Coagulation tests

Erik Lerkevang Grove, Associate Prof, MD, PhD, FESC
Department of Cardiology, Aarhus University Hospital, Denmark

WE ARE THE ESC

Thrombosis ESC Working Group

EUROPEAN SOCIETY OF CARDIOLOGY®

Disclosures

- **None related to this talk.**
- General disclosures:
  - Lecture fees from AstraZeneca, Baxter, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, MSD, Sysmex, and Pfizer.
  - Advisory board meetings for AstraZeneca, Bayer, Boehringer Ingelheim, and Bristol-Myers Squibb.

Outline of talk: Coagulation tests

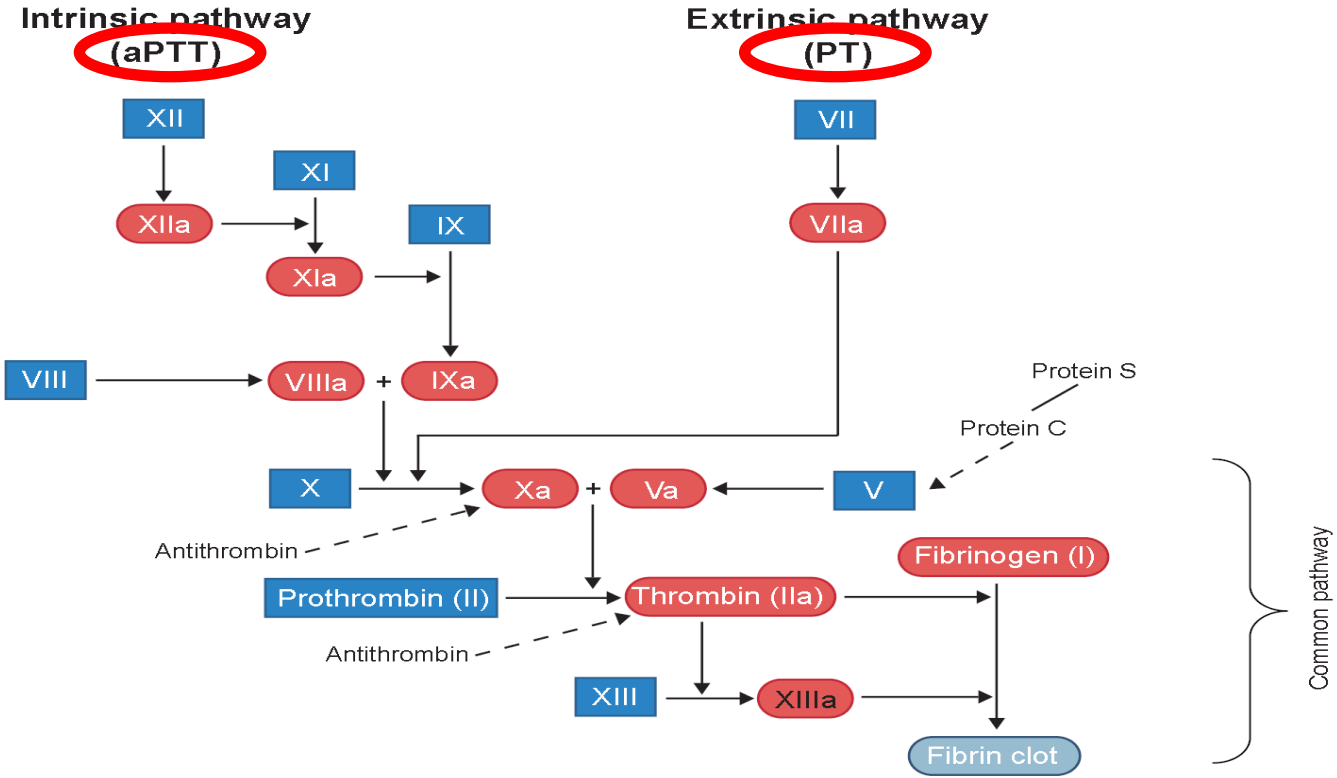
- **Coagulation system**
- **Coagulation tests: why?, how?, when?**
  - PT/INR
  - aPTT
  - ACT
  - Anti-Xa activity
  - Point-of-care testing: TEG & ROTEM
  - Evaluation of coagulation during treatment with NOACs
- **Conclusions**

Evaluating the coagulation system – why?

- Unexplained bleeding
- Pre- and perioperative testing
- Monitoring of anticoagulant treatment
- Research

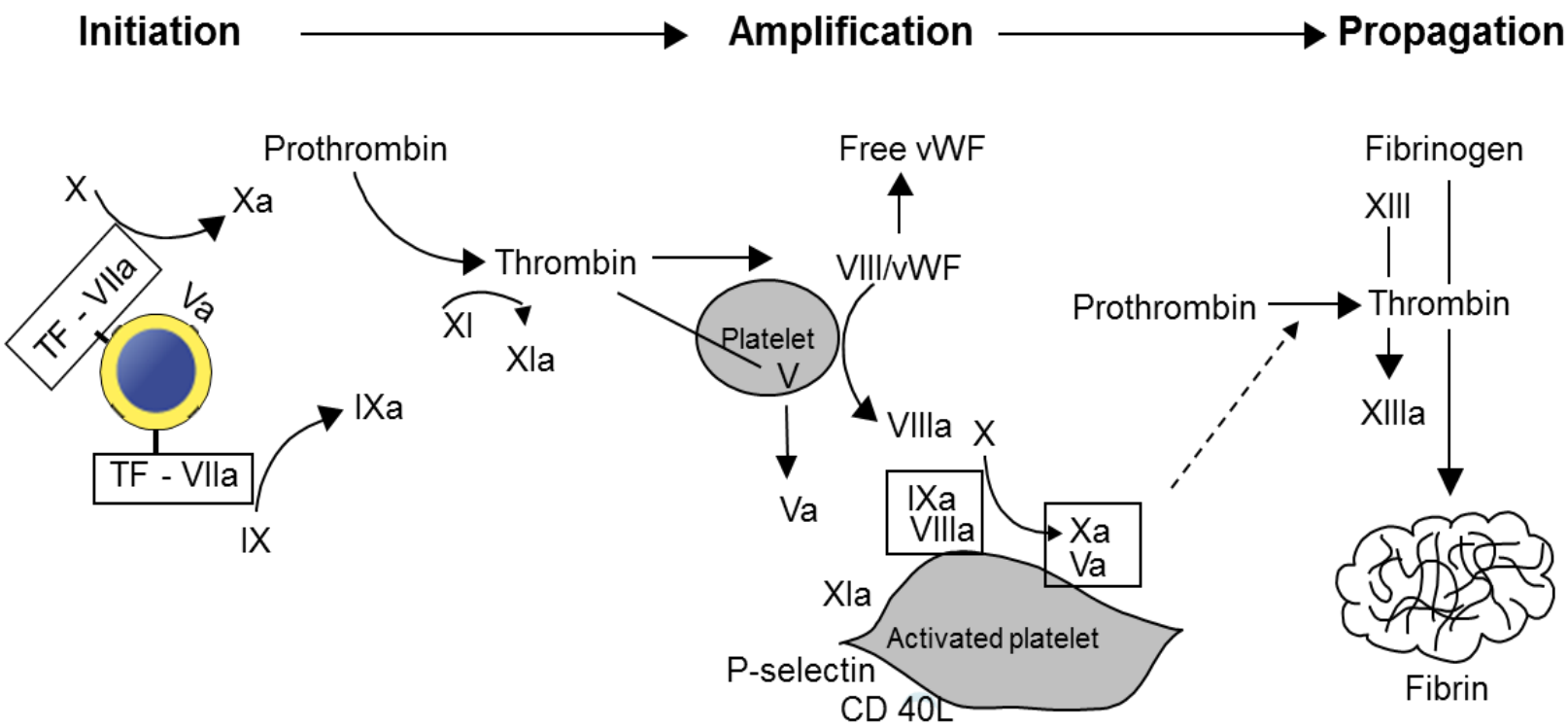
Erik Lerkevang Grove

Coagulation system: *traditional* concept



Hvas AM, Grove EL, Kristensen SD
ESC Textbook of Intensive & Acute Cardiovascular Care, Oxford University Press, 2015

Coagulation system: *current* concept



Modified from De Caterina et al, EHJ 2007.

Prothrombin time (PT) and INR

- **PT measures the time [reference value: 11-13 seconds] it takes plasma to clot when exposed to tissue factor and reflects the 'extrinsic' and 'common' pathways of coagulation.**

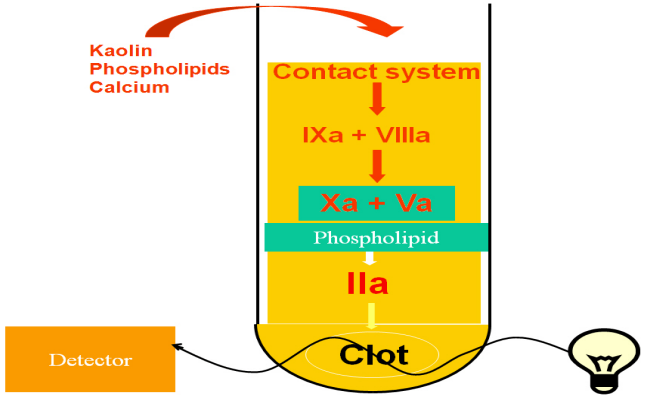
- **International normalized ratio (INR) [ref: 0.8-1.2] = (PT-patient/PT-normal)^ISI**

- **<u>Clinical use</u>: bleeding, liver synthetic function, DIC, warfarin treatment.**

Erik Lerkevang Grove

Activated partial thromboplastin time (aPTT)

- The aPTT measures the time [ref: 25-35 seconds] it takes plasma to clot when exposed to substances that activate the contact factors - and assesses the 'intrinsic' and 'common' pathways of coagulation.



- No standardization.

- <u>Clinical use</u>: Bleeding, DIC, monitoring of unfractionated heparin.

Erik Lerkevang Grove

Activated Clotting Time (ACT)

- **The ACT measures the time [70-180 seconds, dependent on vendor] it takes *whole blood* (rather than plasma) to clot when exposed to an activator of the intrinsic pathway - and assesses both the 'intrinsic' and 'common' pathways of coagulation.**

- **<u>Clinical use</u>: adjusting heparin dosing before/during/shortly after procedures such as CABG, ECMO, PCI etc.**

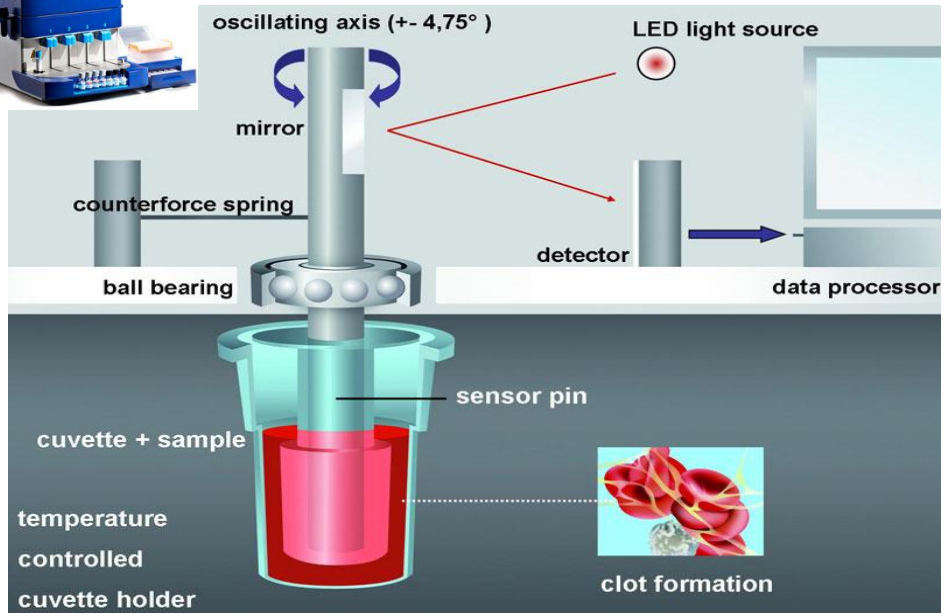
Antifactor Xa activity

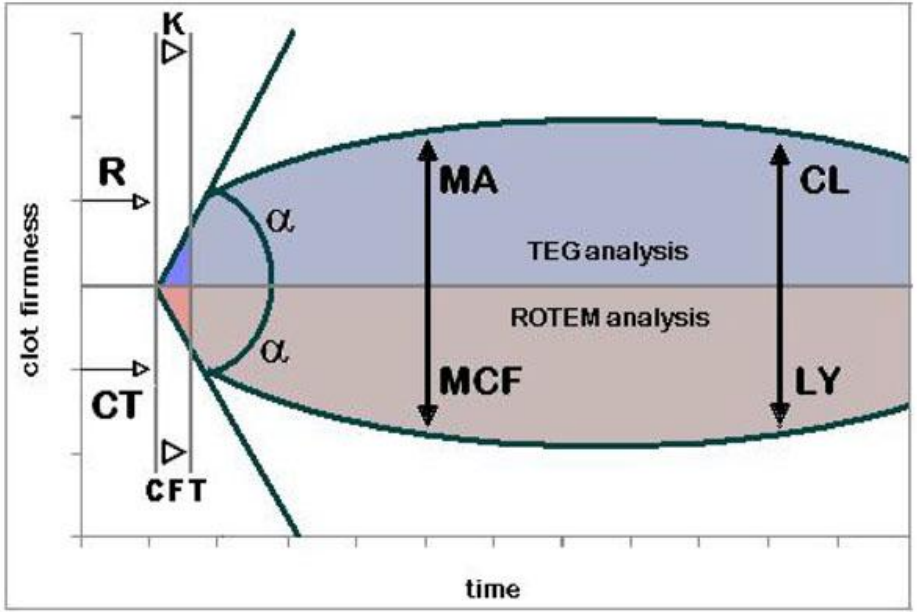
- **Unlike PT, INR, aPTT and ACT, the 'anti-Xa' is a *functional* assay measuring the degree of anticoagulation in units of enzymatic activity.**
- **<u>Clinical use</u>: evaluation of anticoagulant effect in selected patients at risk of accumulation during treatment with LMWH, fondaparinux etc.**
- **Most frequently used in obesity, pregnancy, reduced renal function.**

Point-of-care testing: TEG & ROTEM

- **<u>Point-of-care testing</u>: faster results to improve patient care.**
- **Thus meeting some of the limitations with frequently used 'standard packages' (e.g. platelet count, fibrinogen, aPTT & INR) – that only provide limited information about platelet function and do not predict bleeding risk.**
- **Thromboelastography (TEG) & rotational thromboelastometry (ROTEM) are global tests of haemostasis performed on *whole blood* and reflect platelet function and coagulation, showing kinetics of clot formation, strength, and dissolution – to manage bleeding and assess the response to interventions, e.g. during surgery.**

Point-of-care testing: TEG & ROTEM





Non-vitamin K antagonist oral anticoagulants

- **Routine *monitoring* is not recommended.**
- **…but *measuring* the effect may be considered, in case of e.g.**
  - Bleeding or thrombosis during treatment
  - Suspected overdose
  - Urgent surgery
  - Prior to thrombolysis

- **Standard tests (PT/INR, aPTT, TT) are not recommended but may be used to rule out the presence of NOACs.**
- **Dabigatran: diluted Thrombin Time (e.g. Hemoclot®), Ecarin clotting time.**
- **Factor Xa-inhibitors: anti-Xa analyses.**

Conclusions

- There is no single global test available to adequately evaluate overall haemostasis: The right test for the right purpose!

- Ensure correct sample collection and handling

- Clotting times: PT/INR, aPTT, ACT.
- Functional assays: e.g. 'anti-Xa'
- Dynamic whole blood assays: TEG & ROTOM
- NOACs: aim for specific tests, rather than standard clotting times

- All laboratory tests should be interpreted in a clinical context!

Causes of prolonged PT and/or aPTT

Test result		Causes of test result pattern
PT	aPTT	
Prolonged	Normal	**Inherited**
		Factor VII deficiency
		Acquired
		Mild vitamin K deficiency
		Liver disease
		Warfarin administration*
		Acquired inhibitor of factor VII
		Lupus anticoagulant (more commonly causes isolated prolonged aPTT; may be associated with thrombosis rather than bleeding)
Normal	Prolonged	**Inherited**
		Deficiency of factors VIII, IX, or XI
		Deficiency of factor XII, prekallikrein, or HMW kininogen (not associated with a bleeding diathesis)
		von Willebrand disease (variable)
		Acquired
		Heparin administration*
		Inhibitor of factors VIII, IX, XI, or XII
		Acquired von Willebrand disease
		Lupus anticoagulant (may be associated with thrombosis rather than bleeding)
Prolonged	Prolonged	**Inherited**
		Deficiency of prothrombin, fibrinogen, or factors V or X
		Combined factor deficiencies
		Acquired
		Liver disease
		Disseminated intravascular coagulation
		Supratherapeutic doses of anticoagulants
		Severe vitamin K deficiency
		Combined heparin and warfarin administration
		Direct thrombin inhibitor administration (eg, argatroban, dabigatran)*
		Direct factor Xa inhibitor administration (eg, rivaroxaban, apixaban, edoxaban)
		Fondaparinux administration (slight prolongation)
		Inhibitor of prothrombin, fibrinogen, or factors V or X
		Primary amyloidosis-associated factor X deficiency
		Anticoagulant rodenticide poisoning