
GOOD MORNING

Investigations in bleeding and clotting disorders

CONTENTS

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- CLOTTING DISORDERS
- INVESTIGATIONS
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INTRODUCTION

Blood is an ideal testing material for many systemic conditions because the specimen can be obtained easily and many diseases produce detectable peripheral blood abnormalities.

<u>Laboratory methods</u>
Are considered as screening tests if their results provide evidence of disease.

<u>Definitive methods</u>
Laboratory support for a specific diagnosis.

Text book of oral diagnosis, Gary c. Coleman, 1st edition

CAUSES OF BLEEDING IN ORAL CAVITY

HEMORRHAGE DUE TO LOCAL CAUSE

1. Infection
- Fusospirochetal Infection
- Primary Herpes Simplex infection

2. Local irritant
- Malposed teeth
- Calculus accretions
- Prosthetic appliances

3. Postsurgical

4. Rupture of blood-containing bullae caused by local trauma
Cheek biting

5. Congenital malformation
Hemangiomata
Hereditary hemorrhagic telangiectasia

CLOTTING FACTOR DEFICIENCIES

Deficiencies
Hereditary
- Hemophilia A
- Hemophilia B
- von Willebrand's disease

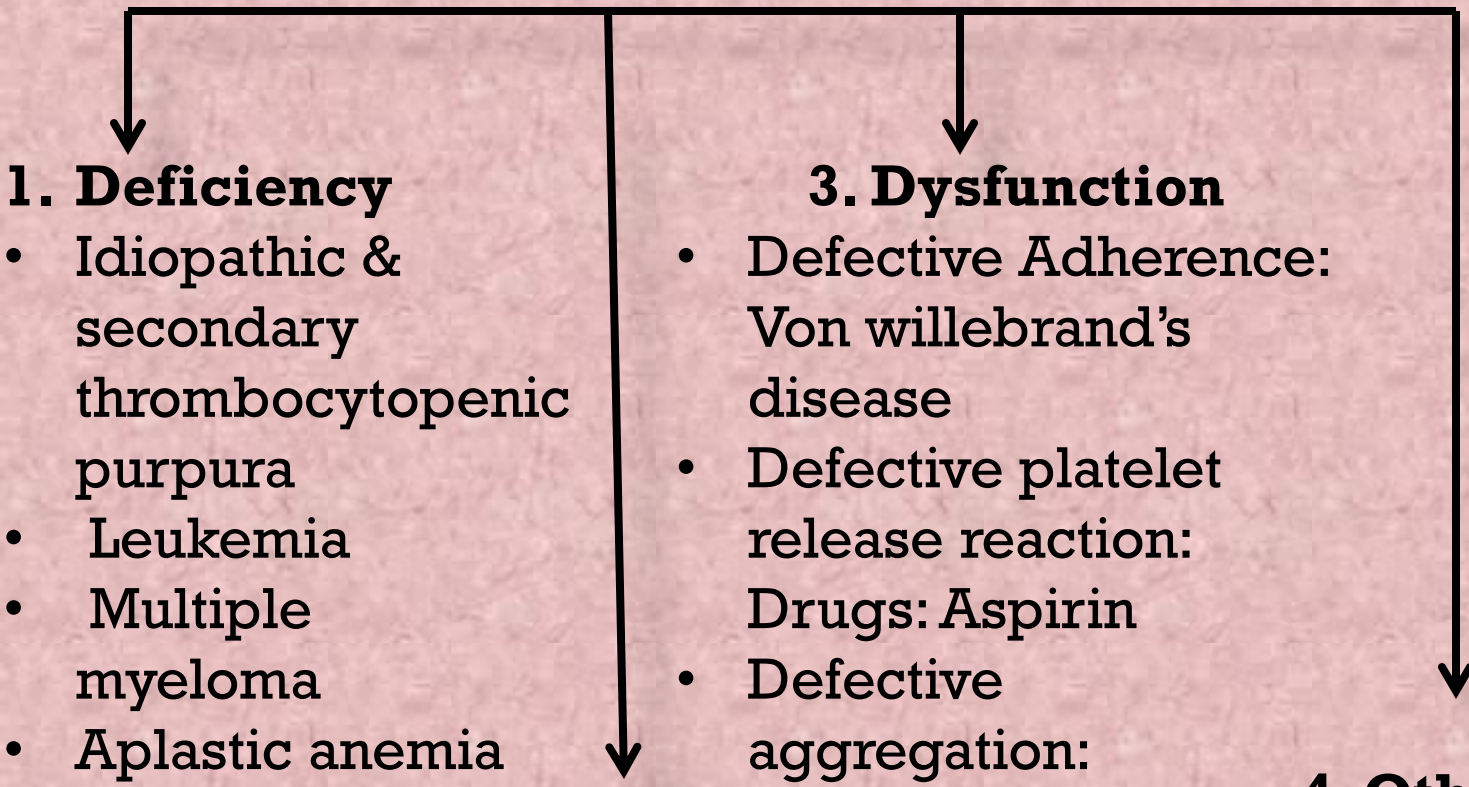
Due to other clotting factor deficiencies

1. Iatrogenic
- Anti coagulant therapy, aspirin
- Drugs other than anticoagulants, valproic acid

2. Liver disease
- Factor II, VII, IX, deficiencies

3. Dysfunction
- Multiple myeloma
- Systemic lupus erythematosus
- Macroglobulinemia

PLATELET DEFICIENCY, EXCESS, DYSFUNCTION



1. Deficiency

- Idiopathic & secondary thrombocytopenic purpura
- Leukemia
- Multiple myeloma
- Aplastic anemia

2. Excess

Thrombocytosis

3. Dysfunction

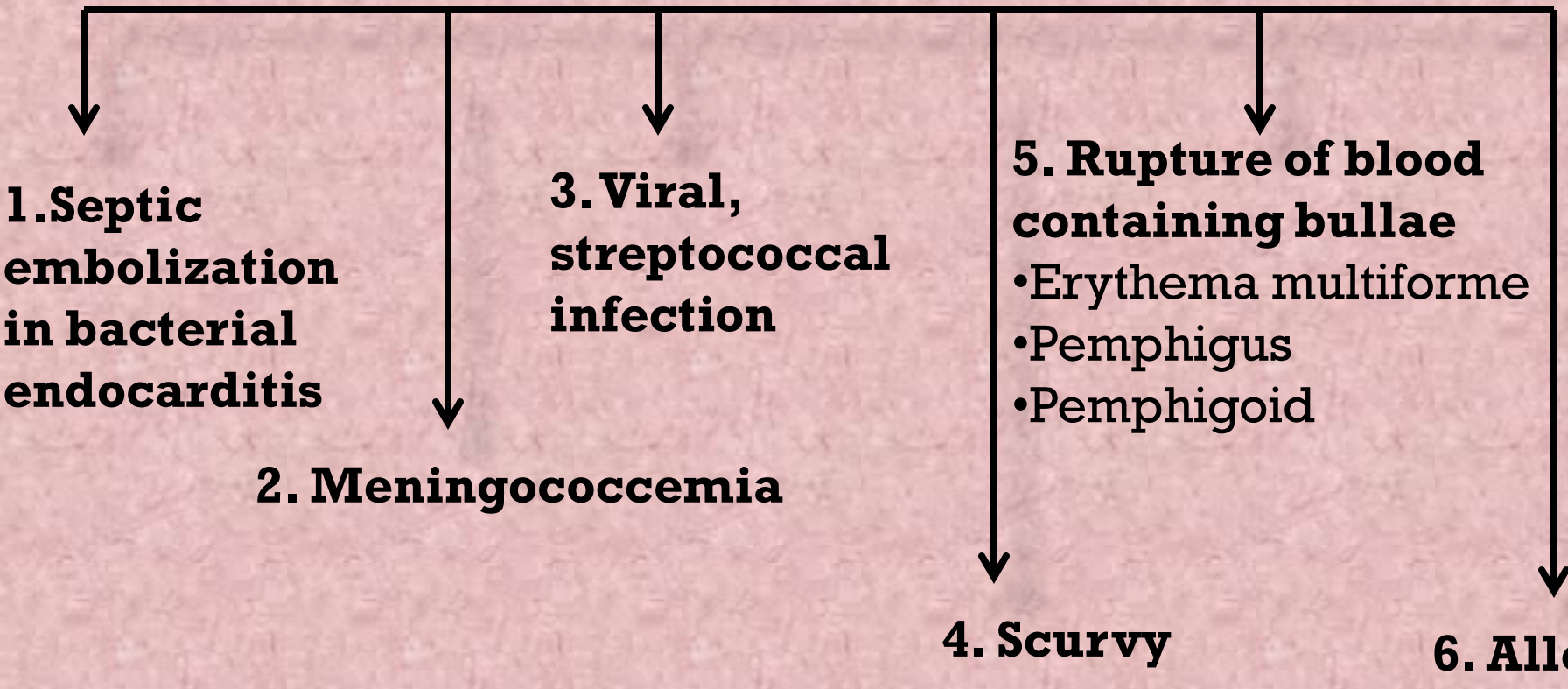
- Defective Adherence: Von willebrand's disease
- Defective platelet release reaction: Drugs: Aspirin
- Defective aggregation: Thrombasthenia

4. Others

- Uremia
- Liver disease
- macroglobulinemia

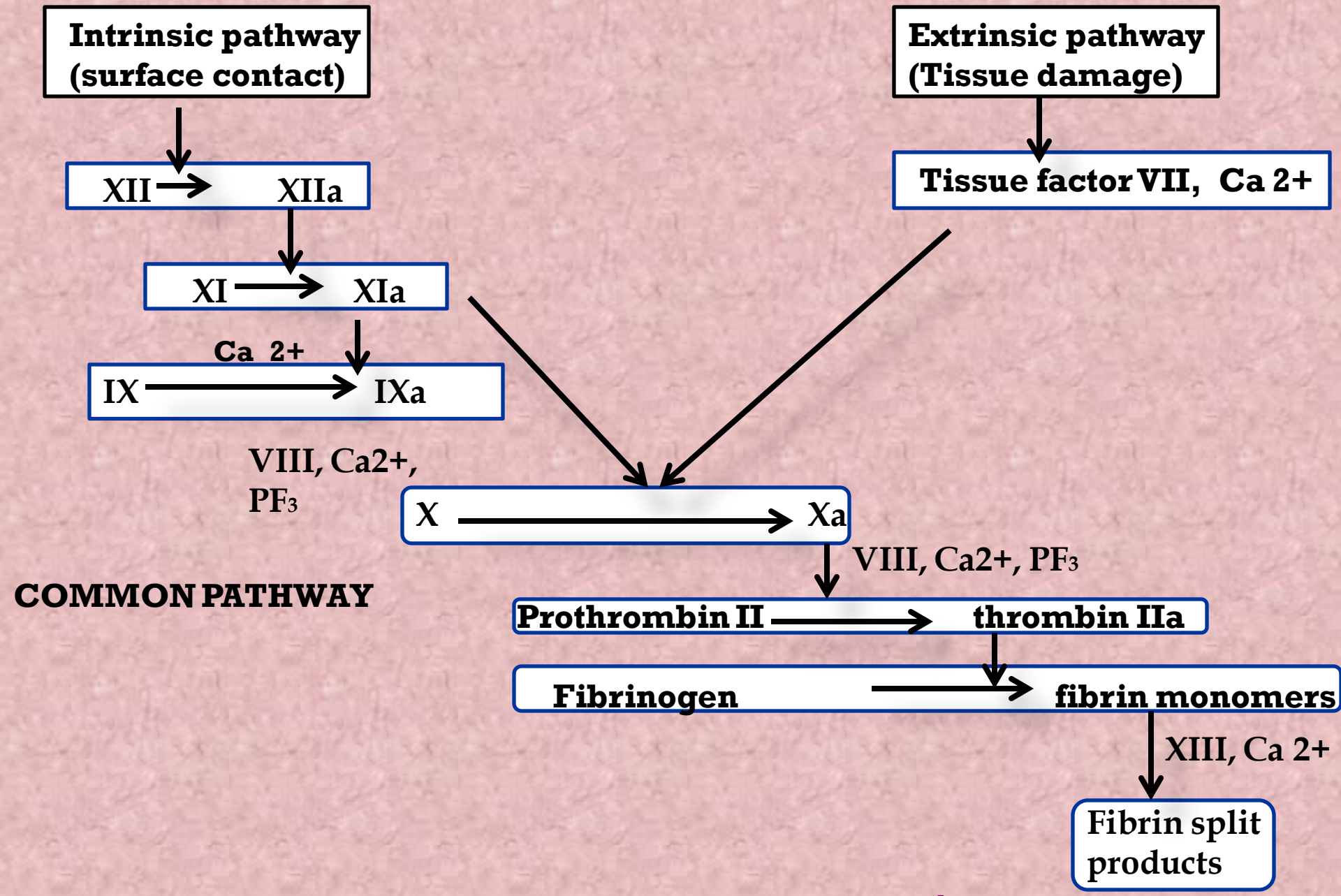
Oral medicine diagnosis and treatment, Burket's 8th edition 7

SYSTEMIC DISEASES OTHER THAN THOSE INVOLVING BLOOD OR BLOOD-FORMING ORGANS



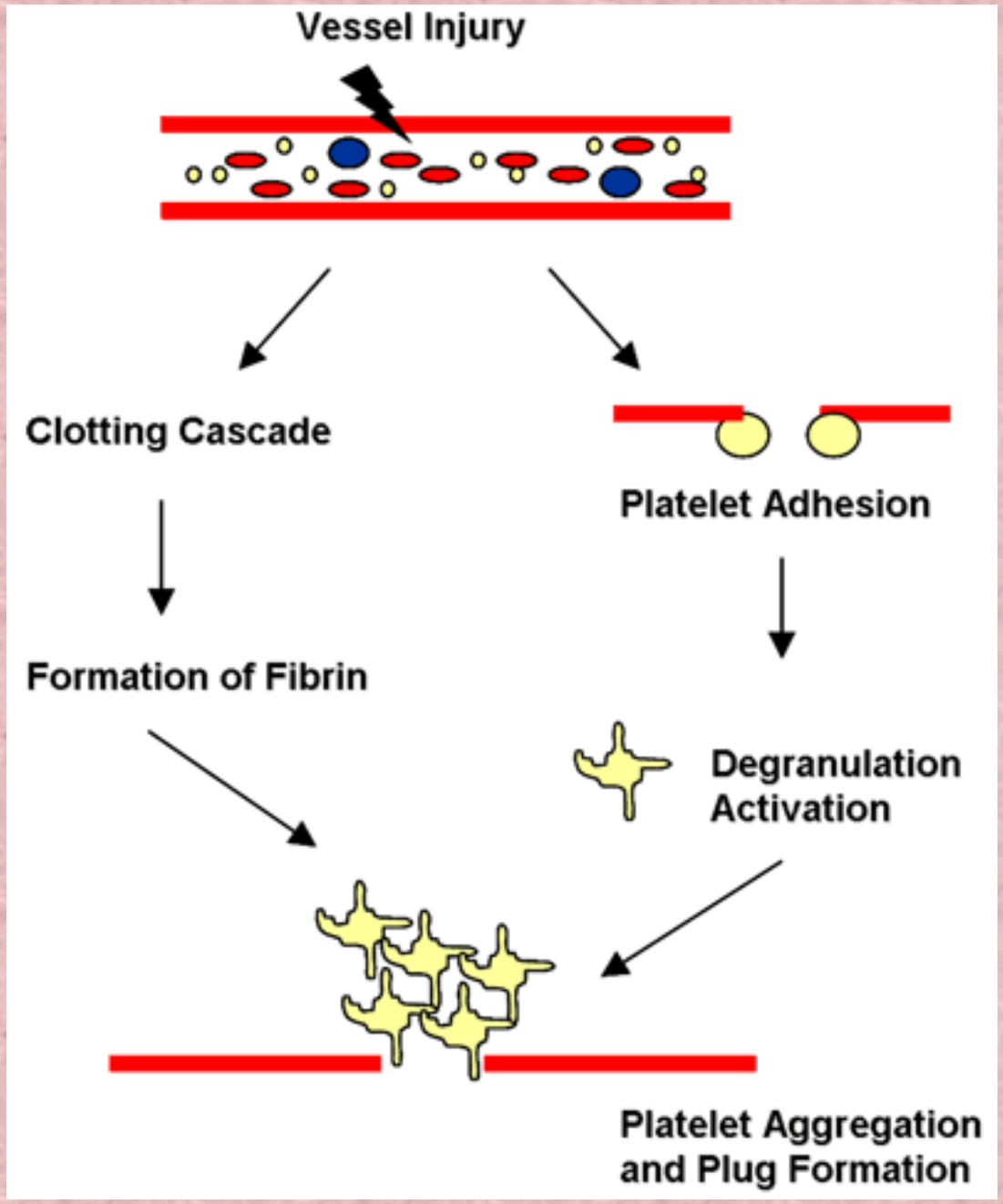
Oral medicine diagnosis and treatment, Burket's 8th edition 8

PATHWAYS OF BLOOD COAGULATION



FACTORS

- Factor I - fibrinogen
- Factor II - prothrombin
- Factor III - tissue thromboplastin (tissue factor)
- Factor IV - ionized calcium (Ca++)
- Factor V - labile factor or proaccelerin
- Factor VI - unassigned
- Factor VII - stable factor or proconvertin
- Factor VIII - antihemophilic factor
- Factor IX - plasma thromboplastin component, Christmas factor
- Factor X - Stuart-Prower factor
- Factor XI - plasma thromboplastin antecedent
- Factor XII - Hageman factor
- Factor XIII - fibrin-stabilizing factor


Vessel Injury
Clotting Cascade
Platelet Adhesion
Formation of Fibrin
Degranulation
Activation
Platelet Aggregation
and Plug Formation

ABOUT BLEEDING DISORDERS

BLEEDING DISORDERS

A group of disorders characterized by defective haemostasis with abnormal bleeding.

The tendency for bleeding may be

Spontaneous

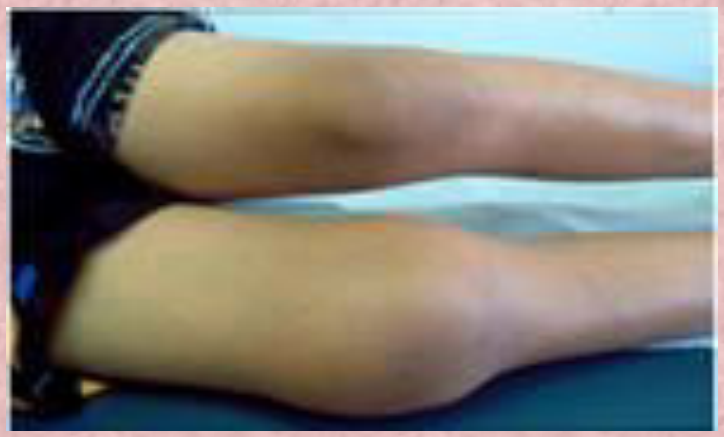
- Petechiae
- Purpura
- Ecchymoses

Following trauma

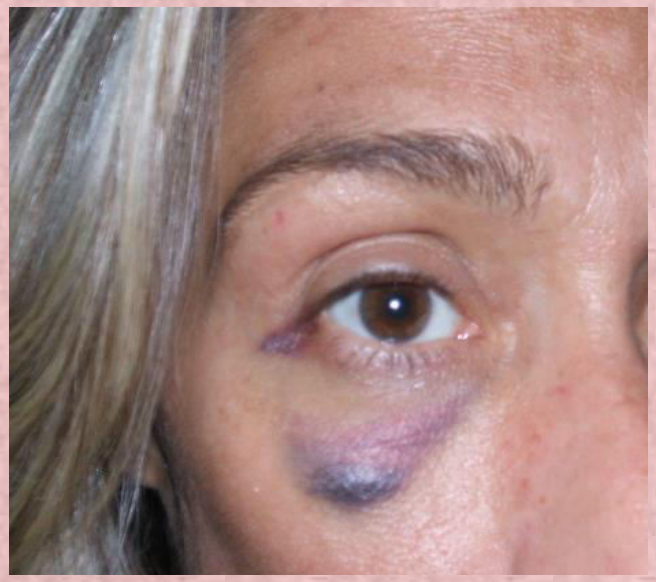
- Hematoma
- Haemarthrosis

ECCHYMOSES

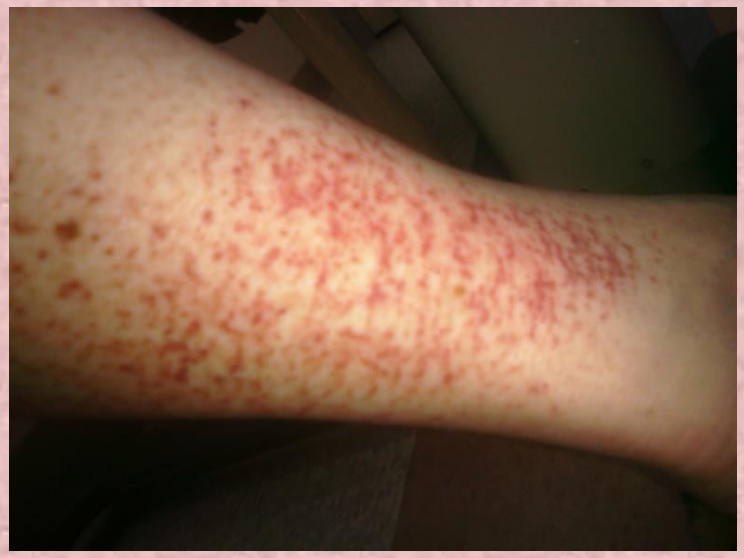
HAEMARTHROSIS



HEMATOMA



PETECHIAE



Know more about
CLOTTING DISORDERS

CLOTTING DISORDERS

Hereditary coagulation disorders :

Due to quantitative or qualitative defect in a single coagulation factor.

- Hemophilia A
- Hemophilia B
- von Willebrand's disease

Acquired coagulation disorders:

Characterized by deficiencies of multiple coagulation factors.

They are:

- Vitamin K deficiency
- Liver disease
- Disseminated intravascular coagulation

HEMOPHILIA

Deficiency of coagulation factors

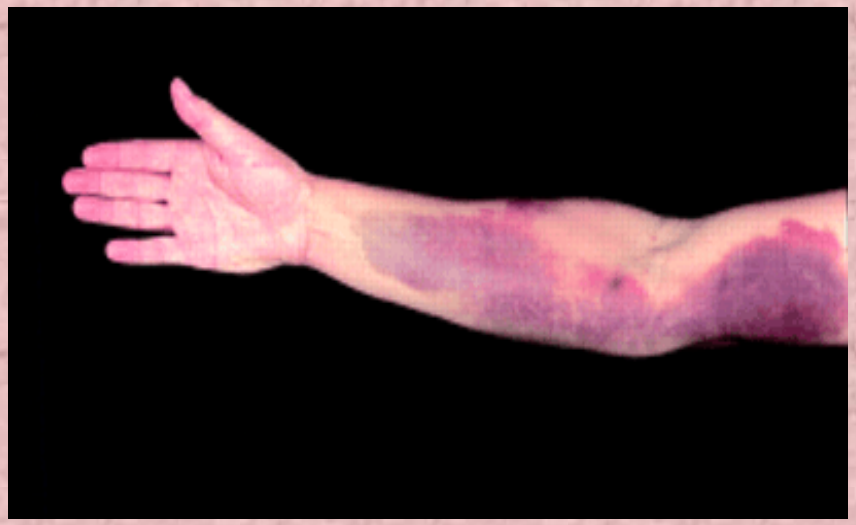
factor VIII
haemophilia A

factor IX
haemophilia B

- Both haemophilias have sex linked inheritance.
- Patients with *moderate to mild conditions:* bleed only after trauma or surgery
- Patients with *severe haemophilia :* spontaneous bleeding into muscles and joints leading to a crippling arthropathy.

VON WILLEBRAND'S DISEASE

PATHOLOGICAL BRUISING IN VON WILLEBRAND'S DISEASE.

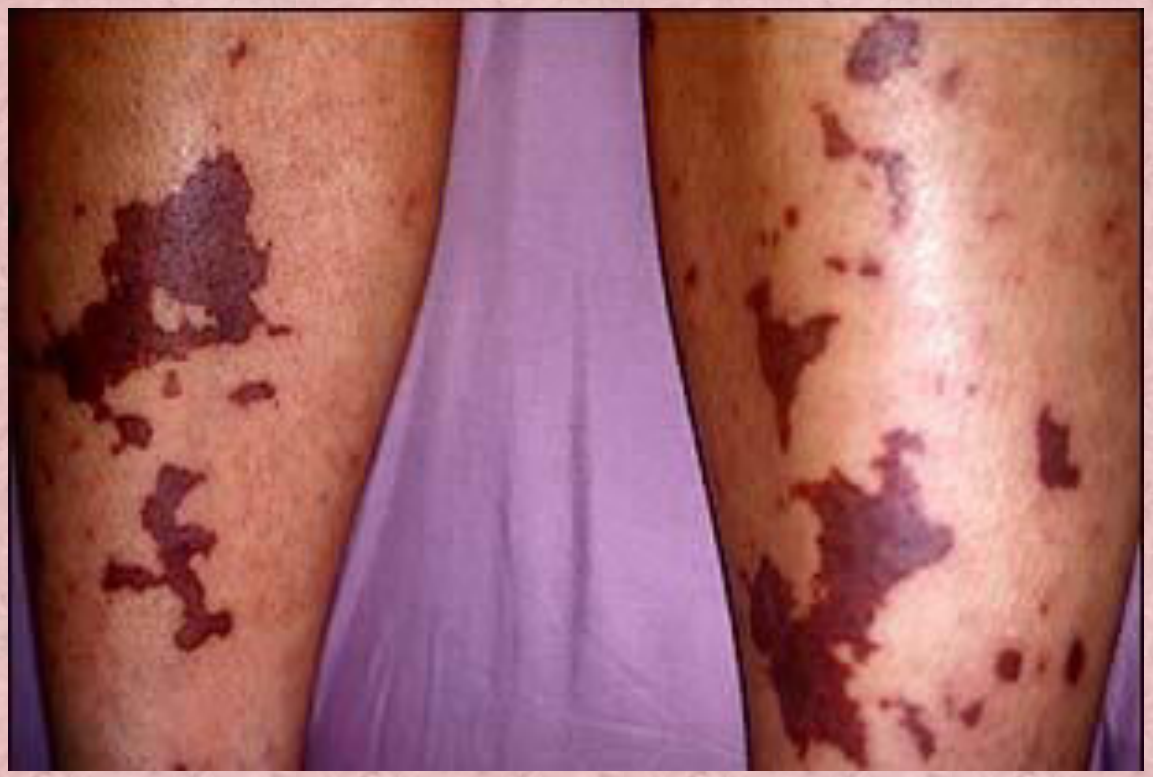


The condition is due to a reduction or structural abnormality of von Willebrand's factor.

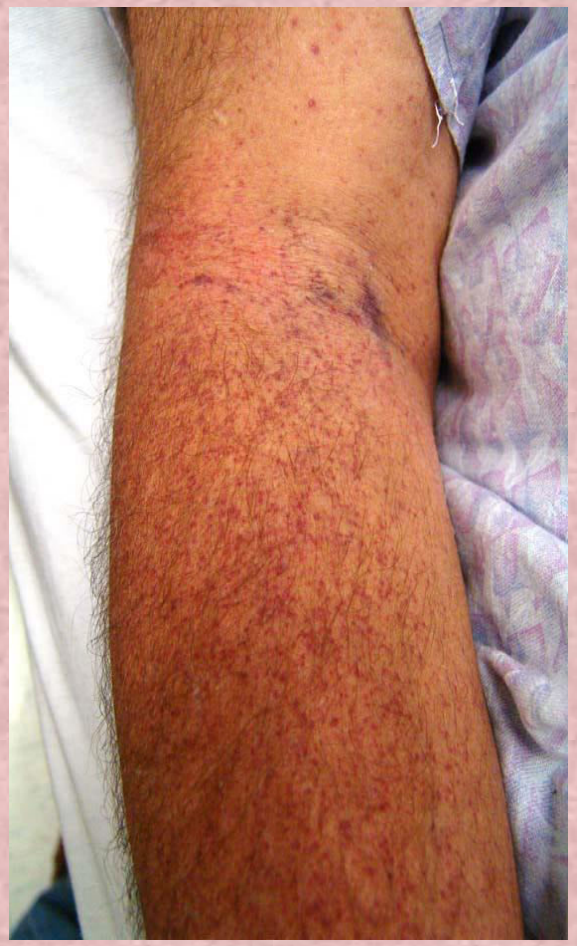
Role of von Willebrand's factor:

1. Promotes normal platelet function
2. Stabilizing coagulation factor VIII.

DISSEMINATED INTRAVASCULAR COAGULATION



- Also known as consumption coagulopathy.
- This condition accelerates clotting, which result in hemorrhage when the clotting factors are exhausted.



THROMBOCYTOPENIA

The disorder is characterized by reduced numbers of circulating platelets in the blood

HYPOPROTHROMBINEMIA

A congenital deficiency of clotting factors that can lead to hemorrhage.

INVESTIGATIONS

Bleeding time:

Time interval from oozing of blood after a cut or injury till arrest of bleeding.

A prolonged bleeding time may be due to:

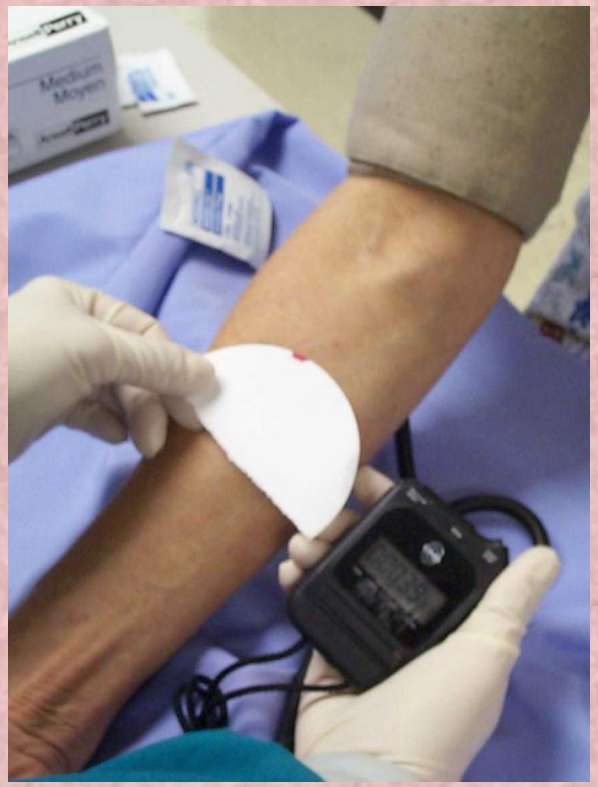
1. Thrombocytopenia
2. Disorders of platelet function
3. von Willebrand's disease
4. Vascular abnormalities
5. Severe deficiency of factor V and XI

IVY TECHNIQUE

- A blood pressure cuff is placed on the upper arm and inflated to 40 mmHg.
- A standard-sized cut is made around 10 mm long and 1 mm deep.
- Every 30 seconds, filter paper is used to draw off the blood.
- The test is finished when bleeding has stopped completely.
- A prolonged bleeding time may be a result from decreased number of thrombocytes or impaired blood vessels.

Normal value: 5 - 6minutes

DUKE METHOD



- The patient is pricked with a special needle or lancet, preferably on the earlobe, fingertip, after having been swabbed with alcohol.
- The prick is about 3-4 mm deep.
- Wipe the blood every 30 seconds with a filter paper.
- The test is complete when bleeding ceases.

Normal time: 7-8 minutes.

International Normalized Ratio

A laboratory test called an INR measures the time it takes for blood to clot and compares it to an average.

Method

To find the INR, a small sample of blood is taken from a fingertip or vein. The time it takes the blood to clot is measured.

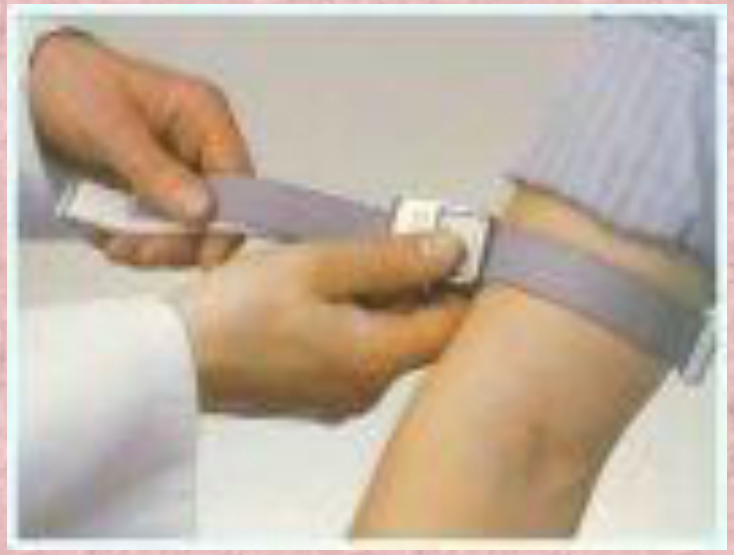
- In healthy people, the INR is about1.0.
- For patients on anticoagulants, INR is 2.0
- Patients with atrial fibrillation, INR is 3.0
- Patients with mechanical heart valves between 3.0 &4.0
- An INR >4.0 may indicate that blood is clotting too slowly
- An INR < 2.0 may not provide adequate protection from clotting.

$$INR = \left(\frac{PT_{test}}{PT_{normal}} \right)^{ISI}$$

Each manufacturer assigns an ISI value (International Sensitivity Index) for any tissue factor they manufacture.

The ISI is usually between 1.0 and 2.0.

Screening test for capillary fragility



•The tourniquet or Rumpel-Leede test evaluates capillary fragility by blocking venous blood return, which increases intraluminal pressure stress.

•Then 5 min later small petechial hemorrhages of the skin are counted in a 2*2cm square proximal to antecubital crease.

• Fewer than 10 petechiae are normal.

• More than 20 indicate capillary fragility.

Investigation of blood coagulation

The normal blood coagulation system consisting of intrinsic and extrinsic pathway.

- **Screening tests:** Tests for blood coagulation system include a battery of screening tests. These are as under:
- **Whole blood coagulation time:** The estimation of whole blood coagulation time done by various capillary and tube methods is of limited value since it is an intensive and nonspecific test.

Lee White method

1 mm of venous blood is placed in each of 4 dry test tubes of standard size, maintained in a water bath. The 1st is tilted at 30sec intervals until the blood no longer flows. The next tube is tilted until the clotting occurs after which 3rd and 4th tubes are similarly treated. The average time between venipuncture and clotting in last 3 tubes is expressed in minutes as clotting time.

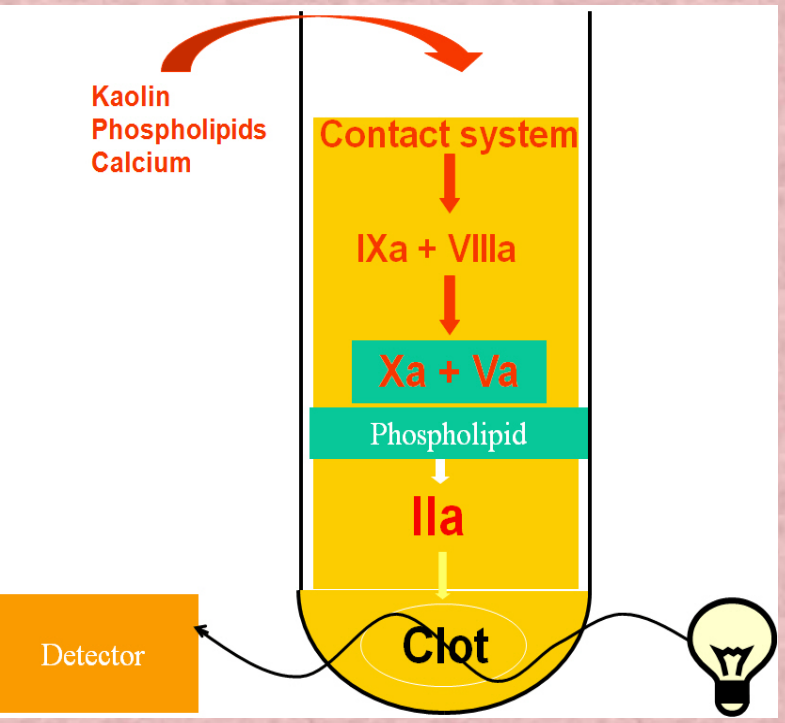
Normal range: 10 to 25 min.

Wright's Capillary tube method

Blood obtained by finger prick taken in a capillary tube.
Broken at intervals of 30seconds into small bits
Until rope formation occurs between the 2 broken ends

Normal time: 3-6 minutes

Activated Partial Thromboplastin Time:



The normal range is 15 to 35sec.

- This test is used to measure the intrinsic system factors as well as factors common to both intrinsic and extrinsic systems.
- The test consist of addition of 3 substances to the plasma- calcium, phospholipid, surface activator such as kaolin.

The causes of a prolonged APTT are:

1. Parenteral administration of heparin
2. DIC
3. Liver disease
4. Circulating anticoagulants.

Thrombin time

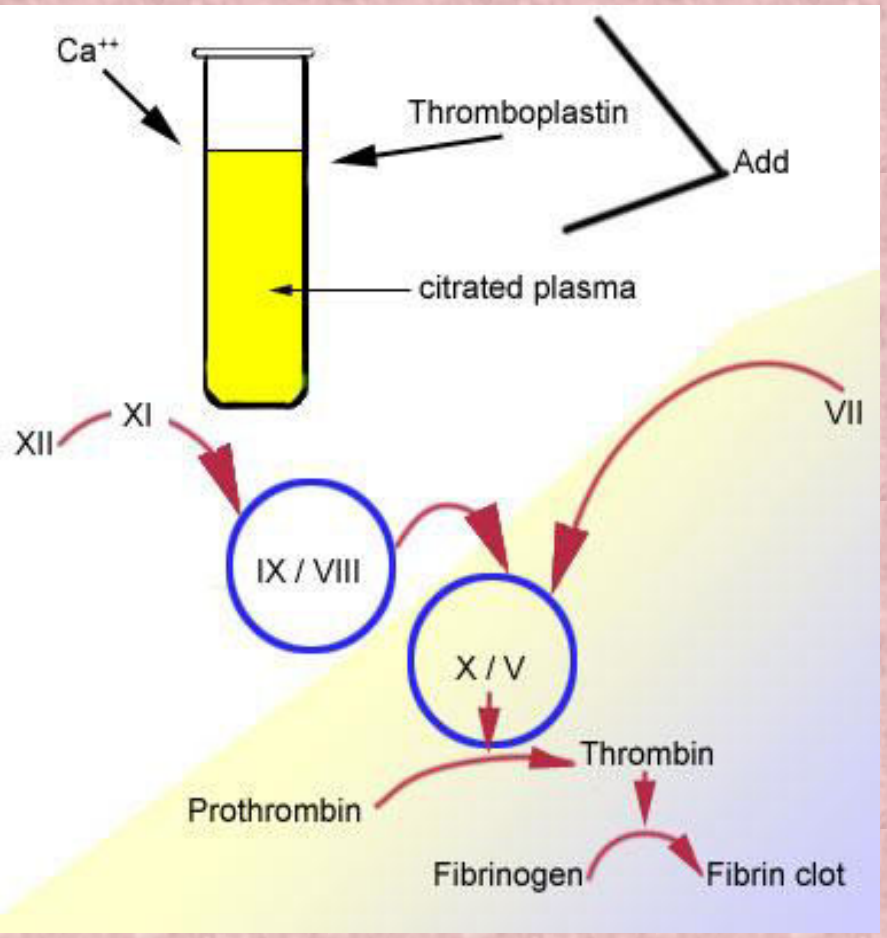
Normal: 12 to 15 sec.

Blood is drawn from a vein.
A standard amount of bovine thrombin is added to a plasma sample from the patient and to a normal plasma control sample.
The clotting time for each sample is compared with the other and recorded.

PURPOSE:

- Used to test the ability to form initial clot from fibrinogen
- Measure the activity of heparin
- Fibrin degradation products
- Para proteins that inhibit the conversion of fibrinogen to fibrin

One stage prothrombin time(PT):



- **The normal PT is 10-14 sec.**

- PT measures the extrinsic system factor VII as well as factors in the common pathway.
- In this test, tissue thromboplastin and calcium are added to the test.

The common causes of prolonged one-stage PT are:

1. Administration of oral anticoagulant drugs
2. Liver disease, especially obstructive liver disease.
3. Vitamin K deficiency
4. Disseminated intravascular coagulation

Measurement of fibrinogen

- The screening tests for fibrinogen deficiency are semi quantitative fibrinogen titre and thrombin time(TT).
- The normal value of fibrinogen titre in plasma dilution up to 32 seconds is considered normal.

The causes for higher values in this test are:

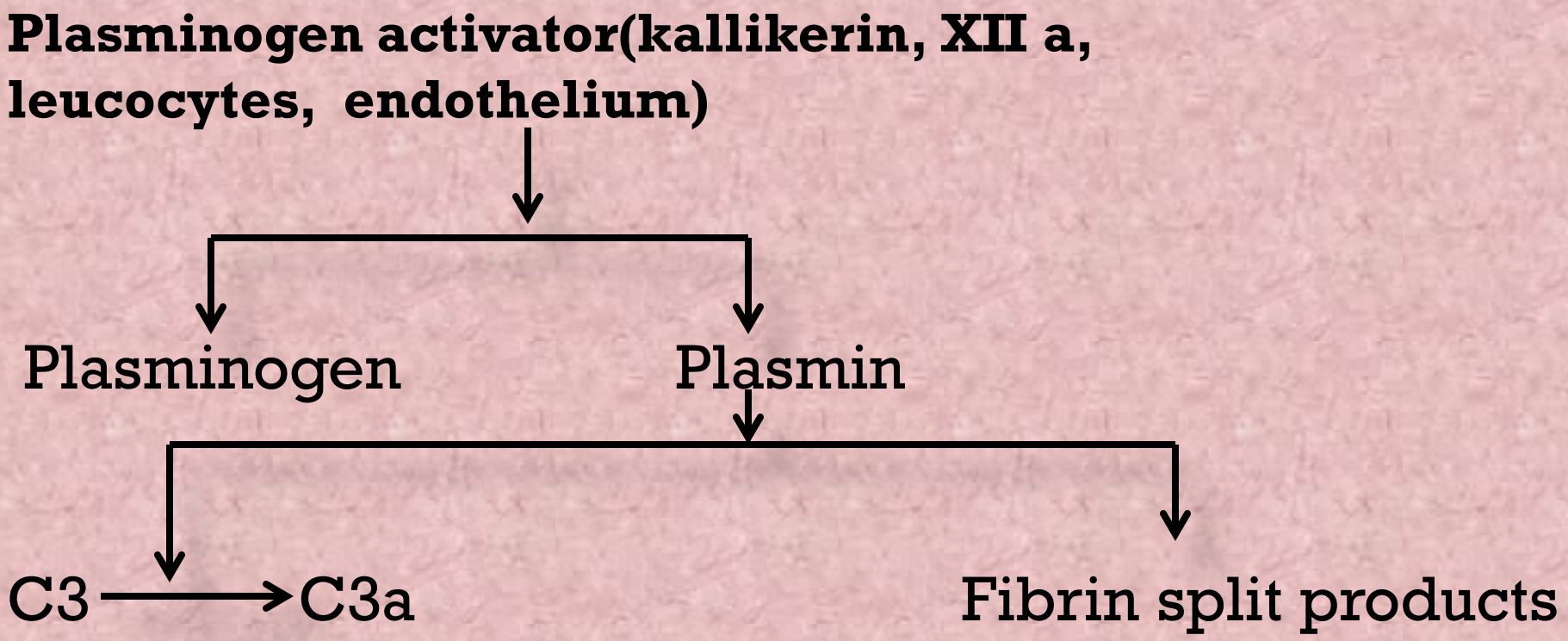
1. Hypofibrinogenaemia
2. Raised concentration of Fibrin degradation products
3. Presence of Heparin

Coagulation factor assays

- These bioassays are based on results of PT test and employ the use of substrate plasma that contains all other coagulation factors except the one to be measured.
- The unknown level of the factor activity is compared with a standard control plasma with a known level of activity.
- Results are expressed as percentage of normal activity

Investigation of fibrinolytic system

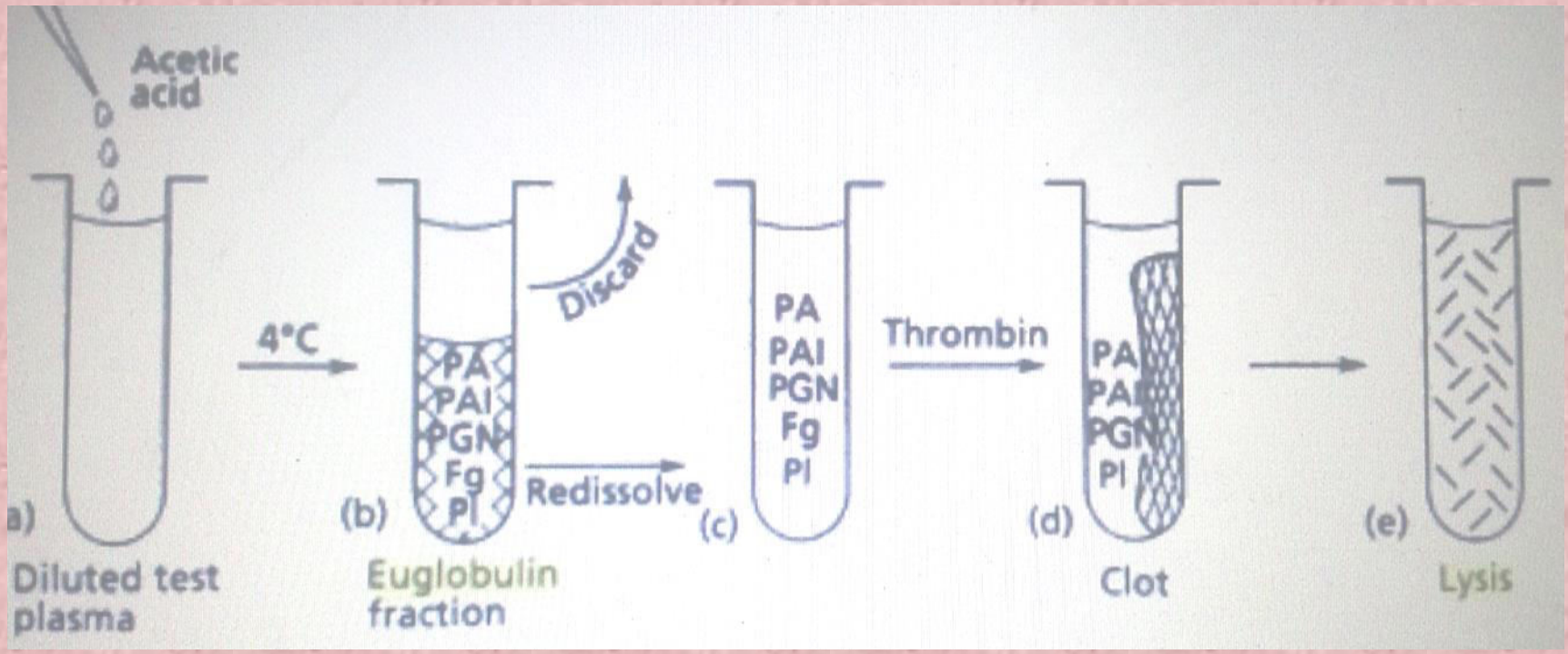
Increased levels of circulating plasminogen activator are present in patients with hyperfibrinolysis.



Screening tests done to assess these abnormalities in fibrinolytic system are:

1. Estimation of fibrinogen
2. **Fibrin degradation products in serum:** evaluate the presence of D-dimer of fibrinogen above normal levels.
3. **Ethanol gelation test**: The ability of ethanol to gel soluble fibrin (fibrin monomer)

4. Euglobulin or whole body lysis time



To see how fast blood clots dissolve.

The clot is observed with an automated clot lysis timer

Normal value 90 min

Thrombosis and hemorrhage, Lippincott Williams & Wilkins, 3rd edition

Investigation of platelets and platelet function

Haemostatic disorders are most commonly due to abnormalities in platelet number, morphology or function.

The screening tests carried out for assessing these are:

1. Peripheral blood count
2. Bleeding time
3. Examination of fresh blood film to see the morphologic abnormalities of platelets

Special tests:

If these screening tests suggest a disorder of platelet function, the following platelet function tests may be carried out:

- **Platelet adhesion test:** Retention in a glass bead column.
- **Aggregation tests:** which are turbidometric techniques using collagen, or ristocetin.
- **Granular content:** of the platelets and their release can be assessed by electron microscopy or by measuring the substances released.
- **Platelet coagulant activity**: is measured indirectly by prothrombin consumption complex.

LABORATORY TEST	FACTO R MEASURED	ASSOCIATED DISORDERS
BLEEDING TIME	Platelet function, vascular integrity	Qualitative disorder of platelets Von Willebrand's disease Quantitative disorders of platelets Acquired vascular disorders
PLATELET COUNT	Quantification of platelets	Thrombocytopenia, Thrombocytosis
PROTHROMBIN TIME	Evaluation of extrinsic and common pathway (Deficiency of factors I, II, V, VII, X)	Oral anticoagulant therapy DIC Liver disease
PARTIAL THROMBOPLASTIN TIME	Evaluation of intrinsic and common pathway (Deficiency of factors I , II, V, VIII, IX, X, XI, XII)	Parenteral heparin therapy DIC Liver disease
THROMBIN TIME	Evaluation of common pathway	Afibrinogenaemia DIC Parenteral heparin therapy

SUMMARY

CONDITION	PRO THROMBIN TIME	PARTIAL THROMBO-PLASTIN TIME	BLEEDING TIME	PLATELET COUNT
Haemophilia	unaffected	prolonged	unaffected	unaffected
von Willebrand disease	unaffected	prolonged	prolonged	unaffected
Factor V deficiency	prolonged	prolonged	unaffected	unaffected
Factor X deficiency	prolonged	prolonged	unaffected	unaffected
Disseminated intravascular coagulation	prolonged	prolonged	prolonged	decreased
Thrombocytopenia	unaffected	unaffected	prolonged	decreased
Glanzmann's thrombasthenia	unaffected	unaffected	prolonged	unaffected
Vitamin K deficiency or warfarin	prolonged	prolonged	unaffected	unaffected
Aspirin	unaffected	unaffected	prolonged	unaffected
Uremia	unaffected	unaffected	prolonged	Unaffected

CONCLUSION

Clinical laboratory methods provide an efficient, effective and relatively inexpensive approach to obtaining diagnostic information from blood specimen.

Effective communications between the pathologist and the clinician is essential in achieving the most accurate diagnosis and optimal management of the patient's condition

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Thank you ...
"The Cure
Is In Your
Hands"