# 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<br><br>Review of systems: (+) for diarrhea |
| **Exam** | BP 98/73 mm Hg $S_pO_2$ 92% breathing air<br>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<br>**Host issues**: smoker, chronic lung disease, immunosuppressed | **GI Symptoms**: diarrhea<br>**Labs**: Hyponatremia<br>**Gram's stain**: many PMNs, no organisms |
| Mycoplasma | School-aged children<br>Military recruits<br>College students | Erythema multiforme<br>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: A Question

How would you interpret these pulmonary function tests?

| Test | Value | Z-score | % Predicted | LLN |
|---|---|---|---|---|
| $FEV_1$ (L) | 2.08 | -1.78 | 69 | 2.20 |
| FVC (L) | 3.02 | -1.50 | 77 | 2.93 |
| $FEV_1$/FVC | 0.69 | -- | -- | 0.64 |
| TLC (L) | 6.96 | +1.30 | 122 | 5.09 |
| DLCO (ml/min/mmHg) | 15.10 | -1.02 | 84 | 17.84 |

1. No definitive evidence of obstructive or restrictive defect
2. Obstructive defect
3. Obstructive defect with hyperinflation
4. Restrictive defect due to intra-parenchymal problem
5. Restrictive defect due to extra-parenchymal problem

LLN: Lower limit of normal

# Changes In PFT Interpretation

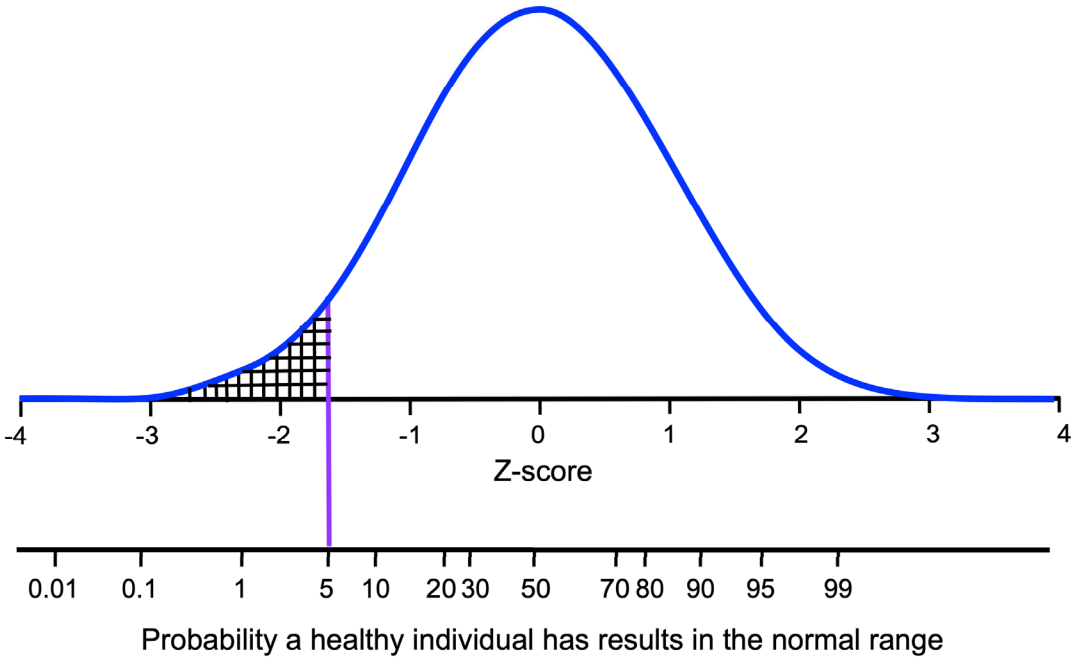
**Problems with percent predicted to define "normal"**

Do not account for age-related changes in measurement variability

Only approximate the lower limit of normal in mid-range of age

Simple but prone to misinterpretation of data

**New reliance on Z-scores**



# Changes In PFT Interpretation

| Interpretation | Old Method | New Method |
|---|---|---|
| Defining normal for $FEV_1$, FVC, TLC, RV and DLCO | 80-120% of predicted | Z = -1.645 to +1.645 |
| Defining normal for $FEV_1$/FVC ratio | GOLD criteria: < 0.7 | Below the lower limit of normal (LLN) |
| Bronchodilator response criteria | 200 mL and 12% change in $FEV_1$ or FVC | Change in $FEV_1$ or FVC > 10% of predicted value |

**Severity for all parameters now based on the z-score**

Source: Stanojevic et al. Eur Respir J 2022. 60: 2101499

# Back To The PFTs In This Case

| Test | Value | Z-score | % Predicted | LLN |
|---|---|---|---|---|
| $FEV_1$ (L) | 2.08 | -1.78 | 69 | 2.20 |
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**FVC low based on % predicted but normal by z-score**

$FEV_1$/FVC below the GOLD cut-off but above the lower limit of normal (LLN), thus ruling out obstruction

**TLC high based on % predicted but normal by z-score**

# Case 3: 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 | % predicted | Z-score |
|---|---|---|
| FVC | 65 | -1.85 |
| $FEV_1$ | 60 | -1.92 |
| $FEV_1$/FVC | 0.85 | LLN 0.69 |

| Test | % predicted | Z-score |
|---|---|---|
| TLC | 70 | -1.72 |
| DLCO | 40 | -2.25 |

**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<br>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

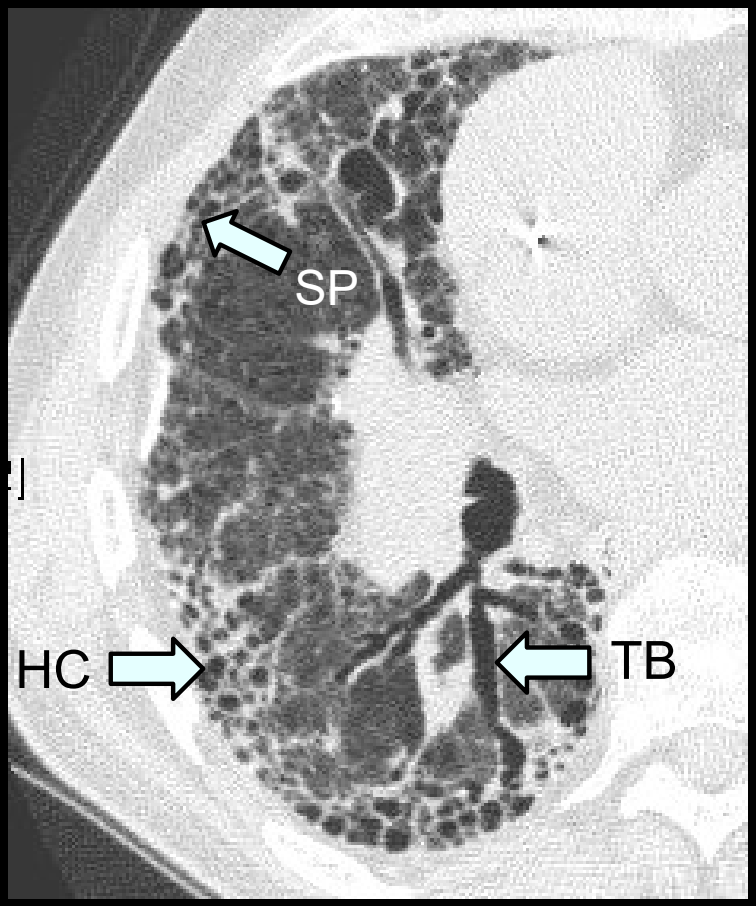
# IPF: Characteristic CT Findings

Basilar predominant opacities

Sub-pleural location (SP)

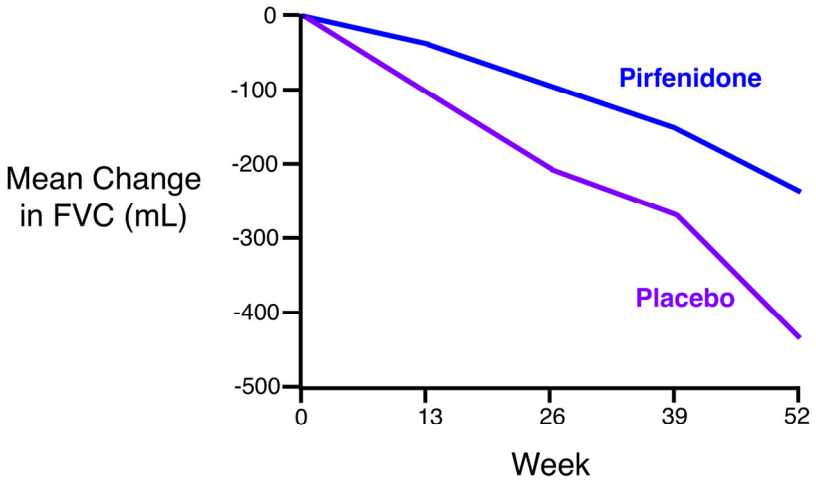
Traction Bronchiectasis (TB)

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<br>Acute and chronic forms |
| Sarcoidosis | Bilateral hilar lymphadenopathy;<br>**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 4: 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<br>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 5: 36 year-old G2P1 Woman

| | |
|---|---|
| **History** | 29 weeks into pregnancy<br>Worsening dyspnea over several weeks with lightheadedness on exertion<br>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<br>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 should 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<br>Decreased serum creatinine |
| **Arterial blood gas** | Compensated respiratory alkalosis |

A key reason people with stenotic valvular lesions or pulmonary hypertension worsen at this stage of pregnancy

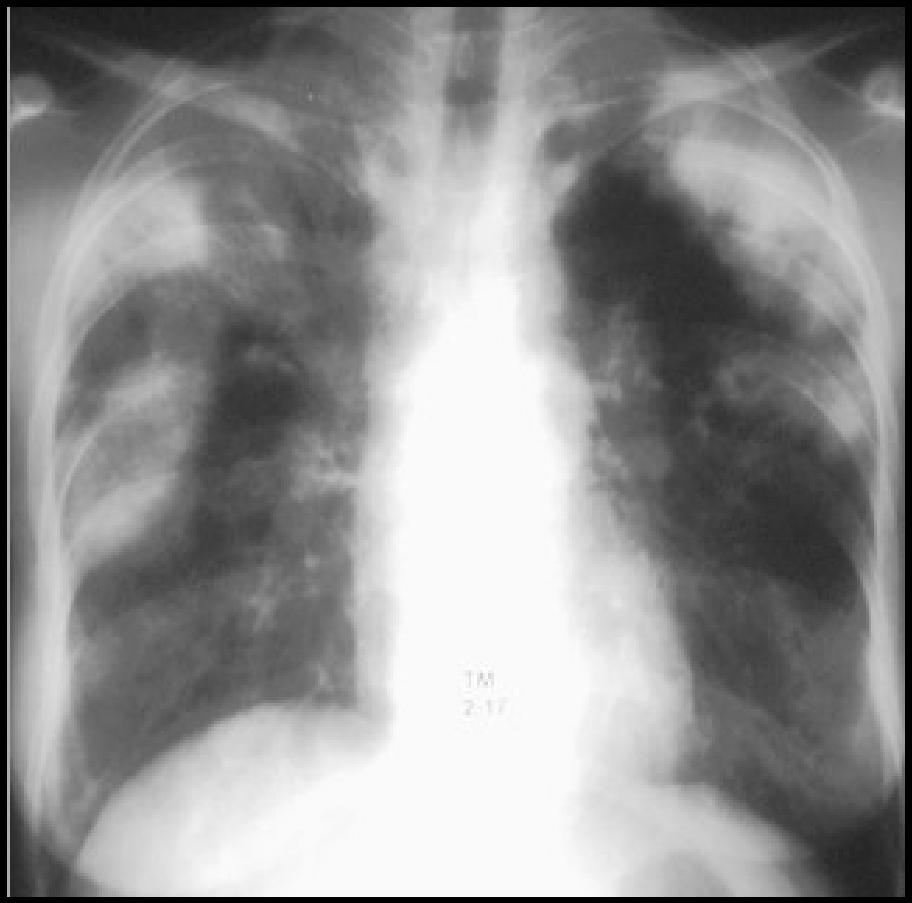
# Acute Respiratory Failure In People Who Are Or Could Be Pregnant

| 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 6: 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<br>Bilateral end-inspiratory crackles |
| **Labs** | WBC 10.5 x $10^3$ cells/μL<br>Differential: 20% eosinophils<br>Serum IgE: 500 IU/mL |

# Case 6: 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

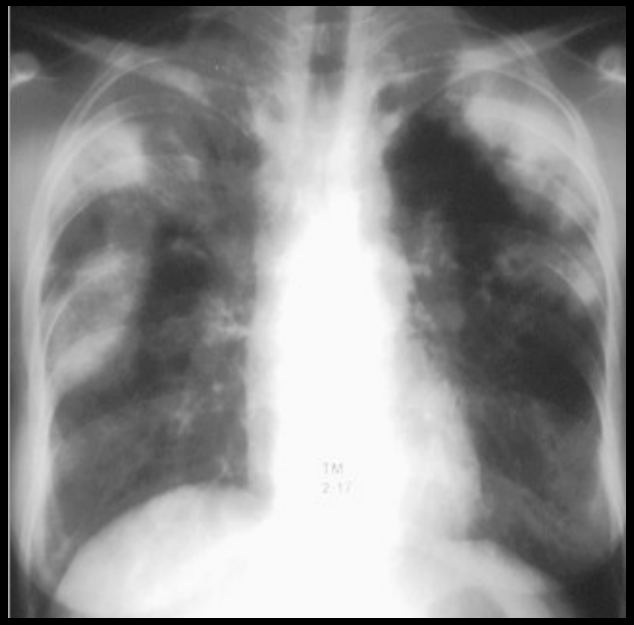
# Differential Diagnosis For Pulmonary Infiltrates And Peripheral Eosinophilia

- 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 7: 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 8: 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 increase risk for CVA and intracerebral abscess by bypassing the filter function of the pulmonary vascular tree**

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

# Case 9: 47 year-old woman

| | |
|---|---|
| **History** | Trekking to Machu Picchu |
| | Flew into Cuzco (elev. 11,000 ft) from Lima (sea level). |
| | Developed headache, loss of appetite and mild nausea 10 hours following arrival |
| **Medical History** | Mild, persistent asthma |
| | No prior travel to high altitude |
| **Exam** | Tired-appearing<br>Mental status normal<br>Normal heel-toe walking |

# A Question

Which of the following medications might have prevented this patient's clinical syndrome?

1. Acetazolamide
2. Dexamethasone
3. Ibuprofen
4. Inhaled budesonide
5. Nifedipine

# Acute Altitude Illnesses

## Acute Mountain Sickness

Most common form of altitude illness

Onset 4-8 hours after ascent to > 8,000 ft

Headache plus one of: Nausea, vomiting, loss of appetite, lassitude, dizziness

## High Altitude Pulmonary Edema

Non-cardiogenic form of pulmonary edema

**Early**: out of breath on exertion, dry cough

**Late**: dyspnea with simple activities, cyanosis, blood-tinged sputum

## High Altitude Cerebral Edema

Causes a global encephalopathy

Main findings include: ataxia, altered mental status

Acute onset of focal deficits should prompt other considerations

# Prevention Of Acute Altitude Illness

## Non-Pharmacologic

Slow ascent!!!

Above 3000 m, do not increase the sleeping elevation by more than 300-500 m/day; Rest days every 3-4 days

## Pharmacologic Prophylaxis

| Medication | Dose |
|---|---|
| AMS and HACE * | |
| Acetazolamide | 125 mg q 12 hr |
| Dexamethasone | 2 mg q 6 hr |
| HAPE ** | |
| Nifedipine SR | 30 mg q 12 hr |
| Tadalafil | 10 mg q 12 hr |

* Reserved for moderate-high risk ascent profiles
** Reserved for those with history of HAPE

Luks et al. Wilderness Environ Med 2019. 30: S3

# The General Approach To Treatment

**Stop Ascending**

**Symptomatic Treatment (e.g. NSAIDs, acetaminophen)**

**+/- Acetazolamide or dexamethasone**

**Okay to go higher if they get better**

**Descend, start oxygen or access a health facility**

**HACE: Dexamethasone**

**HAPE: Nifedipine**

**Mild** **Severe**

**Spectrum of Severity**

# Good Luck On The Boards!

Questions?

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# Answer Key

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