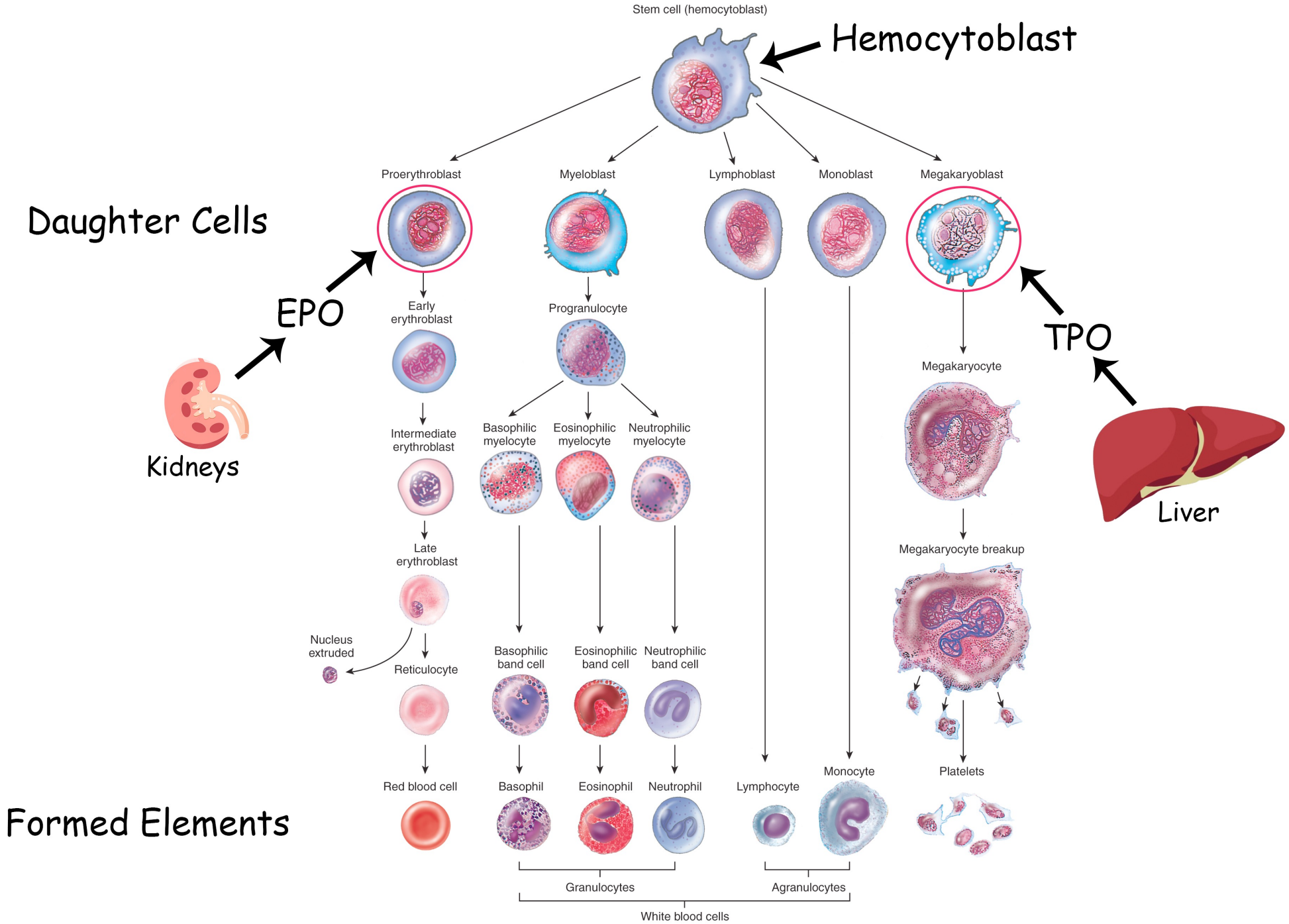
Functions of the Blood

- Transport of gases (oxygen and carbon dioxide)
- Transport of nutrients (amino acids , glucose , fatty acids , vitamins , minerals)
- Transport of waste products (creatinine , urea , uric acid)
- Transport of enzymes and hormones
- Transport of heat
  - Aids in temperature regulation (e.g. blood vessels of the skin)
- Regulation of pH , electrolyte , and water balance
- Protection against pathogens (part of immunity)
- Clot formation

Blood

- Formed Elements / Corpuscles :
  - Erythrocytes / Red blood cells
  - Leukocytes / White blood cells
  - Thrombocytes / Platelets
- Production occurs via hematopoiesis / hemopoiesis
  - Occurs in red bone marrow in post-natal life
  - Liver and spleen can produce corpuscles when levels are extremely low
    - eg , during anemia , leukemia

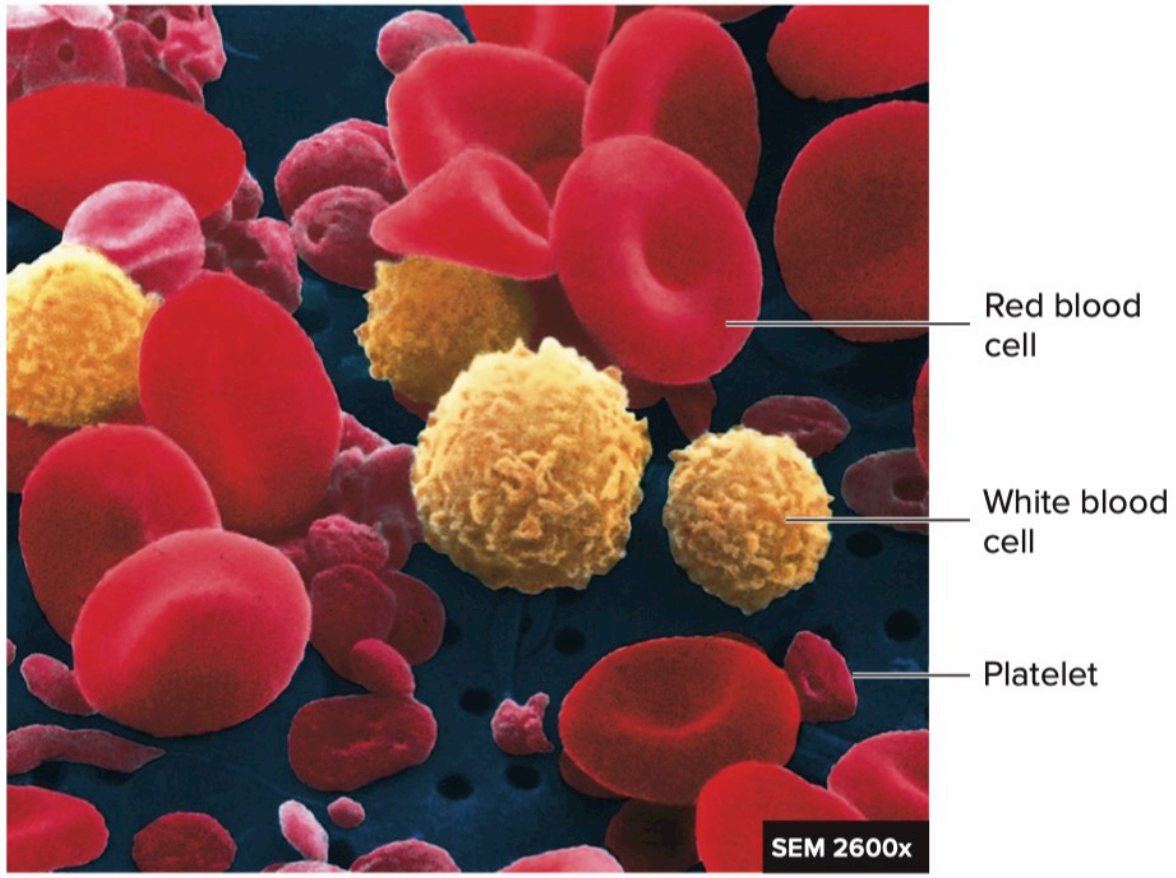

Stem cell (hemocytoblast)
Hemocytoblast
Daughter Cells
Proerythroblast
Myeloblast
Lymphoblast
Monoblast
Megakaryoblast
EPO
Kidneys
Early erythroblast
Progranulocyte
TPO
Megakaryocyte
Liver
Intermediate erythroblast
Basophilic myelocyte
Eosinophilic myelocyte
Neutrophilic myelocyte
Late erythroblast
Megakaryocyte breakup
Nucleus extruded
Reticulocyte
Basophilic band cell
Eosinophilic band cell
Neutrophilic band cell
Red blood cell
Basophil
Eosinophil
Neutrophil
Lymphocyte
Monocyte
Platelets
Granulocytes
Agranulocytes
White blood cells
Formed Elements

Hematopoiesis / Hemopoiesis

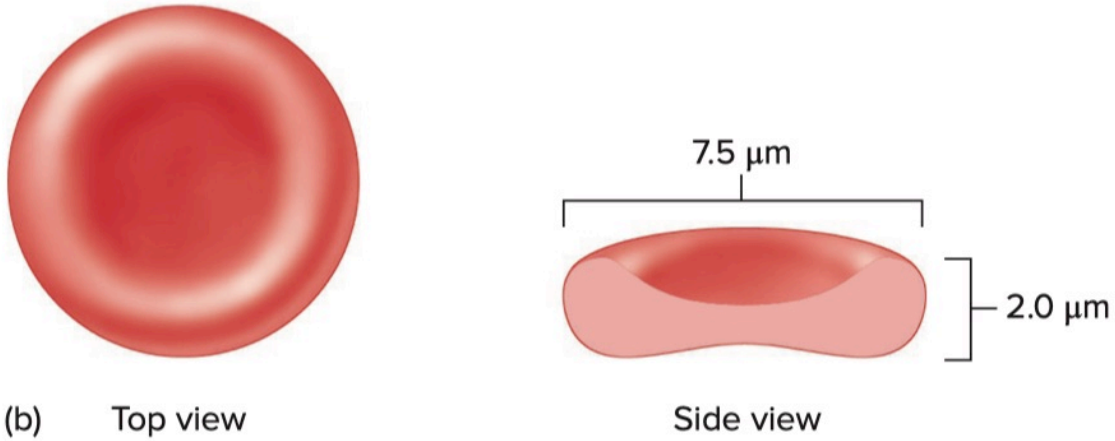
- All corpuscles originate from hemopoieitc stem cells (hemocytoblasts)
  - Give rise to daughter cells that differentiate into various corpuscles
    - **Proerythroblasts** – develop into *red blood cells*
    - **Megakaryoblasts** – develop into megakaryocytes
      - Megakaryocytes fragment and form *platelets*

Regulation of Hemopoiesis

- Erythropoietin (EPO)
  - Produced and released by the kidneys
  - Stimulates proerythroblasts
  - Clinical use
    - Used for those with kidney failure
    - Used for those going through chemotherapy
- Thrombopoietin (TPO)
  - Produced and released by the liver
  - Stimulates megakaryoblasts



(a)



(b) Top view Side view

FIGURE 19.3 Formed Elements

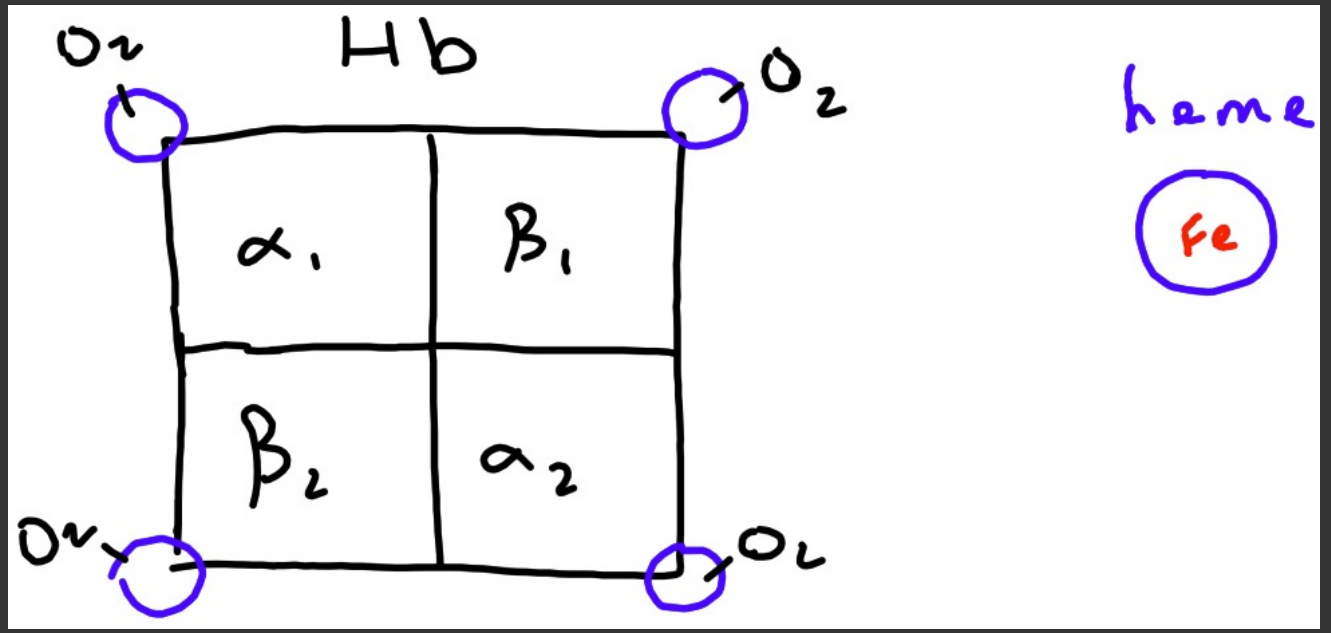
(*a*) Color-enhanced scanning electron micrograph of formed elements: red blood cells (*red doughnut shapes*), white blood cells (*yellow*), and platelets (*red, irregular shapes*). (*b*) Shape and dimensions of a red blood cell.

Red Blood Cells (RBCs) / Erythrocyte

- No organelles
  - eg , no nucleus
    - Provides a greater volume for a greater number of Hb molecules
    - Nucleus present initially but then extruded during development
    - Cannot produce new proteins or divide
  - eg , no mitochondria
    - Can only produce ATP anaerobically

Hemoglobin (Hb)

- 250,000,000 Hb molecules per red blood cell
- Made up of four individual subunits
  - Each subunit contains a heme
    - Each heme contains an iron
      - Each iron can bind an oxygen molecule
        - Each Hb can bind up to 4 oxygens
- **Adult Hb** (HbA)
  - 2 alpha subunits
  - 2 beta subunits



Adult Hemoglobin

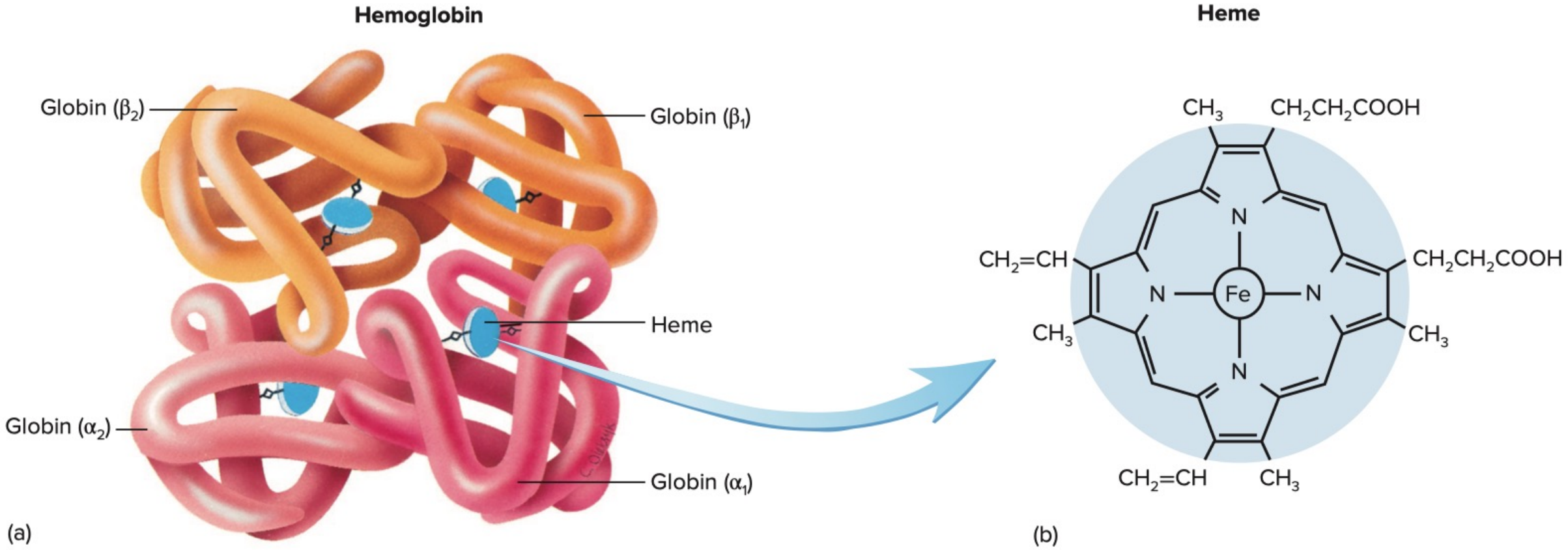


FIGURE 19.4 Hemoglobin

(*a*) Hemoglobin consists of four subunits, each with a globin and a heme. There are two alpha (α) globins and two beta (β) globins. A heme is associated with each globin. (*b*) Each heme contains one iron atom.

Production of Red Blood Cells / Erythropoiesis

- Approximately 2.5 million RBCs produced per second
- Each RBC takes approximately four days to mature

Destruction of RBCs

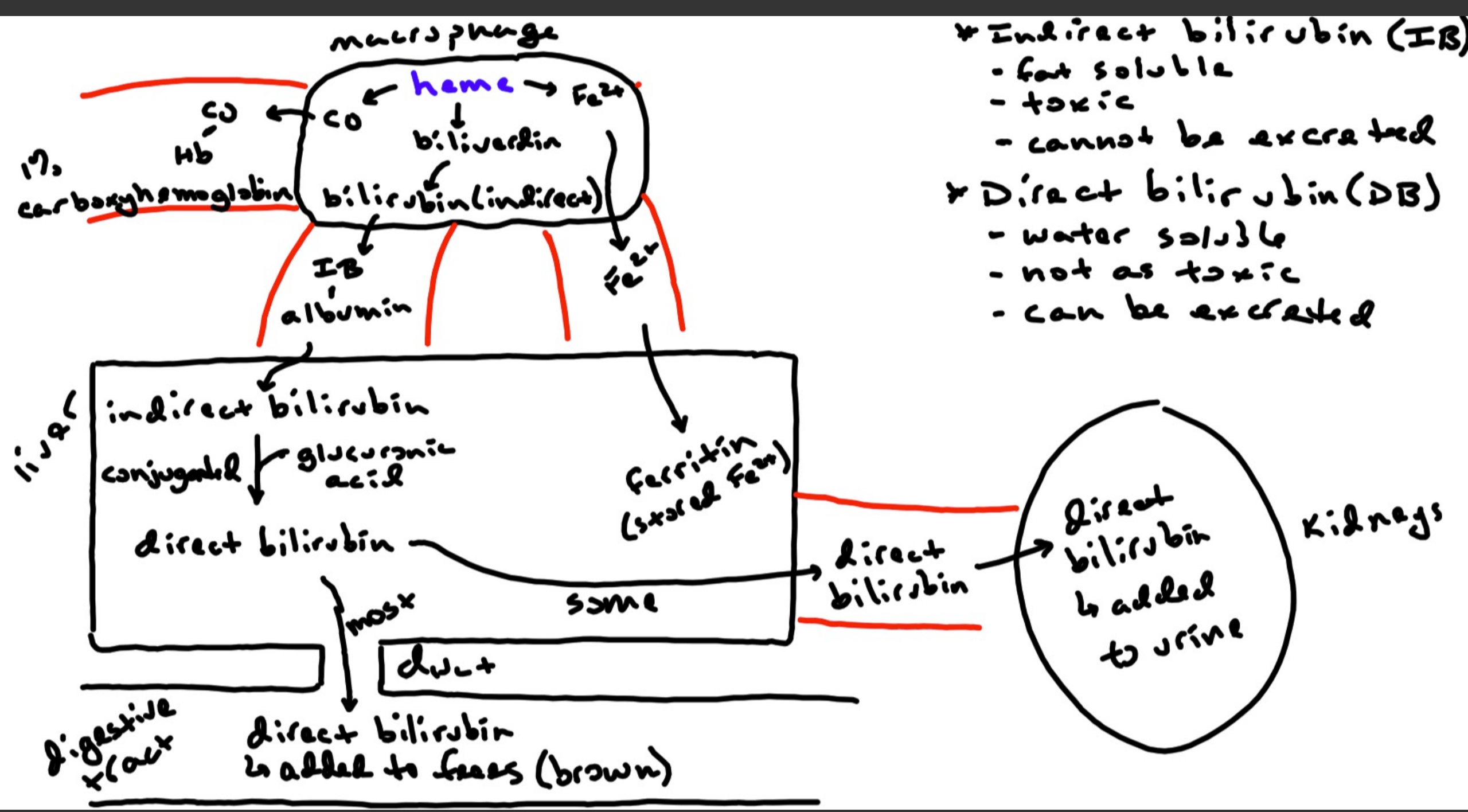
- Approximately 2.5 million RBCs destroyed per second
- Wear rather quickly
  - Lifespan of approximately 120 days
  - Cannot repair properly due to a lack of nuclear genes

- Main product destroyed is hemoglobin
  - Hemoglobin metabolized by macrophages in liver and spleen
  - Catabolism of hemoglobin
    - Subunits broken down into amino acids
    - Heme broken down to:
      - Carbon monoxide
      - Iron
      - Biliverdin

Catabolism of Hemoglobin

- Carbon Monoxide
  - Diffuses into the blood
    - Binds to Hb
      - Carboxyhemoglobin
        - Normally is around 1%
        - Smokers have between 5 to 10%
- Iron
  - Diffuses into the blood
    - Carried via transferrin to various tissues
    - Stored in various areas
      - (eg , liver and spleen)
      - Stored on the protein , apoferritin
        - Ferritin = (apoferritin + iron)

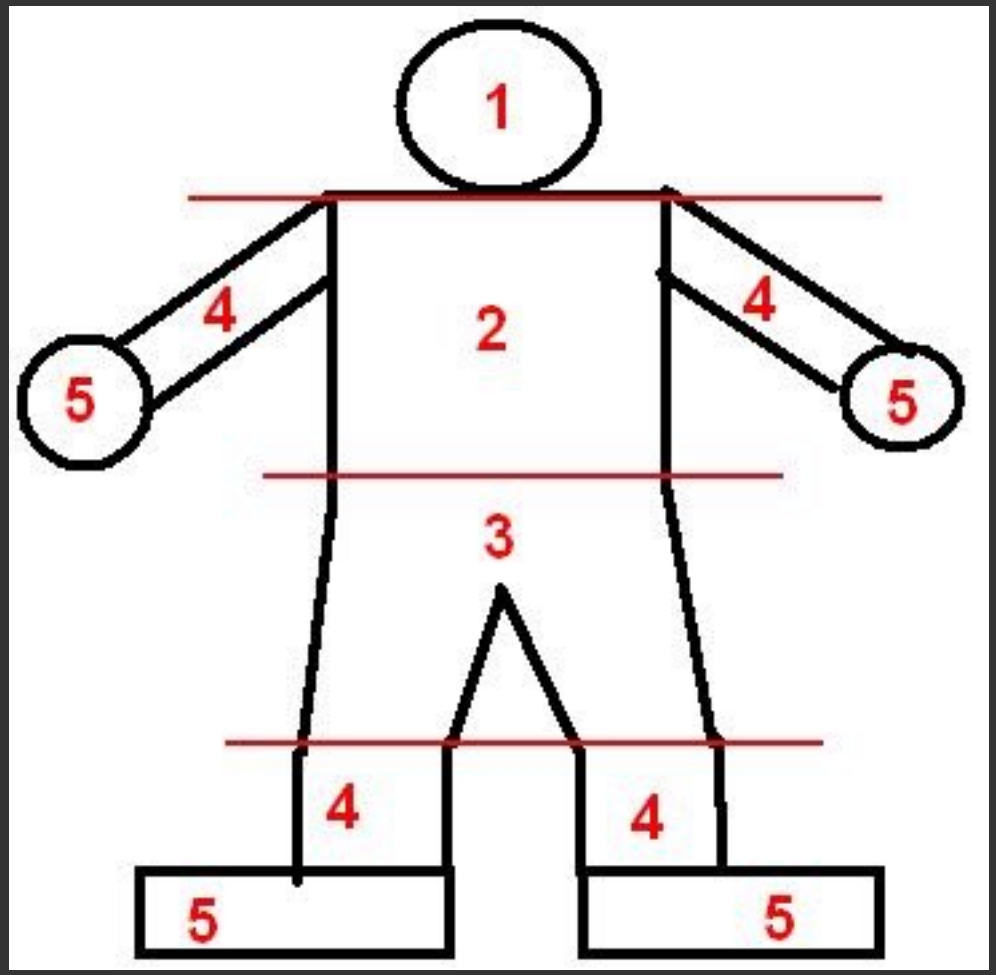
- Biliverdin
  - Subsequently converted to bilirubin (lipid-soluble)
    - Bilirubin diffuses into the blood
  - **Indirect Bilirubin** (lipid-soluble) :
    - Formed from biliverdin
    - also known as "free bilirubin" and "unconjugated bilirubin"
    - Toxic
    - Needs to be water-soluble ... why?
      - So it is no longer toxic
      - So it can be excreted
  - Making Indirect Bilirubin Water Soluble :
    - Indirect bilirubin is carried via albumin to liver and spleen
    - Receptor mediated endocytosis into the liver cell
    - Conjugated with glucuronic acid to create direct bilirubin
    - Most goes into digestive tract
    - Some goes into the kidneys
  - **Direct Bilirubin** (water-soluble) :
    - also known as "conjugated bilirubin"
    - Can now be excreted
    - Most goes to the digestive tract
      - Excreted in feces
        - Reason feces is brown
    - Some diffuses into the blood
      - Goes to the kidneys
        - Excreted in urine
        - Reason urine is yellow



* Indirect bilirubin (IB)
  - fat soluble
  - toxic
  - cannot be excreted
* Direct bilirubin (DB)
  - water soluble
  - not as toxic
  - can be excreted

Jaundice

- Yellowing of the skin , conjunctiva , and mucous membranes
- Due to an increase in indirect and/or direct bilirubin
- Progresses from head , down the torso and then into extremities
- Resolves in the opposite fashion than it progresses
- Three types :
  - Prehepatic
  - Hepatic
  - Posthepatic / Obstructive



Prehepatic Jaundice

- Due to increased RBC destruction
- Causes increased indirect bilirubin in the blood
  - Causes yellowing
  - Liver must conjugate excess bilirubin
    - Causes increased direct bilirubin
      - *Causes yellowing*
      - *Dark-colored feces*
      - *Dark-colored urine*
- Note: urine could be dark if jaundice is severe
  - Due to high Hb levels in urine
- Caused by hemolytic disease and found in newborns

Hepatic Jaundice

- Due to inability of liver to conjugate indirect bilirubin
  - Causes increased indirect bilirubin in the blood
    - Causes yellowing
  - Decreased level of direct bilirubin
    - Pale-colored feces
    - Light-colored / clear urine
- Caused by liver cell damage (e.g. hepatitis or cirrhosis)
- Caused by immature liver in premature babies

Post-Hepatic / Obstructive Jaundice

- Due to blockage of bilirubin transport to small intestine
  - Decreased level of direct bilirubin in feces
    - Pale-colored feces
  - Causes increased direct bilirubin in blood
    - Causes yellowing
    - Increased excretion by kidneys
      - Dark-colored urine
- Caused by gallstones , tumor , pancreatitis

Jaundice Treatment

- Phototherapy / bili light (blue or green light)
  - Performed in infants (will not work in adults)
- Exchange transfusion
  - Performed in infants and adults

Pre-hepatic	Hepatic	Obstructive
* Cause: destruction of too many RBC's - hemolytic disease - new born	* Cause: liver has difficulty conjugating bilirubin - hepatitis - cirrhosis - pre-term baby	* Cause: difficulty getting direct bilirubin to digestive tract - gallstones - tumor - pancreatitis
* Jaundice: ↑↑ indirect bilirubin ↑ direct bilirubin	* Jaundice: ↑↑ indirect bilirubin	* Jaundice ↑↑ direct bilirubin
* Darker feces * Darker urine	* Pale Feces * Light colored urine	* Pale Feces * Dark urine

Kernicterus

- Bilirubin toxicity in the central nervous system
- Almost exclusively seen in infants (rare in adults)
- Some warning signs
  - Lethargy
  - Muscle rigidity
  - High pitched cry
- Can lead to seizures , mental deficits , hearing loss , and death

Hematocrit / Packed Cell Volume

- Percent of RBCs in blood
  - (contained in the bottom layer of a hematocrit tube)
- Normal range for males: 40 – 50%
- Normal range for females: 35 – 45%
- Above values translate into 4 to 6 million RBCs / µl blood

Hemoglobin Concentration

- Normal range for males: 13.5mg to 18mg / dl blood
- Normal range for females: 11.5mg to 16mg / dl blood

Anemia

- Deficiency of hemoglobin
- Signs and symptoms
  - Fatigue
  - Dyspnea (shortness of breath) upon exertion
  - Malaise (general state of discomfort)
  - Pallor (pale skin)

Causes of Anemia – Iron-Deficiency Anemia

- Most common cause of anemia
- Iron is essential component of Hb
- Diagnosed by determining blood iron levels
- Treatment : increase intake of iron

Causes of Anemia – Vitamin B_{12} (cobalamin) Deficiency Anemia

- Pernicious anemia
- Vitamin B_{12} is necessary for RBC maturation
- Commonly due to lack of intrinsic factor in stomach
  - Protein that allows absorption of vitamin B_{12}
- Can also be due to intake deficiency
  - Not found naturally in plant-based food
- Diagnosed by determining blood vitamin B_{12} level
- Treatment: vitamin B_{12} shots or increase intake of B_{12}

Causes of Anemia – Vitamin B_9 (folate) Deficiency Anemia

- Folate is necessary for RBC maturation
- Diagnosed by determining blood folate level
- Treatment : increase intake of folate

Causes of Anemia – Aplastic Anemia

- Due to damaged red bone marrow
  - Bone marrow aplasia
- Thought to be autoimmune
- Can also be caused by certain therapeutic drugs
- Diagnosed with bone marrow biopsy
- Treatment :
  - Immunosuppressive drugs
  - Bone marrow transplant (cure)

Causes of Anemia – Thalassemia

- Defective Hb due to a genetic mutation
- Mild to severe
- Can cause red blood cells to lyse
  - Hemolytic anemia
- Diagnosed with genetic testing
- Treatment
  - Frequent blood transfusions
  - Bone marrow transplant (possible cure)

- Alpha Thalassemia
  - Defective or absent alpha subunit

- Beta Thalassemia
  - Defective or absent beta subunit

Nutrient Deficiency	Bone Marrow damage (aplasia)	Genetic
Iron	Aplastic anaemia	Thalassaemmia - α - β - haemolytic
B_{12}		
B_9		Sickle Cell Anaemia - β - haemolytic

Causes of Anemia – Sickle Cell Anemia

- Defective beta subunit on Hb
  - (HbS hemoglobin)
- Hemolytic anemia
- RBCs sickle / Sickle cell crisis
  - Hb molecules polymerize and RBC dehydrates
  - RBCs clump and block blood flow
    - Vaso-occlusive crisis
    - Ischemia
    - Pain
  - Factors that increase the risk of sickle cell crisis
    - Hypoxia
    - Acidosis
    - Dehydration
    - Infection
- Treatment = blood transfusions

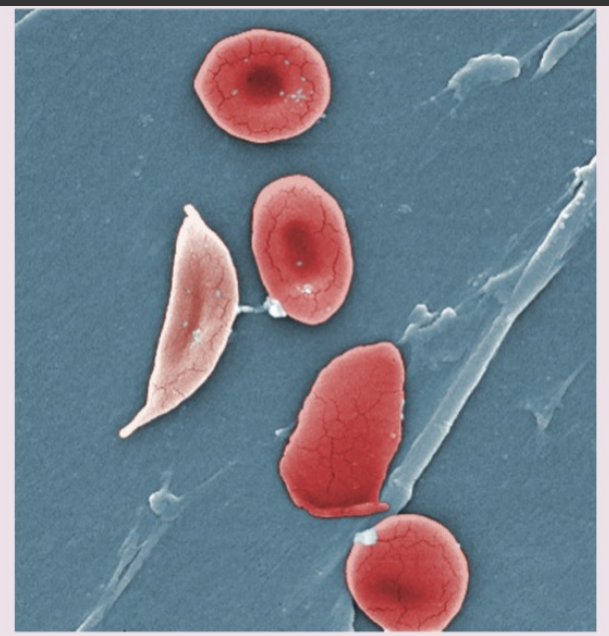
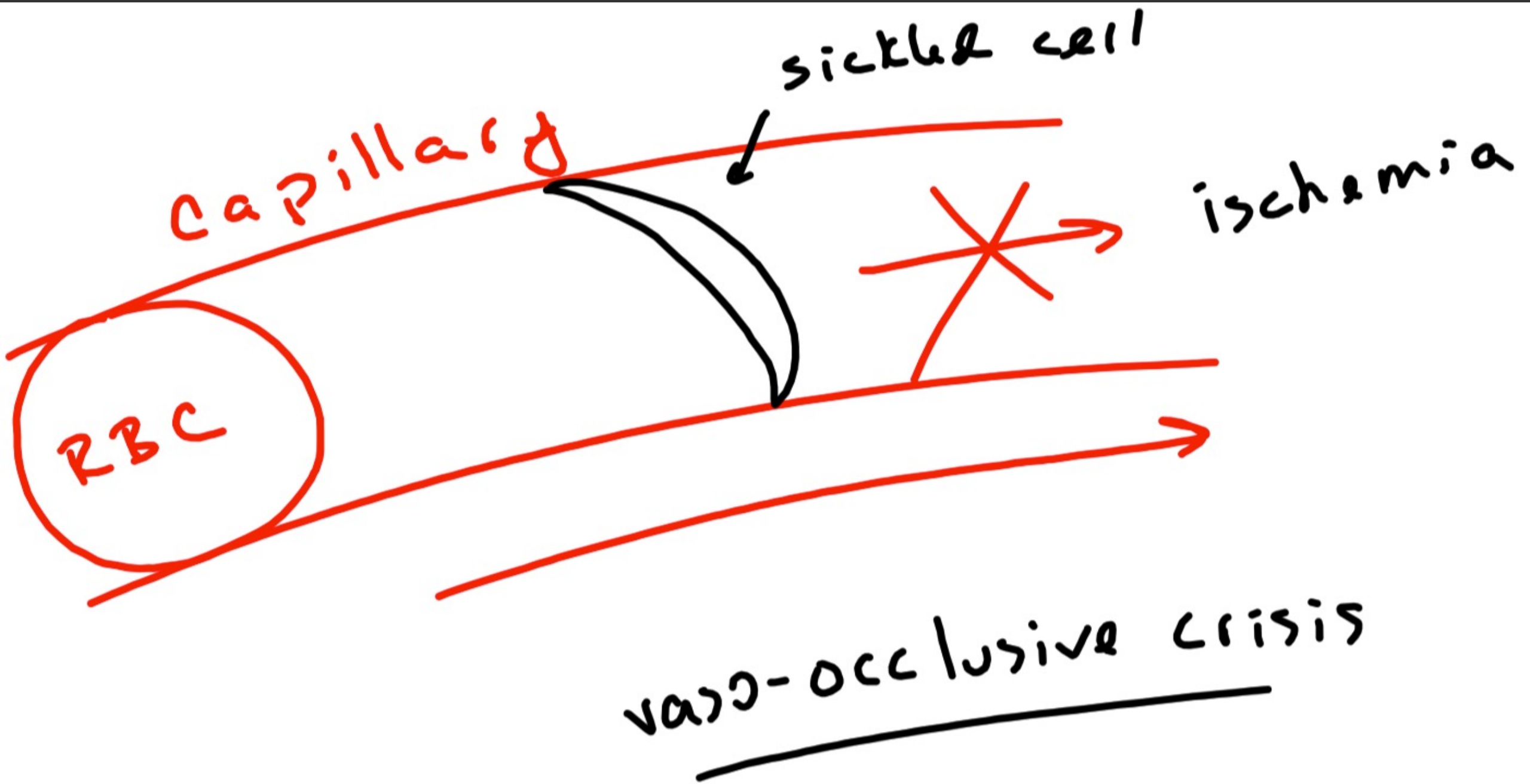


FIGURE 19.5 Sickle-Cell Disease
Red blood cells in a person with sickle-cell disease appear normal in oxygenated blood. In deoxygenated blood, hemoglobin changes shape and causes the cells to become sickle-shaped and rigid. ©CDC/Sickle Cell Foundation of Georgia: Jackie George, Beverly Sinclair/photo by Janice Haney Carr


sickled cell
capillary
ischemia
RBC
vaso-occlusive crisis

Polycythemia

- Increased percentage of RBCs
- Increases viscosity (thickness) of the blood
- Caused by conditions that lower oxygen carrying capacity of blood
  - Low blood oxygen level (hypoxia)
    - Pulmonary disease
    - Cardiovascular disease
    - Smoking
    - High altitude
  - Defective Hb
    - Therefore , can be anemic and polycythemic
  - Above conditions stimulate EPO release from kidneys
    - Stimulates proerythroblast development
- Caused by cancer (polycythemia vera)
- Caused by blood doping
  - Shots of EPO
  - Transfusion of RBCs into a recipient

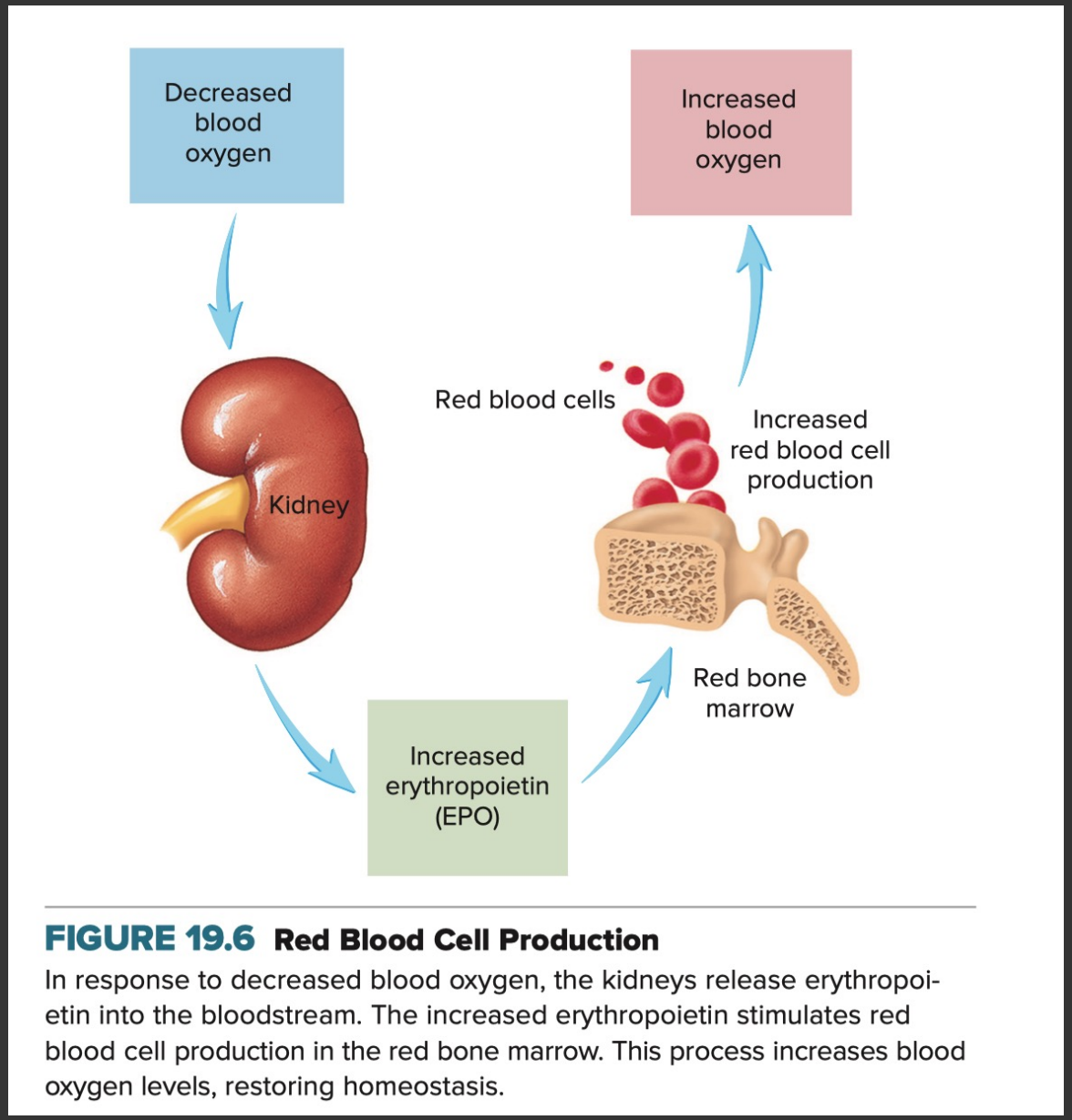


FIGURE 19.6 Red Blood Cell Production
In response to decreased blood oxygen, the kidneys release erythropoietin into the bloodstream. The increased erythropoietin stimulates red blood cell production in the red bone marrow. This process increases blood oxygen levels, restoring homeostasis.

Polycythemia ↑[RBC]

* Cancer
- polycythemia vera

① * Hypoxia (↓O_2 level)
- cardiovascular disease
- pulmonary disease
- smoking
- high altitude

} bad

① Defective Hb (anemic)

* Blood Doping
- transfusing RBC
- EPO

② ↑ EPO release from kidneys → ③ ↑ RBC

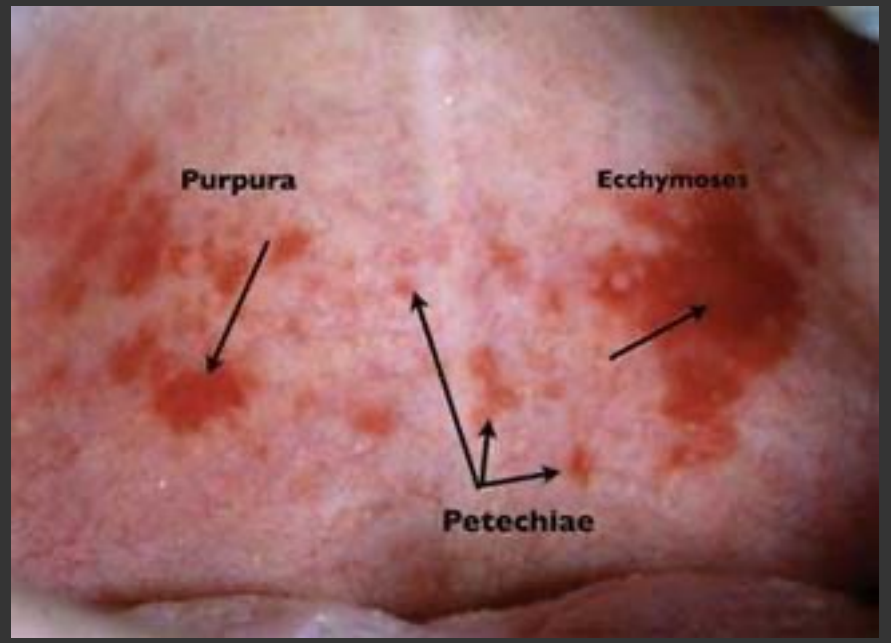
cheating

Leukocytes / White Blood Cells (WBCs)

- Normal range is 5,000 to 9,000 WBCs / µl of blood
- Leukopenia
  - Low WBC count (< 5,000 / µl)
  - Causes
    - Bone marrow aplasia
    - Acquired immune deficiency syndrome (AIDS)
- Leukocytosis
  - High WBC count (> 10,000 / µl)
  - Causes
    - Infection
    - Inflammation
    - Cancer
- Leukemia
  - Cancer of any one type of WBC
    - Crowd out developing RBCs and platelets
      - Results in anemia and thrombocytopenia
    - WBCs are defective and therefore frequent infections occur
  - Most common cancer among children
  - Affects 10 times more adults than children

Thrombocytes / Platelets

- Normal range is ~ 150,000 to 400,000 / µl of blood
- Thrombocytopenia
  - Low platelet count (< 150,000 / µl)
  - Caused by
    - Leukemia – WBCs crowd-out platelets
    - Autoimmune (e.g. lupus)
    - Bone marrow aplasia
  - Signs
    - Typically asymptomatic unless count is very low
    - Clusters of red or purple discolorations of the skin
      - Petechiae - small spots (< 5 mm)
      - Purpura – medium spots (5 – 9 mm)
      - Ecchymoses – large spots (> 10 mm)
    - Bleeding of the mouth , gums , digestive tract , brain
    - < 50,000: danger of uncontrolled bleeding
  - Treatments = platelet transfusion



Thrombocytes / Platelets

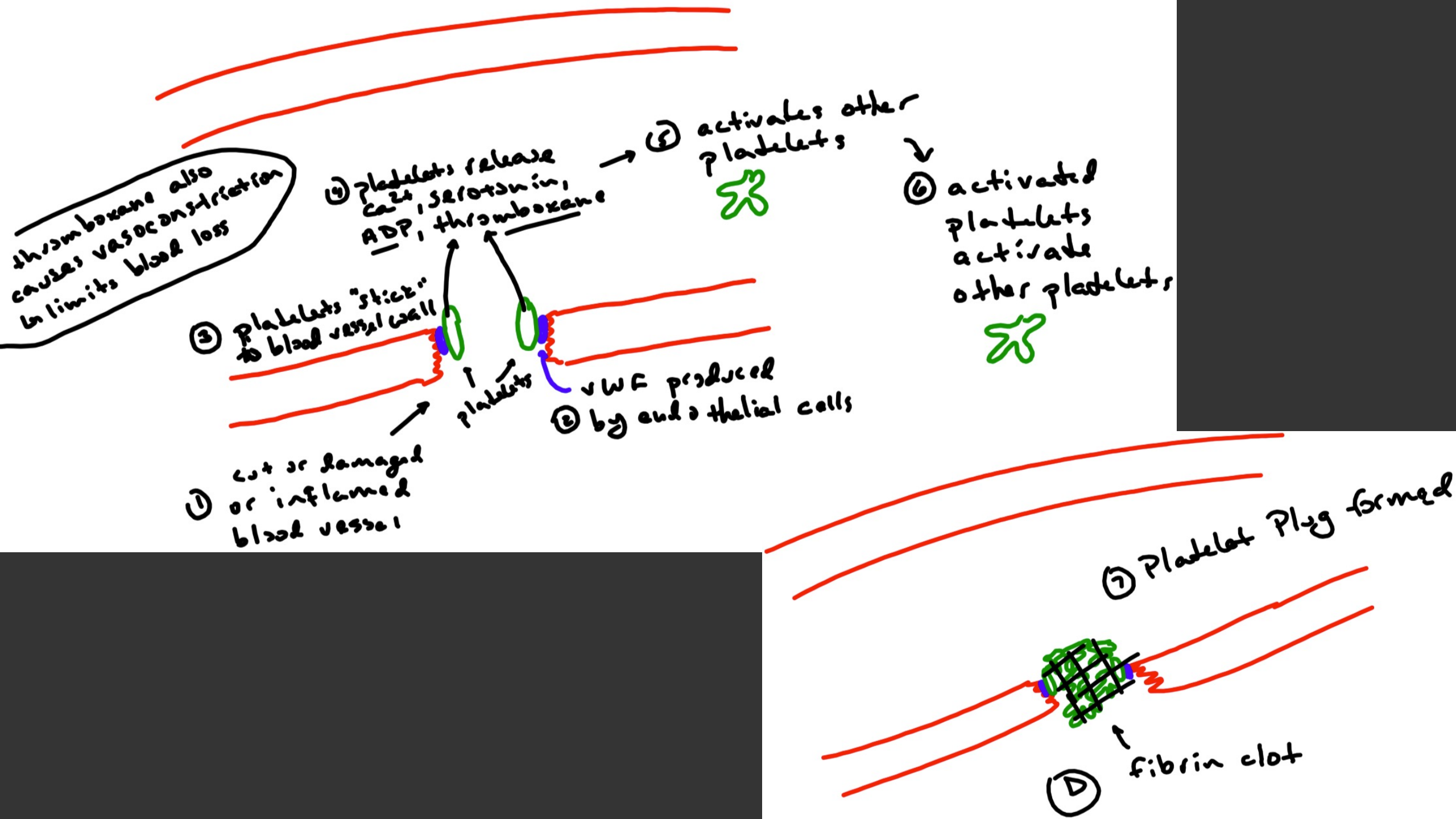
- Normal range is ~ 150,000 to 400,000 / µl of blood
- Thrombocytosis
  - High platelet count (> 400,000 / ul)
  - Typically asymptomatic
  - Platelets could clump together (thrombus)
  - Caused by :
    - TPO oversensitivity of megakaryoblasts
    - Cancer
  - Treatment = Anticoagulants

Hemostasis – Vascular Spasm / Vasospasm

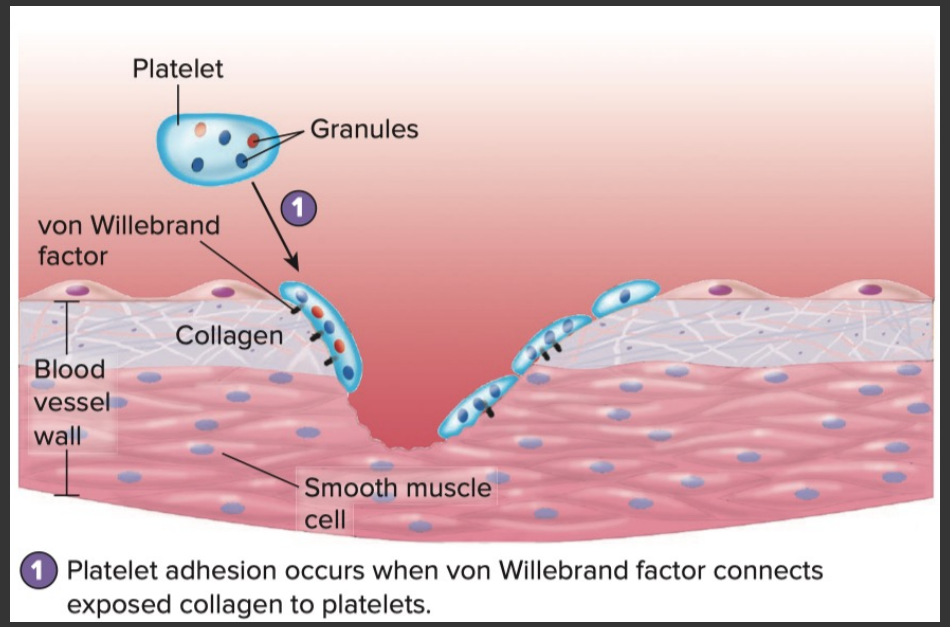
- Vasoconstriction after blood vessel is cut
  - Decreases blood flow and restricts bleeding
  - If blood vessels are small enough , can close them completely
    - Stoppage of bleeding
- Can be effective in small venules and capillaries
- This type of repair occurs continuously

Hemostasis – Platelet Plug

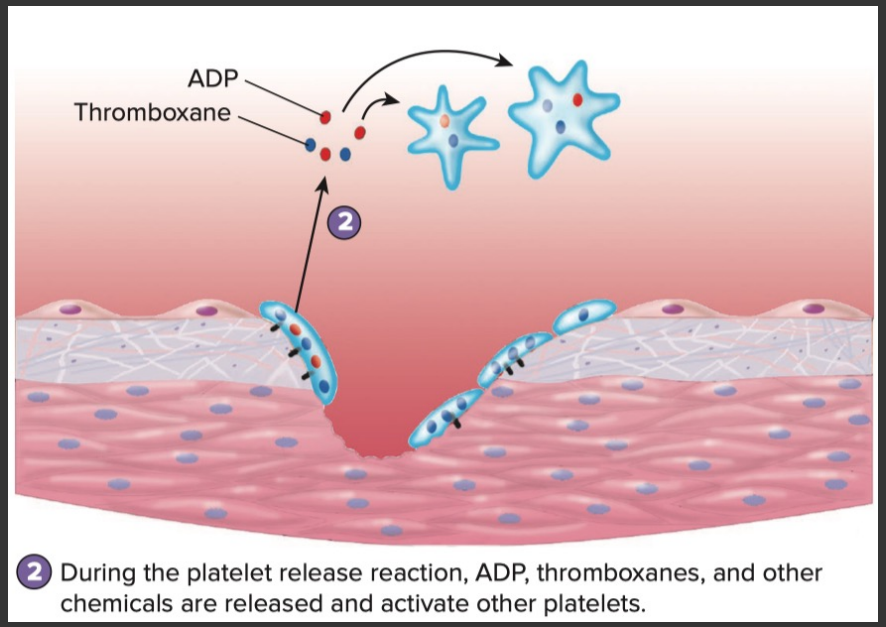
- Endothelial cells of blood vessels secrete **von Willebrand factor** (vWF)
  - Binding protein that aids in the adhesion of platelets to blood vessels
    - Binds to platelet surface receptors and collagen
- Platelets adhere to collagen fibers of damaged blood vessel via vWF
  - Platelets can also bind to collage fibers directly (not as effective)
- Platelets become activated (platelet release reaction)
- Become star-shaped and “sticky”
- Release ADP , thromboxane , serotonin , and calcium
  - ADP and thromboxane activate other platelets
    - Causes these other platelets to become “sticky” as well
    - Causes them to release ADP , thromboxane, etc.
      - This cycle continues (*positive feedback*)
    - Thromboxane also causes vasoconstriction
- Platelets aggregate with each other forming a platelet plug
- If the blood vessel is small enough , platelet plug is sufficient to stop bleeding
  - This type of repair occurs continuously


thromboxane also causes vasoconstriction to limits blood loss
④ platelets release Ca2+, serotonin, ADP, thromboxane
⑤ activates other platelets
⑥ activated platelets activate other platelets
③ platelets "stick" to blood vessel wall
platelets
vWF produced by endothelial cells
① cut or damaged or inflamed blood vessel
⑦ Platelet Plug formed
fibrin clot
D

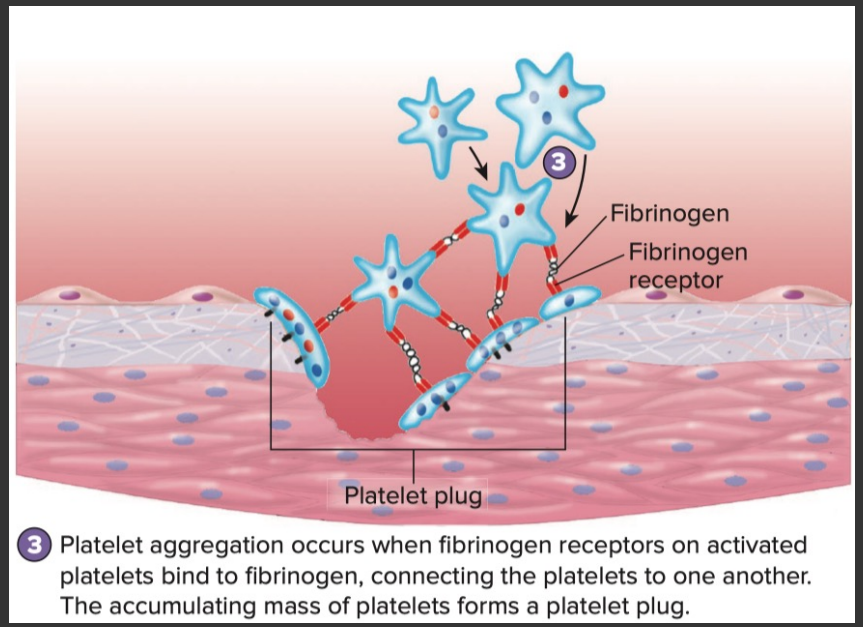
Hemostasis – Platelet Plug Formation



1 Platelet adhesion occurs when von Willebrand factor connects exposed collagen to platelets.

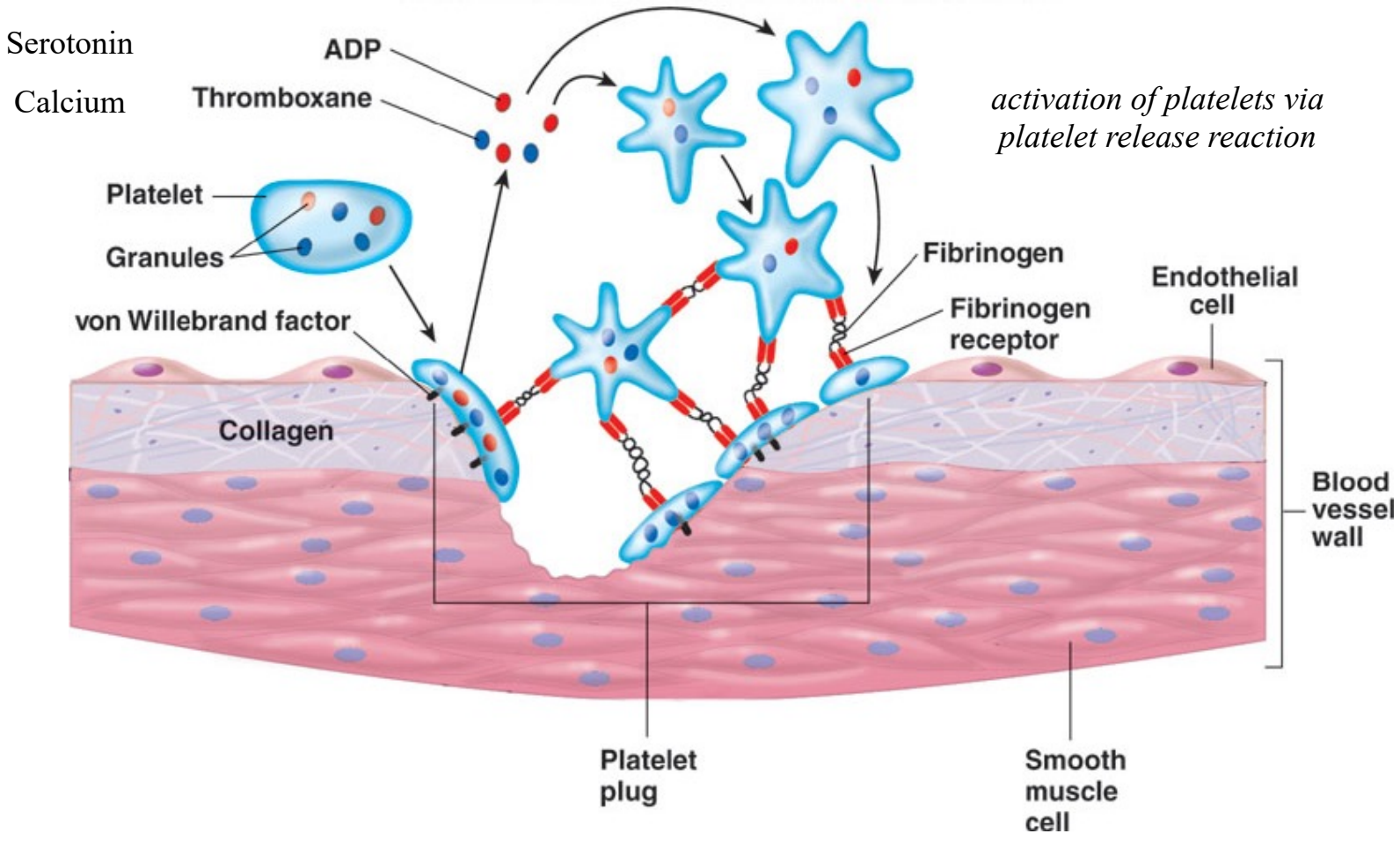


2 During the platelet release reaction, ADP, thromboxanes, and other chemicals are released and activate other platelets.



3 Platelet aggregation occurs when fibrinogen receptors on activated platelets bind to fibrinogen, connecting the platelets to one another. The accumulating mass of platelets forms a platelet plug.

Hemostasis – Platelet Plug Formation



Hemostasis – Blood Coagulation / Blood Clotting

- Two mechanisms : Extrinsic and Intrinsic
- Extrinsic clotting mechanism :
  - *So named because it begins with substances that are outside of the plasma*
  - Rapid (occurs in less than 30 seconds)
  - Release of thromboplastin by damaged tissue (*outside of plasma*)

- Intrinsic clotting mechanism :
  - *So named because it begins with substances that are part of the plasma*
  - Relatively slow (takes minutes) – more steps involved than extrinsic pathway
  - Initiated by activation of Hageman factor (factor 12)
    - Occurs when Hageman factor is exposed to a foreign surface
      - e.g. collagen in connective tissue or glass vial

Coagulation

~90 sec

↓

(pathway)

Intrinsic Mechanism (A)

Hageman factor is activated when exposed to blood vessel wall

~30 sec

↓

(pathway)

Extrinsic Mechanism

Thromboplastin is produced and released into blood by the damaged tissue

↘ ↙

(B)

↘ ↙

Prothrombinase

Hemostasis – Blood Coagulation / Blood Clotting

- Common Pathway for Extrinsic and Intrinsic Clotting Mechanisms :
- Prothrombinase converts prothrombin into thrombin
- Thrombin catalyzes a reaction that fragments fibrinogen (factor I)
  - Long threads of fibrin formed that forms webbing of the clot
    - Traps RBCs and platelets
- Thrombin also stimulates factor XIII , which stabilizes the fibrin clot
- Once blood clot begins to form , promotes more blood clotting
  - (*positive feedback*)

Coagulation

(common pathway)

Ⓒ

Prothrombin (inactive) —Prothrombinase→ thrombin (active)

Ⓓ

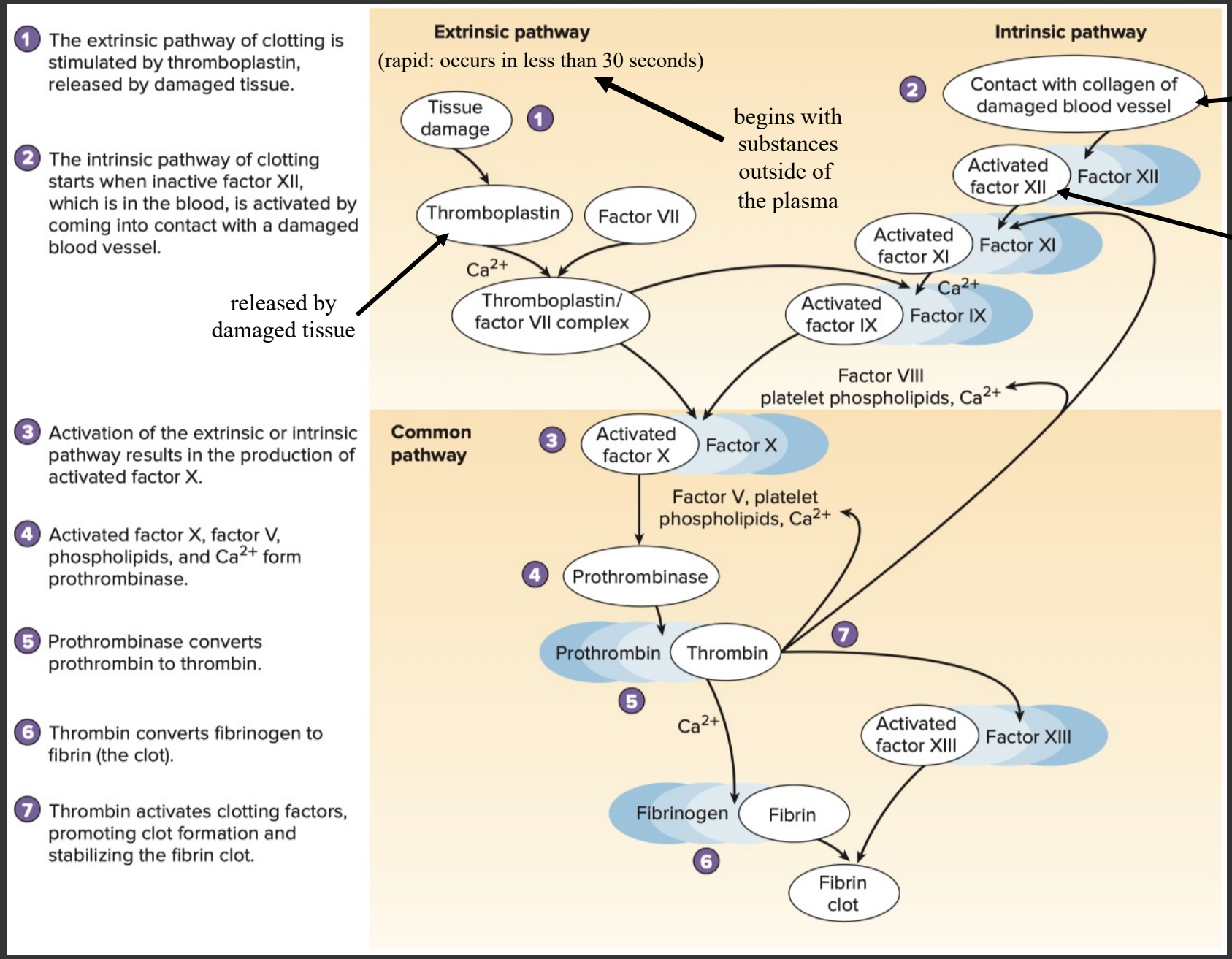
Fibrinogen (inactive) —thrombin→ fibrin (active)

Ⓓ

Factor XIII (inactive) —thrombin→ Factor XIII (active)

Factor XIII (active) —stabilize→ fibrin (active)

Hemostasis – Blood Coagulation / Blood Clotting



Hemostasis – Blood Coagulation / Blood Clotting

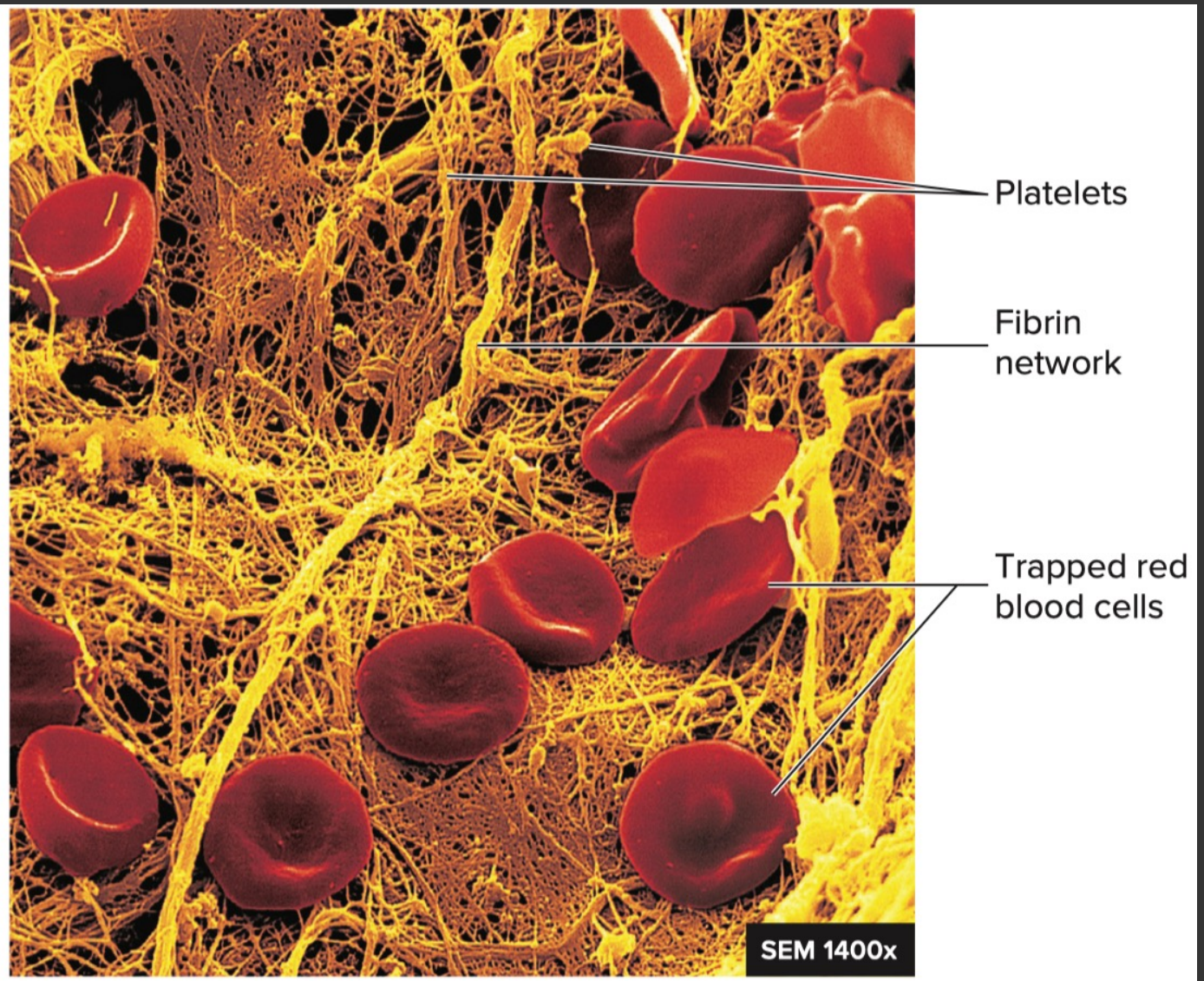


FIGURE 19.11 Blood Clot

A blood clot consists of fibrin, which traps red blood cells, platelets, and fluid.

Hemostasis – Blood Coagulation / Blood Clotting

- Clot Retraction :
  - Platelets contract and pull edges of damaged blood vessel together
  - Platelets release platelet-derived growth factor
    - Stimulates smooth muscle and fibroblasts to repair blood vessel

- Clot Dissolution / Fibrinolysis :
  - Occurs after repair of blood vessel is complete
    - Plasminogen activators (enzymes) released by damaged tissue
      - Converts plasminogen (a plasma protein) into plasmin
        - Plasmin (an enzyme) digests fibrin clot

Causes of Excessive Bleeding

- Hemophilia A :
  - Due to a deficiency of antihemophilic factor (VIII)
    - Therefore , can’t use intrinsic mechanism
  - Most common form of hemophilia (85% of cases)
- Hemophilia B :
  - Due to a deficiency of plasma thromboplastin (factor IX)
    - Therefore , can’t use intrinsic mechanism
- Hemophilia C :
  - Due to a deficiency of plasma thromboplastin antecedent (factor XI)
    - Therefore , can’t use intrinsic mechanism
- Von Willebrand disease :
  - Due to a deficiency of vWF and antihemophilic factor (VIII)
    - Therefore , can’t use intrinsic mechanism

Causes of Excessive Bleeding

- Vitamin K deficiency :
  - Vitamin K needed to synthesize factors II , VII , IX and X
  - Causes :
    - Extensive antibiotic treatment
      - Vitamin K made by “good bacteria” (flora) in colon
        - Antibiotics can kill the flora
    - Lack of vitamin K in the diet
    - Malabsorption diseases (eg , Crohn’s disease)
    - Newborns (lack flora to produce vitamin K)
  - Treatment
    - Replace lost vitamin K with diet or with intramuscular shots
- Liver disease :
  - Liver makes TPO and most of the clotting factors

Abnormally Formed Clot

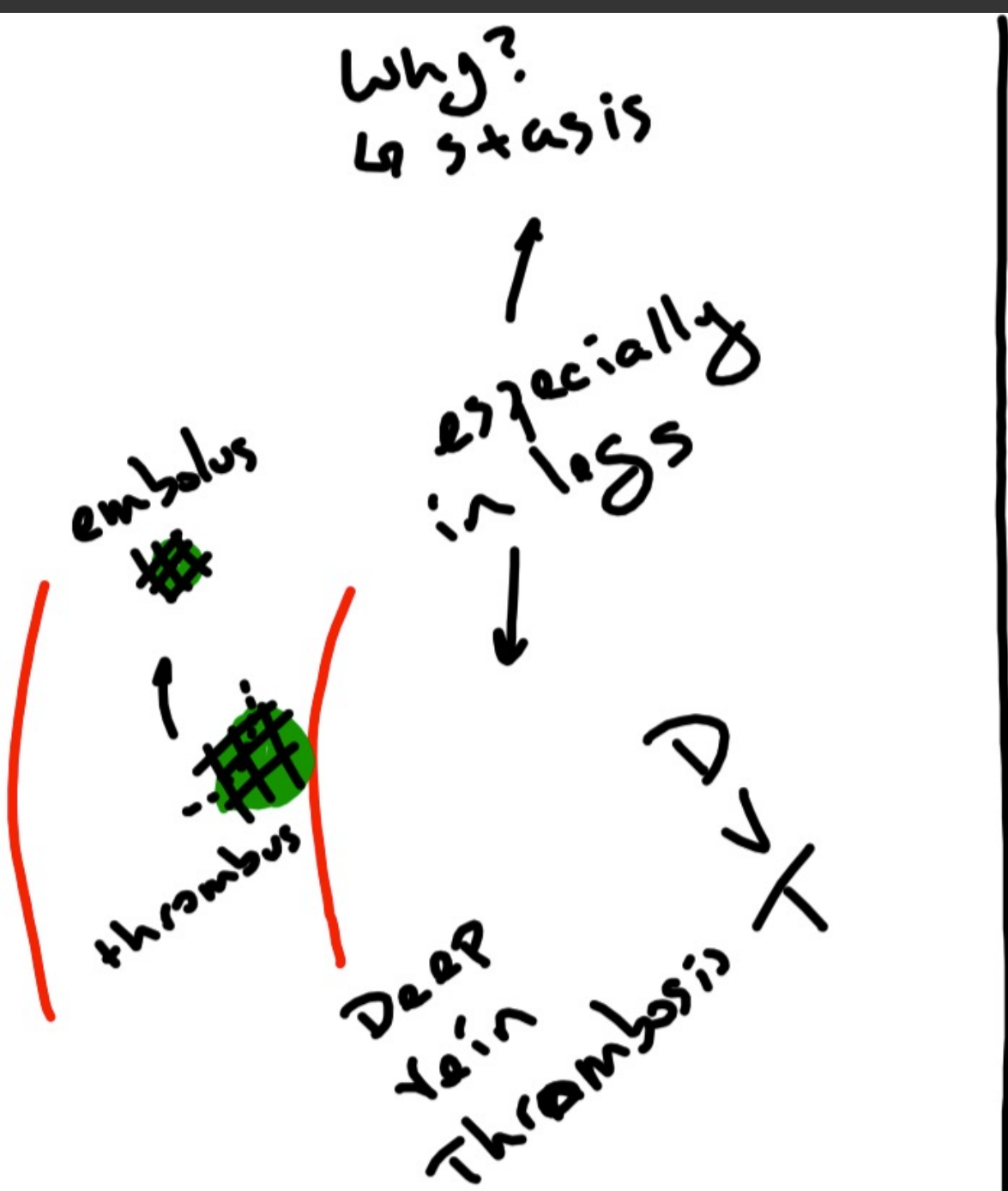
- Thrombus :
  - Part or all of the clot can become dislodged and become an embolus
    - Embolus can become lodged in a smaller blood vessel
      - Condition known as embolism

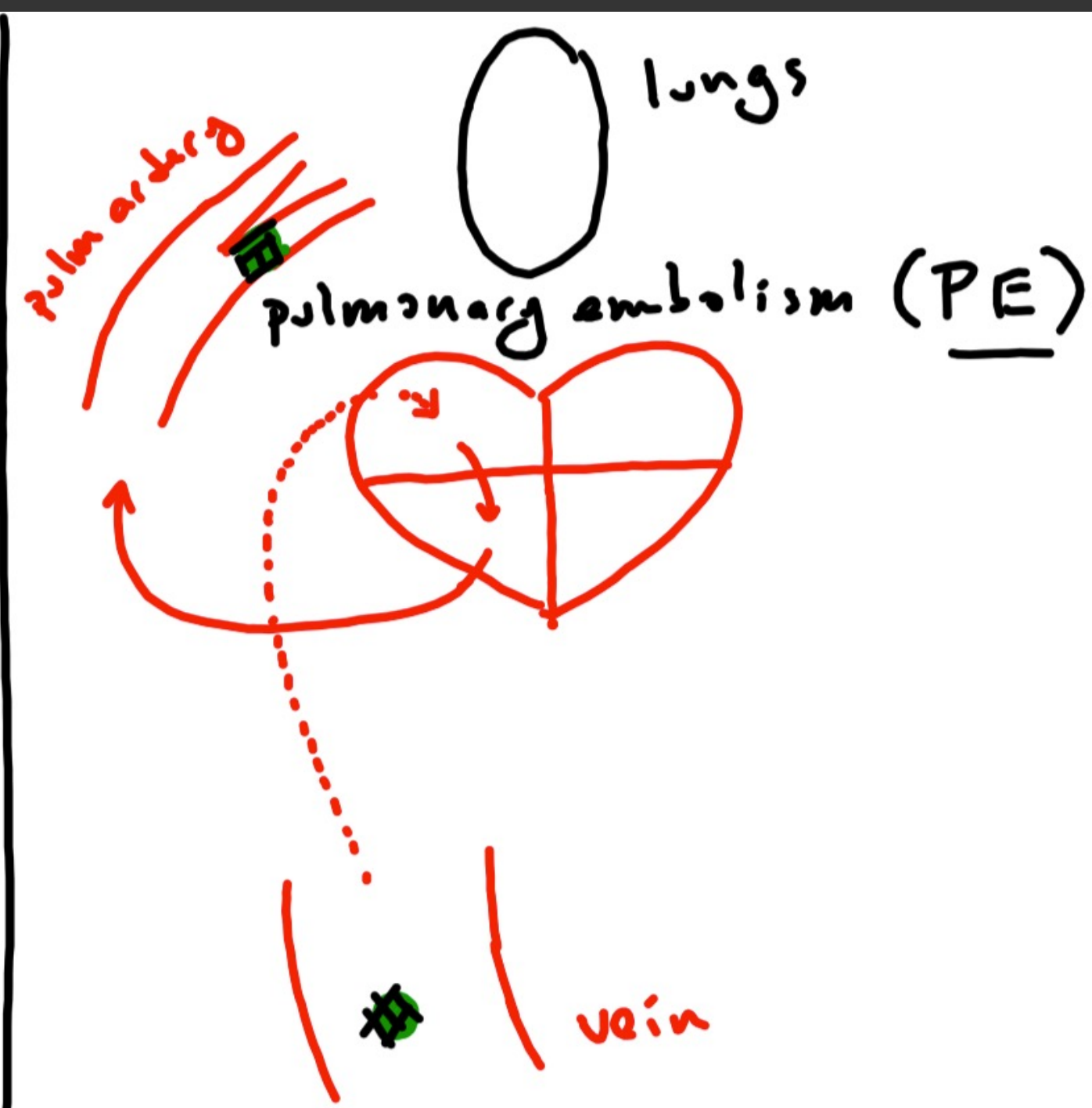
Causes of Excessive Clotting

- Typically caused by damage to or inflammation of blood vessels
  - Activates clotting mechanism
- e.g. atherosclerosis , diabetes , disseminated intravascular coagulation (DIC)
- Disseminated intravascular coagulation (DIC) :
  - Massive clotting due to massive inflammation
    - Causes platelet and clotting factor depletion
  - Massive bleeding
    - Due to platelet and clotting factor depletion
  - Causes :
    - Obstetrics complications
    - Sepsis (especially bacteria)
    - Tissue trauma (e.g. from burns)
  - Treatment :
    - Anticoagulants
    - Clot busting drugs
    - Transfuse platelets
    - Transfuse clotting factors

Causes of Excessive Clotting

- Stasis :
  - Slowed blood flow
    - Leads to accumulation of activated clotting factors
  - Common causes :
    - Congestive heart failure
    - Slow venous blood flow (especially in legs)


Why?
Stasis
especially
in legs
embolus
thrombus
Deep
Vein
Thrombosis
DVT


lungs
pulmonary
pulmonary embolism (PE)
vein

Risk Factors for Excessive Clotting

- Being overweight
- Pregnancy (increased level of estrogen and vein compression by baby)
- Supplemental estrogen (eg , birth control and estrogen therapy)
- Smoking

Control of Clot Formation

- Endogenously present in blood to prevent unwanted clotting
- Antithrombin :
  - Plasma protein that slowly inactivates a number of clotting factors
    - Factors II (thrombin) , VII , IX , X , XI and XII
- Heparin :
  - Activates antithrombin
  - Produced by basophils and endothelial cells
- Prostacyclin :
  - Inhibits platelets from releasing coagulation factors
    - Prevents aggregation of platelets
  - Produced by endothelial cells

Control of Clot Formation

- Anticoagulants :
  - Heparin
  - Coumadin / Warfarin
    - Competes with vitamin K
      - Prevents synthesis of vitamin K dependent clotting factors
  - Eliquis and Xarelto
    - Both inhibit factor X
  - Pradaxa
    - Inhibits thrombin
  - Plavix
    - Blocks ADP receptors on the surface of platelets
      - Platelets not activated and therefore cannot aggregate
  - Aspirin (81 mg / day)
    - Inhibits cyclooxygenase-1 (COX-1 inhibitor)
      - Inhibits thromboxane A2 secreted by platelets
        - Prevents platelet aggregation
        - Effects lasts for days (other NSAIDS last hours)

Control of Clot Formation

- Clot-bursting drugs :
  - Streptokinase and tissue plasminogen activator (tPA)
    - Activate plasminogen to produce plasmin
      - Plasmin digests fibrin (fibrinolysis)

Blood Typing – ABO System

- Named for the antigen (or lack of any antigen) that is in the RBC membrane
- Type A Blood :
  - RBC membrane contains antigen A
  - Plasma contains antibodies to antigen B
  - Genotype: AA or AO
- Type B Blood :
  - RBC membrane contains antigen B
  - Plasma contains antibodies to antigen A
  - Genotype: BB or BO
- Type AB Blood :
  - RBC membrane contains antigens A and B
  - Plasma contains no antibodies to antigens A or B
  - Genotype: AB
- Type O Blood :
  - RBC membrane contains neither A nor B antigen
  - Plasma contains antibodies to antigens A and B
  - Genotype: OO

Type A

Mom (oocyte)	Dad (sperm)	
A	A	→ AA
A	O	→ AO
O	A	→ AO

Type B

Mom	Dad	
B	B	BB
B	O	BO
O	B	BO

Type AB

Mom	Dad	
A	B	AB
B	A	AB

Type O

Mom	Dad	
O	O	OO

A and B genes are dominant

↳ dominant are expressed

O is recessive

↳ two recessive genes needed

to be expressed

Blood Typing – Rhesus (Rh) System

- Antigen D is the most immunogenic of five Rh antigens
- Rh+ blood :
  - RBC membrane contains antigen D
  - Plasma contains no antibodies to antigen D
    - Not made naturally
  - Approximately 85% of the population
  - Genotype: DD or Dd
- Rh- blood :
  - RBC membrane does not contain antigen D
  - Plasma contains no antibodies to antigen D
    - Not made naturally
  - Approximately 15% of the population
    - Genotype: dd

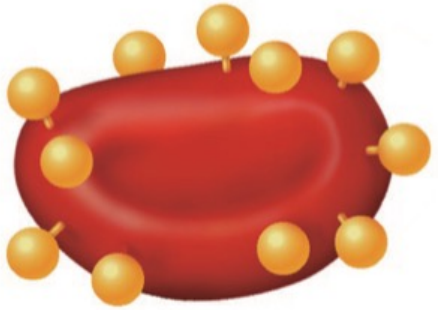
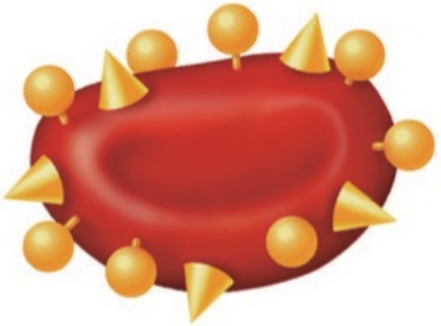
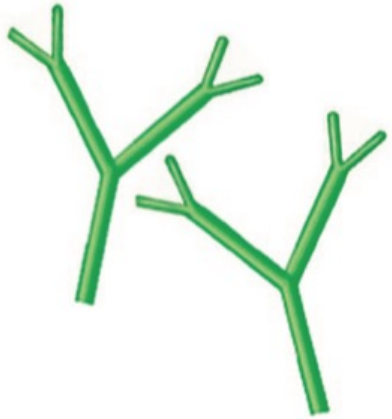
Pos vs Neg Blood Type

Mom	Dad		
D	d	→ Dd	positive
d	D	→ Dd	
D	D	→ DD	

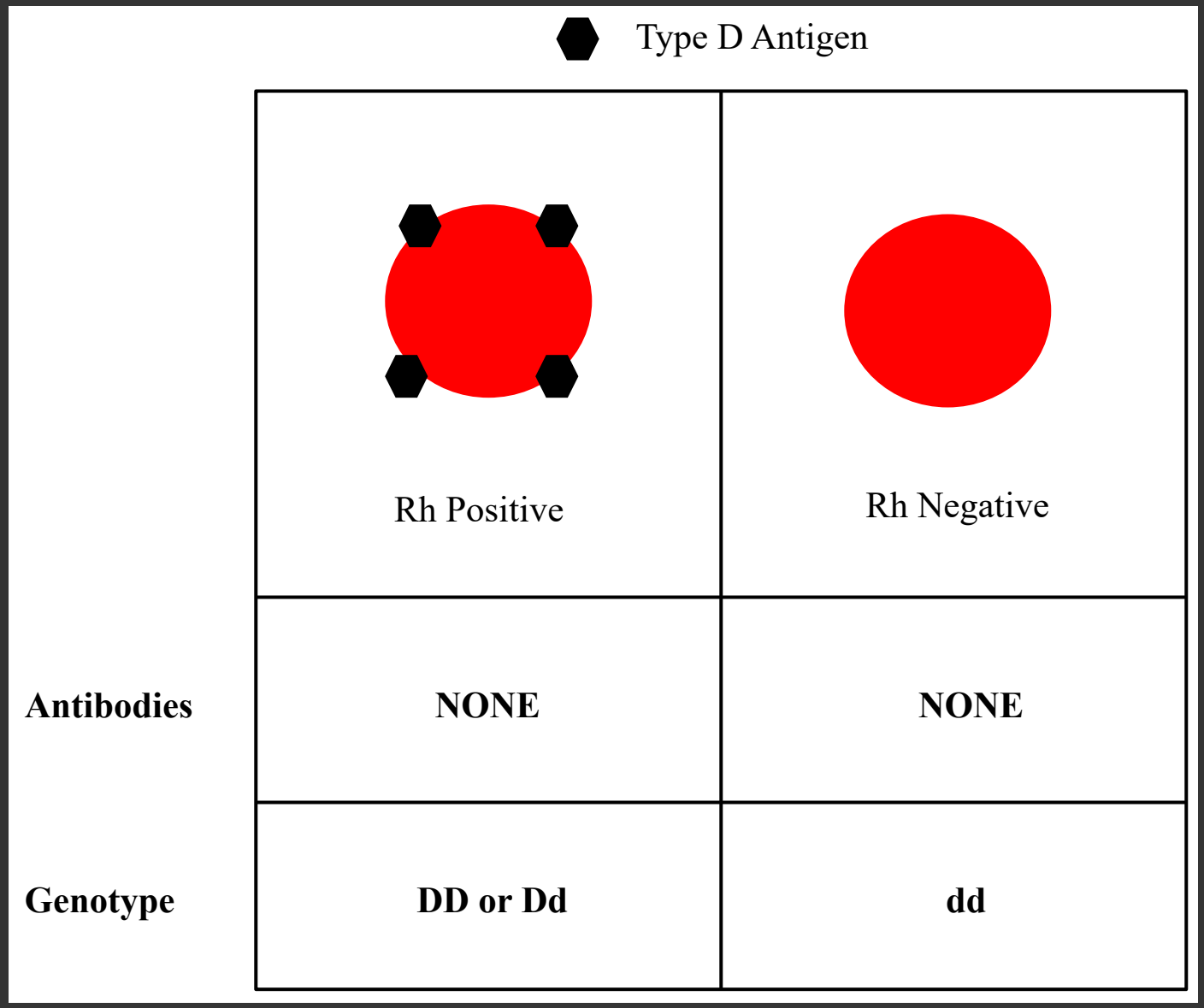
Mom	Dad		
d	d	→ dd	← negative

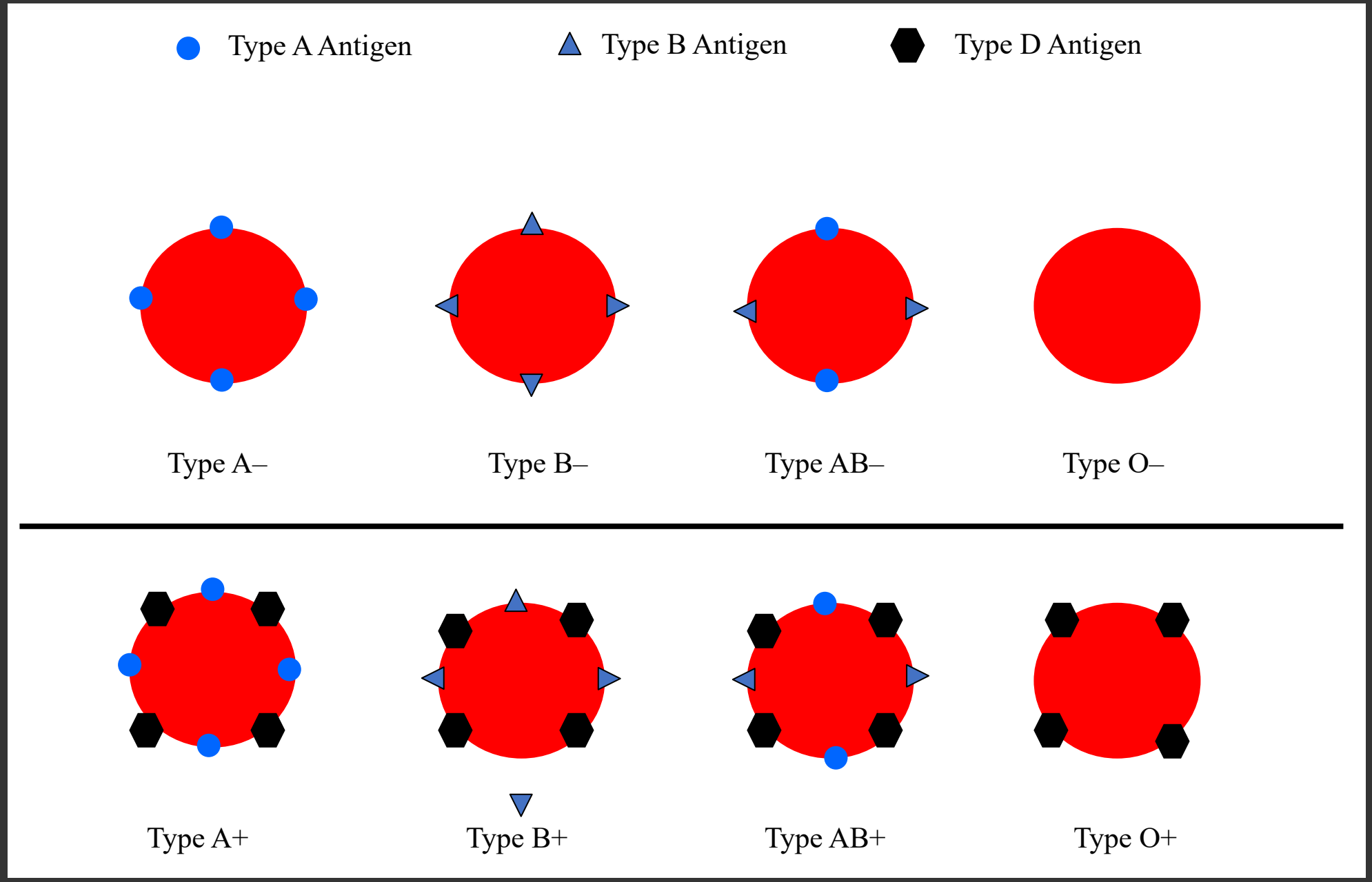
D = dominant

d = recessive

	Type A	Type B	Type AB	Type O
Red blood cells	Antigen A 	Antigen B 	Antigens A and B 	Neither antigen A nor B 
Plasma	Anti-B antibody 	Anti-A antibody 	Neither anti-A nor anti-B antibodies	Anti-A and anti-B antibodies 
	Type A Red blood cells with type A surface antigens and plasma with anti-B antibodies	**Type B** Red blood cells with type B surface antigens and plasma with anti-A antibodies	**Type AB** Red blood cells with both type A and type B surface antigens and neither anti-A nor anti-B plasma antibodies	**Type O** Red blood cells with neither type A nor type B surface antigens but both anti-A and anti-B plasma antibodies

Blood Typing – Rh+ vs Rh-




Type A Antigen
Type B Antigen
Type D Antigen
Type A–
Type B–
Type AB–
Type O–
Type A+
Type B+
Type AB+
Type O+

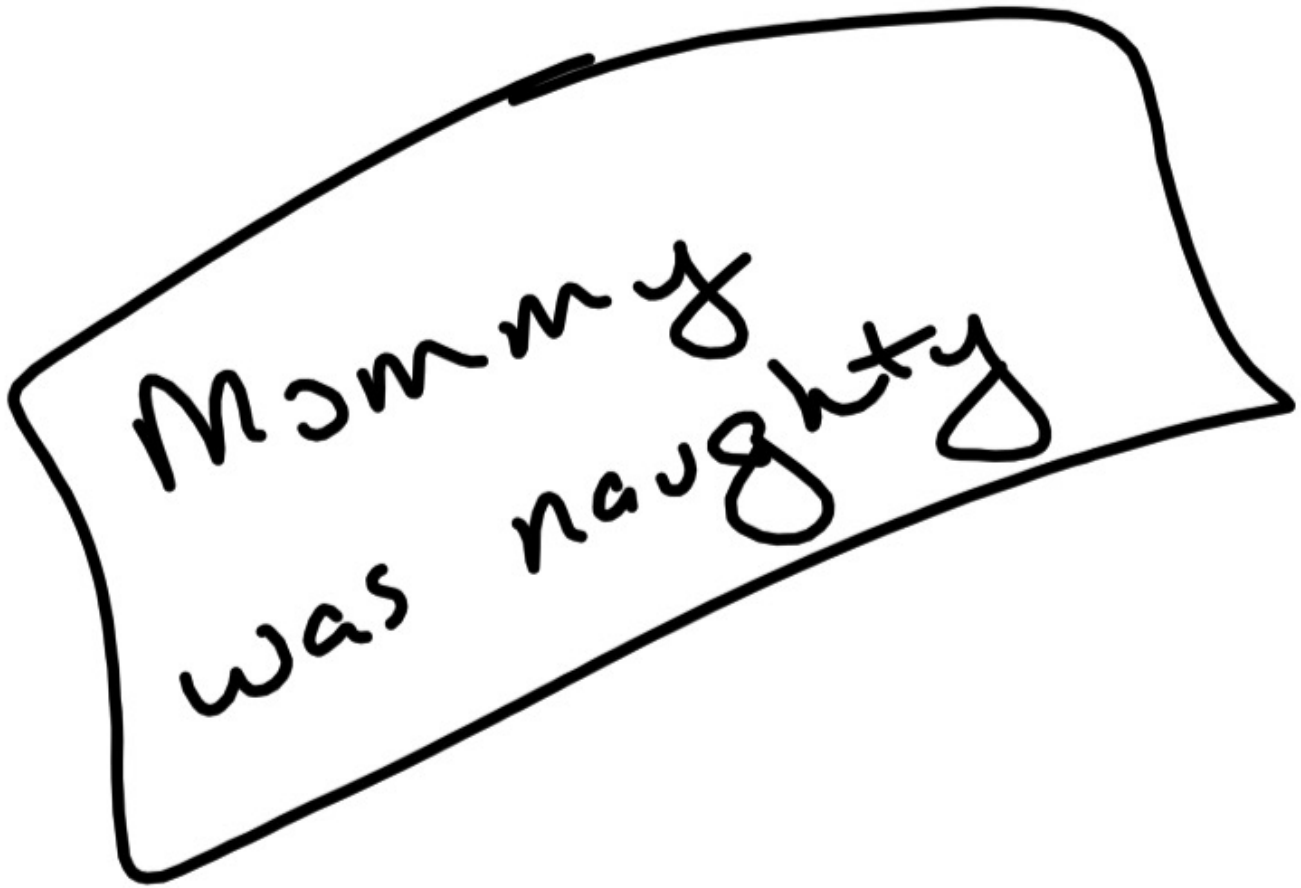
Mom	A+	AODd
Dad	B+	BODd
Baby	O-	OOdd
	O+	OODD or OODd
	A-	AOdd
	A+	AODD or AODd
	B-	BOdd
	B+	BODD or BODd
	AB-	ABdd
	AB+	ABDD or ABDd

Mom	A+	AADD
Dad	B+	BBDD
Baby	AB+	ABDD

Mom A- AOdd

Dad B- BOdd

Baby O+ OODd or OODD



	Type A-	Type A+	Type B-	Type B+	Type AB-	Type AB+	Type O-	Type O+
Antigen on RBC	A	A & D	B	B & D	A & B	A & B & D	none	D
Antibody in the plasma	anti-B	anti-B	anti-A	anti-A	none	none	anti-A anti-B	anti-A anti-B
Genotype	AAdd or AOdd	AADD AADd AODD AODd	BBdd or BOdd	BBDD BBDd BODD BODd	ABdd	ABDD or ABDd	OOdd	OODD or OODd

Blood Type Distribution in the Good Ole' US of A

O+	38%
A+	34%
B+	9%
O-	7%
A-	6%
AB+	3%
B-	2%
AB-	1%

Agglutination

- Occurs because of transfusion incompatibility
- Clumping of RBCs due to antibodies attacking RBC antigens
  - Will lead to hemolysis
    - Consequences could be minor to life threatening

- Examples:
  - Type A donor blood transfused into Type O recipient
    - Anti-A of recipient attacks antigens A of donor cells
  - Type B donor cells transfused into Type A recipient
    - Anti-B of recipient attacks antigen B of donor cells
  - Type O donor plasma transfused into Type B recipient
    - Anti-B of donor attacks antigen B of recipient

Blood Transfusions – Whole Blood Transfusion

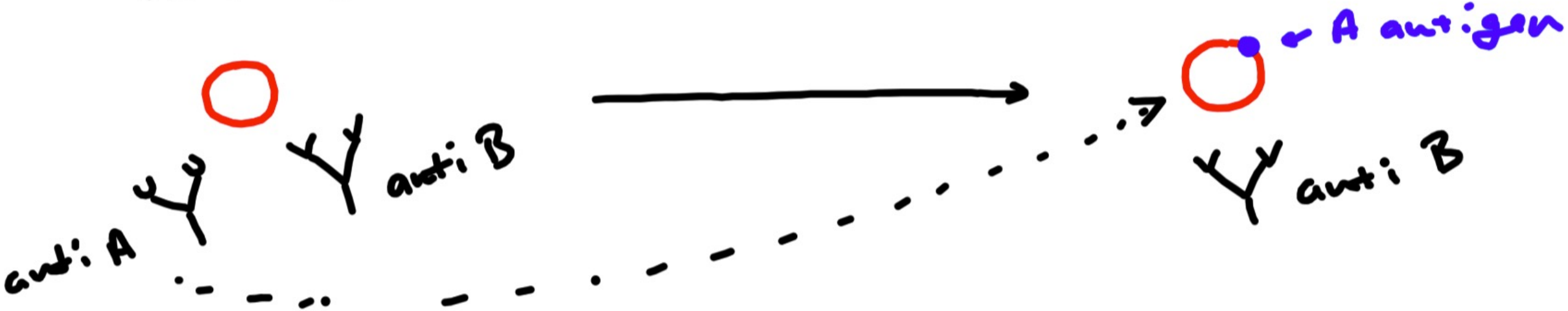
- Donor blood should be of the same type as the recipient blood
- Some reasons for whole blood transfusion
  - Replenish blood lost from trauma , internal bleeding , surgery
- Type O blood can be donated to any blood type but it is not ideal
  - Type O RBCs have no antigen so they cannot be agglutinated
- In case of emergency , any blood type can be donated to any blood type
  - Agglutination could become a serious issue

Transfusions

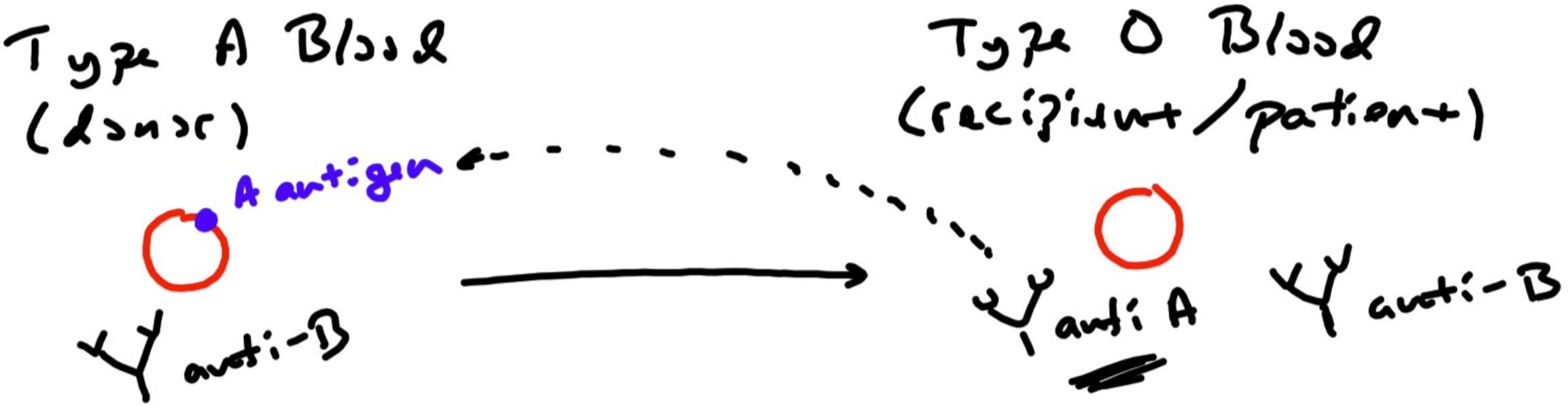
	Whole Blood	Cell	Plasma
RBC (antigen)	✓	✓	✗
Plasma (antibody)	✓	✗	✓

Type O Blood
(donor)

Type A Blood
(recipient/patient)



anti A of donor blood will agglutinate A RBC's



Recipient / Patient anti A agglutinate A RBC's from donor

- Worse
  - Why?
    - activated the immune system of the recipient

Blood Transfusions – Cell Transfusion

- Donated cells should contain the same antigen as the recipient
- Some reasons for red blood cell transfusion :
  - Hemolytic diseases
  - Congestive heart failure
    - Increases RBCs while limiting increase in blood volume

- Universal cell donor :
  - Type O- cells can be donated to any recipient
    - Have no antigen to be agglutinated
- Universal cell recipient :
  - Type AB+ blood can receive any type of red blood cell
    - Have no antibodies to cause agglutination

Cell Transfusions

A Cells	do not give to ...	Type B recipient
		Type O "
B Cells	" " " ...	Type A "
		Type O "
AB Cells	" " " ...	Type A "
		Type B "
		Type O "

O Cells can be given to all blood types

* Neg blood/cells can be given to a recipient w. pos blood

---

* Pos blood/cells can <u>NOT</u> be given to a recipient w. neg blood
  - Why?
    - D antigen is foreign to the immune system of a recipient w. neg blood
      - anti-D will therefore be produced in the recipient

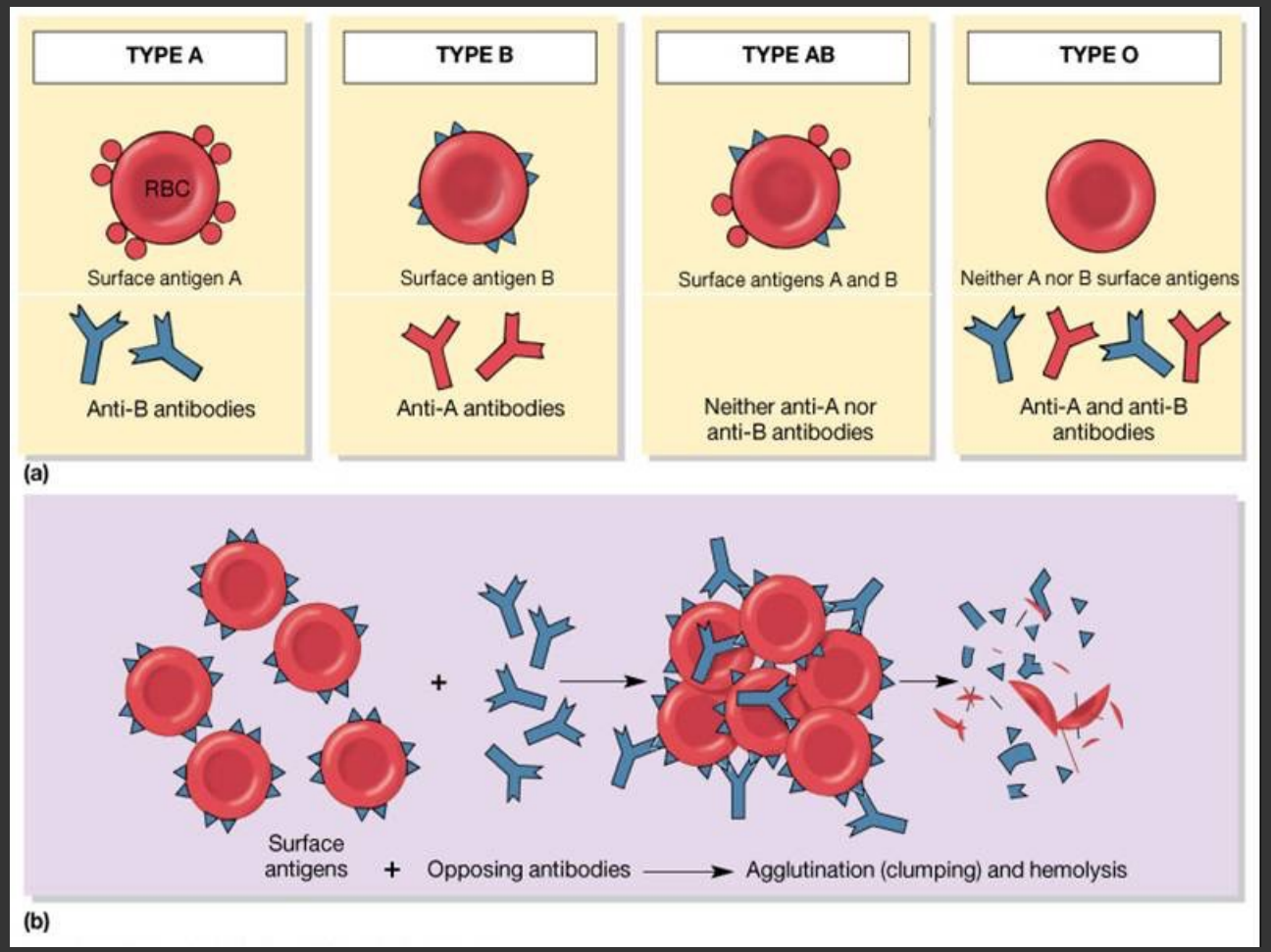
Blood Transfusions – Plasma Transfusion

- Donated plasma should contain the same antibody as the recipient
- Some reasons for plasma transfusion
  - Replenish clotting factors
    - e.g , during liver disease and to treat DIC
  - Prep for a procedure on someone that is on anticoagulants

- Universal plasma donor :
  - Type AB plasma can be donated to any recipient
    - Contains no antibodies
- Universal plasma recipient :
  - Type O blood can receive plasma from any recipient
    - Contains no antigen

Agglutination

Type B donor giving to Type A recipient



Type B Blood (donor)

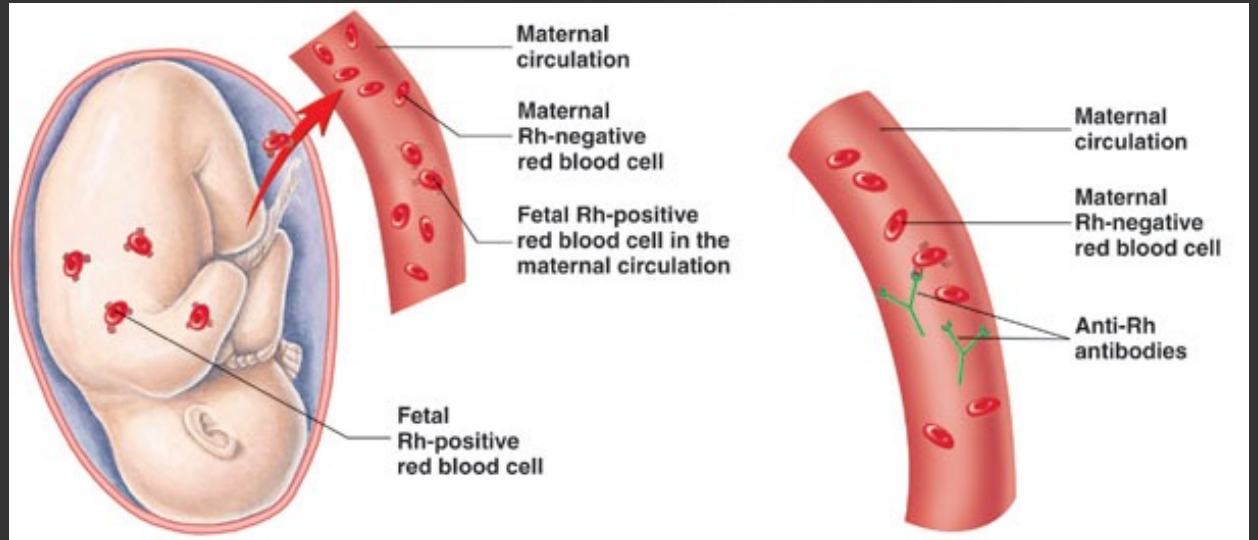
Type A Blood (recipient)

contains Anti-B

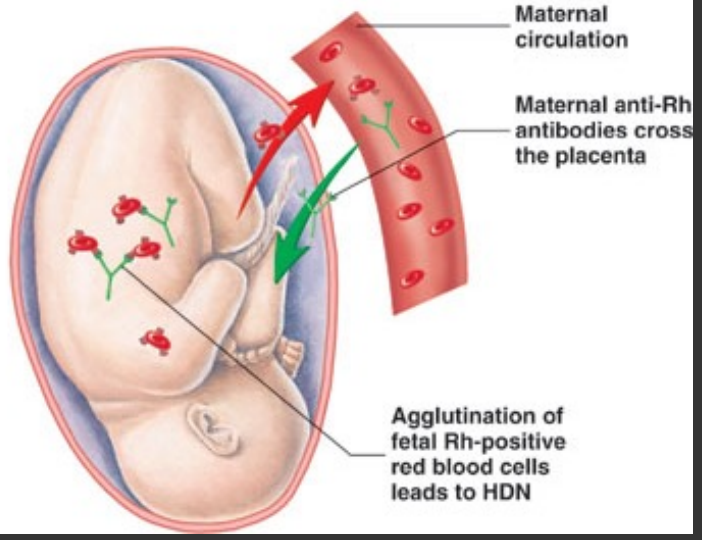
Erythroblastosis Fetalis

- How it occurs :
  - Rh– woman and an Rh+ man have an Rh+ baby
  - Woman exposed to antigen D of baby during birthing
  - Woman subsequently makes anti-D antibodies
    - Anti-D is IgG antibody , which crosses placenta
  - If woman carries an Rh+ child in subsequent pregnancy
    - Anti-D will agglutinate baby's RBCs
  - *Could also occur if woman already has anti-D prior to the first pregnancy

- RhoGAM shot used to prevent the above from occurring
  - Drug that suppresses formation of anti-D antibodies
  - Shot given to Rh– women
    - Given at week 28 of pregnancy
    - Given again within 72 hours of birth if baby is Rh+



a type of hemolytic anemia



E. F.

Mom : neg
Dad : pos
1st baby : pos

} If during birthing, baby's pos blood gets into Mom's neg circulation
↳ Mom produces anti-D

If 2nd baby has pos blood . . . Mom's anti-D will agglutinate baby's D RBC's

Another Incompatibility Due to Rh Factor

- Two successive transfusions of Rh+ blood given to an Rh– recipient
  - Anti-D will be produced in recipient after the first transfusion
  - Anti-D will agglutinate RBCs of subsequent transfused blood

Compatibility Table

Recipient Blood Type	Donated *Cells* Must Be:							
AB+	O-	O+	A-	A+	B-	B+	AB-	AB+
AB-	O-		A-		B-		AB-	
A+	O-	O+	A-	A+				
A-	O-		A-					
B+	O-	O+			B-	B+		
B-	O-				B-			
O+	O-	O+						
O-	O-							

Compatibility Table

Recipient Blood Type	Donated Plasma Must Be:			
AB+				AB
AB-				AB
A+		A		AB
A-		A		AB
B+			B	AB
B-			B	AB
O+	O	A	B	AB
O-	O	A	B	AB