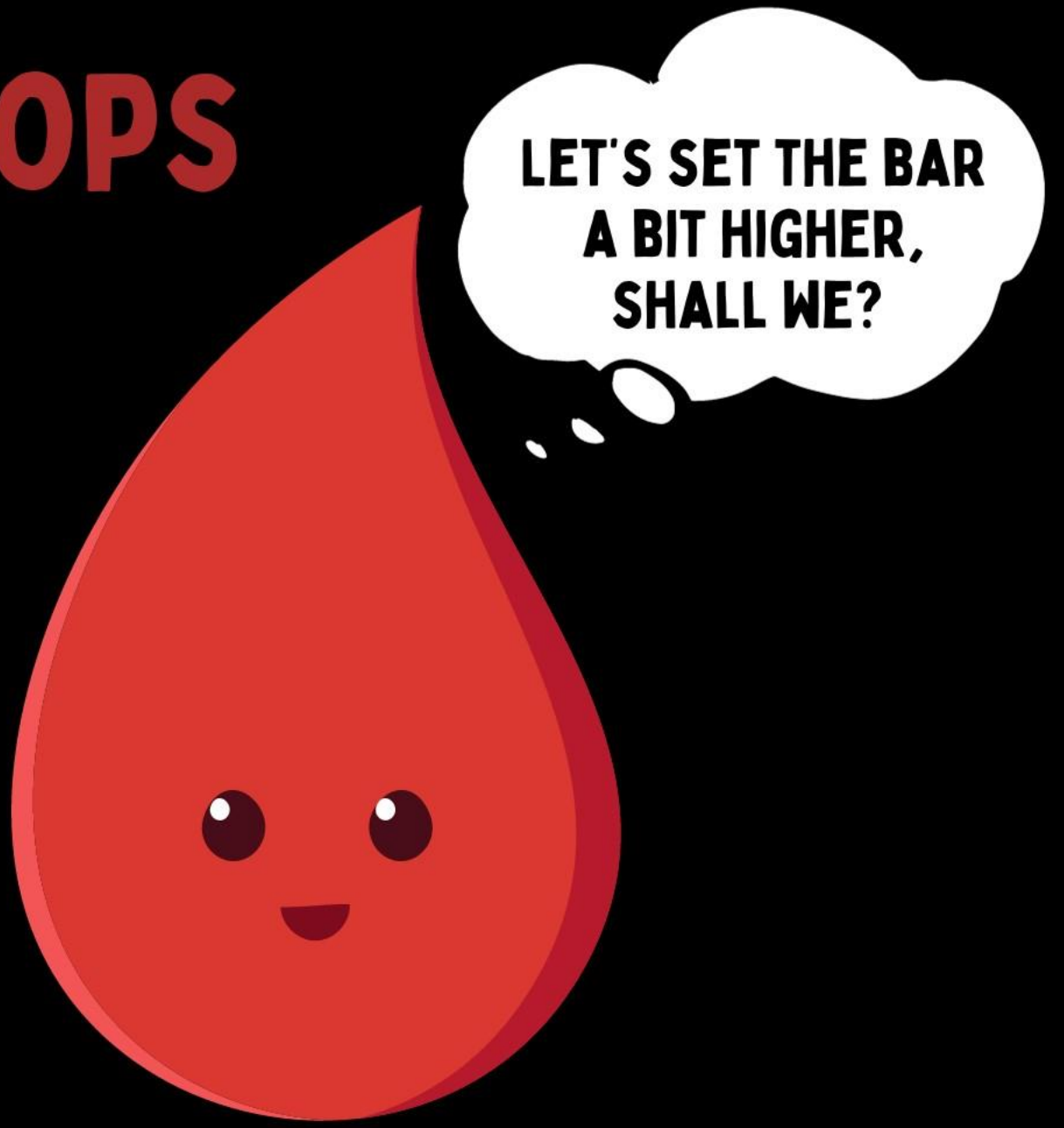
ALL BLEEDING STOPS EVENTUALLY

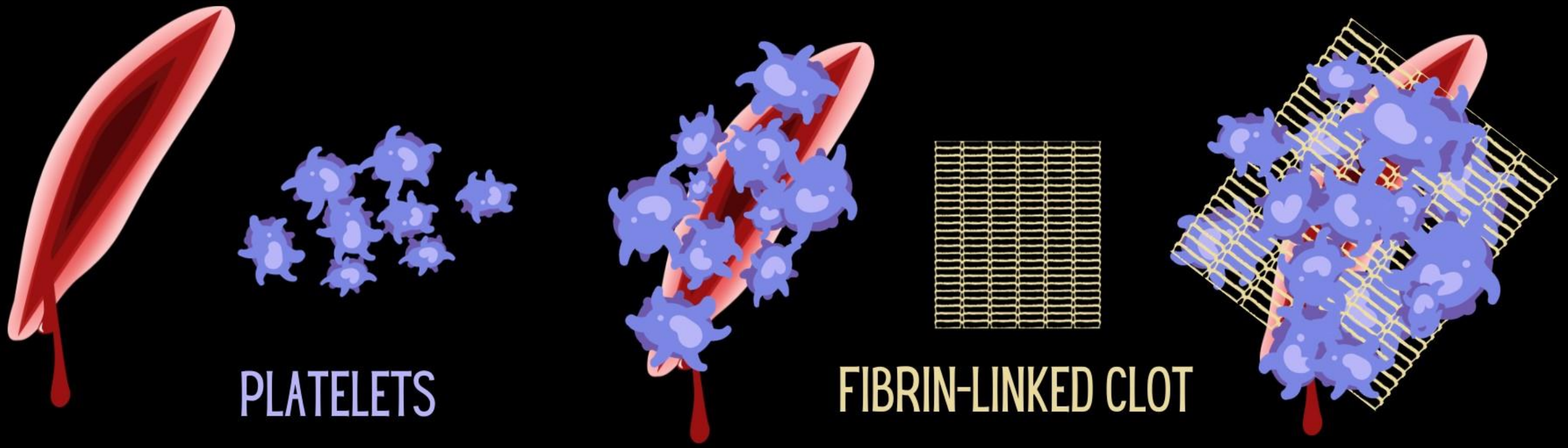
SOME IMPORTANT STUFF ABOUT THE COAGULATION CASCADE



AMY RAMSAY, MD, FACEP
DECEMBER 5, 2023


YOU
ARE
HERE

HEMOSTASIS

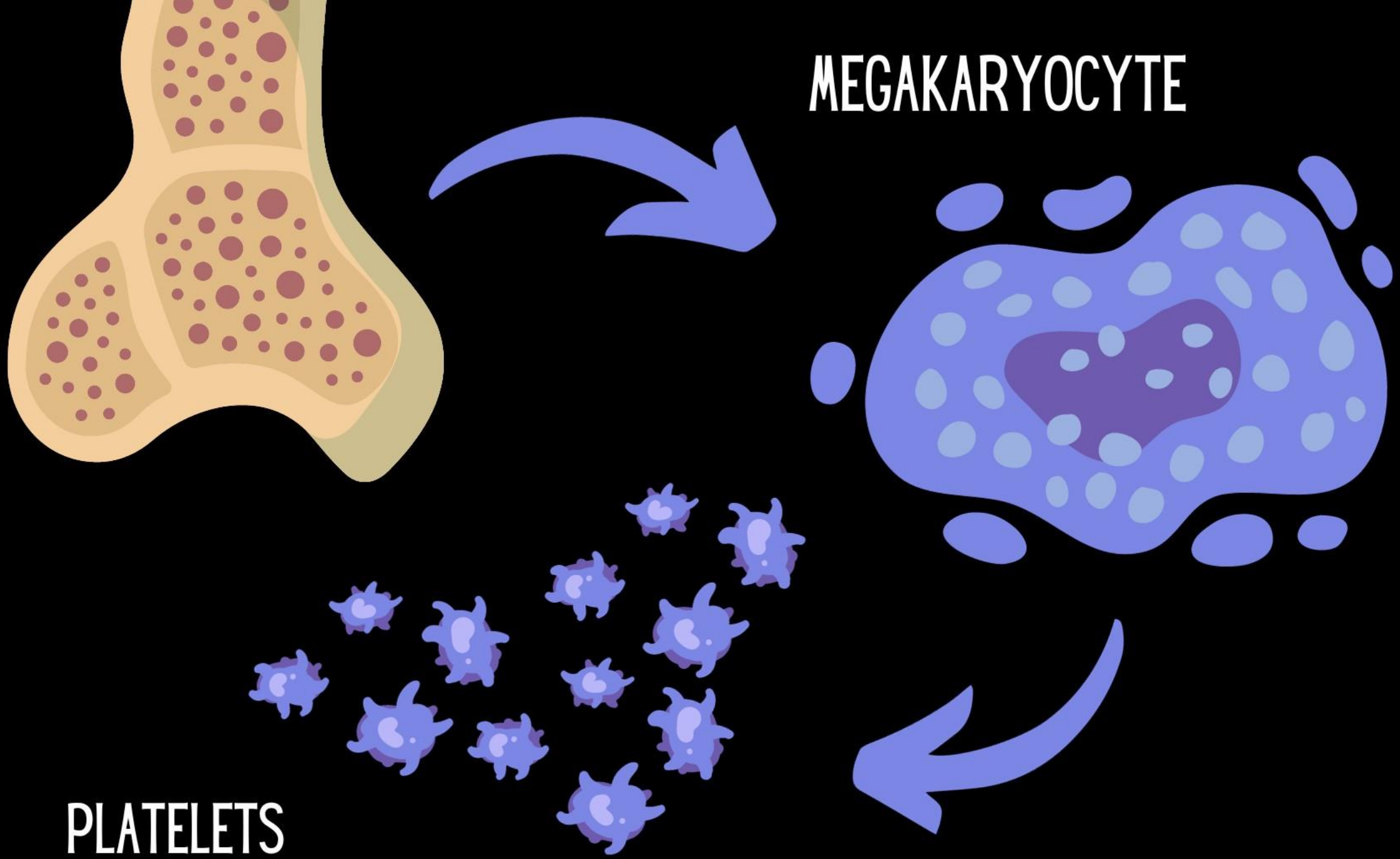


PLATELETS

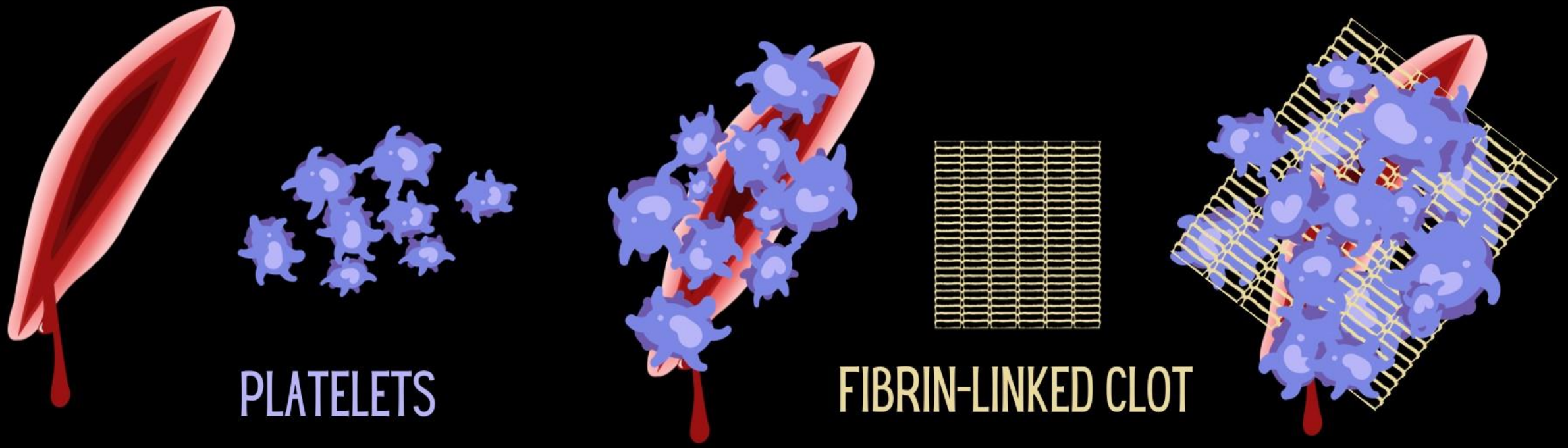
FIBRIN-LINKED CLOT

1

2


MEGAKARYOCYTE
PLATELETS

HEMOSTASIS

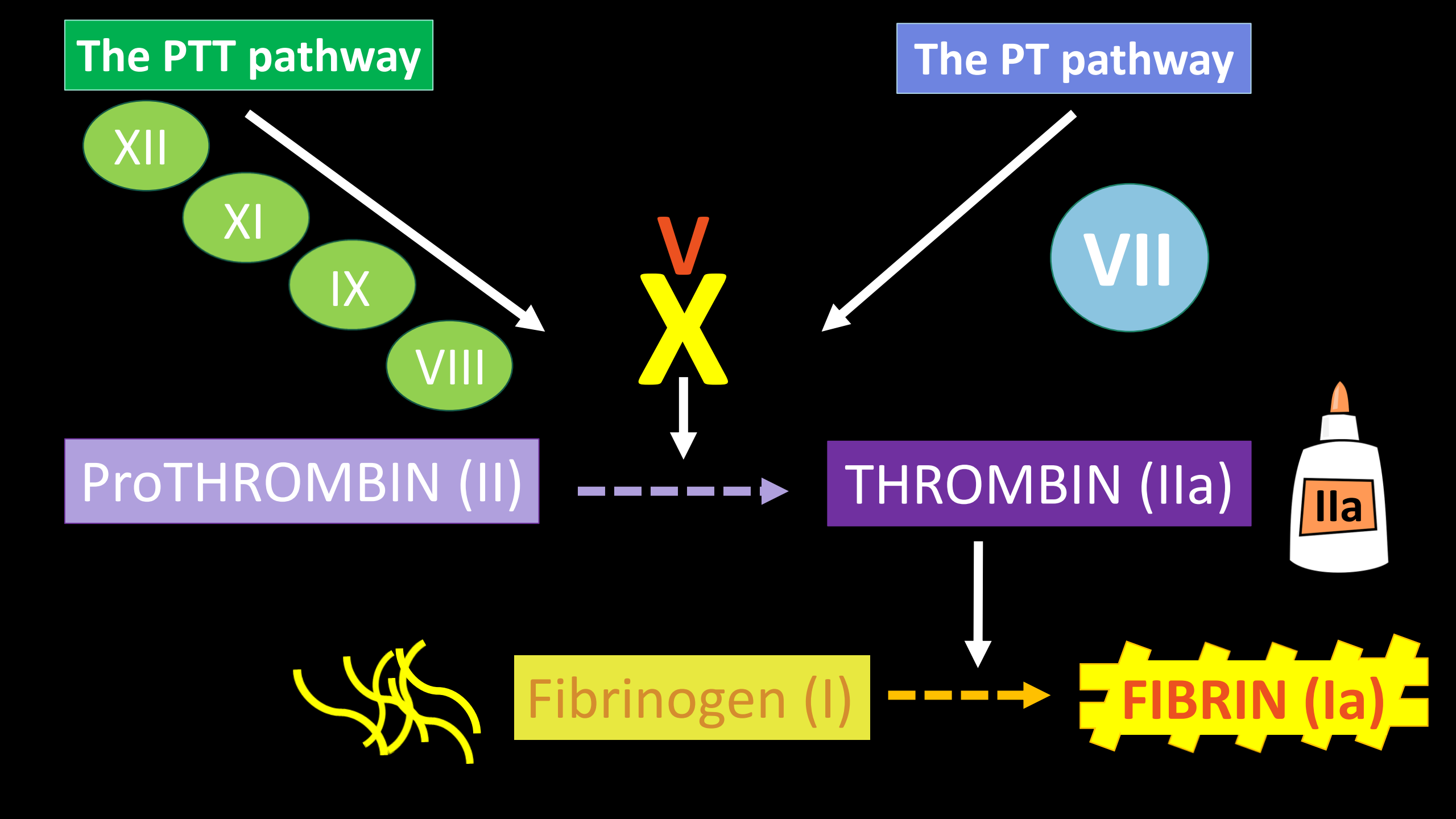


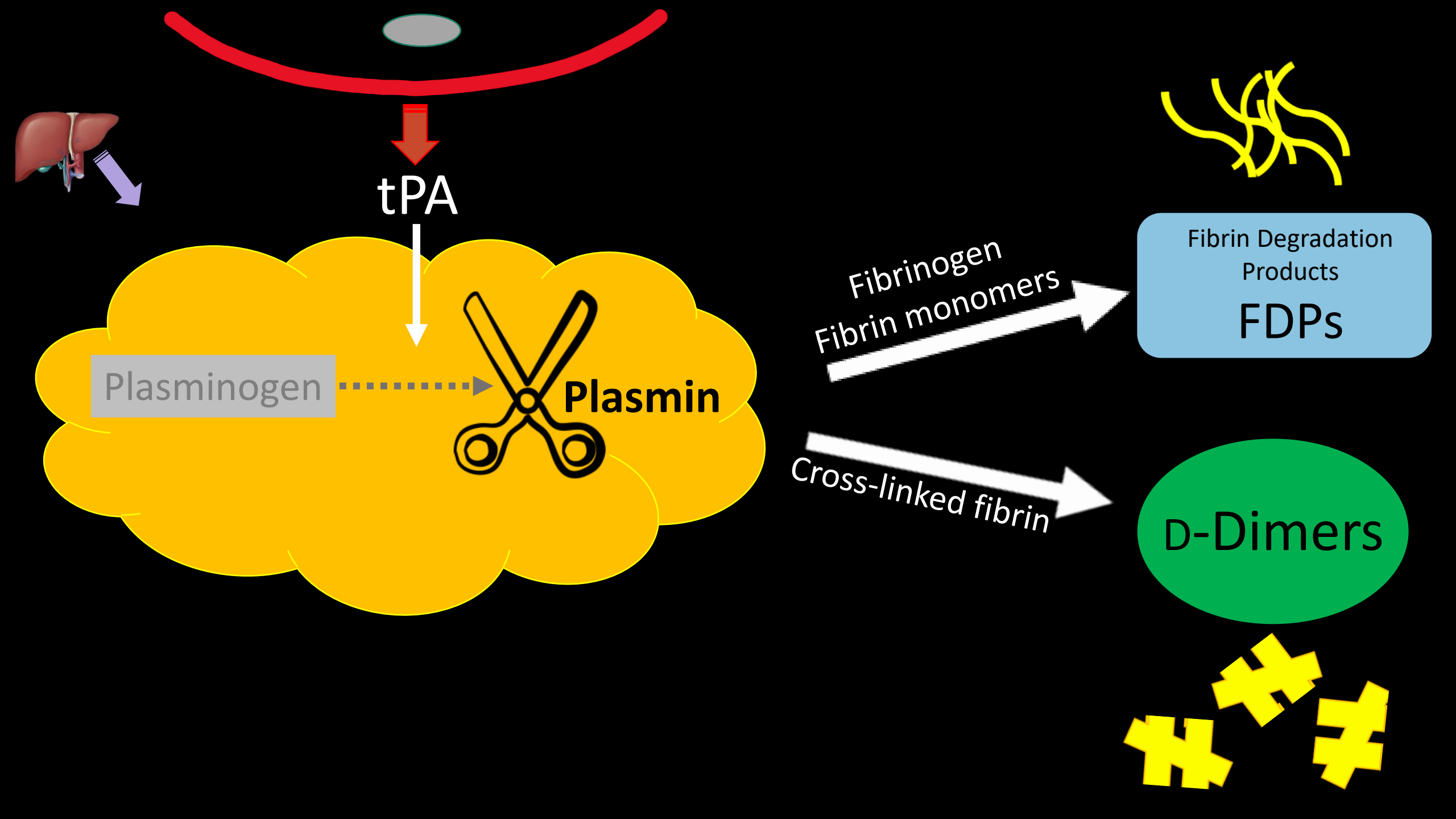
PLATELETS

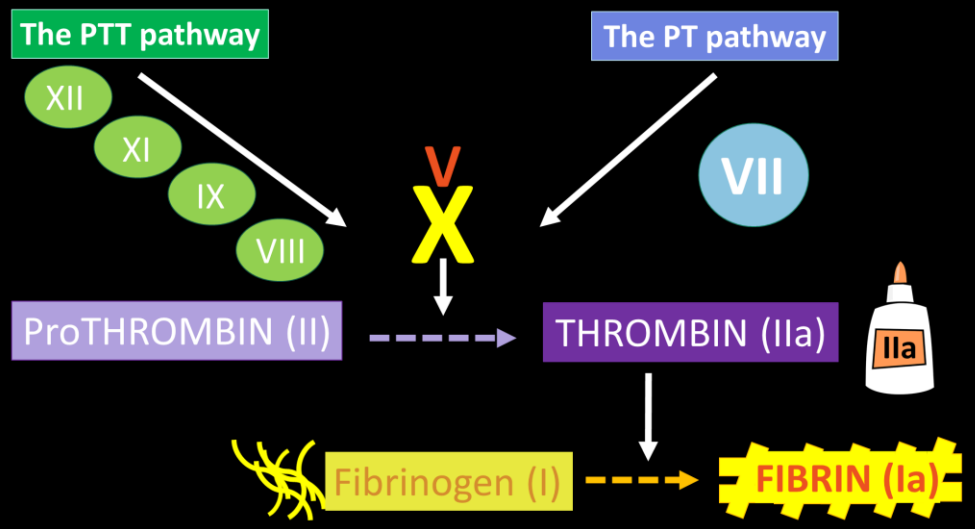
FIBRIN-LINKED CLOT

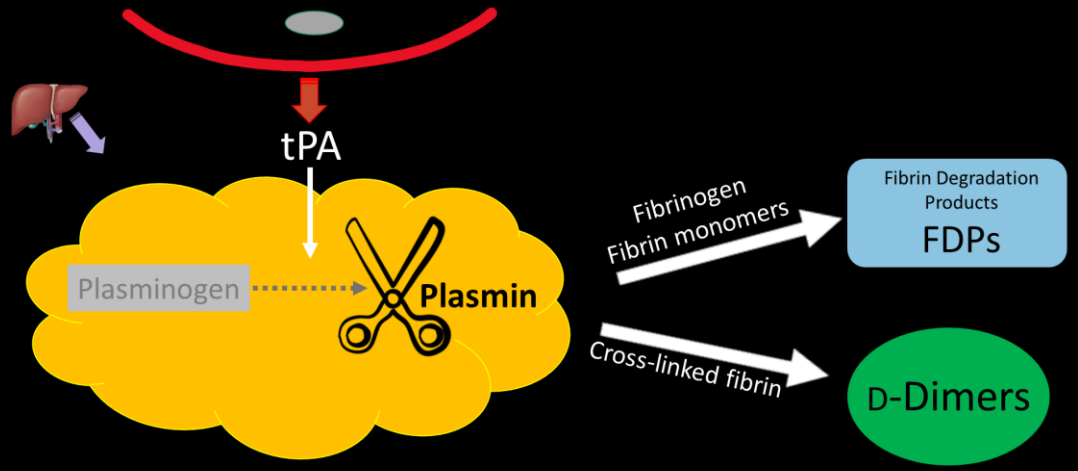
1

2


The PTT pathway
The PT pathway
XII
XI
IX
VIII
V
X
VII
ProTHROMBIN (II)
THROMBIN (IIa)
IIa
Fibrinogen (I)
FIBRIN (Ia)

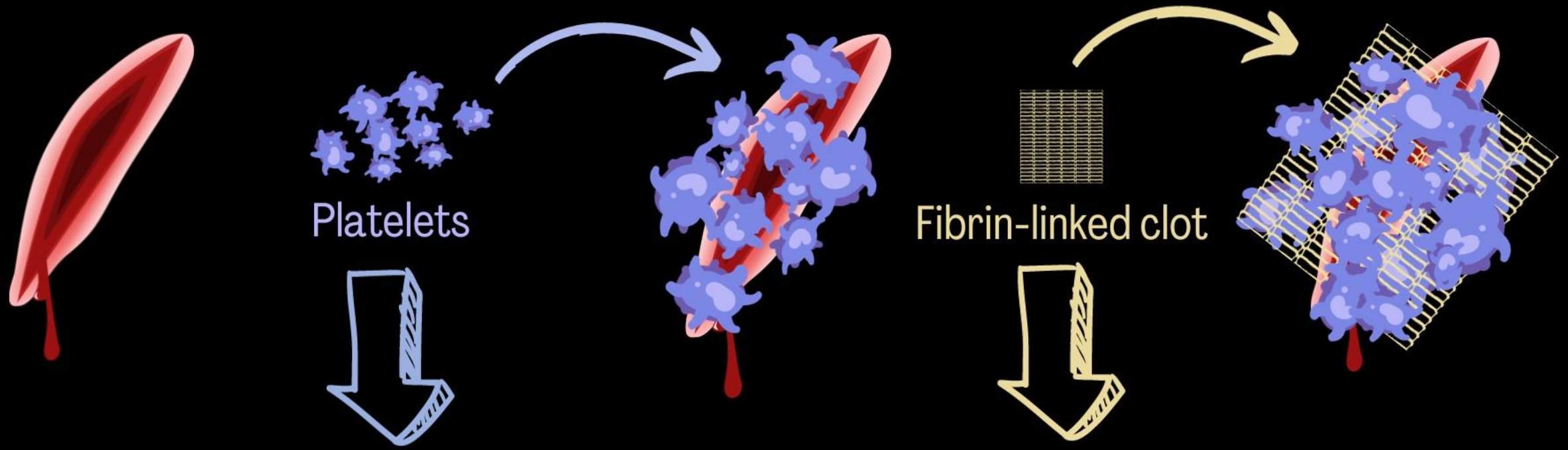

tPA
Plasminogen
Plasmin
Fibrinogen
Fibrin monomers
Fibrin Degradation Products
FDPs
Cross-linked fibrin
D-Dimers





Clot Making

Clot Breaking



PLATELET PROBLEMS

mucocutaneous bleeding

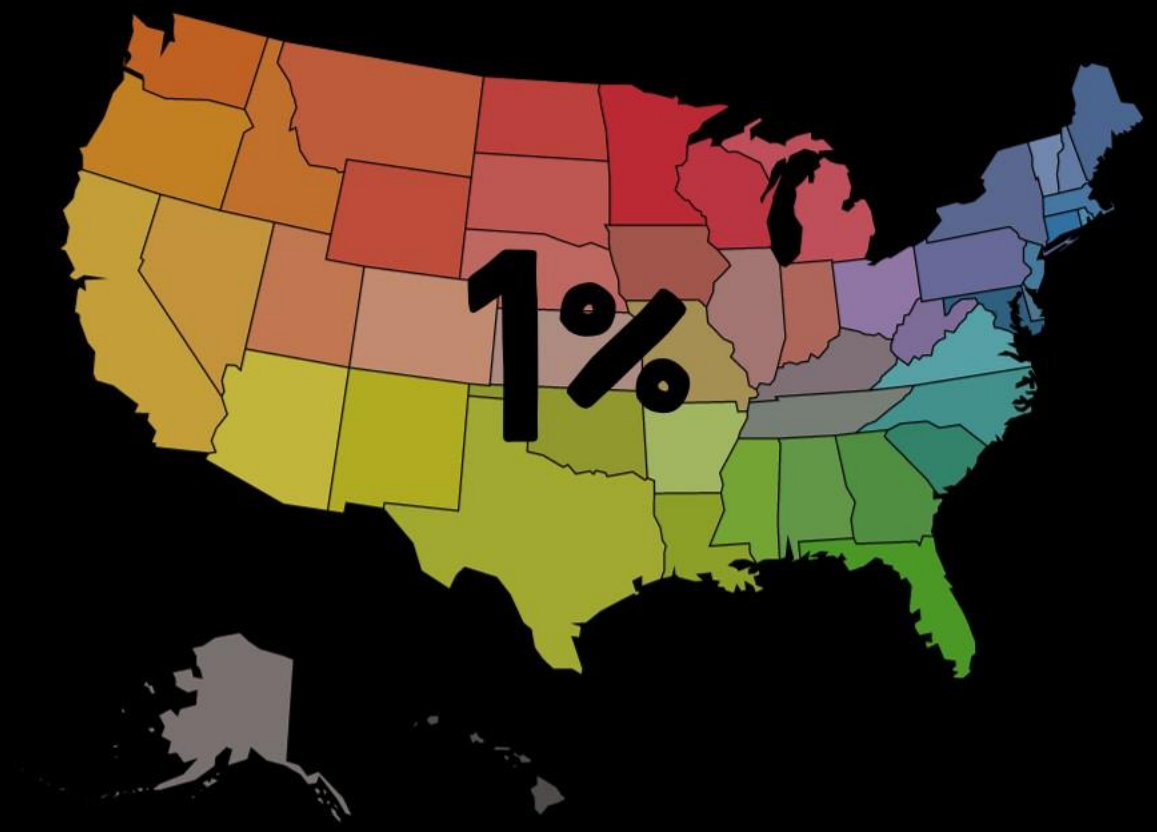
epistaxis
hematuria
petechiae
menorrhagia

FIBRIN CLOT PROBLEMS

deep and delayed bleeding

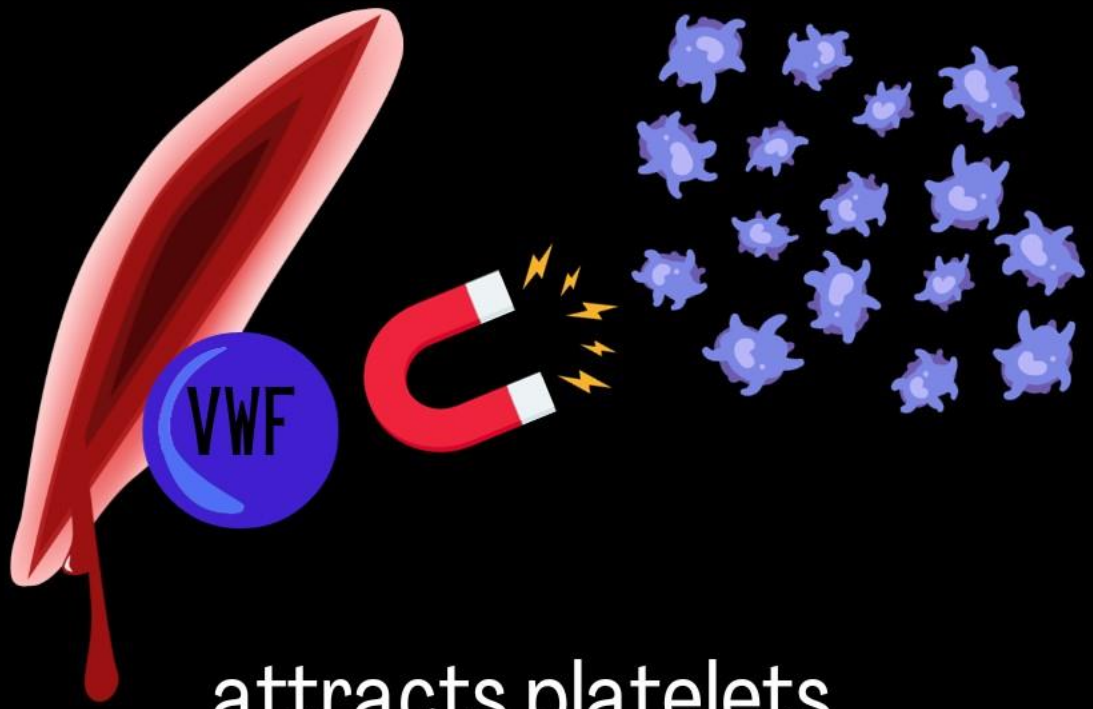
intracranial hemorrhage
retroperitoneal hemorrhage
hemarthrosis

VON WILLEBRAND DISEASE



the most common bleeding disorder

VON WILLEBRAND DISEASE

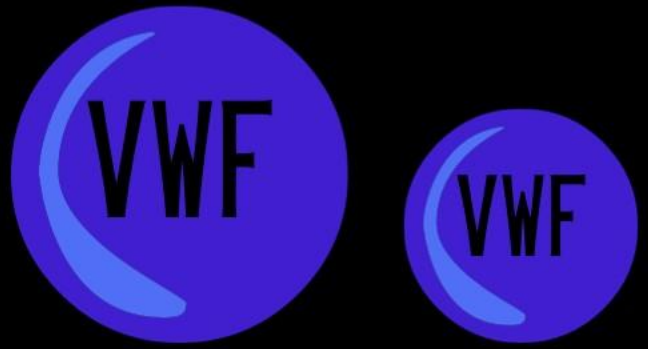


attracts platelets
makes them sticky

stabilizes factor VIII
in coagulation cascade

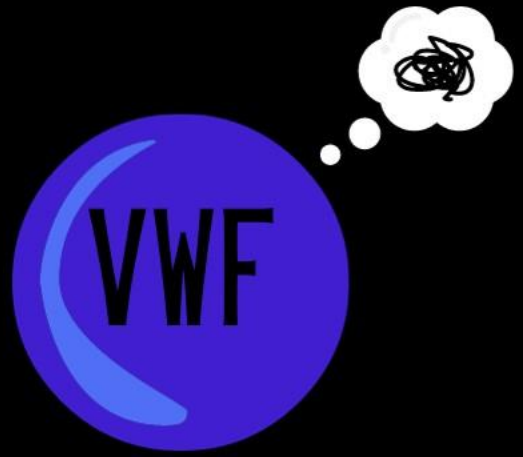
VON WILLEBRAND DISEASE

TYPE 1



reduced levels of vWF
(+/- reduced factor VIII)

TYPE 2

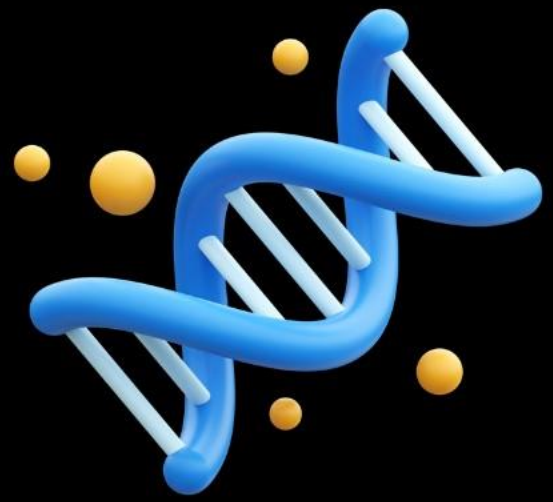


normal level of vWF
dysfunctional

TYPE 3

low/no vWF
low factor VIII

VON WILLEBRAND DISEASE



autosomal dominant inheritance

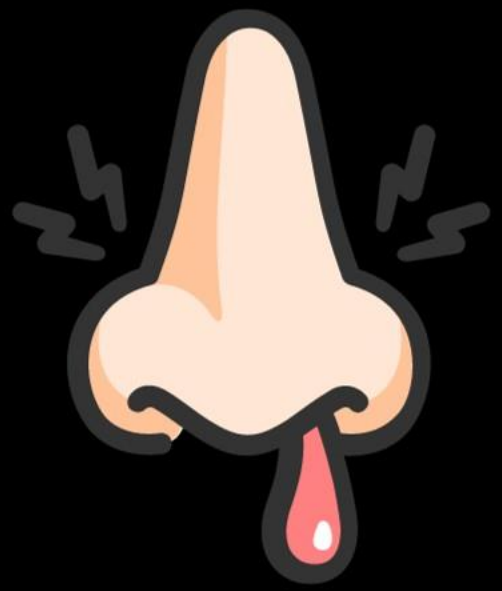
0 alleles
no disease

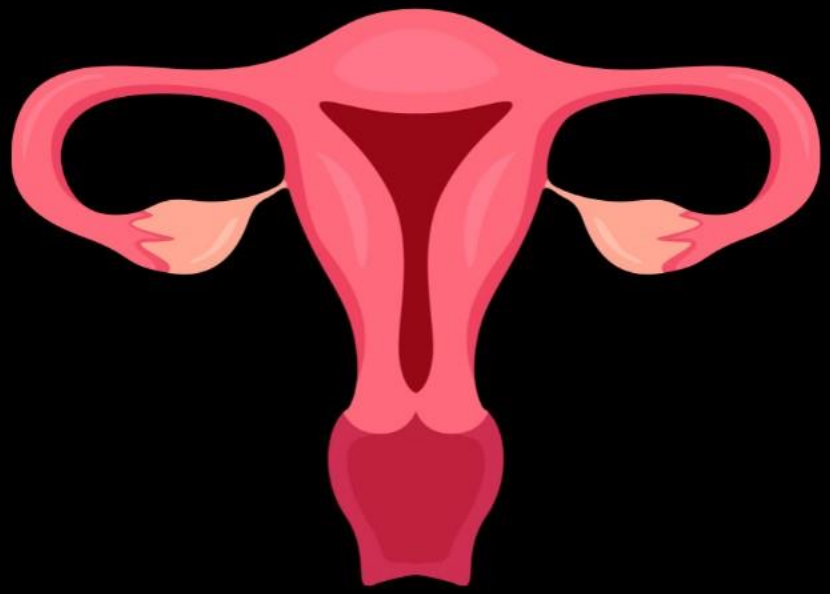
1 allele
mild disease

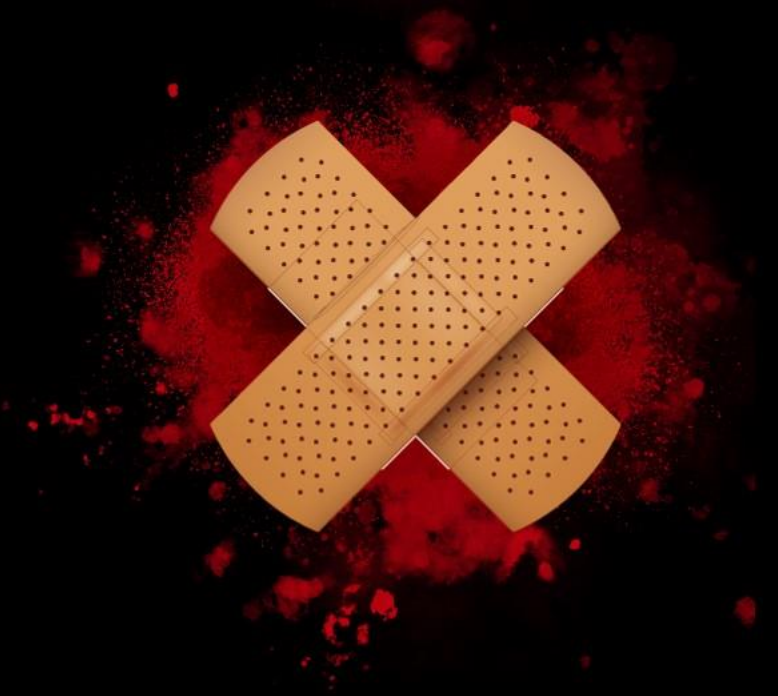
85%

2 alleles
severe disease

VON WILLEBRAND DISEASE

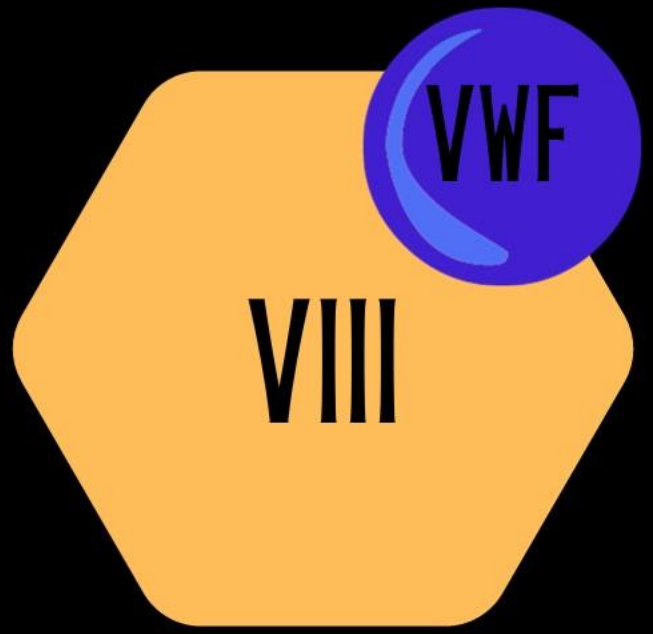




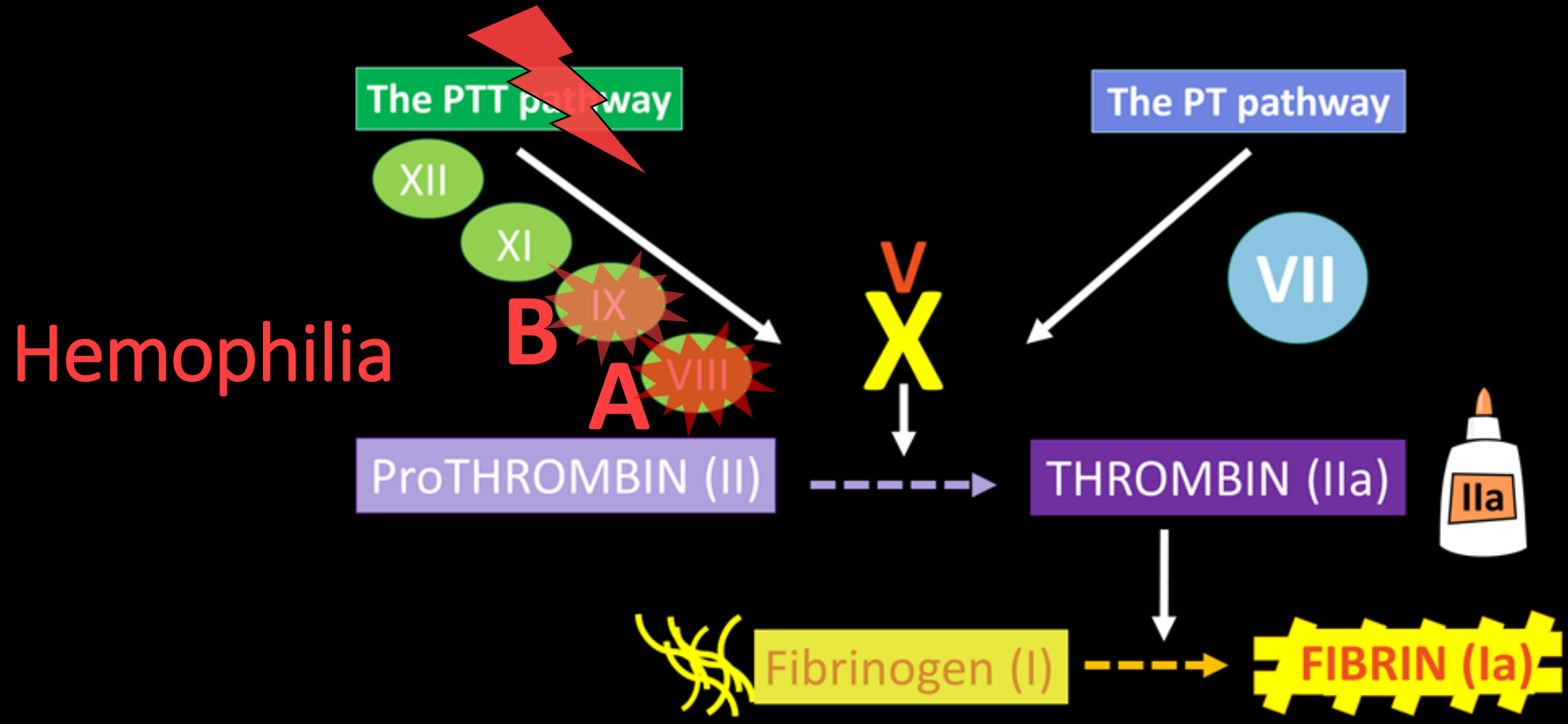


DESMOPRESSIN BOOSTS FACTOR VIII AND VWF LEVELS

0.3
mcg/kg

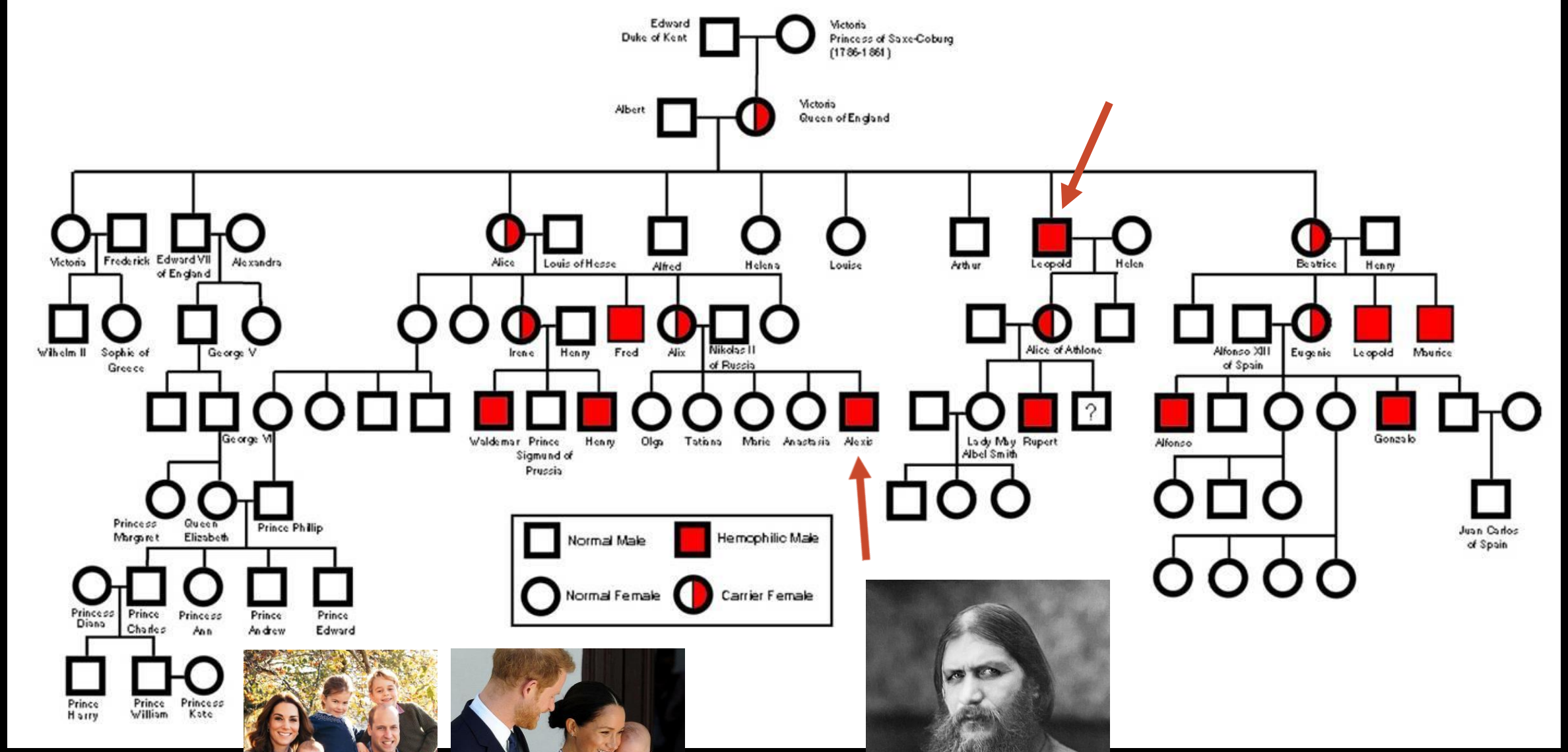


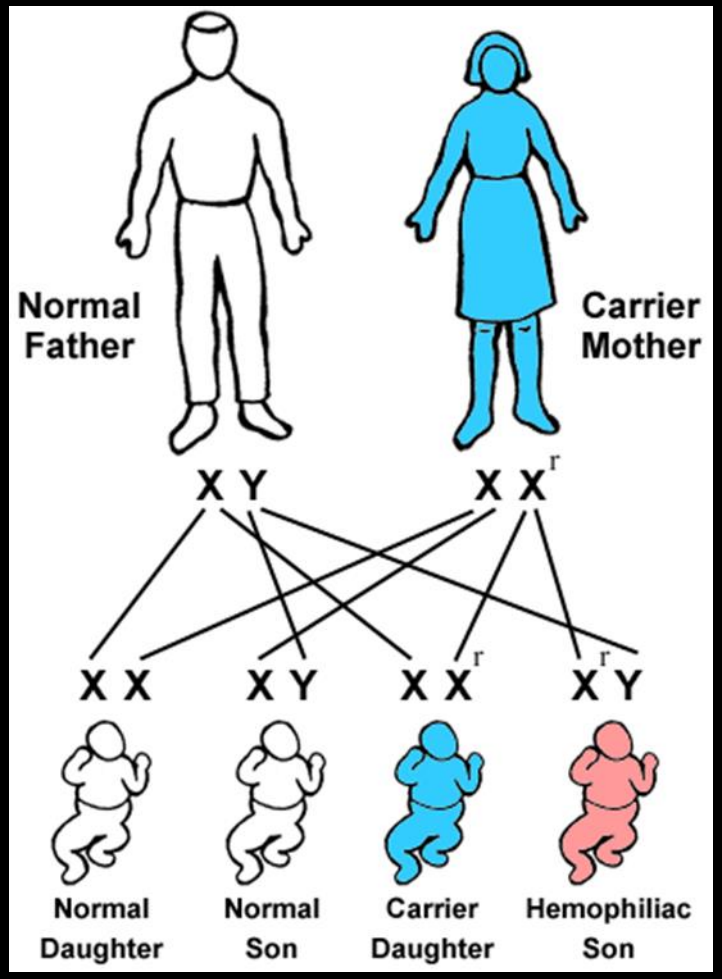

HEMOPHILIA

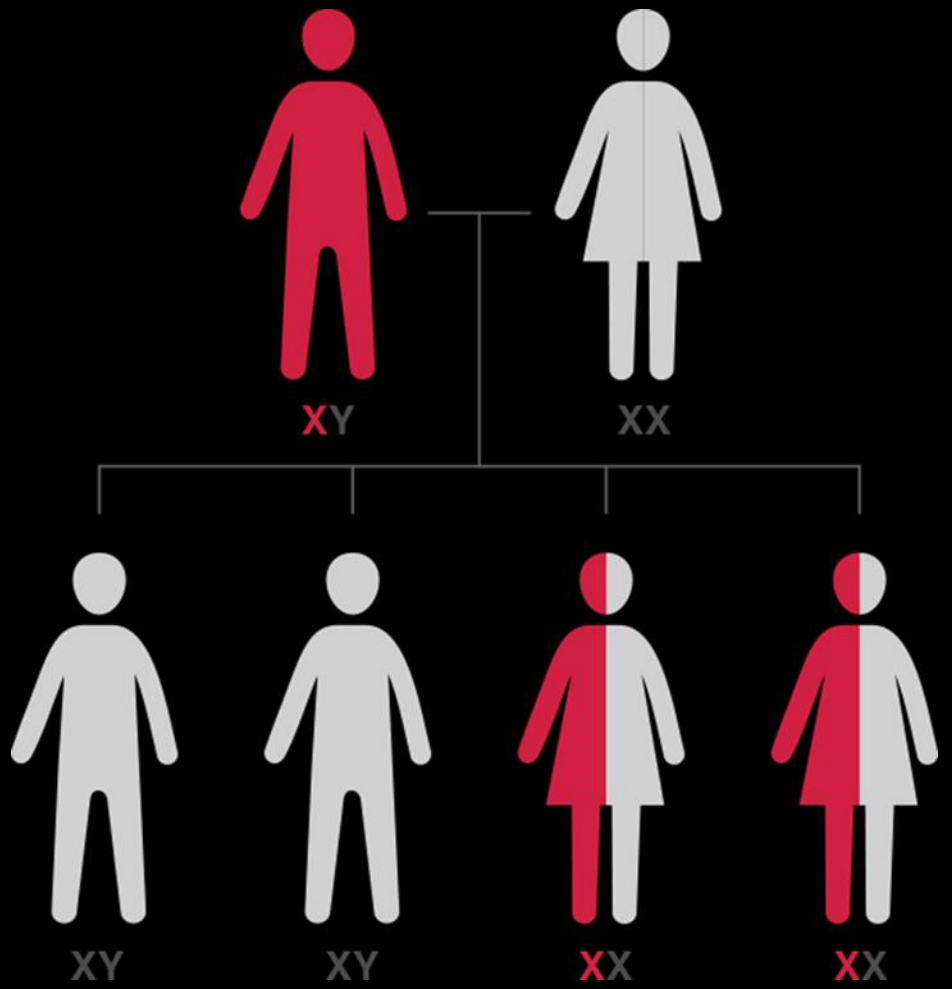


Hemophilia A and B appear clinically the same.

https://www.cdc.gov/ncbddd/hemophilia/data.html


Edward
Duke of Kent
Victoria
Princess of Saxe-Coburg
(1786-1861)
Albert
Victoria
Queen of England
Victoria
Frederick
Edward VII
of England
Alexandra
Alice
Louis of Hesse
Alfred
Helena
Louise
Arthur
Leopold
Helen
Beatrice
Henry
Wilhelm II
Sophie of
Greece
George V
Irene
Henry
Fred
Alix
Nikolas II
of Russia
Alice of Athlone
Alfonso XIII
of Spain
Eugenie
Leopold
Maurice
George VI
Waldemar
Prince
Sigmund of
Prussia
Henry
Olga
Tatiana
Marie
Anastasia
Alexis
Lady May
Abel Smith
Rupert
?
Alfonso
Gonzalo
Juan Carlos
of Spain
Princess
Margaret
Queen
Elizabeth
Prince Phillip
Princess
Diana
Prince
Charles
Princess
Ann
Prince
Andrew
Prince
Edward
Prince
Harry
Prince
William
Princess
Kate
Normal Male
Hemophilic Male
Normal Female
Carrier Female


Normal
Father
Carrier
Mother
X Y
X X r
X X
X Y
X X r
X Y r
Normal
Daughter
Normal
Son
Carrier
Daughter
Hemophiliac
Son

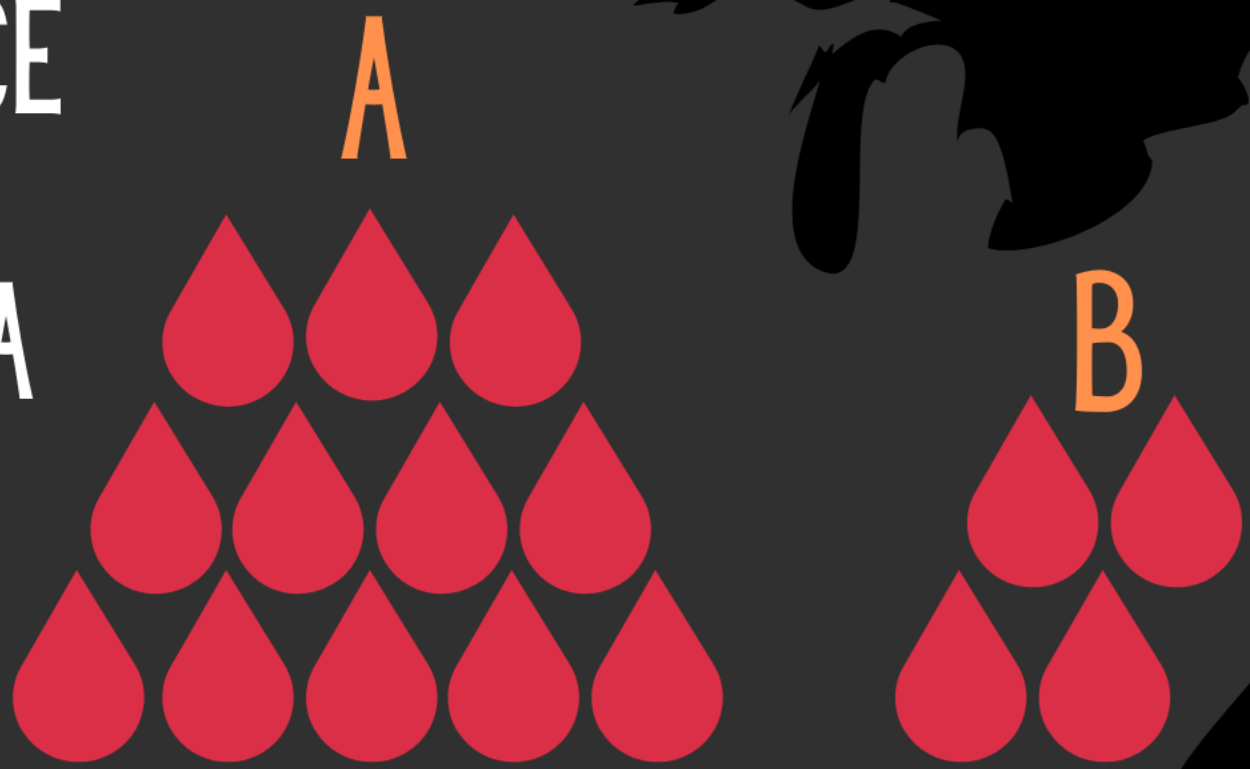

XY
XX
XY
XY
XX
XX

1/3

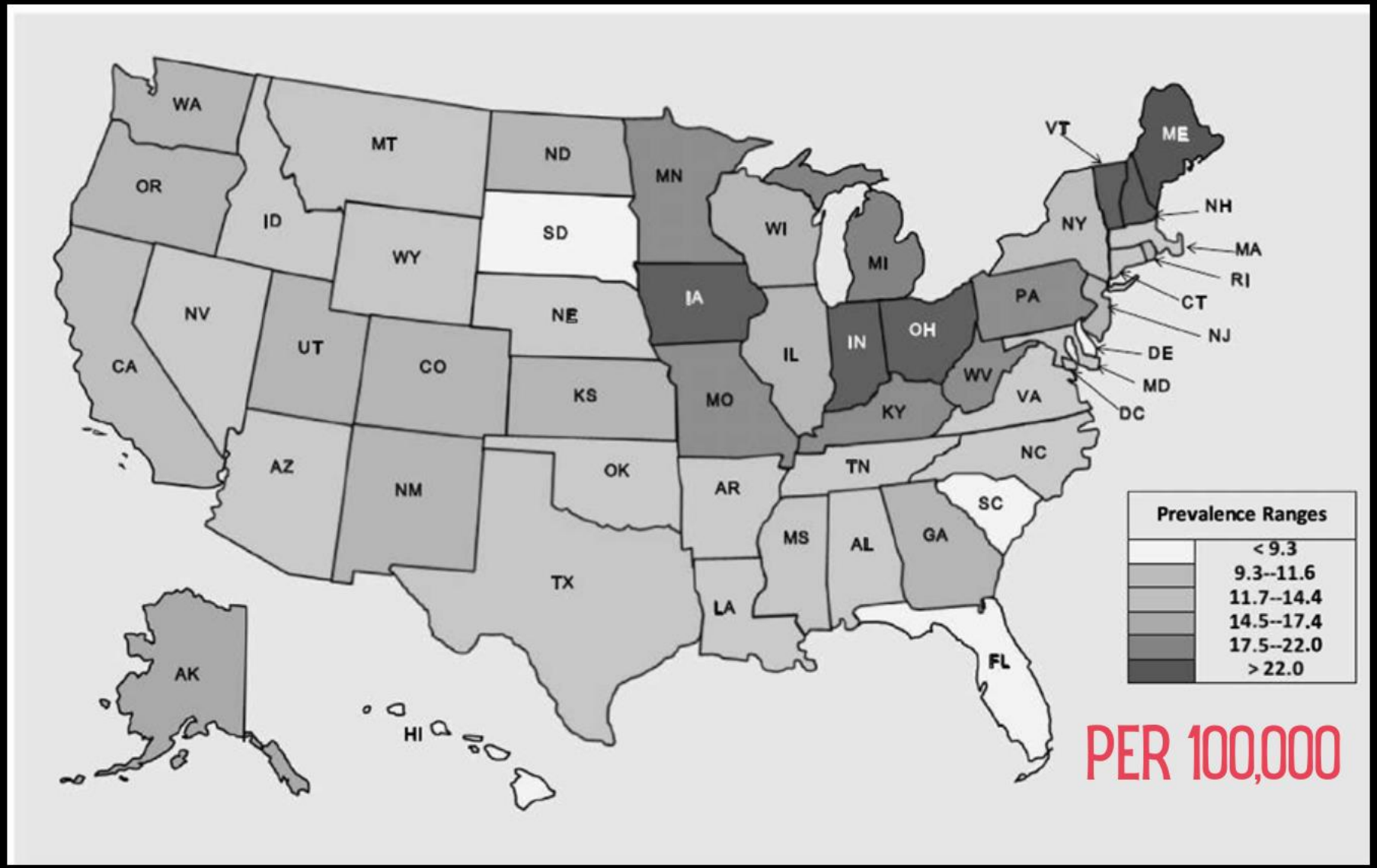
ARISE FROM SPONTANEOUS MUTATIONS

PREVALENCE OF HEMOPHILIA

PER 100,000



STATE-SPECIFIC PREVALENCE

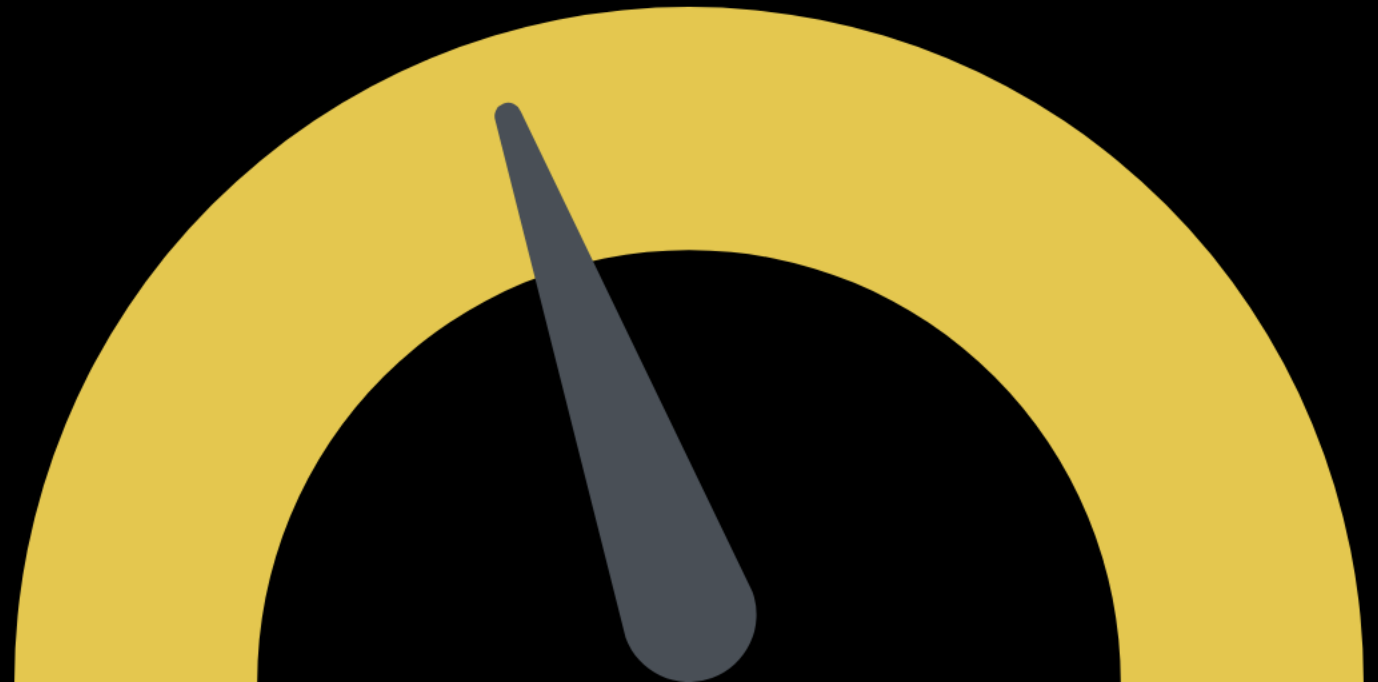


LIVING WITH SEVERE HEMOPHILIA

FACTOR ACTIVITY

5%-40% = MILD DISEASE

USUALLY ONLY BLEED AFTER TRAUMA



1%-5% = MODERATE DISEASE

MAY BLEED SPONTANEOUSLY
BLEED AFTER TRAUMA

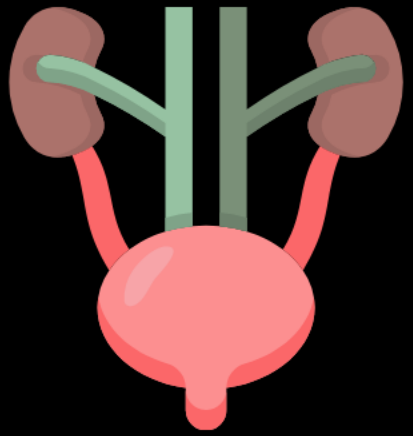
BELOW 1% = SEVERE DISEASE

SPONTANEOUS BLEEDING

MOST COMMON SITES OF BLEEDING

DEEP MUSCLES

JOINTS



URINARY TRACT

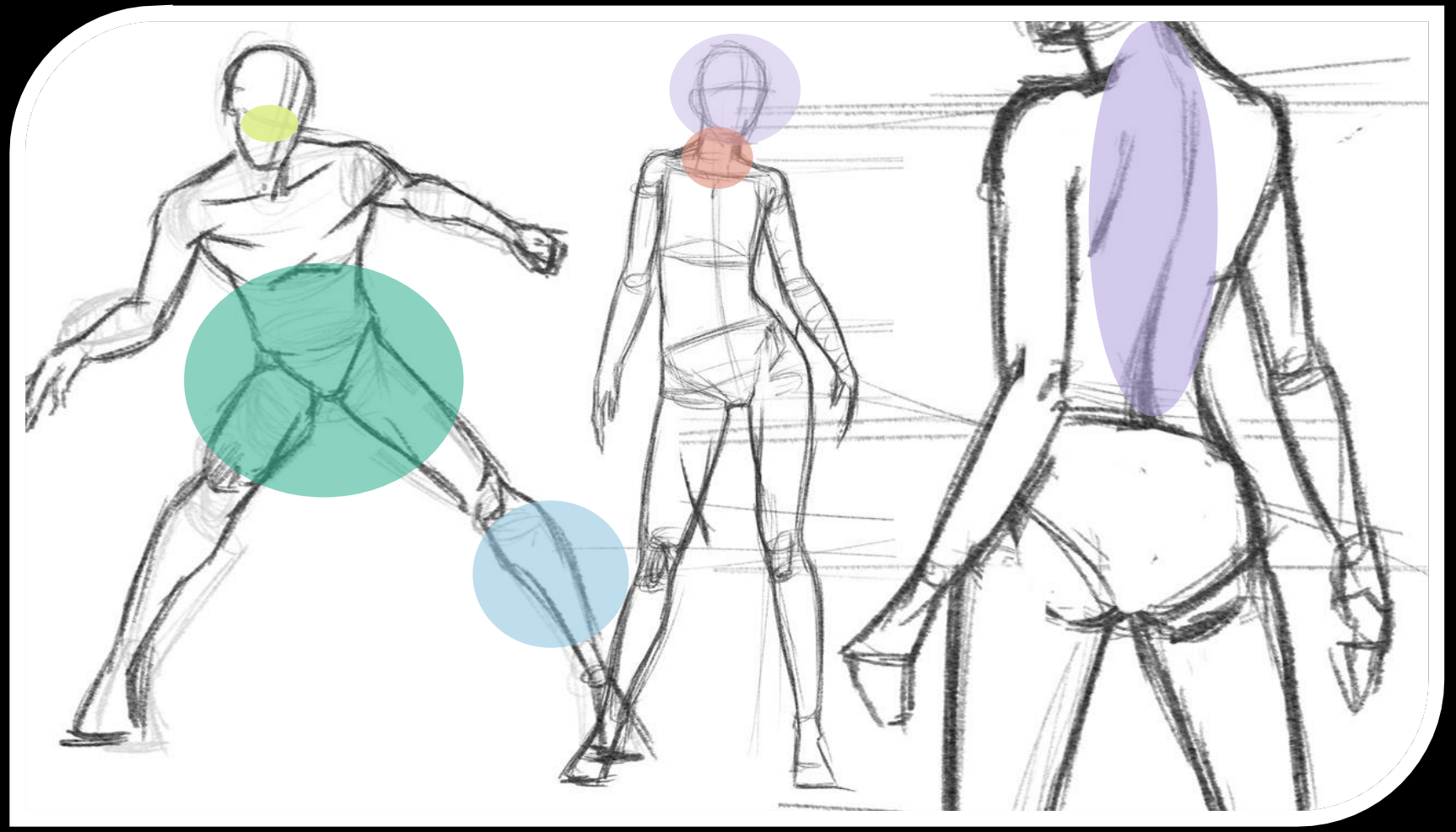
INTRA CRANIAL

Retrobulbar hematoma

Airway compromise

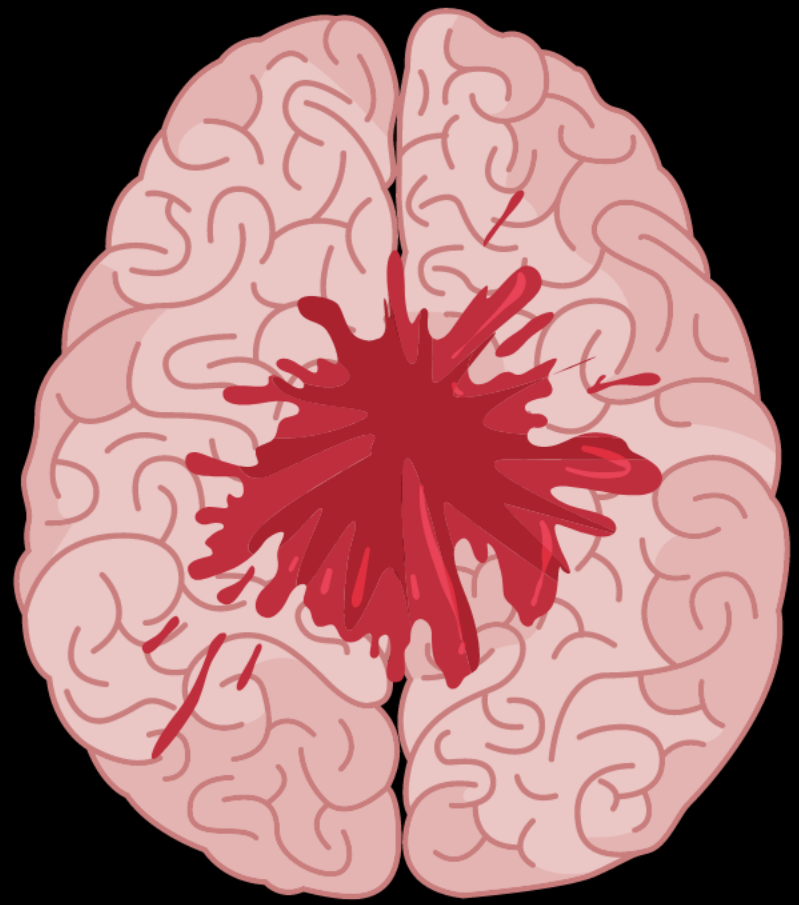
CNS bleeding

Iliopsoas bleeding



Compartment syndrome

INTRACRANIAL BLEEDING IS THE MOST COMMON CAUSE OF DEATH IN ALL AGE GROUPS



HEMARTHROSIS

PROGRESSIVE JOINT DESTRUCTION

EXPECT DELAYED BLEEDING

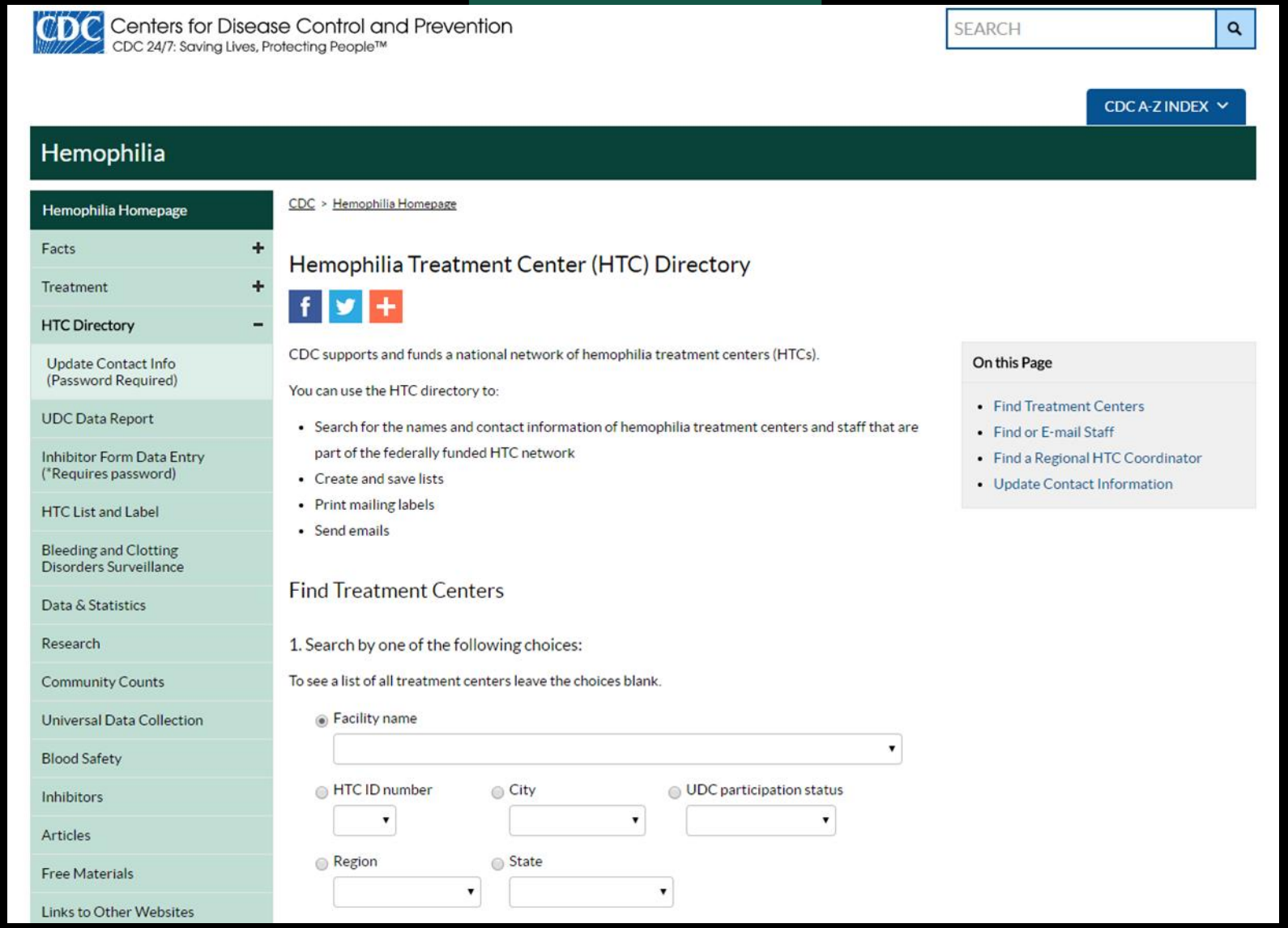
USUALLY BY 8 HOURS

1-5 DAYS OR MORE

MOST MANAGE THEIR BLEEDING AT HOME WITH HEMOPHILIA HOME THERAPY

70%

cdc.gov


Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™
SEARCH
CDC A-Z INDEX
Hemophilia
Hemophilia Homepage
Facts
Treatment
HTC Directory
Update Contact Info (Password Required)
UDC Data Report
Inhibitor Form Data Entry (*Requires password)
HTC List and Label
Bleeding and Clotting Disorders Surveillance
Data & Statistics
Research
Community Counts
Universal Data Collection
Blood Safety
Inhibitors
Articles
Free Materials
Links to Other Websites
CDC > Hemophilia Homepage
Hemophilia Treatment Center (HTC) Directory
CDC supports and funds a national network of hemophilia treatment centers (HTCs).
You can use the HTC directory to:
Search for the names and contact information of hemophilia treatment centers and staff that are part of the federally funded HTC network
Create and save lists
Print mailing labels
Send emails
On this Page
Find Treatment Centers
Find or E-mail Staff
Find a Regional HTC Coordinator
Update Contact Information
Find Treatment Centers
1. Search by one of the following choices:
To see a list of all treatment centers leave the choices blank.
Facility name
HTC ID number
City
UDC participation status
Region
State


BELIEVE
MBARD ST.
AFGHAN KABOB & CAFE
AFGHAN KABOB

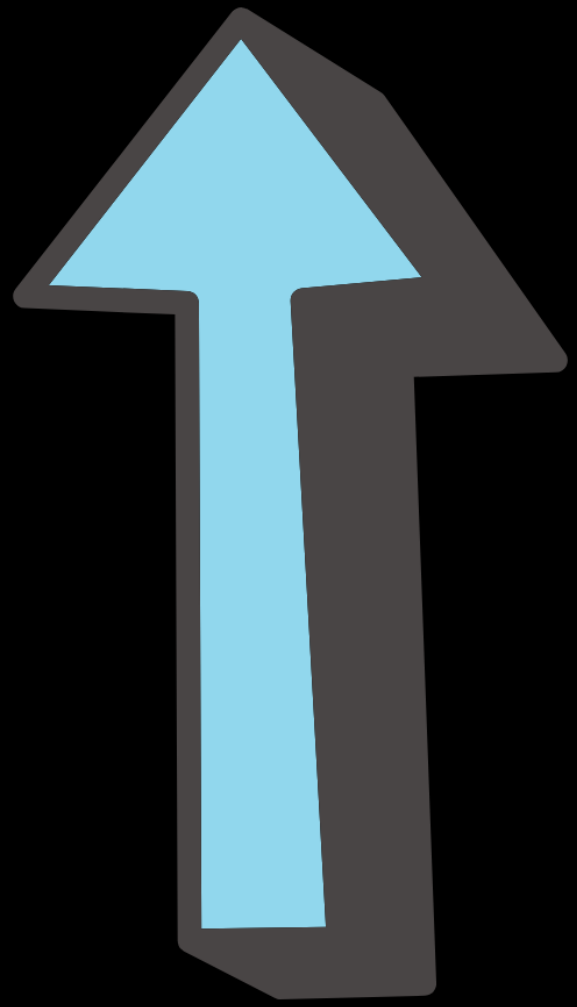
FACTOR FIRST!

REPLACE FACTORS WITH FACTORS WHENEVER POSSIBLE

USE WHAT THEY USE AT HOME

Factor Replacement	Plasma-derived factor 	Recombinant DNA factor 
Cost	✓	
Virus transmission safety		✓
Clotting safety		✓

1 UNIT/KG



2%

DOSE OF FACTOR VIII

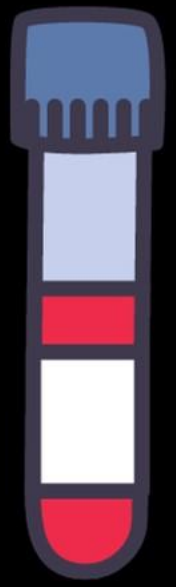
DESIRED PERCENT INCREASE

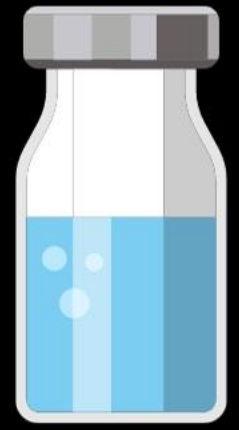
×

WEIGHT IN KG

2

BLEEDING RISK	DESIRED FACTOR VIII LEVEL %	INITIAL DOSE U/KG
MILD	5-10	12.5
MODERATE	20-30	25
SEVERE	50 OR >	50





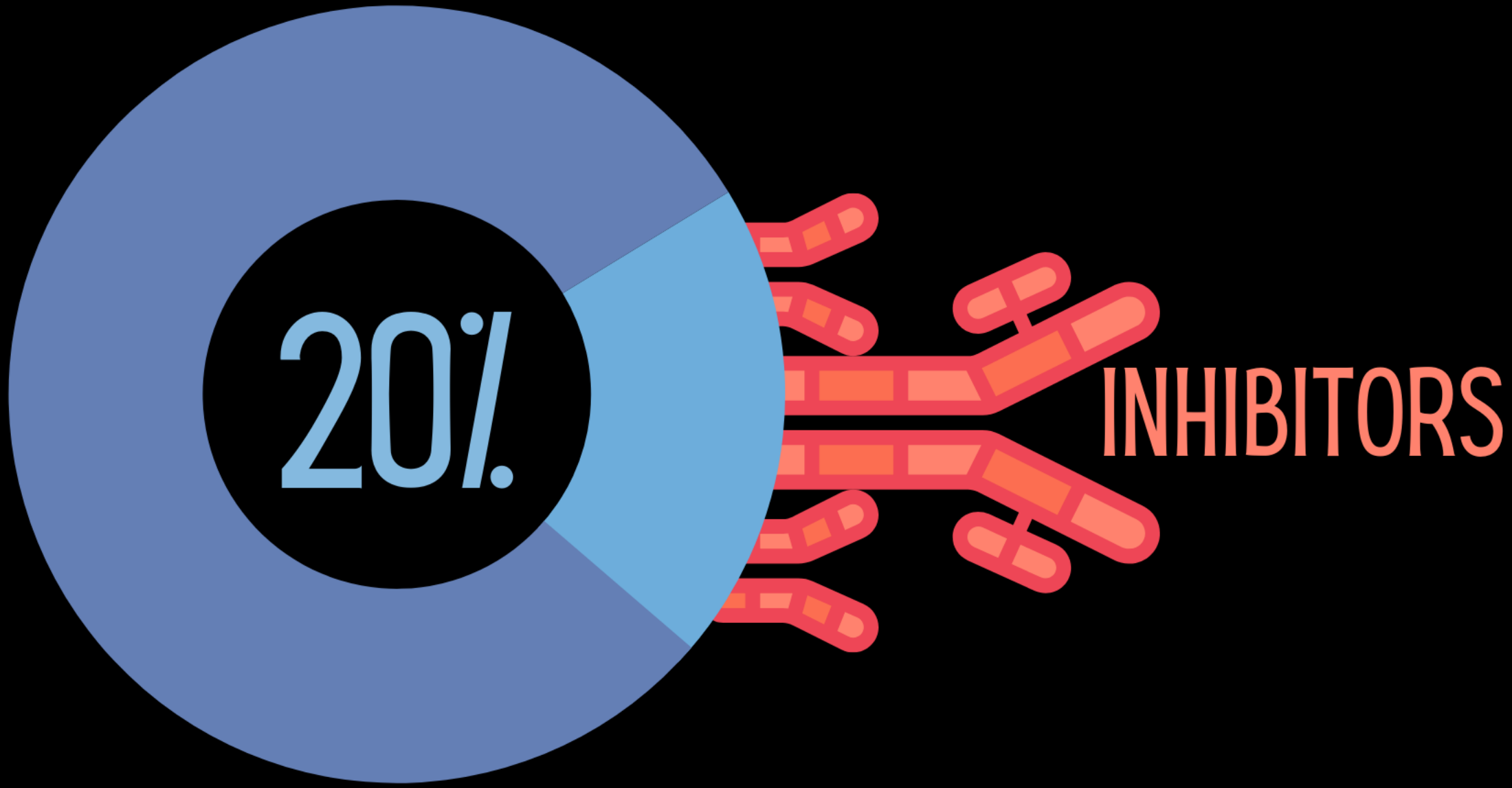
* IN AN EMERGENCY, ASSUME FACTOR LEVEL IS ZERO

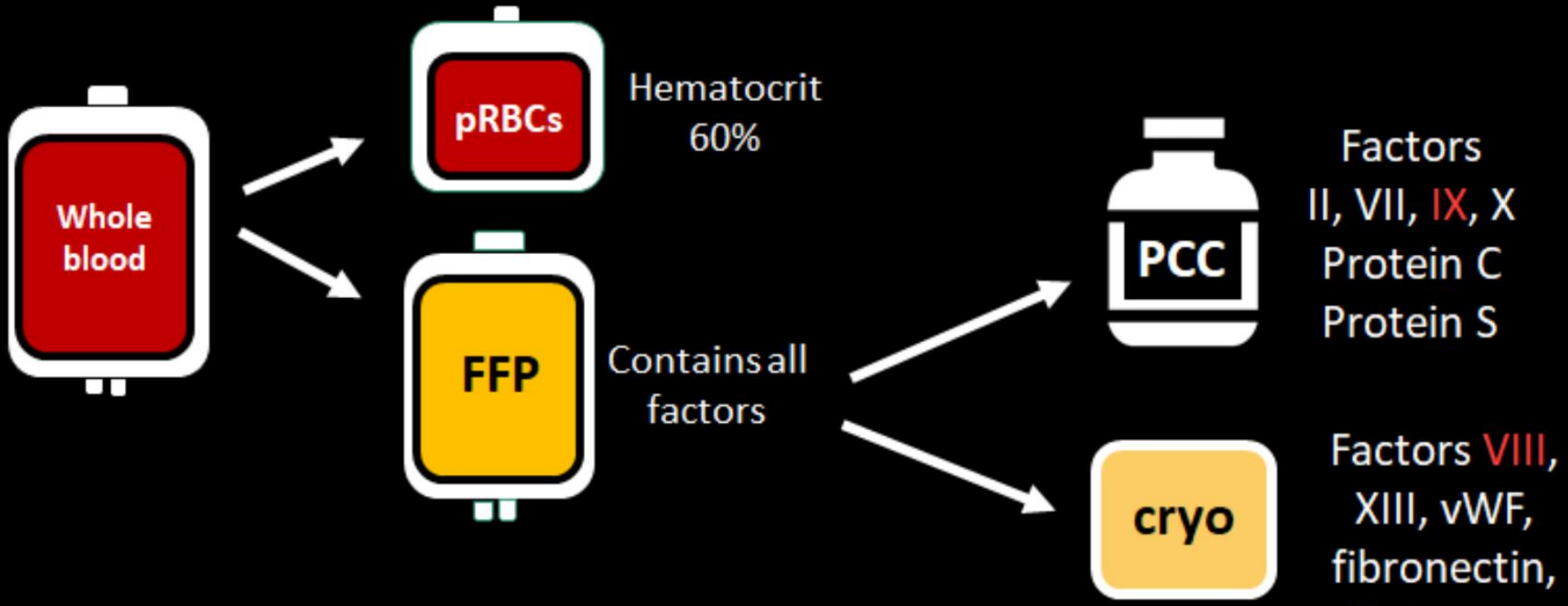
Site	Desired Factor Level %	Hemophilia A Initial dose U/kg	Hemophilia B Initial dose U/kg	Details
Deep skin	-	-	-	Topical thrombin and direct pressure
Deep muscle	40-80	20-40	40-60	Admit: compartment syndrome risk Duration of replacement 1-5 days
Hemarthrosis	30-50	15-25	30-40	Splint and consult ortho Duration of replacement 1-3 days
Epistaxis	40-50	20-25	80-100	Replace until bleeding stops
Oral mucosa	50	25	50	Remove ineffective clot Topical thrombin, TXA
Hematuria	50	25	50	Rest and hydration
GI bleeding	100	50	100	Consult GI for scope to localize source
CNS	100	50	100	Treat before CT Consult Neurosurgery early LP requires factor replacement

From *Tintinalli's Emergency Medicine*


CONSULT
HEMATOLOGY

MEASURE THE FACTOR LEVEL 15 MINUTES AFTER INFUSION


20%
INHIBITORS



WHAT'S IN A UNIT OF WHOLE BLOOD?

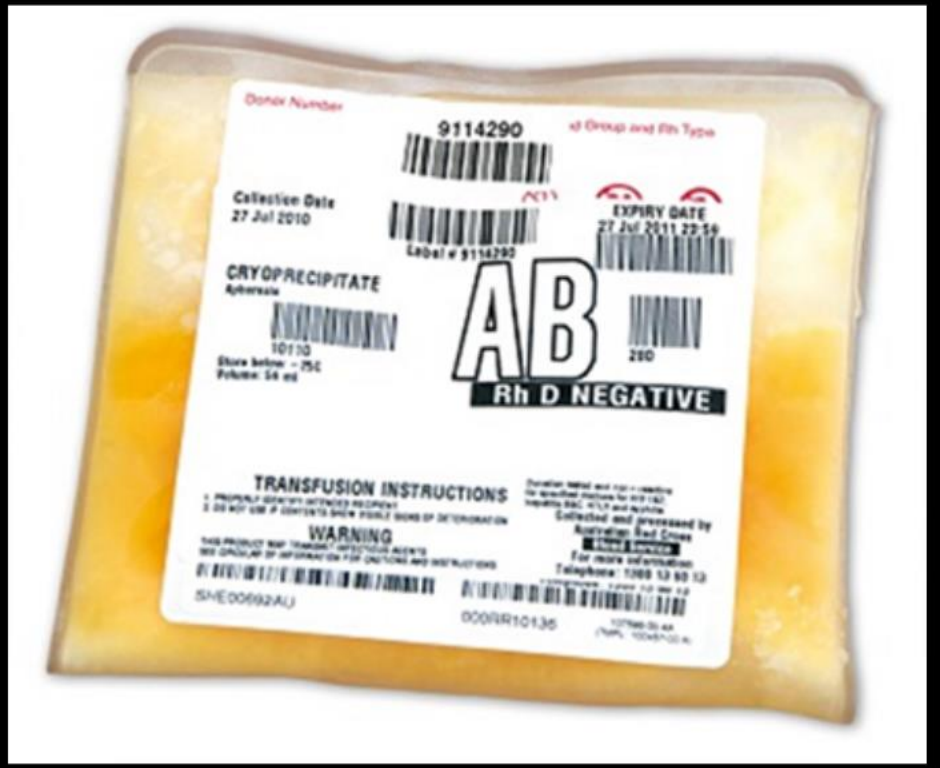
FRESH FROZEN PLASMA

1 CC = 1 UNIT OF ALL FACTORS

15-20 CC/KG

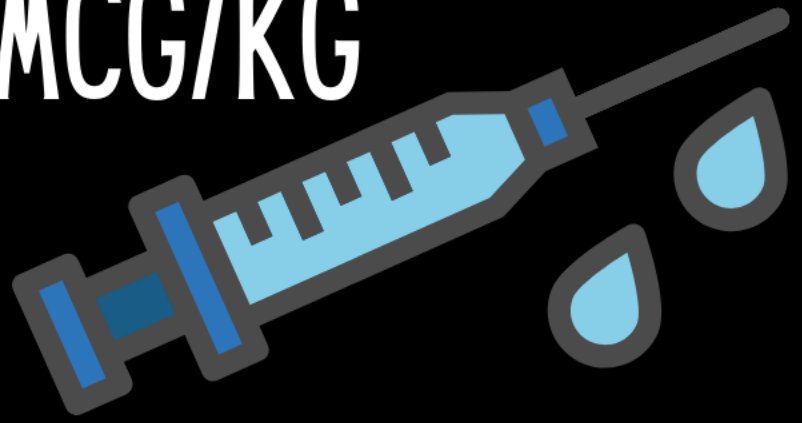
CRYOPRECIPITATE

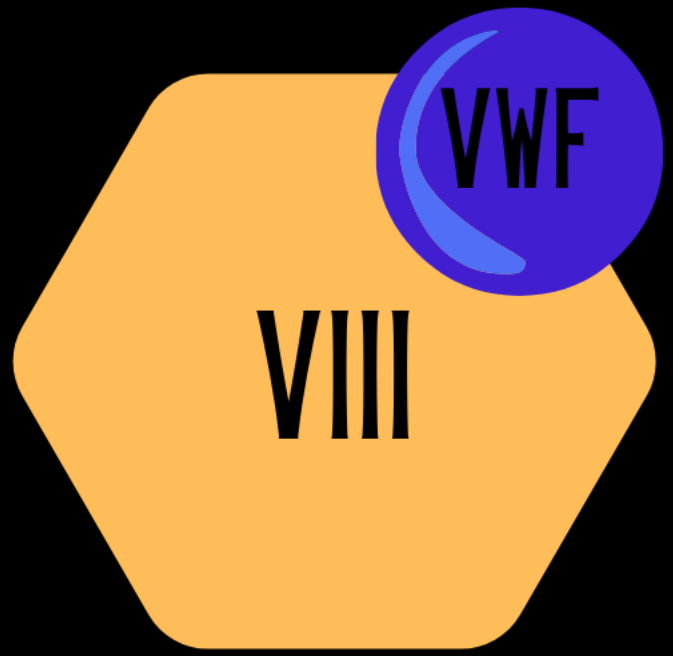
1 UNIT =
80 UNITS
FACTOR VIII

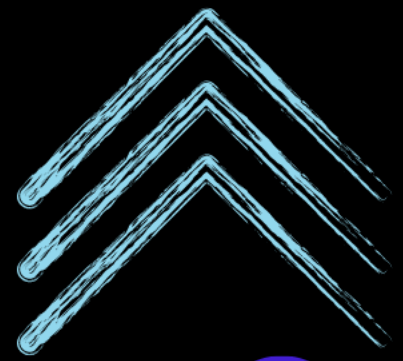


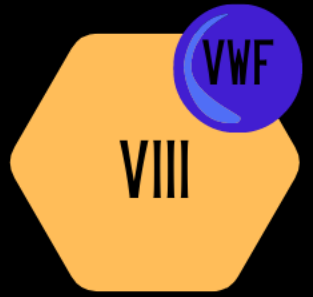
DESMOPRESSIN BOOSTS FACTOR VIII LEVELS

0.3
MCG/KG





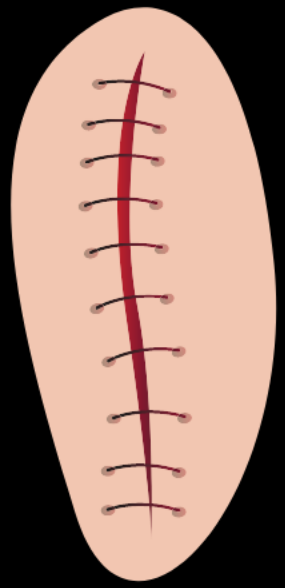


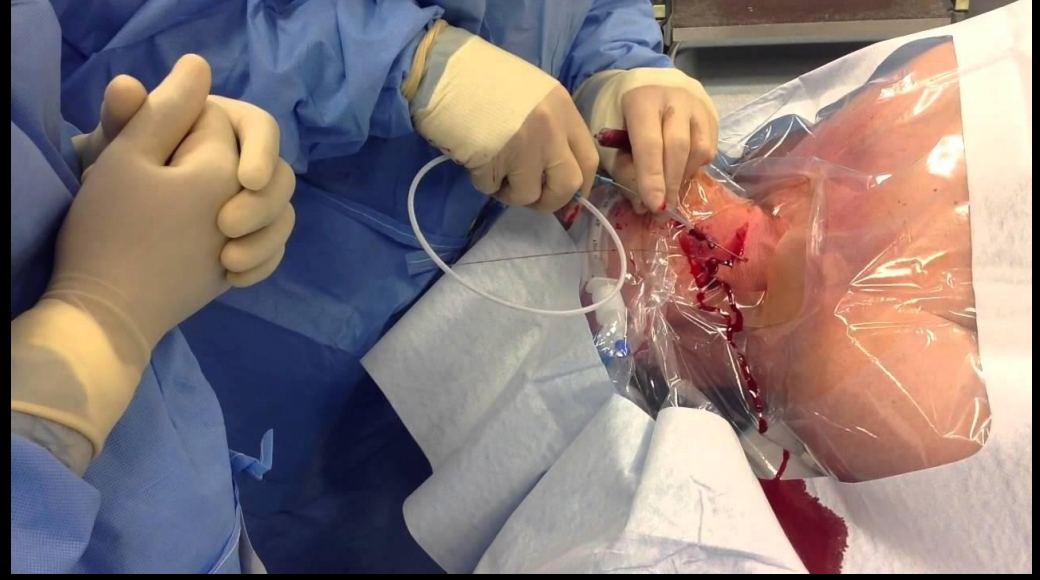


PROTHROMBIN COMPLEX CONCENTRATE

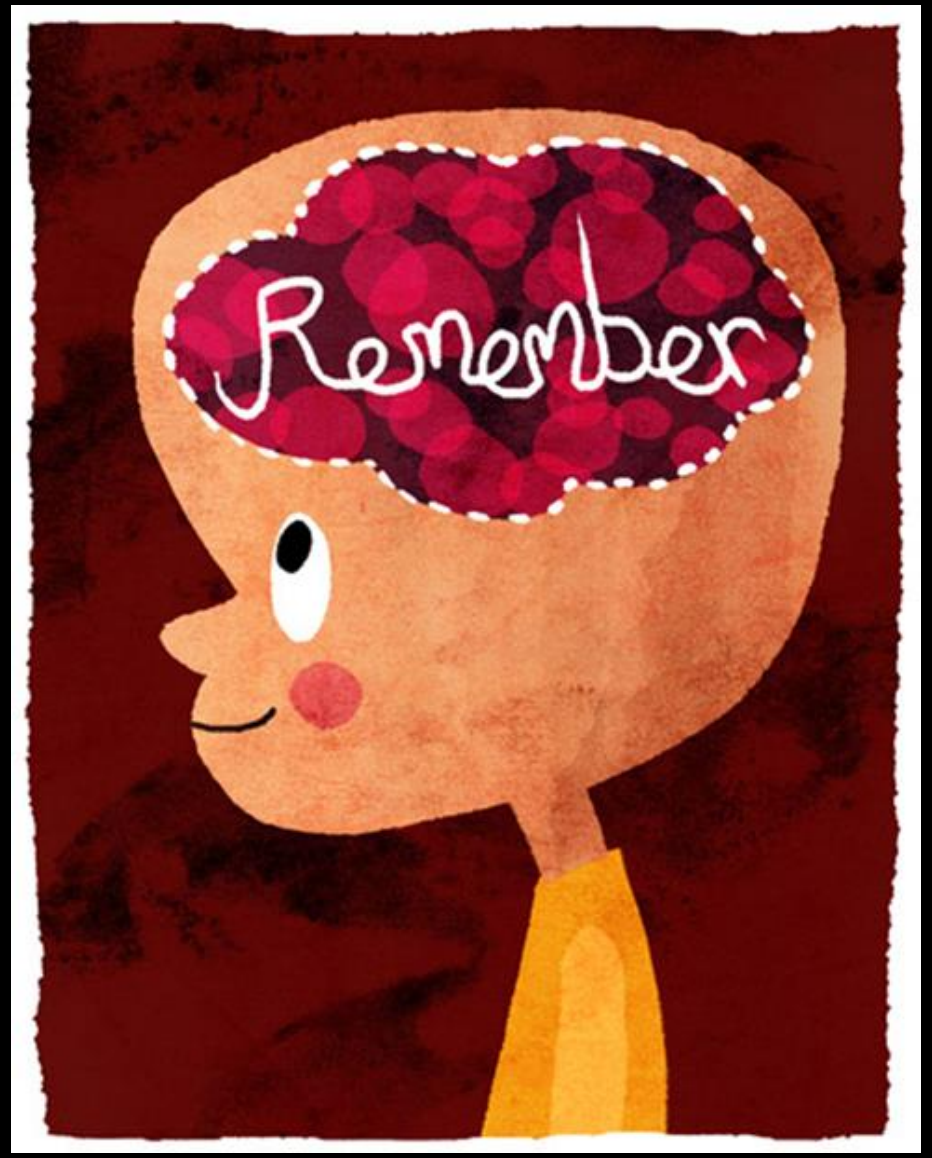
II VII IX X

ADMIT TO OBSERVE FOR DELAYED BLEEDING





GIVE FACTOR BEFORE PROCEDURES


Remember

B BELIEVE

L LOCATION (DEEP)

E EIGHT AND NINE

E EARLY FACTOR REPLACEMENT

D DELAYED BLEEDING

DISSEMINATED INTRAVASCULAR COAGULATION

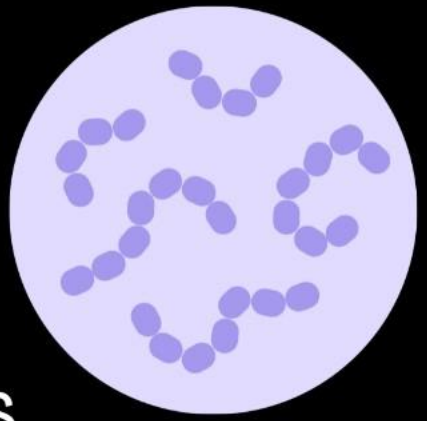
trigger

DISSEMINATED INTRAVASCULAR COAGULATION

obstetrical emergencies

widespread tissue injury

multisystem trauma



sepsis

severe liver disease

DISSEMINATED INTRAVASCULAR COAGULATION

trigger

DISSEMINATED INTRAVASCULAR COAGULATION

trigger

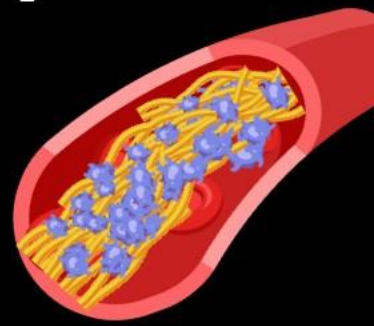
overactive coagulation cascade

DISSEMINATED INTRAVASCULAR COAGULATION

trigger

overactive coagulation cascade

excess fibrin deposited in vessels

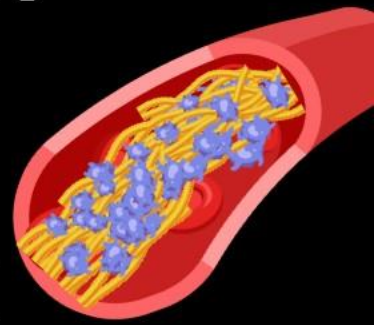


DISSEMINATED INTRAVASCULAR COAGULATION

trigger

overactive coagulation cascade

excess fibrin deposited in vessels



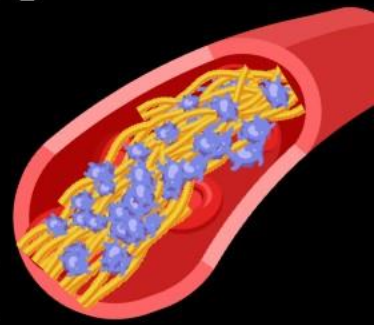
small vessel obstruction and tissue ischemia

DISSEMINATED INTRAVASCULAR COAGULATION

trigger

overactive coagulation cascade

excess fibrin deposited in vessels



small vessel obstruction and tissue ischemia

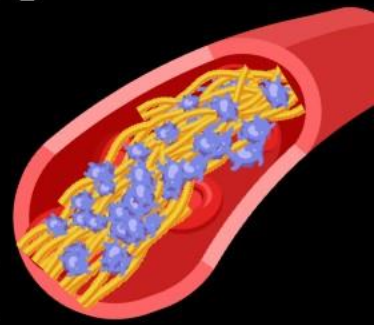
coagulation factors and platelets are depleted

DISSEMINATED INTRAVASCULAR COAGULATION

trigger

overactive coagulation cascade

excess fibrin deposited in vessels

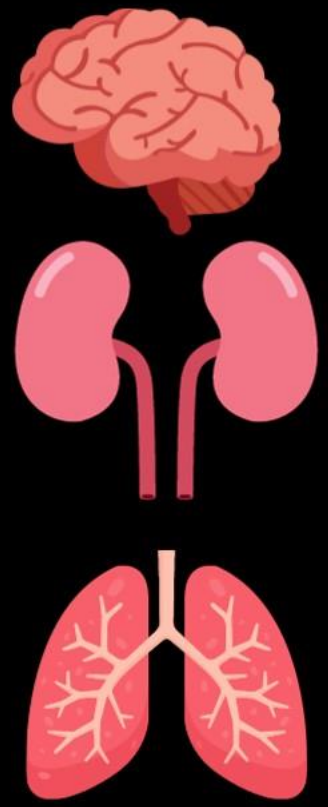


small vessel obstruction and tissue ischemia

coagulation factors and platelets are depleted

hemorrhage

DISSEMINATED INTRAVASCULAR COAGULATION



multiorgan failure

oozing from IV sites

GI bleeding

purpura

DISSEMINATED INTRAVASCULAR COAGULATION

microvascular thrombosis

consumptive coagulopathy

DISSEMINATED INTRAVASCULAR COAGULATION

DIAGNOSIS

schistocytes

fragmented RBCs

microvascular thrombosis

microangiopathic hemolyic anemia

factors
fibrinogen ↓

PT/INR
PTT ↑

The PTT pathway

XII

XI

IX

VIII

The PT pathway

VII

V

X

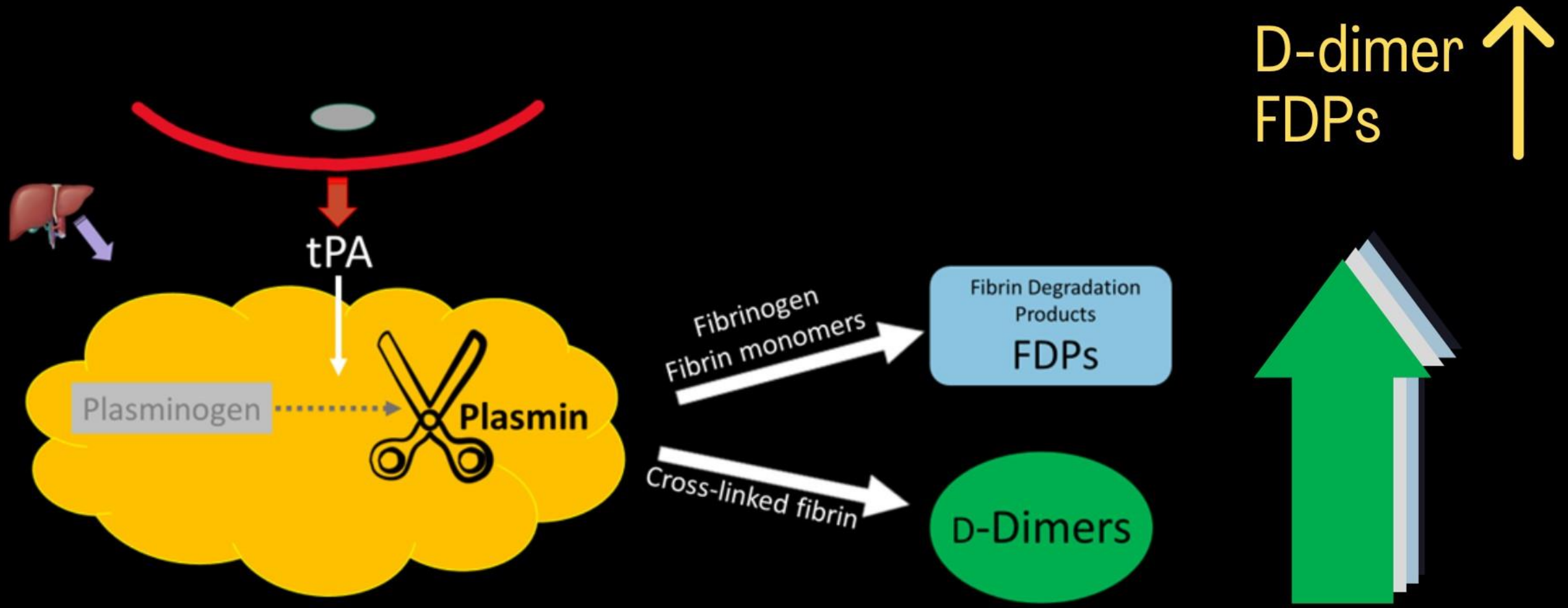
ProTHROMBIN (II)

THROMBIN (IIa)

IIa

Fibrinogen (I)

FIBRIN (Ia)


D-dimer
FDPs
tPA
Plasminogen
Plasmin
Fibrinogen
Fibrin monomers
Fibrin Degradation Products
FDPs
Cross-linked fibrin
D-Dimers

DISSEMINATED INTRAVASCULAR COAGULATION

LAB	RESULT
peripheral blood smear	schistocytes
platelets	low
PT, PT, INR	prolonged
fibrinogen	low
D-dimer/fibrin split products	high

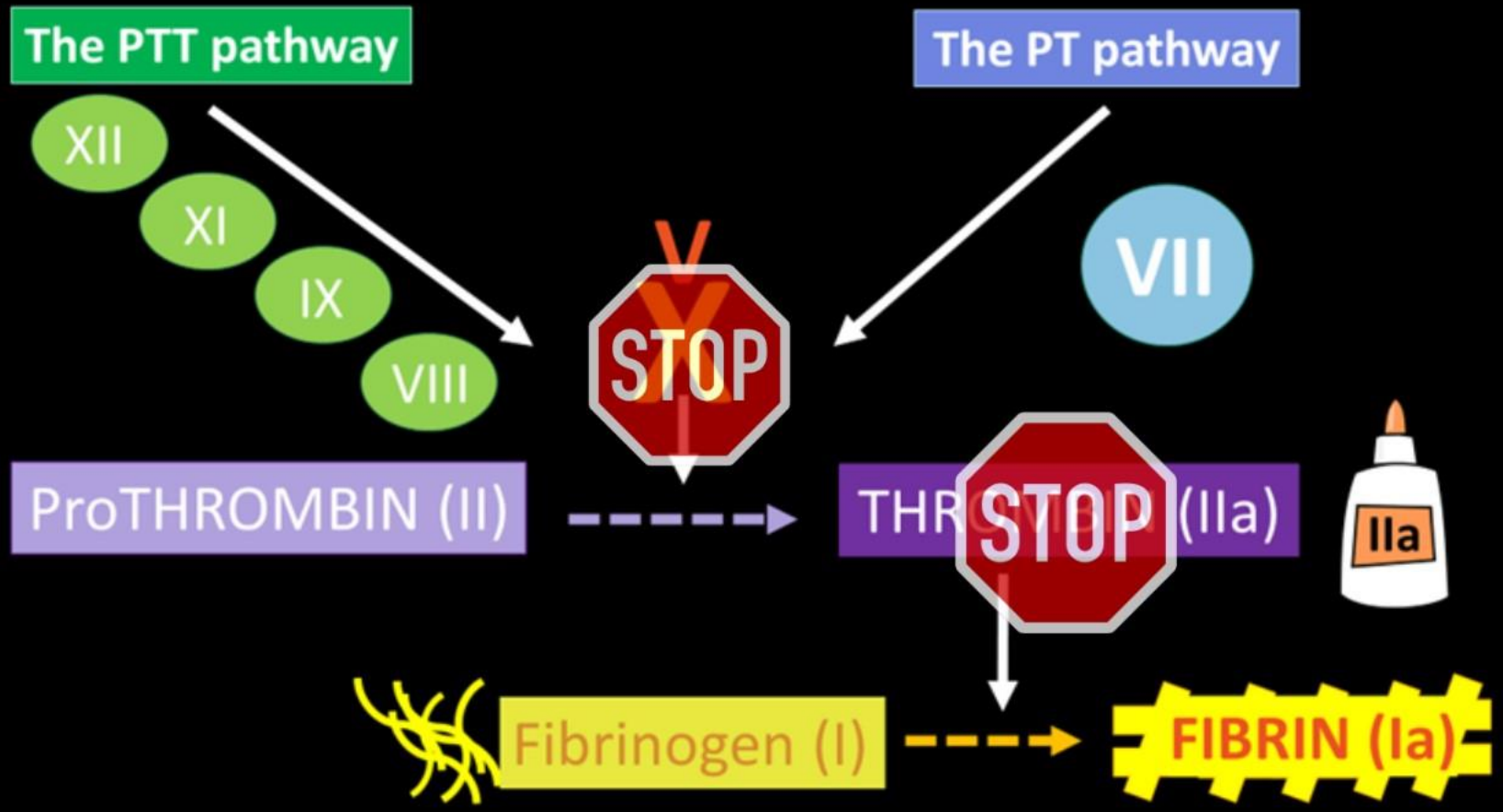
ANTICOAGULANTS

HEPARINS
UFH
LMWH

WARFARIN

DOACS

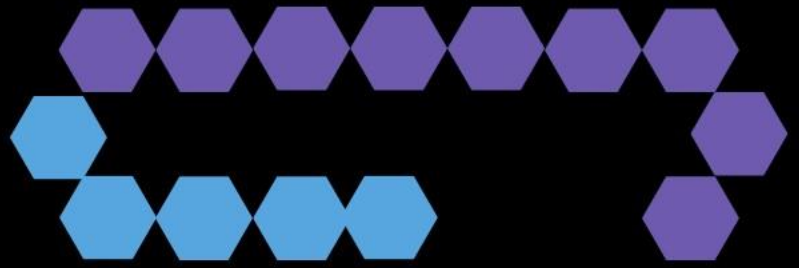
HEPARIN


The PTT pathway
XII
XI
IX
VIII
The PT pathway
VII
STOP
ProTHROMBIN (II)
THR
STOP
(IIa)
IIa
Fibrinogen (I)
FIBRIN (Ia)

UNFRACTIONATED HEPARIN

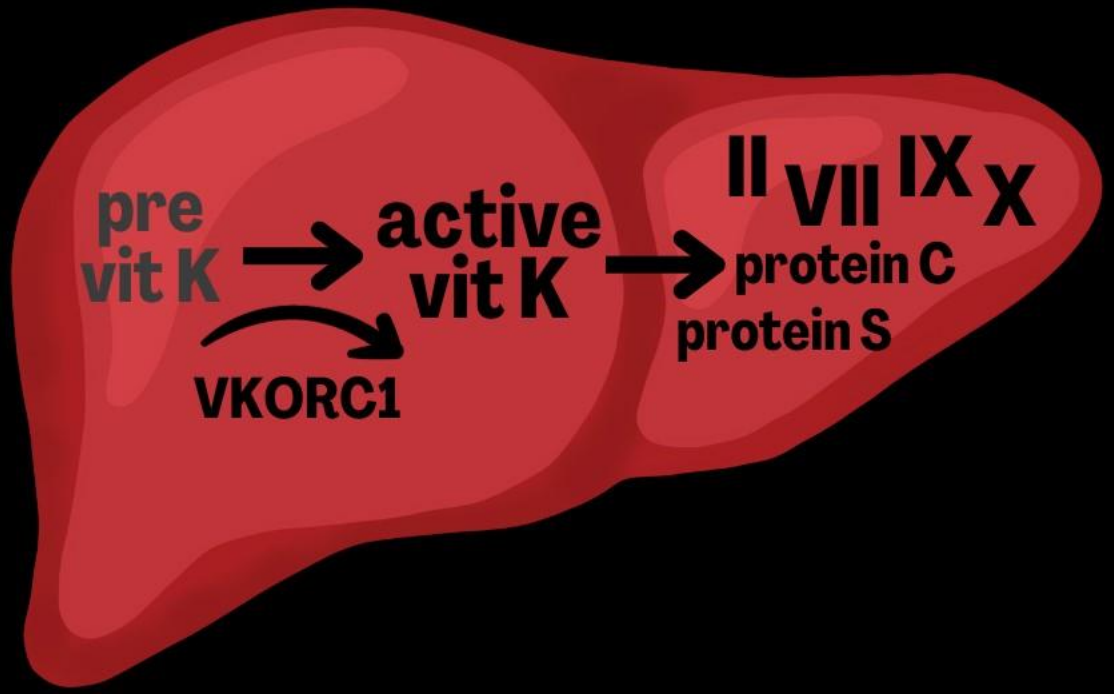
- best when GFR is low
- can stop quickly for procedures

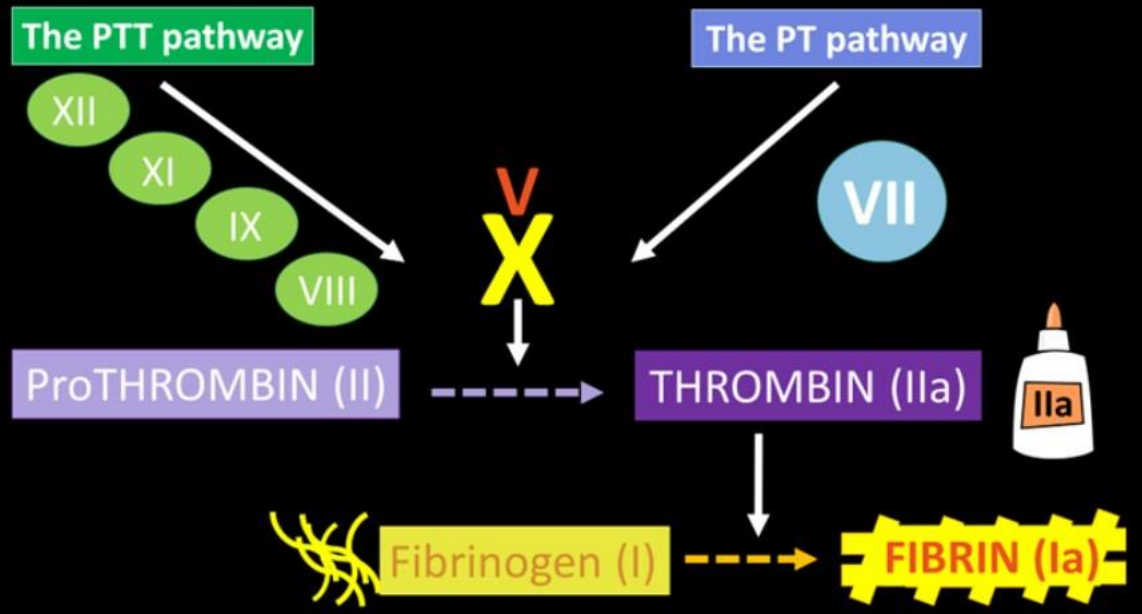
LOW MOLECULAR WEIGHT HEPARIN



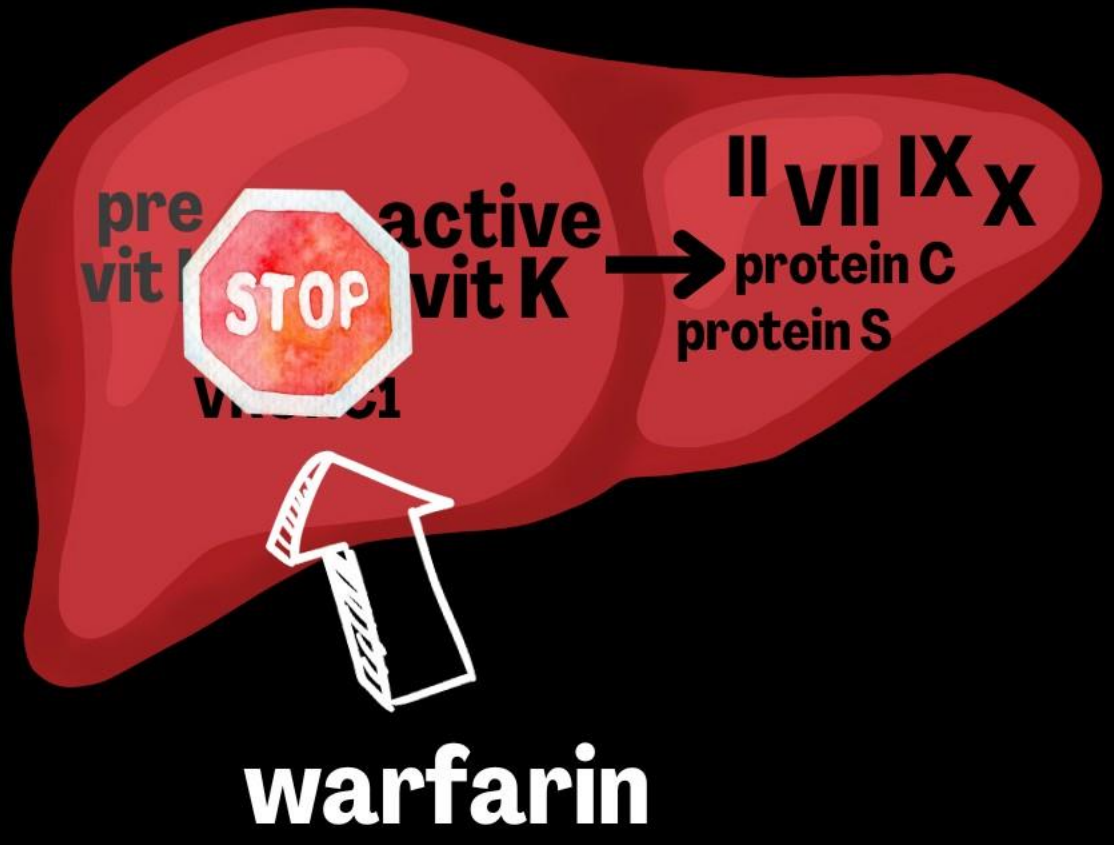
- no IV infusion
- no PTT monitoring
- less risk of bleeding
- lower risk of HIT

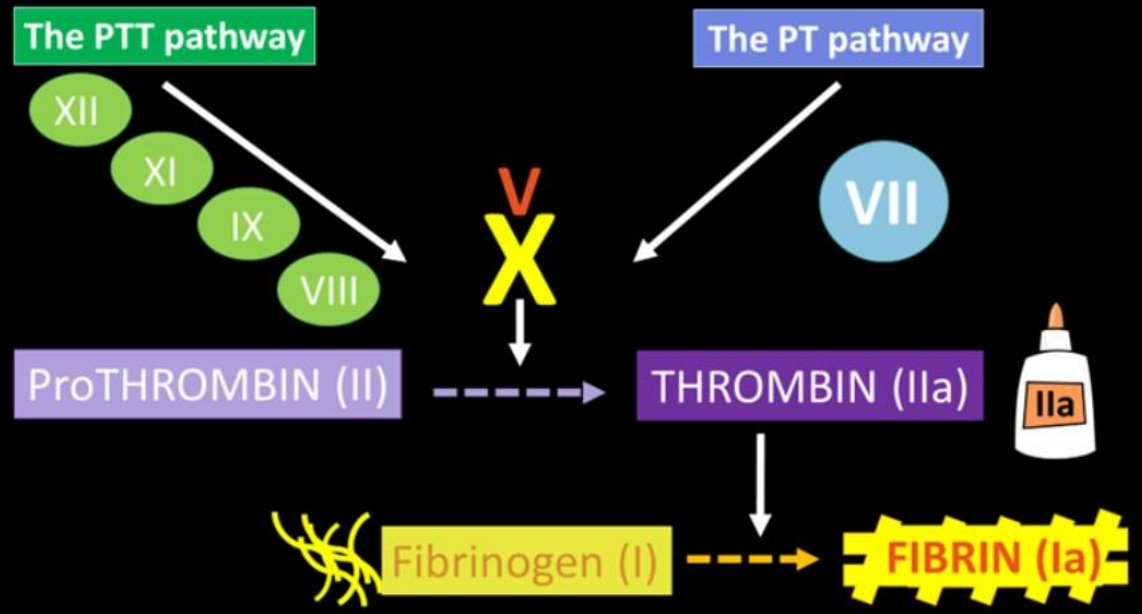
WARFARIN


pre
vit K
active
vit K
VKORC1
II VII IX X
protein C
protein S

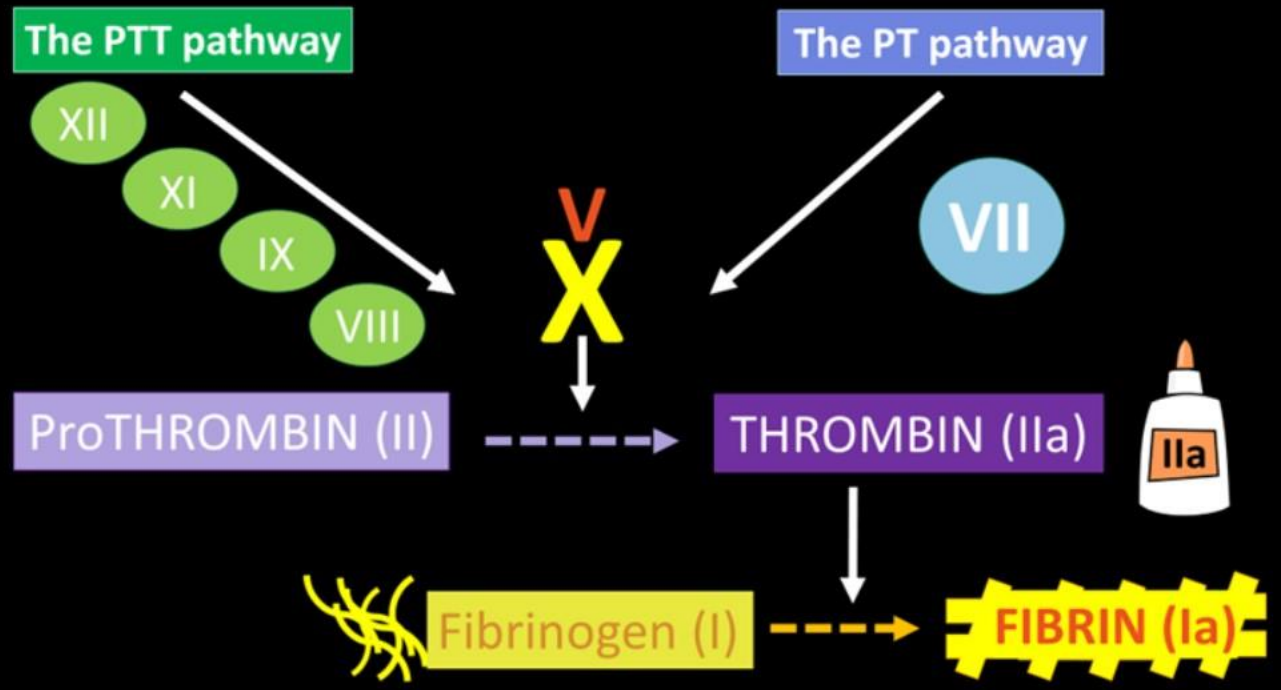

The PTT pathway
The PT pathway
XII
XI
IX
VIII
V
X
VII
ProTHROMBIN (II)
THROMBIN (IIa)
IIa
Fibrinogen (I)
FIBRIN (Ia)

WARFARIN


pre
active
vit K
STOP
II VII IX X
protein C
protein S
warfarin


The PTT pathway
The PT pathway
XII
XI
IX
VIII
V
X
VII
ProTHROMBIN (II)
THROMBIN (IIa)
IIa
Fibrinogen (I)
FIBRIN (Ia)

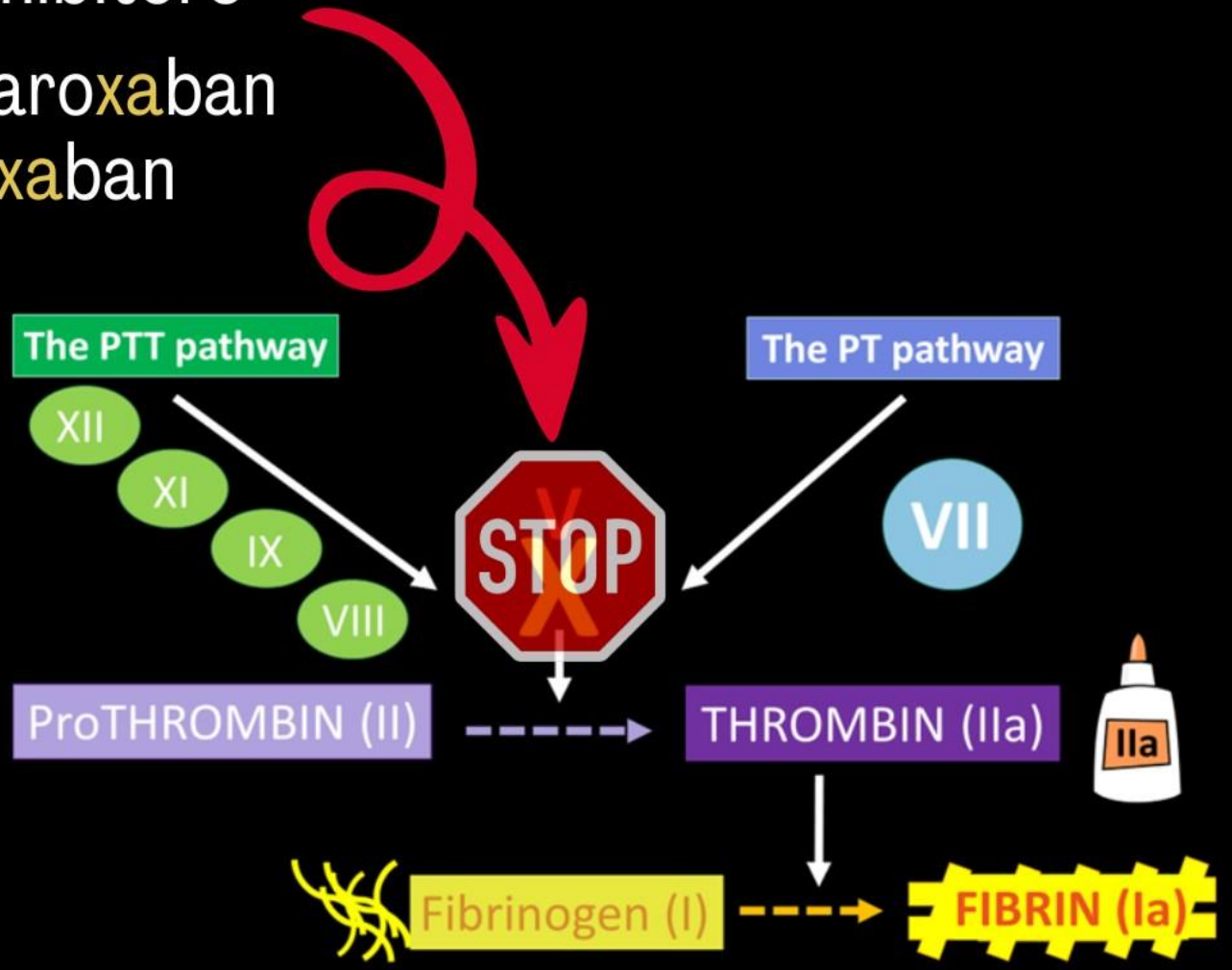
DIRECT-ACTING ORAL ANTICOAGULANTS



DIRECT-ACTING ORAL ANTICOAGULANTS

Factor Xa inhibitors

Rivaroxaban
Apixaban



DIRECT-ACTING ORAL ANTICOAGULANTS

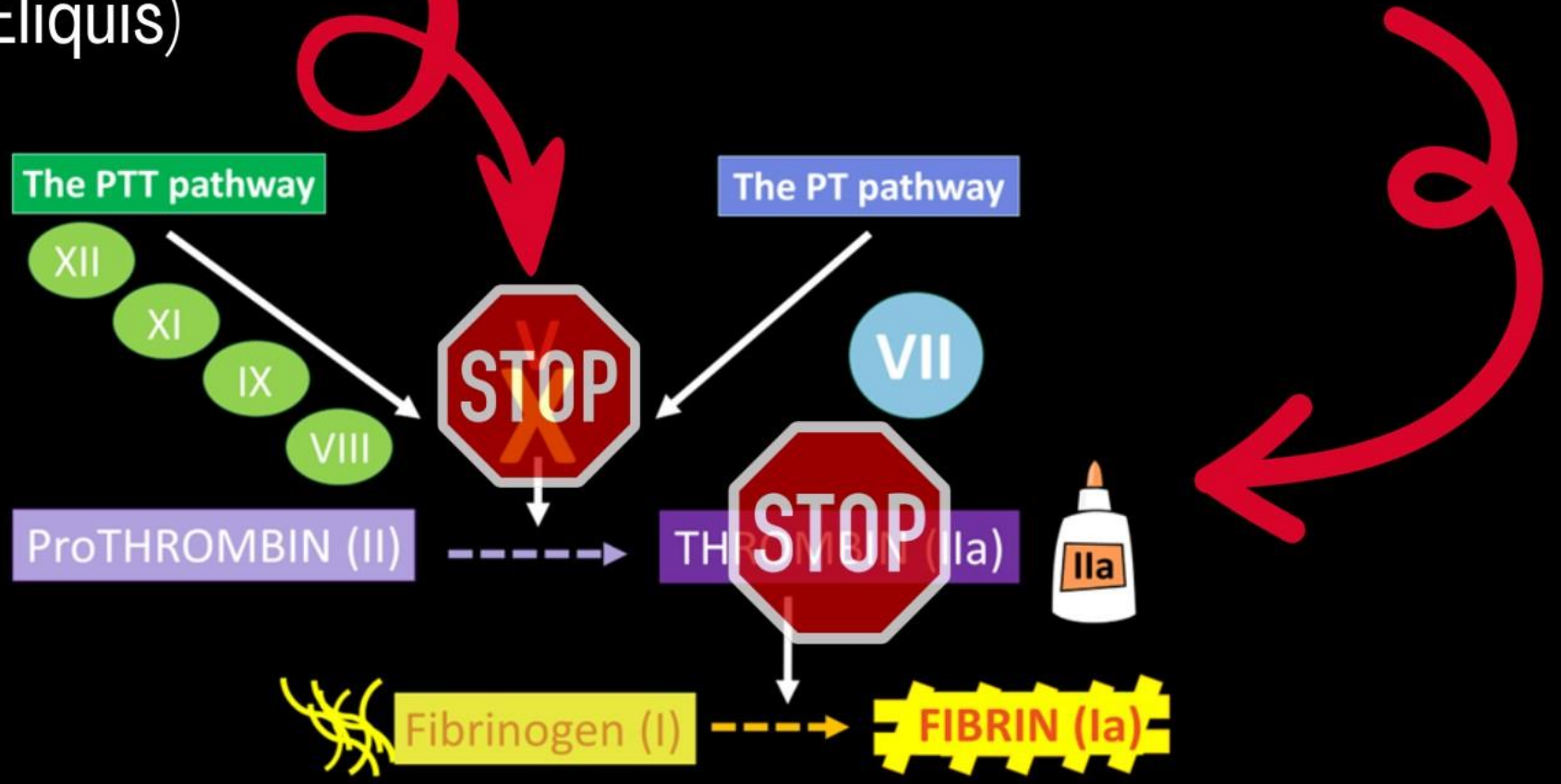
Factor Xa inhibitors

Rivaroxaban (Xarelto)

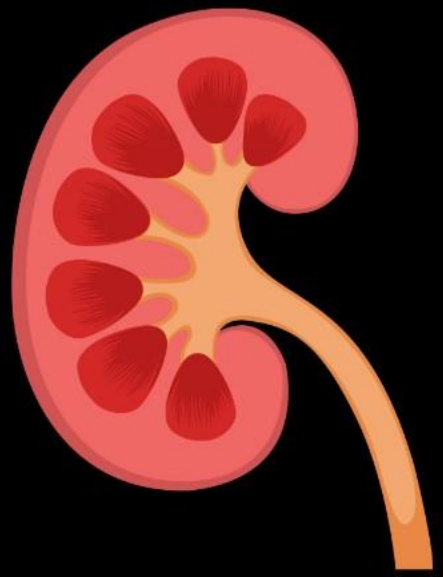
Apixaban (Eliquis)

Direct thrombin inhibitors

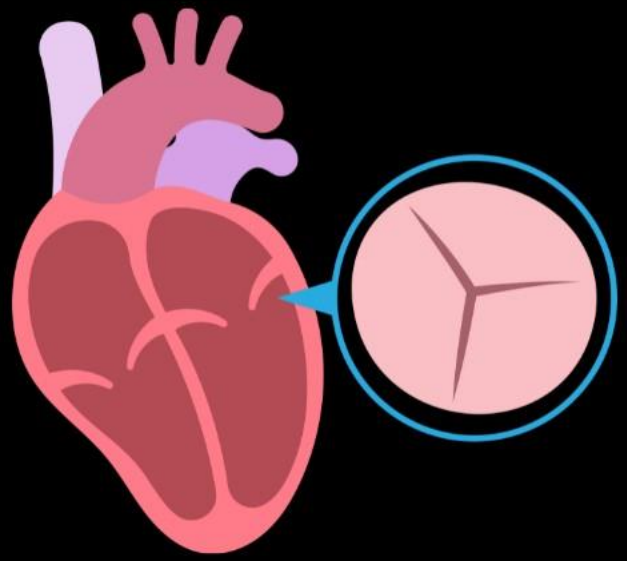
Dabigatran (Pradaxa)



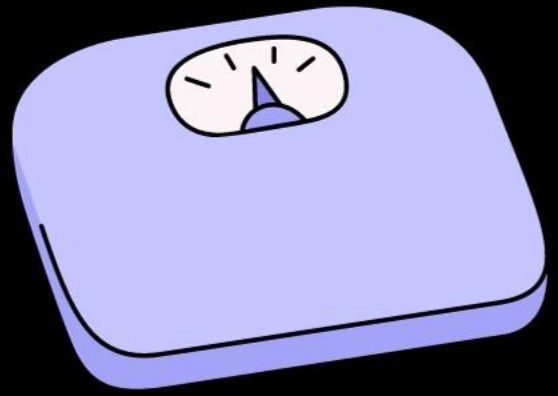
DON'T USE DOACS IN:



kidney disease



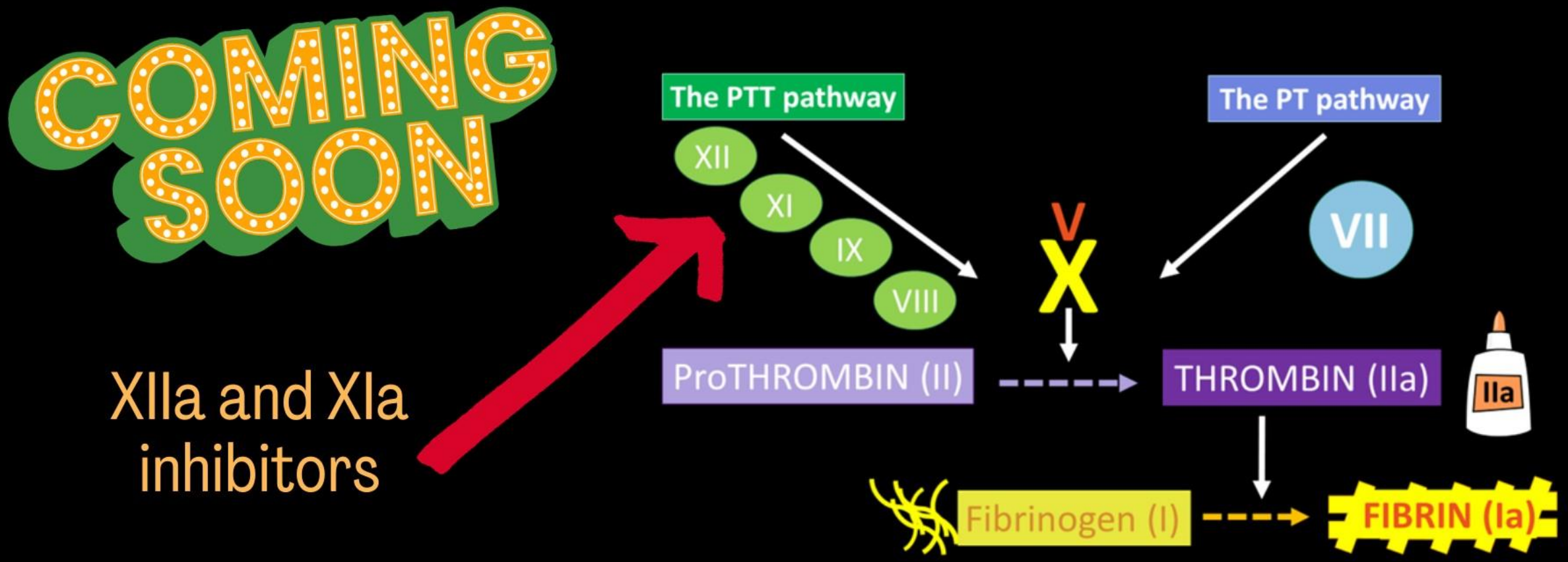
mechanical valve
or native valve disease



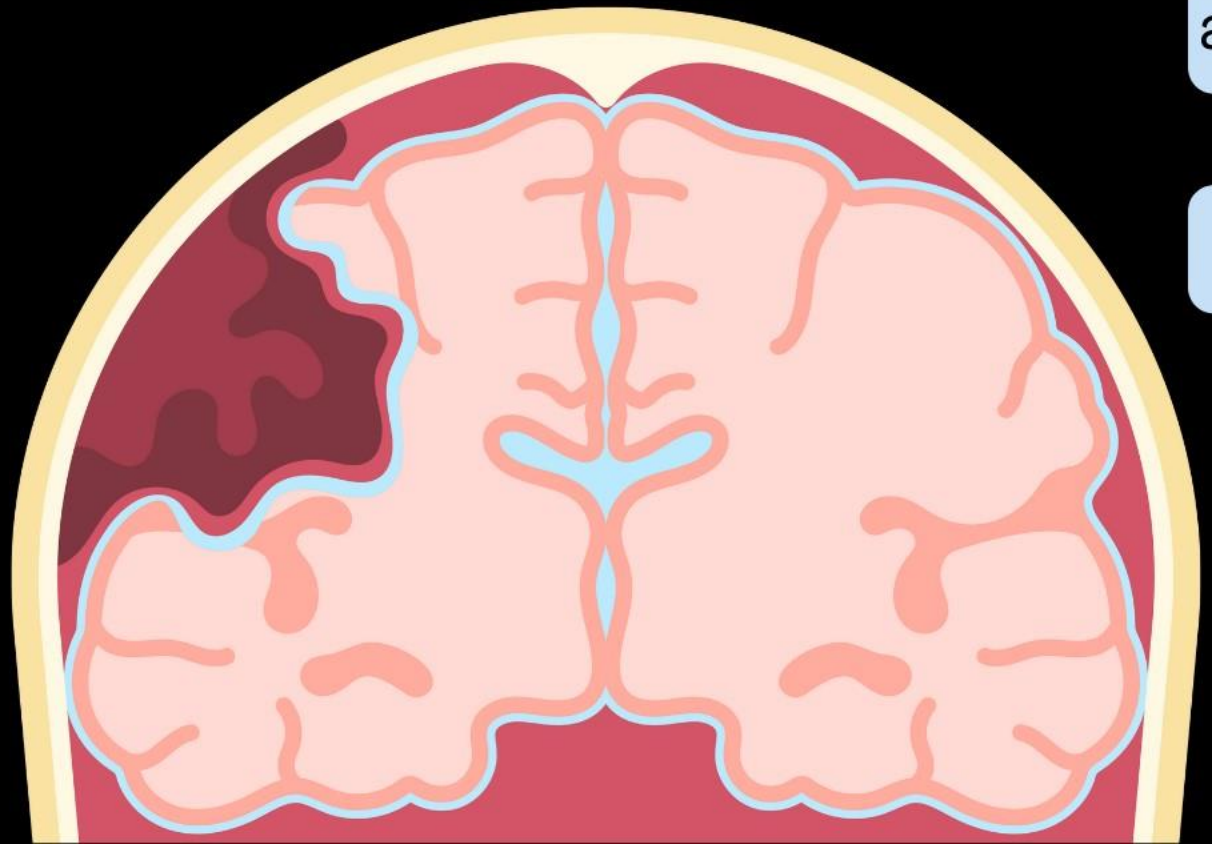
BMI > 70*

BMI > 40 for
dabigatran

DIRECT-ACTING ORAL ANTICOAGULANTS

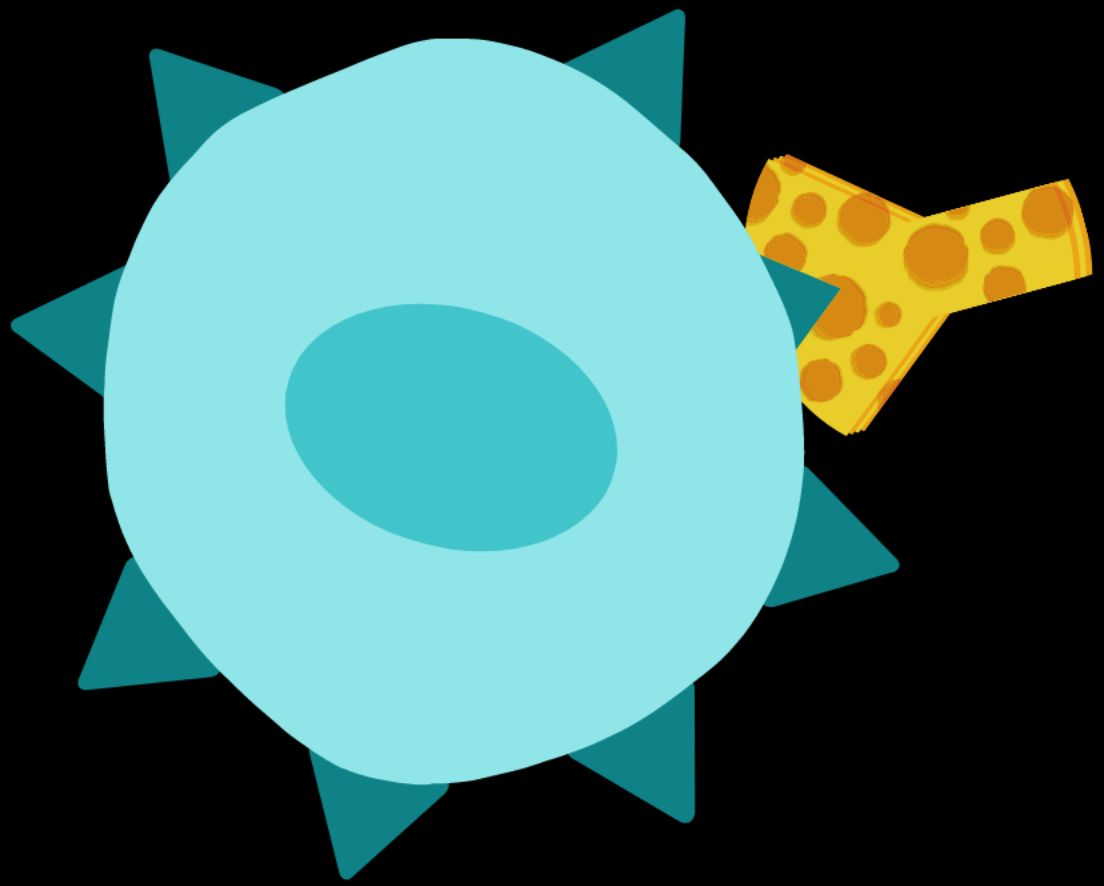


REVERSAL



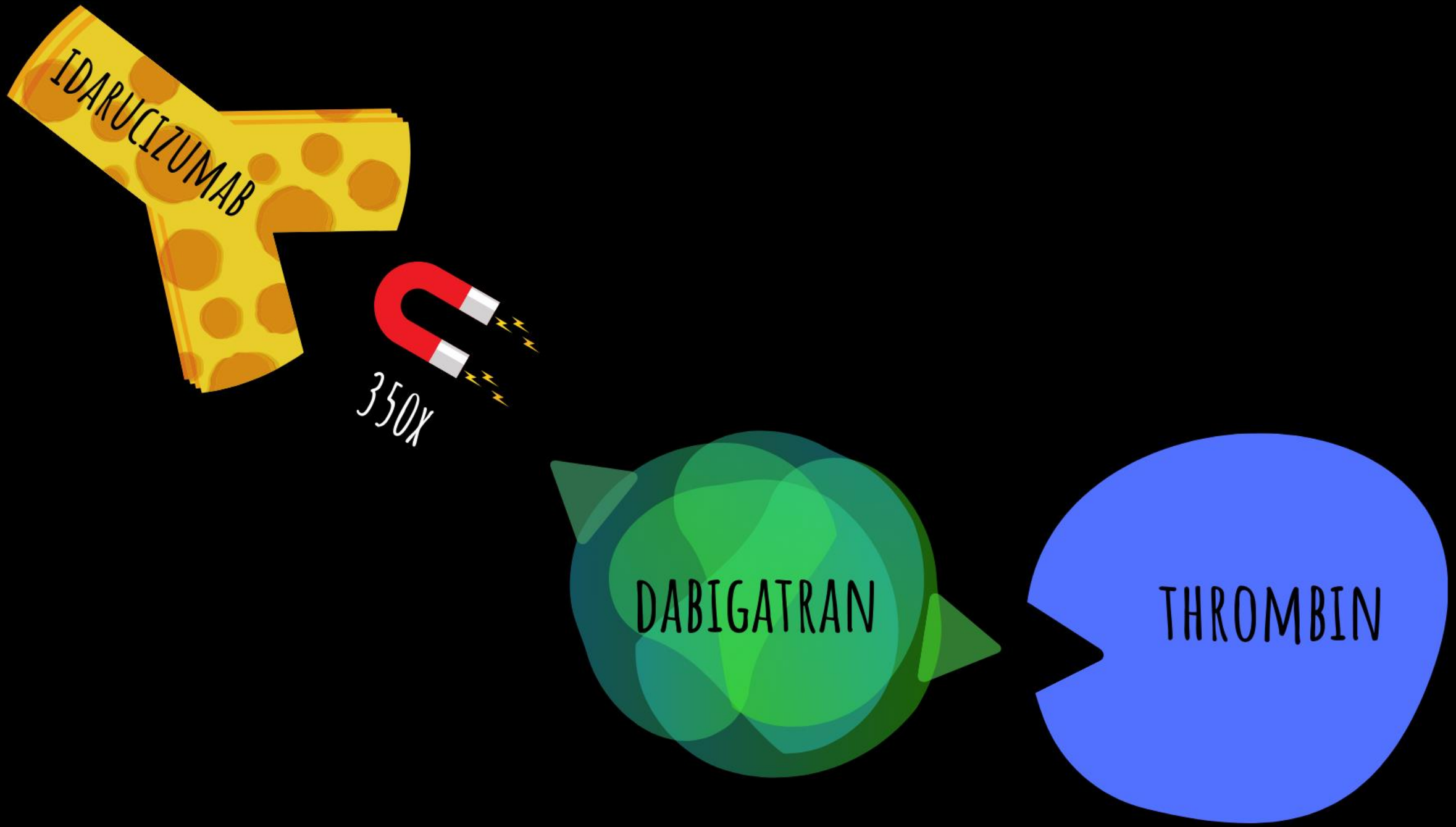
heparin	protamine
warfarin	vitamin K
apixaban/rivaroxaban	andexanet alfa
dabigatran	idarucizumab

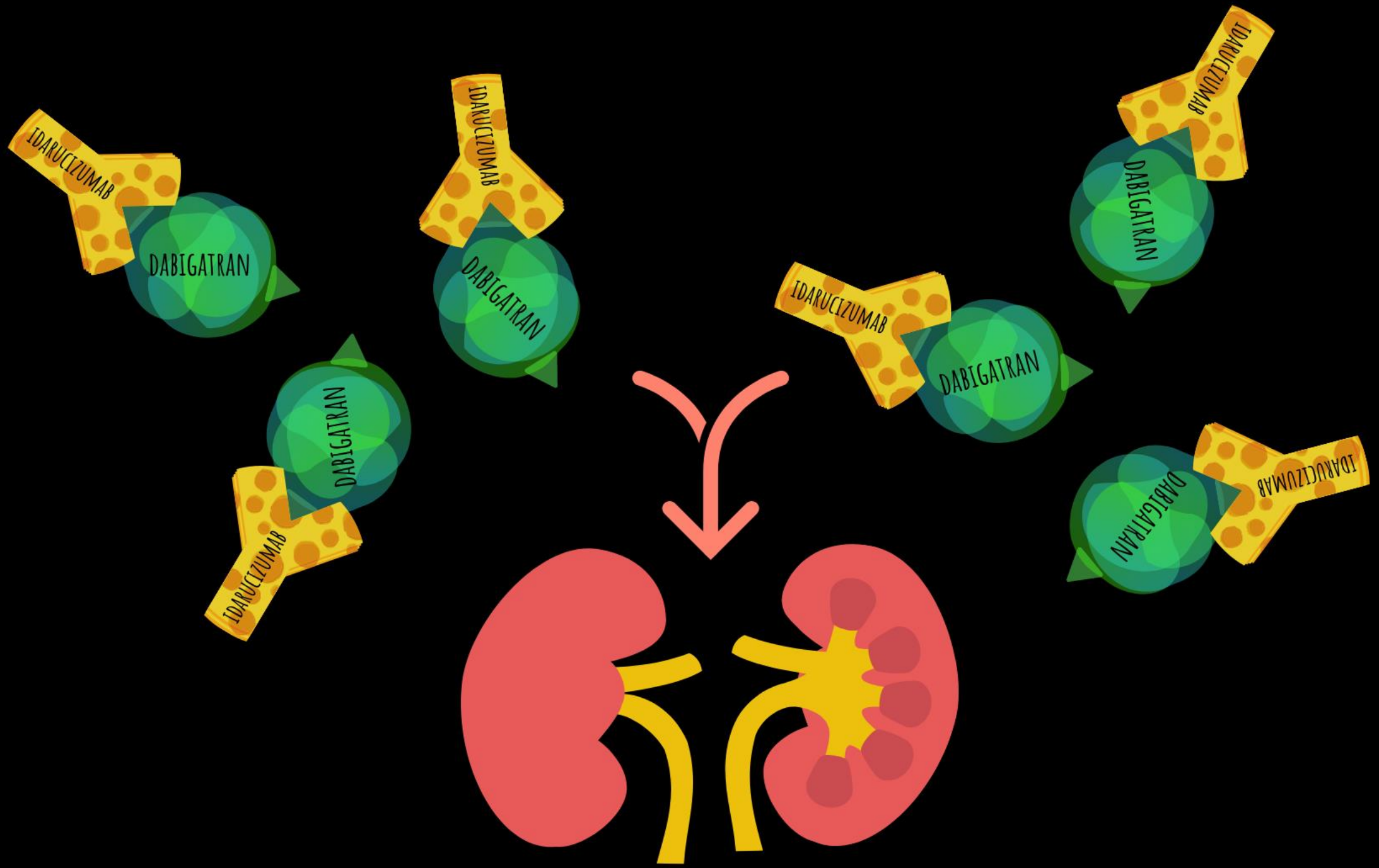
IDARUCIZUMAB

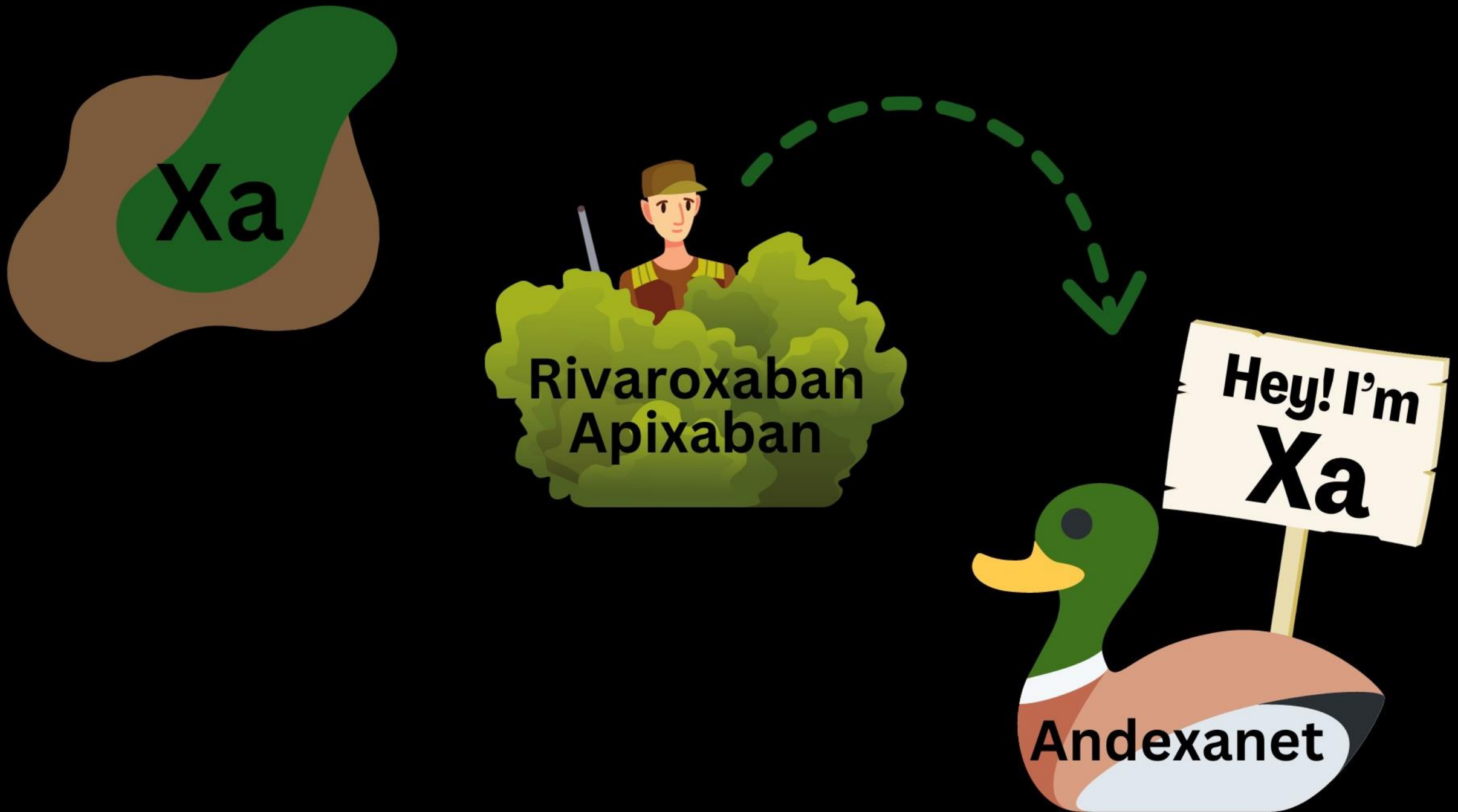


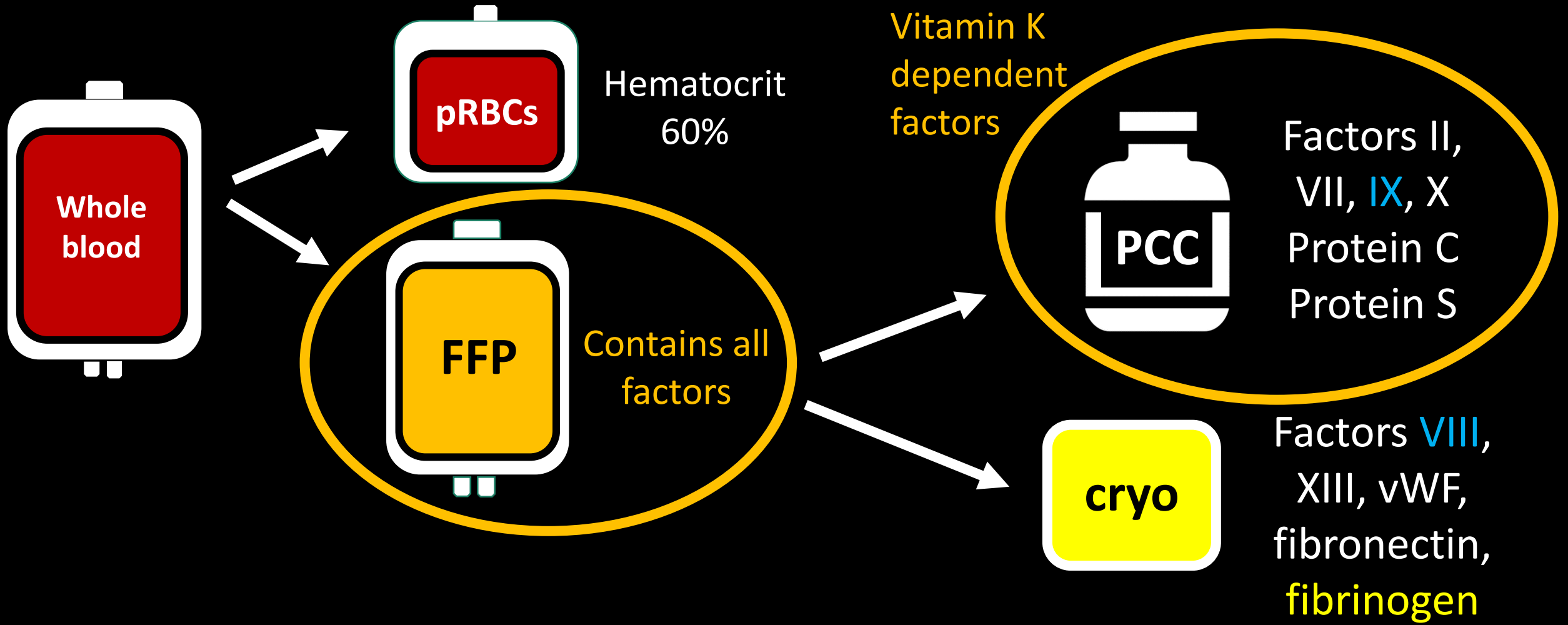
MONOCLONAL ANTIBODY

MADE IN THE LAB TO BIND TO A SINGLE SUBSTANCE


IDARUCIZUMAB
350X
DABIGATRAN
THROMBIN


IDARUCIZUMAB
DABIGATRAN
IDARUCIZUMAB
DABIGATRAN
IDARUCIZUMAB
DABIGATRAN
IDARUCIZUMAB
DABIGATRAN
IDARUCIZUMAB
DABIGATRAN
IDARUCIZUMAB
DABIGATRAN


Xa
Rivaroxaban
Apixaban
Hey! I'm
Xa
Andexanet

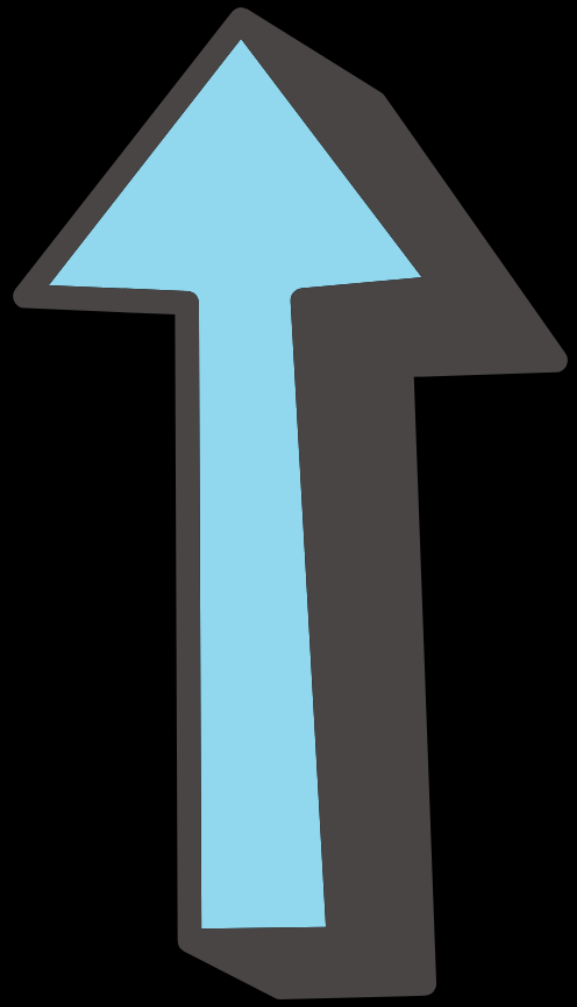


Which blood products would replace affected factors?

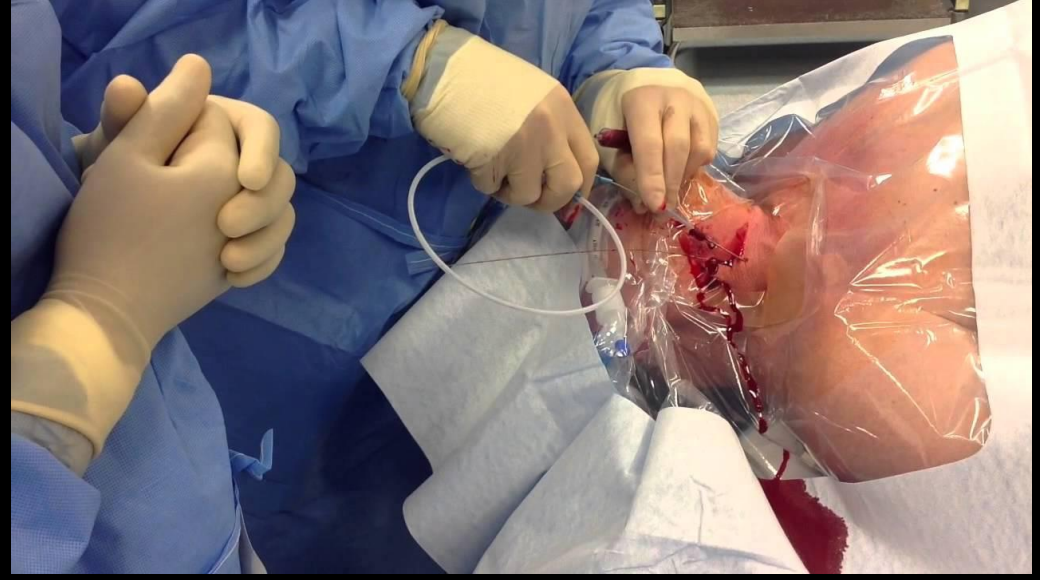
IN SUMMARY...

FACTOR FIRST!

1 UNIT/KG



2%



GIVE FACTOR BEFORE PROCEDURES

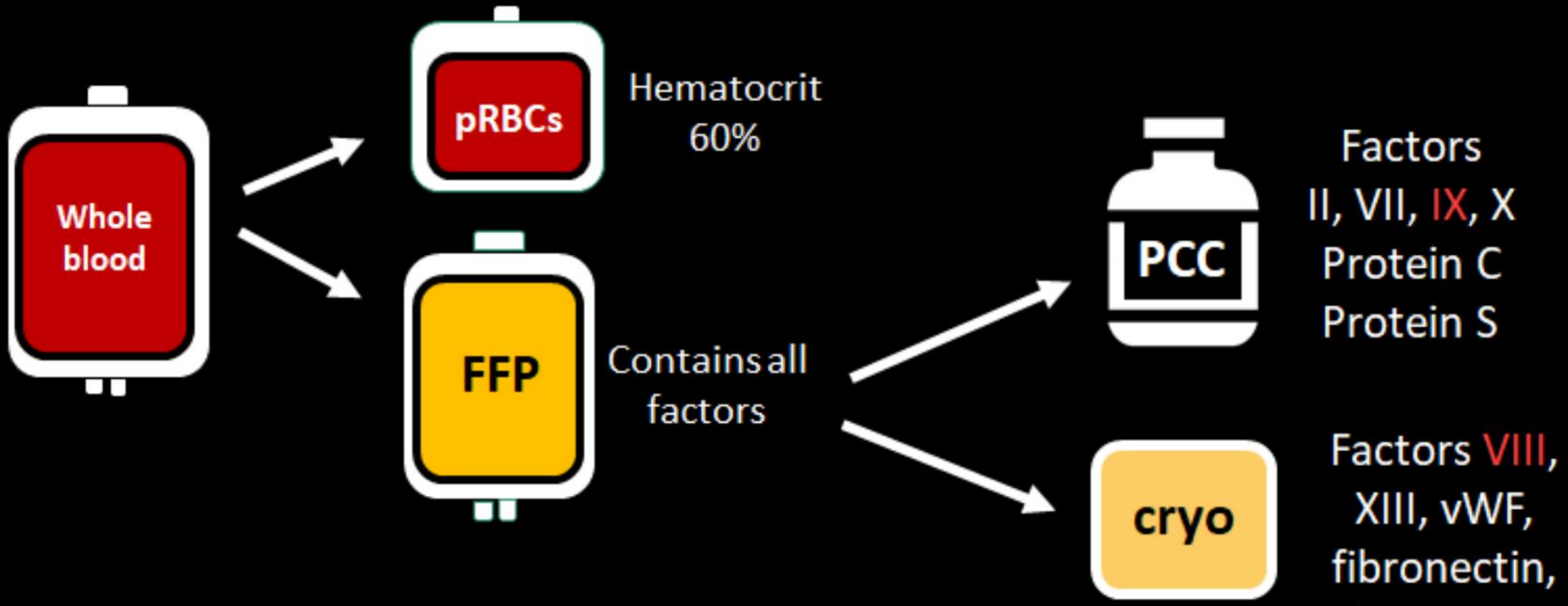
B BELIEVE

L LOCATION (DEEP)

E EIGHT AND NINE

E EARLY FACTOR REPLACEMENT

D DELAYED BLEEDING



WHAT'S IN A UNIT OF WHOLE BLOOD?

QUESTIONS?

Once I became a parent I finally understood the scene where Yoda gets so tired of answering Luke's questions he just dies.