

# **LUNG FIBROSIS FROM THE PATHOLOGIST'S POINT OF VIEW**

**THOMAS V. COLBY MD**

**MAYO CLINIC IN ARIZONA**

# KEY POINTS:

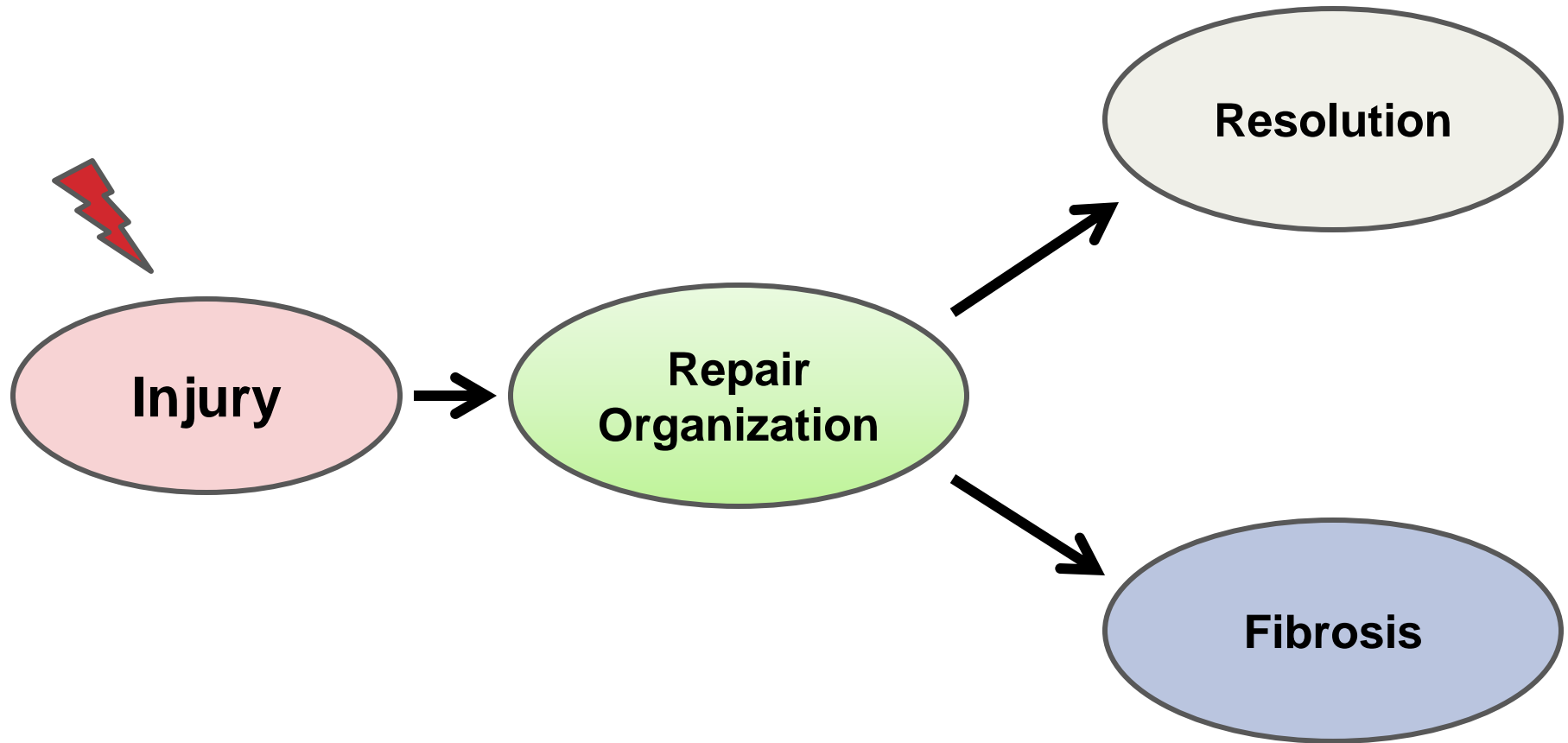
**Not all “fibrosis” in the lung has the same clinical and prognostic implications.**



**Fibroblastic proliferation  $\neq$  Fibrosis**

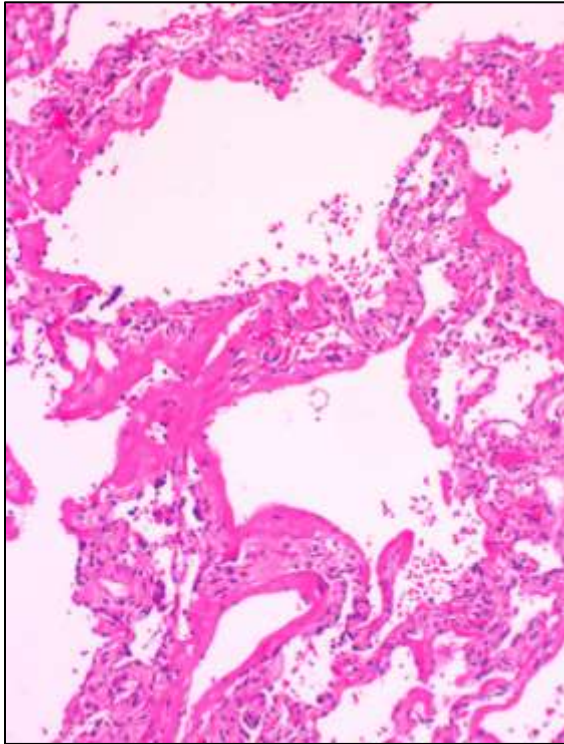
**Not all fibroblastic proliferations in the lung result in irreversible scarring.**

# LUNG INJURY AND FIBROSIS

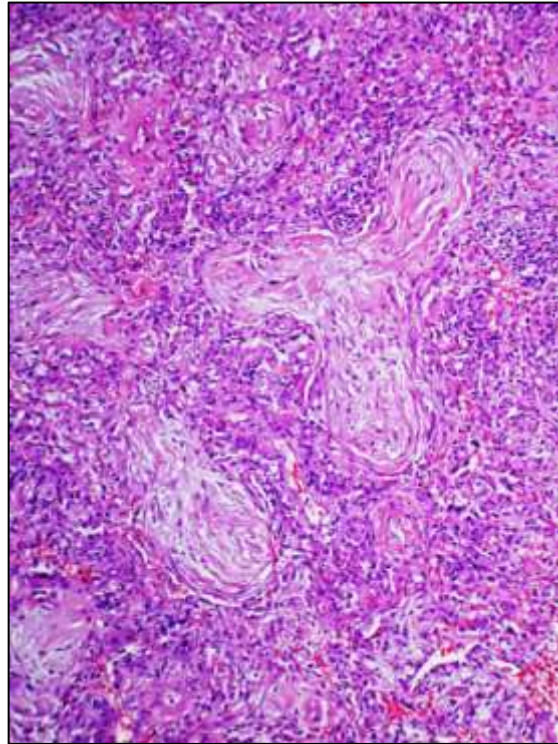


**Clinical presentation (and biopsy) can be at any point**

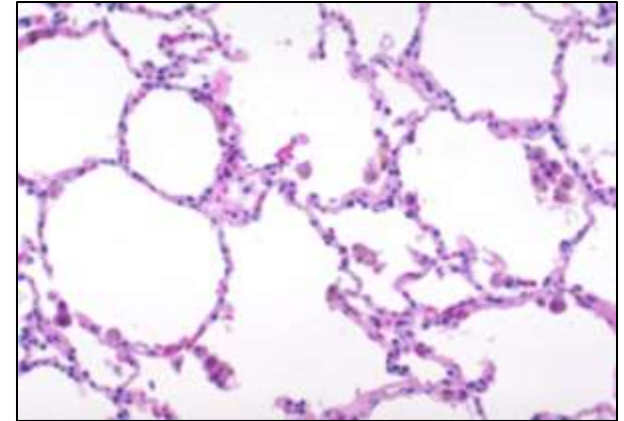
# **EXAMPLE: DIFFUSE ALVEOLAR DAMAGE**



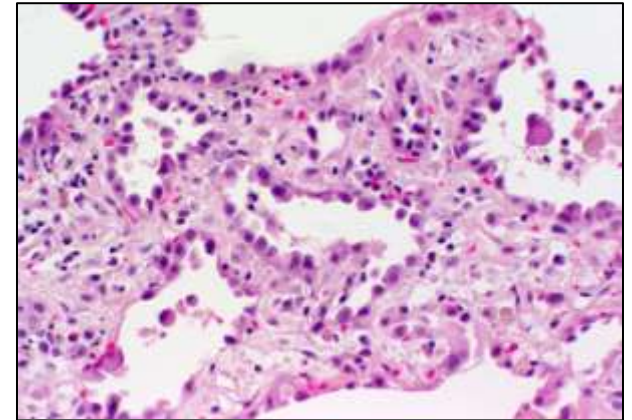
Acute injury with hyaline membranes



Repair with airspace organization

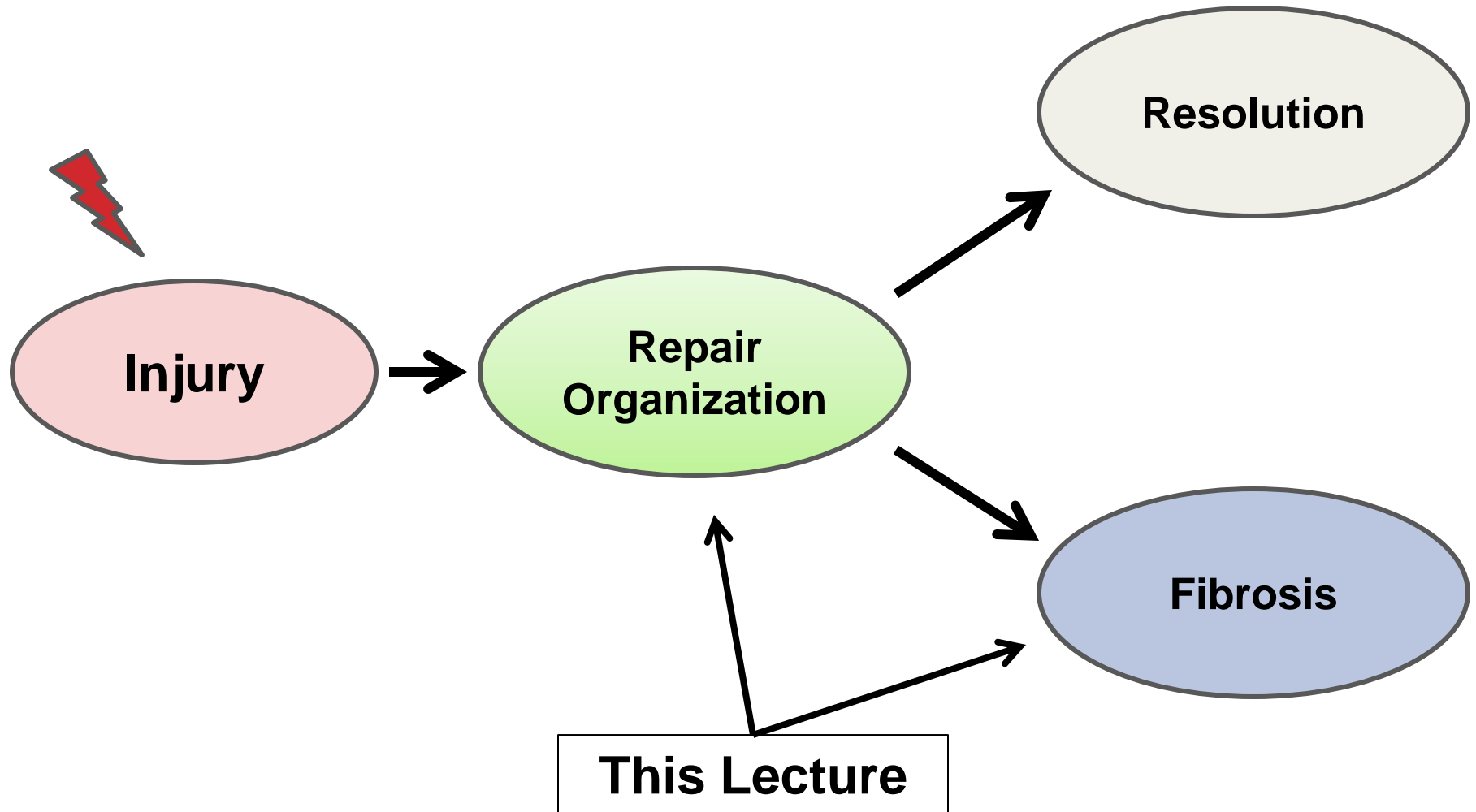


Resolved/healed with normal histology

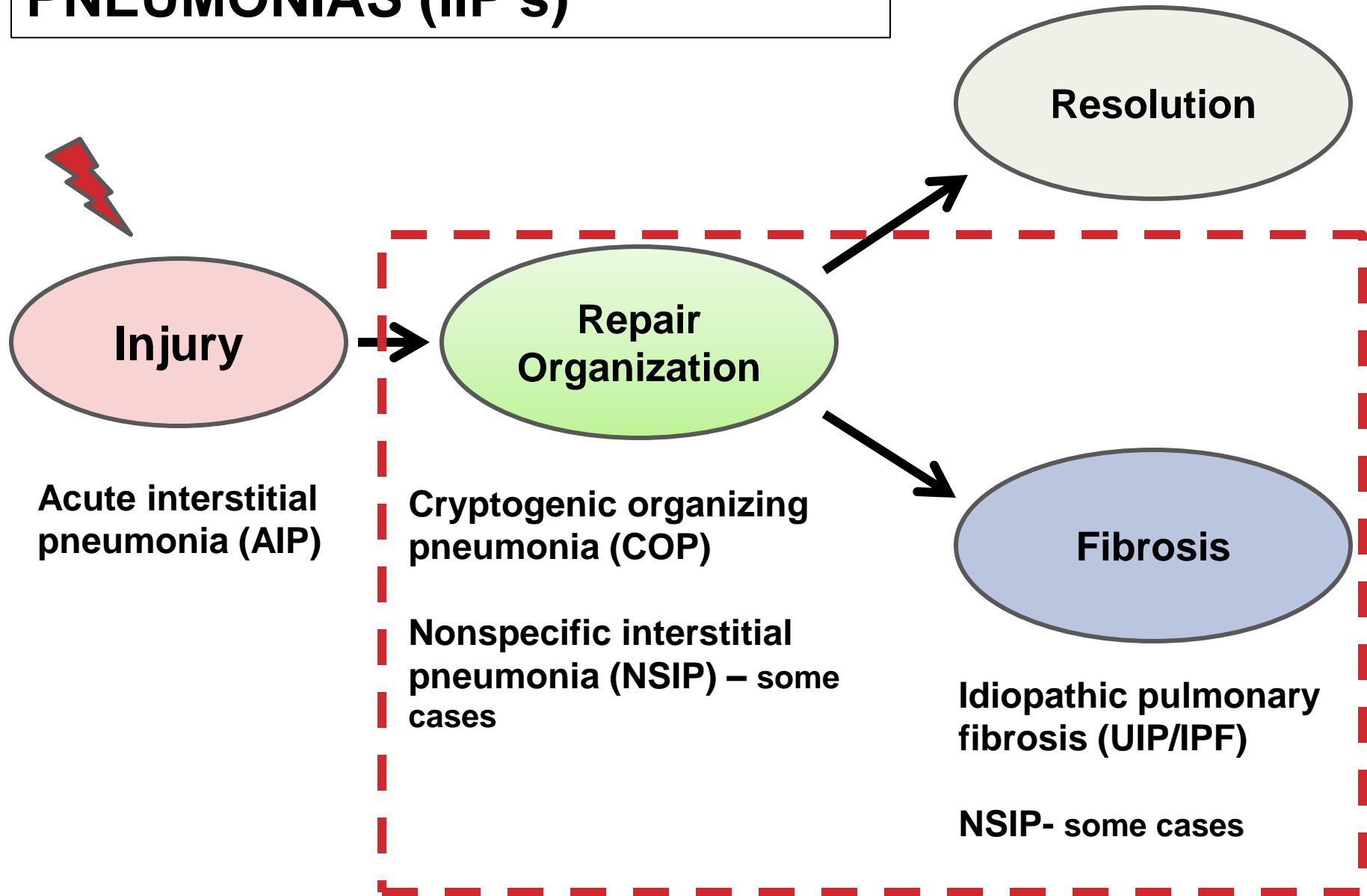


Resolved/healed with interstitial fibrosis

# LUNG INJURY AND FIBROSIS



# IDIOPATHIC INTERSTITIAL PNEUMONIAS (IIP's)



# Patterns seen histologically

## Repair Organization

(These are potentially reversible)

Organizing diffuse alveolar damage  
(ARDS/DAD)

Cryptogenic organizing pneumonia  
(COP)

Eosinophilic pneumonia

Hypersensitivity pneumonitis (HP)

NSIP- some cases

**Some examples**



## Fibrosis

(These are irreversible)

Idiopathic pulmonary fibrosis  
(UIP/IPF)

Other causes of UIP pattern

NSIP- some cases

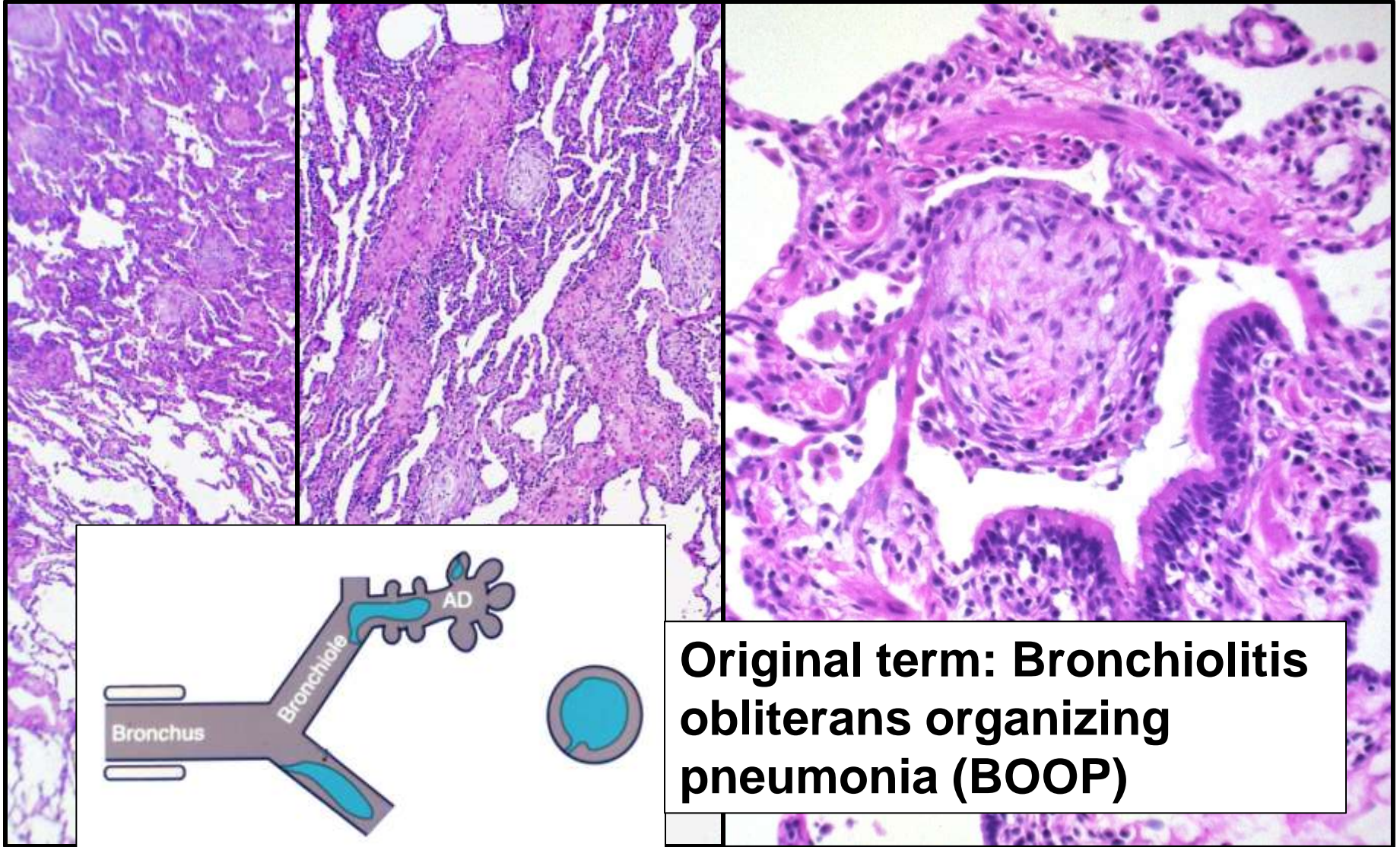
Fibrotic Pulmonary Langerhans  
cell histiocytosis (PLCH)

Pleuroparenchymal fibroelastosis  
(PPFE)

Fibrotic Sarcoidosis



# CRYPTOGENIC ORGANIZING PNEUMONIA (COP)

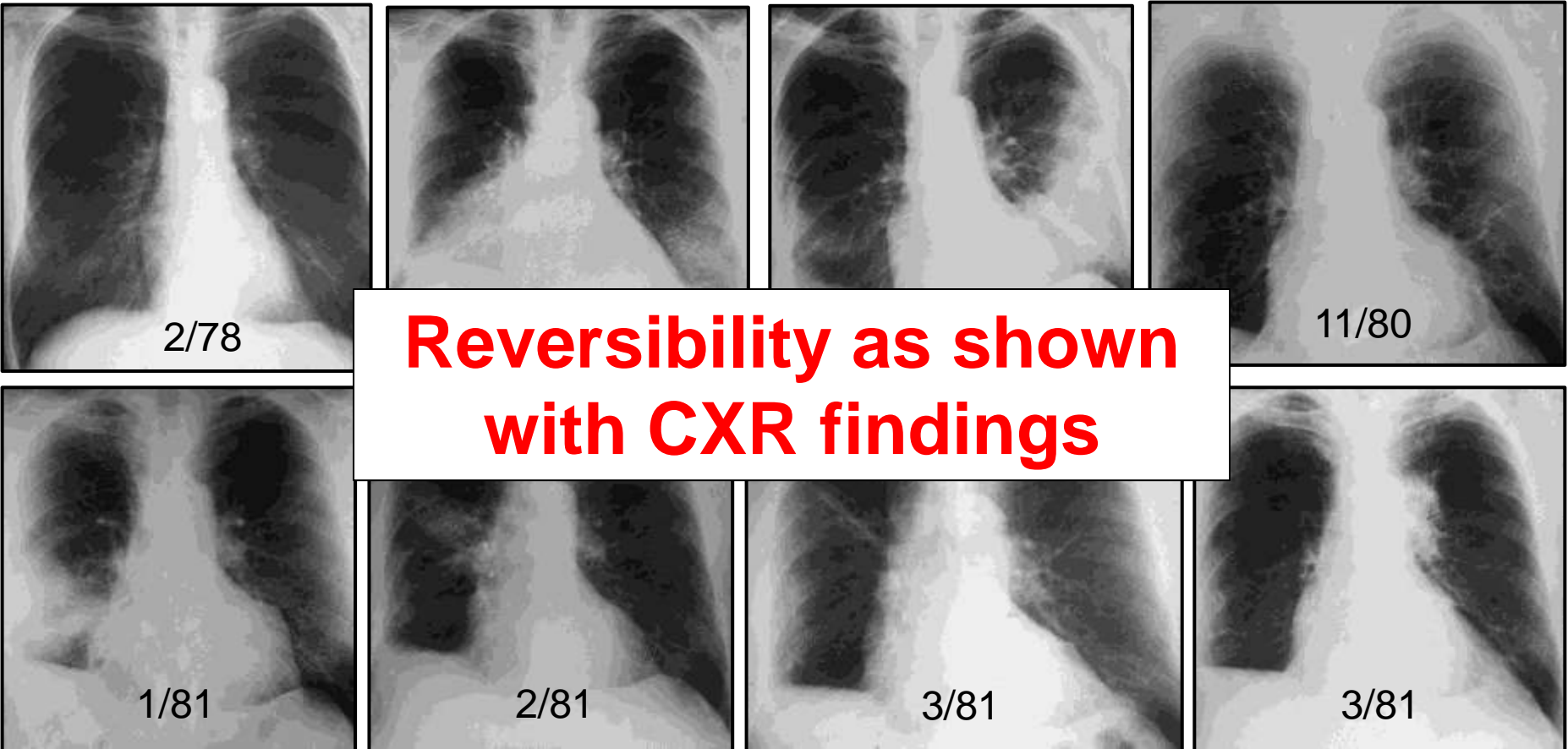


**Original term: Bronchiolitis obliterans organizing pneumonia (BOOP)**



# CRYPTOGENIC ORGANIZING PNEUMONIA (COP)

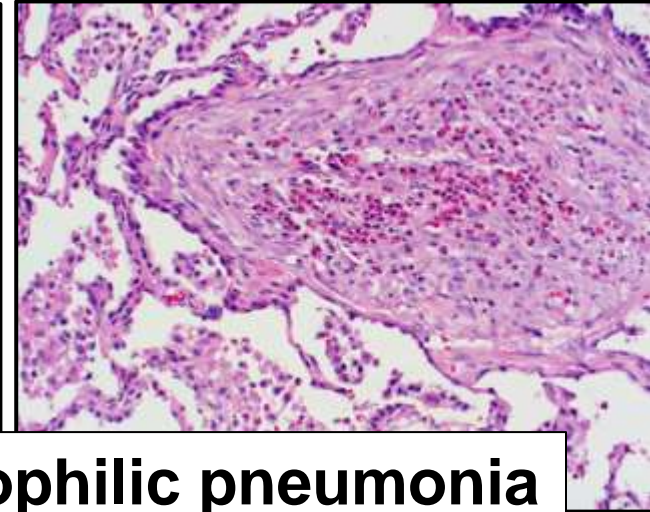
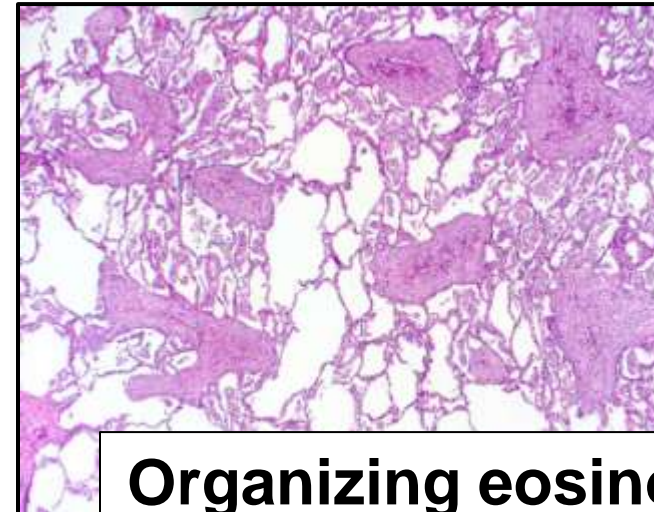
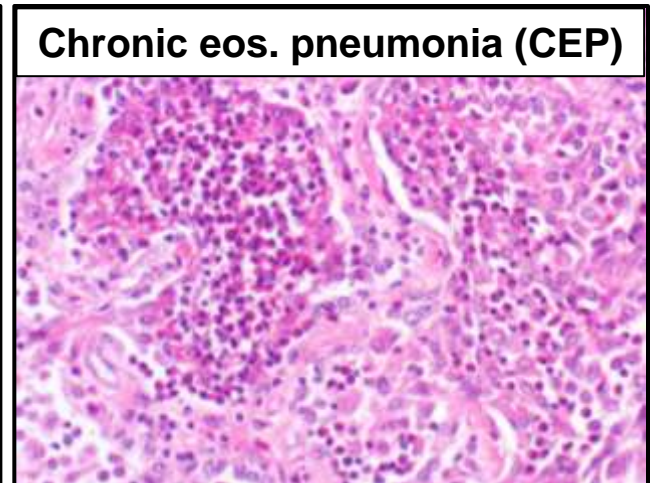
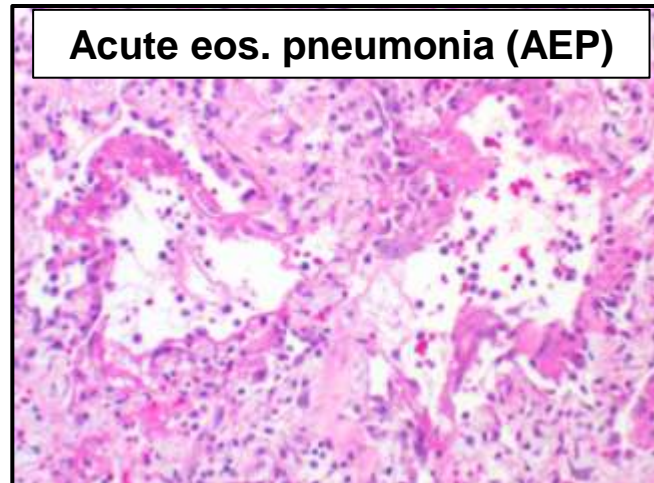
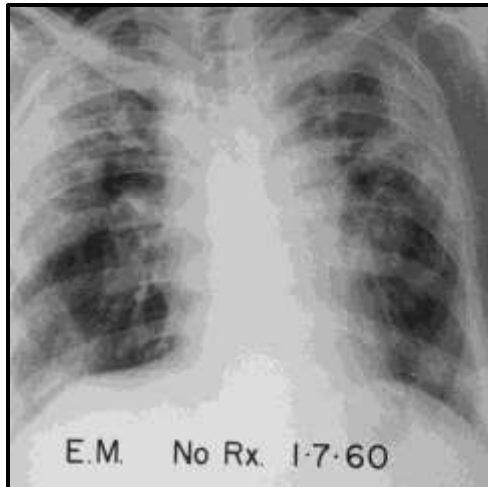
Outcome following steroids: 2/3's resolve completely, 1/3 with recurrent/persistent disease (Schwarz and King 2011)



This case reported in the 1985 NEJM series of BOOP by Epler et.al.

# EOSINOPHILIC PNEUMONIA

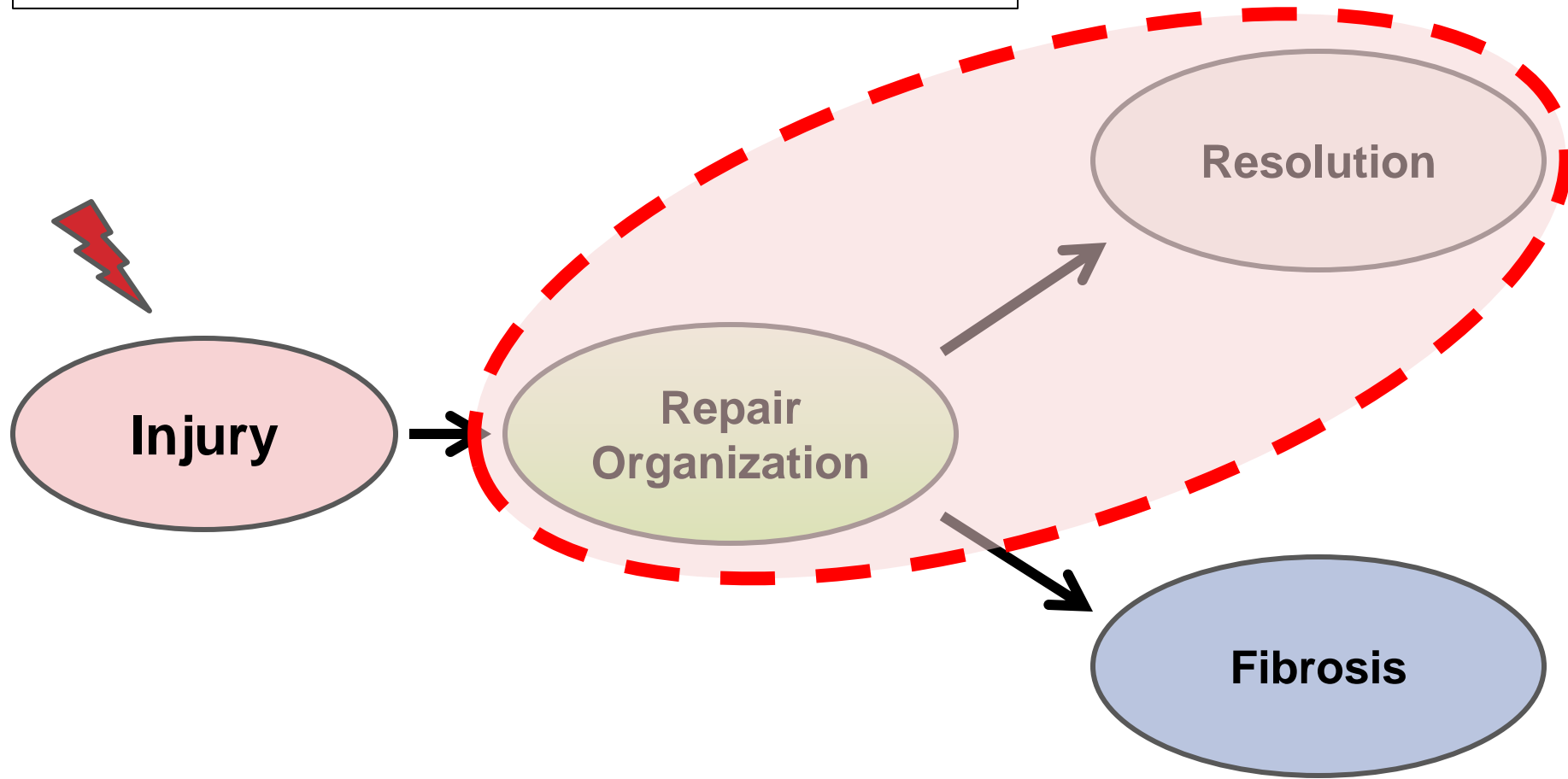
Outcome following steroids: Dramatic response with clearing of infiltrates; long steroids often needed for CEP but not AEP (Schwarz and King 2011)



Original CEP case NEJM 1969

**Organizing eosinophilic pneumonia**

# LUNG INJURY AND FIBROSIS



**Many organizing fibroblastic tissue resolves completely;  
some lead to irreversible fibrosis (eg fibroblast foci)**

# Clinical Syndromes: patterns seen histologically

## Repair Organization

(These are potentially reversible)

Organizing diffuse alveolar damage  
(ARDS/DAD)

Cryptogenic organizing pneumonia  
(COP)

Eosinophilic pneumonia

Hypersensitivity pneumonitis (HP)

NSIP- some cases

## Fibrosis

(These are irreversible)

Idiopathic pulmonary fibrosis  
(UIP/IPF)

Other causes of UIP pattern

NSIP- some cases

Pulmonary Langerhans cell

histiocytosis (PLCH)

Pleuroparenchymal fibroelastosis  
(PPFE)

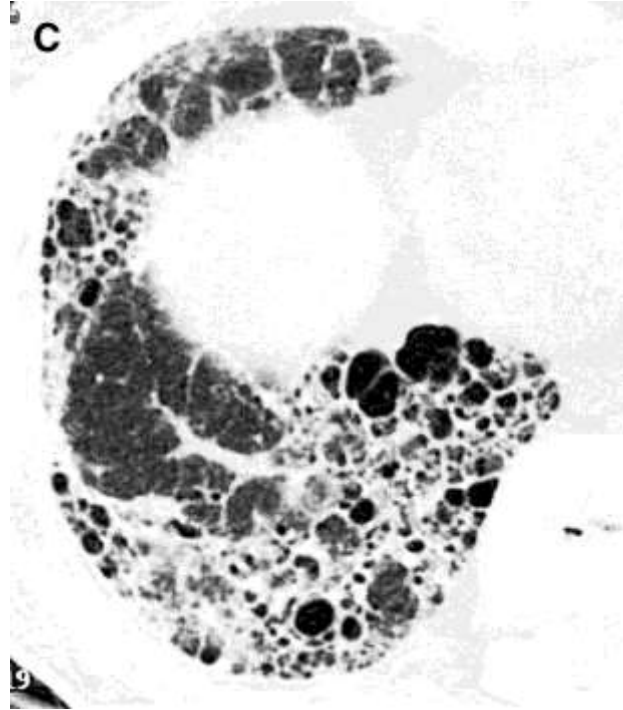
Some examples



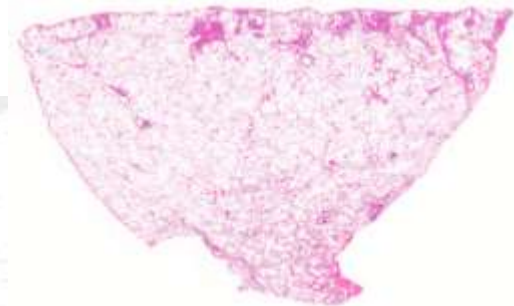
# IDIOPATHIC PULMONARY FIBROSIS (IPF)

Usual interstitial pneumonia histologically

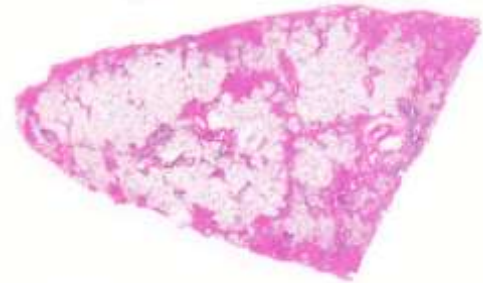
Clinically/radiologically progressive; median survival 3-5 yrs



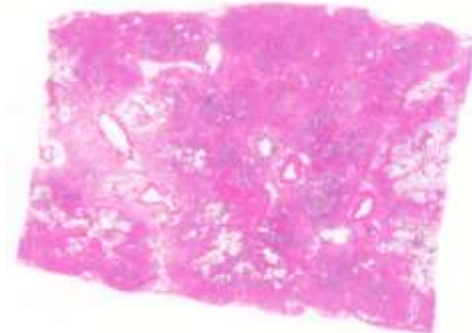
ATS/ERS IIP 2002



RUL

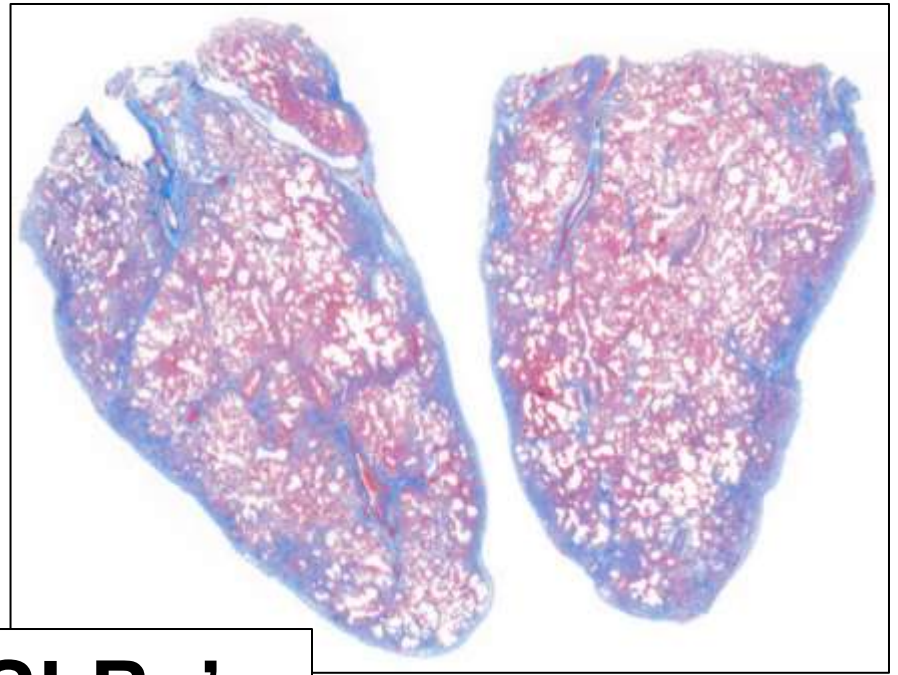
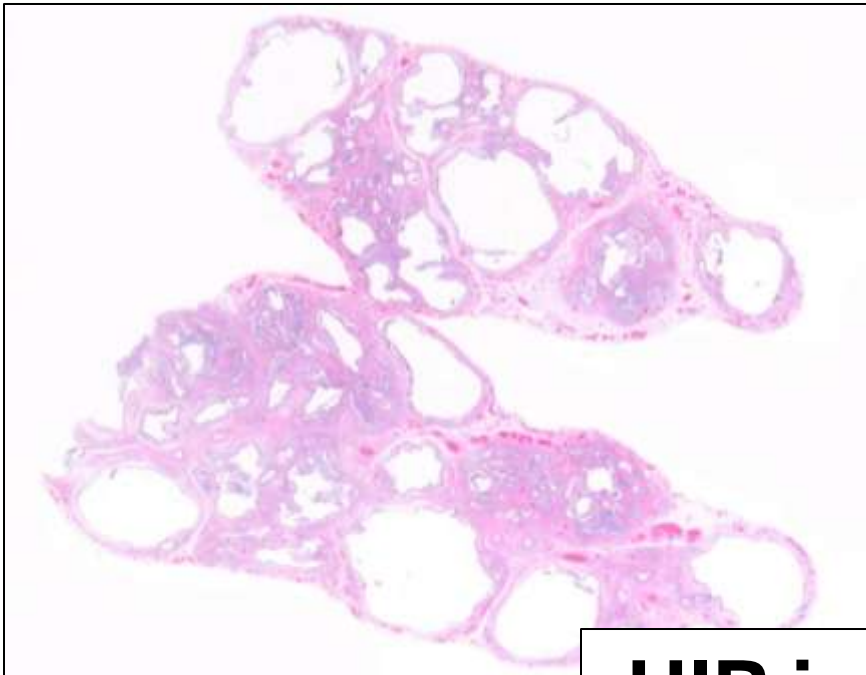


RML

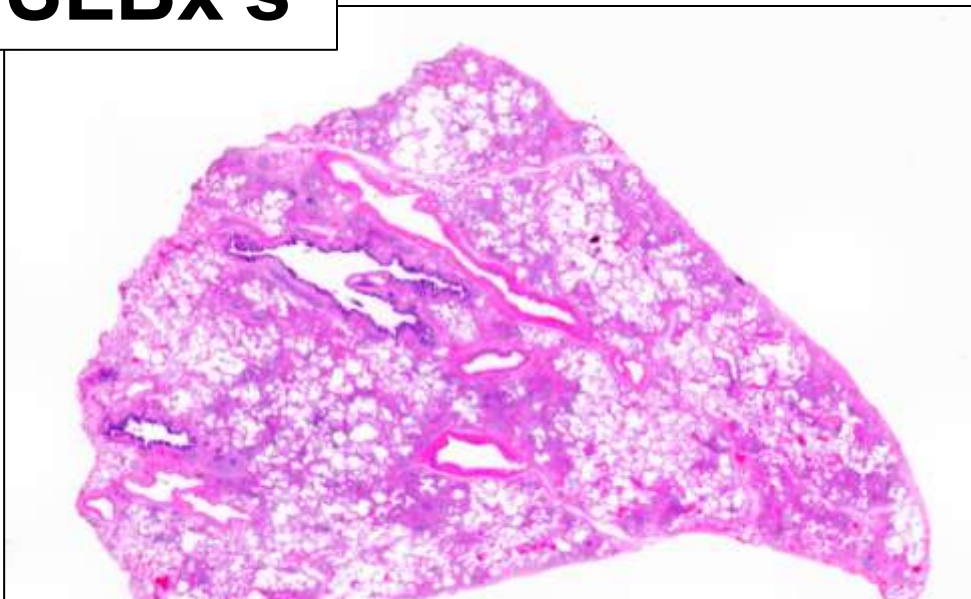
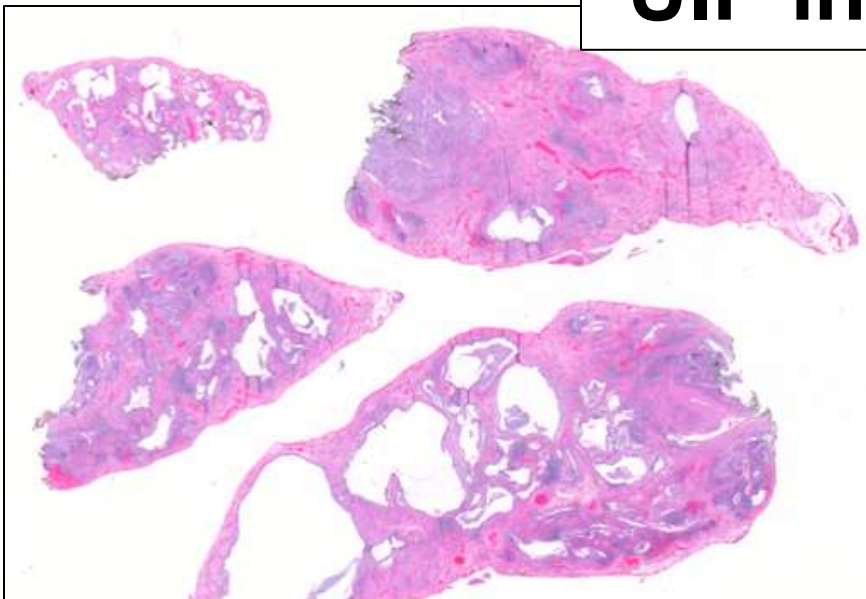


RLL





## UIP in SLBx's



**Note: Patchy, often subpleural, process; Honeycombing not always present**

# FIBROSIS IN UIP/IPF

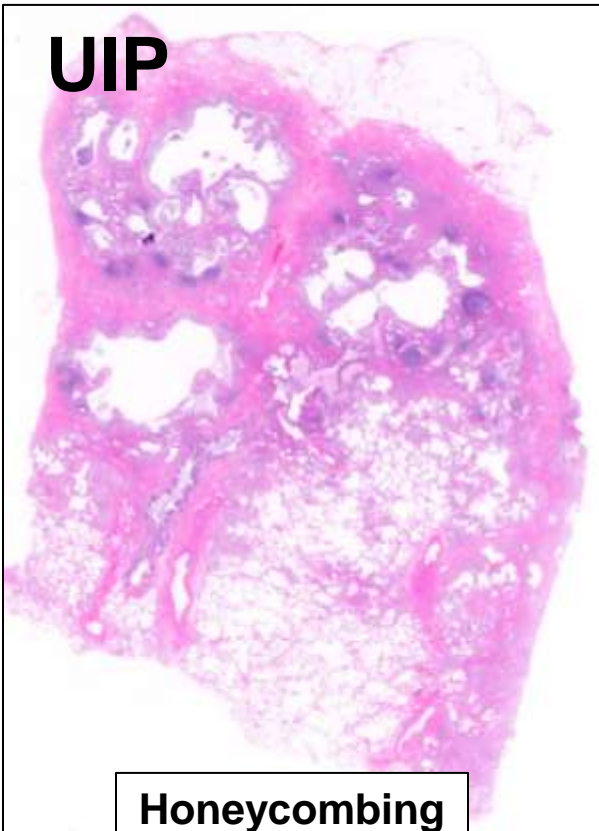
Honeycombing is best known....but....

Honeycombing  $\neq$  UIP/IPF....and....

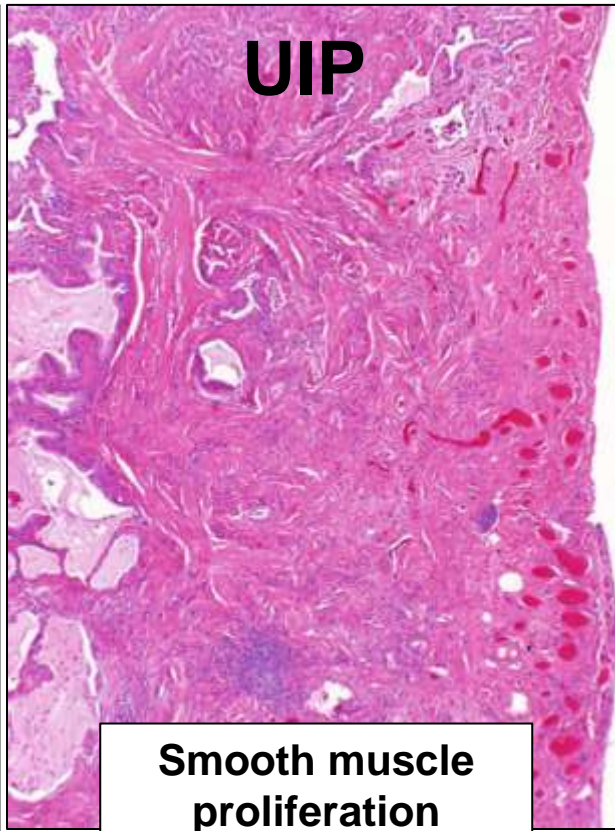
There are cases of UIP/IPF without honeycombing

The essence of UIP/IPF is irreversible destruction of lung architecture by scarring that may manifest as:

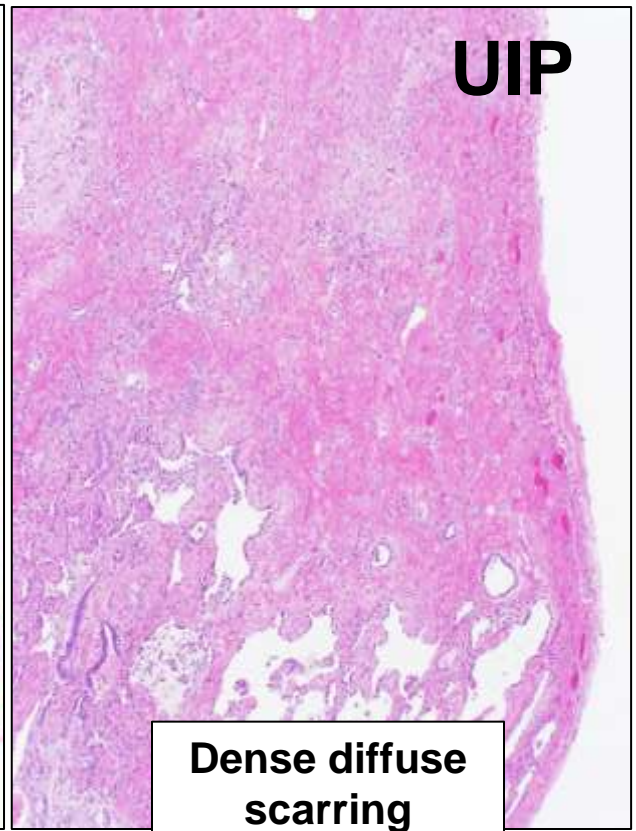
**UIP**



**UIP**



**UIP**



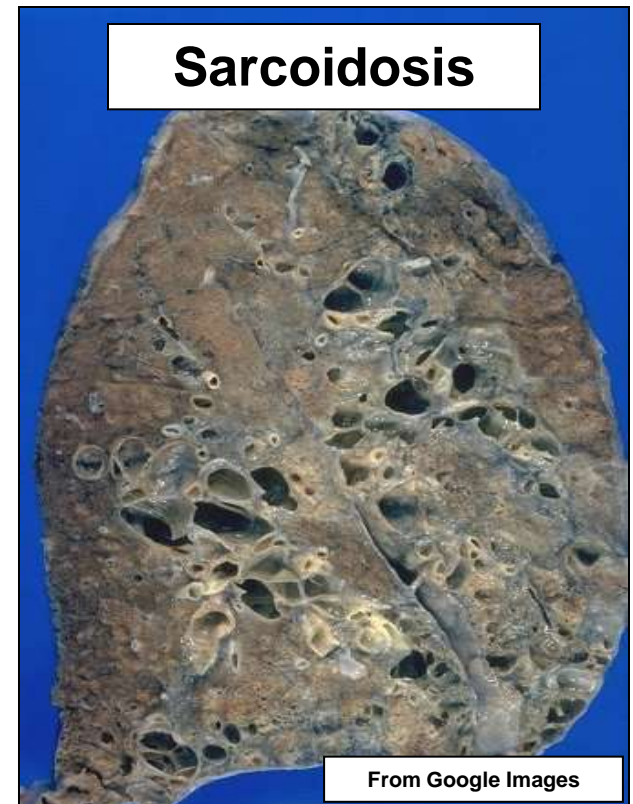


# “HONEYCOMBING”

Honeycombing is not a specific disease. It is the late stage of a number of conditions, of both known and unknown cause, notably asbestosis, usual interstitial pneumonia (UIP) and sarcoidosis



From Google Images



Sarcoidosis

From Google Images

# **HONEYCOMBING: DEFINITION**

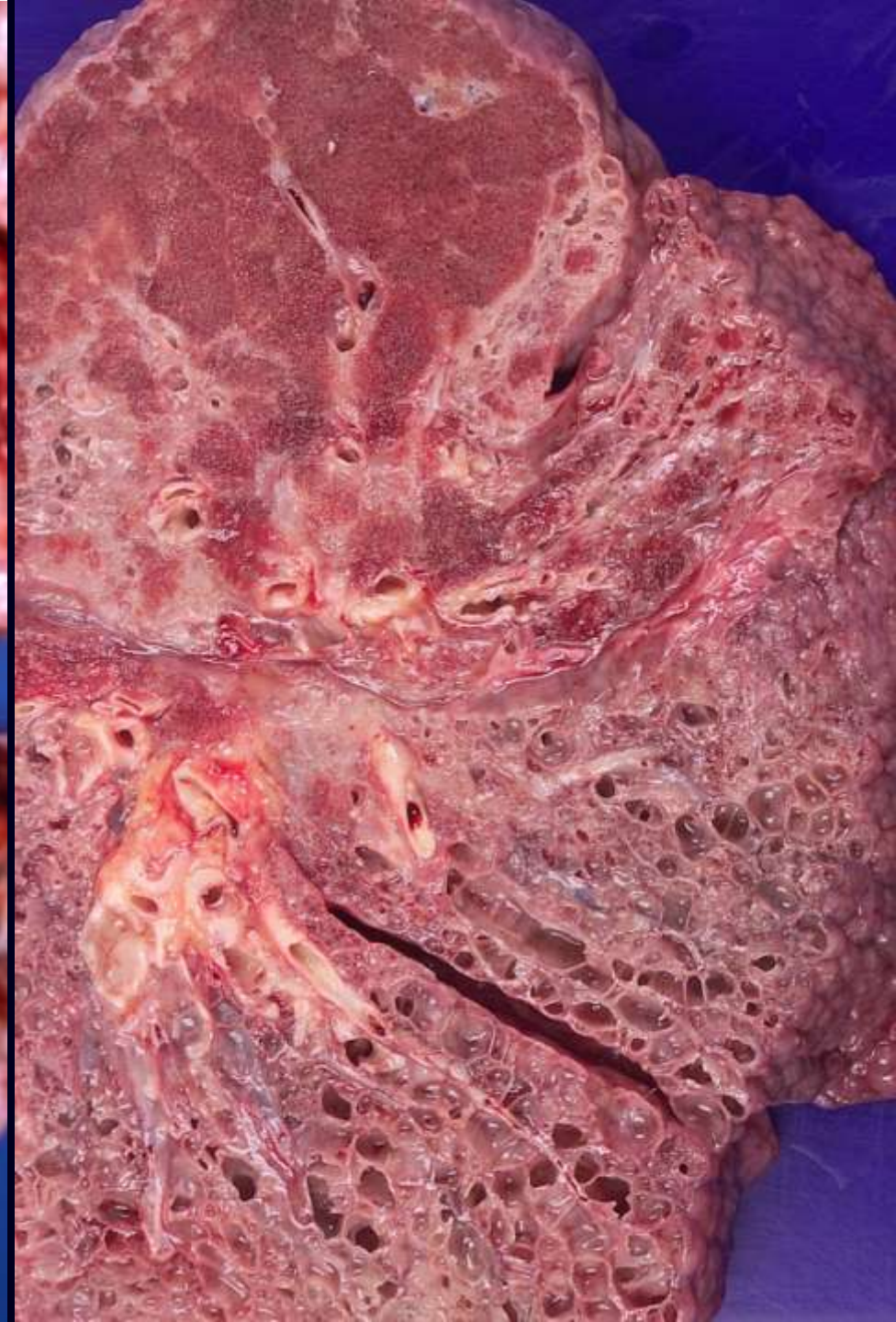
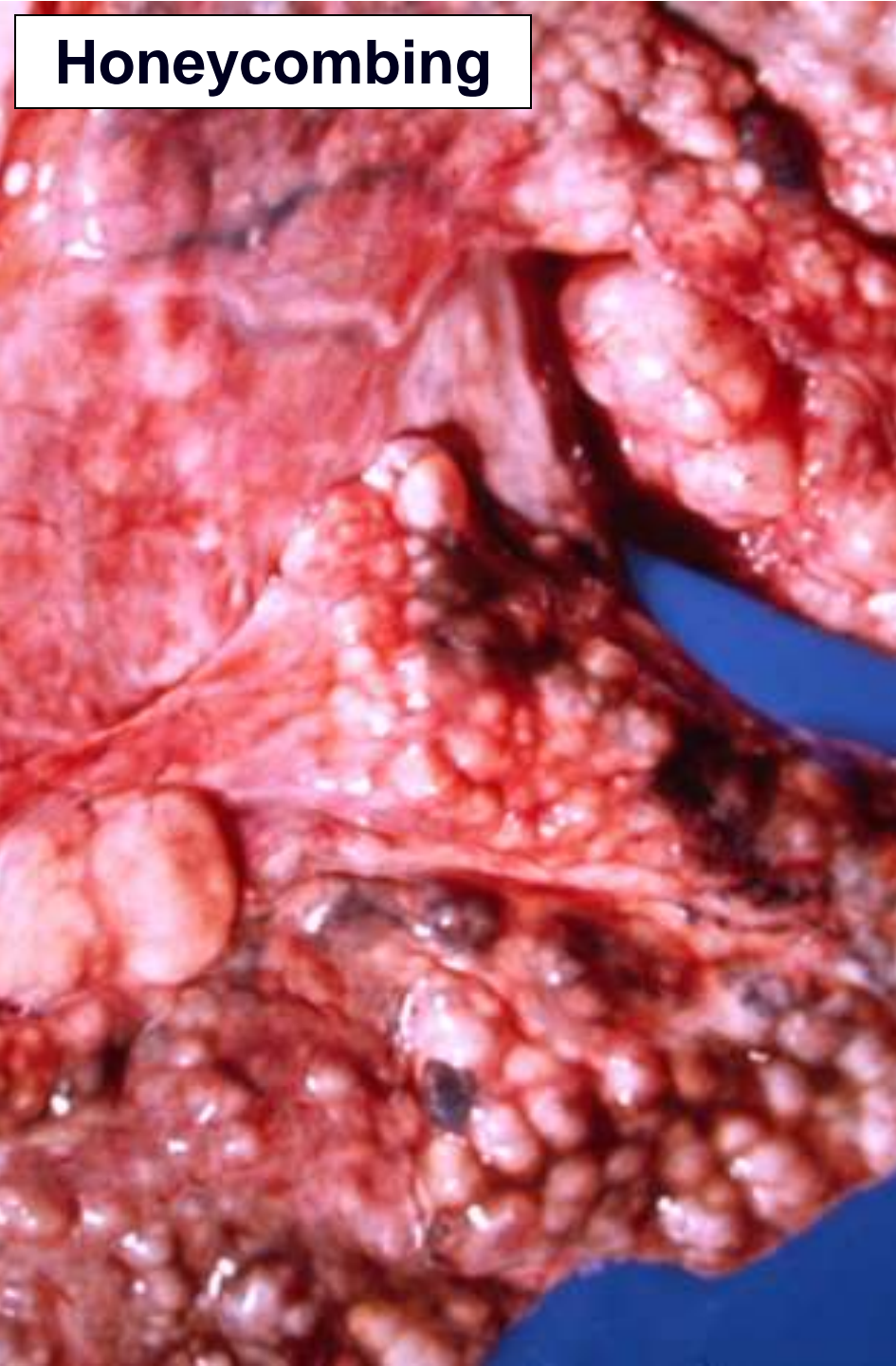
**(HANSELL 2008, FROM GENEREUX)**

**“...destroyed and fibrotic tissue containing...cystic airspaces with thick fibrous walls...with complete loss of acinar architecture...the cysts have variable wall thickness...lined by metaplastic bronchiolar epithelium.”**

**Never uniform throughout the lungs**

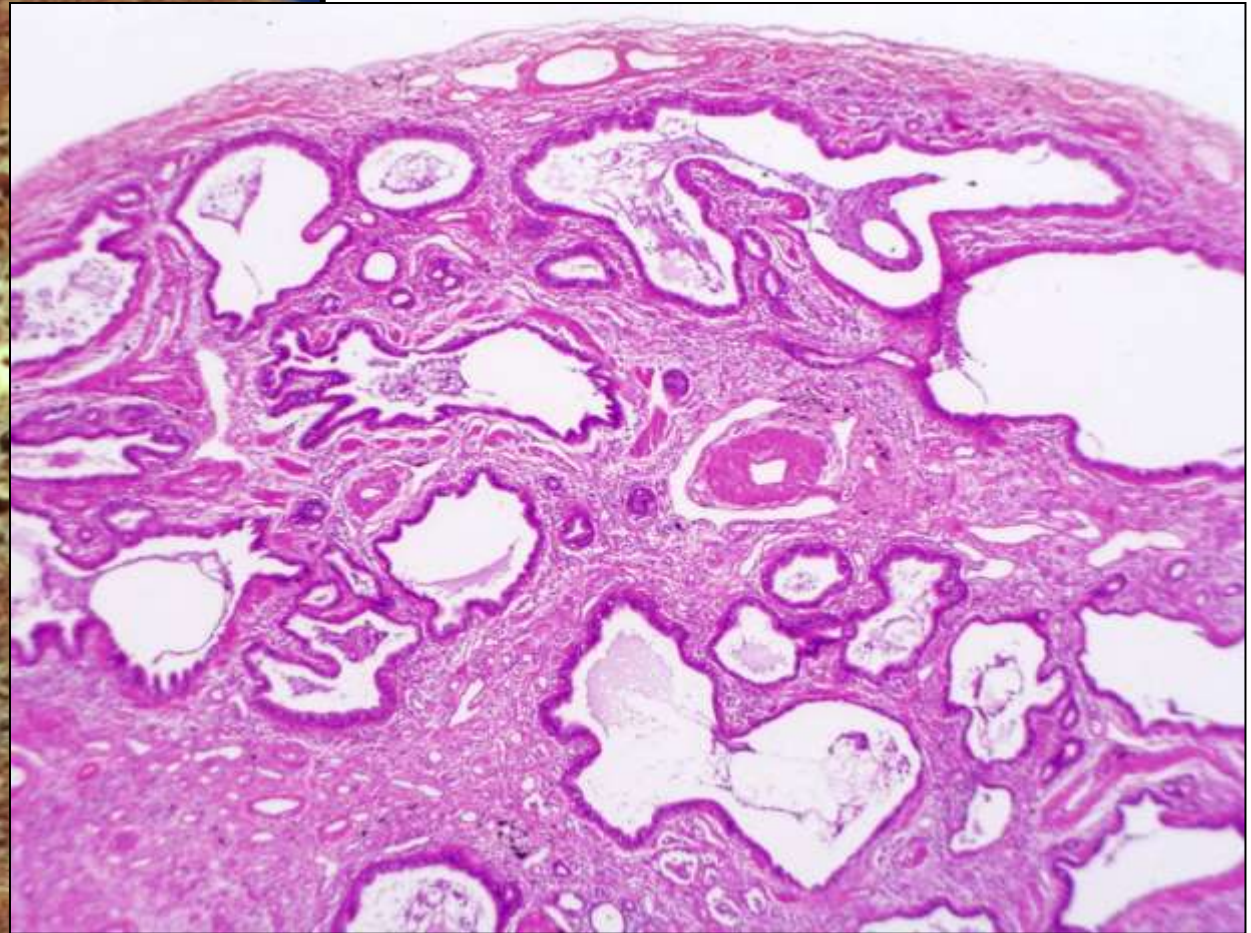
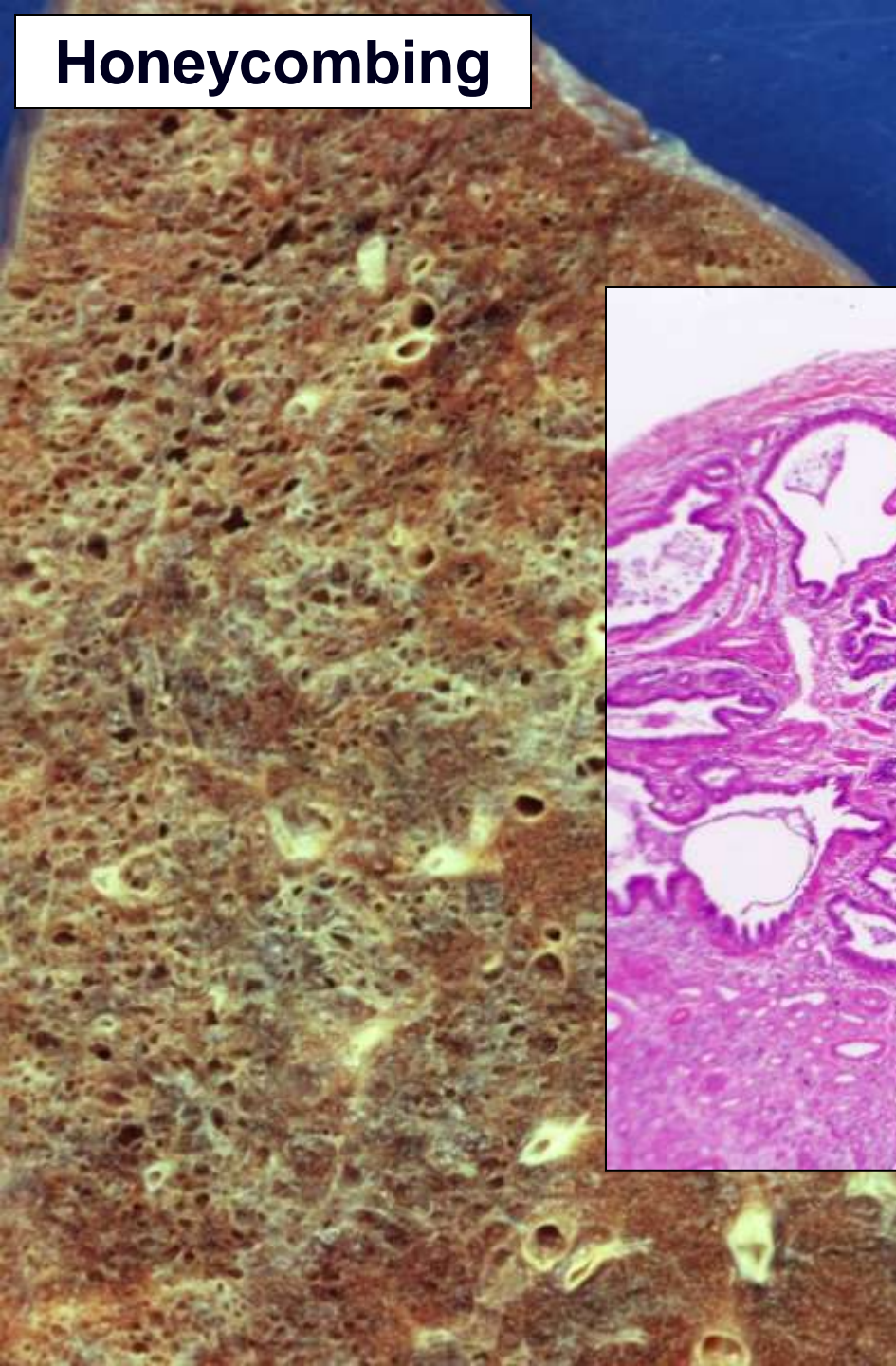


# Honeycombing





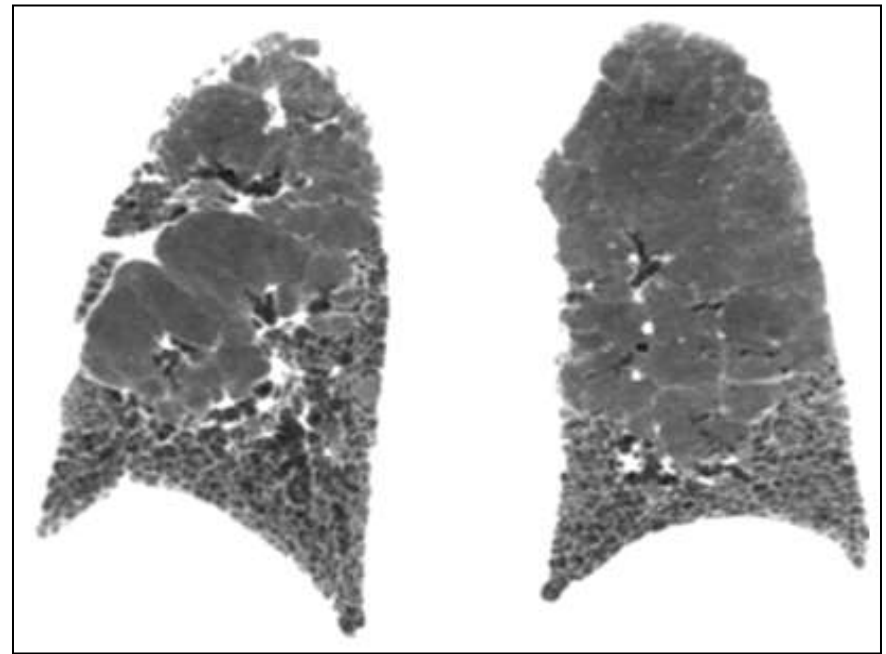
# Honeycombing



# **HONEYCOMBING: DEFINITION**

## **(RADIOLOGIC, FROM HANSELL, 2008)**

**CT: “...clustered cystic airspaces, typically of comparable diameters on the order of 3-10 mm. but occasionally as large as 2.5 cm...usually subpleural ...well defined walls”**

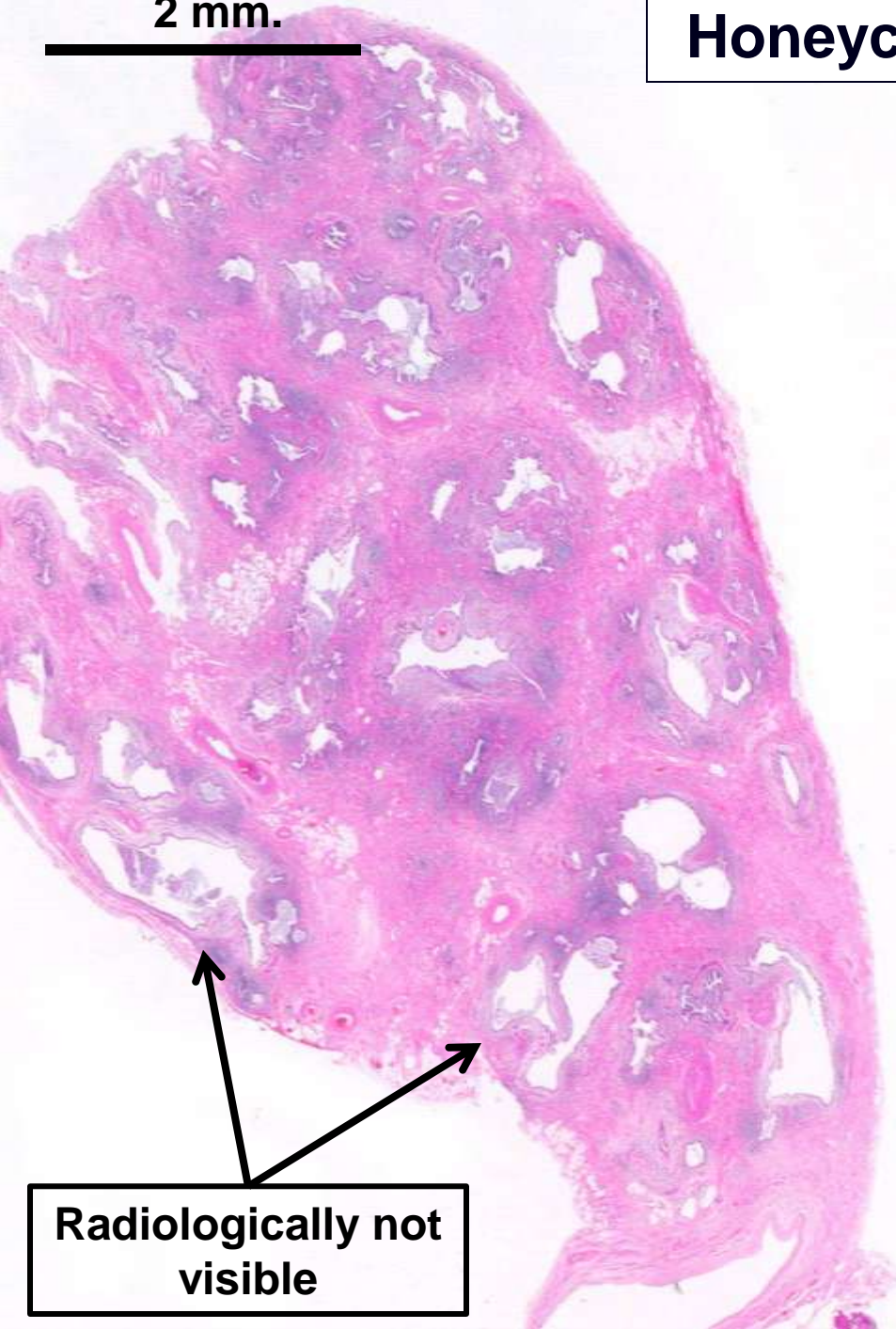




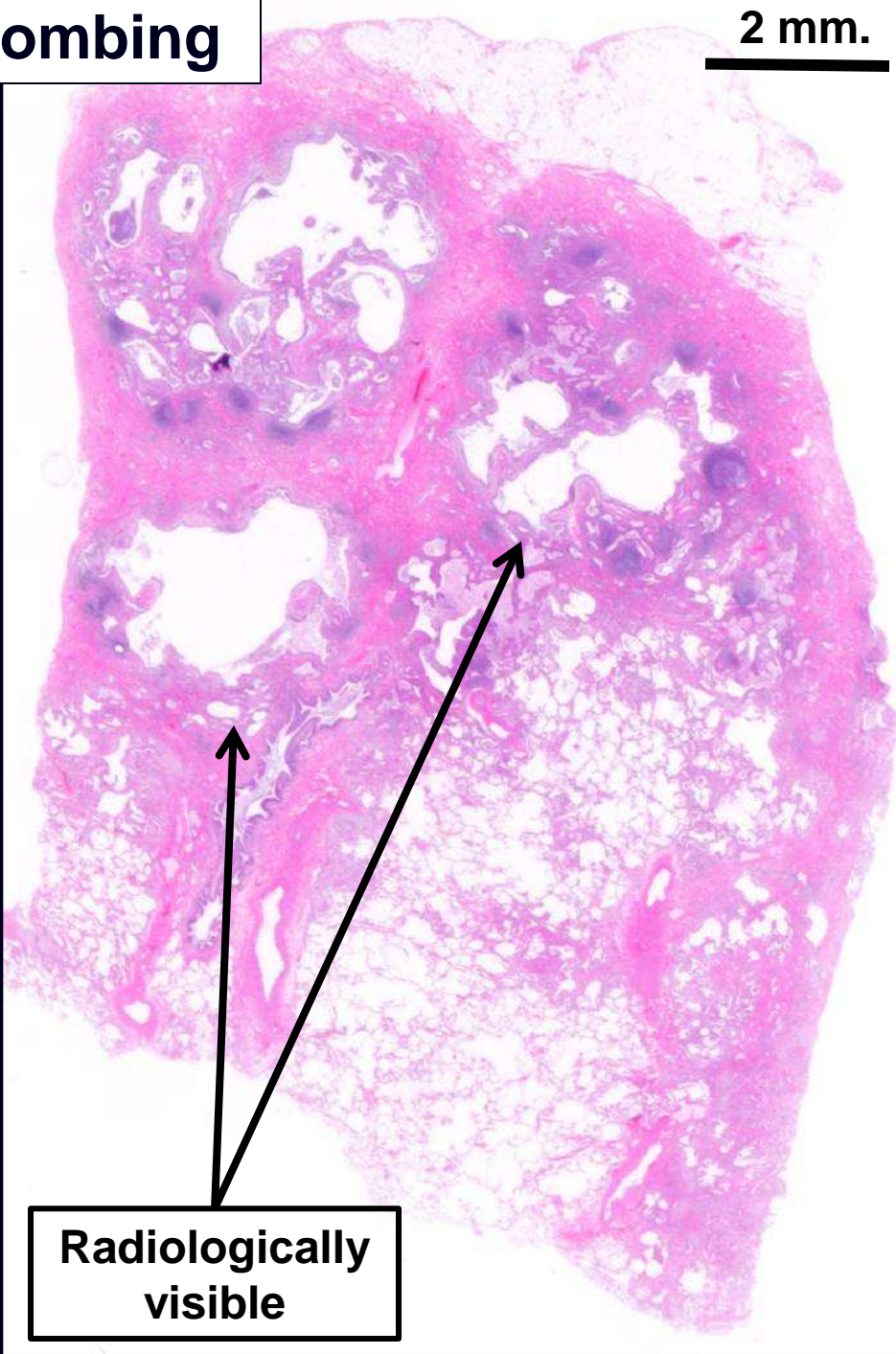
2 mm.

## Honeycombing

2 mm.



Radiologically not visible



Radiologically visible

# **HONEYCOMBING**

**Are radiologic and pathologic honeycombing the same?**

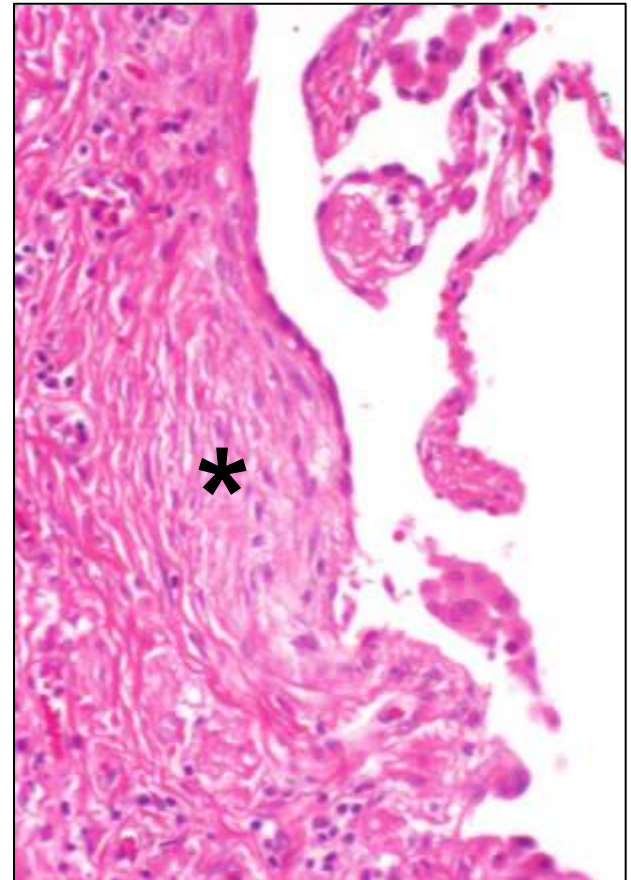
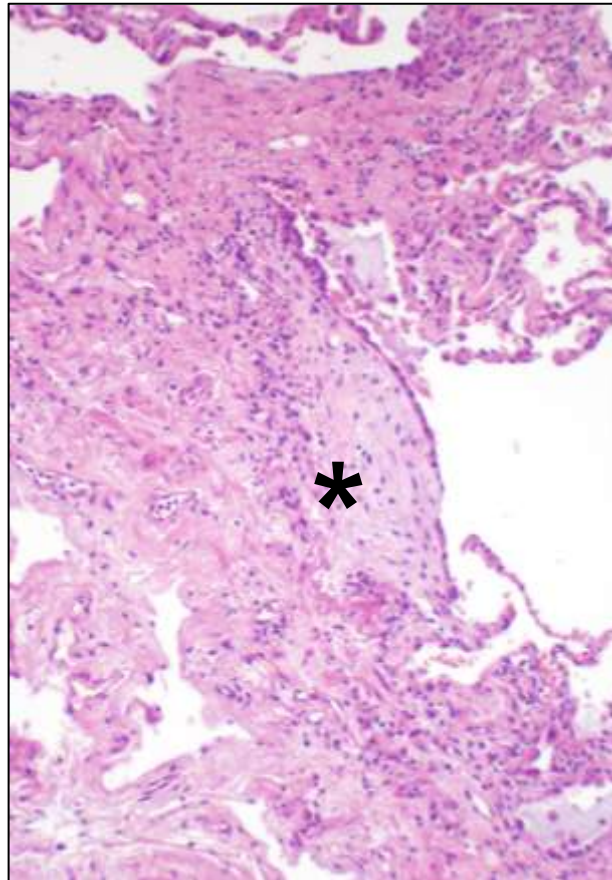
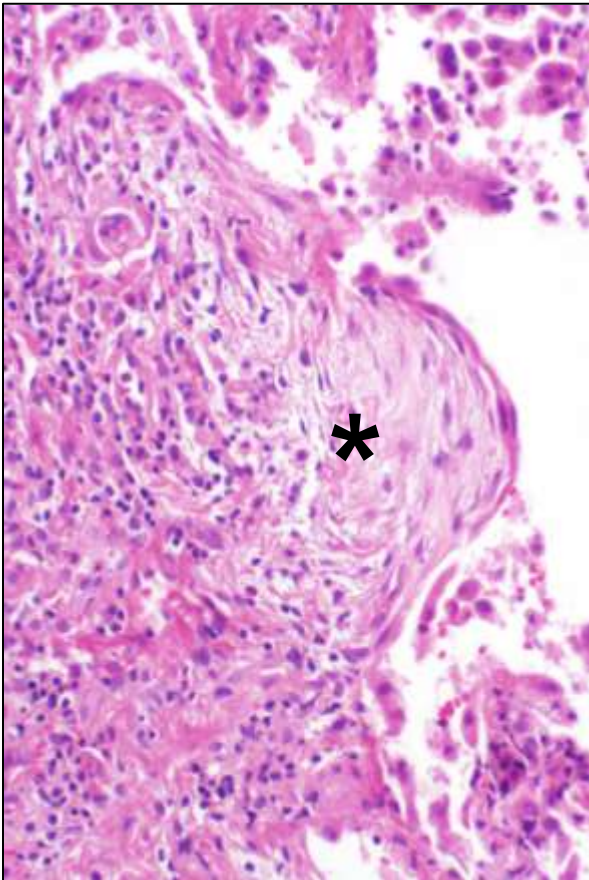
**NO !!**

**Be aware of the implications of the term and the context in which it is used**



# FIBROSIS IN UIP/IPF

Thought to be the end stage of scarring  
that started as fibroblastic foci \*

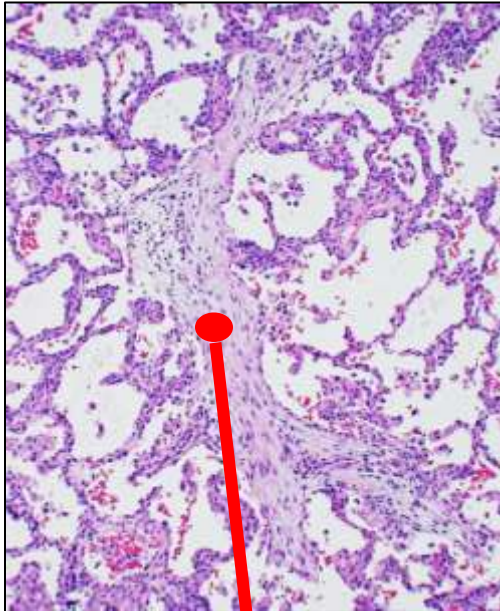




# FIBROSIS IN UIP/IPF

**Fibroblast foci are similar to, and may arise from, microfoci of organizing pneumonia:**

Organizing pneumonia



**Most cases  
reversible**

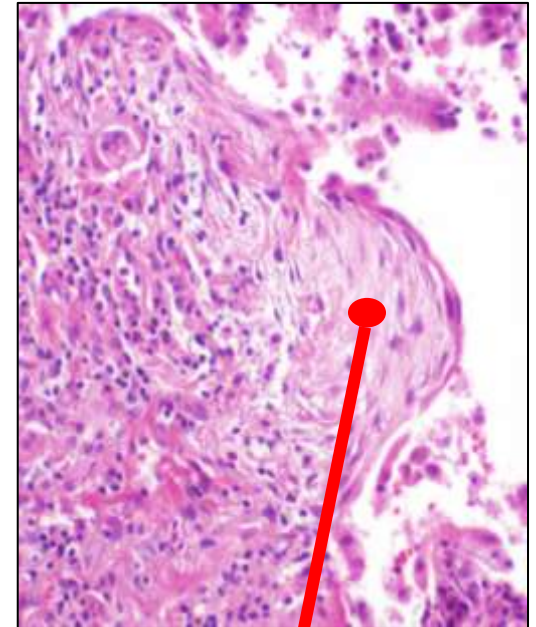
**Both composed of  
fibroblastic tissue**

**OP is seen architecturally  
normal lung**

**Fibroblastic foci are at  
the edge of scarring**

**WHY ??**

Fibroblast focus

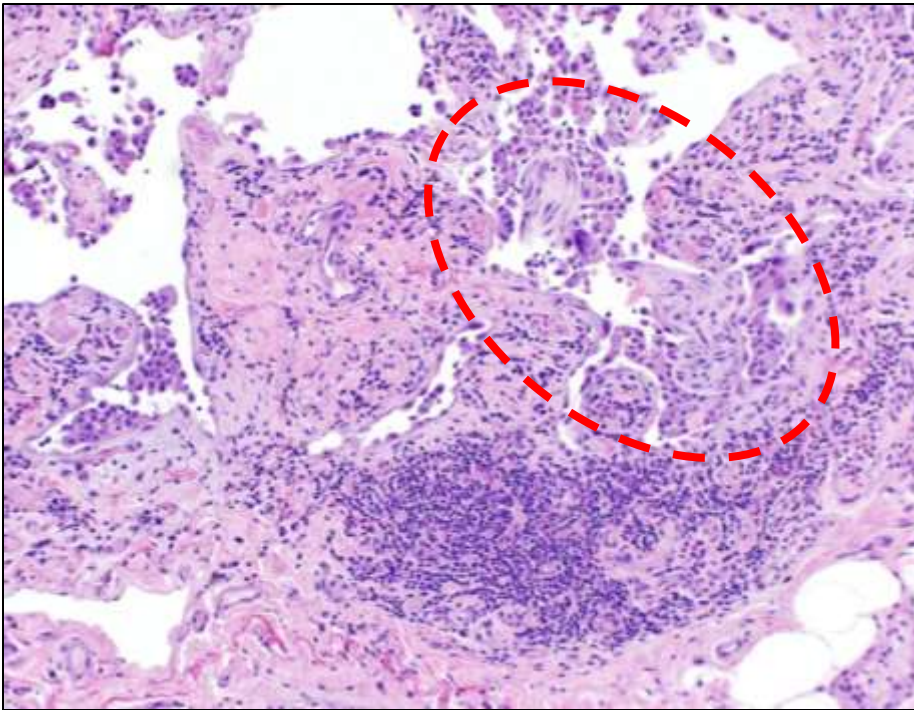


**Progressive  
fibrosis**

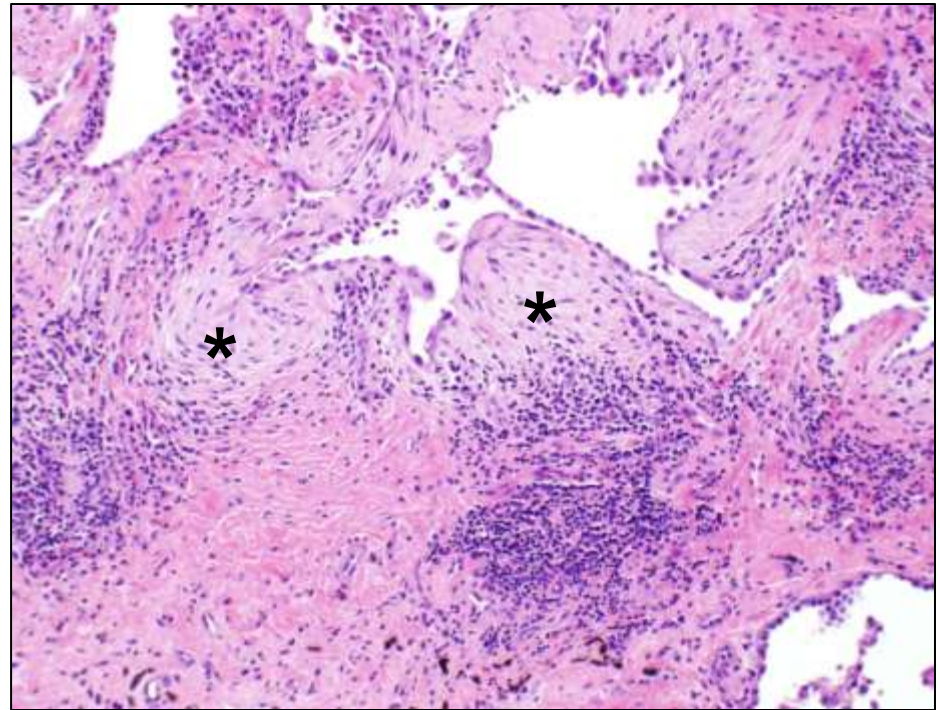
# FIBROSIS IN UIP/IPF

## Fibroblast foci and organizing pneumonia in a case of UIP

Organizing pneumonia

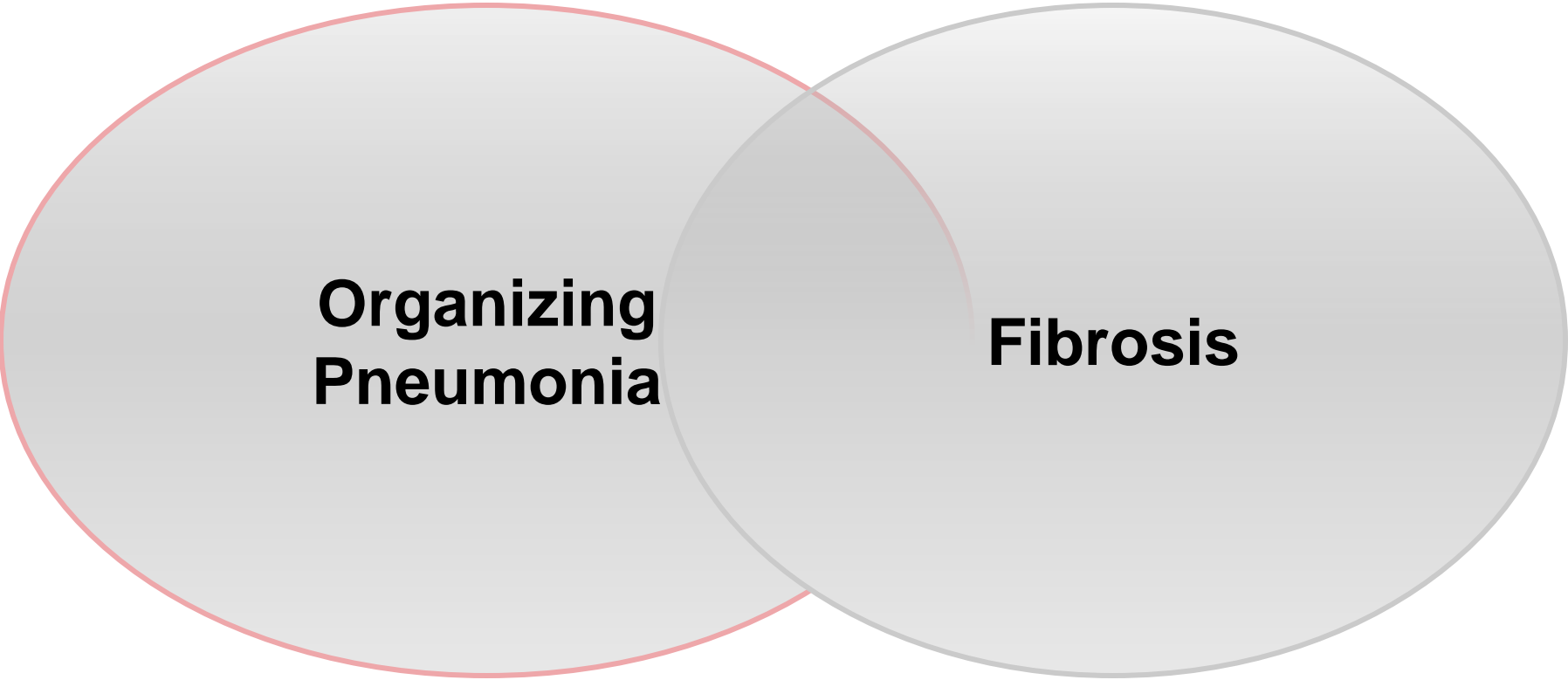


Fibroblast foci\*



In UIP: OP → Fibroblast foci → Irreversible fibrosis

**NOT SURPRISINGLY OVERLAP MAY  
BE ENCOUNTERED**



A Venn diagram consisting of two overlapping circles. The left circle is light gray with a red border and contains the text 'Organizing Pneumonia'. The right circle is light gray with a gray border and contains the text 'Fibrosis'. The overlapping area in the center is shaded a darker gray, representing the intersection of the two conditions.

**Organizing  
Pneumonia**

**Fibrosis**

# **IRREVERSIBLE FIBROSIS:**

## **Non IPF causes of the UIP pattern:**

**Connective tissue diseases**

**Familial interstitial fibrosis**

**Chronic hypersensitivity pneumonitis**

**Some chronic drug reactions**

**Asbestosis (other pneumoconioses)**

**Rare conditions (eg. Hermansky-Pudlak)**

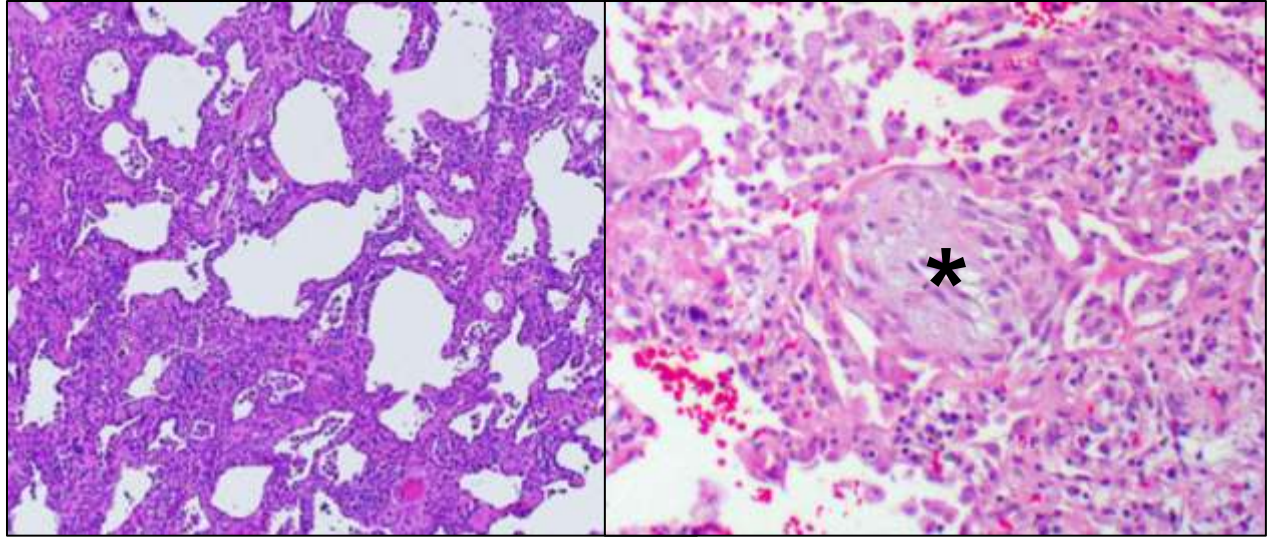
**Pathology UIP  $\neq$  IPF**



# NSIP: THE SPECTRUM

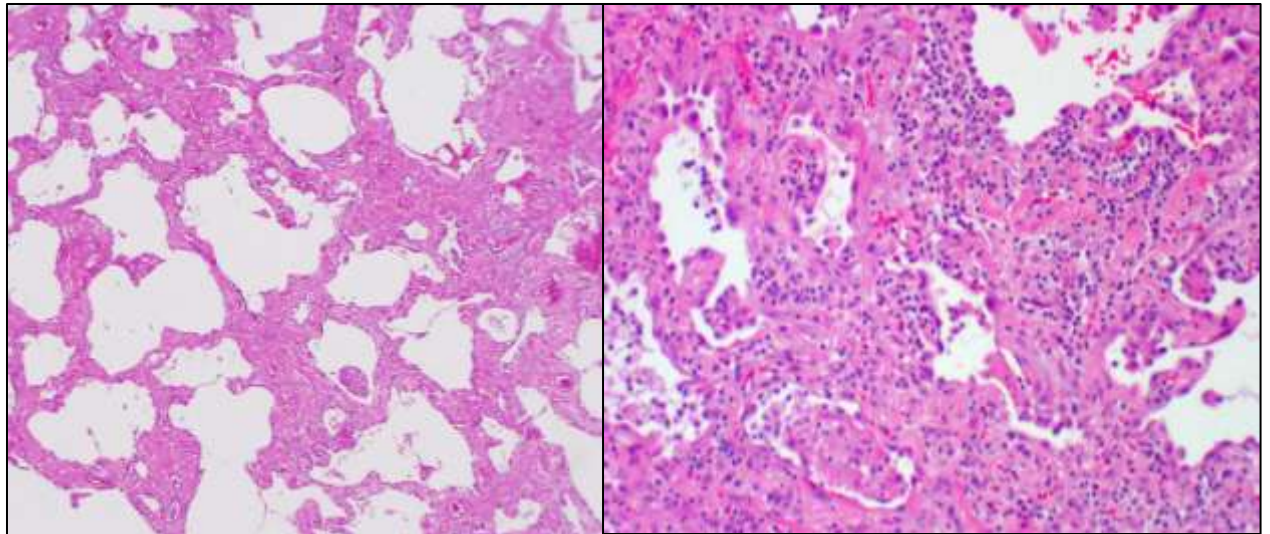
**Cellular NSIP**

**+/- OP\***



**Fibrotic NSIP**

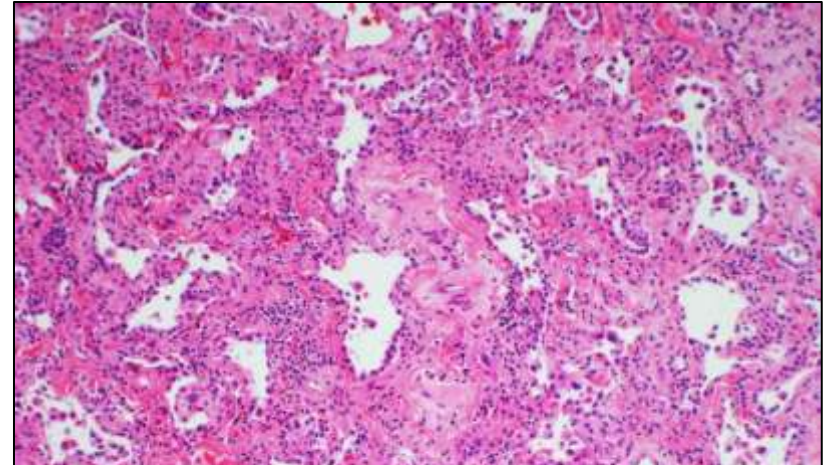
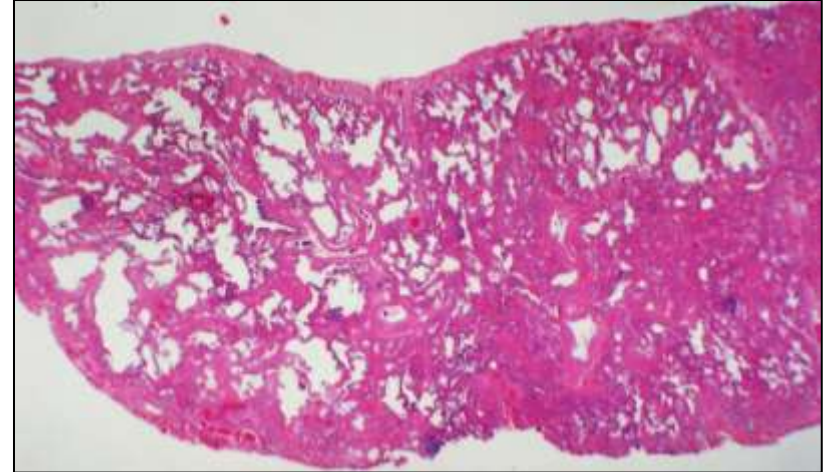
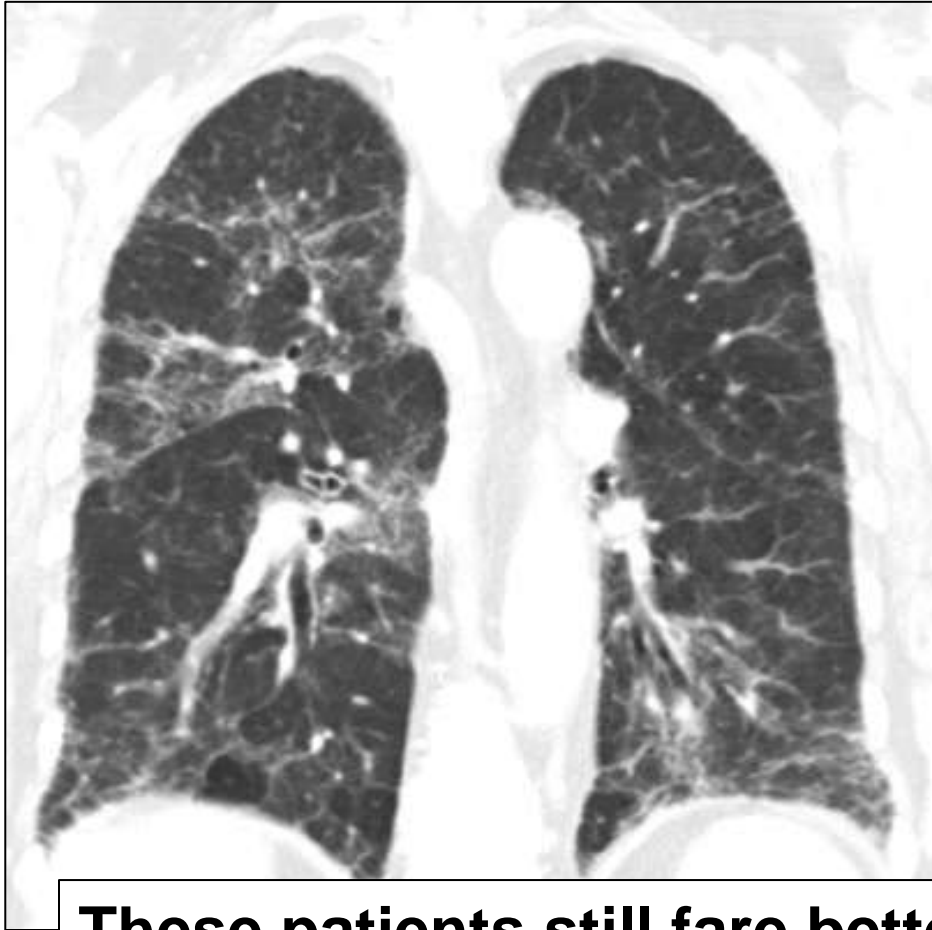
**+/- Inflamm.**





# **IRREVERSIBLE FIBROSIS...**

**...Is seen in some cases of fibrotic nonspecific interstitial pneumonia (NSIP)**

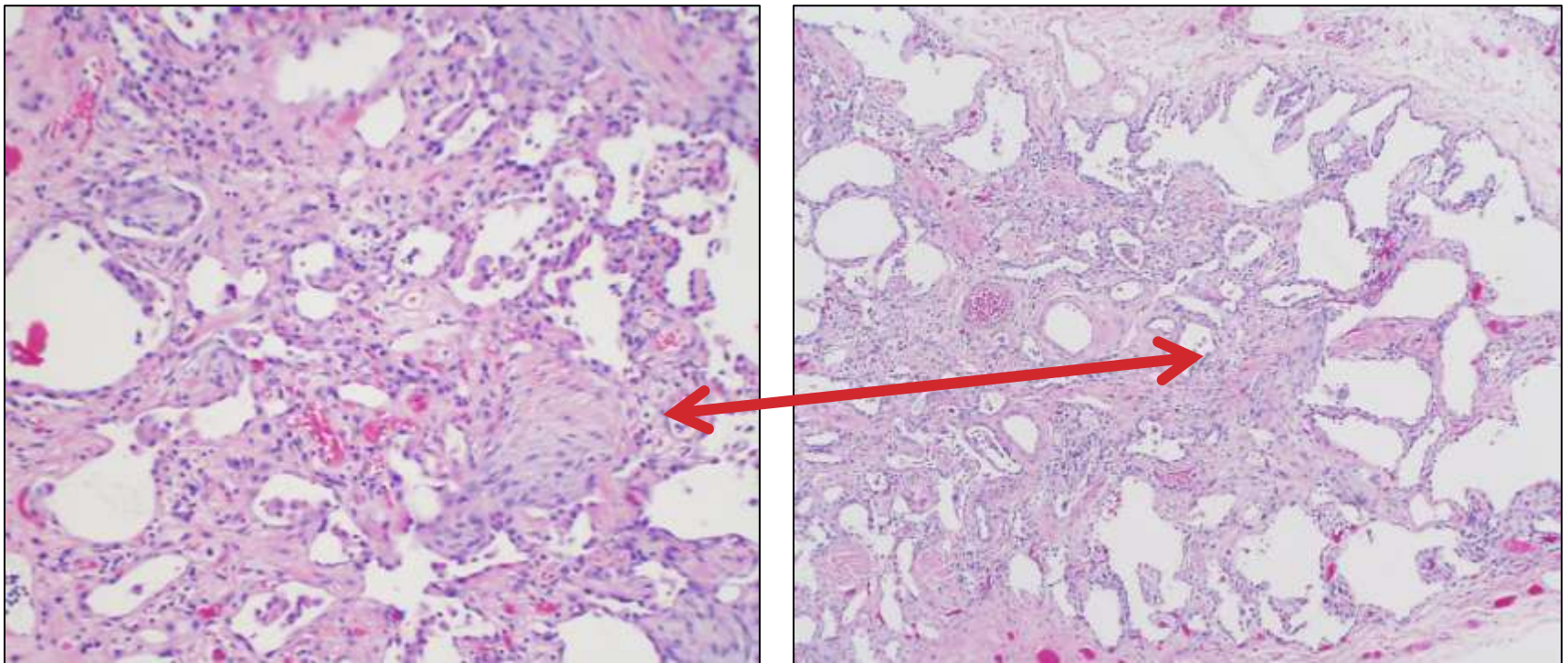


**These patients still fare better than those with UIP/IPF**

# OVERLAP OF OP AND NSIP

**Radiologically some cases of OP evolve into a pattern of NSIP (biopsy-confirmed)**

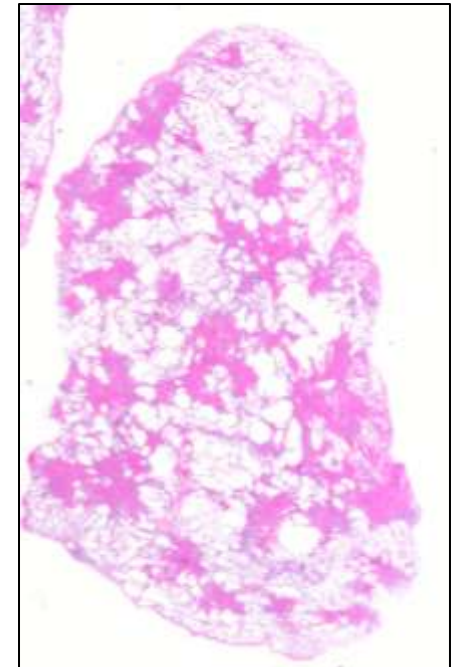
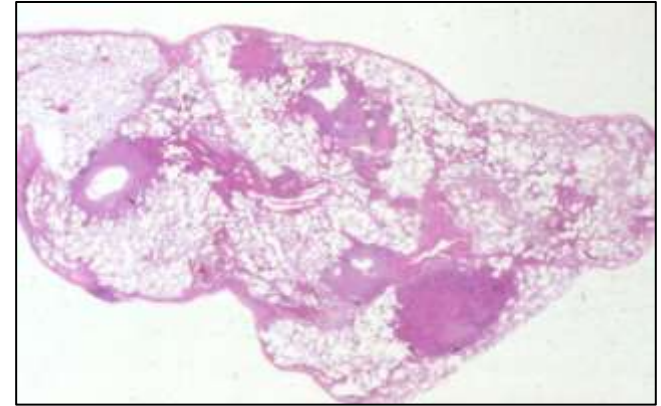
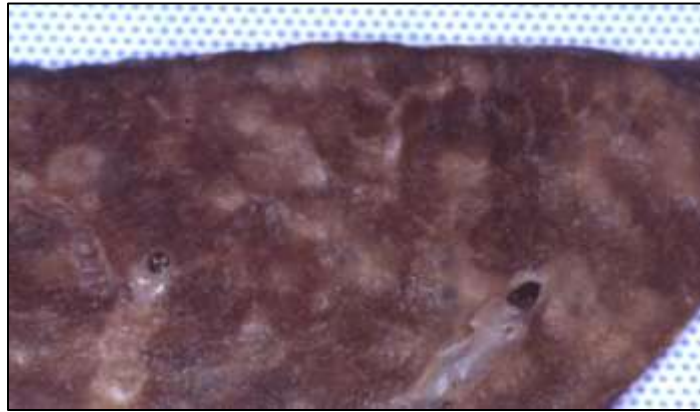
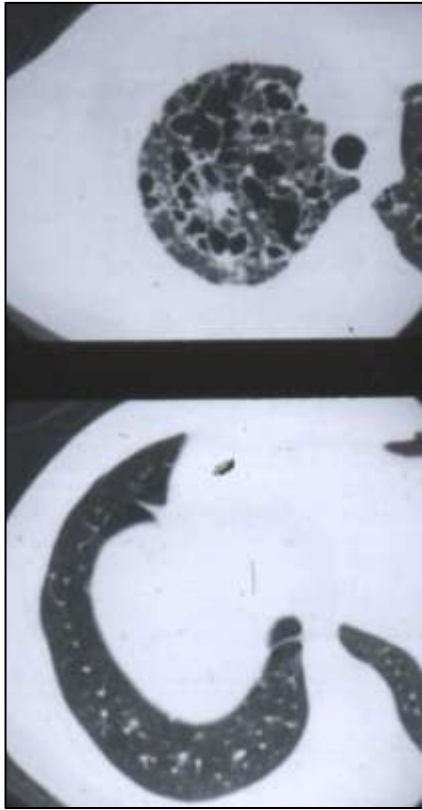
**The overlap can be apparent histologically**





# IRREVERSIBLE FIBROSIS:

Fibrotic/late phase of Pulmonary Langerhans Cell Histiocytosis (PLCH)



Key Feature:

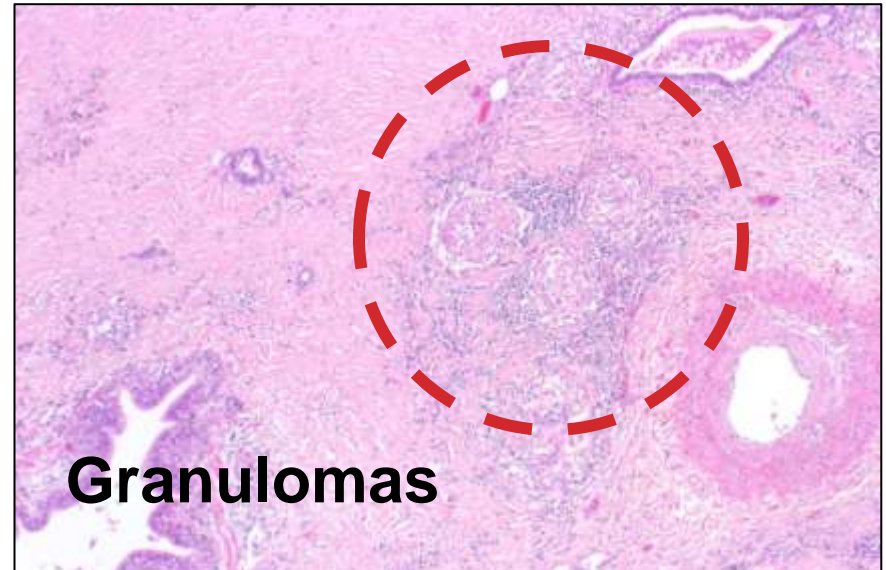
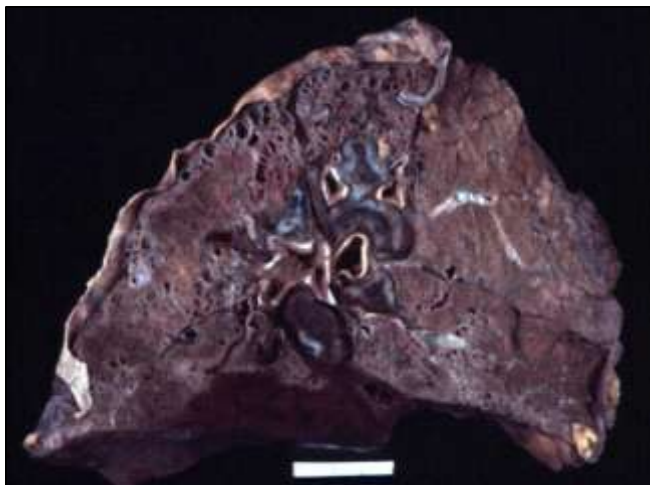
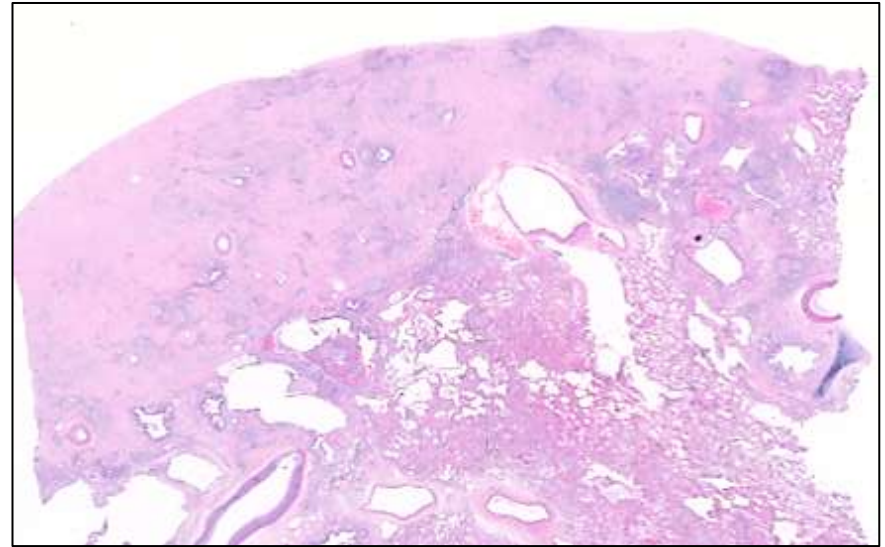
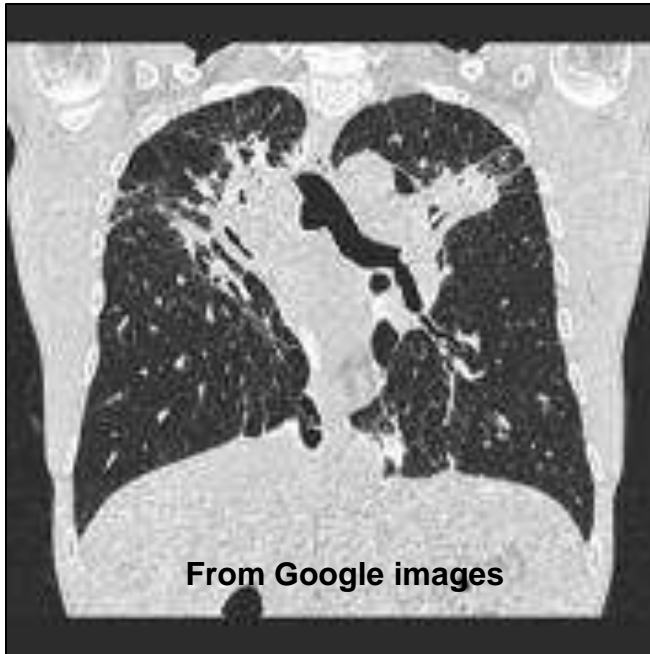
Stellate/centrilobular scar





# IRREVERSIBLE FIBROSIS:

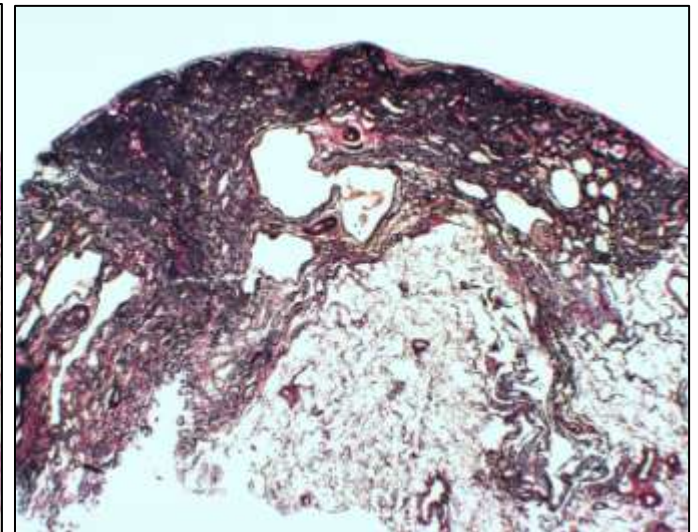
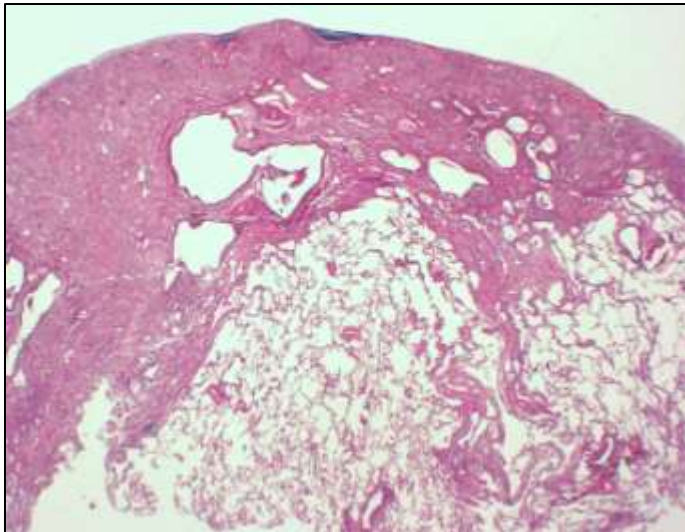
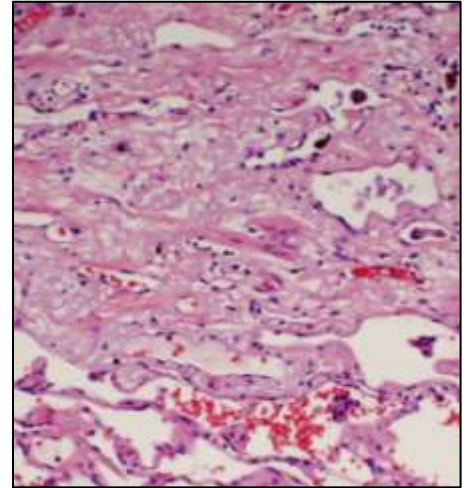
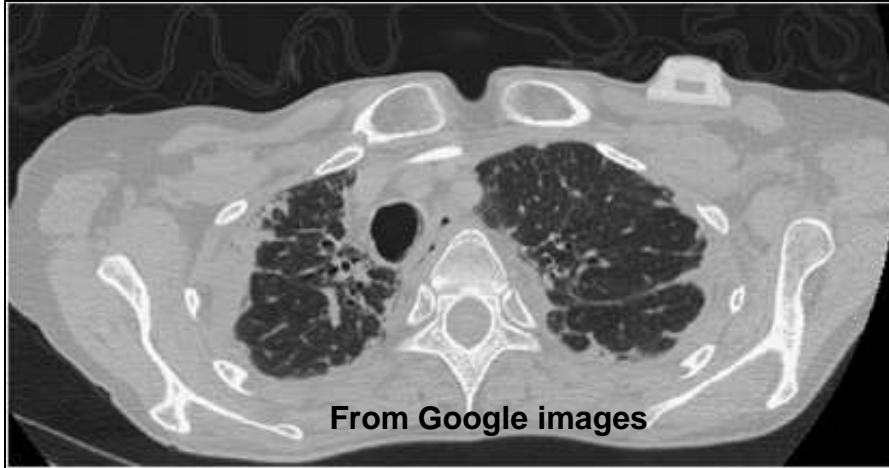
Sarcoidosis: Upper lobe with a lymphangitic distribution



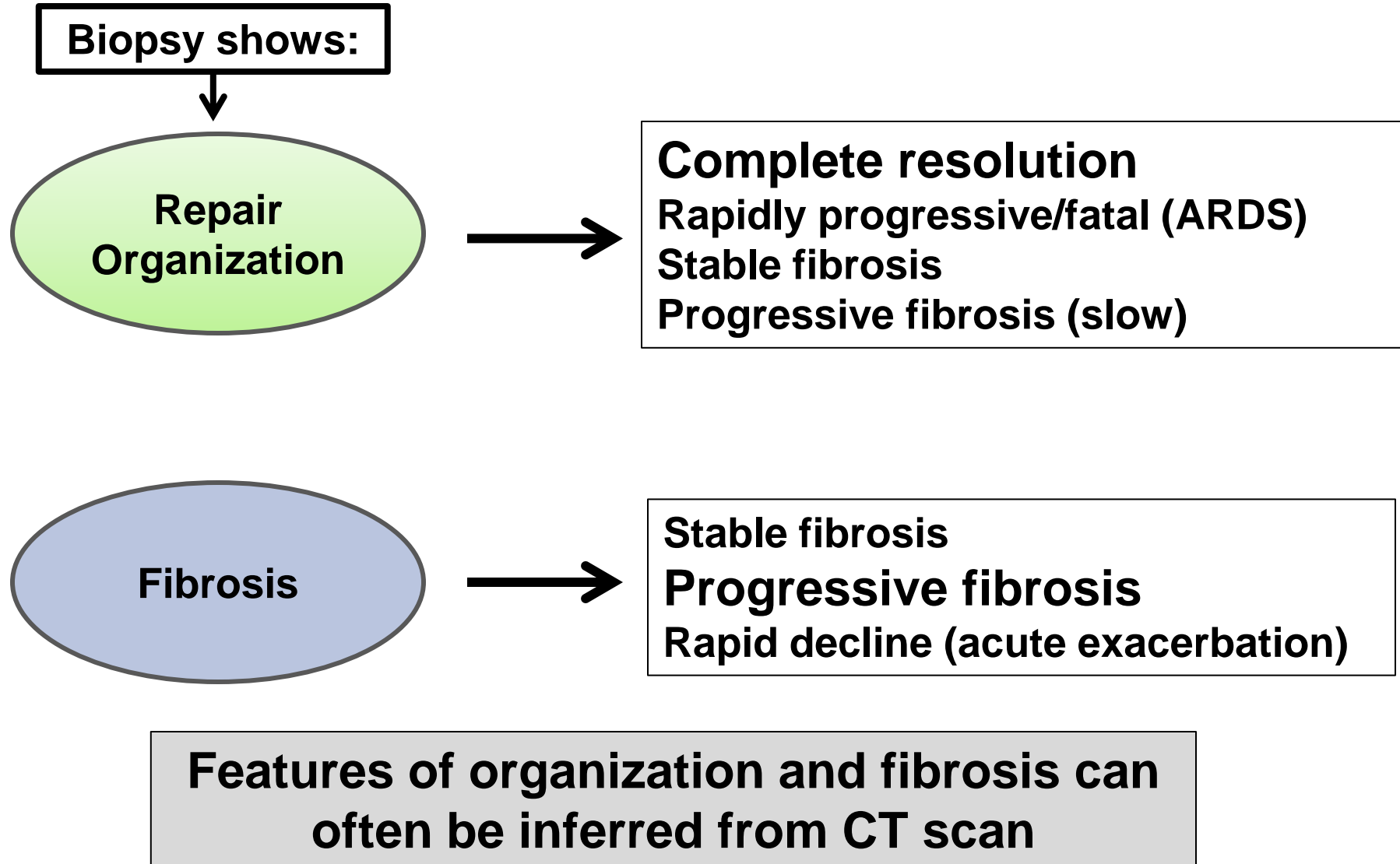
# IRREVERSIBLE FIBROSIS:

PPFE: Pleuroparenchymal fibroelastosis

Keys: Distinctive elastotic fibrosis; upper lobe distribution



# LUNG INJURY AND FIBROSIS: OUTCOME





# **SUMMARY**

- **“Fibrosis” in the lung encompasses a variety of lesions.**
- **Some are reversible and some are not.**
- **Patterns of fibrosis provide clues to reversibility and to etiology.**
- **“Honeycombing” and “fibroblastic foci” are terms that may be misinterpreted as synonymous with UIP/IPF....use them carefully!**

# KEY POINTS:

**Not all “fibrosis” in the lung has the same clinical and prognostic implications.**



**Fibroblastic proliferation  $\neq$  Fibrosis**

**Not all fibroblastic proliferations in the lung result in irreversible scarring.**