Introduction to the Respiratory System

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

Graciously provided by Dr. M. Gardner and modified by Dr. C. Gerin

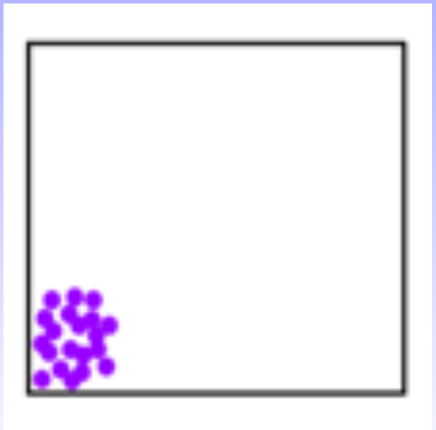
Definitions

- *Respiration* = sequence of events that result in the exchange of oxygen and carbon dioxide between the external environment and the mitochondria. Why do we need O2 and why do we have to exhale CO2?

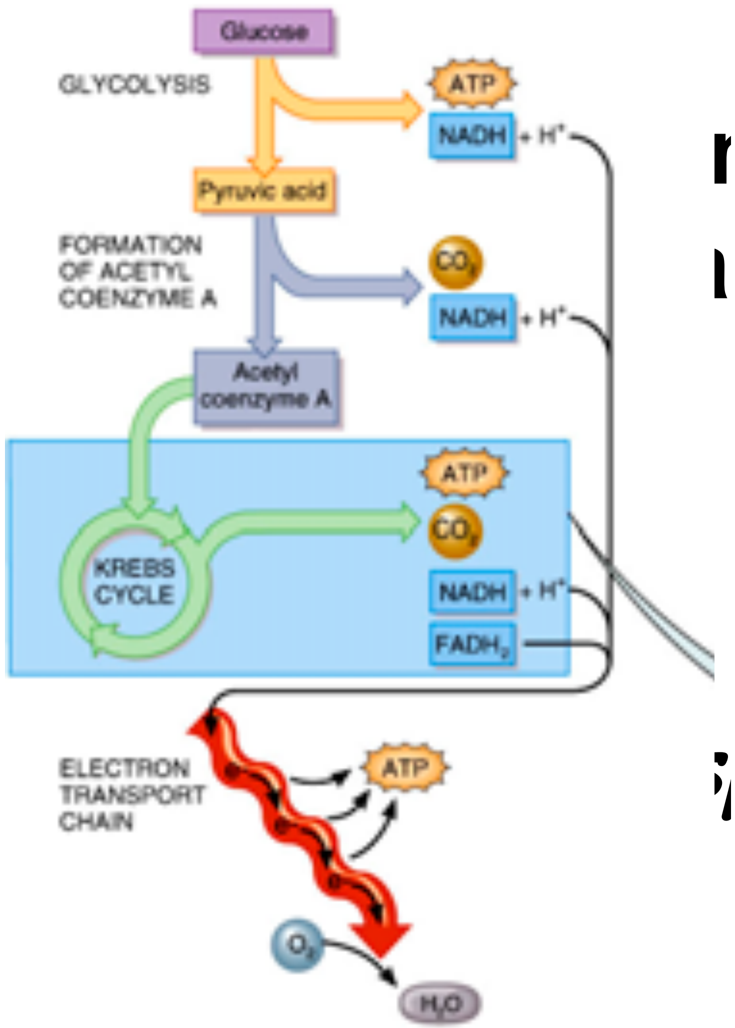
- *External respiration* = gas exchange at the respiratory surface

- *Internal respiration* = gas exchange at the tissues

- *Mitochondrial respiration* = production of **ATP** via oxidation of carbohydrates, amino acids, or fatty acids. **Oxygen is consumed and carbon dioxide is produced**



Diffusion is the movement of molecules from a high concentration to a low concentration.
Gradients can be pressure (gases), electrochemical (ions) or just chemical (glucose)



(a) Cellular respiration

Figure 25.06 Tortora - PAP 12/e

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- Mitochondria consume O_2 to produce **ATP**
- Produce CO_2 in the process. Where?
- Organisms must have mechanisms to obtain O_2 from the environment and get rid of CO_2 . Why get rid of CO2?

- CO2 + H2O ↔ H+ + HCO3-
- An increase in H+, decreases pH

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

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Respiratory systems - diffusion rate

The Fick equation

$$J = -DA\,dC/dx$$

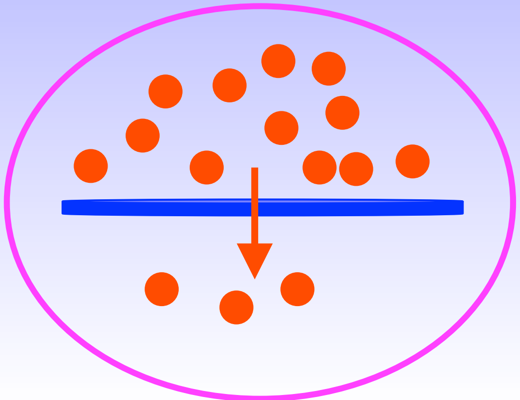
J = rate of diffusion (moles/sec)
D = diffusion coefficient = how easily a substance can diffuse
A = area of the membrane
dC = concentration gradient
dx = diffusion distance

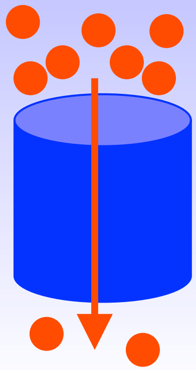
For gases, we usually use partial pressure rather than concentration
Gases will move down pressure gradients. Remember this. From high
Lower pressure

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 <u>thin = short diffusion distance, with a large surface area</u>***



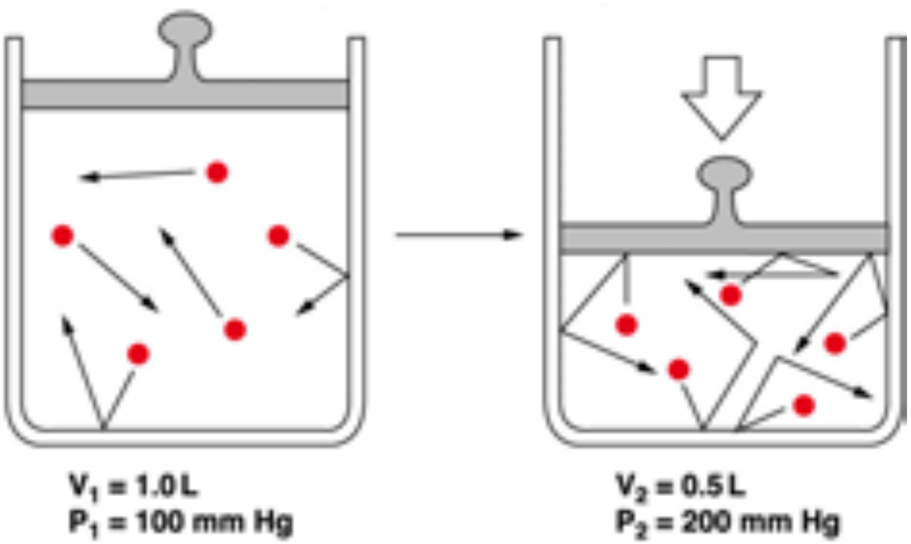


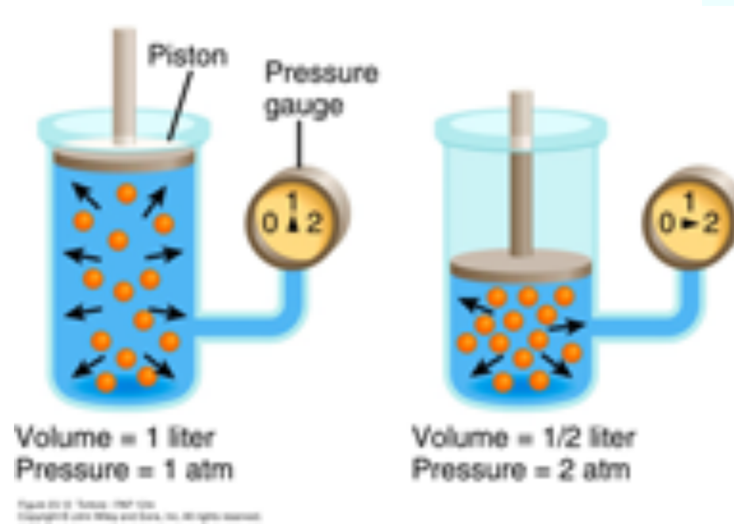
Pulmonary Ventilation

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 changes in volume to cause changes in pressure!

Gases Dissolve in liquids

Henry's Law

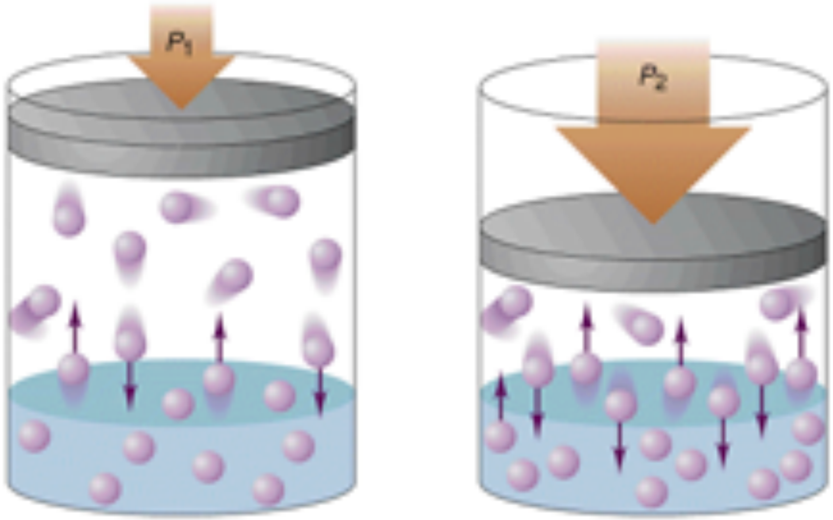
- Gases **have to dissolve before they diffuse**
- When a gas under pressure comes in contact with liquid, the gas dissolves in liquid until equilibrium is reached
- At a given temperature the amount of a gas in solution is proportional to partial pressure of that gas
- What is solubility?

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

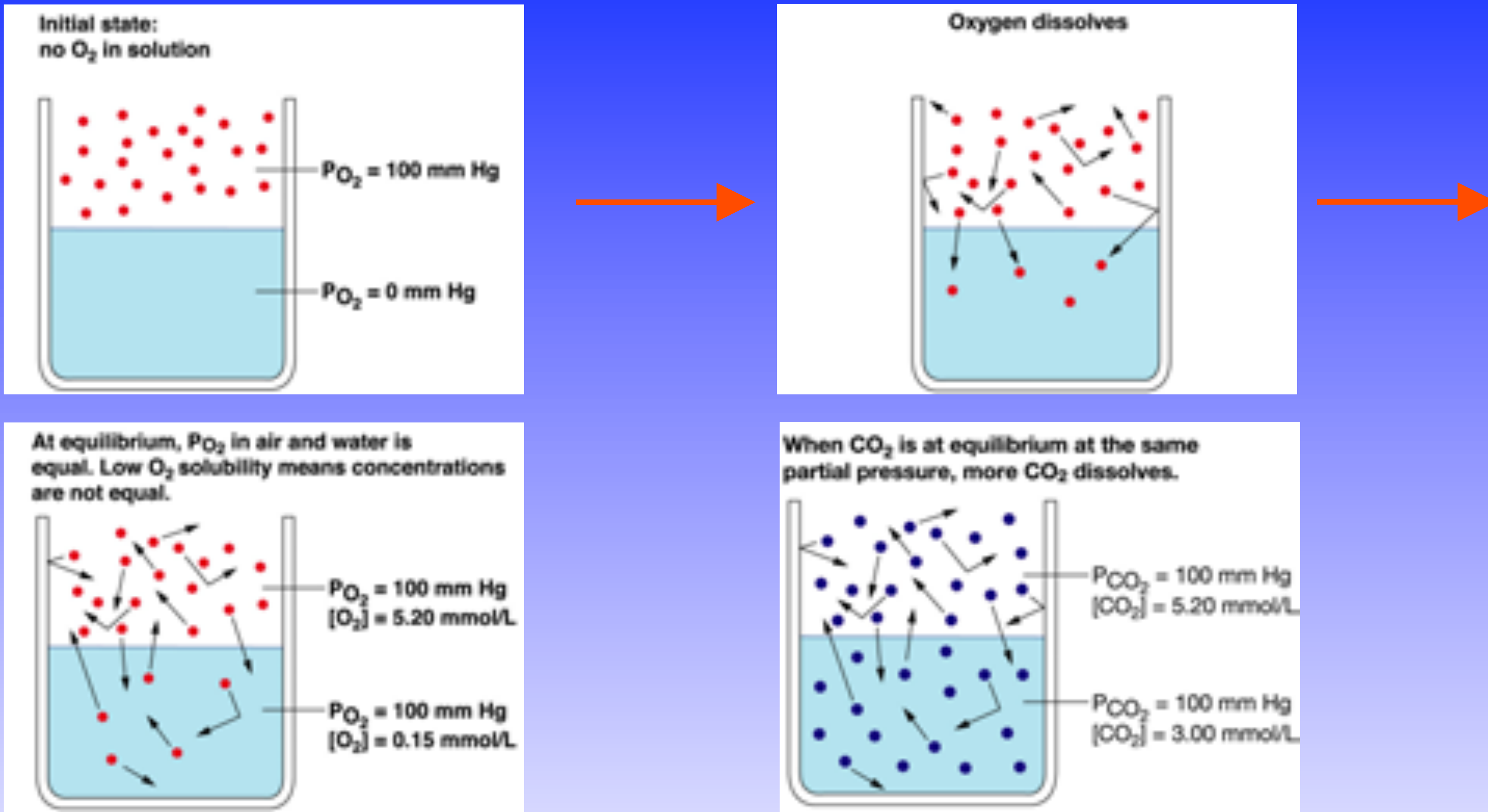
★G is the concentration of the gas in solution

Pgas = Partial pressure of the gas

Sgas = how easily a gas can dissolve in a solution



Gases Dissolve in liquids. Henry's law



CO_2 is much <u>more soluble in water than is O_2</u>. Thus, at the same partial pressure, more CO_2 will 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:

$$\text{Diffusion rate} = \text{solubility}/\sqrt{MW}$$

- O_2 32 atomic mass units
- CO_2 44 amu

- In air "solubilities" are the same (1000 ml/L at 20°C). So oxygen diffuses about 1.2 times faster than CO_2 in air.

- However, CO_2 is about 24 times more soluble in aqueous solutions than O_2. So CO_2 diffuses about 20 times faster than O_2 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_{gas}) = 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

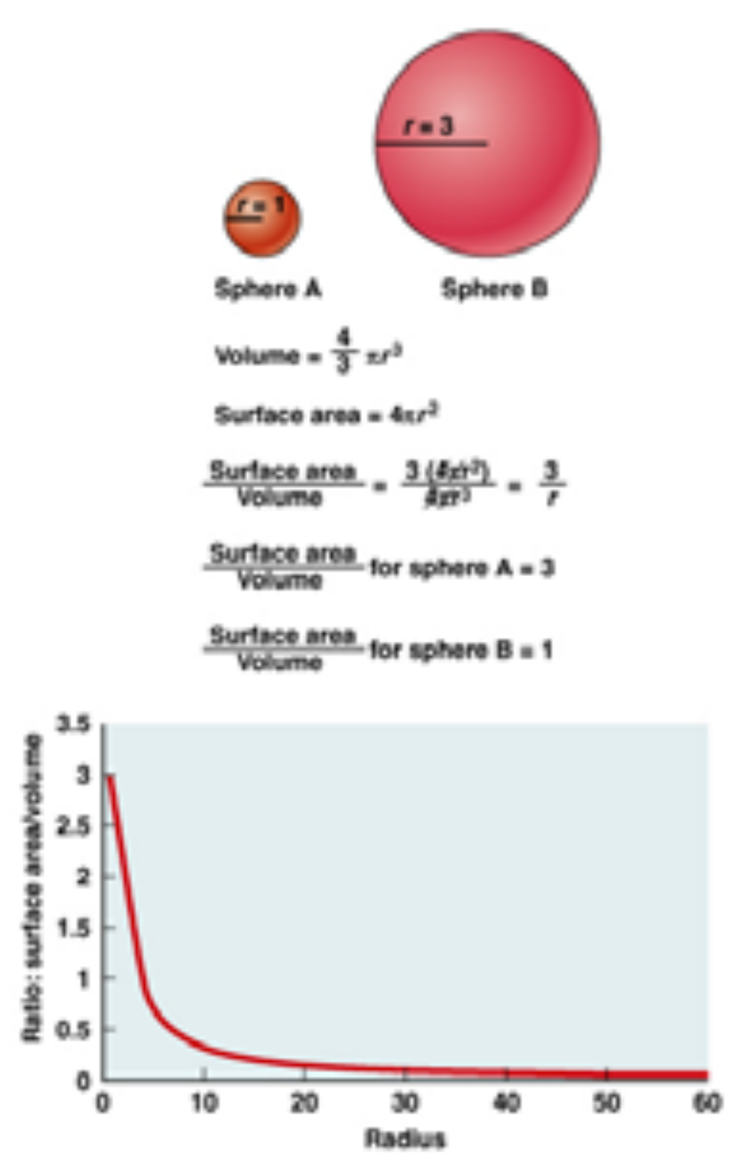
Surface Area to Volume Ratio

- As organisms grow larger, their ratio of surface area to volume **decreases**

- This **limits the area available for diffusion** and **increases the diffusion distance**

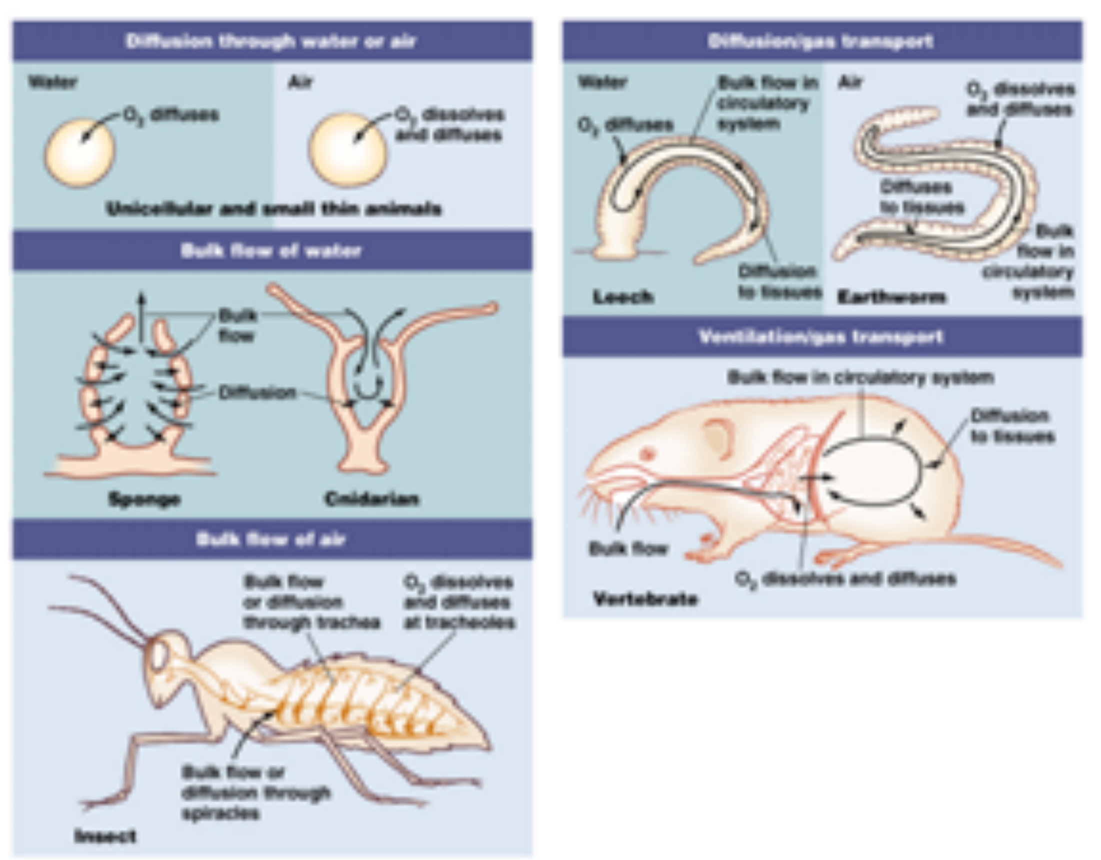
J= -DAdC/dx

That's why we need respiratory systems



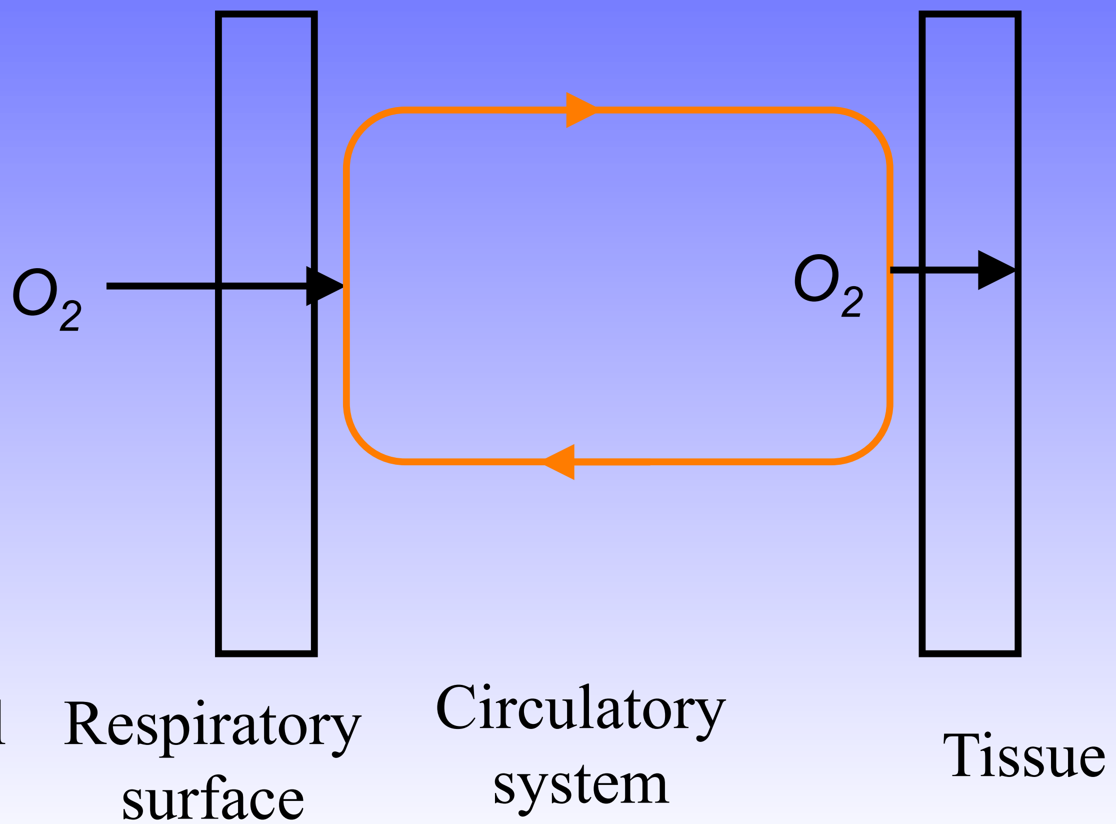
Respiratory strategies of animals

- Unicellular and small multicellular organisms rely on ***diffusion*** for gas exchange
- 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

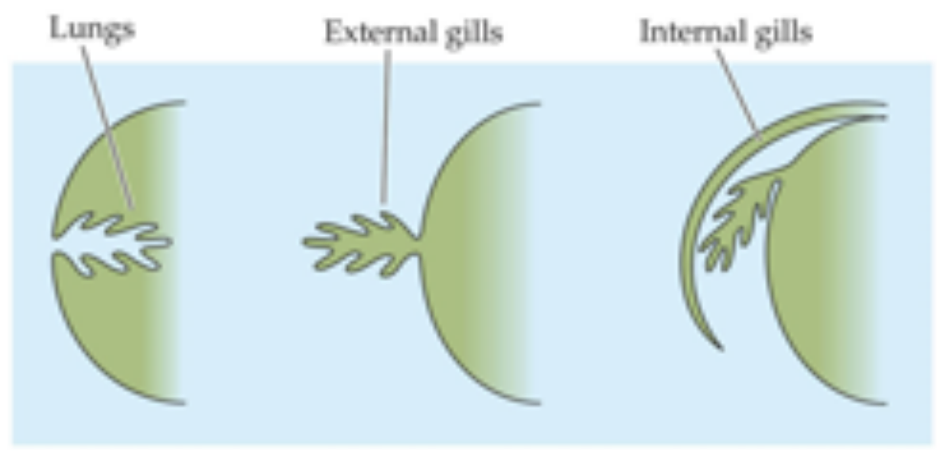
Diffusion of gases across a specialized respiratory surface accompanied by circulatory transport



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 body surface accompanied by **circulatory transport**
  - *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

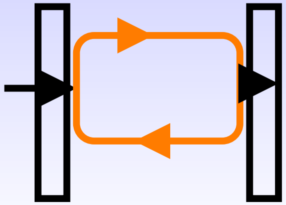
Disadvantages:

- Relatively low surface area
- Conflict between respiration and protection = if skin gets damaged, respiration gets compromised ☹

Salamander

Annelid

Lake Titicaca frog



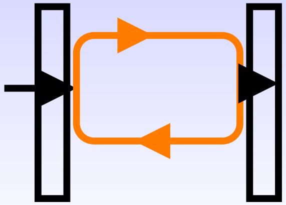
External gills

Gills originate as outpocketings = evaginations

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

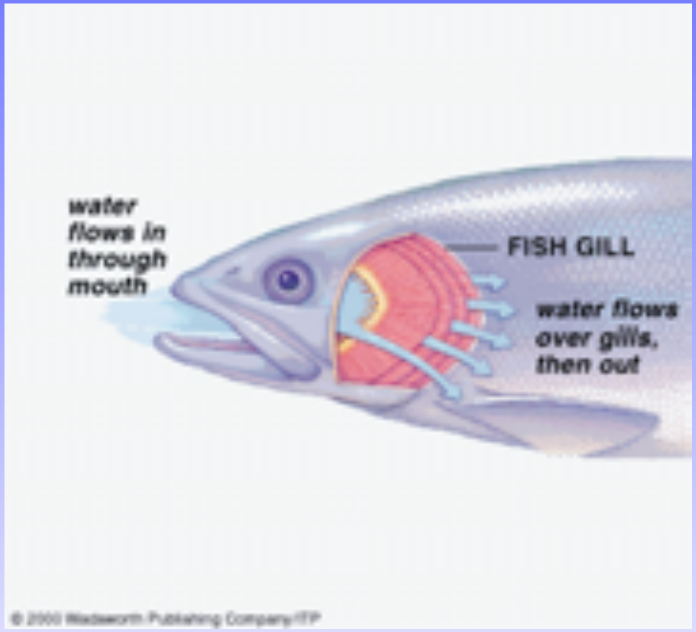
Salamander

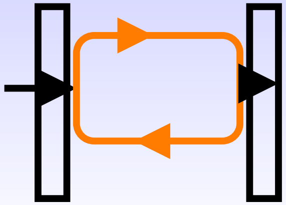
Polychaete



Internal gills

- **Advantages**: High surface area, protected
- **Disadvantages**: not suitable in air = see previous slide, external gills

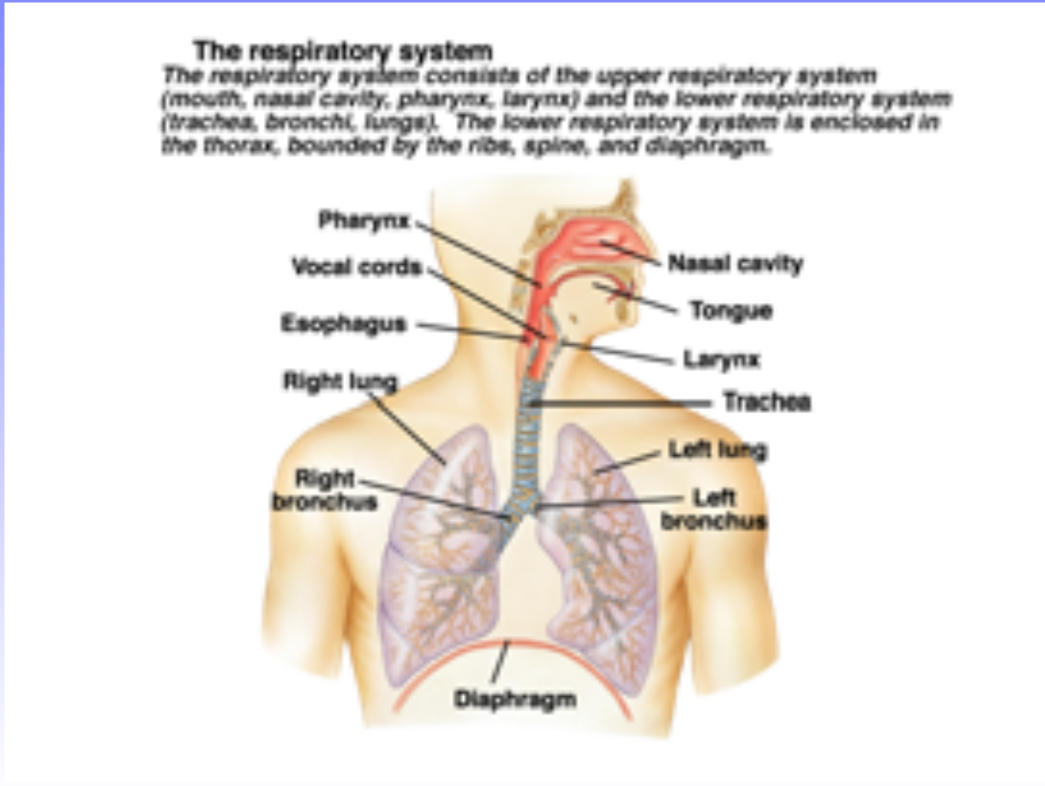




Lungs

Originate as infoldings = invaginations

- **<u>Advantages</u>**: High surface area, protected, suitable for breathing air
- **<u>Disadvantages</u>**: not suitable in water. Why? O2 solubility is very low in fluid and diffusion distance has greatly increased



Ventilation

Ventilation = The active movement of the respiratory medium (air or water) across the respiratory surface. Bulk flow = large quantity of air or water

Flow = $\Delta P/R$ = 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

500 → 100

800 → 400

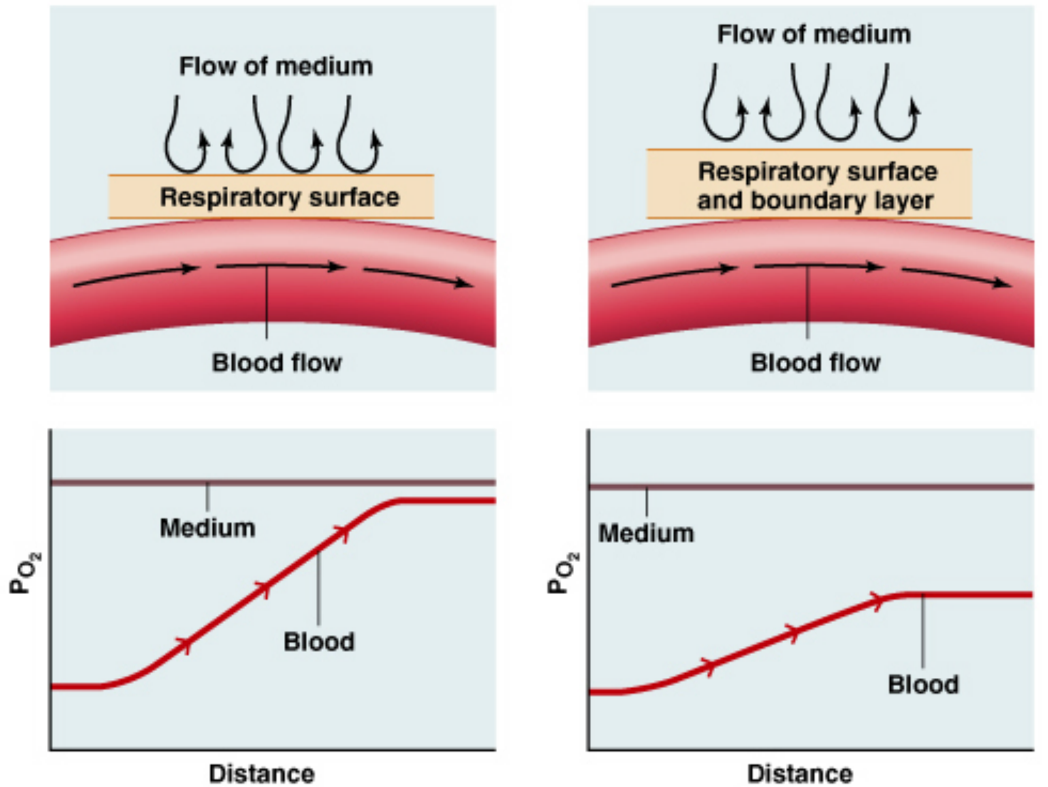
Types of ventilation

- *Nondirectional* - medium flows past 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



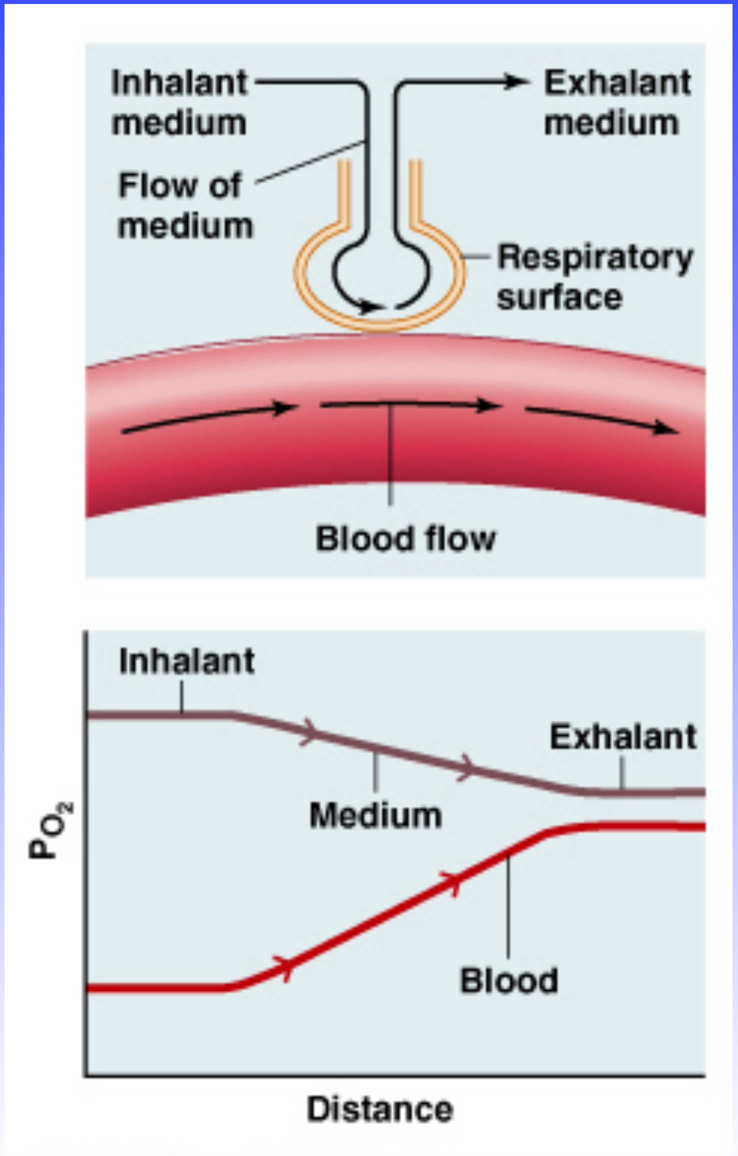
(a) Nondirectional ventilation (fully mixed medium and thin respiratory surface)

(b) Nondirectional ventilation (poorly mixed medium or thick respiratory surface)

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

Tidal ventilation

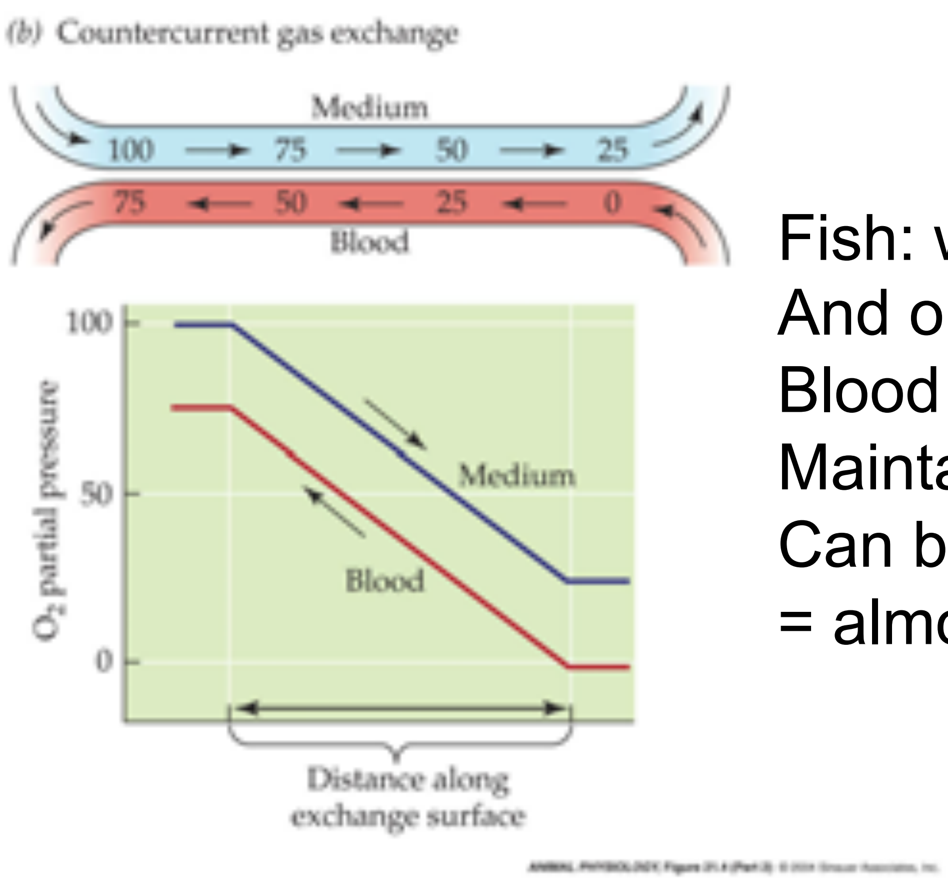
Medium moves in and out the same structure



Lungs

Why less Oxygen at exhalant?

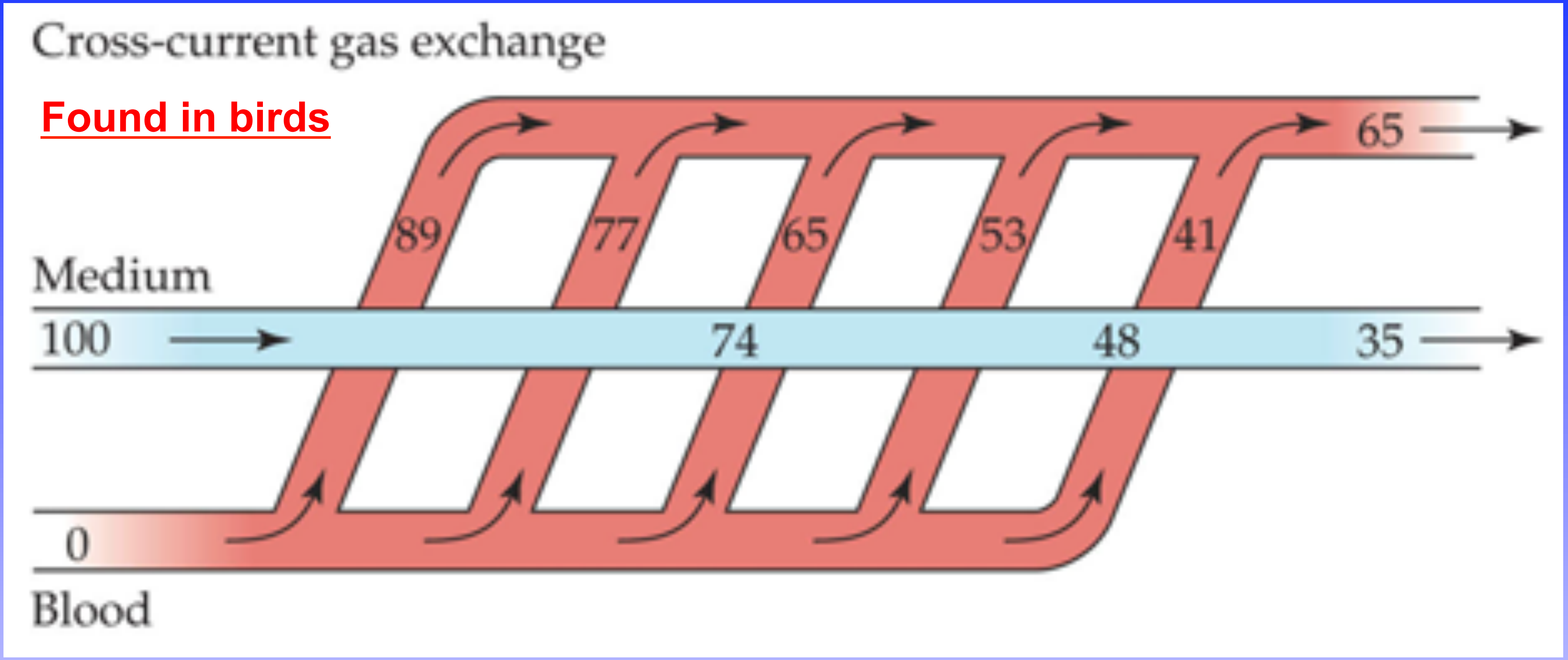
Gas exchange - unidirectional ventilation



Fish: water in at mouth
And out at operculum
Blood flow is countercurrent
Maintain a gradient and so bloo
Can be maximally oxygenated
= almost to saturation

Maintain gradient.
PO_2 of blood approaches that of the inhalant medium

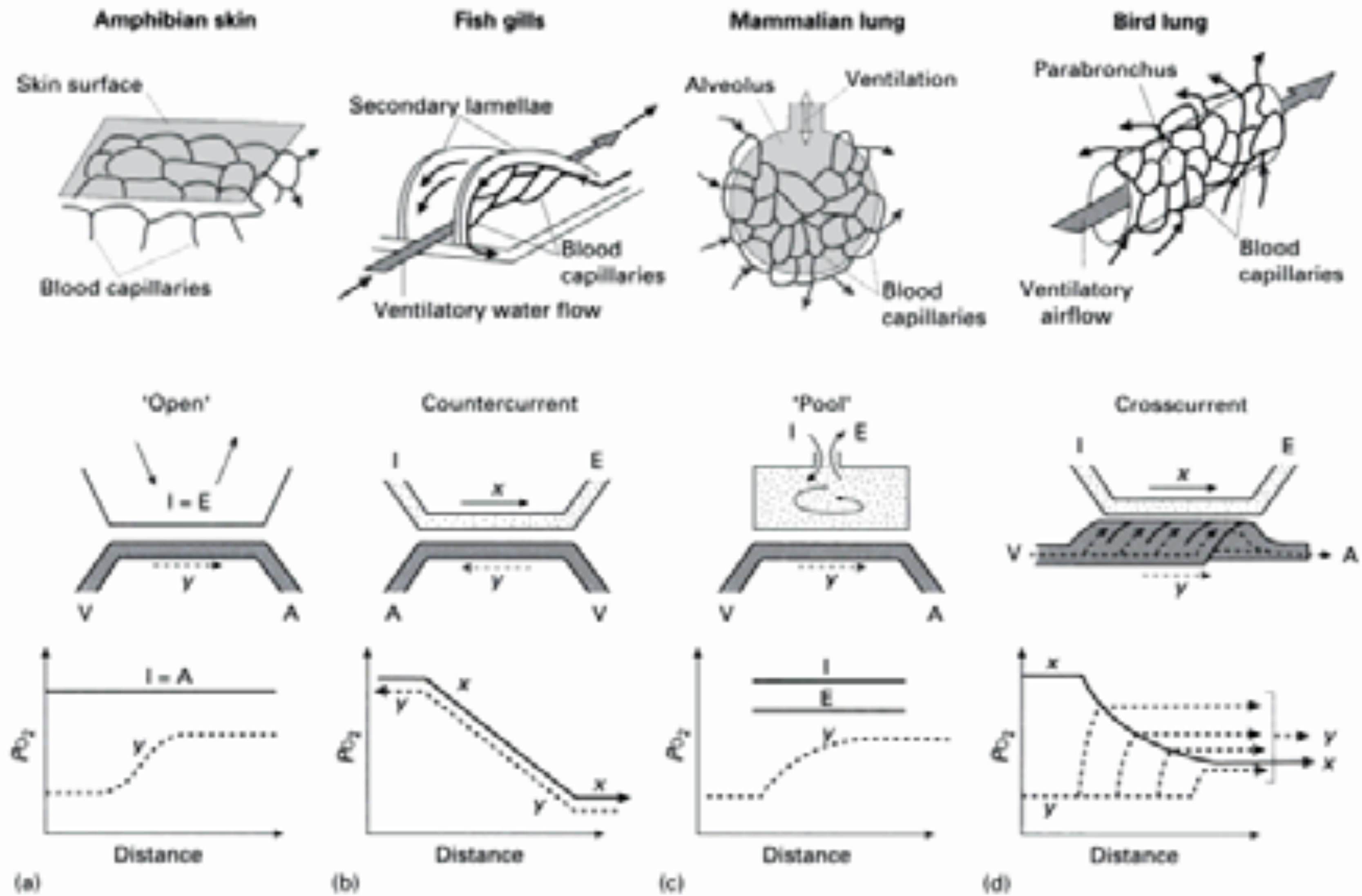
Gas exchange - unidirectional ventilation



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

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

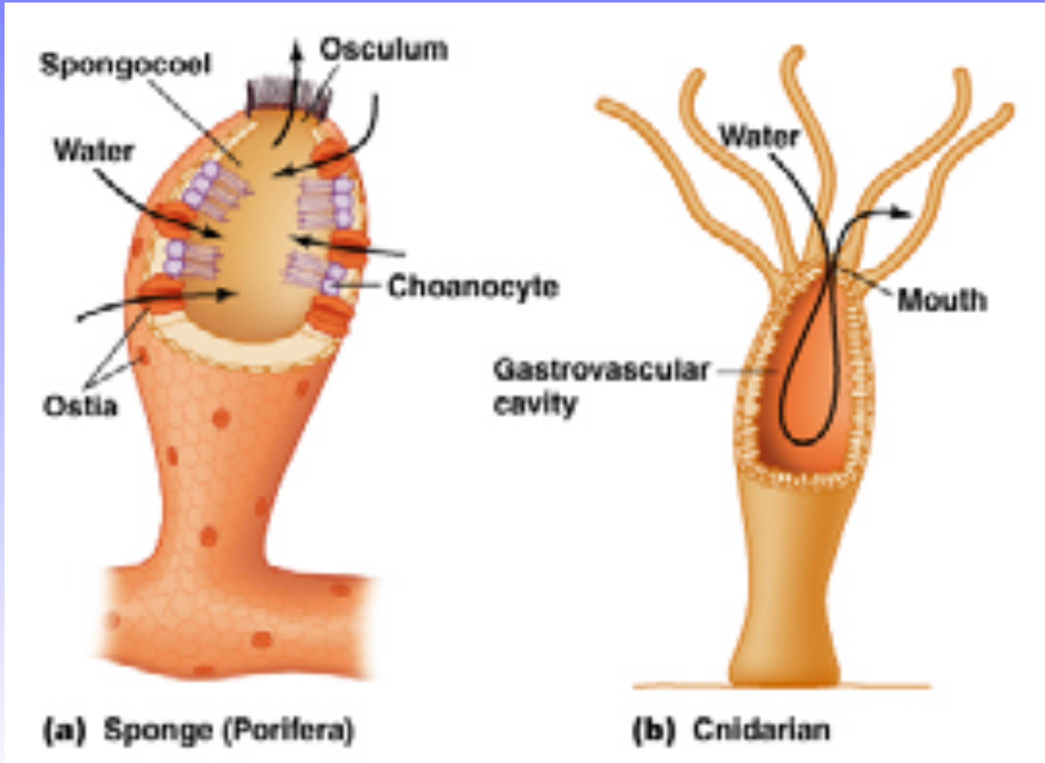
- $[O_{air}]$ greater than $[O_{water}]$. Think Henry's law….
- Water is more dense and viscous than air. Fick's equation….
- Evaporation is only an issue for air breathers

- 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

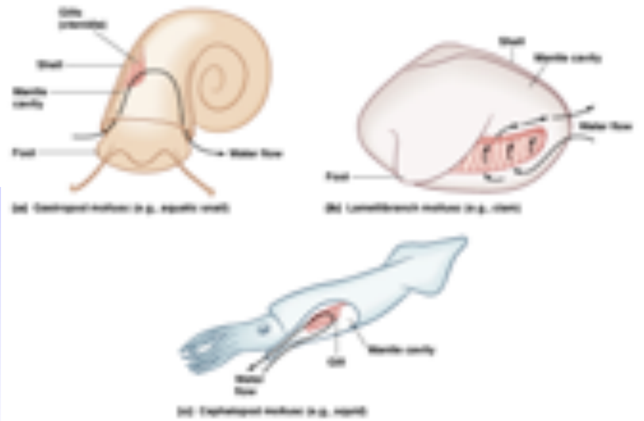
- Circulate the external medium through an internal cavity
- In sponges flagella move water in through *ostia* and out through the *osculum. Flagella in humans = sperm*
- In cnidarians (jellyfish) muscle contractions move water in and out through the mouth



Molluscs - in water

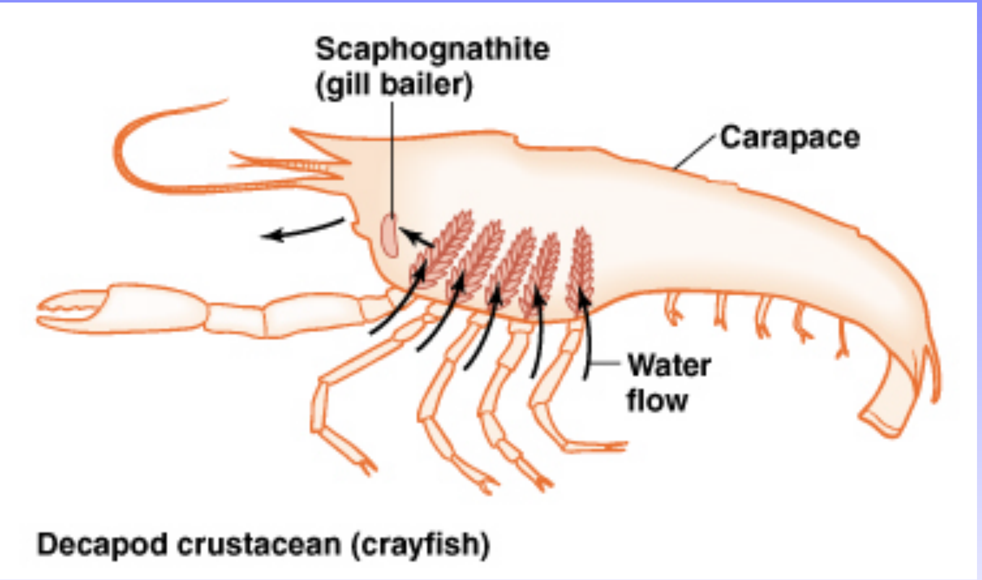
Two strategies for ventilating their gills and mantle cavity

- 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 unidirectionally through the mantle cavity past the gills
  - Blood flow is countercurrent
  - Cephalopods (squid)



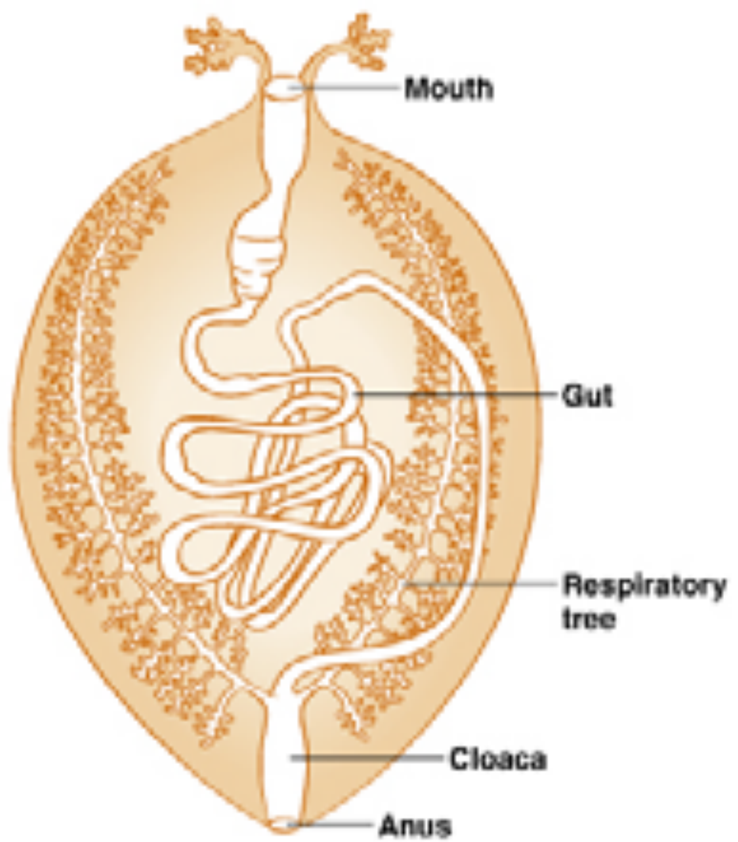
Crustaceans - in water

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



Echinoderms - in water

- Sea cucumbers use muscular contractions of the cloaca and the *respiratory tree* to breathe water tidally though the anus



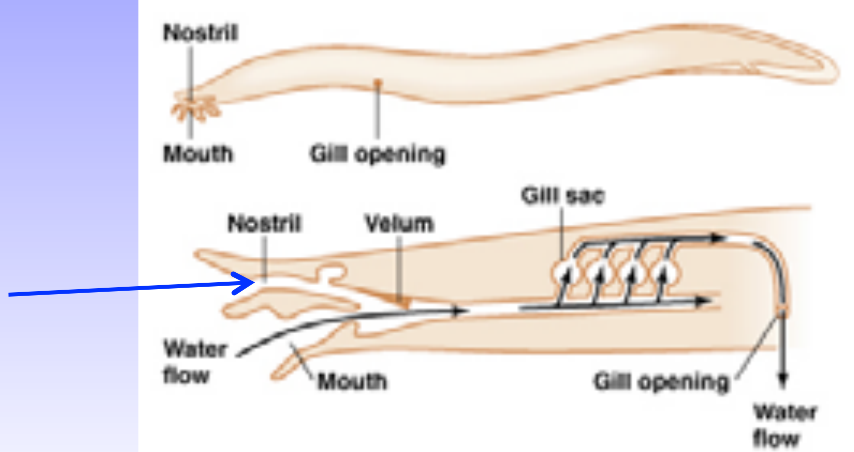
(b) Sea cucumber

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
- Flow is unidirectional
- Blood flow is countercurrent



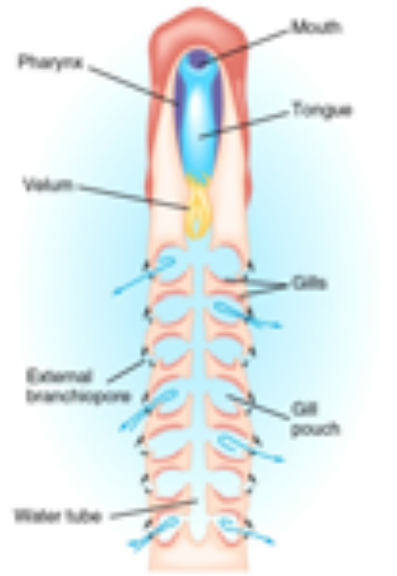
(a) Hagfish (side view and longitudinal section)

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

b Lamprey gill openings (seven pairs)



(b) Lamprey (side view and longitudinal section)

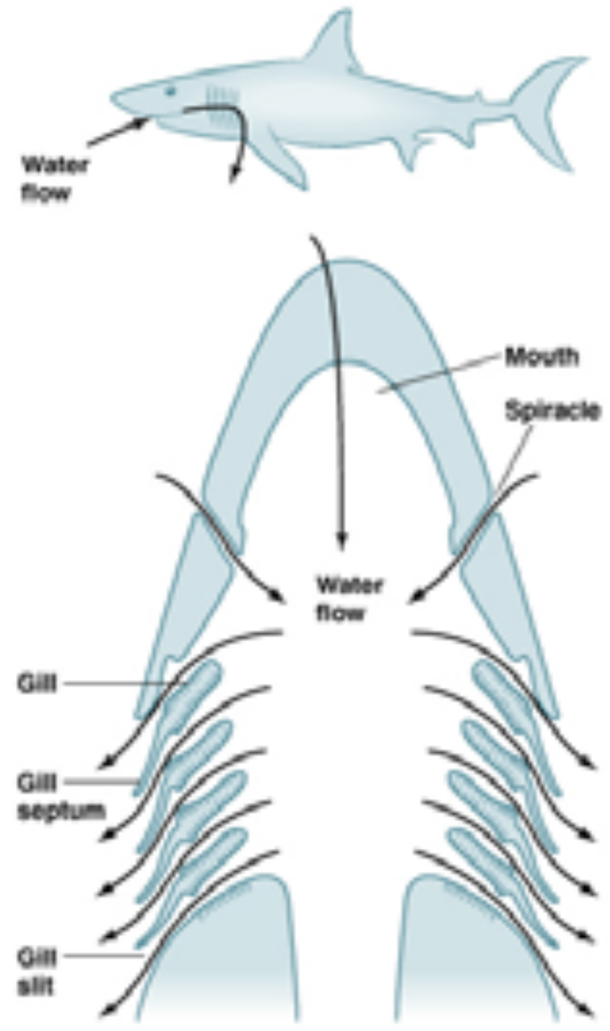
Elasmobranchs – sharks, skates and rays – in water

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

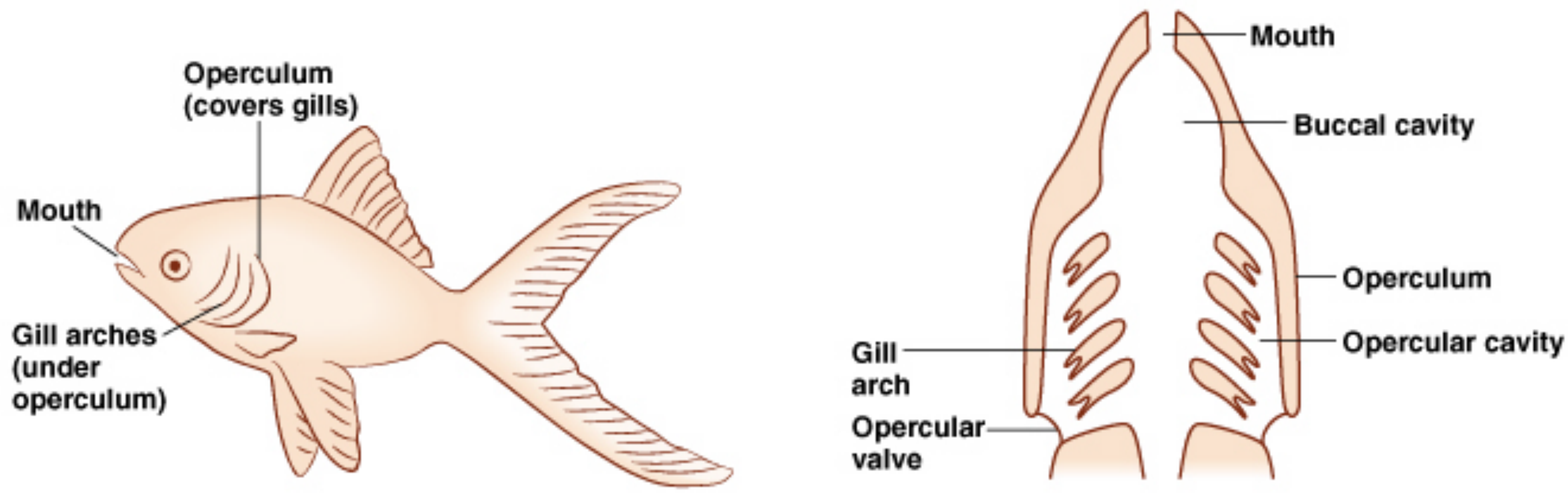
Blood flow is countercurrent

Buccal = relating to mouth



Shark's head (horizontal section)

Teleost Fishes - *in water*



(a) Teleost fish (lateral view and horizontal section)

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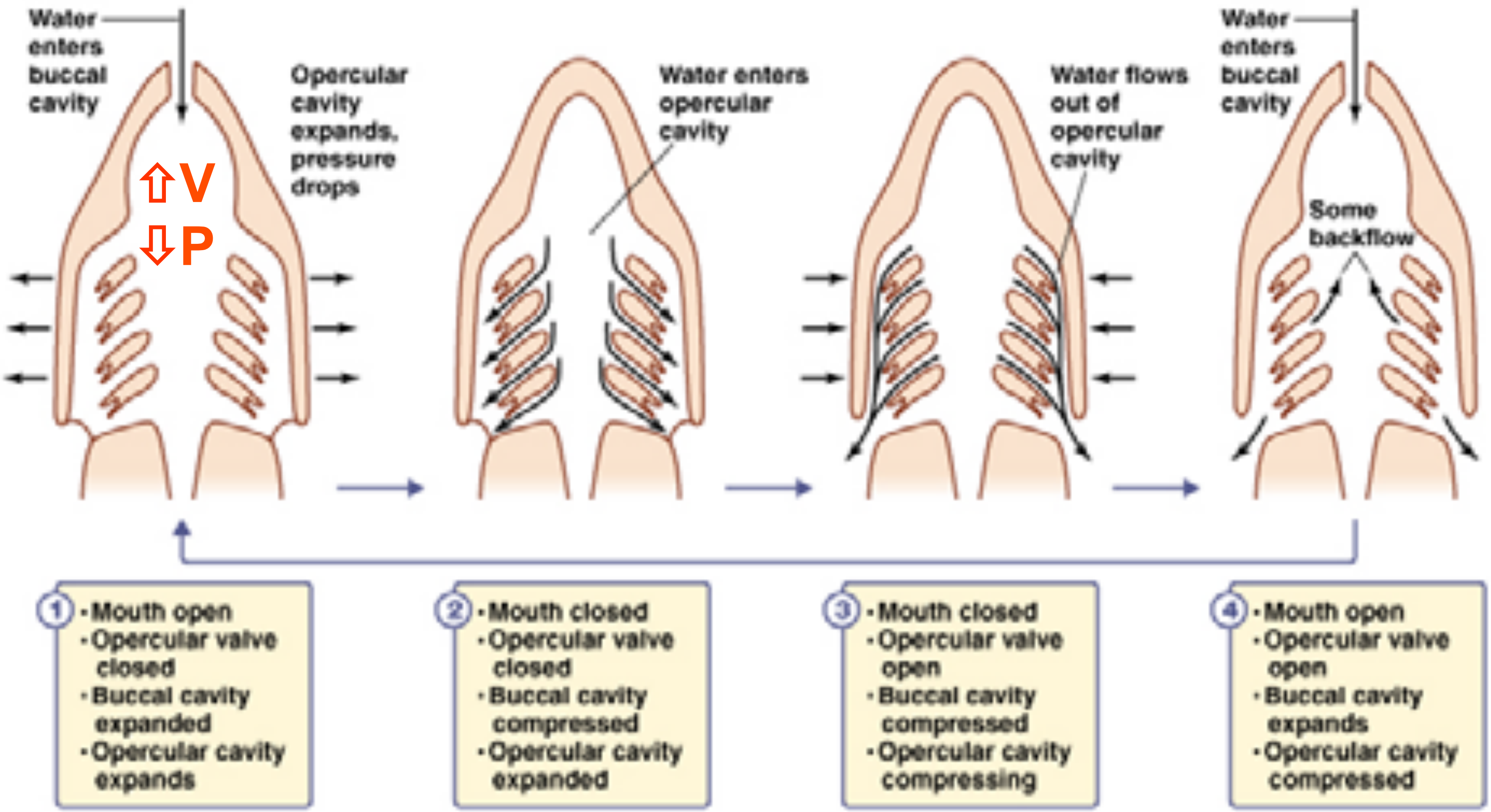
Water flows in via the mouth, out via the opercular opening

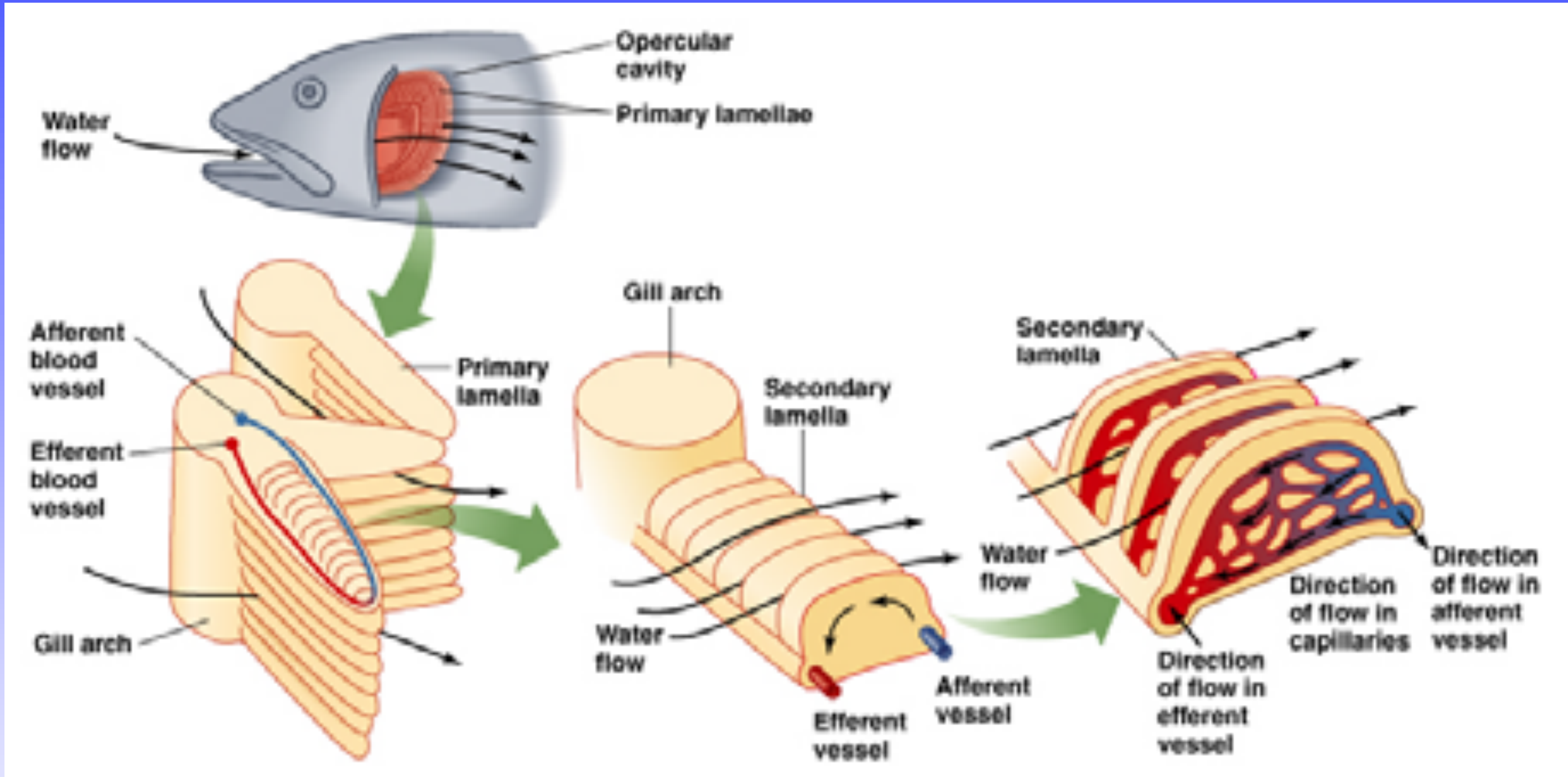
Teleost Fishes



(b) Ventilatory cycle of teleosts

More about fish Gills

Fish gills are arranged for countercurrent flow



Water breathers

Outline and list:

Which water breathing animals use cilia, muscular contractions.

How is water brought into respiratory structure? What is the common method?

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 highly vascularized
- 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&ved=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 (eeeeeeek)

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

Magdalene
Gift from Agnes Lacombe

Crustaceans

Terrestrial crabs

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

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

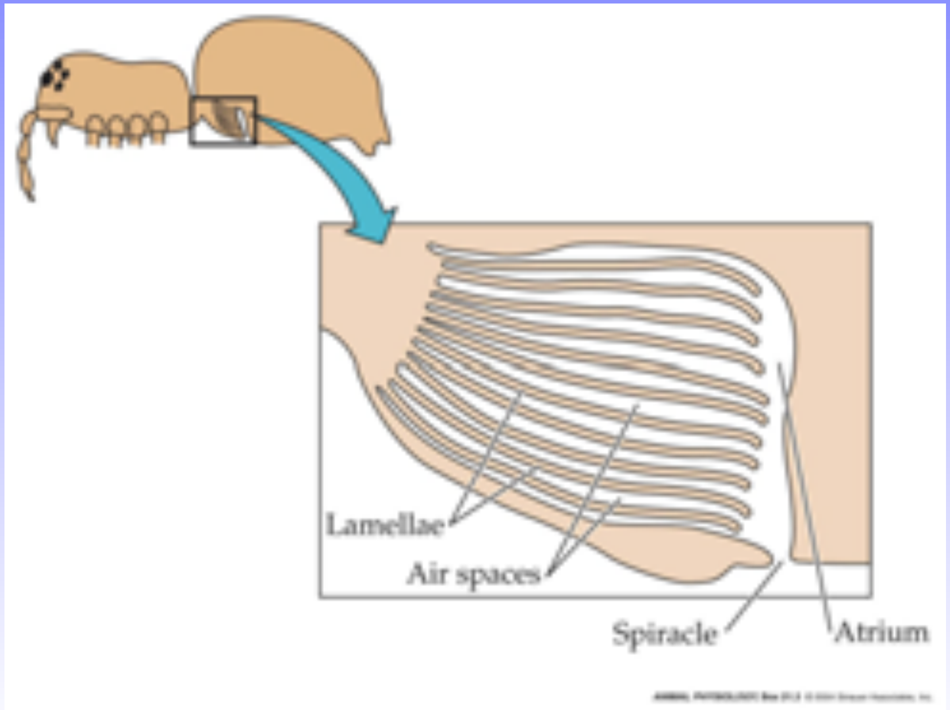
Chelicerates - *Spiders and scorpions*

Have four book lungs

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

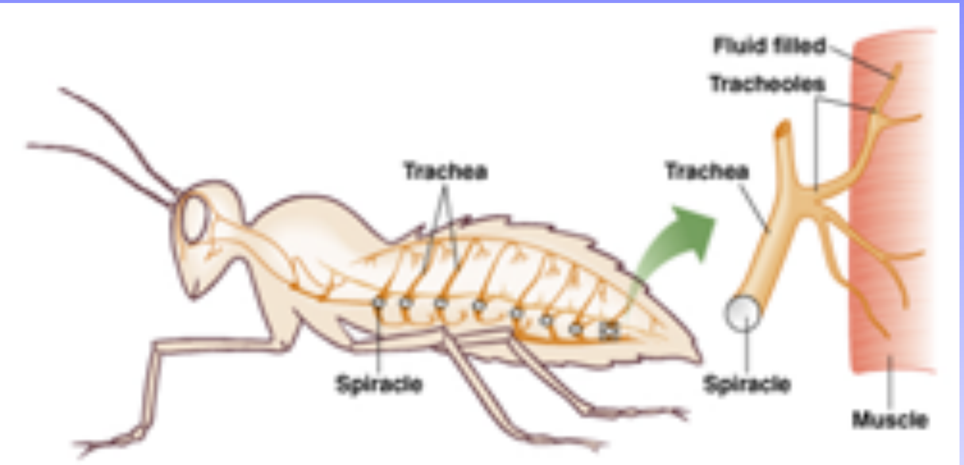
Some spiders also have a *tracheal system* – series of air-filled tubes

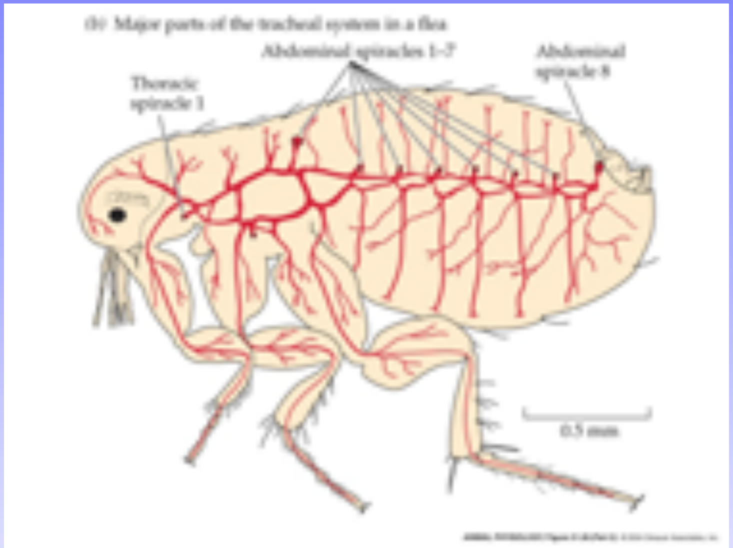
- **Oxygen diffuses into the trachea and dissolves in the interstitial fluid before diffusing into the tissues. Interstitial fluid = outside cells**



Insects

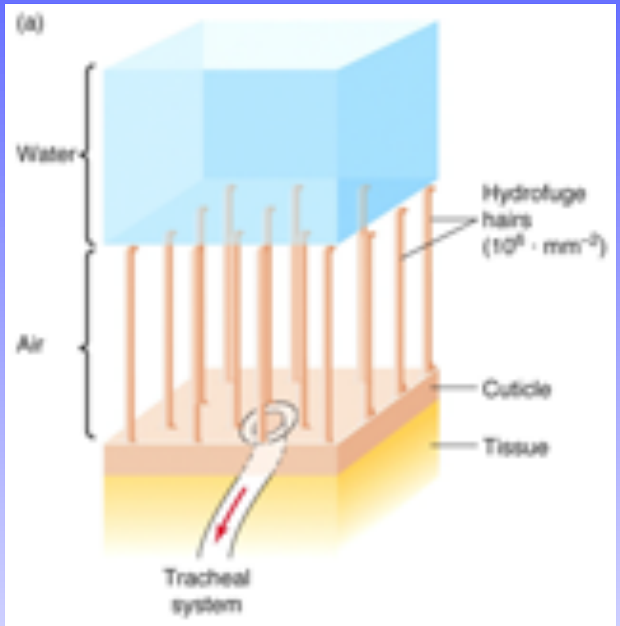
- Have an extensive *tracheal system* - series of air-filled tubes
- *Tracheoles* – terminating ends of tubes that are filled with *hemolymph*
- Oxygen dissolves in the hemolymph = blood of insects
- Open to outside via spiracles
- Gases diffuse in and out
- *High diffusion coefficient of oxygen in air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





Something "cool" about aquatic insects

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



Air breathing vertebrates

- Air breathing evolved in fishes
- 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

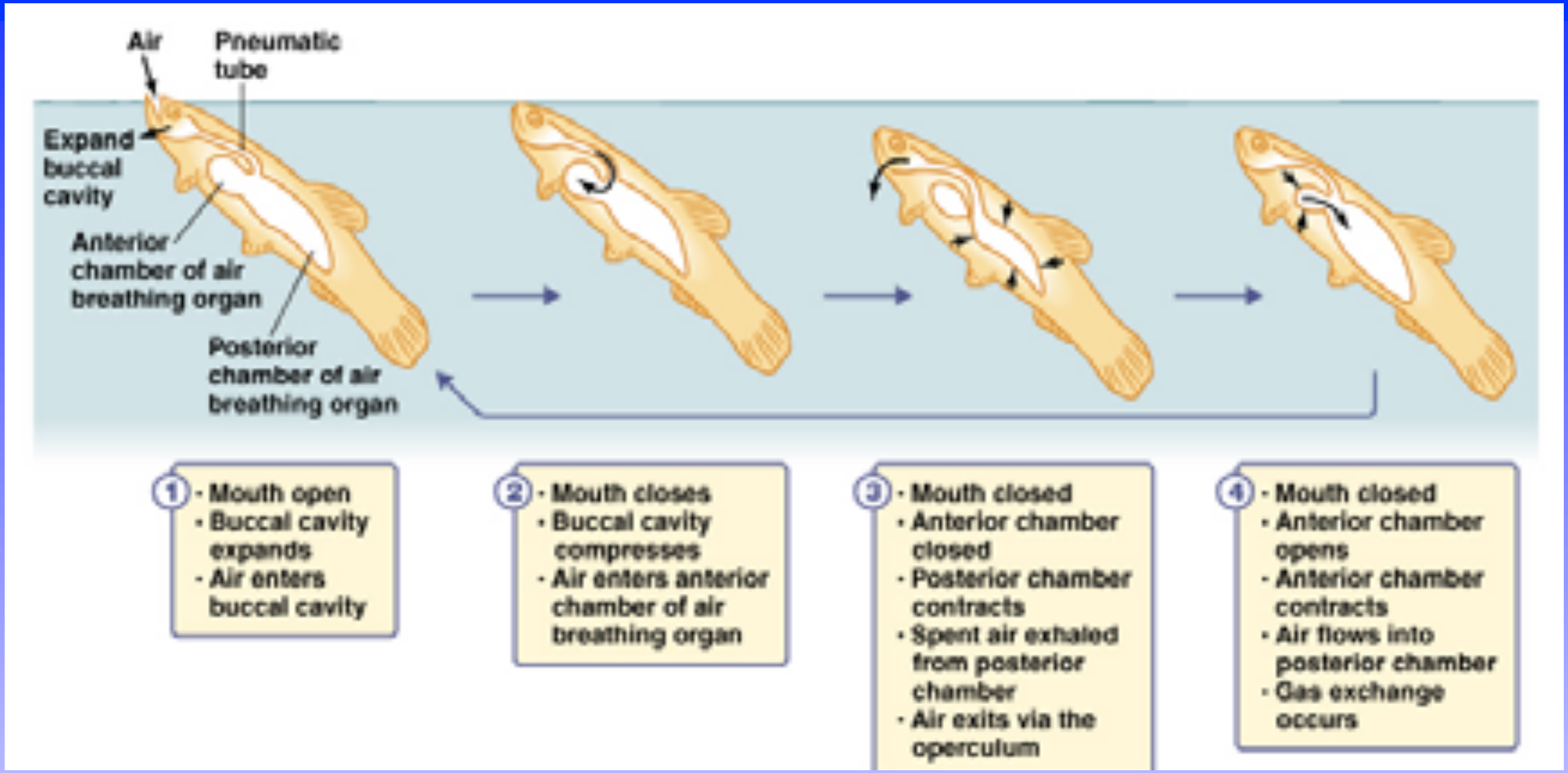
Types of respiratory structures

- 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 tidal 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

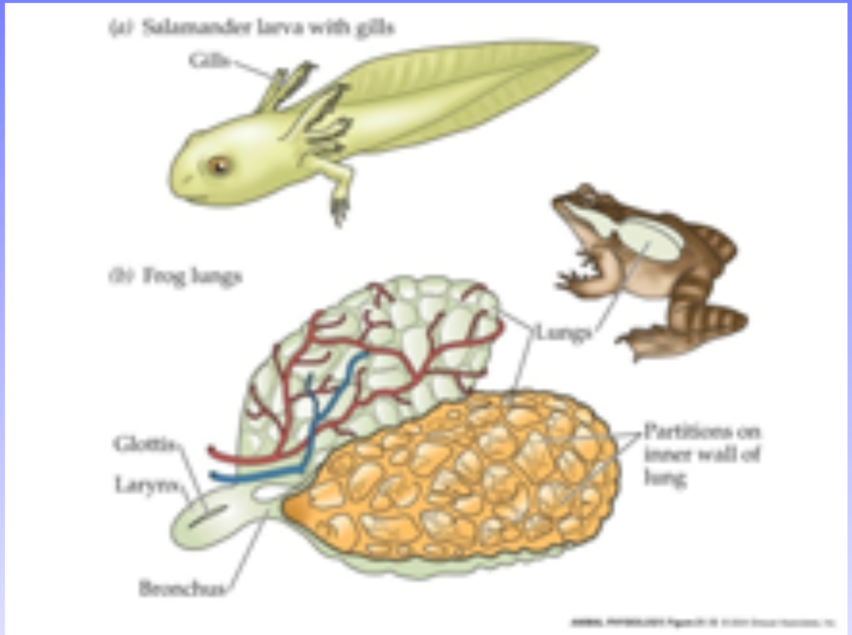
Very little mixing of fresh and old water ☺

Amphibians - ventilation

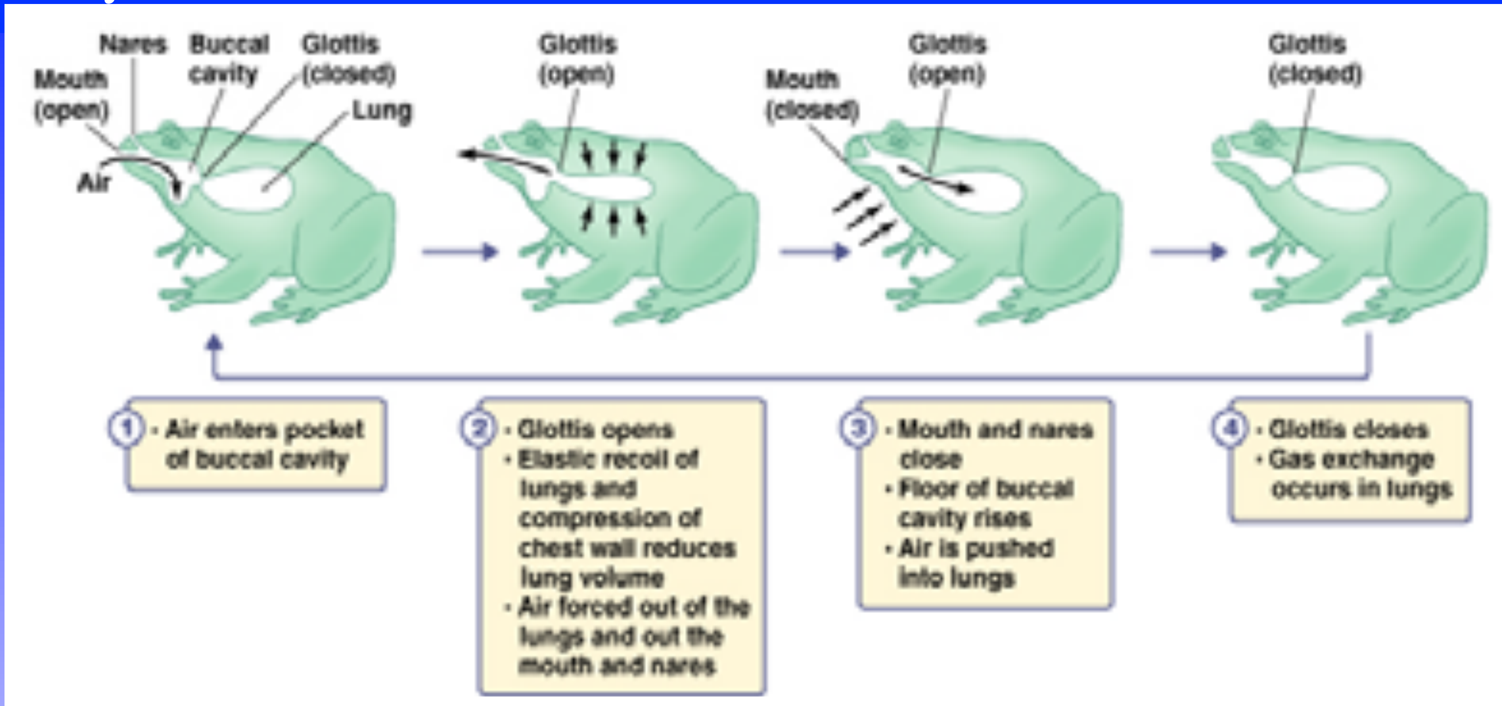
Types of respiratory structures

- Cutaneous respiration = use skin
- 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

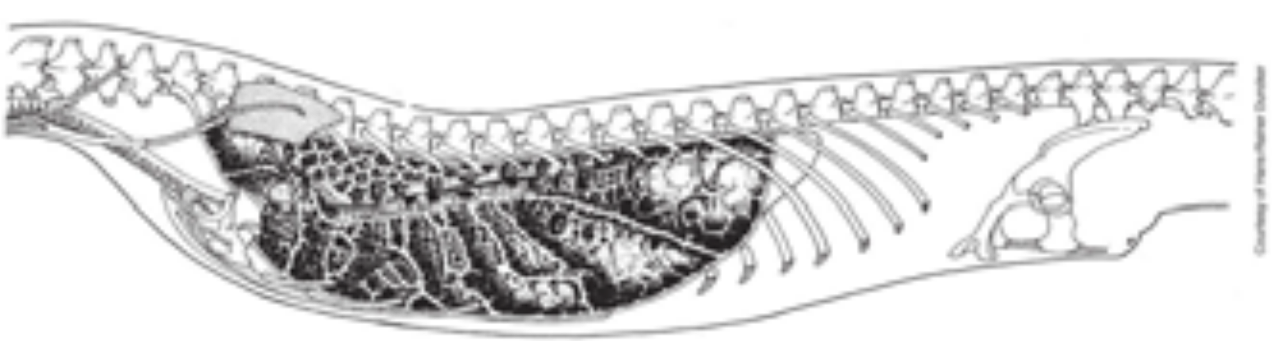
Reptiles

- ***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

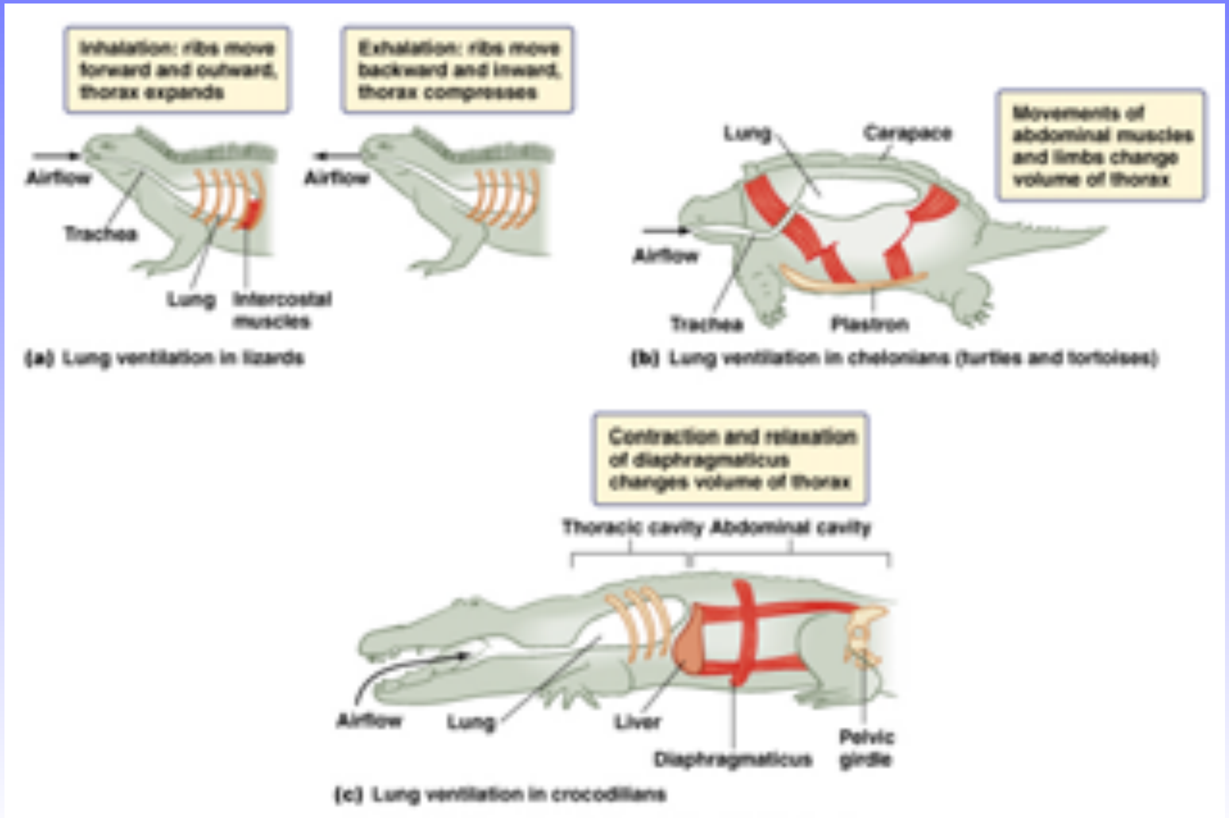
- Tidal
- Rely on suction pumps
- Results in the separation of **feeding and respiratory muscles**
- Two phases: inspiration and expiration
- Use one of several mechanisms to change the volume of the chest cavity. Why do we need to change the volume? To decrease pressure

(c) A multicameral lung in a monitor lizard



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 increases the volume of the lungs. As a result pressure in the lungs *decreases.***

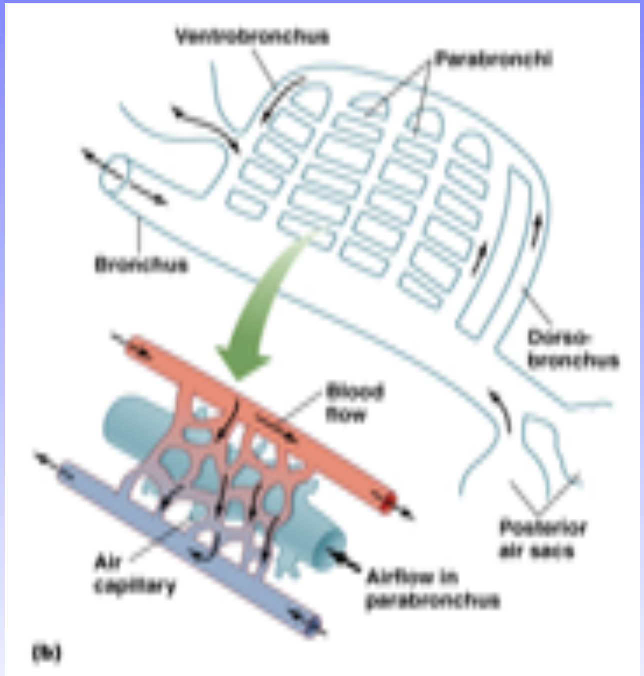


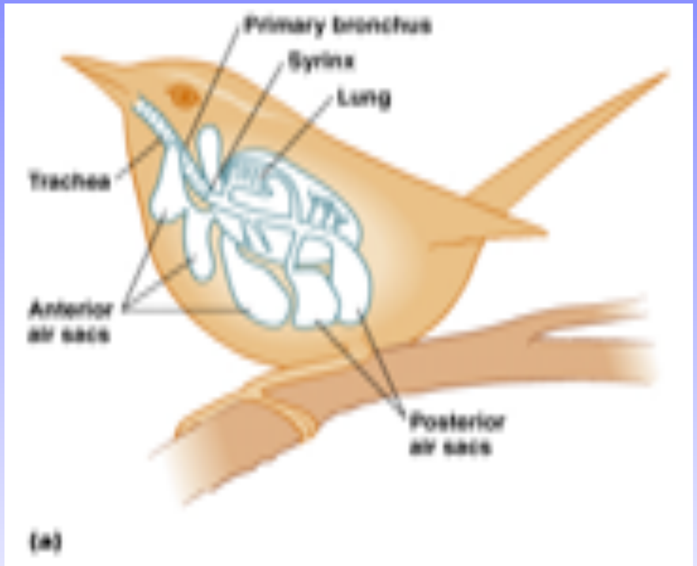
Ventilation in birds and mammals

- Birds use unidirectional ventilation
- Mammals use tidal ventilation

Birds

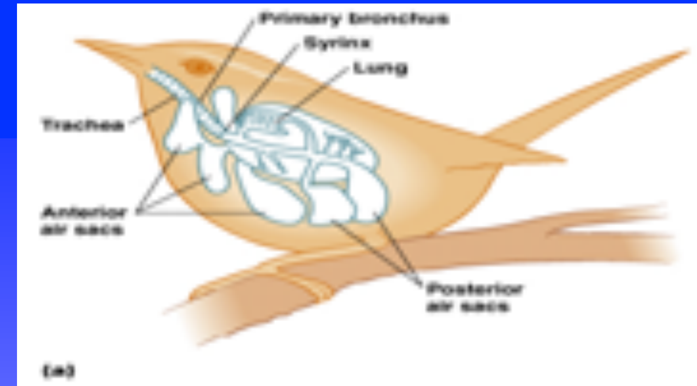
- Lung is stiff and changes little in volume – So how can birds change volume?
- Rely on a series of <u>flexible air sacs. Air sacs allow them to increase volume and decrease pressure</u>
- Gas exchange occurs at *parabronchi*
- *Air sacs = no gas exchange = function is to move air through respiratory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



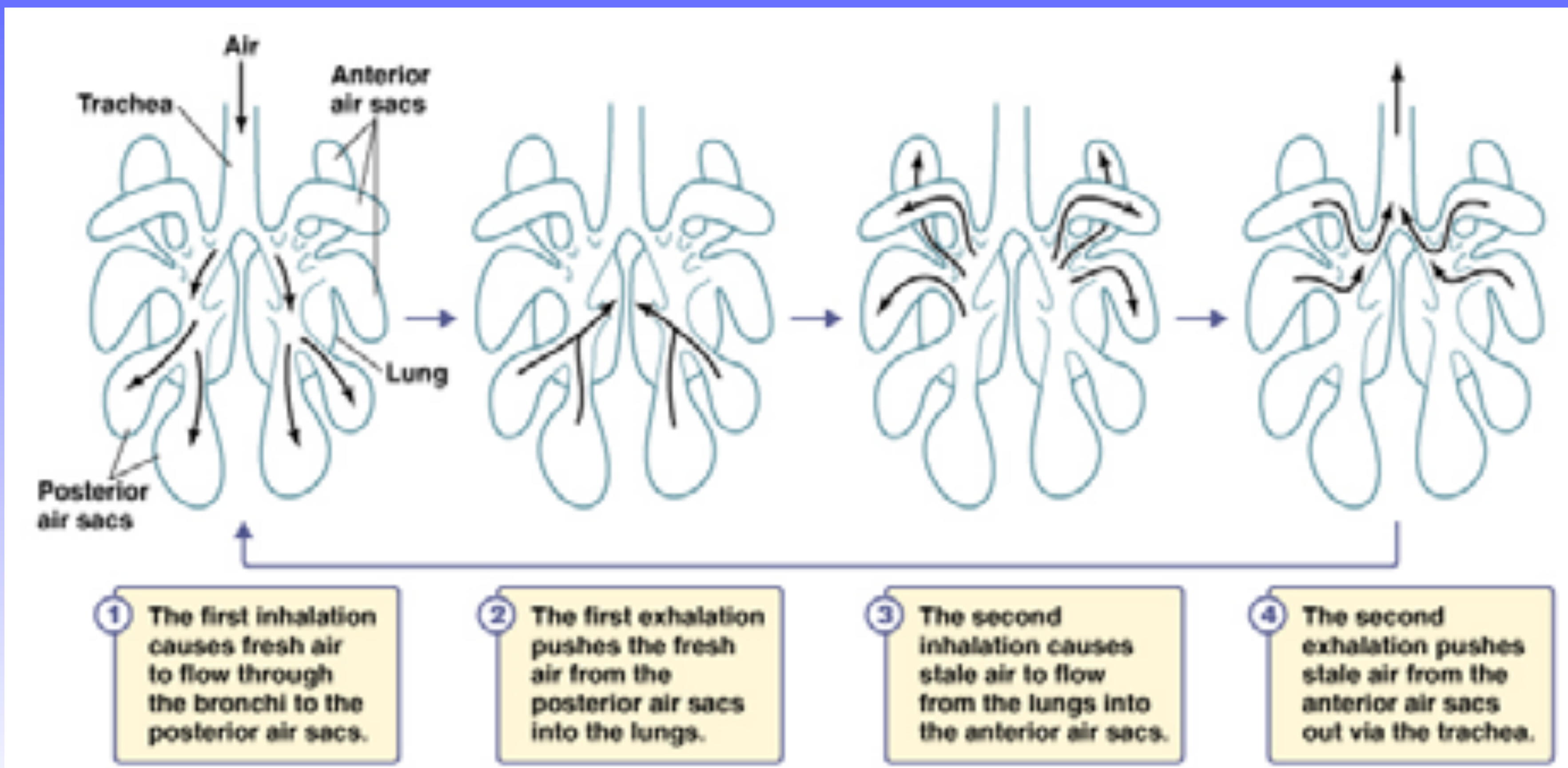


Oxygen extraction efficiency high (up to 90%)

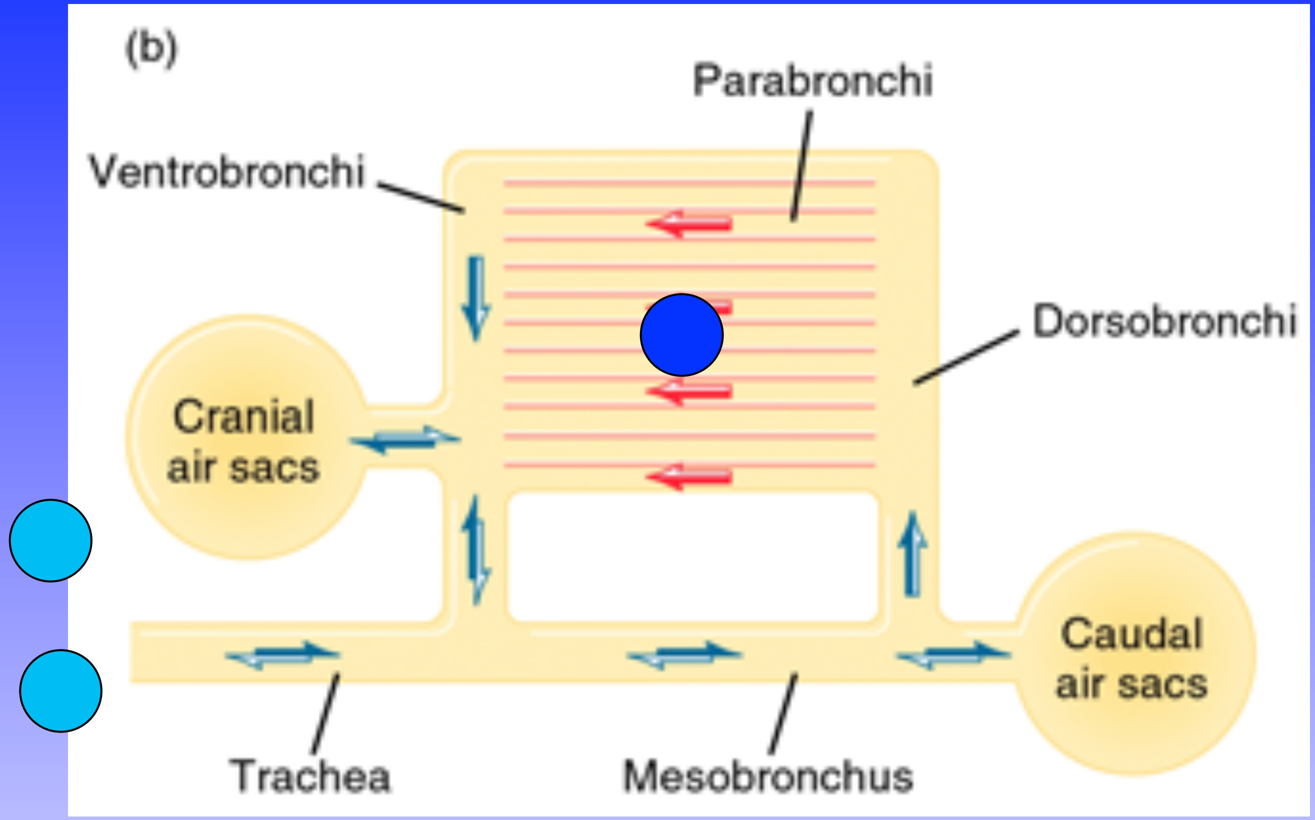
Bird Ventilation



- Requires two cycles of inhalation and exhalation
- Air flow across the respiratory surfaces is unidirectional



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

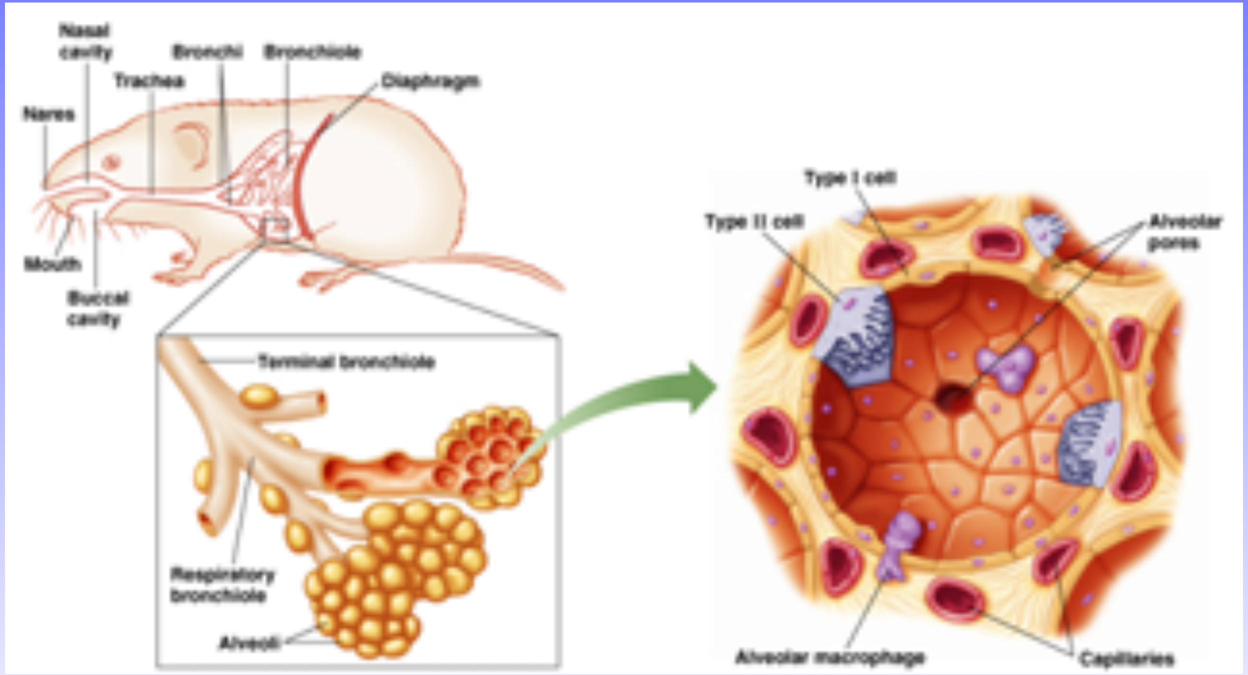
Mammals

Two main parts

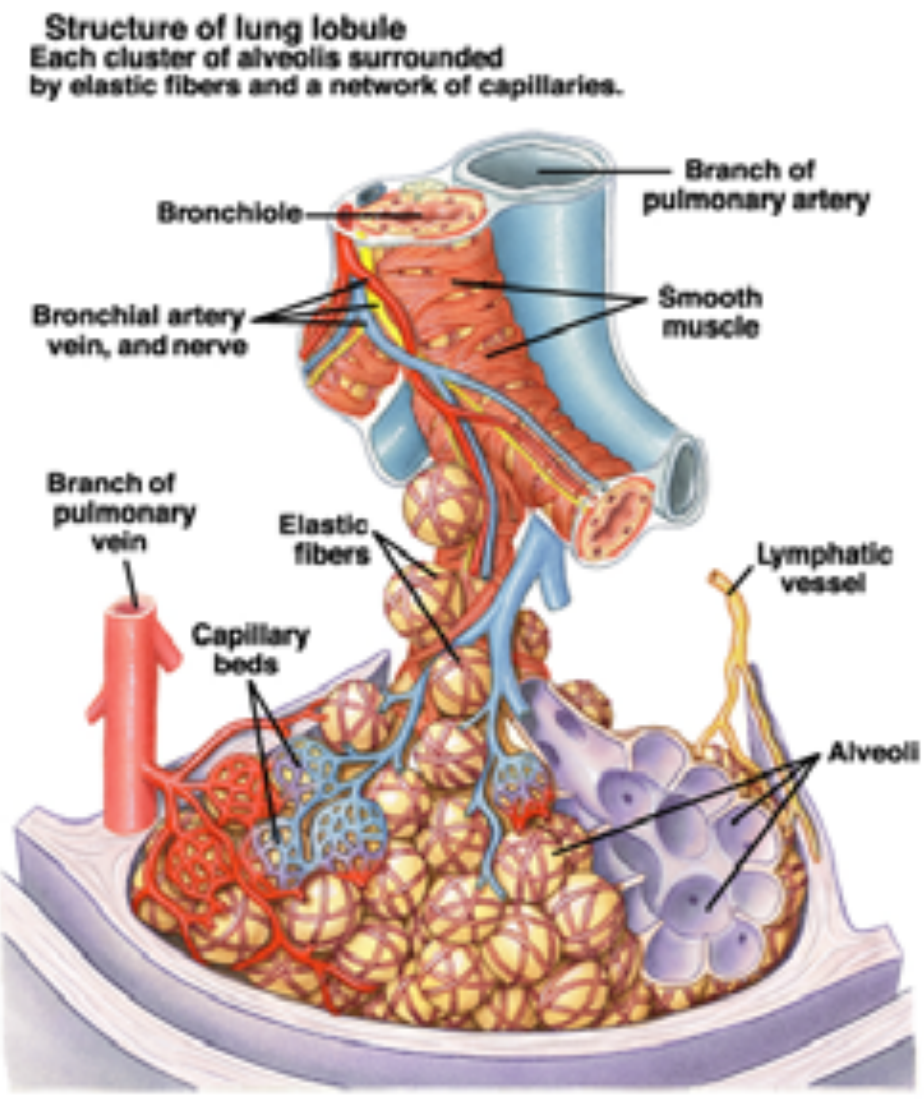
- Upper respiratory tract: mouth, nasal cavity, pharynx, trachea
- Lower respiratory tract: bronchi and lungs

Alveoli are the site of gas exchange

Both lungs are surrounded by a pleural sac



Mammalian lungs



Physical Properties of the Lungs

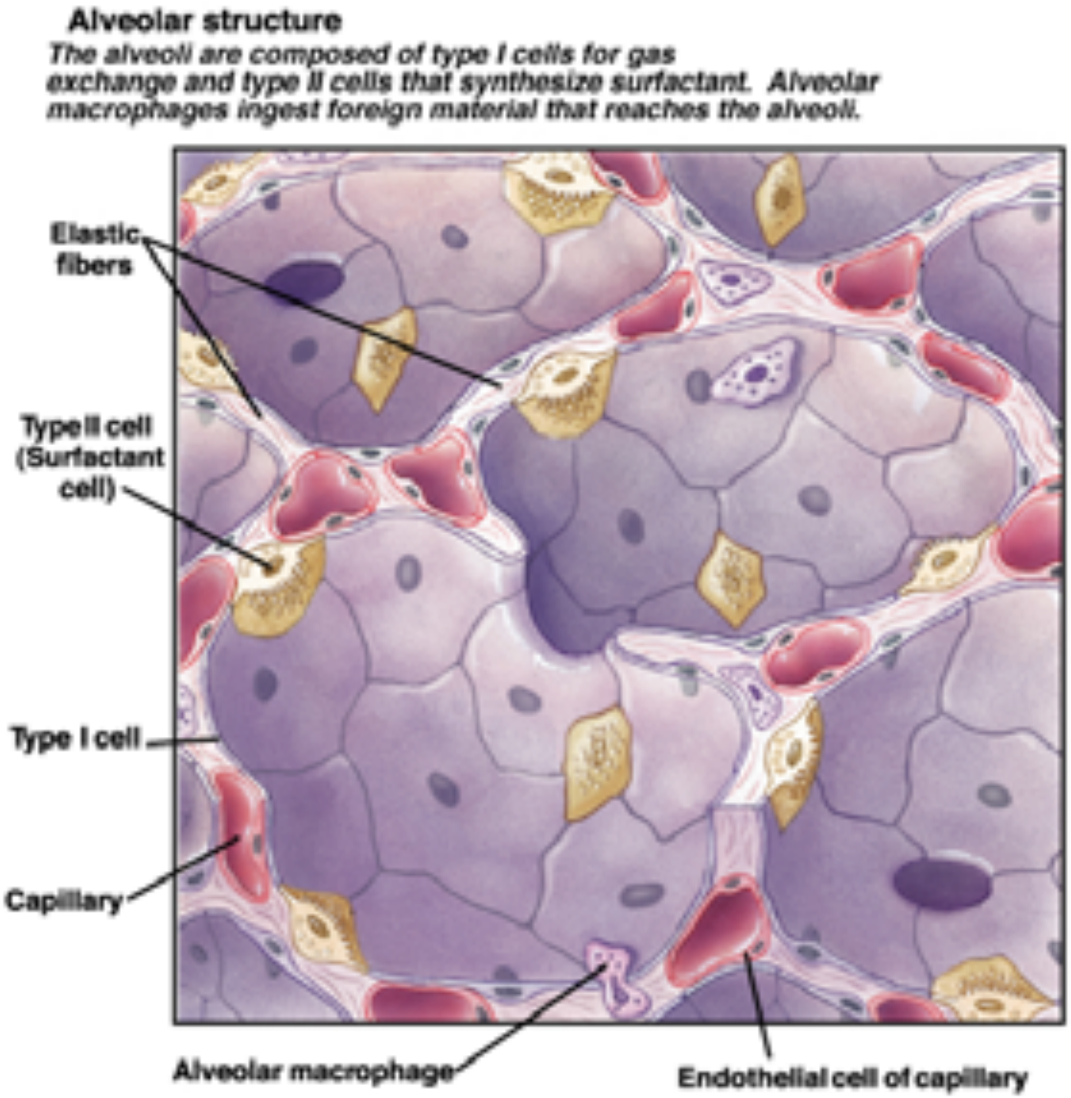
Compliance = Distensibility (stretchability) = Ease with which the lungs can expand. Affected by surfactant. Inhalation = to increase volume which decreases pressure and so air can flow into lungs

Elasticity = Tendency to return to initial size after distension.

- High content of elastin proteins.
- Very elastic and resist distension.
- Recoil ability. Affects exhalation. Exhalation at rest is passive due to elastic recoil

- Inhalation is active = use skeletal muscle
- Exhalation at rest is passive = use elastic recoil

Mammalian lungs - alveoli



Type I cells
  gas exchange

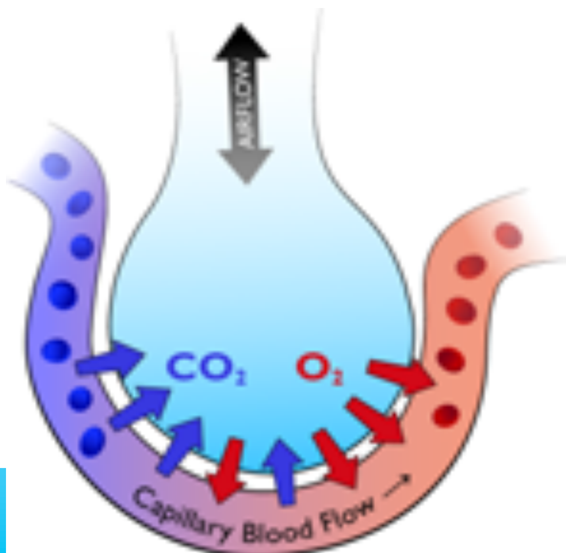
Type II cells
  surfactant secretion

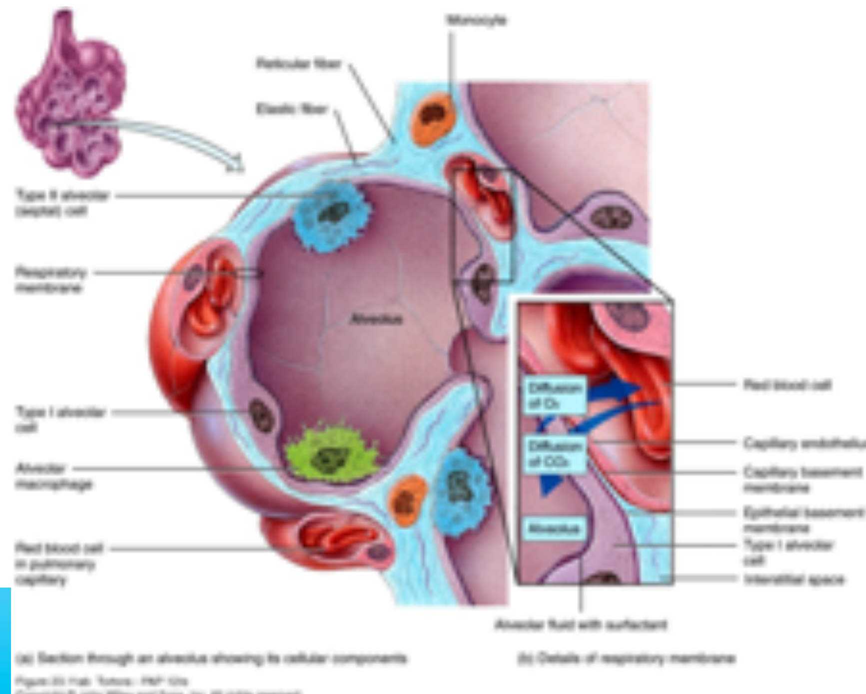
The Lungs - Alveoli

Alveolar Epithelium

- Consists of simple squamous epithelium = one layer and thin = gas exchange
- Consists of thin, delicate **pneumocytes type I = gas exchange**
- Patrolled by **alveolar macrophages**, also called **dust cells**

- Contains **pneumocytes type II** that produce **surfactant.** Surfactants = an oily secretion = Contains phospholipids and proteins



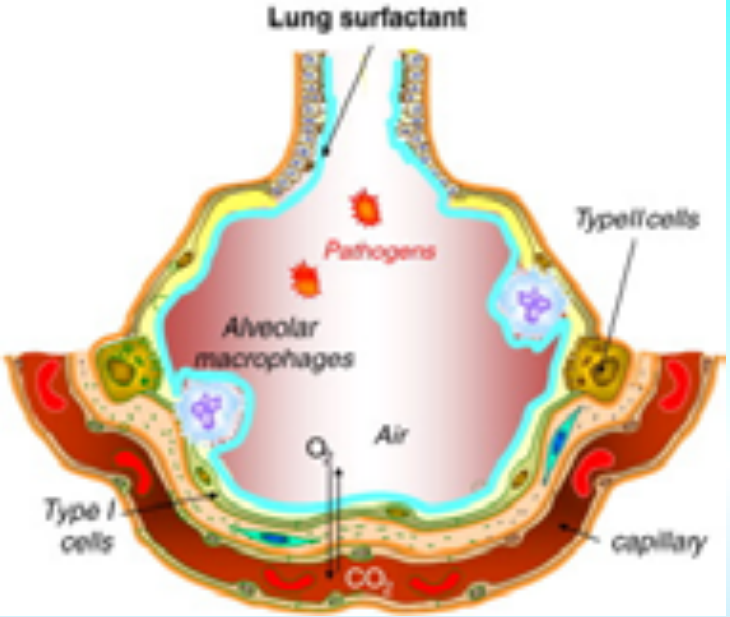


The Lungs - surfactants

Surfactants = Decrease the Work of breathing = less ATP

- Fluid is under tension = like thin membrane being stretched. Why do we need some fluid? Gases have to dissolve before they diffuse

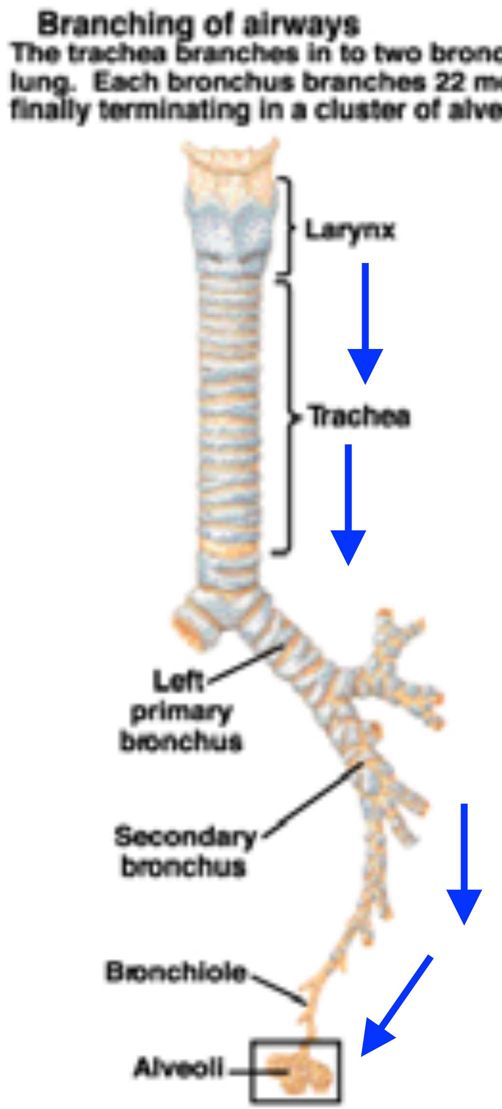
- Surface tension is directed toward the center of the alveoli and this creates pressure → Surfactans decrease the surface tension = increases compliance → easier to increase the volume of the lungs = less work is used.



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

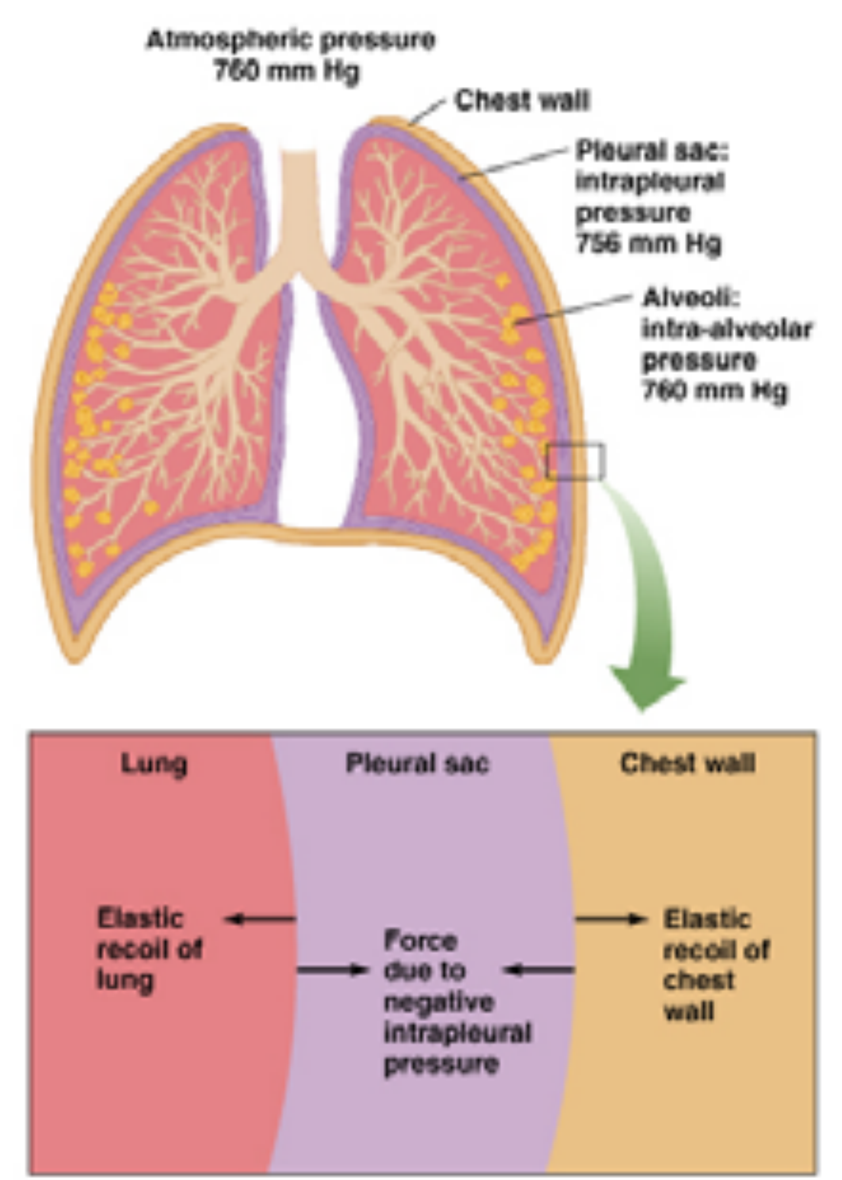


Airways:

Larynx
Trachea
Bronchii
Bronchioles
Alveoli

Important Pressures

- Atmospheric pressure is the pressure of the air outside the body. Has to be higher than inside the lungs to get air in
- Intraalveolar pressure is the pressure inside the alveoli of the lungs. Has to be less than atmospheric pressur for air to move into lungs/alveoli
- Intrapleural pressure is the pressure within the pleural cavity. Pressure is negative, due to lack of air in the intrapleural space



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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 ($1/r^4$). 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
- Bronchodilation – increase in radius = sympathetic nervous system

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. Somatic nervous system controls skeletal muscle

Steps. Don't have to memorize

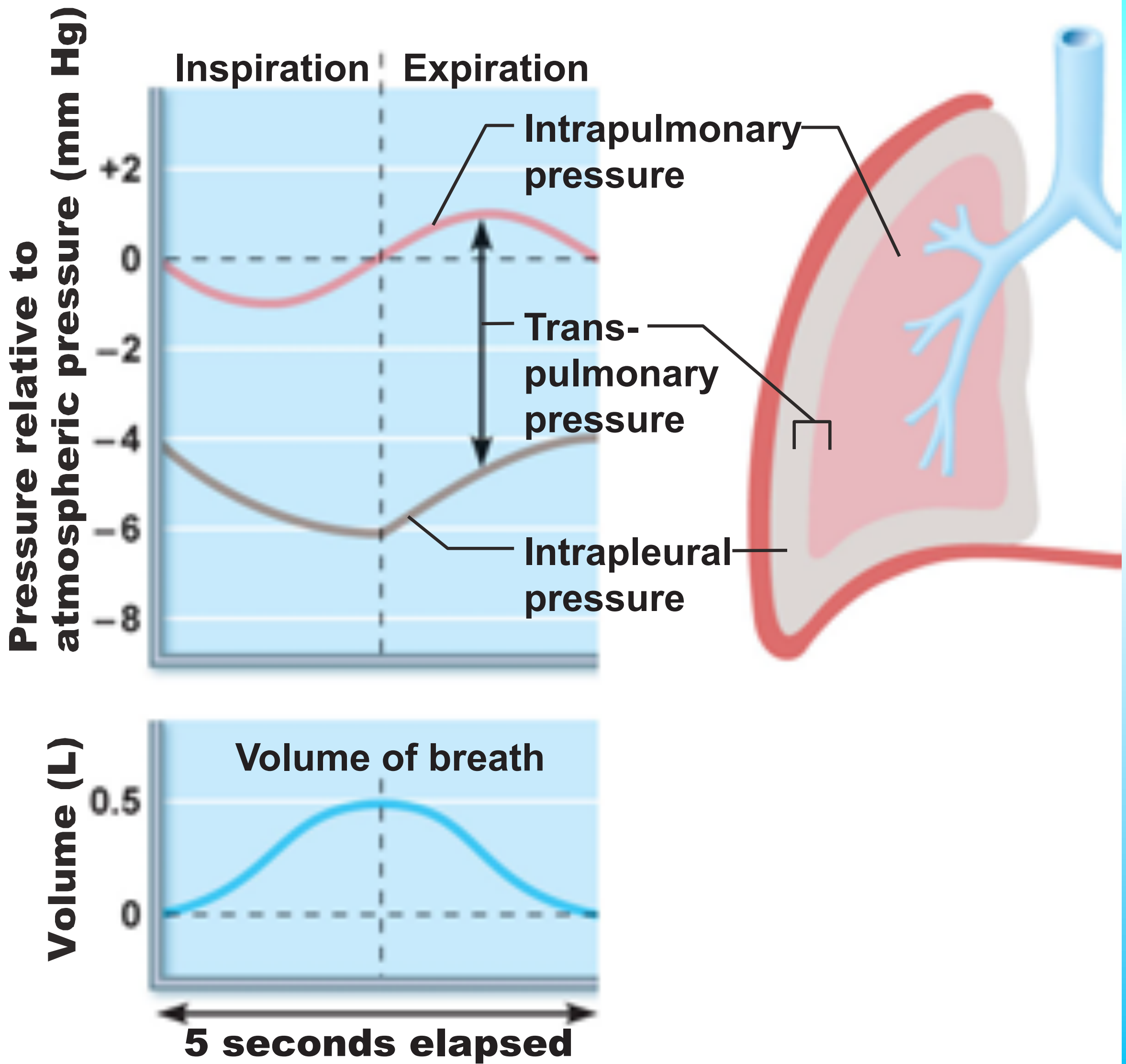
- Inhalation
  - Somatic motor neuron innervation
  - Contraction of the external intercostals and the diaphragm
  - Ribs move outwards and the diaphragm moves down
  - Volume of thorax increases and …..
  - Air is pulled in
- Exhalation
  - Innervation stops = electrical signal stops
  - Muscle relax
  - Ribs and diaphragm return to their original positions
  - Volume of the thorax decreases
  - Air is pushed out via *elastic recoil* of the lungs

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

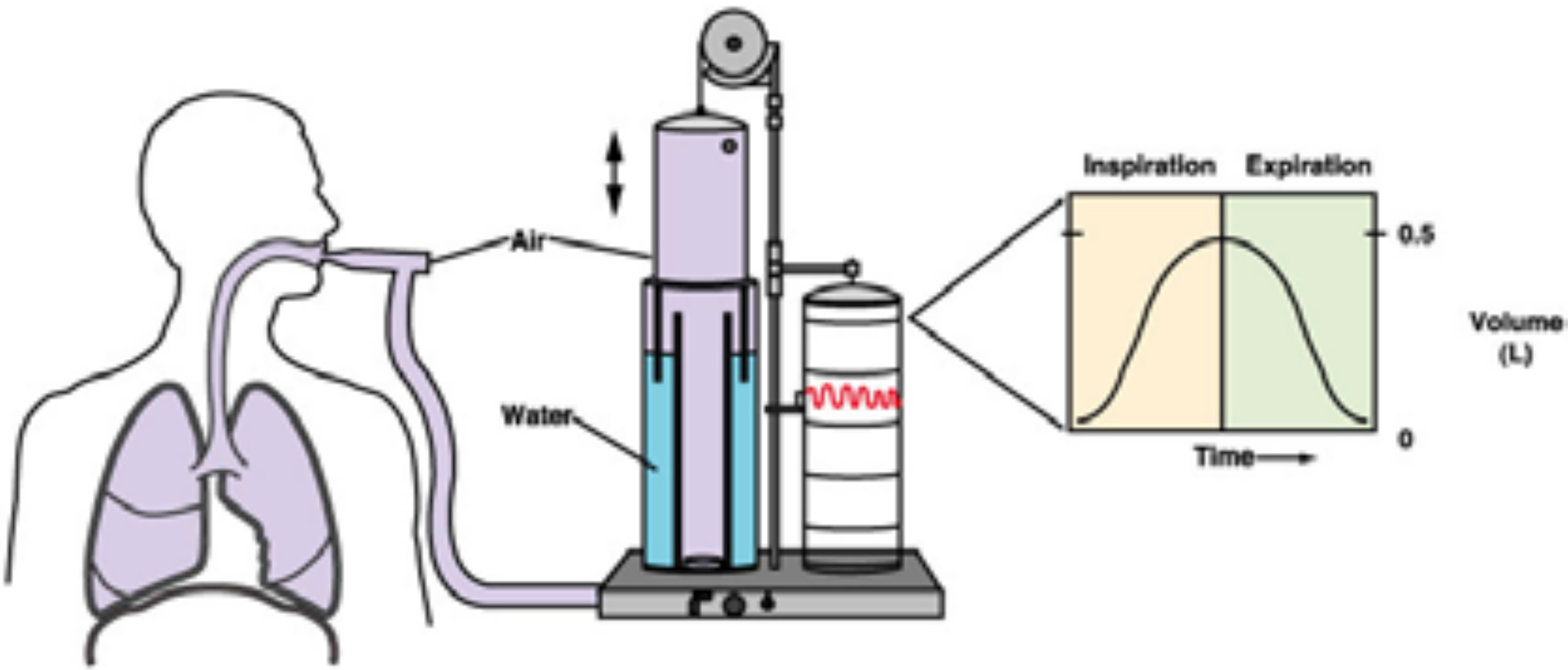
Intrapulmonary pressure. Pressure inside lung decreases as lung volume increases during inspiration; pressure increases during expiration.

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

The Lungs = some diseases

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 **loss of elastic fibers** (smoking, pollution, dust) = creates less surface area for gas exchange

Pulmonary edema = **fluid accumulation** 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

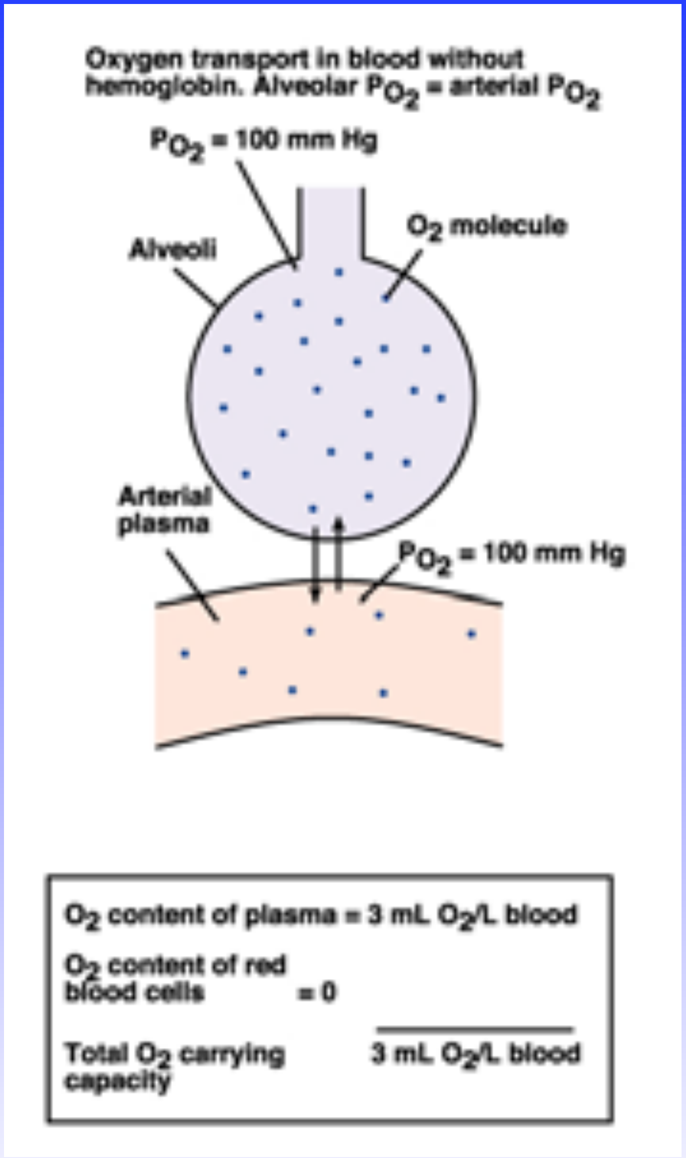
You have learned how water/air enters the respiratory structure

Next step: Gas exchange

Oxygen Transport

- Solubility of oxygen in aqueous fluids is low
- But Respiratory pigments help to increase the amount of O_2 in blood
- By binding oxygen to **carriers**, PO_2 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

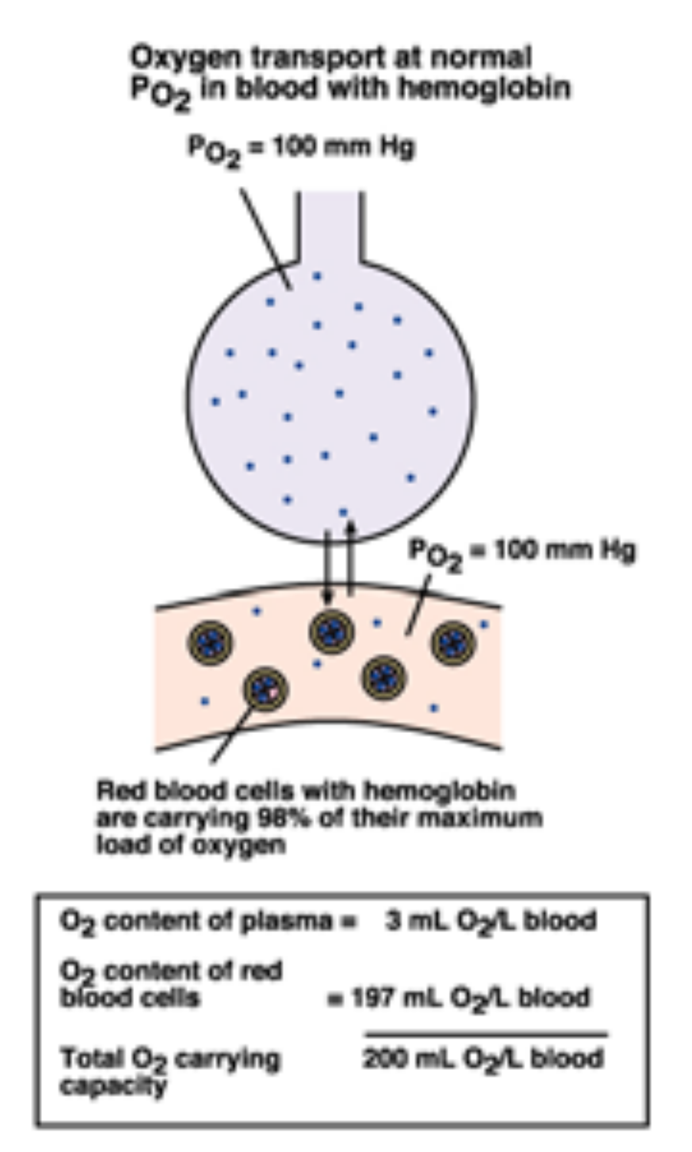


- Because of the low solubility of oxygen in aqueous solutions, only a small amount of oxygen can dissolve in blood
- PO_2 is equal in plasma and lungs, but oxygen content of plasma is much lower

Amount of oxygen that can dissolve in plasma is limited at physiological PO_2

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

Oxygen carrying capacity of blood



- If an oxygen carrier such as hemoglobin is present, some of the oxygen will bind to the pigment
- This oxygen no longer contributes to PO_2
- PO_2 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 within blood cells
  - **Appears red when oxygenated**
  - Myoglobin is found in muscles = holds on very tightly to O2

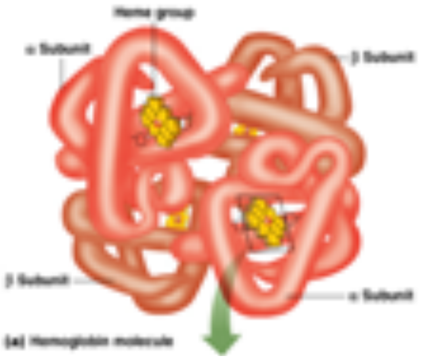
- *Hemocyanins*
  - Arthropods and molluscs
  - Contain *copper*
  - Usually dissolved in the hemolymph
  - **Appears blue when oxygenated**

- *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

Hemoglobin = protein = will eb affected by pH, Temperature, Pressure

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



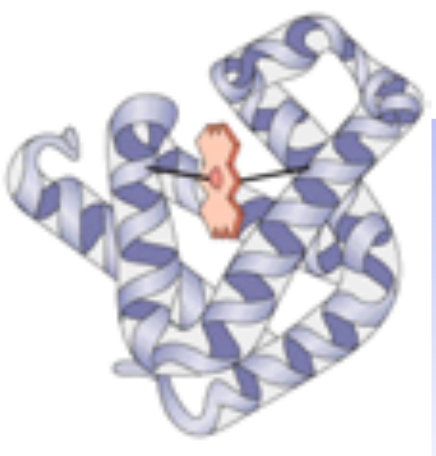
Myoglobin

•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



Myoglobin, a globular protein

Gas Transport - O_2

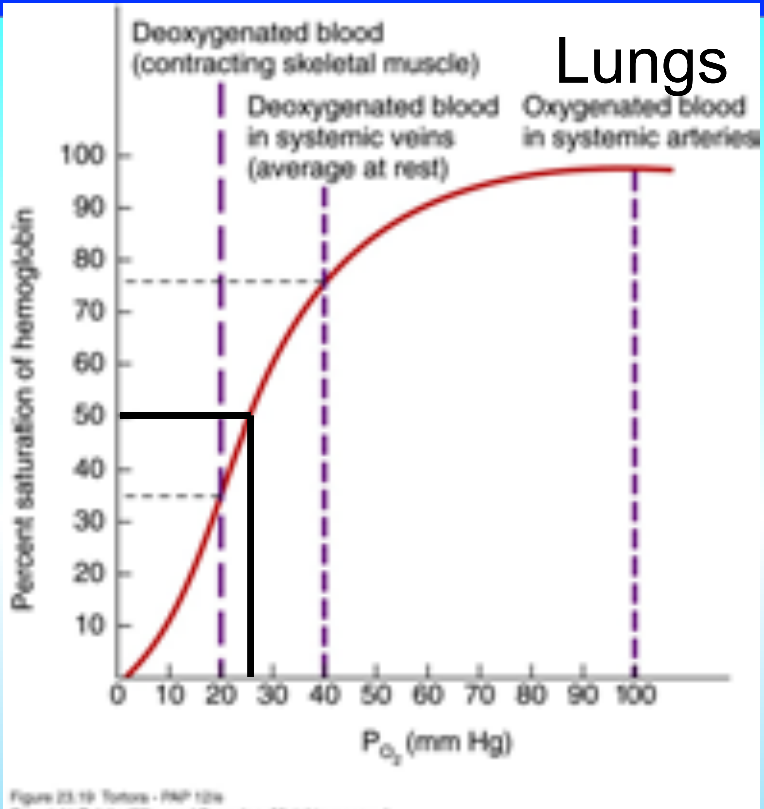
Carrying capacity = the maximum amount of oxygen that can be carried in blood

- **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

- ***P_{50}*** – 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 - O_2

Myoglobin

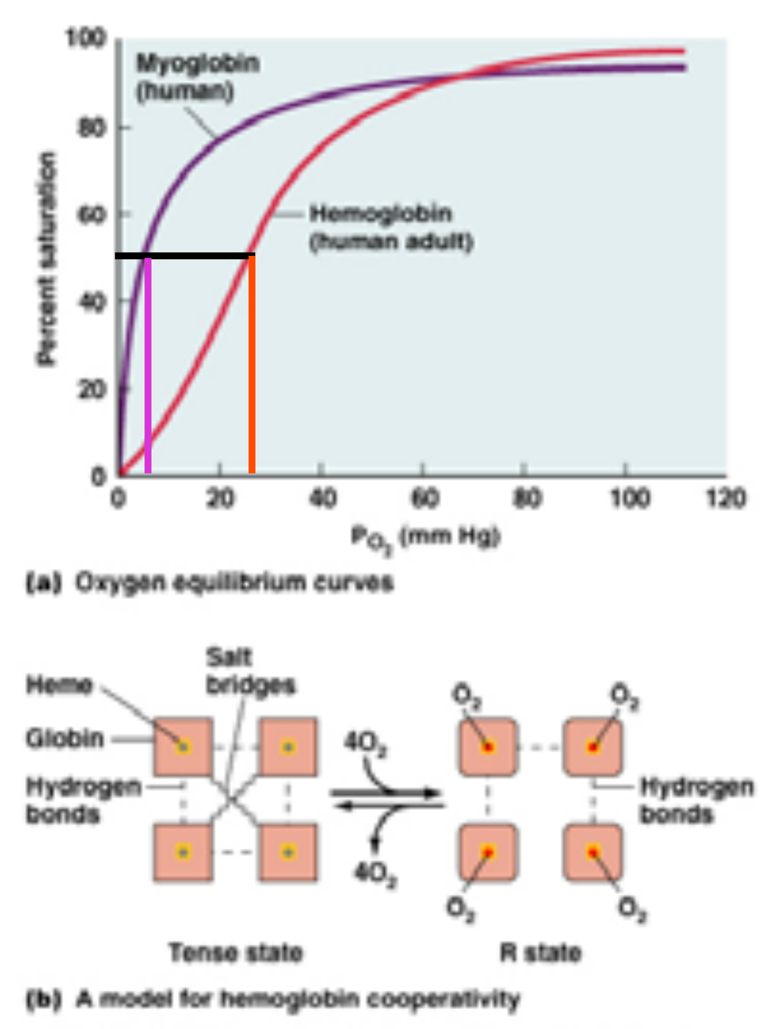
- has a lower P_{50} than Hemoglobin
- Myoglobin has higher oxygen affinity
- PO2 for Myoglobin has to be very low for it to let go of O2 ☺. Helps while exercising

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 O_2 is bound
- Each O_2 bound makes next O_2 binding easier
- Allows Hb to bind O_2 when O_2 levels are low

- Myoglobin only binds one O_2



Gas Transport - O_2

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 CO_2**
  - CO_2 diffuses into RBC
  - An enzyme, called **carbonic anhydrase**, catalyzes reaction with H_2O
  - Produces carbonic acid (H_2CO_3) which dissociates into hydrogen ion (H^+) and bicarbonate ion (HCO_3^-)
  - 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

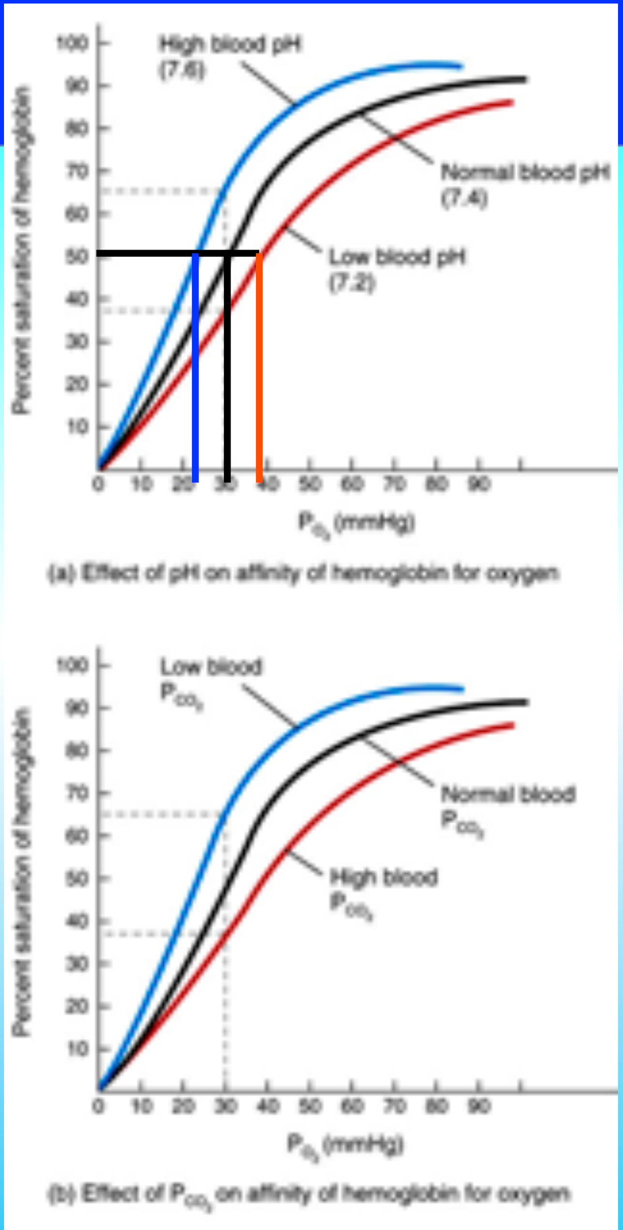
pH

- As pH decreases, affinity of Hb for O_2 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
- <u>Low blood pH can result from high P_{CO2}</u>



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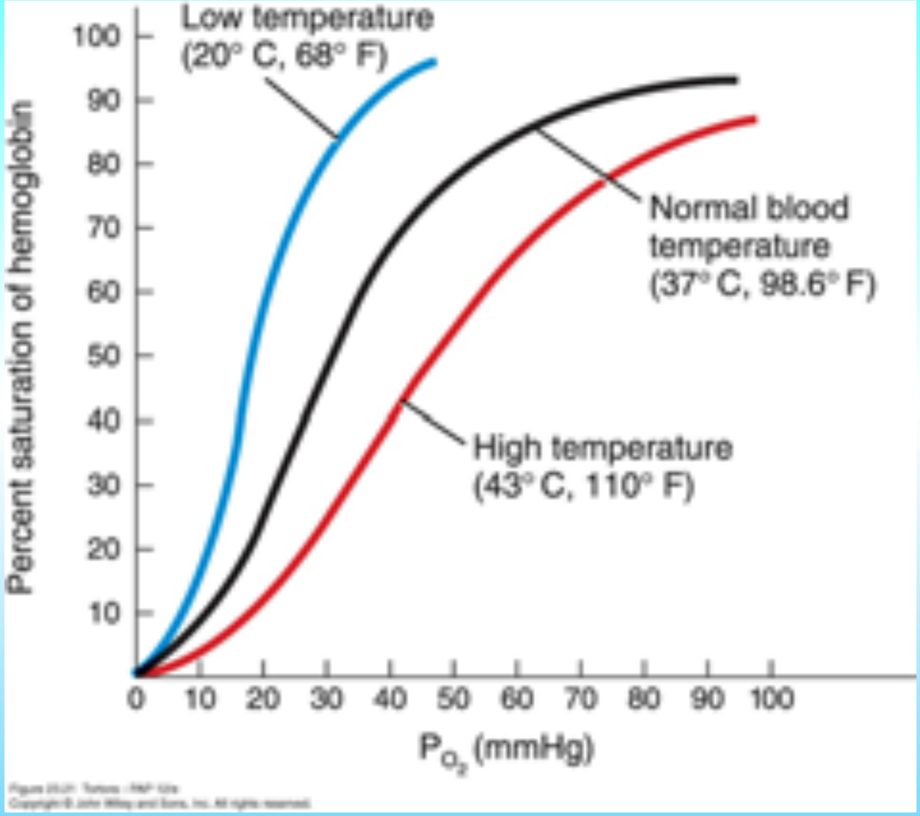
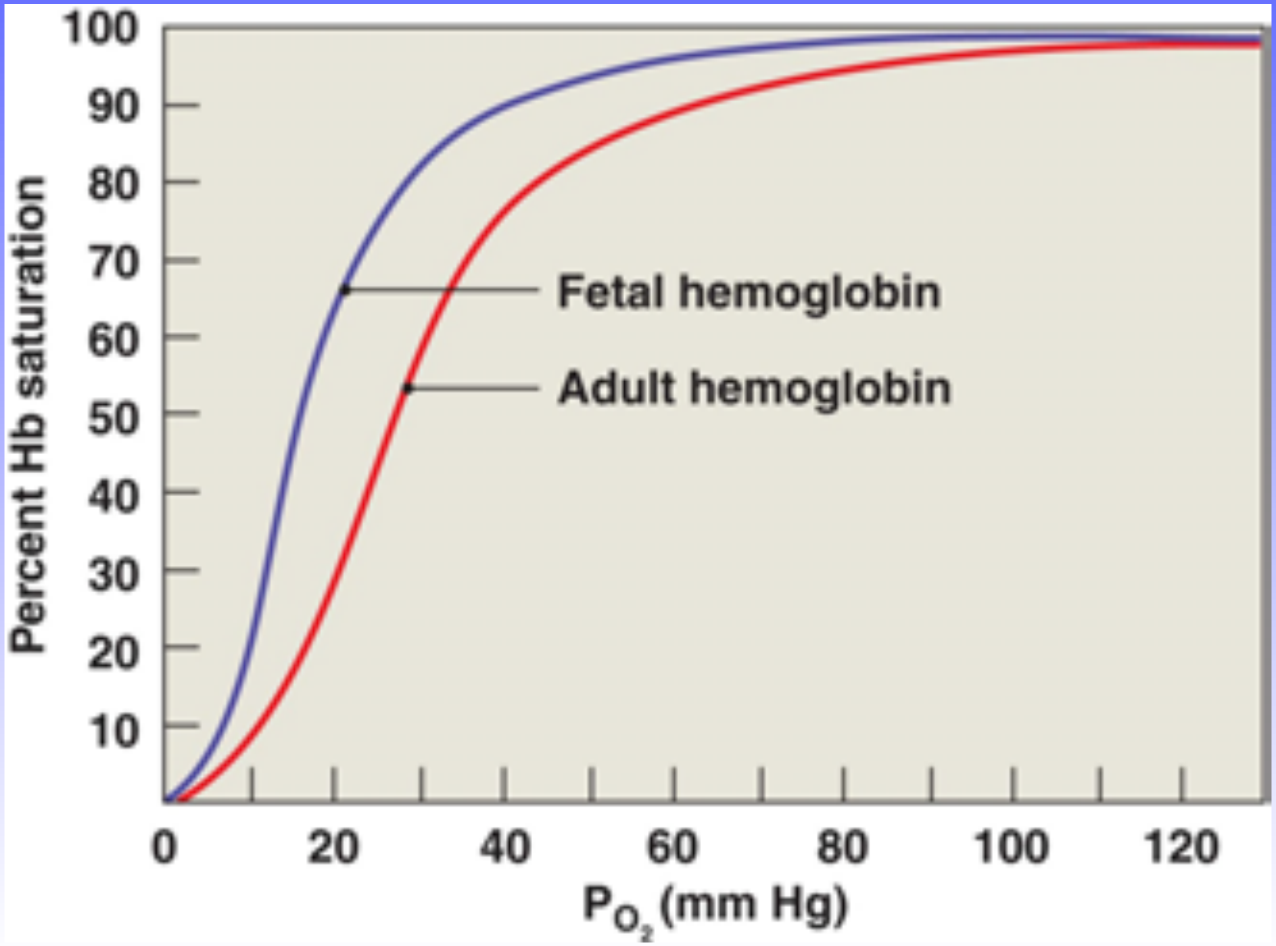
Temperature and Bohr

- 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

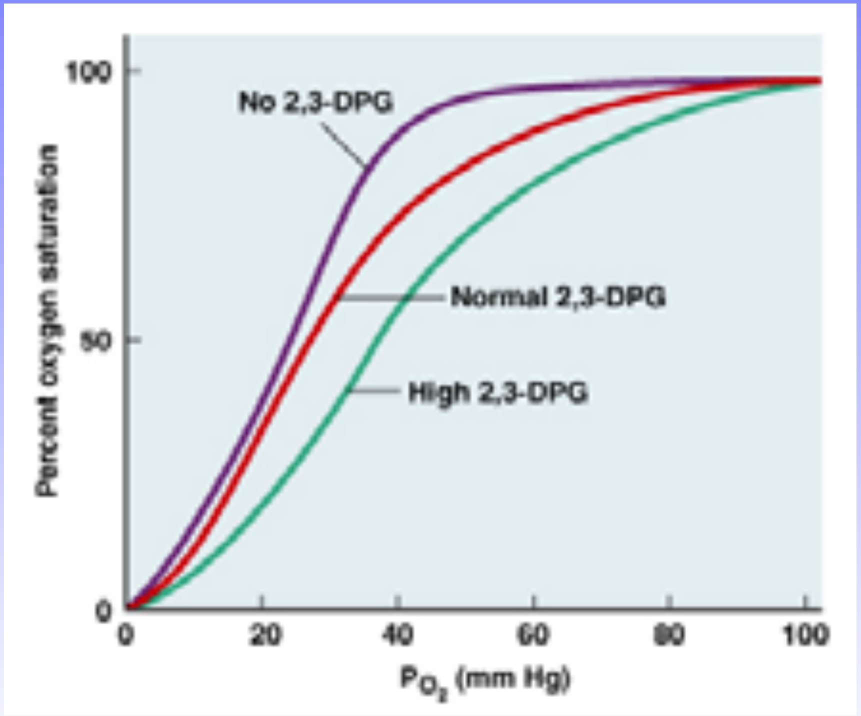
Fetal hemoglobin has a lower P_{50} than maternal hemoglobin. Fetus gets O2 from mom



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

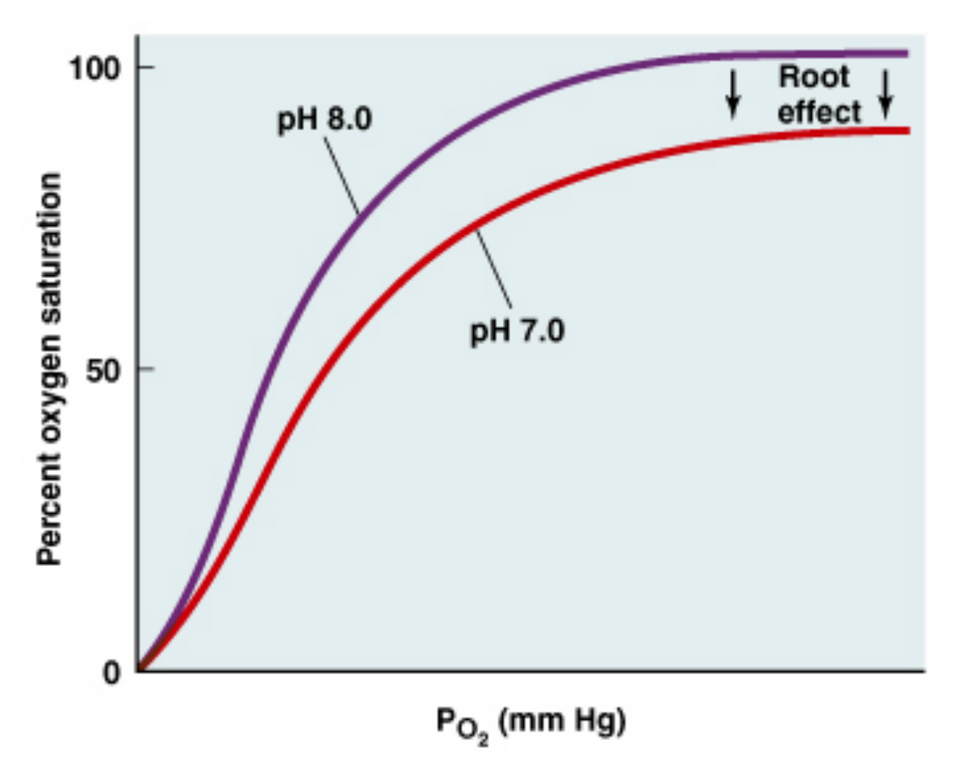


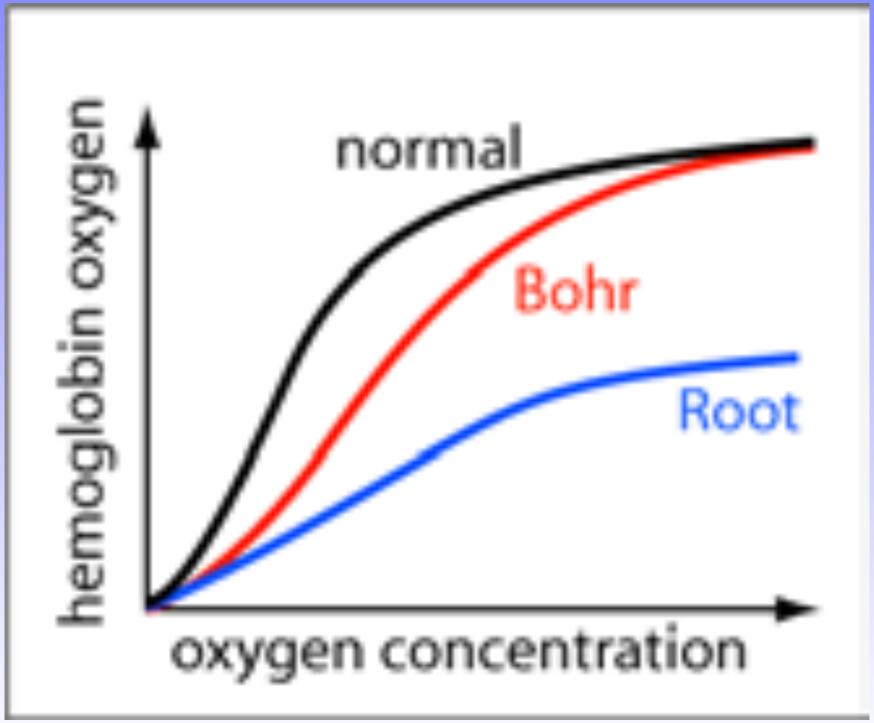
Root effect – something fishy

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

- Seen in hemoglobin of many teleost fishes
- 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

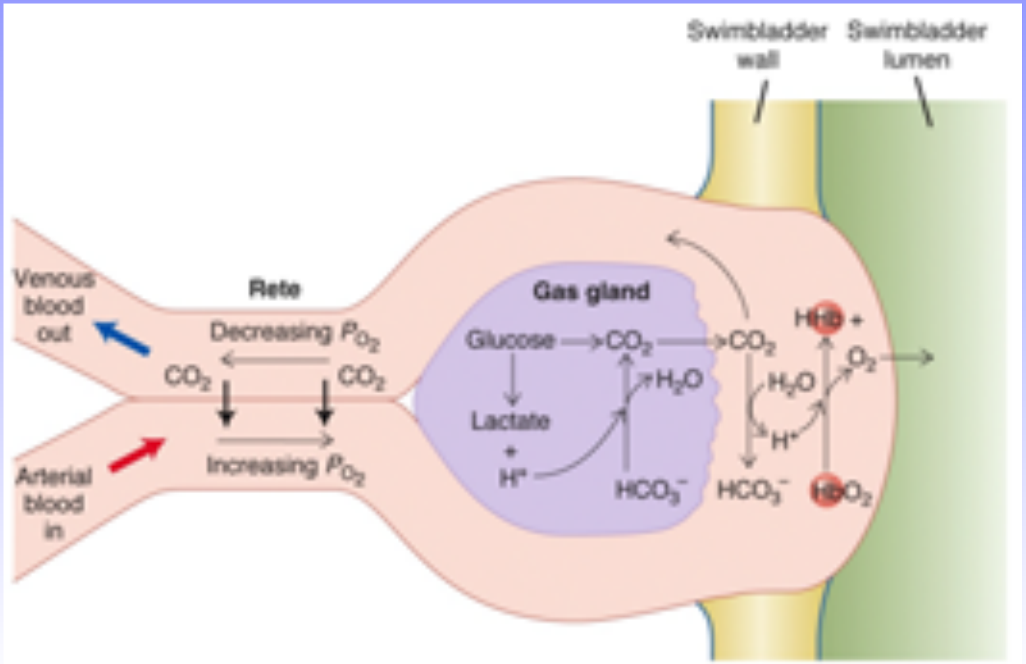


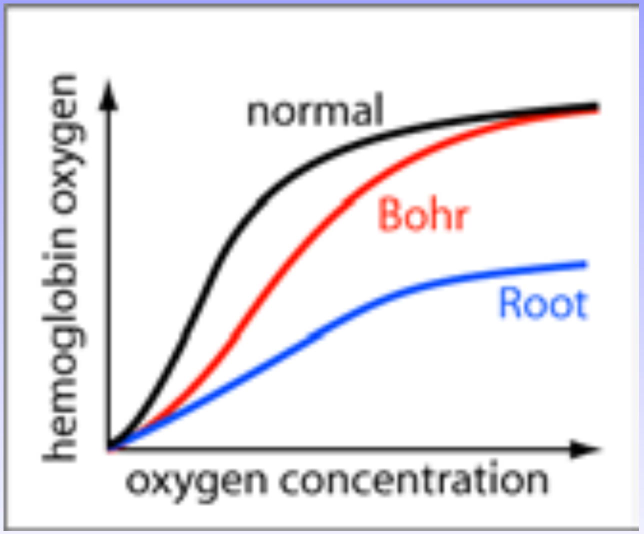


Swim bladder and Oxygen

- 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 **oxygen**

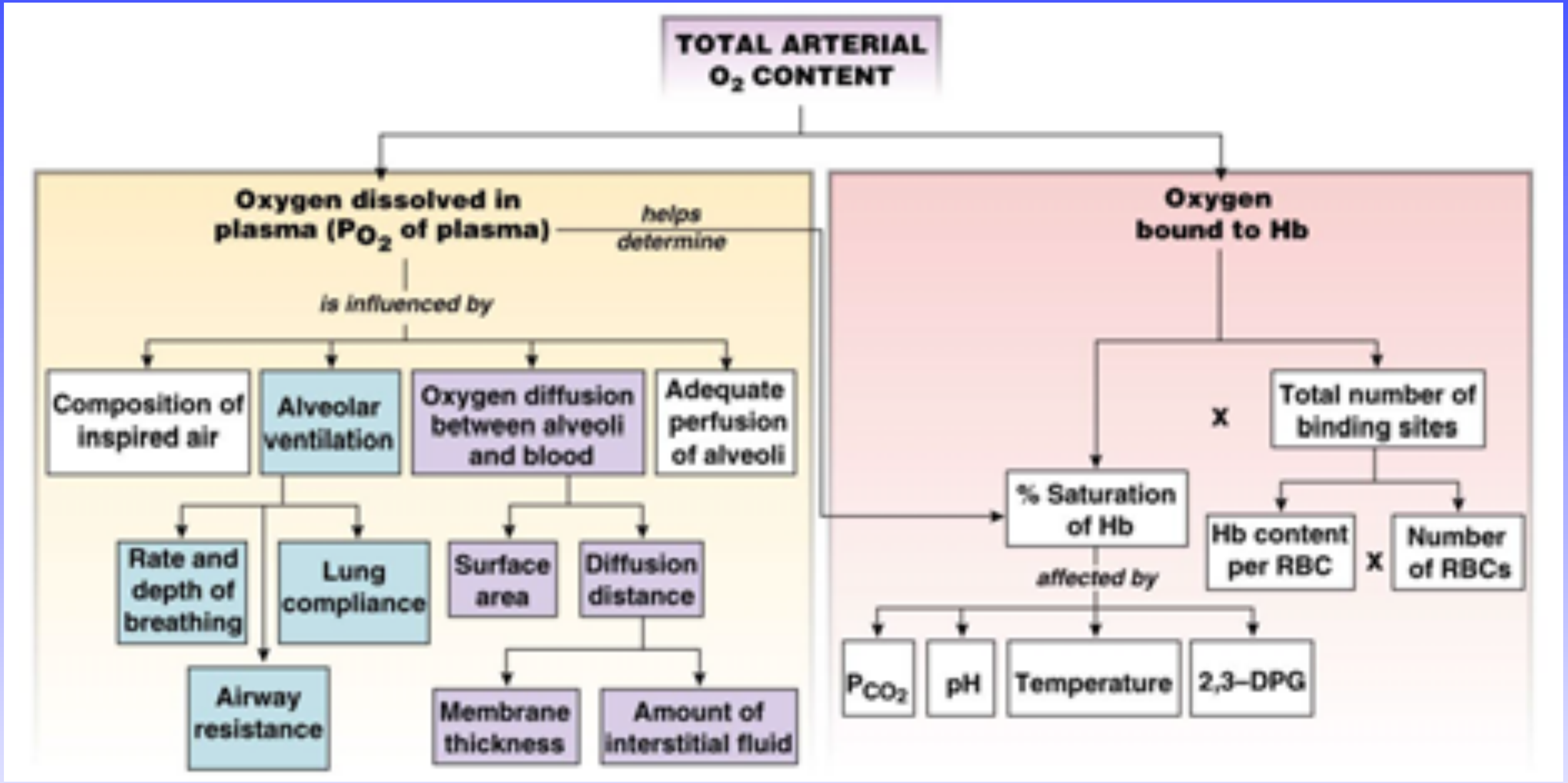
- *Gas gland excretes lactic acid*
- *Acidity causes hemoglobin of the blood to lose its oxygen*
- *Oxygen diffuses into the bladder while flowing through a complex structure known as the rete mirabile*





Summary of oxygen transport

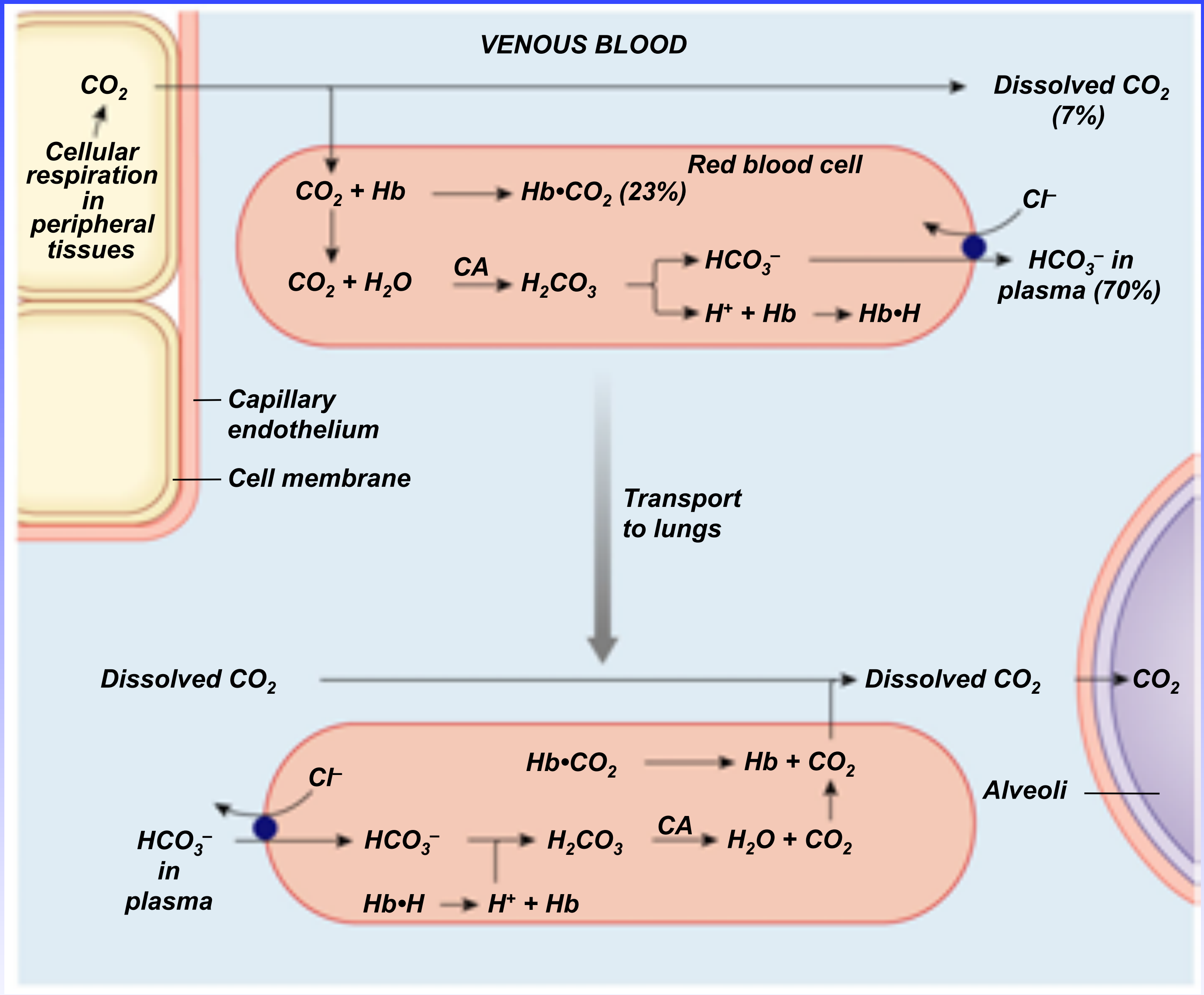
Factors contributing to the total oxygen content of arterial blood



Carbon Dioxide Transport

- ***Carbon dioxide is more soluble in body fluids than oxygen***
- Little CO_2 is transported in the plasma
- Some CO_2 binds to proteins = *carbaminohemoglobin*
- Most CO_2 is transported as bicarbonate
    - $CO_2 + H_2O \Leftrightarrow H_2CO_3$ (carbonic acid) $\Leftrightarrow HCO_3^-$ (bicarbonate) $+ H^+$
- *Carbonic anhydrase* catalyzes the formation of HCO_3^-

Carbon Dioxide Transport



CO2 transport

At tissues:

CO_2 is produced during cellular respiration = Krebs cycle

CO_2 diffuses out into plasma

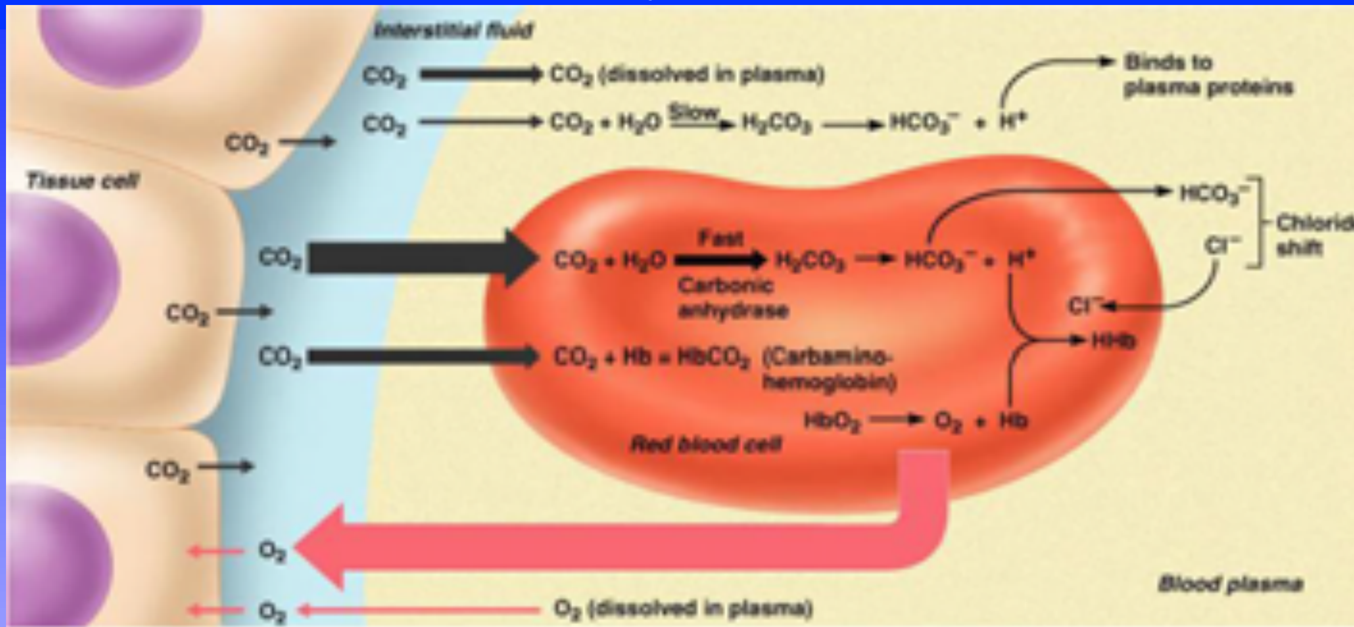
1. Some will stay in plasma dissolved
2. Most will enter RBC:
    1. Some will bind directly to Hb, after Hb has let go of O_2: Hb-C
    2. Most of it will combine with H_2O in presence of carbonic anh
        1. $CO_2 + H_2O \leftrightarrow H^+ + HCO_3^-$
            1. H^+ will bind to Hb after Hb let go of O_2: Hb-H^+
            2. HCO_3^- is removed to the plasma for exchange of Cl^- = chloride shift. Most CO_2 carried back to lungs as HCO_3^-

CO_2 transport

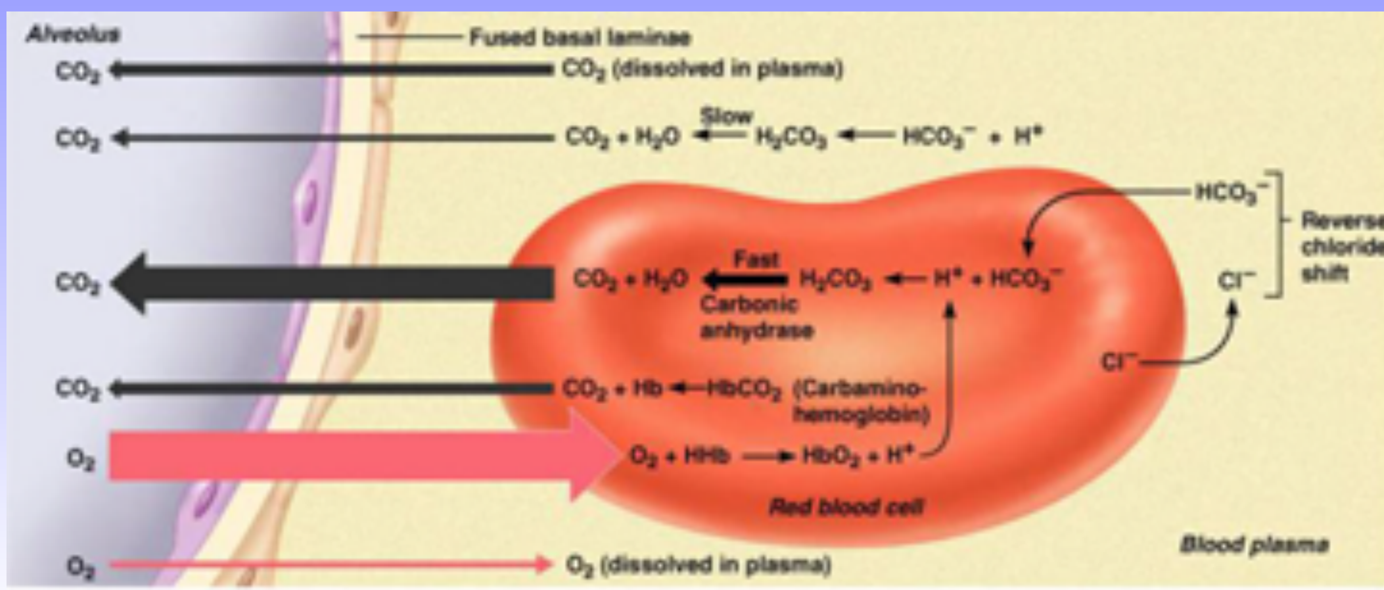
At lungs:

1. The dissolved CO_2 will diffuse out = exhale
2. Within the RBC the Hb will let go of the CO_2 and then can bind O_2. The CO_2 will diffuse out = exhale
3. HCO_3^- is brought back into RBC via reverse chloride shift = Cl^- o
   and HCO_3^- in. $Hb\text{-}H^+$ = will let go of H^+ and so Hb can bind O2
   Then : $HCO_3^- + H^+ \leftrightarrow CO_2 + H_2O$

Carbon Dioxide Transport



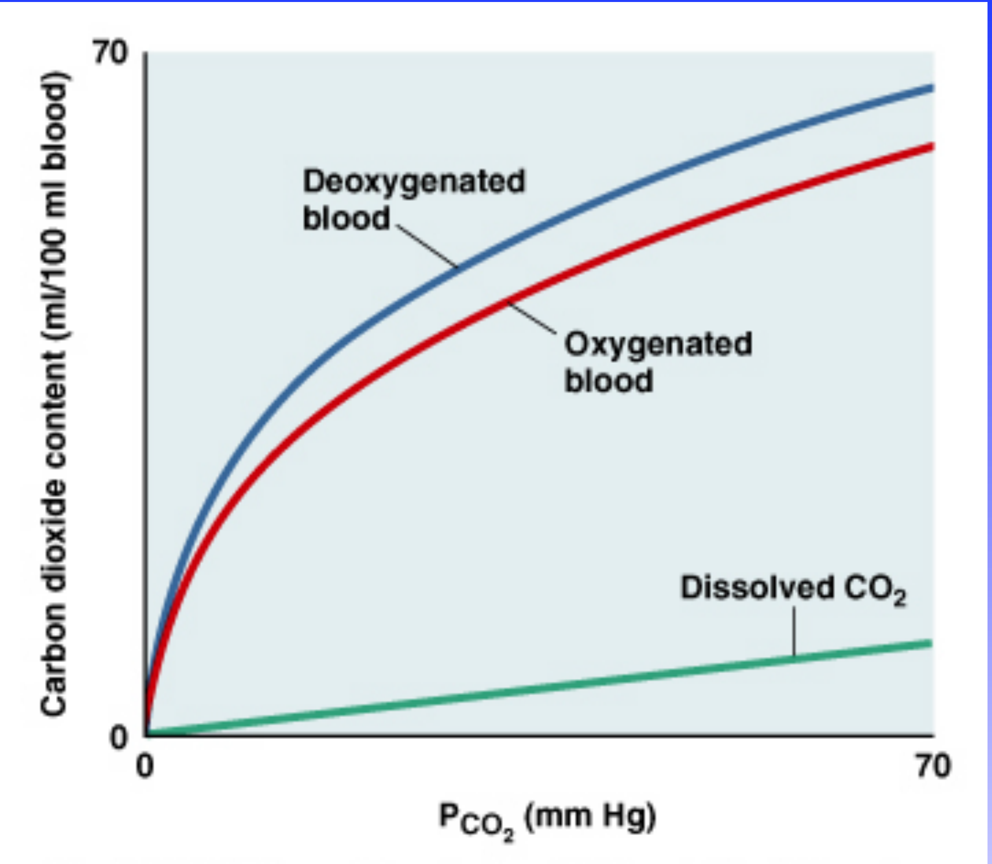
(a) Oxygen release and carbon dioxide pickup at the tissues



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

Carbon Dioxide Equilibrium Curve

- Shows the relationship between P_{CO2} and the total CO_2 content of the blood
- The shape of the curve depends on the kinetics of HCO_3^- formation
- Deoxygenated blood can carry more CO_2 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

→results in CO_2 buildup in blood (high P_{CO_2}) = **hypercapnia**

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

→ results in abnormally low P_{CO_2} = **hypocapnia**

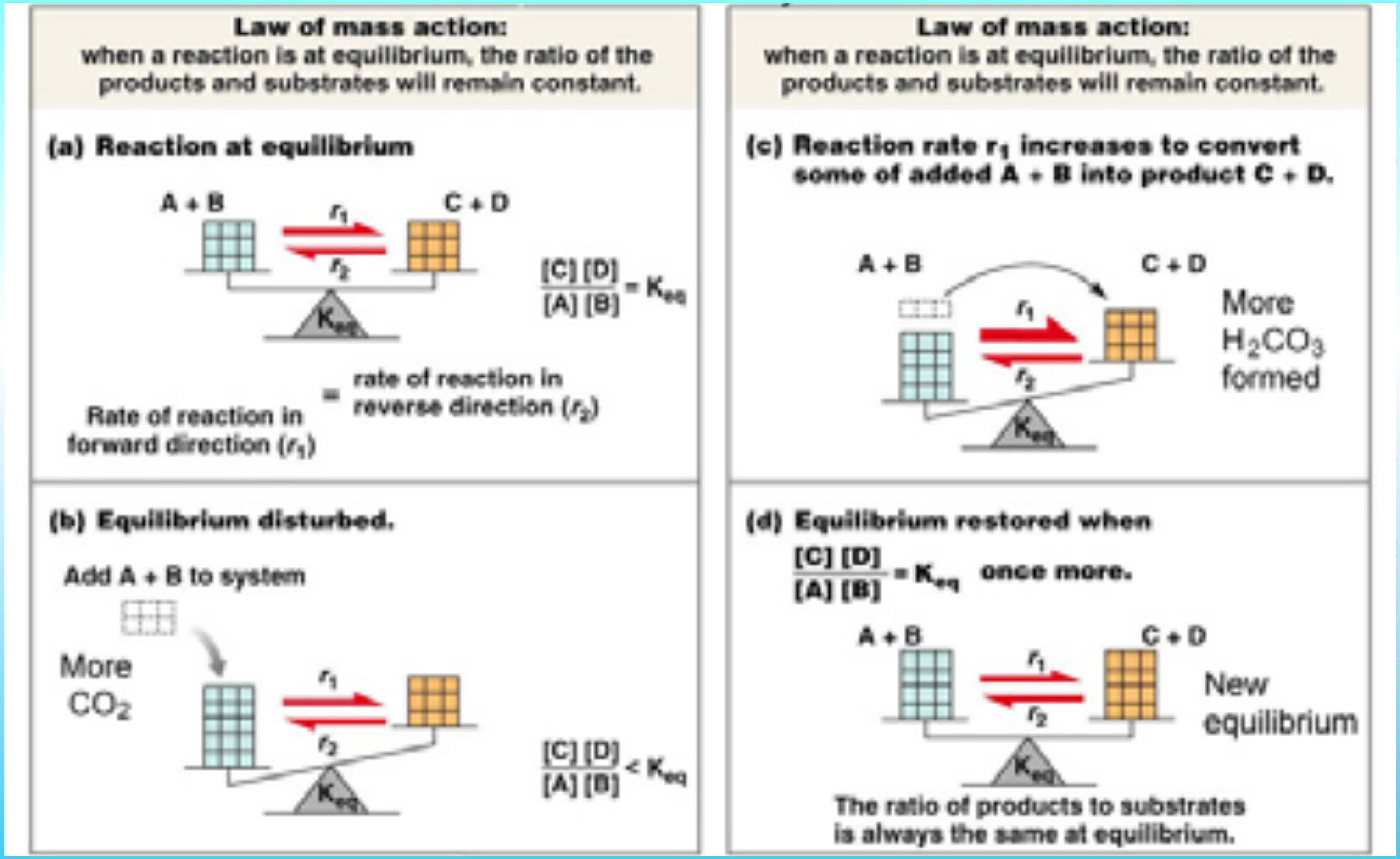
- **Acidosis: ↓ plasma pH = due to increase in H+. Increase in CO2 leads to increase in H+**
- **Alkalosis: ↑ plasma pH = due to decrease in H+. A decrease in CO2 leads to a decrease in H+**

CO2 + H2O ↔ H+ + HCO3-

The effects of CO2 on acid-base homeostasis…

Law of mass action

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



CO_2 and acid-base disturbances

1. **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+

$$CO_2 + H_2O \Leftarrow H_2CO_3 \Leftarrow HCO_3^- + \Uparrow H^+$$

- **How can we fix it?**
  - **Hyperventilate ie CO_2 can be blown off at the lungs**
  - **Renal (kidneys) compensation** - Secretion of H^+ and reabsorption of bicarbonate. Only if kidneys are functioning properly

CO_2 and acid-base disturbances

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

$$\Uparrow \mathbf{CO_2} + H_2O \Rightarrow H_2CO_3 \Rightarrow HCO_3^- + H^+$$

- **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**

CO_2 and acid-base disturbances

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+

$$CO_2 + H_2O \Rightarrow H_2CO_3 \Rightarrow HCO_3^- + \Downarrow \mathbf{H^+}$$

- **How do we fix it?**
- **Must make more H+ as we are losing H+**
  - **Hypoventilate - keep CO2 ie** PCO_2 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

CO_2 and acid-base disturbances

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**

$$\Downarrow \mathbf{CO_2} + H_2O \Leftarrow H_2CO_3 \Leftarrow HCO_3^- + H^+$$

- **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

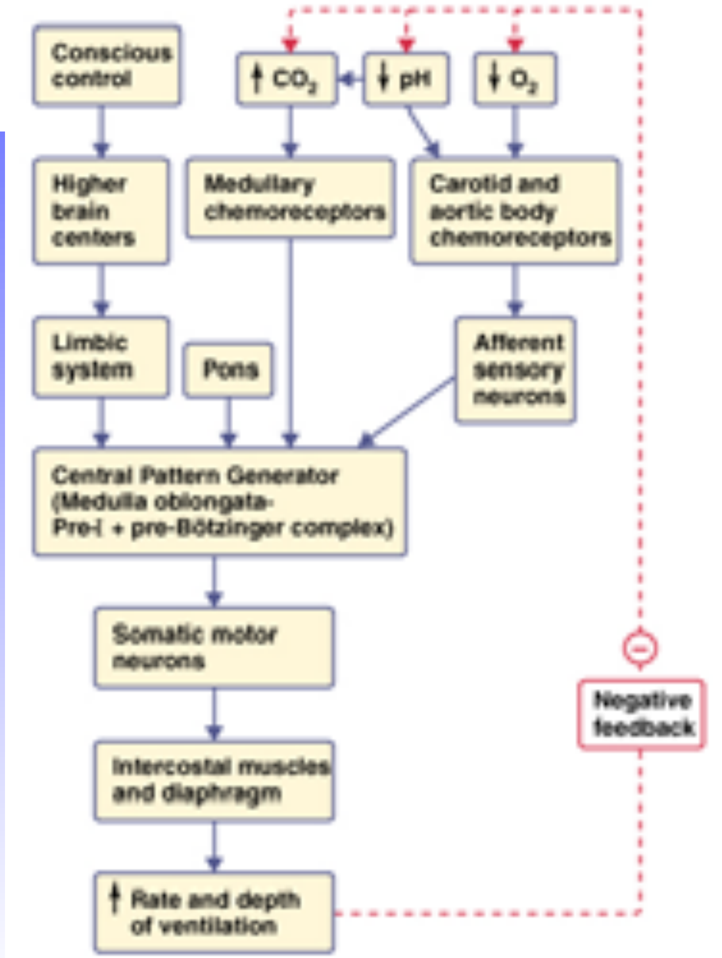
- Ventilation is an automatic process
- Continues even when we are unconscious
- Central pattern generator in medulla

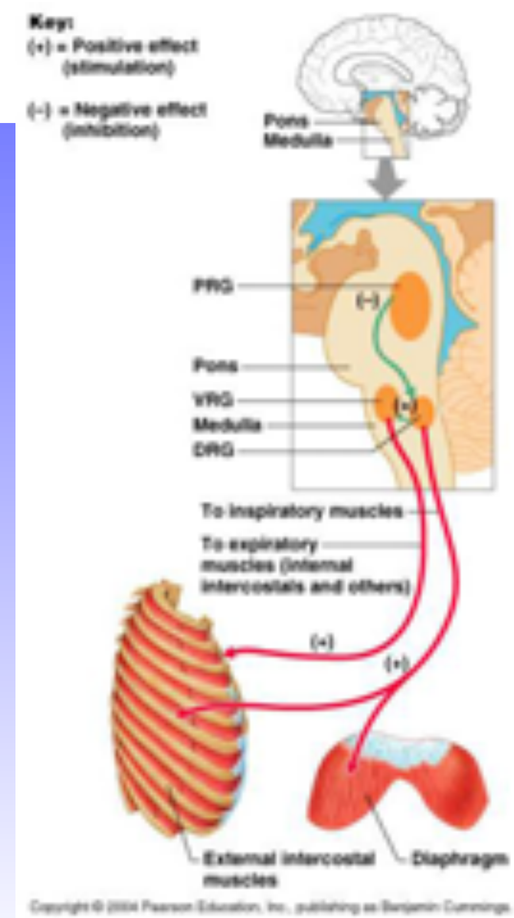
- Rhythmic firing of *central pattern generators* within the medulla initiate ventilatory movements

- 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 CO_2, H^+, and O_2
- Oxygen is the primary regulator in water-breathers while CO_2 is the primary regulator in air-breathers





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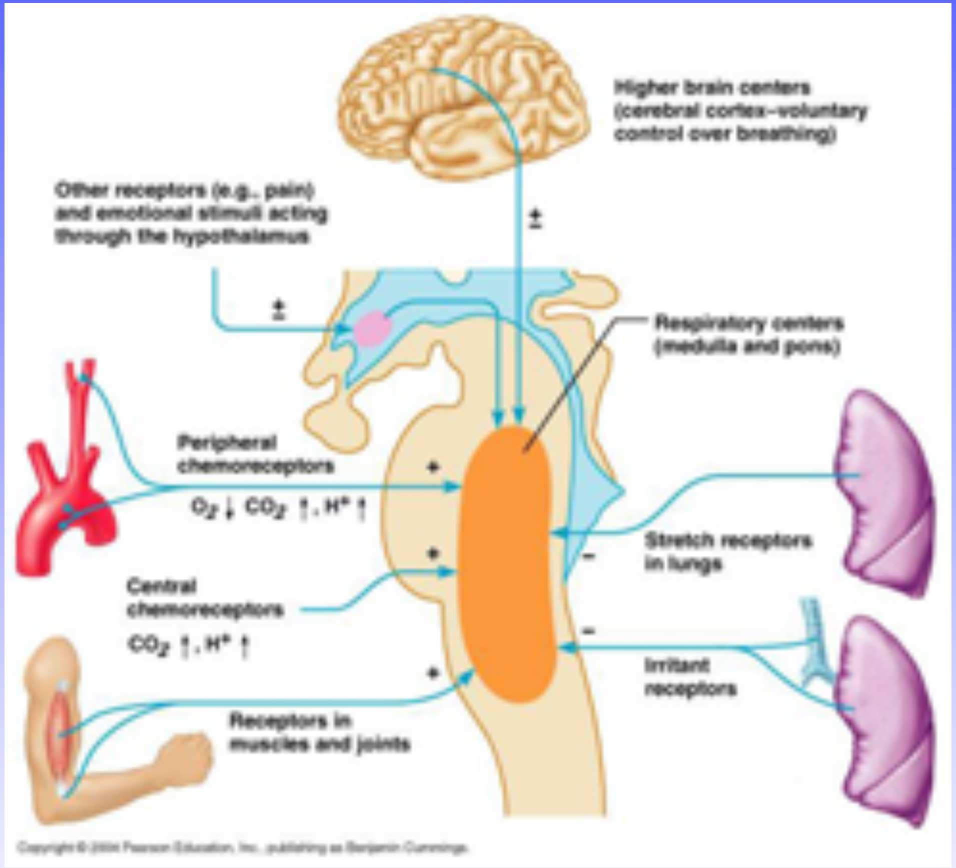
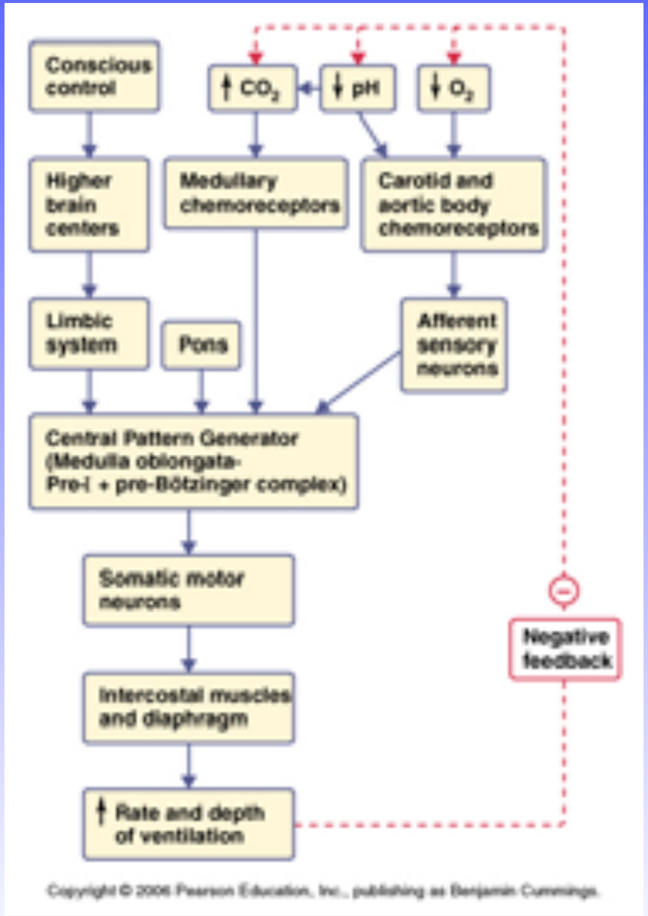
Regulation of ventilation

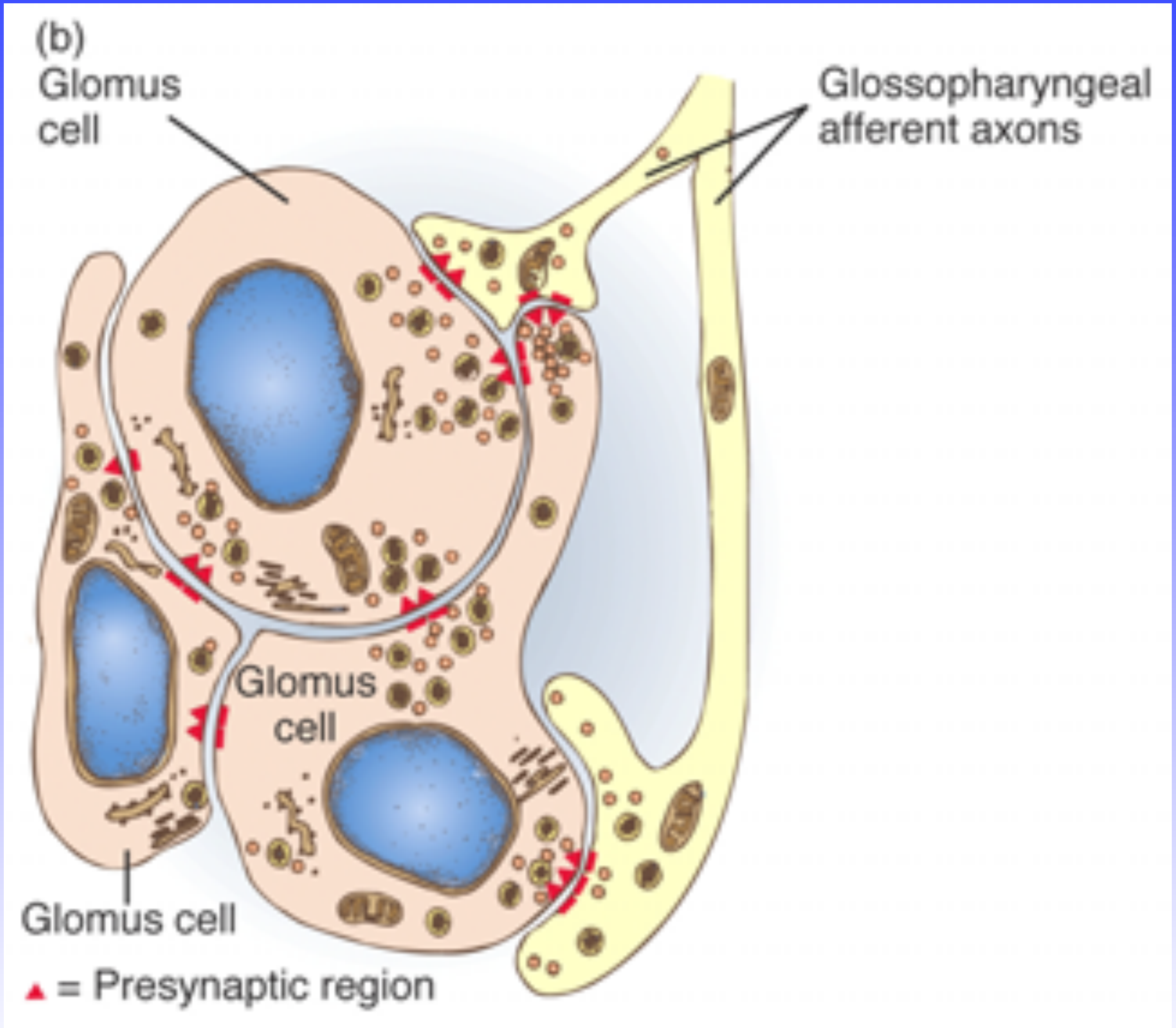
- Ascending sensory input comes from chemosensory neurons in carotid and aortic bodies, in vasculature of lungs, and chemoreceptors in the medulla
- Modulates the rate and depth of breathing
- Negative feedback loop to maintain blood PO_2 and PCO_2 within a narrow range



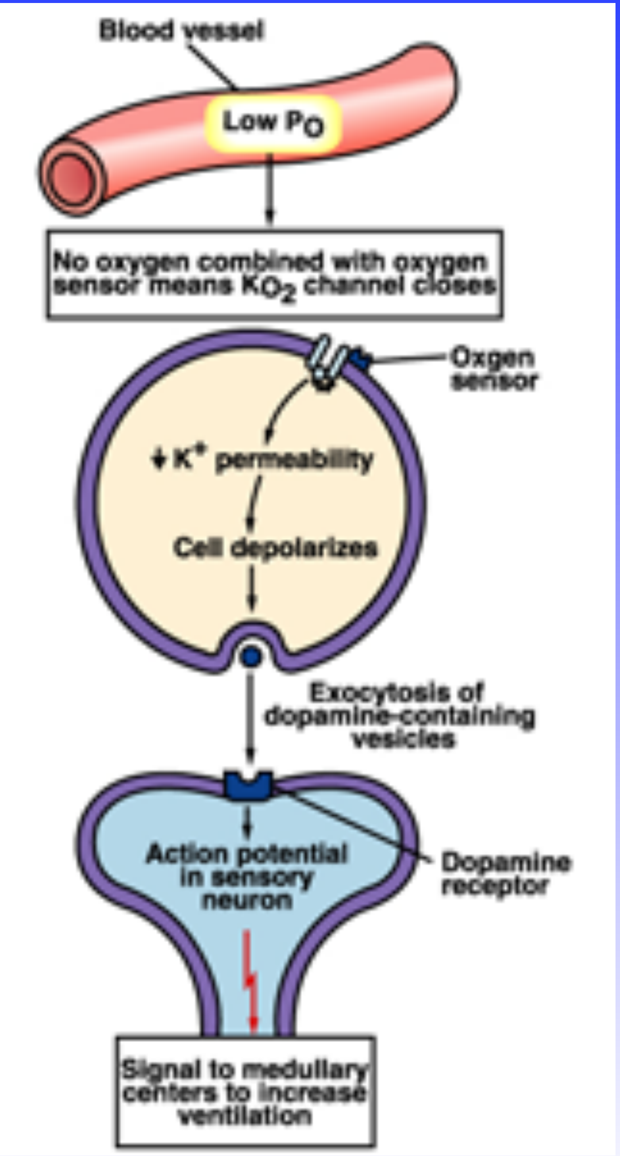


Carotid and aortic chemoreceptors

Glomus cells = chemosensory cells



Low PO2 and mechanism in carotid body

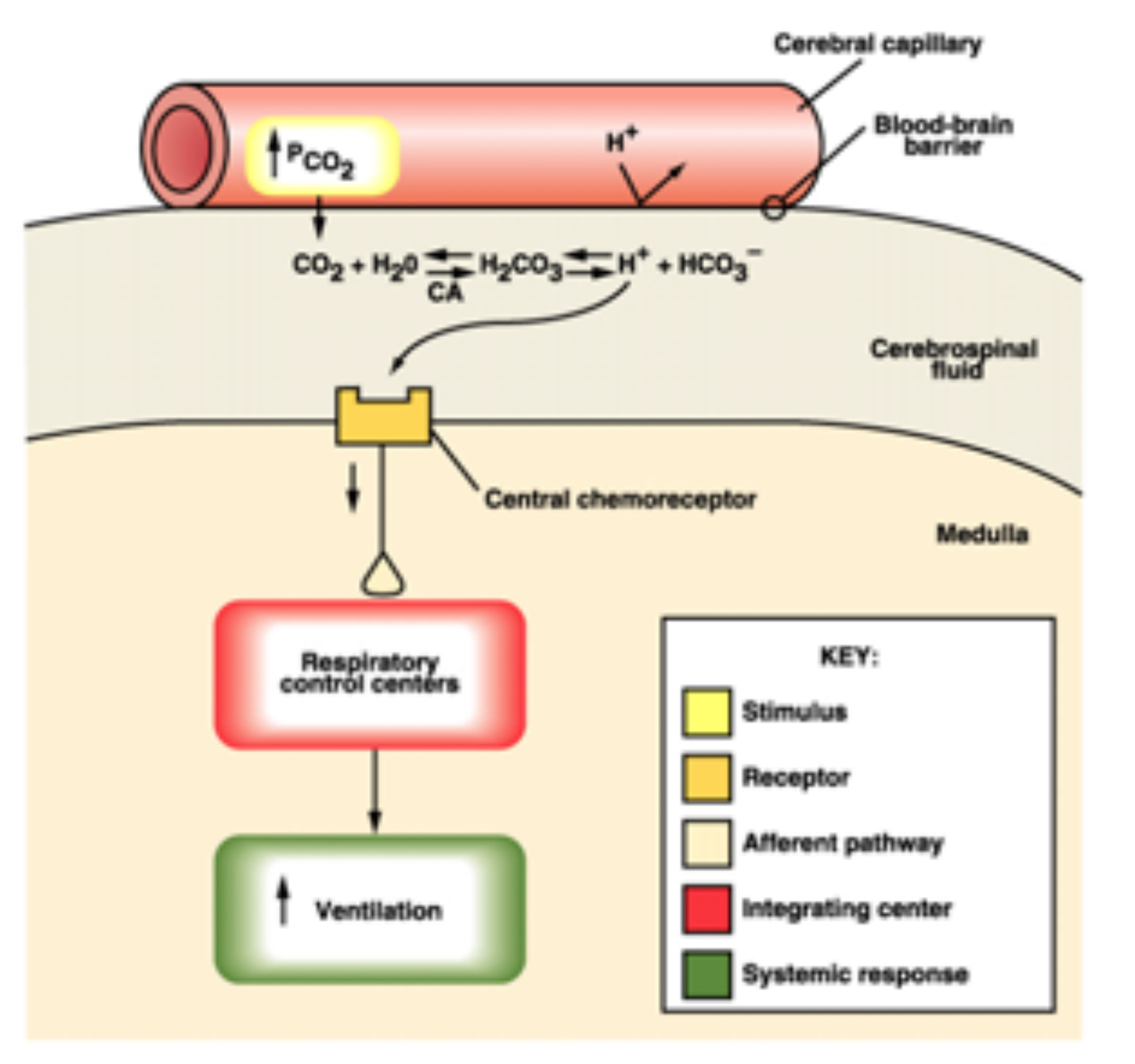


Glomus cells contain oxygen-gated K^+ channels

1. Oxygen sensor detects low PO_2
2. Closes K^+ channels = keep K+ inside cells
3. Cell depolarizes = makes cells more positive
4. 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

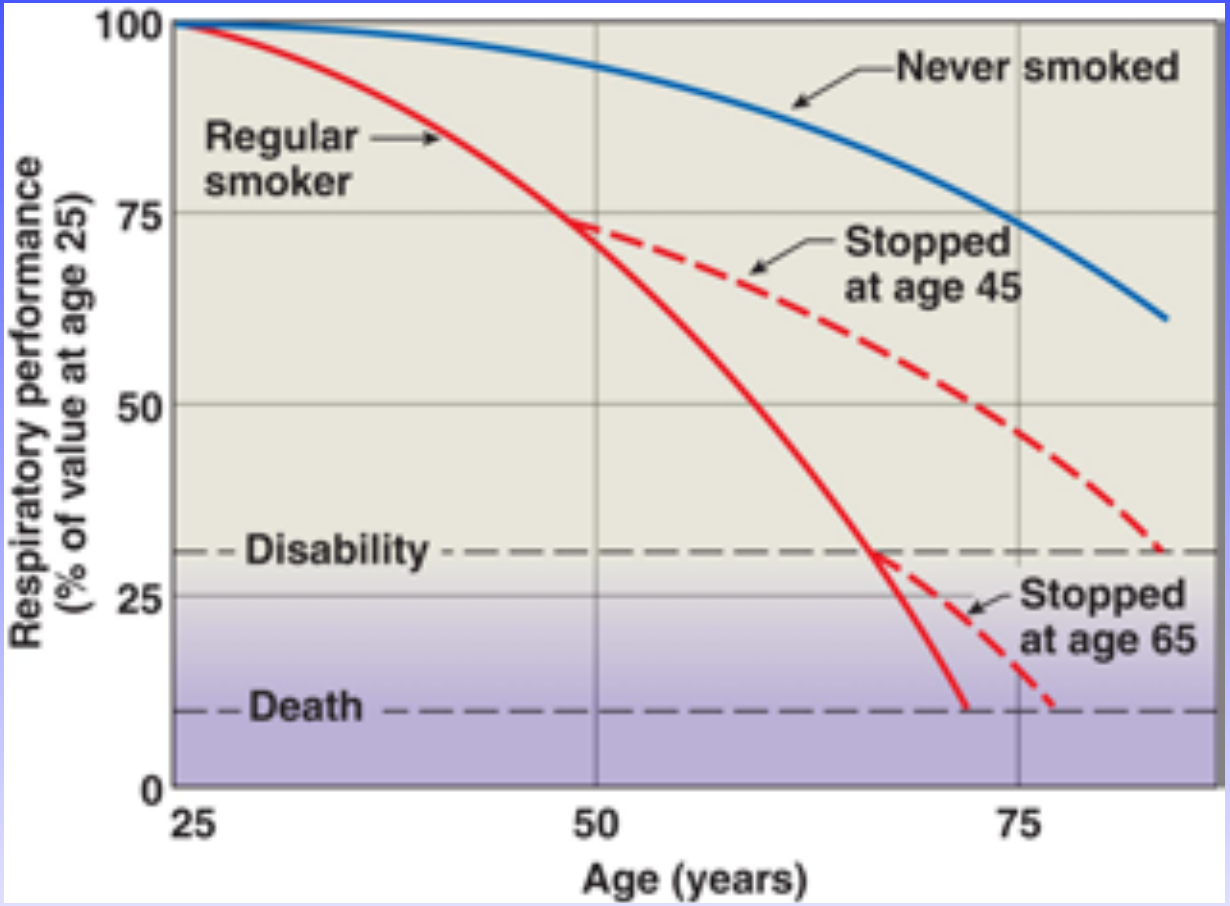
High altitude = get less O2 per breath. Still 21% O2 but PO2 lower

High PCO2 and mechanisms in central chemoreceptors



- Most important controllers in mammals
- Sensitive to changes in PCO_2 and pH
- CO_2 crosses blood/brain barrier
- Carbonic anhydrase converts CO_2 to HCO_3^- 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 (PaO_2 low)*
2. *CO_2 production normal*
3. *Arterial/Carotid chemoreceptors sense low O_2*
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 PO_2*
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

Species	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

Graciously provided by Dr. M. Gardner and modified by Dr. C. Gerin

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 function of surfactants? ____
- How does your body fix a respiratory acidosis? ____________________________________
- What is the significance (why do they matter) of Henry's law, Boyle's law and Dalton's law to the process of respiration? Explain why these laws matter in relation to the respiratory system.

____

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- Diffusion rate increases with a decrease in molecular weight. True or False

Last slide for Test 1