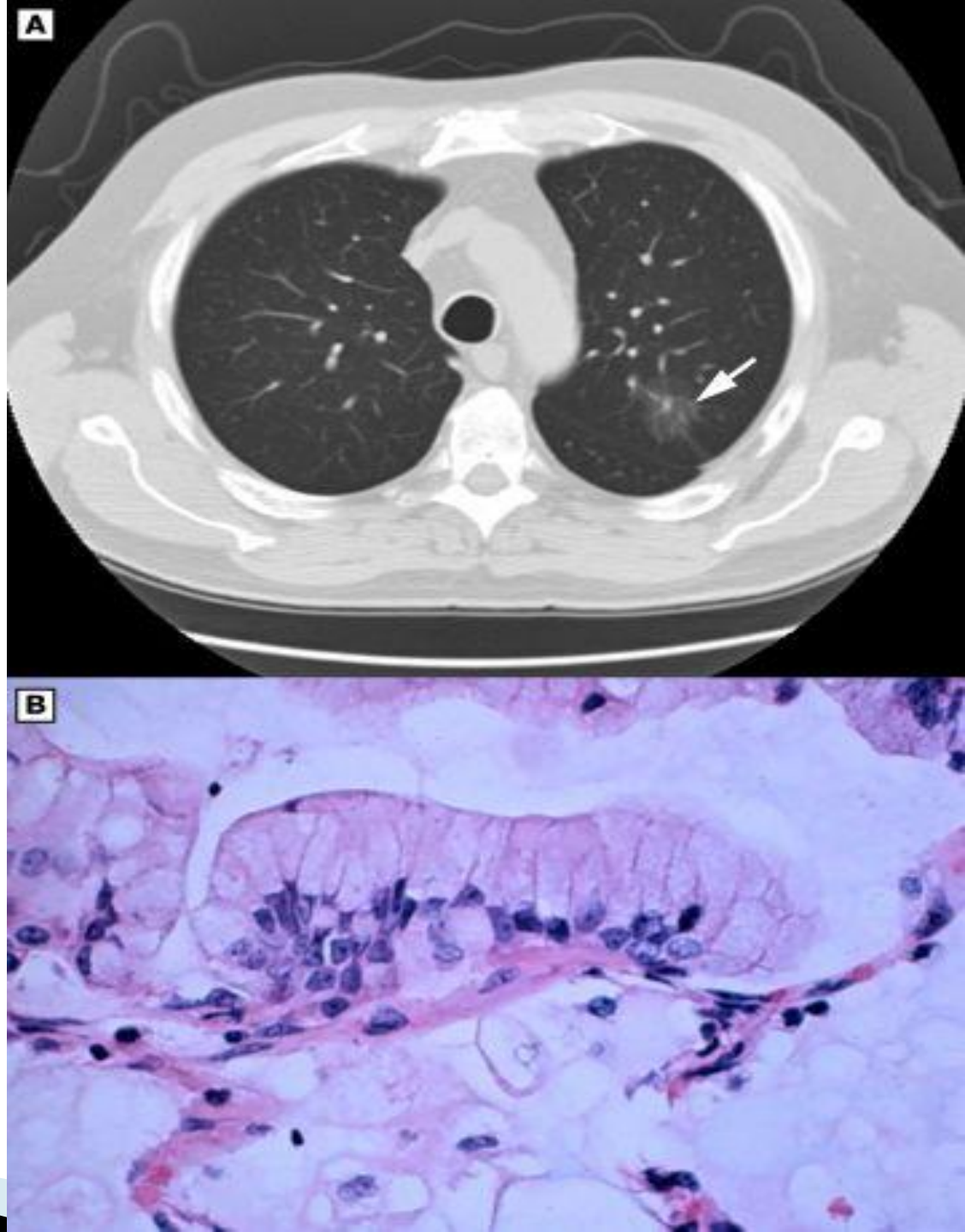
- a type of adenocarcinoma that grows along the alveolar wall in the periphery
- may arise at sites of previous lung scarring (a scar cancer)
- clinical presentation:
  similar to bronchogenic cancer; late metastasis but 45% rate
- treatment and prognosis: solitary lesions are resectable with a 60% 5-year survival rate; overall survival rate is 25%

Alveolar cell cancer
a Diffuse type.
b Localized type.





A) CT from a 75-year-old man showing a 2.5 cm, ground-glass nodule in the left upper lobe that was a bronchioloalveolar carcinoma at resection. B) Histology. Bronchioloalveolar carcinoma (mucinous type) growing on a normal alveolar wall.



Secondary tumours of the lung

- derived from many primary tumours
  breast, kidney, uterus, ovary, testes and thyroid.
- usually multiple and bilateral.
- Often there are no respiratory symptoms
- diagnosis is made on radiological examination.
- Endobronchial deposits are uncommon but can cause haemoptysis and lobar collapse.

Multiple pulmonary metastasis of a renal cancer in a 54-year-old man.