Pulmonary Medicine Board Questions
Selected Topics

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Conflicts of Interest to Disclose

None.

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6th Annual Board Review and Update in Pulmonary and Critical Care Medicine

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Christopher Fanta, MD

Bruce Levy, MD

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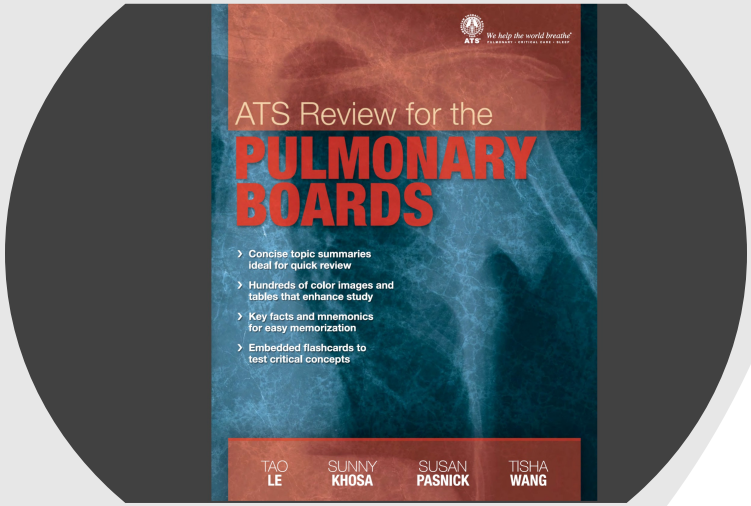

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A 33-year-old woman presents with a 4-month history of cough. She otherwise has no known medical problems, and her only medication is a daily multivitamin. Physical exam is unremarkable—specifically chest is clear and there are no abnormal skin findings. A chest x-ray shows bilateral hilar adenopathy with clear pulmonary parenchyma. Pulmonary function testing reveals normal spirometry and lung volumes, DLCO is in low normal range.

A transbronchial lung biopsy shows well-formed non-caseating granulomas.

Q-1: What are your next steps?

A. ECG, eye exam, recommend oral corticosteroids.
B. ECG, eye exam, recommend inhaled corticosteroids.
C. ECG, eye exam, cardiac echo, recommend oral corticosteroids
D. ECG, eye exam, pending these results discuss treatment vs. observation.
E. ECG, eye exam, recommend methotrexate.

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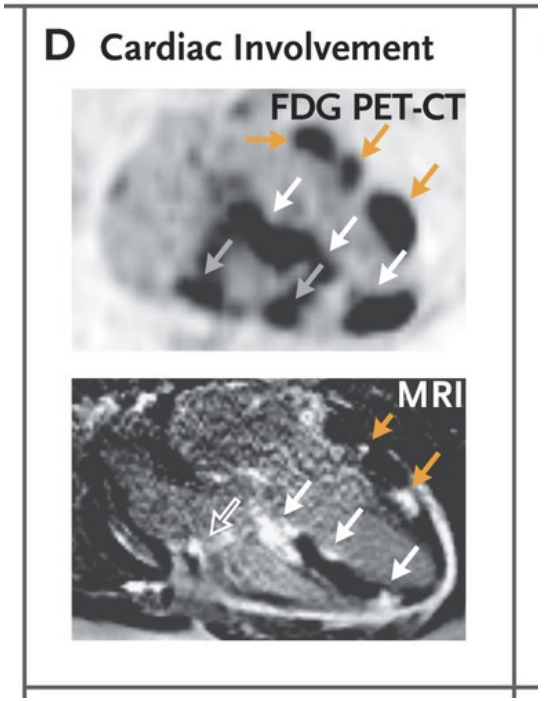
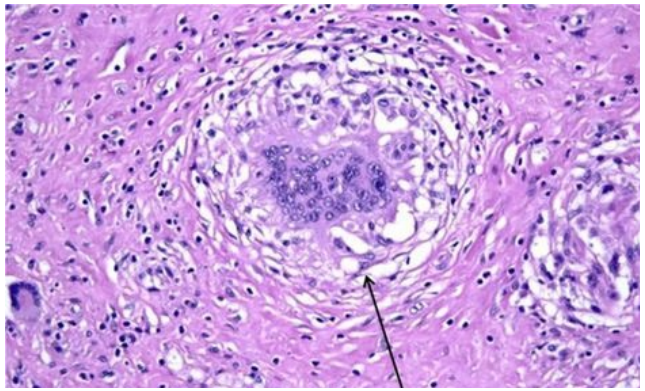
A few words about cardiac sarcoidosis

- 2nd leading cause of death (after lung disease)
- 12 lead ECG part of initial evaluation
- High risk ECG or history should have:
  - Cardiac PET or Cardiac MRI
  - Imaging often sufficient for dx





Drent M, Crouser ED, Grunewald J. Challenges of Sarcoidosis and Its Management. N Engl J Med. 2021 Sep 9;385(11):1018-1032

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A 65 yo man presents with cough, dyspnea on exertion and diffuse parenchymal infiltrates on imaging. After an extensive evaluation, he undergoes a VATS lung biopsy. The findings are consistent with hypersensitivity pneumonitis (HSP).

Q-2: Which of the following statements are true regarding HSP?

A. Antigen avoidance is the cornerstone of management.
B. Serologic assays for specific IgG antibodies are an essential part of the evaluation and frequently provide a definitive diagnosis.
C. Pulmonary function testing, especially DLCO, can differentiate between acute and fibrotic phases of the disease.
D. Glucocorticoids should be instituted in most patients, and treatment is clearly associated with improved outcomes.
E. Transbronchial lung biopsy has an excellent diagnostic yield in HSP.

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A 24-year-old woman is referred to ENT with recurrent and worsening sinus infections. She has not responded to two rounds of oral amoxicillin/clavulanic acid therapy. Her past medical history is significant for frequent sinus infections through her teen years. There is no history GI disease. A culture is obtained and grows mucoid P. aeruginosa. A full evaluation is done, and she is diagnosed with cystic fibrosis (CF).

Q-3: Which of the following is a true statement about appropriate treatment of an adult with newly diagnosed CF?

A. She should be started on triple combination CFTR modulator therapy (ELEXACAFTOR-TEZACAFTOR-IVACAFTOR) to avoid future deterioration.
B. Appropriate treatment with CFTR modulator therapy depends on the patient's CFTR genotype.
C. In the US, CFTR genotypes that are ineligible for CFTR modulator therapy are substantially less common among Black or Hispanic CF patients.
D. Adverse effects of triple combination therapy frequently lead to discontinuation of the drugs.

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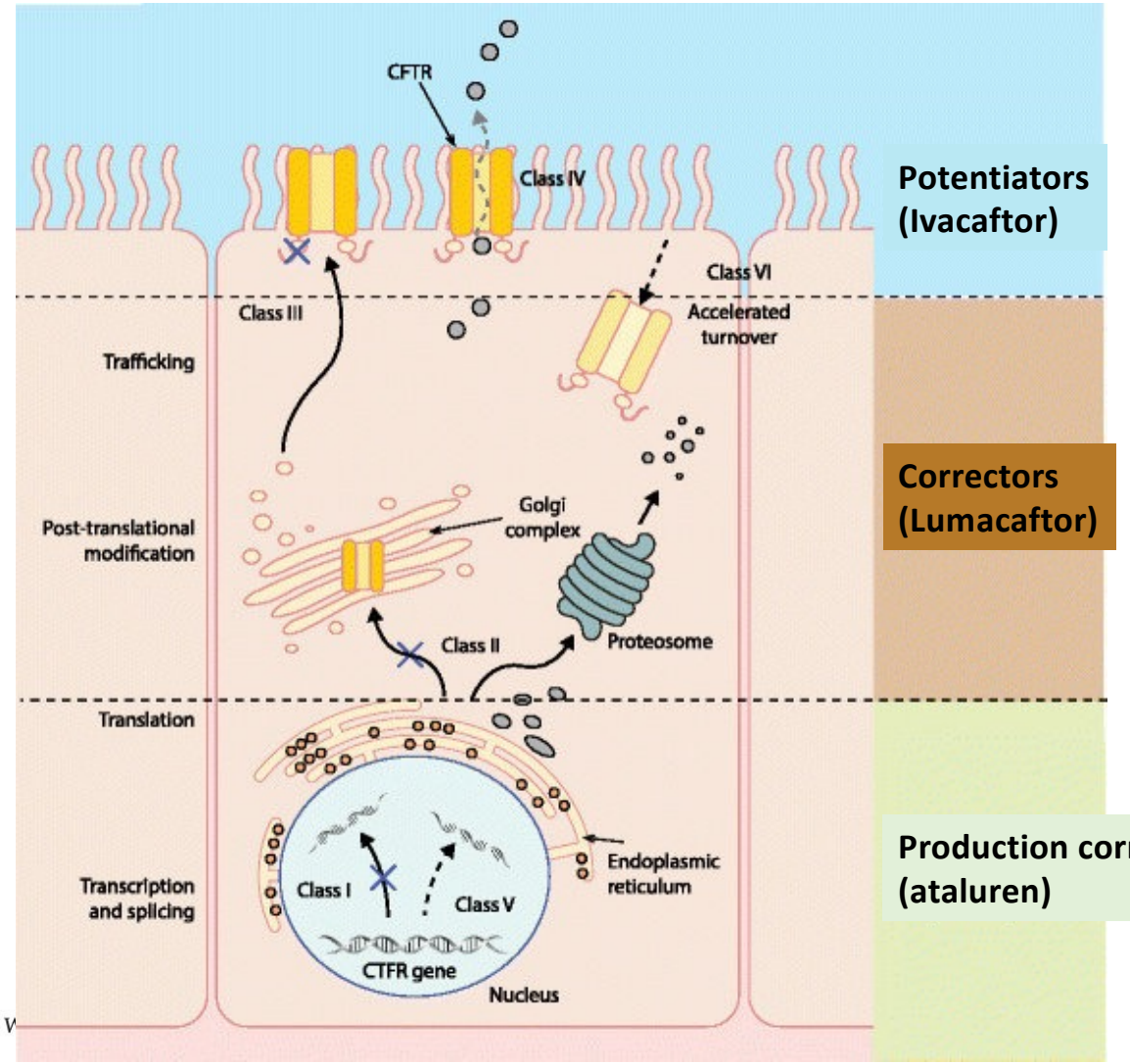
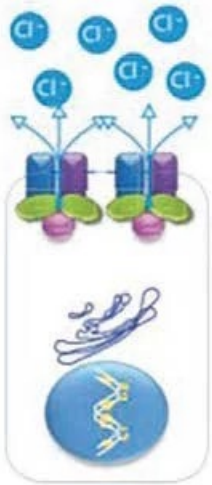


Potentiators (Ivacaftor)

Correctors (Lumacaftor)

Production correctors (ataluren)

FIGURE 1 *CFTR* MUTATIONS



	Normal	Class I	Class II	Class III	Class IV	Class V
DESCRIPTION	CFTR is created, reaches cell surface and functions properly, allowing transfer of chloride and water.	No functional CFTR created.	CFTR protein is created, but misfolded, keeping it from reaching the cell surface.	CFTR protein is created and reaches cell surface, but does not function properly.	The opening in the CFTR protein ion channel is faulty.	CFTR is created in insufficient quantities.
EXAMPLES		G542X W1282X R553X	F508del N1303K I507del	G551D S549N V520F	R117H D1152H R347P	3849+10kbC->T 2789+5G->A A455E

SOURCE OF DATA: Cystic fibrosis patients under care at CF Foundation-accredited care centers in the United States, who consented to have their data entered.
Adapted from: CFTR Modulator Therapies; http://www.cff.org/Life-With-CF/Treatments-and-Therapies/Medications/CFTR-Modulator-Therapies/#section2.
Abbreviations: CF, cystic fibrosis; CFTR, cystic fibrosis transmembrane conductance regulator.

CFTR gene mutations approved for each type of CFTR modulator therapy….

546insCTA	E403D	G628R	L346P	R117H	S912L
711+3A>G	E474K	G970D	L453S	R117L	S945L
2789+5G>A	E588V	G1061R	L967S	R117P	S977F
3141del9	E822K	G1069R	L997F	R170H	S1159F
3272-26A>G	E831X	G1244E	L1077P	R258G	S1159P
3849+10kbC>T	F191V	G1249R	L1324P	R334L	S1251N
A46D	F311del	G1349D	L1335P	R334Q	S1255P
A120T	F311L	H139R	L1480P	R347H	T338I
A234D	F508C	H199Y	M152V	R347L	T1036N
A349V	F508C;S1251N	H939R	M265R	R347P	T1053I
A455E	**F508del***	H1054D	M952I	R352Q	V201M
A554E	F575Y	H1085P	M952T	R352W	V232D
A1006E	F1016S	H1085R	M1101K	R553Q	V456A
A1067T	F1052V	H1375P	P5L	R668C	V456F
D110E	F1074L	I148T	P67L	R751L	V562I
D110H	F1099L	I175V	P205S	R792G	V754M
D192G	G27R	I336K	P574H	R933G	V1153E
D443Y	G85E	I502T	Q98R	R1066H	V1240G
D443Y;G576A;R668C	G126D	I601F	Q237E	R1070Q	V1293G
D579G	G178E	I618T	Q237H	R1070W	W361R
D614G	G178R	I807M	Q359R	R1162L	W1098C
D836Y	G194R	I980K	Q1291R	R1283M	W1282R
D924N	G194V	I1027T	R31L	R1283S	Y109N
D979V	G314E	I1139V	R74Q	S13F	Y161D
D1152H	G463V	I1269N	R74W	S341P	Y161S
D1270N	G480C	I1366N	R74W;D1270N	S364P	Y563N
E56K	G551D	K1060T	R74W;V201M	S492F	Y1014C
E60K	G551S	L15P	R74W;V201M;D1270N	S549N	Y1032C
E92K	G576A	L165S	R75Q	S549R	
E116K	G576A;R668C	L206W	R117C	S589N	
E193K	G622D	L320V	R117G	S737F	

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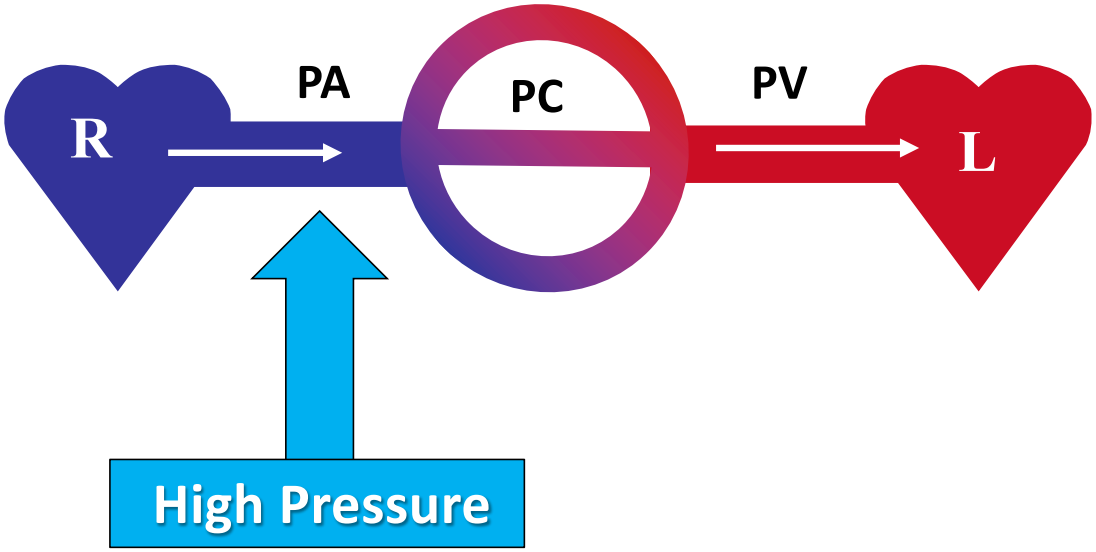
A 55 yo woman presents for evaluation for dyspnea on exertion. PMH is significant for obesity and long-standing systemic hypertension--currently well controlled. An in-depth evaluation reveals no parenchymal lung disease, and a stress test is negative for ischemia. She undergoes a right heart catheterization with the following results:

	Pressure	Mean	Normal values
Right atrium	12		2-8 mmHg
Right ventricle	42/12		15-30/2-8
Pulmonary artery	42/27	32	15-30/4-12
Pulmonary capillary wedge pressure	22		2-10
Cardiac output (L/min)	3.6		6 liters/min
Pulmonary Vascular Resistance?	??		< 1.6 Wood

What is Pulmonary Hypertension?



Old $\Rightarrow$ PA_{mean} > 25 mmHg

New $\Rightarrow$ PA_{mean} > 20 mmHg

Normal $PA_{mean} \leq$ 20 mmHg, *but average ~ 12 mmHg*

Pulmonary Vascular Resistance

Normal PVR < 1.6 Wood Units

Ohm's Law:

$$\Delta P = Flow \times Resistance$$

Rearranging

$$Resistance = \frac{\Delta P}{Flow}$$

$$\text{Pulmonary Vascular Resistance} = \frac{PA_{mean} - LA}{\text{Cardiac Output}}$$

Q-4 Based on these hemodynamic findings, which of the following most accurate?

A. **Pulmonary vascular resistance is 2.8 Wood units; she IS a candidate for pulmonary vasodilator therapy.**
B. **Pulmonary vascular resistance is 5.5 Wood units; she IS a candidate for pulmonary vasodilator therapy.**
C. **Pulmonary vascular resistance is 2.8 Wood units; she is NOT a candidate for pulmonary vasodilator therapy.**
D. **Pulmonary vascular resistance is 5.5 Wood units; she is NOT a candidate for pulmonary vasodilator therapy.**

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Q-5. Based on these hemodynamic findings, how should she be classified?

A. Group 1: Pulmonary arterial hypertension (PAH)
B. Group 2: Pulmonary hypertension owing to left heart disease
C. Group 3: Pulmonary hypertension owing to lung diseases &/or hypoxia
D. Group 4: Chronic thromboembolic pulmonary hypertension (CTEPH)
E. Group 5: Pulmonary hypertension-unclear, multifactorial

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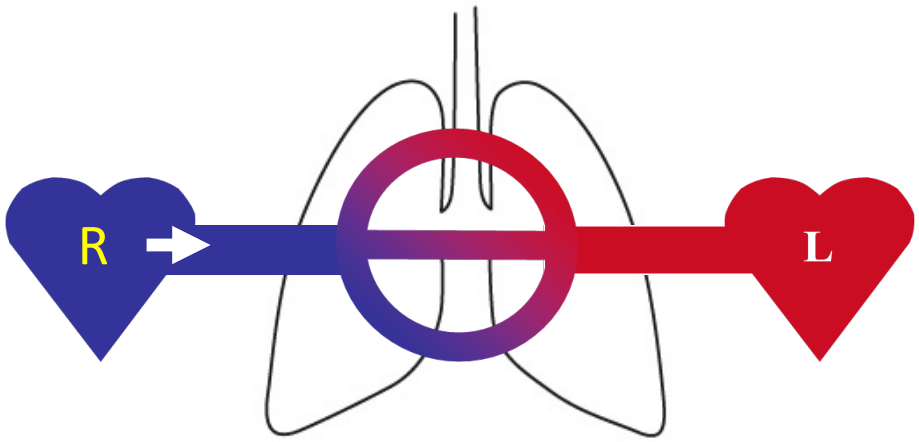
Clinical classification of pulmonary hypertension (NICE, 2018)



1. **Pulmonary arterial hypertension (PAH)**
   - **Idiopathic pulmonary arterial hypertension (iPAH)**
2. **Pulmonary hypertension owing to left heart disease**
3. **Pulmonary hypertension owing to lung diseases &/or hypoxia**
4. **Chronic thromboembolic pulmonary hypertension (CTEPH)**
5. **Pulmonary hypertension-unclear, multifactorial**
   - **Hemoglobinopathies**

A patient with known pulmonary fibrosis has been relatively stable for over a year on pirfenidone. In the last few months, he has noted increased dyspnea on exertion. PFTs are unchanged, but he is found to have right ventricular dysfunction by transthoracic cardiac echo. A right heart catheterization is performed with the following results:

	Pressure	Mean	Normal values
Right atrium	12		2-8 mmHg
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Q-6: Which of the following best describes this patient?

A. She has combined Group 1 and Group 3 PH, PVR = 6.1 Wood. Oral therapy is indicated.

B. She is classified as Group 3 PH, PVR = 6.1 Inhaled treprostinil is indicated.

C. She is classified as Group 3 PH, PVR = 6.1 There are no FDA approved treatments for PH in this setting

D. She is classified as Group 3 PH, PVR = 6.1. Pirfenidone has been ineffective.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Inhaled Treprostinil in Pulmonary Hypertension Due to Interstitial Lung Disease

Aaron Waxman, MD, PhD, *et. al.* January 2021

- **FDA Approves First Drug for Group 3 PH**
- People with Group 3 pulmonary hypertension (PH) associated with interstitial lung disease now have a Food and Drug Administration (FDA)-approved treatment option. Group 3 PH is caused by chronic lung disease or low oxygen levels.

A 32 yo woman delivered a healthy baby girl 12 hours ago. Mom and baby were both doing well until Mom developed the abrupt onset of pleuritic chest pain and shortness of breath which awoke her from sleep.

Q-7: Which of the following statements is most accurate regarding venous thromboembolism in pregnancy?

A. The risk is highest early in the 3rd trimester as the uterus reaches a critical size.
B. The reliability of D-dimer testing does not change with pregnancy.
C. Chest CT scan with pelvic shielding is the recommended imaging method for the diagnosis of PE.
D. Deep venous thrombosis is significantly more common in the right leg.
E. DOACs are contraindicated in pregnancy.

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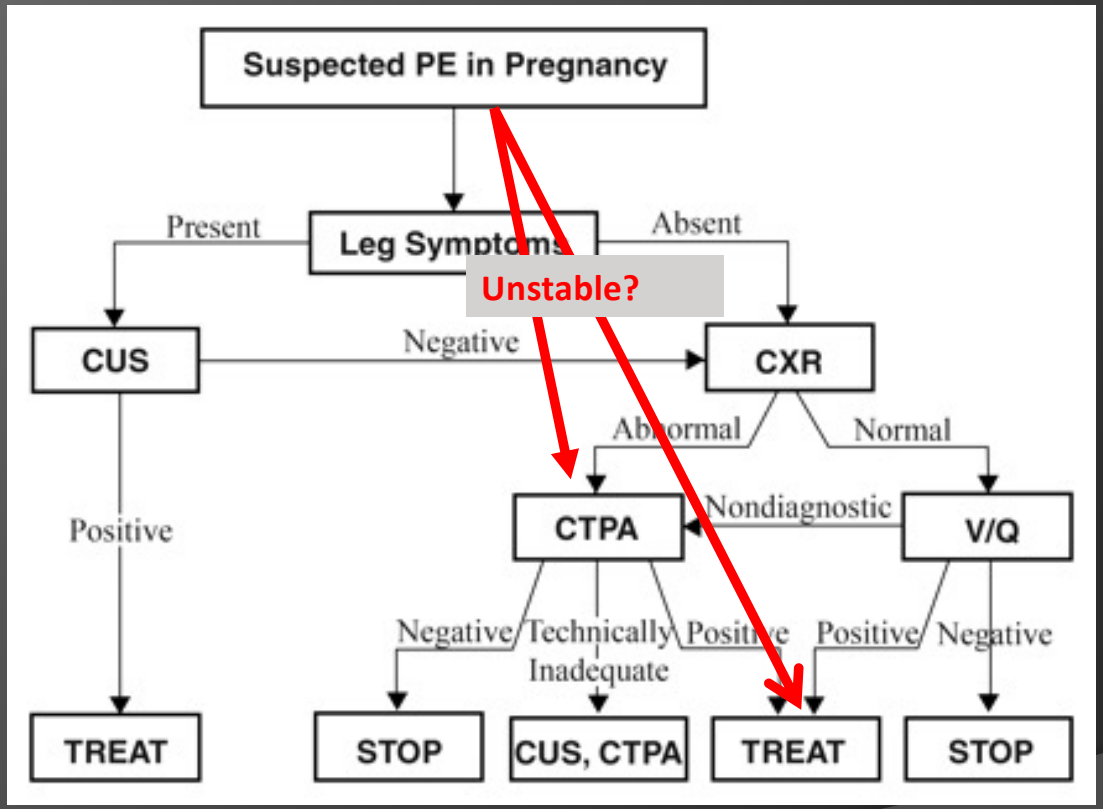
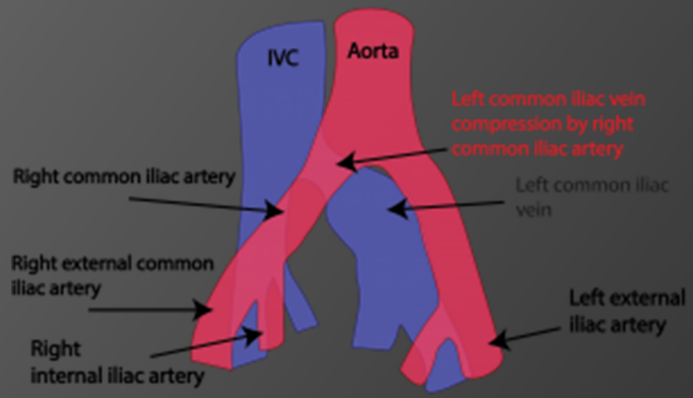
ATS/STR Clinical Practice Guideline

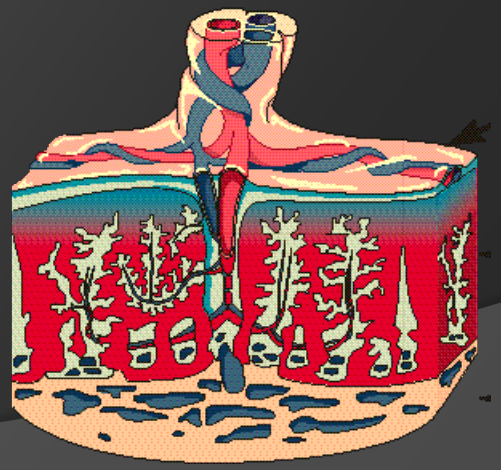


Radiology 262:635, 2012

Pregnancy: Virchow's triad

1. **Stasis**
   - Hormones
   - Compression
     - gravid uterus
     - right iliac artery
2. **Endothelial Injury**
   - Delivery
     - Uteroplacental surface
     - C-section





Predicting DVT in Pregnancy

Table 3. **Results of the Multivariate Analysis of Potential Predictive Variables for Deep Venous Thrombosis in Pregnant Patients**

N = 194 pregnant patient with suspected DVT

Variable	Adjusted Odds Ratio (95% CI)	*P* Value
Symptomatic left leg	44.28 (3.22–609.69)	0.005*
≥2-cm calf circumference difference	26.89 (6.10–118.54)	<0.001*
First trimester	53.43 (7.12–401.02)	0.001*

* Significant predictive variables: $P < 0.05$.

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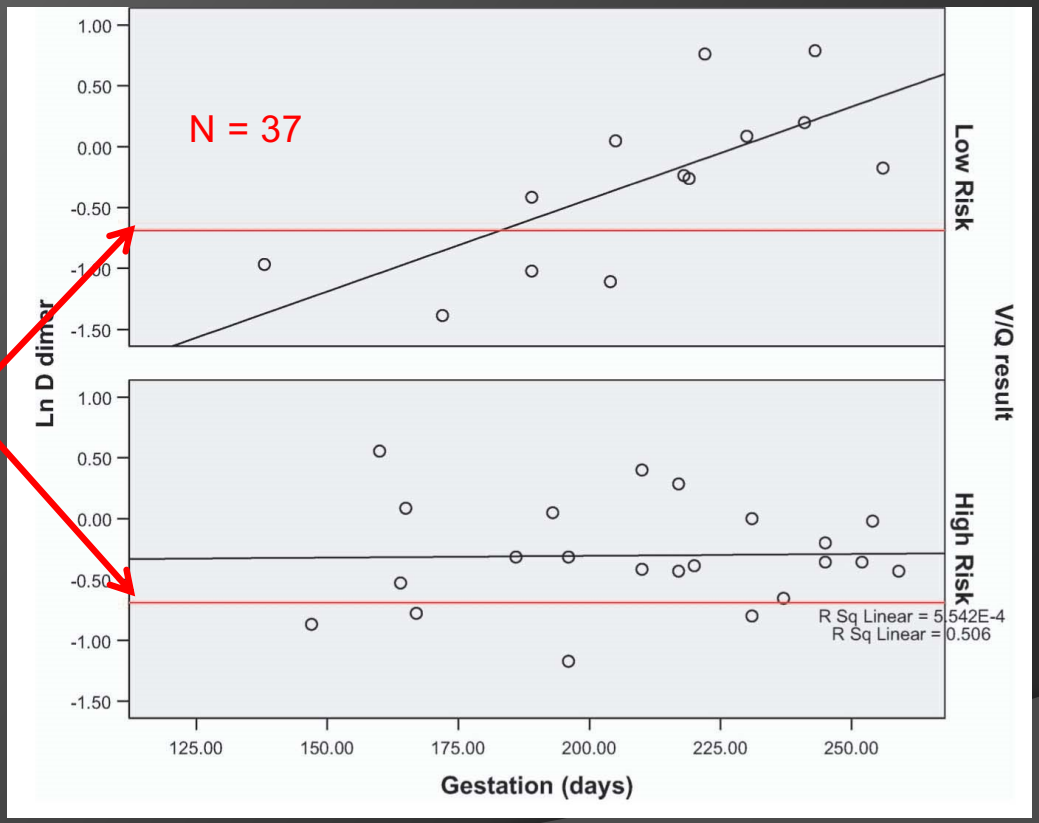
Chan et. al. **Ann Intern Med. 2009;151(2):85-92**

D-dimer in Pregnancy

Normal cutoff



Damadaram JOG 2009

A 55-year-old patient with asthma had three episodes of fever with worsening dyspnea as well as sputum production with brownish mucus plugs in the last 2 months. Chest radiographs show fleeting infiltrates, and an HRCT shows central bronchiectasis. Serum IgE levels are elevated (1200 ng/mL) with peripheral blood eosinophilia (700/mL).

Q-8: What is the most likely diagnosis?

A. Cystic fibrosis
B. Lofgren's syndrome
C. Loffler's syndrome
D. Allergic bronchopulmonary aspergillosis
E. Chronic Eosinophilic Pneumonia

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Q-9: What is the next best step?

A. Immediate skin test to *Aspergillus*
B. Aspergillus specific serum IgE
C. Sweat Chloride testing
D. Hypersensitivity pneumonitis screen
E. A or B

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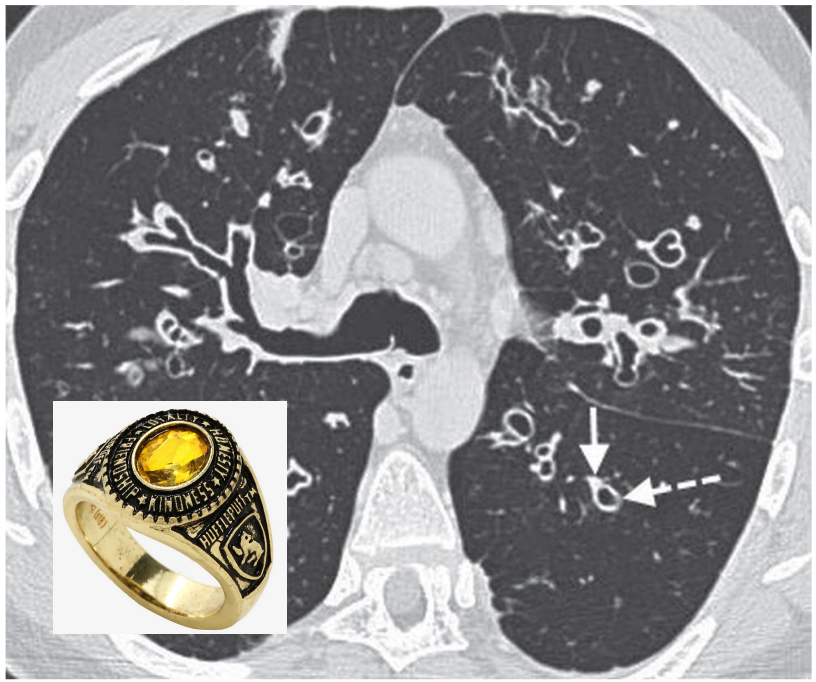
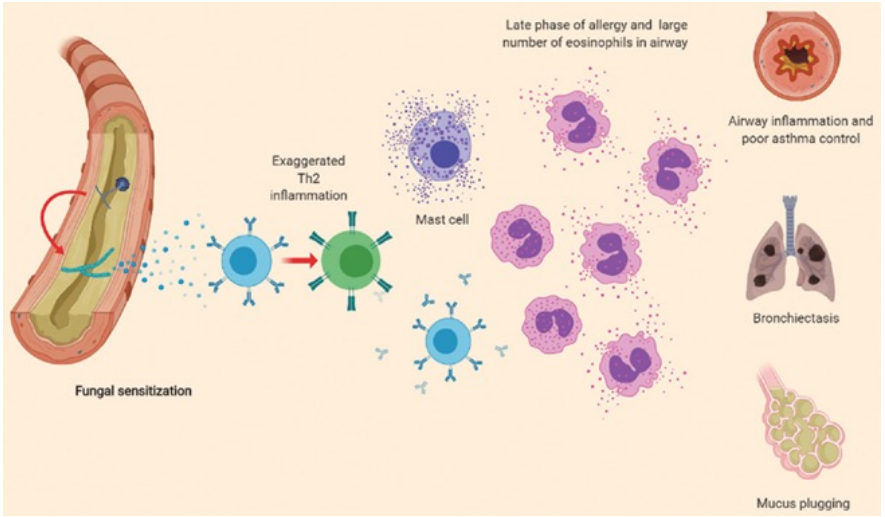
Allergic Bronchopulmonary Aspergillosis

- Hypersensitivity reaction to chronic airway colonization



Prevalence:
Persistent asthma 1-2%
Cystic Fibrosis 2-9%



Diagnostic criteria for allergic bronchopulmonary aspergillosis

International Society for Human and Animal Mycology (ISHAM) working group

Predisposing conditions (one must be present)*:
Asthma **Cystic fibrosis**
Obligatory criteria (both must be present):
Serum IgE levels against *Aspergillus fumigatus* or *Aspergillus* skin test positivity. **Elevated total IgE concentration**
Other criteria (at least two must be present):
Precipitating serum antibodies to *A. fumigatus* or elevated serum *Aspergillus* IgG by immunoassay **Radiographic pulmonary opacities consistent with ABPA** **Total eosinophil count >500 cells/microL in glucocorticoid-naïve patients (may be historical)**

Thank you!