



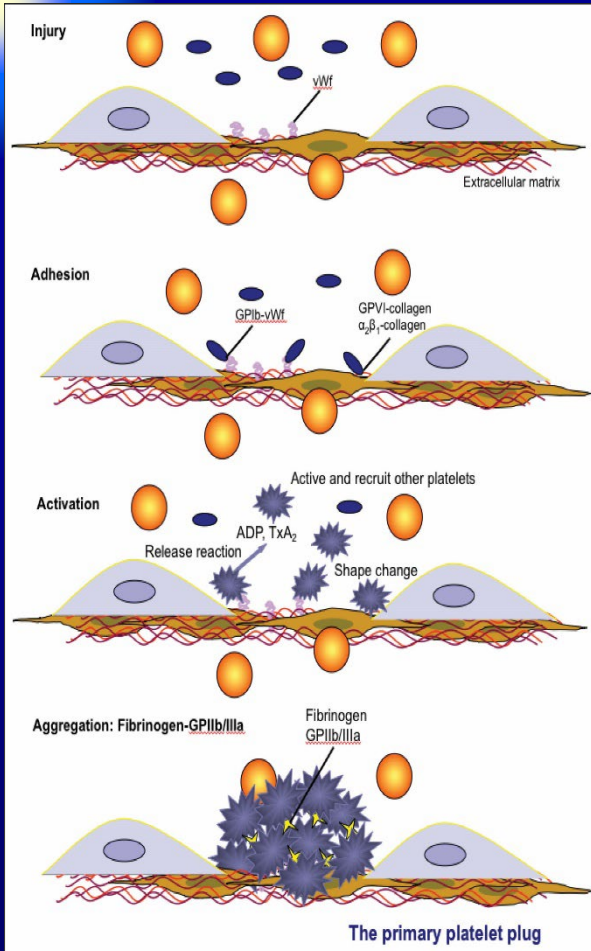
# Hemostáza trochu jinak 😊

prof. MUDr. Miroslav Durila, Ph.D., MHA  
KARIM, 2. LF UK, FN Motol, Praha

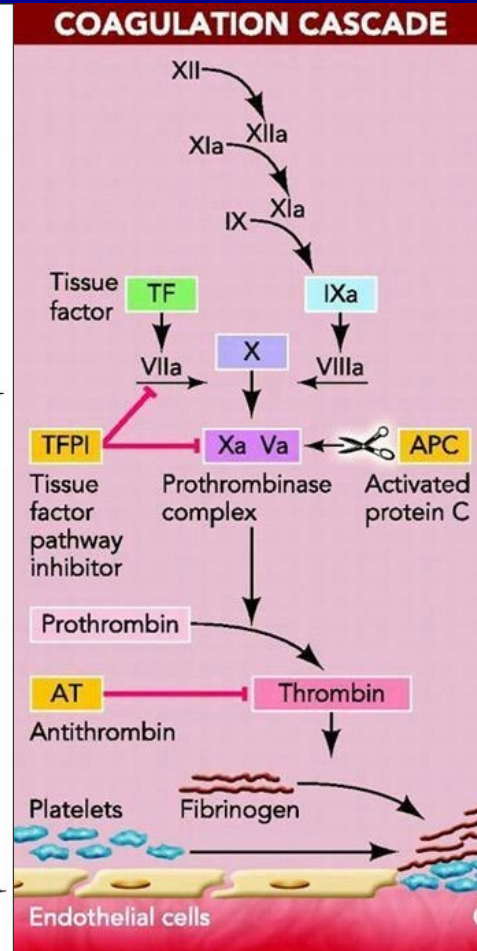
XV. Konference Akutně.cz, 25.11.2023, Brno

# Hemostáza

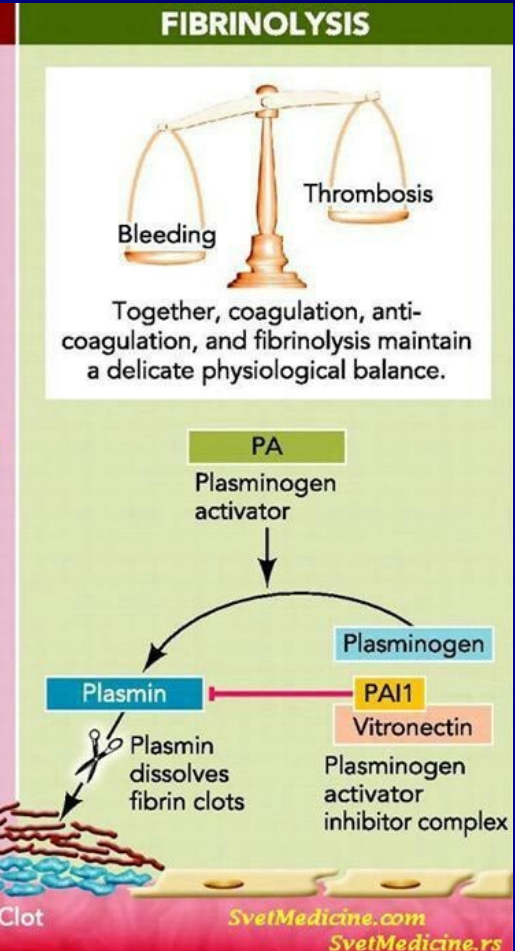
## 1. fáze=Plt zátka



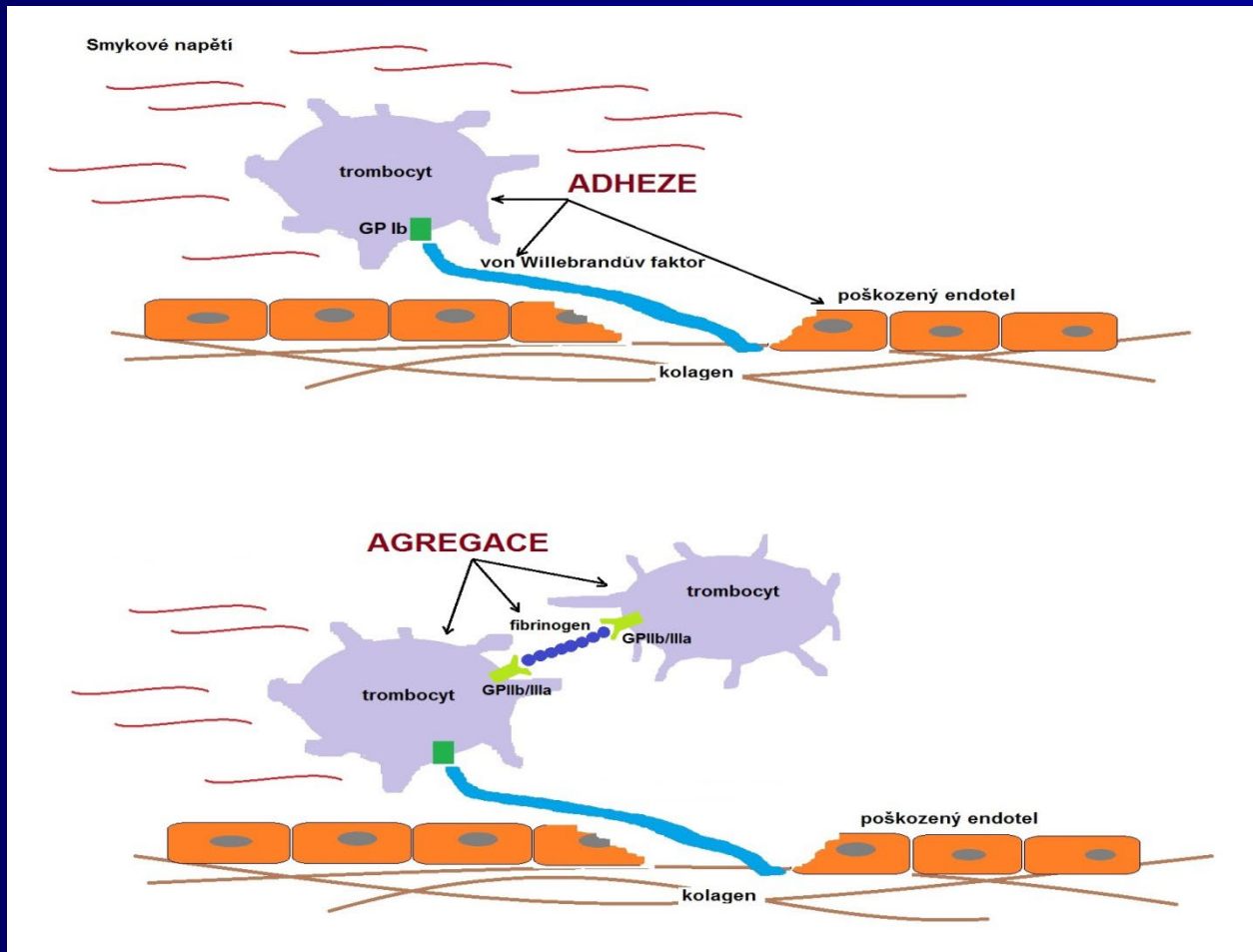
## 2. fáze=fibrin zátka



## 3. fáze=lysis

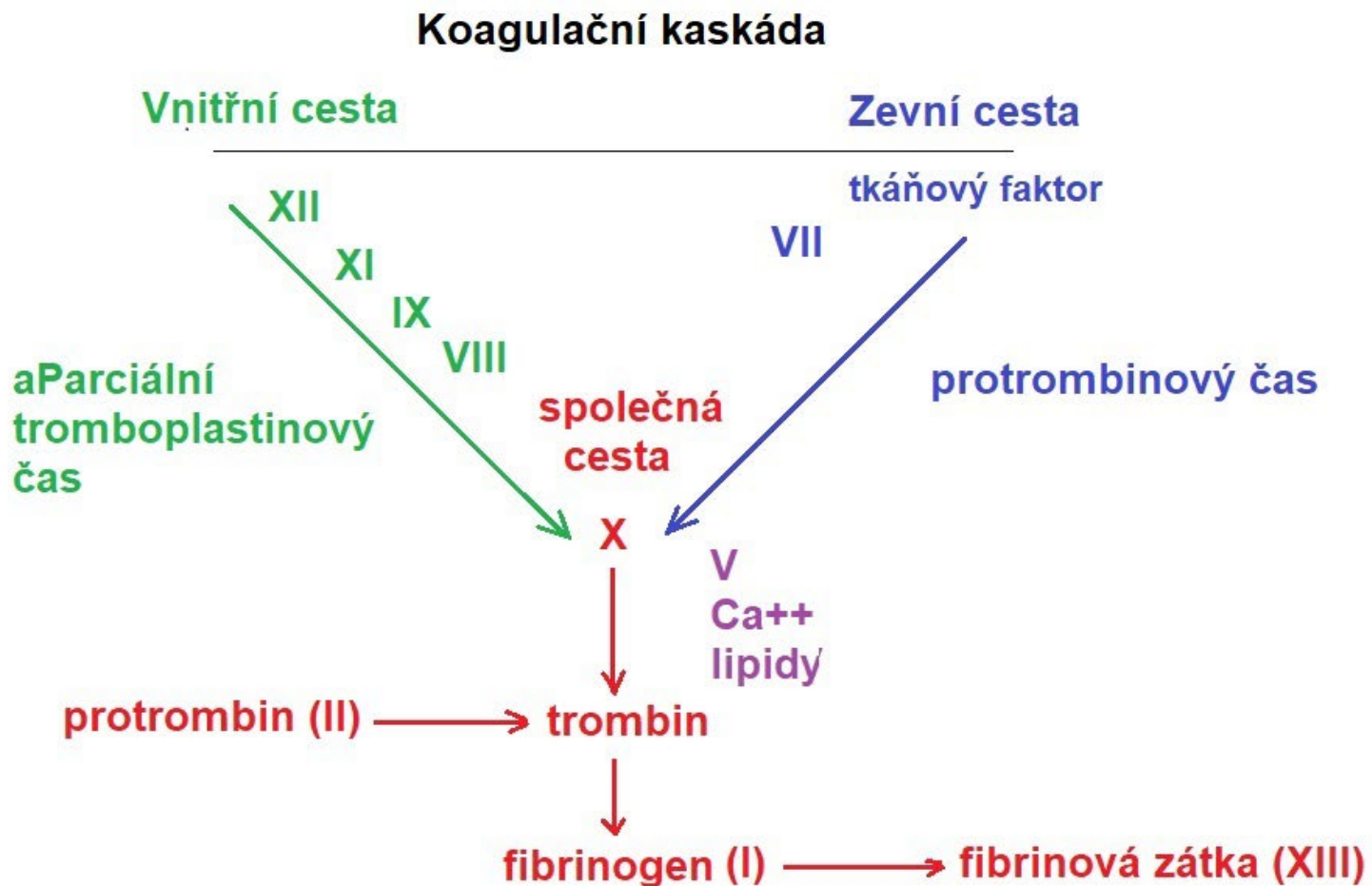


# Dostičkový trombus - primárna hemostáza

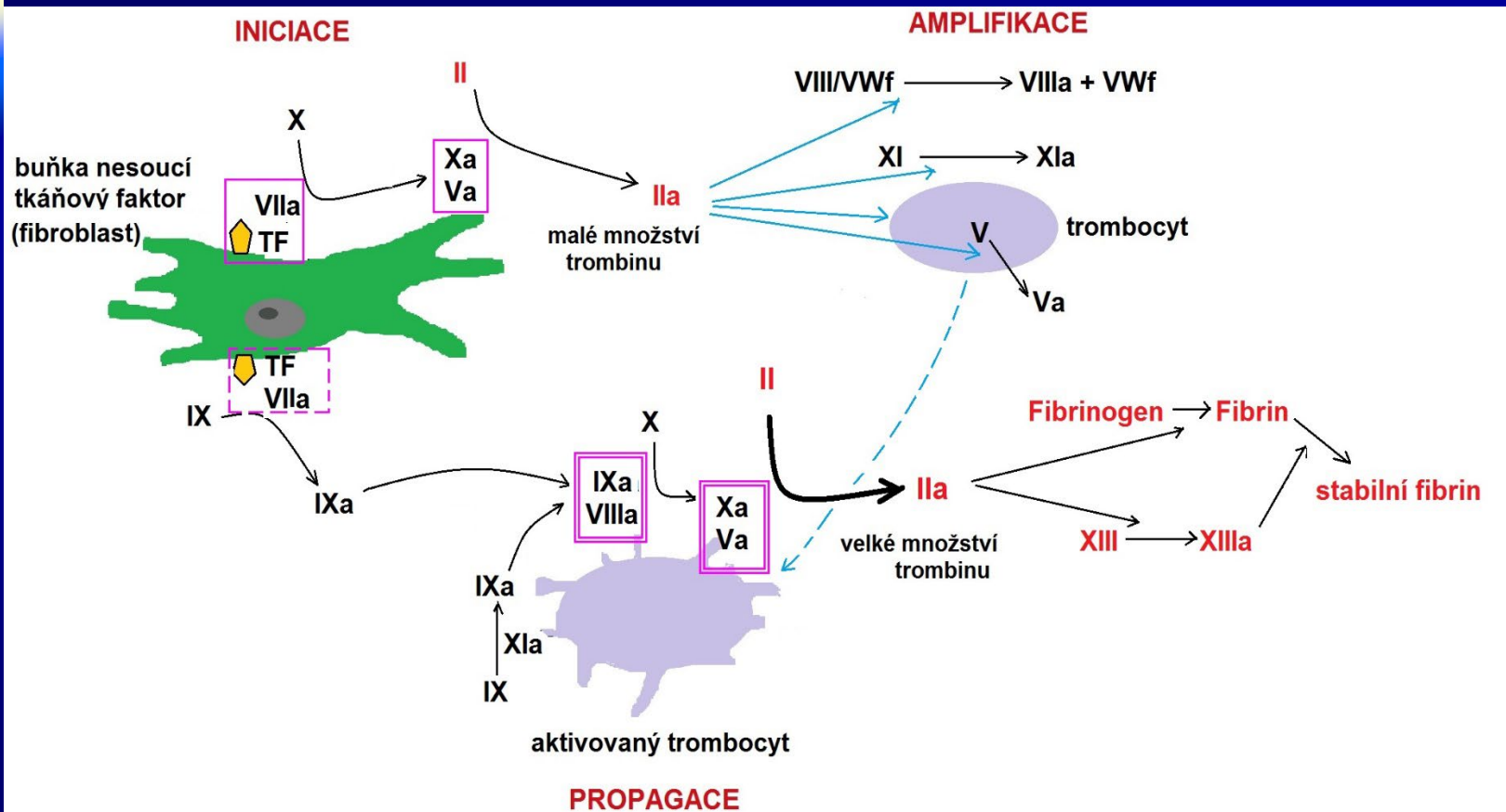


GP Ib/V/IX  
GP IIb/IIIa

# Kaskádový-starý model koagulace



# Buněčný- bunkový- cell based – nový model koagulace - fibrínový trombus – sekundárna hemostáza



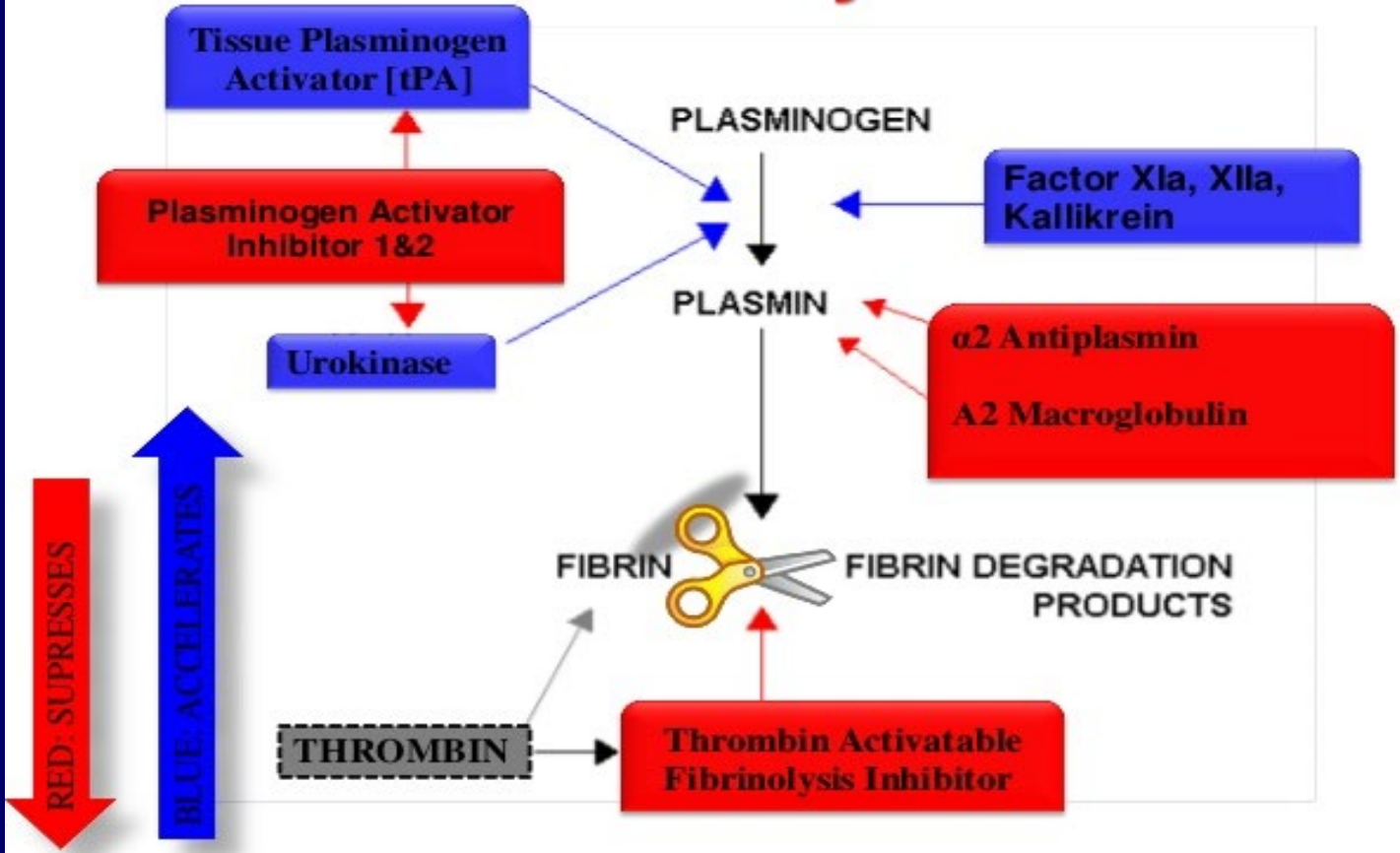
# Retrakcia koagula - terciálna hemostáza



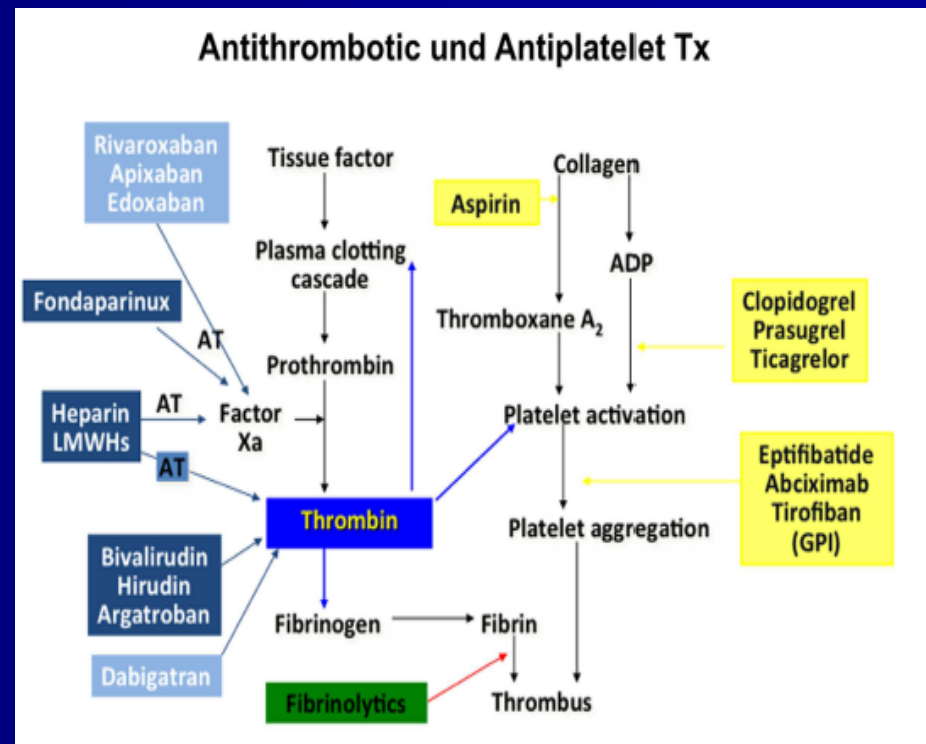
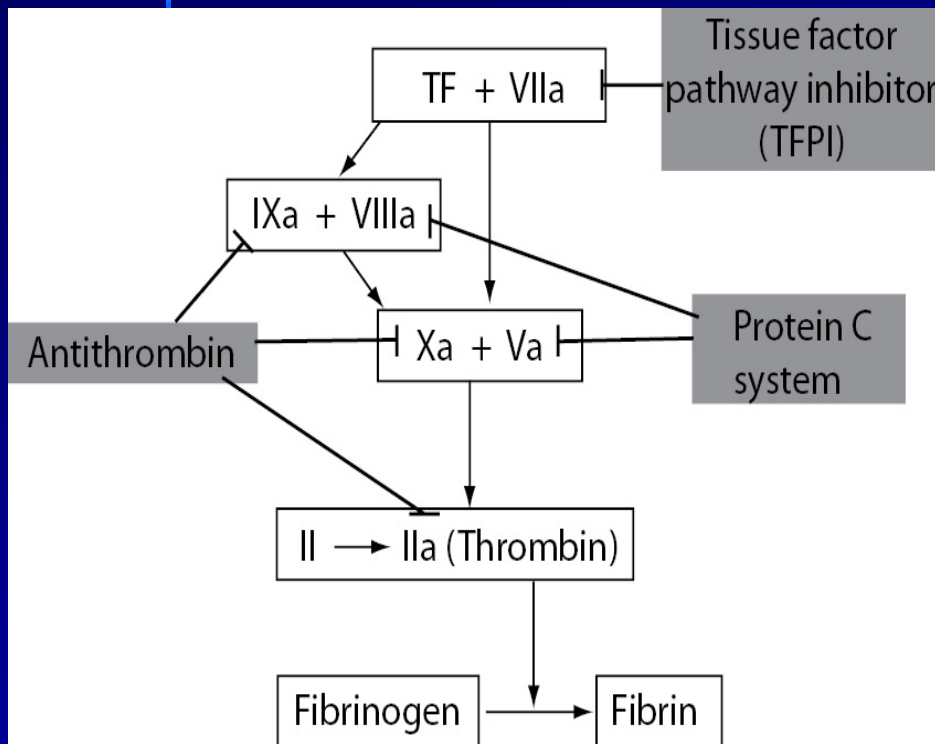
Interakcia  
GP IIb/IIIa a  
Fibrinove vlákna  
nutný FXIIIa

# Fibrinolýza

## Fibrinolysis

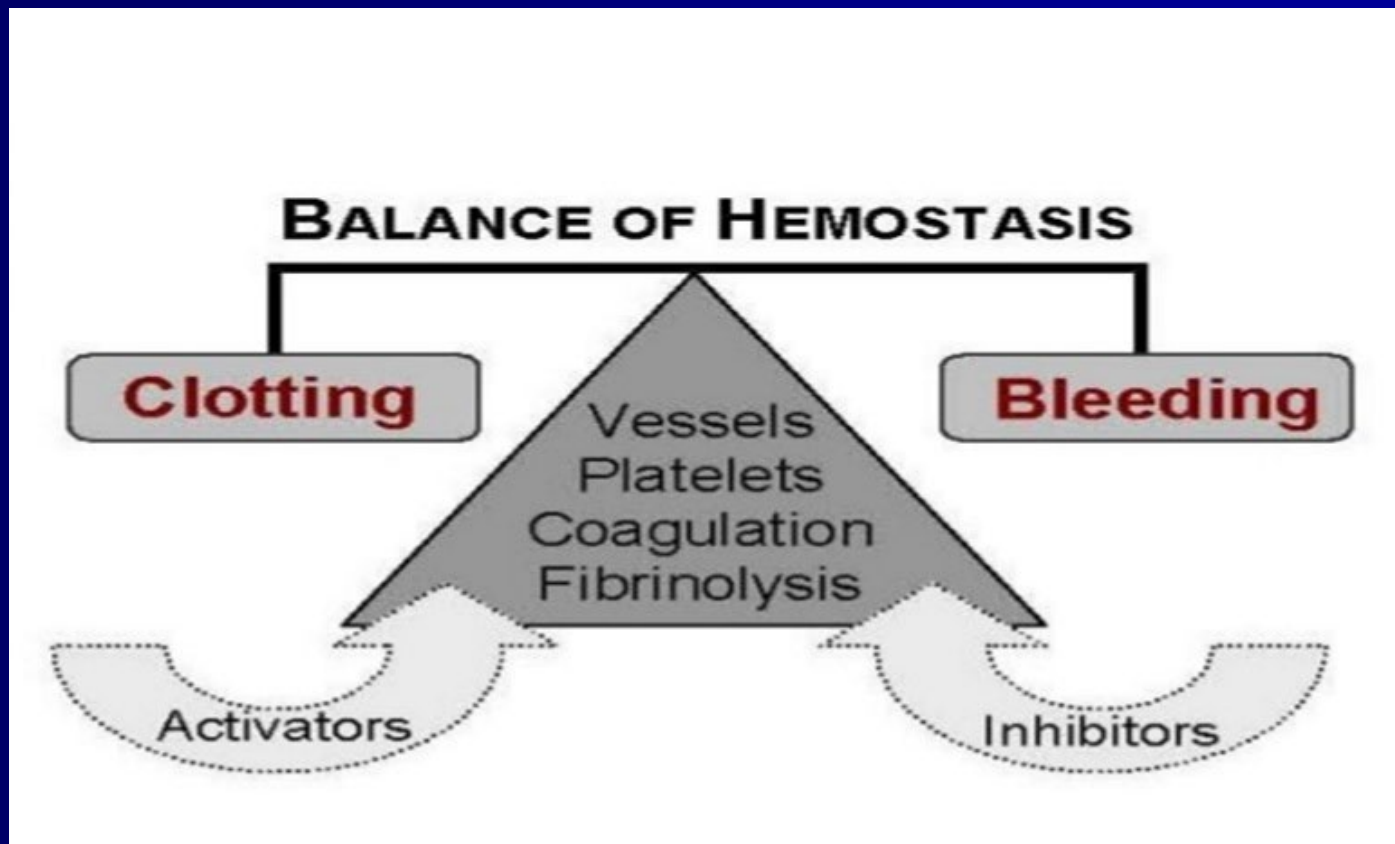


# Antikoagulačné systémy

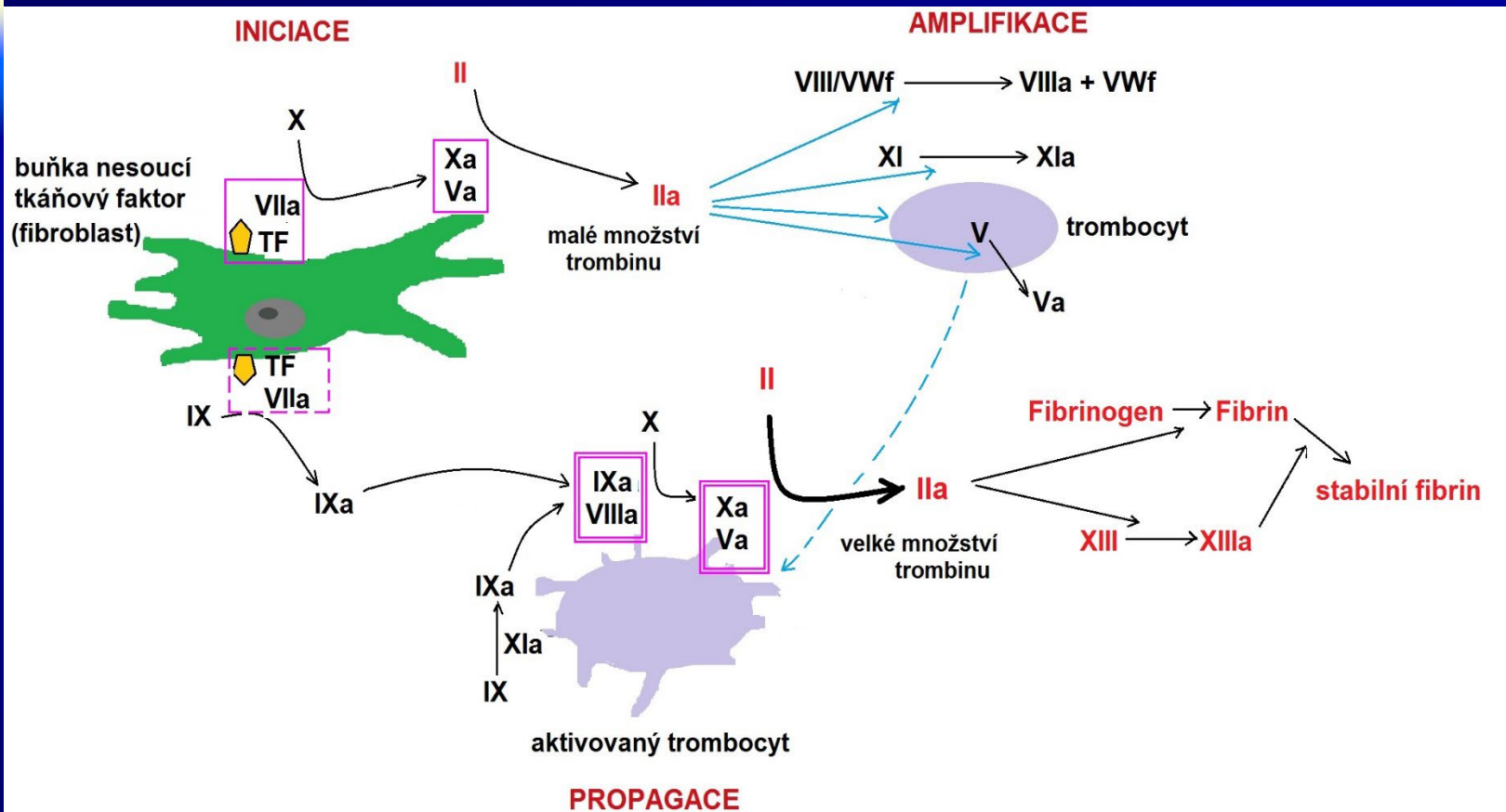




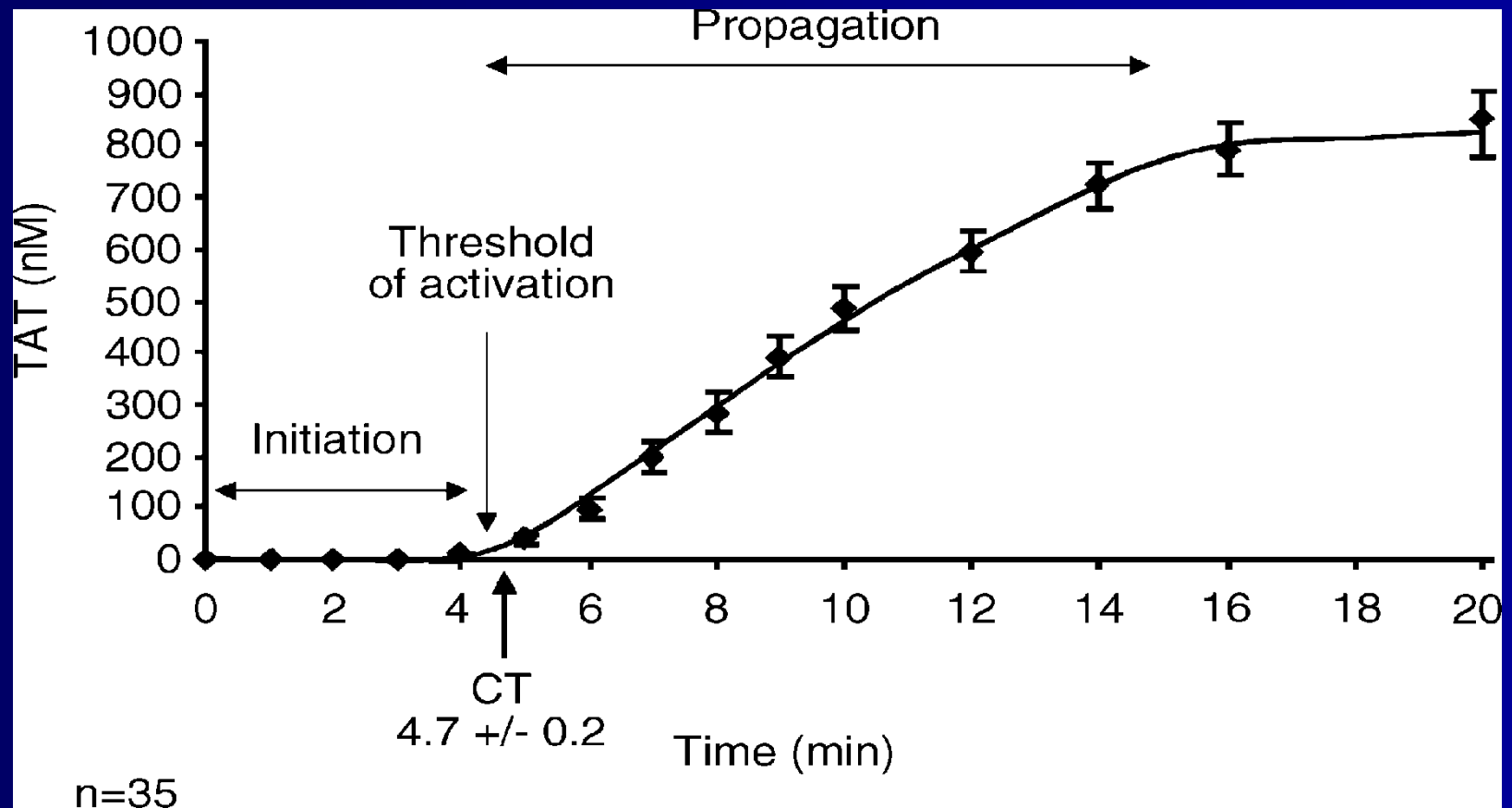
# Výsledok hemostázy nezávisí od rovnováhy...

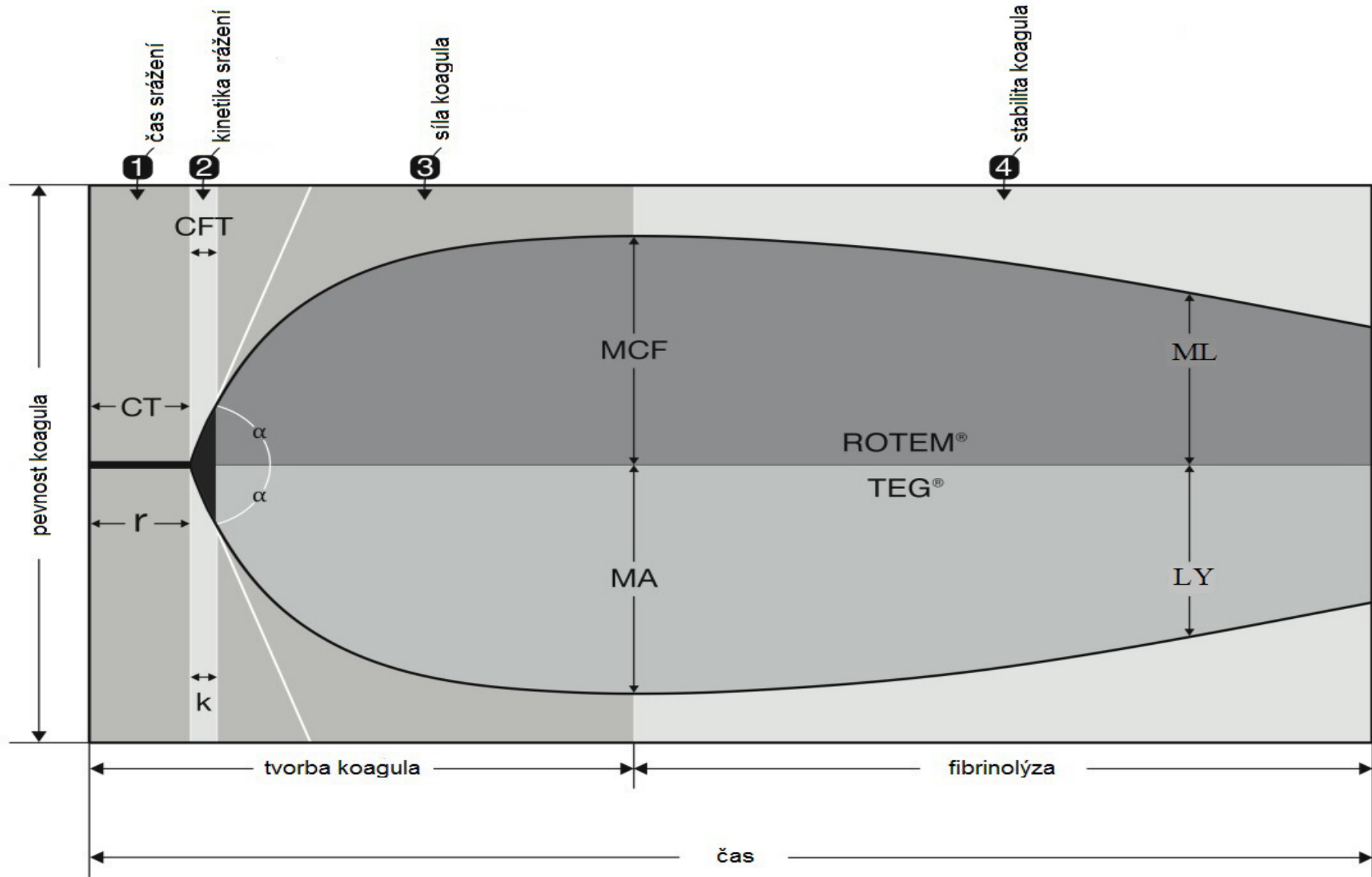


# Buněčný- bunkový- cell based – nový model koagulace - fibrínový trombus – sekundárna hemostáza



Tvorba trombinu pomocou merania trombin–antithrombin (TAT) komplexov je závislá na čase.





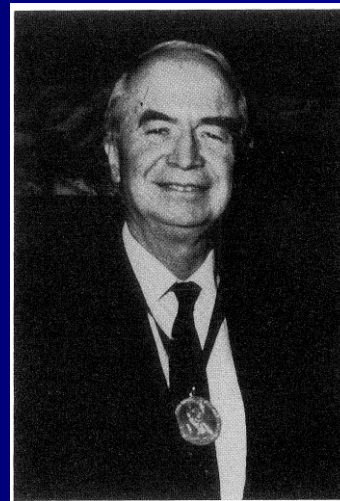
# TEG/ROTEM

## Tromboelastografia/rotačná tromboelastometria

Prof. Helmut Hartert, Nemecko,  
40-te roky minulého storočia

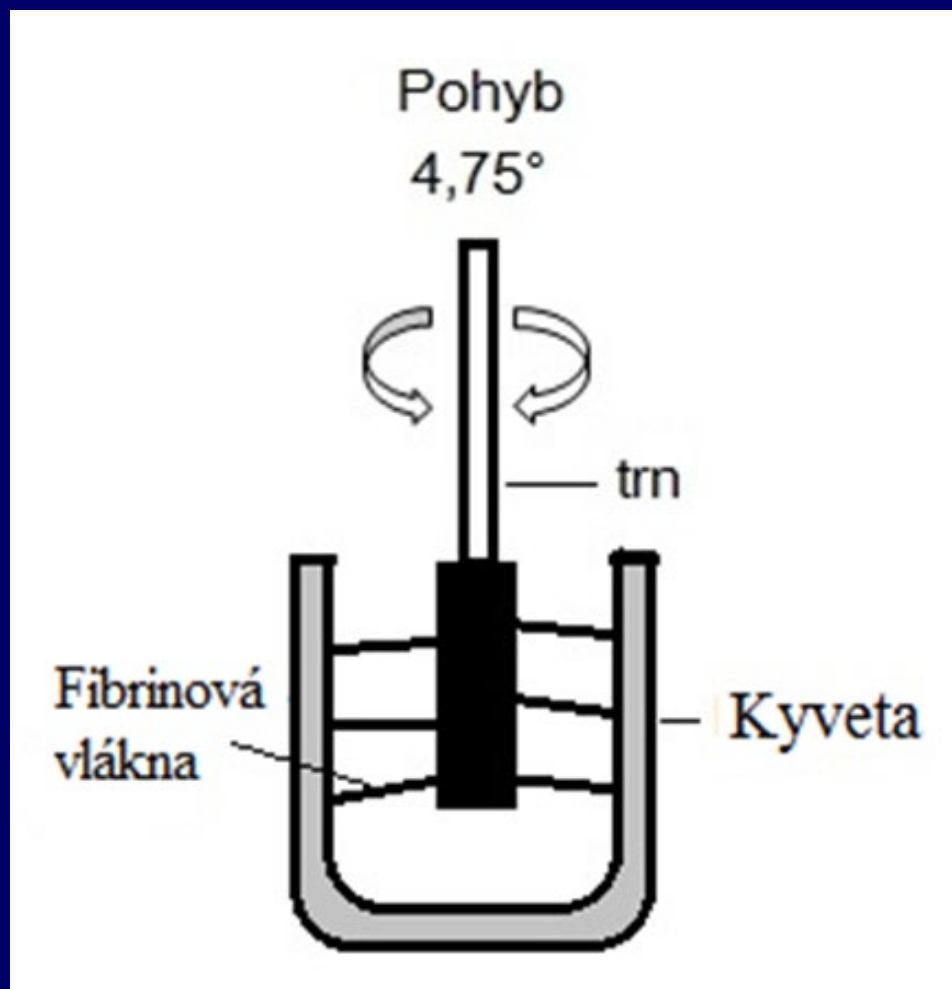


**TEG Haemoscope,  
Niles, IL, USA**



**RoTEM Pentapharm GmbH,  
Munich, Germany**

# Princíp ROTEM



# Sekundárna hemostáza - ROTEM

- Výhody: plná krv (Tr, Er, Leu...) - nekoreluje s PT, aPTT, rýchla diagnostika fibrinolýzy
- Nevýhody a limity: neposkytuje informácie o primárnej hemostáze (chýba endotel a strižné sily) nie pre Dg. vWF, nie antiagregancia...

- **Primárna hemostáza – PFA 200**





## Typy testov ROTEM

EXTEM - obsahuje **aktivátory vonkajšej cesty**

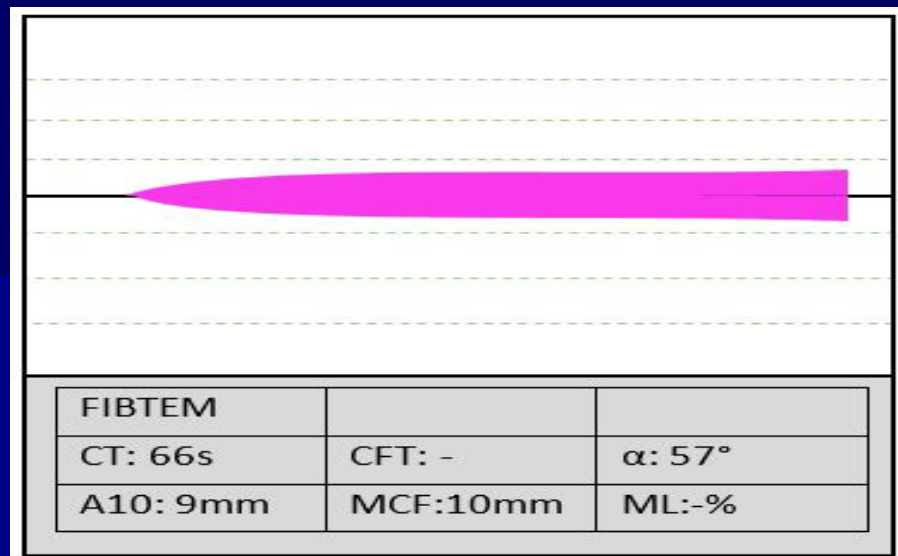
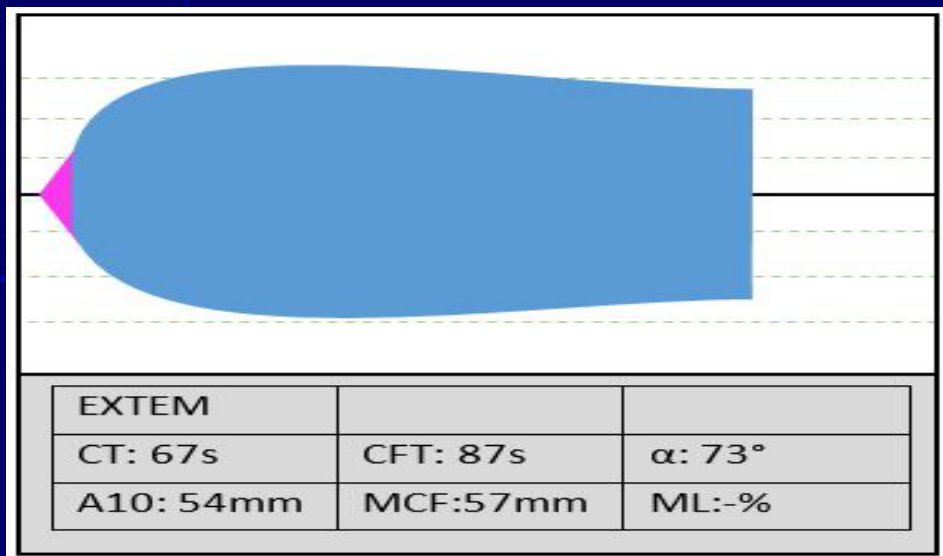
INTEM – obsahuje **aktivátory vnútornej cesty**

FIBTEM – obsahuje **blokátory trombocytov**

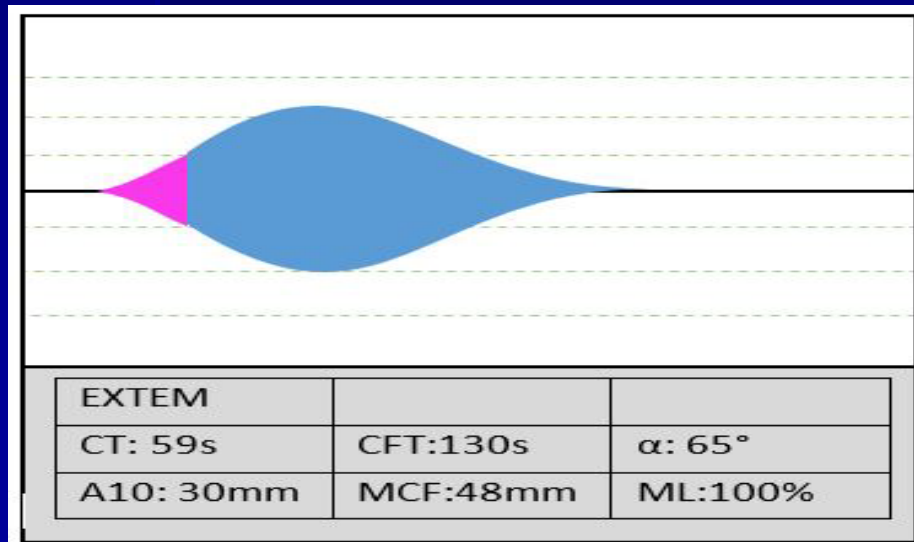
APTEM – obsahuje **aprotinin/tranexamovú kys.**



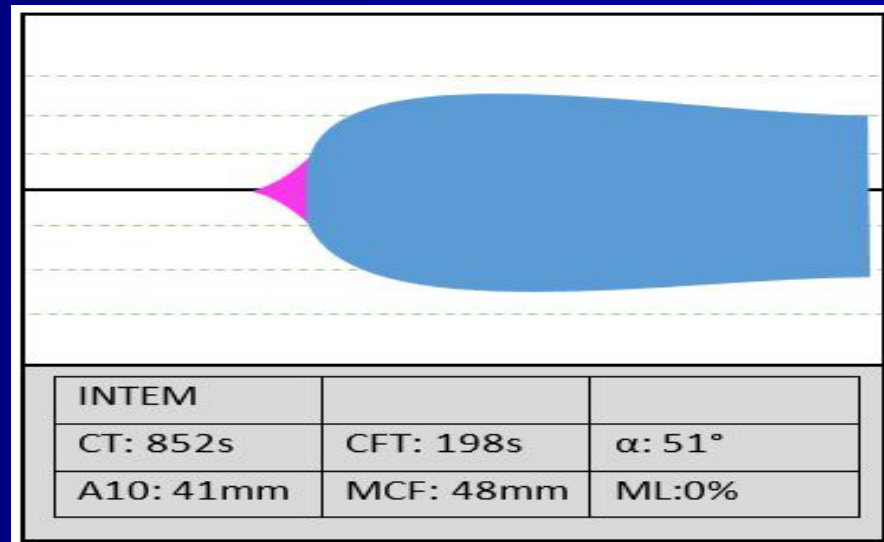
## Normálny nález



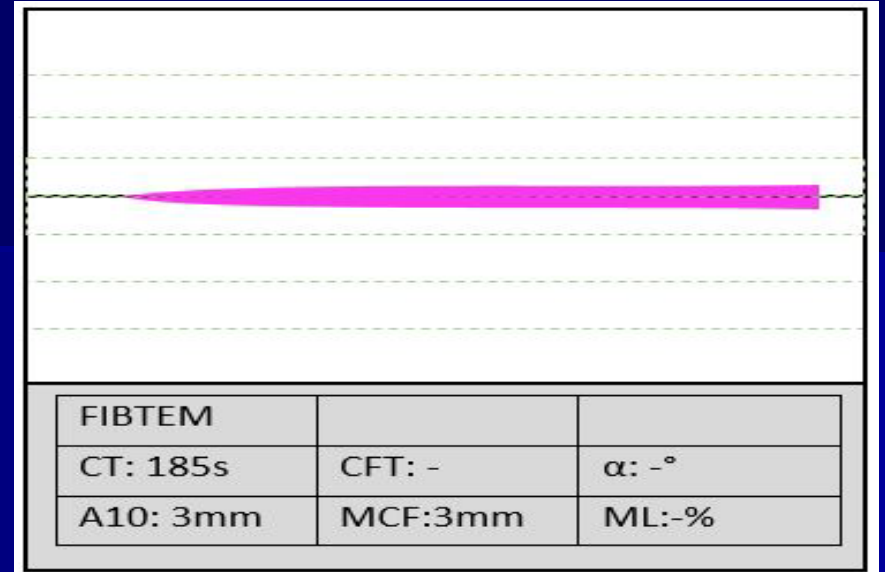
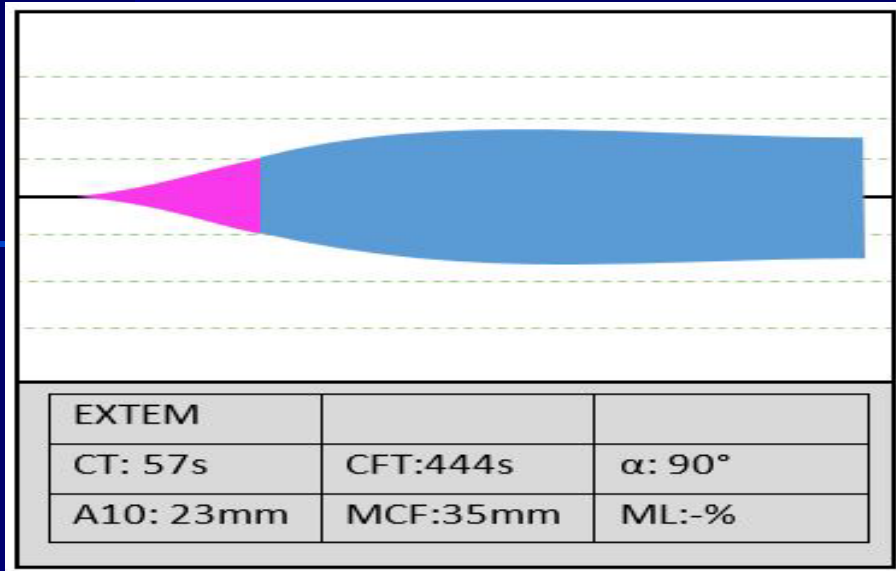
## Hyperfibrinolýza



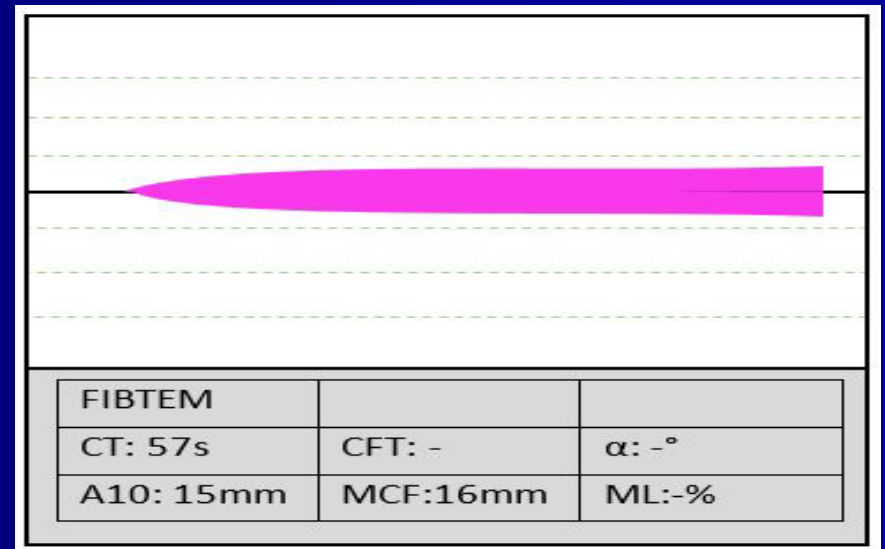
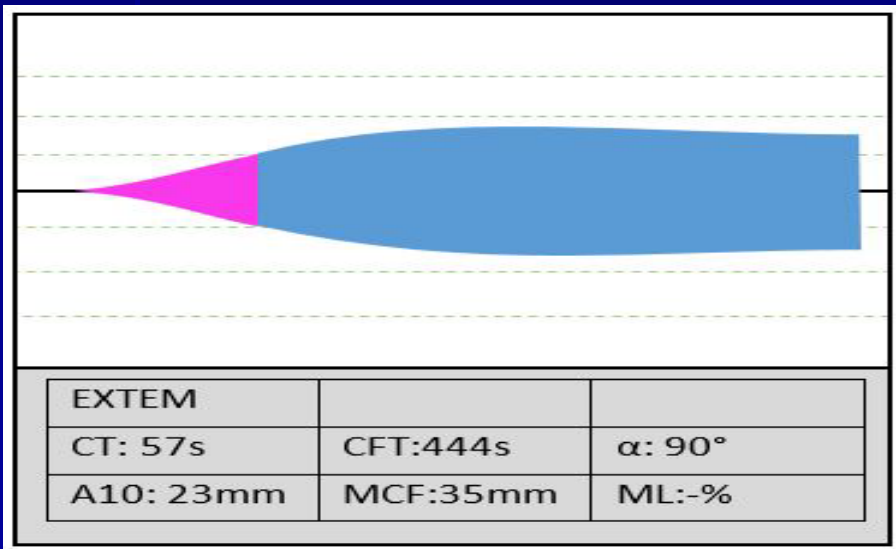
## Hemofília alebo deficti FXII



## Deficit fibrinogenu



## Deficit trombocytov



# ROTEM protocol

EXTEM, FIBTEM, INTEM

**EXTEM CT > 90s**

Th: prothrombin complex concentrate

CT: 90s - 100s = 7,5 units/kg

CT: 101-120s = 15 units/kg

CT: >120s = 22,5 units/kg

**ML > 15% on EXTEM with normal APTEM**

Th: Tranexamic acid 20 mg/kg

(in case of also pathologic APTEM consider deficiency of factor XIII)

**EXTEM MCF < 50 mm a FIBTEM MCF < 10 mm**

Th: Fibrinogen (to get 10 mm MCF of FIBTEM)

calculated dose = required MCF - current MCF x  
6,25mg/kg

**EXTEM MCF < 50 mm a FIBTEM  
MCF ≥ 10mm)**

Th: platelets

**EXTEM MCF < 30-35 mm:**

Th: administer all mentioned products (tranexamic acid, fibrinogen, platelets, prothrombin complex)

In case of normal EXTEM a FIBTEM and bleeding patient, then INTEM should be also performed (prolonged CT may be caused by hemophilia or heparin)

# Význam ROTEM v klinickej praxi?

## ■ 1. Plánované výkony – príprava pacienta

- problematika PT-INR, APTT (nezohľadňuje funkciu Tr, ktoré často vykompenzujú nedostatok faktorov, čiže celkové zrážanie je v norme, napr. sepsa, hepatopatia..., zbytočné podávanie plazmy)

## ■ 2. Ťažké krvácanie – bežné lab. testy sú nepraktické

# 1. ROTEM versus laboratorne testy u detských pacientov

Thromboelastometry as an alternative method for coagulation assessment in pediatric patients undergoing invasive procedures: a pilot study.

**Durila M**, Jonas J, Durilova M, Rygl M, Skrivan J, Vymazal T. Eur J Pediatr Surg. 2019 Jun;29(3):298-301.

Typ invazivního zákroku			
explantace centrálního žilního portu	3x	chirurgická tracheostomie	1x
zavedení hrudního drénu	2x	ileocekální resekce	1x
zanoření ileostomie a kolostomie	2x	resekce jater	1x
apendektomie	2x	hernioplastika	2x
fundoplikace	1x	mastoidektomie	2x
klinovitá resekce plic	1x	tonzilektomie	2x
nefrektomie	1x	hemithyreidektomie	1x
cirkumcize	1x	zavedení centrálního žilního katétru	2x

# 1. ROTEM versus laboratorne testy

British Journal of Anaesthesia 108 (1): 36–41 (2012)  
Advance Access publication 14 November 2011 · doi:10.1093/bja/aer342

BJA

## Comparison of thromboelastometry (ROTEM®) with standard plasmatic coagulation testing in paediatric surgery

T. Haas<sup>1\*</sup>, N. Spielmann<sup>1</sup>, J. Mauch<sup>1</sup>, C. Madjdpour<sup>1</sup>, O. Speer<sup>2,3,4</sup>, M. Schmutz<sup>2</sup> and M. Weiss<sup>1</sup>

<sup>1</sup>Department of Anaesthesia, <sup>2</sup>Department of Haematology, and <sup>3</sup>Children's Research Center, University Children's Hospital Zurich, Steinwiesstrasse 75, Zurich 8032, Switzerland

<sup>4</sup>Zurich Center for Integrative Human Physiology, University of Zurich, Institute of Physiology, Winterthurerstrasse 190, Zurich 8057, Switzerland

\* Corresponding author. E-mail: thorsten.haas@kispi.uzh.ch

### Editor's key points

- Major surgery can result in significant blood loss and coagulopathy in children requiring rapid and accurate assessment of coagulation status.
- This observational study compared standard coagulation testing to rotational thromboelastometry in children undergoing major surgery.
- Standard coagulation testing did not correlate well with thromboelastometry testing except for fibrinogen levels with FibTEM.
- Further studies are needed to develop thromboelastometry-guided transfusion guidelines in children.

**Background.** Thromboelastometry (ROTEM®) might be useful to detect intraoperative coagulation disorders early in major paediatric surgery. This observational trial compares this technique to standard coagulation tests.

**Methods.** Intraoperative blood sampling was obtained in children undergoing elective major surgery. At each time point, standard coagulation tests [activated partial thromboplastin time (aPTT), prothrombin time (PT), and fibrinogen level] and ROTEM® analyses (InTEM, ExTEM, and FibTEM) were performed simultaneously by trained hospital laboratory staff.

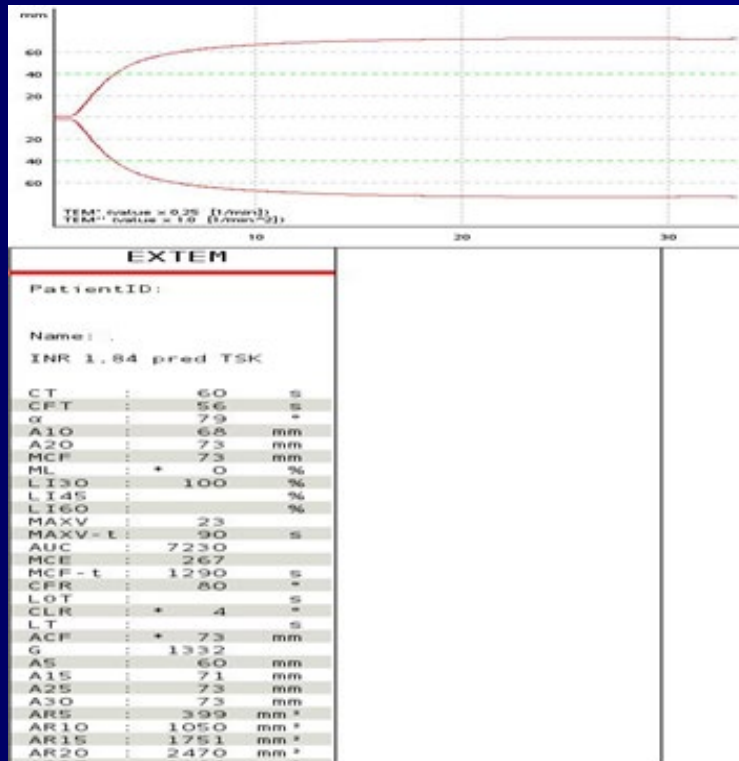
**Results.** A total of 288 blood samples from 50 subjects were analysed. While there was a poor correlation between PT and aPTT to ExTEM clotting time (CT) and InTEM CT, respectively, a good correlation was detected between PT and aPTT to clot formation time, and a very good correlation between fibrinogen level and FibTEM assay ( $r=0.882$ ,  $P<0.001$ ). Notably, 64% of PT and 94% of aPTT measurements were outside the reference range, while impaired CT was observed in 13% and 6.3%, respectively. Standard coagulation test results were available after a median of 53 min [inter-quartile range (IQR): 45–63 min], whereas 10 min values of ROTEM® results were available online after 23 min (IQR: 21–24 min).

**Conclusions.** PT and aPTT cannot be interchangeably used with ROTEM® CT. Based on the results of ROTEM®, recommended thresholds for PT and aPTT might overestimate the need for coagulation therapy. A good correlation was found between the fibrinogen level and the FibTEM assay. In addition, ROTEM® offered faster turnaround times.

# 1. ROTEM versus laboratórne testy u dospelých pacientov

## Evaluation of Thromboelastometry in Sepsis in Correlation With Bleeding During Invasive Procedures.

Lukas P, Durila M, Jonas J, Vymazal T. Clin Appl Thromb Hemost. 2018 Sep;24(6):993-997.



- pacienti s aPTT- R 1.3 - 2.05, PT - INR 1.3 - 2.10
- normálny ROTEM
- žiadna preventívna plazma nepodána a žiadne krvácavé komplikácie

## 2. ROTEM a transplantácia jater/pečene

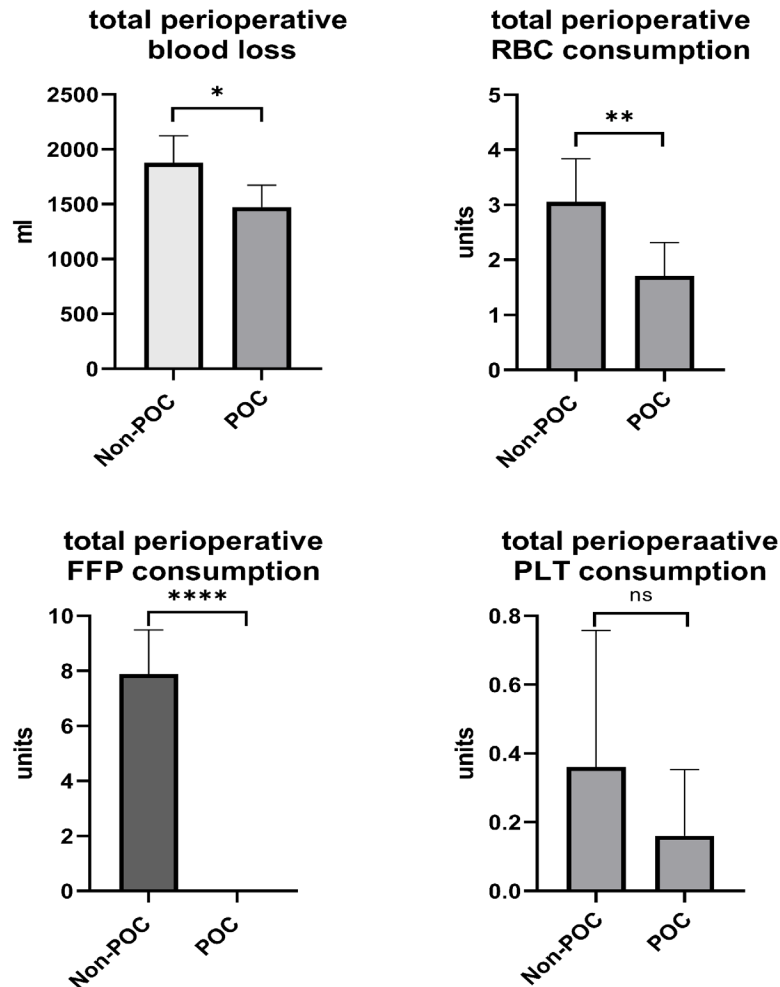
A look into hemostatic characteristics during pediatric liver transplantation using the thromboelastometry (ROTEM®) test.  
Cho JK, Moon YJ, Song IK et al. Liver Transpl. 2022 Mar 30.

### **Conclusions:**

In children undergoing LT, coagulation profiles depend on the etiology for LT. During LT, ROTEM® parameters could help detect thrombocytopenia and hypofibrinogenemia and guide transfusion therapy as a point of care monitoring method.



## 2. ROTEM a transplantácia pľúc



Rotational thromboelastometry reduces blood loss and blood product usage after lung transplantation.

Durila M, Vajter J, Garaj M, Pollert L, Berousek J, Vachtenheim J Jr, Vymazal T, Lischke R.J Heart Lung Transplant. 2021 Jul;40(7):631-641.

# ROTEM

ROTEM je schválený pre používanie v klinickej praxi americkou FDA

**The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition. 1C**

Rossaint R, Bouillon B, Cerny V, et al. Crit Care. 2019 Mar 27;23 (1):98.

**Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology: First update 2016 2C**

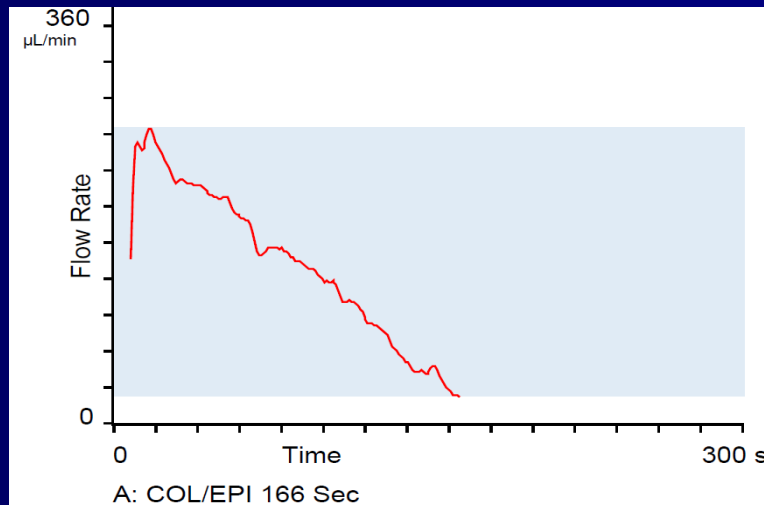
Sibylle A Kozek-Langenecker, Amer B Ahmed, Arash Afshari, et al. Eur J Anaesthesiol. 2017 jun;34 (6):332-395.

**Česko-Slovensky mezioborovy doporučený postup diagnostika a léčba život ohrožujícího krvácení (ŽOK) u dětských pacientů v intenzivní a perioperační péči.** Zaoral T, Blatný J, Vobruba V, et al. Čes-slov Pediat 2018; 73 (1): 57–61.

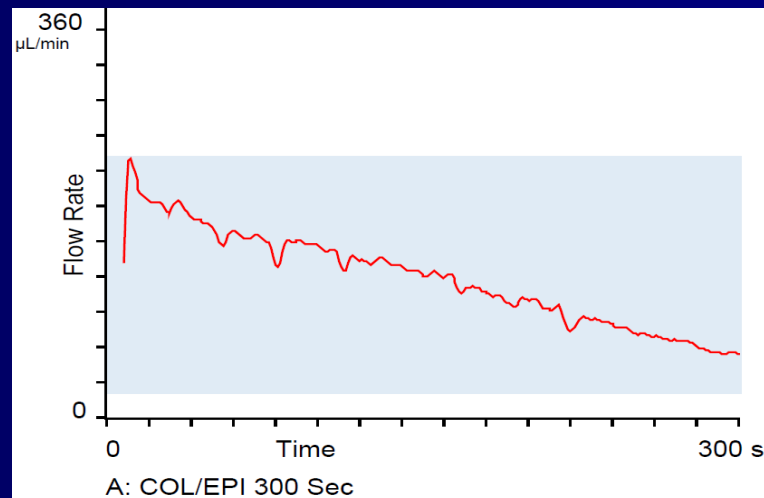
# Primárna hemostáza

## PFA 200

### (platelet function analyser)



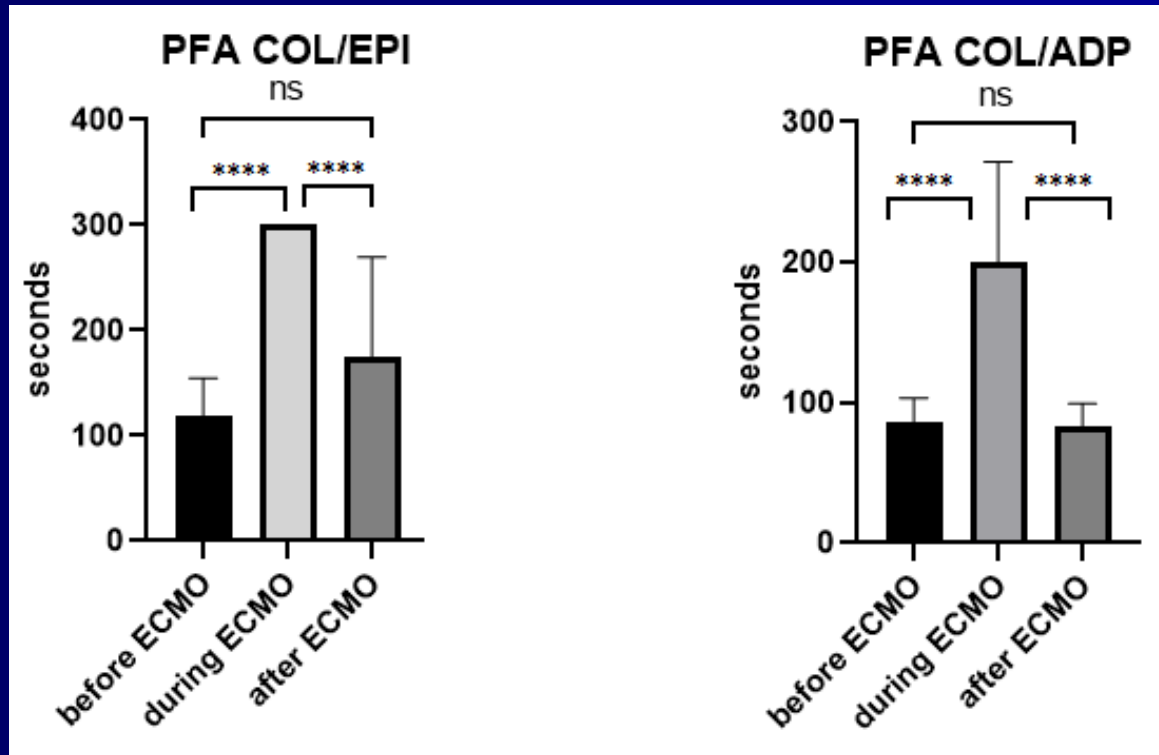
norma



„no closure“

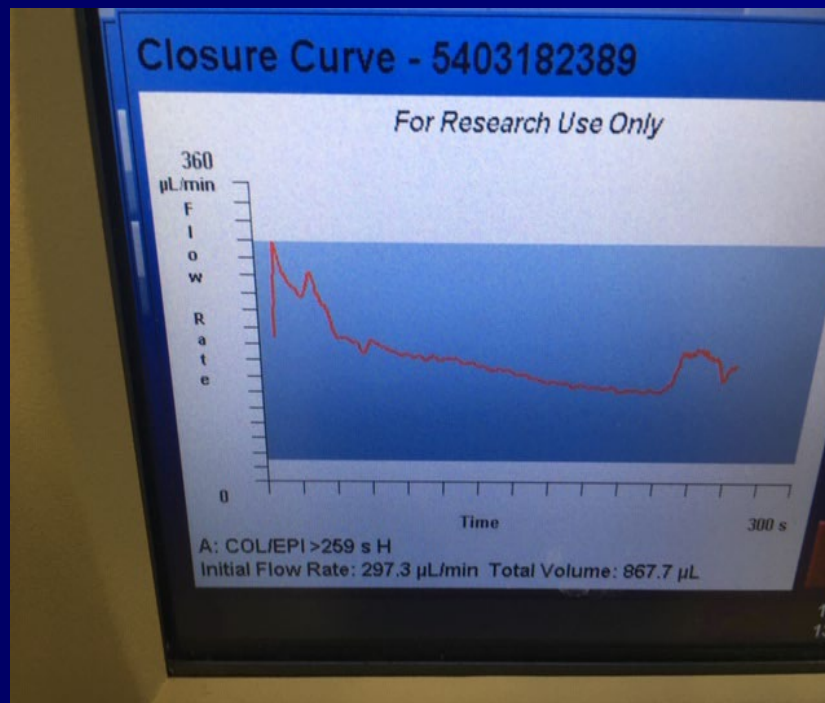


# Primárna hemostáza a ECMO

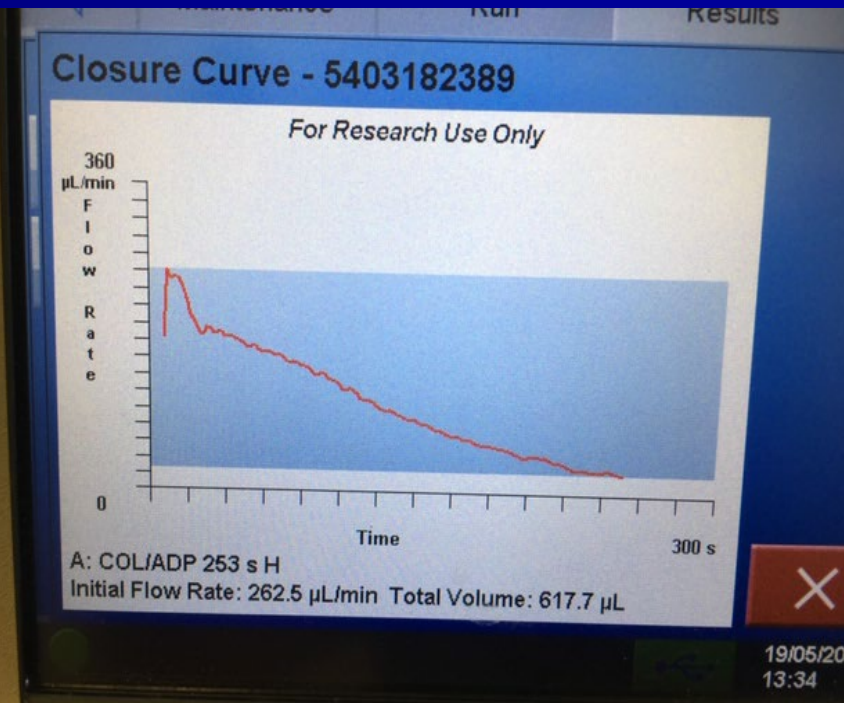


- Acquired primary hemostasis pathology detected by platelet function analyzer 200 seen during ECMO is sufficient to prevent circuit thrombosis. A pilot study. Durila M, Vajter J, Garaj M et al. J Heart Lung Transplant. 2020 Sep;39(9):980-982

# PFA a ECMO



flow 5 litre a krváca



flow 2,5 litra a nekrváca

# Hepatopatia

**Primárná hemostáza** - trombocypenia a znížená funkcia trombocytov (ale môže byť aj zvýšená)!

- je zvýšená funkcia vWF (deficit ADAMS-13)

**„väčšinou balancovaná primárna hemostáza“**

**Sekundárna hemostáza** - deficit FII, FV, FVII, FIX, FX, FXI, FXIII

- deficit AT, proteínu C a S, heparin co-factor II a  $\alpha$ 2-mikroglobulin

- zvýšená hladina FVIII

**„väčšinou balancovaná sekundárna hemostáza“**

**Fibrinolýza** - znížená produkcia jak profibrinolytických, tak i antifibrinolytických faktorov **„väčšinou balancovaná fibrinolýza“**

# Hepatopatia

## Klinické poznámky:

- PT/INR nepredikujú zvýšene riziko spontánneho či periprocedurálneho krvácania, profylaktická korekcia PT/INR pred intervenciou nie je doporučovaná
- profylaktické podávanie krvnej plazmy se ukázalo ako neúčinné, zaťažujúce pacienta komplikáciami a nie je doporučované
- Profylaxia trombózy je u pacientov s hepatopatiou doporučovaná
- Fibringen nad 1g/liter
- Exacyl nie rutinne-neukázal benefit a riziko trombozy

# Neonatologia

## Primárna hemostáza

– trombocyty sú hypofunkčné  
dysfunkcia trombocytov vymizne do 10.-14. dňa po porodu, a to jak u zrelých, tak i nezrelých novorodencov, tj. bez ohľadu na porodný gestačný vek

- u zrelých novorodencov je vyššia hladina vWF (nižšia hladina ADAMTS-13)

**„väčšinou balancovaná primárna hemostáza“**

- u nezrelých novorodencov (<27. týden) sa zistila korelácia medzi PFA-Col/ADP a závažnými krvácavými komplikáciami



# Neonatologia

## Sekundárna hemostáza

- u zrelého novorodenca je hladina koagulačných faktorov vit. K dependentných, ale i iných faktorov FV, FXI a FXII, asi 50 % hodnoty dospelých pacientov. Dospelým hodnotám sa približuje v 6. mesiaci života
- antikoagulačné faktory, ako je antitrombin, protein C, protein S, (protein C a S sú vit. K dependentné) a heparinový kofaktor II, sú tiež znížené na 50 % hodnoty dospelého

**„väčšinou balancovaná sekundárna hemostáza“**

# Záver

- koagulačné testy plnej krvi - ROTEM a PFA lepšie korelujú s klinickým stavom pacienta
- podávanie krevnej plazmy či trombocytov u nekrvácejúcich pacientov alebo profylaktická korekcia plazmatických testov PT/aPTT a počtu trombocytov nepredstavuje pre pacienta benefit, ale skôr rizika
- hodnotenie hemostázy by malo prebiehať komplexne a individuálne s využitím testov plnej krvi-ROTEM a PFA 200

**Ďakujem a prajem**

**pekný deň☺**