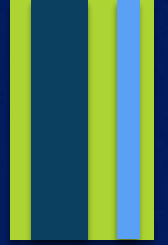


Approach to Non-neoplastic lung disease, especially ILD



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Course Description

5 part primer on the C-R-P approach to the diagnosis of “interstitial lung disease”, (or “ILD”).

Intended audience:

Pulmonologists, Radiologists, and Pathologists
(and their trainees)



Course Description

Part 1: Introduction to Domains and Patterns in ILD: Focus on acute disease

Part 2: Additional patterns of lung fibrosis and inflammatory infiltrates in ILD.

Part 3: Diffuse lung disease with granulomatous features.

Part 4: ILD with airway-centering and bronchiolitis.

Part 5: Non-neoplastic lung disease potpourri



Non-neoplastic Lung Pathology I

Introduction to critical Domains (Clinical, Radiological, Histopathological, Specific diseases)

Basic patterns of lung injury and repair.

KO LESLIE MD

COMMENTARY: TV COLBY MD



Format:

Case Presentation

Introduction to DOMAINS

Acute injury—Prototype: Diffuse Alveolar Damage (DAD)

Subacute injury—Prototype: Organizing pneumonia (OP)

**Chronic injury—Prototype: Pulmonary fibrosis (including
UIP as seen in IPF)**

Common causes of Acute Lung Injury (ALI)



To be discussed:

Typical evolution of acute lung injury

How pulmonary fibrosis occurs

Morphologic patterns: DAD, OP, Pulmonary fibrosis

How different biopsy techniques influence diagnosis

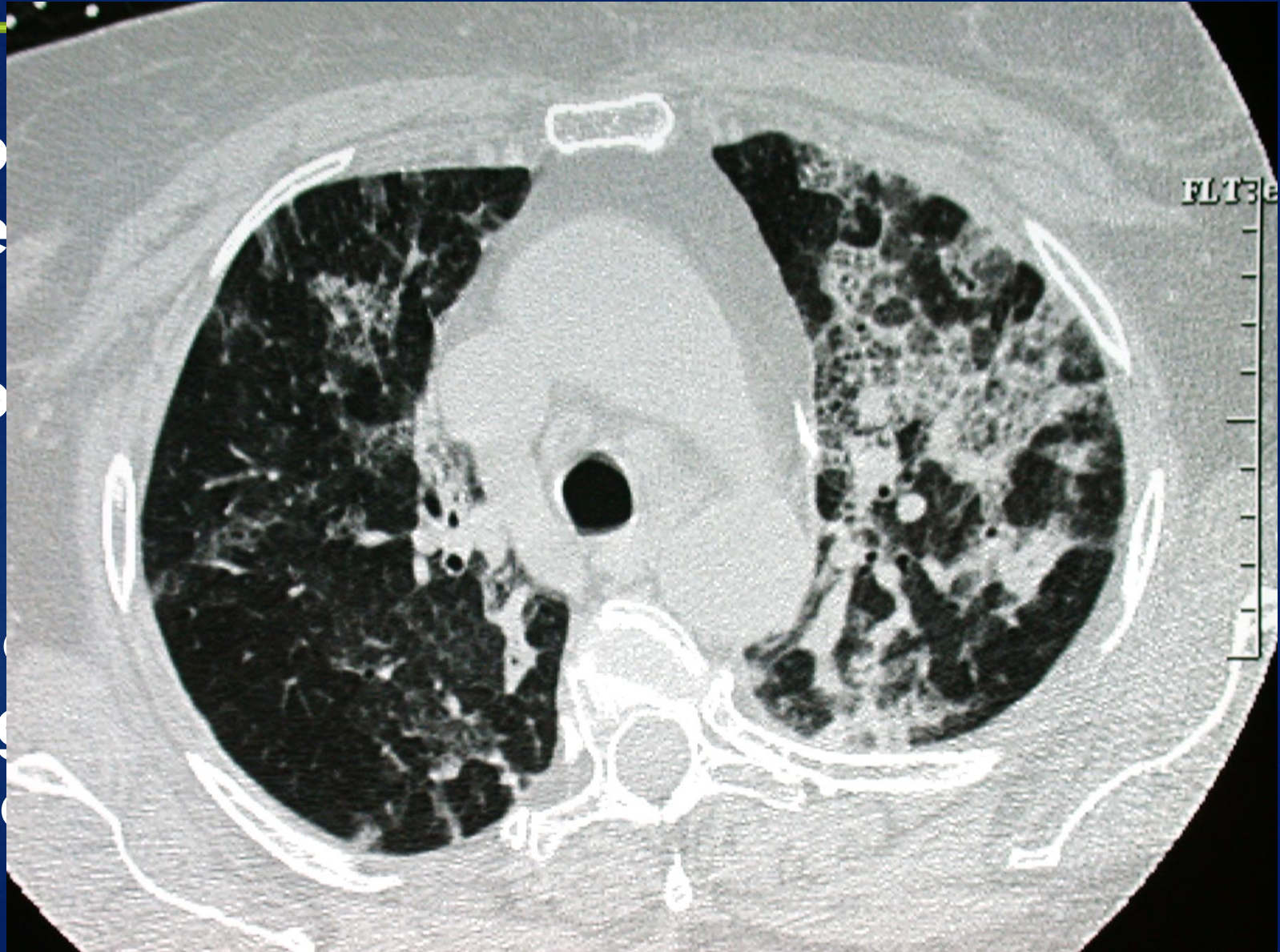


Clinical Case

A 46 year old patient with
progressive respiratory failure.

Chest radiograph shows
infiltrates.

All evaluations of the
patient progress show
hopes of identifying a
diagnosis.





...and the SLB shows



Clinical Case (continued)

Follow up: Query of the family reveals undiagnosed inflammatory arthritis.

All special stains and cultures from the biopsy are negative.

Serological studies reveal a positive ANA and JO-1 consistent with amyopathic polymyositis and the anti-synthetase syndrome.

Case Analysis

Four Domains

Clinical/lab presentation

Radiologic findings

Pathologic injury pattern

Disease entity that fits

Rapidly progressive
dyspnea, arthritis, JO-1

Bilateral ground glass infiltrates

Acute injury with hyaline
membranes = Diffuse alveolar
damage --with DDX

Antisynthetase syndrome with
DAD

Clinical Case

Urgent therapy implemented (high dose solumedrol with pulse-dose cyclophosphamide).

Patient recovered.



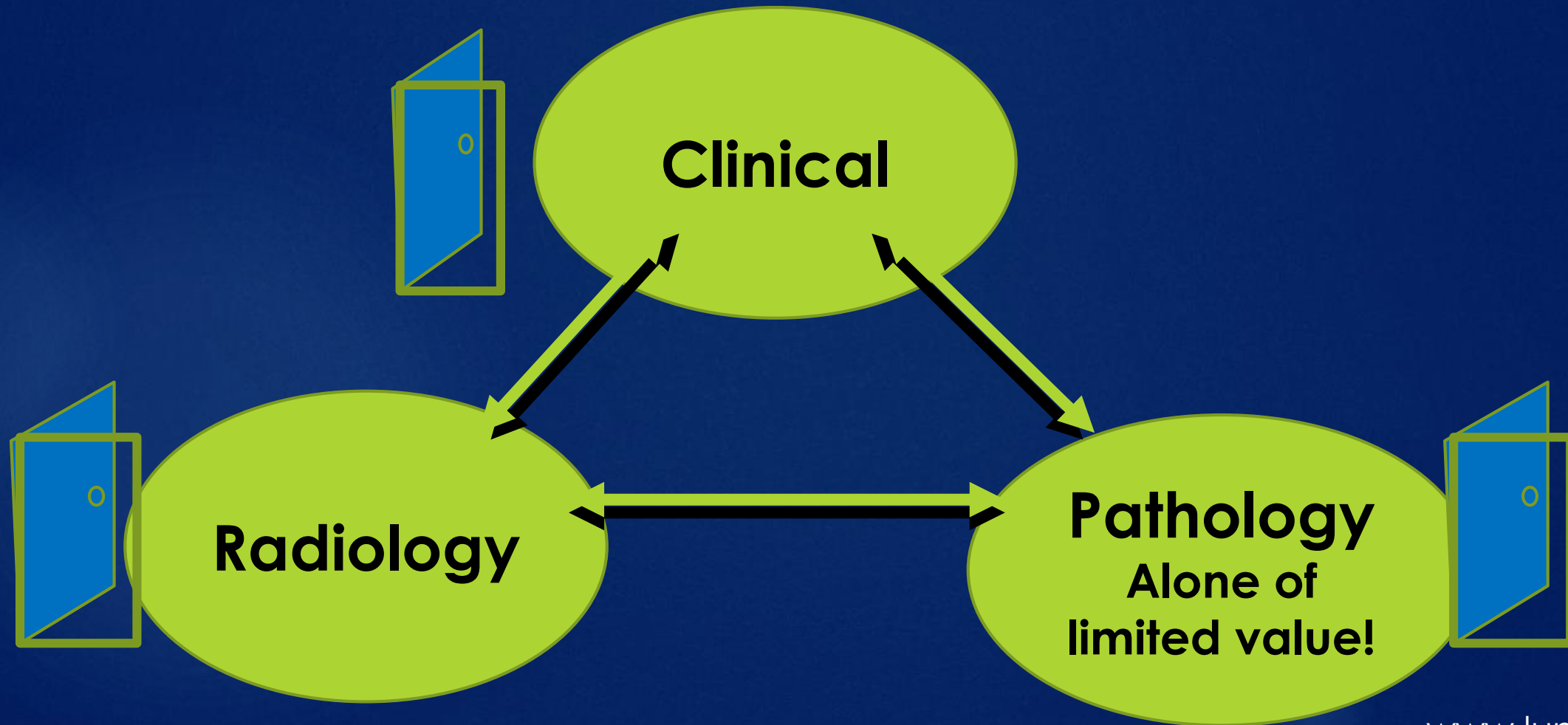


Commentary



LungPath
Consultants

Importance of Clinical-Radiological-Pathological Correlation in ILD



Know the question being asked!

1. Is this a disease with a defined diagnosis and proscribed therapy (like infection or sarcoid)?

2. If not specific, does the pathogenesis have a defined mechanism of injury (e.g. Infection, Trauma, Immunologic?)

3. If not specific, is this a possible condition with available treatments?

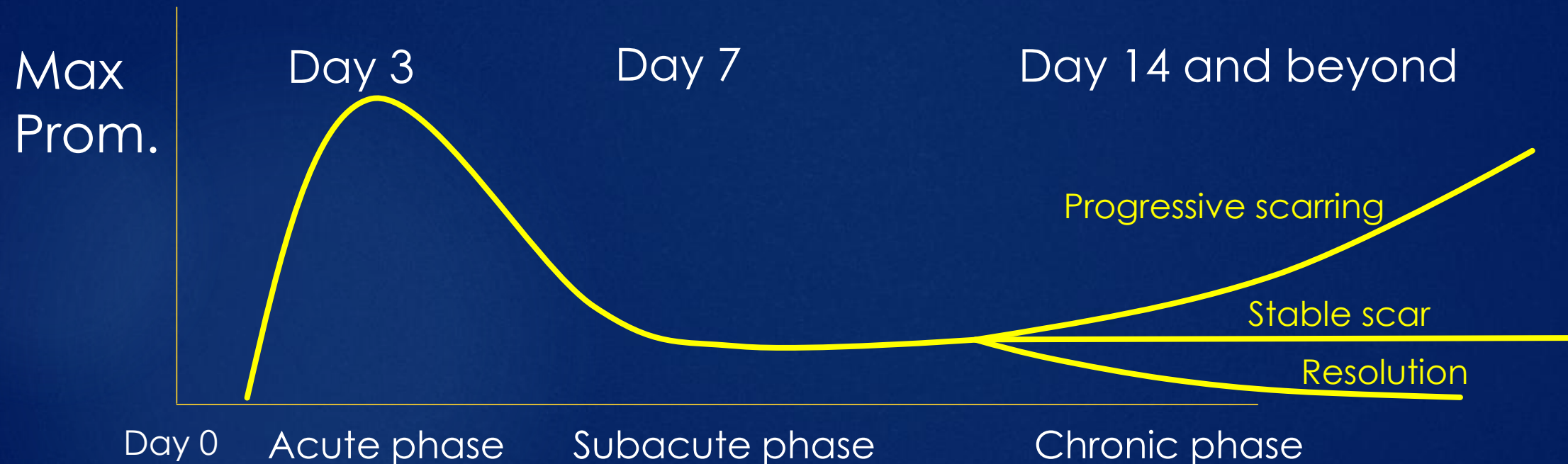
Bronchodilators
Immunoglobulin therapy
Antibiotics
Anti-inflammatory agents
Anti-fibrotic agents
Whole lung lavage
Lung transplant



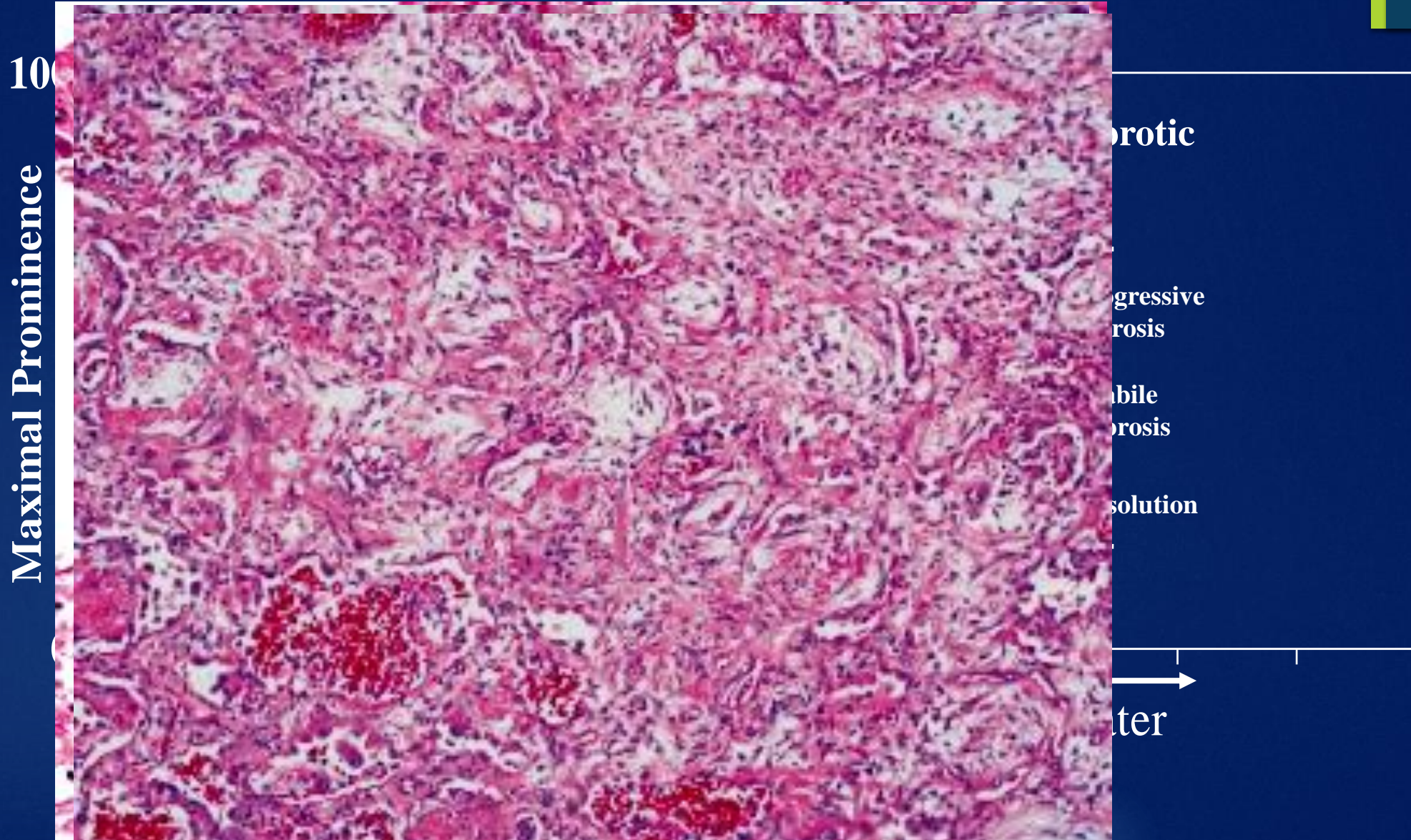
Basic lung reactions to injury



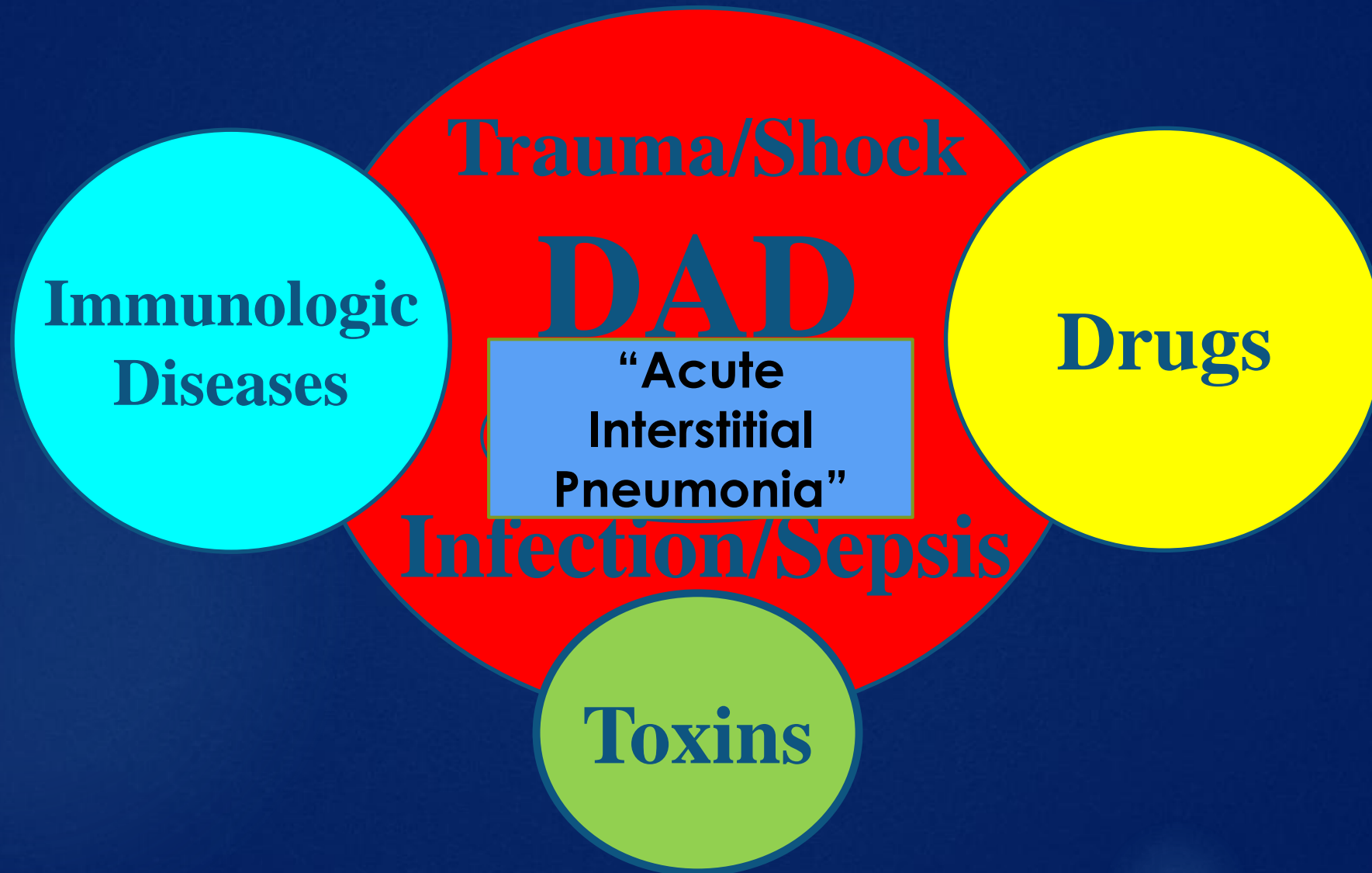
Cellular injury and repair progresses through highly reproducible phases



Phases of Clinical ARDS



Differential Diagnosis for DAD





Commentary

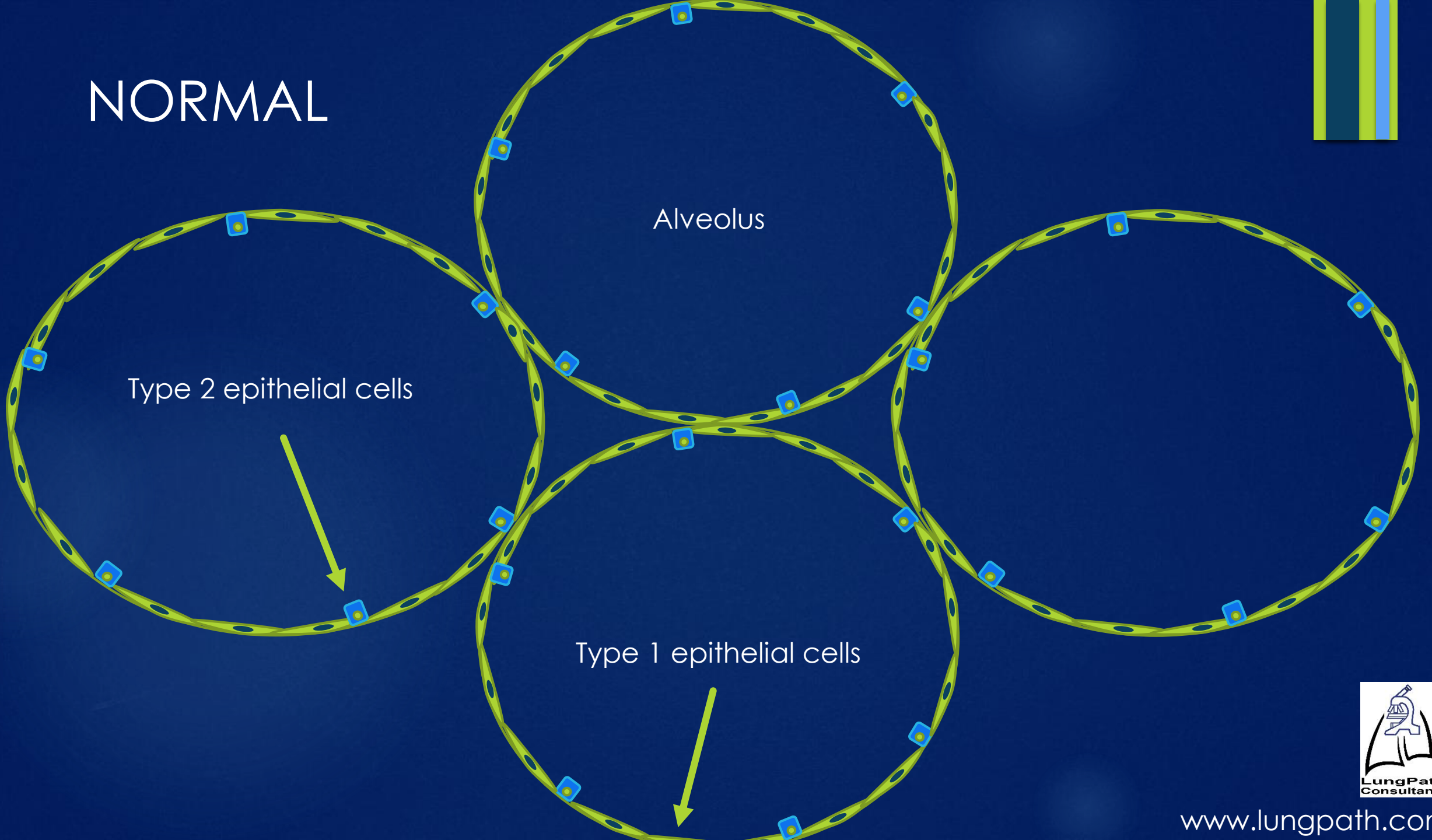


Mechanisms of Lung Repair Following Injury

(Data derived from experimental
models and corroborated in
human observations)



NORMAL

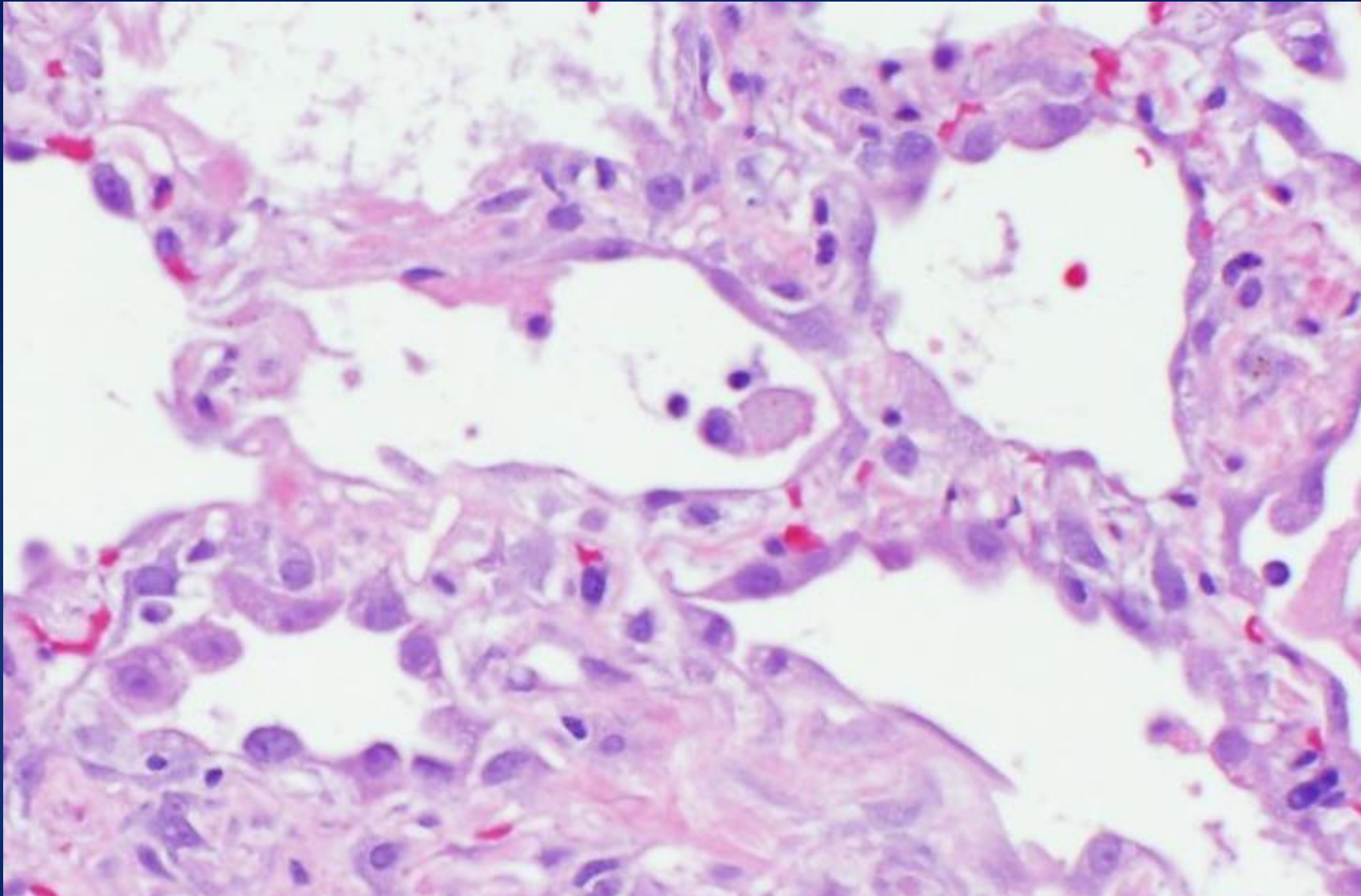


Alveolus



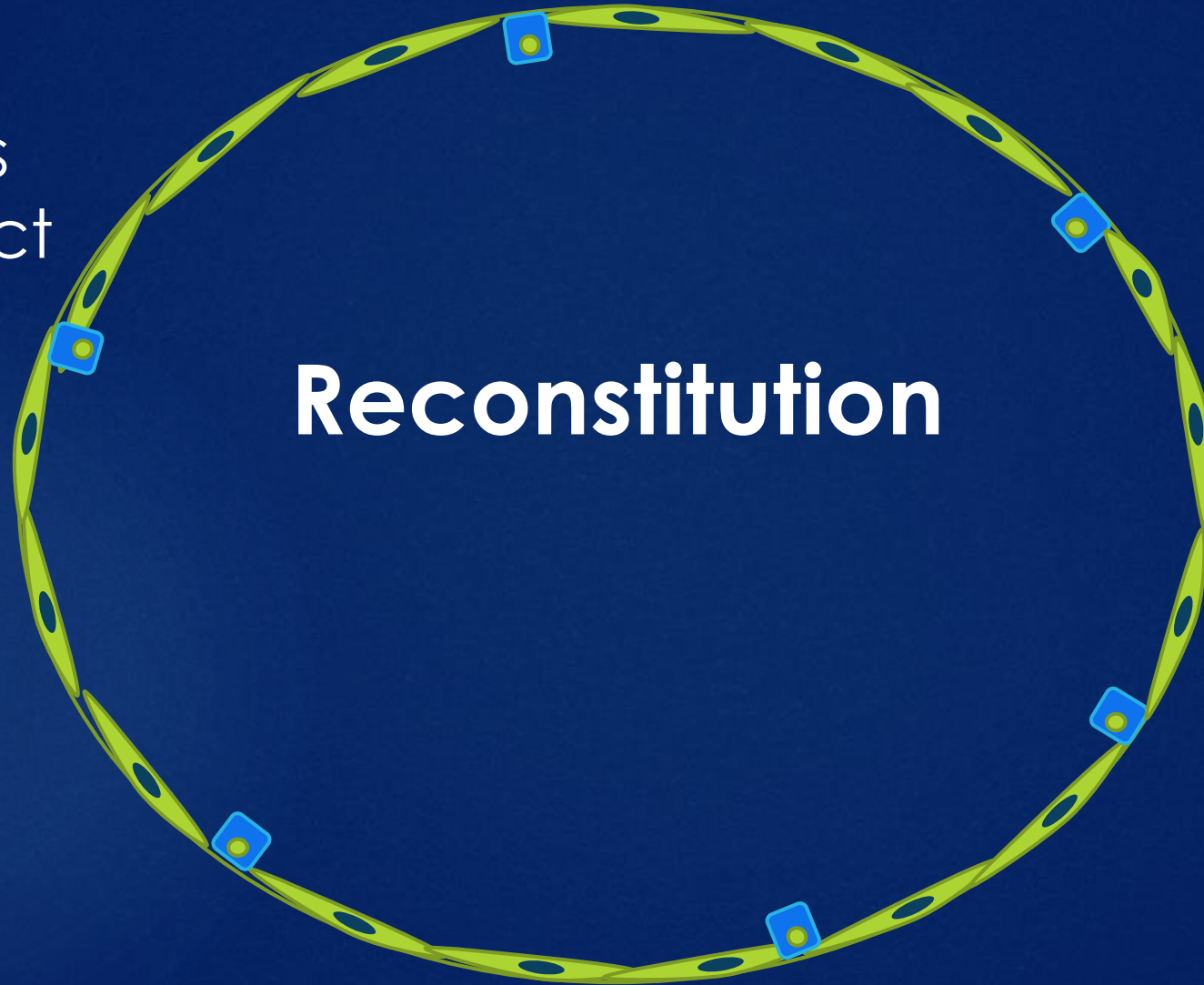
Epithelial injury

Alveolus



IF Injury subsides
AND
Basement
membranes
remain intact

Alveolus



Reconstitution

BUT...

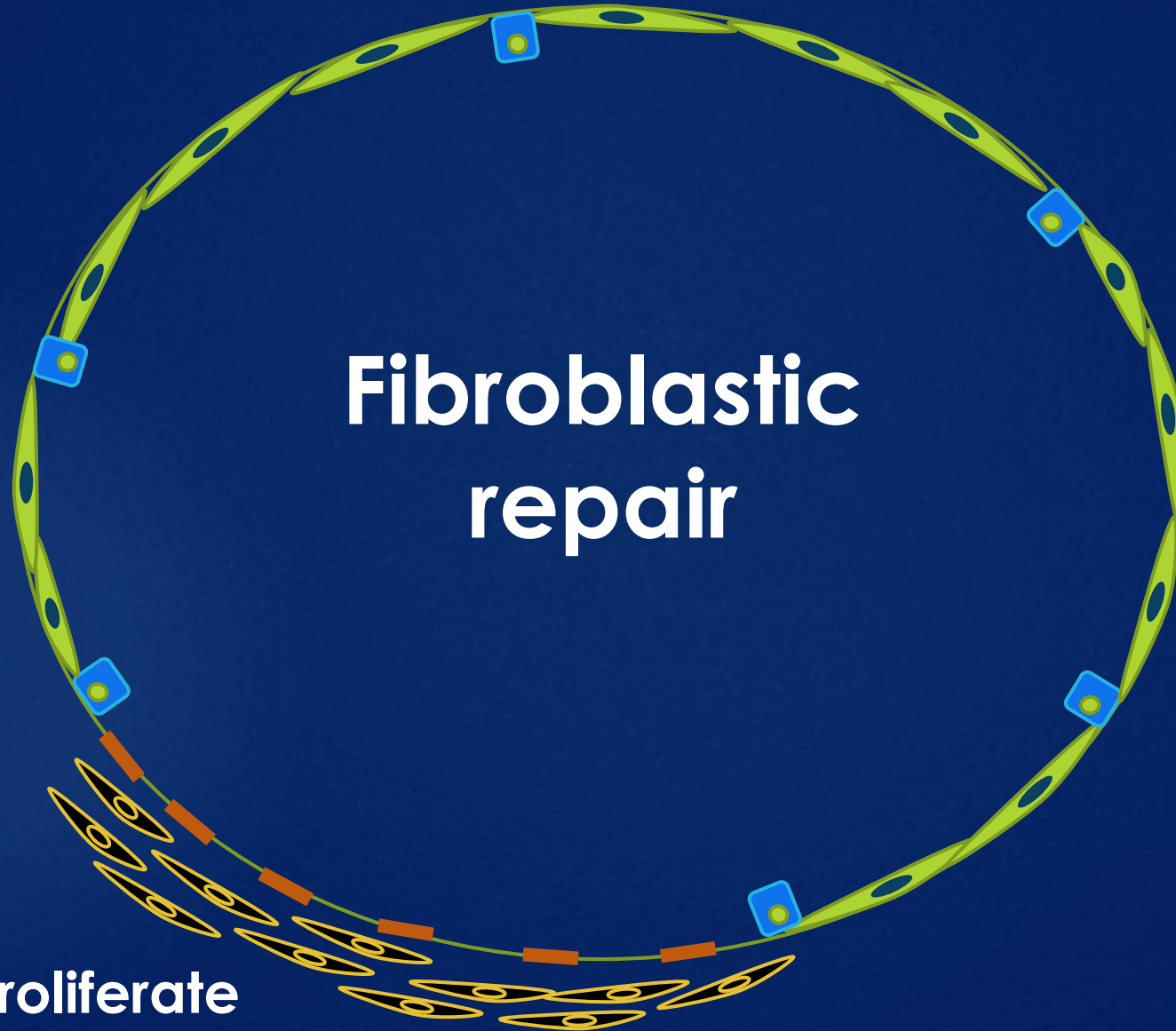
If the injury damages the epithelial
basement membrane...



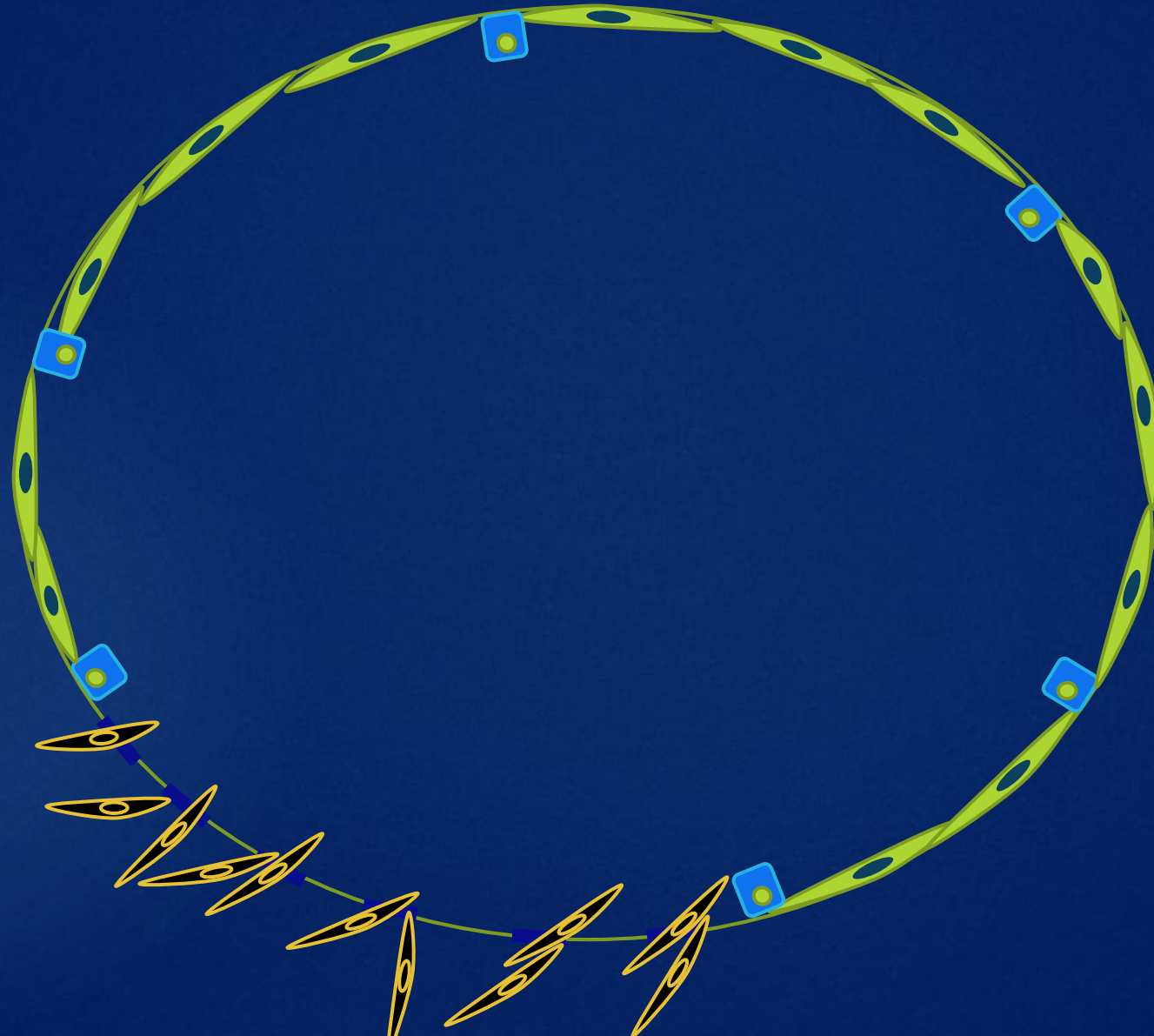
Alveolus

**Fibroblastic
repair**

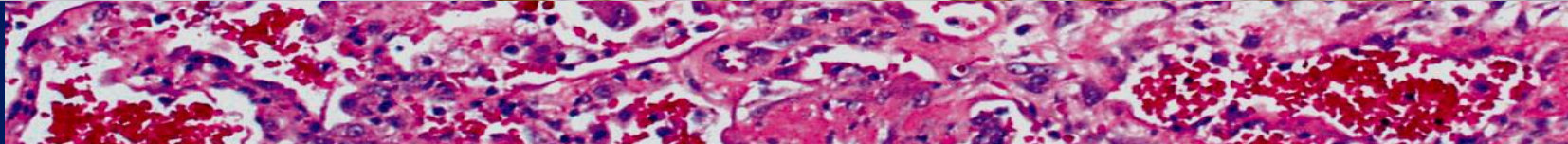
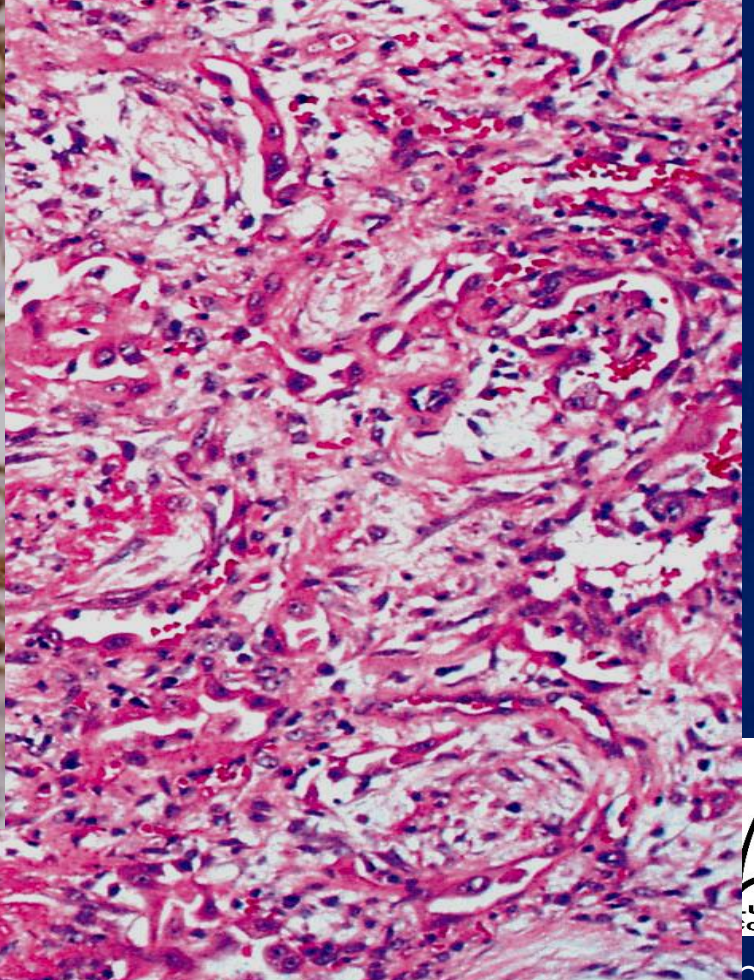
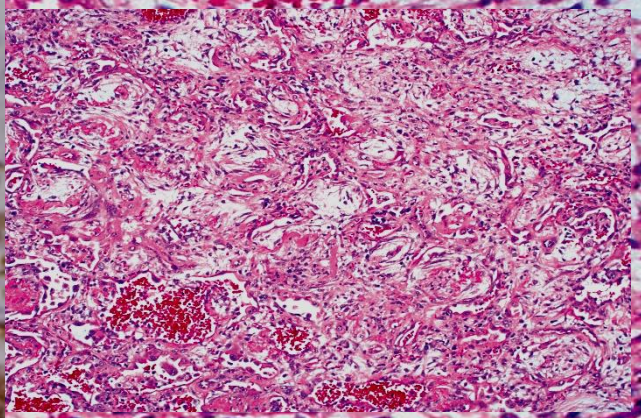
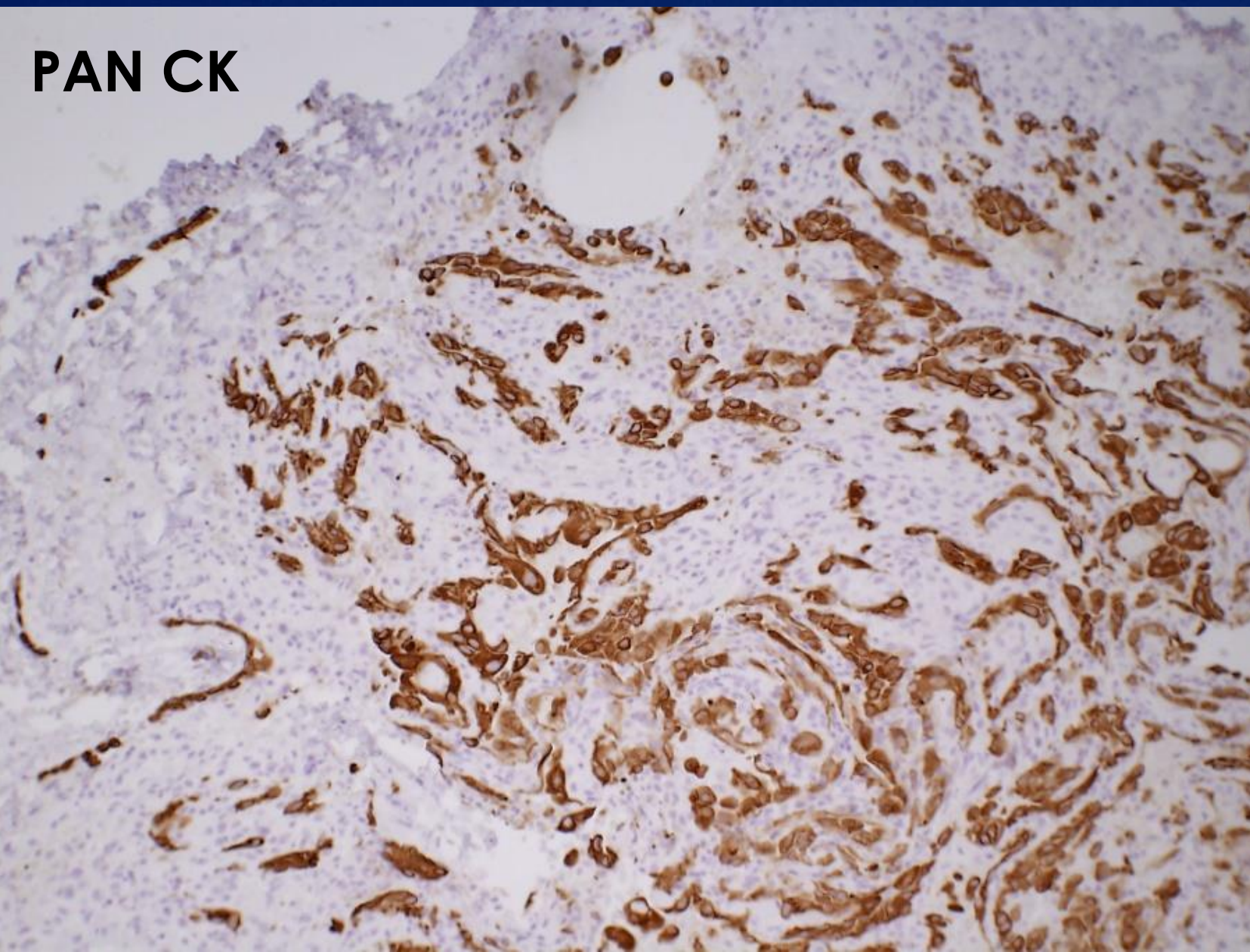
Fibroblasts proliferate



Alveolus

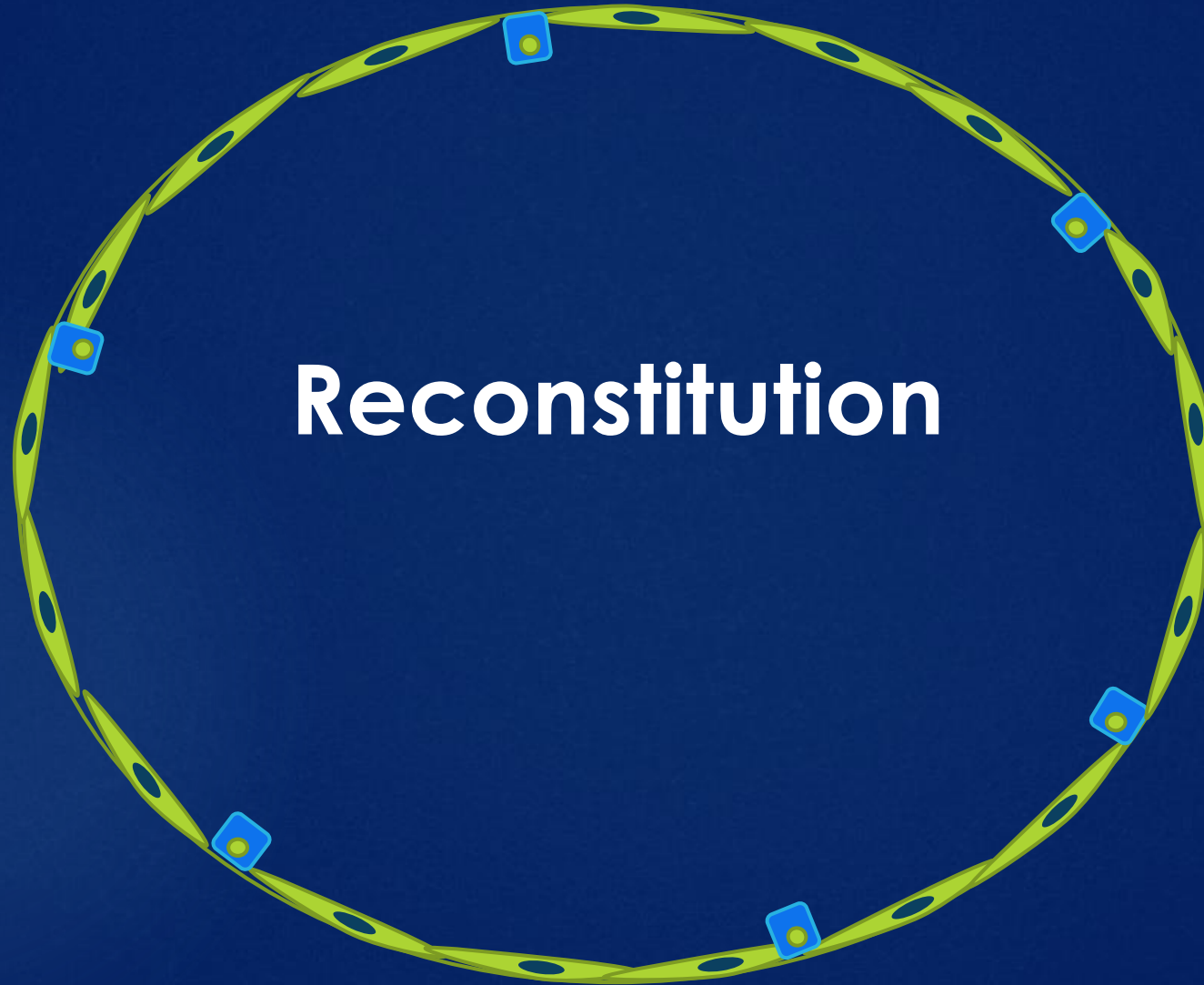


PAN CK

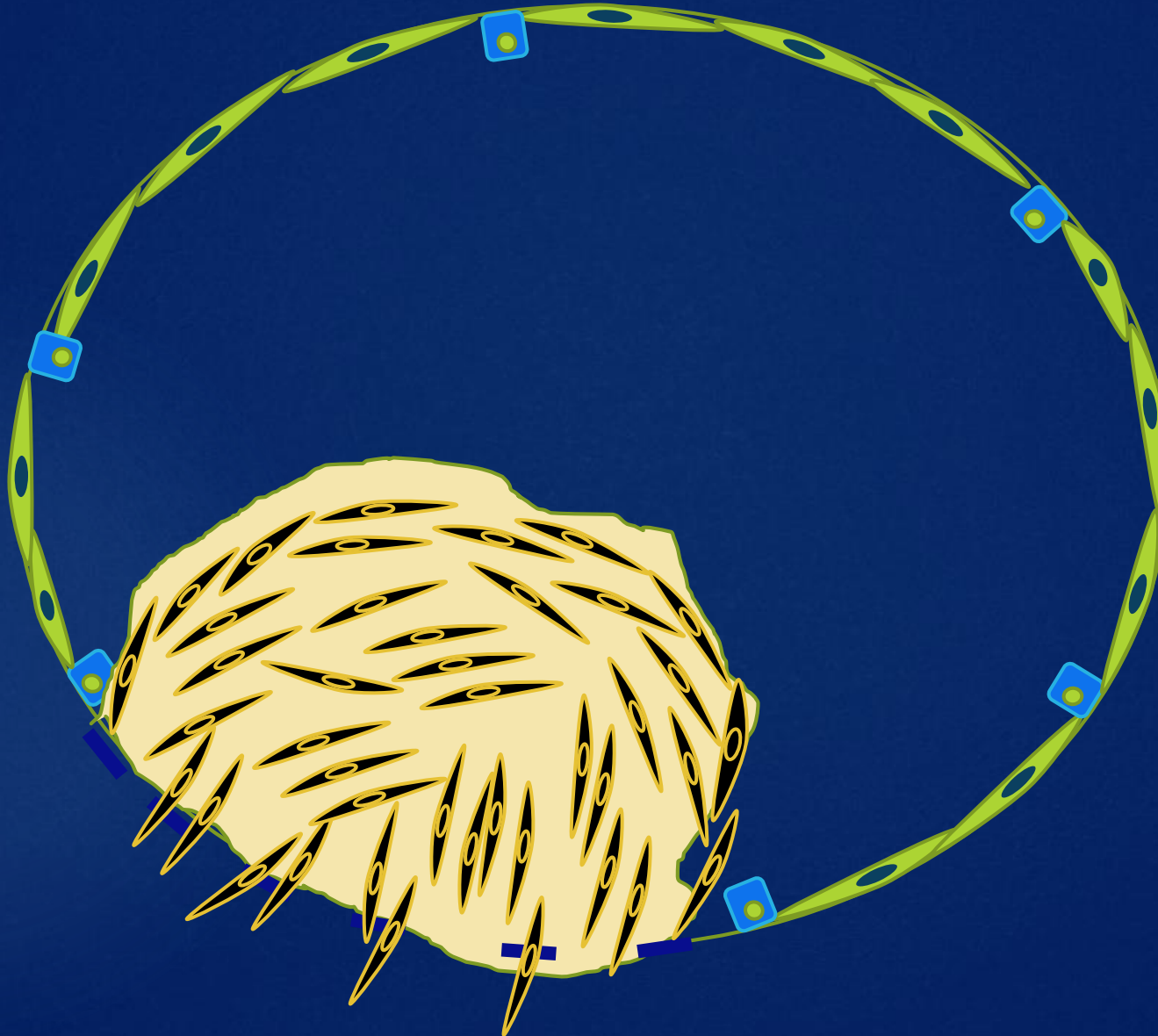


LungPath
consultants

Alveolus

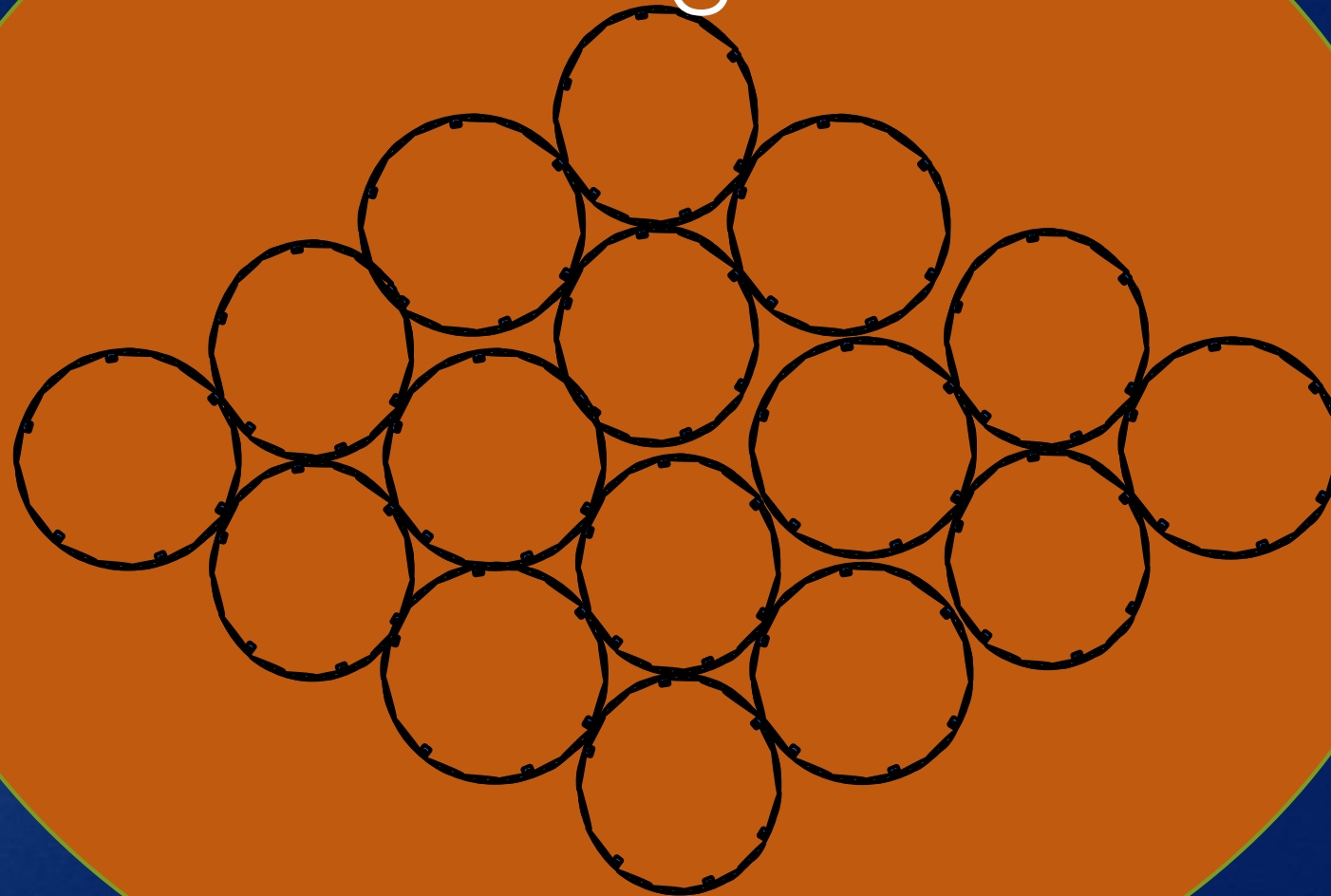


Alveolus



If the injury is severe or prolonged, alveolar destruction and fibrosis occur.

Normal lung structure





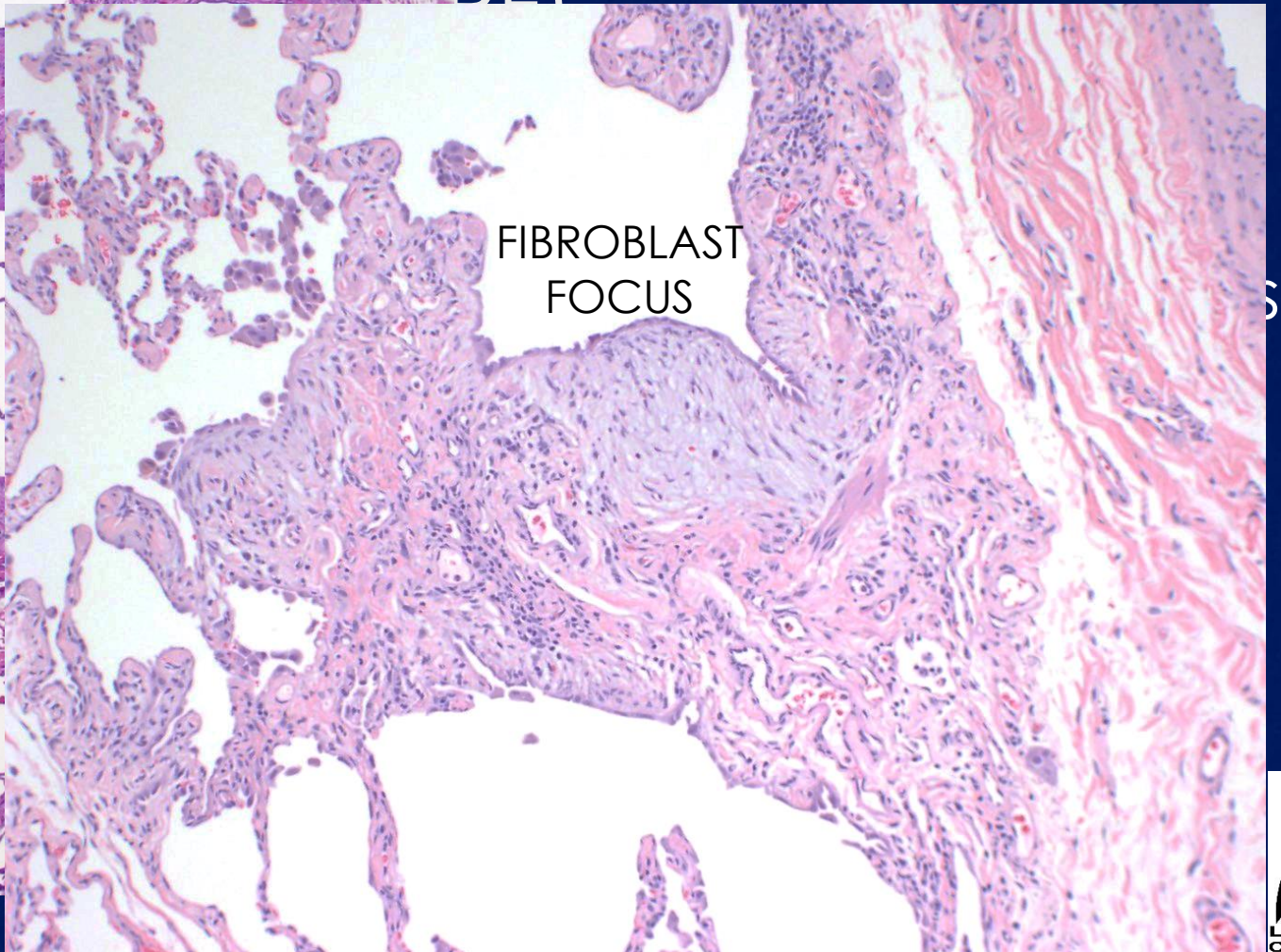
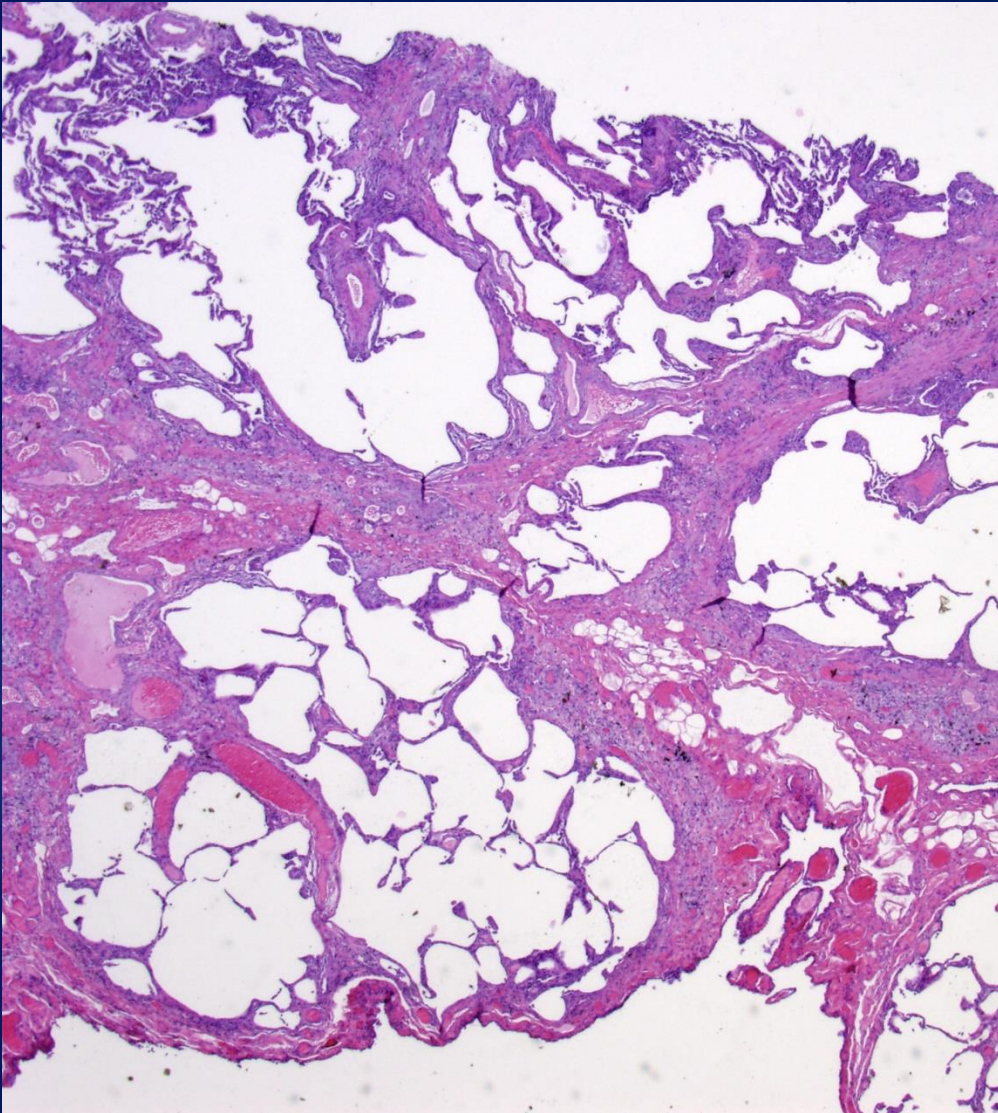
Honeycomb Lung



The most common cause of honeycomb lung

(UIP) in clinical

DE)



FIBROBLAST
FOCUS

sis
for





Commentary



Importance of DOMAINS

The four Domains

Clinical/lab presentation

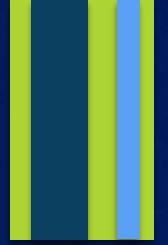
Radiologic findings

Pathologic injury pattern

Disease entity that fits



Clinical Domain



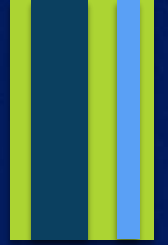
Acute: Hours to days in evolution

Subacute: Weeks to months in evolution

Chronic: Months to years in evolution



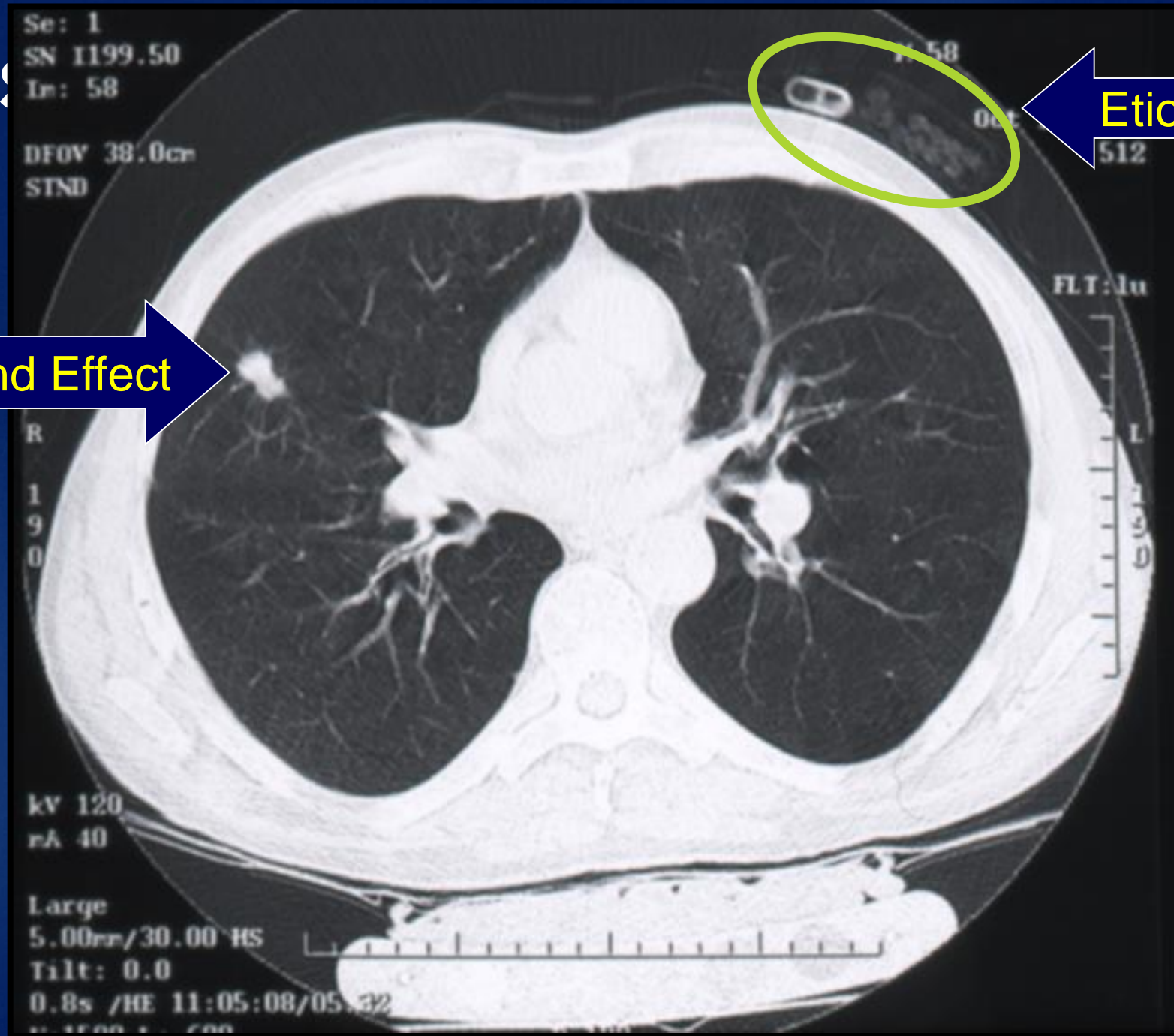
Radiological Domain



1. **Acute:** Ground Glass and consolidation
2. **Subacute:** Ground glass and consolidation
(+/- Air trapping)
3. **Chronic:** Reticulation and structural distortion
(+/- honeycomb cysts)



The Chest domain!

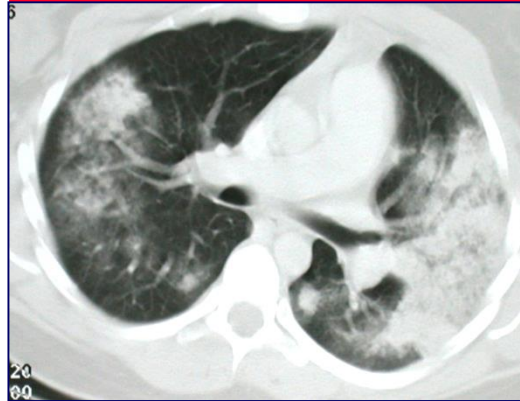


End Effect

Etiology



The 4 CT Patterns of Pulmonary Disease

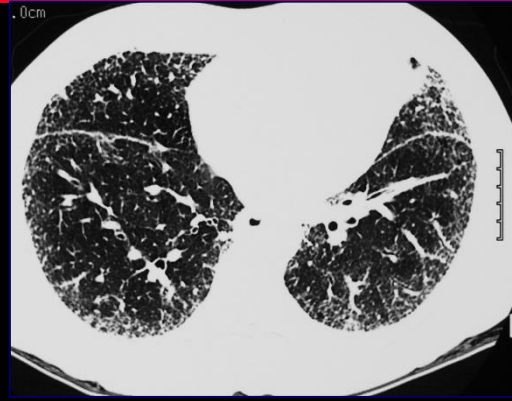


Ground Glass and consolidation

Alveolar Filling
 Neutrophils
 Edema
 Macrophages
 Hemorrhage/Fibrin/protein
 Fibroblasts
 Organizing pneumonia
 (any cause)

Interstitial cells/ protein
 Lymphocytes
 Neutrophils
 Edema/fibrin

Interstitial fibrosis (mild)

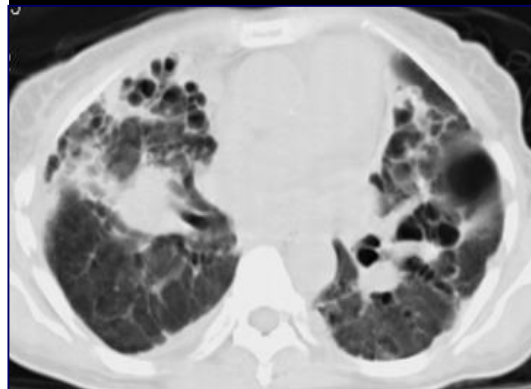


Fibrosis

Alveolar Filling
 Neutrophils
 Edema
 Macrophages
 Hemorrhage/Fibrin/protein
 Fibroblasts
 Organizing pneumonia
 (any cause)

Interstitial cells/ protein
 Lymphocytes
 Neutrophils
 Edema/fibrin

Interstitial fibrosis (mild)



Nodules

Alveolar Filling
 Neutrophils
 Edema
 Macrophages
 Hemorrhage/Fibrin/protein
 Fibroblasts
 Organizing pneumonia
 (any cause)

Interstitial cells/ protein
 Lymphocytes
 Neutrophils
 Edema/fibrin

Interstitial fibrosis (mild)



Mosaic patterns and cysts

Alveolar Filling
 Neutrophils
 Edema
 Macrophages
 Hemorrhage/Fibrin/protein
 Fibroblasts
 Organizing pneumonia
 (any cause)

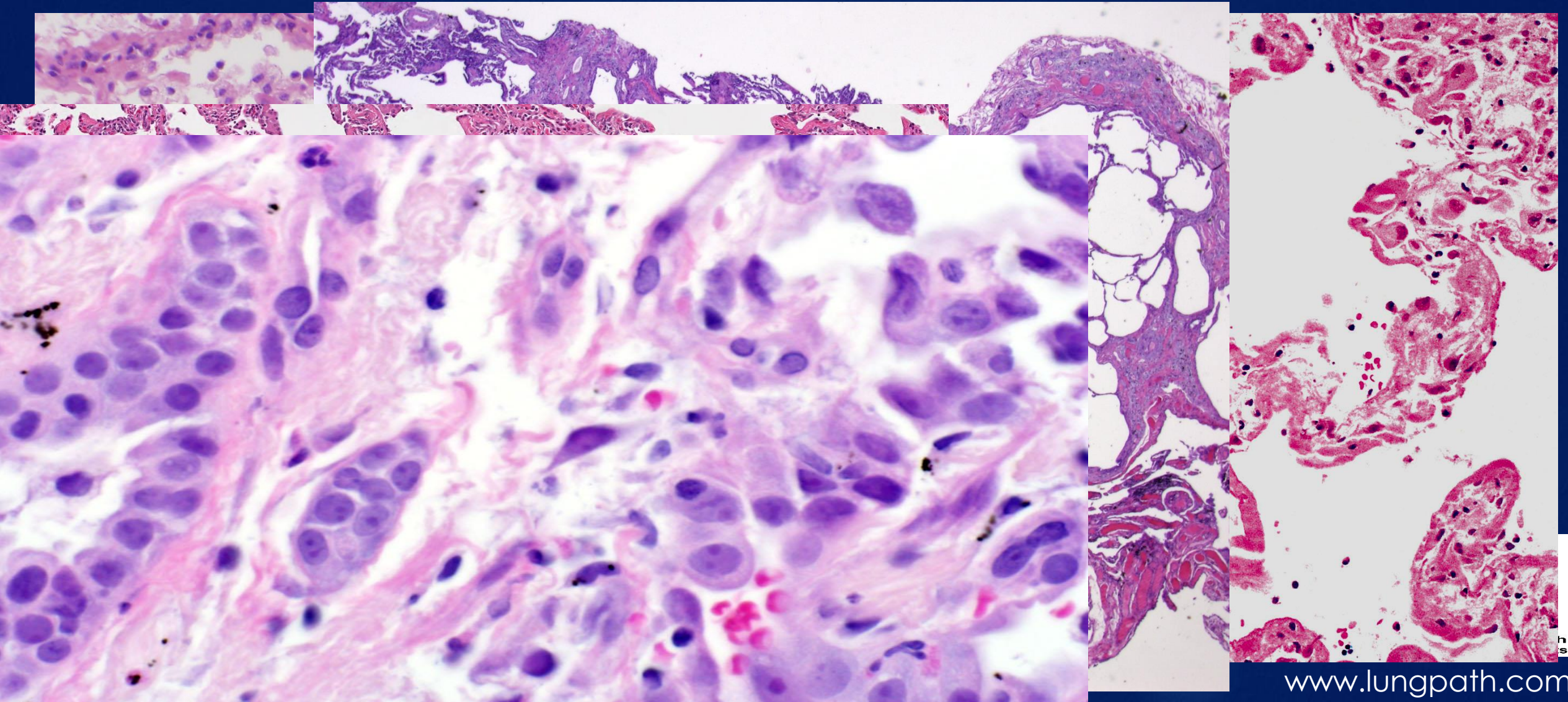
Interstitial cells/ protein
 Lymphocytes
 Neutrophils
 Edema/fibrin

Interstitial fibrosis (mild)

**Differential
 diagnosis**



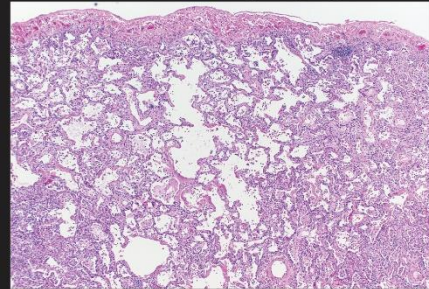
Pathology Domain



The 6 PATTERNS of PULMONARY PATHOLOGY

Kevin O. Leslie, M.D.

1. Acute Lung Injury



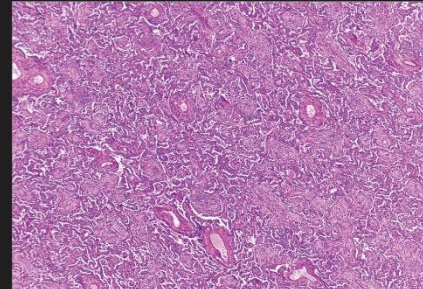
w/ Hyaline membranes (DAD)
Infection
Collagen vascular disease
Drug toxicity
Idiopathic (acute interstitial pneumonia)
Clinical ARDS

w/ Eosinophils
Atopic eosinophilic pneumonia
Drug toxicity
Diffuse alveolar damage in smokers

w/ Necrosis
Infectious
- Viral
- Bacterial
- Fungal
Some tumors

w/ Macrophages
Diffuse alveolar hemorrhage
Collagen vascular diseases
DAD in smokers

4. Alveolar Filling



w/ Macrophages
Smoking related
(RBH/HL/D/DP)
Local fibrosis effect
Airway obstruction

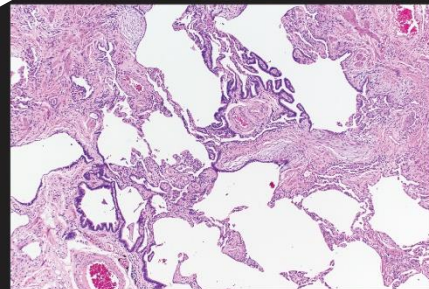
w/ Neutrophils
Infection
Diffuse alveolar hemorrhage

w/ Organizing pneumonia
Drug toxicity
Collagen vascular diseases
Cryptogenic organizing pneumonia
(a.k.a. idiopathic BOOP)

w/ Eosinophilic material
Infection
Collagen vascular diseases
Drug toxicity
Diffuse alveolar hemorrhage
Pulmonary alveolar proteinosis

w/ Hemorrhage
Collagen vascular diseases
Drug toxicity
Diffuse alv. hemorrhage
Atrial
Congestive heart failure

2. Fibrosis



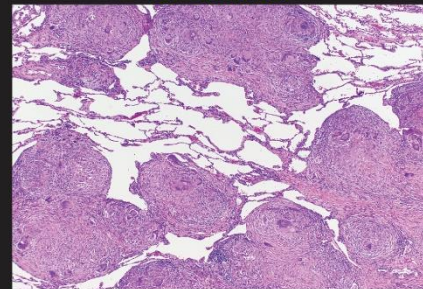
w/ Variable fibrosis
(normal => honeycombing)
Usual interstitial pneumonia/IPF
Asbestosis
Rheumatoid arthritis
Chronic hypersensitivity pneumonitis
Pulmonary Langerhans cell histiocytosis (mainly as reticulate scars)

w/ Honeycombing only
(Diffuse disease on CT scan)
Usual interstitial pneumonia (late)
Epidemic disease in CF
Many causes (e.g. middle lobe syndrome)

w/ Diffuse alveolar wall fibrosis
Collagen vascular disease
Drug toxicity
Sarcoid (with granulomas)
Pneumoconiosis
Fibrotic nonspecific interstitial pneumonia (NSIPF)

w/ Plicaritis
vascular disease

5. Nodules



w/ Lymphoid cells
Wegener's
Diffuse lymphoid hyperplasia
Lymphoma

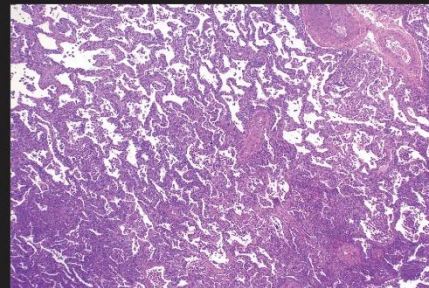
w/ Necrosis
Infections
Nocardiosis
Wegener's

w/ Atypical cells
Infections
Carcinomas
Lymphomas
Sarcomas

w/ Stellate scars
Pulmonary Langerhans cell histiocytosis (PLCH)

With Organizing Pneumonia
Organizing infections
Collagen vascular diseases
Drug toxicity
Wegener's
Organizing aspiration
Infarct

3. Cellular Infiltrates



w/ Lymphocytes and plasma cells
Hypersensitivity pneumonitis
Collagen vascular diseases
Lymphoid interstitial pneumonitis
Nonspecific interstitial pneumonia, cellular form
Certain drug toxicities and infections
Lymphoproliferative diseases

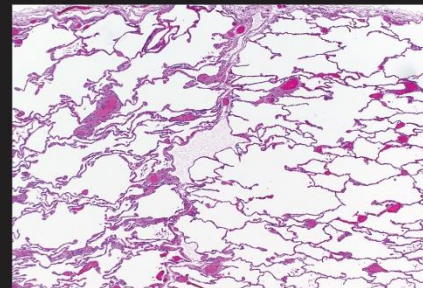
w/ Neutrophils
Infection
Collagen vascular diseases
Hemorrhagic syndromes

w/ Granulomas
Infection
Hypersensitivity pneumonitis
Sarcoidosis/Berylliosis
Aspiration

w/ Focal organizing pneumonia
Infection
Collagen vascular diseases
Drug toxicity
Cryptogenic organizing pneumonia

w/ Plicaritis
Collagen vascular diseases

6. Minimal Changes



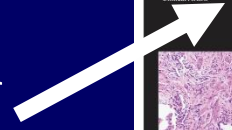
w/ Small Airways Disease
Constrictive bronchiolitis

w/ Vascular Disease
Pulmonary hypertension
Veno-occlusive disease (PVOD)

w/ Cysts
Pulmonary Langerhans cell histiocytosis (PLCH)
Lymphangioleiomyomatosis (LAM)

w/ No specific findings
Early acute injury?
Pulmonary edema?
Sampling error?

Differential diagnosis



Patterns of Acute Injury with DDX

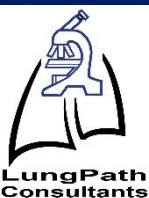
DIFFUSE ALVEOLAR DAMAGE From infection From CVD From unknown cause (AIP)
From drug or toxin In clinical ARDS

ACUTE EOSINOPHILIC PNEUMONIA Asthma From drug From unknown cause (Idiopathic)

ACUTE FIBRINOUS AND ORGANIZING PNEUMONIA (AFOP)

VASCULITIC AND IMMUNOLOGIC DISEASES Granulomatosis w/ polyangiitis (Wegener)
Systemic connective tissue diseases
Anti-GBM disease (Goodpasture)
Microscopic polyangiitis
Churg-Strauss syndrome

ACUTE EXACERBATION OF CHRONIC DISEASE e.g. of IPF



The “Litany” in Cases of Acute Lung Injury

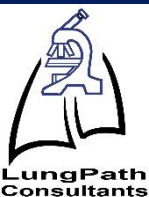
FIRST Look for **Bugs** Do at least AFB and GMS!

NEXT Rule out **Drugs** (clinical record)

THEN Check the **Serology** + CBC + Sed rate

All NEG? Clinician calls it “idiopathic”

Histopathology rarely solves
these issues alone



How different biopsy techniques influence the diagnosis



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



LungPath
Consultants

Key References

Practical Pulmonary Pathology. A Diagnostic Approach, 3rd Ed. Elsevier Sciences. 2015

Leslie, KO: My Approach to Interstitial Lung Disease, J Clin Pathol J Clin Pathol 62:387-401, 2009

Leslie KO: Transbronchial biopsy interpretation in the patient with diffuse parenchymal; lung disease. Arch Pathol Lab Med 131:407-23 2007



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



AUDIENCE

Comments and Questions?

