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# Basics of Factor XI Deficiency

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**NATIONAL HEMOPHILIA FOUNDATION**



# Disclosures

## **Danielle Nance, MD**

Ad boards for Anlylam, Aptevo, Bayer, Bioverativ, Genentech, Octapharma, Shire. Speaker fees from Octapharma, Bioverativ. Grant funding from Bayer.

I am grateful for the opportunity to serve you





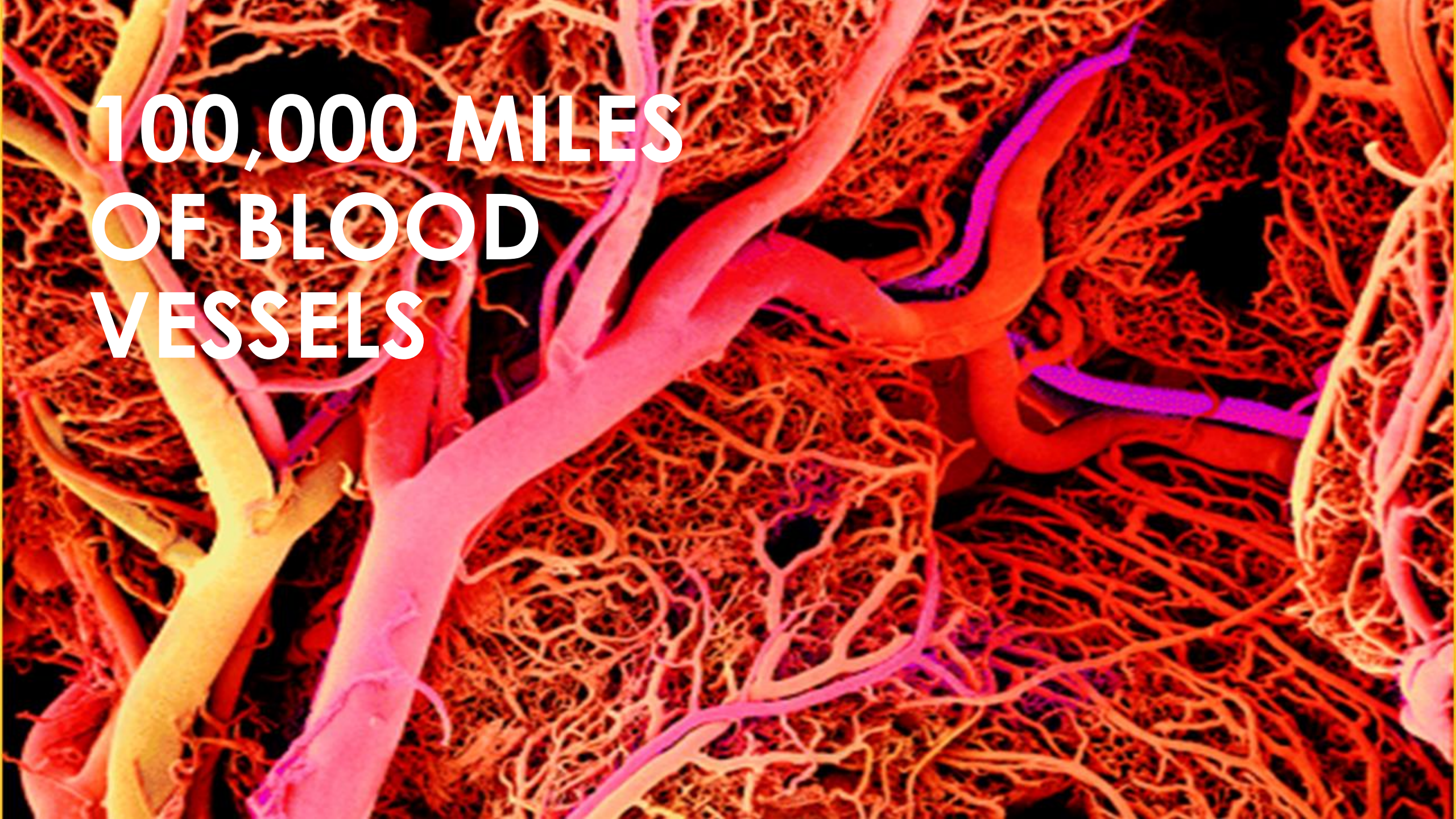


# Contents

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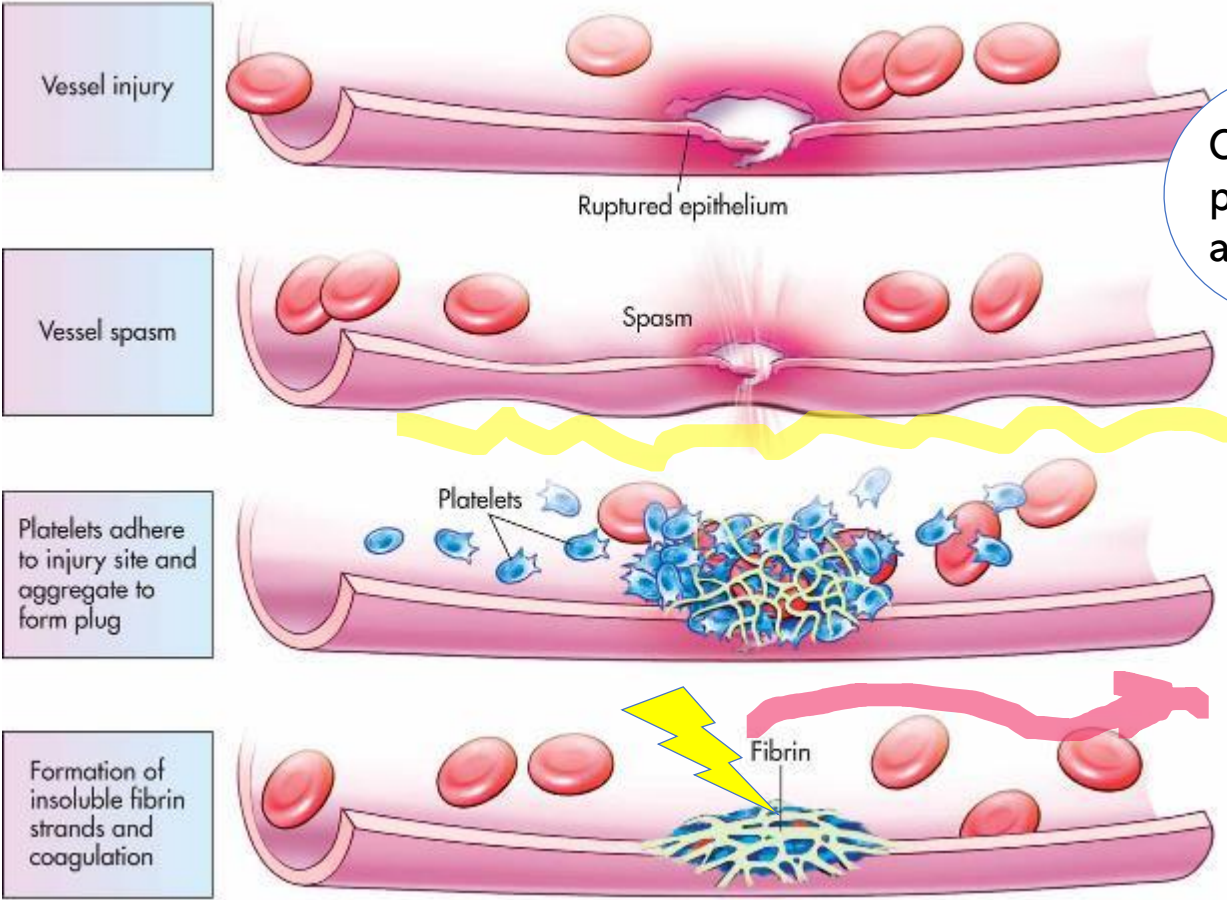
- Hemostasis primer
- Factor XI Statistics
- Factor XI Structure
- Factor XI Function
- Fun facts and wrap up





**100,000 MILES  
OF BLOOD  
VESSELS**

# Hemostasis = Healing

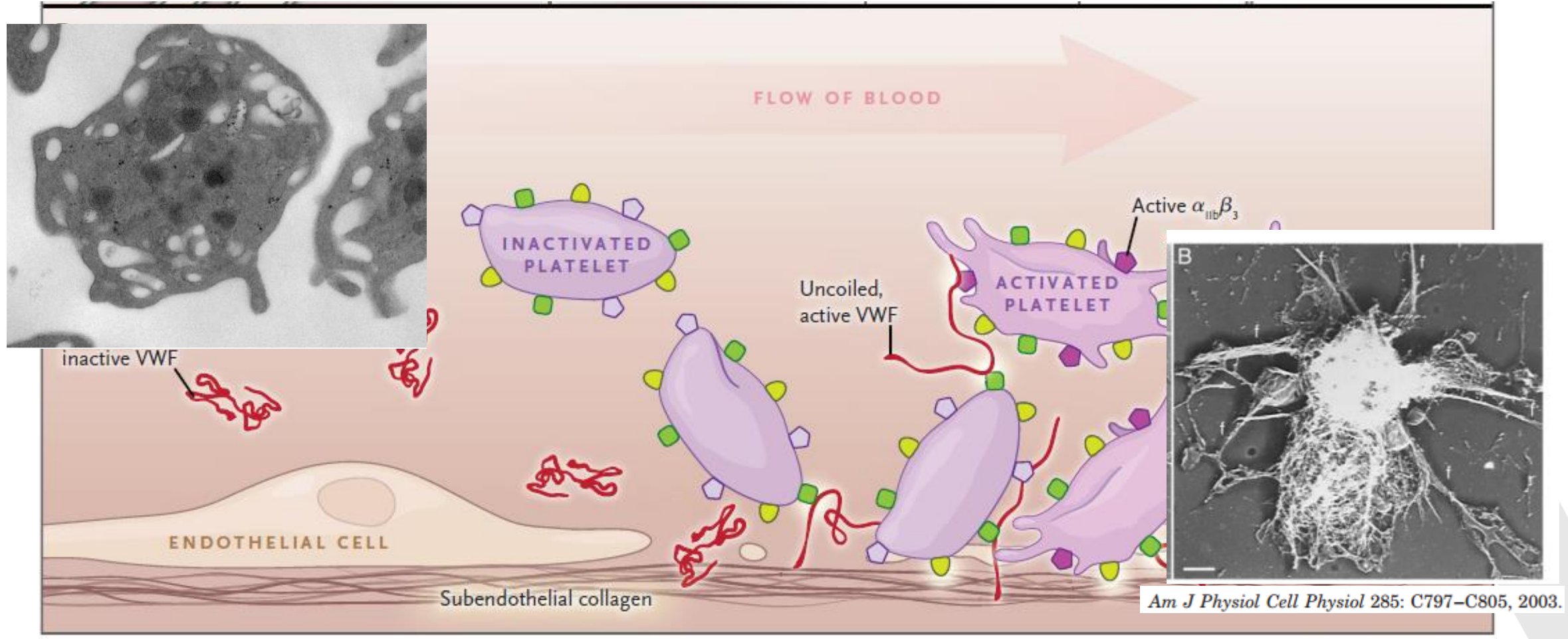


Collagen provides the anchor

VWF is the tether

Platelets are the surface

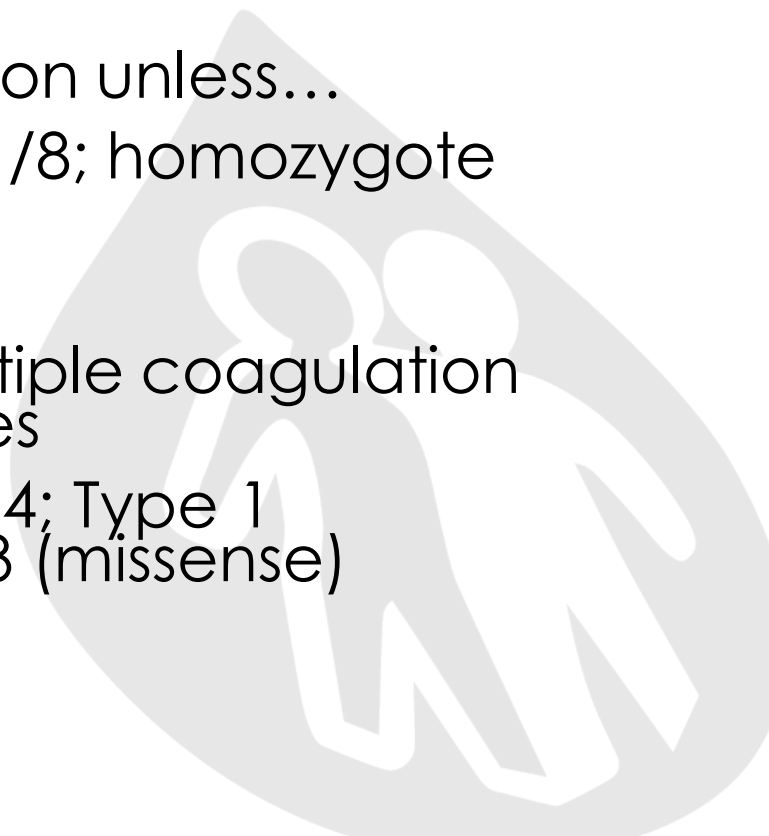
# Platelets + VWF = Happiness





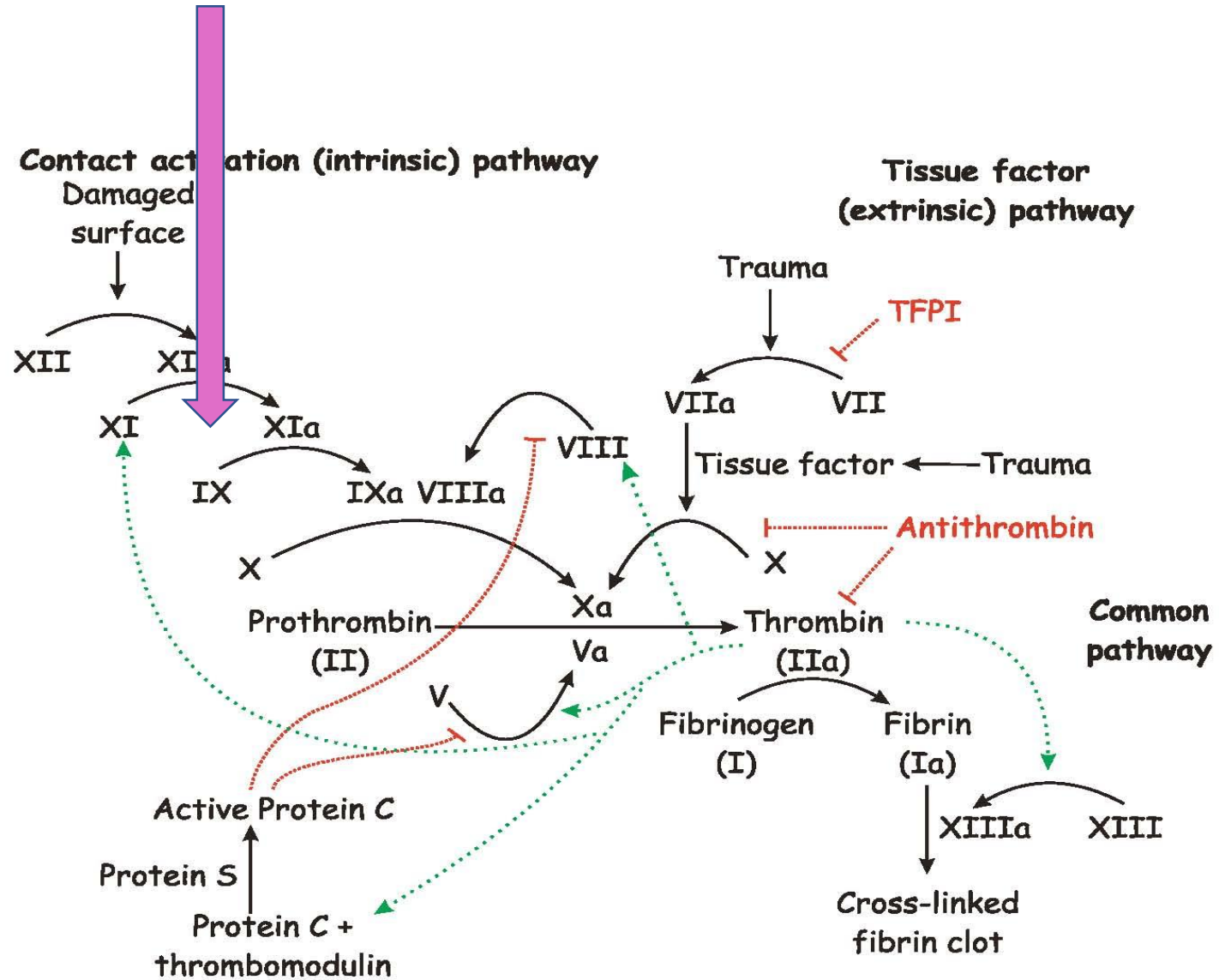
# Factor XI Deficiency = Hemophilia C

- Discovered/described in 1953 (Rosenthal). Index case was bleeding post dental extraction, also called hemophilia C.
- Typically symptomatic when **factor activity is <10%, but exceptions apply**
- Seen in all genetic back grounds, and is 1 in a million unless...
- Ashkenazi Jewish population (heterozygote freq: 1/8; homozygote freq: 1/400)
- Associated with Noonan's syndrome
- Can occur in combination with FMFD (familial multiple coagulation factor deficiencies), Factor VIII/IX, VWF deficiencies
- Autosomal recessive inheritance on chromosome 4; Type 1 (intron/exon junction), Type 2 (stop codon), Type 3 (missense)
- Autosomal dominant for some types



# Factor XI fits here in the cascade

- Synthesized in the liver
- $T_{1/2} = 55$  hrs
- Activated by XIIa, thrombin, platelets
- Inactivated by  $\alpha_1$  antitrypsin, antithrombin (formerly known as ATIII)
- Circulates with HMWK



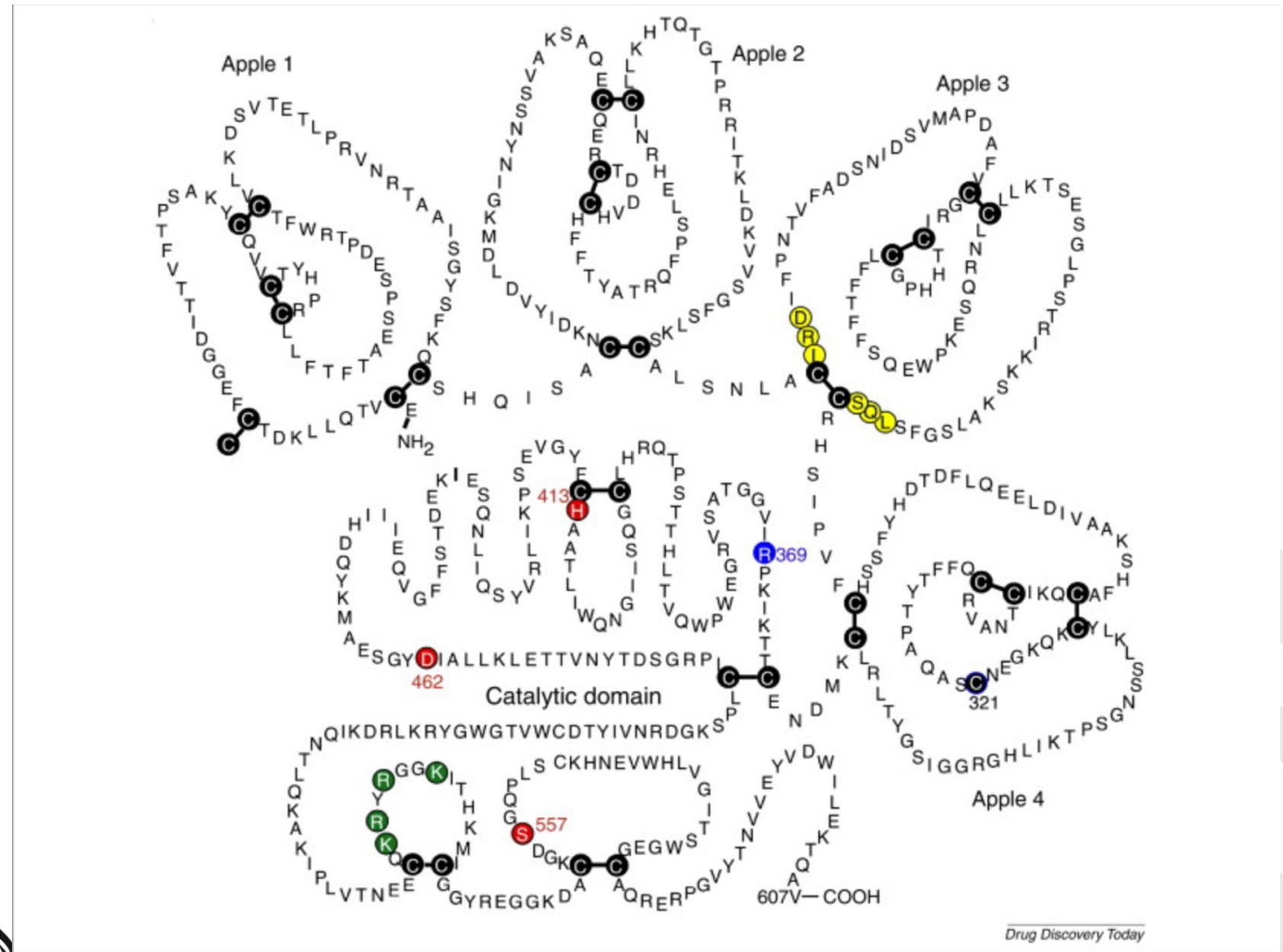
# Diagnosis

- Bleeding symptoms
- Clotting factor activity level
- Family history and genetic testing (when available)

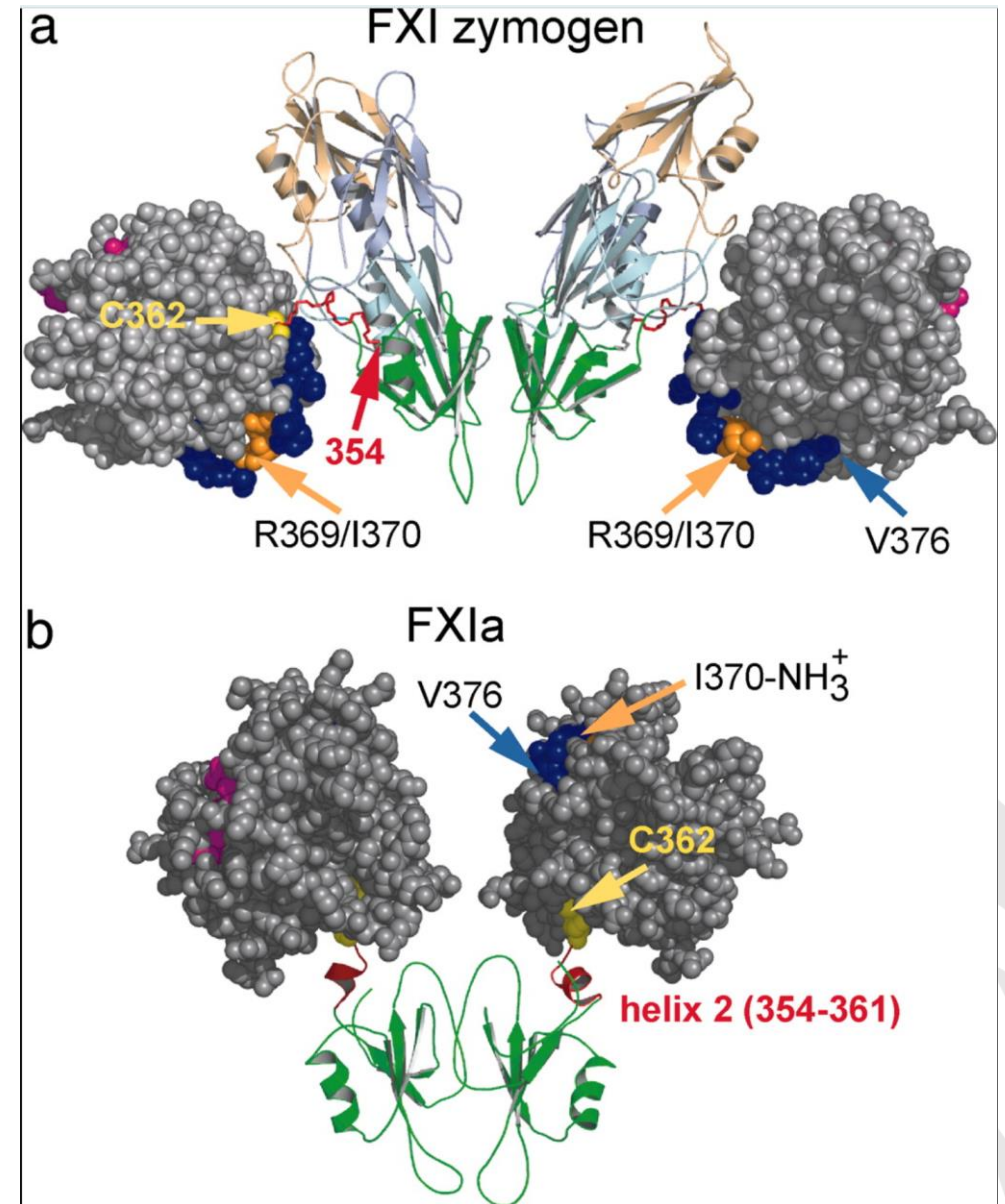
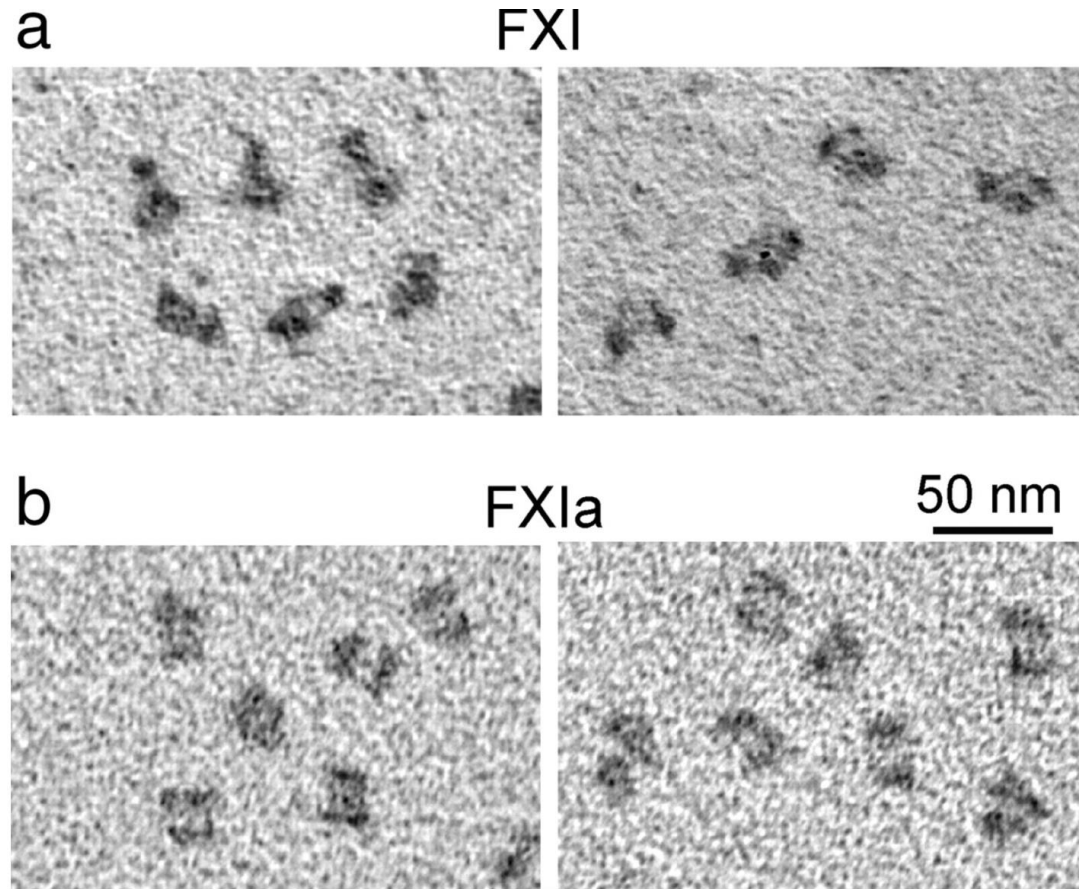


# Factor XI Shape

- 160kd (6ug/ml)
- Four “Apple Domains”
- Circulates as a “homodimer”
- It’s important to help stabilize clots and prevent early break down



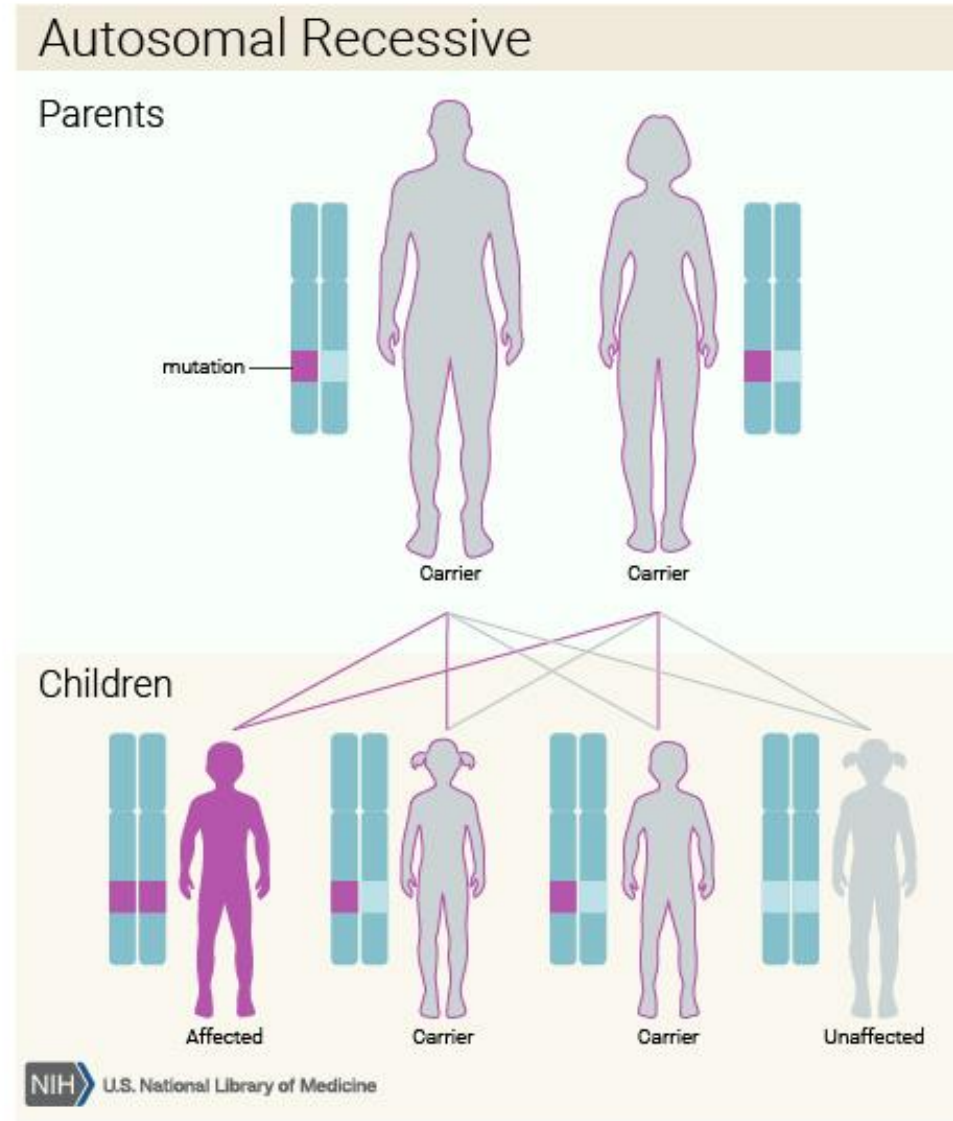
# Shape cont.



# Genetics

Autosomal recessive on chromosome 4;

- Type 1 (intron/exon junction)
- Type 2 (stop codon)
- Type 3 (missense)



<https://ghr.nlm.nih.gov/condition/factor-xi-deficiency#inheritance>



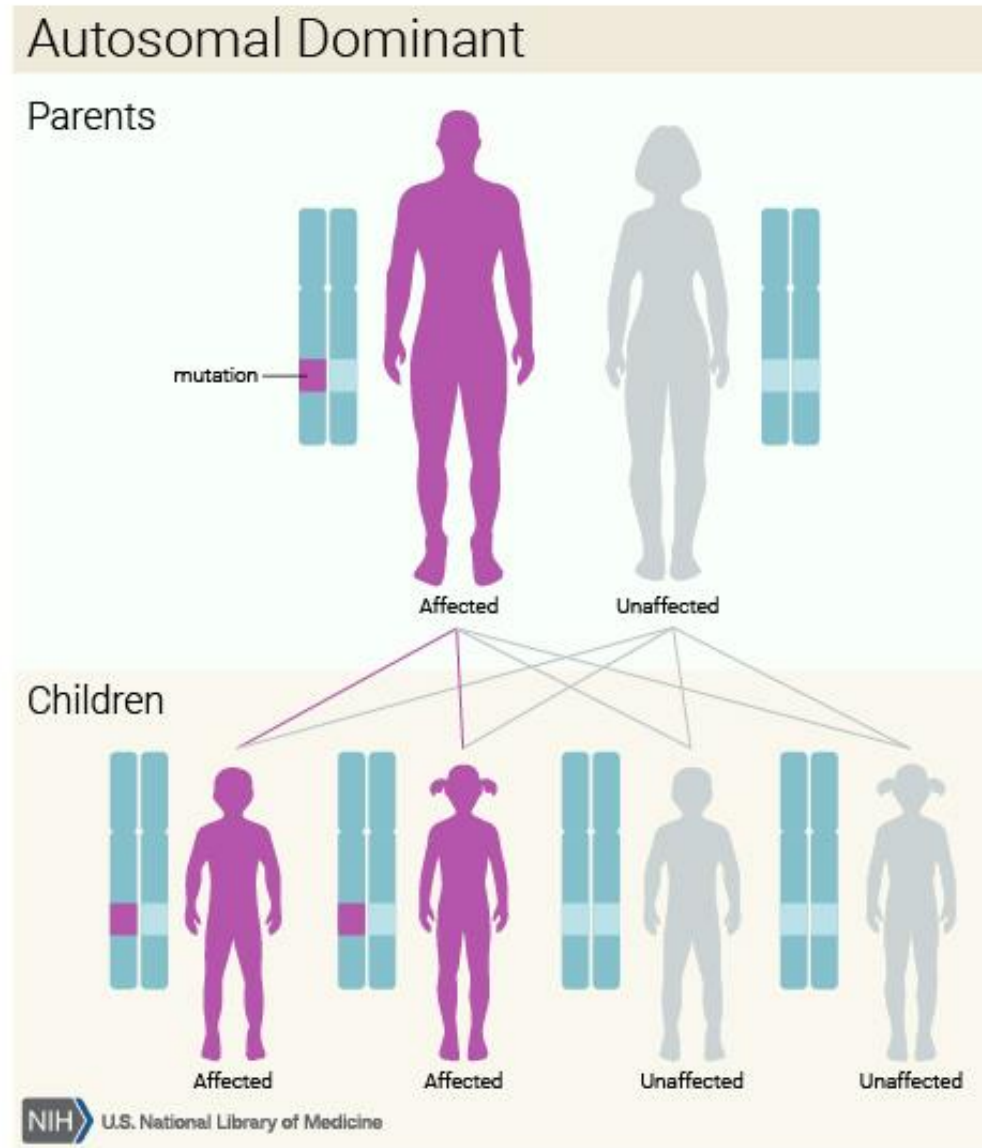
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# Genetics

## Autosomal Dominant

- Reduce protein synthesis
- Can't form dimers
- Can't secrete the protein



<https://ghr.nlm.nih.gov/condition/factor-xi-deficiency#inheritance>



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- 2 1/4 cups all-purpose flour
- 1 teaspoon baking soda
- 1 teaspoon salt
- 1 cup (2 sticks) butter, softened
- 3/4 cup granulated sugar
- 3/4 cup packed brown sugar
- 1 teaspoon vanilla extract
- 2 large eggs
- 2 cups (12-oz. pkg.) [NESTLÉ® TOLL HOUSE® Semi-Sweet Chocolate Morsels](#)
- 1 cup chopped nuts







- 1 1/8 cups all-purpose flour
- 1/2 teaspoon baking soda
- 1/2 teaspoon salt
- 1 stick butter, softened
- 3/8 cup granulated sugar
- 3/8 cup packed brown sugar
- 1/2 teaspoon vanilla extract
- 1 large egg
- 1 cup (6-oz chips)
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# The human genome is like a cookie recipe

- Half of each ingredient is contributed from each parent.
- Variations of some ingredients are tolerated, but others aren't
- Each “cook” adds a special touch (Individual variation that makes that cook special! – that special recipe of grandma's chocolate chip cookies, chunks of a Hershey



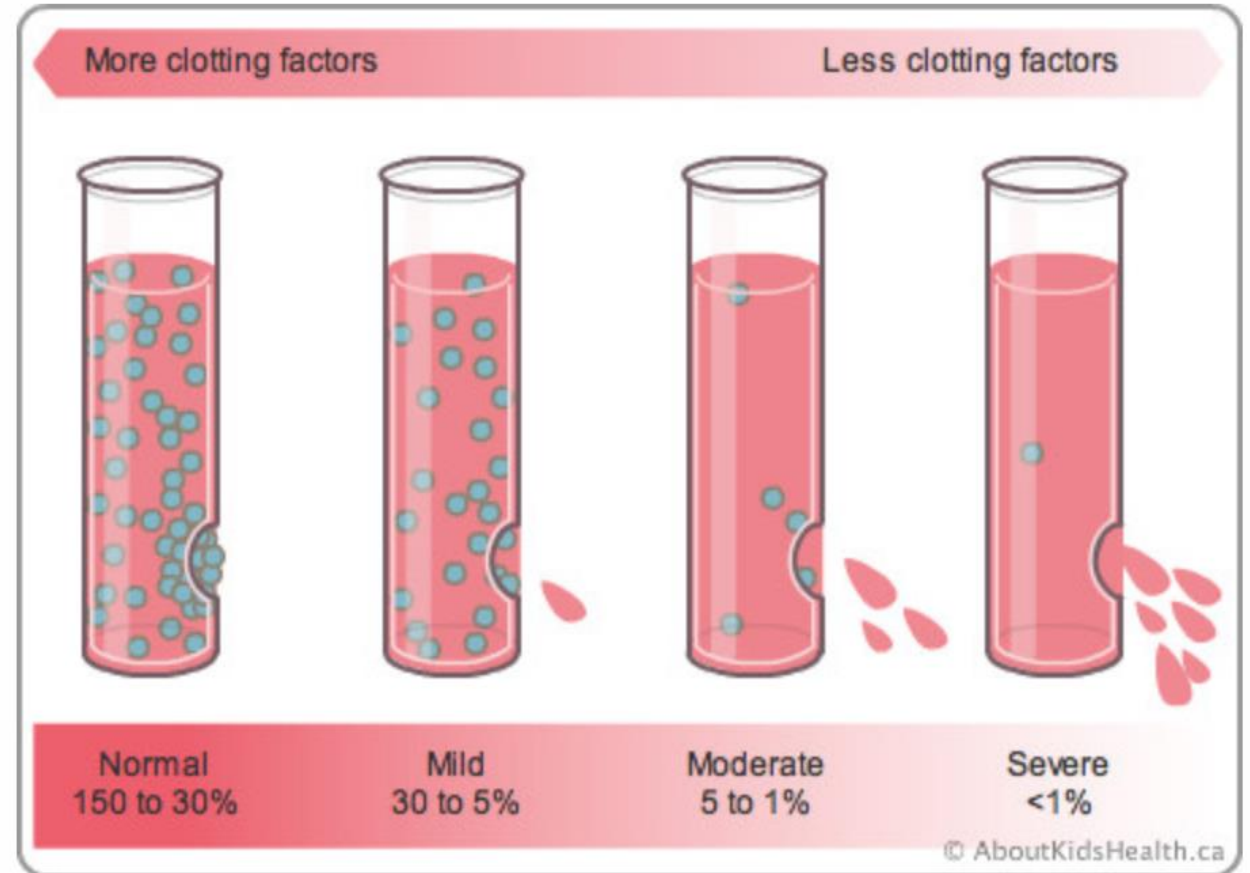
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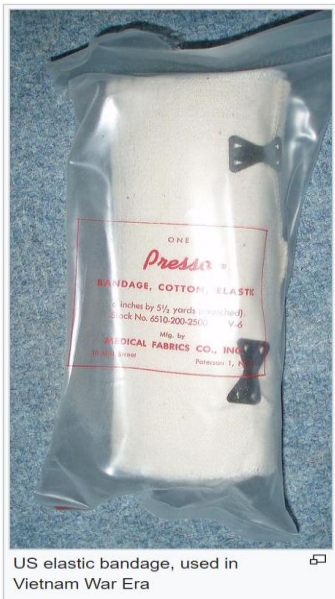
# Low factor levels = symptoms

- Activity levels <10 % have most symptoms of bleeding
- Very rare spontaneous bleeding
- Common bleeding after trauma or surgery, and dental work
- Factor activity levels up to 30-50% have had bleeding symptoms reported.



# Treatment

- First Aid: PRICE
  - Protect
  - Rest
  - Ice
  - Compression
  - Elevation



US elastic bandage, used in Vietnam War Era



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- Antifibrinolytics
- Fresh Frozen Plasma
- Factor Concentrates
  - rFVIIa
  - Factor XI concentrate
- Novel agents
  - siRNA to Antithrombin
  - TFPI inhibitor



<https://www.novoseventrt.com/>

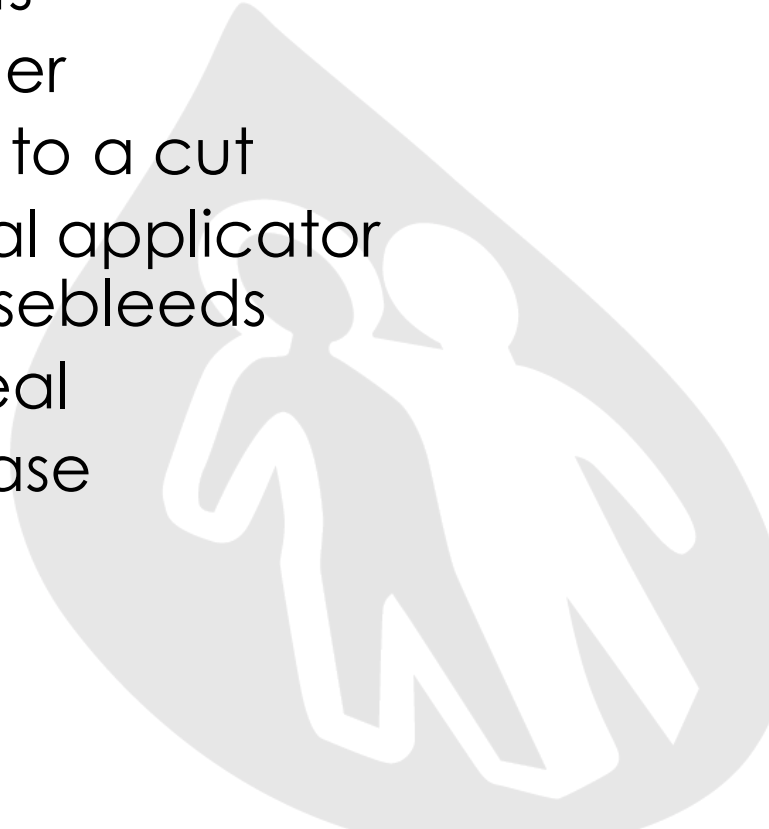
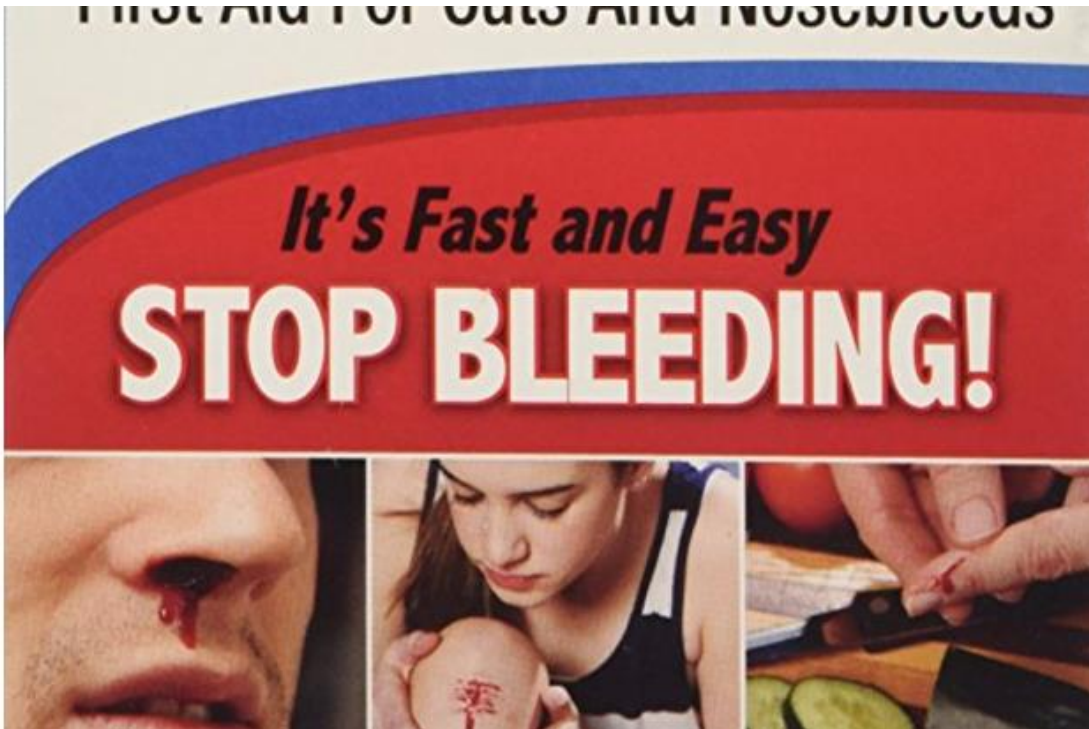


Wikipedia FFP



# Nose bleeding and cuts

- Artificial Clots
  - QR Powder
    - Apply to a cut
    - Special applicator for nosebleeds
  - WoundSeal
  - NasalCease





# NSAIDS

- **Aspirin** – poisons platelets (7-10 days)
- Ibuprofen, Celebrex, naproxen, salsate
  - Stuns platelets for 8-12 hours
- These medicines interfere with platelet function – platelets sticking together
- **When used every day**, they can also cause bleeding ulcers from the stomach, and close off blood flow to the kidneys.



# Get the most out of your visit

- Write down questions you have and record answers for later reference
- Be honest with your concerns
- Be assertive
- Ask the provider to clarify if you don't understand
- Remember you are both on the same team

Reference:

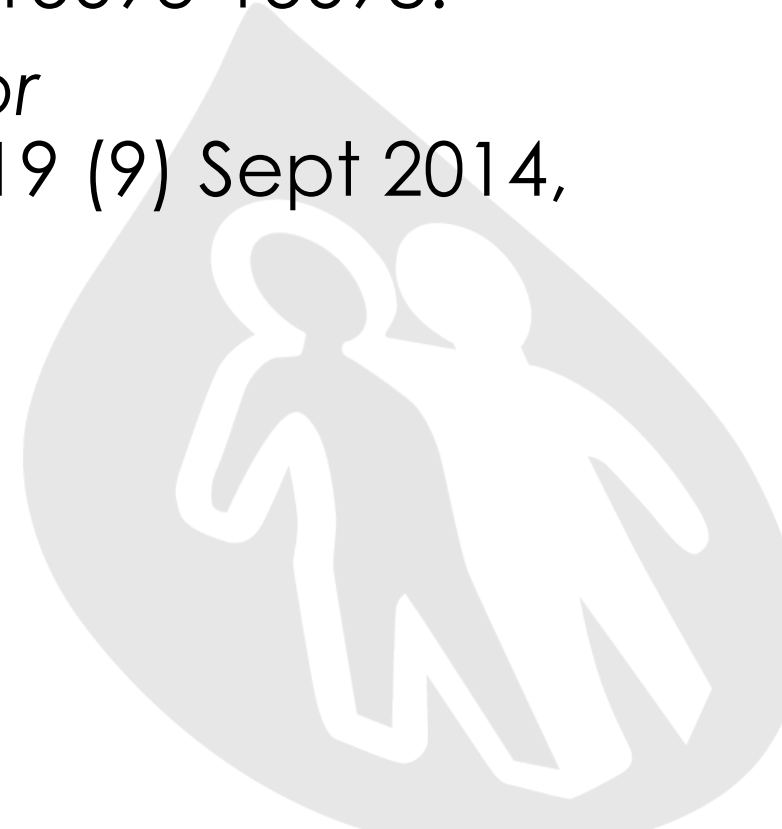
<https://stepsforliving.hemophilia.org/basics-of-bleeding-disorders/navigating-the-health-care-system>





# References

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- Bane CE, Gailani D. *Factor XI as a target for antithrombotic therapy.* *Drug Disc Today* 19 (9) Sept 2014, Pages 1454-1458



# Session Evaluation

Take a few minutes now to fill out the session evaluation:

## Rate this session

- Meaningful?
- Learned new ideas/skills?
- Will implement new ideas/skills?

How could this session be improved?

Comments?

