Lecture_1

Bleeding disorders

fourth year students

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- **Haemostasis**: drives from the Greek meaning "The stoppage of bleeding "

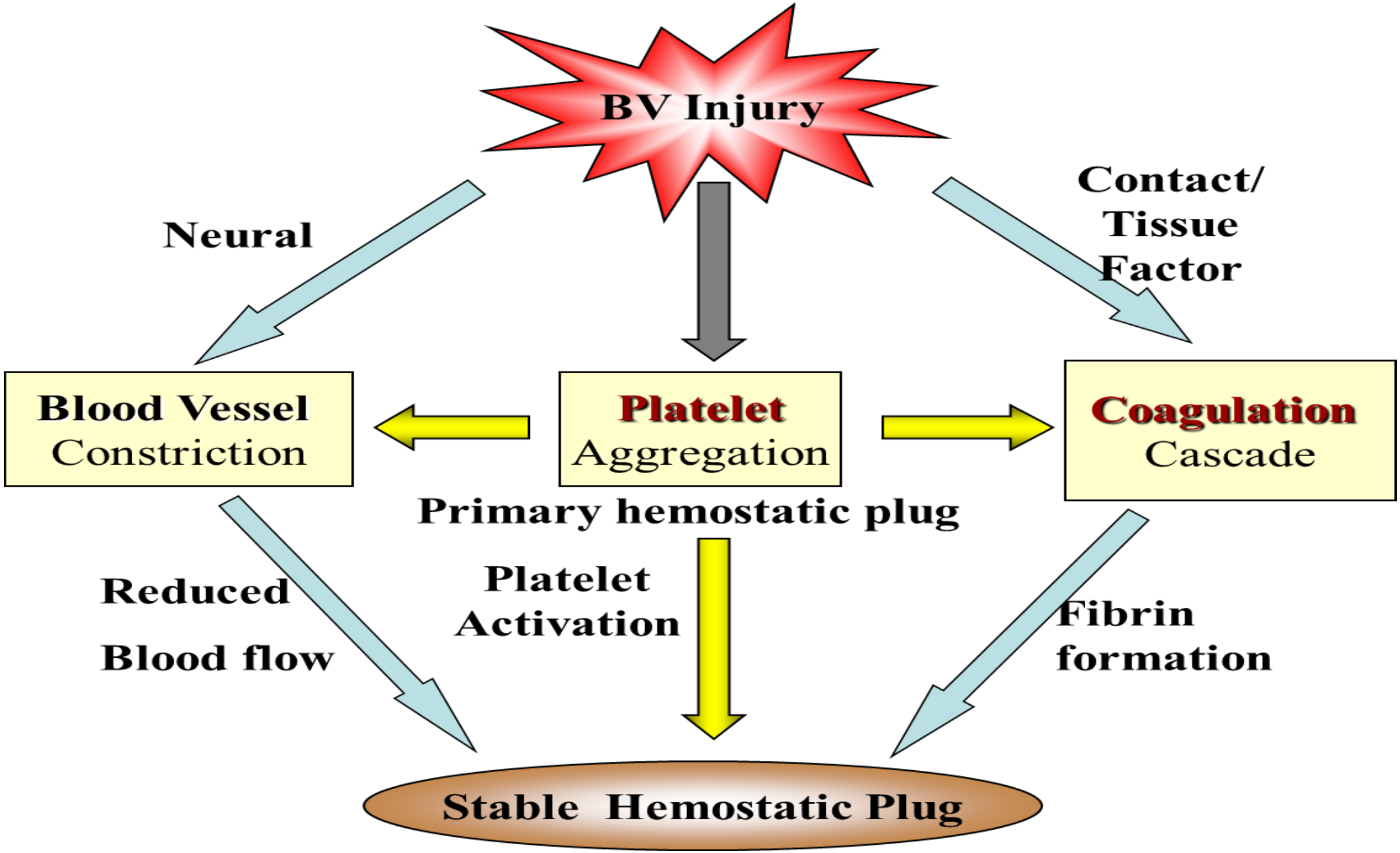
Events preventing excessive blood loss

1. **Vascular spasm**: Vasoconstriction of damaged blood vessels
2. **Platelet plug formation** (von willebrand factor binds damaged vessle and platelets)
3. **Coagulation or blood** clotting

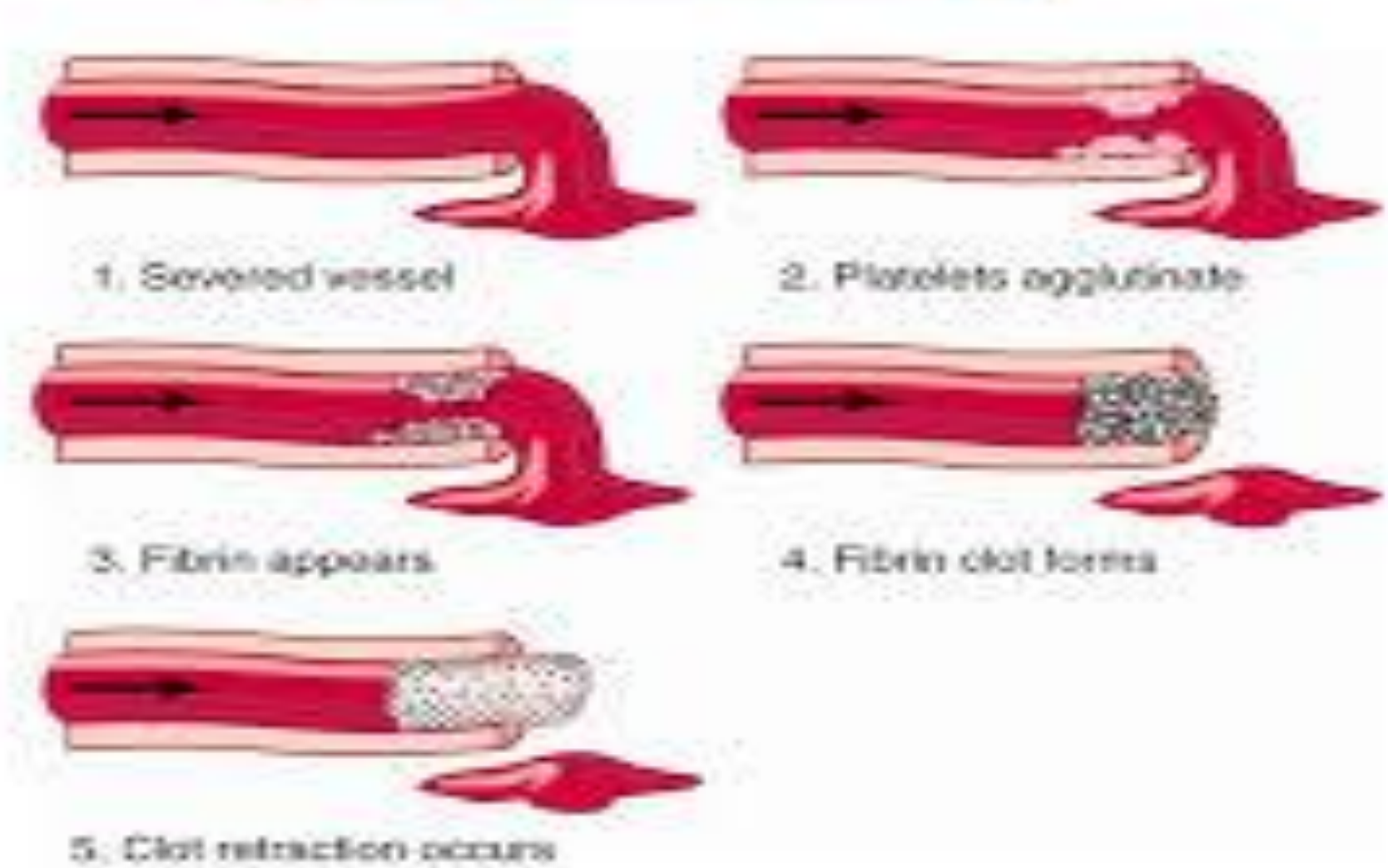
Hemostasis can be divided into two stages:

1. **Primary hemostasis** includes the platelet and vascular response to vessel injury
2. **Secondary hemostasis** includes the coagulation factors response to such injury

Together, platelets, vessels, and coagulation factors combine to stop bleeding and allow for vessel repair through formation of a stable fibrin-platelet plug at the site of injury


BV Injury
Neural
Contact/
Tissue
Factor
Blood Vessel
Constriction
Platelet
Aggregation
Coagulation
Cascade
Primary hemostatic plug
Reduced
Blood flow
Platelet
Activation
Fibrin
formation
Stable Hemostatic Plug

Clot Formation



- Normal bleeding is seen following surgery and trauma

- Pathological bleeding occurs when structurally abnormal vessels rupture or dysfunction of platelets,or the coagulation factors

Disorders of haemostasis

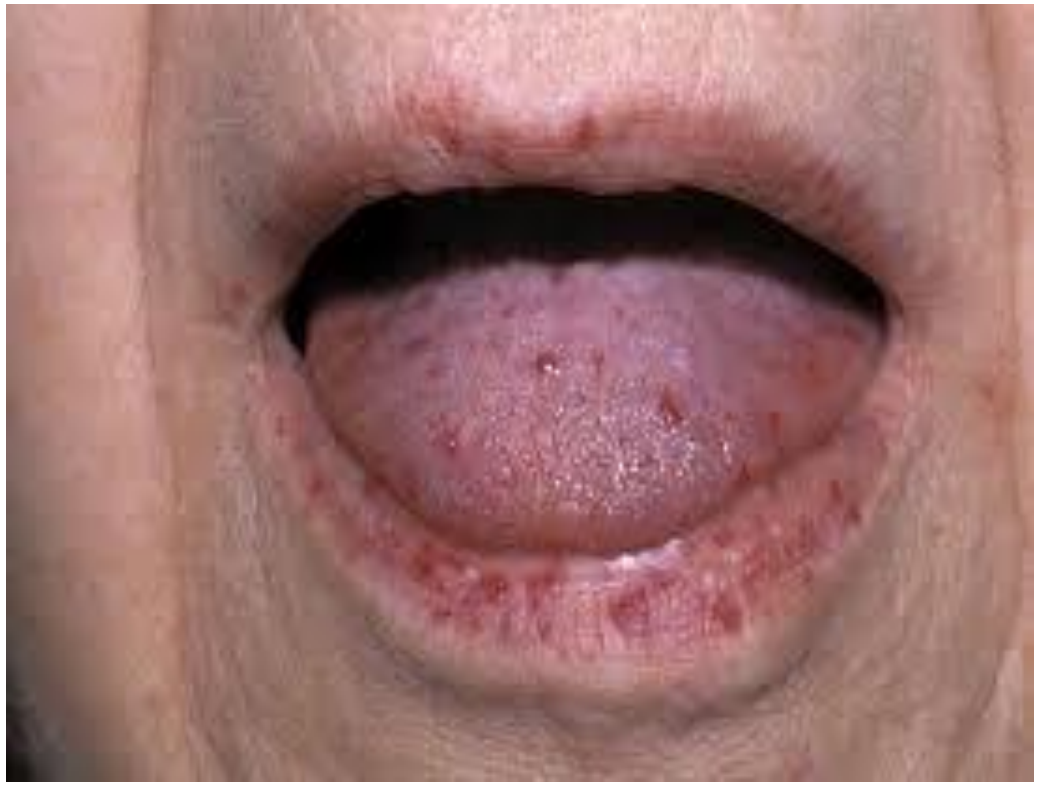
- Vascular disorders
- Platelet disorders
  - Low Number or abnormal function
- Coagulation disorders
  - Factor deficiency
  - Mixed/Consumption: DIC

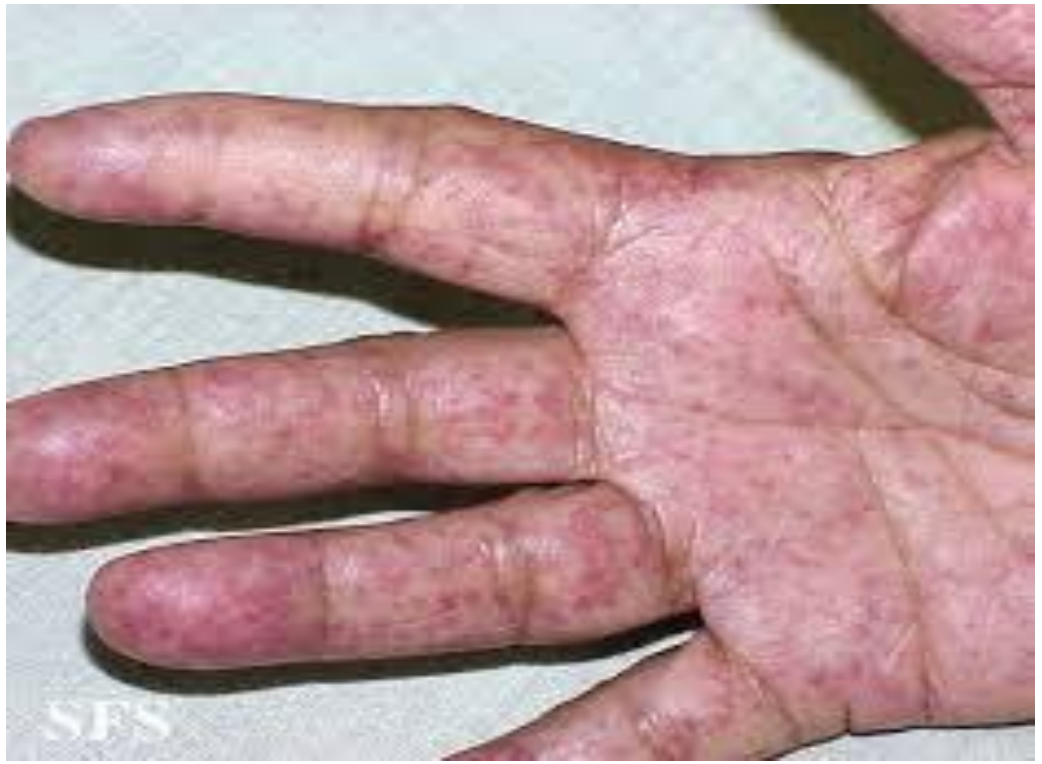
1) Vascular disorders

➢Hereditary haemorrhagic telangiectasia (Osler–Weber–Rendu disease)

- Inherited condition caused by genetic mutations
- Telangiectasia (dilation of the capillaries) and small aneurysms are found on the fingertips, face and tongue, and in the nasal passages, lung and GIT
- Some patients develop larger pulmonary arteriovenous malformations (PAVMs) that cause arterial hypoxaemia due to a right-to-left shunt
- These predispose to paradoxical embolism, resulting in stroke or cerebral abscess

- Patients present either
  - with recurrent bleeds, particularly epistaxis
  - or with iron deficiency due to occult gastrointestinal bleeding
  - Family history (a first-degree relative with HHT)





Diagnosis of HHT

No specific diagnostic

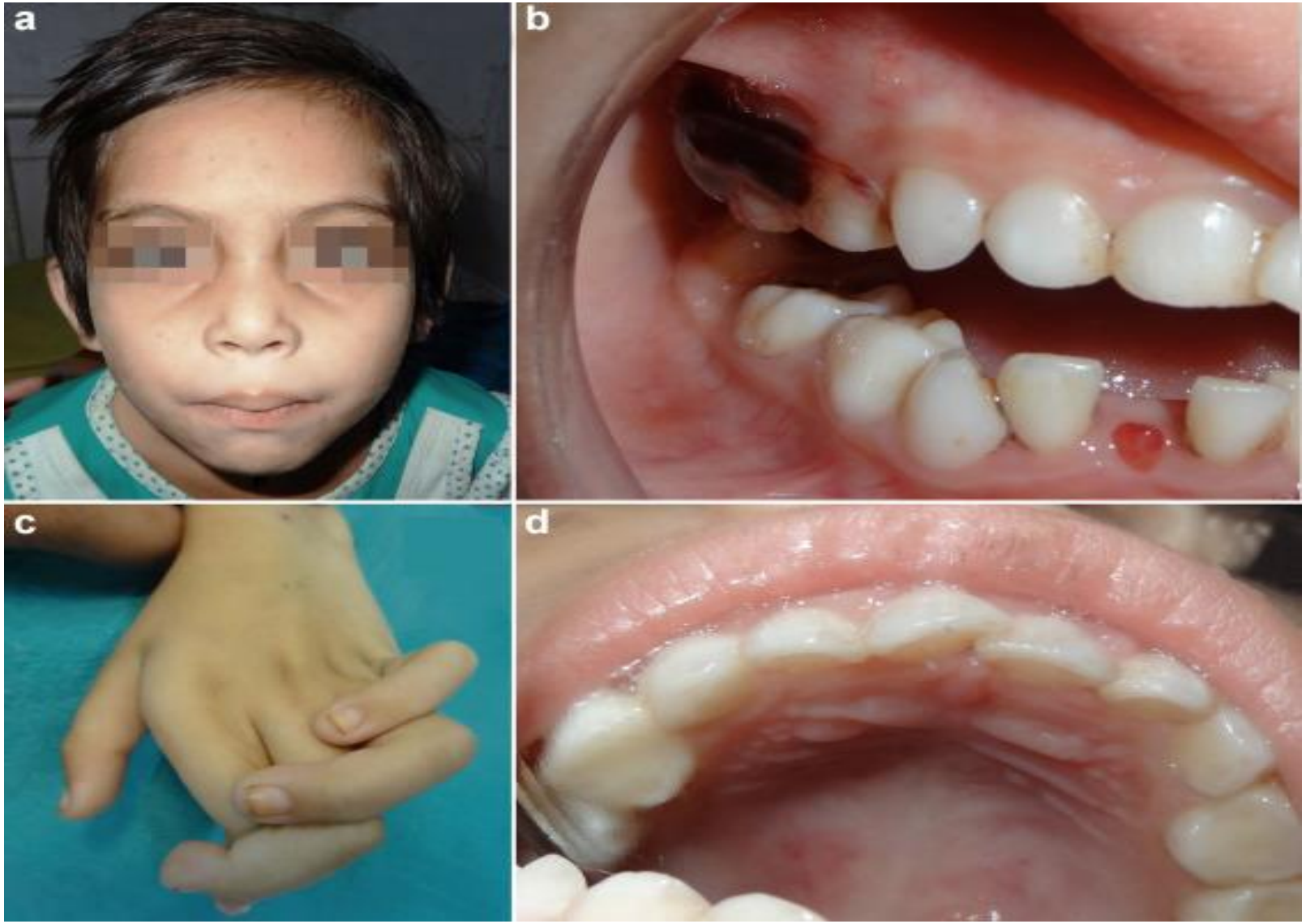
- **All patients with HHT should be screened for PAVMs**

Treatment

- Supportive
- regular iron therapy to compensate for blood loss
- Local cautery or laser therapy may prevent single lesions from bleeding
- A variety of medical therapies have been tried but none has been found to be effective

➢Ehlers–Danlos disease

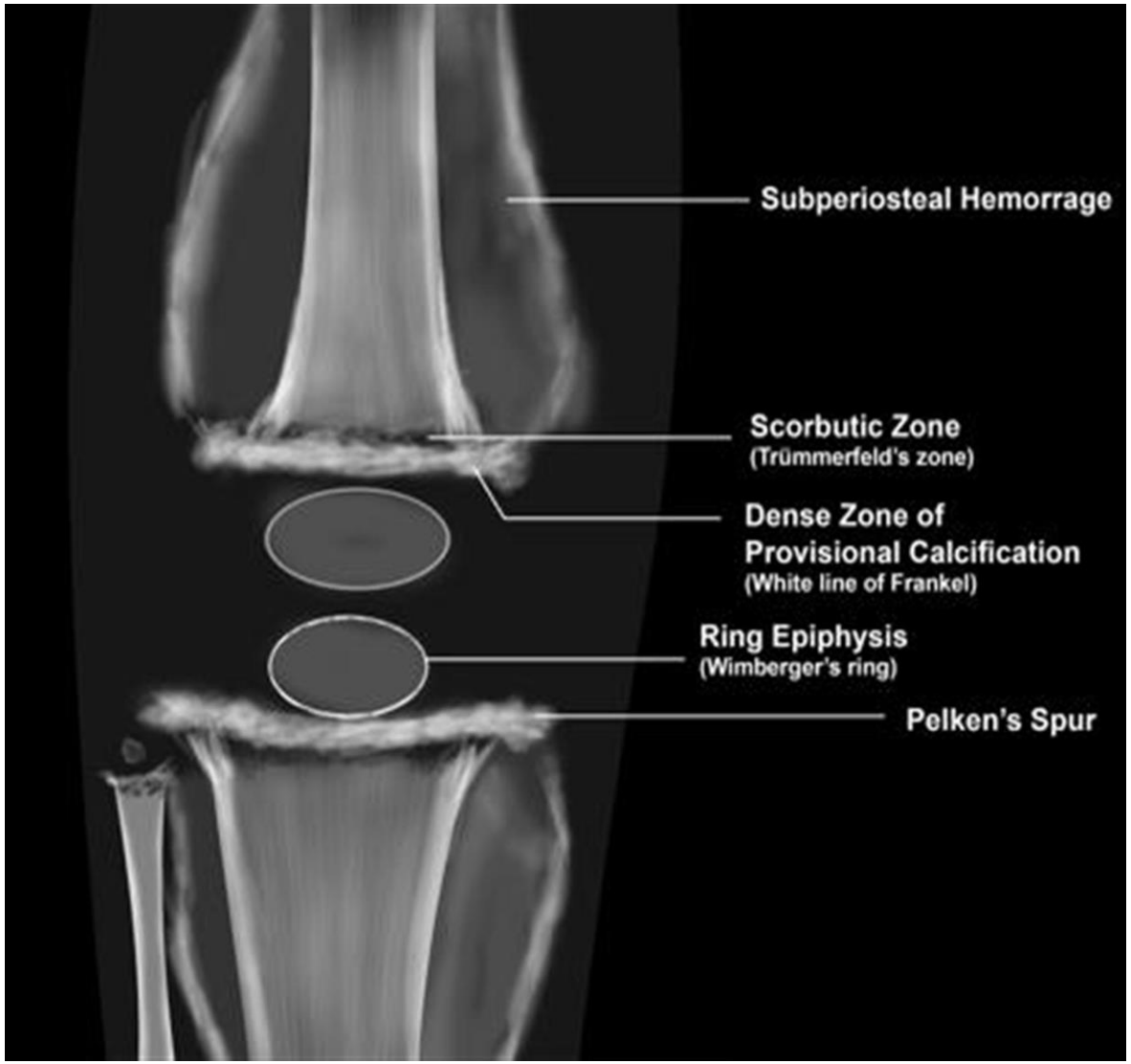
- Is a rare autosomal dominant disorder
- Genetic connective tissue disorders affect the normal synthesis of collagen most typically in the joints, skin, and blood vessels and causes effects ranging from mildly joint hypermobility, skin changes and facial appearance to life-threatening complications
- Bleeding disorder characterised by perifollicular and petechial haemorrhage, bruising and subperiosteal bleeding

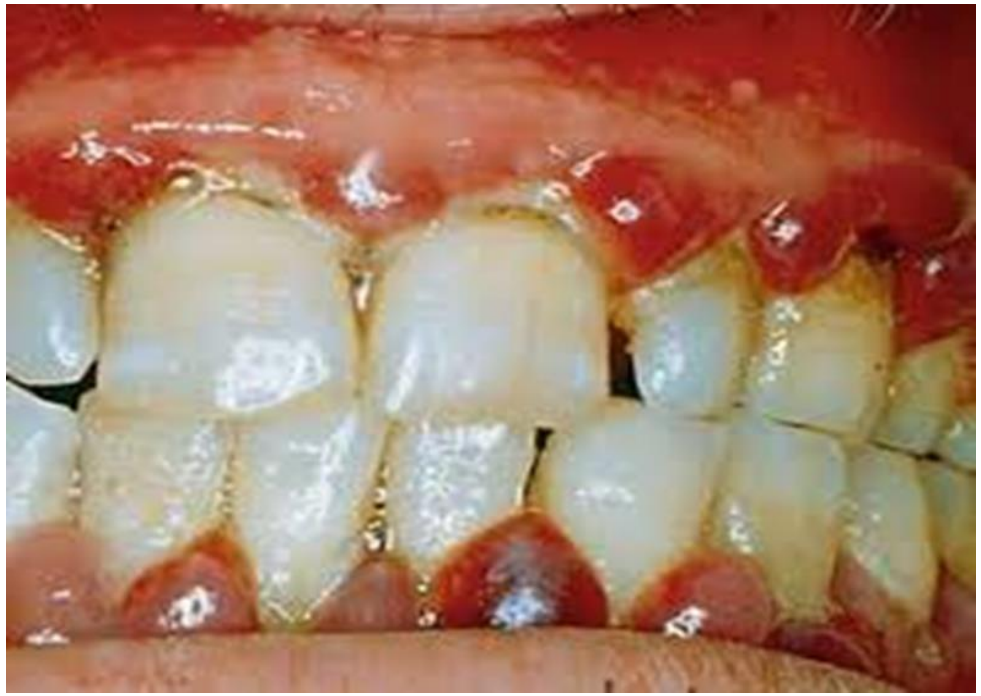

a
b
c
d

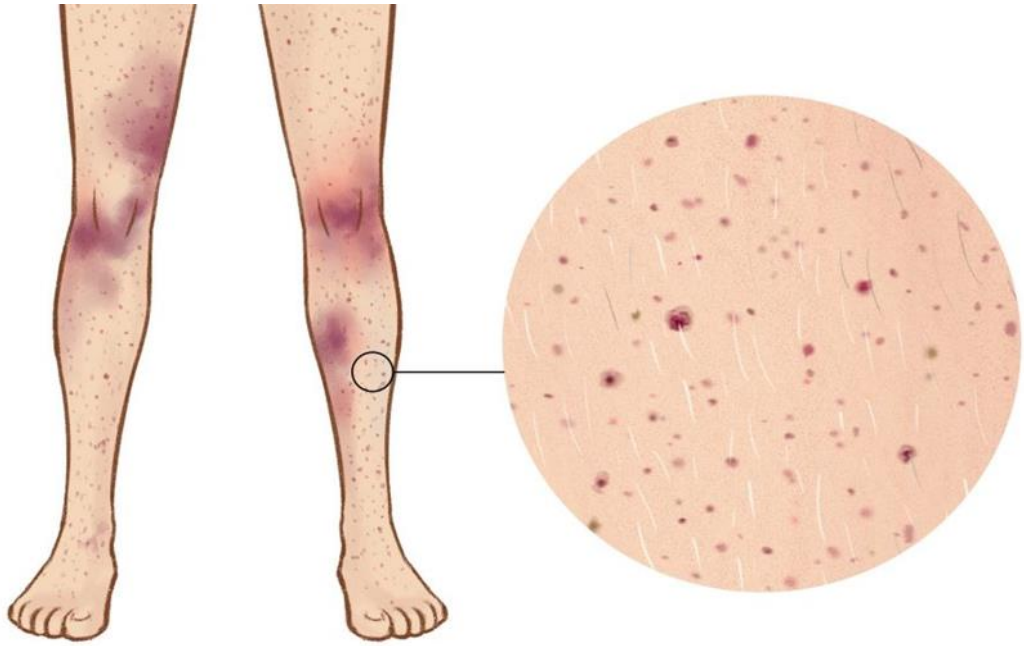
➢ Scurvy (Vitamin C deficiency)

- Deficiency of vitamin C (ascorbic acid) causing abnormal synthesis of collagen
- The human body lacks the ability to synthesize vitamin C and only depends on exogenous dietary sources of vitamin C
- The body's pool of vitamin C can be depleted in 1-3 months
- Clinically: cause bleeding especially perifollicular and petechial haemorrhage, bruising and subperiosteal bleeding
- **Treatment:** vitamin C supplementation

Scurvy


Subperiosteal Hemorrage
Scorbutic Zone
(Trümmerfeld's zone)
Dense Zone of
Provisional Calcification
(White line of Frankel)
Ring Epiphysis
(Wimberger's ring)
Pelken's Spur





2) **Platelet disorders** Normal platelet count = 150 – 400

- Abnormalities of platelet function

- Abnormal low platelet counts (thrombocytopenia)

A. Abnormalities of platelet function

Acquired disorders

- Drug: aspirin, clopidogrel, ticagrelor, dipyridamole
- Uremia
- Paraproteins
- Fibrin degradation products
- Myelodysplasia or a myeloproliferative syndrome

Congenital abnormalities

- Disorders of platelet adhesion (von Willebrand disease, Bernard-Soulier syndrome)
- Disorders of aggregation (Glanzmann thrombasthenia)
- Disorders of secretion
- Disorders of thromboxane synthesis

B. Thrombocytopenia can be can be due to :

1) increased destruction

(1) immune thrombocytopenia (eg, autoimmune, drug-induced)

(2) increased consumption (eg, DIC diffuse/disseminated intravascular coagulation, TTP thrombotic thrombocytopenic purpura)

2) decreased production

Bone marrow failure, such as aplastic anemia, infiltration by leukemia or another malignancy, fibrosis or granulomatous disorders, or tuberculosis

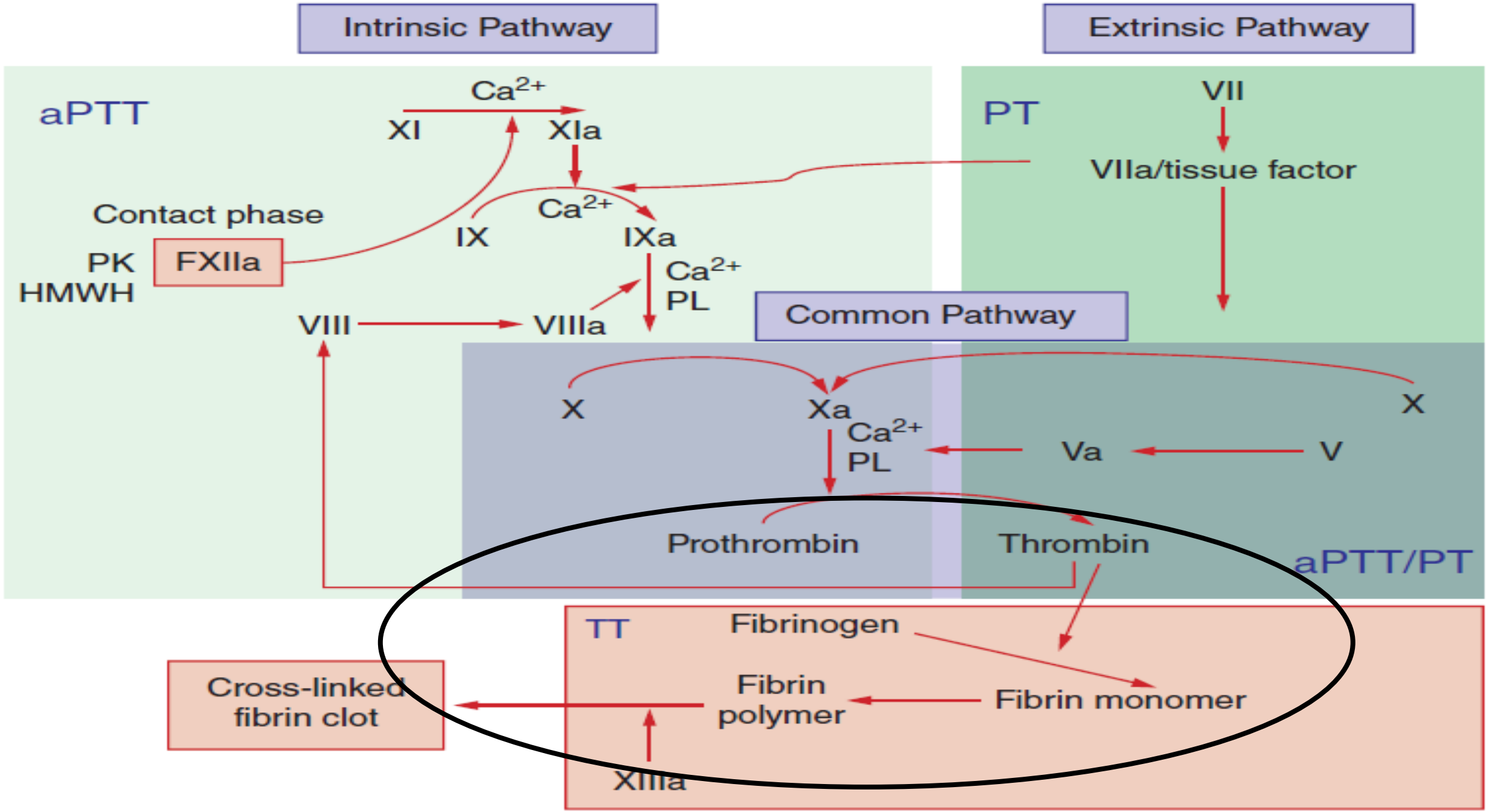
Clinical features and investigations

- The presentation depends on the degree of thrombocytopenia
- Spontaneous bleeding typically occurs only when the platelet count is below $20 \times 10^9/L$
- At higher counts, the patient may complain of easy bruising or sometimes epistaxis or menorrhagia
- Many cases with counts of more than 50 × 109/L are asymptomatic and discovered by chance

Management

1. Most patients are asymptomatic with count of >30 × 109/L and not require treatment except at of surgery
2. First-line therapy for patients with spontaneous bleeding is with high doses of glucocorticoids, either prednisolone (1 mg/kg daily) or dexamethasone (40 mg daily for 4 days), to suppress antibody production and inhibit

3. IV immunoglobulin can raise the platelet by blocking antibody receptors on reticulo-endothelial cells
4. life-threatening bleeding should be treated with platelet transfusion
5. If refractory disease, second-line therapies include the thrombopoietin receptor agonists (TPO-RA), splenectomy and immunosuppression


Intrinsic Pathway
Extrinsic Pathway
aPTT
PT
Ca2+
XI
XIa
VII
VIIa/tissue factor
Contact phase
PK
HMWH
FXIIa
IX
Ca2+
IXa
Ca2+
PL
VIII
VIIIa
Common Pathway
X
Xa
X
Ca2+
PL
Va
V
Prothrombin
Thrombin
aPTT/PT
TT
Fibrinogen
Cross-linked
fibrin clot
Fibrin
polymer
Fibrin monomer
XIIIa

3) Coagulation disorders

- Congenital
- Acquired

Haemophilia A

- Factor VIII deficiency
- A affects 1/10 000 individuals
- Factor VIII is primarily synthesised by the liver and endothelial
- It is protected from proteolysis in the circulation by binding to von Willebrand factor (vWF)
- Factor VIII gene is on the X chromosome, haemophilia A is a sex-linked disorder (Male affected and female is a carrier)

Clinical features

- Spontaneous bleeding into skin, muscle and joints
- Retroperitoneal and intracranial bleeding is also a feature
- Babies with severe haemophilia have an increased risk of intracranial haemorrhage
- In severe haemophilia is bleeding is typically into large joints (knees, elbows, ankles and hips)

Hemophilia B (Christmas disease)

- Aberrations of the factor IX gene
- X link inheretance
- Deficiency of IX level

Management

- Coagulation factor replacement of factor VIII

Von Willebrand disease

- is a mild bleeding disorder caused by a quantitative or qualitative defect of von Willebrand factor (vWF).
- Female> male
- Patients present with haemorrhagic manifestations similar to those in individuals with reduced platelet function
- Superficial bruising, epistaxis, menorrhagia and gastrointestinal haemorrhage are common.
- Bleeding episodes are usually much less frequent

Treatment

- Mild haemorrhage can be treated by local pressure
- Desmopressin which raises the vWF
- Tranexamic acid

Acquired bleeding disorders

- DIC

  is an important cause of bleeding that begins with exaggerated and inappropriate intravascular coagulation. It is discussed under thrombotic disease

- Liver disease

  There is reduced hepatic synthesis, for example, of factors V, VII, VIII, IX, X, XI, prothrombin and fibrinogen

- Renal failure

  Bleeding are due to of platelet dysfunction

- Vitamin K deficiency
- Warfarin therapy
- Antibodies against factor VIII (or other factors)
- Massive transfusion

Thank you