Pulmonary Pathology

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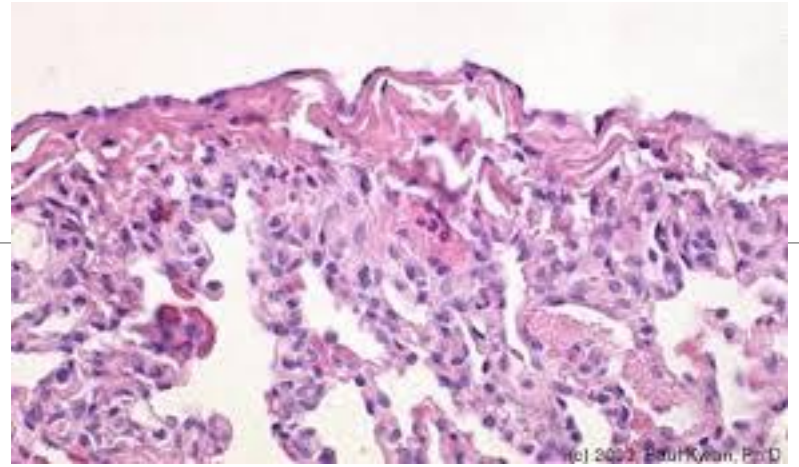
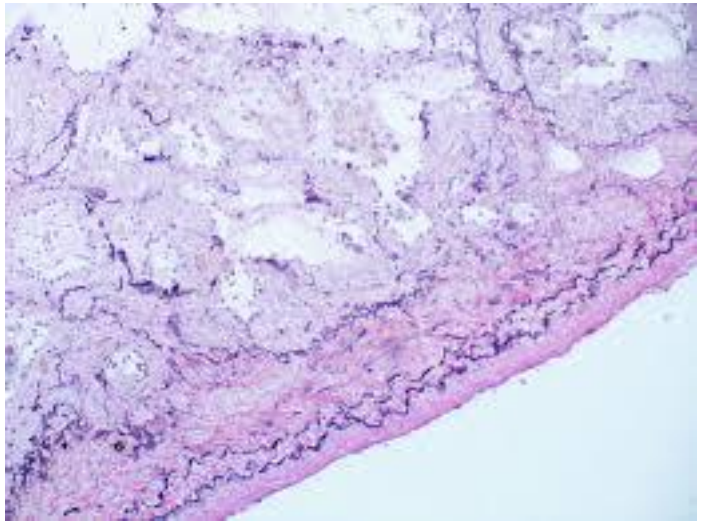
BA MB BCH FRCS FRCPATH

Pleural disease

Normal pleura

- Mesothelial layer
- Connective tissue layer
- Superficial elastic layer
- Loose connective tissue with vessels and lymphatics
- Deep fibro-elastic layer

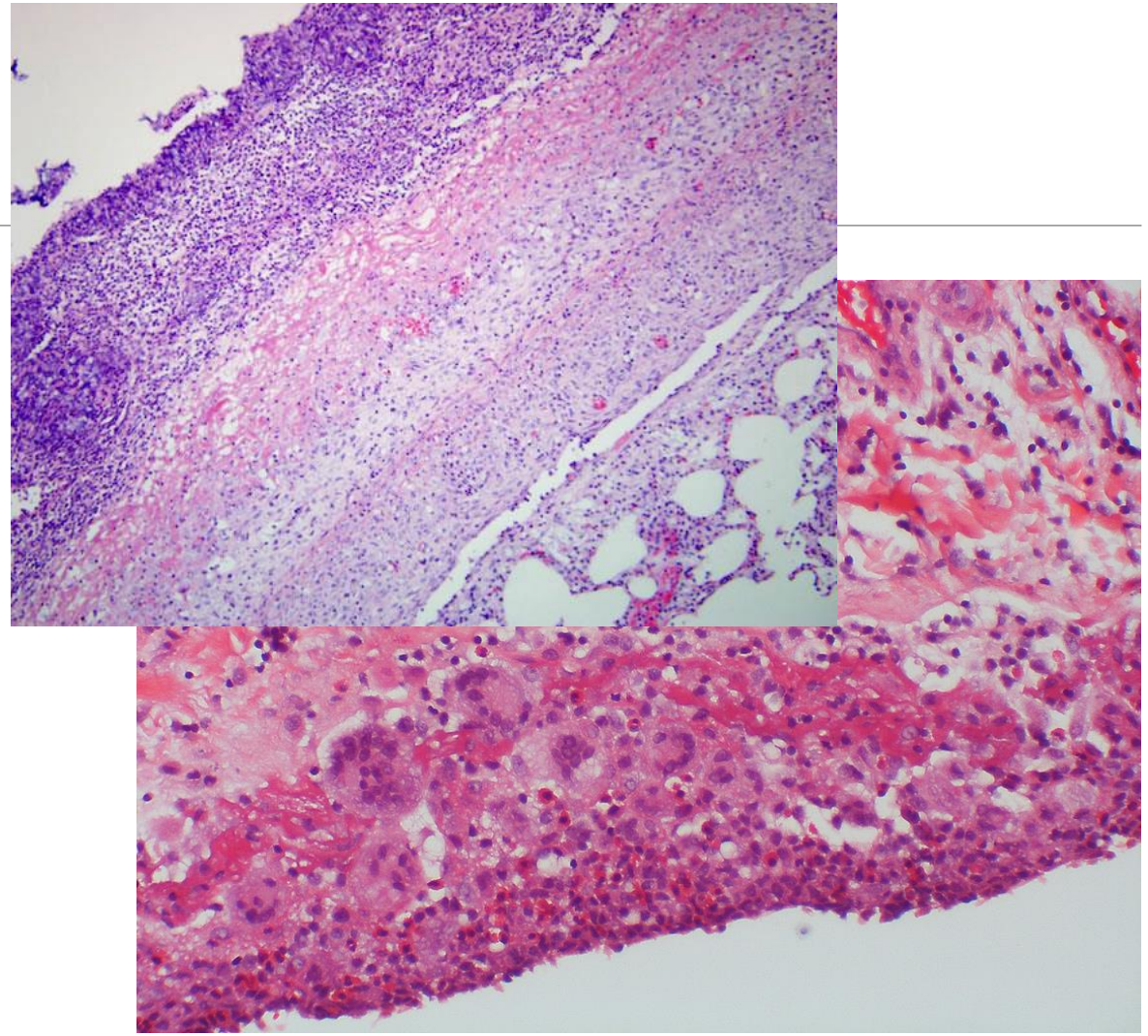




Pleural diseases

Inflammation and fibrosis

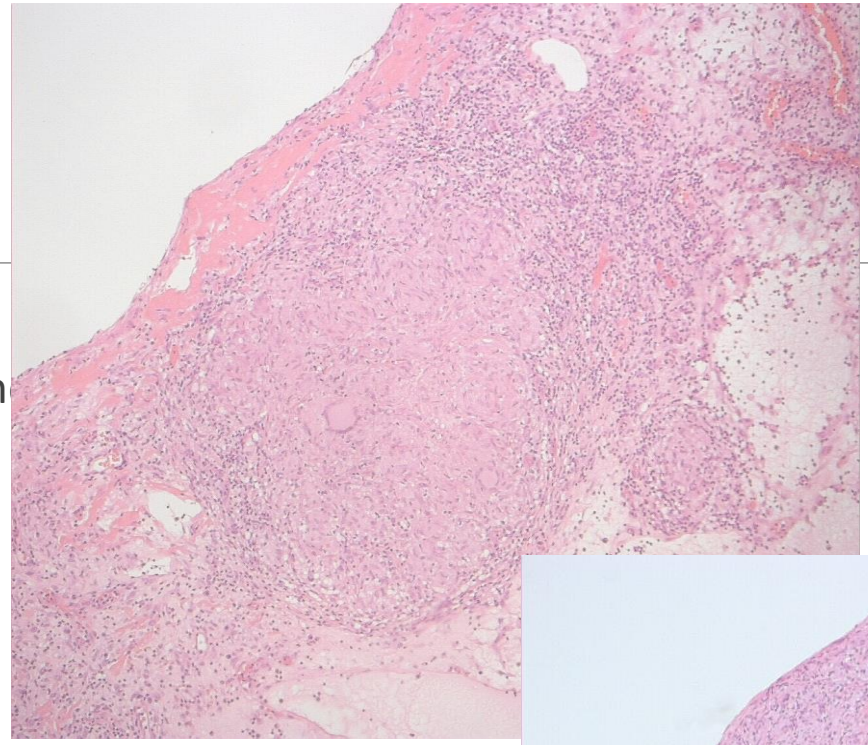
- Infection
- Pulmonary infarction
- Connective tissues disease
- Drugs
- Asbestos
- Pneumothorax
- Sarcoid
- Radiation
- Renal failure

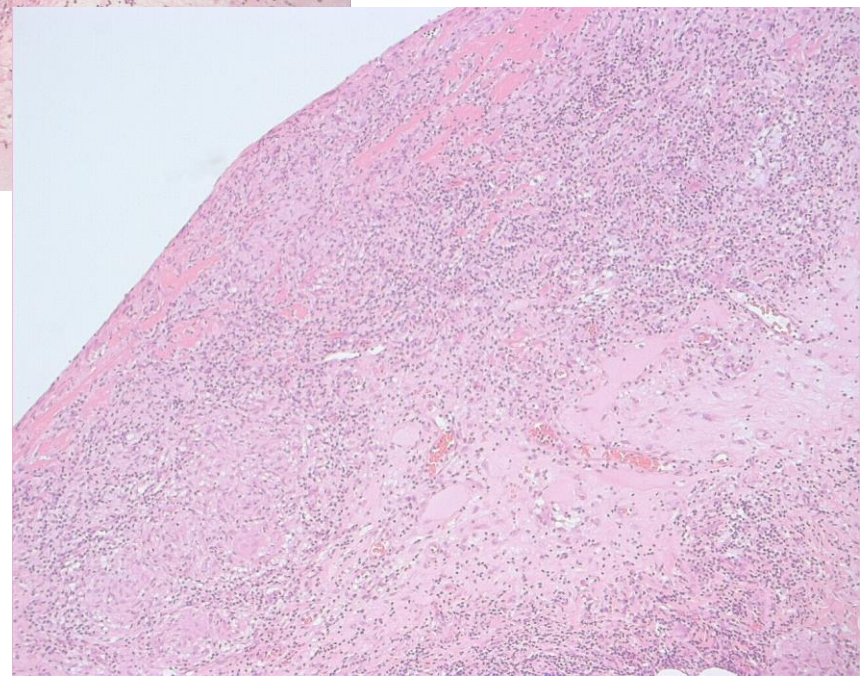


Case 18,

Case 18

- F53 Unexplained pleural thickening an





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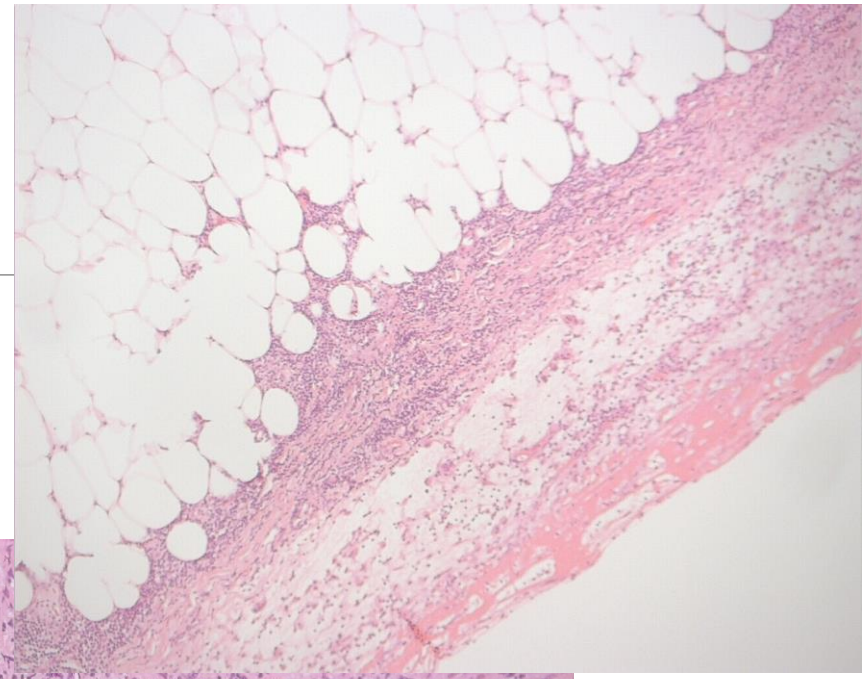
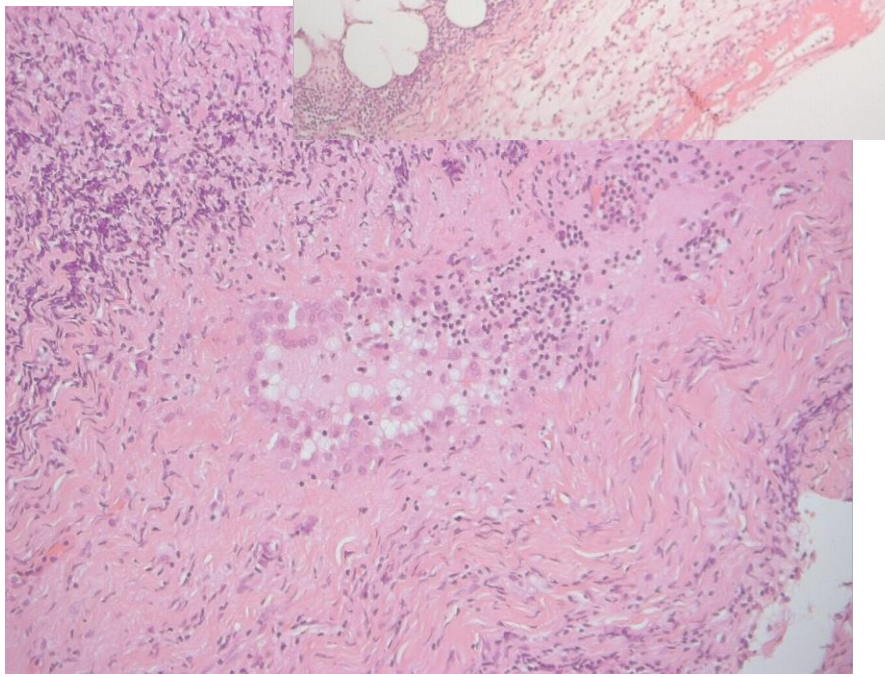
Pitfalls

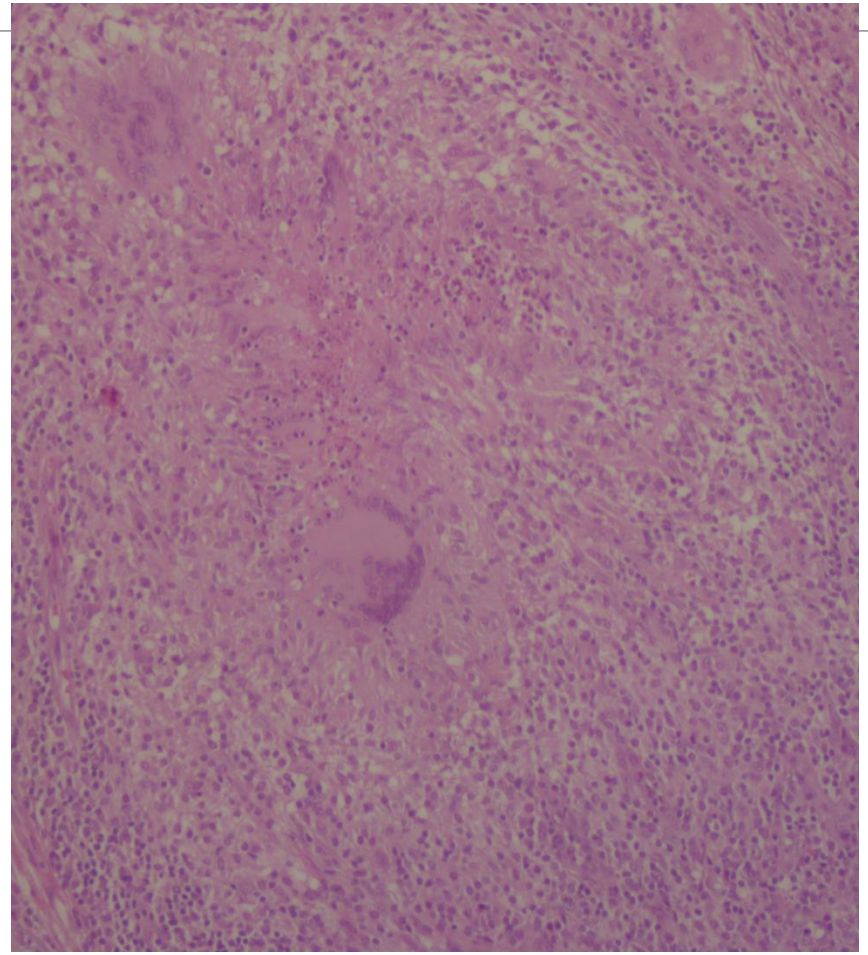
- Layers
- Maturation
- Entrapment

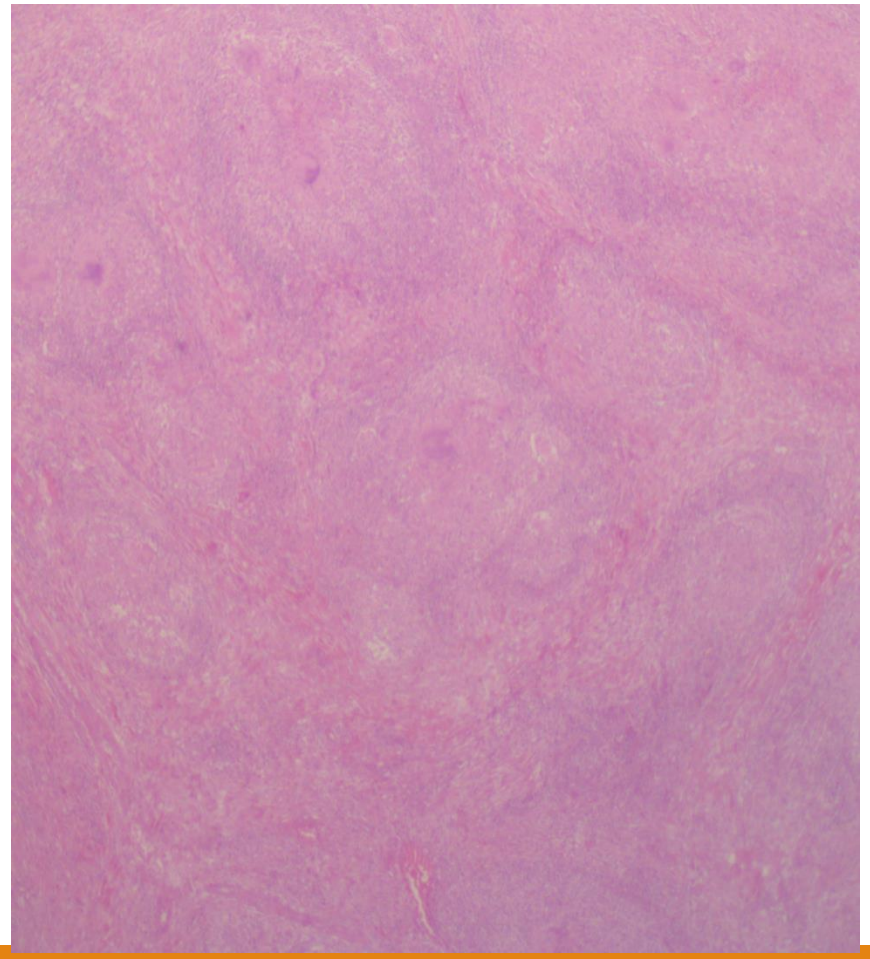


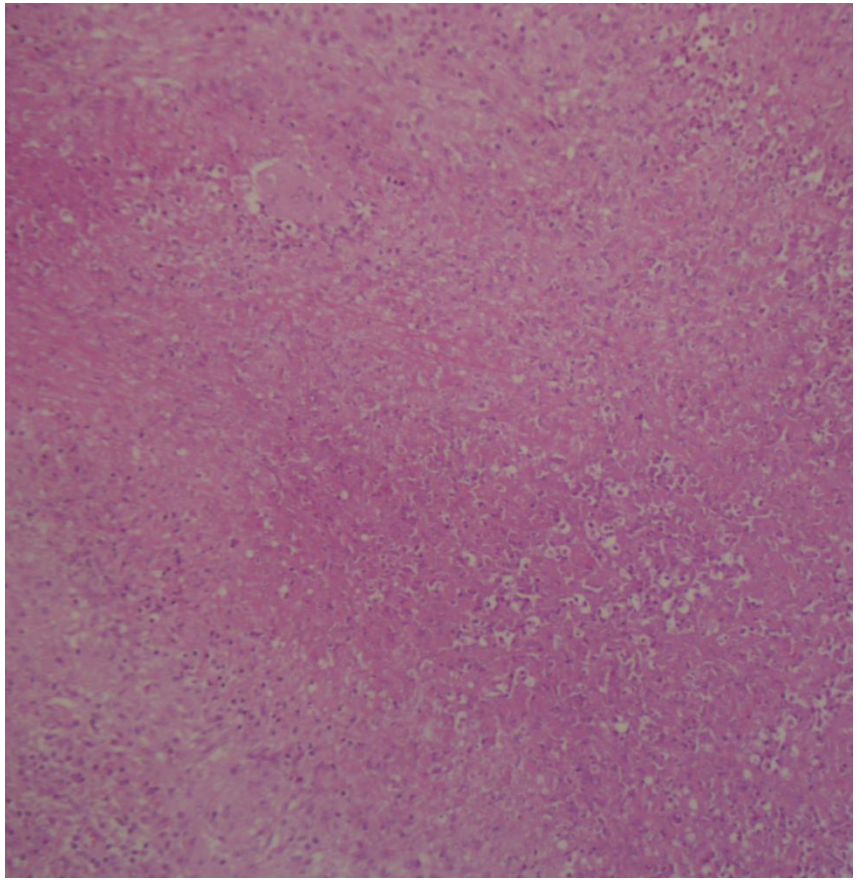


Granulomas

- Sarcoidosis
- Tuberculosis
- Rheumatoid nodules





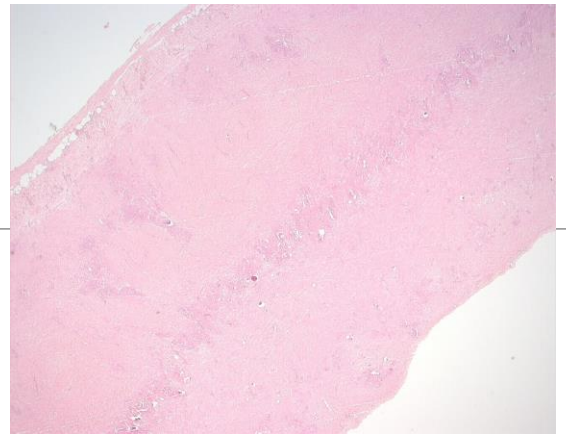


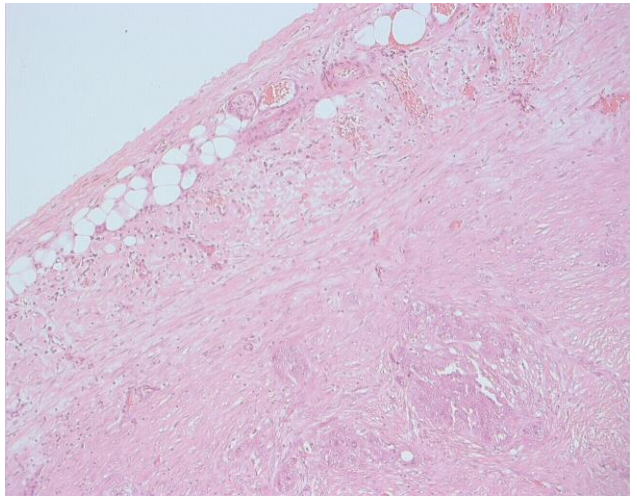
Case 2

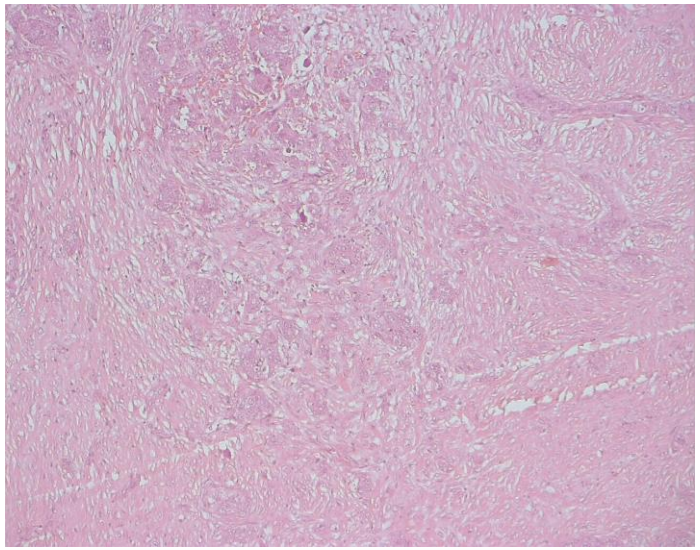
F 66

Increasing shortness of breath

Pleural effusion.







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Differential diagnosis

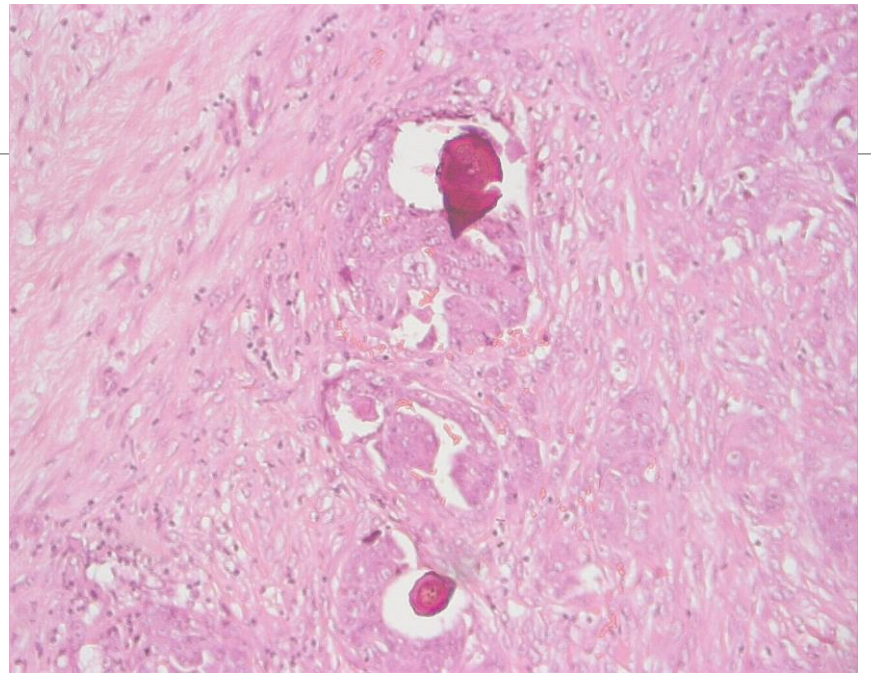
Adenocarcinoma vs Mesothelioma

Immuno panels

Mesothelioma	Adenocarcinoma
CEA, LeuM1, Ber EP4, AUA-1 negative	CEA, LeuM1, Ber EP4, AUA-1 positive
EMA – membrane positivity	EMA – cytoplasmic and cell periphery
CK5/6, calretinin(nuclear), thrombomodulin positive	Negative

2

Marker	Sensitivity %	Specificity %
CK5/6	83	85
Calretinin	82	85
N Cadherin	78	84
WT-1	77	96
Thrombomodulin	61	80



Metastatic Ovarian carcinoma

Mesothelioma vs Mesothelial hyperplasia

Papillary change on surface or entrapment can mimic mesothelioma.

Entrapped – parallel to surface

EMA and p53 – malignant> reactive

Desmin – reactive> malignant

May be helpful but still relies on morphological features

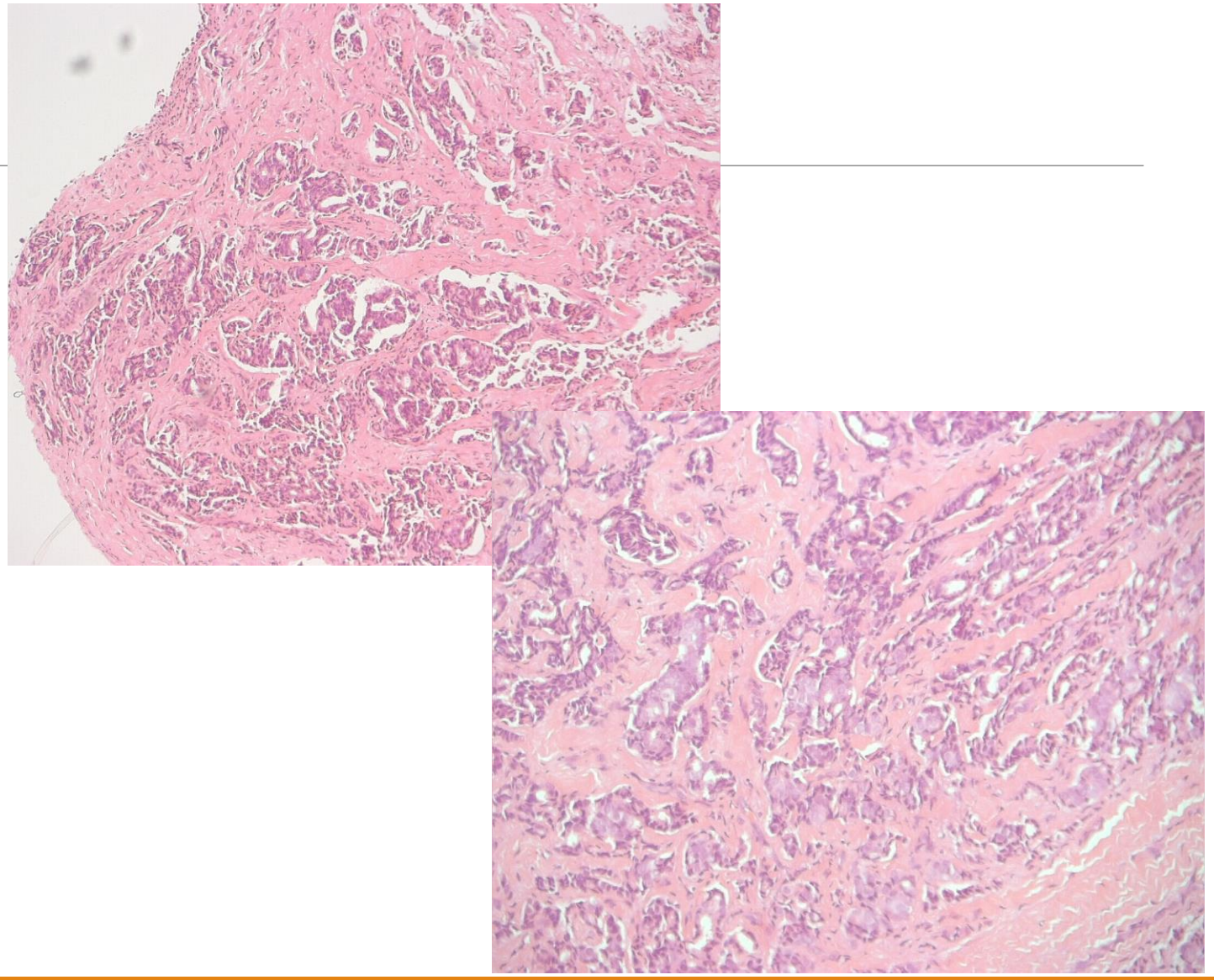
3

F53

Short of breath

No asbestos exposure

Pleural effusion

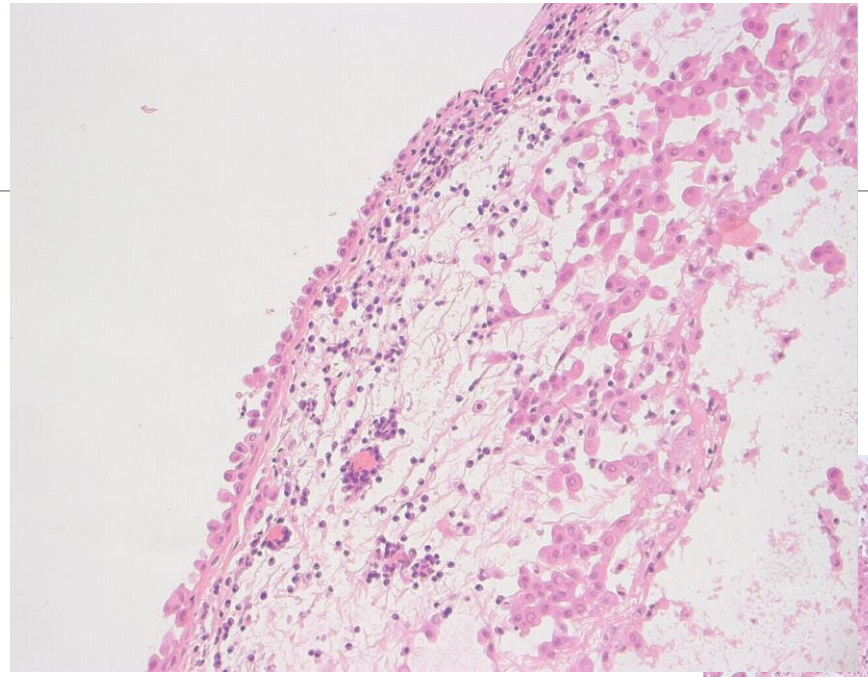


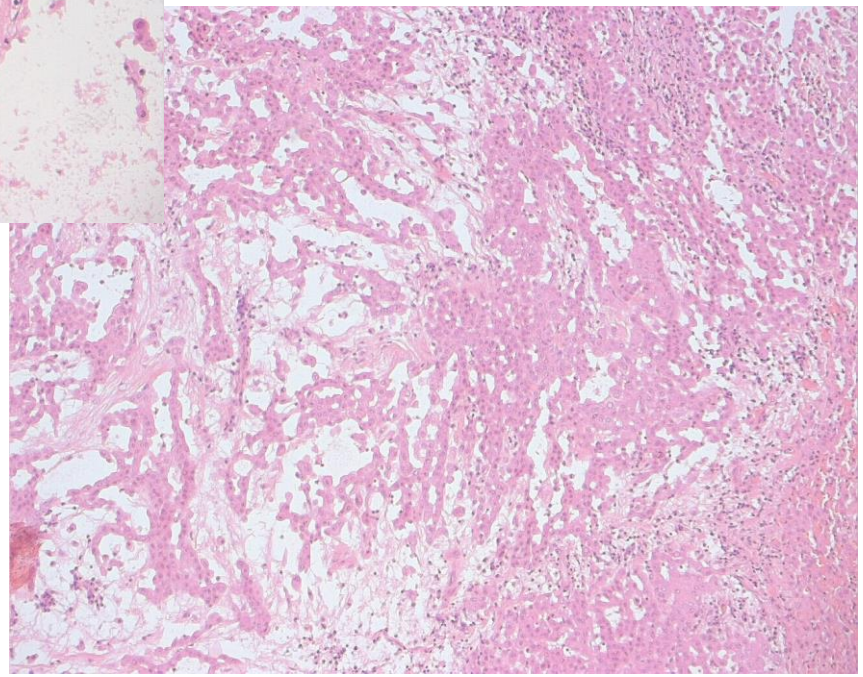
Case 11

M74

Shortness of breath

Pleural effusion





Mesothelioma

Epithelioid

Biphasic

Sarcomatoid

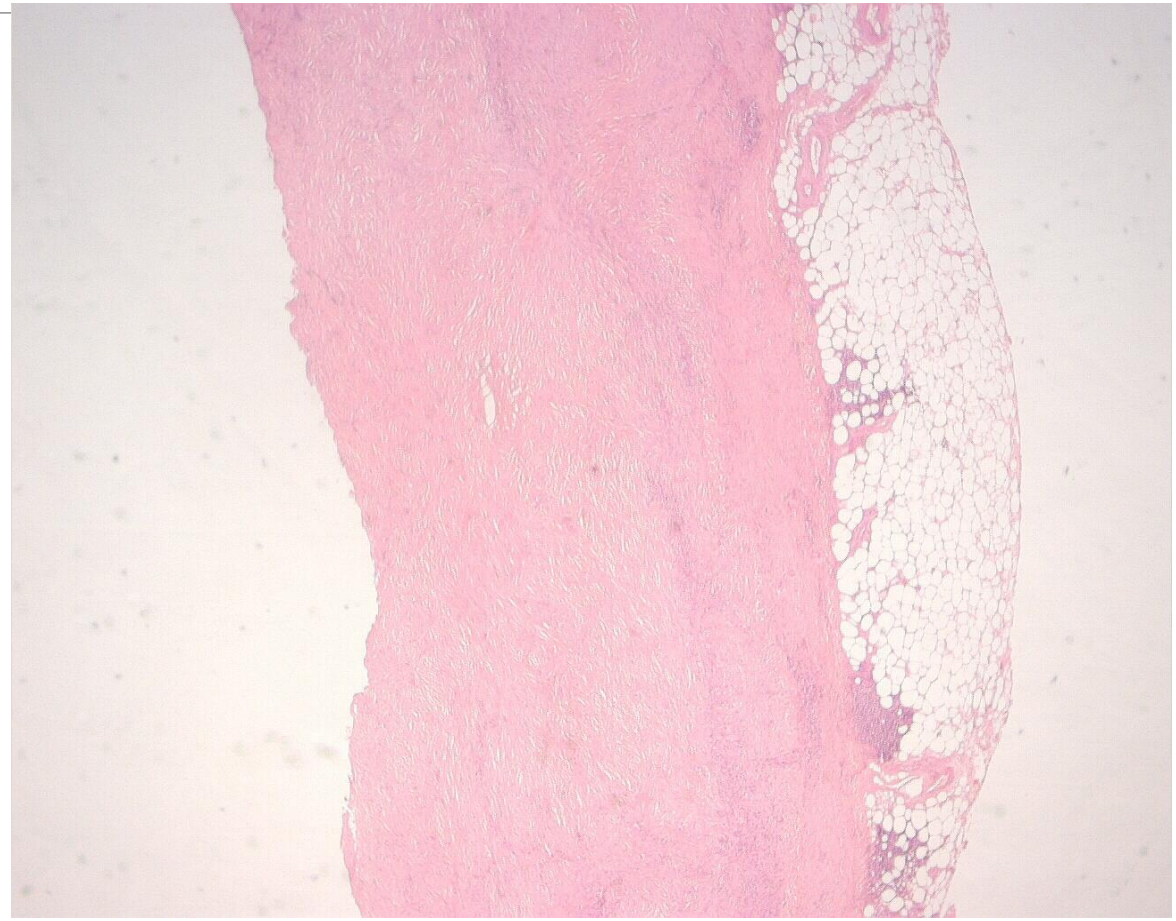
Differential diagnosis

- Epithelioid vs Adenocarcinoma
- Biphasic and other biphasic tumours
- Epithelioid and reactive
- Sarcomatoid and spindle cell tumours
- Sarcomatoid vs fibrosis

Case 29

M71

Pleural effusion and pleural thickening



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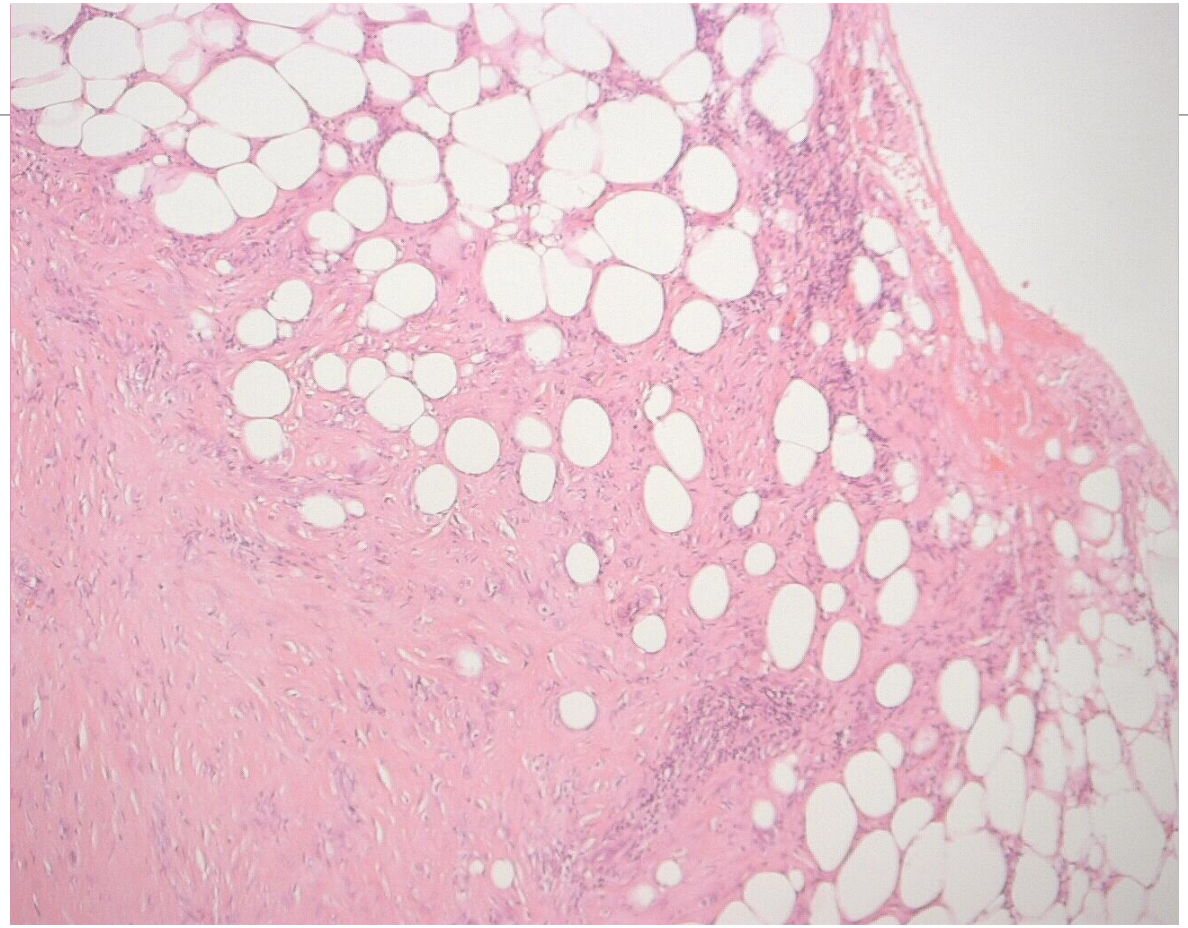
Maturation

Architecture

Fatty infiltration



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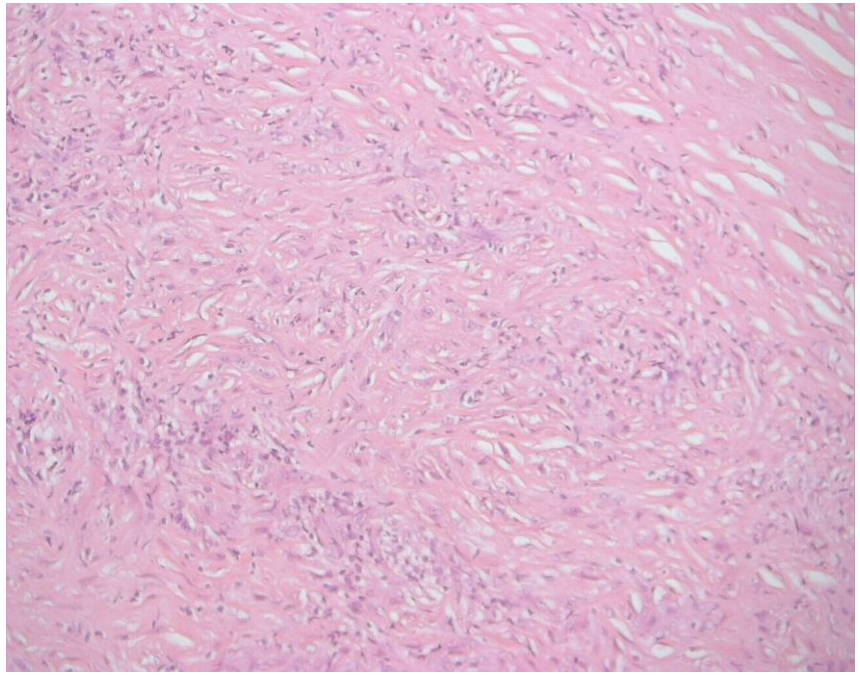
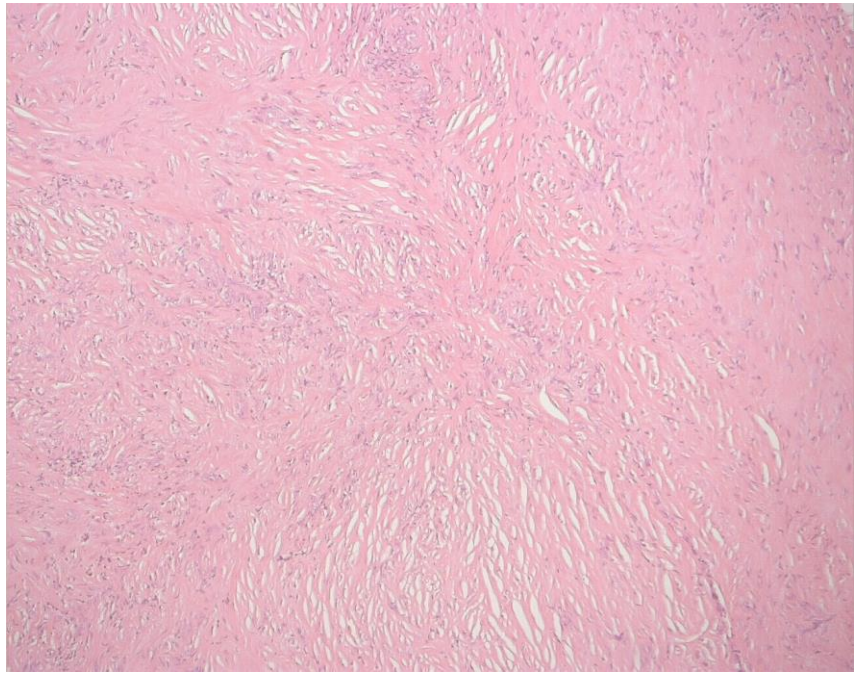




Sarcomatoid mesothelioma

	Pan cytokeratin	CK5/6	Calretinin	Thrombo modulin	SMA	TTF-1	D2/40
Sarcomatoid mesothelioma	70%	rare	70%	70%	60%	0/10	87%
Sarcoma	17%	Rare	17%	38%	58%	Negative	
Sarcomatoid carcinoma	90%	Rare	60%	40%	10%	Positive if pulmonary (maybe)	26%

Solitary fibrous tumour

Origin ultrastructurally in myofibroblasts

Express vimentin +/- actin

Usually attached to the pleura but may be intra-pulmonary or in the chest wall

Histology

Well circumscribed

Variable cellularity in fibrous stroma

Mitoses in more cellular areas

Myxoid change

SFT – Immunohistochemistry

Vimentin, actin +ve

Cytokeratin, EMA –ve

CD34 (80%) (not in MFH or HPCT)

P53 in higher grade tumours

Malignant features

- Hypercellularity
- Mitoses >4/10HPF
- Pleomorphism
- Necrosis

LUNG TUMOURS

LUNG TUMOURS

Risk factors

- Smoking
- Asbestos
- Irradiation
- Arsenic, nickel, chromium, polyaromatic hydrocarbons
- Pulmonary fibrosis – 14x risk
- Hereditary

Pre-malignancy

Squamous metaplasia and dysplasia

Atypical adenomatous hyperplasia and Adenocarcinoma in situ

WHO classification of lung tumours

Adenocarcinoma
- Lepidic, acinar, papillary, micropapillary,solid
- Invasive mucinous carcinoma
- Colloid, foetal,enteric
- Minimally invasive

Squamous cell carcinoma
- Keratinising, non-keratinising, basaloid

Neuroendocrine tumours
- Small cell, Large cell NE
- Carcinoid – typical, atypical

Large cell carcinoma

Adenosquamous carcinoma

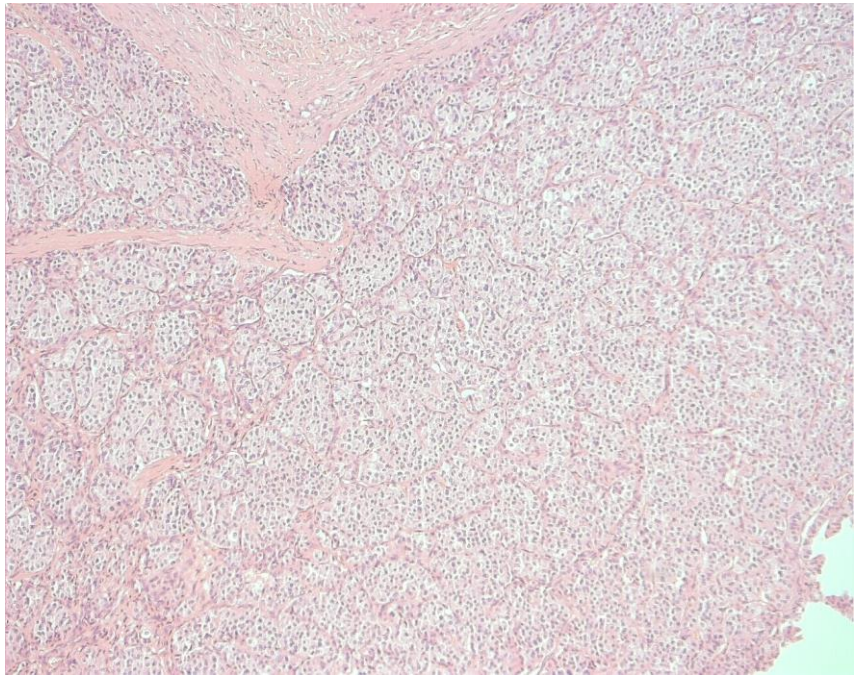
Sarcomatoid carcinoma
- Pleopmorphic
- Spindle cell
- Giant cell
- Carcinosarcoma
- Pulmonary blastoma

7

7

F53

Mass obstructing upper lobe bronchus



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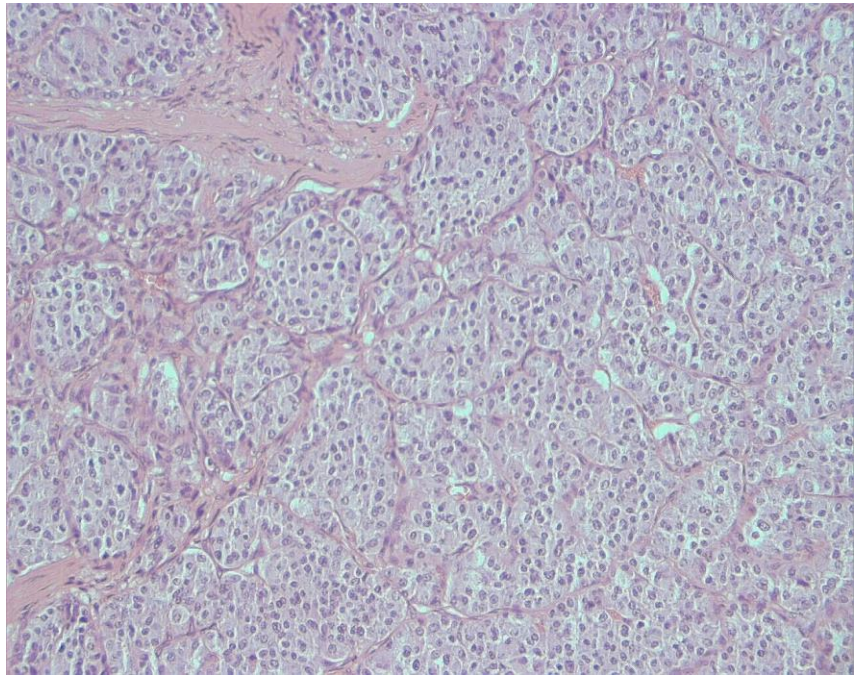
Organoid architecture

Nest and trabeculae

Mitotic rates – Ki67 staining

Immunohistochemistry



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Neuroendocrine tumours of low grade malignancy

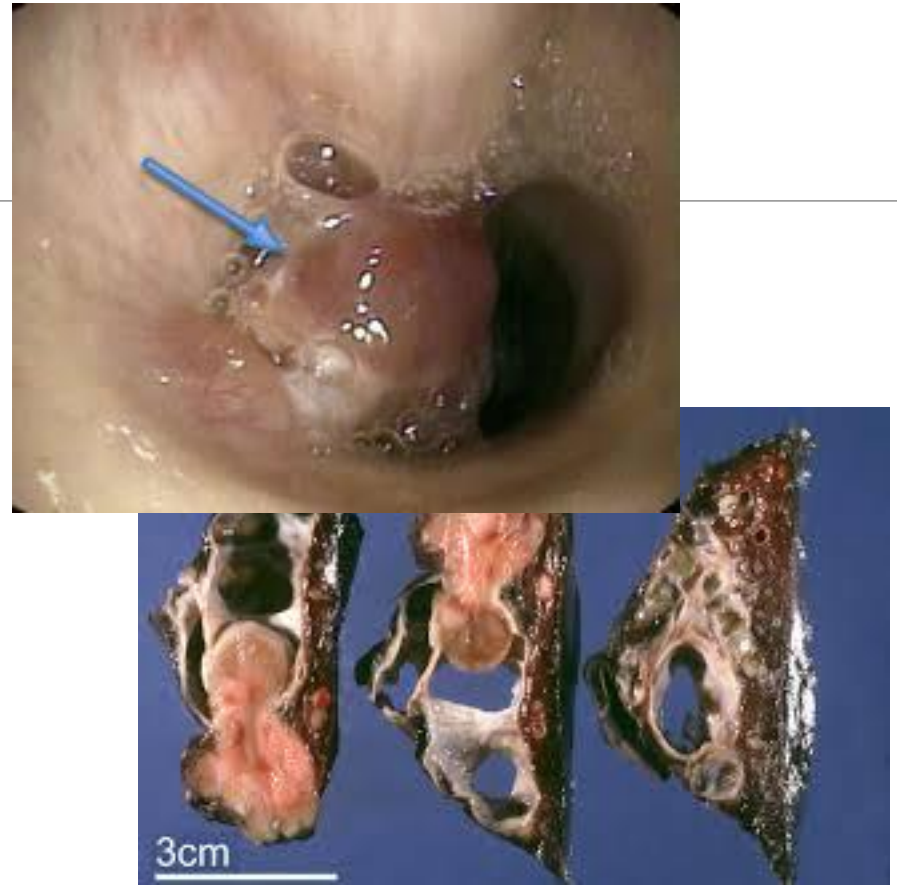
5% of pulmonary tumours

Mean age 50

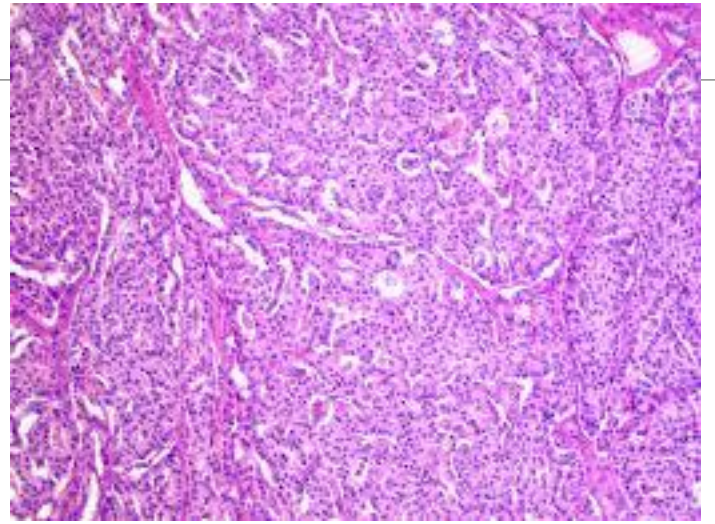
Often in airways leading to obstruction

May extend through wall

Hilar nodes at resection <5%



Trabecular, mosaic patterns

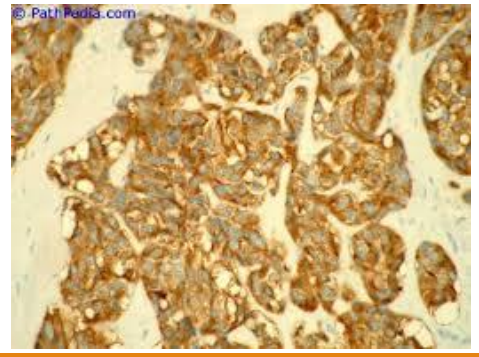


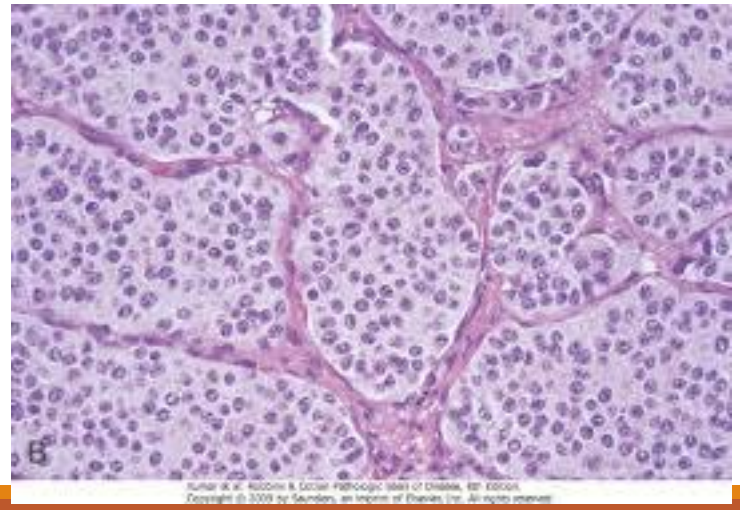
Delicate fibrovascular stroma

Granular chromatin, indisctinct nucleoli

Mitoses <2/2mm^2

CD56, Chromogranin, Synaptophsin





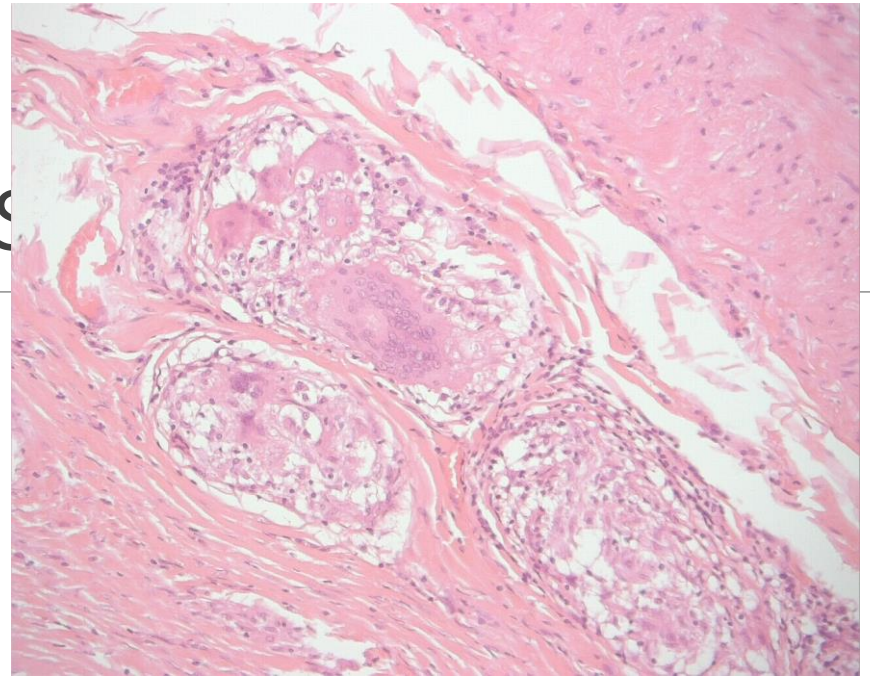
Co-existent sarcoidosis

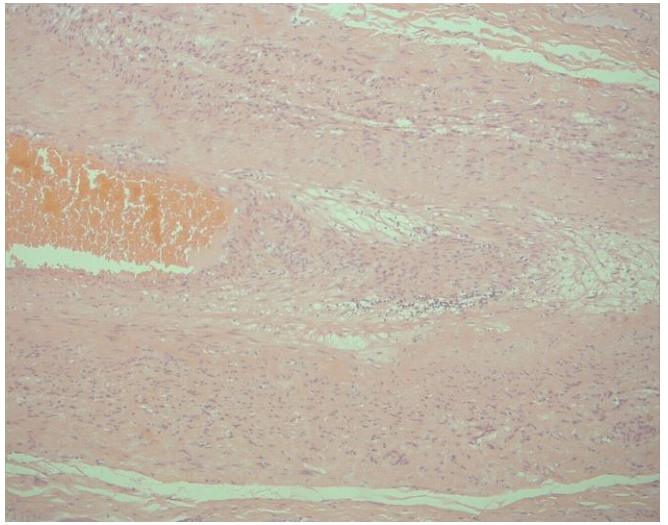
Dual pathologies ae not uncommon

Granulomas

- Always exclude infection

- Infections
- ILD
- Vasculitis
- OLD
- Sarcoid





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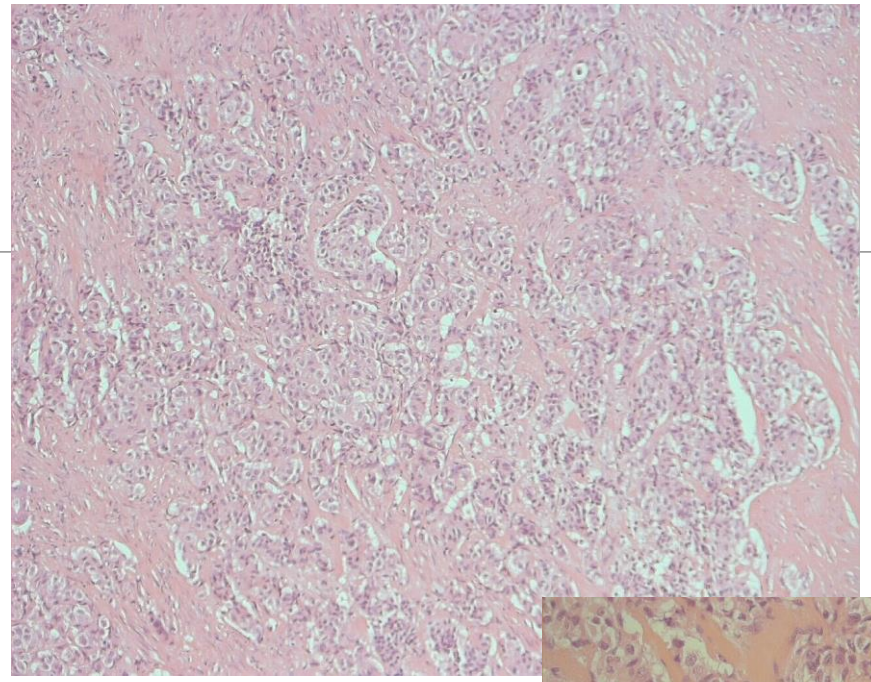
8 M 63

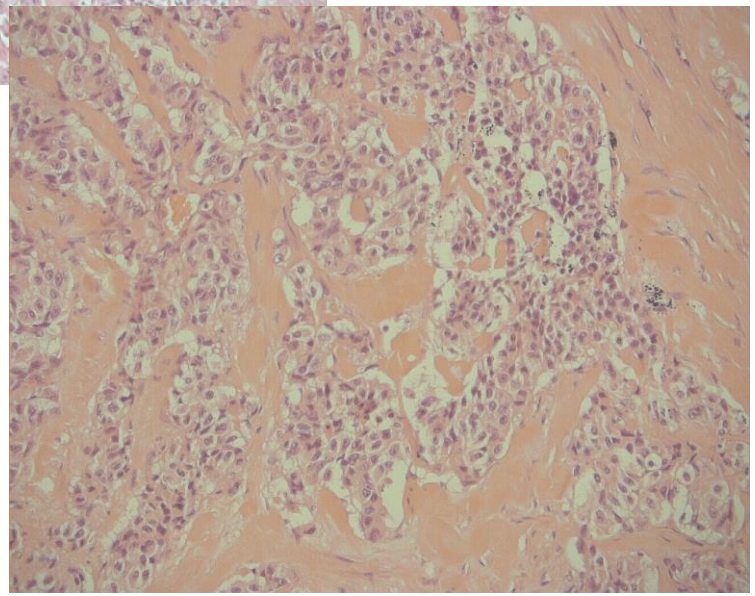
Mass in right bronchus

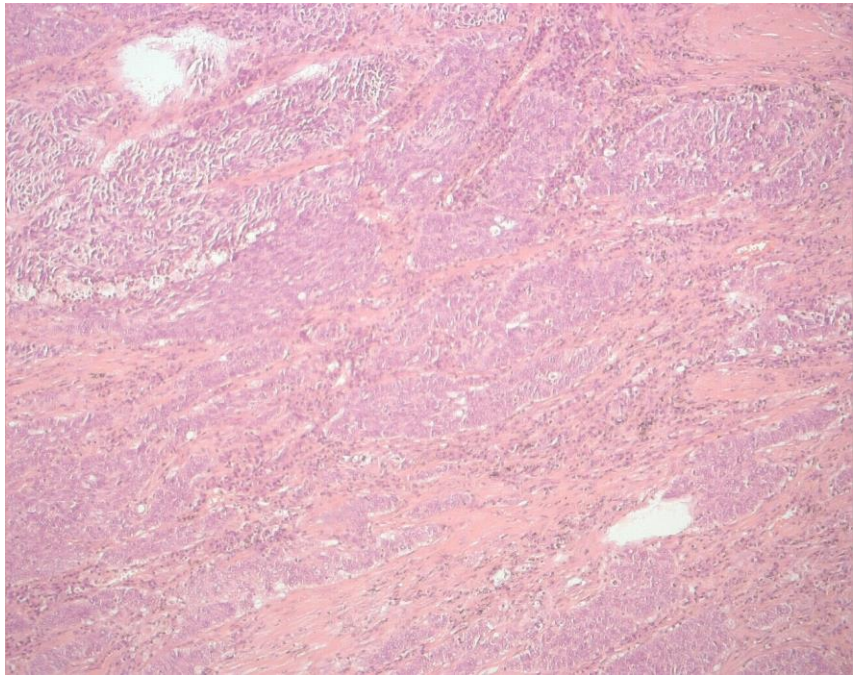
Liver metastases

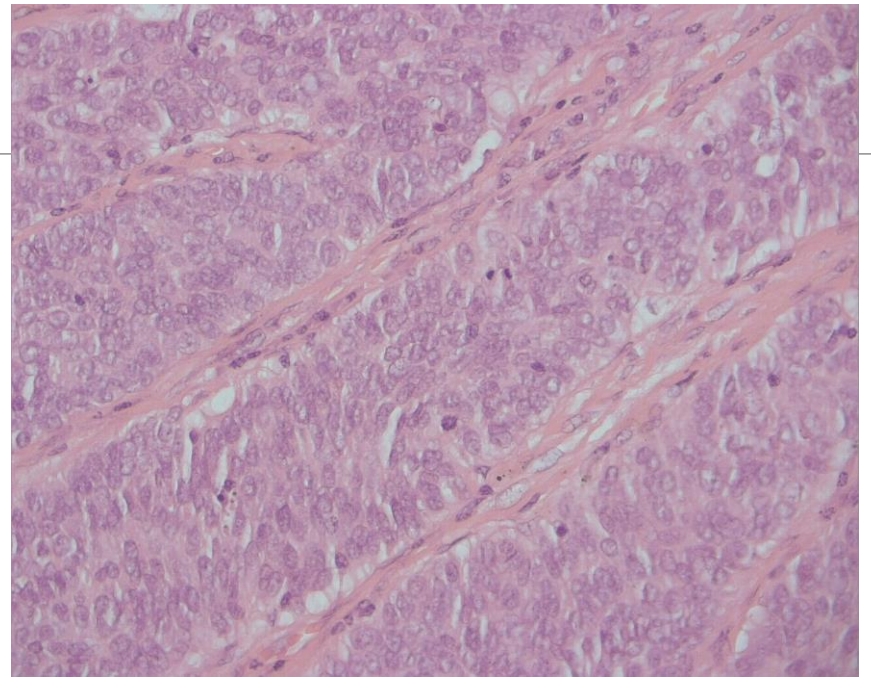
31

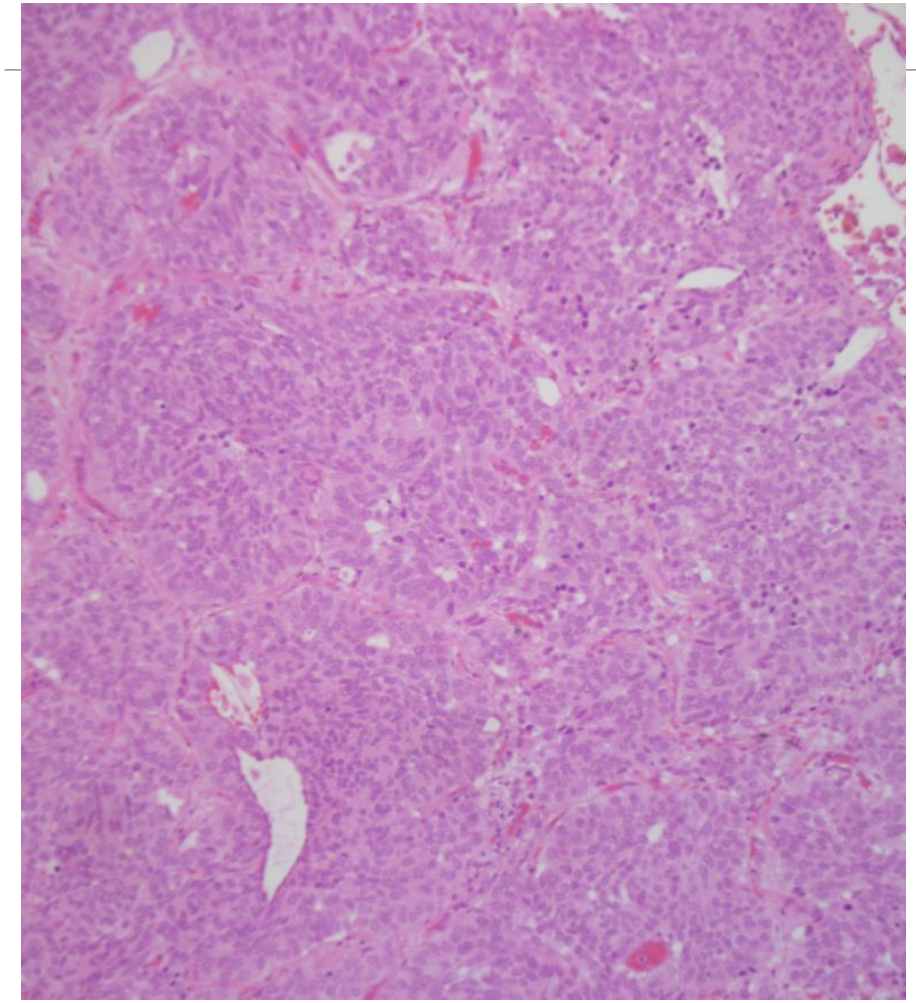
Mass in left upper lobe

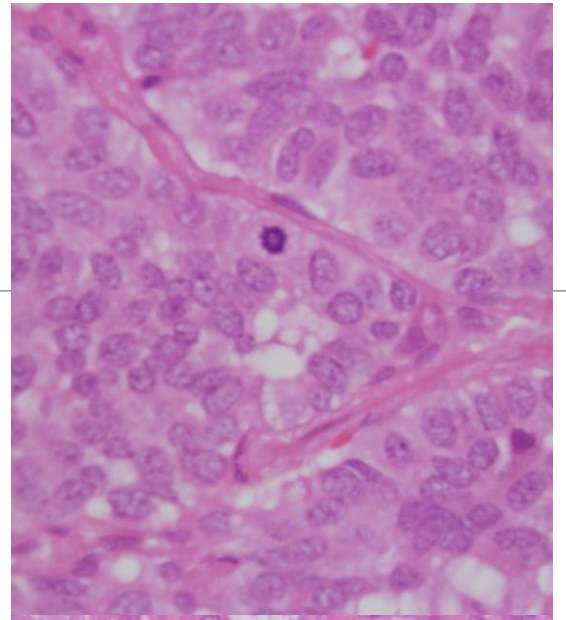


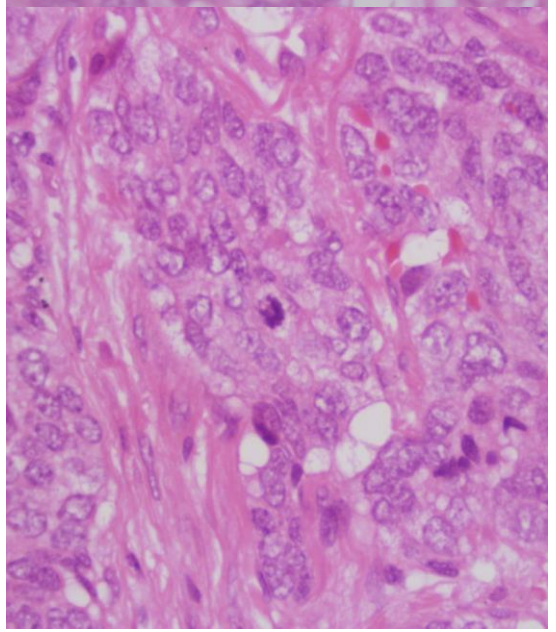












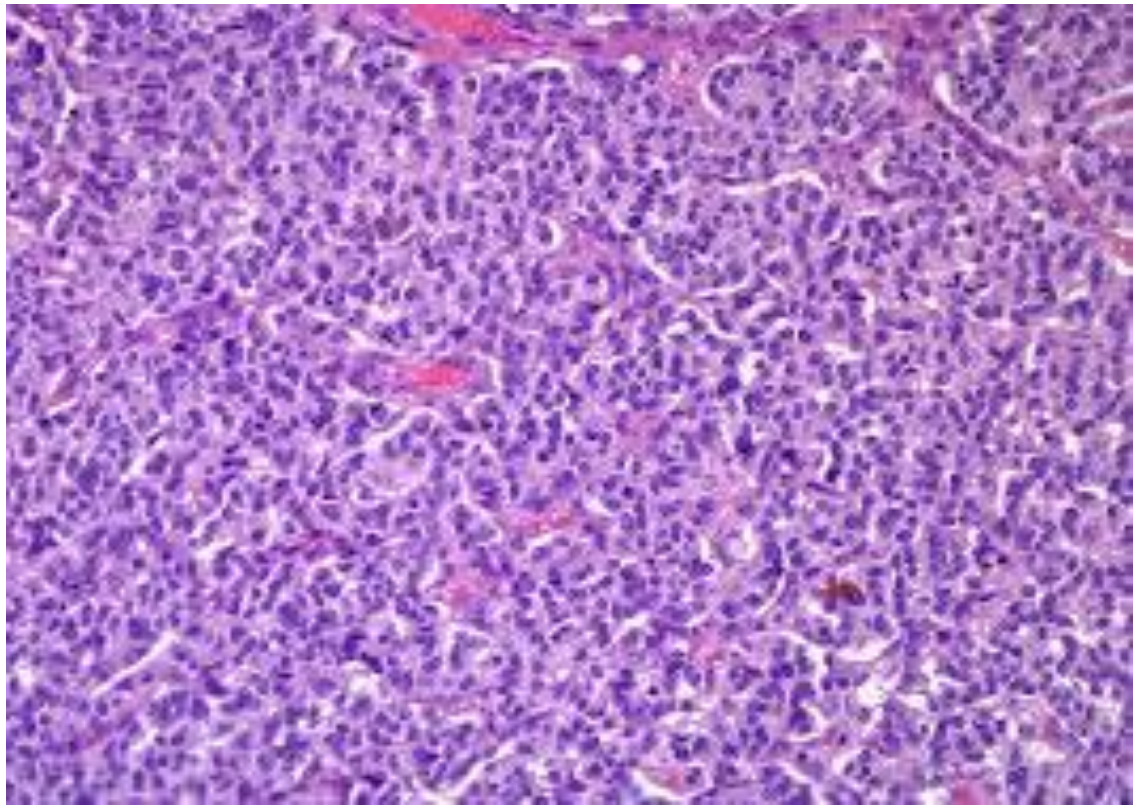
Atypical carcinoid

10% carcinoid tumours

Up to 70% eventually metastasise – 5 year survival 60%

Increased mitotic activity and presence of necrosis.

Pleomorphism, hypercellularity, necrosis, mitoses – 3-10/2mm^2

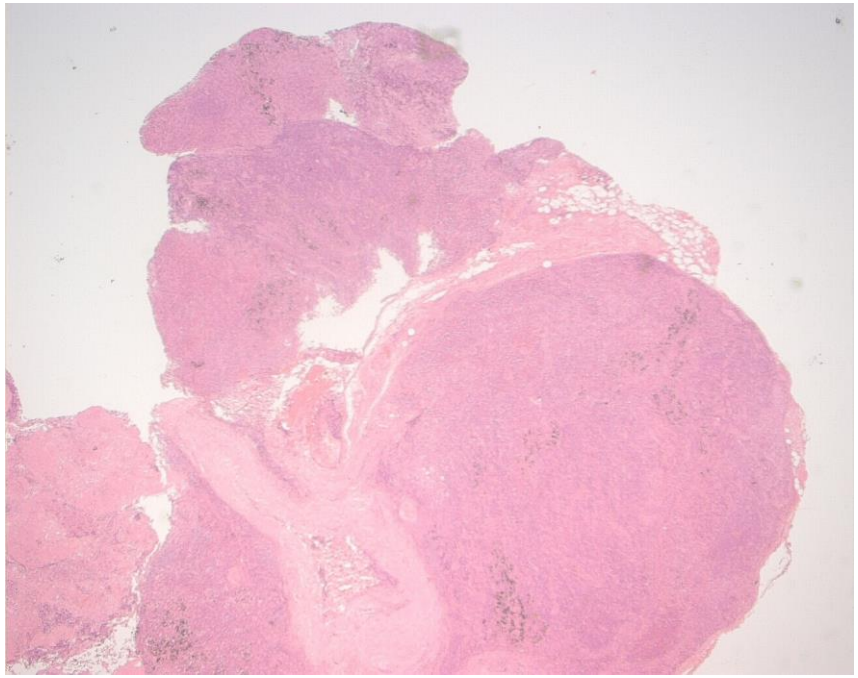


Case 4

F56

Mediastinal mass

Previous excision of thymic cyst



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Small or medium round or elongated cells

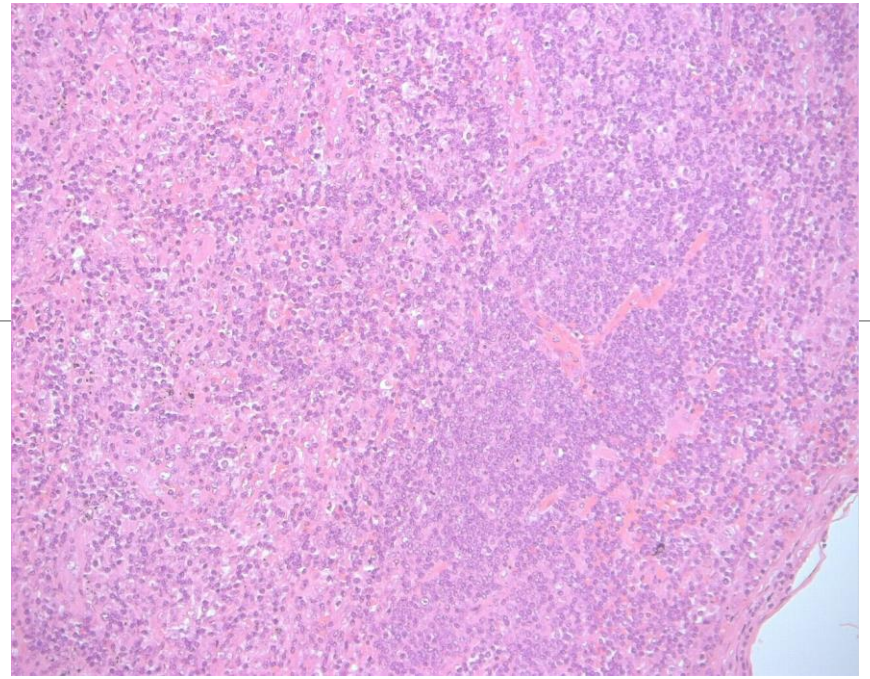
Necrosis

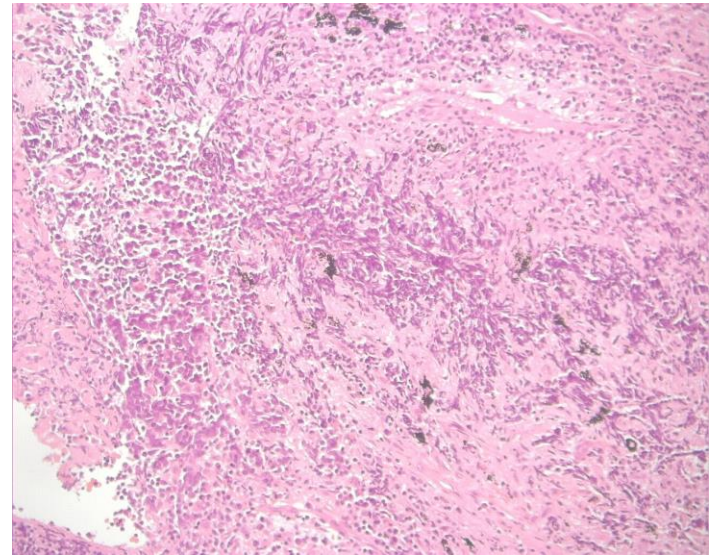
Mitoses

Fine granular chromatin indistinct nucleoli

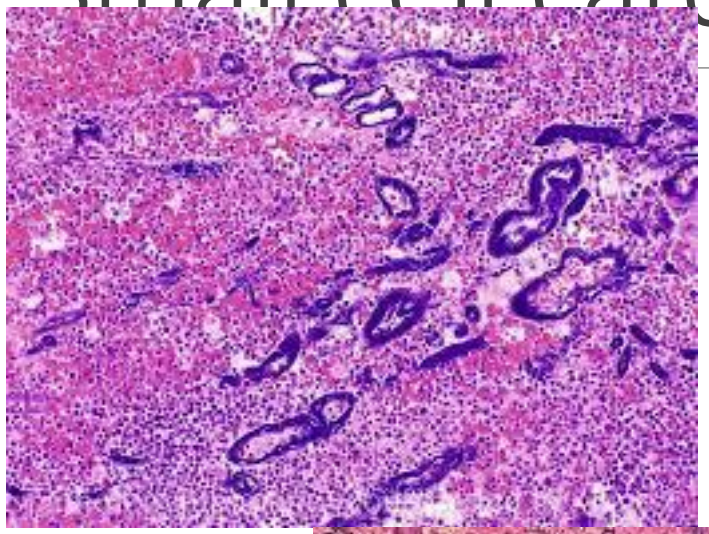
Small amount of cytoplasm

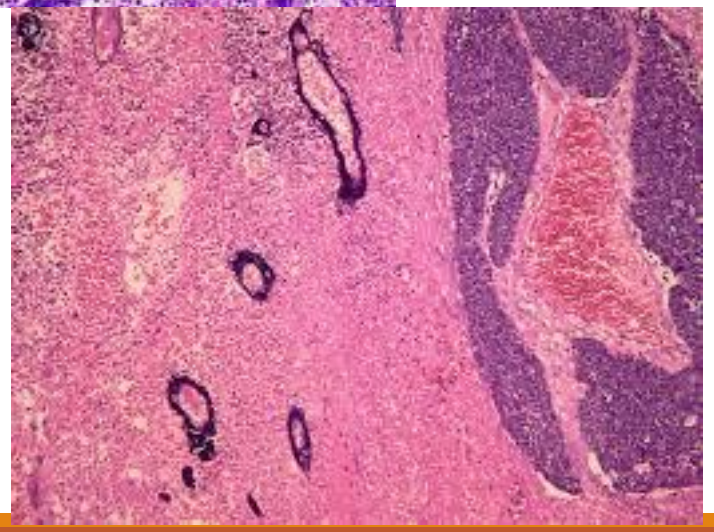
Crush artefact, Azzopardi effect





Small cell carcinoma





	Small cell	Large cell
Cell shape	Round, fusiform	Polygonal
N?C ratio	High	Low
Chromatin	Fine	Coarse
Nuceoli	Indistinct	Prominent
DNA staining of vessels	Frequent	Rare

Small cell immuno

CK7+ve

MNF- paranuclear dot like positivity

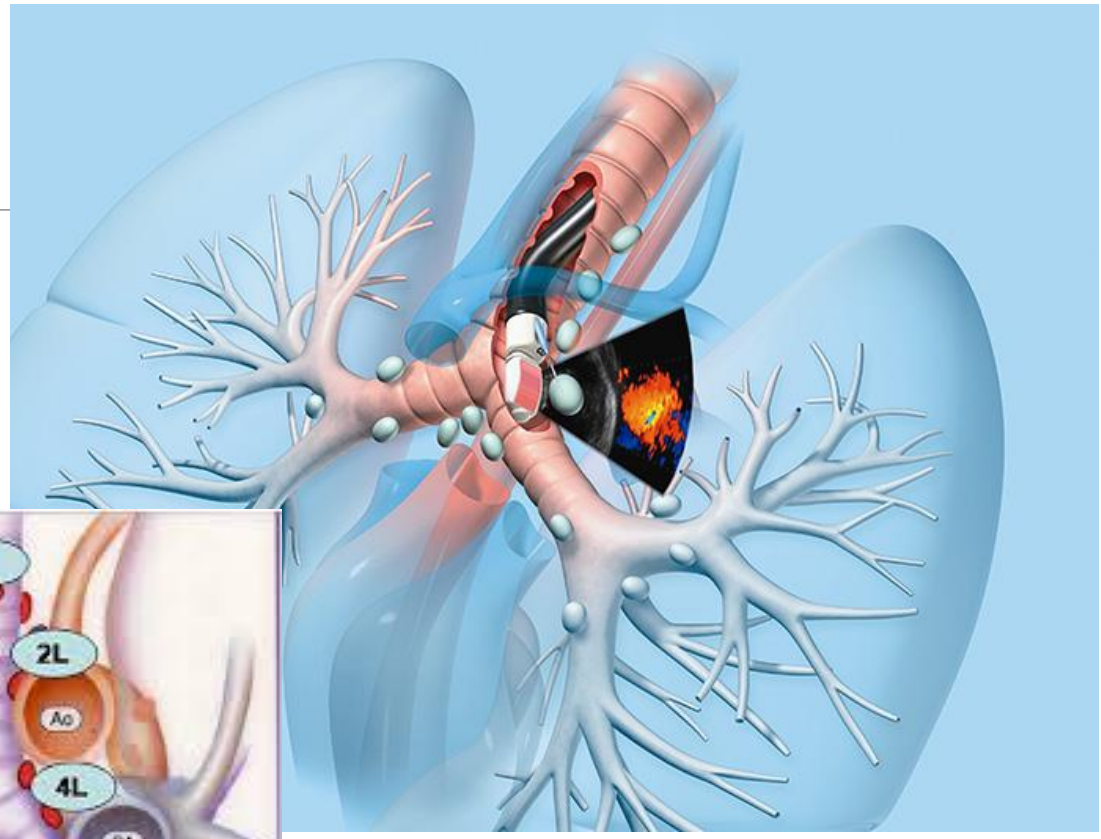
CD56, synaptophysin

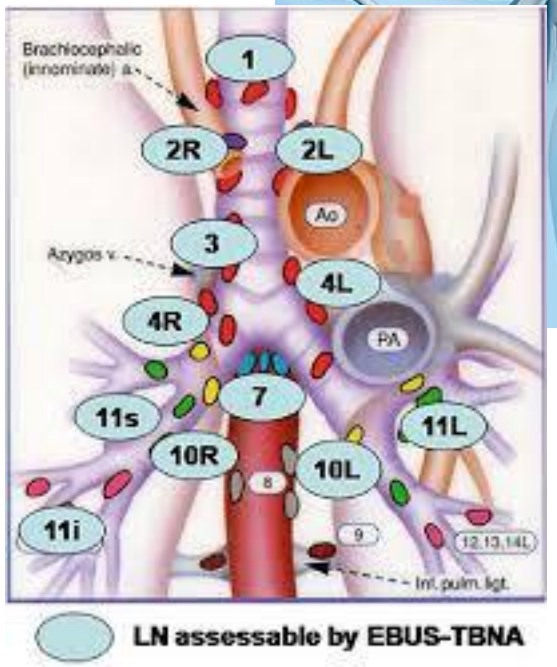
R8

EBUS

Lymph node staging

Diagnostic samples





Squamous carcinoma

May show central necrosis and cavitation

Nests and strands of cells. Irregular nuclei

Keratinisation or intercellular bridges

Variants – papillary, clear cell, small cell and basaloid

Cell type	Usual immunophenotype
Squamous	CK5+, CK7+/-,TTF-1 - , CD56 – p63, p40 +ve
Adeno	CK5-, CK7+, TTF-1 +, CD56 –
Small	CK5-, CK7+, TTF-1+, CD56 +

21

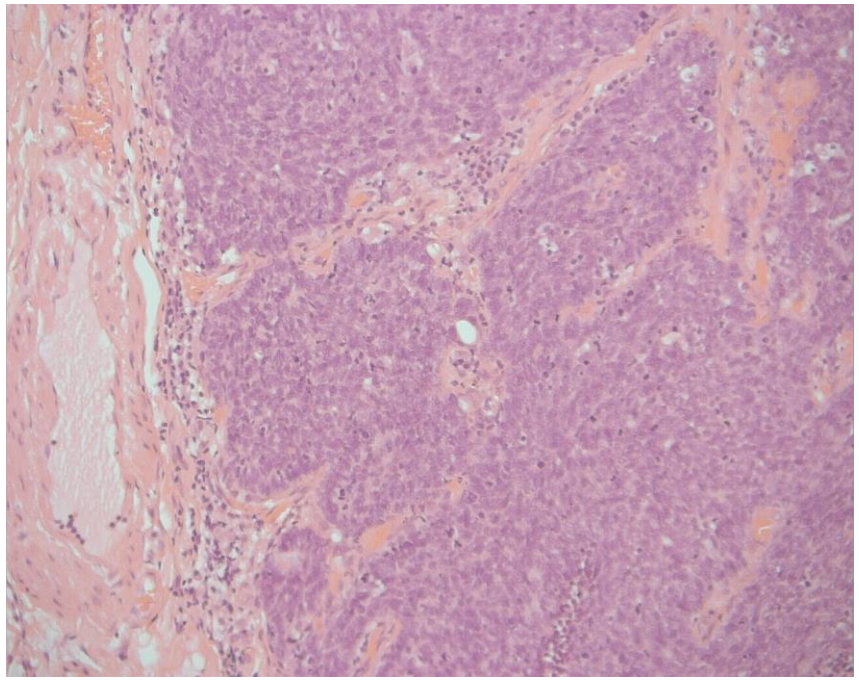
M71

T1 tumour RUL

Peripheral palisade

Small hyperchromatic cells

Some studies suggest worse prognosis



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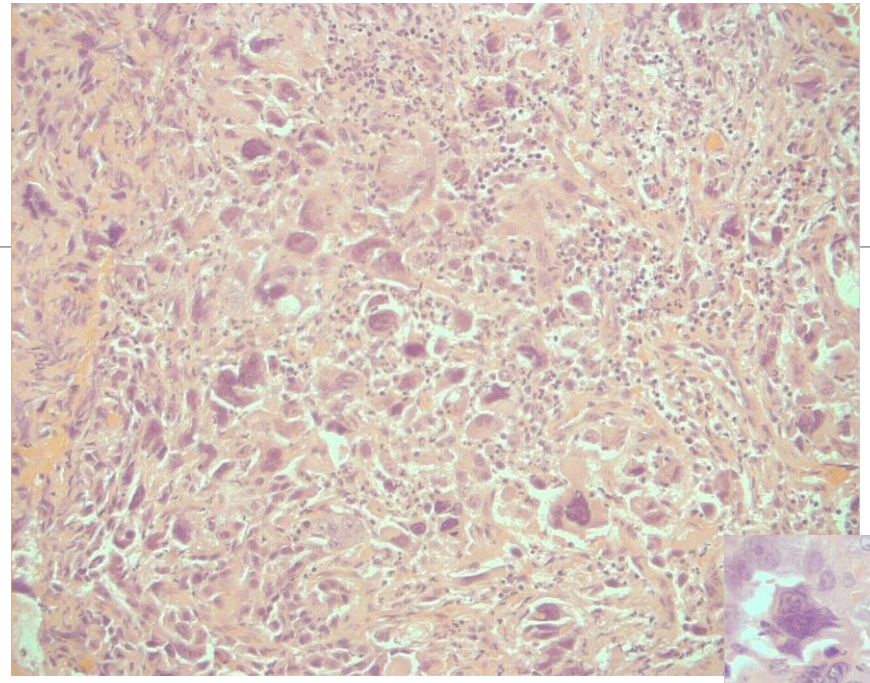
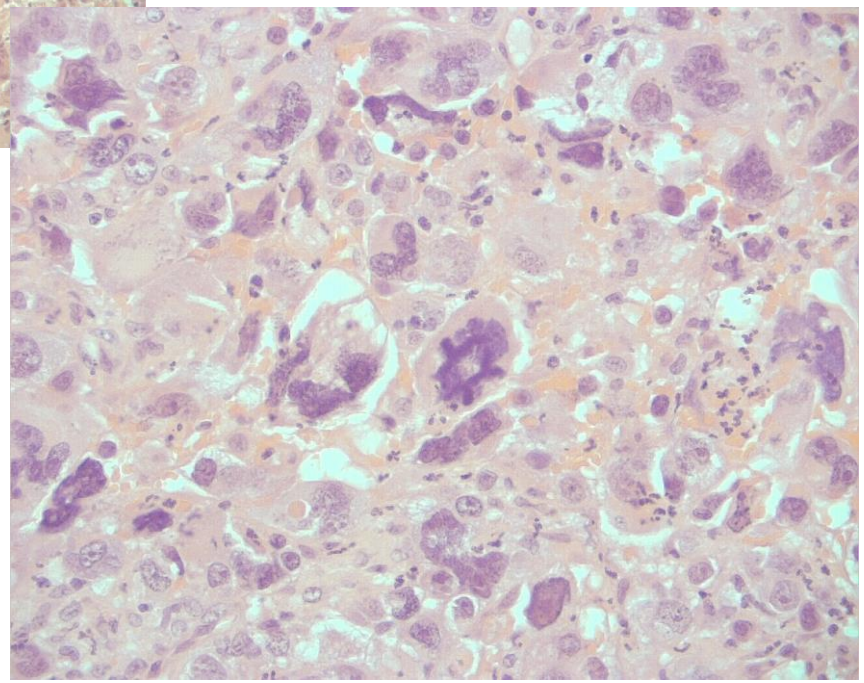
F65

Mass in RUL





Pleomorphic/giant cell carcinoma

Sarcomatoid carcinoma

Spindle cell carcinoma

Giant cell

Pleomorphic carcinoma

1% of all malignancies

Cytokeratin, CEA and EMA usually variably expressed.

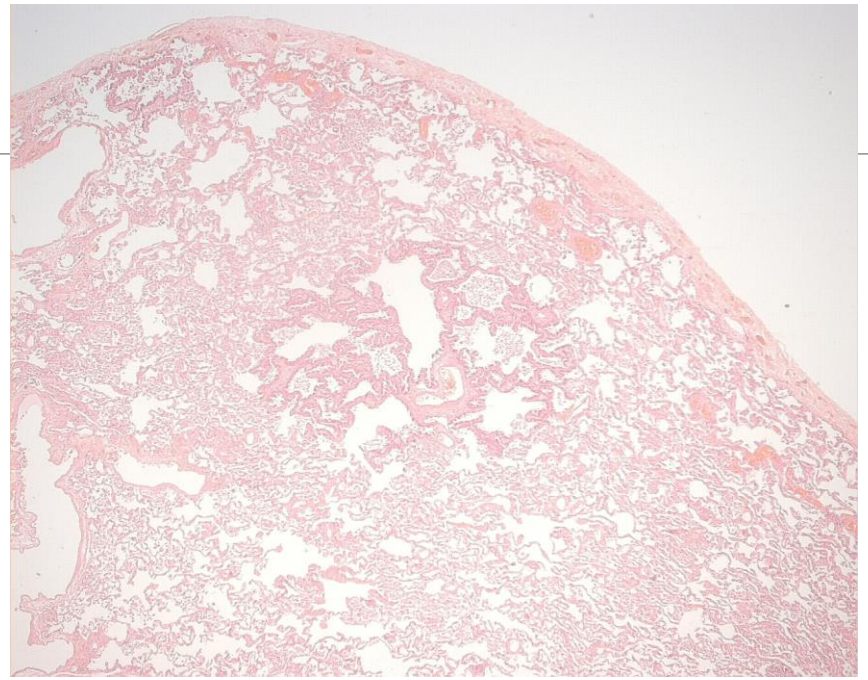
16

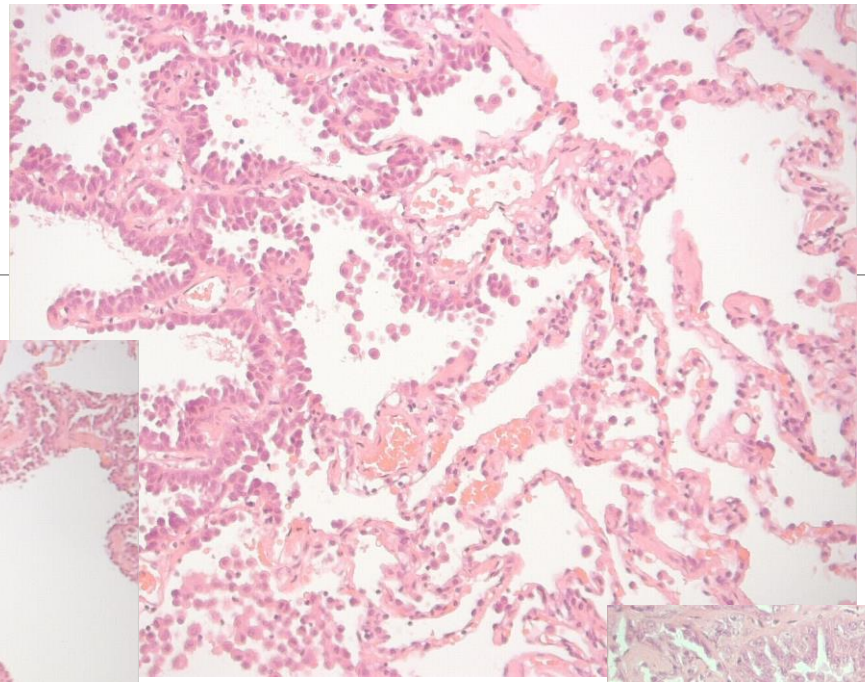
M46

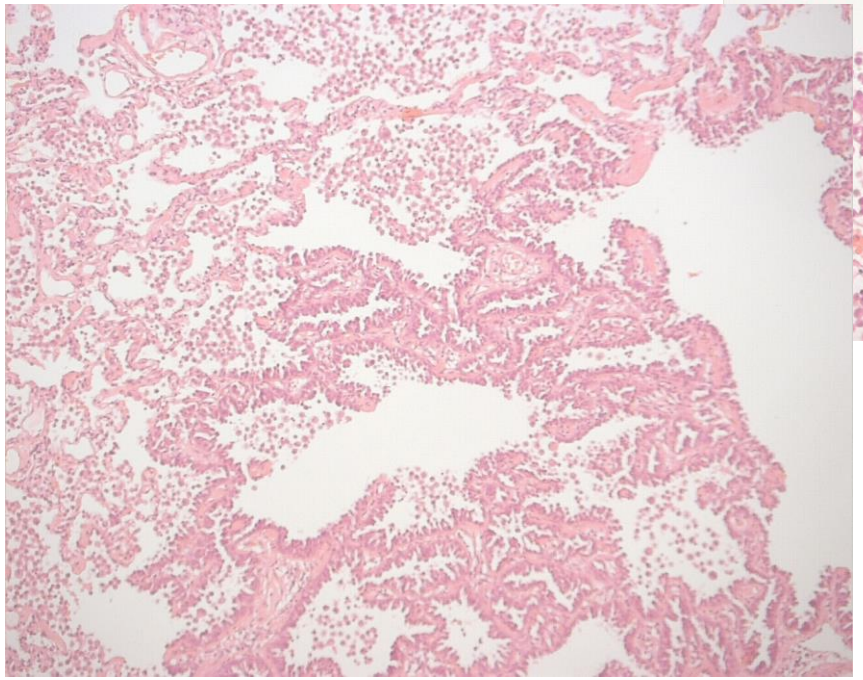
Right upper lobe pneumonia

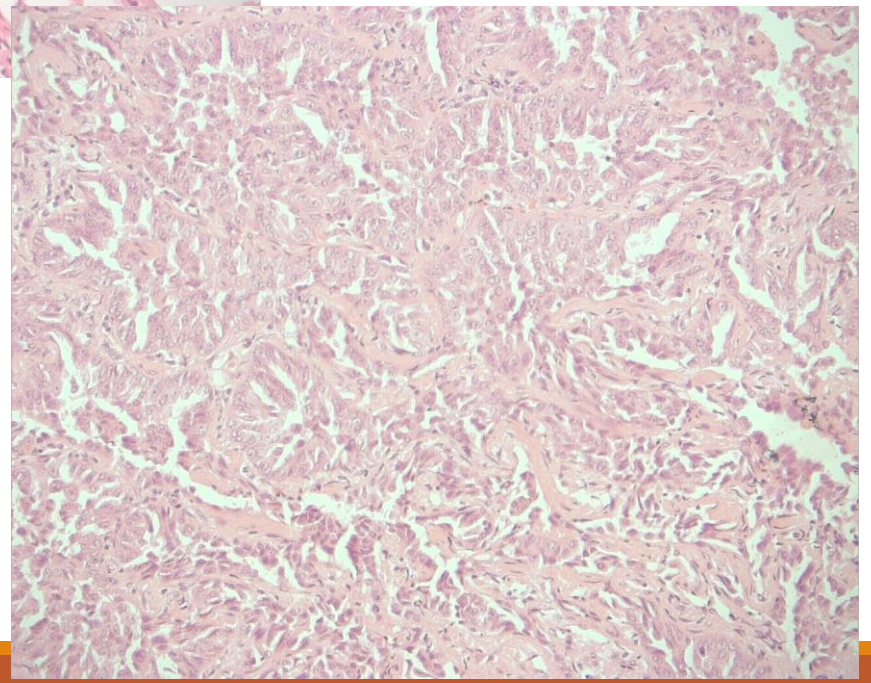
Failed to resolve

Hypoxia









Adenocarcinoma

Patterns

- Lepidic
- Acinar
- Papillary
- Micropapillary
- Solid

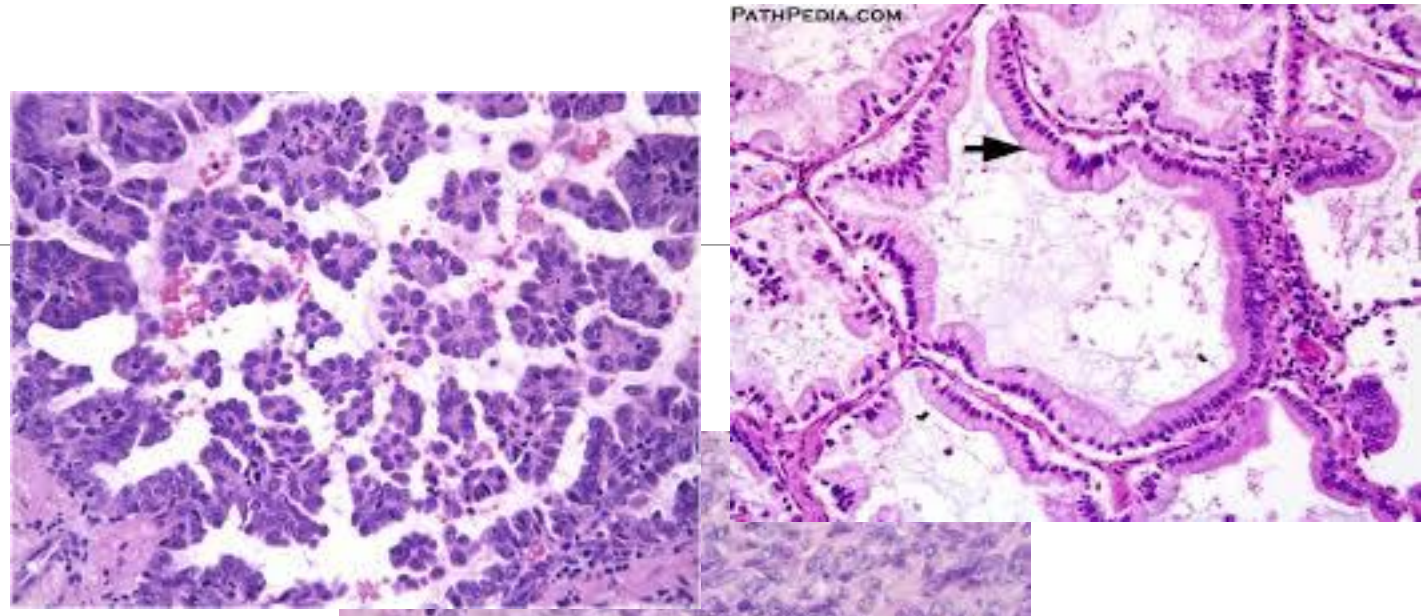
Mucinous adenocarcinoma

Foetal

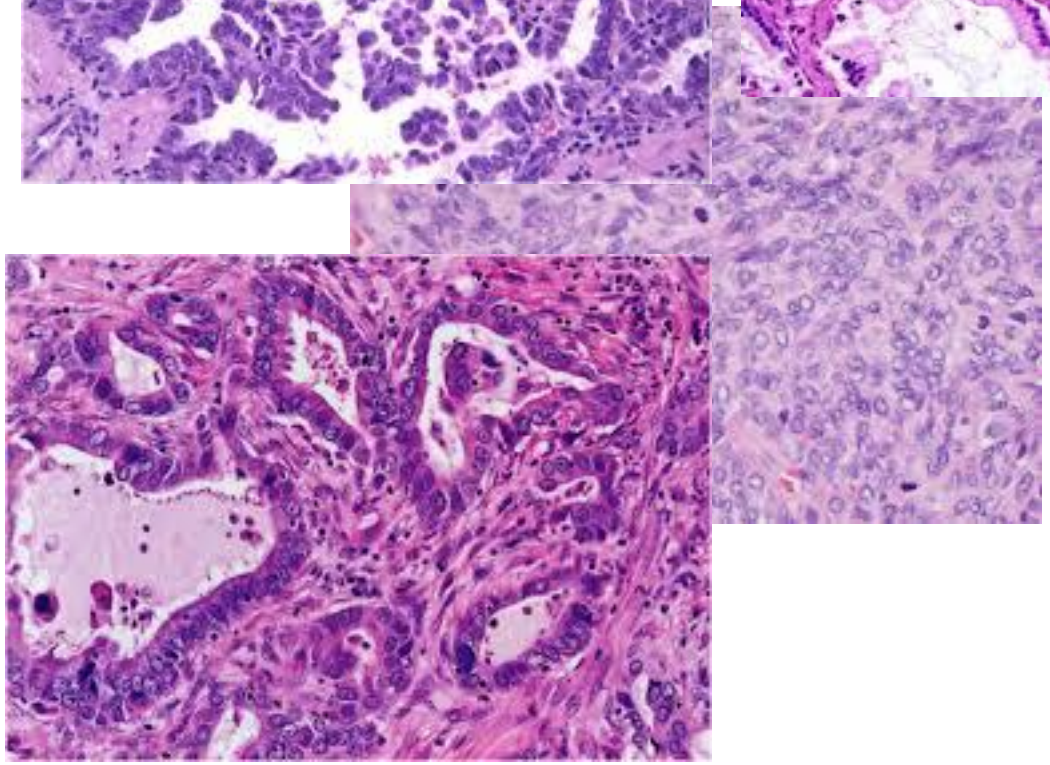
Enteric

Lepidic (BAC)

- Monomorphic cells little atypia may be multifocal
- Aerogenous dissemination



- Immuno
- CK7, TTF-1 +ve
- CEA, Ber EP4, AUA-1
- Mucinous and enteral – CK20, cdx-2



TNM staging 8th edition

Tx Primary tumour not assessed

T0 No evidence of primary

Tis Carcinoma in situ

T1 <30mm
- T1mi minimally invasive
- T1a <10mm
- T1b 10-20mm
- T1c 20-30mm

T2 tumours 30-50mm
- Or+ involves main bronchus
- Invades visceral pleura
- Atelectasis tomhilum
- T2a 30-40mm
- T2b 40-50mm

T3 tumours 50-70 mm
- Or invades parietal pleura, chest wall, phrenic nerve, pericardium, tumour in same lobe

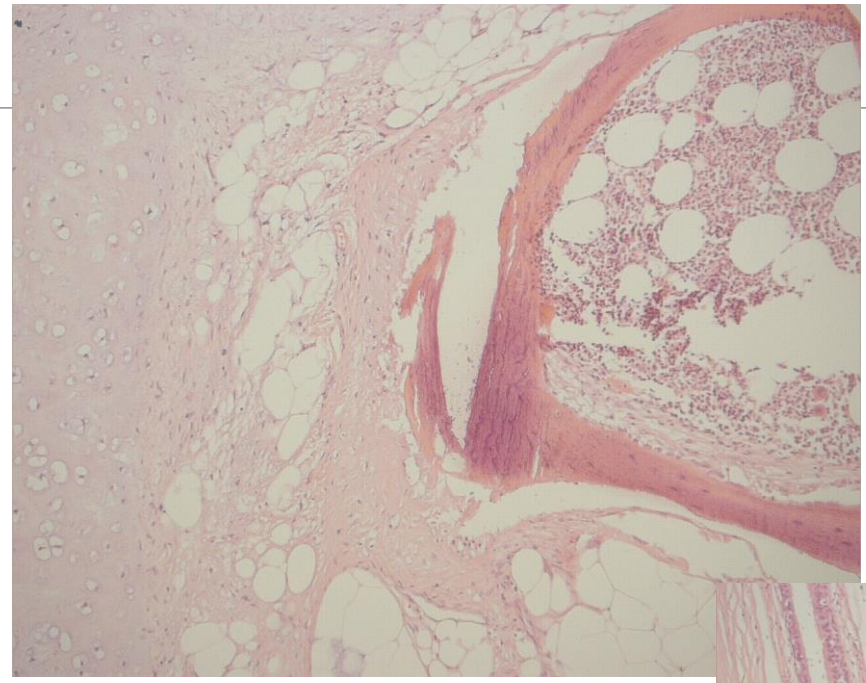
T4 >70mm
- Or in diaphragm,. Heart,vessels, recurrent laryngeal nerve, carina, trachea, oesophagus, vertebra or ipsilateral nerve

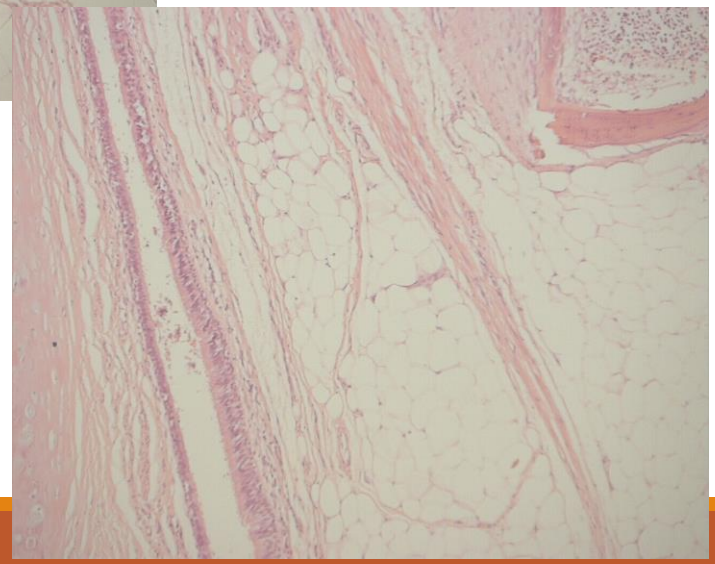
22

F68

Recurrent pneumonia

RUL collapse





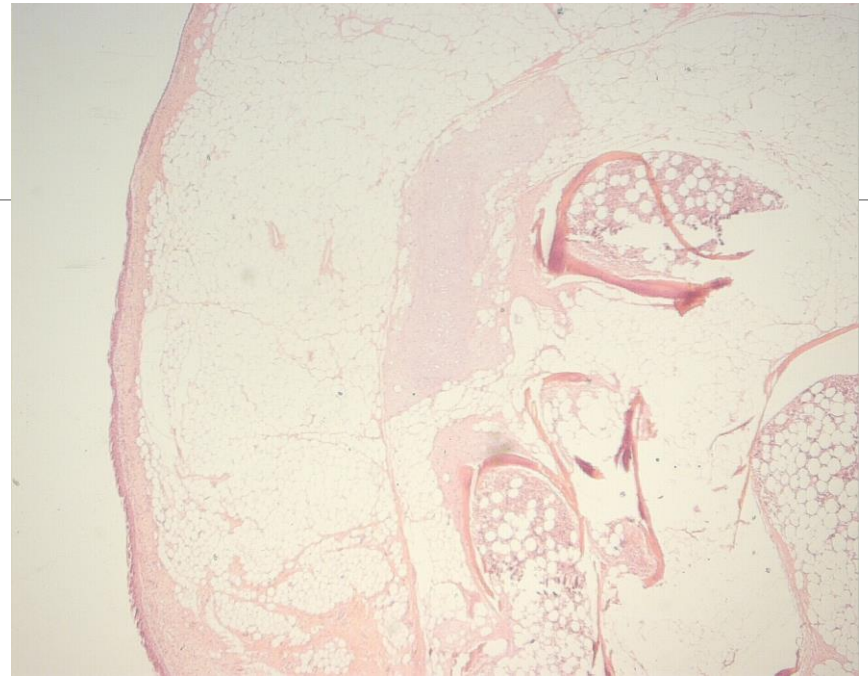
Hamartomas

Disorganised mix of connective and epithelial tissues.

Usually parenchymal, 10% endobronchial

Sharply circumscribed

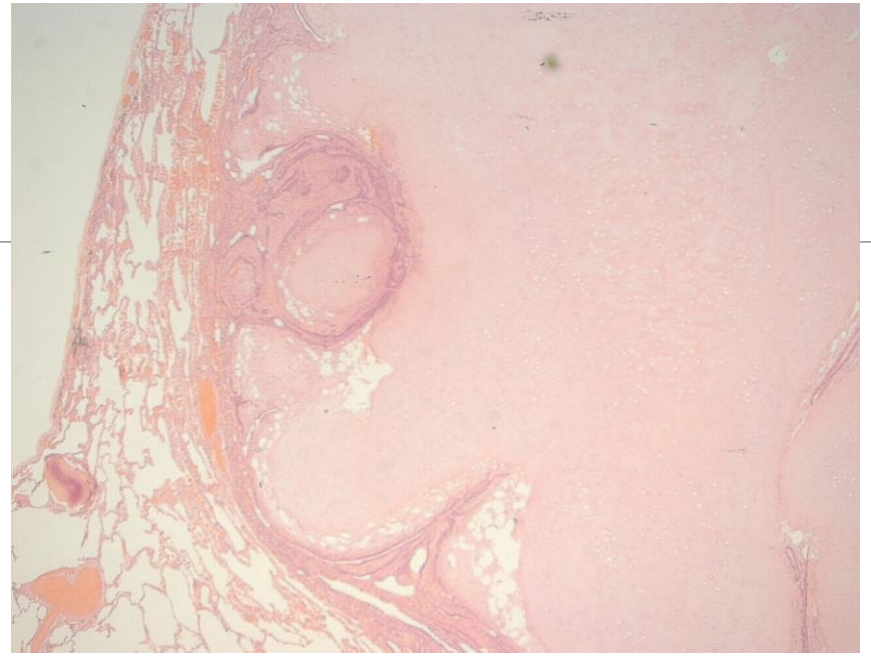
May calcify, ossify



23/30

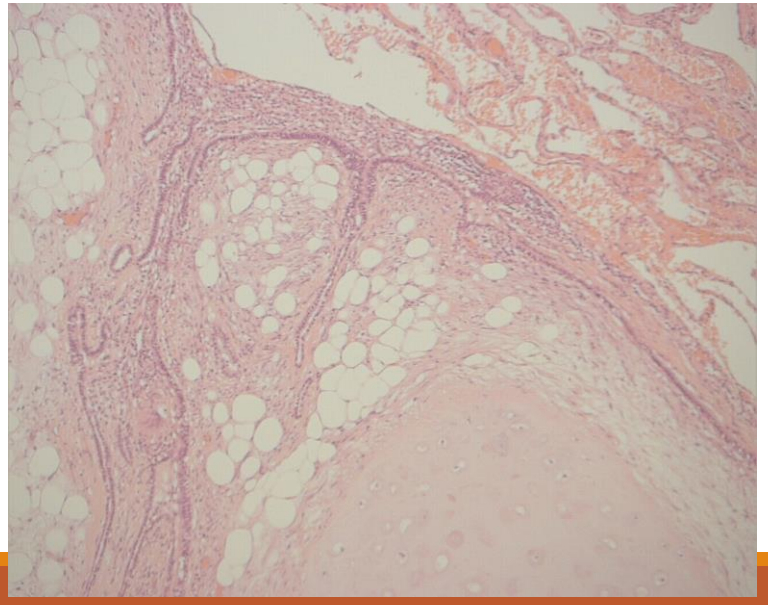
M56

RUL mass at mitral valve surgery

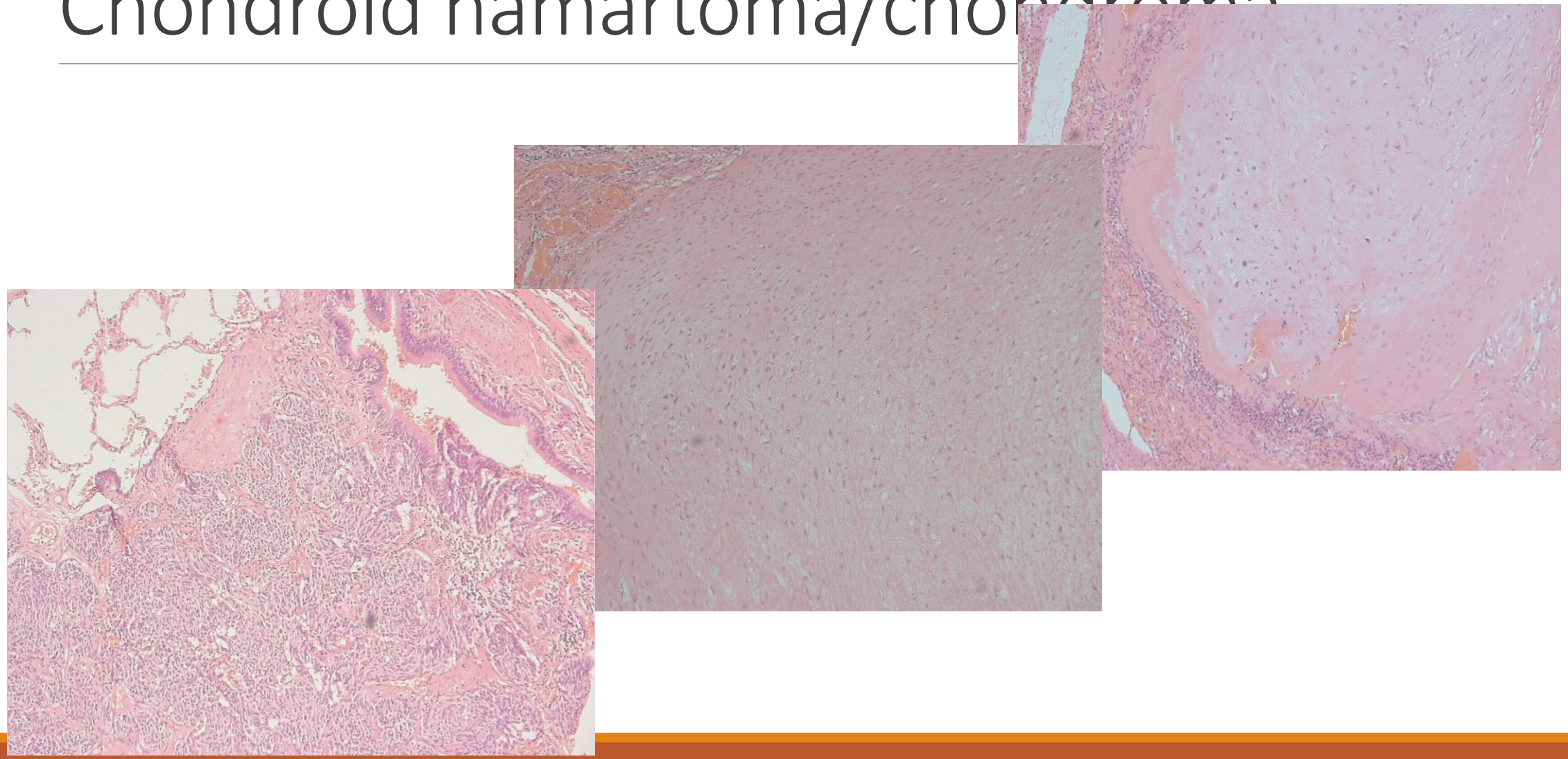


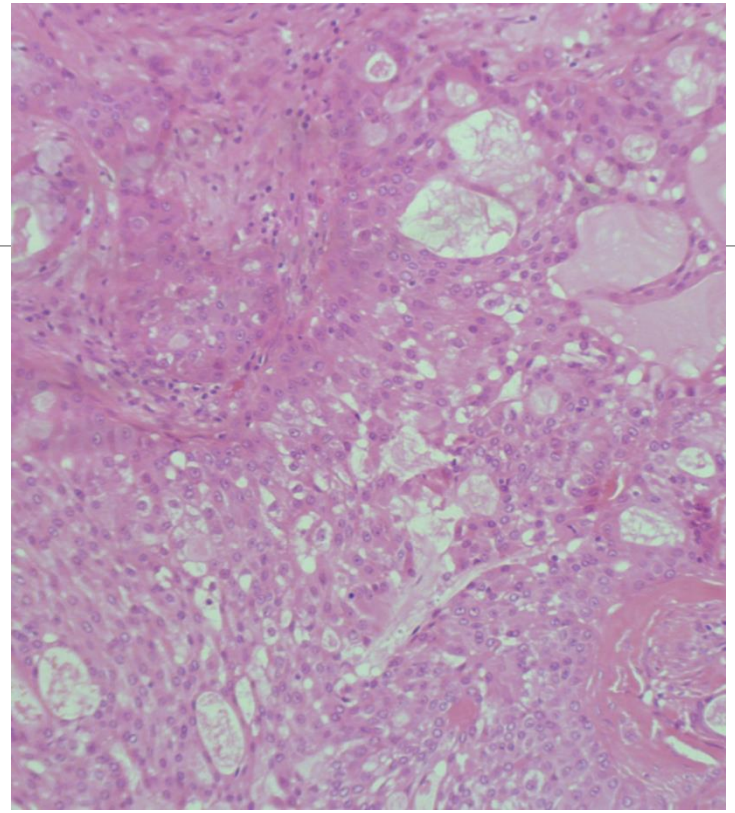
F53

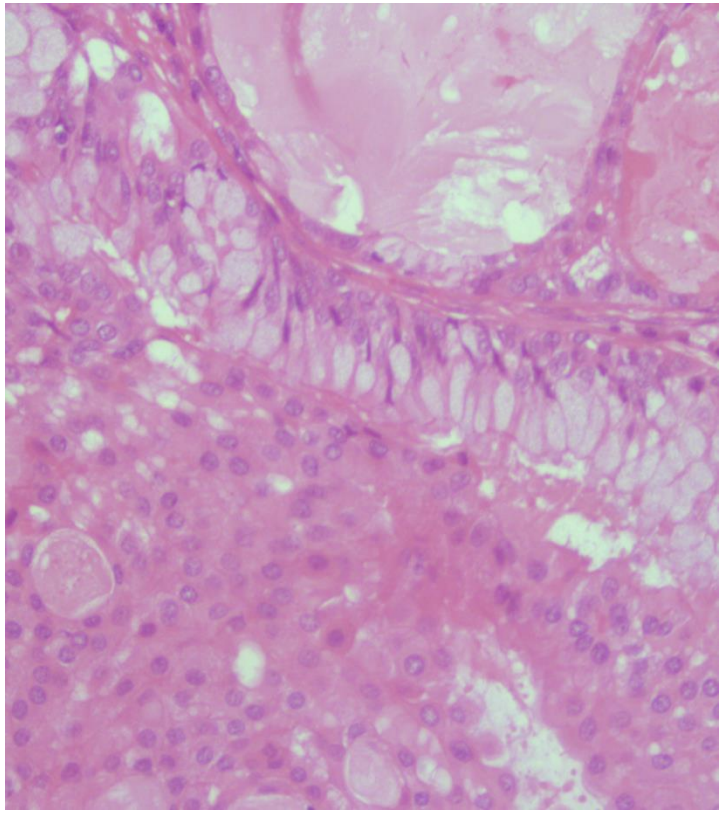
RML nodules

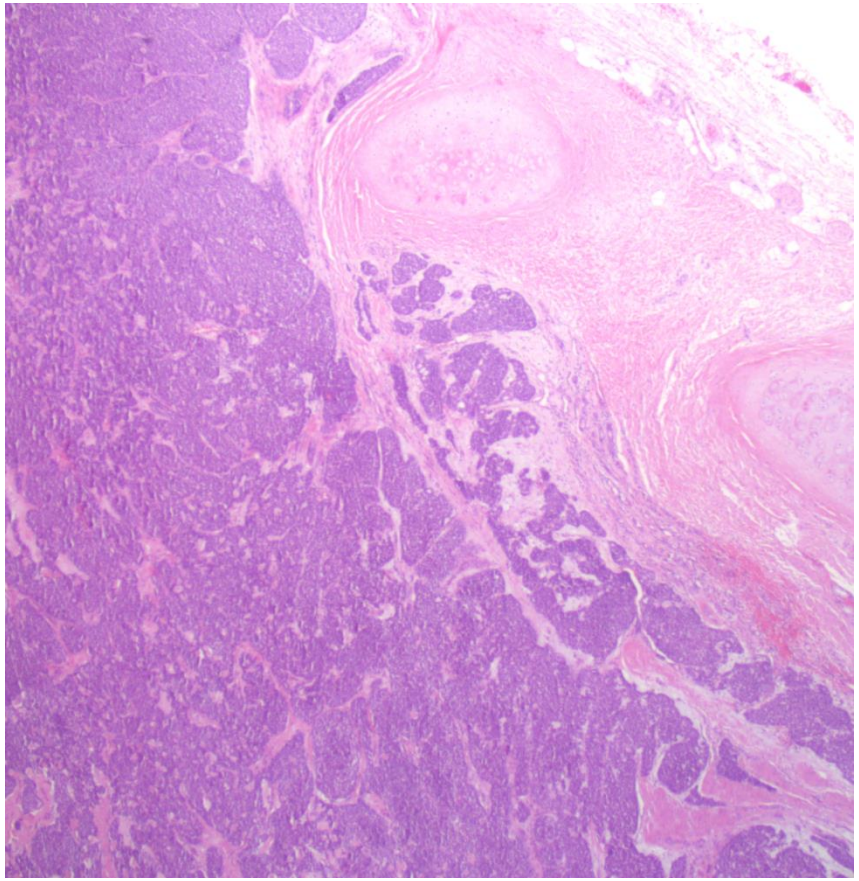


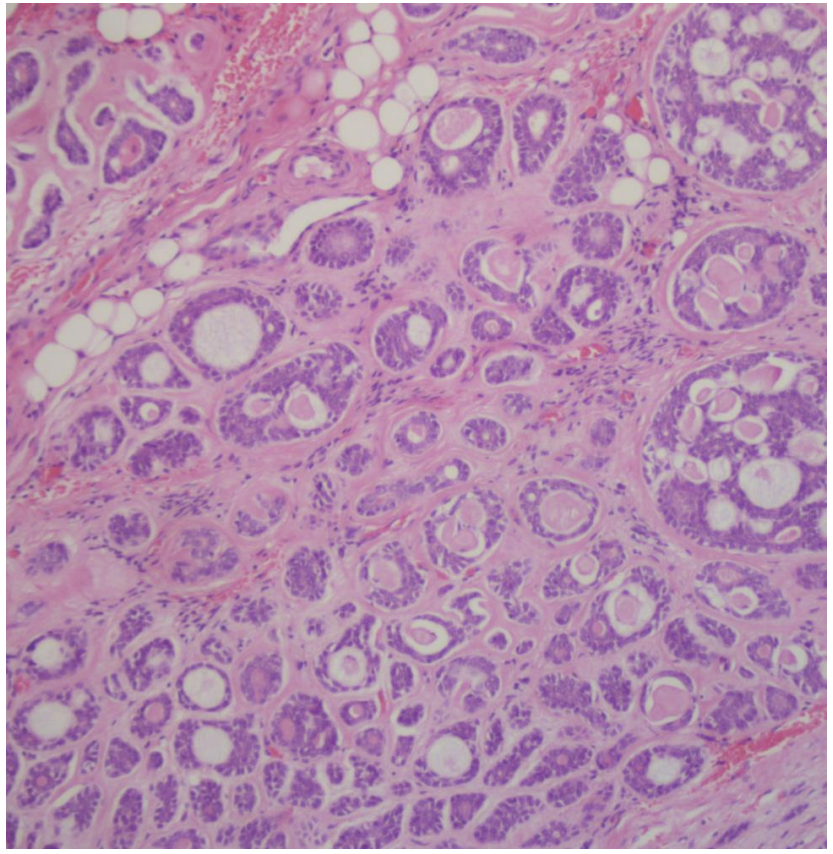
Chondroid hamartoma/chondroma

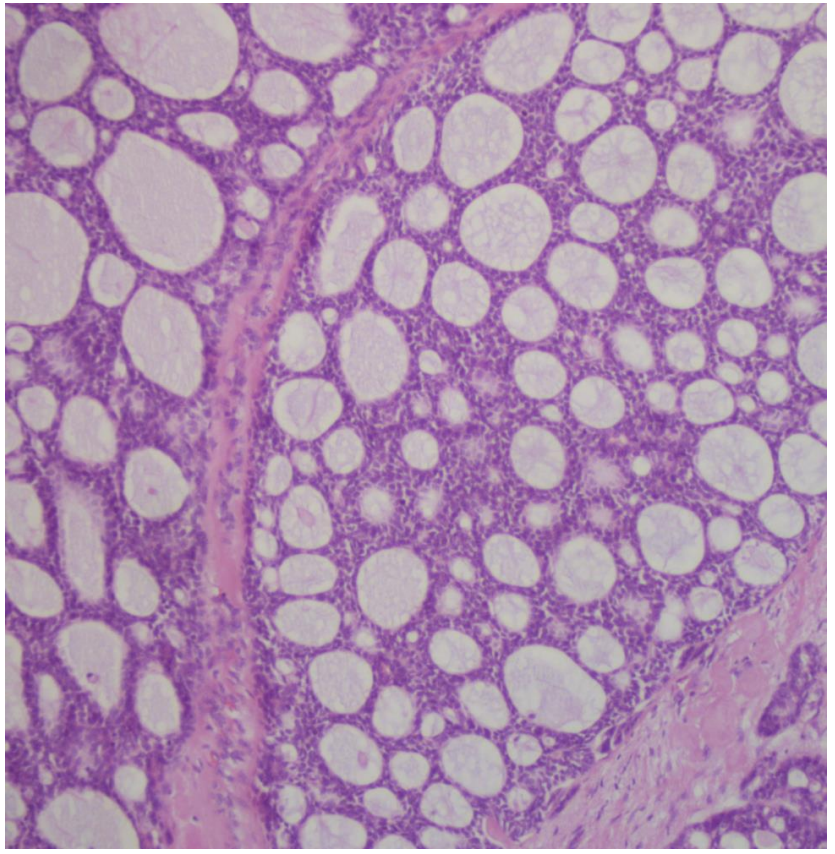












Tracheobronchial gland:Tumours of salivary gland type

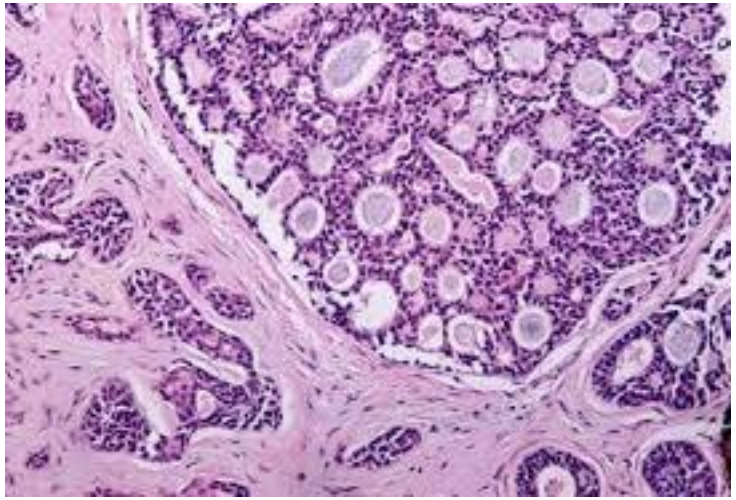
Seromucous galnds of bronchial wall are similar to the minor salivary glands.

Adenoid cystic

Slow growing infiltrative

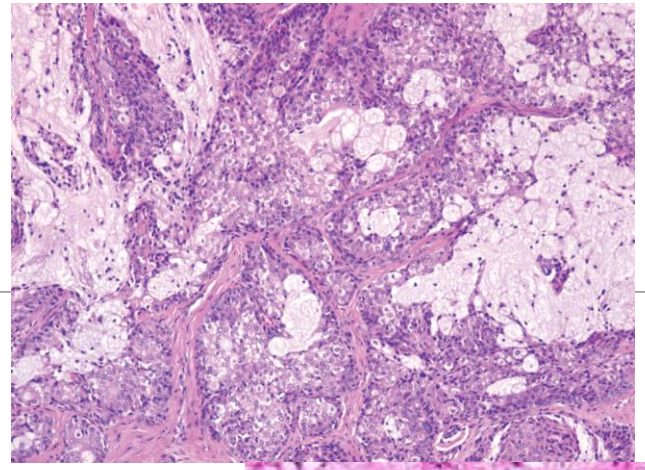
Well demarcated groups with small cyst like spaces

Myoepithelial differentiation

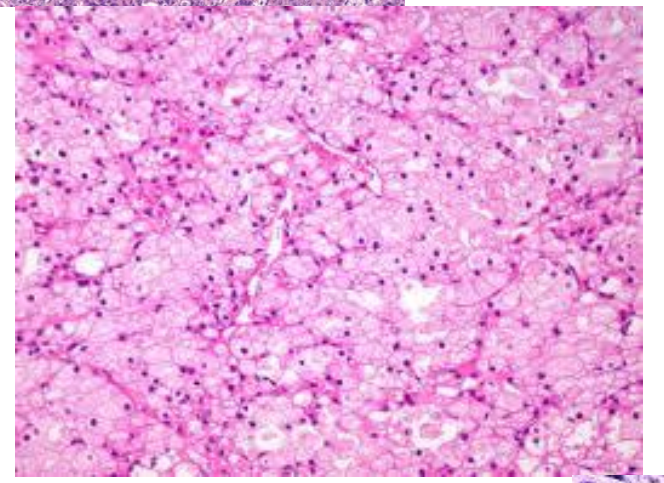


Mucoepidermoid

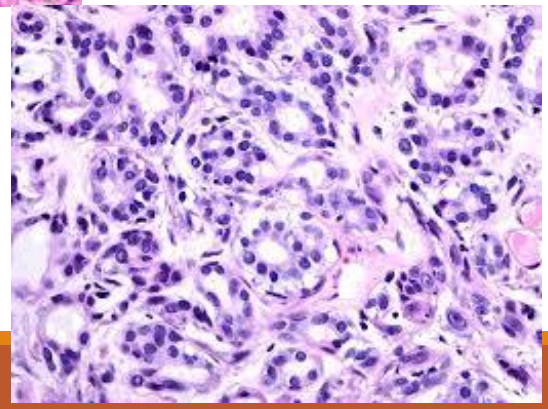
0.1%. Main airways



Acinic cell



Epithelial-myoepithelial carcinoma



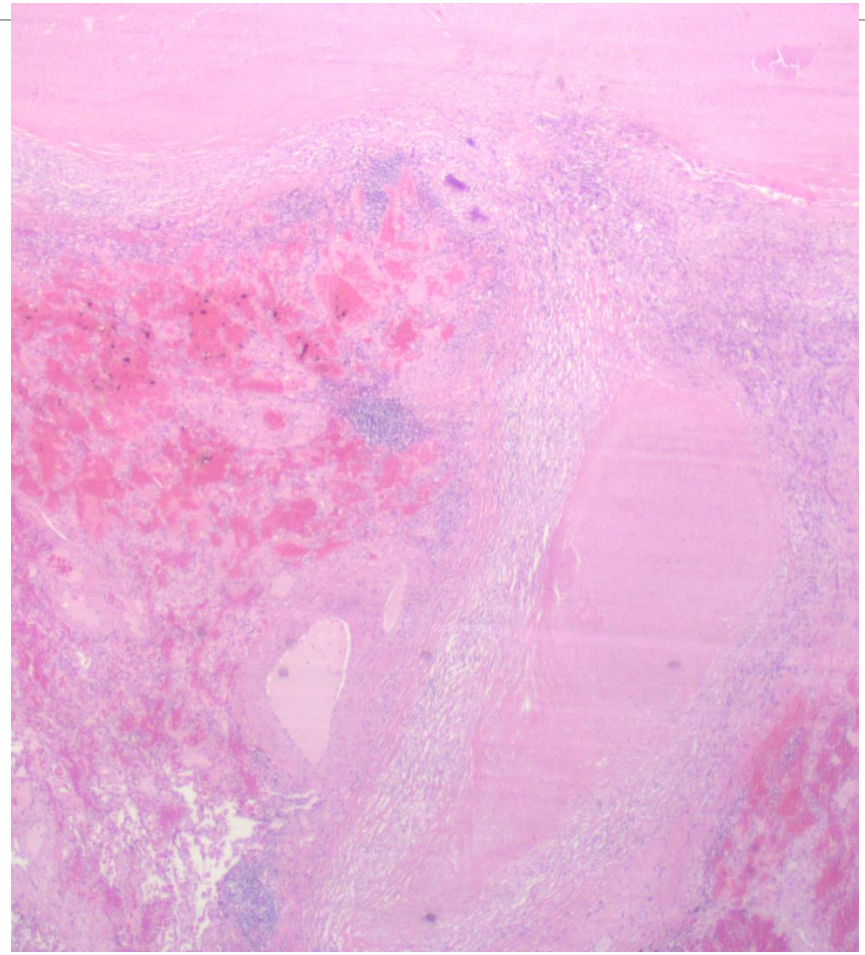
Infections

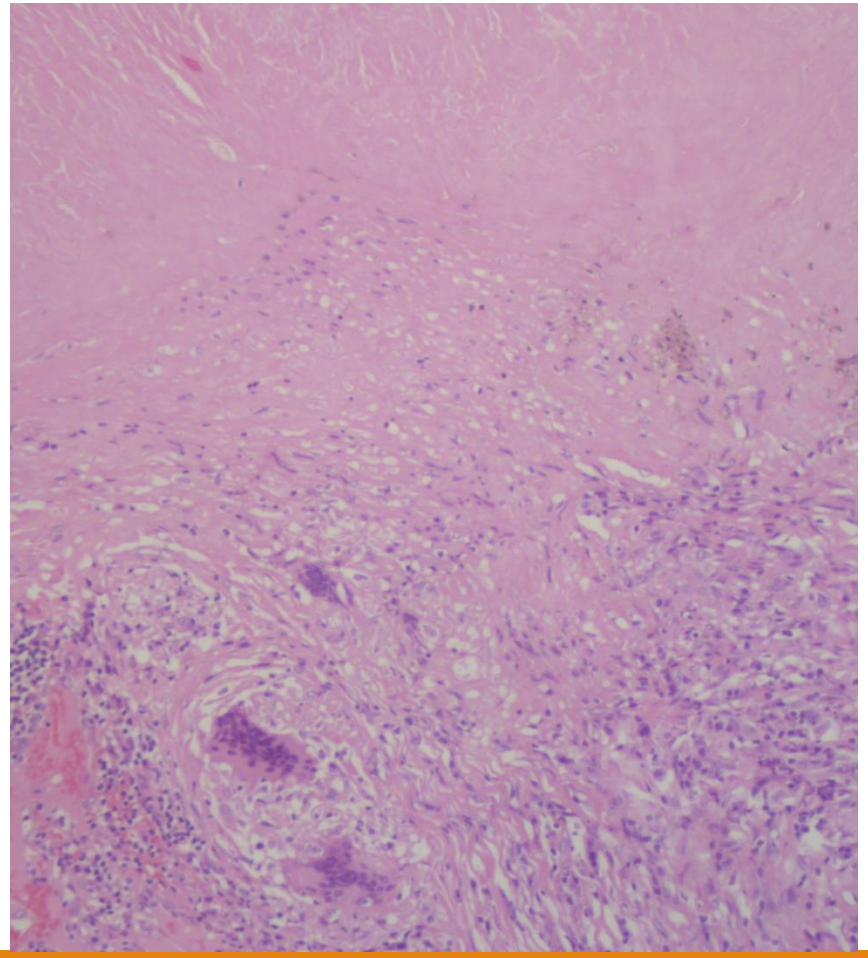
R12

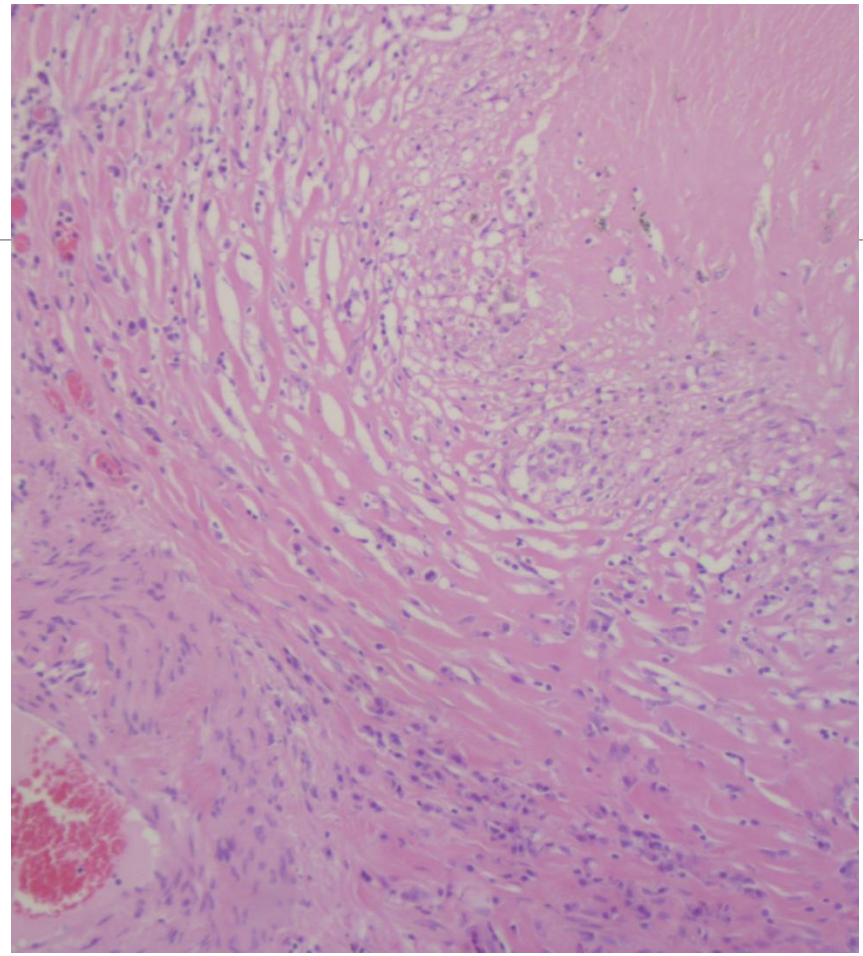
F39

Bronchiectasis

Shadowing ? cause



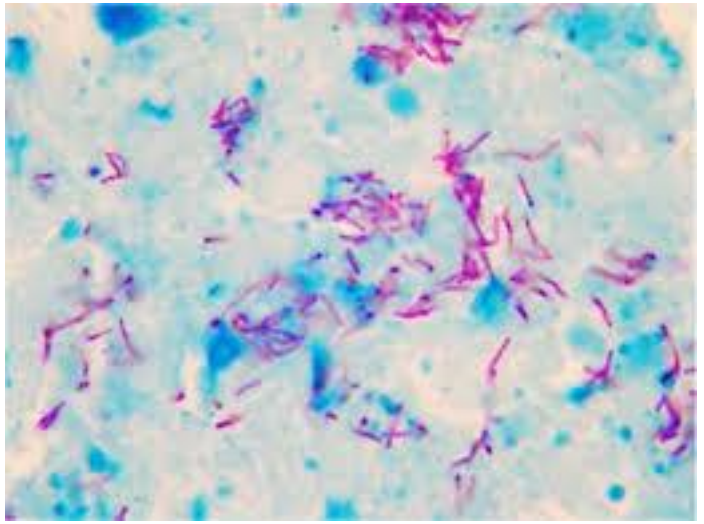




Tuberculosis

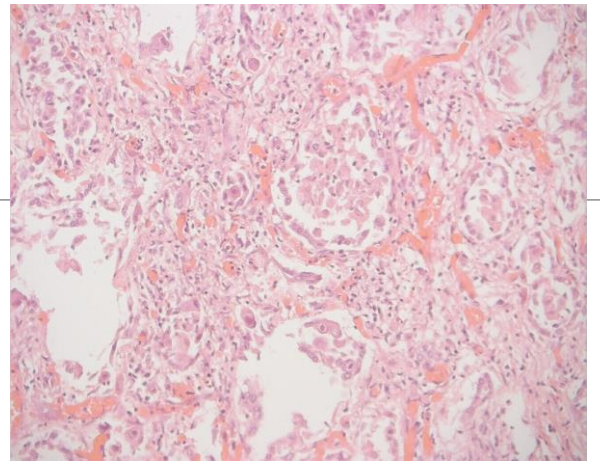
Mycobacterial infection

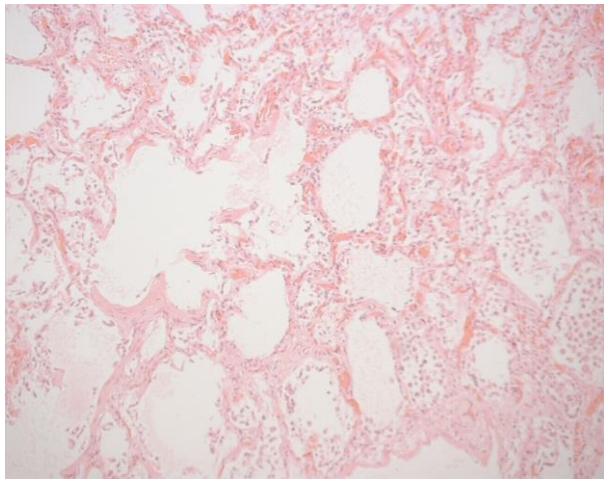
- Organisms often scanty
- Fibro caseous cavitation often apical
- Granulomatous inflammation
- ZN stain

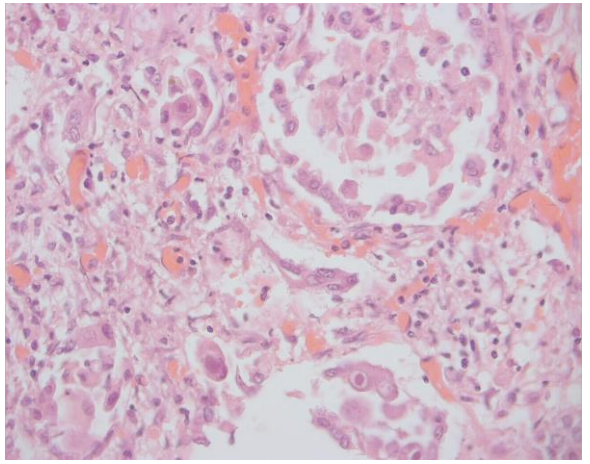


20

Death one month post-lung transplant







Opportunist infections

Usually in the setting of immunosuppression

- Transplant
- Immunological disease
- Haematological malignancy

Viral

CMV, HSV

Fungal

Candida
Aspergillus
Mucor

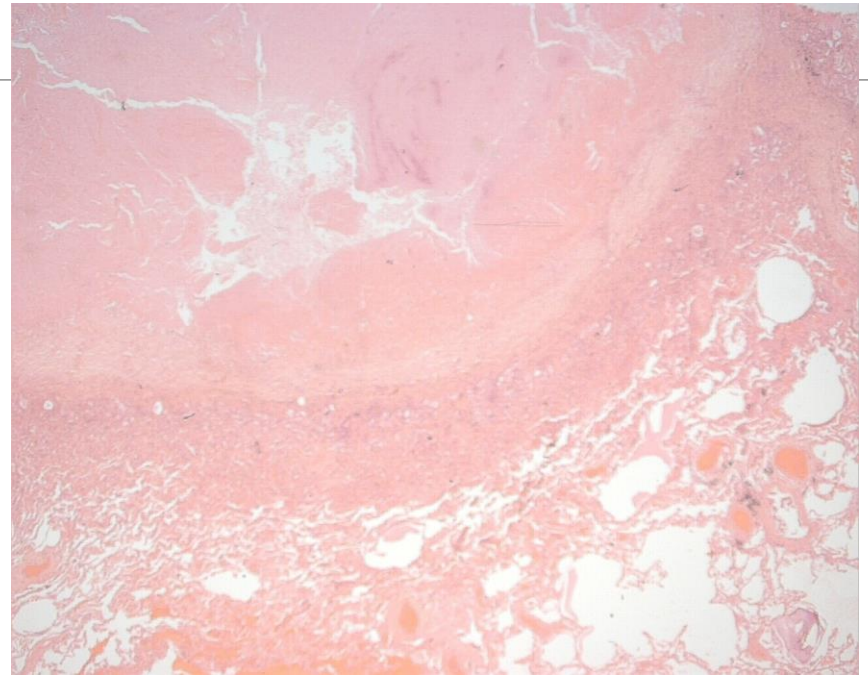
19

M57

Failing renal transplant

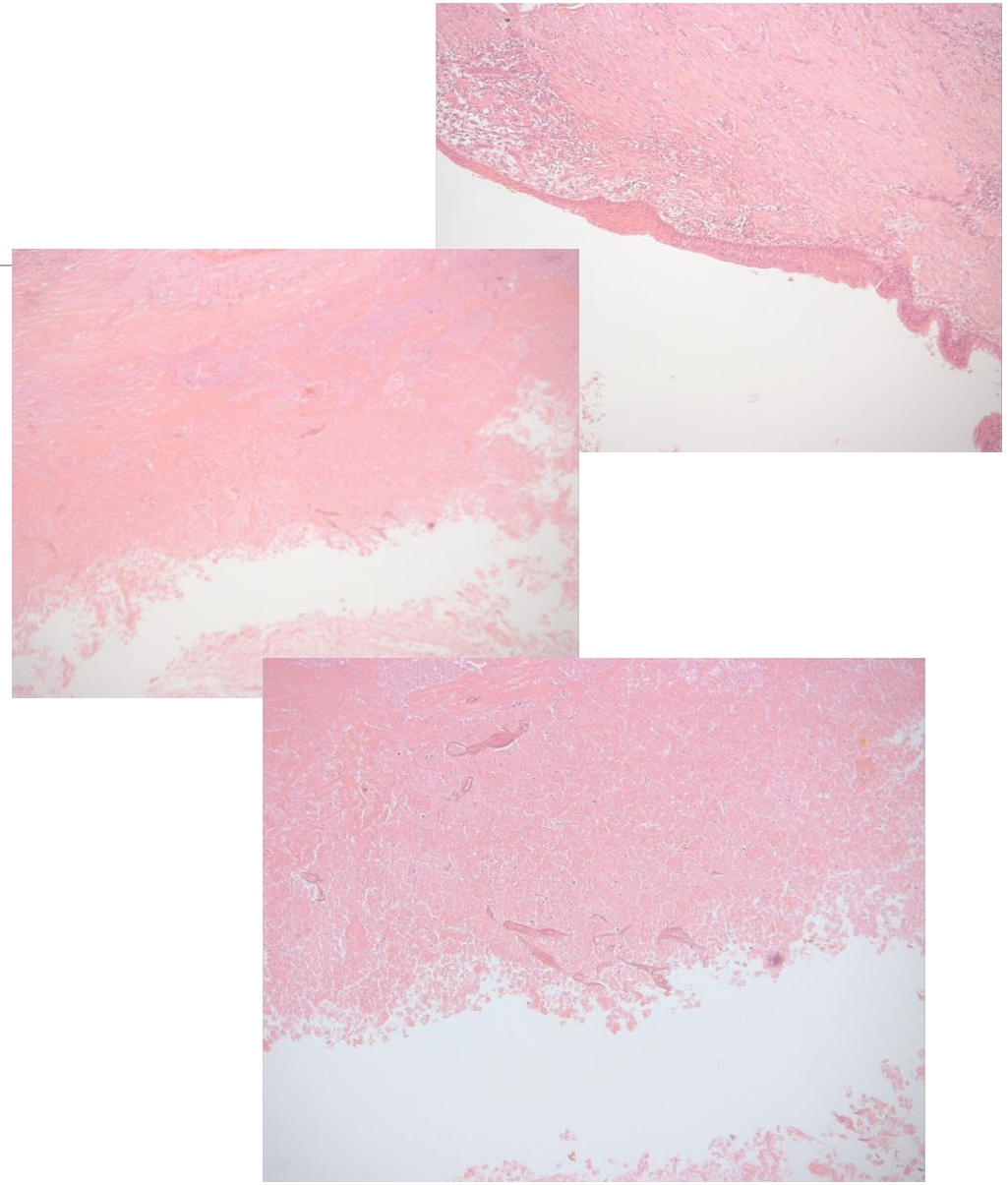
Immunosuppressed

Abscess in RLL post Klebsiella pneumonia



Cavities

- Necrotising pneumonia
- Infarcts
- Vasculitis
- Mycobacteria
- Tumours
- Bronchocoeles

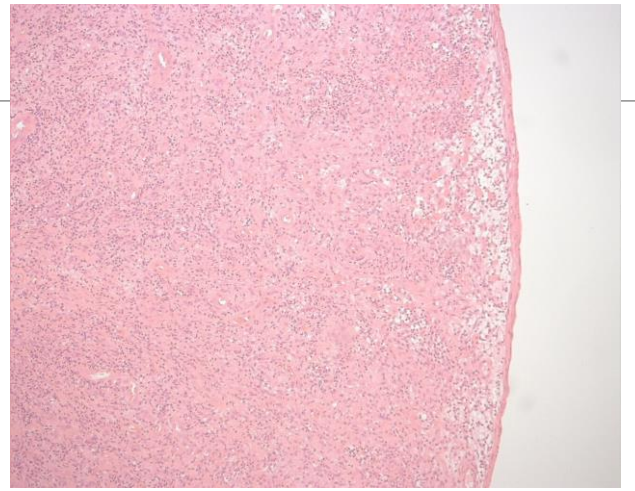


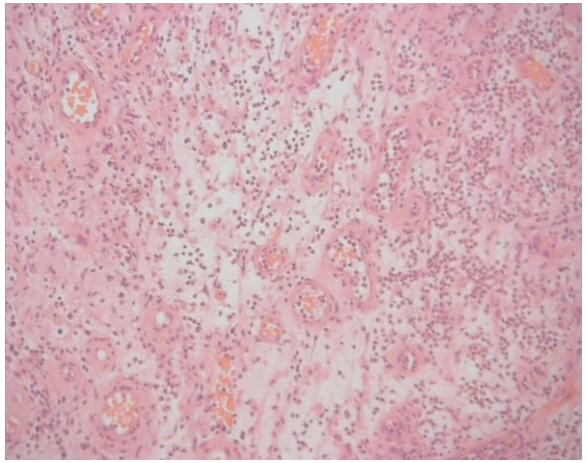
27

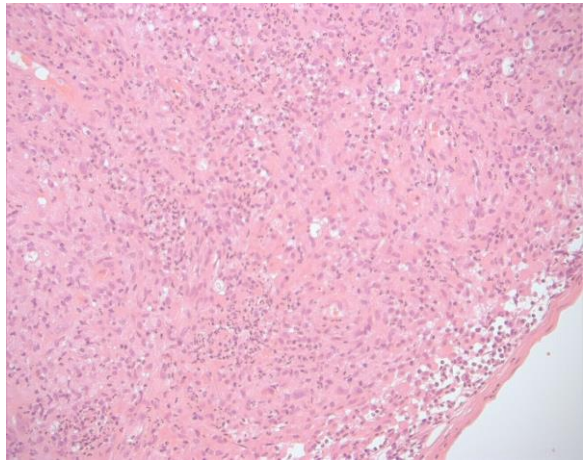
F76

Polypoid mass occluding L main bronchus

Cough Fever ANCA +ve

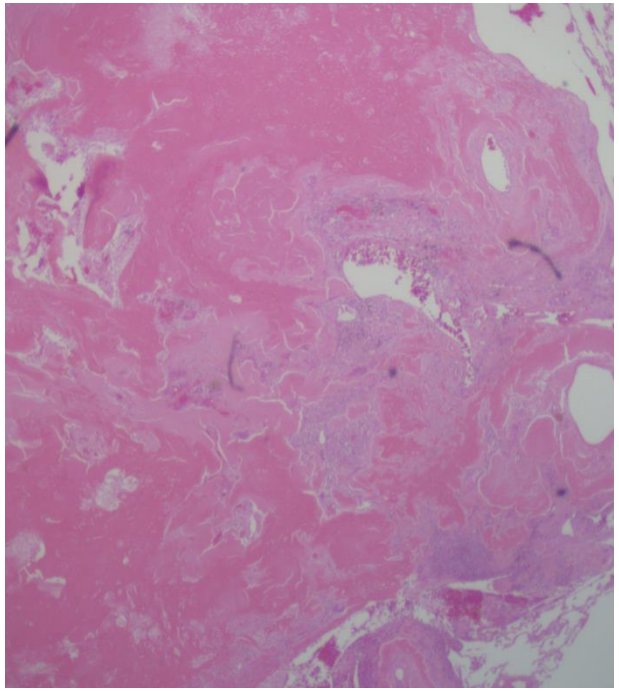


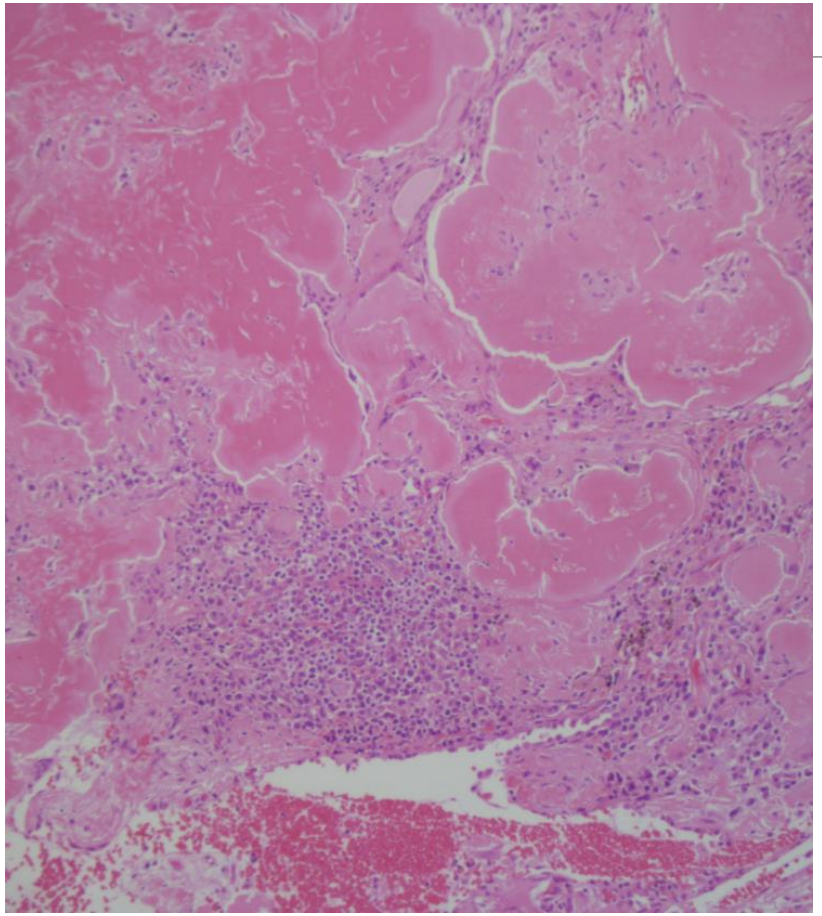


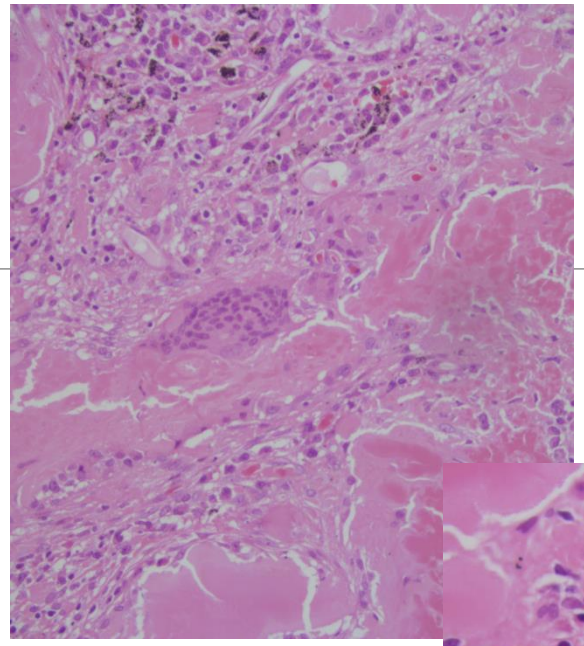


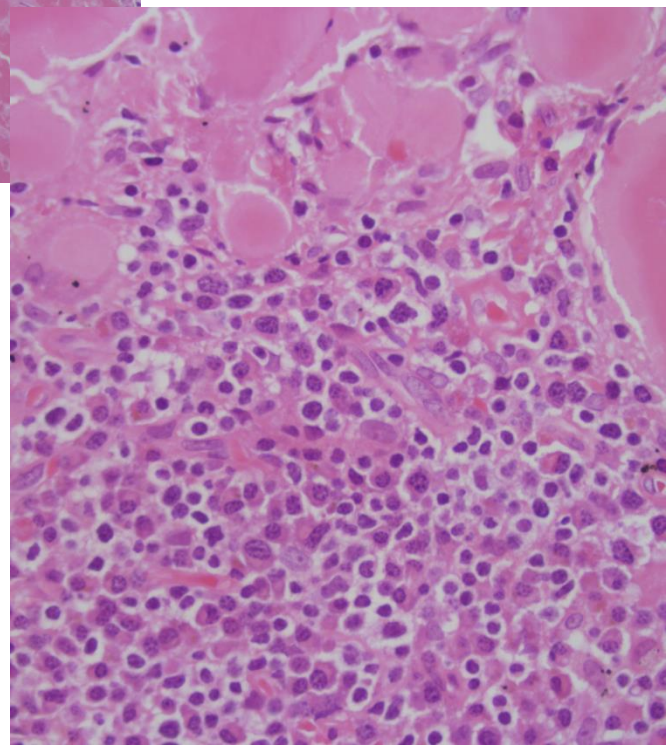
F74

Persistent nodule in right lower lobe









Amyloid

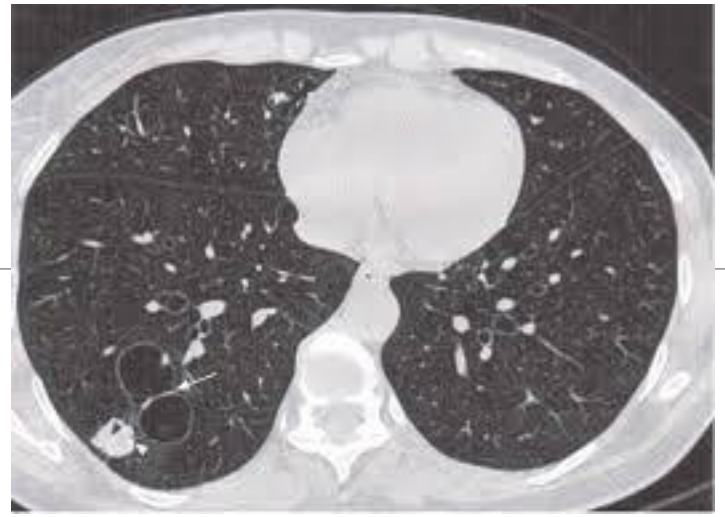
May occur as part of generalised amyloidosis or as isolated disease.

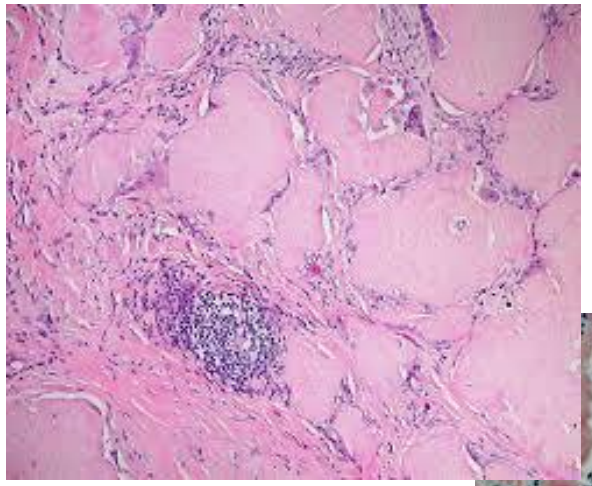
Isolated – tumour like nodules

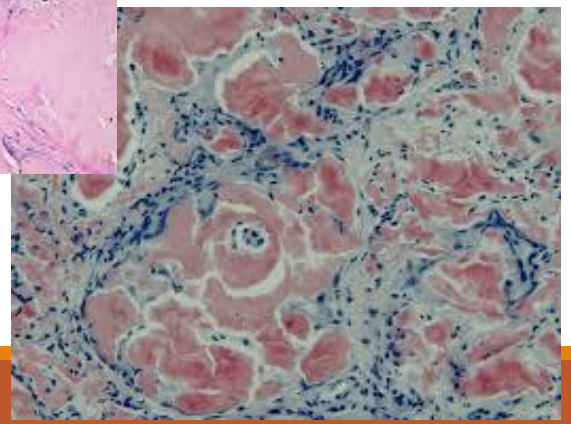
Amorphous eosinophilic material. Giant cell reaction

Mostly light chain

Some senile type transthyretin







INTERSTITIAL LUNG DISEASE

Many diagnosed radiologically

Atypical types get biopsied have atypical histology!

Often have to describe the pattern rather than give a specific diagnostic entity

UIP

NSIP

EAA

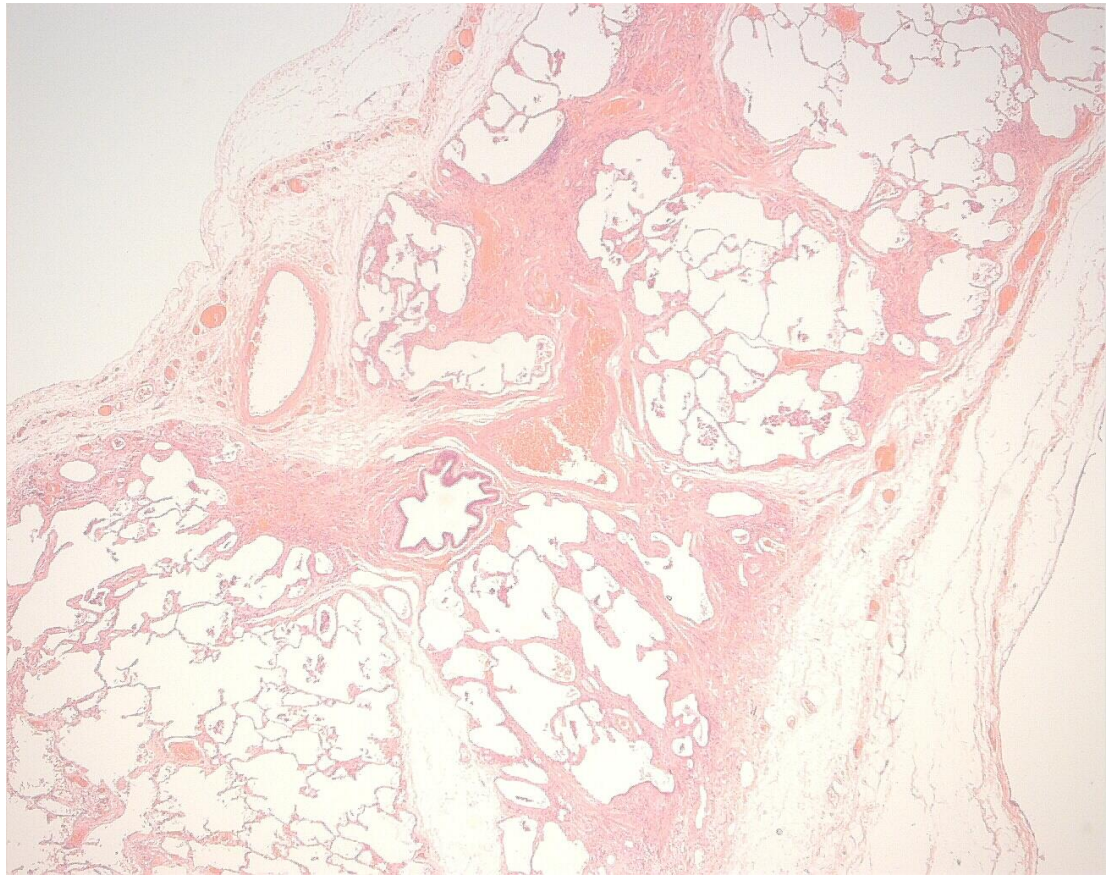
Others

13

13

M44

SOB. Reticular change on CT

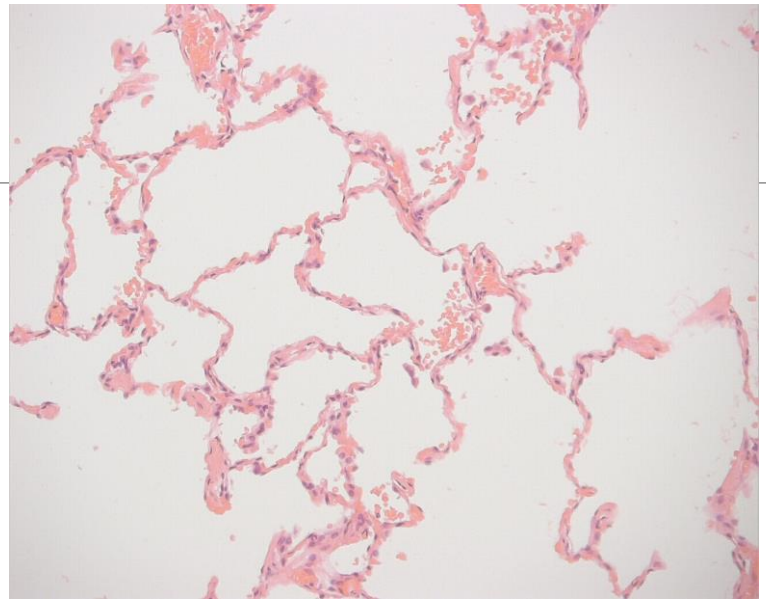


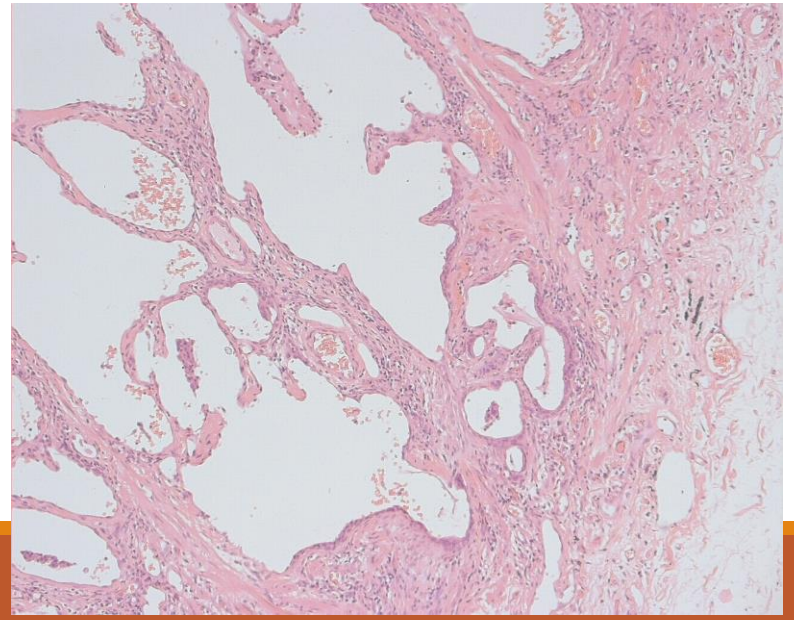
Pleura

Pattern

Heterogeneity

Distribution

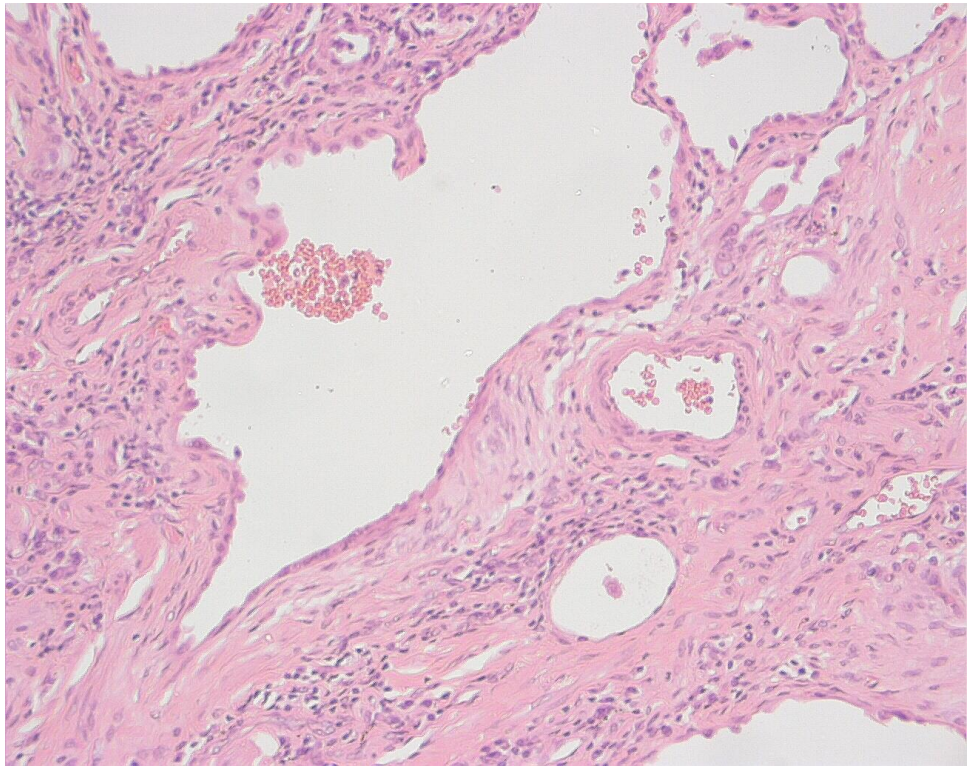




Inflammation

Fibrosis

Epithelial changes



UIP, Idiopathic pulmonary fibrosis

Subpleural and paraseptal predominance

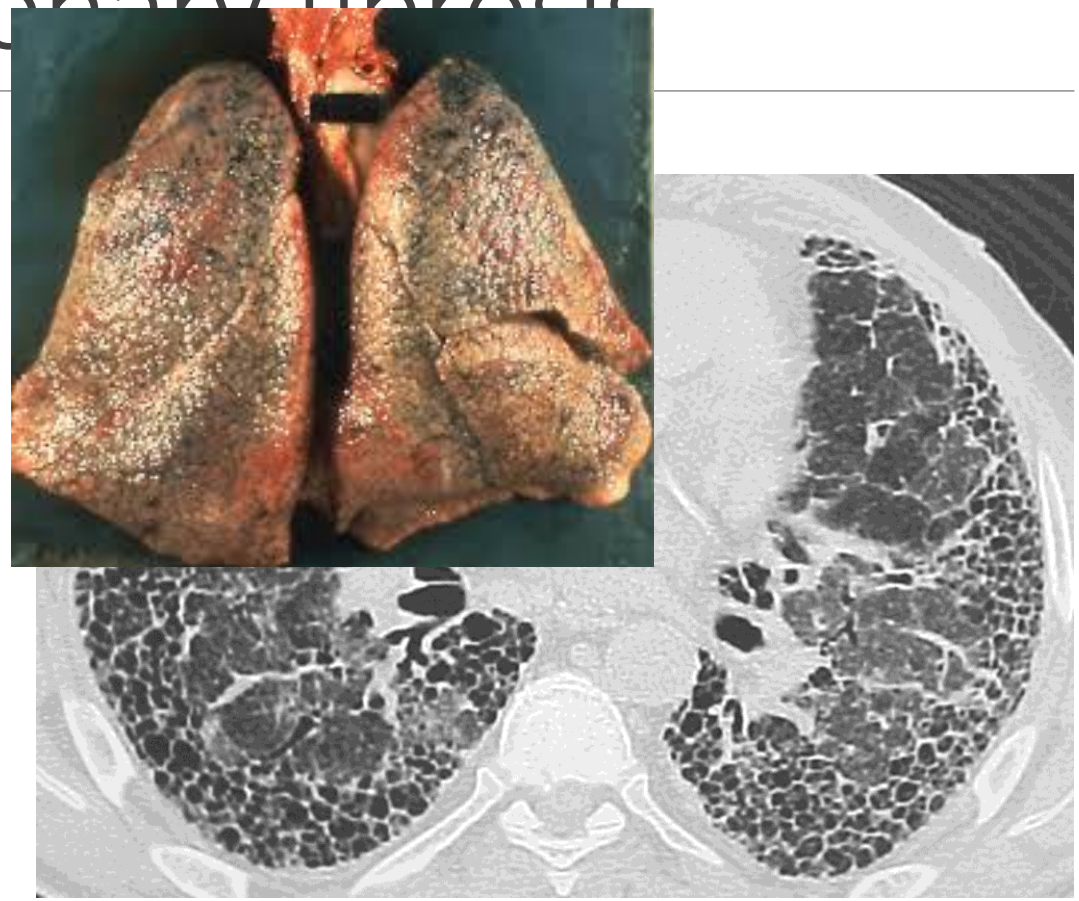
Patchy parenchymal involvement

Fibrosis leading to loss of architecture – honeycombing

Fibroblastic foci

Mild to moderate interstitial inflammation

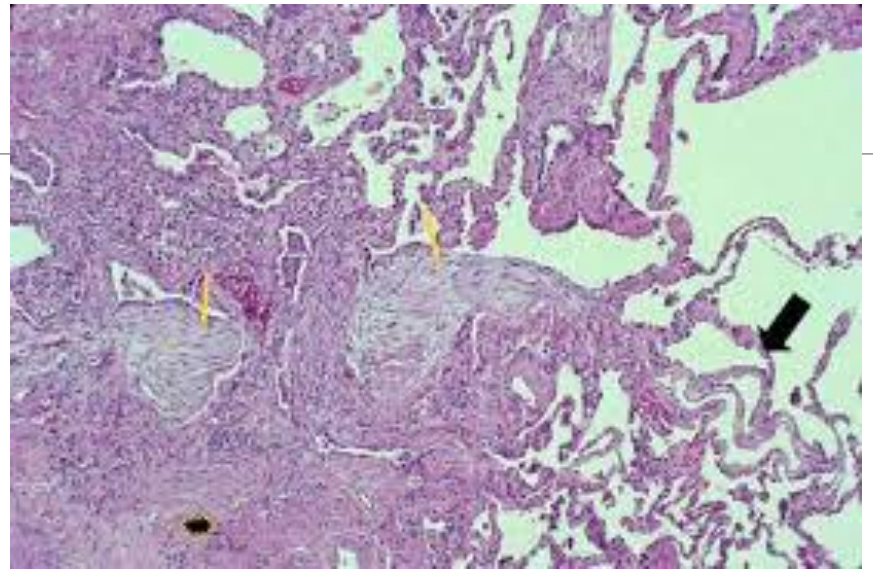
Absence of any other causal feature

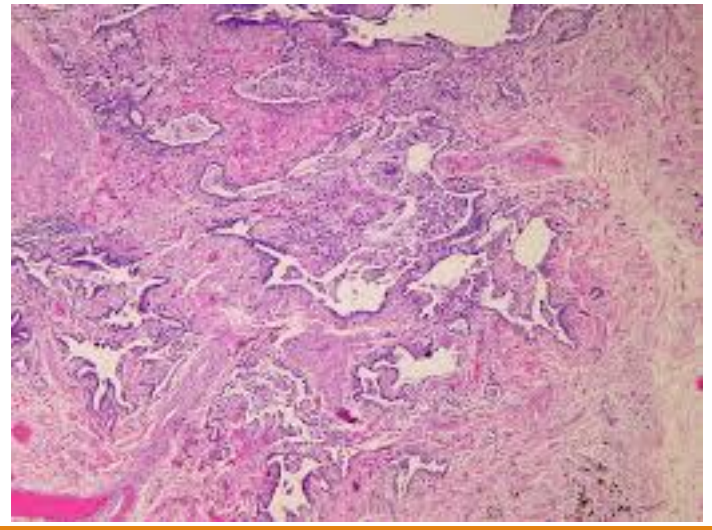


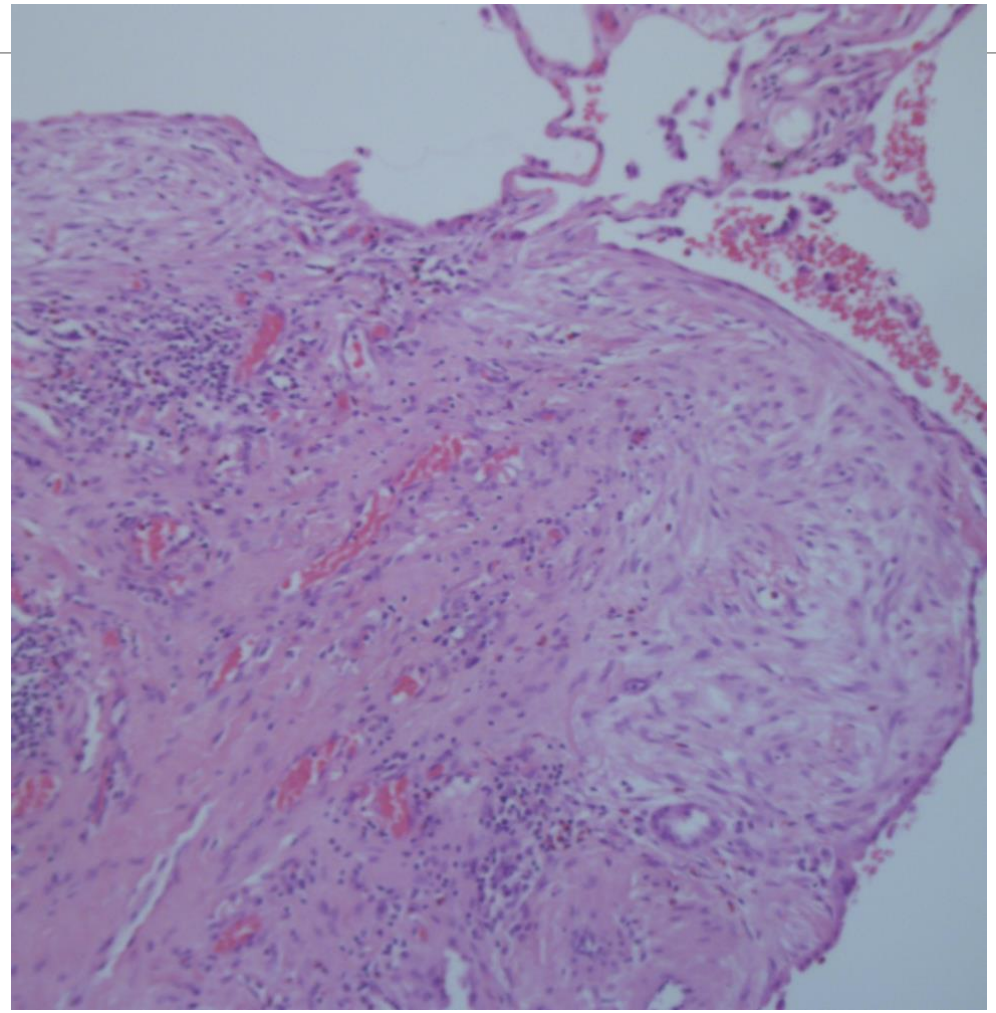
UIP

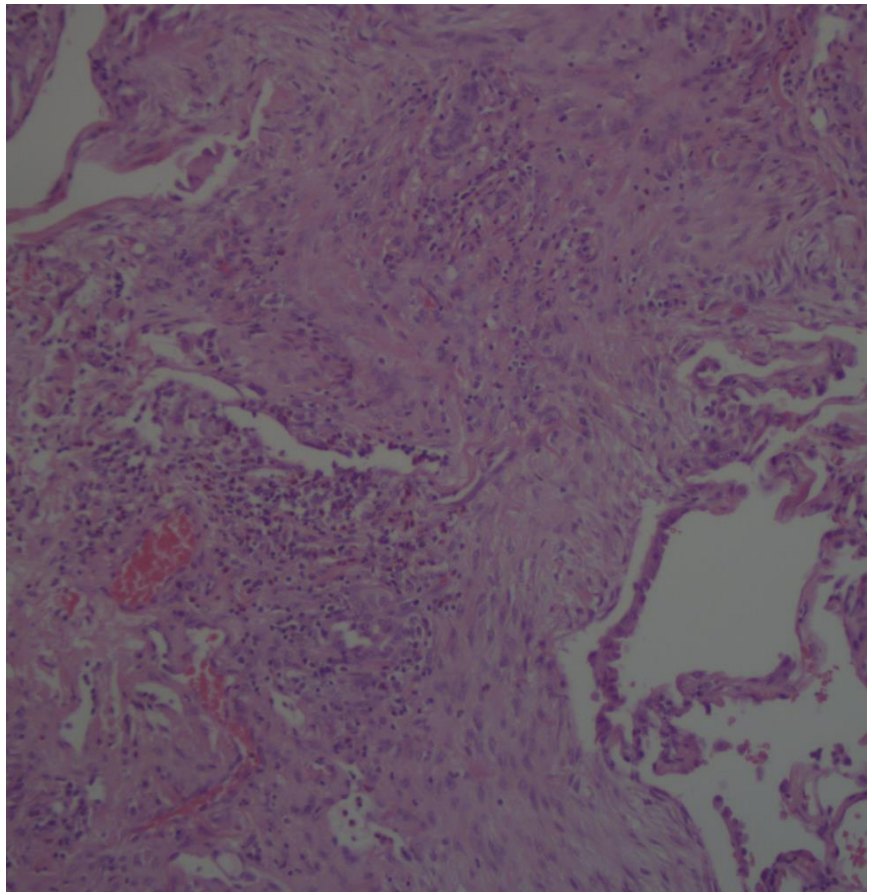
Secondary changes – non specific

- Pneumocyte hyperplasia
- Mucin and debris in air spaces
- Thickened vessel walls
- Smooth muscle cell hyperplasia

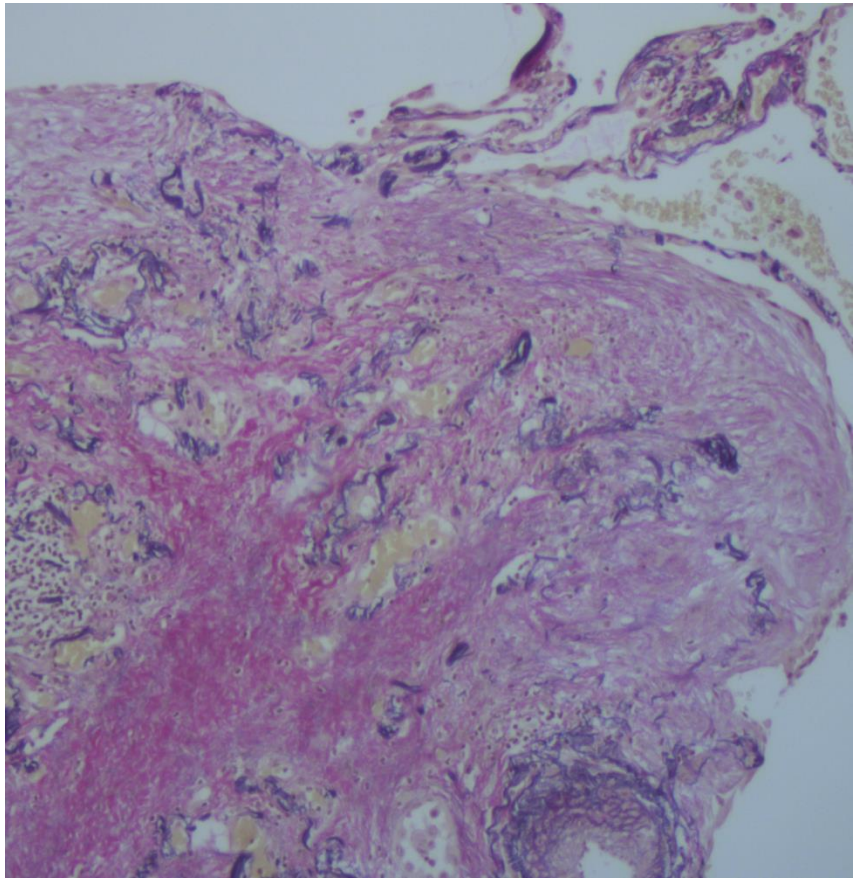


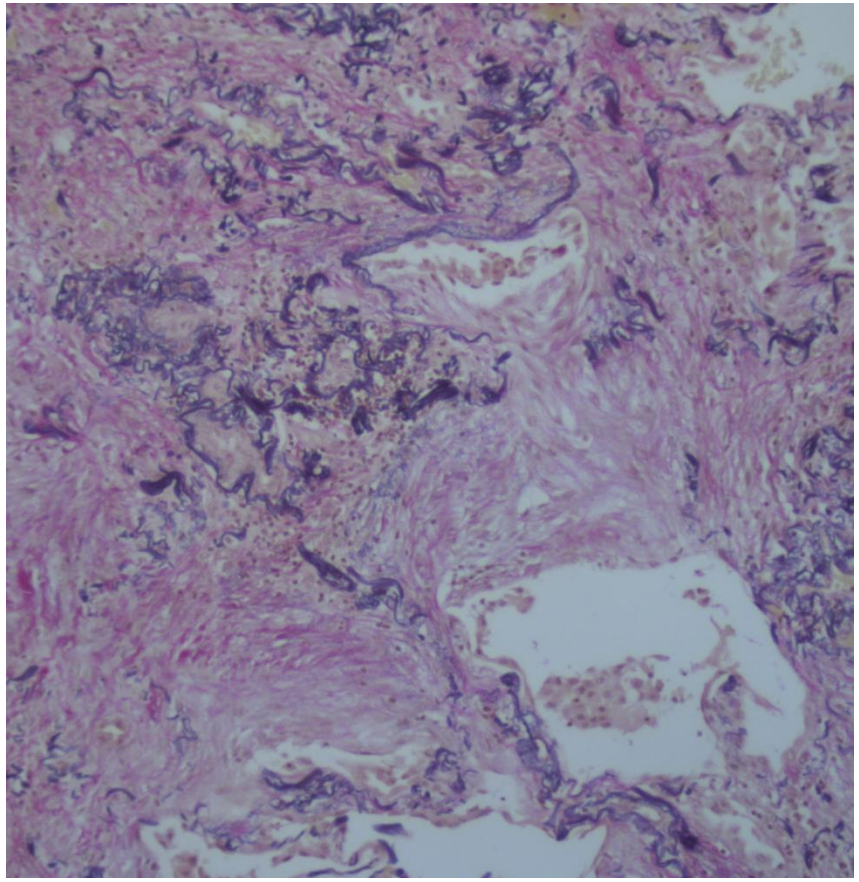






Fibrosing organising pneumonia



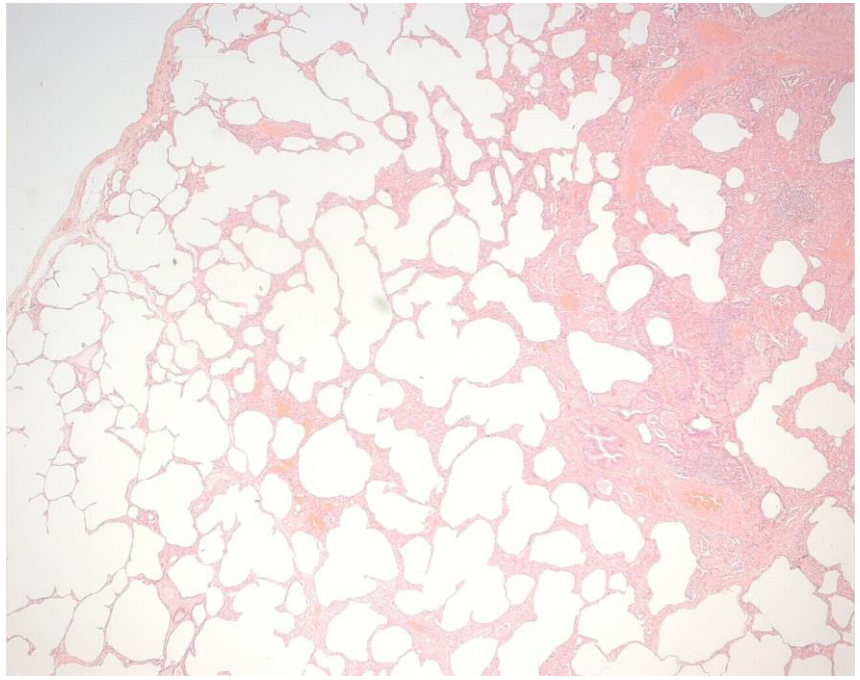


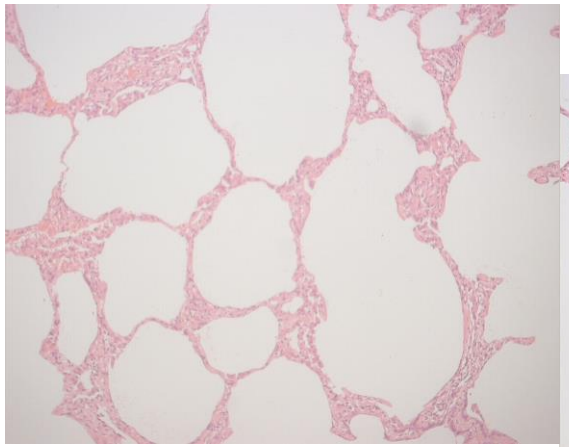
F53

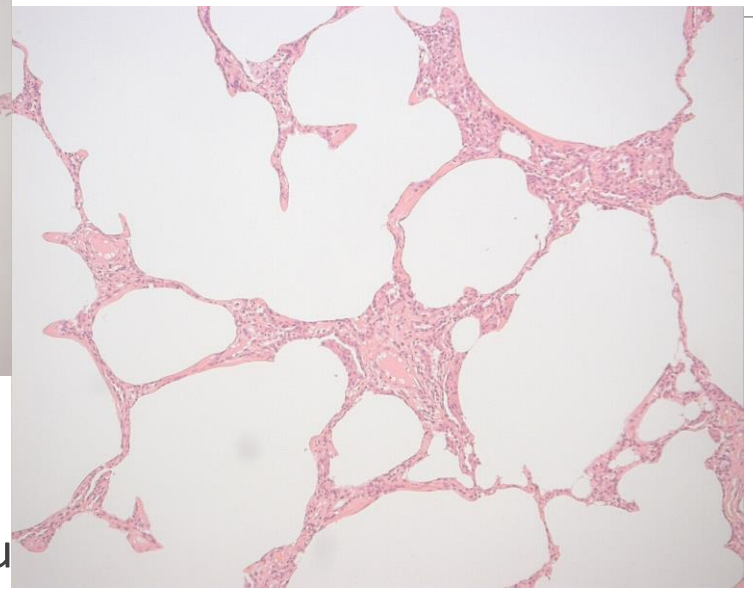
SOBOE

Pernicious anaemia

Raynaud’s disease



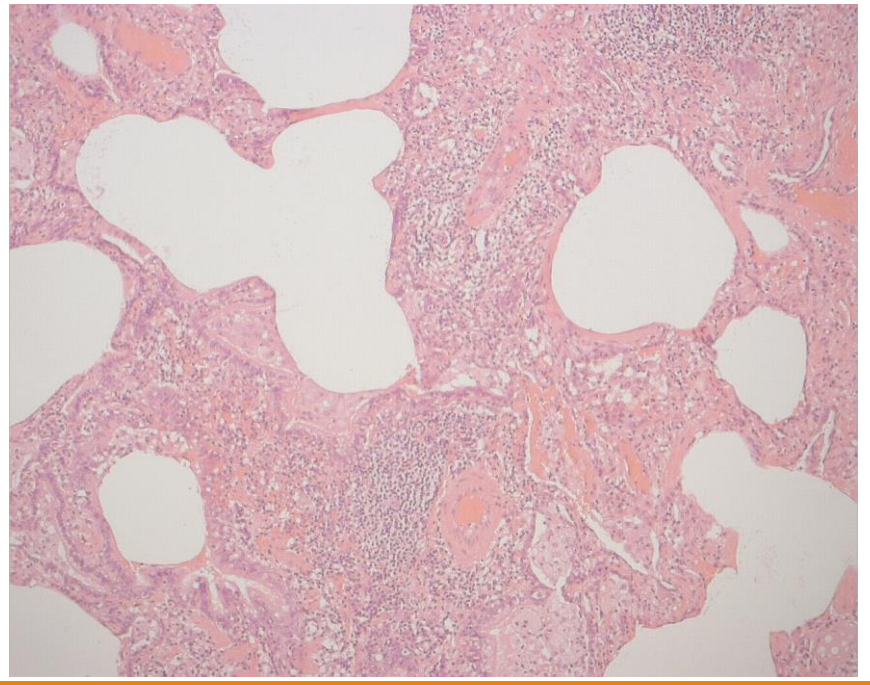




Changes throughou

Uniform but vary in intensity

Architecture preserved.



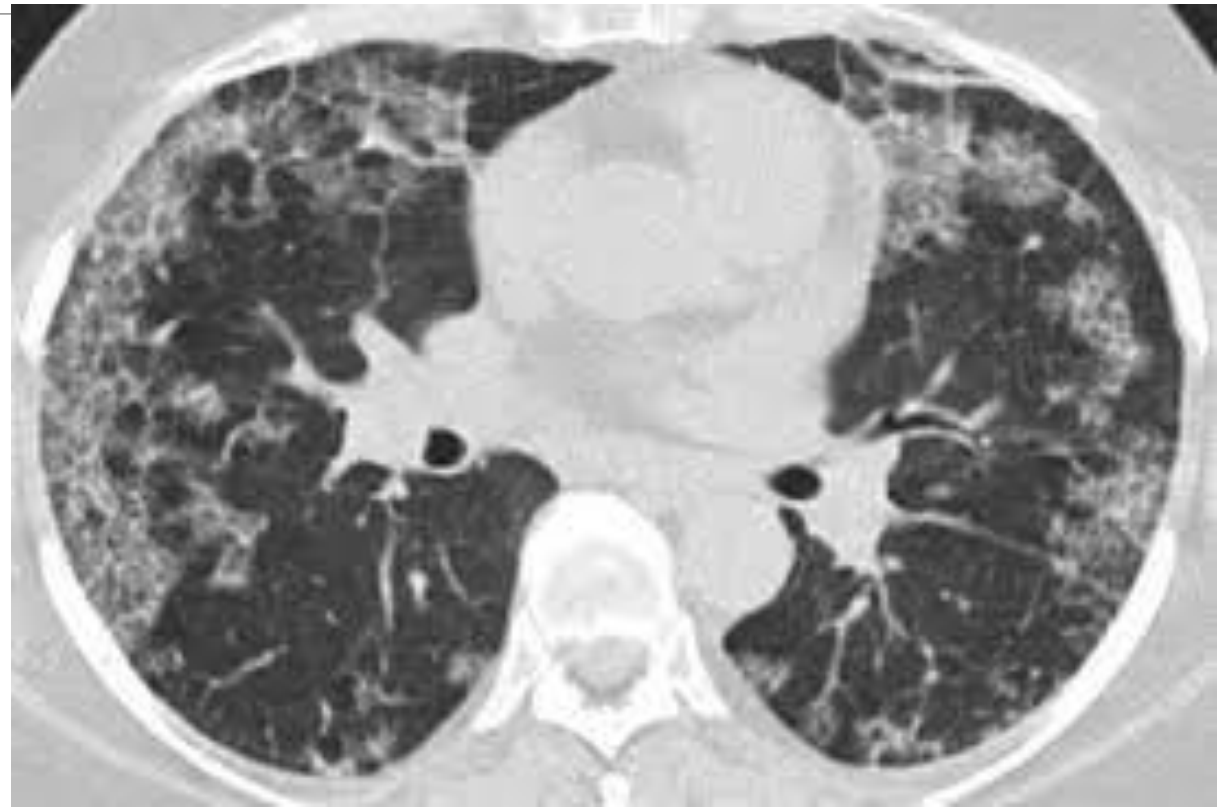
NSIP

Interstitial pneumonia lacking specific features

Multifactorial

Common histological pattern in an number of connective tissues disease.

Defines a pattern or category of disease



NSIP – Cellular and Fibrotic

Cellular	Fibrotic
Diffuse involvement of affected parenchyma	Diffuse involvement of affected parenchyma
Moderate chronic interstitial inflammation	Mild to moderate chronic interstitial inflammation
Little or no fibrosis	Variable degree of interstitial fibrosis
Preservation of alveolar architecture	Little loss of alveolar architecture (no honey combing)

Interstitial Disease Algorithm

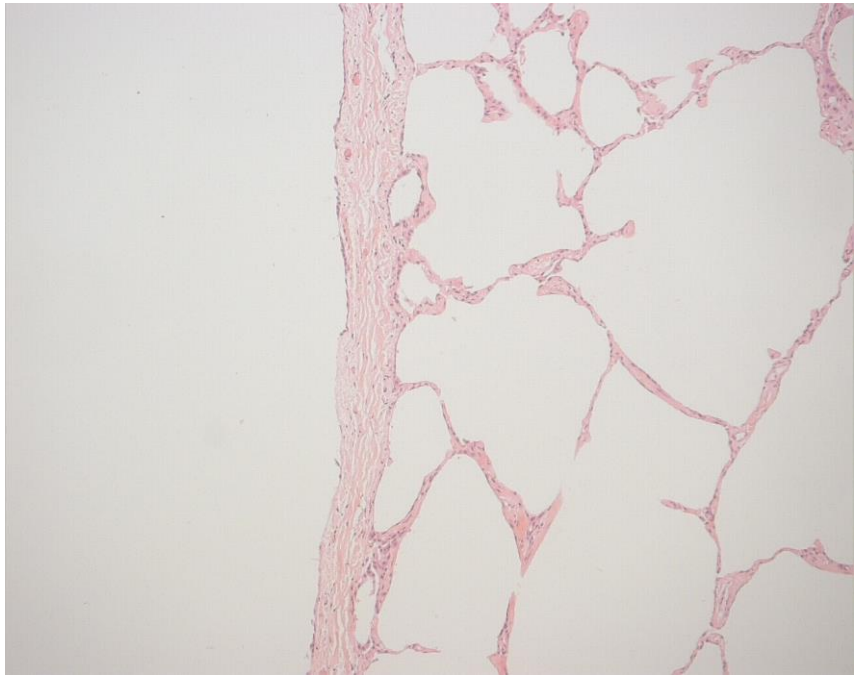
Collagen predominant	Patchy, subpleural and subseptal, loss of architecture, honey combing	UIP
	With chronic peribronchiolar inflammation and possible granulomas	Chronic EAA
	Stellate peribronchiolar scars	Burnt out LCH
	No significant architectural distortion	Fibrotic NSIP
	None of the above	Unclassified fibrosis
Inflammatory predominant	Peribronchiolar granulomas	EAA
	Peribronchiolar with eosinophils and LH cell	LCH
	Peribronchiolar with intraluminal pigmented Macrophages	Respiratory bronchiolitis
	Mild, no specific distribution	Cellular NSIP
	Dense, no specific distribution	Lymphoid interstitial pneumonia
	Non-necrotising granulomas along lymphatics	Sarcoidosis
	Hyaline membranes and fibroblast proliferation	DAD

ILD & CTD

Pleural involvement

Mixed patterns

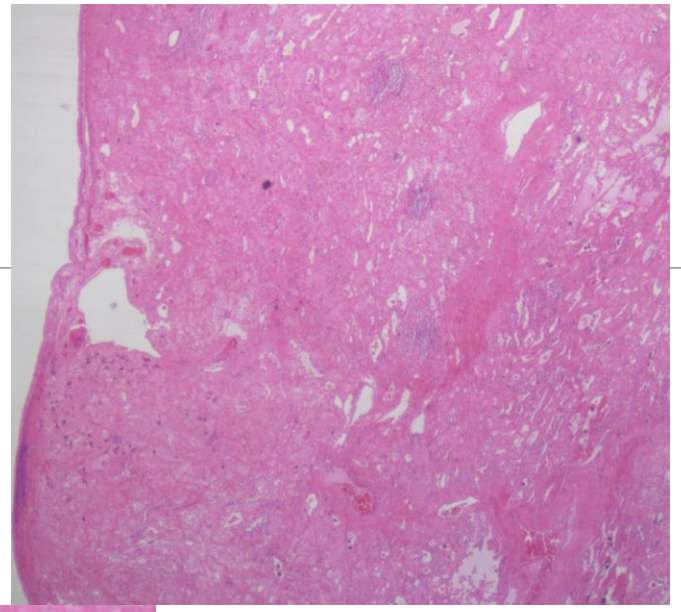
B cells – germinal centres, plasma cells

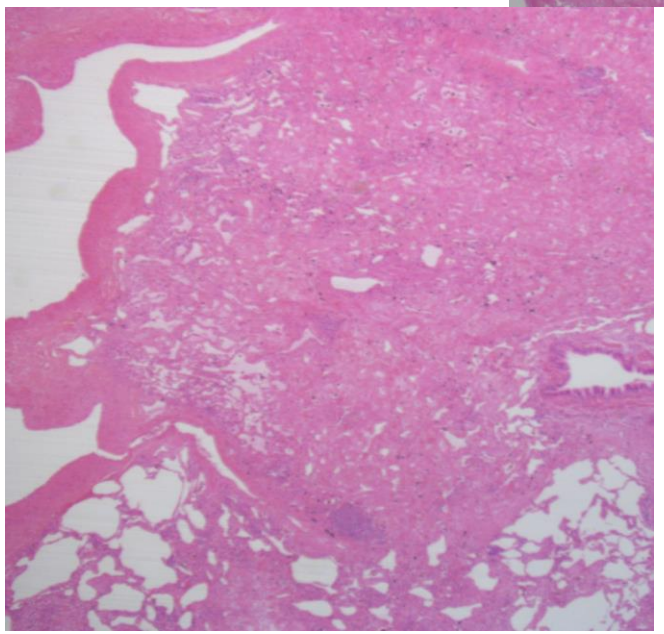


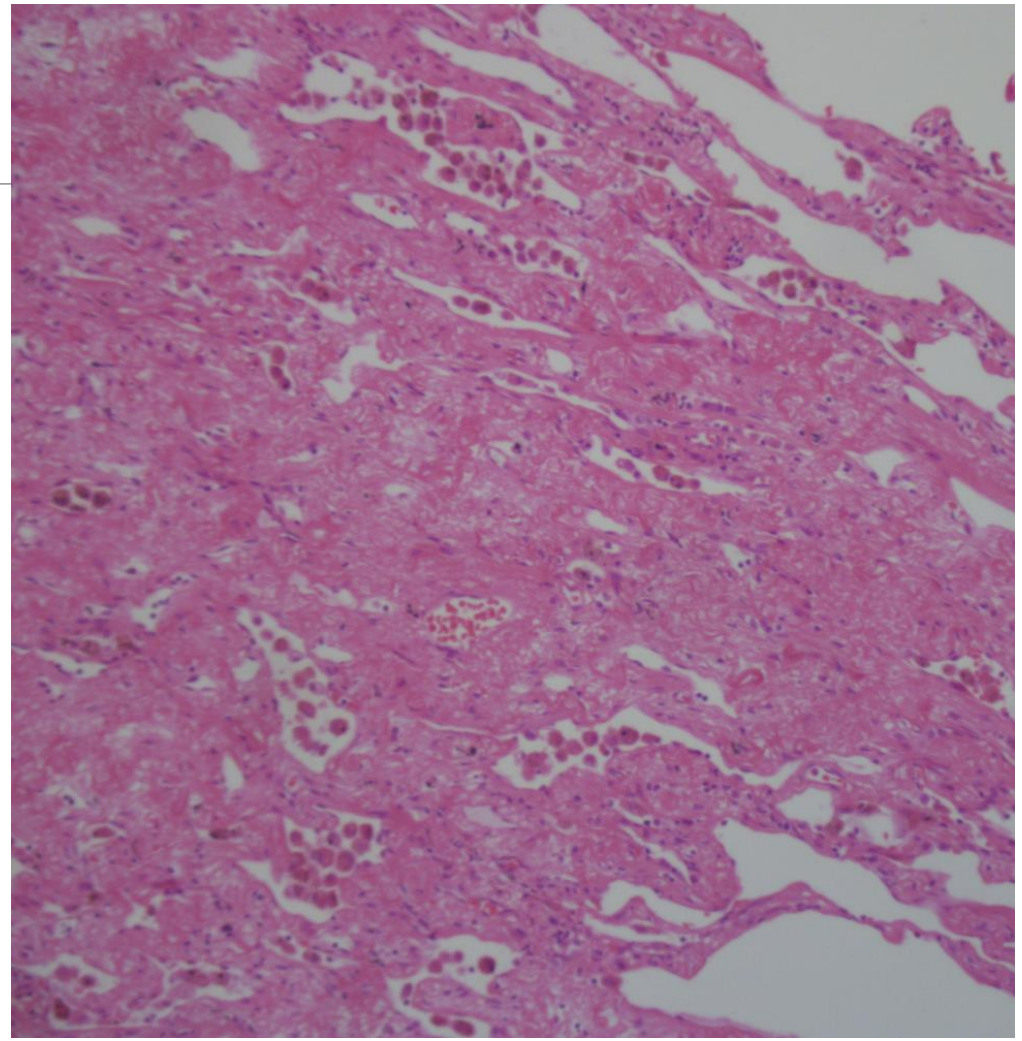
F45

RUL wedge biopsy

?Fibrosis

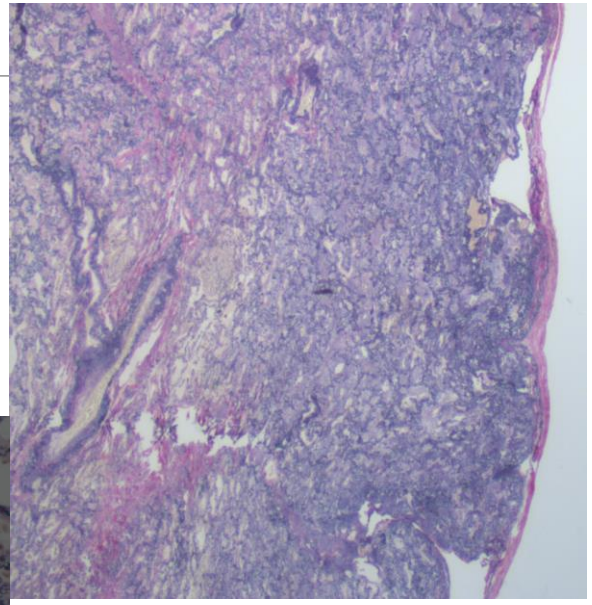


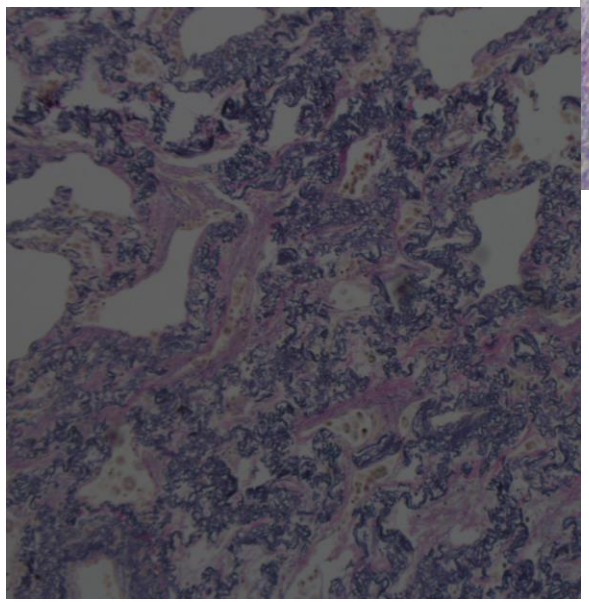




Pleuro-parenchymal fibroelastosis

PPFE





R20

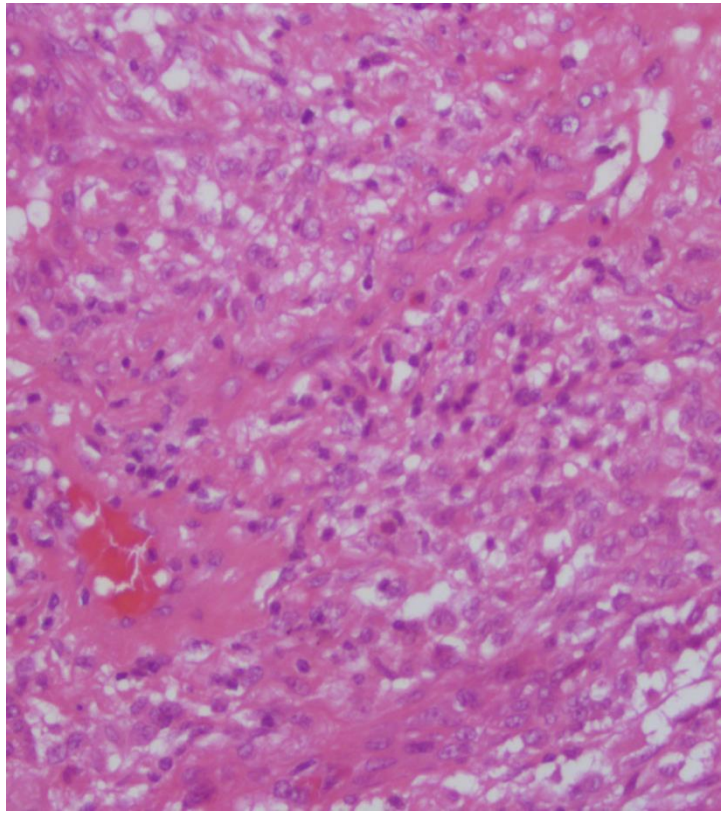
F76

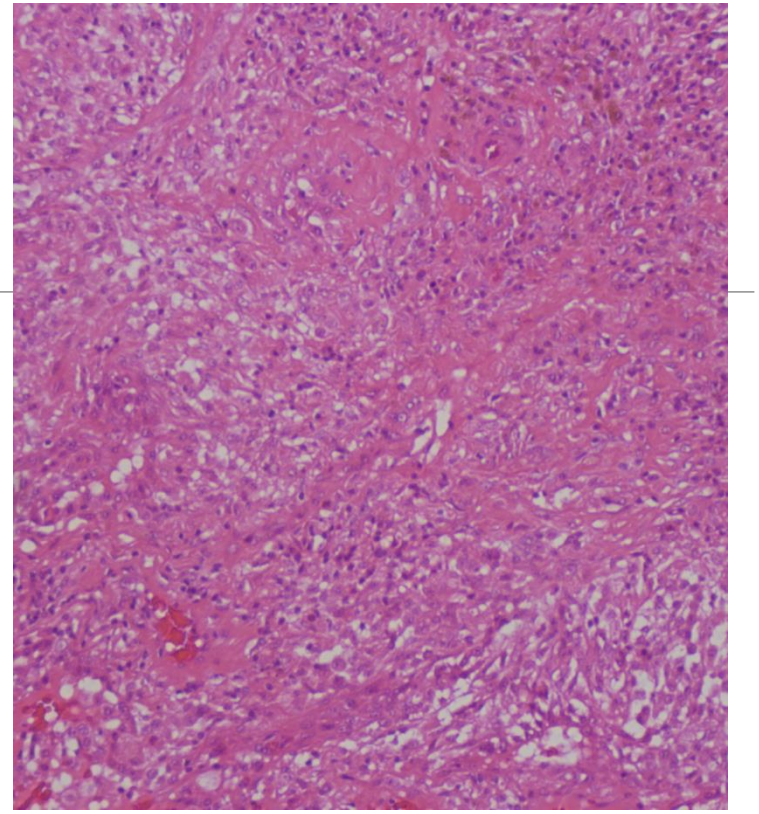
Previous breast

Carcinoma

Interstitial

shadowing





Langerhans cell Histiocytosis

Early lesions of Langerhans cells mingled with eosinophils

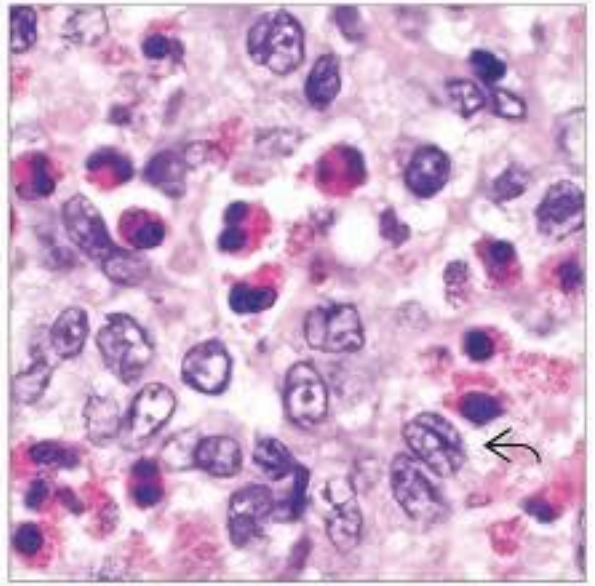
Peribronchiolar distribution

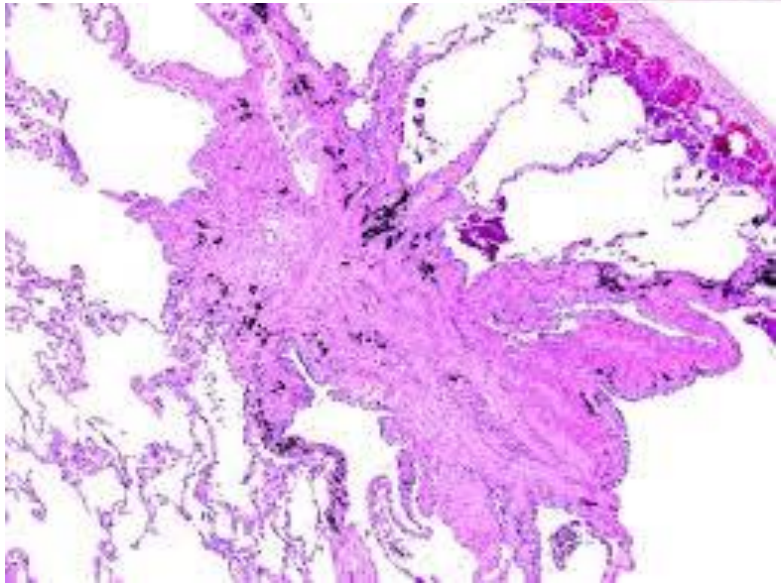
May develop small cavities or cysts – pneumothorax

Progress to stellate fibrous scars

LC and eosinophils less apparent with pigmented macrophages present

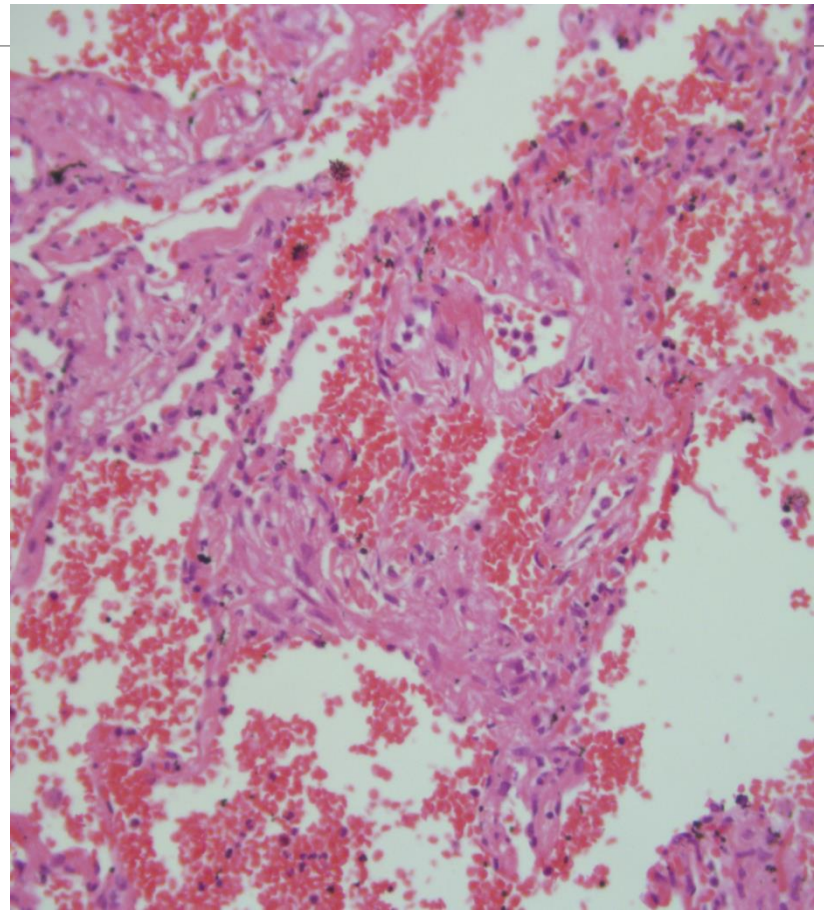
CD1a S100 positive

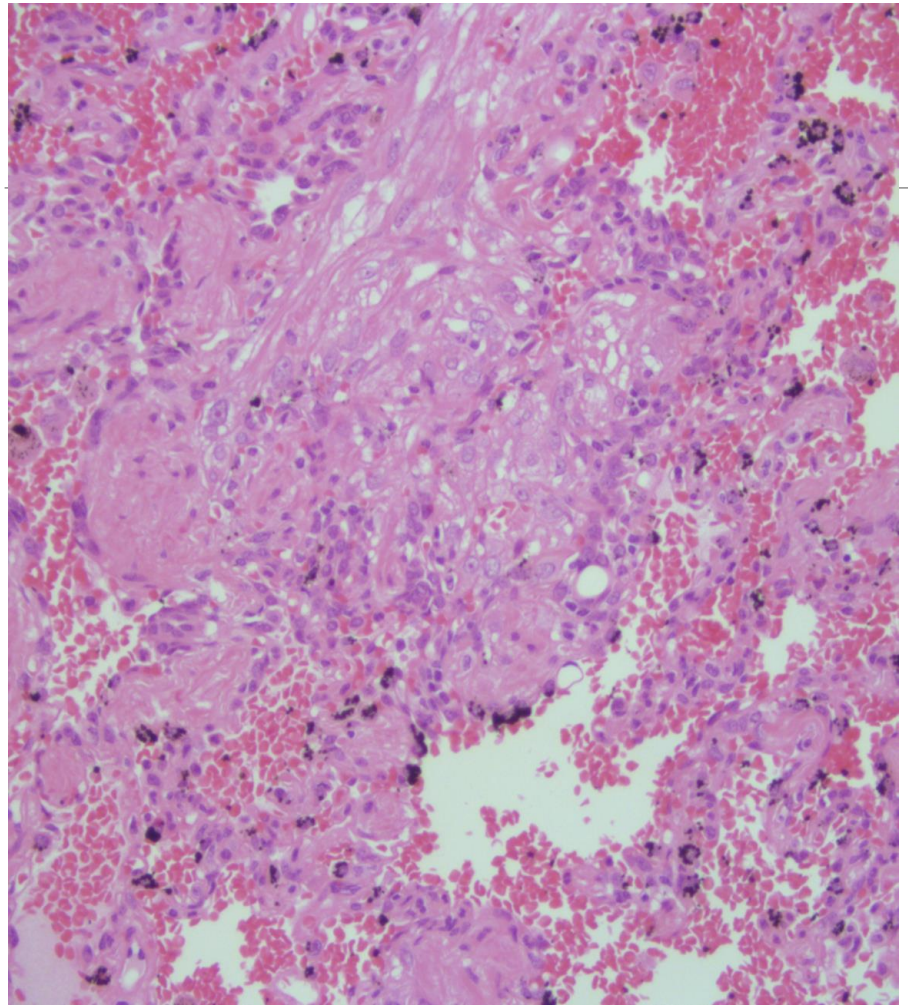


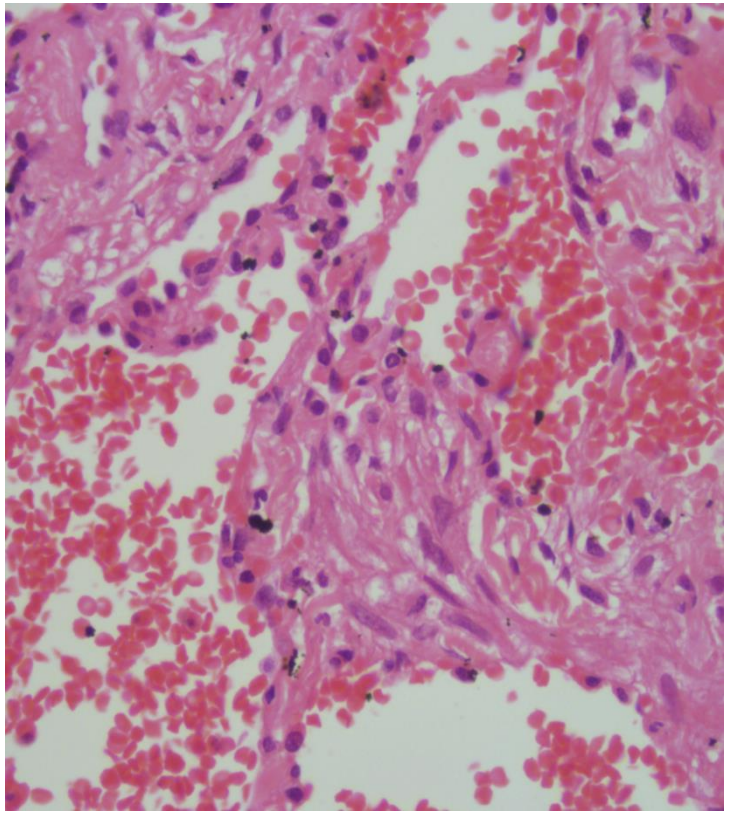


Respiratory failure

Double lung transplant







Lymphangioleiomyomatosis(LAI

Proliferation of unusual smooth muscle cells

Largely confined to women

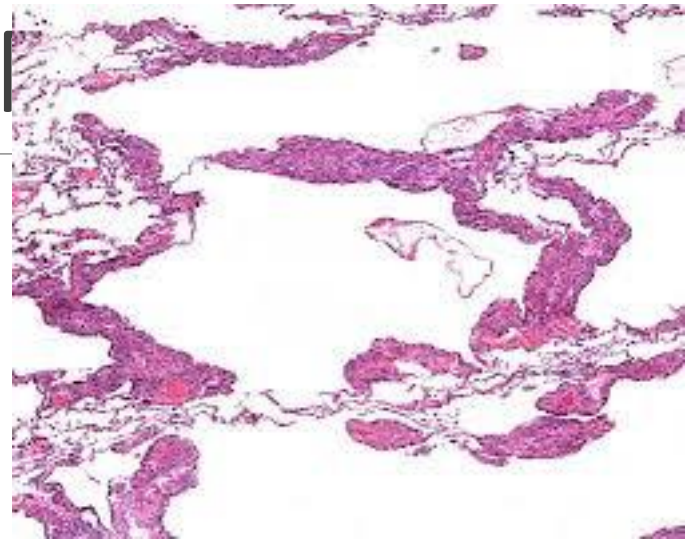
Plump spindle shaped cells

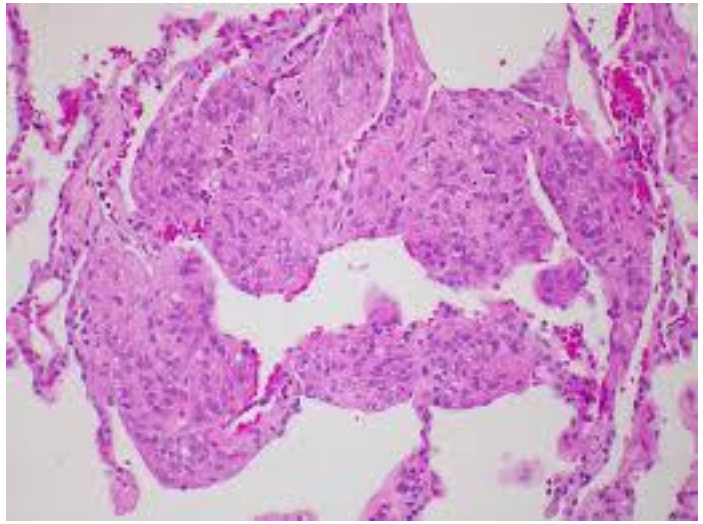
Nodular thickening of alveolar walls

May lead to honeycombing

SMA +ve.

2/3 HMB-45 +ve

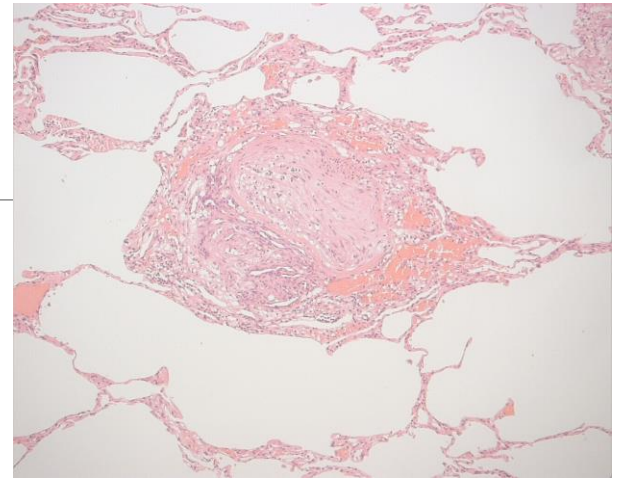




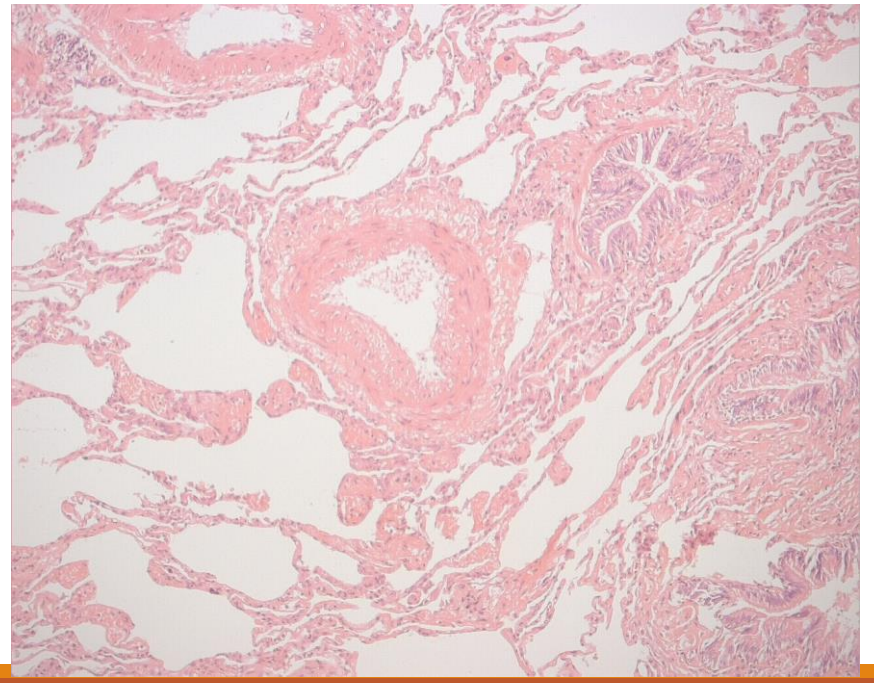
Pulmonary vascular disease

25

F53 bilateral lung transplant



M44 Respiratory failure. Bilateral lung transplant

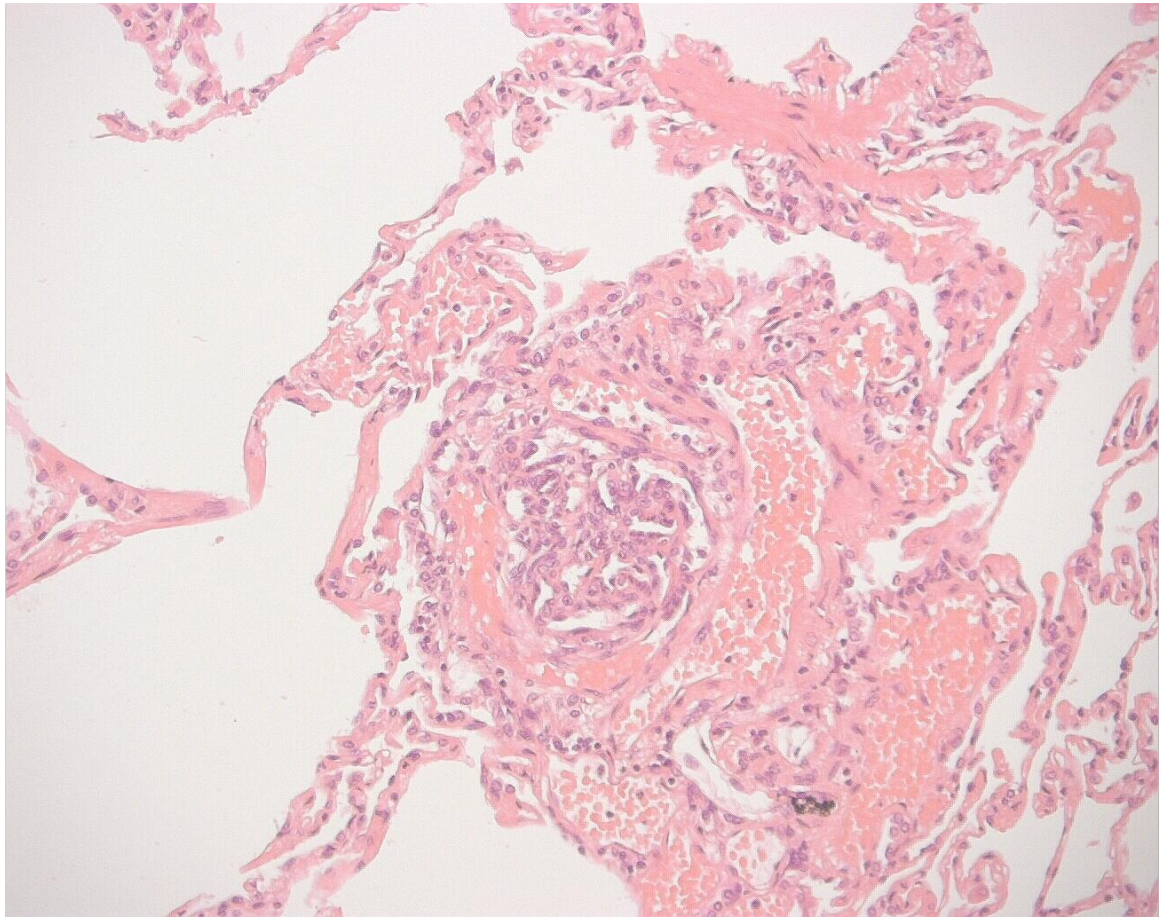


Plexiform lesions

PPH

Liver disease

Congenital heart disease

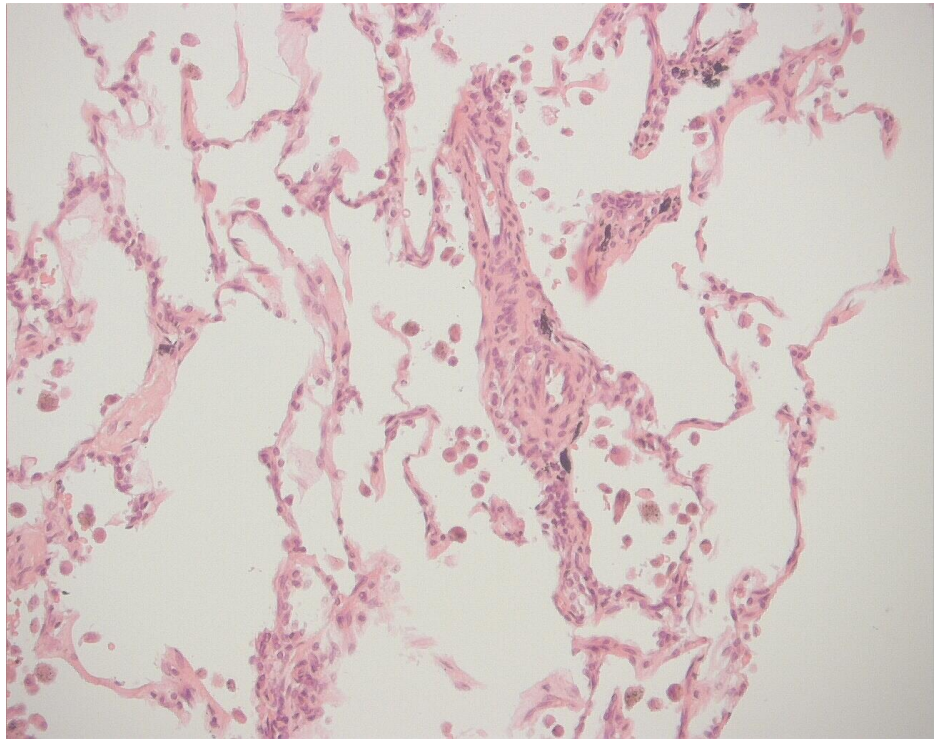


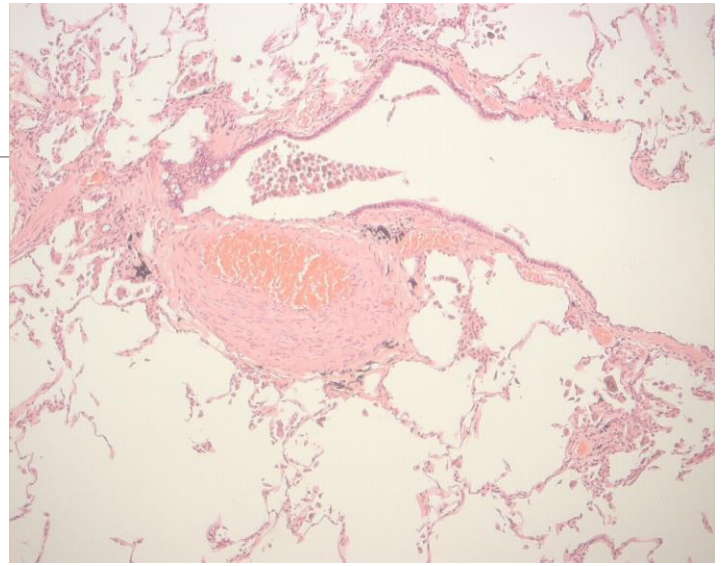
Pulmonary hypertension

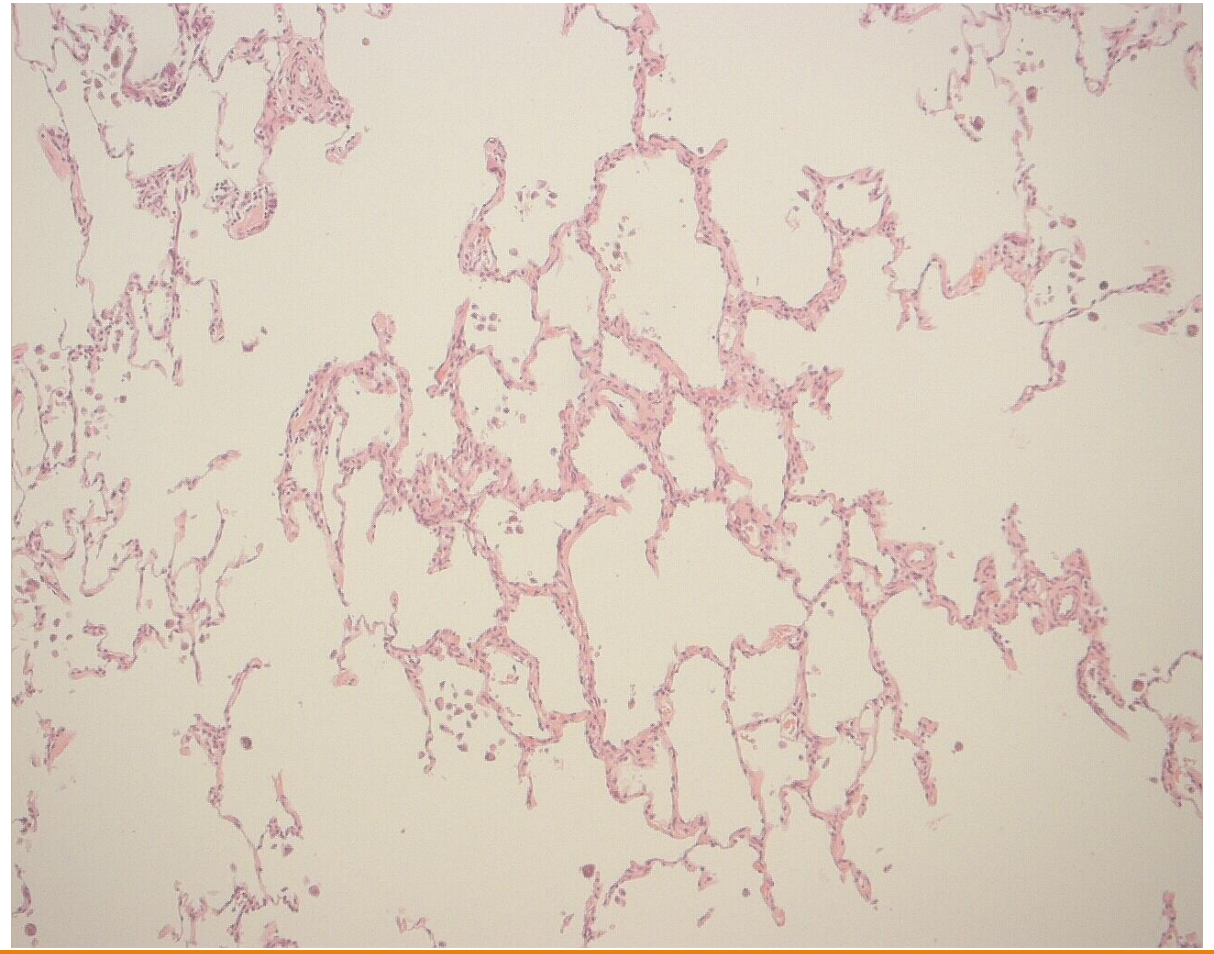
Precapiilary constrictive	
PPH, CHD, Portosytemic shunt – liver, Drugs, HHTelangiectasia, CTD	Plexogenic
Precapillary hypoxic	
High altitude, COPD, OSA	Smooth muscle extension and longitudinal
Precapillary thromboembolic	
CTEPH, Parasites, Tumour	Recanalisation
Capillary	
Pulmonary fibrosis, Capillary haemangiomatosis	
Post capillary	
PVOD, Left sided heart disease	Venous hypertrophy

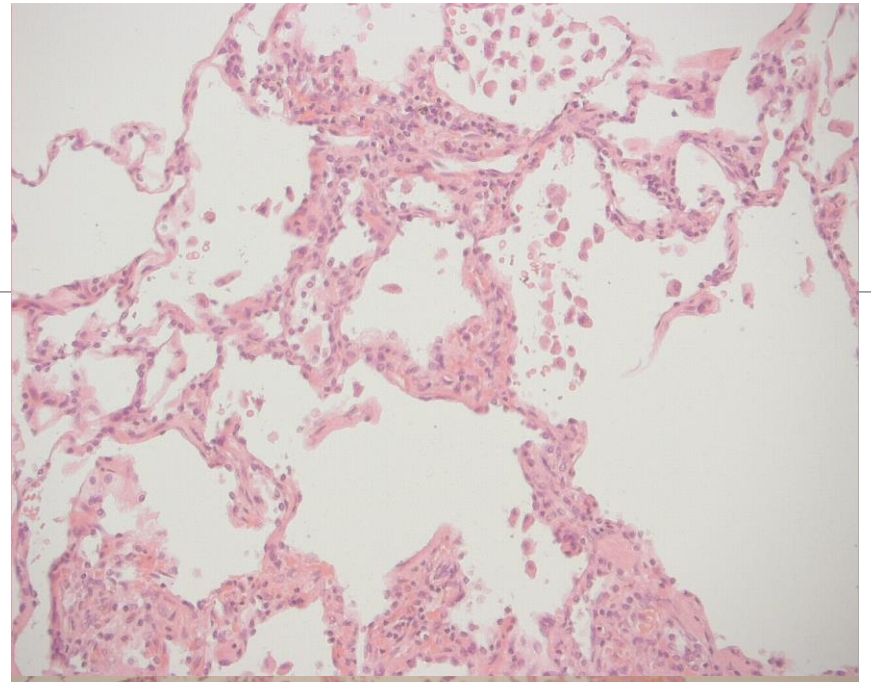
M31

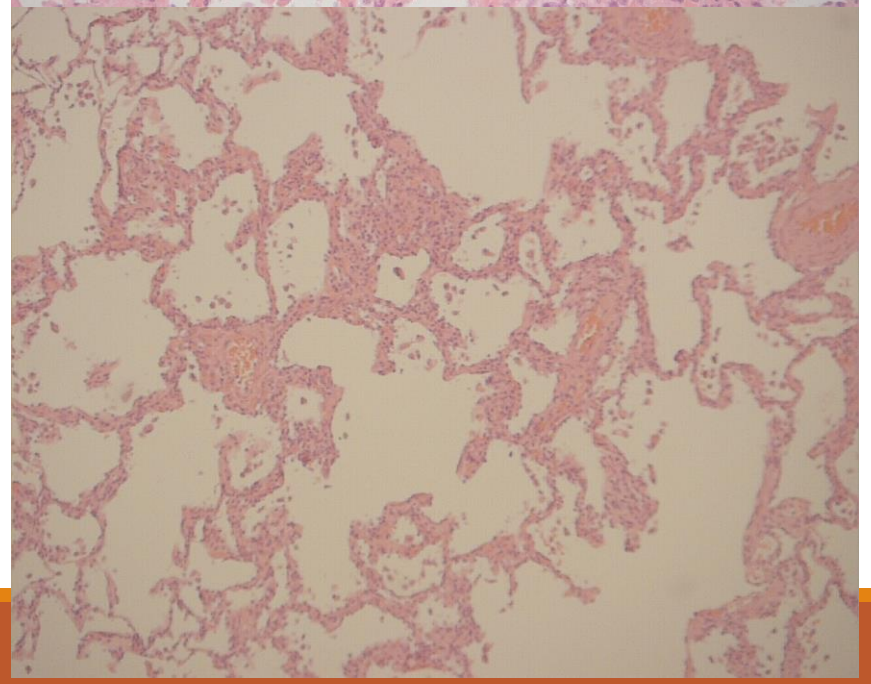
Bilateral lung transplant for pulmonary hypertension











- Microvasculopathy
- PCH
- Centrilobular pattern
- Duplication of capillaries

Very rare

Proliferation of small thin walled capillary vessels

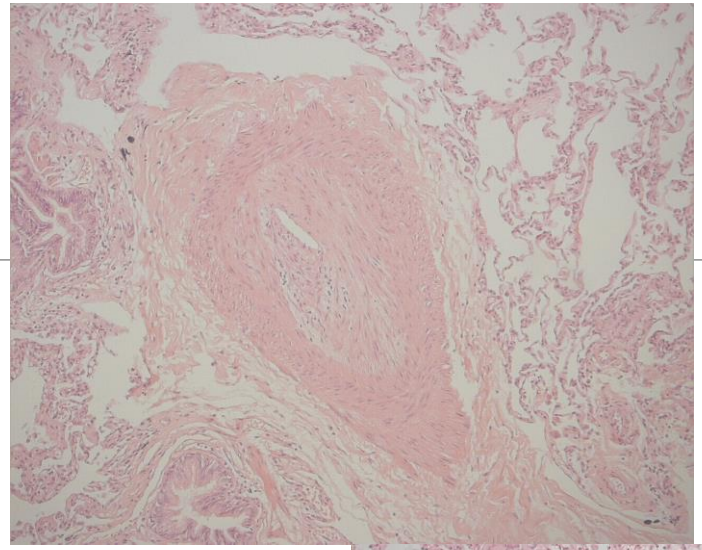
CD34 immunostaining helpful to demonstrate a double layer of capillaries in alveolar walls

Overlap with PVOD

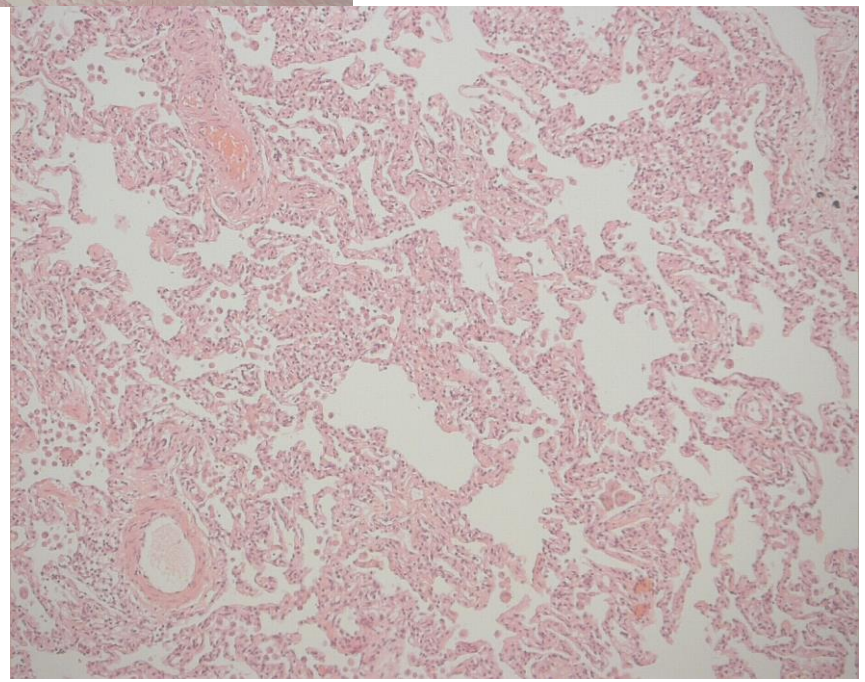
5

M46

Pulmonary hypertension



Lung transplant

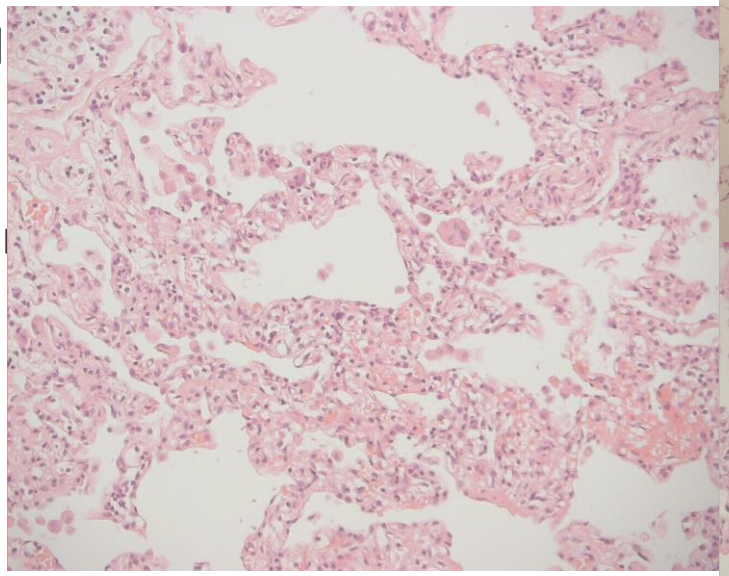


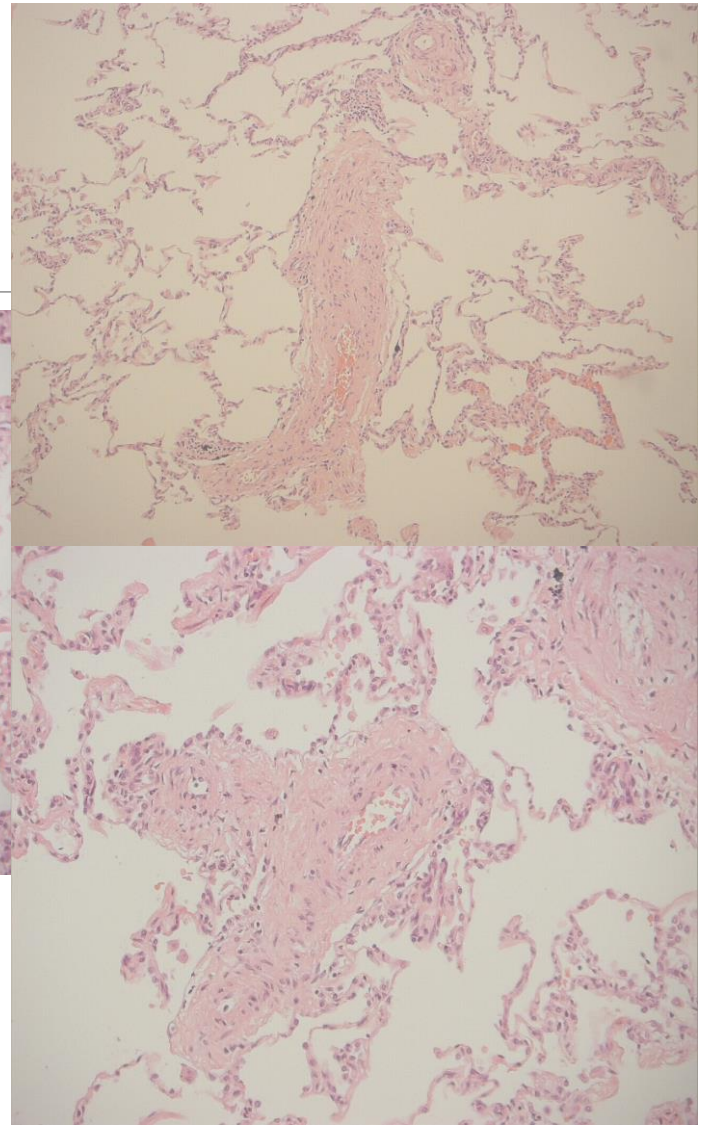
Veno occlusive disease and microvascul

Cellular intimal thickening in the pulmo
veins

Not age related sclerosis

Haemosiderin deposition



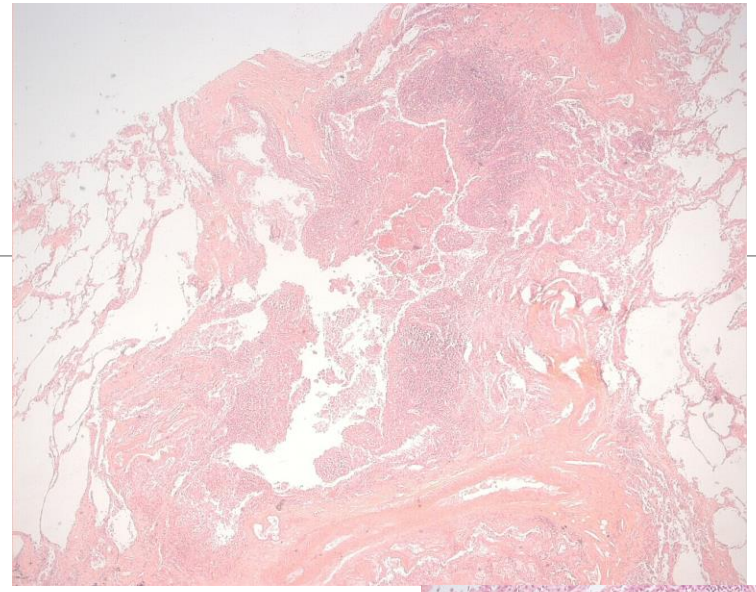


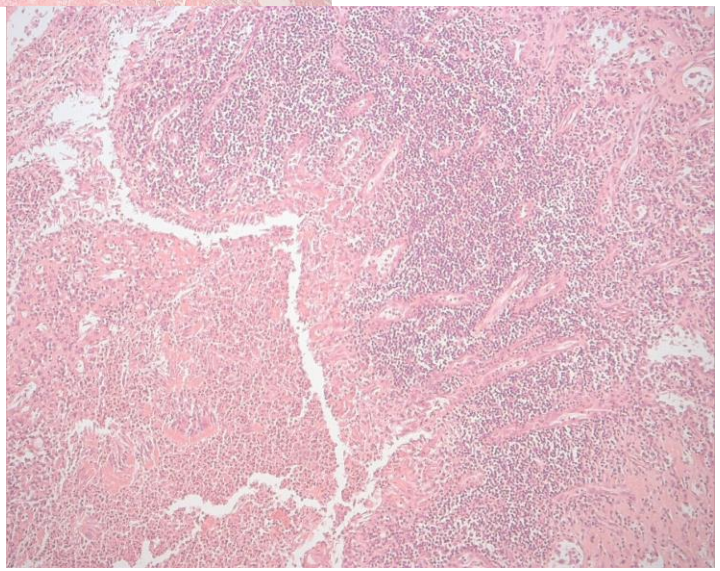
9

F38

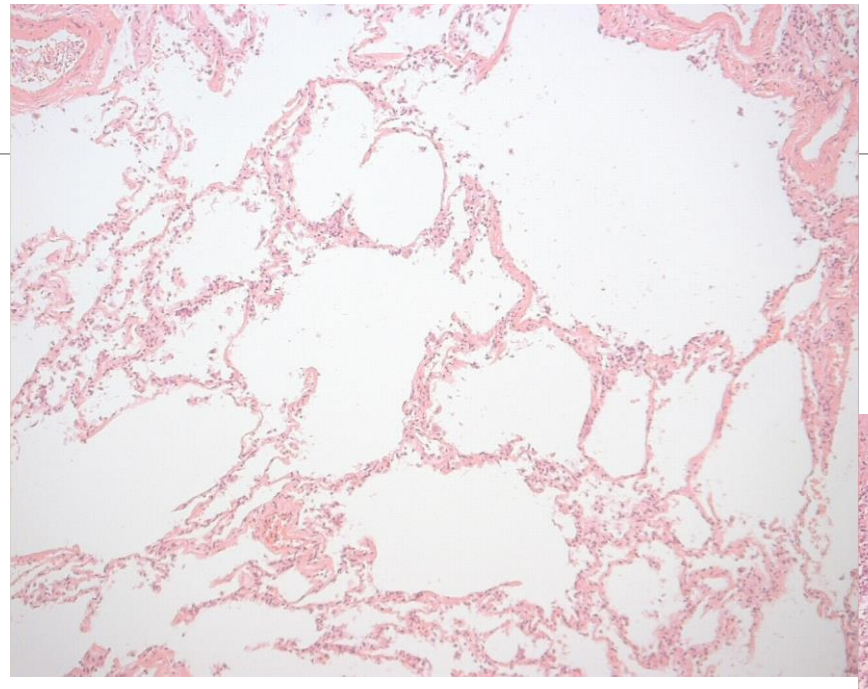
Bilateral lung transplant

Productive cough

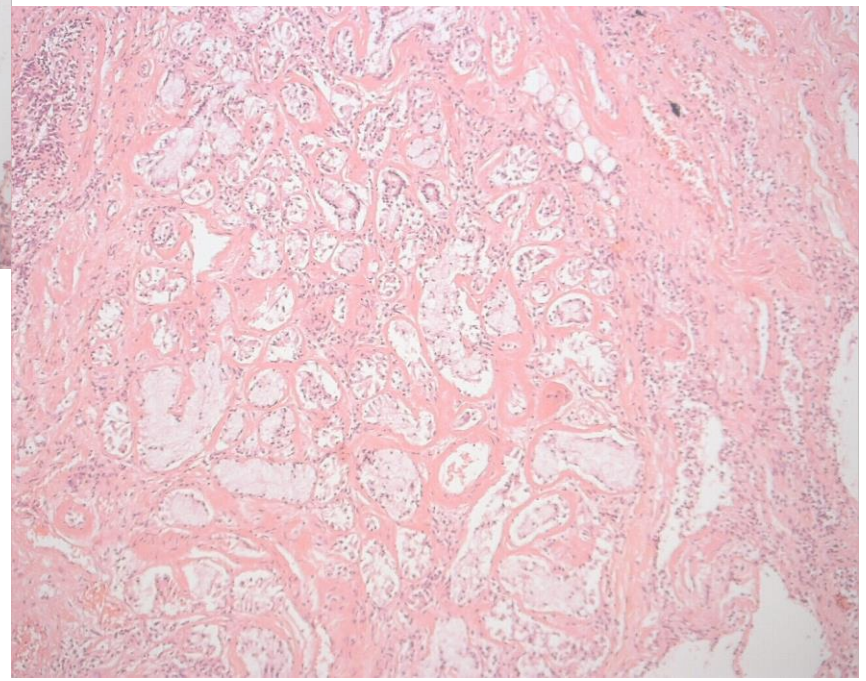




Cystic Fibrosis



Amyloid



Bronchiectasis

Infection – measles, pertussis, adenovirus

Chemical – gases, gastric acid

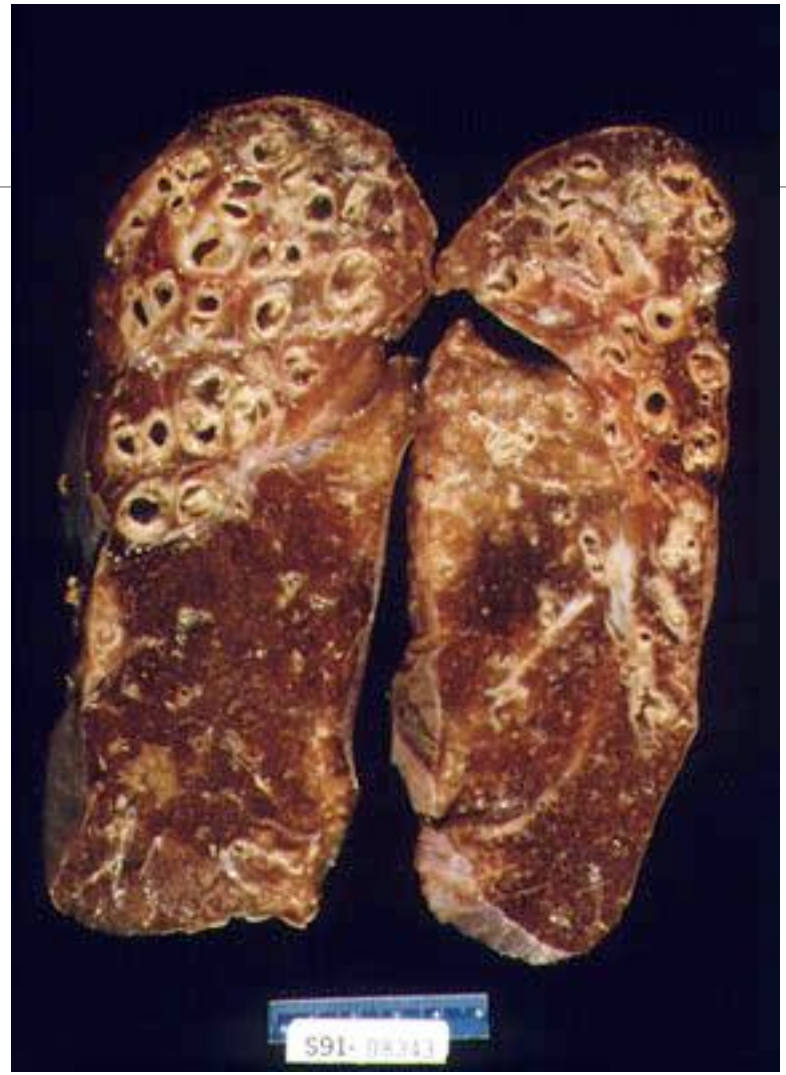
Obstruction – tumour, foreign body extrinsic nodes

Cystic fibrosis, ciliary dyskinesia

Hypogammaglobulinaemia

Autoimmune

ABPA



Bronchiectaisis

Third or fourth order bronchi

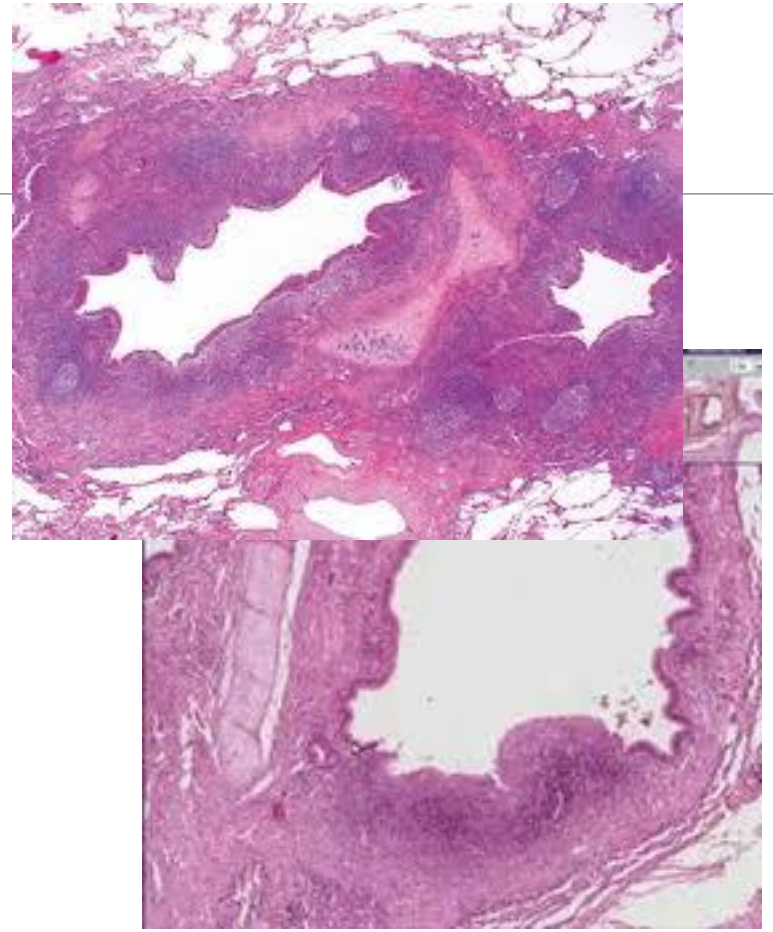
Filled with purulent exudate

Destruction of bronchial wall

Dense inflammatory infiltrate

Distal organising pneumonia

- Abscess
- Empyema



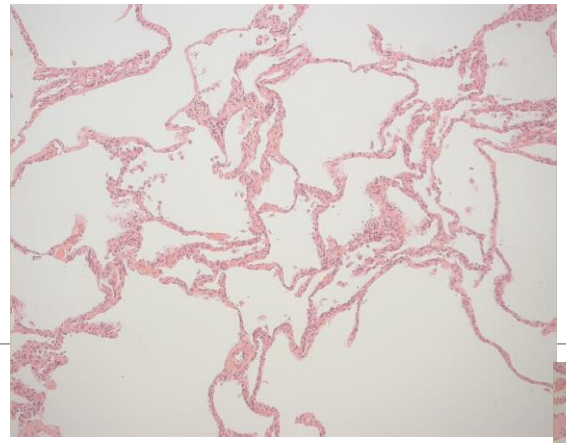
10 and 24

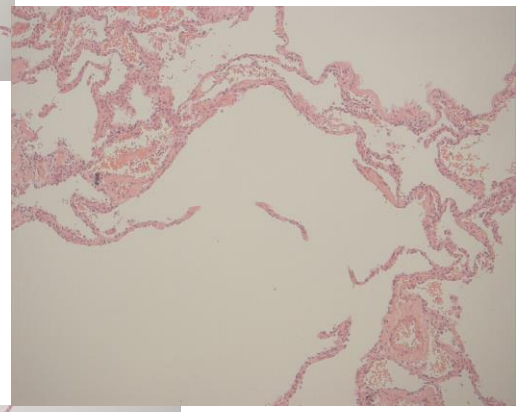
10

F63

Bilateral lung transplant

Emphysema



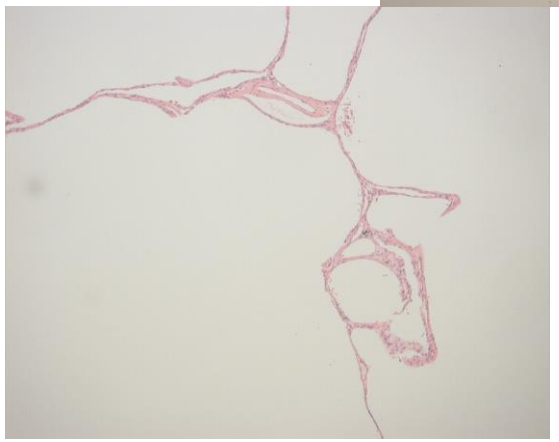


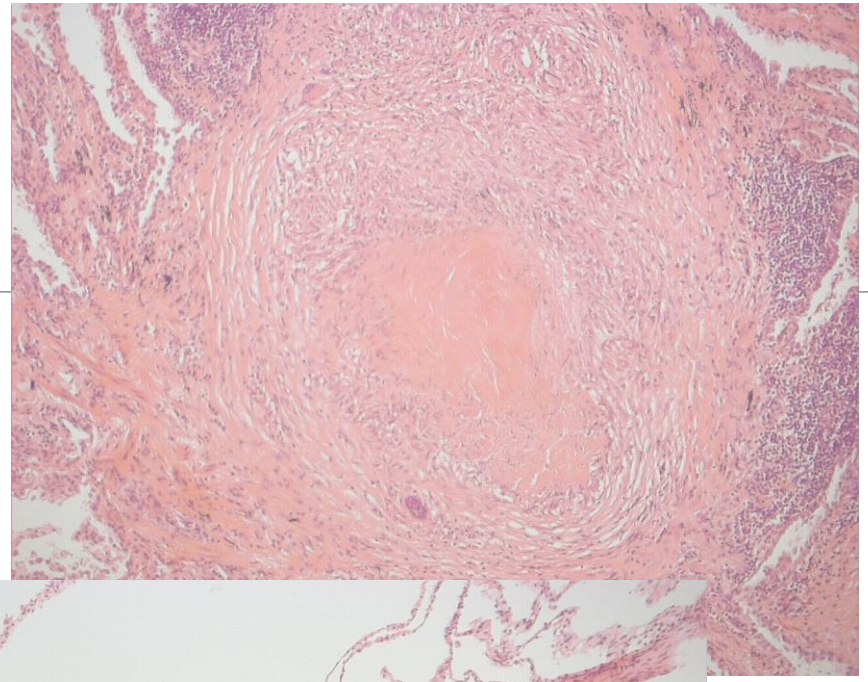
24

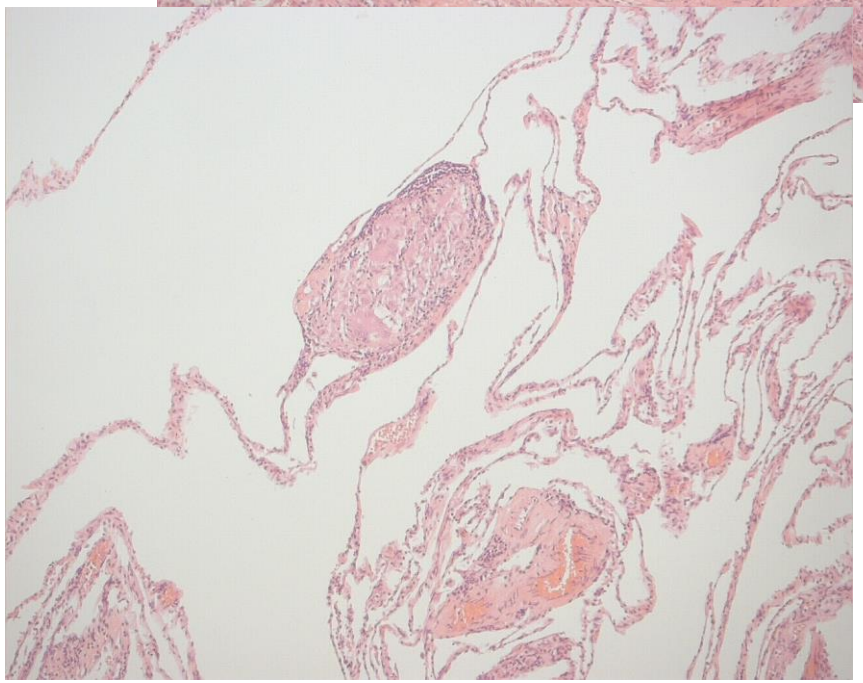
F53

Bilateral lung transplant

Emphysema







THE END