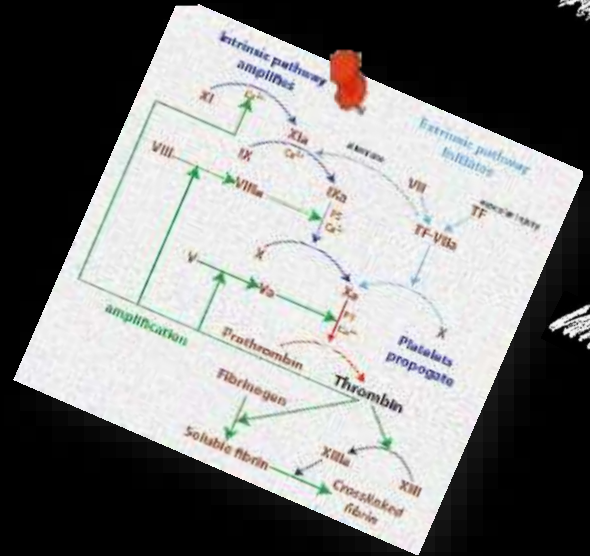
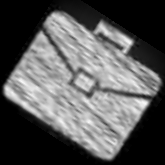
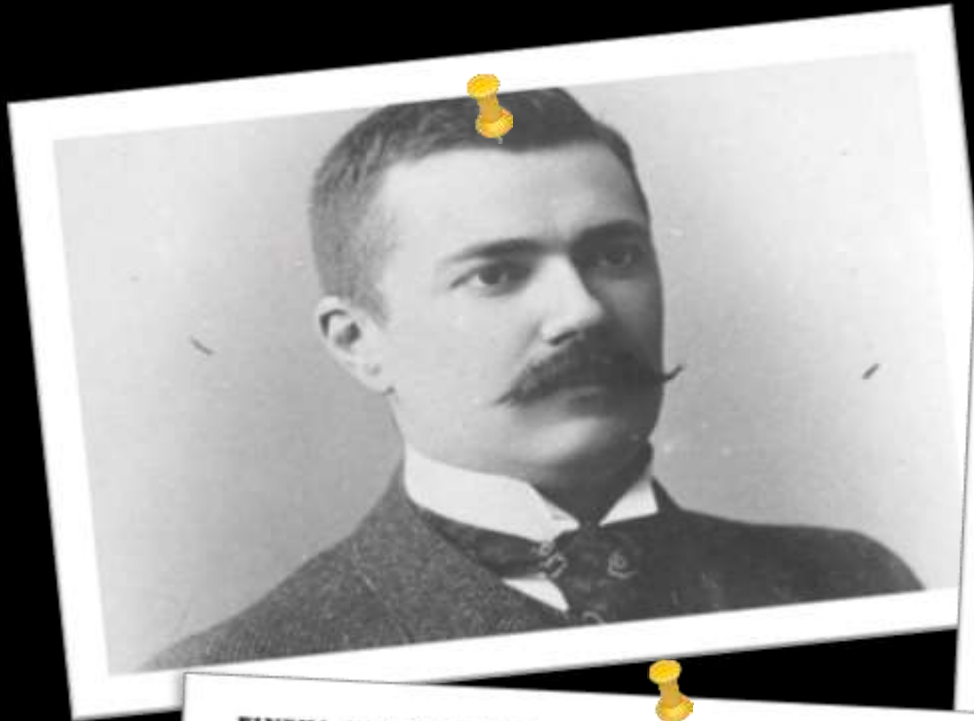


Maladie de Willebrand

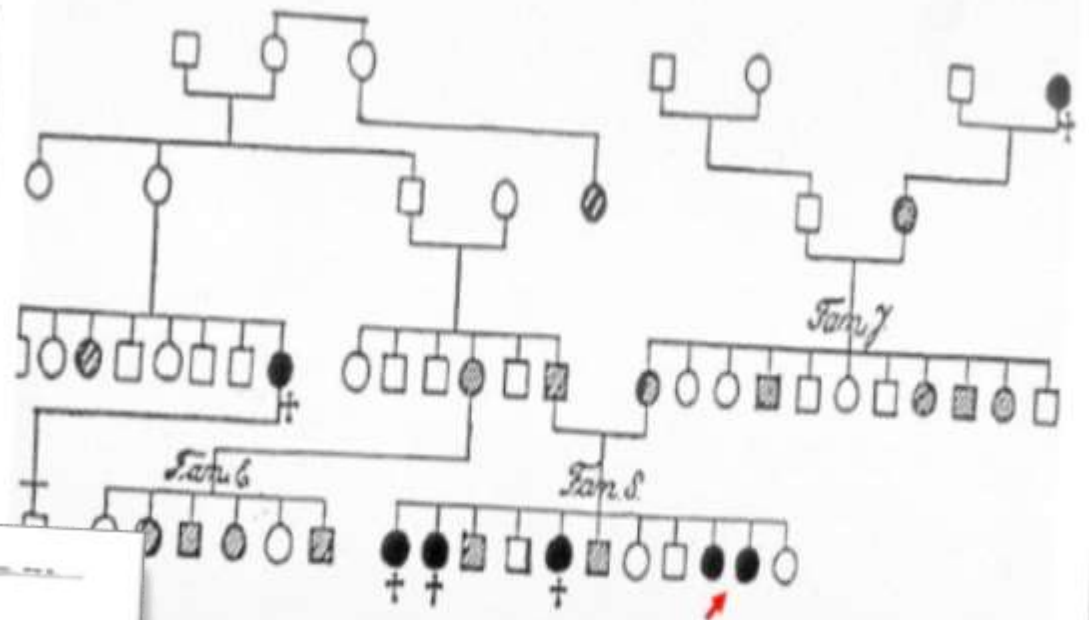


Dr. Abila AMARA PETITJEAN





Äländsk blodarestäkt



histoire

FINSKA LÄKARESÄLLSKAPETS HANDLINGAR
 UDGITT AF
PROF. RICHARD SEEVERS
 BAND LXVIII
 1926 FEBRUARI 1926

INNEHÅLL:

Originalartiklar:

Hereditär pseudo-hemofili.
 af
E. A. v. Willebrand.
 (Med 2 tabeller i texten.)

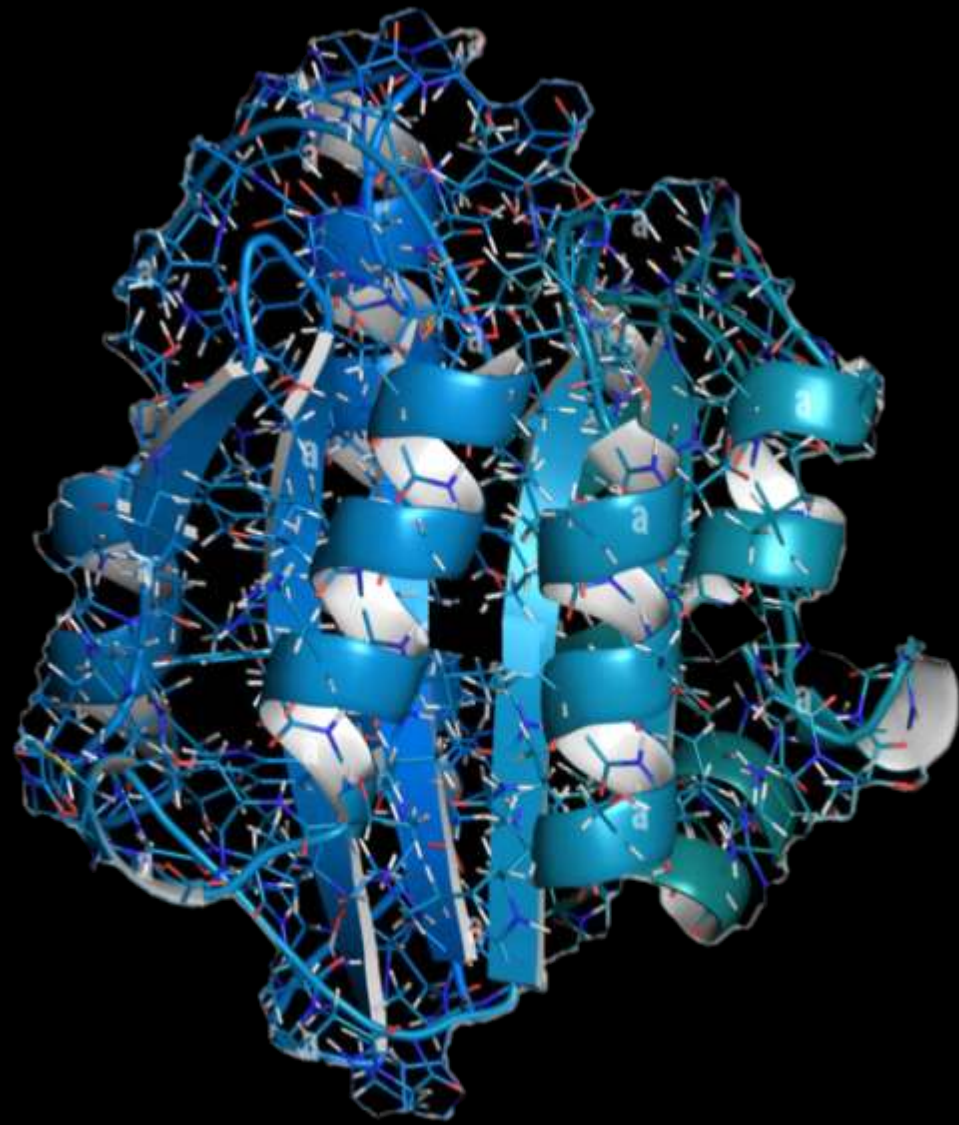
Stämmanderapport. Föregångna årsberättelse till 1926.

...inna icke-blodare. ■ man ○ kvinna med lindrig blodaresjuka ○ kvinna
 blodaresjuka + död av förblödning

1926

E. A. von Willebrand. *Einzelne* i *Åkars-sällskapets Handlingar* 1926: 20: 7-11.

Pseudo hémophilie

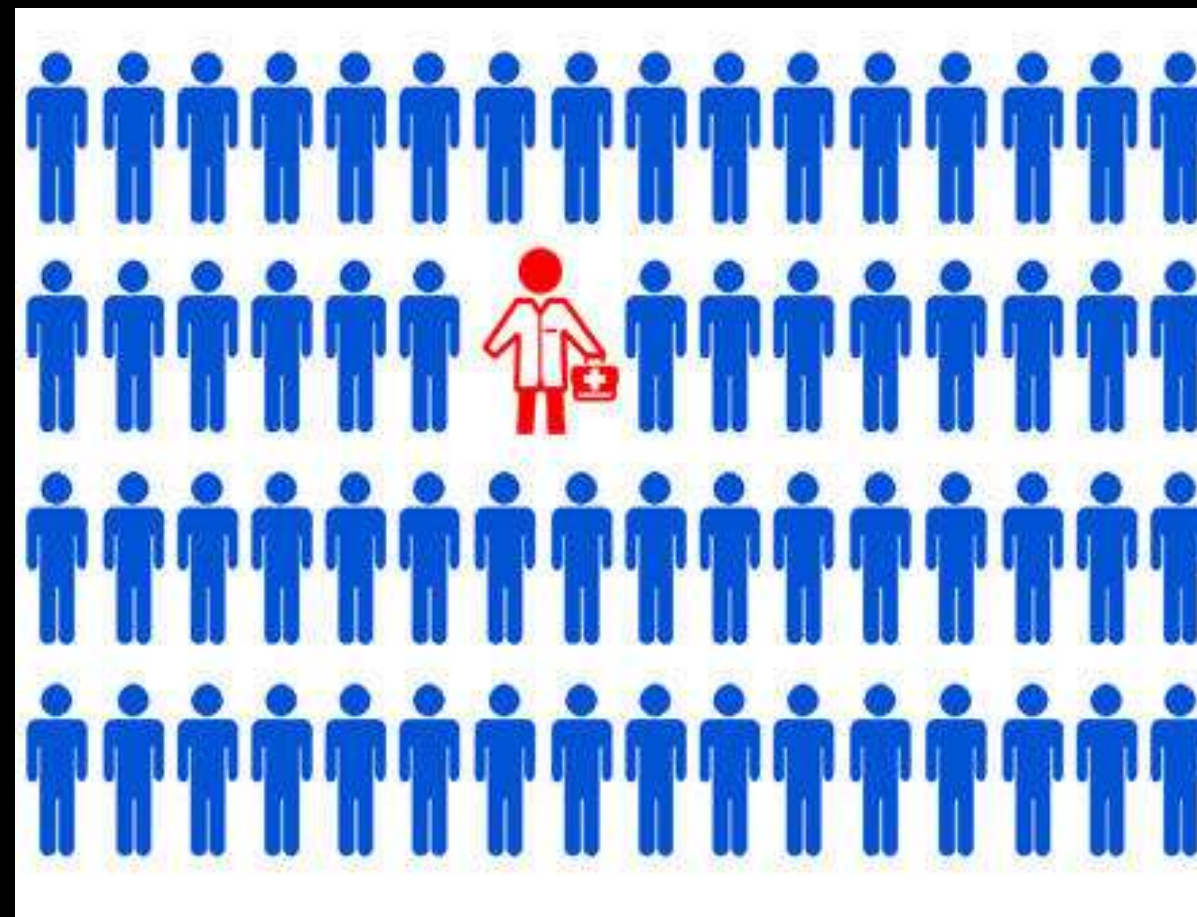


Facteur Von Willebrand

1 % de la population générale

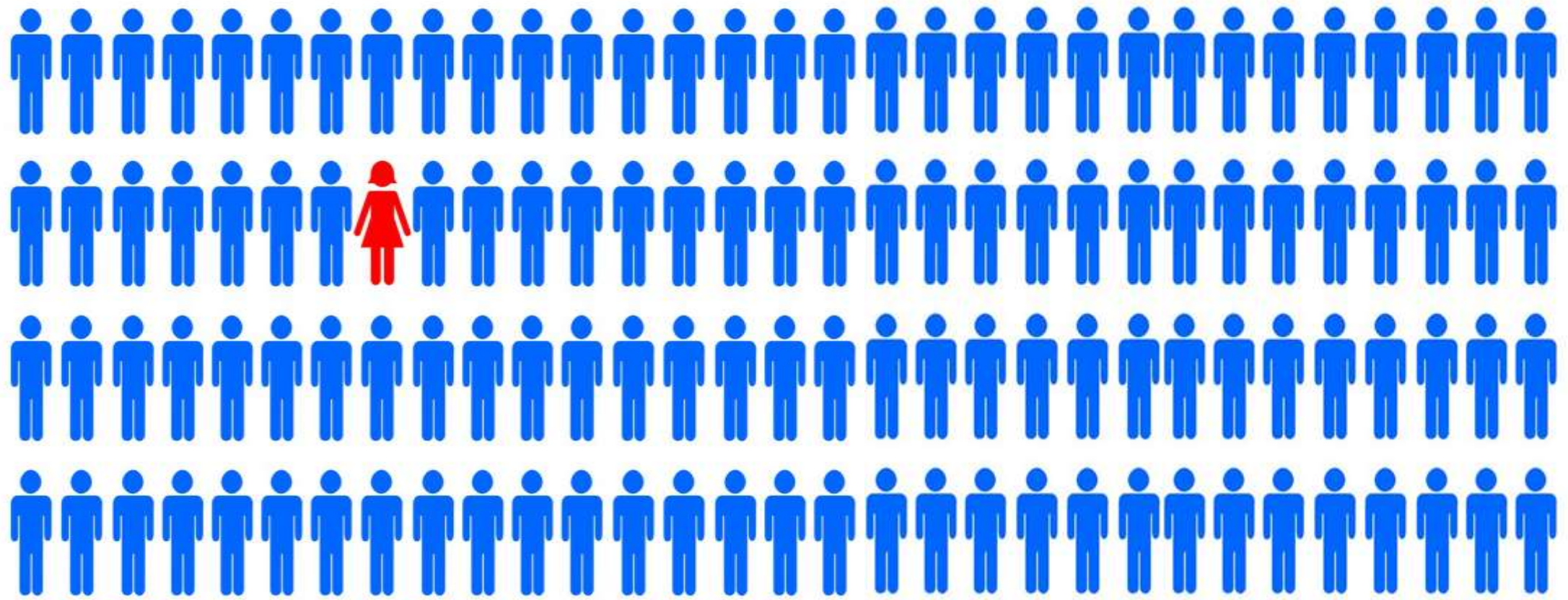


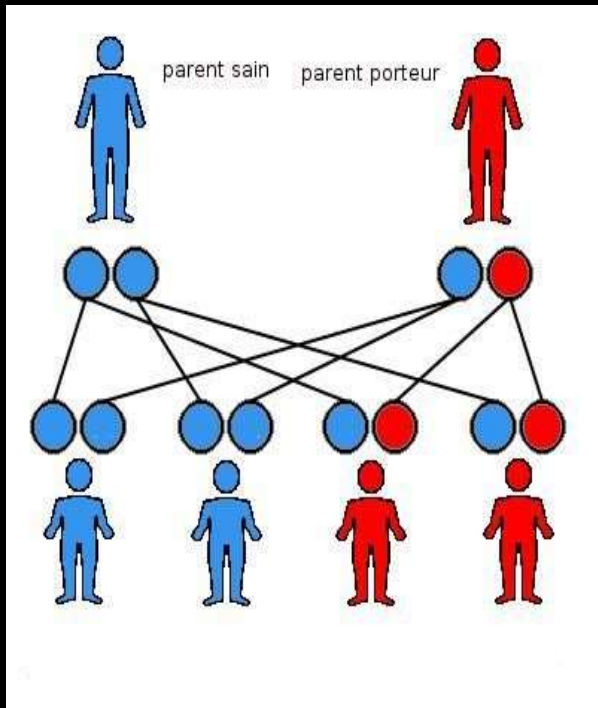
1 sur 10 000



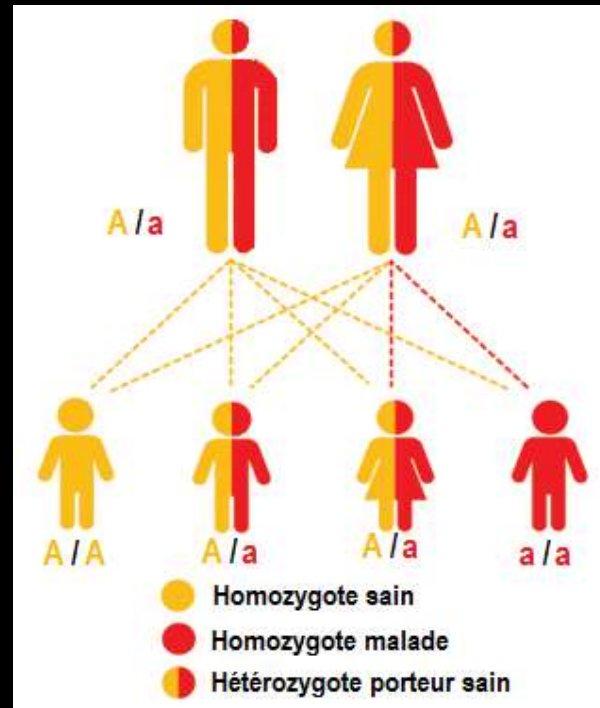
Type 3

1 par million d'habitants

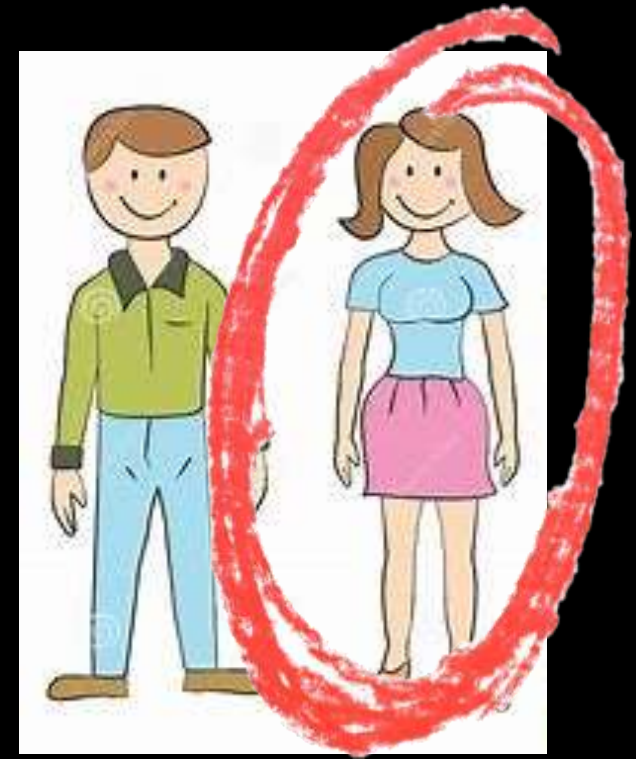




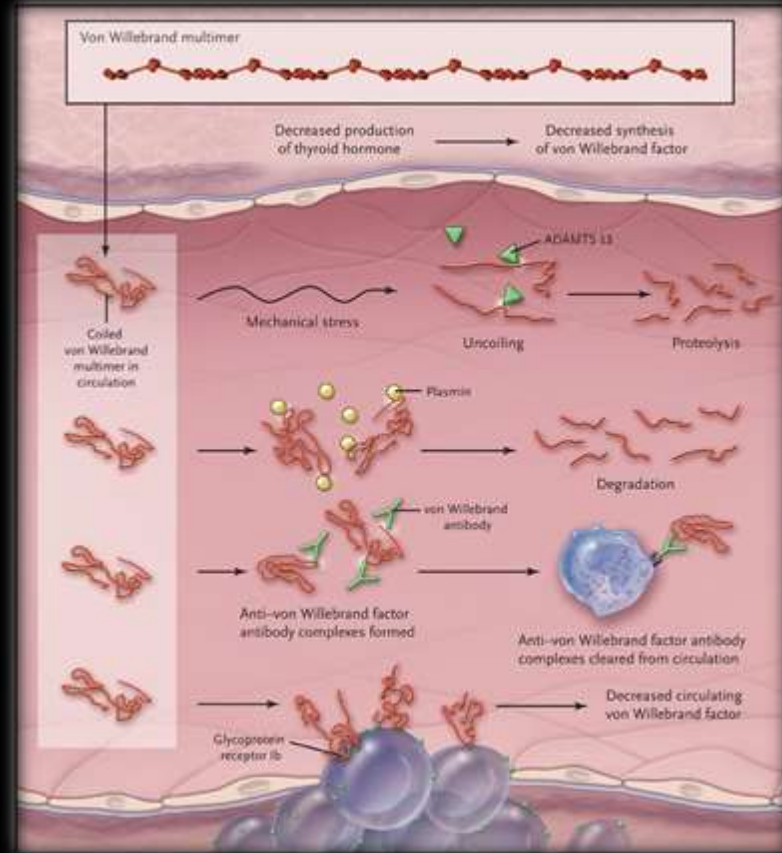
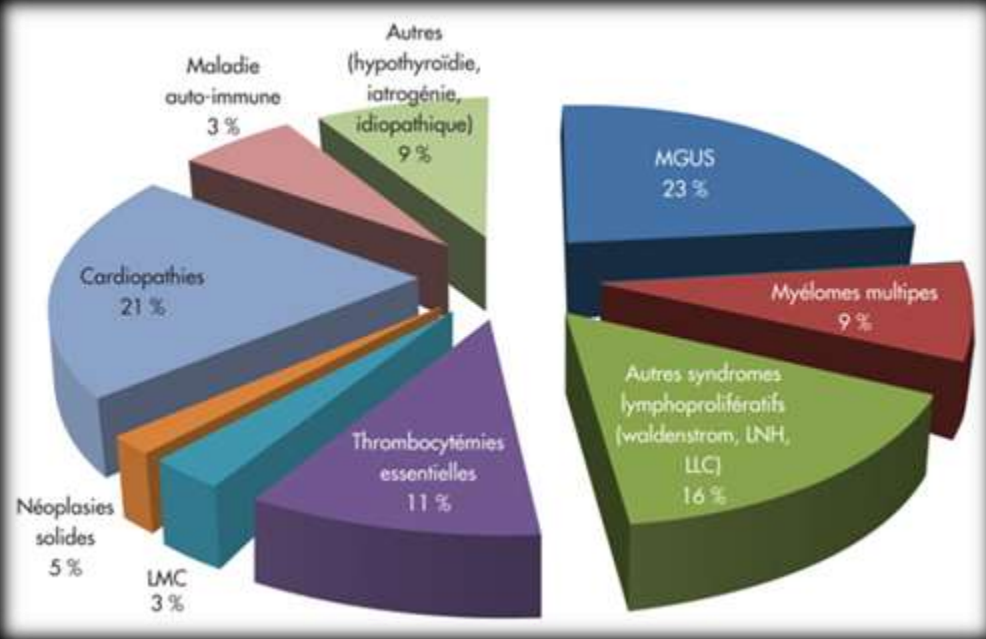
Autosomique dominante (Type 3 et 2N)



Autosomique récessive (Type 1 et 2)



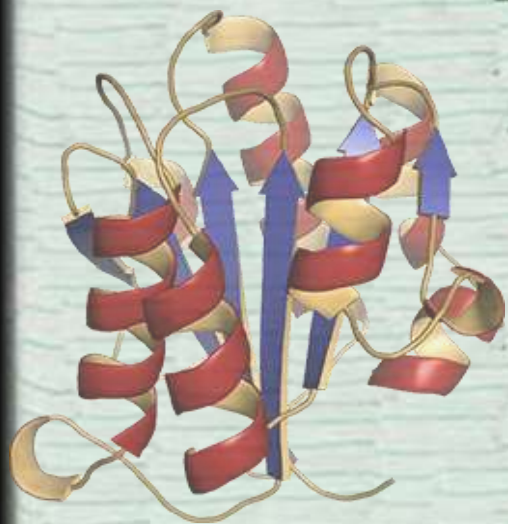
WILLEBRAND ACQUIS



R É P U B L I Q U E F R A N Ç A I S E

CARTE NATIONALE D'IDENTITÉ N° :

Nationalité Française



BS Nom :

Facteur Von Willebrand

Prénom(s) :

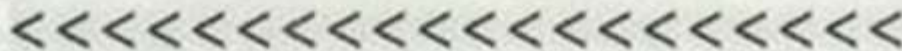
à : Mégacaryocytes, endothelium

Né(e) le : 1926

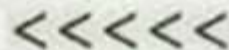
Taille : 500 à 1500 kD

Fonctions : Hémostase primaire / Coagulation

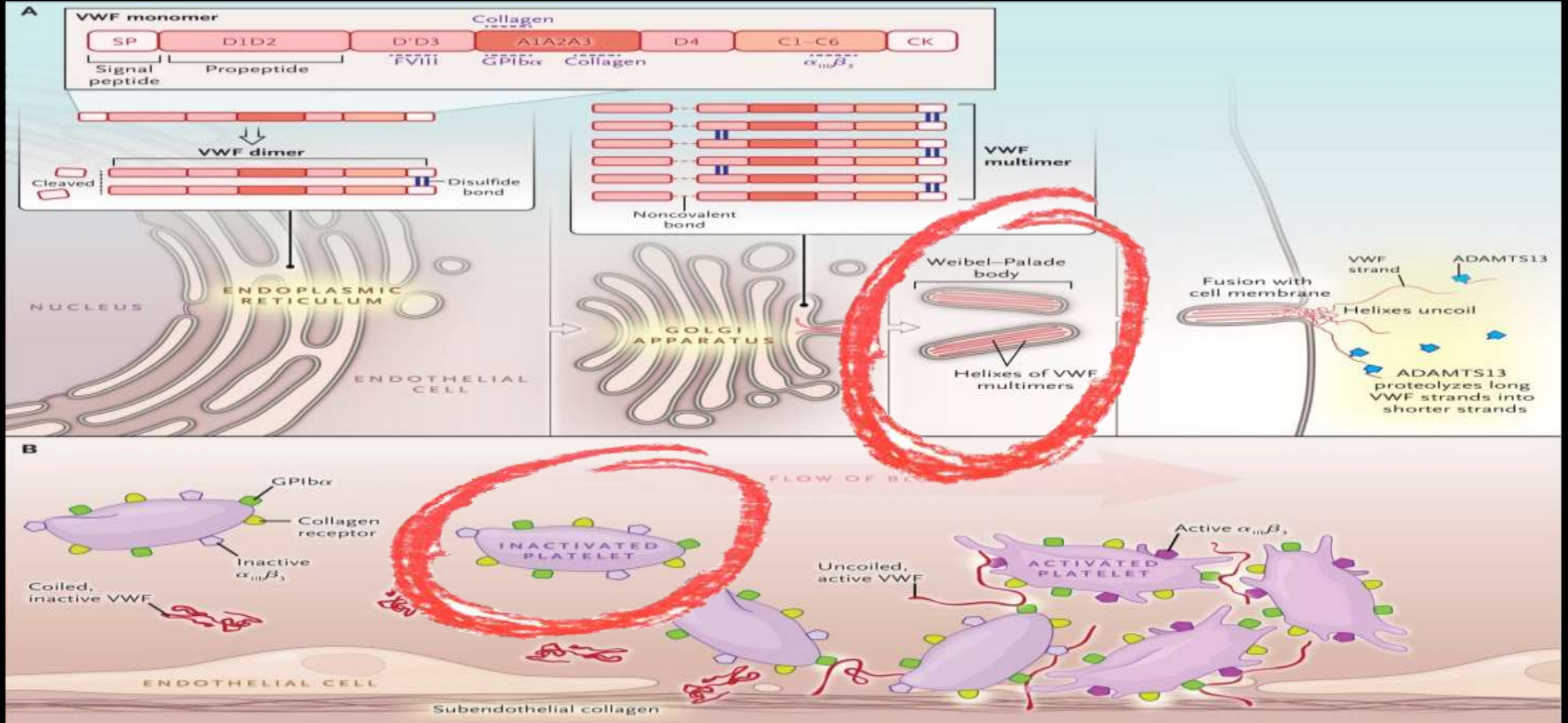
Adresse : Granules α , corps de Weibel Palade



S P É C I M E N



Biosynthesis



Multimères

micro-circulation

Pré-pro-VWF

Dimère de pro-VWF

Multimère de pro-VWF

Multimère de VWF



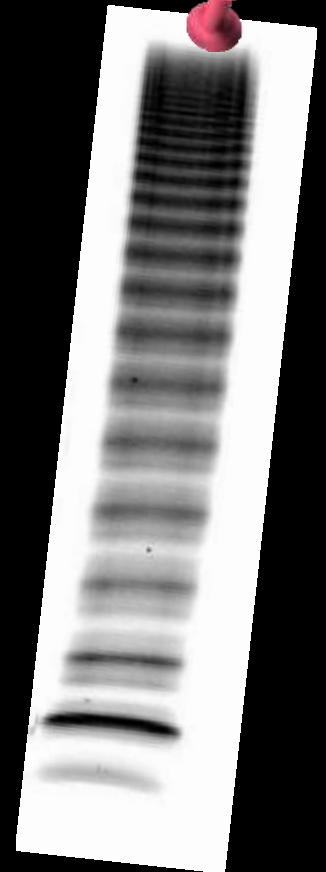
Reticulum
endoplasmique

Golgi

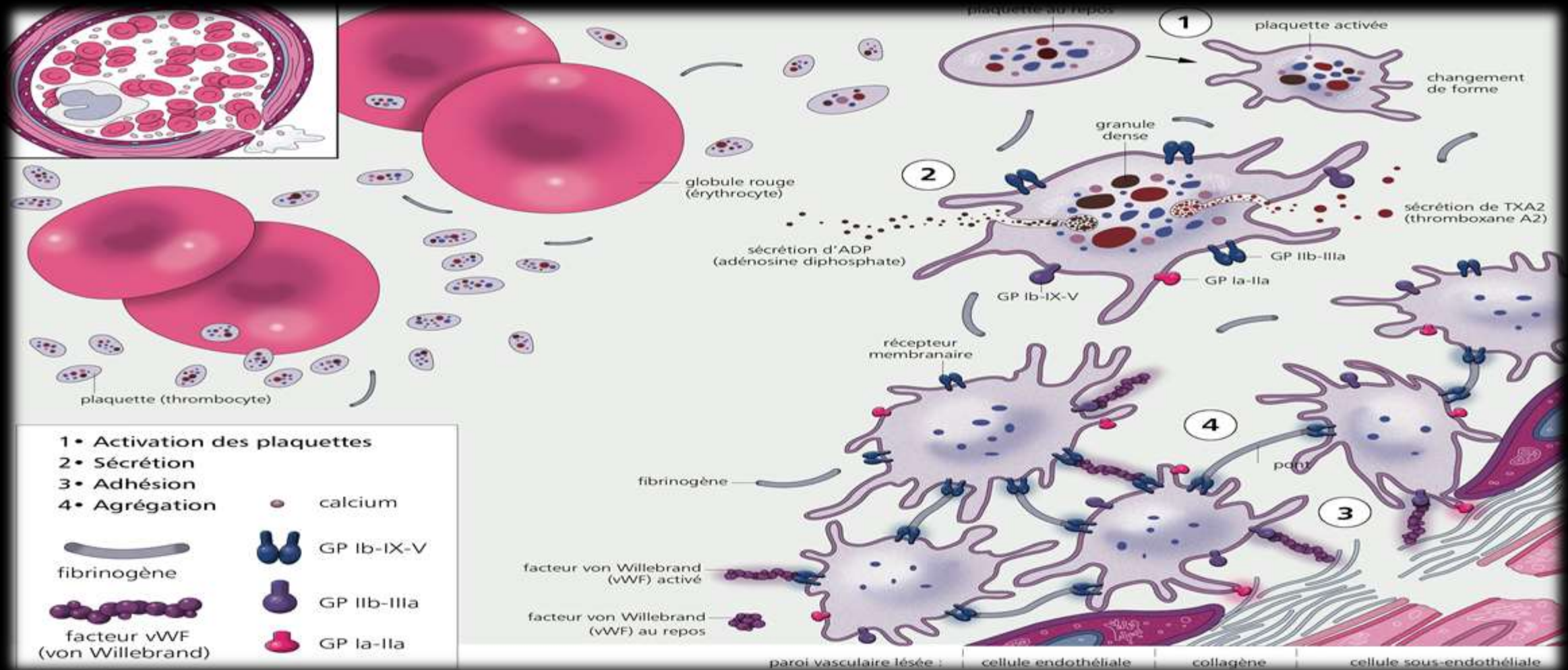
Corps
Weibel-Palade

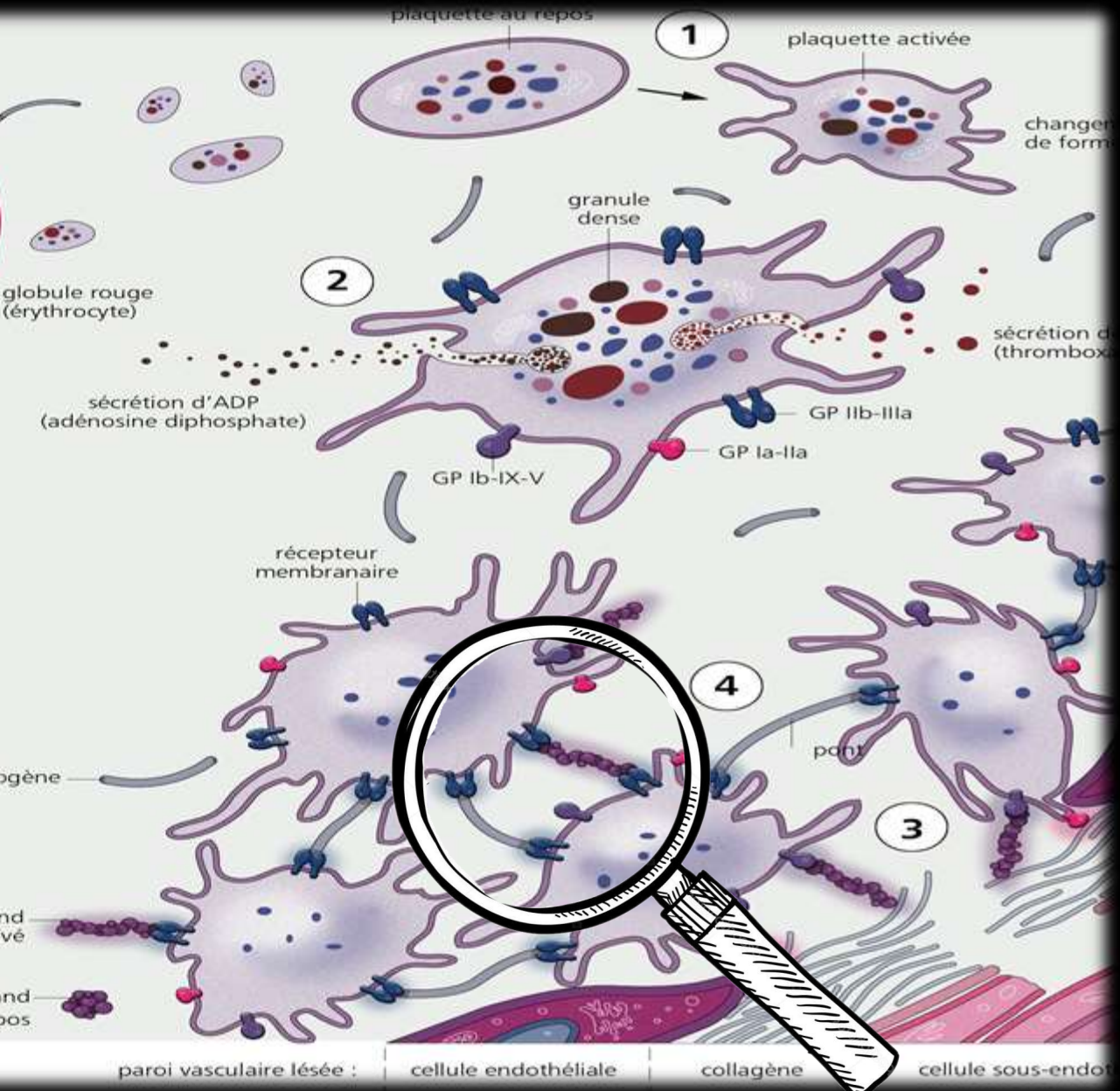
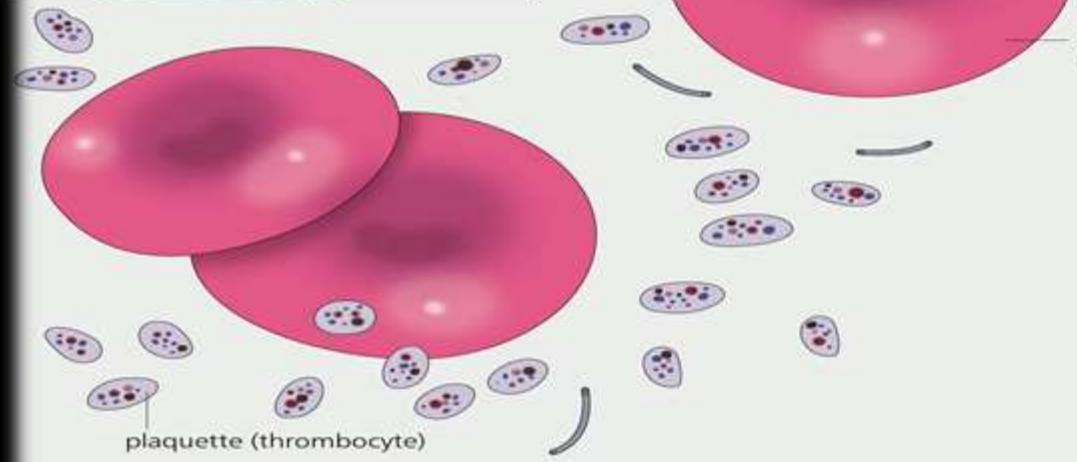
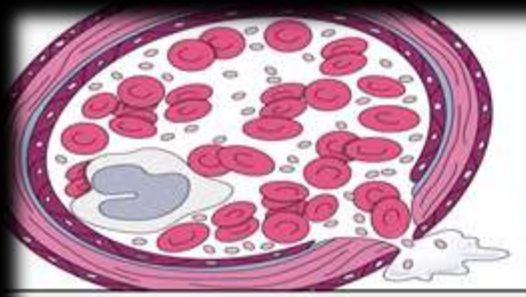
Peptide signal

Polypeptide



liaison des plaquettes aux composants du sous endothélium





1 • Activation des plaquettes
 2 • Sécrétion
 3 • Adhésion
 4 • Agrégation

● calcium

fibrinogène

facteur vWF (von Willebrand)

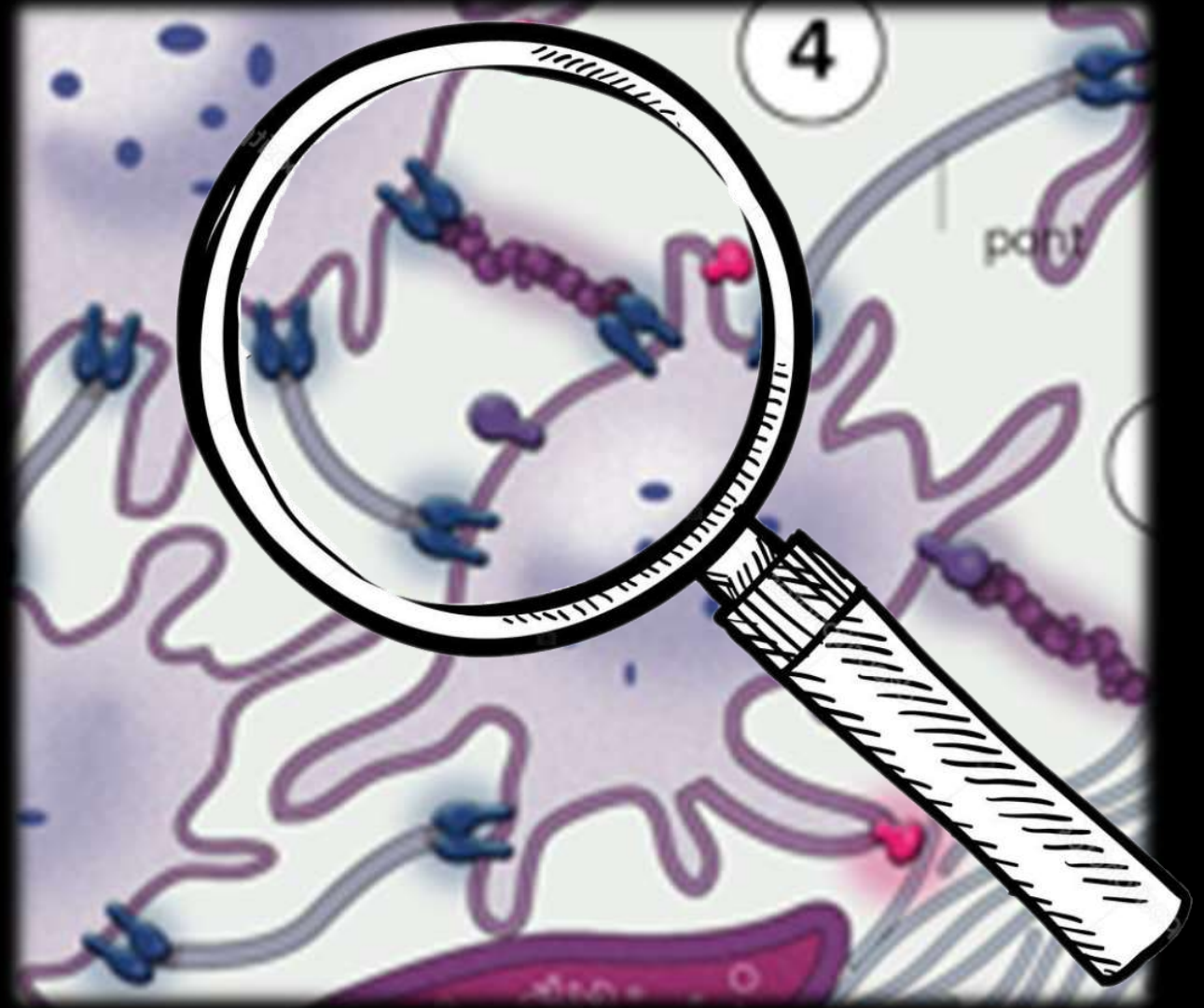
● GP Ib-IX-V

● GP IIb-IIIa

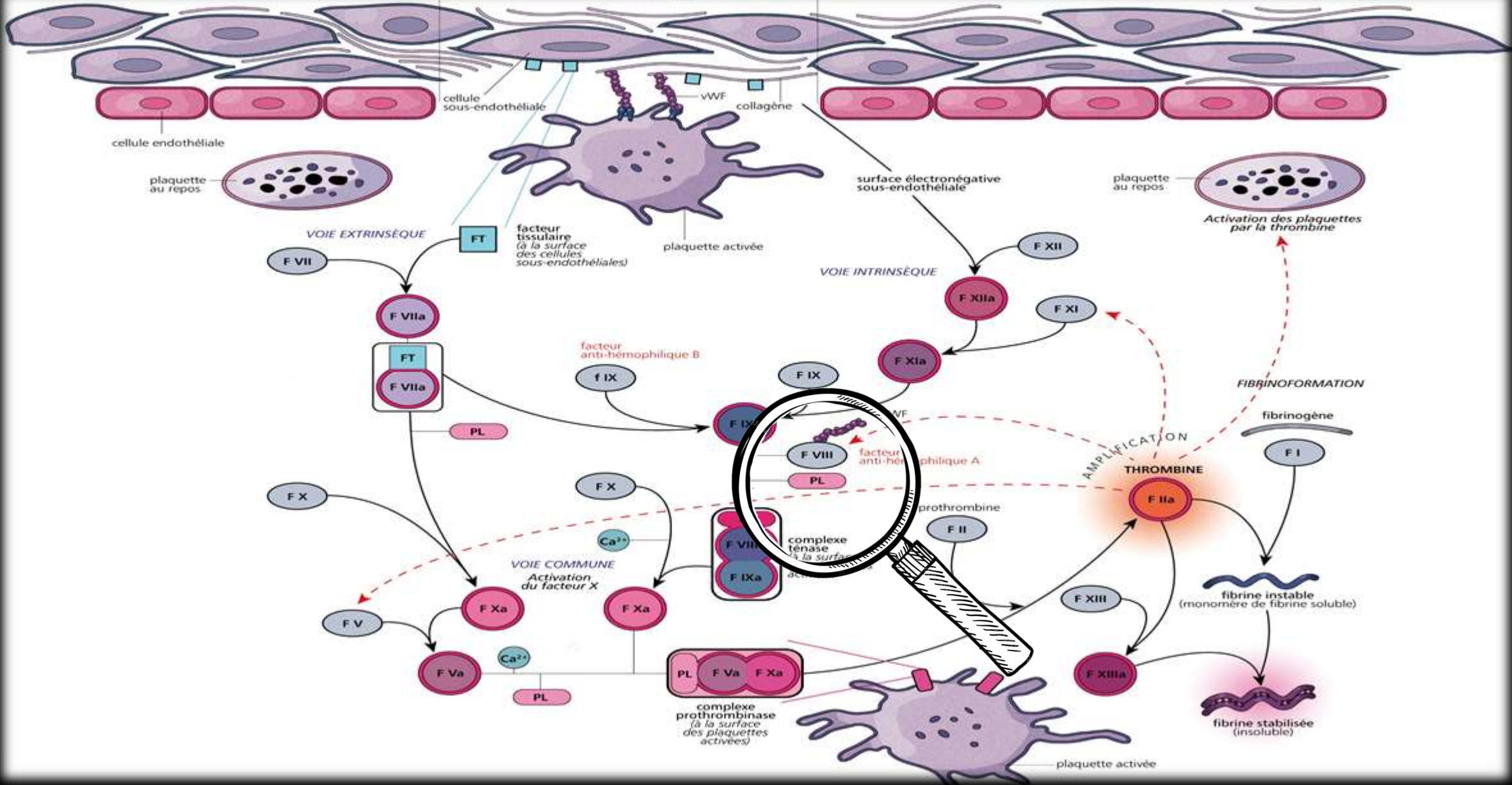
● GP Ia-IIa

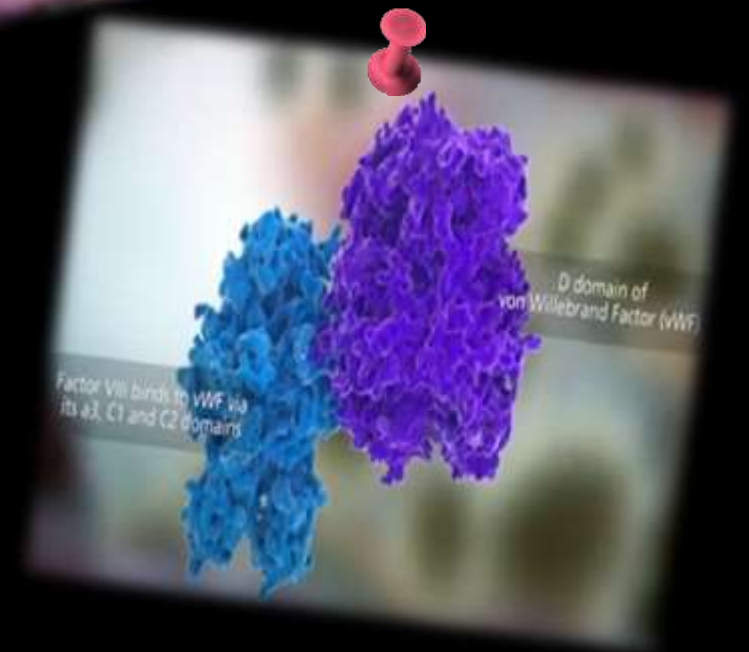
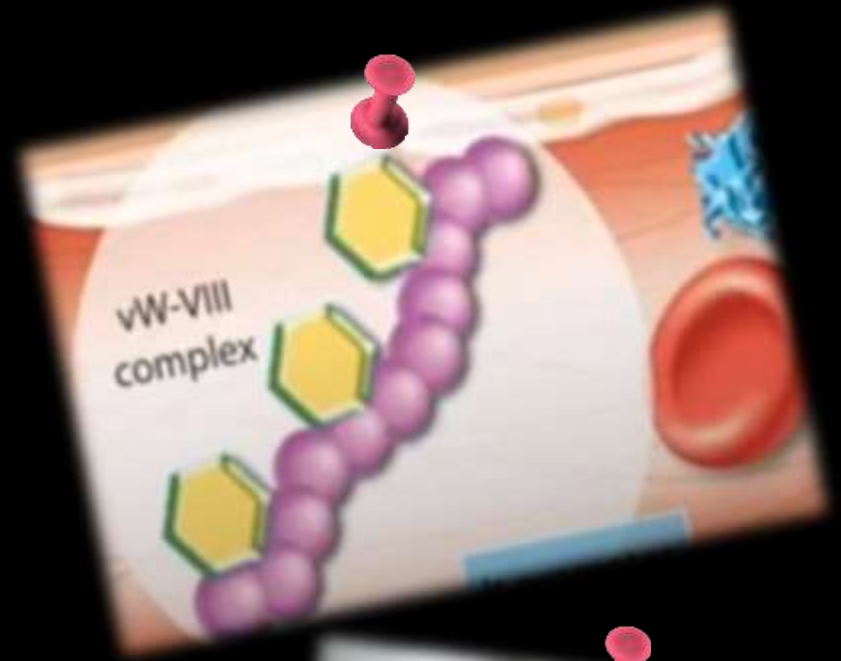
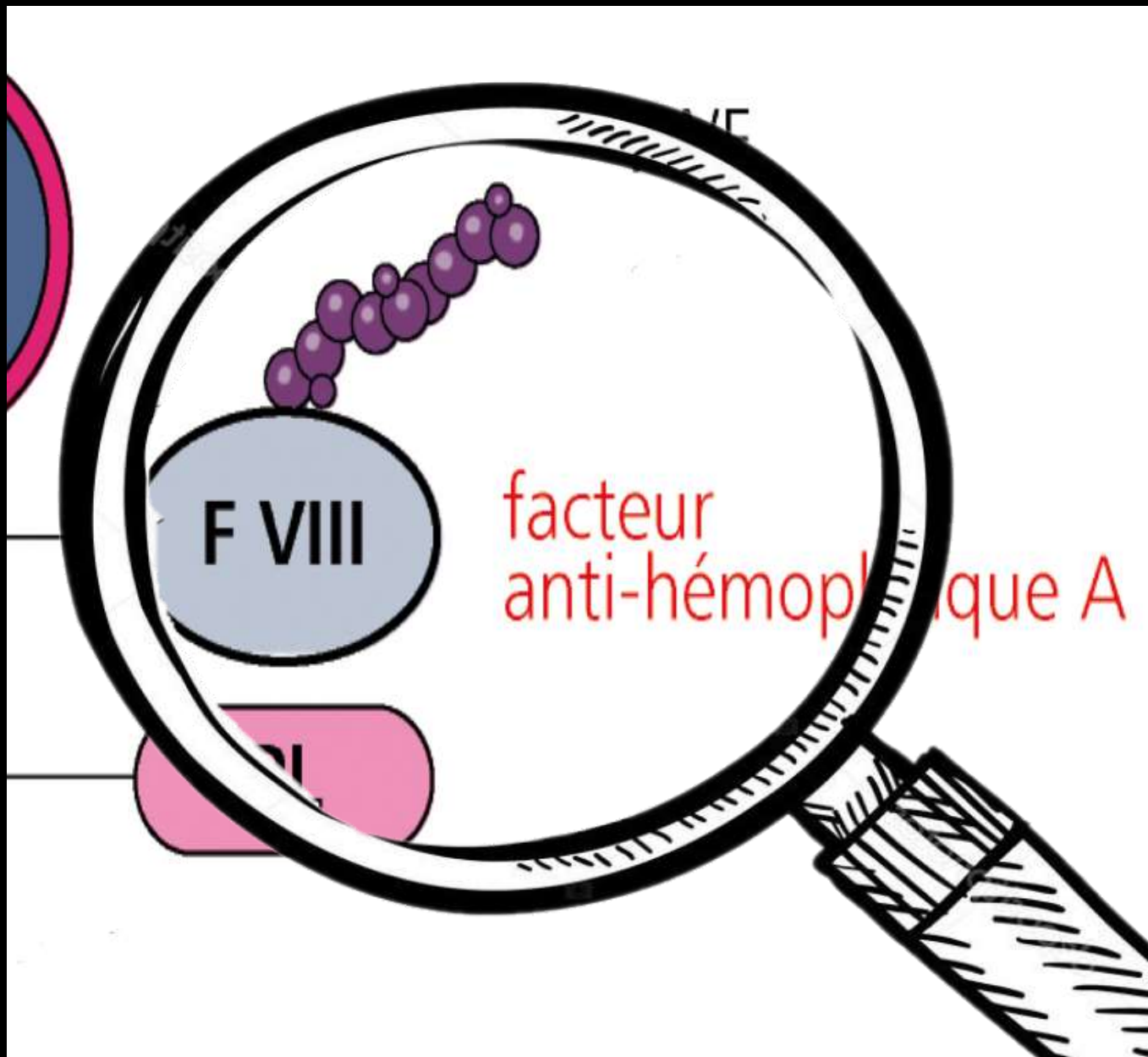
GP IBIX

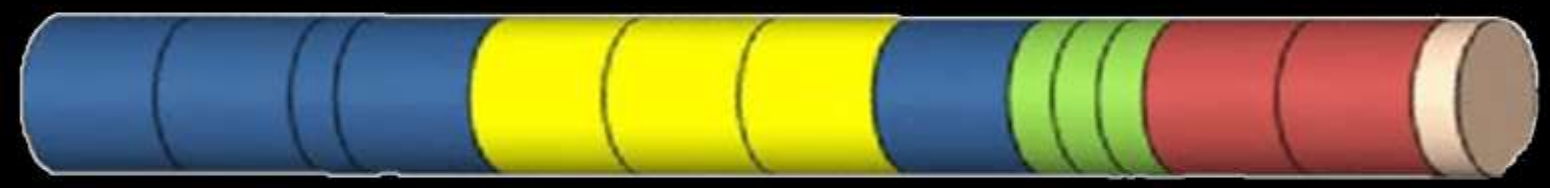
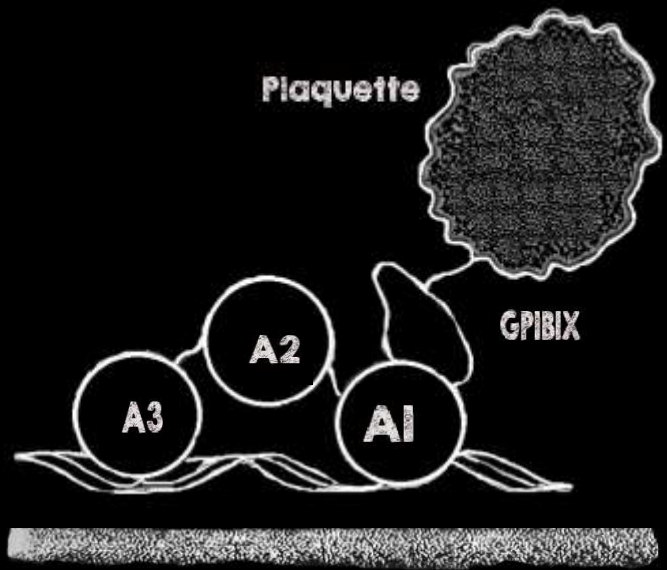
COLLAGENE



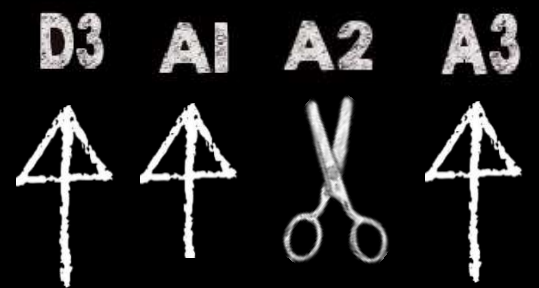
PLAIE VASCULAIRE







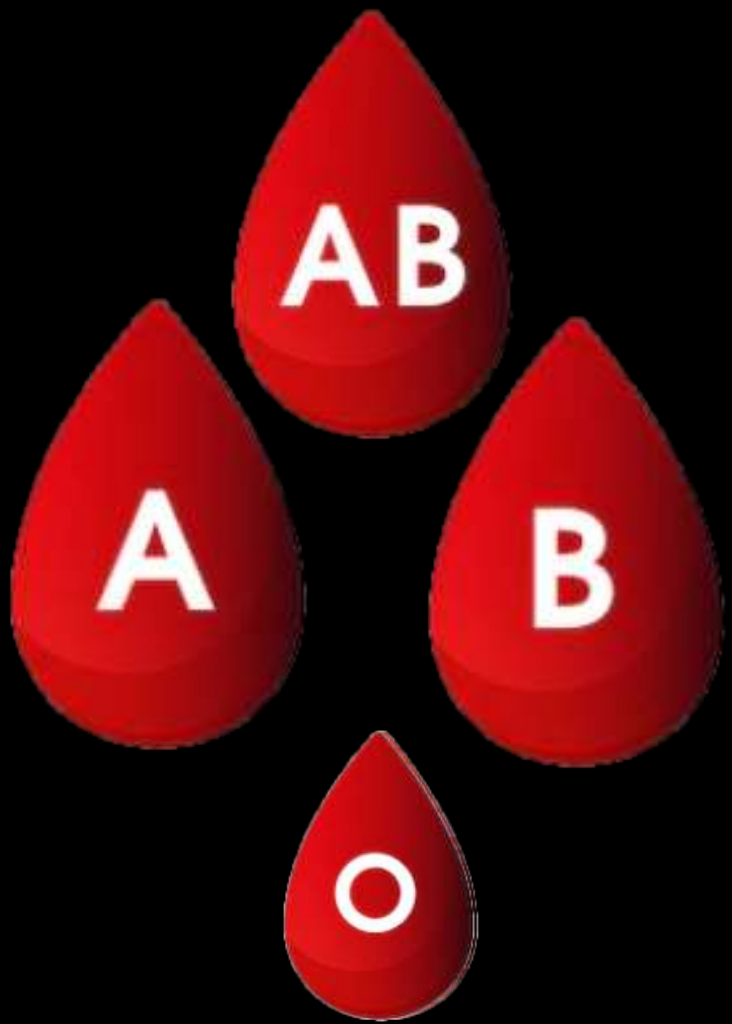
Pro-vWF



FVIII **GPIIB/IIIa** **ADAMTS13** **Collagène**



GPIIb/IIIa



VWF 




Stress

Sepsis Strenuous exercise Severe illness Phlebotomy



Chronic endothelial activation

Cardiovascular disease Hypertension Diabetes



VWF 

CLASSIFICATION



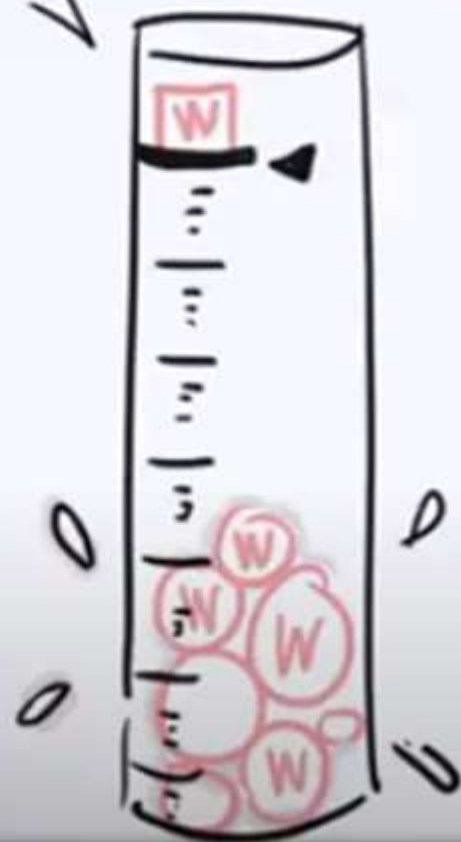
TYPE 1

TYPE 1

TYPE 1

TYPE 1

pas assez.



TYPE 1

TYPE 1

TYPE 1

TYPE 3

TYPE 3

TYPE 3

TYPE 3



TYPE 3

TYPE 3

TYPE 2



TYPE 2

TYPE 2



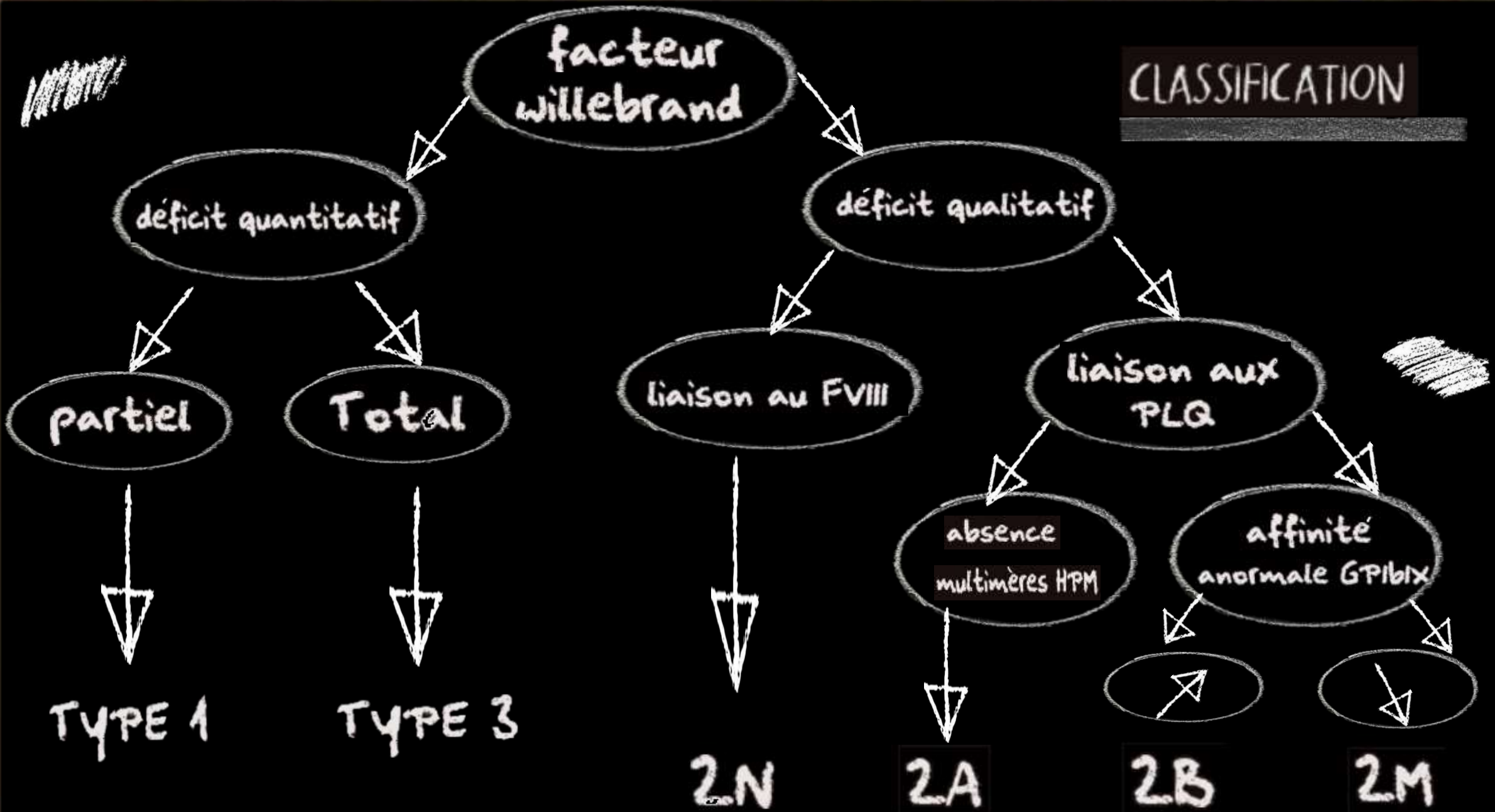
TYPE 2



TYPE 2



CLASSIFICATION





SYMPTOMS

HEMORRAGIES CUTANEO-MUQUEUSES

EMENORRAGIES ONGES



SAIGNEMENTS POST-TRAUMATIQUES POST-CHIRURGICAUX



FORMES SEVERES

HEMARTHROSE DND





DIAGNOSTIC ?





PL SYMT WILLEBRAND
HISTOIRE FAMILIALE



SCORE HEMORRAGIQUE BAT

SCORE 8





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

ISTH-BAT \geq 3 POUR LES $<$ 18 ANS

ADULTES (\geq 4 POUR LES HOMMES, \geq 6 POUR LES FEMMES)

ISTH-BAT \geq 4 POUR LES ADOLESCENTES

Limitations of ISTH BAT scores

Saturable	Adolescent reference range		Few hemostatic challenges
			
Nosebleed - cauterized once BS = 3	15 years old BS = 4	19 years old BS = 4	BS may be lower in those with limited hemostatic challenges
Multiple cauterizations BS still = 3	Positive BS	Negative BS	

Multiple cauterizations
BS still = 3

Positive
BS

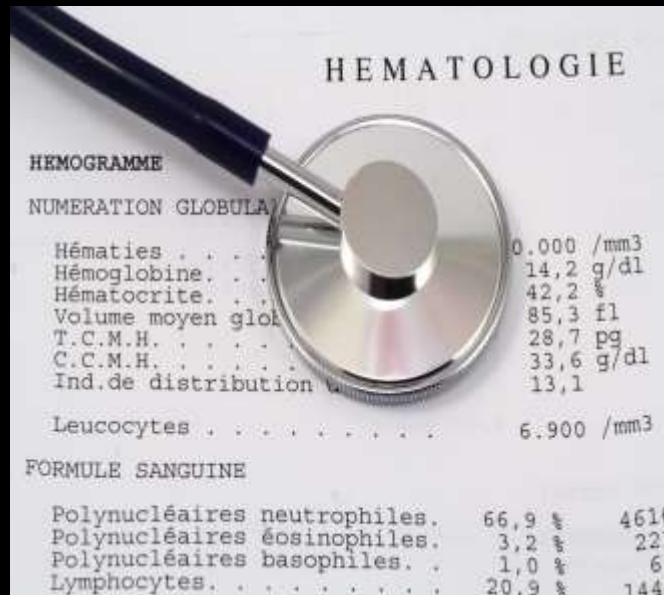
Negative
BS

challenges
hemostatic
with limited

QUEL BILAN PRESCRIRE ?



TESTS DE PREMIERE INTENSION



HEMATOLOGIE

HEMOGRAMME

NUMERATION GLOBULAIRE

Hématies	10.000 /mm ³
Hémoglobine	14,2 g/dl
Hématocrite	42,2 %
Volume moyen glob	85,3 fl
T.C.M.H.	28,7 pg
C.C.M.H.	33,6 g/dl
Ind.de distribution v	13,1

Leucocytes 6.900 /mm³

FORMULE SANGUINE

Polynucléaires neutrophiles	66,9 %	4616
Polynucléaires éosinophiles	3,2 %	221
Polynucléaires basophiles	1,0 %	69
Lymphocytes	20,9 %	1441



NFS (NUMERATION PLAQUETTAIRE)

TEMPS DE CEPHALINE ACTIVE

TEMPS D'OCCLUSION PLAQUETTAIRE (PFA)

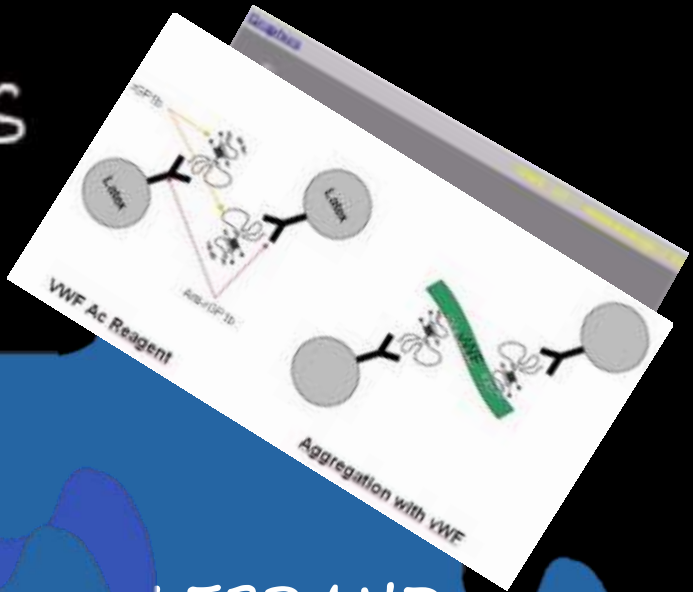
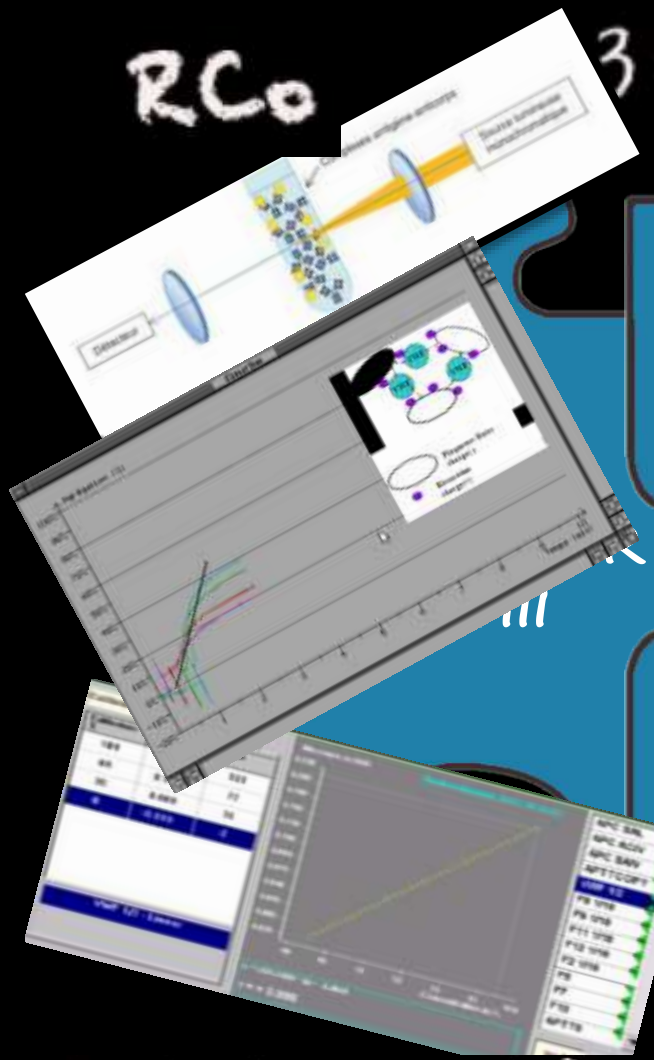
TESTS SPECIFIQUES

Diagnostic



RCo

3 Dosages associables



WILLEBRAND
ACTIVITE

WILLEBRAND
ACTIVITE

GPIIbR

GPIIbM

Seuil de quantification

normes : 50-150 %

Ratios

VWF Act/VWF Ag \rightarrow $>0,7$ TYPE 1
 \rightarrow $<0,7$ 2A 2B 2M

FVIII /VWF Ag \rightarrow $<0,7$ 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

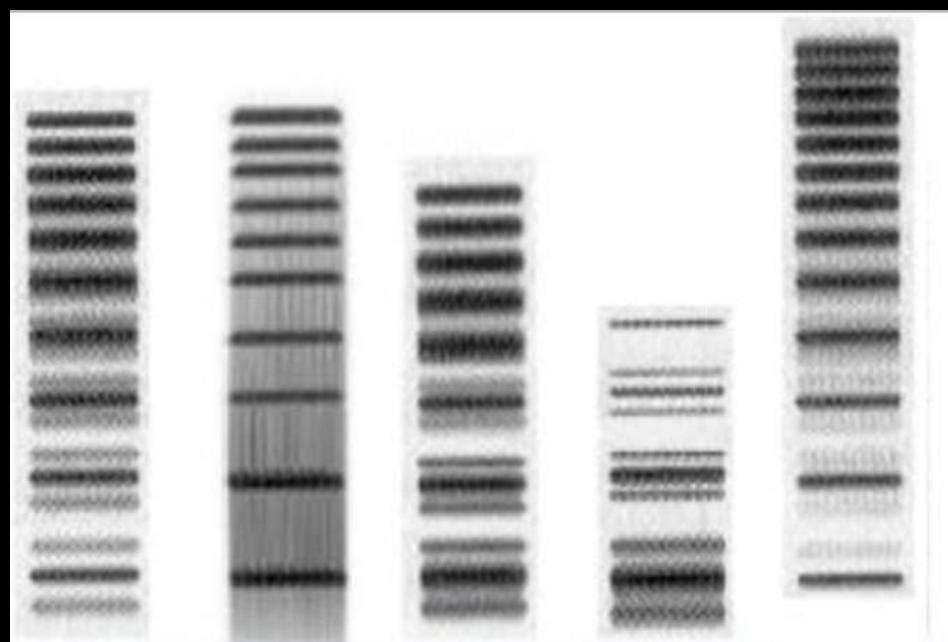
Types ou sous type	2B
TO	↑
TCA	N ou ↑
FVIII	N ou ↓
vWF:Ag	N ou ↓
vWF:Rco	↓↓
FVIII /vWF:Ag	> 0,7
vWF:Rco/WF:Ag	< 0,7

TESTS PLUS SPECIALISES

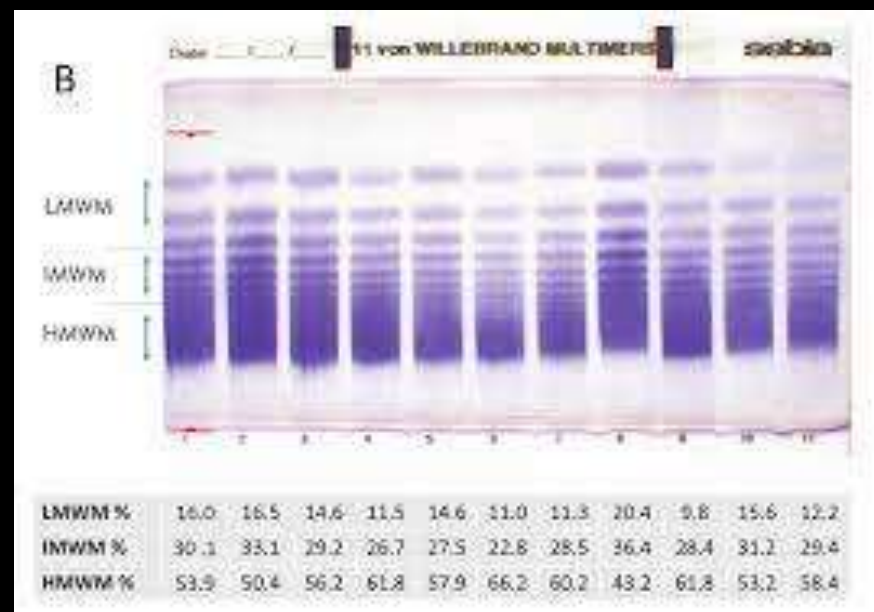
Evaluation du type



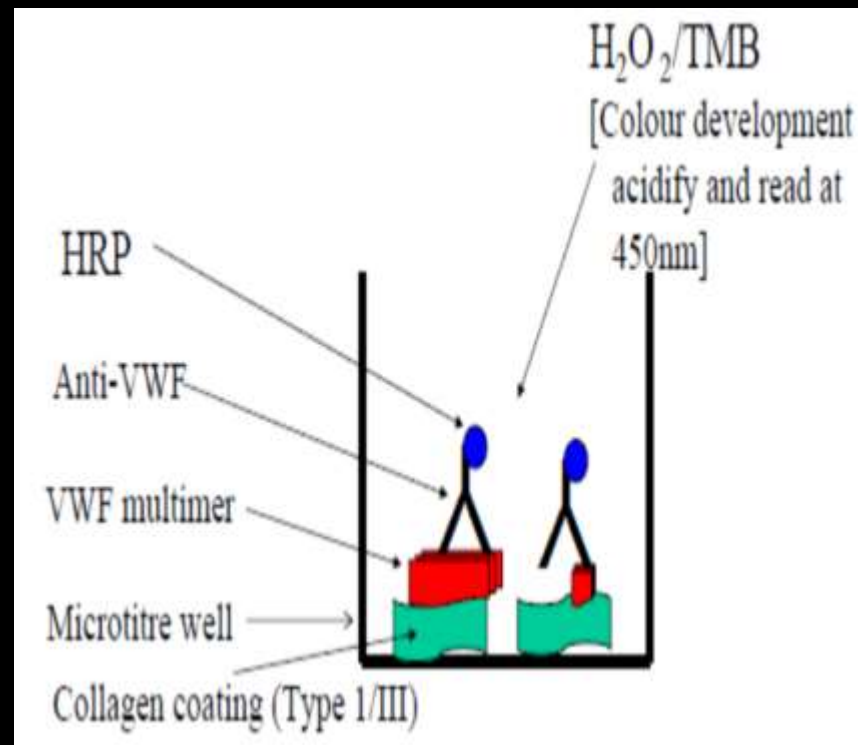
ELECTROPHORÈSE DES MULTIMÈRES DU VWF



PN 2M 2B 2A Vicenza

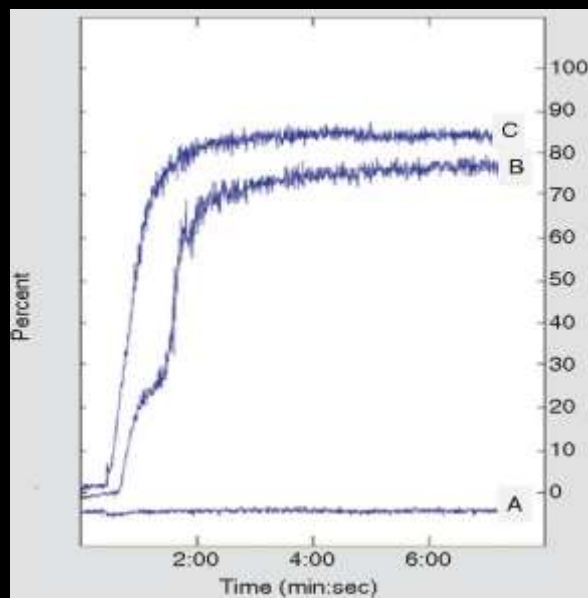


MESURE DE LA CAPACITÉ DE LIAISON DU VWF AU COLLAGÈNE (VWF:CB)



RISTOCETIN INDUCED PLATELET AGGREGATION (RIPA)

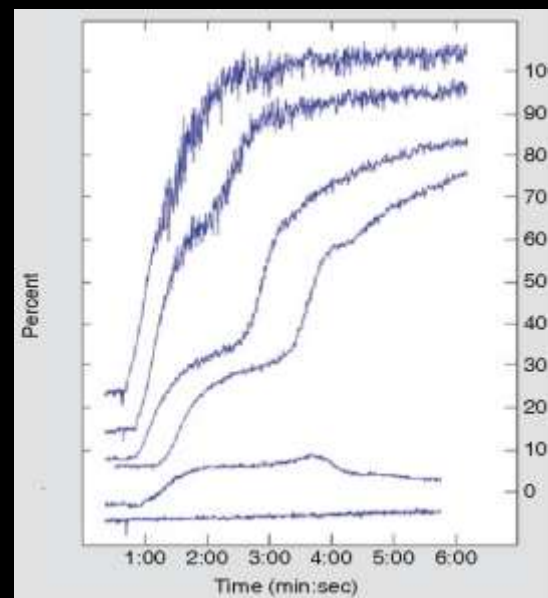
Sujet normal



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

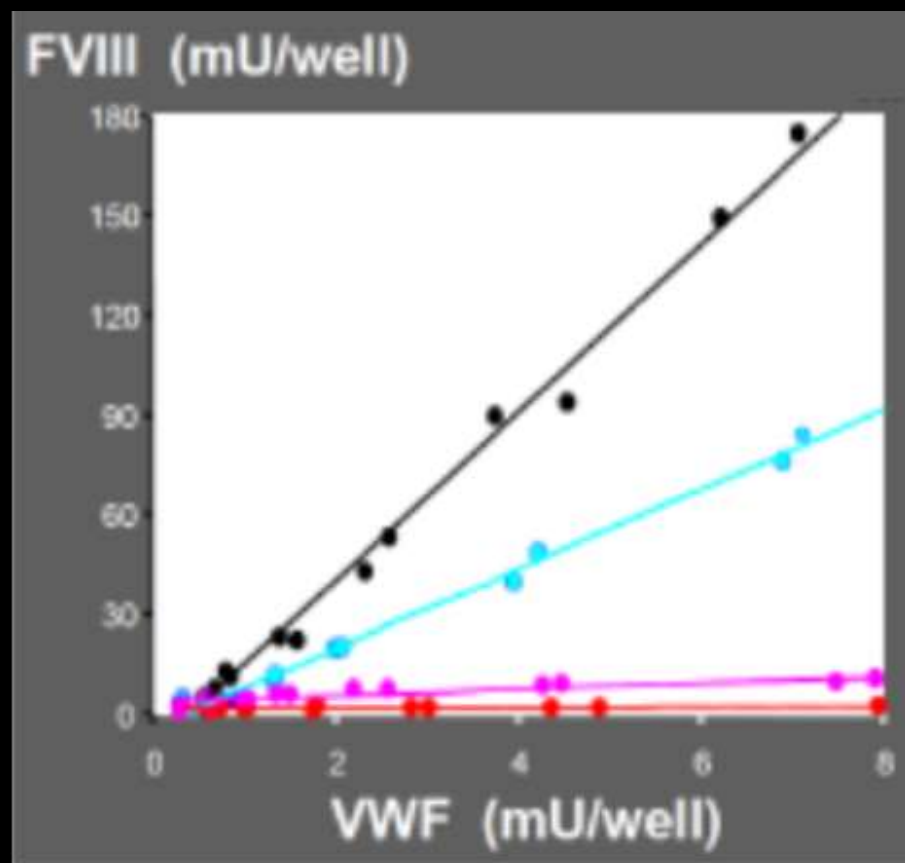
0,3 mg/mL

X

X

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

ELISA



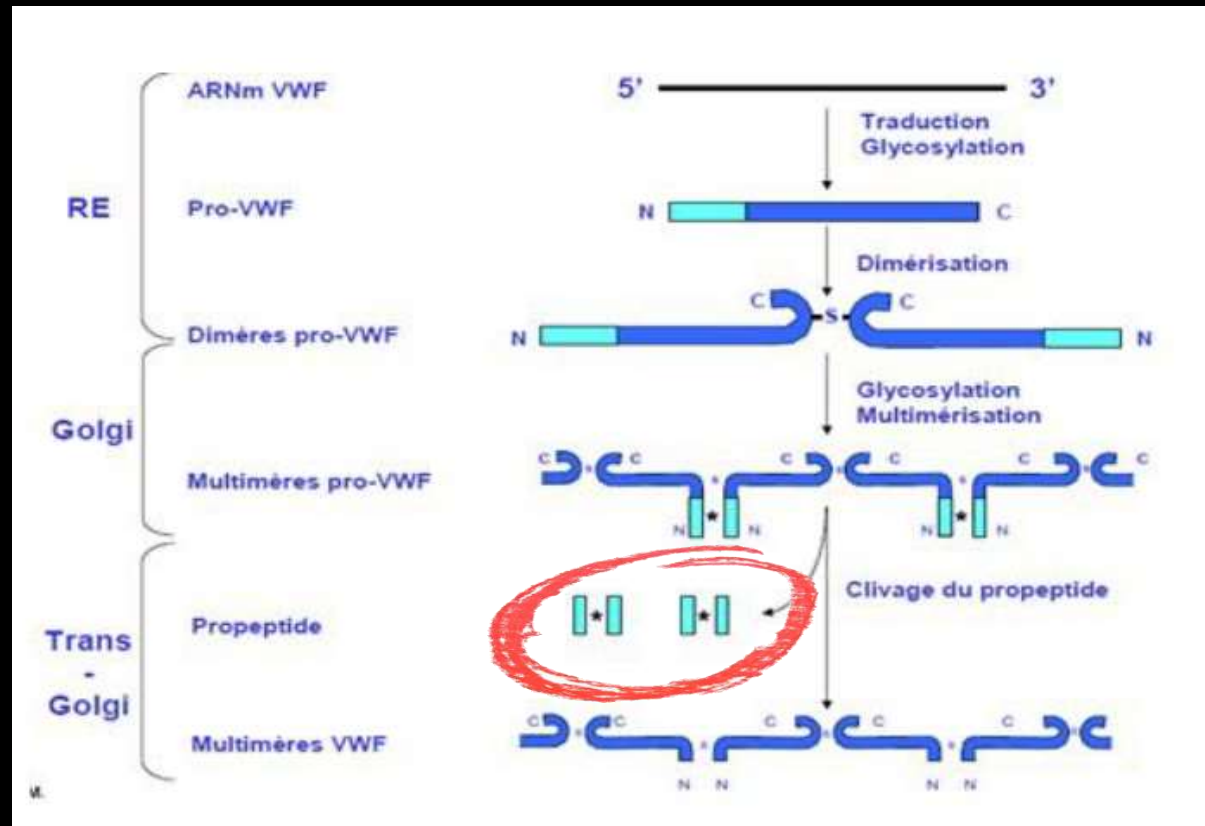
Normal

2N homozygote

2N hétérozygote

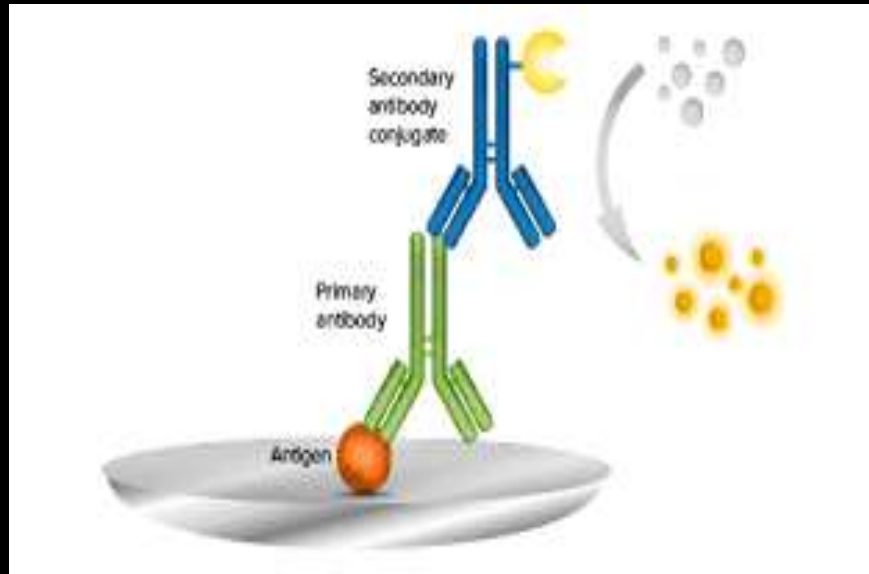
DOSAGE DU PROPEPTIDE VWF:PP

ELISA

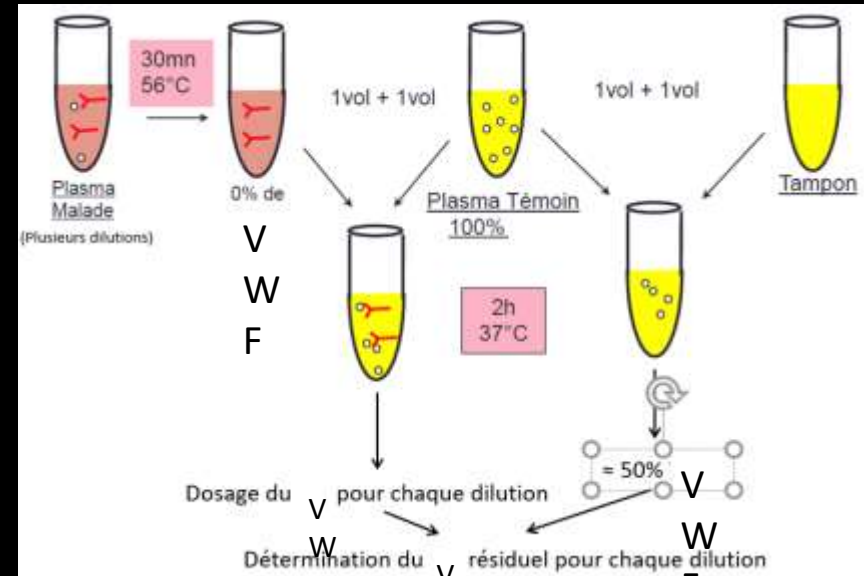


RECHERCHE D'ANTICORPS ANTI-VWF

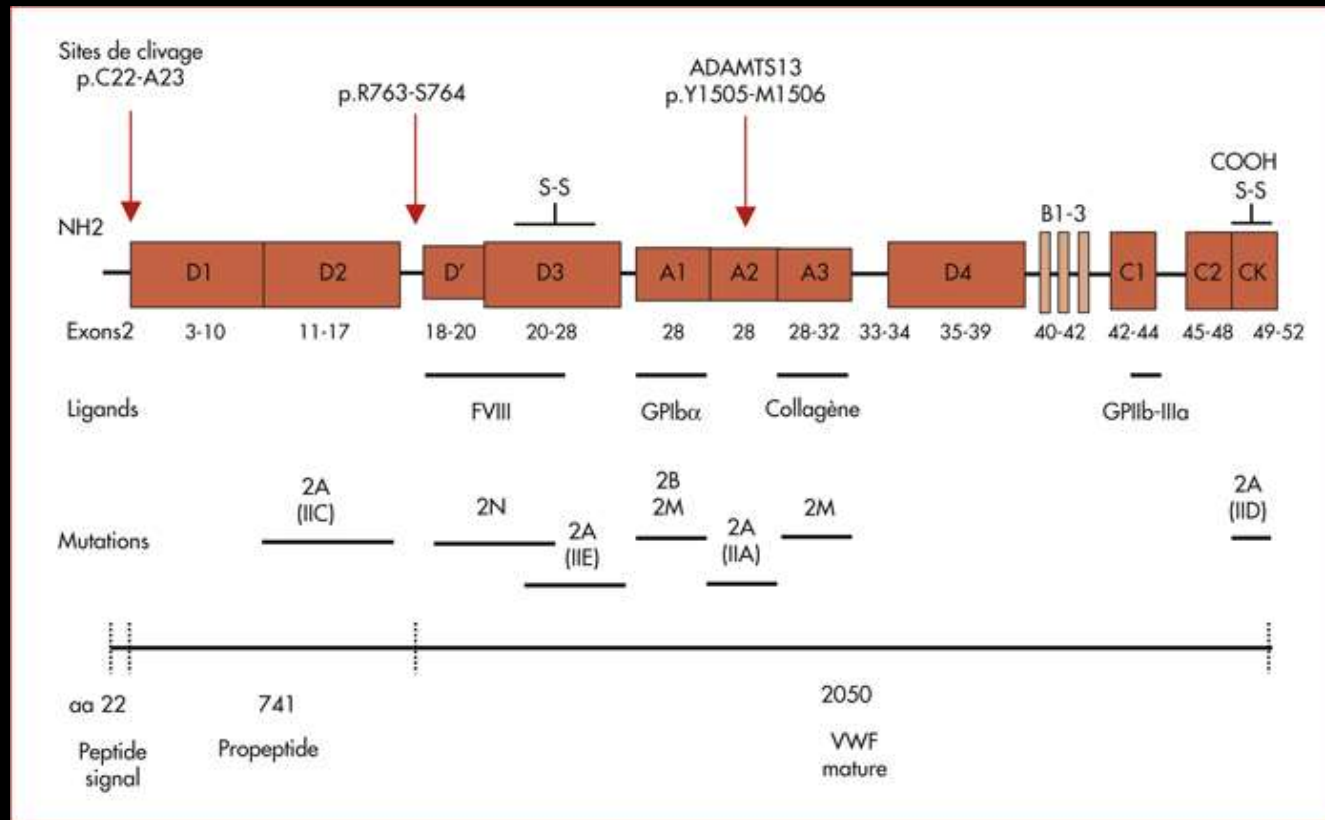
ELISA



Technique Bethesda



ETUDE MOLÉCULAIRE DU GÈNE VWF



PRISE EN CHARGE



maladies rares

CARTE D'URGENCE
Emergency card
Maladie de Willebrand

Personne à prévenir en urgence
Mère/M
Mère/M

Contacts médicaux
Médicaux
Suivi(e) par le centre de : (N°) (adresse)
Tél : (numéro)
Téléphone médical sur le site www.mrhna.fr (Situation d'urgence) et www.mrhna.net (Maladie de Willebrand/urgence)

CRMW orpharjet **MHEMO**

Informations individuelles sur la maladie
Type de maladie de Willebrand : Type 1 (faible quantité de facteur) Type 2A Type 2B Type 2M Type 2N Type 3 (absence de facteur)

Caractéristiques biologiques : VWF : Act (Activité factorielle) Oui Non
VWF Ag (Antigène) Oui Non
Fonction de type 3 inhibiteur anti-VWF Oui Non

Tout à la fois : Oui Non

Médicament substituant la maladie (traitement substitutif ou palliatif en attente de greffe)
Autres informations relatives à la

RECOMMANDATIONS EN CAS D'URGENCE
1. La prise de saignement d'hémorragie grave, en particulier d'hémorragies cérébrales ou des muscles, doit être prise en compte.
2. Pour toute question relative à la prise en charge, contactez le centre de soins habituel du porteur de cette carte (voir le numéro de contact ci-dessous).
3. Compter la coagulation en (premier) en cas d'hémorragie importante, évitez toute intervention chirurgicale (sauf urgence vitale), sans... par injection de concentrateur de facteur Willebrand ou par Desmopressine si bien tolérée.
4. La prise d'aspirine ou d'anti-inflammatoires non-stéroïdiens est contre-indiquée.
5. Ecouter le patient : il connaît sa maladie, son traitement et son centre de soins.

maladies rares

Carte de soins et d'urgence
Emergency healthcare
Maladie de Willebrand
Type Willebrand disease

Indiquer le type de maladie de Willebrand :
 Type 1 Type 2 : paucifactoriel Type 3 Type non déterminé

La maladie de Willebrand est une maladie héréditaire récessive liée à un déficit en facteur Willebrand.

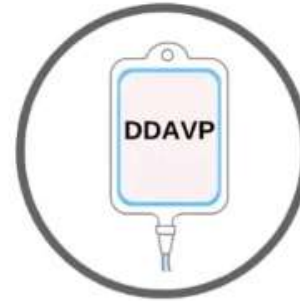
Risque d'hémorragie :
Eviter tout traitement anticoagulant ou antiplaquettaire sans avis médical préalable. Eviter toute intervention chirurgicale ou dentaire sans avis médical préalable.

Carte de soins

Informations et conseils
Maladie de Willebrand

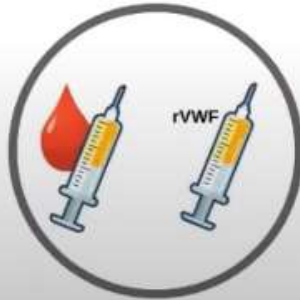


**TRANEXAMIC
ACID**



**DESMOPRESSIN
(DDAVP)**

**VWF
REPLACEMENT
THERAPY**



**IRON &
HORMONAL
THERAPIES**



CLINICAL GUIDELINES • blood advances

ASH ISTH WFH 2021 guidelines on the management of von Willebrand disease

Author: T. Gonsky, M. H. ...

CLINICAL GUIDELINES • blood advances

ASH ISTH NHF WFH 2021 guidelines on the diagnosis of von Willebrand disease

Author: P. ...

Background: von Willebrand disease (VWD) is the most common inherited bleeding disorder in humans. Accurate and timely diagnosis is essential for optimal management.

Objective: These evidence-based guidelines of the American Society of Hematology (ASH), the International Society on Thrombosis and Haemostasis (ISTH), the National Hemophilia Foundation (NHF), and the World Federation of Hemophilia (WFH) are intended to assist patients, clinicians, and other health care professionals in their decisions about VWD diagnosis.

Methods: The ASH, ISTH, NHF, and WFH convened a multidisciplinary guideline panel that included a patient representative and was designed to evaluate evidence from peer-reviewed literature. The guideline was implemented through a process of consensus, including the use of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, including GRADE Evidence-to-Decision (EtD) tables, to evaluate evidence and make recommendations, which were subsequently subject to public comment.

Results: The panel agreed on 11 recommendations.

Conclusions: Key recommendations of these guidelines include the use of bleeding assessment tools in the assessment of patients suspected of VWD, diagnostic design and laboratory utility for type 1 and type 2 VWD, and the use of type 1 and 2 VWD panels with normalized von Willebrand factor (vWF) antigen and activity in plasma assays for types 2B and 2M. Future clinical research priorities are also identified.

Summary of recommendations

These guidelines are derived, developed, and endorsed by the American Society of Hematology (ASH), the International Society on Thrombosis and Haemostasis (ISTH), the National Hemophilia Foundation (NHF), and the World Federation of Hemophilia (WFH). The panel used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to assess the evidence in the evidence and formulate recommendations.

ASH ISTH NHF WFH 2021 guidelines on the management of von Willebrand disease

ASH ISTH NHF WFH 2021 guidelines on the diagnosis of von Willebrand disease



Willebrand



2021

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 accuracy studies ⊕⊕○○).

Recommendation 11

The panel suggests using either VWF:FVIII B 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 ⊕⊕○○).

Recommendation 10

The panel suggests using either VWF:FVIII B 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-VWF:GPIbM, VWF:GPIbR) over the (nonautomated) for the diagnosis (based on low certainty in accuracy studies ⊕⊕○○).

to decide whether the recommendation based on low certainty in the evidence from diagnostic accuracy studies ⊕⊕○○).

studies ⊕⊕○○).

ate probability of VWD (e.g., the panel).

or (n) B, a-tic

Merci



Willet

