PRESENTATIONS OF INHERITED BLEEDING DISORDERS IN CHILDREN

DR MIRABELLE AKWAUGO ANOLUE (FMCPaed)
CONSULTANT PAEDIATRICIAN
DEPARTMENT OF PAEDIATRICS, UNIVERSITY OF PORTHARCOURT TEACHING HOSPITAL.

OUTLINE

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- OVERVIEW OF HAEMOSTASIS
- TYPES OF INHERITED BLEEDING DISORDERS
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INTRODUCTION

- Haemostasis relies on a complex series of events and interaction between the blood vessels wall, platelets and coagulation factors to arrest bleeding.
- Bleeding disorders can be classified into inherited (congenital) and acquired.
- Inherited bleeding disorders are further classified into disorder of primary haemostasis and disorder of secondary haemostasis

INTRODUCTION

- Inherited Bleeding Disorders can be defined as hereditary clotting factor deficiencies. Mode of inheritance can be X-linked as in factor VIII and IX deficiency or autosomal dominance/recessive as in factor XI and Von Willebrand's Disease (vWD).

- The role of the Paediatrician in evaluating bleeding disorders in children is to ascertain whether the patient's symptoms are appropriate to the haemostatic stress or a further laboratory investigation is warranted to determine the cause. So a high index of suspicion is paramount in making the diagnosis

OVERVIEW OF HAEMOSTASIS

- Haemostasis which is the arrest of bleeding from a site of vascular injury is divided into

1. Primary Haemostatic response
2. Secondary Haemostatic response

- Primary haemostasis is triggered by endothelial damage following a vascular injury and the sequential and overlapping phases include VASOSPASM, PLATELET ADHESION TO THE OVERLYING COLLAGEN induced by vWF, PLATELET ACTIVATION AND AGGREGATION.

- The end result is the formation of a PLATELET PLUG which forms a primary clot and arrest of bleeding, this is however short lived.

- Secondary haemostasis sets in to provide a permanent stoppage of the bleeding via the coagulation cascade.

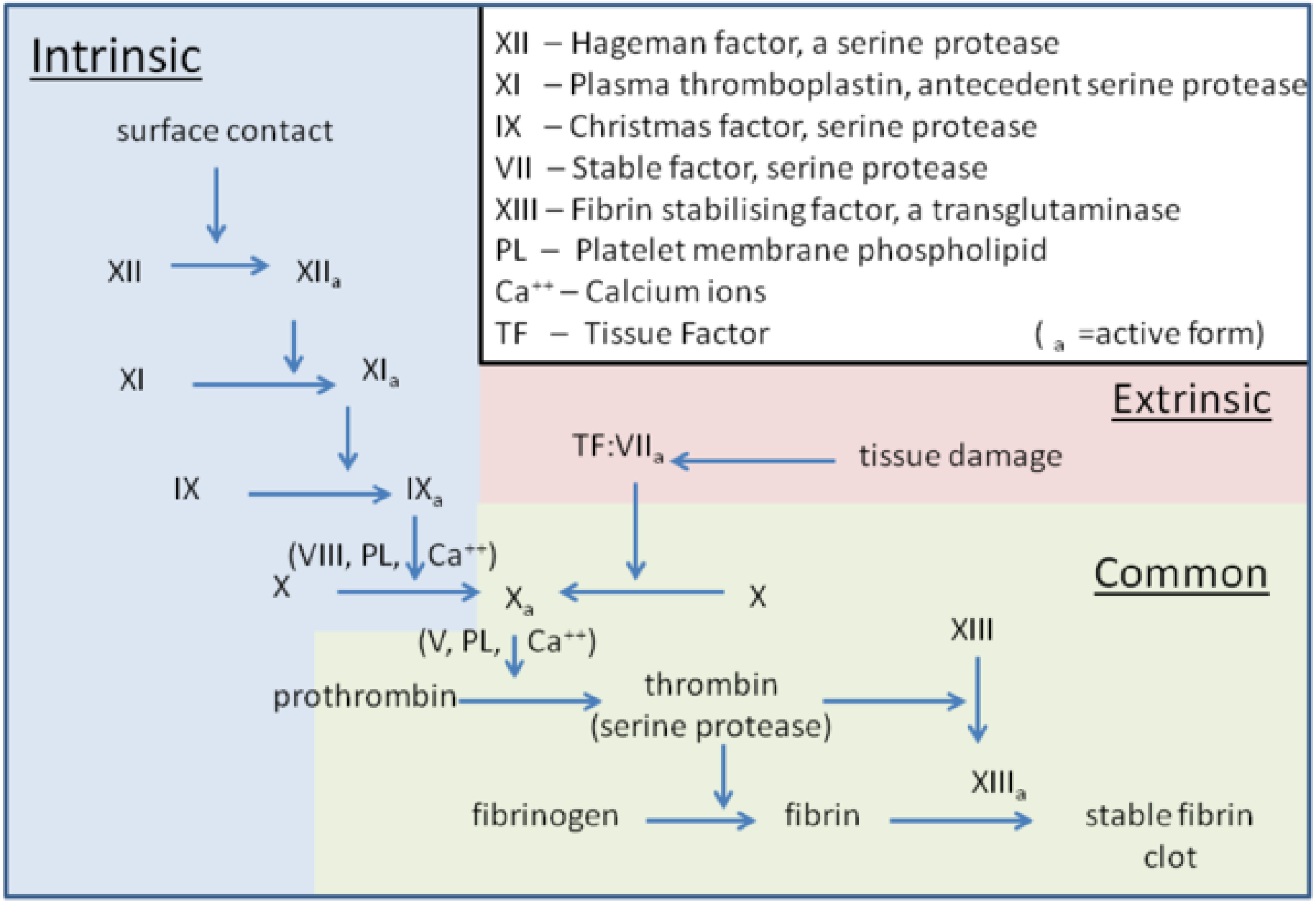
- It involves a series of serine protease zymogens and their cofactors which interacts sequentially on phospholipid surfaces (platelets or damaged endothelial cells) and result in formation of FIBRIN which stabilizes and reinforce the platelet plug.

- The interaction of activated platelets and the clotting cascade gives rise to a haemostatic response that is potentially explosive and if unchecked can give rise to thrombosis and tissue damage

- Coagulation is modulated by a number of mechanism which include removal of activated factors by the Reticuloendothelial system and the fibrinolytic pathway.

- This restores vessel patency following haemostasis , the end product is PLASMIN which is a proteolytic enzyme that degrades fibrin resulting in the formation of fibrin degradation products including D – dimers.

The three pathways that makeup the classical blood coagulation pathway



Classification

Due to Disorder of Coagulation

- Hereditary
  - X-linked recessive trait
    - Haemophilia-A
    - Haemophilia-B
  - Autosomal recessive trait
    - Afibrinogenemia
    - Factor XIII deficiency
  - Autosomal Dominant trait
    - Von-Willbrand Disease
- Acquired
  - Haemorrhagic disease of new born
  - Biliary obstruction
  - Malabsorption of Vitamin K
  - Drugs
  - Liver disease
  - DIC

CLINICAL PRESENTATIONS OF INHERITED BLEEDING DISORDERS IN CHILDREN

- Helpful clinical features to evaluate a bleeding child will include
  - A good medical history of the child
  - Physical examination
  - Laboratory testing

- Features to look out for will include
  - Age of onset: is it in the newborn, a previous dental extraction/surgery without bleeding connotes that bleeding tendency is acquired rather than inherited
  - Sex: Male gender are more likely to have clinical manifestation of haemophilia while female are carriers.

- Family history: A positive family history of bleeding in members is significant particularly for X-linked coagulation disorders like haemophilia.

- Site and type of bleeding

- Mucous membrane bleeding and skin haemorrhages are characteristic of platelet disorders or von Willebrand's disease

- Bleeding into joints and muscles are suggestive of severe coagulation disorders like haemophilia.

- Scarring and delayed bruising is characteristic of factor XIII deficiency or connective tissue disease

CLINICAL PRESENTATIONS

- May go undiagnosed in the newborn in the absence of a positive family history because the patient is asymptomatic
- Bleeding symptoms may be present at birth, it could be sudden and spontaneous or prolonged. Can present with bleeding under the scalp (19.4%), bleeding from heel sticks punctures (10.4%)
- 2% of neonates with haemophilia sustain intracranial haemorrhage following birth trauma.
- 47.9% of male infants with haemophilia bleed with circumcision (post circumcision bleeding)

- Bleeding from a minor traumatic laceration of the mouth (e.g. a torn frenulum) may persist for hours or days. This cause the parents to seek for medical evaluation.

- Obvious symptoms become evident when the babies start crawling and cruising by six to nine months.

  - Easy bruising
  - Petechiae
  - Epistaxis (unrelieved by 15minutes of pressure along the entire sides of the nose)
  - Intramuscular hematoma
  - Hemarthroses (bleeding into the joints) can occur after a minor trauma or spontaneous. This is the hallmark of haemophilic bleeding

- Earliest joint swelling appear most commonly in the ankle
- In older children and adolescent, hemoarthroses of the knee and elbows are common.
- They complain of a warm tingling sensation in the joint, this is the first sign followed by swelling and fluid accumulation in the joint space.
- Repeated bleeding episodes into the same joint leads to a target joint.
- Joint bleeding if left untreated may progress to chronic synovitis and eventual crippling arthropathy.

- Bleeding into the iliopsoas muscles → muscular haemorrhage can cause localized pain an swelling and also lead to → Hypovolaemic shock.
- The hip is held in a flexed, internally rotated position due to irritation of the psoas muscles
- Life threatening bleedings into vital organs like the
  - Central nervous system → seizures, intracranial haemorrhage or cerebrovascular accident (CVA).
  - Exsanguination from gastrointestinal (GIT) bleeding
  - Abdominal pains, dark or bloody stools and haematemesis signifies GIT bleeding from oesophageal varices.

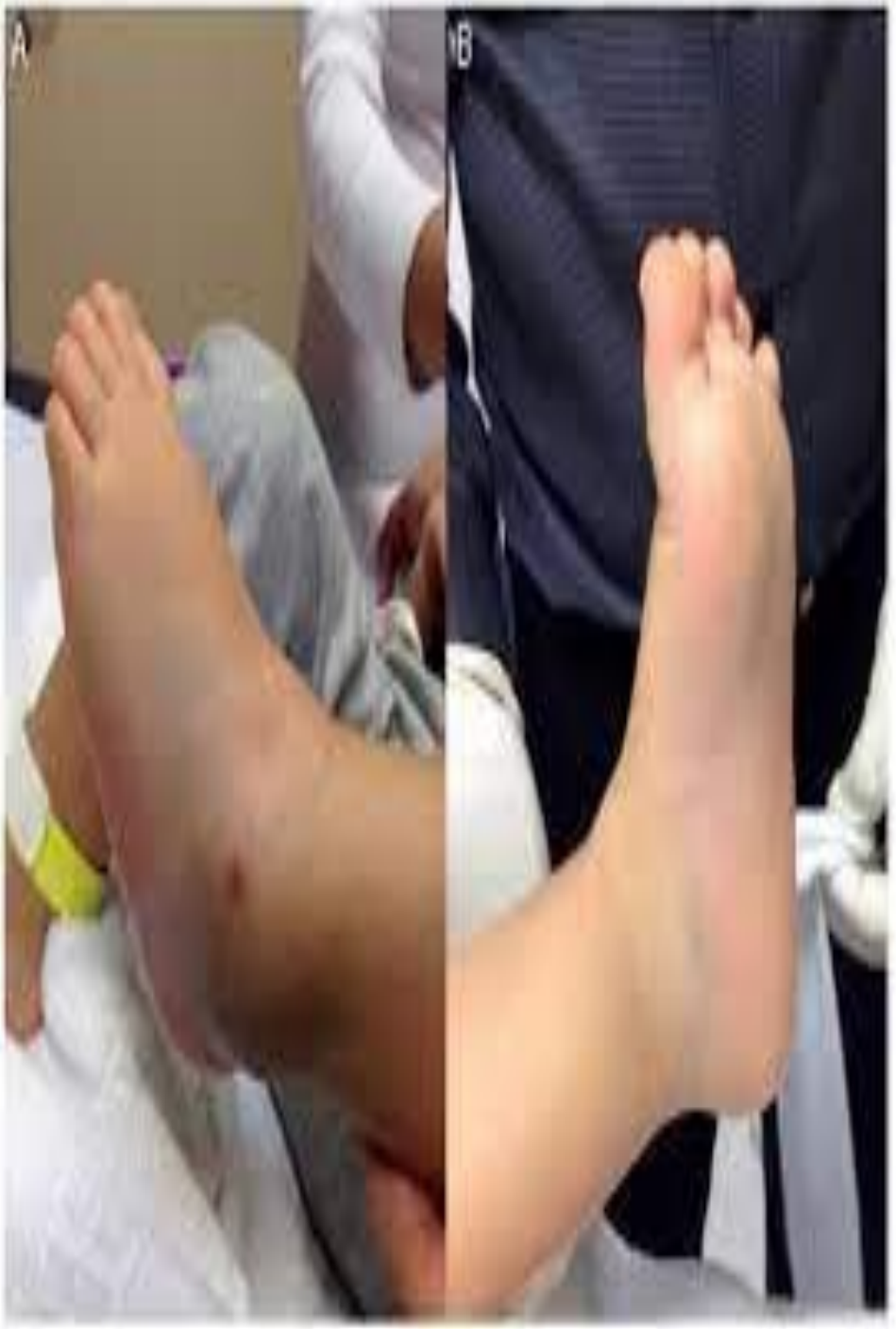
- Menorrhagia in females with Von willibrand disease (vWD).Heavy menstrual flow with clots lasting beyond 7 days
- Prolonged bleeding can occur after a dental work or surgery lasting more than 24 hours. This may require blood transfusion
- Ecchymosis of a size or character incompatible with degree of reported trauma
- It is imperative to treat life threatening haemorrhage promptly with clotting factor concentrates. Treat first, Image second.

PHYSICAL EXAMINATIONS

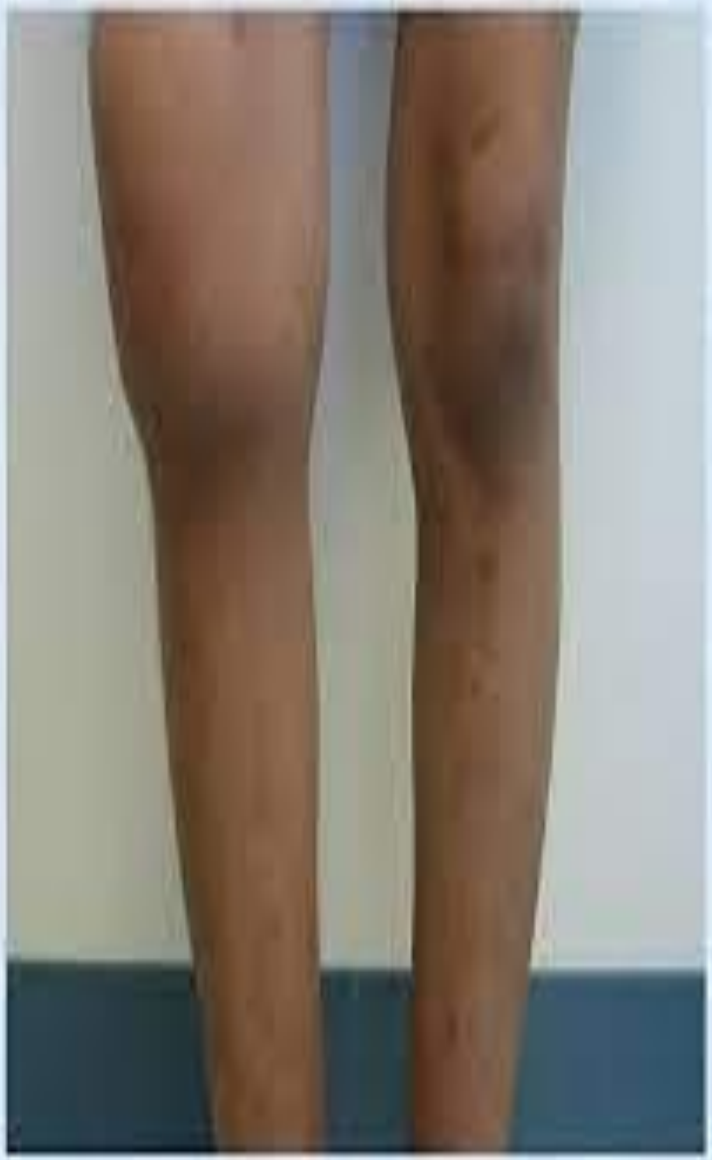
- They may appear pale
- Evidence of bleeding such as petechial haemorrhages, purpura, Ecchymosis
- Mucous membrane haemorrhages
- Gingival bleeding
- Joint swellings

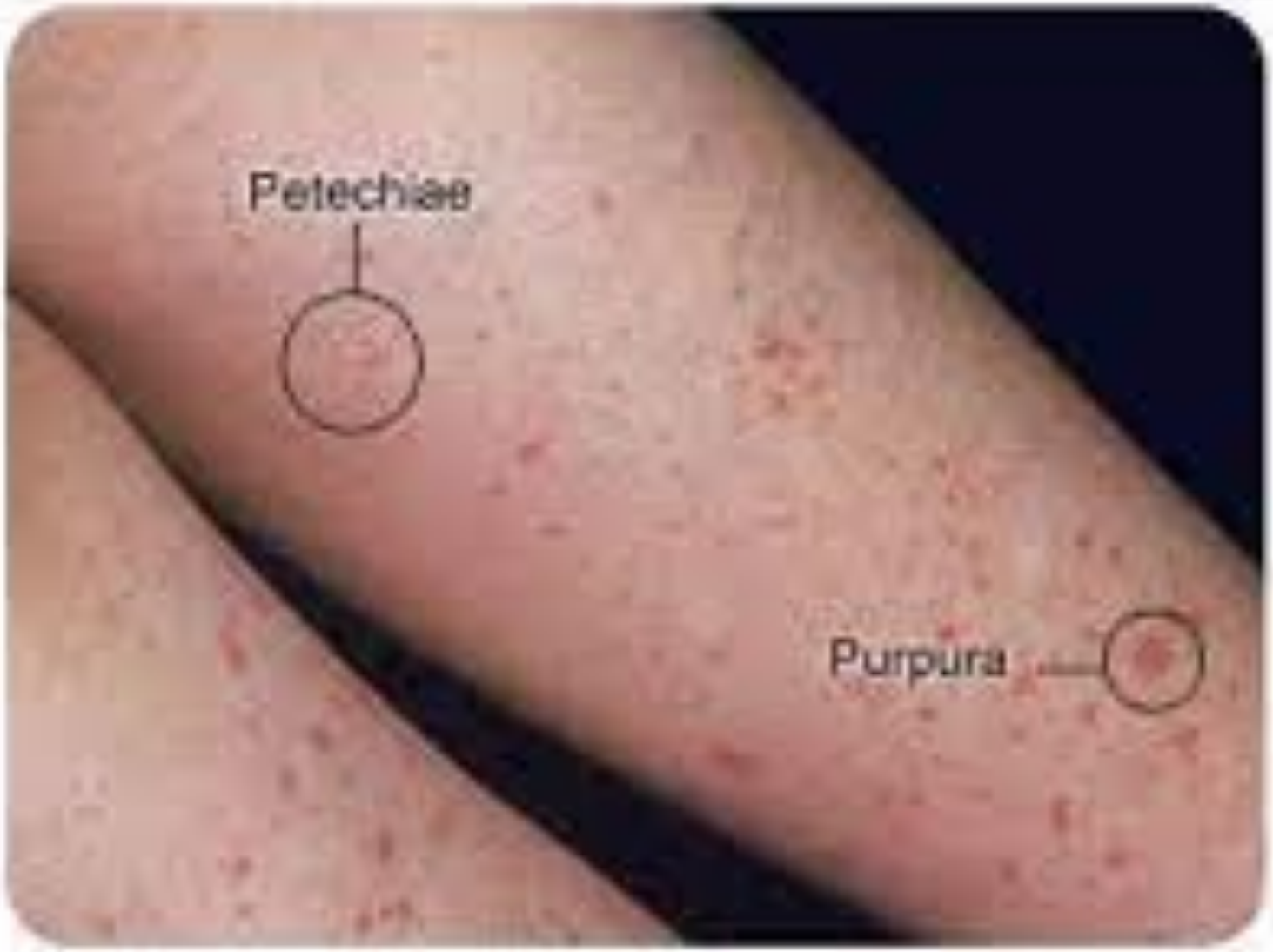
PHYSICAL EXAMINATION

- Deep muscle haematomas
- Haematemesis
- Haematuria
- Evidence of bleeding in the conjunctiva, oral mucosa and optic fundi



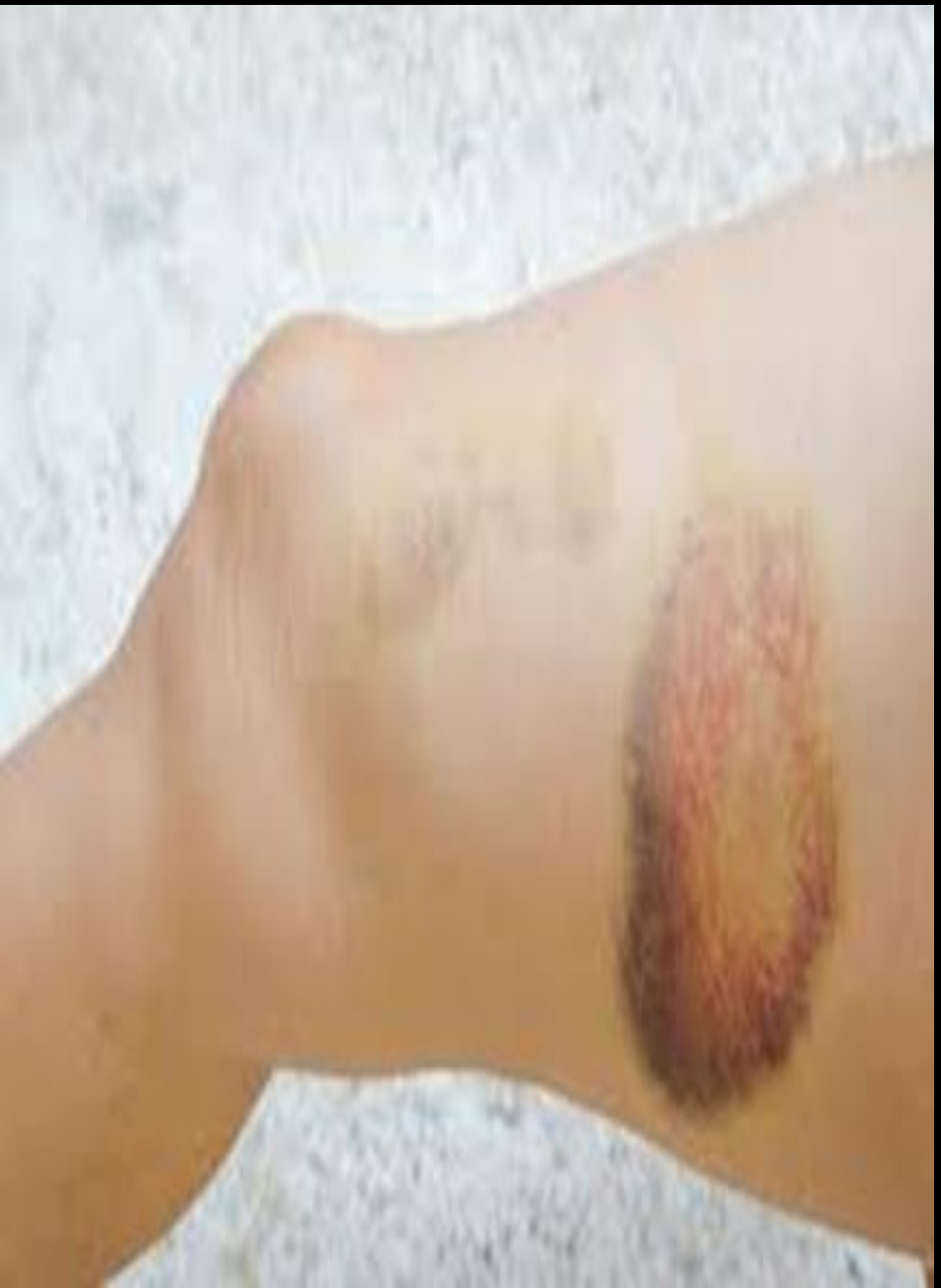
Hemarthrosis (acute)



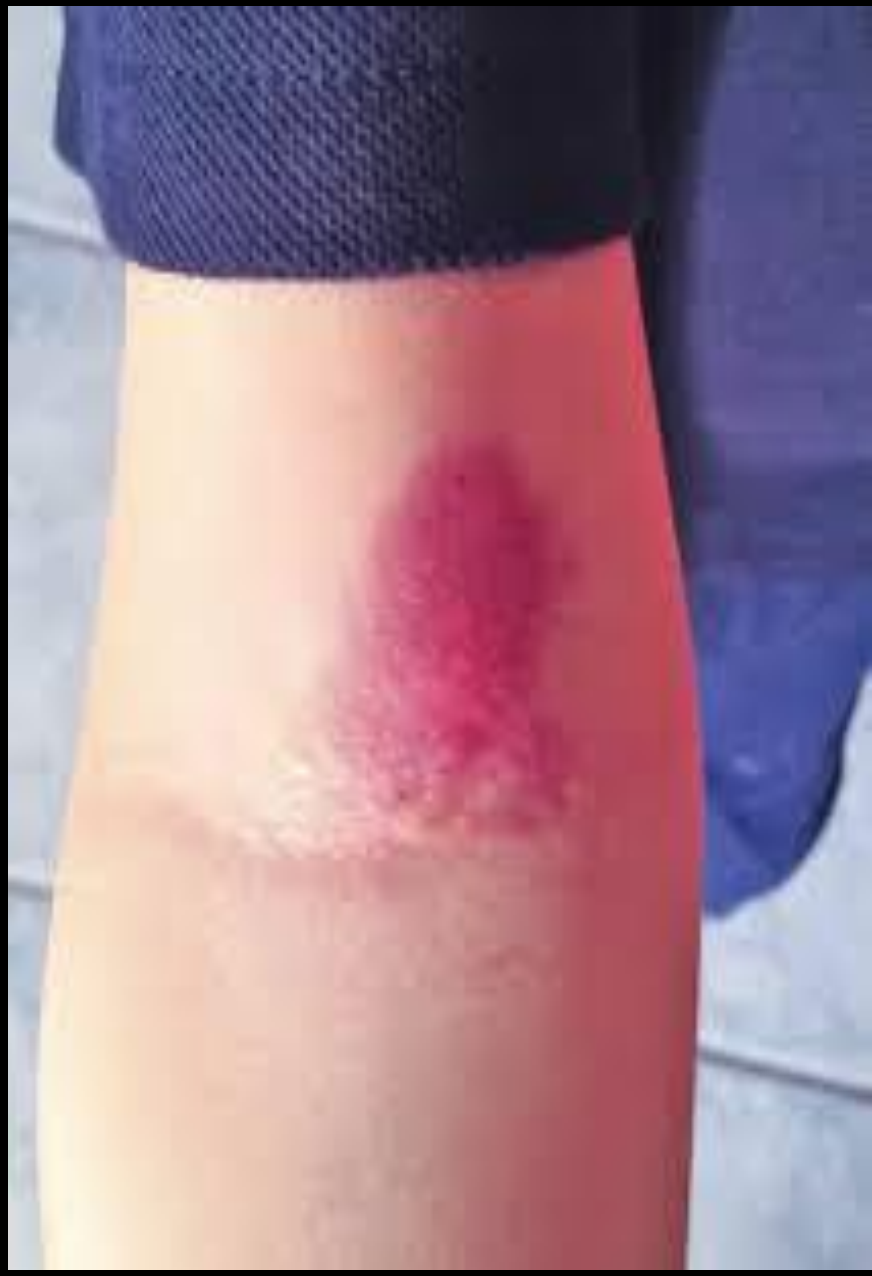


Petechiae	1-3mm
Purpura	3mm-10 mm
Ecchymosis	>10mm

- Deep muscle haematoma



- Swollen bruise and bleed



HAEMOPHELIA BLEEDING SYMPTOMS

VON WILLEBRAND DISEASE

SYMPTOMS

- Bleeding
- Blood in urine
- Easy bruising
- Excessive bleeding during childbirth
- Heavy or prolonged peroids
- Mouth bleeding
- Nose bleeding
- Tendency to bleed easily
- Dental procedure
- Irregugular uterine bleeding

Symptom	Frequency
Hematomas	56%
Easy bruising	48%
Epistaxis	47%
Heavy Menses	45%
Hemarthrosis	38%
Gum bleeding	35%
Circumcision	30%
Umbilical cord	22%
ICH	17%
Hematuria	13%

TABLE 1.

Defects in the Clinical Presentation of Primary Versus Secondary Hemostasis

Primary Hemostasis[a]	Secondary Hemostasis[a]
Mucocutaneous bleeding Epistaxis	Delayed bleeding after surgery or a hemostatic insult
Menorrhagia	Deep tissue bleeding Intramuscular hematoma Hemarthrosis
Easy bruising	
Petechiae	

[a]Considerable overlap exists in the clinical presentation of primary and secondary hemostasis.
Adapted from Rajpurkar and Lusher.[3]

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