Pathology
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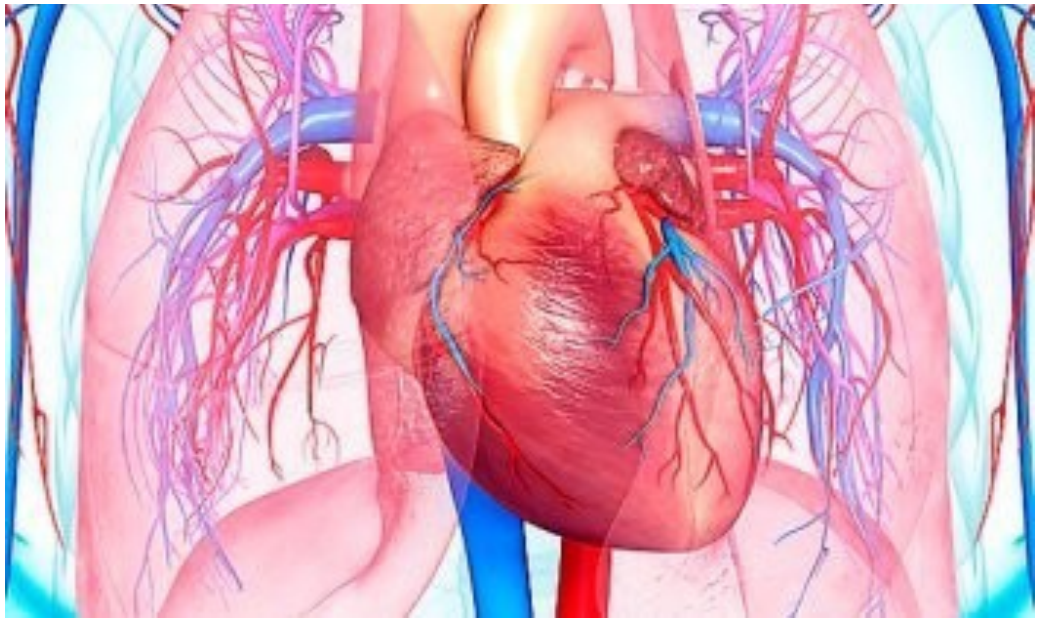
PULMONARY DISEASES OF VASCULAR ORIGIN



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https://www.europeanlung.org/en/lung-disease-and-information/lung-diseases/pulmonary-vascular-disease

PULMONARY DISEASES OF VASCULAR ORIGIN

- Pulmonary Embolism, Hemorrhage, and Infarction
- Pulmonary Hypertension
- Diffuse Alveolar Hemorrhage Syndromes

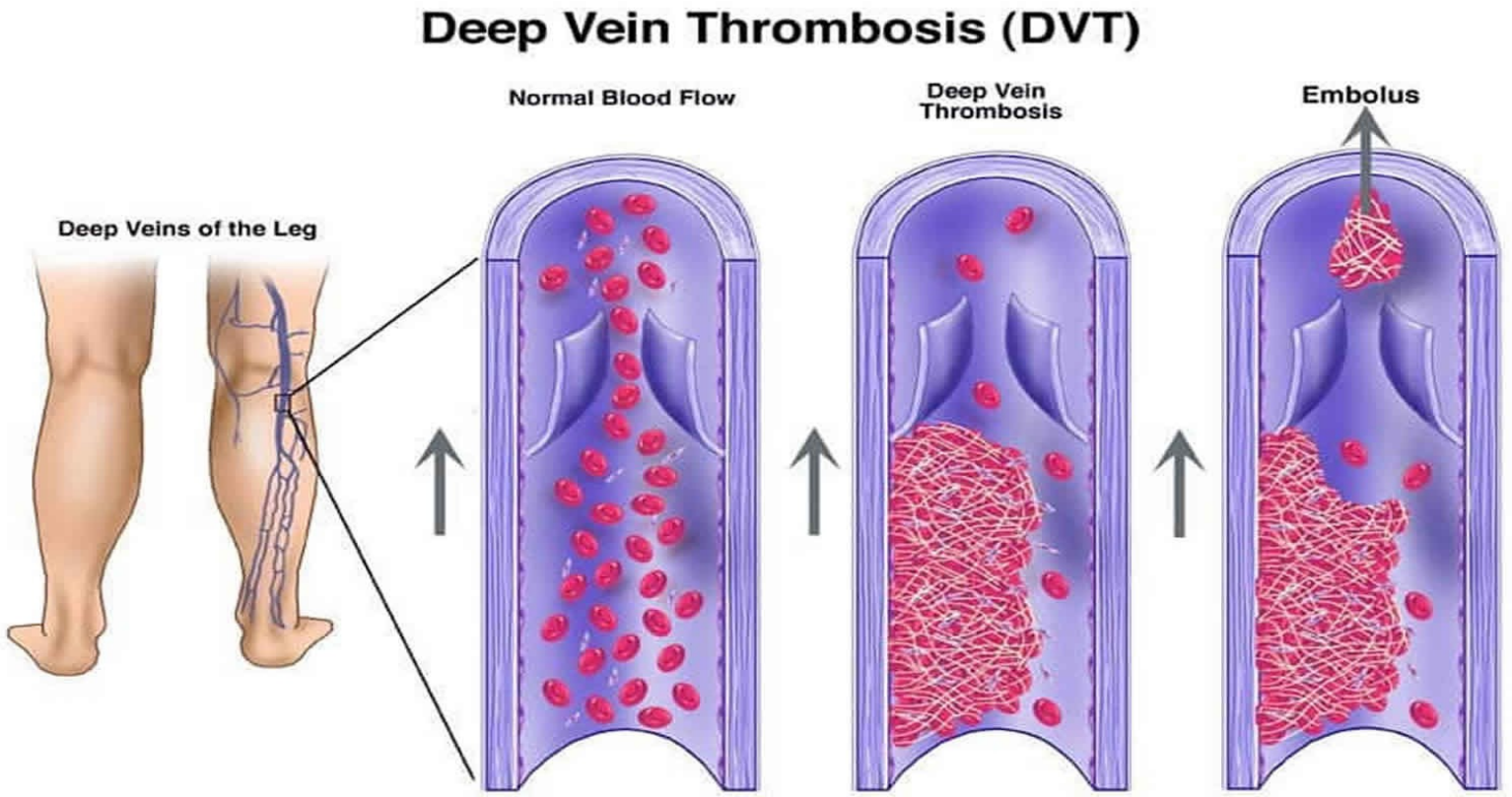
PULMONARY EMBOLISM:

- Thromboembolism
- Nonthrombotic pulmonary emboli

THROMBOEMBOLISM

- Almost all large pulmonary artery thrombi are embolic in Origin.

- >95% of PE (pulmonary emboli) arise from thrombi within the large deep veins of the legs, most often popliteal vein and larger veins above it.



RISK FACTORS FOR VENOUS THROMBOSIS:

1. prolonged bed rest (immobilization of the legs)
2. Surgery (orthopedic surgery on the knee or hip)
3. severe trauma (burns or multiple fractures)
4. congestive heart failure
5. in women, the period around parturition or the use of OCPs (combined oral contraceptive)(high estrogen content)
6. disseminated cancer
7. primary disorders of hypercoagulability (factor V Leiden)

CONSEQUENCES
(of pulmonary arterial occlusion)

1. **Increase in pulmonary artery pressure and vasospasm**

High pulmonary pressure due to blockage of flow, while vasospasm is caused due to release of mediators, e.g. TXA2 and serotonin.
In case of major vessel occlusion, an abrupt increase in the pulmonary artery pressure will follow and the heart will be pumping against higher resistance (pulmonary), which causes decreased CO and right-sided heart failure (acute cor pulmonale). In some cases this can result in sudden death. Meanwhile if it happened in smaller vessels there are no symptoms (clinically silent).

2. **Ischemia of the downstream pulmonary parenchyma.**

The lungs are not only oxygenated by the pulmonary arteries but also the bronchial arteries and directly from the air in the alveoli, so necrosis is uncommon affecting as few as 10% of patients

Pathophysiological CONSEQUENCES:

- **depend mainly on:**

1 size of the embolus

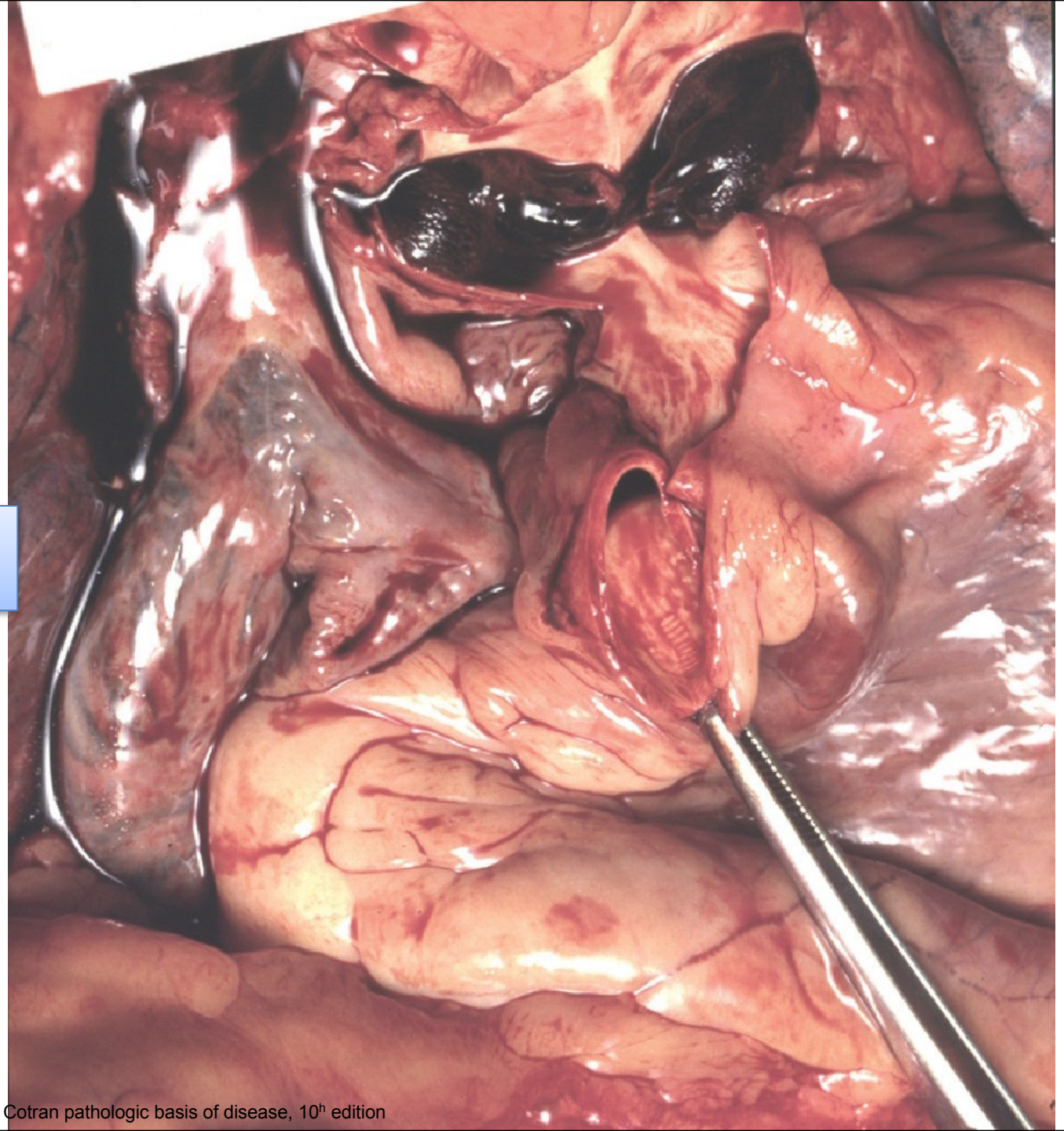
This factor determines the size of the occluded pulmonary artery

- large embolus may embed in the main pulmonary artery or its major branches or lodge at the bifurcation as a saddle embolus
- Smaller emboli become impacted in medium-sized and small-sized pulmonary arteries.

2 the cardiopulmonary status of the patie

The general state of the circulation

Large saddle embolus from the femoral vein.



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MORPHOLOGY:

The morphologic changes of the embolus also depends on the size and the general circulatory status

- **No morphologic alternations**: large emboli

This is because they cause sudden death

- **alveolar hemorrhage**: Smaller emboli

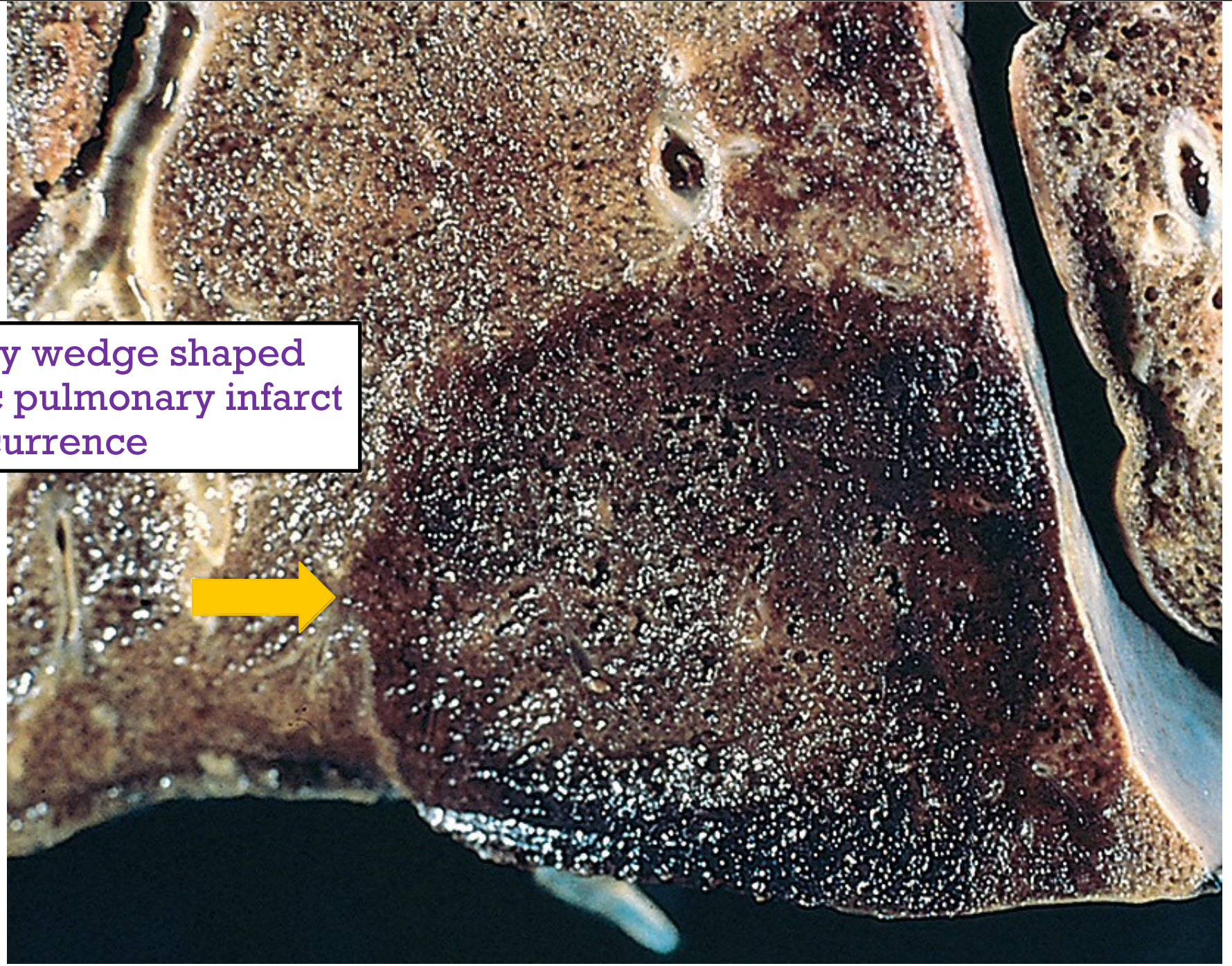
Due to ischemic damage to endothelial cells

- **infarction :**
  - compromised cardiovascular status (congestive heart failure)
  - The more peripheral the embolic occlusion, the higher the risk for infarction.
    - ¾ lower lobes & >50% multiple.
  - **wedge-shaped**, with their base at the pleural surface and the apex pointing toward the hilus of the lung.

PULMONARY INFARCTS

- Typically, hemorrhagic with red-blue areas of coagulative necrosis in the early stages
- The adjacent pleura surface is covered by fibrinous exudate
- The occluded vessel is located near the apex of the infarcted area.
- The red cells begin to lyse within 48 hrs➔ red-brown as hemosiderin is produced ➔ fibrous replacement begins at the margins as a gray-white peripheral zone ➔scar.

Small roughly wedge shaped hemorrhagic pulmonary infarct of recent occurrence



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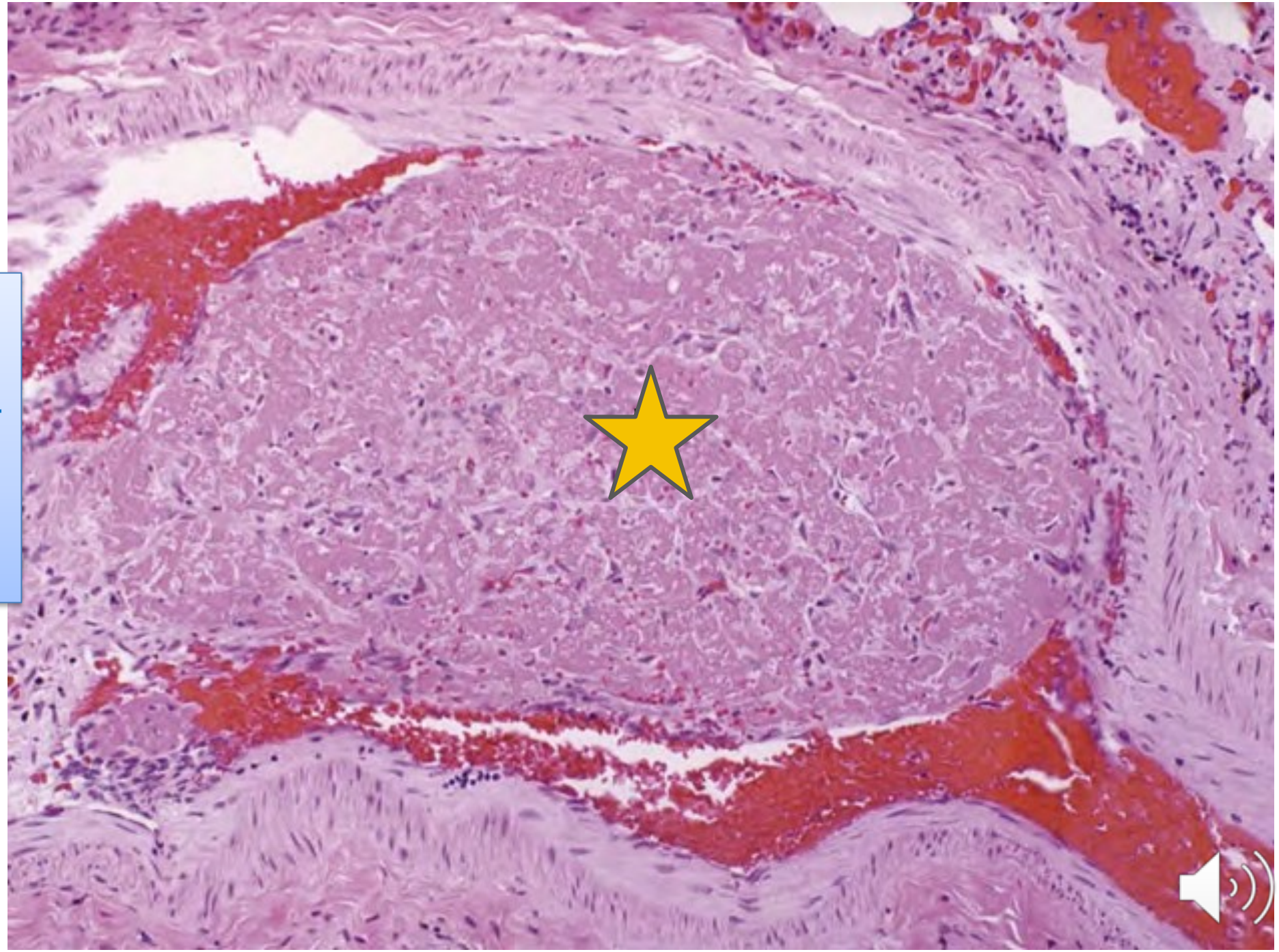
Thromboembolus in the peripheral pulmonary arterial branch.
An increase in its number will cause the vascular bed to diminish, and causes pulmonary hypertension



CLINICAL FEATURES

- 60% - 80% ➔clinically silent
- Small emboli (the bronchial circulation sustains the viability of the effected lung parenchyma)
- embolic mass is rapidly removed by fibrinolytic activity.

•5%➔ death, acute right-sided heart failure, or cardiovascular collapse.

- As in Massive pulmonary embolism: >60% of the total pulmonary vasculature is obstructed by a large embolus or multiple small emboli.

CLINICAL FEATURES

- **10-15%➔ dyspnea**
- Obstruction of small to medium pulmonary branches➔ pulmonary infarction

- **<3% ➔progressively worsening dyspnea**
  - recurrent showers of emboli leading to pulmonary hypertension, chronic right-sided heart failure, and pulmonary vascular sclerosis.

MANAGEMENT:

- Prophylactic therapy: anticoagulation, early ambulation (post op.), elasticstockings, intermittent pneumatic calf compression, and isometric leg exercises for bedridden patients.

- anti-coagulation therapy for patients who develop pulmonary embolism

- thrombolytic therapy for hemodynamically unstable pts with massive pulmonary embolism(shock patients)

NONTHROMBOTIC PULMONARY EMBOLI:

- uncommon but potentially lethal
- such as:
  - air, fat, amniotic fluid embolism,
  - foreign body embolism in intravenous drug abusers
  - Bone marrow embolism:
    - the presence of hematopoietic and fat elements within a pulmonary artery
    - after massive trauma and in patients with bone infarction secondary to sickle cell anemia

PULMONARY HYPERTENSION

The pulmonary circulation is of low resistance, and the pressure is about 1/8 of the systemic pressure

- defined as pressures of **25 mm Hg or more at rest**

- may be caused by a **decrease** in the cross-sectional area of the pulmonary vascular bed or by **increased** pulmonary vascular blood flow.

CLASSIFIED AS FOLLOWING:

- **Pulmonary arterial hypertension:**
  - heritable forms of pulmonary hypertension
  - affects small pulmonary muscular arterioles
    - Examples: connective tissue diseases, human immunodeficiency virus, and congenital heart disease with left to right shunts

- **Pulmonary hypertension due to left-sided heart disease:**
  - including systolic and diastolic dysfunction and valvular disease

- **Pulmonary hypertension due to lung diseases and/or hypoxia**:
    - including COPD and interstitial lung disease
- **Chronic thromboembolic pulmonary hypertension**
- **Pulmonary hypertension with unclear or multifactorial mechanisms**

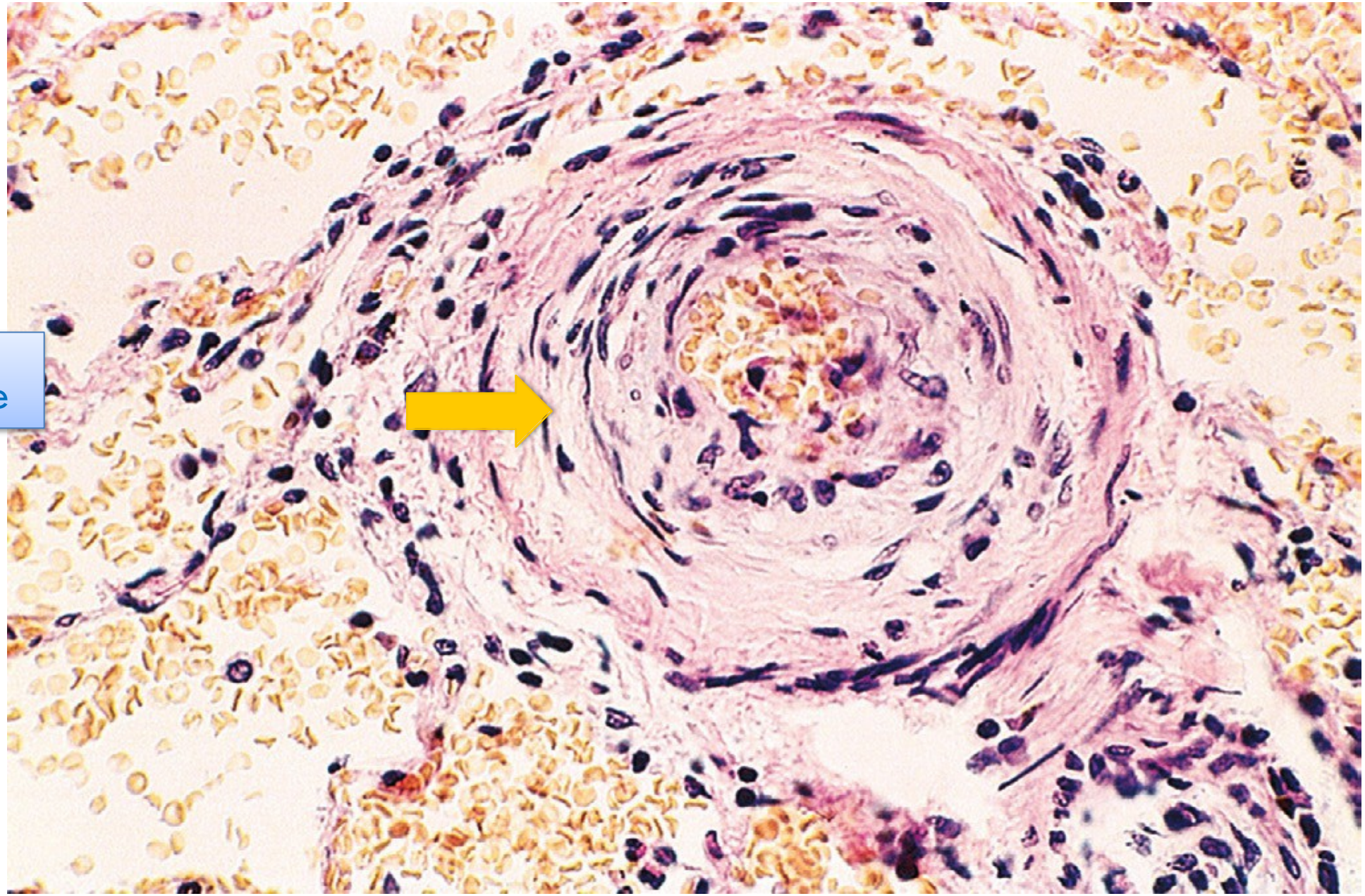
MORPHOLOGY:

- **Medial hypertrophy of the pulmonary muscular and elastic arteries**
  - small arteries and arterioles
- **Pulmonary arterial atherosclerosis**
  - pulmonary artery and its major branches
- **Right ventricular hypertrophy**

-- Organizing thrombi --> recurrent pulmonary emboli as the cause.

-- Diffuse pulmonary fibrosis, severe emphysema and chronic bronchitis --> chronic hypoxia as the initiating event.

Medial hypertrophy affecting an arteriole



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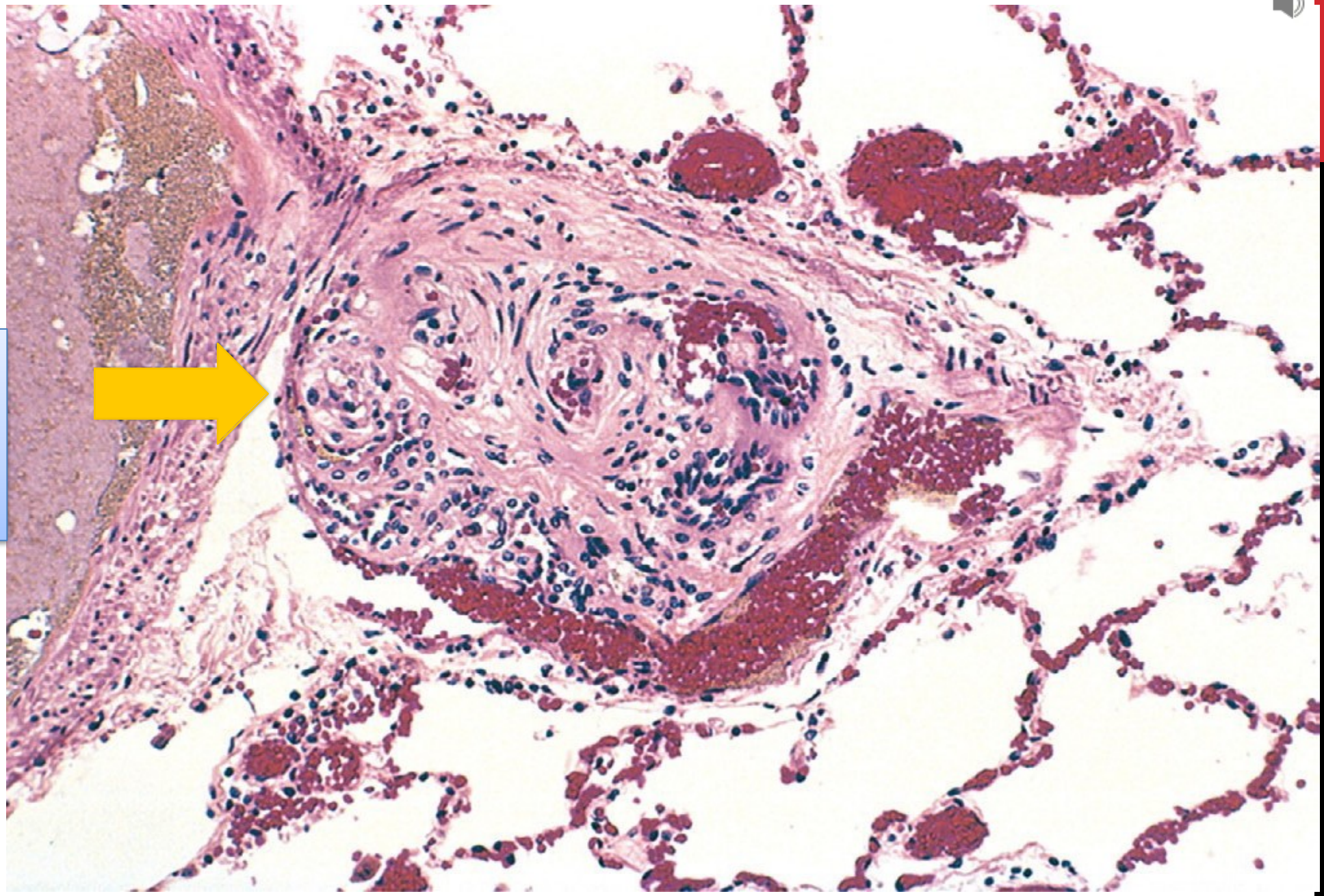
- **Plexiform lesion:**

  - uncommon

  - a tuft of capillary formations producing a network, or web, that spans the lumens of dilated thin-walled, small arteries and may extend outside the vessel.

Plexiform lesion, tuft of capillary formation spanning the lumen of dilated thin-walled vessel



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DIFFUSE ALVEOLAR HEMORRHAGE SYNDROMES

- Complication of some interstitial lung disorders.

Includes:

1. Goodpasture syndrome
2. Granulomatosis with polyangiitis
3. Idiopathic pulmonary hemosiderosis

GOODPASTURE SYNDROME:

- **Is an uncommon autoimmune disease in which lung and kidney injury are caused by circulating autoantibodies against certain domains of type IV collagen.**
    - type IV collagen is intrinsic to the basement membranes of renal glomeruli and pulmonary alveoli
- **Results in necrotizing hemorrhagic interstitial pneumonitis and rapidly progressive glomerulonephritis.**

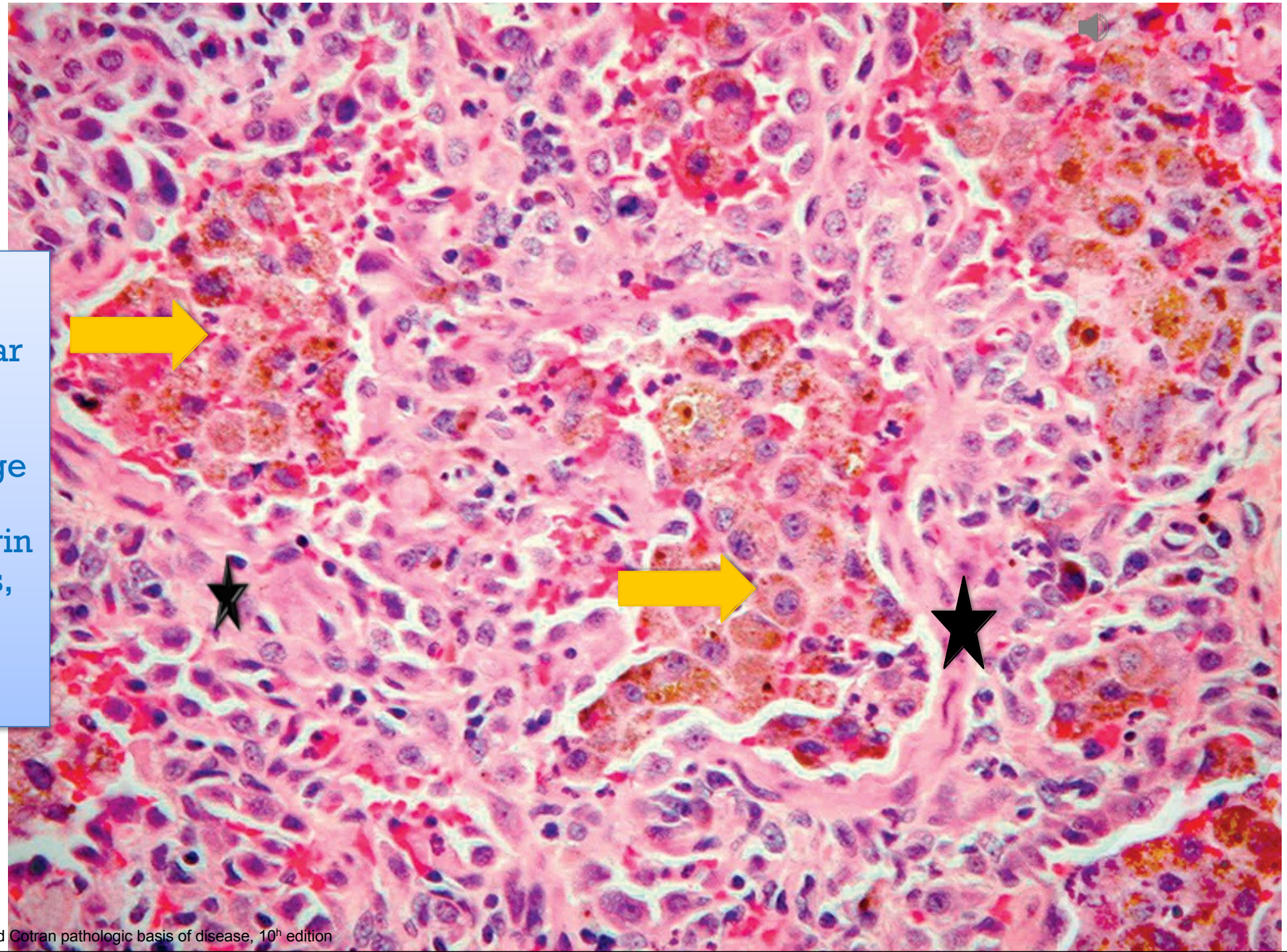
MORPHOLOGY:

- **Grossly,** red-brown consolidation due to **diffuse alveolar hemorrhage**

- **Microscopically:**
  - Focal necrosis of alveolar wall with intra-alveolar hemorrhage,
  - Fibrous thickening of septa
  - Hypertrophic type II pneumocytes.
  - Abundant hemosiderin Due to hemorrhage
  - Linear pattern of immunoglobulin deposition (IgG, sometimes IgA or IgM) seen along the alveolar septa.

This is the hallmark diagnostic finding in the renal biopsy specimen

Lung biopsy from a patient diagnosed with diffused alveolar hemorrhage syndrome, yellow arrows points to large numbers of intra-alverolar hemosiderin laid in macrophages, black stars point at thickened fibrous septa



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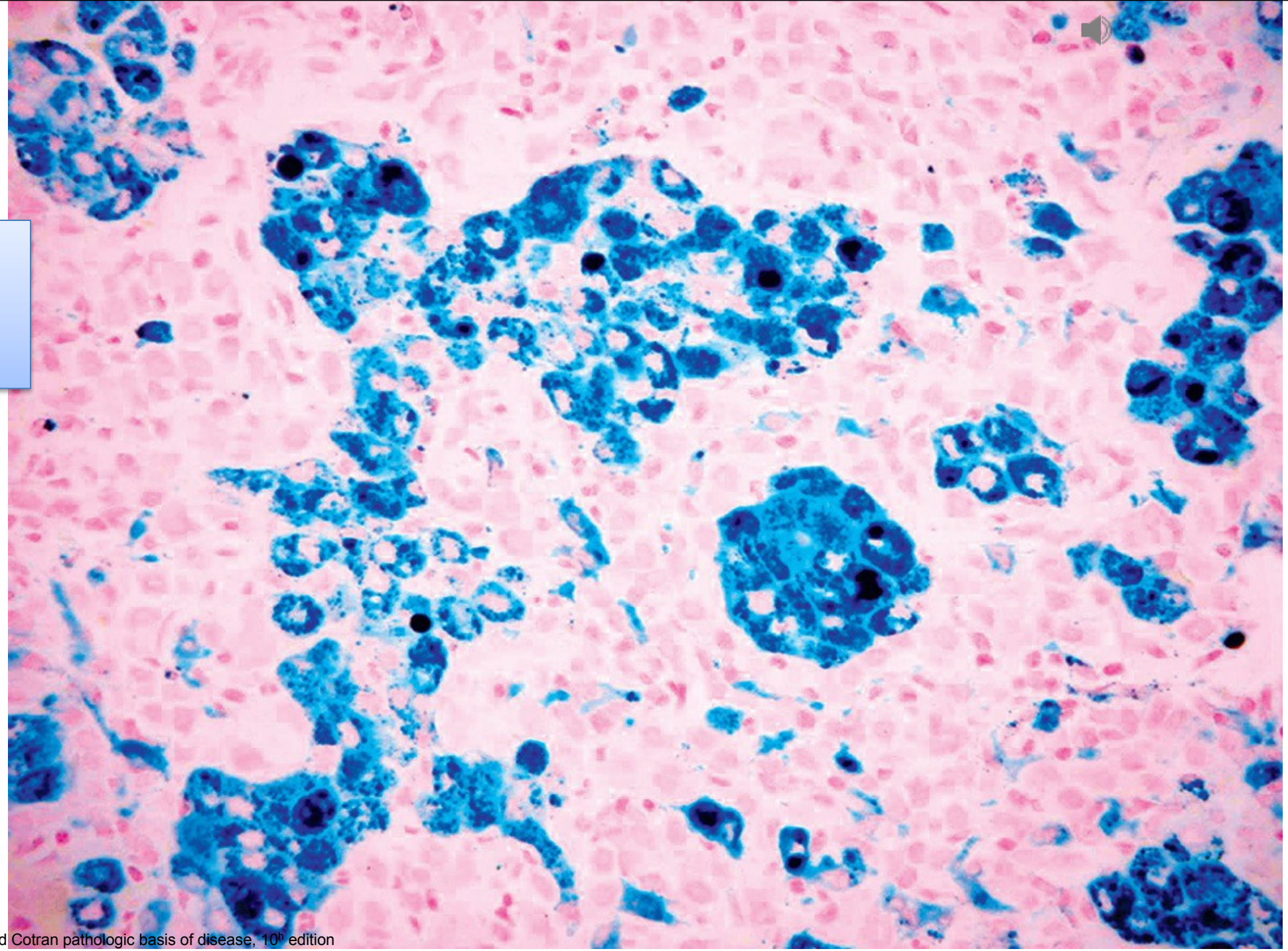
Stained with Prussian blue, to show/highlight hemosiderin deposits



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CLINICAL FEATURES:

- Teens and twenties
- Males > females
- Active smokers
- Plasmapheresis (removes the offending antibodies) and immunosuppressive therapy (inhibit antibody production) , renal transplantation is eventually required

GRANULOMATOSIS AND POLYANGIITIS

- Formerly called **Wegener granulomatosis**
- >80% of patients develop upper-respiratory or pulmonary manifestations.
- The lung lesions are characterized by a combination of necrotizing vasculitis (“angiitis”) and parenchymal necrotizing granulomatous inflammation.

- The signs and symptoms of the **upper-respiratory tract** involvement (chronic sinusitis, epistaxis, nasal perforation) and the **lungs** (cough, hemoptysis, chest pain).

- Focal necrotizing, often crescentic, glomerulonephritis.

- Anti-neutrophil cytoplasmic antibodies (PR3- ANCAs) are present in close to 95% of cases

https://baytowncrimestoppers.com/baytowns-most-wanted/unsolved-crimes/

A 45-year-old gentleman has chronic cough for the last 11 months. Physical examination, shows nasopharyngeal ulcers. on auscultation, the lungs have diffuse crackles bilaterally. Laboratory studies include a serum urea nitrogen level of 75 mg/dL and a creatinine concentration of

6.7 mg/dL. Urinalysis shows 50 RBCs per high-power field and RBC casts. His serologic titer for C-ANCA (proteinase 3) is elevated. A chest radiograph shows multiple, small, bilateral pulmonary nodules. A transbronchial lung biopsy specimen shows a necrotizing inflammatory process involving the small peripheral pulmonary arteries and arterioles. Which of the following is the most likely diagnosis?

A. Granulomatosis with polyangiitis

B. Pulmonary hypertension

C. Goodpasture syndrome

D. Idiopathic pulmonary hemosiderosis

E. Polyarteritis nodosa

Answer : A

ANOTHER CASE?!

A 33-year-old gentleman, medically free, presented with acute onset of hemoptysis. he is afebrile, with normal heart rate, increased respiratory rate and blood pressure. A transbronchial lung biopsy, shows focal necrosis of alveolar walls associated with prominent intraalveolar hemorrhage. Two days later, he has decreased urine output with abnormal serum creatinine and urea nitrogen. Which of the following antibodies is most likely involved in the pathogenesis of his condition?

A Anti–DNA topoisomerase I antibody

B. Anti–glomerular basement membrane antibody

C. Antimitochondrial antibody

D. Anti–neutrophil cytoplasmic antibody

E. Antinuclear antibody

Answer: B

THANK YOU!