Cardiopulmonary Physiology and Anesthesia

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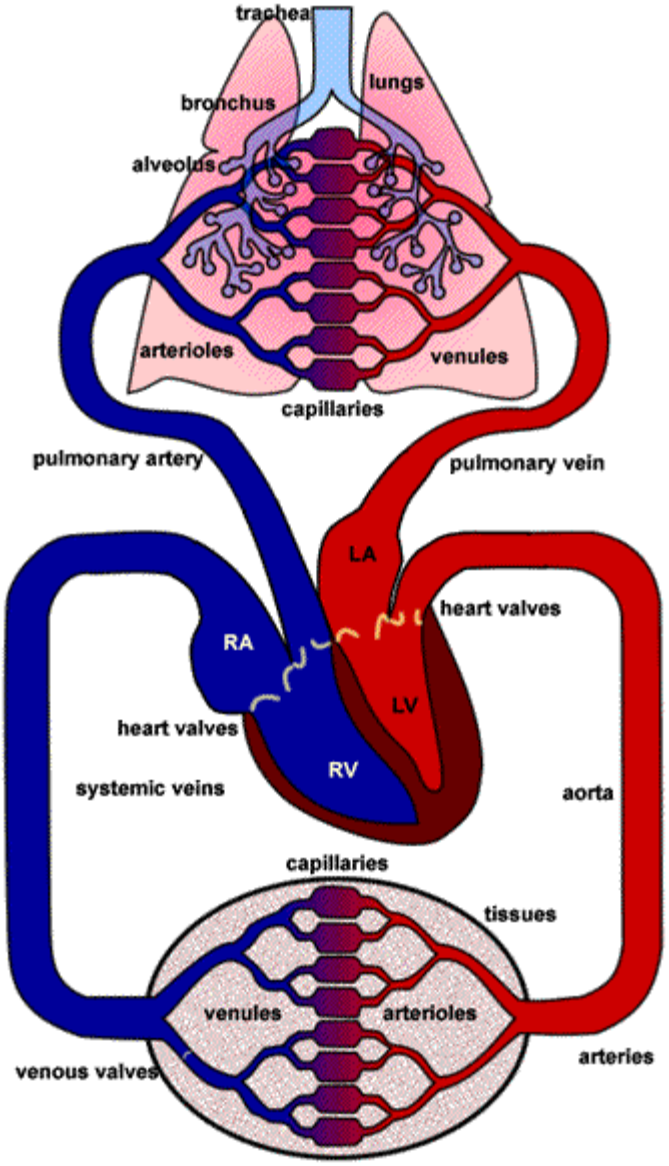
The vascular System

- **Two separate circulations in series**
  - systemic circulation and pulmonary circulation
  - As blood flows through the vascular beds, pressure and velocity drop, and overall cross-sectional area increases

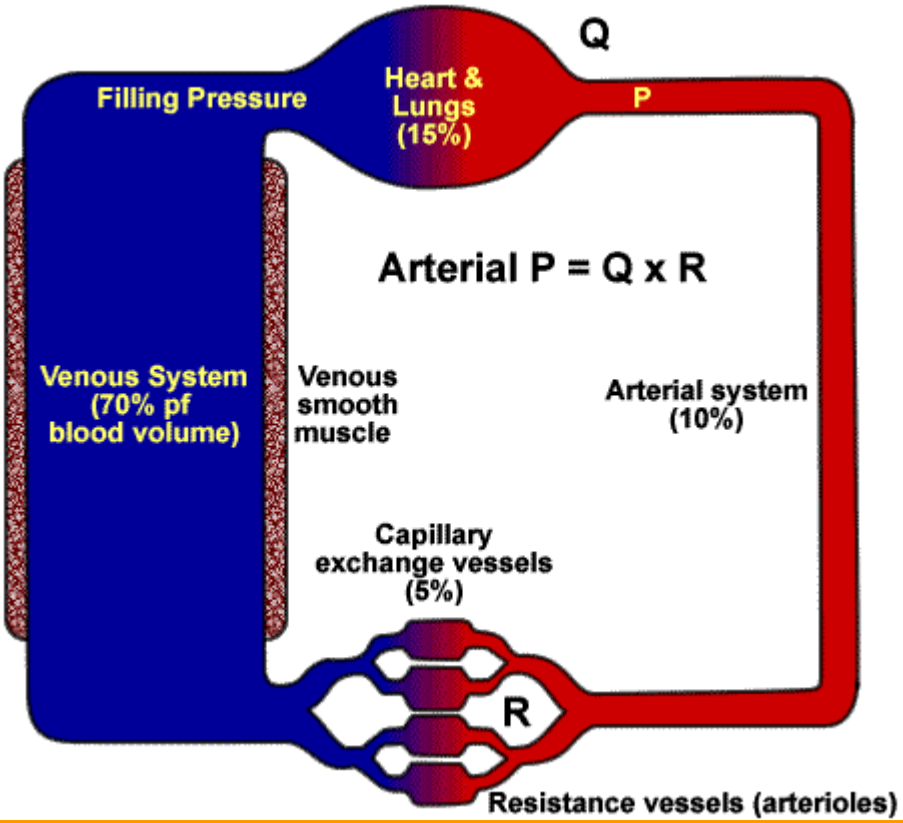
Functional anatomy of the heart & lungs



- **Heart**
  - Composed of four chambers: two atria and two ventricles

- **Blood vessels and volumes**
  - Capacity of blood volumes differs between vessel components.
  - Systemic arteries and arterioles (10%), capillaries (5%), venules and veins (70 %), heart and lung (15 %)

Capacity of blood volumes



- **Blood components**
  - Plasma - water, plasma proteins (colloids), carbohydrates, fats, electrolytes
  - Cells - red cells, white cells, platelets
  - Hemoglobin - oxygen transport
  - Clotting factors

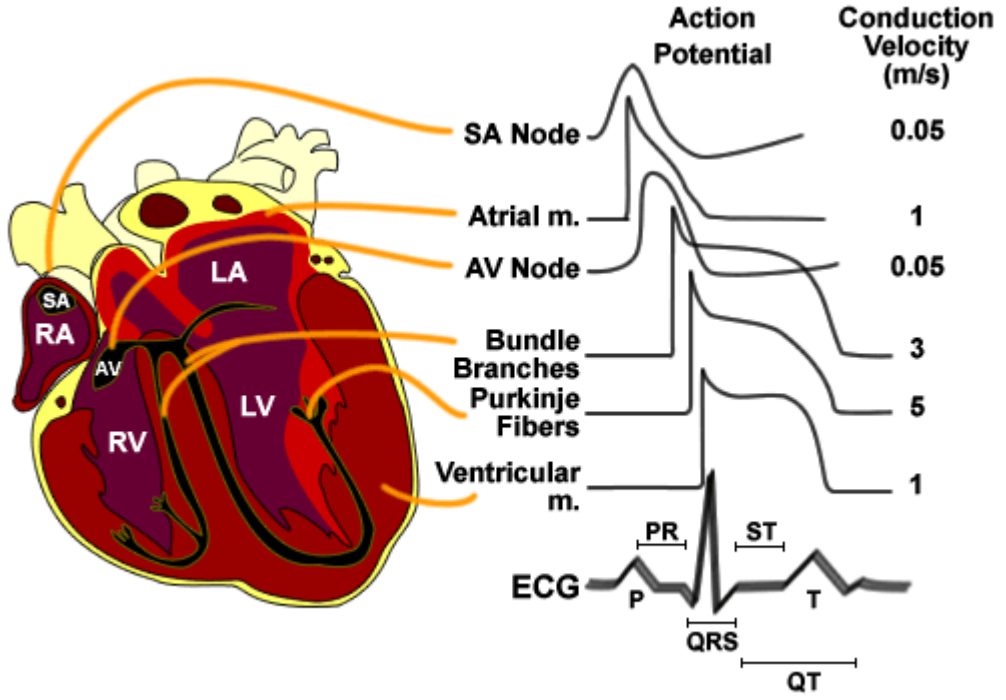
Electrophysiology

- **Cardiac electric activity**
  - electrical activity required for mechanical activity to occur
  - excitation-contraction coupling
  - altered by many anesthetic drugs

- **Ion transport**
  - distribution of sodium, potassium, and chloride responsible for electrical potential across cardiac cellular membranes
  - normal ion transport of ions required for normal electrical activity

- **Electrocardiogram**
  - an algebraic sum of all the action potentials produced by each cardiac cell
  - essential to understand the origin of the components of the normal ECG
  - P-wave: atrial depolarization
  - PR interval: conduction through the atria and AV node (affected by parasympathetic tone)
  - QRS complex: ventricular depolarization
  - QT interval: entire ventricular depolarization and repolarization
  - ST segment: entire ventricular depolarization: the pause between ventricular muscular firing and ventricular muscular repolarization
  - T-wave: ventricular repolarization

Source of the ECG tracing

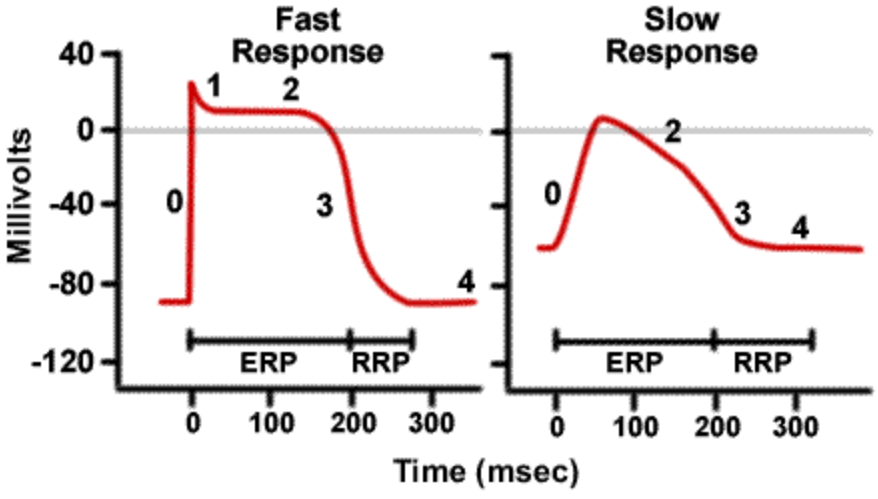


- **Excitability**
  - ability of the heart to initiate an action potential in response to an inward current (depolarization)
  - absolute refractory period (ARP): upstroke of the AP to right after the plateau
  - efferent RP (ERP): slightly longer than ARP, time during which no AP can be initiated
  - relative RP (RRP): following ARP, when repolarization is complete, a period during when AP can be elicited, but more than the usual inward current is required
  - cardiac muscles is different than that of skeletal muscles or nerves
  - lower resting membrane potential (-90 vs -65 mV)
  - greater action potential (130 vs 80 mV)
  - longer duration (150-300 vs 1 msec)

- **Pacemaker action potential (Sinoatrial node)**
  - Phase 0: *upstroke*: much less steep, inward Ca^{++} ↑, note in atria and ventricles upstroke occurs with rapid Na^{+} influx
  - Phase 3: *repolarization*: K^{+} conductance ↑ → outward K^{+} ↑
  - Phase 4: *slow depolarization*: accounts for SA node pace maker activity (automaticity), Na^{+} conductance ↑ → inward Na^{+} ↑
  - There is no phase 1

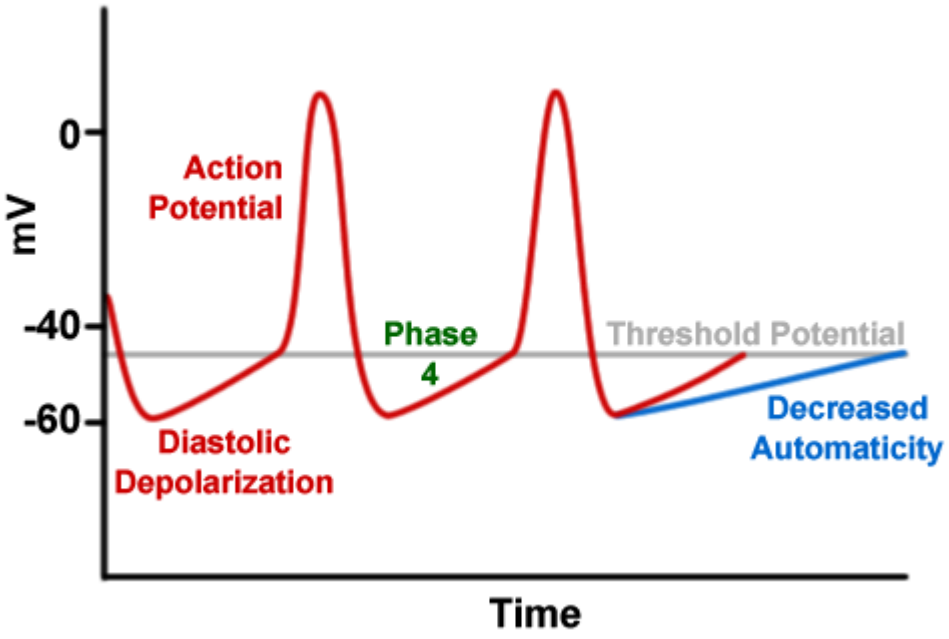
- **Non-pacemaker action potential (atria and ventricles)**
  - Phase 0: *upstroke*: rapid Na^{+} influx depolarizes membrane
  - Phase 1: *initial repolarization*: transient outward movement of K^{+}
  - Phase 2: *plateau*: large but slow inward movement of Ca^{++}, K^{+} conductance ↑, Na^{+} influx ↓
  - Phase 3: *repolarization*: large outward movement of K^{+}
  - Phase 4: *resting*: K^{+} equilibrium

Cardiac Transmembrane Potentials



- **Diastolic depolarization - pacemaker potentials**
  - SA node, AV node, atrial and ventricular Purkinje network causes the unique automaticity of the heart
  - resting potential gradually depolarizes toward a threshold potential, when reached, an action potential is triggered
  - cardiac tissue with the more rapid rate of rise of phase 4 is the pacemaker and determines heart rate (usually SA node)

Diastolic Depolarization



- **Automaticity increased by:**
  - increased heart rate
  - increased temperature
  - mild hypoxia
  - hypokalemia
  - hypercalcemia
  - catacholamines
  - thyroxin

- **Conduction velocity**
  - reflects the time required for excitation to spread in heart tissue, fastest in purkinje system, slowest in AV node

Steps in excitation-contraction coupling

- mainly mediated by calcium
- AP promotes inward Ca current at cell membrane and T-tubule during the plateau
- Ca triggered Ca release from SR → intraceullar Ca ↑
- Ca binds to troponin C which removes inhibition of actin-myosin interaction by troponin I and tropomyosin
- myocardial cell contracts (magnitude depends on Ca concentration)

Cardiac cycle

- Atrial systole (phase 1)
  - preceded by P wave
  - creates fourth heart sound

- Isovolumetric ventricular contraction (phase 2)
  - onset of QRS
  - when ventricular pressure becomes greater than atrial pressure, the A-V valves close, creating 1st heart sound. The mitral valve closes before tricuspid, so 1st sound may split
  - no blood leaves the ventricle

- Rapid ventricular ejection (phase 3)
  - when ventricular pressure becomes greater than aortic pressure aortic valve opens
  - rapid ejection of blood into arota
  - ventricular volume decreases dramatically since most of the stroke volume is ejected during the phase
  - atrial filling begins

- Reduced ventricular ejection (phase 4)
  - ejection continues but is slower
  - ventricular pressure begins to fall
  - aortic pressure also falls because run-off of blood from large arteries into smaller arteries is faster than the flow of blood from the ventricle into the aorta
  - atrial filling continues

- Isovolumetric ventricular relaxation (phase 5)
  - repolarization of the ventricles is complete (T waves)
  - aortic valve, pulmonic valve close, creating 2nd heart sound
  - A-V valves remain closed
  - ventricular volume is constant since all valves are closed

- "blip" following closure of aortic valve corresponds to 'dicrotic notch' or 'incisura'

- Rapid ventricular filling (phase 6)
  - when ventricular pressure decreases below atrial pressure, mitral valve opens, leading to left ventricular filling
  - 3rd heart sound is heard

- Reduced ventricular filling (diastasis) (phase 7)
  - ventricular filling continues, but at a lower rate
  - increased heart rate decreases the time for ventricular filling

- Heart sounds during cardiac cycle
  - First heart sound (S1) - is related to mitral and tricuspid valve closure
  - The closure of the aortic and pulmonic valves contribute to the second sound (S2) production
  - The physiologic third heart sound (S3) - is a low-pitched vibration occurring in early diastole during the time of rapid ventricular filling. Most of the time, is non-audible for human ears.
  - The physiologic fourth heart sound (S4) - is a very soft, low-pitched noise occurring in late diastole, just before S1. S4 generation is related to the ventricular filling by atrial contraction.

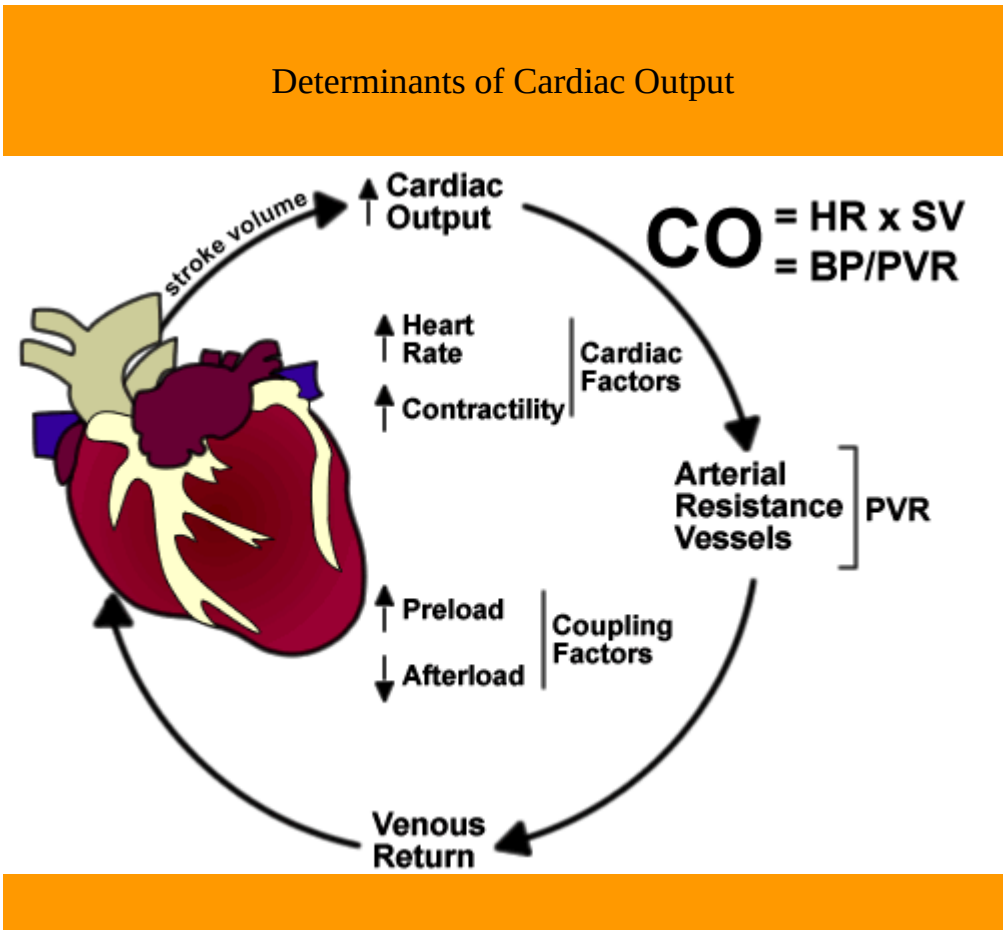
Cardiac performance

- Ultimate goal of the heart is to provide adequate quantities of oxygenated blood to peripheral tissues - cardiac output is the critical variable
- Determinants of cardiac output

$$CO = HR \times SV$$

$$CO = \frac{BP}{SVR}$$

- SV (stroke volume) determined by cardiac contractility, preload and afterload
  - Cardiac contractility (inotropy): intrinsic ability of the heart to generate force; relates directly to physiochemical processes and availablility of intracellular calcium; decreases in cardiac contractility is the key to heart failure following administration of negative inotropes (many anesthetics)
  - Preload: Frank-Starling relationship (increased ventricular volume increases the force of cardiac contraction)
  - Afterload: inverse relationship with cardiac output and direct correlation with myocardial oxygen consumption

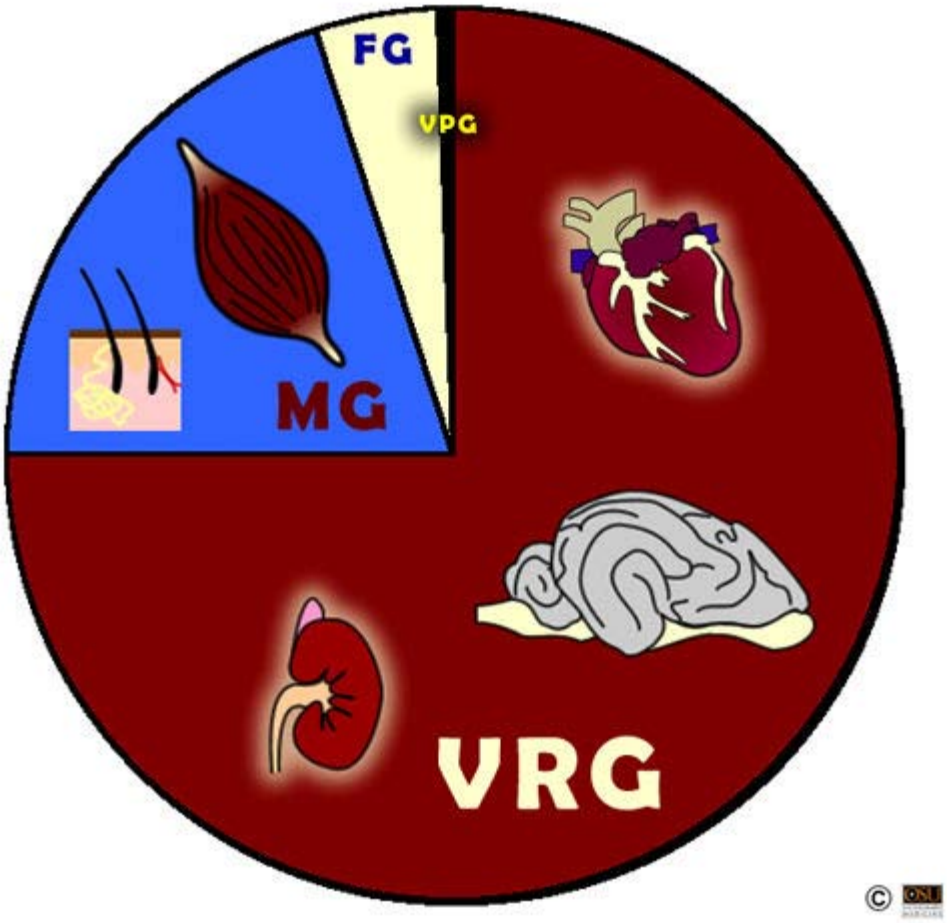


Cardiac output and organ distribution

- Total blood volume (ml/kg):
  - Cats: 60-70
  - Dogs: 80-90
  - Horses (racing): 100
  - Horses (draft): 70
  - Cows: 60
  - Pigs: 60
  - Sheep, goats: 60
  - Humans: 80
- Vessel Rich Group (VRG): 75% of the CO
  - Brain
  - Heart
  - Kidney
  - Liver
  - Lungs
- Muscle Group (MG): 20% of the CO
  - Muscle

- Skin
- Fat Group (FG): 5% of the CO
  - Fat
- Vessel Poor Group (VPG): <1% of the CO
  - Bone, teeth
  - Tendons
  - Ligaments

Distribution of cardiac output

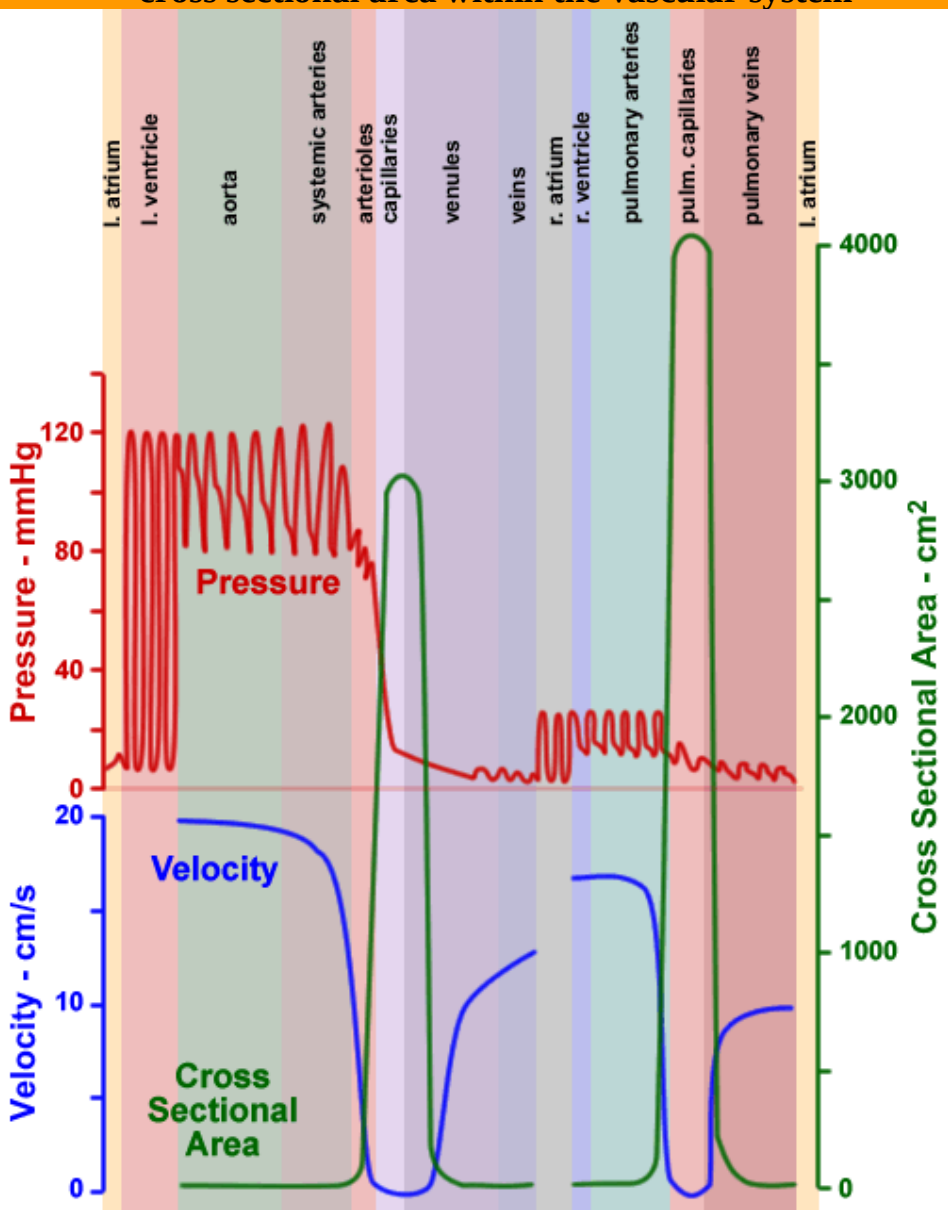


Blood pressure

- Arterial blood pressure is frequently assessed during anesthesia, either directly or indirectly

- Provides a rapid means to assess cardiac function
- Factors that determine blood pressure:
  - heart rate and stroke volume (CO)
  - vascular resistance
  - arterial compliance
  - blood volume
- All of the above factors can change dramatically during the course of anesthesia and surgery, either due to the affects of anesthetic drugs or surgical manipulations
- Blood pressure does not truly indicate tissue perfusion - and one must use clinical judgment to correctly interpret blood pressure measurements (e.g. blood pressure can increase while CO decreases under the effects of several anesthetic drugs)

Relationship between pressure, flow velocity, and cross sectional area within the vascular system



Nervous, humoral, and local control of the cardiovascular system

The autonomic nervous system - significant regulator of CV function

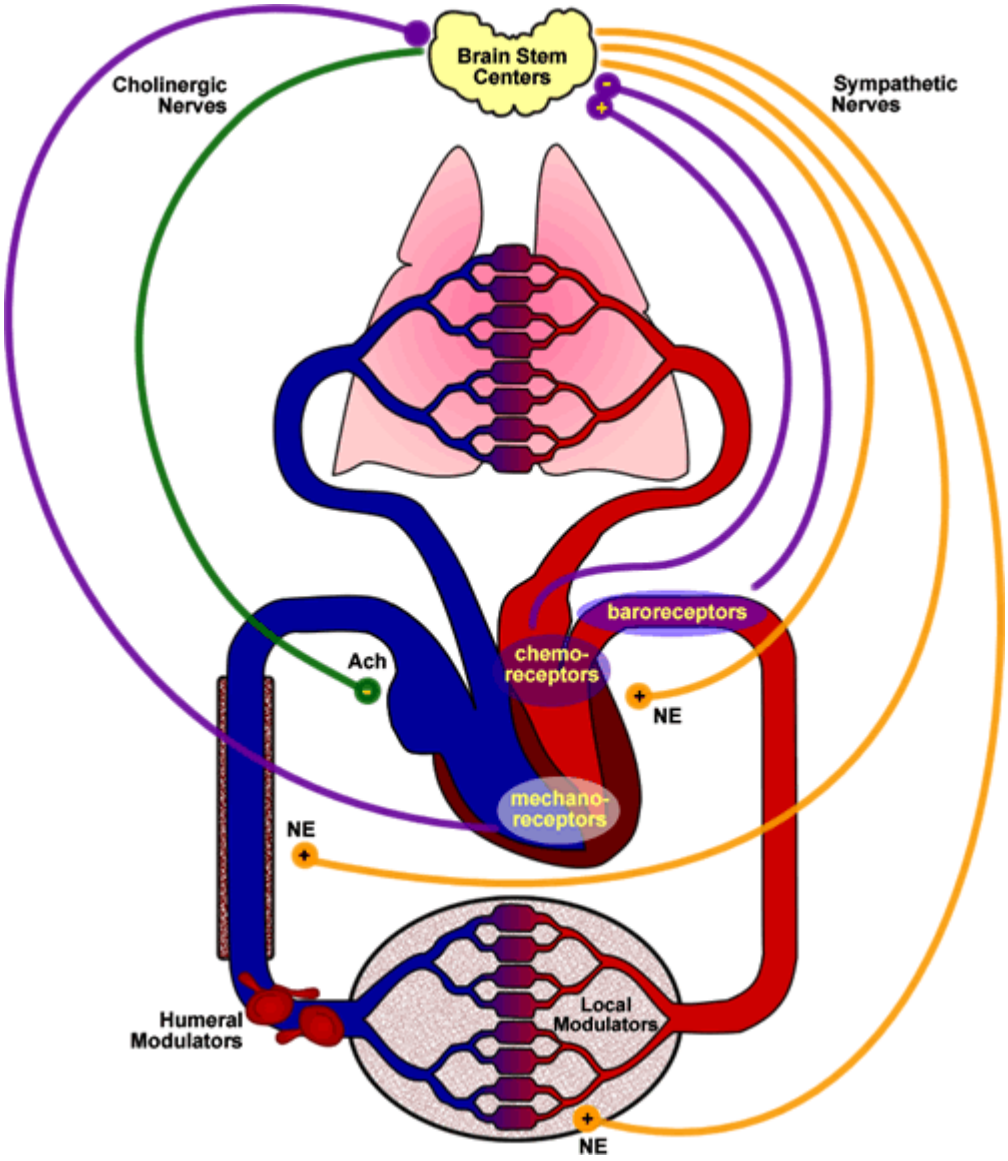
- Sympathetic and parasympathetic outflow affect heart rate, inotropy, and vascular tone to affect cardiac output, blood pressure, and distribution of blood flow
- Parasympathetic (vagus) effects
  - the vagus nerves inhibit the cardiac pacemaker, atrial myocardium and AV conduction tissue, acetylcholine serves a neurotransmitter at muscarinic receptors
  - has negative chronotropic effects (decreased heart rate)
  - has negative dromotropic effects (decreased conduction velocity)
  - has negative inotropic effects (decreased contractility)
- Sympathetic effects
  - innervation is throughout the heart, norepinephrine serves a neurotransmitter at beta 1 receptors
  - has positive chronotropic effects (increased heart rate)
  - has positive dromotropic effects (increased conduction velocity)
  - has positive inotropic effects (increased contractility)
- Peripheral receptors - baroreceptors, chemoreceptors, mechanoreceptors
- Information integrated in brain stem
- Anesthetic agents can and do interfere with this system at all levels
  - depress responsiveness of peripheral receptors
  - depress responsiveness of central integration centers
  - alter sympathetic and parasympathetic outflow

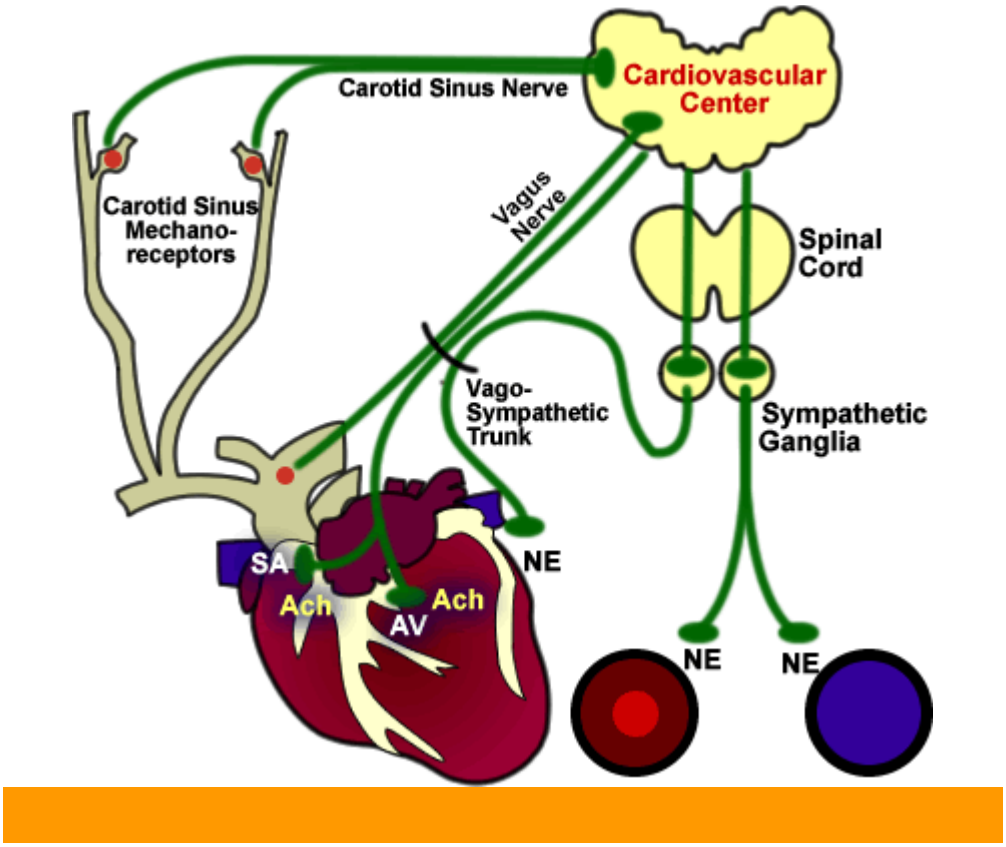
Humoral mechanisms

- **Adrenal medulla**
  - releases epinephrine and norepinephrine into the circulation
  - in response to pain, trauma, hypovolemia, hypotension, hypoxia, hypothermia, hypoglycemia, excercise, stress, and fear
- **Renin-angiotensin**
  - activated within the kidney
  - renin release is stimulated by hyponatremia, decreased extracellular fluid volume, or increased sympathetic tone
  - renin acts on circulating angiotensinogen to release angiotensin I.
  - Angiotensin converting enzyme (ACE) converts angiotensin I to angiotensin II mainly in the lung.
  - Angiotensin II causes peripheral vascular constriction and aldosterone release
  - Aldosterone increases renal resorbtion of sodium and water, thus increasing extracellular volume
- **Arginine vasopressin (ADH)**

- usually released from the hypothalmus in response to increases in plasma solute
- stimulates water conservation within the collecting ducts of the kidney
- also causes vasoconstriction, especially in mesenteric blood vessels, resulting in redistribution of blood flow
- Non-osmotic stimuli that can cause the release of ADH include pain, stress, hypoxia, heart failure, volume depletion, and some anesthetics (opioids, barbiturates)

Nervous, humoral, and local control of the cardiovascular system





Autoregulation

- Ability of blood vessels to adjust flow in response to local metabolic needs and maintain flow in spite of extreme changes in perfusion pressure
- Most tissues regulate flow at a local level by responding to release of metabolites and tissue mediators (eg, histamine, carbon dioxide, NO, H^+)
- The heart, brain, and kidney demonstrate a tight autoregulation

Clinical notes

- Most anesthetics depress cardiovascular performance ranging from hypotension, bradycardia and decreased myocardial contractility
- Avoid these cardiovascular changes by careful dosing and balanced anesthesia
- Overcorrection of cardiac depression with tachycardia and hypertension increase myocardial O_2 consumption, and is detrimental to the heart
- Adequate oxygen delivery to tissues is fundamental - reduced oxygen consumption is the common denominator in all forms of shock and leads to rapid heart failure

Respiratory System

Respiration

- Total process where oxygen is supplied to and used by cells, and carbon dioxide is eliminated

Ventilation

- Movement of gases in and out of the alveoli
- Varies with metabolic needs of the animal

Terms

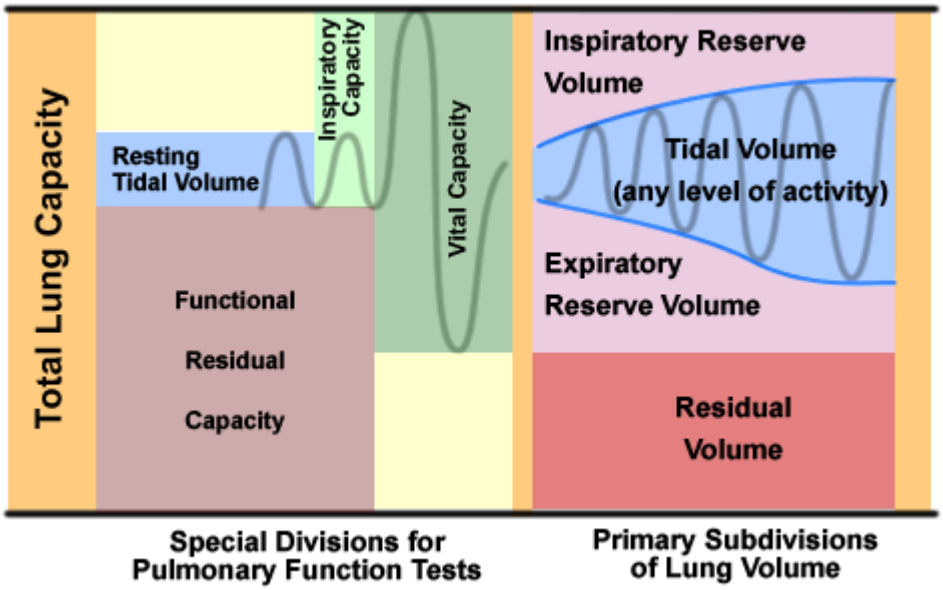
- Apnea: transient cessation
- Apneustic ventilation: long gasping inspirations with several subsequent ineffective exhalation
- Bradypnea: slow regular
- Dyspnea: labored
- Eupnea: ordinary and quiet
- Hyperpnea: fast ± deep, over-respiration
- Hypopnea: slow ± deep, under-respiration
- Polypnea: rapid, shallow panting
- Tachypnea: increased rate
- Hypoxia: any state in which oxygen in the lung, blood and/or tissue is low
- Hypoxemia: insufficient oxygenation of blood to meet metabolic requirement, $PaO_2 < 70$ mmHg at sea level
- Hypercapnia: elevated CO_2 tension in blood, $PaCO_2 > 45$ mmHg
- Hypocapnia: lowered CO_2 tension in blood, $PaCO_2 < 35$ mmHg
- Eucapnia: normal CO_2 tension in blood, 35 mmHg < PaCO2 < 45 mmHg

Volumes and capacities

- Tidal Volume (V_T): the volume of air inspired and expired in one breath
- Inspiratory reserve volume (IRV): the volume of air that can be inspired over and above the normal V_T
- Expiratory reserve volume (ERV): the amount of air that can be expired by forceful expiration after a normal expiration
- Residual volume (RV): the air remaining in the lung after the most forceful expiration
- Minute volume (V_E) (minute ventilation): V_T x respiratory frequency (*f*)
- Inspiratory capacity (IC): V_T + IRV, the amount of air that can be inhaled after a normal expiration and distending the lungs to the maximum amount
- Functional residual capacity (FRC): ERV + RV, the air remaining in the lung after a normal expiration

- Vital capacity (VC): IRV + V_T + ERV, the maximum air expelled from the lungs after filling them to their maximum capacity, take maximum inspiration then take maximum expiration, the exhaled volume is VC
- Total lung capacity (TLC): VC + RV, the maximum volume to which the lungs can be expanded with the greatest possible inspiratory effort

Lung Volumes and Capacities



Components of the ventilatory system:

- neural control mechanisms
- bellows mechanism (chest wall and diaphragm)
- upper airway
- lung parenchyma

Control of respiration

- via an integrated feedback control system, and involves central respiratory centers, central and peripheral chemoreceptors, pulmonary reflexes, and nonrespiratory neural input

Gas exchange

- transfer of gases requires a pressure gradient between the atmosphere and alveoli
- modified by elasticity of lungs and chest walls

- normal ventilation relies on a slight negative pressure within the alveoli during inspiration to draw air into the lungs, and a slight positive pressure within the alveoli during expiration to move air back out of the lungs
- at inspiration, thoracic wall is expanded and diaphragm contracts which leads to decrease in intrapleural pressure and increase in mouth pressure
- following inspiration, intrapleural space reduces which result in increased intrapleural pressure, and air flows reverse to the mouth
- assisted or controlled ventilation provides a positive pressure at the mouth to move air into the lungs - this positive intrapleural pressure has significant cardiovascular effects

Ventilation : perfusion matching

- Matching of alveolar ventilation and capillary blood flow is influenced by gravity, and also that the pulmonary circulation is a low pressure system
- Anesthesia can cause significant abnormalities in ventilation : perfusion matching (termed V/Q mismatching)
- Relationship between alveolar ventilation, hemoglobin oxygen saturation, oxygen content, and arterial partial pressure of carbon dioxide
- Hypoxic pulmonary vasoconstriction (HPV) is a protective mechanism to preserve better V/Q matching
  - limits blood flow to poorly ventilated regions of the lung
  - inhalant anesthetics cause marked reduction in HPV, resulting in continued perfusion of poorly ventilated areas of the lung
  - this results in ventilation : perfusion mismatching, which most greatly affects oxygenation

Carbon dioxide transport

- CO_2 elimination is dependent on pulmonary blood flow and alveolar ventilation
- The amount of CO_2 in the body is a function of CO_2 production and elimination
- CO_2 has a diffusion coefficient 20 times that of oxygen
- There is a continuous gradient of CO_2 tension as CO_2 passes from mitochondria through the cyctoplasma, extracellular fluid, venous blood, and alveolar gas, and then by way of exhalation to the ambient air.

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

- CO_2 transport in the plasma in forms of carbamino compound carried by the plasma proteins, dissolved as CO_2, and carbonic acid (H_2CO_3)
- The action of carbonic anhydrase of erythrocyte on plasma bicarbonate ions contributes about 70% of the CO_2.
- Clinically, administration of an inhibitor of carbonic anhydrase (acetazolamide, as in most of the ophthalmologic cases), almost doubles the CO_2 tension in mixed venous blood and causes a state of acidosis.
- CO_2 transport in the red blood cell: a much large amount of CO_2 combines with hemoglobin to form carbaminohemoglobin. This reaction is facilitated by the

release of oxygen from hemoglobin, making reduced hemoglobin a CO_2 carrier that is 3.5 fold more effective than oxyhemoglobin. This adds another 15-25% of CO_2 transport.

- The carbon dioxide dissolved in plasma amount for 5-10% of CO_2.

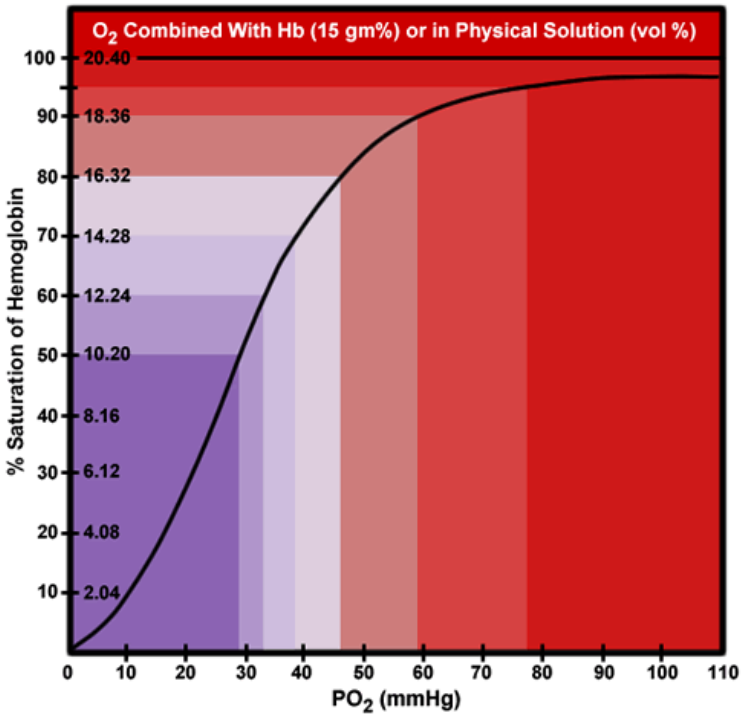
Oxygen transport

Oxygen transport is determined by:

Cardiac output (CO)

Blood oxygen content (CaO_2)

The affinity of hemoglobin for oxygen (affinity determines the position of the hemoglobin dissociative curve-see below)

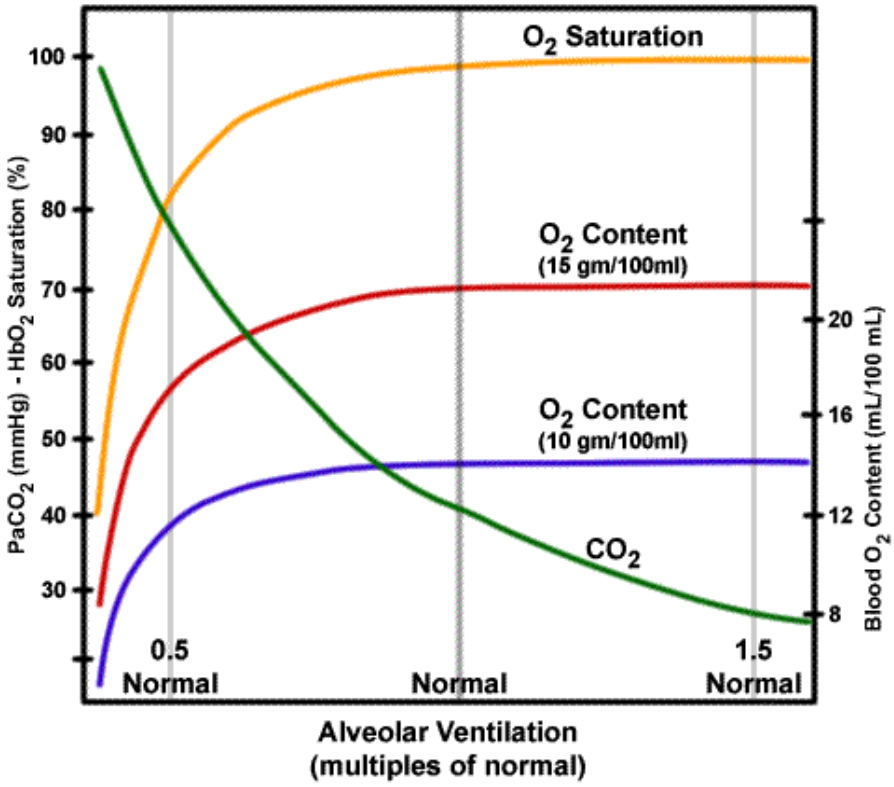


The oxyhemoglobin dissociation curve:

- at complete saturation, each gram of hemoglobin caries 1.36 ml of oxygen
- normal blood contains about 15 gm of hemoglobin/dl
- anemia and reduced blood hemoglobin levels dramatically reduces the oxygen carrying capacity of blood, even with 100% oxygen saturation
- Calculated arterial oxygen content (CaO_2) allows us to know amount of oxygen in the blood.
  - $CaO_2 = (Hb \times 1.39 \times SaO_2/100) + (PaO_2 \times 0.003)$
  - For example, if Hb = 15 g/dl, SaO_2 =100%, and PaO_2 = 100 mmHg, then $CaO_2 = (15 \times 1.39 \times 1) + (100 \times 0.003) =$ **20.85 + 0.3 =21.15** ml/dl
  - At 100% saturation, each gram of hemoglobin caries 1.39 ml of oxygen and normal blood contains about 15 gm of hemoglobin/dl

- Notice that oxygen dissociation in the plasma has little impact upon CaO_2 because it is only 0.3, and hemoglobin carry majority of the oxygen- 20.85
- Majority of the oxygen are carried by hemoglobin
- Clinically, it is better to provide hemoglobin (blood transfusion) than providing 100% oxygen to an anemic patient (see the equation)

Relationship between alveolar ventilation, hemoglobin oxygen saturation, oxygen content, and $PaCO_2$



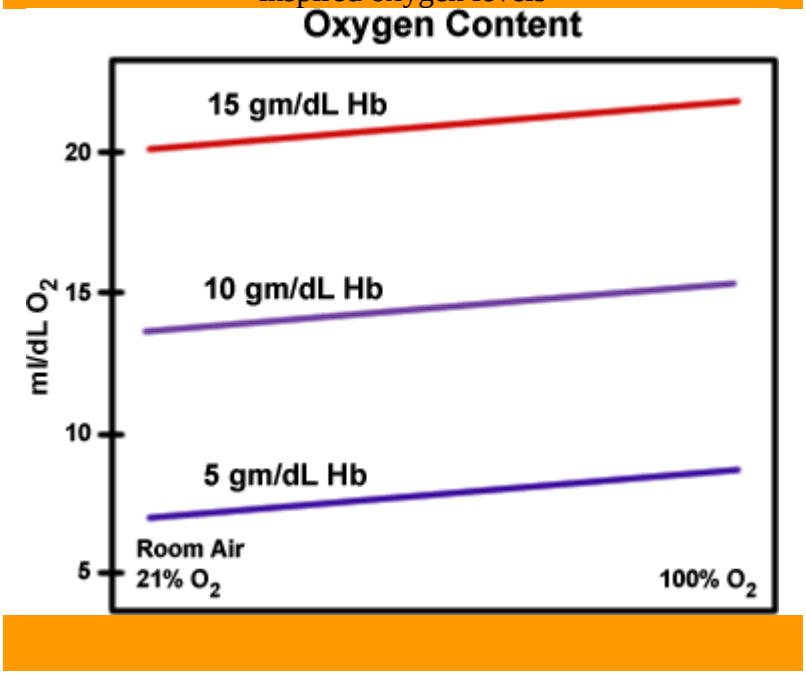
- very little change in saturation (and oxygen content) above 70 mm Hg PO2
- marked change in saturation (and oxygen content) between 10 - 40 mm Hg PO2 (which is commonly found in metabolizing tissues)
- factors that affect the affinity of hemoglobin for oxygen:
  - 2,3-DPG - enhances dissociation of oxygen by competing for oxygen binding sites; decreases 2,3-DPG levels reduce the ability of hemoglobin to deliver oxygen to tissues
  - Carbon dioxide and lactate (metabolic by products) - enhances dissociation of oxygen
  - increased temperature - enhances dissociation of oxygen
- Plasma oxygen
  - only a small component of the total amount of oxygen carried by blood (0.3 ml/dl at 100 mm Hg PO2)
  - high inspired oxygen contents can increase the amount of plasma oxygen modestly (1.8 ml/dl at 650 mm Hg PO2), which results in about a 10% increase in the total oxygen content of blood at normal hemoglobin levels.

- Anemia and reduced blood hemoglobin levels dramatically reduces the oxygen carrying capacity of blood, even with 100 % oxygen saturation

Estimation of normal PaO_2 using FiO2

- Clinically FiO_2 can be related to estimate PaO_2 as measured by the blood gas analyzer.
- If FiO_2 is 1.0 (inspired oxygen at 100%), normal PaO_2 is typically 500-600 mmHg.
- To estimate the normal PaO_2 at different values of FiO_2, we may assume that every 10% oxygen increases 50-60 mmHg of PaO_2.
- Clinical example: what will be a dog's normal PaO_2 in oxygen case with FiO_2 of 0.5 (breathing 50% oxygen) ?
- We expect the normal PaO_2 to be 250-300 mmHg (5 x 50-60mmHg).

Relationship between oxygen content, hemoglobin levels, and inspired oxygen levels



Anesthetic alterations of respiration

- Altered responsiveness of central and chemical chemoreceptors in a dose dependent manner
- Reduction in external signs of impaired ventilation
- Dose dependent decrease in responsiveness to CO_2
- Hypoxic ventilatory drive may be abolished

Clinical notes

- Supplemental oxygen is usually a good idea - even just with sedation
- Intubation and control of the patent airway is usually a good idea
- Controlled ventilation may be considered, depending on anesthetic combination used - however, it is almost always a good idea to have the ability to provide assisted or controlled ventilation whenever general anesthesia is utilized