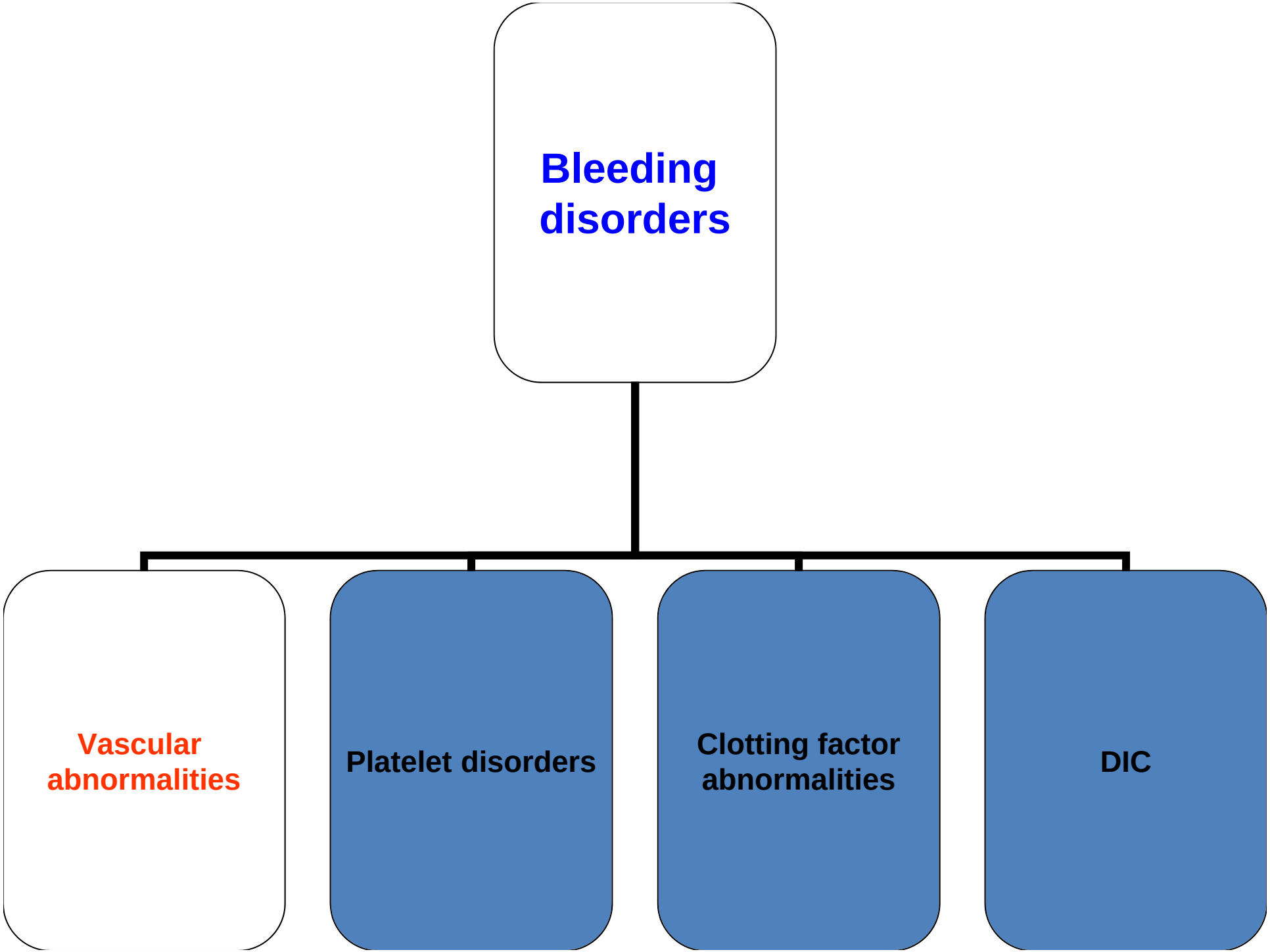
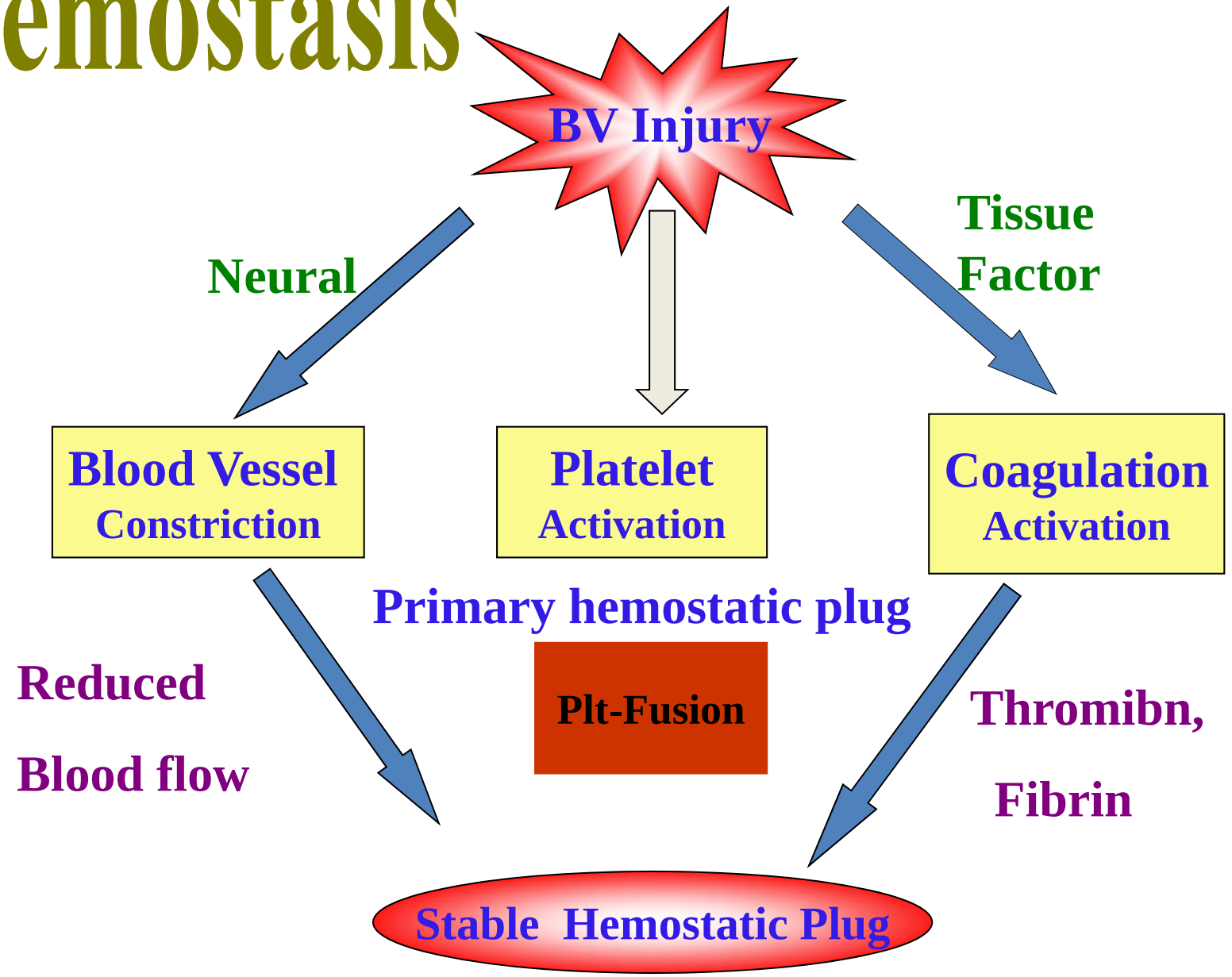

Bleeding disorders
Vascular abnormalities
Platelet disorders
Clotting factor abnormalities
DIC

Hemostasis


BV Injury
Neural
Tissue Factor
Blood Vessel Constriction
Platelet Activation
Coagulation Activation
Primary hemostatic plug
Plt-Fusion
Reduced Blood flow
Thromibn, Fibrin
Stable Hemostatic Plug

Hemostasis

Platelets &vessel wall (Primary hemostasis)

- Thrombocytopenia
- Von willibrands disease
- Drug induced platelet dysfunction

Coagulation & thrombosis (Secondary hemostasis)

- Hemophilia A
- Hemophilia B
- Vitamin K deficiency
- Other coagulation factors Deficiency (v,vii,x,xiii, Protein c,s,antithrombin III

Antiplatelets

Aspirin
Thienopyridines (ticlopidine,clopidogrel)
GpIIa/IIIb antagonists(abciximab,eptifibatide, tirofiban)

Anticoagulant

Heparin (UF,LMWH)

Fibrinolytic drugs

STK,Urikinase,TPA

Primary vs secondary hemostasis

Clinical manifestation	Defects of primary hemostasis	Defects of secondary hemostasis
Onset	immediate	Delayed -hrs/days
site	Superficial mucosal bleed	Deep –joints, muscle,
Physical finding	Petechiae, ecchymosis	Hematoma, hemarthrosis
Treatment response	immediate, local Measures effective	Require sustain Systemic therapy

Disorders of Hemostasis

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

HSP/Anaphylactoid purpura

- Self limited type of vasculitis
- Children & young adults
- Purpuric /urticarial rash on extensor surface of arms,legs& buttocks
- Polyarthralgias/arthritis
- Colicy abdominal pain
- Hematuria (focal glomerulitis)
- Coagulation parameters are normal
- Treatment – glucocorticoids (symptomatic)

Thrombocytopenia

Decreased marrow production eg

Marrow aplasia, infiltration with malignant cells, drugs

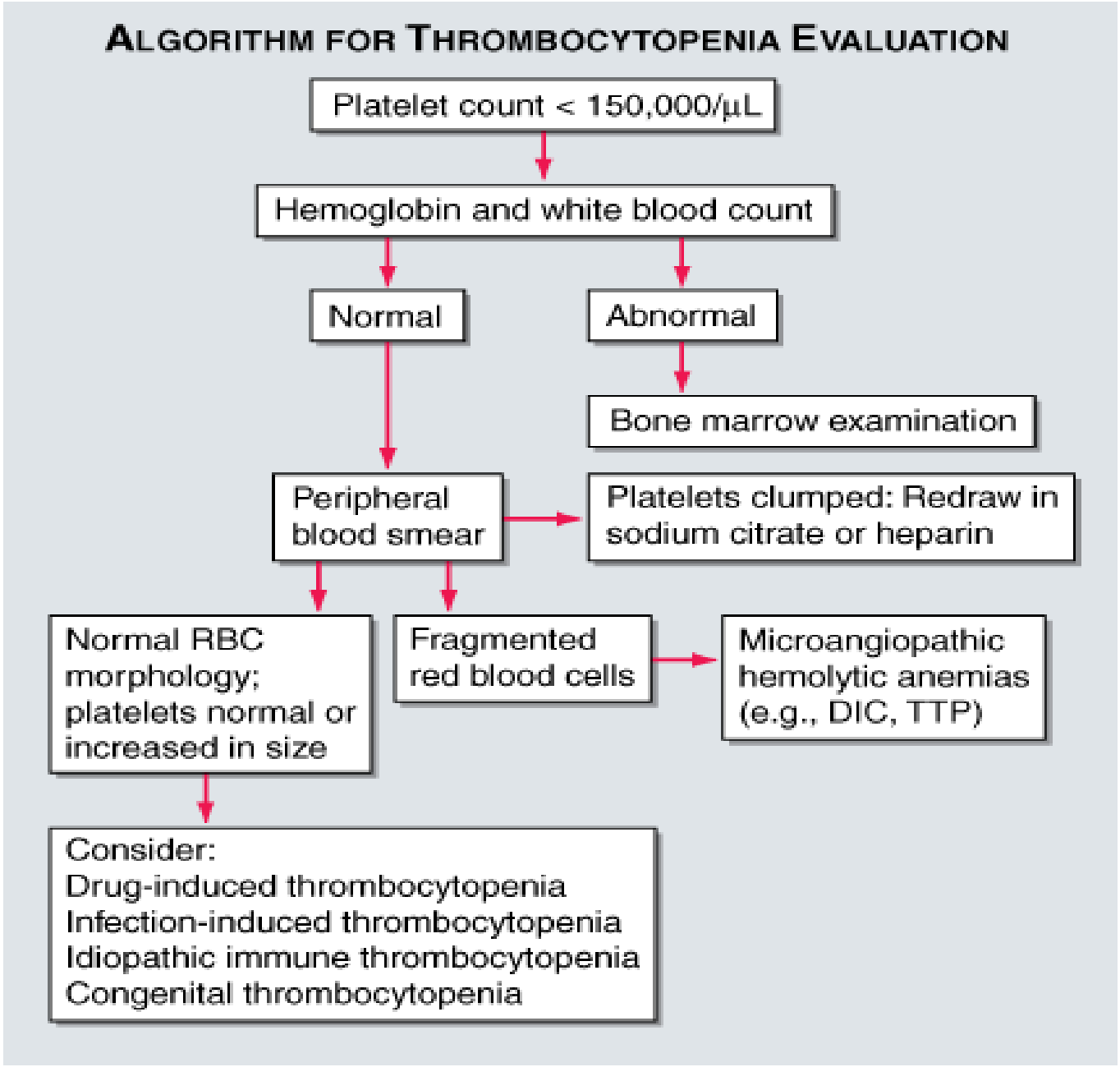
Splenic sequestration eg

portal hypertension, splenic infiltration with tumor cells, myeloproliferative & lymphoproliferative disorders

Accelerated destruction eg HUS

Immunological -viral(dengue), bacterial infection

Drugs , Idiopathic - ITP



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: http://www.accessmedicine.com

Copyright © The McGraw-Hill Companies, Inc. All rights reserved.

Drugs causing thrombocytopenia

- Chemothreapeutic agents Carboplatin, alkylating agents, anthracyclines, antimetabolites
- Antibiotic sufonamides, penicillins, cephalosporins
- Heparins – UF
- Antihypertensive – thiazide diuretics,ACE inhibitors
- Alcohol

Best proof of drug induced etiology is a prompt rise in platelet count when suspected drug is discontinued.

Treatment - stop culprit drug(recover within 7-10 days)
-platelet count <10000 & bleeding
- glucocorticoids
-plasmapharesis/platelet transfusion

Heparin-Induced Thrombocytopenia
HIT

- **Seen in** 3-5% of patients treated with **unfractionated** heparin
- thrombocytopenic after 1-2 weeks of Rx
- **Caused by** IgG antibodies against **platelet factor 4/heparin complexes** on platelet surfaces
- **Exacerbates thrombosis**, both arterial and venous (in setting of severe thrombocytopenia)
  - Antibody binding results in platelet activation and aggregation.
- **Rx - cessation of heparin**

Acute ITP

- Common in children, follows recovery from viral exanthem/URTI
- Sudden onset & thrombocytopenia is often severe.
- 60%recover within 4-6 wks & >90% within 3-6 months
- Mechanism is by formation of immune complex containing viral antigens &formation of antibodies against viral antigens which cross reacts with platelets &lead to their immunological destruction

Chronic ITP

- Common in adults(20-40yrs) – F/M 3:1
- Insidious onset & persist for several years
- Formation of antiplatelet antibodies synthesized in spleen
- Sensitized platelet are destroyed in spleen
- Clinical features – petechiae, hemorrhage, easy brusing, mucosal bleeding from gums, malena
- Lab –thrombocytopenia,BF-largeplatelet,
  marrow -↑no of megakaryocyte with large non lobulated single nuclei
  Platelet survival sudies - ↓ life span
  Coombs test -antiplatelet IgG antibody

Treatment

- <10% cases recover spontaneously
- Steroid prednisolone 60mg/d x 4-6 wks
- Immunosupressive – danazole, azathioprine,cyclophospamide,vincristine,vinblastin,cyclosporin
- Splenectomy
- IVIg

ITP

Feature	Acute	Chronic
Age / Sex	Children	Adult/Female
Onset	Abrupt	Gradual
Predisposing Factors	Viral infection/ vaccine	-
Duration	<2 months	>6mnoths
Pathogenesis	-	IgG against Platelet GP
Peripheral smear	Thrombocytopenia & Giant PLTS	Same
Bone marrow	Normal or ↑Megakaryocytes	Same

ITP

Feature	Acute	Chronic
Tests	Prolonged BT & Normal PT & PTT	Same
Complication (most dangerous)	Intracranial bleed	Same
Clinical course	Spontaneous remission	No
Treatment ▪ PLT. Transfusion ▪ Splenectomy	 If <20,000 No	 If <50,000 Yes (refractory cases)

Thrombotic Thrombocytopenic purpura (TTP)

- Fulminant often lethal disorder initiated by endothelial injury &subsequent release of procoagulant factors eg Vwf
- Cause pregnency, metastatic cancer, mitomycin C, Chemothreapy,HIV,drugs like ticlopidine

Clinical feature

pentard

hemolytic anaemia
thrombocytopenia
neurological finding
renal failure
fever

Treatment

- Removal/correct ppt factors
- Exchange transfusion/intensive plasmapharesis
- Infusion of fresh frozen plasma

Most patient survive a/c illness recover completely with no residual renal or neurological disease

Hemolytic uremic syndrome (HUS)

- Disease of infancy/early childhood

Clinical feature Tetrad

fever
thrombocytopenia
microangiopathic hemolytic anemia
a/c renal failure

- Onset is preceded by minor febrile viral illness
- Epidemic related to infection E.coli (0157H7) has been documented

Treatment

- No therapy effective
- Symptomatic – dialysis for a/c renal failure
- 5%mortality in children
- 10-15% develop CRF

Thrombotic Microangiopathies

HUS	Feature	TTP
Absent	Neurological symptoms	Prominent
Prominent	Acute Renal Failure	Less prominent
Children	Age	Adults
Infection (E.coli O157 : H7)	Cause	Genetic (vWF metalloprotease-ADAMTS 13) deficiency
Supportive	Rx.	Plasma Exchange
Good in children Bad in adults	Prognosis	Better with plasma exchange

Von Willibrands disease

- Most common inherited bleeding disorder
- vonWillibrand factor –heterogeneous multimeric plasma glycoprotein
- Facilitates platelet adhesion
- Plasma carrier for factor VIII (antihemophylic factor)
- Normal plasma vWF level is 10mg/l
- Modest reduction in plasma vWF conc. decreases platelet adhesion &cause clinical bleeding
- Mild cases bleeding occurs only after surgery or trauma
- More severely affected patients have spontaneous epitaxis or oral mucosal, git,genitourinary bleeding

Variants

	Type I	Type II	Type III
Incidence	Most common	Less common	Least common
inheritance	AD	AD	AR
vWF	<50%	↓	↓
RC activity	↓	↓	↓
Multimer pattern	N	↓	A

Lab

- BT- Prolonged
- N -Platelet count
- Reduced plasma vWF concentration
- Defective platelet aggregation with ristocetin.
- Reduced factor VIII activity

Treatment

- Factor VIII concentrate infusion (cryoprecipitate)
- During surgery/trauma factor VIII conc. Infusion given BD X 2-3 days
- Minor bleeding responds to single infusion
- Desmopressin effective only in type I, can be given intravenously or by an intranasal spray (1.5 mg/mL). The peak activity when given intravenously is approximately 30 min, while it is 2 h when given intranasally. The usual dose is 0.3 g/kg intravenously or 2 squirts (1 in each nostril) for patients >50 kg (1 squirt for those <50 kg).