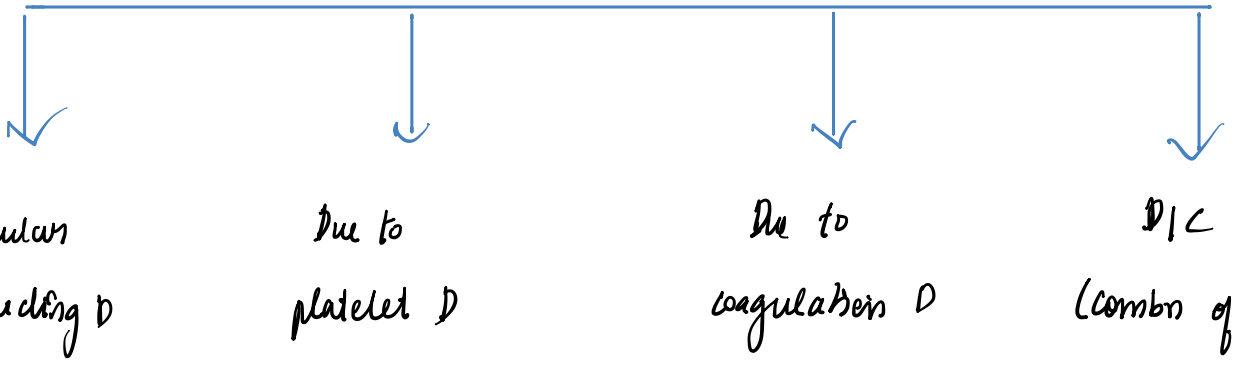
Bleeding disorders



Vascular bleeding D

Due to platelet D

Due to coagulation D

DIC (combn of factors)

1) Vascular bleeding D

Characterised by : Petechiae, purpuras, ecchymoses

Site : Skin & mucous memb

BT, CT, Plat. count, plat func : Normal

→ Inherited VBD

↳ Hereditory hemorrhagic telangiectasia (Osler. weber - Rendu disease)

* Autosomal dominant
* Abnormally dilated blood vessels
* Present with bleeding from stomach, epistaxis

↳ Inherited disorders of connective tissue matrix

→ Acquired VBD

↳ Henoch - schonlein purpura

↳ Infection

↳ Drug reactions

↳ Steroid purpura

↳ Senile purpura

↳ Scurvy

ii) Bleeding due to platelet disorders.

A) Redn in platelet count ie Thrombocytopenias

B) Rise in platelet count ie Thrombocytosis

C) Defective platelet functions

i) Thrombocytopenias

→ Below 1.5 lakhs / µl

→ Associated with abnormal bleeding, spontaneous cutaneous purpura & mucosal haemorrhages

→ Can be due to

* Impaired prodn

a) Generalised BM failure

- Aplastic anaemia, leukemia, myelofibrosis, megaloblastic anaemia

b) Selective suppression of platelet prodn

- Drugs (sulfonamides, PAS, rifampicin, anticancer drugs)

* Accelerated platelet destruction

a) Immunologic thrombocytopenias

- ITP, neonatal, and post-transfusion, drug induced, 2° immune thrombocytopenia (eg. AIDS, SLE)

ii) Increased consumption

- DIC, microangiopathic hemolytic anaemia

* Splenic sequestration

- Splenomegaly

* Dilutional loss

- Massive transfusion

* Inherited

IMMUNE THROMBOCYTOPENIC PURPURA (ITP)

* Idiopathic thrombocytopenic purpura (ITP)

* Immunological destruction of platelets

* Megakaryocytes seen in BM

Pathogenesis:

i) ACUTE ITP

- self limited
- seen commonly in children following a viral illness recovery (eg. hep c, HIV) or an upper resp illness.
- Onset sudden & severe
- Recovery occurs within weeks.
- Mechanism: forms of immune complexes

ii) CHRONIC ITP

- Commonly in adults
- W > M (20-40 yrs)
- Idiopathic
- may be seen associated with SLE, AIDS, AI thyroiditis
- Mechanisms:

form" of "anti-platelet autoantibodies"

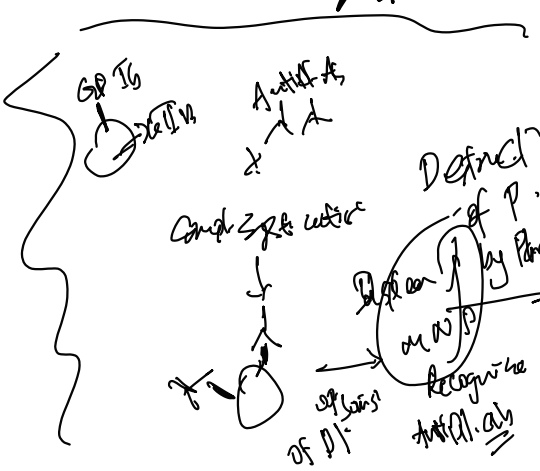
↓

by Platelet-associated IgG humoral Ab (in spleen)

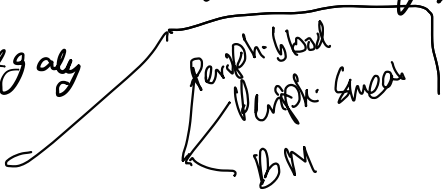
→ Type II hypersensitivity Rxn

Directed against Ag on platelet glycoproteins, GP IIb-IIIa & GP Ib-IX complex

Directed against surface antigens also



- Clinical features:
  - * Petechial hemorrhages
  - * Easy bruising
  - * Mucosal bleeding - nasal bleeding, gum bleeding, haematuria
  - * Splenomegaly & hepatomegaly



- Laboratory features:
  - * Platelet count ↓ (10k - 50k /μL)
  - * Blood smear shows only occasional platelets (often larger in size)
  - * BM shows ↑ed no. of megakaryocytes
  - * Antiplatelet- IgG Ab can be demonstrated on platelet surface

BT - ↑
CT
PT
APTT
} Normal

→ Treatment :

* Spontaneous recovery in Acute ITP
* Corticosteroid therapy, immunosuppressive therapy, splenectomy

→ Peripheral smear :

RBC - microcytic hypochromic anaemia

WBC - normal

Platelets - reduced, giant platelets

→ Bone marrow :

Cellularity : hypercellular

erythropoiesis : Iron def anaemia,

myelopoiesis : Normal

Megakaryopoiesis : Increased, both mature & immature form large cell with basophilic cytoplasm

Storage Fe : ↓

→ BT - Prolonged

CT - normal

HEMOPHILIA

Due to deficiency of factor VIII or reduced activity of factor VIII (Anti-haemophilic factor)

- X linked recessive trait
- Commonly in males, females - carriers
- Inheritance: Gene for factor VIII is on long arm of x-chromosome. Males with mutated factor VIII gene on x chromosome suffer from hemophilia - A
- Clinical features: hemarthrosis, prolonged bleeding, haemorrhage into soft tissue
- Lab findings:

  BT - normal CT - prolonged platelets - normal

  APTT - increased PT - normal

  (Intrinsic pathway)

  factor VIII assay - ↓ fibrinogen assay - normal
- Complications: deforming arthritis, anemia, hep B, C, D, AIDS

DISSEMINATED INTRAVASCULAR COAGULATION

- Defibrination syndrome / consumption coagulopathy
- Intravascular coagulation + haemorrhage
- As 2° complication

ETIOLOGY

* Massive tissue injury - eg. massive trauma, metastatic malignancies, surgery

* Infections : malaria, gram -ve & meningococcal septicaemia
* widespread endothelial damage : Severe burns, aortic aneurysm
* Miscellaneous : Snake bite, Shock, heat stroke

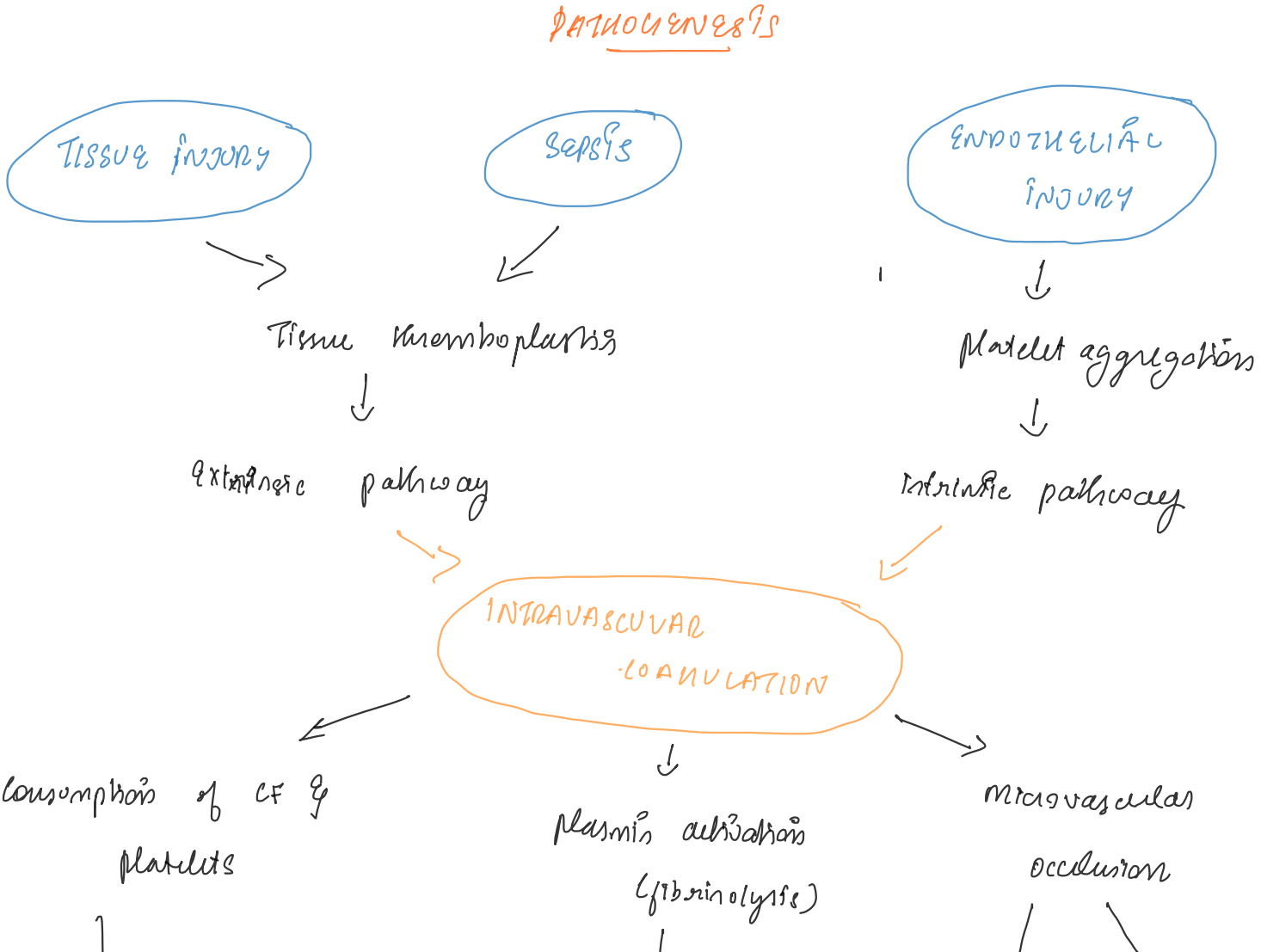
PATHOGENESIS

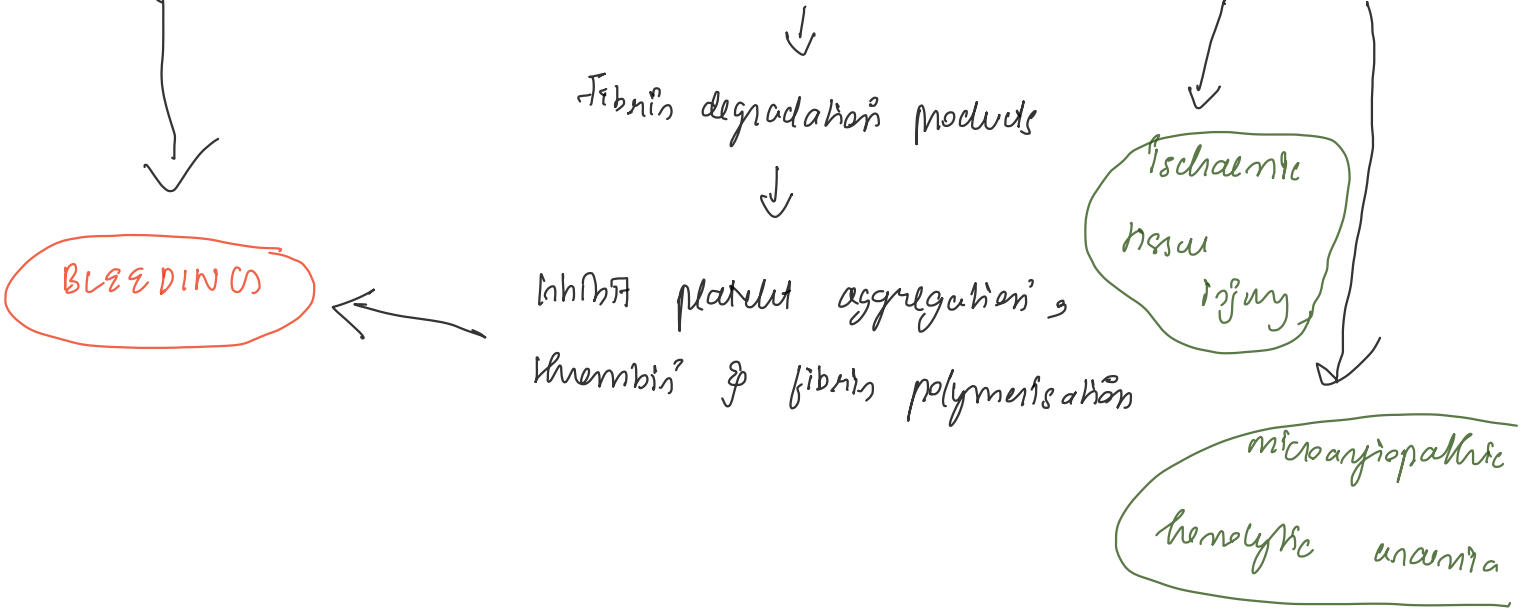
i) Activn of coagulation pathways by release of tissue factor

ii) Thrombotic phase : endothelial damage cause platelet aggregation & adhesion with resultant deposition of small thrombi & emboli throughout the microvasculature

iii) Consumption phase :

iv) 2° fibrinolysis





Laboratory findings :

* BT - ↑
* APTT - ↑
* Platelets - ↓
* Thrombin time - ↑
* PT - ↑

Peripheral smear : microangiopathic hemolytic anaemia with schistocytes

Coagulation disorders

1) CLASSIC HAEMOPHILIA - A

- m/c hereditary coagulation disorders
- Def of CF- VIII (Anti-haemophilic factor) → mutation of F8 gene
  ↳ long arm of X-chromosome
- Sex-linked recessive trait
- m > f (carriers)
- Highest incidence - Britain, Europe, Australia
- 1 in 10000 male births

Pathogenesis

- Quantitative ↓ in factor-VIII (<10%) quantity
- normal / increased level of factor-VIII with reduced activity (10%) quality

Factor VIII → needed for the activation of factor X in intrinsic coagulation pathway

25% factor VIII activity → for normal haemostasis

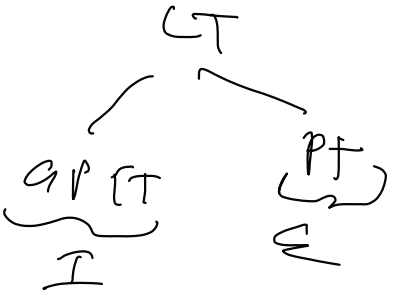
Clinical features

- Bleeding for hrs
- Recurrent painful haemarthroses
- muscle haematomas
- Haematuria (sometimes)
- Spontaneous intracranial haemorrhage } rare
- Oropharyngeal bleeding

Laboratory diagnosis

- Blood CT ↑
- PT - normal
- APTT ↑
- Assay for factor - VIII shows lowered activity

aPTT - intrinsic



Treatment

- treated with factor - VIII replacement therapy [plasma cryoprecipitates]

2) CHRISTMAS DISEASE [Hemophilia B]

- deficiency of factor IX
- Rarer [20% cases]
- 1 in 100,000 cases male births
- Indistinguishable with H - A
- Laboratory diagnosis critical

3) VON - WILLEBRAND DISEASE

- Due to qualitative or quantitative defect in VWF
- 1 in 1000 individuals of either case
- VWF differs from factor VIII in :

* The gene : VWF → chromosome 12 → autosomal dominant

factor VIII → X - chromosome → X - linked recessive

* VWF synthesized in the endothelial cells, megakaryocytes & platelets

factor VIII → liver

* vWF → for adhesion of platelets to subendothelial collagen

factor VIII → activation of factor X (ICP)

Clinical features

Type-I disease → m/c & mild to moderate disease in plasma vWF

synthesis is normal, but release of its multimers inhibited

Type II- disease → much less common

Normal or near normal levels of vWF (functionally defective)

Type III disease → extremely rare

most severe

No detectable vWF activity

Sufficiently low factor VIII levels

Treated with cryoprecipitates

Laboratory features

- Prolonged BT
- Normal platelet count
- Reduced vWF conc
- Defective platelet aggregation
- Reduced factor- VIII activity

4) VIT- K DEFICIENCY

- factor II, VII, IX, X, protein C, protein S
- obtained from green veg, absorbed in SI & stored in livers
- Endogenously synthesized by livers

5) COAGULATION DISORDERS IN LIVER DISEASE

Major site for ↓

* Metabolism of CF
* Produce inhibitors of coagulation such as antithrombin-III & protein C & S [role in clearance of activated factors & fibrinolytic enzymes]

Major causes ↓

A) Morphological lesions

- Portal HT with associated varices, splenomegaly with 2° thrombocytopenia
- Peptic ulceration
- Gastritis

B) Hepatic dysfunctions

- Impaired hepatic synthesis of CF
- Impaired " " of coagulation inhibitors : protein C, S, AT-III
- Impaired absorption & metabolism
- failure to clear activated CF causing DIC & fibrinolysis

C) Complications of Therapy

- following Blood transfusion
- Heparin therapy
- Infusion of activated coagulation proteins

⇒ Prolonged PT, PTTK, mild thrombocytopenia, normal fibrinogen levels & ↓ hepatic stores of vit-K.

i) Acquired

A) AB- Immunohemolytic anaemia

a) AI hemolytic anaemia

- warm AB type (IgG ABs active @ 37°C)
  - 1° [idiopathic), 2° (SLE, lymphoma)
- cold agglutinin type (IgM active below 4–18°C)
  - Acute & chronic
- cold hemolysin type

b) Drug induced immunohemolytic anaemia

c) Isoimmune hemolytic anaemia

B) Mechanical trauma - Microangiopathic HA

C) Direct toxic effects - Malaria

D) Acq. red cell membrane abnormalities - Paroxysmal nocturnal Hburia