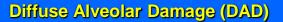
Biennial Pulmonary Pathology Meeting June 2015

Henry D. Tazelaar, M.D. Mayo Clinic Arizona

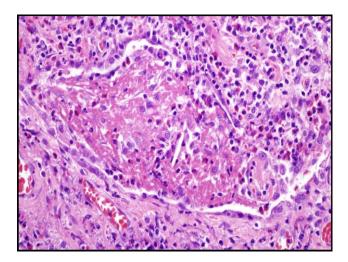


- How do we recognize diffuse alveolar damage?
- Are there clues to the cause of the severe acute lung injury?
- Is the acute respiratory distress syndrome (ARDS) synonymous with DAD?

Acute Lung Injury

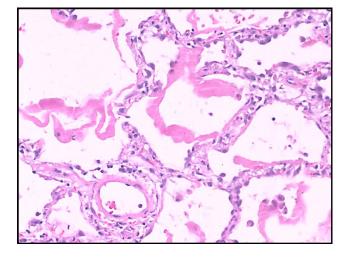
"We use the term acute lung injury pattern in a general sense to encompass diffuse alveolar damage and BOOP. This term emphasizes the relatively recent onset of changes, usually within days to weeks of injury, since they are related to a single injurious event occurring at one specific time..."

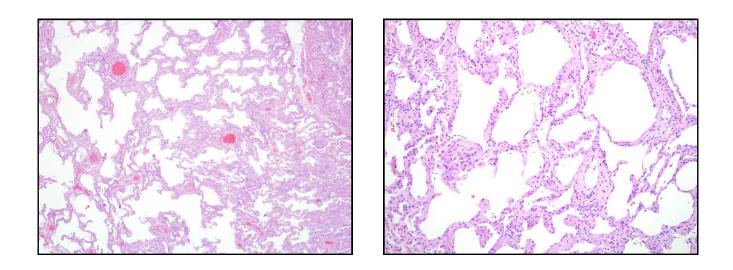
> (atzenstein and Askin's Surgical Pathology of Non-neoplastic Lung Disease, 3rd ed. 1997

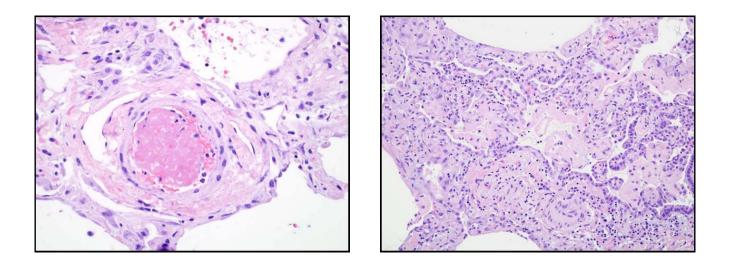


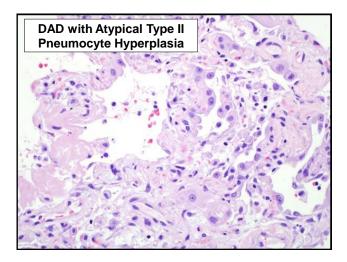
Diffuse Alveolar Damage Histologic Hallmarks

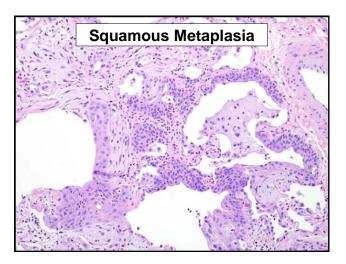
- Homogeneous Geographic "Fibrosis" of same age
- Little architectural distortion
- Associated findings
 - Small thrombi
 - Atypical type II pneumocytes
 - -Squamous metaplasia

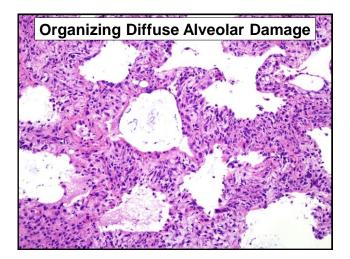


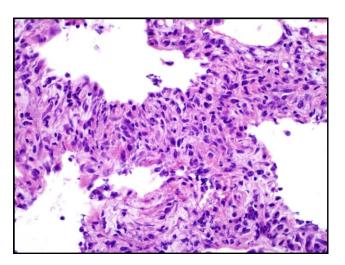












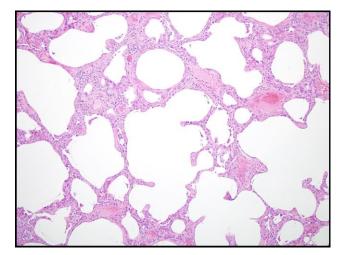
Late Diffuse Alveolar Damage

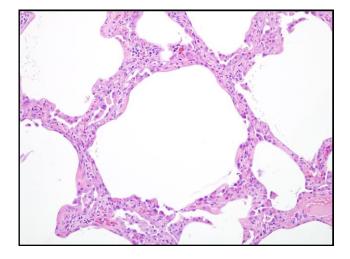
 Previously healthy 56 yr old man who presented <u>3 mos</u> prior to admission with 2-3 days of shortness of breath

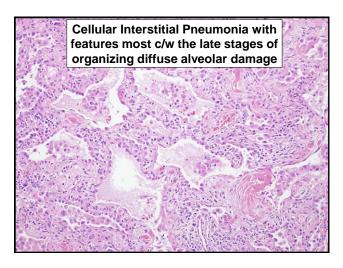
CT: diffuse alveolar infiltrates

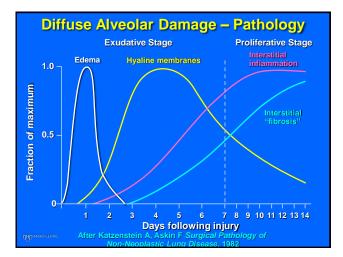
 Treated with steroids and gradually improved, although he then began to get worse

• CT: diffuse ground glass, but no evidence of background fibrosis









Diffuse Alveolar Damage

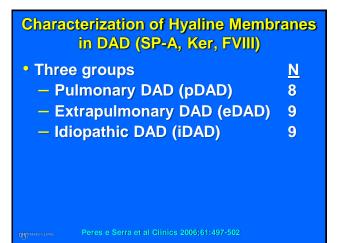
- How do we recognize diffuse alveolar damage?
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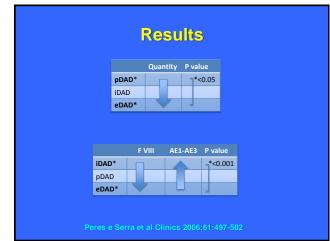
Diffuse Alveolar Damage Can Histology Predict Etiology?

- Pathogenic pathways
- Other pathologic features

Diffuse Alveolar Damage

- Three etiologic forms proposed
 - Idiopathic
 - Primary pulmonary e.g. direct toxic effects/infection
 - Extra pulmonary e.g. sepsis/ shock





Immunohistochemistry of Hyaline Membranes (SP-A, Ker, FVIII)

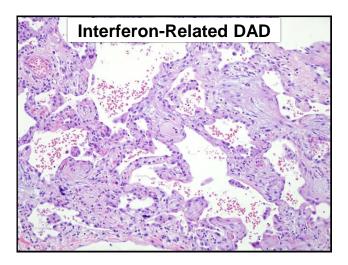
- Propose
 - iDAD: HM's result from simultaneous destruction of type II cells and endothelium
 - eDAD: HM's result from minor endothelial injury, and more epithelial injury
 - pDAD: unclear results

Peres e Serra et al Clinics 2006;61:497-502

Diffuse Alveolar Damage

- Airspace organization —> Extra pulmonary/sepsis
- Airspace and interstitial organization
 Idiopathic or drug-related/
 - primary pulmonary

MOCLINE Kang DT el al. Hum Pathol 2009; 40:1618-27

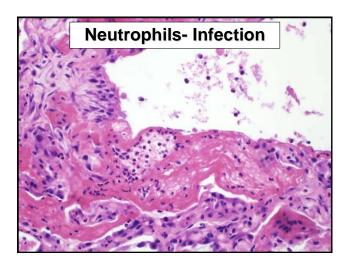


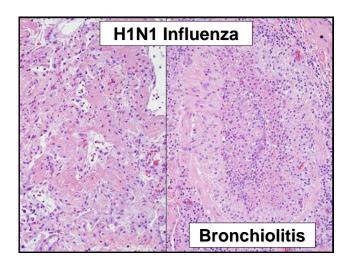
Diffuse Alveolar Damage in Lung Biopsies, N=58

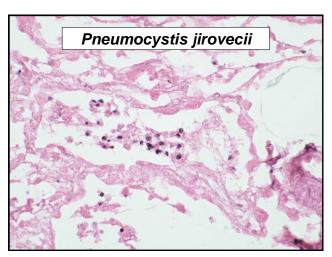
Cause	<u>%</u>
Infection, mostly viral	22
Idiopathic (acute interstitial pneumonia)	21
Non-infectious transplant-related	17
Connective tissue disease-associated	16
Acute exacerbation of IPF	12
Drug reaction	10
Radiation induced	2

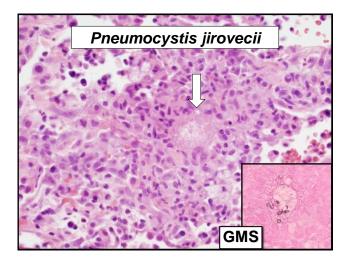
Diffuse Alveolar Damage Can Histology Predict Etiology? Other Pathologic Features

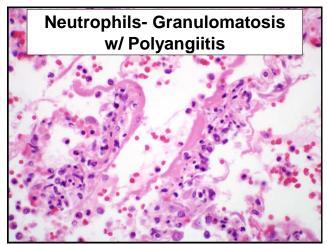
- Neutrophils- sepsis, capillaritis
- Small granulomas- infection, aspiration
- Fibrosis c/w UIP- acute exac. IPF
- Eosinophils- acute eosinophilic pn.
- Foam cells- drug toxicity

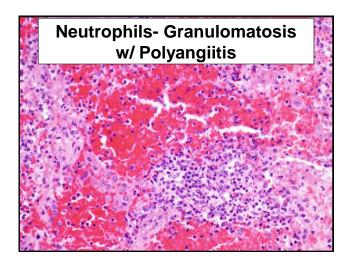


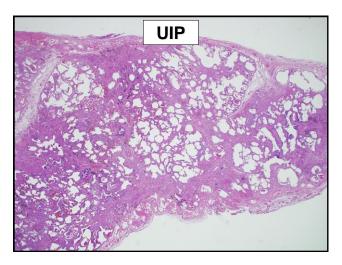


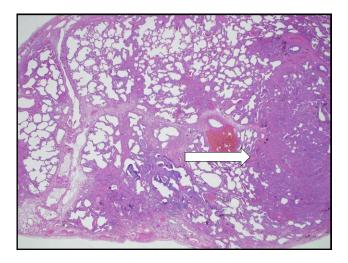


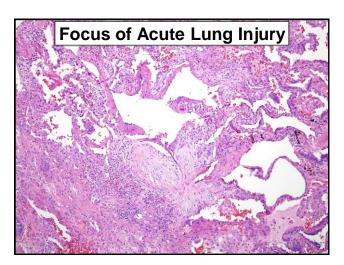


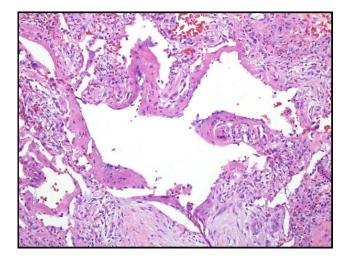






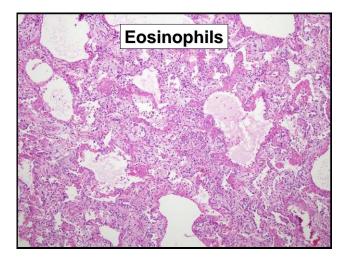


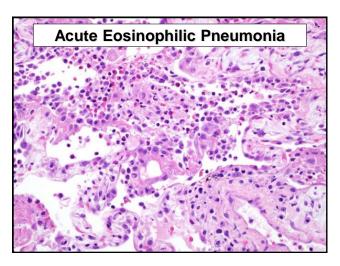


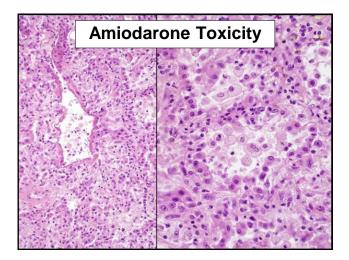


Acute Exacerbation of Idiopathic Pulmonary Fibrosis

- ~15% of IPF patients
- May occur in previously undiagnosed patients
- Common cause of death in IPF
- DDx: aspiration, infection, drug







Diffuse Alveolar Damage Helpful Clues in History

- Connective tissue disease
- Recurrent episodes
 - Multiple pain meds (neurontin, gabepentin, morphine)
 - Aspiration
- Serologies
- Multiple organ dysfunction —> sepsis

Drug Induced Recurrent DAD

- 71 year old woman with longstanding Oxycontin addiction
- 2003 biopsy: acute and organizing diffuse alveolar damage
- Maintained on steroids compression fractures
- Multiple new pain meds
- 2006 biopsy: acute and organizing diffuse alveolar damage (GMS negative)

TO MADGENNE Savici D, Katzenstein AL Hum Pathol. 2001;32:1398-402

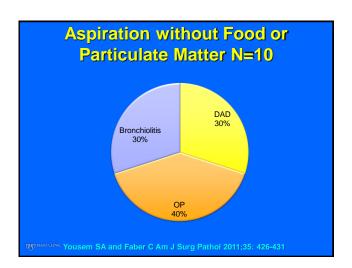
DAD and Recurrent Respiratory Failure N=6

- Narcotics for pain
 4
- Psychotropic drugs
 3
- GERD/hiatal hernia
 5

6

Chronic pain syndromes

TO MANGELINE Savici D, Katzenstein AL Hum Pathol. 2001;32:1398-402



Diffuse Alveolar Damage

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Ф^{р мако сило}

Acute Lung Injury Patterns Definitions of Related Terms

Acute respiratory distress syndrome (ARDS)
 Clinical syndrome: Rapidly progressive

respiratory failure following an identifiable catastrophic event

- Diffuse alveolar damage (DAD)
 Histopathologic changes seen in patients with ARDS
- Acute interstitial pneumonia (AIP) Idiopathic clinicopathologic syndrome: Rapidly progressive interstitial pneumonia (i.e., "idiopathic ARDS")

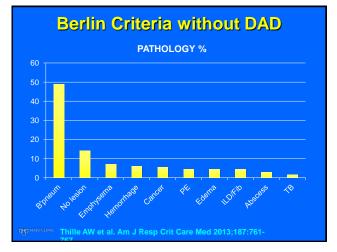
ARDS The Berlin Criteria, 2012			
Timing	1 week of known insult or new/worsening sypmtoms		
Imaging	Bilateral opacities-not fully explained by effusions, lobar/lung collapse, or nodules		
Origin of edema	Resp failure not fully explained by cardiac failure or fluid overload; if no risk factors present, need objective assessment to exclude hydrostatic edema		
Ferguson ND et al. Intensive Care Med 2012;38:1573			

ARDS The Berlin Criteria, 2012					
Oxygenation	Mild	Moderate	Severe		
mmHg	$\begin{array}{l} PaO_2;FiO_2\\ > 200^, \leq 300\\ \text{with}\\ PEEP \text{ or}\\ CPAP \geq 5 \text{ cm}\\ H_2O \end{array}$	$PaO_2:FiO_2 > 100, \le 200$ with PEEP ≥ 5 cm H ₂ O	$\begin{array}{l} \text{PaO}_2:\text{FiO}_2\\ \leq 100\\ \text{with}\\ \text{PEEP} \geq 5\\ \text{cm} \ \text{H}_2\text{O} \end{array}$		
(C) invocurse					

Berlin ARDS and DAD

- Autopsy study of patients who met Berlin criteria
- N=356
- DAD: 45%
 - DAD plus bronchopneumonia 62%
 - DAD more common in patients with ARDS > 72 hours
 - With severe ARDS, 69% had DAD

Thille AW et al. Am J Resp Crit Care Med 2013;187:761-



Diffuse Alveolar Damage Summary

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