Based on: "A Pattern-Based Approach: Atlas of Pulmonary Pathology"
By Drs. Butt and Tazelaar

Prepared by Kurt Schaberg MD
Last updated: 6/18/2024

Medical Lung Diseases

Fibrosis

Dominant finding is **fibrosis**. Appears "**Pink**" (from collagen) at low magnification.

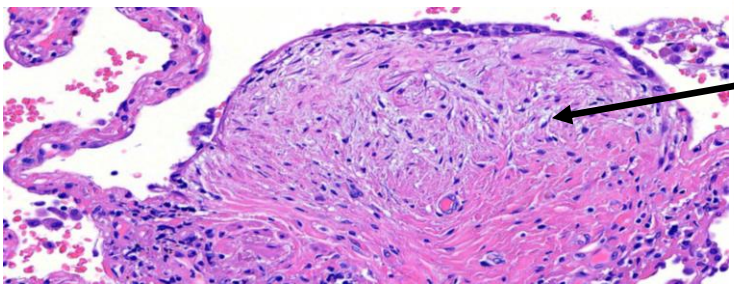
Usual Interstitial Pneumonia (UIP)/Idiopathic Pulmonary Fibrosis (IPF)

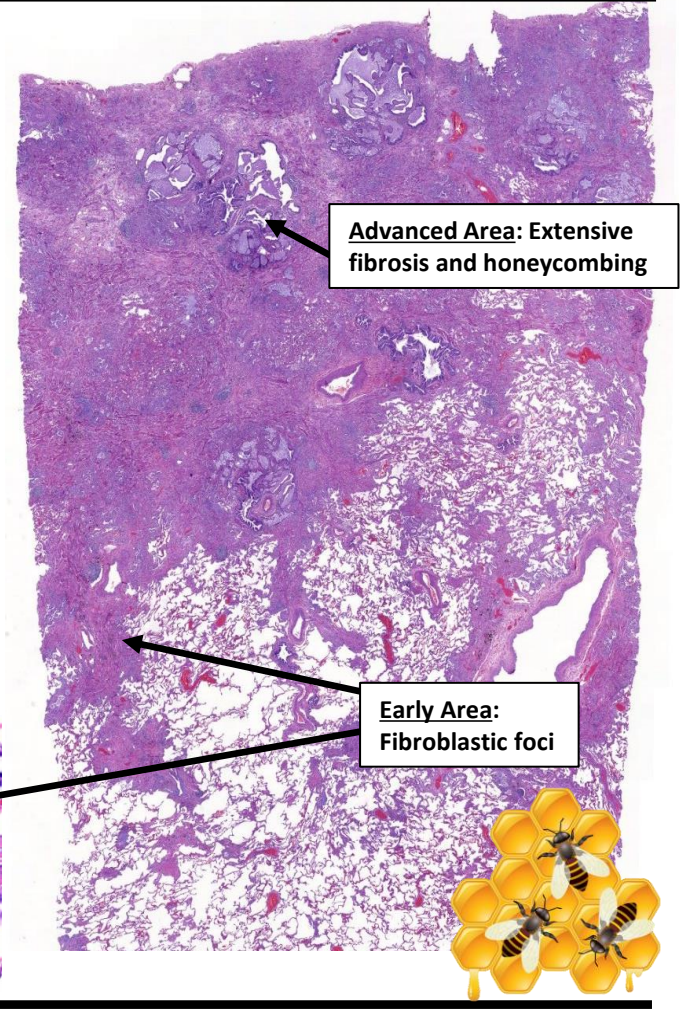
Usual Interstitial Pneumonia (UIP) is a *histologic pattern*, which can be *idiopathic* (and therefore called Idiopathic Pulmonary Fibrosis, IPF), ***or*** due to connective tissue disease, chronic hypersensitivity pneumonitis, or a drug reaction.
UIP→ Pathologic/radiographic Dx
IPF→ Clinical Dx after excluding other etiologies
Typical IPF presentation: Older male with gradually increasing shortness of breath→ eventually *fatal*!

Histologic pattern findings: **Temporally and spatially heterogeneous** (the disease is patchy, with some advanced areas and early areas). Minimal inflammation.

Classic findings: **fibroblastic foci** (immature fibroblastic areas) and **honeycombing** (architecturally distorted cystic spaces with respiratory epithelium and surrounding fibrosis)

Fibrosis is worst in lower lobes adjacent to pleura and septae. (So can't Dx on transbronchial biopsy!)

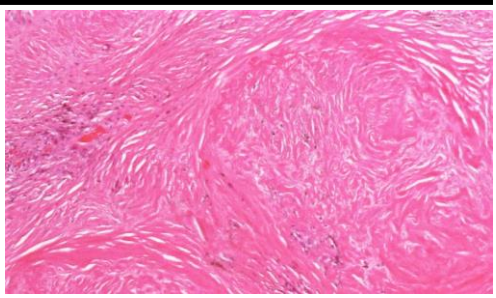




Asbestosis

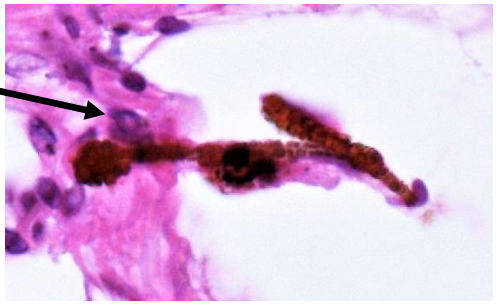
Caused by inhalation of silicate mineral fibers (not just asbestos!)
Often occupational exposure (e.g., miner, construction, shipyards…)

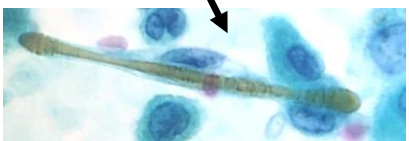
Key finding: 1) Interstitial fibrosis, 2) Asbestos bodies
(however, diagnosis often made clinically)
Minimal associated inflammation. Fibroblastic foci are absent.



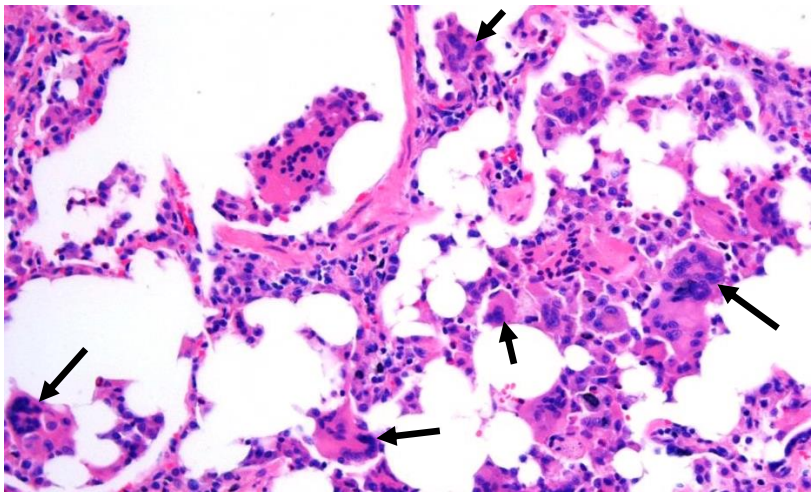
Asbestos bodies: dumbbell-shaped iron deposits (highlight with iron stains)

Often also see pleural plaques.
Increased risk of lung cancer and mesothelioma.





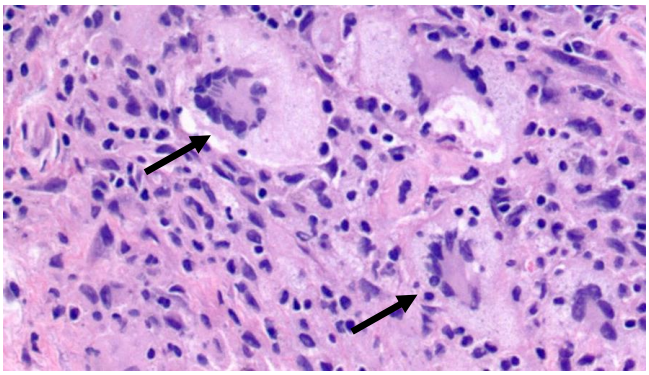
Hard Metal Pneumoconiosis



Caused by inhalation of <u>hard metals</u>, usually <u>cobalt</u>
Other metals: tungsten, titanium
Occupational exposure: manufacturing, drilling/sawing

<u>Histologically</u>: **Giant cell interstitial pneumonia (GIP)**
Intra-alveolar giant cells and fibrosis with variable inflammation. Frequent emperipolesis.

Erdheim-Chester Disease

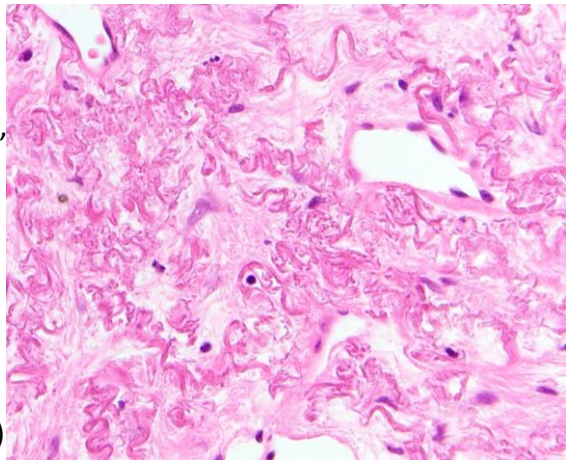


Multisystemic histiocytosis that can involve any organ. (Frequently involves long bones also)

<u>In lung</u>: **Broad fibrotic bands with intermixed foamy to pink histiocytes**. Scattered Touton-type giant cells (→).

IHC: Macrophages stain with CD68, FactorXIIIa. S100 +/-
Some show <u>BRAF V600E gene mutations</u>

Pleuroparenchymal Fibroelastosis



Early: **Upper lobe predominant subpleural fibrosis with mostly <u>elastic fibers</u>** (Highlight with elastin stain. Smaller, lighter-colored, kinkier fibers than collagen).

<u>Rare diffuse interstitial disease</u> that can be idiopathic or associated with stem cell transplantation, medications, exposures, etc…
Minimal to no: inflammation, granulomas, fibroblastic foci.

<u>If localized apical mass lesion</u>: consider "***Apical cap***" (common pleural-based fibroelastotic lesions, which can mimic malignancy)

Other Fibrotic Diseases

Many diseases (that may initially start out in a different pattern) can become fibrosis-predominant if the become advanced enough, so be sure to look for clues to other etiologies!

<u>Smoking-related Interstitial Fibrosis</u>: Hyalinized ropey fibrosis, respiratory bronchiolitis (smokers' macrophages), and emphysema.

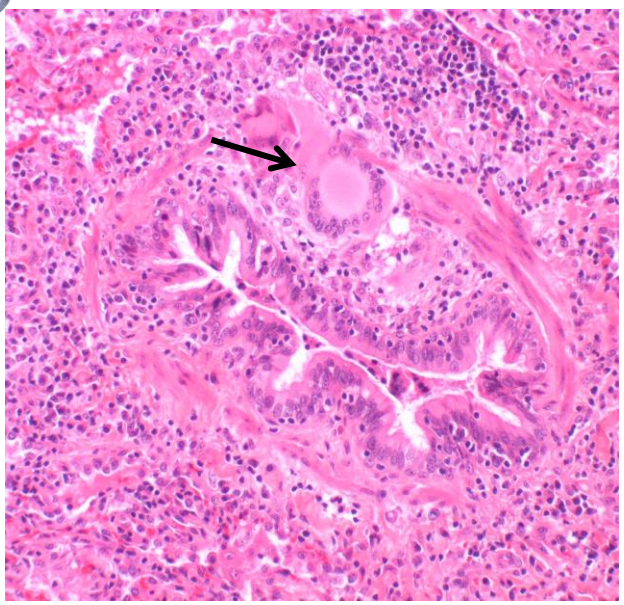
<u>Chronic Hypersensitivity Pneumonitis</u>: Cellular infiltrates, particularly near airways. Loosely formed non-necrotizing granulomas and/or giant cells.

<u>Chronic Nonspecific Interstitial Pneumonia (NSIP)</u>: Histologic pattern with relatively <u>homogenous thickening of alveolar septae by fibrosis of the same age</u> (as opposed to heterogeneity of UIP). Can be due to hypersensitivity pneumonitis, drugs, connective tissue disease, DAD, etc…

Cellular Interstitial Infiltrates

Often appears **Blue** at low power.

Hypersensitivity Pneumonitis



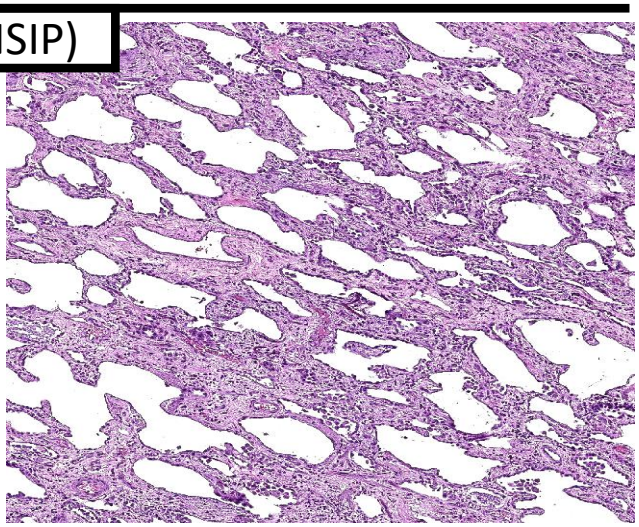
Due to inhalation of small organic or chemical antigens→ stimulate immune response.
Common antigens: Birds ("Pigeon Fancier's Lung"), Molds ("Farmer's lung"), Wood dust, certain industrial chemicals.
Often delayed diagnosis→ insidious onset of dyspnea.

Airway-centric inflammation with:
1) **Peribronchiolar granulomas/giant cells (→)**
2) **Peribronchiolar interstitial chronic inflammation**
3) **Chronic bronchiolitis**

Also often see: Peribronchiolar metaplasia ("Lambertosis"), organizing pneumonia, cholesterol clefts,

If fibrosis→ consider chronic hypersensitivity pneumonitis

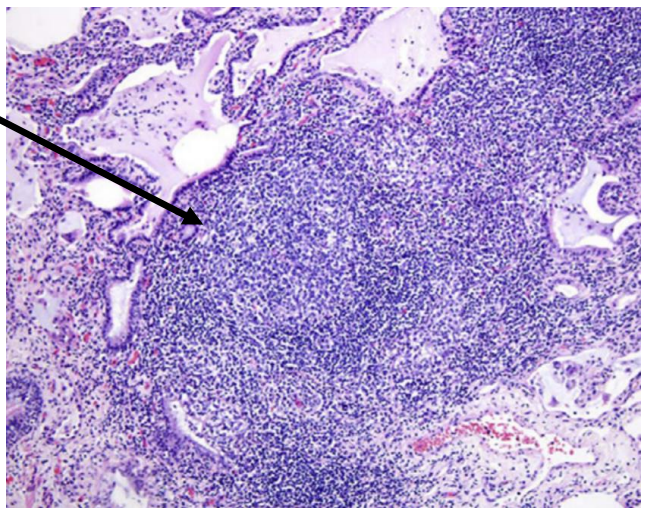
Nonspecific Interstitial Pneumonia (NSIP)



Pattern of inflammation with homogeneous, diffuse thickening of alveolar septae by chronic inflammatory infiltrates.
Can see associated homogenous fibrosis→ chronic NSIP.
Better prognosis than UIP/IPF.

Can be idiopathic, medication-related, hypersensitivity pneumonitis, or, most commonly, due to Connective Tissue Disease.

Connective Tissue Disease (CTD)-associated interstitial lung disease:



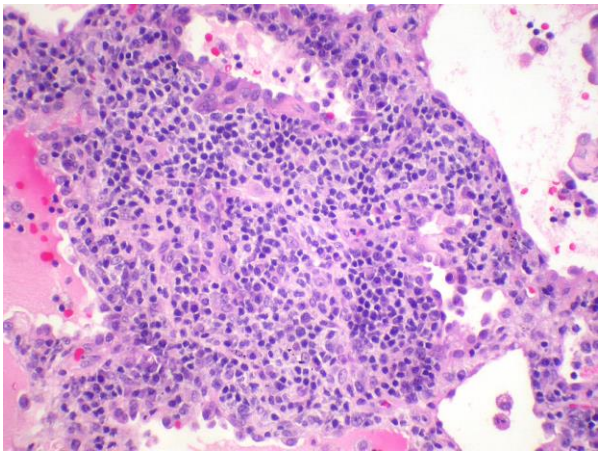
Common findings to suggest this diagnosis:
-**Prominent lymphoid follicles** +/- germinal centers
-**Pleuritis**
-Inflammation/patterns that are hard to explain/classify
If suspicious→ consider suggesting Rheumatology evaluation

Rheumatoid arthritis
Can see rheumatoid nodules.

Systemic Lupus Erythematosus
Can have pretty much any pattern/appearance

Scleroderma
Polymyositis/Dermatomyositis
Sjogren's syndrome
Mixed Connective Tissue Disease

Lymphoid Interstitial Pneumonia (LIP)

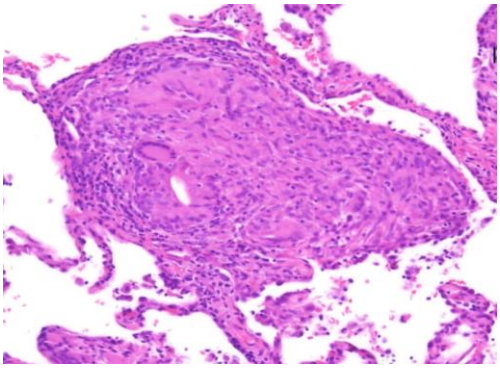


Diffuse, dense interstitial lymphoplasmacytic infiltrate. Mostly polymorphous T cells.

Rare, idiopathic. Must exclude other conditions, particularly Autoimmune diseases, HIV/AIDS, and immunodeficient states (e.g., CVID).
Also, must exclude lymphoma (esp. MALT lymphoma)!

If lots of large lymphoid follicles centered around airways, consider "**Follicular bronchiolitis**" (on a spectrum with LIP with similar DDX)

Hot Tub Lung

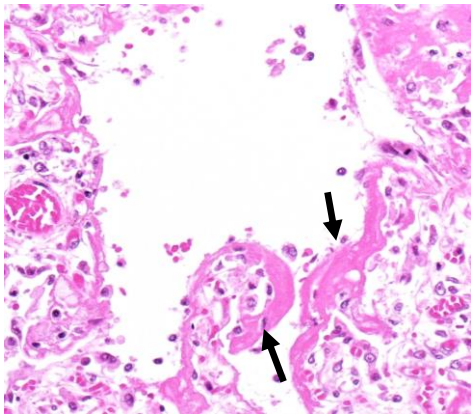


Hypersensitivity pneumonia-like reaction to mycobacterium avium complex (MAC), which is common in water (like indoor hot tubs, saunas, pools, etc…)

Similar appearance to HP (peribronchiolar chronic inflammation), but more prominent and better-formed granulomas, which can be necrotizing.

Alveolar Filling Pattern

Diffuse Alveolar Damage

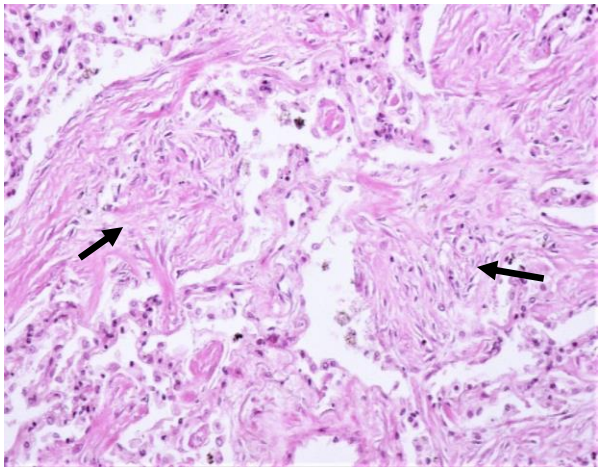


Histologic manifestation of Acute Respiratory Distress Syndrome (ARDS)→ Bilateral diffuse infiltrates, often requiring ventilation.

Can be seen in a variety of settings (common endpoint) including: **Infection, sepsis, drug reactions, toxins, and shock**.
If idiopathic→ "Acute Interstitial Pneumonia" (AIP)

Endothelial/epithelial injury→ leakage of serum proteins → **Hyaline membranes** (→) (fibrinous exudate). Particularly with infection also see **necrosis**, and **acute inflammation.**

Organizing Pneumonia

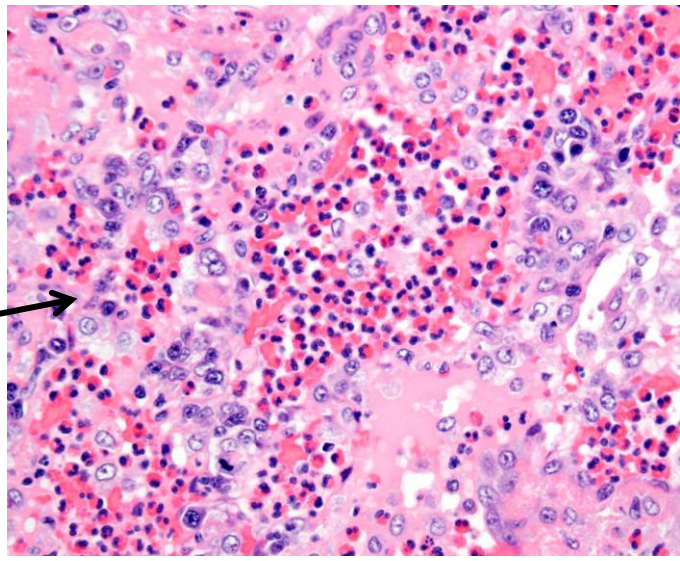


Nonspecific pattern of lung injury/repair.
Can be seen after recent infection/injury, aspiration, connective tissue disease, etc..
If idiopathic→ "Cryptogenic Organizing Pneumonia" (COP)

Accumulation of immature myxoid material and fibroblasts within airspaces.
In airspaces can see **fibroblastic plugs** (branching→) **/polyps** (floating)**.** Intact alveolar septae.

Often resolves after removing inciting agent.

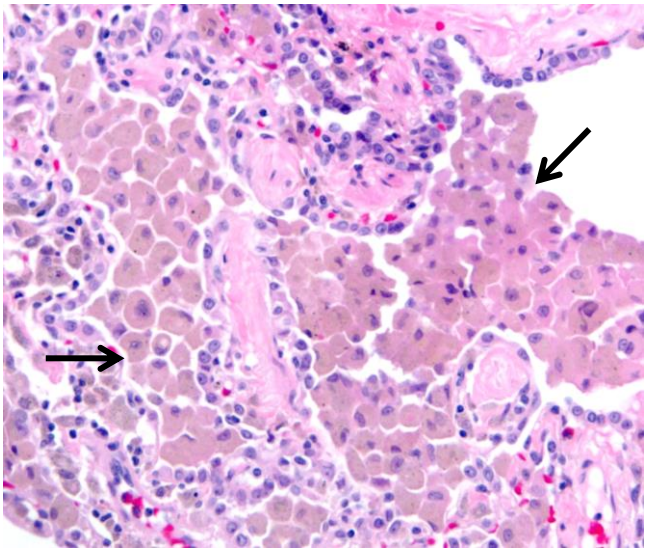
Eosinophilic Pneumonia



Acute Eosinophilic Pneumonia:
Presents with fever and dyspnea of <1 month duration.
Essentially, Diffuse Alveolar Damage with the addition of eosinophil-rich inflammation.
Peripheral eosinophilia and Eos on BAL.
DDX: Infection (parasites), Medications, Cigarettes, Pneumothorax, Idiopathic.

Chronic Eosinophilic Pneumonia:
Insidious onset, relapsing. Responds to steroids.
Intra-alveolar collections of Eosinophils, macrophages, and proteinaceous edema. Also, organizing pneumonia.
DDX: When idiopathic often associated with asthma, medications, allergies, etc…

Desquamative Interstitial Pneumonia (DIP)/ Respiratory Bronchiolitis Interstitial Lung Disease (RB-ILD)



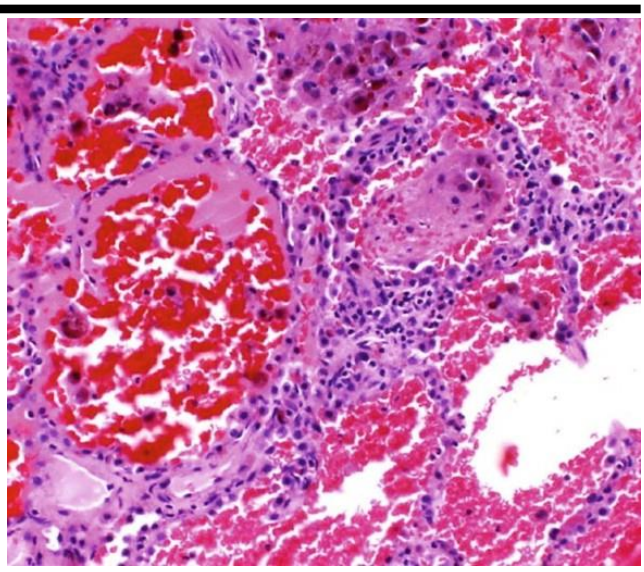
***Spectrum* of disease highly associated with smoking.**

RB: Pigmented "smoker's macrophages" (→) in respiratory bronchioles and adjacent alveoli. Often with associated adjacent mild fibrosis.
Need clinical symptoms/findings to label as RB-*ILD*.

DIP: Filling of alveoli by pigmented macrophages. Often associated fibrosis and mild chronic inflammation.

Note: It can be challenging to distinguish these "smoker's macrophages", which have fine, powdery anthracotic pigment, from hemosiderin-laden macrophages (seen with hemorrhage/congestion), which is more chunky and refractile. Both contain iron.

Alveolar Hemorrhage



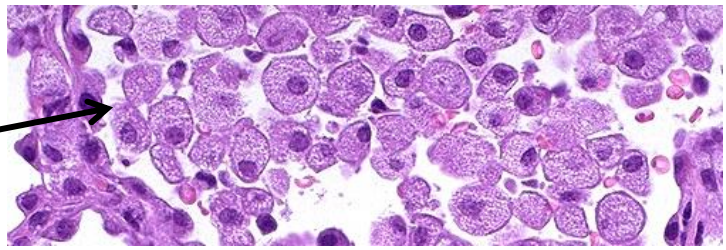
Hemosiderin-laden macrophages and fresh blood in alveoli.

Can be *secondary* to Trauma, Cardiac disease, Vascular disease, Medications, etc..

Diffuse Alveolar Hemorrhage (DAH) is often a result of vasculitis→ be sure to look for capillaritis!

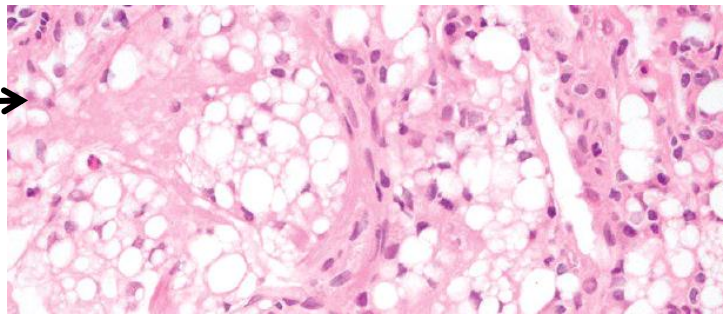
Anti-Glomerular Basement Membrane Disease (Goodpasture Syndrome). Autoantibodies to collagen IV in basement membrane. Impacts capillaries in kidney, lung, or both. In lung→ hemorrhage. In kidney→ crescentic glomerulonephritis.

Lipoid Pneumonia



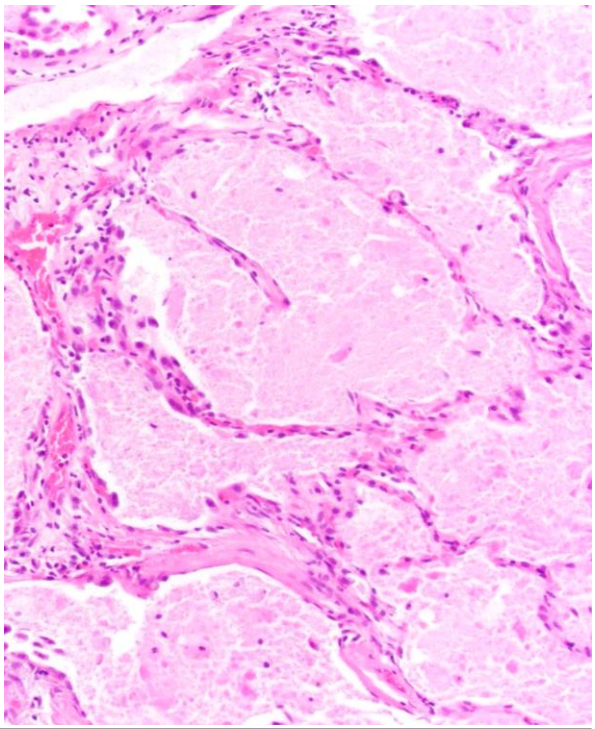
<u>Lipid-rich material</u> and inflammatory cells filling alveolar spaces.

Endogenous/Post-obstructive:
Proximal airway obstruction→ inability to clear secretions→ accumulation of ***<u>finely</u>*** <u>vacuolated macrophages</u> in distal airways.



Exogenous/Aspiration:
Aspiration of lipid-rich material (e.g., mineral oil)
Accumulation of <u>multinucleated giant cells containing ***large*** lipid vacuoles</u> within alveoli.

Alveolar Proteinosis



Filling of alveoli by amorphous eosinophilic, granular proteinaceous material. Occasional crystals and cholesterol clefts. **PASD+** (vs edema, which is PAS negative)
"Crazy Paving" appearance on CT.

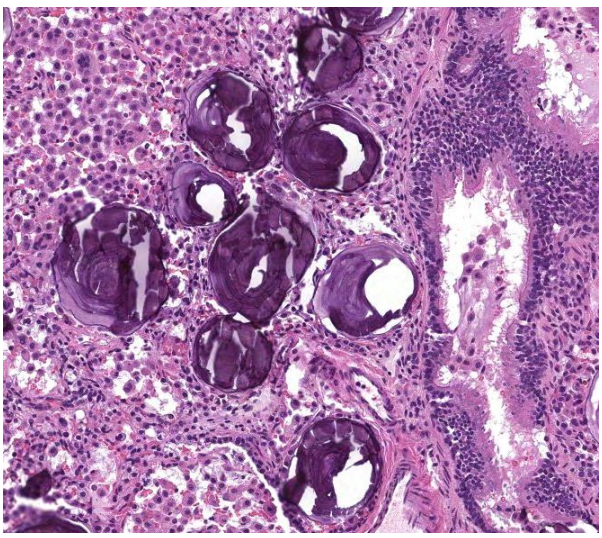
<u>Three forms:</u>
Congenital: Due to mutations of genes encoding surfactant or GM-CSF

Primary: autoantibodies against GM-CSF→ abnormal macrophage function→ accumulation of proteinaceous material.

Secondary: A variety of causes including stem cell transplantation, solid organ transplantation, etc…

<u>Key histologic DDX</u>: Pneumocystis pneumonia→ be sure to get fungal stains, especially if immunocompromised!

Alveolar Microlithiasis



Microliths of calcium phosphate within alveoli with characteristic circular lamellations
(similar to psammoma bodies)

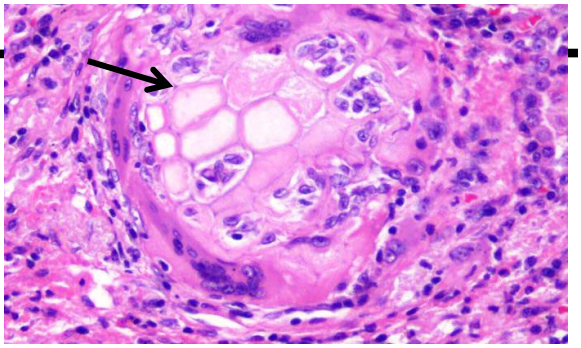
<u>Autosomal recessive disorder</u>: Mutations in SLC34A2 gene → dysfunctional sodium phosphate transport.
Usually causes disease in middle-aged adults, respiratory failure, but usually indolent with slow-progression.

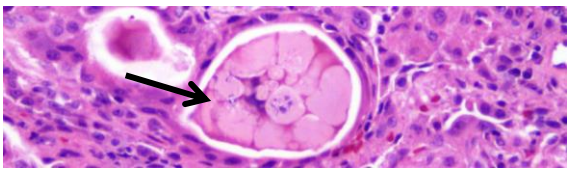
"Sandstorm" appearance on radiology.

DDX: corpora amylacea (normal), dystrophic calcifications, ossification

Nodules

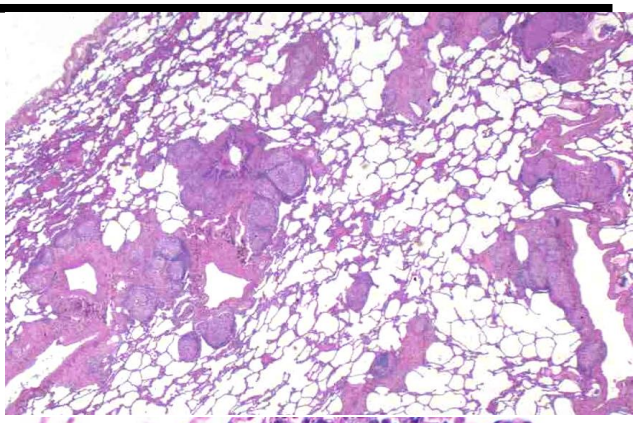
Aspiration

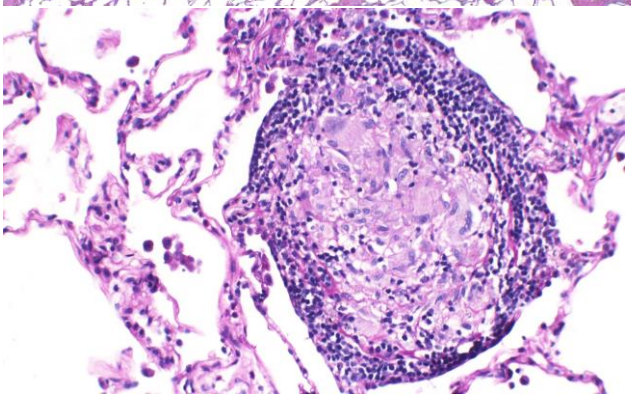




Due to aspiration of food particles.
Can be single or multiple.
Risk factors: Stroke, GERD, obesity, epilepsy, Alcohol.
Airway-centered inflammation with **giant cells** and organizing pneumonia.
Classically: degenerating food particles (→) (but may be focal)
→ may be polarizable, especially some pill particles.
Can also see lipoid pneumonia (see separate section)
Can see abscess formation if superinfected.

Sarcoidosis





Systemic idiopathic granulomatous disease with frequent pulmonary involvement.
Dx requires clinical correlation.

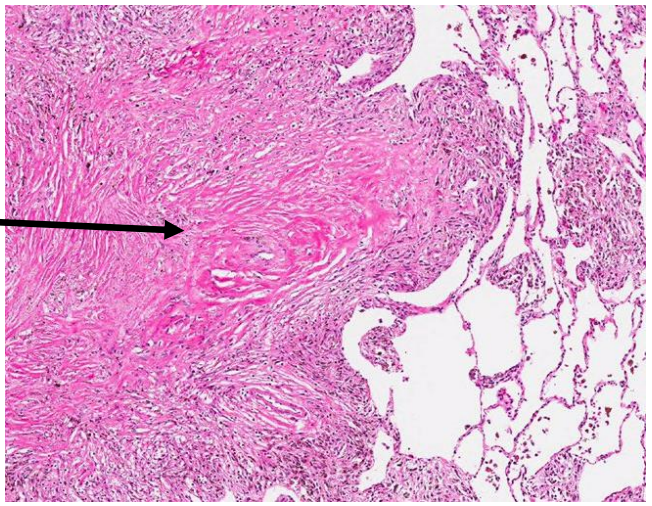
Starts centrally in lung with large airways and hilar lymphadenopathy→ extends outward with progressive fibrosis.

***Classic finding*: tightly formed (mostly) non-necrotizing granulomas with giant cells**→ eventually become more confluent and mass-like with increased hyalinized fibrosis.
Follows lymphangitic distribution (bronchovascular bundle, interlobar septae, pleural). NOT in airspaces.
Sparse lymphoid inflammation at periphery.

No organizing pneumonia or interstitial inflammation.
Extensive necrosis→ favors infectious etiology.

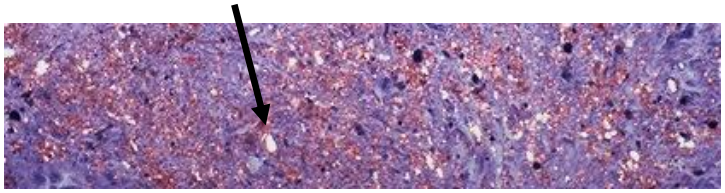
Note: Giant cells can produce some *endogenous* polarizable material (calcium oxalate)→ don't mistake as foreign material!

Silicosis



Caused by inhalation of Silica and related minerals.
Risk factors: construction, manufacturing, mining, etc.

Inhale silica→ engulfed by **macrophages→ form aggregates that increasingly fibrose/hyalinize and coalesce into nodules.**
Silica is **birefringent** if polarized.

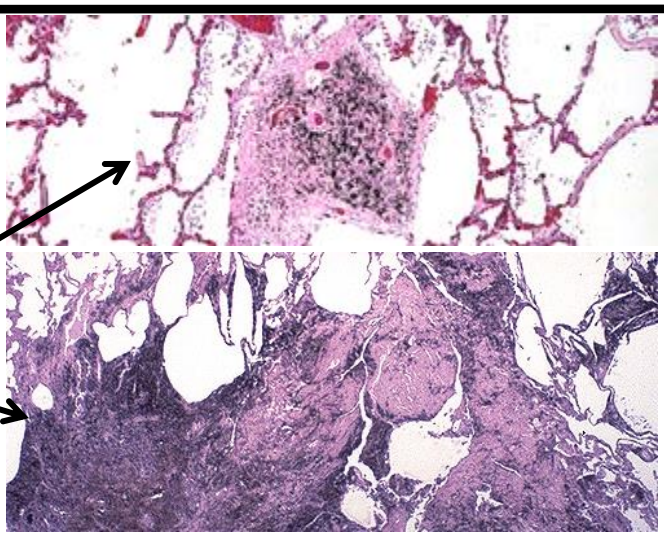


Coal Workers' Pneumoconiosis

"Black Lung Disease"

Caused by exposure to Coal dust.
Common to see concurrent silica/silicosis ("mixed dust," similar exposure while mining).

Dust-laden macrophages in/around terminal bronchovascular bundles → Mild haphazard fibrosis and emphysema → can progress to large nodules with fibrosis.



Vasculitis

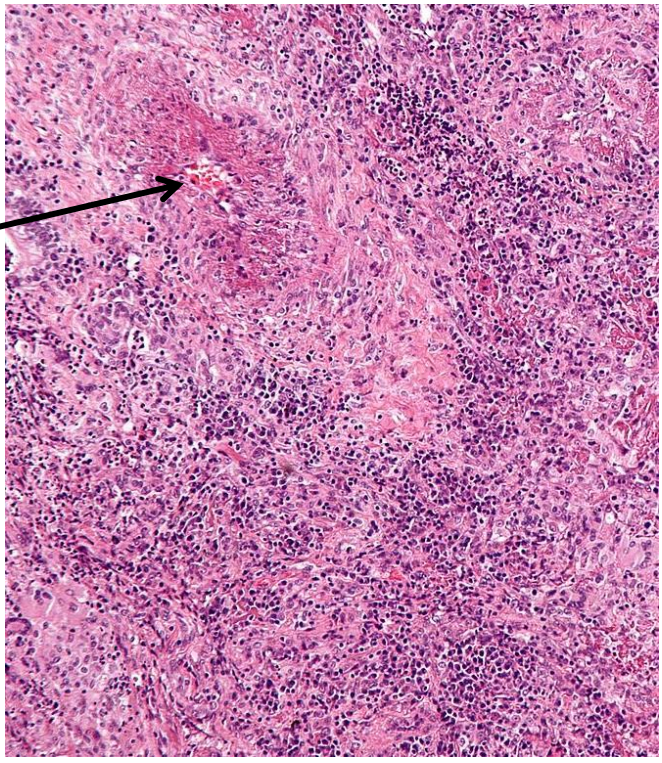
Dx often involves clinical/serologic correlation.
Often ANCA positive.

Granulomatosis with Polyangiitis (Wegner's)

Necrotizing granulomatous inflammation.
Commonly impacts lung, nasal cavity, and kidney.
In lung/head see granulomas with geographic central necrosis and associated vasculitis→ form ulcers and cavitating nodules. In kidney can see crescentic glomerulonephritis.
PR3-ANCA positive (c-ANCA).

Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss)

Eosinophil-rich and necrotizing granulomatous inflammation. Often impacts the lung. Associated with asthma and eosinophilia.
MPO-ANCA usually positive (p-ANCA).



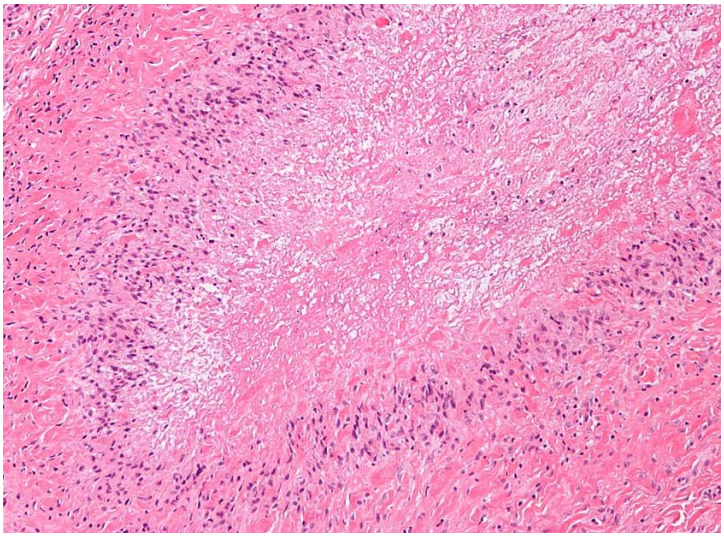
Rheumatoid Nodule

Granulomatous nodules with central fibrinoid necrosis. Palisading histiocytes with lymphoplasmacytic inflammation.

Most *specific* pulmonary findings for Rheumatoid arthritis. (Can see diverse other finding including pleuritis, follicular bronchiolitis, NSIP, UIP, etc…)

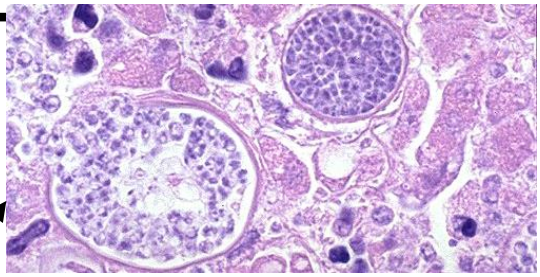
Can see both in lung and pleura.

DDX: Granulomatosis with Polyangiitis, Infection.
→ be sure to get bug stains, etc…



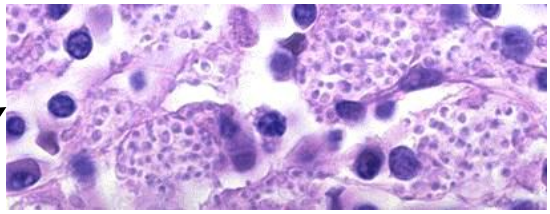
Fungal Infections

Often diagnosed based on imaging and lab studies.
May be focal or diffuse (particularly if immunocompromised).
Often cause **granulomatous** response (+/- necrosis).
Have a low threshold to get a GMS/PAS!

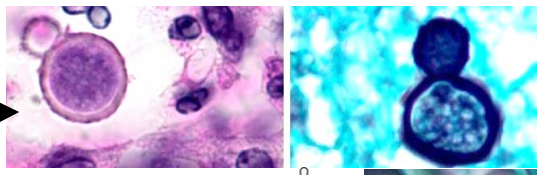


Regardless of immune status:

Coccidioidomycosis: Southwestern US in dry soil. See spherules +/- endospores. "Valley Fever."



Histoplasma Capsulatum: Mississippi/Ohio River valley in soil/caves (bat droppings). Narrow based buds. Small, oval size. Common to have subclinical infection with burnt out hyalinized granulomas. If disseminated→ see in macrophages



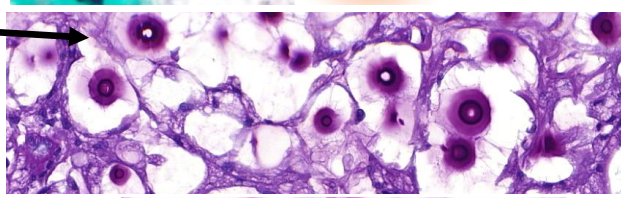
Blastomycosis: Mississippi/Ohio River valley and Northeast in soil. Broad based buds, round, uniform thick double wall.

Paracoccidioides: South and Central America. Radial pattern.

Often immunocompromised:

Pneumocystis jirovecii: Ubiquitous. Infect immunocompromised hosts (classically AIDS). "Crushed ping pong balls" with central dot in foamy alveolar exudate.

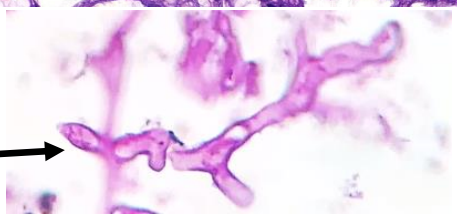
Cryptococcus: Ubiquitous in soil and bird droppings. Round, thick halo. Variable size ("Pleomorphic"). Narrow budding.



Aspergillus: Ubiquitous in soil. Septae hyphae with 45° branching. Can colonize pre-existing cavity→ Aspergilloma (fungus ball). Can also cause allergic response or be tissue/vascular invasive.

Candida: Ubiquitous in skin (can be oral contaminate in BAL). Budding yeast and pseudohyphae.

Mucormycosis: Ubiquitous. Broad "Ribbon-like" hyphae with irregular branching and inconspicuous septae.



Bacterial Infections

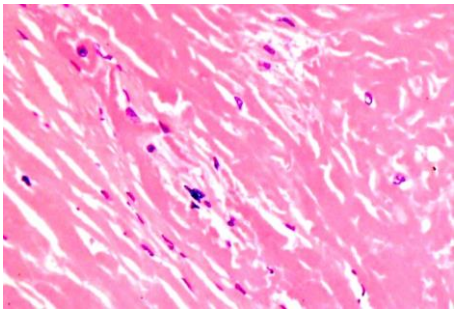
Often diagnosed clinically based on radiology and lab findings, esp. usual bacterial pneumonia.

Mycobacterium tuberculosis: Worldwide, many people are asymptomatically infected leaving behind calcified nodules/lymph nodes (Ghon complex). This can reactivate leading to active cavitating infection, often in the upper lobes. Can disseminate more widely if immunocompromised. Histologically, mostly see necrotizing granulomas and fibrosis. Have a low threshold for getting AFB!

Nocardiosis: Gram-positive filamentous bacteria. Infect immunocompromised. Highlighted by both AFB and GMS. Look like slender tangled strings.

Actinomycosis: Gram-positive filamentous bacteria. Commensal in oral cavity. Can cause abscesses with distinctive "sulfur granules."

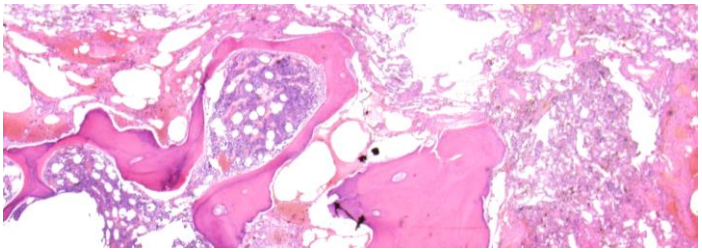
Pulmonary Hyalinizing Granuloma



Pulmonary counterpart to fibrosing mediastinitis
Often considered an exaggerated response to a remote infection, most often histoplasmosis. Can also be associated with IgG4-related disease.

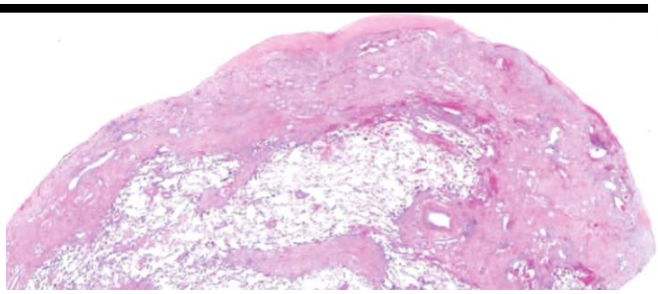
Single or multiple slow-growing nodules.
Well-circumscribed, acellular hyalinized collagen.
Scattered foci of chronic inflammation.

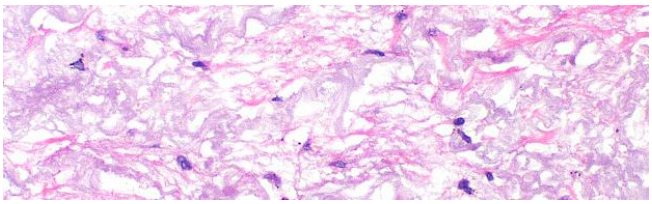
Metaplastic Ossification



Mature lamellar bone. Often incidental finding.
Frequently **response to injury**: scar, aspiration, granulomas, apical caps, etc…

Apical Cap



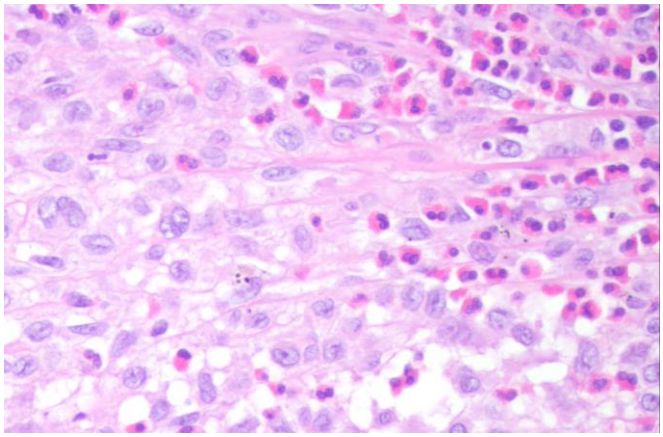


Subpleural fibroelastotic scars seen most commonly in the apices of the upper lobes.

Unclear etiology.
Predominantly elastotic fibers with intermixed collagen.
Triangular-shape (with broad pleural base).
Can radiographically mimic malignancy.

If diffuse → Pleuroparenchymal fibroelastosis (rare type of interstitial lung disease discussed separately)

Pulmonary Langerhans Cell Histiocytosis



aka "Eosinophilic granuloma"

Considered a reactive proliferation (as opposed to extrapulmonary LCH, which is neoplastic)

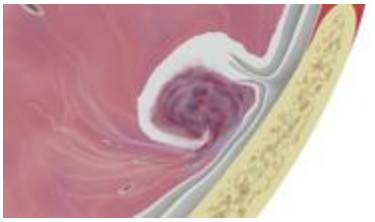
Strongly associated with **smoking** (so often see other smoking-related changes). Stellate nodules centered around airways with surrounding cystic areas.

Early → **Numerous Langerhans cells** (greyish cytoplasm with groove coffee bean nuclei; Stain with S100, Langerin, CD1a) **with associated eosinophils**.
Late → Increased fibrosis

Other Non-Neoplastic Mass-forming Lesions

Berylliosis
Amyloidosis
Light-chain deposition disease
Parasitic infections
Vaping (can cause nodular injury)
Ehler-Danlos Syndrome (from spontaneous vascular injury)

Round Atelectasis

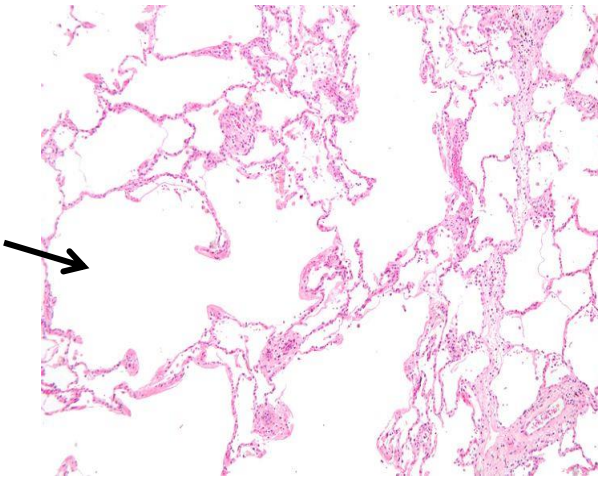


Infolding of lung into underlying parenchyma caused by pleural fibrosis/retraction→ <u>can *simulate* a "Mass."</u>
Most common in lingula. Requires radiographic correlation.

Histologically: **Normal-appearing lung tissue with overlying pleural fibrosis** (no obvious mass-forming lesion).

Near Normal

Emphysema

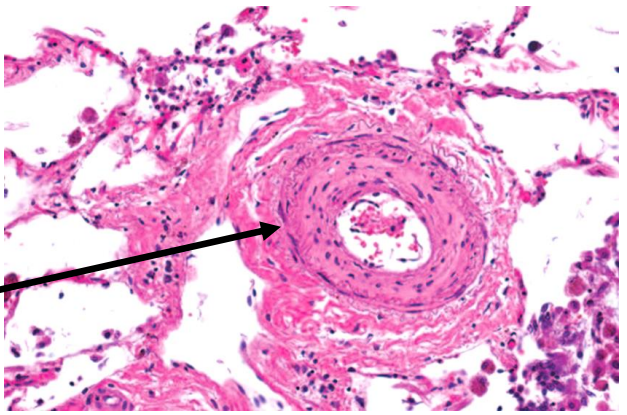


Airspace enlargement due to alveolar septal destruction without significant fibrosis.
Common "background" (incidental) finding in lung.

<u>Often classified by location:</u>
<u>Centrilobular</u>: Destruction near small airways. Classically associated with <u>smoking</u> and upper lobe predominant. Emphysema + Chronic Bronchitis = Chronic Obstructive Pulmonary Disease (COPD). Also see with Coal workers' pneumoconiosis. Eventually expands to panlobular/acinar.

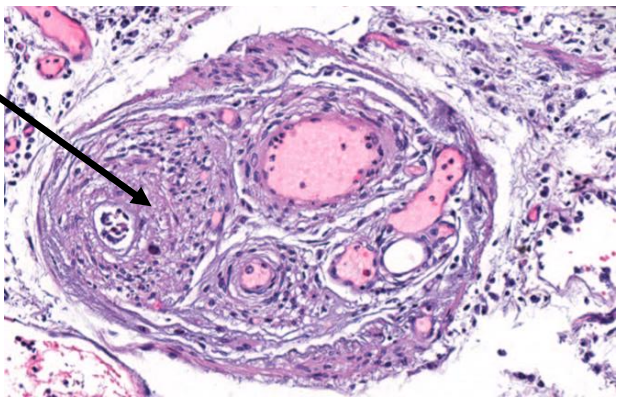
<u>Panacinar</u>: Involves entire lobule from beginning. Classically associated with α1-antitrypsin deficiency. Lower-lobe predominant. Also risk of liver disease.

Pulmonary Hypertension



<u>Clinical diagnosis</u>!
Increased pulmonary vascular pressure.
Common causes: Heart failure, Lung disease (e.g., UIP)
Can be primary/idiopathic.

Pathologic findings may not correlate with symptoms.
<u>Medial hypertrophy</u> of arteries and veins,
Intimal proliferation/fibrosis,



<u>Plexiform lesions</u>, fibrous webs/plugs ("colander-like"), emboli/thrombi.

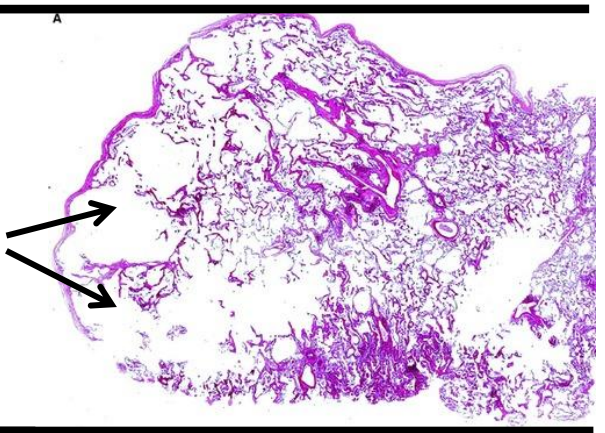
<u>Note</u>: Recanalized thrombi (from a PE) are also plexiform. If the lesion is in a large elastic artery→ think pulmonary embolism!

Birt-Hogg-Dubé Syndrome

Autosomal Dominant.
Mutations in folliculin gene (FLCN).

Multi-organ manifestations:
Lung: Variably sized **thin-walled cysts** underneath pleura near septae or lower lobes→ can rupture→ **pneumothorax**

Skin: Fibrofolliculomas
Kidney: hybrid oncocytic neoplasms (chromophobe renal cell carcinoma + oncocytoma)

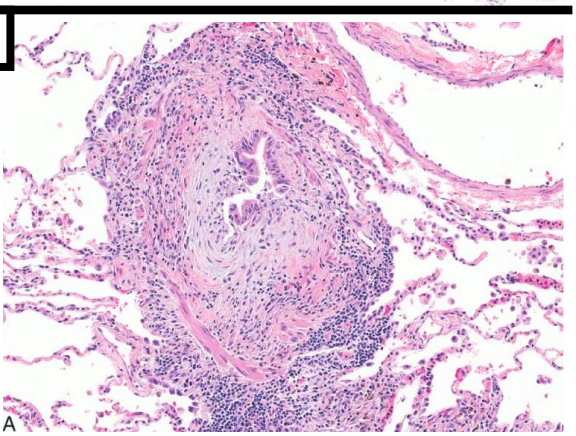


Constrictive (Obliterative) Bronchiolitis

(mainly say Obliterative bronchiolitis in transplant setting)

Fibroinflammatory scarring of bronchioles.
Scarring between epithelium and smooth muscle→ can eventually obliterate lumen.
Elastin stain can highlight elastic layer of obliterated airway and confirm it was there, usually with a remaining paired artery.

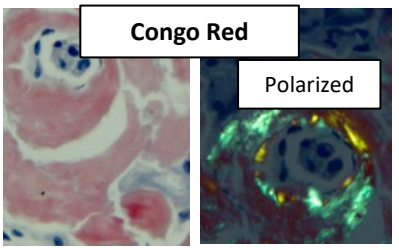
Possible causes: Infection, fumes/toxins, medications, connective tissue disease (especially RA), etc..



Amyloidosis

Can be localized (just lung) vs systemic.
Localized amyloidosis can be nodular or diffuse.

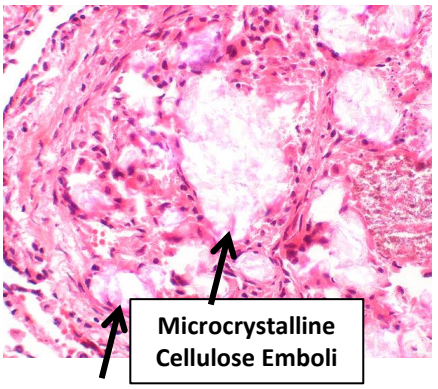
Regardless, appears similar to elsewhere: Waxy pink protein deposition.
(+) Congo Red stain with "Apple green" birefringence

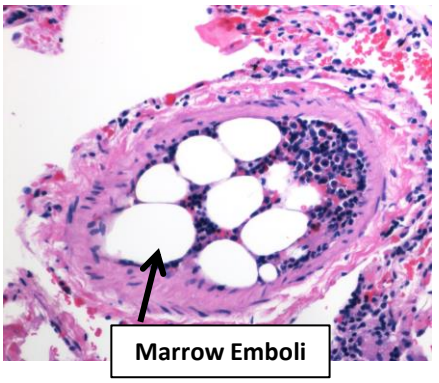


Foreign Material Emboli

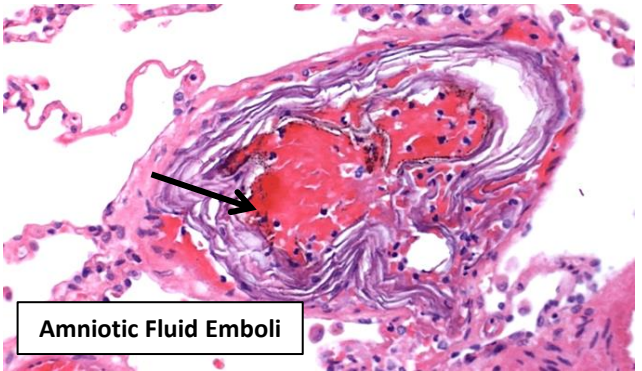
With intravenous drug use, there can be **microcrystalline cellulose emboli**: refractile under polarized light→ causes pulmonary hypertension.

Bone marrow/fat emboli can be seen after bone fractures (including after CPR).





Amniotic fluid emboli can occur during pregnancy/birth → see fetal squamous cells (and other fetal tissues) in pulmonary vasculature → can cause sudden death, hypoxia, DIC, etc..



Lung Transplantation

Surveillance biopsies are often performed to look for rejection at regular intervals post-transplant (e.g., 6, 9, 12 months)

Acute Cellular Rejection

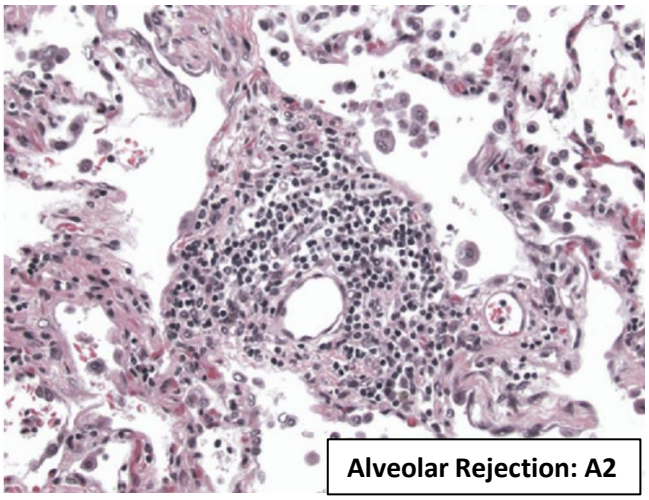
For adequate sensitivity, need 5 pieces of expanded alveolated lung, and multiple levels.

Acute cellular rejection is based on the **presence of perivascular and interstitial T-cell-rich infiltrates**.

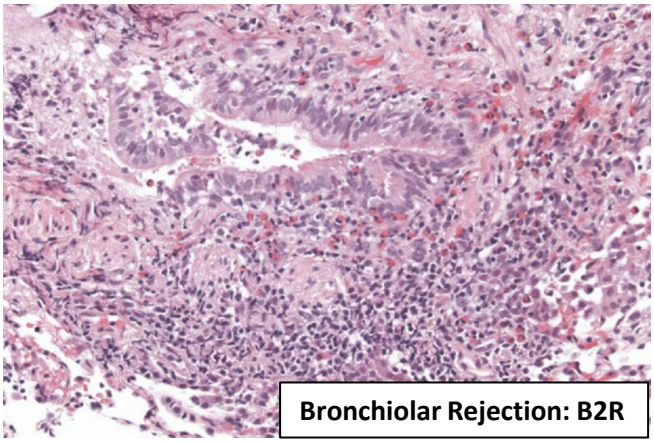
Can also see **lymphocytic bronchiolitis** with a band-like T-cell-rich chronic inflammatory infiltrate in the submucosa of bronchioles (which have no cartilage in the walls)(vs BALT, which is well-circumscribed and B-cell rich)

Note: Perivascular/interstitial and bronchial chronic inflammation is *NOT* specific for rejection! Infection (e.g., CMV, PCP) and PTLD can look similar, so consider other options, particularly if there are lots of neutrophils or plasma cells (features that favor infection).

(See grading on next page)



Alveolar Rejection: A2

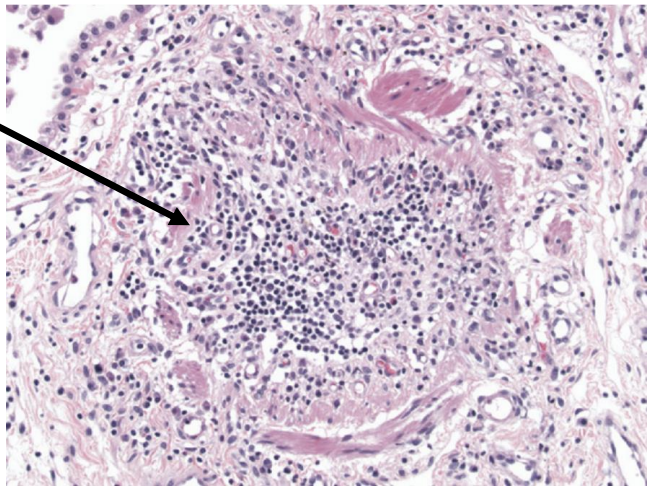


Bronchiolar Rejection: B2R

Chronic Rejection

Obliterative Bronchiolitis: Progressive airway lumen obliteration by inflammation and fibrosis.
Hard to see on surveillance biopsies→ often a clinical diagnosis with reduced FEV_1.
Elastic stains can be used to highlight obliterated bronchioles.

(synonymous with constrictive bronchiolitis in nontransplant setting)



Chronic Vascular Rejection: Myointimal thickening and fibrosis within arteries and veins. Not often seen in biopsies.

Antibody-Mediated Rejection

Less well-defined than in other organs.
Requires: 1) Clinical dysfunction, 2) Positive circulating donor-specific antibodies (DSA), and 3) C4d immunoreactivity.
On H&E: Neutrophilic capillaritis and neutrophilic septal margination.
IHC/IF: C4d strong, linear/donut pattern of staining in septal capillaries.

Transplant Acute Rejection Grading

Based on: Stewart S, et al. J Heart Lung Transplant. 2007 Dec;26(12):1229-42.

Alveolar Rejection		
AX	Ungradable	
A0	None	Normal pulmonary parenchyma without evidence of mononuclear cell infiltration, hemorrhage or necrosis.
A1	Minimal	Scattered, infrequent perivascular mononuclear infiltrates (particularly around venules), < 3 cells thick.
A2	Mild	Conspicuous perivascular inflammation, > 3 cells thick
A3	Moderate	Conspicuous perivascular inflammation, with extension into alveolar septa
A4	Severe	Conspicuous perivascular inflammation, with features of acute lung injury
Bronchiolar Rejection		
BX	Ungradable	
B0	None	No significant airway inflammation
B1R	Low-grade	Submucosal chronic inflammation, without significant intraepithelial inflammation or injury
B2R	High-grade	Submucosal chronic inflammation with intraepithelial lymphocytes, epithelial injury, +/- neutrophils, ulceration, and/or necrosis

Transplant Chronic Grading

Obliterative Bronchiolitis	
C0	Absent
C1	Present
Chronic Vascular Rejection	
D0	Absent
D1	Present

Helpful Tables

Histologic Findings of Idiopathic Interstitial Pneumonias

Adapted from: Practical Pulmonary Pathology by Drs. Leslie and Wick

Feature	Nonspecific Interstitial Pneumonia (NSIP)	Usual Interstitial Pneumonia (UIP)	Desquamative Interstitial Pneumonia (DIP)	Acute Interstitial Pneumonia (AIP)	Lymphocytic Interstitial Pneumonia (LIP)	Cryptogenic Organizing Pneumonia (COP)
Temporal appearance	Uniform	Varied	Uniform	Uniform	Uniform	Uniform
Interstitial inflammation	Prominent	Scant	Scant	Scant	Prominent	Scant
Interstitial fibrosis: collagen	Variable, diffuse	Patchy	Variable, diffuse	No	Some cases	No
Interstitial fibrosis: fibroblasts	Occasional, diffuse	No	No	Yes, diffuse	No	No
OP pattern	Occasional, focal	Occasional, focal	No	Occasional, focal	No	Prominent
Fibroblast foci	Occasional, focal	Typical	No	No	No	No, but see *similar* fibroblastic plugs/polyps
Honeycomb areas	Rare	Typical	No	No	Sometimes	No
Intra-alveolar macrophages	Occasional, patchy	Occasional, focal	Yes, diffuse	No	Occasional, patchy	No
Hyaline membranes	No	No	No	Yes	No	No
Granulomas	No	No	No	No	No	No

Diseases with Bronchocentric Granulomas

Adapted from: "A Pattern-based Approach: Atlas of Pulmonary Pathology"

Disease	Additional Findings
Aspiration	History of stroke, epilepsy, GERD, etc…, Degenerating food/pill particles
Sarcoidosis	Tightly formed granulomas, usually non-necrotizing. Also along pleura and septae.
Infection	Positive cultures or special stains.
Hypersensitivity Pneumonitis	Peribronchiolar chronic inflammation, Chronic bronchiolitis, Peribronchiolar metaplasia ("Lambertosis"), relevant exposure history (e.g., Birds, molds...)
Allergic Bronchopulmonary Aspergillosis (ABPA)	Allergic mucin (Charcot-Leyden crystals and eosinophils), Eosinophilic pneumonia, asthma/asthmatic airway changes, rare fungal elements.
Granulomatosis with polyangiitis	Vasculitis, capillaritis, Diffuse Alveolar Hemorrhage, Positive ANCA, relevant history/clinical findings.
Middle Lobe Syndrome	Limited to middle lobe.
Rheumatoid Arthritis	Rheumatoid nodules. Relevant clinical history (arthritis, RF+, etc…)