BLEEDING DISORDERS

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Learning Objectives

- Introduction
- Thromocytopenia – Classification
- Idiopathic thrombocytopenic Purpura
- Thrombotic thrombocytopenic purpura

BLEEDING DISORDERS

- Group of disorders characterised by defective hemostasis with abnormal bleeding

Hemo – Blood

Stasis – Standing still

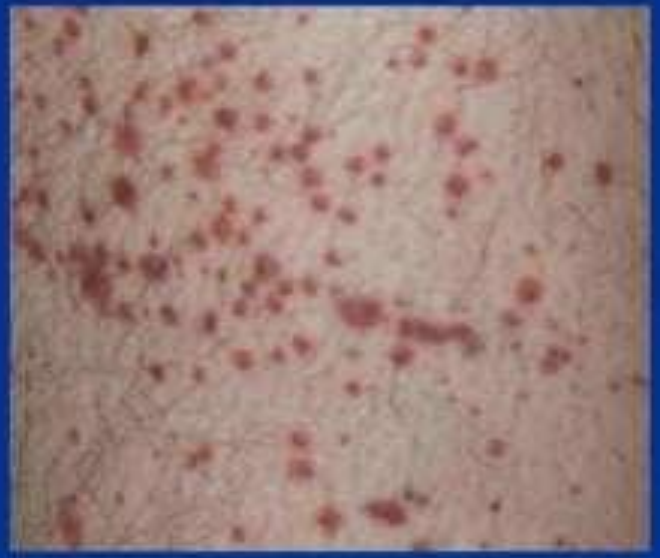
Spontaneous

Petechiae
Purpura
Ecchymosis

Following trivial trauma

Petechiae
(1 – 2 mm)

Purpura
(≥ 3 mm)



Ecchymosis
(> 1 – 2 cms)

Systems Involved in Hemostasis

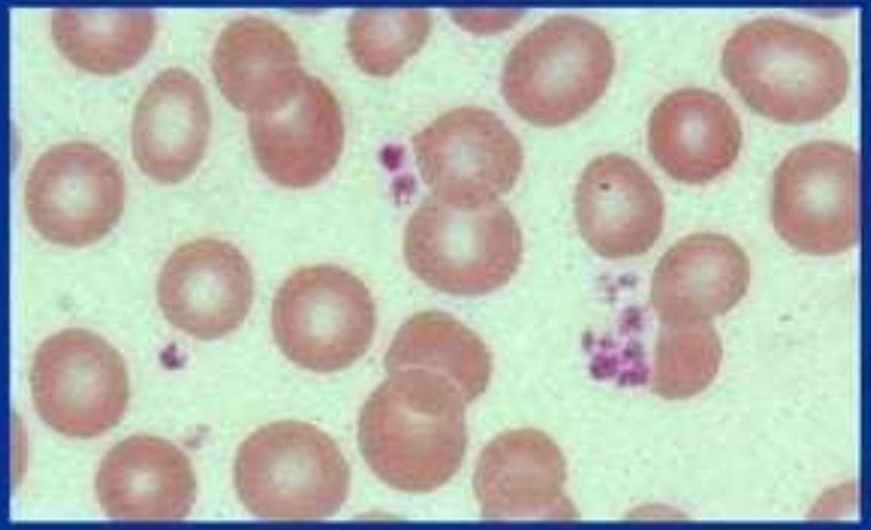
- Vascular system
  - Injured vessel initiates vasoconstriction
- Platelet System
  - Injured vessel exposes collagen that initiates platelet aggregation and help form plug
- Coagulation System
  - protein factors of intrinsic and extrinsic pathways produce a permanent fibrin plug

Disorders of Hemostasis

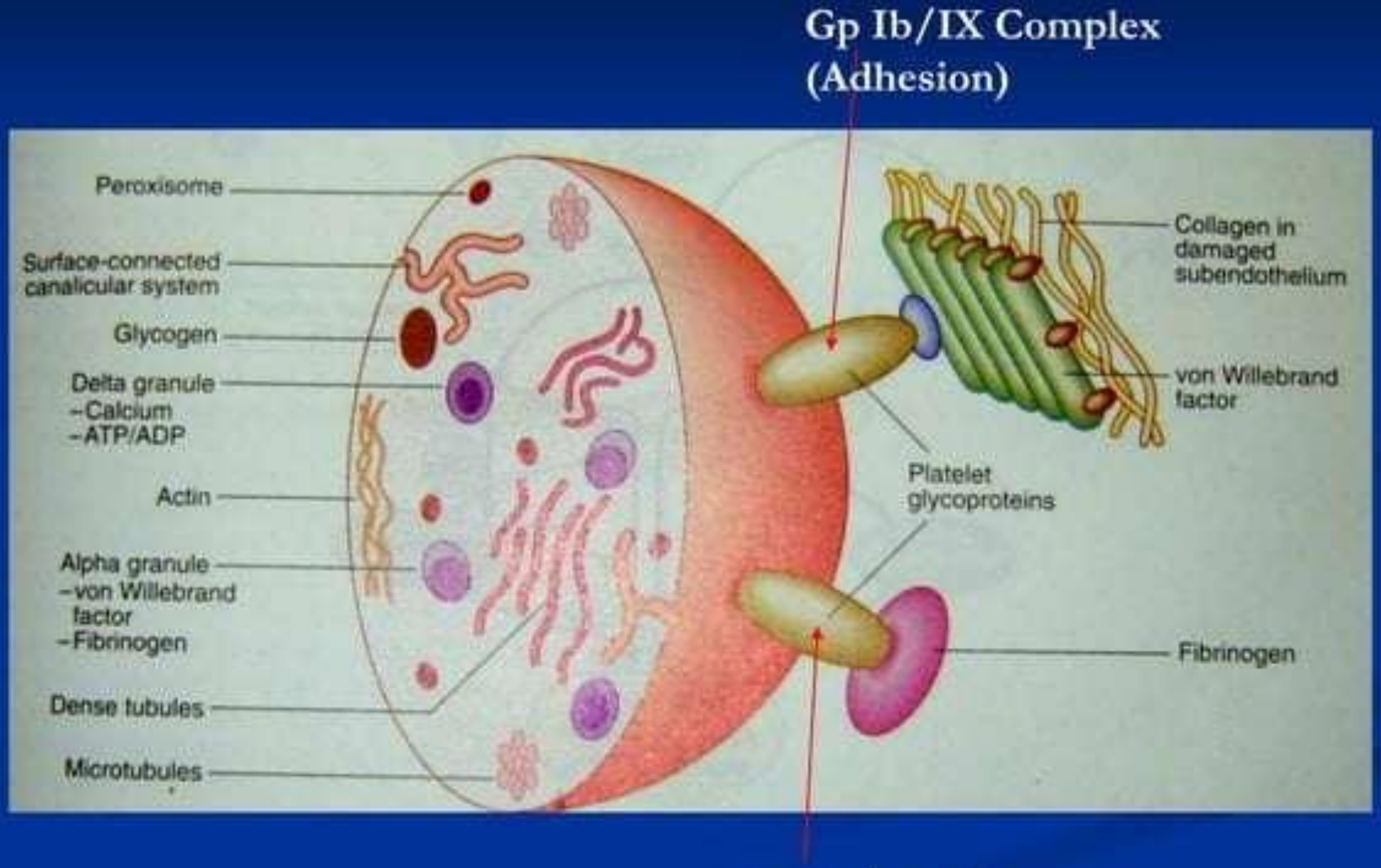
- **Vascular disorders:**
  - Scurvy, easy bruising, Henoch-Schonlein purpura.
- **Platelet disorders:**
  - **Quantitative** - Thrombocytopenia
  - **Qualitative** - Platelet function disorders – Glanzmans
- **Coagulation disorders:**
  - **Congenital** - Haemophilia (A, B), Von-Willebrands
  - **Acquired** - Vitamin-K deficiency, Liver disease
- **Mixed/Consumption:** DIC

PLATELET(Thrombocyte)

- Small discoid(1 – 4 μm) nonnucleate structures containing granules
- Normal count – 1.5 – 4 lakhs
- Life span – 7 – 8 days



Platelet ultra structure



Investigations of platelets and platelet functions

Screening tests

1. Platelet count
2. Bleeding time
3. Peripheral smear

Special tests

1. Adhesion tests
2. Aggregation tests
3. Assessment of grannular content, etc

Hemorrhagic diathesis due to platelet disorders

QUANTITATIVE
↓ in platelet number
(Thrombocytopenia)

QUALITATIVE
Defective platelet function

Congenital

Adhesion defect

Bernard Soulier Synd
VWD

Aggregation defect

Glanzmanns
thrombasthenia

Acquired

1. Aspirin therapy
2. Uremia
3. Multiple myeloma, etc

THROMBOCYTOPENIAS

- Reduction in the platelet number
- Count below 100,000/μl is generally considered to constitute thrombocytopenia
- count<20,000/μl-Spontaneous bleeding
- count20,000 – 50,000/μl – aggrevates post traumatic bleeding

THROMBOCYTOPENIA

↓

rule out pseudothrombocytopenia

↓ PRODUCTION	↑ DESTRUCTION	SEQUESTRATION	DILUTIONAL
• aplasia	• immune auto-immune (ITP, SLE drugs infections allo-immune	splenomegaly	
• infiltration			
• ineffective megakaryopoiesis eg. MDS	• non-immune sepsis DIC, TTP, HUS hypertensive disorders of pregnancy		
• selective impairment of platelet production			
•Drugs			

Idiopathic Thrombocytopenic Purpura (ITP)

Definition

1. Purpura

2. Thrombocytopenia
   - -Thrombocytes or Platelet
   - -Penia or Low

3. Idiopathic & Immune

Incidence

1. 1 / 10,000 Population

2. Children (age < 15 yr.) 50%
   - Girl : Boy = 1 : 1
   - Mortality 0.5 - 1.5%

3. Adults (age 20-40 yr.) 50%
   - Female : Male = 3-4 : 1
   - Mortality rare

Etiology

.ITP is a disease of increased peripheral platelet destruction.

.Most patients produce auto-antibodies to specific platelet membrane glycoproteins.

.Most patients have either normal or increased platelet production in BM.

Clinical Manifestations

1.Purpura

-Petechiae

-Ecchymoses

2.Hemorrhage

Clinical Appearance

1. **Acute ITP (children)**

2. **Chronic ITP (adults)**

Classification

Acute ITP	Chronic ITP
Mostly children	Mostly adults
Male/Female = **1:1**	Male/Female = **1:3-4**
Acute onset	Usaully gradual onset
Plt. Count mostly <20,000/mm^3	Plt. Count 20,000 – 50,000/mm^3
Spontaneous remission frequent	Spontaneous remission rare
Mortality : 0.5-1.5 %	Chronic recurrent course

Common Signs and Symptoms

1. Purpura
2. Menorrhagia
3. Epitaxis
4. Gingival bleeding
5. Recent virus immunization (acute ITP)
6. Recent viral illness (acute ITP)
7. Bruising tendency

Role of Spleen

1. Auto-antibody production
2. Platelet destruction
3. Platelet storage

Common Physical Findings

- Nonpalpable petechiae
- Hemorrhage
- Purpura
- Gingival bleeding
- Signs of GI bleeding
- Spontaneous bleeding
  (plt. < 10,000 /mm^3)
- Menorrhagia
- Retinal hemorrhage
- Evidence of intracranial hemorrhage
- Nonpalpable spleen

Mortality/Morbidity

1.Hemorrhage represents the most serious complication

2.Mortality rate from hemorrhage is approximately 1% in children and 5% in adult

3.Increase risk of severe bleeding in adult ITP

4.Spontaneous remission

: occure in more than 80 % in children

: uncommon in adults

Laboratory Examination

1.Complete Blood Cell Count (CBC)

-Isolated thrombocytopenia

2. Increased Bleeding time

3.Bone Marrow Examination

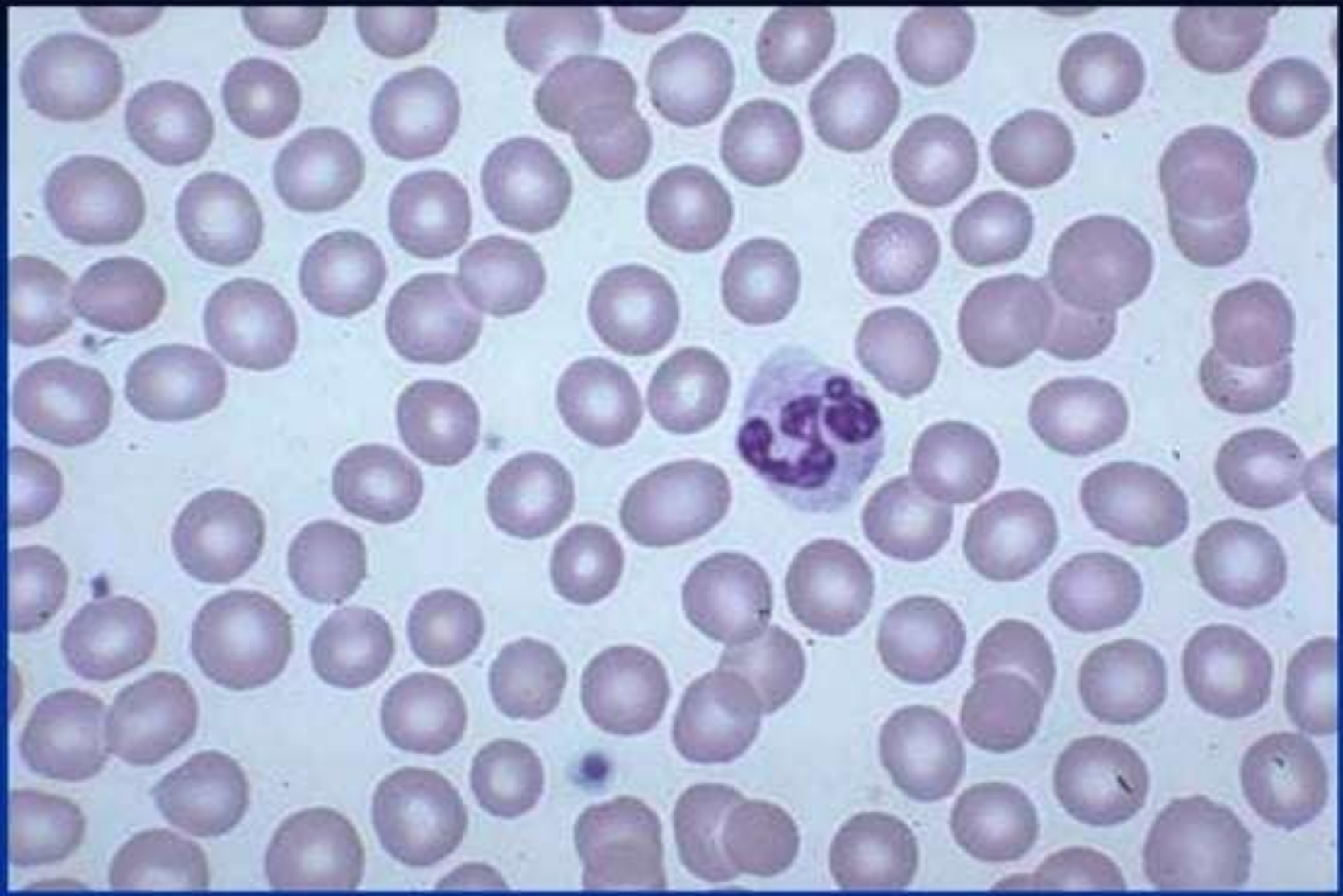
-Megakaryocyte, Megakaryoblast & Promegakaryocyte --> increase/normal

-Other cellular component--> normal

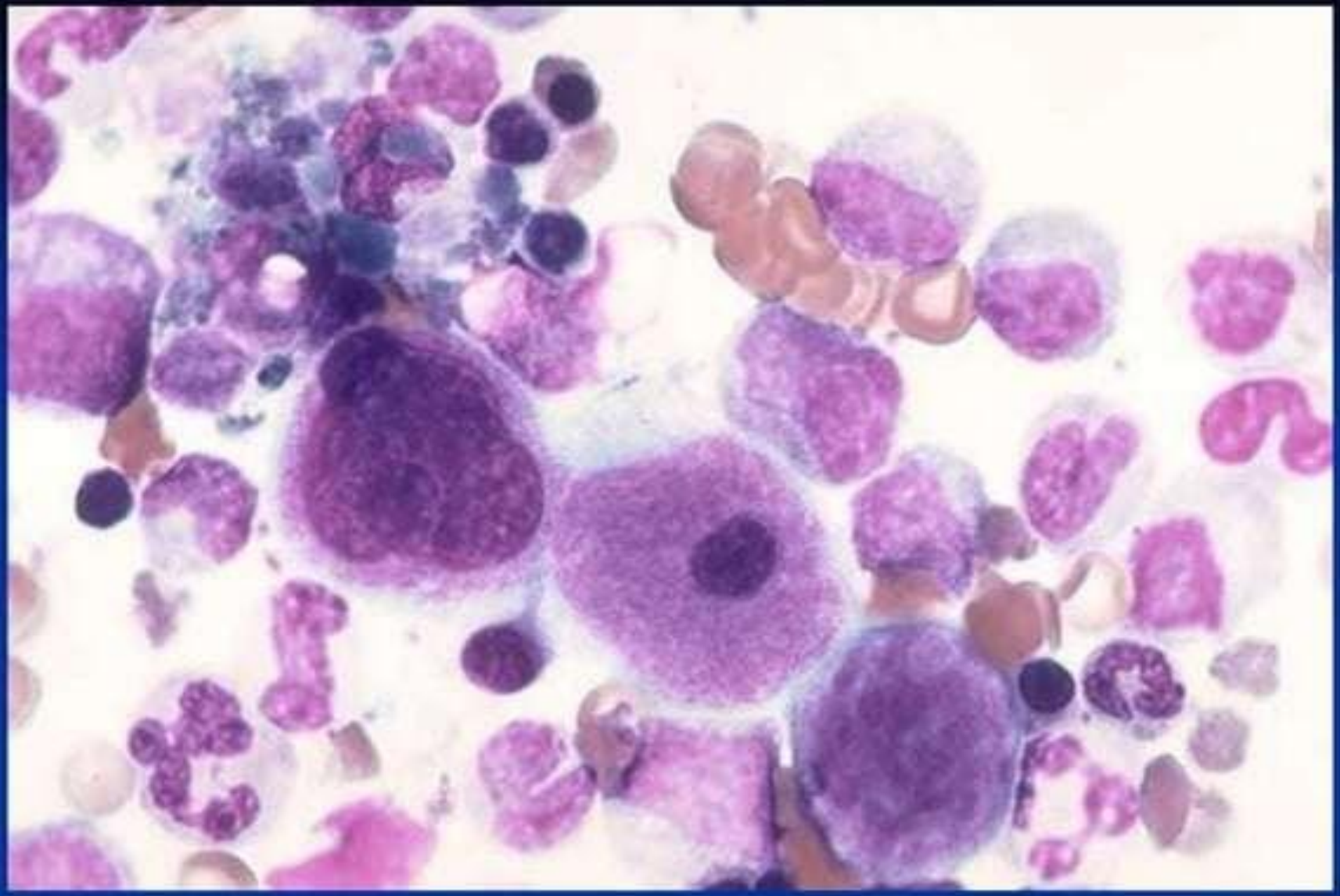
4.Platelet Auto-antibody

-PAIgG (non-specific)

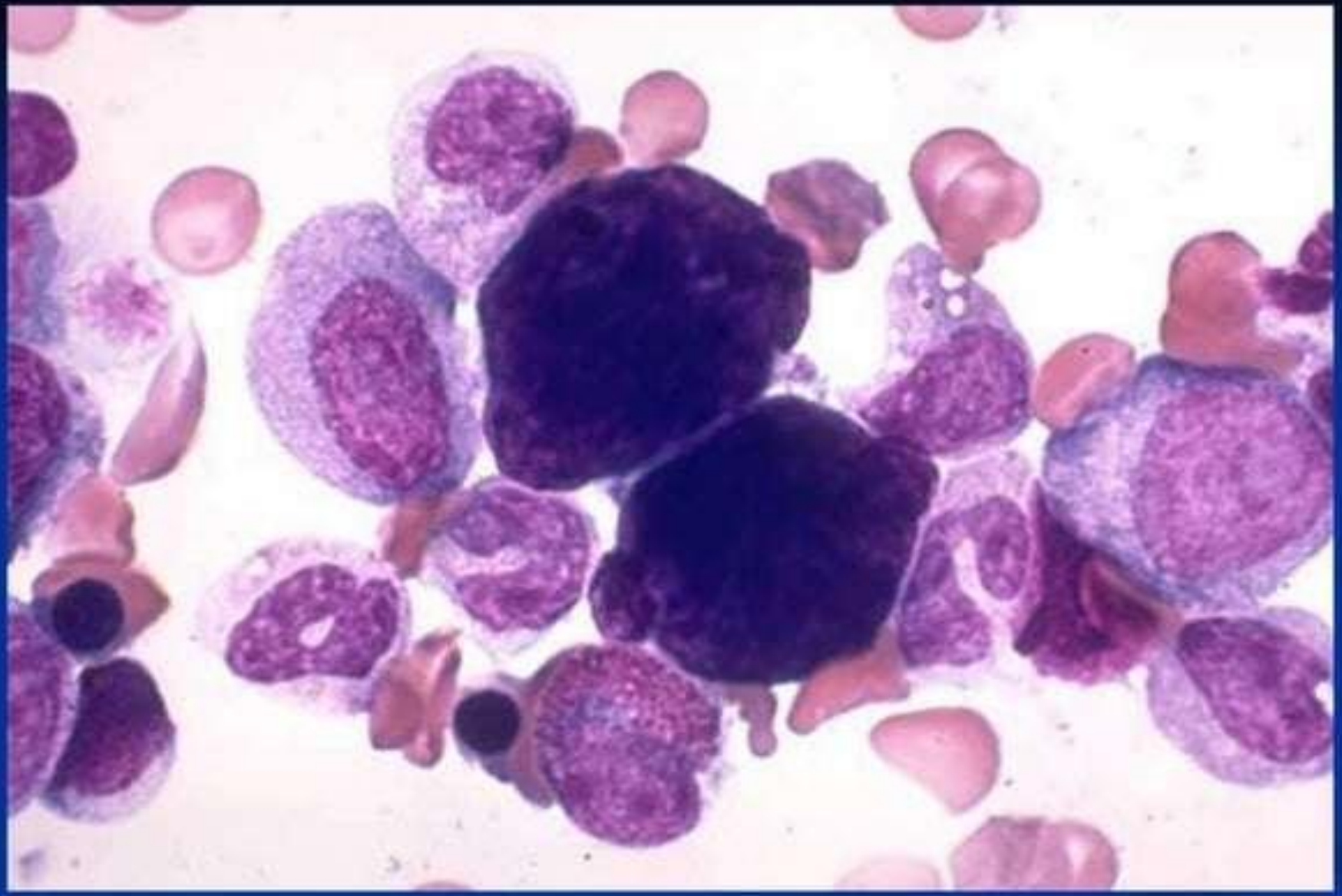
-GP specific antibody



Fewer Platelets than normal.



Two mature megakaryocytes; one with a very high N/C ratio, the other with a very low N/C ratio.



Two bare megakaryocyte nuclear masses

Laboratory Findings

1.Isolated thrombocytopenia

2.No splenomegaly

3.Increase megakaryocytes in BM

4.No other cause of thrombocytopenia

5.Platelet auto-antibody found

Treatment & Prognosis

Acute ITP

1. Self remission 80 %
2. Platelet transfusion in severe bleeding
3. Corticosteroid therapy within 3-4 weeks
4. No response to corticosteroid > 6 months (15 %)
   → consider Splenectomy

Chronic ITP

1. Complete remission (10-20 %)
2. Corticosteroid therapy to reduce phagocytic activity of RE system & suppress antibody production
3. Consider Splenectomy :
   - No response to high dose steroid
   - Cerebral hemorrhage

THROMBOTIC THROMBOCYTOPENIC PURPURA(TTP)

- Fulminant and lethal disorder
- Characterised by the formation of hyaline microthrombi within the microvasculature throughout the body
- The thrombi is composed of platelets and fibrin.

Thrombotic Thrombocytopenic Purpura

Easy to diagnose and treat – if you think of it

The 5 Clinical Features

thrombocytopenia
red cell fragmentation
fever
transient neurologic deficits
kidney failure

Untreated, TTP is deadly
Treatment usually involves replacing the plasma repeatedly until the patient recovers

The usual problem, loss of a protein that removes activated VIII-R, is just now being figured out

RBC fragments

Essential anatomic lesion: Widespread thrombin-platelet microthrombi

Thrombotic Thrombocytopenic Purpura

- A classic pentad of signs:
  - Microangiopathic hemolytic anemia
  - Thrombocytopenia
  - Neurologic dysfunction
  - Renal failure
  - Fever
- Incidence ≈4/million/year
- Often strikes young adults, mainly females
- Untreated, mortality >90%
- Treated with plasmapheresis, mortality <20%

PATHOGENISIS

- Defieciency of enzyme – ADAMTS 13

  (vWF Metalloproteinase)

  ↓

  Accumulation of
  high mol wt multimers of vWF

  ↓

  Promote platelet microaggregate
  formation throughout the microcirculation

- Untreated, mortality >90%
- Treated with plasmapheresis, mortality <20%

Summary

- Thromocytopenia – Classification
- Idiopathic thrombocytopenic Purpura
- Thrombotic thrombocytopenic purpura

Thank you