

Diagnostikk av interstitielle lungesykdommer

”Pattern recognition”

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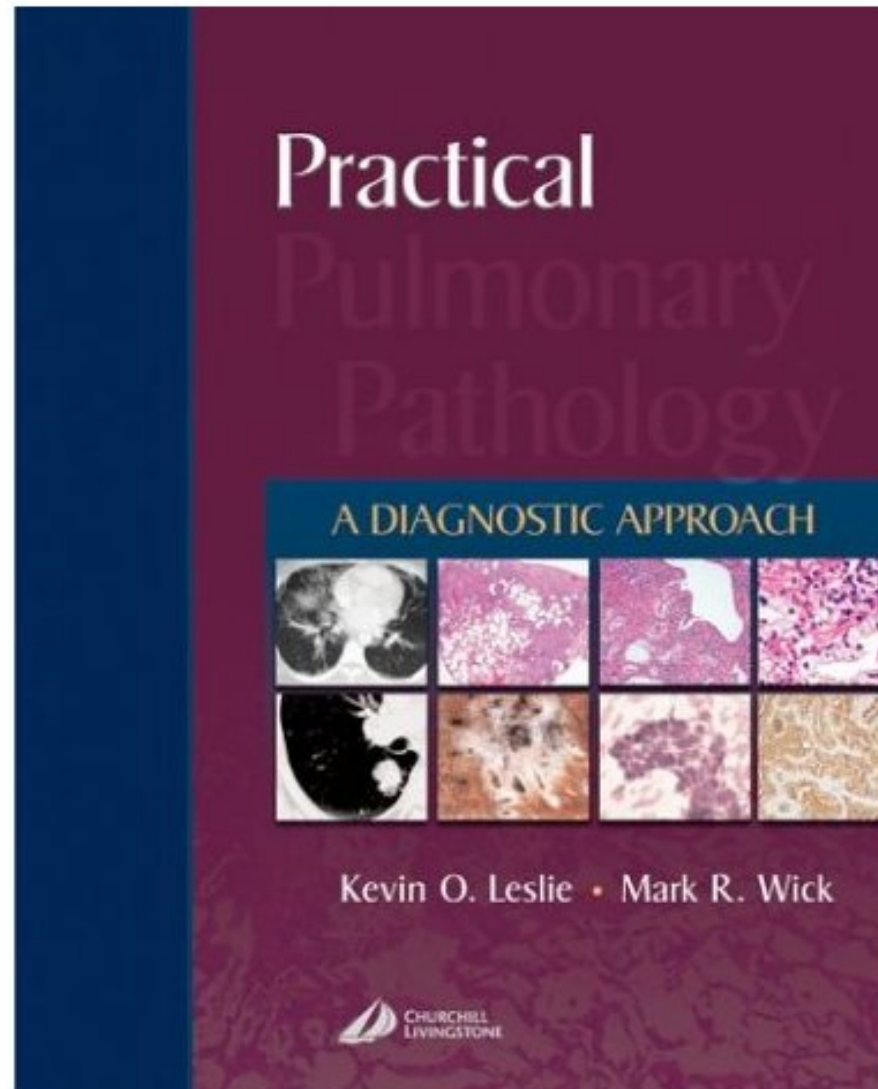
“The Six Pattern Approach”



Professor Kevin O. Leslie



Mayo Clinic Scottsdale, Arizona



Practical Pulmonary Pathology

Royal Society of Medicine 2005 Book of the Year

Introduksjon

1. Diffuse lungelidelser kan være:

- infeksiøse
- immunologisk / toksisk / støv-relaterte
- neoplastiske

2. Ulike mønstre (“patterns”) kan påvises.

Via disse mønstre kan ulike tilstander identifiseres

3. Deretter søkes tilleggsfunn som innsnevrer diff.dignosene.

Identifikasjon av
hovedmønster (pattern)
gjøres ved liten
forstørrelse

The 6 Patterns of Interstitial Lung Disease

Pattern 1	Pattern 2	Pattern 3	Pattern 4	Pattern 5	Pattern 6
ALI	Fibrosis	Cellular IP	Alv. Filling	Nodules	Minimal Δ
Hyaline memb Infection CVD Drug Idiopath	Temp Hetero UIP Asbestosis RA Chr HSP	Lymphs & PC's NSIP, CVD HSP, Drugs, Infection, Lymphoma	Macs Smoking Dis Local fibrosis Obstruction	Lymphoid Lymphoma Foll Bronch Wegener's	SAD Constrictive bronchiolitis
Eosinophils AEP Drug DAD in smoker	Honeycomb Diffuse -Late UIP Focal -Many causes	Polys Infection CVD Hemorrhage	Polys Infection Hem Synd	Granulomas Sarcoid, Asp.	Vascular PHT, PVOD
Necrosis Infections Some tumors	Diff Fibrosis CVD Drug Sarcoid PLCH Pneumocon	Granulomas Infection, HSP Sarcoid/Bery Aspiration	OP Infection, Drug, CVD	Necrosis Infections Tumor Wegener's	Cysts PLCH LAM
Siderophages Hem Synds CVD	Pleuritis CVD	Patchy OP Infection CVD, COP	Eosin material Infection, CVD, Drug, Hem Synd, CHF, PAP	Atyp cells Infections, Ca Lymphomas Sarcomas	Sampling
		Pleuritis CVD	Hemorrhage CVD, Drug, Hem Synd	Stellate scars PLCH	
				OP Infections, CVD Drug, Wegener's, Infarct	

Klinikk ved diffuse lungelidelser

Akutt sykdom

Diffuse alveolar damage
(sjokk/infeksjon)

Akutt eosinofil pneumoni

Medikamentell /toksisk

Revmatiske sykdommer
("collagen vascular disease")

Vaskulitt / Alveoleblødn.

Akutt interstitiell pneumoni (AIP)

Akutt forverring av IPF (UIP)

Subakutt sykdom

Organiserende pneumoni

Cryptogen organiserende
pneumoni (COP)

Hypersensitivitet pneumoni

Lymphocytic interstitial
pneumonia (LIP)

Eosinophilic pneumonia

RBILD/DIP/PLCH

Sarkoidose/Berylliose

Revmatiske sykdommer

Medikamentskade

NSIP

Kronisk sykdom

Pneumoconiose

Lymphangitic tumor

RBILD/DIP/PLCH

Sarkoidose/Berylliose

Revmatiske
sykdommer

Alveolær proteinose

Small airways disease

Amyloidose

UIP/IPF

De 6 mønstre for interstitielle lungesykdommer

<p>1. Akutt lunge skade Prototype: DAD</p>	<p>4. Alveolar Filling Prototype: OP</p>
<p>2. Fibrose Prototype: UIP</p>	<p>5. Noduli Prototype: Wegener's</p>
<p>3. Interstit. betennelse Prototype: Hypersens. pneum.</p>	<p>6. Minimale forandr. Prototype: Small airway disease</p>

Mønster 1: Akutt Lunge Skade

Hovedfunn mønster 1

- Utvidete alveolesepta
- Ødem og fibrin i alveoler
- Reaktive alveoleceller

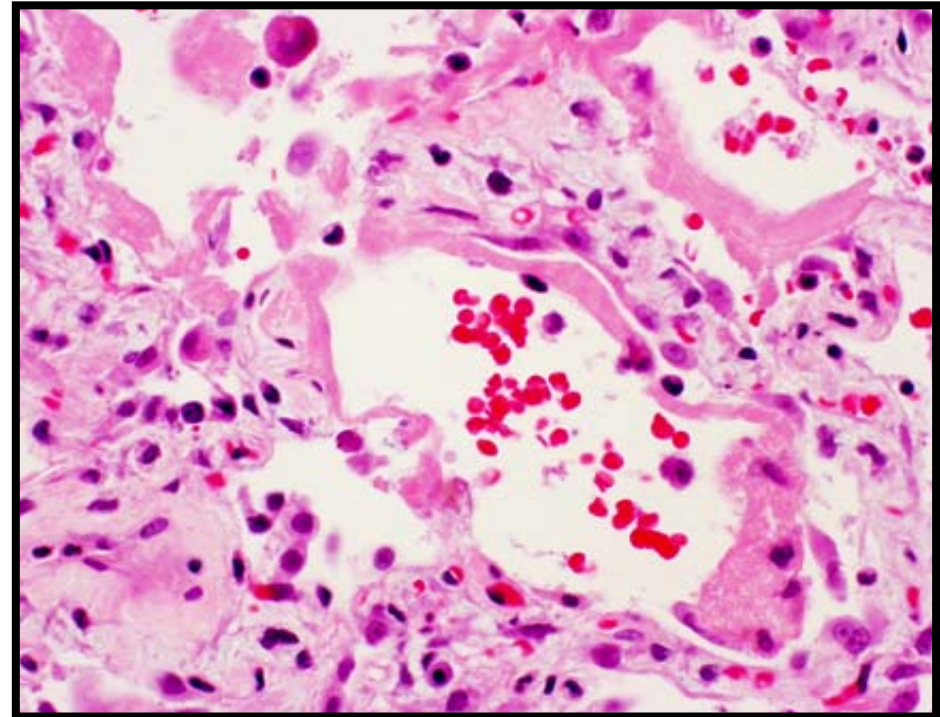
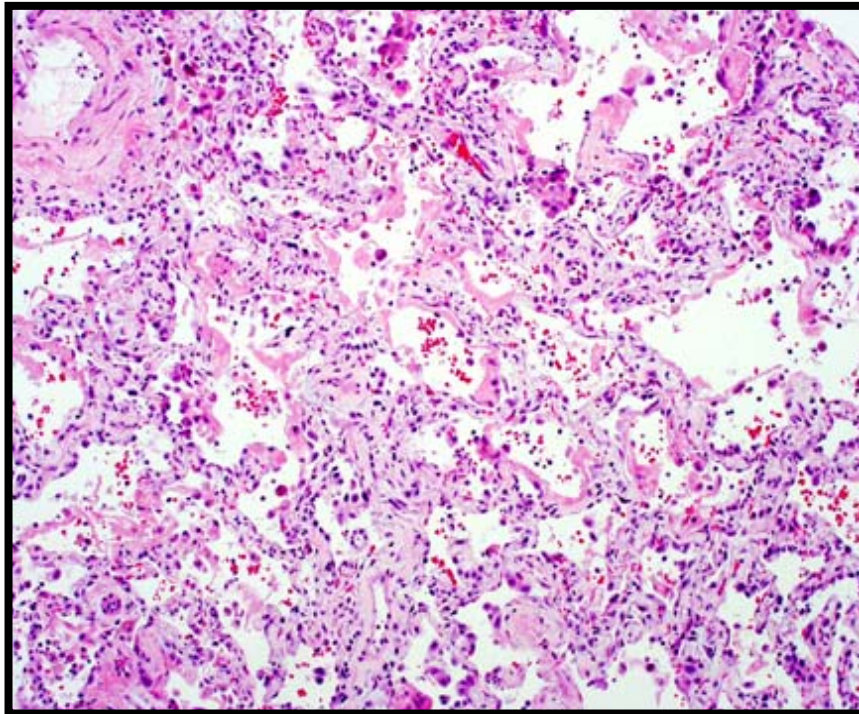
Mønster 1: Akutt lungeskade

Viktige parametere:

- **Hyaline membraner ?**
- **Nekrose ?**
- **Eosinofile ?**
- **Pigmentmakrofager ?**

Mønster 1: Akutt lungeskade

- Med hyaline membraner



Infeksjon Medikamentskade
Revmatiske sykd.

Stråleskade
Idiopatisk (AIP)

Ved akutt lungeskade:

First: Look for **Bugs**

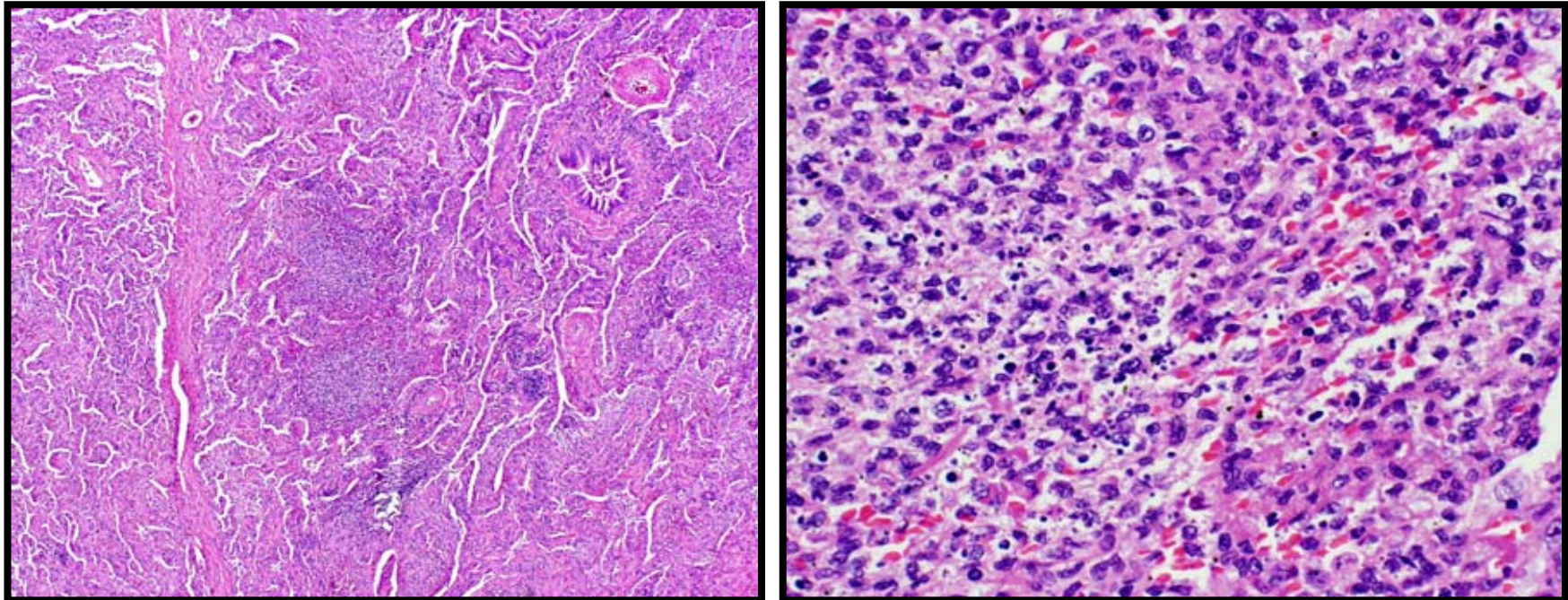
Next: Rule out **Drugs**

Still in doubt: Check the **serology**

When all else fails: Call it **“idiopathic”**

Mønster 1: Akutt lungeskade

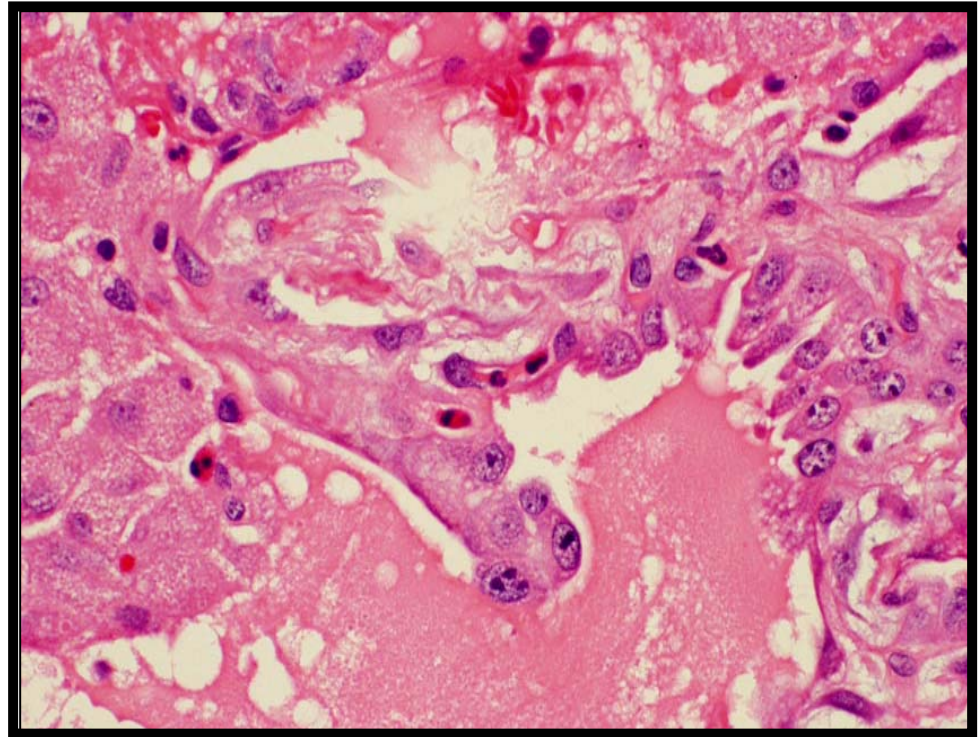
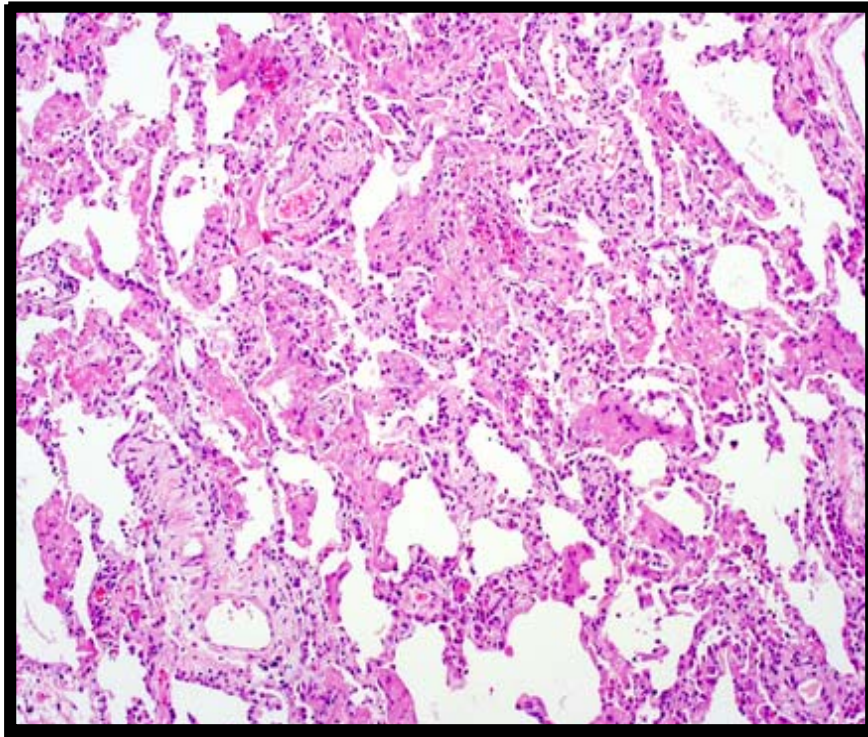
- **Med nekrose**



- Virus (f.eks. Herpes, Adeno)
- Bakterier
- Sopp...sjelden mycobakterier

Mønster 1: Akutt lungeskade

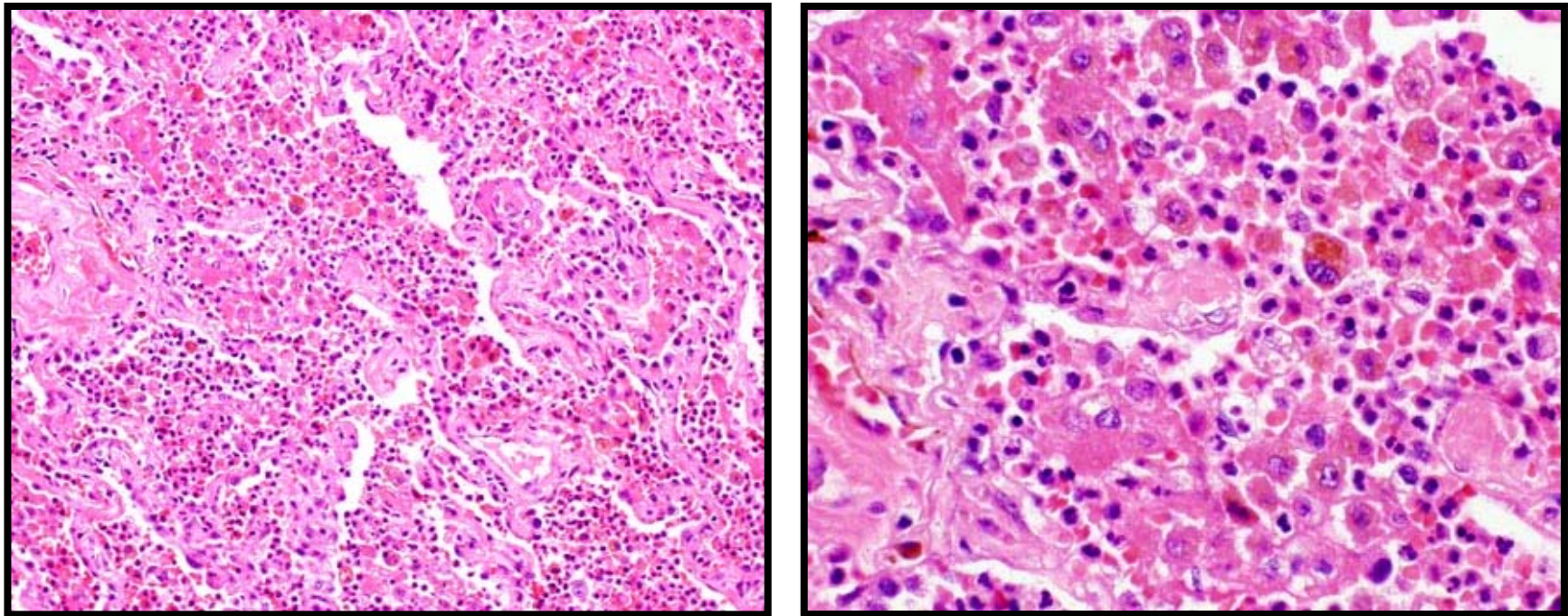
- **Med eosinofile**



- Akutt eosinofil pneumoni (astma, medikament, idiopatisk)

Mønster 1: Akutt lungeskade

- **Med pigmentmakrofager**



Diffus alveoleblødning - alle årsaker

Storrøyker (DIP-liknende) - med DAD

De 6 mønstre for interstitielle lungesykdommer

1. Akutt lunge skade

Prototype: DAD

4. Alveolar Filling

Prototype: OP

2. Fibrose

Prototype: UIP

5. Noduli

Prototype: Wegener's

3. Interstit. betennelse

Prototype:
Hypersens. pneum.

6. Minimale forandr.

Prototype: Small
airway disease

Mønster 2: Fibrose

Idiopatiske

Kjent årsak

UIP

eller

”fibrøs”

NSIP

eller

uspesifisert
fibrose

Revmatiske sykdommer

SLE

MCTD

RA

Sklerodermi

Sjøgren

Dermatomyositt/polymyositt

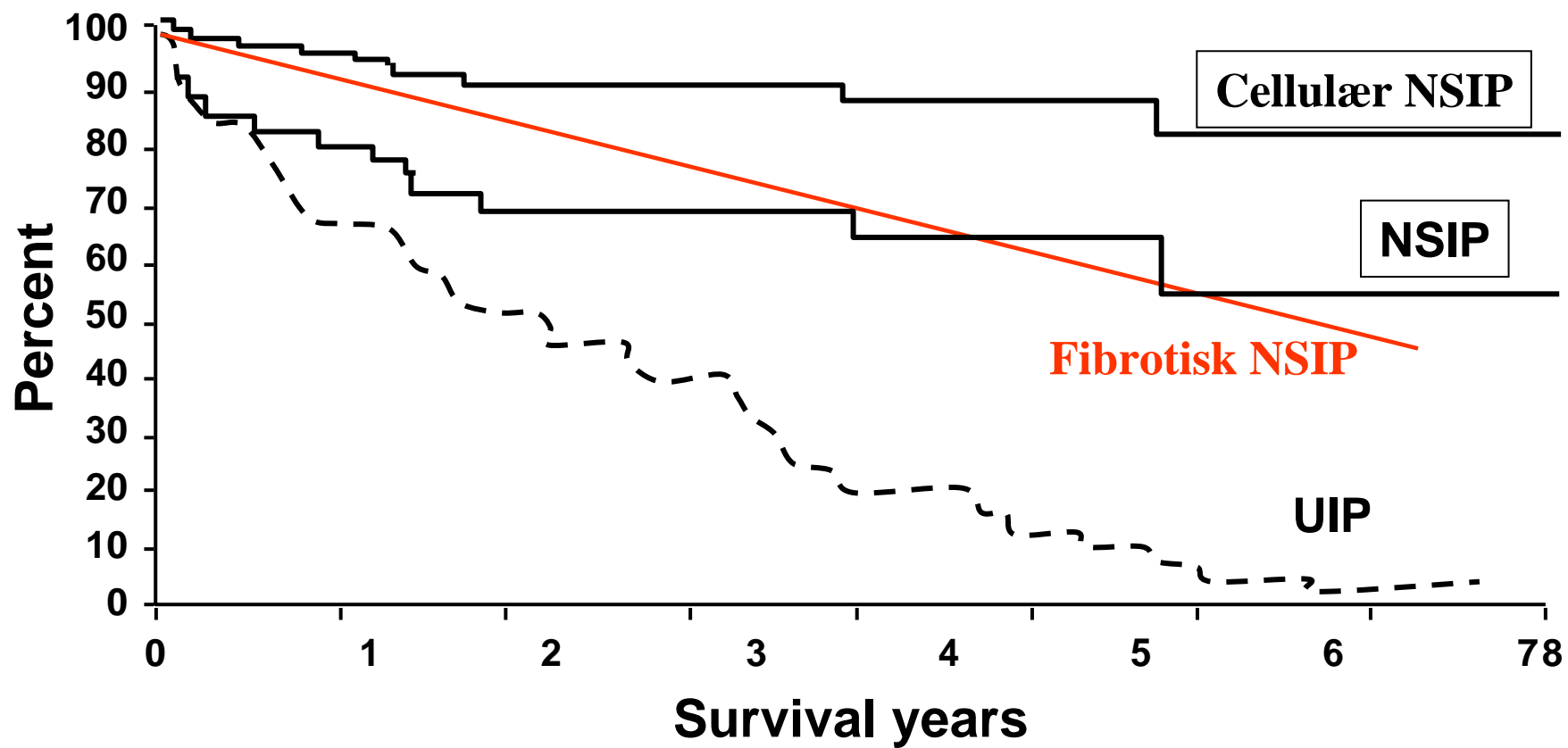
Røykerelaterte sykdommer

RBILD, DIP, Langerhanscelle histiocytose

Kronisk hypersens.pneum. Sarkoidose

Pneumokonioser Andre sjeldne

NSIP vs UIP



Mønster 2: Fibrose

Hovedfunn mønster 2

- Kompakt kollagenavleiring
- Arraktig remodelering
- Mikroskopisk “honeycomb”

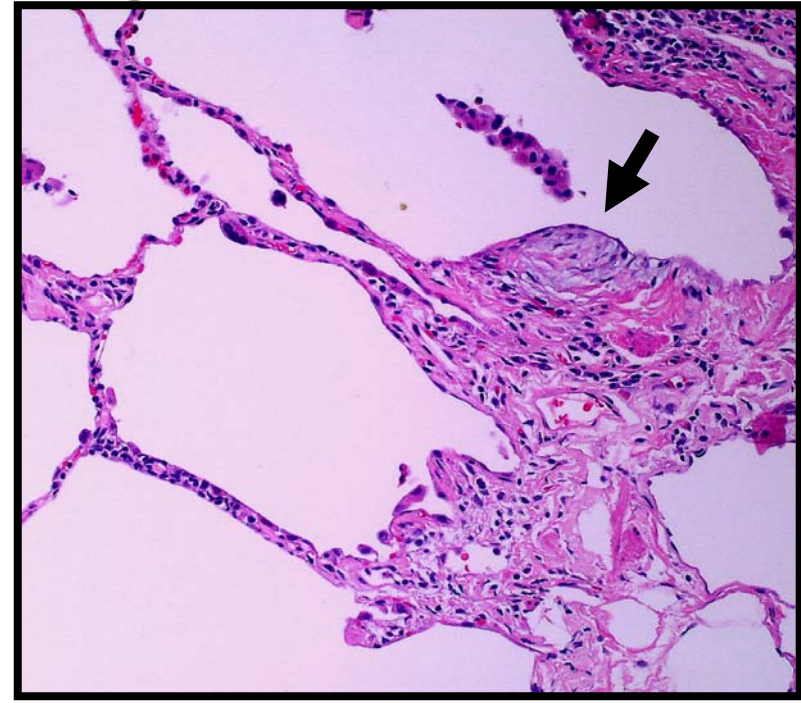
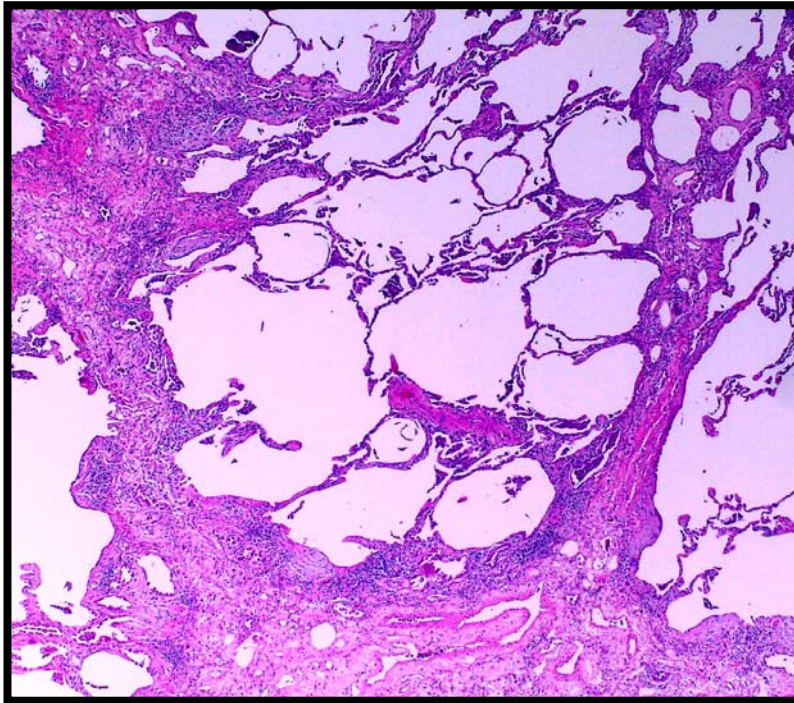
Mønster 2: Fibrose

Viktige parametere:

- **Temporær heterogen fibrose ?**
- **Diffus fibrose** (affiserer alveoleveggene)?
- **Pleuritt ?**

Mønster 2: Fibrose

- **Med temporær heterogen fibrose**



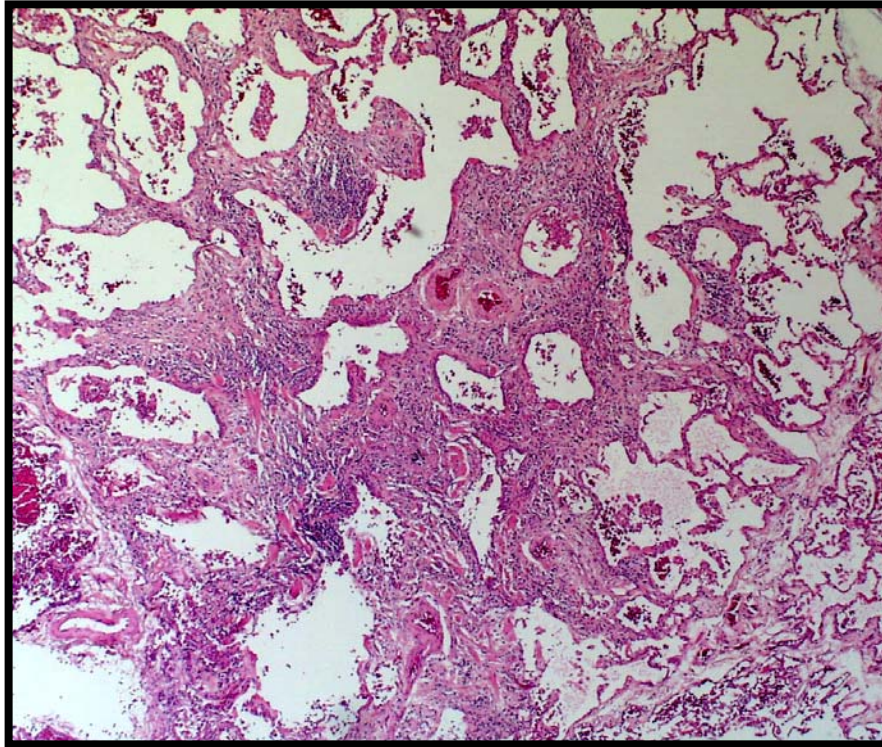
- Usual interstitial pneumonia (UIP)
- Endstage RA
- Asbestose (mulig)
- Kronisk hypersensitivitet (mulig)



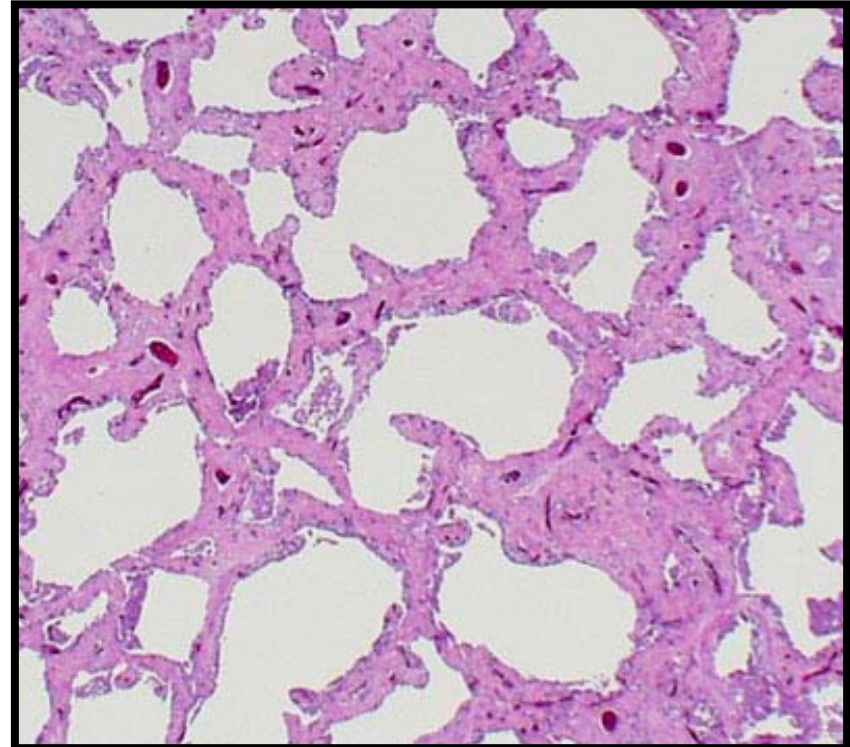
Fibroblast puter

Mønster 2: Fibrose

- **Med diffus fibrose**



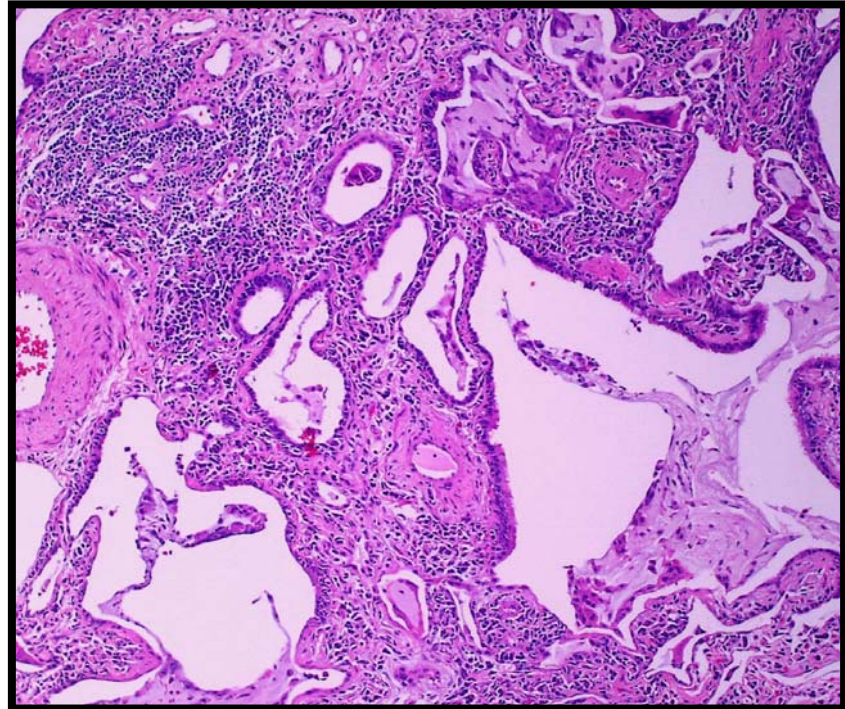
Revmatiske sykdommer
Noen pneumokonioser
Langtkommet sarkoidosis



Kronisk medikamentskade
Langtkommet PLCH
Fibrotisk NSIP

Mønster 2: Fibrose

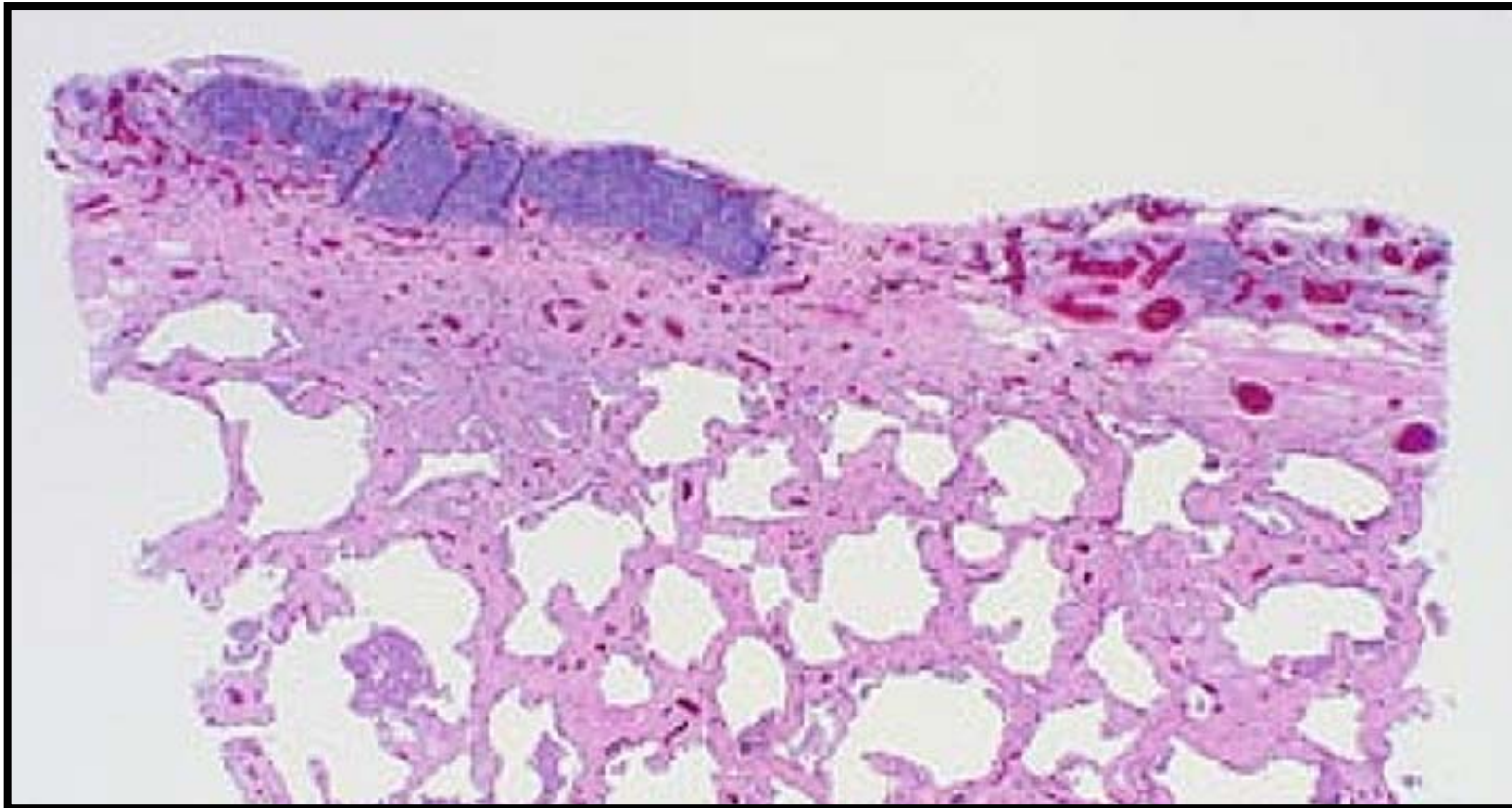
- **Med isolert “honeycomb”** (obs fokal lesjon!)



Mange årsaker, kan være UIP eller uspesifikt

Mønster 2: Fibrose

- **Med pleuritt**



- Revmatiske sykdommer
- Ulike inflammatoriske tilstander i pleura

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6. Minimale forandr.

Prototype: Small
airway disease

Mønster 3: Interstitiell betennelse

Hovedfunn mønster 3

- Lymfocytter, plasmaceller, histiocyttter, og/eller nøytrofile i alveoleseptta
- Lymfoide aggregater/folikler
- Bronkiolitt

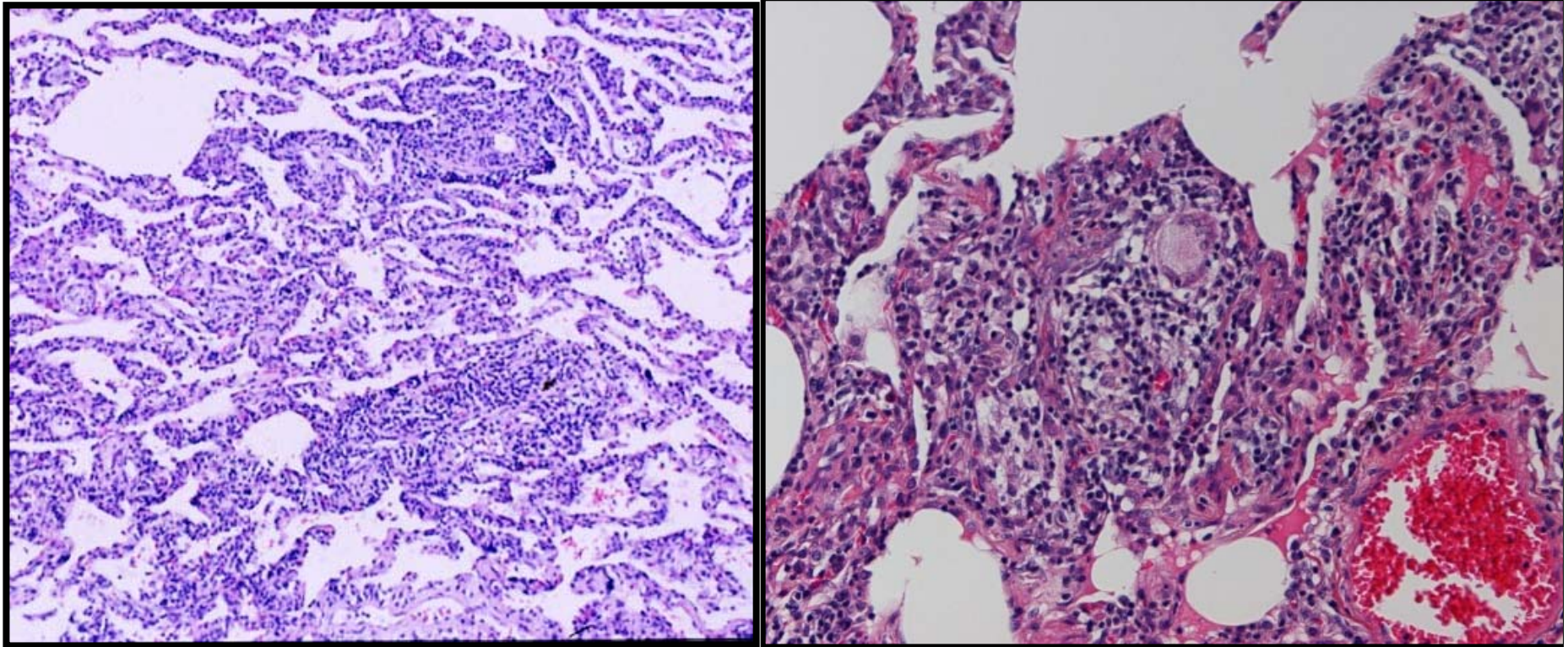
Mønster 3: Interstitiell betennelse

Viktige parametere

- **Lymfocytter og plasmaceller;**
+/- “løse” granulomer ?
- **Velformete granulomer ?**
- **Fokal organisering ?**
- **Nøytrofile ?**
- **Pleuritt ?**

Mønster 3: Interstitiell betennelse

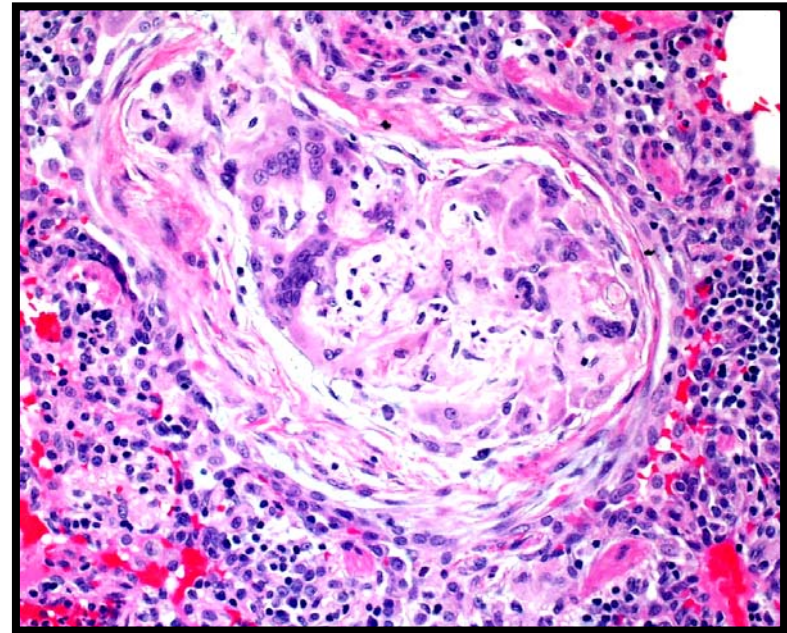
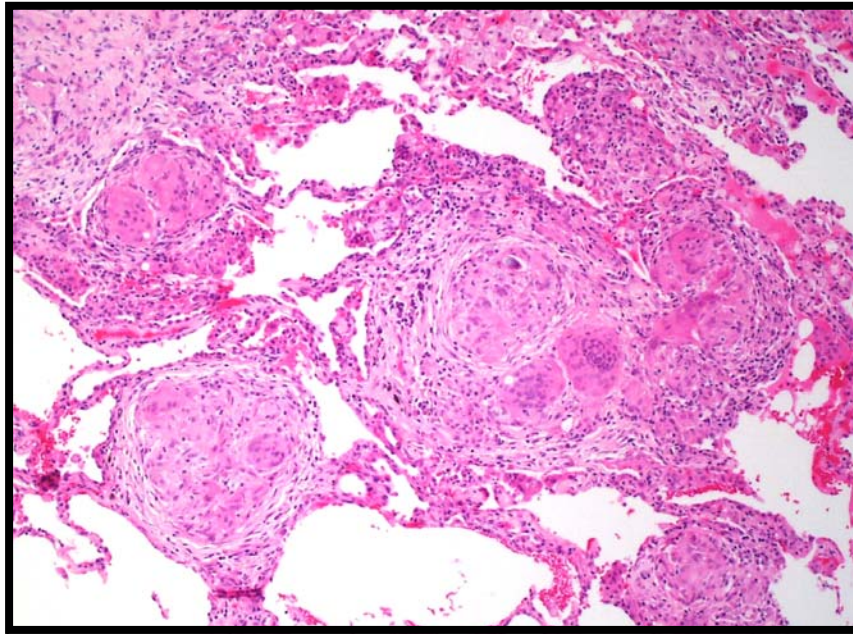
- Med lymfocytter, plasmaceller, +/- “løse” granulomer



- Hypersensitivitets pneumoni
- Nonspecific interstitial pneumonia (NSIP)
- Lavgradig lymfom
- Medikamentreaksjon

Mønster 3: Interstitiell betennelse

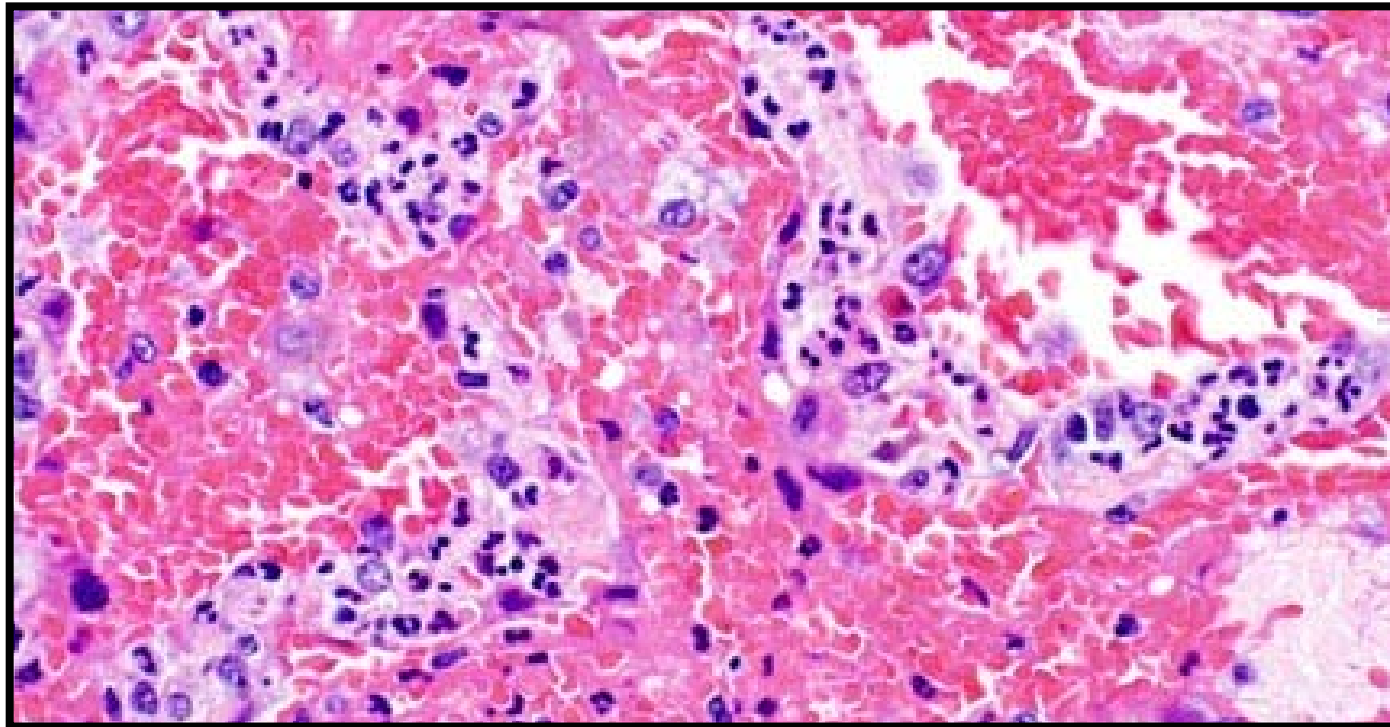
- **Med velformede granulomer**



- Infeksjoner (syrefaste staver og sopp)
- Sarkoidose/berylliose
- Aspirasjon
- I.v. stoffmisbruk

Mønster 3: Interstitiell betennelse

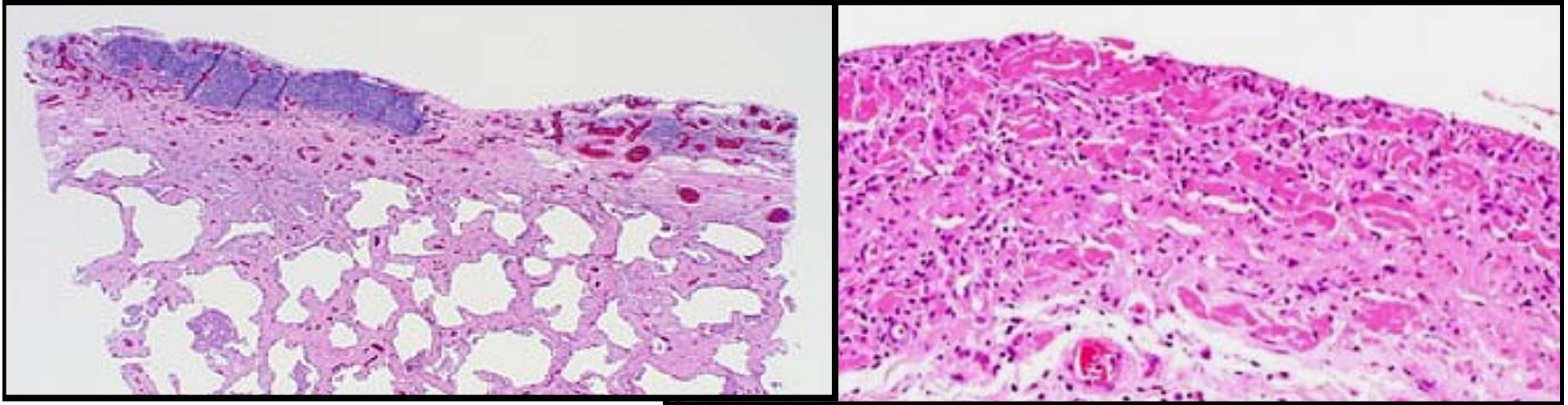
- **Med nøytrofile granulocytter**



- Infeksjoner
- Syndromer med lungeblødning (kapillaritt!)
- Revmatiske sykdommer

Mønster 3: Interstitiell betennelse

- Med pleuritt



- Revmatiske sykdommer
- Ulike inflammatoriske tilstander i pleura

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Prototype:
Hypersens. pneum.

6. Minimale forandr.

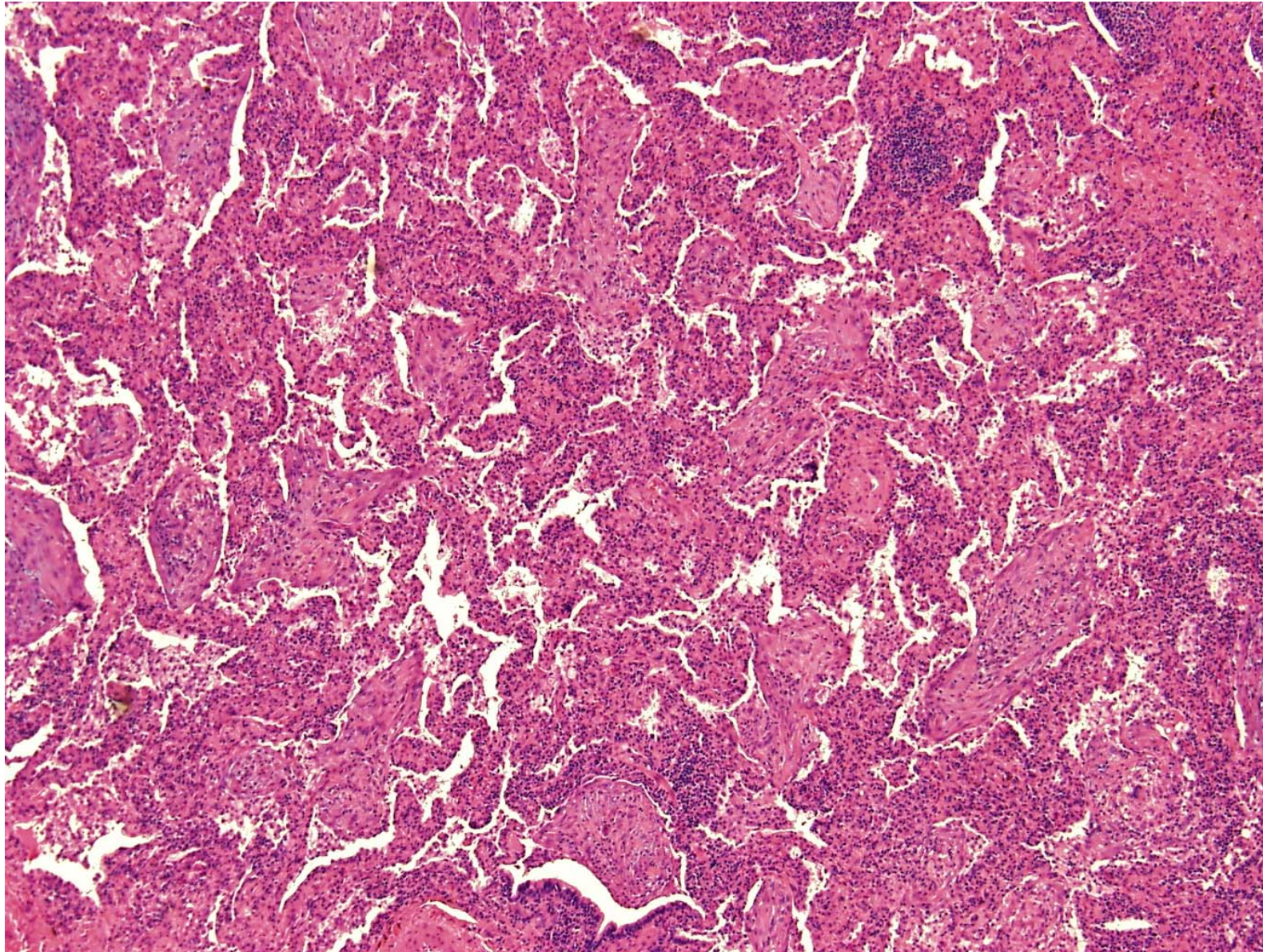
Prototype: Small
airway disease

Mønster 4: Alveolar Filling

Hovedfunn mønster 4

- Alveoler fylt med celler, eksudat eller annet materiale

Mønster 4: Alveolar Filling



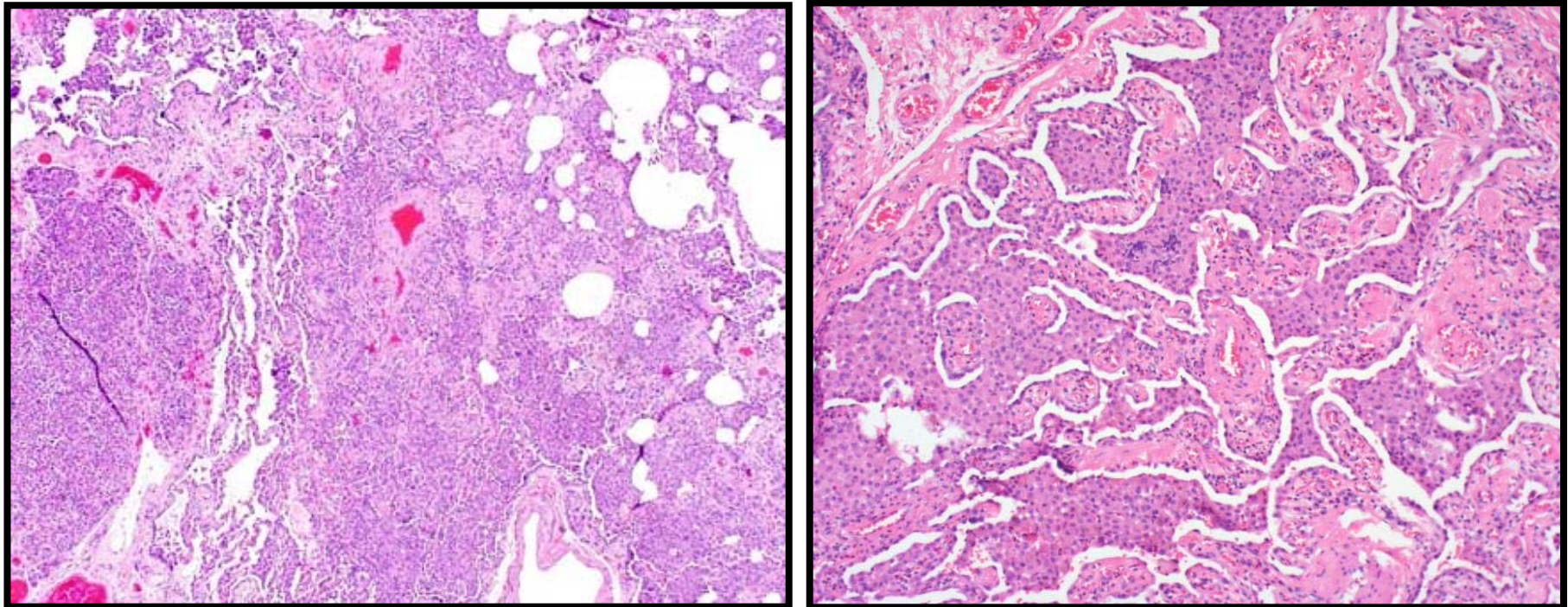
Mønster 4: Alveolar Filling

Viktige parametere

- **Makrofager ?**
- **Nøytrofile ?**
- **Organiserende pneumoni ?**
- **Eosinofilt innhold ?**
- **Blødning ?**
- **Mucin-innhold ?**

Mønster 4: Alveolar Filling

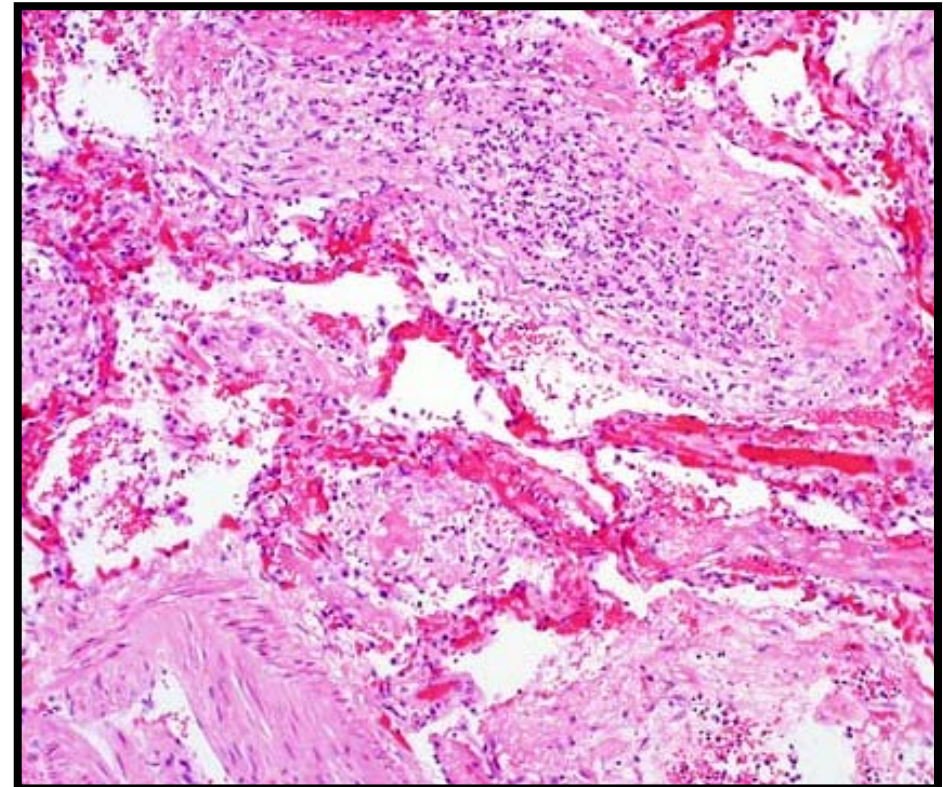
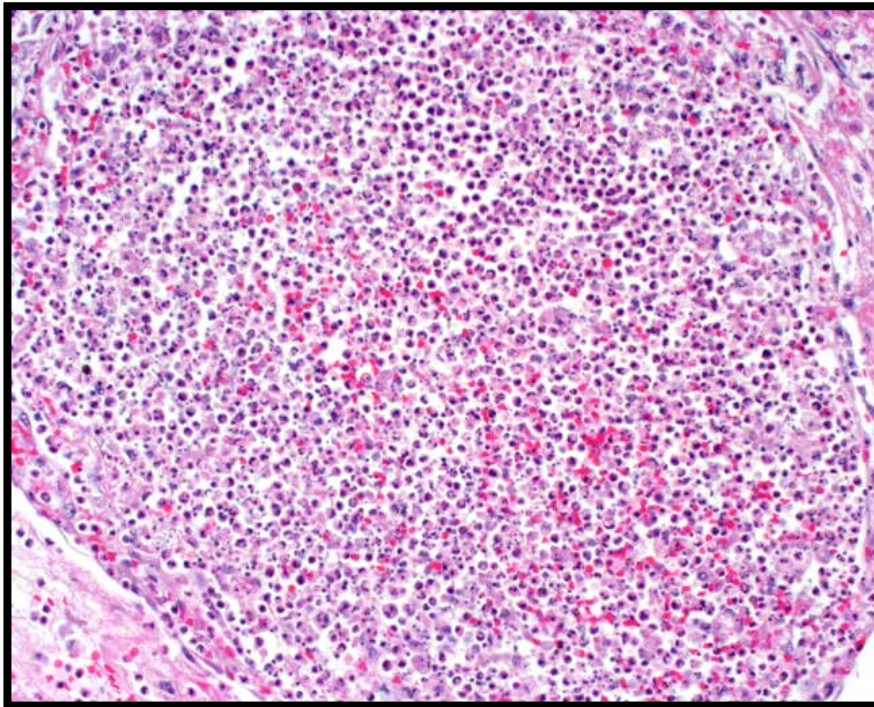
- **Med makrofager**



- Røykerelaterte lungesykdommer (DIP, RBILD, PLCH)
- Makrofag “stase” pga fokal fibrose

Mønster 4: Alveolar Filling

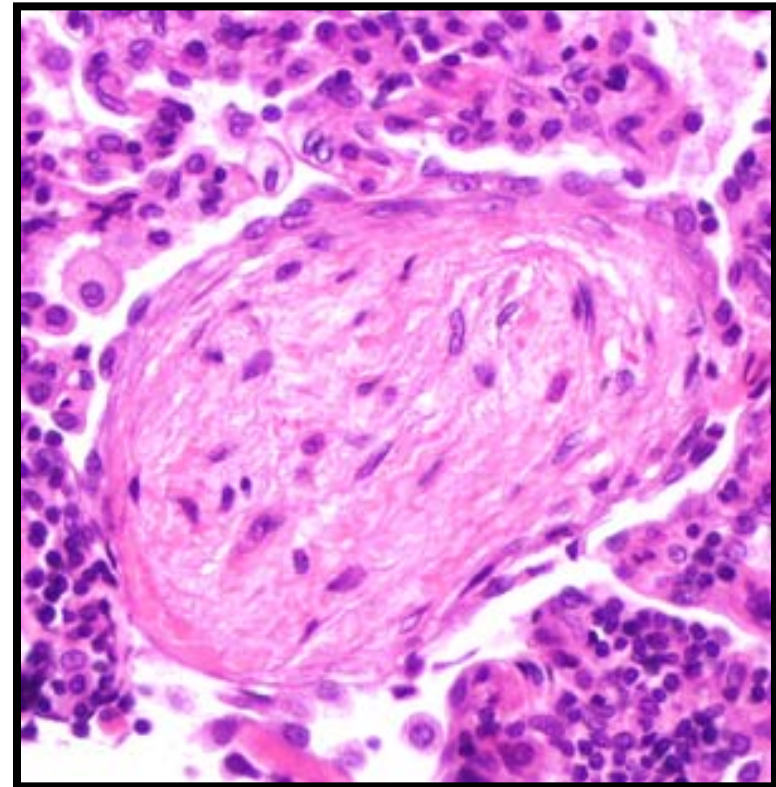
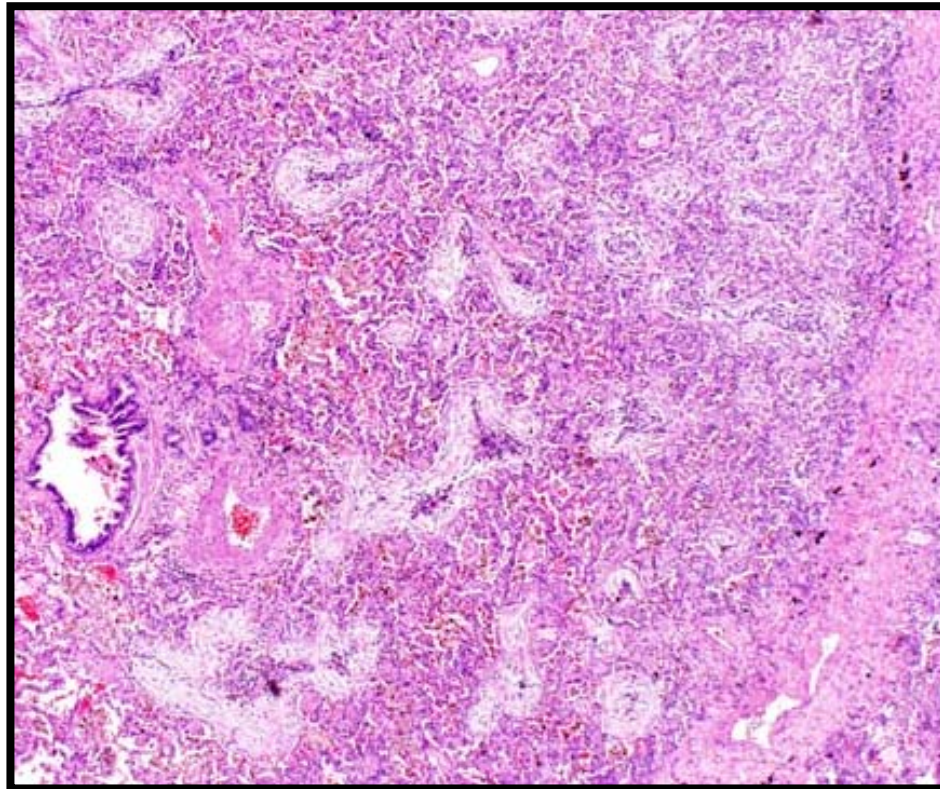
- **Med nøytrofile**



- Bronkopneumonier
- Revmatiske sykdommer
- Syndromer med lungeblødning (obs kapillaritt!)

Mønster 4: Alveolar Filling

- **Med organiserende pneumoni**

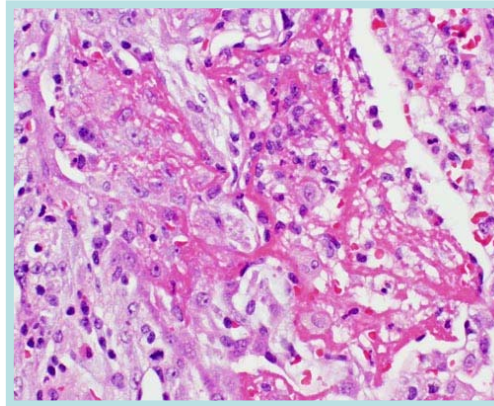


- Infeksjon i organisering
- Reaksjon medik. el. toxin
- Revmatiske sykdommer

Mønster 4: Alveolar Filling

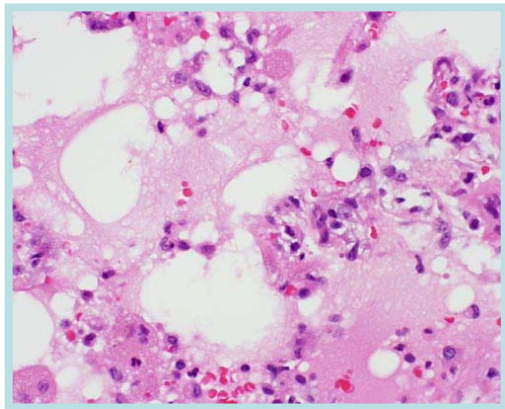
- **Med eosinofilt materiale**

- **Fibrin:**



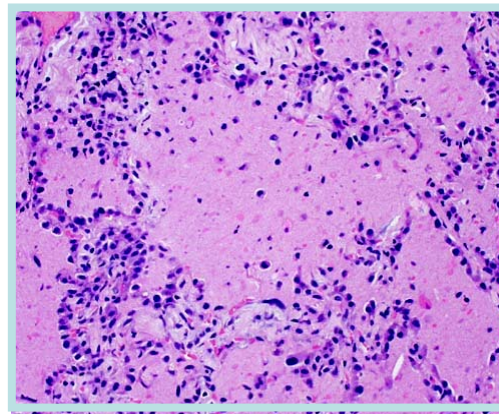
Infeksjon, revma.,
syndr. m. blødning,
medikament

- **Ødem:**



Hjertesvikt, revma.,
medikament

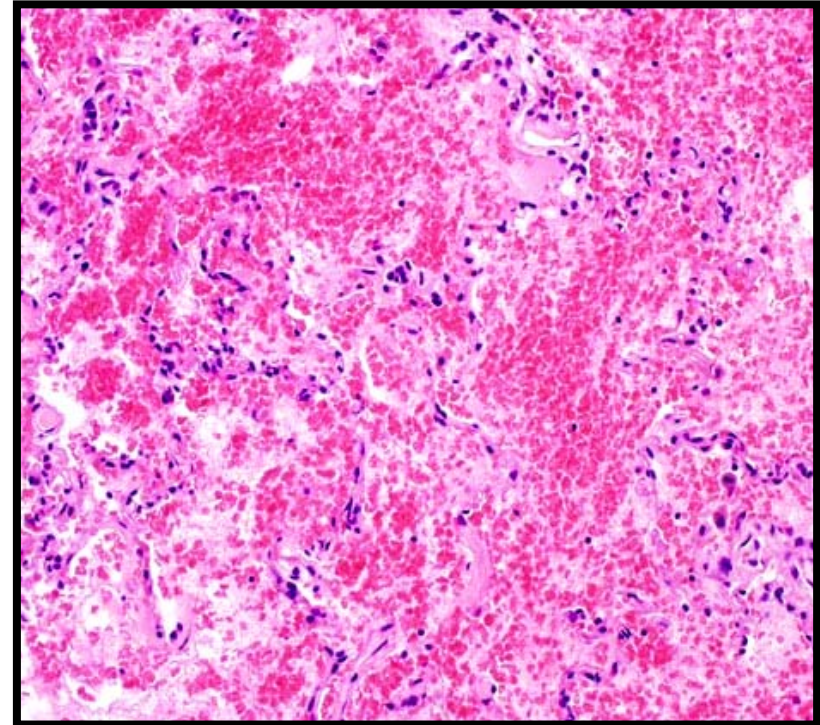
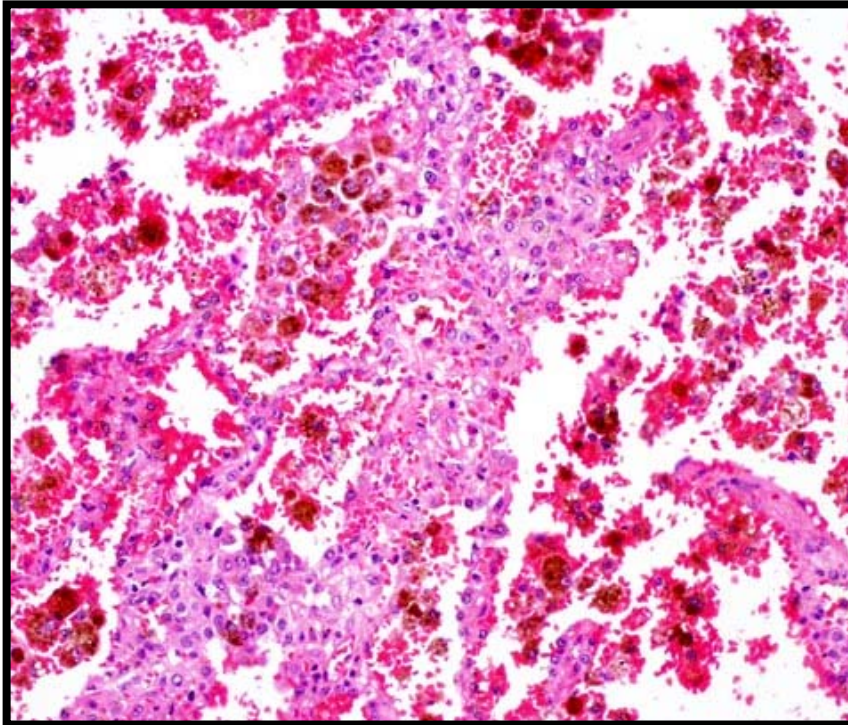
- **Protein:**



Alveolær
proteinose
(PAP)

Mønster 4: Alveolar Filling

- **Med blødning**

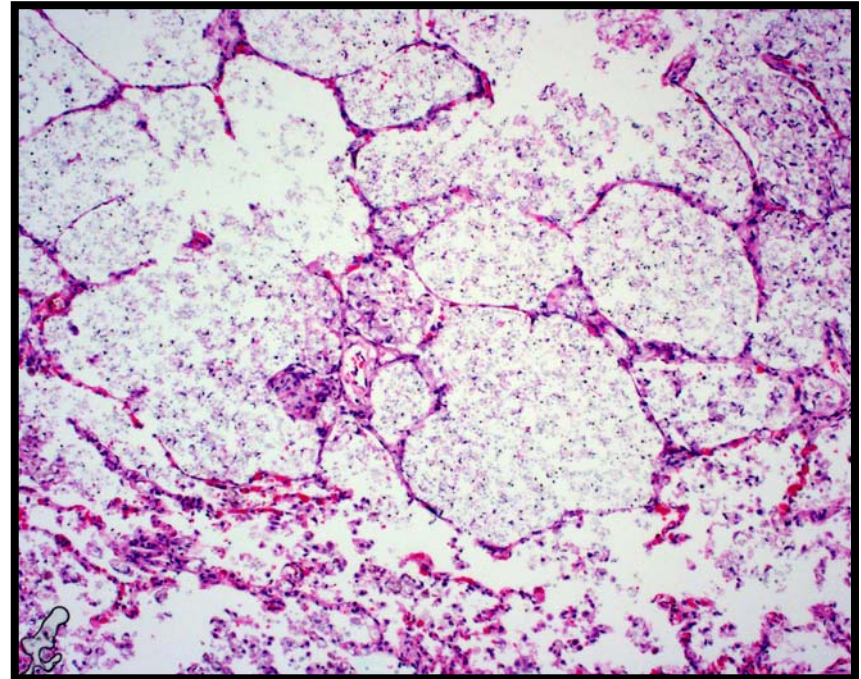
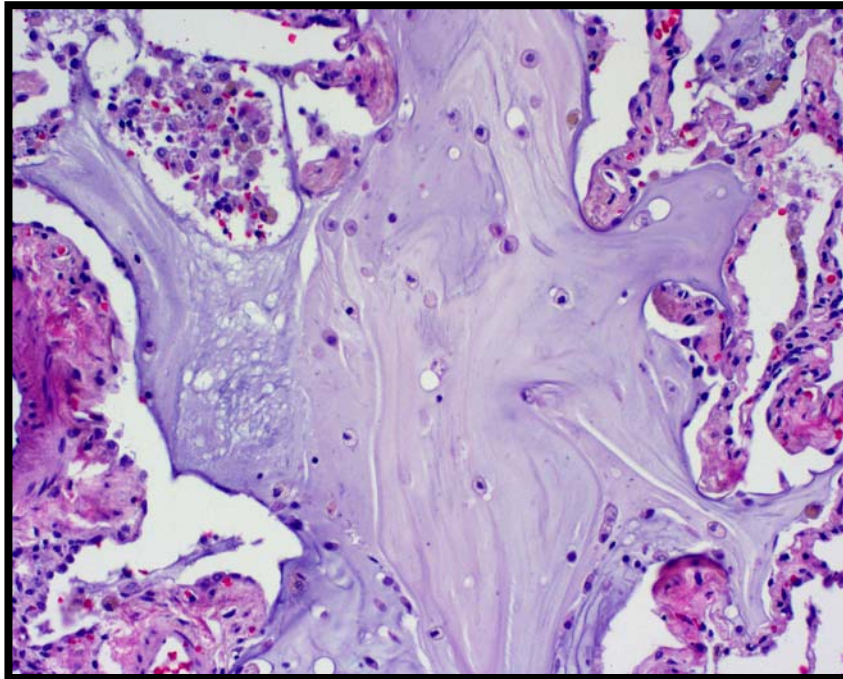


Med fibrin: Revmatiske, lungeblødning, medikamentskade

Uten fibrin eller siderofager: artefakt/blødn. ved biopsiering!

Mønster 4: Alveolar Filling

- **Med mucin**



- Mucostase ved small airway disease (SAD)
- Mucoïd pneumoni (cryptococcus)
- Bronchioloalveolært carcinom

De 6 mønstre for interstitielle lungesykdommer

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Prototype: UIP

5. Noduli

Prototype: Wegener's

3. Interstit. betennelse

Prototype:
Hypersens. pneum.

6. Minimale forandr.

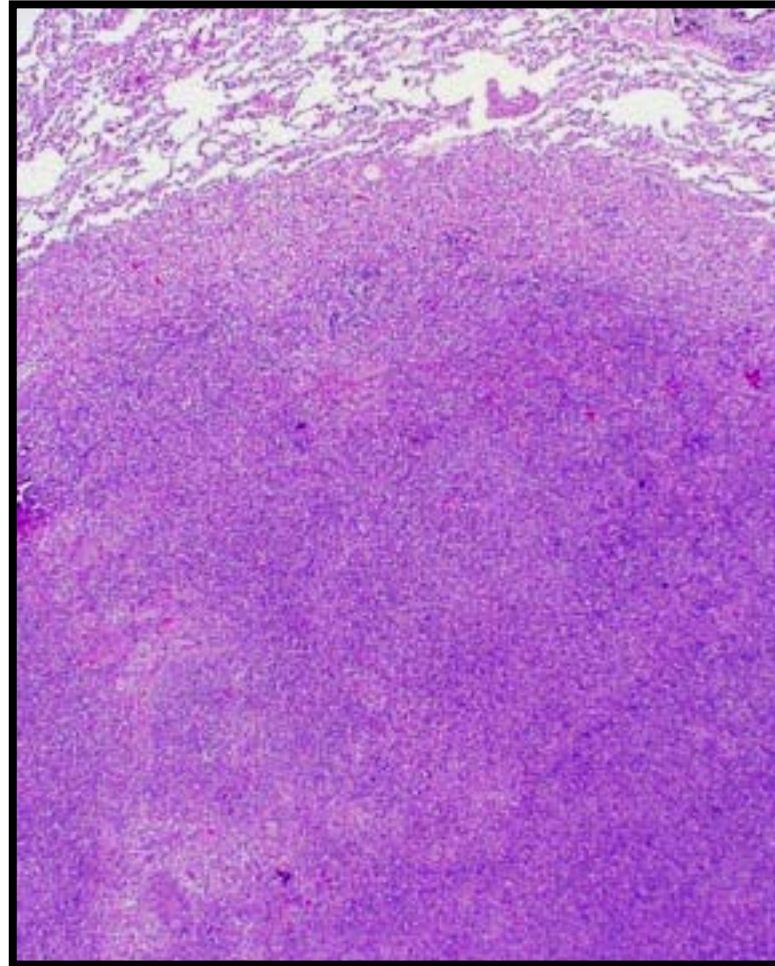
Prototype: Small
airway disease

Mønster 5: Noduli

Hovedfunn mønster 5

Knuteformete infiltrater fokalt i normalt lungevev

Mønster 5: Noduli

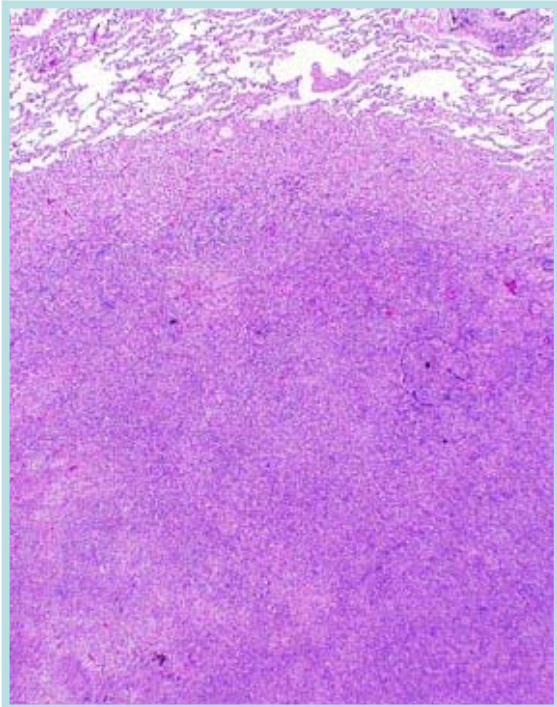


Mønster 5: Noduli

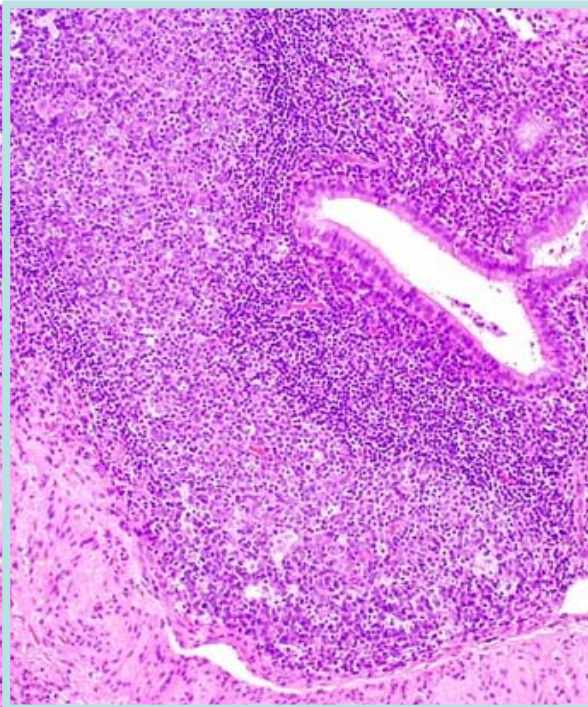
- **Lymfoid vev ?**
- **Granulomer ?**
- **Nekrose ?**
- **Atypiske celler ?**
- **Stjerneformete arr ?**
- **Organiserende pneumoni ?**

Mønster 5: Noduli

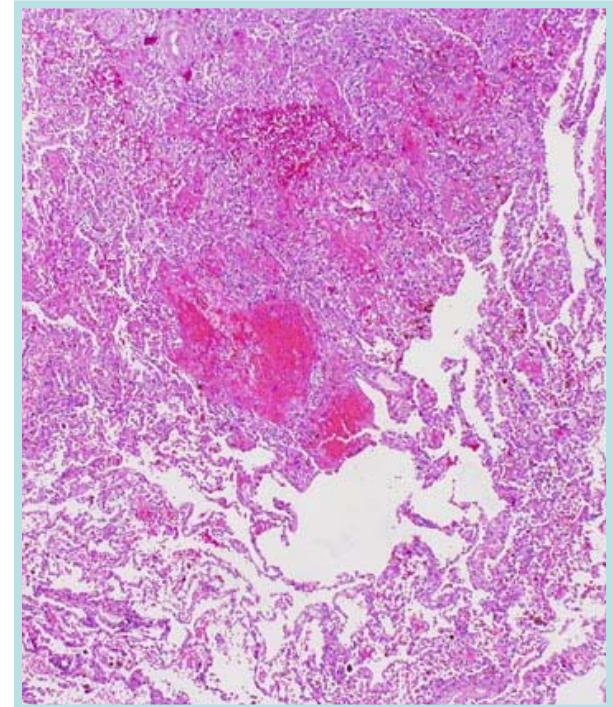
- Med lymfoid vev



Malignt lymfom



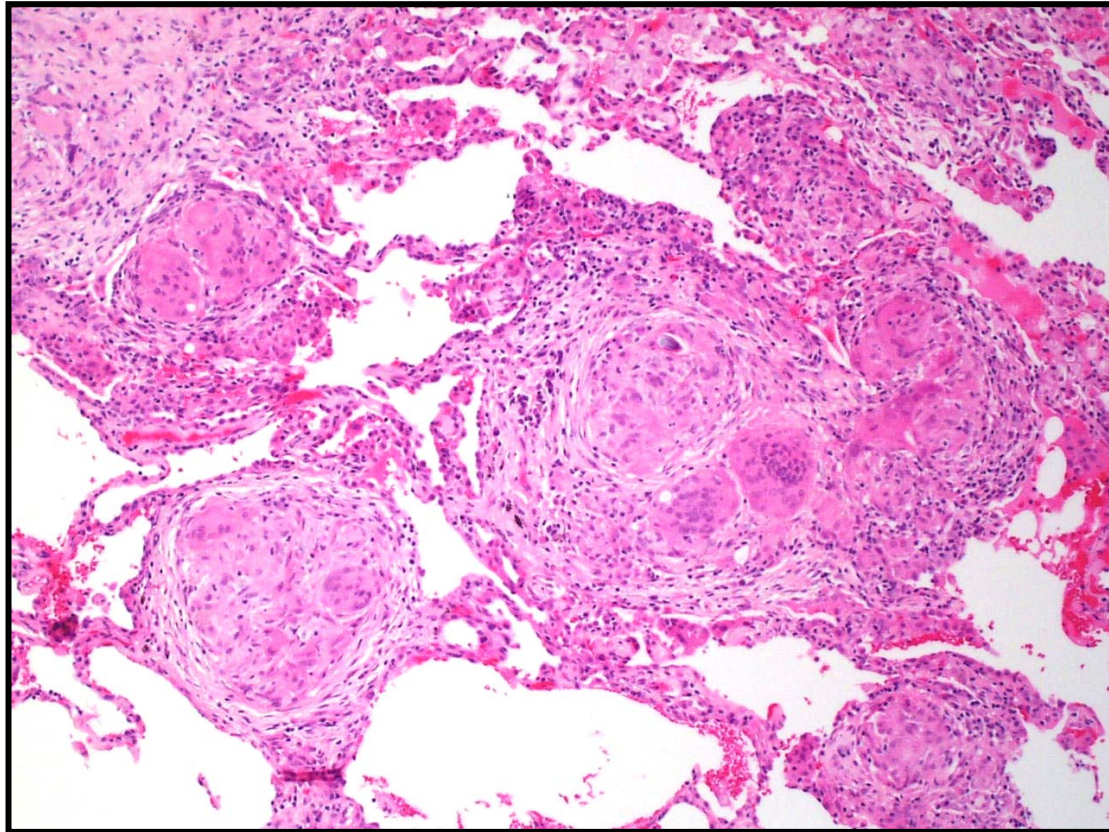
Folikulær
bronkiolitt/
bronkiektasier



Wegener's
granulomatose

Mønster 5: Noduli

- **Med granulomer**



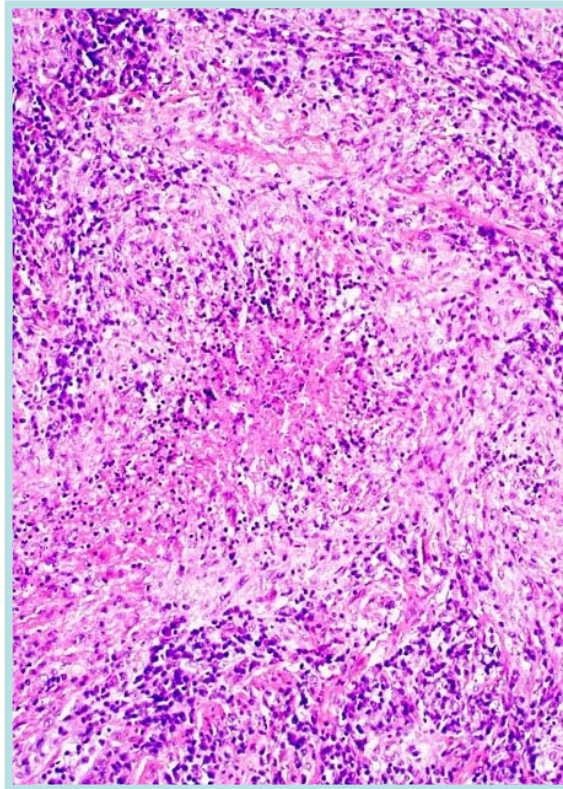
Sarkoidose/berylliose

Infeksjoner

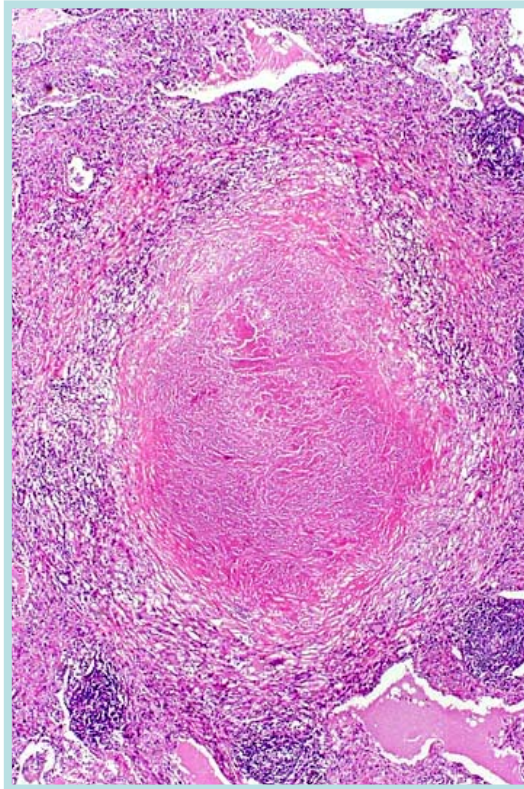
Aspirasjon

Mønster 5: Noduli

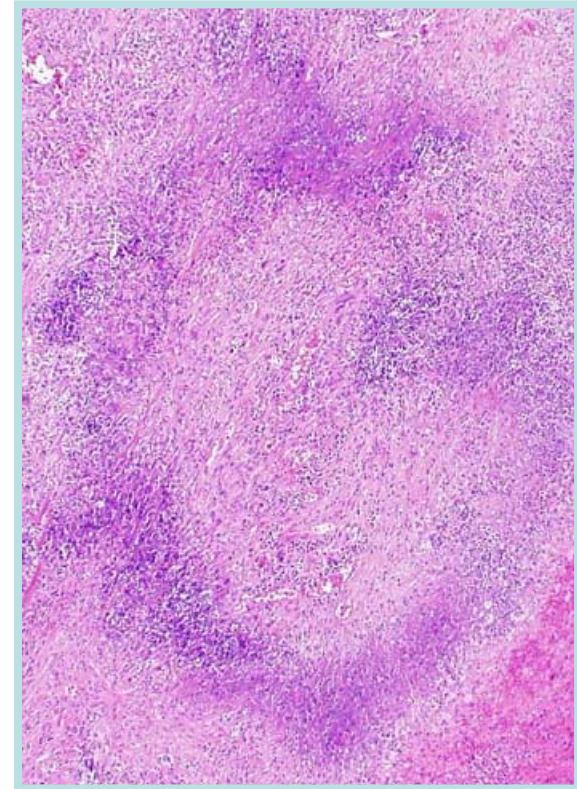
- **Med nekrose**



Infeksjoner



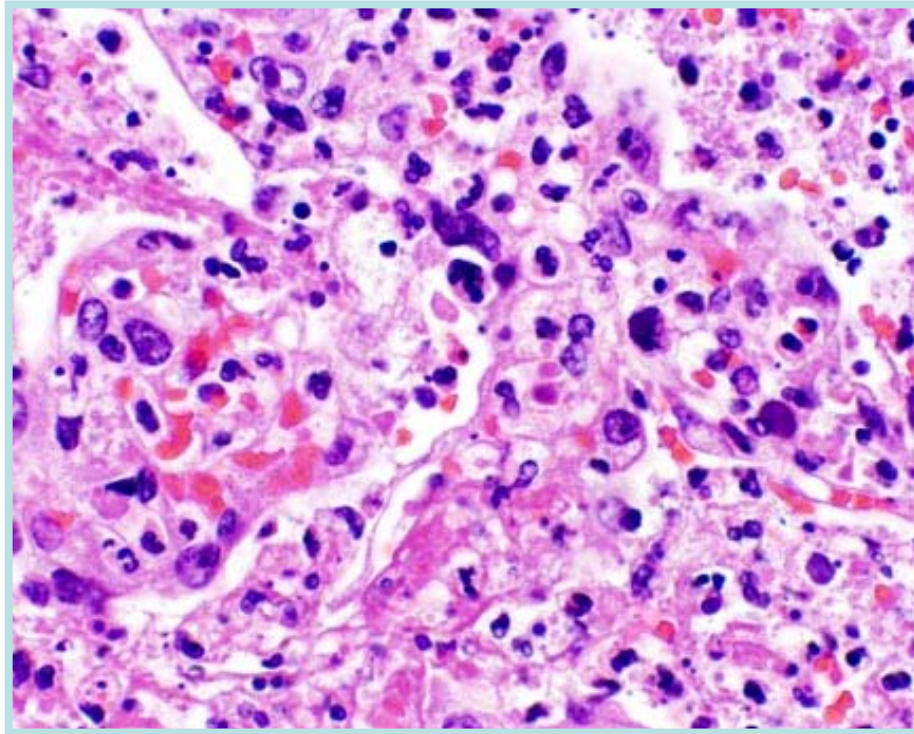
Maligne
tumores



Wegener's

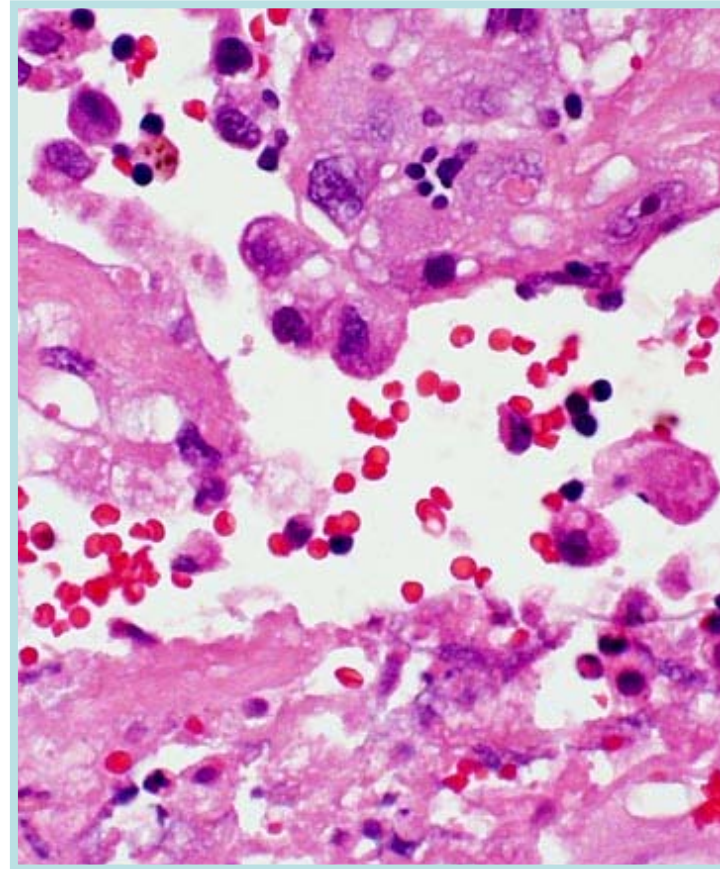
Mønster 5: Noduli

- **Med atypiske celler**



Infeksjoner

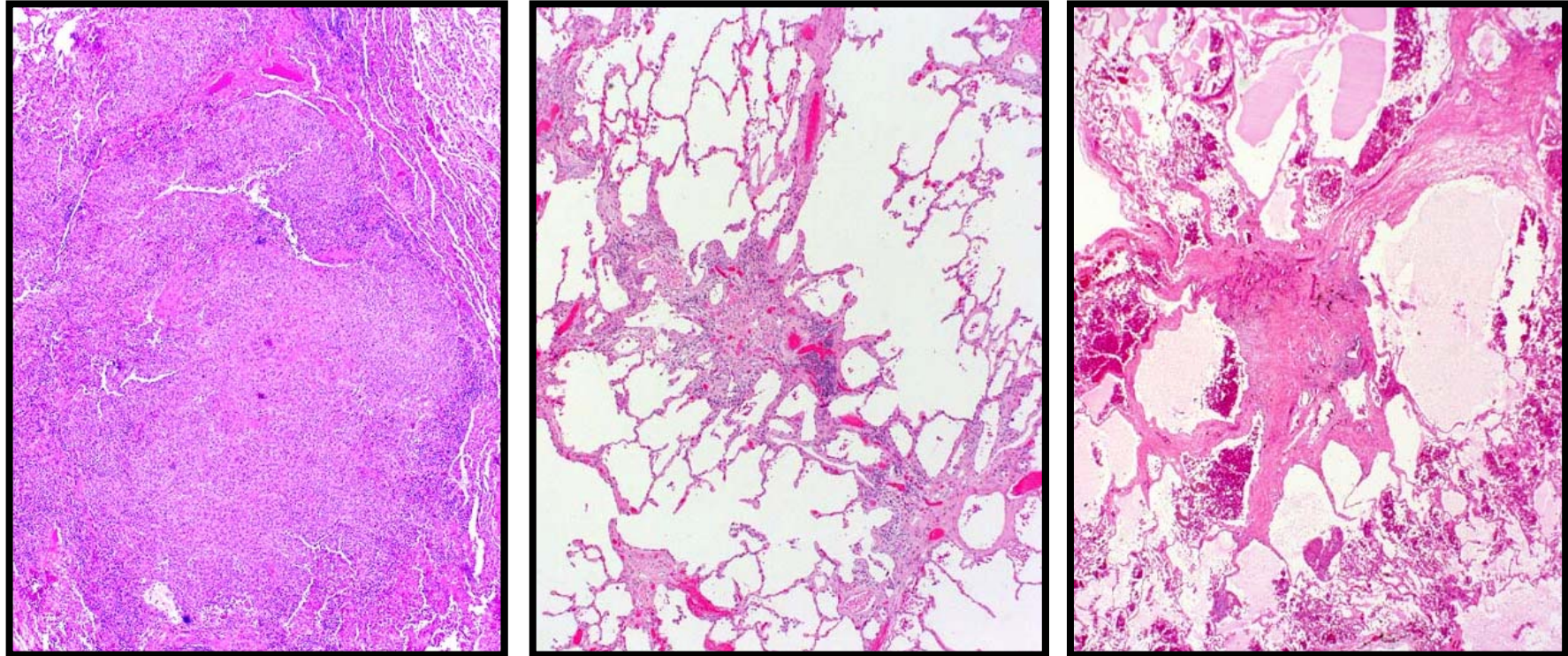
Lymfomer



Carcinomer
og sarkomer

Mønster 5: Noduli

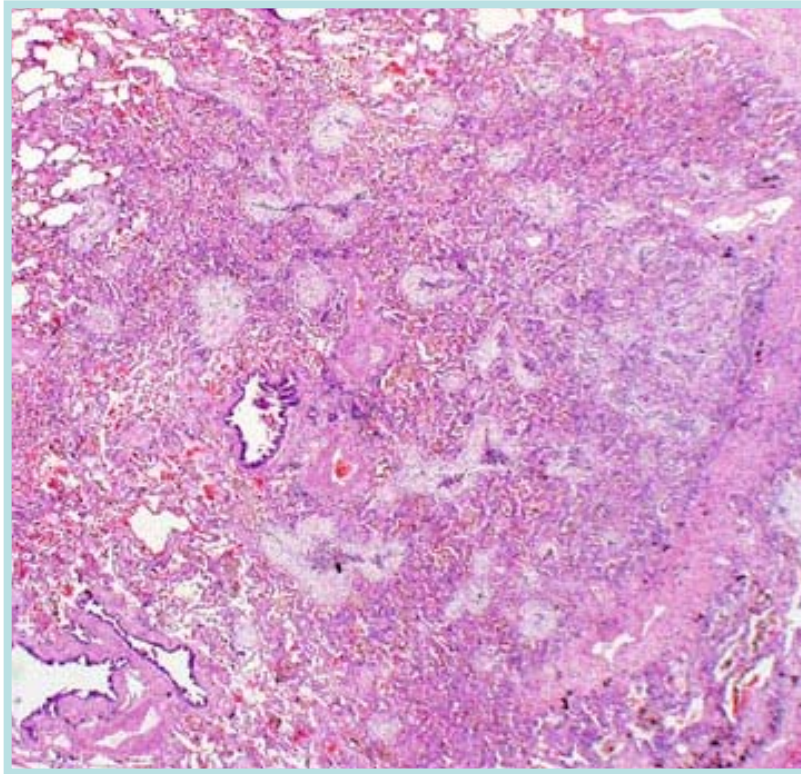
- **Med stjerneformede arr**



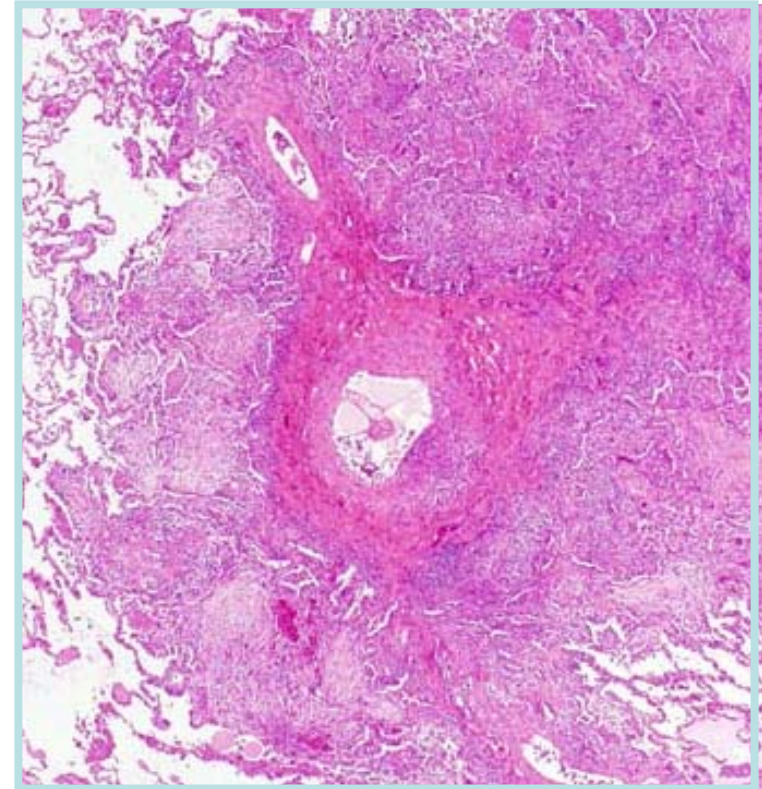
Pulmonal Langerhanscelle histiocytose

Mønster 5: Noduli

- **Med organizing pneumonia**



Infeksjoner
Revmatiske sykd.



Tilhelende infarkt
I periferi av tumor

De 6 mønstre for interstitielle lungesykdommer

1. Akutt lunge skade

Prototype: DAD

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Prototype: UIP

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Prototype:
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6. Minimale forandr.

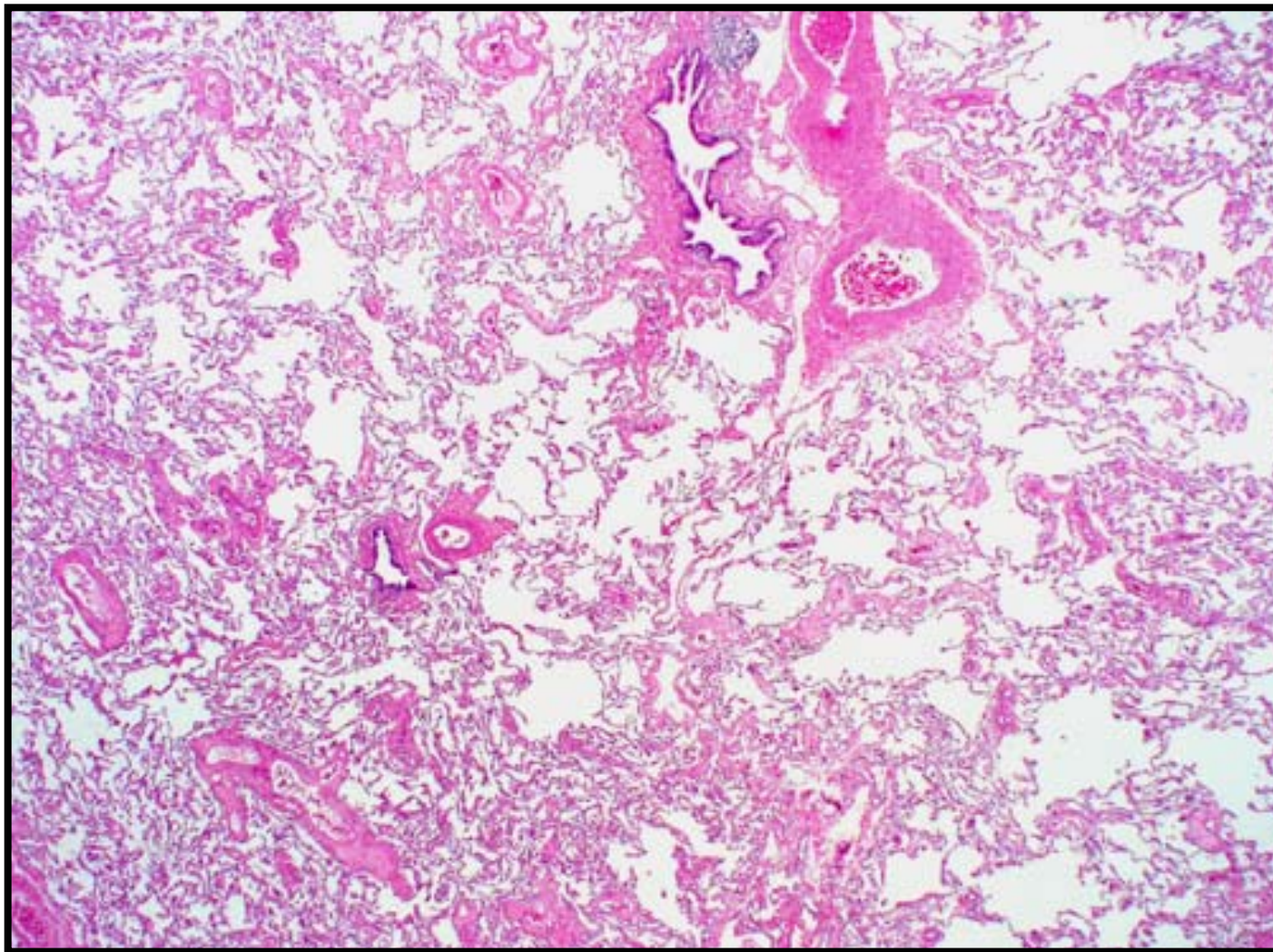
Prototype:
Small airway disease

Mønster 6: Minimale forandringer

Hovedfunn mønster 6:

- Normalt utseende biopsi ved liten forstørrelse.

Mønster 6: Minimale forandringer

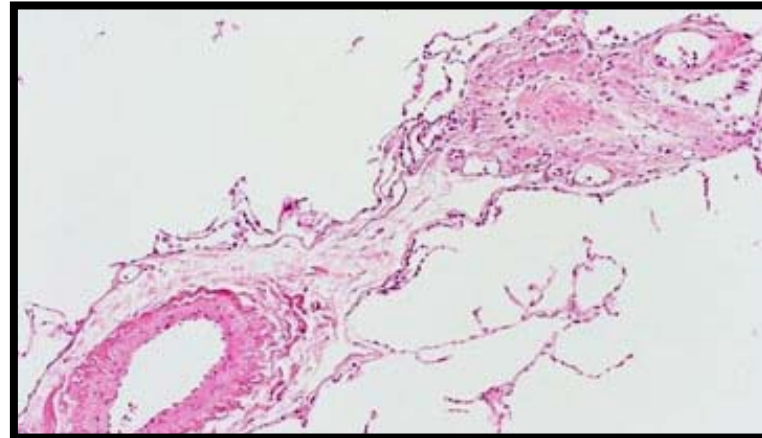
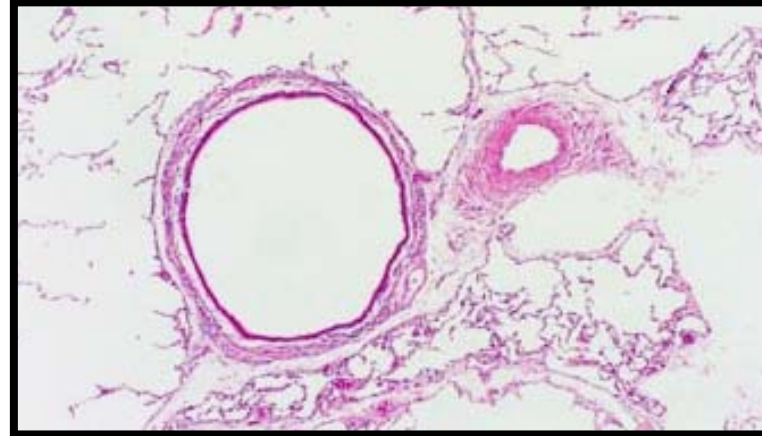
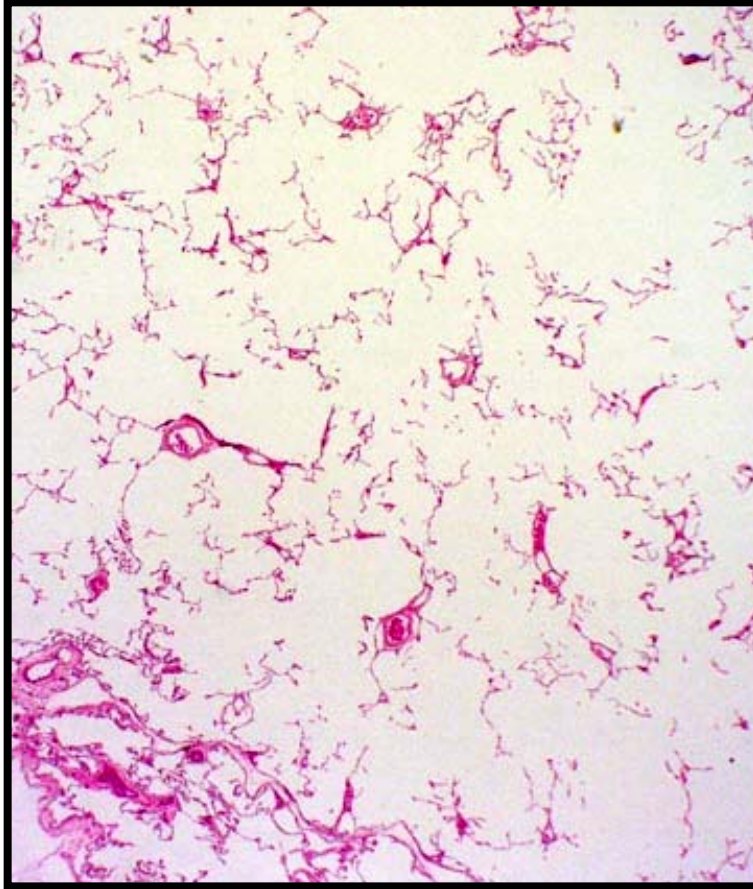


Mønster 6: Minimale forandringer

- **Small airways disease ?**
- **Karforandringer ?**
- **Cyster ?**
- **Sampling problem?**

Mønster 6: Minimal Changes

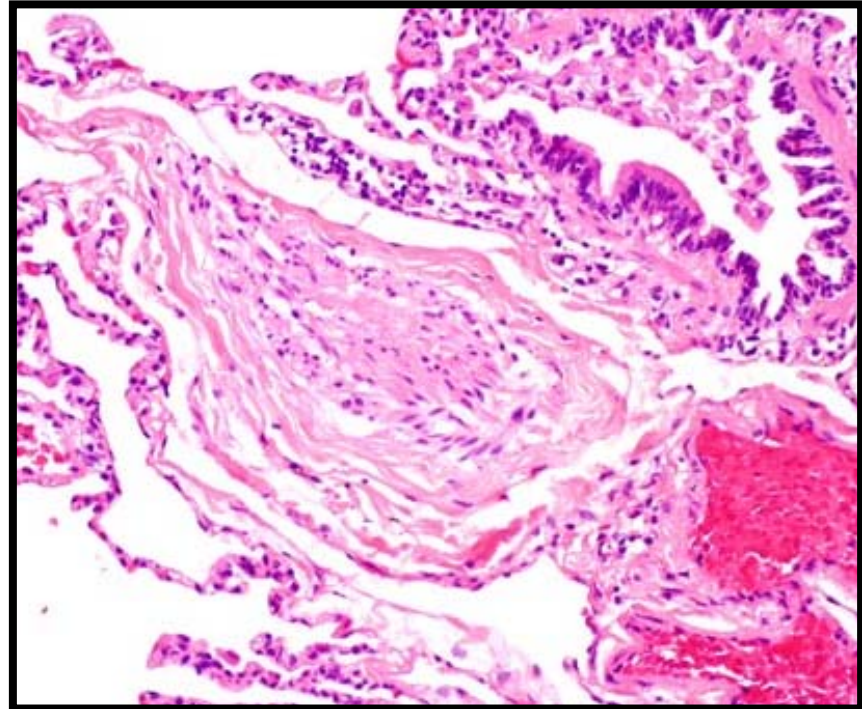
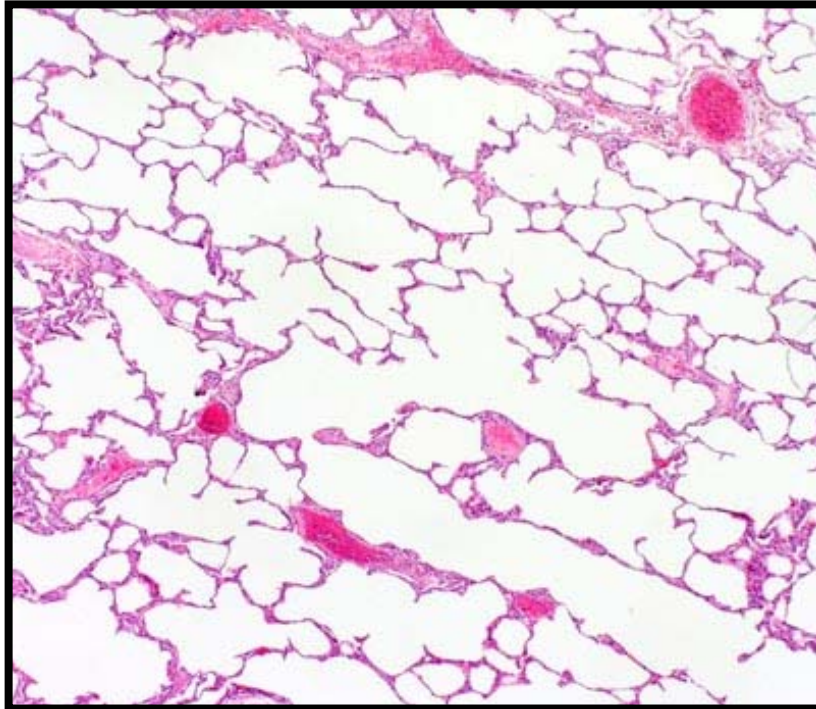
- Med small airway disease (SAD)



Konstriktiv bronkiolitt

Mønster 6: Minimale forandringer

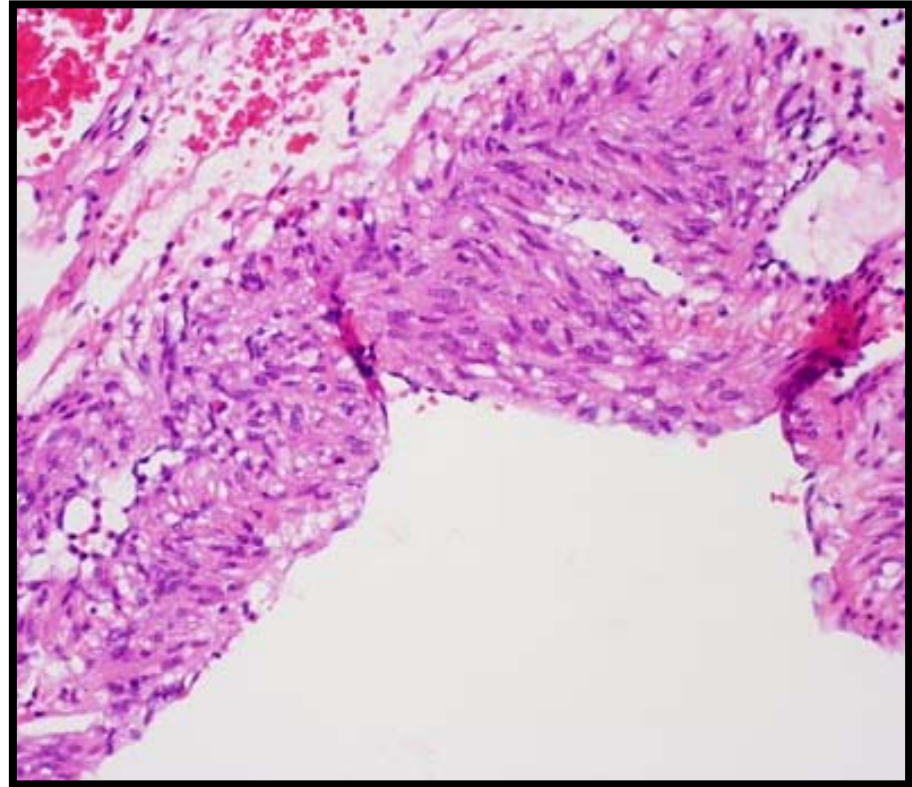
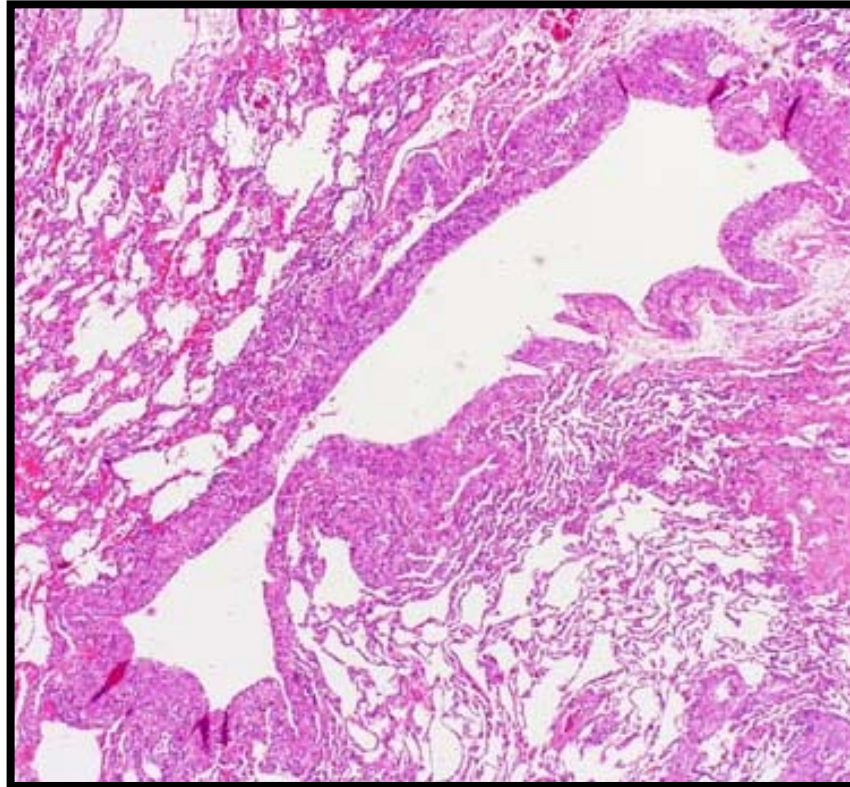
- Med karforandringer



Pulmonal hypertensjon

Mønster 6: Minimale forandringer

- Med cyster



Lymfangioleiomyomatose (LAM)

Pulmonal Langerhanscelle histiocytose

Forkortelser

AEP	Acute eosinophilic pneumonia	NSIP	Non-specific interstitial pneumonia
AIP	Acute interstitial pneumonia	OP	Organizing pneumonia
ALI	Acute lung injury	PAP	Pulmonary alveolar proteinosis
CHF	Congestive heart disease	PHT	Pulmonary hypertension
COP	Cryptogenic organizing pneumonia	PLCH	Pulmonary Langerhans cell histiocytosis
CVD	Collagen vascular disease	PVOD	Pulmonary veno-occlusive disease
DAD	Diffuse alveolar damage	RA	Rheumatoid arthritis
DIP	Desquamative interstitial pneumonia	RBILD	Respiratory bronchiolitis-interstitial pneumonia
HSP	Hypersensitivity pneumonitis	SAD	Small airway disease
LAM	Lymphangiomyomatosis	SLE	Systemic lupus erythematosus
LIP	Lymphocytic interstitial pneumonia	UIP	Usual interstitial pneumonia
MCTD	Mixed connective tissue disease		