Haemostasis cont….

Prof. Niranga Devanarayana

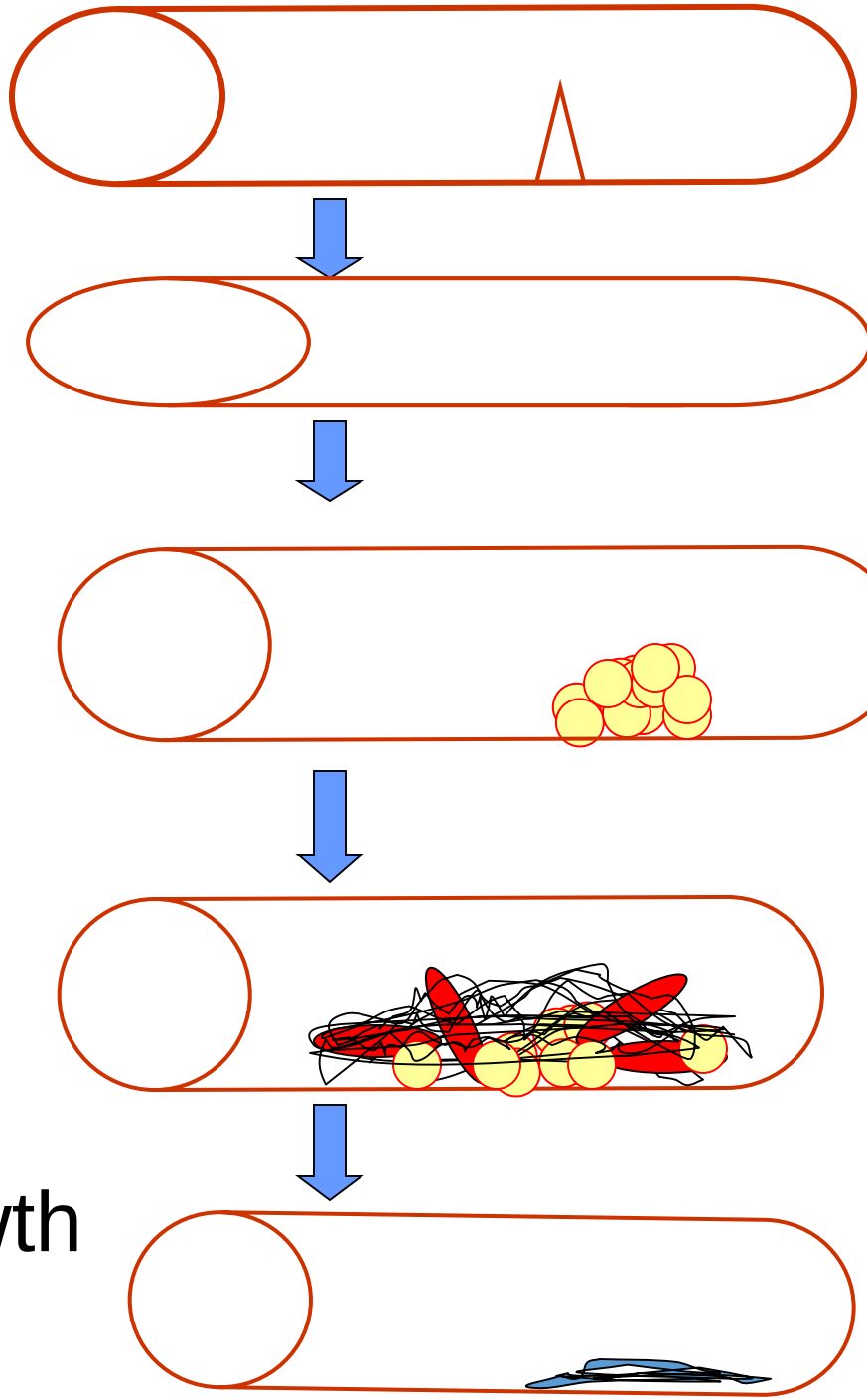
Injury to vessel

vasoconstriction

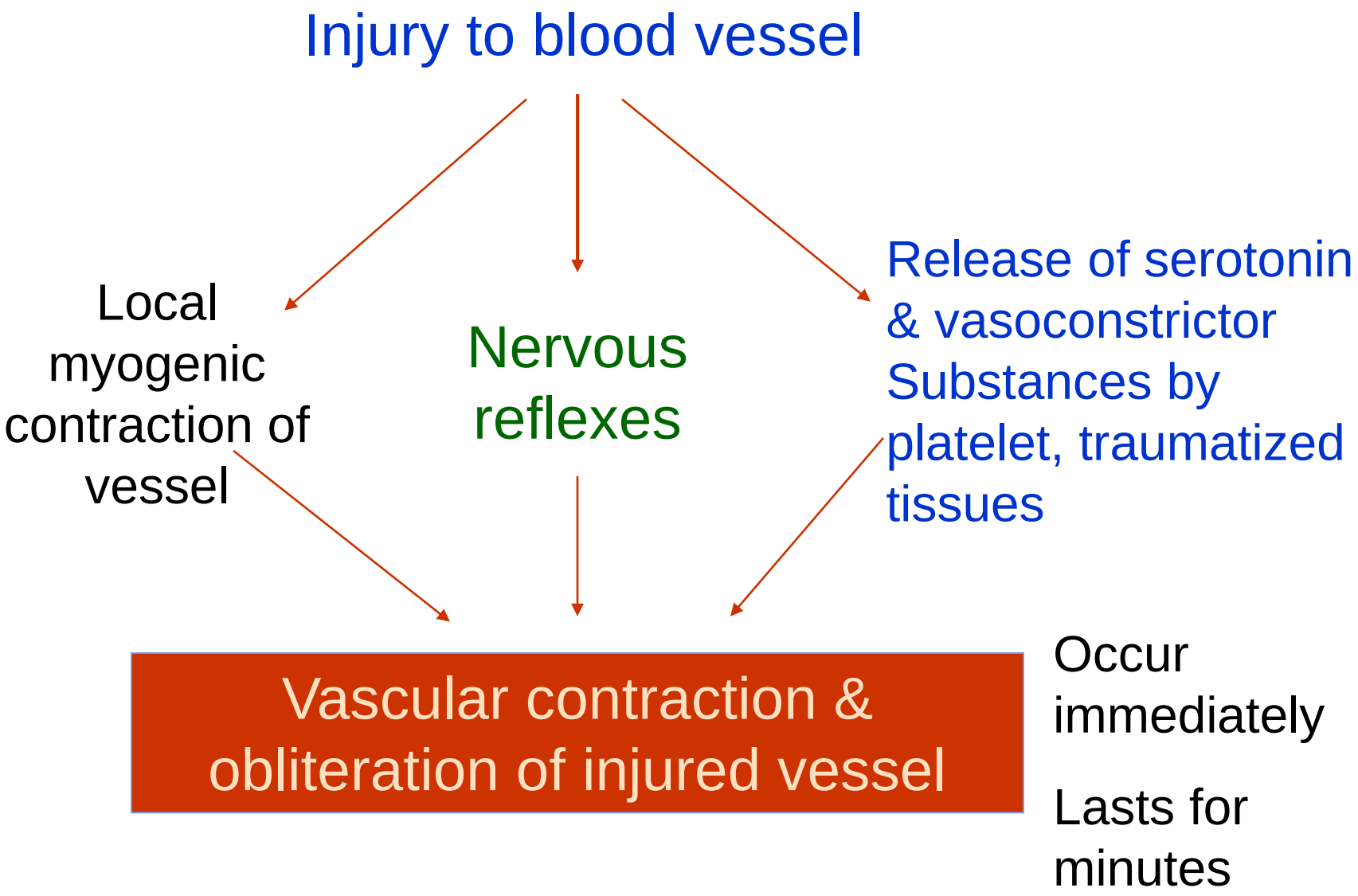
Platelet plug

Coagulation

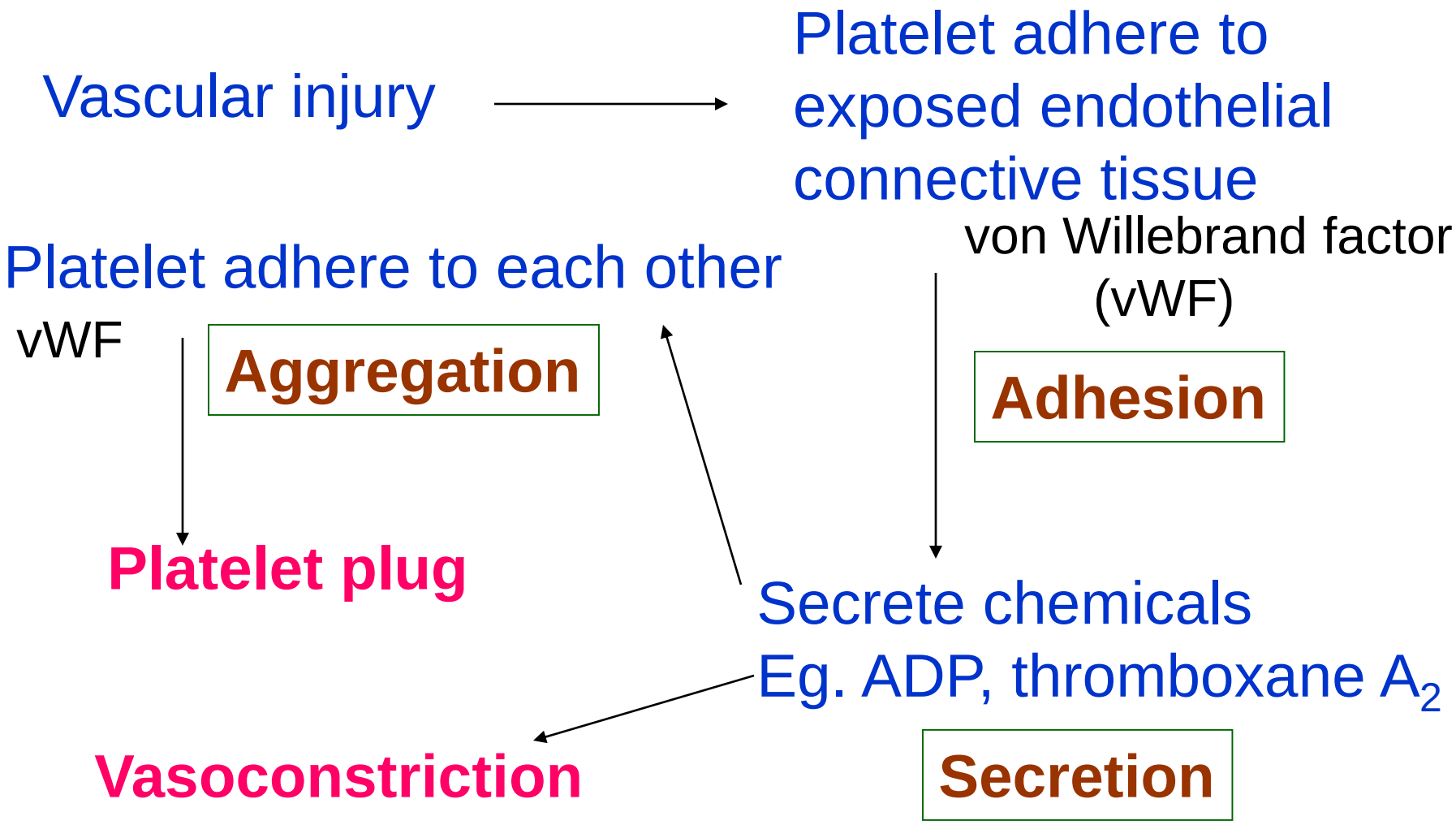
Removal of clot & growth of vascular tissue



1. Vascular spasm

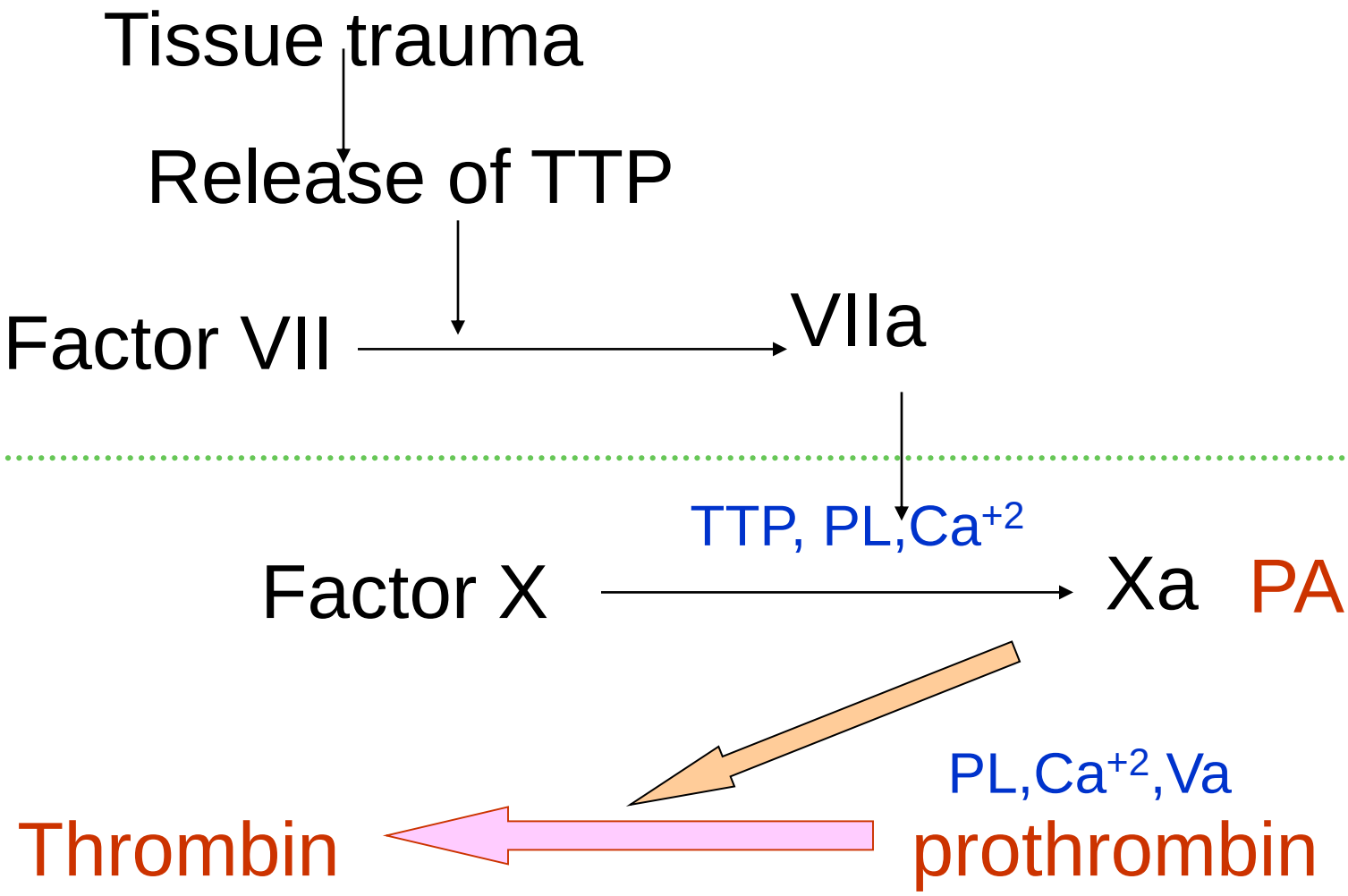


2. Formation of platelet plug



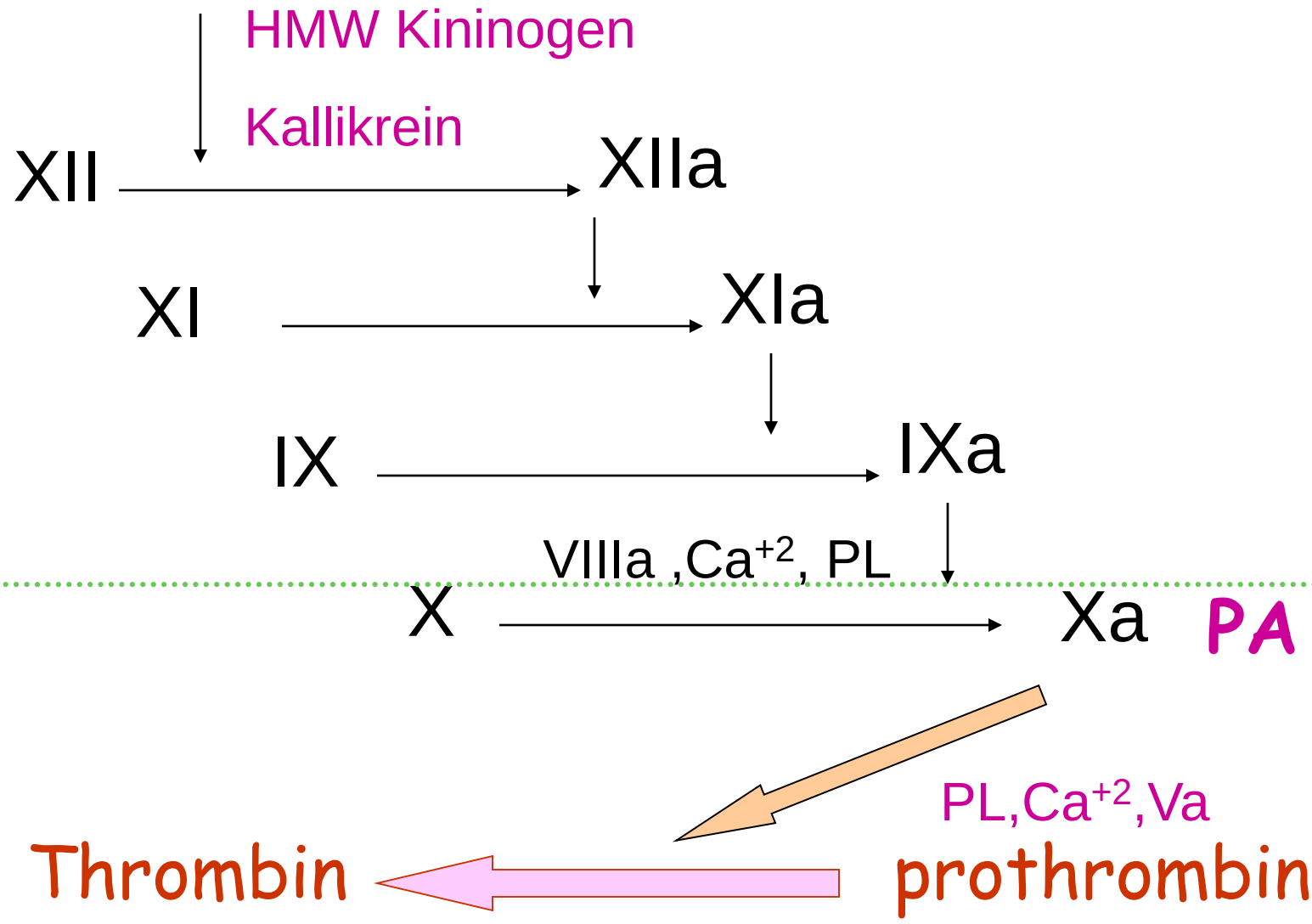
3. Coagulation

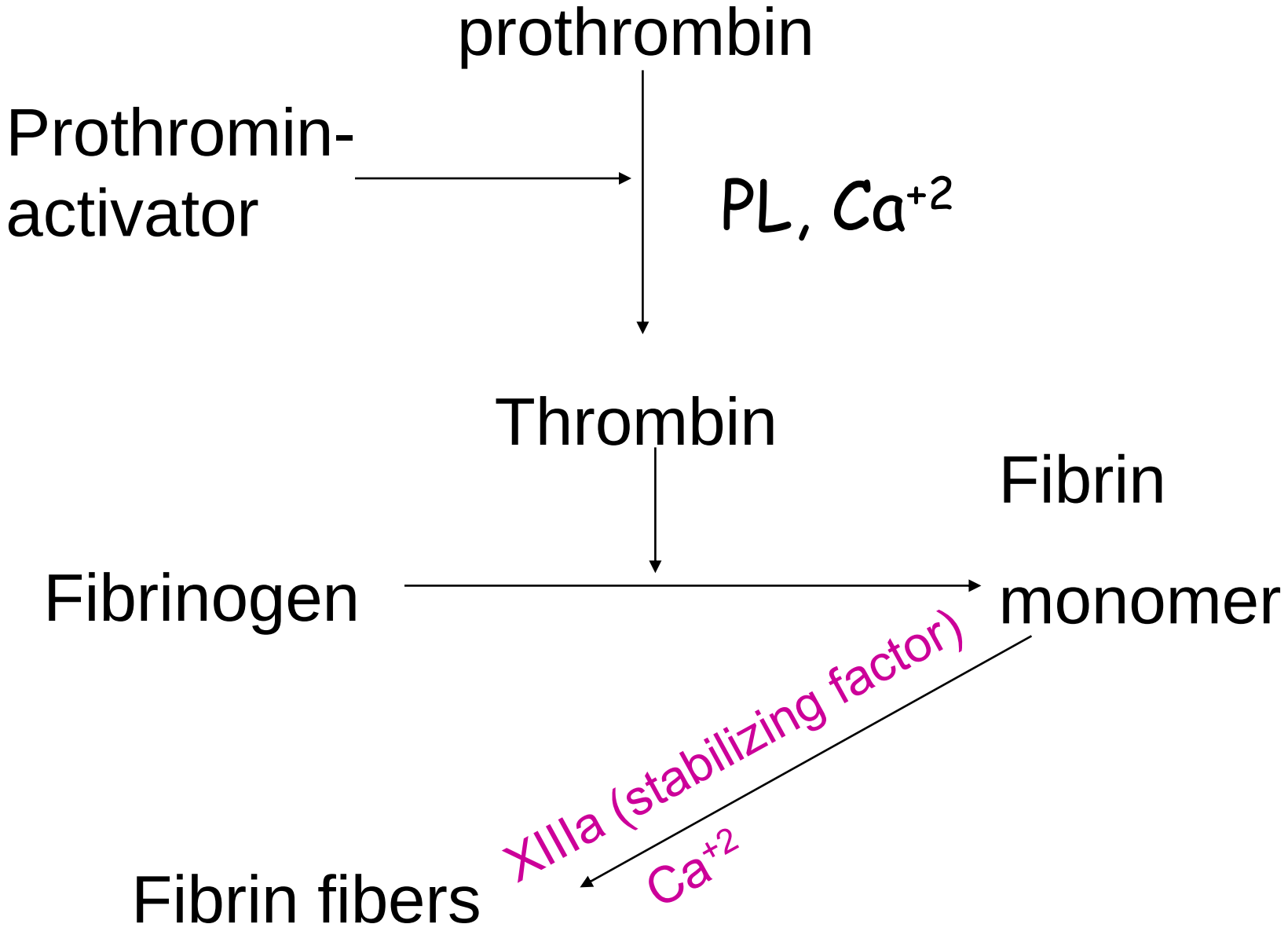
Extrinsic pathway



Intrinsic pathway

traumatized blood cells/exposure to collagen




prothrombin
Prothromin-
activator
PL, Ca+2
Thrombin
Fibrin
Fibrinogen
monomer
XIIIa (stabilizing factor)
Ca+2
Fibrin fibers

ANTI CLOTTING MECHANISMS

Prof. Niranga Devanarayana

ANTI CLOTTING MECHANISM

- The tendency of blood to clot is balanced in vivo by limiting reactions that tend to prevent clotting inside the blood vessels and to breakdown any clots that do form.

- There are several mechanisms operating inside the body as intravascular anticoagulants.

Objectives

1. Describe mechanisms that operate in the body to prevent intravascular thrombosis
   - Properties of the vessels (endothelial factors)
   - Anticlotting mechanisms
   - Fibrinolytic system

2. Giving examples, explain the mechanisms of action of
   - Antiplatelet drugs
   - Anticoagulants
   - Fibrionolytic agents

ANTI CLOTTING MECHANISM CONT.

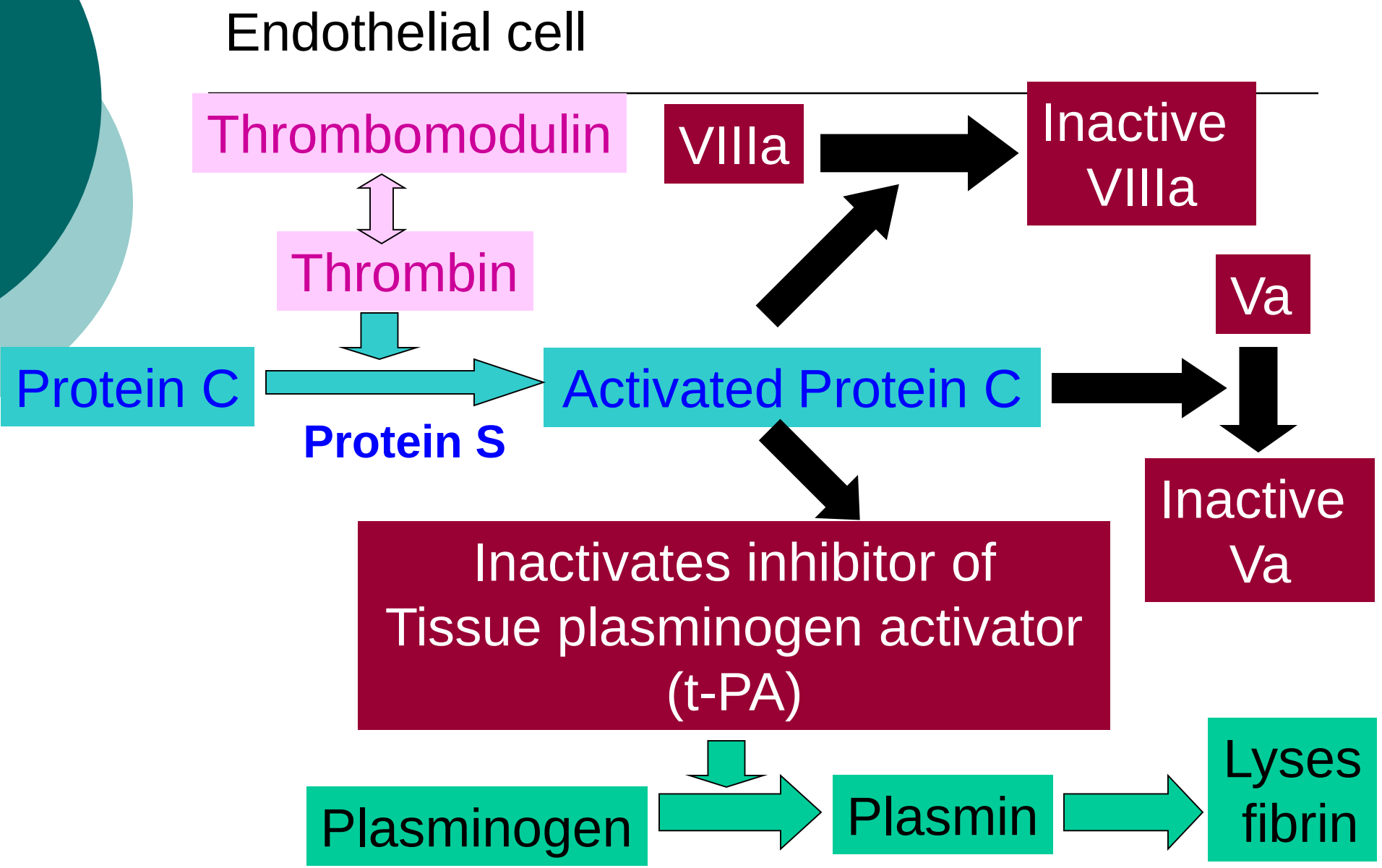
1. Endothelial surface factors

Probably the most important factors for prevention of clotting.

This involves :

- Prostacyclin (↓ platelet aggregation and vasoconstriction).
- Smoothness of the endothelium.
- Surface layer of glycocalyx which repels platelets and clotting factors.
- Thrombomodulin leading to activation of fibrinolytic system.
  - All endothelial cells except cerebral microcirculation produce thrombomodulin, and express it on their surface.

2. FIBRINOLYTIC SYSTEM



3. Antithrombin III

- Antithrombin III is a circulating protease inhibitor that binds to serine proteases in the coagulation system.
- Following binding with thrombin it inhibits active clotting factors II, IX, X, XI & XII.
- Heparin acts as a cofactor and facilitates this binding of antithrombin III with active clotting factors and inactivates them.

ANTICOAGULANTS

- Anticoagulants prevent clotting.

1. **Heparin** is naturally occurring anticoagulant that facilitates the action of antithrombin III. In addition, heparin impairs platelet function

2. Coumarin derivatives like dicumarol and **warfarin** inhibit the action of vitamin K.

   Vitamin K is a cofactor for the conversion of inactive factors II,**VII**,IX,X,Protein C and Protein S to biologically active forms by γ carboxylation of glutamic acid residues.

3. Ca^{++} chelating agents like oxalates, citrates and EDTA can be used as in vitro anticoagulants.

Antiplatelet drugs

- Eg. Aspirin

Cyclo-oxygenase

Arachidonic acid → Prostaglandin

Prostacyclin in vascular endothelium → ↓ platelet aggregation
Vasodilatation

Thromboxane A_2 in platelet → ↑ platelet aggregation
vasoconstriction

Fibrinolytic agents

1. Human tissue plasminogen activator is also produced by recombinant DNA techniques. It is clinically used to lyse clots in coronary arteries in acute myocardial infarction.

2. Streptokinase is a bacterial enzyme which is has similar action to tPA. Used in acute myocardial infarction for thrombolysis.

- https://www.youtube.com/watch?v=R8JMfbYW2p4
- https://www.youtube.com/watch?v=_yQD0U3ZtCs
- https://www.youtube.com/watch?v=cy3a__OOa2M

Question 1

- List the events that takes place after injury to a blood vessel to arrest the bleeding.

[10 marks]

Question 2

- Briefly describe the role of following in relation to haemostasis
  - Platelets [25 marks]
  - von Willebrand factor [15 marks]
  - Liver [15 marks]
  - Vitamin K [15 marks]

Question 3

- Describe the extrinsic, intrinsic and common pathways of clotting

[30 marks]

Question 4

- Describe the mechanisms that operate in humans to prevent abnormal intreavascular thrombosis

[20 marks]

Question 5

- Give one example each for the following and outline their mechanism of action
  - Anticoagulant [10 marks]
  - Antiplatelet drugs [10 marks]
  - Fibrinolytic agents [10 marks]