

Non-neoplastic Lung Pathology II Additional Patterns of Lung Fibrosis and Inflammatory Infiltrates in Interstitial Lung Disease (ILD)

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COMMENTARY: KO LESLIE MD



Format:

- Case presentations
- Cellular infiltrates
- Additional fibrosis patterns
- Disease entities: NSIP, RB-ILD, DIP, PPFE, DAH, Eos Pneum,



To be discussed:

Nonspecific Interstitial Pneumonia (NSIP)

Respiratory bronchiolitis associated ILD (RB-ILD)

Desquamative interstitial pneumonia (DIP)

Pleuroparenchymal fibroelastosis (PPFE)

Smoking-related interstitial fibrosis (SRIF)

Diffuse alveolar hemorrhage (DAH)

Eosinophilic pneumonia (Acute/AEP, Chronic/CEP)

Refs:

Leslie KO and Wick MR. Practical Pulmonary Pathology (Elsevier 2017)

Travis WD et al. ...Idiopathic interstitial pneumonias. Am J Respir Crit Care Med 2013; 188: 733.

Leslie KO. My Approach to ILD.... J Clin Pathol 2009; 62:387

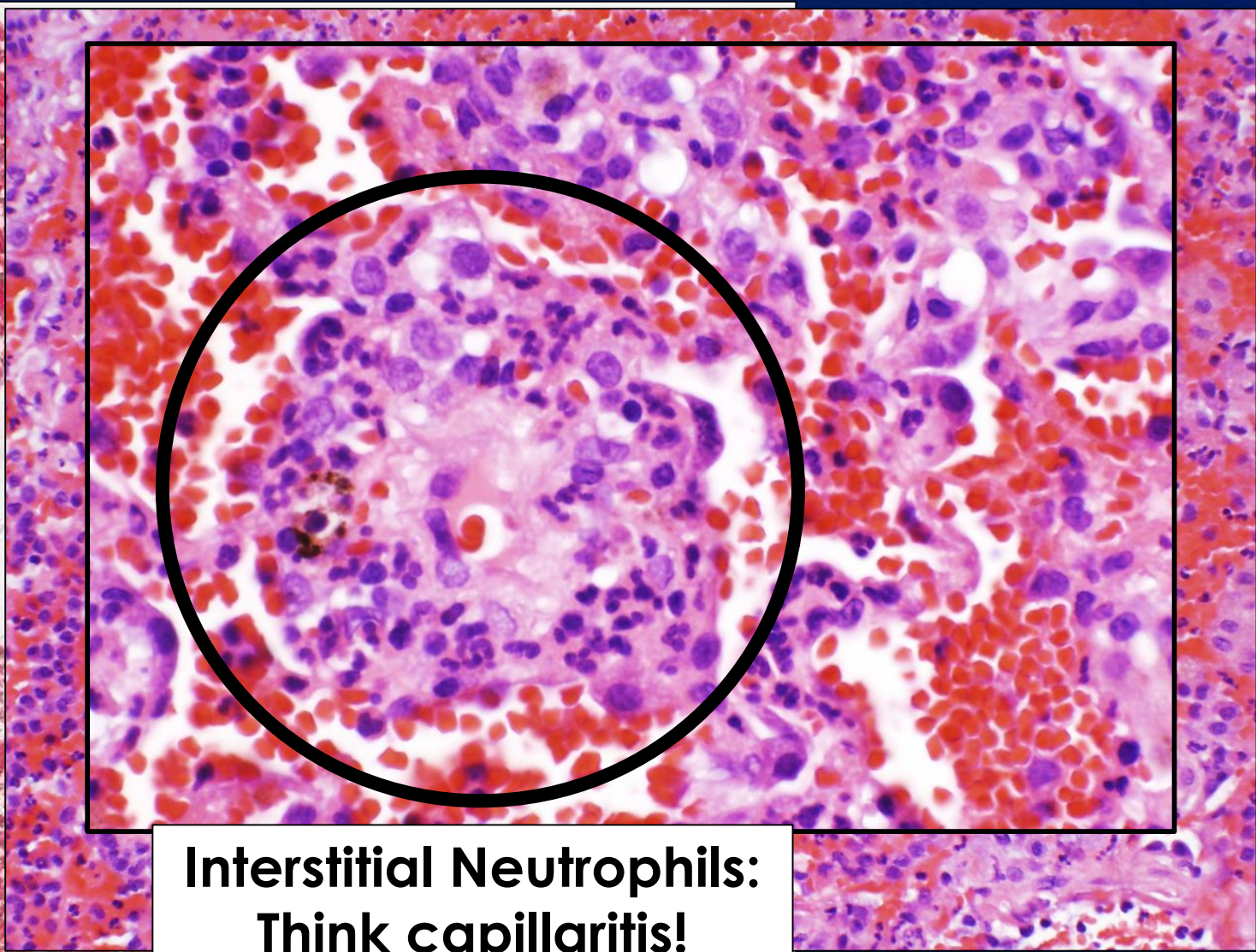
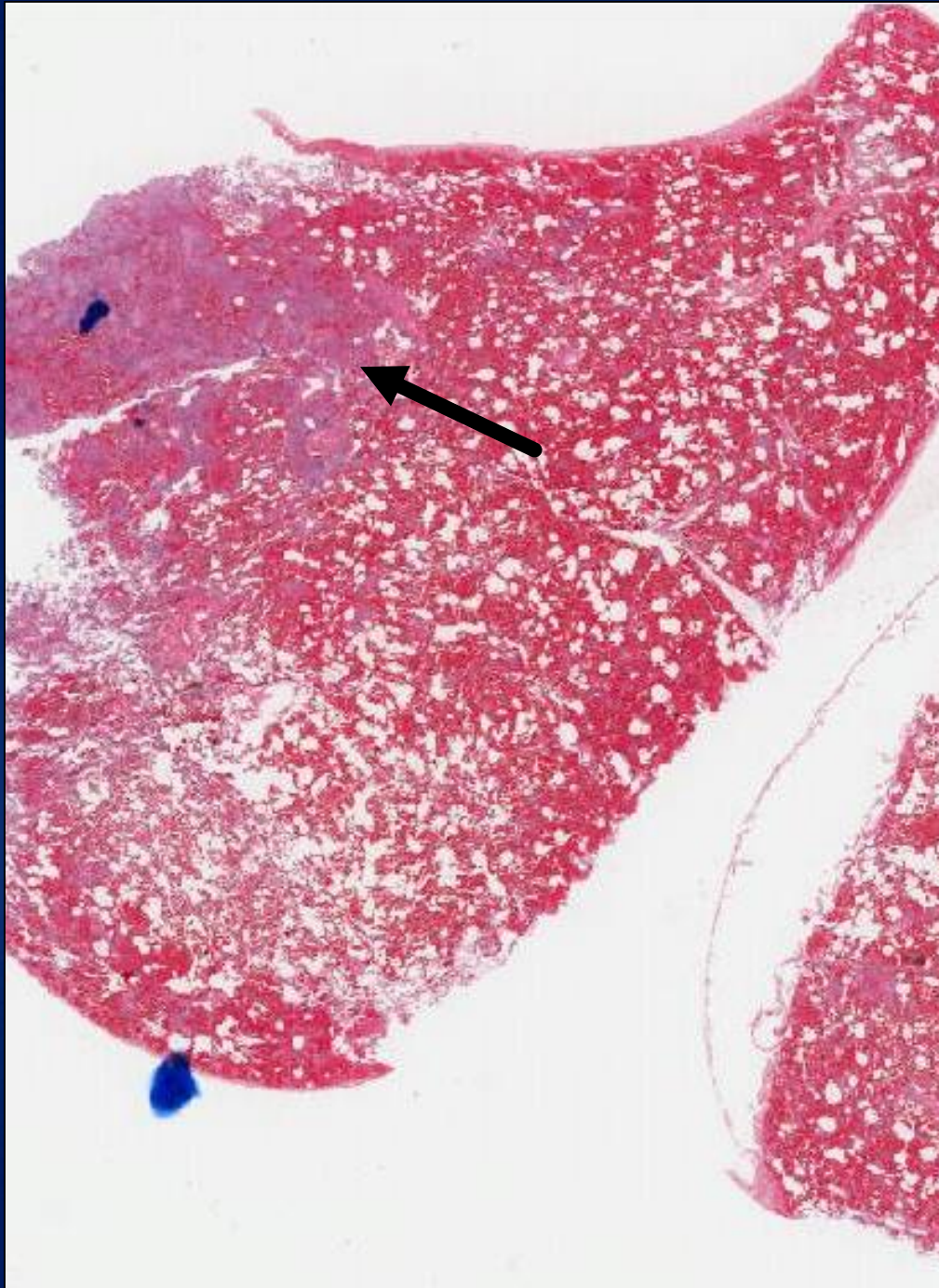


Pathologic diagnosis in non-neoplastic lung disease requires integration of:

1. Information from four domains:
 - a. Clinical /laboratory (?immunosuppressed)
 - b. Radiologic findings (and Dx/Dx)
 - c. Pathologic injury pattern(s) identified
 - d. Individual disease entity that fits
2. Knowledge of the clinical question

“What question(s) am I answering with this Bx?”





**Interstitial Neutrophils:
Think capillaritis!**

CASE ANALYSIS

Four domains

Clinical/Lab presentation

Radiologic findings

Pathologic injury pattern(s)

Disease entity that fits

Acute SOB, hemoptysis,
anemia, +PR3 ANCA

Patchy airspace
disease

Alveolar hemorrhage
with capillaritis

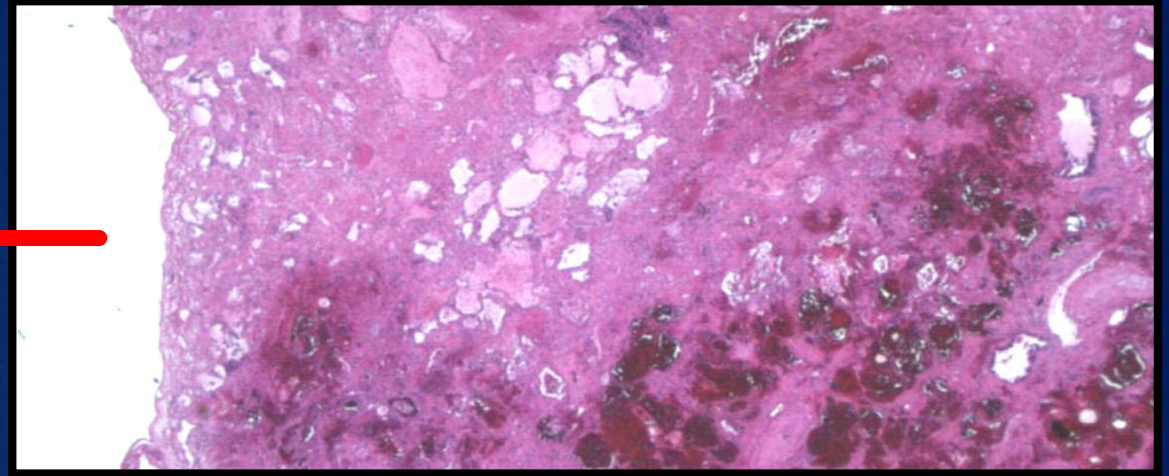
**c/w Granulomatosis
with Polyangiitis (WG)**



LungPath
Consultants

Blood in the lung: Most common cause is trauma of the biopsy procedure:

If in doubt get the history!



Alveolar hemorrhage syndrome/Diffuse alveolar hemorrhage: Pulmonary hemorrhage not due to trauma, airway disease, tumors, or heart failure

Form of severe acute lung injury with bleeding

DIFFUSE ALVEOLAR HEMORRHAGE (DAH)

ANCA-associated: WG, MPA, pulmonary renal syndromes, isolated alveolar hemorrhage

Antibaseophilic Vasculitis- esp GPA/WG

syndromes Collagen Vascular diseases

Immune-mediated Anti-GBM disease

IgA disease Idiopathic Pulmonary Hemosiderosis (IPH)

hemorrhage Miscellaneous (eg. drug)

Immune-mediated mechanism not determined. Imm, isolated alveolar hemorrhage



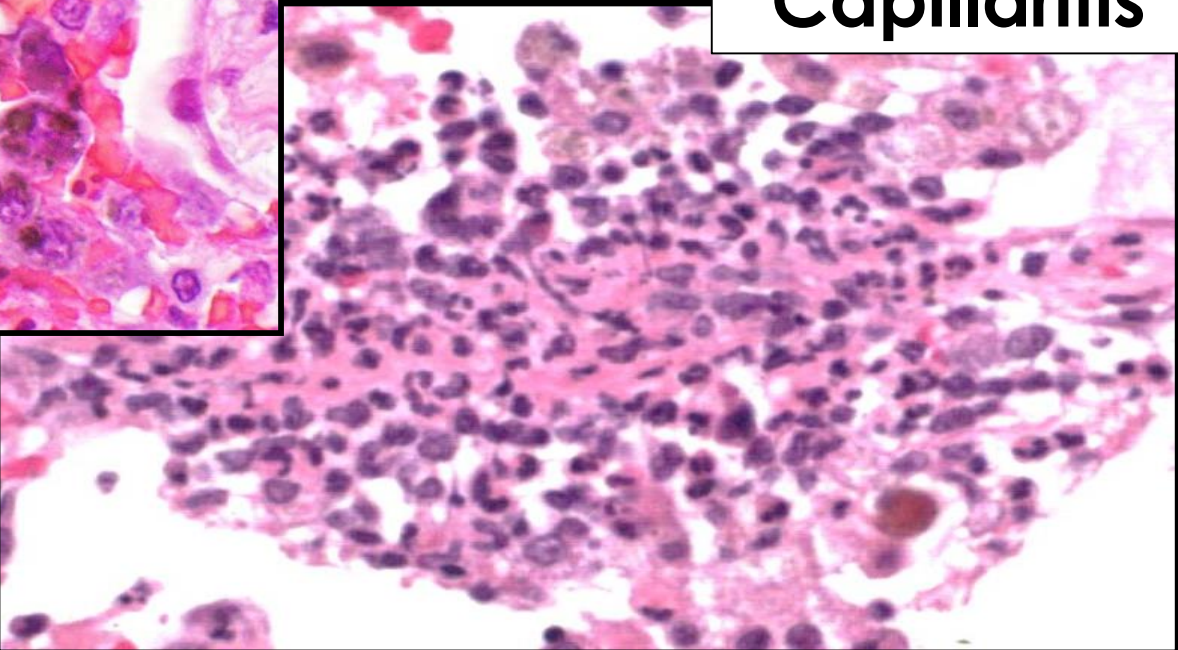
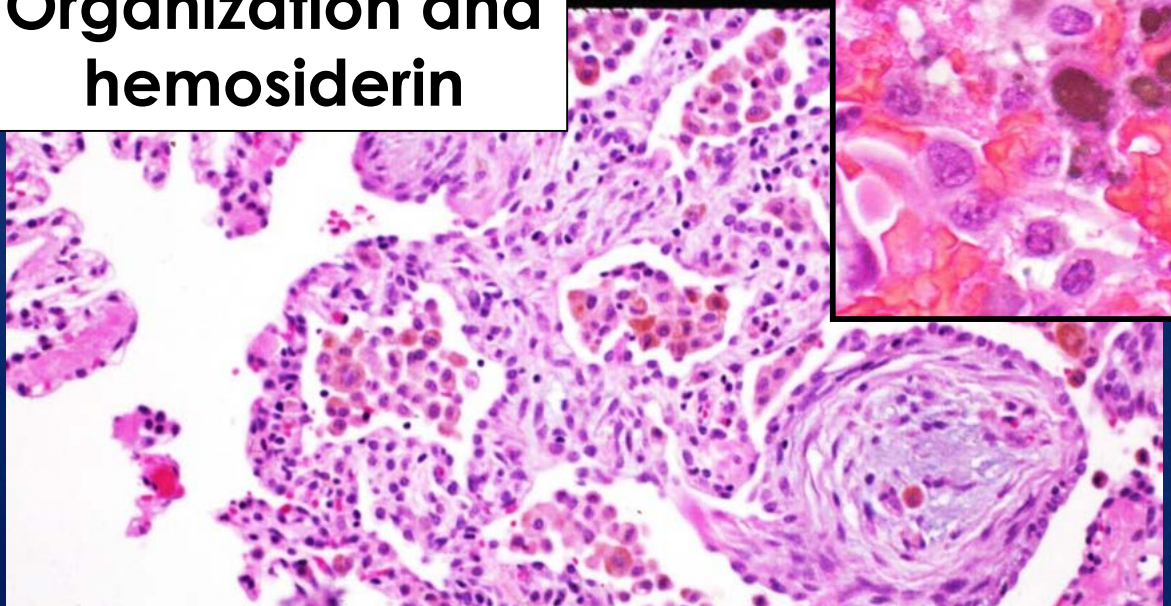
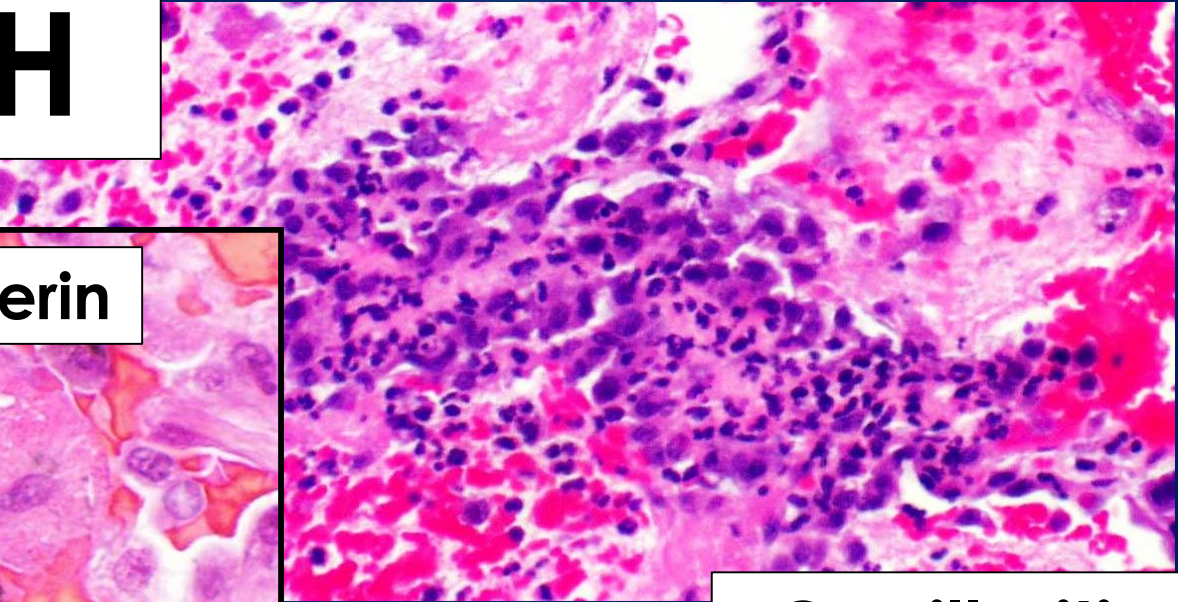
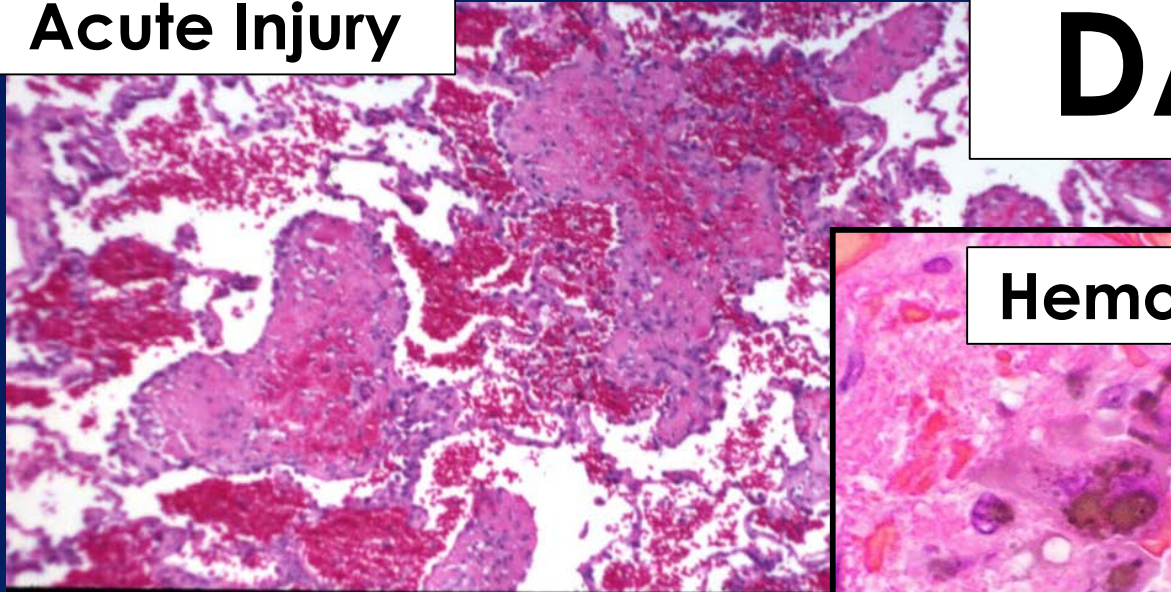
Acute Injury

DAH

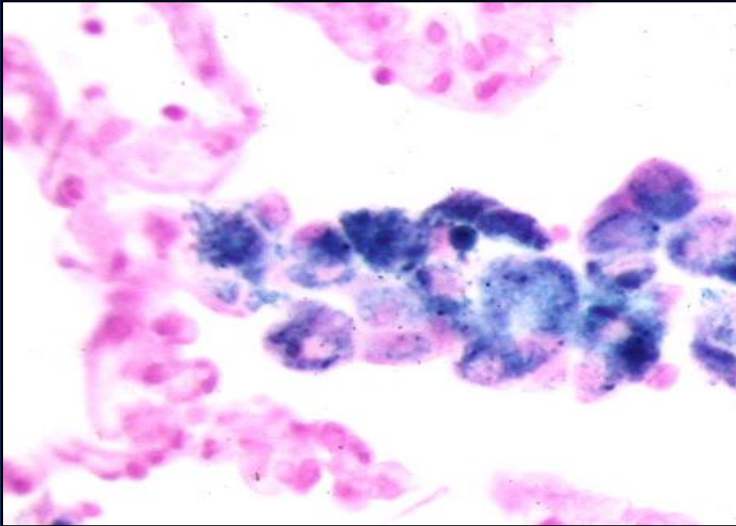
Hemosiderin

Capillaritis

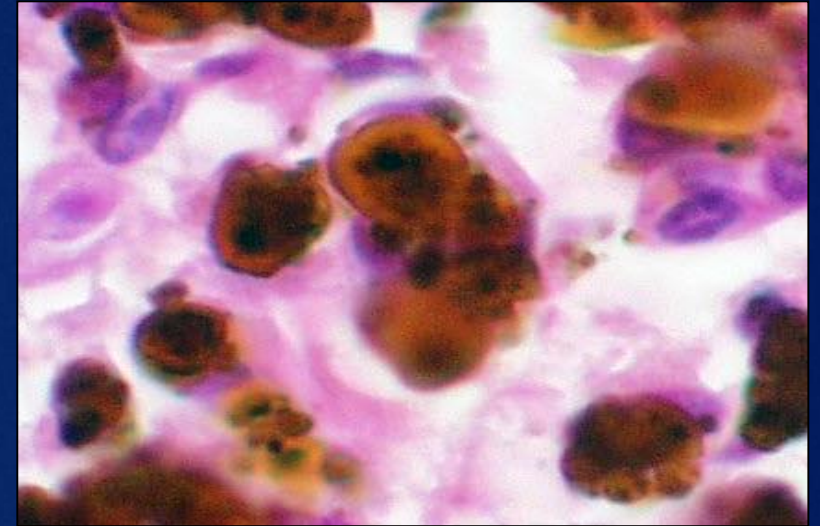
**Organization and
hemosiderin**



Lung Hemosiderin not due to DAH



← Smoking

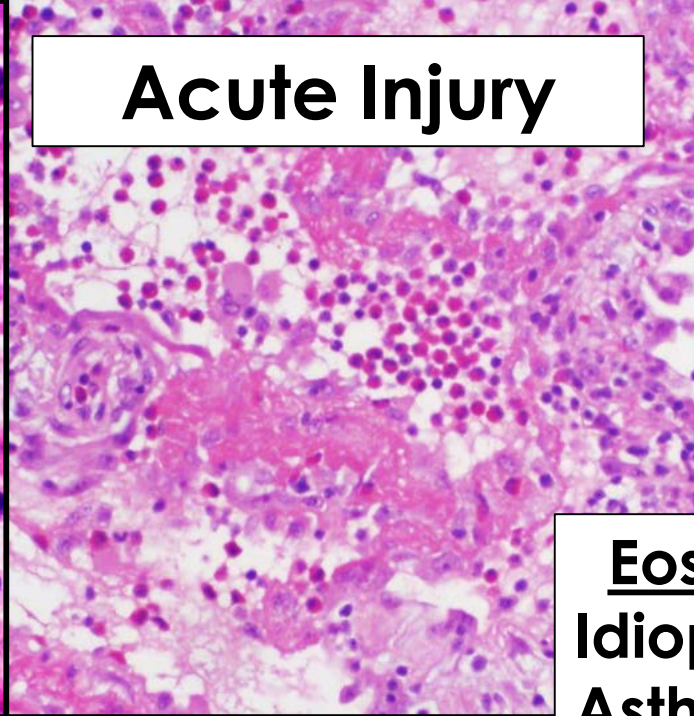
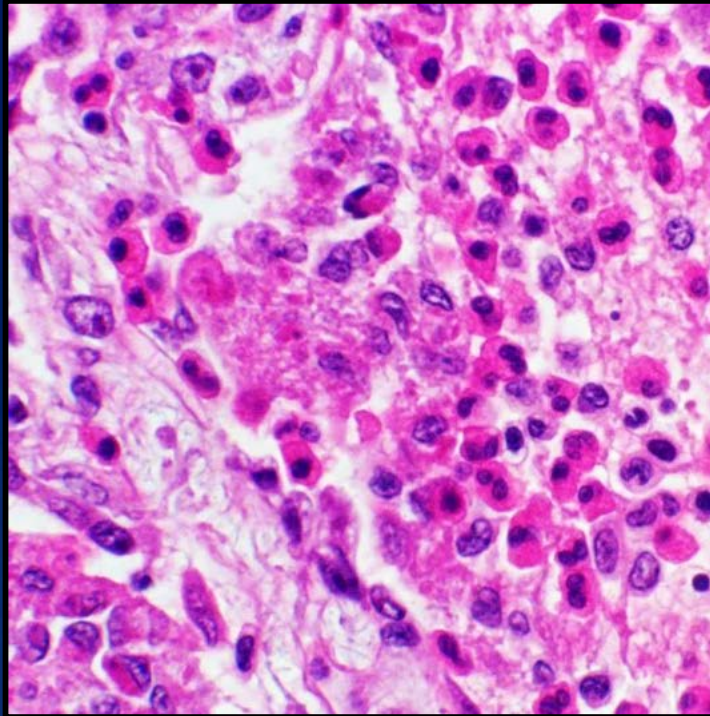


Cardiac disease ↗

Occupational Exposure (eg welder)

Long miscellaneous list

Eosinophils in diffuse lung disease



Eosinophilic Pneumonia:
Idiopathic (Ac and Chr), Drug, Smoking,
Asthma-related, Infex-related, et.al.

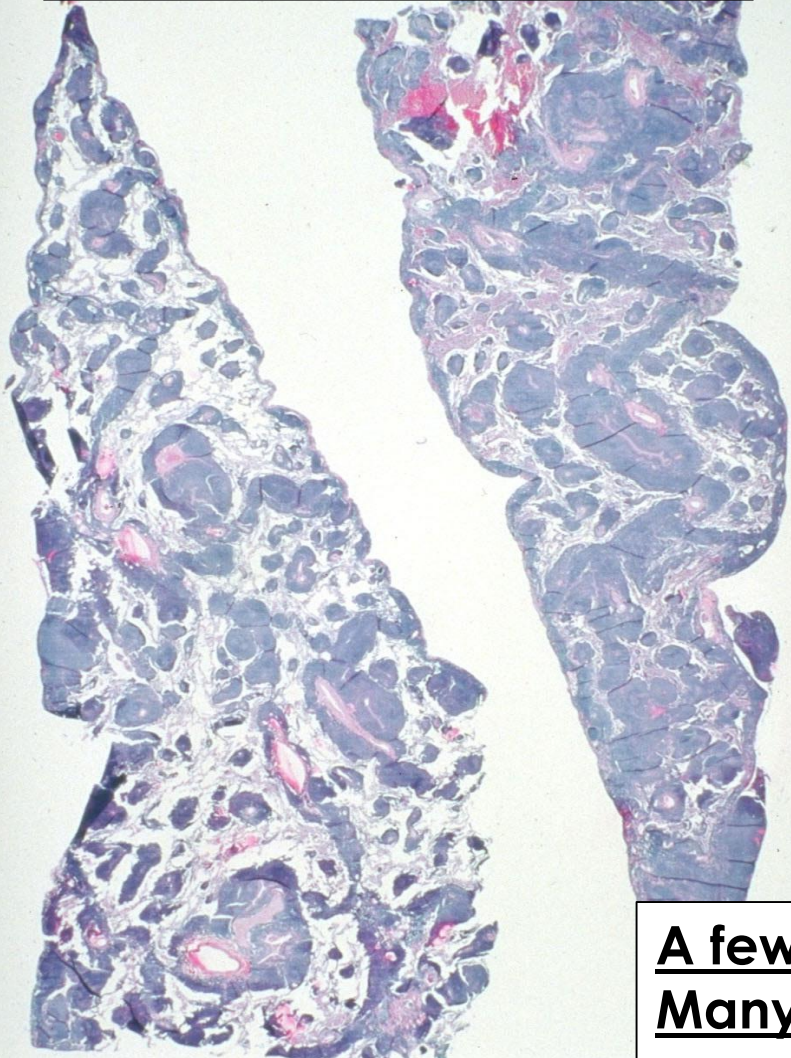
How many? **>10-15 in a hpf**

Greatly narrow the differential diagnosis

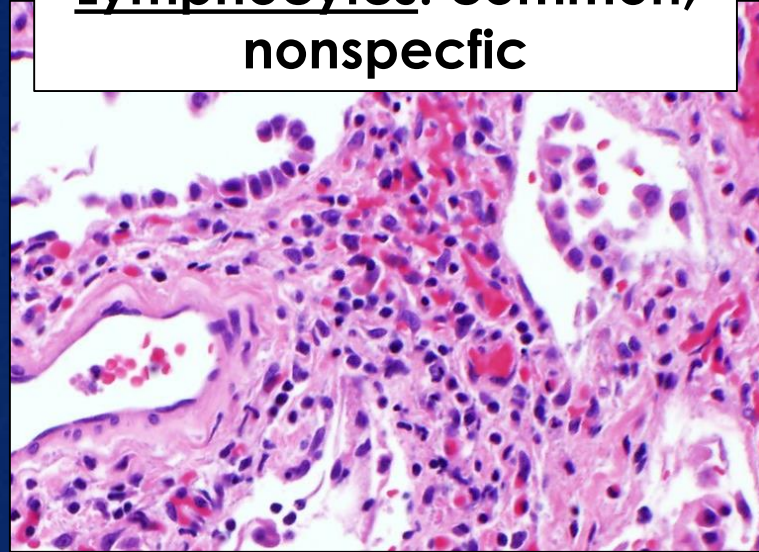


Lymphoid Cells in Diffuse Lung Disease

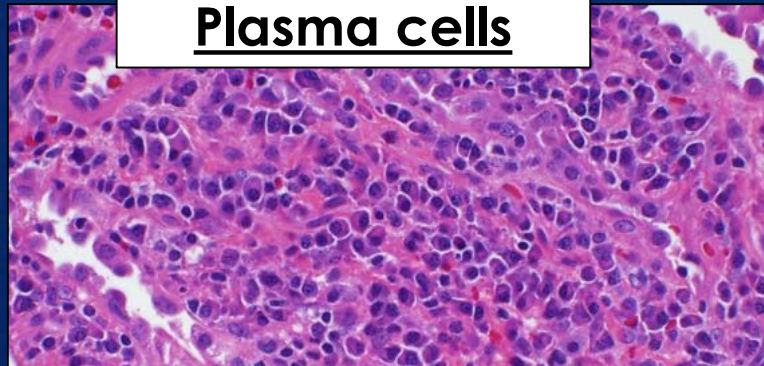
Lymphoproliferative



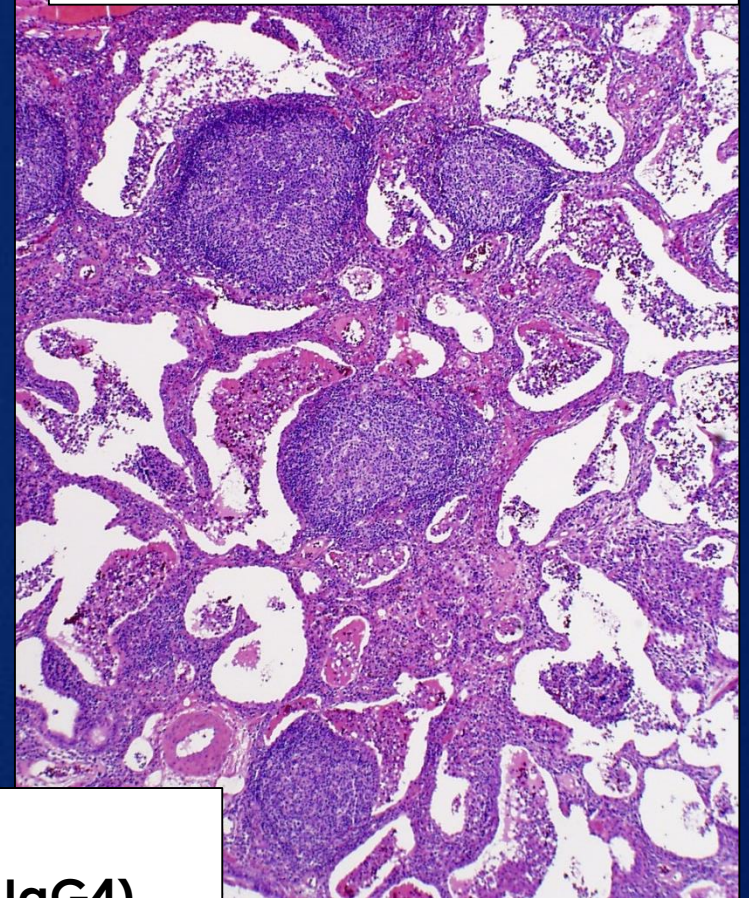
Lymphocytes: common, nonspecific



Plasma cells



Lymphoid Hyperplasia: CVD, Immunodeficiency, Chronic infection

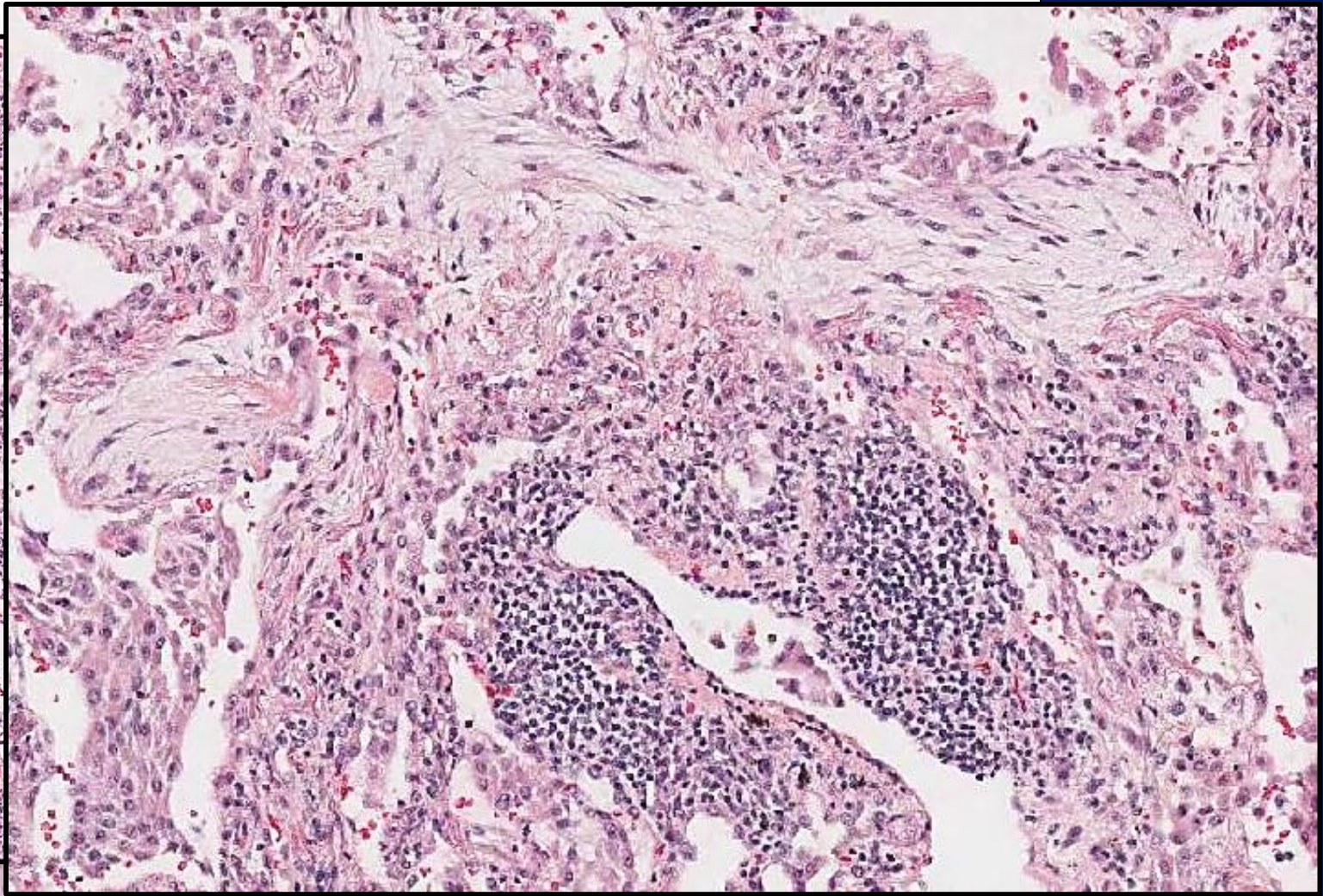
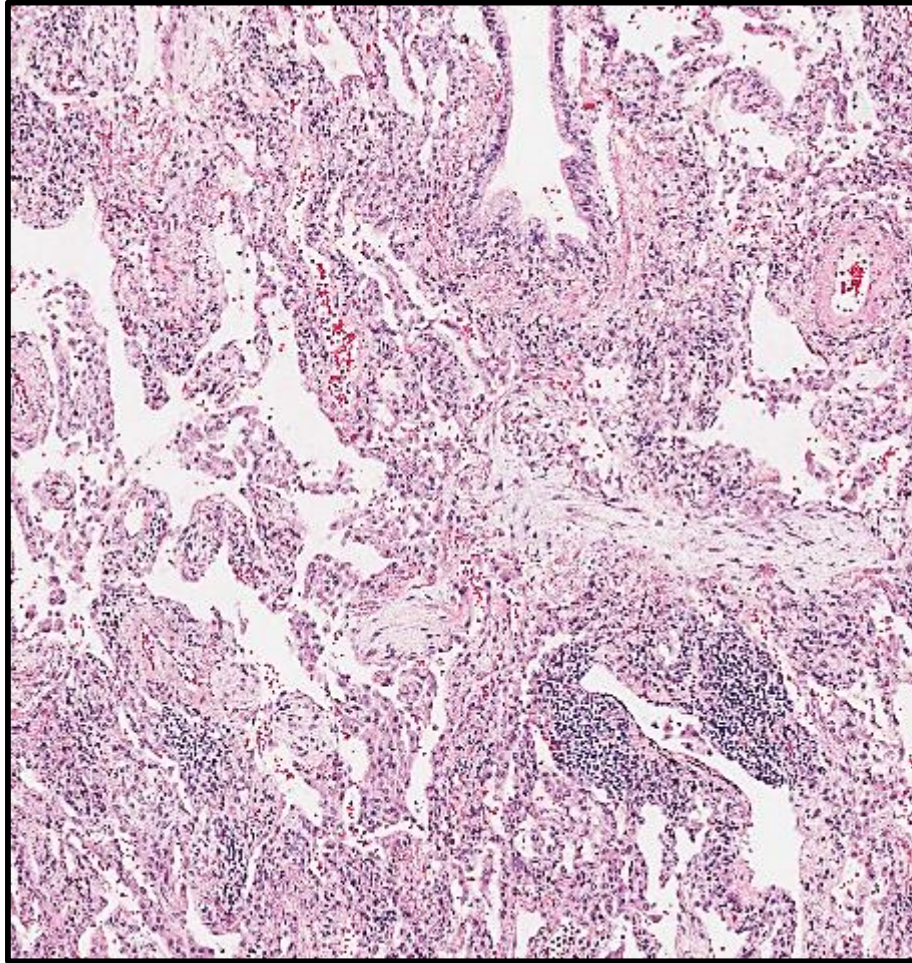


A few: common/nonspecific

Many: Immunologic dis (CVD, drug, HP, IgG4), Ig disorders, Lymphoproliferative dis

Commentary.....





OP D/D: Bugs, drugs, CVD, Idiopathic, many others

Patterns of lung “fibrosis”

Major: Organizing pneumonia (OP) and UIP

Additional:

“Diffuse” fibrosis as in fibrotic NSIP

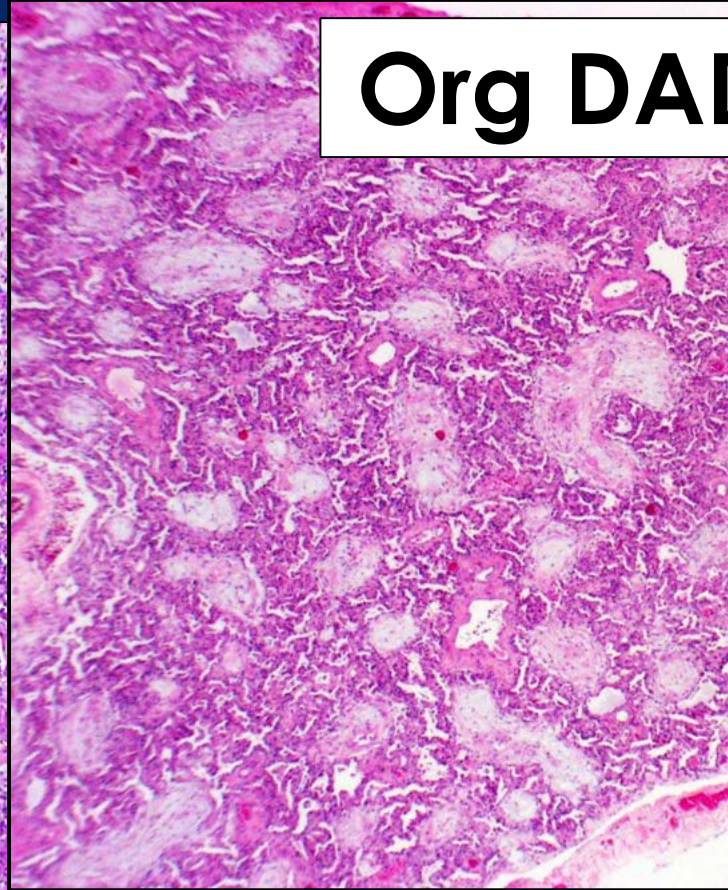
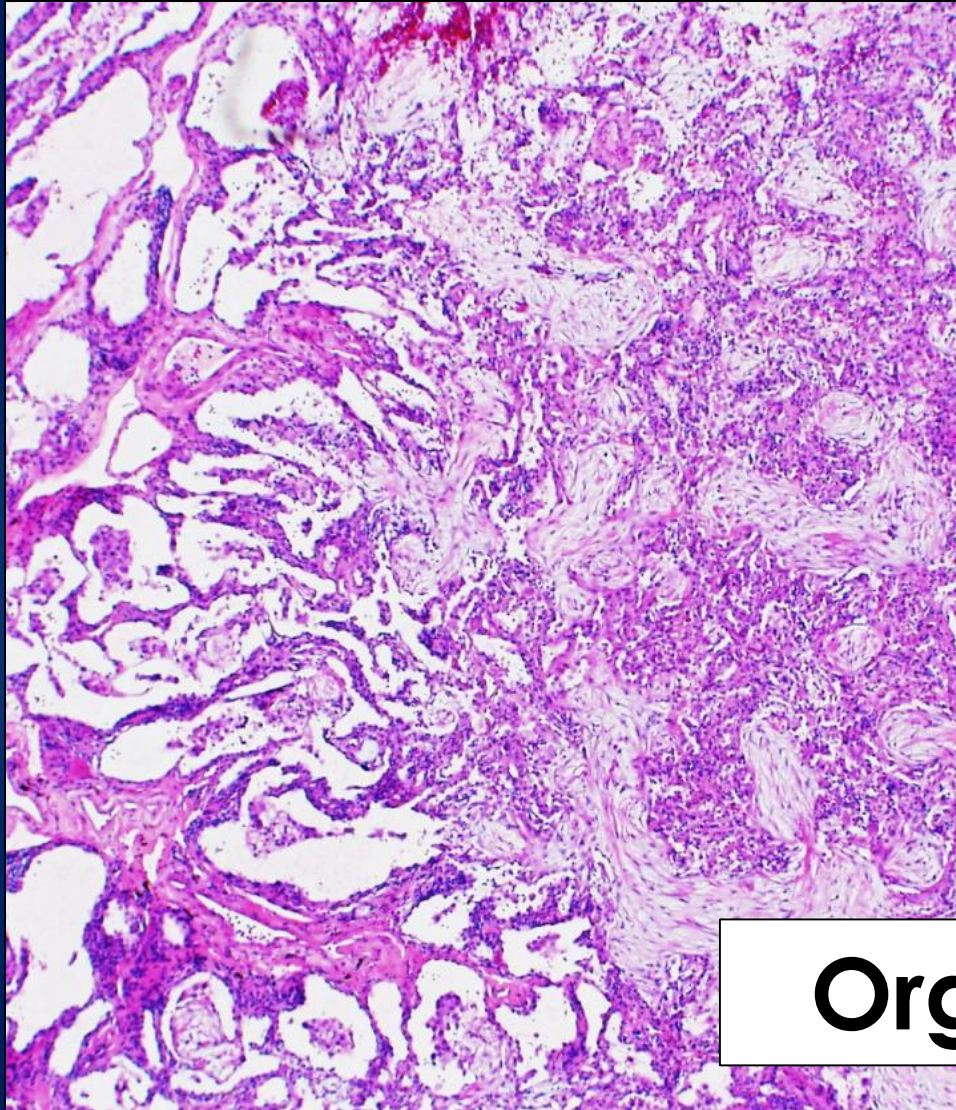
Centrilobular

Smoking-related

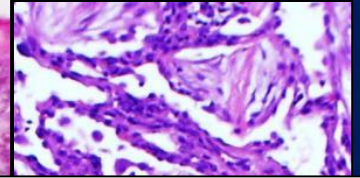
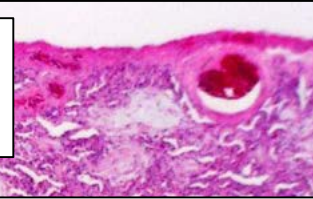
Elastotic



Types of Lung Fibrosis



Org DAD



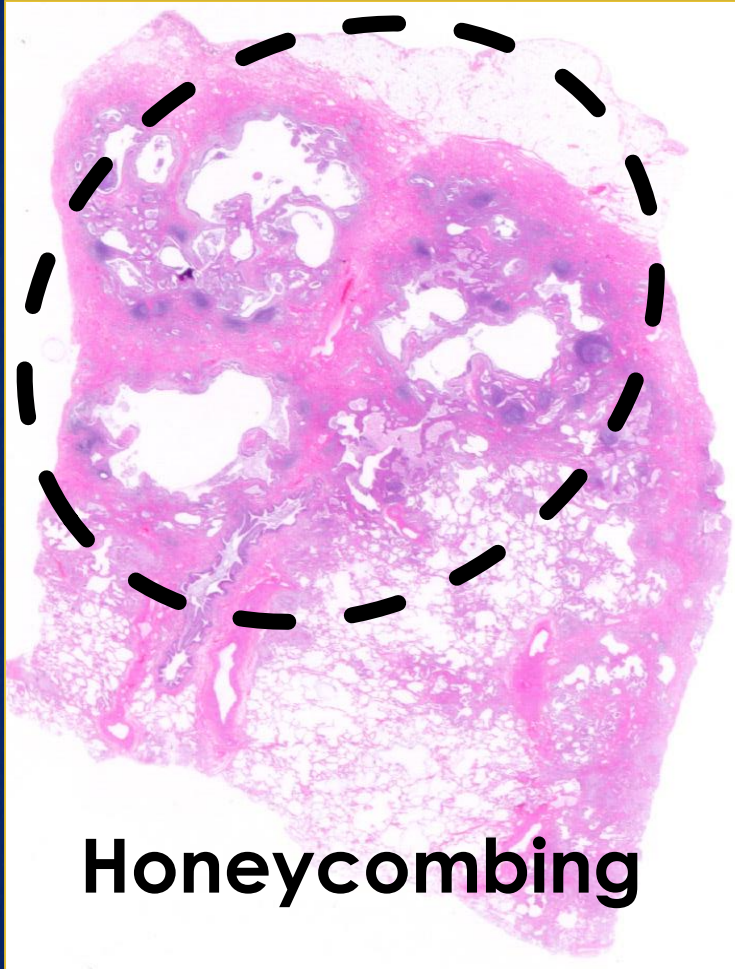
Seen in:

Infection
Drug reaction
CVD
Idiopathic
As a local reaction
Many misc

Organizing pneumonia/OP

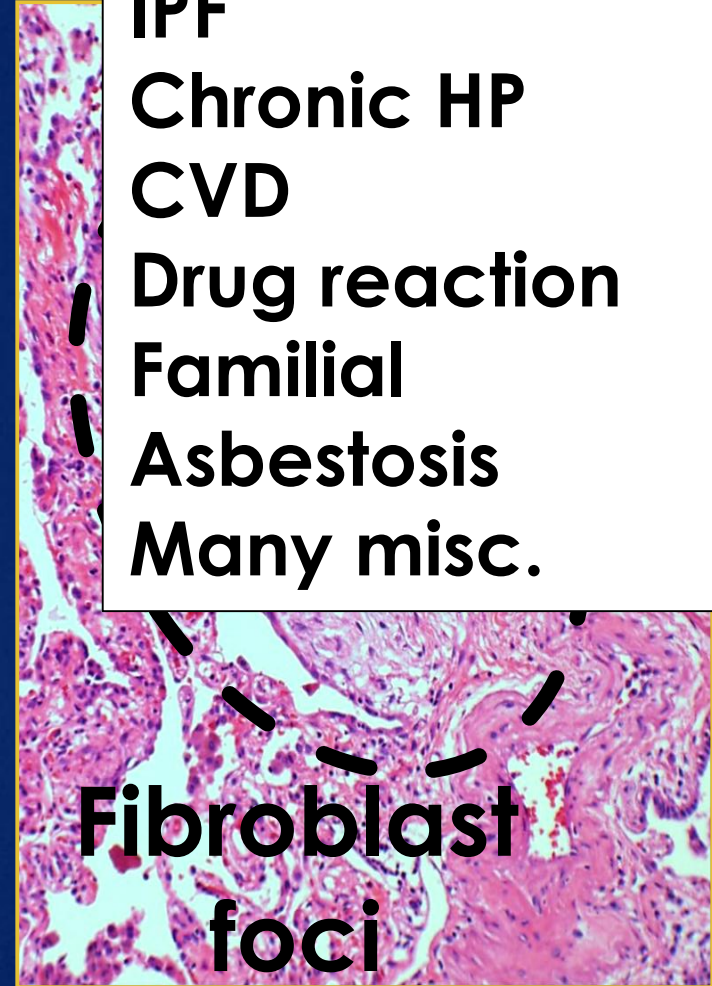
Types of Lung Fibrosis

UIP Fibrosis



Seen in:

IPF
Chronic HP
CVD
Drug reaction
Familial
Asbestosis
Many misc.



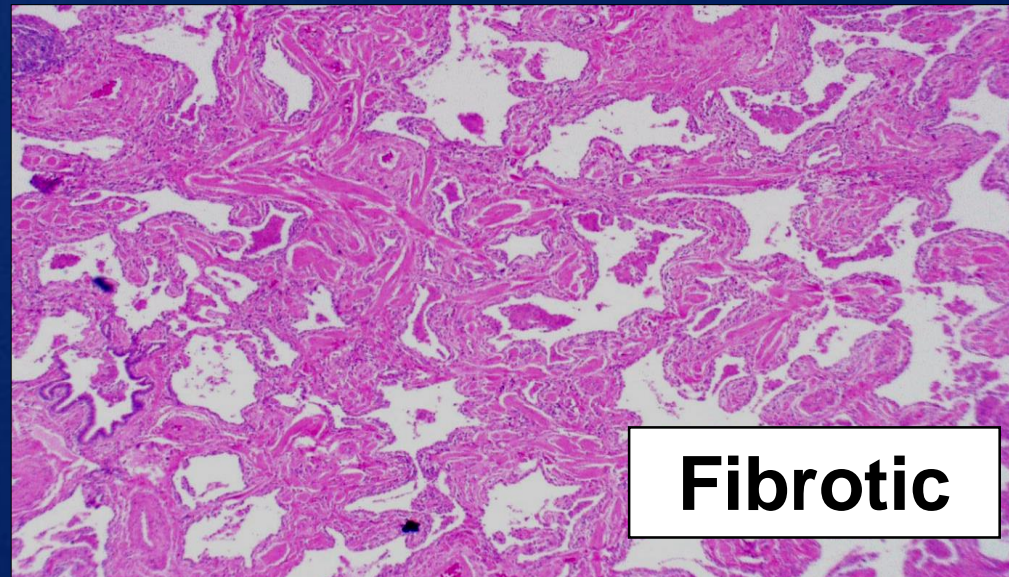
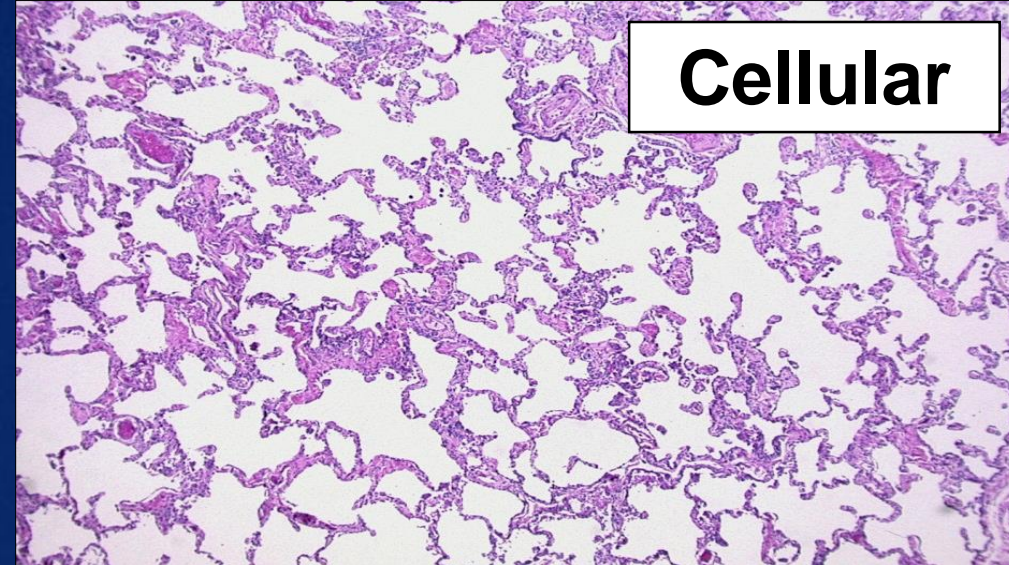
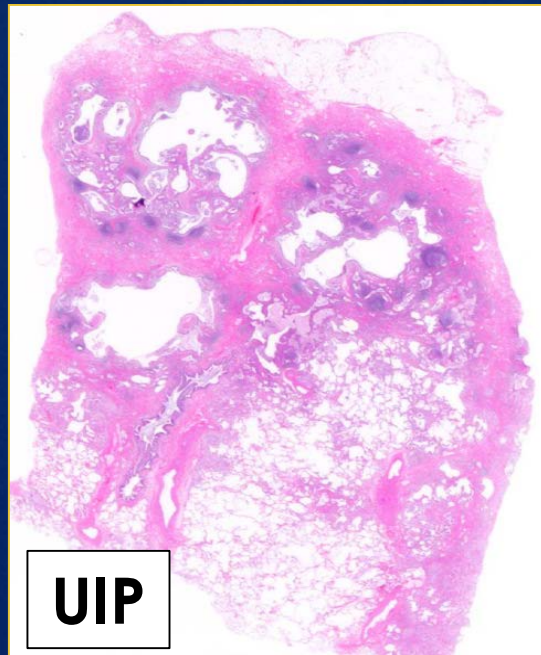
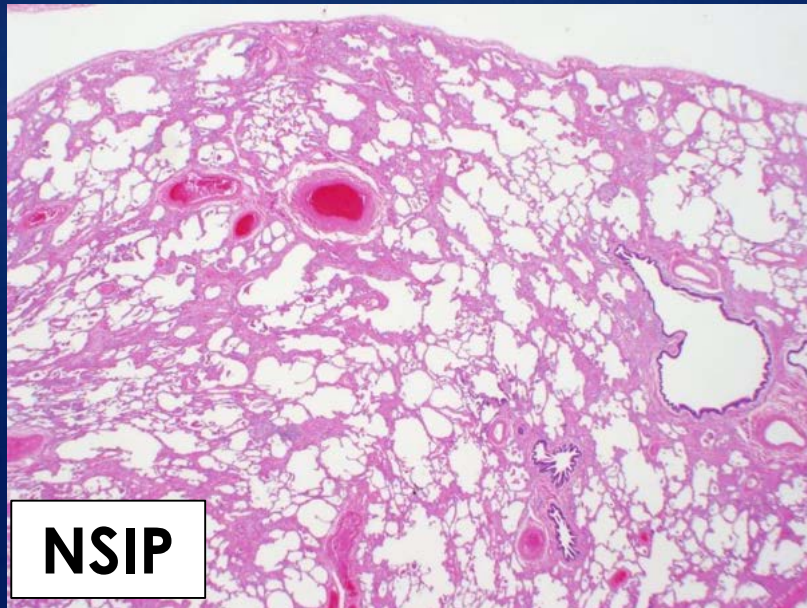
Nonspecific Interstitial Pneumonia (NSIP)

Key features:

Temporally homogeneous

Uniform involvement of tissue

Spectrum from cellular to fibrotic



Types of Lung Fibrosis

Fibrotic NSIP

NSIP seen in:

CVD

Drug reaction

(Chr) HP

Idiopathic NSIP

Many misc.

UIP

Types of Lung Fibrosis

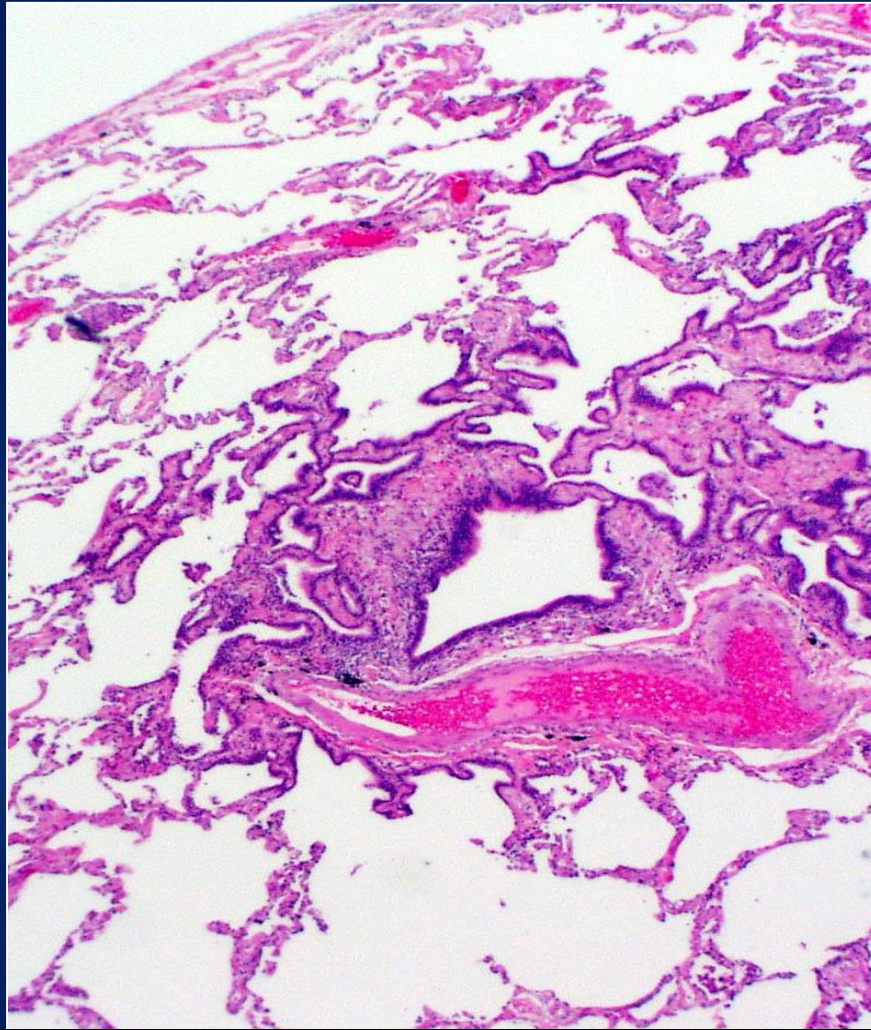
Incidental finding in lobectomy

Clinical ILD

Often subpleural; paucicellular and hyaline-appearing

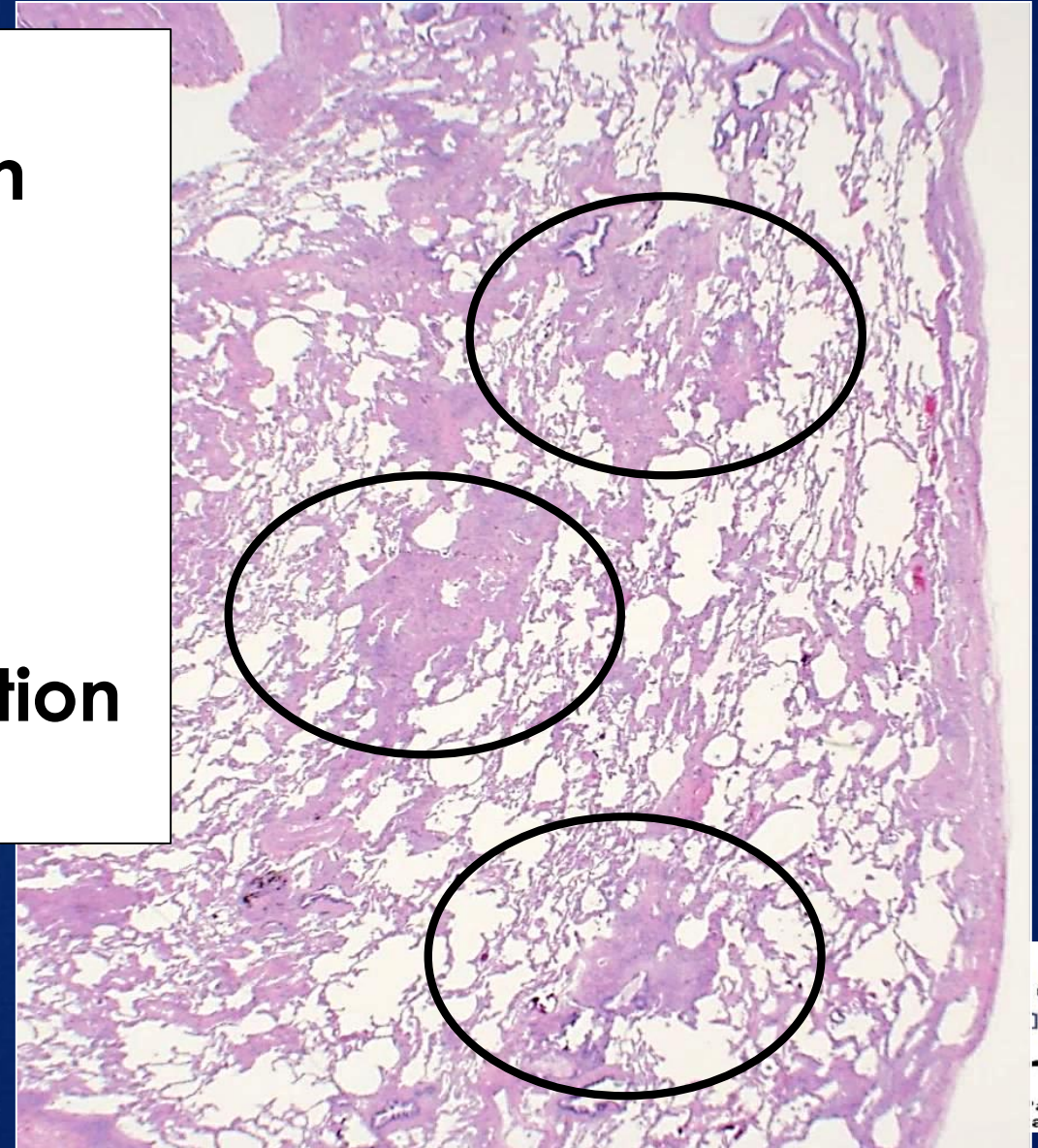
Smoking-related interstitial fibrosis (SRIF)

Types of Lung Fibrosis: Bronchiolocentric



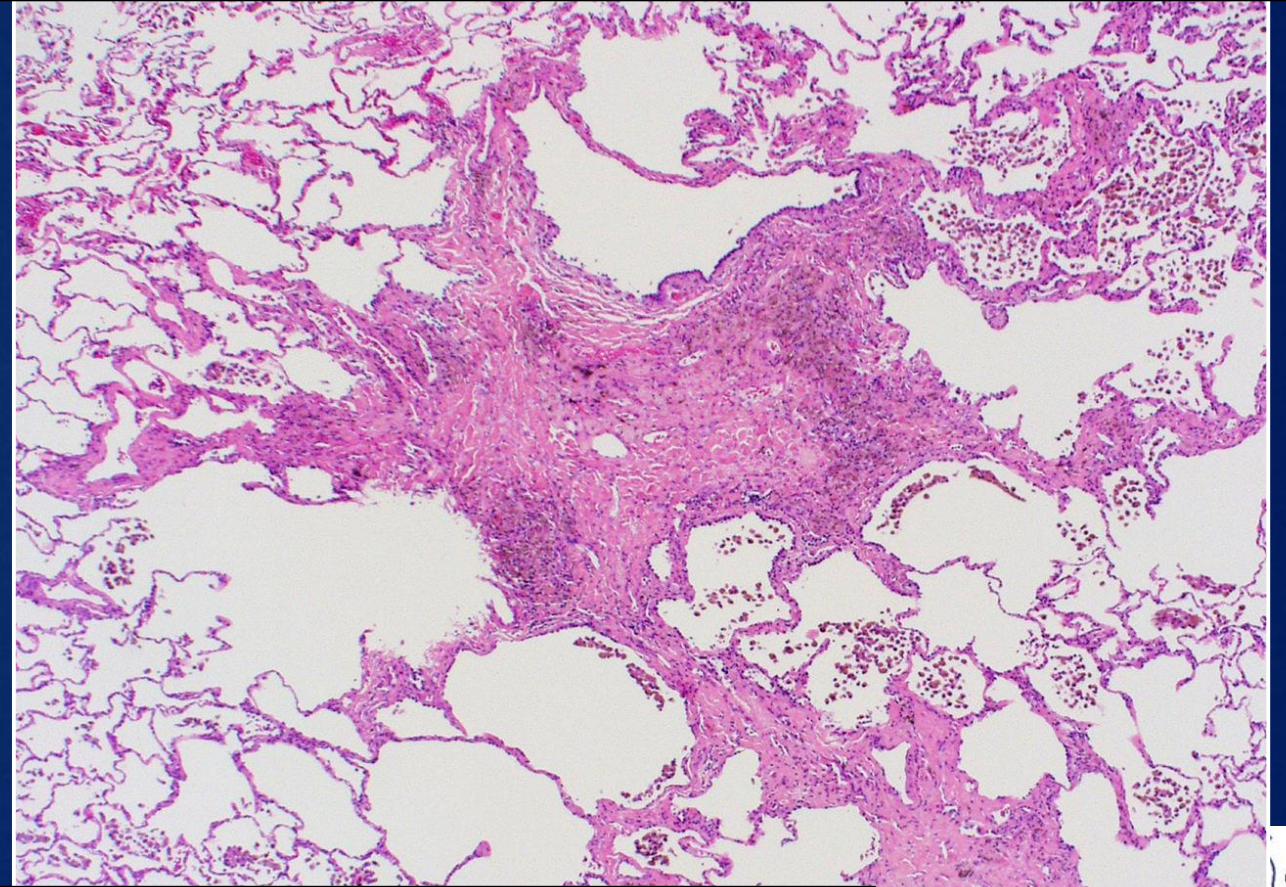
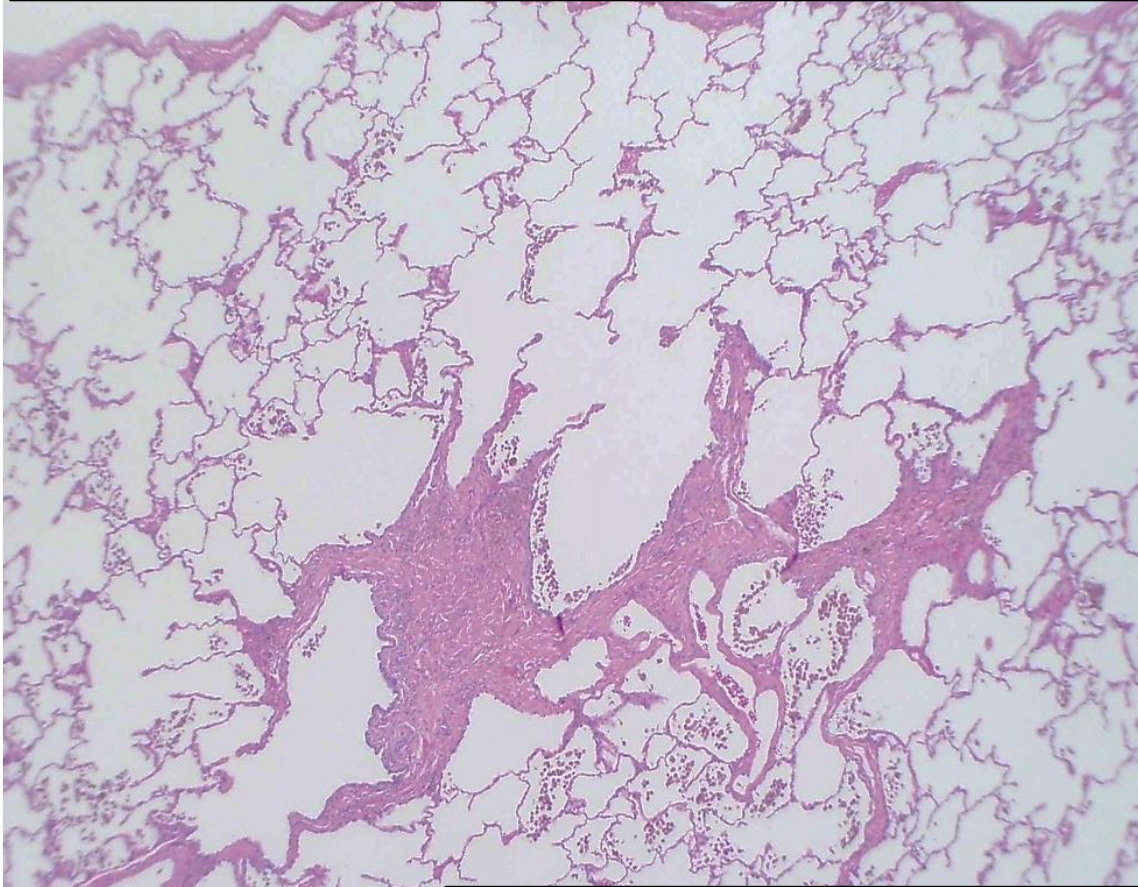
Peribronchiolar Metaplasia/PBM

Seen in:
Post Infection
CVD
PLCH
Chr HP
Aspiration
Idiopathic
A local reaction
Many misc



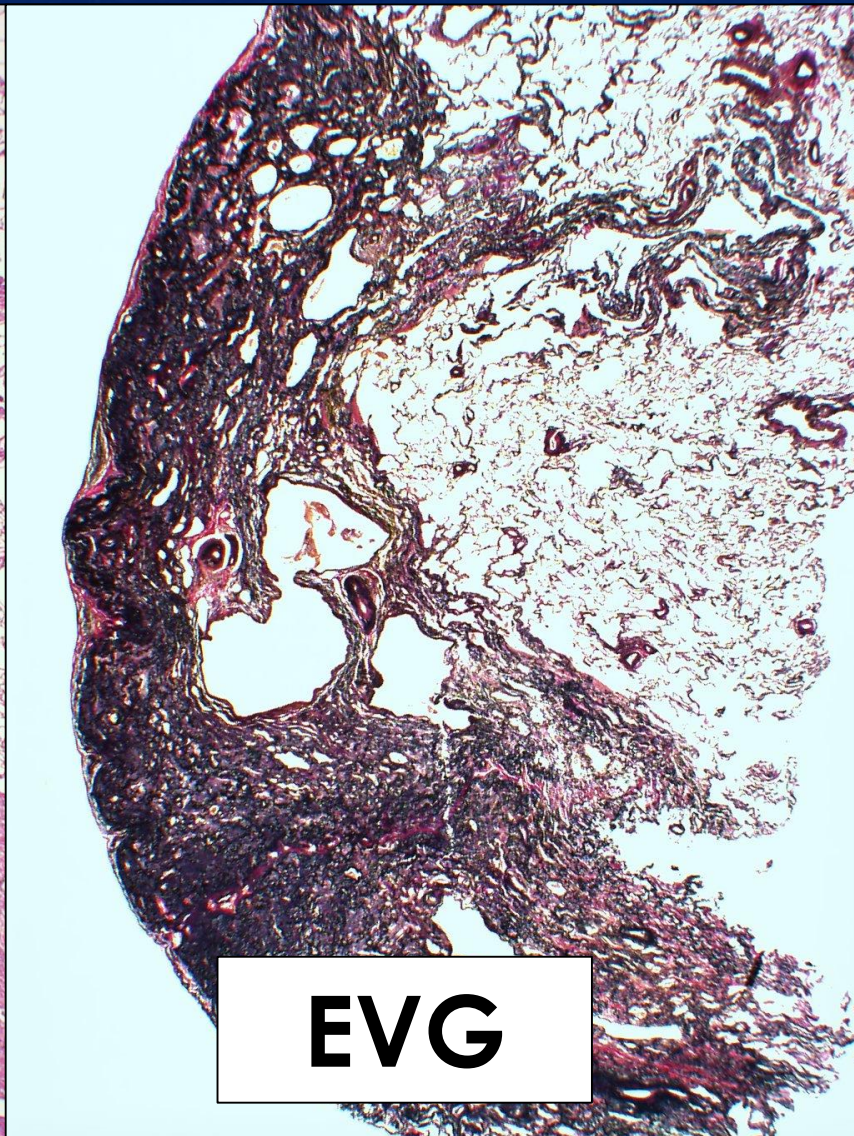
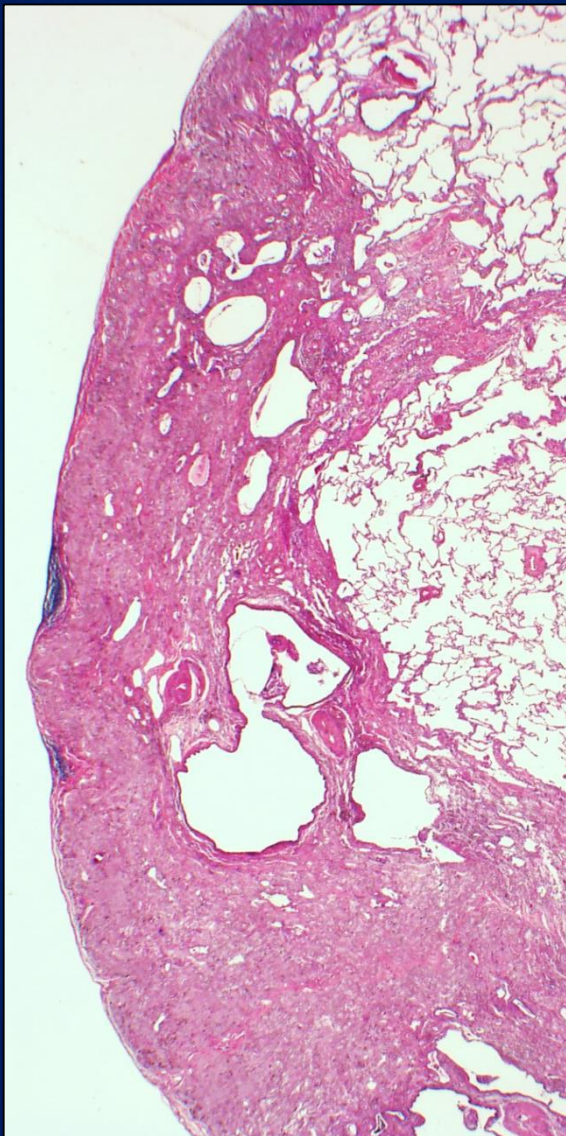
Types of Lung Fibrosis: Bronchiolocentric

Old/healed Pulmonary Langerhans Cell Histiocytosis (PLCH)

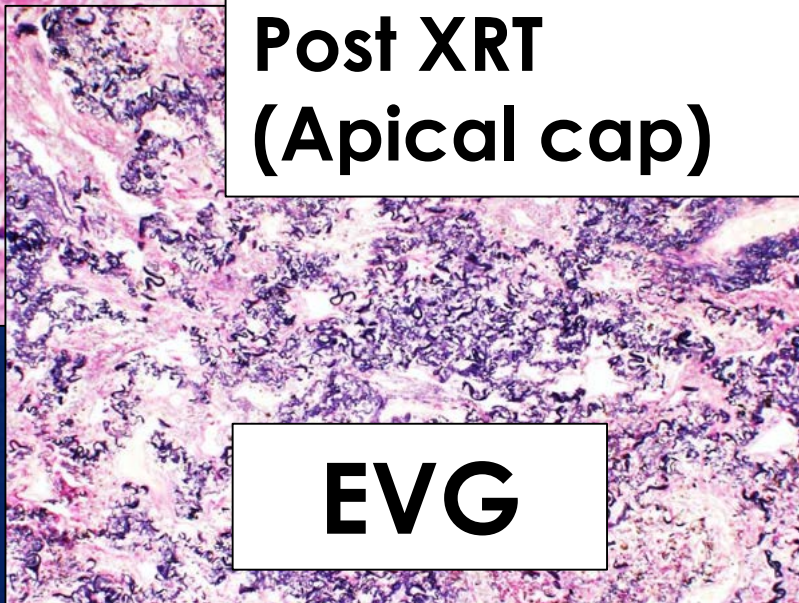
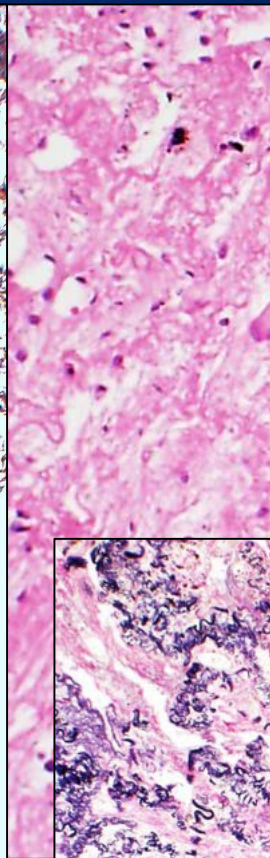


Stellate centrilobular scarring

Types of Lung Fibrosis: Elastotic



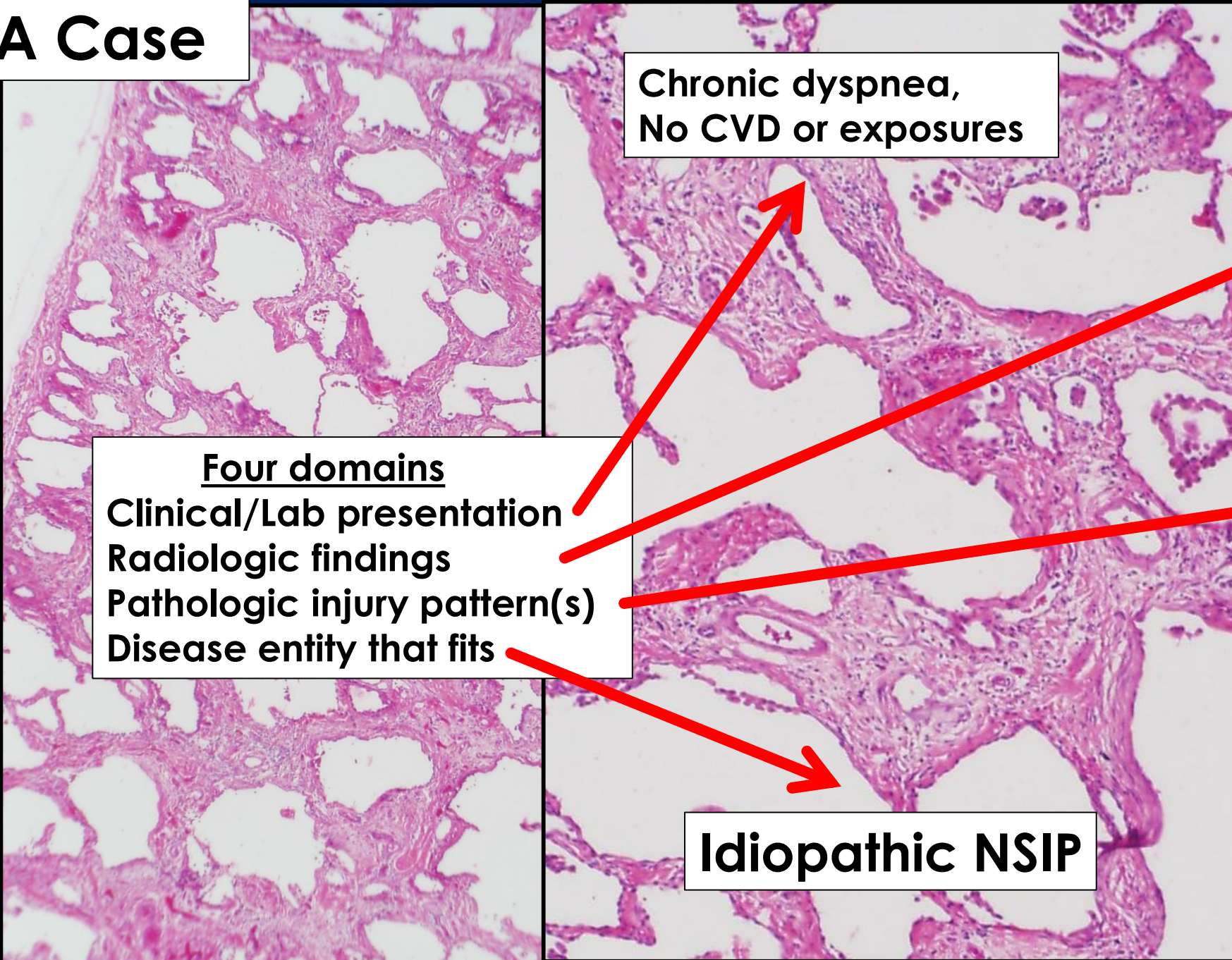
EVG



EVG

Seen in:
Idiopathic PPFE
Post Lung/BM Tx
Drug reaction
CVD
Ancient scars
Post XRT
(Apical cap)

A Case



Chronic dyspnea,
No CVD or exposures

HRCT: Not UIP, c/w NSIP



Fibrotic NSIP
No granulomas
Not centrilobular

NSIP Pattern: Causes
CVD, Drug, HP,
Idiopathic, Misc.

Four domains
Clinical/Lab presentation
Radiologic findings
Pathologic injury pattern(s)
Disease entity that fits

Idiopathic NSIP



Another Case

Four domains

Clinical/Lab presentation

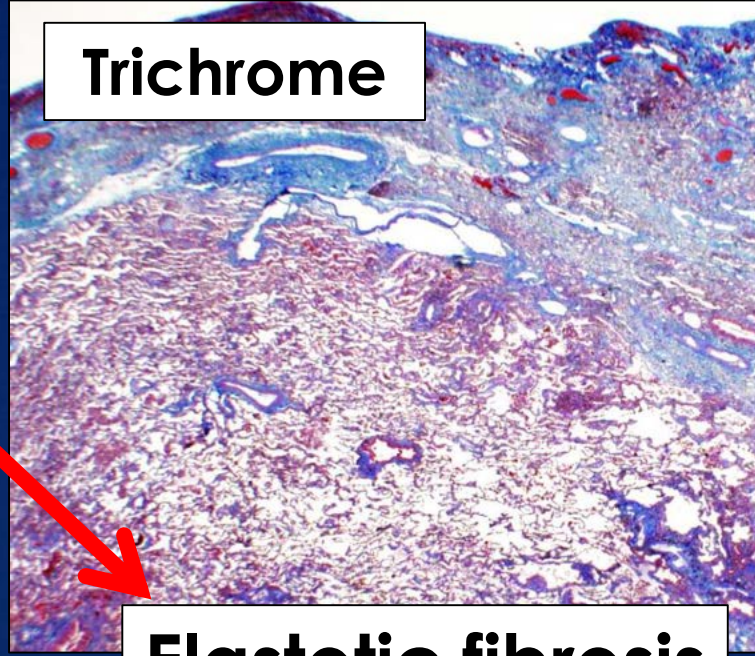
Radiologic findings

Pathologic injury pattern(s)

Disease entity that fits

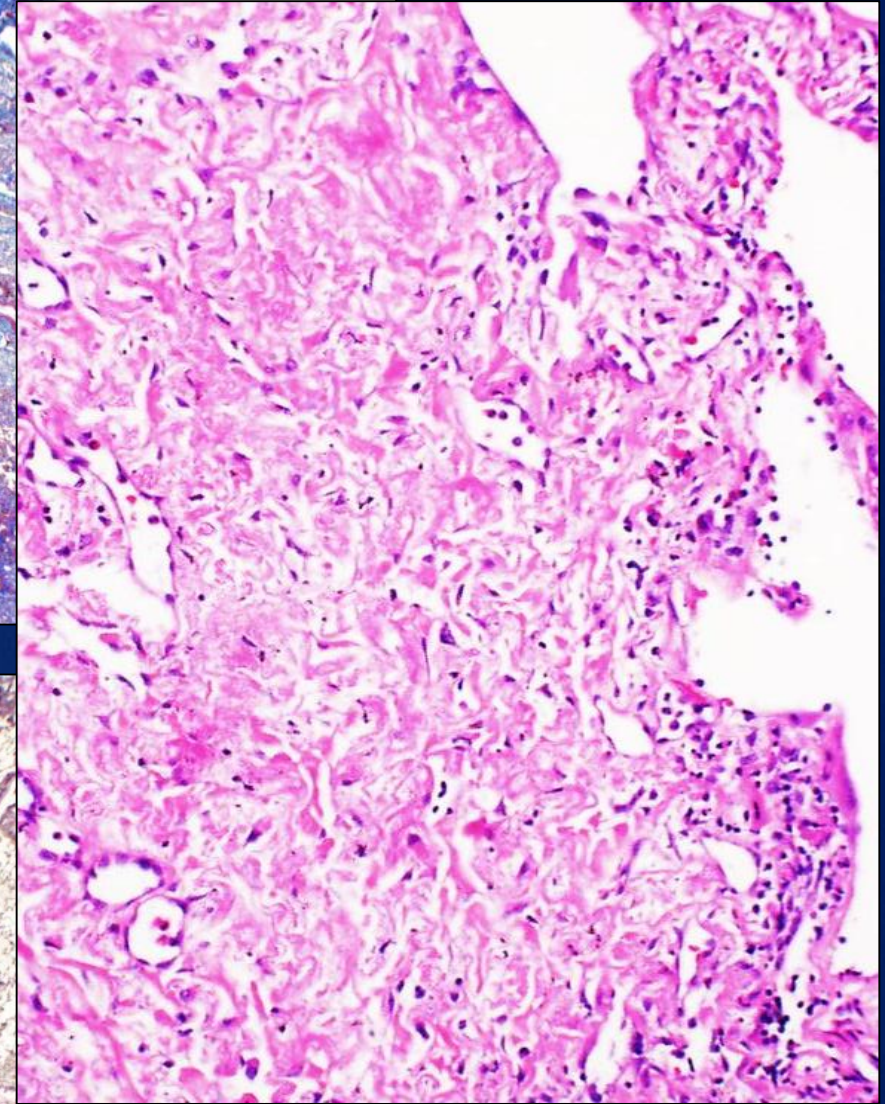
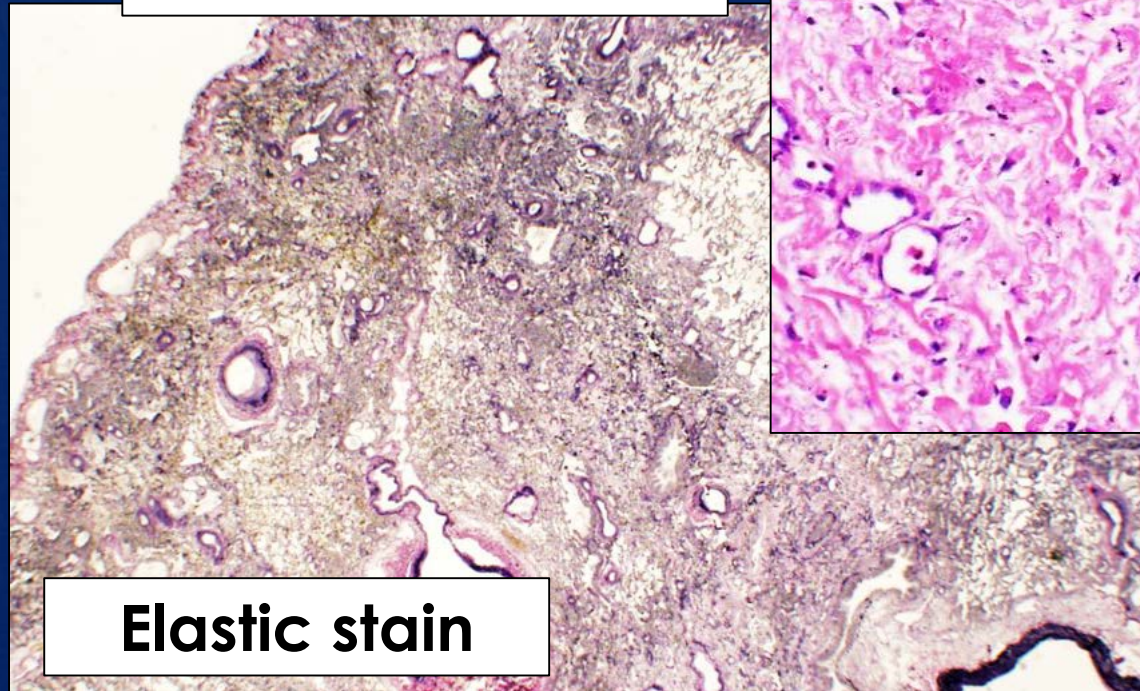


Trichrome



Elastotic fibrosis

Elastic stain



Four domains

Clinical/Lab presentation

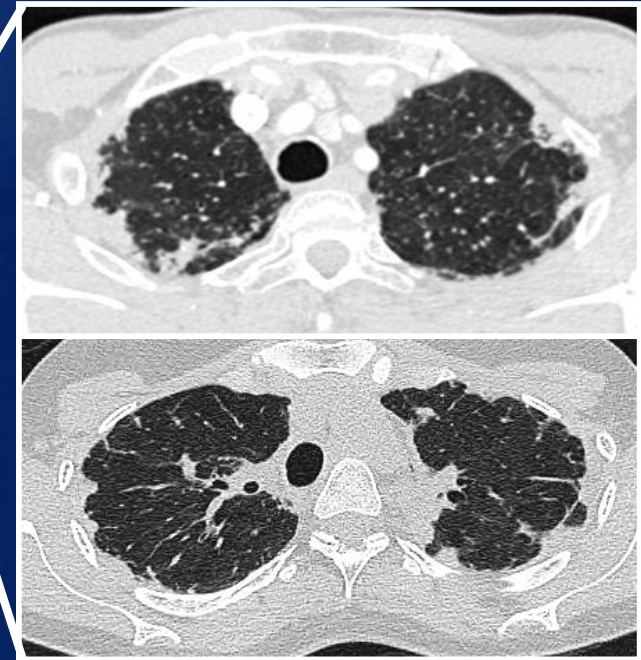
Radiologic findings

Pathologic injury pattern(s)

Disease entity that fits

Bilateral ILD, Chr. dyspnea

HRCT: Upper lobe subpleural infiltrates; Not an apical cap



Elastotic fibrosis

ILD with Elastotic Fibrosis Causes:

Idiopathic Pleuroparenchymal fibroelastosis (PPFE)

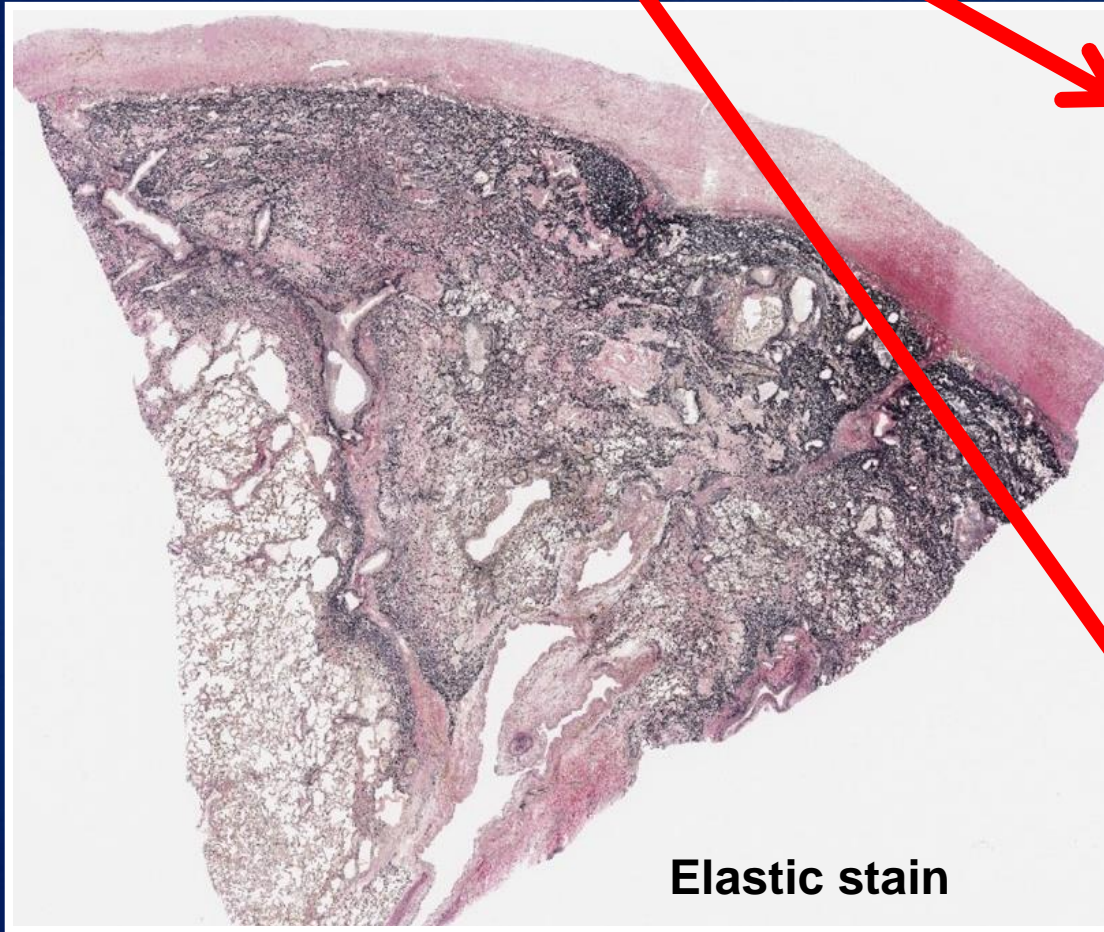
S/P Lung/BM Transplantation

Drug reaction

CVD

Idiopathic PPFE

F>M 6th decade



Elastic stain

How do clinicians view “pulmonary fibrosis”?

Clinicians are now lumping cases into:

*Progressive fibrosing ILD's**

Regardless of cause.....

.....For treatment purposes

As pathologists we should be continue to be
“splitters”

* Eur Respir J 2020 June 25; NEJM 2019; 381: 1718; FDA guideline Mar 9, 2020



Commentary.....



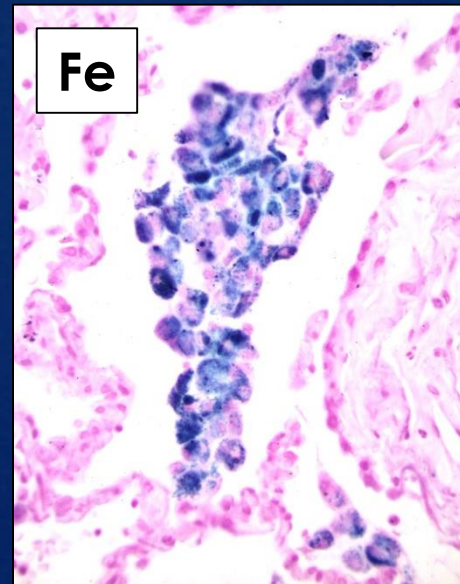
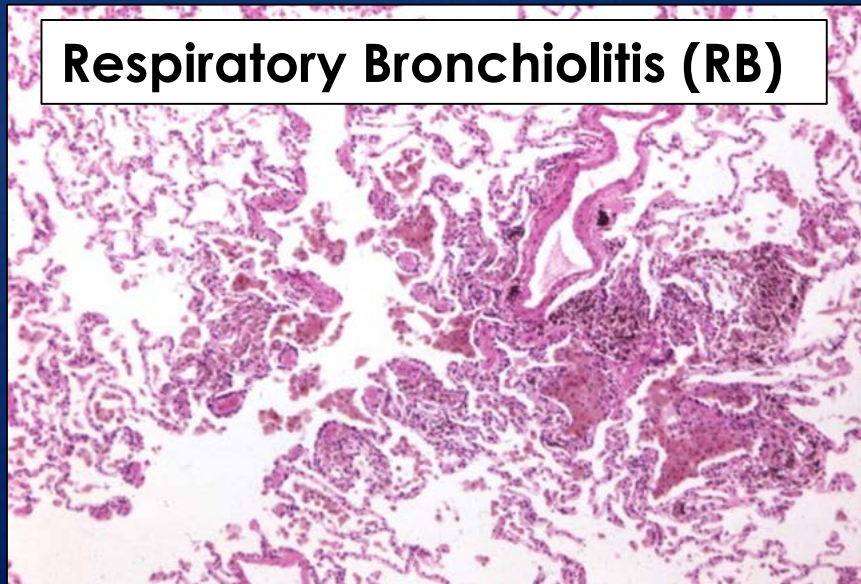
Smoking and Interstitial Lung Disease

Respiratory bronchiolitis ILD (RBILD)*

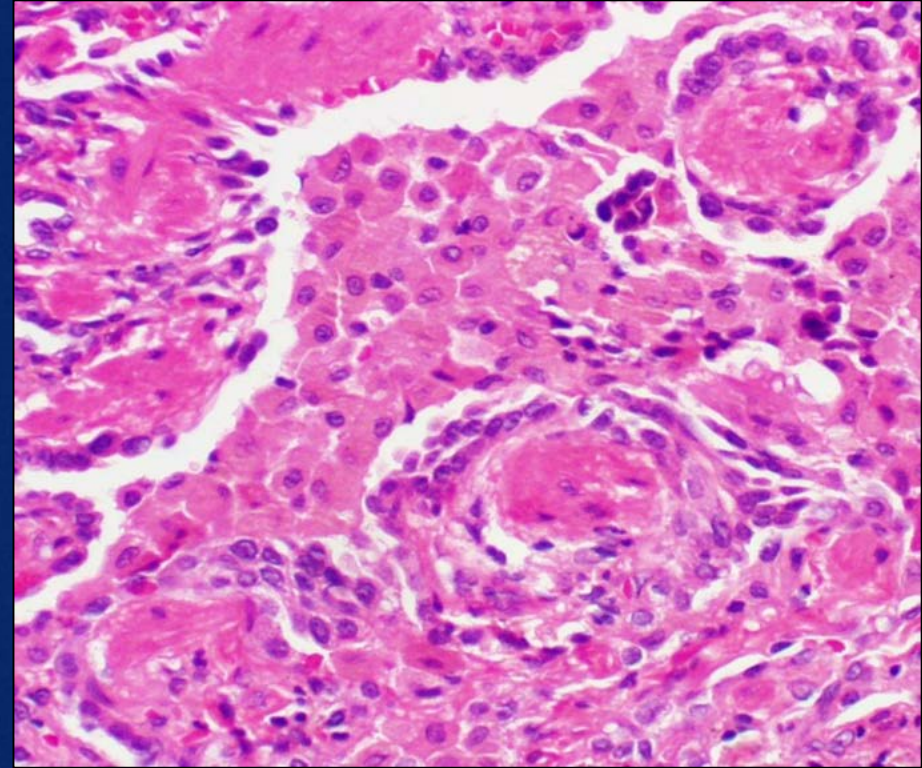
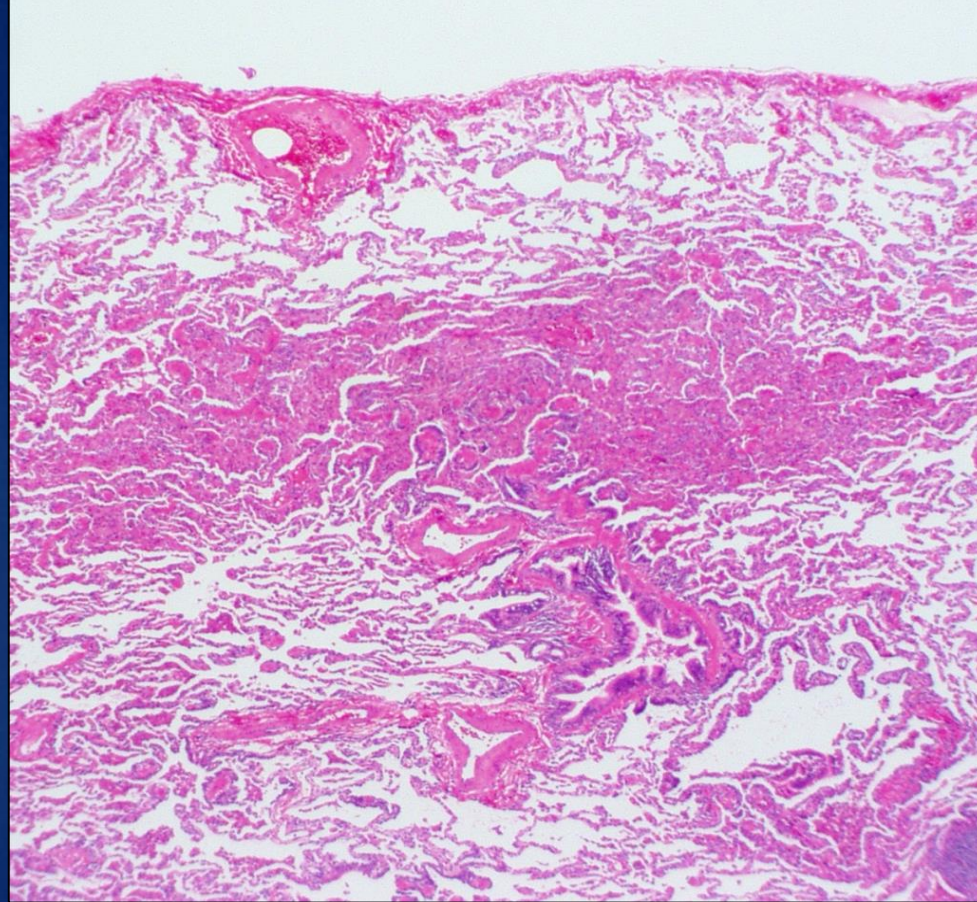
Desquamative interstitial pneumonia (DIP)*

Pulmonary Langerhans Cell Histiocytosis (PLCH)*

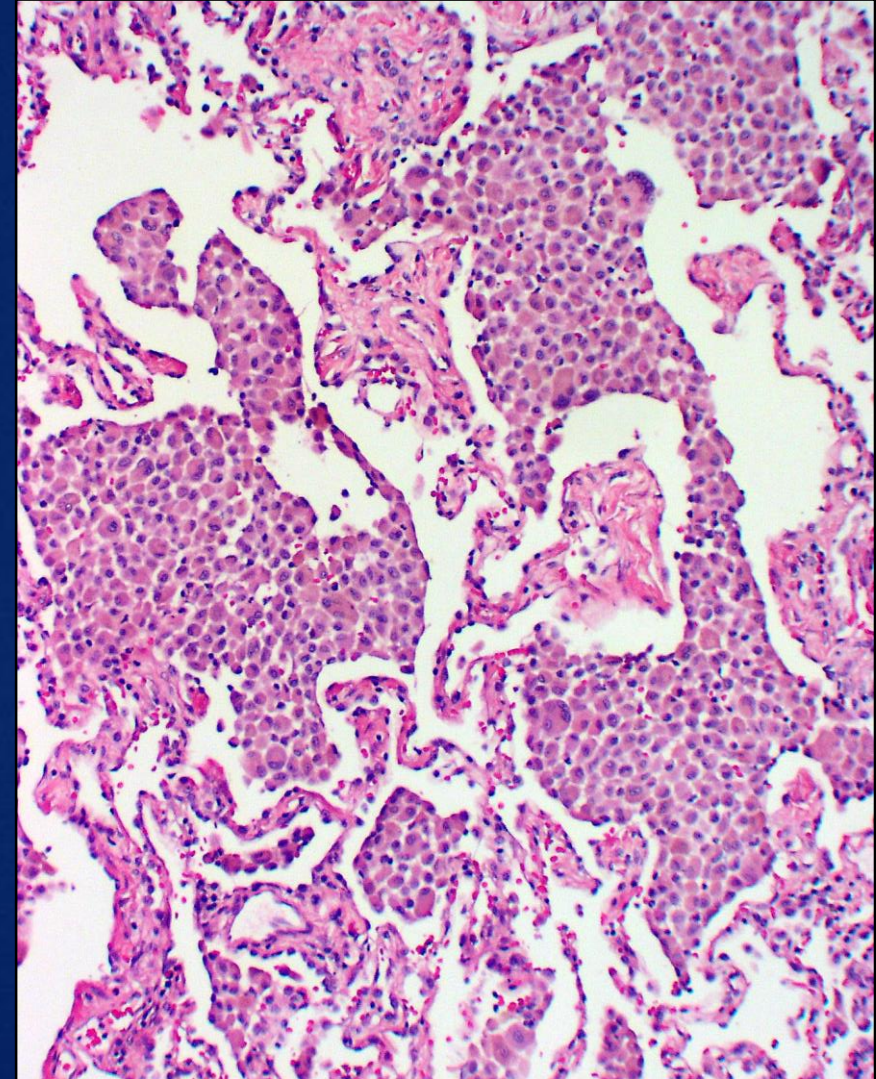
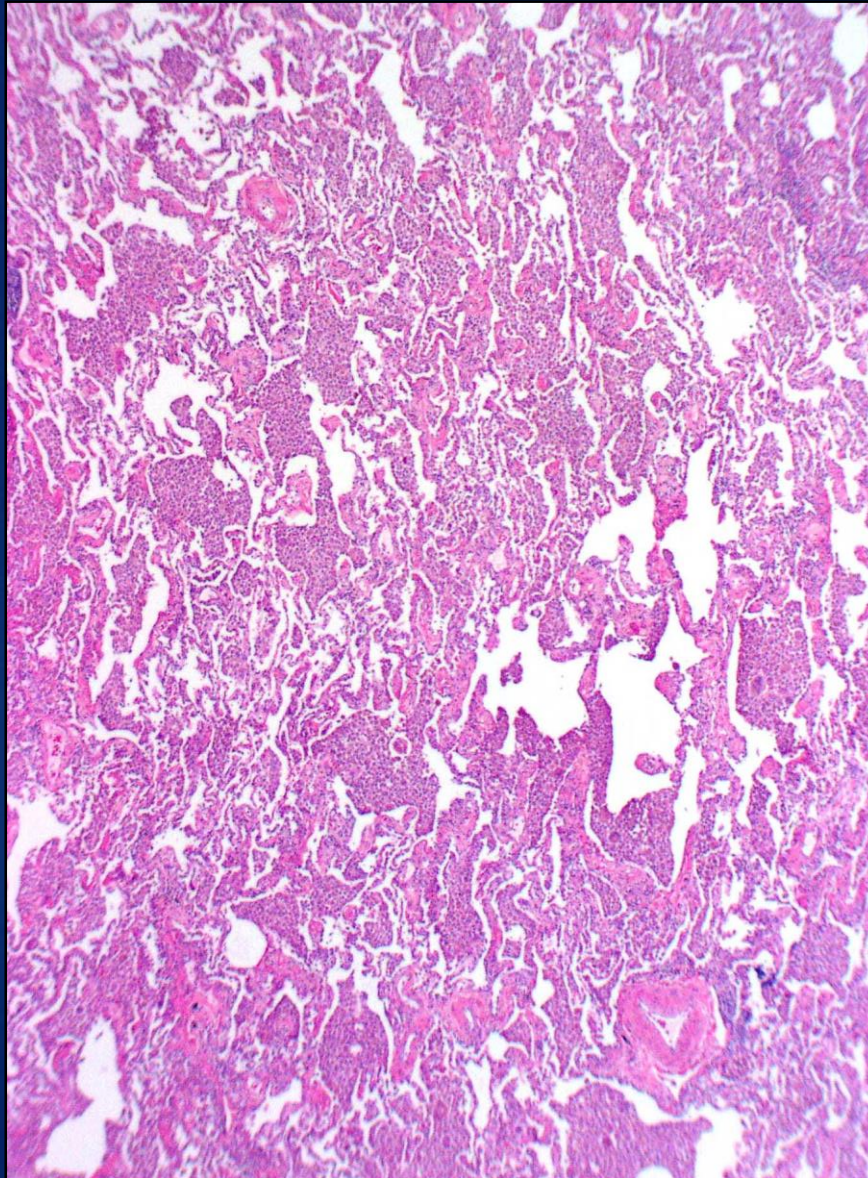
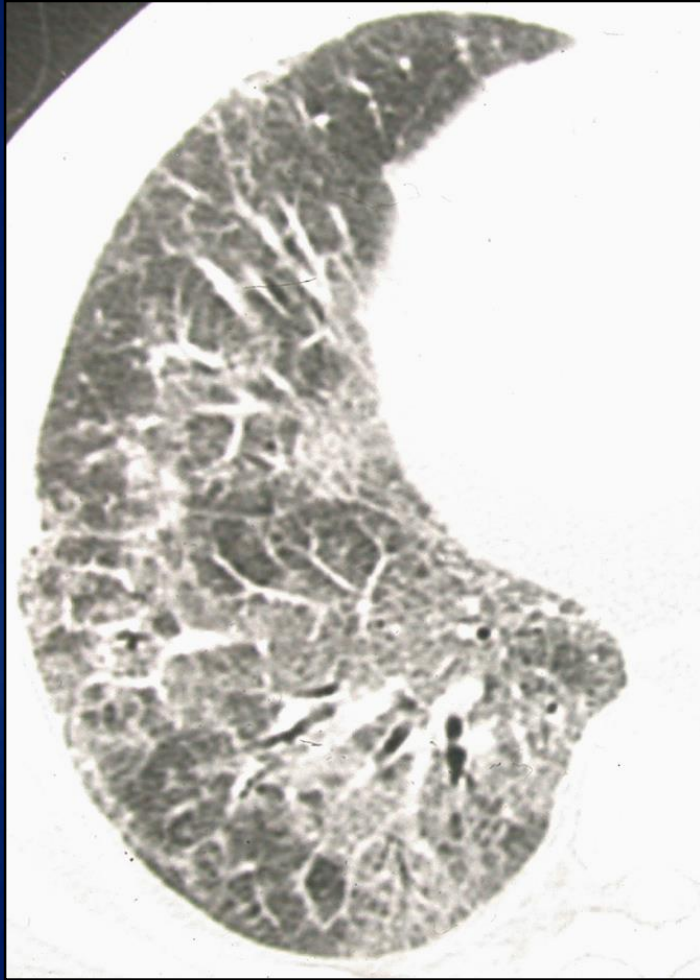
Eosinophilic pneumonia



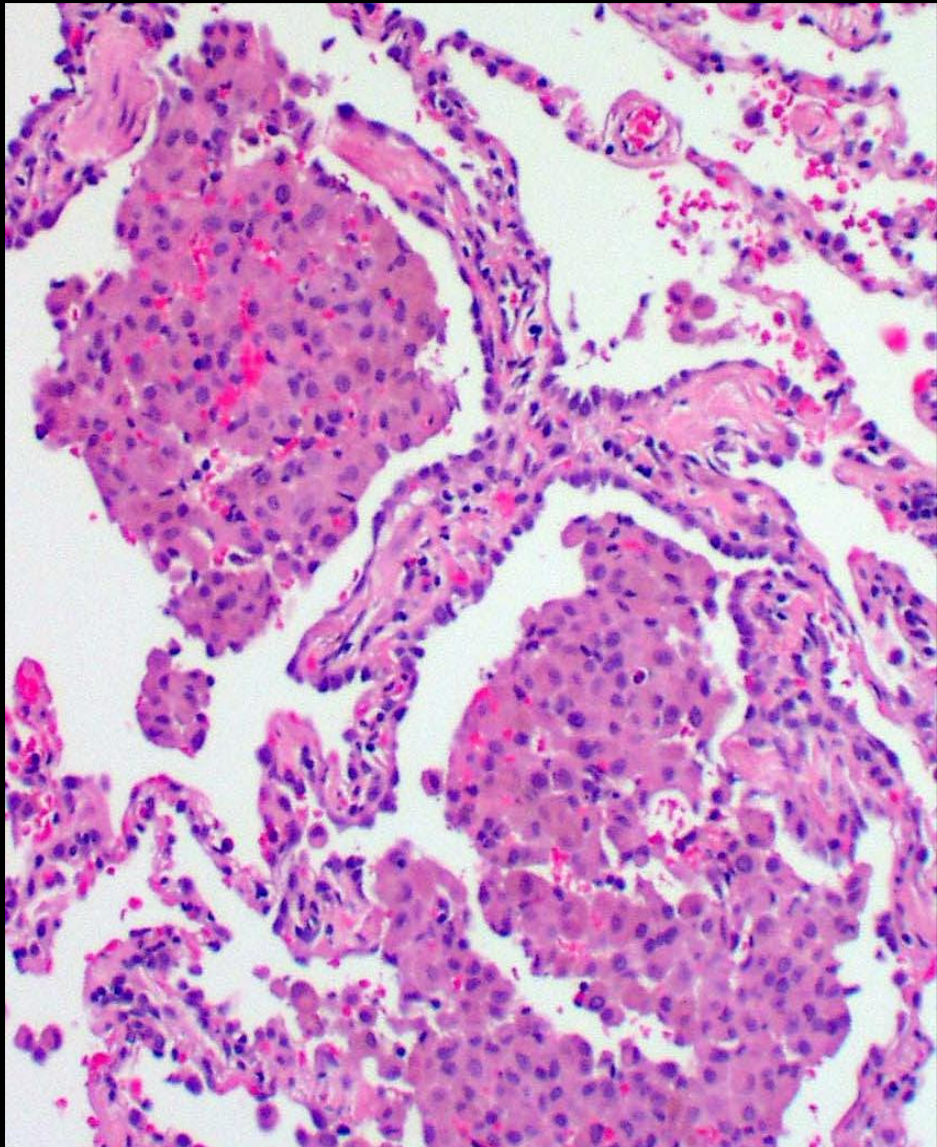
RB-ILD: An exaggerated RB reaction with increased airspace macrophages and greater extent of lung tissue affected



Desquamative Interstitial Pneumonia (DIP)



Airspace filling by macrophages



- Common nonspecific finding
- Smoking-related (RB, RBILD, DIP (incl. marijuana))
- Obstruction (foamy character)
- Aspiration (exogenous lipoid)
- Chronic Hemorrhage (Fe)
- Heart failure (Fe)
- Eosinophilic pneumonia
- Pneumoconioses
- Drug (esp Amiodarone)
- Storage diseases
- Misc.

Case:

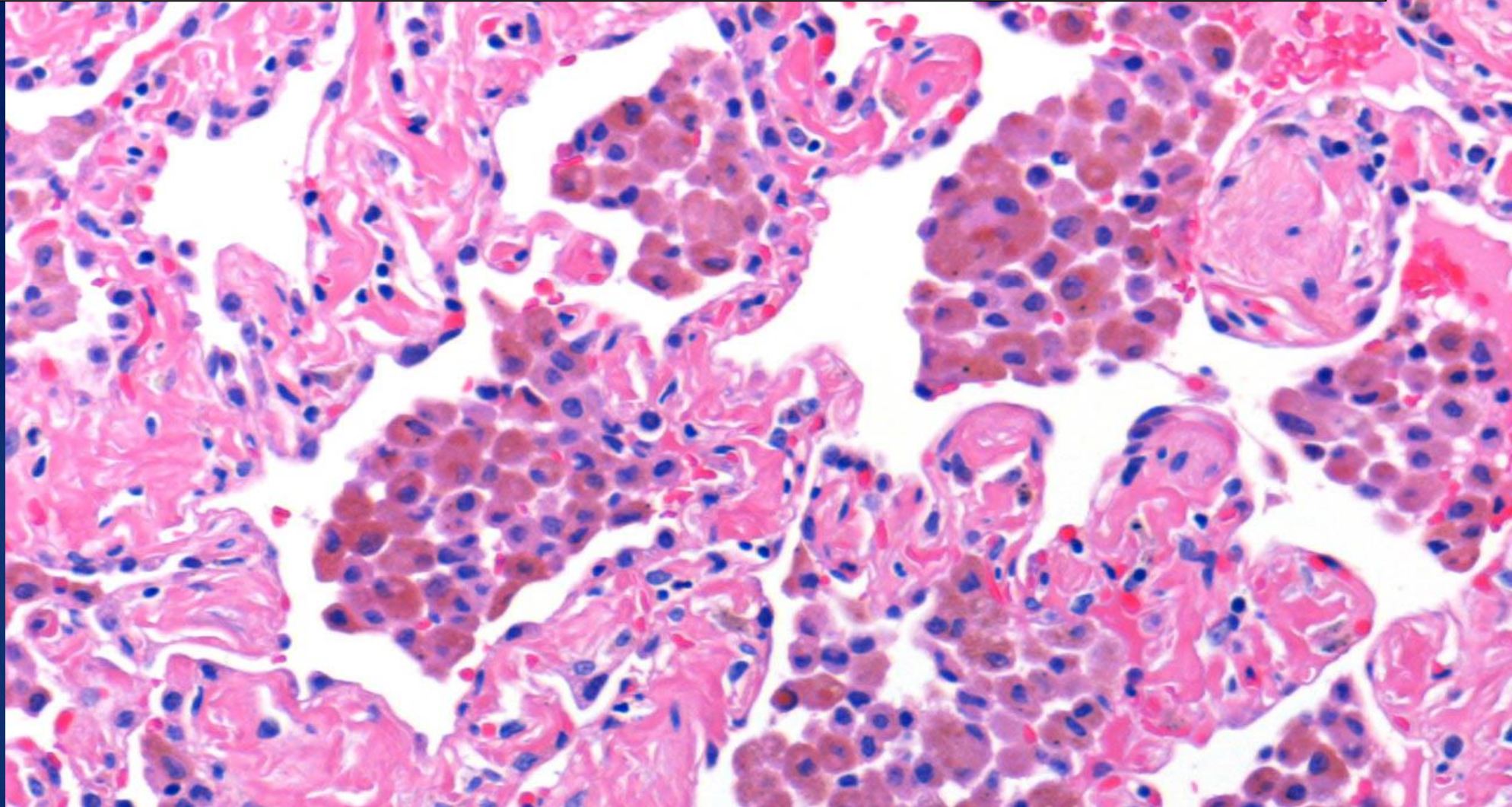
Four domains

Clinical/Lab presentation
Radiologic findings
Pathologic injury pattern(s)
Disease entity that fits

Eosinophilic Pneumonia (Ac or Chr)

Drug reaction
Asthma-related
Infection-related (eg. Cocci)
Smoking-related (esp Acute EP)
Idiopathic
Misc rare...Hyper eos. syndrome

What about this case with histiocytes?



Smoker; Could be DIP or incidental SRIF

Idiopathic Interstitial Pneumonias (IIPs)

(Clinician's point of view)

Major IIPs

Idiopathic Pulmonary Fibrosis (UIP)

Idiopathic NSIP (NSIP)

RB-ILD (RBILD)

DIP (DIP)

Cryptogenic Organizing Pneumonia (OP)

Acute Interstitial Pneumonia (DAD)

Minor IIPs

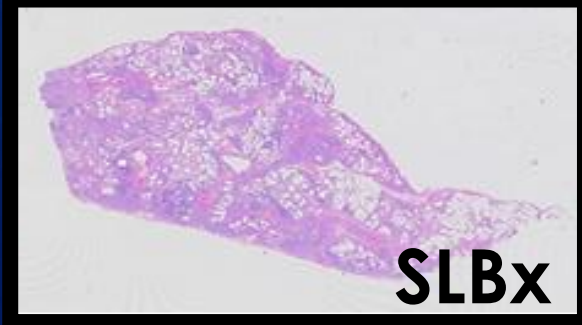
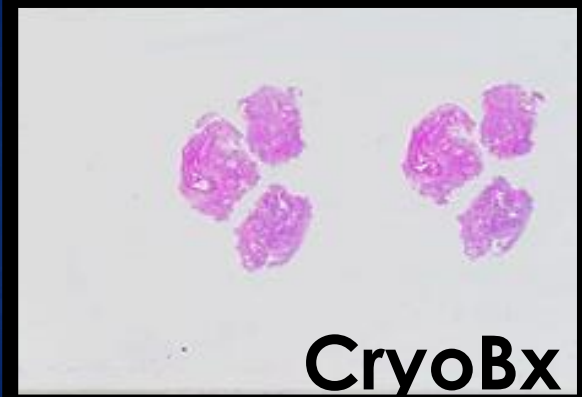
Idiopathic lymphocytic interstitial pneumonia (LIP)

Idiopathic pleuroparenchymal fibroelastosis (PPFE)

Unclassifiable IIPs



Lung Biopsies: Forceps Bx, CryoBx, SLBx



Forceps Bx in ILD ~35% diagnostic

Cryobiopsy in ILD ~75-85% diagnostic

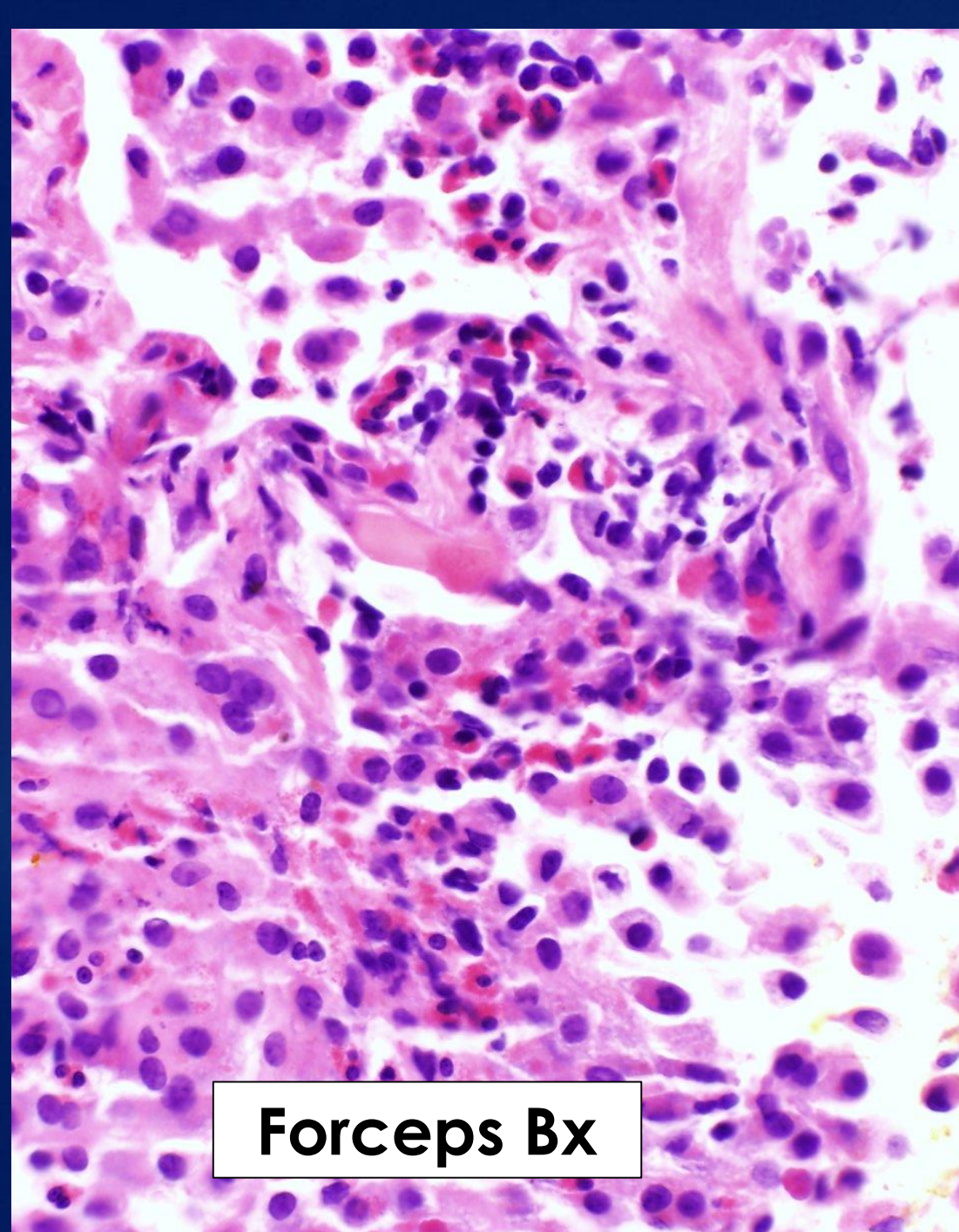
SLBx in ILD ~95% diagnostic

Forceps Biopsies often Nondiagnostic

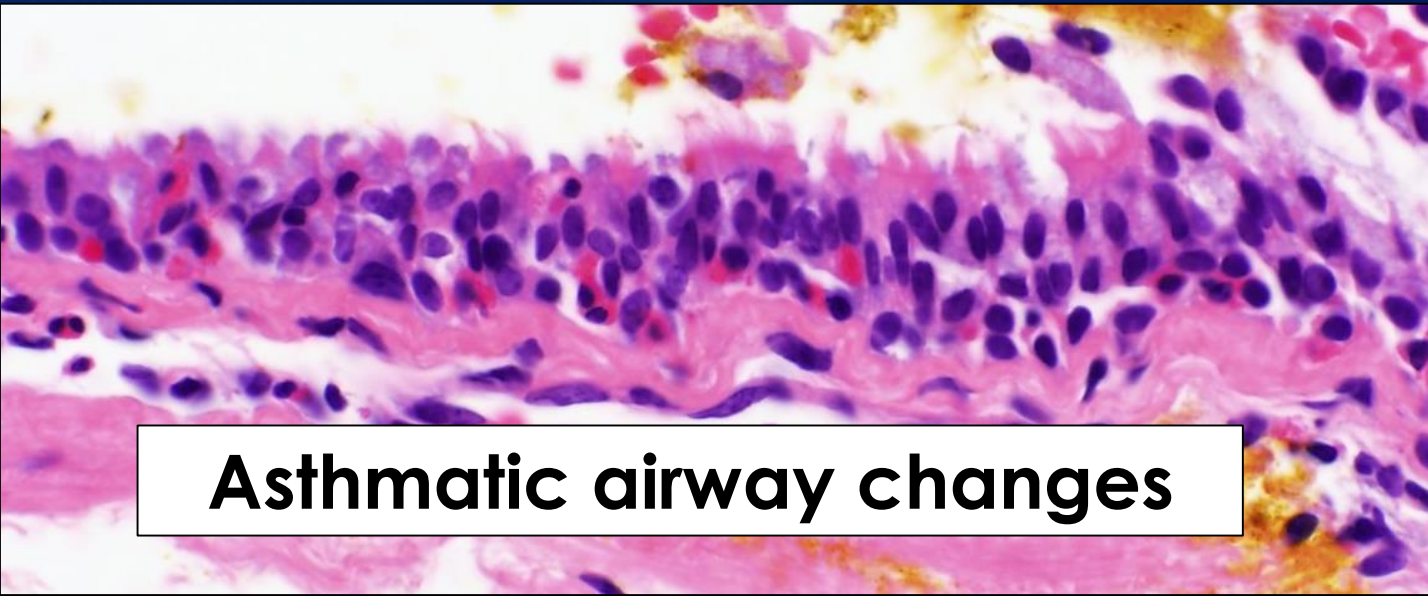
BUT YOU CAN STILL ADDRESS: DO THE FINDINGS ANSWER THE CLINICAL QUESTION?

Some Examples.....





Forceps Bx



Asthmatic airway changes

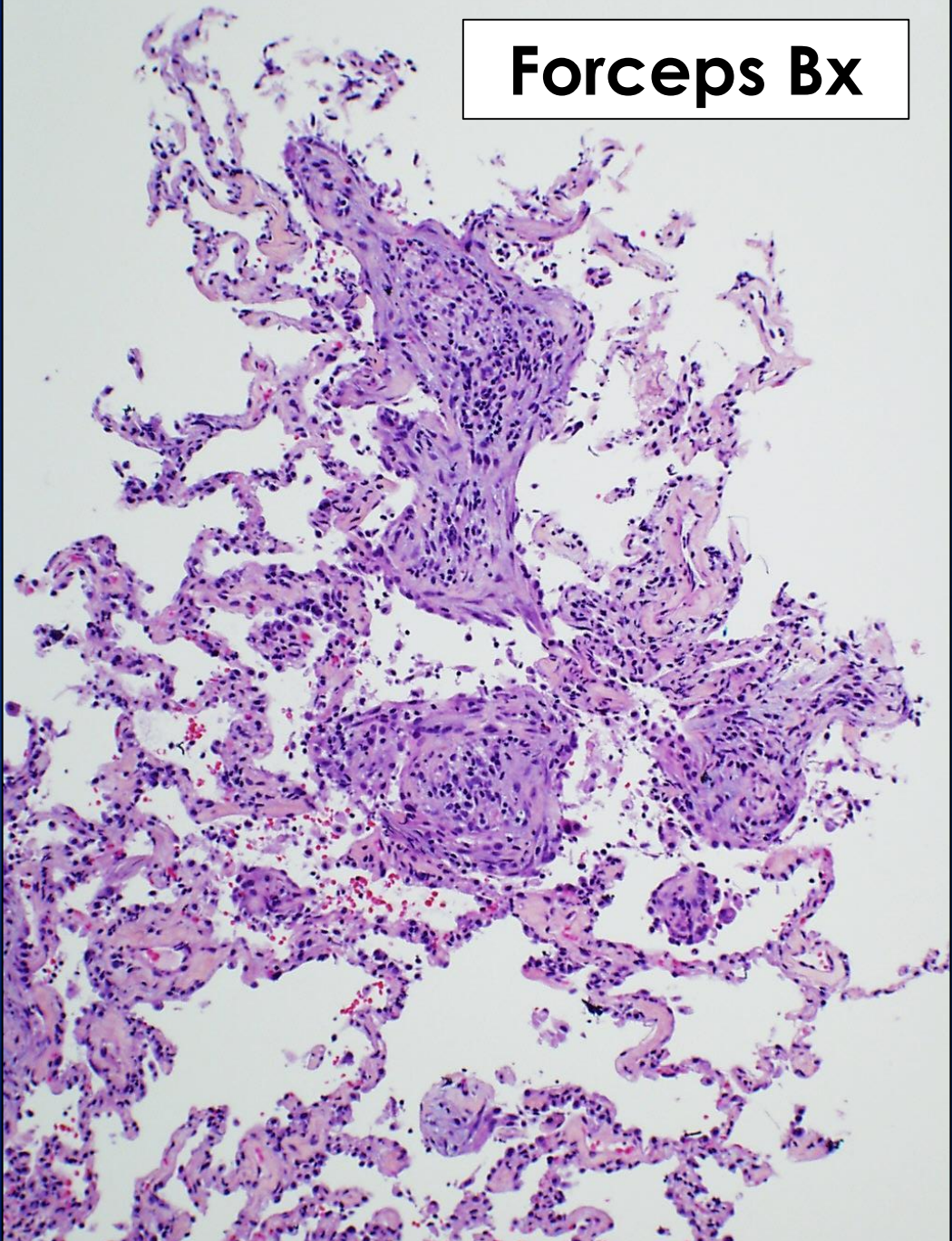
Pathologic Injury: ?Eos pneumonia
Does that answer the clinical findings? which are:

Patchy infiltrates in an asthmatic

Answer- YES



Forceps Bx



Pathologic Injury: **Organizing pneumonia (OP)**

You are given no history (typical!)

What to do?

Be descriptive

Provide a Dx/Dx

Seen in:

Infection

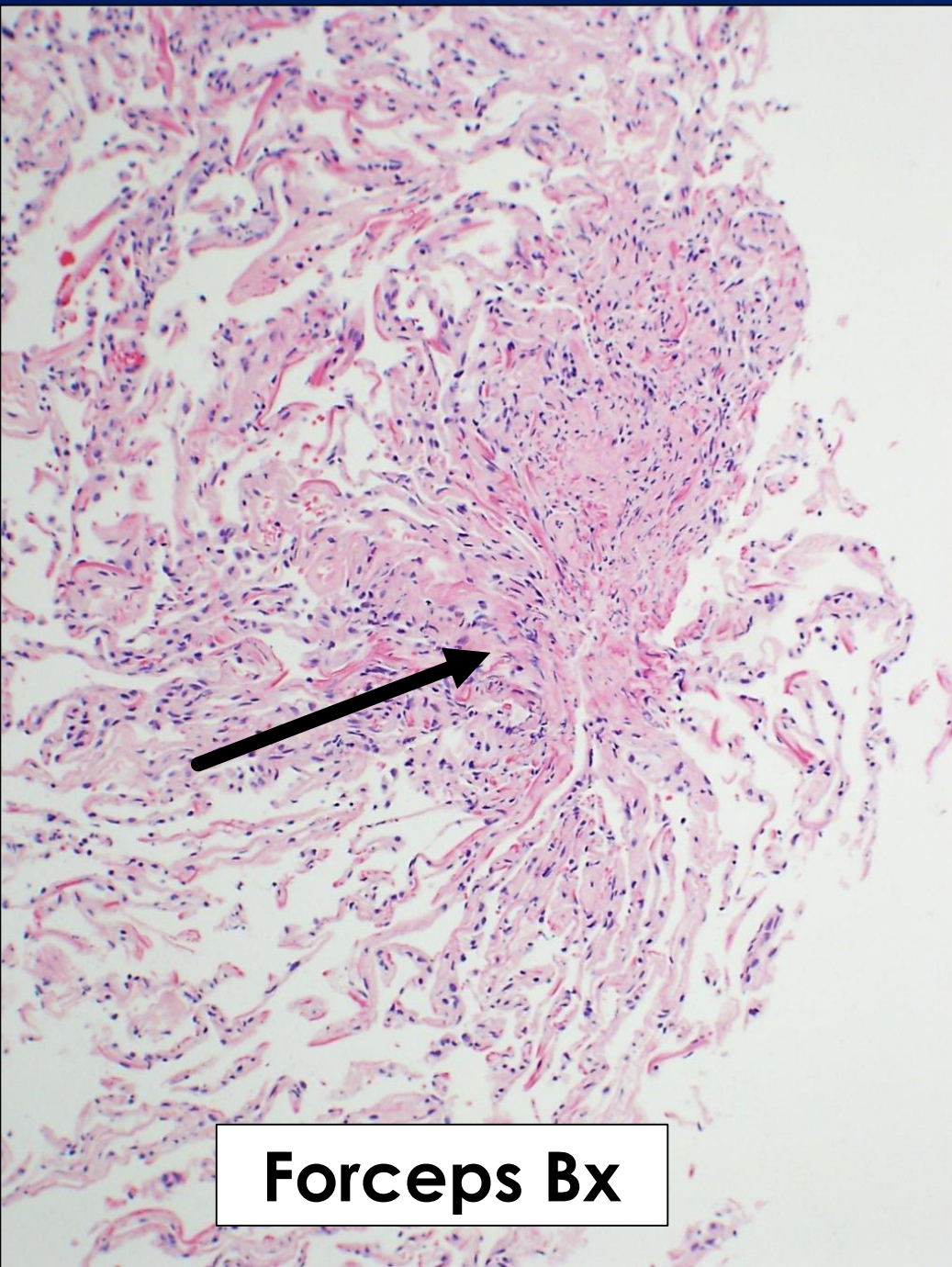
Drug reaction

CVD

Idiopathic

As a local reaction

Many misc



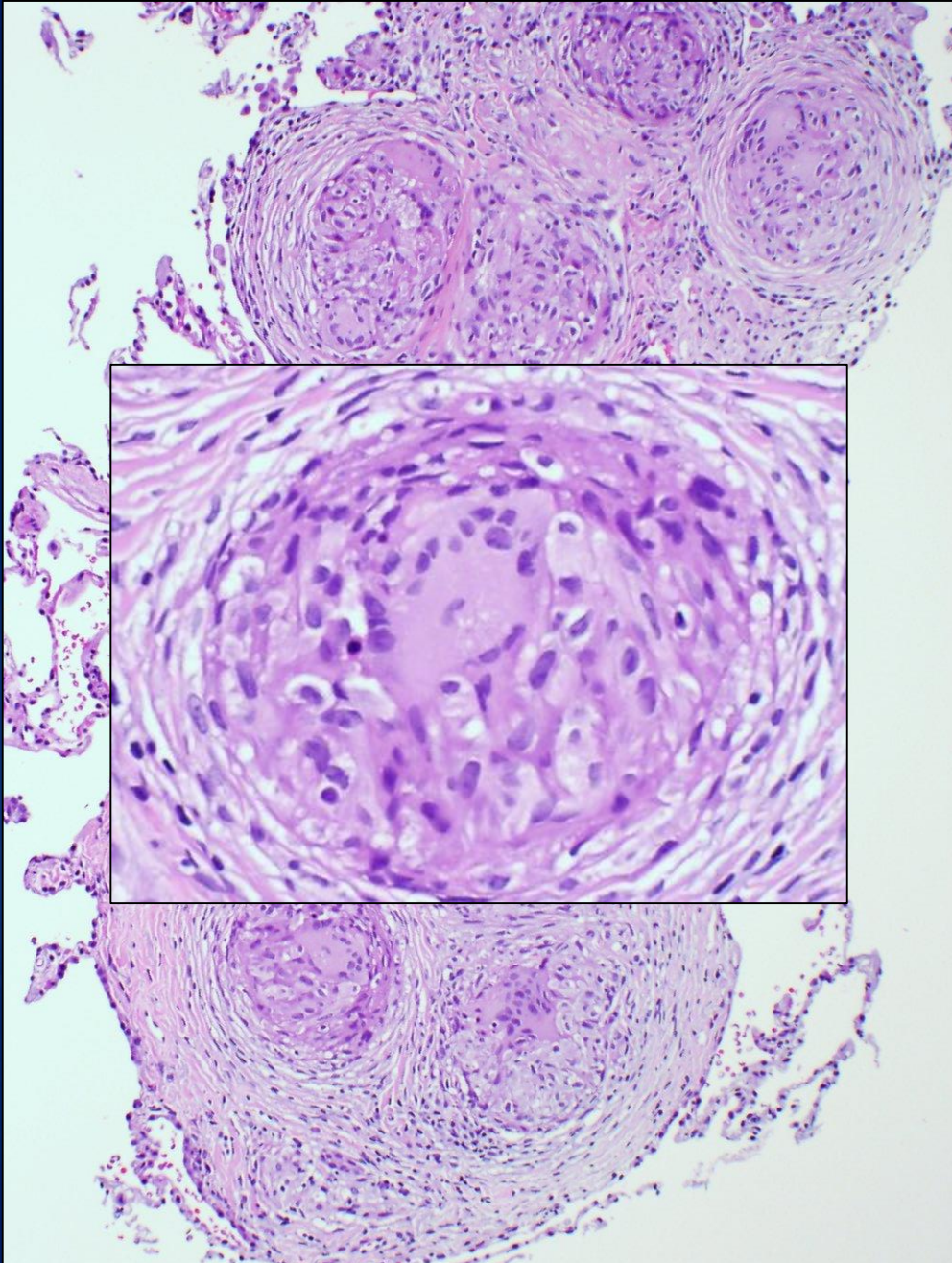
Findings: Lung with pinch artifact
Is anything abnormal?

What to do?

Be descriptive: “Unremarkable lung with Bx artifact”

Nondiagnostic: It does not answer (any) clinical question





Sarcoidosis is often identifiable in small biopsies

When you know if that is the question you can say something like:

“Coalescing non-necrotizing granulomas c/w sarcoid, AFB and GMS stains are negative.”

Common Diagnoses: TbBx v. CryoBx v. SLB

| | Transbronchial Biopsy | Cryobiopsy | Surgical Biopsy |
|---------------------------------|-----------------------|------------|-----------------|
| 1. Malignant tumors | ● | ● | ● |
| 2. Acute-subacute injury | ● | ● | ● |
| 3. Chronic cellular infiltrates | ● | ● | ● |
| 4. Alveolar filling | ● | ● | ● |
| 5. Distinctive non-neoplastic | ● | ● | ● |
| 6. Vasculitis | ● | ● | ● |
| 7. Amyloidosis | ● | ● | ● |
| 8. EG/HX/PLCH | ● | ● | ● |
| 9. LAM | ● | ● | ● |
| 10. RB/RBILD/DIP | ● | ● | ● |
| 11. UIP/NSIP/LIP /COP | ● | ● | ● |
| 12. Constrictive bronchiolitis | ● | ● | ● |
| 13. Pulm HT and PVOD | ● | ● | ● |

Often

Often

Sometimes

Never (alone)

Sometimes

FREQUENT



Commentary.....



When do I get help with a case of non-neoplastic lung disease?

- The domains are at odds

Four domains

Clinical/Lab presentation

Radiologic findings

Pathologic injury pattern(s)

Disease entity that fits

- I have not answered the clinical question?



Course Description

Part 1: Introduction to critical domains (Clinical, Radiological, Histopathological, Specific diseases) and basic patterns of lung injury and repair.

Part 2: Additional patterns of lung fibrosis and inflammatory infiltrates in interstitial lung disease (ILD).

Part 3: Approach to granulomatous lung disease.

Part 4: ILD with airway-centering and bronchiolitis.

Part 5: Non-neoplastic lung disease potpourri



COMMENTARY AND QUESTIONS ??



LungPath
Consultants