Pulmonary Pearls For The Internal Medicine Boards

ACP Internal Medicine Board Review Course

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Case 1: 65 year-old woman

History	Two days of cough, fever and dyspnea several days after a 4-night hotel stay for a convention Review of systems: (+) for diarrhea
Exam	BP 98/73 mm Hg S_pO_2 92% breathing air Right axillary crackles
Labs	Sodium 128 mEq/L Creatinine 1.3 mg/dL
Imaging	Right lower lobe opacity

A Question

Which of the following is the preferred diagnostic test in this situation?

1. Cold agglutinins
2. Modified sputum acid-fast stain
3. Polymerase chain reaction (PCR)
4. Routine sputum gram stain and culture
5. Urinary antigen studies

Clues To The Diagnosis Of Atypical Pneumonia

Organism	Epidemiology	Key Features
Legionella	**Exposure**: hotels, cruise ships **Host issues**: smoker, chronic lung disease, immunosuppressed	**GI Symptoms**: diarrhea **Labs**: Hyponatremia **Gram's stain**: many PMNs, no organisms
Mycoplasma	School-aged children Military recruits College students	Erythema multiforme Hemolysis with cold agglutinins

Other Infectious Pneumonias To Consider

Organism	Key Point
Pneumocystis	Diffuse bilateral opacities; HIV or risk factors for the disease; high dose steroids
Cryptococcus	Can cause pneumonia in immunocompetent patients
Nocardia	Extrapulmonary dissemination common (e.g., brain abscess)
Actinomyces	Bad dental disease; more indolent course; sinus tracts to chest wall

Diagnosing Legionnaire's Disease *

Test	Key Points
Culture	Sensitive; Considered the gold standard but takes 3-5 days and requires special media
Direct fluorescent antibody	Rapid but lacks sensitivity; Cross reacts with other respiratory pathogens
Paired serologies	Reliable but takes too much time; generally used for epidemiologic studies only
Polymerase chain reaction	Preferred test; Detects all legionella species and serotypes. Hard to obtain adequate respiratory samples
Urinary antigen	Commonly used; fast; positive early in disease; Only detects L. pneumophilla serotype 1

*Most cases caused by Legionella pneumophila

Case 2: 60 year-old man

History

6 months of progressive dyspnea on exertion and dry cough

Review of systems: (-) hemoptysis, fevers

Exam

S_pO_2 90% breathing air
Fine, basilar end-inspiratory crackles

Pulmonary Function Tests

Test	Result
FVC	65% predicted
FEV_1	60% predicted
FEV_1/FVC	0.85

Test	Result
TLC	70% predicted
DLCO	40% predicted

Imaging

Bibasilar, reticular opacities

A Question

Which of the following has been shown to improve mortality in this clinical situation?

1. Combination therapy with prednisone and azathioprine
2. Inhaled budesonide and formoterol
3. Nintedanib
4. Pirfenidone
5. No therapy improves mortality

Pulmonary Function Tests In Restrictive Diseases

Test	Result
Spirometry	Low FEV_1 and FVC Normal or high FEV_1/FVC
Total lung capacity	Low
Residual volume	Intraparenchymal restriction: Low
	Extraparenchymal restriction: Normal or high
Diffusion capacity	Intraparenchymal restriction: Low
	Extraparenchymal restriction: Normal

Idiopathic Pulmonary Fibrosis (IPF)

Presentation

Timing: After 6th decade

Symptoms: Progressive dyspnea, dry cough

Review of systems: typically unremarkable

Exam: fine crackles, clubbing, otherwise unremarkable

Work-Up

PFTs: Restrictive pattern, low DL_{CO}

Chest Radiography: Basilar predominant, reticular opacities

Biopsy: not needed if CT characteristic

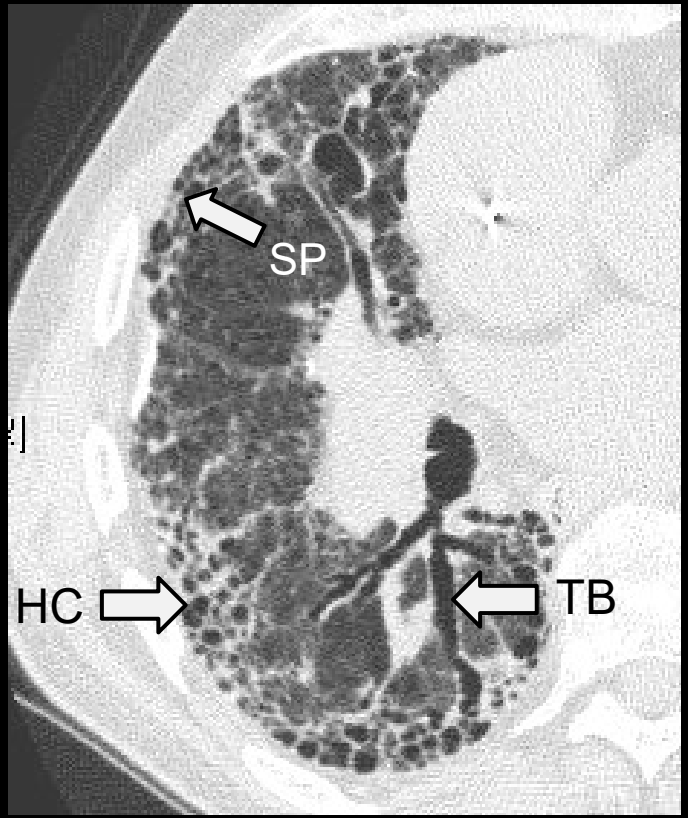
IPF: Characteristic CT Findings

Basilar predominant opacities

Sub-pleural location (SP)

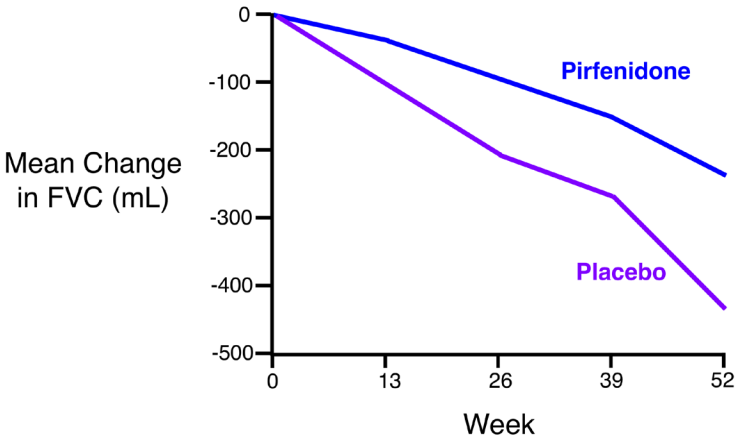
Traction Bronchiectasis (TB)

Honeycombing (HC)



Treatment Of Idiopathic Pulmonary Fibrosis

Pirfenidone slows lung function decline *



King et al. N Engl J Med 2014. 370: 2083

Other components of patient management

Supplemental oxygen

Pulmonary rehabilitation

Early referral for transplant evaluation

Nothing has been shown to improve mortality

* Nintedanib has also been shown to slow lung function decline

Other Diffuse Parenchymal Lung Diseases

Disease	Important Clues
Hypersensitivity pneumonitis	Key exposures: birds; hot tubs Acute and chronic forms
Sarcoidosis	Bilateral hilar lymphadenopathy; **Non**-caseating granulomas
Drug-induced pneumonitis	Nitrofurantoin, amiodarone, methotrexate, bleomycin

Other Diffuse Parenchymal Diseases: Pneumoconioses

Disease	Exposures	Clues
Asbestosis	Shipyards, brake pads; insulation	Pleural plaques; fibrosis
Silicosis	Sandblasting; hard rock mining;	Upper lobes; progressive massive fibrosis
Coal-Workers' Pneumoconiosis	Coal Mining	Upper lobes; progressive massive fibrosis
Berylliosis	Nuclear industry; electronics	Looks like sarcoidosis

Case 3: 37 year-old man

History Thoracentesis performed after chest film done to evaluate dyspnea shows a pleural effusion

Labs

Parameter	Value
Appearance	Milky
Serum Protein	6.8
Serum LDH	180
Pleural fluid protein	4.5
Pleural fluid LDH	323
WBC Differential	80% Lymphocytes 12% Mesothelial cells

A Question

Which of the following is the most appropriate test to order next on the pleural fluid?

1. Adenosine deaminase
2. AFB stain and culture
3. Amylase
4. Cytology
5. Triglycerides

Light's Criteria For An Exudate

LDH_{PF} > 2/3 upper limit of normal for serum value

LDH_{PF}: LDH_S > 0.6

Fluid is exudative if any one of the three criteria are met

$Protein_{PF}$: $Protein_S$ > 0.5

Other criteria incorporate pleural fluid cholesterol > 45 mg/dL

PF: Pleural Fluid; S: serum

Utility Of The WBC Differential

Lymphocytosis (> 65%)

TB Pleurisy

Chylothorax

Yellow nail syndrome

Lymphoma and NSSCA

Eosinophils

Not as useful for diagnosis as eosinophils in blood

Usually due to blood or air in pleural space

Mesothelial Cells

Usually found in large amounts in normal fluid

Values > 5% are ***not*** consistent with TB pleuritis

NSSCA: Non-small cell carcinoma

Other Pleural Fluid Tests

Test	Utility
Adenosine deaminase	> 40-60 mg/dL in TB pleurisy; useful to rule in TB pleurisy in high prevalence regions
Triglycerides	> 110 mg/dL seen in chylothorax
Amylase	Effusions due to acute pancreatitis, pancreaticopleural fistula, esophageal rupture
Glucose	< 30 mg/dL with empyema, TB pleurisy, lupus pleuritis; rheumatoid pleurisy *
Cytology	Sensitivity ~ 60%; If negative on first sample but suspicion for cancer is high, retap

* Same differential for very low pleural fluid pH

Chylothorax

- Definition: chyle in the pleural space
- Etiologies: disruption of thoracic duct
  - Traumatic
  - Non-traumatic: think lymphoma and order a chest CT
- Pleural fluid features:
  - Usually milky *
  - Lymphocyte predominant
  - Triglycerides > 110 mg/dL

* Not seen in patient who is not eating or is severely malnourished

Case 4: 36 year-old G2P1 Woman

History	29 weeks into pregnancy Worsening dyspnea over several weeks with lightheadedness on exertion Increased lower extremity edema
Vitals	BP 100/60 HR 95 RR 26 S_pO_2 95% breathing air
Chest Radiograph	Low lung volumes. No focal opacities. Prominent right atrial shadow. Bilateral hilar fullness
Labs	Creatinine 0.6 mg/dL Urinalysis: 0-2 RBC, 0-2 WBC; No proteinuria

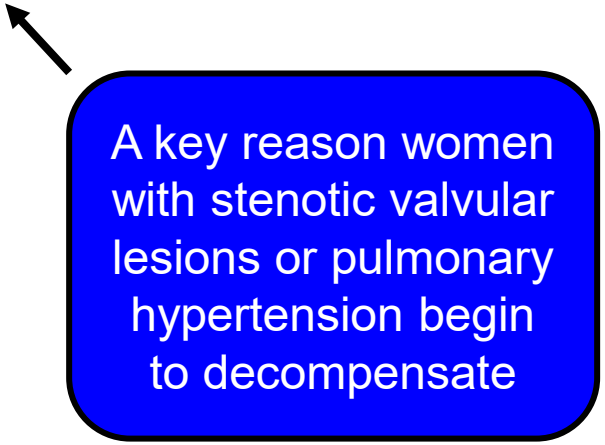
A Question

Which of the following is the most likely diagnosis at this time?

1. Amniotic fluid embolism
2. Diffuse alveolar hemorrhage
3. Peripartum cardiomyopathy
4. Preeclampsia
5. Pulmonary Hypertension

Key Physiologic Differences In Pregnancy

Vitals	Blood pressure be lower than normal through pregnancy and only rise back toward typical values in late term
Volume Status	Plasma volume and cardiac output both increase in early pregnancy and reach their peak in the second trimester
Labs	Physiologic anemia of pregnancy Decreased serum creatinine
Arterial blood gas	Compensated respiratory alkalosis



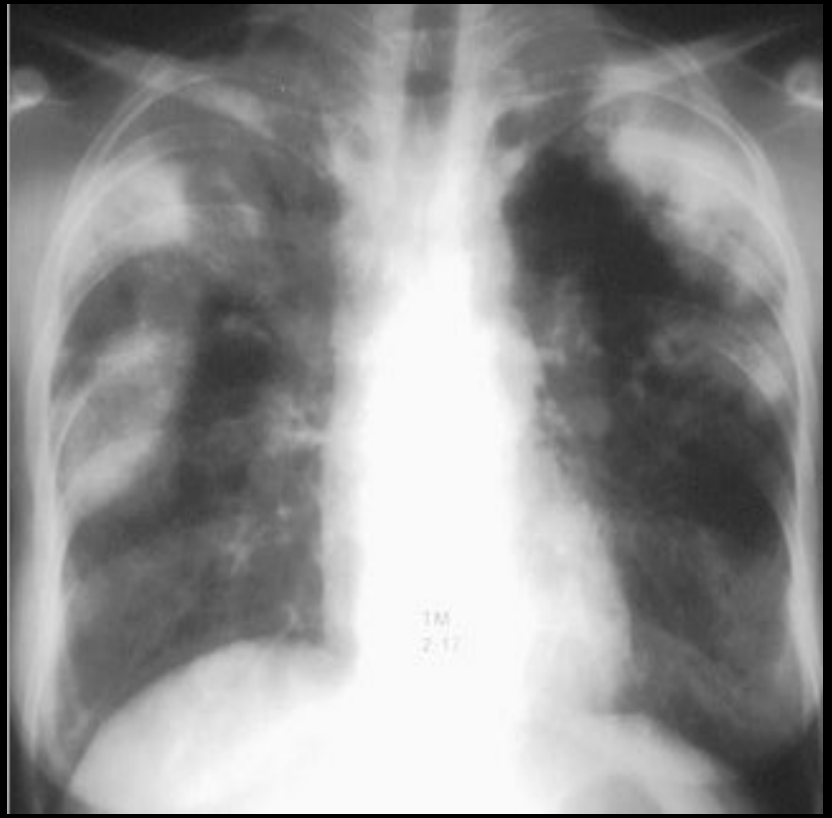
Acute Respiratory Failure In Women Who Are Or Could Be Pregnant

Diagnosis	Diffuse opacities on chest imaging
Amniotic fluid embolism	Yes
Aspiration pneumonitis	Yes
Asthma exacerbation	No
Decompensated pulmonary hypertension	No
Peripartum cardiomyopathy	Yes
Preeclampsia with pulmonary edema	Yes
Pulmonary embolism	No
Tocolytic-induced pulmonary edema	Yes

Case 5: 43 year-old Woman

History	3 months of increasing dyspnea
	Review of systems: (+) for fevers, 20 lb. unintentional weight loss, night sweats
	Social history: sexually active with multiple partners. No injection drug use
Exam	Thin; chronically ill-appearing Bilateral end-inspiratory crackles
Labs	WBC 10.5 x 10^3 cells/μL Differential: 20% eosinophils Serum IgE: 500 IU/mL

Case 5: Chest Radiograph



A Question

Which of the following is the most likely diagnosis in this patient?

1. Allergic bronchopulmonary aspergillosis
2. Chronic eosinophilic pneumonia
3. Granulomatosis with polyangiitis *
4. Pneumocystis jirovecii pneumonia
5. Tuberculosis

* Formerly Churg-Strauss Vasculitis

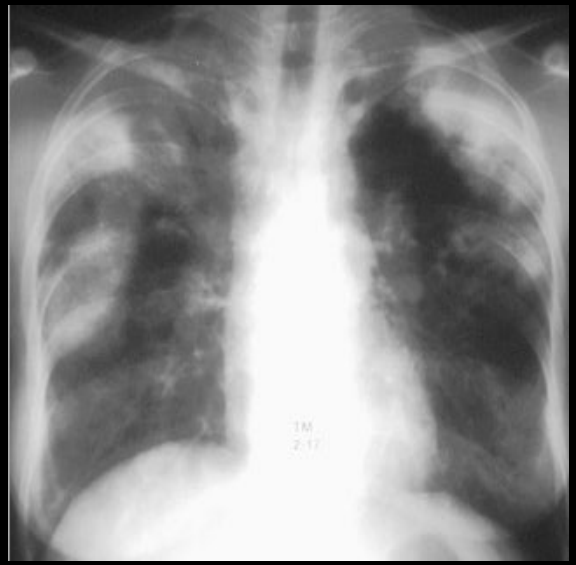
Differential Diagnosis For Pulmonary Infiltrates And Peripheral Eosinophilia

- Acute eosinophilic pneumonia
- Chronic eosinophilic pneumonia
- Simple pulmonary eosinophilia (Loffler's Syndrome)
- Allergic bronchopulmonary aspergillosis
- Eosinophilic granulomatosis with polyangiitis *
- Parasitic infections (e.g., Strongyloides)
- Hypereosinophilic syndrome
- Drug reactions

* Formerly "Churg-Strauss Vasculitis

Chronic Eosinophilic Pneumonia

- Subacute onset cough, fever, dyspnea, weight loss, night sweats
- Pre-existing asthma, atopy
- Labs: peripheral eosinophilia
- Imaging: photographic negative of pulmonary edema
- Diagnosis:
  - Clinical
  - Bronchoscopy with BAL in unclear cases
- Treatment: prolonged oral corticosteroids



What About Acute Eosinophilic Pneumonia?

Epidemiology
Often young, recently started smoking

Presentation
Acute onset dyspnea, hypoxemia and diffuse opacities

Diagnosis
Bronchoalveolar lavage:
> 25% eosinophils

Treatment
Corticosteroids yield very rapid response;
Recurrence unlikely

Case 6: 51 year-old man

History

Echocardiogram performed to evaluate dyspnea reveals: ejection fraction 63%; mild mitral regurgitation; estimated PASP 70 mm Hg

Exam

BMI 47

Studies

HIV negative
Liver panel normal
Arterial blood gas: P_aCO_2 60 mm Hg
Sleep study: obstructive sleep apnea, AHI 55
Chest radiograph: low lung volumes, basilar atelectasis
PFTs: FEV_1/FVC 0.84, TLC 81% predicted

AHI: apnea hypopnea index

A Question

Which of the following is most likely to be the appropriate treatment for this patient:

1. Intravenous epoprostenol
2. Lisinopril, metoprolol and spironolactone
3. Oral bosentan
4. Oral sildenafil
5. Supplemental oxygen

Pulmonary Hypertension

- WHO Definition: ***Mean*** PA pressure > 20 mm Hg * at rest
  - Echo gives an *estimate* of systolic pressure
  - Right heart catheterization: gold standard

- Presentation:
  - Pulmonary arterial hypertension: classically, young to middle-aged woman with isolated dyspnea on exertion
  - Challenging to identify when due to an underlying disease (e.g., COPD or idiopathic pulmonary fibrosis)

* Was previously > 25 mm Hg
WHO: World Health Organization; PA: Pulmonary Artery

WHO Classification Scheme

Group	Basic Problem	Examples of Disorders
1	Disease in small arterioles	**Idiopathic PAH**, anorexigens, collagen vascular disease, HIV, methamphetamine
2	Pulmonary venous hypertension	Left heart failure, valvular heart disease
3	Lung disease, alveolar hypoxia	COPD, IPF, residence at high altitude, obesity hypoventilation
4	Thrombo-embolism	Chronic thromboembolic disease, schistosomiasis
5	Miscellaneous /multifactorial	Fibrosing mediastinitis (e.g., Histoplasmosis); Sarcoidosis

PAH: Pulmonary Arterial Hypertension

Diagnostic Evaluation For Pulmonary Hypertension

- Initial testing to identify the cause:
  - Pulmonary function tests
  - Chest radiograph and V/Q Scan
  - Overnight polysomnogram
  - Labs (ABG, liver panel, ANA, RF, HIV)
  - Review echocardiogram

- Group I Patients: Right heart catheterization to:
  - Confirm pulmonary artery pressure
  - Calculate pulmonary vascular resistance
  - Assess response to pulmonary vasodilators

Treatment Of Pulmonary Hypertension Varies Based On The Cause

Group	General Treatment Strategy
1	Pulmonary vasodilators * based on NYHA class
2	Treat the underlying heart disease
3	Treat the lung disease; supplemental oxygen
4	Anticoagulation; possible surgery
5	Treat underlying process

* Phosphodiesterase-5 inhibitors (e.g., sildenafil), endothelin receptor antagonists (e.g., bosentan), prostacyclin analogs (e.g., epoprostenol, treprostinil, iloprost, selexipag)

Case 7: 45 year-old man

History

One day history of hemoptysis following 2 months of increasing dyspnea, cough and fevers

Negative HIV test 6 months ago

Social history: staying in Union Gospel Mission

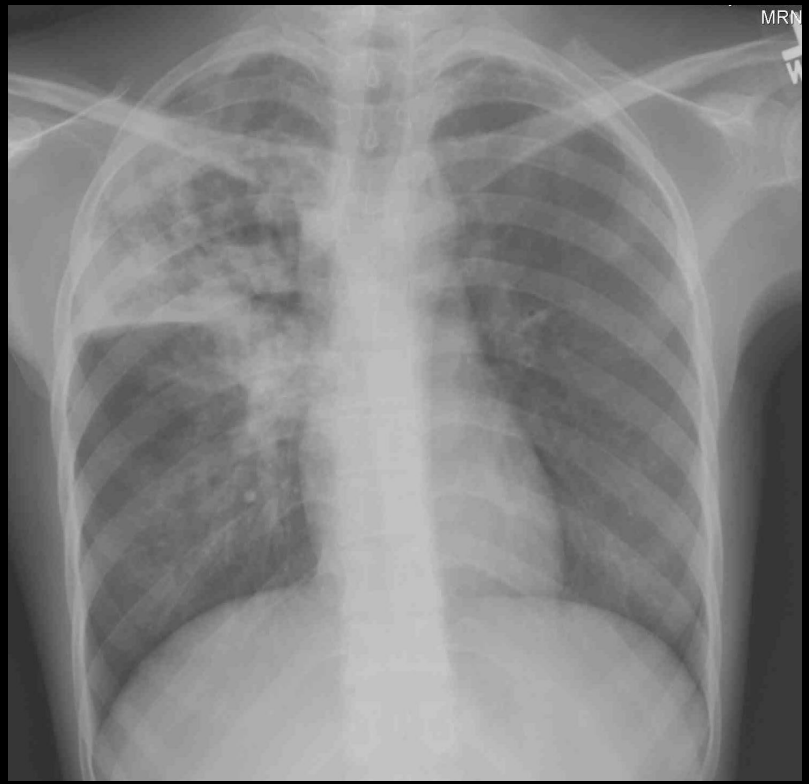
Exam

Thin, chronically ill-appearing
S_pO_2 95% breathing air
Decreased breath sounds over right upper lobe

Studies

Arterial blood gas: P_aO_2 75 mm Hg
WBC 11.6 x 10^3 cells/μL
Hemoglobin 10.3 g/dL

Case 7: Chest Radiograph



A Question

Which of the following is the next most appropriate initial step?

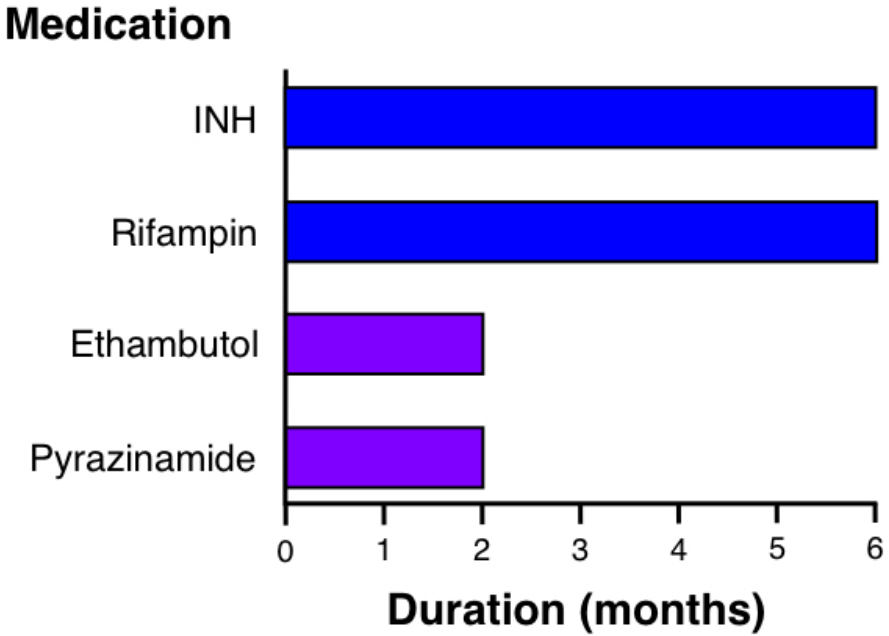
1. Bronchoalveolar lavage for AFB stain and NAAT
2. CT scan of the chest
3. Interferon gamma release assay
4. Spontaneously expectorated sputum for AFB stain and NAAT
5. Start INH and rifampin

NAAT: Nucleic acid amplification testing

Diagnosing Active TB

- TST and IGRA should ***not*** be used to diagnose ***active*** disease
- Culture: gold standard for diagnosis of active TB
- AFB smears of sputum
  - Goal: 3 samples collected at 8-24 hour intervals
  - Not specific for M.TB (e.g., MAC)
- Nucleic acid amplification increases specificity and can identify INH resistance
- Bronchoscopy usually not done until sputa are negative unless there is an urgent need to evaluate for other diagnoses

Active TB Treatment



HIV+: If not on ART, start ART during TB treatment (timing based on CD4 count)

Extend treatment: based on duration of culture positivity and presence of cavitary disease

ART: anti-retroviral therapy

Issues With The TB Medications

Drug	Issues / Major Toxicities
Isoniazid	Peripheral neuropathy (prevent with pyridoxine); Hepatitis
Rifampin	Hepatitis; High drug interaction potential (ART, OCP, warfarin)
Pyrazinamide	Hepatotoxicity; Hyperuricemia; May need to avoid in pregnant women*
Ethambutol	Optic neuritis

OCP: Oral contraceptive pill; ART: antiretroviral therapy

* WHO Guidelines say PZA is okay; Streptomycin is to be avoided in pregnant women

Case 8

A 45 year-old nurse at your hospital goes in for their semi-annual TB skin test (TST). They have no prior positive tests, no recent TB exposure and have not missed testing in over 10 years. Two days later, they have 5 mm of induration and erythema at the site of the test.

A Question

Which of the following is the most appropriate step at this time:

1. Repeat testing in 6 months
2. PA and lateral chest radiograph
3. Start daily isoniazid
4. Start weekly isoniazid and rifapentine DOT
5. Begin 4-drug therapy

DOT: Directly Observed Therapy

Diagnosing Latent TB (LTBI)

- Tuberculin Skin Test (TST)
  - False negatives in 10-25% of cases
  - False positives: Prior BCG vaccination
- Whole Blood IFN-Gamma Assays (IGRA)
  - Preferred test with prior BCG vaccination
  - Less reader bias
  - Repeatability issues with results near the cut-off

Low-intermediate risk of progression*: IGRA preferred
High risk of progression: Use IGRA or TST

* Progression to active TB

Positive TB Skin Tests Are Based On The Patient's Risk Profile

Positive at ≥ 5 mm

Living with HIV

Recent TB contact

Immunosuppressed

Organ transplantation

Fibrotic changes on chest radiography

Positive at ≥ 10 mm

Recent arrival, high prevalence region

IV drug user

Residents/employees of high risk settings

High risk conditions: DM, CKD, silicosis

Target screening for those at high risk of TB or who would benefit from treatment

Case 9: 32 year-old man

History

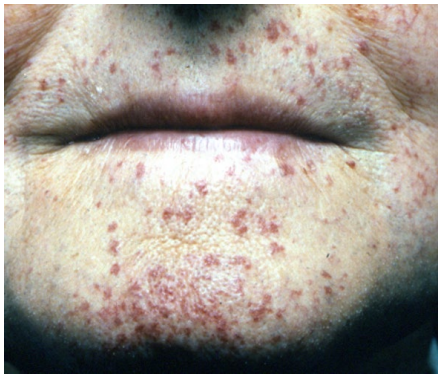
Recurrent epistaxis

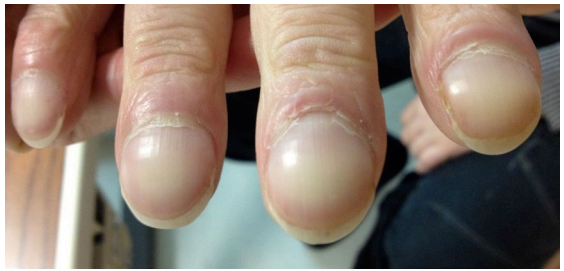
Increasing dyspnea over 9 months; worse when in the upright position

Family history: multiple members with GI bleeding

Exam

S_pO_2 Upright: 88%; Supine 94%





A Question

For which of the following complications is this patient at risk without treatment?

1. Intracerebral abscess
2. Pulmonary hypertension
3. Refractory ascites
4. Ruptured esophageal varices
5. Sudden cardiac death

Hereditary Hemorrhagic Telangiectasia (HHT)

Diagnostic Criteria

Recurrent epistaxis

Mucocutaneous telangiectasias

Visceral arterio-venous malformations

1st deg. relative with HHT

Important Screening

Pulmonary AVMs

Cerebral AVMs

Iron deficiency anemia

Additional screening for SMAD 4 mutation carriers

Pulmonary AVMs can cause CVA and intracerebral abscess

AVM: arteriovenous malformation; CVA: cerebrovascular accident

Another Cause Of Platypnea: Hepato-pulmonary Syndrome

Clinical Features

Cirrhosis and associated findings

Dyspnea with platypnea

Hypoxemia with orthodeoxia

Diagnostic Steps

Impaired oxygenation:
$(A\text{-}a)O_2$ difference $\geq$ 15 or
$P_aO_2 < 80$ on F_IO_2 0.21

Demonstrate IPVDs

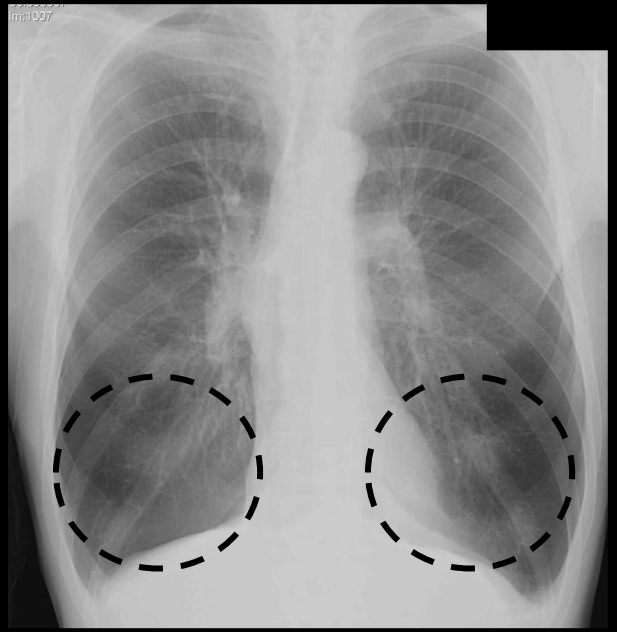
Contrast echocardiogram*
Perfusion scan
Angiography

IPVD: Intrapulmonary vascular dilation
* Preferred study

Some Quick-Hitter Pearls

Be Able To Recognize This Presentation

40 year-old man with 30 pack-year history of smoking presents with worsening dyspnea on exertion. Pulmonary function testing shows an obstructive pattern with an FEV_1 52% predicted.



The Diagnosis: Alpha-1 Antitrypsin Deficiency

… And This Presentation

27 year-old woman develops a headache and nausea after flying to Cuzco (elev. 11,000 ft.) on the way Machu Picchu

Acute Altitude Illnesses
AMS, HACE, HAPE

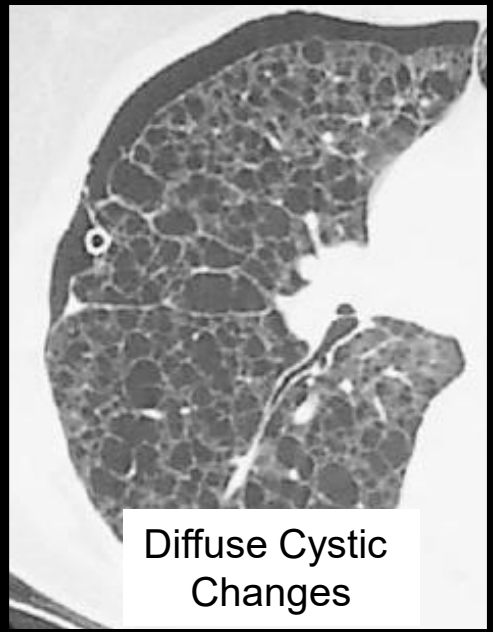
Prevention
Slow Ascent
AMS: acetazolamide
HAPE: nifedipine or tadalafil

Treatment
Descent and/or oxygen
AMS: acetazolamide
HACE: dexamethasone
HAPE: nifedipine

AMS: Acute Mountain Sickness
HACE: High Altitude Cerebral Edema
HAPE: High Altitude Pulmonary Edema

… And This Presentation

30 year-old woman presents with her third spontaneous pneumothorax (PTX) in 3 years. The timing of her pneumothoraces bears no relation to her menstrual periods.



The Diagnosis: Lymphangioleiomyomatosis

DDx for recurrent PTX includes catamenial PTX

Good Luck On The Boards!

Questions?
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Answer Key

Question	Answer
1	4
2	5
3	5
4	3
5	1
6	5
7	4
8	1
9	4