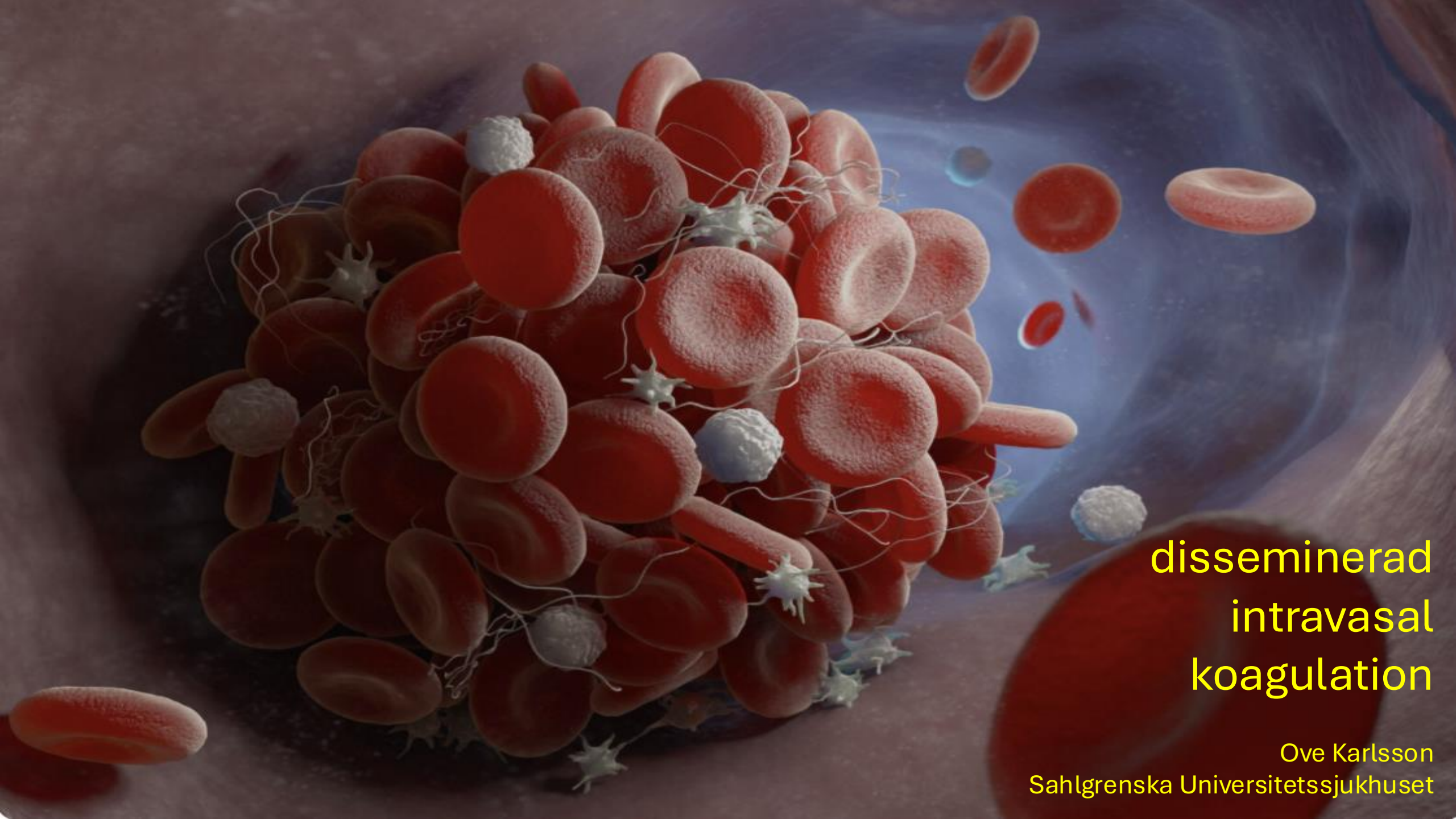


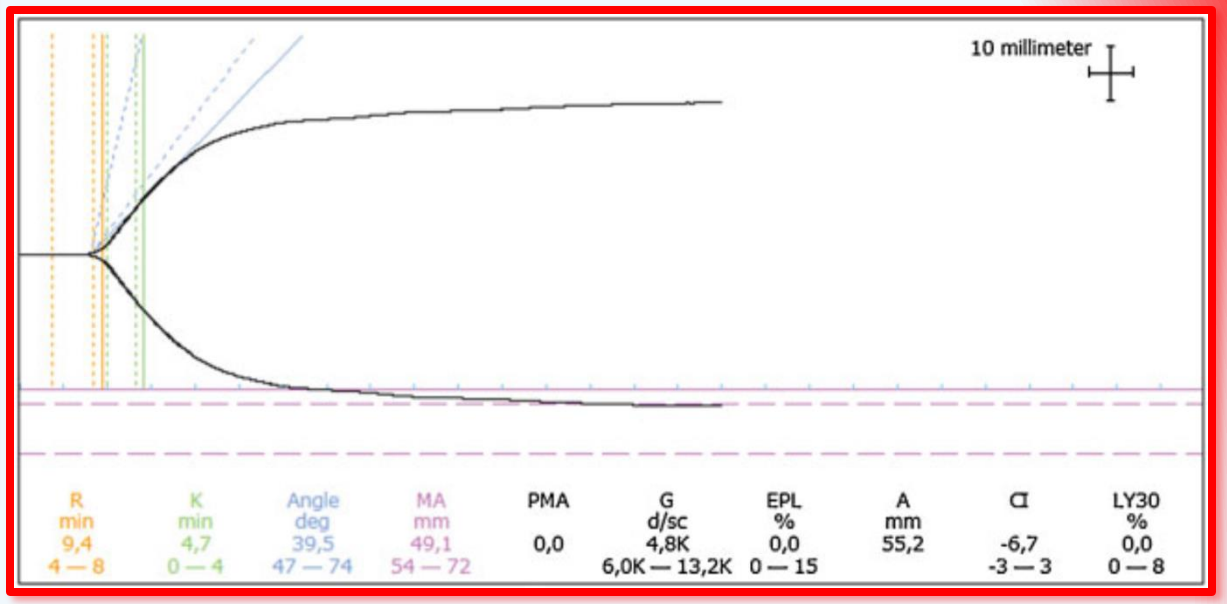
# disseminerad intravasal koagulation

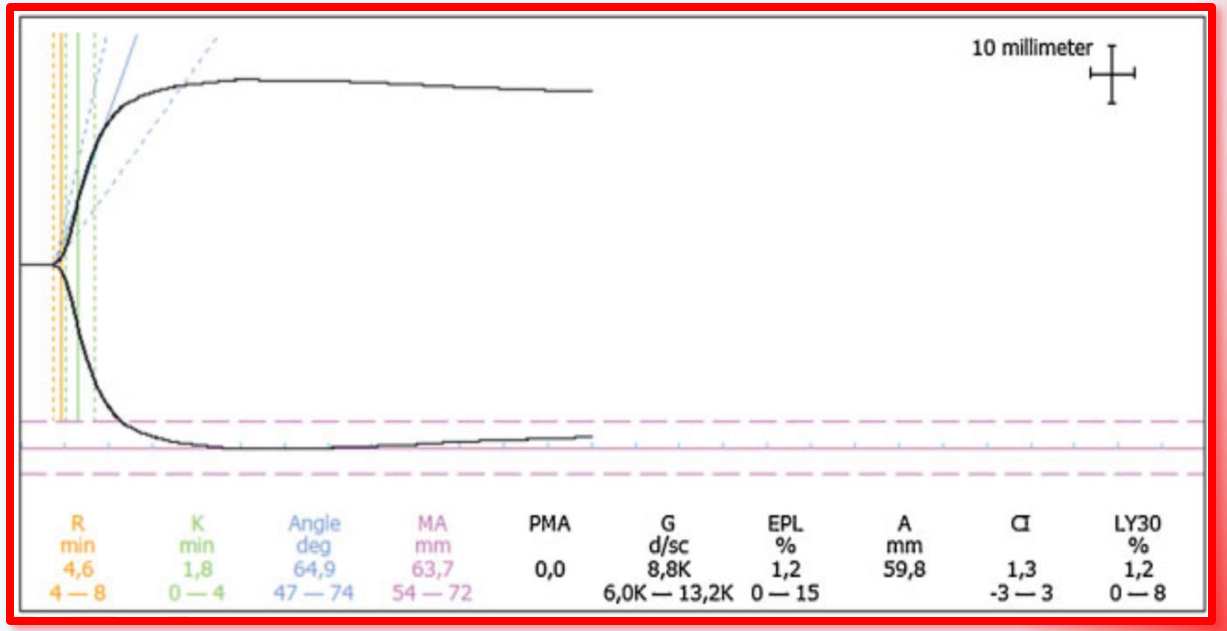
Ove Karlsson
Sahlgrenska Universitetssjukhuset

# Kvinna, 37 år

- Frisk
- Susp Ablatio
- Larmsnitt/urakut snitt
- Tranexamsyra
- Oxytocin, metylergometrin misoprostol karboprost
- Blödning 1500 ml
- Blodprover (ingen TEG)
  - Felaktigt fyllda

- Blod och plasma
- Fibrinogen 4 g
- Tranexamsyra 2 g
- Reoperation
  - TEG
  - Ingen pågående blödning
  - Gammalt 1500 ml



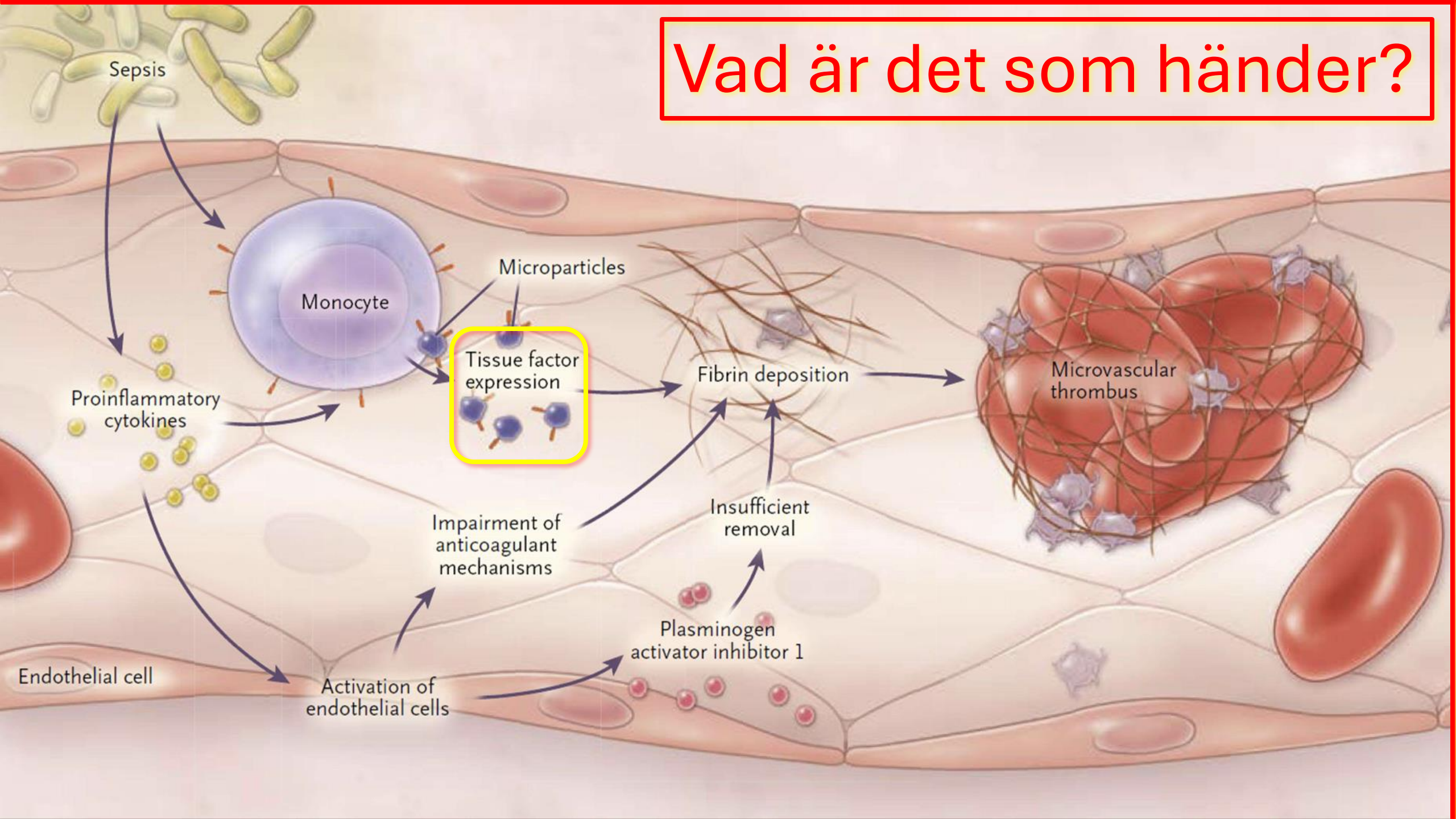

- UVA, stabil ➢
- BB avd. Hb 88 g/l
- BB mår inte bra
- Nya blodprover

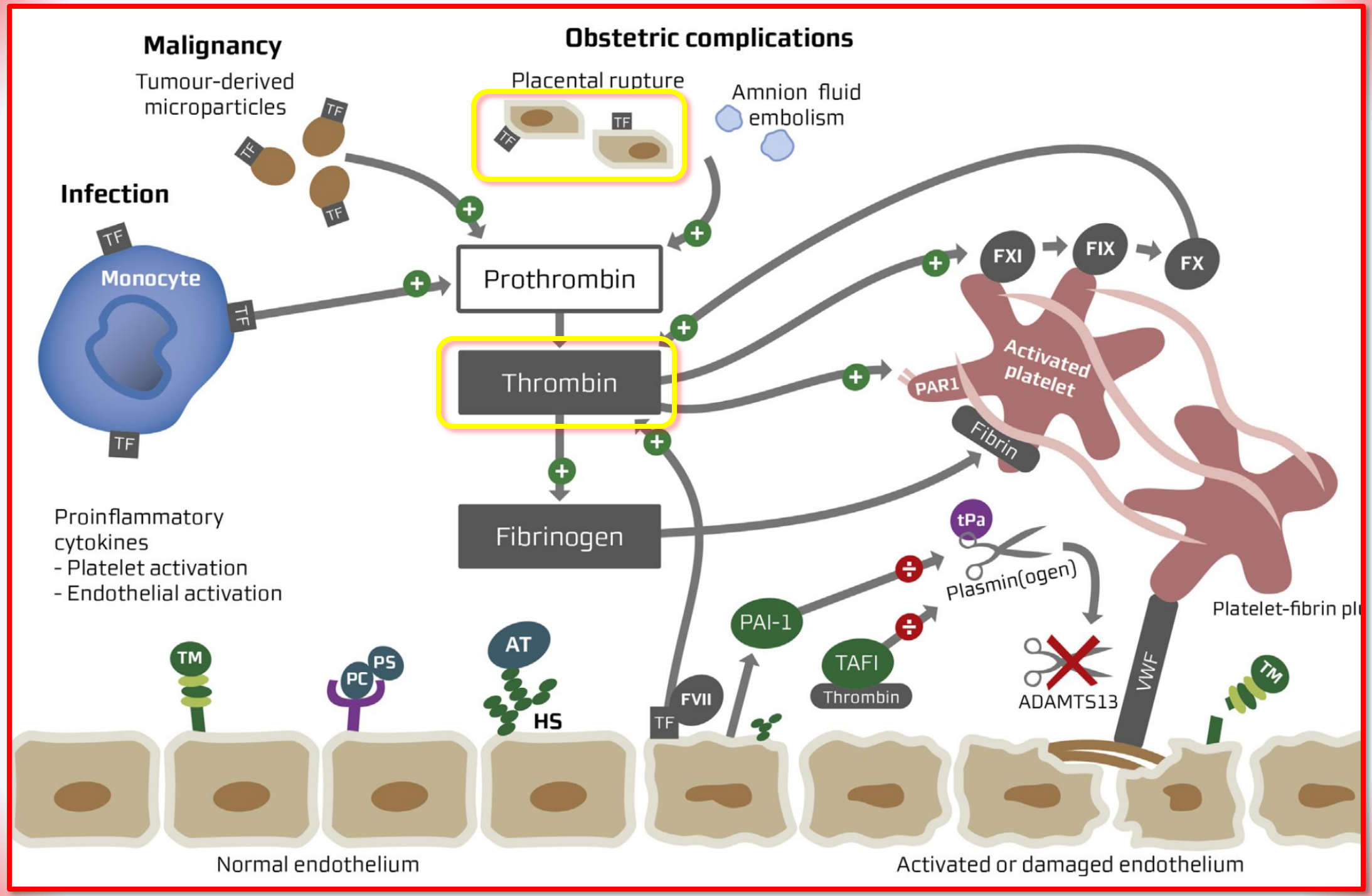
- Hb 70-77
- TPK 123
- APTT PT(INR) normal
- Fibrinogen <0,6 g/l

Reflektioner

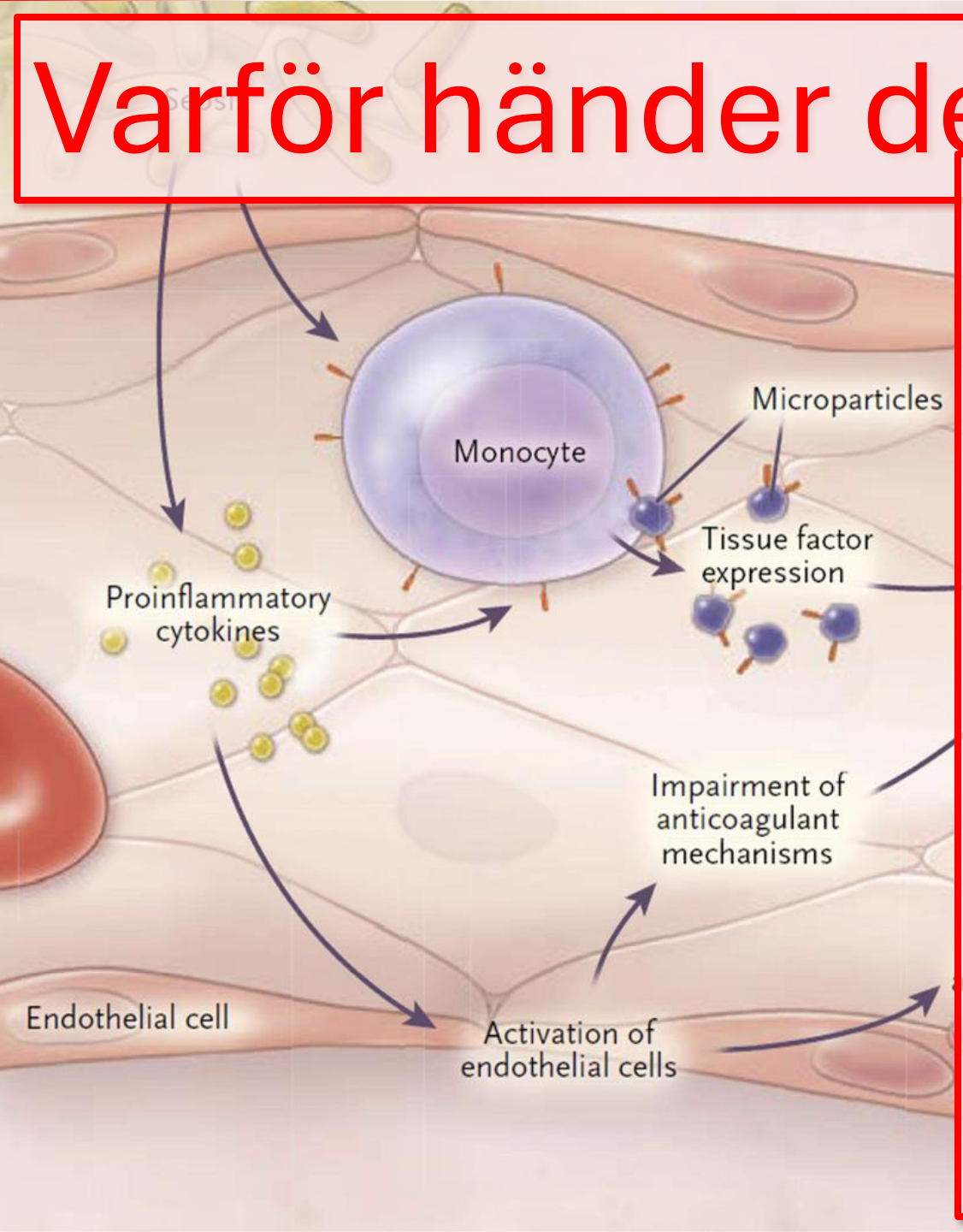
- Hemostarubbning
- Ablatio
- TEG/Rotem, första op!
- Rätt från början ★

# Vad är det som händer?



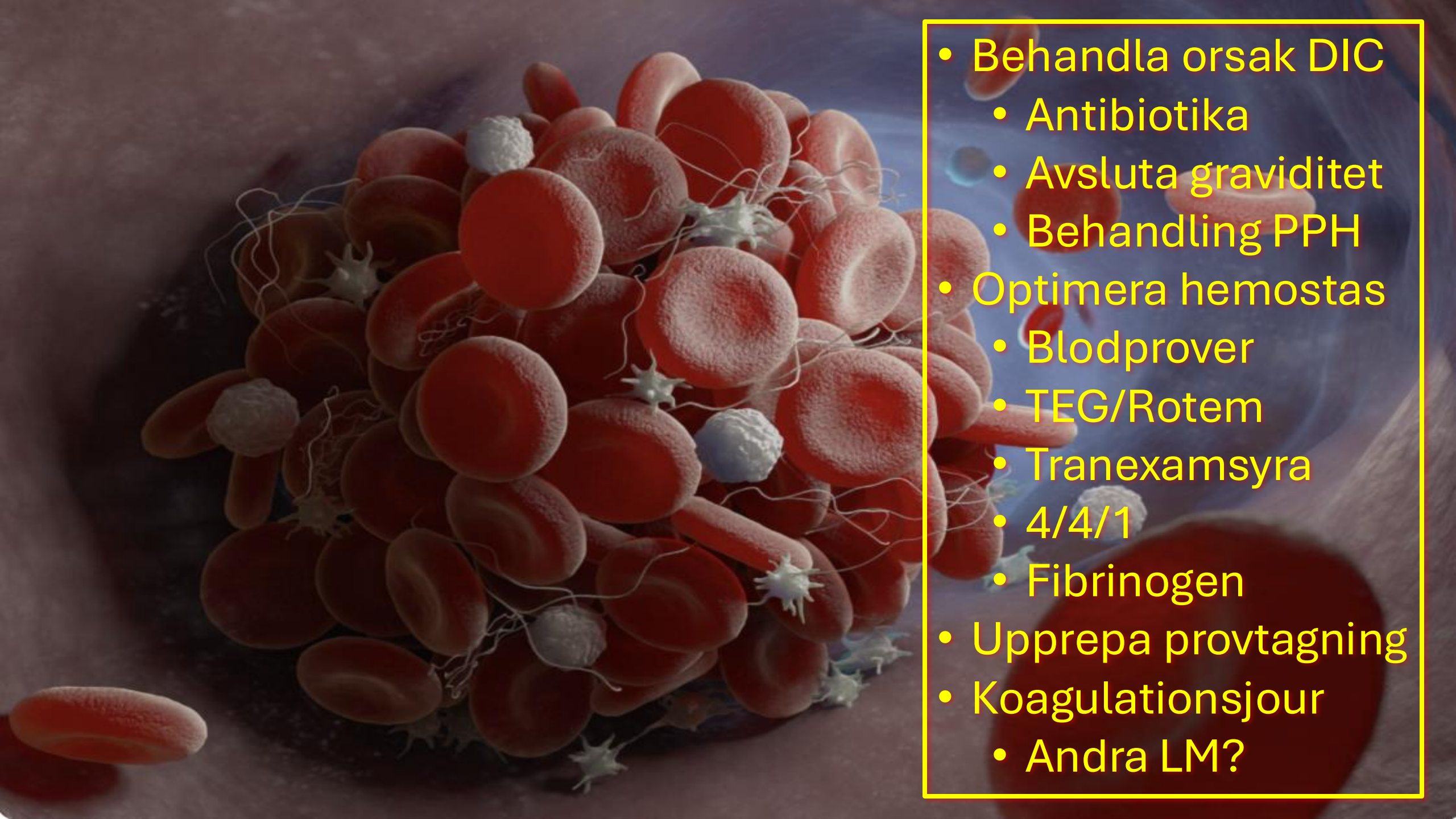

Malignancy
Tumour-derived microparticles
Obstetric complications
Placental rupture
Amnion fluid embolism
Infection
Monocyte
TF
Prothrombin
Thrombin
Fibrinogen
FXI
FIX
FX
Activated platelet
PAR1
Fibrin
Proinflammatory cytokines
- Platelet activation
- Endothelial activation
tPa
Plasmin(ogen)
PAI-1
TAFI
Thrombin
ADAMTS13
VWF
Platelet-fibrin pl
TM
PC
PS
AT
HS
FVII
Normal endothelium
Activated or damaged endothelium

# Varför händer det?




- Ablatio
- Sepsis/infektion
- Postpartum blödning
- Preeklampsi/HELLP
- IUFD
- Akut fettlever
- Fostervattenemboli

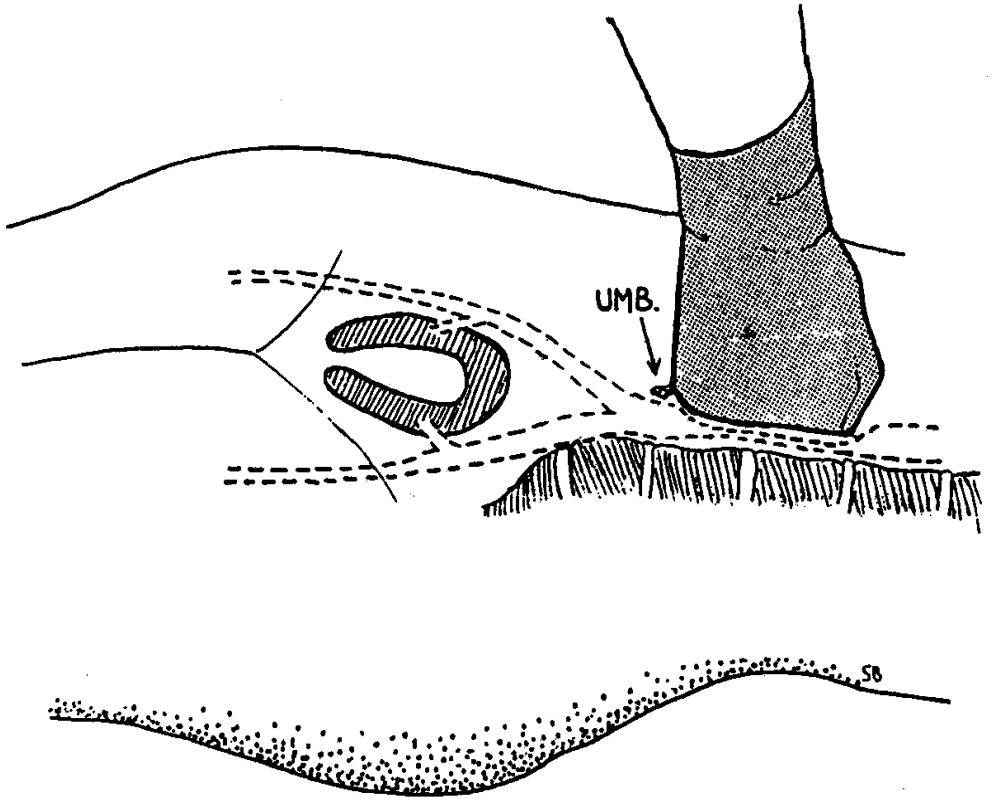

# Vad ska vi göra?



- Behandla orsak DIC
  - Antibiotika
  - Avsluta graviditet
  - Behandling PPH
- Optimera hemostas
  - Blodprover
  - TEG/Rotem
  - Tranexamsyra
  - 4/4/1
  - Fibrinogen
- Upprepa provtagning
- Koagulationsjour
  - Andra LM?

# Initial behandling

- Aortakompression
- Alt bimanuell uterus kompression
- Tillkalla personal
- Sänk huvudända och syrgas 5-10 L/min
- Blodtryck och puls
- 2 grova nålar
- Hb, bastest, hemostasprover, blodgas
- Varma vätskor
  - Ringeracetat
  - Försiktighet > 2000 ml)
  - Risk spädningskoagulopati
- KAD
- Håll patient varm
- Inj Tranexamsyra (Cyklokapron®) 1-2 g iv




**FIGUR 39** - Aortakompression sker lättast i höjd med naveln, som på bukens yta motsvarar projektionen av nedersta delen av bukaorta innan bifurkationen. Ena handen palperar först ljumskens puls. Den knutna andra handen, mjukt och försiktigt anlagd mot naveln, sänks sakta tills aortapulsationerna förnimmes. Ytterligare kompression leder till flödesminskning och -stopp i aorta genom att handen pressar ihop aorta mot kotpelarens framvägg.

# Akut postpartumblödning

**ÖVERVÄG ALLTID AORTAKOMPRESSION OCH UTERUSKOMPRESSION**

## Steg 1
## Blödning >500 ml

- Tillkalla extra BM+USK samt läkare
- Försök lösa placenta med traktion av navelsträng
- Blödningsvagn+protokoll
- PVK+bastest
- Oxytocin totalt 16,6 µg im/iv (max 16,6µg)
- Tappa urinblåsan
- Identifiera orsak och påbörja åtgärder
  - ✓ Atoni, placenta, bristning eller koagulation?

## Steg 2
## Fortsatt blödning

**Säkerställ att åtgärder på steg 1 är utförda**

- Lös placenta
- Metylergometrin 0,2 mg iv/im
- Förstärkt oxytocindropp
- Extra PVK
- Tranexamsyra 1 g iv
- Prostinfenem 0,25 mg im
- Misoprostol 0,2mg 3 tabl subl

## Steg 3
## Blödning >1 000 ml
(eller kliniskt påverkad patient)

**Säkerställ att åtgärder på steg 2 är utförda**

- Kontroller enligt ONEWS2
- Syrgas 10 l/min
- Planläge, höjda ben
- Kroppsvarm Ringer-Acetat 1 l
- Tranexamsyra 1 g iv
- KAD

## Steg 4
## Blödning >1 500 ml

**Time-out i teamet, utvärdera orsak och åtgärder**

Överväg:

- Resursförstärkning (ex anestesiolog, bakjour)
- Fortsatt handläggning på operation
- Transfusion av blodprodukter
- Fibrinogen 2 − 4 g iv
- Följ blodprover: Hb, TPK, PK, APTt, S-Ca, Fibrinogen

**Väg all blödning kontinuerligt**

bjh review

# Disseminated intr
# biomarkers, and r

Kasper Adelborg,[1,2,3] Julie B. La

[1]Department of Clinical Biochemistry
and [3]Department of Clinical Medicin

## Summary

Disseminated intravascular coagula
activation of the coagulation sy
microvascular thrombosis and, si
life-threatening haemorrhage attrib
platelets and coagulation factors. U
infection, cancer, or obstetrical com
for the initiation and propagation
review provides insights into the epi
current understanding of its patho
use of diagnostic biomarkers, curre
dations from international medical
an overview of emerging diagnostic
ers. Last, it provides guidance on ma
that timely and accurate diagnosis
condition is essential for the progno
marily focus on the underlying cau
treatment should be individualised
ing aetiology, patient's symptoms an

## Treatment of underlying clinical condition

- urgent and sufficient antibiotic treatment
- ongoing adjustment of the antibiotics according to microbial cultivation
- drainage of infection focus
- surgical resection of avital tissue
- anticancer drugs or cancer surgery
- accelerated delivery

## Supportive treatment

### Asymptomatic

**Laboratory signs of DIC**
LMWH prophylaxis

### Thromboembolism

**Microthrombi**
LMWH prophylaxis

**Overt VTE**
Therapeutic LMWH or UFH
if minor or no bleeding

**Overt arterial events**
Antiplatelet treatment if
minor or no bleeding

*Optional (low evidence)*
Antithrombin concentrate

### Bleeding

**Minor or no bleeding**
LMWH prophylaxis

Platelet concentrate:
Platelet count < 20 x $10^9$/l

**Major bleeding or need for invasive procedures**
Platelet concentrate:
platelet count < 50 x$10^9$/l

FFP or factor concentrate:
aPTT and PT > 1.5 x normal value

Fibrinogen:
Fibrinogen levels < 1.5 g/l
(< 2.0 g/l in PPH)

Vitamin K:
Suspected vitamin K deficiency

Tranexamic acid:
Hyperfibrinolysis only, otherwise
contraindicated

Journal of E

Open Access Full Text

# DIC in
# Charac

Offer Erez[1]
Maha Othman
Anat Rabinovi
Elad Leron[5]
Francesca Got
Jecko Thachil[7]

[1]Maternity Departm
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Medicine, Faculty of
Gurion University of
Sheva, Israel; [2]Depar
and Gynecology, Hut
Hospital, Wayne Stat
Detroit, MI, USA; [3]D
Biomedical and Mole
School of Medicine,
Kingston, ON, Cana
Hemostasis Unit, He
Soroka University M
Faculty of Health Sci
University of the Ne
Israel; [5]Division of C
Gynecology, Soroka
Center, School of M
Health Sciences Ben
the Negev, Beer She

## Diagnosis and Management of DIC in Pregnancy

**Obstetrical risk factors for DIC**

- Acute post partum hemorrhage
- Placental abruption
- Preeclampsia /HELLP syndrome
- Retained stillbirth
- Sepsis/ intra-amniotic infection
- Acute fatty liver
- Amniotic fluid embolism

**Are there clinical signs of DIC?**

**Yes**

- Prompt treatment including:
  - Delivery of the patient
  - Administration of blood products according to transfusion protocols
  - Treatment of underlying cause
  - Repeated laboratory testing
  - Multidisciplinary approach

**No**

- Clinical and laboratory evaluation
- Consider using of point of care testing
- Apply DIC score for risk assessment

**High risk for DIC**

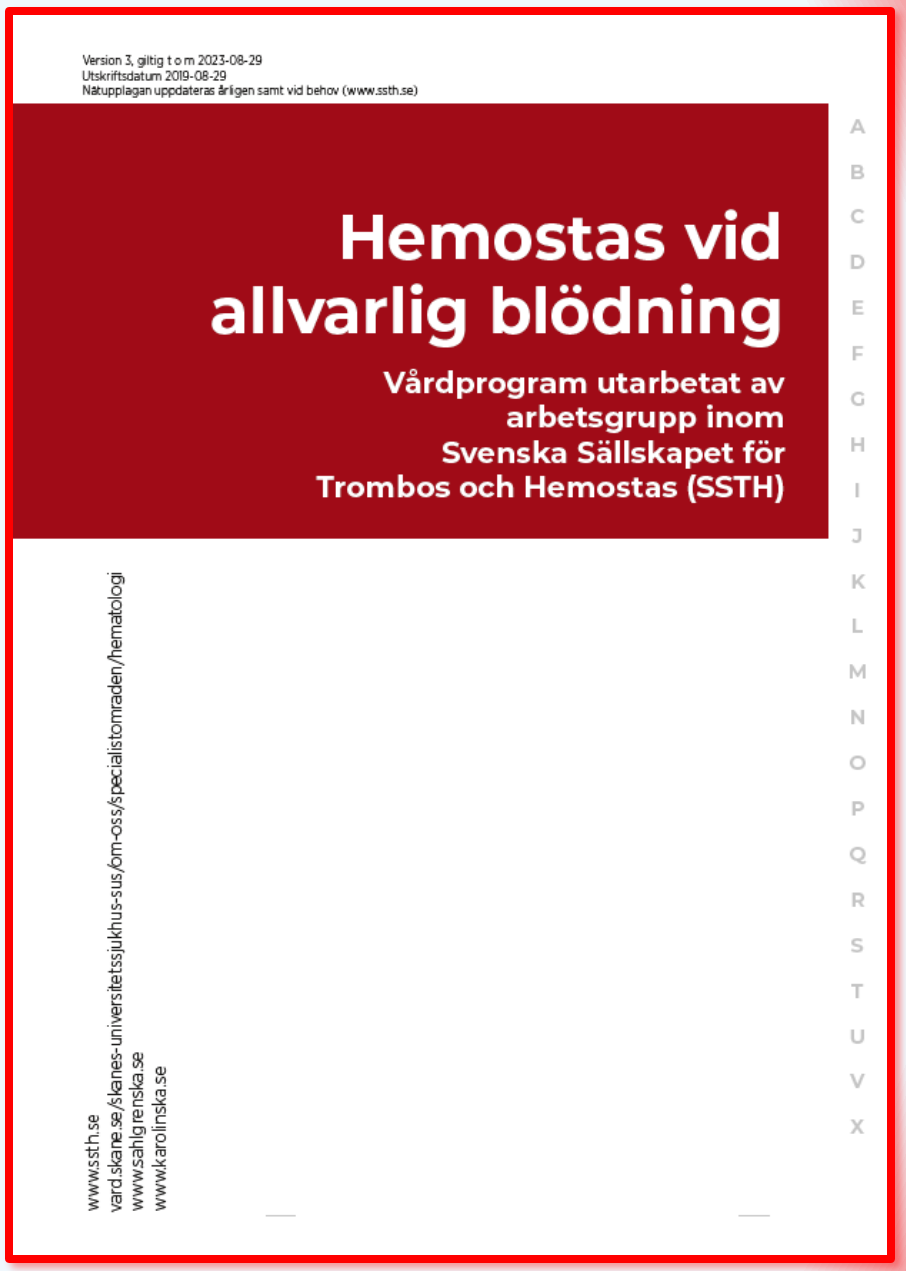
- Consult of multidisciplinary team
- Consider early administration of blood products and supportive measures
- Close clinical and laboratory surveillance

**Low risk for DIC**

Close clinical and laboratory surveillance

# Mål under pågående blödning:

- Hb > 90 g/l
- TPK > 100 (50) x $10^9$/l
- PK < 1,5
- APTT normal
- Fibrinogen > 2,0-2,5 g/l
- Temp > 36,5 ° C
- pH > 7,2
- Jonicerat Ca >1,0
- **Patient nära analysinstrument**
- **Upprepa provtagning!**



# Tranexamsyra

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Tranexamic Acid for the Prevention of Loss after Cesarean Delivery

L. Sentilhes, M.V. Sénat, M. Le Lous, N. Winer, P. Rozenberg, E. Verspyck, F. Fuchs, E. Azria, D. Gallot, D. Korb, R. Desbrière, C. Chauleur, F. de Marcillac, F. Perrotin, O. Parant, L.J. Salomon, F. Bretelle, N. Sananès, C. Bohec, N. Mottet, G. Legendre, V. Letouzey, B. Haddad, D. Vardon, H. Madar, A. Mattuizzi, V. Daniel, S. Regueme, C. Roussillon, A. Benard, A. Georget, A. Darsonval, and C. Deneux-Tharaux, for the Groupe de Recherche en Obstétrique et Gynécologie*

ABSTRACT

BACKGROUND

...h reduced ...t evidence

- Randomiserad 4400 patienter
- Inj Tranexamsyra 1 g alt inj NaCl
- Kalkylerad blödning 550 / 650 ml
- Ingen skillnad uppmätt blödnings mängd, transfusioner, bruk av uterotonika, embolisering mm

BJA

British Journal of Anaesthesia, 129 (6): 937–945 (2022)

doi: 10.1016/j.bja.2022.08.033

OBSTETRIC ANAESTHESIA

## Tranexamic acid dose–response relationship for antifibrinolysis in postpartum haemorrhage during Caesarean delivery: TRACES, a double-blind, placebo-controlled, multicentre, dose-ranging biomarker study

Anne-Sophie Ducloy-Bouthors[1,2,*], Sixtine Gilliot[2], Maeva Kyheng[3,4], David Faraoni[5], Alexandre Turbelin[1], Hawa Keita-Meyer[6], Agnès Rigouzzo..., Benjamin Constant[9], Francoise Broisin[10], Agnès L. Gouez[1...], Louise Ghesquiere[14], Gilles Lebuffe[2,15], Alain Duhamel[3,4], Benjamin Hennart[16], Emmanuelle Jeanpierre[17], Pascal Od...

- Randomiserad blindad: placebo / 0,5 g / 1 g
- Skillnad i fibrinolys, laboratorietetest
- Blödningsmängd inom 6t: 208 / 300 / 134 ml

## Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial

WOMAN Trial Collaborators*

Summary

Background Post-partum haemorrhage is the leading cause of maternal death worldwide. Early administration of tranexamic acid reduces deaths due to bleeding in trauma patients. We aimed to assess the effects of early administration of tranexamic acid on death, hysterectomy, and other relevant outcomes in women with post-partum haemorrhage.

Methods In this randomised, double-blind, placebo-controlled trial, we recruited women aged 16 years and older with a clinical diagnosis of post-partum haemorrhage after a vaginal birth or caesarean section from 193 hospitals in 21 countries. We randomly assigned women to receive either 1 g intravenous tranexamic acid or matching placebo in addition to usual care. If bleeding continued after 30 min, or stopped and restarted within 24 h of the first dose, a second dose of 1 g of tranexamic acid or placebo could be given. Patients were assigned by selection of a numbered treatment pack from a box containing eight numbered packs that were identical apart from the pack number. Participants, care givers, and those assessing outcomes were masked to allocation. We originally planned to enrol 15 000 women with a composite primary endpoint of death from all-causes or hysterectomy within 42 days of giving birth. However, during the trial it became apparent that the decision to conduct a hysterectomy was often made at the same time as randomisation. Although tranexamic acid could influence the risk of death in these cases, it could not affect the risk of hysterectomy. We therefore increased the sample size from 15 000 to 20 000 women in order to estimate the effect of tranexamic acid on the risk of death from post-partum haemorrhage. All analyses were done on an intention-to-treat basis. This trial is registered with ...

...to receive ...e analysis. ...ients vs 191 ...men given ...ebo group, ...sterectomy ...he placebo ...sterectomy ...546 [5·5%] ...events) did

Interpretation Tranexamic acid reduces death due to bleeding in women with post-partum haemorrhage with no adverse effects. When used as a treatment for postpartum haemorrhage, tranexamic acid should be given as soon as possible after bleeding onset.

Lancet 2017; 389: 2105-16

Published Online April 26, 2017 http://dx.doi.org/10.1016/S0140-6736(17)30638-4

This online publication has been corrected. The corrected version first appeared at thelancet.com on May 5, 2017

See Editorial page 2081

*Collaborators listed at end of the report

Correspondence to: Clinical Trials Unit, London School of Hygiene & Tropical Medicine, London, UK thewomantrial@LSHTM.AC.UK

- 20.000 patienter, 21 länder, 193 sjukhus
- Randomiserad, dubbel-blind, placebo kontrollerad
- Inj Tranexamsyra 1g, en andra dos möjlig
- Minskad mortalitet pga minskad blödning

# Tranexamsyra

EJA

*Eur J Anaesthesiol* 2023; **40**:226–304

GUIDELINES

## Management of severe peri-operative bleeding: Guidelines from the European Society of Anaesthesiology and Intensive Care

*Second update 2022*

Sibylle Kietaibl, Aamer Ahmed, Arash A
Giedrius Barauskas, Edoardo De Rob
Anne Godier, Thorsten Haas, Matthias
Zsolt Molnar, Lidia Mora, Niels Rahe-M
Christoph Schlimp, Anne J. Wikkelsø a

**BACKGROUND** Management of peri-operative bl
complex and involves multiple assessment tools a
gies to ensure optimal patient care with the goal of
morbidity and mortality. These updated guidelines from the European Society of Anaesthesiology and Intensive Care (ESAIC) aim to provide an evidence-based set of recommendations for healthcare professionals to help ensure improved clinical management.

**DESIGN** A systematic literature search from 2015 to 2021 of several electronic databases was performed without language restrictions. Grading of Recommendations, Assessment, Development and Evaluation (GRADE) was used to assess the methodological quality of the included studies and to formulate recommendations. A Delphi methodology was used to prepare a clinical practice guideline.

**RESULTS** These searches identified 137 999 articles. All articles were assessed, and the existing 2017 guidelines were revised to incorporate new evidence. Sixteen recommendations derived from the systematic literature search, and four clinical guidances retained from previous ESAIC guidelines were formulated. Using the Delphi process on

**DISCUSSION** Peri-operative bleeding management encompasses the patient's journey from the pre-operative state through the postoperative period. Along this journey, many features of the patient's pre-operative coagulation status, underlying comorbidities, general health and the procedures that they are undergoing need to be taken into account. Due to the many important aspects in peri-operative nontrauma bleeding management, guidance as to how best approach and treat each individual patient are key. Understanding which therapeutic approaches are most valuable at each timepoint can only enhance patient care, ensuring the best outcomes by reducing blood loss and, therefore, overall morbidity and mortality.

**CONCLUSION** All healthcare professionals involved in the management of patients at risk for surgical bleeding should be aware of the current therapeutic options and approaches that are available to them. These guidelines aim to provide specific guidance for bleeding management in a variety of clinical situations.

- Inj Tranexamsyra 1 g iv
- Så snart som möjligt, inom 3 timmar
- Kan upprepas
- Kan övervägas vid högrisk kejsarsnitt
- Ger illamående och kräkningar

Received: 12 March 2023 | Revised: 15 August 2023 | Accepted: 2 October 2023

https://doi.org/10.1016/j.jtha.2023.10.001

jth

REVIEW ARTICLE

## When to use tranexamic acid for the treatment of major bleeding?

Zoe K. McQuilten[1,2] | Erica M. Wood[1,2] | Robert L. Medcalf[3]

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**Funding information**
This study is supported by NHMRC Investigator Grants (GNT1194811, to Z.M.; GNT1177784, to E.W.).

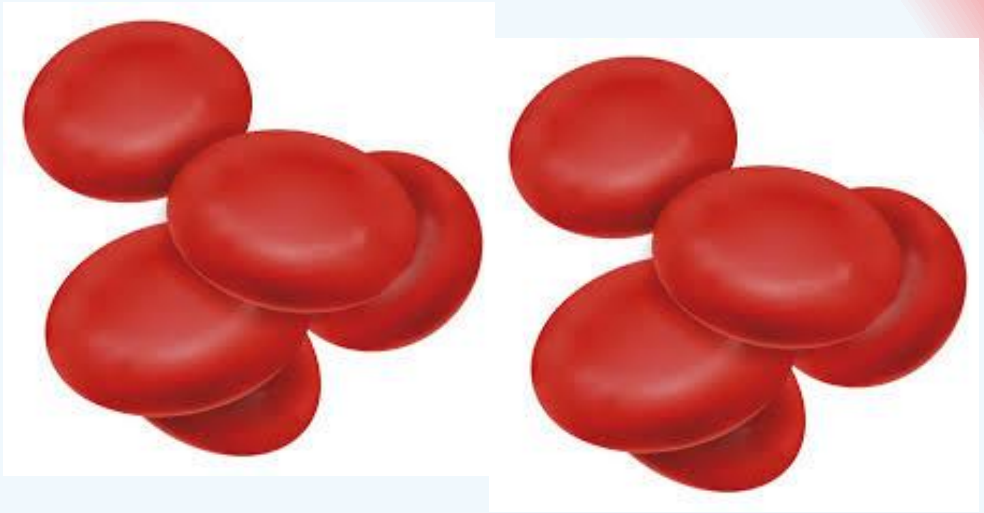
**Abstract**

Tranexamic acid (TXA) is an antifibrinolytic agent originally developed for the management of bleeding in the setting of postpartum hemorrhage (PPH). Over the last 15 years, there has been accumulating evidence on the use of TXA for the treatment of active bleeding in a variety of clinical contexts. Clinical trials have shown that the efficacy and safety of TXA for the treatment of bleeding differ according to the clinical context in which it is being administered, timing of administration, and dose. Early administration is important for efficacy, particularly in trauma and PPH. Further studies are needed to understand the mechanisms by which TXA provides benefit, optimal modes of administration and dosing, and its effect in some clinical settings, such as spontaneous intracerebral hemorrhage. There is no evidence that TXA increases the risk of thrombotic events in patients with major bleeding overall. However, there is evidence of increased risk of venous thrombosis in patients with gastrointestinal bleeding. There is also evidence of increased risk of seizures with the use of higher doses. This review summarizes the current evidence for the use of TXA for patients with active bleeding and highlights the importance of generating evidence of efficacy
he bleeding contexts—as findings
other contexts—and that of indi-
nd other risks, as well as important
imize care and outcomes in these

- Viss effekt på mortalitet vid trauma och PPH
- Tidig administrering bättre
- Ingen ökad risk trombotiska komplikationer

KEYWORDS
fibrinolysis, major hemorrhage, thrombosis, tranexamic acid, transfusion

# Blodtransfusion



Bedöm om blödning kommer att:

Blödning < ½ blodvolym och blödning avstannar

- Transfundera
  - Så lite som möjligt
  - Målriktad terapi
  - Kristalloid

Blödning > ½ blodvolym och blödning pågår

- Transfundera
  - Blod/plasma/trombocyter
  - 4:4:1

EJA

*Eur J Anaesthesiol* 2023; **40**:226–304

GUIDELINES

# Management of severe peri-operative blee
# from the European Society of Anaesthesio
# Intensive Care

*Second update 2022*

Sibylle Kietaibl, Aamer Ahmed, Arash Afshari, Pierre Albaladejo, Cesa
Giedrius Barauskas, Edoardo De Robertis, David Faraoni, Daniela C
Anne Godier, Thorsten Haas, Matthias Jacob, Marcus D. Lancé, Juan
Zsolt Molnar, Lidia Mora, Niels Rahe-Meyer, Charles M. Samama, Eca
Christoph Schlimp, Anne J. Wikkelsø and Kai Zacharowski

**BACKGROUND** Management of peri-operative bleeding is

253 sentences of guid

methodology was used to prepare a clinical practice

outcomes by reducing blood loss and, therefore, overall

guidelines were formulated. Using the Delphi process on

clinical situations.

MBRRACE-UK
Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK

Update guidance on the use of coagulation tests in the context of obstetric haemorrhage including the timelines for availability and how to interpret these, noting that women should not be inappropriately denied clotting products based on a single measure of coagulation in the face of ongoing haemorrhage. **ACTION: National Institute for Health and Care Excellence (NICE), Royal Colle … llege of Physicians, Obstetric Anaesthetists Associatio**

- Patientnära viskoelastiska instr.
- TEG/ROTEM
- Kunskap, tolkning och åtgärder
- Upprepa provtagning

Produce guidance on which beside tests should be … aining to perform and interpret those tests (Knight, Bunch et …

If no haemostatic tests are available, early fresh frozen plasma (FFP) should be considered for conditions with a suspected coagulopathy, such as placental abruption or amniotic fluid embolism, or where detection of PPH has been delayed (Royal College of Obstetricians and Gynaecologists 2016a).

VHA can identify obstetric coagulopathy including hypofibrinogenaemia and reduced platelet level. B

VHA-guided haemostatic treatment reduces the need for blood products. B

In severe postpartum haemorrhage, we suggest a VHA-guided intervention protocol. 2C

travenous iron supplementation improves fatigue and pression score postpartum. B

e suggest assessing fibrinogen levels in parturients with eding, as levels less than 2 g l$^{-1}$ may identify those at k of severe postpartum haemorrhage. 1C

agulopathy risk assessment should include the obstet- associated with PPH not just an estimat-

as opposed to two units in haemodynamic stable with anaemia. 1B

age is well tolerated in obstetric settings, pro- hat precautions are taken against rhesus nisation. C

est that using peri-operative cell salvage during section with high risk of haemorrhage may homologous transfusion. 2B

mend i.v. iron supplementation as this elicits a overy from anaemia with fewer gastrointestinal ts than oral iron treatment. 1B

titution in women with ongoing postpar- e and a fibrinogen level above 2 g l$^{-1}$ or eater than 12 mm is not indicated. 1B

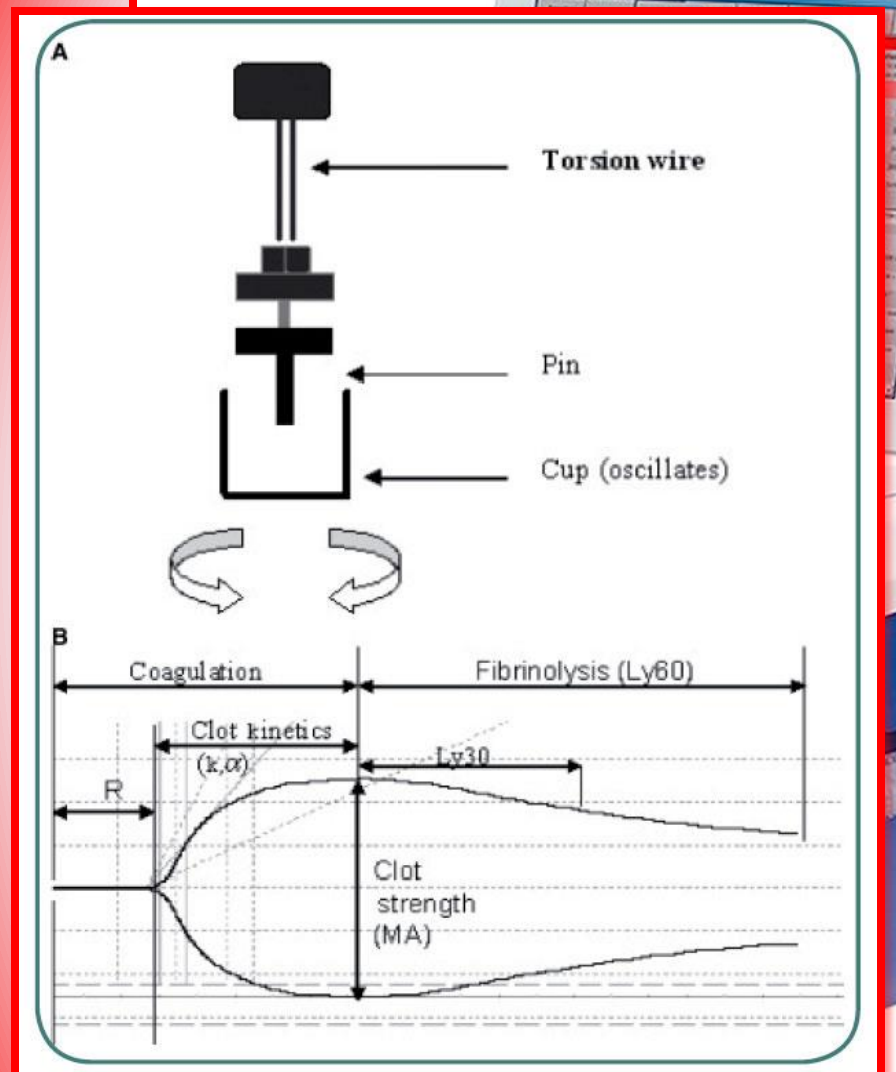
rtum haemorrhage, we suggest a VHA- tion protocol. 2C

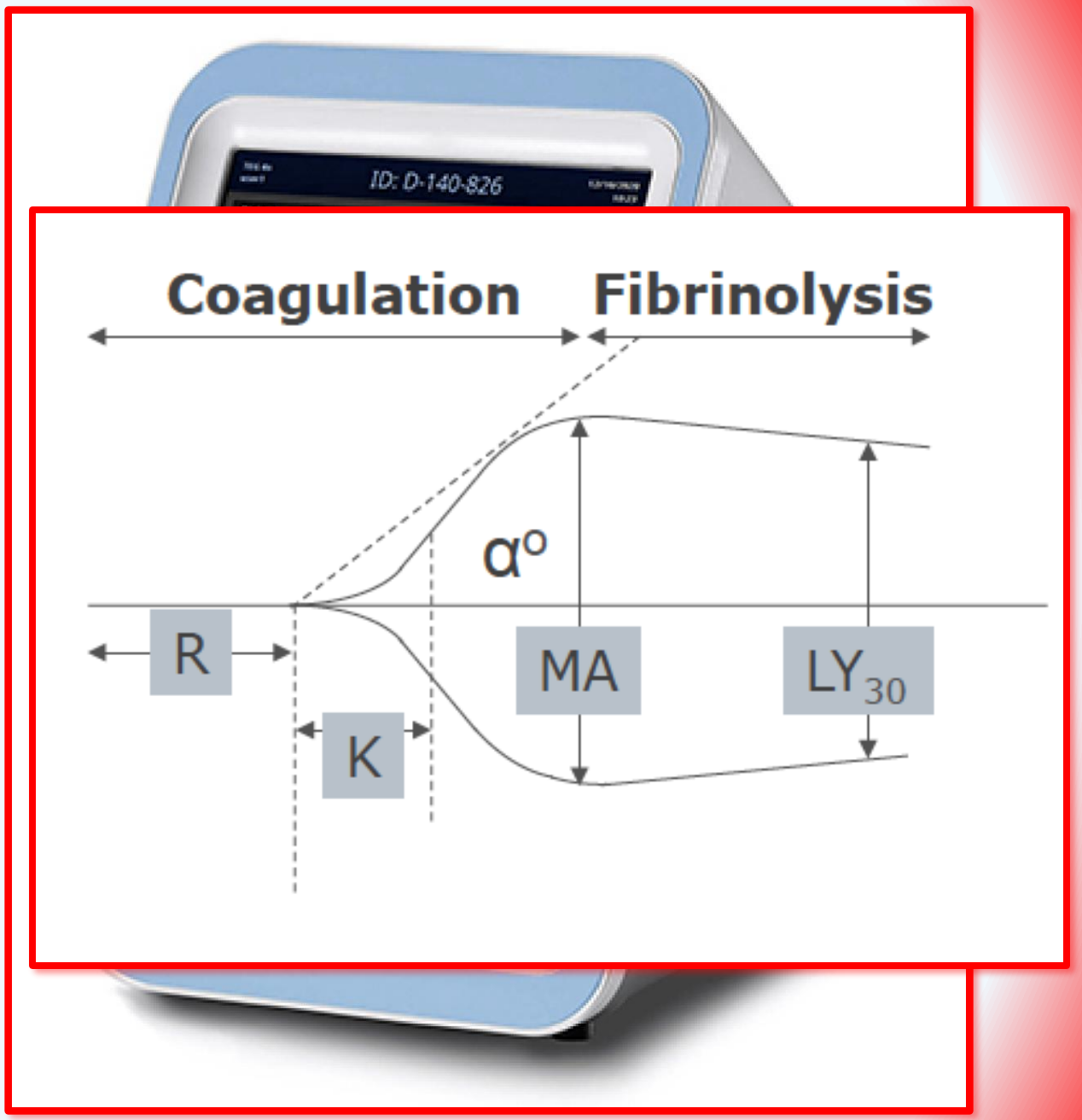
the administration of TXA in postpartum a dose of 1 g intravenously as soon as 3 h, which can be repeated if bleeding

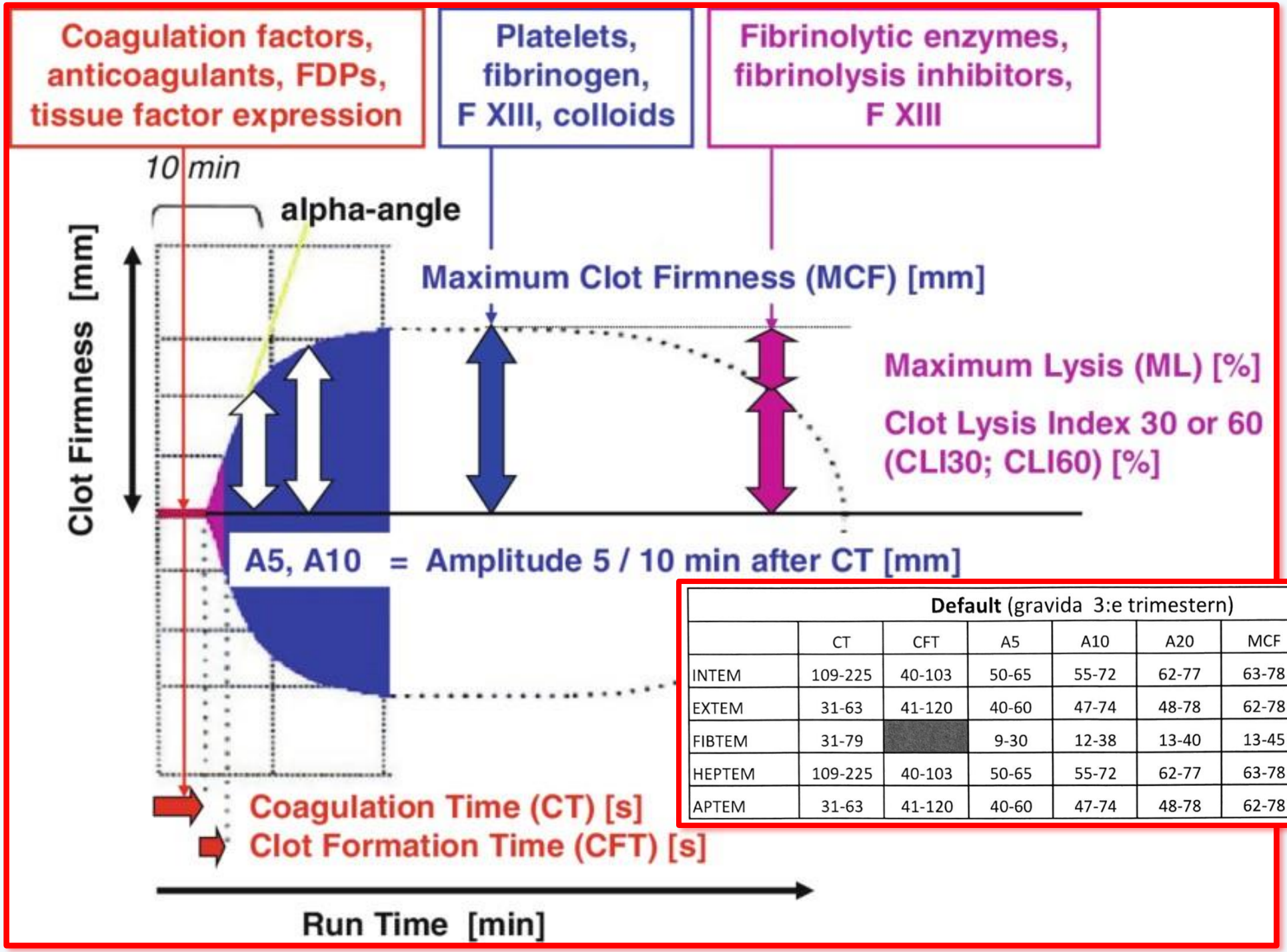
t TXA be considered before high-risk n and vaginal deliveries or cases of ante- g. 2B

We suggest that administration of rFVIIa can be considered for life-threatening postpartum haemorrhage, which cannot be stopped by conventional, surgical or interventional radiological means and/or when comprehensive coagulation therapy fails. 2C

We recommend against a prophylactic/general use of rFVIIa in postpartum haemorrhage because of increased risk of fatal thrombosis. 1C


A
Torsion wire
Pin
Cup (oscillates)
B
Coagulation
Fibrinolysis (Ly60)
Clot kinetics
(k,α)
Ly30
R
Clot
strength
(MA)


ID: D-140-826
Coagulation
Fibrinolysis
α°
R
K
MA
LY30




**Default** (gravida 3:e trimestern)

| | CT | CFT | A5 | A10 | A20 | MCF | LI30 | ML |
|---|---|---|---|---|---|---|---|---|
| INTEM | 109-225 | 40-103 | 50-65 | 55-72 | 62-77 | 63-78 | 94-100 | 0-15 |
| EXTEM | 31-63 | 41-120 | 40-60 | 47-74 | 48-78 | 62-78 | 94-100 | 0-15 |
| FIBTEM | 31-79 | | 9-30 | 12-38 | 13-40 | 13-45 | | |
| HEPTEM | 109-225 | 40-103 | 50-65 | 55-72 | 62-77 | 63-78 | 94-100 | 0-15 |
| APTEM | 31-63 | 41-120 | 40-60 | 47-74 | 48-78 | 62-78 | | |

Journal of Blood Medicine

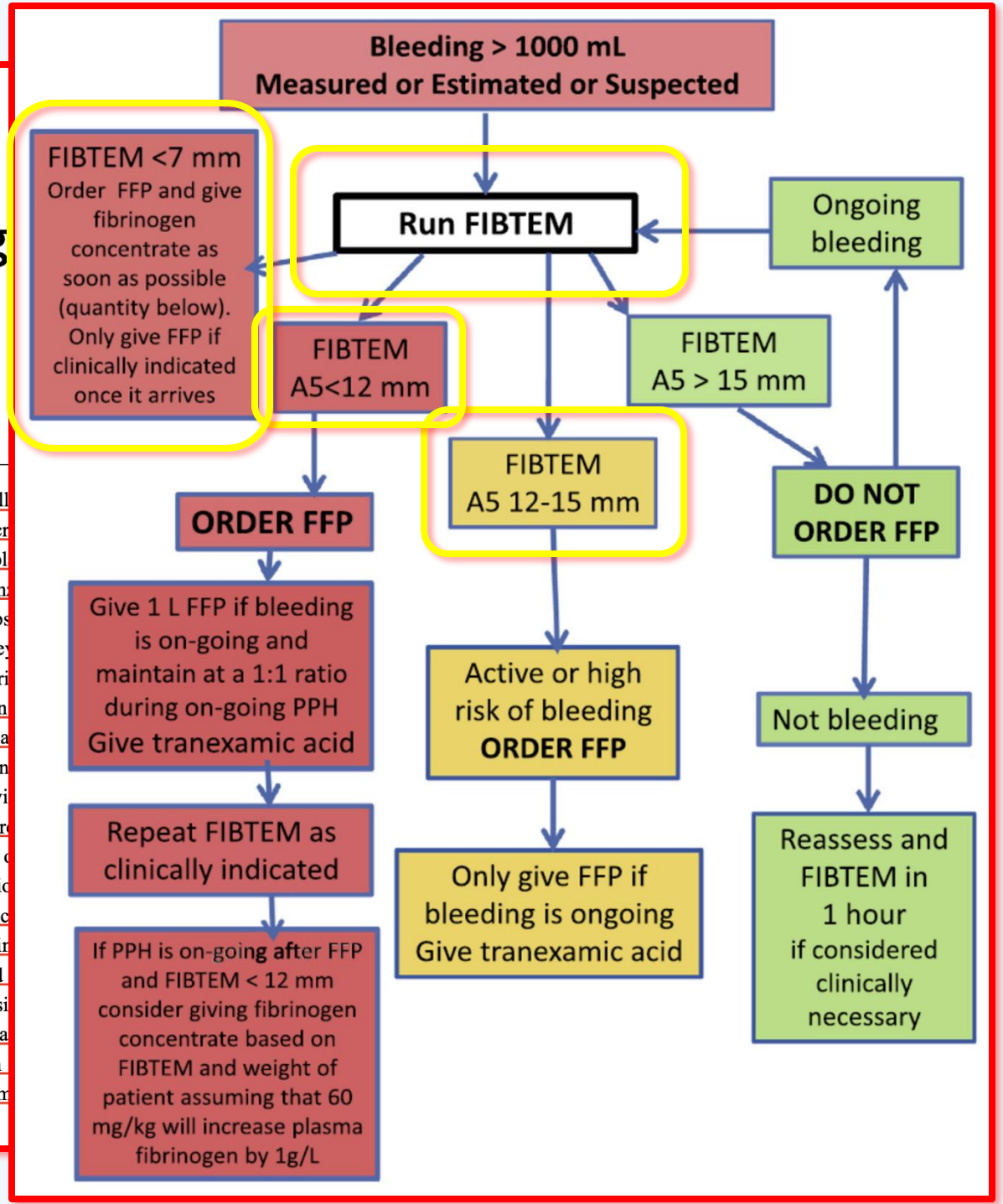
Open Access Full Text Article

# DIC in Pregnancy – Pathophysiolog
# Characteristics, Diagnostic Scores,

Offer Erez[1,2]
Maha Othman[3]
Anat Rabinovich[4]
Elad Leron[5]
Francesca Gotsch[6]
Jecko Thachil[7]

[1]Maternity Department "D", Division of Obstetrics and Gynecology, Soroka University Medical Center, School of Medicine, Faculty of Health Sciences Ben Gurion University of the Negev, Beer Sheva, Israel; [2]Department of Obstetrics and Gynecology, Hutzel Women's Hospital, Wayne State University, Detroit, MI, USA; [3]Department of Biomedical and Molecular Sciences, School of Medicine, Queen's University, Kingston, ON, Canada; [4]Thrombosis and Hemostasis Unit, Hematology Institute, Soroka University Medical Center and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer Sheva, Israel; [5]Division of Obstetrics and Gynecology, Soroka University Medical Center, School of Medicine, Faculty of Health Sciences Ben Gurion University of the Negev, Beer Sheva, Israel;

**Abstract:** Obstetrical hemorrhage and especiall
tion) is a leading cause for maternal mortality acr
maternal and/or fetal complications including pl
HELLP syndrome (hemolysis, elevated liver en
and acute fatty liver of pregnancy. Various obs
a complication; thus, increased awareness is ke
can present to clinicians who may not be experi
and hemostasis. Hence, DIC diagnosis is often
developed uncontrollable bleeding or multi-orga
able scenarios. Beyond the clinical presentation
relation to coagulation test abnormalities. It is wi
prolonged prothrombin time (PT) and partial thr
low fibrinogen, and raised D-dimers. Diagnosis
requires vigilance and knowledge of the physic
facilitated by using a pregnancy specific DIC sc
gen concentrations; 2) the PT difference – relati
patient's plasma and the laboratory control; and
the pregnancy specific DIC score has 88% sensi
ratio (LR) of 22, and a negative LR of 0.125. Ma
a prompt attention to the underlying condition
delivery of the patient, and correction of the hem
of care testing adjusted for pregnancy.



OBSCYMRU
Obstetric Bleeding Strategy for Wales

# ROTEM Protocol

(For use in postpartum haemorrhage)

**Blood loss >1000ml** *or* **Stage 2 activated**
*Measured or suspected*

**Give Tranexamic Acid** *(if not given already)*

**TAKE BLOODS**
**POC:** ROTEM, Lactate, Hb
**Lab:** FBC, Coag, +/- repeat Xmatch *(Alert lab staff)*

**ONGOING BLEEDING *or* CLINICAL CONCERN?**

**OPTIMISE PATIENT**
Temp >36°C  Hb >80g/L  pH >7.2  Ionised $Ca^{2+}$ >1mmol/L

**REVIEW OTHER CAUSES OF BLEEDING**
If coagulation normal, escalate obstetric & anaesthetic care

**NO**
*No blood products required*

**CLINICAL MONITORING**
*Consider HDU care post-op*

**ANY OF THE FOLLOWING?**
**Clinical concern**
**Suspected further bleeding**
*Inc. concealed bleeding*
**>500ml further blood loss**

**YES**

**Only transfuse coagulation products if patient is bleeding**

**REVIEW FIBTEM A5**
*(fibrin polymerisation)*

FIBTEM A5 ≥12mm
*or Fibrinogen >2 g/L* — ***No fibrinogen currently required***

**FIBTEM A5 ≤11mm**
*or Fibrinogen <2 g/L* → **Give fibrinogen concentrate**
A5 7-11mm = 4g
A5 <7mm = 6g

If **FIBTEM A5 ≤11mm** after transfusing fibrinogen concentrate,
*or* **suspicion of abruption/AFE** review EXTEM CT and FBC

**REVIEW EXTEM CT**
*(thrombin generation)*

EXTEM CT <75sec
*or normal PT/APTT* — ***No FFP required***

**EXTEM CT ≥75sec**
*or elevated PT/APTT* → **Give FFP**
Booking Weight ≤ 50Kg = 3 Units
> 50Kg = 4 Units

**REVIEW FBC**
*(platelet deficiency)*

Platelets >75 x$10^9$/L — ***No Platelets required***

**Platelets ≤75 x$10^9$/L** → **Give Platelets**
1 adult unit

**ANY OF THE FOLLOWING?**
**Any blood products given**
**> 500ml further blood loss**
**Clinical concern**

**If you have any concerns discuss with haematologist**

*Haematologist*
*Blood Bank*
*Haematology Lab*
*Porters*

**NB: ROTEM does not reliably detect effects of:** warfarin, aspirin, clopidogrel, reopro, direct oral anticoagulants, LMWH. It will not detect deficiency of von Willebrand factor.

Fibrinogen plays a critical role in achieving and maintaining hemostasis and is fundamental to effective clot formation. There is increasing awareness of the important role of fibrinogen as a key target for the treatment and prevention of acquired bleeding. Fibrinogen is the first coagulation factor to fall to critically low levels (<1.0 g/L) during major hemorrhage (normal plasma fibrinogen levels range from 2.0 to 4.5 g/L), and current guidelines recommend maintaining the plasma fibrinogen level above 1.5 g/L. Fibrinogen supplementation can be achieved using plasma or cryoprecipitate; however, there are a number of safety concerns associated with these allogeneic blood products and there is a lack of high-quality evidence to support their use. Additionally, there is sometimes a long delay associated with the preparation of frozen products for infusion. Fibrinogen concentrate provides a promising alternative to allogeneic blood products and has a number of advantages: it allows a standardized dose of fibrinogen to be rapidly administered in a small volume, has a very good safety profile, and is virally inactivated as standard. Administration of fibrinogen concentrate, often guided by point-of-care viscoelastic testing to allow individualized dosing, has been successfully used as hemostatic therapy in a range of clinical settings, including cardiovascular surgery, postpartum hemorrhage, and trauma. Results show that fibrinogen concentrate is associated with a reduction or even total avoidance of allogeneic blood product transfusion. Fibrinogen concentrate represents an important option for the treatment of coagulopathic bleeding; further studies are needed to determine precise dosing strategies and thresholds for fibrinogen supplementation.



CME Fibrinogen as
critica

Jerrold H

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taining hemostasis and is fundame
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tant role of fibrinogen as a key targ
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REVIEW

# CME Fibrinogen as a therapeutic target for bleeding: a review of critical levels and replacement therapy

*Jerrold H. Levy,[1] Ian Welsby,[1] and Lawrence T. Goodnough[2]*

mation, to fall to low levels.[2] There is increasing awareness regarding the important role of fibrinogen during acute bleeding and as a target for the treatment and prevention of bleeding, especially in perioperative settings. However, in many centers, fibrinogen is not routinely monitored in the critically bleeding patient, despite growing evidence from clinical studies suggesting that fibrinogen is a vital target.[3-5]

Clinical data examining the efficacy and safety of fibrinogen concentrate for the treatment of acquired coagulopathy are reviewed here, as is the current evidence on appropriate plasma threshold levels and dosing across a range of clinical settings.

## THE CRITICAL ROLE OF FIBRINOGEN IN CLOT FORMATION AND HEMOSTASIS

Major blood loss represents a significant challenge across critical care settings, often resulting in coagulopathy and

**ABBREVIATIONS:** CABG = coronary artery bypass graft; CPB = cardiopulmonary bypass; FP24 = plasma frozen with 24 hours of collection; MCF = maximum clot firmness; MTP(s) = massive transfusion protocol(s); PCC = prothrombin complex concentrate; PPH = postpartum hemorrhage; ROTEM = thromboelastometry; TACO = transfusion-associated circulatory overload.

From the [1]Department of Anesthesiology, Duke University School of Medicine, Durham, North Carolina; and the [2]Department of Pathology, Stanford University School of Medicine, Stanford Medical Center, Palo Alto, California.

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Received for publication May 3, 2013; revision received August 14, 2013, and accepted August 14, 2013.

doi: 10.1111/trf.12431

**TRANSFUSION** 2014;54:1389-1405.

- Bra review om fibrinogen
- Plasma innehåller 1-3 g/l
- Fibrinogen koncentrat innehåller 15-20 g/l
- Vid obstetrisk blödning höjer 1 g ca 0,36 g/l

# Benefit Profile of Thrombomodulin Alfa Combined with Antithrombin Concentrate in Patients with Sepsis-Induced Disseminated Intravascular Coagulation

Clinical and Applied Thrombosis/Hemostasis
Volume 28: 1-10

DOI: 10.1177/10760296221077096
journals.sagepub.com/home/cat
SAGE

**Atsushi Mura**
**Goichi Honda**

**Abstract**
Thrombomodulin a
lant agents for the
with infection-indu
from combination
plasma AT level of
tively). Kaplan-Mei
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reduced 28-day mo
tions (ADRs) and
deficiency are canc

**Keywords**
disseminated intrav

International Journal of *Molecular Sciences*
MDPI

*Review*

# Antithrombin as Therapeutic Intervention against Sepsis-Induced Coagulopathy and Disseminated Intravascular Coagulation: Lessons Learned from COVID-19-Associated Coagulopathy

**Christian J. Wiedermann** [1,2]

[1] Institute of General Practice, Claudiana—College of Health Professions, 39100 Bolzano, Italy; christian.wiedermann@am-mg.claudiana.bz.it
[2] Department of Public Health, Medical Decision Making and HTA, University of Health Sciences, Medical Informatics and Technology—Tyrol, 6060 Hall in Tyrol, Austria

**Abstract:** Recent research has contributed significantly to our understanding of the pathogenesis of acute disseminated intravascular coagulation. COVID-19 can be considered as a new underlying condition of disseminated intravascular coagulation. In this narrative review, current evidence is presented regarding biomarker differences between sepsis-induced and COVID-19-associated coagulopathies, supporting the importance of acquired antithrombin deficiency in the early differential diagnosis of septic coagulopathy and its potential impact on treatment with endogenous anticoagulants. Establishing new scoring systems for septic coagulopathy in combination with endogenous anticoagulant biomarker activities may allow for the identification of those in the heterogeneous population of sepsis patients who are more likely to benefit from targeted specific treatment interventions.



**Citation:** Wiedermann, C.J. Antithrombin as Therapeutic

Desmopressin

Trombomodulin

Antikoagulantia

Protein C

## Antitrombin

- Koagulationsjour
- DIC pga sepsis, konsumtionsbild, med låga TPK

# En vanlig natt på förlossningen

**Dag 0, kl 23.38**

- Telefonsamtal
- Frisk
- 3 para
- Gravid v35+1
- MVC, blodtryck 110/65, ingen proteinuri dock illamående
- Ont epigastriet sedan 1 timme
- Hälsas välkommen

**Dag 1, kl 00.28**

- Klinik
  - Ont epigastriet
  - Illamående
  - Smärtpåverkad, kan ej ligga still
  - Mjuk buk
- Ultraljud: HF ua, FR ua, placenta ua
- Inj Ketogan iv

# En vanlig natt på förlossningen?

**Dag 1, kl 01.22**

- CTG
  - Inskränkt variabilitet
  - Komplexa variabla decelerationer
  - Frekvens initialt 120
  - Bradykardi, frekvens 60
- Larm, urakut kejsarsnitt

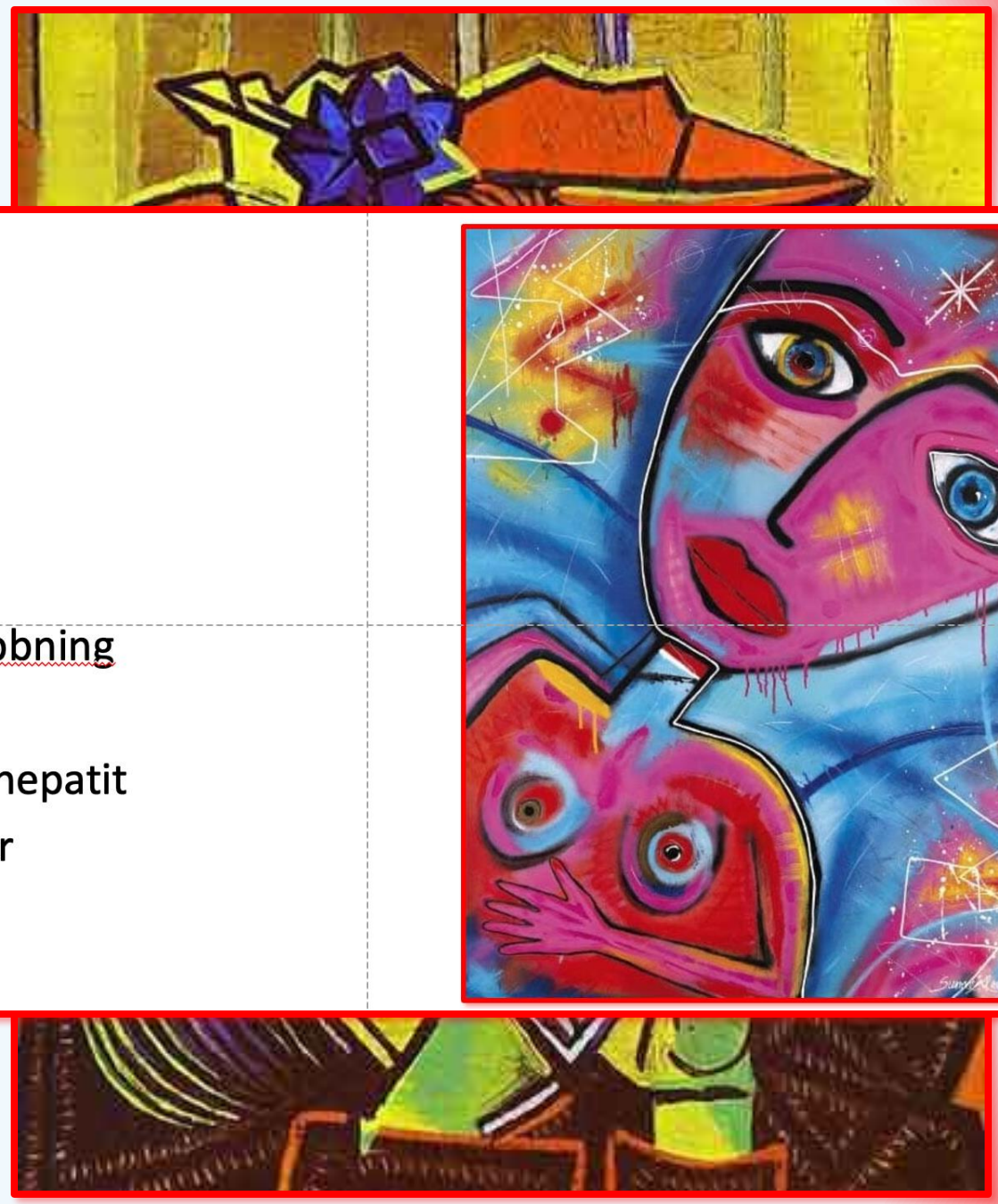
**Dag 1, kl 01.45**

- Födelse pojke
- Oxytocin 5 E + 5 E
- Methergin
- Blödning 200 ml initialt
- Uterus väl kontraherad
- Lever svullen?

# En vanlig natt på operationssalen

**Dag 1, kl 03.12**

- Blödning vaginalt, 1100 m
- Tranexamsyra 2 g
- Oxytocin infusion
- Karboprost (Prostinfenem
- Desmopressin (Octostim)
- Blodprover hemolys
- Transfusion, 4 blod + 2 pla
- Rotem
- Diagnos?

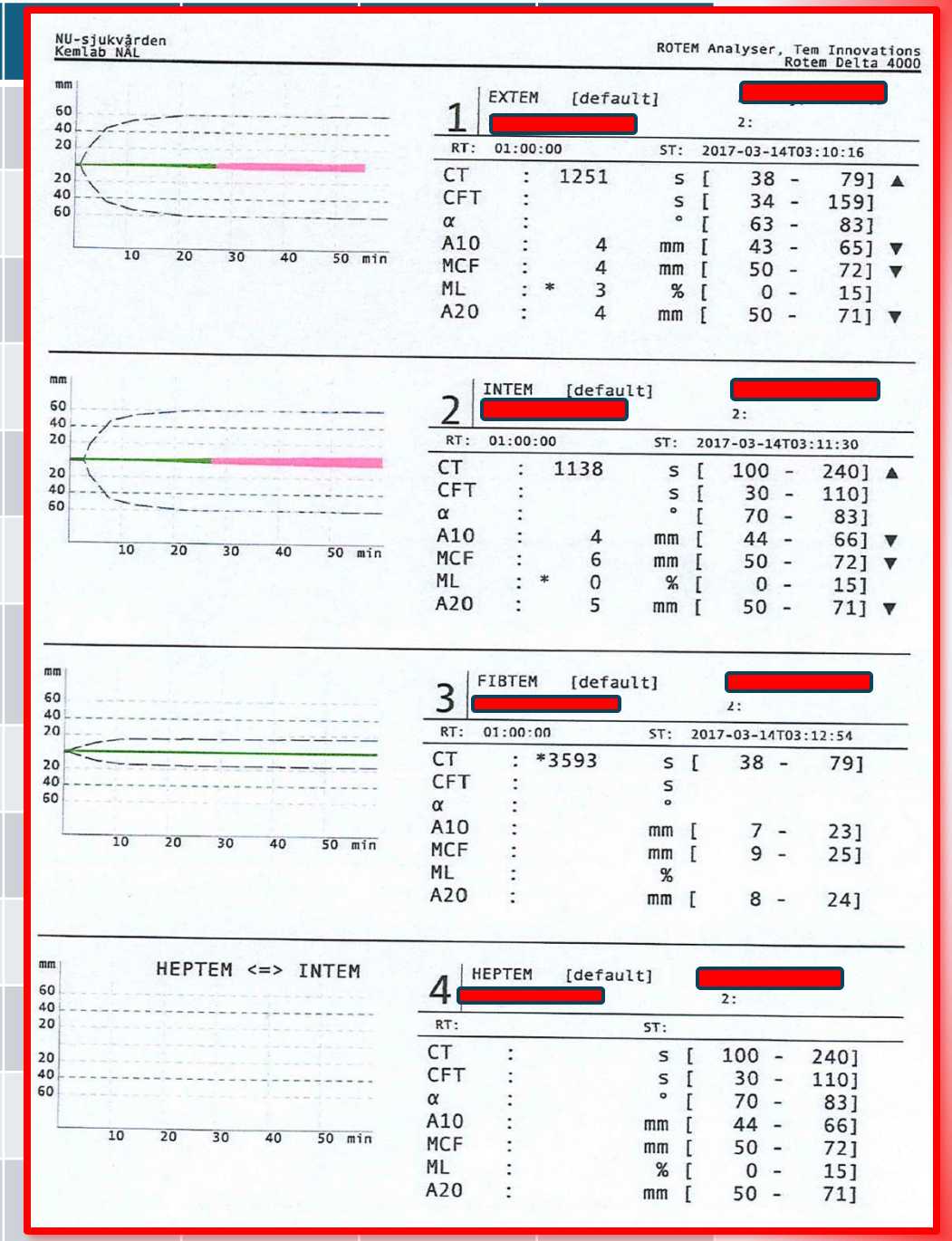


## Diagnos?

1. HELLP
2. Hemostasrubbning
3. Hepatit
4. Autoimmun hepatit
5. Akut fettlever
6. Ingen aning

| Dag 1-3 | 01:00 | 04:00 | 06:00 | 11:30 | 14:30 | 20:30 |
|---|---|---|---|---|---|---|
| Hb | 121 | | | | | |
| LPK | 17.5 | | | | | |
| TPK | 156 | | | | | |
| CRP | 6 | | | | | |
| Asat | Hem | | | | | |
| Alat | Hem | | | | | |
| Bilirubin | Hem | | | | | |
| Kreat | Hem | | | | | |
| PK | Hem | | | | | |
| APTT | Hem | | | | | |
| Fib | Hem | | | | | |
| AT | 0.48 | | | | | |
| Rotem | 03:10 | | | | | |

Fibrinogen 4 g


NU-sjukvården
Kemlab NÄL

ROTEM Analyser, Tem Innovations
Rotem Delta 4000

1 EXTEM [default] [redacted]

RT: 01:00:00 ST: 2017-03-14T03:10:16

| | | | | | |
|---|---|---|---|---|---|
| CT | : | 1251 | s [ | 38 - | 79] ▲ |
| CFT | : | | s [ | 34 - | 159] |
| α | : | | ° [ | 63 - | 83] |
| A10 | : | 4 | mm [ | 43 - | 65] ▼ |
| MCF | : | 4 | mm [ | 50 - | 72] ▼ |
| ML | : * | 3 | % [ | 0 - | 15] |
| A20 | : | 4 | mm [ | 50 - | 71] ▼ |

2 INTEM [default] [redacted]

RT: 01:00:00 ST: 2017-03-14T03:11:30

| | | | | | |
|---|---|---|---|---|---|
| CT | : | 1138 | s [ | 100 - | 240] ▲ |
| CFT | : | | s [ | 30 - | 110] |
| α | : | | ° [ | 70 - | 83] |
| A10 | : | 4 | mm [ | 44 - | 66] ▼ |
| MCF | : | 6 | mm [ | 50 - | 72] ▼ |
| ML | : * | 0 | % [ | 0 - | 15] |
| A20 | : | 5 | mm [ | 50 - | 71] ▼ |

3 FIBTEM [default] [redacted]

RT: 01:00:00 ST: 2017-03-14T03:12:54

| | | | | | |
|---|---|---|---|---|---|
| CT | : | *3593 | s [ | 38 - | 79] |
| CFT | : | | s | | |
| α | : | | ° | | |
| A10 | : | | mm [ | 7 - | 23] |
| MCF | : | | mm [ | 9 - | 25] |
| ML | : | | % | | |
| A20 | : | | mm [ | 8 - | 24] |

HEPTEM <=> INTEM

4 HEPTEM [default] [redacted]

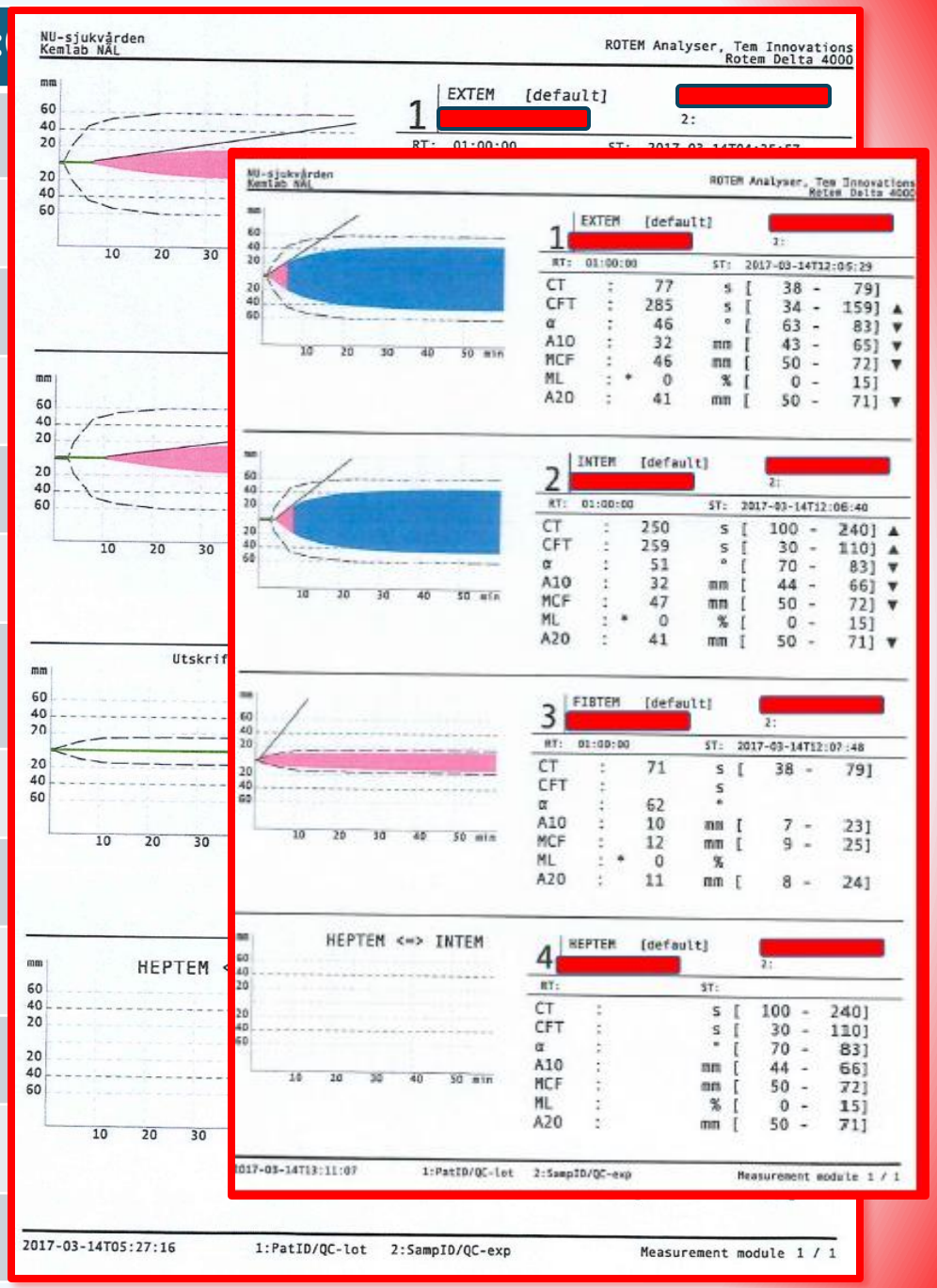
RT: ST:

| | | | | | |
|---|---|---|---|---|---|
| CT | : | | s [ | 100 - | 240] |
| CFT | : | | s [ | 30 - | 110] |
| α | : | | ° [ | 70 - | 83] |
| A10 | : | | mm [ | 44 - | 66] |
| MCF | : | | mm [ | 50 - | 72] |
| ML | : | | % [ | 0 - | 15] |
| A20 | : | | mm [ | 50 - | 71] |

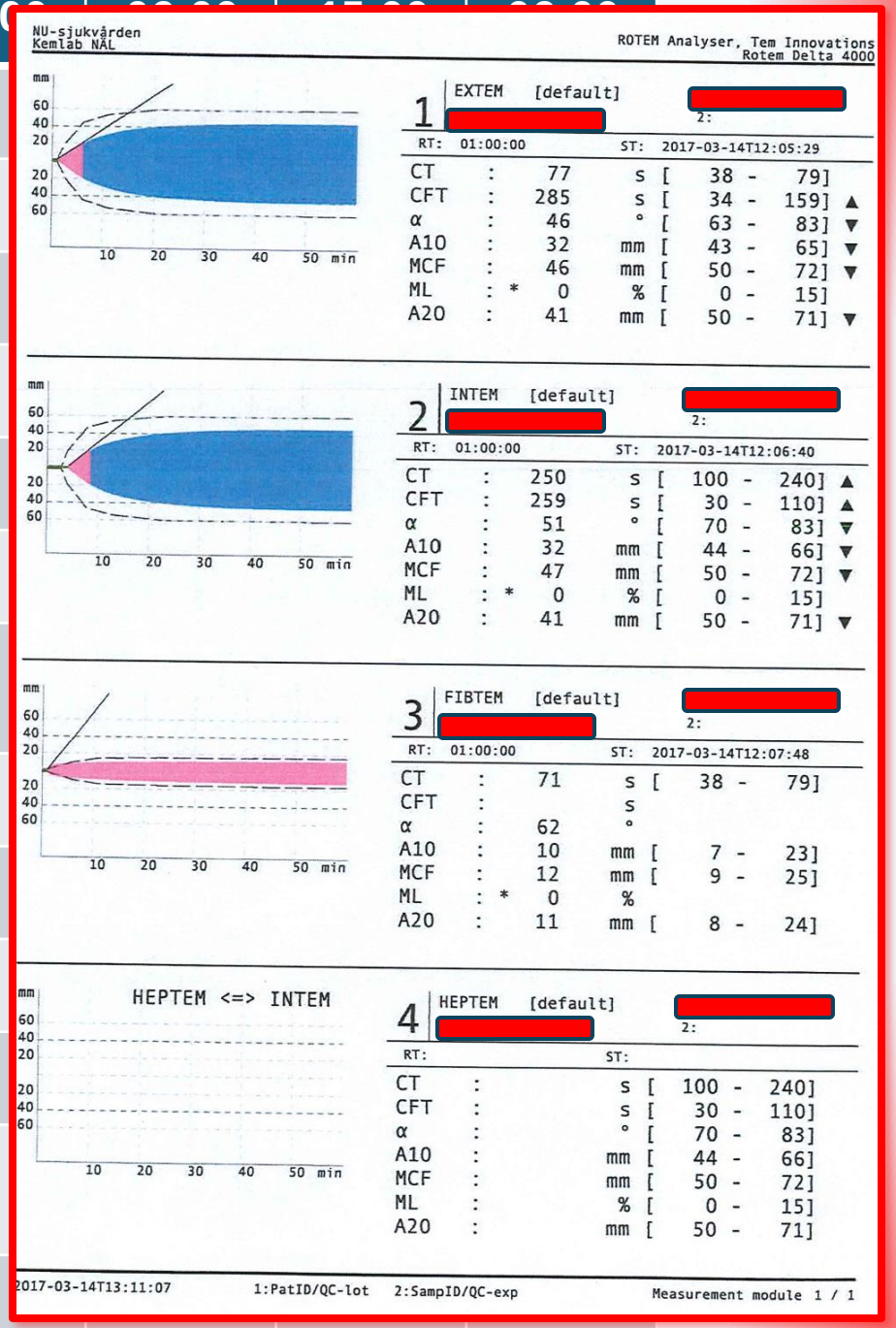
| Dag 1-3 | 01:00 | 04:00 | 06:00 | 11:30 | 14:30 | 20:30 | 03: |
|---|---|---|---|---|---|---|---|
| Hb | 121 | 131 | | | | | |
| LPK | 17.5 | 21.8 | | | | | |
| TPK | 156 | 83 | | | | | |
| CRP | 6 | 4 | | | | | |
| Asat | Hem | Hem | | | | | |
| Alat | Hem | 29 | | | | | |
| Bilirubin | Hem | Hem | | | | | |
| Kreat | Hem | Hem | | | | | |
| PK | Hem | 1.2 | | | | | |
| APTT | Hem | Hem | | | | | |
| Fib | Hem | - | | | | | |
| AT | 0.48 | - | | | | | |
| Rotem | 03:10 | 04:30 | | | | | |

Dag 1, kl 05.00 IVA

- Fortsätter siva från uterus
- Intuberad respirator
- Blodprover hemolys
- Bakri ballong
- Tamponad vagina
- Uterus väl kontraherad
- Diagnos?
- Mer blod, FFP, trombocyter och fibrinogen



| Dag 1-3 | 01:00 | 04:00 | 06:00 | 11:30 | 14:30 | 20:30 | 03:0 |
|---|---|---|---|---|---|---|---|
| Hb | 121 | 131 | 117 | 91 | | | |
| LPK | 17.5 | 21.8 | 21.7 | 13.2 | | | |
| TPK | 156 | 83 | 85 | 45 | | | |
| CRP | 6 | 4 | 5 | | | | |
| Asat | Hem | Hen | Hem | 72 | | | |
| Alat | Hem | 29 | 22 | 19 | | | |
| Bilirubin | Hem | Hem | 78 | 135 | | | |
| Kreat | Hem | Hem | Hem | 147 | | | |
| PK | Hem | 1.2 | 1.2 | 1.2 | | | |
| APTT | Hem | Hem | Hem | 50 | | | |
| Fib | Hem | - | Hem | 1.6 | | | |
| D-dimer | - | - | - | >10 | | | |
| Rotem | 03:10 | 04:30 | 08:00 | 12:00 | | | |


NU-sjukvården
Kemlab NÄL

ROTEM Analyser, Tem Innovations
Rotem Delta 4000

1 EXTEM [default] [redacted] 2:

RT: 01:00:00 ST: 2017-03-14T12:05:29

| | | | | | | |
|---|---|---|---|---|---|---|
| CT | : | 77 | s | [ | 38 - | 79] |
| CFT | : | 285 | s | [ | 34 - | 159] ▲ |
| α | : | 46 | ° | [ | 63 - | 83] ▼ |
| A10 | : | 32 | mm | [ | 43 - | 65] ▼ |
| MCF | : | 46 | mm | [ | 50 - | 72] ▼ |
| ML | : * | 0 | % | [ | 0 - | 15] |
| A20 | : | 41 | mm | [ | 50 - | 71] ▼ |

2 INTEM [default] [redacted] 2:

RT: 01:00:00 ST: 2017-03-14T12:06:40

| | | | | | | |
|---|---|---|---|---|---|---|
| CT | : | 250 | s | [ | 100 - | 240] ▲ |
| CFT | : | 259 | s | [ | 30 - | 110] ▲ |
| α | : | 51 | ° | [ | 70 - | 83] ▼ |
| A10 | : | 32 | mm | [ | 44 - | 66] ▼ |
| MCF | : | 47 | mm | [ | 50 - | 72] ▼ |
| ML | : * | 0 | % | [ | 0 - | 15] |
| A20 | : | 41 | mm | [ | 50 - | 71] ▼ |

3 FIBTEM [default] [redacted] 2:

RT: 01:00:00 ST: 2017-03-14T12:07:48

| | | | | | | |
|---|---|---|---|---|---|---|
| CT | : | 71 | s | [ | 38 - | 79] |
| CFT | : | | s | | | |
| α | : | 62 | ° | | | |
| A10 | : | 10 | mm | [ | 7 - | 23] |
| MCF | : | 12 | mm | [ | 9 - | 25] |
| ML | : * | 0 | % | | | |
| A20 | : | 11 | mm | [ | 8 - | 24] |

HEPTEM <=> INTEM

4 HEPTEM [default] [redacted] 2:

RT: ST:

| | | | | | | |
|---|---|---|---|---|---|---|
| CT | : | | s | [ | 100 - | 240] |
| CFT | : | | s | [ | 30 - | 110] |
| α | : | | ° | [ | 70 - | 83] |
| A10 | : | | mm | [ | 44 - | 66] |
| MCF | : | | mm | [ | 50 - | 72] |
| ML | : | | % | [ | 0 - | 15] |
| A20 | : | | mm | [ | 50 - | 71] |

2017-03-14T13:11:07 1:PatID/QC-lot 2:SampID/QC-exp Measurement module 1 / 1

# Akut fettlever, behandling

- Avsluta graviditet
- Om tid finns
  - Stabilisera patient
  - Optimera hemostas
- Undvik ytterligare leverskada
  - Intensivvård
  - Optimera cirkulation, hjärtminutvolym och blodtryck
  - Undvik vissa LM
  - Acetylcystein?
- Farmakokinetik och farmakodynamik ändrad
- Samarbete och kommunikation
- Levertransplantation vb

SGF Nationella Riktlinjer
2014

På uppdrag av Svensk Gastroenterologisk Förenings styrelse

Nationella riktlinjer
för utredning samt handläggning av

Leversjukdom under graviditet – graviditet vid leversjukdom

2013-10-25

Kontaktperson: Hanns-Ulrich Marschall, Medicinkliniken, Sahlgrenska Universitetssjukhuset, 413 45 Göteborg, 070-8774073, hanns-ulrich.marschall@gu.se

Medlemmar i expertgruppen

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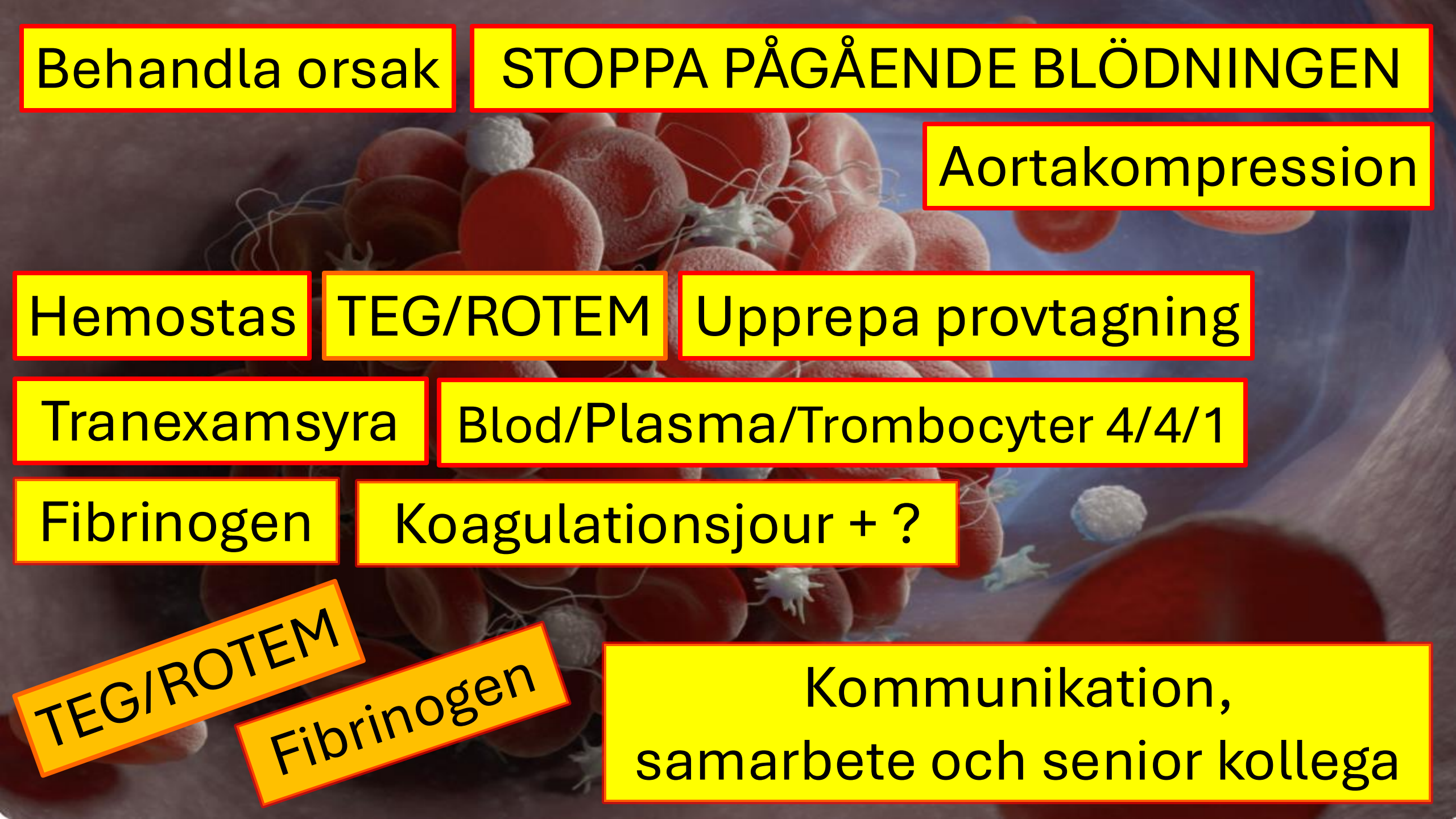
martin.lagging@medfak.gu.se
Olof Stephansson, Kvinnokliniken, Karolinska Universitetssjukhuset, Stockholm
olof.stephansson@ki.se

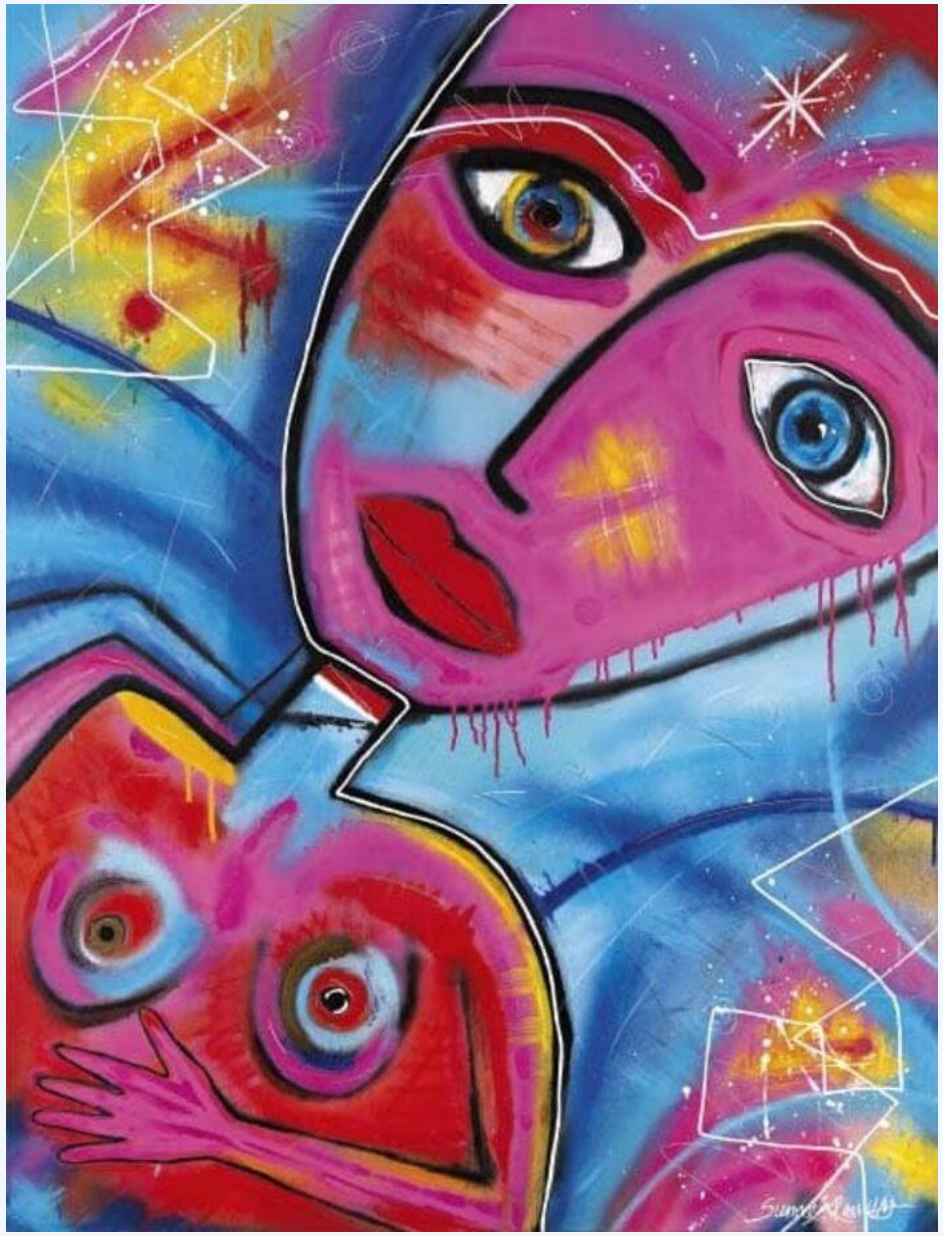
# nliga dygn på IVA

**1 - 8**

- od 3 st (tot 9 blod)
- P 3 st (tot 12 FFP)
- ombocyter 5 st (tot 8 st)
- Fibrinogen (tot 10 g)
- Respirator dag 1-4
- Dialys CRRT dag 3-8
- Sjukhusvård 3 veckor

- FFP 7 st
- Trombocyter 3 st
- Fibrinogen 3 + 3 g
- Tranexamsyra 2 g


Behandla orsak
STOPPA PÅGÅENDE BLÖDNINGEN
Aortakompression
Hemostas
TEG/ROTEM
Upprepa provtagning
Tranexamsyra
Blod/Plasma/Trombocyter 4/4/1
Fibrinogen
Koagulationsjour + ?
TEG/ROTEM
Fibrinogen
Kommunikation,
samarbete och senior kollega



Tack!