*The Complete Preparatory Guide*

# USMLE STEP 1
## Platinum Notes

*Comprehensive Coverage of STEP 1 Exam for Foreign Medical Graduates*

**2nd Edition**

**Important Features**

Latest USMLE-type Questions included
Complete Revision Guide
All subjects covered in detail
High-yield matter with highlighted text matter
Special focus on the latest examination pattern
Image-based questions included

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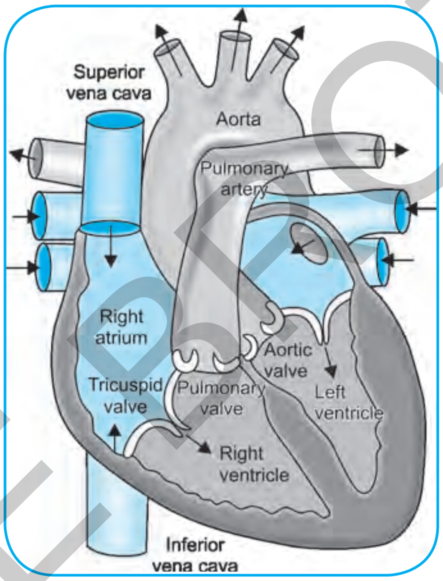
# Contents


Superior
vena cava
Aorta
Pulmonary
artery
Right
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Tricuspid
valve
Pulmonary
valve
Left
ventricle
Right
ventricle
Inferior
vena cava

# PHYSIOLOGY

# Physiology 2

## Basics of Physiology

**$Na^+$ $K^+$ ATPase Pump**

**Two ions are responsible: sodium ($Na^+$) and potassium ($K^+$). An unequal distribution of these two ions occurs on the two sides of a nerve cell membrane because carriers actively transport these two ions: sodium from the inside to the outside and potassium from the outside to the inside. As a result of this active transport mechanism (commonly referred to as the sodium-potassium pump), there is a higher concentration of sodium on the outside than the inside and a higher concentration of potassium on the inside than the outside.**

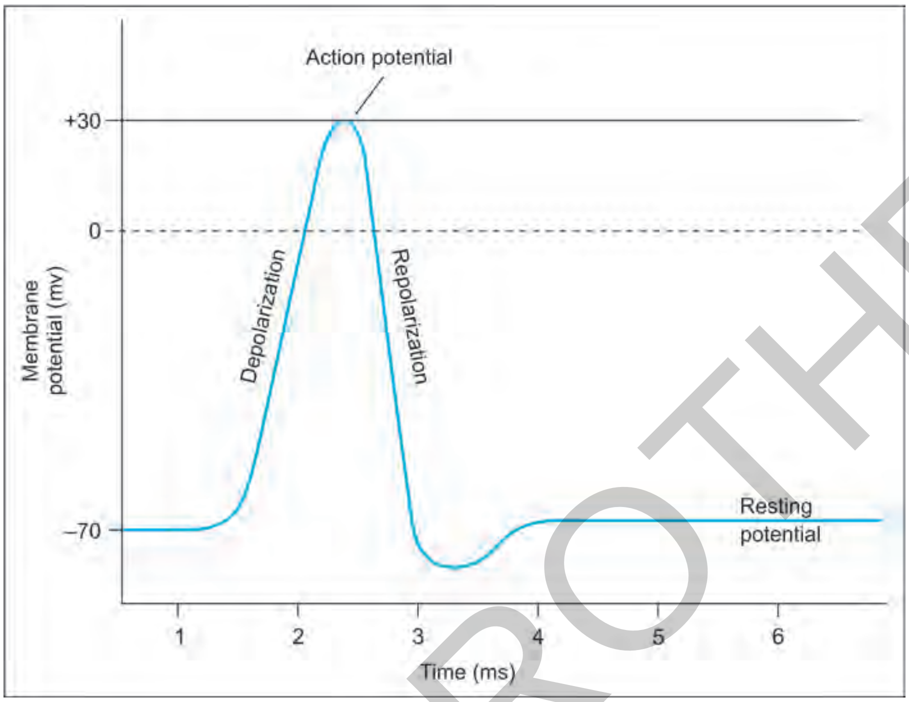
- Na K ATPase Pump is an active, electrogenic pump moving three sodium ions outside and in place two potassium ions inside utilizing ATP. It helps in **intrusion** of $K^+$
- It accounts for 20% of energy utilized by cells
- Thus its coupling ratio is **3:2**
- Extracellular binding site is **Ouabain**
- Its activity is inhibited by **Ouabain and related cardiac glycosides**
- It is a **P type ATPase** (super family of cation transporters)
- Also called **E1/E2 Type ATPase** responsible for carrying ions across cell membranes
- Type: **Heterodimer Heterogeneous**
- **It is an example of active transport**

**RMP (Resting Membrane Potential)**

- Resting membrane potential of a **skeletal muscle** is – **90 mV**
- Resting membrane potential of a **smooth muscle** is – 50 to – 75 mV
- Resting membrane potential of a **cardiac muscle** is – 85 to – 95 mV
- The resting membrane potential in the **nerve fiber is** – **70 mV**
- The resting membrane potential in the **rods** is – 40 mV
- The resting membrane potential of **inner ear cell** is – 60 mV

## The Action Potential

- Neurons transmit information as action **potentials**
- **An action potential is a temporary change in the membrane potential**
- **Usually initiated in the cell body**
- Travels in one direction normally
- Action potential is conducted in an all-or-none fashion
- If the stimulus is too low there is no action potential
- If the stimulus is above a threshold the action potential is always the same size




Action potential

**Electrical changes during action potential**

- Membrane potential depolarizes (becomes more positive)
- After the peak of the spike the membrane repolarises (becomes more negative)
- The potential becomes more negative than the resting potential (negative after potential)
- It then returns to normal
- The action potentials of most nerves last 5–10 milli seconds
- Action potentials are initiated by many different types of stimuli
- Sensory nerves respond to stimuli of many types including chemicals, light, electricity, pressure, touch and stretch
- In the central nervous system most nerves are stimulated by chemical activity at synapses
- Stimuli must be above a threshold level to initiate an action potential
- After a nerve has fired there is a period of time during which it cannot be stimulated again
- This is known as the refractory period

## Concepts

- Resting Membrane Potential is **due to: $K^+$**
- Resting Membrane Potential is **close to** isoelectric potential of: $Cl^-$
- **IPSP is due to $Cl^-$ influx**
- **EPSP is** due to **$K^+$ influx**

- **For action potential; threshold stimulus is required**
- **Nerve conduction follows All or None phenomenon**
- **Axon has the lowest threshold potential in a nerve fiber**
- **Nerve impulse travels in one direction only at synapse**

- **RMP is close to isoelectric potential of chloride**
- **RMP is due to pottasium**
- **IPSP is due to chloride**
- **Amplitude is due to chloride**

- **Most of pottasium is intracellular**
- **Mx pottasium is found in skeletal muscles**
- **In response to tissue injury intracellular pottasium shifts to extracellular space**

## The Cell Membrane: (USMLE Favorite)

- **Main constituent is the protein**
- **Lipids are regular but assymetrically arranged**
- **Membrane lipids are amphiphatic**
- **Are arranged as a bilayer**
- **Signal transduction and enzyme activation are the functions of phospholipid part**
- **The fluidity of cell membrane is increased by Polyunsaturated fatty acids**
- **Lipids and proteins intract by hydrogen bonds**
- **RBC Membrane is specially having spectrin (maintains integrity) and glycophyrin**
- **Lipid bilayer is most permeable to urea**
- **Lipid bilayer acts as a gel**
- **Protein: lipid ratio is 2:1**

## Basement Membrane

- Contains laminin
- Nidogenin
- Enactin
- Type IV collagen
- Degeneration mediated by metalloproteineases

## Functions of Organalles Commonly Asked: (USMLE Favorite)

- **Synthesis of lipids occurs in Agranular Endoplasmic Reticulum**
- **Synthesis of proteins occurs in Rough ER**
- **Intracellular sorting and packing is done in Golgi complex**
- **Cell shape and motility are a function of Microtubules**
- **Catabolism of $H_2O_2$ is a function of Peroxisomes**
- **Site of ATP synthesis is Mitochondria**

## Marker of

- **Plasma membrane: adenyl cyclase, 5 nucleotidase**
- **Golgi bodies: galactosyl transferase**
- **Mitochondria: Glutamic dehydrogenase**

## Fluids and Electrolytes: (USMLE Favorite)

- Water constitutes between 50% and 70% of total body weight
- The water of the body is divided into three functional compartments

- **The intracellular water,** represents between 30% and 40% of body weight
- **The extracellular water** represents approximately 20% of body weight and is divided between intravascular fluid, or plasma (5% of body weight), and interstitial, or extravascular, extracellular fluid (15% of body weight)
- **Intracellular Fluid:** Measurement of intracellular fluid (ICF) is determined indirectly by subtraction of the measured extracellular fluid (ECF) from the measured total body water. The intracellular water is **between 30% and 40% of body weight,** with the largest proportion in the skeletal muscle mass. Because of the smaller muscle mass in the female, the percentage of intracellular water is lower than in the male. The chemical composition of **ICF with potassium and magnesium the principal cations, and phosphates and proteins the principal anions**
- **Extracellular Fluid:** The total ECF volume represents approximately 20% of body weight. The ECF compartment has two major subdivisions. **The plasma volume is** approximately 5% of body weight in the normal adult. **The interstitial, or extravascular, ECF volume,** obtained by subtracting the plasma volume from the measured total ECF volume, accounts for approximately 15% of body weight
- **The interstitial fluid** is further complicated by having a rapidly equilibrating or functional component as well as several more slowly equilibrating, or relatively nonfunctioning, components. The nonfunctioning components include connective tissue water as well as transcellular water, which includes cerebrospinal and joint fluids. This nonfunctional component normally represents only 10% of interstitial fluid volume (1 to 2% of body weight) and is not to be confused with the relatively nonfunctional ECF, often called a third space, found in burns and soft tissue injuries
- The normal constituents of ECF are with **sodium the principal cation and chloride and bicarbonate the principal anions.**

| Electrolyte | Function | Distribution |
|---|---|---|
| **Sodium ($Na^+$)** | • Essential role in fluid and electrolyte balance — **accounts for half the osmolarity of ECF**<br>• Role in **generation of action potentials** | Represents about 90% of extracellular cations<br>Level in blood controlled by aldosterone, ANP and ADH |
| **Potassium ($K^+$)** | • **Establishes resting membrane potential** and essential in the **repolarization phase** of action potentials in nervous and muscle tissue<br>• Aids maintenance of fluid volume in cells<br>• Helps regulate pH. | Most abundant intracellular cation<br>Blood serum level controlled by aldosterone. |
| **Calcium ($Ca^{2+}$)** | • Roles in blood clotting, neurotransmitter release, maintenance of muscle tone, and **excitability of nervous and muscle tissue** | Most abundant mineral in the body due to bone content<br>Principally extracellular<br>Blood level controlled chiefly by Parathyroid hormone (PTH) |
| **Chloride ($Cl^-$)** | • Helps balance anions in different fluid compartments. | Most prevalent extracellular anion<br>Diffuses easily between interstitial space and ICF<br>Level controlled indirectly by aldosterone – due to relationship with sodium |
| **Bicarbonate ($HCO_3^-$)** | • Major buffer of $H^+$ in plasma<br>• Helps maintain correct balance of anions and cations in ECF and ICF | Second most prevalent anions in extracellular fluid<br>A small amount found in intracellular fluid<br>Blood level controlled by kidneys which can both form and excrete bicarbonate |

## Remember

- **If an isotonic salt solution is added to or lost from the body fluids,** only the volume of the ECF is changed. The acute loss of an isotonic extracellular solution, such as intestinal juice, is followed by a significant decrease in ECF volume and little, if any, change in ICF volume. Fluid is not transferred from the intracellular space to refill the depleted extracellular space as long as the osmolality remains the same in the two compartments.

- **If water alone is added to or lost from the ECF,** the concentration of osmotically active particles changes. Sodium ions account for most of the osmotically active particles in ECF and generally reflect the tonicity of other body fluid compartments. If ECF is depleted of sodium, water passes into the intracellular space until osmolality is again equal in the two compartments
- The concentration of most other ions within the ECF compartment can be altered without significant change in the total number of osmotically active particles, thus producing only a compositional change. For instance, a rise of the serum potassium concentration from four to eight mEq per liter would have a significant effect on the myocardium, but it would not significantly change the effective osmotic pressure of the ECF compartment. Normally functioning kidneys minimize these changes considerably, particularly if the addition or loss of solute or water is gradual
- **An internal loss of ECF into a nonfunctional space,** such as the sequestration of isotonic fluid in a burn, peritonitis, ascites, or muscle trauma, is termed a distributional change. This transfer or functional loss of ECF internally maybe extracellular (e.g. as in peritonitis) or intracellular (e.g. as in hemorrhagic shock). In any event, all distributional shifts or losses cause a contraction of the functional ECF space.

## Regulation of Fluid Transfer among Compartments

**The transfer of fluid between vascular and interstitial compartments occurs at the capillary level and is governed by the balance between hydrostatic pressure gradients and plasma oncotic pressure gradients**

**This relation is stated by the Starling equation:**

**Jv = Kf (DP – Dp)**

**Where:**

- Jv is rate of fluid transfer between vascular and interstitial compartments, Kf is the water permeability of the capillary bed
- DP is the hydrostatic pressure difference between capillary and interstitium, and
- Dp is the oncotic pressure difference between capillary and interstitial fluids

Under normal circumstances, interstitial tissue pressure is low, and the DP term in the Starling equation represents the integrated hydrostatic pressure gradient from arteriolar to venular ends of a capillary. Since interstitial fluid is protein poor, the Dp term in the Starling equation represents the oncotic pressure of plasma proteins, principally albumin; five grams of albumin per deciliter of plasma exerts an oncotic pressure of about 15 mm Hg.

## Osmolal gap

It is the difference between measured serum osmolality and calculated serum osmolality. It is typically calculated as: OG = measured serum osmolality – (2 × serum sodium + serum glucose + serum urea) Where: 2 × serum sodium + serum glucose + serum urea = the calculated serum osmolality and all measures are in **mmol/L.** OG = Osmolal gap. In US customary units the calculated osmolarity is: (2 × sodium) + glucose/18 + BUN/2.8

**Causes of an Elevated Osmolal Gap are numerous**

- **Ethanol intoxication**
- **Methanol ingestion**
- **Isopropanol ingestion**
- **Ethylene glycol ingestion**

## 'Acidosis' and 'Alkalosis': (USMLE Favorite)

Refer to the mechanism by which a given acid base disturbance is reached

- **'Primary'** refers to the initiating process of acid base disturbance, while **'secondary'** refers to a compensatory process
- **Mixed** acid base disturbances are combinations of two or more primary acid base disturbances

The pH of arterial blood and interstitial fluid normally ranges between **7.38 and 7.42** despite wide variations in dietary intake of acids or alkali

The arterial pH range over which cardiac function, metabolic activity and CNS function can be maintained is narrow; the widest range of pH values compatible with life is from 6.8 to 7.8, or an interval of one pH unit.

The major buffer system in ECF is the bicarbonate-carbonic acid pair. The relation between pH, bicarbonate and carbonic acid concentrations in ECF maybe expressed according to the familiar Henderson-Hasselbalch equation:

**$pH = pK + \log HCO_3 / H_2CO_3$**

Where pK is the carbonic acid dissociation constant, $HCO_3^-$ is the plasma bicarbonate concentration and $H_2CO_3$ is the plasma carbonic acid concentration. The $H_2CO_3$ concentration is given by a $PaCO_2$, where is the $CO_2$ solubility constant and has a value of 0.0301, and $PaCO_2$ is the arterial carbon dioxide tension. Therefore, the Henderson-Hasselbalch equation becomes

**$pH = 6.1 + \log HCO_3/0.03\ PCO_2$**

**Primary changes** in the numerator (blood bicarbonate concentration) refer to primary metabolic changes, while primary changes in the denominator (blood carbon dioxide tension) refer to primary respiratory changes

**Proton shifts:** Between the ECF and ICF stabilize the plasma pH against acute fluctuations. But the ultimate maintenance of pH balance requires that input of acid or base into the body be matched by output of acid or base so that the $HCO_3^-/H_2CO_3$ ratio and the total bicarbonate content in the ECF remain constant. The cardinal systems involved in these external processes are the kidneys for bicarbonate balance, and the lungs for $CO_2$ balance.

## The Serum Anion Gap

Sodium is the principal cation in extracellular fluids. The sum of plasma chloride plus bicarbonate concentrations is less than the serum sodium concentration; the remaining anions required for electroneutrality, generally not reported with routine serum electrolyte measurements, are referred to as unmeasured anions, or as the serum anion gap. A convenient formula for calculating the serum anion gap is the following:

**Serum anion gap = $Na^+ - (Cl^- + HCO_3^-)$**

Where $Na^+$, $Cl^-$ and $HCO_3^-$ are the serum sodium, chloride and bicarbonate concentrations, respectively

The anion serum gap includes primarily phosphates and sulfates derived from tissue metabolism, lactate and keto acids arising from incomplete combustion of carbohydrates and fatty acids, and negatively charged protein molecules, principally albumin. The normal value for unmeasured anions, or the serum anion gap, is 10 to 12 mEq per liter; albumin and other proteins normally account for about half the anion gap

**An increased serum anion gap generally indicates the presence of metabolic acidosis**

**A reduced serum anion gap provides an index to certain other disorders**

The anion gap will be reduced if the sodium concentration falls while the chloride plus bicarbonate concentrations are unchanged or, in other words, when the concentration of another cation in serum is increased while the serum osmolality remains normal. This may occur in multiple myeloma of the immunoglobulin G (IgG) variety if the myeloma proteins are cationic at pH 7.4. Hyperviscosity syndromes also may result in a reduced anion gap.

## The Urinary Anion Gap

The urinary anion gap, defined as:

**Urinary anion gap = $(Na^+ + K^+) - Cl^-$**

It is useful in evaluating patients with hyperchloremic acidosis. The test provides an approximate index to urinary $NH_4^+$ excretion, as measured by a negative urinary anion gap, that is, urinary $(Na^+ + K^+)$ is less than urinary $Cl^-$. Thus, in hyperchloremic metabolic acidosis, a normal renal response would be a negative urinary anion gap, generally in the range of 30 to 50 mEq per liter. In such an instance, the hyperchloremic acidosis is probably due to gastrointestinal losses rather than a renal lesion. In contrast, a positive urinary anion gap implies a renal tubular disorder.

## Remember

- **Water constitutes roughly 60% of body weight**
- **Na, Cl, $HCO_3$ are predominantly in ECF**
- **K, P, Mg are predominantly in ICF**

## Measurement of Body Fluids

| **Total Body water** | **About 60% of body weight** |
|---|---|
| • ICF | • 40% |
| • ECF | • 20% |

| | |
|---|---|
| • Total body water | Tritrated water, Deuterium Oxide, Antipyrine |
| • ECF | **Inulin**, Mannitol |
| • Plasma volume | Evans Blue, radiolabelled albumin |

- **ECF** is rich in: $Na^+$
- **ICF** is rich in: $K^+$
- **Endolymph** is rich in: $K^+$

## Anion Gap: (Repeat)

- Anion gap = **unmeasured** ions in plasma
- Normal cations in plasma: $Na^+$, $K^+$, $Ca^{++}$, $Mg^{++}$
- Normal anions in plasma: $Cl^-$, $HCO_3^-$, albumin, phosphate, lactate
- Sum of positive and negative charges is equal
- Anion gap = $(\mathbf{Na^+ + K^+}) - (\mathbf{Cl^- + HCO_3^-})$
- Normal AG = **10–12 mmol/l**

## Terms Frequently Asked

- **Endocytosis: Substance transported into cell by infoldings of cell membrane around substance and internalizing it**
- **Pinocytosis: Engulfing liquid substances by enfolding of cell membrane**
- **Phagocytosis: Engulfing soild substances by enfolding of cell membrane**
- **Exocytosis: Reverse of endocytosis**
- **Emiocytosis: Excretion of specific hormones and granules by cell is emiocytosis**
- **Requires calcium**
- **Transcytosis: Vesicular transport within cell. (epithelial cells of intestine)**

## Proteins in Vesicular Transport

| |
|---|
| **AP 1 clathirin: Involved in transportation from Golgi bodies to lysosomes** |
| **AP 2 clathirin: Involved in transportation to endosomes** |
| **CO –PI: Coating proteins in vesicles for transportation between endoplasmic reticulum and Golgi apparatus**<br>**CO –PII: Coating proteins in vesicles for transportation between endoplasmic reticulum and Golgi apparatus** |
| **Dynamin: Vesicle formation from Golgi complex and cell membrane** |
| **Docking protein: V snare protein and T snare proteins present on target cells** |

## Cutaneous Vascular Responses

**White reaction:**
**Appearance of pale stroke line when pointed object is drawn lightly over skin**
**Due to precapillary sphincter contraction**

**Triple response:**

1. **Red reaction: Red line appearing at site of injury**
   **Due to dilatation of precapillary sphincter. (histamine and bradykinin)**
2. **Flare: Diffuse irregular outside red reaction due to dilatation of arteriole and precapillary sphincter**
3. **Wheal: Swelling or localized edema within area of flare**

**Due to increased capillary permeability**

- **Dermatographia: Striking triple response on touching the skin**

## Muscle Contraction

- The skeletal muscle fibers are cylindrical in shape.
- The length varies from 1 mm to 15 cm. The width varies from 10 microns to 80 microns.
- Each muscle fiber has a thick sarcolemma
- The cytoplasm is acidophilic and granular and is composed of **Actin, Myosin and Tropomyosin**.
- The Cytoplasm contains longitudinal **Myo fibrils or Sarcostyles** which are striated transversely.
- Each Myofibril or Sarcostyles is formed of smaller filaments called as **Myofilaments**.
- The Myofilaments are of two types:
- **Thin or Actin Filaments**
- **Thick or Myosin Filaments**
- The Transverse striations are due to presence of dark and light bands
- The **Sarcomere** is the unit of contraction
- It is formed of Actin and Myosin
- Actin is present in light **band** and Myosin is present in the **dark band**

## Remember

- **A:** Anisotropic; broad, dark; **remains constant in width despite degree of contraction**
- **I:** Isotropic; broad, light; only thin filaments (no thick); **narrows during contraction**
- **Z:** (Zwischenscheiben) bisects I band; **drawn together during contraction**
- **H:** (Heller) light band bisects A band; only thick filaments (no thin); **narrows during contraction**
- **M**: (Mittelscheibe) denser band bisects H band.

- **Heads of Myosin** contain actin binding site and possess **ATPase activity**
- **Tropomyosin** is a relaxing protein
  - **Troponin I** inhibits interaction of myosin with actin
  - **Troponin T** binds other troponins to tropomyosin
  - **Troponin C** has binding sites for calcium which initiates contraction
- **Tropomyosin** covers the **active sites of actin**
- **RMP** of skeletal and cardiac muscle is **– 90 mV**
- **Repolarization** is due to **pottasium efflux**
- **Depolarization** is due to **sodium influx**
- **Treppe or stair case phenomenon** is due to increased **availability of Calcium** for binding to troponin C

- **Rheobase** is the **minimum amount of current** to cause excitation
- **Chronaxie** is the **shortest duration** for a stimulation to excite tissue with a current strength twice the rheobase
  - **Newborns have longer chronaxies**
  - **Skeletal muscles have shorter chronaxies**
  - **Cold lenthens chronaxie**
  - **Vagal stimulation shortens chronaxie**
- **For smooth muscle contraction presence of cellular calcium is essential to cause contraction**
- **Force of muscle contraction is independent of amplitude of action potential**

**Nerve fibers and anesthesia:**
**SUSCEPTIBILITY: Type C > Type B > Type A**
**Nerve fibers and pressure**
**SUSCEPTIBILITY: Type C < Type B < Type A**

## Golgi Tendon Organ

- **It is an encapsulated sensory receptor**
- **Detects muscle tension**
- **Involved in inverse stretch reflex**
- **3–25 muscle fibers on an average are attached to golgi tendon organ**
- **Impulses are transmitted by type nerve fibers**
- **It is inhibitory and protective**
- **Golgi tendon reflex is bisynaptic.**

## Muscle Spindle

- **3–12 mm long structure containing intrafusal muscle fibers enclosed in capsule of connective tissue**
- **It is a receptor for myotactic or stretch reflex**
- **Central zone has no actin and myosin**
- **Peripheral zone has actin and myosin**

**Are of two types:**

- **Intrafusal**
- **Extrafusal**

**Intrafusal are of two types:**

- **Nuclear bag and**
- **Nuclear chain fibers**

**Two types of sensory nerve endings are**

- **Primary annulospiral endings**
- **Secondary flower spray endings**

- **Neurapraxia : No anatomic disruption**
- **Axonometesis : Axon and myelin disruption**
- **Neurontemesis : Complete division of nerve**
- **Degeneration distal to cut end : Wallerian degeneration**

The skeletal muscle fibers are two types: **Red Fibers and white fibers**

| **Red Fibers** | **White Fibers** |
|---|---|
| • Have **irregular** striations | • Have **regular** striations |
| • Have **central** nuclei | • Have **periphera**l nuclei |
| • Have **rich vascular** supply | • Have **poorer** blood supply |
| • **Nonfatiguable** | • Are **fatiguable** |
| • **Are poor in mitochondria, Myoglobin, fats** | • **Are rich in Myoglobin, fats** |
| • **Example : Skeletal muscle** | • **Examples: diaphragm, muscles of eye, mastication** |
| • **They react quickly, with brief, forceful contractions, but cannot sustain contraction for long periods** | • **Their contraction in response to nervous stimulation is slow and steady, resulting in their designation as slow fibers** |
| • **They are thus termed fast fibers** | |

## Red Blood Cell

Mature Red cell is **8 micrometer** in diameter

Mature Red cell is **anucleate**

Mature Red cell is **discoid** in shape

Mature Red cell is **pliable**

- Average life of red cell is **100–120** days
- Hematopoiesis is the process by which formed elements of the blood are produced
- In the BM (Bone Marrow) first morphologically recognizable precursor is the **PRO** normoblast **Erythropoietin** is produced by the peritubular cells within the kidney
- There is daily replacement of 0.8–1% of all circulating red cells

**'Hematopoiesis'** is the process by which formed elements of the blood are produced. Stem cells are capable of producing all classes of cells

In the BM (Bone Marrow) first morphologically recognizable precursor is the '**PRO** normoblast.' This cell can undergo **4–5 cell divisions** that result in production of 16–32 mature red cells

**Erythropoietin (EPO)** is produced by the peritubular cells within the kidney. These cells are **specialized epithelial cells**. A small amount of EPO is also produced by **Hepatocytes**.

## Cardiovascular Physiology

- Artery/Arteriole **Resistance Vessel**
- Capillary (Mx Surface area) **Exchange Vessel**
- Vein **Capacitance Vessel**

- **BP** = Cardiac output x Peripheral resistance
- **BP measured by sphygmomanometer is less than arterial BP actually**
- **Small cuff = High BP**
- **Thick walled vessels = High BP**
- **Obesity = High BP**
- **Pulse Pressure** = Systolic pressure – Diastolic Pressure
- **Mean Arterial Pressure** = Diastolic Pressure +1/3 of Pulse Pressure

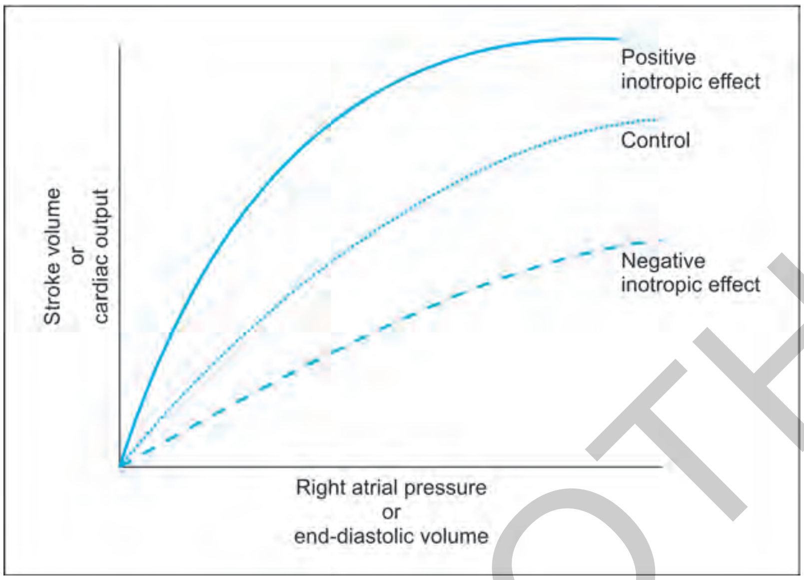
- **Ventricular End Diastolic Volume**: Volume of blood in ventricular cavity at the end of atrial contraction (n) = 120 ml. Determines **Preload**
- **Ventricular End Systolic Volume**: Volume of blood in ventricular cavity at the end of ejection (n) = 40 ml
- **Stroke Volume**: Volume of blood ejected with each heart beat. CO/HR (n) = 70 – 80 ml
- **Ejection Fraction**: Ratio of stroke volume to End Diastolic Volume (SV/EDV) (n) = 50 – 70%
- **Cardiac Output**: Volume of blood expelled from one side of heart per minute

**Can be detected by**:

- Ficks principle
- Echocardiography
- Thermodilution
  - **Cardiac index = CO/Body surface area**
  - **Normal cardiac index IS 3.2**

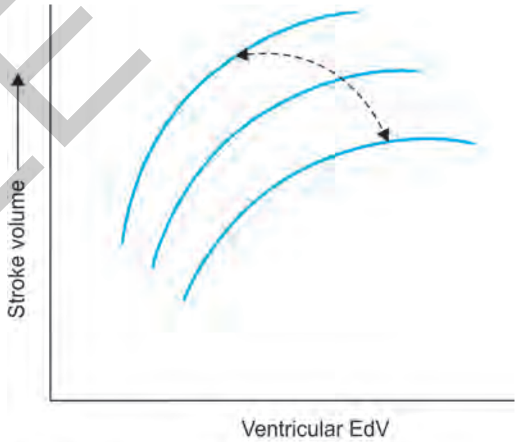
## Frank–Starling Law

**This principle illustrates the relationship between cardiac output and left ventricular end diastolic volume (or the relationship between stroke volume and right atrial pressure.)**




Determinant of cardiac output

- The Frank-Starling principle is based on the length-tension relationship within the ventricle. If ventricular end diastolic volume (preload) is increased it follows that the ventricular fiber length is also increased, resulting in an increased 'tension' of the muscle
- In this way, cardiac output is directly related to venous return the most important determining factor of preload. When heart rate is constant, cardiac output is directly related to preload (up to a certain point.)
- An increase in preload will increase the cardiac output until very high end diastolic volumes are reached. At this point cardiac output will not increase with any further increase in preload, and may even decrease after a certain preload is reached
- Also, any increase or decrease in the contractility of the cardiac muscle for a given end diastolic volume will act to shift the curve up or down, respectively.




Changes in myocardial contractility
Curve shifting down wards and to right as
contractility decreases
(Frank-Starling curve)

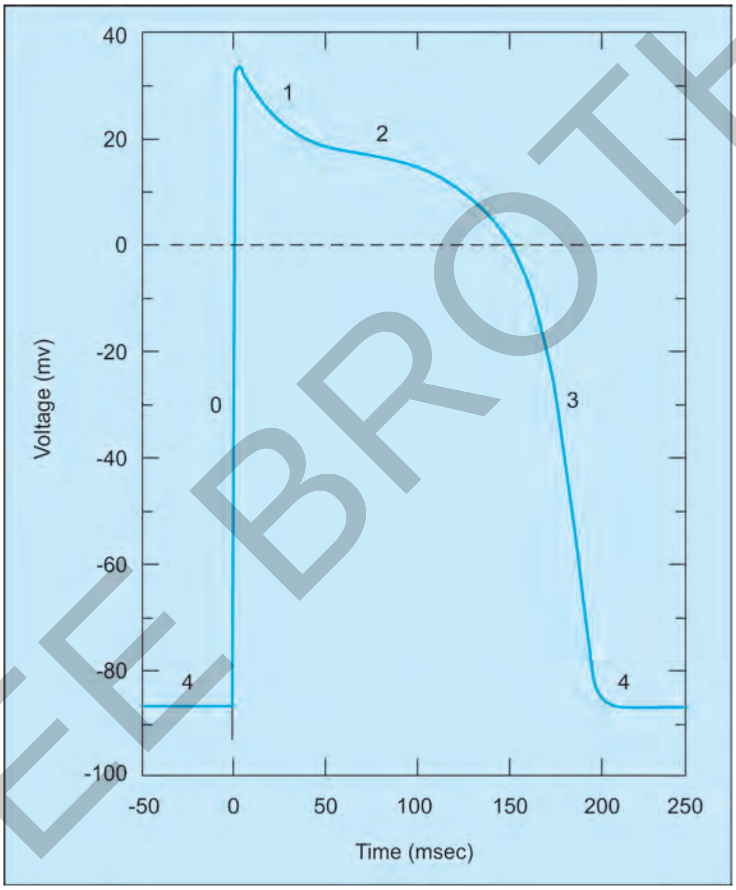
Frank-starling curve

## Regional Blood Flow

- **Blood flow is controlled mainly by arterioles**
- **Velocity of blood is maximum in large veins**

- **Blood flow of liver > kidney > brain > heart**
  - **Carbon dioxide produces vasodilation in brain**
  - **Exercise produces venoconstriction in splanchnic circulation**
  - **Exercise produces increase in coronary circulation**
  - **Hypoxia produces vasoconstriction in pulmonary circulation**
  - **$PGE_1$, $PGI_2$ produce renal vasodilation.**

## Myocardial Action Potential




Phases of myocardial action potential

**Phase 0 — rapid depolarization**
- Rapid **sodium influx**
- These channels automatically deactivate after a few ms

**Phase 1 — early repolarization**
- Efflux of **potassium**

**Phase 2 — plateau**
- Slow influx of **calcium**

**Phase 3 — final repolarization**
- Efflux of **potassium**

**Phase 4 — restoration of ionic concentrations**
- Resting potential is restored by $Na^+/K^+$ ATPase
- There is **slow entry of $Na^+$** into the cell decreasing the potential difference until the threshold potential is reached, triggering a new action potential

# USMLE STEP 1

## Platinum Notes

The USMLE examination is a conceptual examination based on testing the concept of students for practicing in the United States of America. A meticulous effort has been made by the authors to completely update the first edition of the book, taking into account the quality inputs needed for high scoring or high percentile.

The aim of the book is to help the students study the matter needed to get near to 99th percentile. We sincerely hope that the book helps the students achieve their ultimate dream of getting a placement in the USA after getting high scores.

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