

How do you like your mix?

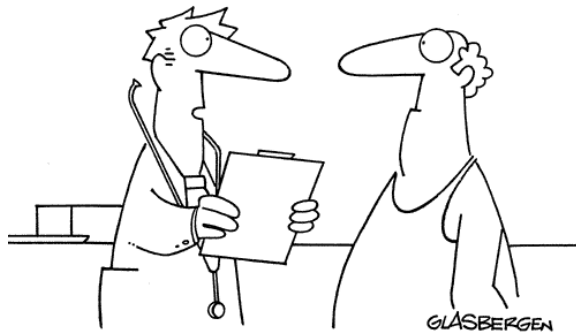
Shaken, not stirred !

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"The handle on your recliner does not qualify as an exercise machine."



SCHWADRON
"YOU'RE FEELING GREAT? THAT'S UNUSUAL...WE'D BETTER RUN SOME TESTS..."



[Mr. L. K.]

- **ID:** 76M living with his wife
- **RFC:** Epistaxis
- **PMH:**
 - AAA rupture 1988 (graft)
 - AS with porcine AVR 2002
 - DMII, BPH, Hypothyroidism, Dyslipidemia
 - No previous hx of bleeding diathesis/thrombophilia
- **Fam Hx:** no coagulation disorder
- **Meds:** ASA, Synthroid, Metformin, Tamsulosin, Pregabalin 75², Fluticasone, Amlodipine 10¹, Lasartan-HCTZ 100/25¹, Atorvastatin 40¹.

[HPI]

- Feeling of easier bruising since summer
 - In retrospect
- **Oct 10th**: Hemorrhagic lesion soft palate.
 - Saw dentist and ENT: prophylactic Penicillin.
 - Spontaneous healing.
- **Mid-Oct**: Recurrent epistaxis and spontaneous right leg hematoma
 - no history trauma. ASA held.

[HPI]

- **Oct 31st:** presented to ER with large epistaxis left nare, stopped with digital compression.
 - **INR normal**
 - **↑ PTT 66**, received 2 u FFPs
 - Hep Adsorbed PTT: 69 (↑)
 - **PTT dilution: 38.8/34.2**
 - seen in ER, patient discharged home with f/u 1 week
- **Nov 3rd:** New visit with more epistaxis:
 - **↑ PTT (55):** 2 U FFP's given.
 - Hb 130→113, plt 288, Fibrinogen N.

At this point, the differential includes...

Factor deficiency, VWD ...



[HPI]

- **Nov 4th**: arrival RVH ER (early AM), then new onset epistaxis right side and bruising right leg.
 - ↑ PTT 66, INR 1.06
 - Hb 106, plt 233
- **From Oct 31st**
 - **Factor VIII** assay **0.02** (↓ ↓). Low for all the dilutions (0.01 to 0.04).
 - Factor IX, XI, XII assays and fibrinogen: N

Factor VIII Deficiency

What about the mix?

-The ptt dilution study, not your martini!

Important testing and treating issues



[Acquired Hemophilia A]

- Acquired inhibitors against factor VIII (FVIII)
- Rare
 - About 1-4 per million/year in general population
 - Hence paucity of evidence-based literature
 - 14.7 per million/year above 85 yo.
 - Same incidence in men/women except 20-30 yo
 - Small peak from 20 to 30 yo because of pregnancy (post-partum inhibitors)

[What are the manifestations?]

- No known genetic inheritance pattern
- Usually in adults
- Median age at presentation is 60-67 yo.
- Bleeding pattern:
 - Congenital: hallmark is hemarthrosis
 - **Acquired: RARELY hemarthrosis**
 - purpura, soft tissue bleeding, muscle bleeding, hematuria, GI bleed and intracerebral bleeds.
- No explanation found to explain difference in bleeding patterns

[How deadly?]

- **Mortality: 8-22%**
 - 3 large studies
 - More recent studies report slightly lower mortality
- Frequently confused with conditions like DIC
- Elderly population already frail
- Most present with severe bleeding
 - 87% requiring transfusions
- **Morbidity:**
 - Compartment syndromes
 - Iatrogenic (angio, arterial punctures...)

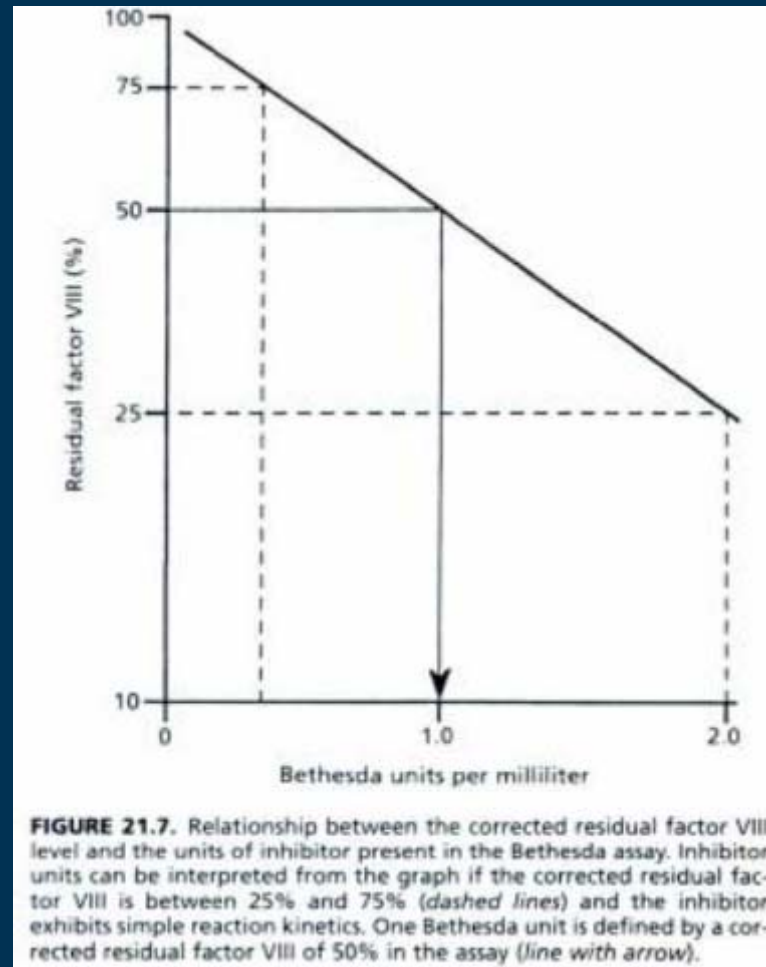
[How to diagnose it?]

- Associated disease/state:
 - Post-partum (often after delivery)
 - 50% idiopathic
 - CTD, malignancy, drugs
- Increased PTT
- R/O heparin contamination
- R/O lupus anticoagulant
- Mixing study with appropriate protocol
 - Indication on the request

[Mixing study]

- Mix with pooled normal control plasma
 - If it corrects: factor deficiency
 - If it does not: inhibitor
- BUT...
- If FVIII inhibitor is suspected, it should be done at 37°C for at least 1h
- It binds FVIII in **time** and **temperature**-dependent manner
- Weak inhibitor might take up to 2 hrs to react
 - Calculated in Bethesda units

[Bethesda Unit]



[Management]

- Acute control of hemorrhage
 - Increase FVIII
 - DDAVP or FVIII concentrate
 - Bypassing Agent
 - aPCC or rFVIIa
 - Important risk of thrombosis
 - Mr K. had a stroke likely due to rFVIIa
- Eradication of inhibitors
 - Immunosuppression
 - Infection is the first cause of death in some registry
 - Rituximab + steroids

[Key points]

- When to suspect it?
 - Rare disease of the elderly
 - Post-partum
- Prognosis?
 - Significant mortality (8-22%) from
 - Bleeding
 - Infection post-treatment

[Key points]

- Approach to diagnosis
 - Pitfall: make sure that mixing study was incubated long enough
- How do you manage it?
 - No clear standard of care, often time rFVIIa in Canada
 - Multiple regimen for long term eradication; Rituximab more and more common
 - Relapse is not uncommon

Ahh, life as a student...

