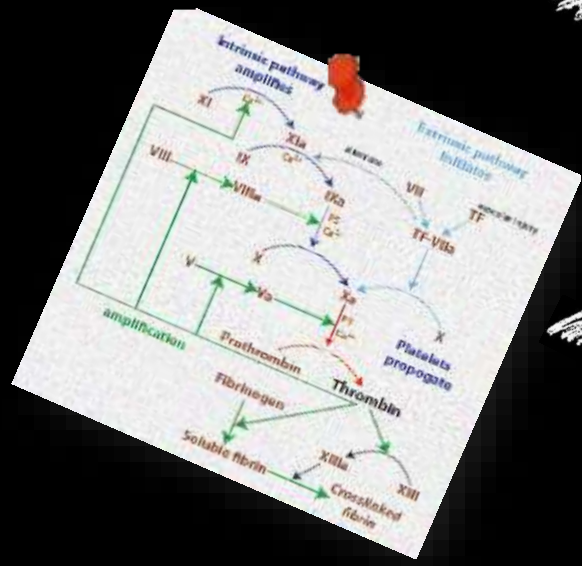
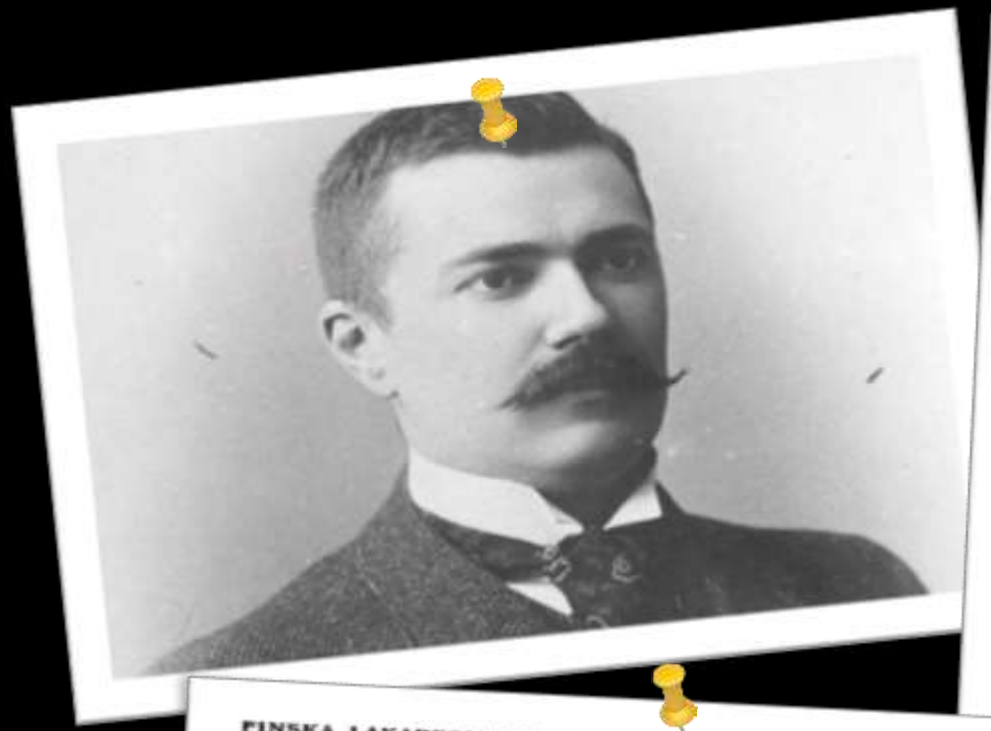
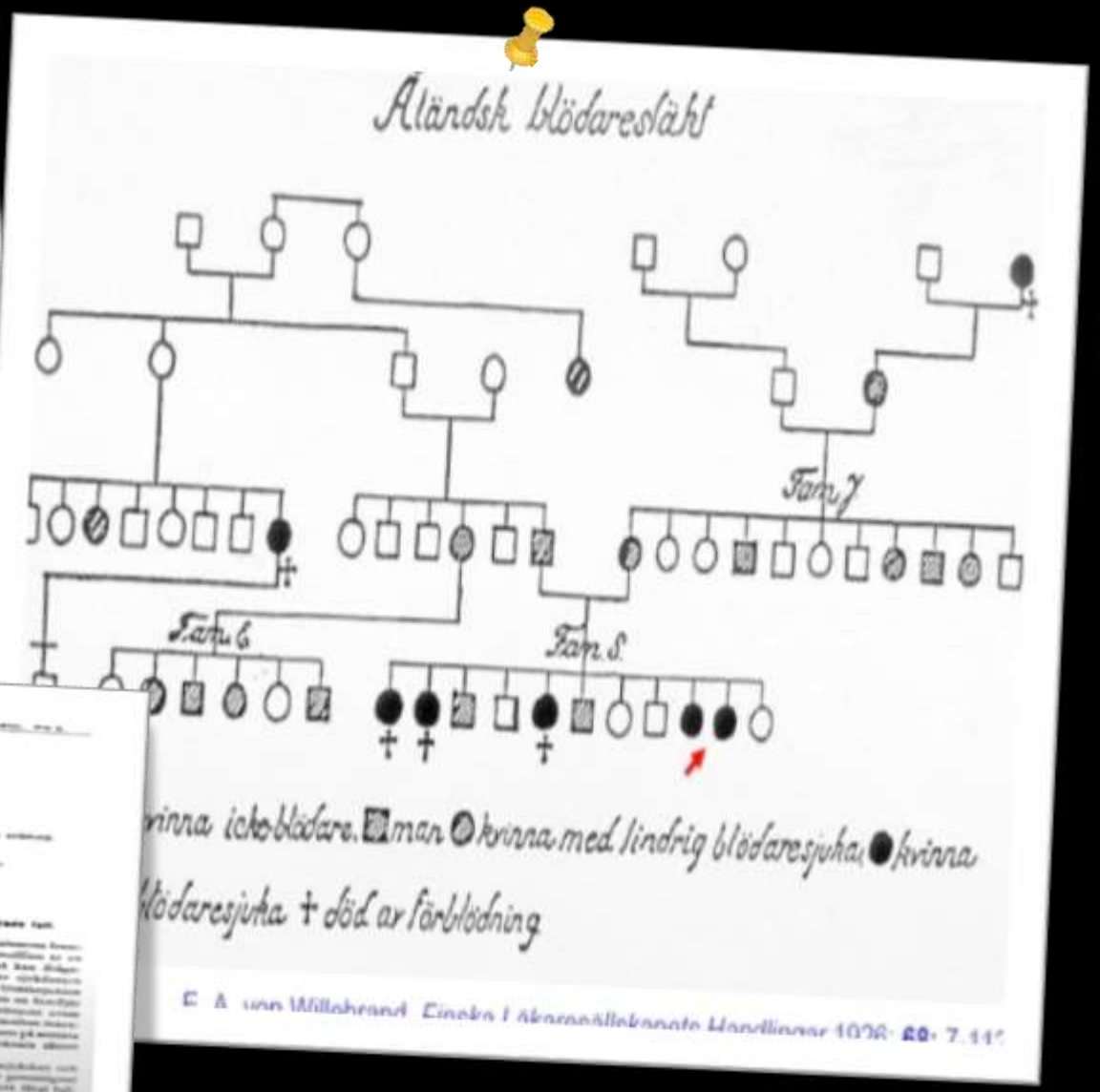
Maladie de Willebrand



Dr. Abla AMARA PETITJEAN

histoire



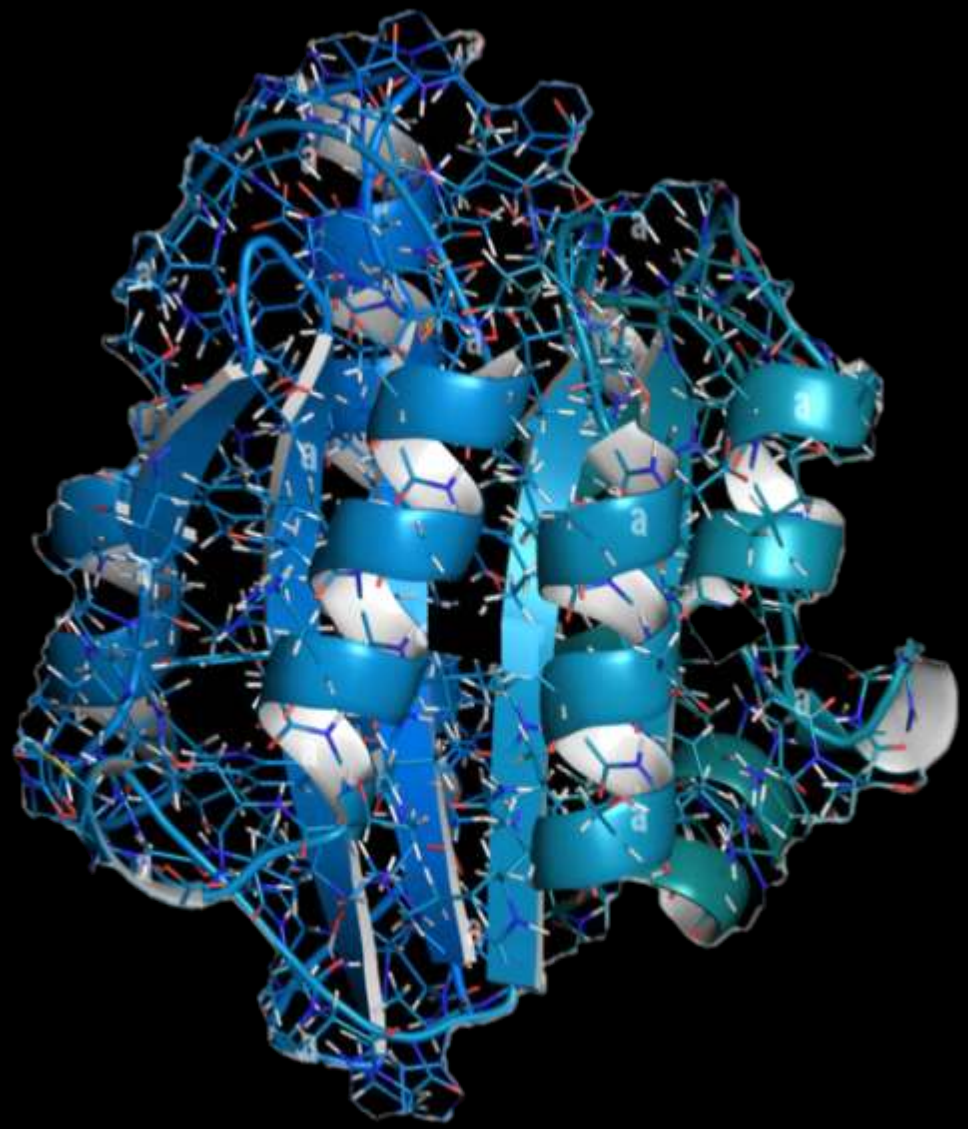


FINSKA LAKARESALLSKAPETS
HANDLINGAR
PROF. RICHARD HEVERS
BAND LXVIII
1926 FEBRUARI 1926

ORIGINALARTIKLAR.

1926

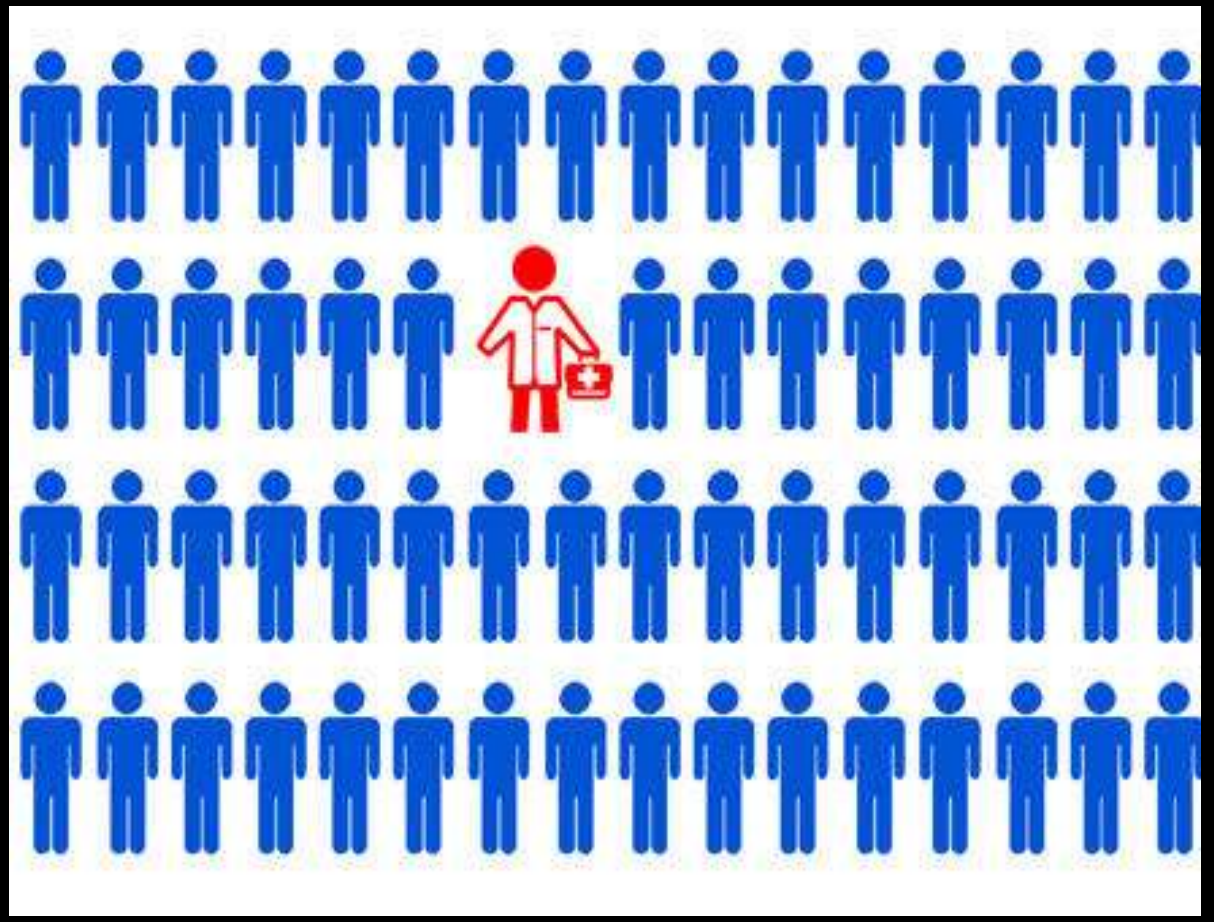
Pseudo hémophilie



Facteur Von Willebrand

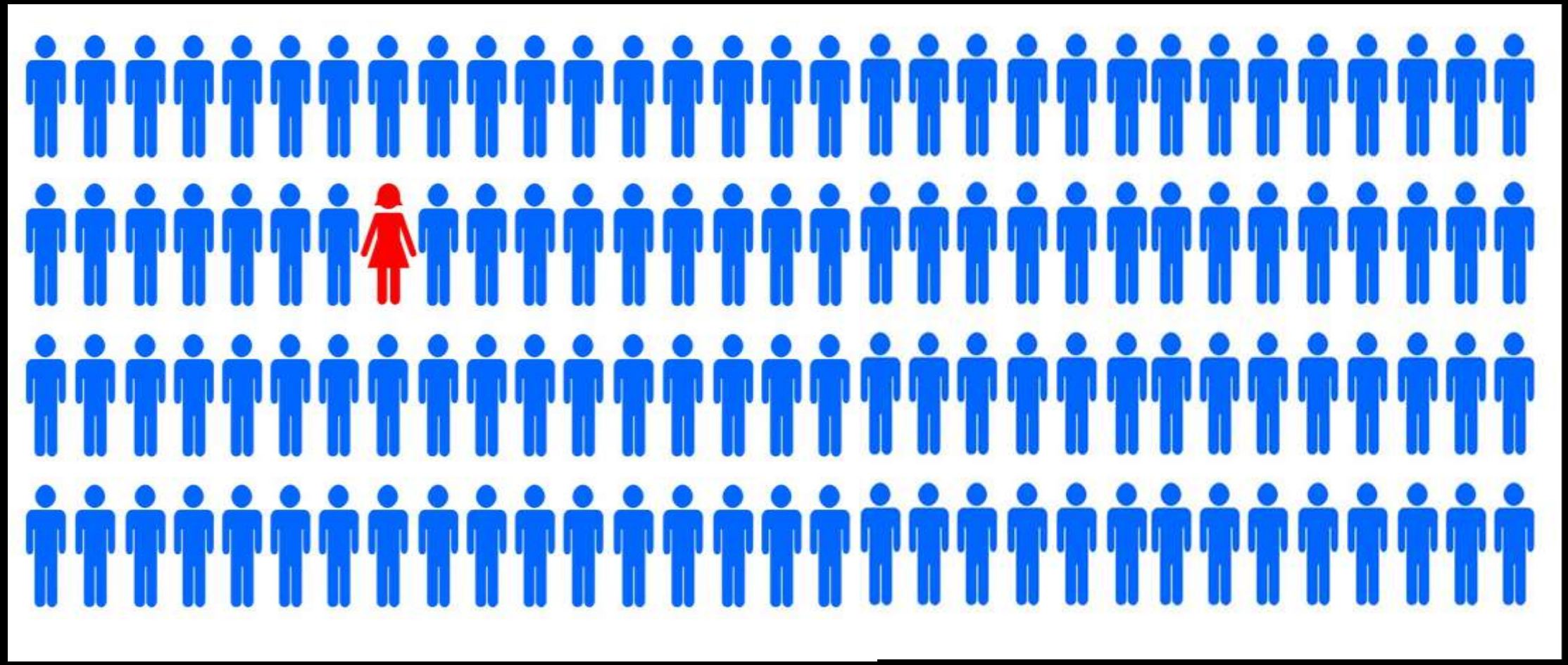
1 % de la population générale

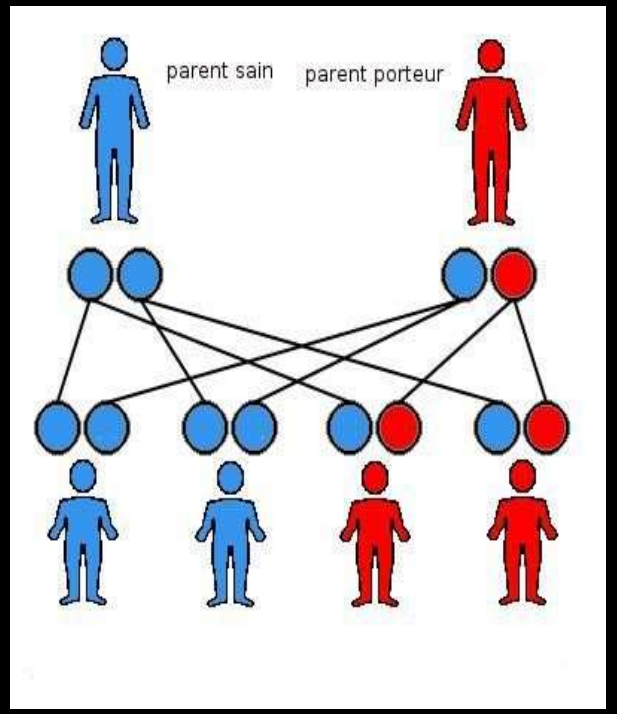
1 sur 10 000



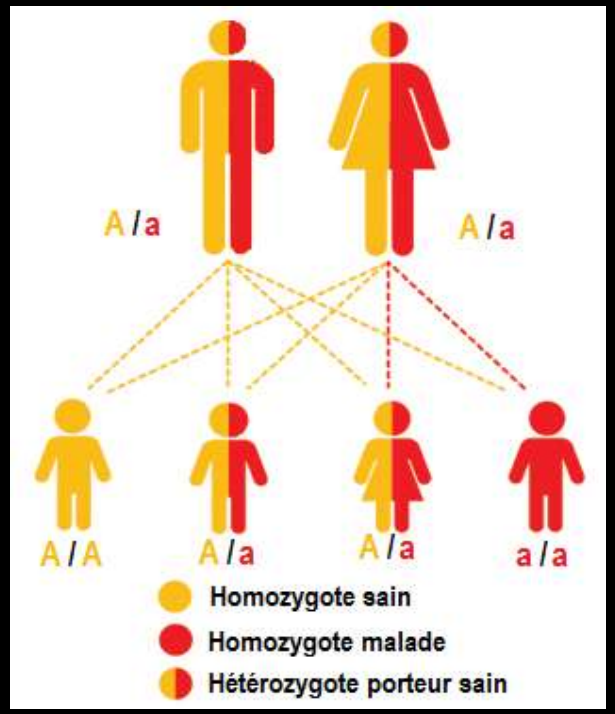
Type 3

1 par million d'habitants

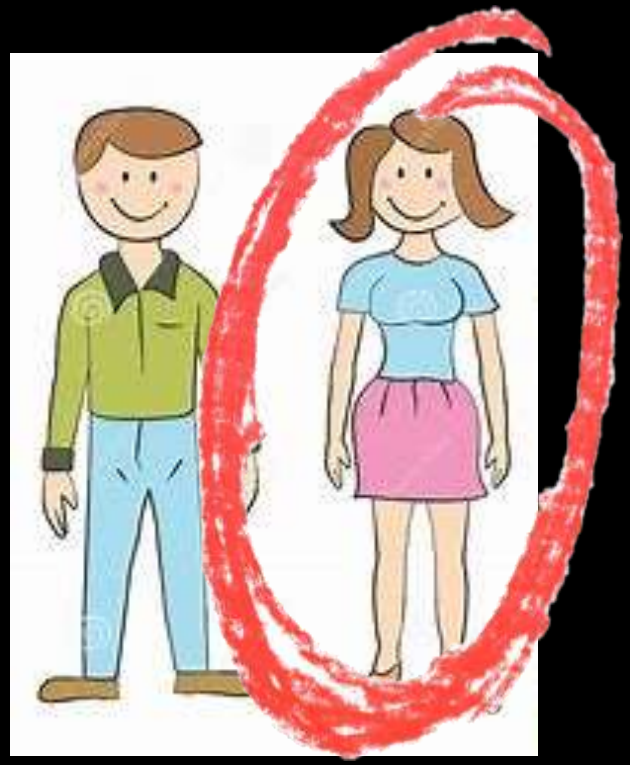




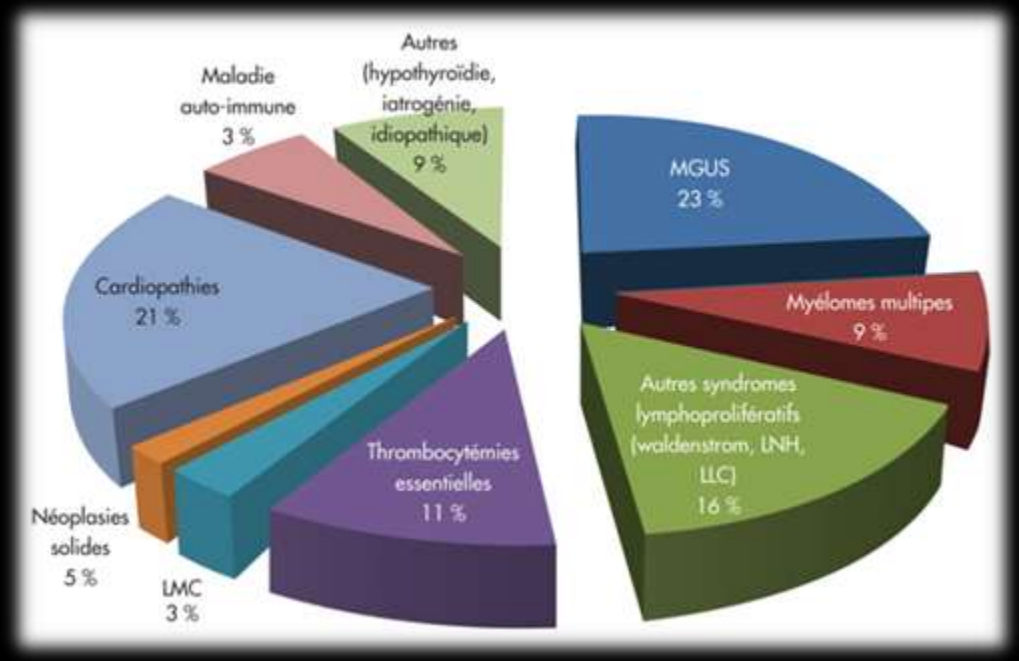
Autosomique dominante (Type 3 et 2N)

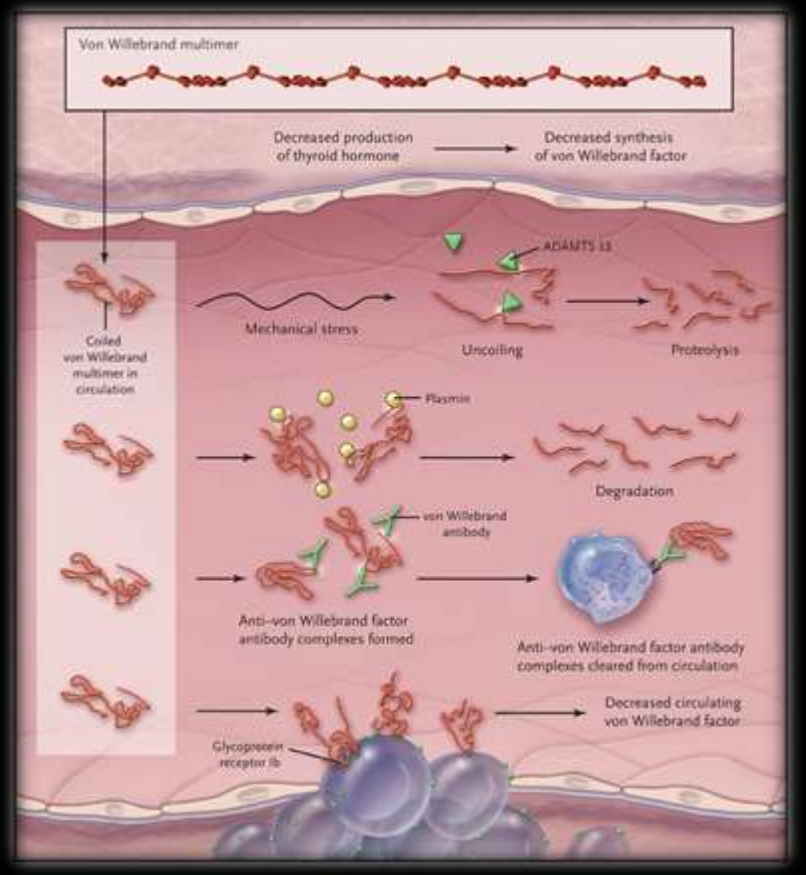


Autosomique récessive (Type I et 2)



WILLEBRAND ACQUIS



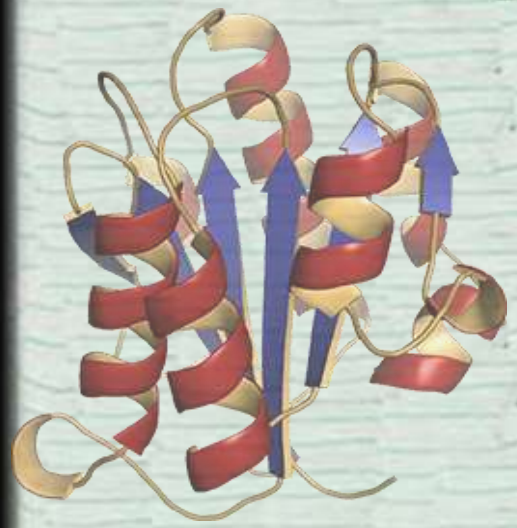


RÉPUBLIQUE FRANÇAISE

CARTE NATIONALE D'IDENTITÉ N° :

Nationalité Française

BS



Nom :

Facteur Von Willebrand

Prénom(s) :

à : Mégacaryocytes, endothelium

Né(e) le : 1926

Taille : 500 à 1500 kD

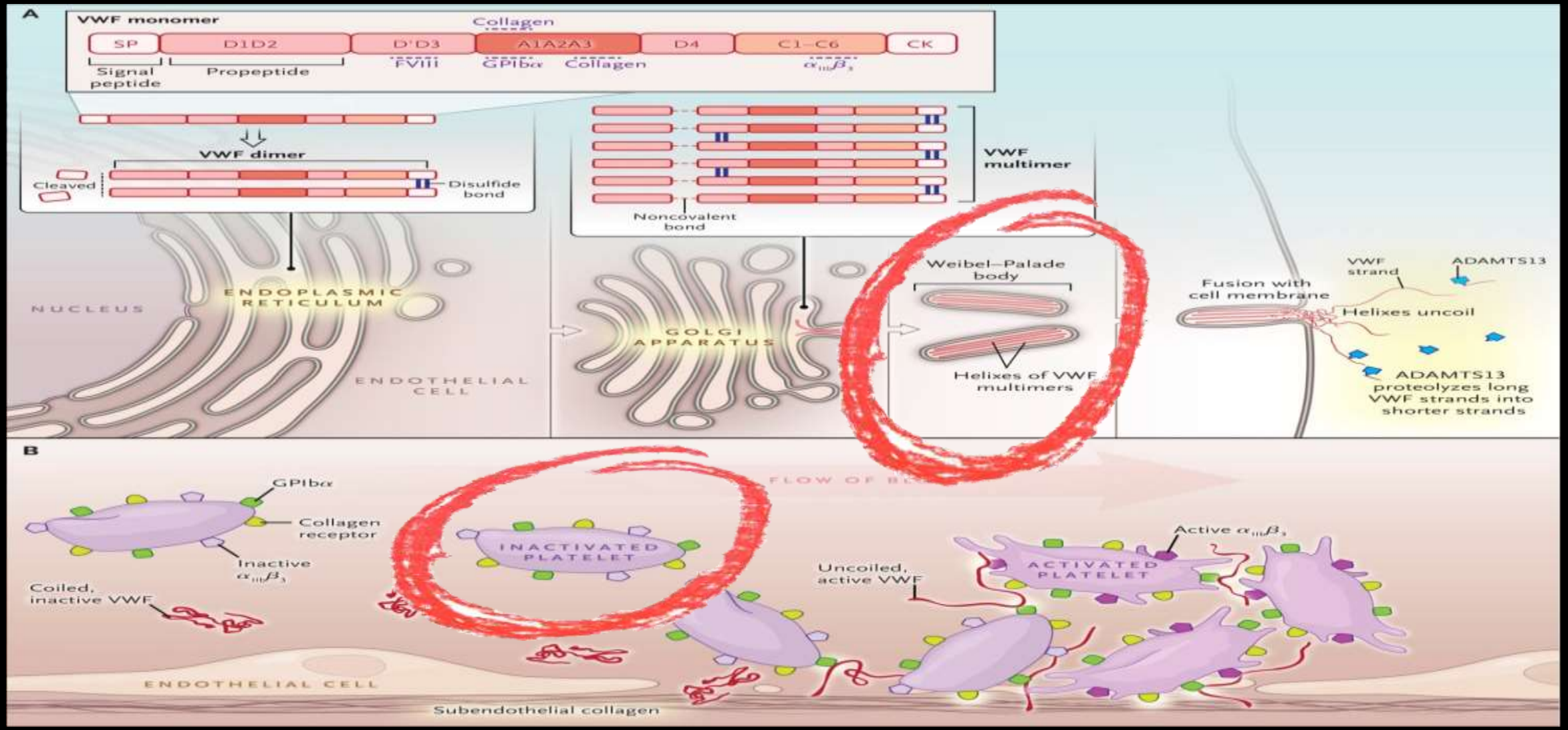
Fonctions : Hémostase primaire / Coagulation

Adresse : Granules α, corps de Weibel Palade

<<<<<<<<<<<<<<<<<<<<<<<<

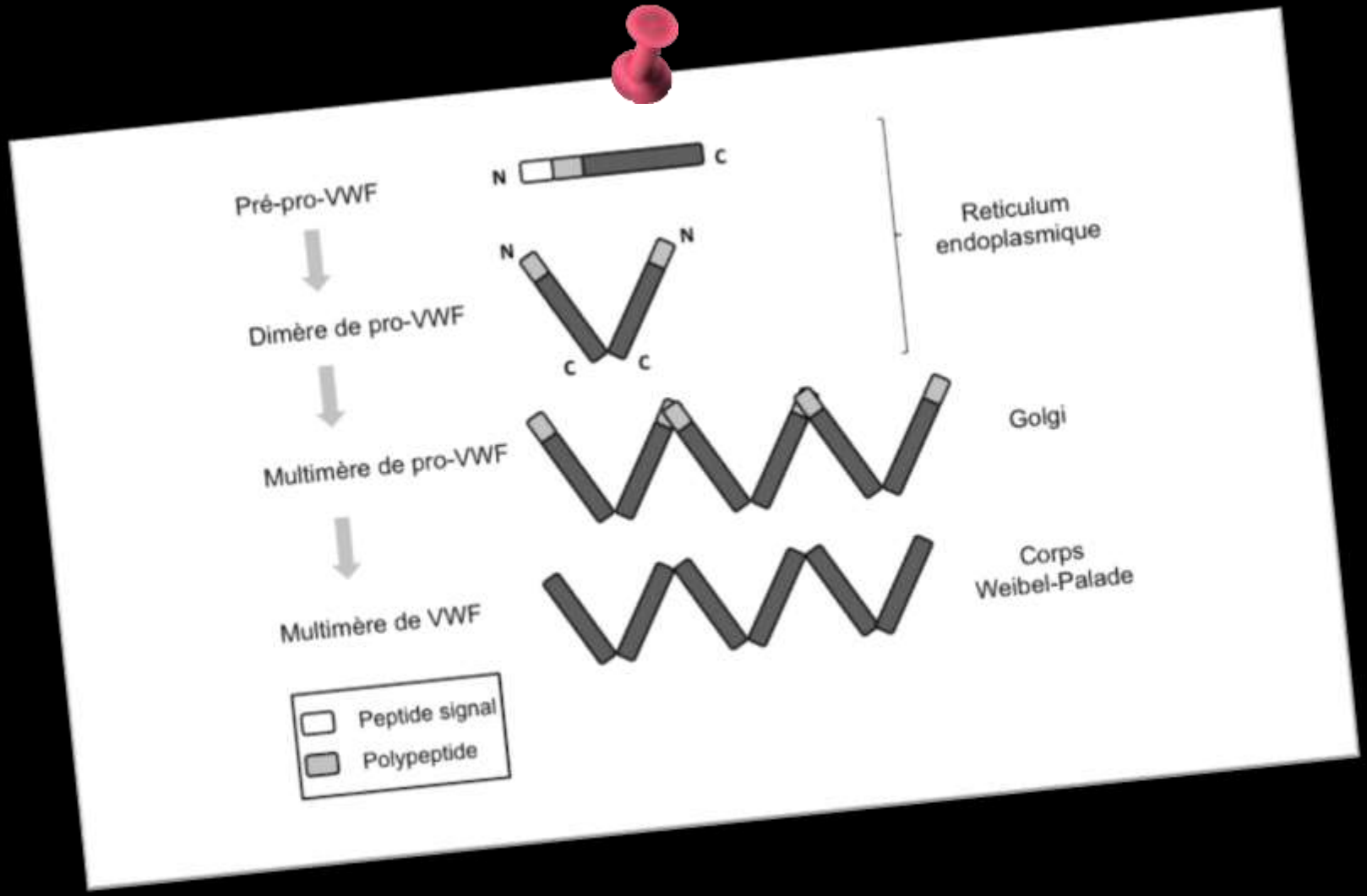
SPÉCIMEN <<<<<<

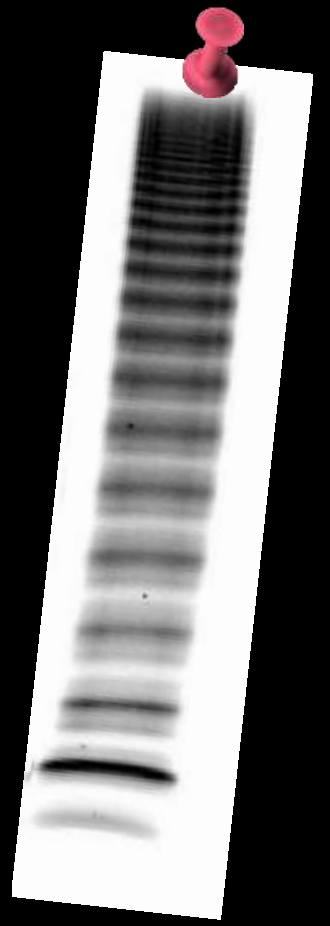
Biosynthèse



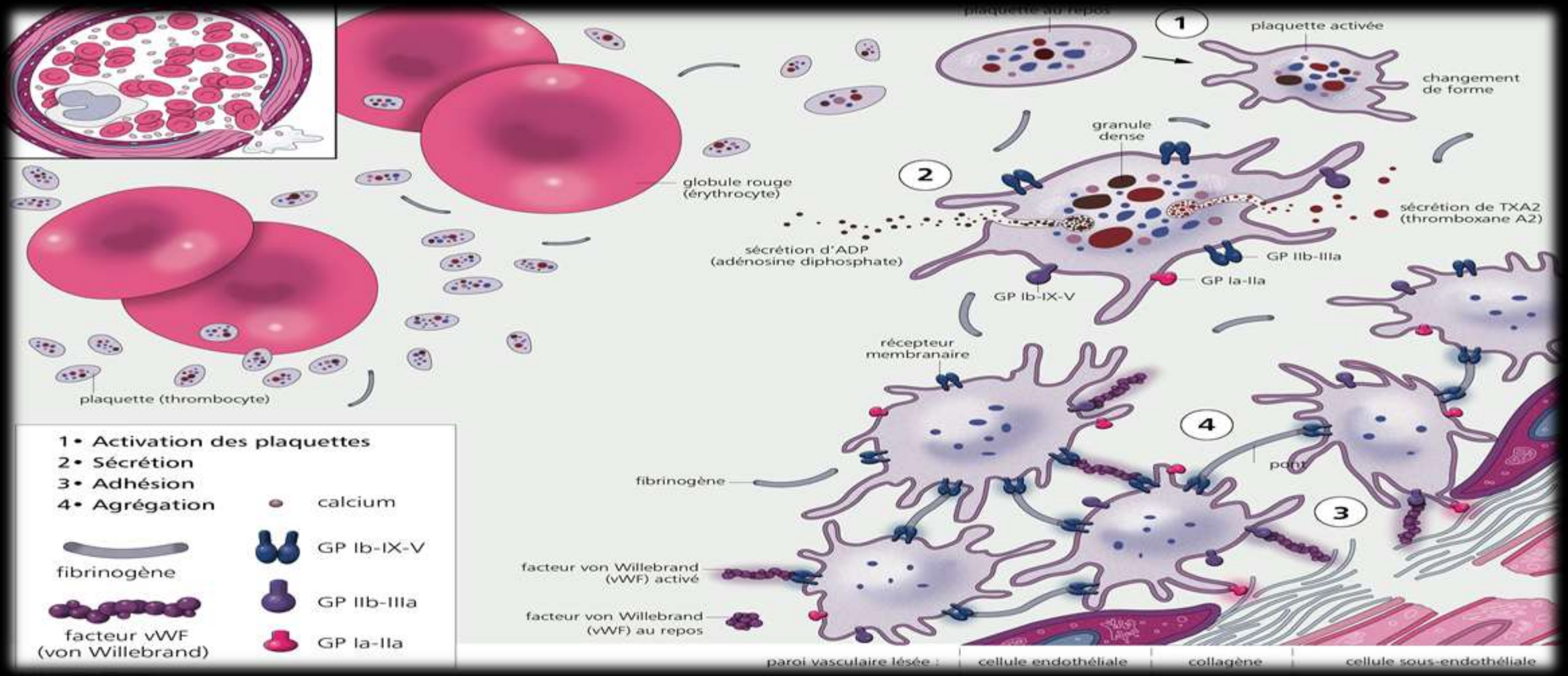
Multimères

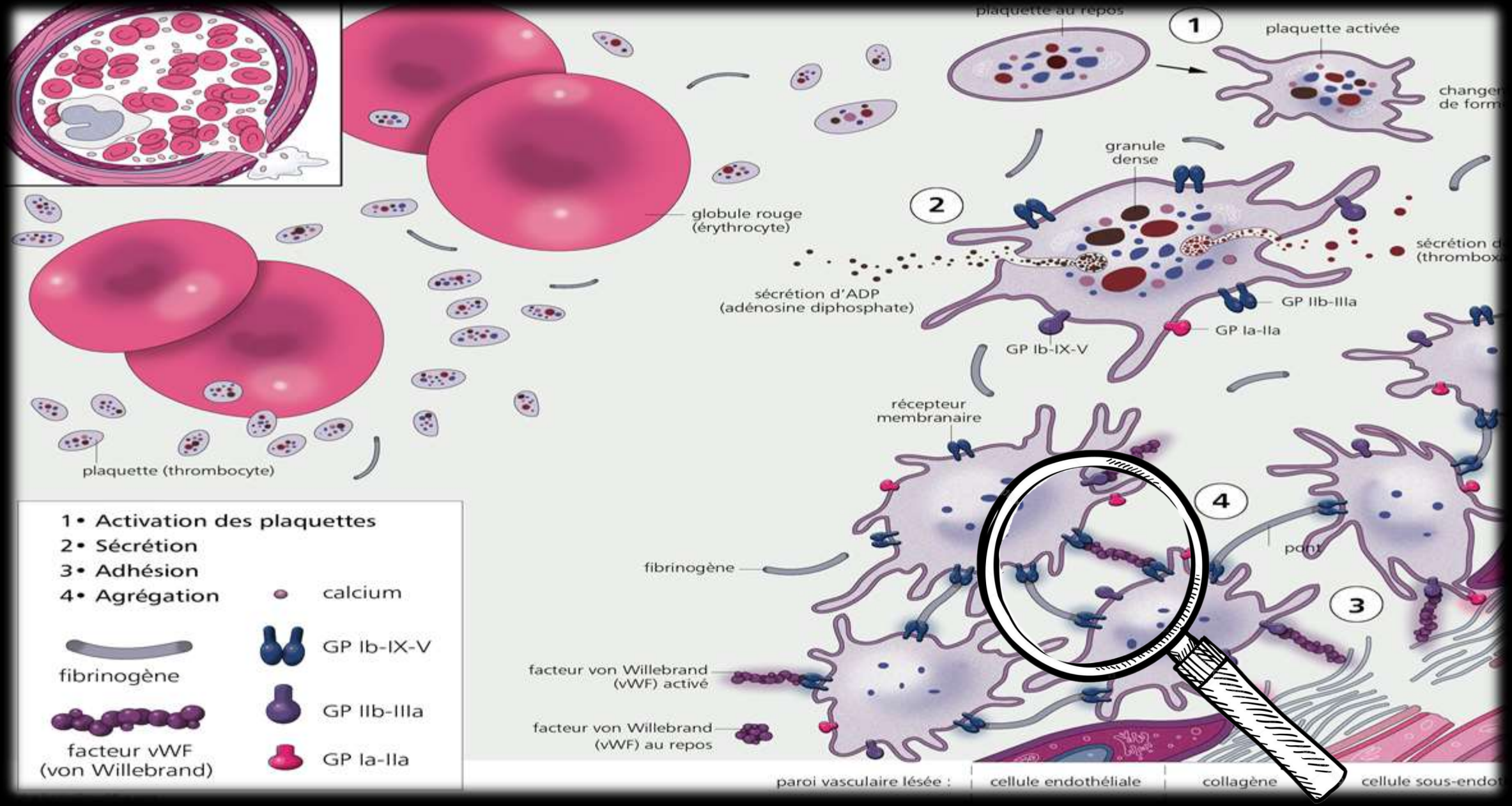
micro-circulation





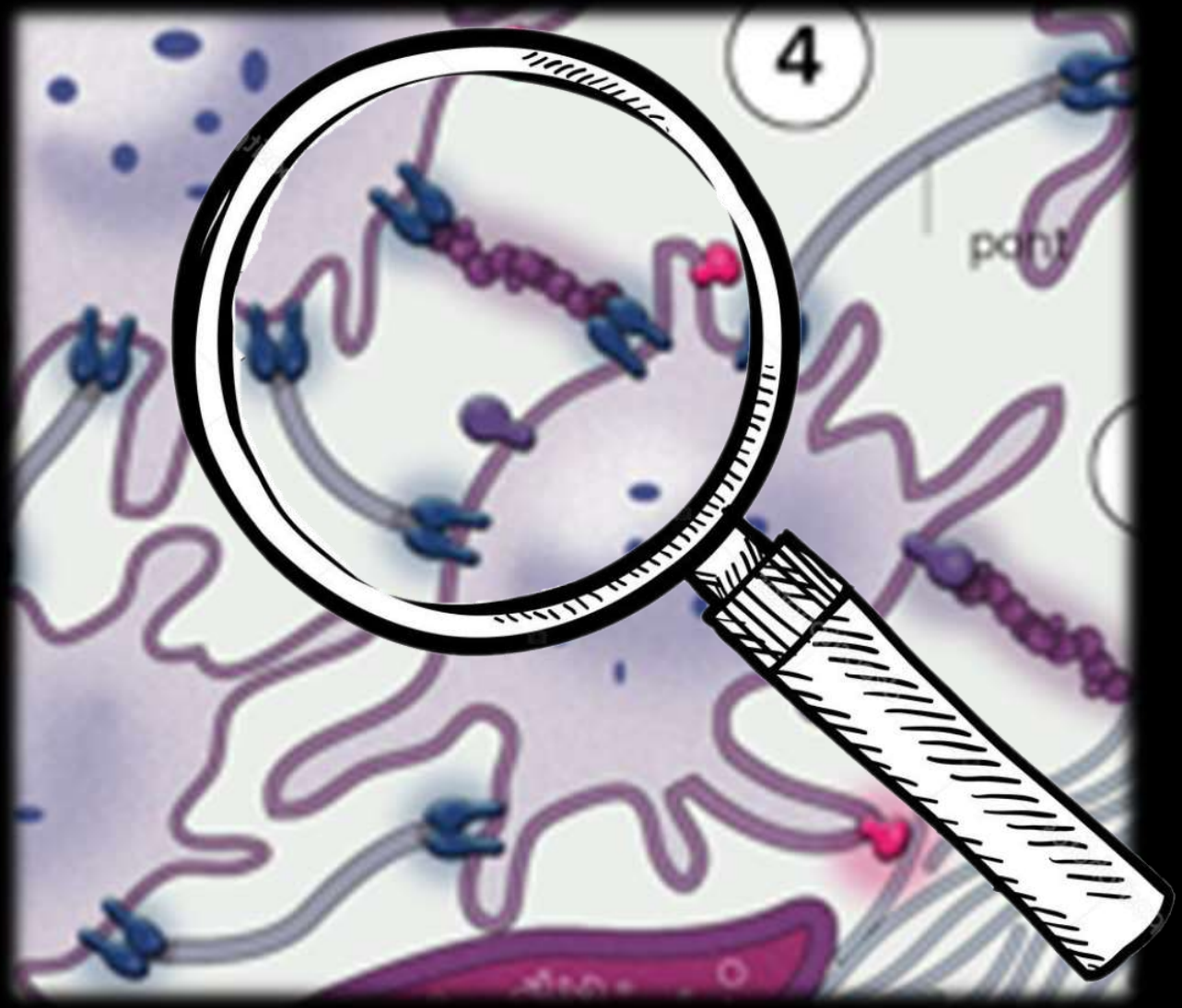
liaison des plaquettes aux composants du sous endothélium

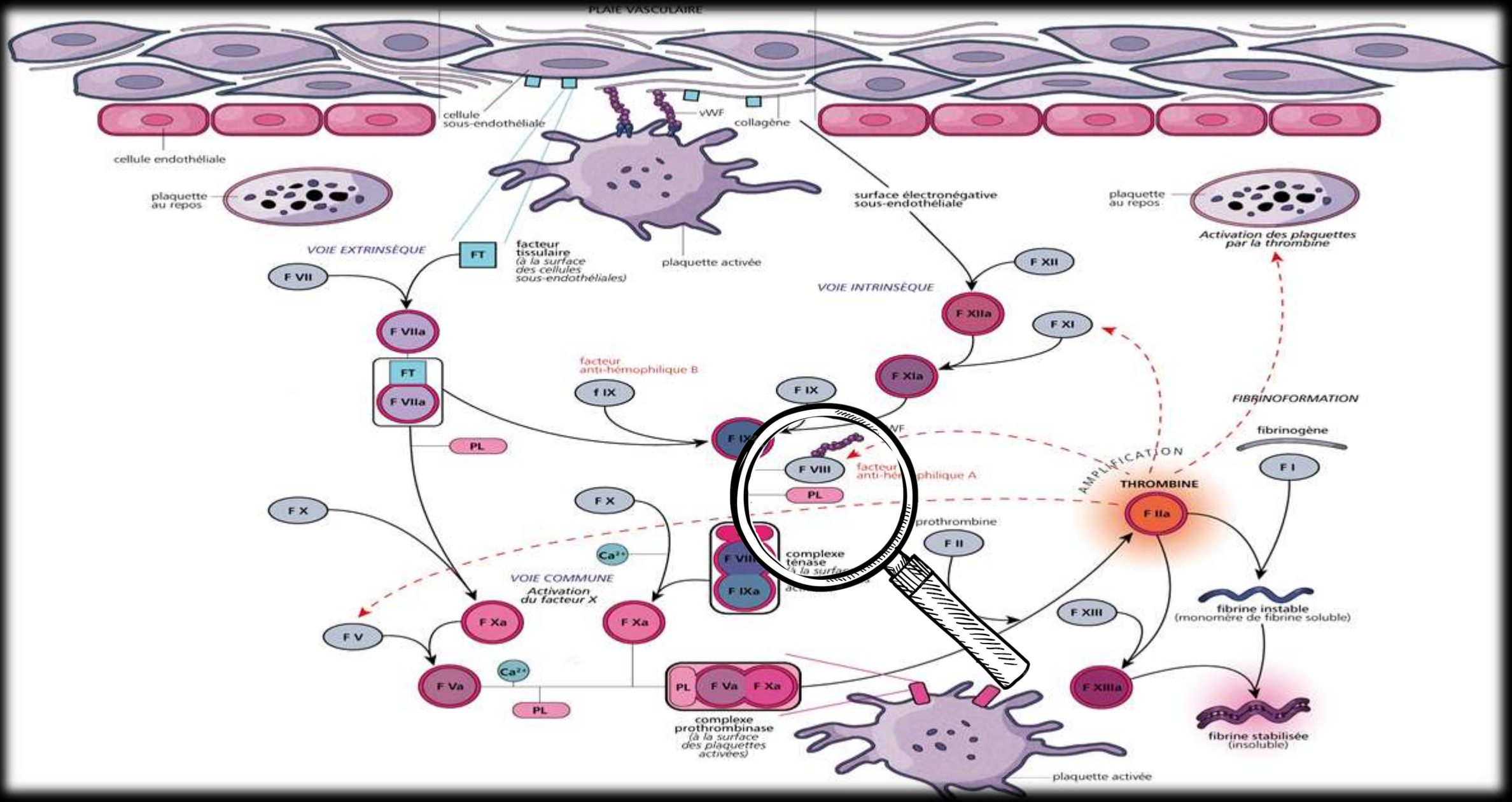


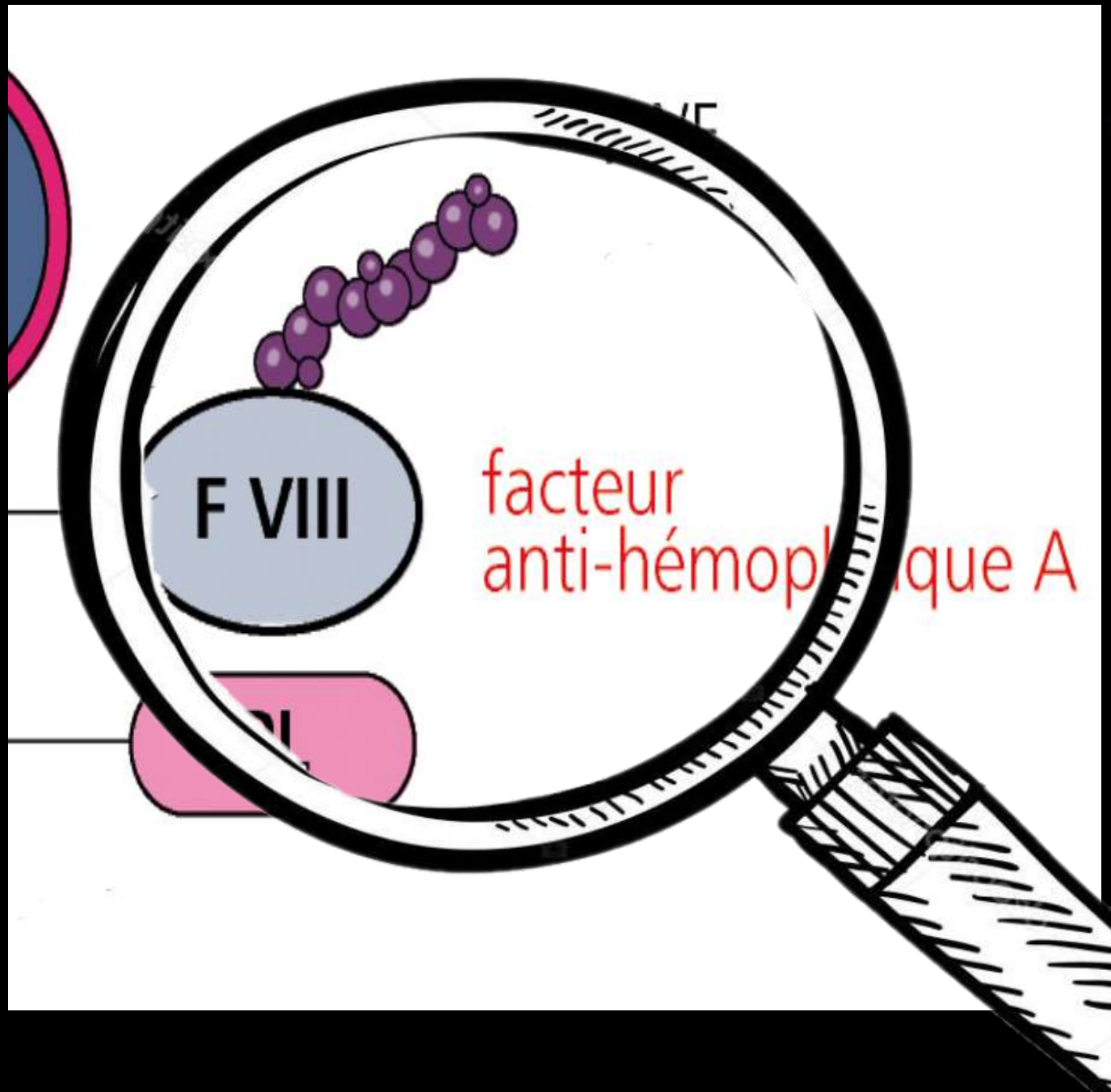

plaquette au repos
1
plaquette activée
granule dense
2
globule rouge (érythrocyte)
sécrétion d'ADP (adénosine diphosphate)
GP IIb-IIIa
GP Ia-IIa
GP Ib-IX-V
plaquette (thrombocyte)
récepteur membranaire
4
pont
3
fibrinogène
facteur von Willebrand (vWF) activé
facteur von Willebrand (vWF) au repos
paroi vasculaire lésée :
cellule endothéliale
collagène
1 • Activation des plaquettes
2 • Sécrétion
3 • Adhésion
4 • Agrégation
calcium
GP Ib-IX-V
fibrinogène
GP IIb-IIIa
facteur vWF (von Willebrand)
GP Ia-IIa

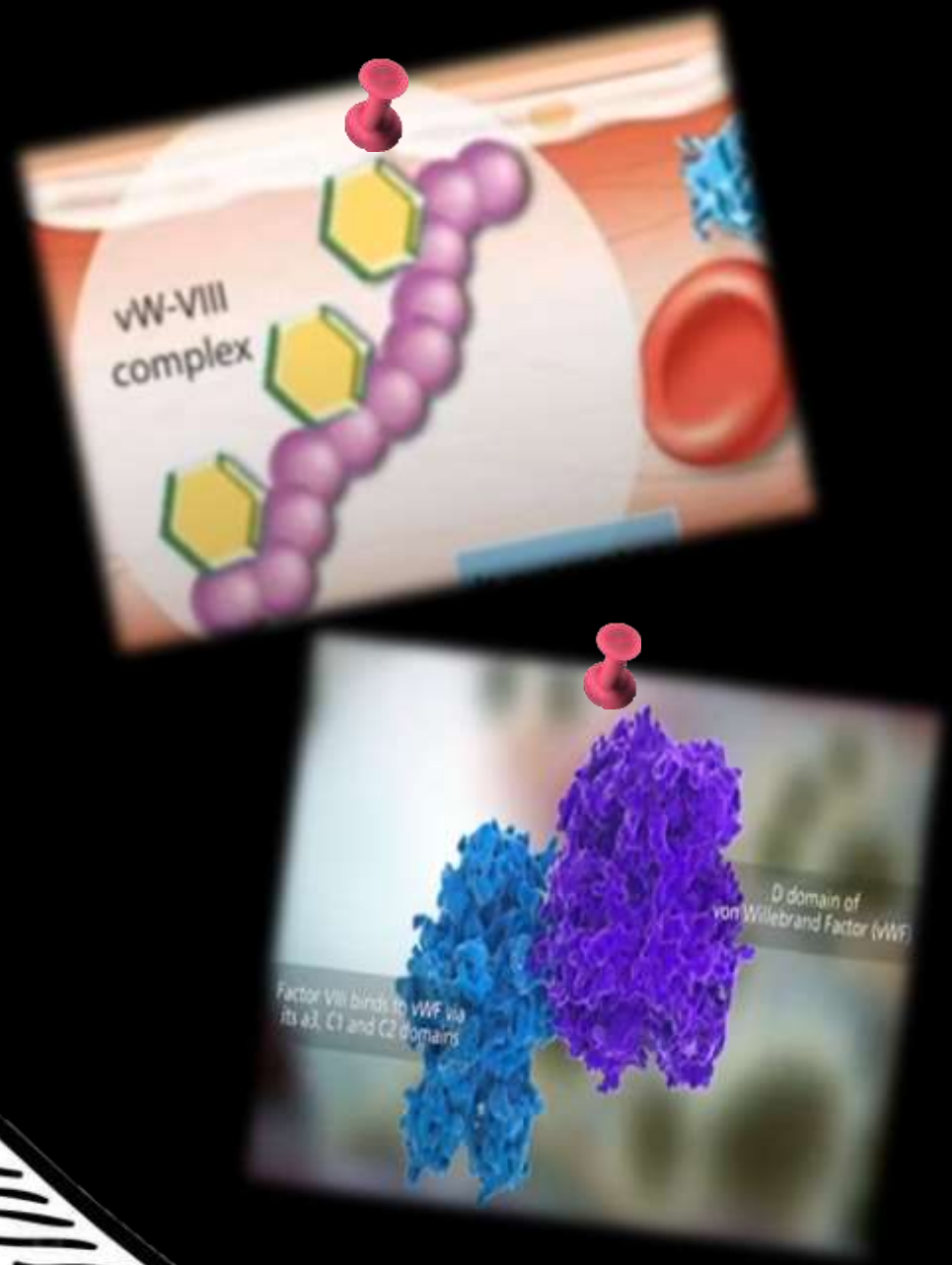
GP IBIX

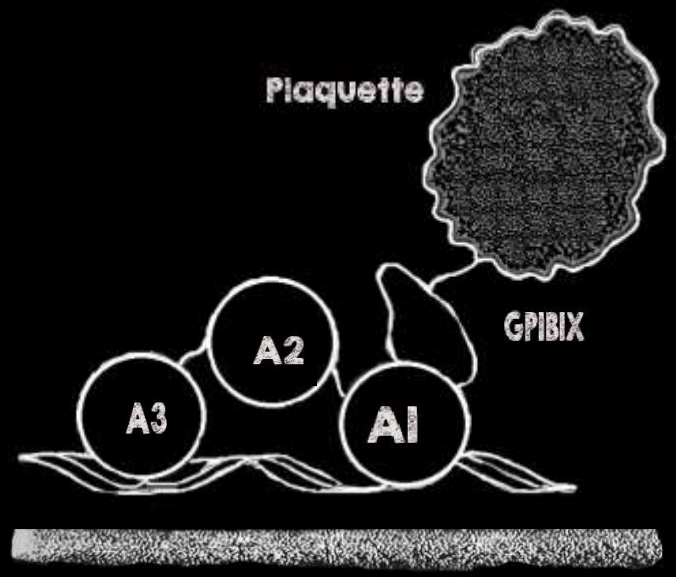
COLLAGENE




PLAIE VASCULAIRE
cellule endothéliale
cellule sous-endothéliale
vWF
collagène
plaquette au repos
plaquette activée
surface électronégative sous-endothéliale
plaquette au repos
Activation des plaquettes par la thrombine
VOIE EXTRINSÈQUE
FT
facteur tissulaire (à la surface des cellules sous-endothéliales)
F VII
F VIIa
FT
F VIIa
PL
VOIE INTRINSÈQUE
F XII
F XIIa
F XI
F XIa
facteur anti-hémophilique B
f IX
F IX
F IXa
F VIII
PL
facteur anti-hémophilique A
FIBRINOFORMATION
fibrinogène
F I
AMPLIFICATION
THROMBINE
F IIa
prothrombine
F II
F X
F X
Ca++
F VIII
F IXa
complexe ténase (à la surface
VOIE COMMUNE
Activation du facteur X
F Xa
F Xa
F V
F Va
Ca2+
PL
PL
F Va
F Xa
complexe prothrombinase (à la surface des plaquettes activées)
F XIII
F XIIIa
fibrine instable (monomère de fibrine soluble)
fibrine stabilisée (insoluble)
plaquette activée


F VIII
facteur
anti-hémop que A

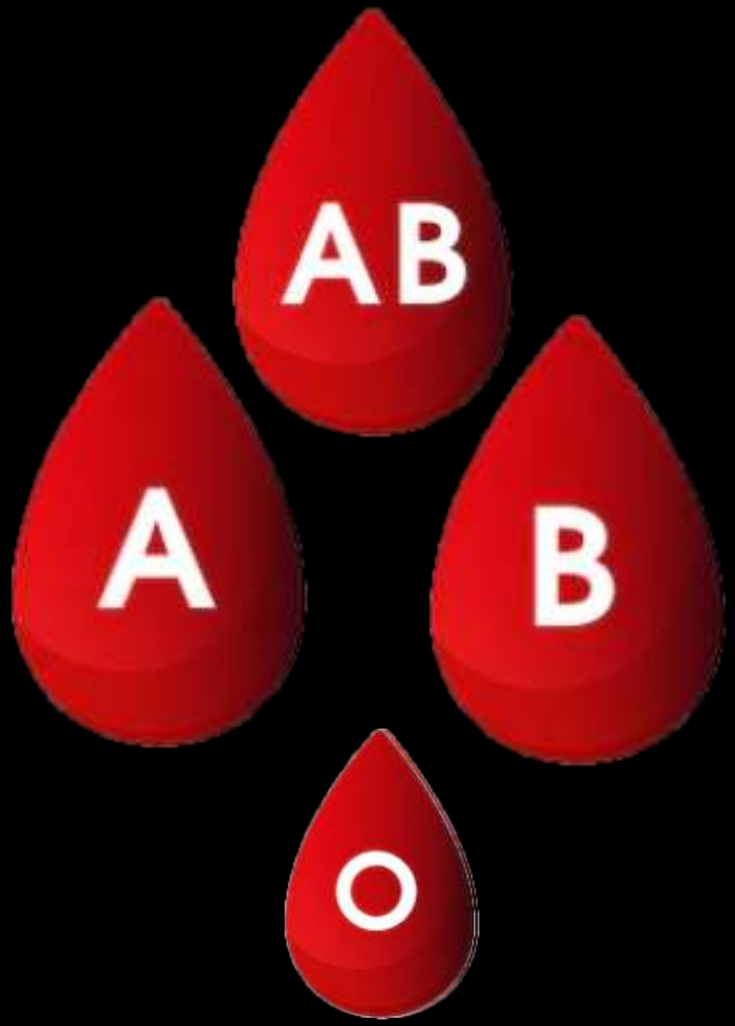

vW-VIII
complex
D domain of
von Willebrand Factor (vWF)



Pro-vWF D3 AI A2 A3 CI

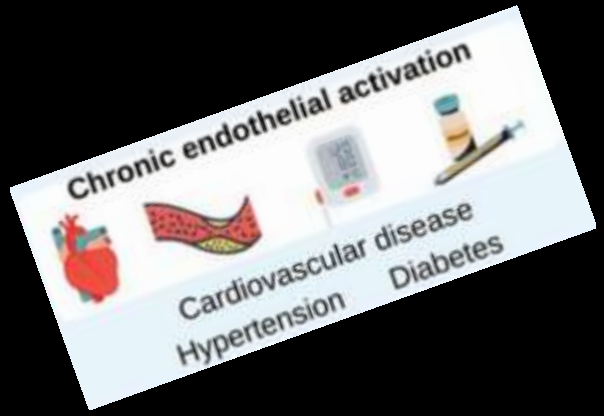
FVIII GPIBIX ADAMTSI3 Collagène GPIIbIIIa

Collagène


AB
A
B
O

vWF ↓


Stress
Sepsis
Strenuous exercise
Severe illness
Phlebotomy


Chronic endothelial activation
Cardiovascular disease
Hypertension
Diabetes

vWF ↑

CLASSIFICATION

TYPE 1

TYPE 1

TYPE 1

TYPE 1

TYPE 1

TYPE 1

TYPE 1

TYPE 1

TYPE 3

TYPE 3

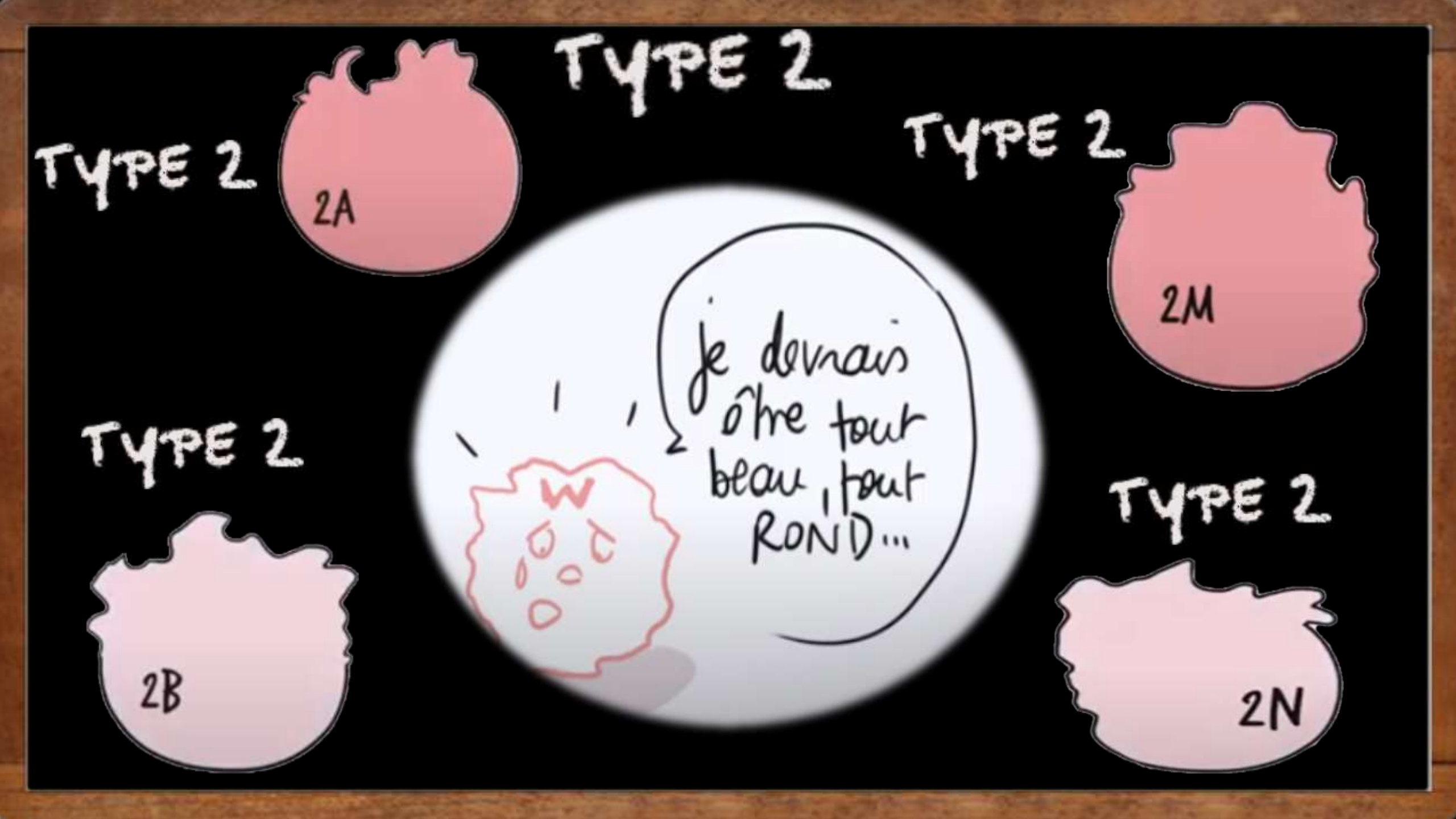
TYPE 3

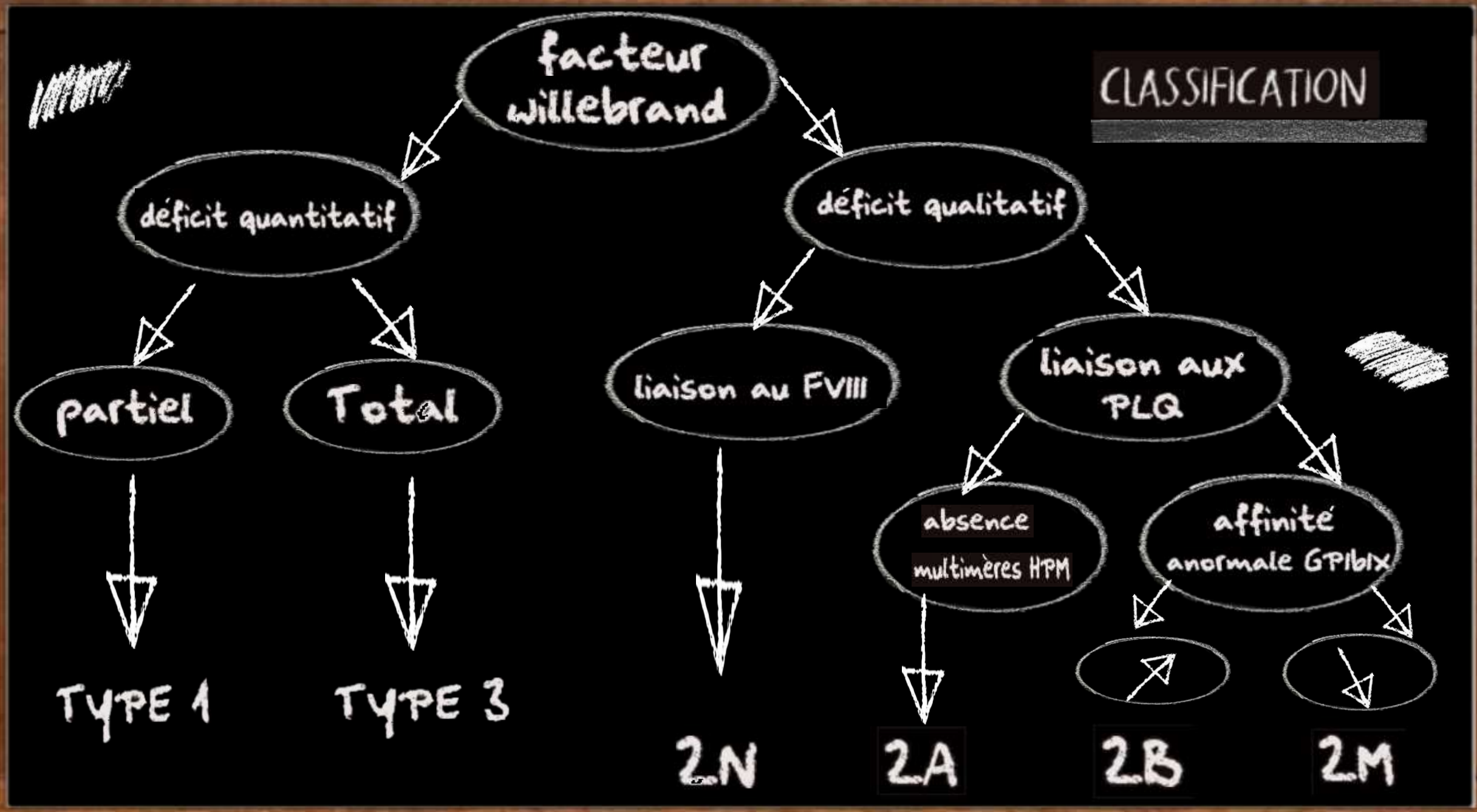
TYPE 3

TYPE 3

TYPE 3

TYPE 3

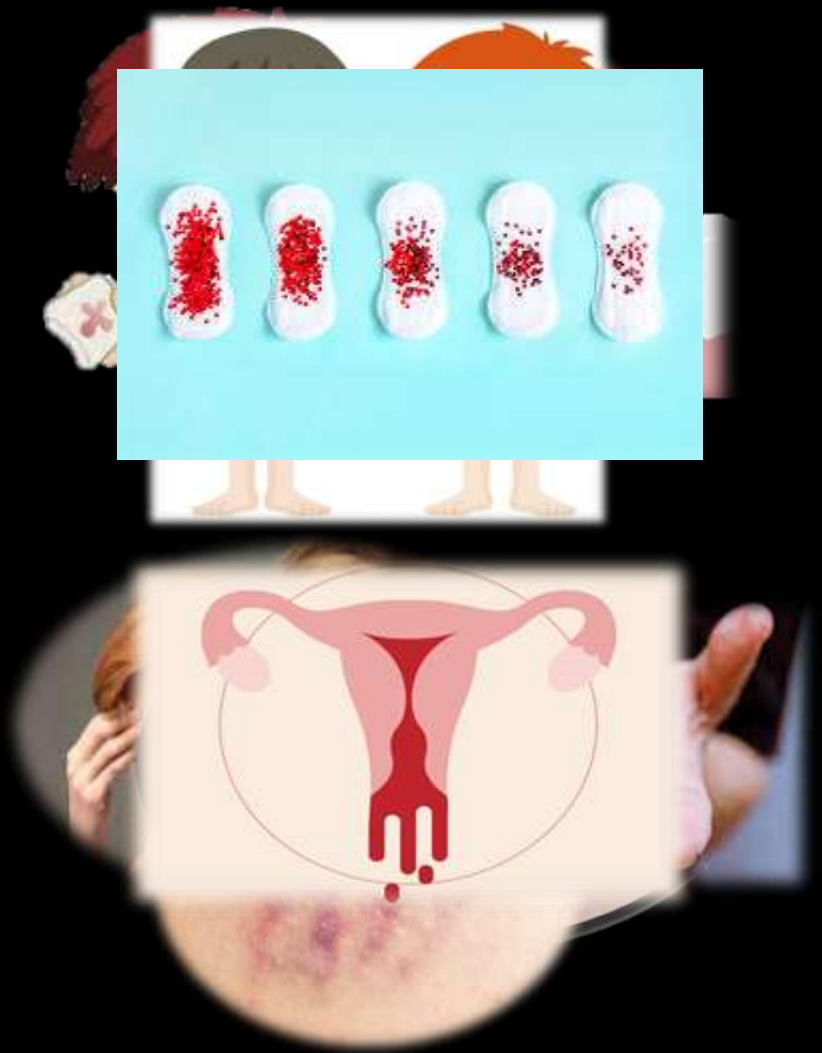

TYPE 2
TYPE 2
2A
TYPE 2
2M
je devrais être tout beau, tout ROND...
TYPE 2
2B
TYPE 2
2N


facteur willebrand
CLASSIFICATION
déficit quantitatif
déficit qualitatif
partiel
Total
liaison au FVIII
liaison aux PLQ
absence multimères HPM
affinité anormale GPIbIX
TYPE 1
TYPE 3
2N
2A
2B
2M

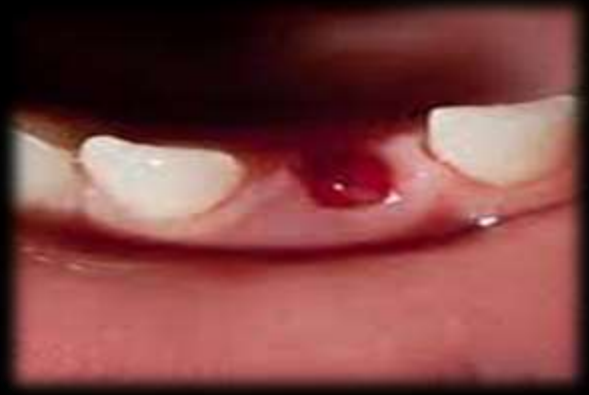

SYMPTOMES

HEMORRAGIES CUTANEO-MUQUEUSES

- MENORRAGIES PROLONGES

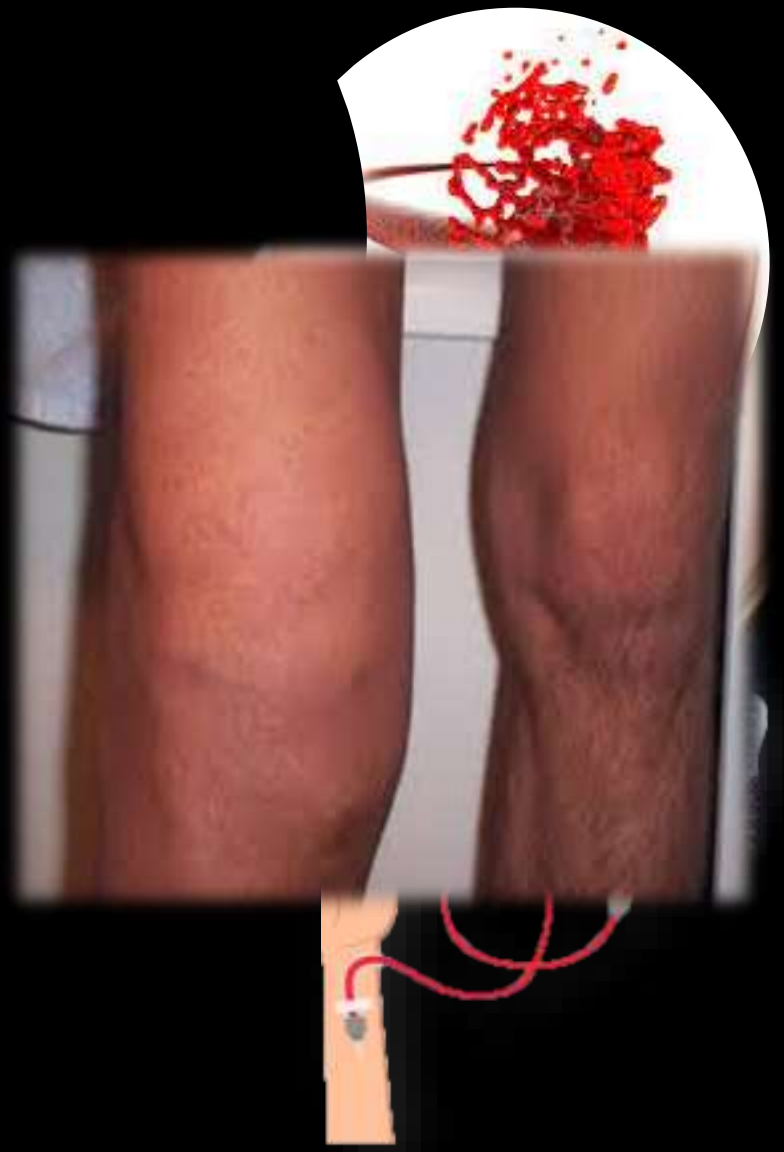


SAIGNEMENTS POST-TRAUMATIQUES POST-CHIRURGICAUX



FORMES SEVERES

HEMARTHROSE OND



DIAGNOSTIC ?

PL SYMT WILLEBRAND

HISTOIRE FAMILIALE

SCORE HEMORRAGIQUE BAT

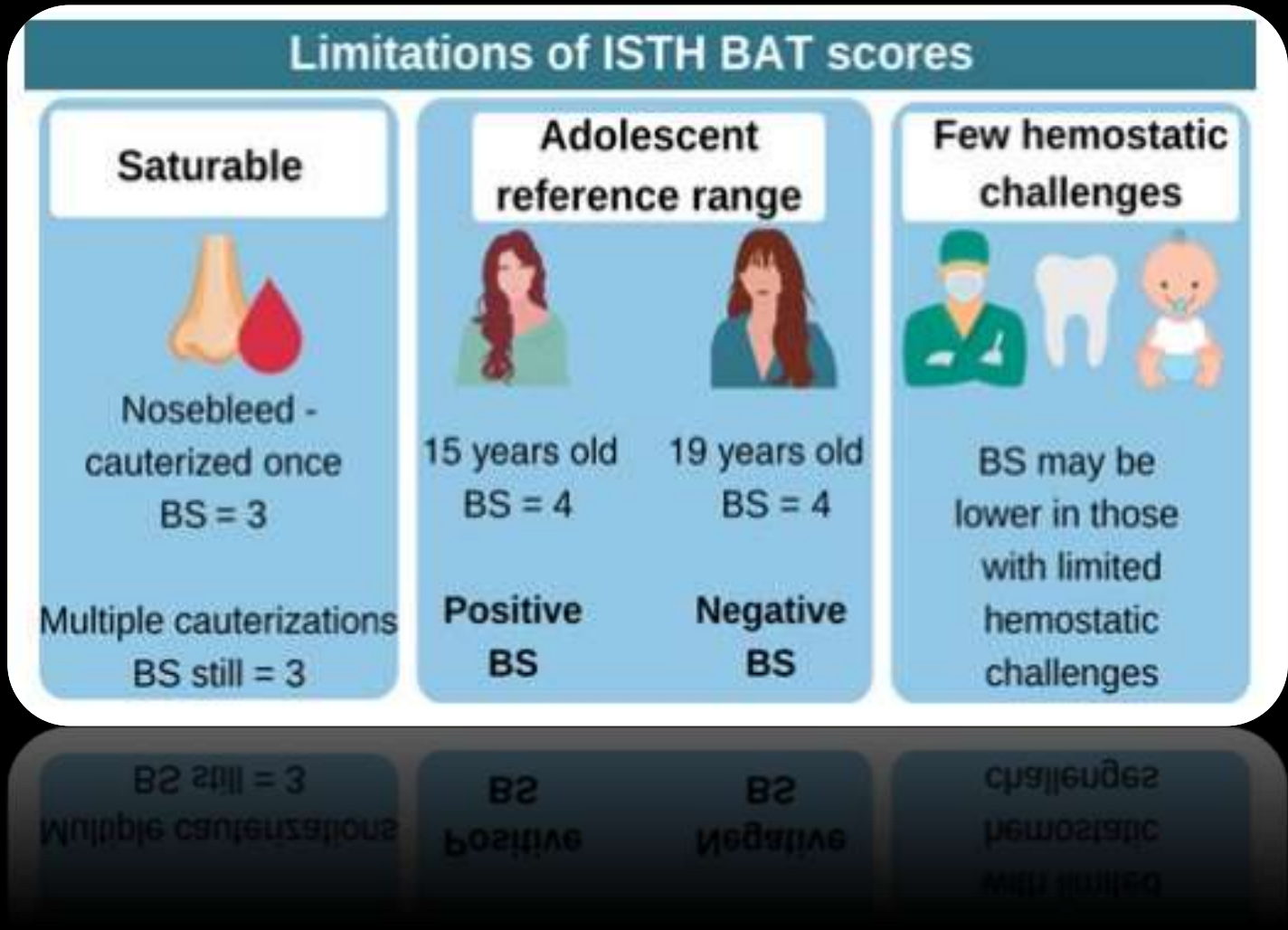
SCORE 8

	SCORE				
SYMPTOMS (up to the time of diagnosis)	0§	1§	2	3	4
Epistaxis	○ No/trivial	● - > 5/year or - more than 10 minutes	○ Consultation only*	○ Packing or cauterization or antifibrinolytic	○ Blood transfusion or replacement therapy (use of hemostatic blood components and rFVIIa) or desmopressin
Cutaneous	○ No/trivial	○ For bruises 5 or more (> 1cm) in exposed areas	○ Consultation only*	● Extensive	○ Spontaneous hematoma requiring blood transfusion
Bleeding from minor wounds	● No/trivial	○ - > 5/year or - more than 10 minutes	○ Consultation only*	○ Surgical hemostasis	○ Blood transfusion, replacement therapy, or desmopressin
Oral cavity	○ No/trivial	○ Present	○ Consultation only*	○ Surgical hemostasis or antifibrinolytic	● Blood transfusion, replacement therapy or desmopressin
GI bleeding	● No/trivial	○ Present (not associated with ulcer, portal hypertension,	○ Consultation only*	○ Surgical hemostasis, antifibrinolytic	○ Blood transfusion, replacement therapy or desmopressin

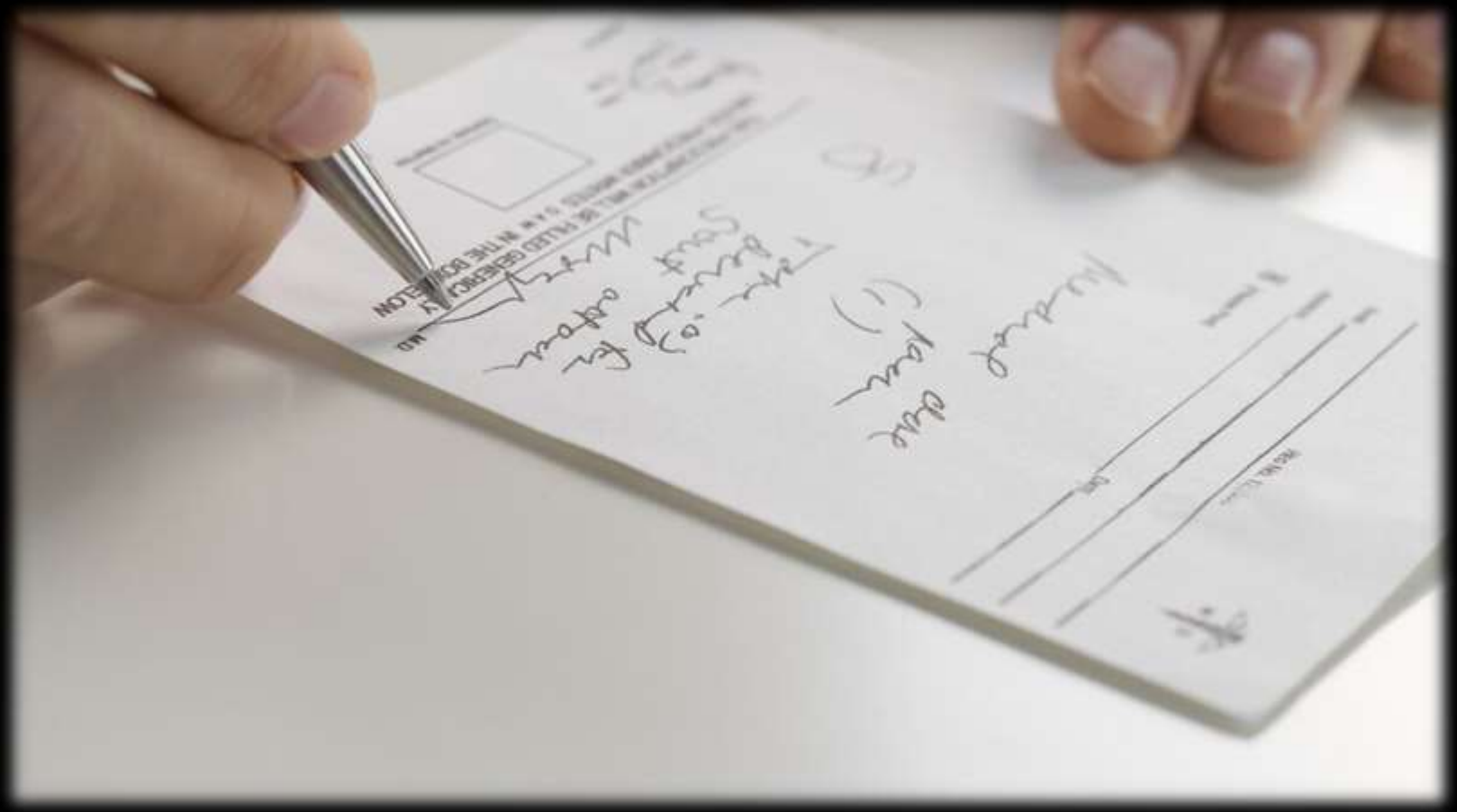
ISTH-BAT ≥ 3 POUR LES < 18 ANS

ADULTES (≥4 POUR LES HOMMES, ≥ 6 POUR LES FEMMES)

ISTH-BAT ≥ 4 POUR LES ADOLESCENTES



QUEL BILAN PRESCRIRE ?



TESTS DE PREMIERE INTENSION

NFS (NUMERATION PLAQUETTAIRE)

TEMPS DE CEPHALINE ACTIVE

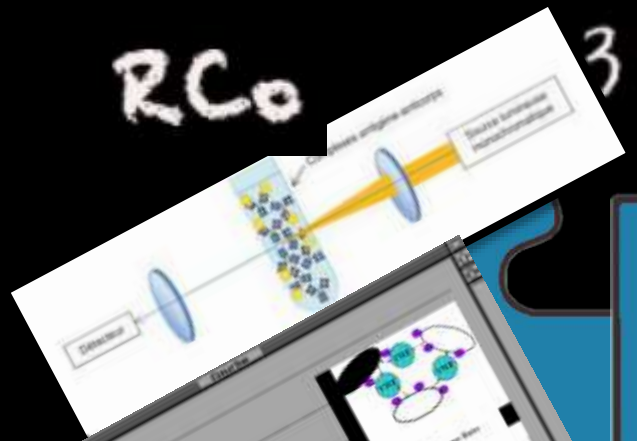
TEMPS D'OCCLUSION PLAQUETTAIRE (PFA)

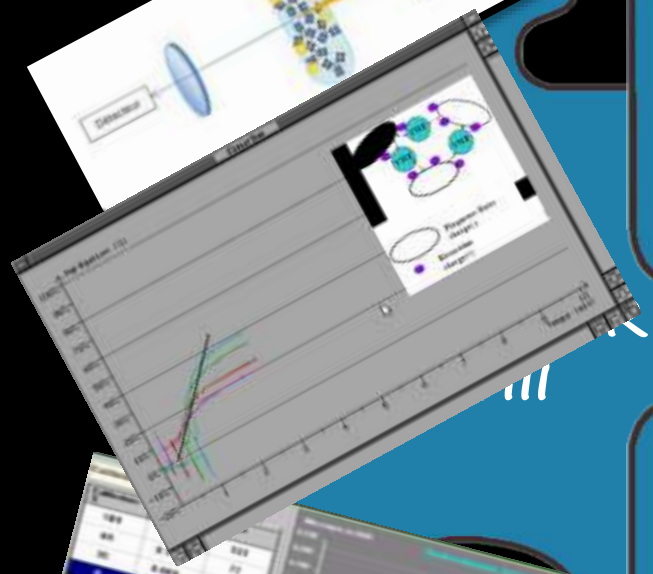
TESTS SPECIFIQUES

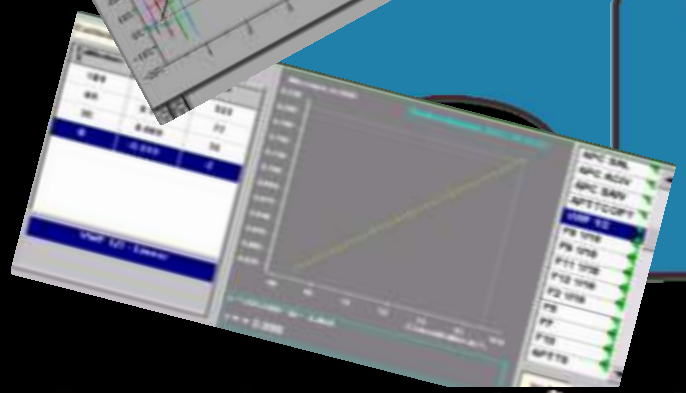
Diagnostic

RCo

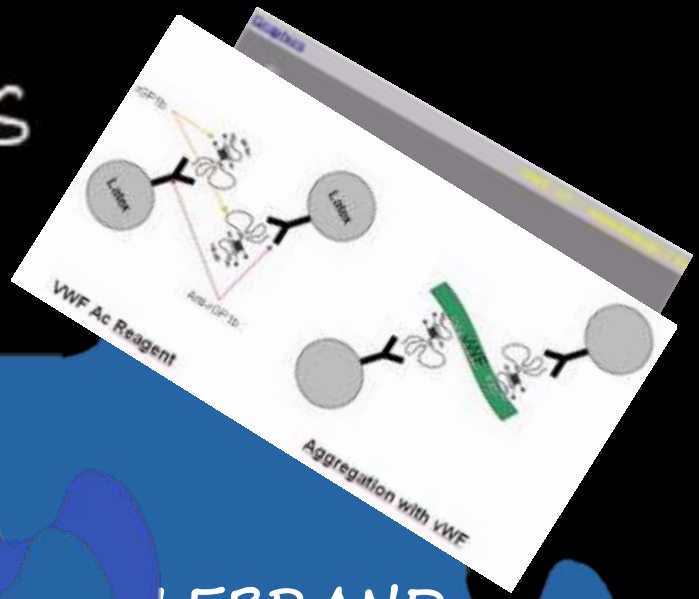
3 Dosag ociables







WILLEBRAND ACTIVITE



LEBRAND CTIVITE

GP1bR

GP1bM

Seuil de quantification

normes : 50-150 %

Ratios

VWF Act/VWF Ag

- >0,7 → TYPE 1
- <0,7 → 2A 2B 2M

FVIII /VWF Ag → <0,7 → 2N hemophilie A

TYPE 1

Type	1
TO	↑
TCA	N ou ↑
FVIII	N ou ↓
vWF:Ag	↓
vWF:Rco	↓
FVIII /vWF:Ag	> 0,7
vWF:Rco/WF:Ag	> 0,7

TYPE 3

Types ou sous type	3
TO	↑↑↑
TCA	↑
FVIII	↓↓↓
vWF:Ag	↓↓↓ ou absent
vWF:Rco	↓↓↓ ou absent
FVIII /vWF:Ag	–
vWF:Rco/WF:Ag	–

2N

TO	N
TCA	↑
FVIII	↓↓ (3-40%)
vWF:Ag	N
vWF:Rco	N
FVIII /vWF:Ag	< 0,5
vWF:Rco/WF:Ag	> 0,7

2M

Types ou sous type	2M
TO	↑
TCA	N ou ↑
FVIII	N ou ↓
vWF:Ag	N ou ↓
vWF:Rco	↓↓
FVIII /vWF:Ag	> 0,7
vWF:Rco/WF:Ag	< 0,7

2A

Types ou sous type	2 A
TO	↑
TCA	N ou ↑
FVIII	N ou ↓
vWF:Ag	N ou ↓
vWF:Rco	↓↓
FVIII /vWF:Ag	> 0,7
vWF:Rco/WF:Ag	< 0,7

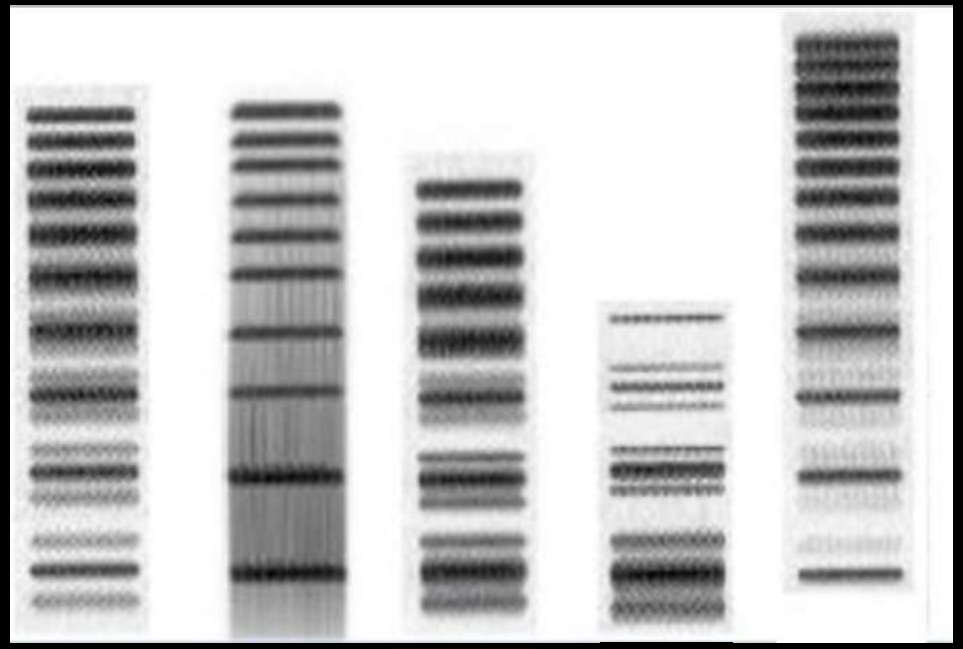
2B

Types ou sous type	2B
TO	↑
TCA	N ou ↑
FVIII	N ou ↓
vWF:Ag	N ou ↓
vWF:Rco	↓↓
FVIII /vWF:Ag	> 0,7
vWF:Rco/WF:Ag	< 0,7

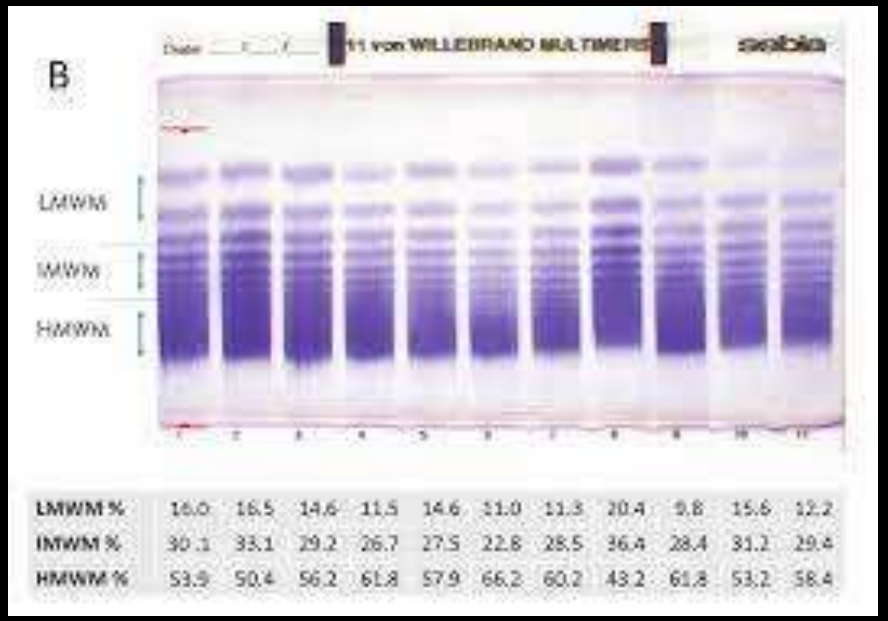
TESTS PLUS SPECIALISES

Evaluation du type

ELECTROPHORÈSE DES MULTIMÈRES DU VWF

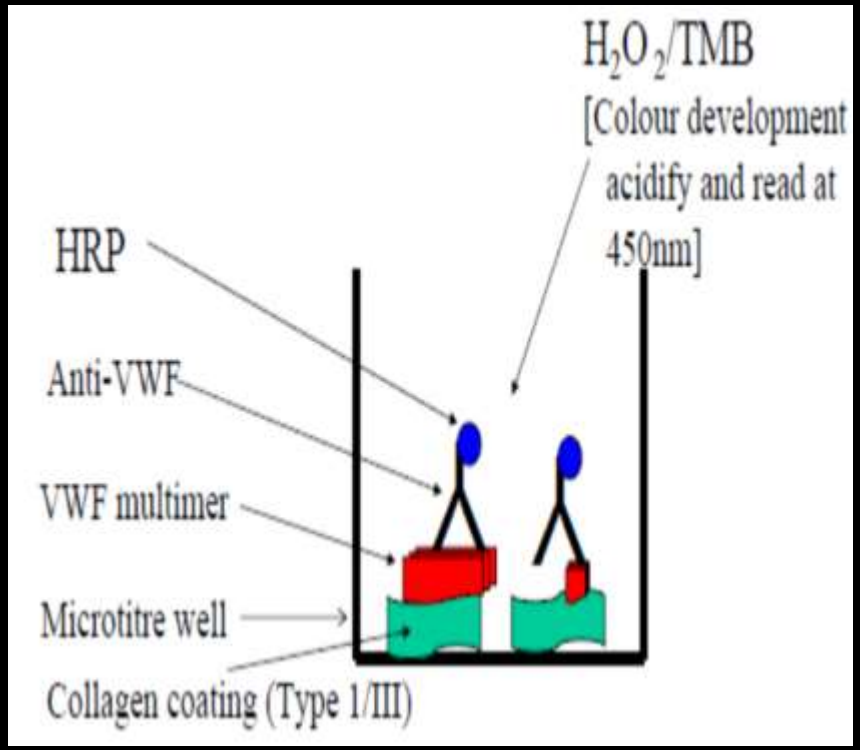


PN 2M 2B 2A Vicenza



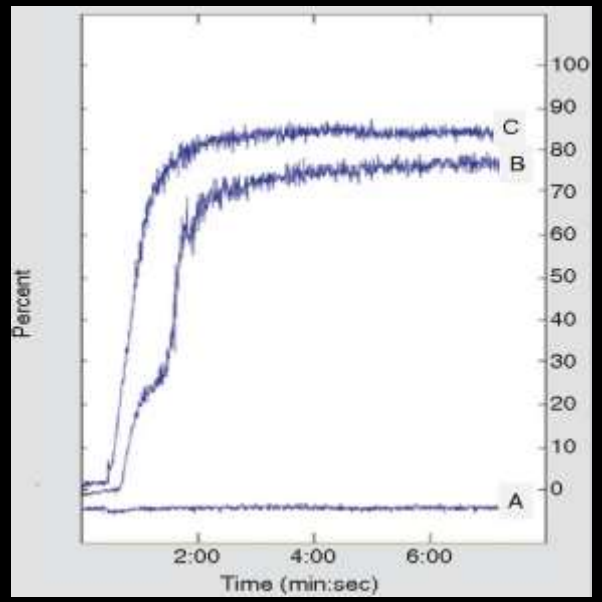
LMWM %	16.0	16.5	14.6	11.5	14.6	11.0	11.3	20.4	9.8	15.6	12.2
IMWM %	30.1	33.1	29.2	26.7	27.5	22.8	28.5	36.4	28.4	31.2	29.4
HMWM %	53.9	50.4	56.2	61.8	57.9	66.2	60.2	43.2	61.8	53.2	58.4

MESURE DE LA CAPACITÉ DE LIAISON DU VWF AU COLLAGÈNE (VWF:CB)



RISTOCETIN INDUCED PLATELET AGGREGATION (RIPA)

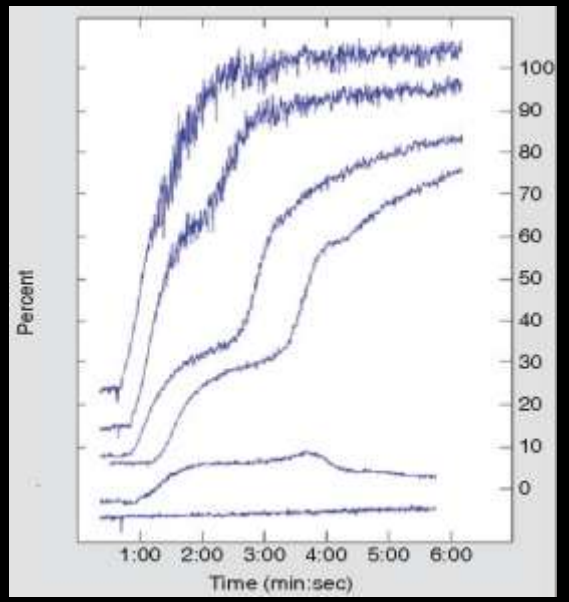
Sujet normal



1 mg/mL
0,8 mg/mL

0,6 mg/mL

Patient 2B

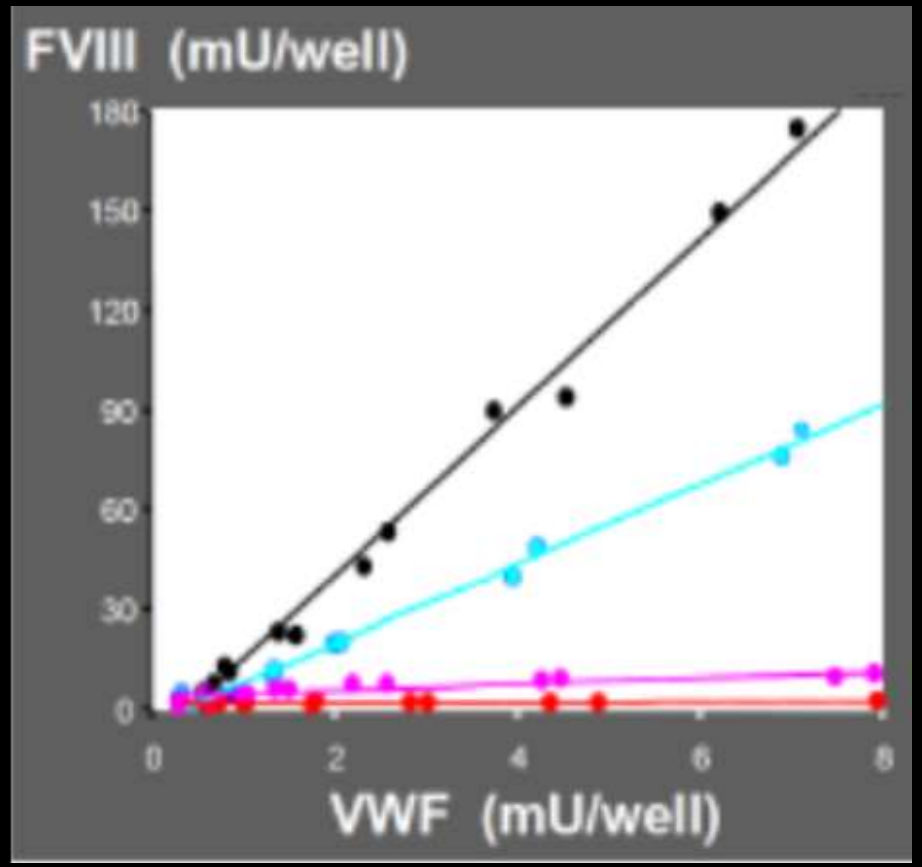


1 mg/mL
0,8 mg/mL
0,6 mg/mL ✗
0,5 mg/mL ✗

0,4 mg/mL
0,3 mg/mL

MESURE DE LA CAPACITÉ DE LIAISON DU VWF AU FVIII (VWF:FVIIIB)

ELISA



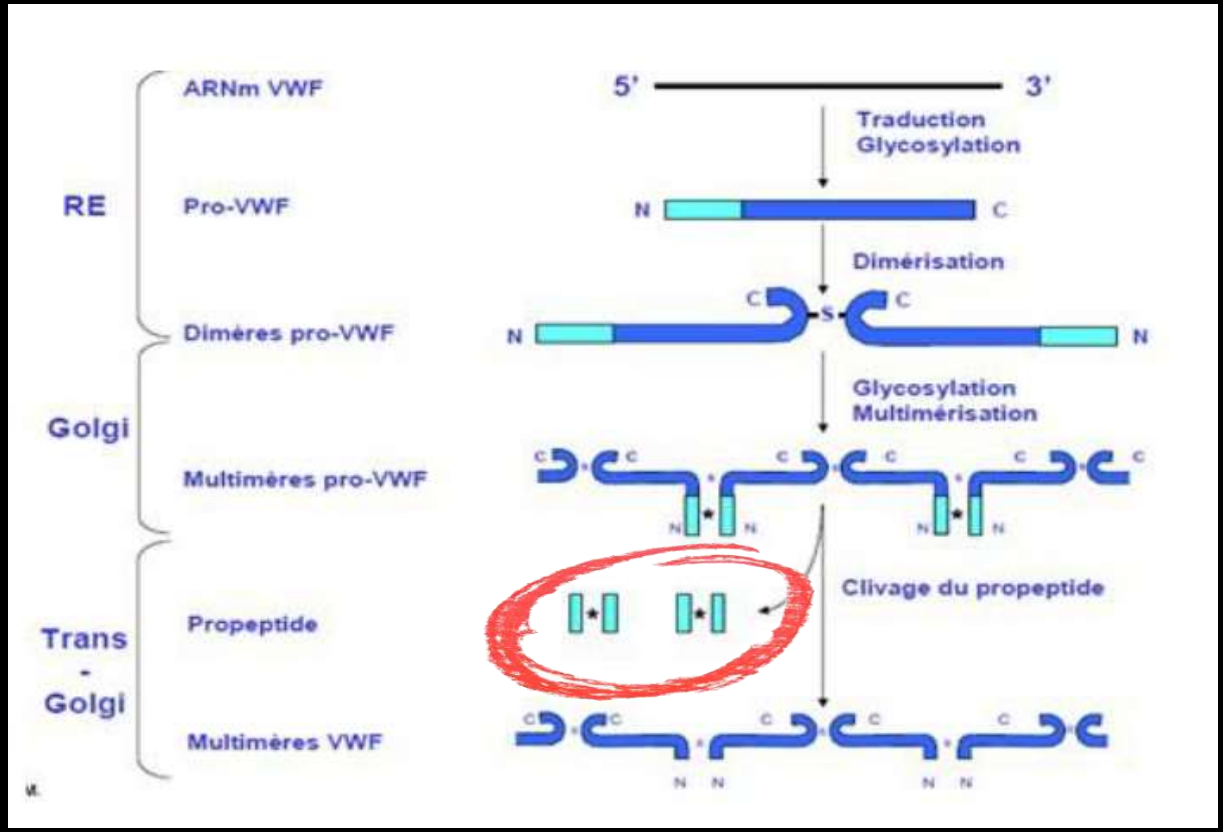
Normal

2N homozygote

2N hétérozygote

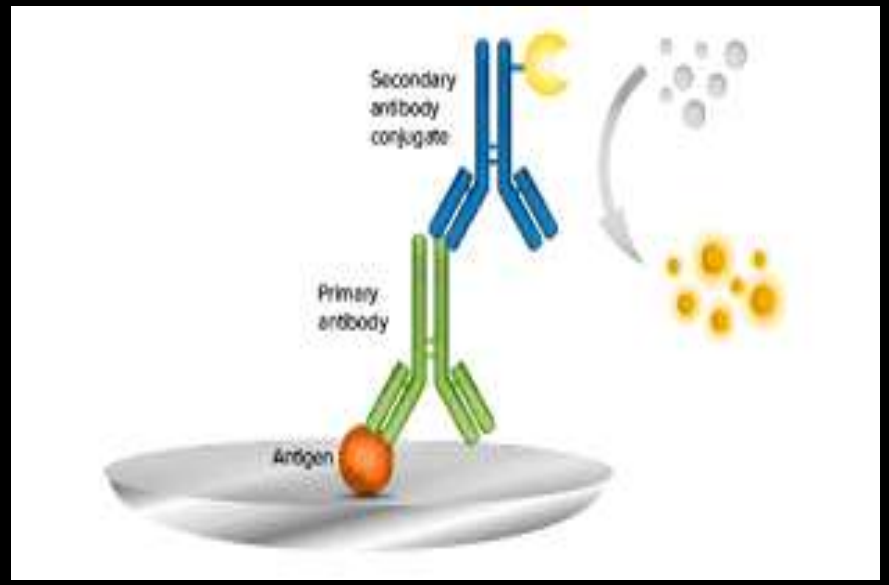
DOSAGE DU PROPEPTIDE VWF:PP

ELISA

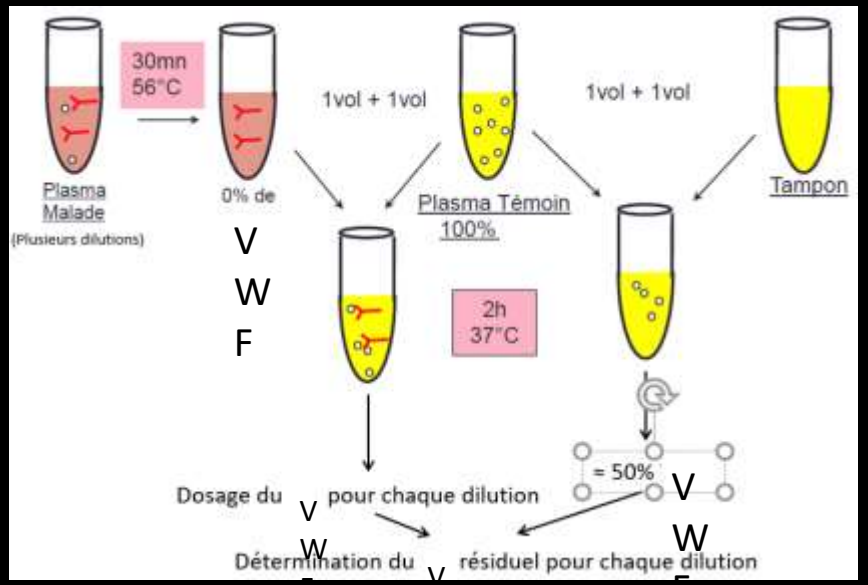


RECHERCHE D'ANTICORPS ANTI-VWF

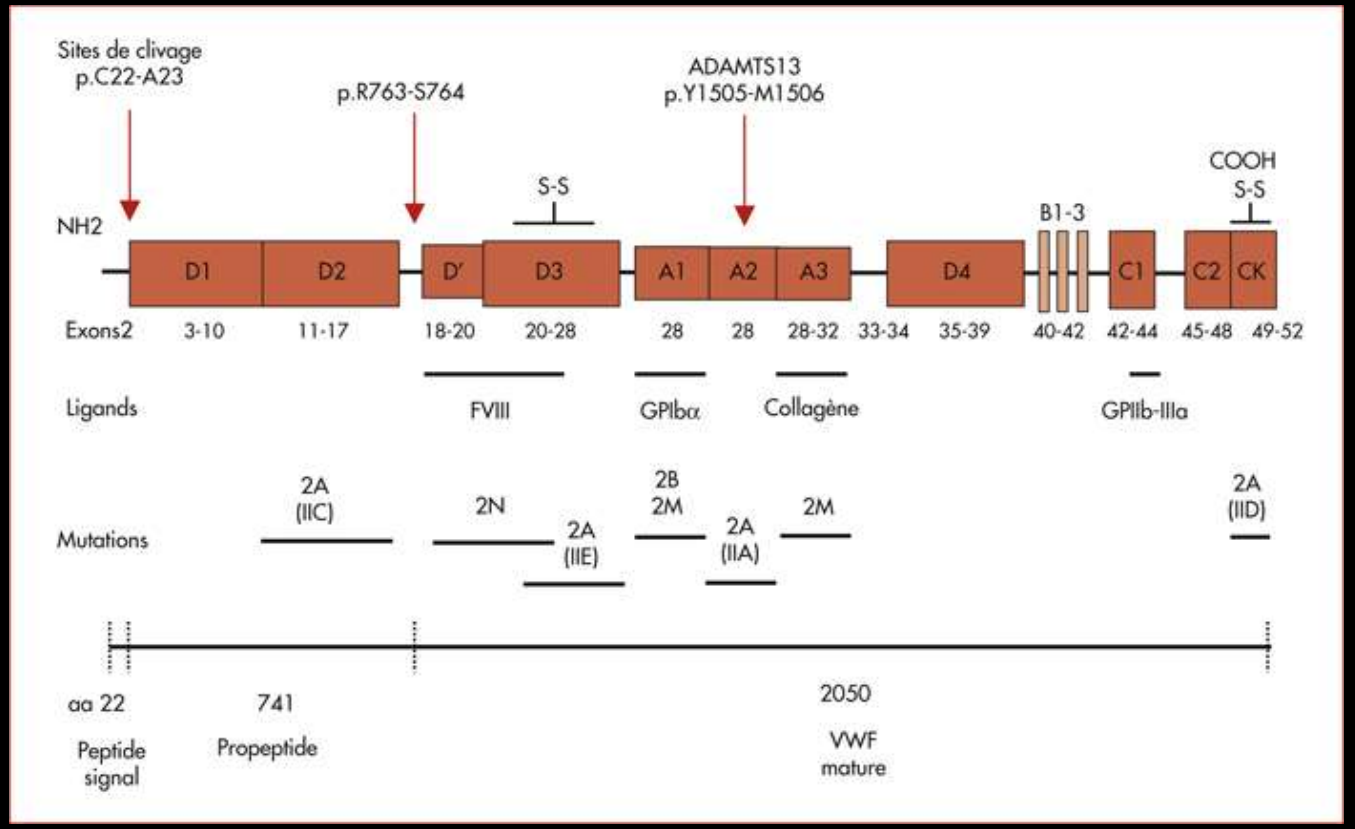
ELISA



Technique Bethesda



ETUDE MOLÉCULAIRE DU GÈNE VWF



PRISE EN CHARGE

TRANEXAMIC ACID

DESMOPRESSIN (DDAVP)

VWF REPLACEMENT THERAPY

IRON & HORMONAL THERAPIES

Willebrand

ISTH

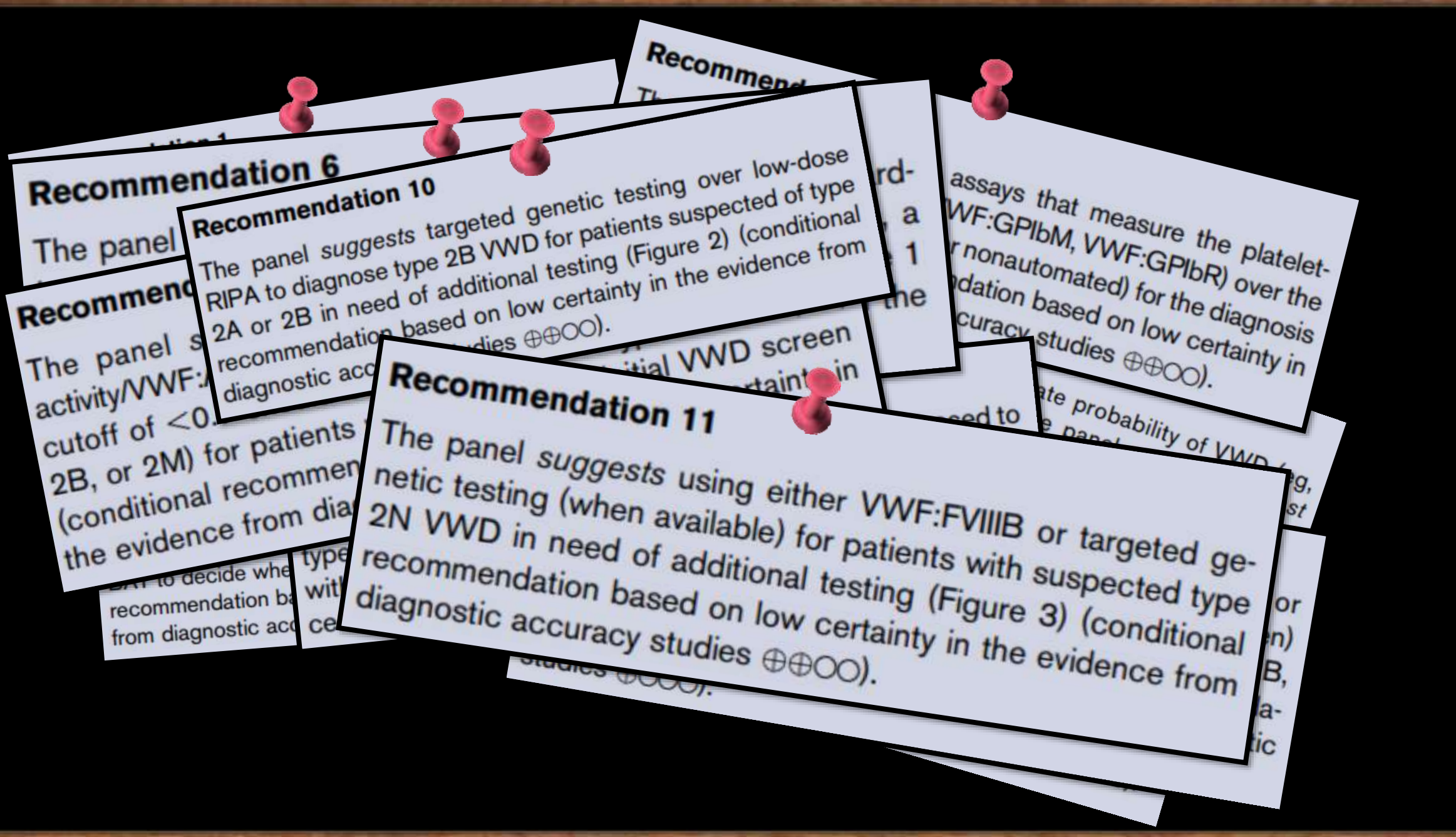
AMERICAN SOCIETY OF HEMATOLOGY

WFH

WORLD FEDERATION OF HEMOPHILIA

2021

NATIONAL HEMOPHILIA FOUNDATION


Recommendation 6
The panel
Recommendation 10
The panel suggests targeted genetic testing over low-dose RIPA to diagnose type 2B VWD for patients suspected of type 2A or 2B in need of additional testing (Figure 2) (conditional recommendation based on low certainty in the evidence from diagnostic acc
Recommendation 11
The panel suggests using either VWF:FVIIIB or targeted genetic testing (when available) for patients with suspected type 2N VWD in need of additional testing (Figure 3) (conditional recommendation based on low certainty in the evidence from diagnostic accuracy studies ⊕⊕◯◯).
assays that measure the platelet-
WF:GPIbM, VWF:GPIbR) over the
nonautomated) for the diagnosis
dation based on low certainty in
curacy studies ⊕⊕◯◯).

Merci