COAGULANTS AND ANTICOAGULANTS

Clotting factors:
I Fibrinogen
II Prothrombin
III Thromboplastin
IV Ionic calcium
V Hereditary labile factor, Activator (AC) globulin, Proaccelerin.
VI Accelerin, supposed to be active form of Factor V
VII Proconvertin; Serum prothrombin conversion accelerator (SPCA)
VIII Antihemophilic factor (AHF)
IX Plasma thromboplastin component (PTC; Christmas factor)
X Stuart-Prower factor
XI Plasma thromboplastin antecedent (PTA)
XII Hageman factor
XIII Fibrin stabilising factor, Fibrinase
XIV Prekallekrein
XV Kallekrein
XVI Platelet factor

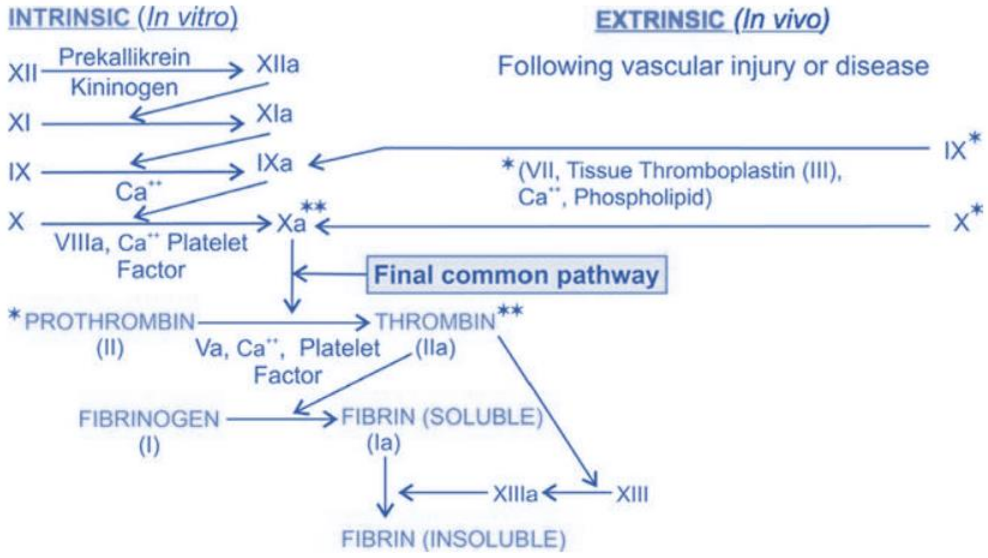


Fig: Blood clotting (* Inhibited by warfarin ** Inhibited by heparin)

The coagulation is initiated in vitro by the intrinsic pathway whereas it is initiated in vivo by the extrinsic pathway (Fig. 33.1). These pathways merge with the generation of factor Xa.

Blood, in the body is generally kept fluid state by:
- The rapid flow of blood.
- Antithrombin III (inactivates all the clotting factors in the blood /thrombin formed in the
- Removal by fibrinolysis
- Deficiency of platelets or clotting factors.

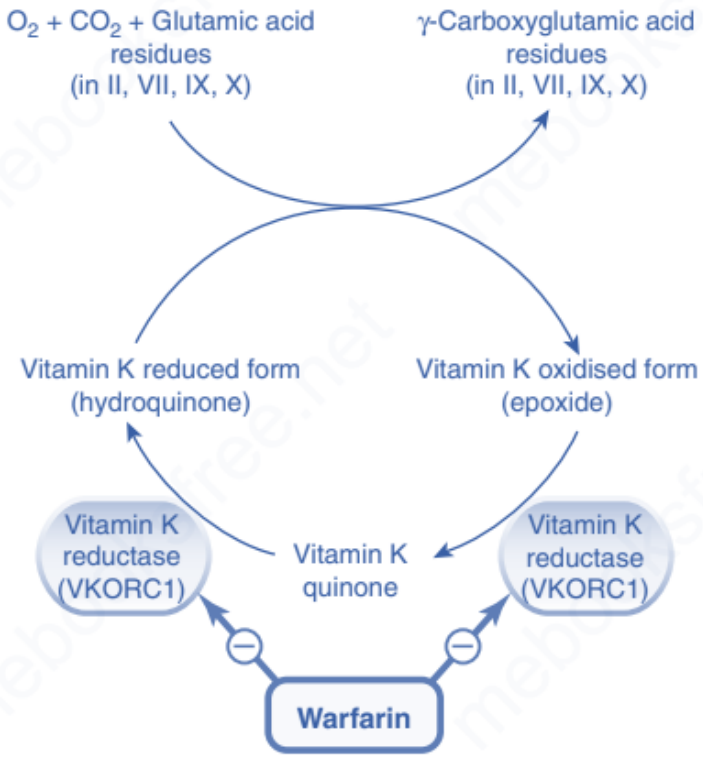
Hypercoagulability is due to:
- Stasis within the venous system
- Injury to or disease of the vessel wall; and
- A hypercoagulable state of blood

Thrombogenesis is a pathological process, leading to an intravascular thrombus formation. It is normally prevented by several regulatory mechanisms such as normal vascular endothelium, PGI_2 , antithrombin, protein C and heparan sulfate.

COAGULANTS

Main coagulant in the body is vitamin K. It is of three types; K1 (phytonadione, occurring naturally in plants), K2 (menaquinone or bacterial menaquinones formed in the gut) and K3 (menadione). Vitamin K is involved in the activation of various clotting factors (like II, VII, IX and X) which are glycoproteins with γ-carboxyglutamic acid (Gla) residues.

Mechanism of vitamin K and of warfarin



(Vitamin K epoxide reductase component 1 (VKORC1), the site of action of warfarin)

Binding does not occur in the absence of γ-carboxylation. Similar considerations apply to the proteolytic activation of factor X by IXa and by VIIa. There are several other vitamin K-dependent Gla proteins, including proteins C and S

Pharmacokinetic

Natural vitamin K1 (phytomenadione) may be given orally or by injection. If given by mouth, it requires bile salts for absorption, and this occurs by a saturable energy-requiring process in the proximal small intestine. A synthetic preparation, menadiol sodium phosphate, is also available. It is water-soluble and does not require bile salts for its absorption. This synthetic compound takes longer to act than phytomenadione. There is very little storage of vitamin K in the body. It is metabolised to more polar substances that are excreted in the urine and the bile.

Clinical uses of vitamin K

- Treatment and/or prevention of bleeding: – from excessive oral anticoagulation (e.g. by warfarin) – in babies: to prevent haemorrhagic disease of the newborn
- For vitamin K deficiencies in adults: – dietary deficiency, prolonged antimicrobial therapy, sprue, coeliac disease, steatorrhoea – lack of bile (e.g. with obstructive jaundice)

ANTICOAGULANTS