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Objectives: the learner will be able to explain the pathophysiology of PE, identify the variable presentation of PE, recognize and carry out the cost-effective diagnostic algorithm of PEs, initiate correct treatment based on hemodynamic stability.

Introduction
A PE is a common form of venous thromboembolism that obstructs the pulmonary artery and its branches. We will focus on the classic VTE form of PE, the other causes (air, septic emboli, fat, etc.) are outside the scope of this review. We can classify PE's based on timing, location, severity of symptoms.
PE's can be acute/subacute (~days-weeks), or chronic (years).
Their location is in the order of most common: lobar/segmental > subsegmental > saddle.

Originally, it was thought saddle emboli were most associated with causing hemodynamic instability, but recent data suggests otherwise. A saddle embolus ≠ "massive PE".

> Massive PE = any PE that causes hemodynamic instability.
> Submassive PE = any PE that causes greater than mild RV strain.

Pathophysiology: PE is caused by one or more aspects of **Virchow's Triad**:
1) **Stasis**: Any type of immobilization (long drives/flights/train trips, *recent surgery*).

2) **Hypercoagulable state** or 3) **Endothelial injury**: pregnancy, cancer, sepsis, fractures, contraceptive pills, or genetics. The most common inherited clotting disorder is **Factor V Leiden**. Prothrombin G20210A, Protein C&S deficiency, and Antithrombin III deficiency are other risk factors. Really, any general inflammatory state can be considered hypercoagulable.

The majority of PEs arise from VTE in the proximal legs. In fact, about 50% of patients with proximal DVT also have a PE on presentation.

PE's can result in significant pathology:
-infarction: segmental or subsegmental PEs. Classically can have Hampton's hump on chest x-ray. Hemoptysis and pleuritic chest pain common.
-V/Q mismatch
-RV strain: increased pulmonary vascular resistance works against the RV and decreases cardiac output.

Presentation
Most common symptom: dyspnea > pleuritic pain > calf pain/swelling > cough …orthopnea, hemoptysis
Most common sign: tachypnea > calf swelling > tachycardia > crackles/rales > murmurs/JVD...

Pearls in the HPI: *true* exertional dyspnea. Instead of asking "do you feel short of breath when exerting yourself?" ask "describe what triggers your dyspnea?" or "give me an example when you feel most short of breath."

Onset of dyspnea is usually sudden and <1 hour.
PE is also a common cause of sudden cardiac death (~8%) of patients, so suspicion should always be high in those presenting with cardiac arrest.
Syncope has been found to not be a major risk factor associated with PE. In 2 large studies, PE prevalence was only about ~1%.

Certain patient populations like those with CHF or COPD can make it difficult to diagnose PE. A recent study suggested up to ~20% of patients with COPD exacerbations had some type of PE (granted this was a single center and some PEs were only subsegmental). Best advice here is to work up their primary complaint and if there is lack of improvement or symptoms/signs suggesting PE > CHF/COPD, do not hesitate to work it up.

Diagnosis
Accessory tests that are usually ordered in dyspneic patients: CBC, BNP, CMP, blood gas, troponin, EKG, CXR.

EKG: Forget what you learned in medical school. The most common finding associated with PE is "normal sinus rhythm" and the most common abnormal finding is "sinus tachycardia" followed by ST segment and T wave changes. *The* most specific sign for PE on EKG is flipped T waves in anterior and inferior leads.
What about that S1Q3T3? Turns out it is not specific at all for PE, however if you see it on EKG in a dyspneic patient, PE workup is not a bad idea.
Other rare EKG findings include evidence of new right heart strain: RVH, RBBB (both <10%)
CXR: most commonly normal. Rarely, a **Hampton's Hump** (hump-shaped opacity in bottom lateral lower quadrant in either lung and often confused with PNA) or **Westermark Sign** (sharp cutoff with pulmonary vessels; "blackout") can be seen. These both are *rare*.
In general, CXR is not going to help you with PE but assist in ruling out other differential diagnoses.

Before proceeding with diagnostic testing, you need to stratify your patient based on risk.
The following diagnostic algorithms are based on the patient's hemodynamic stability (mainly BP):

<u>Hemodynamically **STABLE** nonpregnant patient</u>

The goal is to efficiently diagnose PE and limit unnecessary
testing. We apply Well's, PERC, D-dimer, and CTPA (Figure 1 to
the right). At the end of this document, we will discuss the
evidence behind these tools if you want to learn more.
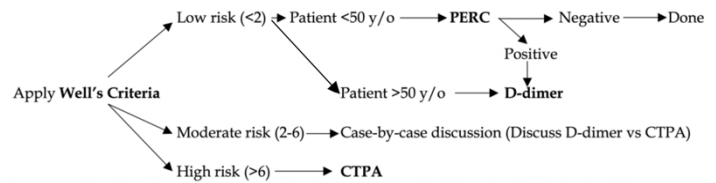
<u>Hemodynamically **UNSTABLE** patient:</u>
High suspicion for PE⟶ *immediate* anticoagulation with continued supportive care until able to proceed with CTPA.
Bedside echocardiography can potentially show evidence of right heart strain. Wall abnormalities, increased RV size, abnormal septal
wall motion, decreased RV function, are all not specific for PE but present in nearly 40% of PE patients. In general RV strain is both
poorly sensitive and specific (53% and 61% respectively).

Treatment
Untreated PE has an associated mortality up to 30%. Anticoagulation clearly reduces mortality and morbidity. Most deaths occur in the first
week from shock (massive PE group), and the other groups can have complicated, more chronic issues (e.g. pulmonary hypertension, poor gas
exchange, etc).

<u>Hemodynamically stable</u>: initiate anticoagulation after confirmed PE diagnosis. LMW in those where oral intake is not feasible.
Otherwise, rivaroxaban, apixaban, or warfarin should be discussed. Their risks, benefits, and cost are outside the scope of this handout.

<u>Hemodynamically unstable:</u>
Thrombolytics: Plasminogen to plasmin (accelerated thrombolysis). tPA is a natural plasma enzyme which binds to fibrin and
enhances affinity for plasminogen as well as plasminogen activation. tPA has been associated with early hemodynamic improvement
but obviously at cost of major bleeding.

Definite indications: persistent hypotension or shock (most widely accepted viewpoint) = "massive" PE
Few studies available, but overall there is improved mortality in these patients.

Considerations as case-by-case basis: severe RV dysfunction ("submassive" PE), cardiac arrest due to PE, free-floating right heart
thrombus.
By far, most controversial finding: right heart strain without hypotension. No randomized trials have shown mortality benefit, but
there have been studies demonstrating those with RV dysfunction and a submassive PE have worse outcomes than those without RV
strain. Better studies are likely coming soon and it is in our opinion this should be handled case-by-case.

Contraindications to thrombolytics: must be measured on the strength of the above indication.
Absolute contraindications: history of intracranial neoplasm or ICH, <2 months of intracranial trauma/injury/surgery, bleeding
condition, ischemic CVA <3 months prior.

<u>Disposition:</u>
Perform PESI (PE Severity Index): this validated score adds patient's age to points assigned to 10 variables. The total score organizes
the patient to classes of increasing risk for mortality, with <66 being the least risk of mortality, and Class V >125 being the highest risk
category.
sPESI is a more truncated approach but of similar accuracy.

<u>Prognosis</u>: risk of recurrence is highest within the 1st two weeks, declining thereafter. Mortality at 5 years is associated most with non-
cardiovascular causes (infection, cancer, etc).

BONUS TIME! More on the protocols used. This is **not an academic journal club discussion but a review of the evidence in support of our approach
to PE workup**.
Well's Criteria: clinically validated. ~50% of physicians use this score incorrectly or not at all. Maybe due to poor application of the criteria, who knows.
Gestalt fairs well against the Wells Criteria and is often just as accurate, but data shows physicians tend to overestimate risks of PE. We suggest taking
the time to calculate Wells in each patient whom PE is high on the working differential.
PERC Criteria: has been clinically validated. One crossover cluster-randomized noninferiority study tested 1916 ED's and found PERC was not inferior
to D-dimer in low risk patients. The application of PERC reduced ED stay (by at least 40 minutes), reduce CTPA usage (by nearly 10%), and only one
patient was found to have an undiagnosed PE at 3 month follow up. PERC should *not* be used where the local population PE prevalence is >7%.
D-dimer: here's the deal. This test is hotly debated. We believe it does have a role, but in a very select group of patients. The test is horribly specific (40-
60%) with a high sensitivity. We support the use of age-adjusted cut-off values as age can reduce the specificity of the test.
Age (if over 50) x 10 = cutoff value in ng/mL
In low risk patients, <500 ng/mL effectively rules out PE. In moderate risk patients, handle this case-by-case → we favor CTPA in most. D-dimer should
not be used in high risk patients.

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Apply **Well's Criteria**

- Low risk (<2) → Patient <50 y/o → **PERC** → Negative → Done
  - **PERC** → Positive → **D-dimer**
- Patient >50 y/o → **D-dimer**
- Moderate risk (2-6) → Case-by-case discussion (Discuss D-dimer vs CTPA)
- High risk (>6) → **CTPA**