

Blood coagulation

Blood and Body Fluids

Factor I	Fibrinogen
Factor II	Prothrombin
Factor III	Thromboplastin
Factor IV	Calcium
Factor V	Labile factor (Proaccelerin or Accelerator globulin)
Factor VI	Presence has not been proved
Factor VII	Stable factor
Factor VIII	Antihemophilic factor (Antihemophilic globulin)
Factor IX	Christmas factor
Factor X	Stuart-Prower factor
Factor XI	Plasma thromboplastin antecedent
Factor XII	Hegman factor (Contact factor) and
Factor XIII	Fibrin stabilizing factor (Fibrinase)

Each of these factors was named after the scientists who discovered them or as per the activity. Only the Christmas factor was named after the patient in whom it was discovered.

SEQUENCE OF CLOTTING MECHANISM

In general, clotting of blood occurs in three stages.

1. Formation of prothrombin activator
2. Conversion of prothrombin into thrombin and
3. Conversion of fibrinogen into fibrin

During the process of blood clotting, the clotting factors, which are in inactive forms, are converted into active forms. And their enzymatic actions produce the successive reactions one after another in a cascading manner.

Thus, the various reactions involved in blood clotting are explained by enzyme cascade theory.

STAGE 1: FORMATION OF PROTHROMBIN ACTIVATOR

Prothrombin activator is formed in two ways.

- a. **Extrinsic pathway:** In this, the formation of prothrombin activator is initiated by the tissue thromboplastin (Fig. 20-1).
- b. **Intrinsic pathway:** In this, the formation of prothrombin activator is initiated by platelets, which are within the blood itself.

Extrinsic Pathway for the Formation of Prothrombin Activator

It occurs in the following sequence:

- i. Tissue thromboplastin (Factor III) initiates this pathway. After injury, the damaged tissues release tissue thromboplastin. The thromboplastin contains proteins, phospholipid and glycoprotein, which act as proteolytic enzymes.

- ii. The glycoprotein and phospholipid components of thromboplastin convert factor X into activated factor X, in the presence of factor VIII.
- iii. The activated factor X reacts with factor V and phospholipid component of tissue thromboplastin to form prothrombin activator. This reaction requires the presence of calcium ions.
- iv. Factor V is activated by thrombin, which is formed from prothrombin. This factor V now accelerates formation of prothrombin activator and the other processes of blood clot. This effect of thrombin is called positive feedback effect of thrombin.

Intrinsic Pathway for the Formation of Prothrombin Activator

Following is the sequence of events in intrinsic pathway:

- i. During the injury, the blood vessel is ruptured. The endothelium is damaged and collagen beneath the endothelium is exposed.
- ii. When factor XII (Hegman factor) comes in contact with collagen, it is converted into activated factor XII.
- iii. The activated factor XII converts factor XI into activated factor XI in the presence of Kinogen and Prekallikrein.
- iv. The activated factor XI activates factor IX in the presence of factor IV (calcium).
- v. Activated factor IX activates factor X in the presence of factor VIII and calcium.
- vi. When platelet comes in contact with collagen of damaged blood vessel, it releases phospholipids.
- vii. Now the activated factor X (as in the case of extrinsic pathway) reacts with platelet phospholipid and factor V to form prothrombin activator. This needs presence of calcium ions.
- viii. Factor V is also activated by positive feedback effect of thrombin.

STAGE 2: CONVERSION OF PROTHROMBIN INTO THROMBIN

Prothrombin activator converts prothrombin into thrombin in the presence of calcium. Thrombin itself can accelerate this reaction by positive feedback mechanism. That is, the initial thrombin activates factor V, This in turn accelerates the formation of both extrinsic and intrinsic prothrombin activator (Fig. 20-1).

STAGE 3: CONVERSION OF FIBRINOGEN INTO FIBRIN

During this, the soluble fibrinogen is converted into insoluble fibrin by thrombin. Initially, the fibrinogen is converted into activated fibrinogen due to loss of 2 pairs

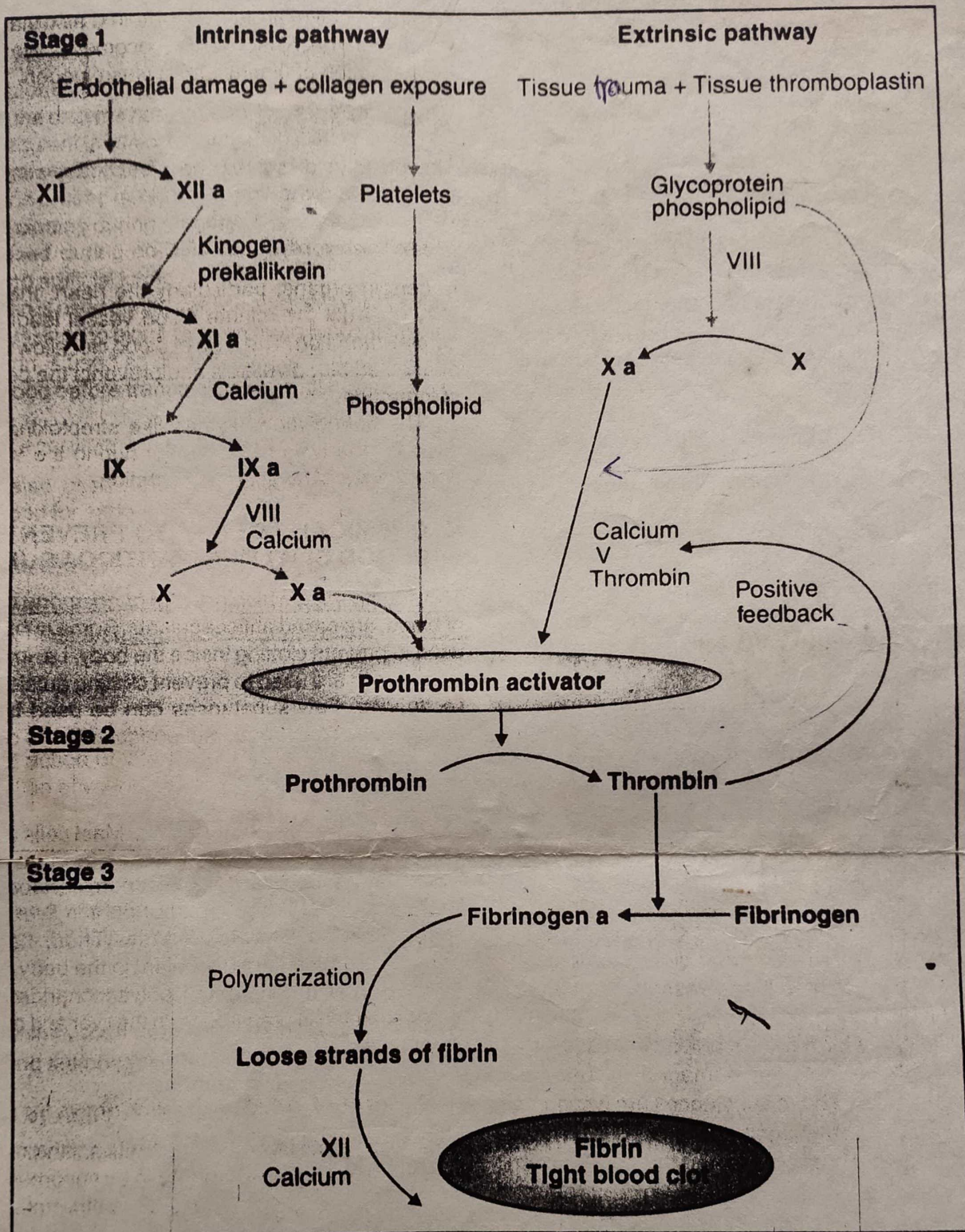


FIGURE 20-1: Stages of coagulation of blood. a = activated

of polypeptides from each fibrinogen molecule. The activated fibrinogen is called fibrin monomer. This polymerizes with other monomer molecules to form fibrin.

The first formed fibrin contains loosely arranged strands. This is modified later into a dense tight aggregate by fibrin stabilizing factor (factor XIII) and this reaction requires the presence of Ca^{2+} .