Pulmonary Complications of Illicit Drugs and Prescription Medications

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Disclaimer: Nothing in this presentation specifically reflects the opinions of my employer

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Other Training/Previous Experience

-One of roughly 50 RTs with the right amount of crazy to earn all of the NBRC specialty credentials

-One of the editors of *Oakes' Respiratory Care Pocket Guide*, 10th Edition

-Cross-trained in cardiac ultrasound

-Former flight respiratory therapist

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-Former EMS supervisor and clinical instructor

-Fellow, Royal Anthropological Institute of Great Britain and Ireland (FRAI)

-Former deputy coroner

-Host of forensic science/true crime podcast (“The Skelecast”)

-Mediocre guitarist

CAUTION:

The following presentation contains attempts at humor, sarcasm, and various historical and pop culture references

Viewer discretion is advised.

Outline

-Substances Associated with Pulmonary Complications

-Mechanisms of Action

-Treatment Options

Sources of Complications

About 300+ medications or drugs of abuse have some form of primary or secondary pulmonary disease described as a complication (Taylor et al, 2016)

Sources of Complications

(Un)fortunately, this means we only have time to get into a few examples substances in any real detail

Me: I promise to not go overboard explaining this stuff

Three drinks later:

Sources of Complications

-Antineoplastic agents (bleomycin)

-Antiarrhythmics (amiodarone)

-Illicit drugs/associated adulterants

-Anti-tuberculars (isoniazid)

Sources of Complications

-Antibiotics (nitrofurantoin)

-Antiparasitics (levamisole)

-Sulfa drugs

-Aspirin

Sources of Complications

-Antihypertensives (ACE inhibitors, beta-blockers)

-Immunosuppressants/Immune modulating agents

-Anticonvulsants

Sources of Complications

-Antipsychotics (chlorpromazine)

-Capoten

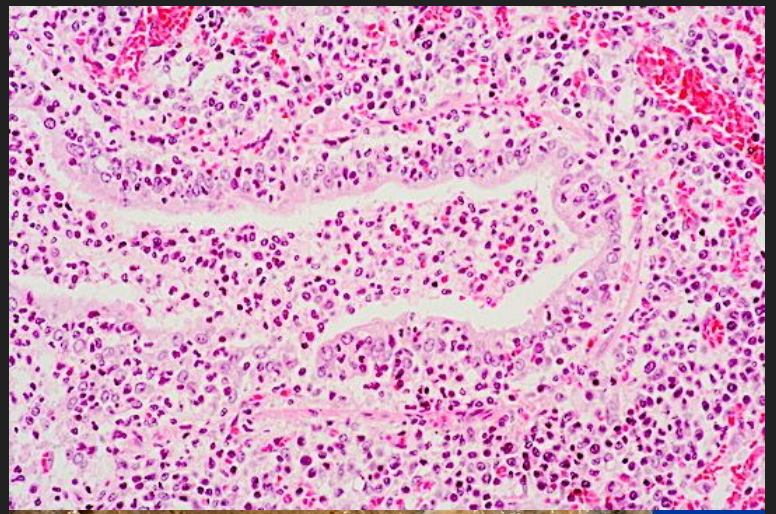
-Methyldopa

-Sulfasalazine: used for rheumatoid arthritis

Mechanisms of Action

-Allergic (asthma, eosinophilic pneumonia, hypersensitivity pneumonitis)

-Inflammation of bronchial mucosa (with or without scarring)

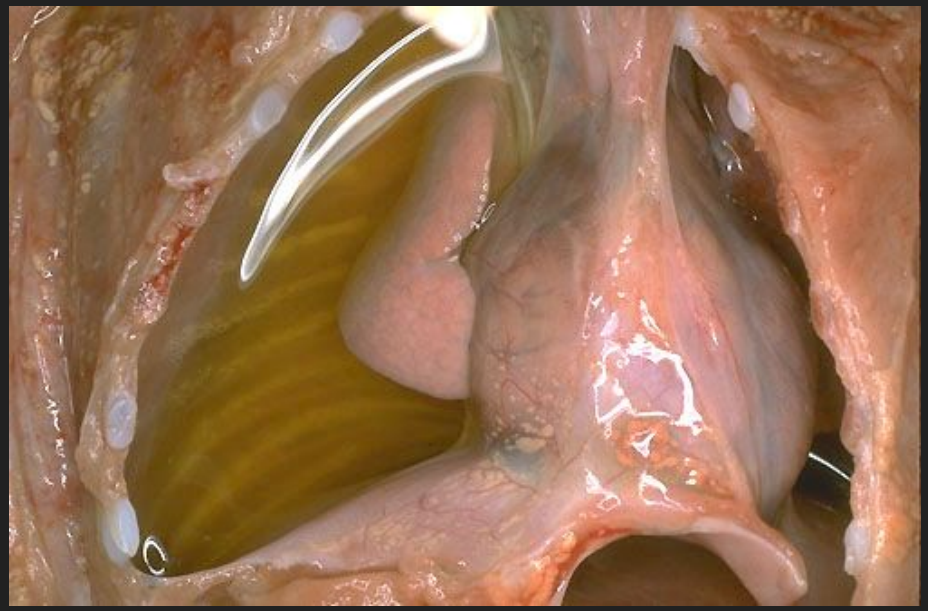


Mechanisms of Action

-Pulmonary edema

-Pleural effusion

-Mediastinitis



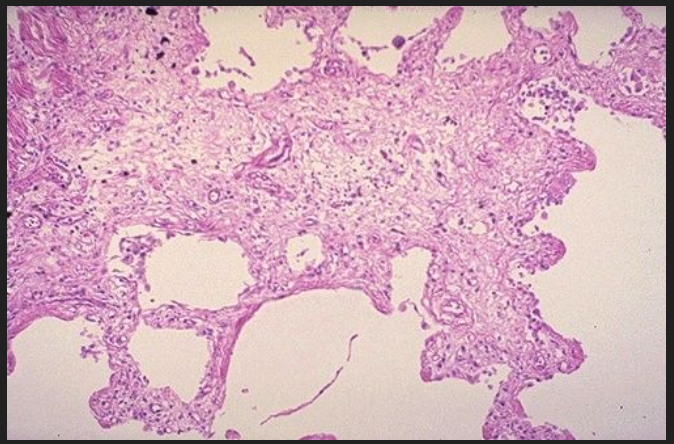
Autopsy and histology images courtesy of WebPath unless otherwise noted

Mechanisms of Action

-Pulmonary vasculitis

-Interstitial fibrosis

-Cytotoxic effects upon pneumocytes



Mechanisms of Action

-Alveolar hemorrhage (uncommon)/hemorrhagic pulmonary infarct (rare)

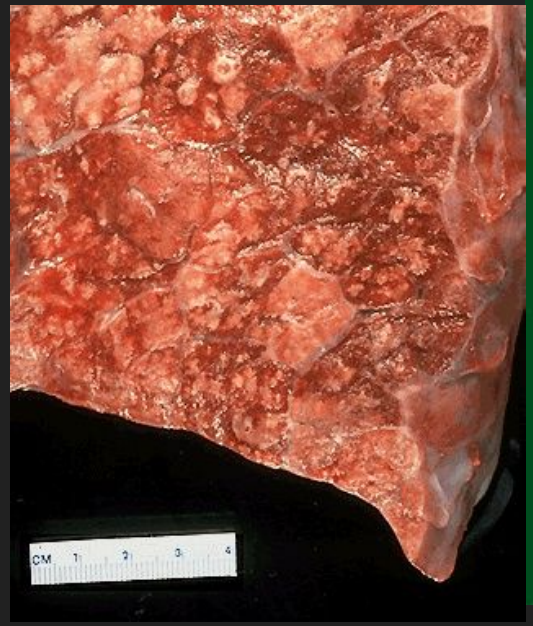
-Drug induced autoimmune responses (drug induced lupus)

Mechanisms of Action

Drug induced autoimmune responses (drug induced lupus)

Mechanisms of Action

-Infectious complications



Antineoplastics

-Bleomycin

-Cyclophosphamide

-Methotrexate

Chemotherapeutic Agents

-Chemotherapeutic driven complications often present with a fever mimicking an infectious process

-About 10-20% present with pulmonary infiltrates

-Often fatal even if it is caught early

Chemotherapeutic Agents

-Some present with a cytotoxic effect
-Can produce microangiopathic hemolytic anemia (presenting as pulmonary edema)
-Or eosinophilic pneumonitis
-Or granulomatous reactions
-Can also kill, alter, or impair type I and type II pneumocytes

QUIZ TIME!

QUESTION FOR STUDENTS:
What form of pulmonary pathology is shown as an example at right?

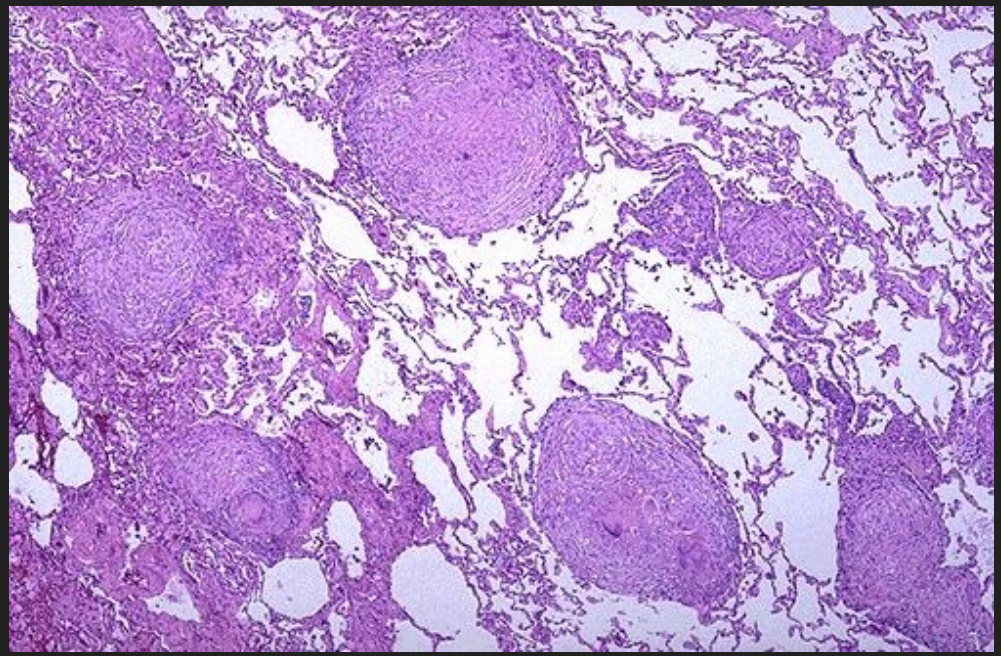
QUIZ TIME

BONUS QUESTION FOR STUDENTS:

What disease is shown as an example at right? (Not a drug complication but it can be related to this discussion!)

Ever wondered...

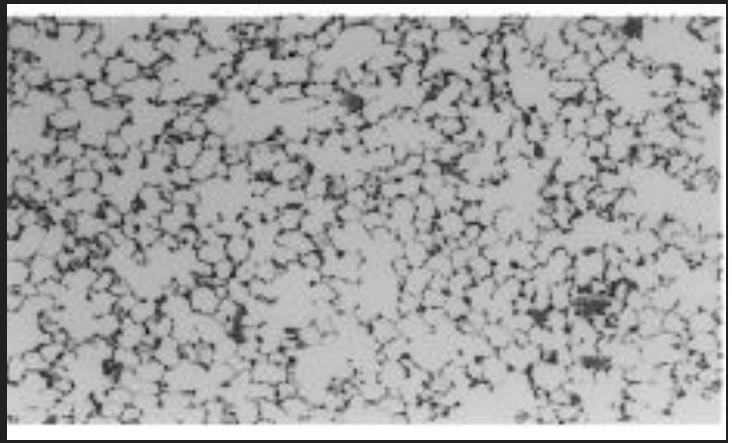
…why you get a reticulonodular pattern on a chest x-ray? This is what the tissue looks like magnified

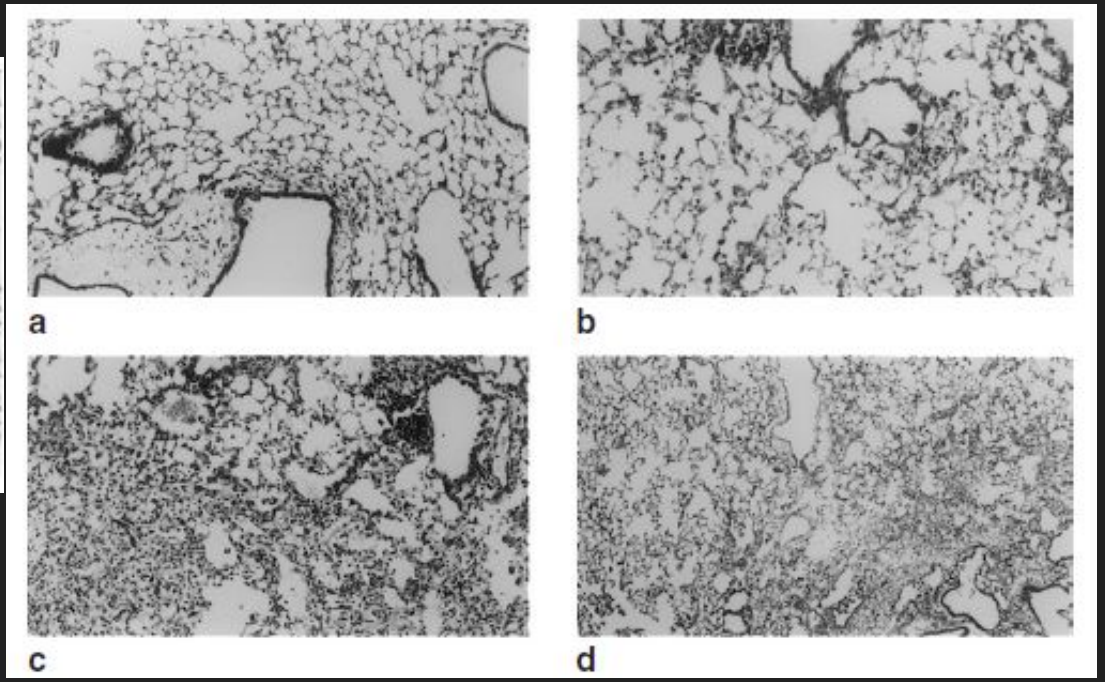


Bleomycin

-Pulmonary fibrosis (fibrosing alveolitis)
-About 10% of people receiving bleomycin
-Main limiting factor in utility of the medication
-Can also cause organizing pneumonia (formerly BOOP)

Bleomycin fibrosis progression (mouse model- 3, 6, 14, 21 days)





Source: Izbicki et al. Int J. Exp Path (2002) 83:111-119

Bleomycin

-Unclear pathogenesis (oxidative damage, deficiency in deactivating enzyme, genetics, inflammatory cytokine release, etc?)

-Higher risk in older patients, renal insufficiency, multi-drug chemotherapy, concomitant radiation therapy, smoking

Bleomycin

-High FiO_2 can cause acute respiratory failure and ARDS in patients previously given bleomycin

-Perioperative protocol was developed using minimal O_2 exposure and judicious IV fluid replacement and this greatly reduced complications

Bleomycin

-Keep in mind “high” is a relative term

Cases have been reported with FiO2 of 33%

Data is inconsistent on how widespread oxygen sensitization is

Bleomycin

-Hypersensitivity pneumonitis is less common but possible

Hypersensitivity pneumonitis presentation

Early stages of acute (inflammatory) variant may be misinterpreted as “asthma” until CXR, CT, and/or PFTs are done (especially in kids)

Coughing, chest tightness, dyspnea, leukocytosis, myalgia, and fever

Eosinophilia on BAL or biopsy

Hypersensitivity pneumonitis presentation

Chronic (fibrotic) form:
Progressive exertional dyspnea, fatigue, cough (often productive), weight loss, basilar crackles, digital clubbing

Restrictive pattern with decreased DLCO

Hypersensitivity Pneumonitis CXR

MAY BE NORMAL OR VARY DURING COURSE

-Numerous poorly defined small (<5 mm) opacities throughout both lungs, sometimes with sparing of the apices and bases

-Airspace disease: usually seen as ground-glass opacities (can be patchy or diffuse, resembling pulmonary edema) or, more rarely, as consolidation

-Pattern of fine reticulation (“lace lung”)

Hypersensitivity Pneumonitis CXR

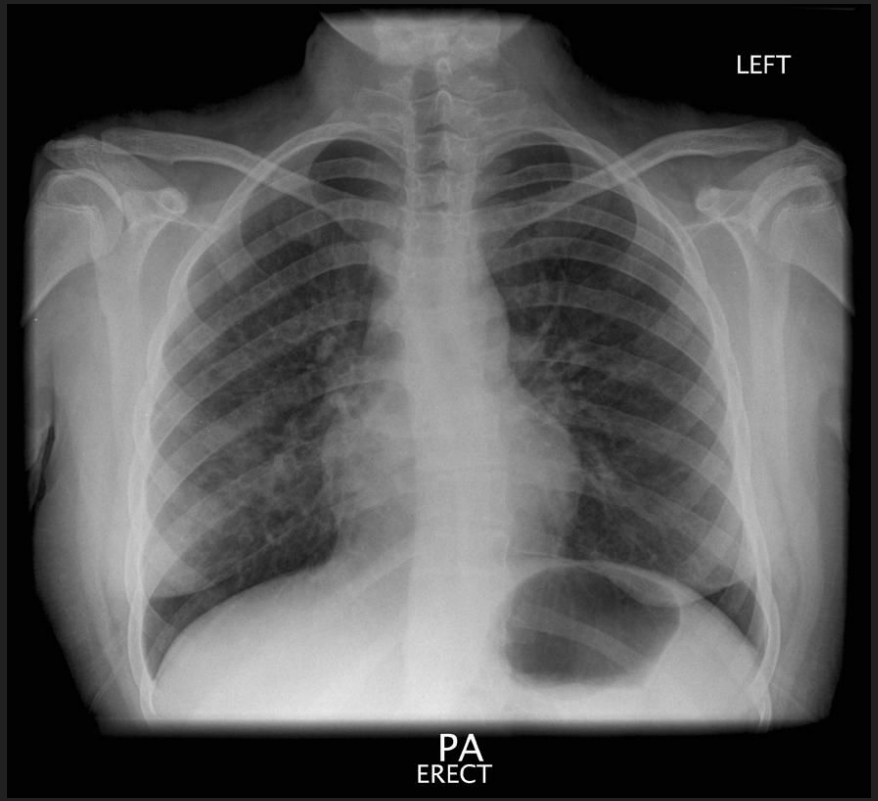
LATE FINDINGS

-Cardiomegaly (cor pulmonale)

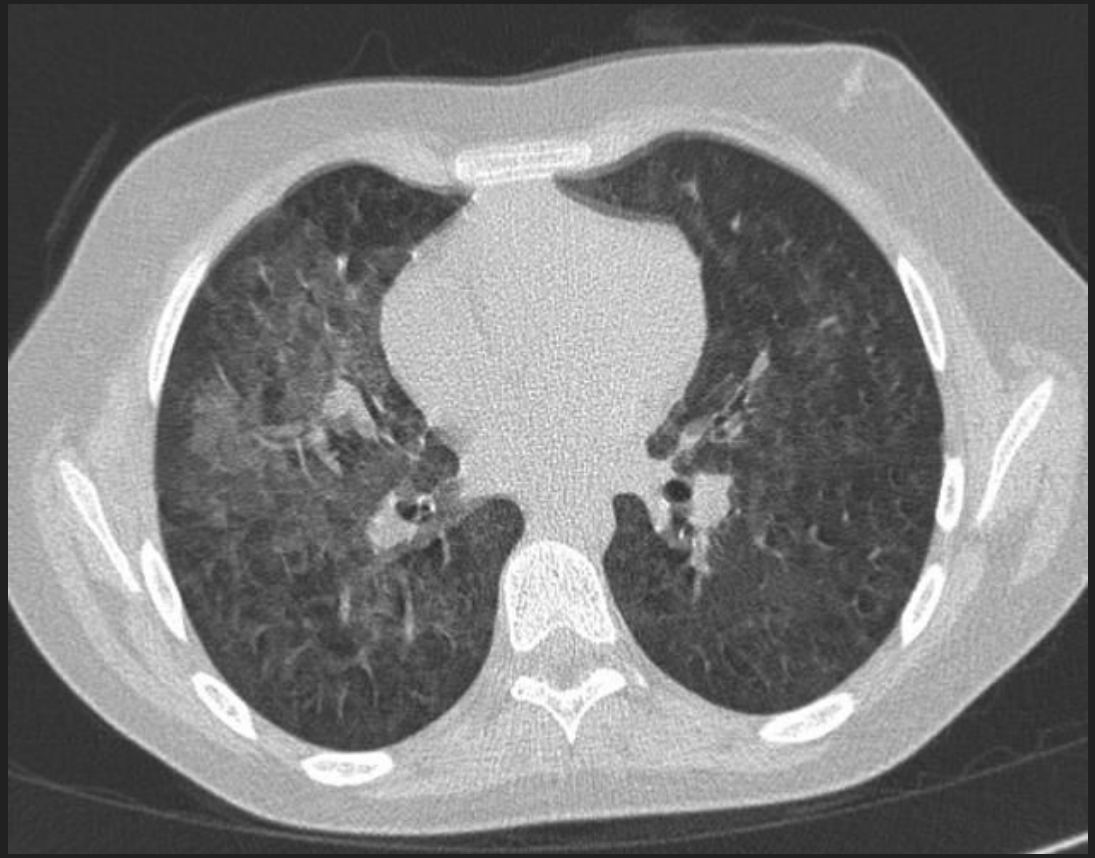
-Honeycombing from fibrosis (usually upper > than lower); ground glass on CT

-Peribronchial thickening

Hypersensitivity Pneumonitis CXR



Hypersensitivity Pneumonitis CT

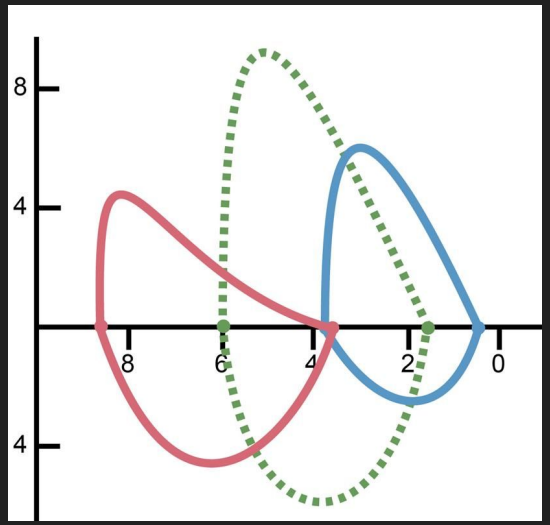


Screening/Monitoring

-Screening PFTs including DLCO on ALL patients receiving bleomycin for comparison with baseline values

-Optimum frequency remains debated

-After every two to four cycles of therapy is a common recommendation



Treatment (Hypersensitivity)

-Permanent and immediate discontinuation of bleomycin upon symptoms or significant alterations in screening PFTs

-Glucocorticoids for symptomatic patients

AFTER INFECTION IS RULED OUT

Methotrexate (MTX)

-Antimetabolite used against a number of cancers
-Induces intracellular deficiency of folate derailing DNA and RNA synthesis (among other things)
-Has antiinflammatory and immunomodulating properties
-Also used to treat psoriasis, RA, Crohn's, MS, and autoimmune diseases

Methotrexate (MTX)

-Pulmonary toxicity usually happens weeks to months into a low-dose oral dosing schedule

-Can happen more rapidly if doses are increased or route is intravenous or intrathecal

-Happens in about 1-8% of patients taking MTX for rheumatoid conditions

Methotrexate (MTX)

Risk factors for pulmonary complications:

-Age >60 years

-Existing rheumatoid effects on pleura or lungs

-Previous or concomitant use of other antirheumatic meds

-Hypoalbuminemia (pre-existing or during therapy)

-Diabetes

Methotrexate (MTX)

Low levels of albumin result in reduced protein binding and thus higher circulating levels of free methotrexate

Hyperinsulinemia alters the metabolism of methotrexate

Methotrexate (MTX)

Other risk factors

-Higher or more frequent doses

-Preexisting lung disease/abnormal baseline PFTs

-Renal insufficiency, ascites, etc (reduced elimination of MTX)

-Possible genetic factors

Methotrexate (MTX)

-Three major types of pulmonary complications:
Inflammatory: Hypersensitivity pneumonitis (most common complication)
-Organizing pneumonia (formerly BOOP)
-Pulmonary fibrosis (often rapid onset and progression)
-Interstitial pneumonia and pulmonary edema
-Pleuritis and pleural effusion (rare)

Methotrexate (MTX)

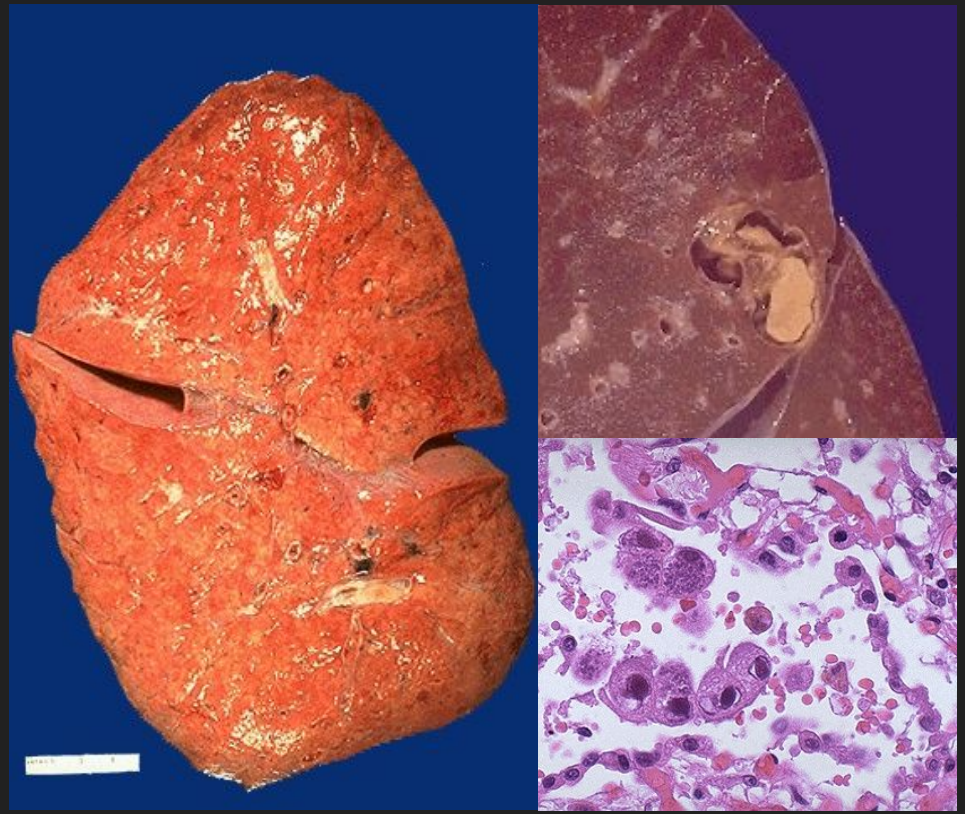
Hypersensitivity pneumonitis

Basically same pattern and treatment as any other hypersensitivity pneumonitis

Methotrexate (MTX)

Infectious: an "indirect" complication

May involve unusual or opportunistic pathogens (*P. jirovecii*, CMV, VZV, *Nocardia*, mycobacteria, *Aspergillus*, etc)



Methotrexate (MTX)

Lymphoproliferative: such as non-Hodgkin (B-cell) and other lymphomas

-Usually regress or go into remission after methotrexate is discontinued

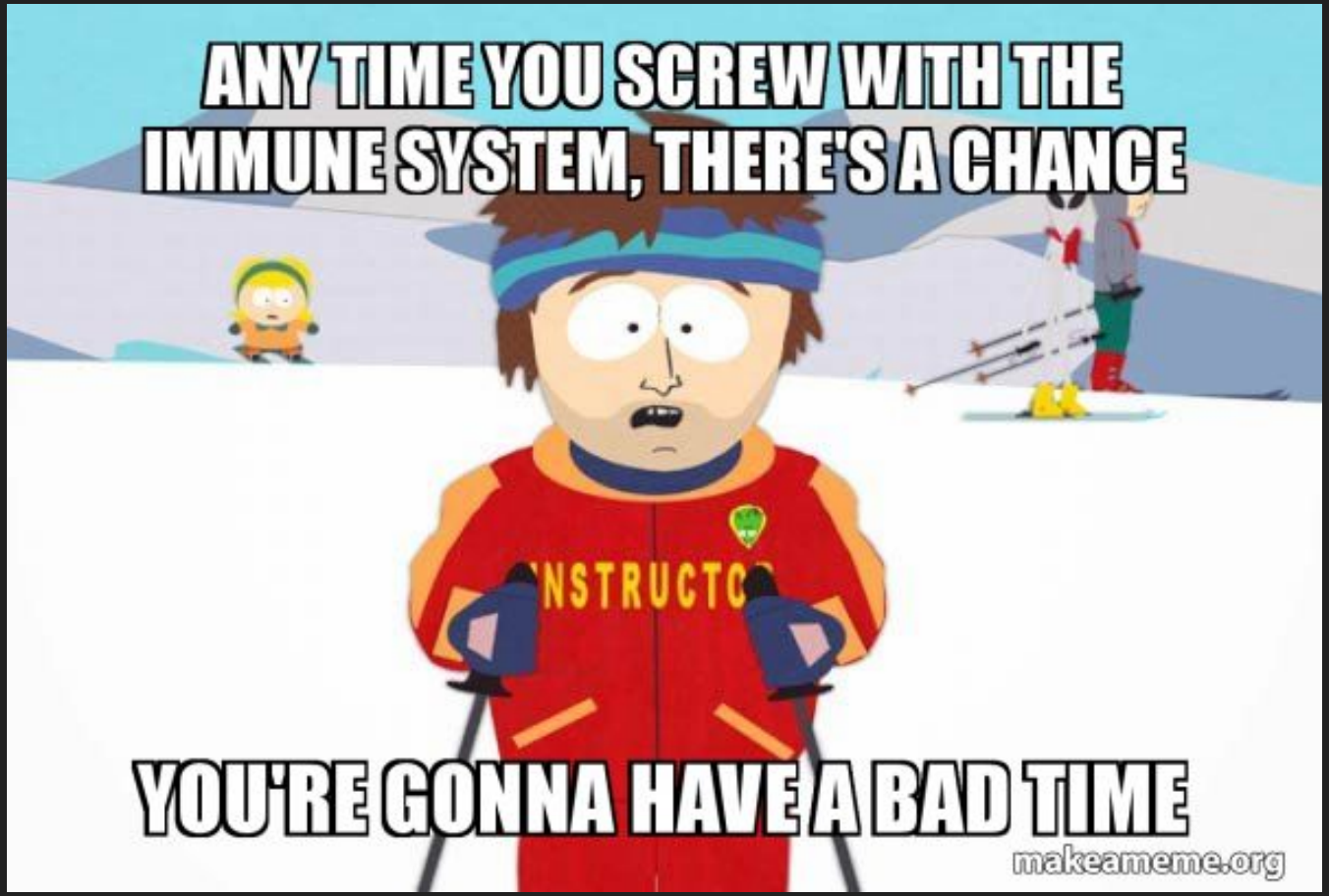
-May be result of suppressed immune surveillance and/or EBV infection

Methotrexate (MTX)

Lung and/or pleura is often not the primary target in MTX related lymphoproliferative states (only 8-21% of cases)

Immunosuppressants and Immune modulating agents

-Direct effects
-Autoimmune complications
-Infection due to the immunosuppression
-Graft rejection
-Lymphoproliferative states (leukemia, lymphoma, monoclonal gammopathies (primary amyloidosis))


ANY TIME YOU SCREW WITH THE IMMUNE SYSTEM, THERE'S A CHANCE
YOU'RE GONNA HAVE A BAD TIME
makeameme.org

“The only thing more difficult than spelling the generic name of a rheumatoid arthritis medication is untangling all its potential complications”

Cardiovascular Medications

-Amiodarone (fibrosis)- roughly 6% of patients taking it

-ACE inhibitors (chronic cough)- about 15% of patients

-Hydralazine (drug induced SLE)

-Procainamide (drug induced SLE)

-Quinidine (drug induced SLE)

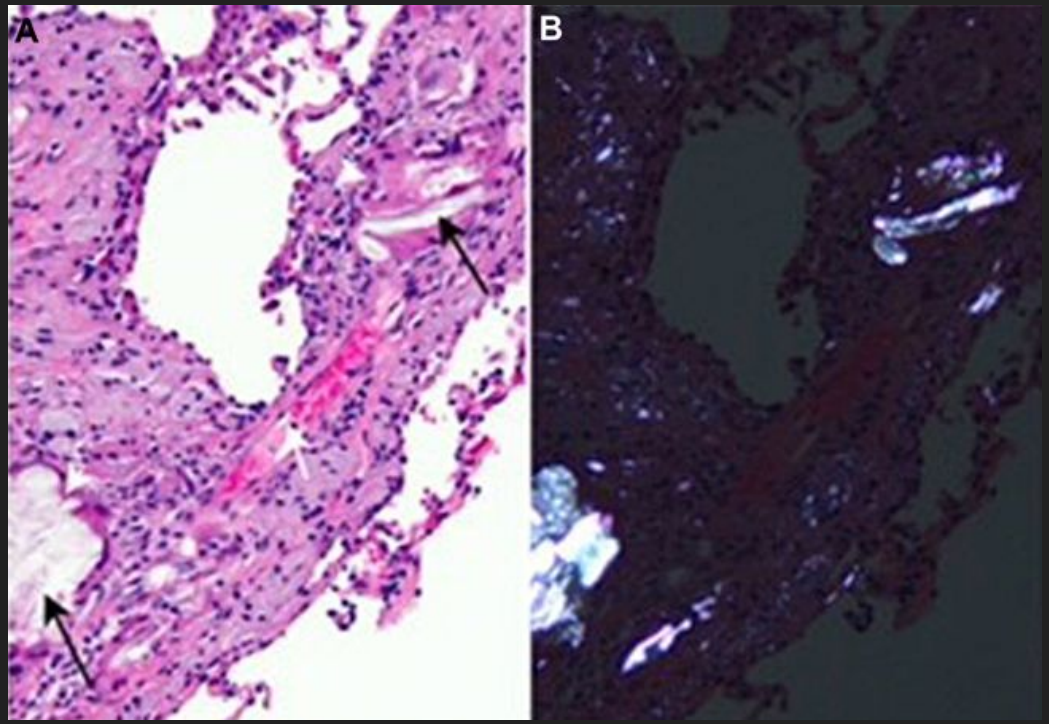
Illicit Drugs

-Often caused by adulterants: the substances the drugs are mixed (cut) with

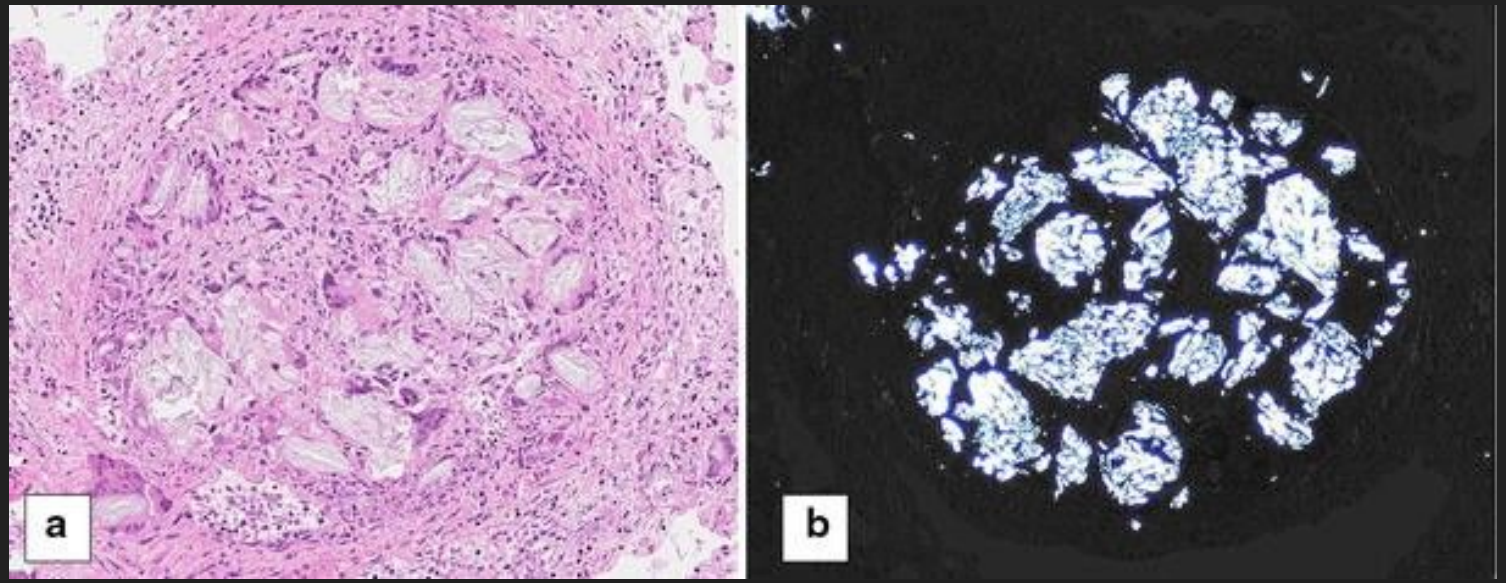
-Talc

-Levamisole (withdrawn antiparasitic medication that is commonly is found cut into cocaine (60-80%); can trigger drug induced SLE or induce agranulocytosis, neutropenia, or vasculitis)

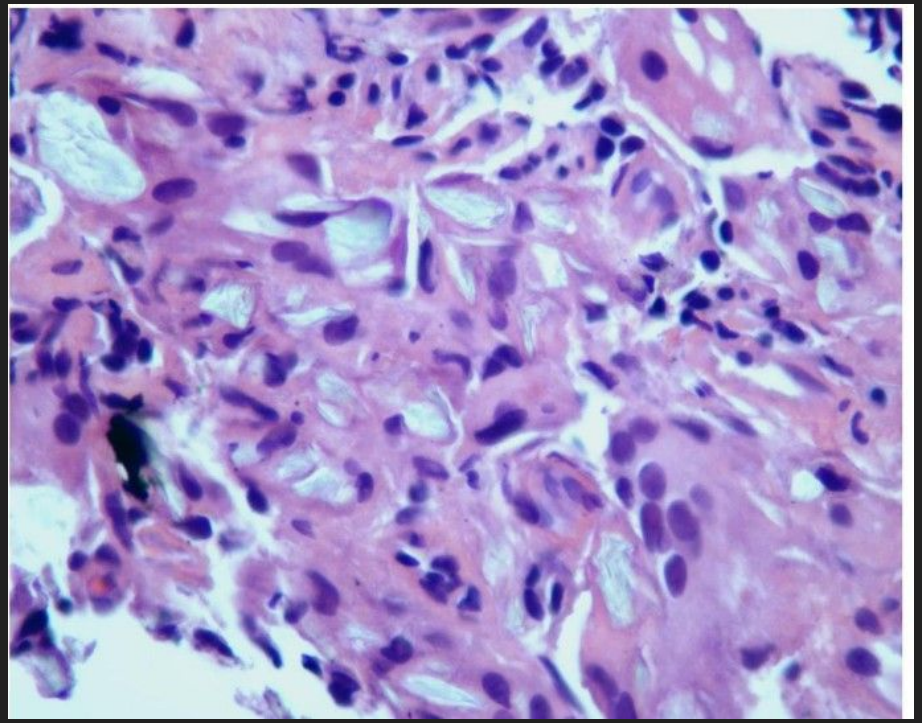
QUIZ: Unusual Pulmonary Emboli



Talc Granuloma



Talc Granuloma



Antibiotics

-Nitrofurantoin

-Sulfa drugs

-Isoniazid

-Minocycline

Antibiotics

Nitrofurantoin is the most common cause

-Acute onset of dyspnea with cough and fever

-Often resolves rapidly with discontinuation

-Can progress to a syndrome mimicking idiopathic interstitial pneumonitis and fibrosis

-The way to differentiate is that the condition improves with discontinuation and corticosteroids

Aspirin

-Aggravation of symptoms in about 5% of asthmatics

-Non-cardiac pulmonary edema in higher doses (>35-40 mg/dL levels)

-A “pseudosepsis” syndrome

Aspirin “Pseudosepsis”

Fever, hypothesis, reduced SVR, leukocytosis (increased bands), etc

Multiple organ system failure: ARDS, encephalopathy, DIC, renal failure

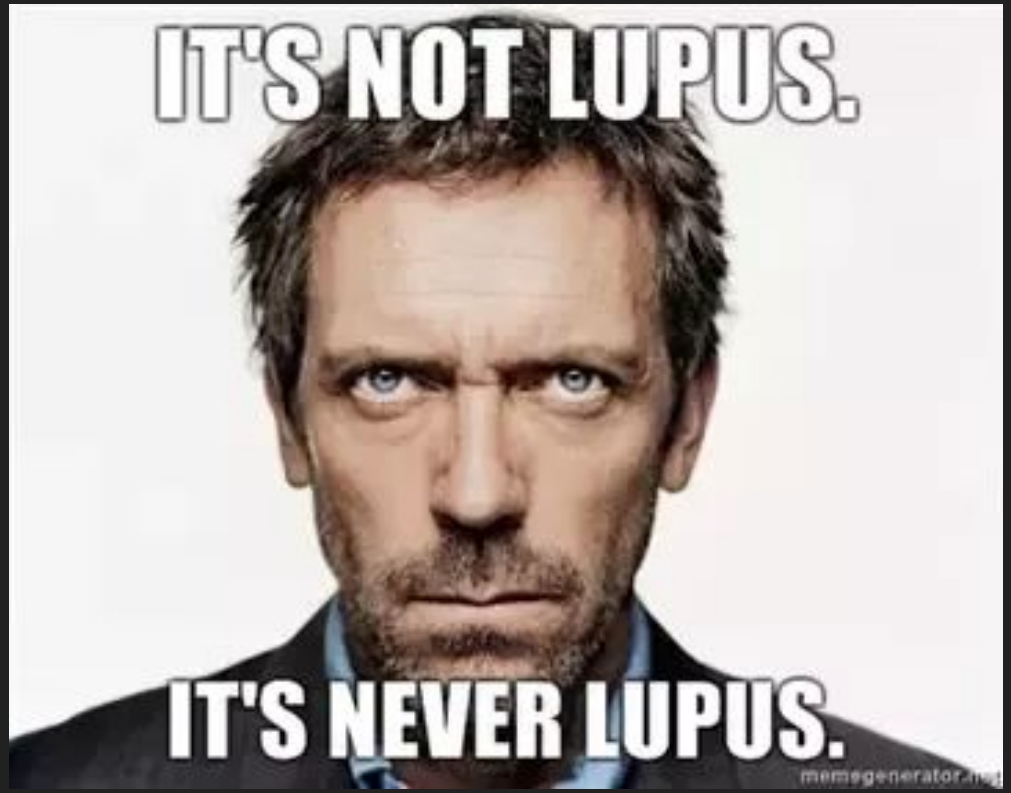
Aspirin “Pseudosepsis”

Can occur with chronic or acute overdose

Overdose recognition is commonly delayed or completely missed (until toxicology at autopsy)

Miscellaneous

Anticonvulsants (SLE)
Capoten (SLE)
Chlorpromazine (SLE)
Methyldopa (SLE)
Sulfasalazine (SLE)- used for rheumatoid arthritis



Except when it is....

Skin rash - malar or discoid

Sensitivity to light (photodermatitis; worsens aforementioned rash)

Serositis - inflammation of serosal surfaces along with effusions

Glomerulonephritis - the worst problem with SLE

Cytopenias - anemia, leukopenia, thrombocytopenia

Arthralgias, myalgias

Vasculitis - anywhere: CNS, skin, kidney, etc

Decreased serum complement - especially C1q

Thrombosis - in arteries or veins

Drug Induced Lupus

-Usually happens after at least 3 months on a medication

-Can produce a wide range of pulmonary issues

Drug Induced Lupus

-Pleural effusions
-Reactive airway disease
-Vasculitis
-Pulmonary emboli
-Interstitial lung disease
-Pulmonary hypertension
-Infectious complications
-Diffuse alveolar hemorrhage
-Acute lupus pneumonitis

Drug Induced Lupus

-Treatment is dependent upon presentation (disease is very heterogeneous)

-Pulmonary hypertension associated with SLE tends to have a better prognosis that from other causes

-Immunosuppressant treatments for SLE carry their own risk of pulmonary complications


WOULD YOU LIKE TO KNOW MORE?

Contact Information

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