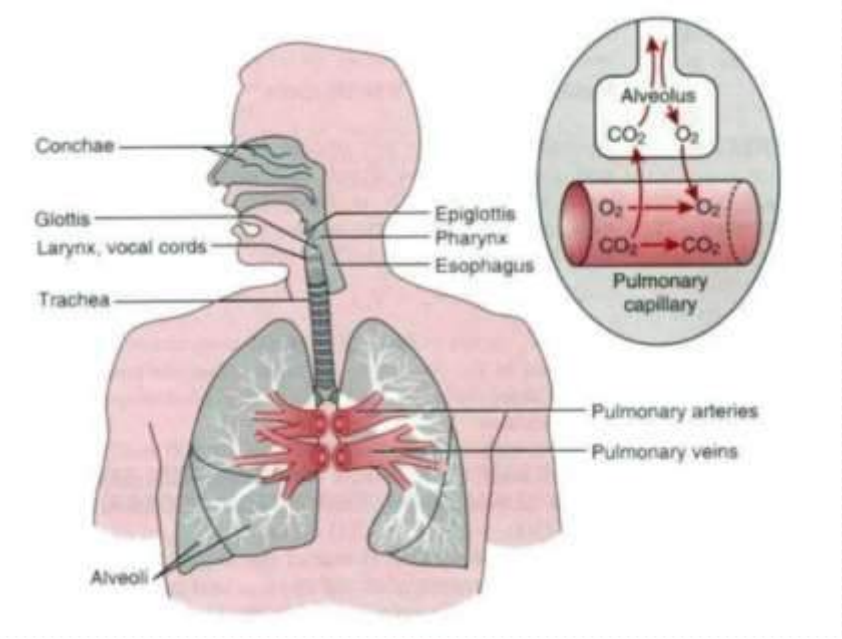
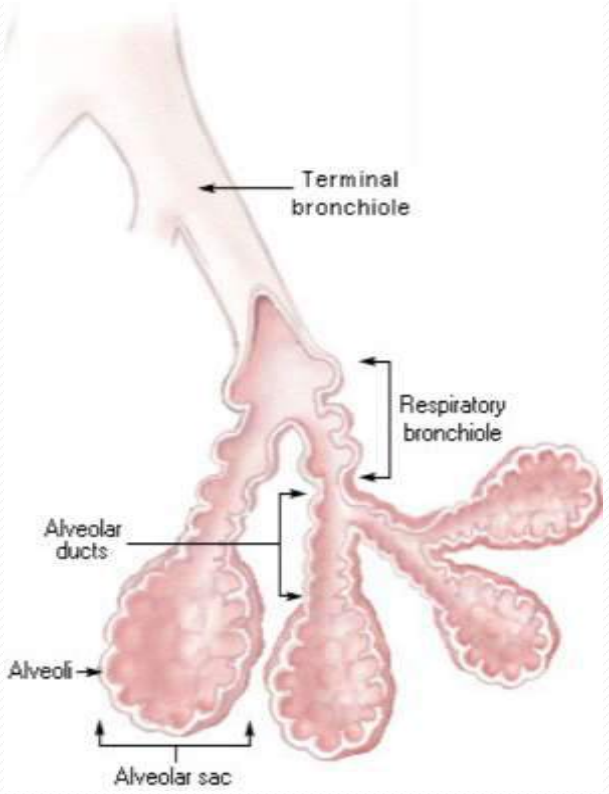
- **Control Of Breathing:**

- **Respiratory Airways:**

Anatomical classification: nose, pharynx ***(upper respiratory tract),***larynx, trachea, bronchi, bronchioles, terminal bronchioles, respiratory bronchioles, alveolar ducts, alveolar sacs, and alveoli***(lower respiratory tract***





Non Respiratory Functions Of The Lung:

1. the pulmonary capillaries within the circulation allows them to act as a filter for debris in the bloodstream. The lungs' high content of heparin and plasminogen activator facilitates the breakdown of entrapped fibrin debris

2. surfactant synthesis.

3. pneumocytes refer a major portion of extra hepatic mixed function oxidation. Neutrophils and macrophages in the lung produce O 2 -derived free radicals in response to infection.

4. The pulmonary endothelium metabolizes a variety of vasoactive compounds, including norepinephrine, serotonin, bradykinin, and a variety of prostaglandins and leukotrienes

5. the lungs can be a major site of histamine synthesis and release during allergic reactions.

6. The lungs are also responsible for converting angiotensin I to its physiologically active form, angiotensin II. The enzyme responsible, angiotensin- converting enzyme, is bound on the surface of the pulmonary endothelium.

Control Of Breathing:

- Spontaneous ventilation is the result of rhythmic neural activity in respiratory centers within the brainstem. This activity regulates respiratory muscles to maintain normal tensions of O 2 and CO 2 in the body. The basic neuronal activity is modified by inputs from other areas in the brain, volitional and autonomic, as well as various central and peripheral receptors (sensors).

Central Respiratory Centers

- The basic breathing rhythm originates in the medulla. Two medullary groups of neurons are generally recognized: **a dorsal respiratory group**, which is primarily active during **inspiration**, and **a ventral respiratory group**, which is active during **expiration**. The close association of the dorsal respiratory group of neurons may explain reflex changes in breathing from **vagal or glossopharyngeal** nerve stimulation. Two pontine areas influence the dorsal (inspiratory) medullary center. A lower pontine **(apneustic) center is excitatory**, whereas an upper pontine **(pneumotaxic) center is inhibitory.** The pontine centers appear to fine-tune respiratory rate and rhythm.

1. *Central Sensors*

The most important of these sensors are **chemoreceptor**s that **respond to changes in hydrogen ion concentration**. Central chemoreceptors are thought to lie on the anterolateral surface of the medulla and **respond primarily to changes in cerebrospinal fluid (CSF) [H +].** This mechanism is effective in regulating Pa co 2 , because the blood–brain barrier is permeable to dissolved CO 2 , but not to bicarbonate ions. Acute changes in Pa co 2 , but not in arterial [HCO 3 –], are reflected in CSF; thus, a change in CO 2 must result in a change in [H +]:

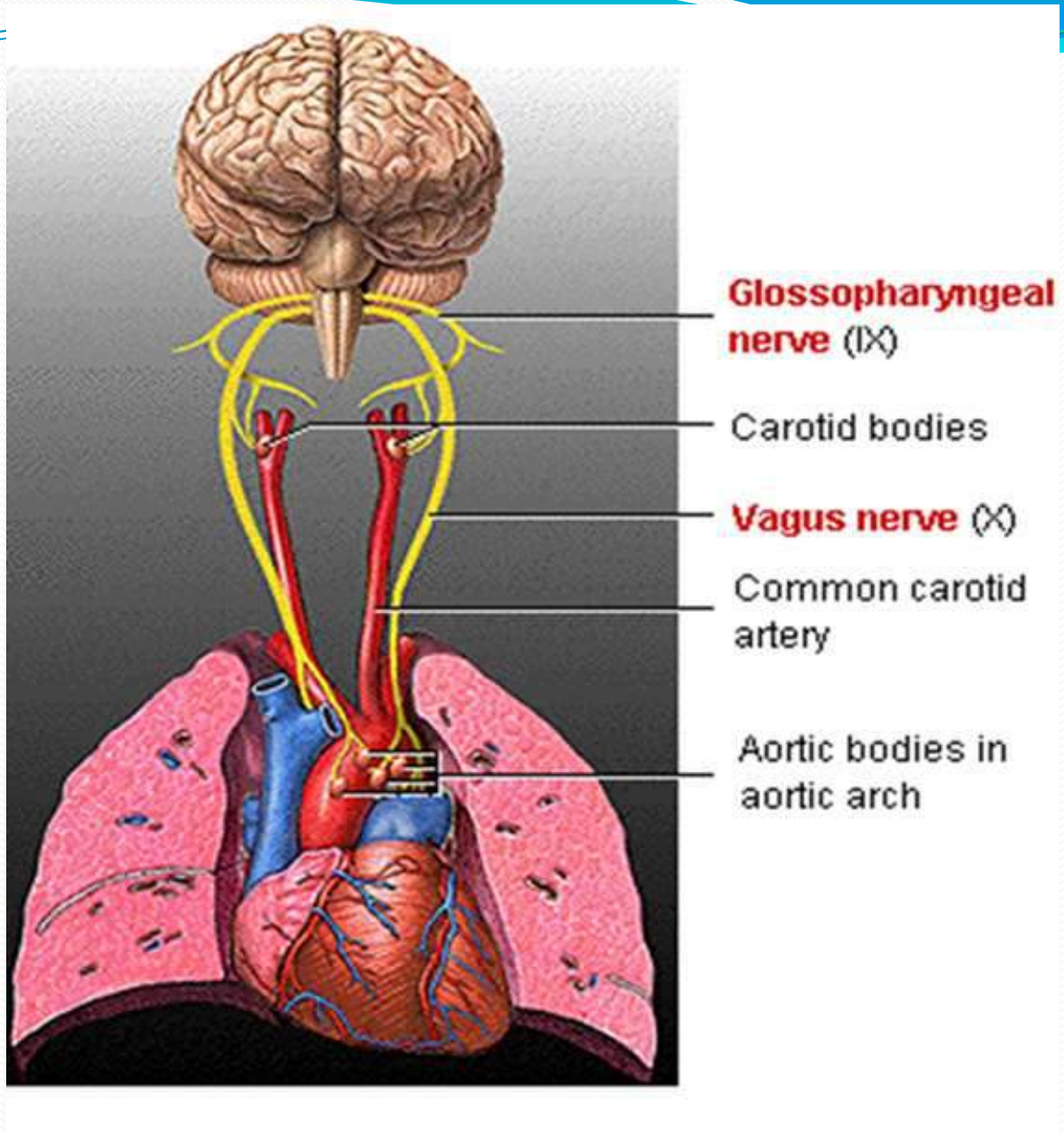
$$CO2 + H2O \leftrightarrow H+ + HCO3-$$

Increases in Pa co 2 elevate CSF hydrogen ion concentration and activate the chemoreceptors. Secondary stimulation of the adjacent respiratory medullary centers increases alveolar ventilation and reduces Pa co 2 back to normal.

2. Peripheral Sensors

- Peripheral chemoreceptors include the **carotid bodies** (at the bifurcation of the common carotid arteries) and the **aortic bodies** (surrounding the aortic arch). The carotid bodies are the principal **peripheral chemoreceptors in humans and are sensitive to changes in Pa o 2 , Pa co 2 , pH, and arterial perfusion pressure**. They interact with central respiratory centers via the **glossopharyngeal nerves, producing**

reflex increases in alveolar ventilation in response to reductions in Pa o 2 , arterial perfusion, or elevations in [H +] and Pa co 2 . Peripheral chemoreceptors are also stimulated by cyanide, doxapram, and large doses of nicotine. In contrast to central chemoreceptors, which respond primarily to Pa co 2 (really [H +]), **the carotid bodies are most sensitive to Pa o 2**


Glossopharyngeal nerve (IX)
Carotid bodies
Vagus nerve (X)
Common carotid artery
Aortic bodies in aortic arch

3-Lung Receptors

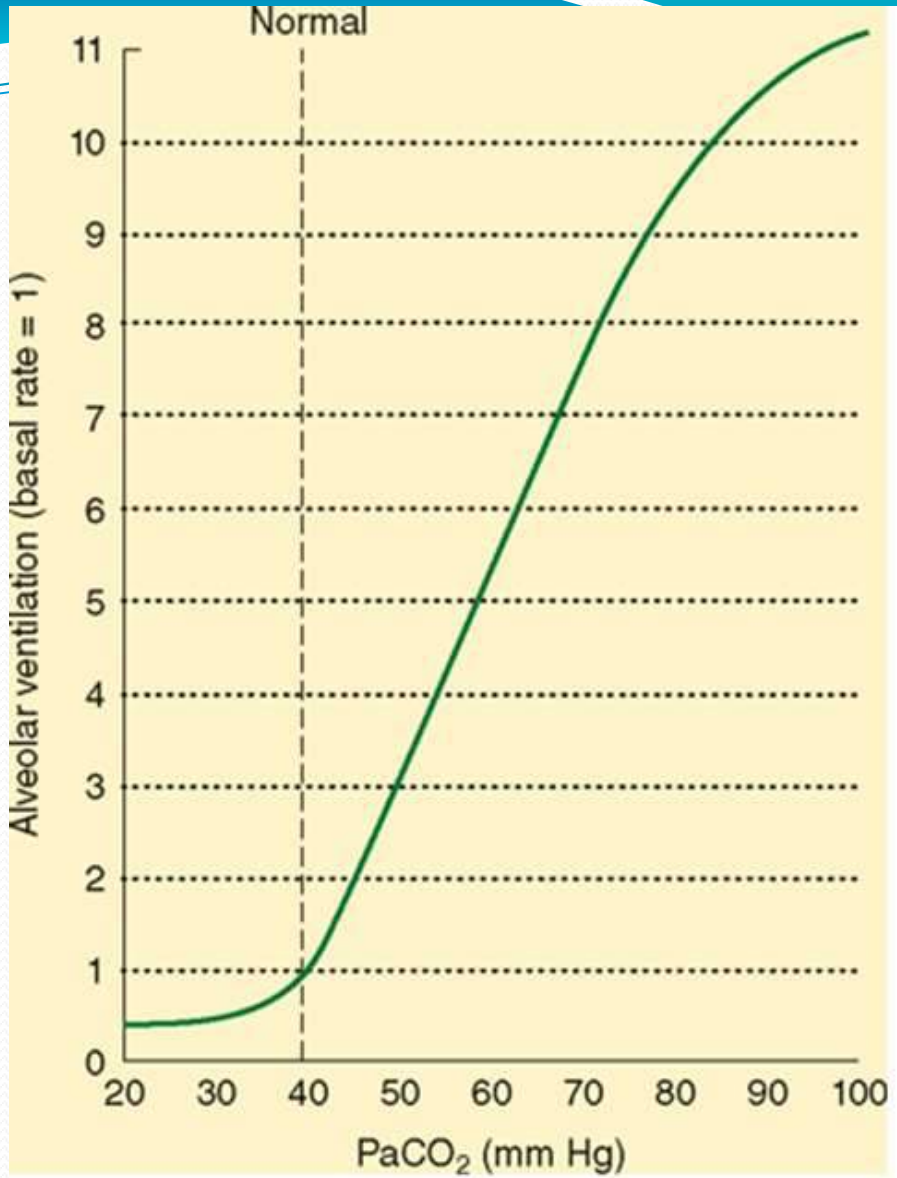
A- **Stretch receptors** are distributed in the smooth muscle of airways; they are responsible for inhibition of inspiration when the lung is inflated to excessive .

B-**Irritant receptors** in the tracheobronchial mucosa react to noxious gases, smoke, dust, and cold gases; activation produces reflex increases in respiratory rate, bronchoconstriction, and coughing.

C-**juxta-capillary receptors** are located in the interstitial space within alveolar walls; these receptors induce dyspnea in response to expansion of interstitial space volume and various chemical mediators following tissue damage.

4-Other Receptors

These **include various muscle and joint receptors on pulmonary muscles and the chest wall**. Input from these sources is probably important during exercise and in pathological conditions associated with decreased lung or chest compliance



Source: Butterworth JF, Mackey DC, Wasnick JD: *Morgan & Mikhail's Clinical Anesthesiology*, 5th Edition: www.accessmedicine.com

Effects of Anesthesia on the Control of Breathing

- The most important effect of most general anesthetics on breathing is:
- 1-a tendency to promote hypoventilation. The mechanism is probably dual: central depression of the chemoreceptor and depression of external intercostal muscle activity.
- 2-The magnitude of the hypoventilation is generally proportional to anesthetic depth. With increasing depth of anesthesia, the slope of the Pa co 2 /minute ventilation curve decreases, and the apneic threshold increases. This effect is at least partially reversed by surgical stimulation.
- 3-The peripheral response to hypoxemia is even more sensitive to anesthetics than the central CO 2 response and is nearly abolished by even sub anesthetic doses of most inhalation agents (including nitrous oxide) and many intravenous agents.

Carbon dioxide narcosis. Loss of consciousness caused by severe **hypercapnia**, i.e. arterial *P*CO2 exceeding approximately (200 mmHg). Thought to be due to a profound fall in pH of **CSF** (under 6.9). Increasing central depression is seen at arterial *P*CO2 greater than (100 mmHg), and CSF pH under 7.1. Other features of hypercapnia may be present. Used by **Hickman** in 1824 to enable painless surgery on animals.

Anesthesia for Patients with Respiratory Disease

Obstructive Pulmonary Disease:

ASTHMA

Asthma is a common disorder, affecting 5% to 7% of the population. Its primary **characteristic is airway (bronchiolar) inflammation and hyper reactivity in response to a variety of stimuli**. Clinically, asthma is manifested by episodic attacks of **dyspnea, cough, and wheezing. Airway obstruction, which is generally reversible, is the result of bronchial smooth muscle constriction, edema, and increased secretions**. Classically, the obstruction is precipitated by a variety factors like

- 1- airborne substances, including pollens, dusts, pollutants, and various chemicals.
- 2-Some patients also develop bronchospasm following ingestion of aspirin, nonsteroidal anti-inflammatory agents, sulfites, or tartrazine and other dyes.
- 3-Exercise, emotional excitement, and viral infections

Restrictive lung disease

- These conditions are different, in that they cause the loss of lung tissue, impair the lung's ability to expand when inhaling, and also lead to less efficiency in transferring oxygen and carbon dioxide between your bloodstream and your airways. Lung cancer and pneumonia are two kinds of restrictive lung diseases
- **Anesthetic Considerations:**
- 1-Patients with poorly controlled asthma or wheezing at the time of anesthesia induction have a higher risk of perioperative complications.
- 2-controlled asthma has not been shown to be a risk factor for intraoperative or postoperative complications. A thorough history and physical examination are of critical importance. The patient should have no or minimal dyspnea, wheezing, or cough.

3-The most critical time for asthmatic patients undergoing anesthesia is during instrumentation of the airway. General anesthesia by mask or regional anesthesia will circumvent this problem, but neither eliminates the possibility of bronchospasm.

4-some clinicians believe that high spinal or epidural anesthesia may aggravate bronchoconstriction by blocking sympathetic tone to the lower airways (T1–T4) and allowing unopposed parasympathetic activity.

5-Pain, emotional stress, or stimulation during light general anesthesia can precipitate bronchospasm.

6-Drugs often associated with histamine release (eg, atracurium, morphine) should be avoided or given very slowly when used

The goal of any general anesthetic is a smooth induction and emergence, with anesthetic depth adjusted to stimulation

Chronic Obstructive Pulmonary Disease(COPD):

defined as a disease state characterized by airflow limitation that is not fully reversible. The chronic airflow limitation of this disease is due to a mixture of small and large airway disease (**chronic bronchitis/bronchiolitis**) and parenchymal destruction (**emphysema**), with representation of these two components varying from patient to patient**.**

Lung Volumes And Capacities

Pulmonary ventilation can be recorded by using the *spirometer* and the process called *spirometry* by which volume of air that is moved in and out of the lung can be recorded. The volumes and capacities of lungs are:

1-The tidal volume (TV):

Is the volume of air inspired or expired with each normal breath and it is about **500 ml** in average young adult man.

2-The inspiratory reserve volume (IRV):

Is the extra volume of air that can be inspired over and beyond tidal volume and it is about **3000 ml.**

3-The expiratory reserve volume (ERV):

Is the amount of air that can be expired after the normal tidal expiration, which is about **1100 ml.**

4-The residual volume (RV):

Is the volume of air still remaining in the lungs after the most forceful expiration, which is about **1200 ml.** This is important because it provides air in the alveoli to aerate the blood even between breaths.

- **Anesthetic Considerations:**

- Patients with COPD should be prepared prior to elective surgical procedures in the same way as patients with asthma.

- Many people with chronic obstructive pulmonary disease have a low partial pressure of oxygen in the blood. Treatment with supplemental oxygen may improve their well-being; alternatively, in some this can lead to the adverse effect of elevating the carbon dioxide content in the blood (hypercapnia) to levels that may become toxic due to peripheral receptors depression.

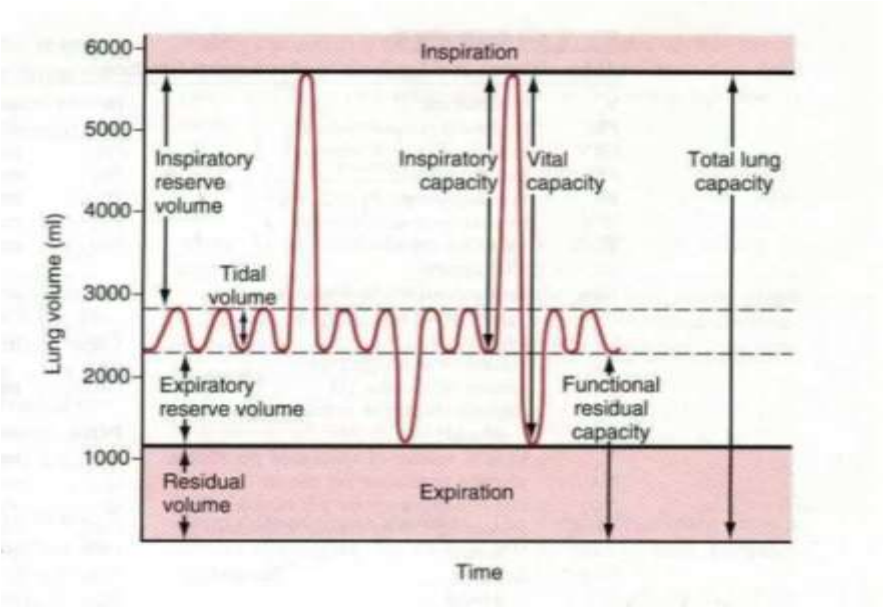
-

5-The inspiratory capacity (IC) = TV +IRV = **500 +3000 = 3500 ml.**

6- The functional residual capacity (FRC)=ERV + RV = 1100 + 1200 = **2300 ml.**

7- The vital capacity (VC)= IRV + TV + ERV = 3000 + 500 + 1100 = **4600 ml.**

8- The total lung capacity (TLC)= VC + RV = 4600 + 1200 = **5800 ml.**



Dead space:

Anatomical Dead Space : the volume of the conducting airways in which no gas exchange takes place, or that part of the inspired volume which is expired unchanged at the beginning of expiration, or "the volume of gas exhaled before CO2 reaches the alveolar plateau

Factors Affecting Anatomical Dead Space

1. **Body Size** anatomical dead space ↑with increasing body size
2. **Age** ↑with increasing age .
3. **Lung Volume** anatomical dead space ↑with increasing lung volume
4. **Posture** anatomical dead space ↓with supine
5. **Hypoxia**: bronchoconstriction ↓ anatomical dead space

7. **Drugs and Anaesthetic Gases** bronchodilatation ↑ anatomical dead space

8. **Lung Disease -** emphysema ↑ anatomical dead space

loss or excision of lung ↓ anatomical dead space

9. **Endotracheal Intubation** ↓ anatomical dead space~ 50%

10. **Position of the Jaw & Neck -** increases with jaw protrusion

Alveolar Dead Space : that part of the inspired gas which passes through the anatomical dead space and enters alveoli, however is ineffective in arterializing mixed venous blood and does not represent the actual volume of these alveoli the cause is failure of adequate perfusion of the alveoli to which gas is distributed.

Factors Affecting Alveolar Dead Space

1. **Age** Alveolar Dead Space ↑with increasing age

2. **Pulmonary Arterial Pressure** decrease in PA pressure (eg. hypotension) decreases perfusion to the upper parts of the lung & ↑ Alveolar Dead Space

3. **Posture :**Alveolar Dead Space increases in the upright and lateral positions due to exaggeration of hydrostatic differences .

4. **Intermittent positive pressure ventilation(IPPV)** increases Alveolar Dead Space due to exaggeration of hydrostatic failure of perfusion also decreases total pulmonary blood flow.

5. **Tidal Volume -** as VT increases, so Alveolar Dead Space increases but the ratio remains constant

6. **Oxygen -** hyperoxic ↑ Alveolar Dead Space . hypoxic ↓ Alveolar Dead Space

7. **Anaesthetic Gases** ↑ Alveolar Dead Space but not known why!

8. **Lung Disease** ↑ Alveolar Dead Space increased in multitude of diseases

Alveolar Dead Space in healthy = 0

Physiological Dead Space

Physiological Dead Space= Total Dead Space

= **anatomical Dead Space**+ **Alveolar Dead Space**

part of the tidal volume which does not participate in gas exchange and is ineffective in arterializing mixed venous blood, because either,

1. it doesn't reach the alveoli (anatomical Dead Space)

2. it reaches alveoli with no capillary flow

3. it reaches alveoli with inadequate flow (Alveolar Dead Space)

in normal supine man

Physiological Dead Space~ anatomical Dead Space ~ 150 ml

Shunts:

One extreme form of ***V/Q*** mismatch, causing **hypoxaemia** Some venous blood passes through the lungs without equilibration with Alveolar gas. This "Venous Admixture" or "Shunt" subsequently mixes with oxygenated blood in the pulmonary veins, and has the effect of reducing PaO2 and elevating PaCO2.

While the slight rise in PaCO2 can be overcome easily by increasing the ventilation to normal alveoli, the same is not true for PaO2. Normal alveoli can blow off twice as much CO2 as usual if ventilated twice as much normal, but never saturate the blood leaving them any more than 100%.

A pure shunt causes hypoxemia that does not correct by increasing inspired oxygen.

A patient with a 50% shunt breathing 100% inspired oxygen will only get a PaO2 of about 60 mmHg, but doubling their ventilation will maintain normocarbia.

Effects Of General Anesthesia :

General anesthesia has a marked effect on ventilation/perfusion ratio V/Q relationships. Following induction of anesthesia,

1-changes in the dimensions f the thoracic cavity due to muscle relaxation, in particular loss of tonic activity in the diaphragm , lead to a 20 % reduction in Functional Residual Capacity (FRC).

2- atelectasis occurs in the dependent parts of the lung resulting in areas of lung that are perfused but not ventilation. increasing shunt and therefore impairing oxygenation.

3- General anesthesia commonly leads to low cardiac output and pulmonary hypotension, resulting in reduced perfusion to nondependent regions.

4-Without compensatory increases in ventilation, these regions of lung lead to reduced carbon dioxide elimination and give rise to the large difference between end-expiratory and arterial Pco2 commonly seen during general anesthesia.

5- during general anesthesia, there is increased scatter of V/Q ratios in different lung regions leading to impairment of both oxygenation and carbon dioxide elimination.

Pressure-Volume Relationships:

In the pulmonary physiology absolute pressure means atmospheric pressure (760 mm Hg at sea levels). The pressures and the pressure differences of the respiratory system are expressed as relative pressures to the atmospheric pressure. When it is said that alveolar pressure is zero, it means that alveolar pressure = atmospheric pressure.

If one excises animal lung and places it in a jar, one could measure the changes in volume with a spirometer through a cannula attached to the trachea. When the pressure inside the jar below atmospheric pressure, the lung expands and the change in its volume is measured and the pressure volume curve is plotted.

When there is no pressure distending the lung there is a small volume of gas in it. As the pressure in the jar is gradually reduced, the volume of the lungs increases.

Even when the pressure outside the lung is increased above the atmospheric pressure, very little further air is lost and the air is trapped in the alveoli. The volume of the air trapped in the lung is increased with age and in some respiratory diseases.

Pressure units are

mmHg= 760mmHg

kilopascals Kpa= 100KPa

bar=1bar

Air has an O2 concentration of approximately 21%; therefore, if the barometric pressure is 760 mm Hg (sea level), the partial pressure of O2 (PO2)in air is normally 160 mmHg

760 mm Hg × 0.21 = 160 mm Hg(approx.).

COMPLIANCE: the volume change per unit pressure is known as ***compliance***. The compliance of the human lung is 0.15 L/cm H2O. However, it gets stiffer (compliance smaller) as it is expanded above the normal range. Compliance is ***reduced*** when:

(1) The pulmonary venous pressure is increased and the lung becomes engorged with blood

(2) There is alveolar oedema due to insufficiency of alveolar inflation.

(3) The lung remains unventilated for a while e.g. atelectasis.

(4) Because of diseases causing fibrosis of the lung e.g. chronic restrictive lung disease

On the contrary in chronic obstructive pulmonary disease (COPD, e.g. emphysema) the alveolar walls progressively degenerate, which ***increases*** the compliance.

In asthma (hyperactive airway smooth muscle) the lung compliance is usually normal..

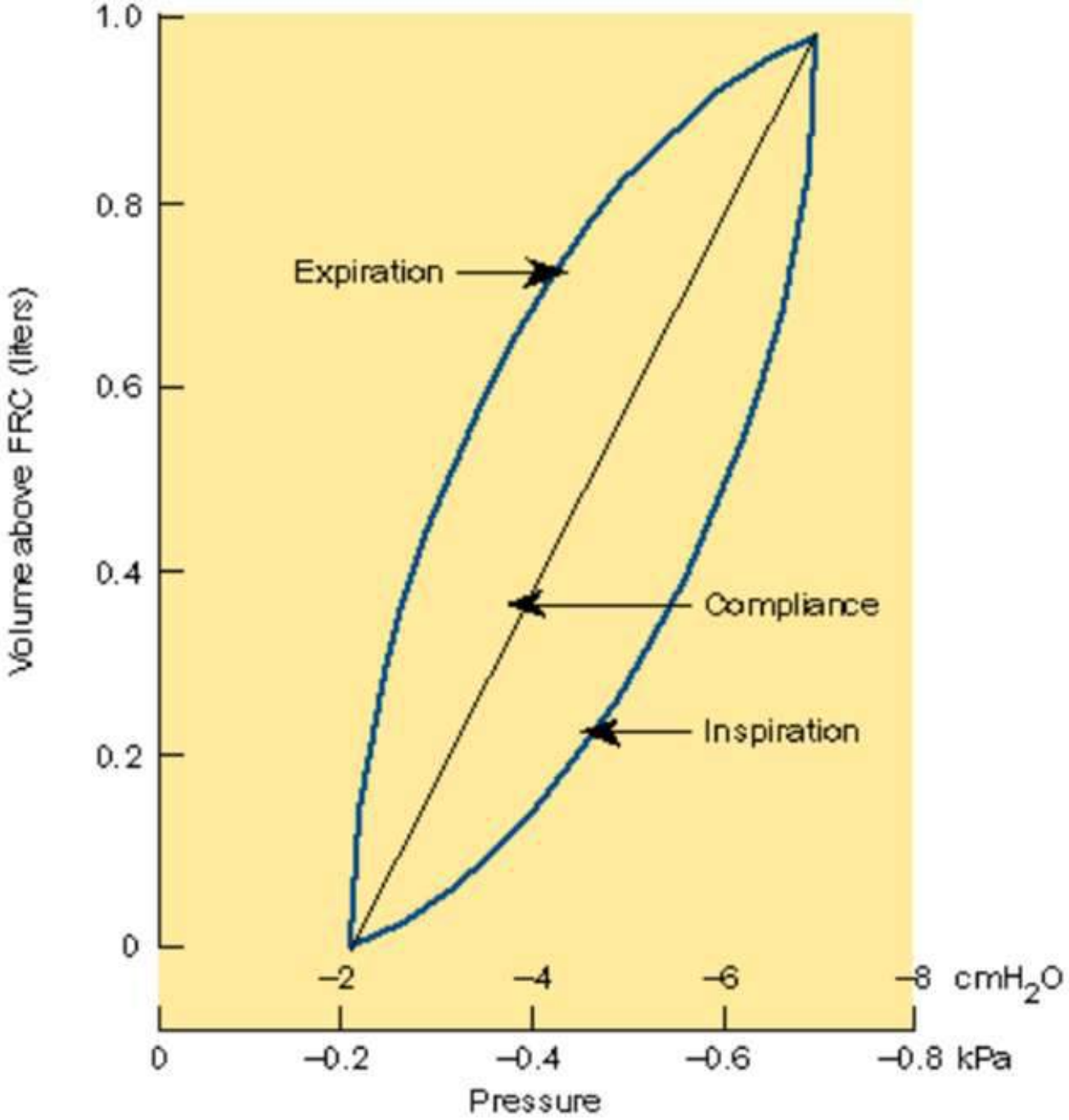
5-At the birth the lung compliance is the smallest and increased with age (until adulthood) due to increase in the size of the lungs.

CHEST WALL COMPLIANCE: Changes in chest wall compliance are less common than changes in the lung compliance:

(1) pathologic situations preventing the normal movement of the rib cage, such as, distortion of the spinal column,

(2) pathologic (cancer) or physiologic (pregnancy) reasons increasing the intra abdominal pressure,

(3) stiff chest, such as broken ribs


1.0
0.8
0.6
0.4
0.2
0
Volume above FRC (liters)
Expiration
Compliance
Inspiration
−2
−4
−6
−8 cmH2O
0
−0.2
−0.4
−0.6
−0.8 kPa
Pressure

Surface Tension: The surface tension arises because the attractive forces between adjacent molecules of the liquid are much stronger than those of between the liquid and the gas. As a result of that the liquid surface area becomes as small as possible.

At the interface between the liquid and the alveolar gas, intermolecular forces in the liquid tend to cause the area of the lining to shrink (the alveoli tend to get smaller).

The surface tension contributes a large part of the static recoil force of the lung (expiration). The surface tension changes with the surface area: The larger the area the smaller the surface tension gets.

The most important component of this liquid film is **surfactant.** It is produced by type 2 alveolar epithelial cells and its major constituent is dipalmitoyl phosphotidylcholine (DPPC), a phospholipid with detergent properties. The phospholipid DPPC is synthesised in the lung from fatty acids that are either extracted from the blood or are themselves synthesised in the lung. Synthesis is fast and there is a rapid turnover of surfactant. If the blood flow to a region of lung is restricted due to an embolus the surfactant may be depleted in the effected area. Surfactant synthesis starts relatively late in fetal life and premature babies without adequate amount of surfactant develop respiratory distress which could be life threatening

What are the advantages of having surfactant and the low surface tension?

1. It increases the compliance of the lung

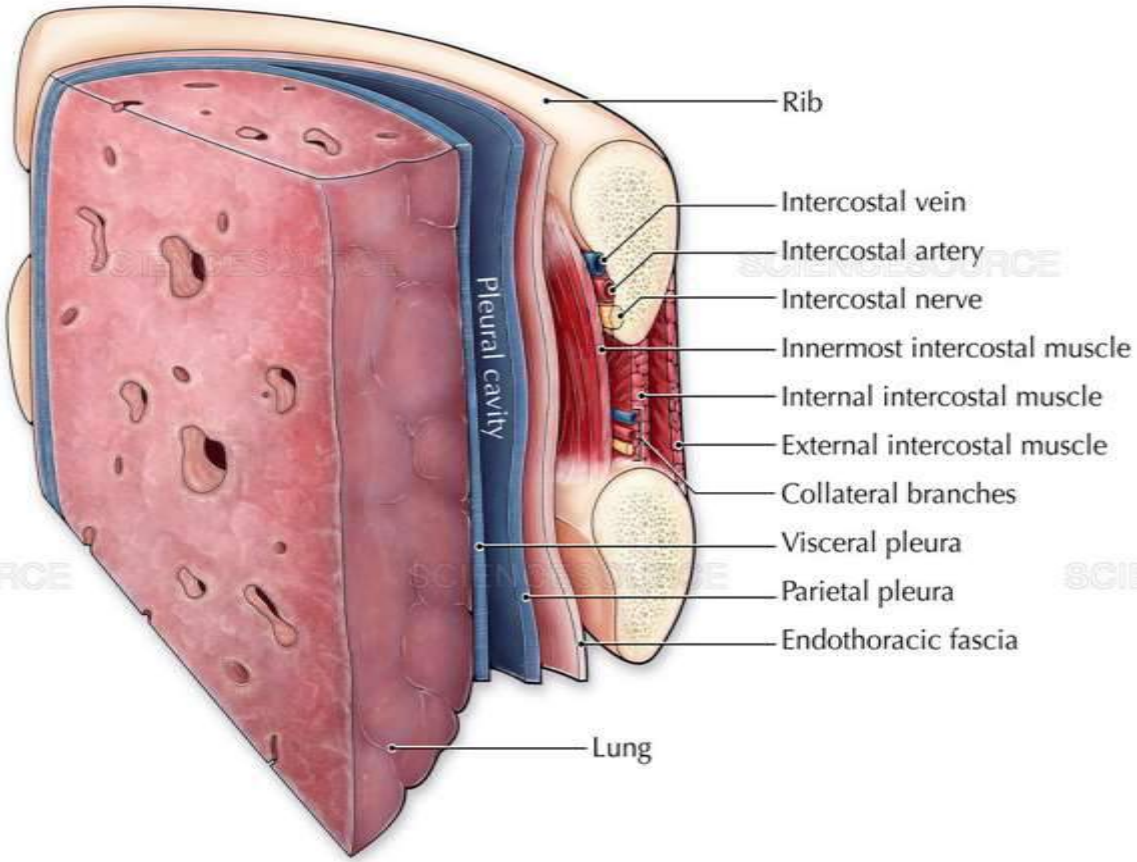
2. It reduces the work of expanding of the lung with each breath

3. It stabilizes the alveoli (thus the smaller alveoli do not collapse at the end-expiration)

4. It keeps the alveoli dry (as the surface tension tends to collapse alveoli, it also tends to suck fluid into the alveolar space from capillaries).

Pleural Pressure:

The pleura is a thin membrane which invests the lungs and lines the walls of the thoracic cavity. The side of the pleura that covers the lung is referred to as the visceral pleura and the side of the pleura which covers the chest wall is called the parietal pleura. These two sides are continuous and meet at the hilum of the lung. The two faces of the pleural membranes are directly opposed to one another, and the entire space within the pleura contains only a few milliliters of serous pleural fluid.


Rib
Intercostal vein
Intercostal artery
Intercostal nerve
Innermost intercostal muscle
Internal intercostal muscle
External intercostal muscle
Collateral branches
Visceral pleura
Parietal pleura
Endothoracic fascia
Pleural cavity
Lung

Pleural pressure is the pressure surrounding the lung, within the pleural space. During quiet breathing, the pleural pressure is negative; that is, it is below atmospheric pressure.

The size of the lung is determined by the difference between the alveolar pressure and the pleural pressure, or the transpulmonary pressure. The bigger the difference, the bigger the lung.

As a result of gravity, in an upright individual the pleural pressure at the base of the lung base is greater (less negative) than at its apex; when the individual lies on his back, the pleural pressure becomes greatest along his back. During active expiration, the abdominal muscles are contracted to force up the diaphragm and the resulting pleural pressure can become positive. Positive pleural pressure may temporarily collapse the bronchi and cause limitation of air flow.

Transpulmonary pressure :

is the difference between the alveolar pressure and the intrapleural pressure in the pleural cavity. During human ventilation, air flows because of pressure gradenit

$P_{tp} = P_{alv} - P_{p}$. Where P_{tp} is transpulmonary pressure, P_{alv} is alveolar pressure, and P_{ip} is intrapleural pressure.

Physiology

Since atmospheric pressure is relatively constant, pressure in the lungs must be higher or lower than atmospheric pressure for air to flow between the atmosphere and the alveoli. If 'transpulmonary pressure' = 0 (alveolar pressure = intrapleural pressure), such as when the lungs are removed from the chest cavity or air enters the intrapleural space (apnumothorax). Under physiological conditions in inspiration the transpulmonary pressure is always positive; intrapleural pressure is always negative and relatively large, while alveolar pressure moves from slightly negative to slightly positive as a person breathes.

Airway Resistance to Gas Flow:

Gas flow in the lung is a mixture of laminar and turbulent flow. Laminar flow can be thought of as consisting of concentric cylinders of gas flowing at different velocities; velocity is highest in the center and decreases toward the periphery.

Turbulent flow is characterized by

1-random movement of the gas molecules down the air passages.

2-Turbulence generally occurs at high gas flows, at sharp angles or branching points, and in response to abrupt changes in airway diameter.

turbulent or laminar flow occurs can be predicted by the Reynolds number, which results from the following equation:

$$\text{Reynolds number} = \frac{\text{Linear velocity} \times \text{Diameter} \times \text{Gas density}}{\text{Gas viscosity}}$$

A low Reynolds number (<1000) is associated with laminar flow, whereas a high value (>1500) produces turbulent flow. Laminar flow normally occurs only distal to small bronchioles (<1 mm). Flow in larger airways is probably turbulent.

A helium–O 2 mixture not only is less likely to cause turbulent flow but also reduces airway resistance when turbulent flow is present

Forced expiratory volume (FEV). Volume of gas forcibly exhaled from full inspiration,

The ratio of the forced expiratory volume in the first second of exhalation (FEV 1) to the total forced vital capacity (FVC) is proportional to the degree of airway obstruction. is then called (FEV1) Normally, FEV 1 /FVC which may be measured using a **spirometer**. FEV1 /FVC provides important information about airway resistance FEV1 /FVC Reduced in obstructive lung disease, In restrictive disease, FEV1 may be normal, but **FVC** is reduced

Effects of Anesthesia on Gas Exchange:

Abnormalities in gas exchange during anesthesia are common. They include

1-increased dead space, hypoventilation. There is increased scatter of V/Q ratios.

2-General anesthesia increases venous admixture to 5% to 10%, and increased intrapulmonary shunting, probably as a result of atelectasis and airway collapse in dependent areas of the lung.

3-Inhalation agents, including nitrous oxide, also can inhibit **hypoxic pulmonary vasoconstriction**

OXYGEN CASCADE & TRANSPORT:

The purpose of the cardio-respiratory system is to extract oxygen from the atmosphere and deliver it to the mitochondria of cells.

OXYGEN CASCADE :

the oxygen cascade describes the process of declining oxygen tension from atmosphere to mitochondria**.**

When air down through the body to the cell, oxygen is diluted down, extracted or otherwise lost , so that at cellular level the PO2 may only be 3 or 4mmHg.

With every breath, the inspired gas mixture is humidified at 37°C in the upper airway. The inspired tension of O2 (PiO2) is therefore reduced by the added water vapor. Water vapor pressure is dependent only upon temperature and is 47 mmHg at 37°C. In humidified air, the normal partial pressure of O2 at sea level is 149 mm Hg:

$$(760 - 47) \times 0.21 = 149 \text{ mmHg(approx.).}$$

The general equation is $PiO_2 = (Pb - PH_2O) \times FiO_2$

Air consists of oxygen and nitrogen, but as gas moves into the alveoli, a third gas, carbon dioxide, is present. The alveolar carbon dioxide level . The alveolar partial pressure of oxygen PAO2 can be calculated from the following equation: PAO2 =PIO2 - PaCO2/R. R is the respiratory quotient, which represents the amount of carbon dioxide excreted for the amount of oxygen utilized, and this in turn depends on the carbon content of food (carbohydrates high, fat low). For now let us assume that the respiratory quotient is 0.8, the PAO2 will then be 149-(40/0.8) = 100mmHg (approx).

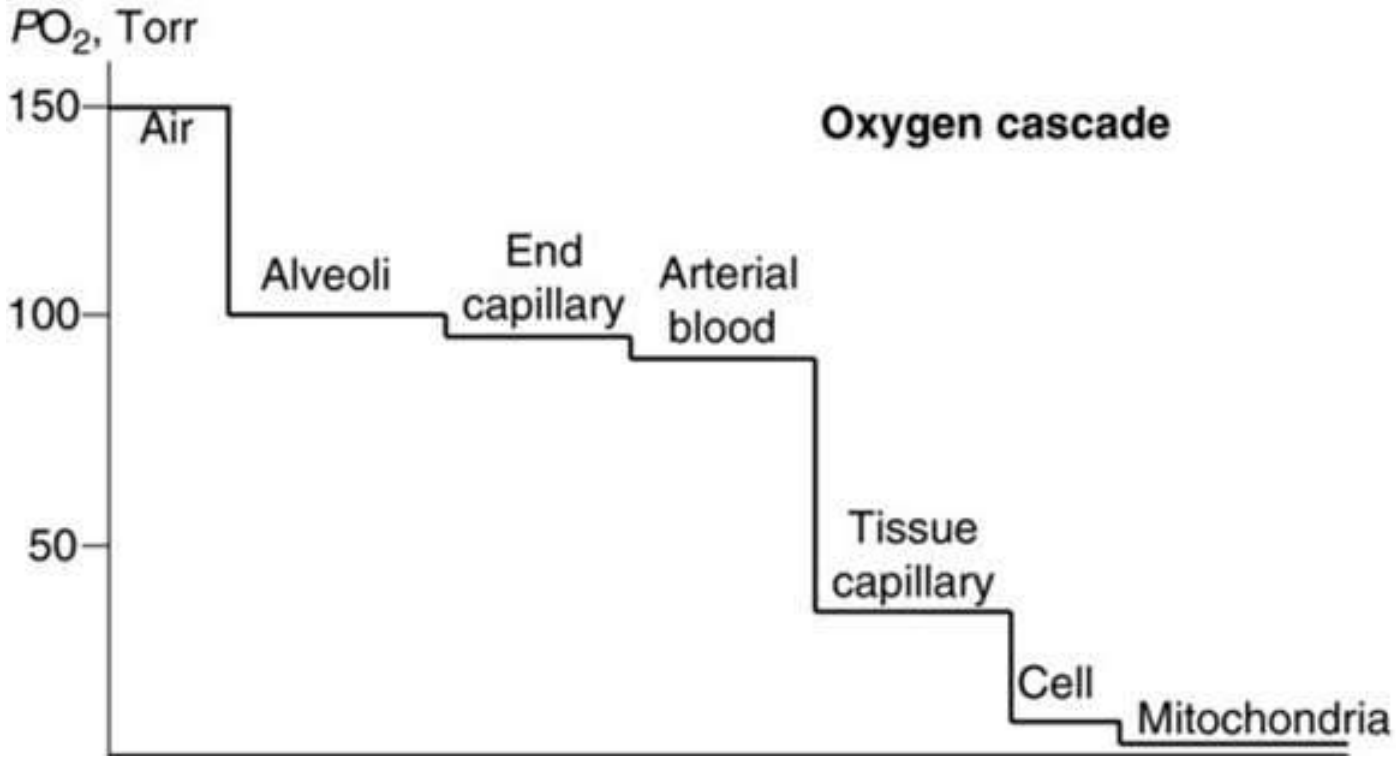
The next step is the movement of oxygen from alveolus to pulmonary capillary (where the partial pressure of oxygen in mixed venous blood, PVO2, is approx (47mmHg) , and as you would expect, there is a significant gradient, usually 5-10 mmHg, explained by small ventilation perfusion abnormalities and the physiologic shunt.

Oxygen is progressively extracted from the capillary network, may only be 3 or 4mmHg.

such that the partial pressure of oxygen in mixed venous blood, PVO2, is approx 47mmHg

- **The amount of oxygen in the bloodstream is determined by the:-**

1. Oxygen binding capacity of Hb
2. The serum hemoglobin level,
3. The percentage of this hemoglobin saturated with oxygen,
4. The cardiac output
5. amount of oxygen dissolved .


PO_2, Torr
150
100
50
Air
Alveoli
End capillary
Arterial blood
Tissue capillary
Cell
Mitochondria
Oxygen cascade

- **Oxygen Transport:**
- Oxygen is carried in the blood in two forms:

1. dissolved in plasma
2. bound to hemoglobin.

Dissolved oxygen obeys Henry's law – the amount of oxygen dissolved is proportional to the partial pressure. For each mmHg of PO2 there is 0.003 ml O2/dl (100ml of blood). The solubility coefficient of oxygen in plasma is 0.003, Therefore, with a Pao2 of 100 mmHg, only 0.3 mL of O2 is transported dissolved per deciliter of plasma.
97-98% Bound to Hb. Hemoglobin is the main carrier of oxygen. Each gram of hemoglobin can carry 1.34ml of oxygen. This means that with a hemoglobin concentration of 15g/dl, the O2 content is approximately 20ml/100ml. With a normal cardiac output of 5.6 L/min in men and 4,9 L/min in women, the delivery of oxygen to the tissues at rest is approximately 1000 ml/min: a huge physiologic reserve.

Hemoglobin has 4 binding sites for oxygen, and if all of these in each hemoglobin molecule were to be occupied, then the oxygen capacity would be filled or saturated. The amount of oxygen in the blood is thus related to the oxygen saturation of hemoglobin.

Oxygen Saturation:

Oxygen Saturation is the Ratio of oxygen bound to Hb compared to total amount that can be bound with Oxygen**.**

Up to four oxygen molecules can bind to one hemoglobin (Hb).

O2 Content in blood :

The sum of O2 carried on Hb and dissolved in plasma

- 97-98% Carried in Combination With Hb
- 2% Dissolved in Plasma

We can calculate the oxygen content of blood where the PO2 is 100mmHg, when the hemoglobin concentration is 15g/L :

O2 content in 100 ml blood (if normal adult with Hb 15 gm/dl) ~ 20 ml/dl

(20 ml as OxyHb + 0.3 ml in plasma)

Hemoglobin:

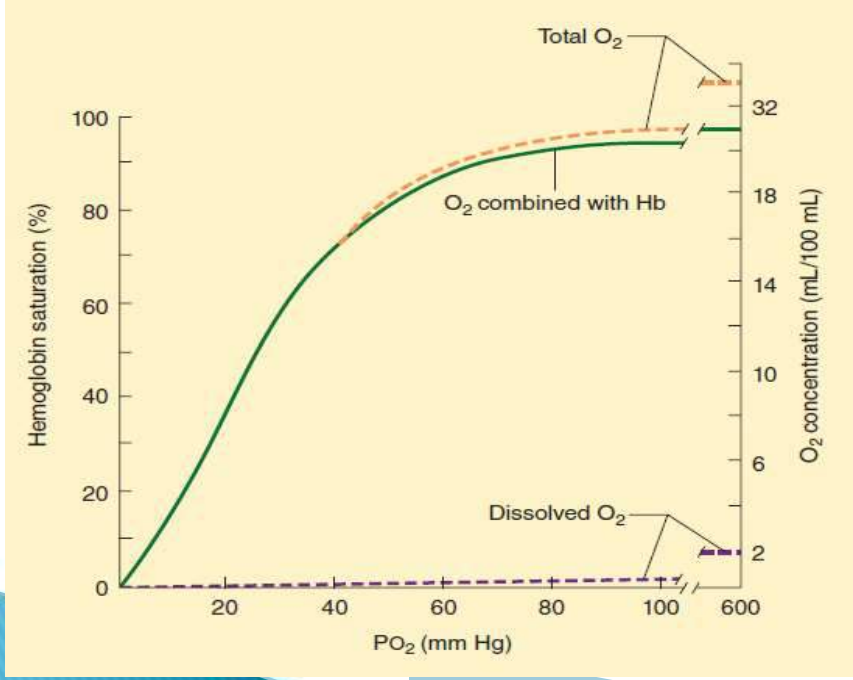
Hemoglobin is a complex molecule consisting of:-

- four heme. Heme is an iron–porphyrin compound that is have four O2 -binding sites
- four protein subunits.

Each gram of hemoglobin can theoretically carry up to 1.34 mL of O2 .

Hemoglobin Dissociation Curve

Represent the relationship between the partial pressure of oxygen and the saturation of oxygen.



The complex interaction between the hemoglobin subunits results in nonlinear (an elongated S Sigmoid shape) binding with O2.

Combination Of 1st Heme with O2 increases affinity of 2nd Heme and **so on** The last reaction is responsible for the accelerated binding between 25% and 100% saturation.

At about 90% saturation, the decrease in available O2 receptors flattens the curve until full saturation is reached.

P 50 , the O2 tension at which hemoglobin is 50% saturated .it measure affinity of haemoglobin for oxygen .

Normal P50 value is 26.7 mm Hg.

As P50 increases/decreases, we say the "curve has shifted". To right or left .

– P50 less than 27: Shift to the left.

– P50 greater than 27: Shift to the right.

Po2	**So2**
27	50
40	75
60	90
250	100

- **Factors Influencing the Hemoglobin Dissociation Curve:**
- Important factors altering O2 binding include

1. hydrogen ion concentration,
2. CO2 tension,
3. temperature

Each factor shifts the dissociation curve either to the right (increasing P 50) or to the left (decreasing P 50).

A rightward shift in the oxygen–hemoglobin dissociation curve lowers O2 affinity, displaces O2 from hemoglobin, and makes more O2 available to tissues; (At cellular site)

left ward shift increases hemoglobin's affinity for O2 , reducing its availability to tissues. (the lower CO2 content in pulmonary capillaries increases hemoglobin's affinity for O2 again, facilitating O2 uptake from alveoli.) The normal P 50 in adults is 26.7 mm Hg (3.4 kPa).

Abnormal Ligands & Abnormal Forms of Hemoglobin's

Carbon monoxide, cyanide, nitric acid, and ammonia can combine with hemoglobin at O2 –binding sites. They can displace O2 and shift the saturation curve to the left . Carbon monoxide is particularly potent, having 200–300 times the affinity of O2 for hemoglobin, combining with it to form carboxyhemoglobin. Carbon monoxide decreases hemoglobin's O2 -carrying capacity and impairs the release of O2 to tissues

Arterial Oxygen Content:

The total O2 content of blood is the sum of that in solution plus that carried by hemoglobin .

Total O2 content is expressed by the following equation:

Arterial Oxygen Content CaO2 (ml/dL) = (SaO2 x Hb x 1.34) + (PO2 x0.003)

where Hb is hemoglobin concentration in g/dL blood,

and SaO2 is hemoglobin saturation at the given PO2 .

Using the above formula and a hemoglobin of 15 g/dL, the normal O2 content for both arterial and mixed venous blood and the arteriovenous difference can be calculated as follows:

$Cao2 = (0.003 \times 100) + (0.97 \times 15 \times 1.34) = 20$ mL/dL blood

$Cvo2 = (0.003 \times 40) + (0.75 \times 15 \times 1.34) = 15$ mL/dL blood

$Cao2 - Cvo2 = 5$ mL/dL blood

Oxygen Transport :

O2 transport is dependent on both respiratory and circulatory function. Total O2 delivery (Do2) to tissues is the product of arterial O2 content and cardiac output:

O2 delivery = 20 mL O2/dL blood × 50 dL per blood/min = 1000 mL O2/min

Body normally consumes only 25% of the O2 carried on hemoglobin(250mL)

O2 delivery.

Oxygen Stores:

The concept of O2 stores is important in anesthesia. When the normal flux of O2 is interrupted by apnea existing O 2 stores are consumed by cellular metabolism; if stores are depleted, hypoxia and eventual cell death follow. This amount includes :

1-The O2 remaining in the lungs

2- That bound to hemoglobin and myoglobin

3-That dissolved in body fluids.

The O2 contained within the lungs at FRC (initial lung volume during apnea), therefore, becomes the most important source of O2 . Of that volume, however, probably only 80% is usable. Apnea in a patient previously breathing room air leaves approximately 480 mL of O 2 in the lungs. (If fraction of inspired oxygen (FiO2) = 0.21 and FRC = 2300 mL, O2 content = FiO2 × FRC.) The metabolic activity of tissues rapidly depletes this reservoir severe hypoxemia usually occurs within 90 sec. The onset of hypoxemia can be delayed by increasing the FiO2 prior to the apnea. Following ventilation of O2 ; this delays hypoxemia following apnea for 4–5 min. This concept is the basis for preoxygenation prior to induction of anesthesia.

2. Carbon Dioxide;

Carbon dioxide is transported in blood in three forms:

1. dissolved in plasma,
2. as bicarbonate
3. combine with proteins in the form of carbamino compounds .

The sum of all three forms is the total CO2 content of blood

Dissolved Carbon Dioxide:

Carbon dioxide is more soluble in blood than O2 ,

Bicarbonate:

In aqueous solutions, CO 2 slowly combines with water to form carbonic acid and bicarbonate, according to the following reaction:

$H2O + CO2 \leftrightarrow H2CO3 \leftrightarrow H+ + HCO3-$

In plasma, although less than 1% of the dissolved CO2 undergoes this reaction, the presence of the enzyme **carbonic anhydrase** within erythrocytes and endothelium greatly accelerates the reaction. As a result, bicarbonate represents the largest fraction of the CO 2 in blood .

Carbamino Compounds:

Carbon dioxide can react with amino groups on proteins, At physiological pH, only a small amount of CO2 is carried in this form, mainly as carbaminohemoglobin. Deoxygenated hemoglobin (deoxyhemoglobin) has a greater affinity (3.5 times) for CO2 than does oxyhemoglobin.

Carbon Dioxide Stores:

Carbon dioxide stores in the body are large (approximately 120 L in adults) and primarily in the form of dissolved CO 2 and bicarbonate.

Hypoxia :

Hypoxia is defined as lack of oxygen at tissue level.

Anoxia :

Anoxia is defined as complete absence of oxygen in the tissues

Types of hypoxia

A. Hypoxic hypoxia
B. Anaemic hypoxia
C. Stagnant(ischaemic) hypoxia
D. Histotoxic hypoxia

A. Hypoxic hypoxia

- It is characterized by low arterial pO_2 when oxygen carrying capacity of blood and rate of blood flow to tissues are normal or elevated
- It is characterised by

i. Low arterial pO_2
ii. Low arterial % O_2 saturation of haemoglobin
iii. Low A-V pO_2 difference

Hypoxic hypoxia.

Causes:

1) Low pO_2 of inspired air
2) Decreased pulmonary ventilation
3) Defect in exchange of gases
4) Venous arterial shunts

B.Anaemic hypoxia

In anaemic hypoxia arterial pO_2 is normal but the amount of haemoglobin available to carry oxygen is reduced.

Causes :

i. Anemia

ii. Hemorrhage

iii. Conversion of haemoglobin to some abnormal form

Anaemic hypoxia

- Characterized by:

i. Normal arterial pO_2

ii. arterial oxyhemoglobin are reduced

iii. A–V pO_2 difference is normal

C. Stagnant(ischemic) Hypoxia

Blood flow to the tissue is so low that adequate oxygen is not delivered to them .despite normal arterial pO_2 and haemoglobin concentration

Causes :

i. Circulatory failure

ii. Haemorrhage via baroreceptors leading to reflex vasoconstriction

Stagnant hypoxia

Characterized by:

i. Normal arterial pO_2

ii. Normal arterial hemoglobin content

iii. normal arterial % O_2 saturation of haemoglobin

iv. A–V difference more than normal

D.Histotoxic hypoxia

- Amount of oxygen delivered to the tissues is adequate but because of the action of toxic agents the tissues cannot make use of the oxygen supplied to them.
- **Cause :** *Cyanide poisoning* causing damage to enzyme cytochrome oxidase.
- **Characterized by:**

i. Normal pO_2

ii. A-V pO_2 difference is less than normal

Clinical features of hypoxia

1) Hyperventilation is seen in all types of hypoxia except anemic hypoxia.
2) In all types of hypoxia the first symptoms are like that of alcohol overdose(drowsiness, depression/excitement, emotional outburst).

If oxygen saturation of hemoglobin falls below 60% there unconsciousness within 20 seconds, causing death in 4-5 minutes.

3) Severe hypoxia(except anemic) causes increase in heart rate and systemic blood pressure.
4) Associated symptoms- nausea, vomiting and anorexia

Treatment of hypoxia

1. Treatment of the underlying cause- depending upon the type of hypoxia
2. Oxygen therapy-

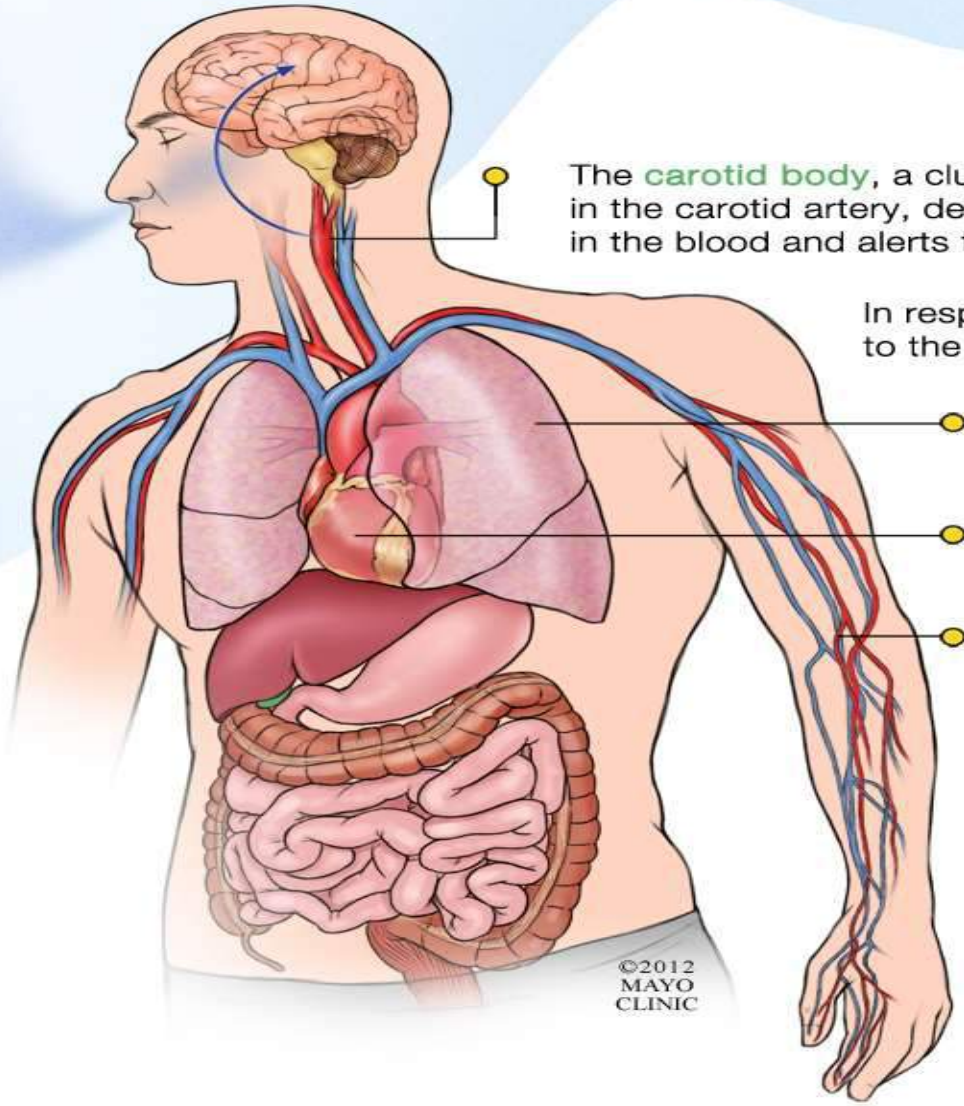
i. Inhalation of 100% pure oxygen

ii. Hyperbaric oxygen therapy

Effects of Hypoxia

(hi-pok´se-ah)
: a condition in which the body as a whole or a region of the body is deprived of adequate oxygen supply.
/hy·pox·ia/ - noun

Low oxygen pressure at high altitude



The carotid body, a cluster of specialized cells in the carotid artery, detects low oxygen levels in the blood and alerts the brain.

In response, the brain sends signals to the rest of the body to...

- increase breathing rate and constrict vessels in the lung
- increase heart rate
- dilate peripheral blood vessels in arms, legs, hands, and feet

CYANOSIS

Bluish discoloration of skin and/or mucus membrane due to the presence of at least 5gm of reduced haemoglobin per 100ml of blood in capillaries.

Sites to be examined:

i. Mucus membrane of undersurface of tongue
ii. Lips
iii. Ear lobes
iv. Nail beds
v. Tip of nose

Types of cyanosis:

1. **Central cyanosis**– Due to a circulatory or ventilatory problem that leads to poor blood oxygenation in the lungs.

It develops when arterial saturation of blood with oxygen is ≤85%. Cyanosis may not be detected until saturation is 75% in dark-skinned individuals

2. **Peripheral cyanosis**–Due to inadequate circulation.

All factors contributing to central cyanosis can also cause peripheral symptoms to appear, however peripheral cyanosis can be observed without there being heart or lung failures.

Causes of cyanosis

1. Hypoxic hypoxia
2. Stagnant hypoxia
3. Polycythemia
4. Exposure to mild cold(approx 20^0 C) produces cyanosis while exposure to severe cold (appprox. 10^0 C or below) does not produce cyanosis.

categories of lung disease:

Obstructive and restrictive Pulmonary Disease:

Obstructive and restrictive breathing are the two most common abnormal patterns, as determined by PFTs.

Obstructive lung diseases are the most common form of pulmonary dysfunction. They include:

asthma, emphysema, chronic bronchitis, cystic fibrosis, and bronchiolitis.

The primary characteristic of these disorders is:

- resistance to airflow.
- (forced expiratory volume <70% [FEV 25–75%]).

in adult males and females are normally >2 and >1.6 L/sec, respectively. As the disease progresses, both forced expiratory volume in 1 sec (FEV 1) and the FEV 1 /FVC (forced vital capacity) ratio are less than 70% of the predicted values.

- Elevated airway resistance and air trapping lead to:

1. Increase the work of breathing
2. respiratory gas exchange is impaired because of ventilation/ perfusion ($\dot{V}/\dot{Q}$) imbalance.
3. residual volume and total lung capacity (TLC) increase.
4. Wheezing is a common finding and represents turbulent airflow.

It is often absent with mild obstruction that may be manifested initially only by prolonged exhalation.

Condition	Main site	Major changes	Causes	Symptoms
hronic bronchitis	Bronchus	Hyperplasia and hyper secretion of mucus glands	Tobacco smoking and air pollutants	Productive cough
Bronchiolitis	Bronchiole	Inflammatory scarring and bronchiole obliteration	Tobacco smoking and air pollutants	Cough, dyspnea
Bronchiectasis	Bronchus	Dilation and scarring of airways	Persistent severe infections	Cough, purulent sputum and fever
Asthma	Bronchus	• Smooth muscle hyperplasia • Excessive mucus • Inflammation • Constriction	Immunologic or idiopathic	Episodic wheezing, cough and dyspnea

ASTHMA

Asthma is a common disorder, affecting 5% to 7% of the population. Its primary characteristic is

- airway (bronchiolar) inflammation
- hyper reactivity in response to a variety of stimuli.
- Airway obstruction, bronchial smooth muscle constriction.

❖edema.

❖increased secretions.

causes

- a variety of airborne substances, including pollens, animal dander, dusts, , and various chemicals.
- Some patients also develop bronchospasm following ingestion of aspirin, nonsteroidal anti-inflammatory agents, sulfites, or tartrazine and other dyes.
- Exercise, emotional excitement, and viral infections

Clinically, asthma is manifested by episodic attacks of dyspnea, cough, and wheezing

Asthma is classified as acute or chronic. Chronic asthma is further classified as intermittent(mild, moderate, and severe persistent disease) .

Diagnosis:

expiratory airflow measurements such as FEV 1 , FEV 1 /FVC, , and peak expiratory flow rate FEF —help in assessing the severity of airway obstruction

Anesthetic Considerations:

- Patients with poorly controlled asthma or wheezing at the time of anesthesia induction have a higher risk of perioperative complications.
- Well controlled asthma has not been shown to be a risk factor for intraoperative or postoperative complications.
- Patients with frequent or chronic bronchospasm should be placed on an optimal bronchodilating regimen.

Intraoperative Management:

- Regional anesthesia will circumvent this problem, but some clinicians believe that high spinal or epidural anesthesia may aggravate bronchoconstriction by blocking sympathetic tone to the lower airways (T1–T4) and allowing unopposed parasympathetic activity
- Drugs often associated with histamine release (eg, atracurium, morphine, and meperidine) should be avoided or given very slowly when used.

COPD

defined as a disease state characterized by airflow limitation that is not fully reversible

Most patients with COPD are asymptomatic or only mildly symptomatic, but show expiratory airflow obstruction upon PFTs. With advancing disease, mal distribution of both ventilation and pulmonary blood flow results in areas of low ($\dot{V}/\dot{Q}$) ratios (intrapulmonary shunt), as well as areas of high ($\dot{V}/\dot{Q}$) ratios (dead space).

Anesthetic Considerations:

Patients with COPD should be prepared prior to elective surgical procedures in the same way as patients with asthma (above).

Intraoperative Management:

- regional anesthesia is often considered preferable to general anesthesia, high spinal or epidural anesthesia can decrease lung volumes, restrict the use of accessory respiratory muscles, and produce an ineffective cough, leading to dyspnea and retention of secretions
- Preoxygenation prior to induction of general anesthesia prevents the rapid oxygen desaturation often seen in these patients and retention of secretions

Restrictive Pulmonary Disease:

Restrictive pulmonary diseases are characterized by

- decreased lung compliance.
- Lung volumes are typically reduced,
- both FEV 1 and FVC are reduced, but the FEV 1 /FVC ratio is normal.

Restrictive pulmonary diseases include many acute and chronic intrinsic pulmonary disorders, as well as extrinsic (extrapulmonary) disorders involving the pleura, chest wall, diaphragm, or neuromuscular function.

Reduced lung compliance lead to

- increases the work of breathing characteristic rapid, but shallow, breathing pattern.
- Respiratory gas exchange is usually maintained until the disease process is advanced

Restrictive lung diseases are often divided into two groups, depending on their cause is intrinsic or extrinsic.

Intrinsic restrictive lung disorders cause an internal abnormality, usually leading to the stiffening, inflammation , and scarring of the lung tissues.

Types of diseases and conditions involved in intrinsic restrictive lung disease can include:

pneumonia , tuberculosis , sarcoidosis ,idiopathic pulmonary fibrosis

interstitial lung disease , lung cancer ,fibrosis caused by radiation ,rheumatoid arthritis ,infant and acute respiratory distress syndrome ,inflammatory bowel disease (IBD) and systemic lupus

Extrinsic restrictive lung disease is caused by complications with tissues or structures outside of the lungs are often associated with

- weakened muscles.
- damaged nerves.
- stiffening of the chest wall tissues.

Types of diseases and conditions involved in extrinsic restrictive lung disease can include:

- pleural effusions, or the buildup of excessive fluid between tissue layers surrounding the lungs
- scoliosis, or twisting of the spine
- neuromuscular disease such as Lou Gehrig's disease
- muscular dystrophy intermittent muscle weakness
- obesity

- malignant tumors
- rib damage, especially fractures
- ascites, or abdominal swelling connected with liver scarring or cancer
- diaphragm paralysis
- kyphosis, or hunching of the upper back
- diaphragmatic hernia
- heart failure

Symptoms

- Most people with restrictive lung diseases have similar symptoms, including:
- shortness of breath, especially with exertion
- inability to catch their breath or get enough breath
- chronic or a long-term cough, usually dry, but sometimes accompanied by white sputum or mucus
- weight loss
- chest pain
- wheezing or gasping breath
- fatigue ,depression and anxiety

Preoperative Management

Patients with acute pulmonary disease should be procedures

- oxygenation and ventilation should be optimized preoperatively to the greatest extent possible.
- Fluid overload should be treated with diuretics.
- heart failure may also require vasodilators .

Commonly used tests for restrictive lung disease include:

- **Forced vital capacity (FVC) test**, which involves inhaling and filling the lungs with as much air as possible, then exhaling with as much force as possible. The FVC of those with restrictive lung diseases is typically decreased. **Forced expiratory volume in 1 second (FEV1) test**, which measures the amount of air exhaled during the first second of the FVC test. Most people expel about three-quarters of the air inhaled during this initial period of exhalation. In restrictive disease, because the FVC is usually reduced, the FEV1 will be lower, proportionally.

FEVI to FVC ratio test, which compares the amount of air expelled during the first second of exhalation (FEV1) to the total amount of air exhaled during an FVC test. This ratio is often normal or even increased in those with restrictive lung disease.

- **Chest X-ray**, which creates images of the entire chest and lung area for evaluation.
- **Computed tomography (CT) scans**, which create more detailed images of the chest and lung area compared to chest X-rays.
- **Bronchoscopy**, where a flexible tube with a camera is inserted through the nose or mouth into the airways of the lung for examination

Respiratory Failure

Respiratory failure exists whenever the exchange of O_2 for CO_2 in the lungs cannot keep up with the rate of O_2 consumption & CO_2 production in the cells of the body. This results in a fall in arterial O_2 tension (hypoxemia) and a rise in arterial CO_2 tension (Hypercapnia).

Respiratory failure is considered acute if the lungs are unable to maintain adequate oxygenation in a previously healthy person, with or without an impairment of carbon dioxide elimination and the lung usually returns to its normal original states, But in chronic respiratory failure the structure damage is irreversible.

Causes of Acute Respiratory Failure (ARF):

a- Intrapulmonary:

- Lower airway and alveoli diseases (COPD, Asthma, Pneumonia…..)
- Pulmonary Circulation: {Pulmonary Embolism}
- Alveolar capillary membrane (Acute respiratory distress syndrome, inhalation of toxic gases, near drowning, drug overdose)

b-Extrapulmonary:

- Brain (e.g. Drug overdose)
- Spinal Cord(e.g. Guillain-Barré syndrome)
- neuromuscular system(e.g. Myasthenia gravis)
- thorax(e.g. Massive obesity)
- pleura (e.g. Pleural effusion)
- upper airway Obstruction(e.g. Sleep apnea)

Classification of acute respiratory failure:

Based on the pattern of blood gas abnormality:

1- Type I Hypoxaemic respiratory failure,

- In which the PaO_2 is less than 50 mmHg and the $PaCO_2$ is normal or low.

-The major pathophysiologic mechanisms causing hypoxaemic respiratory failure usually is a combination of ventilation- perfusion (V/Q) mismatching and shunting.

- Type II Hypercapnic/ Hypoxaemic respiratory failure,

- In which the $PaCO_2$ >45mmHg, accompanied by a lower than normal PaO_2.

-Pathophysiology caused by alveolar hypoventilation.

Chronic respiratory failure:

is an ongoing condition. It gradually develops over time and requires long-term treatment.

Chronic respiratory failure usually happens when the airways that carry air to your lungs become narrow and damaged. This limits air movement through the body, which means that less oxygen gets in and less carbon dioxide gets out.

Chronic respiratory failure can also be classified as hypoxemic or hypercapnic respiratory failure. Low blood oxygen levels cause hypoxemic respiratory failure. High carbon dioxide levels cause hypercapnic respiratory failure.

symptoms of chronic respiratory failure:

Symptoms of chronic respiratory failure may not be noticeable at first. They usually occur slowly over an extended period of time. When symptoms do develop, they may include:

- difficulty breathing especially when active
- coughing up mucous
- wheezing
- bluish tint to the skin, lips, or fingernails
- rapid breathing
- fatigue
- anxiety
- confusion
- daily headache
- people may develop an abnormal heart rhythm, stop breathing, or slip into a coma.

causes chronic respiratory failure:

Certain lung diseases can cause chronic respiratory failure. Conditions that affect the way in which the brain, muscles, bones, or surrounding tissues support breathing can also cause chronic respiratory failure.

Diseases and conditions that commonly lead to chronic respiratory failure include:

- COPD
- Complicated pneumonia
- Cystic fibrosis
- spinal cord injuries
- strock
- Muscular dystrophy
- injury to the chest
- drug or alcohol misuse
- smoking

Pathophysiology:

Hypoxemia is the result of impaired gas exchange and is the hallmark of acute respiratory failure. Hypercapnia may be present, depending on the underlying cause of the problem. The main causes of hypoxemia are:

- alveolar hypoventilation
- ventilation/perfusion (V/Q) mismatching
- intrapulmonary shunting.

Type I respiratory failure usually results from V/Q mismatching and intrapulmonary shunting, whereas type II respiratory failure usually results from alveolar hypoventilation, which may or may not be accompanied by V/Q mismatching and intrapulmonary shunting.

Ventilation/Perfusion (V/Q) Mismatching.

V/Q mismatching occurs when ventilation and blood flow are mismatched in various regions of the lung in excess of what is normal. Blood passes through alveoli that are under ventilated for the given amount of perfusion, leaving these areas with a lower-than-normal amount of oxygen. V/Q mismatching is the most common cause of hypoxemia and is usually the result of alveoli that are partially collapsed or partially filled with fluid.

Intrapulmonary Shunting.

The extreme form of V/Q mismatching, intrapulmonary shunting, occurs when blood reaches the arterial system without participating in gas exchange. The mixing of unoxygenated (shunted) blood and oxygenated blood lowers the average level of oxygen present in the blood. Intrapulmonary shunting occurs when blood passes through a portion of a lung that is not ventilated. This may be the result of alveolar collapse secondary to atelectasis alveolar flooding with pus, blood, or fluid

Alveolar Hypoventilation.

Alveolar hypoventilation occurs when the amount of oxygen being brought into the alveoli is insufficient to meet the metabolic needs of the body. This can be the result of

- increasing metabolic oxygen needs
- decreasing ventilation

Hypoxemia caused by alveolar hypoventilation is associated with hypercapnia and commonly results from extrapulmonary disorders.

Clinical manifestations:-

1. Tachypnea (40b/min).
2. Shallow breathing (dyspnea)
3. Retraction of the intercostal & suprasternal areas during inspiration.
4. Hypoxemia fails to respond to O_2 therapy in case of intrapulmonary shunting, but in other case will.

5- Cerebral hypoxia (anxiety, confusion, irritability, drowsiness,

6- Hypoxia of the heart (Tachycardia, dysrhythmias & hypotension).

Diagnostic Tests:

1. Arterial Blood Gas Monitoring.
2. Chest X-ray.
3. Pulmonary Function Test.

Laboratory investigations:

1. Blood gases
2. HCT, Hb,.
3. Electrolytes

- **Management of Acute Respiratory Failure:**

Assessment of Baseline values for:

- Vital signs:

- Respiratory rate.

- Symmetry of air entry.

- Synchronization of chest movement with the ventilator.

- Blood pressure.

- Premature ventricular contractions, an increase (indication of hypoxemia) or decrease (vagal stimulation)in heart rate.

- Central venous pressure (CVP).

- Temperature.

- Level of consciousness.

Autonomic control of the cardiovascular system

- Chronotropy : heart rate
- Dromotropy : conduction velocity- how fast a signals going from one cell to the next.
- Inotropy: contractility, the force heart muscle contraction.
- Lusitropy : the relaxation .
- Bathmotropy : the excitability

Cardiovascular centers:

These centers located in medulla oblongata (lower part of brain stem) and its functions is regulation of cardiovascular system function by controlling sympathetic and parasympathetic systems.

Parts of cardiovascular centers

1. **Cardiac centers:**

a) Cardiac accelerated center(CAC): act by sympathetic system increasing heart rate, contractility, stroke volume and cardiac output.

b) Cardiac inhibitory center(CIC): act by parasympathetic system decreasing heart rate and cardiac output

1. **Vasomotor centers:**

a) Vasoconstrictor centers: vasoconstriction by increasing sympathetic discharge to blood vessels

b) Vasodilators centers: vasodilatation by inhibition to vasoconstriction.

Parasympathetic:

The right vagus nerve supplies the SA node, whilst the left vagus nerve supplies the AV node. Atrial muscle is also innervated by parasympathetic neurons, but ventricular muscle is not (and is therefore unaffected). Parasympathetic nervous system activity, therefore, affects heart rate and conduction, but has little effect on the force of contraction:

- ✓ Negative chronotropy (decrease HR): the intrinsic rate of SA node is 90-120bpm. At rest there is continuous parasympathetic nervous discharge at SA node known as vagal tone, which decrease the resting HR to 60-80bpm.
- ✓ Decrease conduction velocity through the AV node.

Sympathetic:

The heart is innervated by post-ganglionic sympathetic fibers from upper thoracic chain (mainly T1-T3). Increase sympathetic nervous system activity causes release of noradrenaline at sympathetic nerve endings and release of adrenaline from adrenal medulla. Both noradrenaline and adrenaline act at cardiac B1 adrenergic receptor, a G protein-coupled receptor whose activation resulting in:

- ✓ Positive chronotropy(increase HR): in SA node increasing Na influx thereby increasing the gradient of pacemaker potential which increase HR.
- ✓ Positive inotropy(increase myocardial contractility): in the cardiac myocytes increase intracellular Ca concentration which increase the strength of contraction.
- ✓ Shorter action potential duration.
- ✓ Increase rate of transmission through AV node.

The autonomic control of systemic vasculature is primarily sympathetic and their principle function is to regulate vascular tone. Variation of arterial vascular tone serve to **regulate blood pressure and the distribution of blood flow to the various organs**, whereas **variation in venous tone alter vascular capacity, venous pooling, and venous return to the heart.** The vasculature has sympathetic vasoconstrictor and vasodilator fibers. Sympathetic induced vasoconstriction (via a1-adrenergic receptors) can be potent in skeletal muscle, kidney and skin but least active in the brain and heart. The most vasodilator fibers are those feeding skeletal muscle mediating increased blood flow (via B2-adrenergic receptors) in response to exercise, vasodepressor (vasovagal) syncope which can occur following intense emotional strain associated with high sympathetic tone, results from reflex activation of both vagal and sympathetic vasodilator fibers.

Table show The effects of sympathetic and parasympathetic system on heart and blood vessels.

HEART	Sympathetic	parasympathetic
Chronotropy (rate)	Increased heart rate (HR) +++	Decreased heart rate (HR) - - -
Inotropy (contractility)	Increased force of contraction	Decreased force of contraction -
Dromotropy (conduction velocity)	Increased conduction velocity ++	Decreased conduction velocity - - -
Bathmotropy (excitability)	Increased excitability ++	Decreased excitability - -
Blood Vessels	Arterial constriction (α1), dilatation) +++ 0 Venous constriction (α1) , dilatation) +++ 0	

Control of arterial blood pressure:

Arterial blood pressure is regulated by a series of immediate, intermediate, and long-term adjustments that involve complex neural, humoral, and renal mechanisms.

Immediate control:

- Minute-to-minute control of blood pressure is primarily the function of ANS reflexes.
- Changes in arterial BP are sensed both centrally (hypothalamus and brain stem areas) and peripherally (baroreceptors).
- Decrease in BP result in increase sympathetic tone, increase adrenal secretion of epinephrine and reduced vagal activity. The resulting systemic vasoconstriction, increased heart rate, and enhanced cardiac contractility serve to increase blood pressure.
- Peripheral baroreceptors are located at the bifurcation of the common carotid arteries and aortic arch.
- Elevation in BP increase baroreceptor discharge inhibiting systemic vasoconstriction and enhancing vagal tone and the converse is also true.

B. Intermediate control:

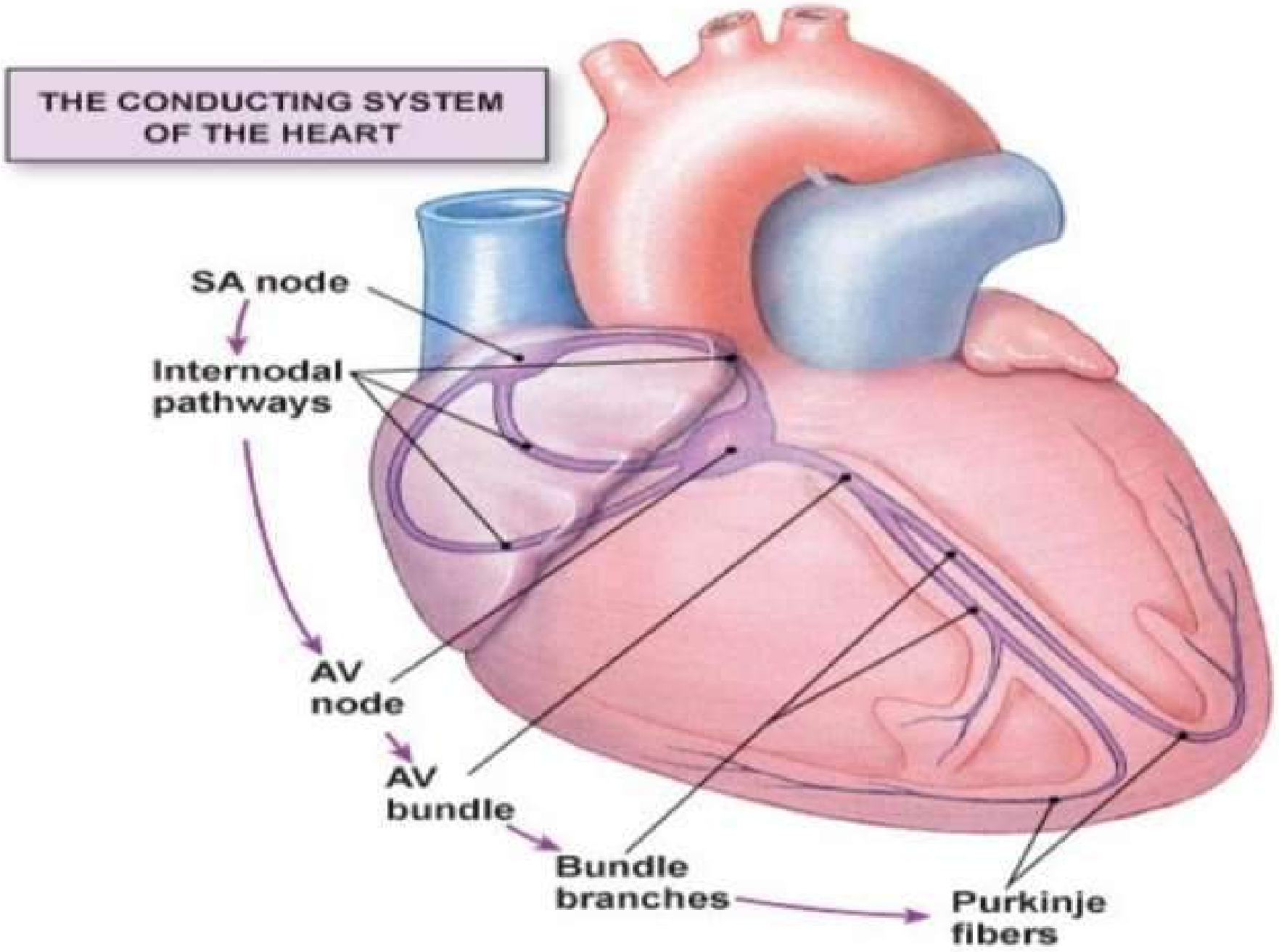
- Occur in the course of few minutes.
- Changing in BP activate the renin-angiotensin II - aldosterone system, increase secretion of arginine vasopressin (AVP) and alter normal capillary fluid exchange.
- Both angiotensin II and AVP are potent arteriolar vasoconstrictors.
- Hypertension increase interstitial movement of intravascular fluid, whereas hypotension increase reabsorption of interstitial fluid.

C.Long-term control:

- Occur within hours of sustained change in BP.
- The kidney alters total body sodium and water balance to restore BP to normal.
- Hypotension result in sodium and water retention, whereas hypertension generally increase sodium excretion in normal individuals.

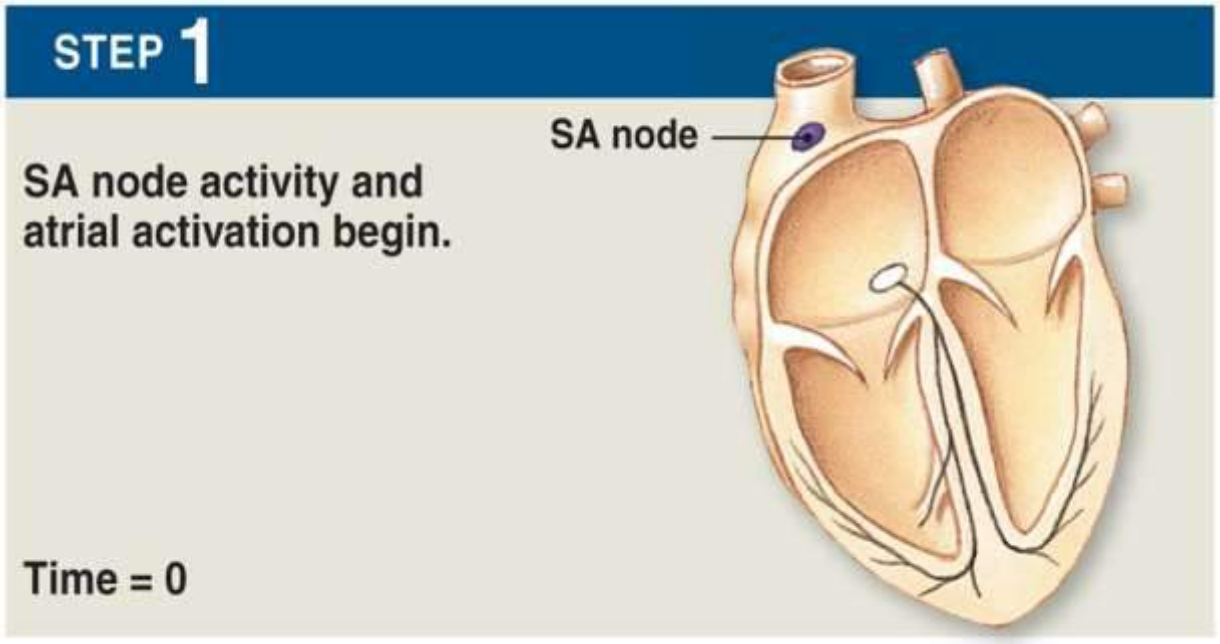
Cardiac cycle

- **Heartbeat**
  - A single contraction of the heart.
  - The entire heart contracts in series, First the atria then ventricle.
- **Structures of the Conducting System**
  - Conducting cells - throughout myocardium.
  - Sinoatrial (SA) node - wall of right atrium.
  - Internodal pathway.
  - Atrioventricular (AV) node - junction between atria and ventricles.
  - His bundle.
  - Bundle branches.
  - Purkinje fibers


THE CONDUCTING SYSTEM OF THE HEART
SA node
Internodal pathways
AV node
AV bundle
Bundle branches
Purkinje fibers

The Sinoatrial (SA) Node

- In posterior wall of right atrium.
- Contains pacemaker cells.
- SA node generates 80–100 action potentials per minute.
- Connected to AV node by internodal pathways.
- Begins atrial activation (step 1).



Internodal pathway:

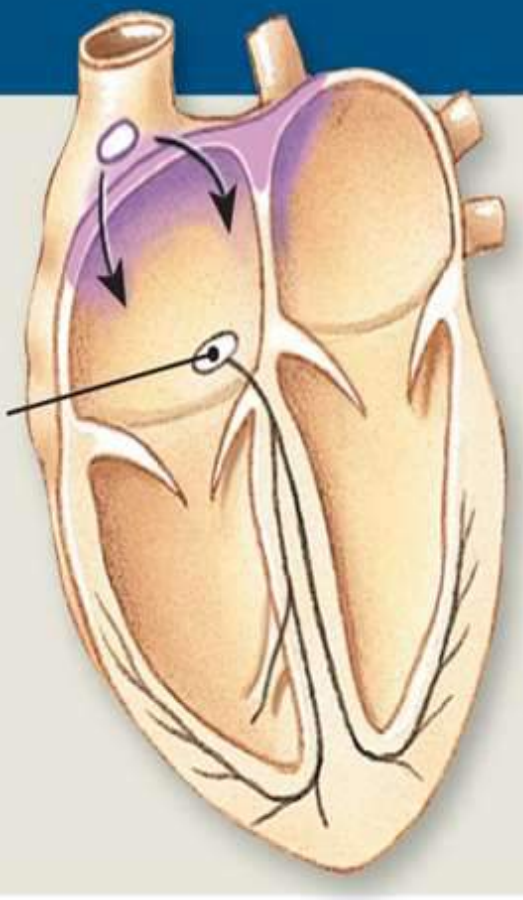
- Interconnect SA and AV nodes.
- Distribute stimulus through myocardium in the atrium.

The Atrioventricular (AV) Node:

- In floor of right atrium.
- AV node generates 40–60 action potentials per minute.
- Receives impulse from SA node (Step 2).
- Delays impulse (Step 3).
- Atrial contraction begins.

STEP 2

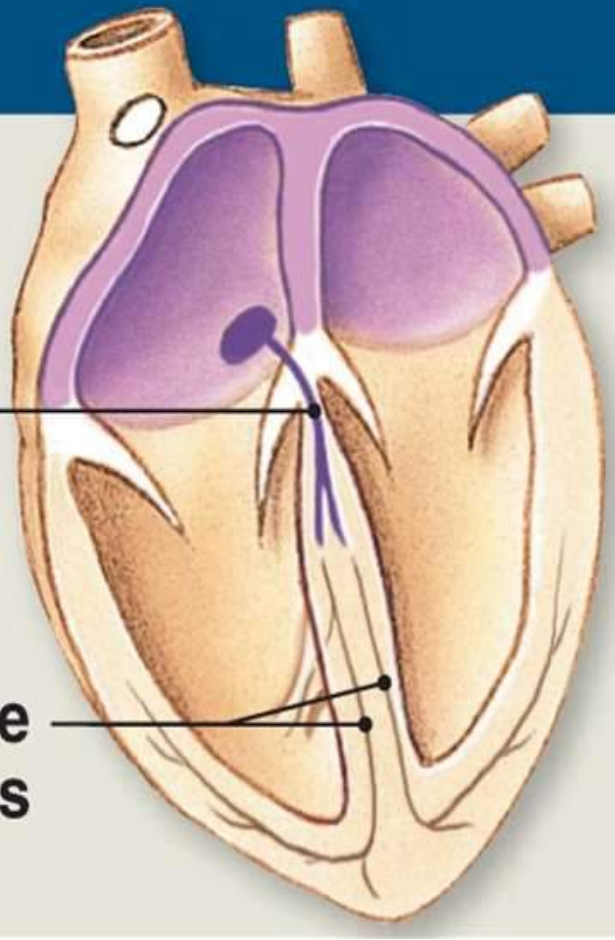
Stimulus spreads across the atrial surfaces and reaches the AV node.



Elapsed time = 50 msec

STEP 3

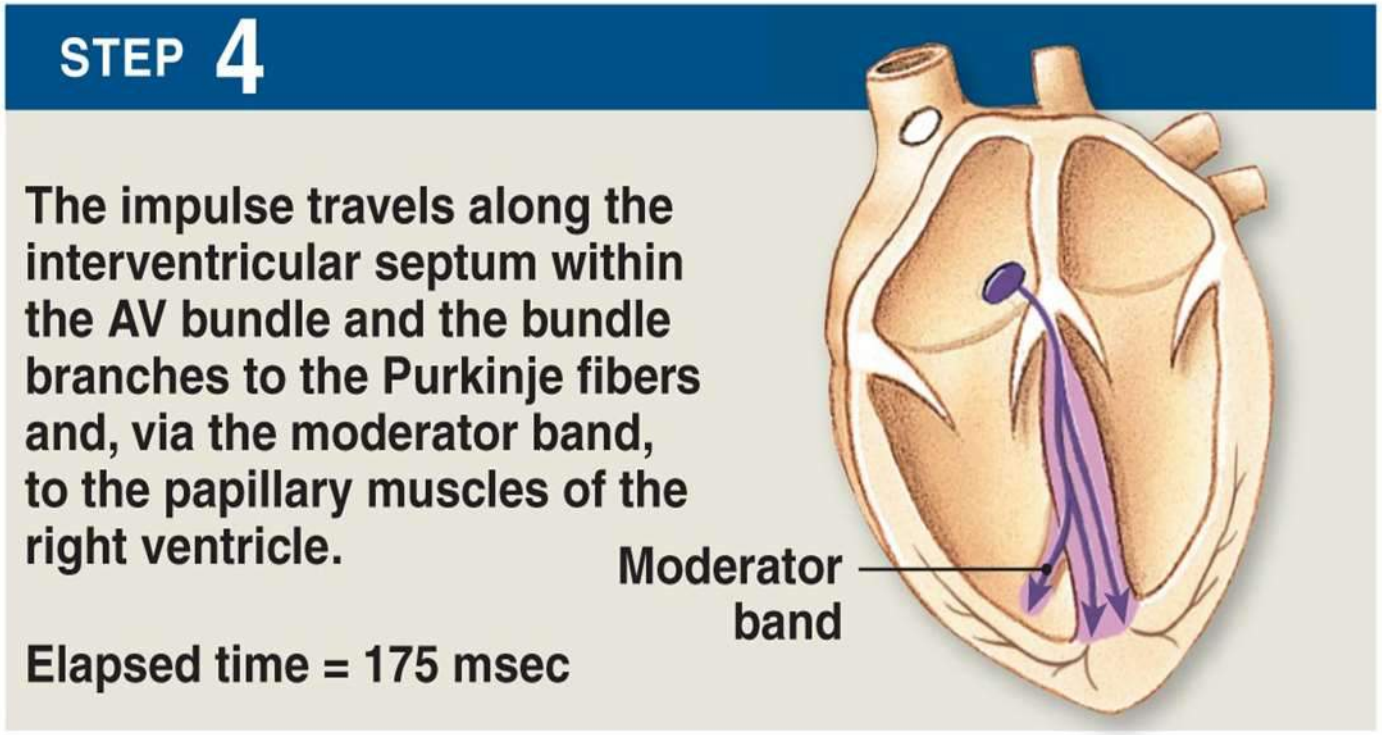
There is a 100-msec delay at the AV node. Atrial contraction begins.



Elapsed time = 150 msec

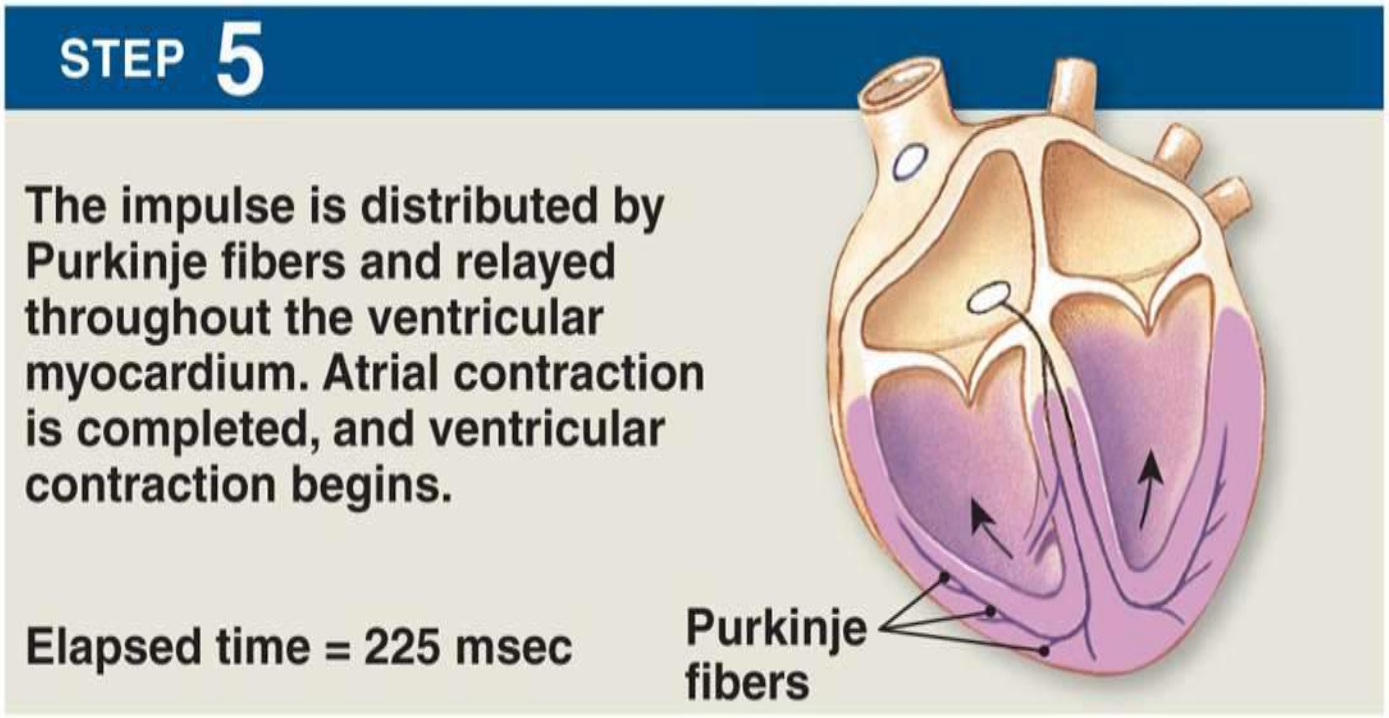
His bundle:

- In the septum.
- Carries impulse to left and right bundle branches.
- Which conduct to Purkinje fibers (Step 4).
- And to the moderator band Which conducts to papillary muscles.



Purkinje Fibers

- Distribute impulse through ventricles (Step 5).
- Atrial contraction is completed.
- Ventricular contraction begins.



Cardiac cycle

The cardiac cycle refers to the complete consequence of events that occur in the heart from the beginning of one heart beat to the beginning of the next. Each heart beat consists of two major periods called systole and diastole.

- Systole: period of ventricular contraction (ventricles contract and eject blood into the aorta and pulmonary artery).
- Diastole: period of ventricular relaxation. (ventricles fill with blood).

Phases of cardiac cycle:

Divided into five phases (and duration of phases)

1. Late diastole (0.11s)
2. Atrial Systole (0.11s – 0.53s)
3. Isovolumetric Ventricular Contraction (0.05s)
4. Ventricular Ejection (0.22-0.27s)
5. Isovolumetric Ventricular Relaxation (0.08s)

Late diastole :

- As the mitral valve open, the left ventricular pressure decrease due to its relaxation while the volume increase.
- Both the aortic and left atrial pressure will be decrease.
- On heart sound its **S3**.

Atrial Systole:

- As the atria contract, the atrial pressure increase this will cause opening of mitral and tricuspid valves and blood flows into ventricles.
- During this phase, ventricular volume will be tops up but the ventricular pressure will not be raised.
- In ECG its preceded by **P** wave.

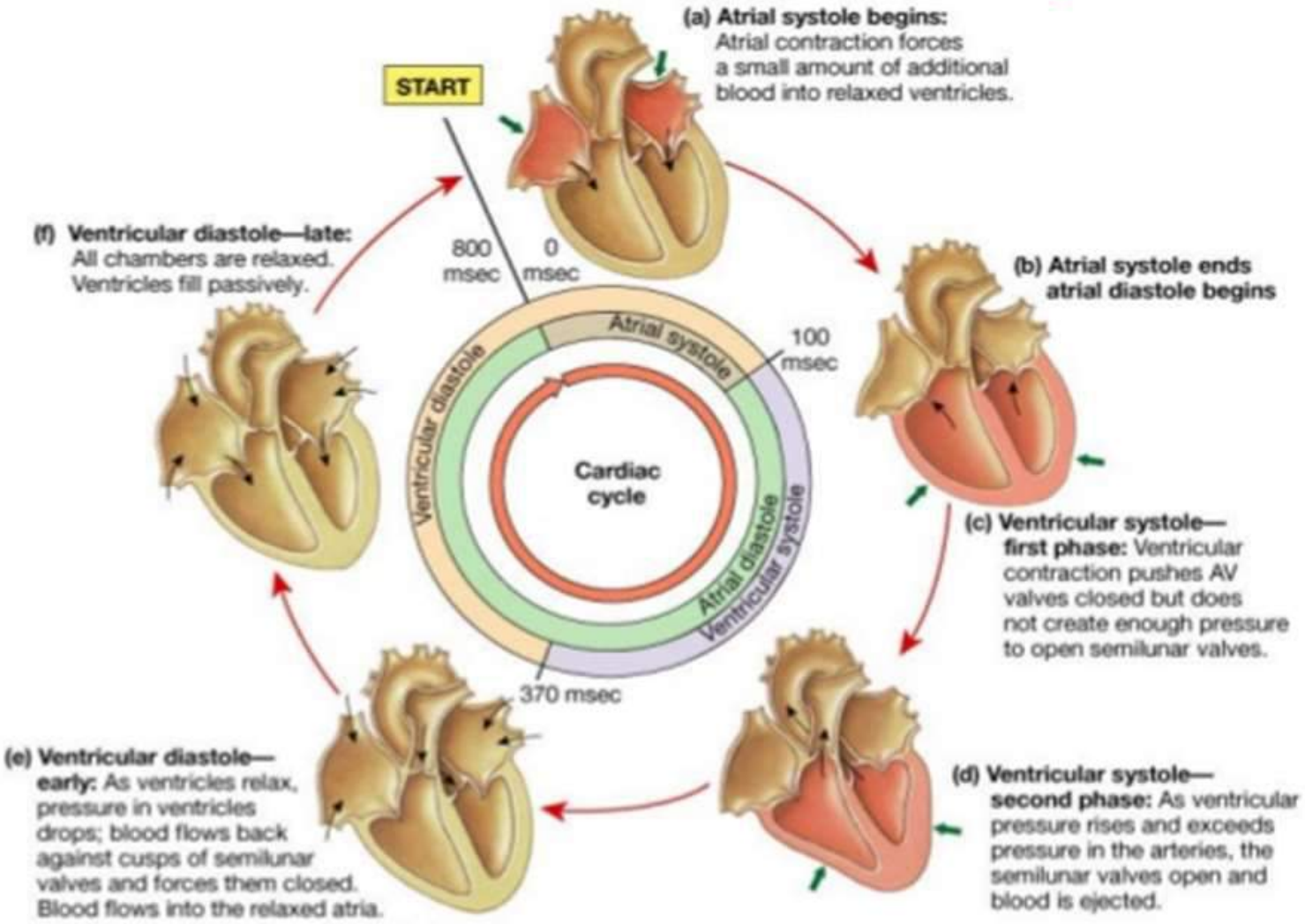
Isovolumetric Ventricular Contraction:

- When the left ventricle begins to contract, the mitral valve close and this will lead to increase left ventricular pressure.
- Ventricular volume remains constant.
- In ECG its QRS complex.
- Its S1 on heart sound

Ventricular Ejection:

- While the ventricles still contracted and the pressure increase inside it more than the aortic pressure.
- the aortic valve open and most of the stroke volume of blood will be ejected.
- The volume of blood that eject causes increase in aortic pressure.

Phases of the Cardiac Cycle



Cardiac output(CO):

- Is the volume of the blood ejected from the heart per minute.
- The usual resting value for adult 5 L/min.
- ***SV*** is the volume of blood ejected from LV per heart beat.
- The cardiac output is the product of heart rate(HR)and stroke volume(SV).

CO = HR x SV.

- ***EDV.*** is The volume of blood within the ventricle at the end of atrial contraction.
- ***LVEDV*** the volume of blood in the LV prior to contraction .135ml
- LVESV the volume of blood remaining in LV after contraction.65ml
- SV=LEDV - LESV, SV=70ml

* EDV=135ml
* ESV=65ml
* SV=135 – 65=70ml
* HR=72 b./min.
* C.O=70 × 72 5 L./min..

Preload: is the end diastolic volume that stretches the right or left ventricle of the heart to its greatest dimensions under variable physiologic demand. factors increasing the preload are :

1. Hypervolemia.
2. Regurgitation of cardiac valves.
3. Heart failure (HF).

After load: Is the force against which the ventricle must contract to eject blood, is affected by the ventricular radius and ventricular systolic pressure. Factors increasing afterload are:

1. Hypertension.
2. Vasoconstriction.

Causes of low preload:

1-Hypovolemia

May result from bleeding or fluid losses.

2-Vasodilation

Occurs with general anesthesia and may be even more prominent in the presence of neuraxial anesthesia.

3-Tension pneumothorax and cardiac tamponade

Which prevent ventricular filling due to increase pressure around the heart, even though blood volume and filling pressure are adequate.

4-Pathological problems on the right side of the heart

May prevent filling of the left ventricle. Pulmonary embolism and other causes of pulmonary hypertension prevent the right side of the heart from pumping a sufficient volume to fill the left side of the heart.

Ejection fraction (EF):

- It's the ratio of stroke volume to end diastolic volume and commonly used to measure the cardiac performance.
- Its expressed as percentage%
- Normally its more than 55%.
- EF provides a non-Specific index of ventricular function. EF=SV/EDV

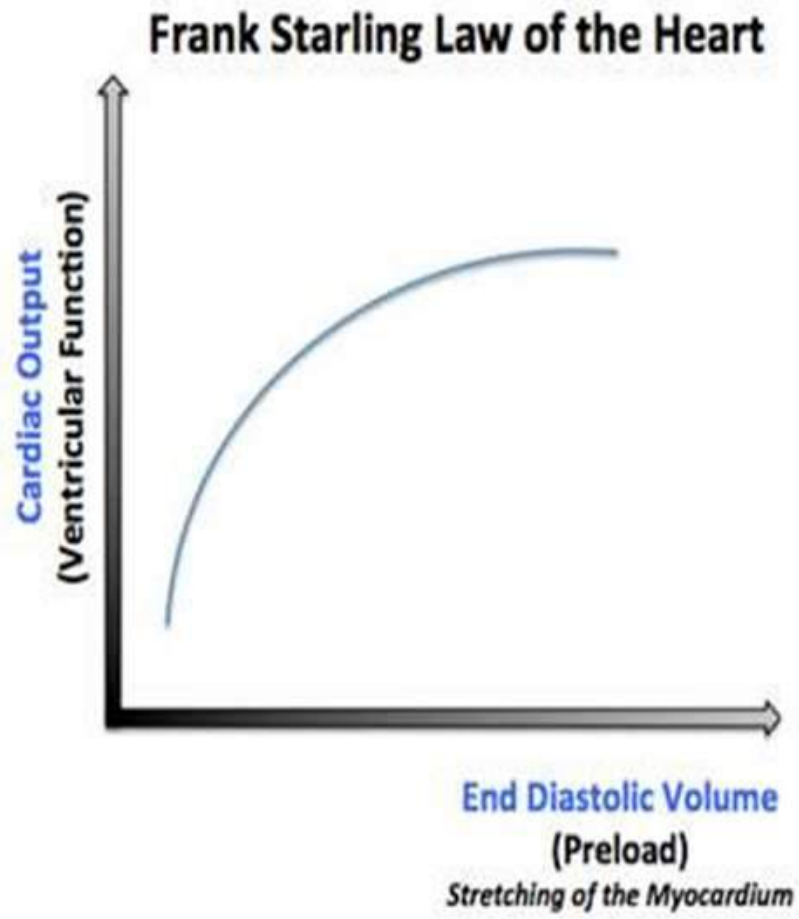
heart sounds*:* 4 heart sounds:

- 1st& 2^{nd}.heart sounds (usually heard).
- 3rd& 4^{th}.heart sounds (sometimes detected).
  - 1^{st}. heart sound: produced by vibration generated by closure of the mitral and tricuspid valves, it corresponds to the end of diastole and beginning of ventricular systole.
  - 2^{nd}. Heart sound: produce by the closure of aortic and pulmonary valves.
- Important for diagnosis of valvular heart diseases (murmurs).

Starling law of the heart

- As described in previous, cardiac output increase or decreases in response to changes in heart rat or stroke volume. When a person stand up for example, cardiac output falls because a fall in central venous pressure lead to a decrease in stroke volume. As another example, limb movement during exercise enhances venous return to the heart, which causes an increase in stroke volume. In the late 19th century Otto Frank found using isolated frog hearts that the strength of ventricular contraction was increased when the ventricle was stretched before to contraction. This observation was extended by the elegant studies of Ernest Starling and colleagues in early 20th century who found that increasing venous return to the heart which increased the filling pressure(LVEDP) of the ventricle led to increased stoke volume, conversely decreasing venous return decreased stoke volume

- This cardiac response to change in venous return and ventricular filling pressure is intrinsic to the heart and does not depend on extrinsic neurohumoral mechanisms. In honor of these two early pioneers **the ability of *the heart to change its force of contraction and therefore stroke volume in response to changes in venous return is called Frank-Starling mechanism or starling law of the heart***


Frank Starling Law of the Heart
Cardiac Output
(Ventricular Function)
End Diastolic Volume
(Preload)
Stretching of the Myocardium

What is cardiac failure?

Cardiac failure (or heart failure) is said to occur when the heart is unable to provide sufficient cardiac output to meet the demands of the tissues. Heart failure may either be:

* ***High output heart failure***: cardiac output is normal but the tissue O2 demand is high; for example, pregnancy and thyrotoxicosis
* ***Low output heart failure***: the tissues O2 demand is normal but the cardiac output is insufficient to meet it. In this type the right or left ventricles may be affected, resulting in RVF or LVF respectively.

In addition, progressive pump failure of LV may lead to RVF this knowing as congestive cardiac failure

* ***Systolic heart failure***: in which the pump function of the heart is impaired that is ejection fraction (EF) is reduced to below 45%. Systolic heart failure occurs when the strength of myocardial contraction is inadequate due to:

- ✓ Dysfunction of myocytes as a result of ischemia, inflammation (myocarditis), congenital disease. Leading to decrease SV, increasing LVEDV and increased size of the heart, this pathological dilatation of the heart is known as cardiomegaly.
- ✓ Chronically raised afterload for example, systemic hypertension or aortic stenosis. Chronically increased afterload causes a compensatory left ventricular hypertrophy.

- ***Diastolic heart failure***: in which ventricular compliance is reduced, either as a result of impaired ventricular relaxation (ischemic heart disease, restrictive cardiomyopathy) or as a result of pathological ventricular hypertrophy (hypertension, obstructive cardiomyopathy).

Functions of the Heart

1. Generating blood pressure
2. Routing blood: separates pulmonary and systemic circulations
3. Ensuring one-way blood flow: valves
4. Regulating blood supply:Changes in contraction rate and force match blood delivery to changing metabolic needs

Circulatory System Function

Move circulatory fluid (blood) around body

1. Gas Transport
2. Nutrient Transport
3. Waste Transport
4. Cell Signal Transport
5. Distribute secretions of endocrine glands
6. Hydraulic Force
7. Heat Conductance
8. Immunity

Path of Blood

Pulmonary Circuit

Blood flow between the lungs and heart

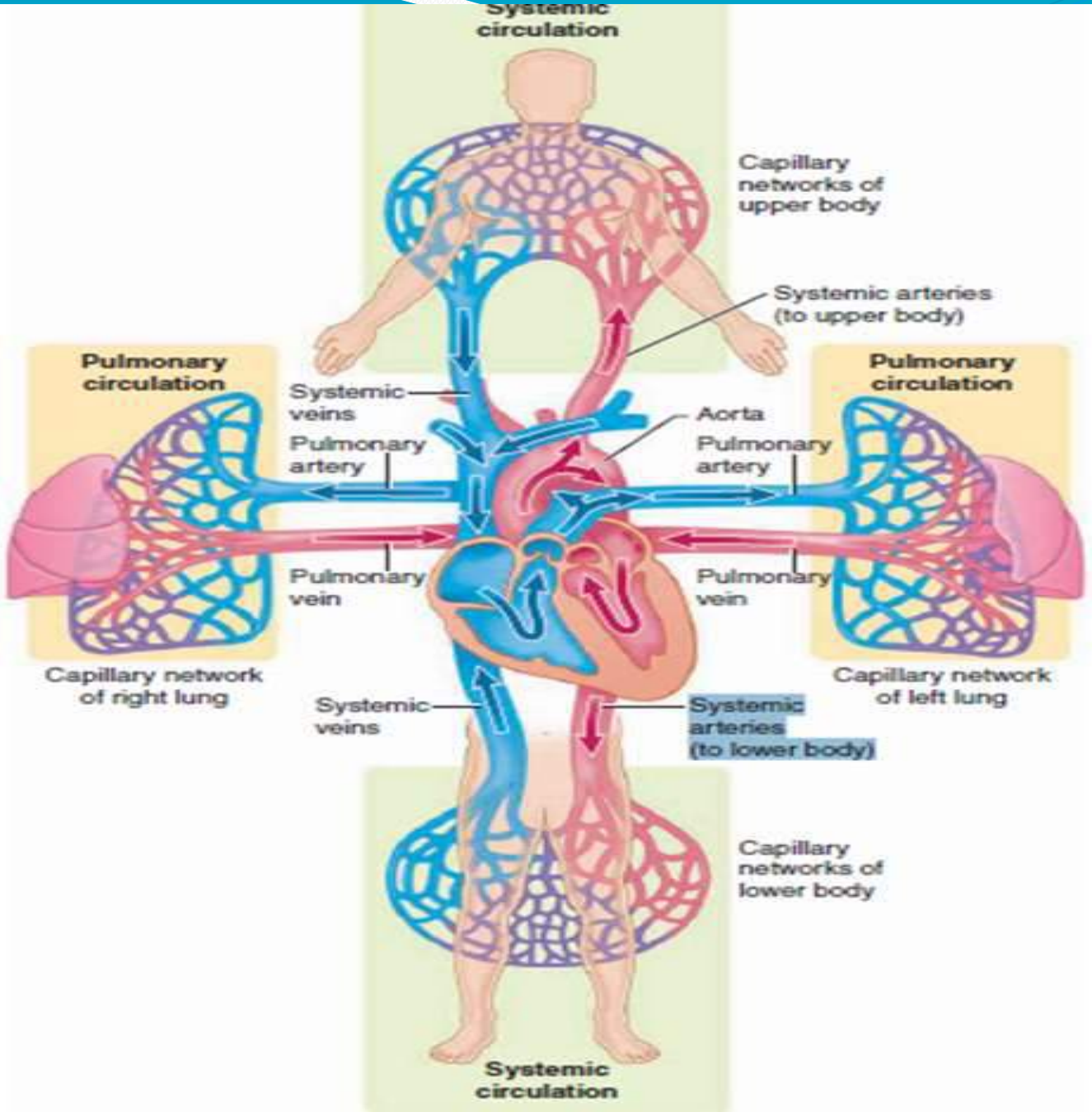
Supplied by the *Right* side of the heart

Systemic Circuit

Blood flow between the rest of the body and heart

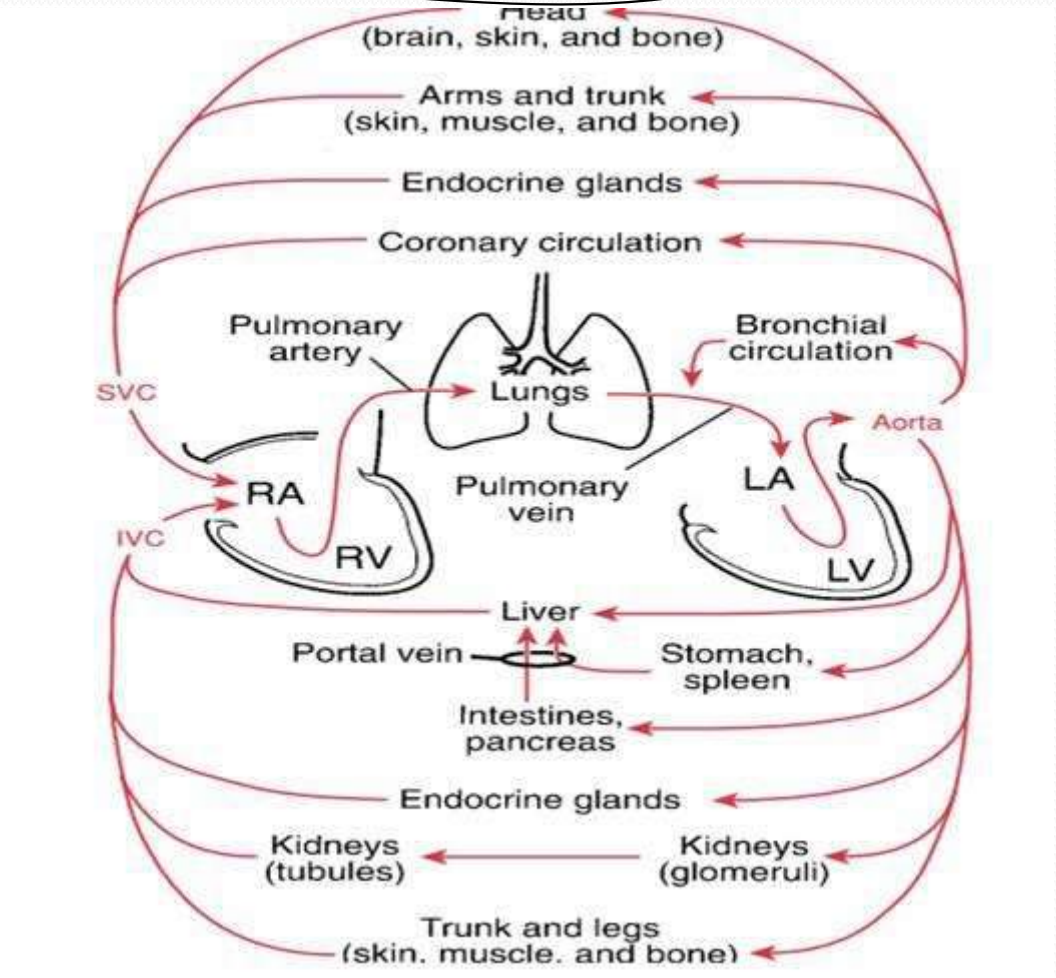
Supplied by the *Left* side of the heart

Pulmonary circulation

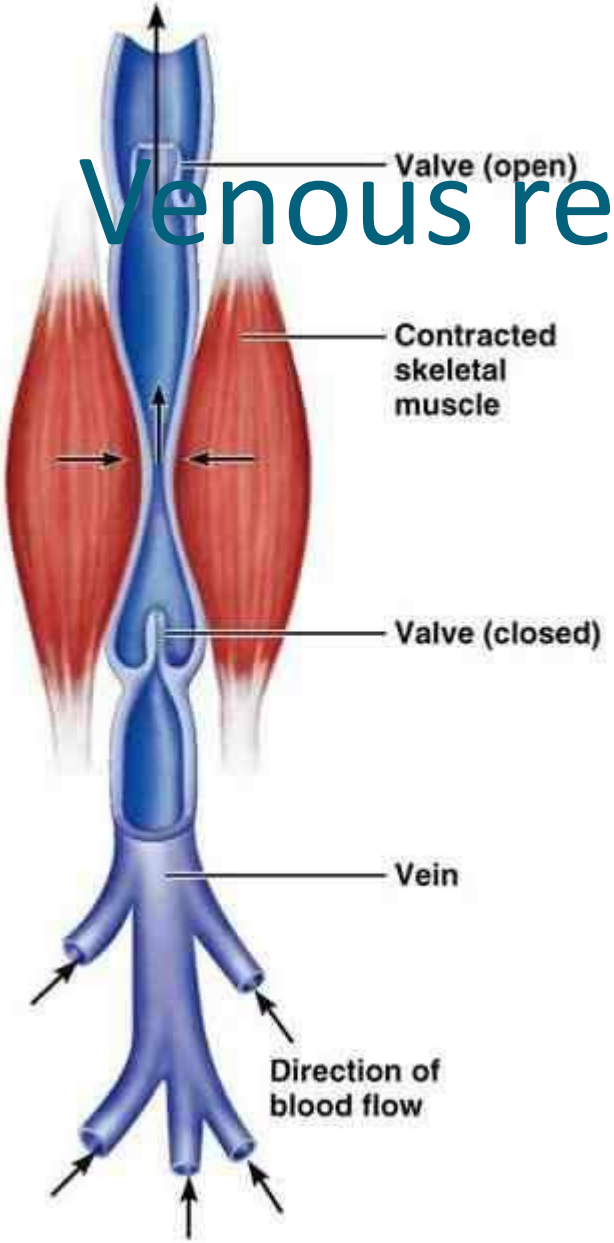


Systemic circulation

/greater circulation / peripheral circulation.



Venous return



is aided by both structural and functional adaptations.

- Structural

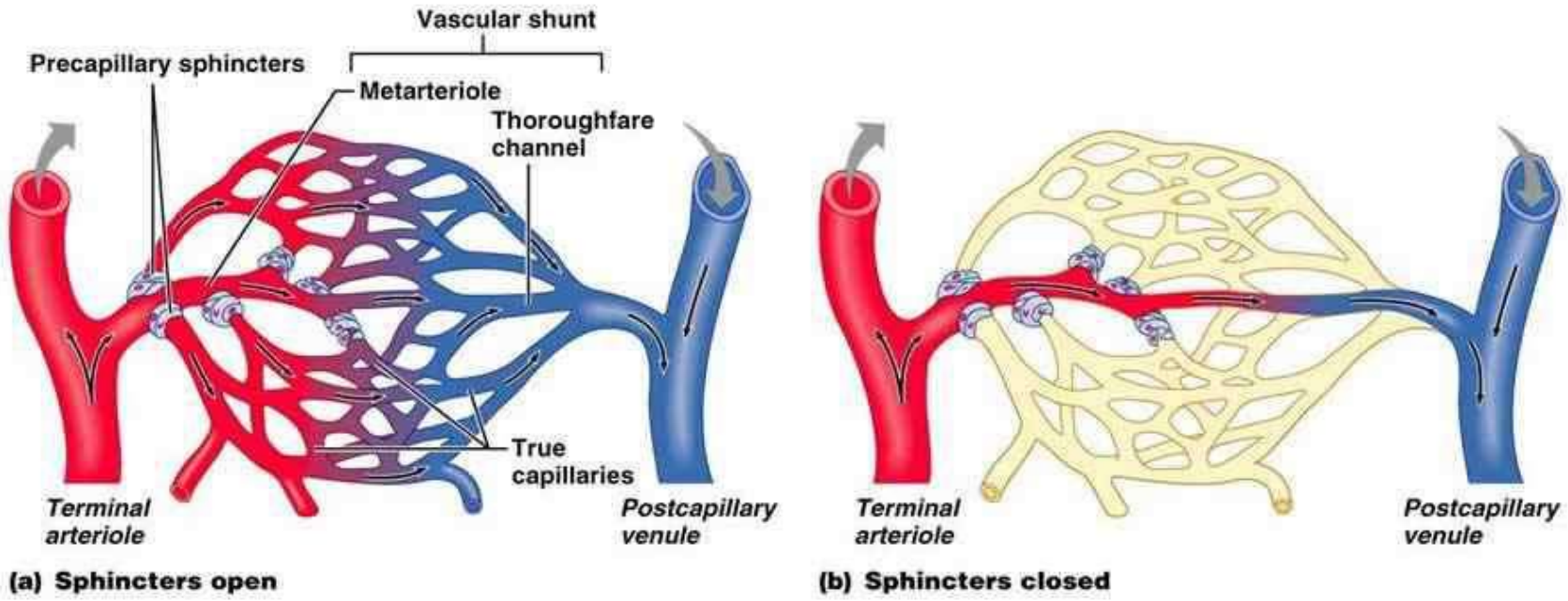
-Valves - present mostly in extremities, none in ventral body cavity

2. Functional

-Respiratory Pump

-Muscular Pump

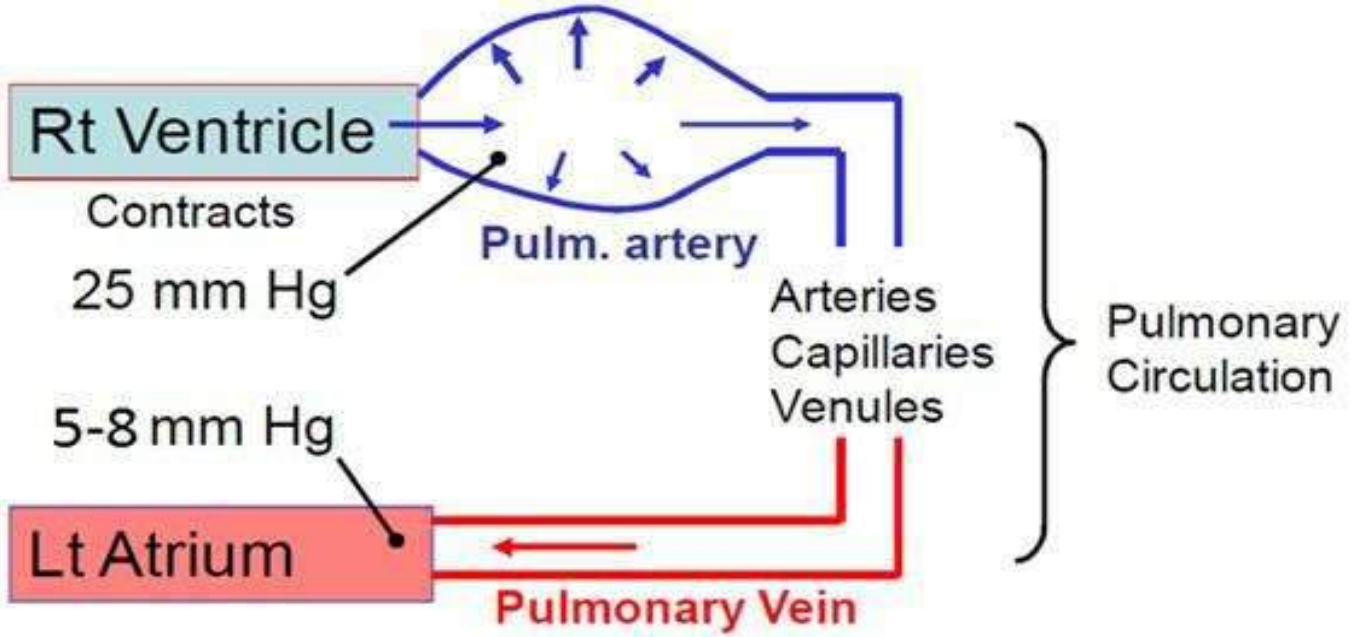
-Smooth muscle layer under sympathetic control


Vascular shunt
Precapillary sphincters
Metarteriole
Thoroughfare channel
True capillaries
Terminal arteriole
Postcapillary venule
(a) Sphincters open
Terminal arteriole
Postcapillary venule
(b) Sphincters closed

Functions of circulation

- Supply the tissues with nutrients.
- Removal the waste product of tissue metabolism.
- Regulate the heat lose.
- Aides in defense mechanism by delivered the antibodies ,platelet and leukocytes.

The pulmonary system is similar but works at lower pressures



Blood Flows through the Pulmonary Circulation because of the Pressure Gradient between RV and LA

Concept of pressure

Pressure gradient between LV and RA 100 to 0 mm Hg.

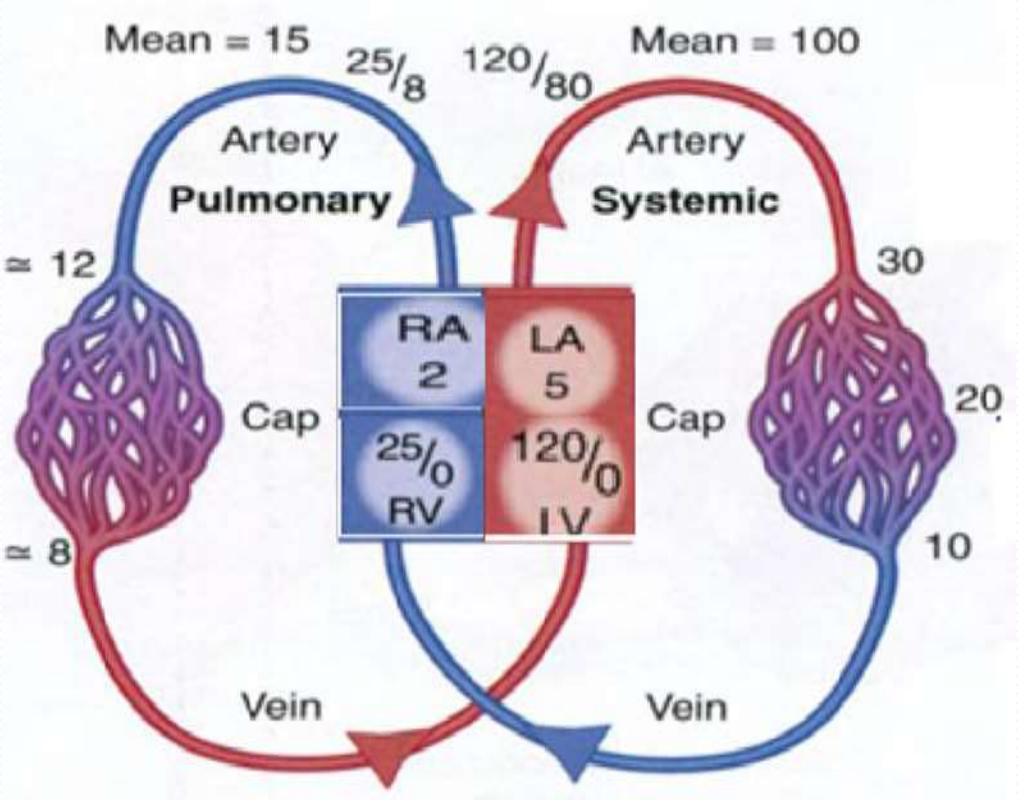
Pressure gradient between RV and LA 25 to 5-8 mm Hg.

Pressure gradient is the force that drives the blood around the circulation .

Pressure gradient is created by the mechanical work done by the ventricular in contracting.

Pulse pressure=systolic-diastolic

Mean arterial pressure=diastolic +pulse pressure/3


Mean = 15
25/8
120/80
Mean = 100
Artery
Pulmonary
Artery
Systemic
≃ 12
30
RA
2
LA
5
Cap
Cap
20
25/0
RV
120/0
LV
≃ 8
10
Vein
Vein

Pressures in the Pulmonary Circulation		Pressures in the Systemic Circulation	
Right ventricle	25/0 mm Hg	Left ventricle	120/0 mm Hg
Pulmonary artery	25/8 mm Hg	Aorta	120/80 mm Hg
Mean pulm. art.	15 mm Hg	Mean art. blood p	93 mm Hg
Capillary	7–9 mm Hg	Capillary: skeletal renal glomerular	30 mm Hg 45–50 mm Hg
Pulmonary venous	5 mm Hg	Peripheral veins	15 mm Hg
Left atrium	5–10 mm Hg	Right atrium (central venous)	0 mm Hg
Pressure gradient	15–5 = 10 mm Hg	Pressure gradient	93–0 = 93 mm Hg

Blood flow is the volume of blood flowing:

through a vessel, organ, or the entire circulation ml/min

(controlled in relation to the tissue need)

Blood flow= ΔP/total peripheral resistance (TPR)

TPR=viscosity x length/$(radius)^4$

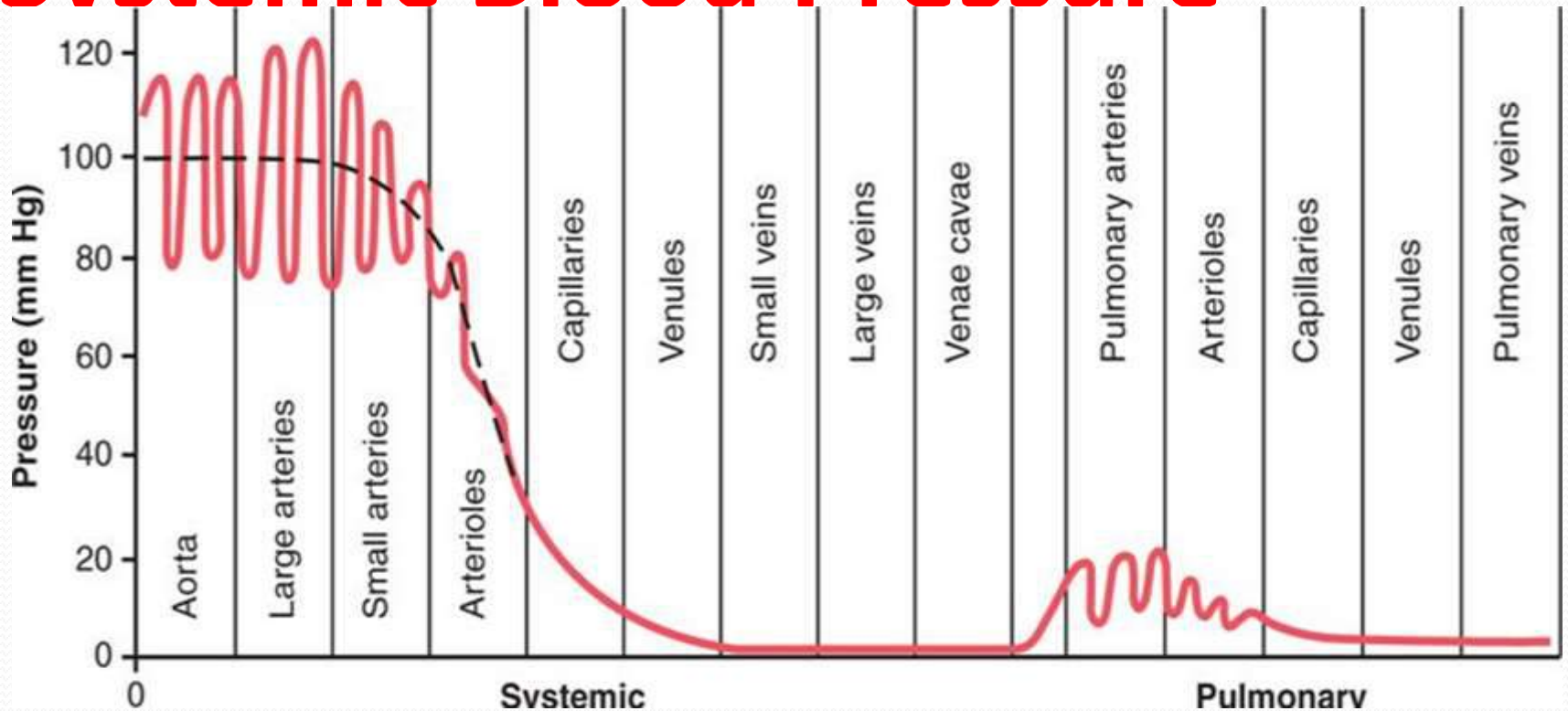
Blood pressure is the force per unit area exerted by the blood against a vessel wall (mm Hg). (by the tension at the end of the arterioles)

Resistance is friction between blood and the vessel wall,.

Significant difference between pulmonary and systemic circulation

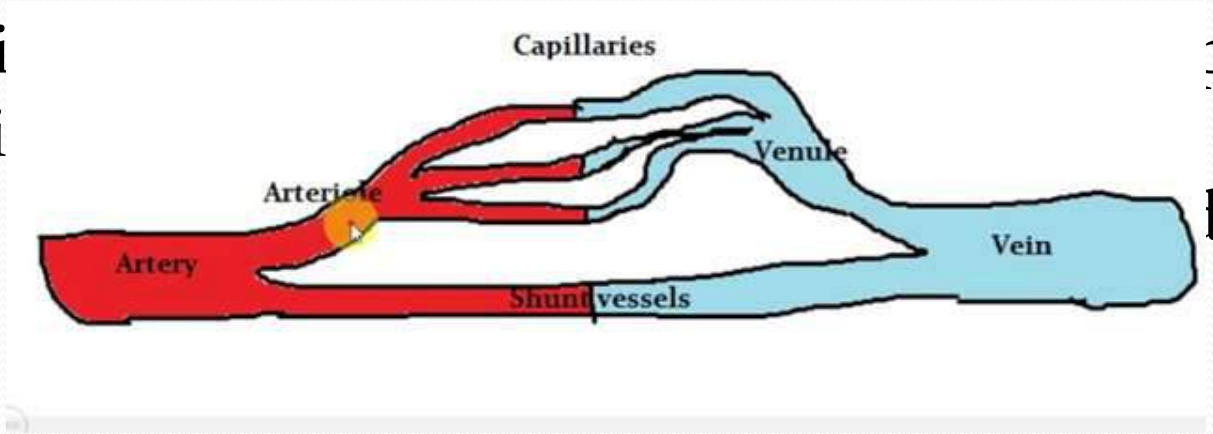
- Cardiac output and heart rate in tow circuit are equal so the stroke volume are the same
- All pressures are higher in the systemic circuit this show the vessels of circuit are very different (the systemic circuit has much high resistance and much low compliance than the pulmonary circuit
- The lower pressure mean that the work of the right ventricle is much lower
- In addition the lower capillary pressure protected against the development of pulmonary edema .

Systemic Blood Pressure



Types of blood vessels

- distensible vessels (aorta , pulmonary artery and their large branches)
- Resistance vessels (arterioles, metarterioels and precapillary sphincter)
- Exchange vessels (capillaries)
- Capacitation vessels (veins, venules)
- shunt vessel A blood vessel: that links an artery di pass the capi control lilation.



Compliance of blood vessels

The compliance or capacitance of blood vessels discredit the volume of blood the vessels can hold at given pressure .compliance is related to distensiblity and is given by the following equation:

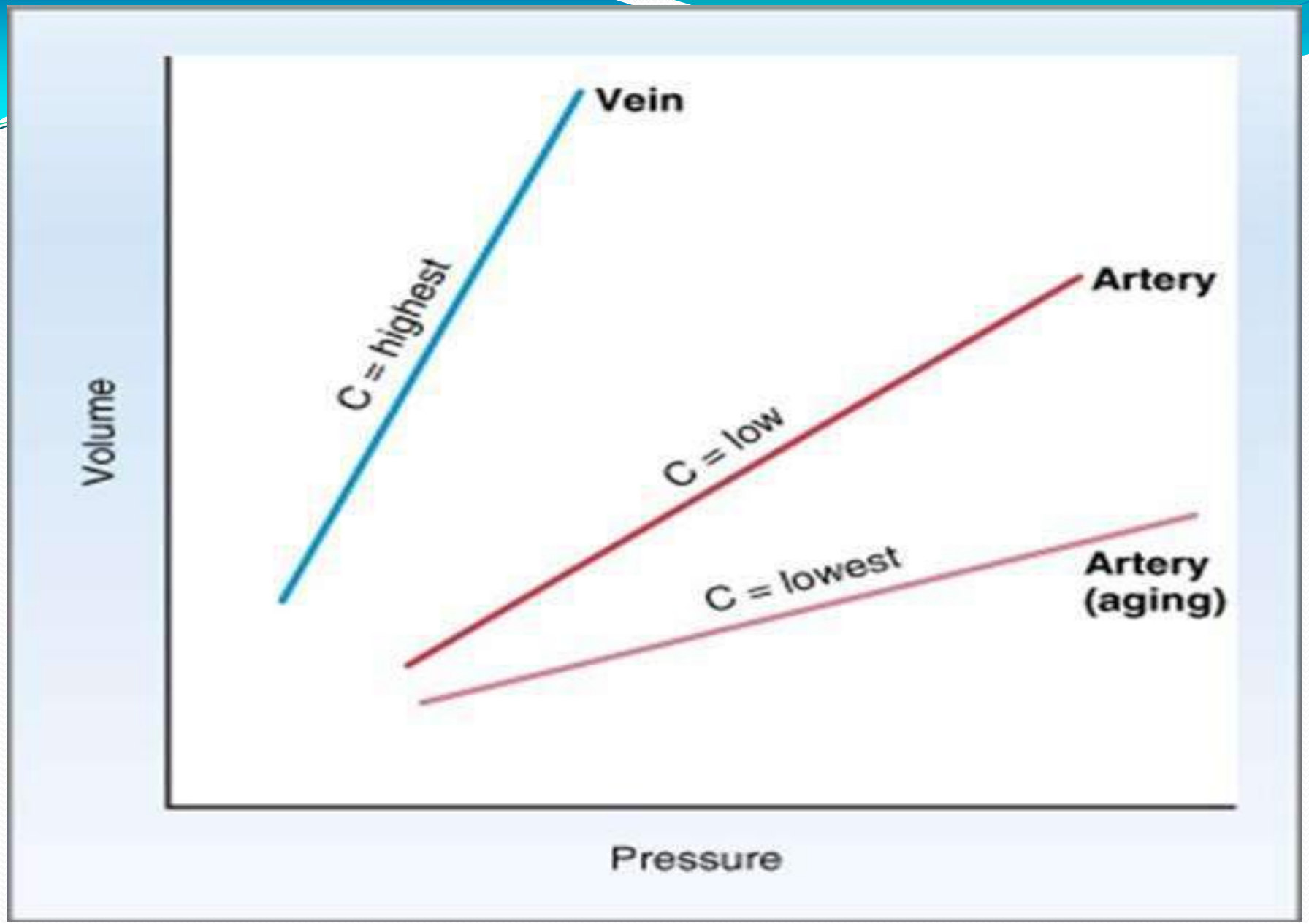
$$C=V/P$$

Where C =compliance ml/mm Hg

V= volume ml

P =pressure mm Hg

If the vessels easy to stretched its considered very compliant ,the apposite noncompliant or


Vein
C = highest
Artery
C = low
C = lowest
Artery
(aging)
Volume
Pressure

Elasticity is the inverse of compliance .vessels that has high elasticity has low compliance

Blood volume:

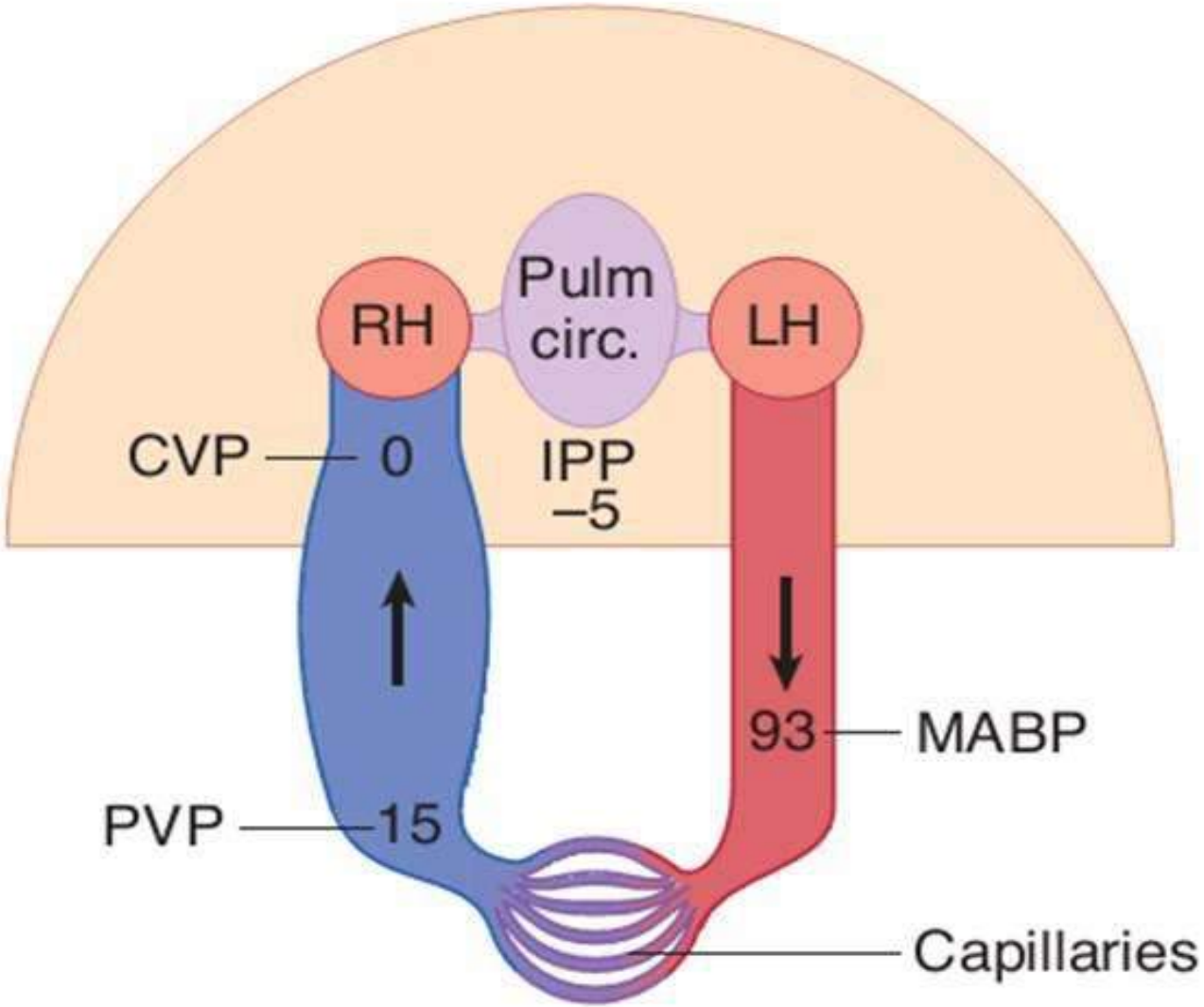
The largest blood volume in CVS is in the systemic veins

The second largest blood volume in the pulmonary veins

The systemic and pulmonary veins have very high compliance compared to the systemic arteries ,this is primary responsible to the blood distribution.

Characteristic of systemic veins

- systemic veins about 20 time more compliant than systemic arteries .
- Veins contain 70% of the systemic blood and thus represent major blood reservoir .
- In venous system small change in blood pressure causes large change in venous volume.


RH
Pulm
circ.
LH
CVP
0
IPP
–5
93
MABP
PVP
15
Capillaries

Volume loading (infusion of fluids)

- Increases venous pressure that's lead to distends the vein ,this is passive dilation
- The volume of blood stored in veins increases ,which means that some of infused volume will not contribute with cardiac out put
- The complaint nature of veins act buffer to buffer change in the venous return and cardiac output

Velocity of blood stream:

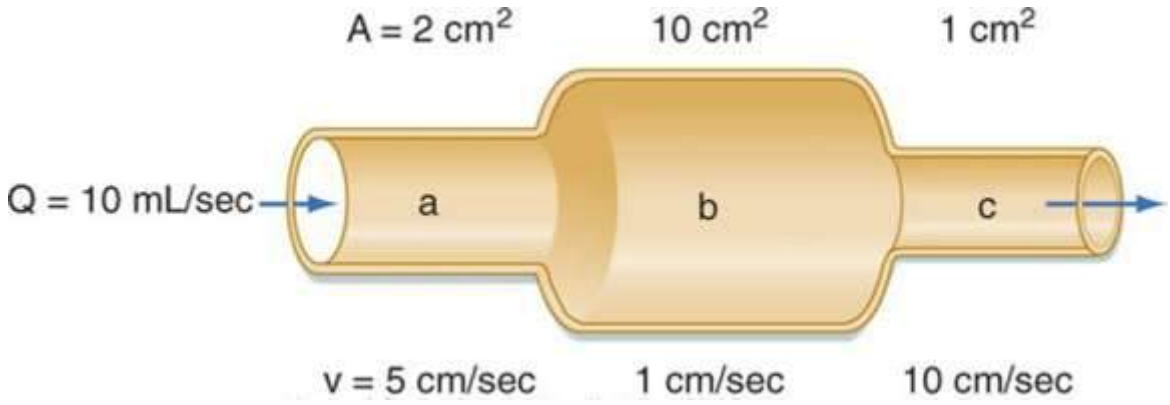
1. **Velocity: as related to fluid movement ,is the distance that practical of fluid travel with the respect to time (e.g. cm/sec).**

2. **Flow: is the rat of displacement of a volume of fluid. And it is expressed in unit of volume per unit time ($e.g.\ cm^3$/sec)**

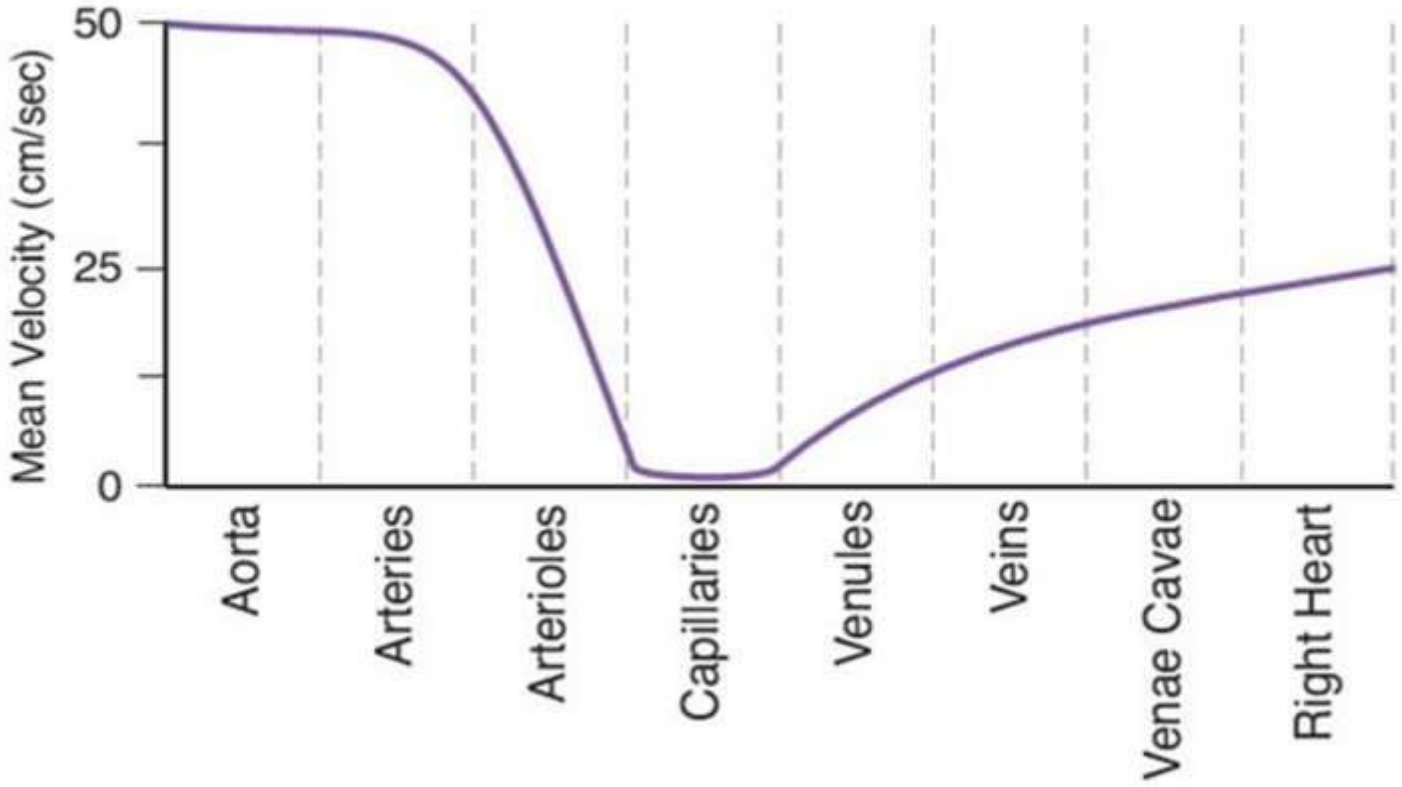
In rigid tube velocity (V) flow (Q) are related to the another by cross section area (A) of tube

The velocity of blood flow is slowest through the capillaries because the have the largest total cross sectional area.

Velocity =flow /cross sectional area



Velocity


Mean Velocity (cm/sec)
50
25
0
Aorta
Arteries
Arterioles
Capillaries
Venules
Veins
Venae Cavae
Right Heart

Factor influence on velocity

- Cross section area of segment
- Phase : systolic increase velocity and diastolic decrease velocity
- Viscosity :increase viscosity lead to decrease velocity
- Velocity decrease in heart failure

Starling law of capillary

Fluid filtration

The hydrostatic pressure in the capillaries tends to force fluid and its dissolved substances through the capillary pores into the interstitial spaces.

Osmotic pressure caused by the plasma proteins, called colloid osmotic pressure tends to cause fluid movement by osmosis from the interstitial spaces into the blood. This osmotic pressure exerted by the plasma proteins normally **prevents significant loss of fluid volume from the blood into the interstitial spaces**.

Lymphatic system returns to the circulation the small amounts of excess protein and fluid that leak from the blood into the interstitial spaces

Starling's Law of the Capillary

P_c = hydrostatic pressure of capillary
π_c = protein (oncotic) pressure of capillary
P_i = hydrostatic pressure of interstitial fluid
π_i = protein osmotic (oncotic) pressure of the interstitial fluid

Net movement out of capillary into interstitium (ml/min)

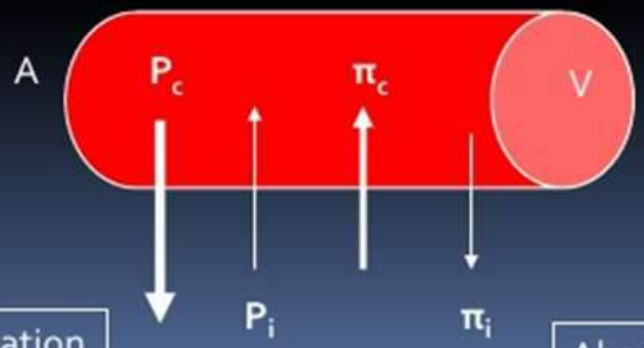
$$FLOW_{net} = (P_c - P_i) - (\pi_c - \pi_i)$$

Basically, movement is governed by (hydrostatic pressure – protein (oncotic) pressure)

P_c = *30 mmHg*
π_c = 28 mmHg
P_i = -3 mmHg
π_i = 8 mmHg

Net = +13 mmHg

Filtration



P_c = *10 mmHg*
π_c = 28 mmHg
P_i = -3 mmHg
π_i = 8 mmHg

Absorption

Net = -7 mmHg

1. ***The capillary hydrostatic pressure (Pc)***, which tends to force fluid outward through the capillary membrane.

2. ***The interstitial fluid pressure (Pi)***, which tends to force fluid inward through the capillary membrane when Pi is positive but outward when Pif is negative.

3. ***The capillary plasma colloid osmotic pressure (***πc), which tends to cause osmosis of fluid inward through the capillary membrane.

4. ***The interstitial fluid colloid osmotic pressure (***πi), which tends to cause osmosis of fluid outward through the capillary membrane.

If the sum of these forces, the net filtration pressure, is positive, there will be a net fluid filtration across the capillaries. If the sum of the Starling forces is negative, there will be a net fluid absorption from the interstitial spaces into the capillaries.

The net filtration pressure (NFP) is calculated as:

$NFP = (Pc + \pi i) - (Pi + \pi c)$

The rate of fluid filtration in a tissue is also determined by

1. the number and size of the pores in each capillary
2. number of capillaries in which blood is flowing.

These factors are usually expressed together as the capillary filtration coefficient (Kf).

The Kf is therefore a measure of the capacity of the capillary membranes to filter water for a given NFP and is usually expressed as ml / min / mmHg net filtration pressure.

The rate of capillary fluid filtration is therefore determined as:

Filtration = Kf x NFP

Exchange of Fluid Through Membrane

The average capillary pressure at the arterial ends of the capillaries is 25-30 mm Hg greater than at the venous ends. Because of this difference, fluid "filters" out of the capillaries at their arterial ends, but at their venous ends fluid is reabsorbed back into the capillaries.

Reabsorption pressure is considerably less than the filtration pressure at the capillary arterial ends, but the venous capillaries are more numerous and more permeable than the arterial capillaries, so that less reabsorption pressure is required to cause inward movement of fluid. The reabsorption pressure causes about 9/10th of the fluid that has filtered out of the arterial ends of the capillaries to be reabsorbed at the venous ends. The remaining 1/10th flows into the lymph vessels and returns to the circulating blood. In other capillaries, the balance of Starling forces is different and, for example, fluid moves out of almost the entire length of the capillaries in the renal glomeruli. On the other hand, fluid moves into the capillaries through almost their entire length in the intestines.

Edema :refers to the presence of excess fluid in the body tissues. In most instances, edema occurs mainly in the extracellular fluid compartment, but it can involve intracellular fluid as well.

Intracellular Edema :

Depression of the metabolic systems of the tissues Lack of adequate nutrition to the cells When blood flow to a tissue is decreased, the delivery of oxygen and nutrients is reduced. If the blood flow becomes too low to maintain normal tissue metabolism, the cell membrane ionic pumps become depressed - osmosis Sometimes this can increase intracellular volume of a tissue area to two to three times normal. Intracellular edema can also occur in inflamed tissues. Inflammation usually has a direct effect on the cell membranes to increase their permeability, allowing sodium and other ions to diffuse into the interior of the cell, with subsequent osmosis of water into the cells

Extracellular Edema:

Extracellular fluid edema occurs when there is excess fluid accumulation in the extracellular spaces. There are two general causes of extracellular edema:

1-abnormal leakage of fluid from the plasma to the interstitial spaces across the capillaries

Increased capillary hydrostatic pressure or decreased plasma colloid osmotic pressure

2- failure of the lymphatics to return fluid from the interstitium back into the blood

Lymphatic Blockage Causes Edema When lymphatic blockage occurs, edema can become severe because plasma proteins that leak into the interstitium have no other way to be removed. The rise in protein concentration raises the colloid osmotic pressure of the interstitial fluid, which draws even more fluid out of the capillaries.

Blockage of lymph flow can be severe with

- infections of the lymph nodes, such as occurs with infection by filaria nematodes.
- Blockage of the lymph vessels can occur in certain types of cancer
- after surgery in which lymph vessels are removed or obstructed. For example, large numbers of lymph vessels are removed during radical mastectomy, impairing removal of fluid from the breast and arm areas and causing edema and swelling of the tissue spaces - temporary

Edema Caused by Heart Failure :

In heart failure,

- the heart fails to pump blood normally from the veins into the arteries; this raises venous pressure and capillary pressure, causing increased capillary filtration.
- In addition, the arterial pressure tends to fall, causing decreased excretion of salt and water by the kidneys, which increases blood volume and further raises capillary hydrostatic pressure to cause still more edema.
- Also, diminished blood flow to the kidneys stimulates secretion of renin, causing increased formation of angiotensin II and increased secretion of aldosterone, both of which cause additional salt and water retention by the kidneys.

- In patients with left-sided heart failure, blood is pumped into the lungs normally by the right side of the heart but cannot escape easily from the pulmonary veins to the left side of the heart because this part of the heart has been greatly weakened. Consequently, all the pulmonary vascular pressures, including pulmonary capillary pressure, rise far above normal, causing serious and life-threatening pulmonary edema. When untreated, fluid accumulation in the lungs can rapidly progress, causing death within a few hours

Edema Caused by Decreased Kidney Excretion of Salt and Water

Most sodium chloride added to the blood remains in the extracellular compartment, and only small amounts enter the cells. Therefore, in kidney diseases that compromise urinary excretion of salt and water, large amounts of sodium chloride and water are added to the extracellular fluid. Most of this salt and water leaks from the blood into the interstitial spaces, but some remains in the blood. The main effects of this are to cause

- (1)widespread increases in interstitial fluid volume (extracellular edema)
- (2) hypertension

Edema Caused by Decreased Plasma Proteins

One of the most important causes of decreased plasma protein concentration is loss of proteins in the urine in certain kidney diseases, a condition referred to as nephrotic syndrome. Multiple types of renal diseases can damage the membranes of the renal glomeruli, causing the membranes to become leaky to the plasma proteins and often allowing large quantities of these proteins to pass into the urine. When this loss exceeds the ability of the body to synthesize proteins, a reduction in plasma protein concentration occurs. Serious generalized edema occurs when the plasma protein concentration falls below 2.5 g/100 ml.

Cirrhosis of the liver is another condition that causes a reduction in plasma protein concentration. Cirrhosis means development of large amounts of fibrous tissue among the liver parenchymal cells. One result is failure of these cells to produce sufficient plasma proteins. The liver fibrosis sometimes compresses the abdominal portal venous drainage vessels as they pass through the liver before emptying back into the general circulation. Blockage of this portal venous outflow raises capillary hydrostatic pressure throughout the gastrointestinal area and further increases filtration of fluid out of the plasma into the intraabdominal areas. When this occurs, the combined effects of decreased plasma protein concentration and high portal capillary pressures cause transudation of large amounts of fluid and protein into the abdominal cavity, a condition referred to as ascites.

Increased capillary pressure

A. Excessive kidney retention of salt and water

1. Acute or chronic kidney failure

2. Mineralocorticoid excess

B. High venous pressure and venous constriction

1. Heart failure

2. Venous obstruction

3. Failure of venous pumps (a) Paralysis of muscles (b) Immobilization of parts of the body (c) Failure of venous valves

C- **Decreased plasma proteins** :

A. Loss of proteins in urine (nephrotic syndrome)

B. Loss of protein from shed skin areas 1. Burns 2. Wounds

C. Failure to produce proteins

d. Liver disease (e.g., cirrhosis)

e. Serious protein or caloric malnutrition

D-Increased capillary permeability

A. Immune reactions that cause release of histamine and other immune products

B. Toxins

C. Bacterial infections

D. Vitamin deficiency, especially vitamin C

E. Prolonged ischemia

F. Burns

E-Blockage of lymph return

A. Cancer

B. Infections (e.g., filaria nematodes)

C. Surgery

D. Congenital absence or abnormality of lymphatic vessels

Tachycardia

is a common type of heart rhythm disorder (arrhythmia).

heart beats are normal for your heart rate to rise during exercise or as a physiological response to stress, trauma or illness. But in tachycardia the heart beats faster than normal in the upper or lower chambers of the heart or both while at rest.

Your heart rate is controlled by electrical signals sent across heart tissues. Tachycardia occurs when an abnormality in the heart produces rapid electrical signals that quicken the heart rate, which is normally about 60 to 100 beats a minute at rest.

In some cases, tachycardia may cause no symptoms or complications. But if left untreated, tachycardia can disrupt normal heart function and lead to serious complications, including:

- Heart failure
- Stroke
- Sudden cardiac arrest or death.

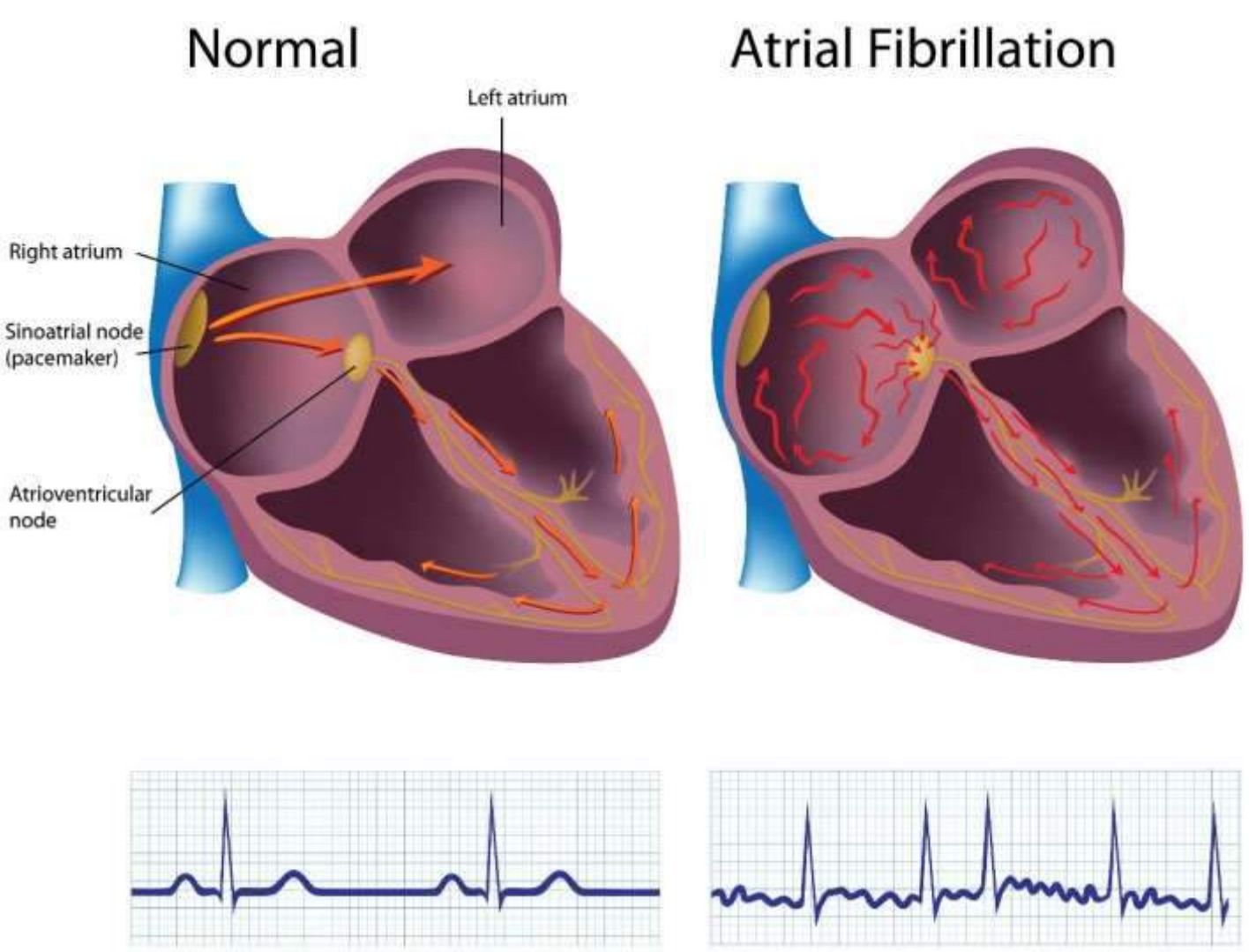
There are many different types of abnormal tachycardia. They're classified according to the origin and cause of the abnormally fast heartbeat. Common types of tachycardia include:

1-Supraventricular tachycardia (SVT). Supraventricular tachycardia is an abnormally fast heartbeat that originates somewhere above the ventricles. It's caused by abnormal circuitry in the heart that is usually present at birth and creates a loop of overlapping signals.

Atrial fibrillation: Atrial fibrillation is a rapid heart rate caused by chaotic, irregular electrical impulses in the upper chambers of the heart (atria). These signals result in rapid, uncoordinated, weak contractions of the atria.

Atrial fibrillation may be temporary, but some episodes won't end unless treated.

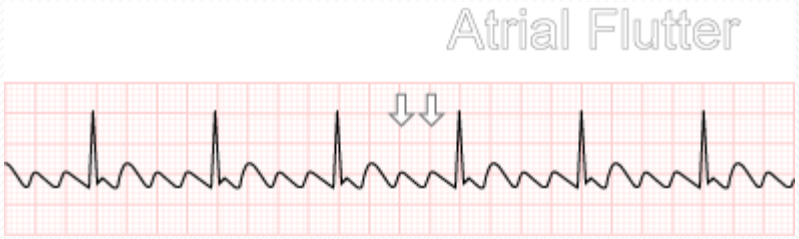
Atrial fibrillation is the most common type of tachycardia. Most people with atrial fibrillation have some structural abnormalities of the heart related to underlying conditions such as **heart disease or high blood pressure.** Other factors that may contribute to atrial fibrillation include **a heart valve disorder, hyperthyroidism or heavy alcohol use.**

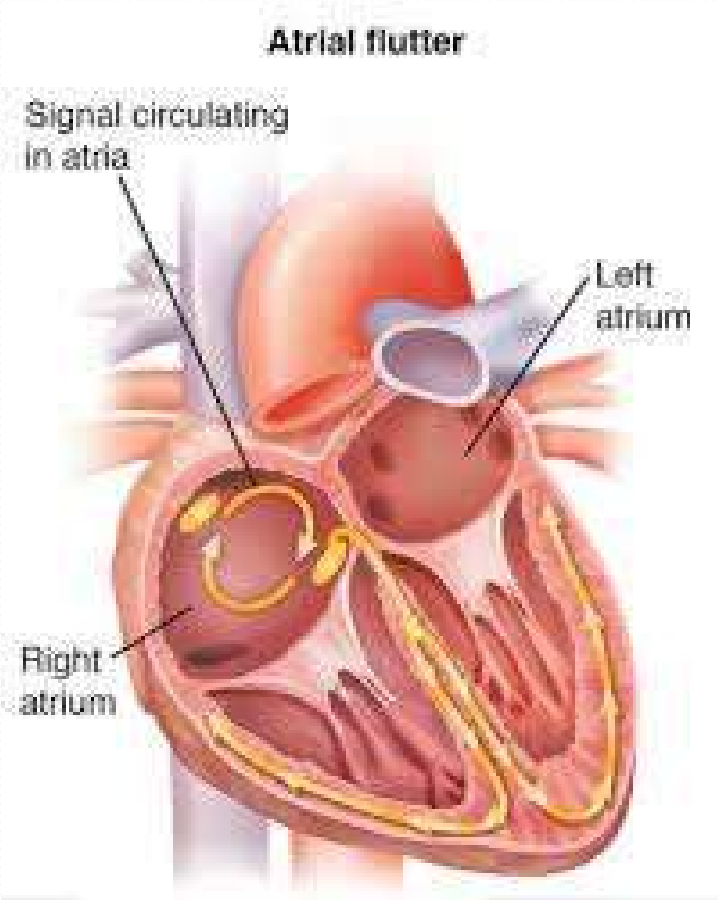

Normal
Atrial Fibrillation
Left atrium
Right atrium
Sinoatrial node
(pacemaker)
Atrioventricular
node

Atrial flutter. In atrial flutter, the heart's atria beat very fast but at a regular rate. The fast rate results in weak contractions of the atria.

Atrial flutter is caused by irregular circuitry within the atria. Episodes of atrial flutter may resolve themselves or may require treatment.

People who experience atrial flutter also often experience atrial fibrillation at other times.





2-Ventricular tachycardia. Ventricular tachycardia is a rapid heart rate that originates with abnormal electrical signals in the lower chambers of the heart (ventricles). The rapid heart rate doesn't allow the ventricles to fill and contract efficiently to pump enough blood to the body.

Ventricular tachycardia episodes may be brief and last only a couple of seconds without causing harm. But episodes lasting more than a few seconds can become a life-threatening medical emergency.

Ventricular fibrillation. Ventricular fibrillation occurs when rapid, chaotic electrical impulses cause the ventricles to quiver ineffectively instead of pumping necessary blood to the body. This can be fatal if the heart isn't restored to a normal rhythm within minutes with an electric shock to the heart (defibrillation).

Ventricular fibrillation may occur during or after a **heart attack**. Most people who experience ventricular fibrillation **have an underlying heart disease** or have experienced **serious trauma**, **such as being struck by lightning**.

When your heart is beating too fast, it may not pump blood effectively to the rest of your body. This can deprive your organs and tissues of oxygen .

Hypotension

Hypotension is abnormally low blood pressure . Blood pressure is the force of blood pushing against the walls of the arteries as the heart pumps out blood.

blood pressure is measured as systolic and diastolic pressures. "Systolic" refers to blood pressure when the heart while pumping blood. "Diastolic" refers to blood pressure when the heart is at rest between beats.

You most often will see blood pressure numbers written with the systolic number above or before the diastolic number, such as 120/80 mmHg.

Normal blood pressure in adults is 120/80 mmHg.

Hypotension is blood pressure that's lower than 90/60 mmHg.

Symptoms

For some people, low blood pressure signals an underlying problem, especially when it drops suddenly or is accompanied by signs and symptoms such as:

- Dizziness or lightheadedness
- Fainting (syncope)
- Blurred vision
- Nausea
- Fatigue
- Lack of concentration

Conditions that can cause low blood pressure

Medical conditions that can cause low blood pressure include:

Pregnancy. Because the circulatory system expands rapidly during pregnancy, blood pressure is likely to drop. This is normal, and blood pressure usually returns to your pre-pregnancy level after you've given birth.

Heart problems. Some heart conditions that can lead to low blood pressure include extremely low heart rate (bradycardia), heart valve problems, heart attack and heart failure.

Endocrine problems. Thyroid conditions , adrenal insufficiency (Addison's disease), low blood sugar (hypoglycemia).

Dehydration. When your body loses more water than it takes in, it can cause weakness, dizziness and fatigue.

Fever, vomiting, severe diarrhea, overuse of diuretics and strenuous exercise can lead to dehydration

Blood loss. Losing a lot of blood, such as from a major injury or internal bleeding, reduces the amount of blood in your body, leading to a severe drop in blood pressure.

Severe infection (septicemia). When an infection in the body enters the bloodstream, it can lead to a life-threatening drop in blood pressure called septic shock.

Severe allergic reaction (anaphylaxis).

Common triggers of this severe and potentially life-threatening reaction include foods, certain medications, insect venoms and latex. Anaphylaxis can cause a dangerous drop in blood pressure

Lack of nutrients in your diet. A lack of the vitamins B-12 can keep your body from producing enough red blood cells (anemia), causing low blood pressure.

Shock

Extreme hypotension can result in this life-threatening condition. Signs and symptoms include:

- Confusion, especially in older people
- Cold, clammy, pale skin
- Rapid, shallow breathing
- Weak and rapid pulse

Effect of blood lose on C.V.S

Hemorrhagic shock is a clinical syndrome resulting from decreased blood volume (hypovolemia) caused by blood loss, which leads to reduced cardiac output and organ perfusion.

Blood loss can be external (e.g., externally bleeding wound) or internal (e.g., internal bleeding caused by ruptured aortic aneurism).

The severity of hemorrhagic shock and associated symptoms depends on the volume of blood that is lost and how rapidly it is lost.

Generally, a blood loss of <15% of total blood volume leads to only a small increase in heart rate and no significant change in arterial pressure.

When blood loss is 15 to 40%, mean arterial and pulse pressures fall, and heart rate increases,. If the hemorrhage is stopped, the arterial pressure slowly recovers and heart rate declines as long-term compensatory mechanisms are activated to restore normal arterial pressure. The time for recovery is longer when there is a greater loss of blood.

.

Resuscitation efforts, which include the administration of fluids to increase blood volume, can speed up this recovery. A greater than 40% blood loss is life threatening, and resuscitation is generally essential for survival because prolonged, severe hypotension leads to organ failure and death.

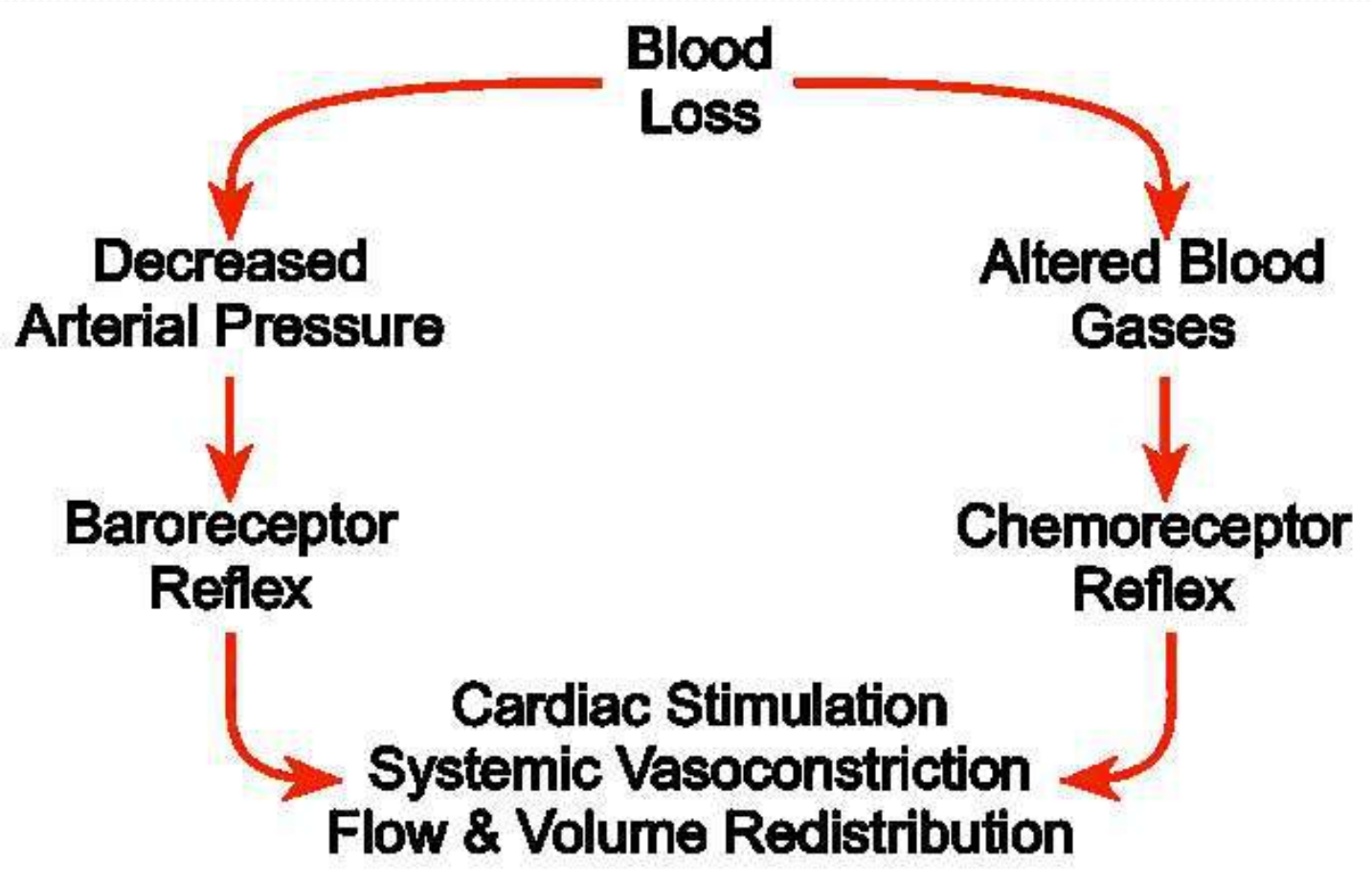
Compensatory mechanisms

The reduction in blood volume during acute blood loss causes a fall in central venous pressure and cardiac filling. This leads to reduced cardiac output and arterial pressure. The body has a number of compensatory mechanisms that become activated in an attempt to restore arterial pressure and blood volume back to normal. These mechanisms include:

- Baroreceptor reflexes
- Chemoreceptor reflexes
- Renal reabsorption of sodium and water
- Activation of thirst mechanisms
- Reabsorption of tissue fluids

he body can quickly sense a fall in blood pressure through its arterial and cardiopulmonary baroreceptors , and then activate the sympathetic adrenergic system to stimulate the heart (increase heart rate and contractility) and constrict blood vessels (increase systemic vascular resistance).

Sympathetic activation has little direct influence on brain and coronary blood vessels, so these circulations can benefit from the vasoconstriction that occurs in other organs (particularly in the gastrointestinal, skeletal muscle and renal circulations) that serve to increase systemic vascular resistance and arterial pressure. In other words, cardiac output is redistributed from less important organs to the brain and myocardium, both of which are critical for survival. Reduced organ blood flow caused by vasoconstriction and reduced arterial pressure


Blood Loss
Decreased Arterial Pressure
Altered Blood Gases
Baroreceptor Reflex
Chemoreceptor Reflex
Cardiac Stimulation
Systemic Vasoconstriction
Flow & Volume Redistribution

Critical closing pressure

Critical closing pressure :is the internal pressure at which a blood vessels collapses and closes completely. If blood pressure falls below critical closing pressure, then the vessels collapse. This happens during the measurement of blood pressure with a sphygmomanometer At resting state the arterial critical closing pressure is ~ 20 mmHg .

In severe hemorrhage , blood loss leads to a significant reduction in pressure. This, combined with activity in the sympathetic autonomic nerve supplying smooth muscle , leads to vasoconstriction to the extent that the vessels may collapse. This occurs at the critical closing pressure, closing off blood supply to tissue, which can lead to toxic shock.

Cyanosis

Cyanosis :is bluish discoloration of the skin and mucous membrane that results

1. when the absolute level of reduced hemoglobin (Deoxyhemoglobin) in the capillary bed exceeds 5g/DL. or
2. increased concentration of abnormal Hemoglobine derivatives (eg. Methemoglobinemia, sulphaemoglobinemia) in the superficial blood vessels

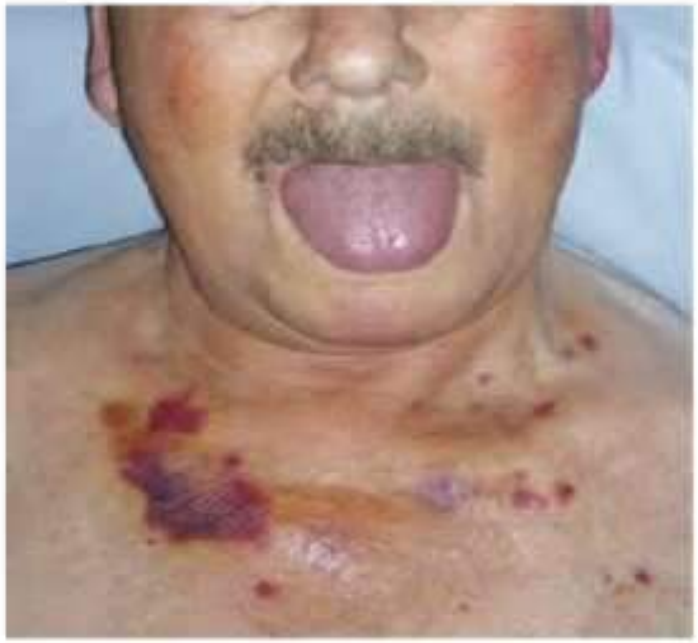
Mechanism of cyanosis

1. Alveolar hypoventilation
2. Diffusion impairment
3. Ventilation-perfusion mismatch
4. Hemoglobinopathy (including methemoglobinemia, sulphaemoglobinemia) that limits oxygen transport

Central cyanosis

1. Pathologic condition caused by reduced arterial oxygen saturation (SO2).
2. Involves highly vascularized tissues, such as the lips, tongue and mucous membranes, through which blood flow is brisk and the arteriovenous difference is minimal.
3. Cardiac output typically is normal, and patients have warm extremities

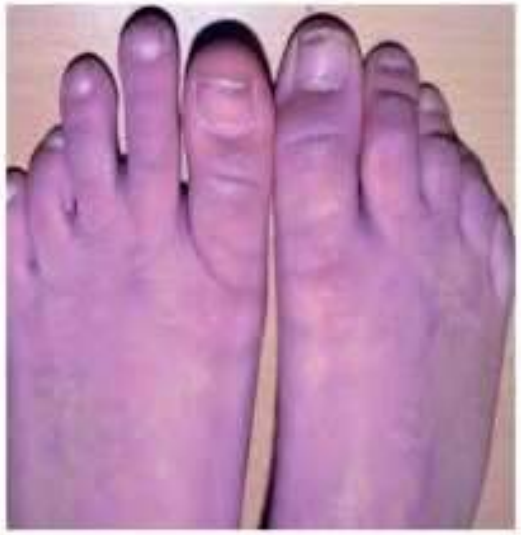
Central cyanosis

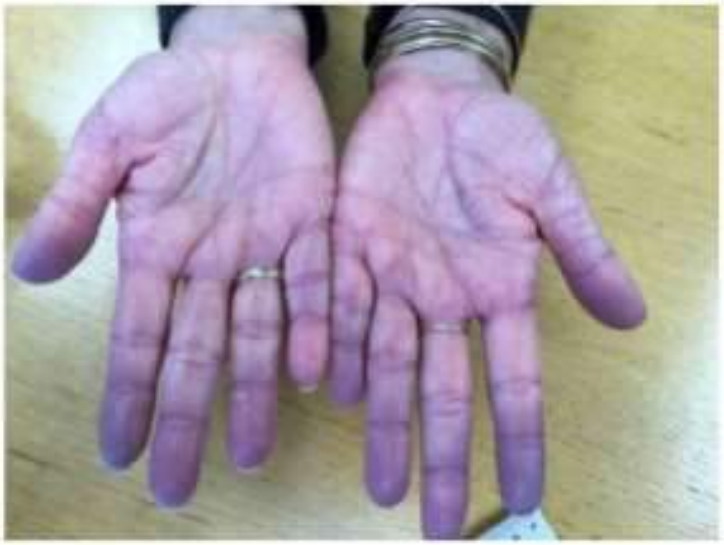


Peripheral cyanosis

1. Normal systemic arterial oxygen saturation and increased oxygen extraction from peripheral blood, resulting in a wide systemic arteriovenous oxygen difference
2. The increased extraction of oxygen results from sluggish movement of blood through the capillary circulation.
3. Affects the distal extremities, and circumoral areas .

Peripheral cyanosis

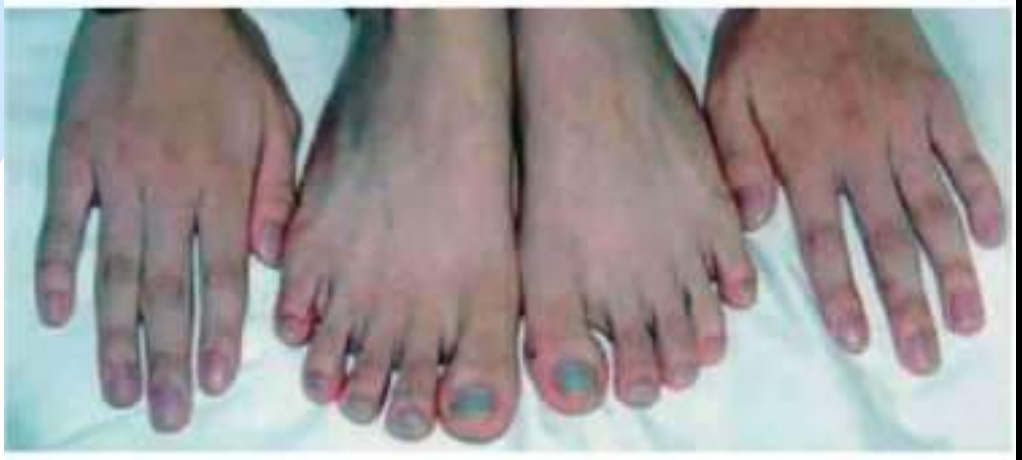


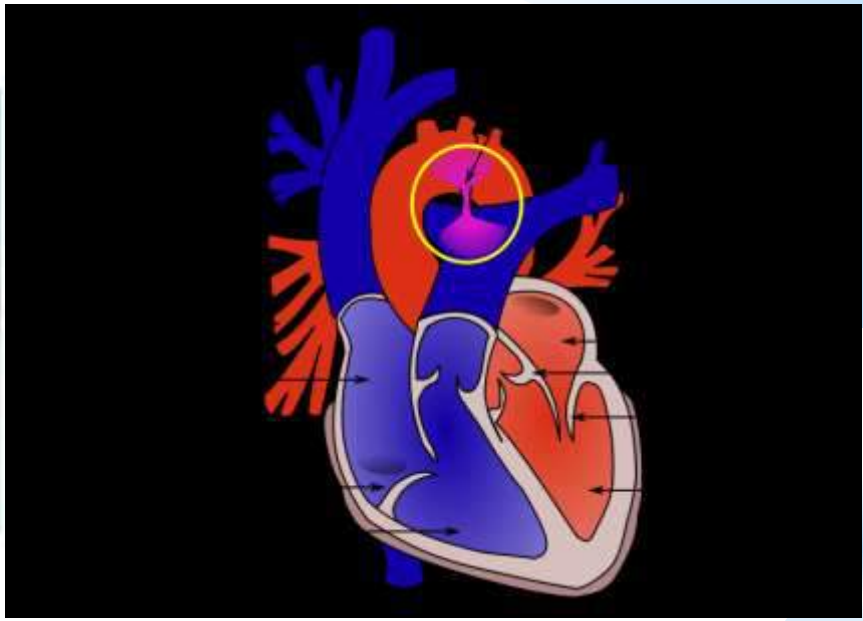


	central cyanosis	Perpheral cyanosis
Area	generalize	localize
Tongue	involve	Not involve
Hand shake	Feel warm	Feel cold
clubbing	Usually present	Not present
On O2 application	Pulmonary cause improved	Not improved
Application of warming	Not improved	improved
Mechanism	Diminution of oxygen saturation	Diminution of blood flow
Capillary refill time	<2 sec	>2 sec

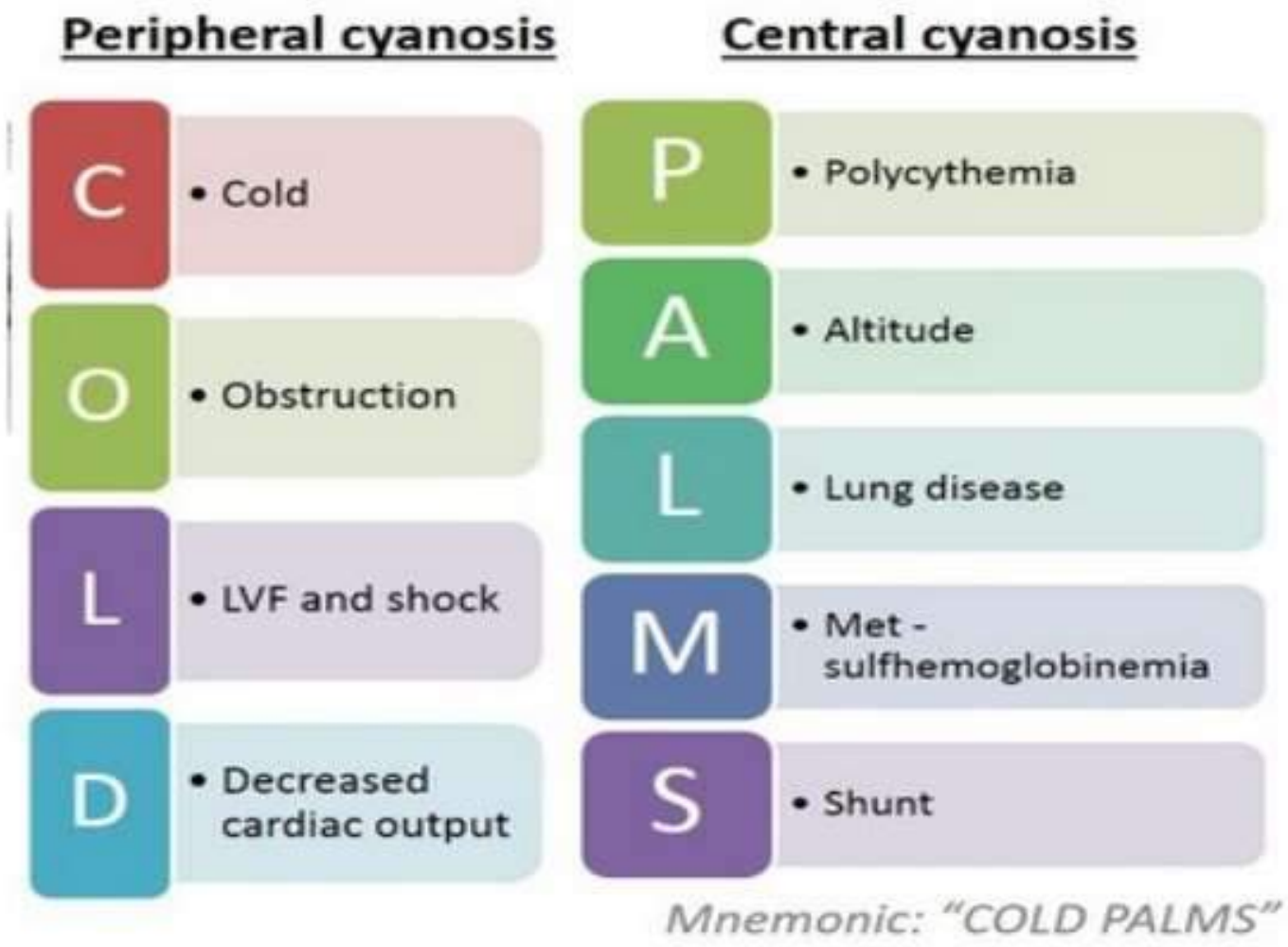
Differential cyanosis

When cyanosis is present only in the toes but not in the fingers, * it is called Differential cyanosis. It is seen in Patent ductus arteriosus PDA.





ETIOLOGY


Peripheral cyanosis
C
• Cold
O
• Obstruction
L
• LVF and shock
D
• Decreased cardiac output
Central cyanosis
P
• Polycythemia
A
• Altitude
L
• Lung disease
M
• Met - sulfhemoglobinemia
S
• Shunt
Mnemonic: "COLD PALMS"

pulmonary causes

1. Alveolar hypoventilation

A. Central nervous system depression: asphyxia, maternal sedation, intraventricular hemorrhage, meningitis, encephalitis

B. Neuromuscular disease: myasthenia gravis, phrenic nerve injury

C. Airway obstruction: choanal atresia, laryngotracheomalacia,,

2. Ventilation/perfusion mismatch

A. Airway diseases: pneumonia, cystic adenomatoid, diaphragmatic hernia, pulmonary hypoplasia, lobar emphysema, atelectasis, pulmonary hemorrhage, transient tachypnea of the newborn

B. Extrinsic compression of lungs: pneumothorax, thoracic dystrophy.

3. Diffusion impairment

A. Pulmonary edema: left-sided obstructive cardiac disease, cardiomyopathy

B. Pulmonary fibrosis

C. Congenital lymphangiectasia

4-Cardiac causes:

1-Decreased pulmonary blood flow-

A. Tetralogy of Fallot

B. Tricuspid valve anomaly

C. Pulmonary valve atresia

D. Critical valvular pulmonary stenosis

2. Severe heart failure

A. Hypoplastic left heart syndrome

B. stenosis of the aorta

C. Interrupted aortic arch

D. Critical valvular aortic stenosis

4- Hemoglobinopathy :

Methemoglobinemia: congenital or secondary to toxic exposure >1.5gm/dl

sulphaemoglobinemia: secondary to toxic exposure >0.5gm/dl .

Factors affecting the detection of cyanosis

1-Hemoglobin concentration

Detected at higher levels of saturation in polycythemic than in anemic patients.

Significant oxygen desaturation can be present in an anemic patient without clinically detectable cyanosis

2. Fetal hemoglobin

* Binds oxygen more avidly than adult hemoglobin.
* The oxygen dissociation curve is shifted to the left, so that for a given level of oxygen tension (PO2), the oxygen saturation (SO2) is higher in the newborn than older infants or adults .
* It explains that for a given level of oxygen saturation(SO2), the PO2 is lower in newborns.
* As a result, cyanosis is detected at a lower PO2 in newborns compared with older patients.

3. Skin pigmentation

Less apparent in the skin of patients with darker pigmentation. . Examination should include the nail beds, tongue, and mucous membranes, which are less affected by pigmentation

Treatment of cyanosis

Treatment of cyanosis thus focus on the Treatment of underlying disease rather than the symptom alone.

- Symptomatic treatment of cyanosis

1. Warming of the affected areas- Peripheral cyanosis brought about by exposure to cold or Raynaud's phenomenon may be treated symptomatically using gentle warming of the fingers and toes.

2. Oxygenation as a treatment for , Sometimes a breathing machine or ventilator might be required.

3.Intravenous fluids- Children who have difficulty in feeding due to cyanosis and heart failure due to an underlying cyanotic heart disease need to be administered intravenous fluids.

*pallor

*pallor is a pale color of the skin and mucous membrane due to reduce in amount of hemoglobin

*there are many causes of pallor :

1. Anemia : which is the most common cause
2. Leukemia
3. Heart disease
4. Sleep deprivation
5. Shock : whether it is septic , Anaphylactic, Cardiogenic, Neurogenic and hypovolemic shock
6. syncope =decrease in the blood supply to the brain=hypotension leading to pallor .

7-long steady diabetic patient lead to keratin deposition in the skin

8. Hypothyroidism with or without anemia

9. hypopituitarism leads to decrease in the melanin stimulatory hormone .

Pallor is seen in :

* Palm creases
* Conjunctiva.
* mucous membranes

*Anemia

ANEMIA :is a reduction in the number of RBCs, the quantity of hemoglobin, or the volume of RBCs

- Hb level below than 10 g/dl is considered as a significant level to assess anemia
- Because the main function of RBCs is oxygenation, anemia results in varying degrees of hypoxia depending on the degree of anemia and the rapidity of development but its independent on the cause.
- symptom of anemia : like fatigue ,headache ,dizziness Palpitation , dimness of vision and others
- signs : the most important is pallor and others like : Tachycardia, and edema

Types Of Anemia

* Iron deficiency anemia
* Megaloplastic anemia
* Hemolytic anemia
* aplastic anemia
* Anemia of chronic dis.

Iron Deficiency Anemia The most common type Etiology

1. Inadequate dietary intake Found in 30% of the world's population
2. Malabsorption due to in duodenum GI surgery
3. Blood loss 2 ml blood contain 1mg iron

* Investigation

1. Blood film : Hemoglobin level reduced, mean corpuscular volume reduced .
2. bone marrow aspiration : iron stores is empty
3. serum ferritin reduced and the total binding capacity with transferrin increased.
4. gastrointestinal tract endoscopy.

Megaloblastic Anemia *

- The causes of this type of anemia is deficiency of both B12 and folic acid that are important for DNA synthesis .
- Any disorder in the DNA will cause abnormalities in rapidly proliferative tissue including the hematopoietic tissue.

Diagnosis :

1. mcv ,blood film :oval macrocytosis , Platelet count and leucocyte tend to be low.
2. bone marrow show hypercellularity ,megaloblastic changes in erythroid series.
3. plasma Lactate dehydrogenase LDH elevated due to increase in the destruction of RBC

Common forms of megaloblastic anemia is :

1. Cobalamin deficiency (vitamin B12) known as pernicious anemia

* Inadequate diet
* ,intrinsic factor deficiency (congenital or due to gastrostomy)
* disease of the terminal ileum(e.g. Crohn's disease),
* may be removed from gut by bacterial proliferation

2. folate deficiency

* Poor intake
* Malabsorption (Coeliac disease)
* increase demand(pregnancy)or drugs.

Hemolytic Anemia *

- Various abnormalities lead to decrease in the life span of the RBC & development of anemia when the bone marrow output no longer compensates
- increasing in BM activity will be reflected as increasing in reticulocyte count in peripheral blood
- the catabolic pathways for hemoglobin degradation are overloaded and a modest increase in unconjugated bilirubin in the blood and increase absorption urobilinogen from the gut that excreted in urine

Causes Of Hemolytic Anemia

1-CONGENITAL

membrane abnormalities :

*hereditary spherocytosis

*hemoglobinopathies:

thalassemia: in lack of Hb chain synthesis

sickle cell anemia :amino acid substitution or alternation of Hb chain

membrane defect : Glucose-6-phosphate dehydrogenase deficiencyG6PD def.

2-AQUIRED

*Immune : Autoimmune disease like SLA –

* Non Immune : like, malaria and drugs

* Aplastic Anemia

the basic problm in this type of anemia is failure of stem cell to a varying degree, producing hypoplasia of marrow elements

Etiology :

- Congenital :Chromosomal alterations
- Acquired :Results from exposure to ionizing radiation, chemical agents, viral and bacterial infections

investigation :

- A full blood count demonstrate a pancytopenia, neutropenia is the most marked aspect of leukopenia , RBCs are normocytic – normochromic , platelet production is severely affected

* Anemia of chronic disease

- This is a commen type of anemia , characterized by :
- Anemia occurs in chronic infection , inflammation , or neoplasia
- Anemia is not related bleeding , hemolysis or marrow infiltration
- Anemia is mild , with normal MCV and normocytic – noromchromic RBC
- the serum iron is low but iron stors is normal or increased

Anemia of chronic disease

- several mechanism are implicated including:
- Relative deficiency of erythropoietin
- diminished erythropoiesis due to toxic effect of uremia reduce red cell survival.
- increased blood loss due to capillary fragility and poor platelet formation.
- reduced dietary intake and absorption of iron.

Homeostatic

The term homeostasis is used by physiologists to mean maintenance of nearly constant conditions in the internal environment.

Essentially all organs and tissues of the body perform functions that help maintain these constant conditions. For instance, the lungs provide oxygen to the extracellular fluid to replenish the oxygen used by the cells, the kidneys maintain constant ion concentrations, and the gastrointestinal system provides nutrients.

Fluid and Electrolyte Imbalances

Electrolytes are ions that can have either a negative or positive charge. Electrolytes play roles that are essential to life. For example,

- ions contract muscles
- move fluids about within the body
- produce energy and they perform many other roles in the body

The body's electrolytes are positively or negatively charged as shown below:

Sodium Na^+ ,Potassium K , Calcium Ca^+, Magnesium Mg^+ ,Chloride Cl ,Hydrogen phosphate $HPO4^-$, Bicarbonate HCO3 and Sulfate SO4.

Sodium

The normal range for sodium is 135 to 145 milliequivalents per liter (mEq/L).

Sodium plays a primary role in the body's fluid balance and it also impacts on the functioning of the bodily muscles and the central nervous system.

This electrolyte is most abundant in the blood plasma, and bodily water goes where sodium is. For example, high levels of fluid in the plasma will occur when the plasma has high sodium content and the converse is also true.

Hypernatremia, that is a sodium level higher than 145 mEq/L can result from different factors such as

- diabetes insipidus
- dehydration, as the result of a fever, vomiting, diarrhea, diaphoresis, extensive exercise ,exposures of long duration to environmental heat
- Cushing's Syndrome.

❖ It must be noted, however, that a rapid reduction of sodium in the body can lead to the rapid flow of water which can result in cerebral edema, permanent brain damage which lead death.

❖ The treatment of hypernatremia, like other electrolyte disorders includes the correction and management of any underlying causes and dietary sodium restrictions.

Hyponatremia, that is a sodium level of less than 135(mEq/L). can result from the syndrome of

- inappropriate antidiuretic hormone
- some medications like diuretics
- some antidepressants
- water intoxication
- Some diseases and disorders such as , cirrhosis, renal failure,, diabetes insipidus, Addison's disease, primary polydipsia, severe diarrhea or vomiting.

The treatments of hyponatremia include

- the correction and management of any underlying causes
- diuretic medications
- fluid restrictions, intravenous sodium,
- if Addison's disease is the cause then hormone replacement may be necessary.

Potassium

The normal potassium level is 3.7 to 5.2 mEq/L. Unlike sodium that is an extracellular electrolyte that is found in the blood plasma, potassium is most abundant in the cells of the body; it is primarily an intracellular electrolyte. This electrolyte promotes and facilitates electrical impulses that are necessary for muscular contractions and also for the normal functioning of the brain.

Hyperkalemia: which is a potassium level greater than 5.2 mEq/L, can be life threatening. Hyperkalemia is most frequently associated with renal disease, but it can also occur as the result of some medications.

Life threatening hyperkalemia is treated with renal dialysis and potassium lowering medications. Lower less threatening levels of hyperkalemia can sometimes be treated with the restriction of dietary potassium containing foods

Hypokalemia, which is a potassium level less than 3.7 mEq/L, most often as the result of bodily fluid losses that occur as the result of diarrhea, vomiting, and diaphoresis as well as some medications like diuretics and laxatives, and with other disorders and diseases such as ketoacidosis.

to treating the underlying cause of this electrolyte imbalance, supplemental potassium is typically administered

Calcium

The normal level of calcium is between 8.5 - 10.6 mg/dL.

The levels of calcium in the body are managed by calcitonin which decreases calcium levels and parathyroid hormone which increases the calcium levels. Calcium is essential for bone health and other functions.

Hypercalcemia, which is a calcium level of more than 10.6 mg/dL, is most often associated with

- the endocrine disorder of hyperparathyroidism,
- some forms of cancer such as breast cancer and cancer of the lungs, with multiple myeloma

The treatment of hypercalcemia can include intravenous fluid hydration and medications like diuretics

Hypocalcemia, which is a calcium level less than 8.5 mg/dL, can occur as the result of renal disease,

- inadequate dietary calcium, a vitamin D deficiency because vitamin D is essential for the absorption of calcium
- a low level of magnesium, pancreatitis, hypoparathyroidism
- an eating disorder, and certain medications such as anticonvulsants,

The treatment of hypocalcemia includes the monitoring of the patient respiratory and cardiac status in addition to providing the patient with calcium supplements coupled with vitamin D because vitamin D is necessary for the absorption of calcium

Magnesium

The normal level of magnesium in the blood is 1.7 to 2.2 mg/dL. Magnesium plays an important role in enzyme activities, brain neuron activities, the contraction and relaxation of muscles. Magnesium also plays a role in the metabolism of calcium, potassium and sodium.

Hypermagnesemia, which is a blood magnesium level of more than 2.2 mg/dL, is most frequently found secondary to renal failure, dehydration, diabetic acidosis, hyperparathyroidism, Addison's disease, and with the excessive and prolonged use of magnesium containing laxatives .

- The treatment for hypermagnesemia typically includes the cessation of causative medications like magnesium containing laxatives, renal dialysis, and the administration of calcium gluconate, calcium chloride and/or intravenous dextrose .

Hypomagnesemia, on the other hand, is a blood magnesium level less than 1.7 mg/dL. Hypomagnesaemia often occurs as the result of the prolonged use of diuretics, uncontrolled diabetes, hypoparathyroidism, diarrhea and gastrointestinal disorders such as Chron's disease, severe burns, malnutrition,.

The treatment of hypomagnesaemia can include medications to decrease pain ,administration of intravenous fluids and magnesium

Phosphate

The normal level of serum phosphate is from 0.81 to 1.45 mmol/L.

Hyperphosphatemia is defined as a phosphate level greater than 1.45 mmol/L. The greatest risk factor for hyperphosphatemia is severe and advanced renal disease, but other risk factors can include hypoparathyroidism, diabetic ketoacidosis, serious systemic infections, and rhabdomyoysis which is the destruction of muscular tissue.

Hyperphosphatemia can be asymptomatic and may be patient have signs and symptoms of muscular spasms and cramping, weakness of the bones, tetany, and crystal accumulations in the circulatory system and in the body's tissue that can lead to calcifications in the subcutaneous tissue.

The treatment of hyperphosphatemia includes the restriction of dietary food products containing phosphates including foods like milk and egg yolks,

- **Hypophosphatemia**, which is defined as a phosphate level less than 0.81 mmol/L, is associated with risk factors such as
- chronic diarrhea,
- severe burns
- hyperparathyroidism
- severe malnutrition
- alcoholism
- lymphoma, leukemia
- hepatic failure
- osteomalacia, genetics, the long term use of some diuretics

Treatments for hypophosphatemia include cardiac monitoring, oral and intravenous potassium phosphate, and the encouragement of high phosphorous foods like milk and eggs

Chloride

The normal level of chloride is from 97 to107 mEq/L.

- **Hyperchloremia**, which is a chloride level greater than 107 mEq/L can adversely affect the oxygen transportation in the body. Hyperchloremia can occur as the result of dehydration, some medications, renal disease, diabetes, diarrhea, hyperparathyroidismia, and some medications such as supplemental hormones and some diuretics.
- **The treatments**, in addition to identifying and treating an underlying disorder, include the cautious administration of fluids because too rapid rehydration efforts can lead to cerebral edema and other complications, the elimination of problematic medications, and the correction of any renal disease and hyperglycemia.
- **Hypochloremia**, which is a low chloride level of less than 97 mEq/L, can occur as the result of vomiting, metabolic alkalosis, respiratory acidosis, high bicarbonate levels and hyponatremia.
- Treatments for this electrolyte imbalance can include the administration of chloride replacements, and, at times, the administration of hydrochloric acid and a carbonic anhydrase inhibitor like acetazolamide for an acute episode of hypochloremic alkalosis.

Disorders of fluids

Hypervolemia is an abnormal increase in the volume of fluid in the blood, particularly the blood plasma .

Hypervolemia, which is often referred to as fluid overload, can occur as the result of

- increased sodium in the body which is hypernatremia
- excessive fluid supplementation that cannot be managed effectively by the body.
- disorders and diseases such as hepatic failure, renal failure and heart failure.

The signs and symptoms of hypervolemia include

- Hypertension
- Dyspnea
- adventitious breath sounds such as crackles
- abdominal ascites
- bulging and distended jugular veins with pulsations
- peripheral edema in hands, feet and/or ankles, tachycardia, and strong pulse.

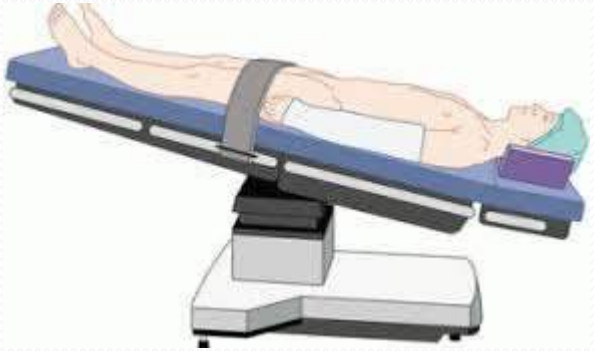
In addition to treating the underlying cause whenever possible other treatments for hypervolemia include fluid and sodium restrictions and diuretics.

Hypovolemia: is a deficit of bodily fluids. can occur as the result of

- secondary to bleeding and hemorrhage
- severe dehydration
- vomiting, and diarrhea.
- This fluid deficit can lead to complications such as
- decreased cardiac output.
- hypovolemic shock.
- metabolic acidosis.
- multisystem failure.
- coma and death

the treatment of an underlying disorder are

- intravenous rehydration with fluids such as lactated Ringers.
- The placement of the patient in the Trendelen burg position.
- administration of plasma expanders, blood and blood products as indicated by the nature of the patient status and the severity of the hypovolemia.



vomiting and diarrhea are not illness themselves, but are common symptoms of many other common illnesses. The most common cause of vomiting and diarrhea is a stomach or intestinal infection, typically caused by a virus, but occasionally can be caused by a bacteria or parasite. illnesses that can cause vomiting and diarrhea include:

- Strep throat infection
- Urinary tract infection
- Respiratory or sinus infection
- Meningitis
- Ear infection
- Appendicitis
- Milk or food allergy
- Side effects from oral medications (usually antibiotics)

treatment vomiting and diarrhea It is important to prevent dehydration through

- drinks plenty of fluids even though they may not be thirsty
- oral rehydration solution.
- avoid sugar-based beverages such as sports drinks, soda, or juices. The sugar can draw water into the intestines and away from the rest of the body making the diarrhea worse and increasing the risk of dehydration. Additionally, these beverages may not contain electrolytes that need to be replenished

Diabetic ketoacidosis

Diabetic ketoacidosis (DKA) is a life-threatening problem that affects people with diabetes . It occurs when the body starts breaking down fat at a rate that is much too fast. The liver processes the fat into a fuel called ketones, which causes the blood to become acidic.

Causes

- DKA happens when the insulin in the body is so low that:
- Glucose (blood sugar) can't go into cells to be used as a fuel source.
- Fat is broken down too rapidly for the body to process.

The fat is broken down by the liver into a fuel called ketones(water soluble molecules acetoacetat , beta hydroxybyturat and aceton) . Ketones are normally produced when the body breaks down fat after a long time between meals. When ketones are produced too quickly and build up in the blood and urine, they can be toxic by making the blood acidic. This condition is known as ketoacidosis.

DKA is sometimes the first sign of type 1 diabetes in people who have not yet been diagnosed. It can also occur in someone who has already been diagnosed with type 1 diabetes.

People with type 2 diabetes can also develop DKA, but it is less common and less severe. It is usually triggered by prolonged uncontrolled blood sugar.

Anesthesia, surgery and fluid balance

Many patients are dehydrated before theatre owing to prolonged fasting, the use of purgatives or diuretic therapy. Therefore, a general tendency towards hypovolaemia is usually present leading to thirst and vasopressin secretion.

There are two main components to the stress response to surgery:

- the neuroendocrine response
- cytokine response.
- The neuroendocrine response is stimulated initially by painful afferent neural stimuli reaching the CNS and central baroreceptors which cause increased ADH activity. It may be diminished by dense neural blockade from anesthesia.

The cytokine response is stimulated by local tissue damage at the site of surgery itself (the more extensive the surgery the higher the response) and is independent of neural blockade.

The most important response to anesthesia and surgery in the perioperative period is sodium and water retention. In general, the tendency to retain water is directly related to the magnitude of surgery. A number of factors may contribute to this including:

- the effects of anesthetic agents on renal blood flow and GFR.
- effects of intraoperative hypotension or hypovolaemia on renal function
- increased sympathetic tone and circulating catecholamines causing renal vasoconstriction
- increased plasma cortisol and aldosterone levels in response to the stress of surgery

One of the most important of these is the increase in ADH activity. during surgery the ADH concentration may increase 50–100-fold. This concentration falls at the end of surgery but does not return to normal for 3–5 days (similar to the period of postoperative oliguria). This response is partly related to

- drugs
- pain
- the stress of surgery
- loss of intravascular fluid into cells
- sequestration and immobilization in damaged tissues

- **Acid-base balance**
- **Acid-base balance means regulation of $[H^+]$ in the body fluid.**
- Only slightly changes in $[H^+]$ from the normal value can cause marked alteration in the rates of chemical reactions in the cell.
- For this reason the regulation of $[H^+]$ is one of the most important aspects of homeostasis.

$$\textbf{pH} = \log \frac{1}{[H^+]} \quad \textbf{or} \quad = -\log [H^+]$$

- **Acidosis :** low pH and high $[H^+]$
  - **Alkalosis :** high pH and low $[H^+]$

- **De To prevent acidosis or alkalosis, several control systems are available:**
- **Acid-base buffer system**
- **Respiratory system**
- **Renal system**
- **Acid-base buffer system**
  a. Consist from weak base acid and it base

  a. present in all body fluids

  b. combine immediately with any acid or alkali

- $$pH = Pk + \frac{\{base\}}{\{acid\}}$$

pK= log dissociation constant of weak acid

For the bicarbonate buffer system the formula may be expressed as Follow:

- $$\mathbf{pH = 6.1 + \log \frac{[HCO_3^-] \text{ in mmol/l}}{[CO_2] \text{ in mmol/L}}}$$
- This is called the **Henderson— Hasselbalch equation** and by using it one can calculate the pH of a solution.

[1] The bicarbonate buffer system

- It consists of mixture of (H_2CO_3) - ($NaHCO_3$) [carbonic acid-sodium bicarbonate].
- When a strong acid such as HCl is added:
  - **$HCl + NaHCO_3 \rightarrow H_2CO_3 + NaCl$**
  - strong HCl is converted into a very weak carbonic acid .
- When a strong base such as NaOH is added to this buffer, the following takes place;
  - **$NaOH + H_2CO_3 \rightarrow NaHCO_3 + H_2O$**
  - The net result is exchange of the strong base NaOH for the weak base $NaHCO_3$.

[2] Phosphate buffer system

- It is composed of H_2PO_4 and Na_2HPO4
- The phosphate buffer is especially important in

the tubular fluid of the kidney because of high concentration in the tubules.

When a strong acid such as HCl is added:

HCL+NaHCO3→H2p04 +NaCl

- When a strong base such as NaOH is added to this buffer, the following takes place;

$NaOH + H_2pO_4 \rightarrow HpO_4 + H_2O$+Na

[3] The protein buffer system

- NH_2 -Protein-COOH → Undissociated protein(buffer).
- Behave as weak acids and weak bases.
- The most plentiful buffer of the body is the plasma and cells proteins.

Hb as a buffer System

- There are 38 histidine units in the Hb molecules.
- Histidine is an amino acid which contains additional—NH2 and -COOH groups, thus Hb is a good buffer.
- Reduced Hb- which is base
- Reduced Hb + H^+ H-Hb which is a very weak acid.

Respiratory Regulation of Acid-Base Balance

- change rate of breathing ….. change rate of CO_2 washing(acid gas) …….. readjust $[H^+]$ back to normal within 1 -15 minutes

❖ Recalling the Henderson-Hasselbalch equation

- **$[HCO_3^-]$ in mmol/l**

  - **pH = 6.1 + log ----------**

- **$[CO_2]$ in mmol**

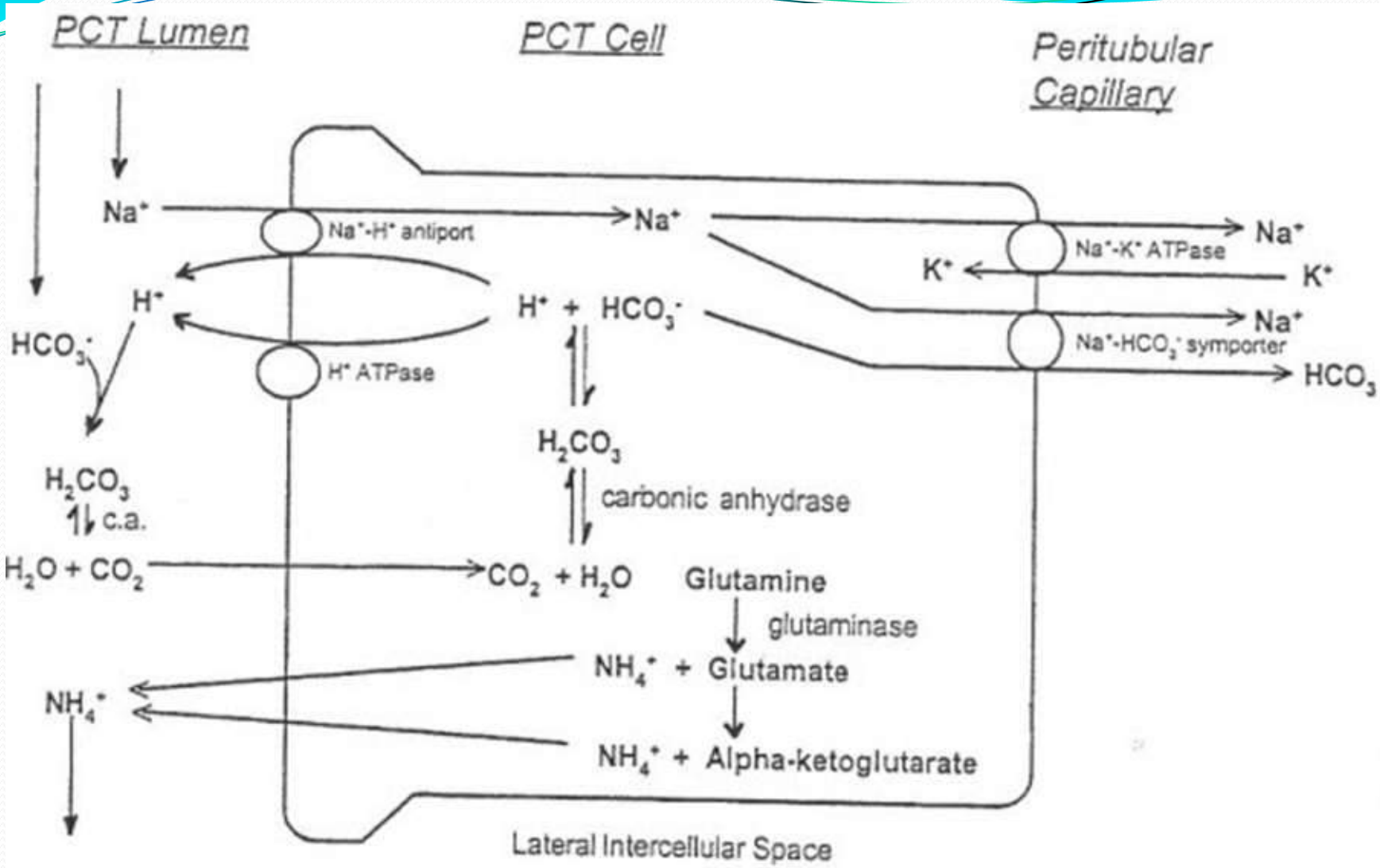
- **Inverse relationship between CO_2 concentration in the body fluids and pH.**

❖ The CO_2 concentration in the ECF depends on:

  - the rate of metabolic production of CO2.
  - the rate of pulmonary ventilation(CO2 washing).

Inverse relationship between CO_2 concentration in the body fluids and pH.

- The CO_2 concentration in the ECF depends on:
  - the rate of metabolic production of CO2.
  - the rate of pulmonary ventilation(CO2 washing).
- Since alveolar ventilation can be reduced to zero or increased to about 15 times normal, thus, activity of the respiratory system has marked effects on pH of the body fluids.
- On the other hand, a change in blood CO_2 concentration or blood $[H^+]$ affects the rate of alveolar ventilation by a direct action of H^+ on the respiratory center .
- The overall buffering power of the respiratory system is one to two times as great as that of all the chemical buffers combined.


PCT Lumen
PCT Cell
Peritubular Capillary
Na+
Na+-H+ antiport
Na+
Na+-K+ ATPase
Na+
K+
K+
H+
H+ + HCO3-
Na+-HCO3- symporter
HCO3-
HCO3
H+ ATPase
H2CO3
H2CO3
c.a.
carbonic anhydrase
H2O + CO2
CO2 + H2O
Glutamine
glutaminase
NH4+ + Glutamate
NH4+
NH4+ + Alpha-ketoglutarate
Lateral Intercellular Space

Renal regulation of acid-base balance

- Renal excretion of acidic or alkaline urine ….. readjust the [H^+] back to normal within hours to several days.
- The most powerful of all the acid-base regulatory systems.
- The kidneys regulate H^+ conc. principally by increasing or decreasing the HCO_3^- in the body fluid.
- Normally H^+ secretion = HCO_3^- filtration, and they titrate each other in the renal tubules the end products being CO_2 and water.
- The basic mechanism by which the kidney corrects either acidosis or alkalosis is by incomplete titration of H+ against HCO3-, leaving one or the other of these to pass into the urine and therefore to be removed from the extracellular fluid .

Clinical applications

1. Respiratory acidosis(CO2 retention)

- Alveolar ventilation is not enough to wash CO2 produced by metabolism.
- increased PCO_2 , carbonic acid and fall of pH
- **Pathological causes are:**

1-airway obstruction

2-Pneumoinia(infection of alveoli)

3-chest deformities

4-paralysis of respiratory muscles

- All decrease gas exchange resulting in low PO2 and high PCO2.

2-Respiratory alkalosis (CO_2 washout or deficit)

- Over breathing ……. loss of carbonic acid …….occurs in:
- 1- Hysteria

  2-Mechanical respirator

  3- Meningitis or encephalitis.

3-Metabolic acidosis

Accumulation of acids other than carbonic acid in the body or as a consequence of body depletion of the base bicarbonate Causes are :

1-Increased lactic acid (vigorous exercise).

2-Ketoacidosis: accumulation of ketone bodies (uncontrolled diabetes mellitus).

3-Renal diseases

4- Metabolic alkalosis

Abnormal loss of HCl (prolonged or severs vomiting).

newborn children with pyloric obstruction.

Excessive ingestion of alkaline drugs such as sodium bicarbonate for the treatment of peptic ulcer.