DDx

Extrathoracic

- NM Disease (refer)
- Thoracic Disease (refer)
- Pleural Disease (refer)

Intrathoracic

- Alveolar Disease (refer)
  - Alveolar Hemorrhage
  - Alveolar Proteinosis
  - Alveolar Edema
- Interstitial Lung Disease (ILD)
  - Mechanism: Insult to alveolar septal interstitium → fibrosis → decreased compliance and increased elasticity → decease in ALL lung volumes and decrease in diffusion → V/Q mismatch → vasoconstriction → dyspnea, non productive cough, fatigue, dry crackles/rales, pulmonary HTN → cor pulmonale, clubbing, cyanosis
  - Can be acute/subacute/chronic
  - Most ILDs are idiopathic but it is important to try to find a cause b/c it offers the best chance for Tx
  - Imaging: in general rarely diagnostic, 15% normal, CXR: interstitial changes (reticular/nodular/honeycombing vs HRCT: interstitial changes (ground-glass opacities), late findings include traction bronchiectasis
  - Transbronchial/Surgical Bx is often necessary to make Dx
  - Idiopathic
    - **Idiopathic Pulmonary Fibrosis (IPF), Interstitial Pulmonary Fibrosis (IPF), Usual Interstitial Pneumonitis (UIP)**
      - Epidemiology: old male smokers
      - CXR: usually peripheral lower lobe dz, bibasal/subpleural opacities
      - S/S: insidious Sx, no extra-pulm involvement
      - Dx: DOE, biopsy (spatially and temporally heterogenous pattern of fibrosis interspersed w/ normal lung = "fibroblastic foci"), NB any end stage diffuse lung disease can look like IPF
      - Tx: distinctly poor response to Tx including steroids/immunosuppressants (consider IFN, NAC, Bosentan, Imatinib) and prognosis compared to other ILDs w/ 50% mortality at 3yrs w/ only Tx being transplant
    - **Cryptogenic Organizing Pneumonia (COP) aka Bronchiolitis Obliterans w/ Organizing Pneumonia (BOOP)**
      - Epidemiology: old women
      - Mech: ILD that looks/acts just like an infectious pneumonia but no localized infection or response to antibiotics, 2/2 viral infection, medications, CTDs, radiation, inhalational toxins, etc but most are idiopathic (said to represent 25% of all chronic infiltrative lung diseases)
      - S/S: subacute ILD w/ significant systemic Sx
      - Dx: differentiate from IPF by the presence of neutrophils/lymphocytes on Bx/BAL, no diagnostic CXR/HRCT but often bilateral consolidation picture
      - Tx: spontaneous recovery or steroids
    - **Lymphangioleiomyomatosis (LAM)**
      - Mech: sporadic (or associated w/ tuberous sclerosis esp w/ renal angiomyolipomas) proliferation of smooth muscle cells
      - Epidemiology: young women
      - Complications: recurrent spontaneous PTX (often presenting Sx), hemoptysis, chylous effusions, atypical cp
      - CXR/CT: above but paradoxic hyperinflation and cysts
      - Tx: progesterone hormone but slowly progressive requiring lung transplant, b/c of recurrent PTX consider pleurodesis
    - **Pulmonary Langerhan's Cell Histiocytosis X**
      - Mech: abnormal proliferation of abnormal Langerhan's Cells aka Histiocytes and can be associated w/ systemic diseases (Letterer-Siwe Dz and Hand-Schuller-Christian Syndrome)
      - Epidemiology: young smoker
      - Complications: spontaneous PTX, lytic bone disease, diabetes insipidus
      - Dx: abnormal histiocytes containing intracellular Birbeck Granules on Bx

- CXR/CT: cysts/nodules in mid/upper zones, classically there is lack of disease at costophrenic angles
- Tx: variable course if severe steroids and lung transplant

▪ **Chronic Eosinophilic Pneumonia**
- Mech: eosinophilic infiltration of interstitium + eosinophilia
- Types
  - Primary (Simple aka Loeffler's Syndrome from Ascaris lumbricoides, Acute, Chronic)
  - Secondary (Drugs, Parasite, Fungal, Vasculitis, ABPA, Asthma)
- Tx: responds to steroids but relapses occur 75% of chronic cases
- Complications: hypereosinophilic syndrome (peripheral eosinophilia infiltrates other organs esp heart causing damage)

▪ **Diffuse Aveolar Hemorrhage**
- 2/2 Good Pasteure's, Wegener's, Churg-Straus, Idiopathic Pulmonary Hemosiderosis, CHF Hemorrhage

▪ **Pulmonary Alveolar Proteinosis**
- Mech: rare accumulation of surfactant/phospholipids in alveoli and septum, primary or in association w/ hematologic malignancy or autoimmune dz
- Epidemiology: adult males
- CXR: bat-shaped alveolar infiltrates in middle zones
- Dx: anti-GM-CSF
- Tx: periodic lung lavage, granulocyte colony stimulating factor infusion, NO steroids b/c pts are at increased r/o infection
- Complications: unusual infections w/ Nocardia, MAC, PCP

▪ **Nonspecific Interstitial Pneumonia (NSIP)**
- similar to IPF but younger pts, better prognosis
- Tx w/ steroids

▪ **Desquamative Interstitial Pneumonia (DIP) and Respiratory Bronchiolitis Associated Interstitial Lung Disease (RB-ILD)**
- Seen in young male smokers
- BAL shows pigmented macrophages
- Tx: steroids

▪ **Acute Interstitial Pneumonia (AIP) aka Hamman-Rich Syndrome**
- Acute dz that progresses to respiratory failure over 2wks
- Systemic Sx + ILD then Sx that looks like ARDS
- Tx: steroids but 75% die w/in 2mo

▪ **Lymphoid Interstitial Pneumonia (LIP)**
- Very rare
- Seen in women
- ILD Sx w/ systemic Sx
- BAL reveals lymphocytes looking like lymphoma
- Associated w/ underlying autoimmune dz esp Sjogren's or immunodeficiency esp HIV

o Systemic

▪ **Sarcoidosis**
- Multisystem chronic non-caseating granulomatous disease of unknown etiology possibly infectious (NB transmission has occurred in heart/bone transplants)
  - Pulmonary (100%): ILD
  - MS (50%): arthralgia
  - General (30%): constitutional Sx
  - Derm (25%): erythema nodosum, apple butter plaques, subcutaneous nodules
  - Ophtho (25%): uveitis w/ blindness (most common cause of morbidity), conjunctivitis
  - GI (25%): infiltrative liver dz, parotid swelling
  - Heme (25%): cytopenias, palpable LNs
  - CV (5%): arrhythmias (most common cause of mortality)
  - CNS (5%): Bell's Palsy, optic nerve dysfxn, papilledema, peripheral neuropathy
  - NB renal/GI/GU is rare

        - NB Lofgren's Syndrome (acute onset, mainly Caucasians, S/S: F + bilateral hilar LAD + EN + Arthralgia, resolves on own w/o Tx in 90% of cases), Heerfordt's Syndrome (F + Uveitis + Parotid Enlargement + Bell's Palsy)
    - Epidemiology: young black & northern European females, smoking is protective, very unique clustering in certain occupations (nurses, firefighters, etc), first responders to World-Trade Center bombing resulted in a sarcoid like illness
    - Dx
        - Clinical
        - Bx (non-caseating granulomas and exclusion of other causes, in some cases you don't need to do a Bx if S/S/imaging is clear)
        - CXR (Siltzbach): Stage 0 (normal, seen in 10% of pts!!!) → Stage 1 (bilateral hilar/mediastinal LAD) → Stage 2 (bilateral hilar LAD + interstitial infiltrates, 50% of pts) → Stage 3 (interstitial infiltrates) → Stage 4 (fibrosis)
        - Skin Anergy (False Negative PPD 2/2 depressed T lymphocyte fxn)
        - High ACE Level (neither sensitive nor specific)
        - High VitD Levels
        - BAL (lymphocytosis)
        - Lymphopenia/Eosinophilia
        - Always check a CXR, PPD, EKG, Ophtho exam, PFTs
    - Tx: most resolve spontaneously in 2yrs and thus require no Tx but if symptomatic OR critical organ involvement (CV, CNS, Eye, Hypercalcemia/uria, Stage 2/3 CXR) then Tx w/ systemic corticosteroids (30mg/d x2mo then taper over the next 10mo), hydroxychloroquine, methotrexate, anti-TNF, etc
- Autoimmune: **SLE, RA, SS, Sjogrens, PM/DM, AS, Vasculitis**
- Cancer
    - **Psuedolymphoma**
    - **Pulmonary Lymphoma**
    - **Lymphoid Granulomatosis**
    - **Lymphangitic Carcinomatosis**
- Other: **Amyloid**

o <u>Exposure</u>

- Inorganic Dusts (Pneumoconiosis)
    - **Asbestos** (used as a fire-retardant, exposure during mining/manufacturing, shipbuilding/repairing, building construction, etc, parietal pleural thickening w/ plaques at base w/ lower lobe ILD, r/o malignant lung cancer and mesothelioma, complication: bronchogenic carcinoma)
    - **Silicosis** (found in mining, stone cutting, glass manufacturing, etc, acute vs chronic disease, increased r/o TB (hence if pt also has a fever then check for TB), but no increased r/o cancer, localized upper lobe / peribronchial nodular fibrosis w/ eggshell calcifications of hilar LNs)
    - **Beryllium** (found in power plants, ceramic industry, etc, acute vs chronic disease similar to sarcoid)
    - **Aluminum**
    - **Titanium**
    - **Cobalt**
    - **Coal**
- Organic Particles (Hypersensivity Pneumonitis, acute flu-like illness vs chronic ILD, check serum precipitin Ab)
    - Fungi (**Aspergillus, Actinomycetes, Alternaria, Cladosporium, Aureobasidium spp.**) most common
    - Bacteria (**Thermophilic spp**. aka Farmer's Lung, Humdifier Lung, Hot-Tub Lung, etc)
    - Mycobacteria (**Atypical spp**.)
    - Amoeba (**Naegleria, Acanthamoeba spp**.)
    - Animal/Insect Proteins
        - **Avian Droppings/Feathers/Serum** aka Bird Breeder's Disease
        - **Mammal Pelts/Urine/Serum** aka Animal Handler's Disease
- Chemical
    - **Isocyanates**
    - **Trimellitic Anhydride**
    - **Copper Sulfate**
- Drugs
    - Chemo (**Bleomycin, Busulfan, Methotrexate**)

        - Abx (**Nitrofurantoin, Sulfa**)
        - CV (**Amio, Hydralazine**)
        - NSAIDs (**Gold, Penicillamine**)
        - Recreational (**Cocaine**)
    - Radiation