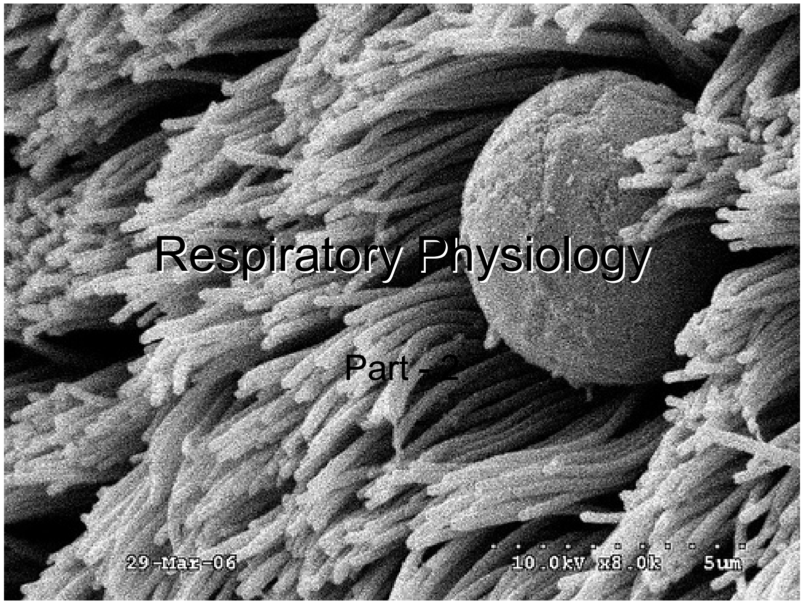
Respiratory Physiology

Part - 2



Lecture Outline

- Basics of the Respiratory System
  - Functions & functional anatomy
- Gas Laws
- Ventilation
- Diffusion & Solubility
- Gas Exchange
  - Lungs
  - Tissues
- Gas Transport in Blood
- Regulation of Ventilation & Impacts on
  - Gas levels, pH

Ventilation & Gas Exchange

Relationship

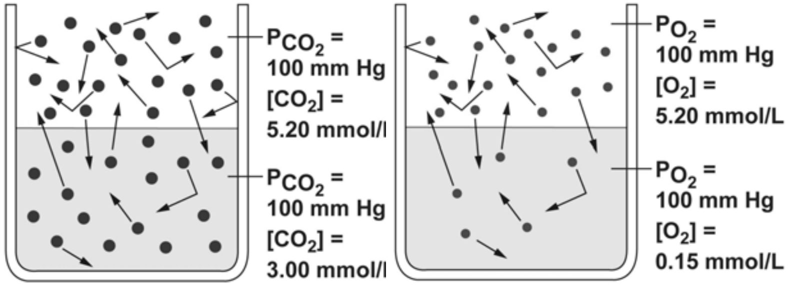
- Net effect of ventilation is to exchange air within the alveoli to
  - Maintain a partial pressure gradient which is required for gas exchange in the tissues and in the lungs!
- Blood flow and ventilation rate are optimized to ensure a usable gradient remains despite changing conditions, this is mainly controlled at the local (lung) level by
  - the pulmonary capillaries collapse at low bp, diverting blood to areas of the lung with higher bp (away from the apex, towards the base)
  - Bronchiole diameter is affected by CO_2 levels
    ↑P_{CO_2} in expired air = ↑ in bronchiole diameter (and vice versa)
  - Arteriole diameter in the lungs, controlled by blood gas levels
    - With a ↑ P_{CO_2} and a ↓ P_{O_2}, the pulmonary arterioles constrict
    - With a ↓ P_{CO_2} and a ↑ P_{O_2}, the pulmonary arterioles dilate weakly

Gas Exchange

External Respiration

- The exchange of gases
  - Diffusion between the alveolar air and pulmonary capillary blood
  - Driven by
    - partial pressure (P) gradients for O_2 and CO_2
    - Solubility of gas which is affected by
      - Pressure gradient
      - Solubility coefficient for the particular gas
      - Temperature
      - Given the same pressure gradients and temp, O_2 will reach equilibrium at a lower dissolved content than will CO_2…. Why?

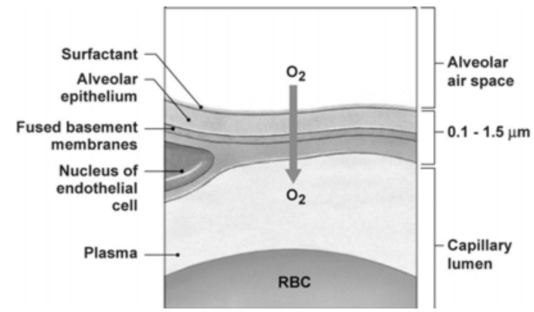
Solubility



Gas Exchange

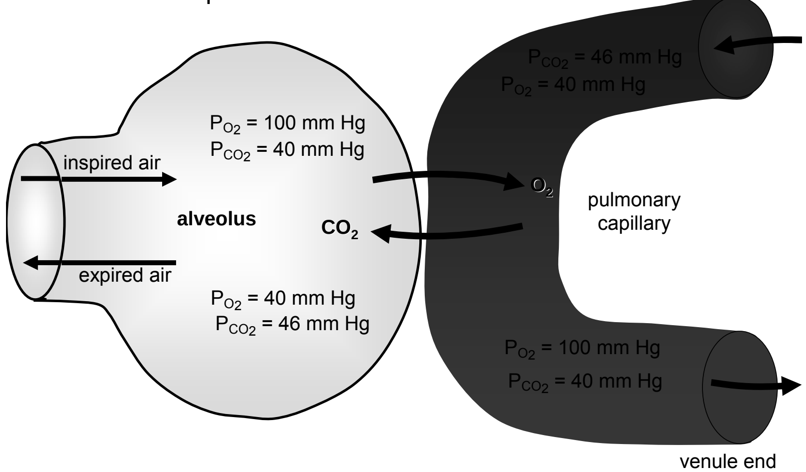
External Respiration

- The exchange membrane components and organization



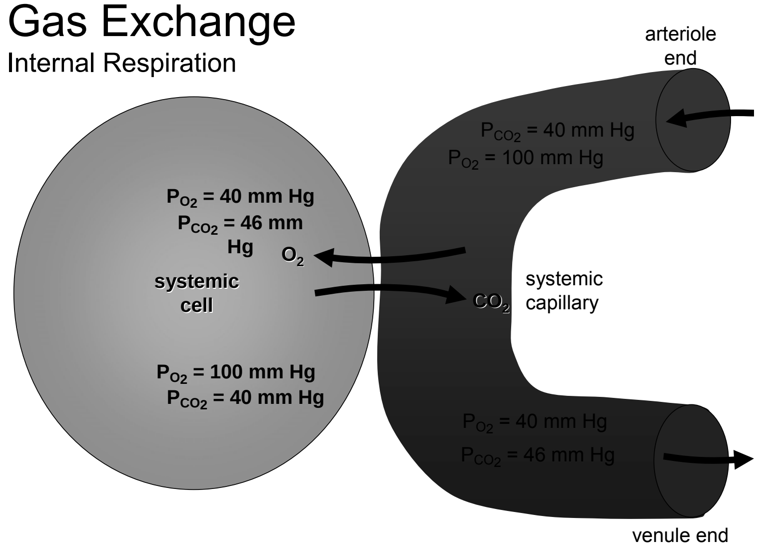
Gas Exchange

External Respiration



Gas Exchange

Internal Respiration



Gas Exchange

- What happens when alveolar P_{O_2} drops?
  - Solubility rules indicate that
    - If P_{O_2} drops, then the amount dissolved in blood also drops!
    - Creating a hypoxic condition
- Factors that may cause low arterial P_{O_2}
  1. Not enough O_2 reaching alveoli
  2. Exchange between alveoli and pulmonary capillaries has a problem
  3. Not enough O_2 transported in blood

Gas Exchange

Hypoxia classifications

Hypoxic hypoxia	Low arterial P_{O_2}	↑altitude, hypoventilation, ↓lung diffusion capacity, altered ventilation-perfusion ratio, asthma
Anemic hypoxia	↓Total O_2 bound to Hb	hemorrhage, low Hb, CO poisoning, altered Hb binding
Ischemic hypoxia	Hypoxia from reduction in blood flow	heart failure (systemic anemia), shock (peripheral hypoxia), thrombosis (single organ hypoxia)
Histotoxic hypoxia	cells being poisoned, and can't use O_2	Cyanide, H_2S, alcohol, narcotics

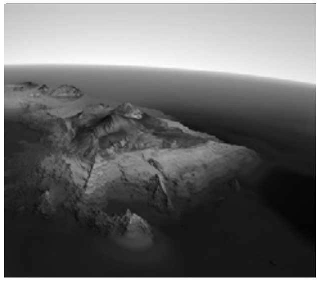
Gas Exchange

Hypoxia Problems

1. Not enough O2 in alveoli…
   - High elevation
     - Denver (5,280 ft above San Diego) where atmospheric pressure = 628 mm Hg
       - P_{O_2} then must be 132 mm Hg, instead of the 160 mm Hg here
       - A 17.5% decrease in available oxygen in the blood!
     - What about top of Mt. Everest at 29,029 ft above San Diego?
       - Atmospheric pressure = 30kPa or 225 mm Hg
       - P_{O_2} then must be 47.25 mm Hg
       - A nearly 71% decrease in available oxygen in the blood!
         - » To compensate ventilations increase from 15 per minute to between 80-90 ventilations per minute
   - Other ideas?

Which is harder?

- To breath at the top of the world's tallest mountain, or second tallest mountain?

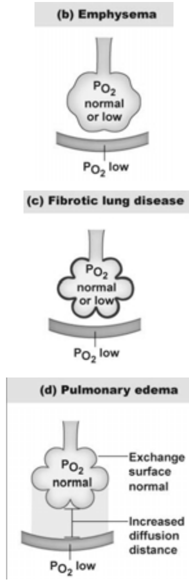


Peak of Mauna Kea – some 33,476 ft. above its base

Peak of Mt. Everest – some 29,029 ft. above its base

Gas Exchange
Hypoxia Problems

2. Interference with alveolar capillary exchange
   - Alveolar air is normal but the exchange isn't
   - Caused by
     - Less surface area for exchange (b)
     - Increased thickness of alveolar membrane (c)
     - Increased distance between alveolar membrane and capillary membrane (d)



Gas Exchange
Hypoxia Problems

2. Not enough O_2 transported in blood (anemia)
   - Review causes from prior notes (table 16-3)

TABLE 16-3 Causes of Anemia

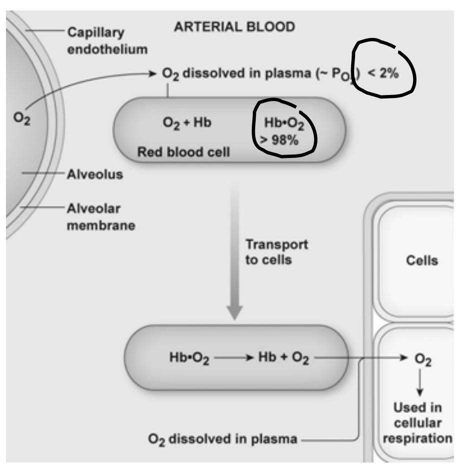
ACCELERATED RED BLOOD CELL LOSS
Blood loss: cells are normal in size and hemoglobin content but low in number
Hemolytic anemias: cells rupture at an abnormally high rate
Hereditary
Membrane defects (example: hereditary spherocytosis)
Enzyme defects
Abnormal hemoglobin (example: sickle cell anemia)
Acquired
Parasitic infections (example: malaria)
Drugs
Autoimmune reactions

TABLE 16-3 Causes of Anemia

DECREASED RED BLOOD CELL PRODUCTION
Defective red blood cell or hemoglobin synthesis in the bone marrow
Aplastic anemia: can be caused by certain drugs or radiation
Inadequate dietary intake of essential nutrients
Iron deficiency (iron is required for heme production)
Folic acid deficiency (folic acid is required for DNA synthesis)
Vitamin B_{12} deficiency (B_{12} is required for DNA synthesis): may be due to lack of intrinsic factor for B_{12} absorption.
Inadequate production of erythropoietin

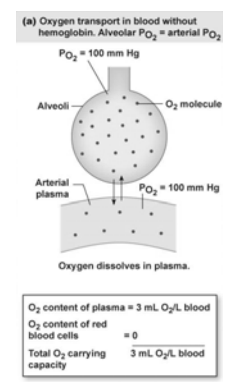
Gas Transport
General Process

- Oxygen once in blood will
  - A. remain as dissolved oxygen
  - B. Bind to hemoglobin (Hb) to make HbO_2



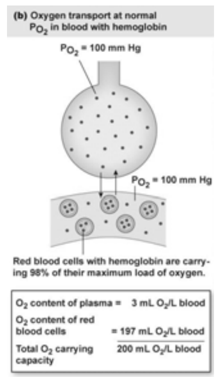
Gas Transport
General Process

- TOTAL blood O_2 content = quantity dissolved in plasma + amount bound to Hb (HbO_2)
- Why have hemoglobin?
  - To ensure enough systemic O_2!
    - Dissolved oxygen content in blood volume
      - 15 ml O_2/min reaching the systemic tissues
      - O_2 requirement at rest = ~250 ml O_2/min
  - Oxygen bound to hemoglobin, allows the total amount of oxygen in the blood to exceed 250 ml O_2/min



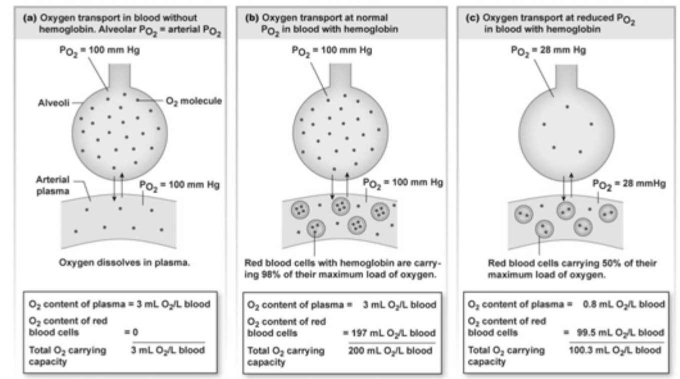
Gas Transport
General Process

- O_2 in blood quickly associates with hemoglobin (Hb), forming oxyhemoglobin (HbO_2)
  - allows for blood to carry an extra 985 ml of oxygen/min in an average blood volume of 5L
    - Dissolved = 15ml O_2/min transported
    - Associated with Hb = 985 ml O_2/min
  - **Total Oxygen carrying capacity = 1000ml/min or 1L/min**
    - 4x's greater than "at rest" demand



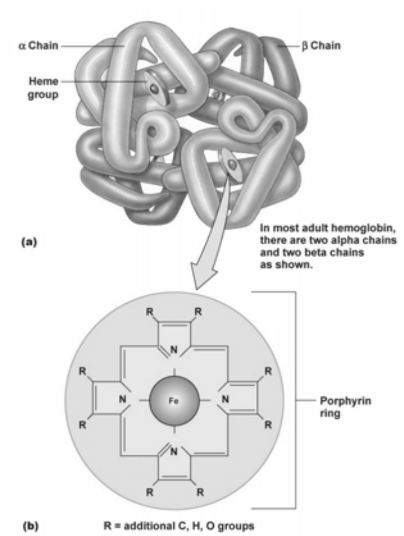
Gas Transport
oxygen binding to Hb

- What is the driving force for oxygen to bind to Hb?
  - Plasma P_{O2}



Gas Transport
Hemoglobin

- Why is hemoglobin so effective?
  - Each subunit of the quaternary structure has a binding site for oxygen
    - The heme group of each subunit contains a prophyrin ring with an iron atom (Fe^{2+}) a the center
      - This Fe^{2+} reversibly binds O_2 in accordance with the law of mass action
      - Typically P_{O2} drives this reaction



Gas Transport
Hemoglobin

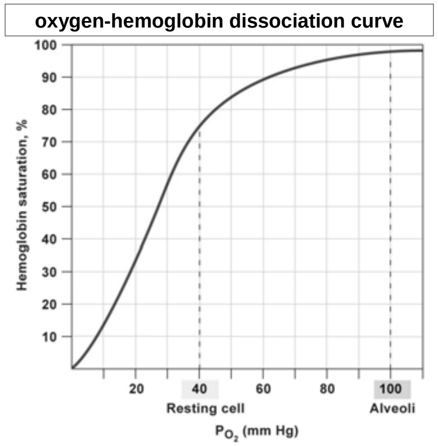
- Hb structure can vary
  - Adult Hb
    - The subunits are alpha, beta, gamma, delta
    - Most common arrangement is 2 alpha, and 2 beta units (HbA) >95%
    - Also some where:
      - 2 alpha & 2 delta subunits present (HbA_2) ~2.5%
      - 2 alpha & 2 gamma subunits present (HbF) rare
  - Fetal Hb (HbF)
    - Gamma chains in place of the beta chains.
    - Creates Hb molecules with a higher affinity for oxygen

Hydroxyurea treatment in adults with sickle cell anemia stimulates development of more HbF than HbA

Gas Transport

Oxygen-hemoglobin dissociation curve

- The binding (association/ dissociation curve) is NOT linear, it is rather a sigmoid (S shaped) curve.



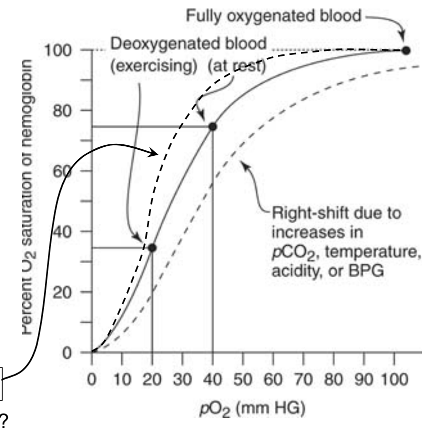
Gas Transport

Oxygen-hemoglobin dissociation curve

- The binding of O2 on Hb is influenced by
  - Temperature
  - P_{CO_2}
  - pH
  - 2,3-DPG (BPG)

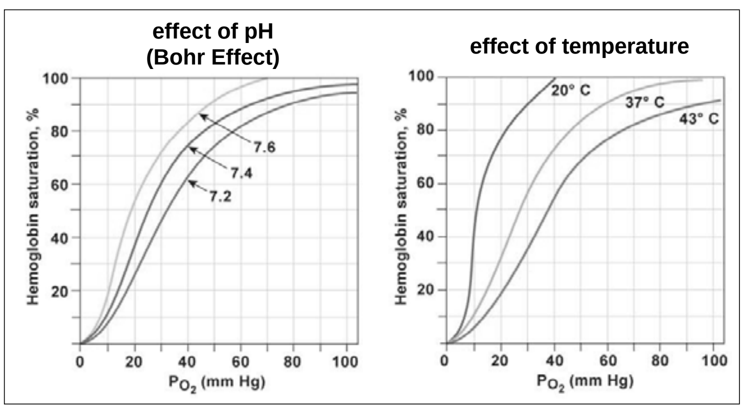
What would create a left-shift?

Which curve would represent HbF?



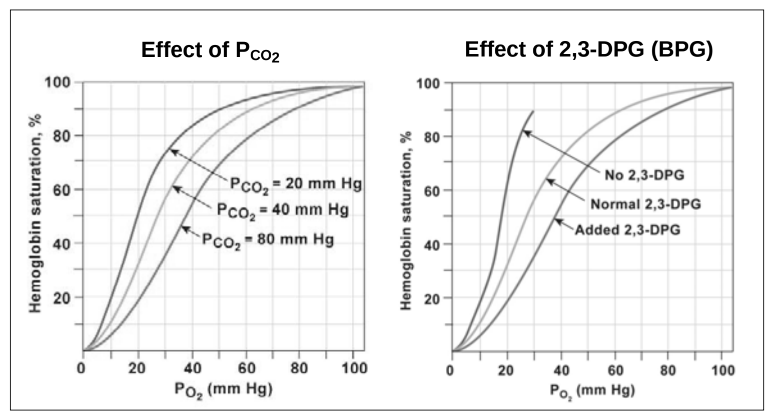
Gas Transport

oxygen-hemoglobin dissociation curves

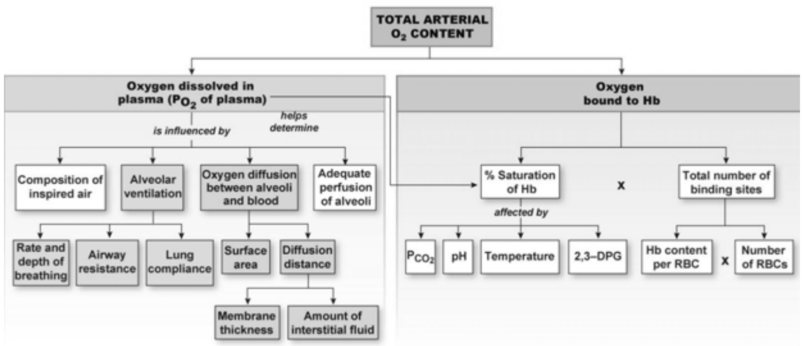


Gas Transport

oxygen-hemoglobin dissociation curves



Gas Transport
Oxygen Summary



Gas Transport
Carbon Dioxide

- Why be concerned with CO2 transport?
- Transported three ways:
  - Dissolved in blood (~7%)
  - Converted to bicarbonate ions (~70%)
  - Attaches to Hb (~23%)
    - $CO_2 + Hb \leftrightarrow Hb{\cdot}CO_2$(carbaminohemoglobin)

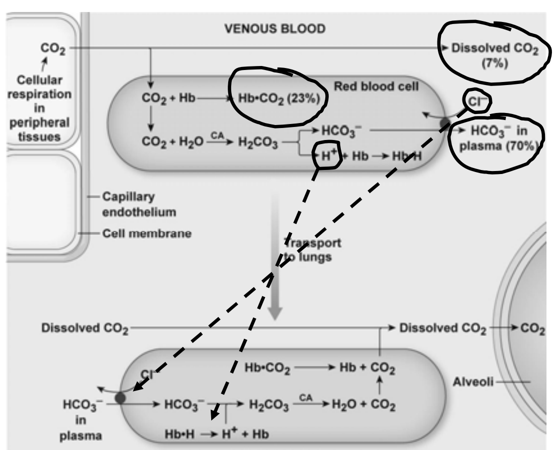
Gas Transport
Carbon Dioxide

Important things to consider!

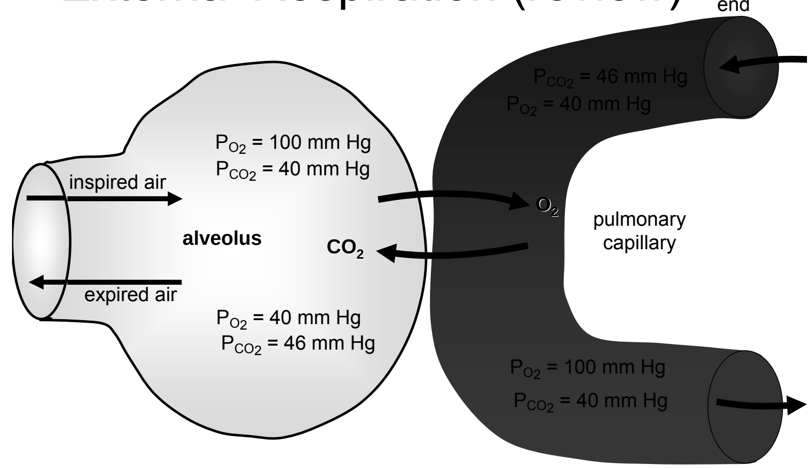
1. The H^+ created during bicarbonate ion formation
2. The transport of HCO_3^- out of the cell occurs with the movement of Cl^- into the cell

called the chloride shift

Both must reverse in the lungs!



External Respiration (review)



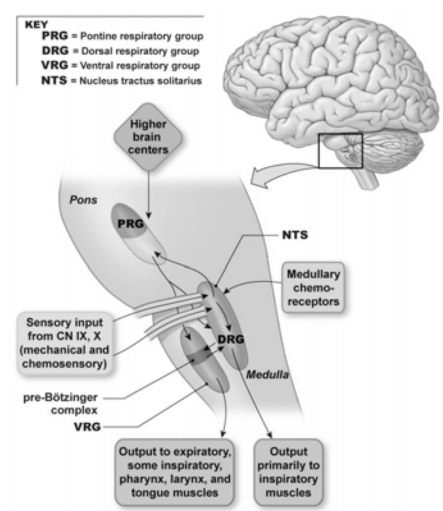
Regulation of Ventilation

- Ventilation is controlled in the brain stem by a neural network
  - It is influenced by
    - Gas levels
    - pH
    - Emotions
    - Voluntary efforts
      - Tend to be very temporary!

Regulation of Ventilation

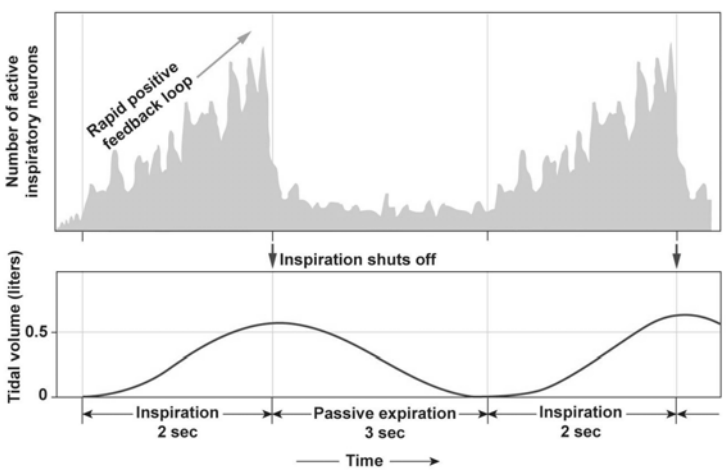
Brain Stem

- Control Model
  1. Rhythmic ventilation is due to spontaneously discharging neurons
     - Pre-Bötzinger complex (pacemaker)
  2. Respiratory neurons in medulla (DRG & VRG) control inspiratory & expiratory muscles
  3. Neurons in the Pons (PRG) integrate sensory input and influence activity of the medullary neurons
  4. Ventilation is under continuous modulation by reflexes and higher brain centers



Regulation of Ventilation

Neural Output Levels



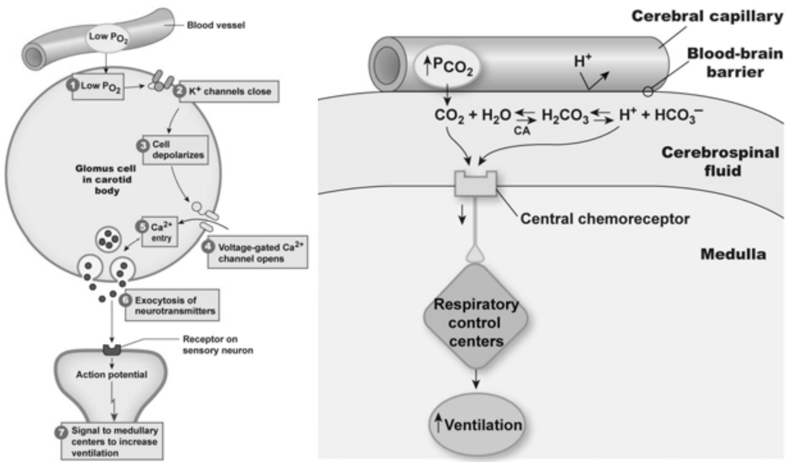
Regulation of Ventilation

Influencing Factors

- CO_2, O_2 and pH levels all influence ventilation
  - CO_2 has the biggest influence on ventilation rates
  - O_2 and H^+ (pH) are influencing factors as well, but to a smaller extent
- Monitored by
  - peripheral and central chemoreceptors
    - Peripheral in the carotid and aortic bodies
    - Central in the medulla oblongata

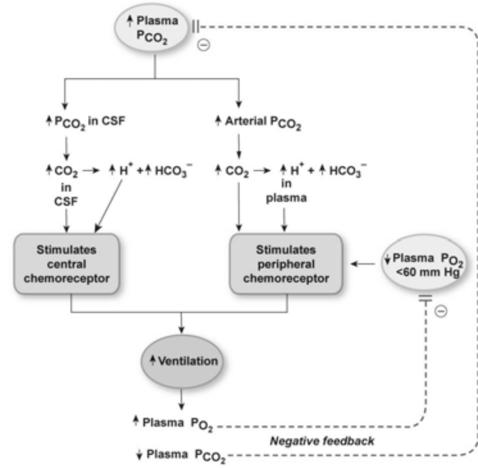
Regulation of Ventilation

Peripheral & Central Chemoreceptors



Regulation of Ventilation

Ex. Chemoreceptors responses to plasma CO_2



Regulation of Ventilation

Protective Measures

- Irritant receptors in airway cause
  - bronchoconstriction
  - coughing
  - sneezing
- Hering-Breuer inflation reflex
  - Prevents over-inflation of lungs
    - Stops inspiration
      - Rare in adults, infants may use this to limit ventilation volumes… why?

Regulation of Ventilation

Higher Brain Center Influence

- Higher brain function NOT required for normal ventilation and regulation of respiratory cycles
- Conscious and unconscious controls
  - Emotional state
    - Fear/anxiety/excitement = increased respiratory cycle rate
    - Depression…
  - Holding your breath?
  - Hyperventilation before breath holding… good or bad?

Control of Ventilation Overview