

Blood physiology

Tharunya Kurusanth

Platelets & red blood cells

Platelets

- Function and origin
- Hemostasis
 - Primary hemostasis
 - Secondary hemostasis
 - Disorders of hemostasis
 - Drugs that affect hemostasis

Red blood cells

- Function and origin
- Blood type ABO and Rh
- Serological conflict
- Hemoglobin

Platelets (PLT's)

- 150.000 - 400.000 cells/ μ L
- Small (2–3 μ m), anuclear
- Cell membrane: phospholipids, glycoproteins
- **Thrombopoietin** from the **liver** (and kidney)
- Life span \approx 10 days

Platelets: *spends hours to clot my injury*

8 y/o me: *scratches the clot because its itchy*

Platelets:



Hemostasis

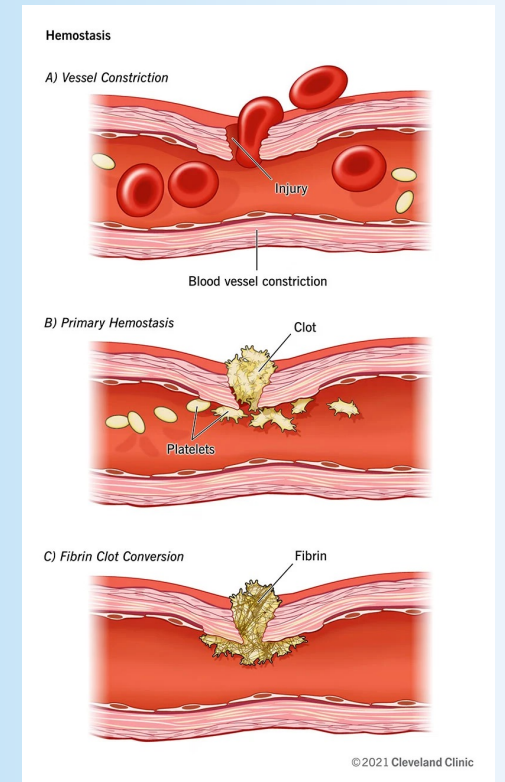
- Stopping of blood flow and prevention of blood loss

3 stages:

1. Vasoconstriction

2. Formation of temporary «**platelet plug**»

3. Activation of coagulation cascade and formation of «**fibrin plug**»



Hemostasis



	Primary	Secondary
Goal	Platelet plug	Fibrin plug
Mechanism	Vasoconstriction Platelet aggregation	Coagulation cascade
Clot characteristics	Unstable	Stable

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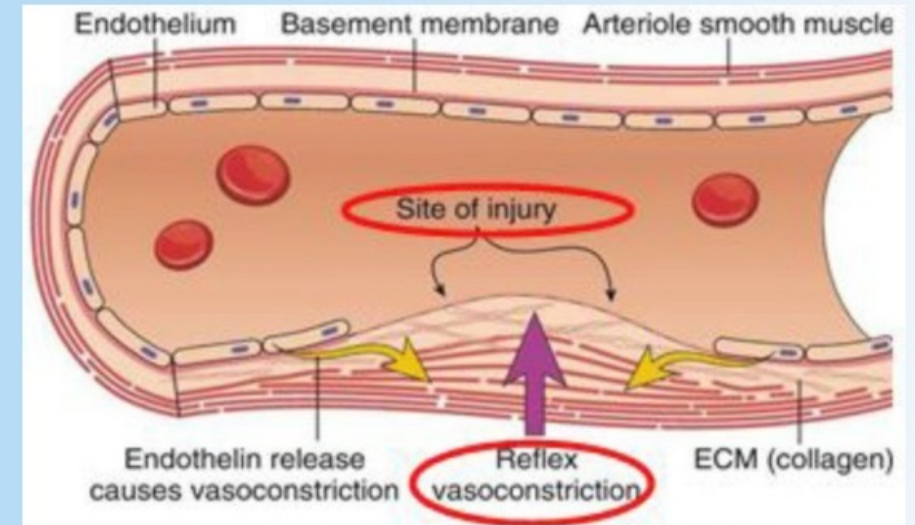
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Primary hemostasis

Vasoconstriction

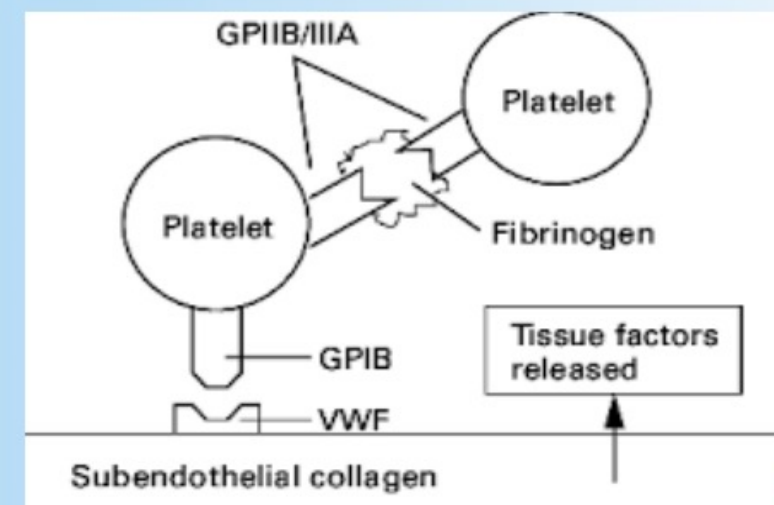
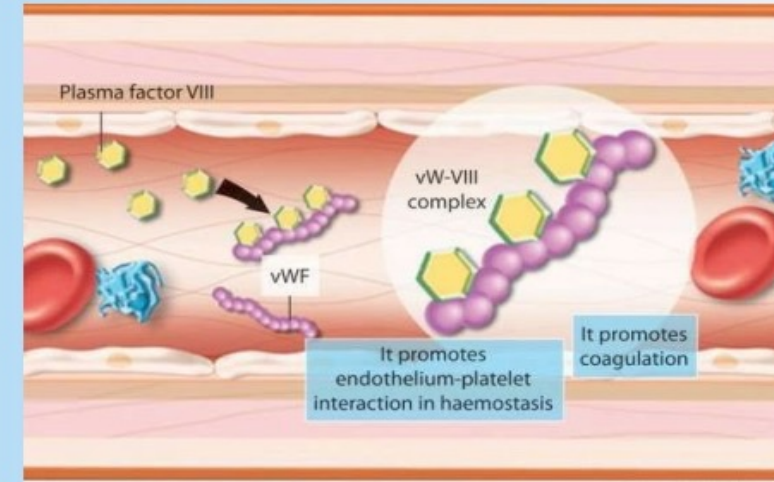
- *Damage to endothelium* →
- Sympathetic reflex
 - Arteriolar smooth muscle contraction
- Vasoconstrictors
 - Thromboxane A₂
 - Serotonin



Primary hemostasis

PLT activation

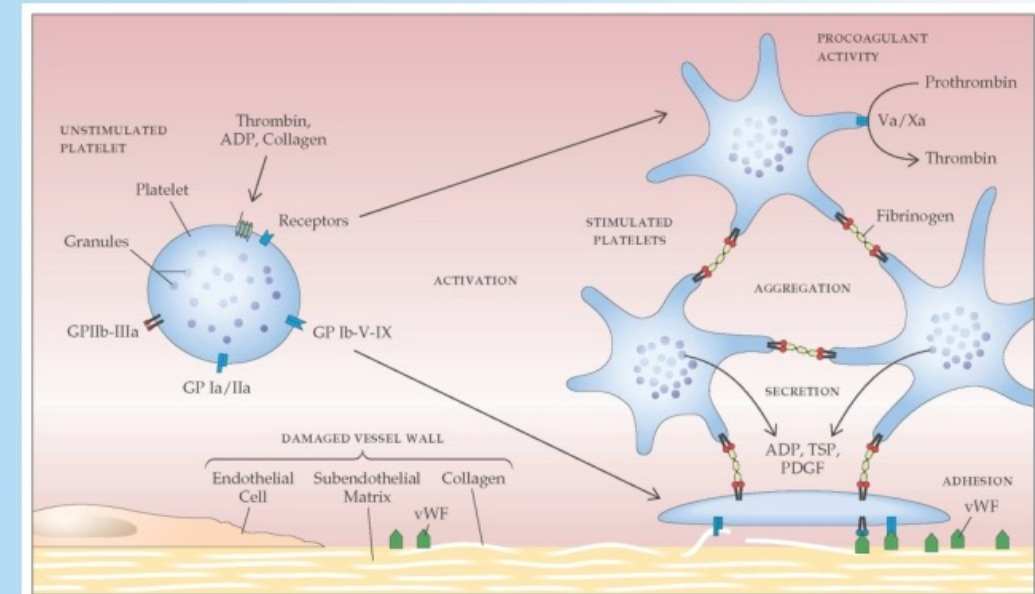
- Subendothelial collagen – PLT activation
- Release of PLT granules:
 - *TXA₂, serotonin, ADP*
 - *Activate nearby PLT's*
- *Von Willebrand factor (vWF)*
 - PLT adherence
 - GPIIB/IIIA
 - Clotting factor VIII



Primary hemostasis

PLT aggregation

- **ADP** - change of PLT shape, GPIIB/IIIA expression
- **Thromboxane A₂ (TXA₂)** - PLT aggregation
- **Fibrinogen** binds to GPIIB/IIIA, and ties platelets together



Platelets & red blood cells

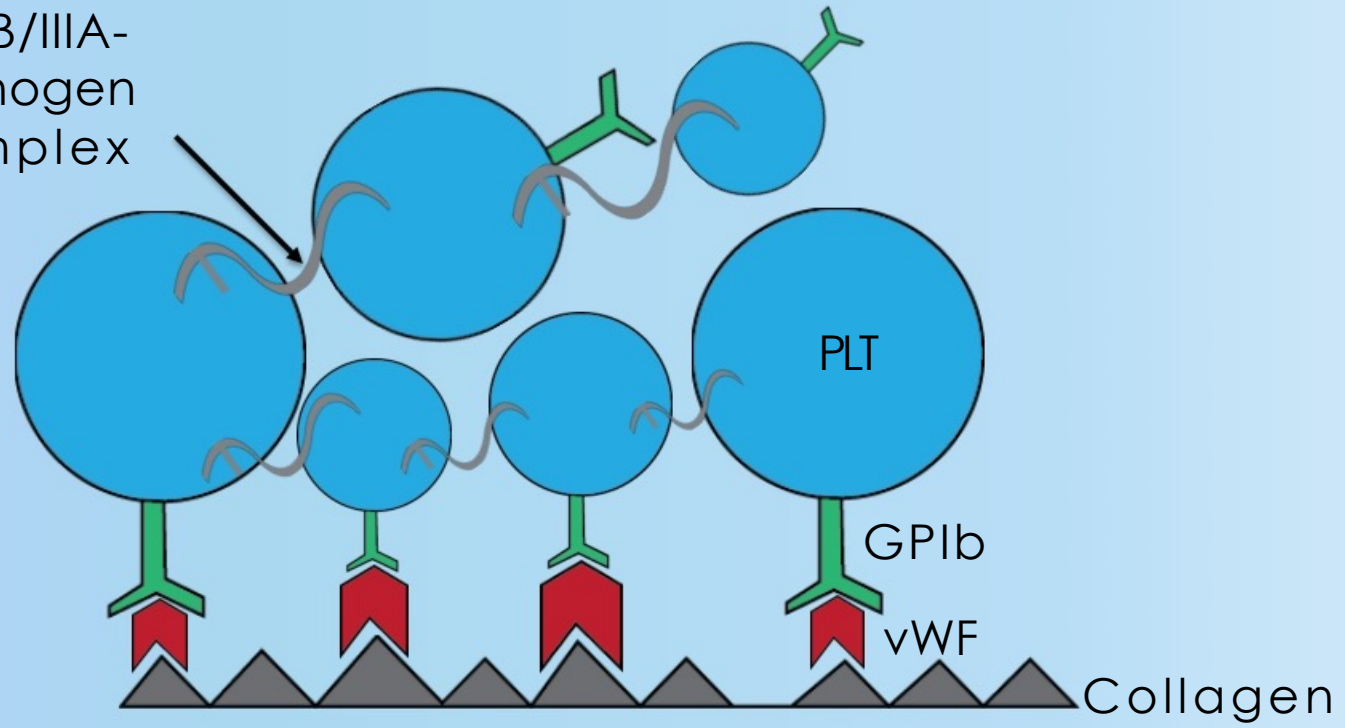
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Red blood cells

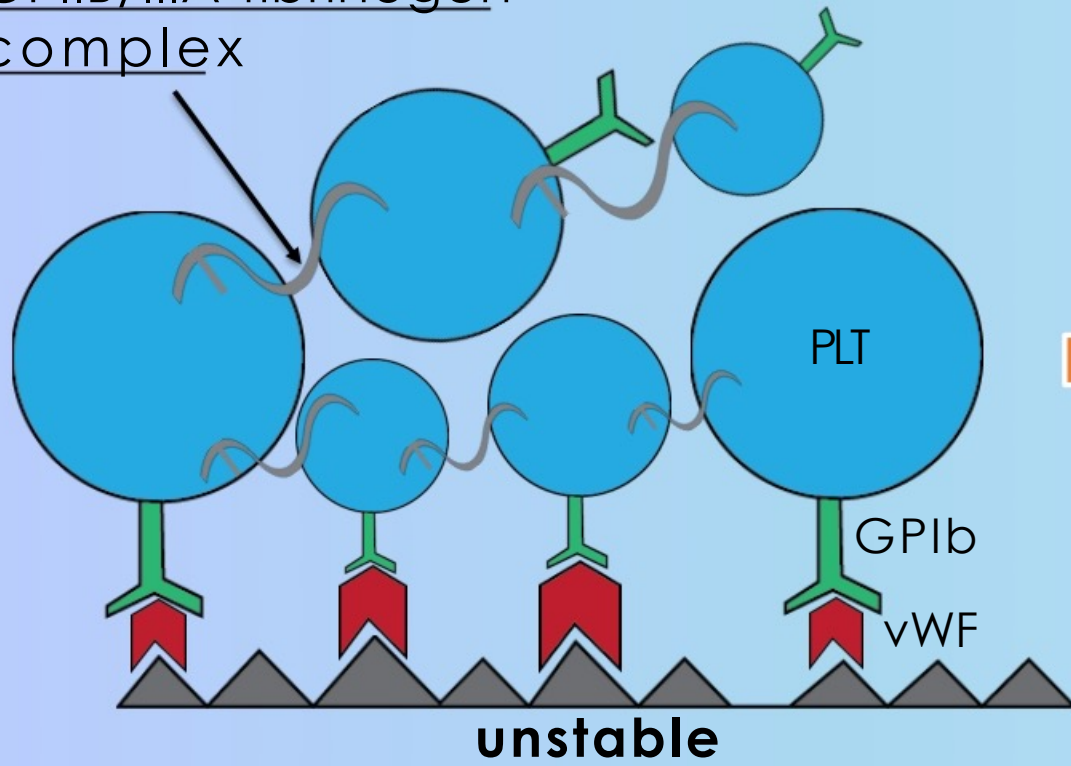
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GPIIB/IIIA-
fibrinogen
complex

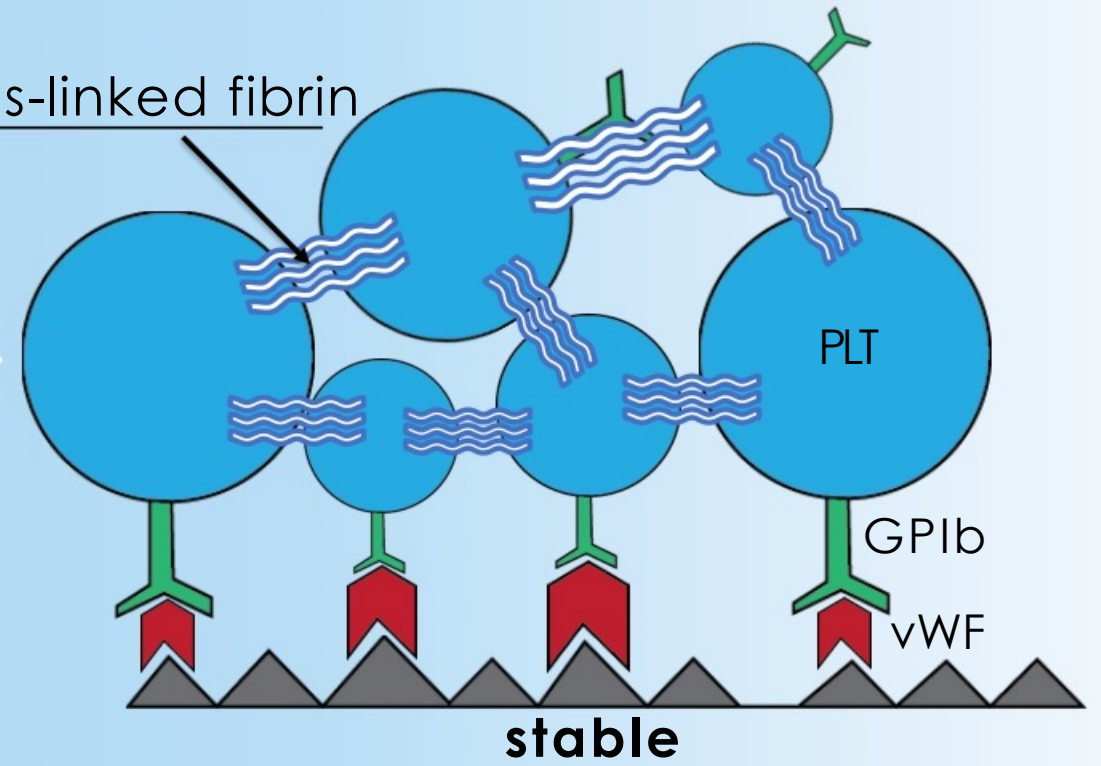


What is the goal?

GPIIB/IIIa-fibrinogen complex



Cross-linked fibrin

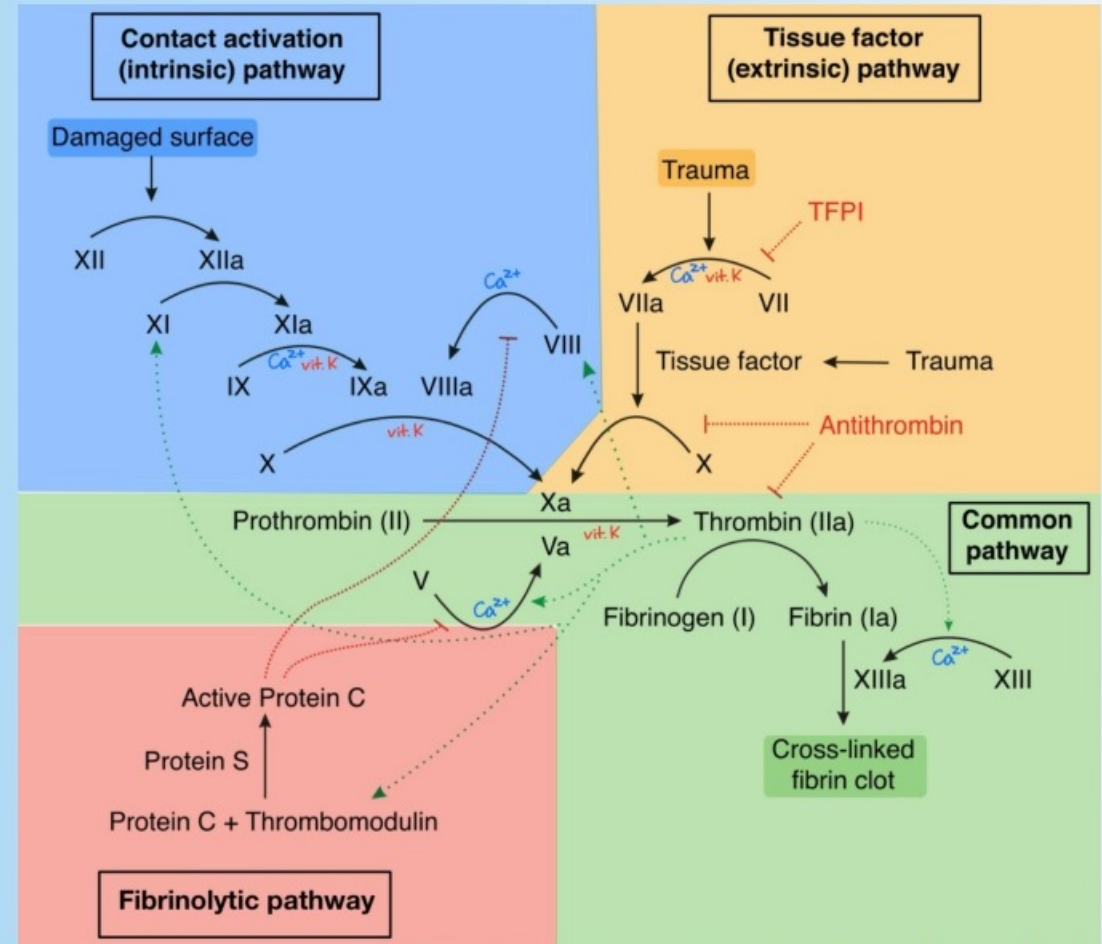


Secondary hemostasis

Coagulation cascade

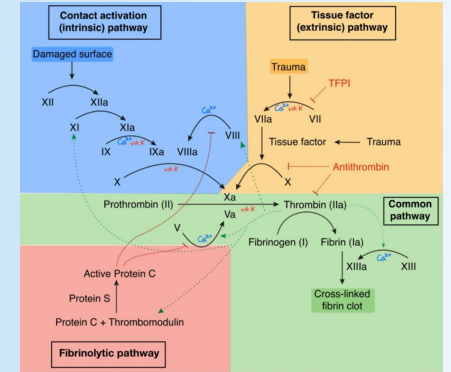
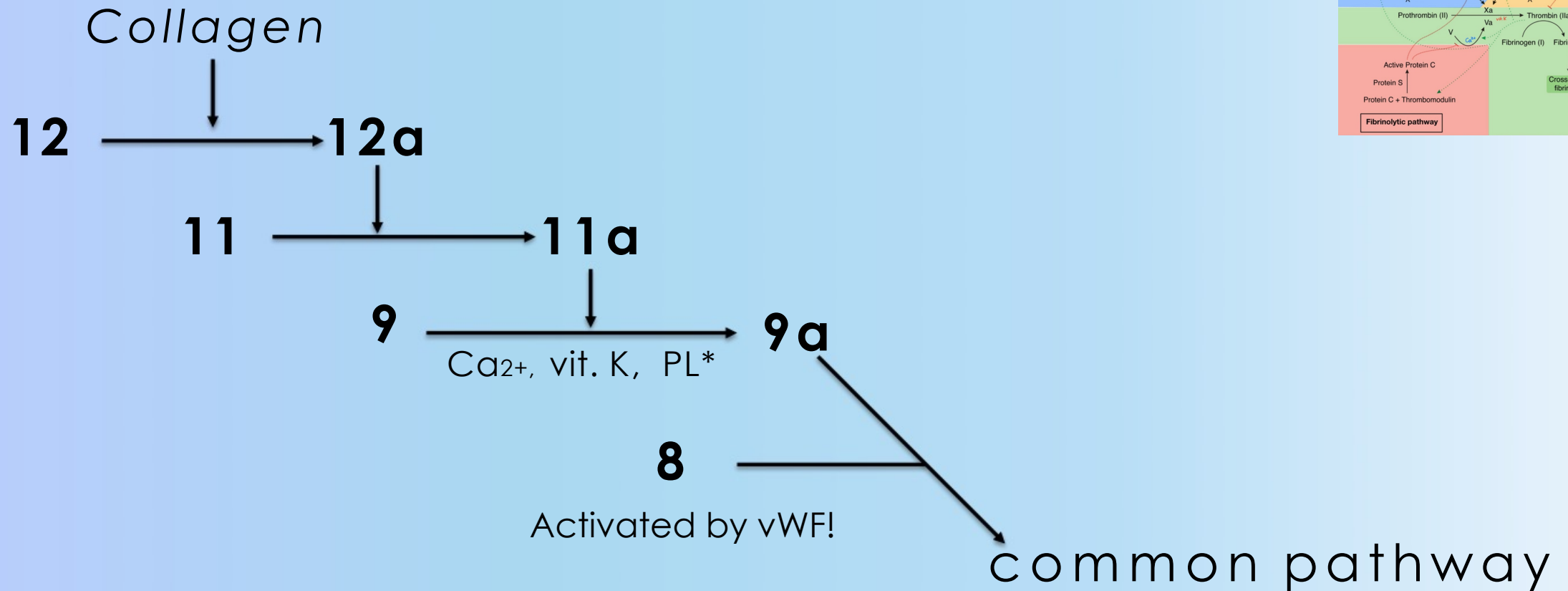
4 pathways:

- Intrinsic pathway
- Extrinsic pathway
- Common pathway
- Fibrinolytic pathway



Coagulation cascade

Intrinsic pathway



*PL = platelet phospholipids

Coagulation cascade

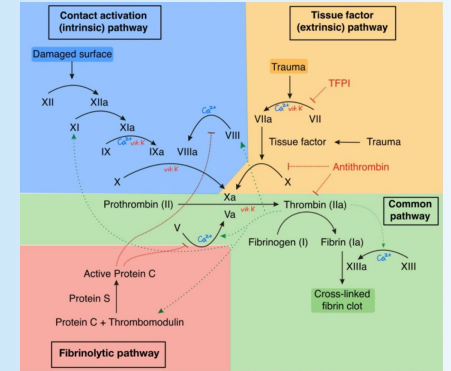
Extrinsic pathway

external *trauma*

tissue factor (*thromboplastin*)

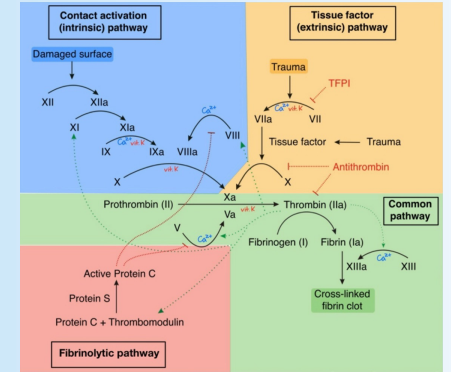
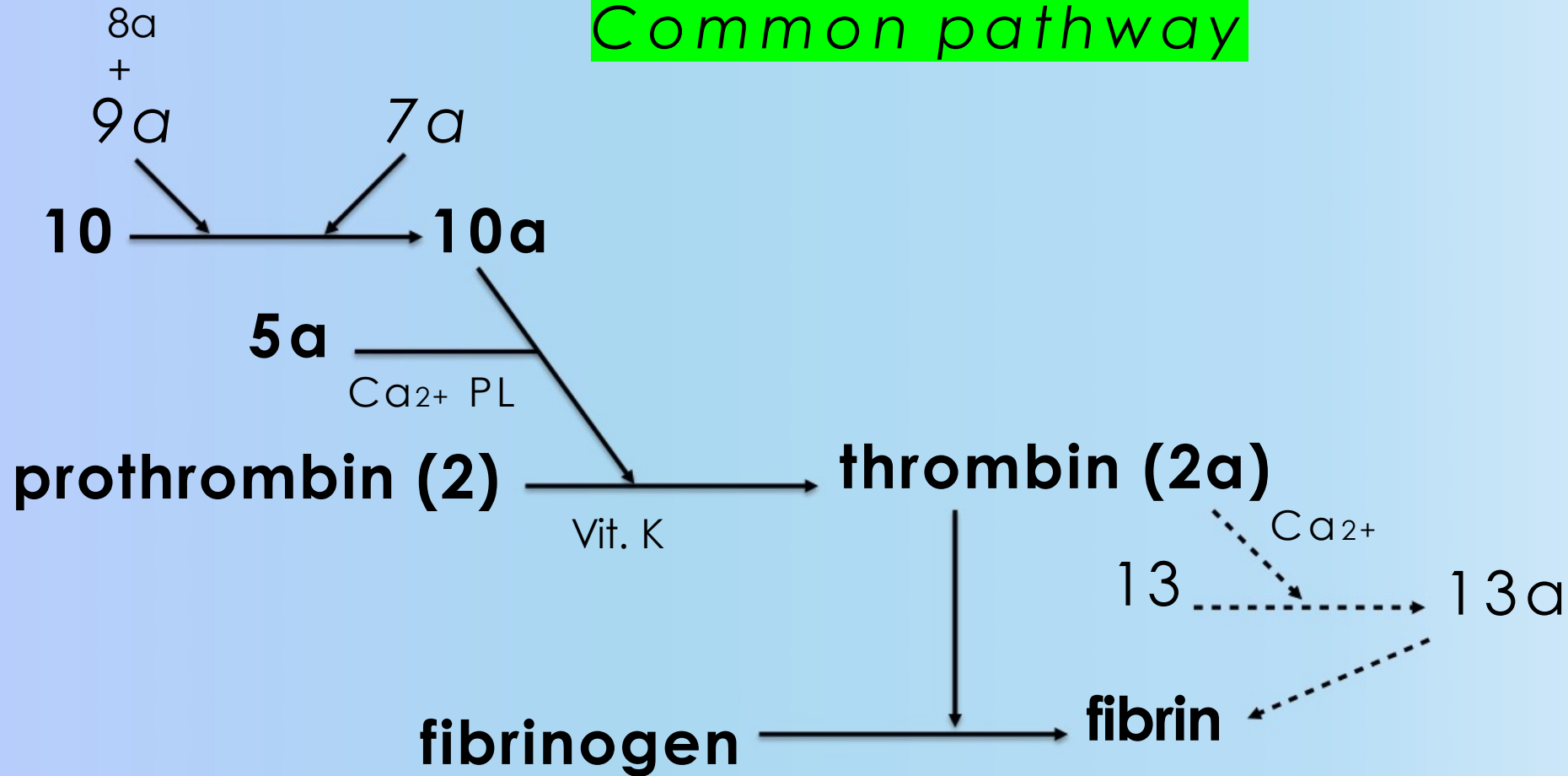


common pathway



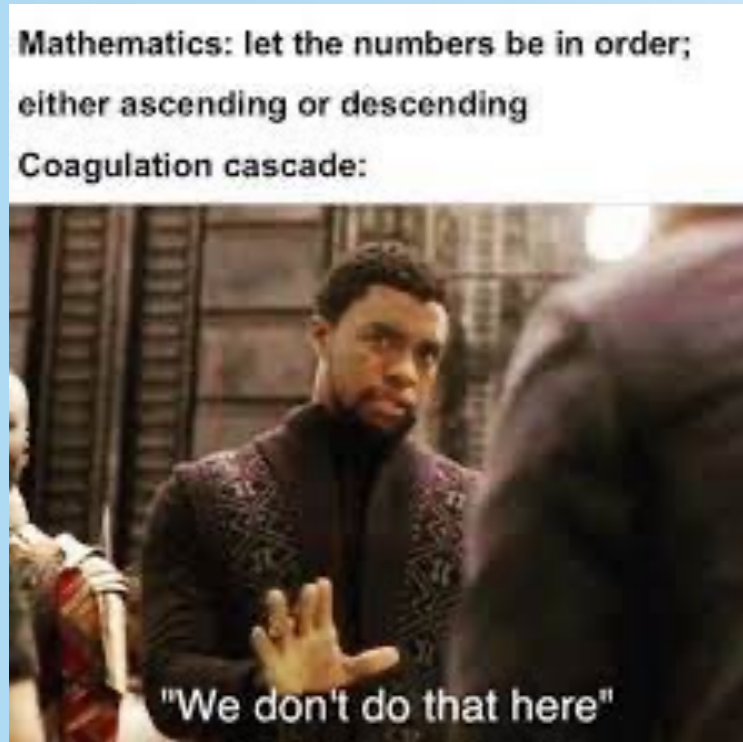
Coagulation cascade

Common pathway



Clotting factors

1. *Fibrinogen*
2. *Prothrombin*
3. *Tissue factor*
4. *Calcium*
5. **L**abile factor (proaccelarin)
7. **S**tabile factor
8. **A**nti-haemophilic factor
9. **C**hristmas factor
10. **S**tuart - Prower factor
11. **P**TA (plasma thromboplastin antecedent)
12. **H**ageman factor
13. **F**ibrin stabilizing factor

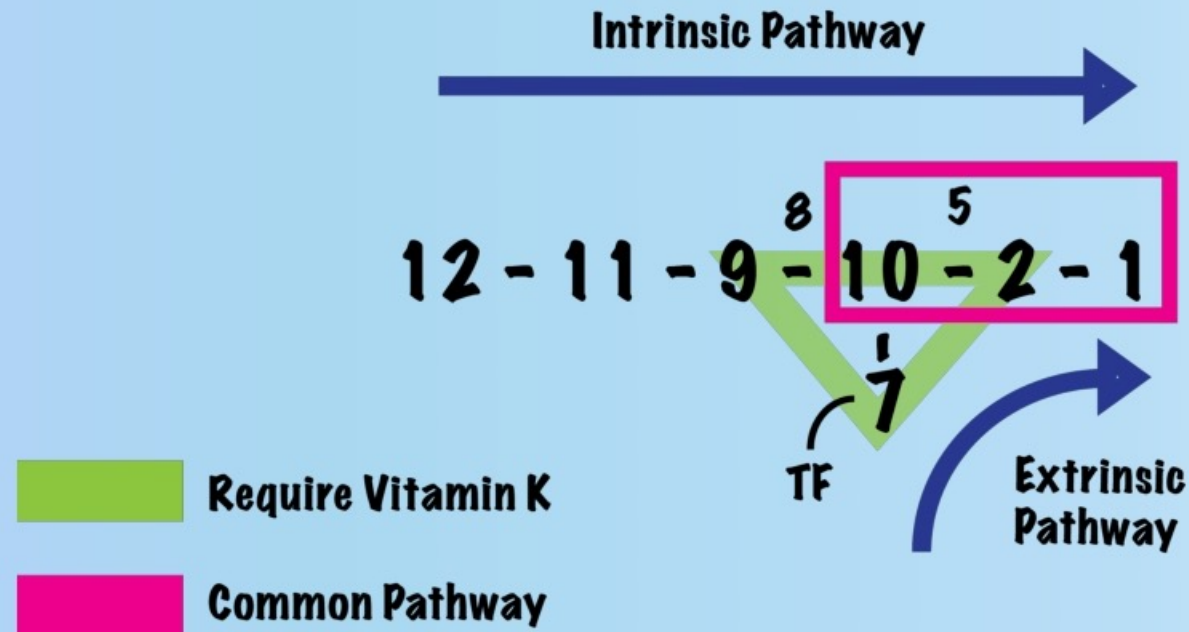


Foolish **P**eople **T**ry **C**limbing **L**ong **S**lopes **A**fter **C**hristmas, **S**ome **P**eople **H**ave **F**allen

Secondary hemostasis

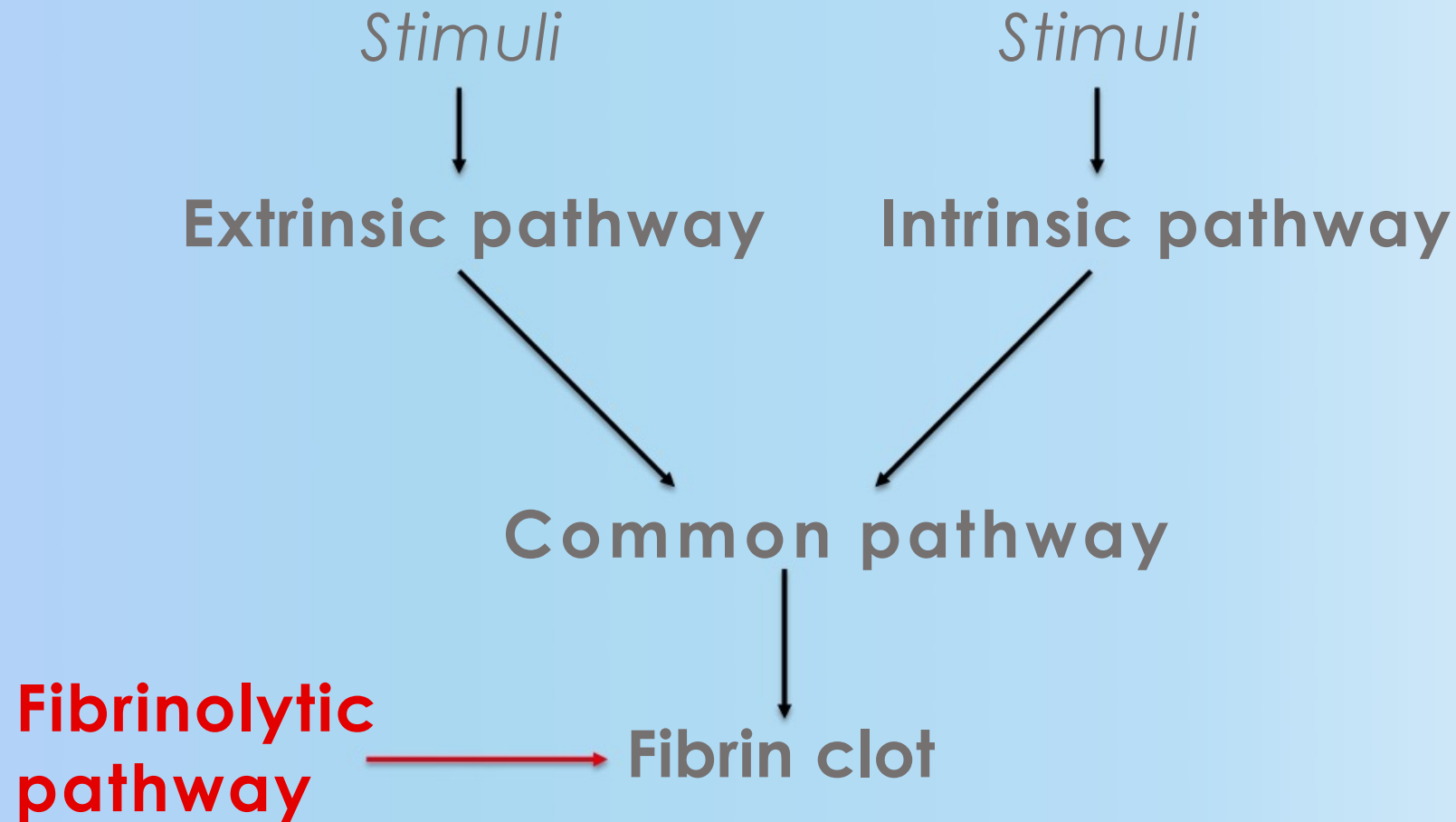
Coagulation cascade

Vit. K dependent <ul style="list-style-type: none">• 10, 9, 7 & 2▸ «1972»	Synthesized in liver <ul style="list-style-type: none">• 1, 2, 5, 7, 8, 9, 10, 11, 12• Protein C	Ca²⁺ dependent <ul style="list-style-type: none">• 5, 7, 8, 9 & 13
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Coagulation cascade

Fibrinolytic pathway

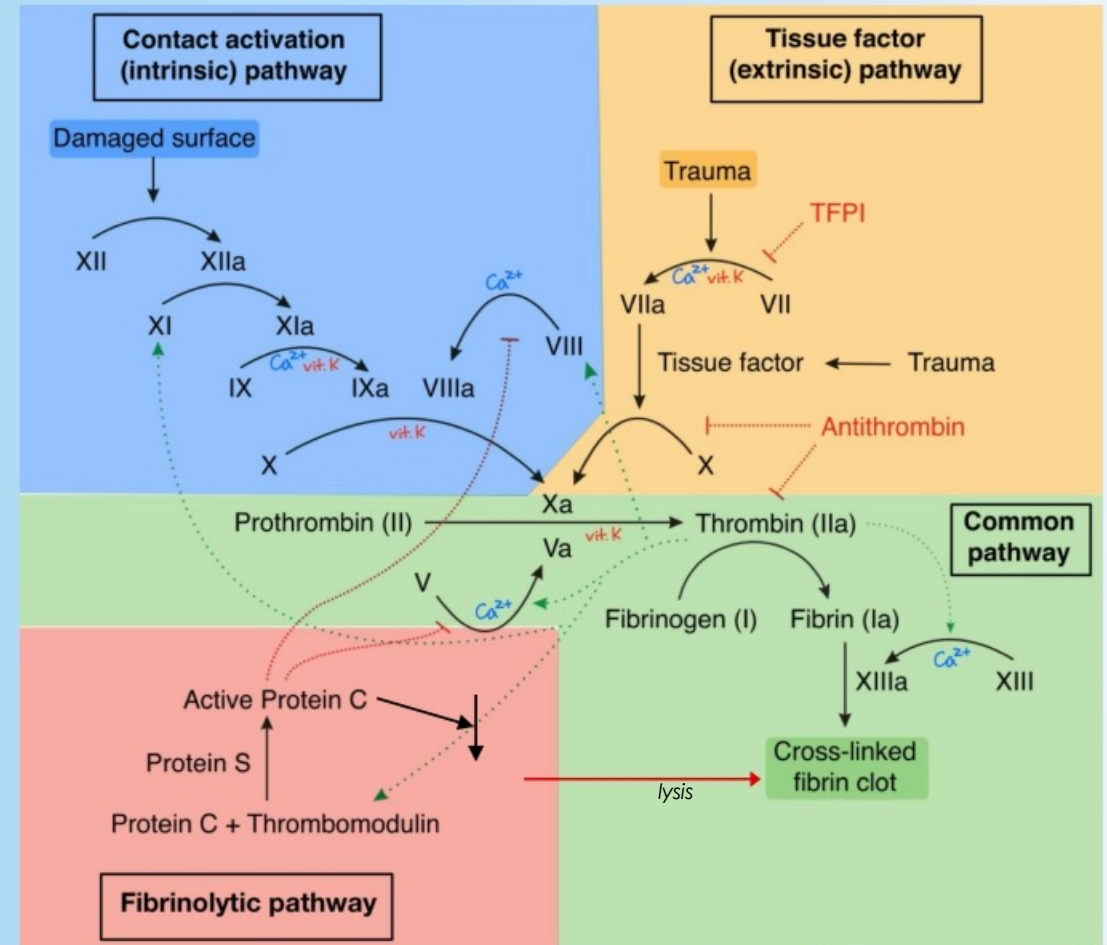


Coagulation cascade

Fibrinolytic pathway

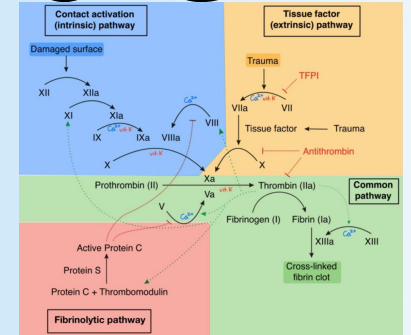
Goal:

- Destroy pre-existing clots:
thrombolysis
- Stop new clots from forming:
anticoagulation



Coagulation cascade

Fibrinolytic pathway



Thrombin (2a)

Thrombin-thrombomodulin complex

Thrombomodulin

Protein C

APC

t-P A

8

Plasminogen

Plasmin

5

lyses fibrin

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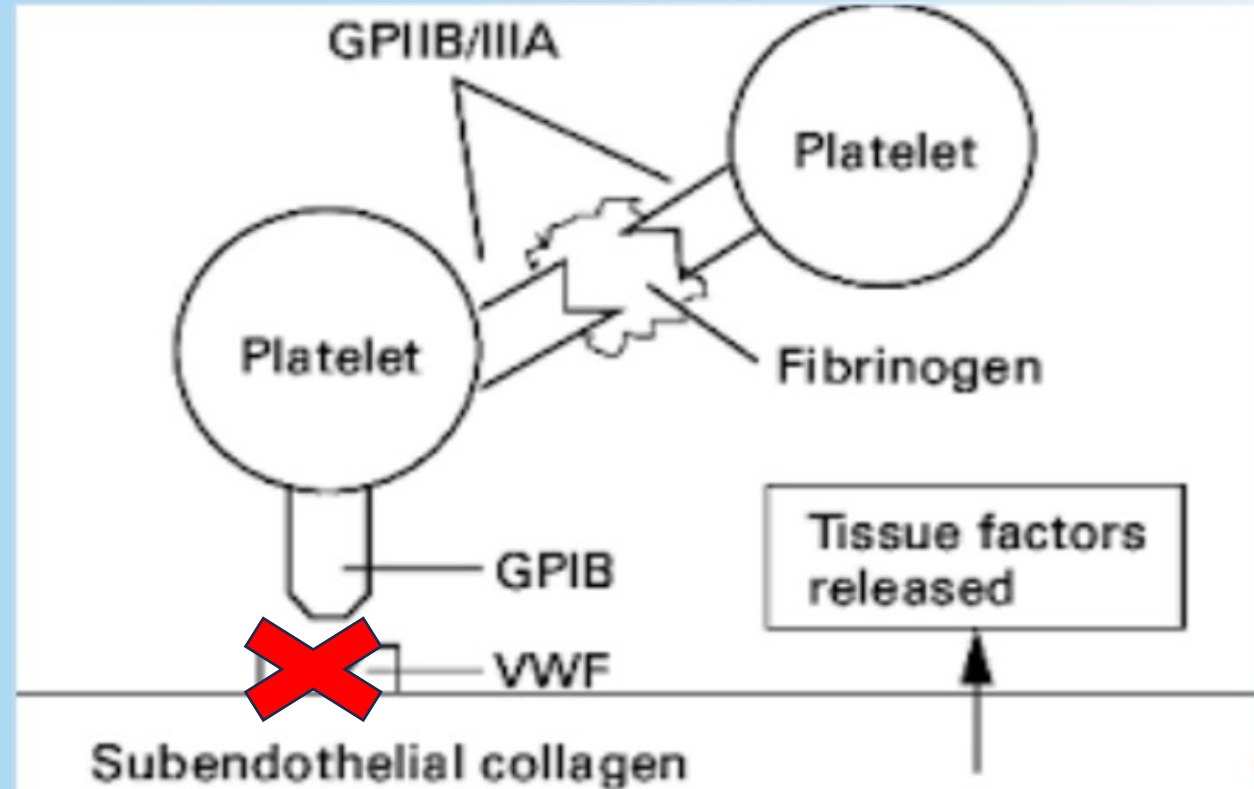
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Clotting disorders – von Willebrand disease

- ↓vWf or no vWf
- Primary hemostasis

Ppl w/ vWD Nosebleeds



Clotting disorders – secondary hemostasis

Hemophilia A

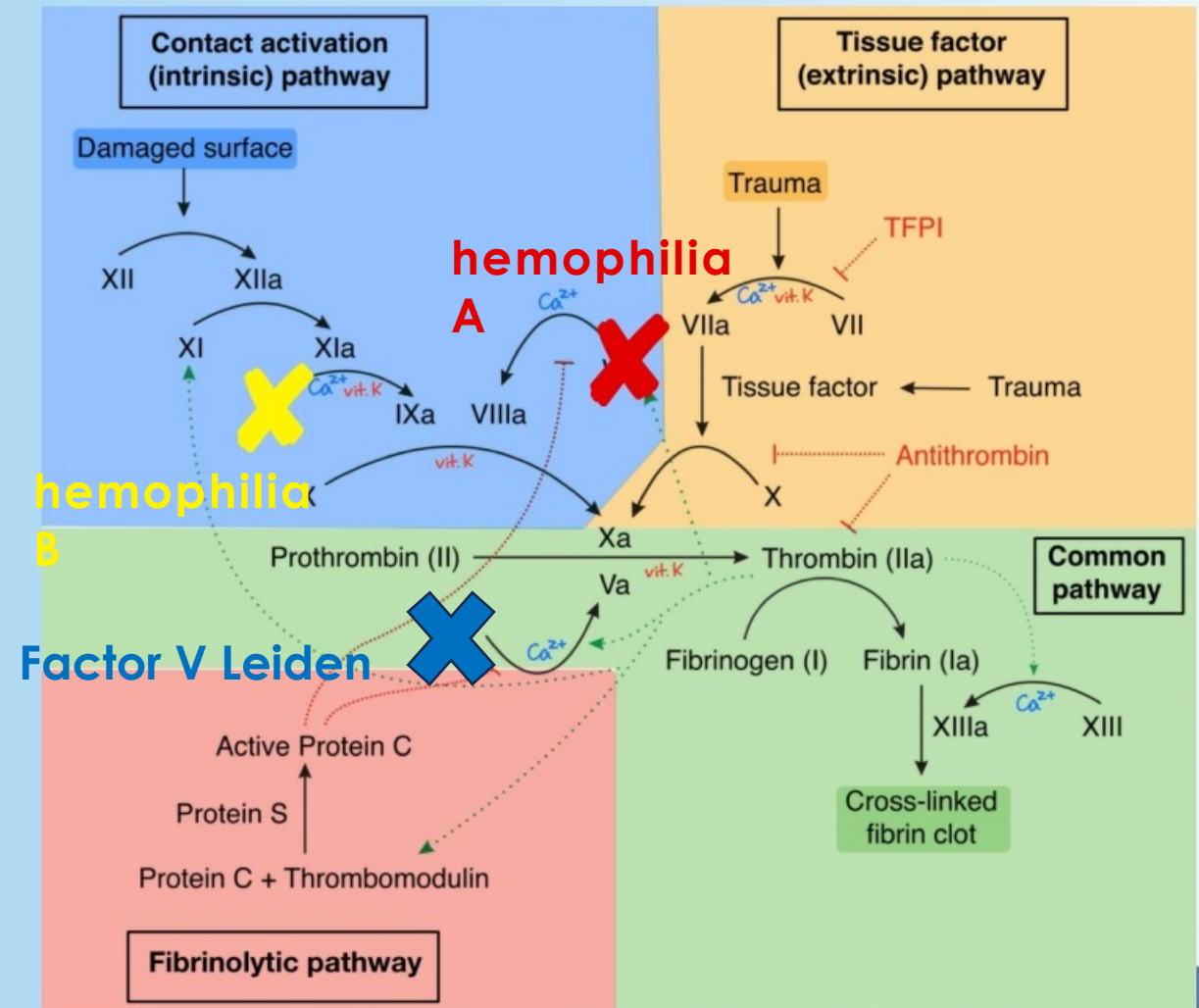
- Deficiency of **clotting factor 8**
«*hemophilia Aight*»

Hemophilia B

- Deficiency of **clotting factor 9**

Factor V Leiden

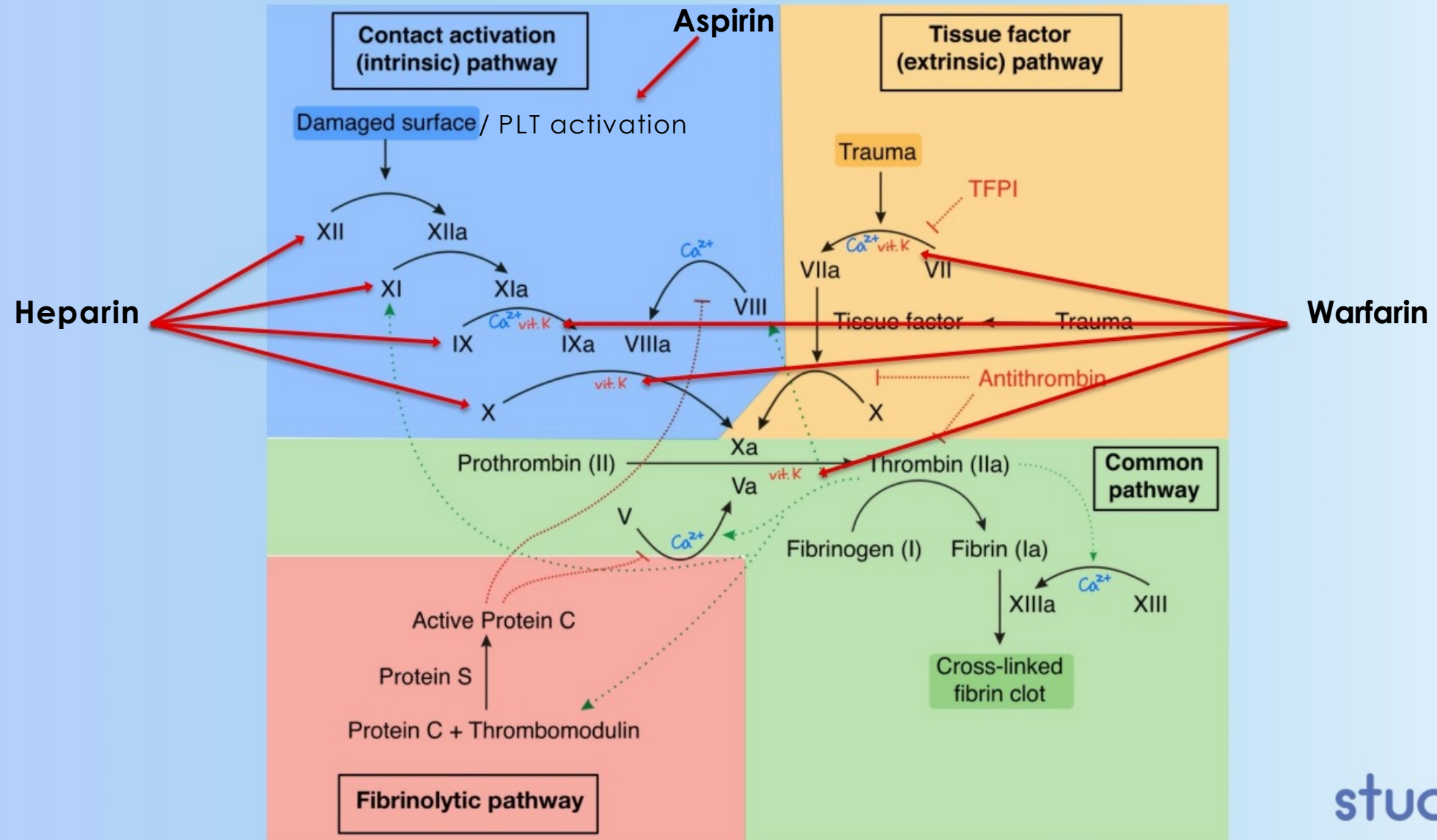
- Mutation of **clotting factor 5**



Clotting disorders

	Haemophilia	Von Willebrand disease	Factor V leiden	Vitamin K deficiency
Disorder type	Hypocoagulative state of secondary hemostasis	Hypocoagulative state of primary hemostasis	Hypercoagulative state of secondary hemostasis	Hypocoagulative state of secondary hemostasis
Pathophysiology	Hemophilia A: Deficiency of factor VIII Hemophilia B: deficiency of factor IX	Deficiency of vWF	Mutation of factor V	Insufficient activation of clotting factors 2, 7, 9 & 10
Mechanism	X-linked recessive inheritance	Autosomal dominant inheritance	Inherited	Liver disease Malabsorption Warfarin overdose

Drugs that inhibit clotting



Drugs that inhibit clotting

	LMW Heparin	Aspirin	Warfarin
Effect	Anticoagulant	Antiplatelet	Anticoagulant
Mechanism of action	When conjugated with antithrombin-III, inhibits factor IX, X, XI, XII	Inhibits synthesis of TXA ₂	Inhibits vitamin K
Used in	<ul style="list-style-type: none"> - Always present in blood - Thromboembolism 	<ul style="list-style-type: none"> - Heart attack - Cardiovascular diseases 	Hypercoagulative disorders

Platelets & red blood cells

Platelets

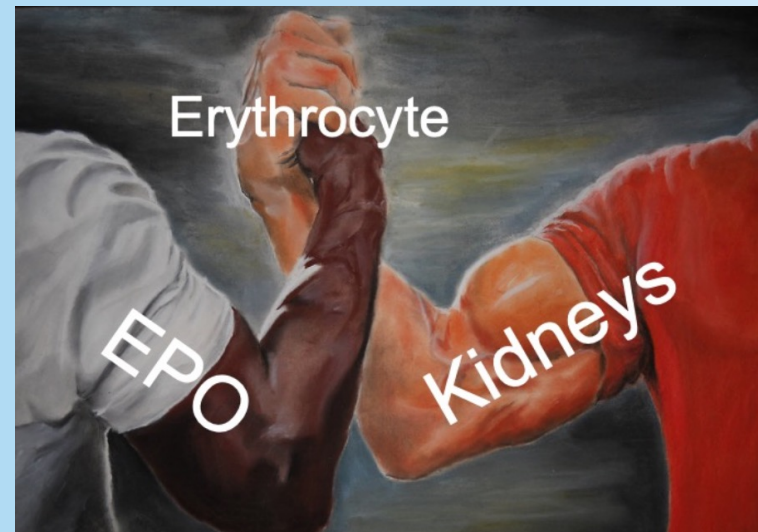
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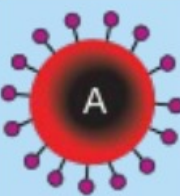
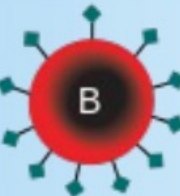
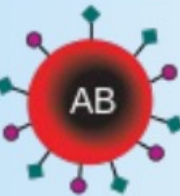




Red blood cells (RBC's)

- 4 - 6 million cells per microliter
- 6–8 μm , anuclear
- Stimulated by **erythropoietin** from the **kidney**
- Life span \approx 120 days
- Function: **oxygen transport**



Blood types




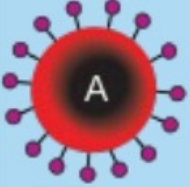
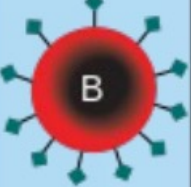
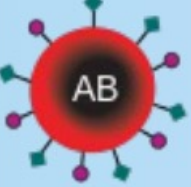




- Blood type **A**, **B**, **AB** or **O** - proteins are present/absent RBC surface
- Antibodies against the proteins that are **absent**
 - Type A = antibody B
 - Type B = antibody A
 - Type O = antibody A and B
- Rhesus proteins: **+** or **-**
 - Rh- = Rh antibody

	Group A ●	Group B ◆	Group AB ◆●	Group O
Red blood cell type				
Antibodies in Plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B

Blood types

Blood transfusion

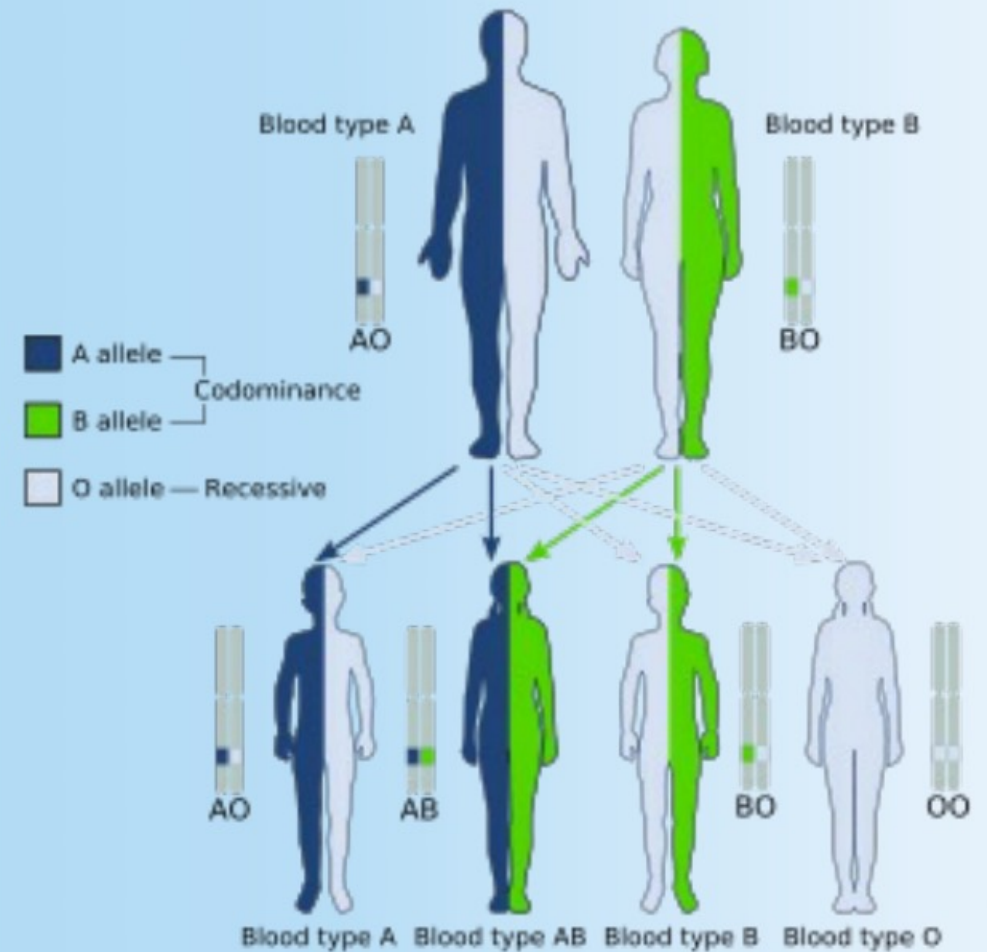
- Blood type AB+ = universal recipient
- Blood type O- = universal donor

	Group A 	Group B 	Group AB 	Group O
Red blood cell type				
Antibodies in Plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B

Blood type - inheritance

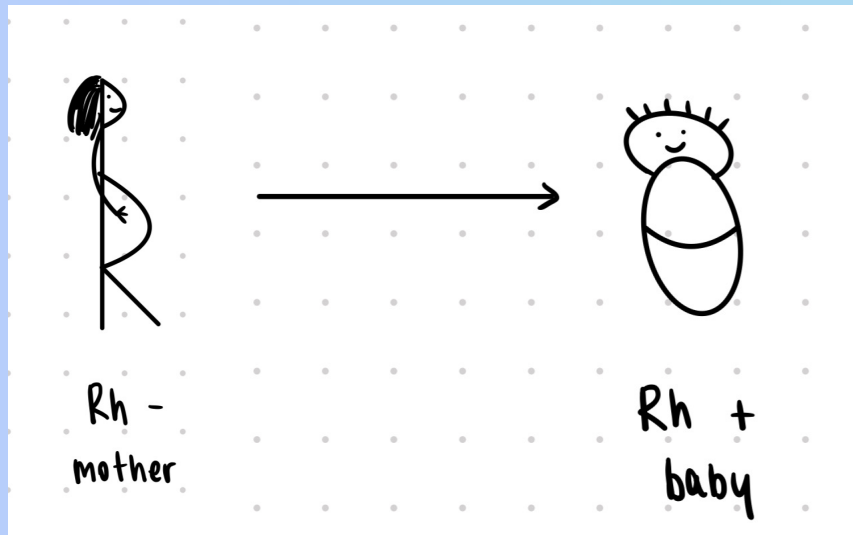
A = dominant }
 B = dominant } *Codominant*
 O = recessive

ABO genotype in the offspring		ABO alleles inherited from the mother		
		A	B	O
ABO alleles inherited from the father	A	A	AB	A
	B	AB	B	B
	O	A	B	O

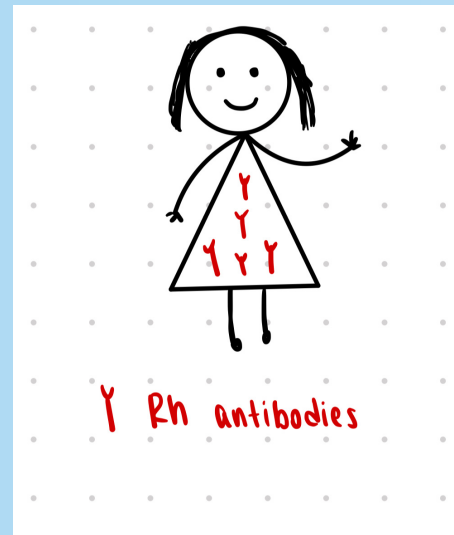


Serological conflict

1st pregnancy



Between pregnancies

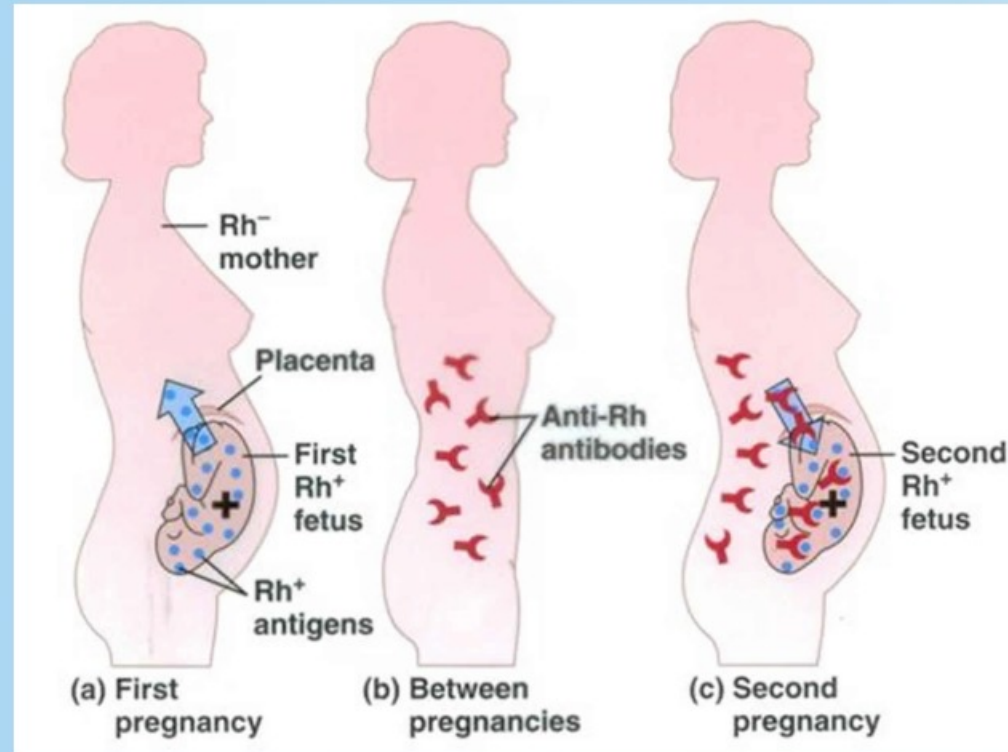


2nd pregnancy



Hemolysis →
Jaundice, anemia

Serological conflict - prophylaxis



- Rh blood-typing
- Anti-D immunoglobulin within 72 hrs!

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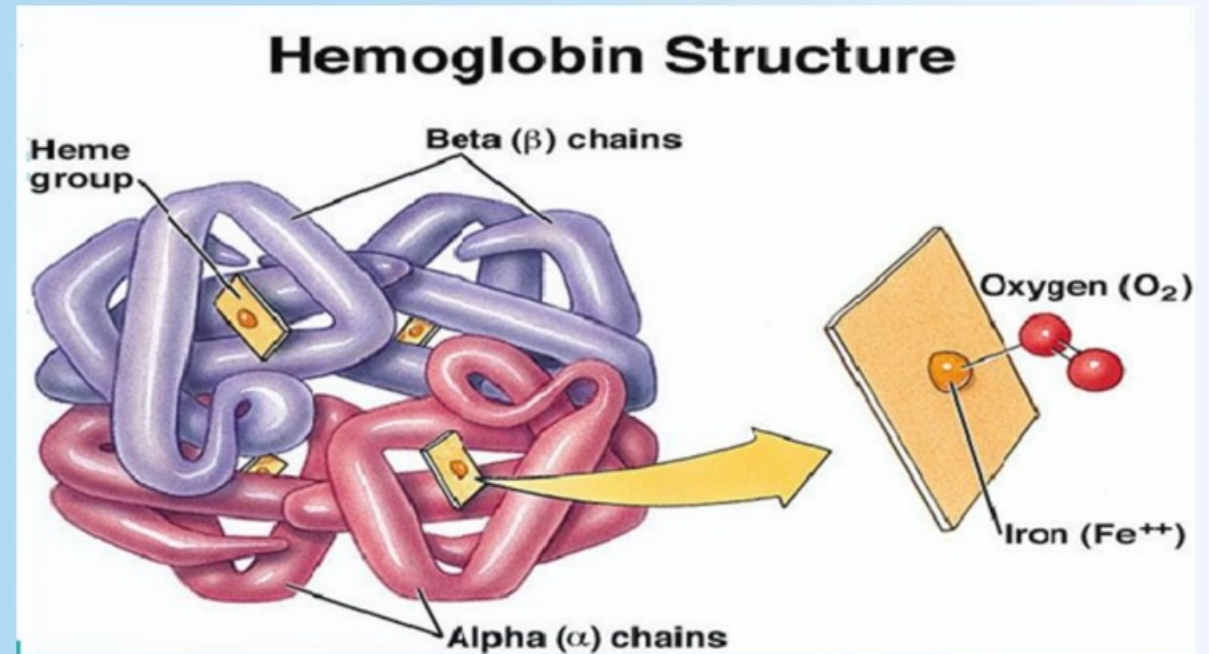
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- Hemoglobin

Hemoglobin (Hb)

- A protein (globin): **4 subunits**
- Subunit: **1 heme** group
- Heme group: **1 Fe²⁺**
- Fe²⁺ binds **1 O₂**

Quick maths: 1 Hb = 4 O₂



Hb - subunits

Adults

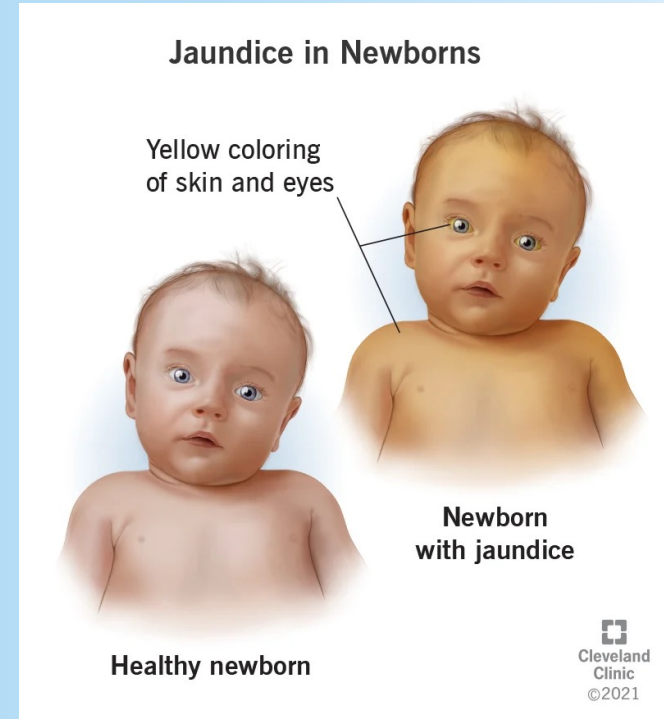
- HbA: $\alpha_2\beta_2$

Fetus:

- HbF: $\alpha_2\gamma_2$
- Higher affinity to oxygen

Clinical significance - fetal jaundice:

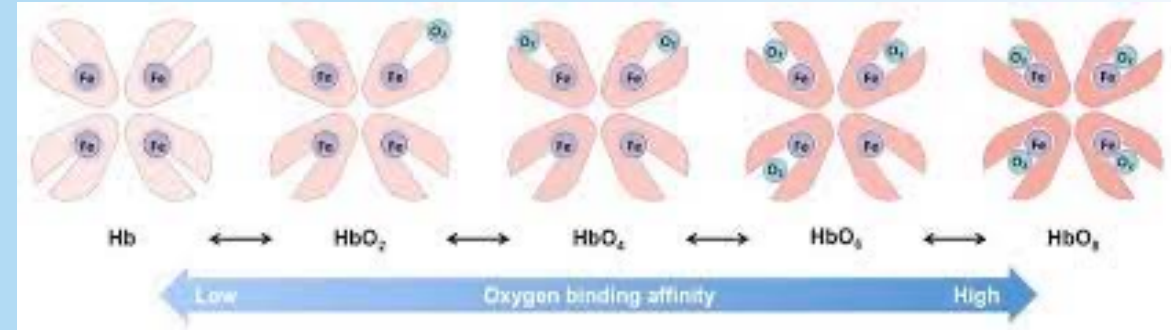
A normal process where fetal RBC's are removed from circulation to replace fetal hemoglobin with adult hemoglobin, causing jaundice. Bilirubin is the breakdown product of RBC's, that why the skin is yellow!



Hb - oxygen binding

Oxygen needs to be:

- Picked up in the lungs
- Released in peripheral tissues



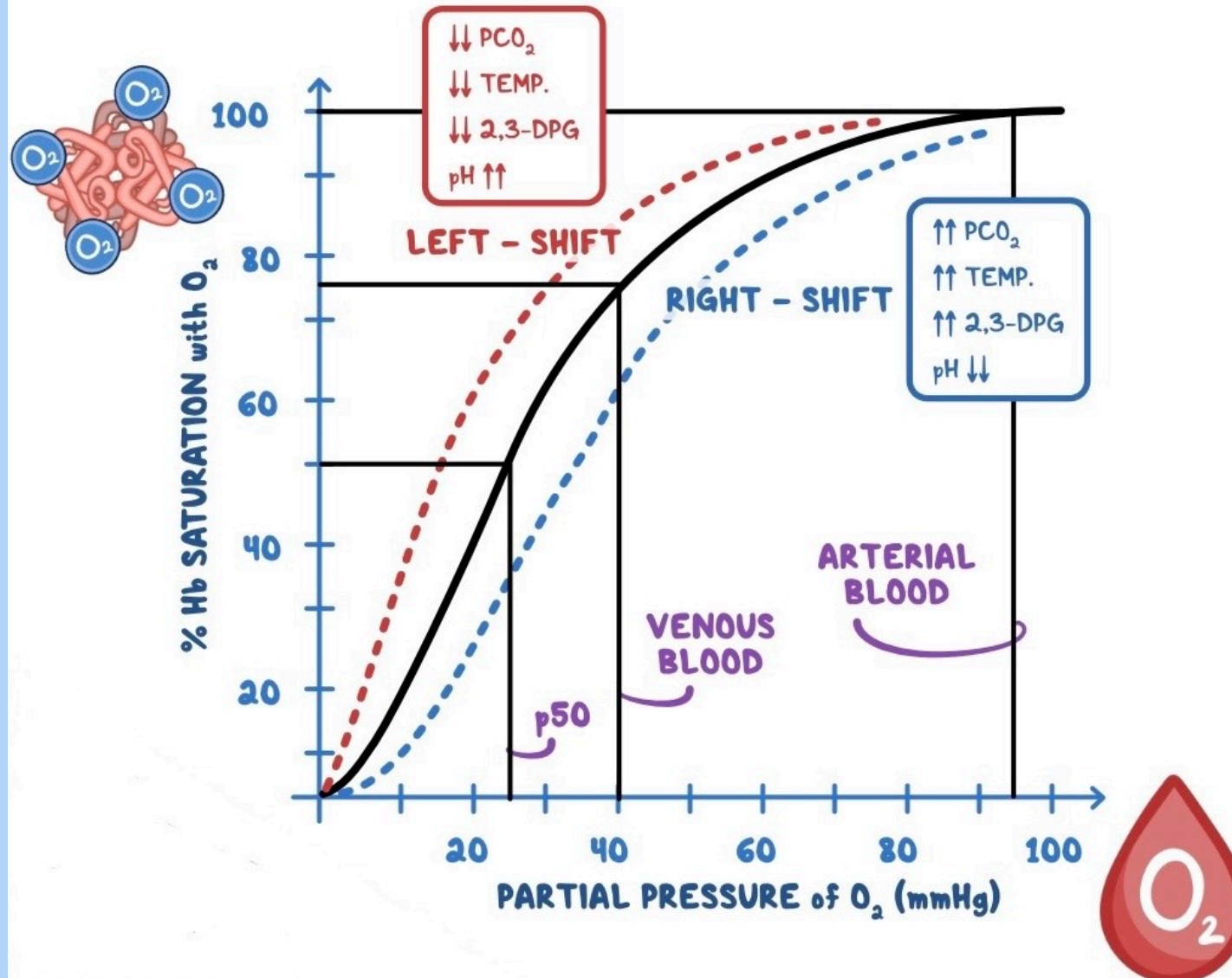
Arterial blood

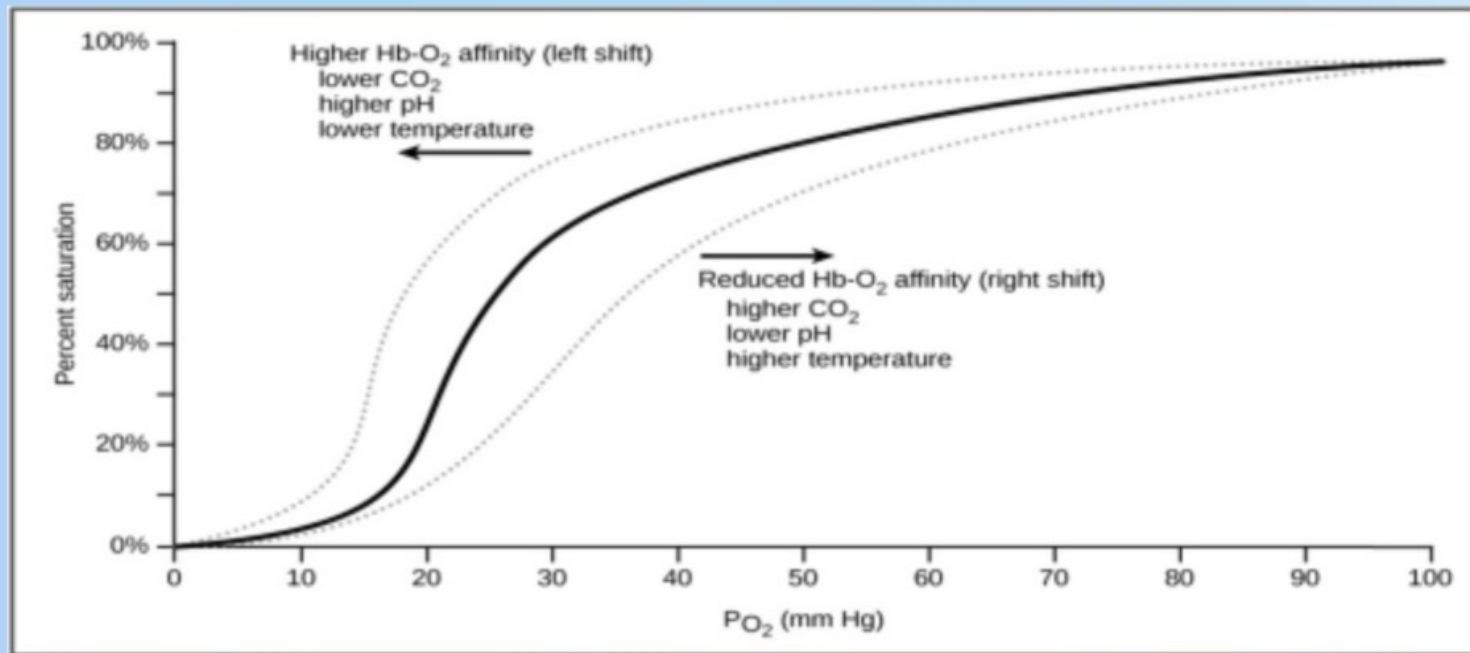
- Oxyhemoglobin ($\approx 97\%$ O₂ saturation)
- R (relaxed) - configuration

Venous blood

- Deoxyhemoglobin ($\approx 70\%$ O₂ saturation)
- T (tense) - configuration

OXYGEN - HEMOGLOBIN DISSOCIATION CURVE





Left shift

↓O₂ unloading to tissues, ↑O₂-Hb affinity

Left = Lower P₅₀

- ↓H⁺ (↑pH, base)
 - ↓CO₂ (weak acid)
- ↓ 2,3-BPG concentration
- ↓temperature
- HbF (γ subunit)
- R-state

Right shift

↑O₂ unloading to tissues, ↓ O₂-Hb affinity

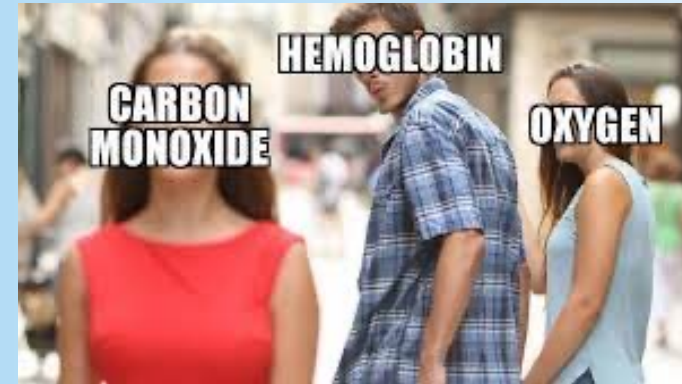
Right = **ACE BATS** are **right** handed

- ↑H⁺ (↓pH, **A**cid)
 - ↑**C**O₂ (weak acid)
 - **E**xercise
- ↑2,3-**B**PG concentration
- High **A**ltitude
- ↑**T**emperature
- T-state

Hb - clinical significance

Carbon monoxide (CO) poisoning

- CO: **240 - fold greater affinity** to Hb than O₂
- Forms **carboxyhemoglobin**
—> hypoxia



Methemoglobinemia

- Heme groups with Fe³⁺ in place of Fe²⁺
- **Fe³⁺ doesn't bind O₂** —> decreased O₂-saturation (≈ 85%)
- Fe³⁺ induces conformational changes to hemoglobin that **increase O₂ affinity to Fe²⁺**
—> hypoxia



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Event code
BLOODP