Thrombosis pot-pourri

March 20, 2025

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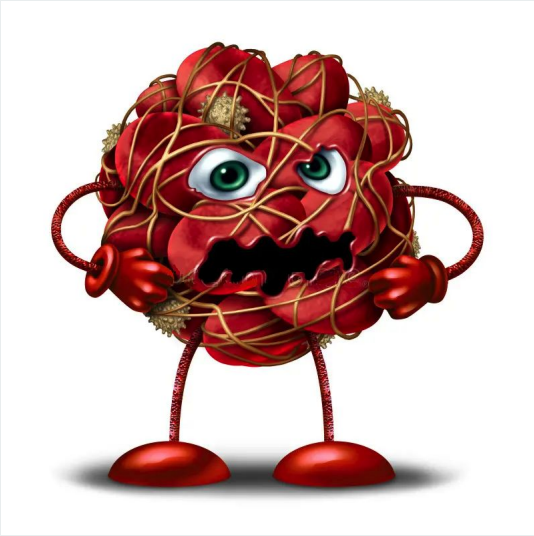
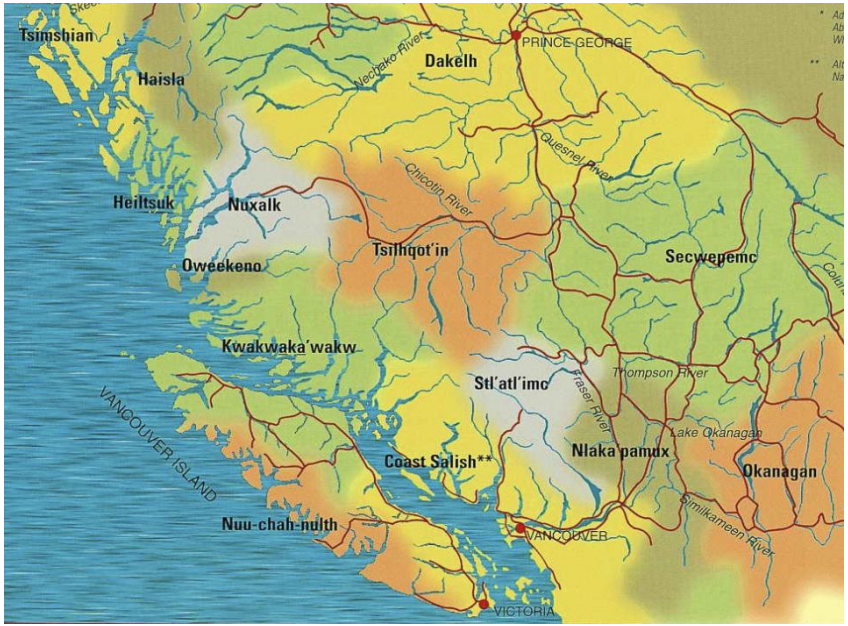


Acknowledgment

I am speaking to you today from Coast Salish territories, as an uninvited guest on the unceded lands of the xʷməθkʷəy̓əm (Musqueam), Sḵwx̱wú7mesh (Squamish), and səlilwətaʔɬ (Tsleil-waututh) Nations.



Disclosures

I have no conflicts of interest or financial disclosures

Objectives

1. Review some clinical presentations of thrombosis
2. Review factors promoting thrombogenesis
3. Approach to VTE
    a. Classification + risk stratification
    b. Management
4. Considerations in special cases

Case 1: HPI

Previously healthy 52 M from Burkina Faso, arrived to Canada 1 week ago.

Presents to ED with sudden onset SOB starting yesterday.

- No fevers, dry cough in the past 2-3 days with no sputum production, no hemoptysis, no other infectious symptoms.
- No constitutional symptoms.
- No history of chest pain or exertional symptoms, no orthopnea or PND.
- Flew from Burkina Faso > Nairobi > Montreal > Vancouver with total travel time 22 hours.
- Does not report any significant leg pain or swelling.
- No smoking history.

Case 1: Initial investigations

- CBC, lytes, creatinine normal
- Troponin and BNP normal
- Viral swabs pending

- CXR normal
- ECG shows sinus tachycardia

Case 1: Physical Exam

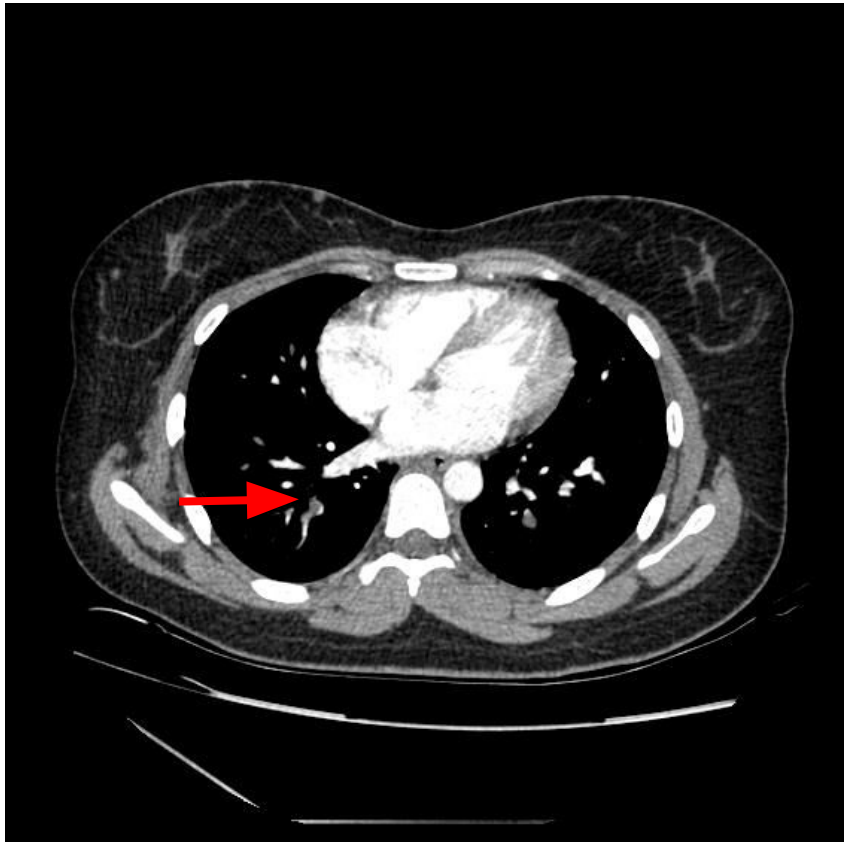
- BP 124/87, HR 108, RR 22, SpO2 93% on RA, afebrile.
- Looks well, no acute distress, alert & oriented
- Lungs are clear to auscultation
- Normal S1/S2, no S3/S4, no murmurs, JVP nondistended
- Abdomen unremarkable
- No obvious leg swelling, erythema, or tenderness, no skin lesions/rashes

Case 1: Bedside US

- Cardiac US:
  - Visual normal LV size + systolic function
  - Normal RV size and TAPSE (RV systolic function)
  - No septal bowing or flattening
  - No effusion
- Lung US:
  - A lines throughout with only occasional B lines in the bases (<3 per field)
  - Regular appearing pleura
  - No areas of consolidation visualized

Case 1: CT-PE

- CT-PE shows segmental pulmonary embolism in the posterior basal branch of the right lower lobe
- RV/LV ratio 0.8
- No contrast reflux into IVC



Pulmonary embolus: Clinical Presentation

Common presentation:

- Dyspnea +/- hypoxemia
- Chest discomfort

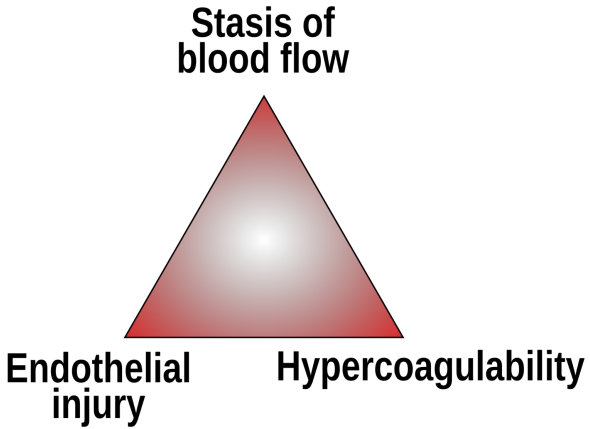
Other possible presentations:

- Cough
- Hemoptysis
- Palpitations / tachycardia
- Syncope / presyncope
- Hypotension
- Cardiac arrest (typically PEA)

Basic principles of thrombosis

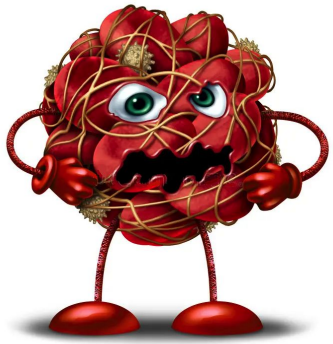
Clot forms when something disturbs the homeostasis of thrombogenesis and thrombolysis

Virchow's triad:

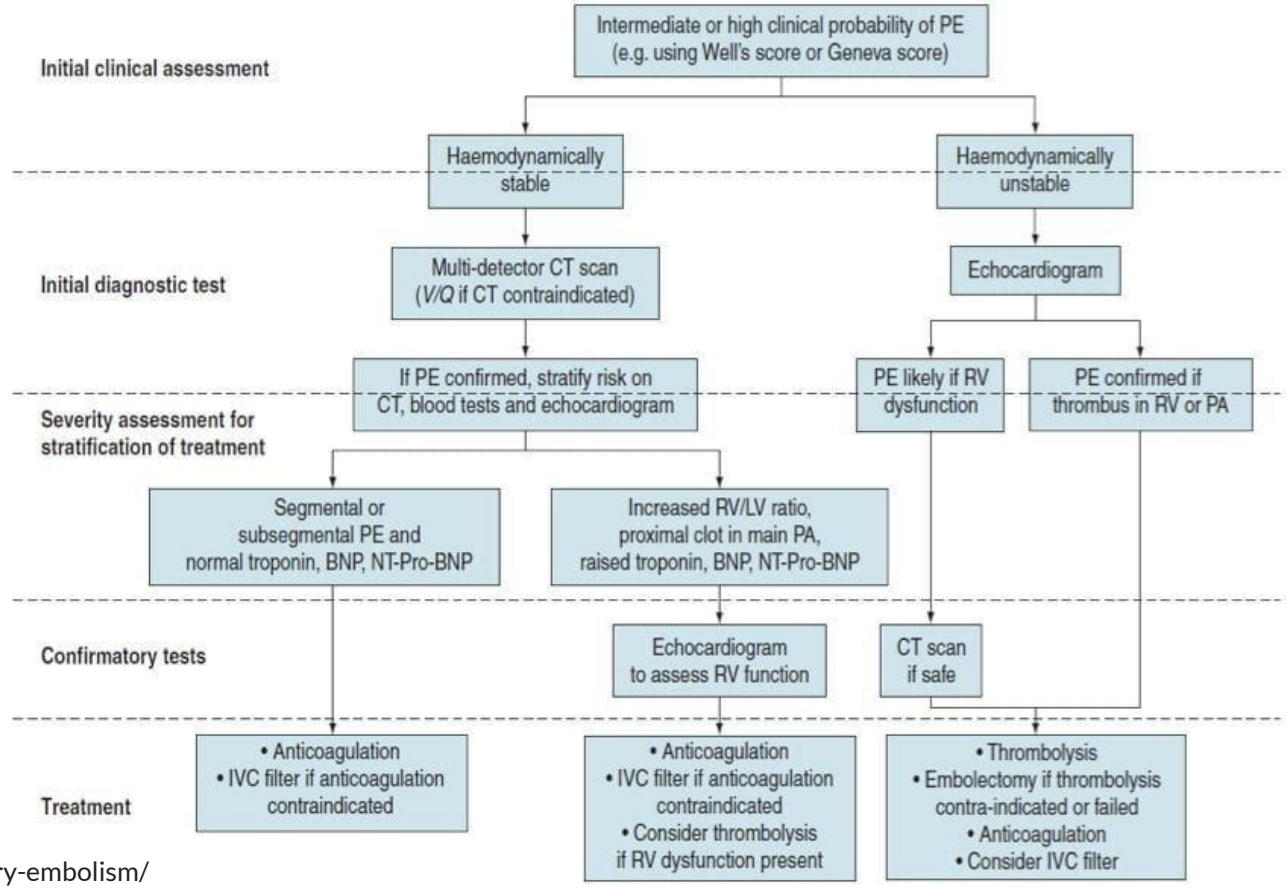


Approach to VTE

Step 1: Stable or unstable?
Step 2: High risk features?
Step 3: Treatment options
Step 4: Duration of treatment



Approach to PE



https://litfl.com/pulmonary-embolism/

Approach to PE

Step 1: Stable or unstable?
Step 2: High risk features? ● RV dysfunction ● Myocardial ischemia ● Decreased cardiac output ● Proximal clot or large clot burden

Risk stratification and disposition?

PESI (Pulmonary Embolism Severity Index)

- Score < 85 (Class I or II) = low risk of 30 day mortality

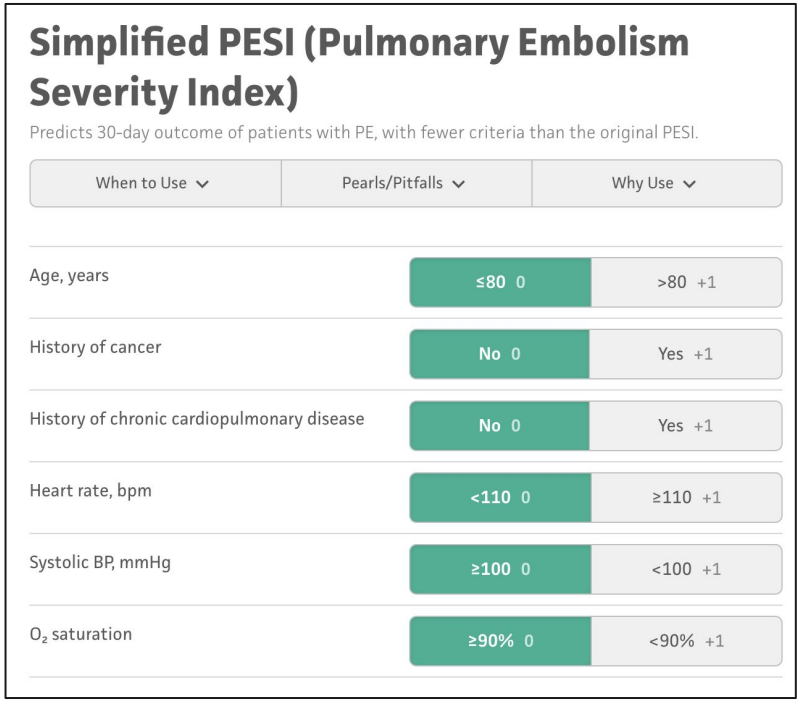
Simplified PESI

- Score 0 = low risk of 30 day mortality
- Score ≥ 1 = increased risk of 30 day mortality

Other increased risk situations might include:

- Elevated lactate, troponin or BNP
- Syncopal event
- Large clot burden, concomitant large DVT

Low risk patients can likely be treated as outpatient, if otherwise well enough to go home



Anticoagulant	The good	The bad
DOACs • Apixaban • Rivaroxaban • Edoxaban • Dabigatran	• Effective in most VTEs, including cancer-associated • Lower bleeding risk than warfarin • Ease of administration	• Reversal agent may not be readily available • Different absorption depending on patient and diet factors • Drug interactions
VKA • Warfarin	• Affordable • Useful in APS, mechanical or rheumatic valves, breastfeeding • Reversible	• DRUG INTERACTIONS • Diet interactions • Frequent INR testing • Teratogenic
LMWH • Enoxaparin • Dalteparin • Tinzaparin	• Effective in most VTEs, including cancer-associated	• Needles • Moderately expensive if not covered • Comes from pigs - concerns for animal rights or religious beliefs
UFH	• Use if procedures anticipated • Fast on/off, reversible	• IV infusion + frequent labs • Difficult to titrate

Duration of treatment? Depends on…

- Persistent vs. transient risk factors
- Major vs. minor risk factors
- Risk of recurrent clot vs. risk of bleeding

Strong risk factors (odds ratio ≥ 10)

- Fracture (hip or leg)
- Hip or knee replacement
- Major general surgery
- Major trauma
- Spinal cord injury

Moderate risk factors (odds ratio 2 to 9)

- Arthroscopic knee surgery
- Central venous lines
- Chemotherapy
- Congestive heart or respiratory failure
- Hormone replacement therapy
- Malignancy
- Oral contraceptive therapy
- Paralytic stroke
- Pregnancy/postpartum
- Previous venous thromboembolism
- Thrombophilia

Weak risk factors (odds ratio < 2)

- Bed rest > 3 days
- Immobility due to sitting (eg, prolonged car or air travel)
- Increased age
- Laparoscopic surgery (eg, cholecystectomy)
- Obesity
- Pregnancy/antepartum
- Varicose veins

Prognostication: Risk of recurrent VTE

	1 Year after Stopping Anticoagulants	5 Years after Stopping Anticoagulants
Surgical/Major	1-2%	3%
Non-surgical/Minor (e.g., hospitalization, plaster cast immobilization, hormonal therapy*, flight of > 8 hours, medical illness with immobilization)	5%	15%

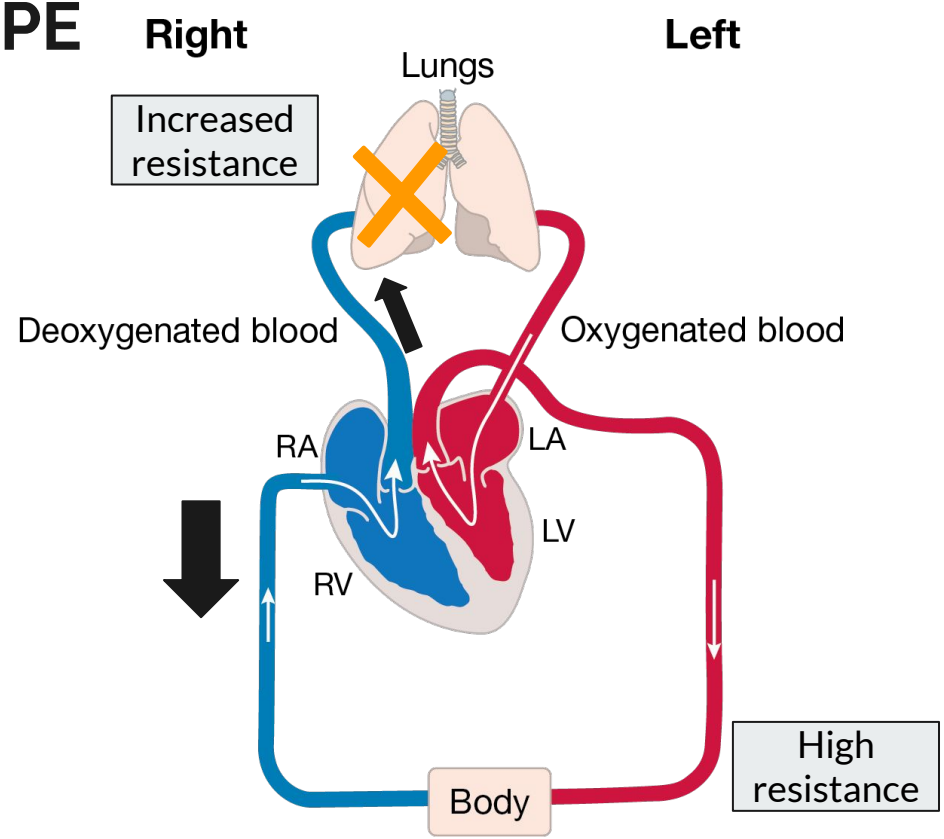
- HERDOO2 (females only)
- DASH
- Persistent risk factors (eg. malignancy, thrombophilia, etc.)

Duration of treatment

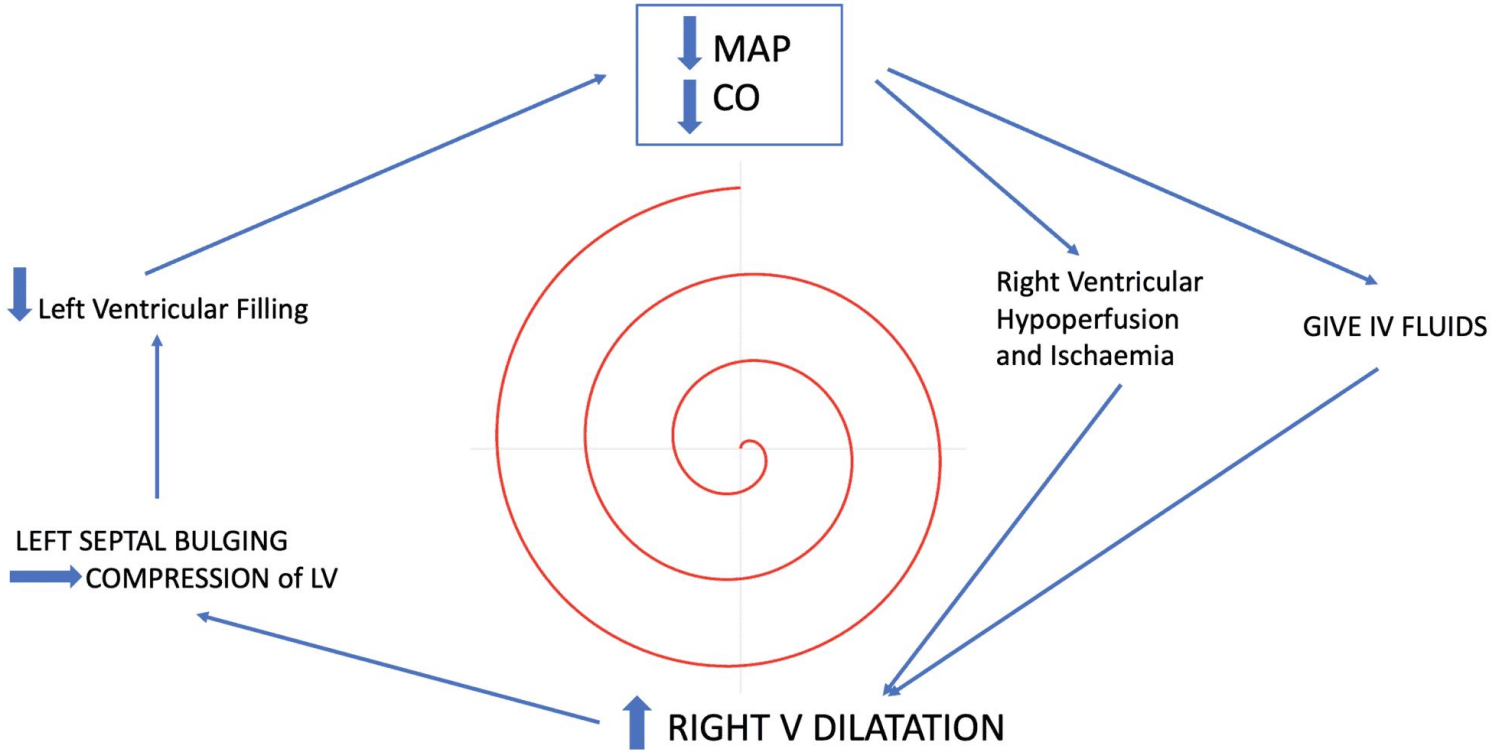
- Unprovoked VTE: Minimum 3 months, then reassess
  - If low/moderate risk of bleeding → continue indefinitely
  - If high risk → risk/benefit discussion
- Provoked by transient risk factor: 3 months
- CVC-associated VTE: 3 months after CVC removed
- Isolated distal DVT: 3 months
- Cancer or chemo-associated VTE: Continue until 6 months remission and/or chemo stopped
- APS / thrombophilia: Indefinite anticoagulation

A brief note about massive PE (Not the focus of this talk)

- Patients with PE don't typically die from hypoxemia, they die from hemodynamic failure (obstructive shock, RV failure)
- **If at all possible, avoid intubating for PE**
- Positive pressure ventilation + sedation ⇒ ⬇️ preload
- Which can cause cardiac arrest or lead you into the RV spiral of death



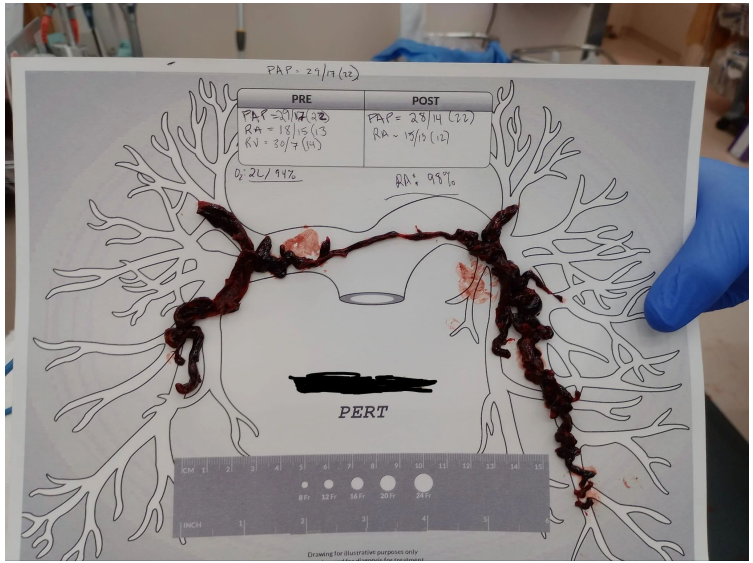
The RV spiral of death
(Still not the focus of this talk)

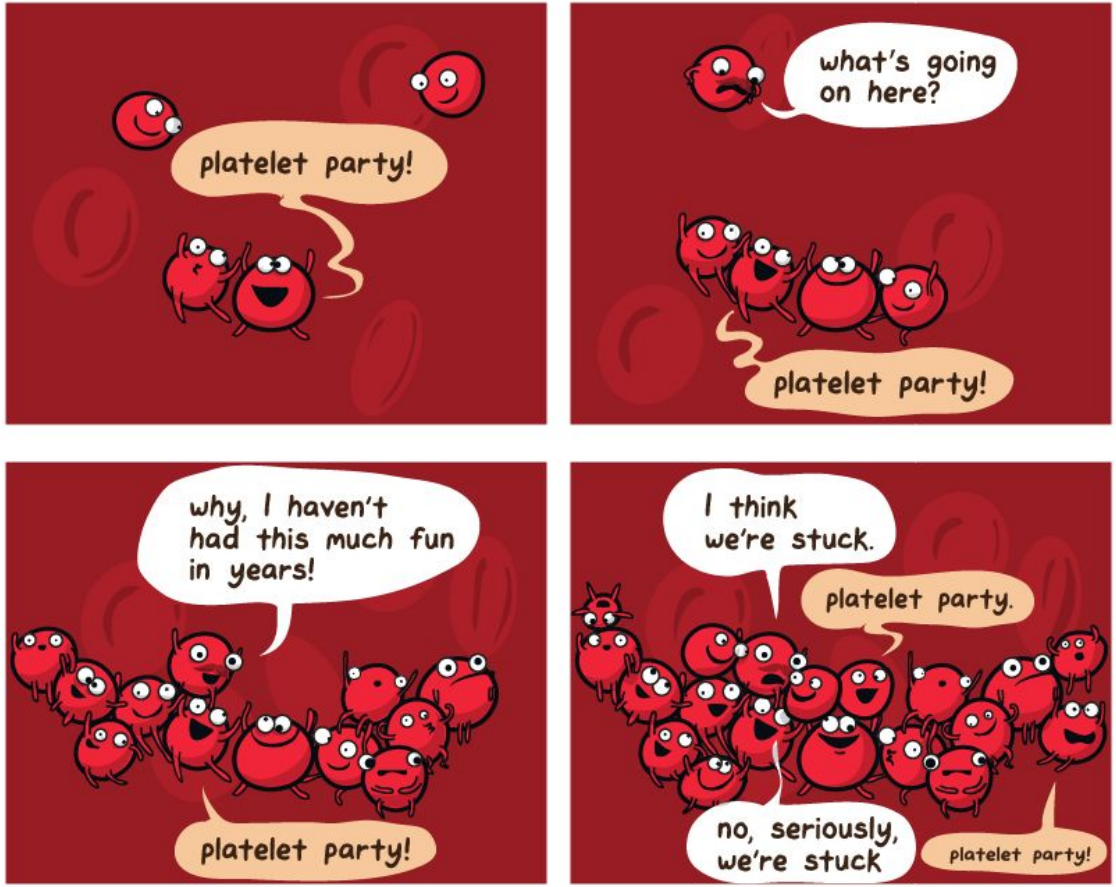


THE PE SPIRAL

Bottom line:

- Goal is to remove obstruction (aka the clot)
- If signs of early RV strain but no shock → anticoagulate
- If shock or evidence of significant RV failure → thrombolysis
- If failed anticoagulation, OR contraindication to systemic thrombolysis → thrombectomy or catheter-directed thrombolysis





theAwkwardYeti.com

Case 2: HPI

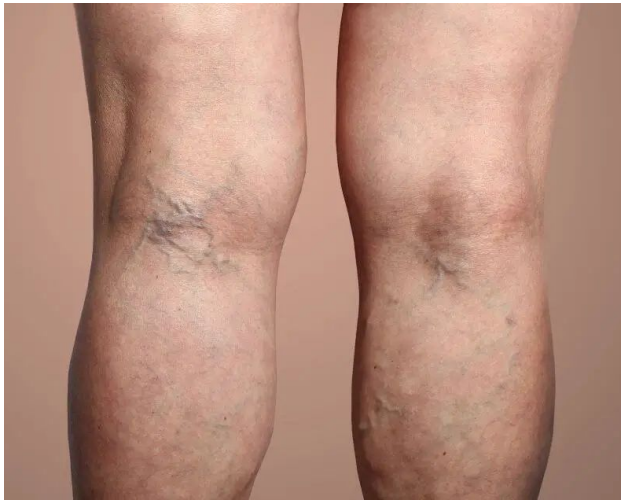
Previously healthy 36 F refugee from Syria, G3 P0 A2 at 32+3 weeks GA

Presents with 24h history of acute onset pain in the back of the left knee. No SOB, chest pain, palpitations, presyncope. Mild bilateral pedal edema since about 6 weeks ago but no calf swelling. Review of systems otherwise unremarkable.

- History of varicose veins
- 2 prior miscarriages in Syria at < 10 weeks
- No prior history of VTE
- Uncomplicated pregnancy to date, natural conception
- No recent travel, immobilization, trauma, or surgery
- No family history of VTE, recurrent pregnancy loss, or autoimmune disease
- Current meds: PNV, ASA, calcium supplement

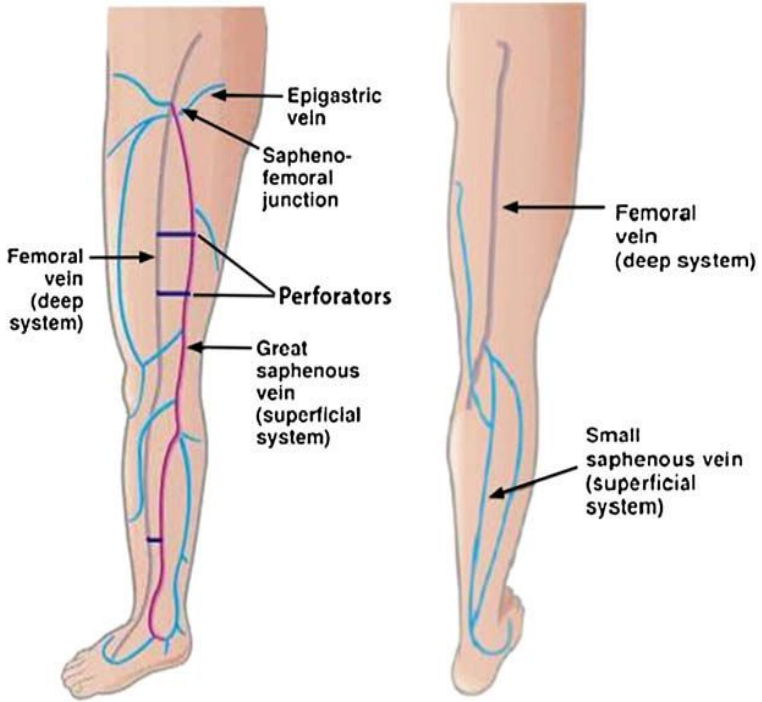
Case 2: Physical exam

- BP 116/67, HR 86, RR 18, SpO2 98% RA, afebrile
- Looks well, alert, oriented, NAD
- Cardiac and respiratory exam unremarkable
- Gravid abdomen, nontender, normal fetal movements
- Tenderness and palpable firmness of varicose veins in lateral popliteal fossa
- Mild symmetrical bilateral pedal edema



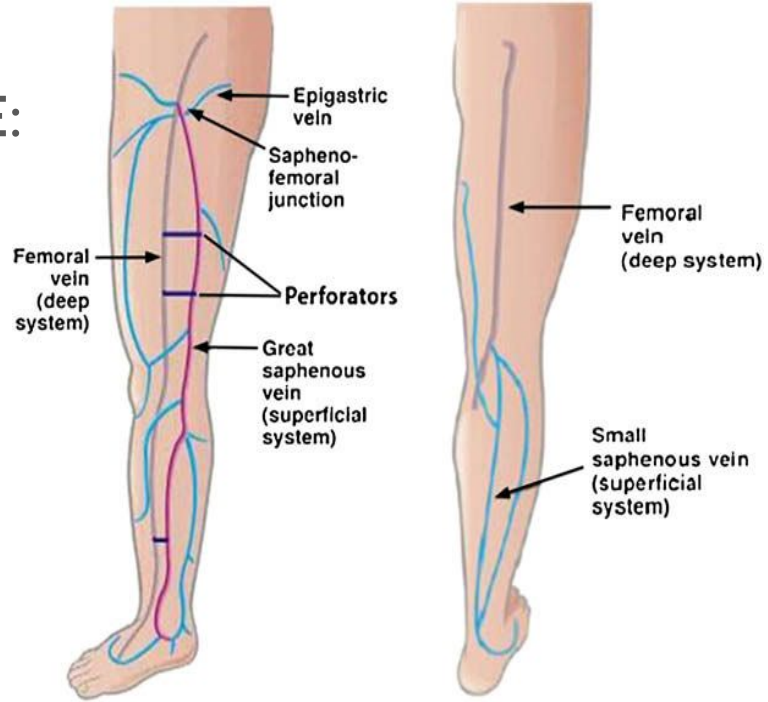
Doppler says...

- No deep vein thrombosis seen
- “Superficial venous thrombophlebitis present in the small saphenous vein measuring 3.6 cm in length, 3.5 cm distal to the saphenopopliteal junction, extending distally into several tortuous small superficial branches”



Superficial vein thrombosis

- Anticoagulate if **increased risk of VTE**:
  - SVT > 5 cm length
  - Proximity to deep vein
    ie. < 3 cm away from SFJ or SPJ
  - Positive medical risk factors



Thrombosis in pregnancy

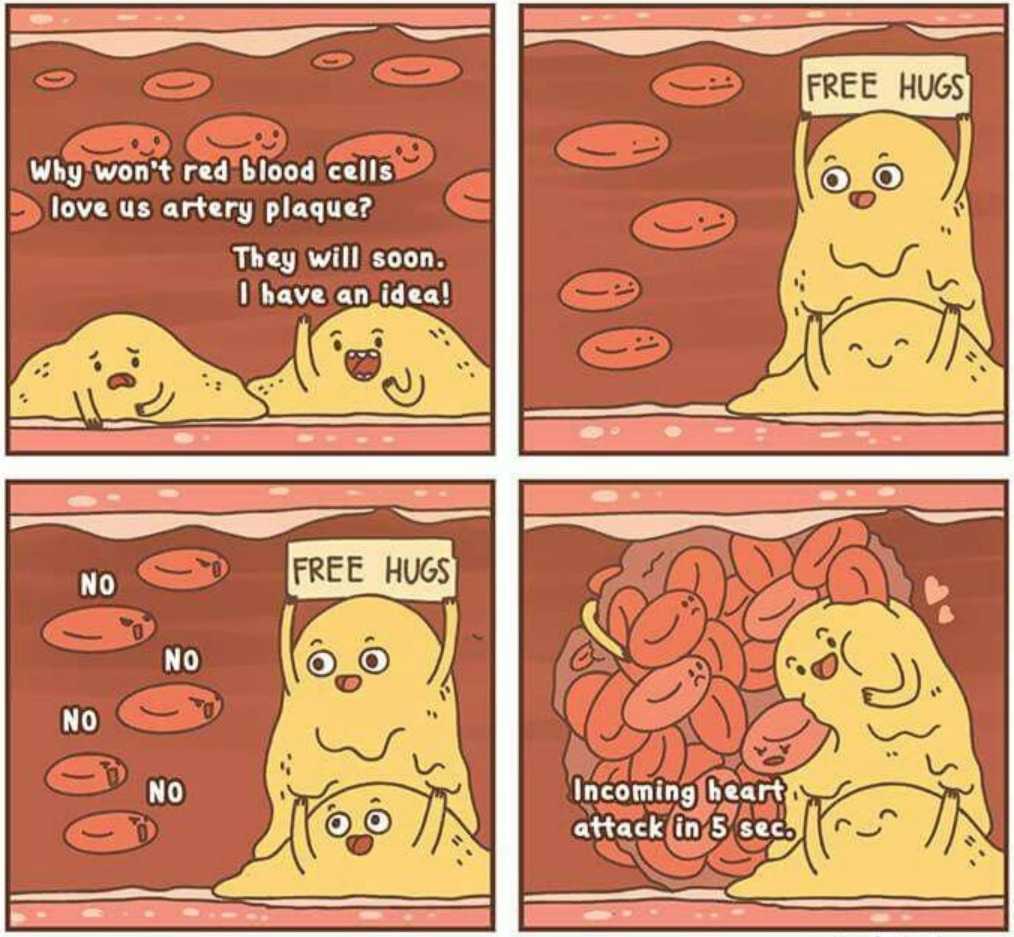
- **Thromboprophylaxis and anticoagulation in pregnancy → LMWH**
- For acute VTE in pregnancy → therapeutic LMWH
- For SVT in pregnancy → LMWH (no clear agreement on dose)
- For pregnant women with:
  - Prior history of unprovoked VTE
  - Prior history of hormone-related VTE (OCP, pregnancy)

  → prophylactic LMWH during pregnancy and until 6 weeks PP
- For pregnant women with:
  - Obstetrical APS and no prior VTE

  → ASA + prophylactic LMWH during pregnancy and until 6w PP
- Breastfeeding women → LMWH or warfarin

For our patient…

- Risk-benefit discussion with the following considerations:
  - Risk of progression to VTE
  - Bleeding risk
  - Proximity to delivery & delivery plan
  - Desire for neuraxial anesthesia?
  - Cost of LMWH
  - Ability to return for care urgently if needed
- Ultimately decided to go with prophylactic dose LMWH and repeat lower extremity Doppler US in 1 week


Why won't red blood cells love us artery plaque?
They will soon. I have an idea!
FREE HUGS
NO
NO
NO
NO
FREE HUGS
Incoming heart attack in 5 sec.
accordingtodevin.com

Case 3: History

63M active, independent at baseline, presenting with a 10 day history of progressive LUQ pain.

PMHx:

- Remote STEMI 24 years ago, received TNK. Subsequent angiogram showed no significant CAD. Normal LVEF at that time.
- Dilated cardiomyopathy NYD
    - Acute onset SOBOE 6 months ago, with LVEF 10-15% on echo. Repeat angiogram showed minimal nonobstructive CAD.
    - Cardiomyopathy workup including cardiac MRI, pyrophosphate scan, SPEP, UPEP, SFLC, TSH, ferritin, viral serologies, all negative.

Medications:

- Sacubitril/valsartan (Entresto) 24/26 mg BID, Dapagliflozin 10 mg daily, Bisoprolol 5 mg BID, ASA 81 mg daily.

Case 3: History

HPI:

- Went to Vancouver 10 days ago for his cardiac MRI, and while there had abrupt onset of LUQ pain
- Pain fluctuates in intensity but is persistent and worsening over the past 10 days
- Today the pain started to radiate to his left shoulder and throat
- No associated SOB or HF symptoms, although when the pain intensity increases he finds it hard to breathe through the pain
- No nausea or vomiting, no post-prandial pain, no change in bowel movements
- No infectious symptoms, no sick contacts or recent travel
- No constitutional symptoms, weight stable

Case 3: Physical Exam

- BP 126/80, HR 65, RR 16, SpO2 99% on RA, afebrile.
- Appears well, alert, oriented, no acute distress.
- Normal S1/S2, no S3/S4, no murmurs or rubs. JVP 3 to 4 cm ASA. No peripheral edema. Laterally displaced apical impulse.
- No increased work of breathing. Chest clear.
- Large left upper quadrant mass palpable, tender. Abdomen soft and nontender elsewhere.
- No palpable lymphadenopathy.

Case 3: Investigations

Labs:

- WBC 18.5, Hb 116, MCV 95, PLT 615
- Na 136, K 4.2, Cl 104, HCO3 27, Ca 2.41, Mg 0.89, PO4 1.23, Cr 76, GFR 92, BUN 5.8
- ALT 24, AST 84, GGT 82, ALP 387
- Total bilirubin 20, LDH 780, haptoglobin <0.01, reticulocytes 136 (H), DAT negative
- Ferritin 106, TSat 0.11, Vit B12 311
- Peripheral smear shows normocytic anemia with no schistocytes or spherocytes
- ANCA negative
- Troponin 1635 → 1839 → 12436
- UA shows positive glucose and trace hemoglobin

Diagnostics:

- ECG shows sinus rhythm with possible LA enlargement, nonspecific interventricular conduction delay, and nonpecific inferior and lateral ST changes.
- Echo shows LVEF has improved somewhat to 25%, mild to moderate MR, trivial TR, normal RVSP. No obvious LV thrombus, however no contrast used.

Case 3: Further investigations

- **CT abdomen w/ contrast:**

  “Severe splenomegaly, 20 cm in craniocaudal length. Large 6x6x6 cm enhancing mass centrally in the spleen. Multiple peripheral wedge-shaped areas of low-density in the superior spleen which may represent infarcts or additional splenic lesions. A short segment of nonocclusive thrombus is seen in the splenic vein. Linear hypodensity in the left lobe of the liver, favored to represent a short segment of portal vein thrombosis. No intra-abdominal lymphadenopathy is seen.”

- **Coronary angiogram:**

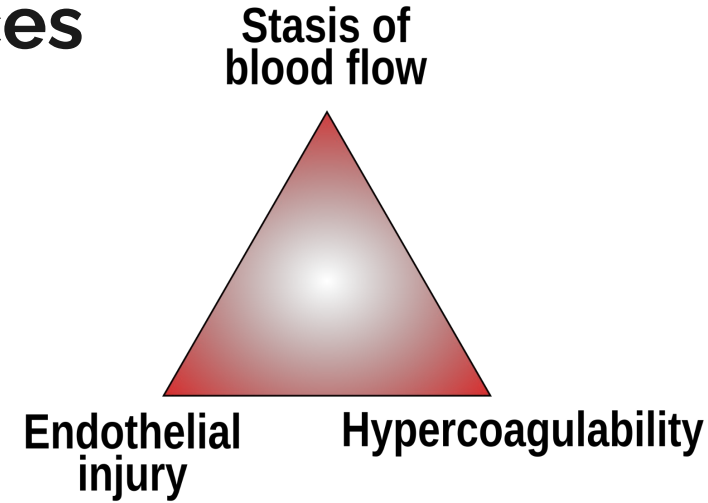
  Thrombosis seen in the left circumflex, felt to be embolic or thrombosis in situ, without evidence of significant CAD

Anticoagulation? Clots in weird places

- **Portal vein thrombosis**
  - Symptomatic or extensive PVT: Anticoagulate for 3-6 months
  - Asymptomatic: Less clear, but if underlying malignancy then treatment recommended
  - Up to 30% of non-cirrhotic PVT have MPN, JAK2 testing recommended
- **Mesenteric vein thrombosis**
  - Similar to PVT
- **Splenic vein thrombosis**
  - No strong evidence, treat underlying cause
  - Anticoagulate if embolic etiology suspected
- **Hepatic vein thrombosis**
  - Anticoagulate indefinitely

Workup: Clots in weird places

- Malignancy?
  - US Abdomen
  - Tri-phasic CT Abdomen
  - CT Chest and Neck
  - PET-CT
  - BM biopsy
- Thrombophilia?
  - APS antibodies triple negative
  - Peripheral flow cytometry
  - JAK2



1 week later

- **Flow cytometry: Positive for PNH clones**

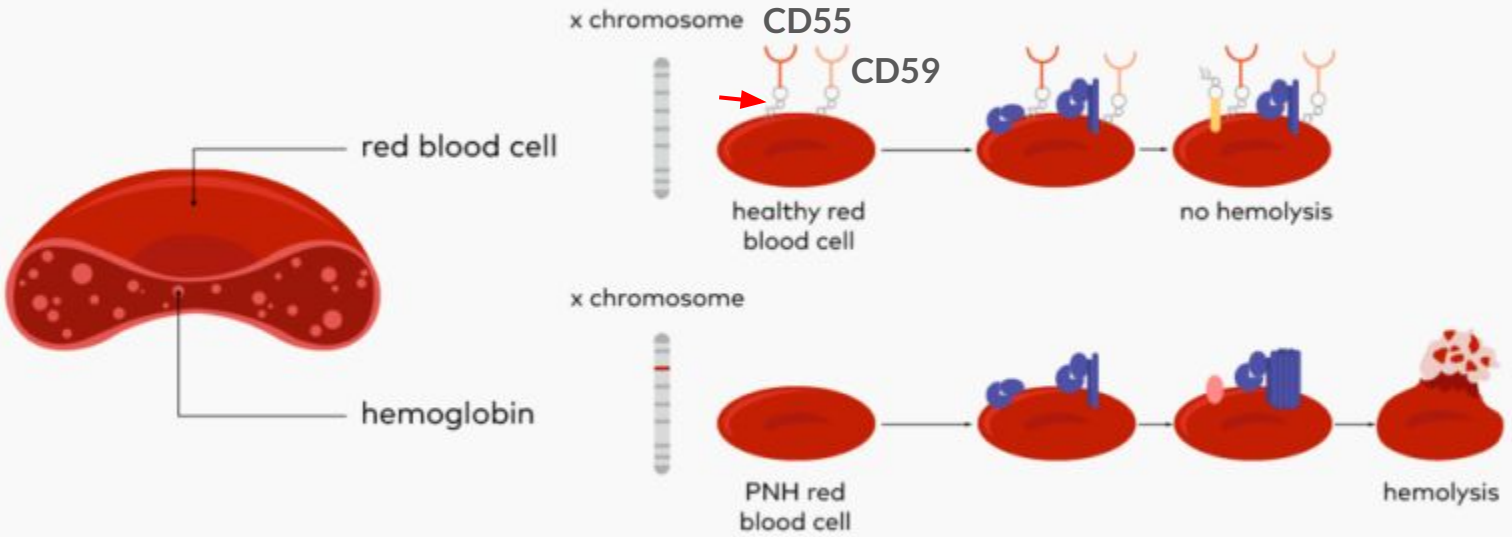
- **Bone marrow: Hypercellular bone marrow with megakaryocytic hyperplasia** and expanded sinusoids. The overall morphologic findings are **consistent with a Myeloproliferative Neoplasm** with the differential including Pre-fibrotic Myelofibrosis, Essential Thrombocythaemia and less likely Masked Polycythemia Vera.

- **JAK2 gene testing positive** for V617F mutation

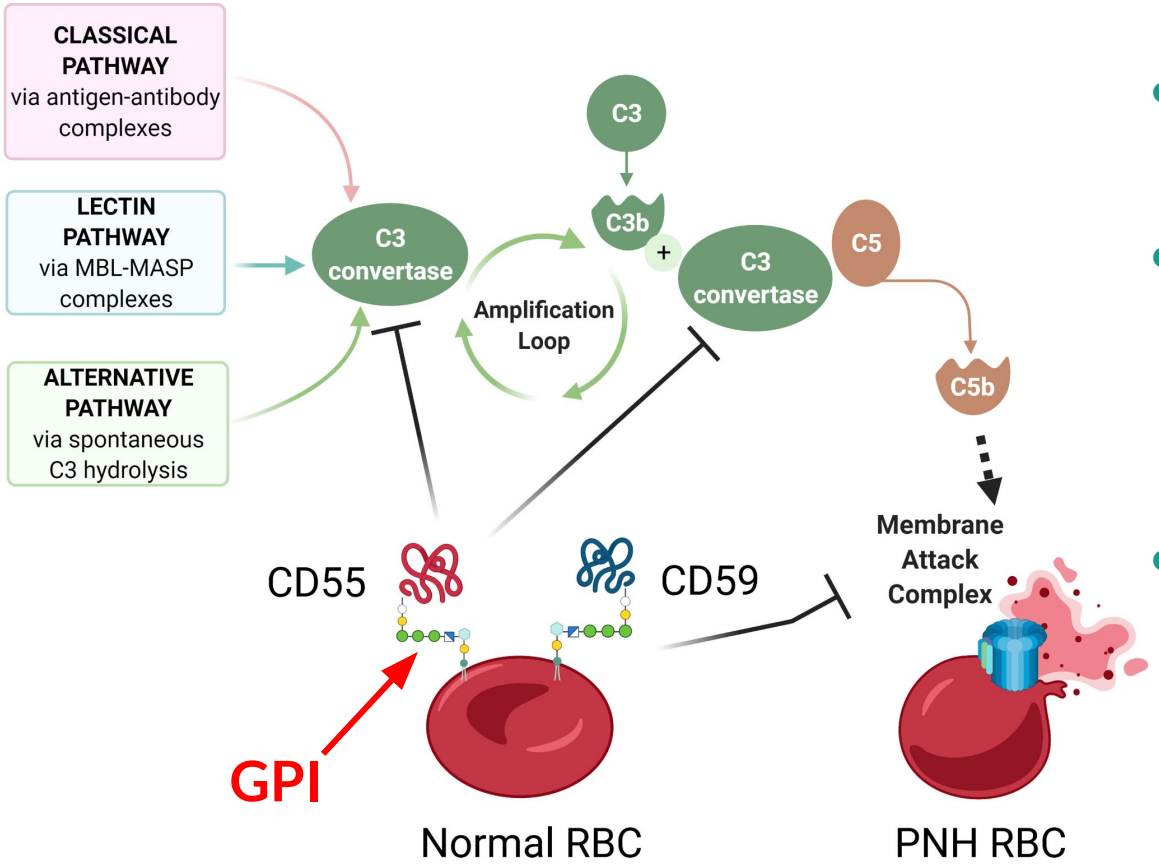
What the heck is PNH?

Paroxysmal Nocturnal Hemoglobinuria*

Acquired clonal disorder of hematopoietic stem cells affecting RBCs and WBCs



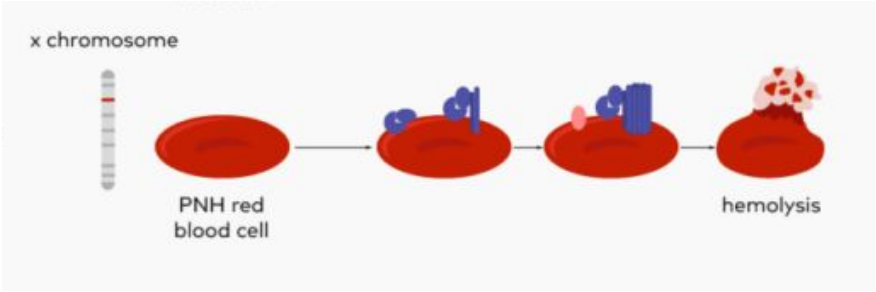
* Note: It's not actually paroxysmal OR nocturnal



- CD55 and CD59 are protective markers against complement destruction
- Gene mutation leads to absence or deficiency int the enzyme that makes GPI glycoproteins, which attach CD55 and CD59 to RBC surface
- RBCs missing CD55 and CD59 are susceptible to MAC attack → both intravascular and extravascular hemolysis

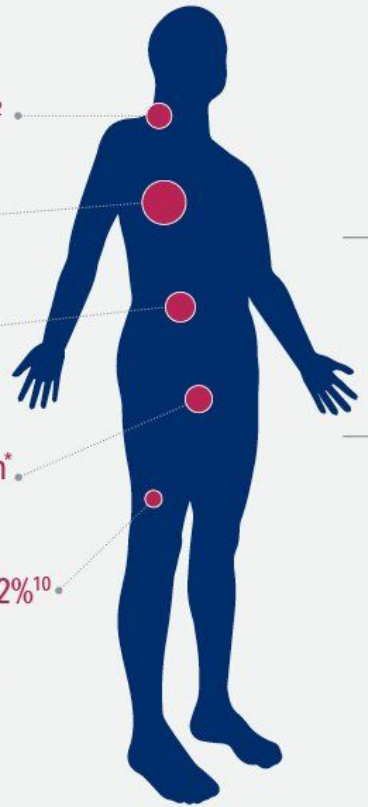
Clinical Presentation of PNH

- Classically characterized by:
  - Anemia or pancytopenia
  - DAT negative hemolysis
  - Clots, often in weird places
    - Especially splanchnic or mesenteric circulation, or CVST



- Intra and extravascular hemolysis → inflammatory cytokines and oxidative stress precipitates thrombosis
- Hemoglobinuria

SIGNS AND SYMPTOMS OF PNH



Thrombosis
causes 40 to 67% of deaths[1,9]

Renal Failure
causes 8 to 18% of deaths[1]

Pulmonary Hypertension
affects 47% of patients[14]

Adapted from[6]

Case 3: Treatment

Multifocal thrombosis

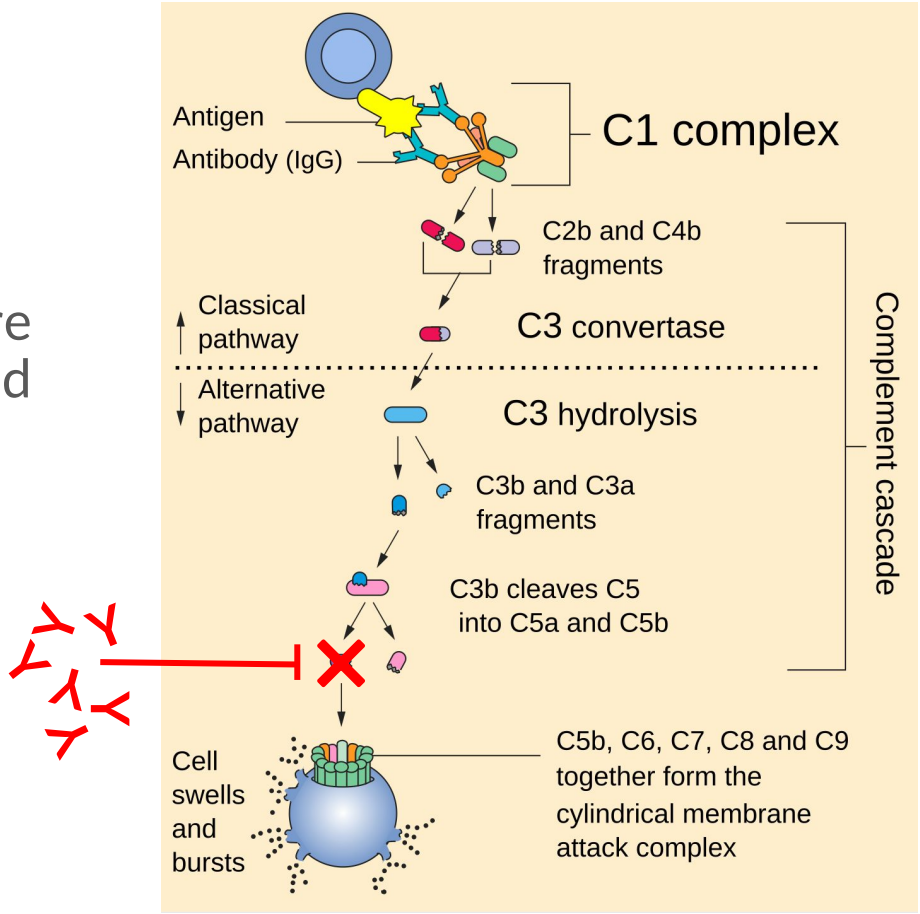
- LMWH
- After 1 month his symptoms are improving and he is transitioned to apixaban
- ASA ongoing

JAK2 positive MPN

- Hydroxyurea

PNH

- Eculizumab = C5b inhibitor



Resources:

1. Thrombosis Canada Clinical Guides. https://thrombosiscanada.ca/hcp/practice/clinical_guides
2. Ortel TL, et al. American Society of Hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. Blood advances. 2020 Oct 2;4(19):4693-738. https://doi.org/10.1182/bloodadvances.2020001830
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Thank you!

Questions?

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