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# THROMBOEMBOLIC COMPLICATIONS IN IBD

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# COI Disclosure

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- In the last 36 months:
  - Personal Funding or has sat on Advisory Boards
    - Astra Zeneca, Precisions Biologics, Hemostasis Reference Laboratories, and Syneos Health
  - Prepared educational materials and/or presented talks on behalf
    - Bayer, Pfizer, and CSL Behring
  - Has participated in various medicolegal activities relating to thrombosis, anticoagulant drugs, or other aspects of hematological practice
  - He has also worked with a variety of for-profit and not-for-profit entities such as Up To Date.

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# INTERNATIONAL CONSENSUS ON THE PREVENTION OF VENOUS AND ARTERIAL THROMBOTIC EVENTS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

# Why is this a relevant topic?

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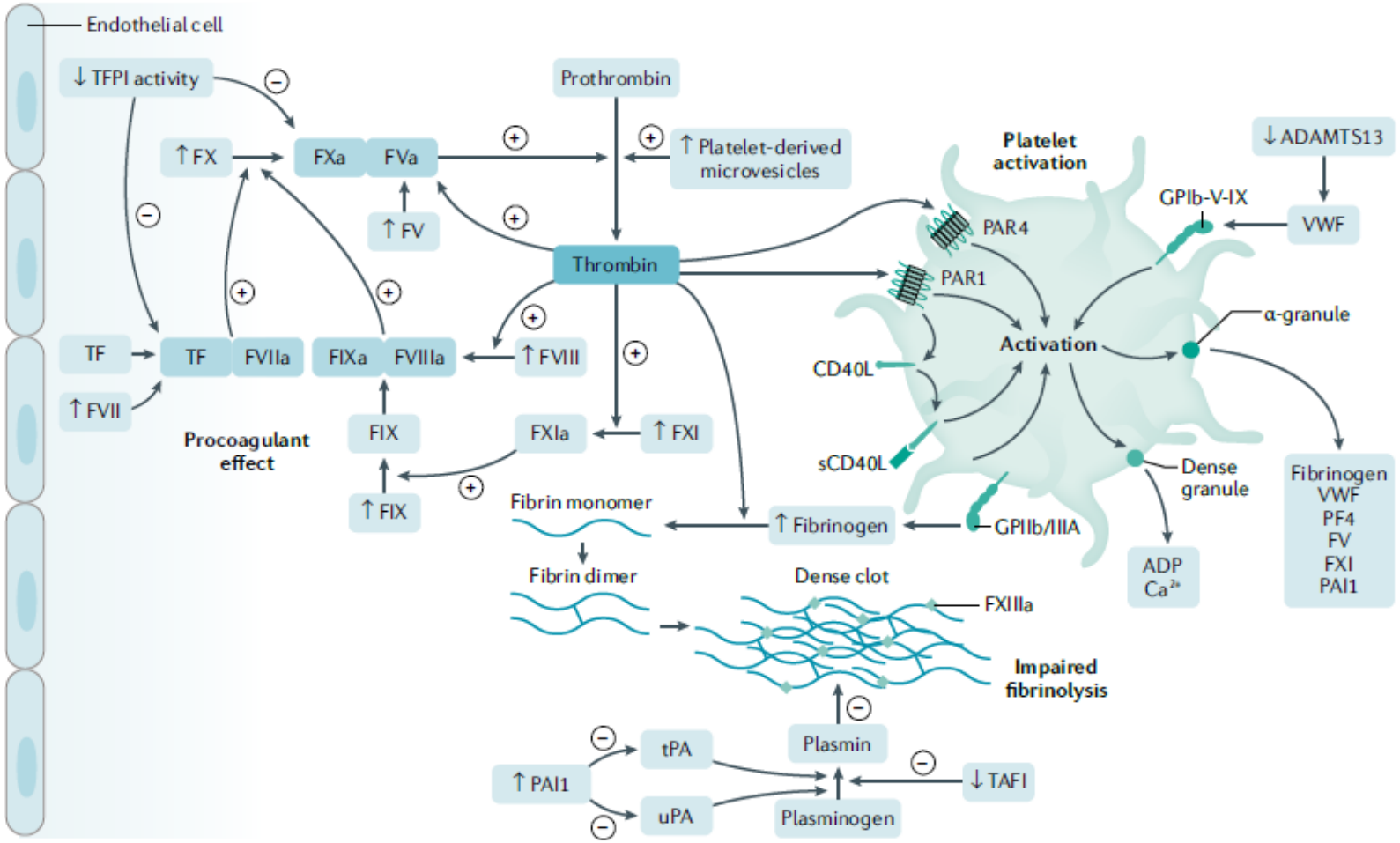
## Venous thrombosis

- Relative risk of 2.20 (95% CI 1.83 – 2.65) for DVT and PE
  - Ulcerative colitis (RR 2.57, 95% CI 2.02–3.28)
  - Crohn's disease (RR 2.12, 95% CI 1.40–3.20)

- Risk is increased by coincident risk factors frequently seen in patients with IBD
  - Need for surgery
  - Immobilization and hospitalization
  - Pregnancy
  - Disease activity and systemic inflammation

- Mitigating risk
  - Address risk factors that can be ameliorated
  - Use prophylaxis when indicated
  - Some ambulatory patients may require prophylaxis

# Egad… Figure 2



# Arterial thrombosis

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- Patients with IBD probably have an increased risk of arterial events compared with matched patients who do not have IBD

  - Some risk factors are the same in the general population
  - Risk may be disproportionate in women

    - Population-based study from Copenhagen County that included 108,789 participants (of whom 1,203 had IBD)
      - IBD patients - higher prevalence of CVD than the general population
        - »13.2% versus 10.9%; P = 0.009)
      - IBD patients had higher levels of CRP and fibrinogen
        - »May reflect the impact of chronic systemic inflammation as a risk factor for CVD

# Mitigation that is specific to IBD

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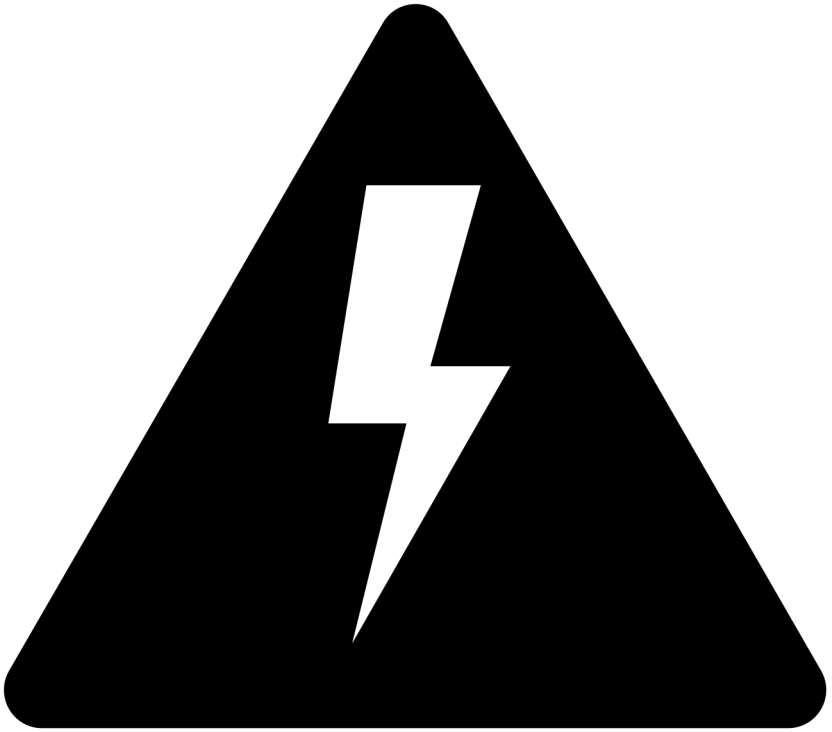
- Drugs used in IBD therapy modify the risk of VTE
  - ASA derivatives may decrease the risk
  - Steroids may increase the risk
- Generally – controlling disease activity reduces the risk of arterial and venous thromboembolism
- "Standard of practice" interventions should be aggressively pursued
  - Mobilization
  - Pharmacological prophylaxis



# A quick note on thrombophilia testing

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NO

# 2022: Anticoagulation options

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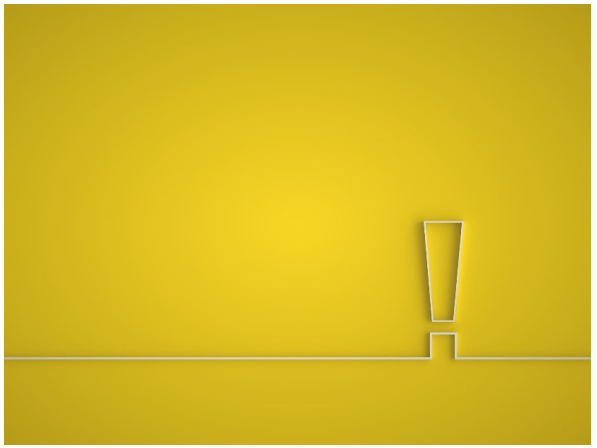
- **Heparins**
  - **UFH**
    - Complex to administer, reversible and titratable
    - May have pleiotropic effects
    - Not dependent on renal clearance
  - **LMWH**
    - Predictable anticoagulant effect
    - Easy to administer
    - Irreversible
    - Some degree of renal dependence



# 2022: Anticoagulation options

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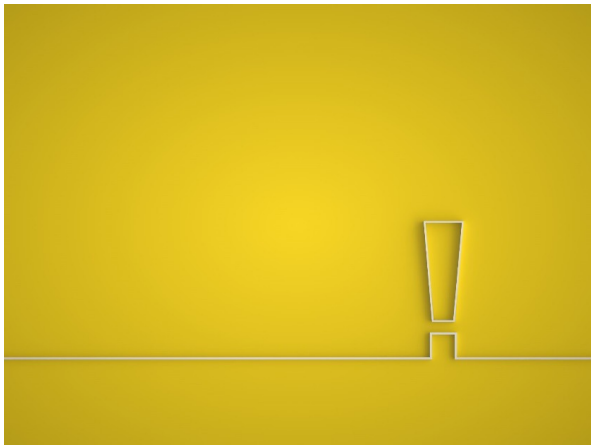
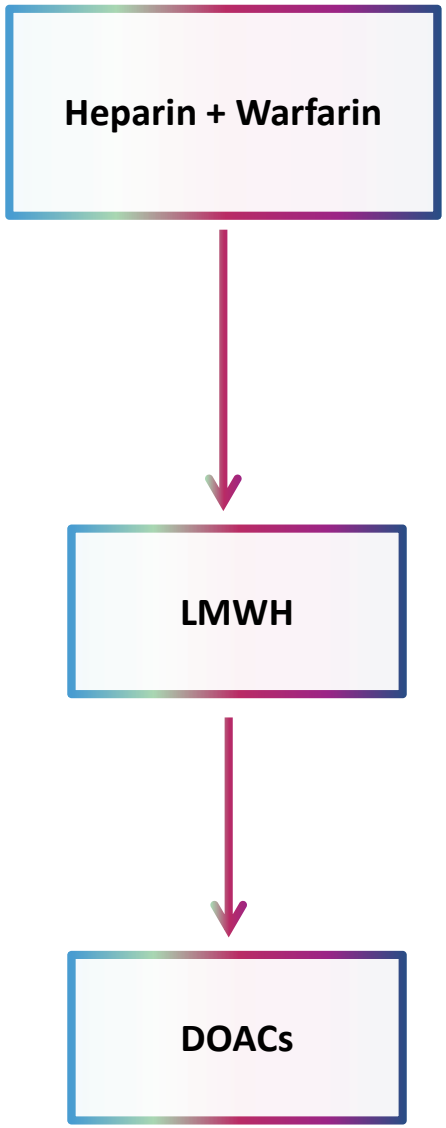
- **Warfarin**
  - Complex to administer, reversible and titratable
  - Not dependent on renal clearance
  - Still has a place in modern therapy
- **DOACs**
  - **Dabigatran**
    - Predictable anticoagulant effect
    - GI side effects
    - Reversible and no liver interactions (***)
    - Very significant renal dependence
  - **Xa inhibitors**
    - Predictable anticoagulant effect
    - Irreversible
    - Some renal dependence
- **A whole bunch of others as well**



# The evolution of anticoagulation

- As time passes and people become more comfortable with medications, use increases and the “eligible population” expands
- LMWH heparin, for example are widely used in patients with renal failure and those with a high risk of bleeding despite:
  - Renal dependence
  - Irreversible effects
- Over time, Xa inhibitors which have similar PK profiles as LMWH will be used with increasing frequency
  - Availability of a reversal agent may increase comfort and use
- The case supports this in that LMWH was chosen to treat an actively bleeding patient despite the fact it is not reversible



# Anticoagulation may be counterintuitive

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- Unpublished data on the efficacy of DOACs in patients with splanchnic vein thrombosis
- Caveat – generally low-quality data
- Major bleeding in non-cirrhotic patients
  - Use of a DOACs to treat SVT compared with no anticoagulation
    - OR = 0.09; 95% CI: 0.03, 0.29; I2=0%, n=3 studies
  - Use of a DOACs to treat SVT compared with no LMWHs
    - OR = 0.13; 95% CI: 0.03, 0.29; I2=0, n=1 study
  - Use of a DOACs to treat SVT compared with VKAs
    - OR = 0.12; 95% CI: 0.02, 0.69; I2=24%; n=2 studies
- No significant differences compared to no anticoagulation, LMWHS, and VKAs in cirrhotic patients.

# The Rock and the Hard place of anticoagulation

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- Thrombosis requires anticoagulation
- IBD is associated with bleeding, which anticoagulation will exacerbate

- Planning for anticoagulation should consider:

  – What type of TE does the patient have, and what are the risks of both direct effects of that TE and of acute extension/recurrence?
  – What was the impact of potential bleeding?
  – Are there modifiable risk factors for bleeding?

- Remember that IV UFH is a perfectly acceptable anticoagulant and is the only completely reversible anticoagulant we currently have

- IBD with clinically important VTE is one circumstance within which worsening bleeding may be tolerated as a “cost” of anticoagulation

# Need for surgery

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- Patients who may require immediate surgery should be treated with UFH
- It is reversible and does not interfere as significantly with anesthetic options
- Patients who may require surgery in the future can be treated with either LMWH or DOAC
  - Pharmacokinetics are very similar
  - Bridging is **NOT** required
- **Warfarin should be avoided**

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## Drug-drug interactions

- LWMH/UFH do not have drug-drug interactions
- Warfarin has lots of drug-drug interactions, but they are easy to deal with
- DOACs are rumoured to have many drug-drug interactions, but very few are clinically important

## Pregnancy

- Pregnancy, and the post-partum period, are high-risk periods for VTE
- DOACs are not known to be safe in pregnancy or with breast-feeding
  - The X the placenta
- Pregnancy is generally managed with LMWH
  - Requires delivery planning, particularly if the patient is on therapeutic doses
- Highest risk period for VTE is 6 weeks AFTER delivery

# A clinical case…

**Loosely based on reality**

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- 24-year-old woman with know UC presents with a disease flare and progressive jaundice
- Despite therapy for IBD reports increasing RUQ pain
- Initial ultrasound does not reveal any pathology but hepatic engorgement leads to a search for hepatic vein thrombosis
- Treated with IV UFH transitioned to LMWH then to warfarin
- Complete recovery in hepatic function
- Achieved long-term remission of UC

# Seven years later…

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- Calls to say she just had a positive pregnancy test
- I will not have anything useful to say about pregnancy and IBD or pregnancy and prior BC other than I immediately informed her gastroenterologist
- With respect to her hx of VTE
  - Immediately stop the DOAC
  - Switch to weight-adjusted, therapeutic dose, LMWH
- No need for routine monitoring during pregnancy except for adjustment based on her weight changes

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- Planned delivery with discontinuation of LMWH > 24 hours beforehand to allow the preferred type of anesthesia/analgesia

- Immediate reinstitution of LMWH
  - She planned on breastfeeding so continues for ~ four weeks until she was tired of injecting and switched to warfarin

- Remains on warfarin while breast-feeding with intent to switch back to a DOAC

# Summary

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- IBD is associated with an increased risk of VTE and ATE
- Procoagulant state is probably multifactorial
- Risk factors may be identified that can be mitigated
- Bleeding may need to be tolerated in patients with significant thrombotic burden
  - UFH is preferred
- Control of underlying disease reduces the risk of thrombosis