Hemorrhagic disorder

Learning Objectives

At the end of lecture student should be able to know :

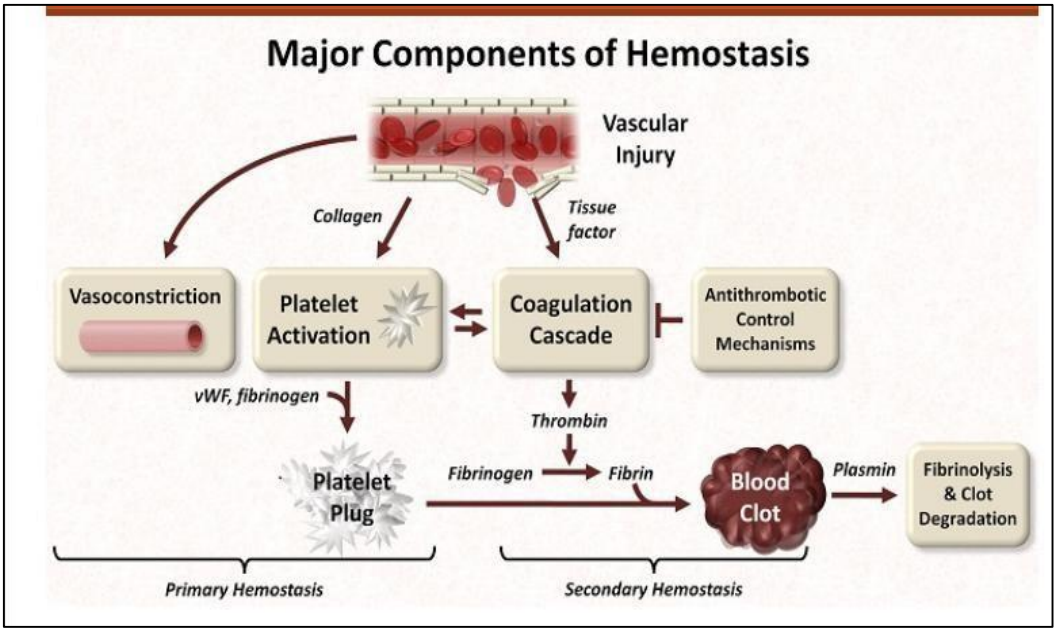
- *The approach to a child who presents with bleeding tendency through:*
  - *Clinical history and physical examination*
  - *Laboratory investigations and its interpretation*
  - *Important lines of treatment*

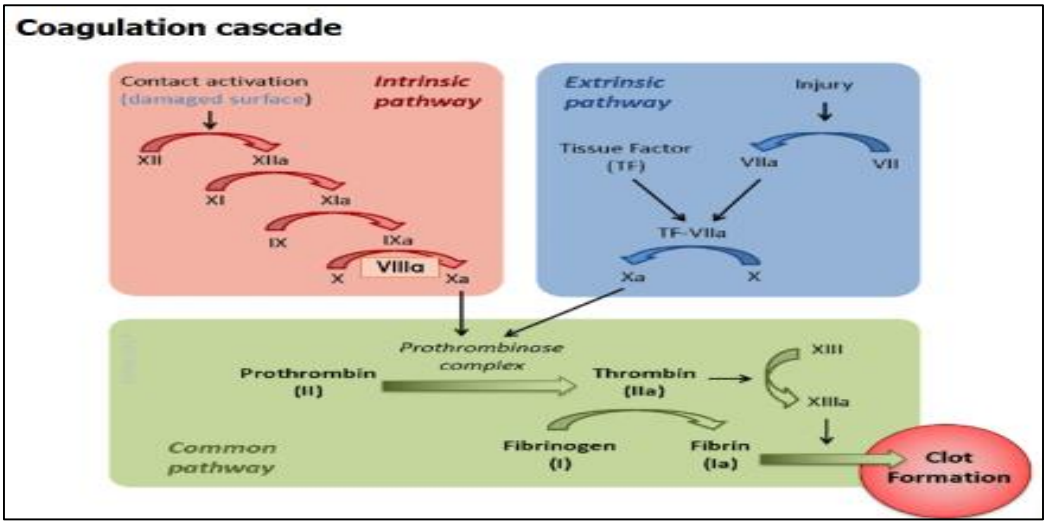
- **Hemorrhagic disorder**: is a condition characterized by excessive bleeding due to defect in one or more components of the hemostatic system
- **Hemostasis: i**s the process of appropriate physiologic response to vascular injury that provides prompt control of blood loss

- **Physiology of Hemostasis**

As a result of injury to the blood vessel endothelium, three events take place concurrently:

1. **Vasoconstriction** (vascular phase).
2. **Platelet plug formation** (primary hemostatic mechanism—platelet phase).
3. **Fibrin thrombus formation** (coagulation cascade-secondary hemostatic mechanism)





Evaluation of a patient for a hemostatic defect generally include the following :

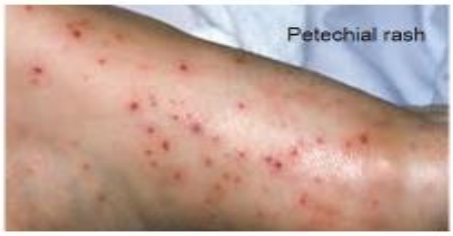
1. Detailed history

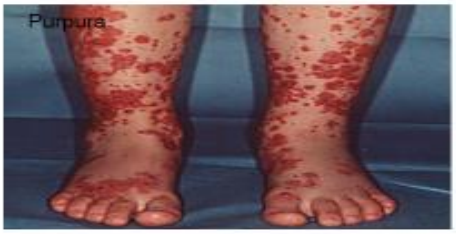
Site of bleeding	Epistaxis, gingival bleeding, easy bruising, menorrhagia, hematuria, gastrointestinal (GI) bleeding, hemarthrosis, hematoma ,prolonged bleeding after intramuscular injection or surgery dental procedures,
Spontaneous bleeding	Spontaneous or after trauma, severity of trauma and duration between trauma and developing of bleeding
Medications	Antiplatelet drugs ,NSAID, anticoagulants (warfarin, heparin, prolonged use of antibiotics causing vitamin K deficiency,
Underlying medical conditions	e.g. liver disease, renal failure, malabsorption
Personal history Family history	Recurrent bleeding or known bleeding disorder

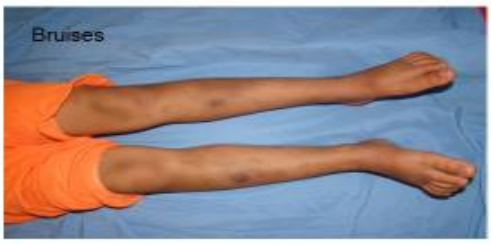
2. Physical examination

The physical examination should focused on whether bleeding symptoms are:

- **Mucous membranes or skin (mucocutaneous bleeding)**
- **Muscles and joints (deep tissue bleeding)**







- **Ecchymosis** (bruises): are large area 1 to 2 cm in size or more.
- **Petechiae**: pinpoint non raised lesion<2 mm
- **Purpura** : (>3 mm)red to purple ,group of adjoining petechiae
- **Hematomas** : have a more diffuse elevated border than other purpura (raised palpable ecchymoses).

Localize the hemostatic defect

Clinical manifestation	Primary hemostasis (PLT disorder)	Secondary hemostasis (Coagulating factor)
Site of bleeding	Skin, mucous membrane	Deep in soft tissue and joint
Petechiae	yes	no
Echymosis	Small, superficial	Large, deep
Hemartherosis	no	common
hematoma	Rare	common

3. Laboratory evaluation

Initial screening tests:

- Complete blood count (CBC) :platelet count
- Bleeding time, Prothrombine time (PT) ,INR and partial Thromboplastin time (PTT)

Normal platelet count is 150-450 × 10^9/L

- **Thrombocytopenia** refers to a reduction in platelet count to <150×10^9/L
- **Thrombasthenia** referred to platelet dysfunction
- Defect in no. or function of plts. lead to bleeding disorder

Bleeding time (normal 4-8 min)

- **Bleeding time is prolonged in:**
  Platelet disorders(No. or function) and Von willebrand dz

Partial Thromboplastin Time (normal: 25-40 sec)

- Prolonged in deficiency of intrinsic pathway factors (II,V,VIII,IX,X,XI,XII) and common pathway

Prothrombine time (normal**:** 12-14 sec**)**

- Measure of extrinsic pathway (VII) and common pathway

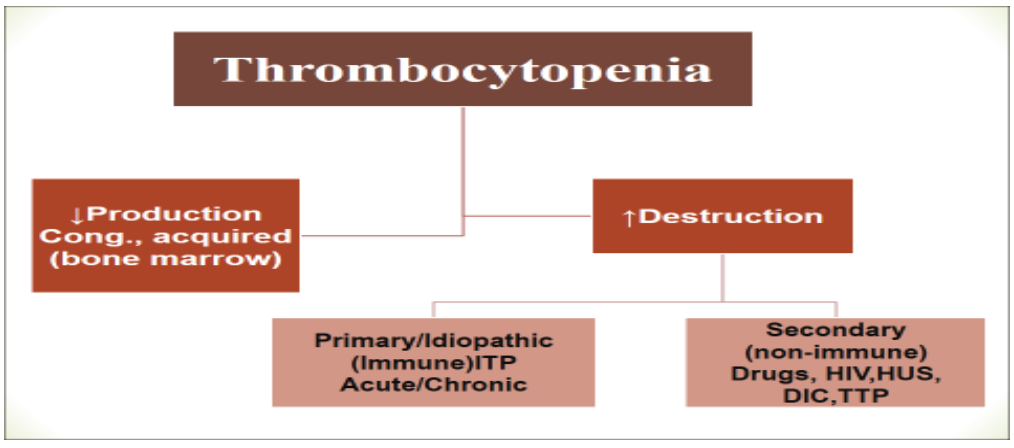
Thrombin time (normal 11-15 sec)

- test for deficiency or dysfunction of fibrinogen

In individuals with abnormal screening tests, further evaluation with specific should be based on those results:

- **PLT function test**
- **Mixing study**
- **VWAg and activity**
- **Fibrinolysis tests**
- **BM study**

Platelets disorder

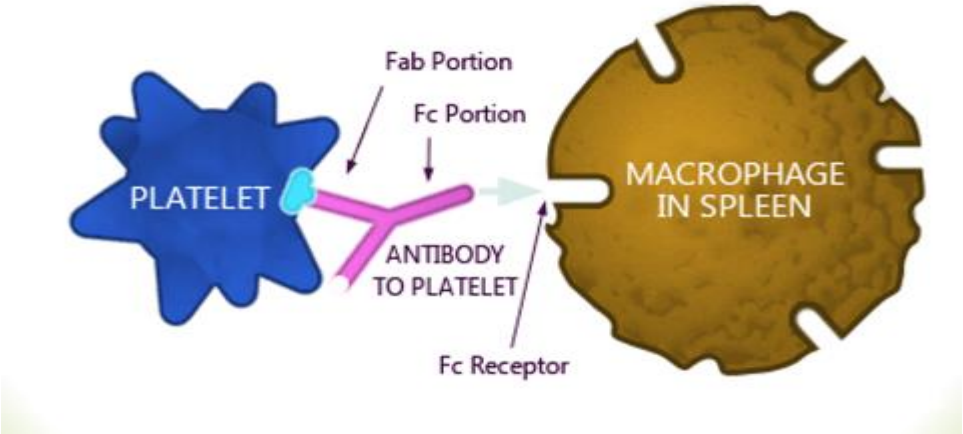


Immune Thrombocytopenic Purpura " ITP"

- ITP is the most common cause of acquired and acute thrombocytopenia in children of any age but with a peak occurrence between 2 and 5 years
- There is a seasonal pattern to ITP with a peak in late winter and early springtime, presumably mimicking the pattern of viral illnesses.
- There does not appear to be a race or sex predilection

Pathophysiology:

- An acute infection often is the initial trigger
- Antibody-mediated destruction
- Most identified autoantibodies are directed against the platelet surface
- Antibody-coated platelets are destroyed by activated Fc receptors on splenic macrophages lead to thrombocytopenia



Clinical Manifestations

- Typically, patients are otherwise well and present with abrupt onset petechiae, purpura, and ecchymoses 1-3 weeks after almost any viral infection
- Mucous membrane bleeding (muco-cutaneous bleeding)
- Physical examination are normal apart from signs of bleeding
- Pallor is usually absent unless there has been significant bleeding
- Absence of hepatosplenomegaly, lymphadenopathy

Diagnosis

- **CBC and blood film morphology**
  Revealed isolated thrombocytopenia with otherwise completely normal CBC and blood smear (particularly red cell and white cell morphology)

- **Bone marrow aspiration and biopsy indicated when there is** :
  - Unexplained anemia
  - Abnormal WBC count or differential
  - Organomegaly or lymphadenopathy

- **Finding:** Increased numbers of megakaryocytes, some are appear to be immature reflective of increased platelets turnover

Treatment:

- Treatment The goal of therapy in ITP is to increase the platelet count enough to prevent serious hemorrhage
- Plts count > 20.000 c/mm³ to decreased risk of spontaneous and life threatening bleeding
- Intracranial hemorrhage which increase when plt < 10.000 c/mm³

Therapy:

1. Intravenous immunoglobulin(IVIG):

- Dose 0.8-1 g/kg/day for 1-2 days induces a rapid rise in plt count (usually >20.000c/mm) in 95% of patients within 48 hr.
- **Side effect:** headache, vomiting, suggestive of aseptic meningitis.
- IVIG appear to induce a response by downregulating Fc-mediated phagocytosis of antibody-coated platelets

2. Prednisone (corticosteroid therapy):

- In a dose 1-4 mg/kg/day continued for 2-3 wks with taper to avoid the long term side effect of corticosteroid therapy(especially growth failure ,DM and osteoporosis)
- **Mechanism of action of steroids:**
  - Inhibit the phagocytosis of antibody-coated platelets.
  - Inhibit platelet antibody production

Note

- Plt. Transfusion is contraindication in ITP only in life threatening bleeding. Because anti plt antibodies bind to transfused plt as well as they do to autologus plt so will lead to more plt destruction that cause more thrombocytopenia

Chronic ITP

- Patient with acute ITP who have persistent thrombocytopenia for > 12 month are said to have chronic ITP (20%)
- Should exclude secondary causes of chronic ITP e.g. SLE, HIV, immunodeficiency , H.pylori

Medical therapy in chronic ITP :

- IVIG,corticosteroid,IV antiD
- Rituximab
- Agents that stimulate thrombopoiesis:
  - Romiplostim(Nplate)
  - Eltrombopag

Role of splenectomy in ITP:

The role of splenectomy in ITP should be reserved for 2 circumstances:

- The older child ≥ 4 yr with severe chronic ITP. and whose symptoms are not easily controlled with therapy

- When life-threatening hemorrhage (ICH) complicates acute ITP, if the PLTs count cannot be corrected rapidly with transfusion of PLTs and administration of IVIG and corticosteroid

References

- **Nelson Textbook of Pediatrics**
- **Nelson essentials Textbook of Pediatrics**
- **Illustrated textbook of pediatrics**