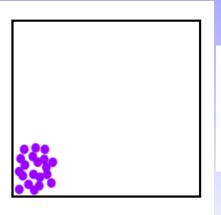
Introduction to the Respiratory System

- Describe <u>primary functions</u> of the respiratory system
- Describe the <u>anatomy</u> of the respiratory system. Identify organs involved
- Define and compare external respiration and internal respiration
- Understand the mechanics of breathing
- Understand <u>diffusion of gases from the lungs into the blood</u> and <u>then to the tissues</u>
- Understand how <u>carbon dioxide is transported</u> in the blood and removed from the body
- Describe the <u>structure of hemoglobin</u>, its importance in gas transport and factors that affect its <u>shape</u>
- Understand <u>the Oxygen–Hemoglobin Saturation Curve</u>, which factors affect its shape and implications on physiology
- Describe <u>how respiration is regulated</u>.
- Understand how <u>acid-base homeostasis</u> is maintained and how acid-base disturbances are corrected
- Be able to compare and contrast respiratory strategies of different species.

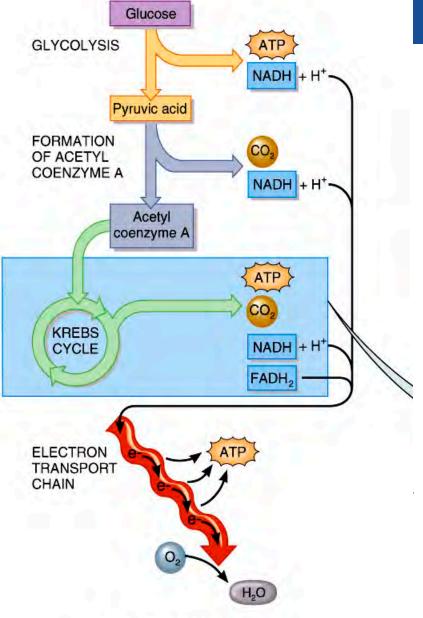
Definitions

- <u>Respiration</u> = sequence of events that result in the <u>exchange of oxygen and carbon</u> dioxide between the external environment and the mitochondria. Why do we need O2 and why do we have to exhale CO2?
- <u>External respiration</u> = gas exchange at the <u>alveolar membrane (lungs)</u> level
- <u>Internal respiration</u> = gas exchange at the <u>tissue</u> level
- <u>Mitochondrial respiration</u> = production of ATP via oxidation of carbohydrates, amino acids, or fatty acids. <u>Oxygen is consumed and carbon dioxide is produced</u>



<u>Diffusion</u> is the movement of substrate molecules <u>from a high</u> concentration to a low concentration.

<u>Gradients</u> can be pressure (gases), electrochemical (ions) or just chemical (glucose)



- (a) Cellular respiration
- Figure 25.06 Tortora PAP 12/e Copyright © John Wiley and Sons, Inc. All rights reserved.

- Mitochondria consume O₂ to produce ATP
- Produce CO₂ in the process. Where?
- Organisms must have mechanisms to obtain
 O₂ from the environment and get rid of CO₂.
 Why get rid of CO₂?
- CO2 + H2O ↔ H+ + HCO3-
- An increase in H+, decreases pH

First, we will look at how gases behave.....

Respiratory systems - diffusion rate

Fick equation

J = -DAdC/dx

J = rate of diffusion (moles/sec)

D = diffusion coefficient = how easily a substance can diffuse

A = surface area of the membrane

dC = concentration gradient

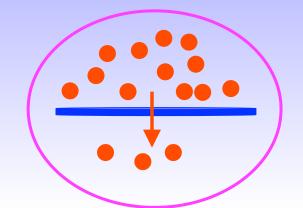
dx = diffusion distance

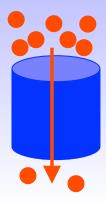
For gases, we usually use <u>partial pressure</u> rather than concentration <u>Gases will move down pressure gradients. Remember this. From high Lower pressure</u>

Respiratory systems - diffusion rate

J = -DAdC/dx

- Rate of diffusion will be greatest when the diffusion coefficient (D), area of the membrane (A), and energy gradients (dC/dx) are large, but the diffusion distance is small
- *Consequently, gas exchange surfaces are typically thin = short diffusion distance, with a large surface area



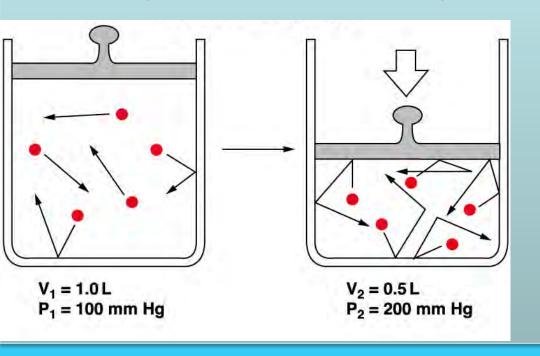


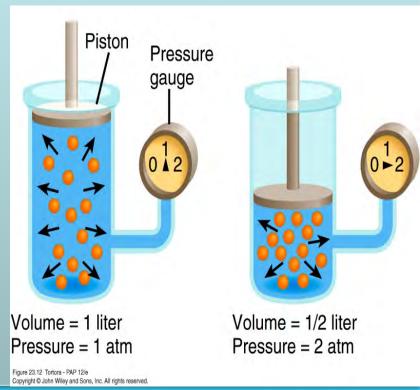
Pulmonary Ventilation

Boyle's Law = pressure of a gas in a closed container is inversely proportional to the volume of the container

*Boyle's Law: $P_1V_1 = P_2V_2$

https://www.youtube.com/watch?v=q6-oyxnkZC0





*Respiratory systems use <u>changes in volume to cause changes in pressure</u>!

Gases Dissolve in liquids

*Henry's Law

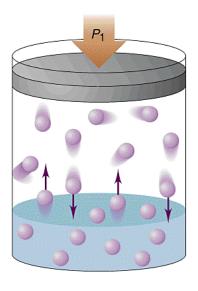
- *Gases have to dissolve before they diffuse
- When a gas under pressure comes in contact with liquid, the gas dissolves in liquid until equilibrium is reached
- *At a given temperature the amount of a gas in solution is proportional to partial pressure of that gas
- What is solubility?

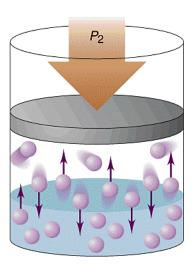
★*Henry's law: [G] = P_{gas} x S_{gas}

★[G] is the concentration of the gas in solution

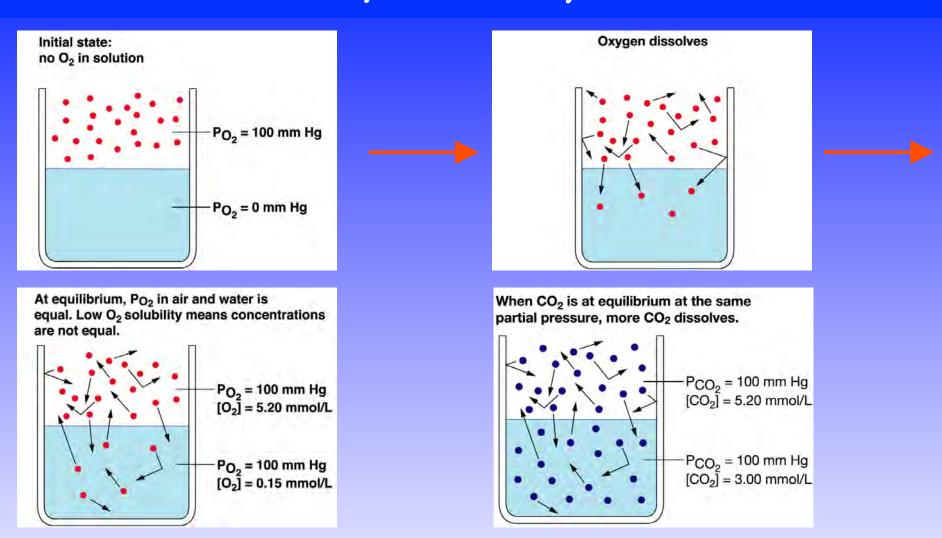
Pgas = Partial pressure of the gas

Sgas = how easily a gas can dissolve in a solution





Gases Dissolve in liquids. Henry's law



*CO₂ is much <u>more soluble in water than is O₂.</u> Thus, at the same partial pressure, more CO₂will be dissolved in a solution than will oxygen. *Need a O2 carrier due to low SO2

Diffusion Rates and molecular weight

*Graham's law = The relative diffusion of a given gas is proportional to its solubility in the liquid and inversely proportional to the square root of its molecular weight:

- * Diffusion rate = solubility/√MW
- O₂ 32 atomic mass units
- CO₂ 44 amu
- In air "solubilities" are the same (1000 ml/L at 20°C). So oxygen diffuses about 1.2 times faster than CO₂ in air.
- However, CO₂ is about 24 times more soluble in aqueous solutions than O₂. *CO₂ diffuses about 20 times faster than O₂ in water.

Again, why do we care? If we don't get rid of CO2, acid-base homeostasis is mucked up ⊗

Diffusion Rates at a constant temperature

*****Combining the Fick equation with Henry's and Graham's laws:

*Diffusion rate =
$$dP_{gas} \times A \times S_{gas} / X \times \sqrt{(MW)}$$

At a constant temperature the rate of diffusion is proportional to

- Partial pressure gradient (dP_{qas}) = high to low
- Cross-sectional area (A) = doesn't change much as adult
- Solubility of the gas in the fluid (S_{gas})

and inversely proportional to

- Diffusion distance (X)
- Molecular weight of the gas (MW)

So what do all of these equations really mean?

Fish versus Terrestrial animals

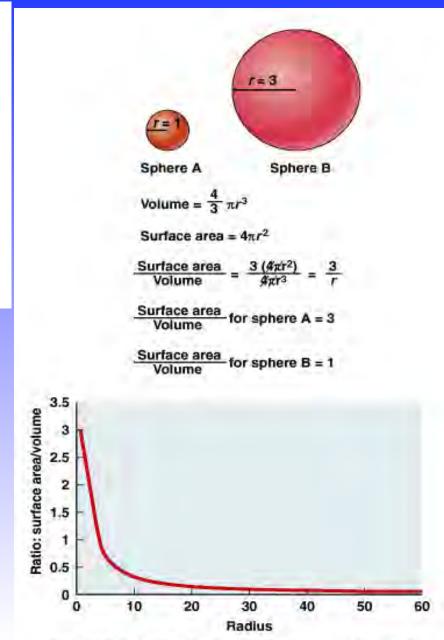
Surface Area to Volume Ratio

- *As organisms grow larger, their ratio of surface area to volume <u>decreases</u>
- This <u>limits the area available for</u>

 <u>diffusion</u> and <u>increases the diffusion</u>
 <u>distance</u>

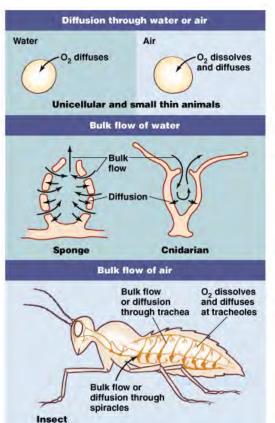
 J= -DAdC/dx

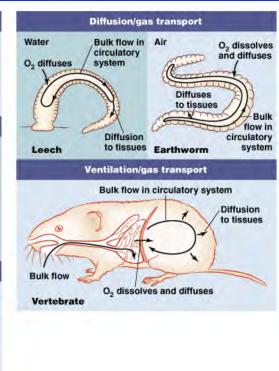
That's why we need respiratory systems



Respiratory strategies of animals

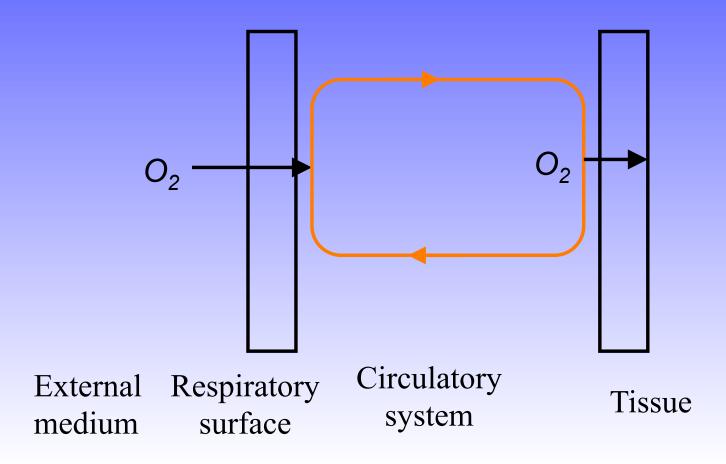
- *Unicellular and <u>small</u> multicellular organisms rely on <u>diffusion for gas exchange</u>
- *Larger organisms must rely on a combination of bulk flow and diffusion for gas exchange, i.e. they need a respiratory system
- *Bulk flow = large amount of medium = air or water
- *Then the gases are exchanged by diffusion





Most animals have a circulatory system

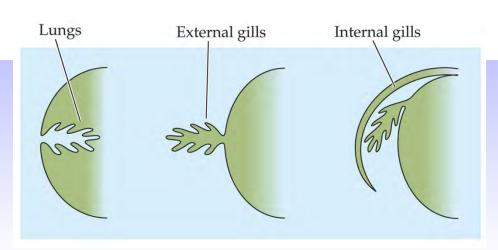
Diffusion of gases across a specialized respiratory surface accompanied by *circulatory transport



Respiratory Strategies

Animals more than a few millimeters thick use one of three respiratory strategies

- Circulating the external medium through the body = Sponges, cnidarians (jellyfish) and insects
- Diffusion of gases across the <u>body surface</u> accompanied by <u>circulatory transport</u>
 - Cutaneous respiration = skin
 - Most aquatic invertebrates, some amphibians, eggs of birds
- *Diffusion of gases across a specialized respiratory surface accompanied by circulatory transport
 - Gills = evaginations; lungs =invaginations
 - Vertebrates



Cutaneous respiration

Respiration through skin

Found in some aquatic invertebrates and a few vertebrates

Disadvantages:

Relatively low surface area

• Conflict between respiration and protection = if skin gets damaged, respiration

gets compromised (3)



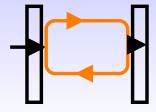
Salamander



Annelid



Lake Titicaca frog



External gills

Gills originate as outpocketings = evaginations

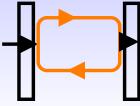
- Advantages: high surface area, exposed to medium
- **Disadvantages**: easily damaged, not suitable in air
- Gills dry out and collapse in air. Why is drying out bad? If dried out, gases cannot diffuse because they <u>must first dissolve</u>. If collapse, surface area reduced



Salamander

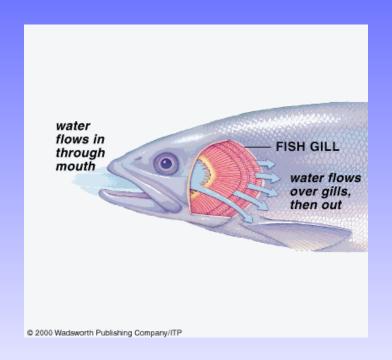


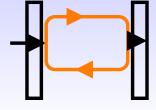
Polychaete



Internal gills

- Advantages: High surface area, protected
- <u>Disadvantages</u>: not suitable in air = see previous slide, external gills





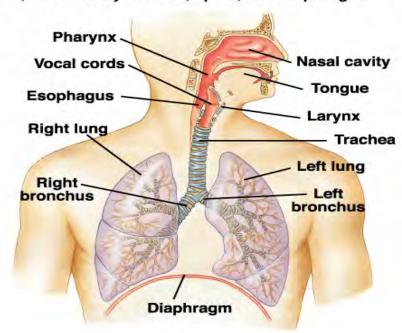
**Lungs

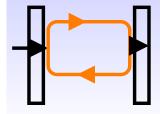
Originate as infoldings = invaginations

- Advantages: High surface area (2 tennis courts), protected, suitable for breathing air
- Disadvantages: not suitable in water. Why? O2 solubility is very low in fluid and diffusion distance has greatly increased

The respiratory system

The respiratory system consists of the upper respiratory system (mouth, nasal cavity, pharynx, larynx) and the lower respiratory system (trachea, bronchi, lungs). The lower respiratory system is enclosed in the thorax, bounded by the ribs, spine, and diaphragm.





Ventilation

*Ventilation = <u>active movement of the respiratory medium</u> (air or water) across the respiratory surface. Bulk flow = large quantity of air or water

**Flow = \triangle P/R = pressure gradient/resistance. Flow in the two tubes is equal because pressure gradients are equal. Animals will affect pressure gradients by changing volume. Increase volume to decrease pressure and air/water will go down pressure gradients

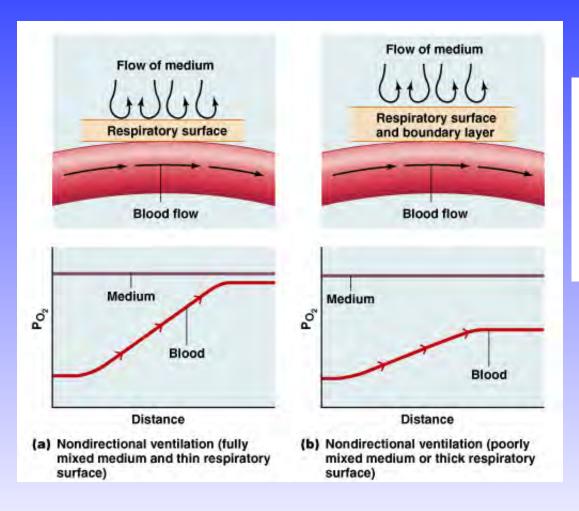
Types of ventilation

- Nondirectional medium flows passing the respiratory surface in an unpredictable pattern = air across frog skin
- *Tidal medium moves in and out the same structure = lungs in mammals
- Unidirectional medium enters the chamber at one point and exits at another
 in fish.. More later

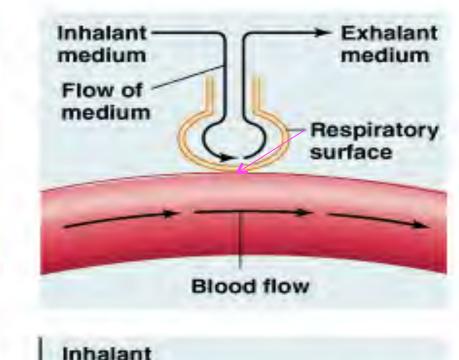
Note: *Air and water will move down pressure gradients.

Nondirectional ventilation

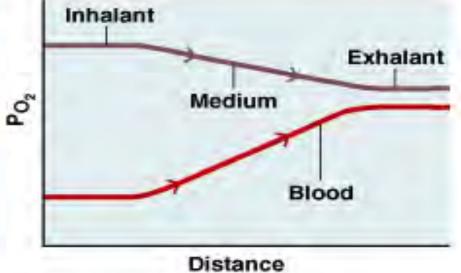
Medium flows past the respiratory surface in an unpredictable pattern



Example frog skin:
If frog is ill and has barrier such as slime on skin,
less O2 can be picked up across skin

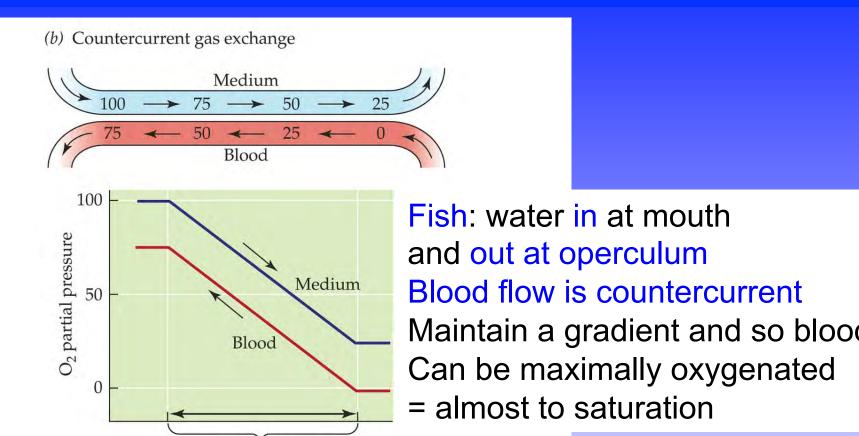


Lungs



Why less Oxygen at exhalant?

Gas exchange - unidirectional ventilation



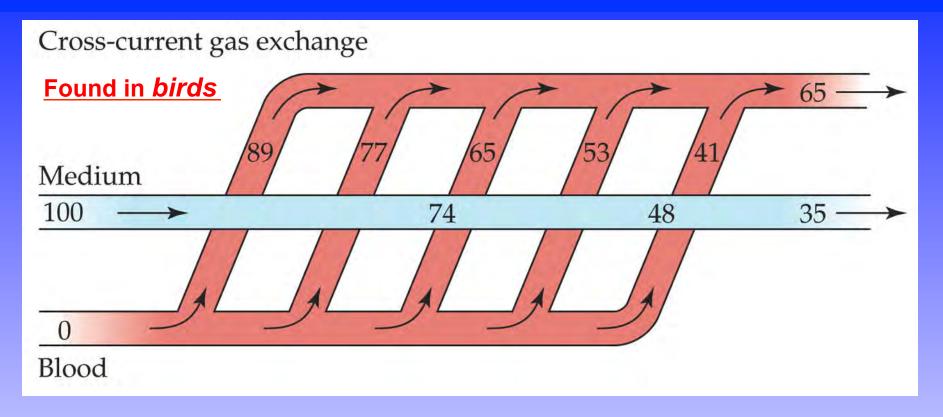
ANIMAL PHYSIOLOGY, Figure 21.4 (Part 2) @ 2004 Sinauer Associates, Inc.

Maintain gradient.

***PO₂ of blood approaches that of the inhalant medium

Distance along exchange surface

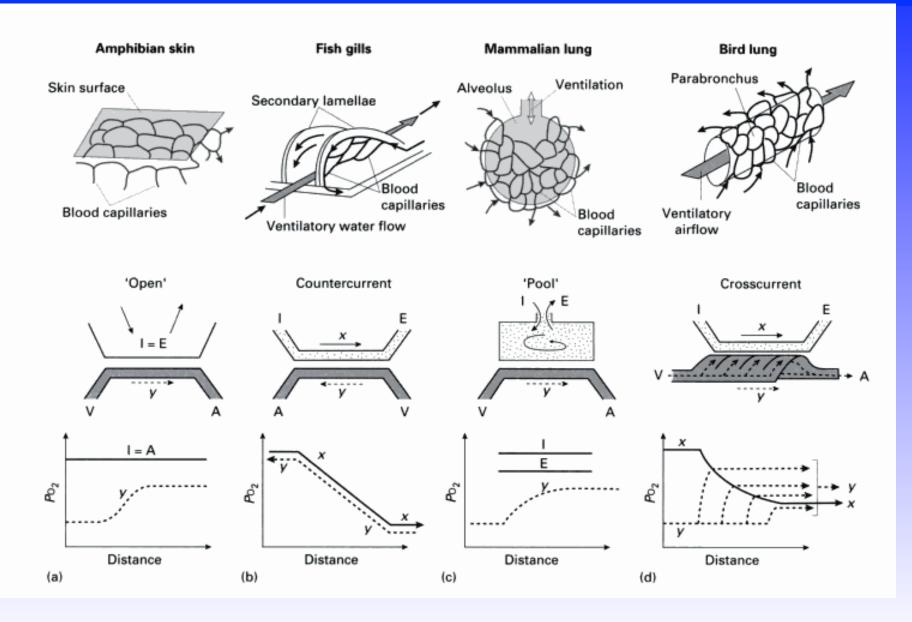
Gas exchange - unidirectional ventilation



The P_{O2} of arterial blood is derived from a mixture of all serial air-blood capillary units and exceeds that of the exhaled P_{O2} .

$$(89+77+65+53+41)/5 = 65$$

Types of ventilation - Summary



Ventilation and Gas Exchange

Because of the different physical properties of air and water, animals use different strategies depending on the medium in which they live

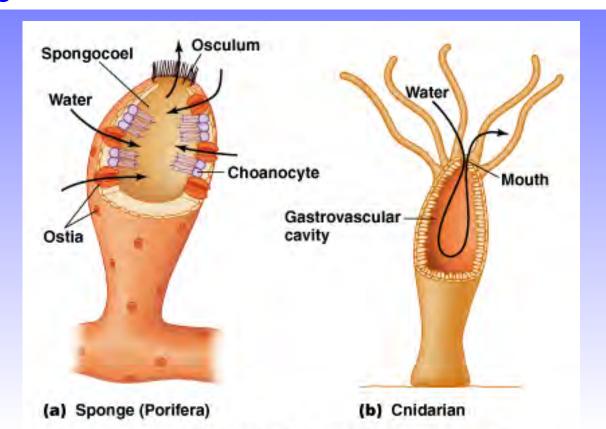
Differences

- [O_{air}] greater than [O_{water}]. Think Henry's law....
- Water is more dense and viscous than air. Fick's equation....
- *Evaporation* is only an issue for air breathers
- Solubility of O2 in water a lot less so fish/aquatic animals have to worry more about O2

What strategies are being used? Next slides

Sponges and Cnidarians - in water

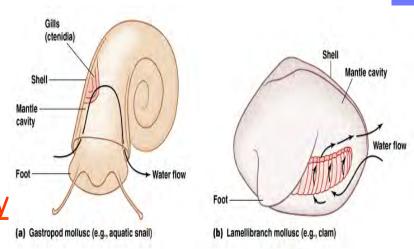
- Circulate the external medium through an internal cavity
- In <u>sponges flagella</u> move water in through ostia and out through the osculum. Flagella in humans = sperm
- In cnidarians (<u>jellyfish</u>) <u>muscle contractions</u> move water in and out through the mouth



Molluscs - in water

Two strategies for ventilating their gills and mantle cavity

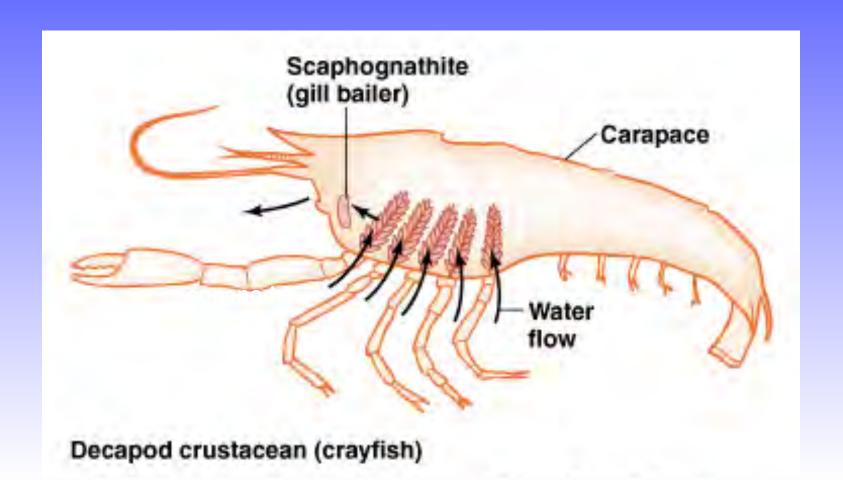
- Beating of cilia on gills move water across the gills unidirectionally. Cilia are structures that beat rhythmically and move "stuff"
 - Blood flow is countercurrent
 - Snails and clams
- Muscular contractions of the mantle propel water <u>unidirectionally</u> through the mantle cavity past the gills
 - Blood flow is <u>countercurrent</u>
 - Cephalopods (<u>squid</u>)



(c) Cephalopod mollusc (e.g., squid)

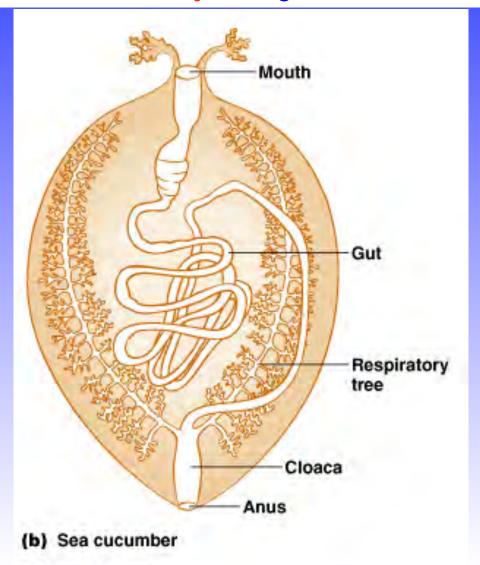
Crustaceans - in water

- Shrimp, crabs and lobsters, have gills derived from modified appendages located within a branchial cavity
- Movements of the <u>gill bailer</u> propels water out of the branchial chamber;
 the <u>negative pressure sucks water across the gills</u>



Echinoderms - in water

Sea cucumbers use <u>muscular contractions</u> of the cloaca and the *respiratory* tree to <u>breathe water *tidally* through the anus</u>



Jawless Fishes - Hagfish - in water

Lamprey and hagfish have multiple pairs of gill sacs

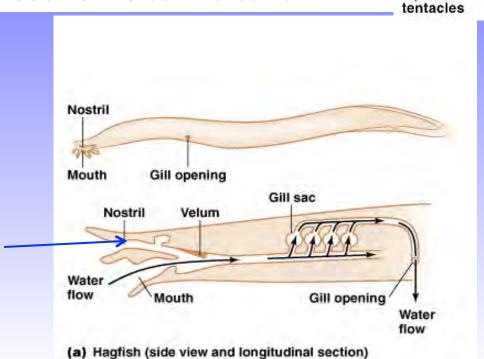
Hagfish

- A muscular pump (= velum) propels water through the respiratory cavity
- Water enters the median nostril and leaves through a gill opening

gill slits (twelve pairs)

mucous glands

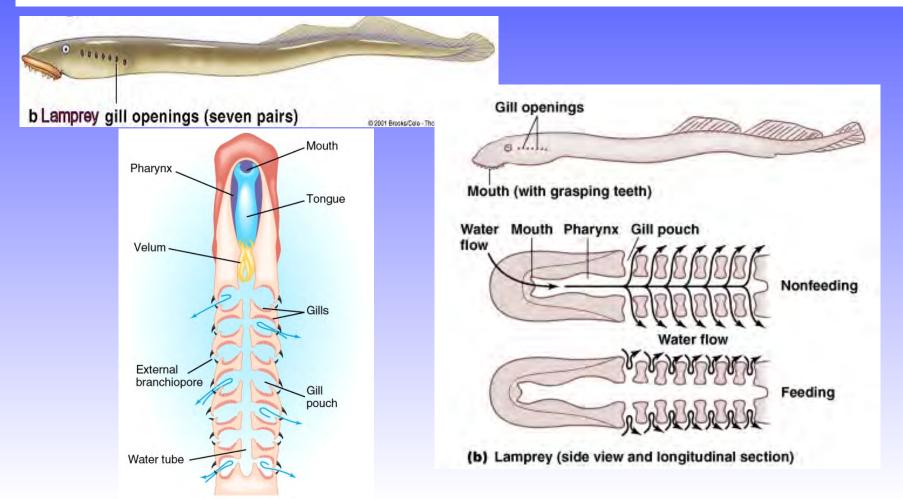
- Flow is unidirectional
- Blood flow is countercurrent



Jawless Fishes - Lamprey - in water

Lamprey

- Ventilation is similar to that in hagfish when not feeding
- When feeding the mouth is attached to a prey (parasitic)
- Ventilation is tidal though the gill openings when feeding



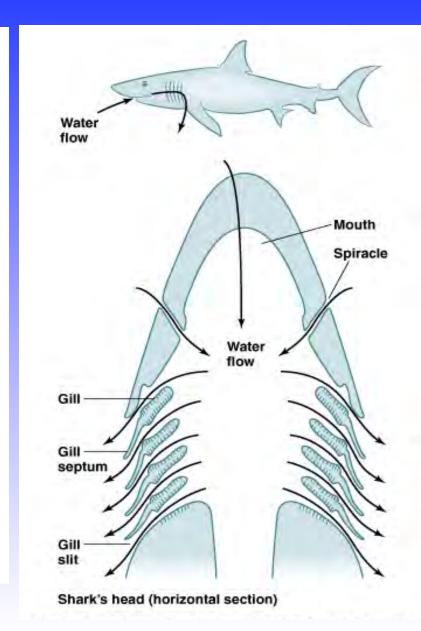
**Elasmobranchs - <u>sharks</u>, skates and rays in water

Steps in ventilation

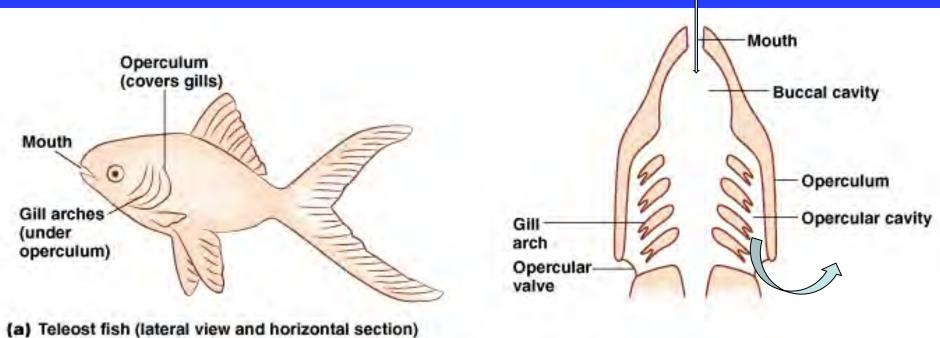
- Expand the buccal cavity = this increases the volume and so decreases the pressure and water flows down pressure gradients
- Increased volume sucks fluid/water into the buccal cavity via the mouth and spiracles (hoels/pores)
- Mouth and spiracles close
- Muscles around the buccal cavity contact forcing water past the gills and out the external gill slits
- Water flow is unidirectionally

Blood flow is countercurrent

*Buccal = relating to mouth



Teleost Fishes - in water

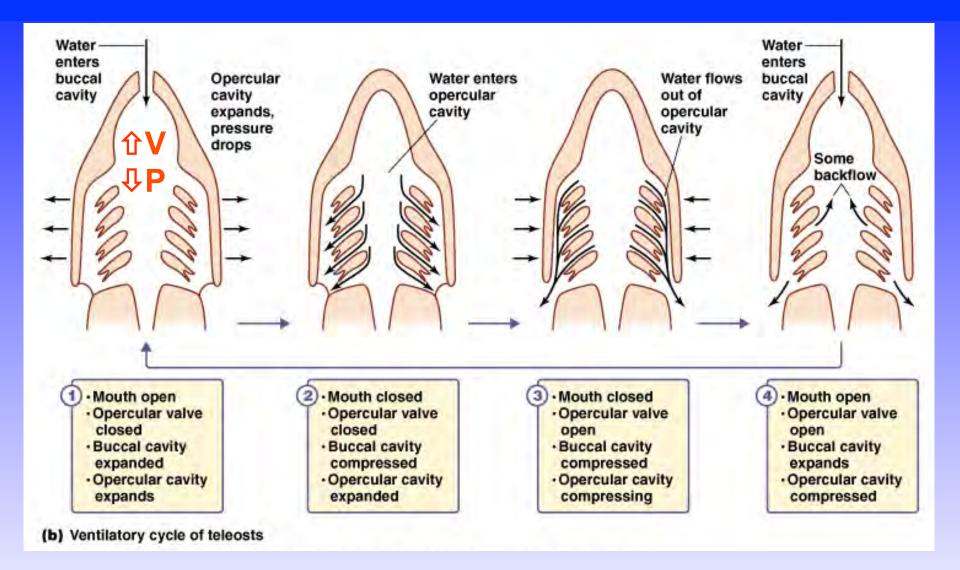


a) releast iisii (lateral view and nonzontal section)

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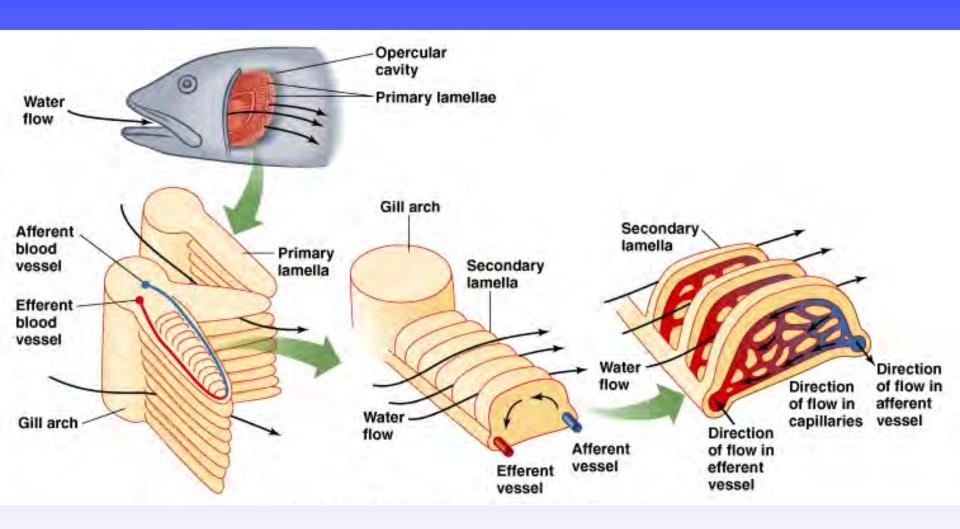
Water flows in via the mouth, out via the opercular opening

Teleost Fishes



More about fish Gills

Fish gills are arranged for countercurrent flow



Water breathers

Outline and list:

Which water breathing animals use cilia, muscular contractions. Sponges

How is water brought into respiratory structure? What is the common method? Movement of water through gills

Ventilation and Gas Exchange in Air

- Arthropods (eeeekkkk)
- Vertebrates

Ventilation - terrestrial molluscs

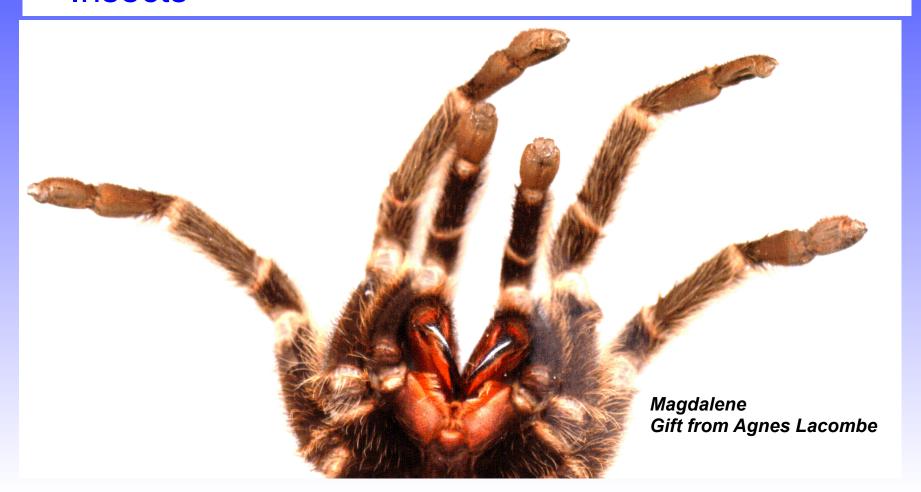
- The "pulmonate" molluscs lack gills (or have highly reduced gills)
- Instead, mantle cavity is <u>highly vascularized</u>
- Garden snails and terrestrial slugs are pulmonates
- Pumping of the mantle cavity moves air in and out



https://www.google.com/search?q=pulmonate +lung&source=lnms&tbm=isch&sa=X&ei=MMqLU-37FsmTqgb724D4Dw&ve d=0CAYQ_AUoAQ&biw=1440&bih=817#q=pulmonate+lung +slugs&tbm=isch&facrc=_&imgdii=_&imgrc=GPRFDb2RpYJE6M%253A %3BdyNMp_2HzkoJSM%3Bhttp%253A%252F %252Fwww.comoxvalleynaturalist.bc.ca%252Fassets%252Fimages %252Fmisc%252Fbanana_slug.jpg%3Bhttp%253A%252F %252Fwww.comoxvalleynaturalist.bc.ca%252Fknowing_nature %252F2005%252Fslugs.html%3B300%3B225

Arthropods (eeeeeek)

- Crustaceans = crabs, woodlice and sowbugs
- Chelicerates = spiders and scorpions
- Insects



Crustaceans

Terrestrial crabs

- Respiratory structures and the processes of ventilation are <u>similar to</u> <u>marine relatives</u>, but
 - Gills are stiff so they do not collapse in air
 - Branchial cavity is <u>highly vascularized</u> and acts as the primary site of gas exchange
 - Movements of the gill bailer propels <u>air</u> in and out of the branchial chamber

Remember: *Gills in marine animals collapse and dry out in air.

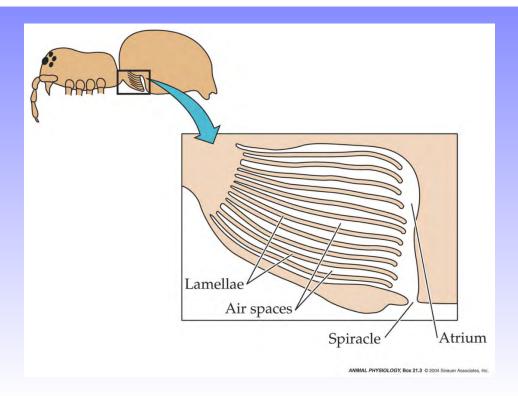
Chelicerates - Spiders and scorpions

Have four book lungs

- Consists of 10-100 lamellae = high surface area
- Open to outside <u>via spiracles</u>
- Gases diffuse in and out

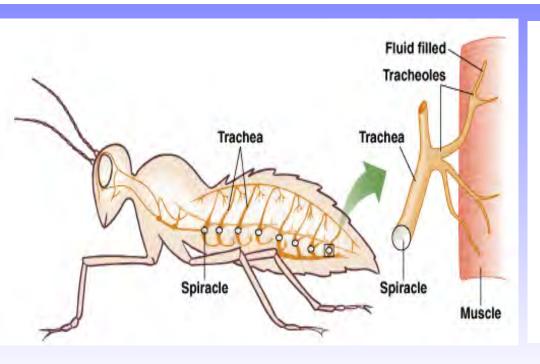
Some spiders also have a tracheal system – series of air-filled tubes

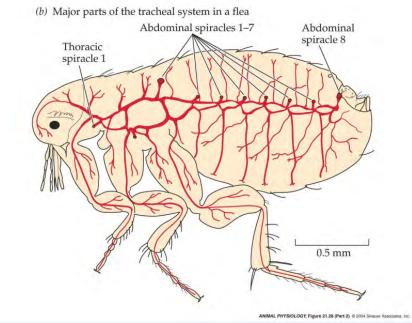
 Oxygen <u>diffuses into the trachea</u> and <u>dissolves in the interstitial fluid</u> before diffusing into the tissues. *<u>Interstitial fluid = outside cells</u>



Insects

- Have an extensive tracheal system series of air-filled tubes
- Tracheoles terminating ends of tubes that are filled with <u>hemolymph</u>
- Oxygen <u>dissolves in the hemolymph = blood of insects</u>
- Open to outside via <u>spiracles</u>
- Gases diffuse in and out
- High diffusion coefficient of oxygen in air allows oxygen to diffuse through the tracheal system

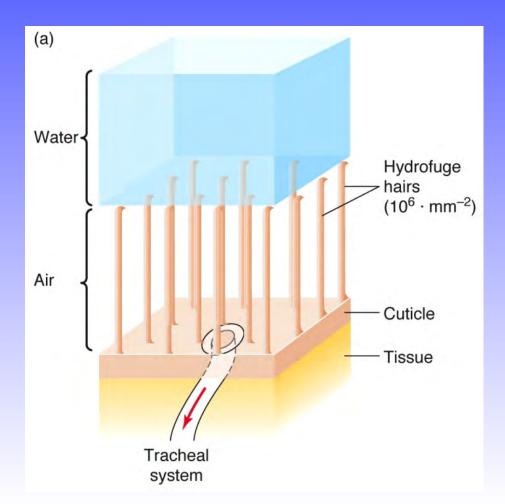




Something "cool" about aquatic insects



- Most aquatic insects breathe air
- Mosquito larvae have "snorkel"



Air breathing <u>vertebrates</u>

- Air breathing evolved in <u>fishes</u>
- Aquatic habitats can become hypoxic = low O2
- Under these conditions, the ability to breathe air is a substantial benefit

We will discuss

- Air-breathing Fish
- Amphibians
- Reptiles
- Birds
- Mammals

Evolution of air breathing

Air breathing has evolved multiple times in fishes

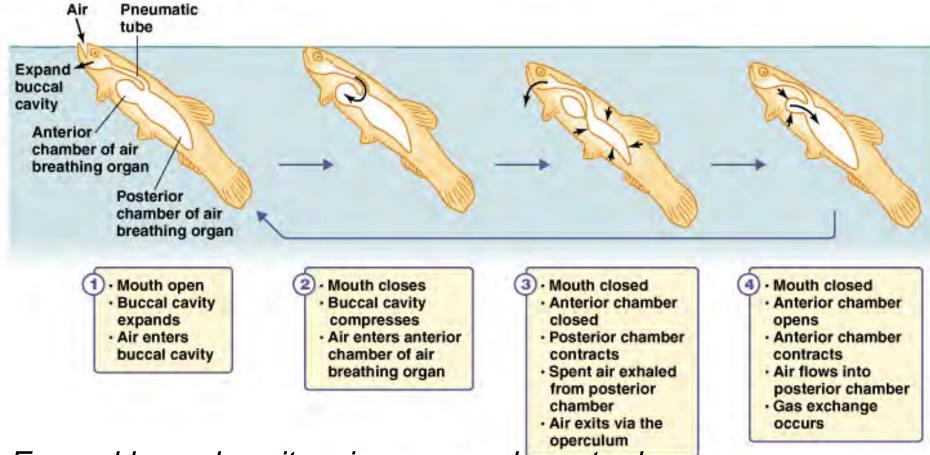
Types of respiratory structures

- Reinforced gills that do not collapse in air = such as stiff gills
- Mouth or pharyngeal cavity for gas exchange = highly vascularized = lots of superficial blood vessels in mouth or pharyngeal cavity to take up O2
- Vascularized stomach = blood vessels in stomach take up O2
- Specialized pockets of the gut = also high vascularized
- Lungs

Ventilation is <u>tidal</u> using buccal force similar to other fish = helps to push air into respiratory structure

Note: Some fish use "aquatic surface respiration" when hypoxic = Swim to the surface and ventilate gills with water from the thin well-oxygenated water layer near surface

Air-breathing fish



Expand buccal cavity = increase volume to decrease pressure

Very little mixing of fresh and old water

Output

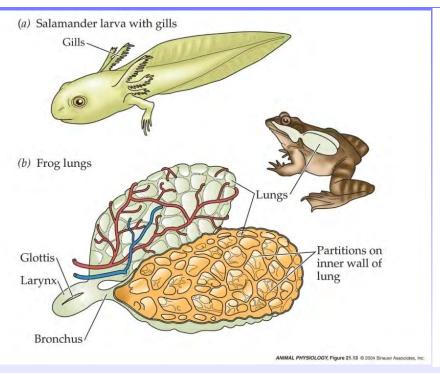
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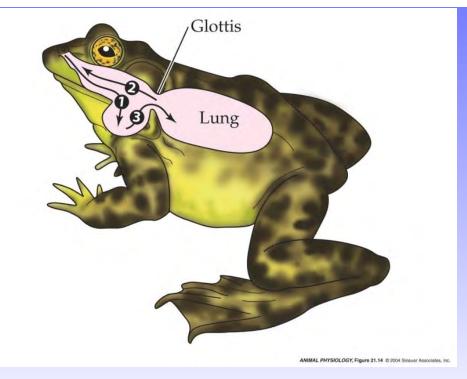
Amphibians - ventilation

Types of respiratory structures

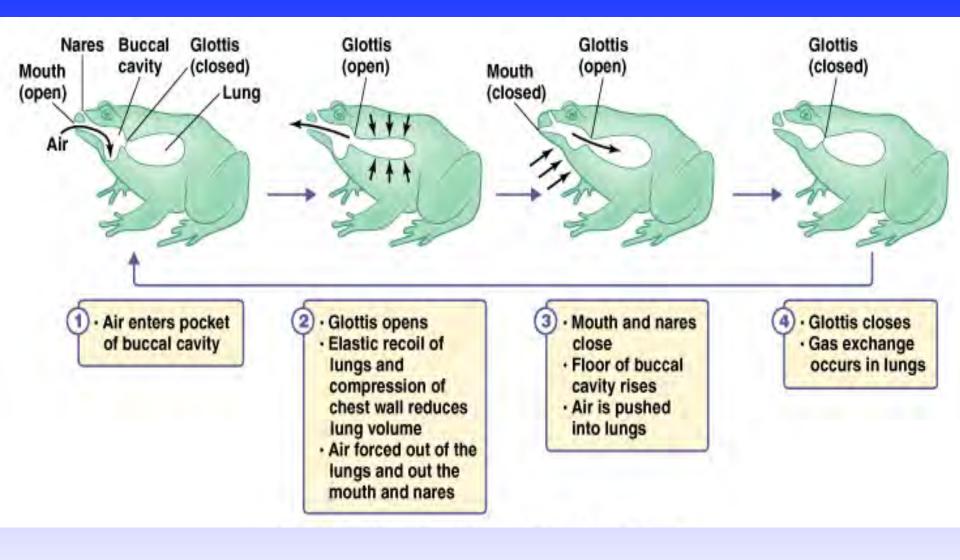
- Cutaneous respiration = <u>use skin</u>
- External gills what were advantages/disadvantages?
- Simple bilobed lungs; more complex in terrestrial frogs and toads

Ventilation is tidal using a buccal force pump





Amphibians



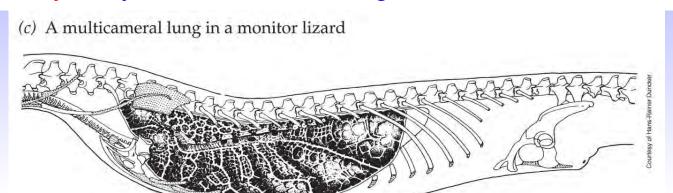
Ventilation is tidal using a buccal force pump

Reptiles (ex: lizard)

- Have two lungs
- Can be simple sacs with honeycombed walls or highly divided chambers in more active species
 - More divisions result in more surface area

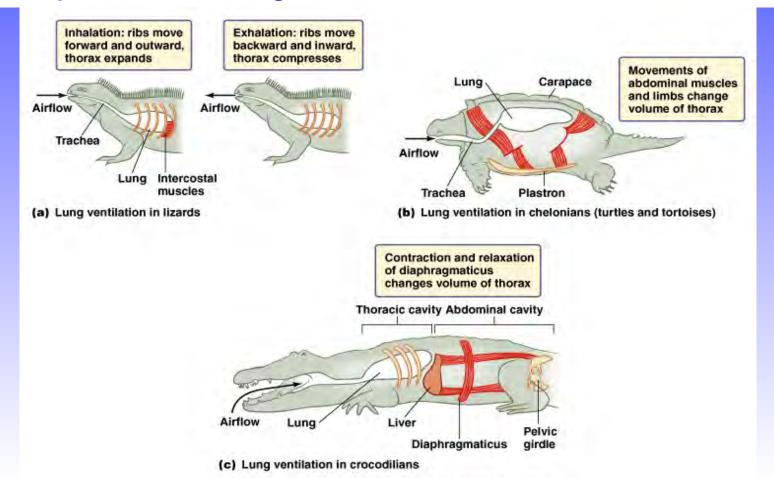
Ventilation

- Tidal
- Rely on <u>suction pumps</u>
- Results in the <u>separation of feeding and respiratory muscles</u>
- Two phases: inspiration and expiration
- Use one of several mechanisms to <u>change the volume of the chest</u> <u>cavity</u>. Why do we need to change the volume? To decrease pressure



Reptiles: mechanisms to change the volume

- Snakes and lizards: use ** intercostal muscles
- Turtles and tortoises: use *abdominal muscles
- Crocodilians: **Diaphramaticus muscles contract which decreases the volume in the abdominal cavity and <u>increases the volume of the lungs</u>. As a result pressure in the lungs decreases.



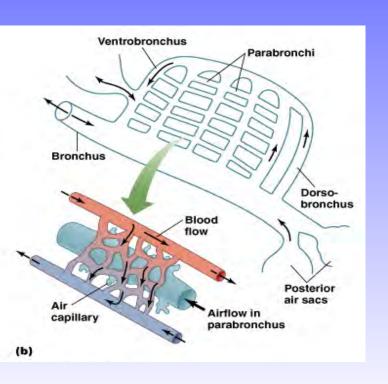
Ventilation in birds and mammals

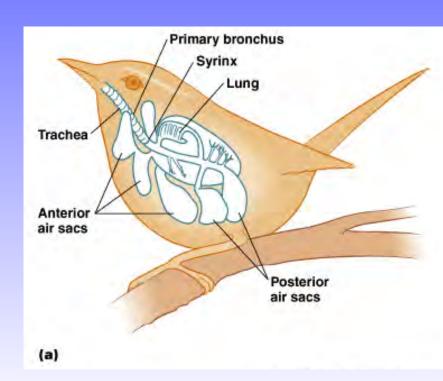
- Birds use unidirectional ventilation
- Mammals use *tidal ventilation



Birds

- *Lung is stiff and changes little in volume So how can birds change volume?
- Rely on a series of <u>flexible air sacs</u>. Air sacs allow them to increase volume and <u>decrease pressure</u>
- Gas exchange occurs at parabronchi
- Air sacs = no gas exchange = function is to move air through respiratory tract

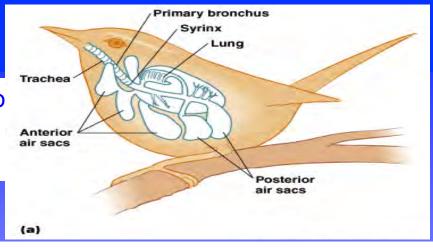


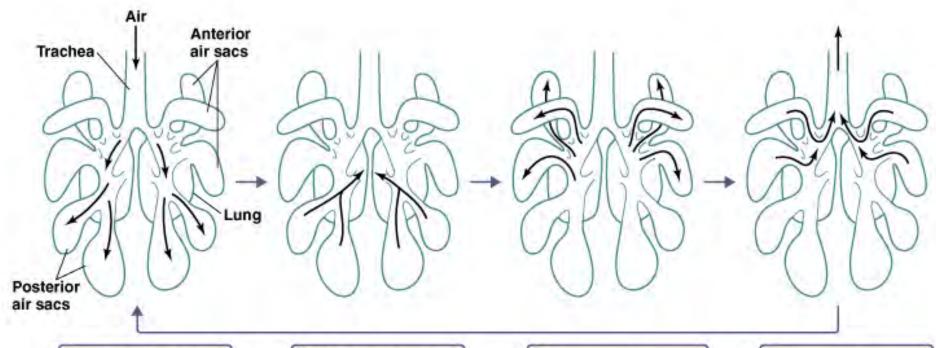


****Oxygen extraction efficiency high (up to 90%)

Bird Ventilation

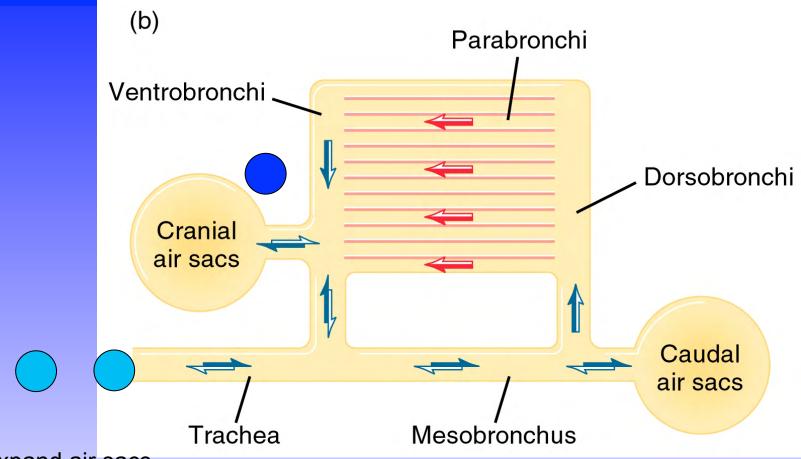
Requires <u>two cycles of inhalation</u> and exhalatio Air flow across the respiratory surfaces is <u>unidirectional</u>





- 1 The first inhalation causes fresh air to flow through the bronchi to the posterior air sacs.
- 2 The first exhalation pushes the fresh air from the posterior air sacs into the lungs.
- 3 The second inhalation causes stale air to flow from the lungs into the anterior air sacs.
- 4) The second exhalation pushes stale air from the anterior air sacs out via the trachea.

Bird Ventilation



Inhalations expand air sacs Exhalation = compress air sacs

Inhale = air into caudal or anterior air sacs

Exhale = air into lungs = gas exchange = O2 into blood

Inhale = air into cranial or posterior air sacs

Exhale = air out

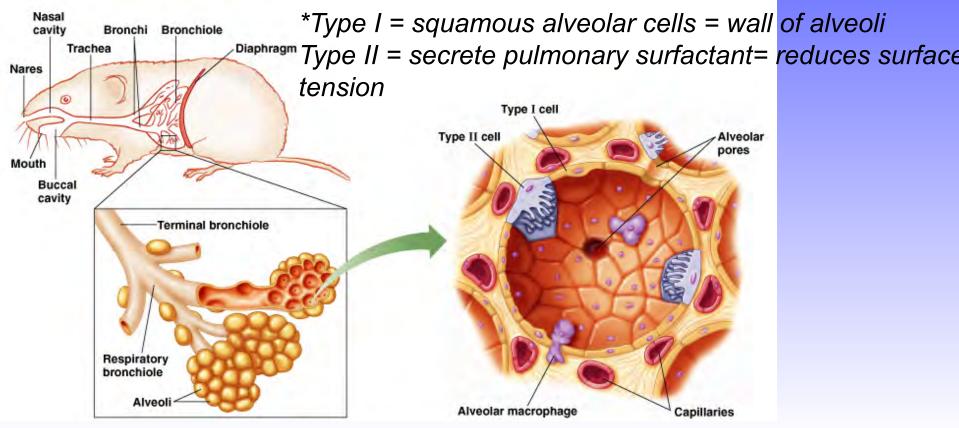
*Mammals

*Two main parts

- Upper respiratory tract: Nasal cavity, mouth, pharynx, larynx trachea
- Lower respiratory tract: trachea, I ary bronchi and lungs

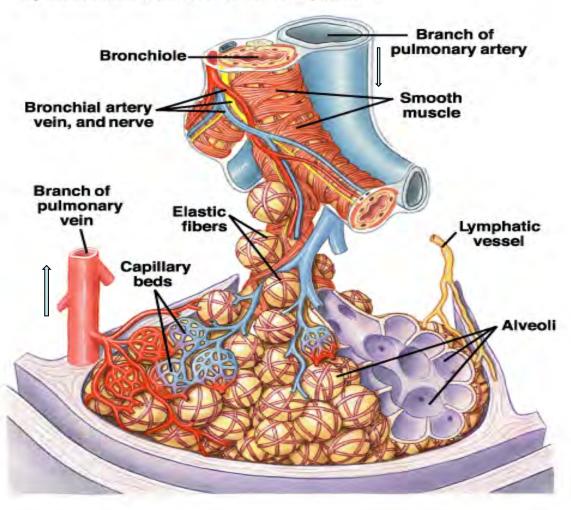
*Alveoli are the site of gas exchange

Both lungs are surrounded by a * pleural sac



*Mammalian lungs

Structure of lung lobule Each cluster of alveolis surrounded by elastic fibers and a network of capillaries.



*Physical Properties of the Lungs

*Compliance = Distensibility (stretchability) = Ease with which the lungs can expand. Affected by surfactant. Inhalation = to increase volume which decreases pressure and so air can flow into lungs

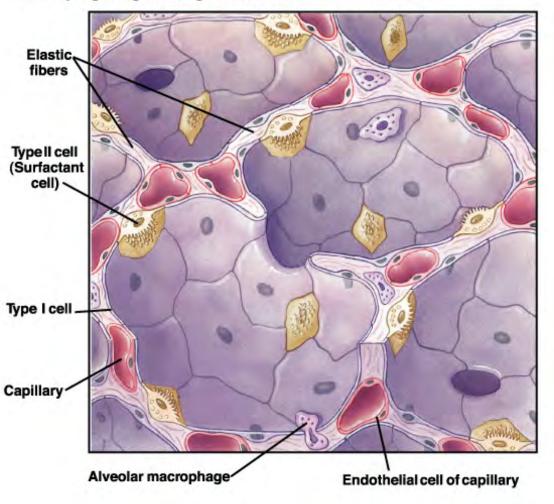
- *Elasticity = Tendency to return to initial size after distension.
 - High content of elastin proteins.
 - Very elastic and resist distension.
 - *Recoil ability. Affects exhalation. <u>Exhalation</u> at rest is <u>passive</u> due to elastic recoil

- *Inhalation is active = use external intercostal and diaphragm muscles
- Exhalation at rest is passive = use elastic recoil

Mammalian lungs - alveoli

Alveolar structure

The alveoli are composed of type I cells for gas exchange and type II cells that synthesize surfactant. Alveolar macrophages ingest foreign material that reaches the alveoli.



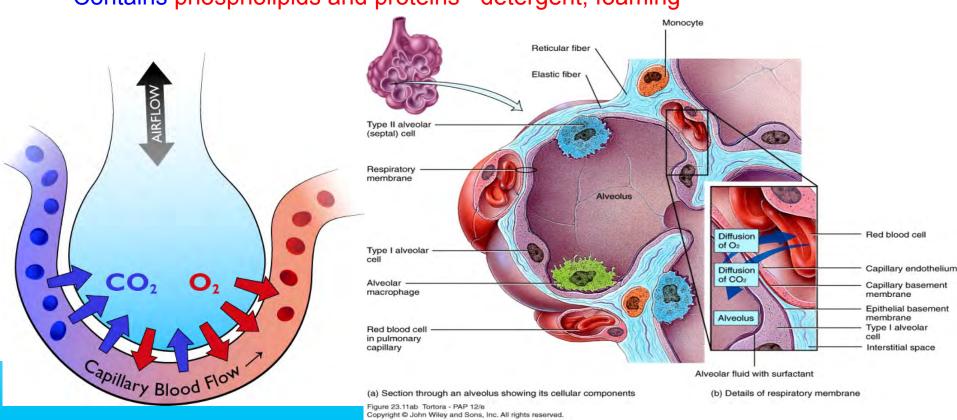
Type I cells gas exchange

Type II cells surfactant secretion

The Lungs - Alveoli

Alveolar Epithelium

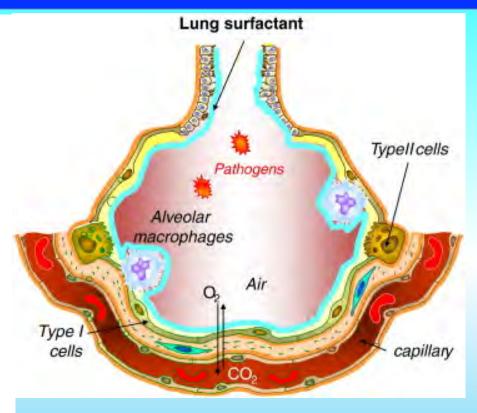
- Consists of <u>simple squamous epithelium</u> = one layer and <u>thin</u> = gas exchange
- pneumocytes type I = gas exchange
- · Patrolled by alveolar macrophages, also called dust cells
- pneumocytes type II that produce surfactant. Surfactants = an oily secretion =
 Contains phospholipids and proteins =detergent, foaming



* Lung - surfactant

Surfactants = <u>Decrease the Work</u> <u>of breathing</u>

- Fluid is under tension = like thin membrane being stretched. Why do we need some fluid? Gases have to dissolve before they diffuse
- Surface tension is directed toward the center of the alveoli and this creates pressure →
 Surfactans decrease the surface tension = increases compliance → easier to increase the volume of the lungs = less work is used.

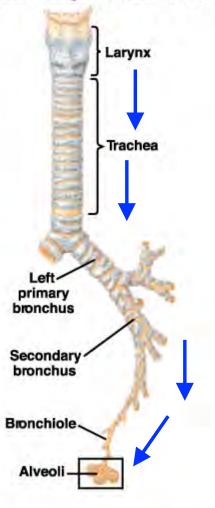


From: Role of lipid ordered/disordered phase coexistence in pulmonary surfactant function
Cristina Casals and Olga Cañadas.
Biochimica et Biophysica Acta (BBA) – Biomembranes;
Volume 1818, Issue 11, November 2012, Pages 2550–2562

Compliance = measure of how easy it is to inflate lungs

Mammalian lungs

Branching of airways
The trachea branches in to two bronchi, one to each lung. Each bronchus branches 22 more times, finally terminating in a cluster of alveoli.

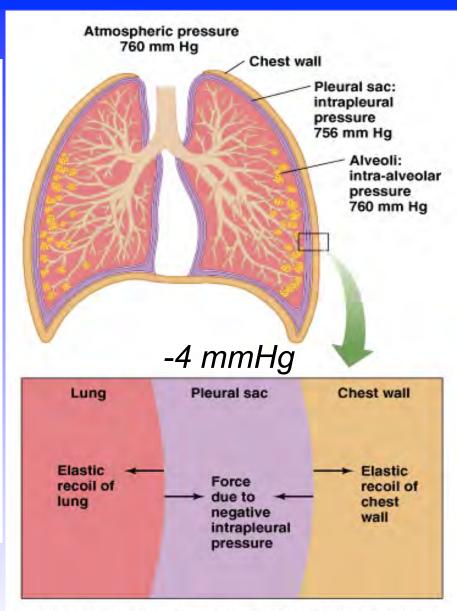


Airways:

Larynx
Trachea
Bronchii
Bronchioles
Alveoli

Ventilation and Pressures

- Atmospheric pressure
 of the air outside the body (1 atm). Has to
 be higher than inside the lungs to get air
 in
- Intraalveolar pressure
 inside the alveoli of the lungs (< atm
 during inhalation). Has to be less than
 atmospheric pressur for air to move into
 lungs/alveoli
- Intrapleural pressure
 within the pleural cavity (always negative
 (-4mmHg).



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**Flow and airway resistance

- *Flow = ΔP/R , ΔP = pressure gradients; R = resistance to flow
- *If resistance increases, a greater ΔP is needed to maintain the same flow
- *Airway resistance is inversely proportional to airway radius to the 4th power (1/r⁴).* What does this mean in terms of radius? Small changes in radius lead to big changes in flow
- *Bronchoconstriction reduction in airway radius. *Histamine* causes brochoconstriction think allergic reaction and antihistamine
- <u>*Bronchodilation</u> increase in radius = sympathetic nervous system= A and NA= sympathomimetic = *Beta2 adrenoreceptors*

Resistance (R) is directly proportional to the length (L) of the "tube" and the viscosity (η), and inversely proportional to the radius to the fourth power (r^4).

$$R = \frac{\eta * L}{r^4}$$

Mammals - **Ventilation

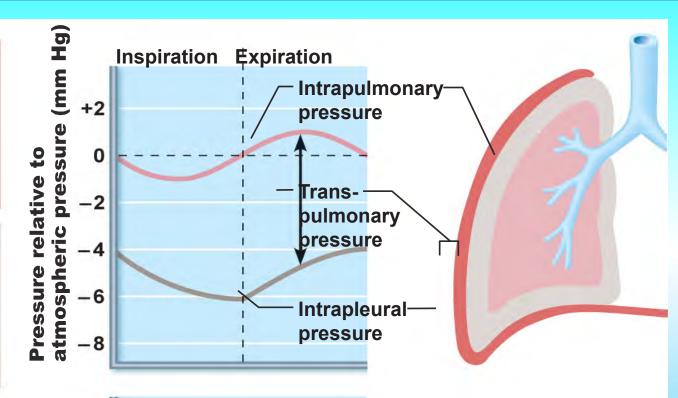
- *Tidal ventilation= measure of tidal volume.
- *Steps. To know
 - Inhalation
 - motor neuron innervation from inspiratory center in medulla oblongata
 - Contraction of the external intercostals and the diaphragm
 - Ribs move outwards and the diaphragm moves down
 - Volume of thorax increases and
 - Air is pulled in
 - Exhalation
 - Inhibition of the inspiratory neurons by the expiratory center => electrical signal to inspiratory muscles stops
 - Inspiratory muscles relax
 - (Ribs and) diaphragm and lungs return to their original positions
 - Volume of the thorax decreases
 - Air is pushed out due to elastic recoil the alveoli of the lungs

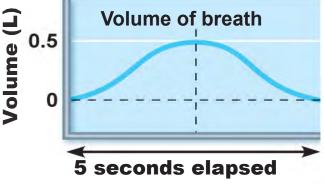
Air moves into and out of the lungs along pressure gradients that are the result of volume changes

Intrapulmonary
pressure. Pressure
inside lung decreases as
lung volume increases
during inspiration;
pressure increases
during expiration.

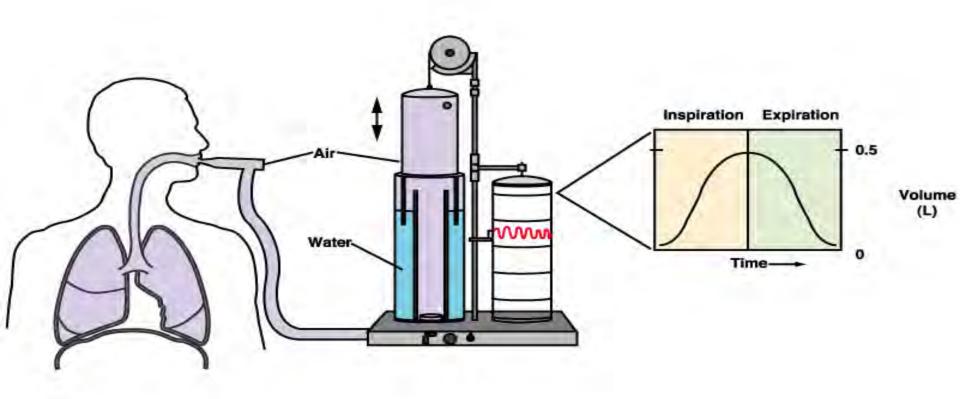
Intrapleural pressure.
Pleural cavity pressure
becomes more negative
as chest wall expands
during inspiration.
Returns to initial value
as chest wall recoils.

Volume of breath.
During each breath, the pressure gradients move 0.5 liter of air into and out of the lungs.





Spirometry



Method for measuring pulmonary function

*Lung pathologies

Pneumonia = acute infection or inflammation of the alveoli = Causes fluid to leak into alveoli and will compromise respiration

Emphysema = destruction of the walls of the alveoli = due to <u>loss of elastic fibers</u> (smoking, pollution, dust) = creates less surface area for gas exchange

Pulmonary edema = <u>fluid accumulation</u> in interstitial spaces and alveoli = could be due to high capillary pressures or increased fluid loss of capillaries

SIDS = sudden infant death syndrome = more common in infants of drug abuse, smokers, premature babies, etc.

Chronic bronchitis = excessive secretion of **bronchial mucous** = leading cause is smoking = cilia are compromised

Air breathers:

Summarize respiratory strategies Structures involved ie muscles. Types ie unidirectional, tidal

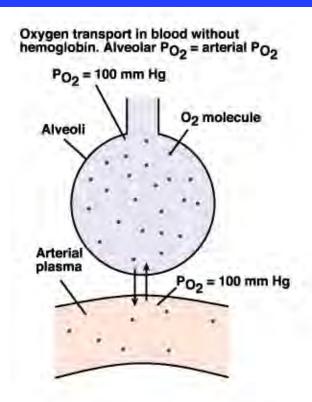
You have learned how water/air enters the respiratory structure

Next step: Gas exchange

Oxygen Transport

- Solubility of oxygen in <u>aqueous fluids is low</u>
- But Respiratory pigments help to increase the amount of O₂ in blood
- By binding oxygen to <u>carriers</u>, PO₂ in the blood remains low and results in improved oxygen extraction
- Contain metal ions
- Gives them a strong colour (e.g. hemoglobin red)
- Oxygen binds reversibly to the metal ion
- Bind to the pigment at the lungs
- Releases from the pigment at the tissues

Oxygen carrying capacity of blood



O₂ content of plasma = 3 mL O₂/L blood
O₂ content of red
blood cells = 0

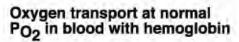
Total O₂ carrying 3 mL O₂/L blood
capacity

- Because of the low solubility of oxygen in aqueous solutions, only a small amount of oxygen can dissolve in blood
- PO₂ is equal in plasma and lungs, but oxygen content of plasma is much lower

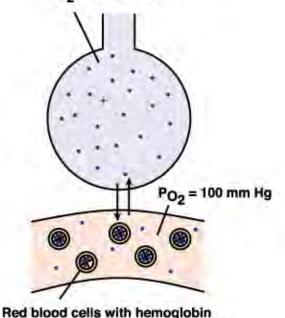
Amount of oxygen that can dissolve in plasma is limited at physiological PO₂

Henry's Law: $[O_2] = PO_2 * S_{O_2}$

Oxygen carrying capacity of blood



PO2 = 100 mm Hg



O₂ content of plasma = 3 mL O₂/L blood

are carrying 98% of their maximum

O2 content of red blood cells

load of oxygen

= 197 mL O2/L blood

Total O₂ carrying capacity

200 mL O₂/L blood

- If an oxygen carrier such as hemoglobin is present, some of the <u>oxygen will bind to the</u> <u>pigment</u>
- This oxygen no longer contributes to PO₂
- PO₂ is the same as in the previous example, but oxygen content is higher. The oxygen carrying capacity is much higher with metalloproteins.
- PO2 = partial pressure of O2

Henry's Law: $[O_2] = PO_2 * S_{O_2}$

Respiratory Pigments

Three major types

- Hemoglobins
 - Vertebrates, nematodes, some annelids, crustaceans, and insects
 - Consist of a protein globin bound to a heme molecule containing iron
 - Usually located <u>within blood cells</u>
 - Appears red when oxygenated
 - Myoglobin is found in muscles = holds on very tightly to O2
- Hemocyanins
 - Arthropods and molluscs
 - Contain copper
 - Usually dissolved in the hemolymph
 - Appears <u>blue when oxygenated</u>
- Hemerythrins
 - Sipunculids, priapulids, some annelids = Worms
 - Contains *iron* directly bound to the protein
 - Usually found inside coelomic cells
 - Appears violet-pink when oxygenated

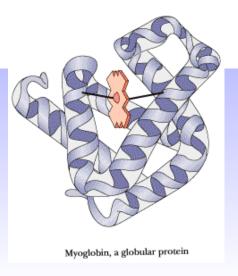
Hemoglobin and Myoglobin

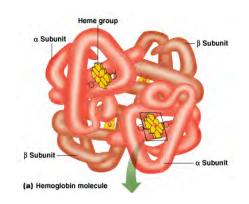
<u>Hemoglobin = protein = will eb affected by pH, Temperature, Pressure</u>

- Each contains a heme group
- Each heme group can bind 1 molecule of oxygen
- Therefore 1 Hb molecule can bind 4 oxygen molecules

Myoglobin

- •Type of hemoglobin found in vertebrate muscle
- Each Mb molecule binds one molecule of oxygen
- "stores" O2 in skeletal muscle
- Holds onto the O2 strongly





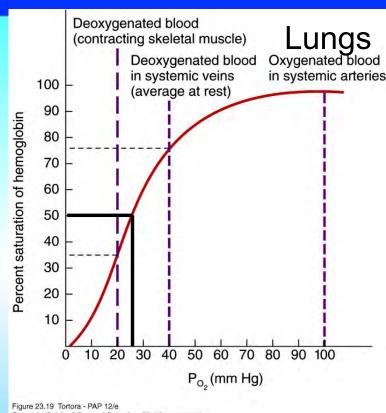
Gas Transport - O2

Carrying capacity = the maximum amount of oxygen that can be carried in blood

Total O_2 in blood = dissolved $O_2 + O_2$ bound to respiratory pigment

Oxygen-Hemoglobin Saturation Curve:

- shows the relationship between partial pressure of oxygen in the plasma and the percentage of oxygenated respiratory pigment in a volume of blood
- <u>P₅₀</u> oxygen partial pressure at which the pigment is 50% saturated. Used as an indicator of affinity. In the figure the P50 is about 28 mmHg. This means that for this protein (Hb), at 28 mmHg 50% are saturated with O2



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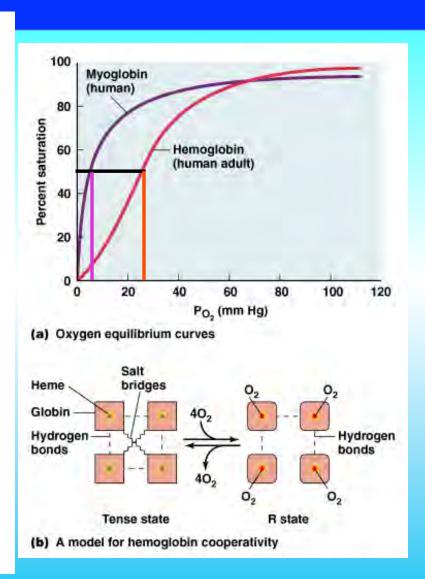
Gas Transport - O2

Myoglobin

- has a <u>lower P₅₀</u> than Hemoglobin
- Myoglobin has higher oxygen affinity
- PO2 for Myoglobin has to be very low for it to let go of O2 ©. Helps while exercising

Also note the difference in the shapes of the curve

- The hemoglobin curve is sigmoidal
- Myoglobin curve is hyperbolic
- Hb changes shape each time a molecule of O₂ is bound
- Each O₂ bound makes next O₂ binding easier
- Allows Hb to bind O₂ when O₂ levels are low
- Myoglobin only binds one O₂



Gas Transport - O2

The Bohr Effect = the effect of pH on hemoglobin-saturation curve = the effect of CO2/pH on the behaviour of hemoglobin. Don't forget proteins are affected by their environement

- Caused by CO₂
 - CO₂ diffuses into RBC
 - An enzyme, called carbonic anhydrase, catalyzes reaction with H₂O
 - Produces carbonic acid (H₂CO₃) which dissociates into hydrogen ion (H⁺) and bicarbonate ion (HCO₃⁻)
 - An increase in CO2 can cause a decrease in pH
- When pH drops more oxygen is released → Curve shifts to right
- When pH rises less oxygen is released → Curve shifts to left

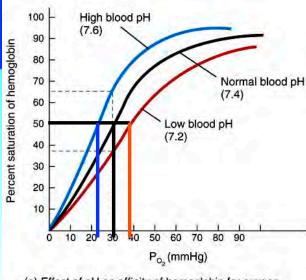
Bohr effect

pН

- As pH decreases, affinity of Hb for O₂
 decreases = enhances unloading === Shifts
 curve to right
- Hemoglobin is a protein that will change shape in response to its environment. At low pH, will change shape and let go sooner of O2. At high pH, will change shape and let go later of O2
- The more active you are, the more CO2 you will produce, also the H+ will produced. The more active, the more O2 you need. SO the the Hb will sense change in activity and the Hb will let go sooner of O2 = right shift = lower affinity ☺

P_{CO2}

- Also shifts <u>curve to right</u>
- As P_{CO2} rises, Hb unloads oxygen more easily
- Low blood pH can result from high P_{CO2}



(a) Effect of pH on affinity of hemoglobin for oxygen

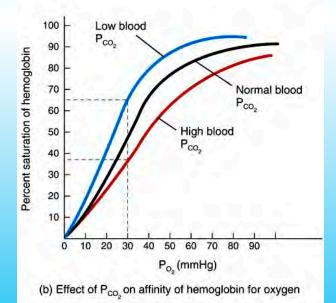
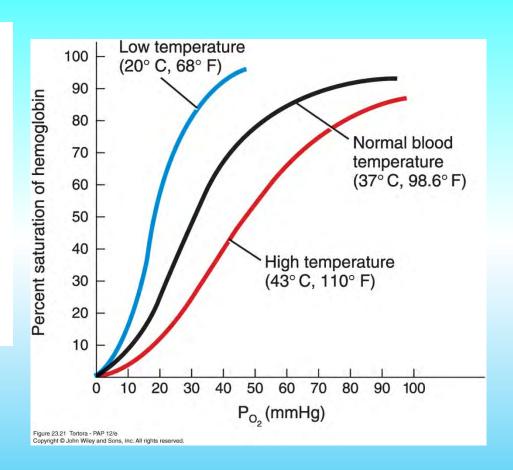


Figure 23.20 Tortora - PAP 12/e Copyright © John Wiley and Sons, Inc. All rights reserved.

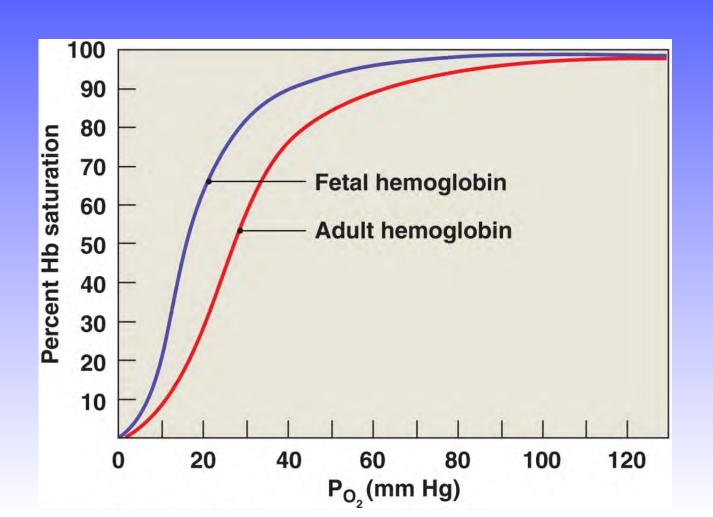
Temperature and Bohr

- As temperature increases, more oxygen is released from Hb. Why? When Temperature increases, more activity, and so let go sooner of O2
- During hypothermia, more oxygen remains bound. Why? Allows to bring O2 to tissues that are farther from heart because blood flow has decreased = at cooler temperatures, holding onto O2 helps to get it to little toe



Structure of the pigment

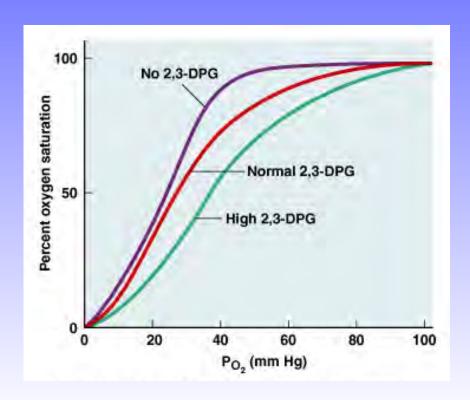
Fetal hemoglobin has a lower P₅₀ than maternal hemoglobin. Fetus gets O2 from mom



Conditions That Affect Oxygen Affinity

Organic modulators (e.g., 2,3-DPG, ATP, GTP); DPG = Diphosphoglycerate = byproduct of RBC activity = always have some

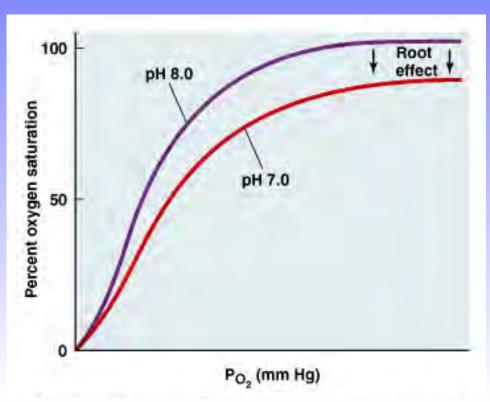
- Increases in these modulators decrease oxygen affinity; right shift
 - Helps oxygen unloading at tissues
 - High DPG = just means you are running amok = let go of O2 sooner

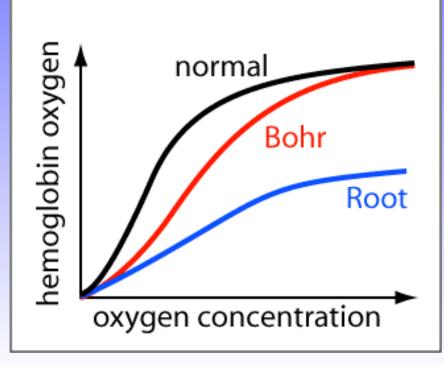


Root effect - something fishy

Root effect – a Bohr effect with a reduction in the oxygen carrying capacity

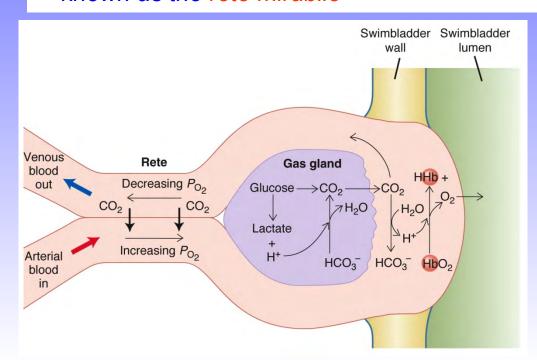
- Seen in hemoglobin of many <u>teleost fishes</u>
- Helps in oxygen delivery to eye and swim bladder = affects buoyancy
- Root effect is a right shift with a reduction in carrying capacity = O2 will diffuse into the swim bladder = increase buoyancy

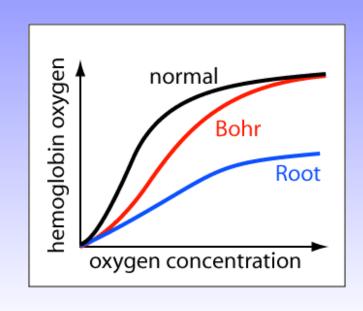




Swim bladder and Oxygen

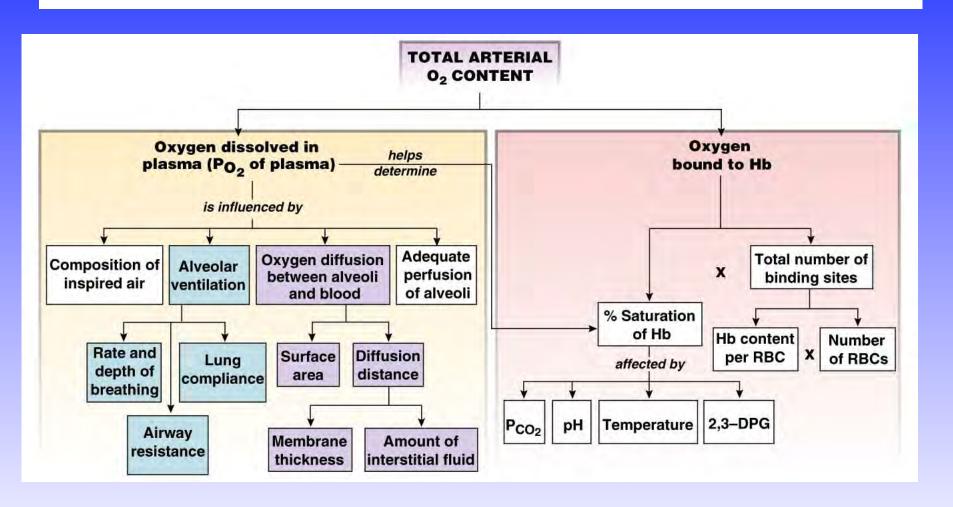
- Many bony fish have a swimbladder that helps to maintain neutral buoyancy
- Gas-filled sac
- Fill with gas to increase buoyancy
- Remove gas to reduce buoyancy
- In most species this gas is <u>oxygen</u>
- Gas gland excretes lactic acid
- Acidity causes hemoglobin of the blood to lose its oxygen
- Oxygen diffuses into the bladder while flowing through a complex structure known as the rete mirabile





Summary of oxygen transport

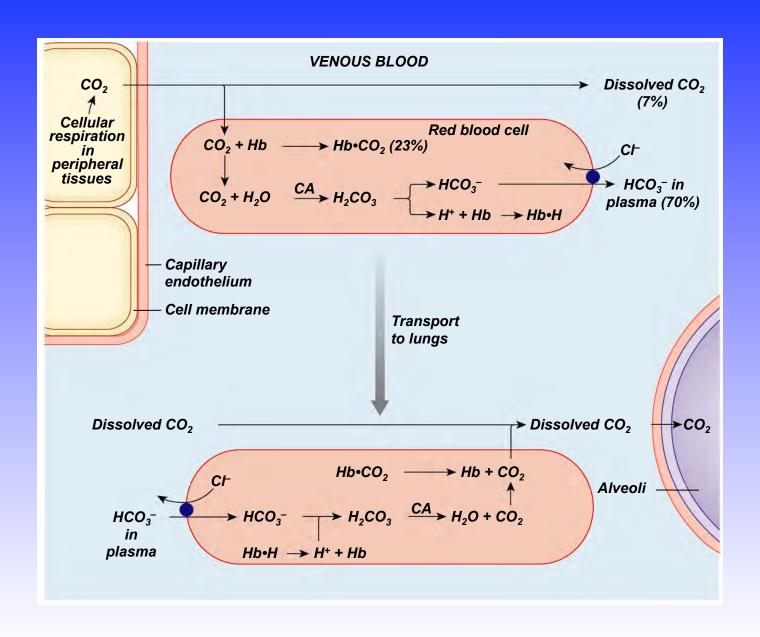
Factors contributing to the total oxygen content of arterial blood



Carbon Dioxide Transport

- Carbon dioxide is more soluble in body fluids than oxygen
- Little CO₂ is transported in the plasma
- Some CO₂ binds to proteins = *carbaminohemoglobin*
- Most CO₂ is transported as bicarbonate
 - CO₂ + H₂O ⇔ H₂CO₃ (carbonic acid) ⇔ HCO₃⁻ (bicarbonate) + H⁺
- Carbonic anhydrase catalyzes the formation of HCO₃⁻

Carbon Dioxide Transport



CO2 transport

At tissues:

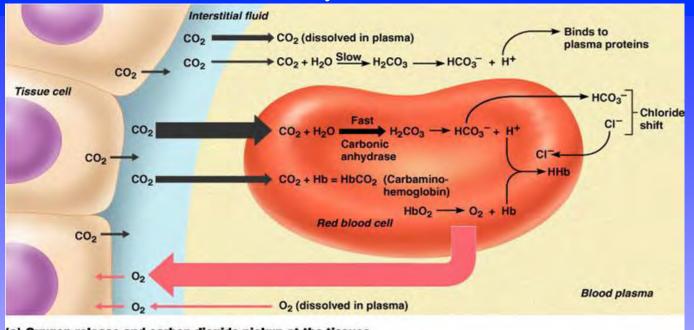
- CO2 is produced during cellular respiration = Krebs cycle CO2 diffuses out into plasma
- 1. Some will stay in plasma dissolved
- 2.Most will enter RBC:
 - 1. Some will bind directly to Hb, after Hb has let go of O2: Hb-0
 - 2. Most of it will combine with H2O in presence of carbonic and
 - 1. CO2 + H2O ↔ H+ + HCO3-
 - 1. H+ will bind to Hb after Hb let go of O2: Hb-H+
 - 2. HCO3- is removed to the plasma for exchange of Cl-= chloride shift. Most CO2 carried back to lungs as
 - HCO3-

CO2 transport

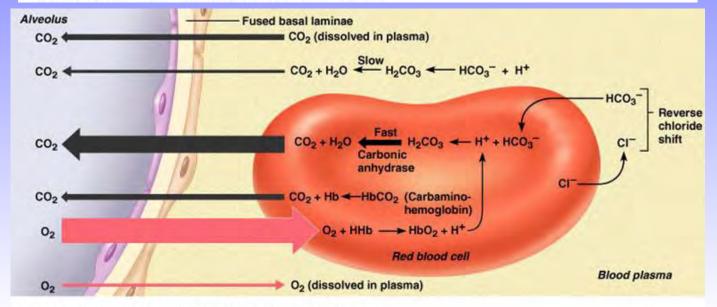
At lungs:

- 1.The dissolved CO2 will diffuse out = exhale
- 2.Within the RBC the Hb will let go of the CO2 and then can bind O2. The CO2 will diffuse out = exhale
- 3. HCO3- is brought back into RBC via reverse chloride shift = Cl- and HCO3- in. Hb-H+ = will let go of H+ and so Hb can bind O2
 Then: HCO3- + H+ ↔ CO2 + H2O

Carbon Dioxide Transport



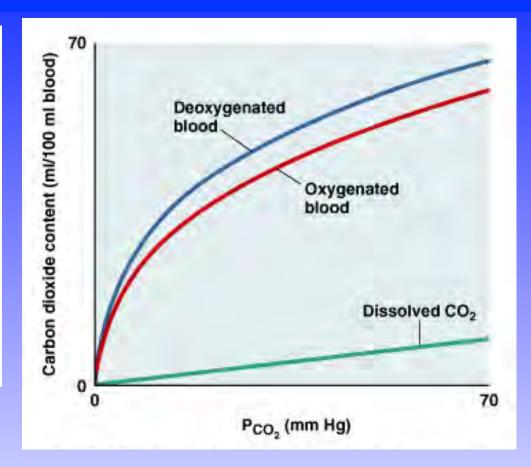
(a) Oxygen release and carbon dioxide pickup at the tissues



(b) Oxygen pickup and carbon dioxide release in the lungs

Carbon Dioxide Equilibrium Curve

- Shows the relationship between P_{CO2} and the total CO₂ content of the blood
- The shape of the curve depends on the kinetics of HCO₃⁻ formation
- Deoxygenated blood can carry more CO₂ than oxygenated blood = Haldane effect
 - Removal of oxygen from hemoglobin increases hemoglobin's affinity for carbon dioxide



Regulation of Respiratory Systems

- Respiratory systems are closely regulated
- Respond to changes in external and internal environment
- Must be able to supply sufficient oxygen to meet metabolic demands
- Must be able to remove carbon dioxide to prevent pH disturbance

Vertebrate respiratory and circulatory systems work together to regulate gas delivery by

- Regulating ventilation
- Altering oxygen carrying capacity and affinity
- Altering perfusion

Definitions

Hypoventilation = Abnormally low respiration rate = like holding your breath \rightarrow results in CO₂ buildup in blood (high P_{CO_2}) = **hypercapnia**

Hyperventilation = Abnormally high respiration rate. Not exercise = exercise is good ☺. Panic attack is an example

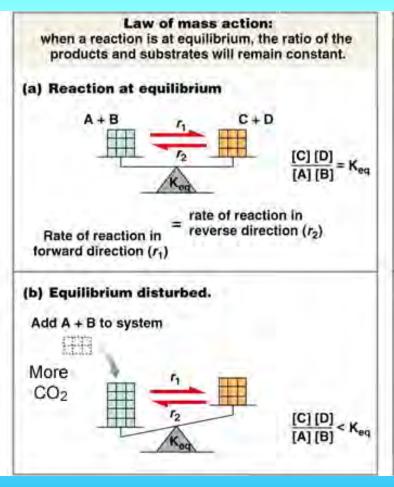
- \rightarrow results in abnormally low P_{CO_2} = hypocapnia
- Acidosis: ↓ plasma pH = due to increase in H+. Increase in CO2 leads to increase in H+
- Alkalosis:
 † plasma pH = due to decrease in H+. A decrease in CO2 leads
 to a decrease in H+

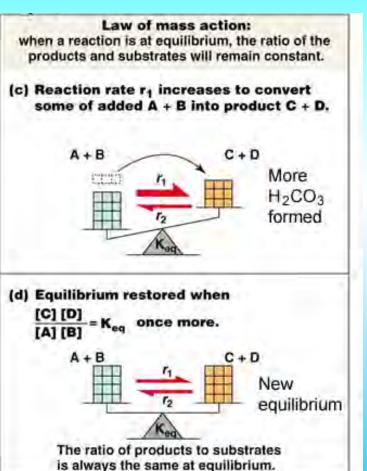
CO2 + H2O ↔ H+ + HCO3-

The effects of CO2 on acid-base homeostasis...

Law of mass action

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





- Metabolic acidosis = too much acid; pH is decreased = due to too many H+.
 Your lungs are working fine. When you exercise H+ increase due to ATP hydrolysis = will hyperventilate = blow off CO2
 - What causes metabolic acidosis?
 Proton accumulation, ketoacids (from breakdown of fats or amino acids), kidney disease = pee out H+ but kidneys are not peeing out H+

$$CO_2 + H_2O \leftarrow H_2CO_3 \leftarrow HCO_3^- + \mathbf{1}$$

- How can we fix it?
 - Hyperventilate ie CO₂ can be blown off at the lungs
 - Renal (kidneys) compensation Secretion of H⁺ and reabsorption of bicarbonate. Only if kidneys are functioning properly

- 2. Respiratory acidosis = lungs cannot remove all of the carbon dioxide the body produces; ph is decreased due to increase in H+. Now lungs are messed and so cant use lungs to fix problems
 - What causes respiratory acidosis?

Hypoventilation which could be due to a wet lung, some obstruction in respiratory system. Anything that prevents CO2 exhalation such as fluid

$$^{\bullet}$$
 CO₂ + H₂O \Rightarrow H₂CO₃ \Rightarrow HCO₃ + H⁺

- How can we fix it?
 - Renal (kidneys) compensation only Secretion of H⁺ and reabsorption of bicarbonate.
 - Cant use lungs to fix it because the lungs are mucked up

3. Metabolic Alkalosis = Loss of protons; pH is elevated above normal

What causes metabolic alkalosis?

Loss of protons due to vomiting, etc. Puke = puke up HCl-. Diarrhea = loss of ions, including H+

$$CO_2 + H_2O \Rightarrow H_2CO_3 \Rightarrow HCO_3^- + \checkmark H^+$$

- How do we fix it?
- Must make more H+ as we are losing H+
 - Hypoventilate keep CO2 ie PCO₂ increases. By holding your breath, you will: Keep CO2 in and CO2 + H2O ↔ HCO3- + H+ and now we have more H+
 - Renal (kidneys) compensation bicarbonate excreted and H⁺ reabsorbed

- 4. Respiratory Alkalosis = removing too much CO_2 across lungs.
 - What is the cause? Due to hyperventilation = panic attack. Cant use lungs to fix it cause lungs are messed up

$$\P$$
CO₂ + H_2 O \Leftrightarrow H_2 CO₃ \Leftrightarrow HCO_3 + H

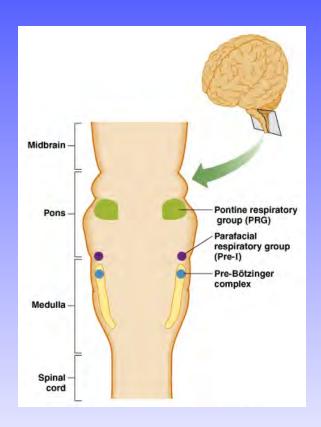
How do we fix it?
 Renal (kidneys) compensation only - bicarbonate excreted and H⁺ reabsorbed

Breathing into a bag will allow you to rebreathe CO2 and thus not lose it

Regulation of Ventilation

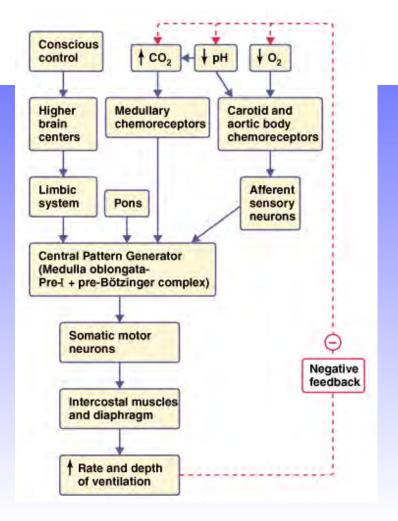
- Ventilation is an automatic process
- Continues even when we are unconscious
- Central pattern generator in medulla

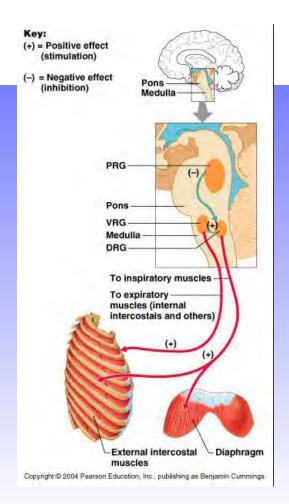
- Rhythmic firing of *central pattern generators* within the medulla initiate ventilatory movements
- Pre-Botzinger complex is an important respiratory rhythm generator in mammals



Regulation of Ventilation

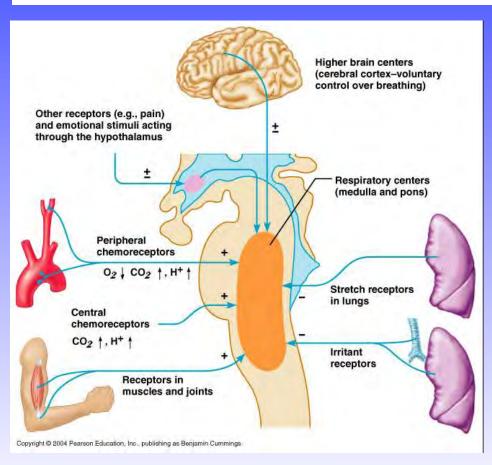
- Chemosensory input helps modulate the output of the central pattern generators
- Chemoreceptors detect changes in CO₂, H⁺, and O₂
- Oxygen is the primary regulator in water-breathers while CO₂ is the primary regulator in air-breathers

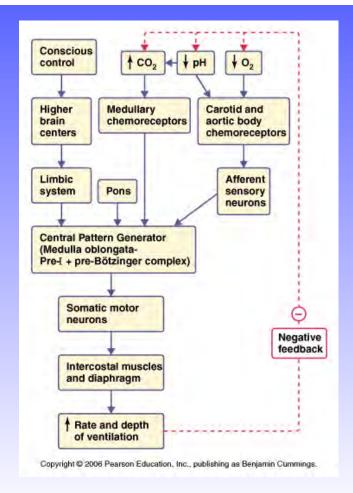




Regulation of ventilation

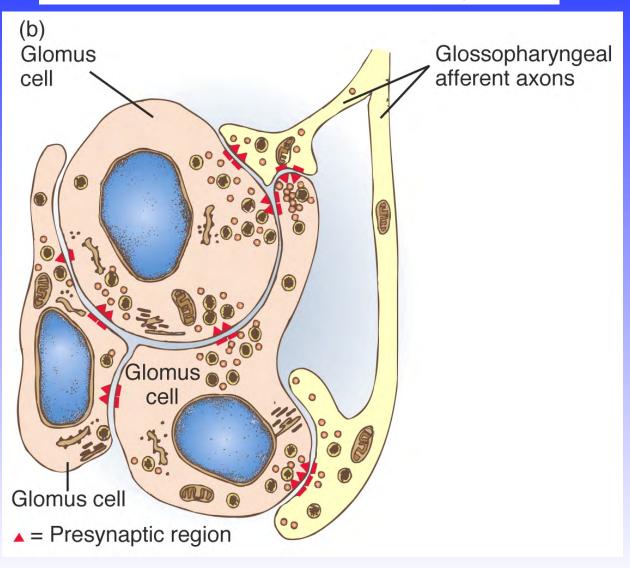
- Ascending sensory input comes from chemosensory neurons in carotid and aortic bodies, in vasculature of lungs, and chemoreceptors in the medulla
- Modulates the <u>rate and depth of breathing</u>
- Negative feedback loop to maintain blood PO₂ and PCO₂ within a narrow range



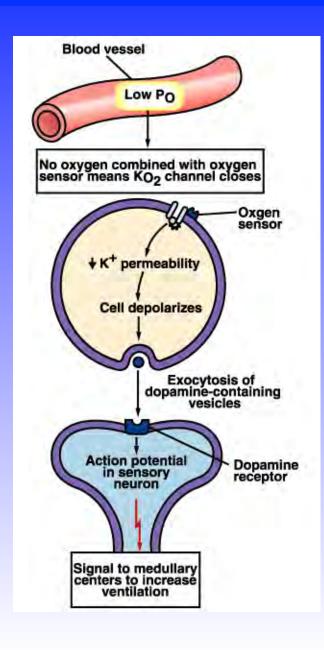


Carotid and aortic chemoreceptors

Glomus cells = chemosensory cells



Low PO2 and mechanism in carotid body

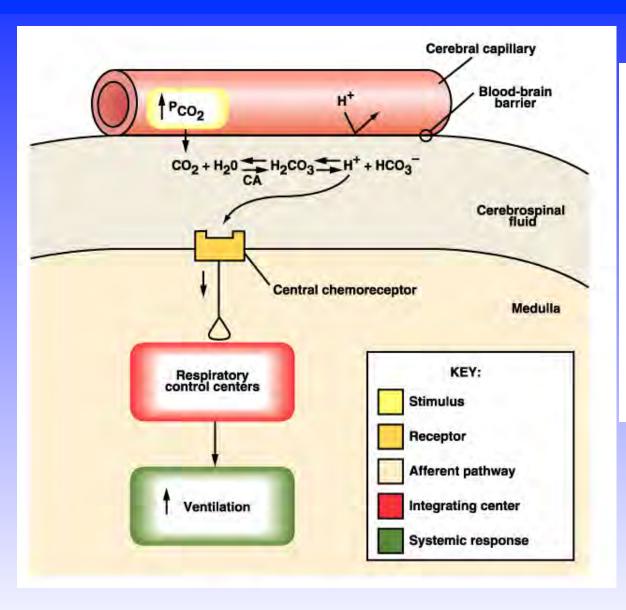


Glomus cells contain oxygen-gated K⁺ channels

- 1. Oxygen sensor detects low PO₂
- 2. Closes K⁺ channels = keep K+ inside cells
- 3. Cell depolarizes = makes cells more positive
- Causes release of dopamine = electrical signal will result in release of chemical messenger = dopamine
- 5. Stimulates sensory neuron
- 6. Send signal to CNS = start breathing more

High altitude = get less O2 per breath. Still 21% O2 but PO2 lower

High PCO2 and mechanisms in central chemoreceptors



- Most important controllers in mammals
- Sensitive to changes in PCO₂ and pH
- CO₂ crosses blood/brain barrier
- Carbonic anhydrase converts CO₂ to HCO₃⁻ and H⁺
- H⁺ stimulates receptor
- Stimulates ventilation = exhale CO2

Respiratory Performance and smoking



Oxygen at Altitude - a special case

- Pressure declines as altitude increases
- Oxygen delivery to body dependent on partial pressure of oxygen
- Concentration of oxygen doesn't change but you get less oxygen per breath
- At 12,000ft you get ~40% less oxygen per breath

Moderate Altitude – initial symptoms

- Headache
- Nausea
- Fatigue
- Loss of appetite
- Difficulty sleeping
- Frequent Urination

High Altitude – symptoms

- Confusion
- Reduced mental acuity
- Loss of coordination
- Cerebral edema
- Pulmonary edema
- Death

Oxygen at Altitude - a special case

Sleeping patterns

- 1. Low inspired oxygen (PaO₂ low)
- 2. CO₂ production normal
- 3. Arterial/Carotid chemoreceptors sense low O₂
- 4. Increase rate and depth of breathing to bring in O2 even at rest
- 5. = Hyperventilate = blow off more CO2 than produced
- 6. Leads to Hypocapnia = low CO2 in blood due to Respiratory Alkalosis. Also pee more to keep H+ due to kidneys being more active = pee more
- 7. Intermittent breathing (especially at night)
- 8. Causes difficulty sleeping

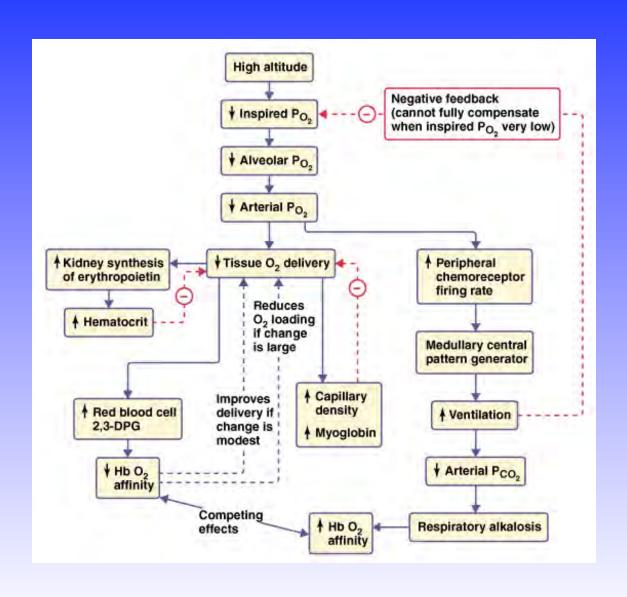
Lungs = later

- 1. Inspired air low PO₂
- 2. Sensors in lung detect low oxygen
- 3. Causes vasoconstriction in lung
- 4. Reduces blood flow
- 5. Increases blood pressure
- 6. Can lead to pulmonary edema

Solution = later

- Increased EPO = RBC increase
- Increased hematocrit
- Peripheral vasodilation

Oxygen at Altitude - a special case



How do diving mammals deal with the lack of oxygen ie cant breathe under water

Dive response

Dive Response

- Apnea = breath hold
- Bradycardia = decrease of Heart rate from resting/baseline = conserve O2.
- Peripheral Vasoconstriction = reduce blood flow to non-essential tissues = helps to conserve O2
- Cooling of tissues to conserve energy

Oxygen Stores

- Lungs but many collapse lungs
- Blood = higher carrying capacities of O2
- Muscle = higher Myoglobin

Respiratory mechanics

High flow rates minimize the time for exhalation/inhalation cycle = rapid breaths allow animals to spend most of their travel time below the surface where drag is less

Hb and Mb

- Marine mammals have exceptionally high [Hb] values compared to terrestrial mammals.
- [Mb] in diving mammals are 10 to 30 times that found in terrestrial mammals.

O2 stores in different species

<u>Species</u>	mL O2 kg-1	Lung %	Blood %	Muscle %
Human	20	24	57	15
Odontocetes	35	22	30	48
Otariids	40	13	54	33
Phocids	60	7	65	28
Sea Otter	55	55	29	16
Manatee	21	33	60	7

Some questions

The common passageway shared by the respiratory and digestive systems is the
The sites of gas exchange within the lungs are
Most of the oxygen transported by the blood is
In humans the most important chemical regulator of respiration is
Define hypercapnia.
Air moves out of the lungs when the pressure inside the lungs is
Carbon dioxide is more soluble in water than oxygen. To get the same amount of oxygen to dissolve in
plasma as carbon dioxide, you would have to
Define affinity. How is Hemoglobin's affinity for O2 affected?
Hyperventilation will CO2 exhaled and thus pH. Use increase and/or decrease.

Some questions

What is the significance (why do they matter) of Henry's law, Boyle's law a process of respiration? Explain why these laws matter in relation to the resp	
process of respiration? Explain why these laws matter in relation to the resp	catory system
	alury system.

Last slide for Test 1