HAEMORRHAGIC DIATHESES DUE TO VASCULAR DISORDERS

- Vascular bleeding disorders, also called non-thrombo-cytopenic purpuras or vascular purpuras,
- characterised by petechiae, purpuras or ecchymoses.
- may be inherited or acquired

Inherited Vascular Bleeding Disorders

1. **Hereditary haemorrhagic telangiectasia (Osler-Weber-Rendu disease):**

- Autosomal dominant disorder
- characterised by abnormally telangiectatic (dilated) capillaries
- Bleeding can occur through mucous membranes of the nose (epistaxis), tongue, mouth, and eyes and throughout the gastrointestinal tract.

2. Inherited disorders of connective tissue matrix:

Have fragile skin vessels and easy bruising.

- **Marfan's syndrome**: defective fibrillin
- **Ehlers-Danlos syndrome**: defective collagen synthesis
- **Pseudoxanthoma elasticum**: fragmentation and mineralisation of elastic fibres.

Acquired Vascular Bleeding Disorders

1. **Henoch-Schönlein purpura**

- hyper-sensitivity vasculitis
- Circulating immune complexes are deposited in the vessel wall consisting of IgA, C3 and fibrin
- purpuric rash on the extensor surfaces of arms, legs and buttocks
- Haematuria due to acute nephritis
- Bleeding into the GIT

2. Infections: Meningococcemia, rickettsia and infective endocarditis.
3. Drug reaction: Penicillin- leucocytoclastic vasculitis.
4. Steroid purpura:

- Long-term steroid therapy or Cushing's syndrome
- defective vascular support.

5. Senile purpura: Atrophy of the supportive tissue of cutaneous blood vessels in old age.
6. Scurvy: defective collagen synthesis.
7. Amyloid infiltration of blood vessels: perivascular deposition of amyloid and consequent weakening of blood vessel wall

HAEMORRHAGIC DIATHESES DUE TO PLATELET DISORDERS

Platelets produce bleeding disorders by one of the following 3 mechanisms:

- Due to reduction in the number of platelets i.e thromboyctopenia
- Due to rise in platelet count i.e. thrombocytosis.
- Due to defective platelet functions.

THROMBOCYTOPENIAS

Thrombocytopenia may result from 4 main groups of causes:

1. Impaired platelet production.
   - Aplastic anaemia
   - Megaloblastic anaemia
   - Leukemia
2. Accelerated platelet destruction
   - Immune- ITP, SLE, Post transfusional
   - Non-immune- TTP, HUS, DIC
3. Splenic sequestration/hypersplenism- splenomegaly
4. Dilutional loss- massive blood transfusion.

Immune Thrombocytopenic Purpura (ITP)

- **Primary/ Idiopathic ITP**
  - Acute ITP
  - Chronic ITP
- **Secondary ITP**
  - SLE
  - AIDS
  - Viral infections
  - Drugs

Acute ITP

- frequently seen in children, M=F
- following viral illness (e.g. hepatitis C, infectious mononucleosis, CMV infection, HIV infection) or an upper respiratory illness.
- Interval between onset of purpura and infection is 2 weeks.

Mechanism-

- immune complexes containing viral antigens
- formation of antibodies against viral antigens which cross react with platelets and lead to their immunologic destruction.
- Self- limiting course (6 months)
- Steroid- if thrombocytopenia is severe.

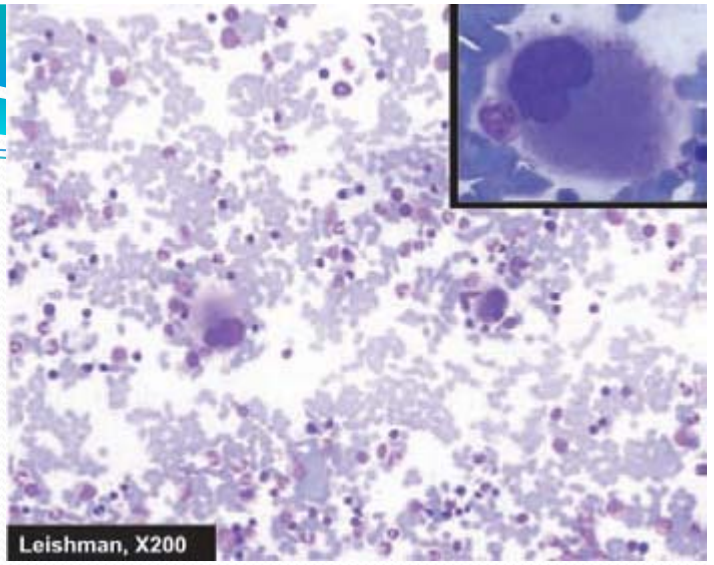
Chronic ITP

- Adults, particularly in women of child-bearing age.
- **Pathogenesis:**
- Anti-platelet autoantibodies- IgG class against Gp IIb-IIIa and Gp Ib-IX complex.
- Antibodies are synthesized in spleen
- Sensitised platelets are destroyed mainly in the spleen by cells of the reticuloendothelial system.

CLINICAL FEATURES

- petechial haemorrhages
- mucosal bleeding such as nasal bleeding, bleeding from gums, malena
- haematuria.
- Hepatospenomegaly.

LABORATORY FINDINGS



- Platelet count is markedly reduced, usually 10,000-50,000/µl.
- Blood film shows giant platelets.
- Bleeding time is prolonged with normal PT and aPTT.
- Bone marrow shows increased number of mega-karyocytes which have large non-lobulated single nuclei and may have reduced cytoplasmic granularity and presence of vacuoles.
- anti-platelet IgG antibody can be demonstrated on platelet surface or in the serum of patients.

Spleen:

- Usually normal in size
- Congestion of sinusoids
- Hyperplasia of splenic follicles with formation of germinal centres.
- Sometimes scattered megakaryocytes are present in sinusoids- milder form of extra-medullary hematopoiesis.

Treatment

- Steroids
- Immunosuppressive drugs
- Spleenectomy.

Drug-Induced Thrombocytopenia

- Result from immunologically mediated destruction of platelets after drug ingestion.
- In most cases, an immune mechanism by formation of drug-antibody complexes is implicated.
- The drugs most commonly involved are quinine, quinidine, sulfonamide antibiotics, and heparin

Heparin-induced Thrombocytopenia

Type-I Heparin-induced Thrombocytopenia:	Type-II Heparin-induced Thrombocytopenia
More common	Less common
occurs rapidly after onset of therapy	occurs 5 to 14 days after commencement of therapy
modest in severity	more severe
results from a direct platelet-aggregating effect of heparin	caused by an immune reaction directed against a complex of heparin and platelet factor 4, that activate platelets, promoting thrombosis
resolve despite continuation of heparin therapy.	Immediate discontinuation of therapy

HIV-Associated Thrombocytopenia

- Thrombocytopenia are most common complication of HIV.

Mechanism:

- **Decreased Platelet Production**:
  - CD4 receptors -target of HIV, has also been demonstrated on megakaryocytes.
  - Infected megakaryocytes are prone to apoptosis leading to decreased platelet production.
- **Increased Destruction:**
  - Antibodies directed against gp IIb-III complex is detected which cross react with HIV associated gp120
  - They act as opsonins and cause phagocytosis of platelets by splenic phagocytes