Hemophilia

[DEPTH OF BIOLOGY]

Hemo → Blood ; Philia → loving

Love to Bleed

because Hemostasis is Impaired

Blood flow ↓ stop

Inherited deff. either → Qualitative / Quantitative

Normally,

after cut or damage to the endothelium or Inner lining of blood vessel walls, there's an immediate vasoconstriction or narrowing of blood vessle which limits the amount of Blood flow.

↓

Then some platellets adhere to damaged vessel wall and become activated and the recruit additional platellete to form a plug.

⇒ Formation of platellet plug is called Primary Hemostasis after that coagulation cascade is activated

[DEPTH OF BIOLOGY]

Blood clotting factors mostly has proteins synthesized by the liver, that are inactive and simply float around the blood.

[DEPTH OF BIOLOGY]

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The coagulation cascade begins when one of these proteins gets Proteolytically cleaved (activating it)

↓

This active protein then proteolytically cleaves and activates the next clotting factors, & soon

↓

This cascade has a great degree of amplification and takes only a few minute from Injury to clot formation.

[DEPTH OF BIOLOGY]

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The final step is activation of the protien fibrinogen (factor-1) to fibrin which deposit & polymerise to form a mesh around a platellet.

*So, these steps heading upto fibrin reinforcement of the platellet plug make up the process called Secondary hemostasis ⟶ results in hard clot at the site of Injury

⇒ In most cases of Haemophili there is a ↓se in the amount and function of one or more of the clotting factors that makes Secondary Hemostasis occurs less effective

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leads to more bleeding.

The coagulation cascade can be started in 2 ways :-

1° Extrinsic Pathway

2° Intrinsic Pathway.

1° Extrinsic Pathway :-

Start when tissue factor get exposed by the Injury of the endothelium

↓

Tissue factor goes tworns Inactivate (Inactive) factor VII into activate factor VII a (a= active)

& then

↓

Tissue factor goes onto bind the newly formed factor VII a to form a complex that tworns factor X into activate factor X a

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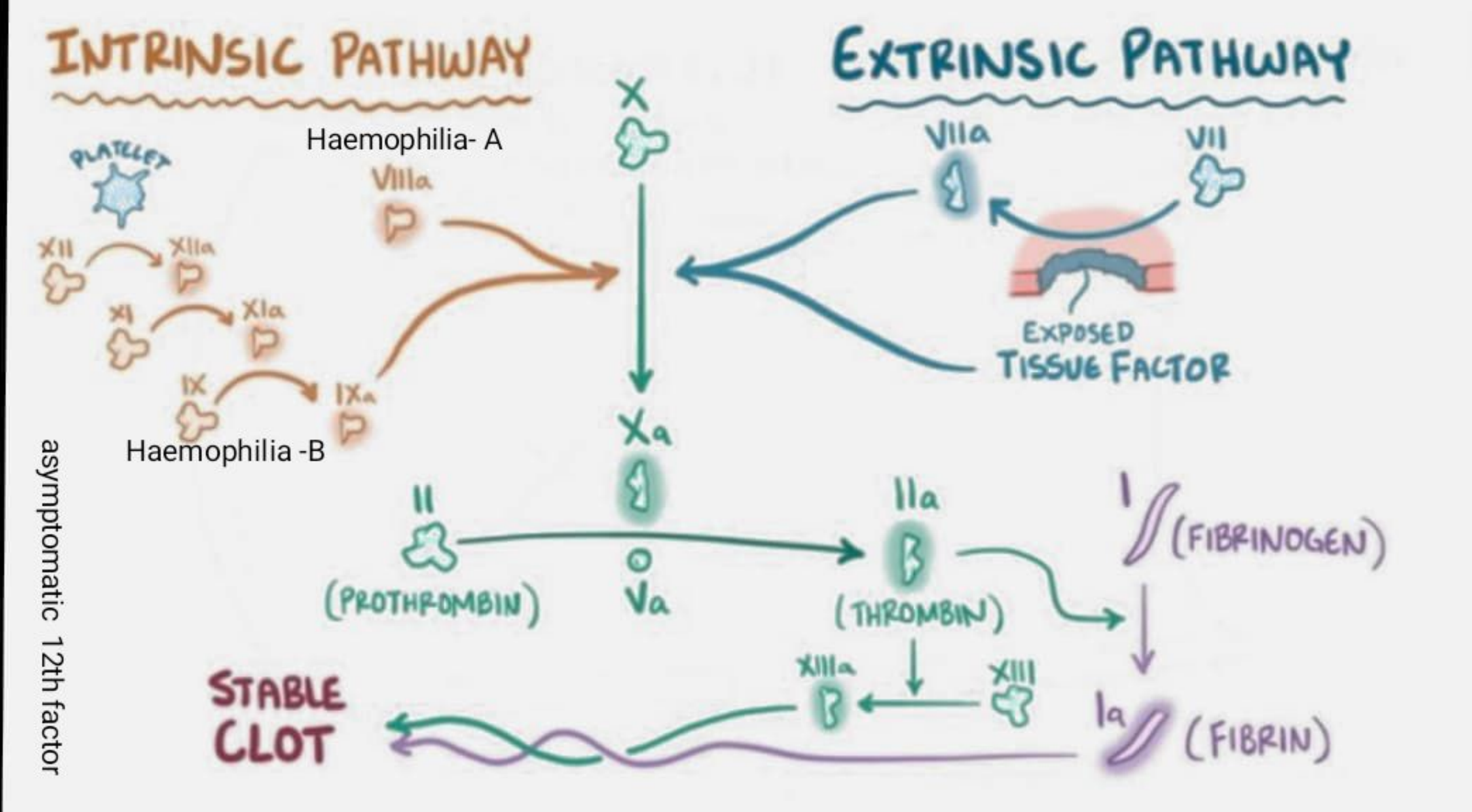

asymptomatic 12th factor

↓

factor X a with factor Va (as a cofactor)
turns factor II (also called prothrombin)
into factor IIa or thrombin

↓

Thrombin then turns factor I or fibrinogen,
which is soluble into factor I or a fibrin
(which is insoluble and ppt. out of the blood at
the site of injury)

↓

[DEPTH OF BIOLOGY]

Thrombin also turns factor XIII into factor XIIIa
which cross link fibrin to form a stable clot.

The second way is the Intrinsic pathway:-
starts when,

Platellet near the blood vessle Injury
activate factor XII into factor XIIa

↓

which then activate factor XI to factor XIa

↓

which then activate factor IX ⟶ IXa

↓

this IXa along with VIIIa work together to activate

[DEPTH OF BIOLOGY]

factor X → Xa

↓

at that point it follow same fate as before,
so both ext. and Int. pathways basically converge
on a single final path called Commaan Pathway

* An insufficient conc. or decreased activity of any coagulation factor can cause

Haemophillia

↓

except factor XII deficiency → which is asymptomatic

⇒ By far most commaan of these are defficiencies are factor VIII which rise to factor VIII a and is stabalized by another factor called Von Willebraand factor cause Haemophilia A or Classic Haemophilia

* Decrease of factor IX → Haemophilia B

also called as Christmas Disease

→ So, in severe Von Willebraand factor defficiency, factor VIII gets broken down faster and can become defficient too.

[DEPTH OF BIOLOGY]

Causes

1. Some acquired causes of Haemophilia are liver failure.
since the liver synthesize factors I, II, V, VII, VIII, IX, X, XI, XIII

[DEPTH OF BIOLOGY]

2. Vitamin K defficiency.
as vitamin k is needed by liver to synthesize and release factor — II, VII, IX & X.

3. Autoimmunity against a clotting factor.
causing autoimmune response

4. Dessiminated Intravascular coagulation (Consume clotting factor)

Now, [DEPTH OF BIOLOGY]
The mutated gene in Haemophilia A → F8 and Haemophilia B is F9 are on the X chromosome
Both conditions are X-linked recessive
↓
Hence, it usually affect men, ∵ they have only one X chromosome and ∴ will have only copy of diseased gene F8 or F9 genes.
Hence they get diseased. [DEPTH OF BIOLOGY]

On the other hand Women,
Who have only one copy of mutated gene and the other X chromosome is healthy so they do not get haemophilia but become carrier and generally remain asymptomatic.

Hence men are symptomatic and can have haemophilia.

[DEPTH OF BIOLOGY]

Clinical Manifestations

of Haemophilia A and Haemophilia B is nearly identical.

As,
factor VIII a & IX a ⟶ together in coagulation cascade to activate factor X.

→ easy bruising (ecchymosis)
→ Hematomas ⟶ collection of Blood outside blood vessle (often in the muscles)
→ Prolonged bleeding after cut or surgery.
→ oozing after tooth extraction.
→ Gastrointestinal bleeding
→ Hematuria (Blood in urine)
→ Severe nose bleeding.
→ Hemarthrosis (Bleeding Into Joint Spaces)

[DEPTH OF BIOLOGY]

→ A dangerous Complication ⇒
Is Bleeding into the brain
it causes ↓
- stroke
- Increase ICP (Intracranial Pressure)
5-15 mmHg in Normal Adults

*Symptoms depends on mutation.

[DEPTH OF BIOLOGY]

Diagnosis

1. Lab test
   - → Platellet (Normal)
   - → Prothrombin time (test ext. & Commun pathway)
   - → Partial Thromboplastin time (test Inter. & Commun Pathway)

Partial Thromboplastin time is prolonged in Haemophilia A and B

2. Confirmation (for Haemophilia A or B) → test for specific factor activates and Mutation testing.

[DEPTH OF BIOLOGY]

Treatment

* Injection of Missing or Non functional Clotting factor.

* If the patient has severe defficiency (where Intrinsic production of the factor is ⊖ absent or very low). [DEPTH OF BIOLOGY]

In this condition supplement factor can be seen as foreign by the Immune system which results in the production of antibodies that tery to eliminate the Injected clotting factor which are called <u>Inhibitores</u>

↓

and also sometimes cause Anaphylaxis

⇒For Haemophilia A → Desmopressin (DDAVP) helpful for mild factor 8 defficiency.

Desmopressin stimulate → Von Willebrand factor released from endothelial cells.

↓

[DEPTH OF BIOLOGY]

which promote Stabalisation of residual factor 8.

* Avoid Contact sports and Certain Medications (Aspirin)