C E E A

Târgu Mures

9-11 December 2015

Management of severe peripartum bleeding

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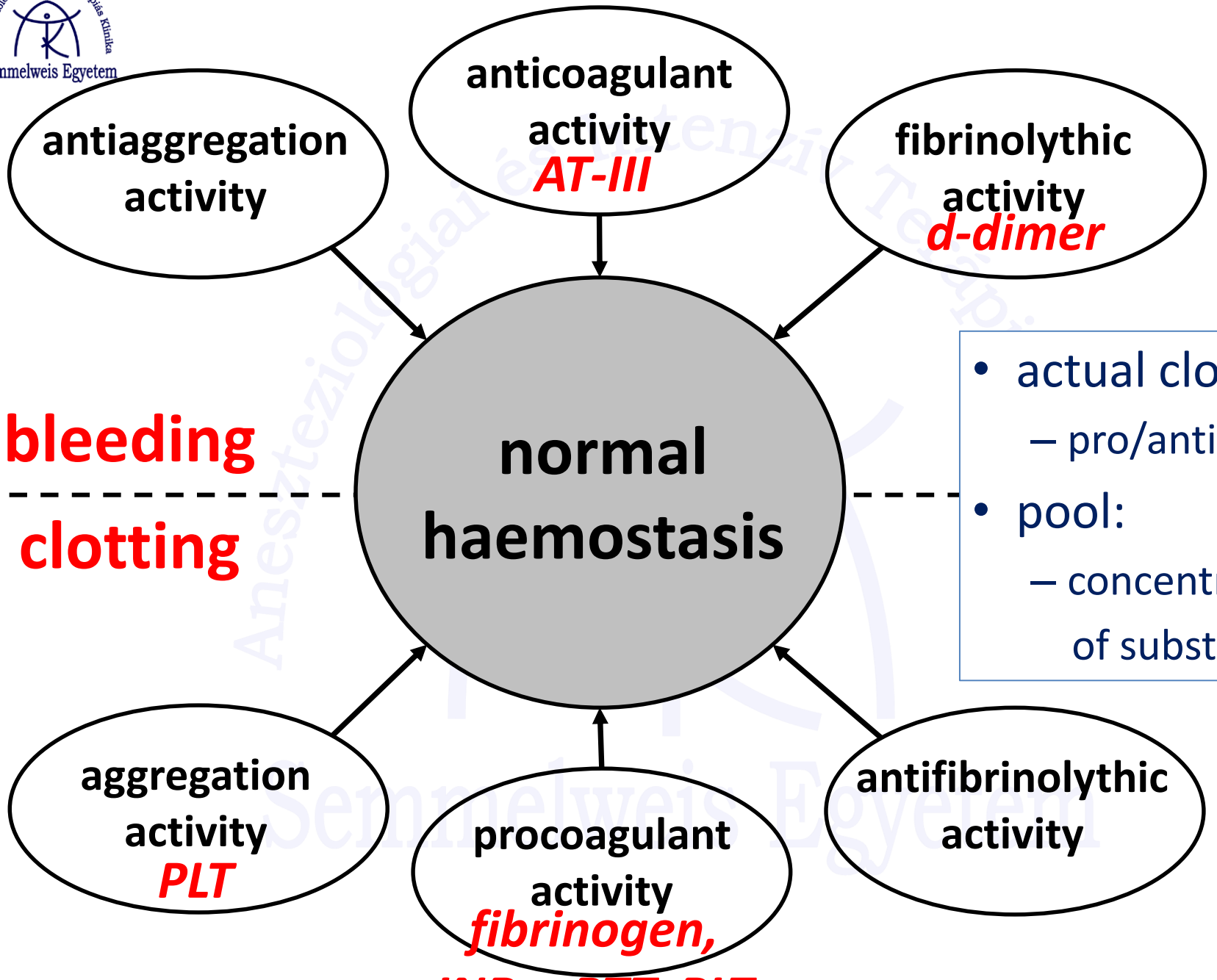
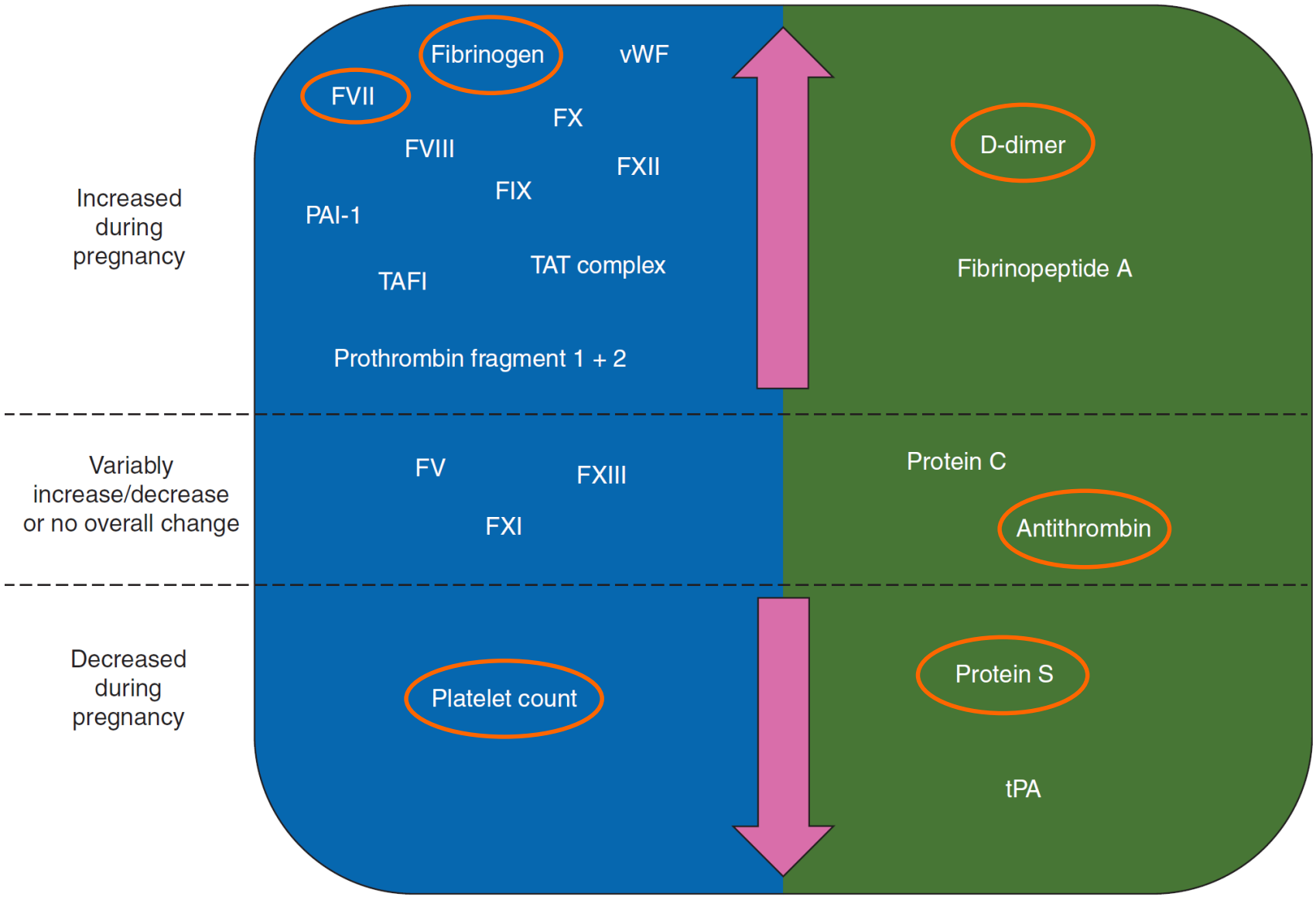


Levy AnesthAnalg 2010, modified

Hemostasis of the pregnant

- Cause/aim
  - 9 month preparation for delivery and blood loss
  - Support of the uterus (and phoetus)
- Haematology
  - Blood volume, „physiologic anaemia”
  - hypercoagulation state
    - It can mask former clotting disorder
- Circulation
  - Vasodilatation
  - CO
  - blood flow of uterus↑ (25% of CO)
  - caval vein syndrome

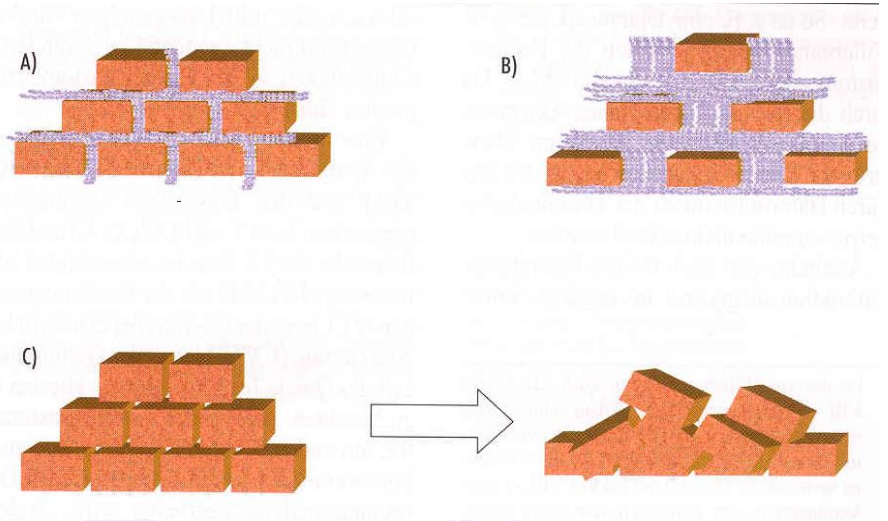
Semmelweis Egyetem



Solomon-BrJAnaesth-2012

Normal values

- aptt, INR: norm
- fibrinogen 3,5-6,5 g/L
- platelet: slightly decreased
- d-dimer: elevated
- placenta: procoagulant
  - high blood flow, harmful (much TF)



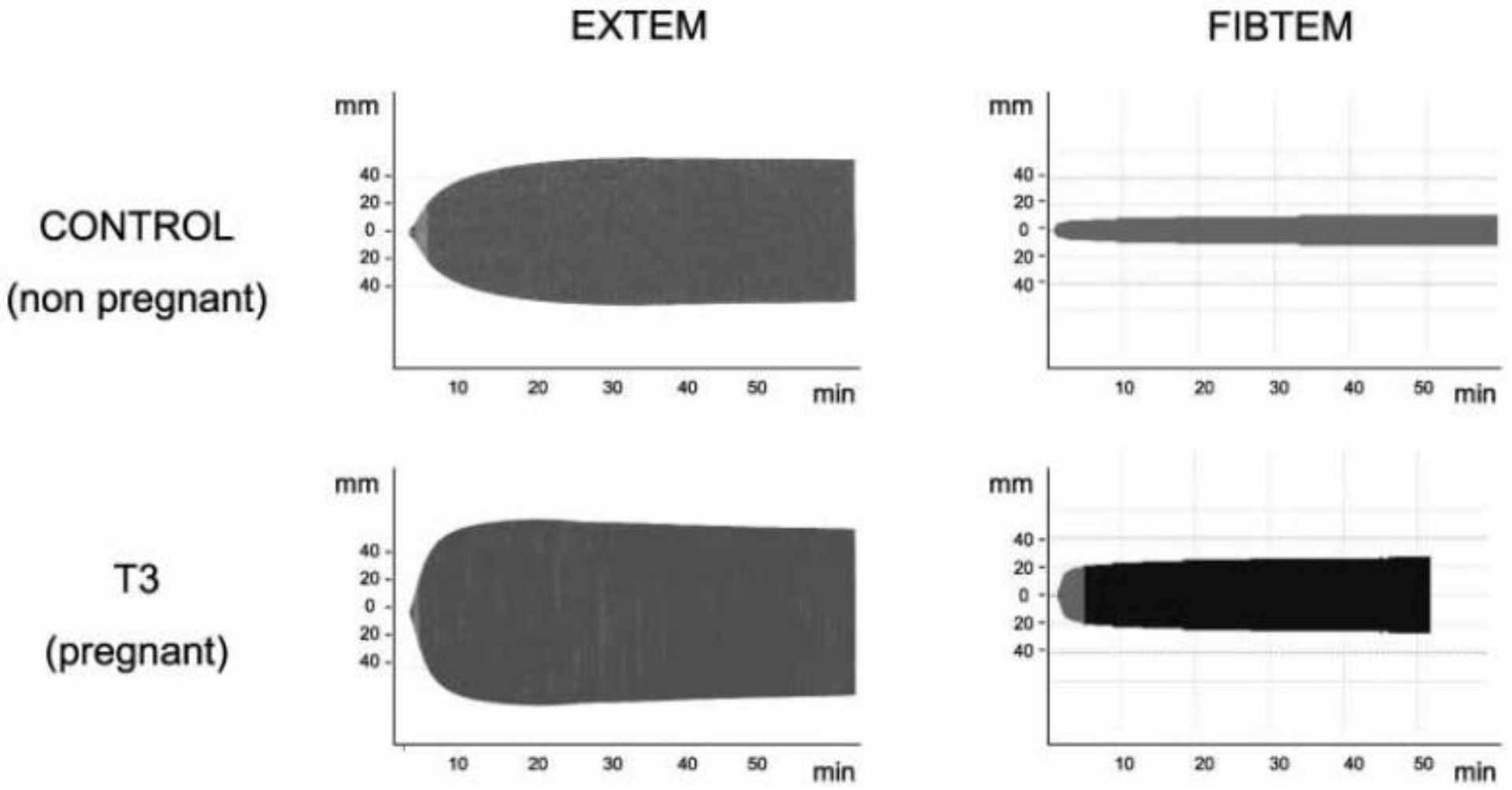
British Journal of Anaesthesia **112** (5): 852–9 (2014)
Advance Access publication 31 January 2014 · doi:10.1093/bja/aet480

BJA

Peri-partum reference ranges for ROTEM® thromboelastometry

N. M. de Lange[1*], L. E. van Rheenen-Flach[2], M. D. Lancé[3], L. Mooyman[4], M. Woiski[5], E. C. van Pampus[6], M. Porath[7], A. C. Bolte[2], L. Smits[8], Y. M. Henskens[9] and H. C. Scheepers[4]

ROTEM pregnant vs. non-pregnant



Huissoud-ThrombHaemost-2009

PPH – role of fibrinogen

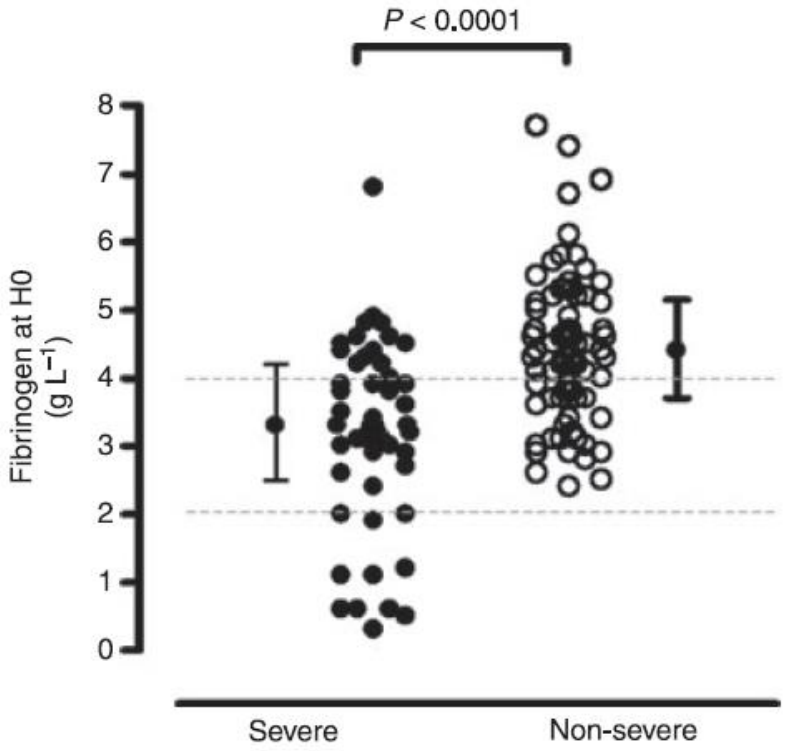


Fig. 2. Individual fibrinogen plasma concentrations at H0 in women with severe (●) or non-severe (○) postpartum hemorrhage. Mean ± SD values are reported for both groups.

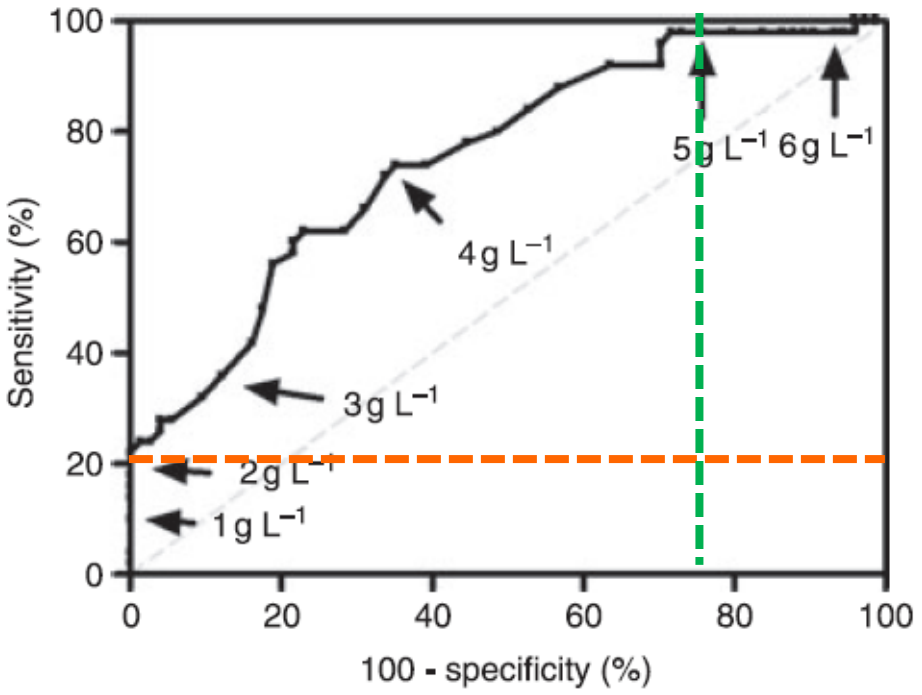


Fig. 3. ROC curve of fibrinogen plasma concentration at H0 for the diagnosis of severe postpartum hemorrhage.

- No pool, decreases quickly in case of bleeding, dilution in case of volume therapy, colloids cause pseudo-elevation
- Substitution: not much in FFP ☹

Charbit-JThrombHaemost-2007

MASSIVE BLEEDING =

= MASSIVE HAEMOSTATIC DISORDER

Semmelweis Egyetem

EJA

Eur J Anaesthesiol 2013; **30:**270–382

GUIDELINES

Management of severe perioperative bleeding

Guidelines from the European Society of Anaesthesiology

Sibylle A. Kozek-Langenecker, Arash Afshari, Pierre Albaladejo, Cesar Aldecoa Alvarez Santullano, Edoardo De Robertis, Daniela C. Filipescu, Dietmar Fries, Klaus Görlinger, Thorsten Haas, Georgina Imberger, Matthias Jacob, Marcus Lancé, Juan Llau, Sue Mallett, Jens Meier, Niels Rahe-Meyer, Charles Marc Samama, Andrew Smith, Cristina Solomon, Philippe Van der Linden, Anne Juul Wikkelsø, Patrick Wouters and Piet Wyffels

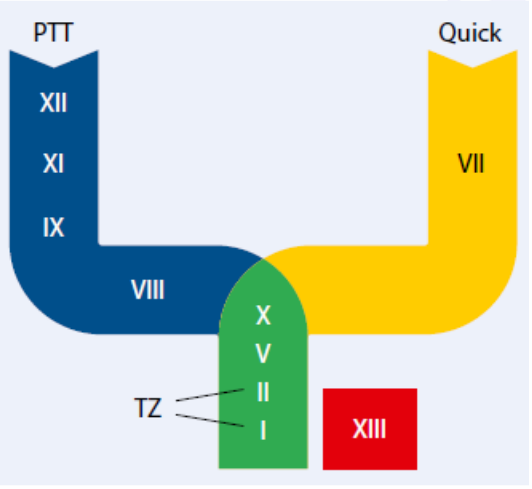
•Kozek-Lagenecker SA et al: Management of severe perioperative bleeding Guidelines from the… Eur j Anaesthesiol 2013;30:270

ESA 2013

- **Traditional tests**
  - **Originally designed for deficiences and drug monitoring, NOT for prognosting bleeding or guiding clotting therapy**
  - **Too slow in emergency cases**
    - **aPTT, PTT (INR)**
      - » Just until the formation of the first fibrin filaments
    - **Fibrinogen level**
      - » Indirect method: interferency with heparin, FDP, colloids
    - **Platelet count**
    - **FII, FV, FVII, FVIII, FIX, FX, FXIII**
      - » Deficiences
    - other: e.g. D-dimer
- **Viscoelastic POC tests**
  - Fast intraoperative diagnosis

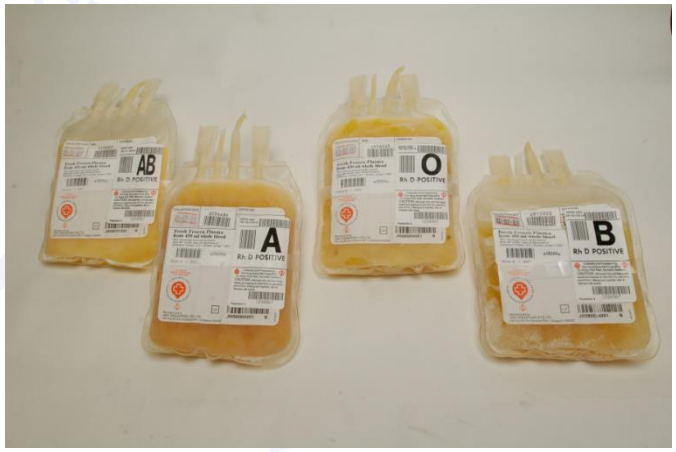
•Kozek-Lagenecker SA et al: Management of severe perioperative bleeding Guidelines from the… Eur j Anaesthesiol 2013;30:270

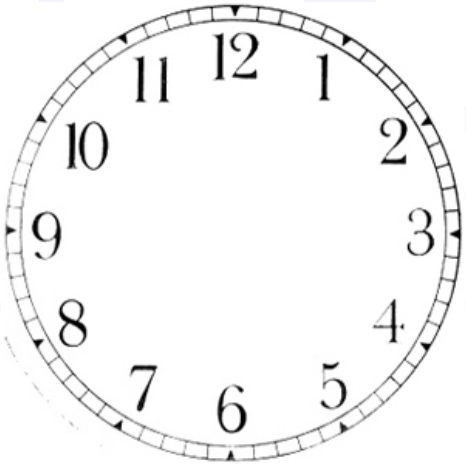
Clotting, diagnosis and therapy

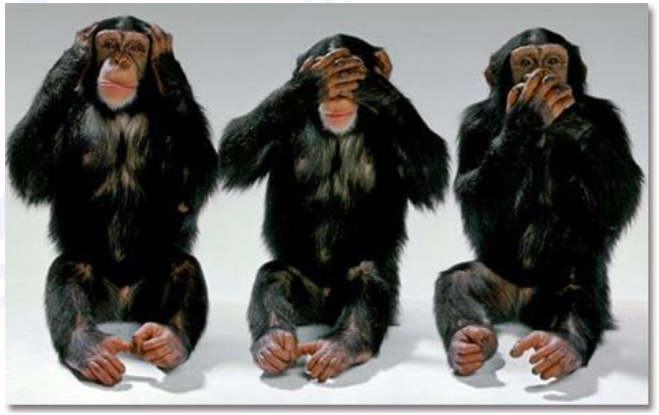


INR↑, aptt↑ ⟹

(fibrinogen?, AT-III?, d-dimer?)

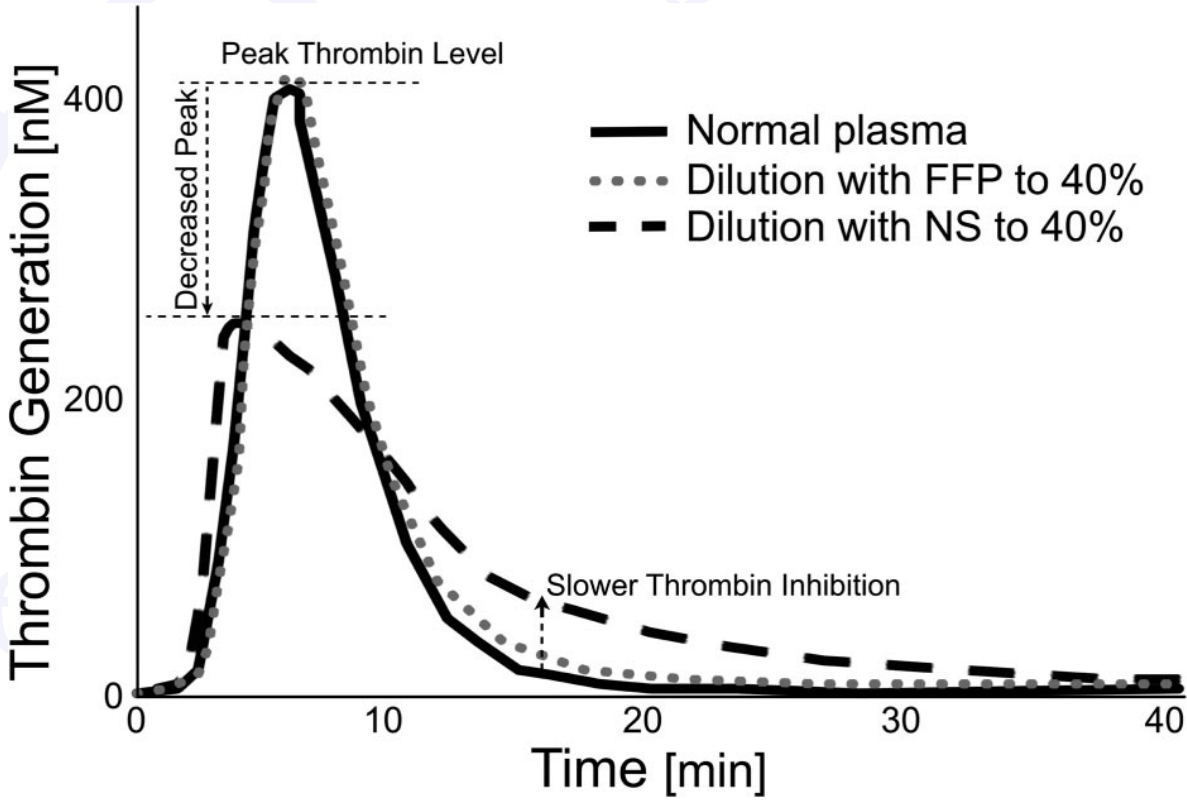






Side effects of infusions on clotting

- Dilution effects (cristalloids + colloids)
  - Clotting factors, plt, hgb
- Colloids
  - Inhibition of PLT function
  - Inhibition of fibrin polimerisation
  - Induction of acquired vW syndrome
  - Fibrinolythic tendency



Bolliger-Anesthesiol-2010

Massive bleeding, substitution w. FFP

- hypothermia!
  - -10% factor activity/-1°C
  - Measurement on 35-37°C pseudonormalisation

Table 1. Critical Level of Hemostatic Factors and the Inversely Predicted Corresponding Blood Loss (95% Confidence Interval) as Percent of Calculated Blood Volume

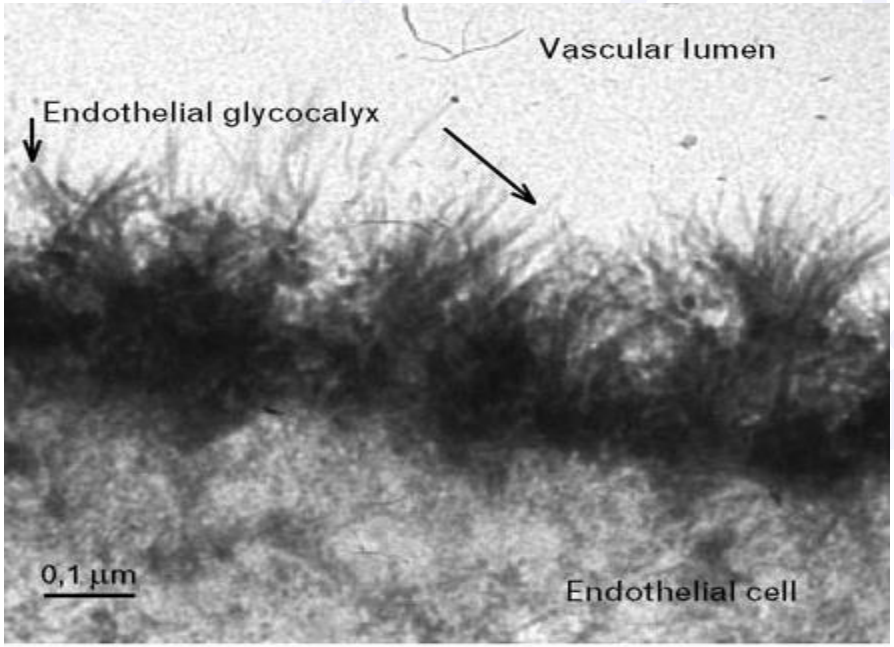
Hemostatic factor	Critical level	Blood loss (%)
Platelets	$50 \times 10^3/mm^3$	230 (169–294)
Fibrinogen	1.0 g/L	142 (117–169)
Prothrombin	20	201 (160–244)
Factor V	25	229 (167–300)
Factor VII	20	236 (198–277)

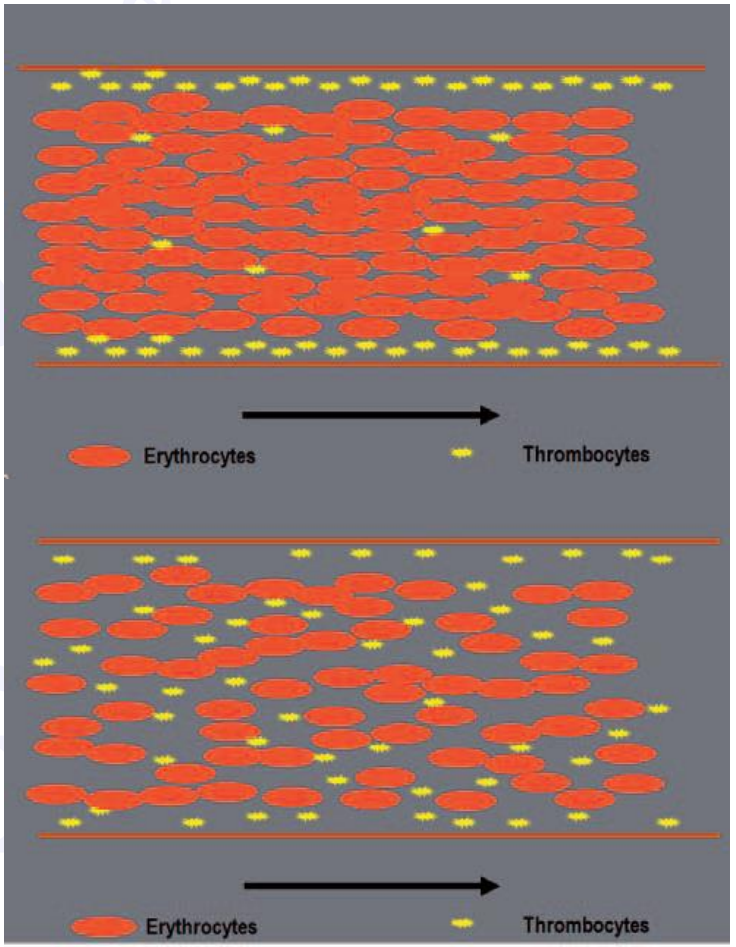
	Group 1 (12 ml/kg FFP)			Group 2 (33 ml/kg FFP)		
	Preinfusion	Postinfusion	Observed increment	Preinfusion	Postinfusion	Observed increment
PT (s)	22·8 (17–222)	19 (15–36)		24 (17–44)	16 (14–20)	
aPTT (s)	46·4 (30–223)	37 (30–158)		41 (28–198)	30** (24–45)	
FI (g/l)	2·7 (0·2–4·4)	3·4 (0·2–7·2)	0·4 (−1·5–2·9)	1·5 (0·4–4·5)	2·7 (1·7–4·1)	1·0 (−0·9–2·4)
FII (IU/dl)	36·5 (22–65)	56 (43–76)	16 (7–42)	35 (16–73)	83** (60–102)	41* (15–61)
FV (IU/dl)	36 (2–126)	58 (14–121)	10 (−4·7–37)	41 (10–99)	69 (39–119)	28* (−16–51)
FVII (IU/dl)	43 (6·6–99)	55 (17–114)	11 (4–32)	48 (16–91)	85** (54–127)	38* (−3–75)
FVIII (IU/dl)	146 (8–391)	159 (18–360)	10 (−49–46)	157 (58–535)	175 (120–313)	17 (−250–96)
FIX (IU/dl)	83 (29–165)	98 (41–167)	8 (−6–30)	73 (43–174)	114 (65–156)	28* (−35–53)
FX (IU/dl)	49 (28–133)	61 (50–94)	15 (−73–43)	53 (16–94)	88** (65–104)	37* (−5–65)
FXI (IU/dl)	38 (20–105)	48 (38–101)	9 (−4·3–32)	34 (15–58)	55** (41–80)	23* (6–37)
FXII (IU/dl)	39 (27–64)	57 (44–83)	30 (1–37)	30 (5–69)	73** (60–105)	44* (23–66)

Wolberg JtTauma 2004, Hippala AnesthAnalg 1995, Chowdoury BrJHaemat 2004

Plasma

- 75% - dinamic plasma (depends on htc)
  - We measure here, treat here
  - If the cascade activates here: DIC
- 25% - static plasma (+glycocalix)
  - Here happens everything





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Massive transfusion = dilution

Table 2—*Whole Blood Composition Compared With Component Therapy*

Whole Blood (500 mL)	Component Therapy (660 mL)
Hematocrit 38%-50%	1 unit PRBC = 335 mL with hematocrit 55%
Platelets 150-400 K/μL	1 unit platelets = 50 mL with 5.5×10^{10} platelets
Plasma coagulation factors = 100%	1 unit plasma = 275 mL with 80% of the coagulation activity compared with whole blood
Thus, 1 unit PRBCs + 1 unit platelets + 1 unit FFP = 660 mL with hematocrit 29%, platelets 88 K/μL, and coagulation activity 65% compared with whole blood. PRBC = packed red blood cells.	

Sihler-Chest-2010

Postpartum haemorrhage (PPH)

- Leading cause of maternal mortality/morbidity
- Should be avoided
- The treatment is suboptimal in many cases
- Causes: 4Ts

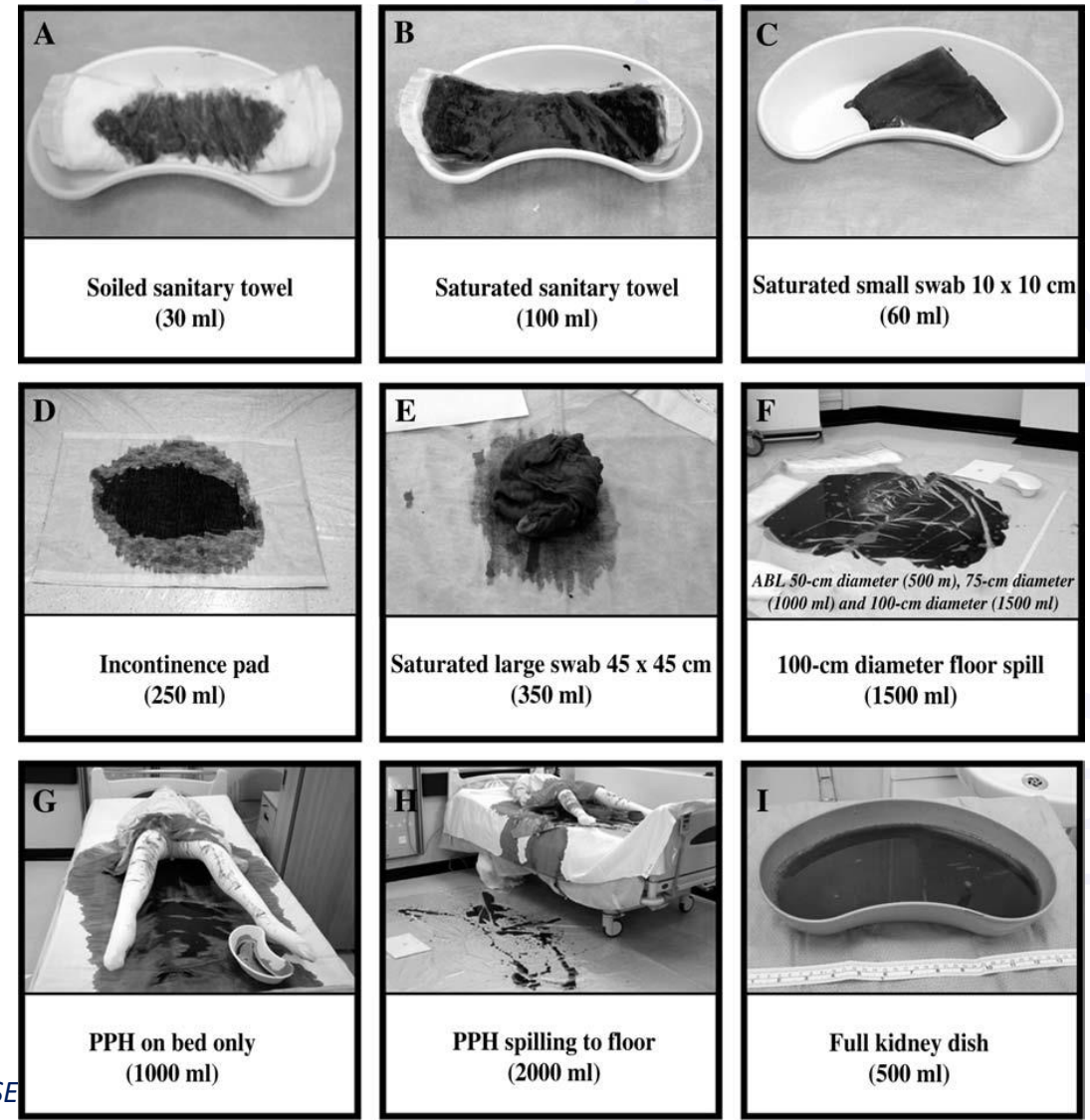
- Excessive blood loss:
  - pvn delivery: >500 ml;
  - Caesarean section: >1000 ml /0-24.ó

- Severe PPH:
  - >1500ml loss or
  - Hgb↓ >40 g/L or
  - PRBC demand ↑ >4 U or
  - Demand for intervention

- How much was that?

There have been some bleeding…

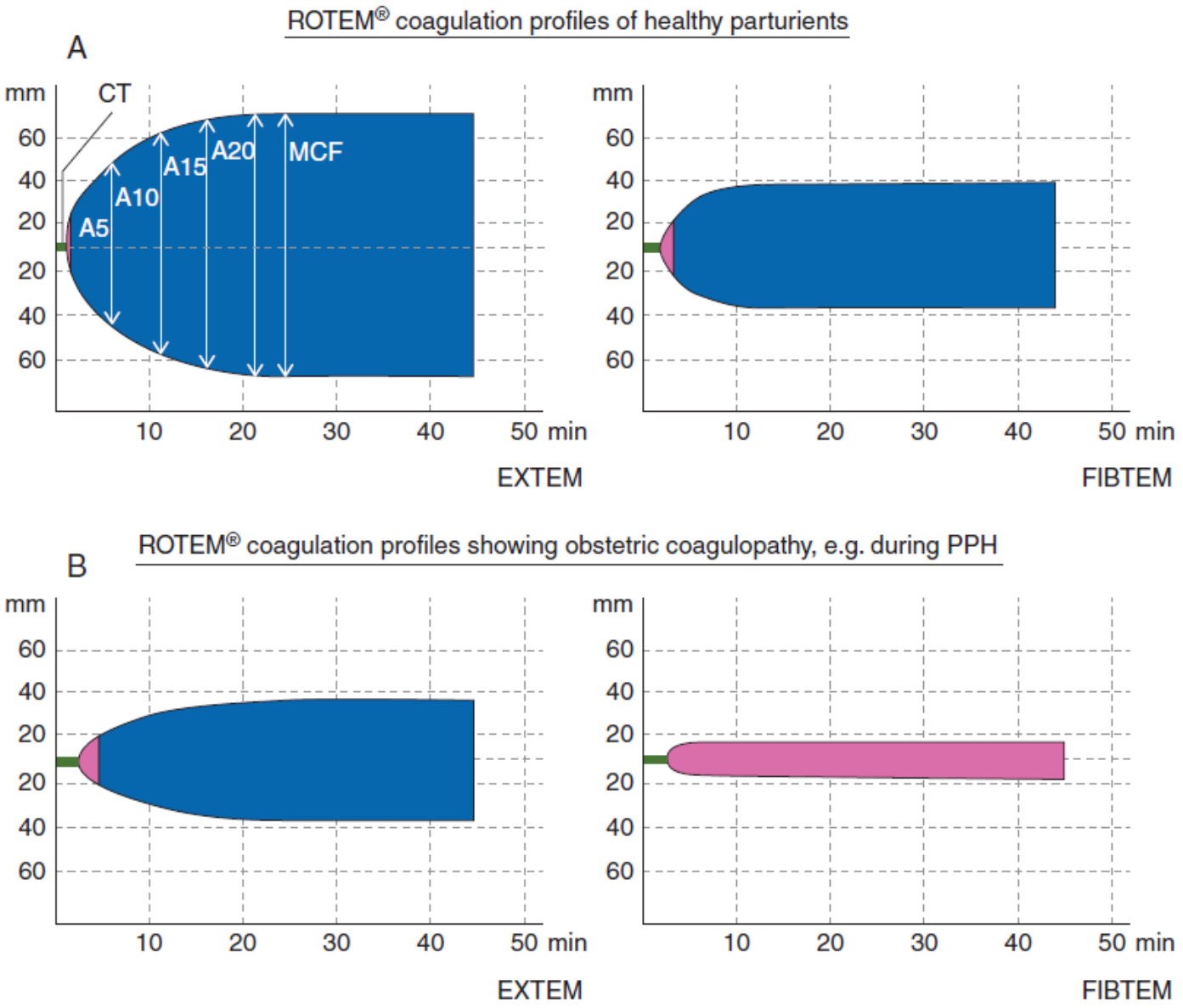
- Normal blood loss: pvn delivery <500ml; Caesarean section <1000ml
- Severe PPH: >1500ml or >4U PRBC or ΔHb>40 or intervention/embolisation



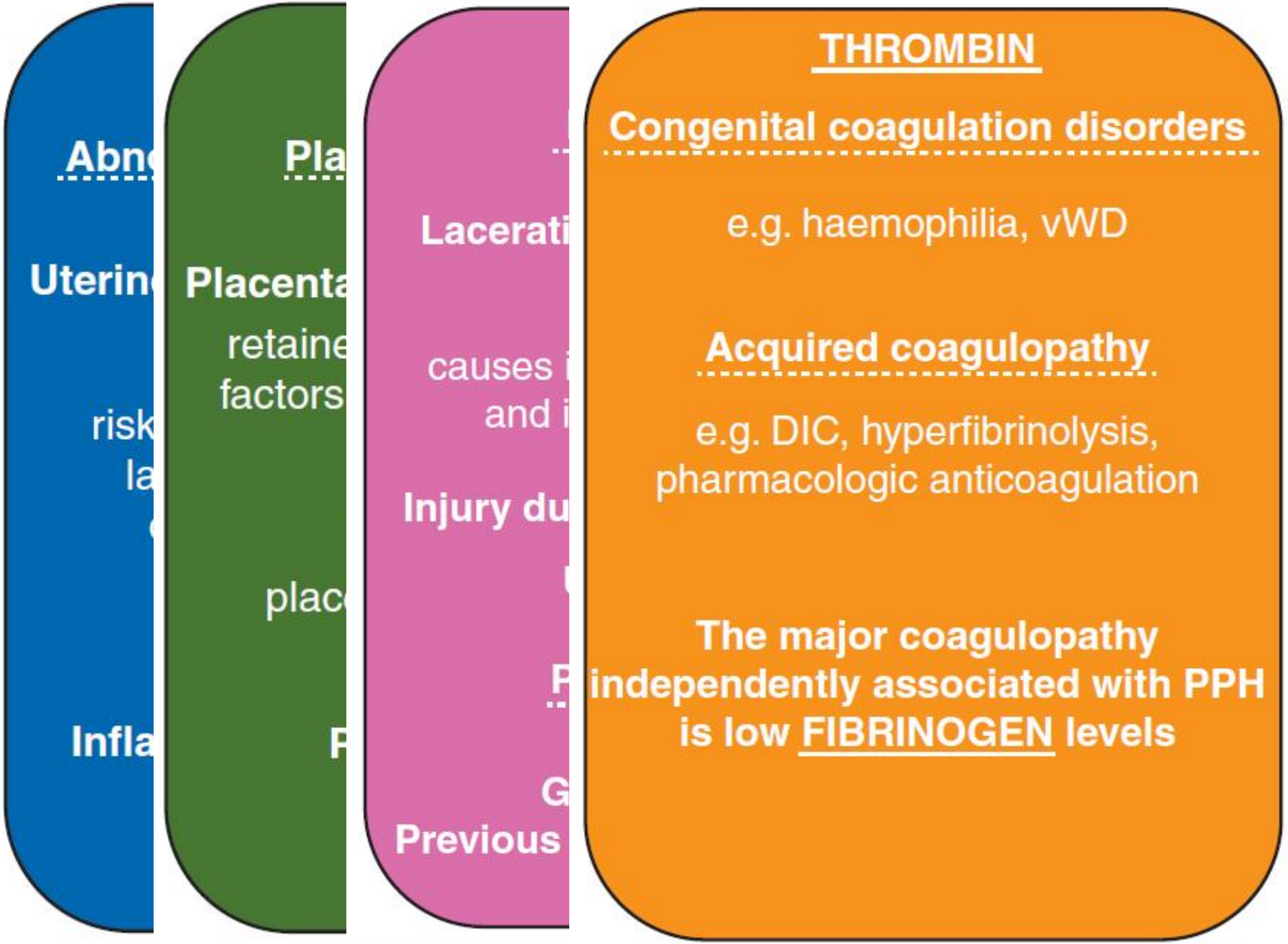
Swabs with blood	ml
10x10cm swab	60
30x30cm small swab	140
45x45cm large swab	350
1kg saturated swab	1000
Ø 50cm pool on the floor	500
Ø 75cm pool on the floor	1000
Ø100cm pool on the floor	1500
Blood only in the bed	<1000
Blood in the bed and on the floor	>1000

Bose-BJOG-2006

ROTEM during PPH



Solomon-BrJAnaesth-2012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Congenital coagulation disorders
e.g. haemophilia, vWD
Acquired coagulopathy
e.g. DIC, hyperfibrinolysis, pharmacologic anticoagulation
The major coagulopathy independently associated with PPH is low FIBRINOGEN levels

Causes of PPH – 4Ts

- **T**ONE
  - Uterine atony
  - Inflammation due to infection
- **T**ISSUE
  - Placental complications (e.g. placenta previa, abruption)
- **T**RAUMA
  - Physical injury (e.g. lacerations of cervix, perineum, vagina; injury during Caesarean section, etc.)
- **T**ROMBIN
  - Congenital disorders
  - Acquired disorders (hyperfibrinolysis)
  - Low fibrinogen level

Risk factors of PPH

- aptt/INR remaines normal for a long time during bleeding
- Result of lab tests tend to come slow (1 hour)
- Fast decrease in platelet count
- Fibrinogen level <2 g/L; this is the first to decrease
- FIBTEM-MCF: decreases earlier than the fibrinogen level

- Infusio, FFP: dilutes the clotting factors ☹
- Colloids: deminishes clotting ☹
- Bleeding patient tends to become hypothermic
- Do not detect fibrinolysis

Problems in PPH

- Delay in therapy due to underestimation of blood loss
- Delayed approach to blood products (PRBC, FFP, PLT)
- Lack of ”local major haemorrhage protocols”
- Lack of knowledge and education
- Insufficient interdisciplinal communication
- Chaos

- Ideal algorithm
  - Obstetritian
  - Anesthetist
  - Hemostazeologist

Girard-CurrOpinAnesthesiol-2014

ESA 2013

- Management of PPH
  - Multidisciplinary team (obstetritian, anaesthetist, hemostazeologist)
  - Escalation protocol
    - uterotonics, surgical/endovascular procedures, procoagulants
  - Use cell saver during Caesarean section
- Diagnostics
  - The availability of aPTT and INR is not sufficient
  - TEG/ROTEM can prove coagulopathy and hyperfibrinolysis
  - Have to measure fibrinogen level for a pregnant who is bleeding
    - <2: high risk of severe PPH
- Therapy
  - Use transfusion protocol
  - Therapeutic trigger of fibrinogen level should be higher
  - Give tranexamic acid during Caesarean section and at PPHs
  - rFVIIa last choice (when fibrinogen and PLT is normal(ized))

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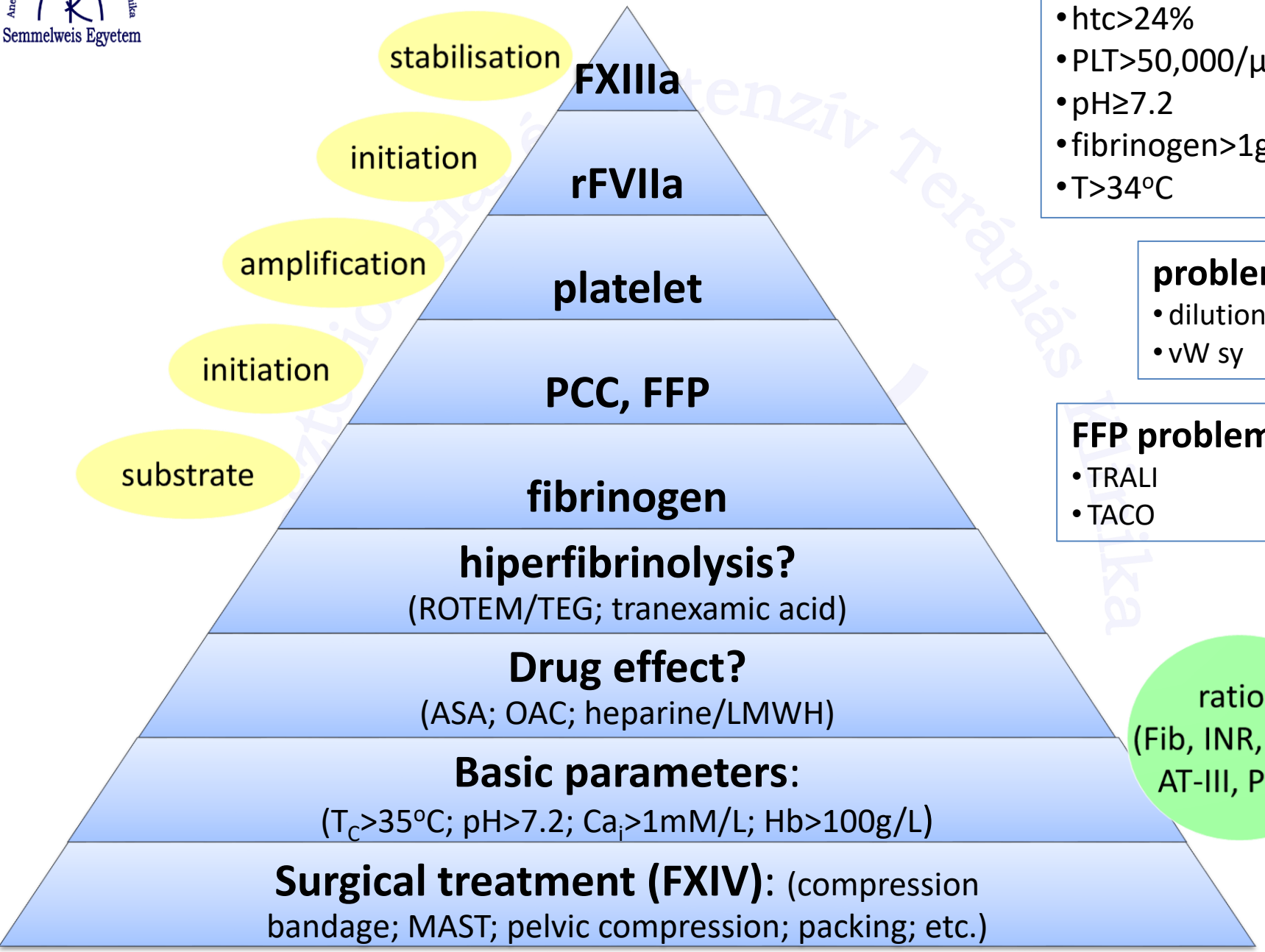

rFVIIa conditions
- htc>24%
- PLT>50,000/µL
- pH≥7.2
- fibrinogen>1g/L
- T>34°C

problems
- dilution
- vW sy

FFP problems
- TRALI
- TACO

ratio?
(Fib, INR, aptt, AT-III, PLT?)

Modified after Görlinger, Kozek, Fazakas

Semmelweis Egyetem
Aneszteziológiai és Intenziv Terápiás Klinika

Postpartum hemorrhage treatment algorithm

After vaginal delivery or postoperatively after cesarean section

	Clinical symptoms	General/surgical measures	Medication
STEP 1	Maximal duration: 30 minutes after diagnosis	Call for senior obstetrician/inforn anesthesiologist	
	• **Vaginal bleeding** > 500 ml after vaginal delivery > 1000 ml after cesarean section beware: underestimation !use measuring system! • **Stable hemodynamics**	• 2 intraevnous accesses (at least 1 large bore) • Cross match blood/emergency labs • Volume (e.g. crystalloids/colloids) • Foley catheter • Measure blood loss • Fast detection of bleeding cause (4 Ts) • Uterine tone (Tone) • Placental inspection (Tissue) • Inspect via speculum (Trauma) • Coagulation (Thrombin) • Uterine compression - ultrasound	PARALLEL • **OXYTOCIN** 3–5 U as short infusion and 40 U in 30 min (controlled infusion) OR • **CARBETOCIN** (off-label use) 100 µg as short infusion Severely persistent hemorrage STEP 2, moderately persistent hemorrhage consider • **MISOPROSTOL** (off-label use) 800 µg sublingual/rectal
STEP 2	Duration maximal further 30 min. (= 60 min after diagnosis)	Call for anesthesiologist/alert OR-team/organize operating room consider transfer	
	• **Persistente severe bleeding** • **Stable hemodynamics**	• Prepare operating room • Exclude uterine rupture • Palpation/ultrasound • Suspected placentral retention • Manual removal • Curettage (controlled by ultrasound)	**Order RBC, plasma, platelets** (Cross match, prepare blood products) • Sulprostone 500 µg (maximum 1500 µg/24h) as controlled infusion only • 2 g tranexamic acid i.v. before fibrinogen In case of persistent severe hemorrhage approx. 1500 ml blood loss • Fibrinogen 2–4 g • Consider RBC, plasma
STEP 3		Consider transfer/call for senior anesthesiologist Inform the persons with the best clinical expertise	
	• **Refractory severe bleeding with hemodynamic stability** OR • **Hemodynamic shock** AIM • Hemodynamic stability • (Temorary) cessation of bleeding • Improve coagulation and anemia • Organize STEP 4	**Uterine tamponade** Balloon: • Insert balloon under ultrasound control sufficient filling of balloon (continue sulprostone) • Use slight traction • Alternatively: Gauze packing of the uterus Cessation of bleeding: • Intermediate/high-dependency care • **Deflate balloon** after 12–24 hours (potentially after transfer to large center) Persistence or resurgence of bleeding: (bleeding with balloon in situ or after deflation) • Consider repeating balloon ("bridging") • Go to STEP 4	Target values: • Hemoglobin > 80–100 g/l (5–6.2 mmol/l) • Platelets > 50 Gpt/l • Systolic BP > 80 mmHg • pH ≥ 7.2 • Temperature > 35° C • Calcium > 0.8 mmol/l
STEP 4		Call in the persons with the best clinical expertise	
	• **Persistent bleeding**	Definite treatment/(surgical) therapy	
		In-stable hemodynamics Stop the bleeding ↓ Laparotomy/vascular clamps/compression Stabilization Hemodynamics/temperature/coagulation consider rFVIIa	**Stable hemodynamics** Definite surgical therapy • Compression sutures • Vascular ligation • Hysterectomy Embolisation
	Criteria for transfer • Lack of surgical or interventional equipment or lack of experienced personel • Temporary stop of bleeding through tamponade • Hemodynamic stability for transport • Existing SOP with the target hospital	**Recombinant FVIIa** (Off-label use!) • Initial 60–90 µg/kg (bolus) • Might be repeated after 20 min in case of persistent bleeding	**Conditions:** pH ≥ 7.2 Fibrinogen > 1.5 g/l Platelets > 50 Gpt/l Hyperfibrinolysis excluded/treated

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Step 1 (max 30 min)

CALL FOR HELP!

Vaginal bleeding>500/1000 ml AND stabile haemodynamics

- 2 large bore veins
- Cross match blood
- Volume
- Urinary catheter
- MEASURING blood loss

- Causes (4T)
  - Tone?
  - Tissue?
  - Trauma?
  - Trombin?
- Uterine compression (ultrasound)

- OXITOCIN

  3-5 IU as short infusion, majd 40 IU/30 min

or

- CARBETOCIN (off-label use)

  100 µg as short infusion

- Moderately persistent haemorrhage consider
  - MISOPROSTOL (off-label use) (PGE_1)
    - 100 µg SL/PR
- Severely persistent haemorrhage → Step 2

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Step 2 (max further 30 min) CALL FOR HELP!

Persistent severe bleeding AND stabile haemodynamics

- Prepare operating room
- Exclude uterine rupture
- Palpation / Ultrasound
- Suspected placental retention
- Manual removal
- Curettage (controlled by ultrasound)

Logistics of blood products

- SULPROSTON (PGE_2)
  500 µg (max. 1500 µg/24h) in infusion
- 2 g tranexamic acid IV before fibrinogen
- In case of severe blood loss (>1500 ml)
  - Fibrinogen 2g
  - Consider RBC/FFP

Girard-CurrOpinAnesthesiol-2014

Step 3

CALL FOR HELP!

Refractory severe bleeding AND stabile haemodynamics

or

shock

- Aims:
  - Hemodynamic stability
  - (Temporary) cessation of bleeding
  - Improve coagulation and anemia
  - Organize Step 4

Uterine tamponade

- Balloon (or gauze packing)
- Cessation of bleeding
  - I/HDU
  - Deflate balloon after 12-24 h
- Persistent or resurgence of bleeding
  - W. balloon in situ or after deflation
  - Consider repeating balloon
  - Step 4
- Target values
  - Hb >80-100 g/L; PLT: > 50 G/L
  - SBP > 80 Hgmm; pH: >7.2
  - T: >35°C, Ca_i: >0.8 mM/L

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Step 4

CALL FOR HELP!

Persistent bleeding

Unstabile haemodynamics

- Definite (surgical) treatment
  - Laparatomy / vascular clamps / compression

↓

- Stabilization
  - Hemodynamics / temperature / coagulation (consider rFVIIa)

Criteria for transfer

- Lack of surgical/interventional equipments of lack of experienced personel
- Temporary stop of bleeding through tamponade
- Hemodynamic stability for transport
- Existing SOP in the target hospital

→

Stabile haemodynamics

- Definite (surgical) treatment
  - Compression sutures
  - Vascular ligation
  - Hysterectomy
- Embolisation

Conditions of rFVIIa

- pH >7.2
- Fibrinogen >1.5 g/L
- PLT: >50 G/L
- Hyperfibrinolysis excluded/treated

Dosage: 60-90µg/kg bolus,
Can be repeated after 20 min

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Take Home Messages

- Vigilance (something may happen…)
- Avoid underestimation of blood loss
- Fast diagnosis and fast therapy
  - POC, if availble (lab tests can be too slow)
  - Substitute differencially
  - Substitution of PRBC
- Tranexamic acid!, fibrinogen!, platelets!
  - give rFVIIa if everything is normal(ized)
- Importance of good organization
  - **Local interdisciplinary algorithms are needed!!!**

Semmelweis Egyetem

Mulţumesc ☺