

---

---

# Pathophysiology 1

---

---



# Course Outline

- Section 1
  - Definitions of Health
  - The Study of Pathophysiology
  - Medical and Pathological Terms
  - Cellular Adaptation
  - Factors Affecting Adaptation to Stressors
  - Aspects of the Disease Process
  - Levels of Disease Prevention
  - Cell Injury

## Section 2

- Blood Cells and the Hematopoietic System
- Blood Elements
- Hematopoiesis
- Anemia
- Hemostasis
- Blood Groups
- Polycythemia
- Infectious Mononucleosis
- Hodgkin Disease and Non-Hodgkin Disease
- Leukemia
- **Test 1 after Section 1 & 2**

# Section 3

- Source of infection
- Patterns and Defenses against Infections
- Spread of infections
- Pathogenesis of Bacterial Infections
- MRSA, H-PYLORI, VRSA-VISA, VRE
- The Lymphatic System

# Section 4

- The Immune System
- Innate immunity
- Adaptive Immunity
- Immune Response
- Acquired immunodeficiency syndrome (AIDS)
- Inflammation
- Hypersensitivity Disorders
- **Test after section 3 and 4**

# Section 5

## Mental Health

- Stress
- Insomnia
- Sleep Disorders
- Anxiety Disorders
- Phobias
- OCD
- Mood Disorders
- Depression
- Bipolar Disorder
- Eating Disorders
- Schizophrenia
- Test
- **FINAL EXAM**

# Definition of Health



“Health is a state of complete physical, mental, and social well-being and not merely the absence of disease and infirmity.”

Definition from the WHO in 1948 and has not been amended since

# Determinants of Health



- For many people attaining health based on the true definition is an unrealistic goal. The US Department of Health and Human Services in “Healthy People 2020” describe the determinants of health to as
  1. Attain lives free of preventable disease, disability, injury and premature death
  2. Achieve Health equity and eliminate disparities
  3. Promote good health for all
  4. Promote healthy behaviors across the lifespan



## Medical and Pathological Terminology

# Study of Physiology



- Branch of biology that deals with the functions and activities of life or of living matter (such as organs, tissues, or cells) and of the physical and chemical phenomena involved

# Study of Pathology

- study of the body's response to dysfunction or disease



# Pathophysiology

- The study of the physiology of altered health



# Pathology Types

**Pathology** - Underlying processes and changes in an organ or tissue, related to disease. At the cellular level it is called ***Histopathology*** & at the tissue level, it is called ***Gross Pathology***

**Forensic Pathology** - determination of a cause of death through examining human remains at the gross & cellular levels.

# Definitions

- **Disease:** The interruption, cessation, or disorder of a body system or organ structure.
- **Etiology:** Cause or causes of the disease
- **Pathogenesis:** Step by step development of the disease
- **Symptoms:** Subjective manifestation of the disease such as pain
- **Signs:** Objective (measurable) manifestations of the disease such as heart rate, BP, Size of swelling etc
- **Diagnosis:** Designation of the nature or cause of a health problem
- **Prognosis:** A prediction of the outcome of the pathological process or disease.

# Disease Progression

- **Remission:** Disease gets better - Decrease or complete disappearance of the disease
- **Exacerbation:** Disease gets worse

Autoimmune conditions such as rheumatoid arthritis, MS, & fibromyalgia often have periods of remission and exacerbation (AKA "flare ups").

**Complications:** Secondary problem due to the initial problem ex. My friend with diabetes has now developed peripheral neuropathy as a complication

**Healing:** Process by which damaged tissues are restored towards normal

**Resolution:** Perfect healing

# Disease Classifications - Congenital

- **Congenital disease:** When the individual is *born with* the disease. This could be due to:
  - a genetic or inherited problem of the DNA such as in Down Syndrome or Cystic fibrosis
  - problems in the uterine environment such as congenital birth defects from exposure to the rubella virus or taking the drug Thalidomide
  - problems during birth, such as cerebral palsy due to a lack of oxygen during the birth process.

# Disease Classifications - Acquired

Any disease that is NOT present at birth is said to be an **acquired disease**.

Diseases can be acquired in different ways:

**Infection:** Disease due to a pathogenic organism such as a virus, bacteria, fungi or parasite. These diseases can be further classified into **contagious** (able to spread to others) and **non-contagious**.

**Degenerative disease:** Disease caused by the structure or function of the tissues changing for the worse over time. Common examples are osteoarthritis, osteoporosis and coronary artery disease which are all very common findings in elderly people.

# Disease Classifications - Acquired

**Traumatic disease:** Disease caused by injury

**Neoplastic disease:** Uncontrolled growth of cells AKA Cancers

**Deficiency Disease:** caused by lack of a certain nutrient eg Scurvy from lack of Vit C, anemia from lack of iron

**Autoimmune disease:** a malfunction of the body's immune system that causes it to attack components of our body ex. Rheumatoid arthritis, Multiple Sclerosis

**Idiopathic disease:** The medical professional does not know the cause of the disease

**Iatrogenic disease:** A disease caused by a medical intervention or mistake, such as paralysis after surgery or kidney disease caused by a toxic medication

# Testing for Diseases

**Predictive value:** Extent to which an observation or test result is able to predict the presence of a given disease or condition.

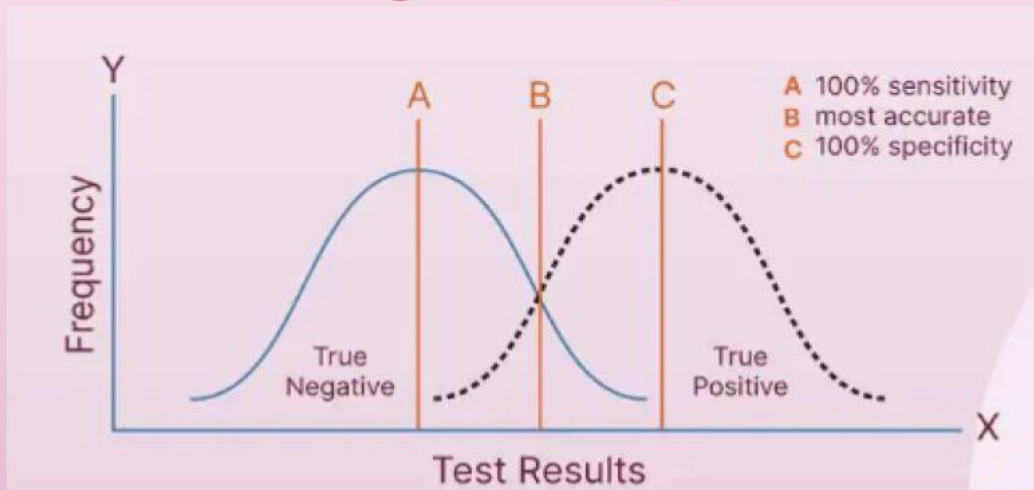
**Sensitivity:** The sensitivity of a test refers to how well the test is able to find people with the disease. A highly sensitive test has very few false negatives and so is very good at identifying those with the condition.

**Specificity:** The specificity of a test refers to how well the test can rule OUT healthy people, with very few false positives.

<https://youtu.be/UsOv0DcXk6w?feature=shared>

# Sensitivity vs Specificity

## Difference Between Sensitivity & Specificity



**SPPIN** - A highly **specific** test, when **positive**, rules **in** a disease

**SNNOUT** - A highly **sensitive** test, when **negative**, rules **out** a disease

# Epidemiology

**Epidemiology** is the study of how a disease affects a population of people.

**Morbidity:** The number of diseased persons in a given locality, nation etc. describes the effects of an illness on a person's life

- Concerned with the incidence, persistence, and long-term consequences of disease

**Prevalence:** The number of people affected by the disease currently in any defined population.

**Incidence:** The number of new cases arising in a population at risk during a specified time

**Mortality:** The number of deaths that have occurred in any defined population due to a specific disease or cause.

# Problems with Blood Oxygenation

- **Anemia:** A condition in which a person doesn't have enough healthy red blood cells or hemoglobin to carry adequate oxygen to his/her tissues.
- **Hypoxia:** Inadequate oxygen supply
- **Ischemia:** Loss of blood supply resulting in damaged tissues
- **Cyanosis:** A bluish discoloration of the skin and mucous membranes due to an excessive concentration of reduced (deoxygenated) hemoglobin in the blood

# Terms related to blood

- **Embolus:** A clot, usually part or all of a thrombus, carried by a larger vessel and forced into a smaller vessel, thus obstructing blood flow.
- **Embolism:** The sudden blocking of an artery by a clot of material (embolus). The process of the formation of an embolus.
- **Hematemesis:** Vomiting blood.
- **Hemoptysis:** Coughing-up blood.
- **Hematoma:** A localized collection of extravasated blood, usually clotted.
- **Hemorrhage:** Discharge of blood.
- **Syncope:** A temporary loss of consciousness due to insufficient cerebral blood flow; fainting.

# Definitions

- **Abscess:** A localized collection of pus in a cavity formed by the disintegration of tissue.
- **Cyst:** An abnormal sac filled with gas, fluid, or semi-solid material that is lined by a membrane.
- **Polyp:** A spheroidal mass that protrudes upwards or outwards from a normal surface. Polyps may be hyperplastic, inflammatory, or neoplastic.
- **Edema:** An abnormal accumulation of fluid in the cavities and intercellular spaces of the body.
- **Ulcerated:** Having a local defect or excavation of the epithelium of an organ or tissue through the basement membrane.

# Continued

- **Dyspnea:** Difficult breathing.
- **Fistula:** An abnormal, tube-like passage from a hollow organ to the surface or from one organ to another
- **Gastroenteritis:** Inflammation of the lining of the stomach and intestine.
  
- **Jaundice:** Yellow staining of the skin and sclera (the whites of the eyes) by abnormally high blood levels of the bile pigment (bilirubin).
- **Necrosis:** The morphologic changes indicative of cell death, indicated by characteristic nuclear and cytoplasmic changes.

# Continued

- **Imperforate:** Closed (when it should be open), ex. imperforate anus
- **Infarct:** A localized area of ischemic necrosis produced by the occlusion of the blood vessels - either arterial supply or venous drainage.
- **Lesion:** An alteration or abnormality in a tissue or cell; a pathological change.
- **Metastatic:** A tumor that has transferred from one organ (or part) to another not directly connected to it
- **Malignant:** Having the properties of anaplasia, invasiveness and metastasis; tending to become progressively worse and to result in death
- **Patent:** Open (when it should be closed), exposed or unobstructed. e.g. patent ductus arteriosus - an abnormal persistence after birth of an open lumen in the ductus arteriosus, between the pulmonary artery and the aorta.

# Continued

- **Splenomegaly:** Enlargement of the spleen.
- **Hepatomegaly:** Enlargement of the liver.
- **Cardiomegaly:** Enlargement of the heart.
  
- **Hemiplegia:** Weakness/paralysis on one side of the body
- **Hemiparesis:** Weakness/partial paralysis on one side of the body
- **Quadriplegia:** Weakness/paralysis bilateral upper & lower extremities
- **Paraplegia:** Weakness/ paralysis bilateral lower extremities

# Suffixes

- -algia: Pain
- -itis: Inflammation
- -pathy: Disease
- -paresis: Partial paralysis
- -lysis: Destruction, separation
- -oma: Tumor
- -penia: Deficiency





Factors Affecting Adaptation to Stressors

## STRESS & HEALTH

# A few more definitions

- **Homeostasis** - tendency of organisms to auto-regulate and maintain their internal environment in a stable state
- **Stress** - is a condition in which the human system responds to changes in its normal balanced state.
- **Stressor** - anything that is perceived as challenging, threatening or demanding
- **Adaptation** - is the change that takes place as a result of the response to a stressor



# Stress Response

## A Control System

- The Stress response
  - A collection of control systems in the brain that serve to control nerve activity, regulate information flow that ultimately control behavior. They mediate the physical, emotional and behavioral reactions to stressors
- Parts of a control System
  - Sensor – Detects change
  - Integrator – compares incoming data with normal
  - Effector – Tries to reverse the change
- More complex Stressor invoke more complex control systems and sometimes the stress response cannot restore balance or homeostasis
- <https://youtu.be/QAeBKRaNri0?si=MV7DugKXORFn2H9q>

# Stress & Adaptation

- Humans usually have alternative mechanisms for adapting and have the ability to control many aspects of the environment
- Many of the bodies physiologic disturbances are controlled by moment by moment feedback mechanisms that limit their application and duration of action
- Systems that control physiologic responses are specific, where as psychological disturbances are not regulated with same degree of specificity and feedback control
- General Adaptation Syndrome HPA Axis

# HPA Axis & General Adaptation Response

- Discovered by Dr. Hans Selye
- Response to a perceived stressor,, physical or mental/emotional, causes a response by the **HPA Axis**:

**Hypothalamus -> Pituitary gland -> Adrenal Gland**

ultimately resulting in the production of more *cortisol* hormone and an increased *sympathetic nervous system* response

-General Adaptation Syndrome has 3 phases: alarm, resistance, & exhaustion

- If the stressor persists & the General Adaptation response cannot restore homeostasis, that is when the exhaustion phase sets in. Symptoms include: fatigue, burnout, decreased tolerance of stressors & more frequent illness.

# Factors that affect Adaptation

- Adaptation implies an individual has created a new balance between the stressor and ability to deal with it
- How we cope with stressful events depends on how we perceive and interpret the event
- Factors that affect our ability to adapt include
  - **Physiologic and Anatomic Reserve**
  - **Time**
  - **Genetics**
  - **Age**
  - **Gender**
  - **Health Status**
  - **Nutrition**
  - **Sleep-wake cycles**
  - **Resilience**
  - **Psychosocial Factors**

# Physiologic & Anatomic Reserve

- The ability of body systems to increase their function given the need to adapt is Physiologic Reserve
- Many body organs are paired which provide an anatomic reserve (kidneys)



# Time

- Adaptation is most efficient when changes occur gradually rather than quickly
- Ex – losing blood over a week with a GI bleed will likely not manifest signs of shock, where as happening suddenly it would



# Genetics

- Adaptation is further affected by availability of adaptive responses and flexibility to select the appropriate one
- Genetics can ensure that systems for adaptation function adequately



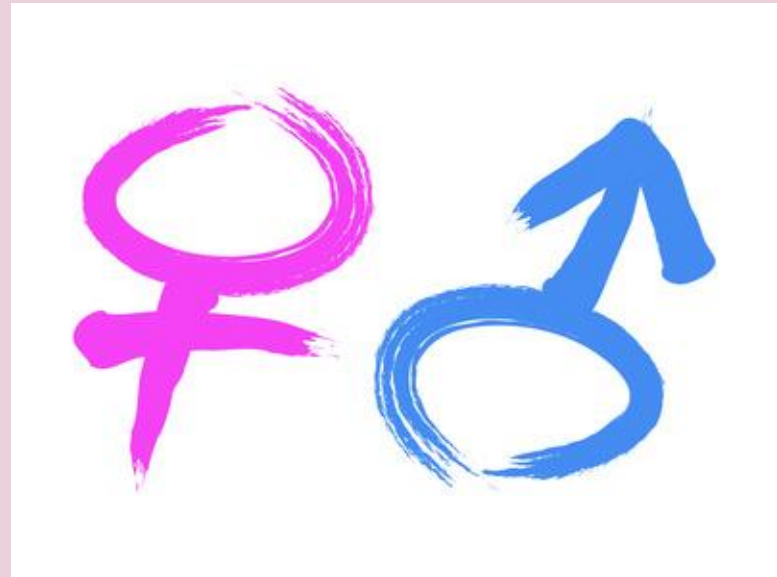
# Age

- Capacity to adapt is decreased at extremes of age
- Ability in infants is impaired by immaturity of body etc.
- Ability in elders due to decline in functional reserve



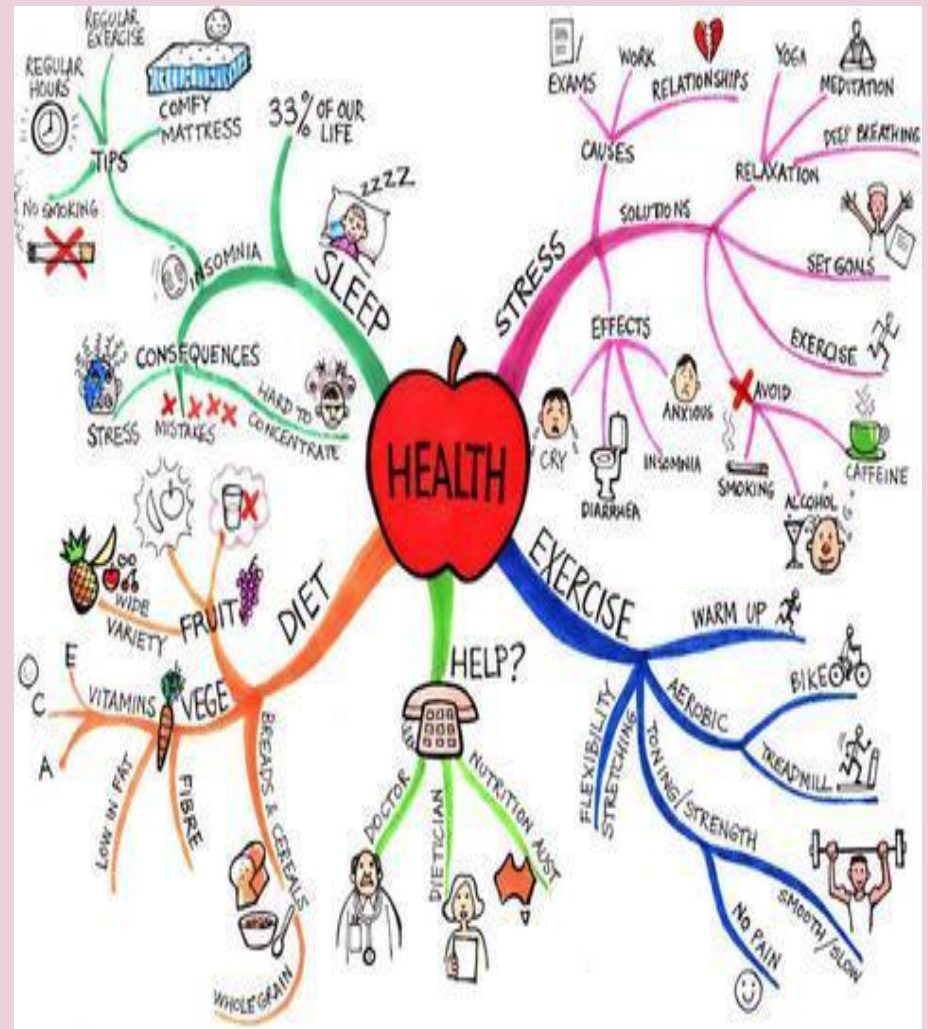
# Gender

- Premenopausal women tend to have a lower activation of their sympathetic nervous system than men in response to stressors
- This may account for differences in susceptibilities to diseases which the stress response plays a causal role



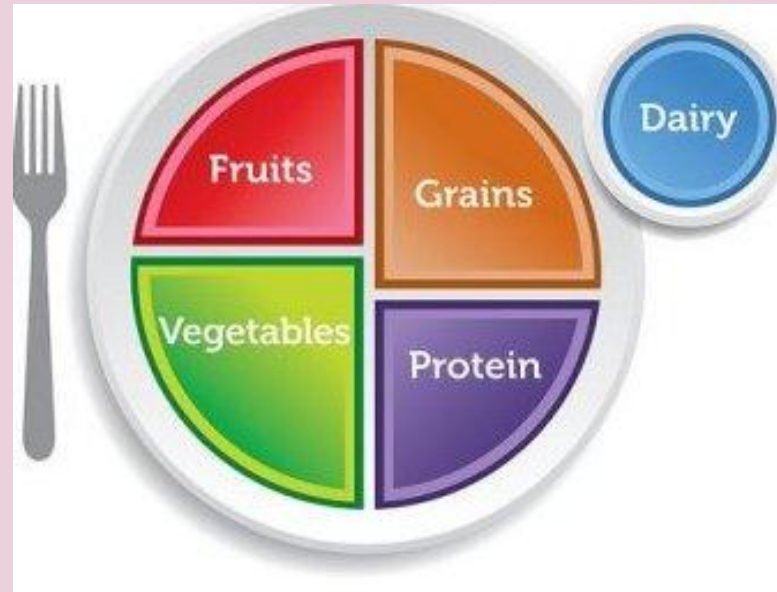
# Health Status

- Strong Determinant of the ability to adapt
- Has an effect on physiologic and anatomical reserves
- Ex – heart disease less able to deal with stresses that require cardiovascular responses



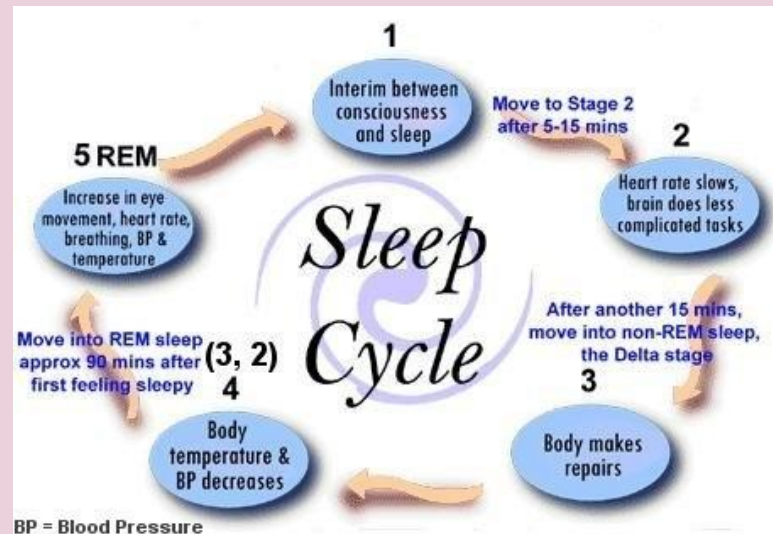
# Nutrition

- Lack of or excesses in any essential nutrient can impair the body's ability to adapt



# Sleep-Wake Cycles

- Sleep is restorative in which energy is restored and tissues are regenerated
- Sleep deprivation has been shown to alter immune responses, hormone secretion, physical and physiological functioning
- Lack of Sleep affects health



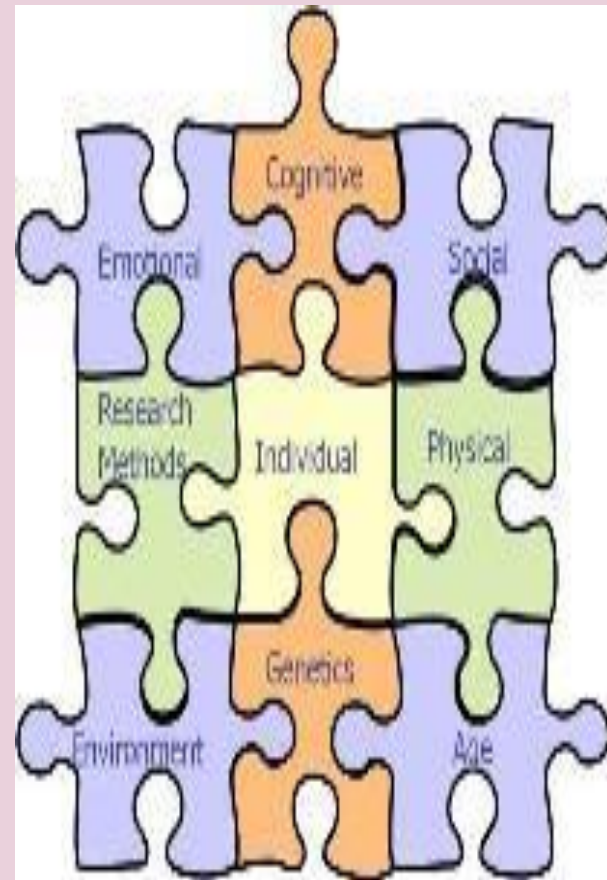
# Resilience or Hardiness

- Personality characteristic that includes: Sense of control over one's life, sense of purpose, ability to look at stressors as challenges rather than a threat. Studies suggest that hardiness is related to positive health outcomes
- Can be improved through many exercises including mindfulness meditation
- <https://youtu.be/v-t1Z5-oPtU?si=hfkx-xLnOrFVzG0t>



# Psychosocial Factors

- People who can mobilize strong supportive resources from within their social relationships are better able to withstand negative effects of stress on their health



1. Physiologic & Anatomic Reserve

2. Time

3. Age

3. Genetics

5. Gender

6. Nutrition

7. Health Status

8. Psychosocial Factors

9. Sleep-Wake Cycles

10. Resilience



[Berkeley Greater Good in Action](#)

# REVIEW OF FACTORS THAT AFFECT ADAPTATIONS TO STRESSORS



ASPECTS OF THE DISEASE PROCESS

# Aspects of the disease process

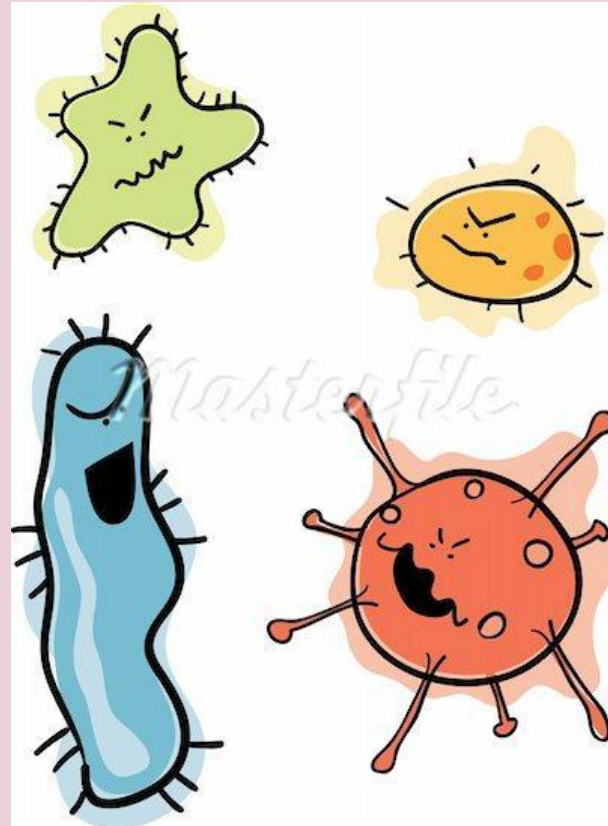
- Etiology
- Pathogenesis
- Morphologic changes(morphology of the tissue changes)
- Clinical manifestations
- Diagnosis
- Clinical course

# Etiology

- Causes of disease known as Etiologic factors
- Recognized etiologic agents
  - Biologic Agents (bacteria, viruses)
  - Physical Forces (Burns, Trauma, radiation)
  - Chemical Agents (Poisons, Alcohol)
  - Genetic Inheritance
  - Nutritional excesses or deficits
- Many different agents can cause disease of a single organ
- A single agent can cause disease to a number of organs or systems (cystic Fibrous)
- Most diseases are multifactorial in nature (cancer, heart disease)

# Etiology Continued

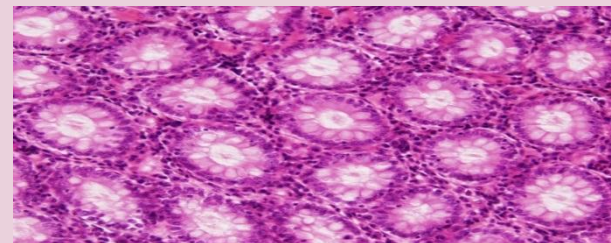
- Diseases can be grouped as either congenital (present at birth) or acquired





# Morphologic Changes

- Refers to the fundamental structure or form of cells or tissues
- concerned with both gross anatomic and microscopic changes that are characteristic of a disease
- Histology – Study of cells, extracellular matrix of body tissues
- Plays an important role in diagnosing many types of cancers



# Clinical Manifestations

- Disease can Manifest in many different ways
  - Some processes manifest quickly and display signs quickly like fever
  - Some are silent at onset and usually diagnosed when examining for other reasons or when disease are far advanced
    - **Signs** (objective, observable, often measurable)
    - **Symptoms** (subjective, hard to measure) used to describe the changes that accompany disease



# Diagnosis

- Designation as to nature of the health problem
- Involves
  - Physical exam
  - Health History
  - Diagnostic Tests
- Development of diagnoses involves competing possibilities and selecting the most likely one from among the conditions that might be responsible for the persons clinical presentation.
- This is referred to as Differential Diagnosis.

# Clinical Course

- Describes evolution of disease
- Acute, Subacute and chronic course possibilities
- Chronic can have stages of remission or aggravation
- Infectious diseases can run a course from preclinical to persistent chronic infection (HepB)
- Possible to transmit to others in preclinical stage
- Subclinical not clinically apparent and not always destined to become clinical. Diagnosed with antibodies or cultures
- Clinical stage manifested by signs and symptoms
- Persistent chronic infection can last years or a lifetime. Carrier has organism but is not infected but can pass an infection to others

# Acute vs Subacute vs Chronic

**Based on the duration and type of symptoms**

Acute:	<2weeks	<ul style="list-style-type: none"><li>■ Early acute</li><li>■ Late acute(4-5days)</li></ul>
Subacute:	2weeks—6weeks	Less virulent - more immune
Chronic:	>6 weeks	

These timeframes can vary a little, based on what type of disease. This chart refers to Infectious diseases.



# LEVELS OF DISEASE PREVENTION

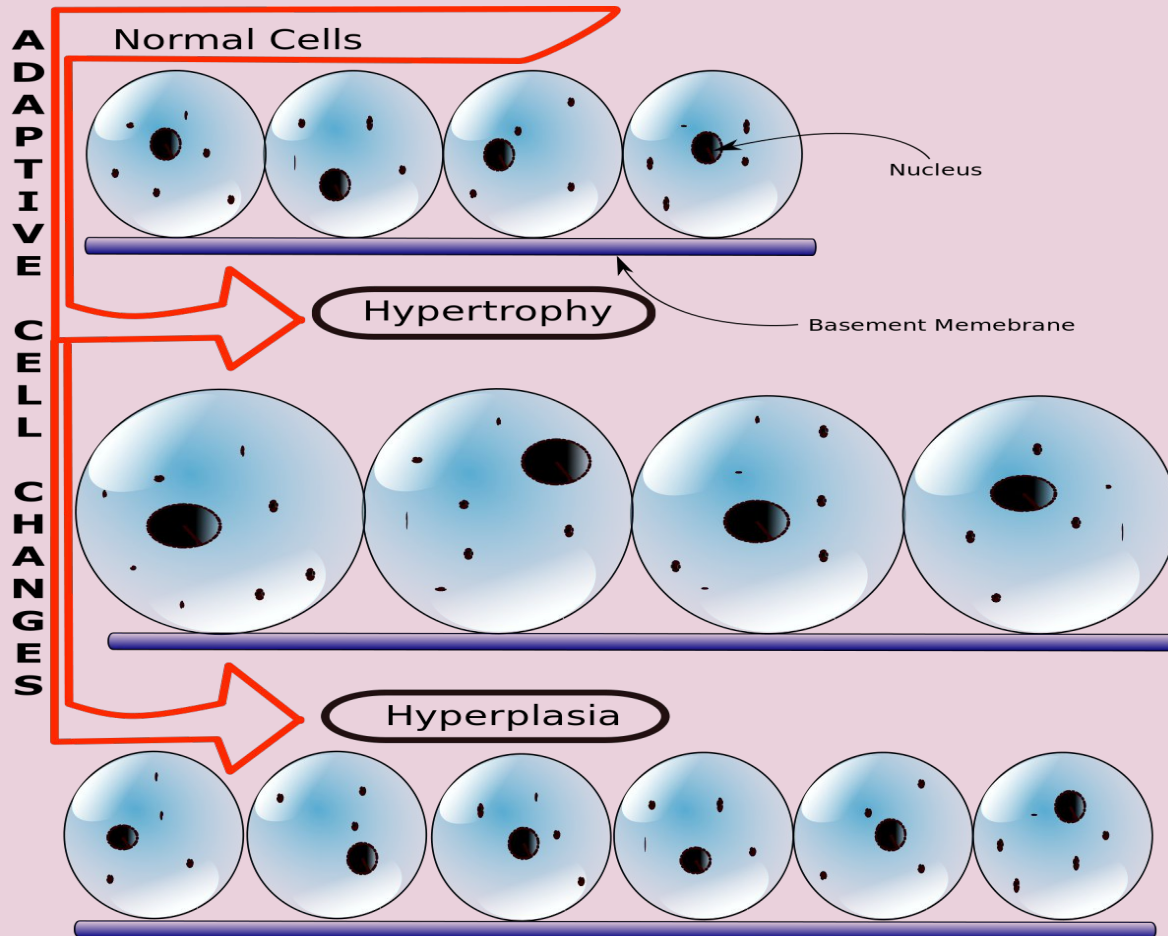
# Three levels of Prevention

- Leading a healthy life contributes to the prevention of disease. The three fundamentals of prevention include:
  - **Primary Prevention** (e.g., immunizations, using seatbelt): removing risk factors so disease does not occur, we use primary prevention methods before the person gets the disease. Primary prevention aims to prevent the disease from occurring. So primary prevention reduces both the incidence and prevalence of a disease
  - **Secondary Prevention** (e.g., Pap smears): detecting disease while it is still curable, Secondary prevention is used after the disease has occurred, but before the person notices that anything is wrong.
  - **Tertiary Prevention** (e.g., antibiotic use): preventing further deterioration or reducing complications of disease, Tertiary prevention targets the person who already has symptoms of the disease.

# Goals of Tertiary Prevention



- Prevent damage and pain from the disease
- Slow down the disease
- Prevent the disease from causing complications
- Give better care to people with the disease
- Return the person to health again and return them to their normal activities of living



# CELLULAR ADAPTATION

# Cellular Adaptation

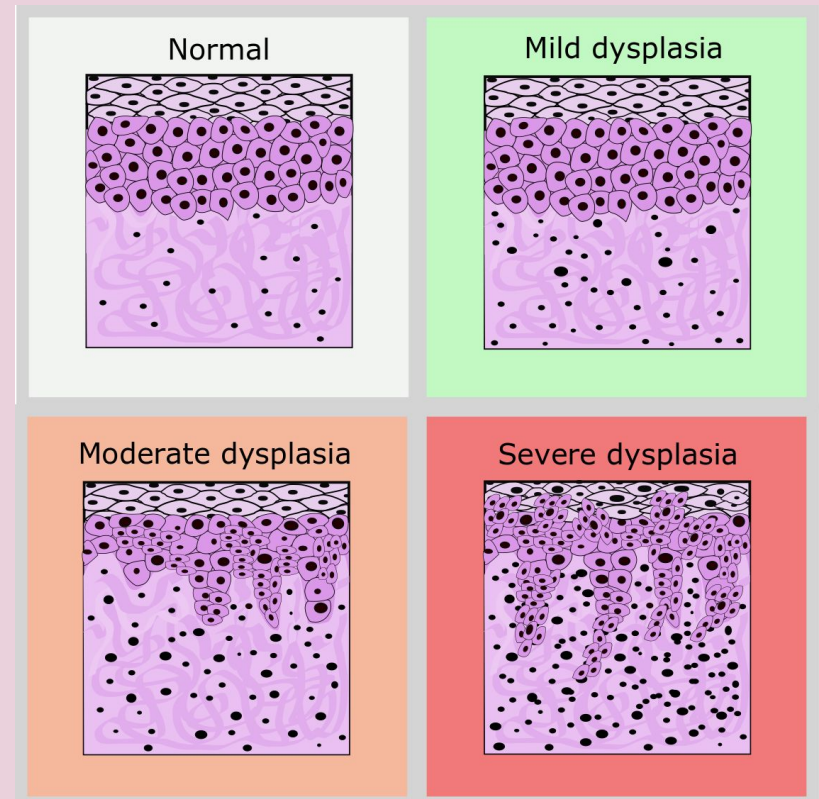
- Occurs when cells are confronted with stresses that endanger its normal structure and function
- These changes permit survival and maintenance of function
- Cell injury and death occur when stress is overwhelming or adaptation is ineffective
- Cells adapt to changes in the internal environment

# How Cells Adapt

- Cells may adapt by undergoing changes in size, number, and type
- These changes occur singly or in combination, may lead to different types of **dysplasia**, either singly or in combination:
  - 1) **Atrophy**
  - 2) **Hypertrophy**
  - 3) **Hyperplasia**
  - 4) **Metaplasia**
- Adaptive cellular responses also include intracellular accumulations and storage of products in abnormal amounts

# Dysplasia

- Characterized by deranged cell growth of a specific tissue that results in cells that vary in shape, size and organization
- Dysplasia is abnormal
- Can be **potentially reversible** as it is an adaptive response to chronic inflammation or irritation



# Atrophy

- **Reverting to a smaller size is known as atrophy**
- An adaptation to decrease in work demands or adverse environmental condition
- Cell functions more efficiently
- General causes
  - Disuse
  - Denervation
  - Loss of endocrine stimulation
  - Inadequate nutrition
  - Ischemia or decreased blood flow

# Hypertrophy

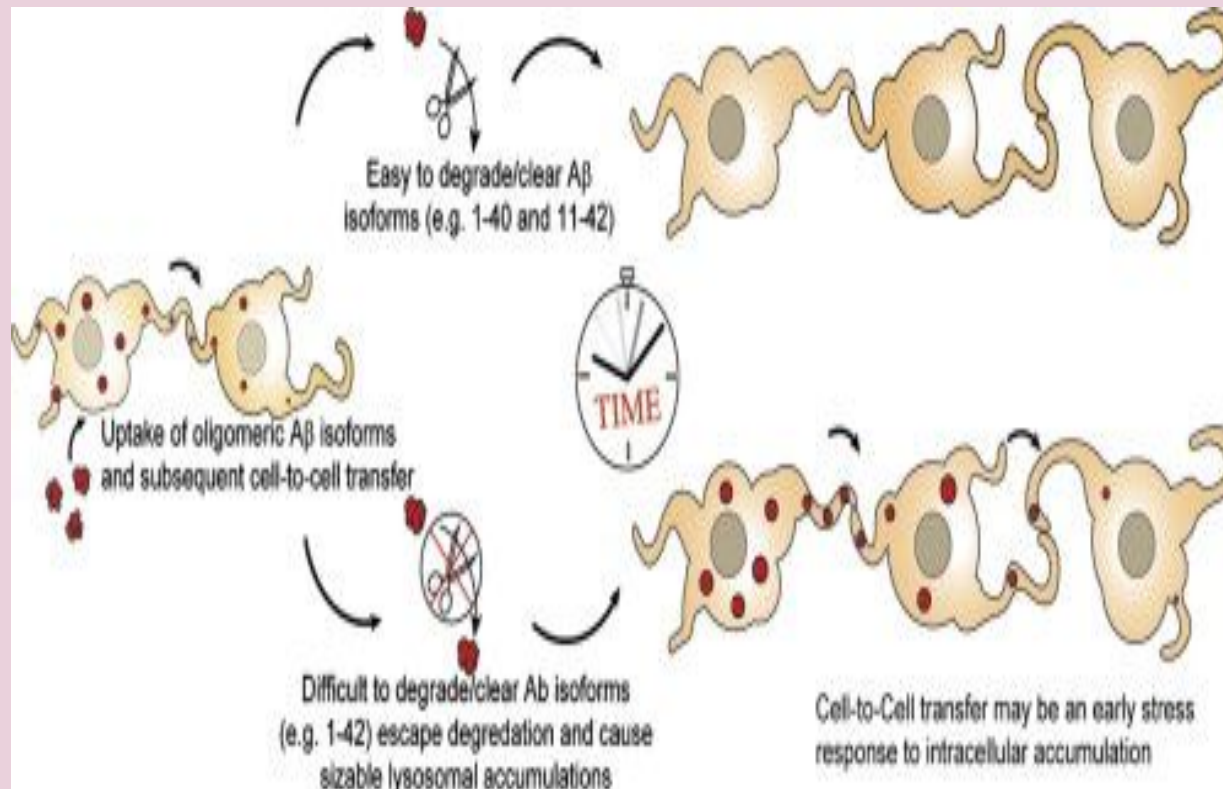
- **Increase in cell size** , increase in the amount of functioning tissue mass
- Results from an increased workload imposed on a organ or body part
- Commonly found in skeletal and cardiac muscle, which cannot adapt by formation of new cells
- May result as normal physiologic or abnormal pathologic conditions (skeletal, myocardial hypertrophy)

# Hyperplasia

- **Increase number of cells** in an organ or tissue
- Occurs in epidermis, intestinal epithelium, glandular tissue – cells that do a lot of mitotic division
- Rarely seen in neurons because of their slow & low rate of mitosis
- 2 types of **physiologic** (normal) hyperplasia
  - Hormonal – breast enlargement during pregnancy
  - Compensatory – regeneration of liver after surgery
- Non physiologic, **pathological** hyperplasia
  - Mostly due to excessive hormonal stimulation
  - Can be caused by effects of growth factors on target tissues
- Hypertrophy and hyperplasia often work together

# Metaplasia

- **A reversible change in cells in which one adult (epithelial or mesenchymal) is replaced by another cell type**
- Thought to involve reprogramming of undifferentiated stem cells that are present in the tissue undergoing the metaplastic changes
- Usually results from chronic irritation or inflammation
- Never oversteps boundaries of original cell type – epithelium – epithelium
- Ex. Squamous epithelial to columnar-lined epithelium for those suffering GERD. Becomes a risk factor for adenocarcinoma ( \*classic example of metaplasia - know this)
- [Review of Cellular Adaptations](#)

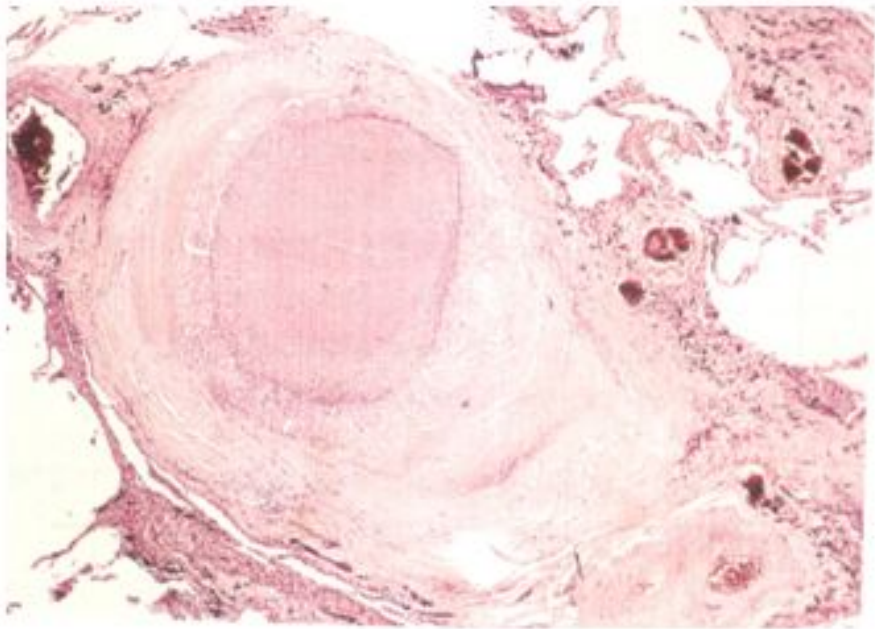


# INTRACELLULAR ACCUMULATIONS

# Intracellular Accumulations

- Build up of substances that cells cannot immediately use or eliminate
- May accumulate transiently or permanently, harmless or toxic
- Grouped into three categories
  - Normal body substances
    - Lipids, proteins, carbohydrates, melanin, etc.
  - Abnormal endogenous products
    - Those resulting from inborn errors of metabolism
  - Exogenous products
    - Environmental agents and pigments not broken down by the cell
    - <https://youtu.be/0GnTCuJt74o>

## Calcification of the lymph nodes



PATHOLOGIC CALCIFICATION

# Pathologic Calcifications

- Occurs when Calcium salts are deposited in tissues where it is not supposed to be. Eg arteries, lung, kidney tubules, lymph node
- Contrast with Physiologic Calcification in which Calcium is deposited where it is supposed to be ie. Teeth, bone
- Abnormal tissue deposits of calcium salts, together with smaller amounts of iron, magnesium and other minerals.
- **Dystrophic** calcification – when occurs in *injured, dying or dead tissue*. Eg atherosclerosis, damaged heart valves
- **Metastatic** Calcification – *occurs in normal tissues as a result of high serum calcium (hypercalcemia)*. Eg calcifications in lung, kidney and blood vessels as a result of hyperparathyroidism, Paget disease etc



CELL INJURY

# Causes of Cell Injury

- Damage can occur in many ways
- Grouped into five categories:

## 1) Injury from physical agents

- Mechanical forces
- Extremes of temperature
- Electrical forces

## 2) Radiation injury

- Ionizing radiation
- Ultraviolet radiation
- Nonionizing radiation

## 3) Chemical agents

- Drugs
- Carbon tetrachloride
- Lead toxicity
- Mercury

# Continued

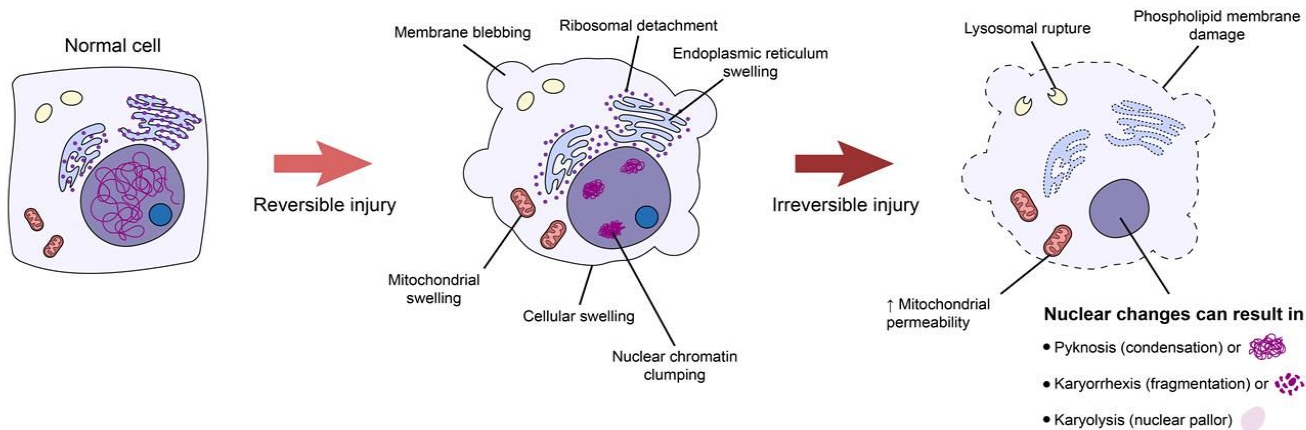
## 4) Injury from biologic agents

- Viruses, parasites, bacteria

## 5) Injury from nutritional imbalances

- Excesses and shortnesses

# Cell Injury



# Mechanisms of Cell Injury

- The cellular response to injurious stimuli depends on the type of injury, its duration, and its severity. Thus, low doses of toxins or a brief duration of ischemia may lead to reversible cell injury, whereas larger toxin doses or longer ischemic intervals may result in irreversible injury and cell death.

# Hypoxic Cell Injury

- Deprives the cell of oxygen and interrupts oxidative metabolism and the generation of ATP
  - Acute cellular swelling (edema)
  - The longer the tissue is hypoxic, the greater chance of irreversible cellular injury.
- Causes of hypoxia:
  - Inadequate amount of oxygen in the air
  - Respiratory disease
  - Inability of the cells to use oxygen
  - Edema
  - Ischemia

# Reversible Cell Injury

- Impairs cell function but does not result in cell death
- Two patterns of reversible cell injury occur:
  - Cellular swelling: impairment of the energy-dependent  $\text{Na}^+/\text{K}^+$  ATPase membrane pump, usually as the result of hypoxic cell injury.
  - fatty change: linked to intracellular accumulation of fat

# Cell Death

- **Apoptosis (programmed Cell Death)**
- This process eliminates cells that are:
  - Worn out – natural life cycle of cell
  - Have been produced in excess
  - Have developed improperly
  - Have genetic damage
- **Necrosis:**
  - Refers to cell death in an organ or in tissues that are still part of a living person
  - Often interferes with cell replacement and tissue regeneration
  - Gangrene occurs when a considerable mass of tissue undergoes necrosis
  - <https://youtu.be/1vaEVcMfa1E>

# Gangrene

- The term gangrene is applied when a considerable mass of tissue undergoes necrosis due to a lack of blood flow or a bacterial infection. Gangrene most commonly affects the extremities, including toes, fingers and limbs, but it can also occur in muscles and internal organs. Treatments for gangrene include surgery to remove dead tissue, antibiotics and other approaches. The prognosis for recovery is better if gangrene is identified early and treated quickly.

# Dry Gangrene

- begins at the distal part of the limb due to ischemia, and often occurs in the toes and feet of elderly patients due to arteriosclerosis
  - The affected tissue becomes dry and shrinks, the skin wrinkles, and its color changes to dark brown or black. The spread of dry gangrene is slow.



# Wet Gangrene

- occurs in naturally moist tissue and organs such as the mouth, bowel, lungs, cervix, and vulva. This condition is characterized by thriving bacteria and has a poor prognosis (compared to dry gangrene) due to septicemia resulting from the free communication between infected fluid and circulatory fluid.
  - The affected area is cold, swollen, and pulseless. The skin is moist, black, and under tension. Blebs form on the surface, liquefaction occurs, and a foul odor is caused by bacterial action.
  - The spread of tissue damage is rapid.



**Wet  
gangrene**

**Intestine**

# References

Lippincott Williams & Wilkins

<http://www.who.int/about/definition/en/print.html>

<http://undp.by/en/who/healthforall>

[www.cdc.gov](http://www.cdc.gov)

<http://kidshealth.org>

[onlinelibrary.wiley.com](http://onlinelibrary.wiley.com)

[www.merckmanuals.com](http://www.merckmanuals.com)

[www.princeton.edu](http://www.princeton.edu)

[www.cliffsnotes.com](http://www.cliffsnotes.com)

<http://biology.about.com>

<https://youtu.be/1vaEVcMfa1E>

<https://www.propofs.com/quiz-school/quizshow.php?title=pathophysiology-practice-test-i&q=1>

---

---

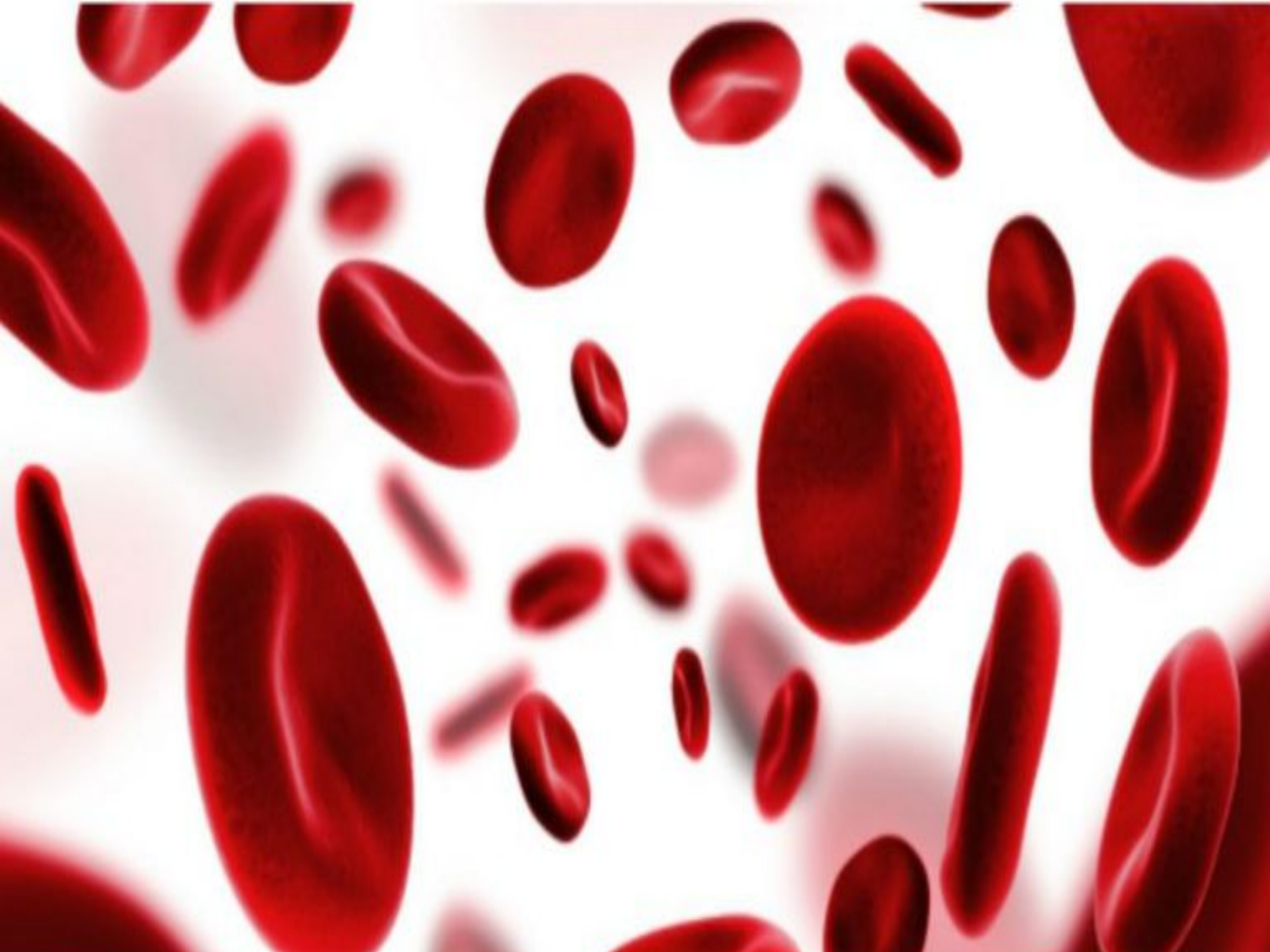
# Hematology

Section 2

— Study of the pathophysiology of Blood —  
The Human Body in Health and Illness  
Ch 15, pg 284

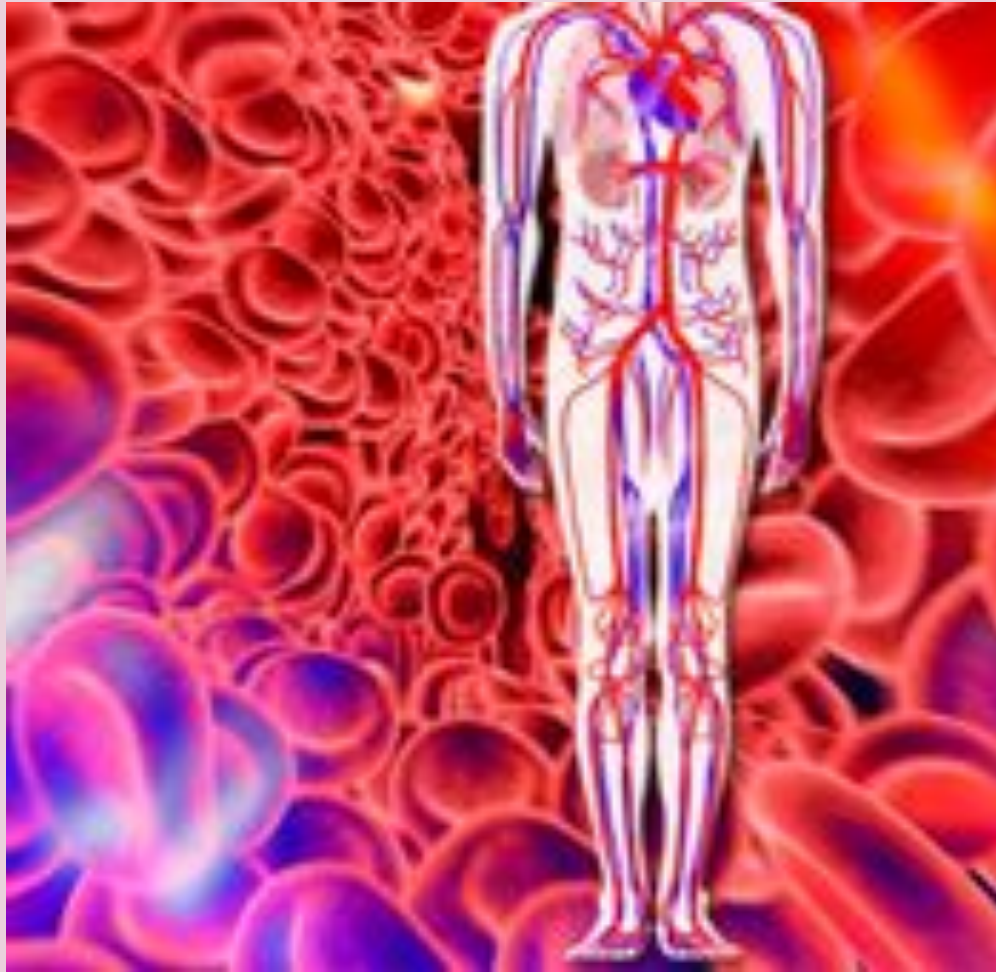
---

---



# Outline

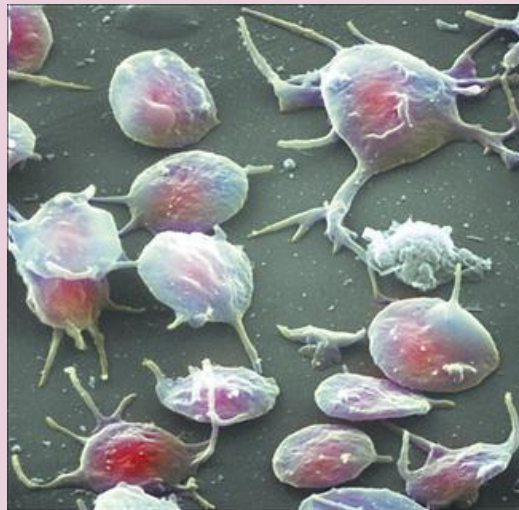
- Blood Cells and the Hematopoietic System
- Blood Elements
- Hematopoiesis
- Anemia
- Hemostasis
- Blood Groups
- Polycythemia
- Infectious Mononucleosis
- Hodgkin Disease and Non-Hodgkin Disease
- Leukemia



# BLOOD CELLS AND THE HEMATOPOIETIC SYSTEM

# Cardiovascular System

- The cardiovascular system consists of three interrelated components: the blood, the heart, and blood vessels.
- Blood contributes to homeostasis by transporting respiratory gasses, nutrients, and hormones to and from your body's cells. It helps regulate body pH and temperature, and provides protection through its clotting mechanisms and immune defenses

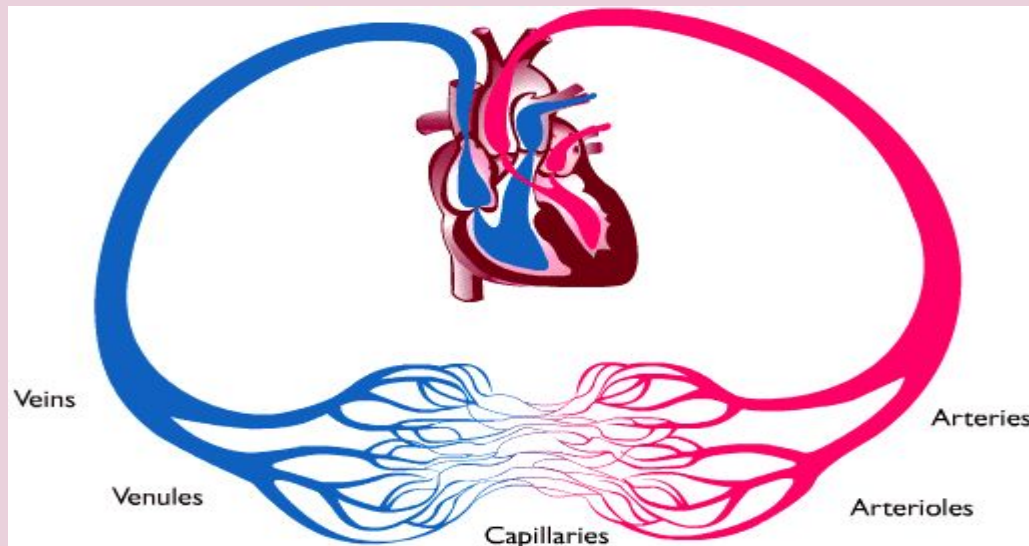


# Blood

- A *connective tissue* composed of liquid extracellular matrix called blood plasma that dissolves and suspends various cells (Erythrocytes, Leukocytes) and cell fragments (Platelets)
- Interstitial fluid is the fluid that bathes the body cells and is constantly renewed by the blood.
- Blood transports oxygen from the lungs and nutrients from the gastrointestinal tract, which diffuse from the blood into the interstitial fluid and then into the body cells. Carbon dioxide and other wastes move in the reverse direction, from body cells to interstitial fluid to blood. Blood then transports the wastes to various organs-the lungs, kidneys, and skin-for elimination from the body.

# Blood Continued

- The colour of blood varies with its oxygen content. When it has high oxygen content it is bright red. When it has low oxygen content it is dark red. Blood is approximately 8% of the total body mass, and totals between 4-6 litres.



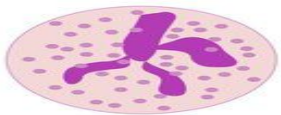
# Functions of the Blood

- Blood has 3 functions:
- 1. Transportation-oxygen, nutrients, heat, waste products
- 2. Regulation-pH, body temperature, and the water content of cells
- 3. Protection-clotting after injury, white blood cells (WBC) through phagocytosis, antibodies, interferons, and complement protect against disease
- <https://youtu.be/UlvU-OuZHww>

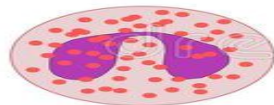
# Components of Blood

- Blood has two components: about 55% blood plasma and about 45% formed elements.
  - Plasma is a straw-coloured watery liquid extracellular matrix that contains 91.5% water and 8.5% solutes, most of which are plasma proteins.
  - Formed Elements are cells and cell fragments. More than 99% are red blood cells (RBCs), and less than 1% are platelets and white blood cells (WBCs)

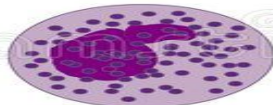
## White blood cells



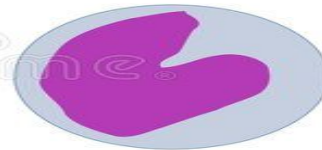
neutrophil



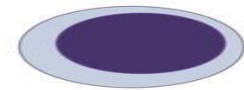
eosinophil



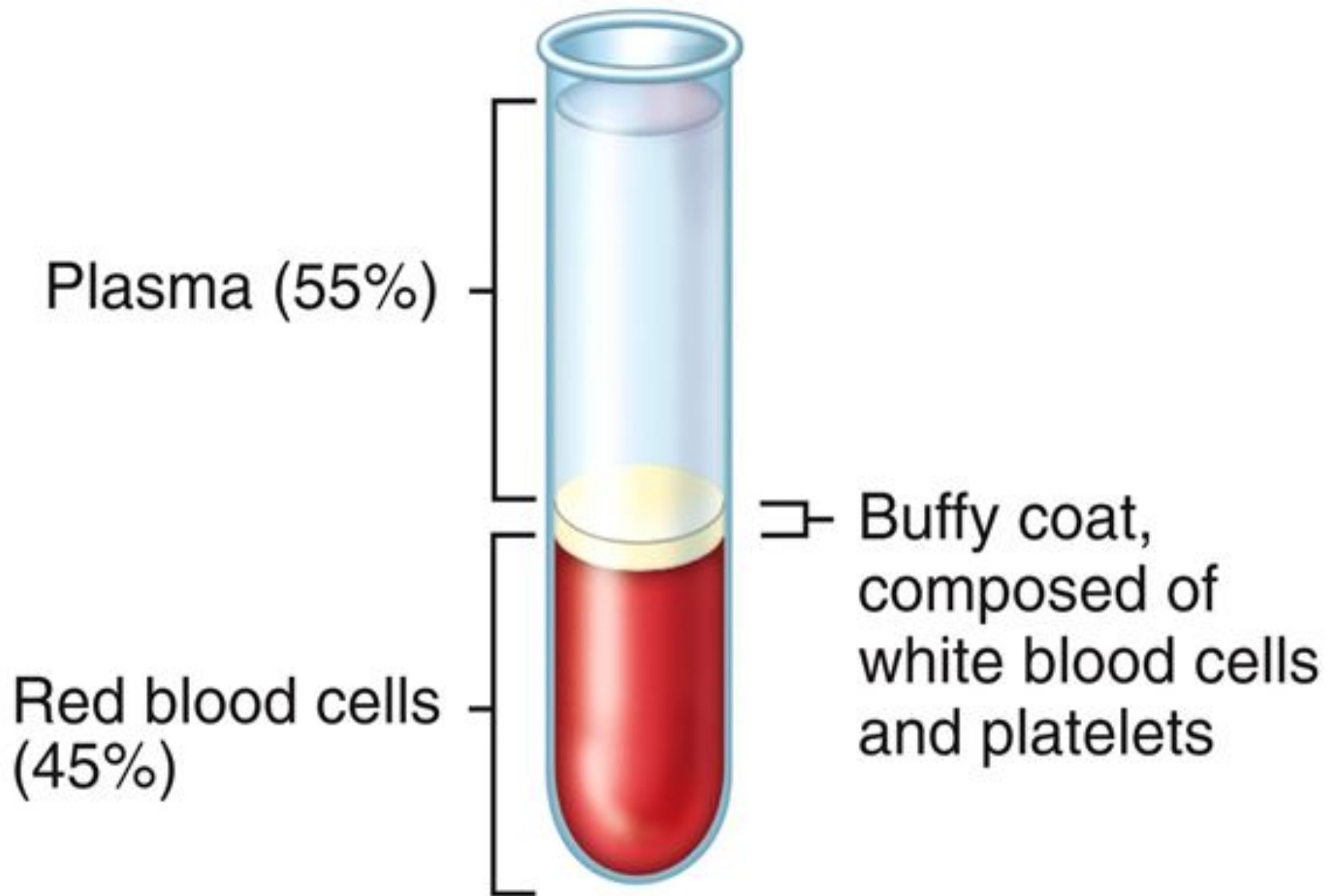
basophil



monocyte



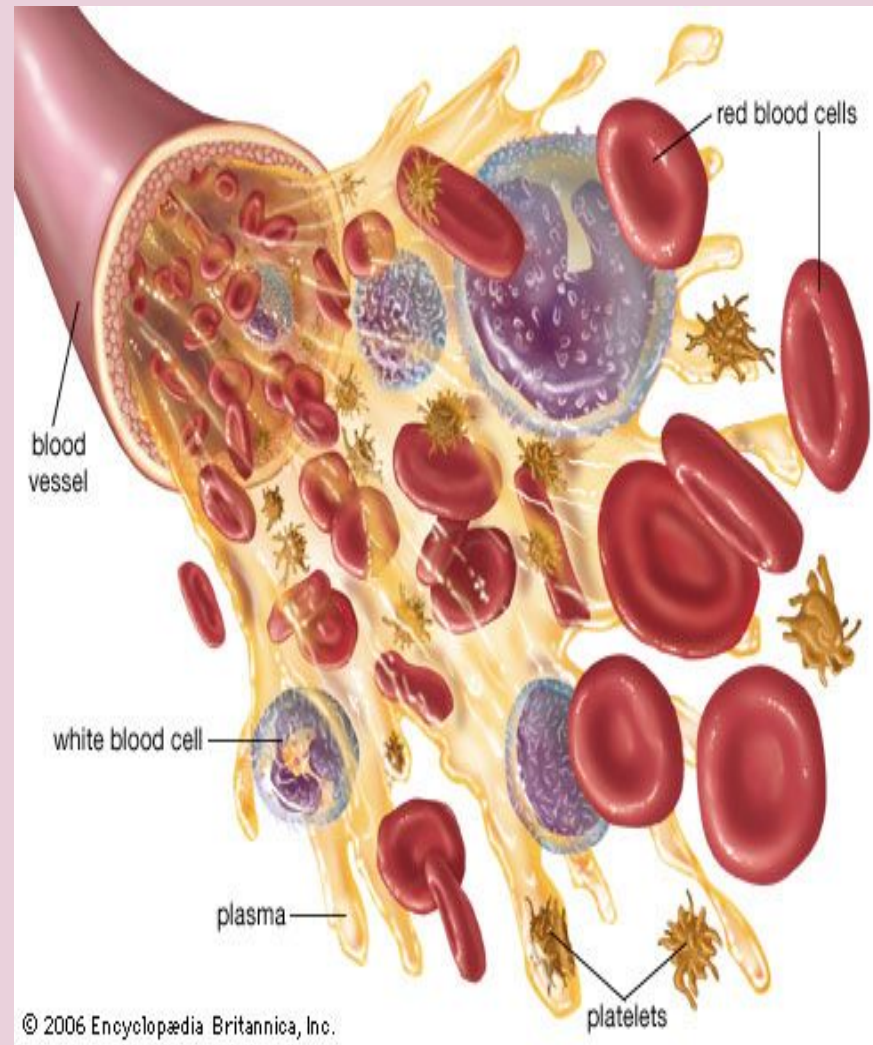
lymphocyte



(a) Appearance of centrifuged blood

# Functions of Plasma

- Carries the cells that transport gases
- Aids in body defenses
- Prevents blood loss



# Plasma Proteins

- Some of the proteins in blood plasma are found elsewhere in the body, but those confined to blood are called Blood proteins
- Hepatocytes synthesize most of the plasma proteins.
- Plasma proteins include
  - **Albumins**
  - **Globulins**
  - **Fibrinogen**
- Other solutes include electrolytes, nutrients, regulatory substances (enzymes, hormones), gases, waste products (urea, uric acid, creatinine, ammonia & bilirubin)

<https://youtu.be/stmYYdpdV-E>

# Continued

## ● Albumin

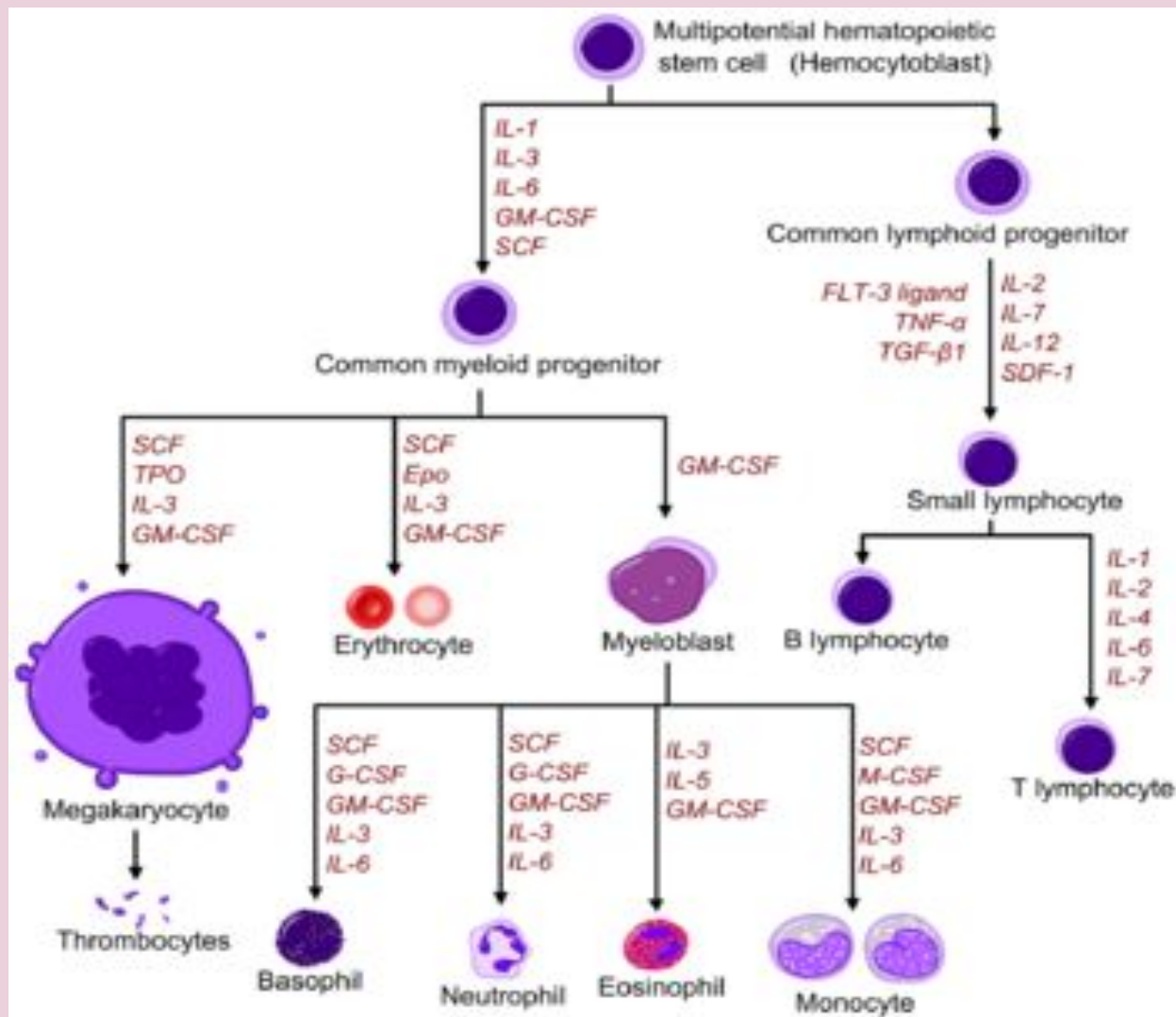
- Comprises approximately 54% of the plasma proteins
- Contributes to plasma osmotic pressure and the maintenance of blood volume
- Serves as a carrier for certain substances

## ● Globulins

- Comprise approximately 38% of plasma proteins
- Alpha globulins transport bilirubin and steroids.
- Beta globulins transport iron and copper.
- Gamma globulins constitute the antibodies (immunoglobulins) of the immune system.

## ● Fibrinogen

- Make up approximately 7% of the plasma proteins
- Converted to fibrin in the clotting process



HEMATOPOIESIS/HEMOPOIESIS

[HTTPS://YOUTU.BE/CM8IK24RRVA](https://youtu.be/cm8ik24rrva)

# Hematopoiesis

- The process by which the formed elements of blood develop is called **Hematopoiesis**.
- Before birth, hematopoiesis occurs in the *spleen & liver*.
- After birth & throughout life, *Red bone marrow* is the source of blood cells.
- Red bone marrow is a highly vascularized connective tissue located in the microscopic spaces between trabeculae of spongy bone tissue. It is chiefly found in the *axial skeleton, pectoral, and pelvic girdles*, and the proximal epiphyses of the humerus and femur. Once blood cells are produced they enter the bloodstream through sinusoids (sinuses)-enlarged and leaky capillaries that surround red bone marrow cells and fibers.

# Continued

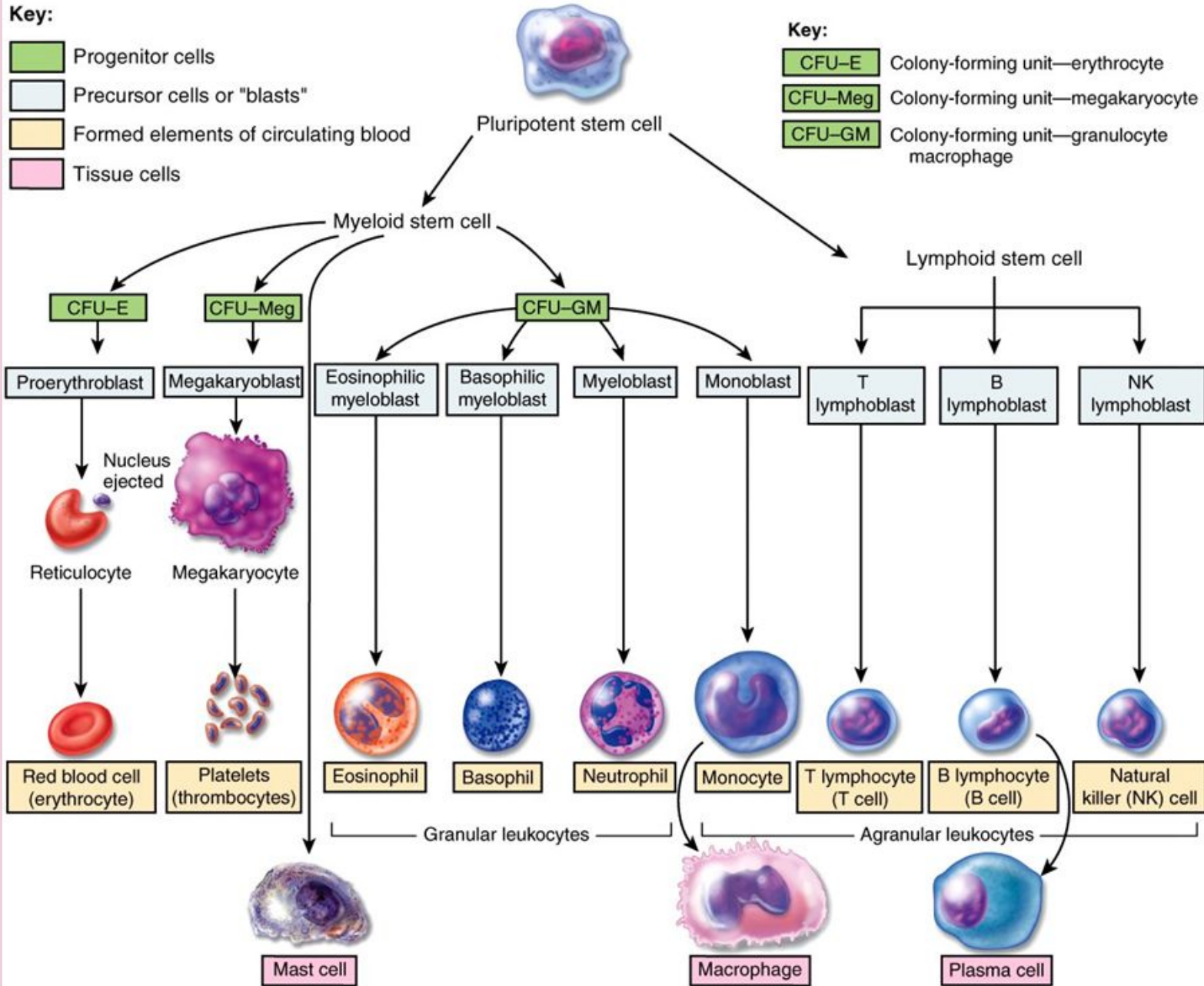
- Blood cells originate from pluripotent stem cells in the bone marrow
- The proliferation, differentiation, and functional abilities of the various blood cells are controlled by ***cytokines***
- Cytokines are hormone-like growth factors
- Hematopoietic Growth Factors
  - Increase peripheral stem cells for transplantation
  - Accelerate cell proliferation after bone marrow engraftment
- <https://youtu.be/0deCbmh7PHs>

**Key:**

- Progenitor cells
- Precursor cells or "blasts"
- Formed elements of circulating blood
- Tissue cells

**Key:**

- CFU-E Colony-forming unit—erythrocyte
- CFU-Meg Colony-forming unit—megakaryocyte
- CFU-GM Colony-forming unit—granulocyte macrophage



# Red Blood Cells

- RBCs contain the oxygen carrying protein **hemoglobin**, which is a pigment that gives whole blood its red colour. To maintain normal numbers of RBCs, new mature cells must enter the circulation at the astonishing rate of at least **2 million per second**, a pace that balances the equally high rate of RBC destruction
- RBCs are biconcave discs without nuclei that contain hemoglobin . Their plasma membrane is both strong and flexible, which allows them to deform without rupturing as they squeeze through narrow capillaries. RBCs lack of a nucleus means it can neither reproduce nor carry on extensive metabolic activities.
- The cytosol of RBCs contains hemoglobin molecules; these important molecules are synthesized before loss of the nucleus during RBC production and constitute about 33% of the cell's weight.



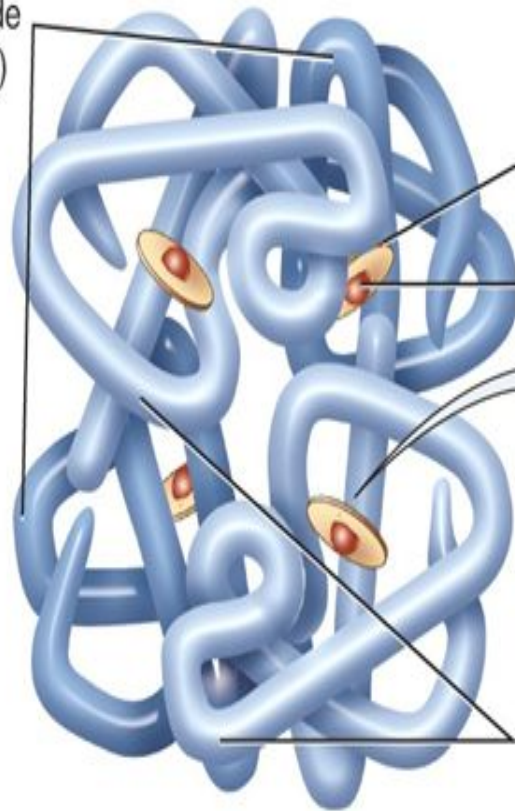
Surface view



Sectioned view

(a) RBC shape

Beta polypeptide chains (globins)

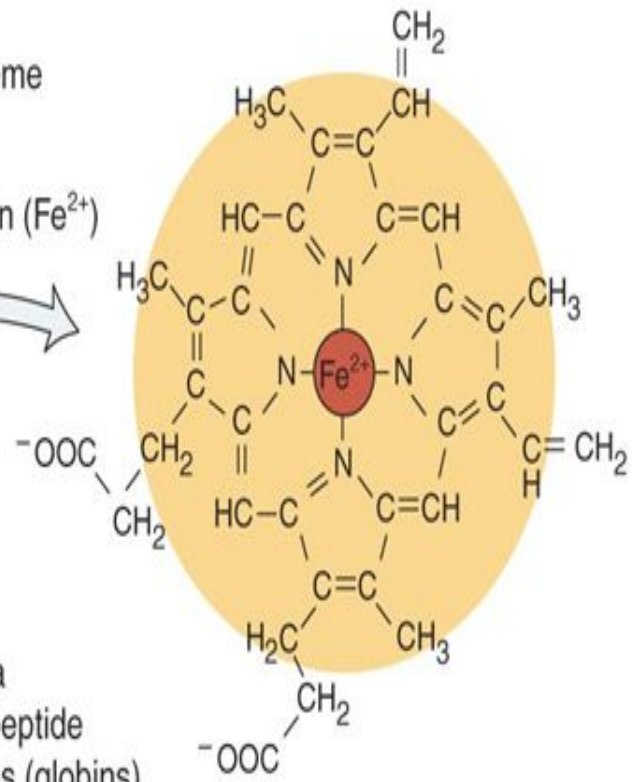


Heme

Iron ( $\text{Fe}^{2+}$ )

Alpha polypeptide chains (globins)

(b) Hemoglobin molecule



(c) Iron-containing heme

# RBC Physiology

- specialized for their oxygen transportation function because they have **no nucleus**, all their internal space is available for oxygen transport
- **lack mitochondria** so they cannot generate ATP aerobically, they do not use up any of the oxygen they transport. (they create ATP through glycolysis only)
- Contains 280 million hemoglobin molecules.
- A hemoglobin consists of a protein called a globin, composed of 4 polypeptide chains, and a heme, composed of a ringlike non protein pigment. At the center of each heme ring is an iron ion that can combine reversibly with one oxygen molecule, allowing ***each hemoglobin to combine with 4 oxygen molecules***

# Hemoglobin, Nitric Oxide & Blood Pressure

- Hemoglobin also functions in blood pressure regulation.
- The gaseous hormone **nitric oxide (NO)**, produced by endothelial cells that line the blood vessels, binds to hemoglobin. Under some circumstances, hemoglobin releases the NO, which then causes **vasodilation**. Vasodilation improves blood flow and enhances oxygen delivery to cells near the site of the NO release.
- <https://youtu.be/-EnL3bDG5J0>
- FYI- Foods that boost NO: beets, garlic, dark chocolate, leafy green vegetables (lettuce, spinach, spinach), celery, citrus fruits

# RBC Life Cycle

- Red blood cells only live about **120 days**
- Worn out RBCs are removed from circulation and destroyed by fixed phagocytic macrophages in the spleen and liver, and the products are recycled.
  - 1. Phagocytosis of worn out RBCs
  - 2. The globin portion is split from the heme
  - 3. Globin is broken down into amino acids, which can be reused for protein synthesis
  - 4. The iron in the heme portion travels to the liver where it is stored as ***Ferritin***. The rest of the heme molecule becomes a component of bile which is produced in the liver.

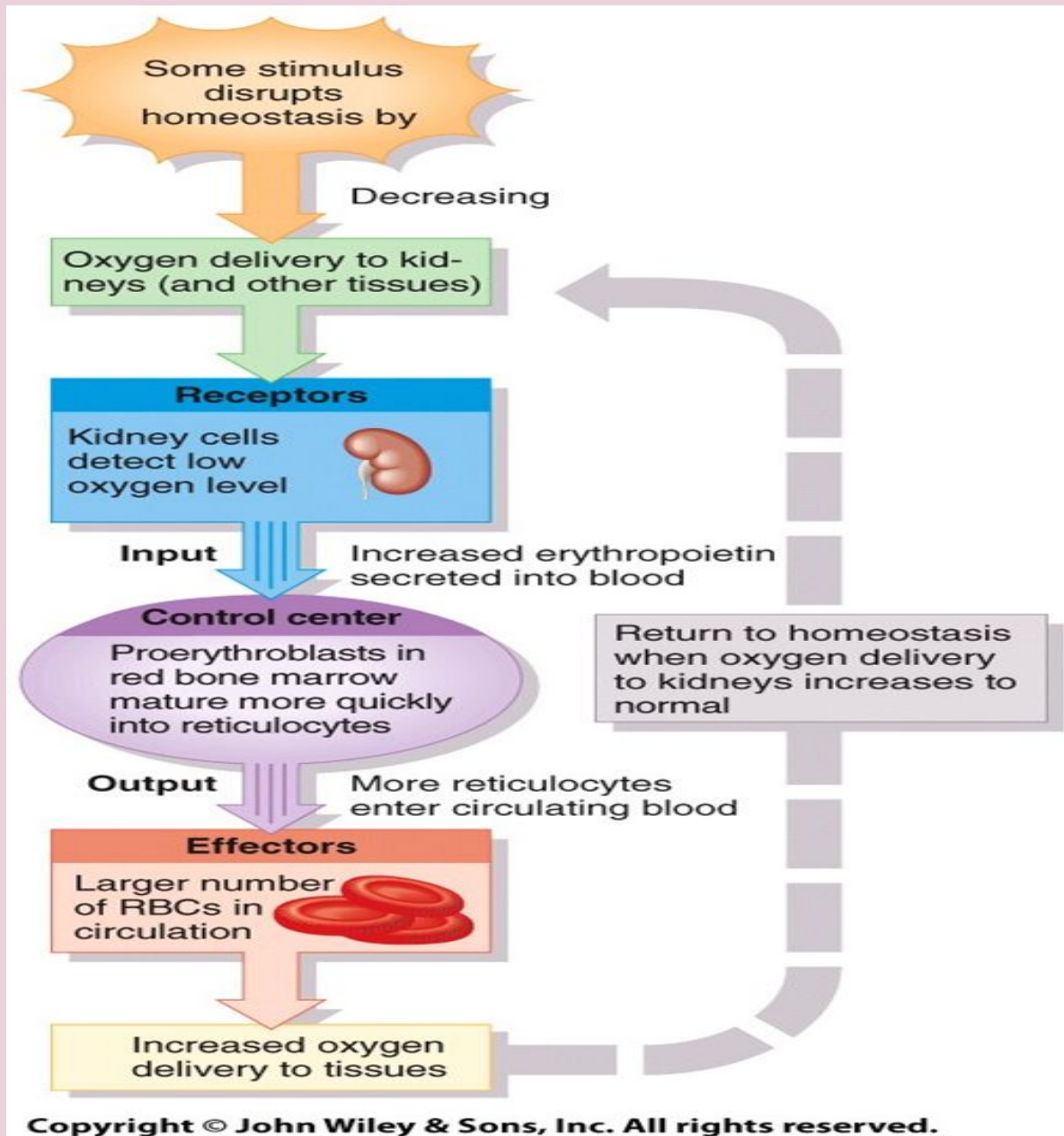
# Iron Overload

- Under normal conditions plasma contains almost no free iron. Iron should be bound to hemoglobin in the RBCs or stored in the liver as ferritin.
- If the amount of iron present in the body builds up, iron overload results which causes diseases of the liver, heart, pancreatic islets, and gonads. Iron overload also permits iron dependent microbes to flourish. Such microbes are normally not pathogenic, but they multiply rapidly and can cause lethal effects in a short time when free iron is present.
- **Primary Iron Overload** - Genetic inheritance, most commonly Hereditary Hemochromatosis
- **Secondary Iron Overload** - Excessive intake of Iron, transfusion, hemolysis
- Iron overload is more likely to occur in men because female menses is protective against iron buildup.
- Treatment is primarily blood donation.



# Erythropoiesis: Production of RBCs

- Erythrocyte formation, called erythropoiesis, occurs in adult red bone marrow of certain bones. Ultimately a cell near the end of the development sequence ejects its nucleus and becomes a reticulocyte. Loss of the nucleus causes the center of the cell to indent, producing the RBCs distinctive biconcave shape. Reticulocytes mature into RBCs within 1 to 2 days after their release from red bone marrow.
- Normally creation and destruction of RBCs proceed at roughly the same pace. If the oxygen carrying capacity of the blood falls because erythropoiesis is not keeping up with RBC destruction, a negative feedback system steps up RBC production
- [.https://youtu.be/8cCgBp8DAb8](https://youtu.be/8cCgBp8DAb8)

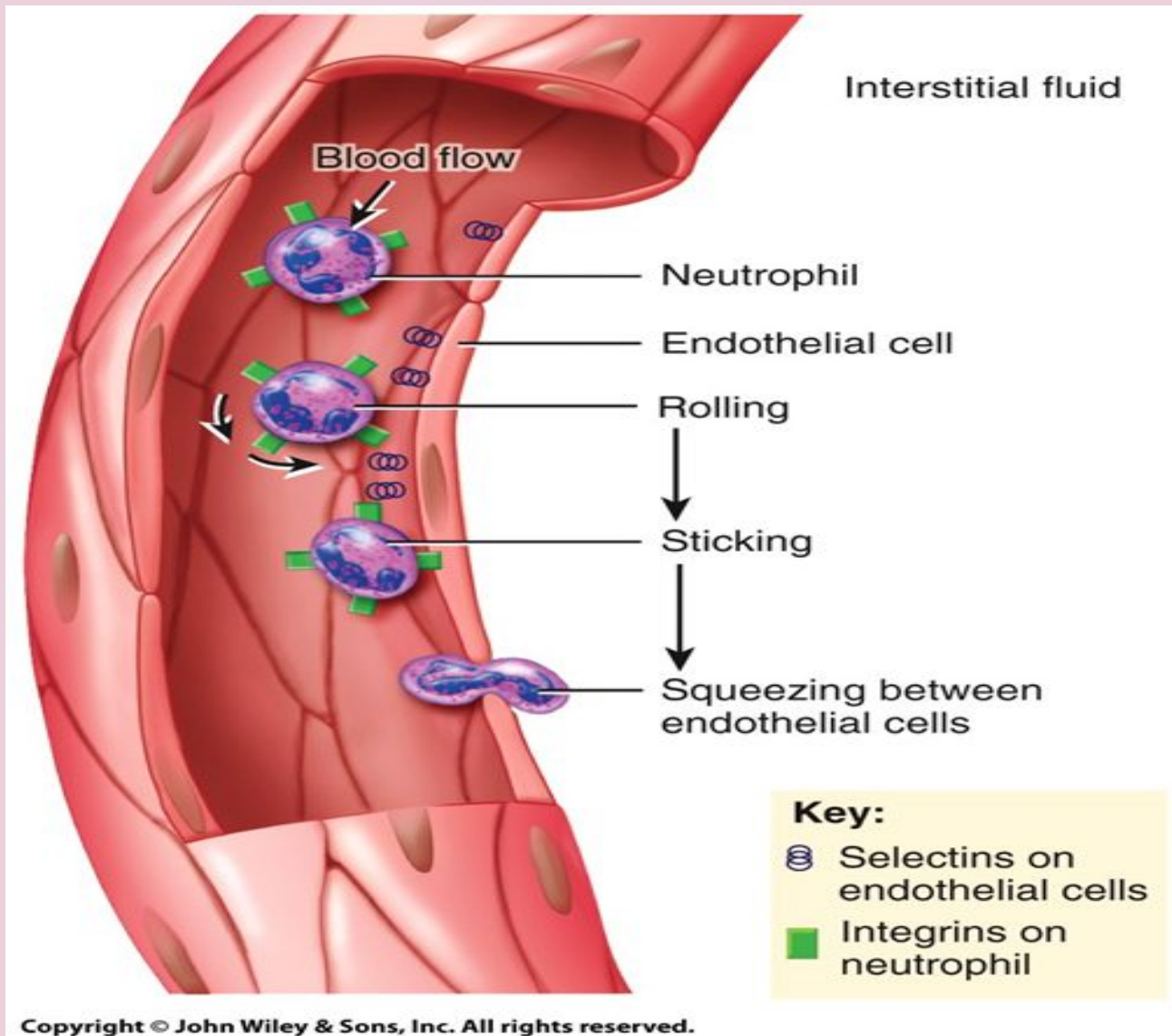


# Leukocytes (White Blood Cells)

- Leukocytes (white blood cells or WBCs) are **nucleated** cells and do not contain hemoglobin.
- These cells are classified as either **granular** (neutrophils, eosinophils, basophils) or **agranular** (lymphocytes and monocytes), based on the straining of the granules under the microscope.
- **Agranular leukocytes** do not have cytoplasmic granules and include the *lymphocytes* and *monocytes*, which differentiate into *macrophages* (fixed and wandering). Leukocytes have surface proteins, as do erythrocytes. They are called major histocompatibility antigens (MHC), are unique for each person (except for identical siblings), and can be used to identify a tissue.

# Functions of White Blood Cells

- White blood cells can live for several months or years but **usually live for only a few hours or a few days.**
- Normal blood contains 5,000-10,000 leukocytes/mm<sup>3</sup>, they are **outnumbered by RBCs about 700:1.**
- **Leukocytosis** refers to an increase in the number of WBCs.
- **Leukopenia** refers to an abnormally low number of WBCs.
  
- *The general function of leukocytes is to combat inflammation and infection.*
- Once pathogens enter the body, WBCs leave the bloodstream by the process of *diapedesis*, and collect at the site of invasion.
- Some WBCs, particularly neutrophils and macrophages, are active in phagocytosis and can ingest bacteria and dispose of dead matter. The chemical attraction of WBCs to a disease or injury site is termed *chemotaxis*.



## Diapedesis

# Continued

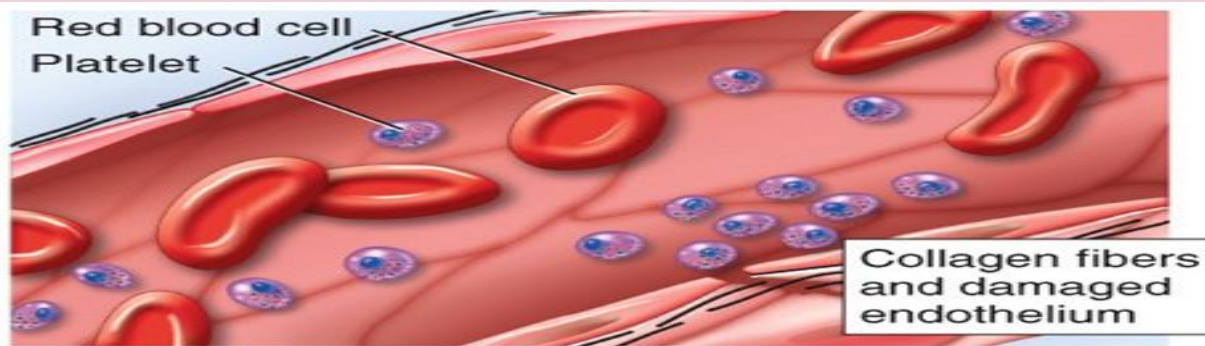
- Different WBCs combat inflammation and infection in different ways:
- **A) Granular Leukocytes**
- 1. **Neutrophils** do so through *phagocytosis*.
- 2. **Eosinophils** combat the effects of histamine in allergic reactions, phagocytize antigen-antibody complexes, and combat *parasitic worms*.
- 3. **Basophils** develop into *mast cells* that liberate heparin, histamine, and serotonin in *allergic reactions* that intensify the inflammatory response e.g allergic and hypersensitivity reactions.
- **B) Agranular Leukocytes**
- 4. **B lymphocytes**, in response to the presence of foreign substances called antigens, differentiate into tissue *plasma cells* that *produce antibodies*.
- 5. **T lymphocytes** *destroy foreign invaders directly*.
- 6. **Monocytes** – *Phagocytic action*
- <https://youtu.be/p5Ovu2uBYvc>

# Platelets

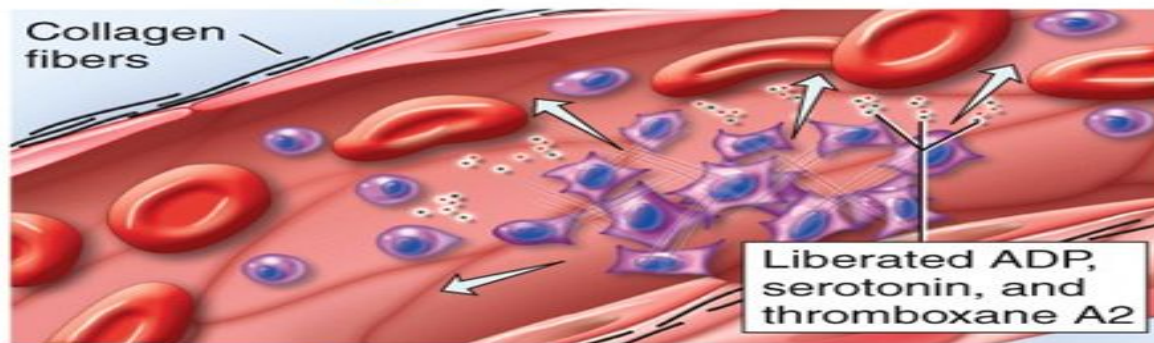
- Besides the immature cells that develop into RBCs and WBCs, hematopoietic stem cells also differentiate into cells called **megakaryocytes** that produce platelets by breaking apart.
- Normal blood contains 250,000 to 400,000 platelets/mm<sup>3</sup>.
- Platelets have a **lifespan of 5 to 9 days**;
- Aged and dead platelets are removed by fixed macrophages in the spleen and liver.
  
- Platelets help stop blood loss from damaged vessels by forming a *platelet plug*. Their granules also contain chemicals that promote blood clotting.
- <https://youtu.be/gZnjCT17bHM>

# Hemostasis

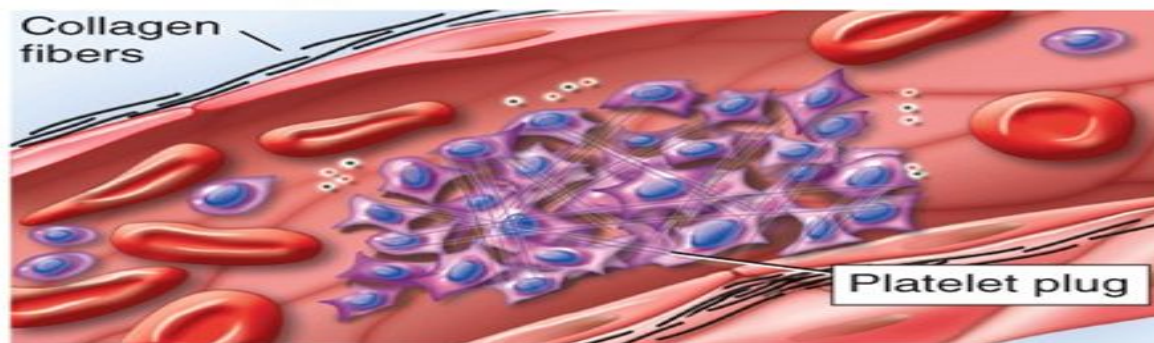
- **Hemostasis refers to the stoppage of bleeding.** When blood vessels are damaged or ruptured, the hemostatic response must be quick, localized to the region of damage, and carefully controlled. When successful, hemostasis prevents hemorrhage.
- Hemostasis (a sequence of responses that stops bleeding), requires: ***platelets, calcium, vitamin K and Clotting factors.***
- Three mechanisms reduce blood loss:
  - 1) **vascular spasm** -the smooth muscle of a blood vessel wall contracts to stop bleeding.
  - 2) **platelet plug formation**-clumping of platelets around the damage to stop the bleeding.
  - 3) **blood coagulation (clotting)**



**1** Platelet adhesion



**2** Platelet release reaction



**3** Platelet aggregation

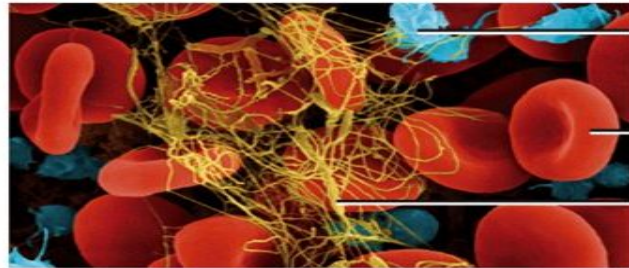
# Clotting

- A clot is a gel consisting of a network of insoluble protein fibers (fibrin) in which formed elements of blood are trapped .The chemicals involved in clotting are known as ***coagulation (clotting) factors***; most are in blood plasma, some are released by platelets, and one is released from damaged tissue cells. Blood clotting involves a complex cascade of reactions that may be divided into three stages:

1) **formation of prothrombinase (prothrombin activator)**

2) **conversion of prothrombin into *thrombin***

3) ***conversion of soluble fibrinogen into insoluble fibrin.***



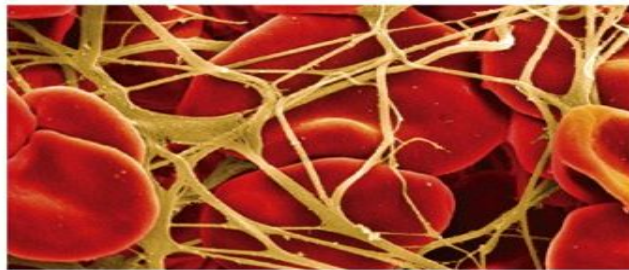
Platelet

Red blood cell

Fibrin threads

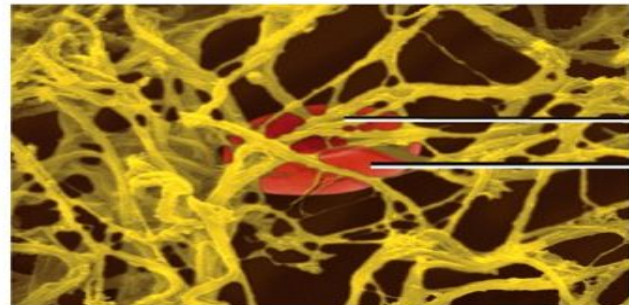
**SEM** 1,445x

(a) Early stage



**SEM** 900x

(b) Intermediate stage



Fibrin threads

Red blood cell

**SEM** 3400x

(c) Late stage showing red blood cells trapped in fibrin threads

(a, c) Dennis Kunkel Microscopy, Inc./Phototake; (b) Steve Gschmeissner/Photo Researchers, Inc.

# Clotting Pathway

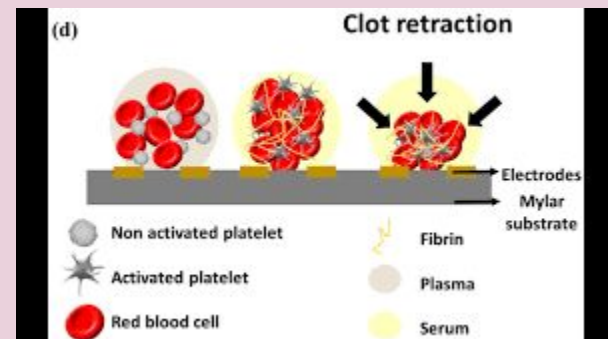
- Either the **extrinsic pathway** or the **intrinsic pathway** can initiate the clotting cascade.
- Extrinsic or primary hemostasis begins with the release of *Tissue factor* from *external trauma*
  - Intrinsic or secondary hemostasis begins with exposure of *collagen & von Willebrand factor* from the *damaged lining of a blood vessel*.

**Both types of hemostasis still require platelets, Vitamin K, Calcium & clotting factors.**



# Clotting Retraction/Healing

- Clot retraction is a consolidation or tightening of the fibrin clot. The fibrin threads attached to the damaged surfaces of the blood vessels gradually contract as platelets pull on them. As the clot retracts it pulls the edges of the damaged vessel closer together, decreasing the risk of further damage.
- During contraction some serum can escape between the fibrin threads, but the formed elements in blood cannot.
- In time, fibroblasts form connective tissue in the ruptured area, and new endothelial cells repair the vessel lining.
- <https://youtu.be/DKFSH5MMPLM>



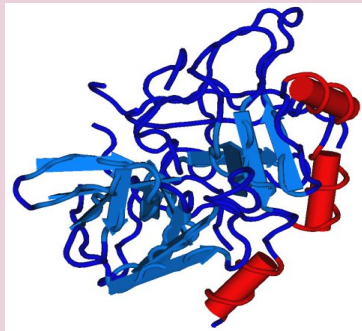
Normal coagulation requires **vitamin K**. It is required for the synthesis of *4 of the clotting factors*. Normally produced by bacteria that inhabit the large intestine, vitamin K is a *fat-soluble vitamin* that can be absorbed through the lining of the intestine and into the blood if absorption of lipids is normal.

Many times a day little clots start to form, often at a site of minor roughness or at a developing atherosclerotic plaque inside a blood vessel. The **fibrinolytic system** dissolves small, inappropriate clots and clots at a site of damage once the damage is repaired.

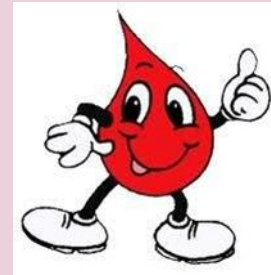
**Plasmin** (fibrinolysin) can *dissolve a clot* by digesting fibrin threads and inactivating substances such as fibrinogen, prothrombin, and factors V, VIII, and XII.

# Homeostatic Control Mechanisms in Clotting









- Clots are *generally localized* due to fibrin absorbing thrombin into the clot, clotting factors diffusing through blood, and the production of prostacyclin, a powerful inhibitor of platelet adhesion and release.
- Substances that ***inhibit coagulation, called anticoagulants***, are also present in blood. An example is *heparin*.
- Patients who are at increased risk of forming blood clots may receive an anticoagulant drug such as heparin or warfarin



# Continued



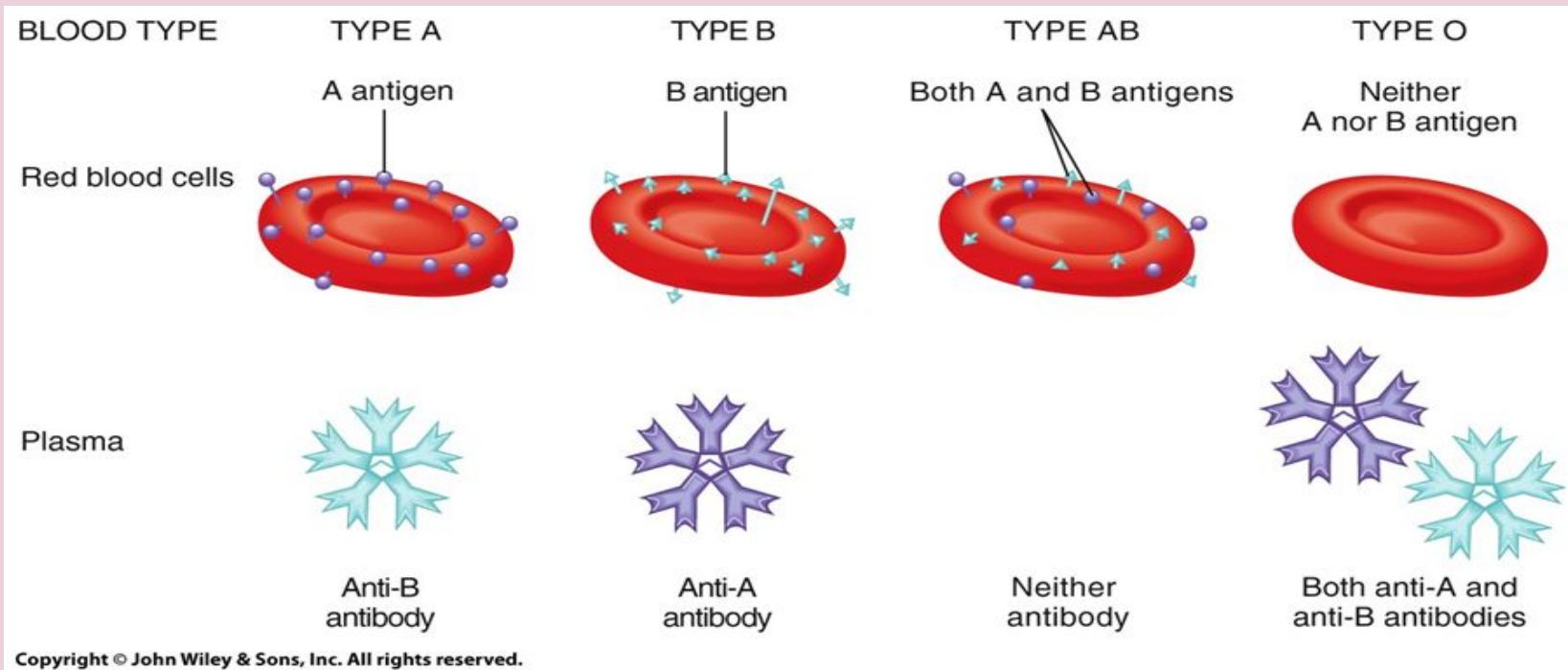
- Despite the *anticoagulating* and *fibrinolytic* mechanisms, blood clots sometimes form within the cardiovascular system. Clotting in an unbroken blood vessel is called **thrombosis**.
- A thrombus (clot), bubble of air, fat from broken bones, or piece of debris transported by the bloodstream that moves from its site of origin is called an **embolus**.
- If the embolus blocks the blood supply to an organ or area of tissue, it is called an **embolism**. Eg a pulmonary embolism is a blockage in the circulation of the lungs.
- 
- At low doses aspirin inhibits vasoconstriction and platelet aggregation thereby reducing the chance of thrombus formation. Thrombolytic agents are injected into the body to dissolve clots that have already formed. <https://youtu.be/gExUCrpAKyQ>

<p><b>O-</b></p> 	<p><b>A-</b></p> 	<p><b>B-</b></p> 	<p><b>AB-</b></p> 
<p><b>O+</b></p> 	<p><b>A+</b></p> 	<p><b>B+</b></p> 	<p><b>AB+</b></p> 

# BLOOD GROUPS AND TYPES

# Blood Groups and Types

- <https://youtu.be/ttjn1jVACk8>
- The *surfaces of red blood cells* contain genetically determined blood group *antigens*, called agglutinogens.
- Blood is categorized into different blood groups based on the presence or absence of various antigens.
- Within a blood group there may be two or more different blood types. Major blood groups are the **ABO and Rh groups**. Other blood groups include the Lewis, Kell, Kidd, and Duffy systems.
- **ABO Group**
  - In the ABO system, agglutinogens (antigens) A and B determine blood types.
  - Plasma contains agglutinins (antibodies), designated as A and B, that react with agglutinogens that are foreign to the individual.

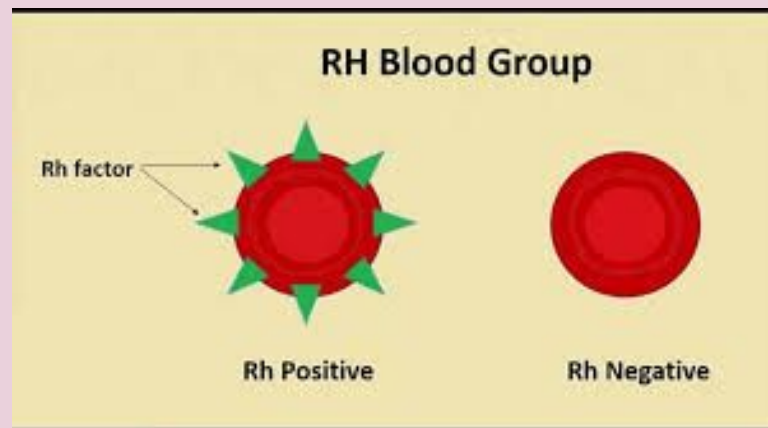


**Type AB individuals are “universal recipients”** because they have neither anti-A nor anti-B antibodies in their serum that would destroy transfused RBCs.

**Type O individuals are “universal donors”** because their RBCs have no antigens on the cell surface that can potentially react with the recipient's serum.

# RH Blood Group

- In the Rh system, individuals whose *erythrocytes have Rh proteins are classified as Rh+*. Those who lack the protein are Rh-.
- *Normally, blood plasma does not contain anti-Rh antibodies;* individuals whose RBCs have the Rh antigen are said to be Rh+ while those who lack the Rh antigen are Rh-



# Rh Continued

- Rh incompatibility can cause problems with any blood transfusion, so it is screened just as carefully as the ABO group.
- biggest problem with Rh incompatibility, however, involves mother and child in pregnancy.
- **If blood from an Rh+ fetus sensitizes an Rh- mother during birth, anti-Rh antibodies will form in the blood of that woman.**
- During her next pregnancy those antibodies can cross the placenta to affect the next baby.
- Hemolytic disease of the newborn (HDN) results when an Rh+ fetus develops in the womb of an Rh- woman, To prevent HDN, mothers who are Rh- are given an injection of RhoGAM - a commercially produced anti-Rh antibody - at 28 weeks pregnancy or within 72 hours of birth.

# BLOOD TESTING

- **Obtaining Blood Specimens**

- Skin puncture (capillary blood)
- Venipuncture
- Arterial puncture
- Bone marrow aspiration

- **Diagnostic Tests**

- Blood count – CBC measures # of RBCs, diff. Leukocytes, and platelets. Also includes RBC indices & hemoglobin also included.
- **Erythrocyte sedimentation rate**- + inflammation = + cytokines= + rate of fall of RBCs in 1 hour = high ESR. Normal is < 15 (men) or 20 (women)
- Bone marrow aspiration and biopsy- For very sick people – investigate possible cancers, unexplained anemia, genetic disorders.
- Aspiration examines fluid component & cell morphology. Biopsy removes a solid chunk of innermost bone for microscopic examination.

# Transfusions

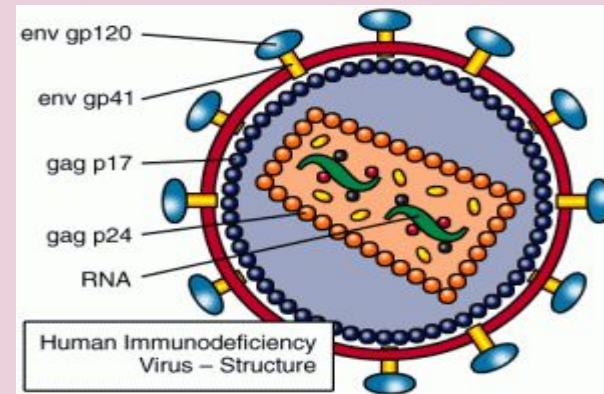
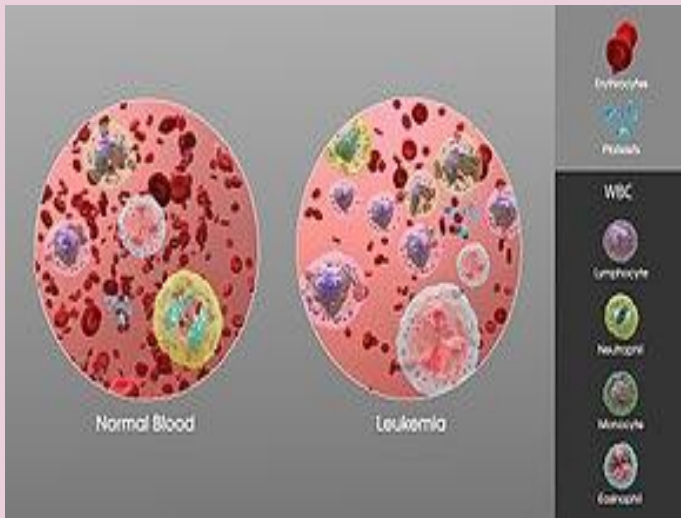
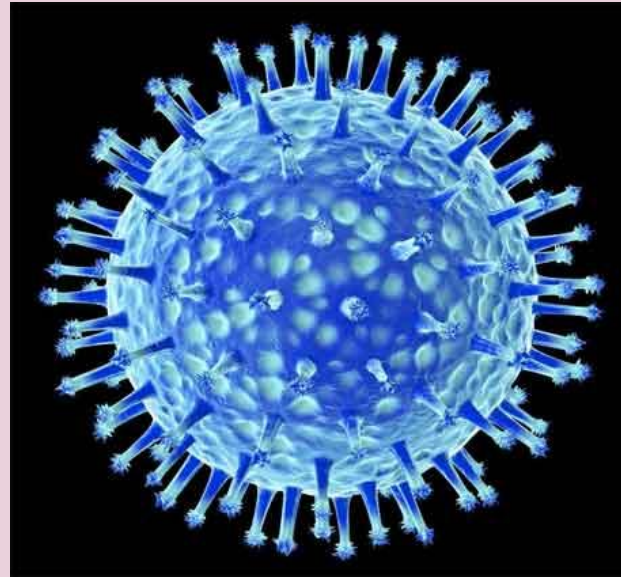
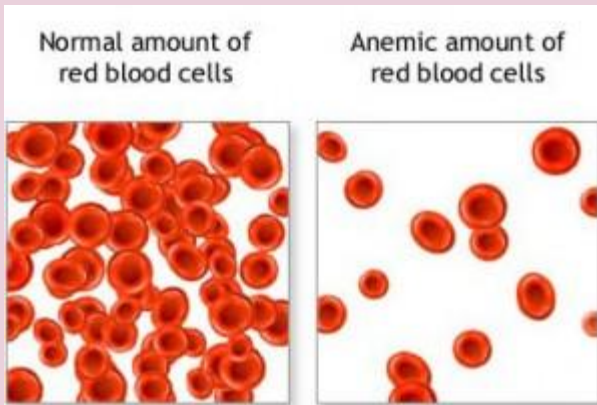
- Blood transfusion is the process of transferring blood or blood products from one person to another. Donated blood can be separated into its various components to make better use of it.
- History of transfusions: <https://youtu.be/qcZKbjYyOfE>

## Types of Transfusions:

- Whole blood - most common
- Red blood cells - for anemia
- Platelet - for thrombocytopenia
- Plasma - used for severe burns, infections and liver failure
- Leukocyte-reduced blood cells - most blood products have the WBCs filtered out to reduce adverse immune reactions
- Frozen red blood cells - used to increase the storage time for rare types of RBCs
- Immunoglobulins- Gamma globulin(aka antibody) transfusions to help support the immune system

# Transfusion Reactions

- In a blood transfusion, if the recipient receives the wrong blood type, antigen-antibody reactions will cause a rapid destruction (hemolysis) of the donor red blood cells
- Giving the wrong type blood can cause the patient to develop a fever, develop serious renal failure, or go into shock.
- Signs and Symptoms of Transfusion Reactions:
  - Sensation of heat along the vein where the blood is being infused
  - Flushing of the face
  - Urticaria, headache, pain in the lumbar area
  - Chills, fever, constricting pain in the chest
  - Cramping pain in the abdomen
  - Nausea, vomiting
  - Tachycardia, hypotension, and dyspnea



# DISORDERS OF THE BLOOD

# Conditions that increase Coagulability

- **Genetic Conditions**

- - Factor V Leiden <https://youtu.be/25SZBFTEPoQ>

## **Acquired Hypercoagulability**

- Long Periods of Inactivity- bed rest, extended travel
- Older Age
- Cancers
- Cancer treatments
- Drugs that help increase red blood cells such as Epoetin
- Long term IV Catheter or port use
- Congestive Heart Failure
- Atrial Fibrillation
- Diabetes
- HIV
- Vasculitis

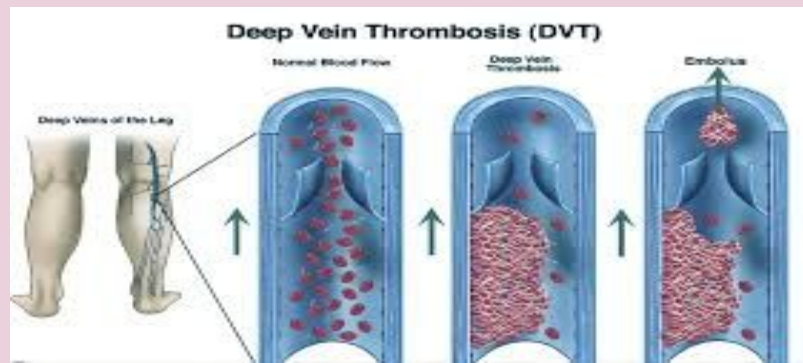
# Conditions that cause temporarily Accelerated Coagulation

- Smoking
- Obesity
- Pregnancy
- Use of oral contraceptives
- Post-surgical state
- Dehydration

## DVT - Deep Vein Thrombosis

RED FLAG SIGNS & SYMPTOMS - Unilateral Pain, Swelling

- <https://youtu.be/SqR8EIVOMQE>



# Coagulation and Vitamin K

- Vitamin K is an essential cofactor for synthesis of clotting factors.
  - It is *Fat-soluble vitamin synthesized by intestinal bacteria*
  - In vitamin K *deficiency*, the liver produces inactive clotting factor, resulting in *abnormal bleeding*.



# Disorders of Bleeding - less Coagulability

- **Thrombocytopenia**

- Decrease in the number of circulating platelets

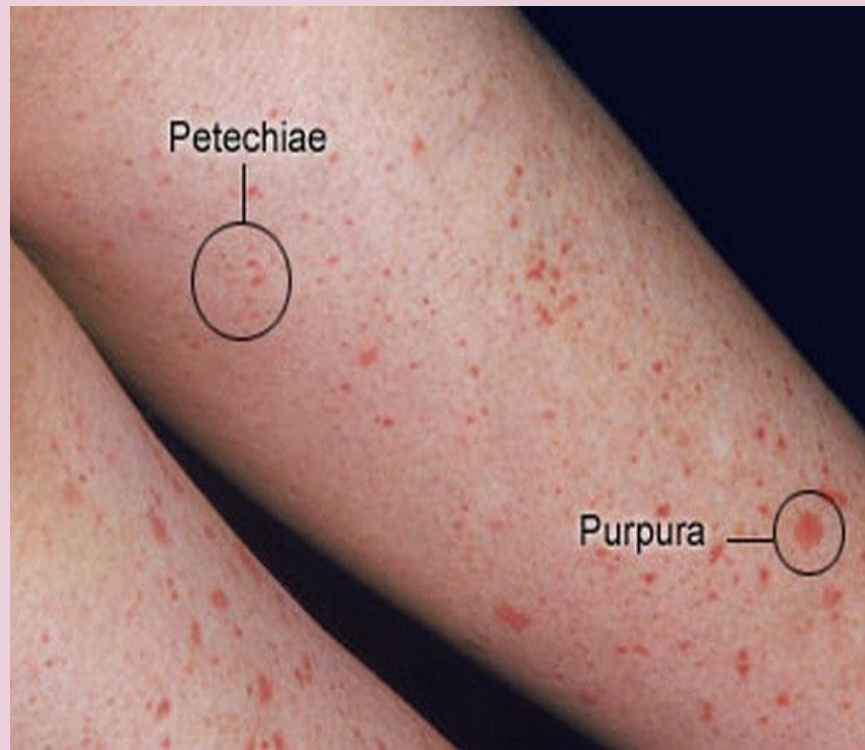
- Depletion of platelets must be relatively severe before hemorrhagic tendencies of spontaneous bleeding occur.

- Impaired platelet function

- Bleeding resulting from platelet deficiency commonly occurs in small vessels and is characterized by petechiae and purpura.

- **petechiae** - red or purple spot on the skin, caused by a minor bleed from broken capillary blood vessels. *<4 mm in diameter*

- **Purpura** - is a condition of red or purple discolored spots on the skin that *do not blanch* on applying pressure. The spots are caused by bleeding underneath the skin *> 4mm in diameter*



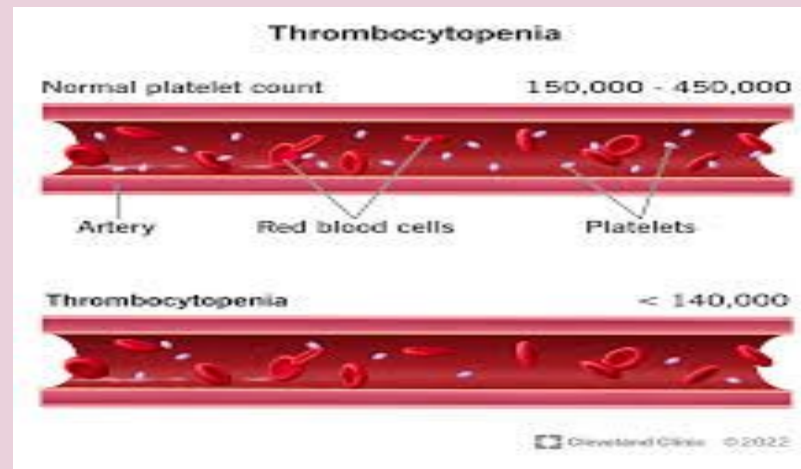
# Platelets Defects - Thrombocytopenia

<https://youtu.be/VLdhfsM5RHc>

Results from: a decrease in platelet production, increased sequestration of platelets in the spleen, or decreased platelet survival

## ● Types:

- *Drug-induced thrombocytopenia*
- *Idiopathic thrombocytopenic purpura*
- *Thrombotic thrombocytopenic purpura*

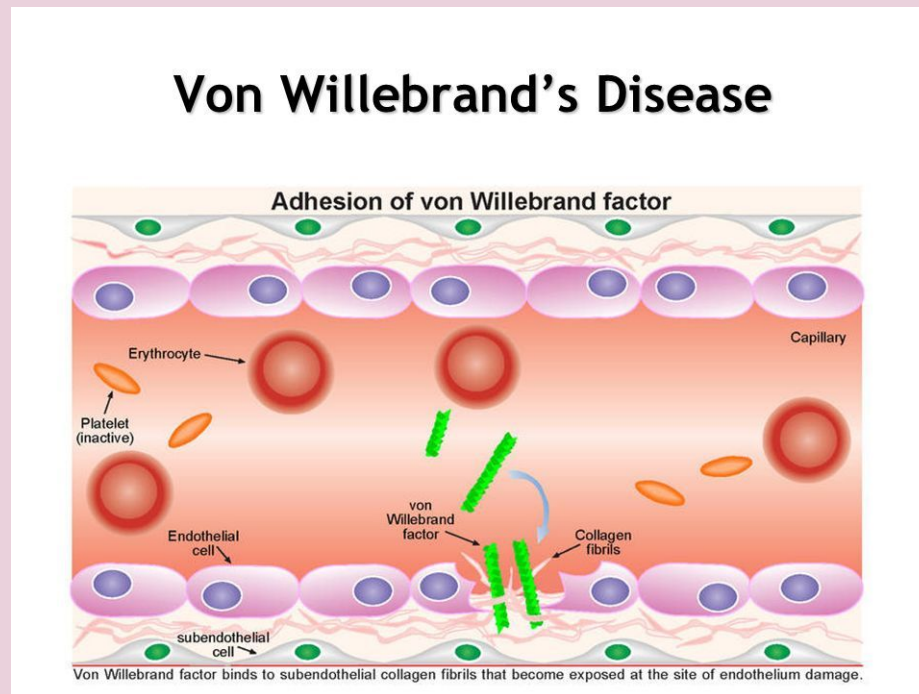


# Coagulation Defects

- Deficiencies can arise because of defective synthesis, or inherited disease.
- Hereditary disorders: <https://youtu.be/BoXBuJSURTI>
- **Hemophilia A**, people with this are at risk for severe bleeding.
  - an *X-linked*, recessive disorder caused by deficiency of functional plasma **clotting factor VIII** (FVIII), which may be inherited or arise from spontaneous mutation. Several members of European royal families were sufferers.
- **Hemophilia B**
  - disorder causing easy bruising and bleeding due to an inherited mutation of the gene for **factor IX**, and resulting in a deficiency of factor IX. It is *less common* than factor VIII deficiency (haemophilia A).

# Coagulation Defects

- **Von Willebrand disease** <https://youtu.be/I-uYvkTVwiM>
  - There are various types of VWD. All the different types are caused by a problem with the von Willebrand factor (VWF). This is a protein in blood which is necessary for proper blood coagulation, or clotting.
  - When there is not enough VWF in the blood, or when it does not work the way it should, the blood takes longer to clot
  -



# Vascular disorders that cause bleeding

- **Hemorrhagic telangiectasia**

- An uncommon autosomal-dominant disorder characterized by thin-walled, dilated capillaries and arterioles

- **Vitamin C deficiency (scurvy)**

- Results in poor collagen synthesis and failure of the endothelial cells to adhere to one another properly, causing a fragile wall

- **Cushing disease**

- Causes protein wasting and loss of vessel tissue support because of excess cortisol

- **Senile purpura (bruising in elderly persons)**

- Caused by the aging process. Collagen becomes less abundant & less organized with advanced age, resulting in stiffer, weaker blood vessel walls

# Polycythemia

- Definition
  - A condition in which the ***red blood cell mass is increased***
- Types
  - **Relative polycythemia:** results from a loss of vascular fluid (ie. dehydration) and is corrected by replacing the fluid
  - **Primary polycythemia(Polycythemia Vera):** a proliferative disease of the bone marrow with an absolute increase in total red blood cell mass accompanied by elevated white cell and platelet counts. Can progress to *myelofibrosis* where scar tissue in bone marrow prevents hematopoiesis.
  - <https://youtu.be/jFxCZ91sDpl?feature=shared>
  - **Secondary polycythemia:** results from *increased erythropoietin* levels caused by *hypoxic* conditions such as chronic heart and lung disease

# Clinical Manifestations

- Variable and related to an increase in RBCs, hemoglobin level, and hematocrit with increased blood volume and viscosity
  - Splenomegaly
  - Depletion of iron
  - Disrupted cardiac output
  - Hypertension
  - Decreased cerebral blood flow
  - Venous stasis
  - Thromboembolism and hemorrhage

# Decreased Red Blood Cells (Anemia)

<https://youtu.be/hJsH9VRjBQk>

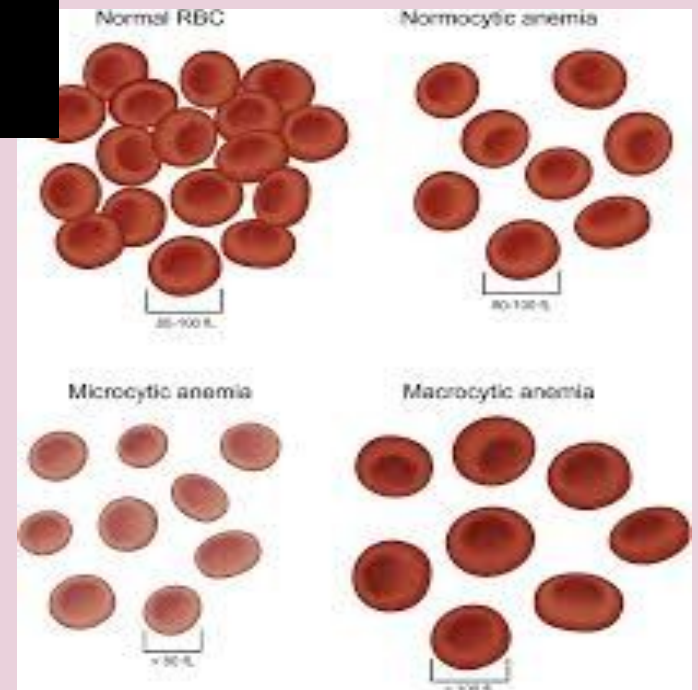
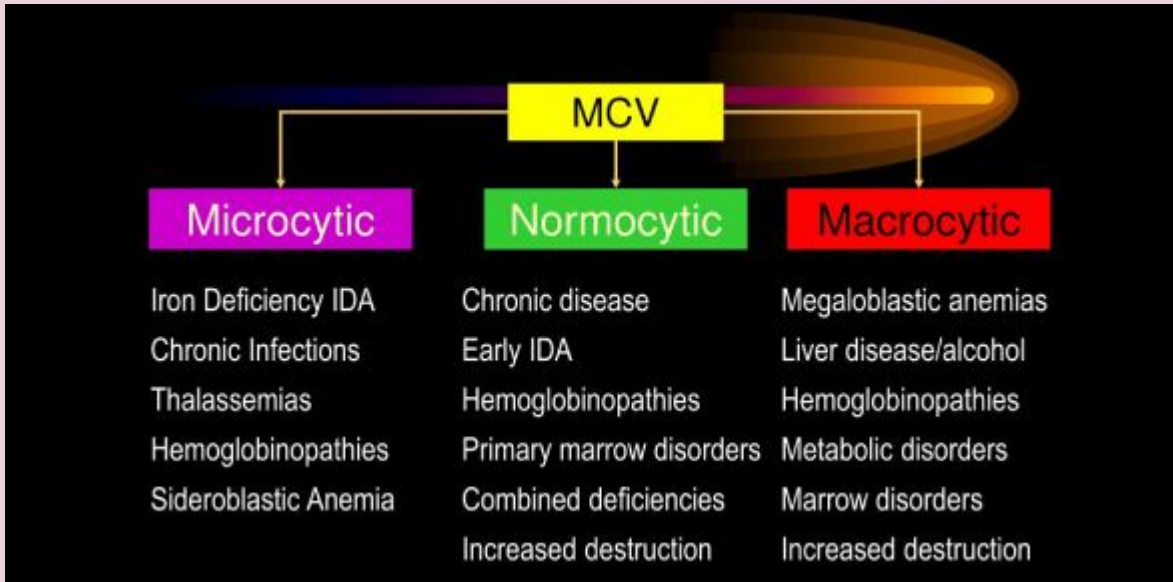
## -Low red Blood Cells

- *RBCs may be Normal, Microcytic, or Macrocytic*
- **Common causes:** Iron deficiency, B12 Deficiency, excessive bleeding, cancers, genetic conditions such as thalassemia
- Peripheral blood smear and a reticulocyte count and index
  - Studies to rule out comorbid conditions such as malignancy, gastrointestinal conditions that cause bleeding, and pernicious anemia

## OR Age-associated decline in the hematopoietic reserve

- Reduction in hematopoietic progenitors
- Reduced production of hematopoietic growth factors
- Inhibition of erythropoietin
- Inflammatory cytokines interfere with interaction of erythropoietin with its receptors.

# Anemia - FYI

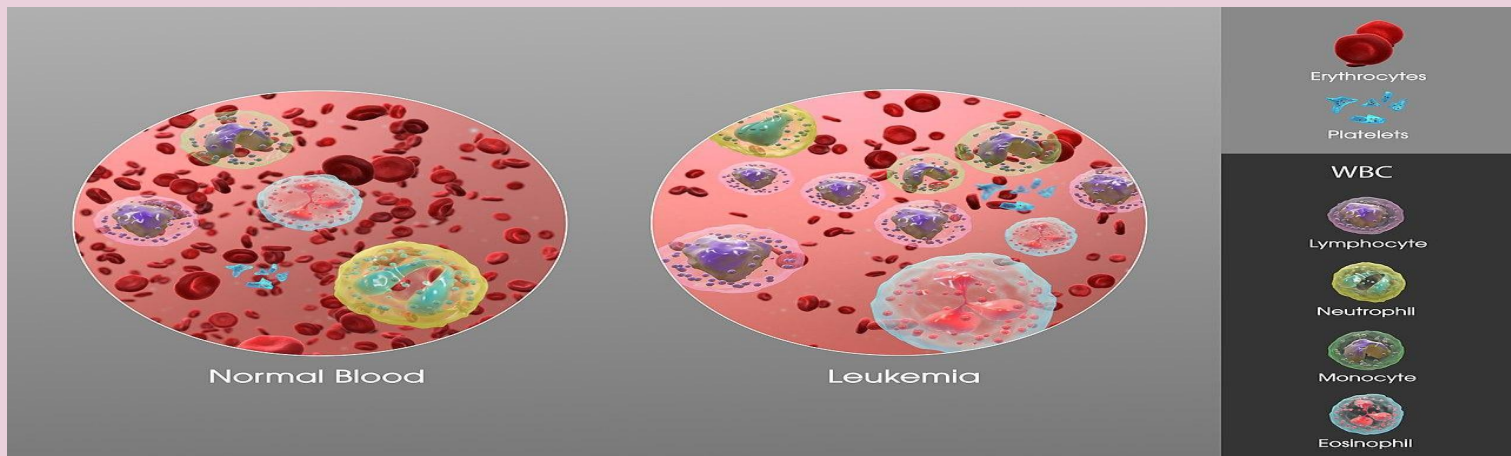


# Infectious Mononucleosis

- <https://youtu.be/U-LHnufQK4Q>
- Definition
  - Self-limited lymphoproliferative disorder
- Causes and characteristics
  - Caused by the B-lymphocytotropic *Epstein-Barr virus*, a member of the herpes virus family; transmitted in saliva
  - Characterized by fever, generalized lymphadenopathy, sore throat, and the appearance in the blood of atypical lymphocytes and several antibodies
  - Highest incidence in adolescents and young adults
  - Treatment is symptomatic and supportive

# Neoplastic Disorders of Hematopoietic and Lymphoid Origin

- Represent the most important pathology of the white cell disorders
- Include somewhat overlapping categories
  - Lymphomas (Hodgkin disease and non-Hodgkin lymphoma)
  - Leukemias
  - Plasma cell dyscrasias (multiple myeloma)



# Hodgkin & Non-Hodgkin Lymphoma

- **Hodgkin disease**

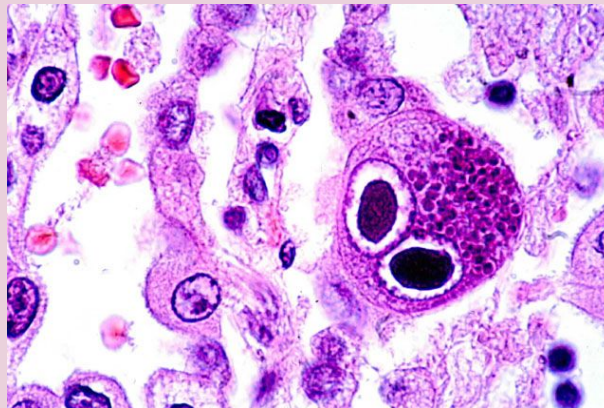
- Lymphoma arises in a single node or chain of nodes, usually upper body
- Can spread through nodes quickly
- **Reed-Sternberg cells ARE present**
- *Young Adults*
- Better Prognosis

- **Non-Hodgkin disease**

- Lymphoma originates at any lymph tissue- Any node & extranodal sites. Spread less likely.
- **Reed-Sternberg cells are NOT present**, (Reed-Sternberg cells are derived from B lymphocytes)
- Affects typically *50+ adults*
- Hepatosplenomegaly
- -Leukemic phase

# Reed-Sternberg Cells

- Reed-Sternberg cells
- Large, multi-nucleated cell that is characteristic of Hodgkin's disease.
- Derive from a B lymphocyte precursor that escapes apoptosis
- The number of Reed-Sternberg cells increases as the disease worsens
- Seen against a sea of B cells, they give the tissue a moth-eaten appearance



# Symptoms of Hodgkin's Disease

- Stage A
  - Lacks constitutional symptoms
  - -Swollen glands, esp. at the throat or underarms
- Stage B (40% of persons with Hodgkin disease)
  - Significant weight loss, fevers, pruritus (itching), or night sweats
- Advanced stages
  - Fatigue and anemia
  - Liver, lungs, digestive tract, and CNS may be involved
  - <https://youtu.be/qW3uP8D3mSs>

# Treatment of Hodgkin's & Non-Hodgkin's Disease

- Depends on the histologic type, stage of the disease, and clinical status of the person
- Types
  - Radiation
  - Combination chemotherapy
- For NHL only
  - Adjuvant radiation therapy
  - Monoclonal antibodies

# Leukemia

- Definition
  - Malignant neoplasms arising from the transformation of a single blood-cell line derived from hematopoietic stem cells

Can be **acute** (affects immature, “blast” cells) or **chronic** (affects mature, fully differentiated cells)
- Classification according to cell lineage
  - **Lymphoid** (lymphocytes)
  - **Myeloid** (granulocytes, monocytes)
- <https://youtu.be/6xdgRo97YZM>

# Leukemic Cells

- Immature and poorly differentiated
- Proliferate rapidly and have a long life span
- Do not function normally
- Interfere with the maturation of normal blood cells
- Circulate in the bloodstream
- Cross the blood-brain barrier
- Infiltrate many body organs
  
- *Most common leukemia is CLL – chronic lymphocytic ( 5 yr survival rate 83%)*
- Worst prognosis is AML – acute myeloid (5 yr survival 26%)

# Warning signs/complications of Acute Leukemia

## Signs

- Fatigue
- Pallor
- Weight loss
- Repeated infections
- Easy bruising
- Nosebleeds
- Other types of hemorrhage.

## Complications

- Leukostasis
- Tumor lysis syndrome
- Hyperuricemia
- Blast crisis
- <https://youtu.be/hp9XfGk4DQ8>

# Multiple Myeloma

Definition: a plasma cell dysplasia characterized by expansion of a single clone of immunoglobulin-producing plasma cells and a resultant increase in serum levels of a single monoclonal immunoglobulin or its fragments

Remember – what is a plasma cell? <https://youtu.be/vceIglmSuTI>

- Main sites involved: bones and bone marrow
- Proliferation and activation of osteoclasts that leads to bone resorption and destruction (Pathologic fractures, Hypercalcemia)
- Signs & symptoms: *back pain*, protein in urine, fractures, anemia
- <https://youtu.be/XHsmJ8u-T4>