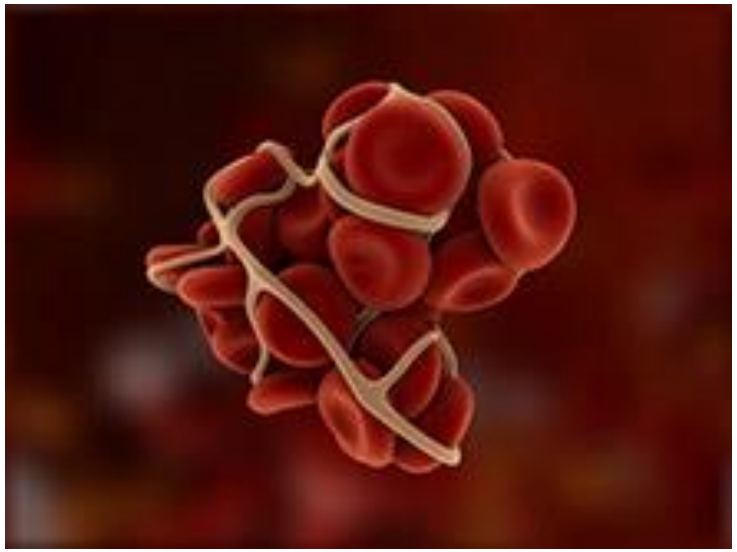
Haemostasis

- Vessel wall
- **Platelets**
- Clotting factors
- Fibrinolysis

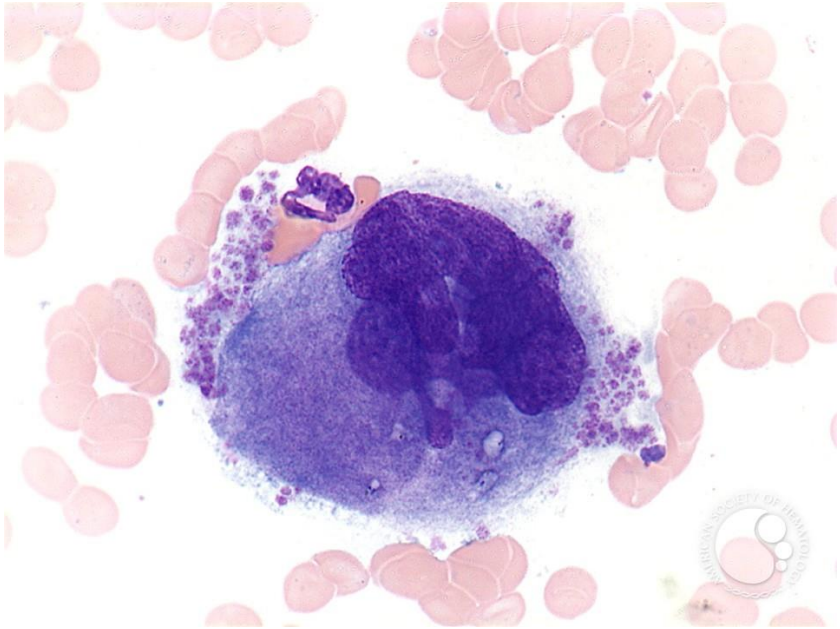


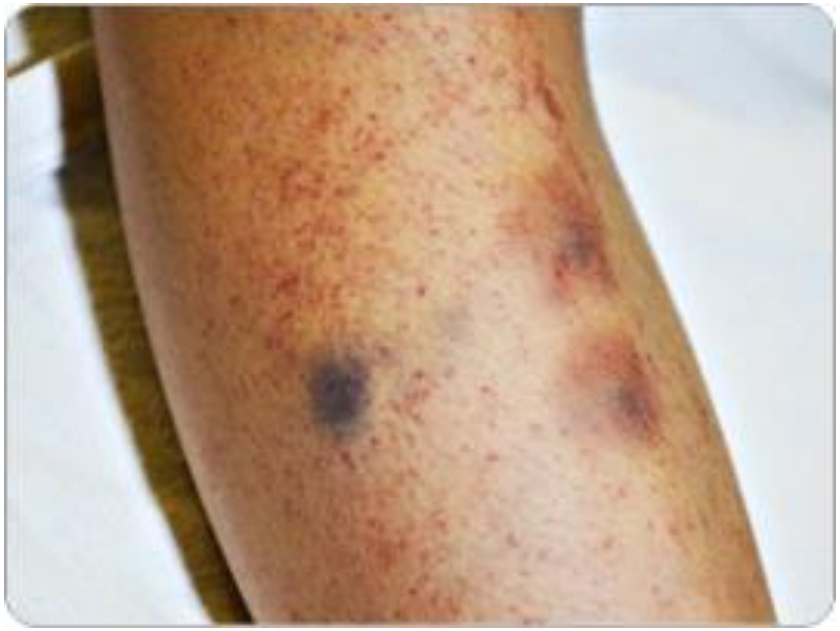
Platelets

Number(Quantity)

Function(quality)

THROMBOCYTOPENIA





Dr Durga Moratuwagama

Platelets

- Produced in BM from Megakaryocytes
- About 1000-5000 platelets are produced from each Megakaryocyte
- Normal platelet production is ~35,000-50,000/µl of whole blood per day
- Can be increased 8-fold when needed
- Normal platelet count-150,000-450,000/µl

Mechanisms of Thrombocytopenia

1. Failure of production

2. Increased destruction

3. Dilutional thrombocytopenia-Massive transfusion

4. Abnormal distribution-Splenomegaly

1.Decreased Platelet Production

Selective megakaryocyte depression

(a)Congenital

TAR

May-Hegglin anomaly

Wiskott-Aldrich syndrome

(b)Acquired

Drugs ,viruses

As a part of general BMF

Cytotoxics/radiotherapy

AA

Leukaemia

MDS

MM

MF

BM infiltration

Megaloblastic anaemia

HIV infection

2. Increased platelet destruction

(A) Immune –

(a) Auto immune → Idiopathic

↘ 2 ry-SLE,CLL ,Lymphoma

(b)Infections - Viruses, malaria

(c) Drug induced

(d)Post transfusion purpura

(e)Feto maternal alloimmune thrombocytopenia

(B) DIC

(C)TTP

HW

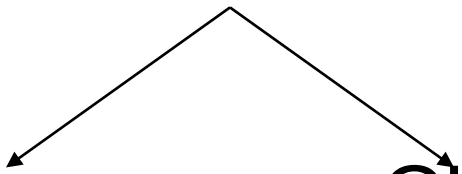
- Make a list of drugs causing thrombocytopenia

Overview of ITP

1. Clinical presentation
2. Pathogenesis
3. Initial evaluation
4. Management

2(A)(a)Auto immune (idiopathic) thrombocytopenic purpura

1. Isolated thrombocytopenia with otherwise normal FBC and blood picture.
2. No other conditions or factors that may cause thrombocytopenia.



ACUTE CHRONIC

Chronic immune (idiopathic) thrombocytopenic purpura

- Relatively common
- Females>Males
- Age 15-50y
- Assoiations-SLE,CLL,HIV,AIHA

Clinical presentation

- Often incidental finding

Common signs/symptoms:

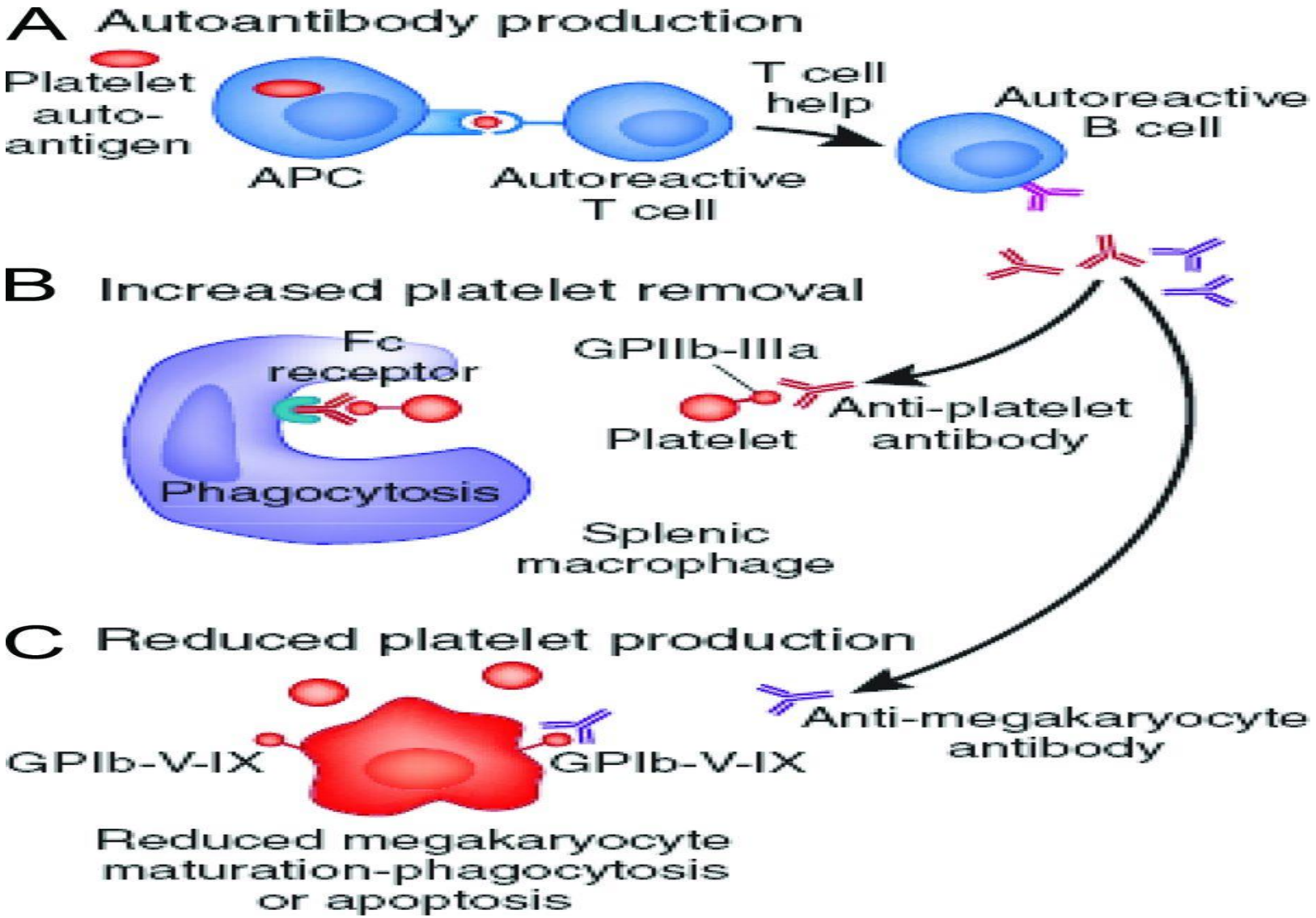
- Mucocutaneous bleeding-gum bleeding
  epistaxis
- Purpura
- *Eschymoses*
- Menorrhagia
- *ICH-rare*

Skin bleeding

Mucosal bleeding-Oral

Pathogenesis of ITP.

(A) T cells are activated upon recognition of platelet-specific antigens on the APCs and therefore induce antigen-specific expansion of B cells.



Diagnostic work-up

- History & physical examination
- Careful examination of medication list
- **FBC**
- **BP**

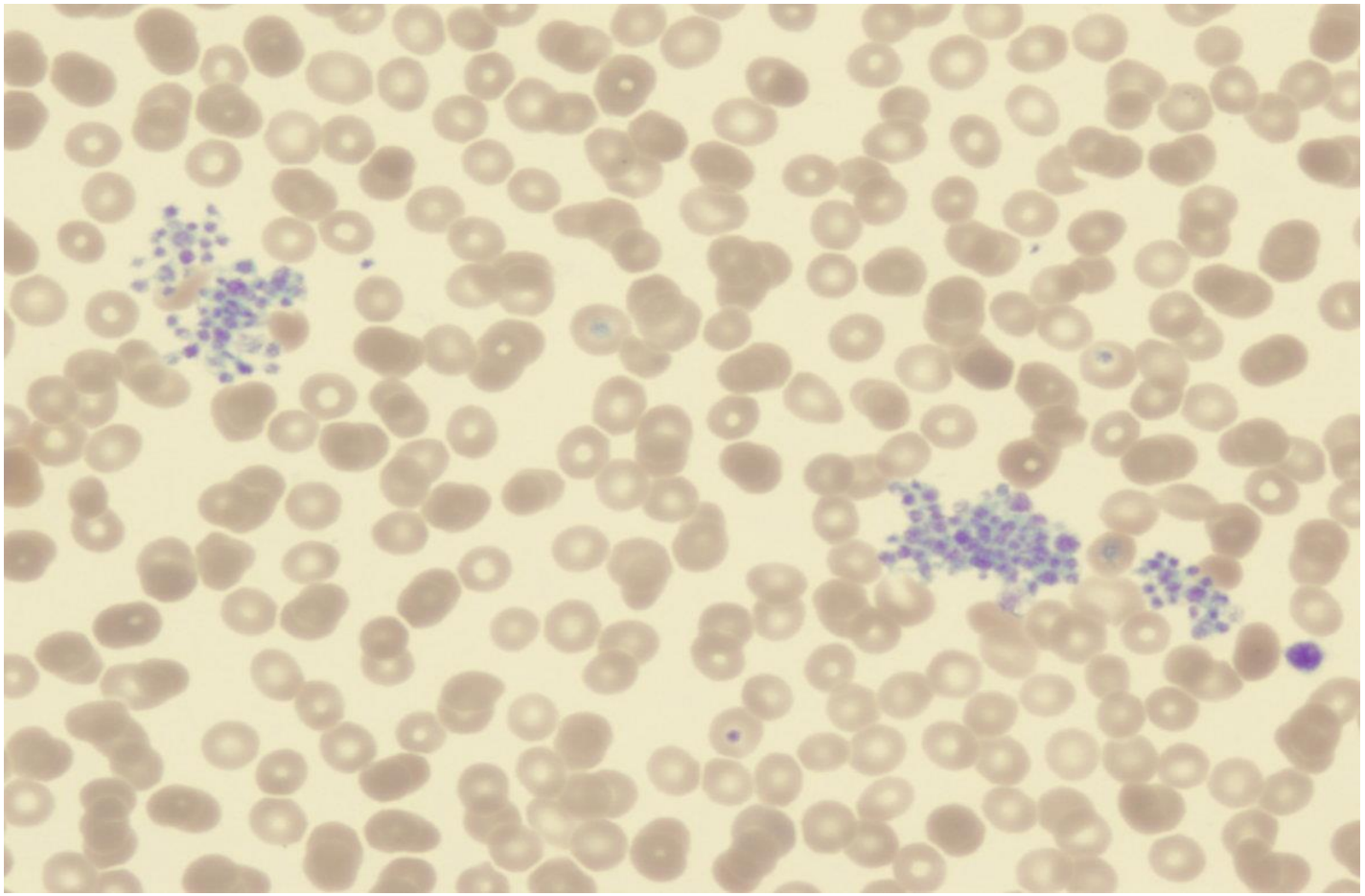
  - Pseudo thrombocytopenia (due to platelet clumping)

  -Giant platelets in congenital thrombocytopenia

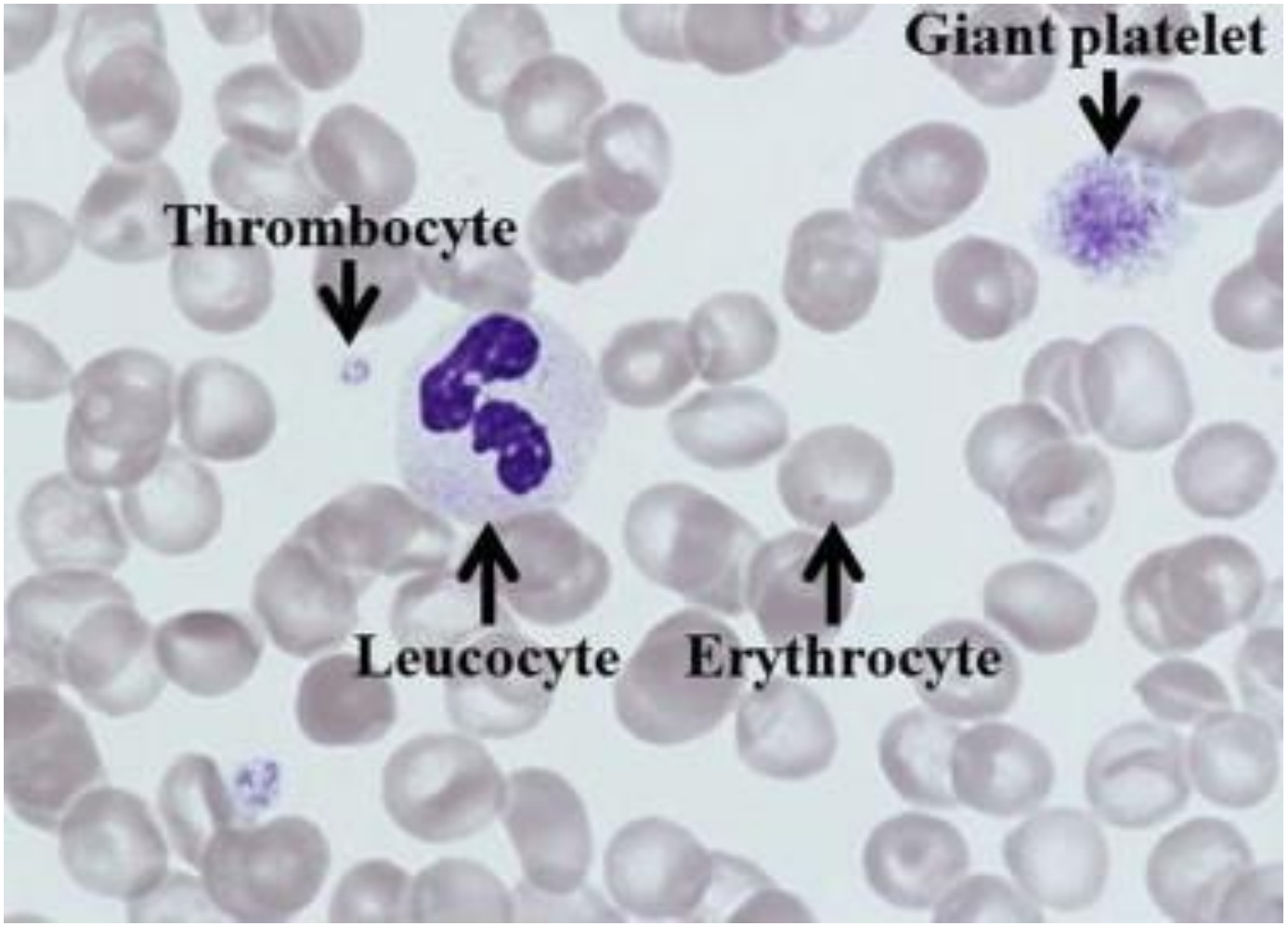
  -Red cell fragments (Schistocytes) in MAHA

  - large platelets in ITP

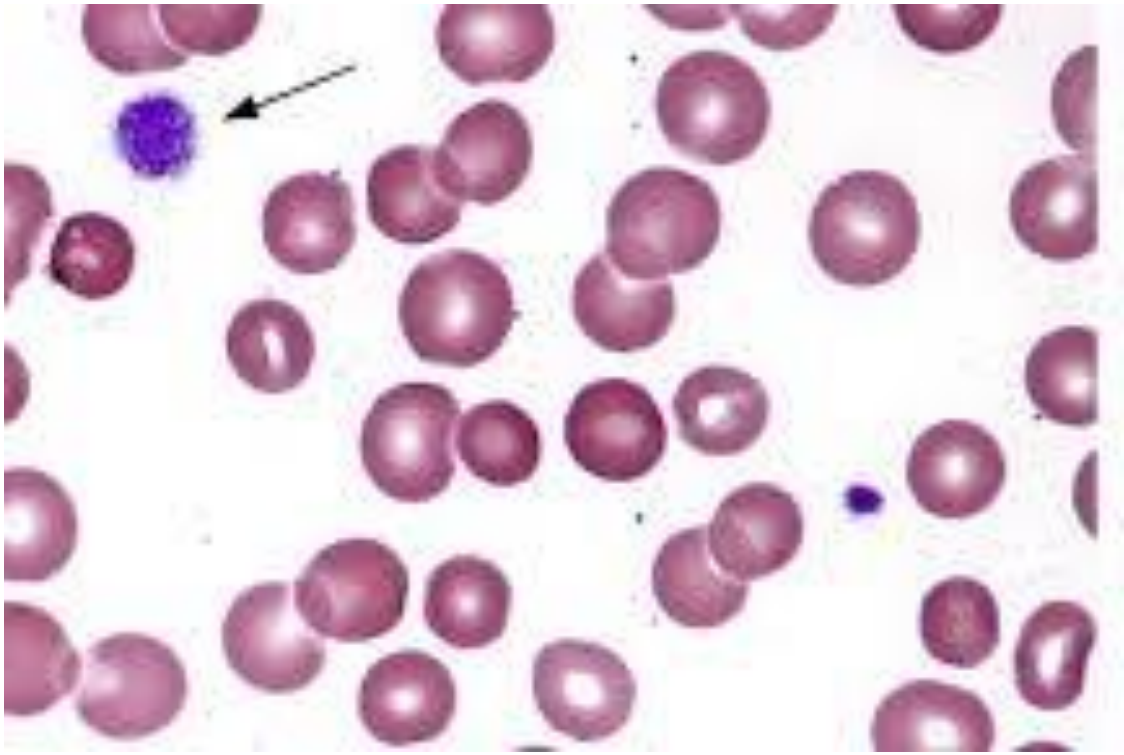
Pseudothrombocytopenia -platelet clumpping



Giant Platelets



Blood picture- ITP



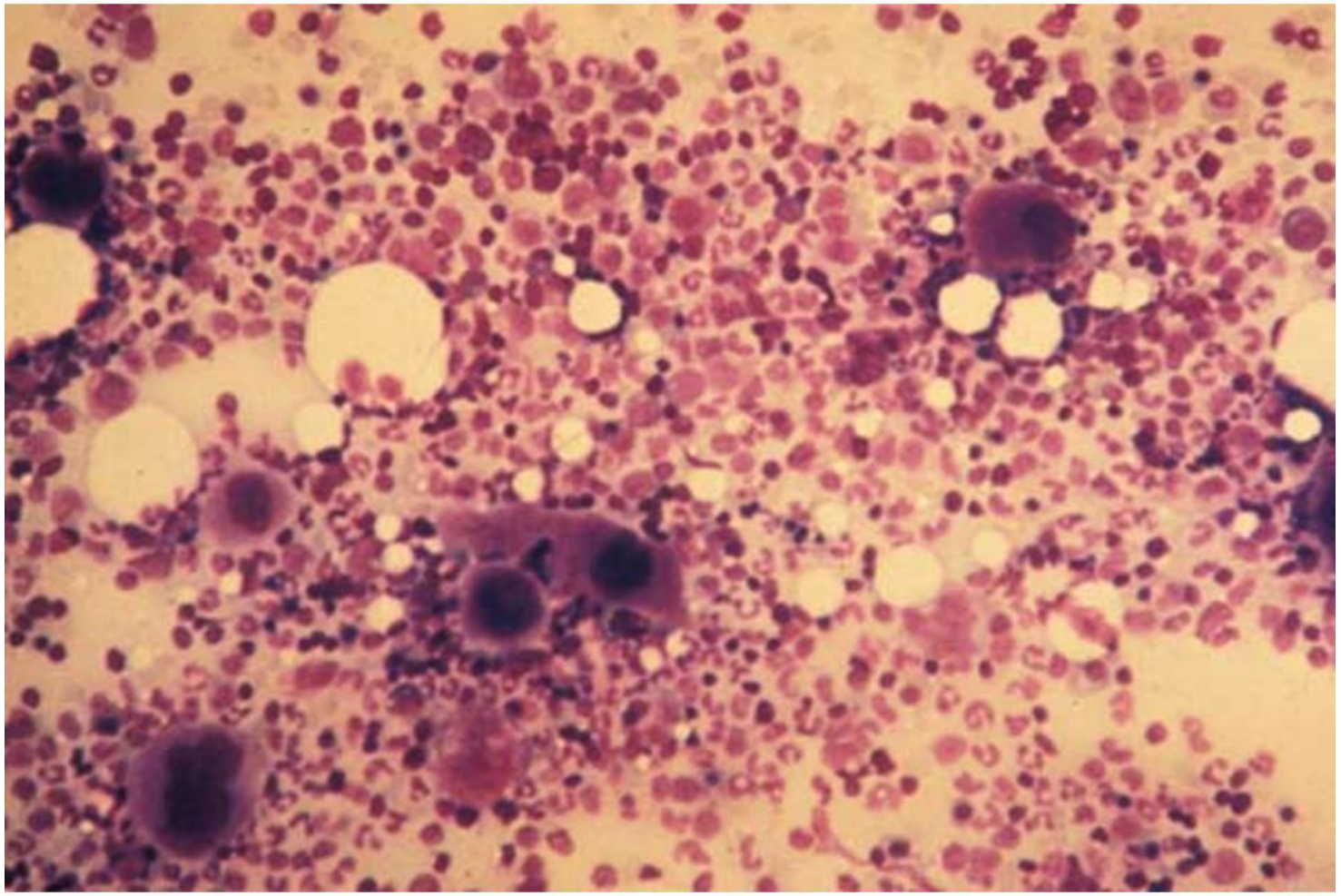
Diagnostic work-up cont.

- HIV /hepatitis C/Dengue serologies in patients with risk factors
- Screening for autoimmune diseases/LPD
- Bone marrow biopsy in selected patients

Bone marrow biopsy

- Indications:
  - Other abnormal cell lines (WBC or Hb)
  - Lack of response to treatment
  - Red flags: Fever, weight loss, bone pain

ITP-BM



Management

Avoid treatment in patients with mild, asymptomatic disease

Plt > 30,000 and asymptomatic

Indications for Treatment

Treat if:

- Plt < 10,000

Consider treatment if:

- Plt > 30,000 and mucous membrane bleeding

Hospitalize if:

- Severe bleeding, regardless of platelet count

Treatment Options

First line

- Corticosteroids
- IVIG
- IV anti-D

Second line

- Splenectomy
- Rituximab
- Other immunosuppressant
- Thrombopoietin receptor agonists(TRA)

- Severe bleeding/hospitalized:

– IVIG 1 g/kg IV for 2 days

– Methylprednisolone 1 gram/day for 3 days

– Dexamethasone 40mg/d for 4 days

– Platelet transfusions(only in life threatening bleeding)

First line treatment

- Steroids
  Prednisone 1-2 mg/kg/day
  response rate-2/3
  platelet count begins to increase after 3-5 d
- IVIG 1 g/kg IV for 2 days
- IV Anti-D

  Dose 50-75 mcg/kg/day IV

H/W- List the side effects of steroids

Many patients will relapse after initial response.

- Consider:

  Repeating the initial Rx

  Second line treatment

  Avoid further Rx if plt > 30,000 and no significant bleeding

Second line treatment

- **Splenectomy**

Consider in the following pts.:

Poor response to first line treatment

Requirement for high-dose steroids->10 mg prednisone /day

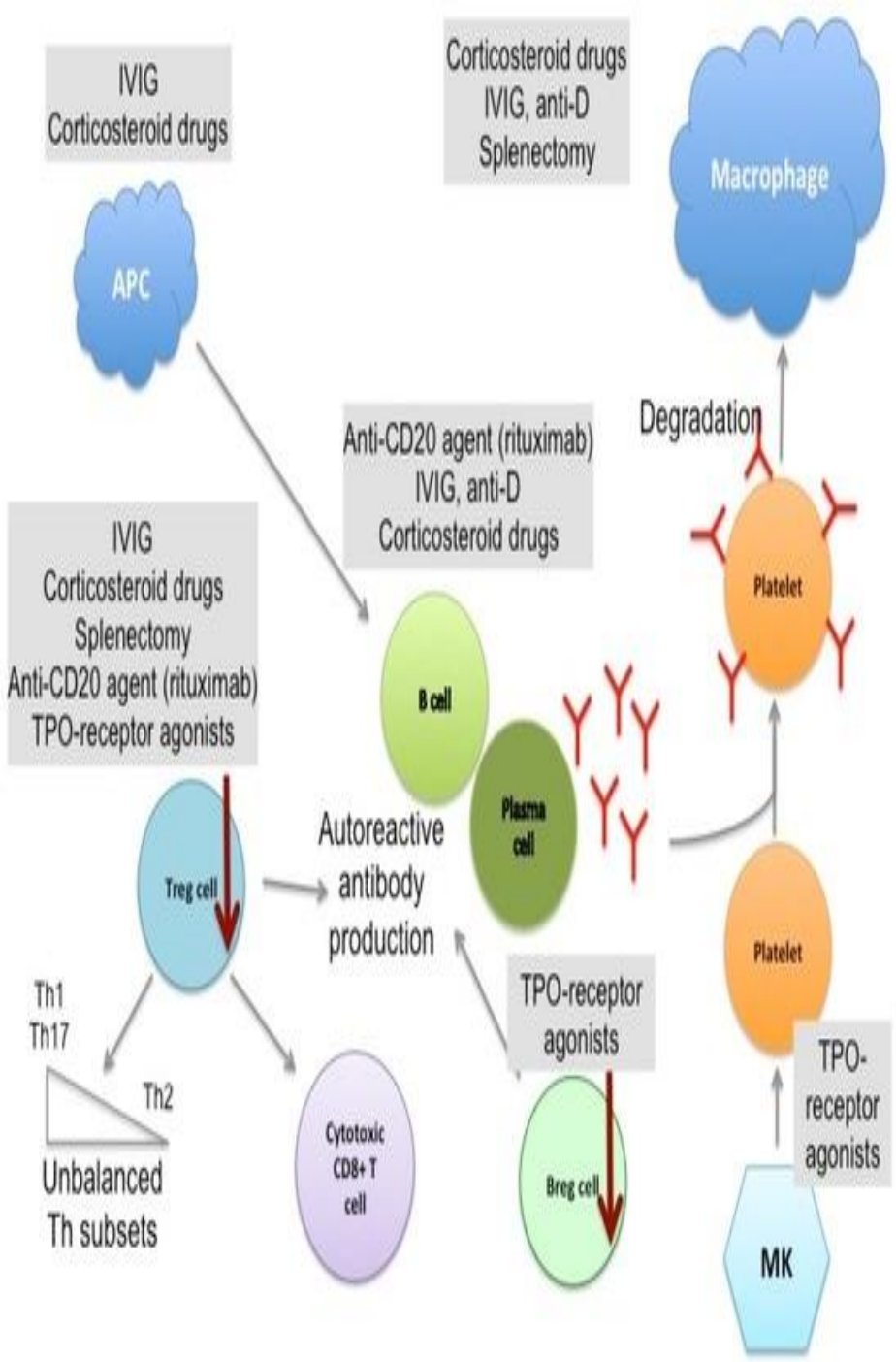
Response rate ~65%

- **Rituximab(anti CD 20 ab)**

Response rate ~50%

Other drugs

- Azathioprine
- Danazol
- Mycophenolate mofetil
- Cyclosporin
- Cyclophosphamide
- Vincristine



Corticosteroids,* azathioprine,† danazol,‡ and other non-specific immunosuppressants

→ Targets T cells to impair production of platelet autoantibodies[11]

*May also impair the destruction of platelets by macrophages within the bone marrow.[11,20]

Intravenous immunoglobulin,† anti-D immunoglobulin

→ Block the Fcγ receptors on macrophages to impair clearance of autoantibody-bound platelets[11]

†May also decrease antibody production.[11]

Rituximab†§

→ Destroys B cells to lower production of antiplatelet autoantibodies[19]

§May also block Fcγ receptors on macrophages.[19]

Splenectomy¶

→ Impairs clearance of antibody-coated platelets by macrophages[11]

¶May also result in impaired antibody production.[11]

Refractory ITP

- Plt < 50,000 for 3 months

despite glucocorticoids and splenectomy

- No consensus on when or how to treat

Acute idiopathic thrombocytopenic purpura

- In children
- Following vaccination/infections
- Spontaneous remission -90%

2. Increased platelet destruction

(A) Immune –

(a) Auto immune → Idiopathic

→ 2 ry-SLE,CLL ,Lymphoma

(b)Infections - Viruses, malaria

(c) Drug induced

(d)Post transfusion purpura

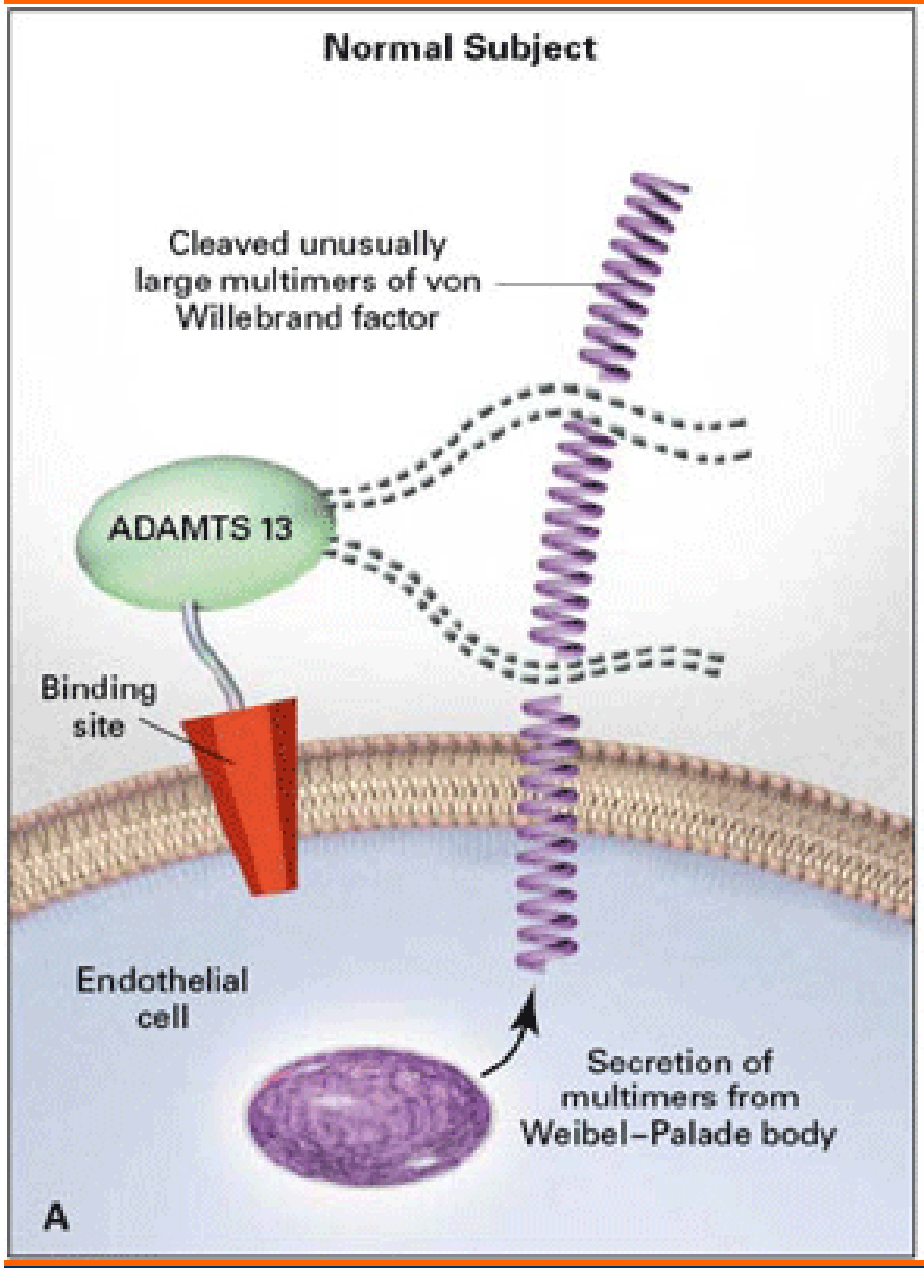
(e)Feto maternal alloimmune thrombocytopenia

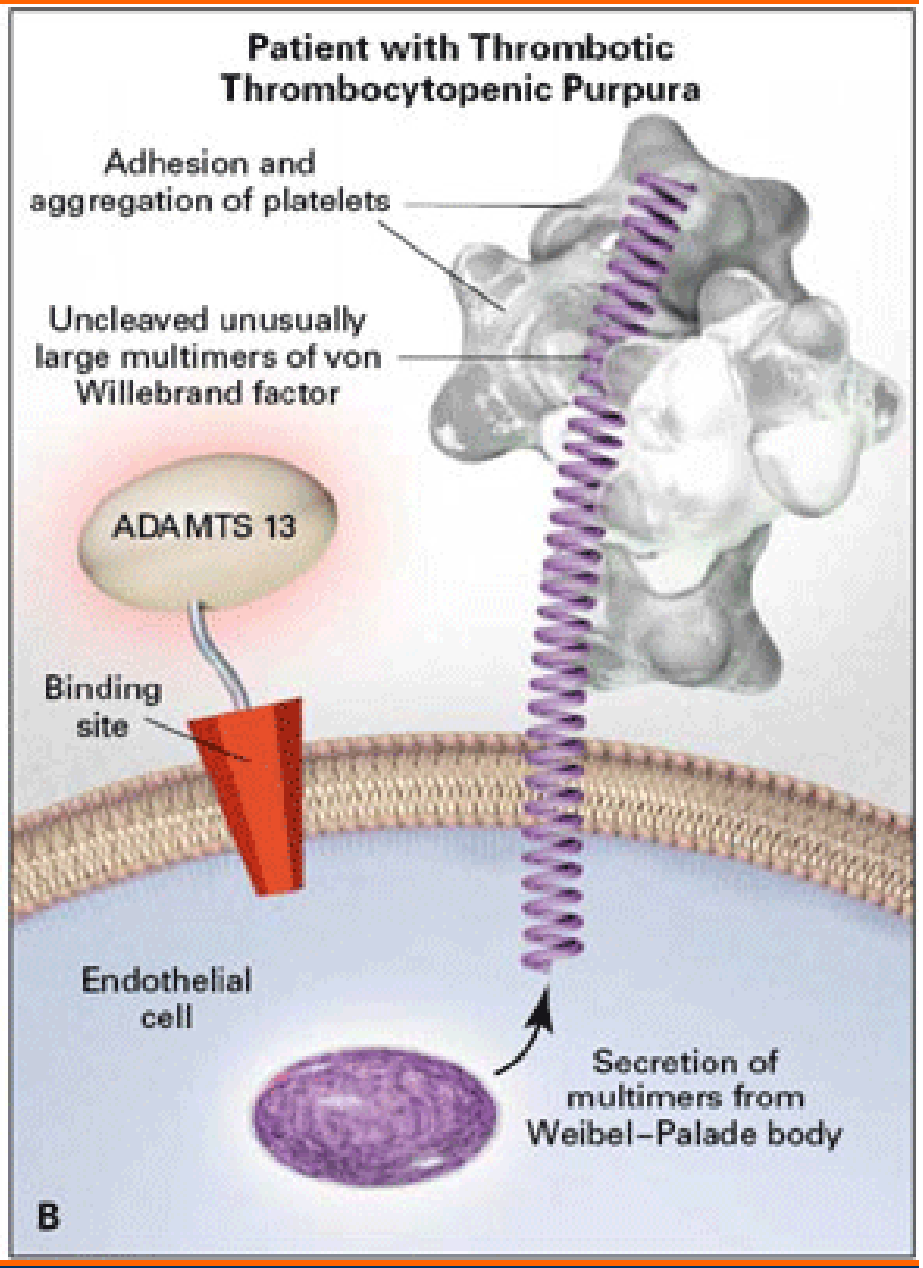
✓(B) TTP

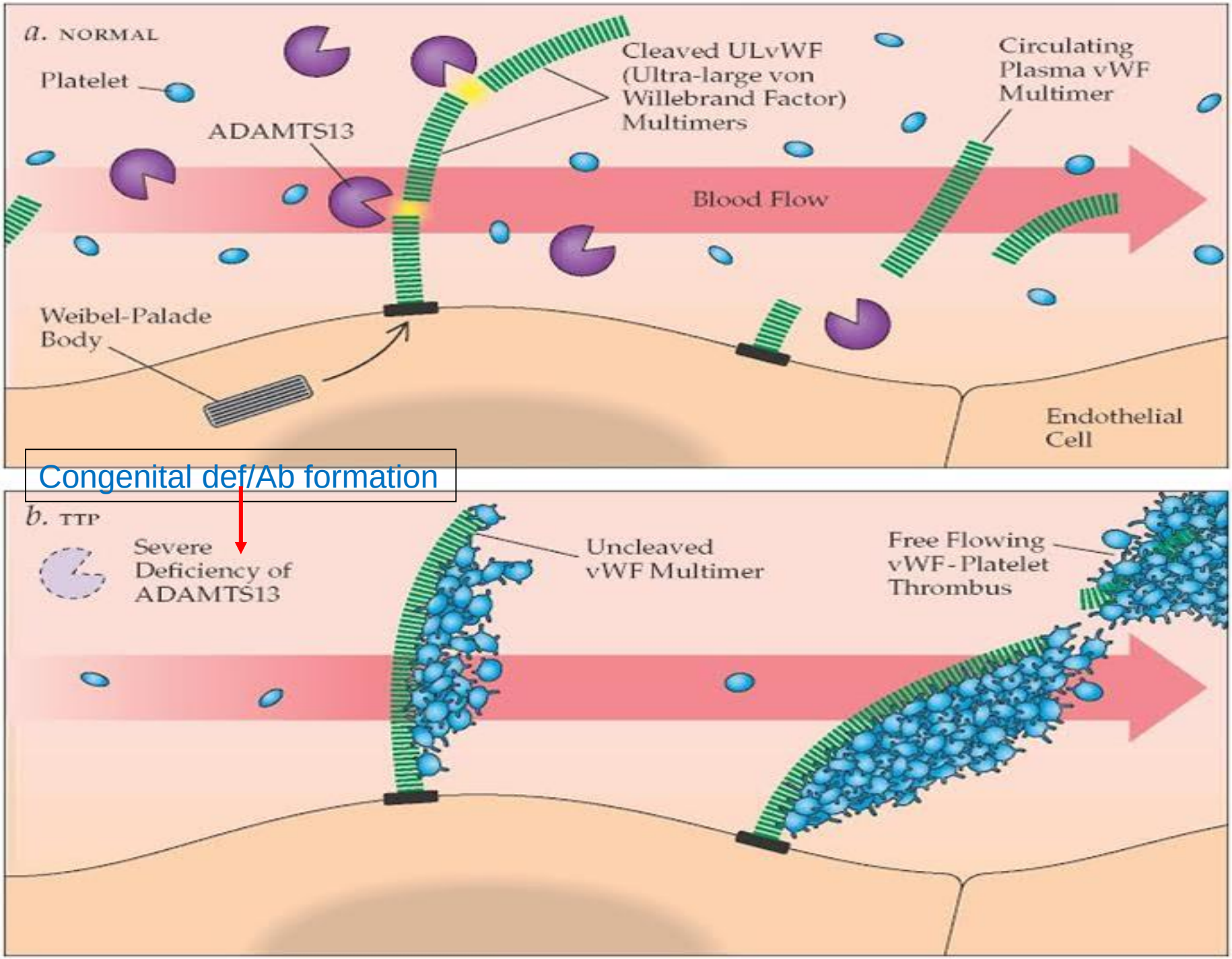
(C) DIC

Thrombotic thrombocytopenic purpura (TTP)

1. Thrombocytopenia
2. MAHA
3. Neurologic abnormalities
4. Fever
5. Renal failure

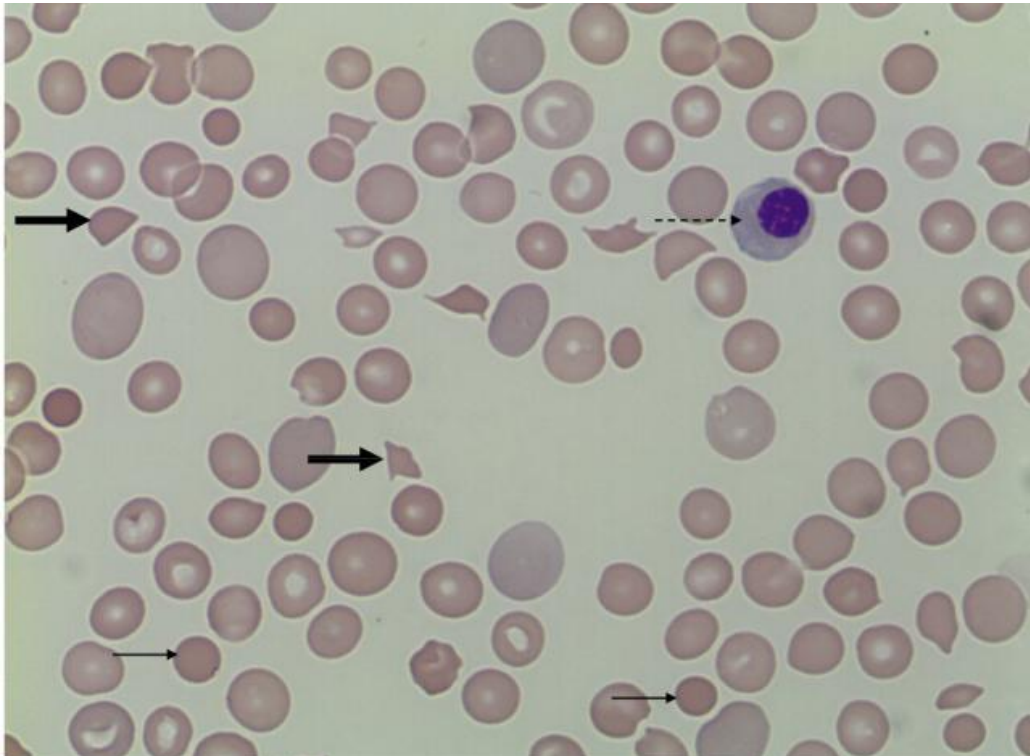





a. NORMAL
Platelet
ADAMTS13
Cleaved ULvWF (Ultra-large von Willebrand Factor) Multimers
Circulating Plasma vWF Multimer
Blood Flow
Weibel-Palade Body
Endothelial Cell
Congenital def/Ab formation
b. TTP
Severe Deficiency of ADAMTS13
Uncleaved vWF Multimer
Free Flowing vWF-Platelet Thrombus

Diagnosis

- Clinical features
- FBC+BP
- Raised LDH
- Clotting tests-Normal
- ADAMTS 13 –Low
- Impaired renal function



Treatment

- Replenish ADAMTS 13
- Remove antibodies
- FFP -emergency

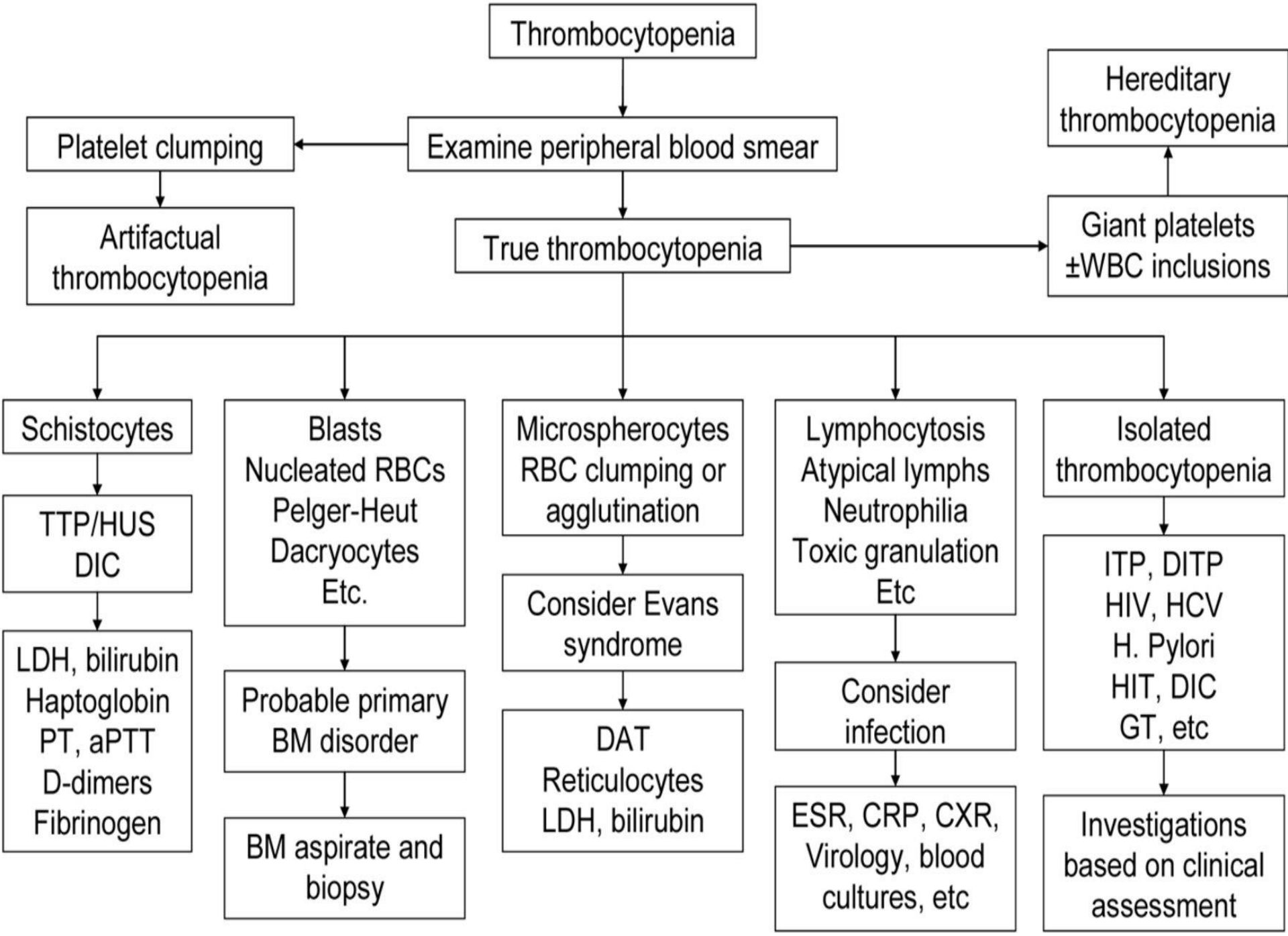
} Plasma exchange

Platelet transfusion

Haemolytic uraemic syndrome(HUS)

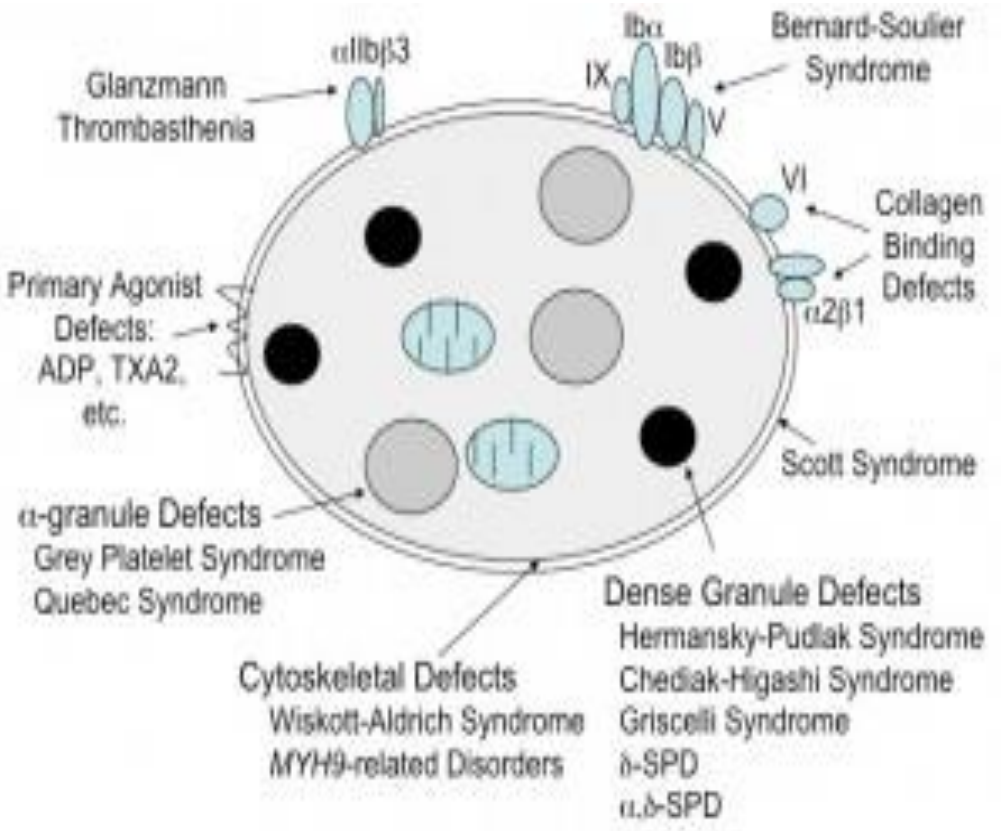
- Predominantly renal impairment
- *HTN*
- *Fits*
- History of diarrhea
- Associated with *E coli /shigella*
- *Dialysis*
- *Control of HTN/Fits*

Feature	ITP	DIC	TTP


Thrombocytopenia
Examine peripheral blood smear
Platelet clumping
Artifactual thrombocytopenia
True thrombocytopenia
Hereditary thrombocytopenia
Giant platelets ±WBC inclusions
Schistocytes
TTP/HUS DIC
LDH, bilirubin Haptoglobin PT, aPTT D-dimers Fibrinogen
Blasts Nucleated RBCs Pelger-Heut Dacryocytes Etc.
Probable primary BM disorder
BM aspirate and biopsy
Microspherocytes RBC clumping or agglutination
Consider Evans syndrome
DAT Reticulocytes LDH, bilirubin
Lymphocytosis Atypical lymphs Neutrophilia Toxic granulation Etc
Consider infection
ESR, CRP, CXR, Virology, blood cultures, etc
Isolated thrombocytopenia
ITP, DITP HIV, HCV H. Pylori HIT, DIC GT, etc
Investigations based on clinical assessment

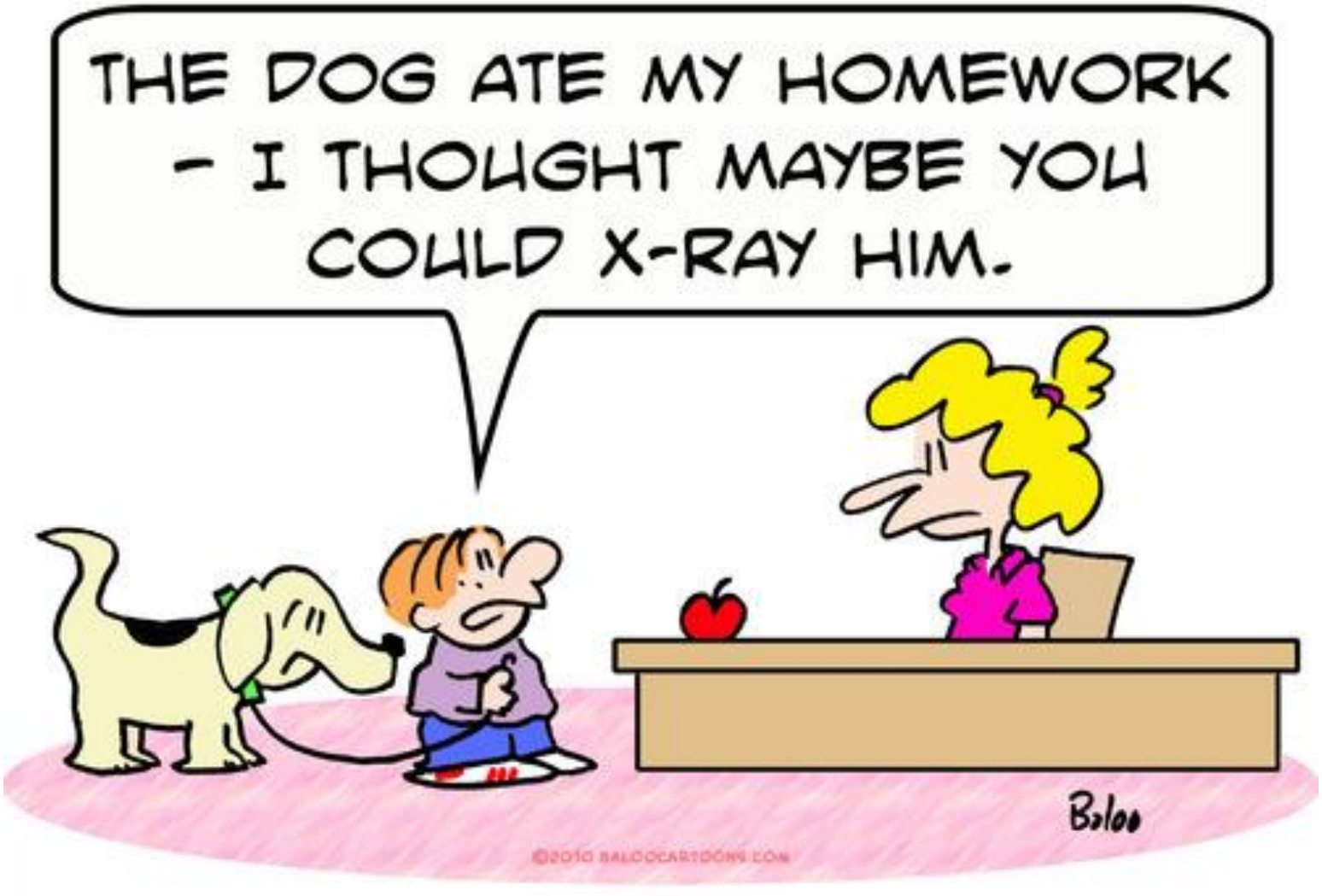
Platelet function disorders

- Congenital vs Acquired
- Adhesion/Aggregation/Secretion



Disorder of Platelet Function

1. Adhension
   - Bernard soulier syndrome
   - Collagen receptor deficiency
   - Plt-type vWD
2. Aggression
   - Galmzman's thrombobasthenia
3. Secreation
   - αgranule : gray plt syndrome
   - δgranule (dense) : storage pool disease, Hermansky-Pudlak syndrome, Chediak-Higashi syndrome, Wiskott- Aldrich syndrome, Thrombocytopenia and absent radii
4. Acquired disorder
   - Drug induced : analgesics, antibiotics, cardiovascular drugs, psychotropic drugs
   - Uremia
   - Disorder of hematopoietic system: MDS, MPD, paraproteinemias
5. Platelet procoagulant activity defect
   - Scott syndrome


THE DOG ATE MY HOMEWORK - I THOUGHT MAYBE YOU COULD X-RAY HIM.
Baloo
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