ALVEOLAR DAMAGE AND ITS OUTCOME: VIEW OF THE PATHOLOGIST

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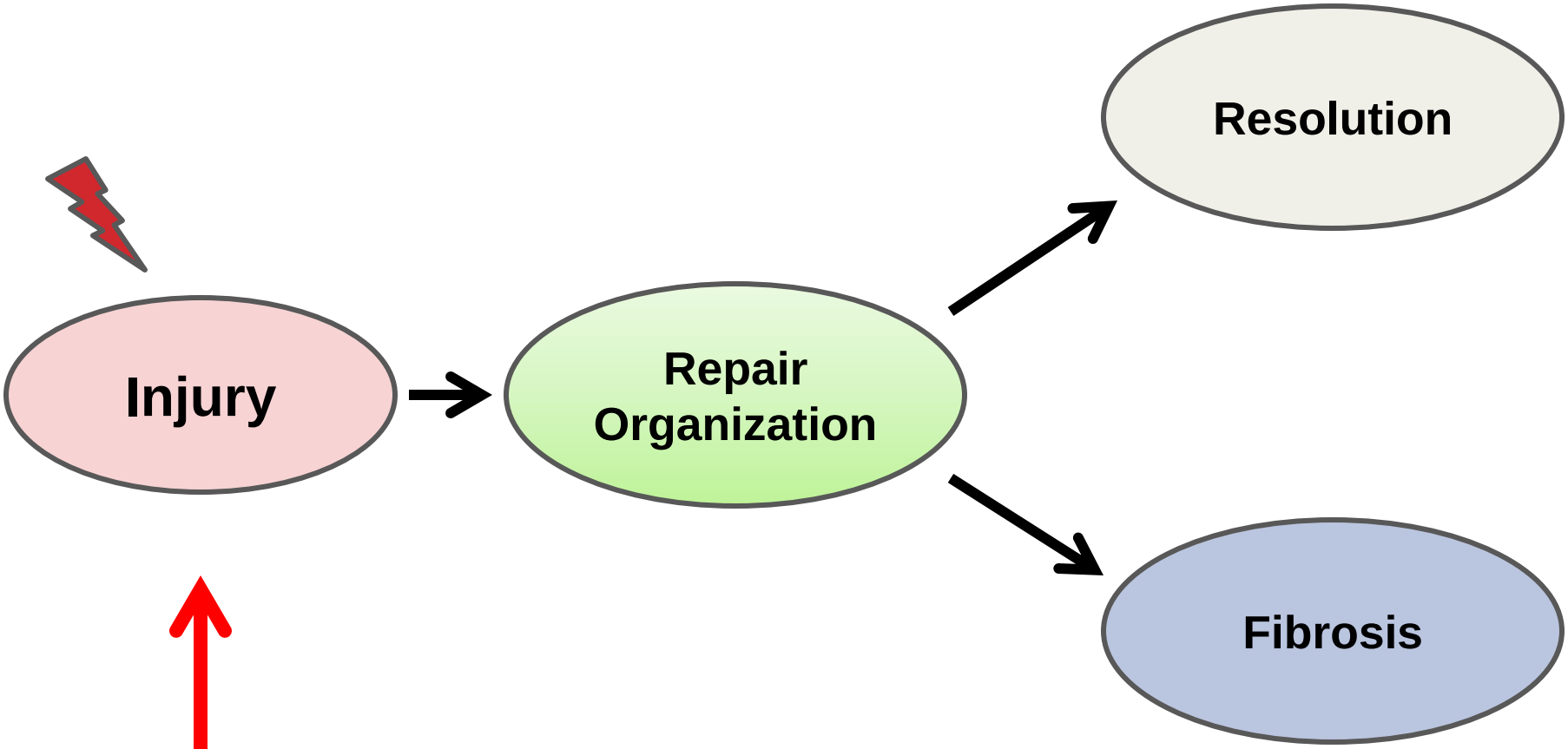
LUNG INJURY AND FIBROSIS

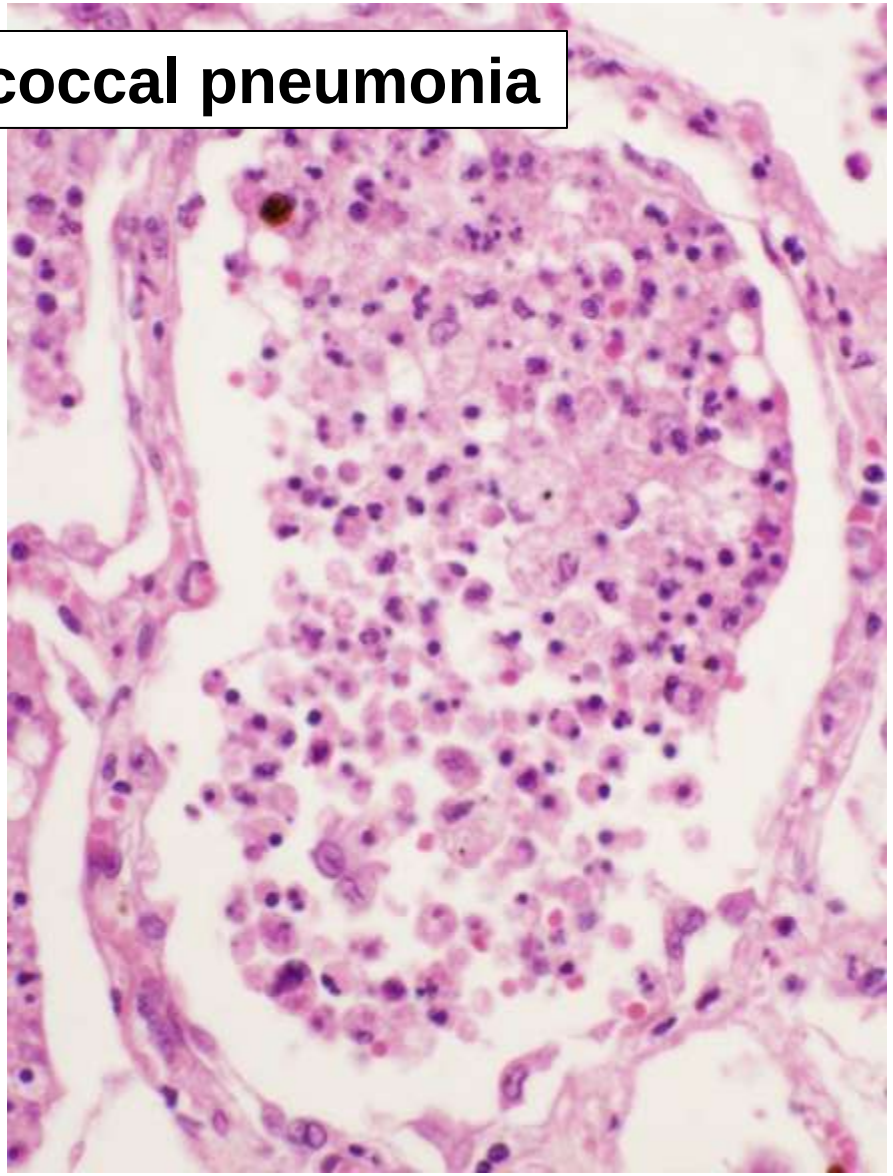


This Lecture

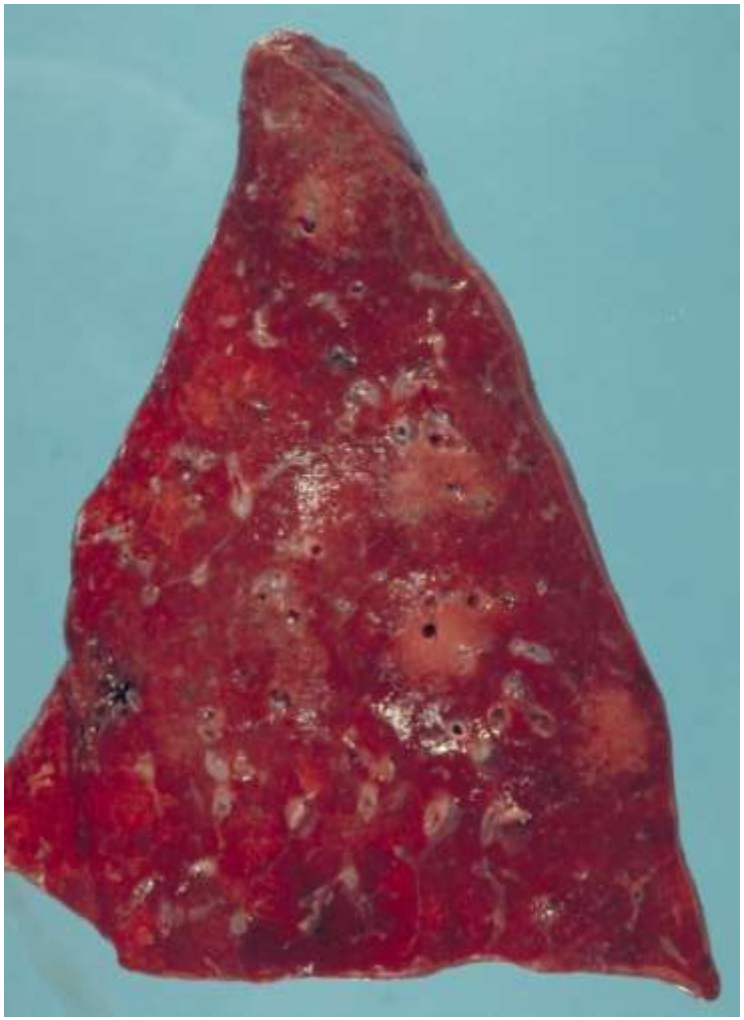
NOTE: Acute injury with neutrophils which is usually infectious (ie. bronchopneuonia) is not discussed

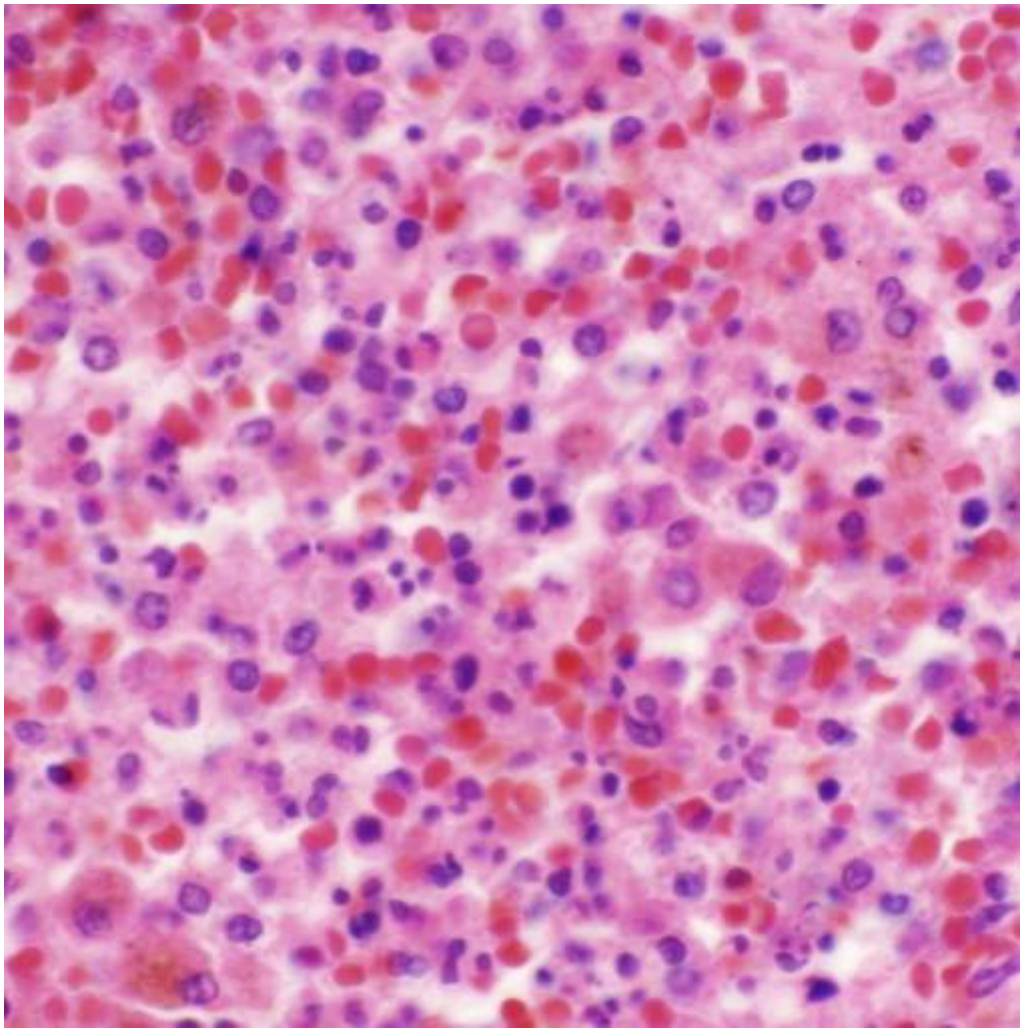
BACTERIAL PNEUMONIA

Lobar pneumococcal pneumonia

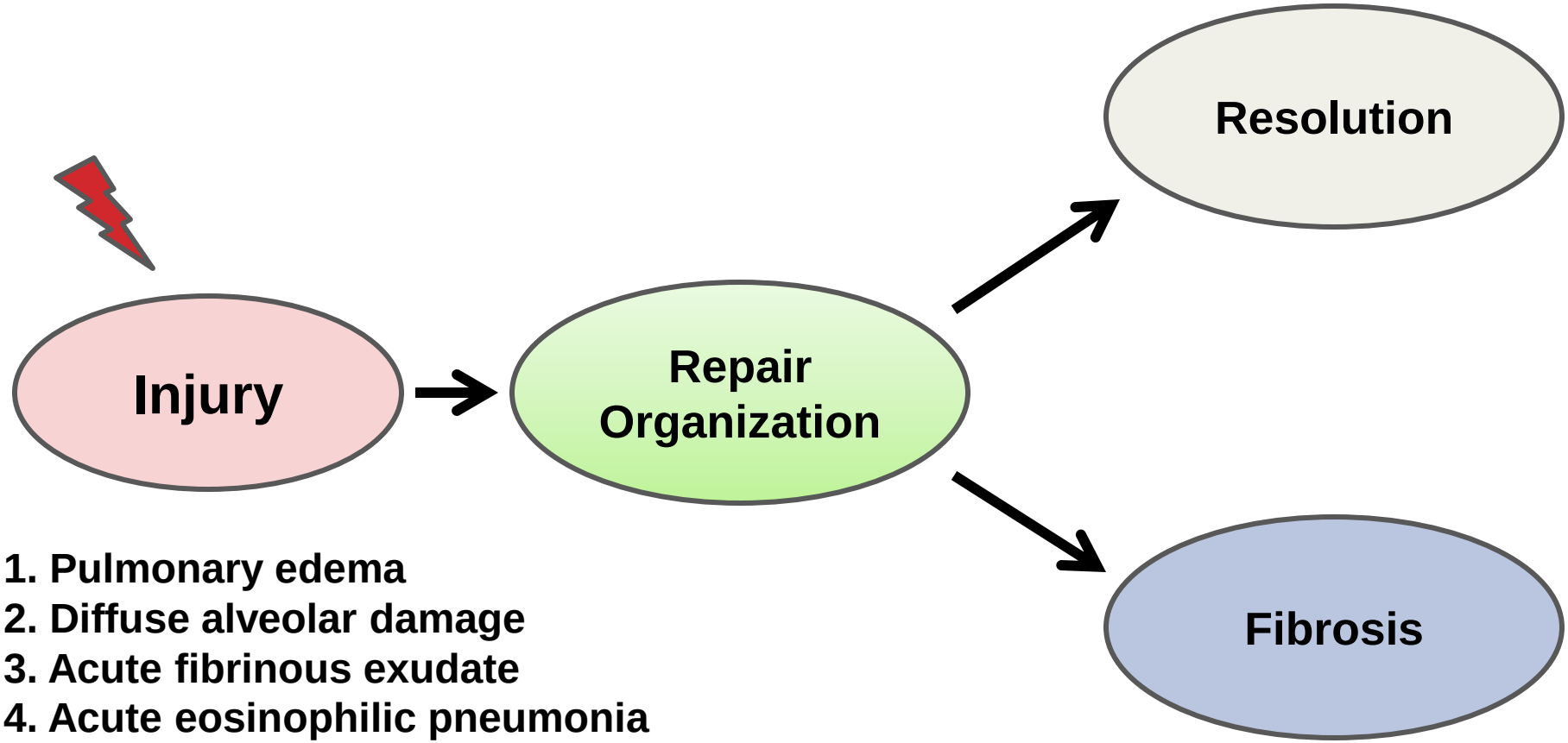


BACTERIAL BRONCHOPNEUMONIA



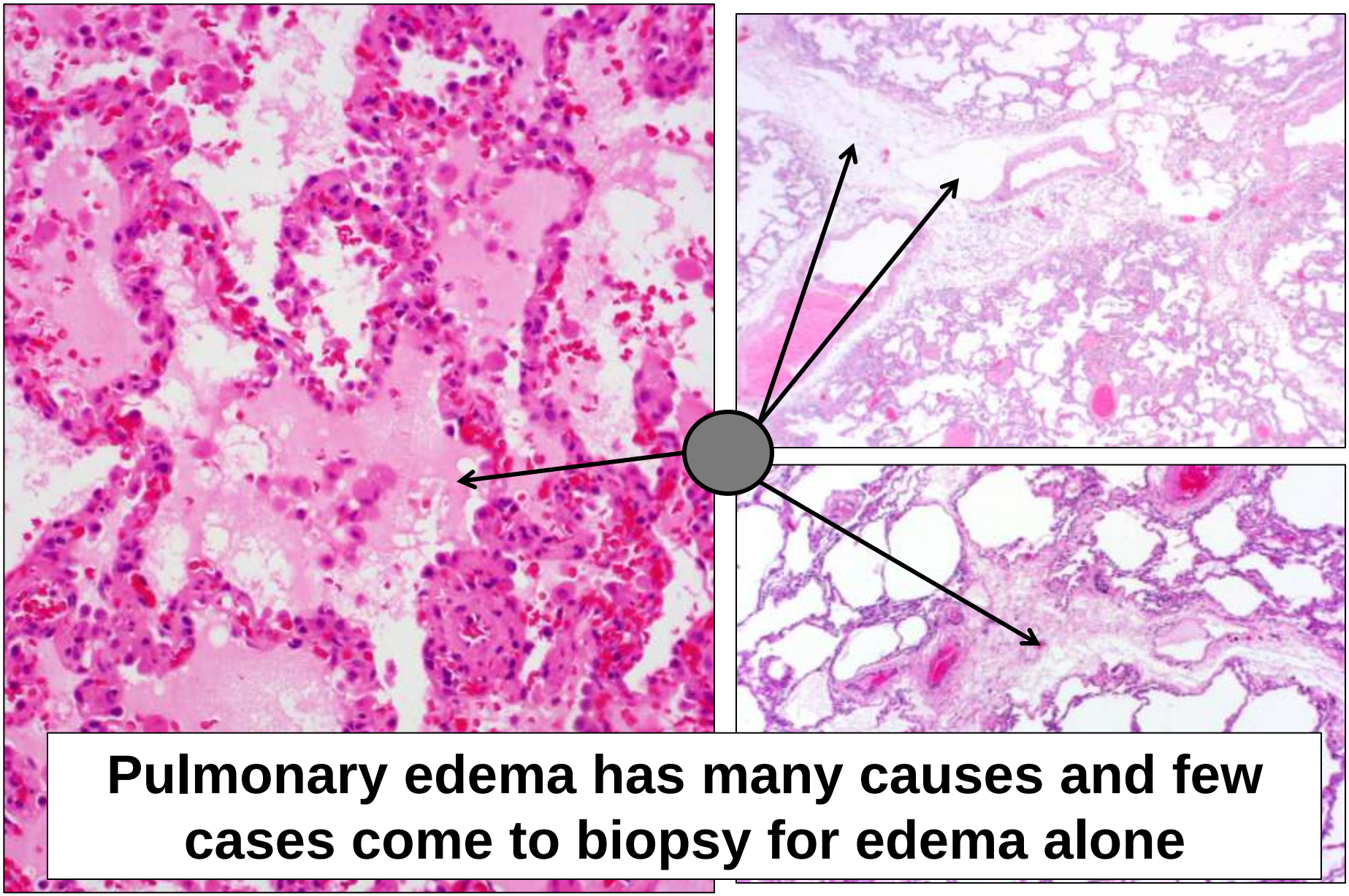


ACUTE ALVEOLAR INJURY PATTERNS



1. Pulmonary edema
2. Diffuse alveolar damage
3. Acute fibrinous exudate
4. Acute eosinophilic pneumonia
5. Alveolar hemorrhage syndromes

1. PULMONARY EDEMA



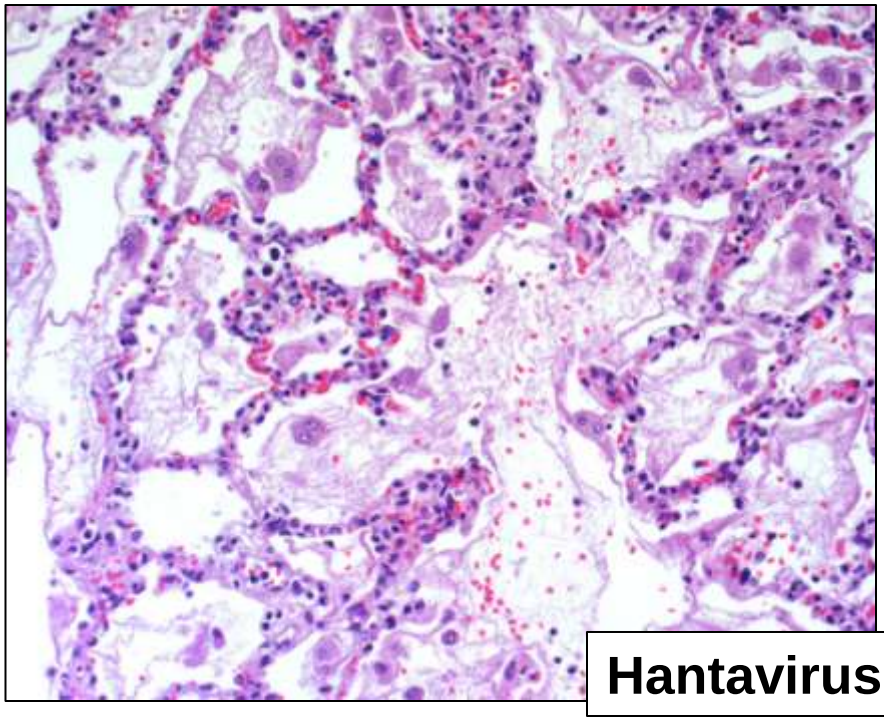
Pulmonary edema has many causes and few cases come to biopsy for edema alone

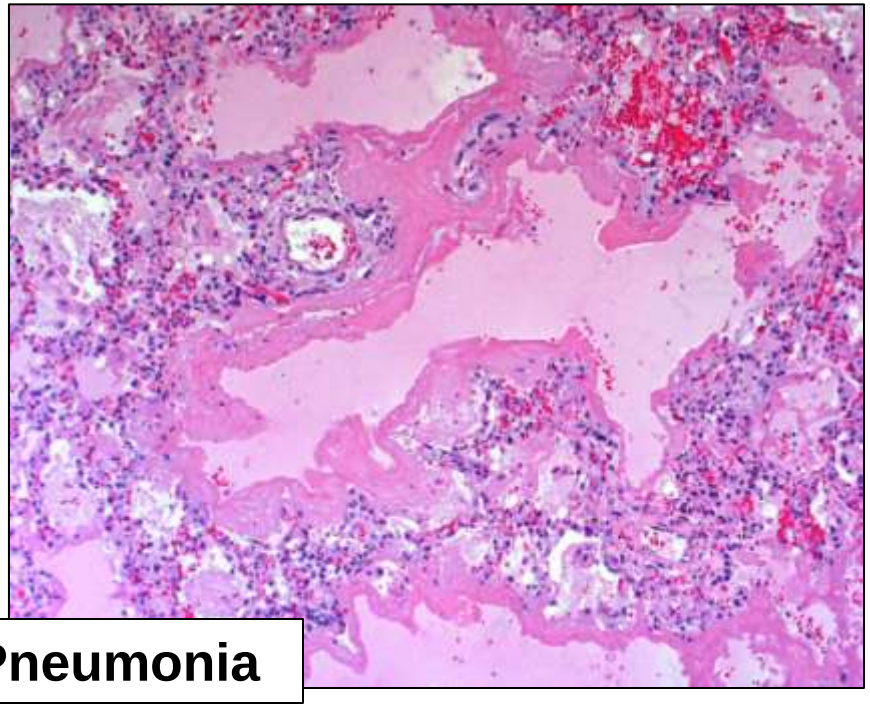
1. PULMONARY EDEMA

Pulmonary edema is often the earliest change in diffuse alveolar damage

Death in < 24 hrs
Massive pulm. edema

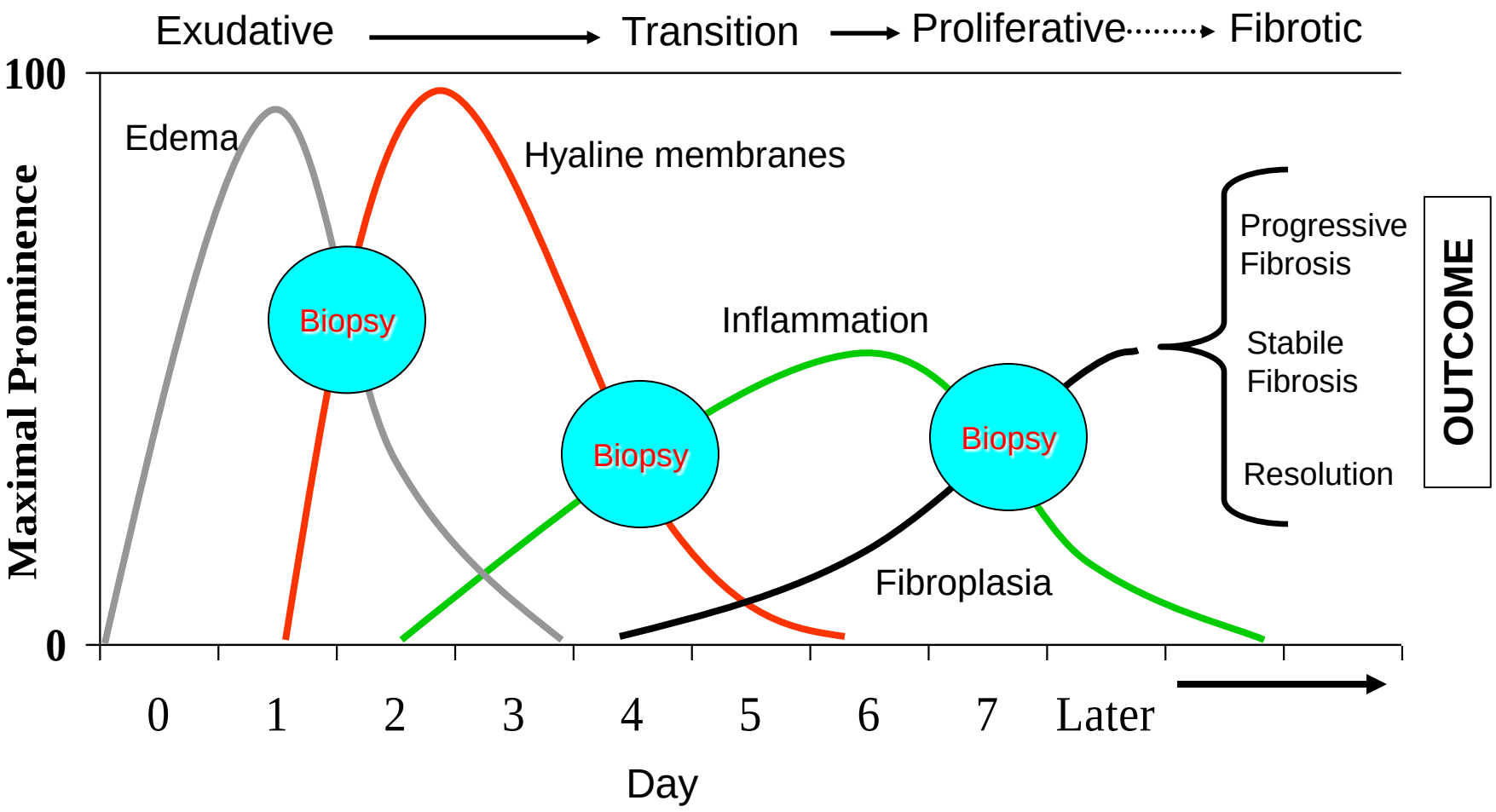
Death in 72 hrs
Hyaline membranes





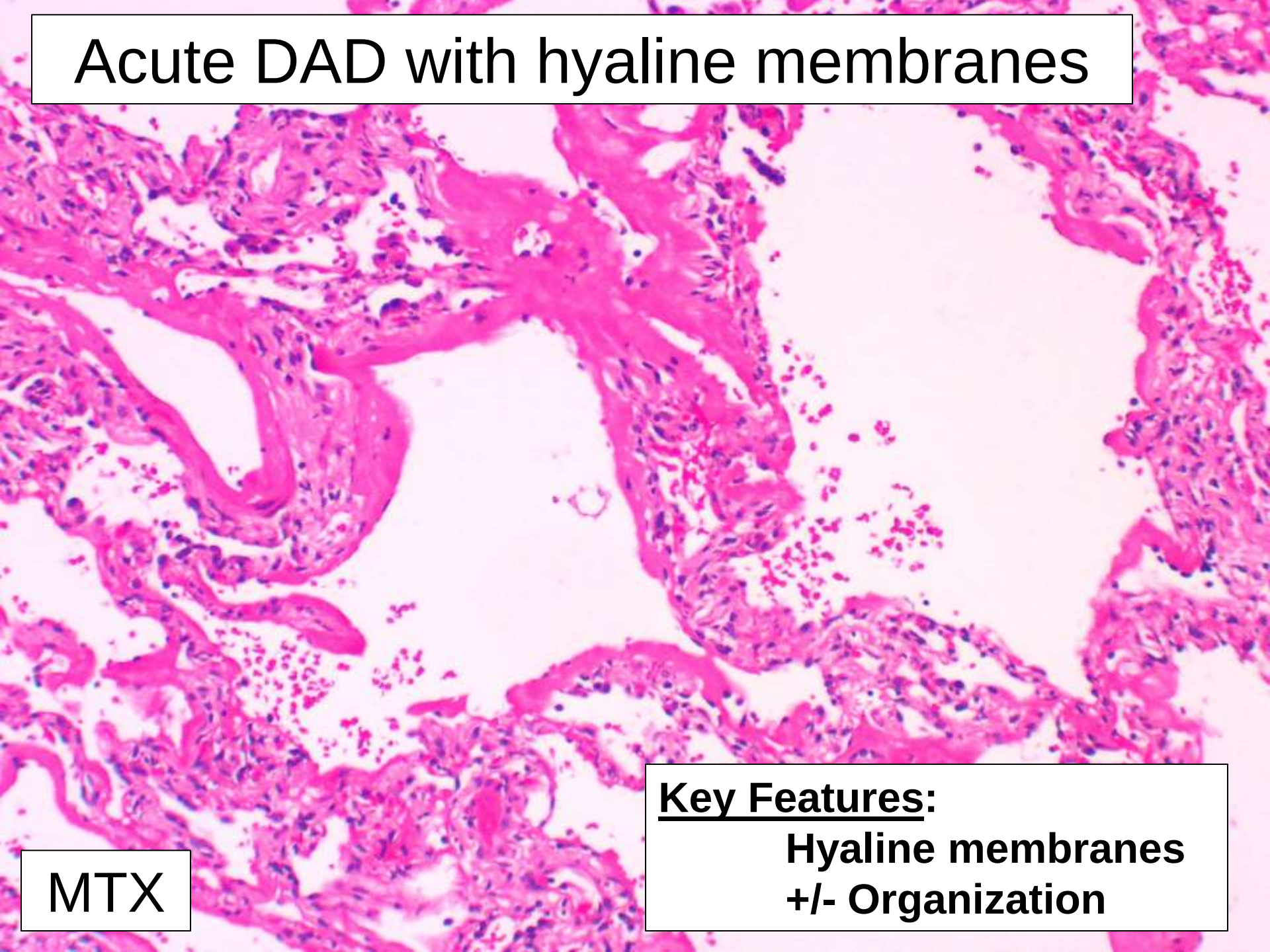
Hantavirus Pneumonia

2. DIFFUSE ALVEOLAR DAMAGE (DAD)



Slide courtesy KO Leslie

Acute DAD with hyaline membranes

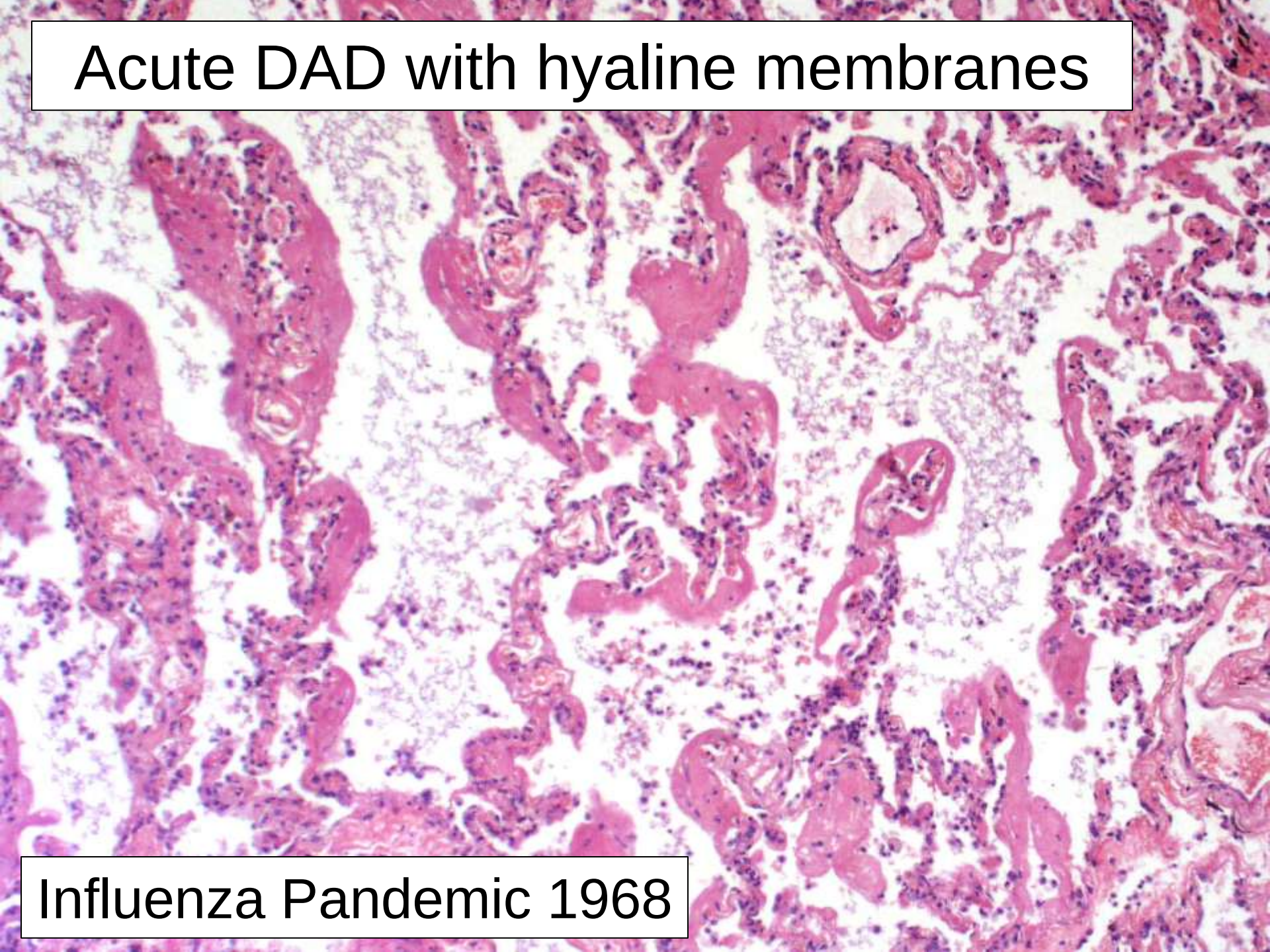


Key Features:

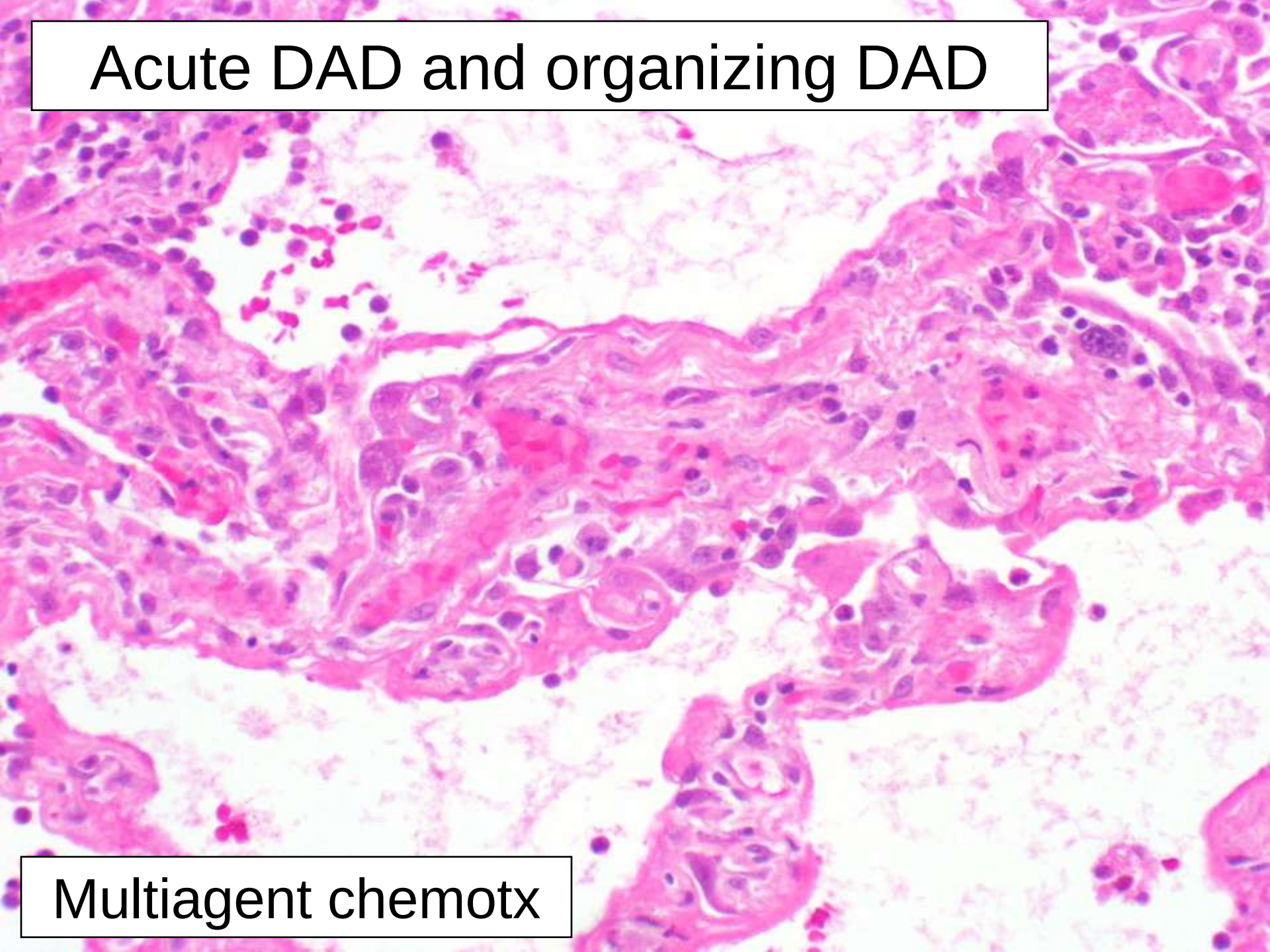
Hyaline membranes

+/- Organization

MTX

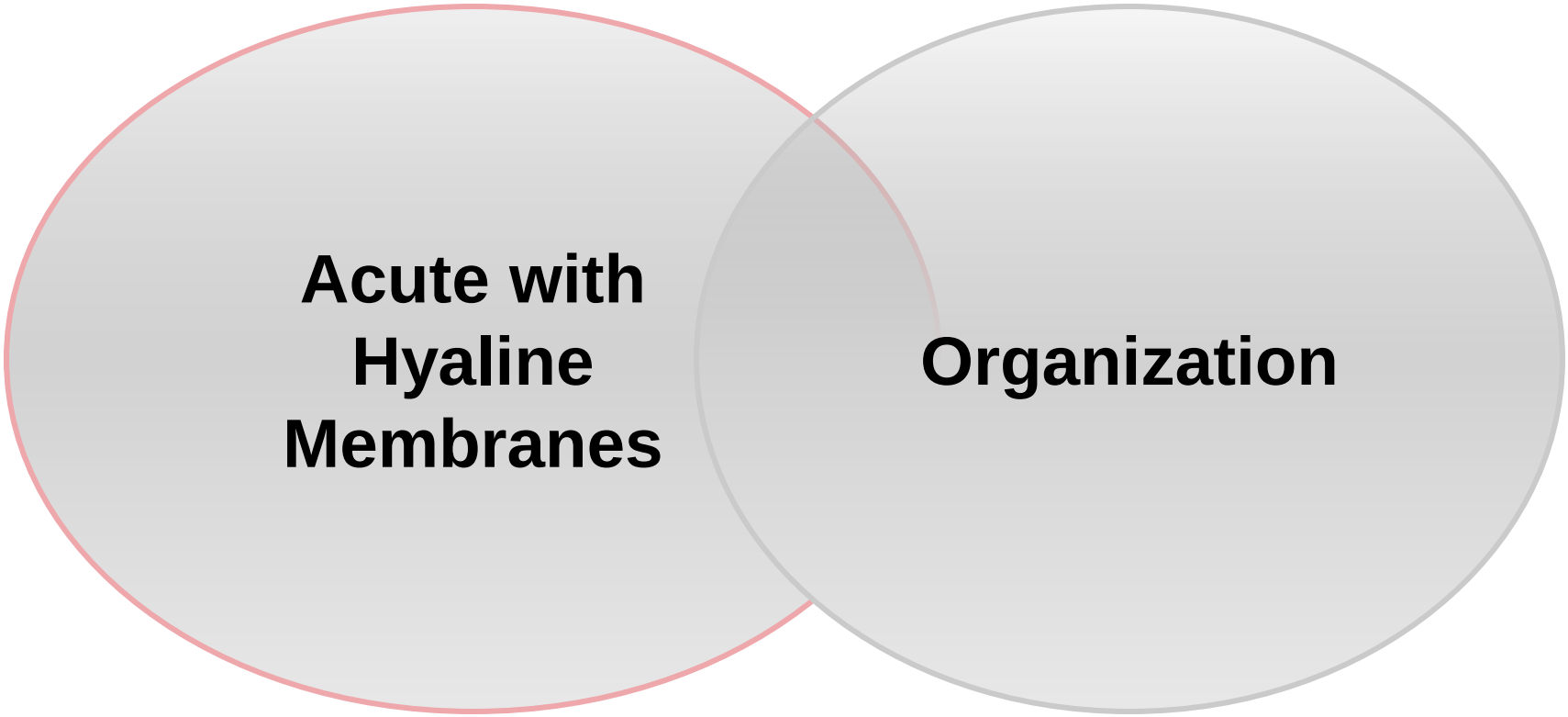

Acute DAD with hyaline membranes
Influenza Pandemic 1968

Acute DAD and organizing DAD



Multiagent chemotx

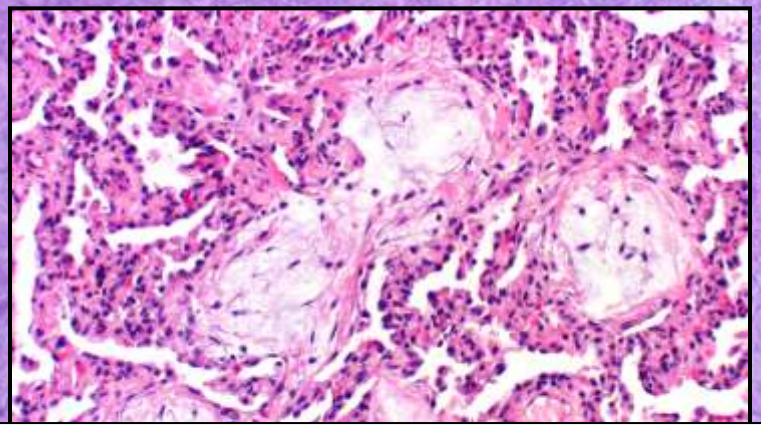
NOT SURPRISINGLY OVERLAP MAY BE ENCOUNTERED

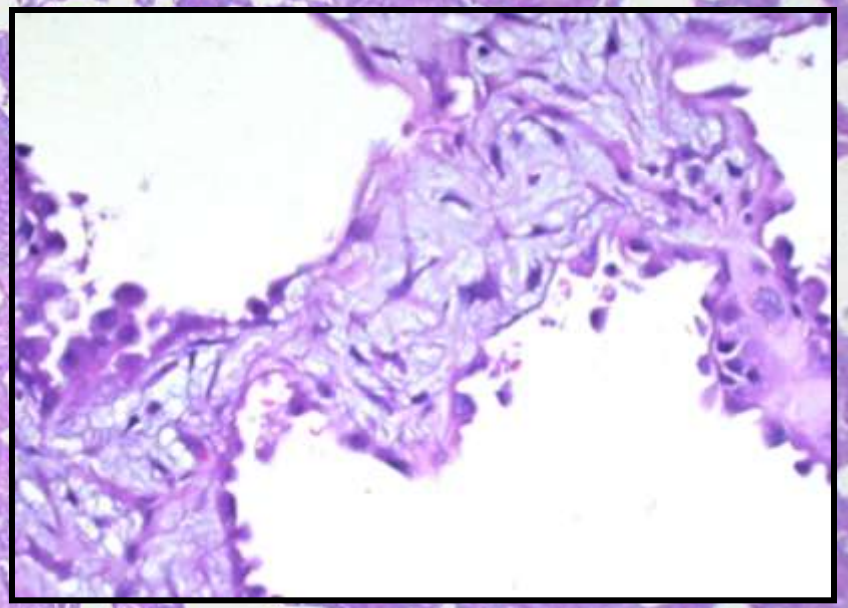


Organizing DAD

AIP

Organizing pneumonia/BOOP Foci



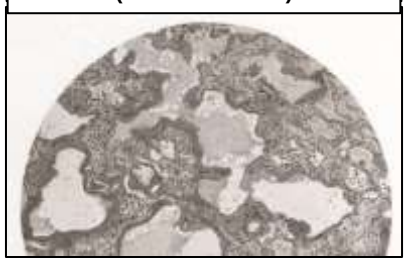


<u>Key Feature</u>: Fibroblastic tissue rather than fibrotic tissue

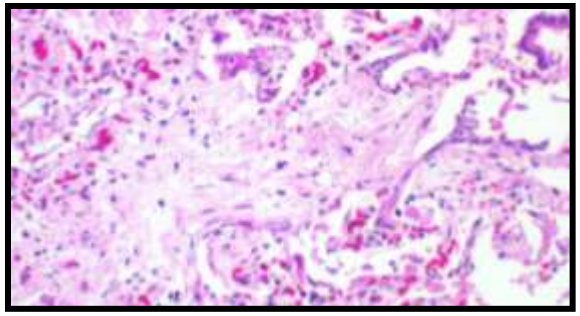
Phases of DAD

Death can occur at any point

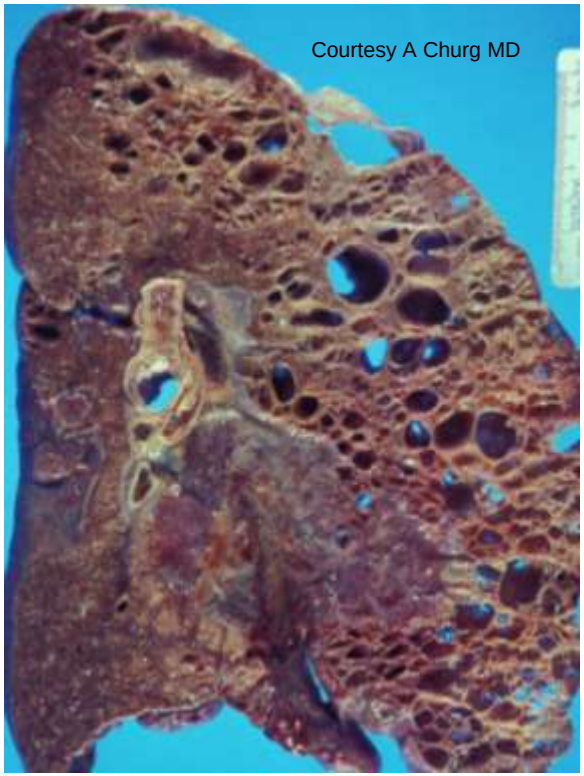
(From Winternitz)



Acute (1918 flu)

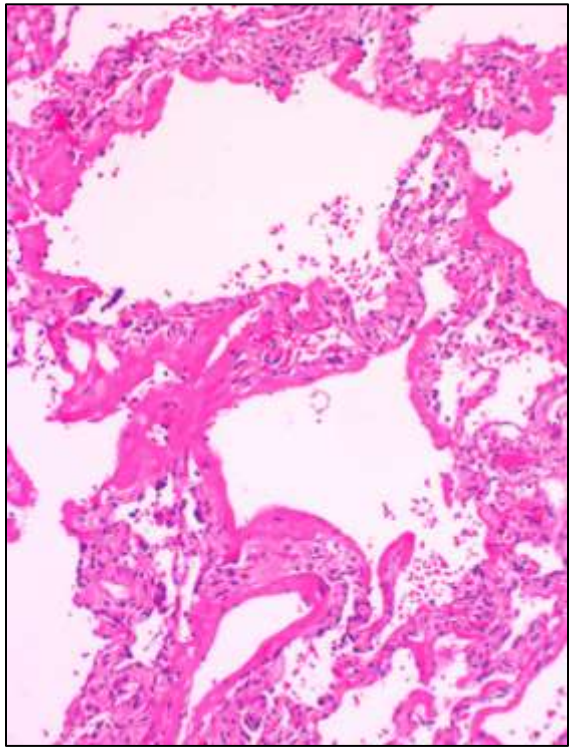


Organizing phase

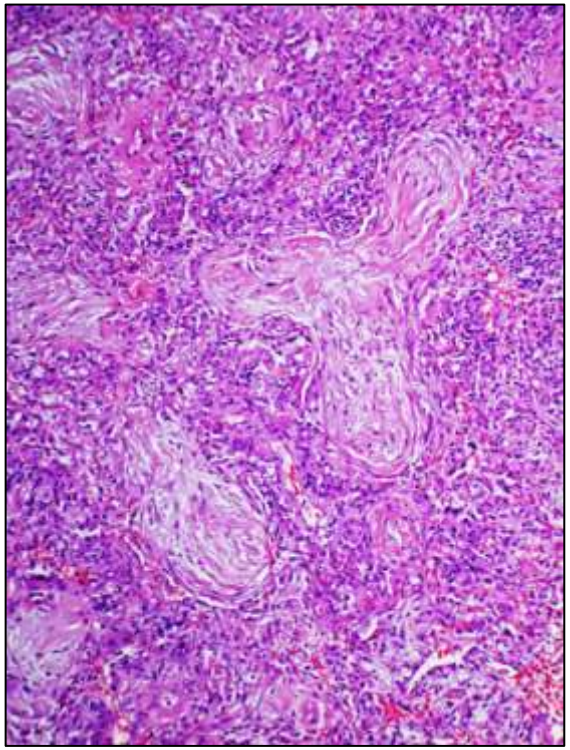


Late/organized
Resembles honeycombing

DIFFUSE ALVEOLAR DAMAGE

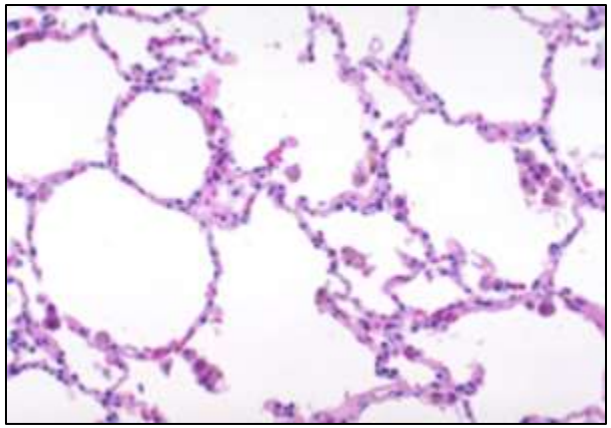


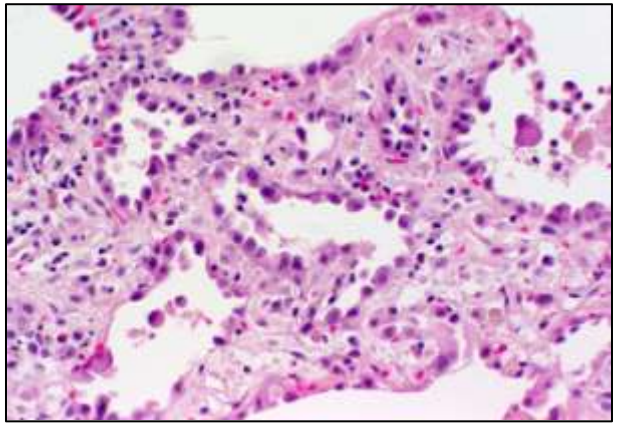
Acute injury with hyaline membranes



Repair with airspace organization

Resolved/healed with normal histology





Resolved/healed with mild interstitial fibrosis

WHERE DOES HAMMAN-RICH SYNDROME FIT ??

(BULL JOHNS HOPKINS HOSP 74: 177, 1944)

Case 1 47M with cough, SOB; died 3 mos

Case 2 21F; "chest cold", SOB; died 1.5 mos

Case 3 37F with SOB; died 1 month

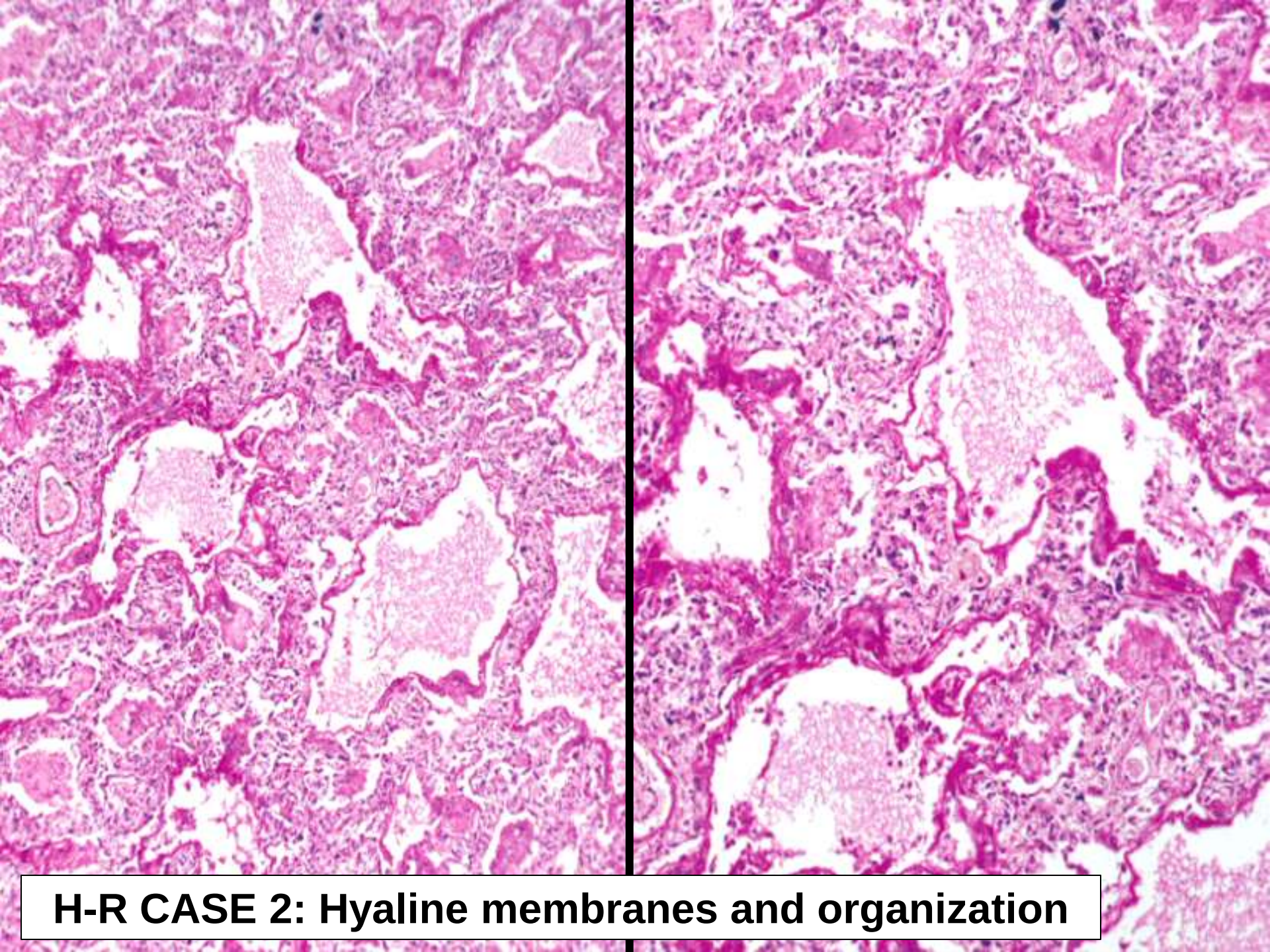
Case 4 68F with cough, SOB; died 2 mos

Hamman-Rich syndrome: "rapidly progessive lung fibrosis"

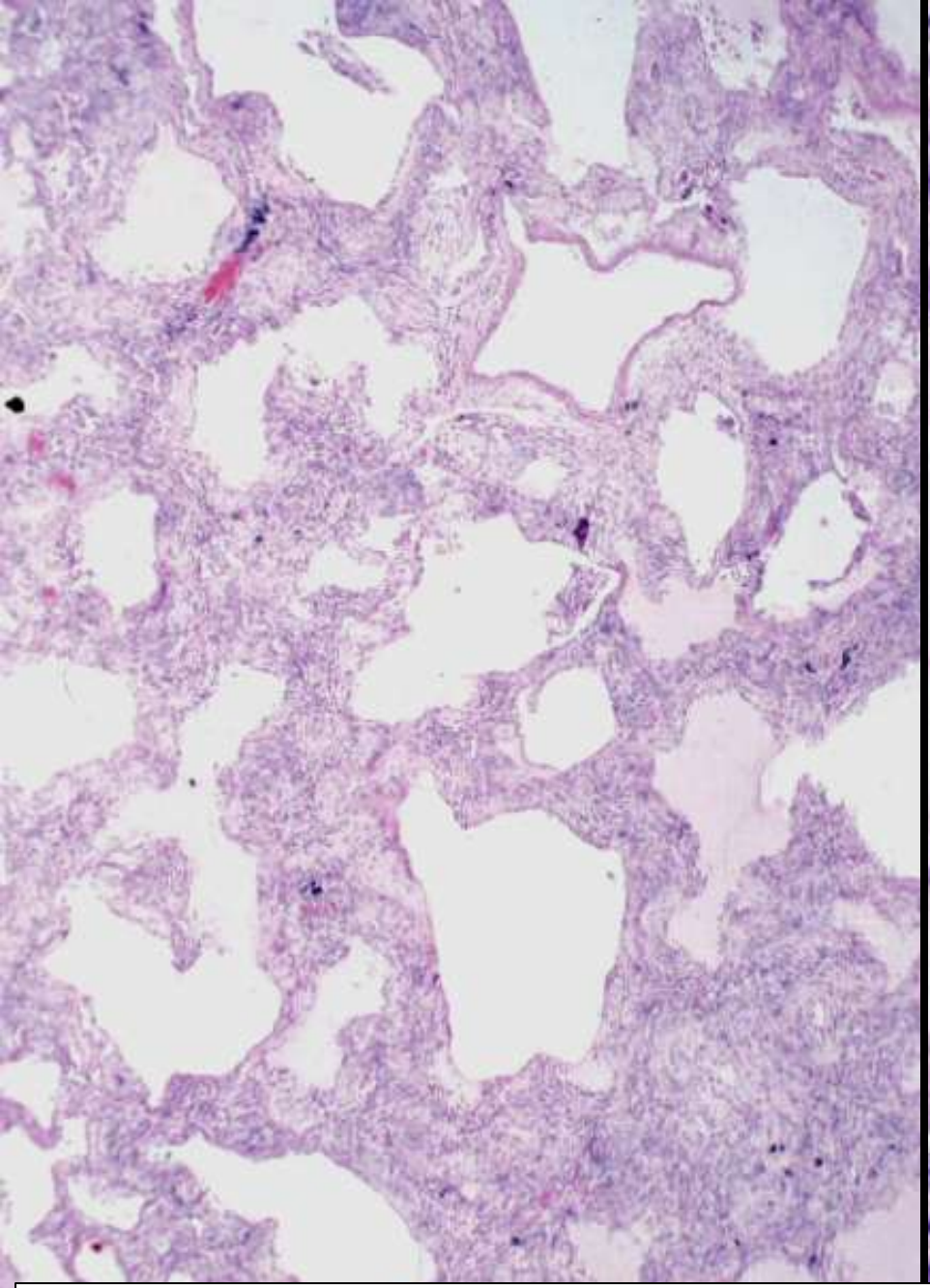
- Not synonomous with IPF
- More akin to DAD
- But from a bygone time with no ventilators, oxygen therapy etc.

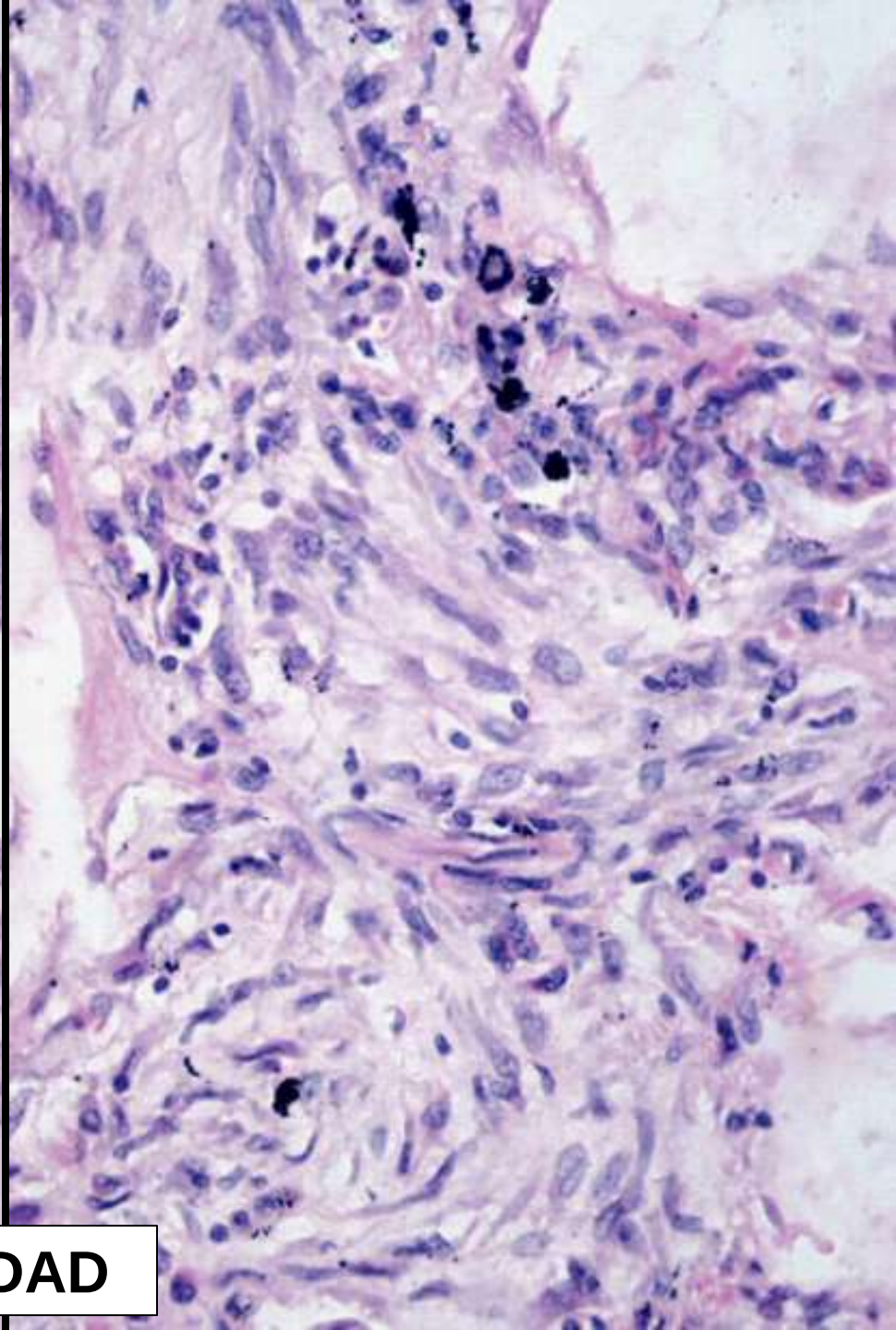
Rich

Hamman



H-R CASE 2: Hyaline membranes and organization





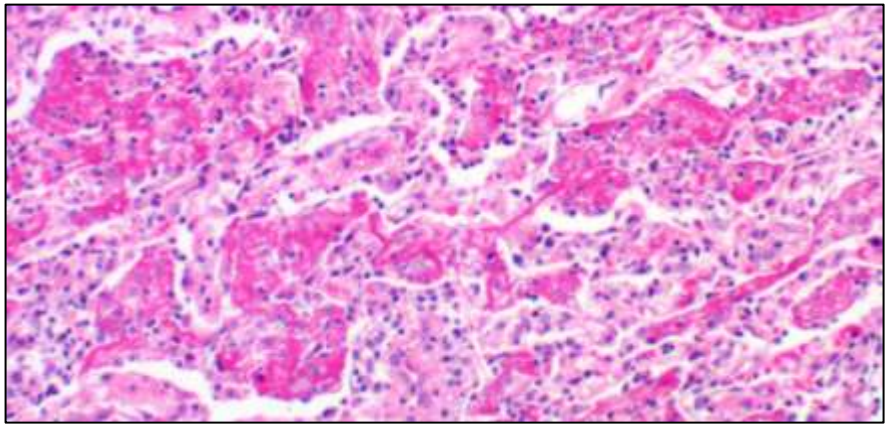
H-R CASE 3: c/w organizing DAD

DAD: CAUSES/DIFFERENTIAL DIAGNOSIS

- Infection: many implicated
- Toxic injury
- Drugs; esp chemotherapeutics
- Shock
- Sepsis
- Collagen vascular disease\
- Unknown (Acute interstitial pneumonia//AIP)
- Misc.

3. FIBRINOUS EXUDATES

<u>Airspace fibrin</u> is very common in acute alveolar injury regardless of cause; it is a good marker for acute injury



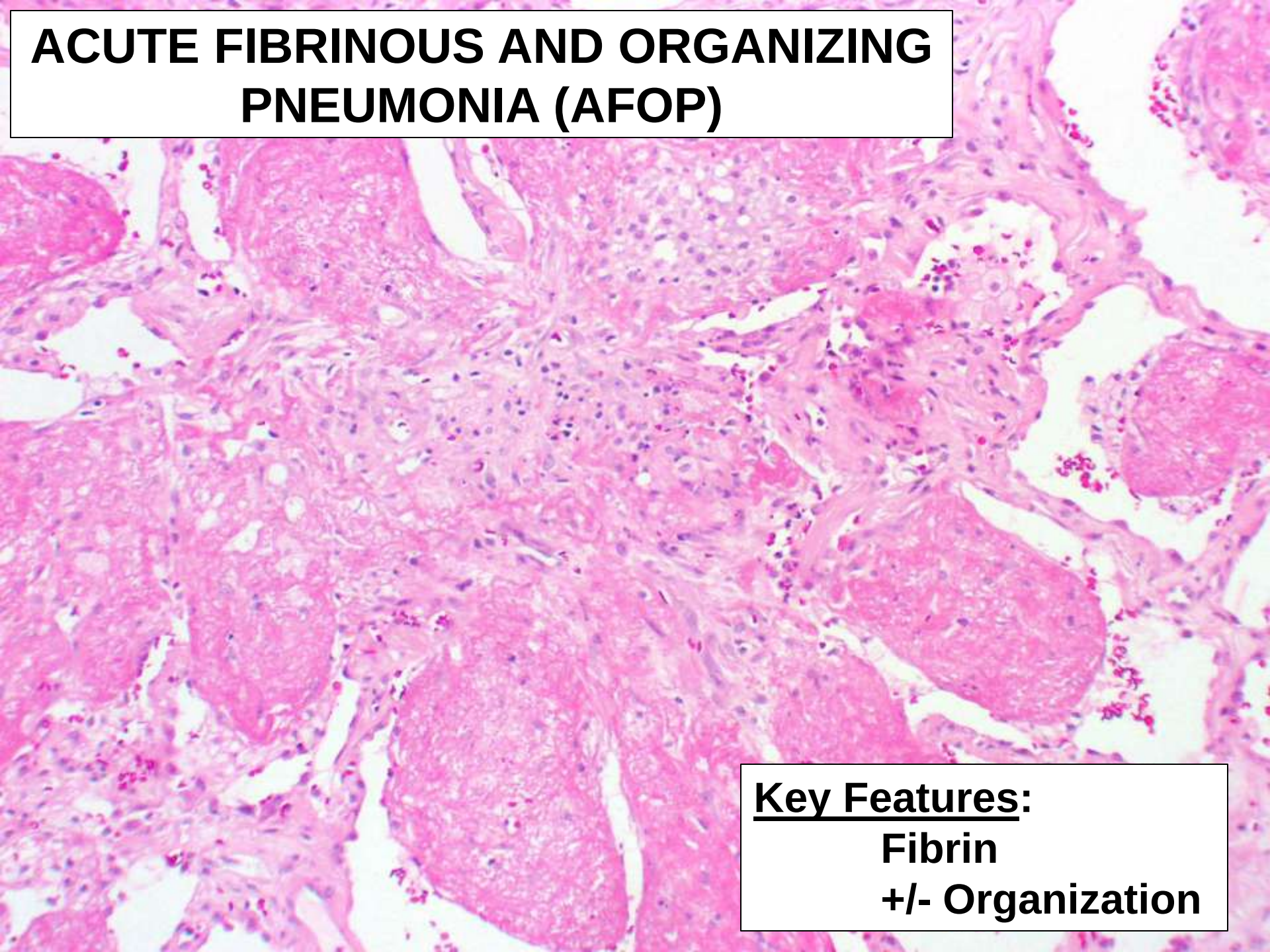
From original BOOP cases: NEJM 1985

<u>Acute fibrinous and organizing pneumonia//AFOP</u>

(Beasley MB, et al. Arch Pathol Lab Med. 2002;126:1064)

- **Acute lung injury dominated by airspace fibrin and organization**
- **Overlaps with DAD and OP patterns**
- **A recognizable pattern of acute lung injury**

ACUTE FIBRINOUS AND ORGANIZING PNEUMONIA (AFOP)



Key Features:

Fibrin

+/- Organization

ACUTE FIBRINOUS AND ORGANIZING PNEUMONIA (AFOP)

Beasley MB, et al. Arch Pathol Lab Med. 2002;126:1064-70.

17 cases; 10M, 7F; (Aged 33-78 yrs)

“Dominant pattern of fibrin and OP”

Associations: CVD, drugs, infections, et al. (None in 6)

Course: Rapid death (9), Subacute with recovery (8)

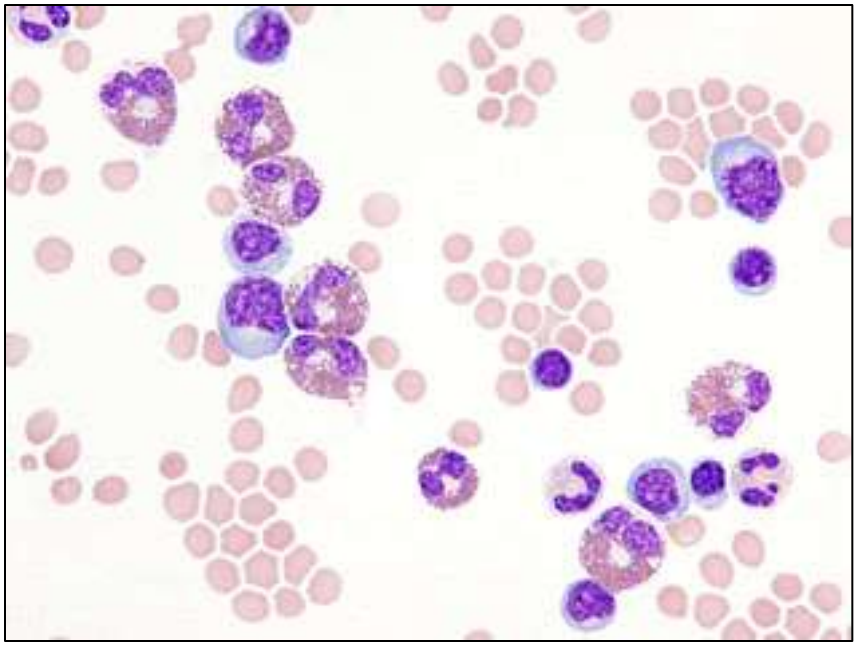
Key feature is recognizing the acute injury and considering the differential

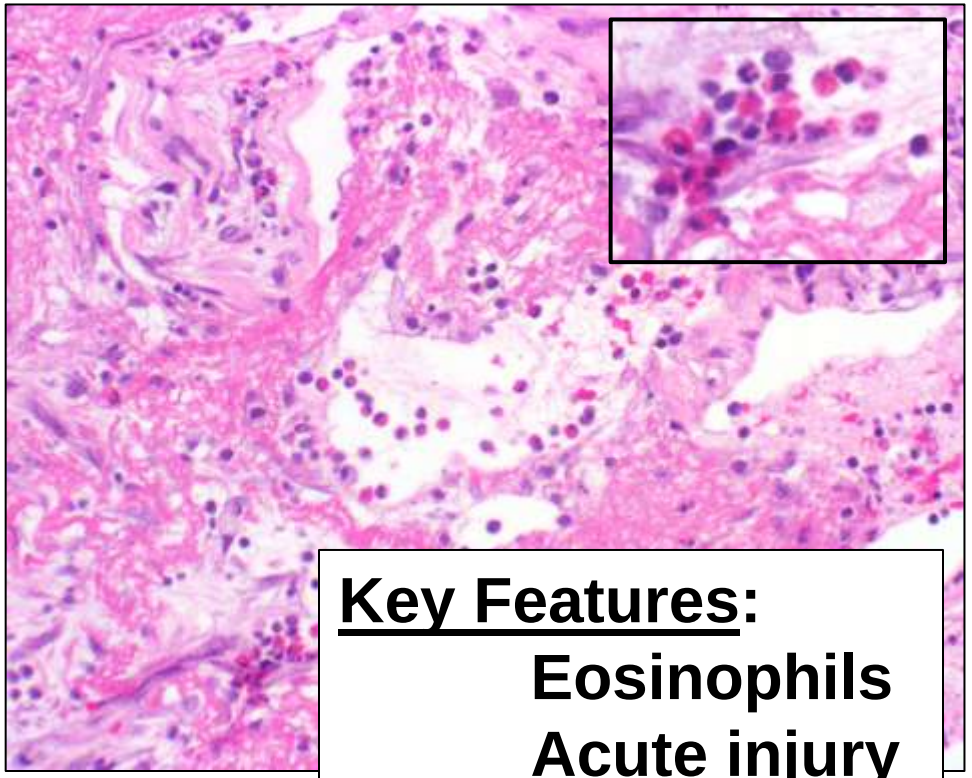
4. ACUTE EOSINOPHILIC PNEUMONIA (AEP)

Acute eosinophilic pneumonia

BAL: >25-40% eosinophils

Biopsy: DAD with ↑↑ eosinophils





Key Features:

Eosinophils

Acute injury

IDIOPATHIC ACUTE EOSINOPHILIC PNEUMONIA:A STUDY OF 22 PATIENTS

(PHILIT ET AL. IN AM J RESPIR CRIT CARE MED 2002;166:1235)

Criteria: 1. Acute febrile illness (< 1 mo) 2. Bilateral infiltrates 3. Hypoxemia 4. Lung eosinophilia (> 25% eos on BAL) 5. Absence of known cause or association (. Eg, drug, infection, etc)

TABLE 3. BLOOD AND LUNG LABORATORY FINDINGS AT THE TIME OF HOSPITALIZATION

Parameter	Mean ± SD
WBC, 10^9/L	20.7 ± 10.9
Neutrophils, 10^9/L	17.6 ± 10.4
Eosinophils, 10^9/L	0.98 ± 1.5
C reactive protein, mg/L	121.1 ± 93.7
Pa_{O_2} on room air, mm Hg (n = 12)	46 ± 8
$Pa_{O_2}/F_{I_{O_2}}$ (n = 9)	118 ± 49
Sp_{O_2} on room air, % (n = 1)	86
Total BAL cell count, cells/μl	765.6 ± 527.7
BAL eosinophils, %	54.4 ± 19.2
BAL macrophages, %	19.4 ± 13.5
BAL neutrophils, %	13.0 ± 14.0
BAL lymphocytes, %	12.5 ± 12.7

Definition of abbreviations: BAL = bronchoalveolar lavage; WBC = white blood cells.

EOSINOPHILIC PNEUMONIA SYNDROMES: Approach

- Rule out infection-associated
- Rule out drug/toxin-associated
- Consider idiopathic eosinophilic pneumonia syndromes (AEP, CEP)
- Miscellaneous other syndromes

AEP Outcome: Prompt resolution on steroids in most cases; rarely fatal

5. DIFFUSE ALVEOLAR HEMORRHAGE (DAH) IS A FORM OF ACUTE ALVEOLAR INJURY

MAJOR CAUSES:

ANCA-associated vasculitis

- **Granulomatosis with polyangiitis (GPA/Wegener's)**
- **Microscopic polyangiitis (MPA)**

Collagen Vascular diseases

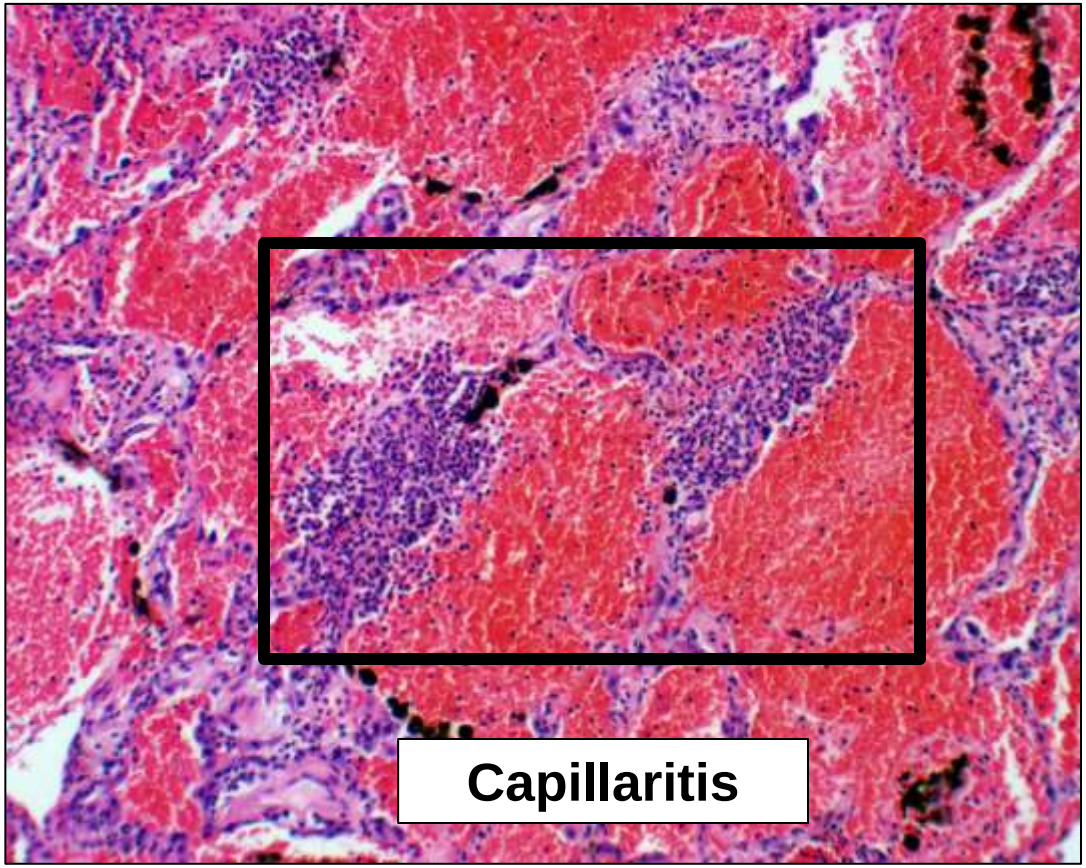
Anti-GBM disease (Goodpasture's syndrome)

Idiopathic Pulmonary Hemosiderosis (IPH)

Miscellaneous

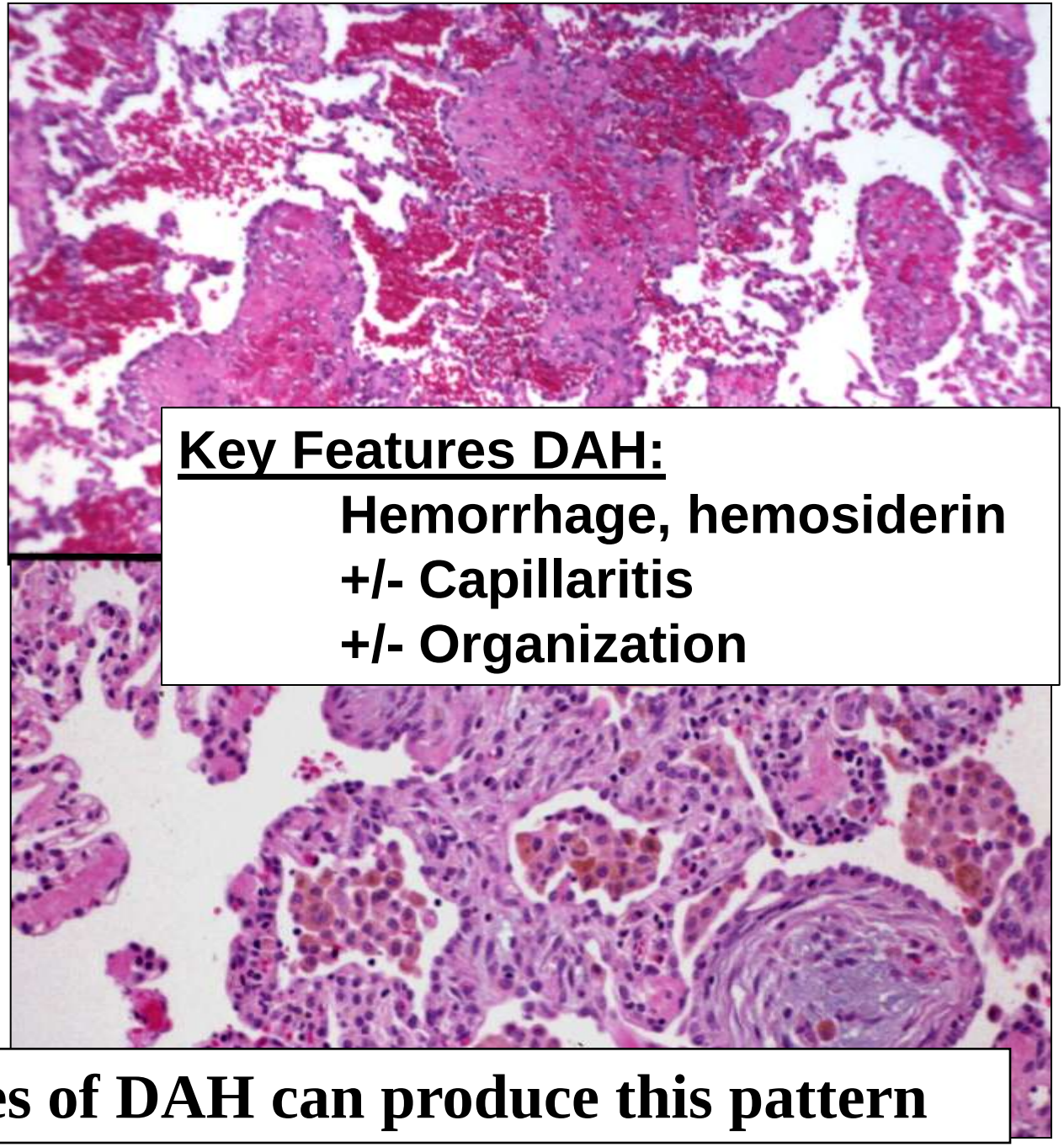
Early aggressive therapy is critical for a favorable outcome

5. ACUTE/DIFFUSE ALVEOLAR HEMORRHAGE (DAH)



Diffuse Alveolar Hemorrhage

(Anti-GBM Disease)



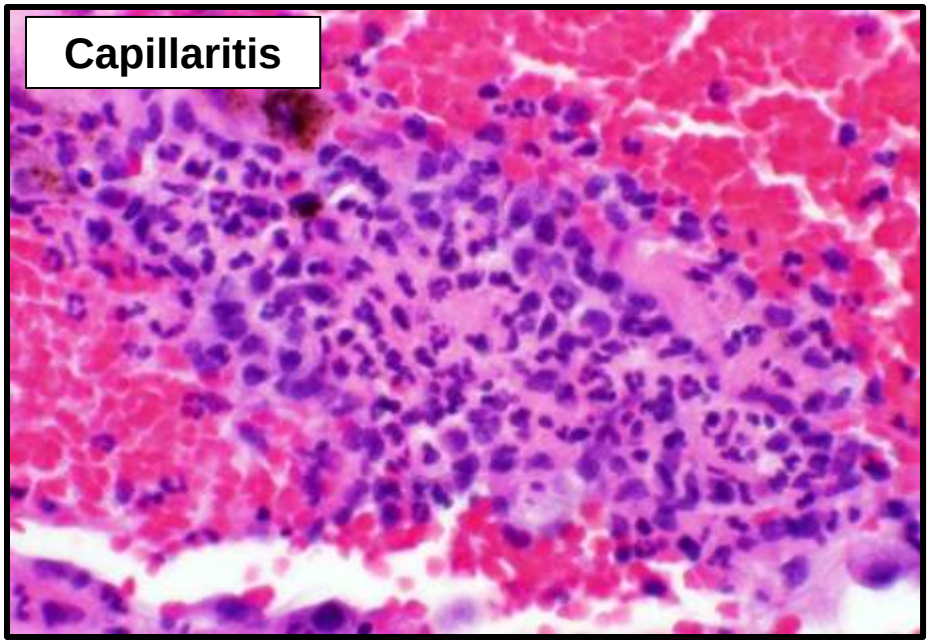
Key Features DAH:

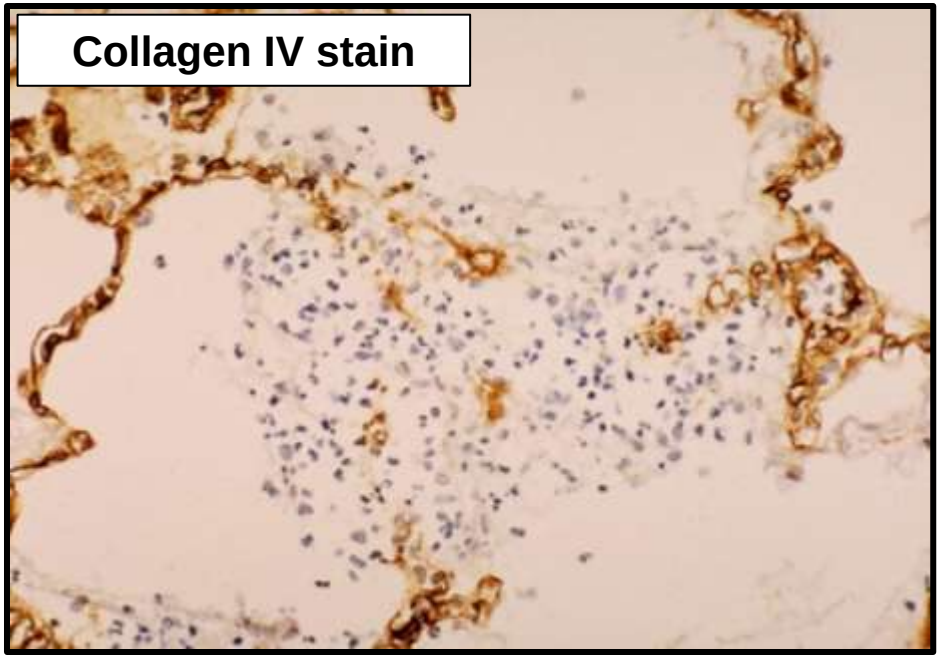
Hemorrhage, hemosiderin
+/- Capillaritis
+/- Organization

= Organizing pneumonia with hemosiderin

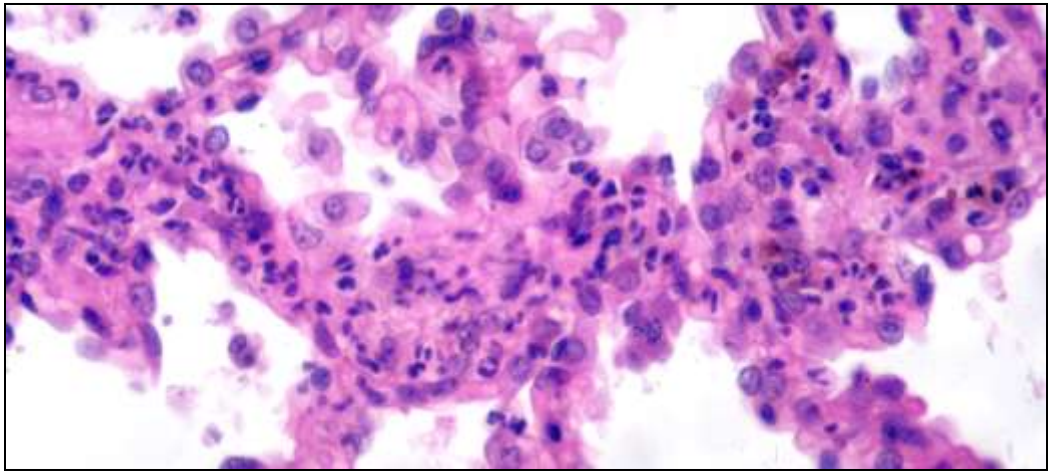
Any of the causes of DAH can produce this pattern

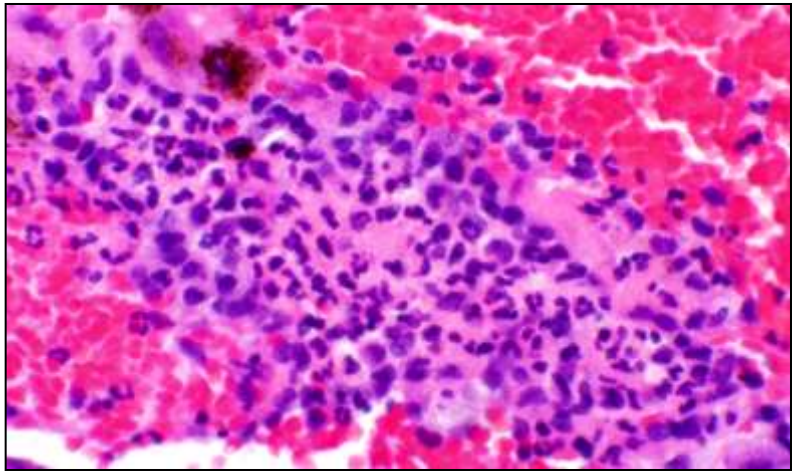

Photo courtesy A. Churg MD


Capillaritis


Collagen IV stain

CAPILLARITIS IN DAH





Capillaritis=Acute inflammation of alveolar septum/capillary

Capillaritis is common in DAH

Capillaritis is analogous to leukocytoclastic vasculitis in the skin

Capillaritis is not specific

Capillaritis is not a disease

SUMMARY

The various forms of acute alveolar/lung injury show histologic overlap but biopsies can usually be put into one of five categories: Edema, DAD, AFOP, AEP, DAH

The causes of DAD are generally similar to those of AFOP

Acute eosinophilic pneumonia and acute diffuse alveolar hemorrhage have much more limited differential diagnoses

Outcome (All patterns): May resolve completely, be fatal, or may leave scarring