Lupus & the Cardiopulmonary System

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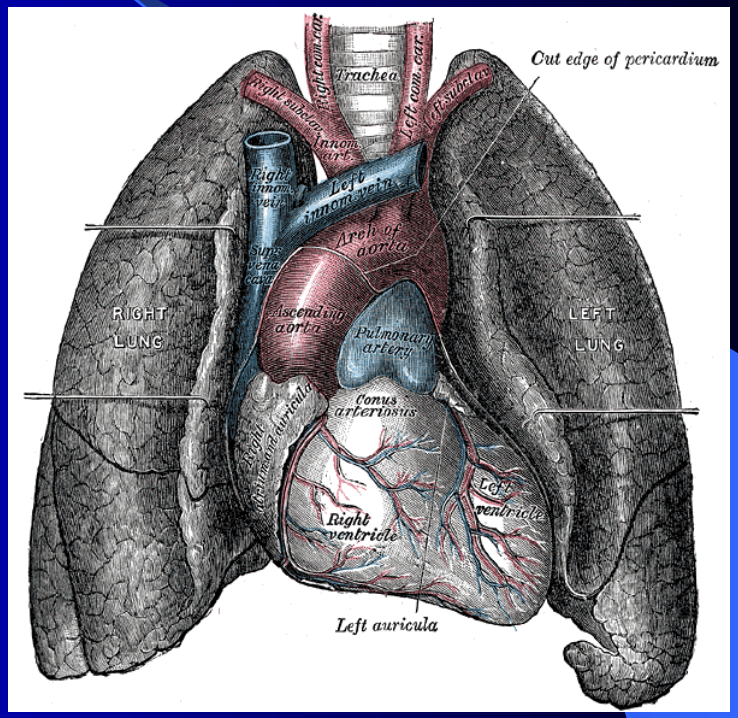
Cardiopulmonary Disease in Lupus

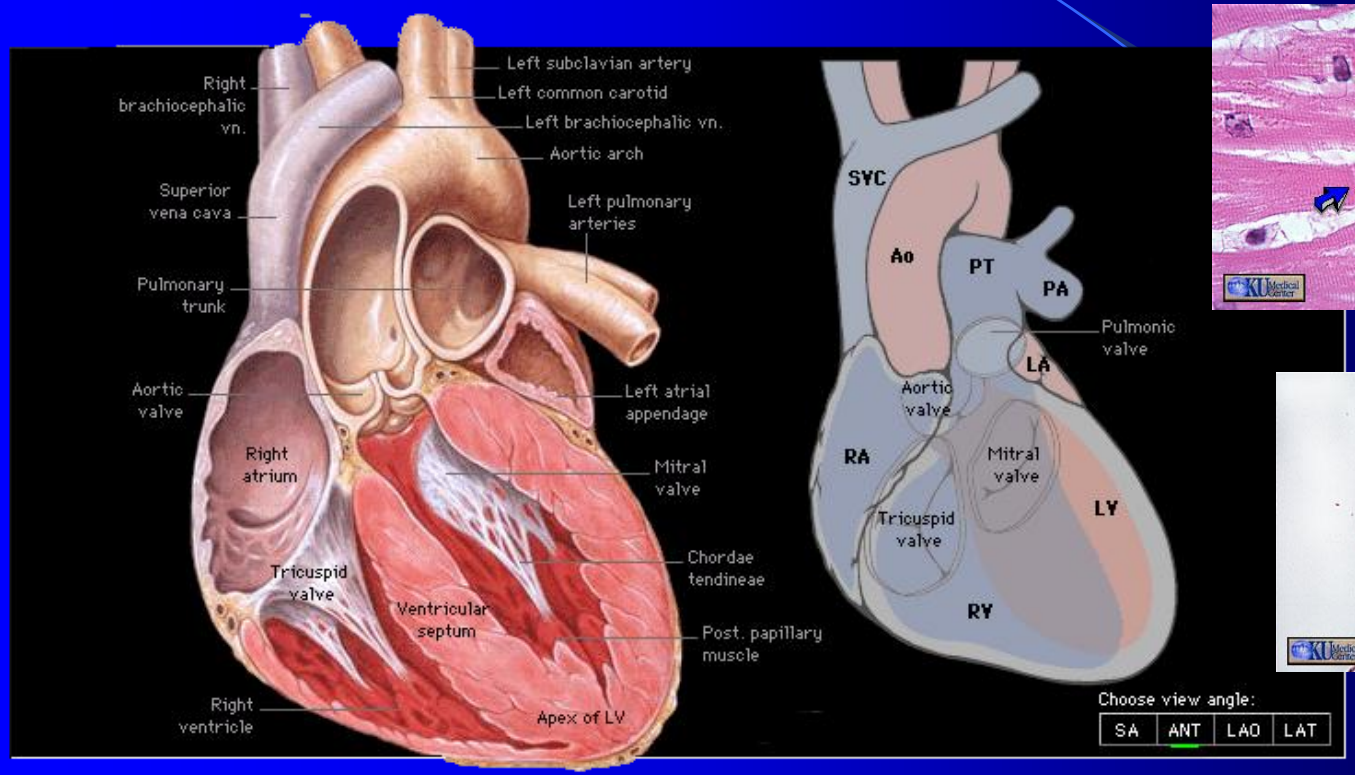
- Overview:
  - Vocabulary
  - Lupus manifestations
    - Lung effects
    - Heart effects
    - Blood vessel effects
  - Accelerated atherosclerosis
    - Epidemiology
    - Risk factors
    - Management

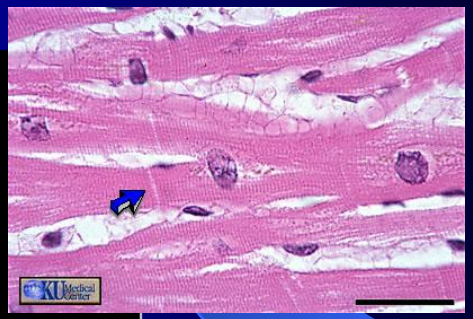
Lupus and the Heart

- Cardiac anatomy
  - Pericardium
    - Thin layer of tissue around the heart and great vessels
  - Myocardium
    - Muscle tissue that functions as a pump
  - Coronary arteries
    - Major blood vessels that deliver oxygen and nutrients to the myocardium
  - Valves
    - Separate chambers, direct blood flow



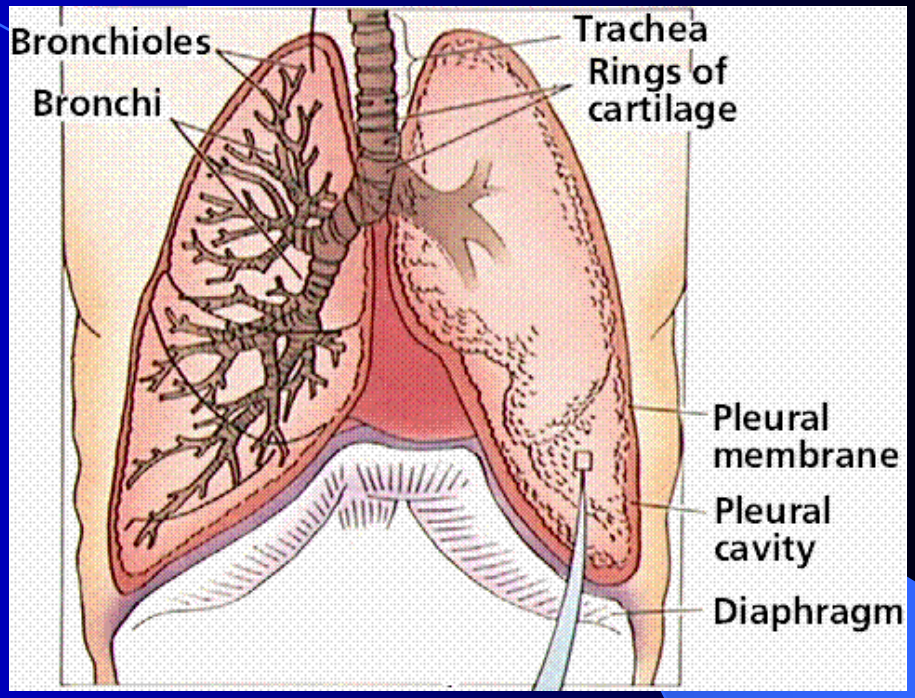
Lupus and the Heart

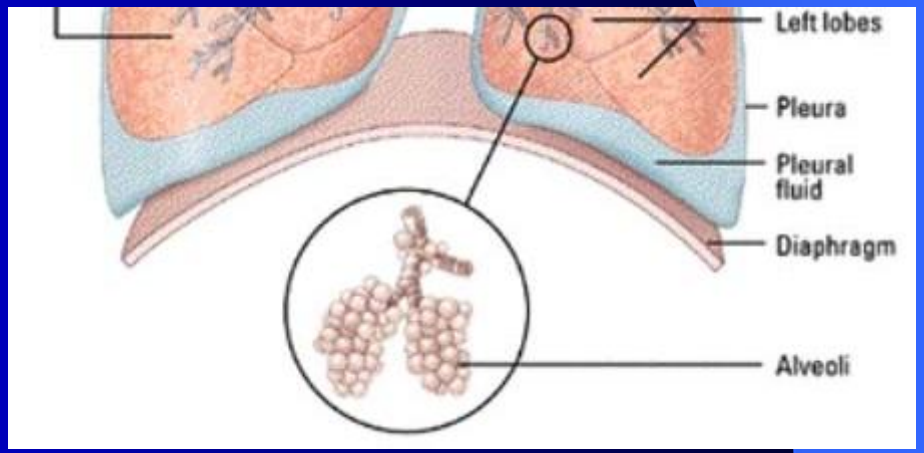




Lupus and the Lungs

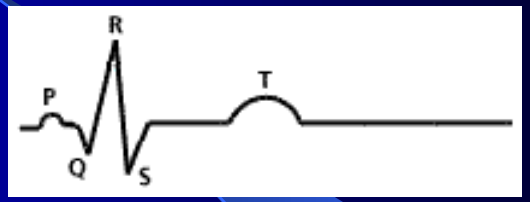
- Lung anatomy
  - Pleura
    - Thin layer of tissue around the lungs
  - Parenchyma
    - Tissue of the lung
      - Airways
      - Alveoli
  - Pulmonary arteries
    - Major blood vessels deliver blood through the lung
  - Chest wall
    - Muscles and connective tissue
    - Diaphragm

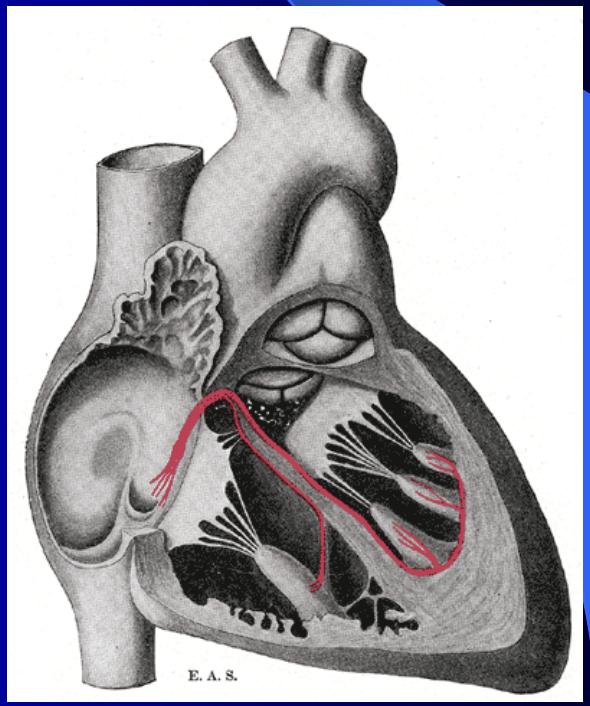




Lupus and the Heart: Medical Vocabulary

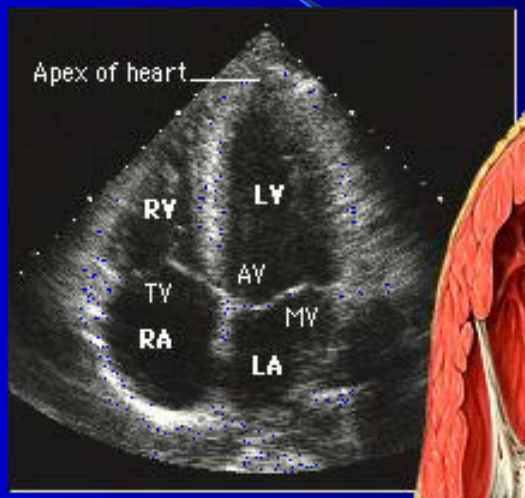
- ECG (electrocardiogram)
  - Measures heartbeat rhythm and assesses electrical movement around the heart
  - Can detect pericarditis, myocardial ischemia (low blood flow), dysrhythmia

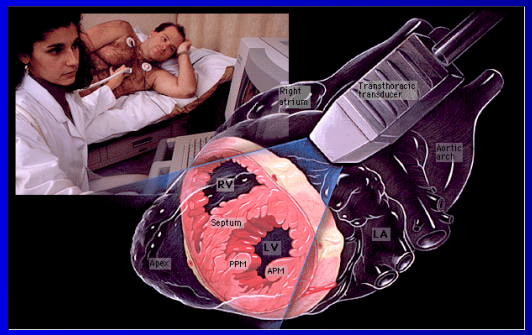




Lupus and the Heart: Medical Vocabulary

- Echo (echocardiogram)
  - Ultrasonographic image of the heart
  - Assesses:
    - Ejection fraction
      - Ability of heart to pump blood
    - Valve structure, patency, and viability
    - Pericardial fluid



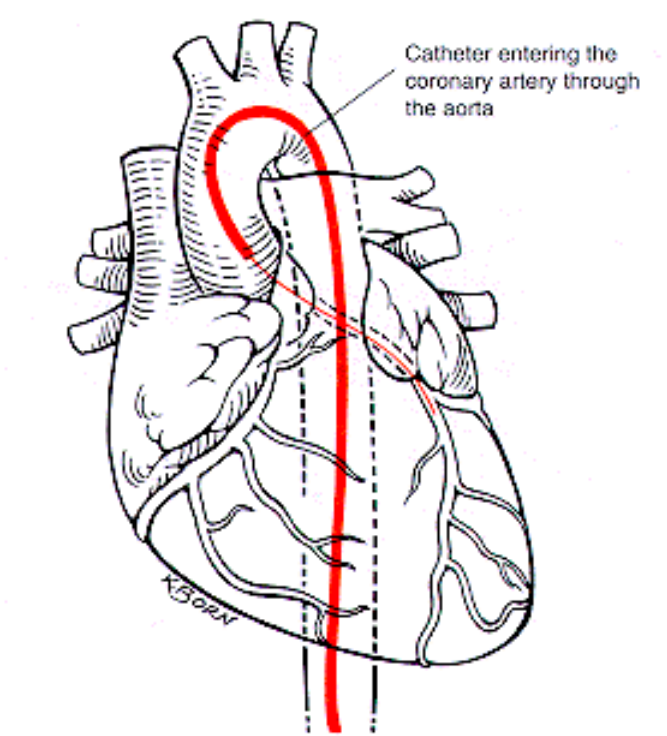


Lupus and the Heart: Medical Vocabulary

- Stress test
  - Means of assessing risk for heart attack by detecting areas of inadequate bloodflow (low oxygen delivery)
    - Exercise
    - Persantine
    - Dobutamine
  - Measure myocardial stress via ECG leads or by perfusion
    - Thallium
    - Cardiolyte

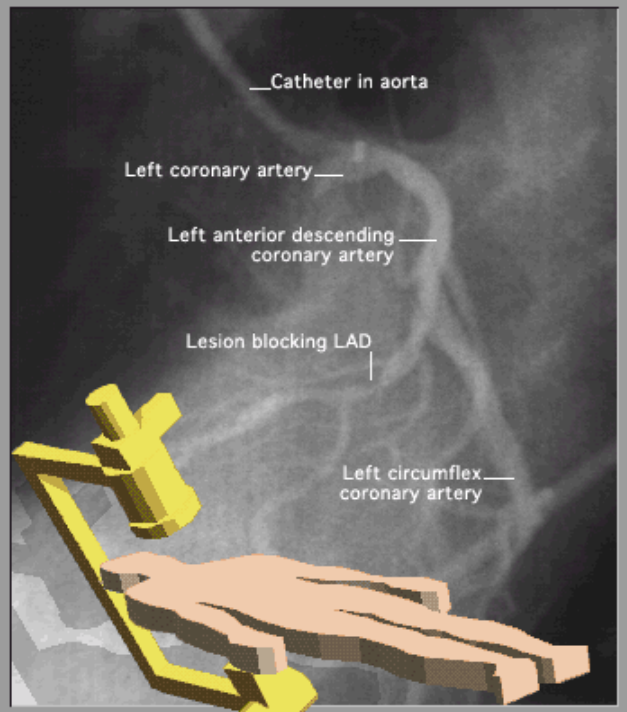
Lupus and the Heart: Medical Vocabulary

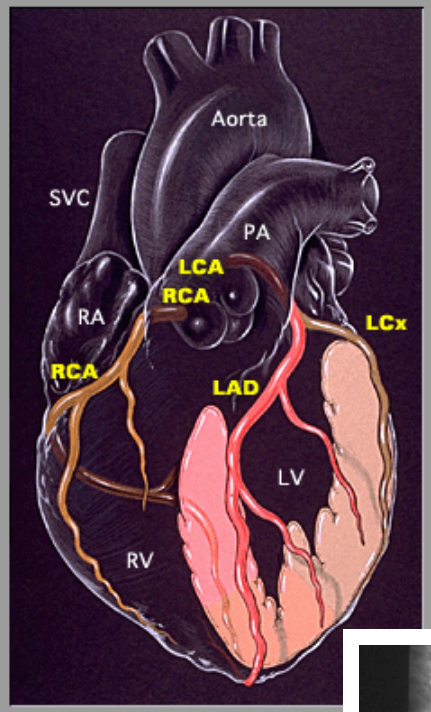
- Cardiac Catheterization
  - Placement of catheters directly into either side of the heart
    - Left heart cath:
      - Measures EF
      - Visualize coronary arteries
      - Can perform interventions
        - Angioplasty
        - Stent deployment
    - Right heart cath
      - Measure right sided pressures
      - Myocardial biopsy

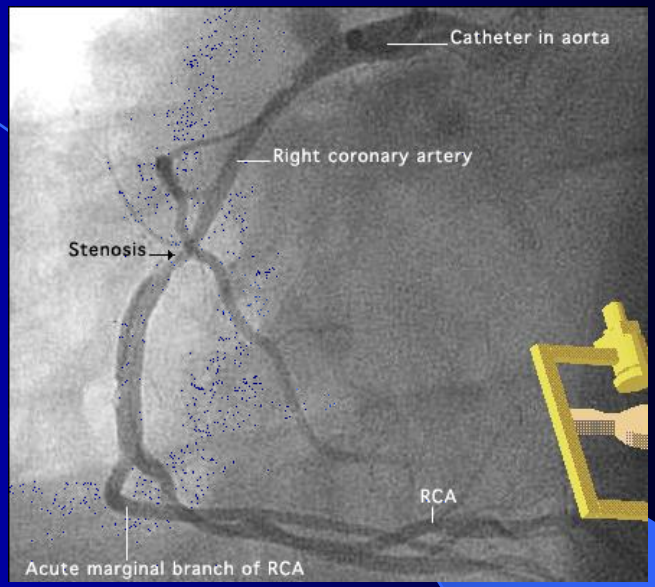


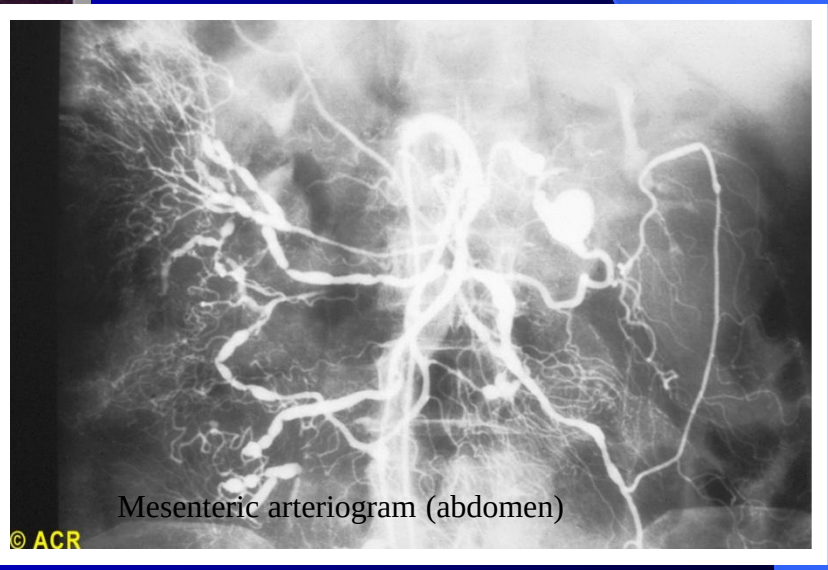
An angiogram is a kind of x-ray test that can show if you have clogged arteries that can lead to heart attack.

Arteriograms





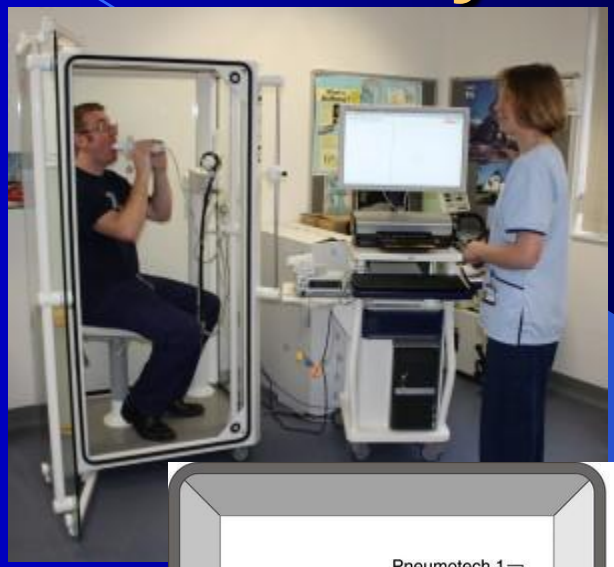


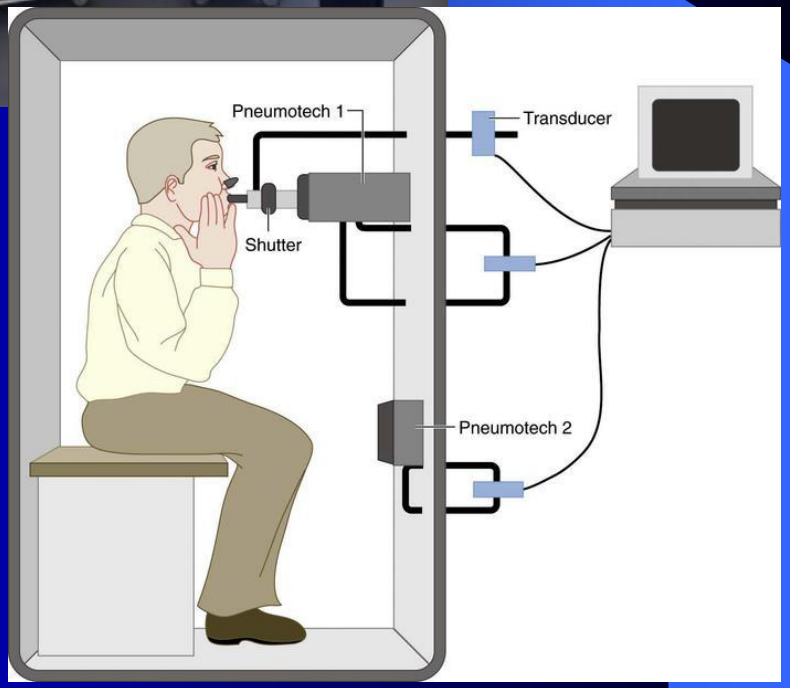


Mesenteric arteriogram (abdomen)

Lupus and the Lung: Medical Vocabulary

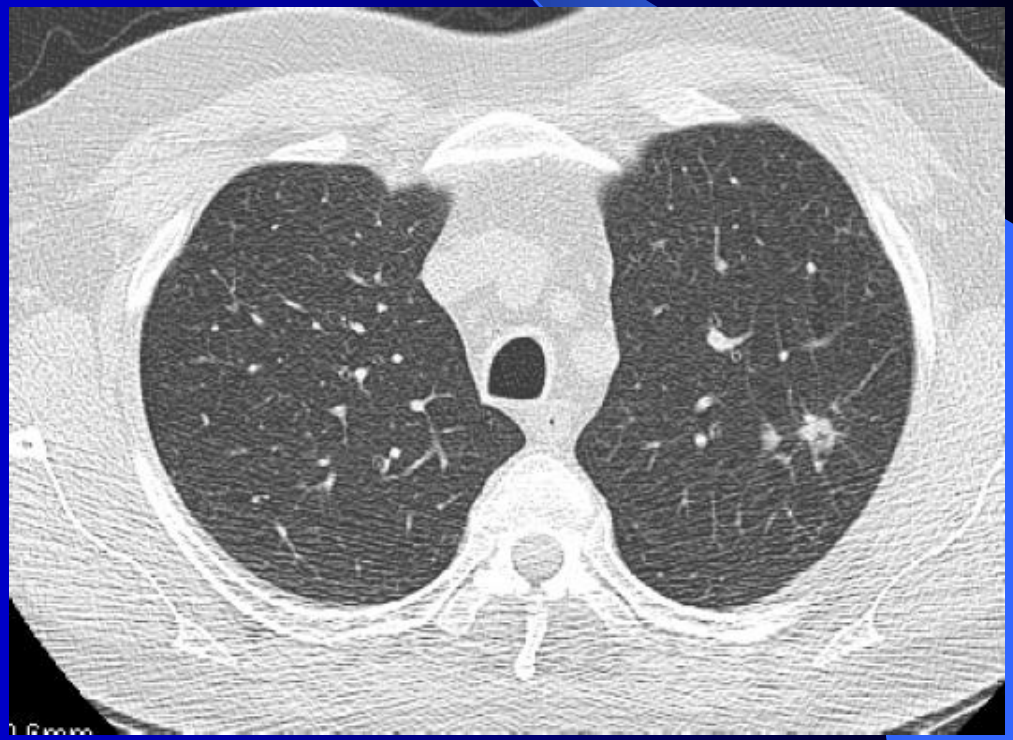
- Pulmonary function tests
  - Non-invasive testing of lung function
    - Measures lung volumes
    - Measures diffusing capacity
- 6 minute walk test
  - Estimates functional status
  - Predicts morbidity in chronic lung disease
- V:Q scan
  - Overlays air movement and blood flow
  - Detects blood clots





Lupus and the Lung: Medical Vocabulary

- CT scan
  - Radiograph imaging of lung
  - High-resolution
    - Non-contrasted
    - Images patient supine and prone
    - Detects small airway and interstial disease (ILD)
  - CTA
    - Uses contrast infusion
    - Detects blood clots

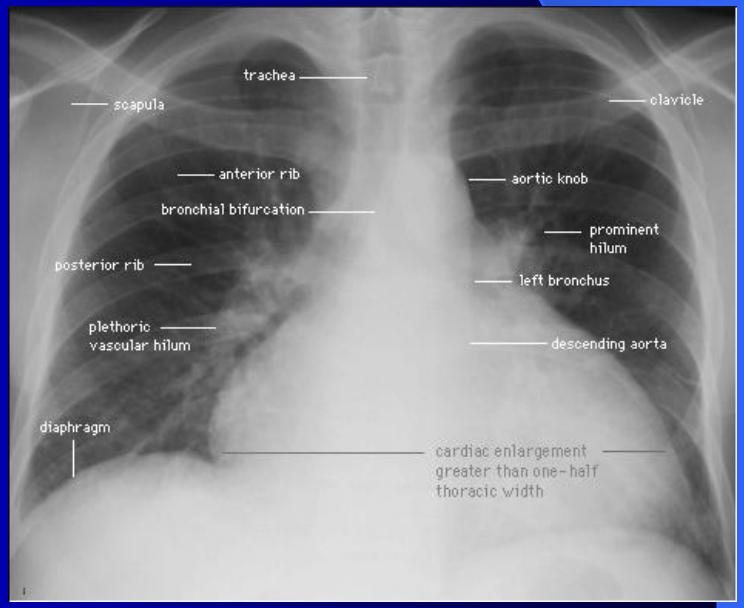


Lupus Cardiac Manifestations

- Pericarditis
  - Inflammation of the lining around the heart
    - May reslt in accumulation of inflammatory fluid
  - Clinical presentation
    - Anterior chest pain, sharp or stabbing
    - Pain worsens with inspiration and reclining
  - Complications
    - Pericardial effusion
    - Pericardial tamponade
  - Treatment
    - NSAIDs
    - Corticosteroids (with caution)

Lupus Cardiac Manifestations

- Myocarditis and Cardiomyopathy
  - Inflammation of the myocardium
    - Loss of ventricular contractile strength
  - Clinical presentation:
    - Typically asymptomatic until heart failure develops
    - Can be associated acutely with pericarditis
  - Diagnosis:
    - Echocardiogram
    - Catheterization to rule out vasculitis/ischemia
    - May require myocardial biopsy
  - Treatment:
    - Immunomodulatory:
      - Corticosteroids
      - Intravenous immunoglobulin
    - Supportive care
      - ACE inhibitors
      - Spironolactone
      - Beta blocker

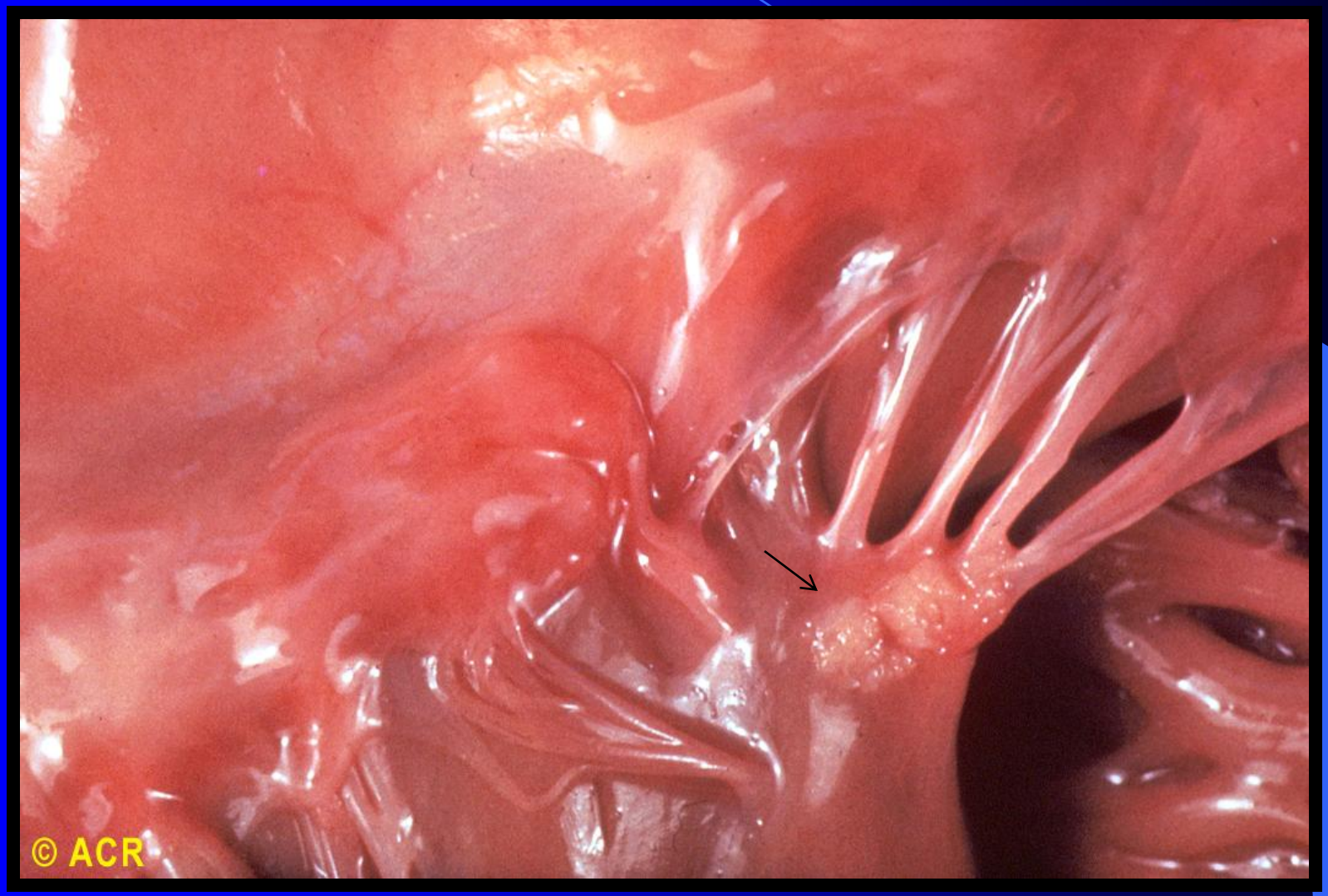


Lupus Cardiac Manifestations

- Libman-Saks endocarditis
  - Bland (non-infectious) vegetations on the heart valves
  - Clinical presentation:
    - May be asymptomatic
    - May present with stroke or peripheral ischemia of vegetations are embolized
    - Rarely cause valvular injury
  - Associated with antiphospholipid antibodies
  - Diagnosis:
    - Echocardiogram (transesophageal)
  - Treatment:
    - Prophylactic antibiotics
    - Anticoagulation
    - Valve replacement surgery

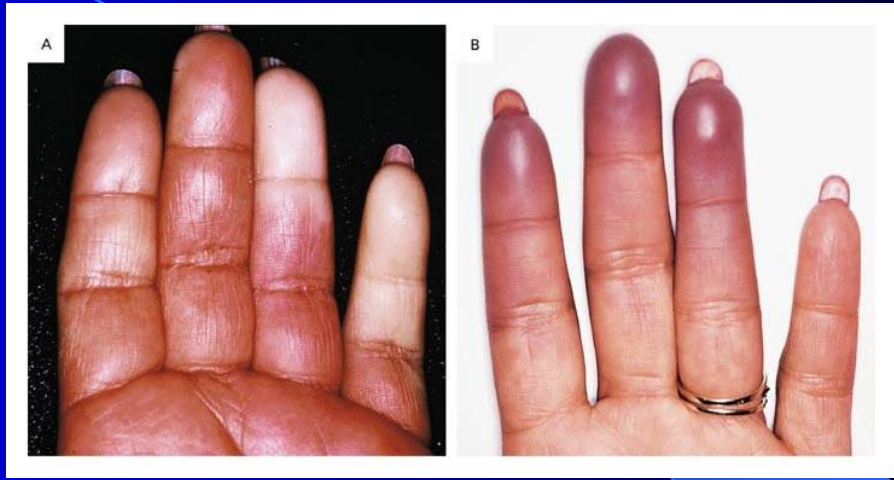
Lupus Cardiac Manifestations

Libman-Saks Endocarditis



SLE: Vascular manifestations

- Raynaud's phenomenon
  - White→Blue→Red
  - Incidence: 34-60%
  - Management:
    - Temperature hygiene
    - Calcium channel blockers
    - Anti-platelet therapies
- Digital vasculitis
  - Digital gangrene
  - Differentiate from APS
  - Management:
    - immunosuppression



Wigley, F. M. N Engl J Med 2002;347:1001-1008

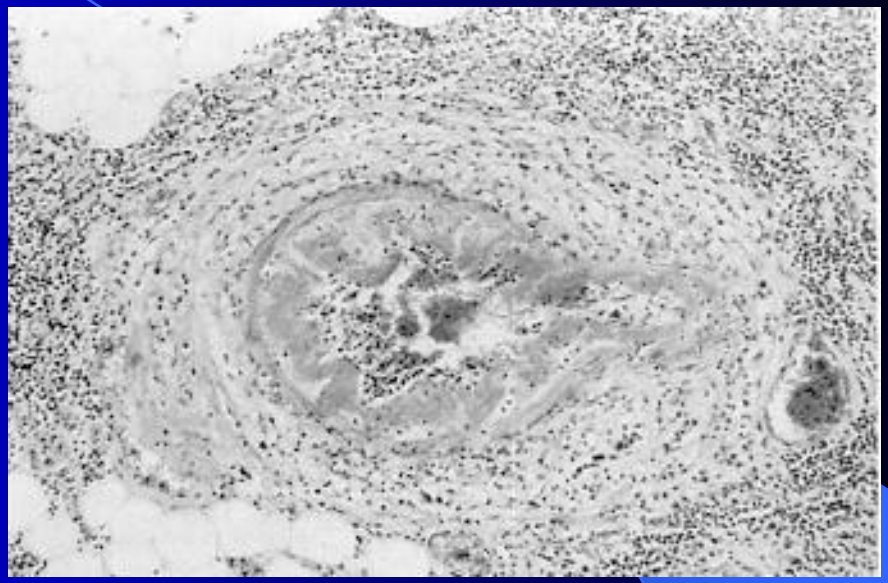
Bluto, M. J. et al. N Engl J Med 2002;347:992

Lupus Vascular Manifestations

- Vasculitis
  - Inflammation of the wall of a blood vessel
    - Ordinarily involves arteries
    - Results in blood vessel narrowing or occlusion
  - Clinical presentation:
    - Depends of the size, number, and location of vessels involved
    - Features reflect impaired blood flow to organs supplied by the inflamed vessels
  - Diagnosis:
    - Arteriogram, biopsy, clinical impression
  - Treatment:
    - Corticosteroids (high dose)
    - Cytotoxic agents (cyclophosphamide)

Vasculitis

- Coronary arteritis (rare)
  - Presents as angina or myocardial infarction
- Mesenteric vasculitis
  - Presents as food avoidance, abdominal pain, weight loss
  - Can cause bowel necrosis and acute abdomen
- Cutaneous vasculitis
  - Usually easier to treat but includes digital vasculitis (which can progress to gangrene)



Vasculitis

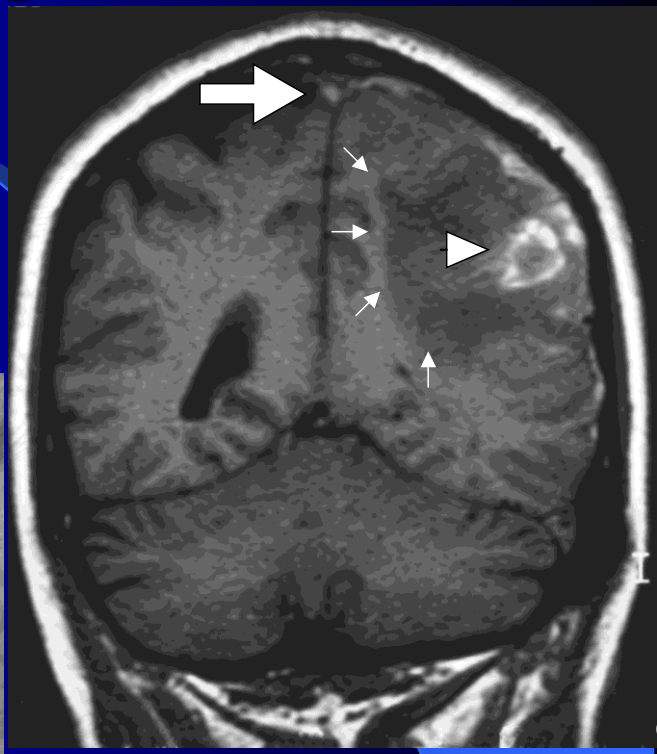

Nailfold infarcts
© ACR


Cutaneous vasculitis at the elbow

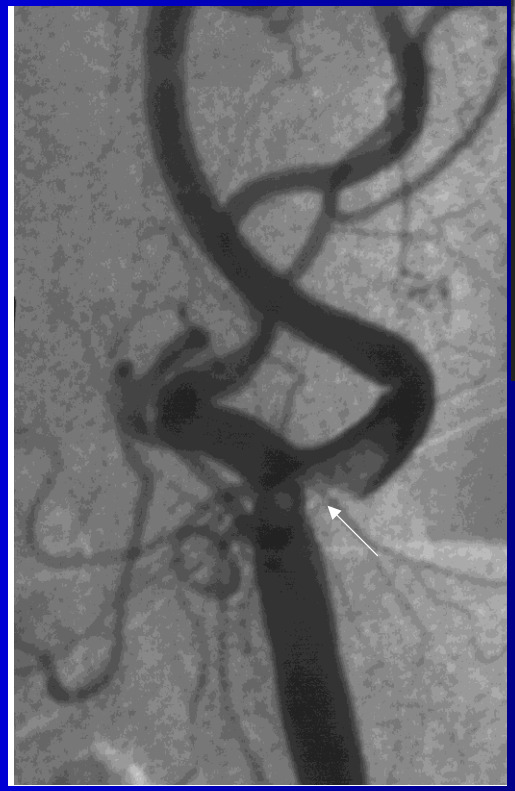

Palpable purpura
© ACR

Antiphospholipid antibody syndrome: Clinical features

- Thrombosis
  - Venous (DVT, pulmonary embolus) or arterial (stroke, mesenteric ischemia, myocardial infarction)
  - Recurrent thromboses favor same vascular bed
  - Occasional bland endocarditis (Libman-Saks)
- Pregnancy loss
  - Single miscarriage late 1st trimester or beyond
  - Three consecutive early 1st trimester miscarriages
  - Absence of other causes (hormonal, genetic, anatomic, exposure)
- Antiphospholipid antibody
  - Anti-cardiolipin antibody
    - strongest association with IgG antibodies
  - Lupus anticoagulant
    - Prolonged PTT, fails to correct with mix + confirmatory study
  - False positive syphilis test



APLS: Superior saggital sinus thrombosis with large venous infarct



APLS: ICA thrombosis caused multiple cerebral infarcts via embolization

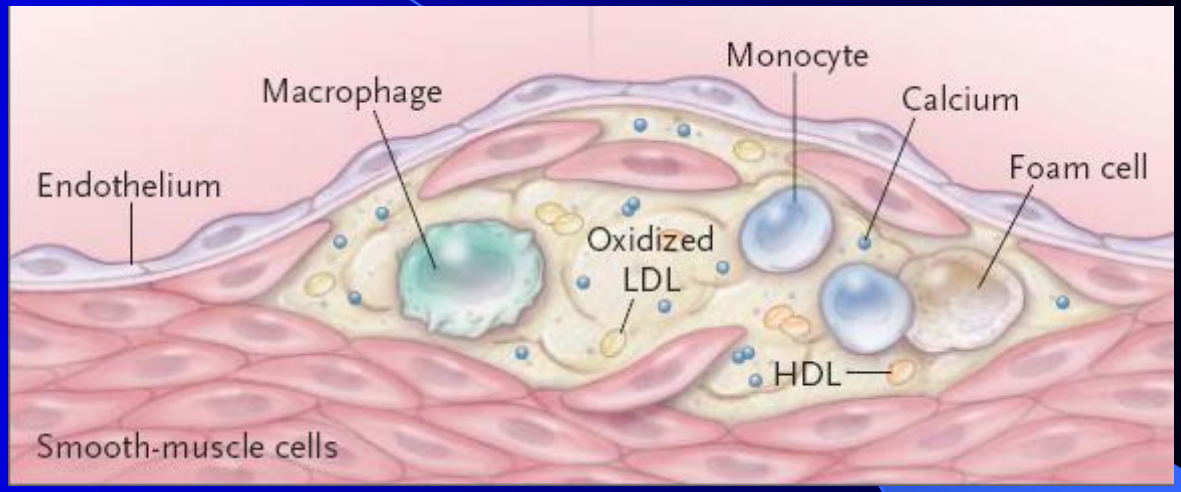
Shanahan JC, Ortel TL, *Sem Cerebrovascular Dis Stroke*, 2002

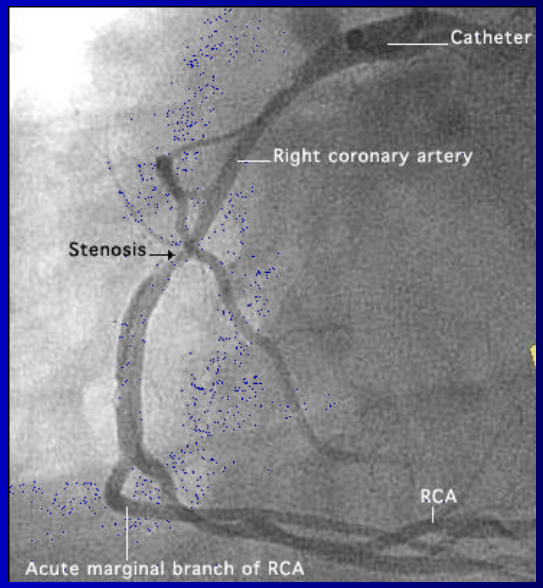
Accelerated Atherosclerosis

- Mortality
  - The leading cause of death in patients with SLE is complications of atherosclerotic coronary artery disease
- Risk
  - Myocardial infarction:
    - 5%-45% SLE patients
    - Among women with SLE <45 yrs old, risk of MI is 50 times that of age-matched healthy controls
    - Nurses Health Study: 2-fold increase risk for CAD w/ lupus diagnosis
  - Independent of standard risk factors, SLE treatment
    - Risk associated with higher disease activity/severity

Atherosclerosis

- Plaques
  - Inflammation
    - Foamy macrophages
  - Deposits
    - Oxidized cholesterol
    - Lipids (fat)
    - Calcium
  - Fibrous caps
- Plaque rupture
  - Exposes tissue factor
  - Results in thrombus formation and occlusion of the vessel





Atherosclerosis in SLE

- Estimated prevalence:
  - Odds ratio for atherosclerosis in SLE:
    - 4.9 (Roman, *NEJM*) – 9.8 (Asanuma, *NEJM*)
    - Assessed by carotid ultrasound (IMT) (Roman)
    - Assessed by external beam CT (detects coronary calcium) (Asanuma)

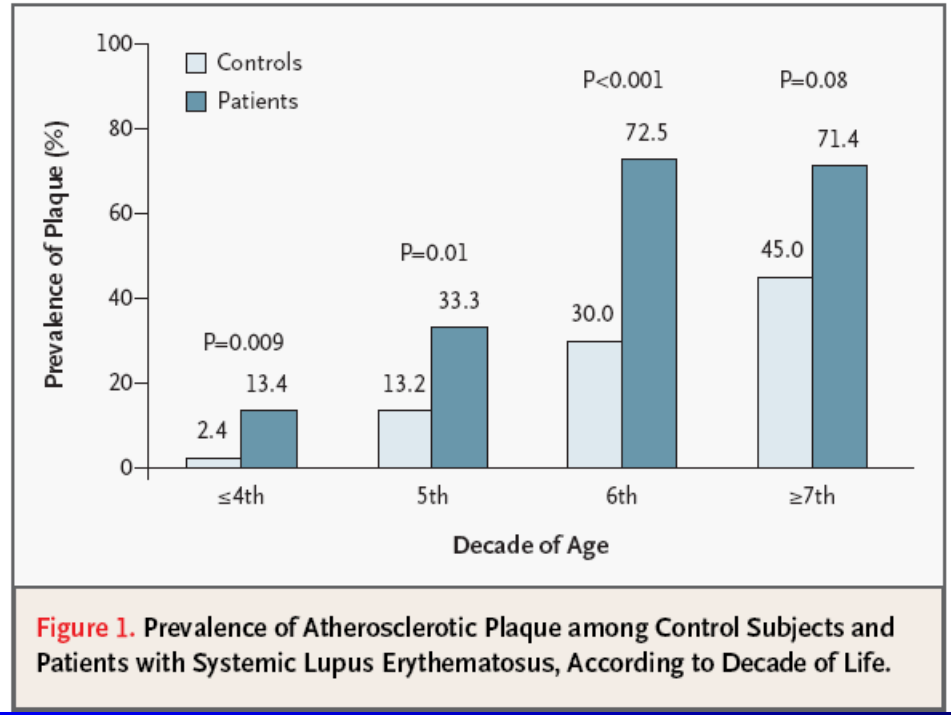


Figure 1. Prevalence of Atherosclerotic Plaque among Control Subjects and Patients with Systemic Lupus Erythematosus, According to Decade of Life.

Atherosclerosis in SLE

- Traditional risk factors:
  - Male gender
  - Age over 50
  - Hypertension
    - Higher rates of HTN in SLE
    - 11.5-75%
  - Family history
    - Parent/sib w/ heart attack
  - Hyperlipidemia
    - Higher rates of HL in SLE
    - 11.5-75%
  - Smoking
  - Diabetes mellitus
    - Metabolic syndrome
      - Overweight, HTN, HL, hyperuricemia/gout, insulin resistance
  - Overweight
- SLE risk factors
  - Younger age at diagnosis of SLE
  - Disease duration
  - Anti-smith autoantibodies
  - Antiphospholipid antibodies
  - Dyslipidemia
  - Corticosteroid use

Atherosclerosis in SLE: Management

- Goal blood pressure:
  - Systolic < 140
    - SBP 130-135 may be better but not at risk of side effects
    - J-shaped curve of risk suggests pressure < 126 is without much benefit
    - If type II diabetes and CAD present- consider treat to <120
  - Diastolic <90
    - DBP below 60-70 could increase stroke risk in some patients
- Goal cholesterol
  - Step 1: fasting lipid panel
  - Step 2: establish presence of coronary heart disease or equivalents
  - Step 3: assess CHD risk factors
  - Step 4: CHD risk calculator
    - http://hp2010.nhlbihin.net/atpiii/calculator.asp?usertype=prof
  - Step 5: Treat based on risk and LDL

Atherosclerosis in SLE: Management

ATP III LDL-cholesterol goals and cutpoints for therapeutic lifestyle changes and drug therapy in different risk categories

Risk category	LDL-cholesterol goal	LDL-cholesterol level at which to initiate therapeutic lifestyle changes	LDL-cholesterol level at which to consider drug therapy
Coronary heart disease (CHD) or CHD risk equivalent (10-year risk >20 percent)*	<100 mg/dL (2.58 mmol/L)	≥100 mg/dL (2.58 mmol/L)	≥130 mg/dL (3.36 mmol/L); drug optional at 100 to 129 mg/dL (2.58 to 3.33 mmol/L)•
2 or more risk factors (10-year risk ≤20 percent) Δ	≤130 mg/dL (3.36 mmol/L)	≥130 mg/dL (3.36 mmol/L)	10-year risk 10 to 20 percent: >130 mg/dL (3.36 mmol/L) 10-year risk <10 percent: ≥160 mg/dL (4.13 mmol/L)
0 to 1 risk factor◇	≤160 mg/dL (4.13 mmol/L)	≥160 mg/dL (4.13 mmol/L)	≥190 mg/dL (4.91 mmol/L); LDL-cholesterol lowering drug optional at 160 to 189 mg/dL (4.13 to 4.88 mmol/L)

Atherosclerosis in SLE: Management

- Screening for risk factors
  - Annual: Blood pressure, fasting lipid panel, hgb a1c or fasting AM glucose
- Early, aggressive intervention for risk factors
  - Control hypertension
  - Smoking cessation
  - Treat hyperlipidemia
    - Dietary adjustment, “Statins”
    - SLE associated with “atherogenic” lipid profile
  - Weight control
    - Diet, exercise
  - Careful monitoring of blood sugar, weight , blood pressure
    - Particularly if chronic corticosteroids are necessary

Atherosclerosis in SLE: Management

- Control SLE
  - Hydroxychloroquine
  - ACE inhibitors for chronic proteinuria
  - Routine rheumatology evaluation and lab assessment
    - Quarterly appointments
    - CBC, chemistries, complement, urinalysis, anti-DNA at each visit
    - Antiphospholipid antibody screen, fasting lipid panel performed annually

Atherosclerosis in SLE: Is there something more?

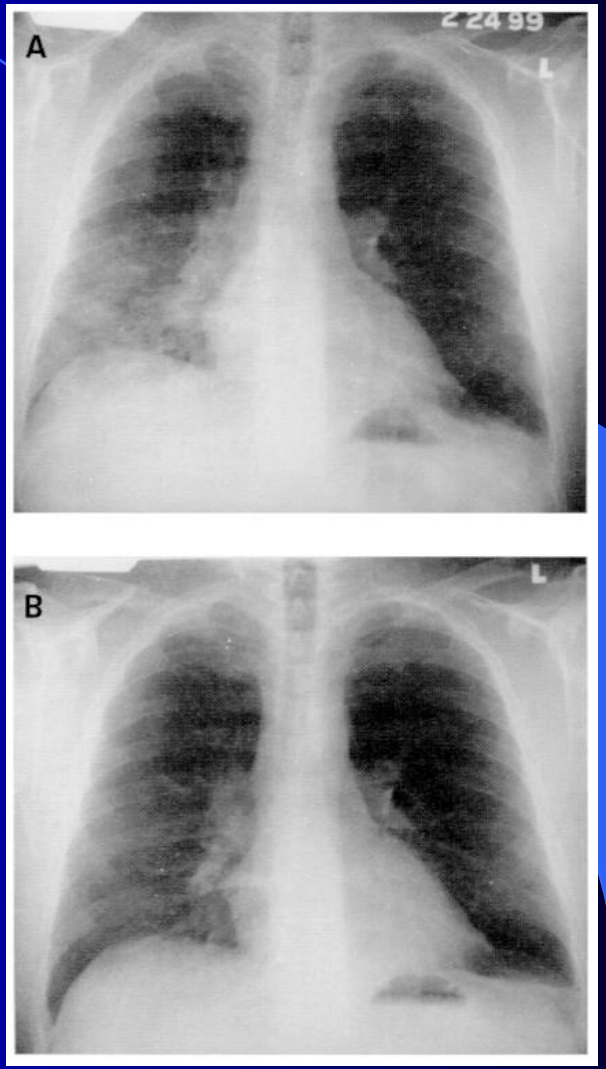
- Impact of inflammation
  - Uncertain role of inflammation
  - CRP levels are independent risk for coronary artery disease
- Endothelial cell injury
  - Now four separate studies that confirm widespread endothelial dysfunction in SLE
    - Independent of atherosclerotic disease burden

Summary

- Atherosclerosis prevention and management must be aggressive
- Multiple diagnostic techniques, including biopsy, may be necessary to understand the etiology of lupus-associated cardiovascular disease
- Questions??

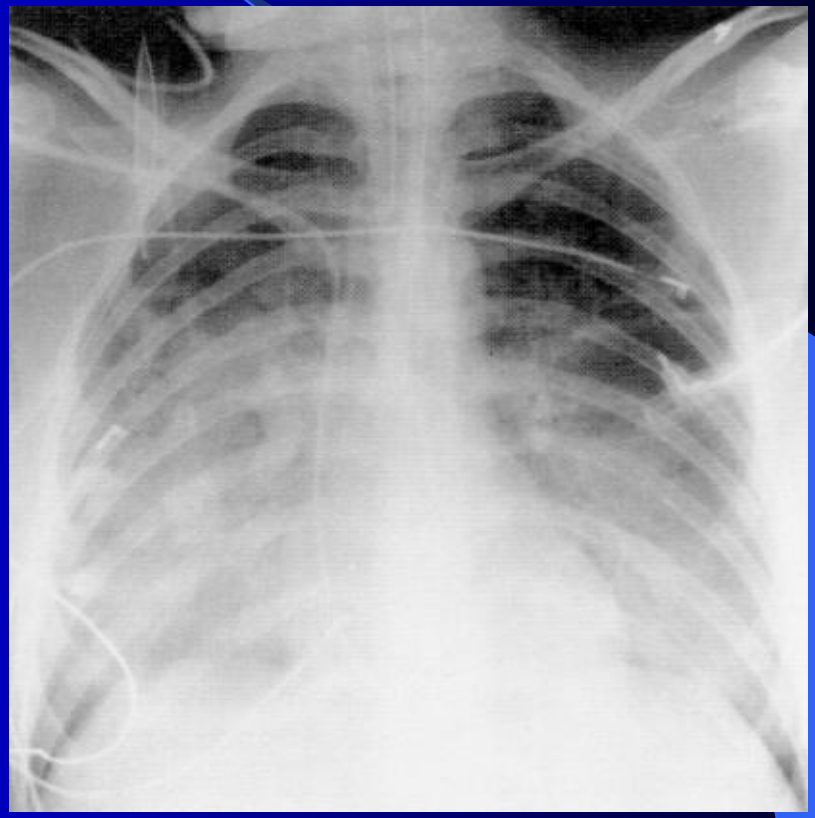
SLE: Acute Lupus Pneumonitis

- Prevalence
  - < 10%
- Presentation
  - Acute dyspnea
  - Cough
  - Fever
  - Hemoptysis
  - Chest pain/pleurisy
  - Hypoxemia
  - Preceded/ associated w/ infxn
- Prognosis:
  - Mortality 50%
- Treatment:
  - Steroids
  - PE
  - CYC/AZA



SLE: Diffuse Alveolar Hemorrhage

- Prevalence
  - 2%
- Presentation
  - Acute dyspnea
  - Cough
  - Chest pain/pleurisy
  - Hypoxemia
  - Anemia
- Prognosis:
  - Mortality 50%
- Treatment:
  - Steroids
  - PE
  - CYC/AZA



SLE: Chronic Interstitial Lung Disease

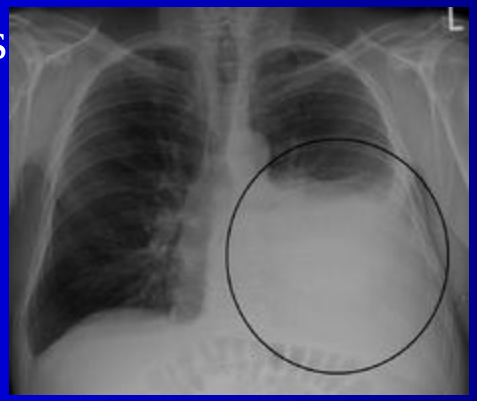
- Also called “pulmonary fibrosis”
- Prevalence:
  - Up to 3%
- Presentation:
  - Dyspnea
  - Cough
  - Decreased FVC, DLCO
- Pathology:
  - Purely inflammatory (NSIP) has best prognosis, easiest to treat
  - Mixed inflammation and scar (NSIP w/ fibrosis)
- Diagnosis
  - Abnormal PFDs
  - Abnormal CT scan findings
  - Bronchoalveolar lavage
    - Confirm inflammation
    - Rule out chronic infection
    - Rule out cancer
  - Open lung biopsy
- Prognosis variable
- Management:
  - Corticosteroids
    - For isolated NSIP
  - AZA/CYC/MMF
    - For fibrosing disease

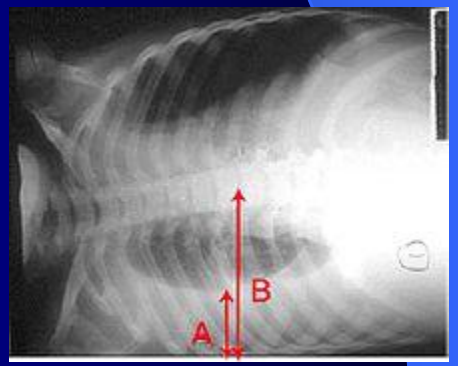
SLE: Chronic Interstitial Lung Disease

- Interstital lung disease
  - Clinical symptoms & signs
    - Cough
    - Dyspnea
    - Pleural rub or dry rales
  - Imaging
    - Interstitial infiltrates (early)
      - CT: “ground glass” opacities
    - Scarring (late)
      - CT: “honeycombing,” traction bronchiectasis
  - Pulmonary function
    - Restrictive pattern
      - Depressed lung volumes

SLE: Pleurisy and Pleural Effusion

- Pleurisy
  - Chest pain, typically sharp and stabbing and localized
  - Occurs with deep inspiration
  - Caused by inflammation of the pleura (similar to and may c-occur with pericarditis and peritonitis
  - Differential diagnosis
    - Rule out Pulmonary embolus!!
    - Pneumonia
    - Pneumothorax
    - ALP
    - Muscle strain
    - Costochondritis
- Diagnosis
  - Friction rub on exam
  - CXR occasionally shows fluid
- Management:
  - NSAIDs
  - Corticosteroids
  - Drainage if large effusion forms





SLE: Shrinking lung syndrome

- Slowly progressive dyspnea with exertion
- Rare, < 2%
- Diagnosis:
  - Decreased breath sounds
  - Reduced lung volumes on PFDs
  - Changing CXR lung aeration

Pathology:

Probably pleural fibrosis/scar

Management

Azathioprine

Corticosteroids

Chen,W. et.al. Hong Kong Clinical Meetings, 2004. www.hkresp.com

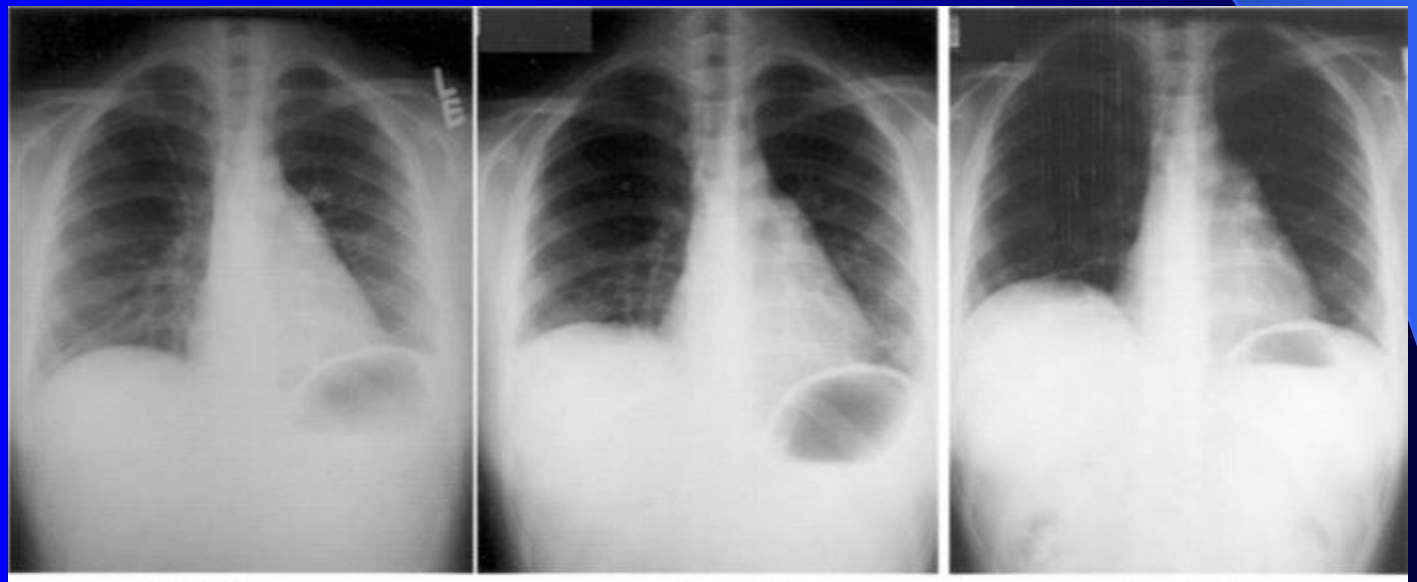
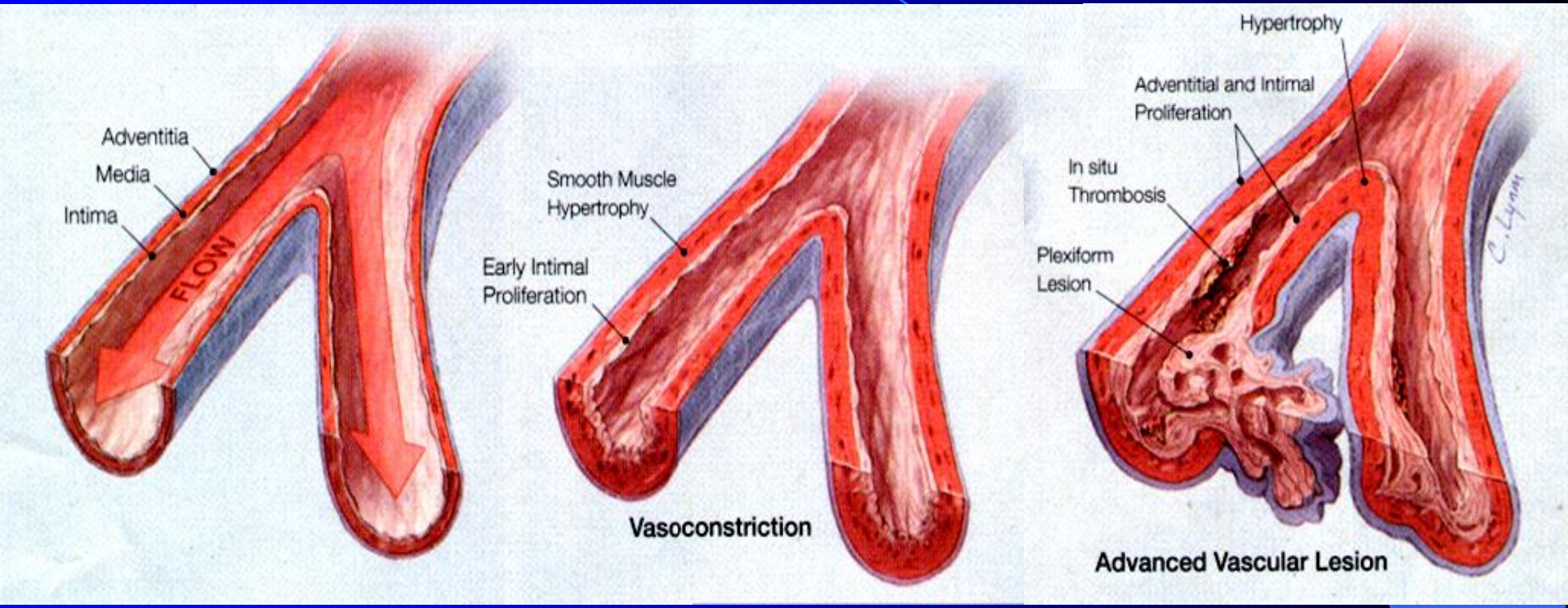


Fig. 2: Chest radiographs showing progressive lung shrinkage over 4 months

SLE: Pulmomary arterial hypertension

- Also called PAH
- Progressive shortness of breath followed by right heart failure
- Due to inflammation, damage, dysfunction of the small pulmonary arteries
- Effectively slows blood flow through the lung, forcing the right ventrivcle to pump harder
- Three different causes with three different management startegies in patients with SLE

Increased Pulmonary Resistance and Pressure



Pre-Symptomatic — Symptomatic — Severely Symptomatic

High flow, low resistance vessel → Low flow, high resistance vessel

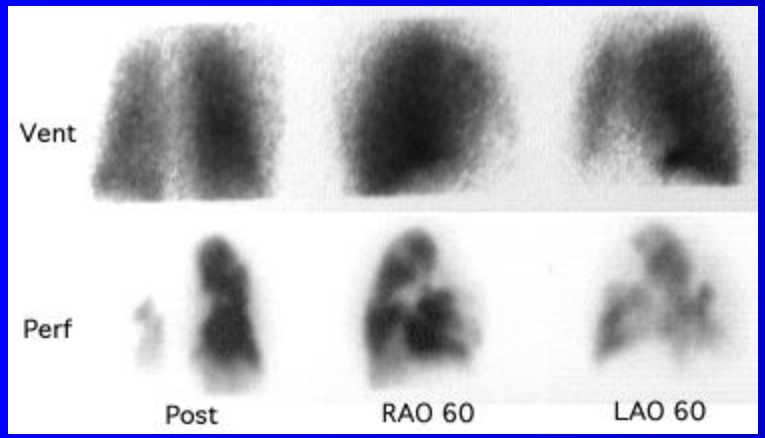
Adapted from Gaine, et al. *JAMA* 2000.

SLE: Pulmomary arterial hypertension

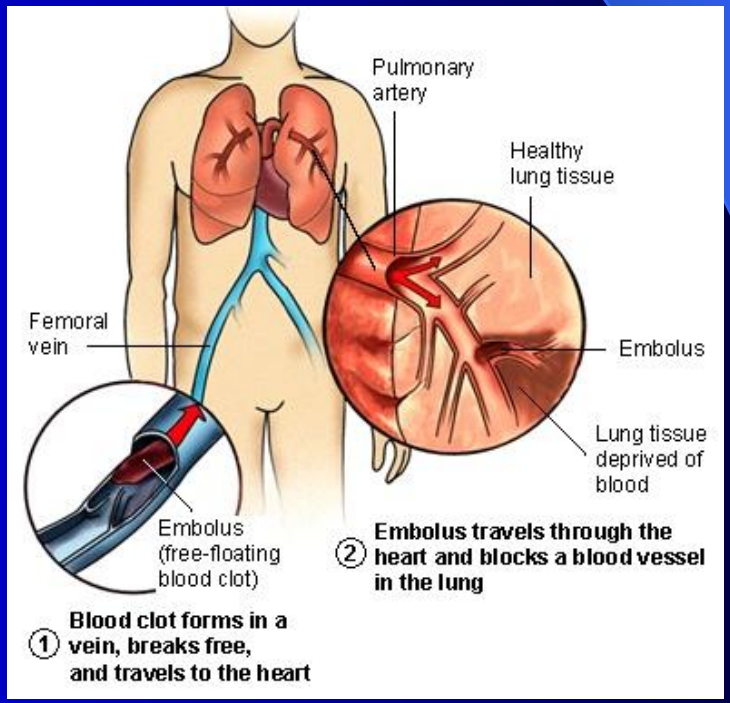
- Type I:
  - Inflammatory vascular disease
  - Reversible with aggressive immunosuppression (Cyclophopshamide and corticosteroids)
  - No way presently to distinguish from chronic Scleroderma-like vascular disease excpet possibly presence of RNP antibodies or cutaneous manifestations of scleroderma
- Type II:
  - Chronic venous thromboembolic disease (CTEPH)
  - Treatment includes anticoagulation along with:
    - Surgical thrombectomy
    - Adempas (riociguat) for inoperable CTEPH
- Type III:
  - Scleroderma- spectrum PAH
  - Treatment:
    - Supplemental O2
    - Treat associated interstitial lung disease or sleep apnea
    - Meds:
      - Endothelin antagonists
      - Prostanoids
      - Adempas
      - 5' PDE inhibitors

SLE: Pulmomary embolus

- Blood clot in the lung
  - Interferes with blood flow through part of the lung
  - If clot is large enough can cause massive vascular collapse and sudden death
  - Triggers:
    - Stasis
    - Tramua (surgery)
    - Malignancy
    - Hypercoaguable states (APLS)



- Diagnosis
  - Clinical:
    - Acute dyspnea, pleuritic chest pain, low BP
  - ECG:
    - S1, Q3,T3
  - V:Q scan or CTA



Lupus Cardiopulmonary Disease

- Numerous potential disease manifestations
- Difficult clinically to sort out causality without diagnostic testing
- Very important to get to the root of the problem as long term outcome and treatment options are variable among diagnoses
- Questions

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