

This lecture is about vascular and obstructive lung disease. We will cover Vascular diseases first.

Vascular Lung Diseases

APPROVED

Robbins Questions of Vascular Lung
Disease:

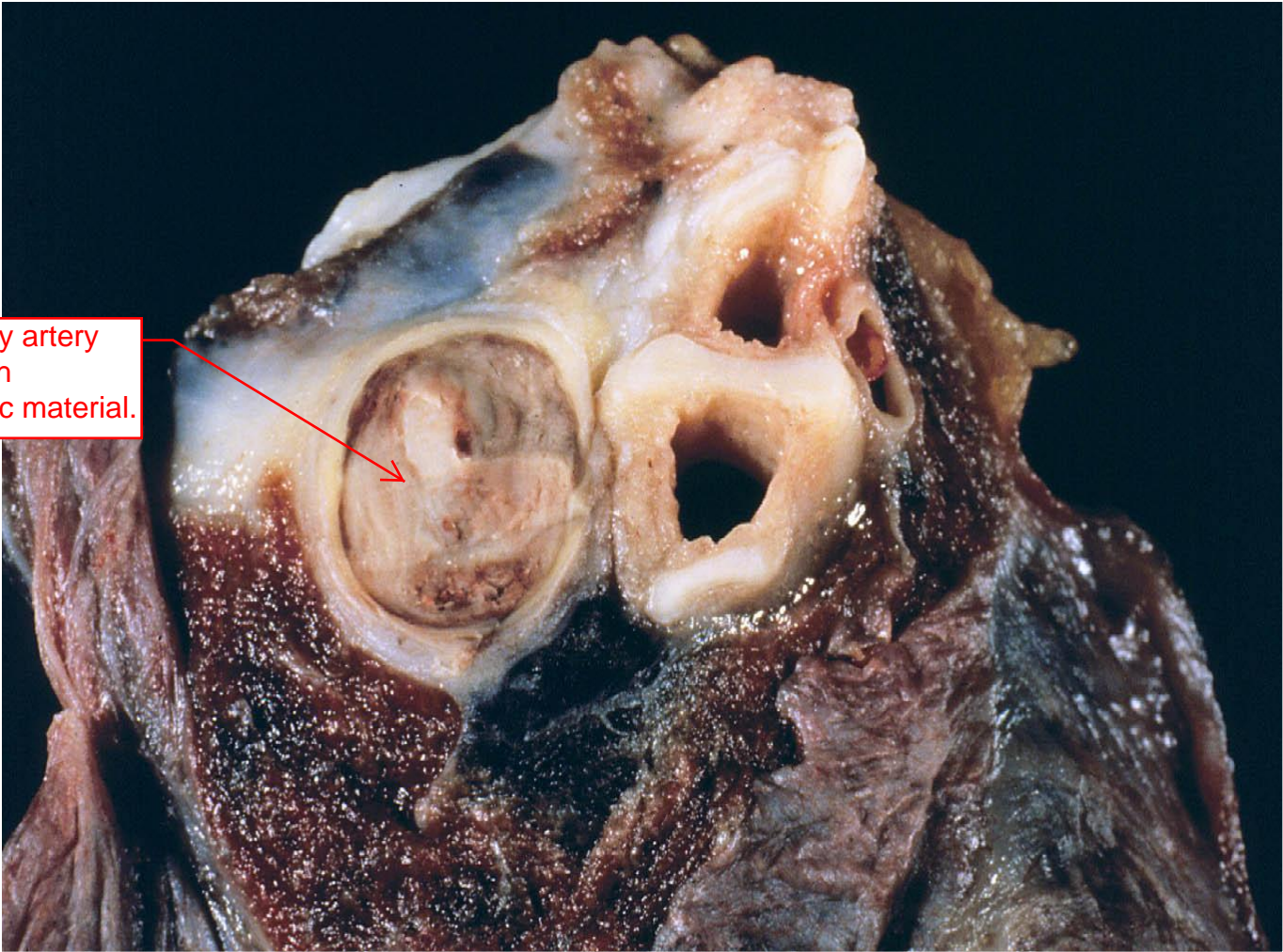
6, 30, 34, 43, 50, 53

SESSION SPECIFIC OBJECTIVES

- List the major types of vascular lung disease
- Recognize and describe the pathology of vascular lung disease:
 - Pulmonary embolism, thrombosis, hypertension, and diffuse pulmonary hemorrhage (Goodpasture's, SLE, Wegener's, idiopathic)

Vascular Lung Diseases

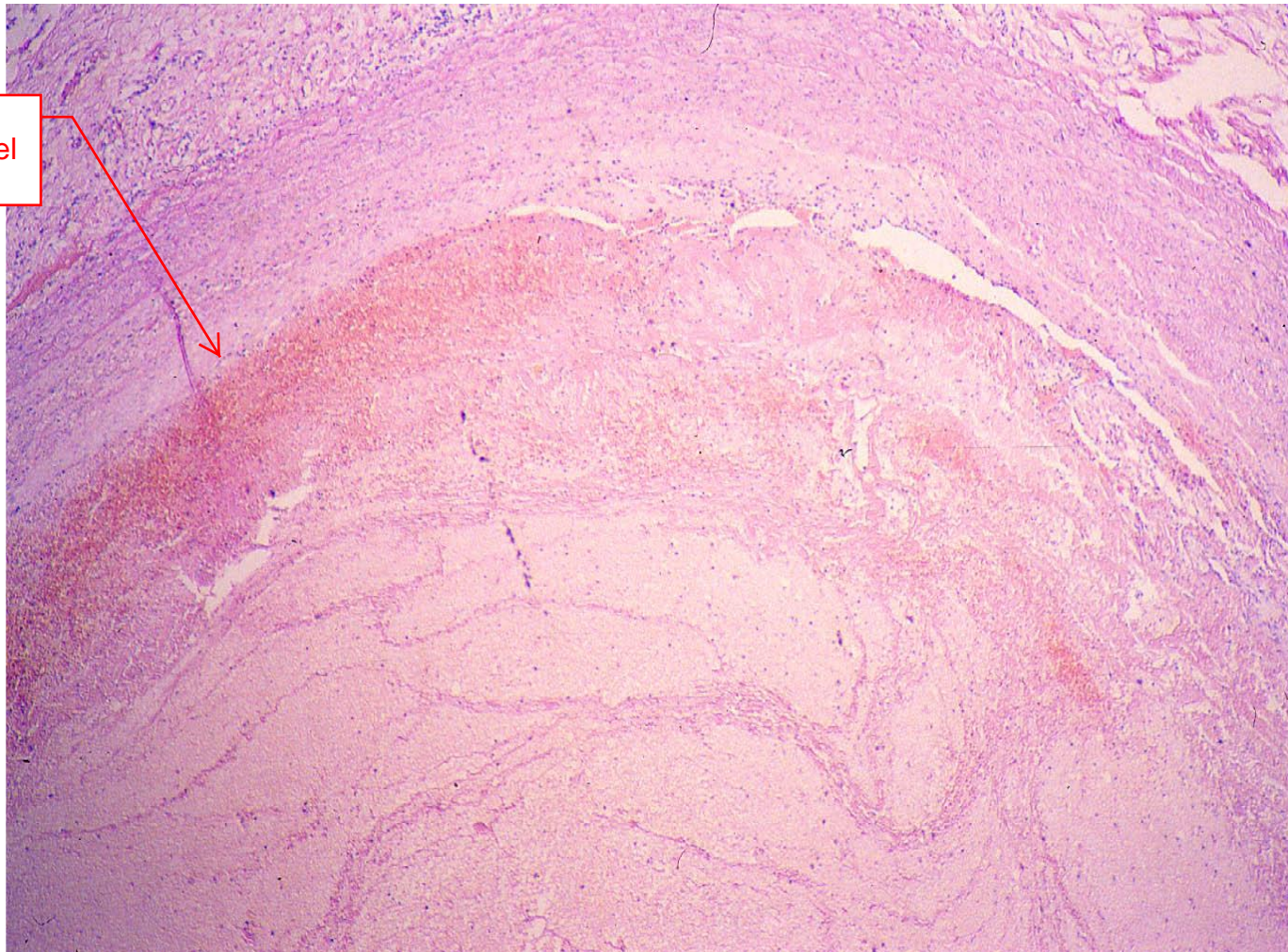
- Pulmonary thromboemboli
- Pulmonary emboli of other types
- Pulmonary thrombosis an unusual disease
- Pulmonary hypertension
- Diffuse pulmonary hemorrhage syndromes



Main pulmonary artery
that is filled with
thromboembolic material.

**Pulmonary Embolus,
right main pulmonary artery**

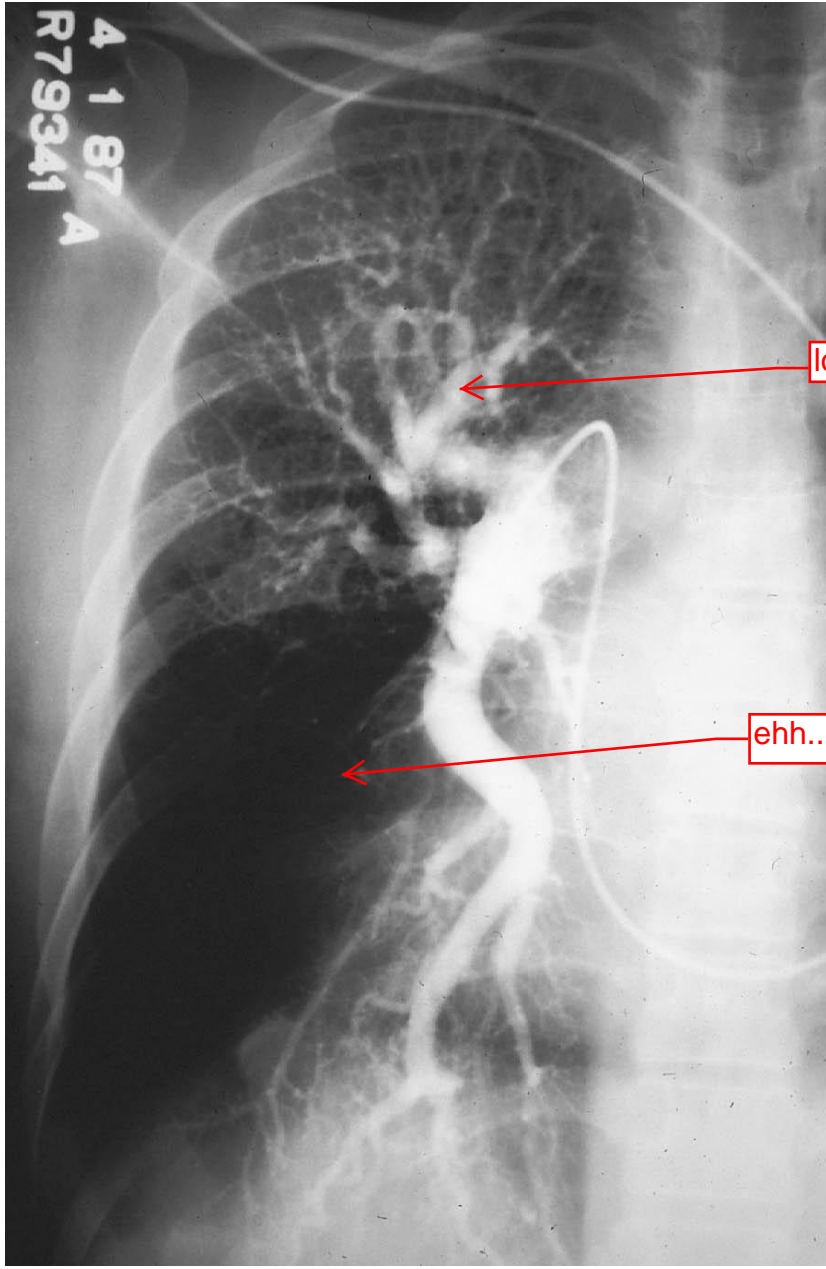
Usually emboli are thrombotic in origin, but they can be from other sources



attachment of
embolus to vessel
wall

Pulmonary Embolus with lines of Zahn (H&E)

the lines of Zahn indicate that the embolus was formed in situ and is not a postmortem clot. They occur over time as RBC's and Platelets mixed with fibrin add onto the thrombus as blood flows over it. Think of it as similar to the way an oyster makes pearls, except that these thrombi can kill you when they embolize get lodged in your lungs.

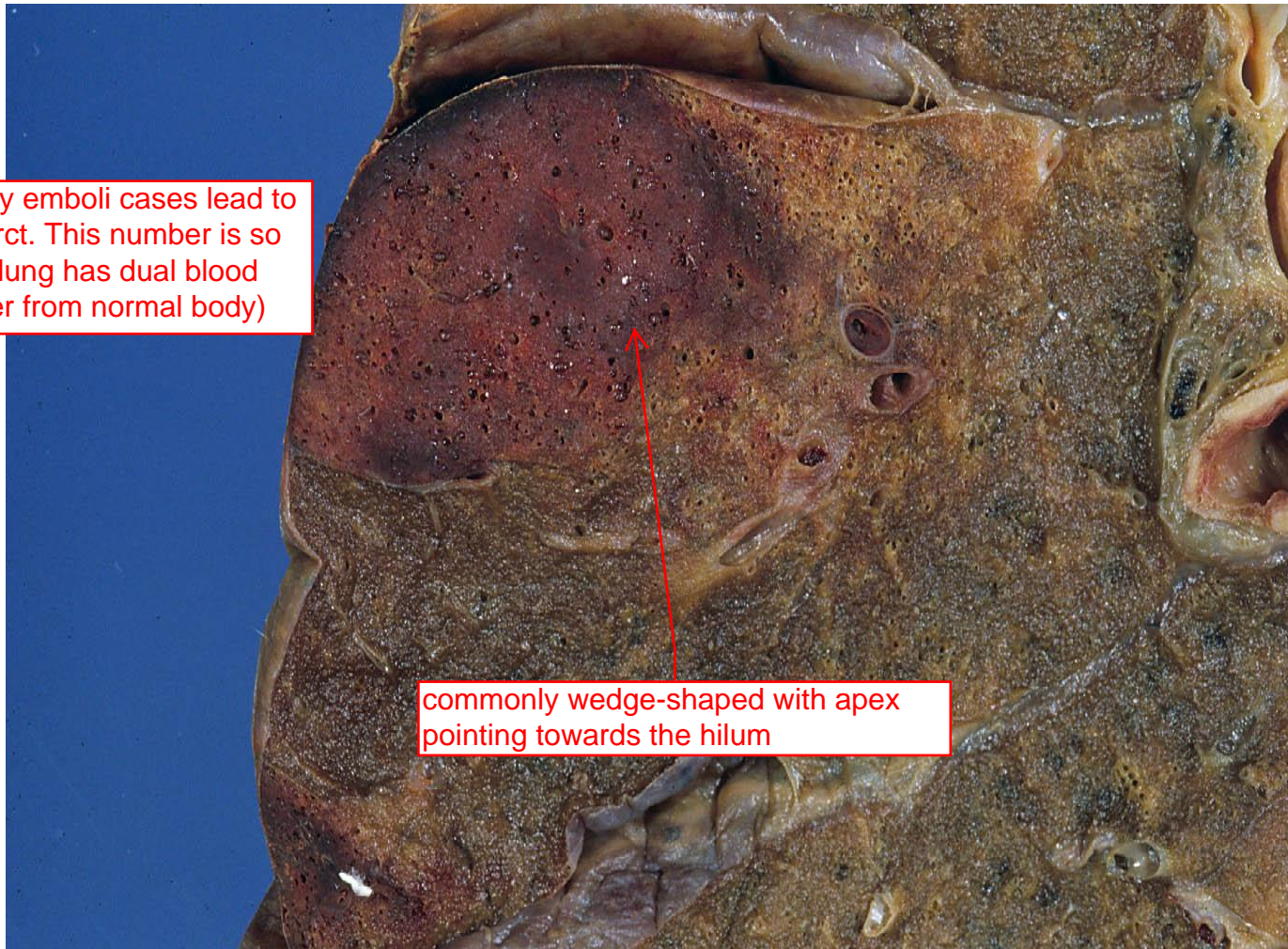


Pulmonary arteriogram, with right lower lobe filling defect

looks normal

ehh... not so normal here

CT angiograms are probably going to replace this type of arteriogram



10% of pulmonary emboli cases lead to a pulmonary infarct. This number is so low because the lung has dual blood supply (remember from normal body)

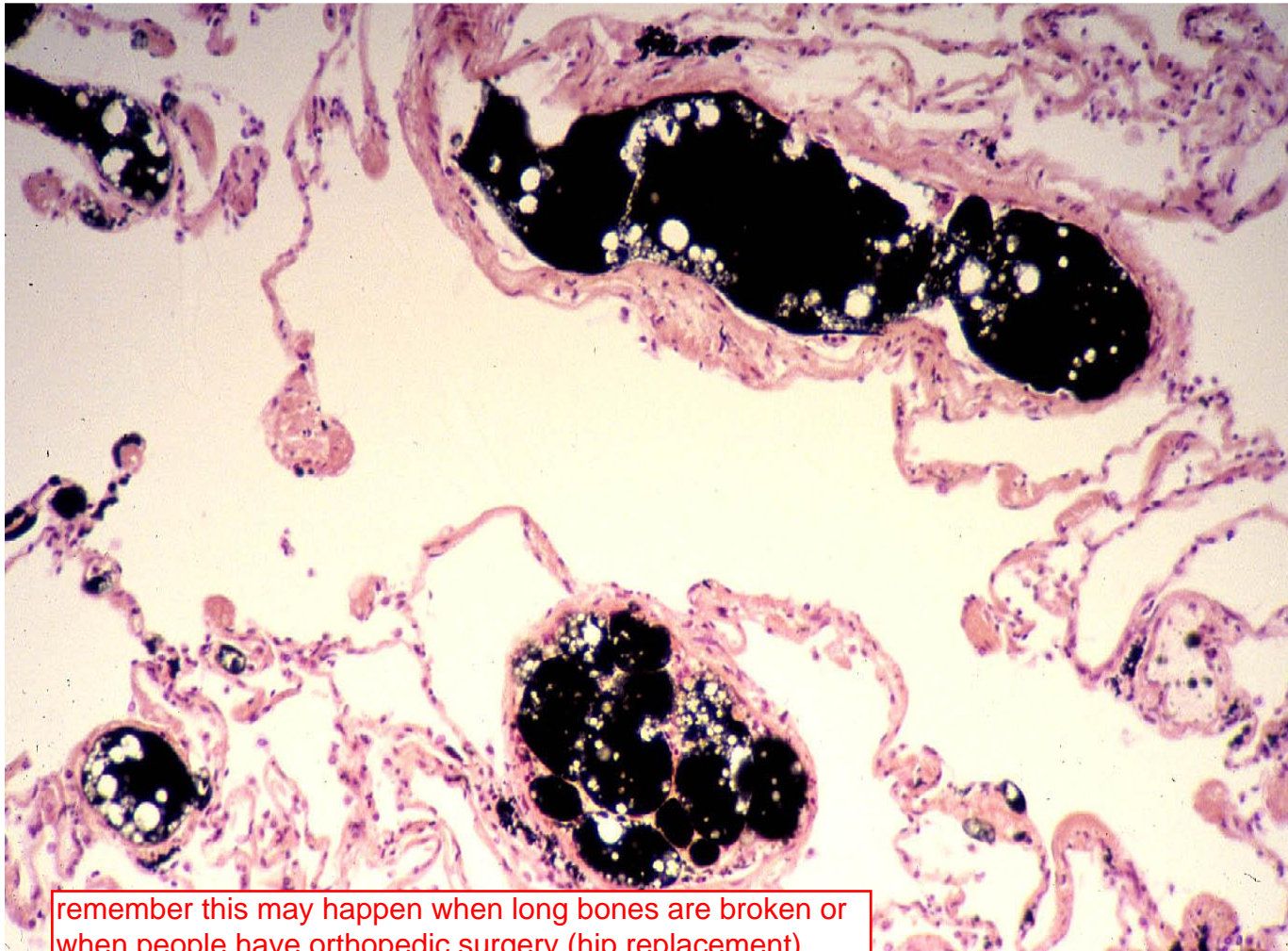
commonly wedge-shaped with apex pointing towards the hilum

Pulmonary infarct, right lung

usually pulmonary infarcts arise when patients have systemic diseases such as CHF. This type of disease will lead to less blood getting into the lungs through the bronchial arteries (thus less dual supply) and it also predisposes an individual to forming venous clots (usually in deep leg veins) because of an overall increase in stasis. (remember Virchow's triad: Stasis (or other hemodynamic changes like turbulence), endothelial damage, and hypercoagulability)

PULMONARY EMBOLI OF OTHER TYPES

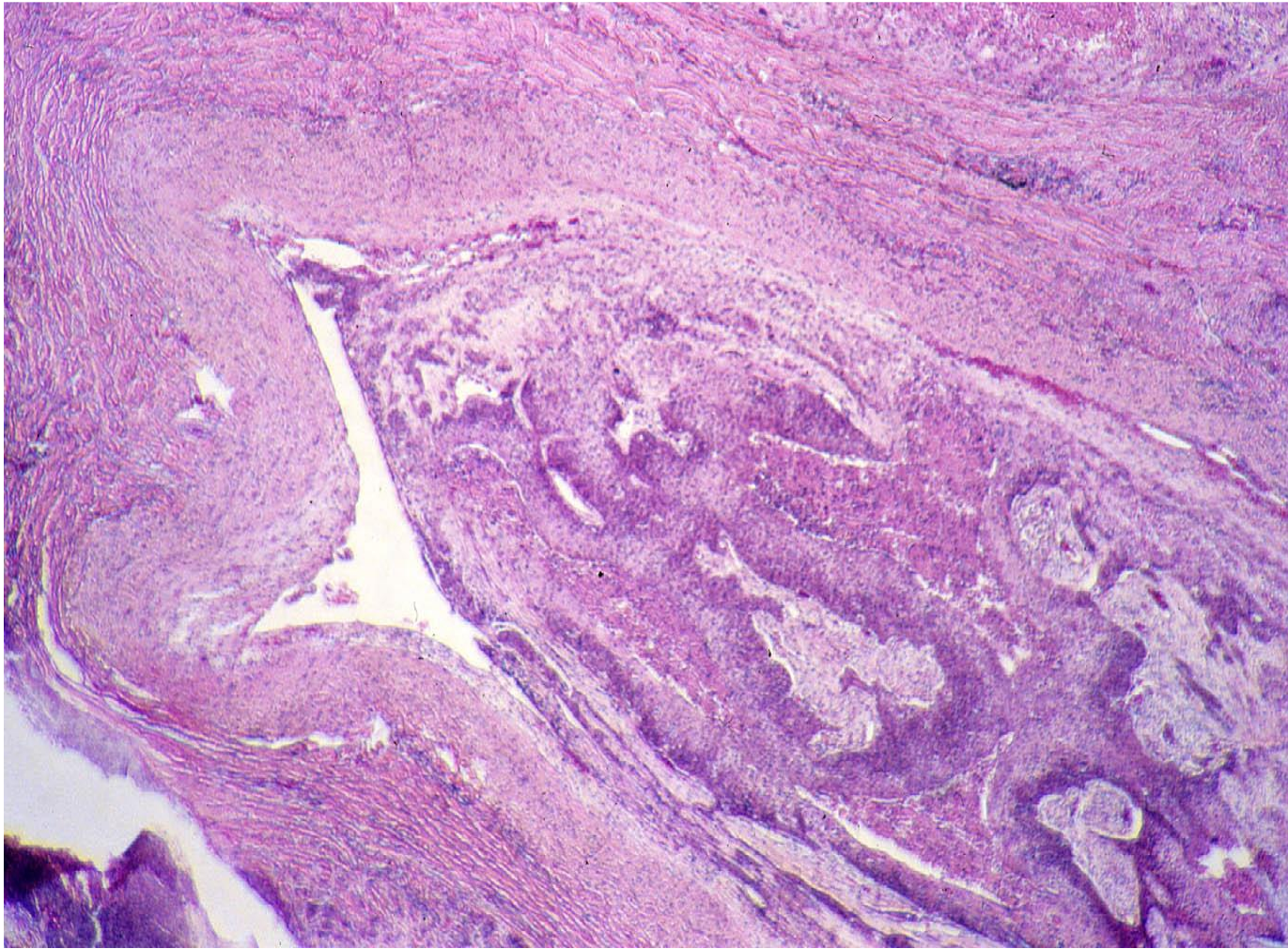
- Fat emboli (injury to long bones) Also during surgery (like hip replacement)
- Tumor emboli (metastatic cancer)
- Air emboli (venous system) usually an iatrogenic problem
- Talc emboli (IV drug abuse) using drugs meant for oral consumption inappropriately by crushing them up and injecting them. Bad for probably more than one reason, but for this lecture we are worried about the filler material in the drug acting as an embolus
- Amniotic fluid emboli (pregnancy complication)



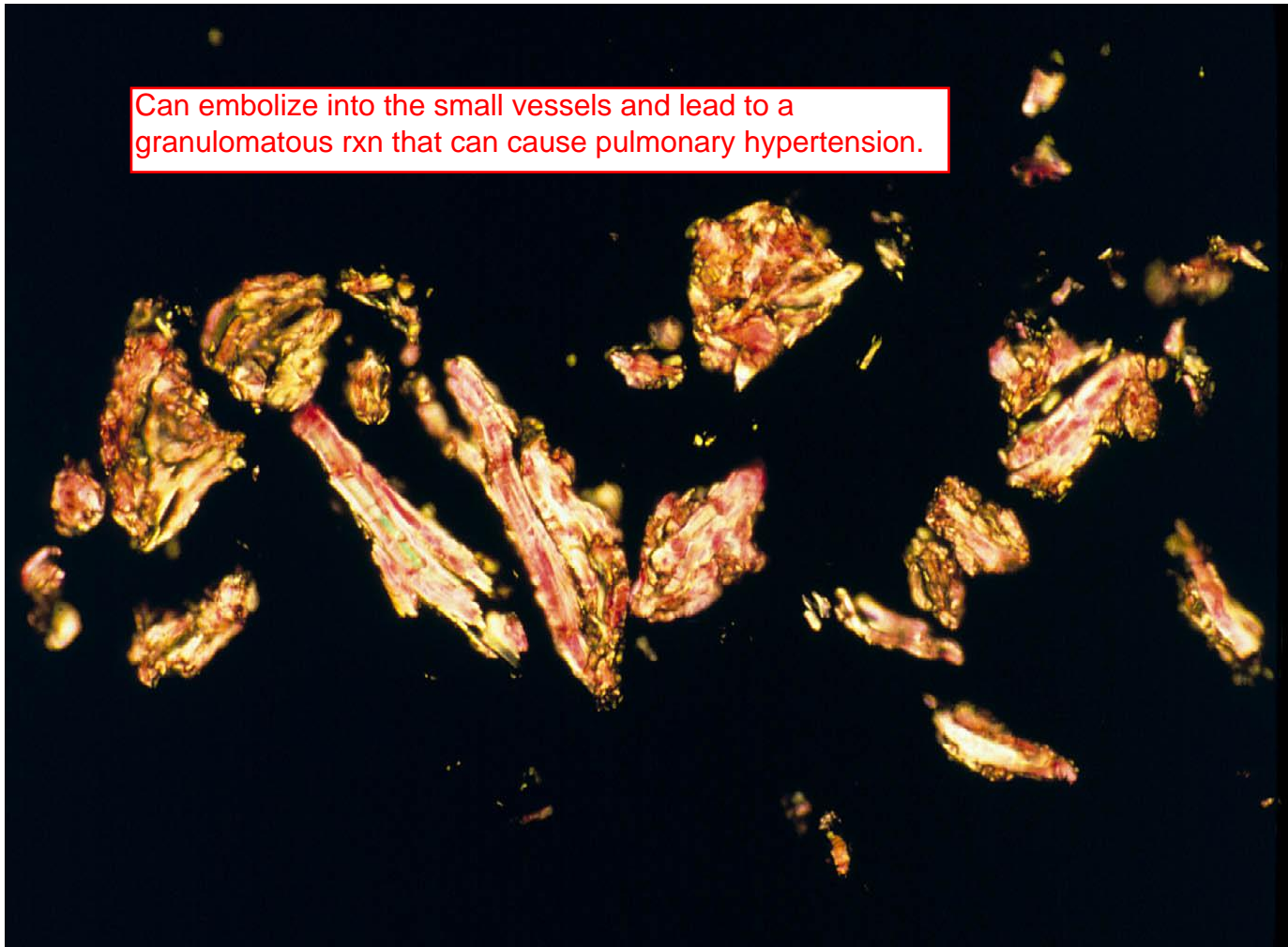
remember this may happen when long bones are broken or when people have orthopedic surgery (hip replacement)

Fat emboli, lung (osmium post fixation)

in addition to the fat blocking the vessels, lipases in the endothelium become activated and convert the fat into fatty acids which can cause further damage downstream in the microvasculature leading to pulmonary edema (add that to your differential diagnosis of pulmonary edema, haha). This is a common problem in people with massive fat emboli. Usually occurs 24 hrs after an ortho procedure.



Tumor Embolus, pulmonary artery



Can embolize into the small vessels and lead to a granulomatous rxn that can cause pulmonary hypertension.

Microcrystalline cellulose (Darvocet tablet), polarized light


present in a lot of meds (like oxycodone)

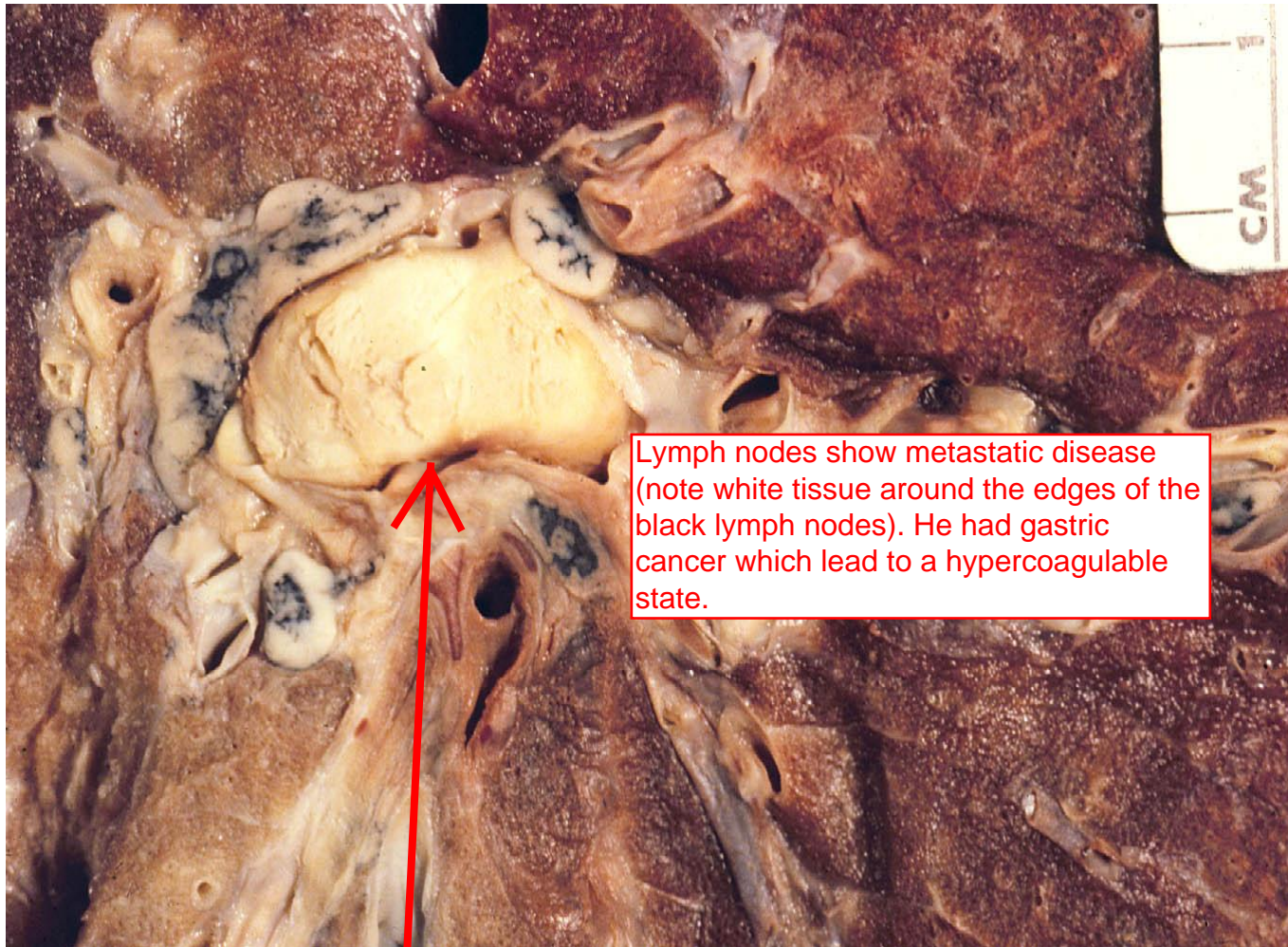
PULMONARY IN SITU THROMBOSIS

"very uncommon"

- Most often occurs in malignancy (hypercoagulation) or pulmonary hypertension
- Thrombi are pale and form "casts" of arterial tree made primarily of platelets and fibrin.

remember seeing the
cast in the roadshow?





Lymph nodes show metastatic disease (note white tissue around the edges of the black lymph nodes). He had gastric cancer which lead to a hypercoagulable state.

Pulmonary artery thrombosis

PULMONARY HYPERTENSION

Used to be a reason for lung transplant,
but now there are drugs that can help

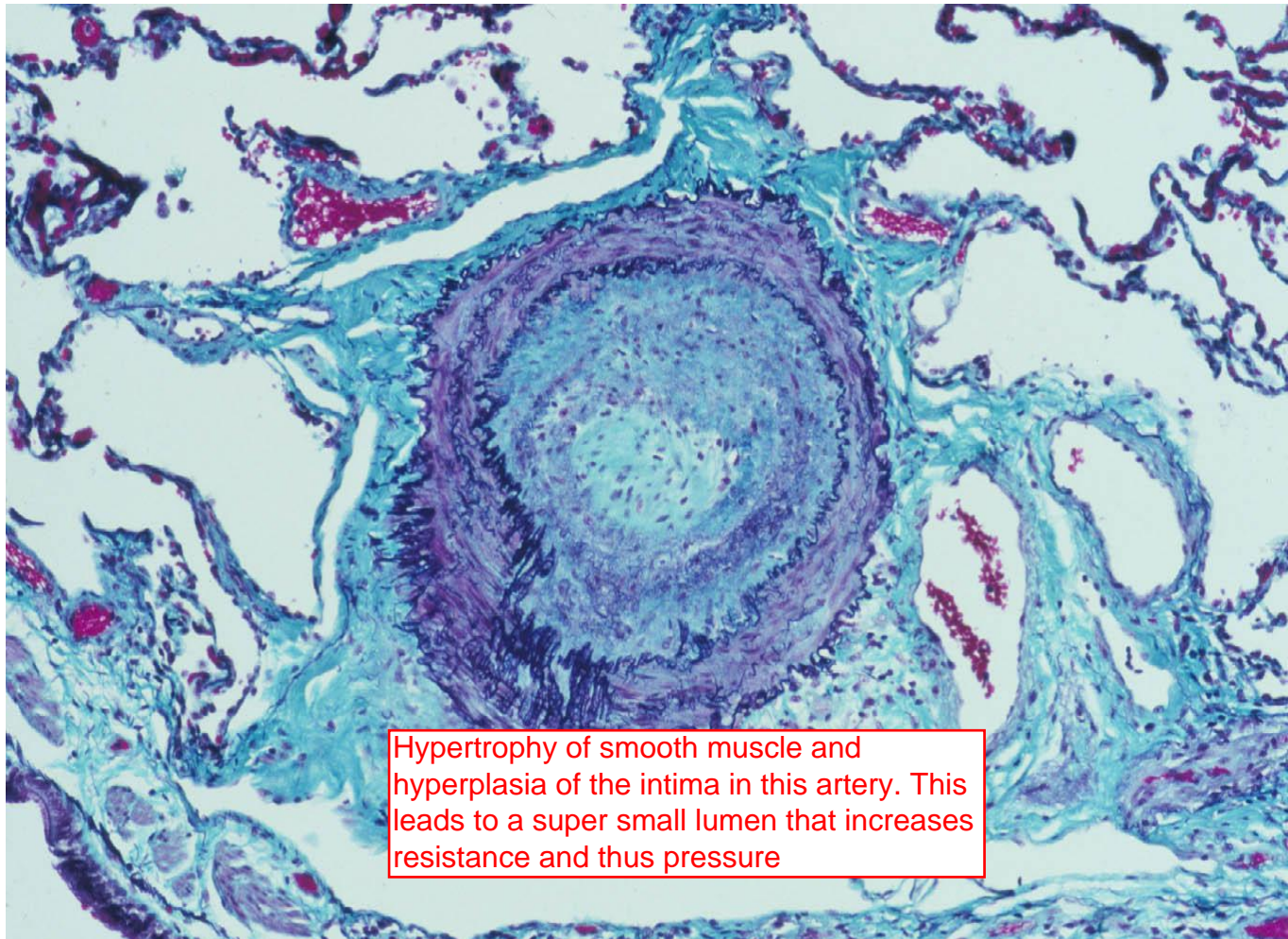
From FA2011: Bosentan is used to treat Pulm HTN; it competitively antagonizes endothelin-1 receptors, decreasing pulmonary vascular resistance

problem is of unknown origin but normally arises in the pulmonary system itself

- Primary pulmonary hypertension
 - Pulmonary arterial hypertension (PAH)
 - Pulmonary veno-occlusive disease
- Secondary pulmonary hypertension
 - Chronic pulmonary emboli
 - Congenital heart disease (ASD, VSD)

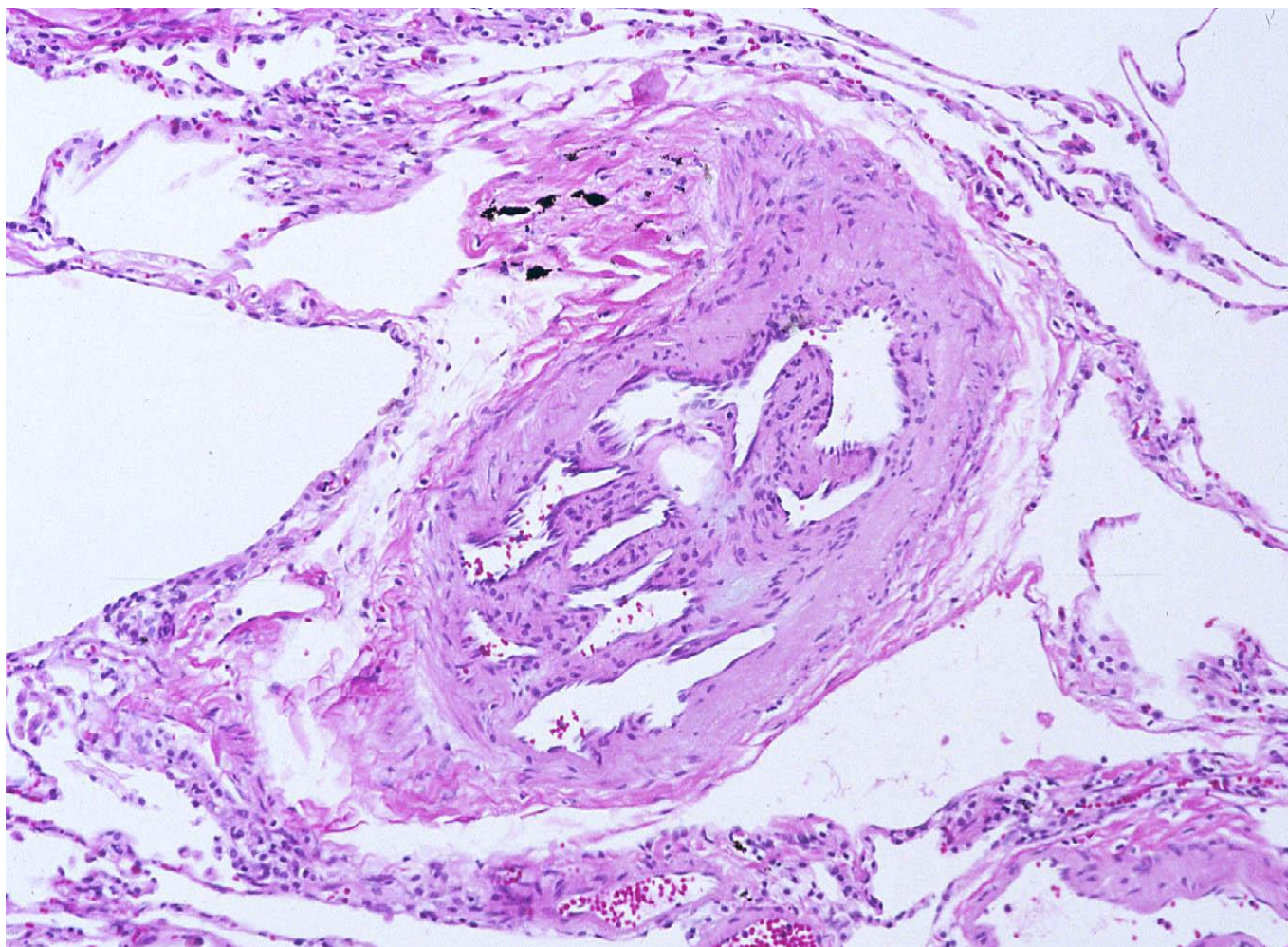
showering emboli from leg veins over a long time

leads to higher right sided pressures



Hypertrophy of smooth muscle and hyperplasia of the intima in this artery. This leads to a super small lumen that increases resistance and thus pressure

Pulmonary arterial hypertension elastic stain

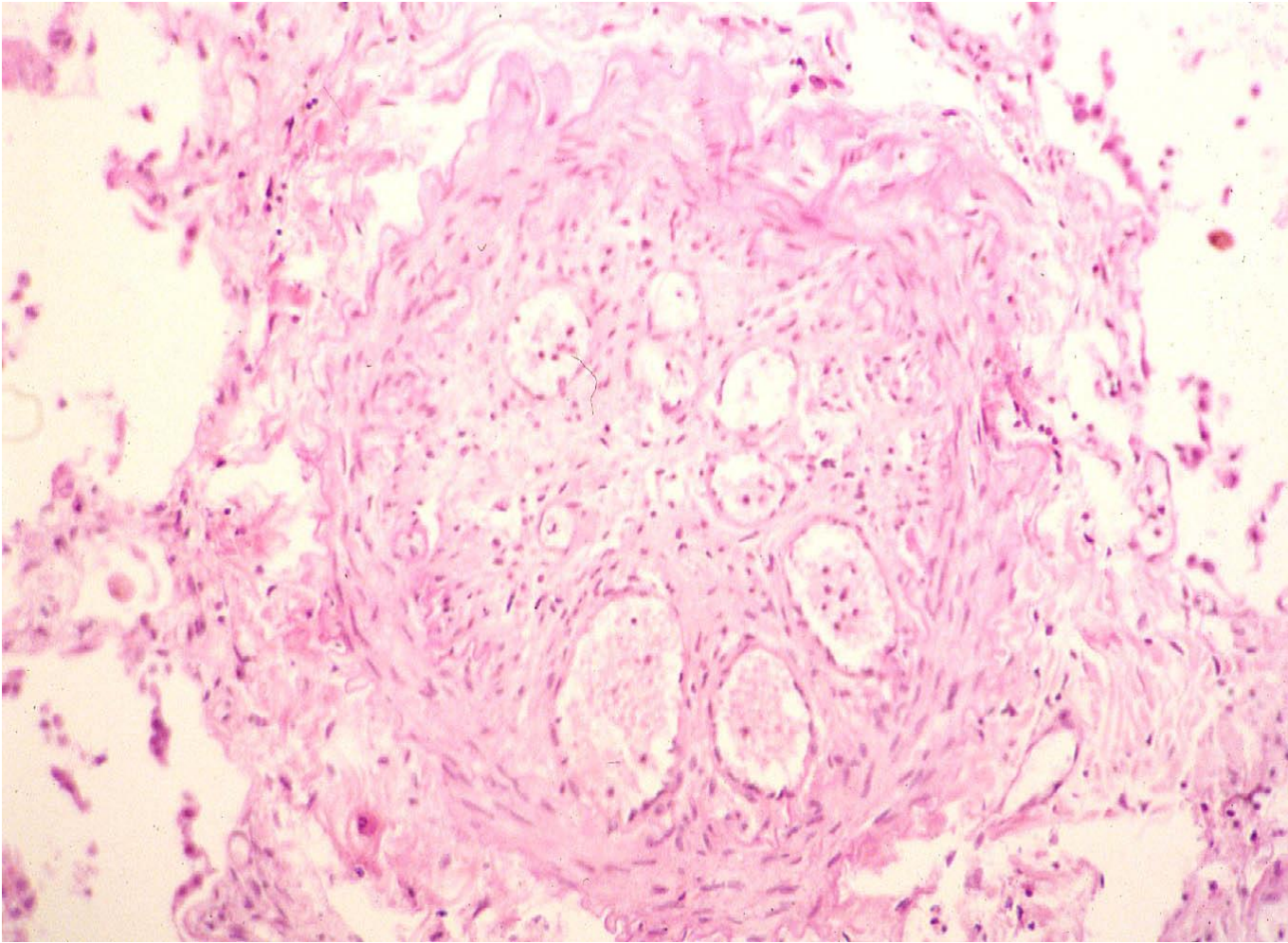


Pulmonary arterial hypertension

plexiform lesion

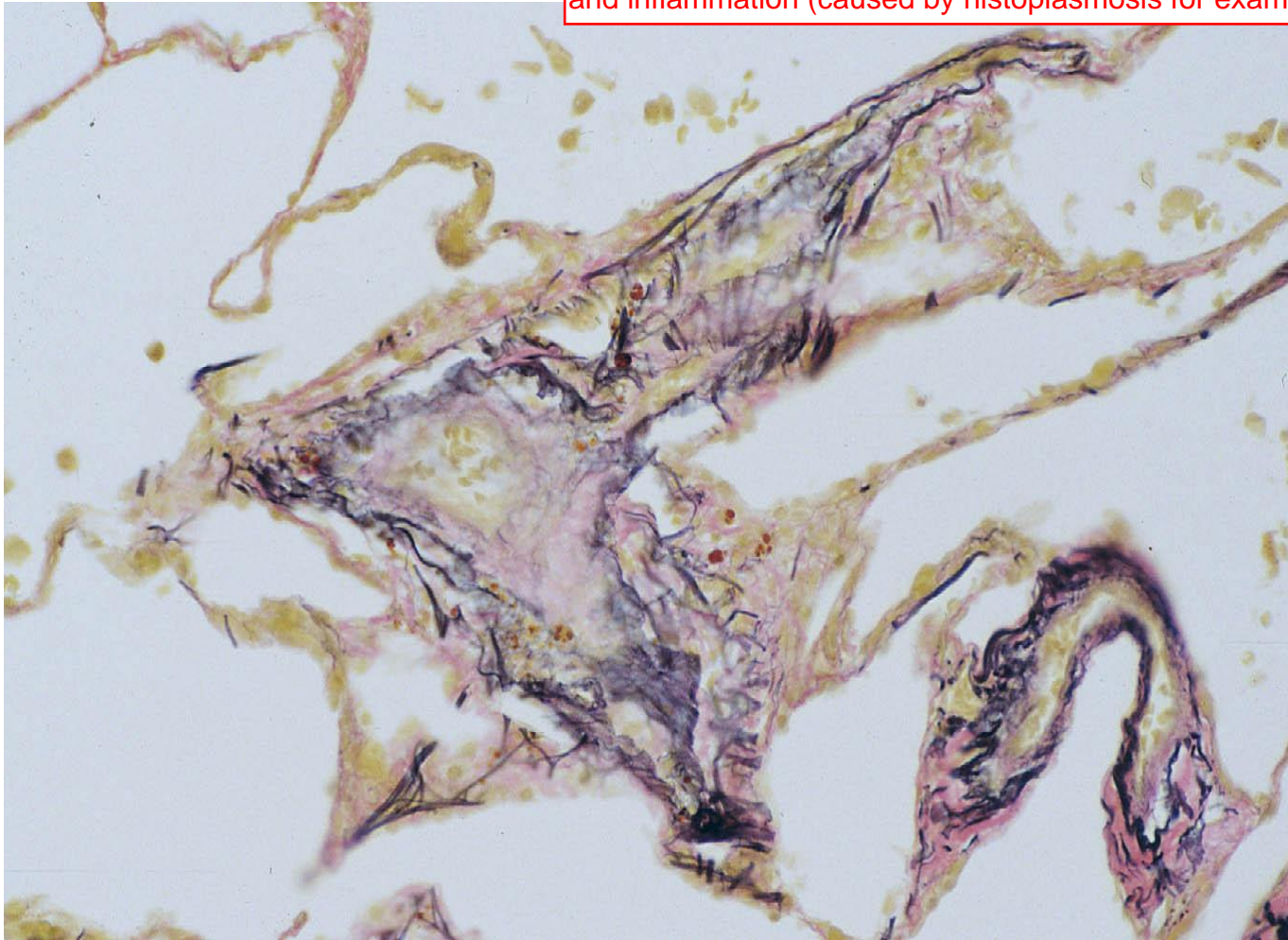
Hallmark of hypertension

usually indicates emboli that
have been re-canalized



**Recanalized pulmonary embolus,
chronic thromboembolic disease**

Usually of unknown cause, but can be associated with chemotherapy and inflammation (caused by histoplasmosis for example)



Pulmonary veno-occlusive disease, elastic stain

small veins of the lung become occluded by fibrous tissue. Clinically very difficult to distinguish from the other hypertensive states. This is a problem because it does not respond to the treatment that is used in the other cases

Thickened and distended RV.



Right ventricular hypertrophy,
primary pulmonary hypertension

Cor pulmonale: Failure of the right side of the heart due to chronic pulmonary hypertension

DIFFUSE PULMONARY HEMORRHAGE

"not common but
important"

usually fatal if not
caught in time

- Goodpasture's syndrome
- Systemic lupus erythematosus
- Wegener's granulomatosis
- Idiopathic

both can be treated
with corticosteroids
and cytotoxic agents

Immunologic Lung Disease (Gell & Coombs)

Immune reaction	Mediator	Histology	Example
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Type I IgE	Reaginic AB	Eosinophils	Asthma
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Type II IgG	Cytotoxic AB	Alveolar hemorrhage	Goodpasture's Syl Ab's directed against glomeruli and alveolar basement membranes
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Type III	Immune complexes	Vasculitis	SLE
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Type IV	Sensitized lymphs	Granulomas	Sarcoidosis HP
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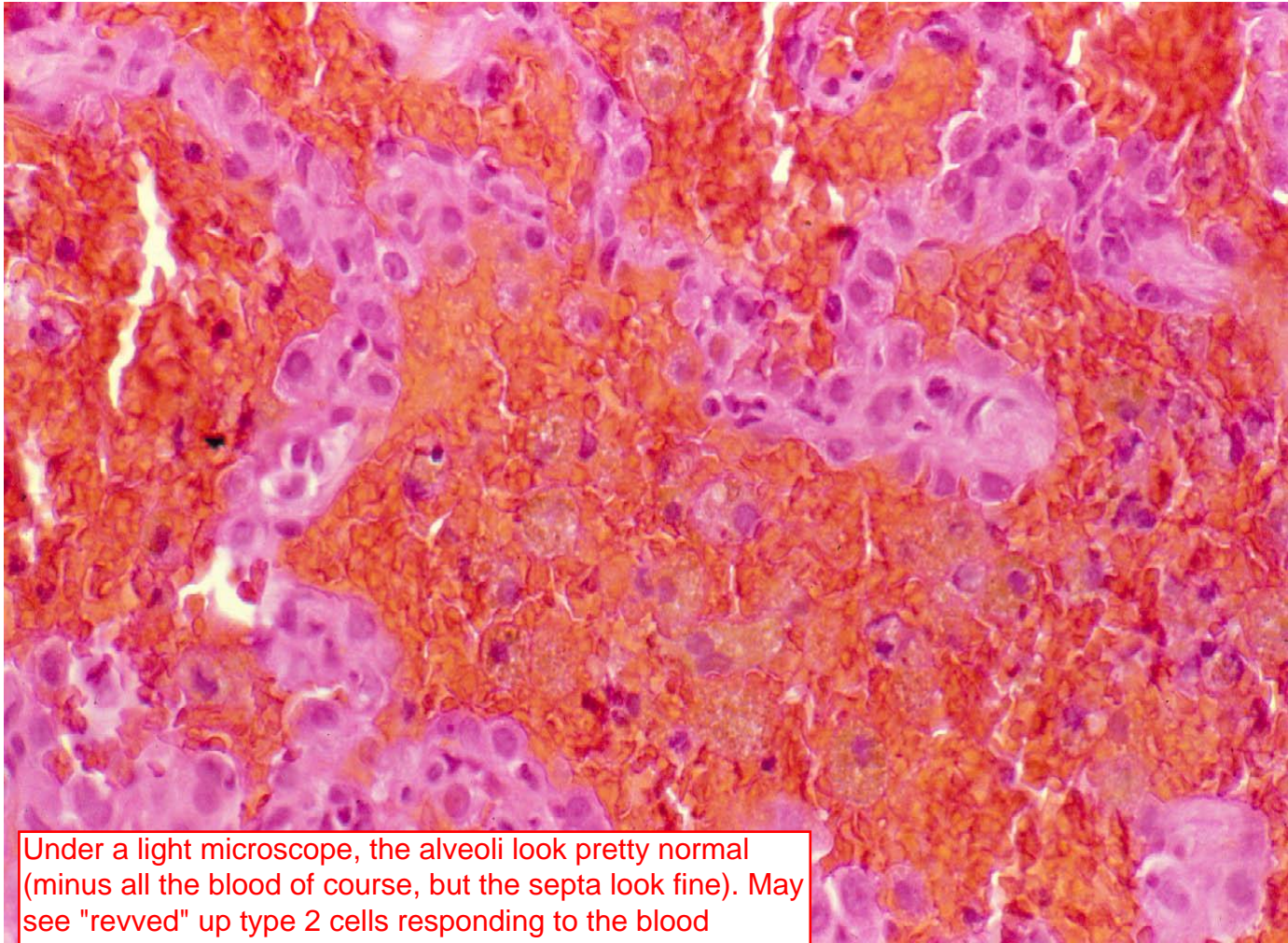
another example is autoimmune hemolytic anemia

Goodpasture's Syndrome



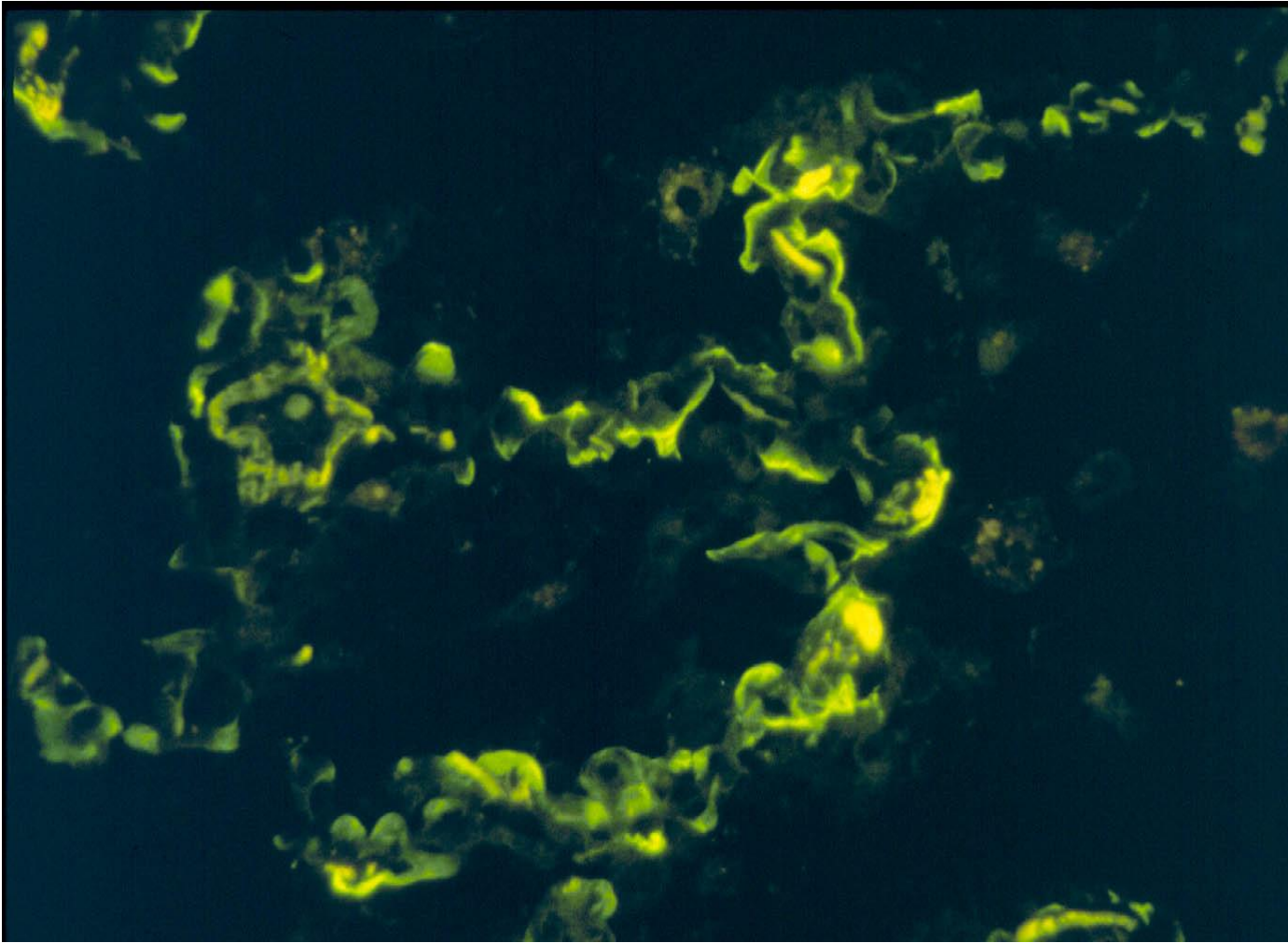
congested blood filled lung

Young males in their 30's have a flu like symptoms and then present with extreme SOB and sometimes hemoptysis



Under a light microscope, the alveoli look pretty normal (minus all the blood of course, but the septa look fine). May see "revved" up type 2 cells responding to the blood

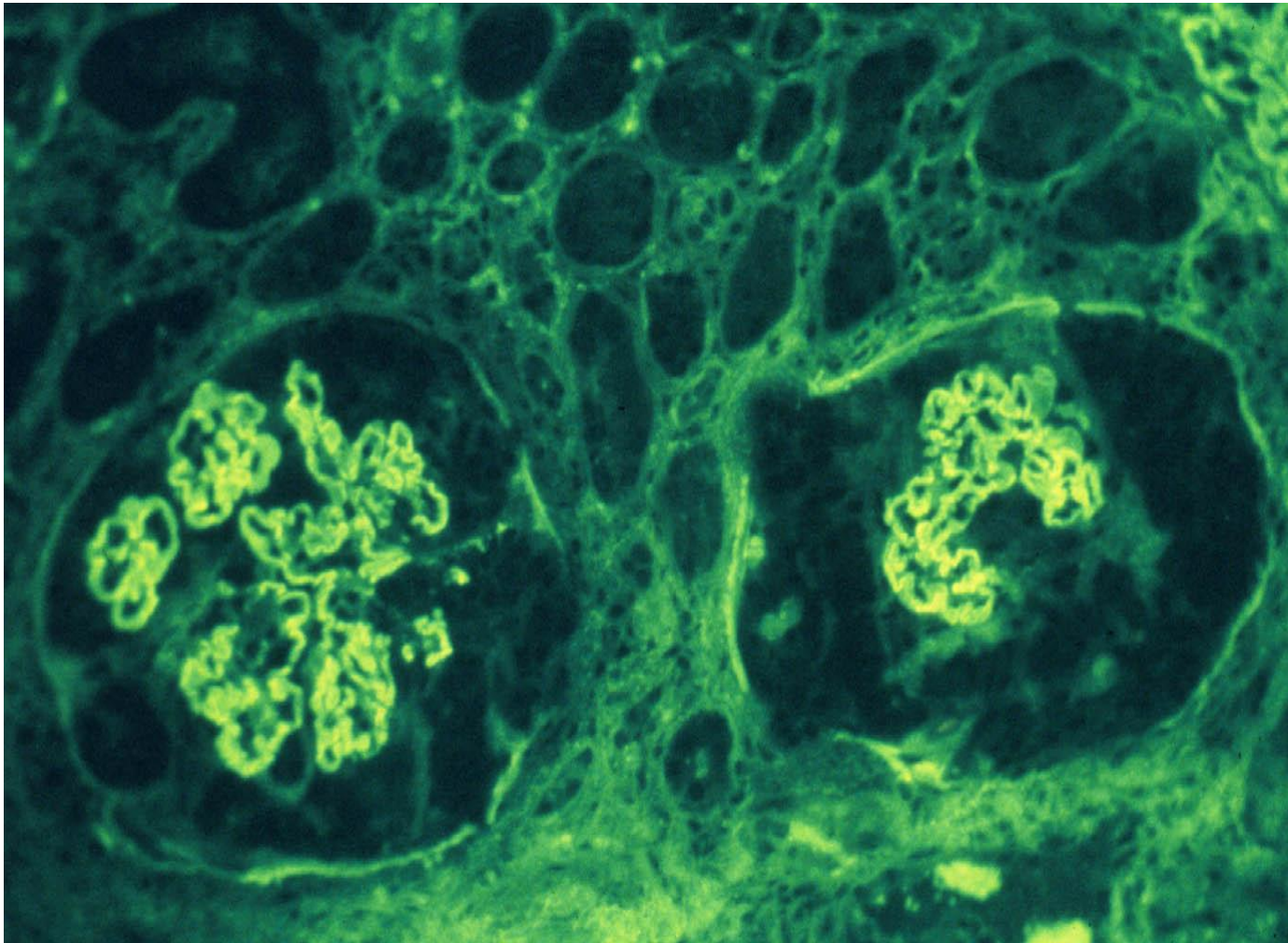
Goodpasture's Syndrome with intra-alveolar hemorrhage



Goodpasture's Syndrome, lung

IgG immunofluorescence

demonstrates
linear deposition

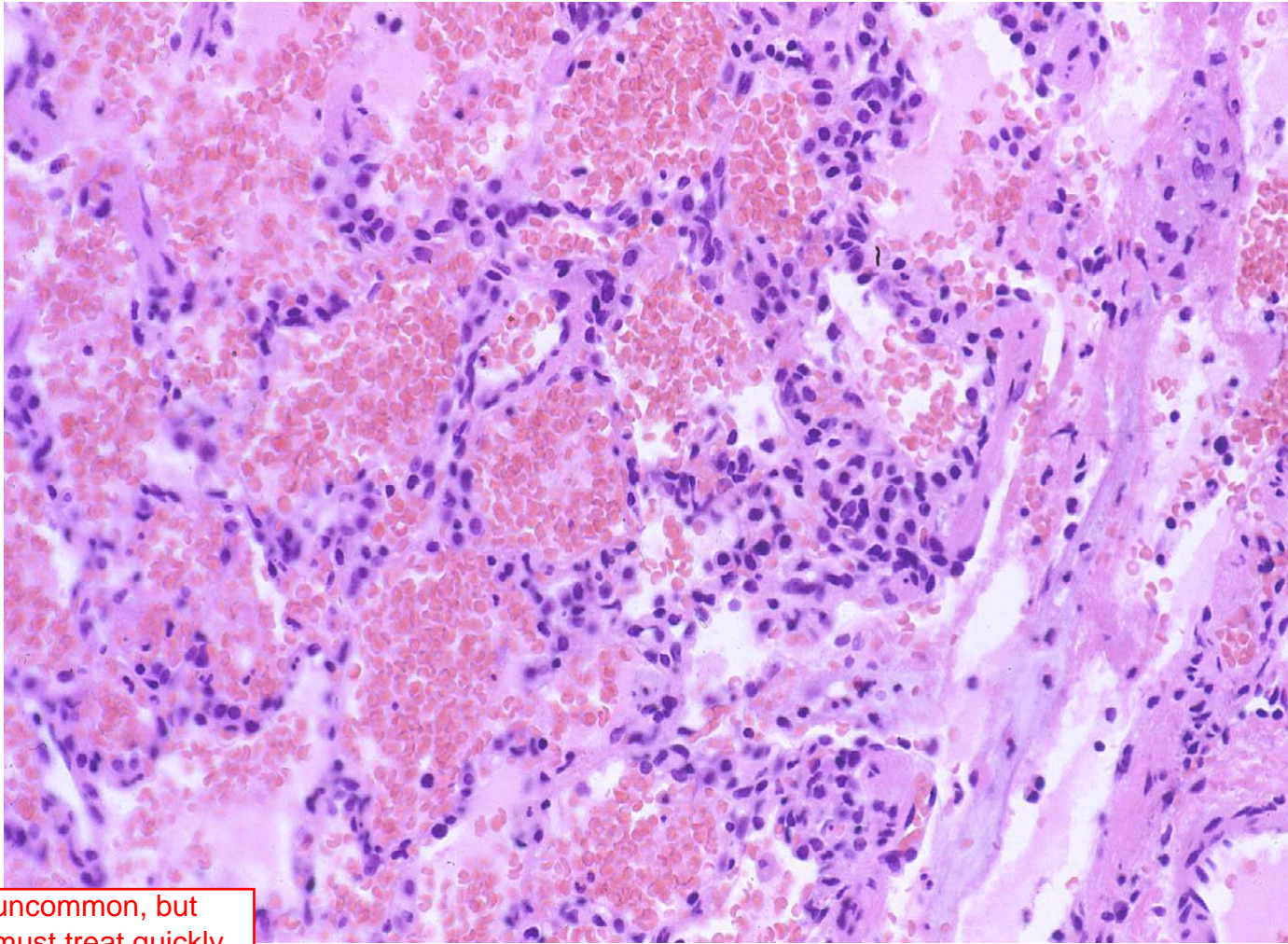


Goodpasture's Syndrome, kidney

IgG immunofluorescence

same type of linear deposition

Side Note: A granular (non-linear) type of deposition is indicative of immune complex deposition (type 3). Such as those formed in SLE



uncommon, but
must treat quickly

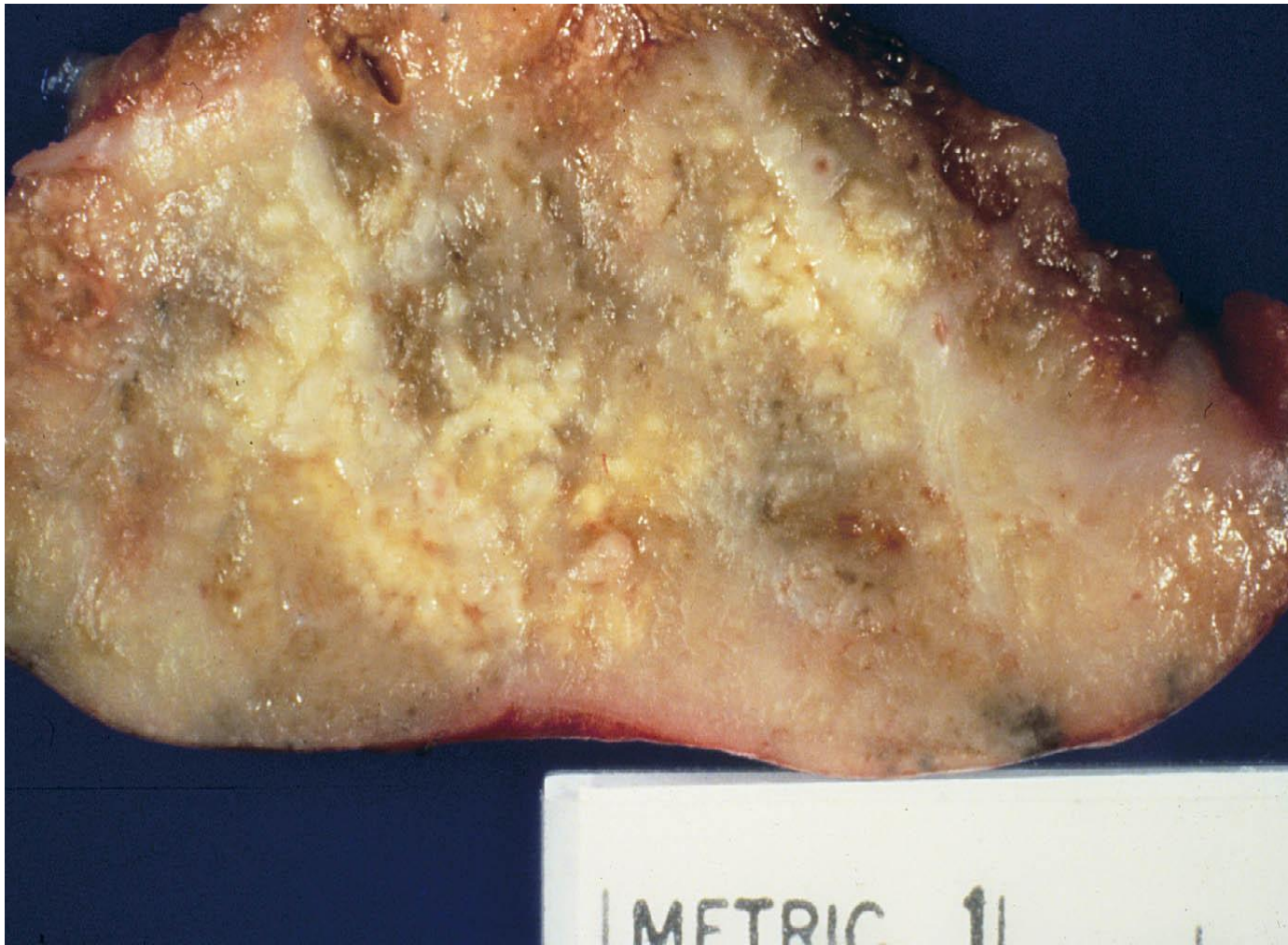
Pulmonary capillaritis (microangiitis), H&E

lupus, wegeners, and
iodopathic causes

A case "reverse pneumonia". Neutrophils are in the alveolar capillary walls and RBC's are in the alveolar space

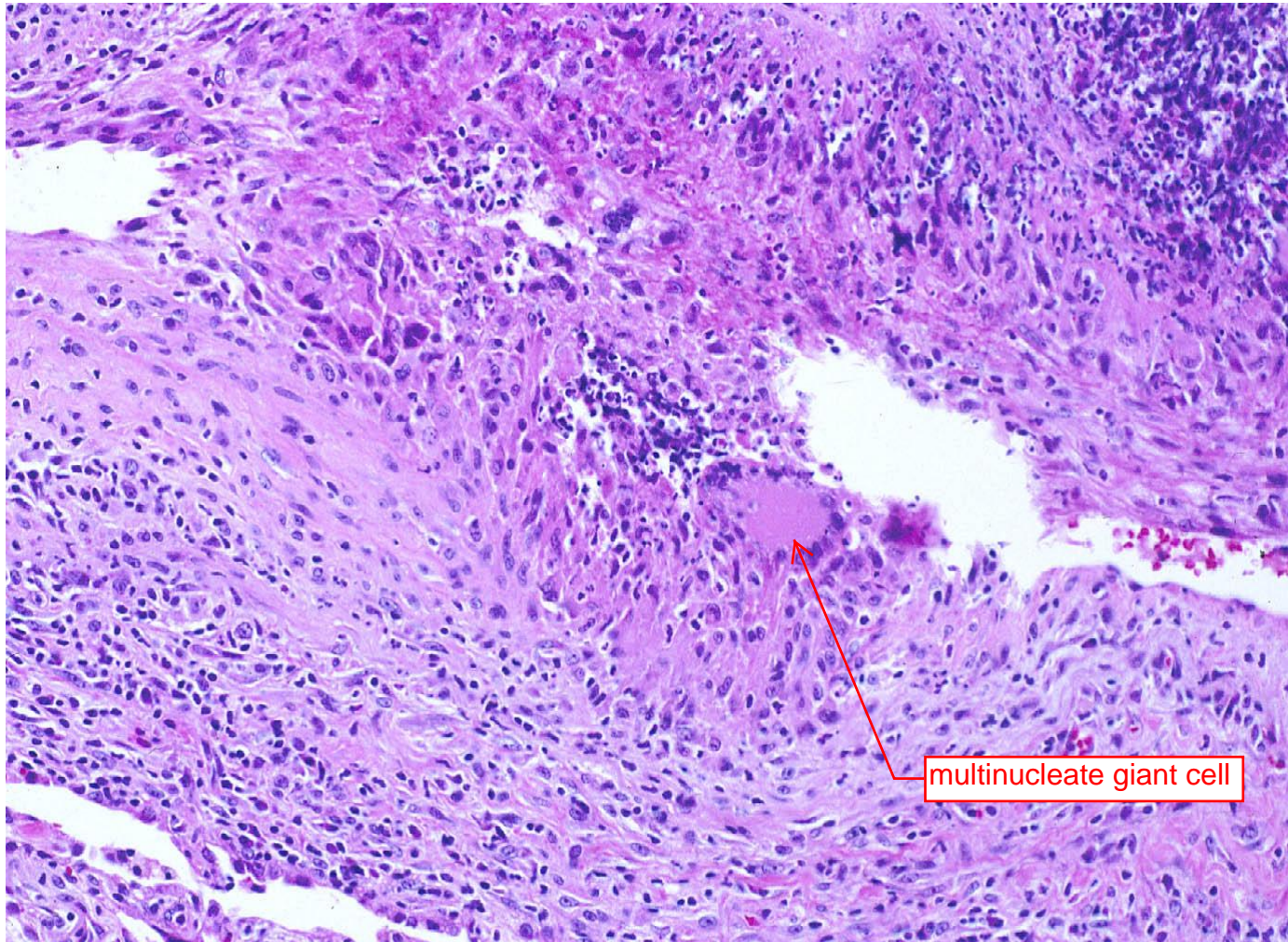
CLASSIC WEGENER'S GRANULOMATOSIS

- Necrotizing granulomatous arteritis of lungs
- Necrotizing inflammation of upper respiratory tract like the larynx, ear, nose, or eyes
- Glomerulonephritis crescentic type glomerulonephritis that is often pauci-immune (meaning little or no immune complexes)

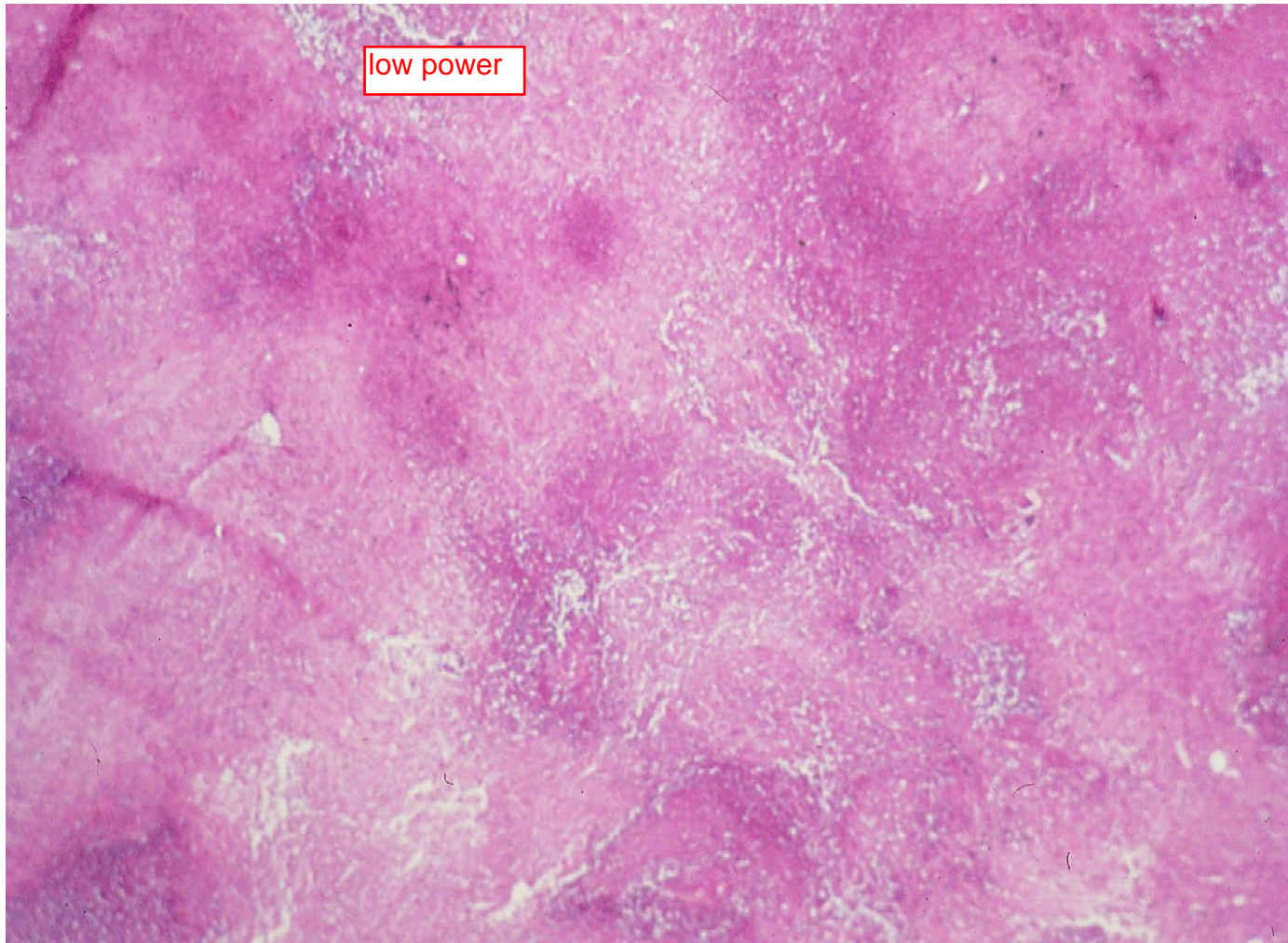


Necrobiotic nodule, Wegener's granulomatosis

fever, chills, SOB, malaise,
and loss of appetite



Necrotizing granulomatous arteritis,
Wegener's (H&E)



Geographic necrosis, variable in shape and size. Helps distinguish Wegener's from TB and histoplasmosis
Wegener's granulomatosis (H&E)



Back wall of my den

part 2!

Obstructive Lung Disease

SESSION SPECIFIC OBJECTIVES

- List the major types of obstructive lung disease
- Recognize and describe the pathology of obstructive lung disease
 - Emphysema, small airways disease, large airways disease, bronchiectasis, and asthma

OBSTRUCTIVE LUNG DISEASE

- Emphysema
- Small airways disease
- Large airways disease
- Bronchiectasis
- Asthma

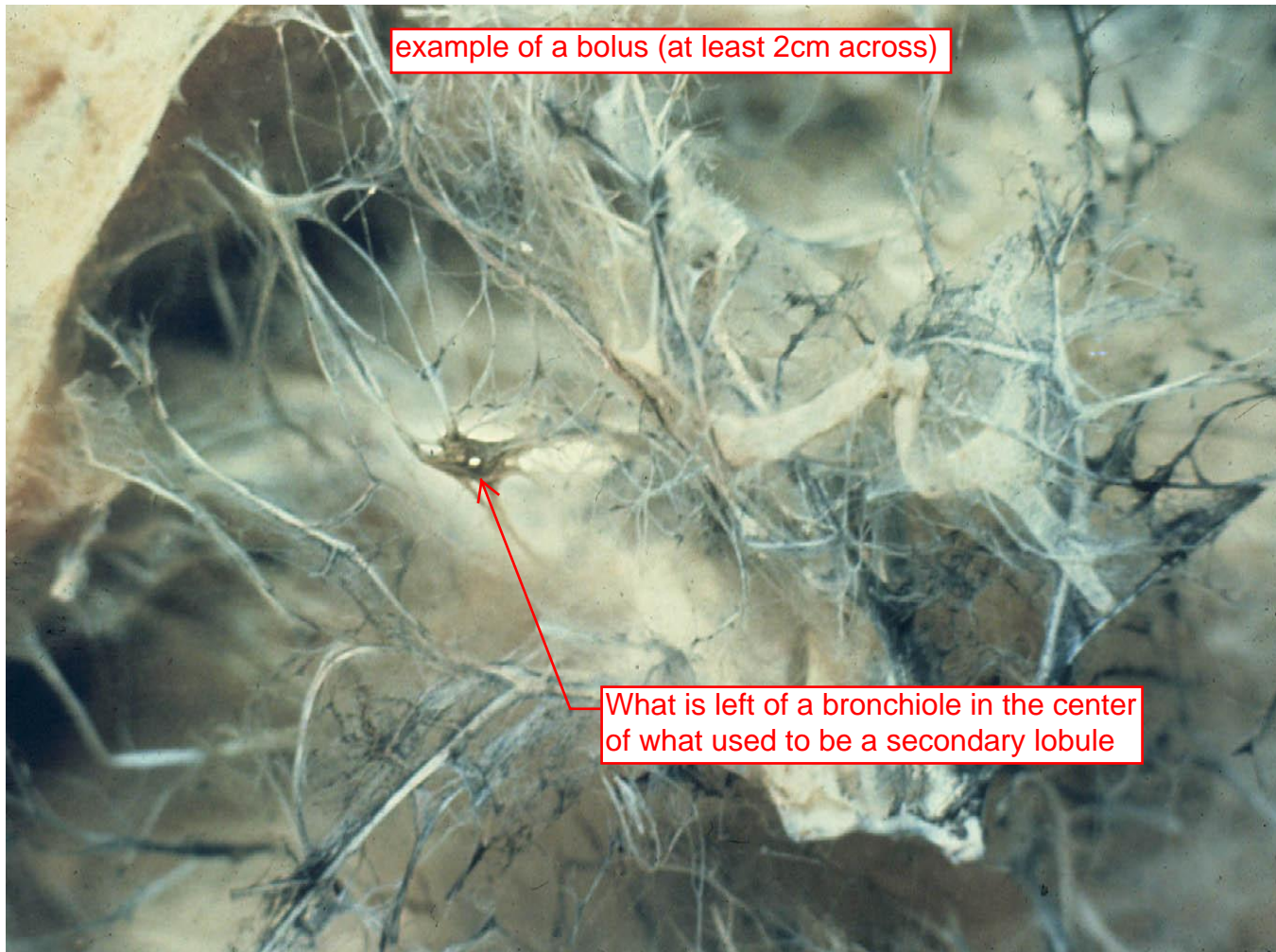
These three can be caused by smoking

CLASSIFICATION OF EMPHYSEMA

Anatomical definition: dilation of the airways of the lung associated with destruction of the lung parenchyma

mostly caused
by smoking

- Centrilobular (85%) Centriacinar
- Panlobular (5%) Panacinar
- Paracicatricial (5%) irregular
- Localized (5%) paraseptal or distal

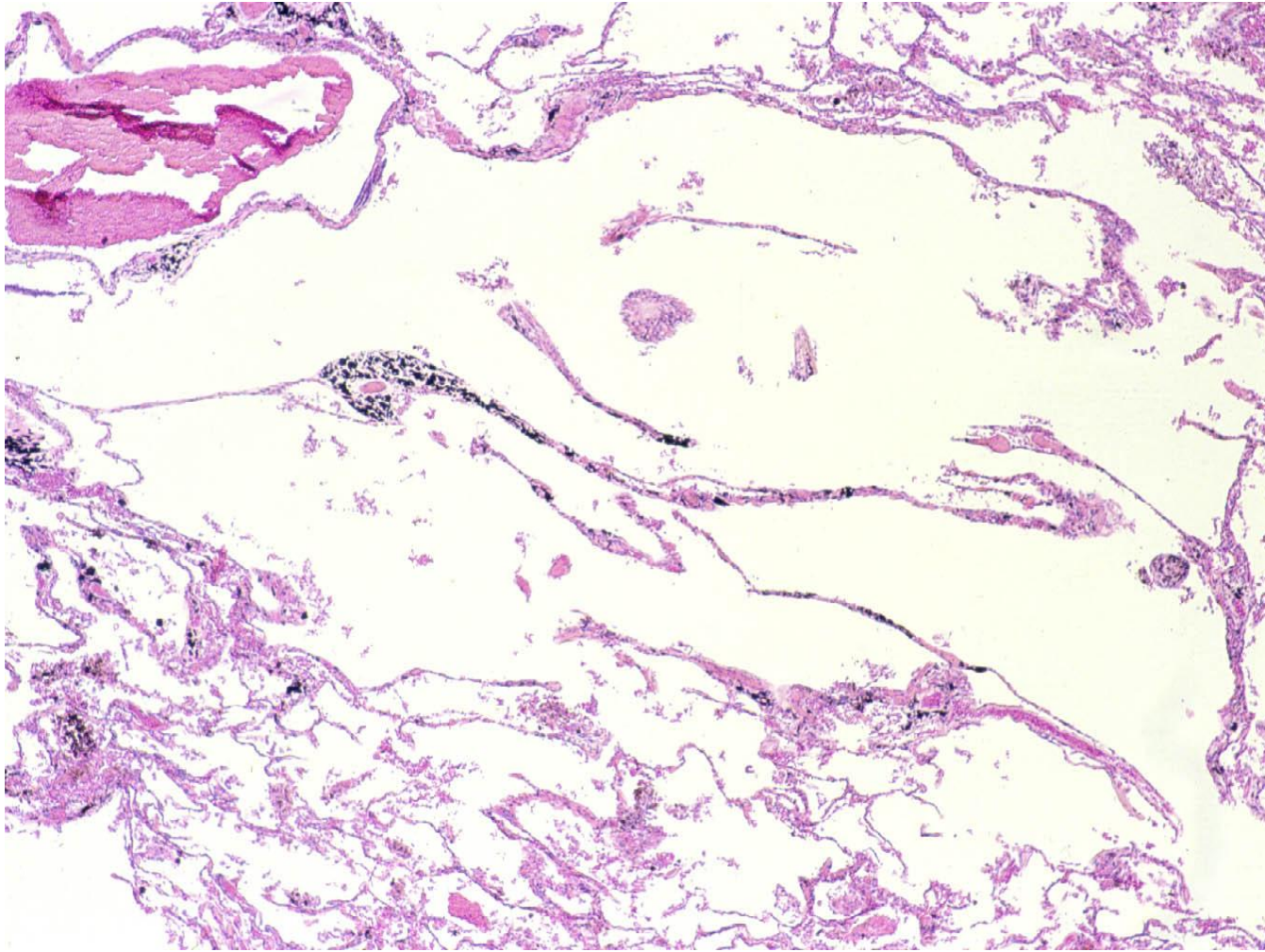


example of a bolus (at least 2cm across)

What is left of a bronchiole in the center of what used to be a secondary lobule

Centrilobular emphysema (gross)

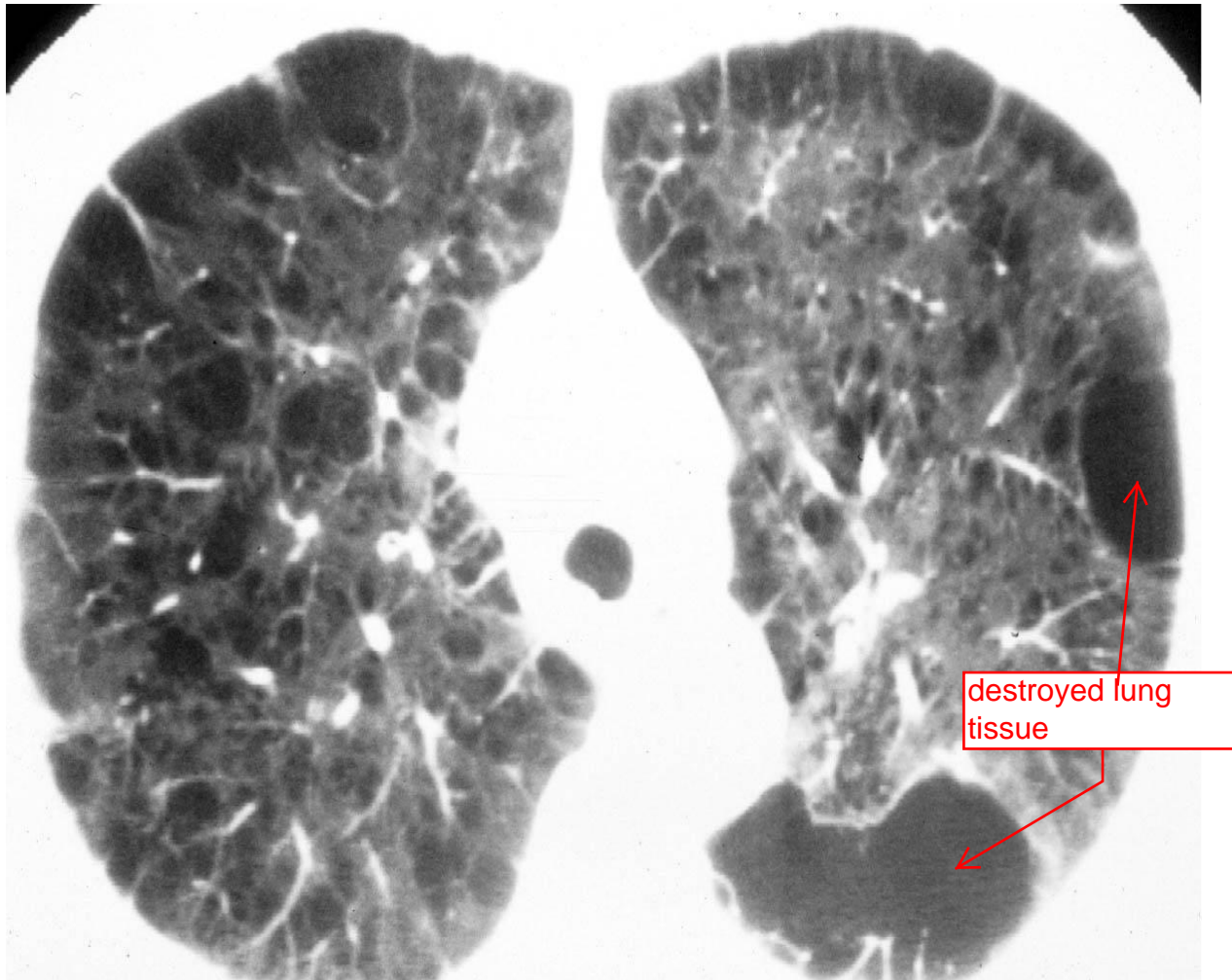
Commonly begins in the central part of the secondary lobule, but can spread to destroy the whole lobule



Microscopic Hallmark

Centrilobular emphysema “free floating” alveolar septa

Only looks "free floating" in 2D



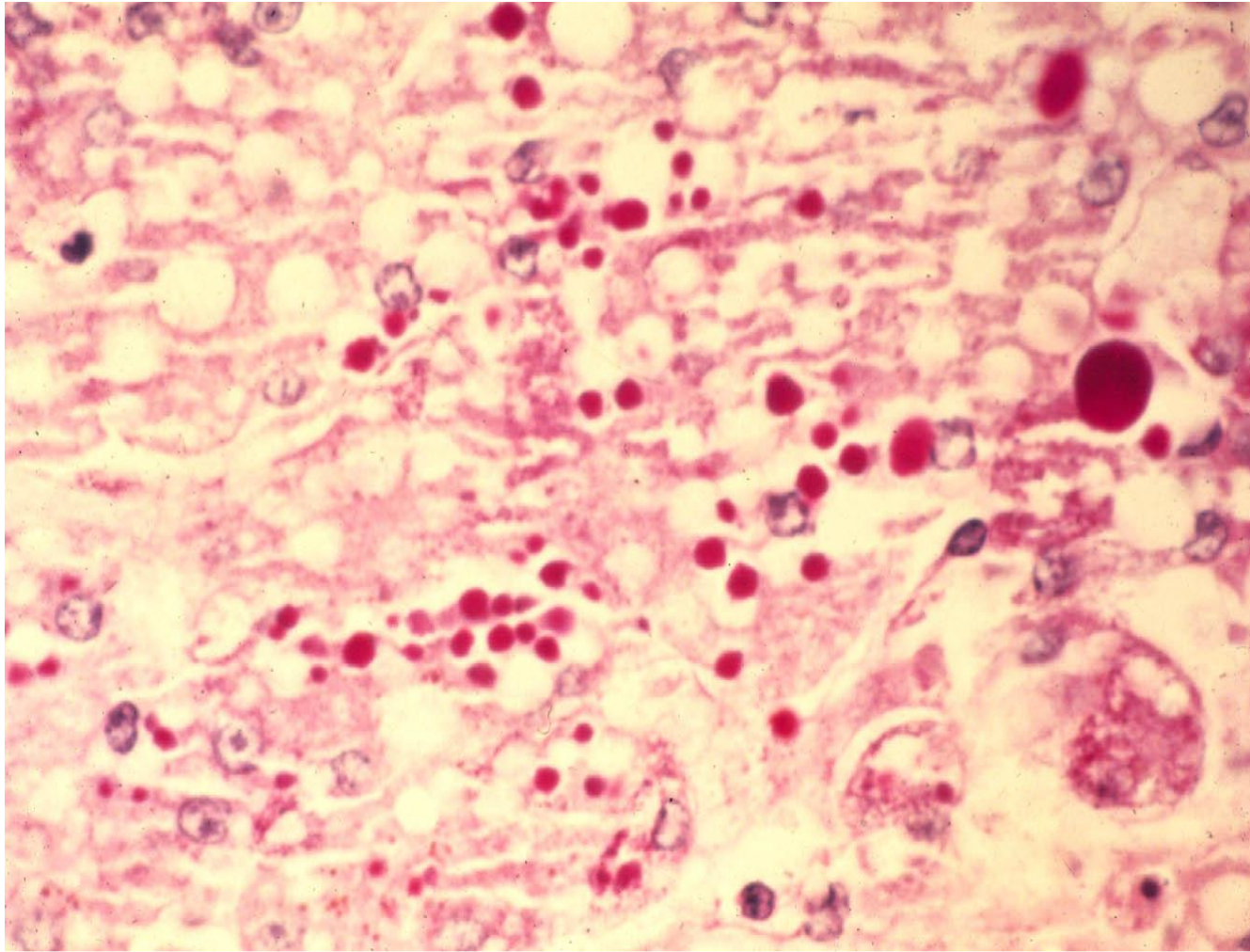
CT of thorax -Centrilobular emphysema

usually diagnosed radiographically or clinically



Panlobular emphysema (gross)

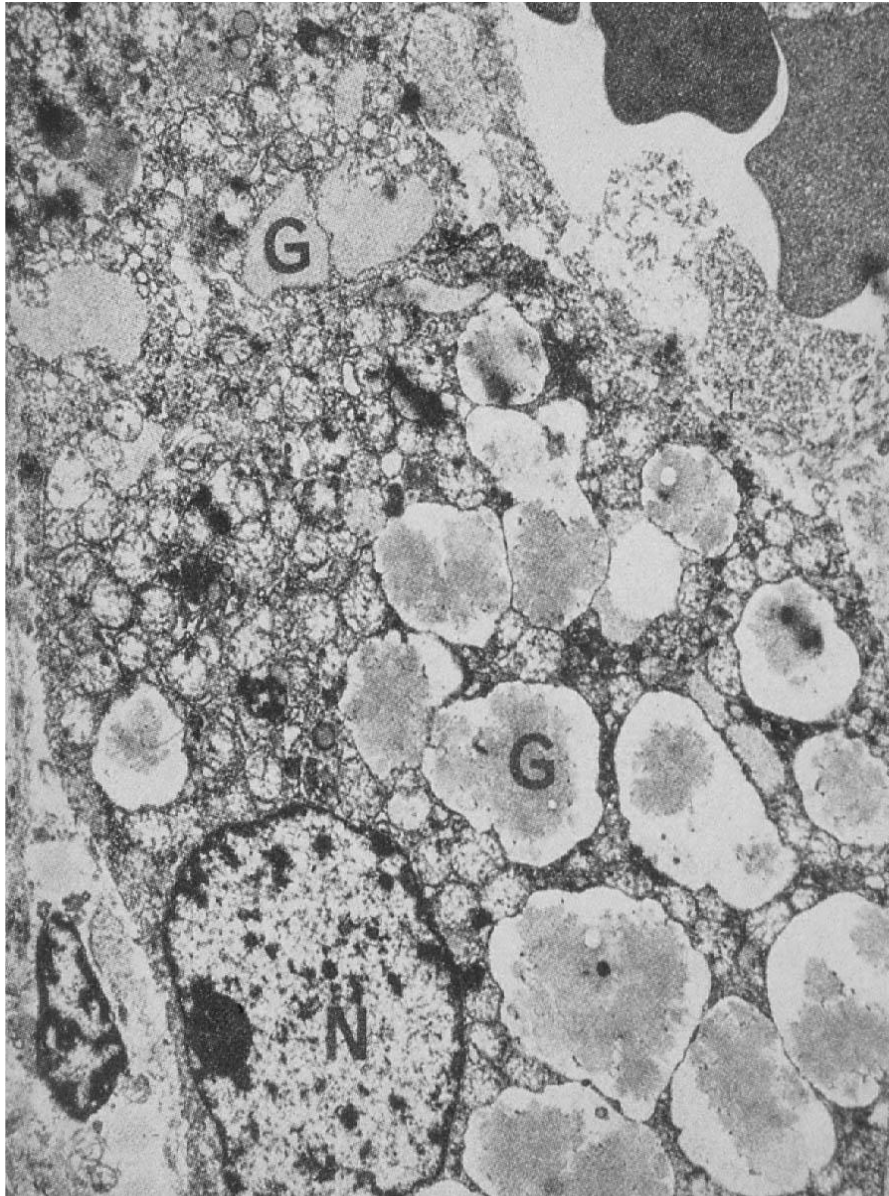
Whole lobule. Often worse in lower lobes (reason to come)



Liver with globules of alpha-1 antitrypsin

(PAS Stain)

Hepatocytes can't export alpha-1 antitrypsin because of the z mutation in alpha-1-antitrypsin that prevents attachment of carbohydrates important for intracellular trafficking through the ER

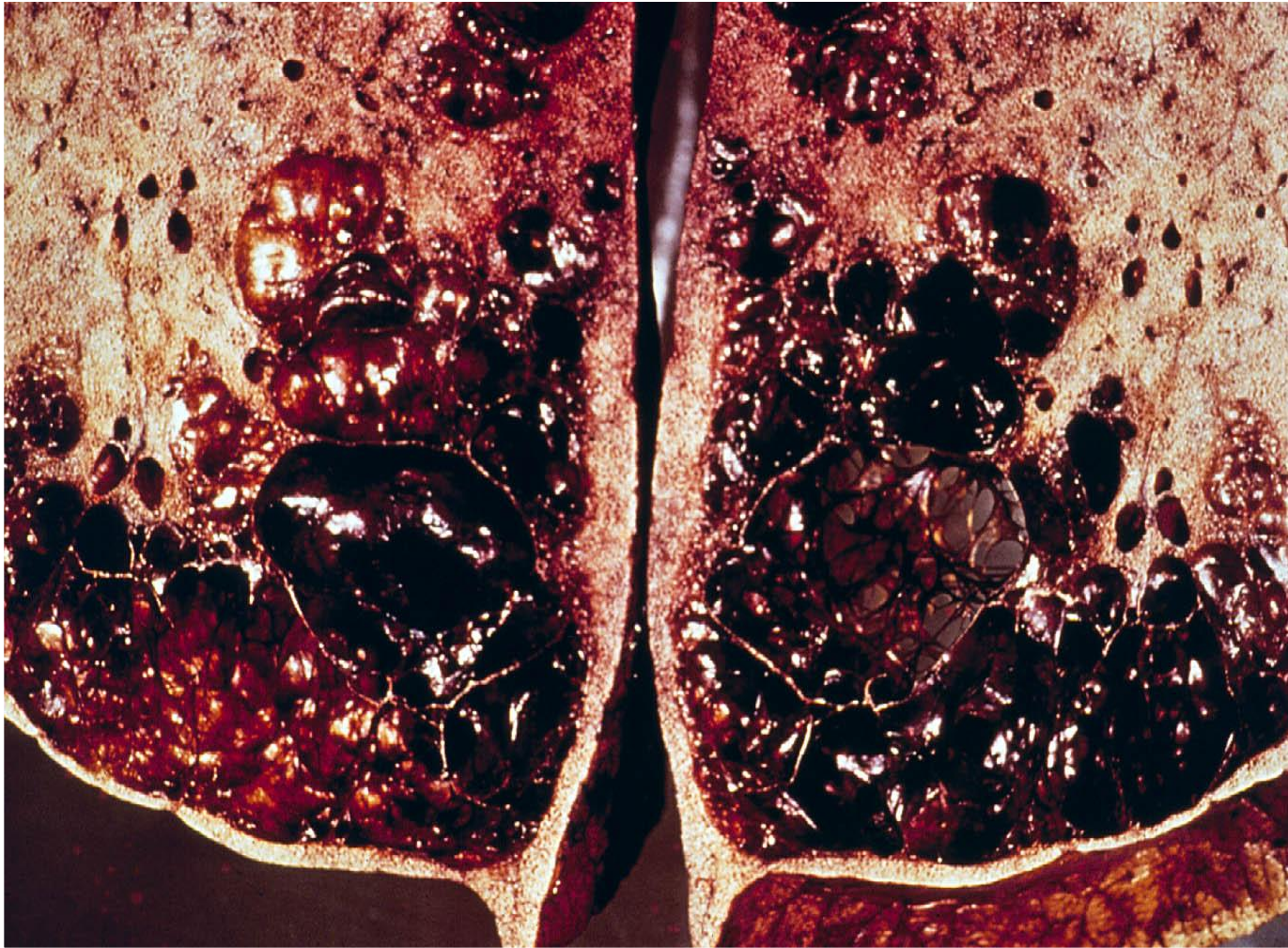


Ultrastructure of
liver in alpha-1
antitrypsin deficiency



Paracatricial "beside a scar"
emphysema,
tuberculosis

Tb scar that leads to
emphysematous
destruction around it



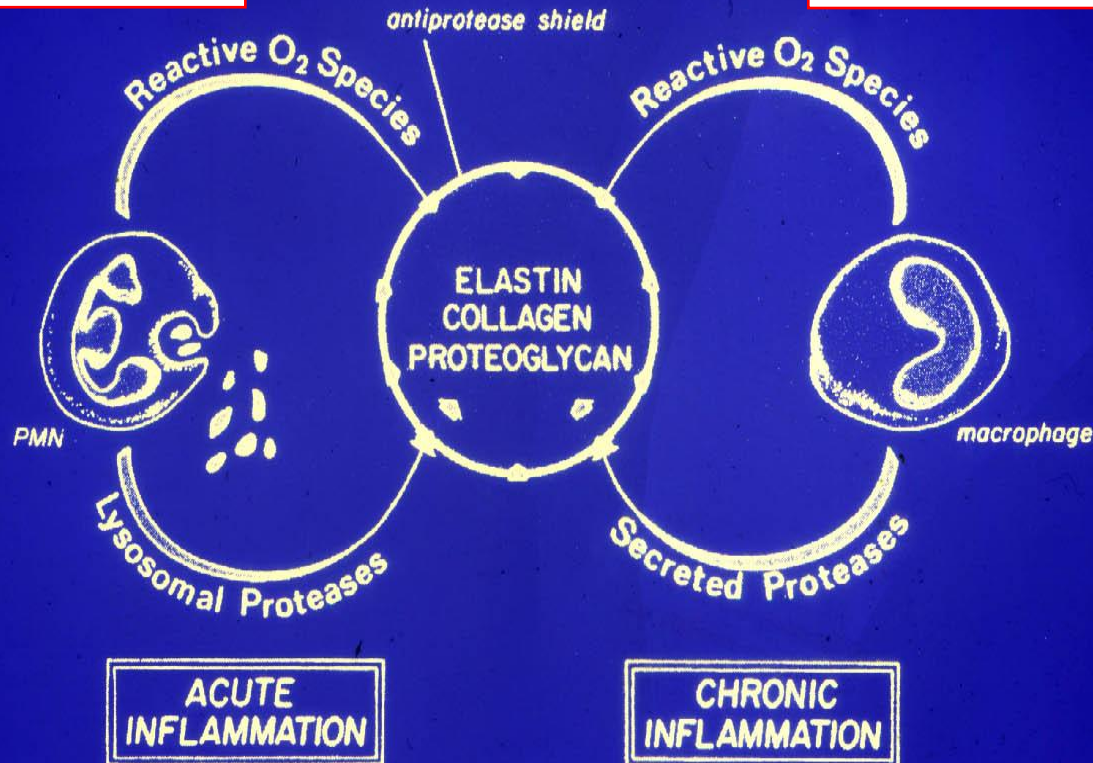
Localized emphysema (gross)

only in one area of the lung. Not know why (possibly due to bacteria like pseudomonas that produce elastases).
Quick question: who remembers from our single day of antibiotics how to treat pseudomonas? (answer on next slide)

PROPOSED PATHWAY OF TISSUE INJURY IN MICROENVIRONMENT OF INFLAMMATORY CELLS

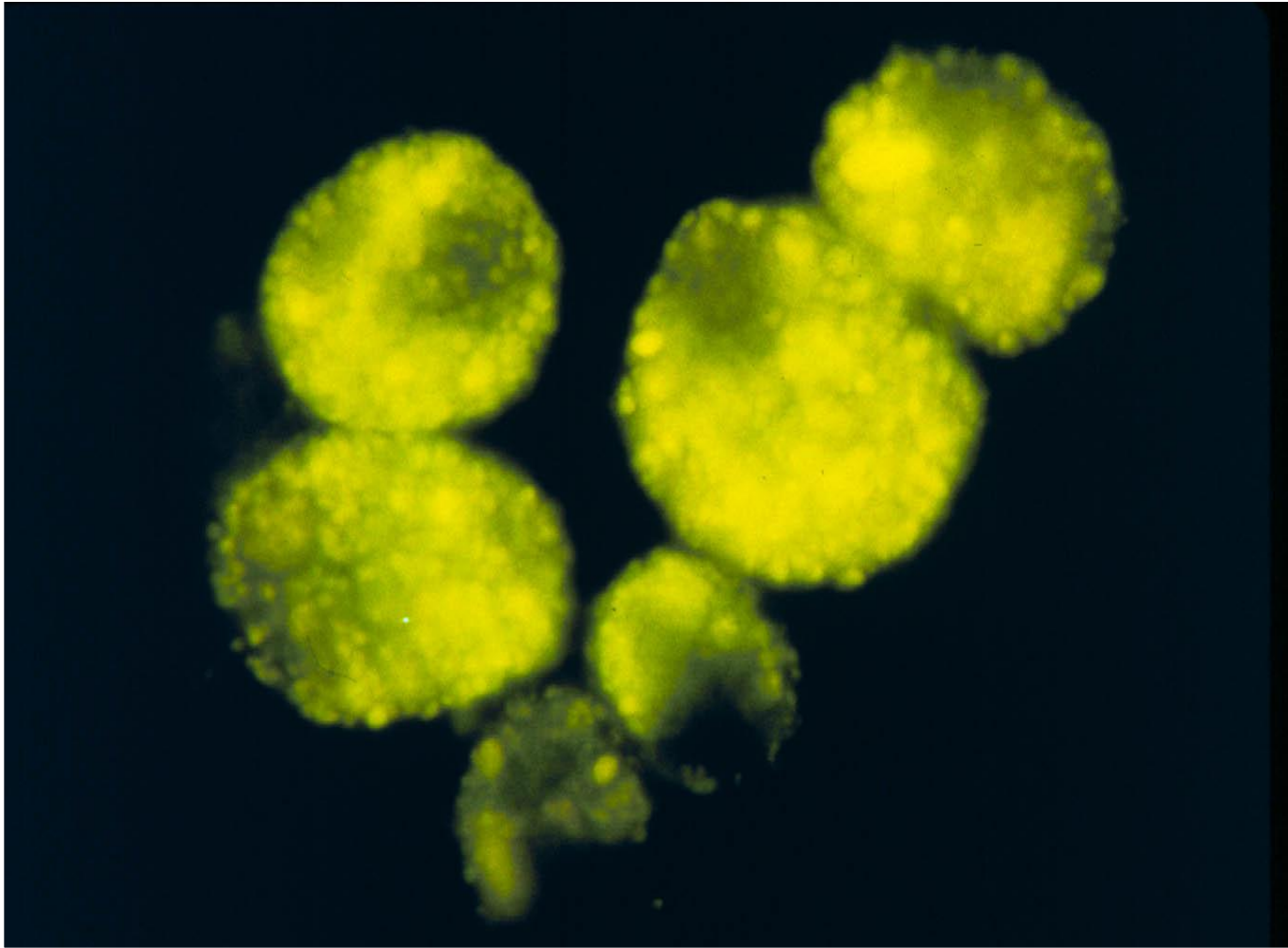
the lung is the graveyard of neutrophils--
antiproteases are crucial for balancing the
release of proteases from dying neutrophils

General mechanism of emphysema is an
imbalance of proteases and antiproteases.
Antiproteases from the blood stream.
Proteases released from inflammatory cells

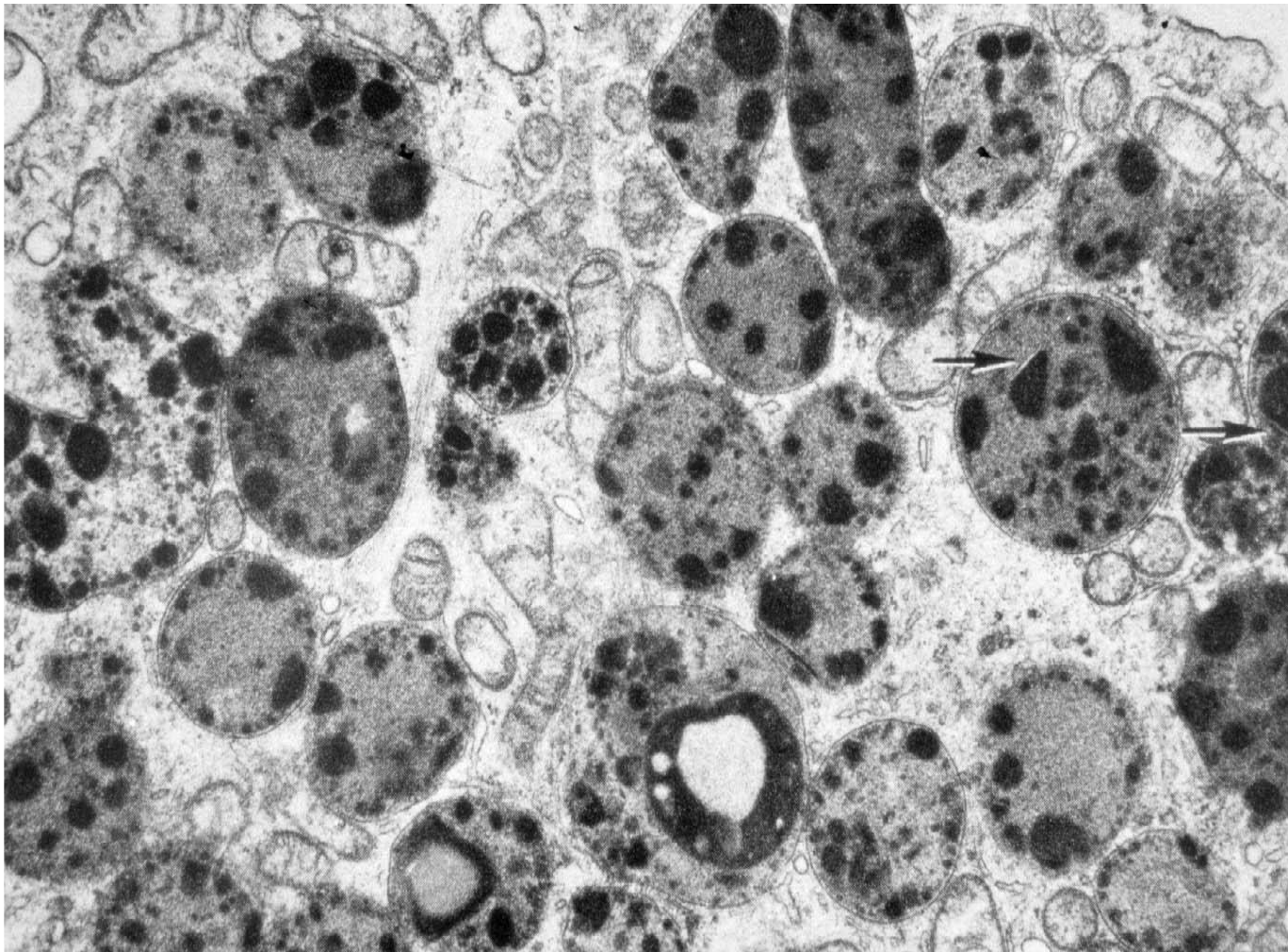


smoking also irreversibly blocks the active
site of alpha1-antitrypsin, increasing
imbalance of protease-antiprotease

A: Ceftazidime, cefepime, aztreonam, quinolones
(but there is rising resistance) aminoglycosides,
piperacillin, ticarcillin, carbapenems (but not
ertapenem), and probably some others. I think if
you remembered any of those you're in good shape



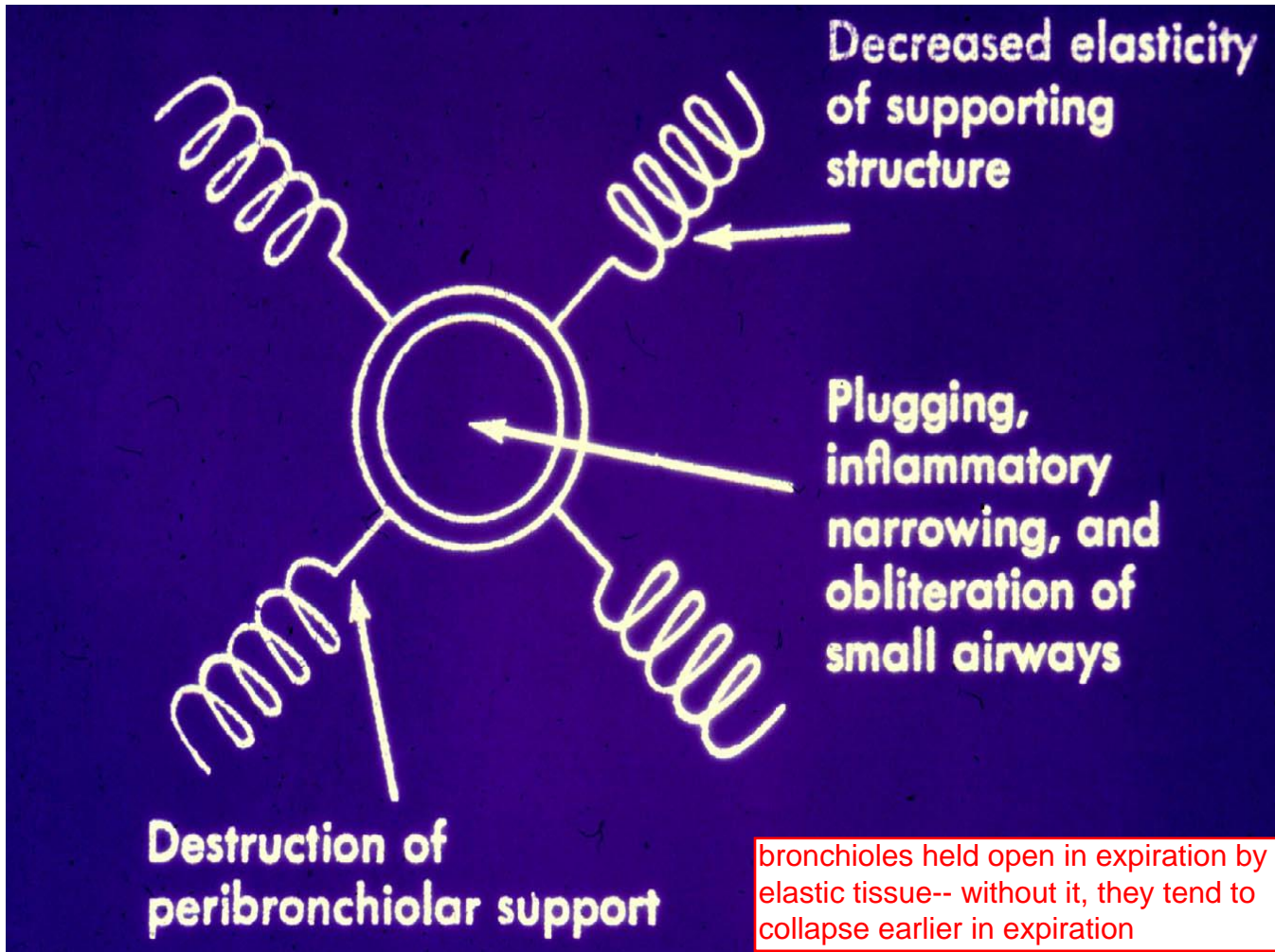
Autofluorescent smoker's macrophages

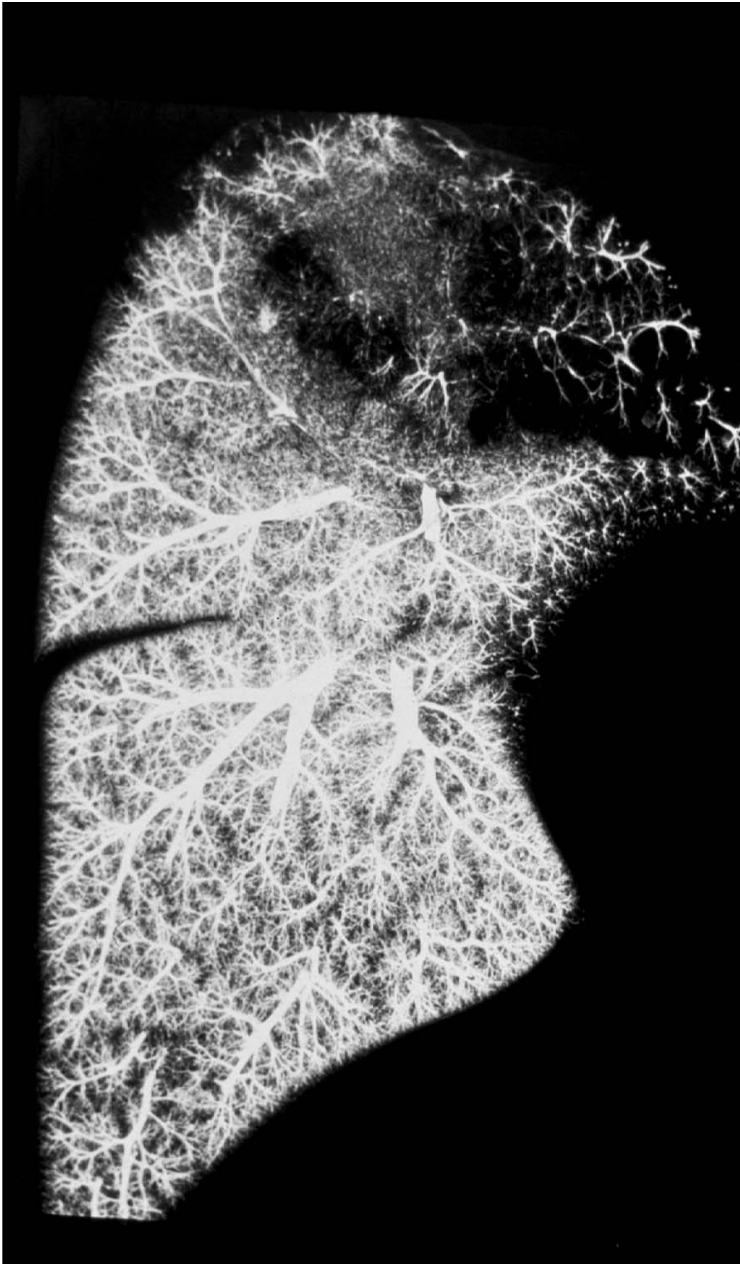


Ultrastructure of smoker's macrophages with numerous secondary lysosomes containing particulate material

CONSEQUENCES OF EMPHYSEMA

- Pulmonary obstruction (\uparrow TLC, \downarrow FEV₁)
- Diminished elastic recoil
- Diminished D_LCO





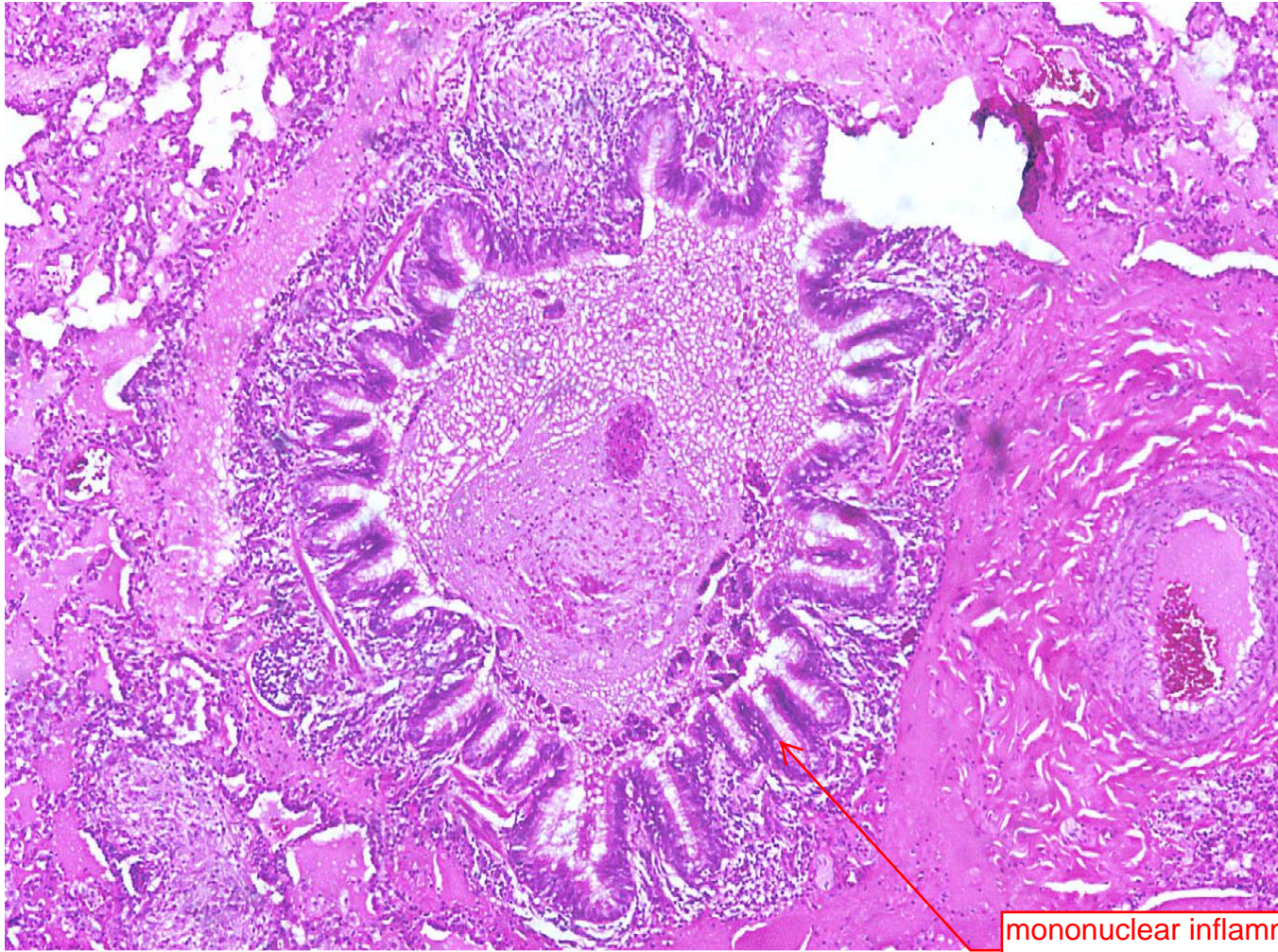
Centrilobular emphysema post-mortem pulmonary artery injection

diffusion capacity diminishes
with vascular destruction

larger vessels remain
intact, but capillaries and
small vessels are lost

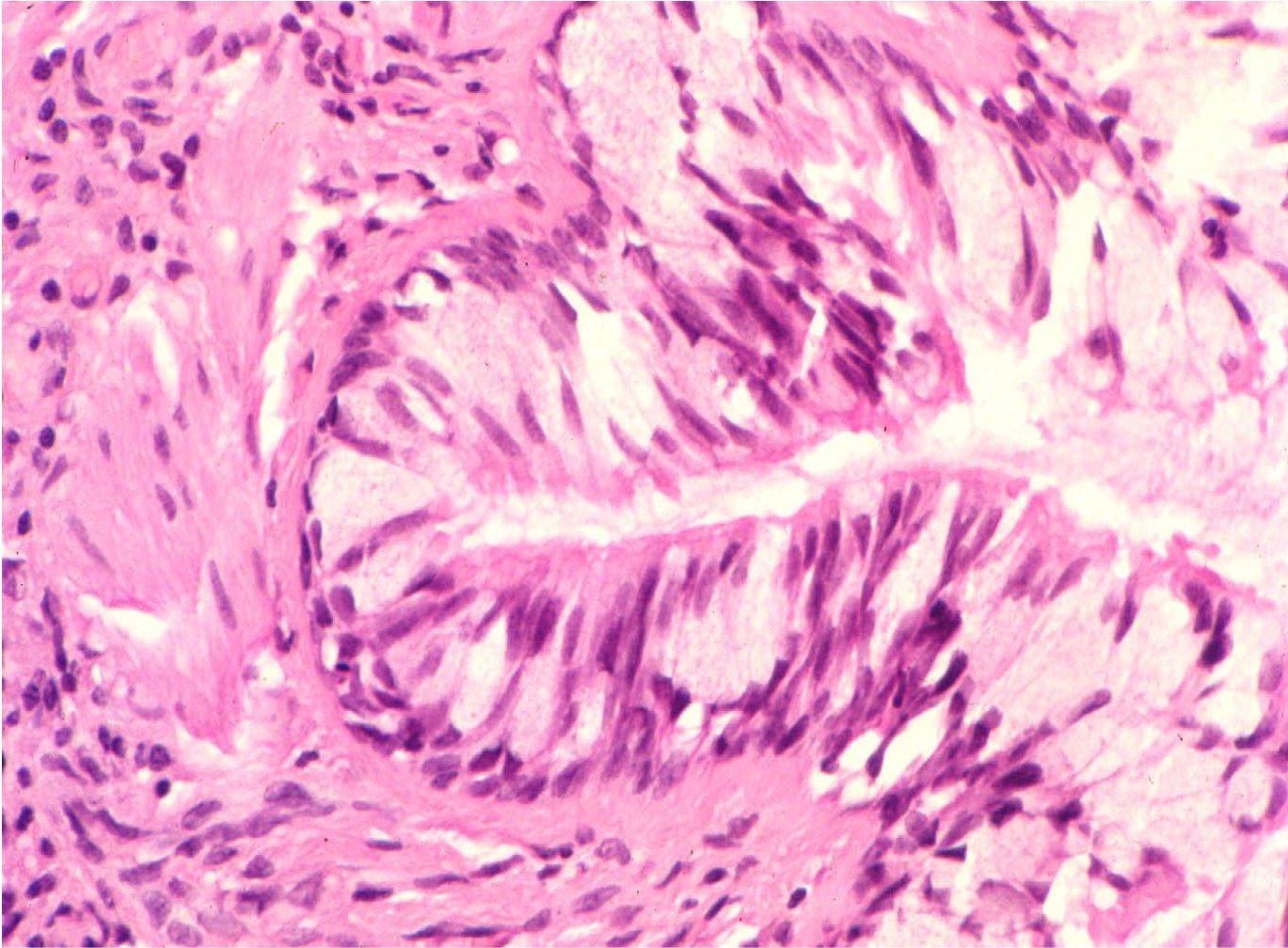
SMALL AIRWAYS DISEASE

- Mucous plugging
- Goblet cell metaplasia
- Chronic inflammation
- Peribronchiolar fibrosis



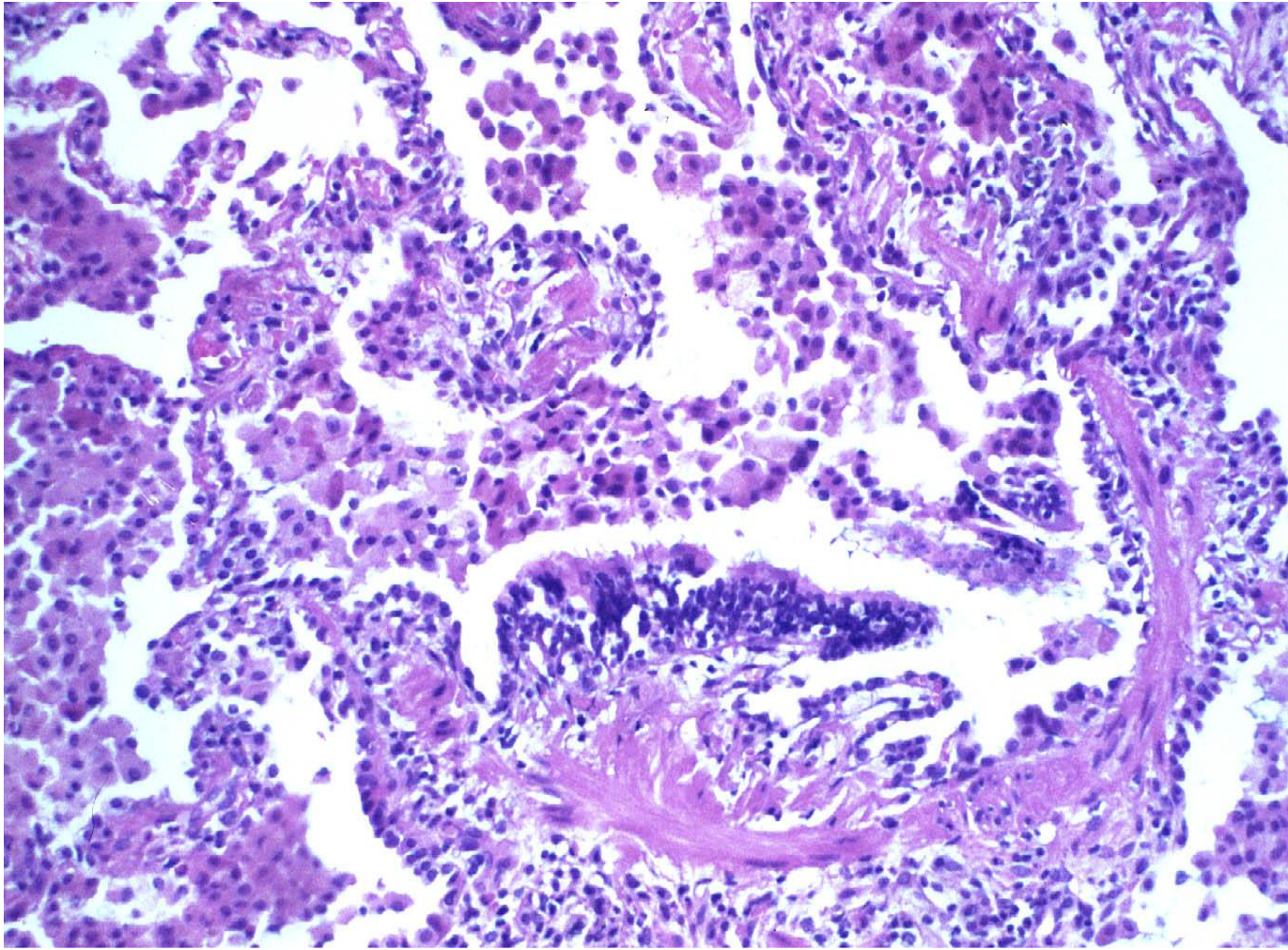
mononuclear inflammatory
infiltrate in the walls

Small airways disease with mucous plugging (PAS)

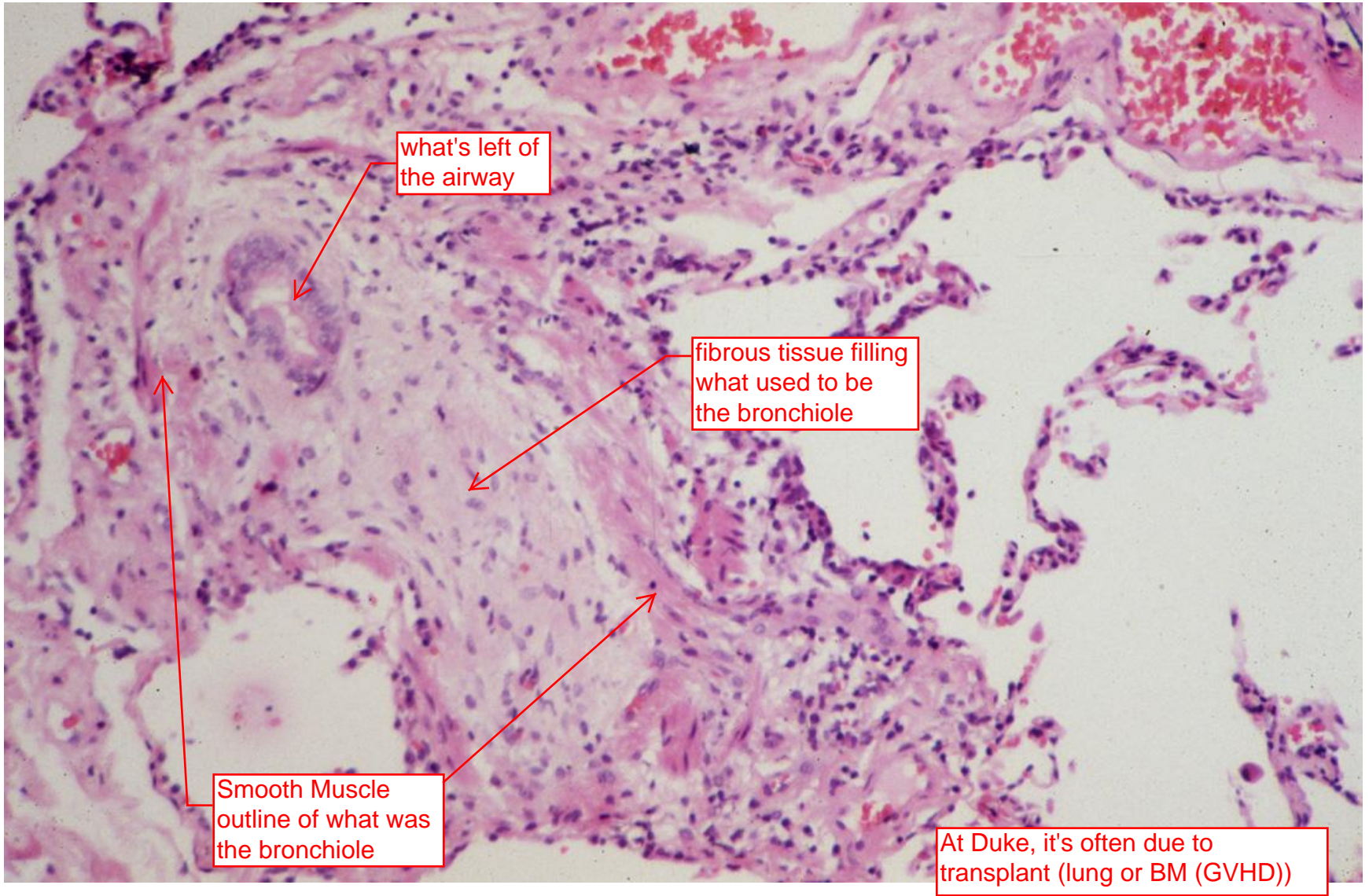


Small airways disease with goblet cell metaplasia

goblet cells in small airways
is a bad thing-- metaplasia

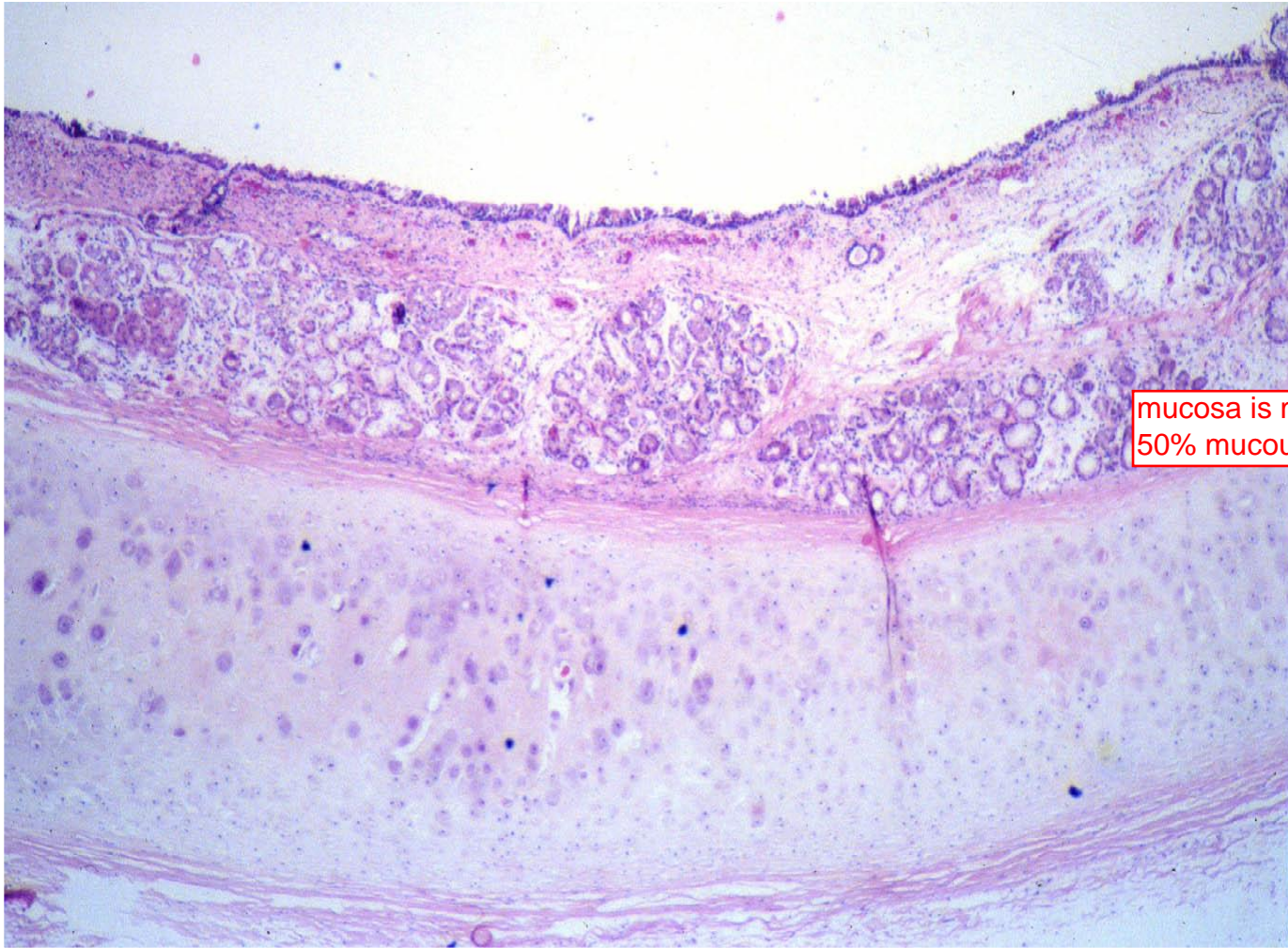


Respiratory bronchiolitis with numerous smokers macrophages



Bronchiolitis obliterans secondary to Adenovirus infection

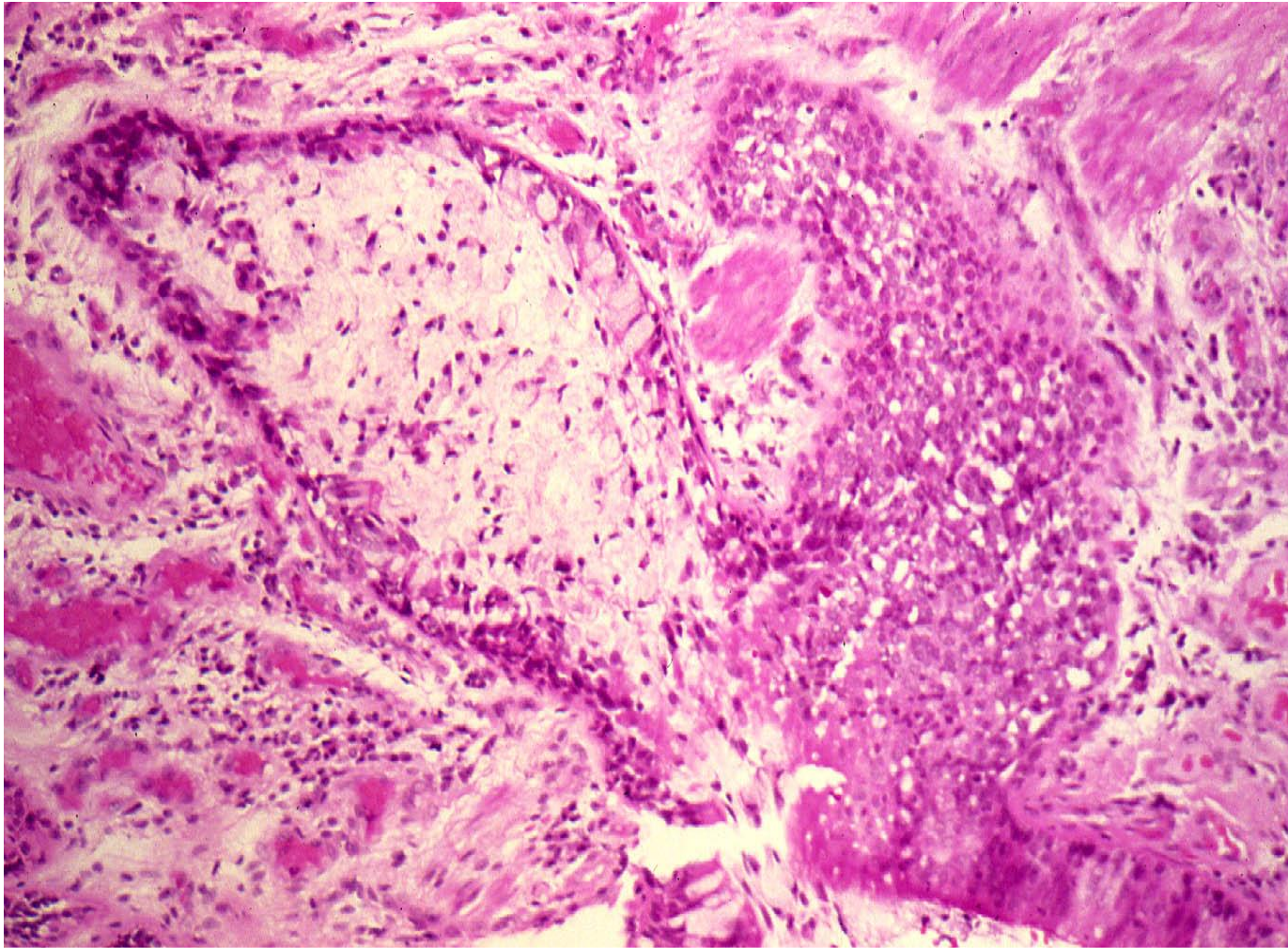
not really associated with cigarette smoking



mucosa is more than
50% mucous glands

Bronchial wall: mucous gland hyperplasia

chronic bronchitis-- productive cough that
occurs for at least 3 months per year for 2
years that doesn't have a better explanation



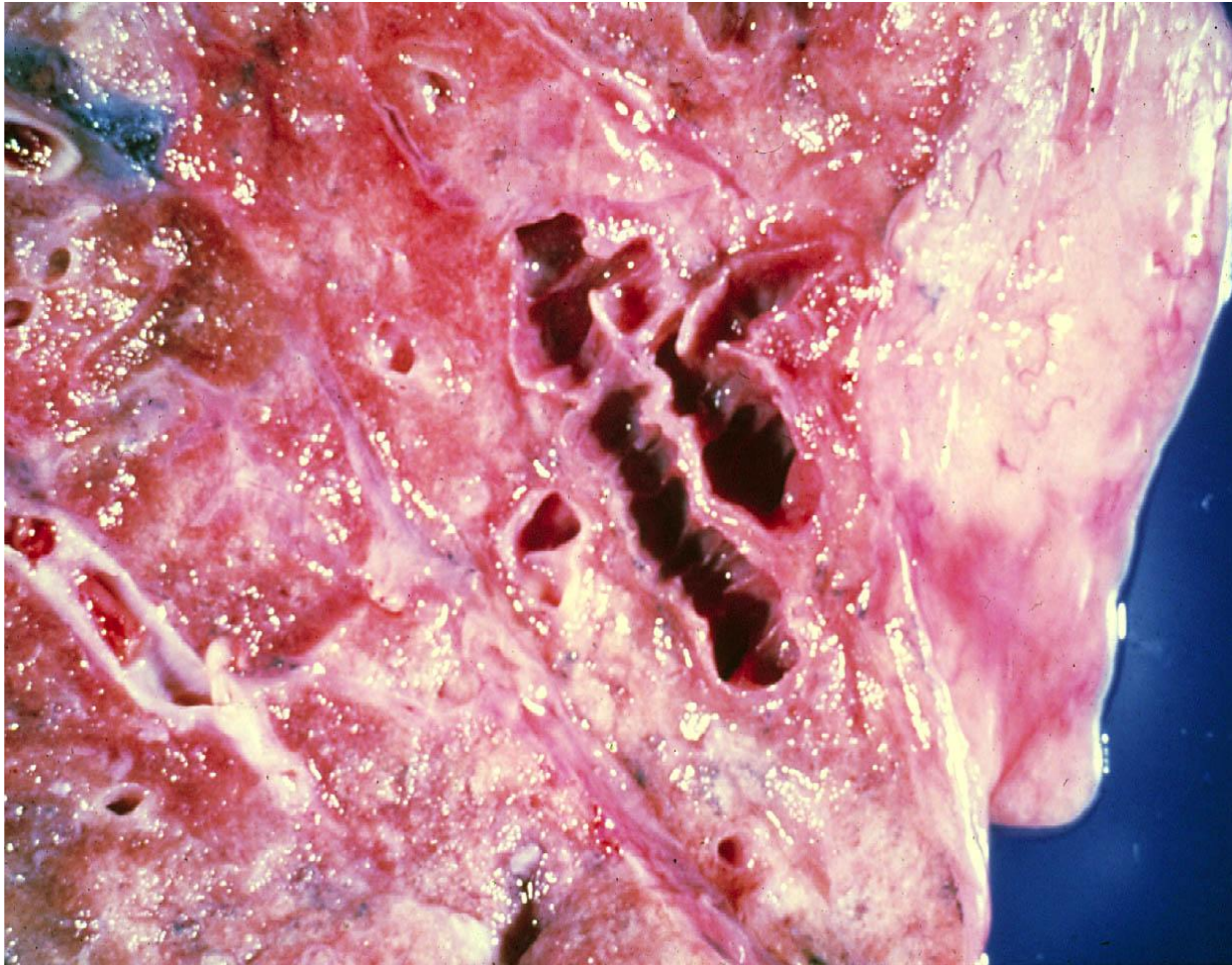
Chronic bronchitis with dilated mucous duct

BRONCHIECTASIS

bronchi become abnormally dilated and fail to taper as they go further into the lung

- Obstruction (foreign body)
- Genetic (CF, primary ciliary dyskinesia)
- Infection (children)
- Traction (sarcoidosis)

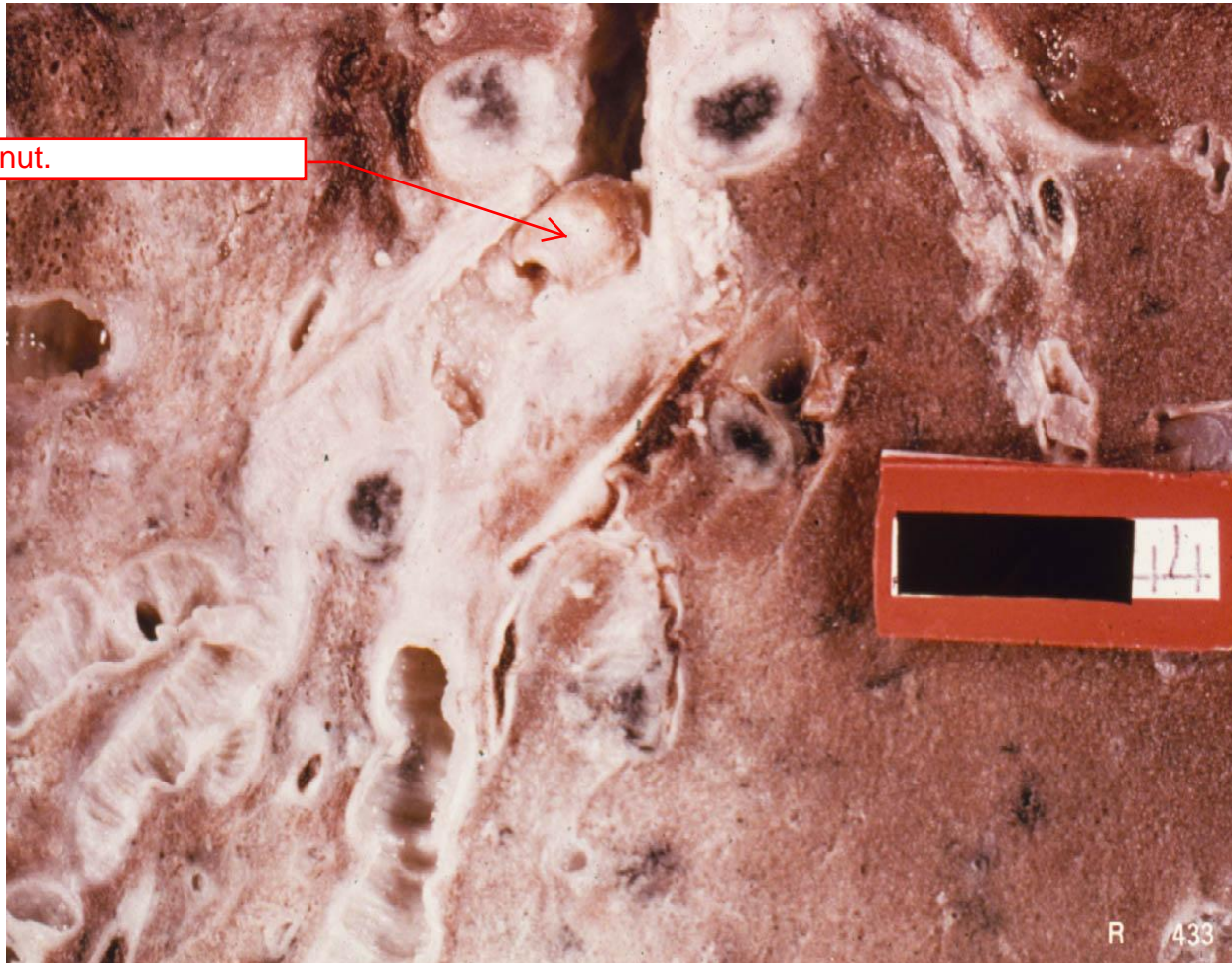
in fibrotic lung diseases, as fibrotic scars shrink, they pull open the bronchi



Bronchiectasis (gross)

transverse ribbing-- atrophy of longitudinal smooth muscle and hypertrophy of circular smooth muscle

note peanut.



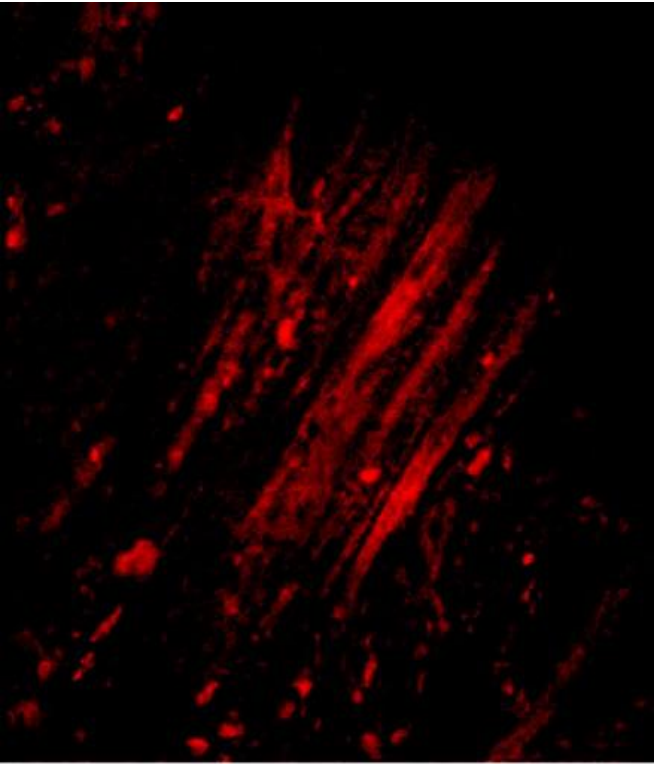
Bronchiectasis secondary to peanut aspiration (gross)



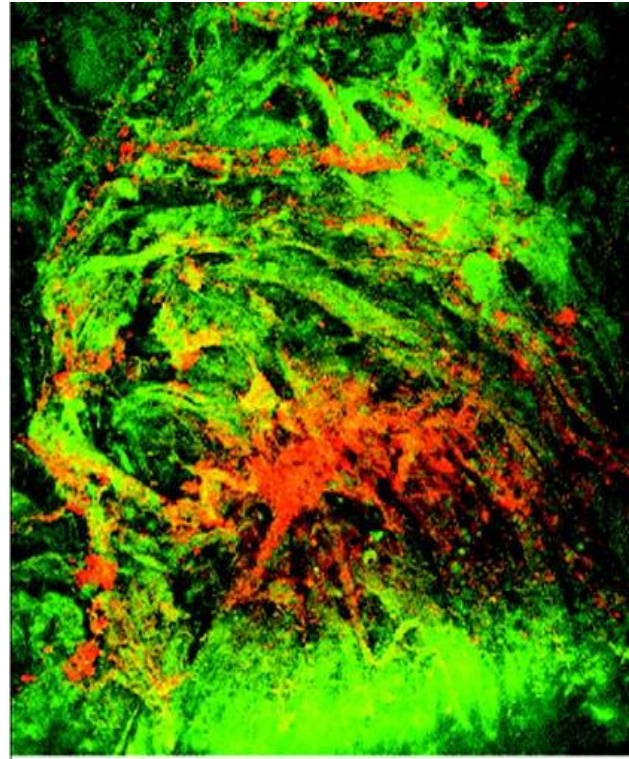
Saccular bronchiectasis cystic fibrosis

many bronchi occluded
by mucoid secretions

red is mucous
protein, green
is DNA

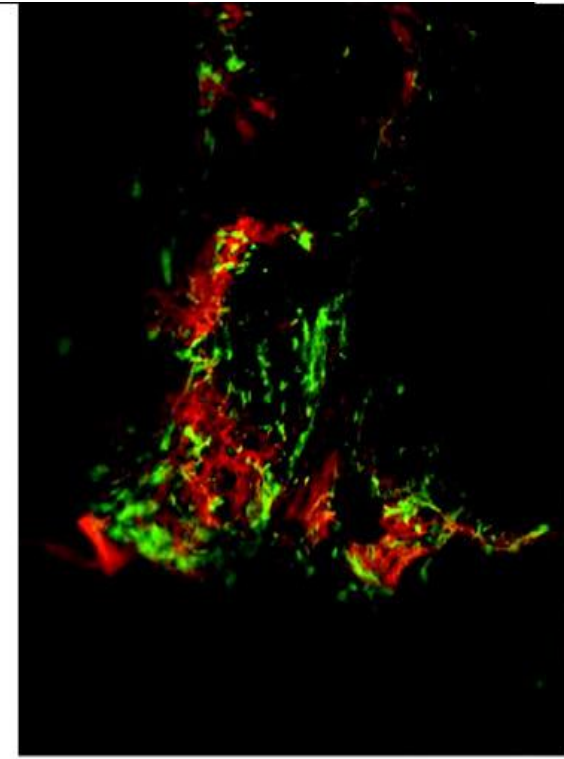


A Normal mucus

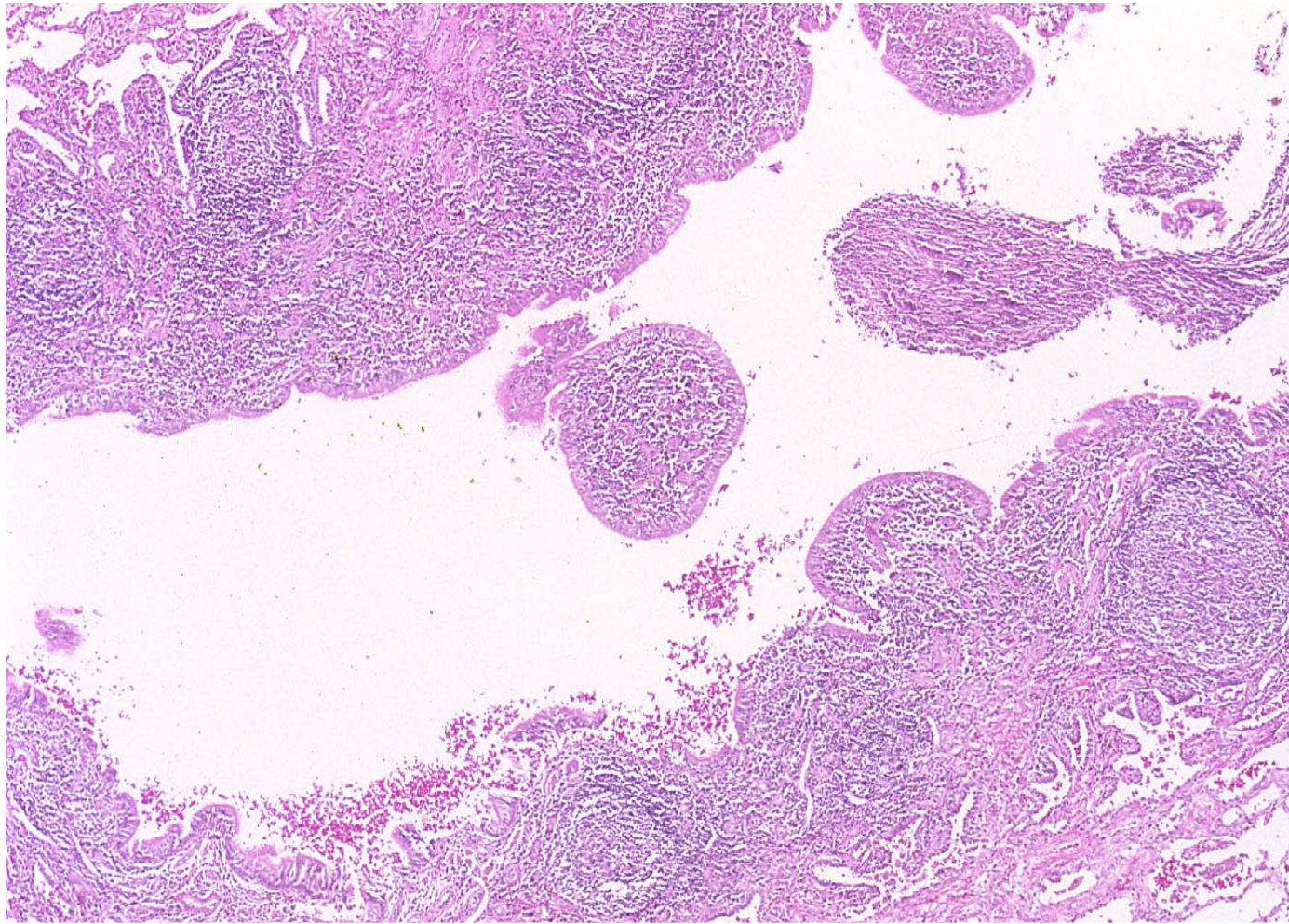


B CF sputum

DNA is mostly (80%) from
host neutrophils, but also
some (20%) from bacteria



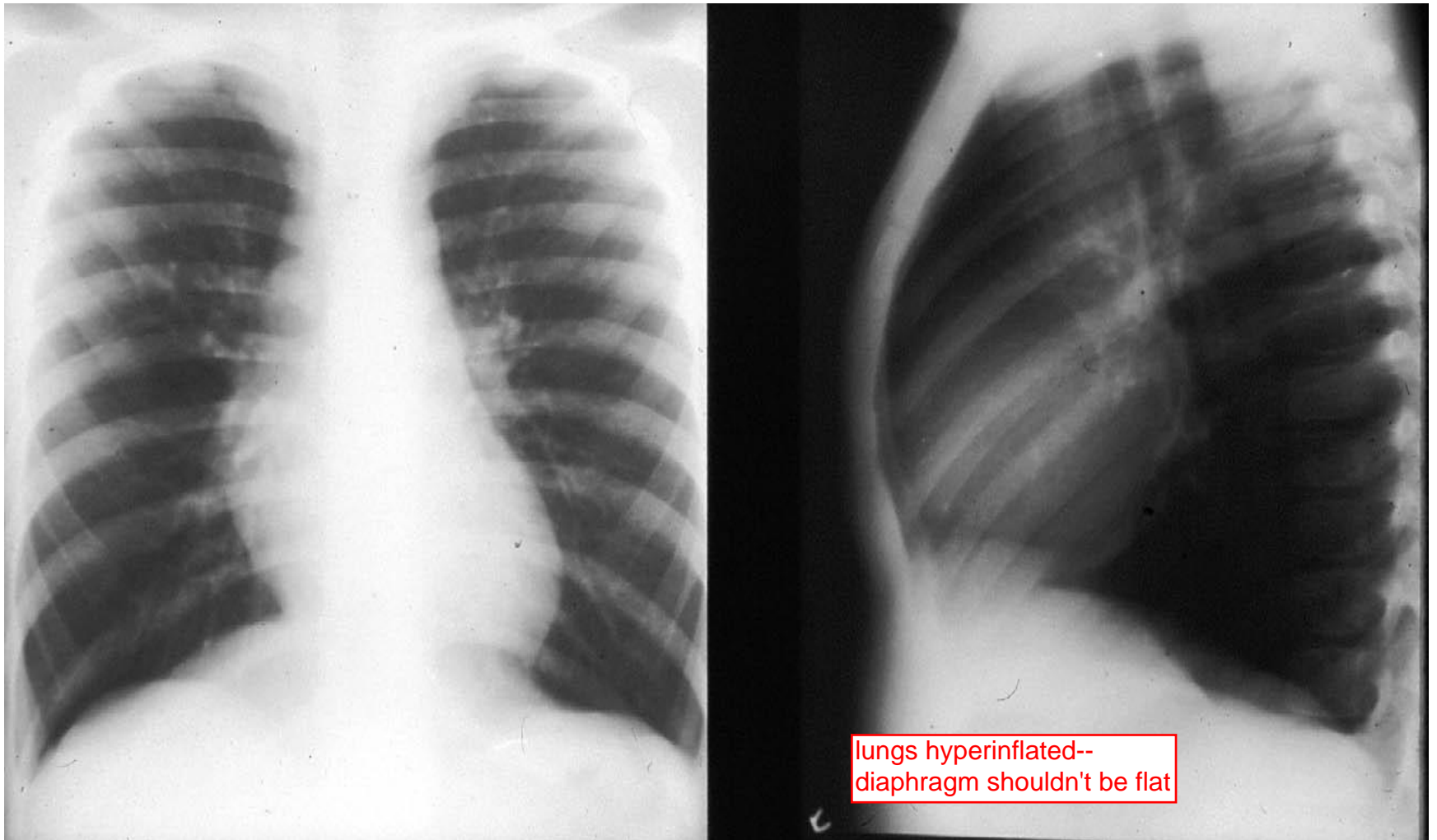
C Plastic bronchitis



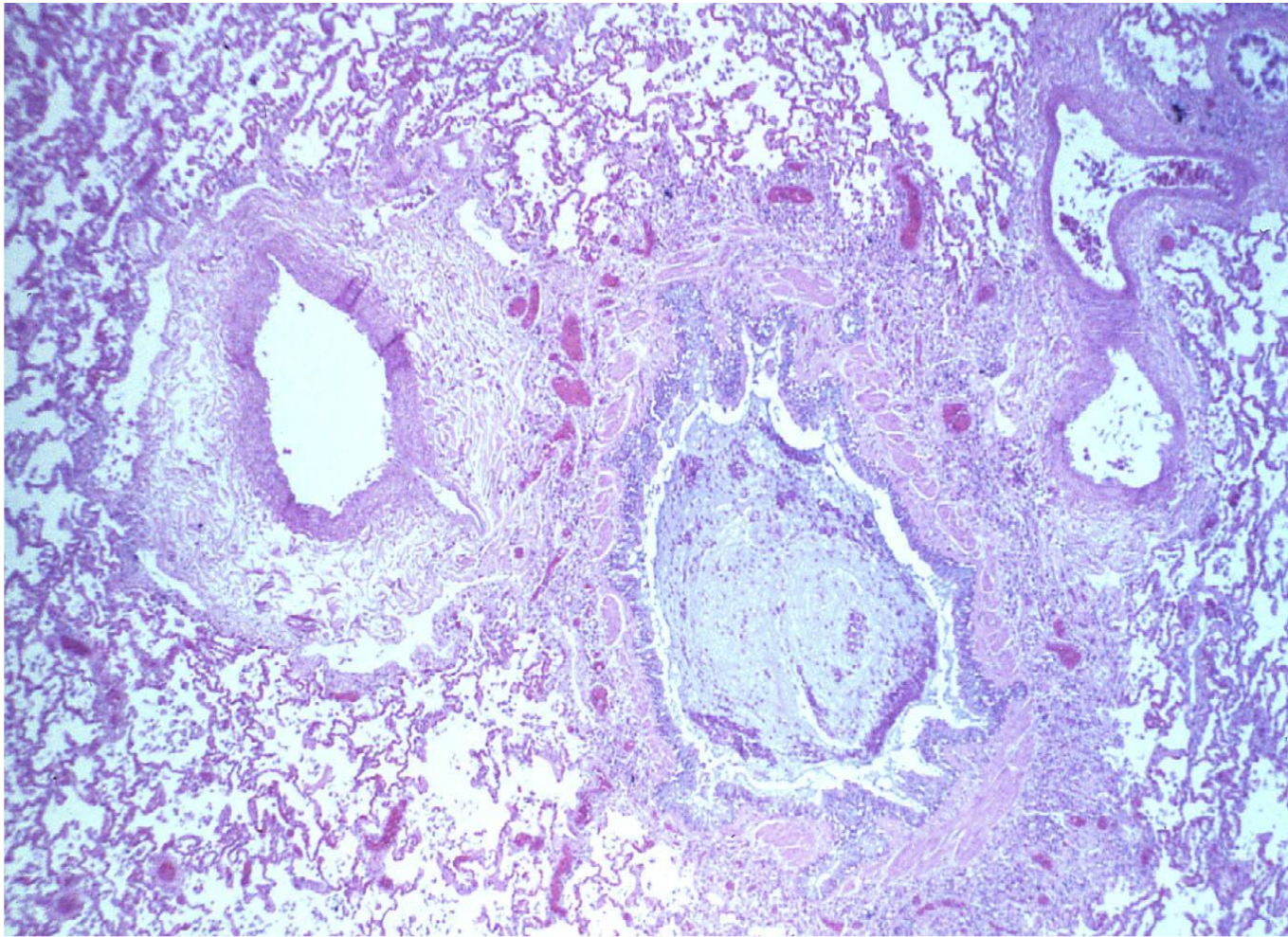
Bronchiectasis, (H&E)

ASTHMA

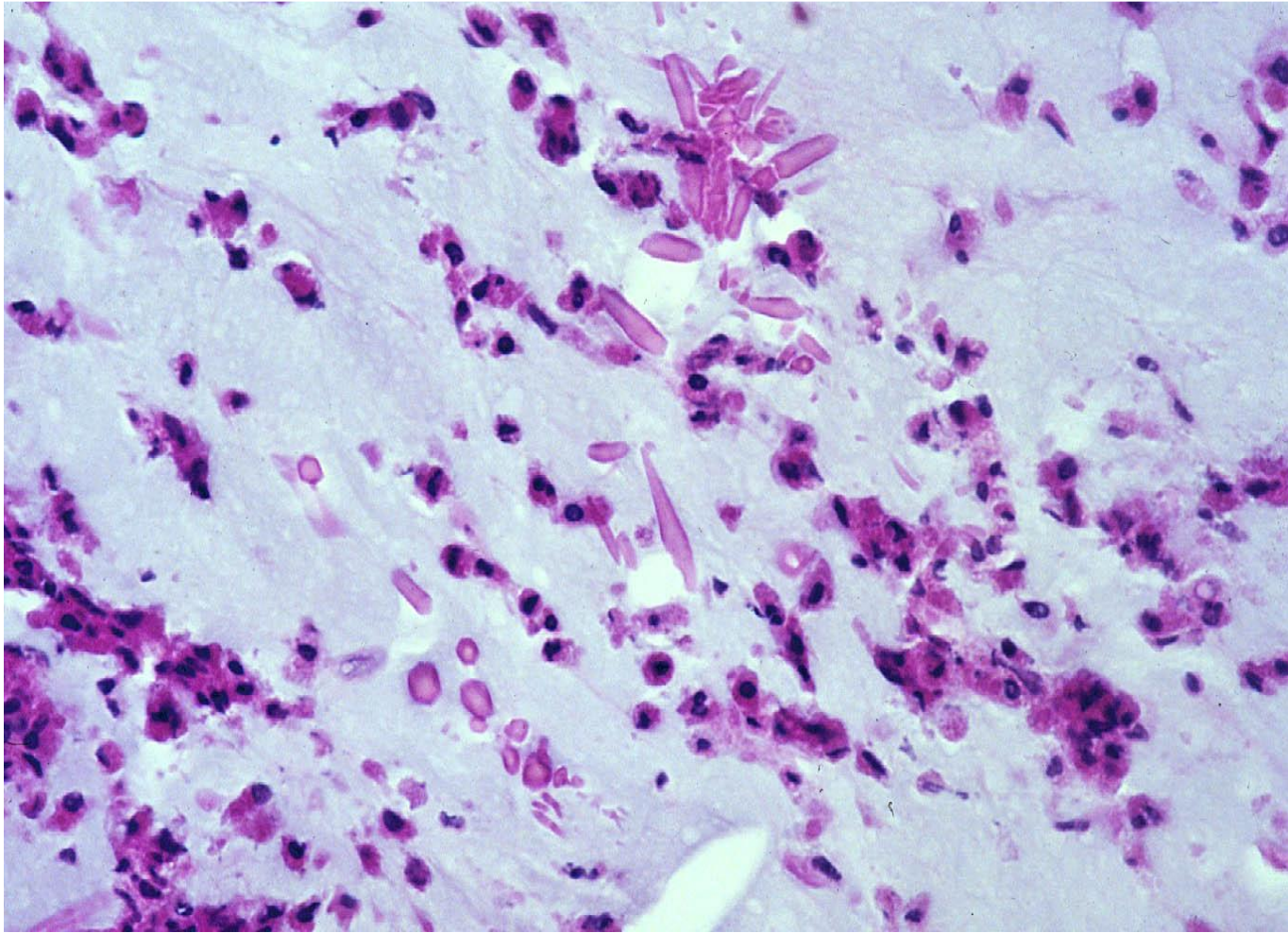
- Goblet cell metaplasia
- Mucous plugging
- Smooth muscle hyperplasia
- Thickened basement membrane
- \pm eosinophils



Chest x-ray in asthma (PA & Lateral)
with hyperinflation



Status asthmaticus with mucous plugging
(H&E)



Bronchial mucous plug (asthma) with

Charcot-Leyden crystals

made by eosinophils,
indicative of an allergic rxn



Wasting away in Margaritaville