What should the anaesthesiologist know about the inherited bleeding disorders

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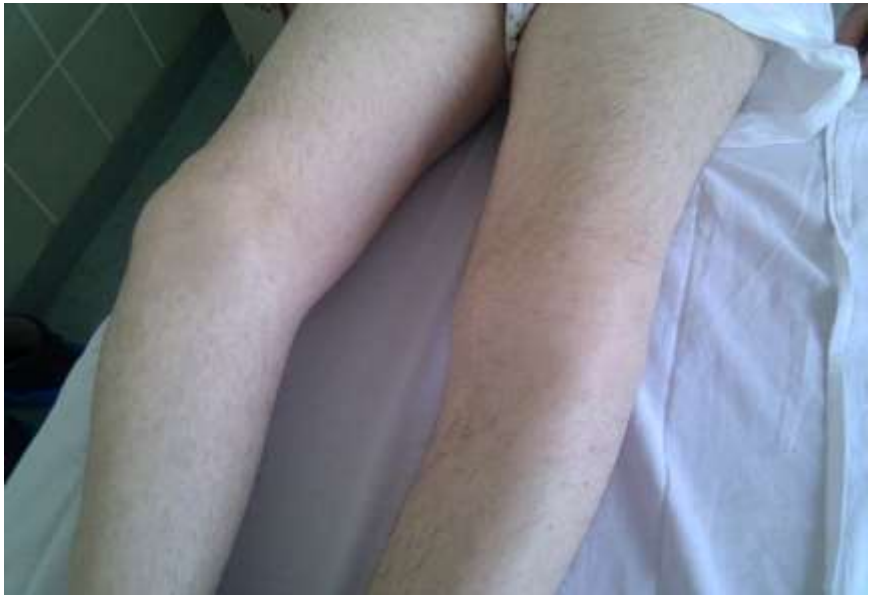
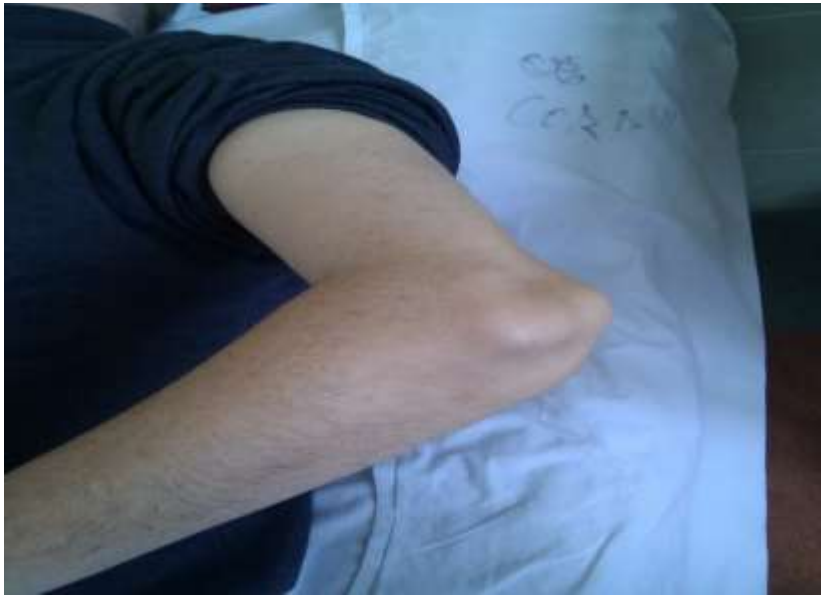
Disclosure

- I received in the past travel grants and speaker fees from Bayer, GSK, Novo-Nordisk, Pfizer and Sanofi-Aventis
- Co-author of 2013 European Guidelines on management of the trauma bleeding patients – unrestricted grant from CLS Behring and LFB France
- Co-author of 2013 ESA Guidelines on management of the severe perioperative bleeding

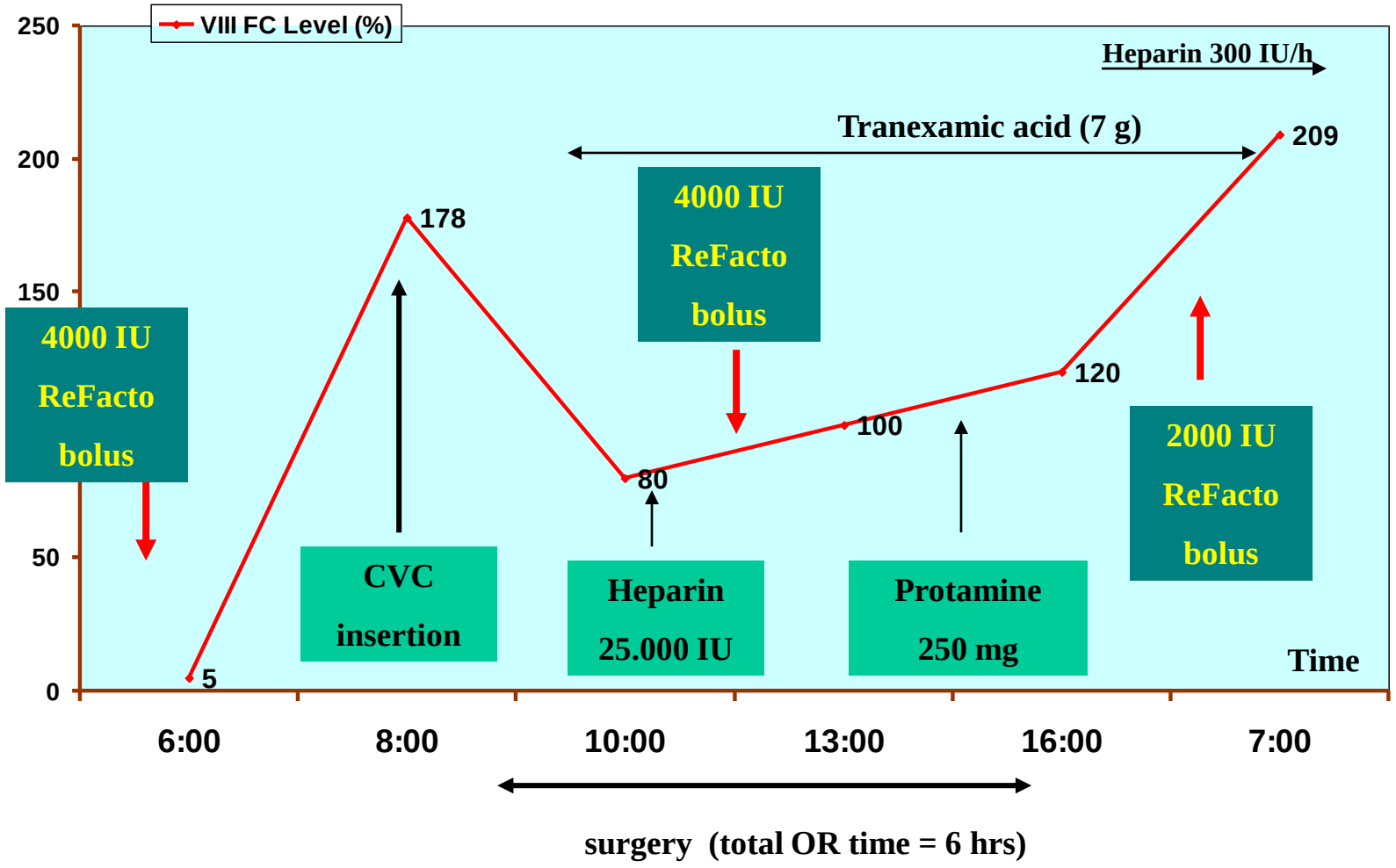
Case presentation



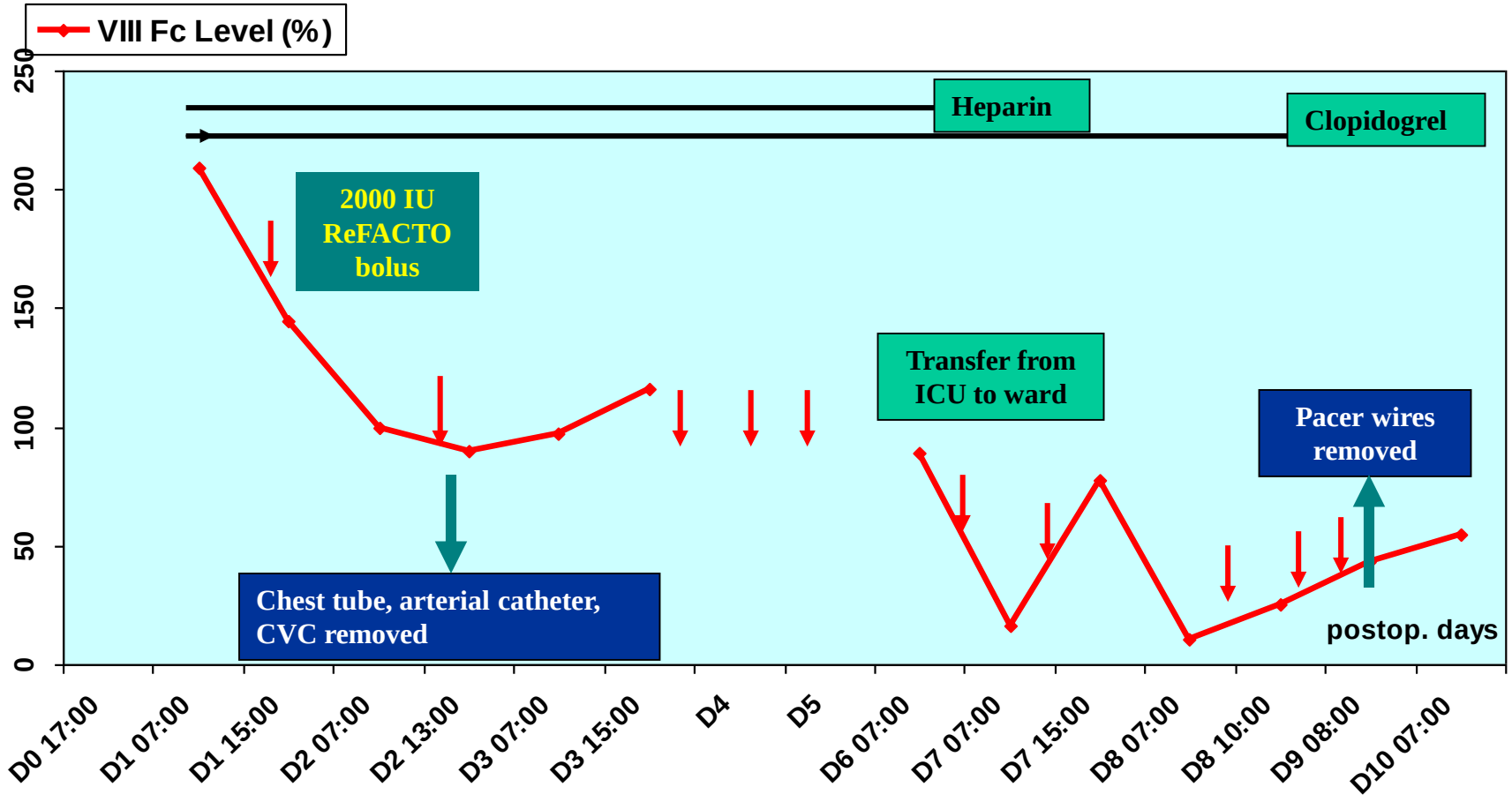


42-year-old man, 64 kg weight
Moderate haemophilia: Fc VIII 5%
Spontaneous bleeding episodes (nazal)
Haemophilic arthropathy - knees and elbows
Orhtopedic surgery (14 yrs ago): wedge osteotomy with metal plate and screws
Perioperative Fc VIII replacement therapy; No inhibitors
Scheduled for CABG surgery

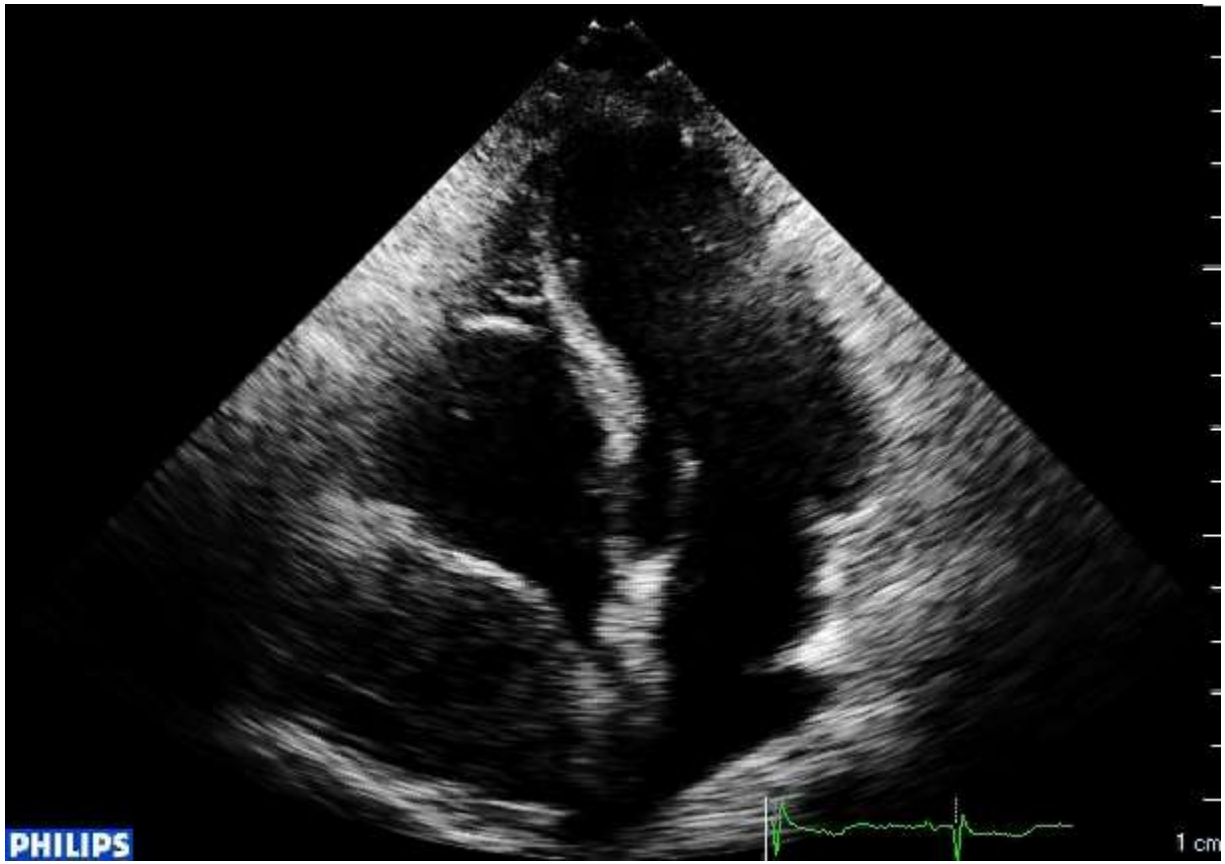
Perioperative Factor VIII levels and Fc VIII replacement (surgery and day 0)



Postoperative Factor VIII levels and Fc VIII replacement (day 1-day 10)

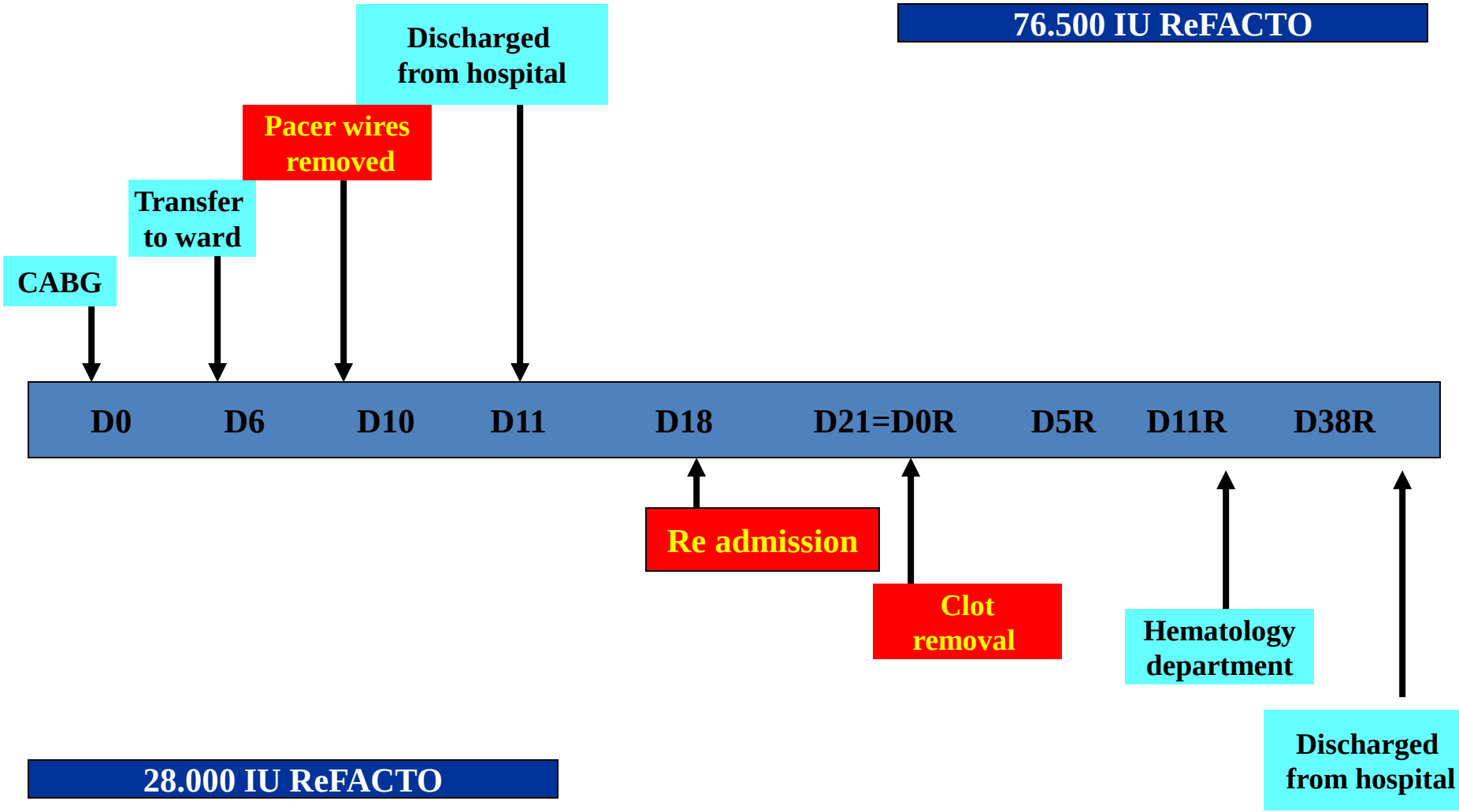


Re admission - late cardiac tamponade
(pericadial clot with compression of right atrium, SVC and IVC)



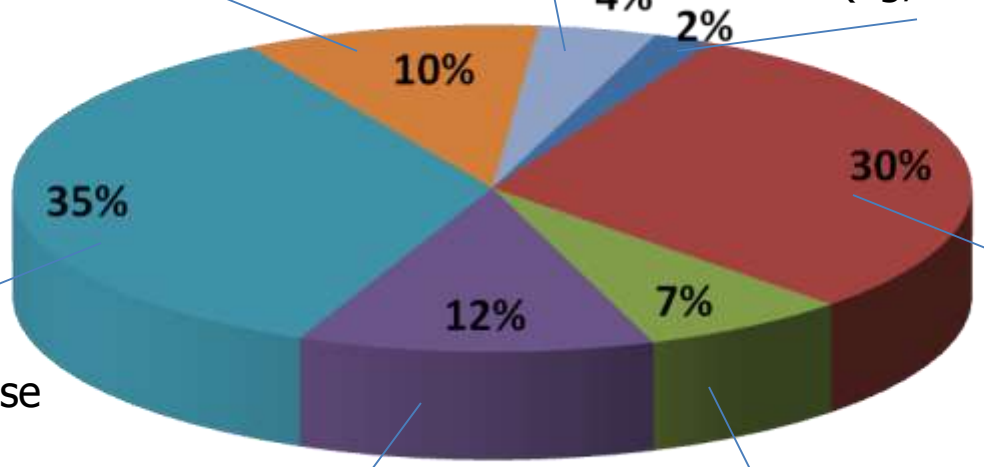
TTE, apical 4 chambers- extrinsec compression of right atrium

Postoperative evolution



Inherited bleeding disorders

N = 489



• **disorders of primary haemostasis**

Von Willebrand disease
• VWF ↓

Haemophilia A
• VIII↓

• **disorders of secondary haemostasis**

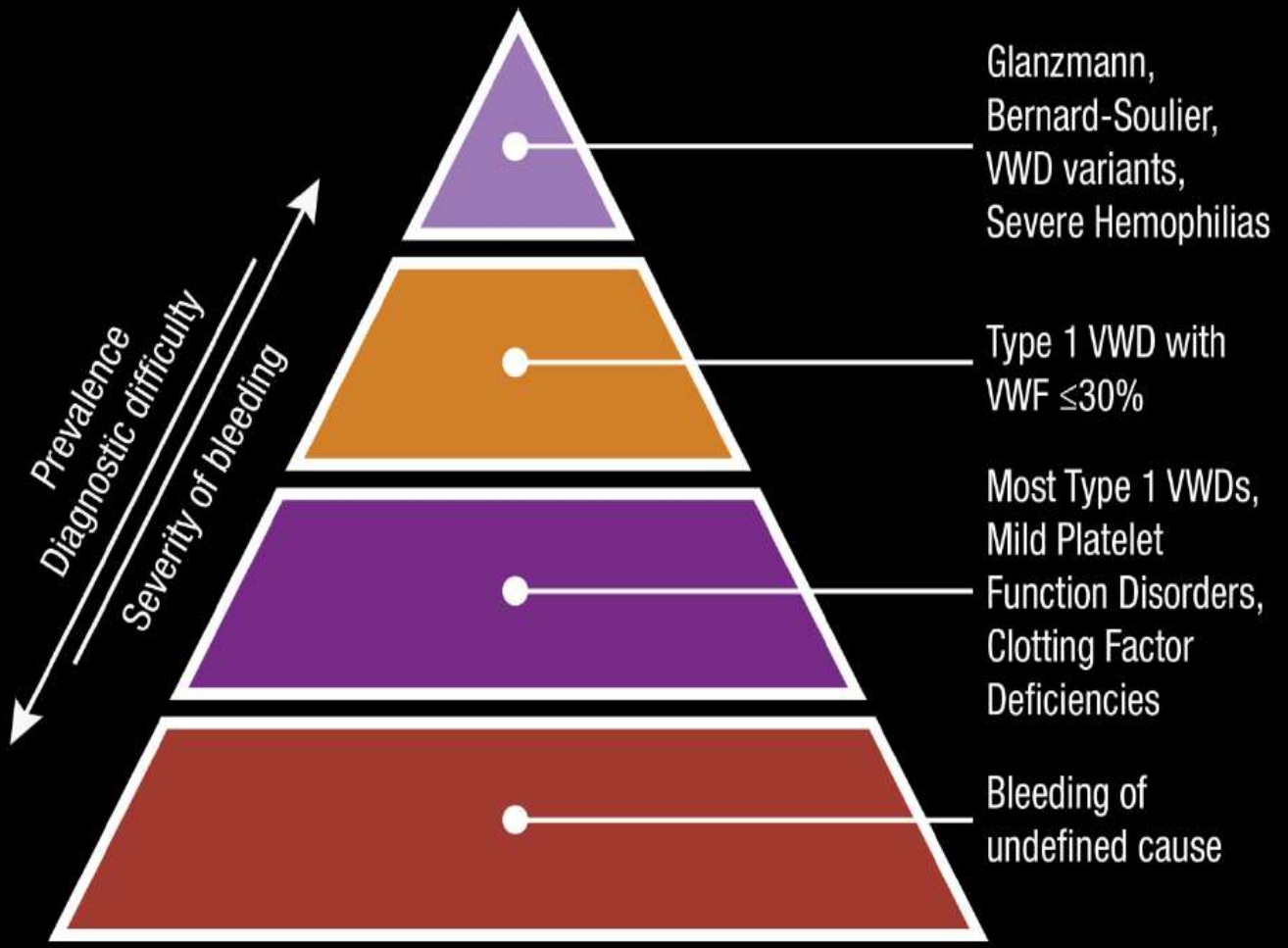
Other coagulation disorders
• (eg, VII↓, XI ↓)

Haemophilia B
• IX↓

BLOOD CME CENTER

Modified from www.bloodcmecenter.org
Image courtesy of Victor S. Blanchette, MD, FRCP

Bleeding Severity, Diagnostic Difficulty, and Prevalence of Inherited Bleeding Disorders



Posted with permission from Quiroga T, et al. *Hematology Am Soc Hematol Educ Program*. 2012;2012:466-474.

Von Willebrand disease

von Willebrand factor

- Synthesis in endothelium and megakaryocytes
- Forms large multimers
- Carrier of factor VIII
- Anchors platelets to subendothelium
- Bridge between platelets

Lison S, et al. Anaesthesia and Analgesia 2012:73

VWD - Classification

Table 1. Phenotypic Classification and Genetic Transmission of von Willebrand's Disease.

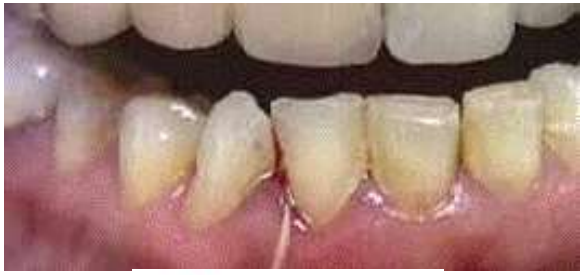
Phenotype	Mechanism of Disease	Genetic Transmission
1	Partial quantitative deficiency of von Willebrand factor (and factor VIII)	Autosomal dominant*
2	Qualitative defects of von Willebrand factor	Autosomal dominant†
A	Defective platelet-dependent von Willebrand factor functions, associated with lack of larger multimers	
B	Heightened platelet-dependent von Willebrand factor functions, associated with lack of larger multimers	
M	Defective platelet-dependent von Willebrand factor functions, not associated with multimer defects	
N	Defective von Willebrand factor binding to factor VIII	
3	Severe or complete deficiency of von Willebrand factor and moderately severe factor VIII deficiency	Autosomal recessive

From: Mannucci PM. NEJM 2004: 683-694

VWD - Clinical manifestations

Symptom	Frequency (%)
Epistaxis	50
Surgery-related	50
Dental-related	50
Easy bruising	80
Menorrhagia	80
Postpartum hemorrhage	30

Images from www.bloodcmecenter.org



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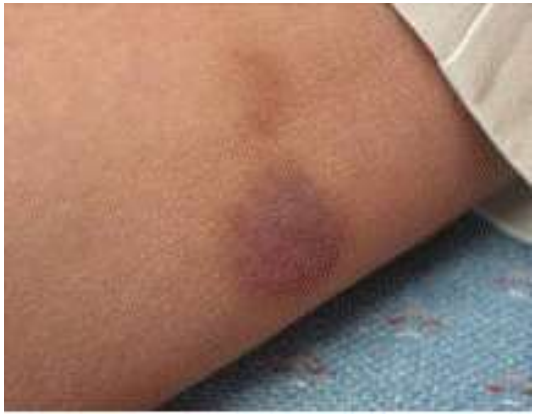
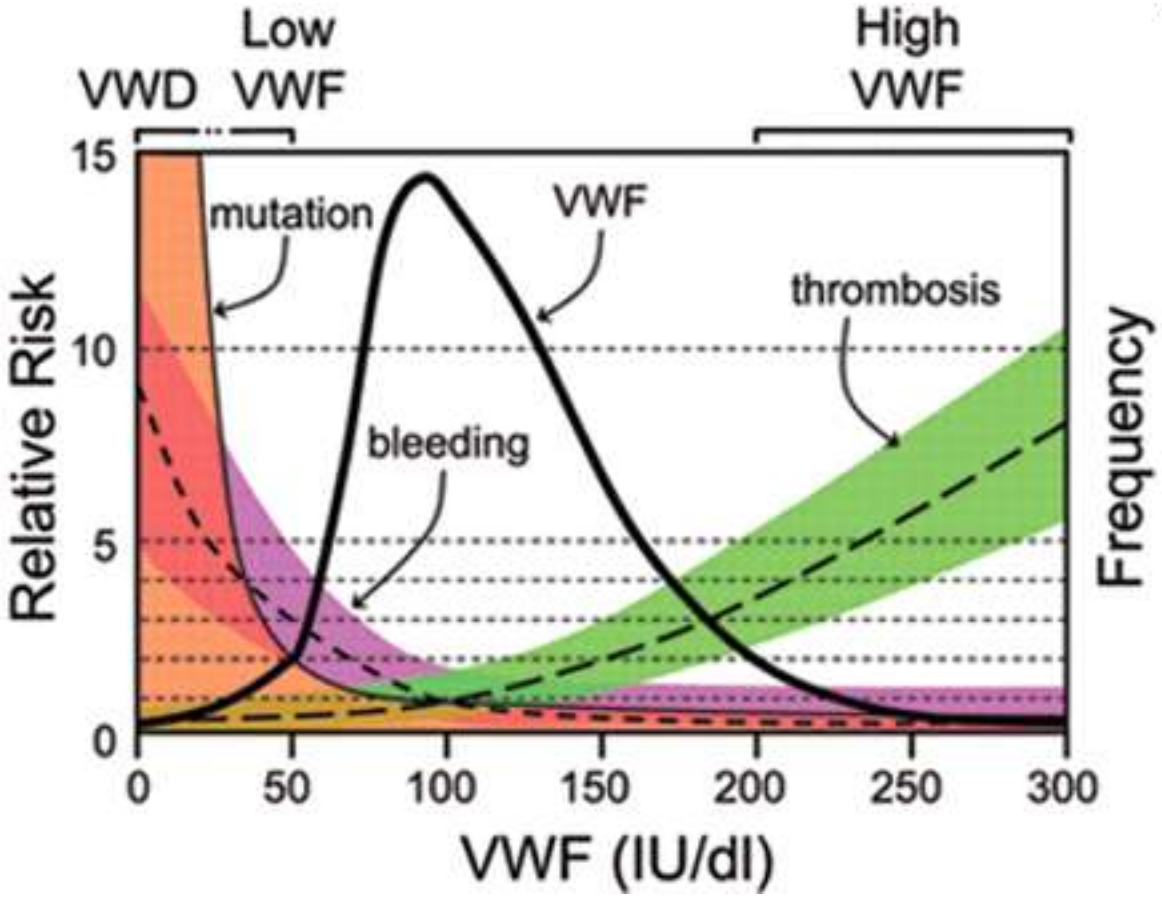


Low von Willebrand factor: sometimes a risk factor and sometimes a disease

J. Evan Sadler[1]

ASH Education Book 2009;1:106-112



Treatment of VWD

- **Endogenous VWF release by desmopressin**
- **Replacement therapy with VWF containing plasma-derived products**
- **Promoting haemostasis with antifibrinolytics and platelet transfusion**

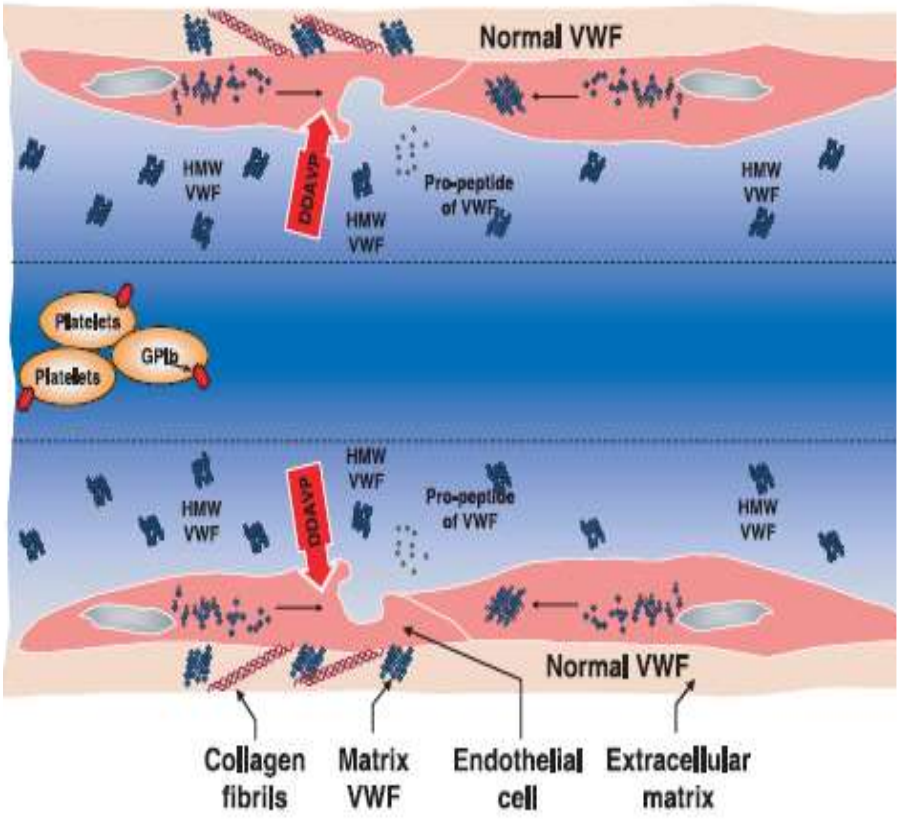
Desmopressin

- Synthetic analog of vasopressin
- Acts on V_2 receptors:

induces an increase (3-5 x) in plasma levels of VWF and FVIII

- First choice treatment

of type 1 VWD, variable effective in type 2, ineffective in type 3



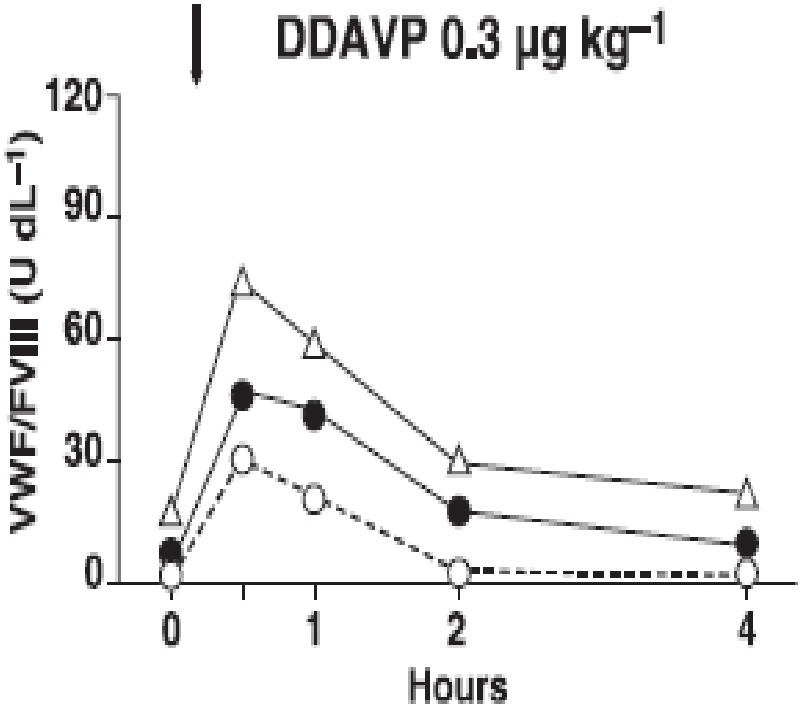
Picture from: Federici AB, et al. Haemophilia 2008 (Suppl. 1):5-14

Desmopressin – dose and monitoring

- 0.3 µg kg−1 in 30–50 mL of normal saline given over 30 min. and **repeated every 12 to 24 hours**, generally 2-4 doses

- Peak increases in VWF and FVIII are observed between 30 and 90 min after infusion

- A **test-infusion** should be given to all patients with clinically relevant VWD

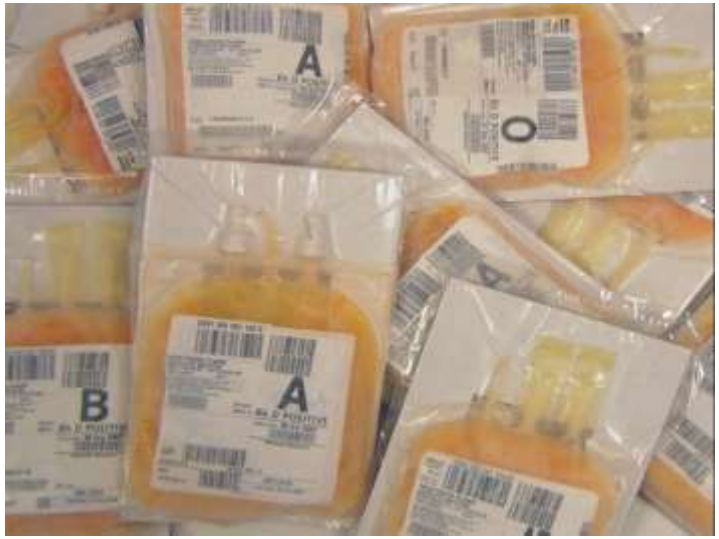


From: Federici AB et al. Hemophilia 2008, 14(Suppl. 1): 5-14

VWD - replacement therapy

- **Plasma derived factors containing VWF (pd-VWF)**

- **Fresh frozen plasma (FFP)**
- **Cryoprecipitate (CP)**



Haemostatic components of cryoprecipitate and FFP

Component	Cryoprecipitate (per mL)	FFP (per mL)
FXIII activity, U	2.8 ± 1.5	1.2 ± 0.3
FXIII antigen, mg	0.031 ± 0.01	0.0096 ± 0.003
FVIII activity, U	6.3 ± 1.9	1.1 ± 0.3
Fibrinogen, mg	8.8 ± 2.6	2.9 ± 0.6
vWF:Ag, U	**8.6 ± 2.7**	**0.9 ± 0.2**
vWF:RCo, U	**8.0 ± 1.8**	**0.9 ± 0.2**
Bag volume, mL	21.3 ± 2.7	245 ± 29

Modified from: Caudil J et al. Transfusion 2009;49:765

Treatment of von Willebrand disease with FVIII/VWF concentrates

Giancarlo Castaman

Blood Transfus 2011; 9: s9-s13

Table I - FVIII/VWF concentrates available in Italy for VWD treatment.

Product	Purification	Viral inactivation	Specific activity* (U/mg protein)	VWF:RCo/Ag (ratio)	VWF:RCo FVIII:C (ratio)	Other proteins
Alphanate (Grifols, Los Angeles, USA)	Affinity chromatography (heparin)	Solvent/detergent + 72 h at 80 °C	>100	0.94	1.21	Albumin +
Fanhdi (Grifols, Barcelona, Spain)	Affinity chromatography (heparin)	Solvent/detergent + 72 h at 80 °C	>100	0.83	1.48	Albumin +
Haemate® P (CSL Behring, Marburg, Germany)	Multiple precipitation	Pasteurisation 10 h at 60 °C	40±6	0.96	2.54	Albumin +
Immunate (Baxter, Wien, Austria)	Ion exchange chromatography	Detergent + vapour heat 10 h at 60 °C, 1 h at 80 °C	100±50	0.47	1.10	Albumin +
Wilfactin (LFB, France)	Aluminium hydroxide gel adsorption ion exchange + Affinity chromatography	Solvent/detergent; dry heat; 72 h at 80 °C; 35 nm nanofiltration	≥50*	0.95	>10	Albumin +

Replacement therapy
FVIII/VWF concentrates

- Products with a VWF/FVIII ratio >1 should be preferred
- Patients undergoing elective surgery should receive a concentrate infusion a couple of hours before the procedure in order to allow enough time for new synthesis of endogenous FVIII
- In emergency situations, VWF concentrates containing large quantities of FVIII may be preferred to accelerate the effect of haemostasis
- Supernormal levels of VWF/FVIII may increase the thromboembolic risk

Nichols WL, Haemophilia 2008:171-232

Recommendations of peri-procedural replacement therapy

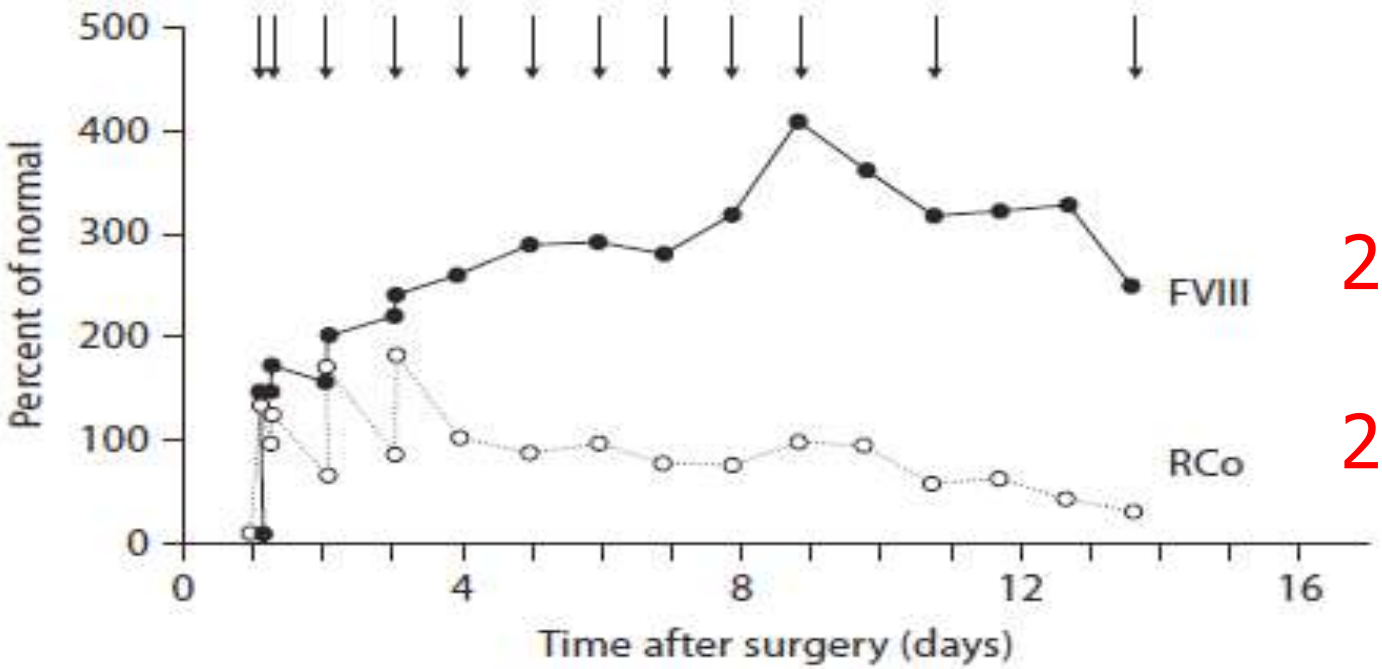
Type of haemorrhage	Target levels of VWF/ FVIII (IU/dL)		Frequency of administration
	initial	Subseq.	
Major surgery	100	> 50	Every 8-24 hrs 7-14 days
Minor surgery	> 30-50	> 30-50	Every 12-48 hrs 1-5 days
Diagnostic procedures	> 50		Single dose
Delivery	> 50	> 50	Daily before delivery 3-4 days postpartum

Nichols WL, et al. Haemophilia 2008:171; Mannucci PM , et al. Blood Transf 2009:117

Managing Patients with von Willebrand Disease Type 1, 2 and 3 with Desmopressin and von Willebrand Factor-Factor VIII Concentrate in Surgical Settings

Jan Jacques Michiels[a, c] Huub H.D.M. van Vliet[b] Zwi Berneman[a]
Wilfried Schroyens[a] Alain Gadisseur[a]

Acta Haematol 2009;121:167–176



250-300 IU/dL

200 IU/dL

Haemophilia (2012), 18, e173–e187 DOI: 10.1111/j.1365-2516.2012.02758.x

REVIEW ARTICLE *von Willebrand disease (VWD)*

Thrombotic adverse events to coagulation factor concentrates for treatment of patients with haemophilia and von Willebrand disease: a systematic review of prospective studies

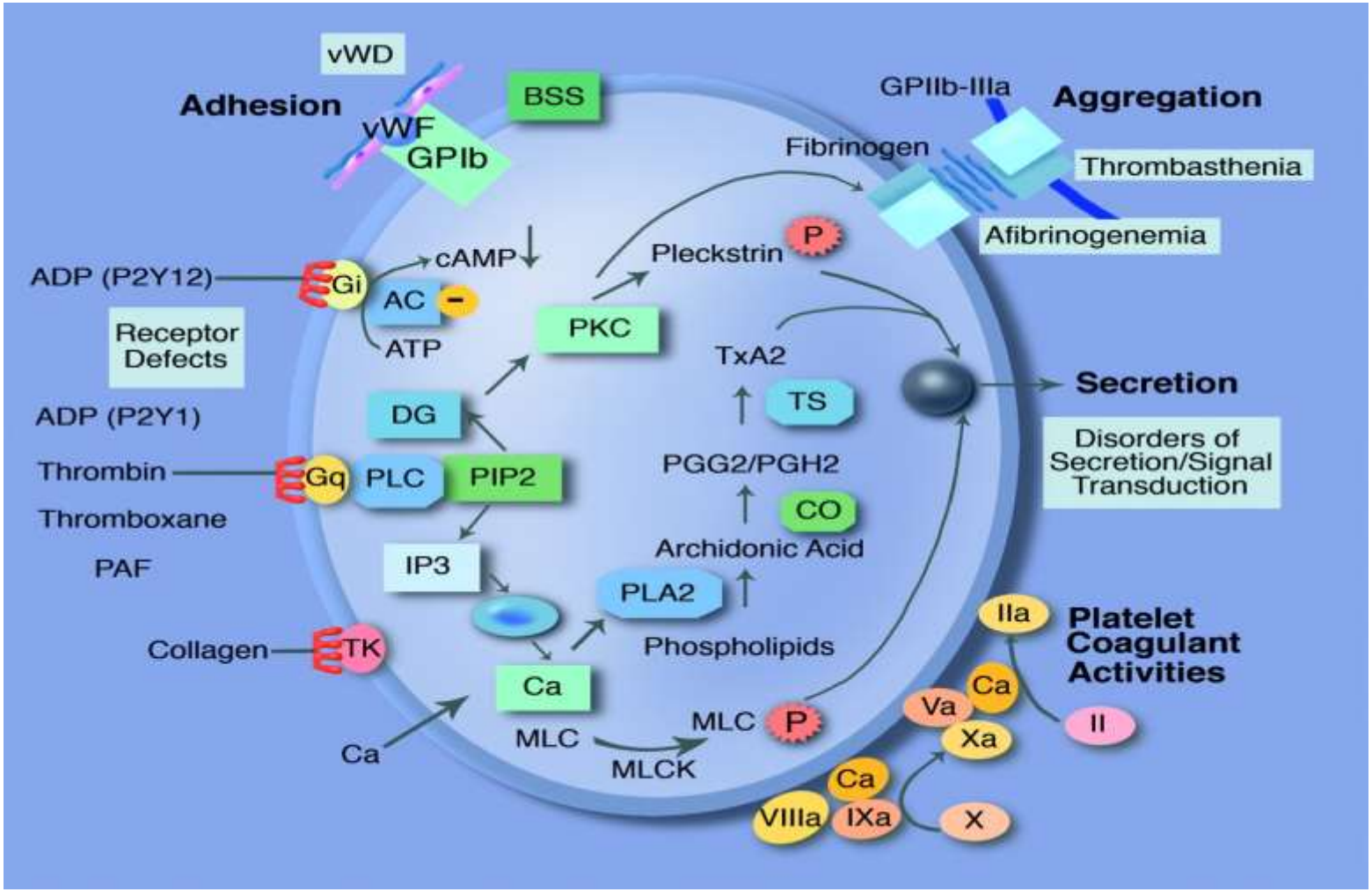
A. COPPOLA,* M. FRANCHINI,† M. MAKRIS,‡ E. SANTAGOSTINO,§ G. DI MINNO* and P. M. MANNUCCI¶

1990-2011
71 prospective studies
5528 patients
27 different concentrates

20 thrombotic adverse events (3.6 per 10^3patients)
2 major thromboses (3.6 per 10^4 patients) both in VWD

Inherited platelet defects

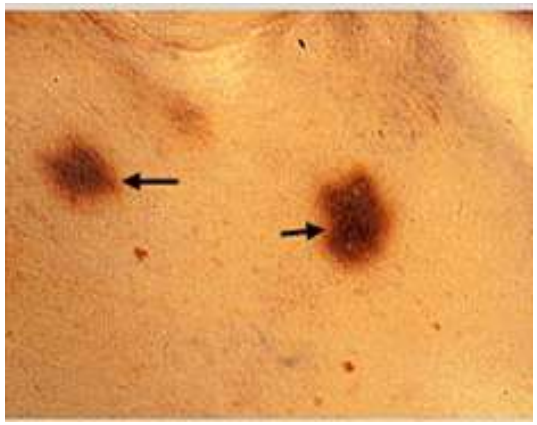
ash-sap™



Arnold DM , et al. ASH-SAP 2010:241-262

Inherited platelet defects

- Mild to moderate muco-cutaneous bleeding tendency (echimosis, petechia, purpura, gingival)
- No deep tissue bleeding or haemarthroses
- Could present particularly abundant bleeding after surgery, trauma or invasive procedures



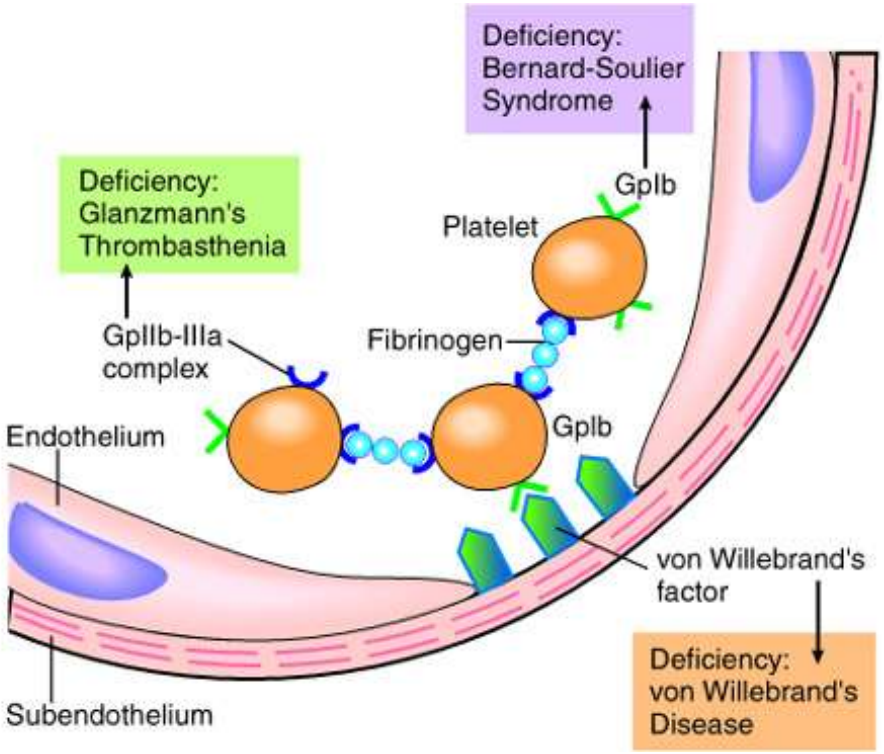
Images from www.bloodcmecenter.org
Courtesy by David Green, eAtlas of Pathology, and Peter A. Kouides

BLOOD CME CENTER

Inherited severe platelet defects

Bernard-Soulier syndrome is due to dysfunction or absence of a platelet membrane receptor (GP Ib/IX/V) resulting in abnormal adhesion of platelets to subendothelial-bound von Willebrand factor during the formation of platelet plug

Glanzmann thrombasthenia is characterized by a deficiency or functional defect of platelet GP IIb/IIIa resulting in abnormal aggregation



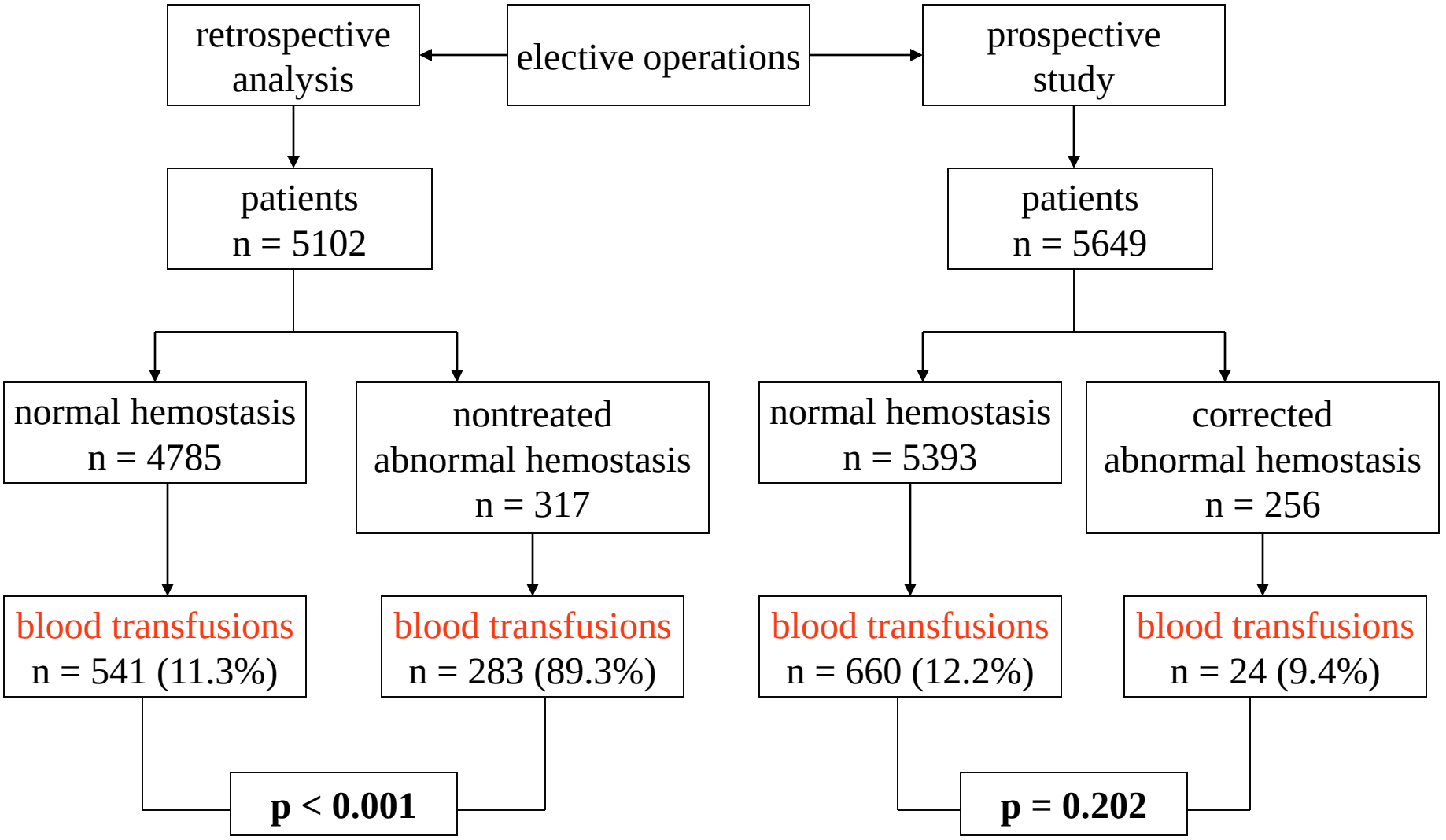
Alamelu J & Liesner R. Brit J Haematol 2010;813-829
Bolton-Maggs PHB et al. Brit J Haematol 2006;135:603-633

Inherited platelet defects - therapy

- **Desmopressin**
- **Antifibrinolytics**
- **Platelet transfusion**
- **Recombinant factor VIIa**

Alamelu J & Liesner R. Brit J Haematol 2010;813-829
Seligsohn U. Haemophilia 2012;18:161-165

A practical concept for preoperative management of patients with impaired haemostasis



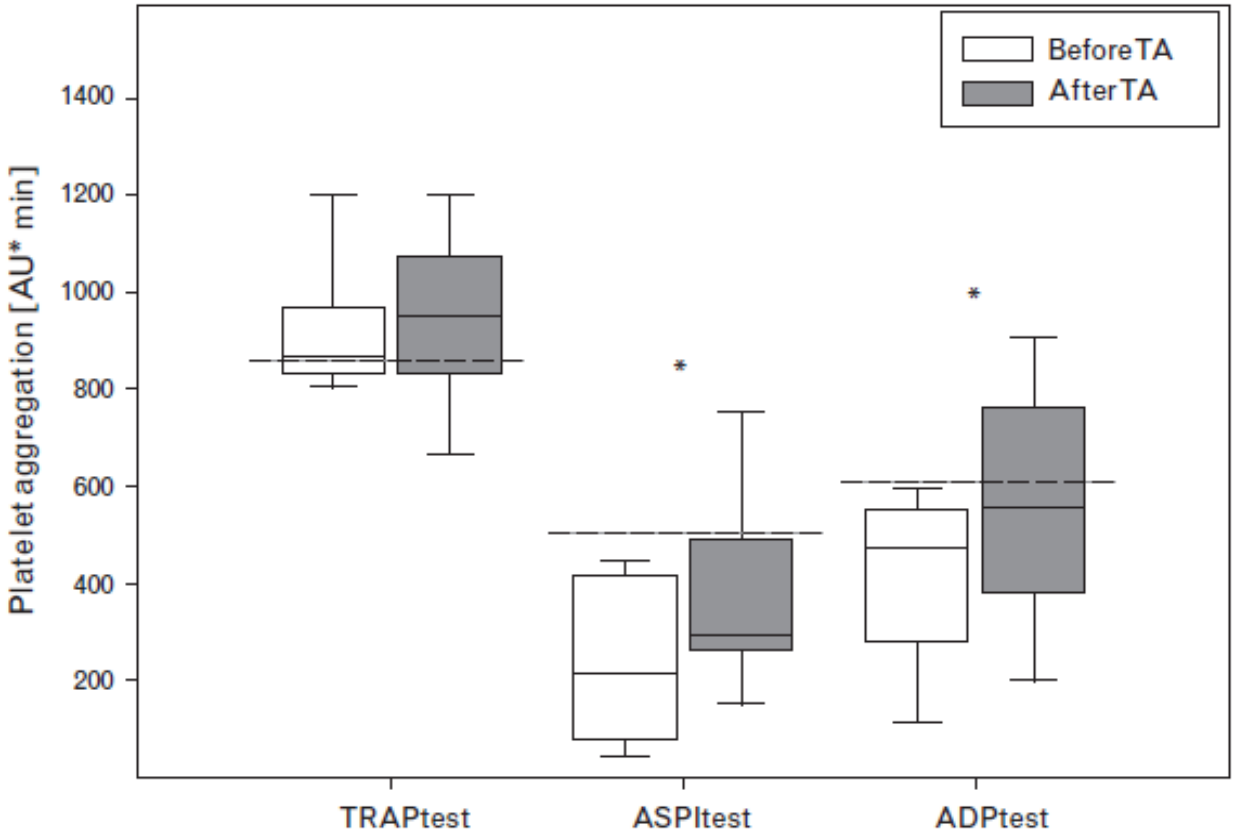
From: Koscienly J et al. Clin Appl Thrombosis.Hemostasis 2004: 155-166

ORIGINAL ARTICLE

Tranexamic acid partially improves platelet function in patients treated with dual antiplatelet therapy

Christian F. Weber, Klaus Görlinger, Christian Byhahn, Anton Moritz, Alexander A. Hanke, Kai Zacharowski and Dirk Meininger

Eur J Anesthesiol 2011:57-62



aspirin & clopidogrel

Drug Design, Development and Therapy

Dovepress

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REVIEW

Evidence supporting the use of recombinant activated factor VII in congenital bleeding disorders

Pär I Johansson
Sisse R Ostrowski

rFVIIa is licensed for thrombastenia Glanzmann

No RCTs in patients with congenital platelet defects !

Platelet transfusion

To reduce the risk of allo-immunization and the risk of refractoriness:

- HLA and ABO-matched donors
- leucodepleted blood components
- apheresis units from single donors

Seligsohn U. Haemophilia 2012;18:161-165

Disorders of secondary hemostasis

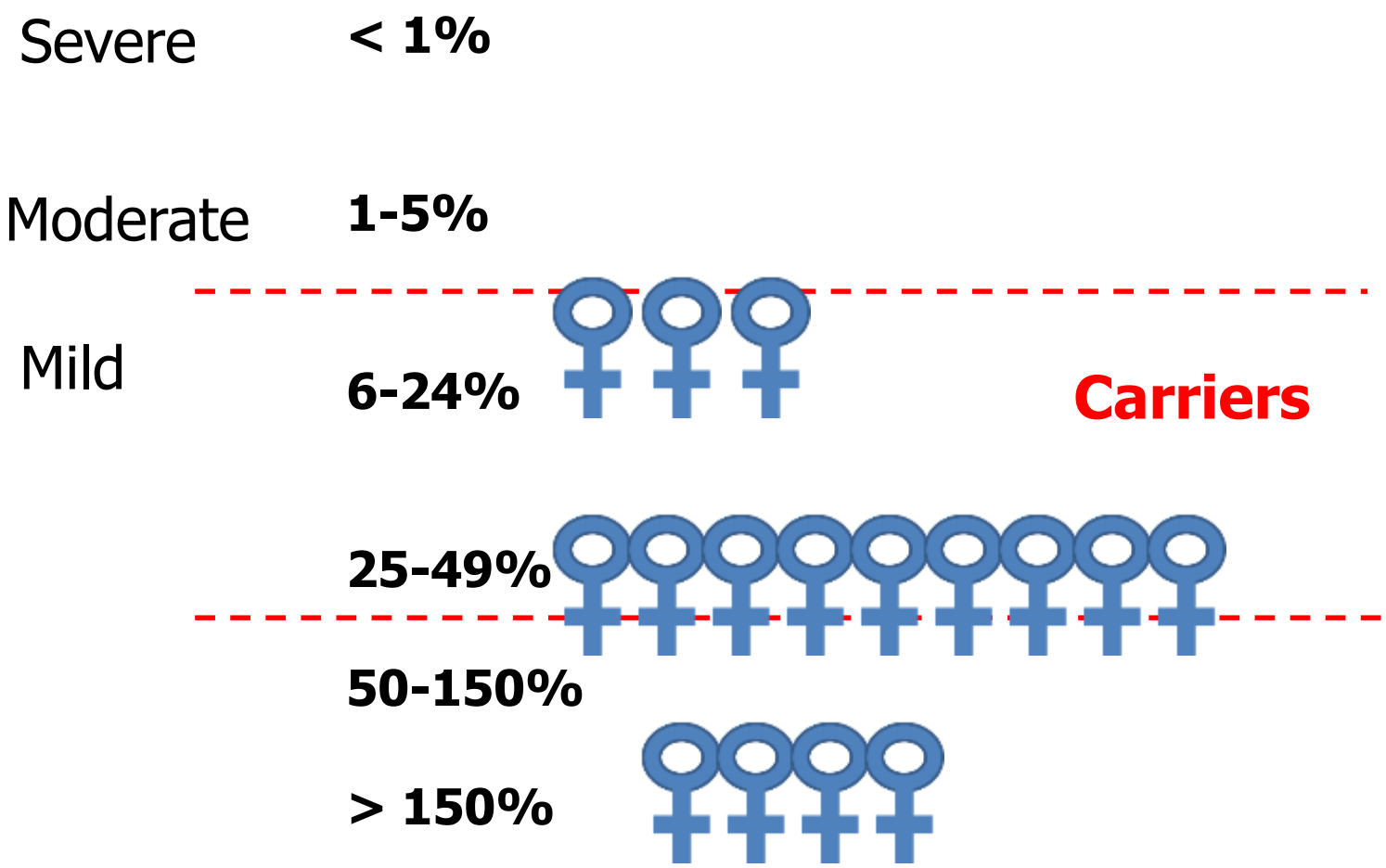
- **Haemophilia A**
  - deficit of F VIII
  - prevalence 1/10 000 male births

- **Haemophilia B**
  - deficit of F IX
  - prevalence 1/60 000 male births

Sex-linked disease affecting males
Reported prevalence varies among countries

Negrier C. Hemophilia A. www.orpha.net 2011

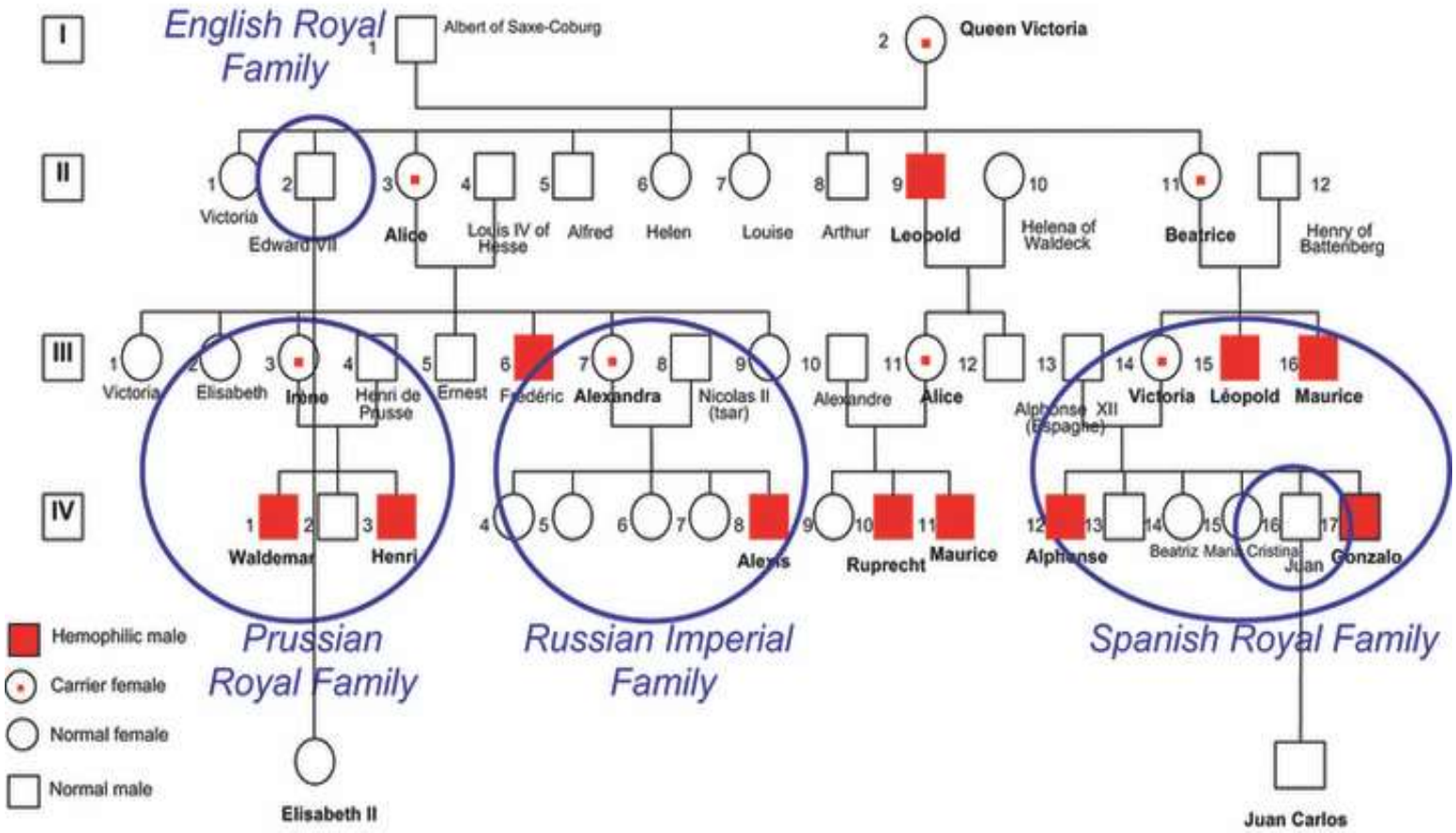
Factor VIII or IX levels and severity of haemophilia



Guidelines for the Management of Hemophilia p. 8, Table 1.1, www.wfh.org

Martlew VJ. Peri-operative management of patients with coagulation disorders. BJA 2000 Sep; 85 (3) :446-55. PubMed PMID:11103188

The 'royal disease'– haemophilia A or B? A haematological mystery is finally solved



From: Heremans LN. Haemophlilia 2010;16: 833-847

Haemophilia - Clinical manifestations

Lack of excessive hemorrhage from minor cuts or abrasions, due to normal platelet function
A major bleed about 20 times/year

- **Haemarthosis**
- **Haemorrhages into the skin, muscles, soft tissues and mucous membranes**
- **Prolonged bleeding post-surgery or trauma**

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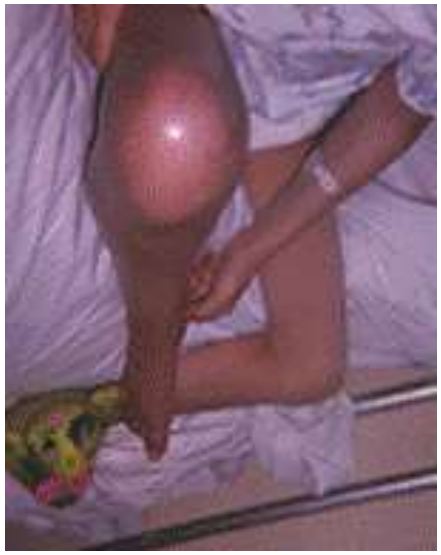
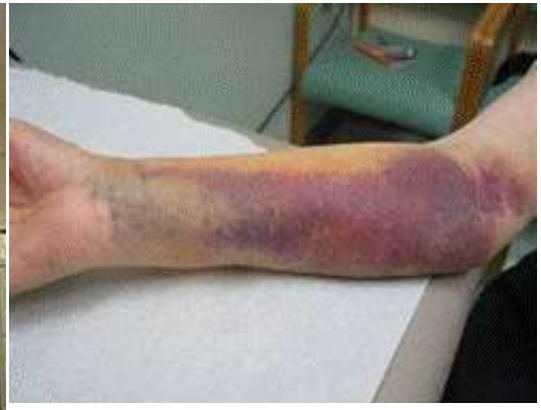
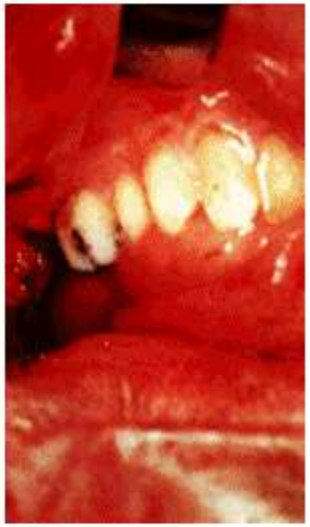
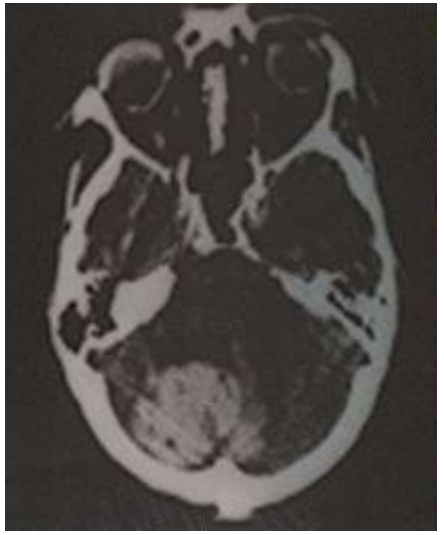


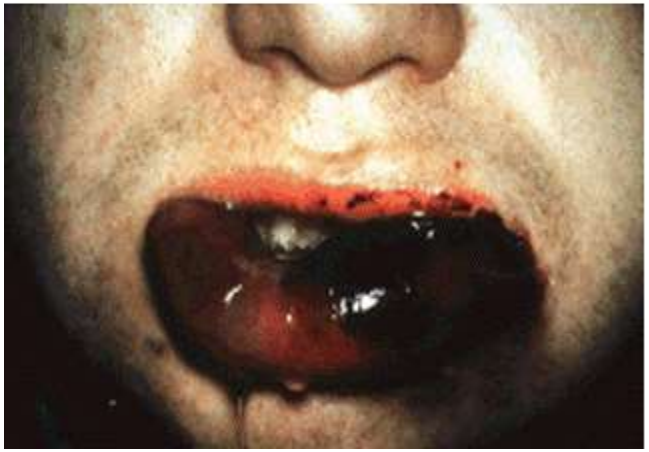


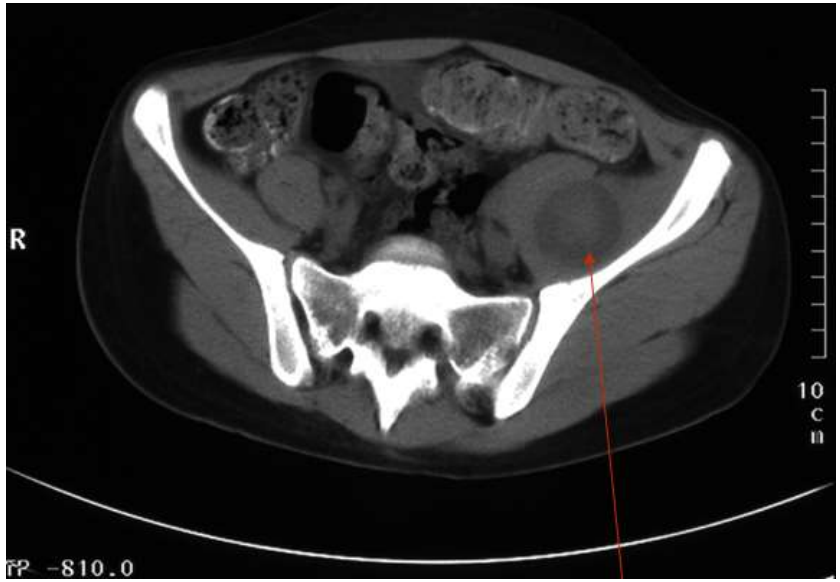
Images courtesy by
Peter A. Kouides, MD
www.bloodcmecenter.org

Life-threatening bleedings









Images courtesy by Peter A. Kouides and Guy Young
From www.bloodcmecenter.org

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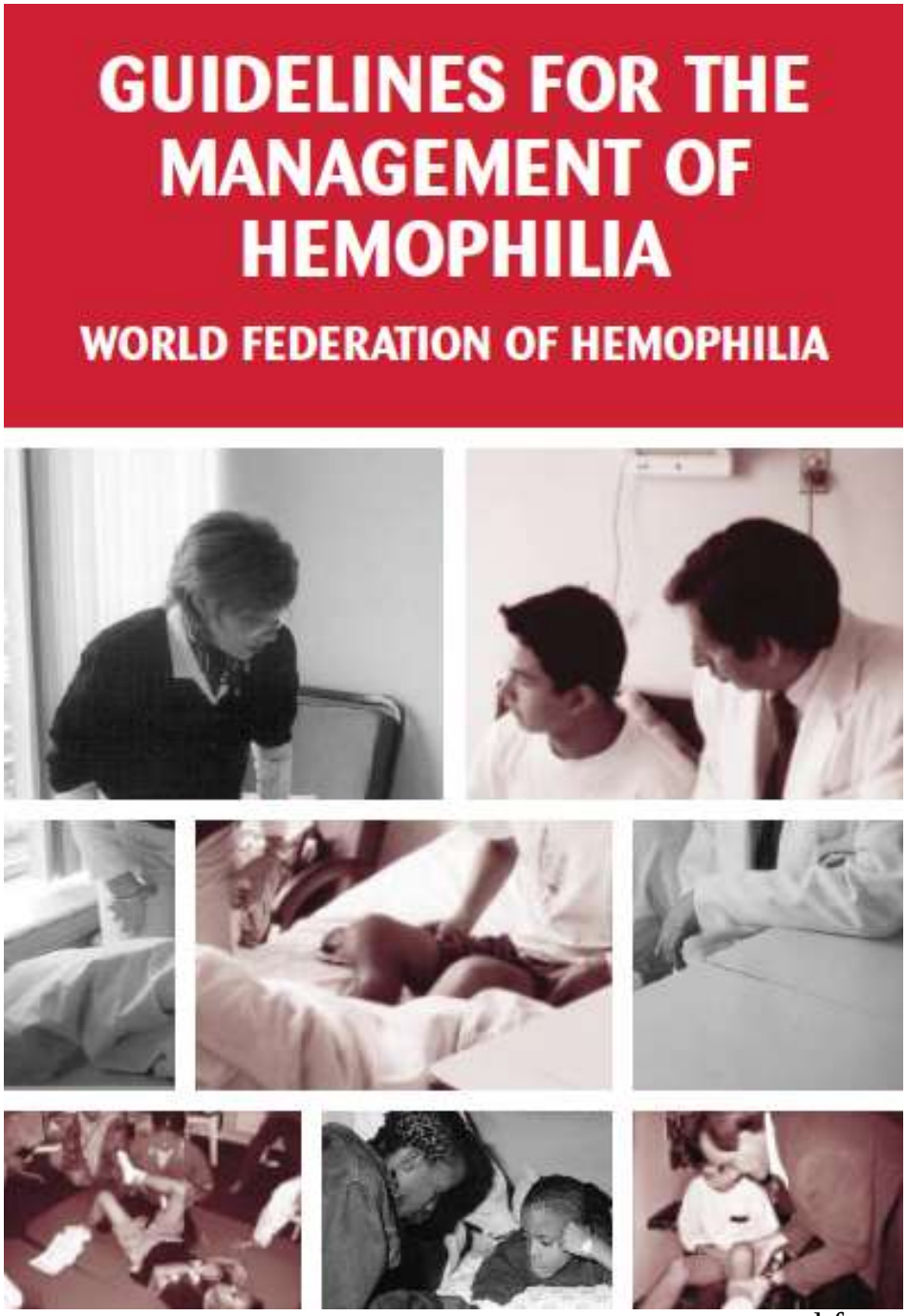


www.whf.org

Replacement therapy

- Factor concentrates
  - plasma derived
  - recombinant
- Cryoprecipitate/plasma

Desmopressin

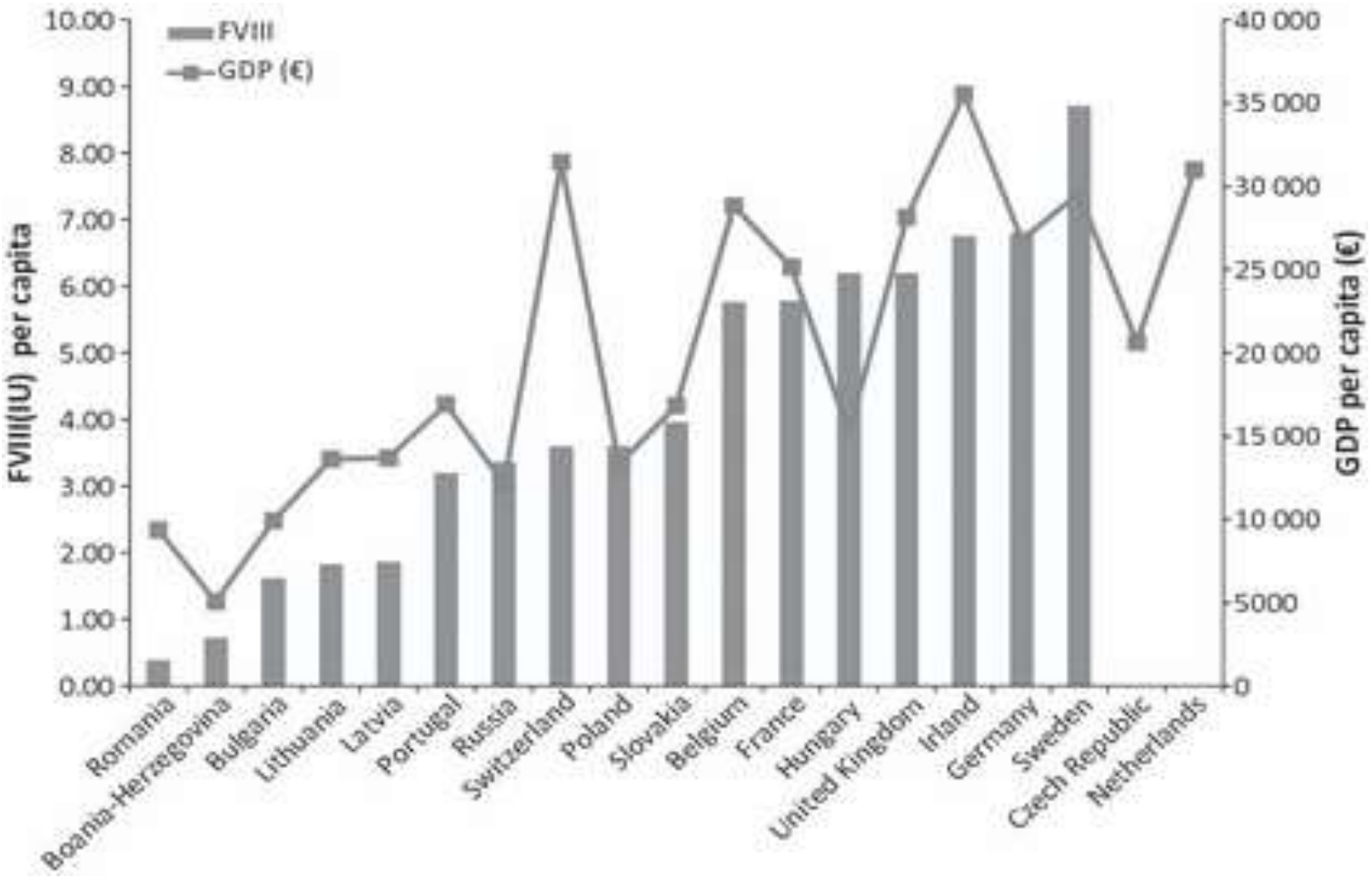
mild haemophilia A

Antifibrinolytic agents

adjuvants

BUT 70% of haemophiliacs in the world are either **not** or **poorly** treated

Haemophilia care in Europe: a survey of 19 countries



From: O'Mahony B et al. Haemophilia 2011;17:35-40

Targeted factor levels for surgical management of patients with haemophilia

Srivastava A, et al. Haemophilia 2013;19:e1-e47

Surgery	FVIII		FIX	
	Target level (%)	Duration of treatment (days)	Target level (%)	Duration of treatment (days)
Major surgery	80-100		60-80	
	60-80	1-3	40-60	1-3
	40-60	4-6	30-50	4-6
	30-50	7-14	20-40	7-14
Minor surgery	50-80		50-80	1-5
	30-80	1-5	30-80	1-5

30-50% less in limited resources sites!

Subclinical deep venous thrombosis observed in 10% of hemophilic patients undergoing major orthopedic surgery

C. HERMANS,* F. HAMMER,† S. LOBET* and C. LAMBERT*

*Division of Haematology and †X-Ray Department, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium

J Thromb Haemost 2010; 8: 1138–40.

- 24 haemophilia pts.
- Grade 1 stockings
- No DVT, PE

- **10% subclincal DVT**

Haemophilia with inhibitors

Inhibitors represent the most serious complication

- neutralization and inactivation of residual endogenous FVIII and exogenous FVIII
- resistance to clotting factor replacement therapy

Up to 30% of patients with severe haemophilia A and 6% in haemophilia B

Bethesda assay used to confirm presence of inhibitors
An inhibitor is considered as strong when the titer is >5 BU

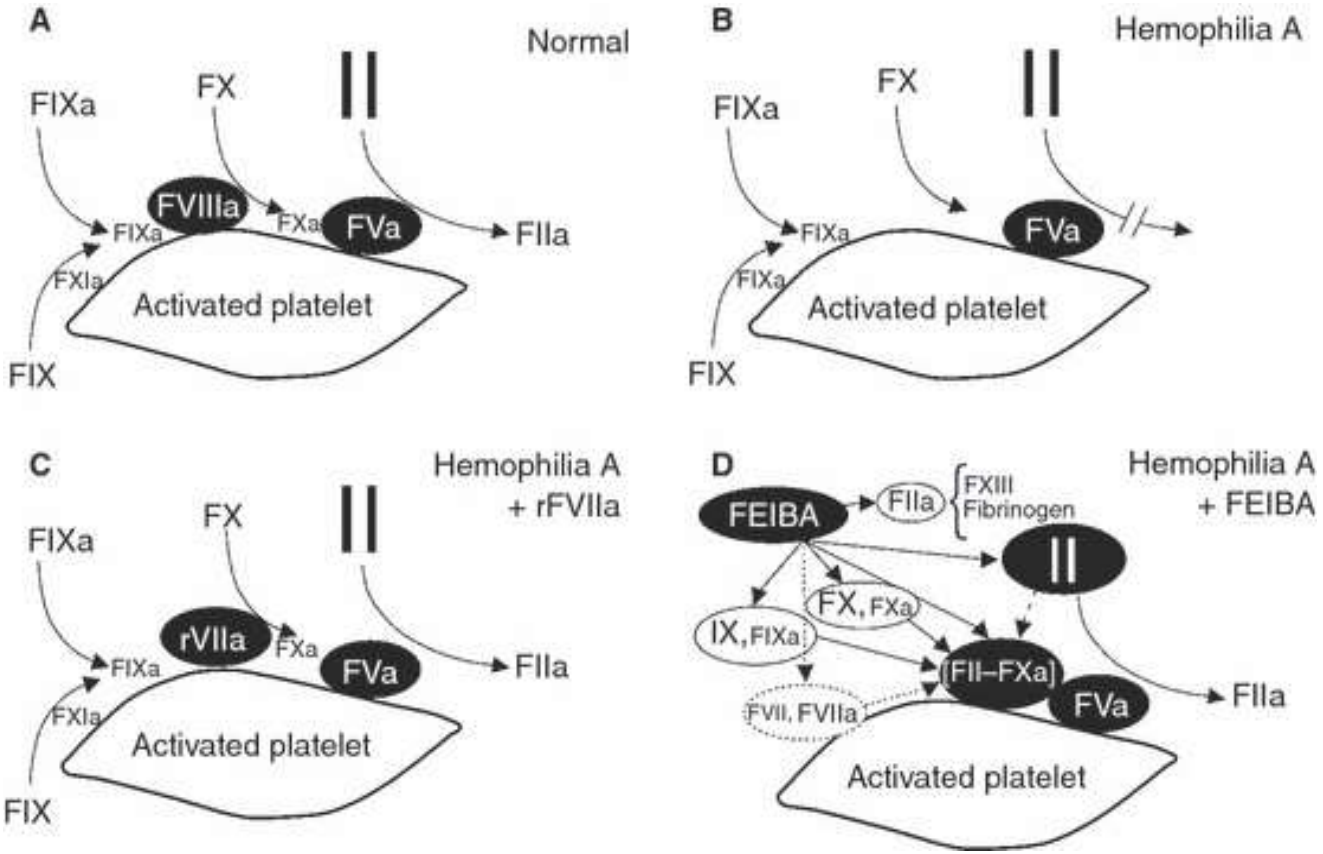
Treatment choices in haemophilia patients with inhibitors

rFVIIa	aPCC
- Recombinant product	- Plasma-derived product containing a mixture of activated factors II, VII, IX, X
- Short half-life (2-3 hr), as measured by FVII activity	- Longer hafl-life than rFVIIa (4-7 hrs)
- Potential for thrombogenicity	- Potential for thrombogenicity
	- Potential for transmission of human viruses
	- Anamnesis noted because of residual FVIII content
-Variable patient response	- Variable patient response
- 90 µg/kg every 2 hrs	- 50-75 IU/kg every 6-8 hrs

Bypassing therapy should be continued for 10-14 days postop.

Kempton CL, White GC. Blood 2009;113:1-13
Teitel JM, et al. Haemophilia 2009;15:227-239
Berntorp E. Haemophilia 2009;15:3-10

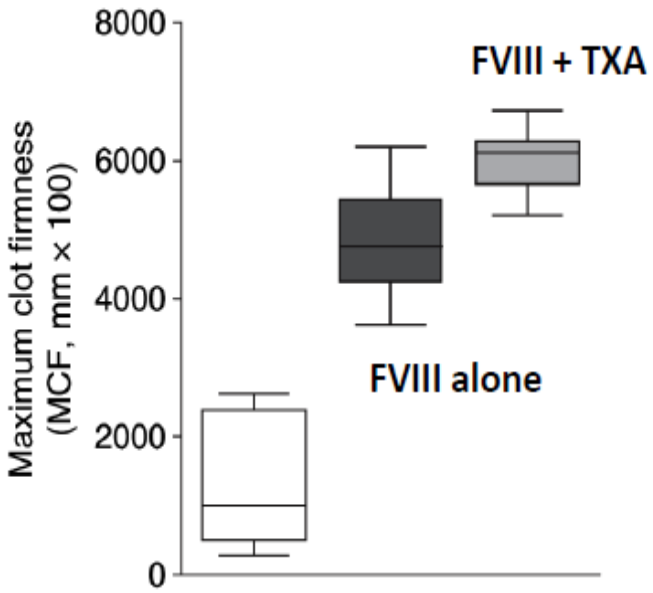
Mechanisms of by-passing agent therapy

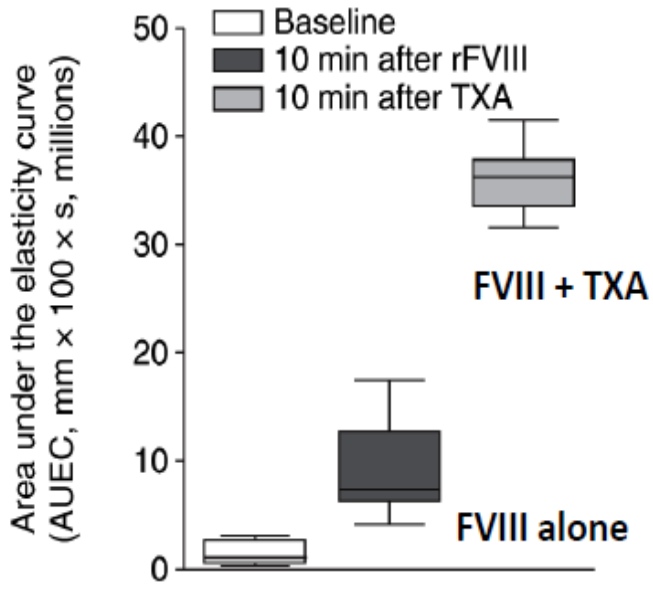


Hoffman M& Dargaud Y. J Thromb Haemost 2012:10:1478-1485

Antifibrinolytic agents

Tranexamic acid (TXA) combined with recombinant factor VIII in severe hemophilia A





Increased clot stability with combination of FVIII and TXA

From: Hvas AM, et al. J Thromb Haemost 2007;5:2409-2414

Inherited deficiencies of coagulation factors (rare bleeding disorders)

Factor	Bleeding severity
I afibrinogenemia,hypofibrinogenemia, dysfibrinogenemia	Usually mild, except in afibrinogenemia
II	Usually mild
V	Usually mild
Combined V + VIII	Usually mild
VII	Severe with low levels
X	Moderate; severe with low levels
Vitamin K dependent	Usually mild
XI	Mild- moderate with low levels
XIII	Severe

Inherited deficiencies of coagulation factors (rare bleeding disorders)

Association between level and clinical bleeding

Strong: FI, FII, FX, FXIII

Poor: FV, FVII

No!: FXI

Peyvandi F et al. Journal of Thromb Haemost 2012;10:1938-1943
Peyvandi F et al. Journal of Thromb Haemost 2012;18:148-153

Inherited deficiencies of coagulation factors (rare bleeding disorders)

Typical symptoms

- ✓ Umbilical cord, mucosal, gastrointestinal tract (GI), genitourinary or central nervous system (CNS) bleeding
- ✓ Hemarthrosis and haematomas
- ✓ Spontaneous rupture of the spleen
- ✓ Bleeding after trauma, surgery and post-partum

Thromboembolic complications!!!

FI deficiency (afibrinogenemia, dysfibrinogenemia)

FVII deficiency

Peyvandi F et al. Journal of Thromb Haemost 2012;10:1938-1943
Peyvandi F et al. Journal of Thromb Haemost 2012;18:148-153
Marty S et al. Haemophilia 2008;14:564-570
Mannucci PN et al. Blood 2004;104:1243-1252

Therapeutic options for RBDs

Tailored to the individual situation

Factor	Treatments
I	Fibrinogen concentrate, Cryoprecipitate, FFP
II	PCC, FFP
V	FFP, rFVIIa, platelet transfusion
V + VIII	FFP, FVIII concentrate, desmopressin
VII	Recombinant FVIIa, FVII concentrate, PCC, FFP
X	FX concentrate, PCC, FFP
Vitamin K dependent	Vitamin K, PCC, FFP, rFVIIa
XI	FXI concentrate, FFP, Antifibrinolytic drugs, rFVIIa, desmopressin
XIII	FXIII concentrate, recombinant FXIII, Cryoprecipitate, FFP

Peyvandi F et al. Haemophilia 2012;18:148-153; Peyvandi F et al. Haemophilia 2008:202
Napolitano M et al. Orphanet J Rare Dis 2010;5:21-29; Franchini M et al. Ann Hematol 2009;88:931-935
Huang JN, Koerper MA. Haemophilia 2008;14;1164-1169

Therapeutic recommendatios for RBDs

Factor	Target	Plasma half-life	Administration
FI	100-200mg/dl	2-4 days	Every 2-4 days
FII	20-30 IU/dl	3-4 days	Every 2-3 days
F V	15 IU/dl	36 hours	Daily
FVII	10-15 IU/dl	4-6 hours	Every 6-8 hours
FX	10-20 IU/dl	40-60 hours	Daily
FXI	30-40 IU/dl	40-70 hours	Daily or alternate days
FXIII	3-10 IU/dl	11-14 days	Every 20-30 days

Peyvandi F et al. Journal of Thromb Haemost 2012;18:148-153; Bornikova L et al. Journal of Thromb Haemost 2011;9:1687-1704; Bolton-Maggs PHB et al. Haemophilia 2004;10:593-628; Mannucci PN et al. Blood 2004;104:1243-1252

Guiding principles for surgery in patients with inherited bleeding disorders

- **Only perform surgery if it is needed and is in the best interest of patient**
- **Do not allow elective surgery to turn into an emergency-get prepared!!**
- **Use the safest haemostatic product that are available**

http://i298.photobucket.com/albums/mm258/Claudiu_2008/19%20Claudiu/image005-3.jpg

Peri-operative plan in patients with inherited bleeding disorders

Preoperative

- **Bleeding history**
  Patient/ Family
  Assessment of bleeding phenotype (non-bleeder, mild vs. severe bleeder)
- **Check for other bleeding risk factors**
  Medications, co-morbidities
- **Type of surgery**
  Risk of intraoperative & postoperative bleeding
- **Assess the risk of venous thromboembolism**
- **Check the serological status** (HIV, hepatitis and vaccination)

- Team meeting: surgeon, anesthesiologist, haematologist, nurses
- Training on factor preparation

Peri-operative plan in patients with inherited bleeding disorders

Preoperative

- **Check the factor level**
  - Measurement of response to therapy
  - Dose titration of therapy
- **Inhibitor screening**
  - If positive, check titre, peak, type of response
- **Check the lab capability**
  - Serial level measurements
- **Check the availability of substitution product**
  - Type, dose, regimen, sampling requirements

Summary of the peri-operative plan in patients with inherited bleeding disorders

Day of surgery

- Schedule the surgery early in the week and early in the day for optimal laboratory and blood bank support
- Check the availability of blood products
- Use oral premedication. Avoid any intramuscular injection
- Careful planning of the venous access. Reserve one iv. line for substitution therapy

Summary of the peri-operative plan in patients with inherited bleeding disorders

Day of surgery

- **Reconstitute the factor product immediately prior to dosing,** to avoid loss of activity and minimize the risk of bacterial contamination

- Check immediately prior to the procedure, that the factor is raised to the desired level and document the patient's response to the replacement therapy

- **Care during intubation of the airway**
Avoid naso-tracheal intubation

- Careful positioning of the extremities

Summary of the peri-operative plan in patients with inherited bleeding disorders

Postoperatively

- Maintain daily contact with the specialized haematologist

- Check daily the factor level

- If postoperative bleeding, check the trough factor level

Summary of the peri-operative plan in patients with inherited bleeding disorders

Postoperatively

- Prompt surgical intervention is required if bleeding continues despite adequate replacement therapy

- No injection and no invasive procedures without replacement

- Use paracetamol, selective cox-inhibitors or opiods for analgesia
- No ASA or NSAIDs

-Consider thromboprophylaxis in selected cases

Replacement therapy for invasive procedures in patients with haemophilia: literature review, European survey and recommendations

THE EUROPEAN HAEMOPHILIA THERAPY STANDARDISATION BOARD

Survey

- **15 European countries**
- **26 centres**
- **3633 severe haemophilia pts.**
- **Interventions per year per centre**
  - 2-4 major interventions
  - 6-10 minor
  - > 10 dental

Literature review

- **35 case series**
- **1114 pts.**
- **1328 surgical procedures**
- **707 orthopedic**

Bleeding rate: 10%

Hermans C et al. Haemophilia 2009;15:369-658

General Surgery in Patients With a Bleeding Diathesis: How We Do It

Aryal K.R. et al. World J Surg (2011) 35:2603–2610

- **Prospectively collected data**
- **113 pts. with bleeding disorders**
  - 46% haemophilia A
  - 38% VWD, 6% haemophilia B
  - 5% FX deficiency
  - 4% other
- **Age 18-86**
- **144 procedures:**

  86 surgical and 58 endoscopic

  15 urgent

  35% major

2 deaths; mortality 1.4%
4% haemorrhagic complications
10% for major operations

Do patients with haemophilia undergoing cardiac surgery have good surgical outcomes?

Michele Rossi[a,*], Raja Jayaram[b], Rana Sayeed[a]

Interact Cardiovasc Thorac Surg 2011

Type of haemophilia	Type of surgery	Total fc VIII consumption	Antifibrinolytics	Thromboprophylaxis
Mild haemophilia	Implantation of a biological aortic valve	51.000 IU Advate	Tranexamic acid	Fragmin 5000IU x 1 In 6 weeks postop
Mild haemophilia	Ventricle resection (DOR) and mitral valve reconstruction	70.000 IU Advate		Aspirin 75 mg x 1
Mild haemophilia	CABG X 3	63.000 IU Kongenate		
Moderate haemophilia	Implantation of a biological aortic valve CABG X 1	94.500 IU Advate	Tranexamic acid	Fragmine 7500 IU x 2 D 1-10 5000 IU x 2 D 11-M 3
Severe Haemophilia	CABG X 4	50.000 IU ReFacto	Tranexamic acid	Fragmine 7500 IU x 2 D 1-10 5000 IU x 2 D 11-M 3
Mild haemophilia	Aorta valve replacement CABG X 1	69.000 IU Advate	Tranexamic acid	Fragmine 5000 IU x 1 D1-5 5000 IU x 1 M1

Tang M, et al. Haemophilia 2010

Haemophilia
The Official Journal of the World Federation of Hemophilia, European Association for Haemophilia and Allied Disorders and the Hemostasis & Thrombosis Research Society

Haemophilia (2013), 19, 833–840 DOI: 10.1111/hae.12189

ORIGINAL ARTICLE *Clinical haemophilia*

Applicability of the European Society of Cardiology guidelines on management of acute coronary syndromes to people with haemophilia – an assessment by the ADVANCE Working Group

P. STARITZ,* P. DE MOERLOOSE,† R. SCHUTGENS‡ and G. DOLAN§ ON BEHALF OF THE ADVANCE WORKING GROUP

**Department of Internal Medicine, Hemophilia Care Center Heidelberg, SRH Kurpfalzkrankenhaus, Heidelberg, Germany; †Hemostasis Unit, University Hospitals and Faculty of Medicine of Geneva, Geneva, Switzerland; ‡Department of Hematology, Van Creveldkliniek, University Medical Center Utrecht, Utrecht, The Netherlands; and §Department of Haematology, Queens Medical Centre, Nottingham University Hospitals, Nottingham, UK*

Final tips for success
HAVE A PLAN !!!

- **Accurate diagnosis and knowledge of the severity of the bleeding disorder are essential**
- **Patients with inherited bleeding disorders should be managed peri-operatively in collaboration with a haematologist**
- **Appropriate peri-operative replacement therapy is the mainstay of therapy**
- **Thromboprophylaxis should be discussed in cases with associated risk factors**
- **Good communication is key**