Bleeding disorders in children

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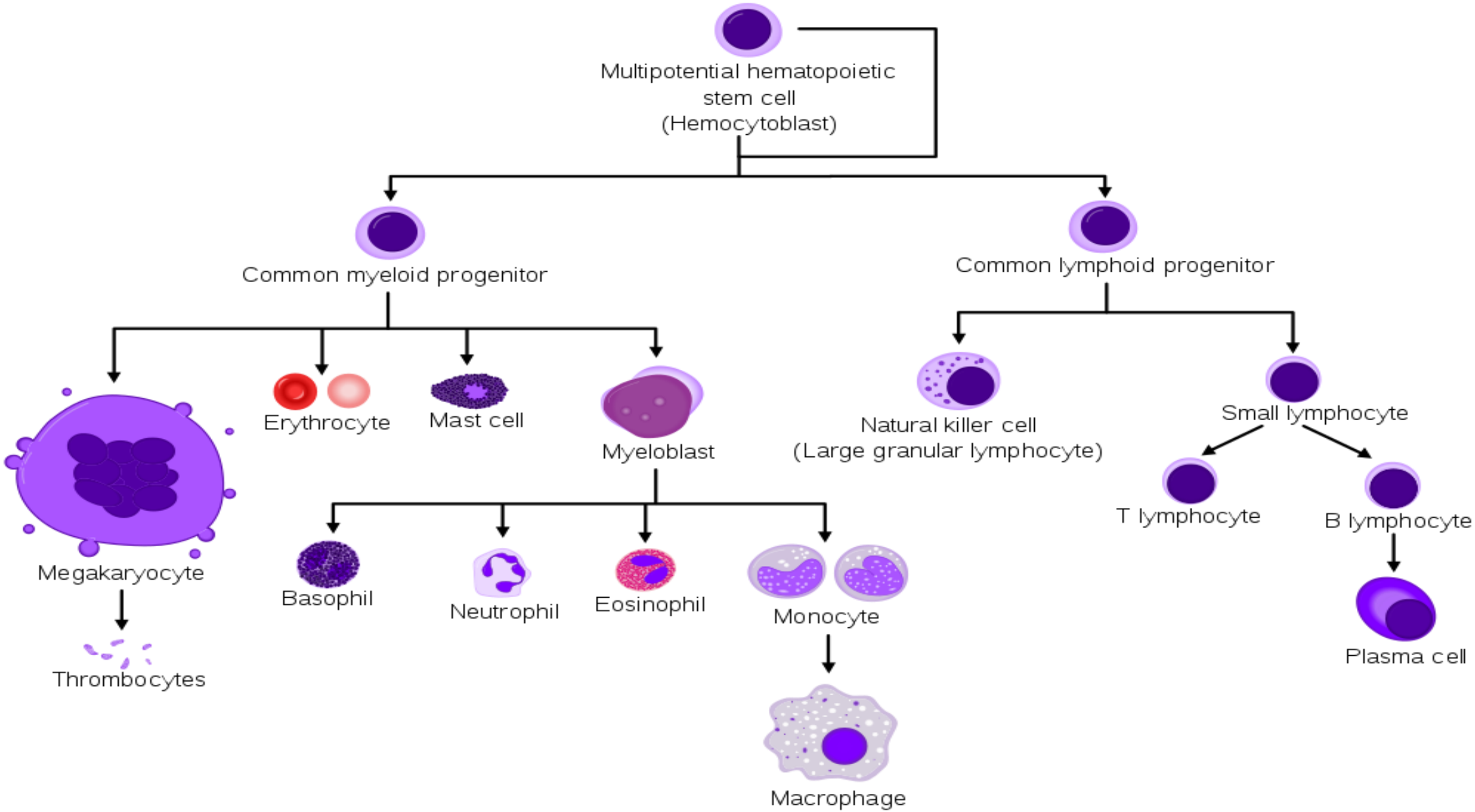

Multipotential hematopoietic stem cell (Hemocytoblast)
Common myeloid progenitor
Common lymphoid progenitor
Megakaryocyte
Thrombocytes
Erythrocyte
Mast cell
Myeloblast
Basophil
Neutrophil
Eosinophil
Monocyte
Macrophage
Natural killer cell (Large granular lymphocyte)
Small lymphocyte
T lymphocyte
B lymphocyte
Plasma cell

Hemostasis

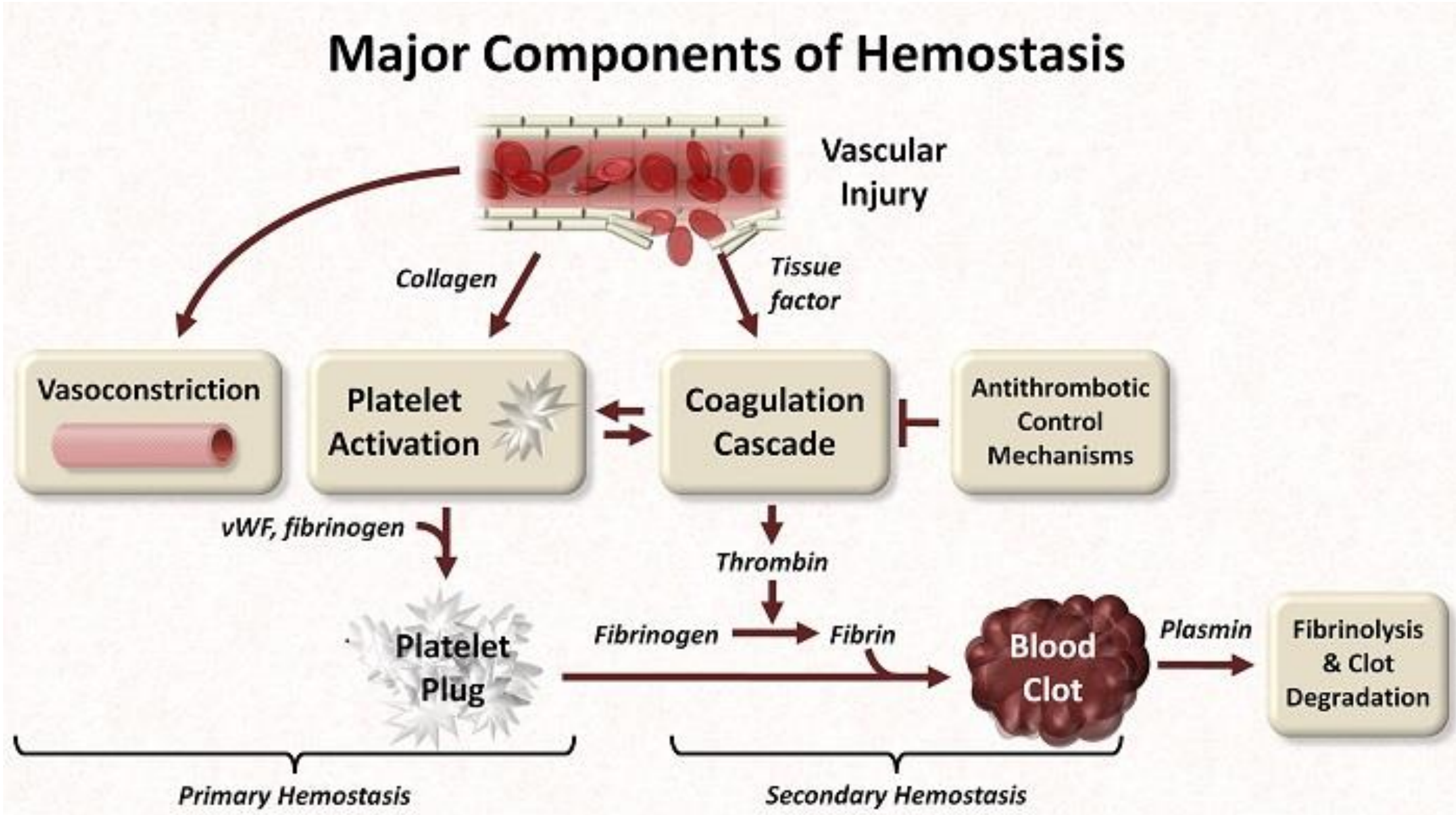
- Megakaryocytes are giant, multinucleated cells derived from the primitive stem cell.

- Thrombopoietin is the primary regulator of platelet production. Platelets adhere to damaged endothelium and subendothelial surfaces via specific receptors for the adhesive proteins, von Willebrand factor (vWF), and fibrinogen.

- Platelets also have specific granules that readily release their contents after stimulation and trigger the process of platelet aggregation.

- Platelets circulate for 7 to 10 days and have no nucleus.

Major Components of Hemostasis



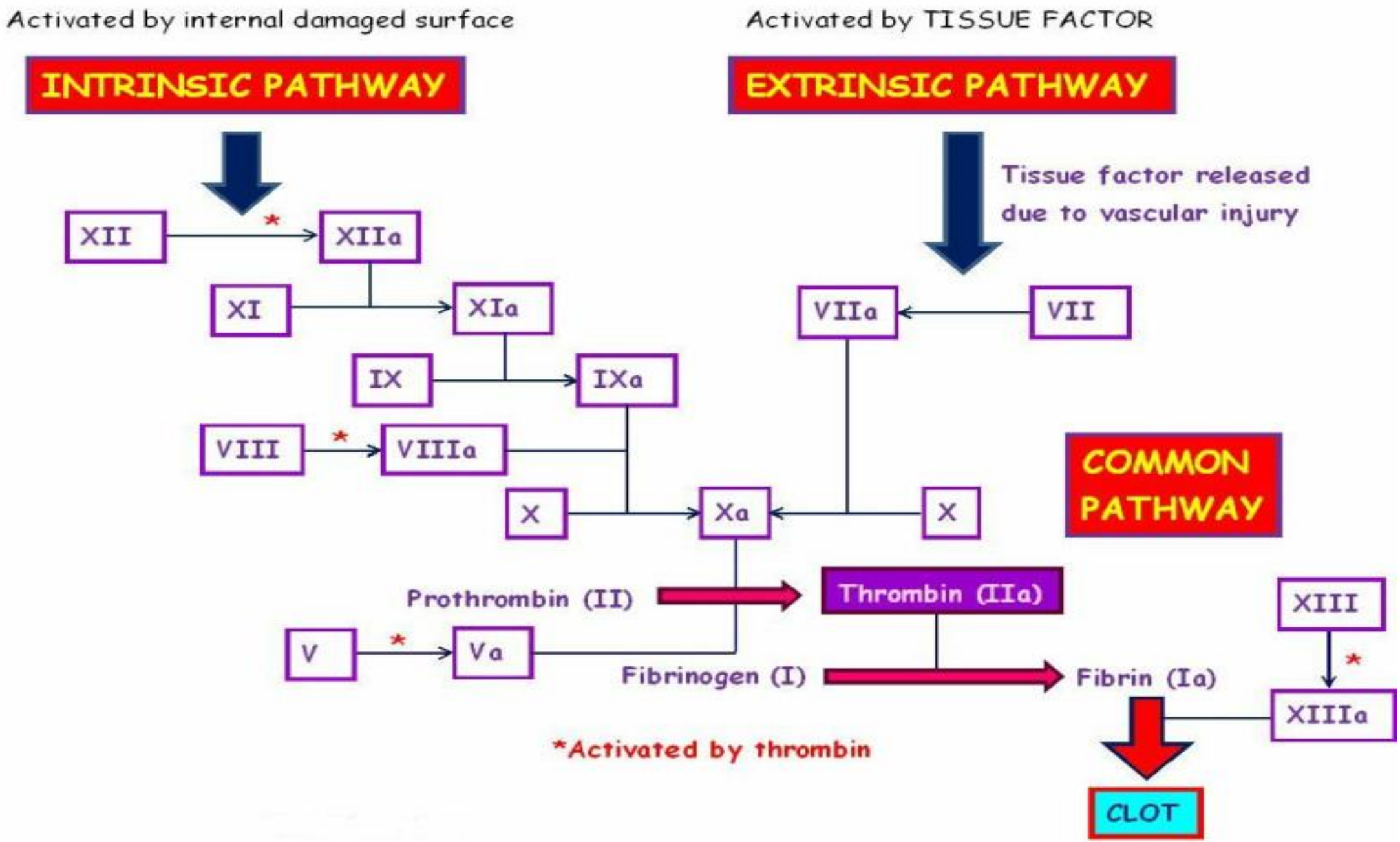

Activated by internal damaged surface
Activated by TISSUE FACTOR
INTRINSIC PATHWAY
EXTRINSIC PATHWAY
Tissue factor released due to vascular injury
XII
XIIa
XI
XIa
IX
IXa
VIII
VIIIa
VIIa
VII
X
Xa
X
COMMON PATHWAY
Prothrombin (II)
Thrombin (IIa)
V
Va
Fibrinogen (I)
Fibrin (Ia)
XIII
XIIIa
*Activated by thrombin
CLOT

Table 502.1

Coagulation (Clotting) Factors

CLOTTING FACTOR	SYNONYM	DISORDER
I	Fibrinogen	Congenital deficiency (afibrinogenemia) or dysfunction (dysfibrinogenemia)
II	Prothrombin	Congenital deficiency or dysfunction
V	Labile factor, proaccelerin	Congenital deficiency (parahemophilia)
VII	Stable factor or proconvertin	Congenital deficiency
VIII	Antihemophilic factor	Congenital deficiency is hemophilia A (classic hemophilia)
IX	Christmas factor	Congenital deficiency is hemophilia B (sometimes referred to as Christmas disease)
X	Stuart-Prower factor	Congenital deficiency
XI	Plasma thromboplastin antecedent	Congenital deficiency (sometimes referred to as hemophilia C)
XII	Hageman factor	Congenital deficiency is not associated with clinical symptoms
XIII	Fibrin-stabilizing factor	Congenital deficiency

Factor	Site of synthesis	Levels in infancy	Half-life	Vitamin K-dependent	Other
Fibrinogen (I)	Liver	Normal	2-4 d	No	High fibrinogen increases ESR
Prothrombin (II)	Liver	Low	3 d	Yes	
Factor V	Liver Megakaryocytes	Low	36 hr	No	
Factor VII	Liver	Low	3-6 hr	Yes	
Factor VIII	Liver Endothelial Cells	Normal/ High	8-12 hr	No	Circulates with VWF Increased by DDAVP
Factor IX	Liver	Low	22 hr	Yes	
Factor X	Liver	Low	40 hr	Yes	
Factor XI	Liver	Low	80 hr	No	
Factor XIII	Liver/Macrophage	Low	10 d	No	Important in wound healing
VWF	Endothelial cells Megakaryocytes	Normal/ High	12 hr	No	Stored in Weibel-Palade bodies in endothelial cells

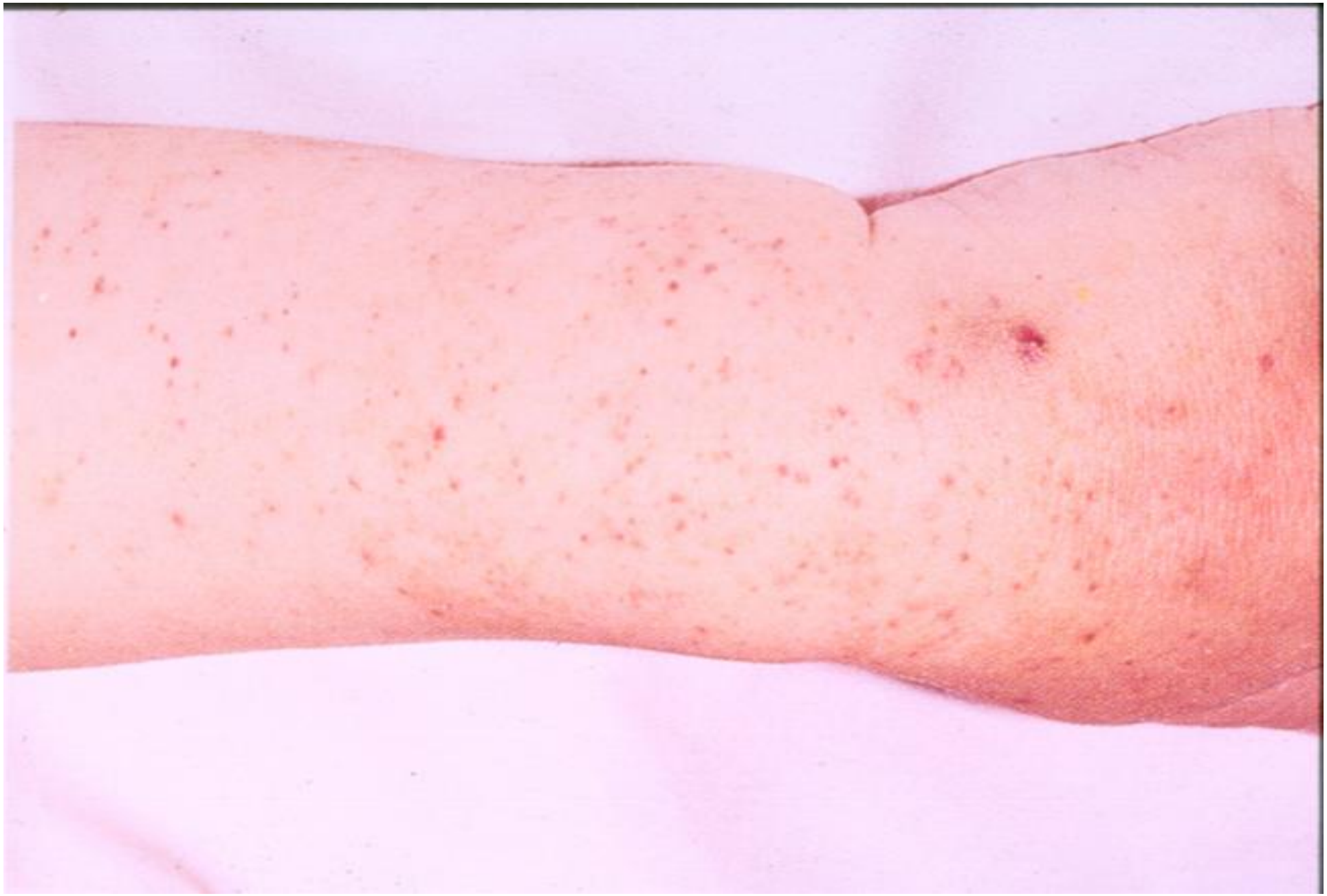
All coagulation factors are made in the liver with the exception of VWF.

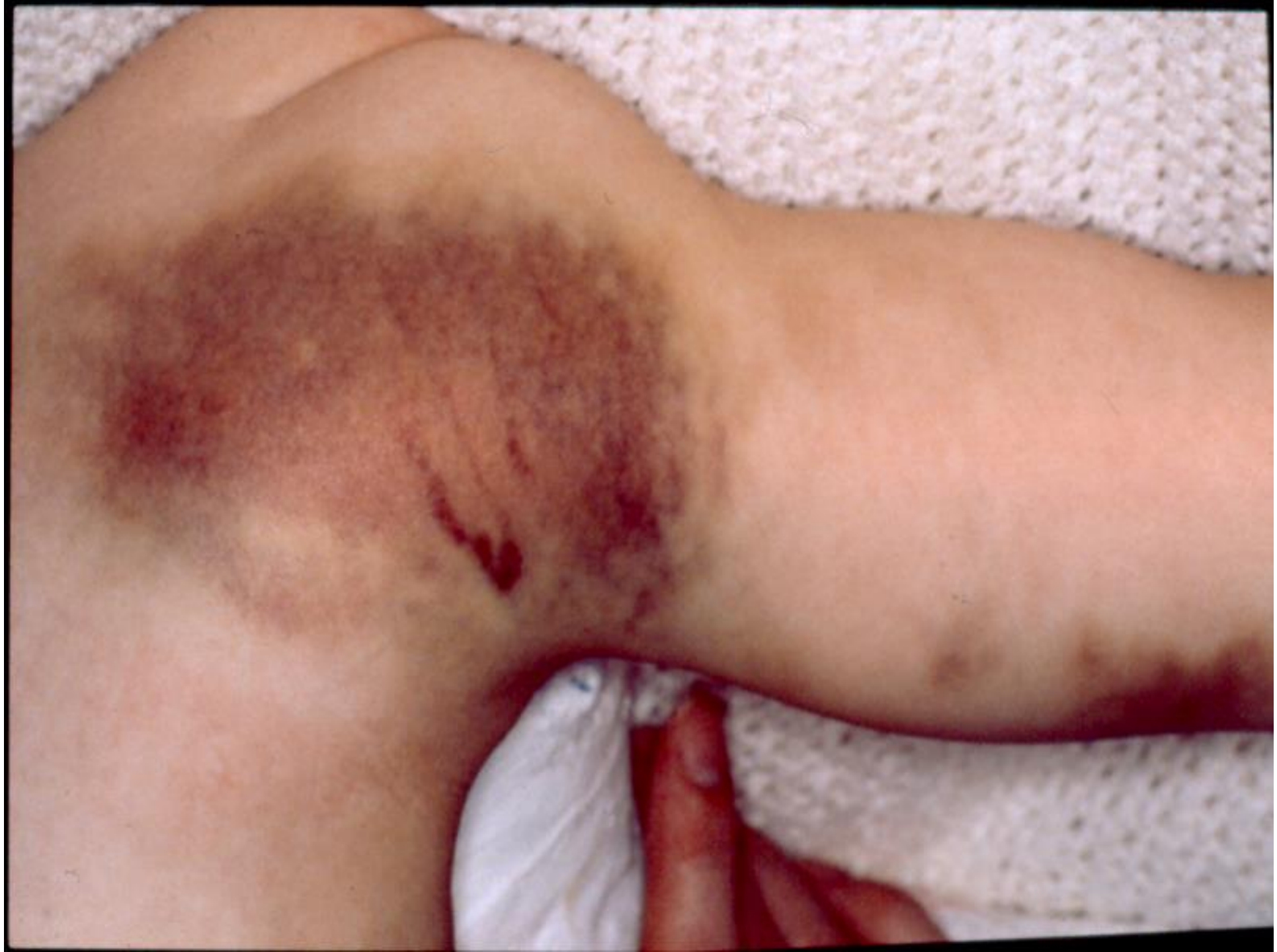
Factor VII has the shortest half-life of 3-6 hours (earliest to drop in liver failure) and factor XIII has the longest half-life of 10 days.

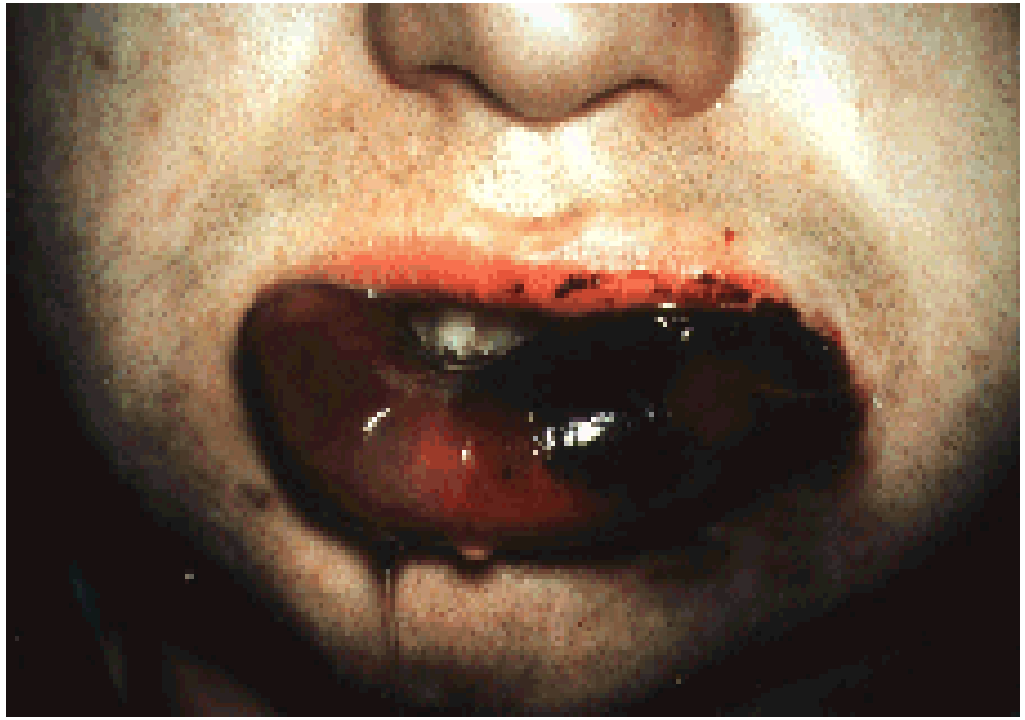
Vitamin K dependent coagulation factors include factors II,VII,IX and X in addition to protein C and protein S.

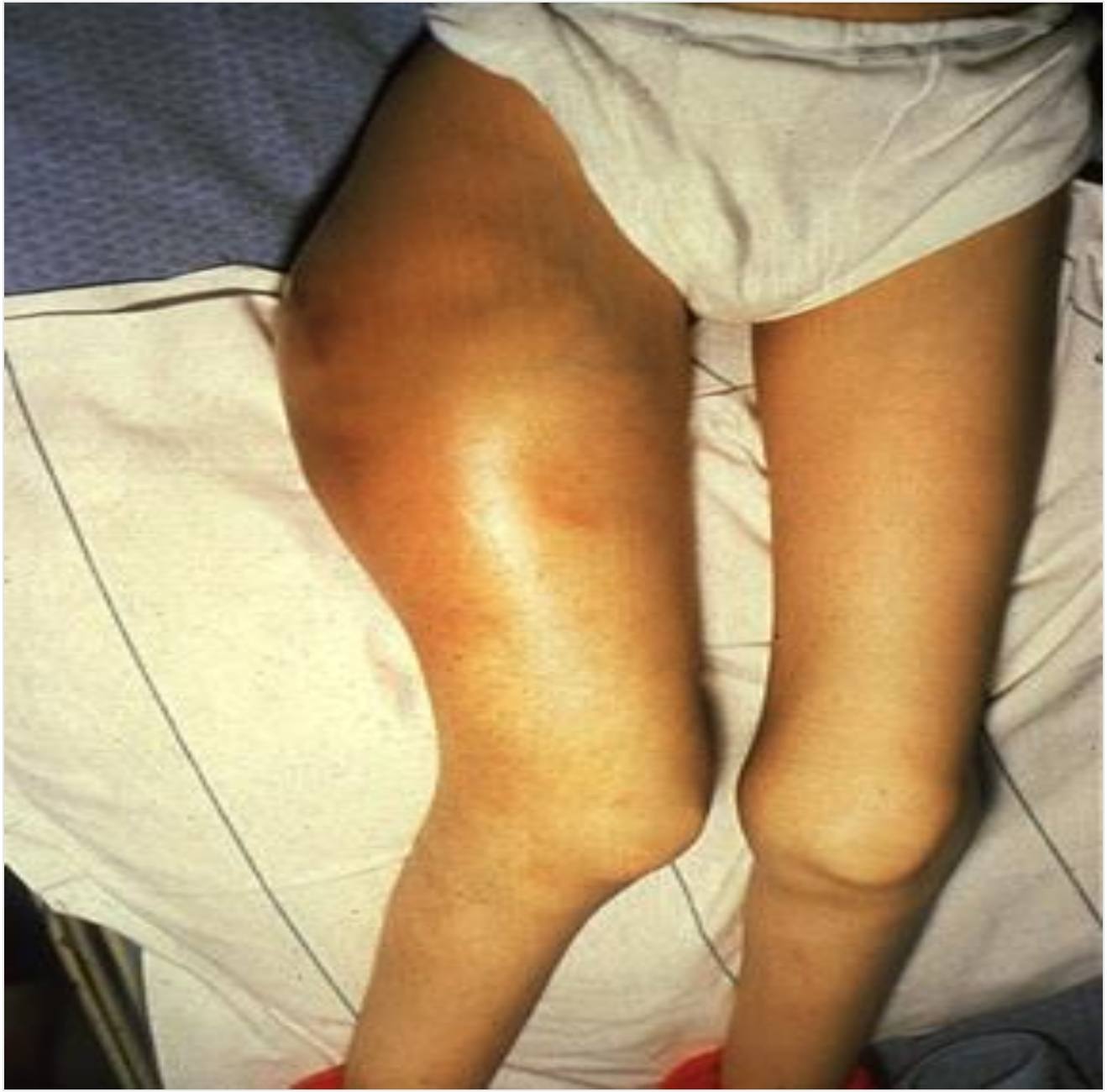
Functional Classification of Bleeding Disorders

- **Abnormal vessels**
  - Ehler Danlos
  - HSP
- **Defects of platelets**
  - Number: Infection, ITP, Leukemia
  - Function: vWD, BS, GT, Drugs
- **Abnormal coagulation**
  - Congenial: Hemophilia A or B
  - Acquired: Liver disease, Vit K deficiency , DIC









Clinical findings	Disorders of coagulation*	Purpuric disorders •
Skin - petechiae	Not usually seen	Characteristic
Ecchymosis	Common - large one or more	Characteristic - small or many scattered
Soft tissue hematoma	Characteristic	Rare
Joint hemorrhages	Characteristic - hallmark of the disease	Not usually seen
Delayed bleeding	Common	Rare
Bleeding from superficial skin abrasions	Uncommon	Common and persistent
Family history of bleeding	Common	Rare
Sex of the patient	Predominantly male	Predominantly female

History

Neonatal bleeding

Bleeding after circumcision

Delayed bleeding from umbilical stump (factor XIII)

Deep hematoma after I.M injections

Epistaxis Unilateral vs bilateral

Tooth extraction, tonsils

Site of bleeding: skin, mm, joints

Family history of bleeding disorders

Drug exposure

Injury child abuse

Physical examination

Petichiae

Ecchymosis

Joint bleeding and deep seated hematomas

Significant lymphadenopathy

Hepatosplenomegaly

Active and playful vs ill looking

Telangietic vessels

Hemangiomas

Loose joints and lax skin associated with easy bruising (Ehlers-Danlos syndrome)

- A male infant who is starting to walk and presents with a painful swollen joint after a fall has hemophilia until proven otherwise.

- An adolescent girl who presents with excessive menstrual bleeding, recurrent nosebleeds, and pallor may have von Willebrand Disease (vWD), the most common inherited bleeding disorder

- A five-year-old child who is not clinically ill but presents with moderate mucocutaneous purpura in the wake of a viral infection most likely has acute post-infectious immune thrombocytopenia

- A teenage girl with easy bruising and mild pallor presenting to a pediatrician's office with a strong family history of autoimmune disorders may have chronic ITP

- A ten-day-old infant with bleeding from the umbilical stump should be evaluated for factor XIII deficiency ,Intracranial hemorrhage in an infant without other risk factors should also prompt consideration of this diagnosis.

Coagulation Screen

Common screening tests:

1-Platelet count and morphology.

2-Bleeding time

3-Partial Thromboplastin Time (PTT).

4-Prothrombin Time (PT).

5-Thrombin time (TT).

Specialized tests:

1-FXIIIA quantitative test

2-Mixing studies

3-Factors assay

4-VW Factor quantitative assay

5-Platelet aggregation

6-Other rare tests

Diagnosis of Coagulation Disorders Screening Tests

Complete blood count :

- Thrombocytopenia when less than 150,000/mm3

- Platelet count is essential in the evaluation of the child with a positive bleeding history because thrombocytopenia is the most common acquired cause of a bleeding diathesis in children.
- **Pseudo thrombocytopenia** Examination of the peripheral blood smear is essential in patients with low platelet counts in order to exclude the presence of pseudo thrombocytopenia caused by platelet aggregation after using EDTA as an in vitro anticoagulant

- **Prothrombin time (PT) :**

- The production of fibrin via the extrinsic pathway and the final common pathway requires tissue thromboplastin (tissue factor), factor VII, factors X, V, prothrombin (factor II), and fibrinogen.

- This test bypasses the intrinsic pathway and uses "complete" thromboplastins (ie, tissue factor) capable of activating the extrinsic pathway.

- The PT is sensitive to alterations in the vitamin K-dependent coagulation factors, especially factors II, VII, and X, and is used to monitor treatment with vitamin K antagonists

- **Activated partial thromboplastin time (aPTT)**

- The aPTT measures the intrinsic and common pathways of coagulation
- This aPTT is routinely used to evaluate intrinsic coagulation and the degree of heparin anticoagulation.

- The aPTT is sensitive to deficiencies of factors XII, XI, IX, and VIII and to inhibitors such as heparin

- It is less sensitive than the PT to deficiencies within the common pathway (eg, factors X, V, prothrombin, and fibrinogen) and is unaffected by alterations in factors VII and XIII.

- **Thrombin Time:**

- Thrombin time measures the final step in the clotting cascade, in which fibrinogen is converted to fibrin.

- The normal thrombin time varies between laboratories but is usually 11-15 sec.

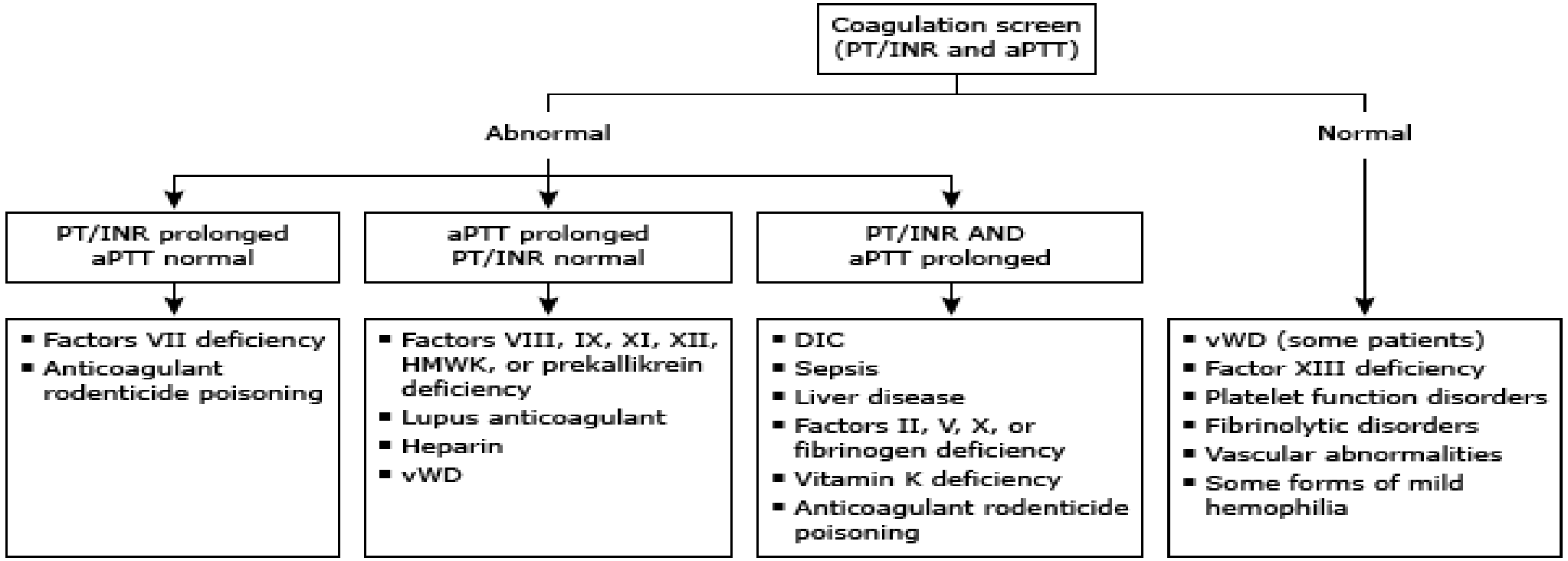
- Prolongation of thrombin time occurs with reduced fibrinogen levels (hypofibrinogenemia or afibrinogenemia), and dysfunctional fibrinogen (dysfibrinogenemia)

- **Bleeding Time:**
- Bleeding time assesses the function of platelets and their interaction with the vascular wall
- Bleeding time is a difficult laboratory test to standardize
- **Platelet Function Analyzer:**
- evaluate the early stages of hemostasis (platelet function and VWF interaction under high shear
- **The PFA-100** measures platelet adhesion -aggregation in whole blood at high shear when exposed to either collagen-epinephrine or collagen-ADP.
- Results are reported as the closure time measured in sec.
- **VWF Antigen**
- **Platelet aggregation test**
- **Clotting Factor Assays:**

Test result		Causes of test result pattern
PT	aPTT	
Prolonged	Normal	**Inherited**
		Factor VII deficiency
		Acquired
		Mild vitamin K deficiency
		Liver disease
		Warfarin administration*
		Acquired inhibitor of factor VII
Normal	Prolonged	**Inherited**
		Deficiency of factors VIII, IX, or XI
		Deficiency of factor XII, prekallikrein, or HMW kininogen (not associated with a bleeding diathesis)
		von Willebrand disease (variable)
		Acquired
		Heparin administration*
		Inhibitor of factors VIII, IX, XI, or XII
		Acquired von Willebrand disease
		Lupus anticoagulant (may be associated with thrombosis rather than bleeding)

PT	aPTT	
		Inherited
		Deficiency of prothrombin, fibrinogen, or factors V or X
		Combined factor deficiencies
		Acquired
		Liver disease
		Disseminated intravascular coagulation
		Supratherapeutic doses of anticoagulants
		Severe vitamin K deficiency
Prolonged	Prolonged	Combined heparin and warfarin administration
		Direct thrombin inhibitor administration (eg, argatroban, dabigatran)*
		Direct factor Xa inhibitor administration (eg, rivaroxaban, apixaban, edoxaban)
		Inhibitor of prothrombin, fibrinogen, or factors V or X

Algorithm for identifying causes of bleeding symptoms in children based on results of coagulation screen



Refer to UpToDate topic on the evaluation of bleeding symptoms in children for additional details.

PT: prothrombin time; INR: international normalized ratio; aPTT: activated partial thromboplastin time; vWD: von Willebrand disease; HMWK: high molecular weight kininogen; DIC: disseminated intravascular coagulation.

- Mixing studies can help delineate the etiology of an elevated PTT. If mixing the patient’s sample with normal plasma corrects the elevation in PTT the underlying cause is a factor deficiency and if not, it’s related to an inhibitor.

- If there is an unexplained prolongation of the PT, PTT, or thrombin time, a mixing study is usually performed. Normal plasma is added to the patient's plasma, and the PTT or PT is repeated.

- Correction of the PT or PTT by 1:1 mixing with normal plasma suggests the deficiencies of a clotting factor

Disorders of Platelets

- **Mucocutaneous bleeding** is the hallmark of platelet disorders
- Children with platelet counts less than 20,000/mm3 are at risk for **spontaneous bleeding.**
- The etiology of thrombocytopenia may be organized into two mechanisms:

1 Decreased platelet production: usually small size platelets or low MPV

2 Increased destruction: usually large platelets or high MPV(mean platelet volume):

A Autoimmune

B Hypersplenism,

C Mechanical destruction (Microangiopathic hemolytic Anemia)

Decreased Platelet Production

Thrombocytopenia with absent radii syndrome (TAR):

- Severe thrombocytopenia in association with orthopedic abnormalities.
- The thrombocytopenia usually improves over time

Congenital A megakaryocytic Thrombocytopenia (CAMT):

- Severe thrombocytopenia, but no other congenital anomalies.
- The marrow is devoid of megakaryocytes and usually progresses to aplasia of all hematopoietic cell lines.

Decreased Platelet Production

- **Wiskott-Aldrich syndrome** An X-linked disorder characterized by hypogammaglobinemia, eczema, and thrombocytopenia
- Small platelets are seen on a peripheral blood smear.

- **Acquired thrombocytopenia** as a result of decreased production is **rarely an isolated finding**.

- It is seen more often in the context of pancytopenia resulting from **bone marrow failure** caused by infiltrative or aplastic processes.

Peripheral destruction

Immune Thrombocytopenic Purpura

- Autoimmune thrombocytopenic purpura of childhood (childhood ITP) is a common disorder that usually follows an acute viral infection.

- The most common cause of acute onset of thrombocytopenia in otherwise healthy child

- Incidence in Males=females

- Peak incidence between 1 – 4 years of age

- Childhood ITP is caused by an antibody (IgG or IgM) that binds to the platelet membrane.

- As the immune system tries to clear a viral infection, it starts by making IgM antibodies. Later class switching occurs and IgG titers rise in a matter of a few weeks. Occasionally, these IgG antibodies my cross react with some of the platelet common antigens if they share similarities with viral antigens.

- Once the platelets are coated by these antibodies, they'll be phagocytosed by macrophages in the reticuloendothelial system as they pass through it causing thrombocytopenia

- Splenic destruction of antibody-coated platelets leading to sever thrombocytopenia < 10.000 platelets/mm3.

- Clinical Manifestations. Young children typically exhibit ITP 1 to 4 weeks after viral illness, with abrupt onset of petechiae, purpura, and epistaxis.

- The thrombocytopenia usually is severe.

- No Significant adenopathy or hepatosplenomegaly

- Red blood cell (RBC) and white blood cell (WBC) and differential are normal.

- The diagnosis of ITP usually is based on clinical presentation and the platelet count and does not often require a bone marrow examination.

Immune Thrombocytopenic Purpura

- **If atypical findings are noted, however, marrow examination is indicated to rule out an infiltrative disorder (leukemia) or an aplastic process (aplastic anemia).**

- **BM study before steroid treatment**

- Increased megakaryocytes and normal erythroid and myeloid elements.

Treatment

- Therapy is seldom indicated for platelet counts greater than 20,000/mm^3 .
- For moderate and severe clinical bleeding with severe thrombocytopenia (platelet count <10,000/mm3)

- Therapeutic options include **prednisone**, 2 to 4 mg/kg/24 hours for 2 weeks or **IVIG**, 1 g/kg/24 hours for 1 to 2 days or **Anti D** Immunoglobulin

- Splenectomy is indicated in acute ITP only for life-threatening bleeding.

- Platelet transfusion in ITP is usually indicated in life threatening bleeding.

- Approximately 80% of children have a spontaneous resolution of ITP within 6 months after diagnosis.

- Serious bleeding, especially intracranial bleeding, occurs in fewer than 1% of patients with ITP.

- ITP that persists for 6 to 12 months is classified as chronic ITP.

- Repeated treatments with IVIG, IV anti-D, or high-dose pulse steroids are effective in delaying the need for splenectomy.

- **Rituximab** (anti CD20) induces remission in 50% of cases

- **Thrombopoietin agonists (Eltrombopag)**

- Secondary causes of chronic ITP, especially SLE ,HIV infection , and immune deficiency should be ruled out.

- **Splenectomy** induces a remission in 70% to 80% of childhood chronic ITP cases.

- The risks of splenectomy (surgery, sepsis from encapsulated bacteria) must be weighed against the risk of severe bleeding.

- **Hemolytic uremic syndrome** occurs as a result of exposure to a toxin that induces endothelial injury, fibrin deposition, and platelet activation and clearance

- **Thrombotic thrombocytopenic purpura** platelet consumption, precipitated by a congenital or acquired deficiency of a metalloproteinase that cleaves von Willebrand factor.

- **Disseminated Intravascular Coagulation**

Disorders of Platelet Function

- **Primary disorders** of platelet function may involve receptors on platelet membranes for adhesive proteins.
- Autosomal recessive disorders
- **Characterized by prolonged bleeding time**
- **Glanzmann thrombasthenia** is an **autosomal recessive** disorder characterized by diminished ability of platelets to aggregate and form a clot as a result of deficient adhesive glycoprotein IIb/IIIa (receptor for fibrinogen) on the platelet cell membrane.
- Usually normal platelet count.

Disorders of Platelet Function

- **Bernard–Soulier syndrome** is an **autosomal recessive** disorder characterized by decreased platelet adhesion as a result of absence of platelet membrane glycoprotein Ib (receptor for collagen).

- Severe hemorrhage may occur, **mild thrombocytopenia** and **large unusual platelets** are seen on blood smear.

Secondary disorders

- systemic illnesses, e.g., liver disease, kidney disease (uremia).

- Drugs (valproic acid, Aspirin, NSAIDS drugs)

- **Disorders of platelet function present with mucocutaneous bleeding and a prolonged bleeding time or abnormal platelets aggregation**

Disorders of Clotting Factors

- **Congenital clotting factor disorders.** These disorders include deficiency of **factor VIII** and **von Willebrand disease** (both of which are factor VIII–related disorders) and deficiency of **factor IX**.

- **Factor VIII disorders** include two inherited disorders

- **Hemophilia A** represents a defect in factor VIII procoagulant activity and normal Platelet function.

- **Von Willebrand disease**

- Factor VIII procoagulant activity is variable, but platelet function is defective because of a decrease or defect in **von Willebrand factor,** a protein required for platelet adhesion to blood vessel wall.

- It also functions as a carrier protein for factor VIII.

Factor VIII deficiency—hemophilia A

- **Inheritance** is **X-linked** and occurs in 1 in 5000–10,000 male births.
- Only 2% of neonates with hemophilia sustain intracranial hemorrhages.

- 30% of male infants with hemophilia bleed with circumcision.

- **Hemarthroses** (involving the knees, elbows, and ankles most commonly) and **deep soft tissue bleeding** are the **hallmarks.**

- **Bleeding into the iliopsoas muscle** may be especially severe as a result of delayed recognition of the bleeding and the potential for significant blood accumulation.

Factor VIII deficiency—hemophilia A

Severe, moderate, and mild forms exist based on the activity level of factor VIII protein.

- **Severe: spontaneous bleeding** (<1% factor VIII protein activity)
- **Moderate: bleeding only with trauma** (1–5% factor VIII protein activity)
- **Mild: bleeding only after surgery or major trauma** (>5% factor VIII protein activity)
- **Central nervous system (CNS) bleeding** is the most dreaded complication and is usually the result of head trauma.

Factor VIII deficiency—hemophilia A

Laboratory findings

- **Prolonged aPTT** (in mild form, aPTT may be normal)
- **Normal PT, platelet count,** and **platelet function assay**
- **Low factor VIII protein activity** in the presence of normal von Willebrand factor assay

Factor VIII deficiency—hemophilia A

- **Management.** Treatment includes prevention of trauma and replacement of factor VIII.

- **Desmopressin acetate (DDAVP)** causes the release of stored factor VIII from the patient's own cells and may be useful in mild hemophilia A.

Treatment

- Early, appropriate **replacement therapy** is the hallmark of excellent hemophilia care.
- Treatment includes prevention of trauma and replacement of factor VIII.

- Prophylactic therapy starting in infancy has greatly diminished the likelihood of chronic Arthropathy in children with sever hemophilia.

- Recombinant factor VIII (FVIII).

- **Novo Seven for inhibitors**

- For mild to moderate bleeding episodes (hemarthroses), a 40% level for factor VIII or a 30% to 40% level for factor IX is appropriate.

- The dose can be calculated using the knowledge that 1 U/kg body weight of factor VIII increases the plasma level 2%, whereas 1.5 U/kg of recombinant factor IX increases the plasma level 1%.

- Desmopressin acetate is a synthetic vasopressin analog with minimal vasopressor effect is used in mild Hemophilia A.

Complications

Long-term complications of hemophilia A and B include :

- Chronic arthropathy
- development of an inhibitor to either factor VIII or factor IX.
- Risk of transfusion-transmitted infectious diseases (with plasma derived not with recombinant factors)

Factor IX deficiency hemophilia B

- This **X-linked disorder** has clinical features similar to those of hemophilia A and occurs in 1 in 50,000 males.
- aPTT is prolonged and low factor IX activity is found.
- PT and platelet count are normal.
- Management includes factor IX replacement.

Factor XIII Deficiency

- Factor XIII is responsible for the cross linking of fibrin or the stabilization of fibrin clot.
- The longest half-life of all the clotting factors (10 days).
- Screening coagulation tests (PT and PTT) are normal.
- Factor XIII deficiency is associated with poor wound healing.
- Delayed separation of umbilical stump (can also occur with leukocyte adhesion deficiency) and intracranial hemorrhage.

Von Willebrand disease

- Von Willebrand Disease (VWD) is the most common inherited bleeding disorder, with an estimated prevalence at 1 : 100 to 1 : 10,000.

- VWF has several functions in coagulation. First, VWF serves to tether platelets to injured subendothelium via binding sites for platelets and for collagen. Second, VWF serves as a carrier protein for factor VIII.

- Von Willebrand factor (VWF) is a large glycoprotein that is synthesized in megakaryocytes and endothelial cells.

- VWD is inherited as an autosomal pattern , the gene on Chromosome 12
- Type 1: quantitatively reduced is the most common type(85%),AD
- Type 2: Qualitatively abnormal, AR or AD
- Type 3: Absent, AR

Von Willebrand disease

- **Most patients** have mild to moderate bleeding, usually involving mucocutaneous surfaces.

- More profound bleeding occurs in type III disease.

- **Common signs and symptoms** include epistaxis, **menorrhagia,** bruising, and bleeding after dental extraction or tonsillectomy

- **Hemarthroses are unusual.**

Diagnosis

- Prolonged bleeding time.
- In type 3, prolonged PTT.
- Abnormal tests for VWF antigen, VWF activity.
- Plasma factor VIII activity.

Treatment

- Treatment of VWD is directed toward increasing the plasma level of VWF
- Synthetic desmopressin (DDAVP) induces the release of VWF from the endothelial cells.
- It works in most cases of VWD but not in type 2, or type 3, Where treatment is by giving replacement therapy using plasma-derived VWF concentrates.
- **Cryoprecipitate**, which contains intact vWf, may be used for serious bleeding, for extensive surgeries, or for type III disease (**also contains fibrinogen , factor 8 and factor 13**)

Table 151-3 Comparison of Hemophilia A, Hemophilia B, and von Willebrand Disease

FEATURE	HEMOPHILIA A	HEMOPHILIA B	VON WILLEBRAND DISEASE
Inheritance	X-linked	X-linked	Autosomal dominant
Factor deficiency	Factor 8	Factor 9	vWF, factor 8
Bleeding site(s)	Muscle, joint, surgical	Muscle, joint, surgical	Mucous membranes, skin, surgical, menstrual
Prothrombin time	Normal	Normal	Normal
Activated partial thromboplastin time	Prolonged	Prolonged	Prolonged or normal
Bleeding time/PFA-100	Normal	Normal	Prolonged or normal
Factor 8 coagulant activity	Low	Normal	Low or normal
von Willebrand factor antigen	Normal	Normal	Low
von Willebrand factor activity	Normal	Normal	Low
Factor 9	Normal	Low	Normal
Ristocetin-induced platelet agglutination	Normal	Normal	Normal, low, or increased at low-dose ristocetin
Platelet aggregation	Normal	Normal	Normal
Treatment	DDAVP* or recombinant factor 8	Recombinant factor 9	DDAVP* or vWF concentrate

Acquired clotting factor disorders

- **Vitamin K deficiency**

- A fat-soluble vitamin, is essential for the synthesis of both procoagulant and anticoagulant factors, such as **factors II, VII, IX, and X** and **proteins C and S.**

- **Dietary deficiency is unusual,** except during early infancy.

- Pancreatic insufficiency, biliary obstruction, and prolonged diarrhea may result in diminished ability to absorb vitamin K.

- **Medications** may interfere with vitamin K metabolism (e.g., cephalosporins, rifampin, isoniazid, warfarin).

- **Hemorrhagic disease of the newborn** is the result of vitamin K deficiency.

- It may occur early (within 24 hours after birth), within the first week of life (**classic form**)**,** or late (1–3 months after birth).

- **Clinical features.** Clinical manifestations include bruising, oozing from skin puncture wounds and bleeding into organs.

- **Haemorrhagic disease of the newborn is characterized by serious bleeding in the early and late forms**

- CNS bleeding may occur occasionally.

- **Laboratory findings** include **prolonged aPTT and PT.**
- **Management.** Treatment includes administration of vitamin K.
- **Intramuscular administration of vitamin K after birth prevents hemorrhagic disease of the newborn.**
- In severe disease, fresh-frozen plasma (FFP) may be needed.

Liver disease

- The liver is the major site of production of most coagulation factors.
- Vitamin K– dependent factors most severely affected .
- **Laboratory findings. prolonged PT and aPTT, and thrombocytopenia.**
- **Management.** Treatment includes vitamin K, FFP, and platelets as needed.

Disseminated Intravascular Coagulation

- It is a condition where there is consumption of clotting factors, platelets, and anticoagulant proteins.
- Resulting in widespread intravascular deposition of fibrin leading to tissue ischemia and necrosis , generalized hemorrhage and hemolytic anemia
- The initiating event is clotting that leads to consumption of procoagulant factors and resultant haemorrhage.
- DIC is a secondary phenomenon that occurs in response to local factors (large hemangiomas as seen in Kasabach–Merritt syndrome) and systemic factors (e.g., sepsis, hypothermia, malignancy, heat stroke, snakebite, burns).

Clinical features:

- Signs include cutaneous and internal organ bleeding.
- Bleeding from puncture sites and surgical incision.
- Skin petechiae and ecchymosis.
- Tissue necrosis and infarctions.
- Anemia(MAHA)
- In neonate mainly at venipuncture site ,GI bleeding , and IVH.

Laboratory findings:

- **Thrombocytopenia**
- **Prolongation of PT and PTT**
- **Reduction in clotting factors** (especially **fibrinogen** and factors II, V, and VIII),
- Fragmented , helmet-shaped RBCs , and **schistocytes** on blood smear.
- Increased FDP, and d-dimers level.

- **Management.** Therapy includes treatment of the underlying cause and transfusions of fibrinogen, FFP, and platelets as needed. Heparin may be useful if the underlying defect cannot be corrected.