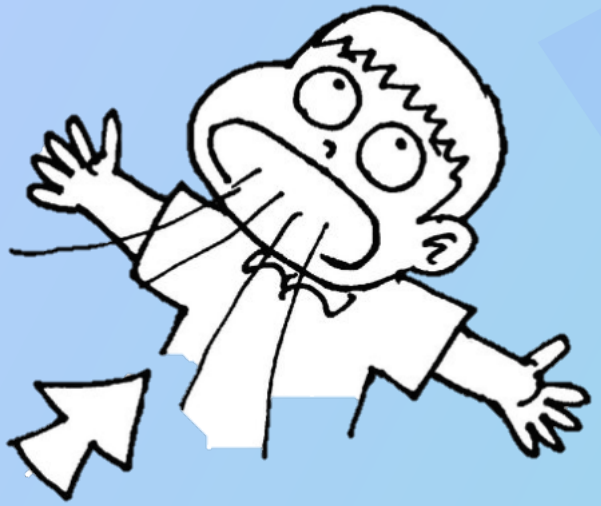
Ventilation/ Perfusion Relationships

And then some…



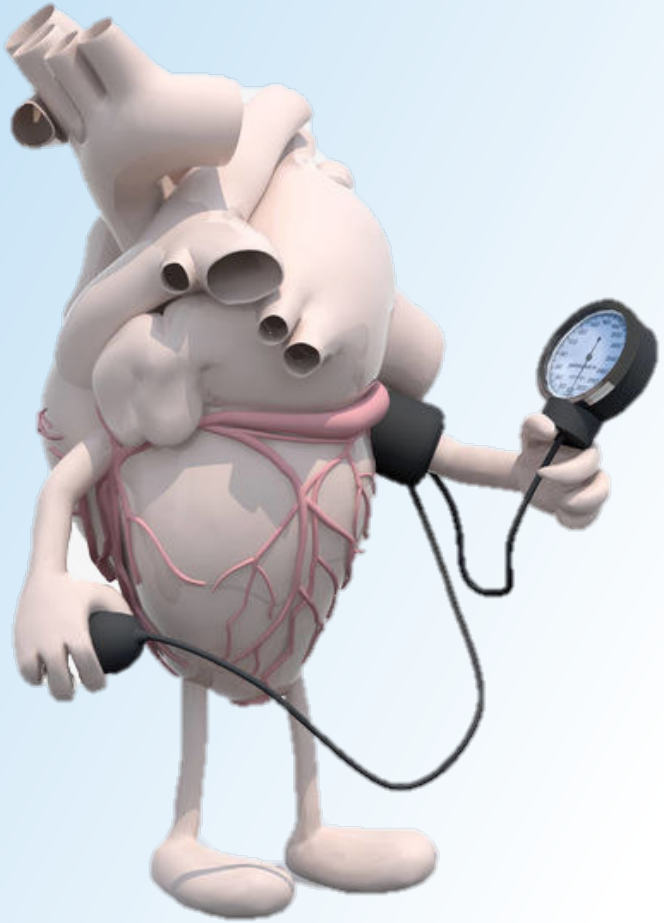
Pulmonary blood flow

Not quite like systemic circulation

[Blood flow] = [blood flow in systemic circulation]

BUT

- Much lower pressures (25/8)
- Much lower resistances
- Hypoxic vasoconstriction!



Hypoxic vasoconstriction

- Decreases in PA_{O2} causes pulmonary vasoconstriction
  - Opposite effect is seen in other vascular beds
- Redirects blood flow to well-ventilated regions of the lung
  - Protective in certain lung diseases (no change in pulmonary resistance)

- Mechanism:
  - Determined by ALVEOLAR O_2 ($PA_{O2} < 70$ mm Hg)
  - May also be determined by NO?

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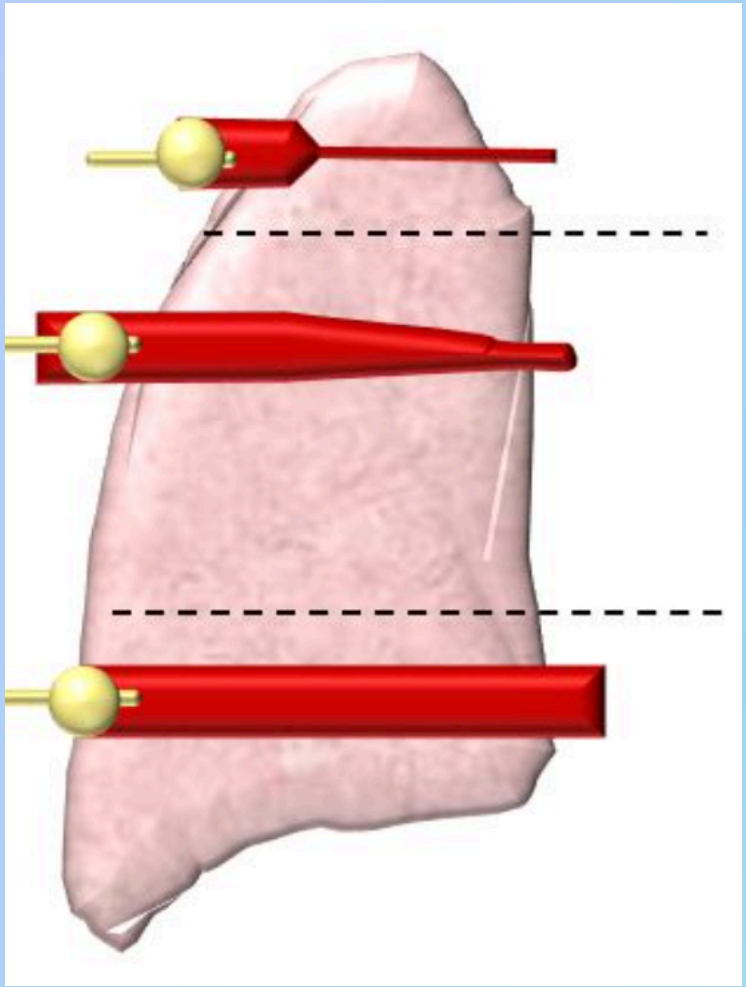
Other regulators of blood flow

- Thromboxane A_2 – constricts
- Prostacyclin (prostaglandin I_2) – dilates
- Leukotrienes – constrict *airways*

Substance	Concentration	Lumen diameter
Oxygen	Decreased ↓	Decreased ↓
NO	Increased ↑	Increased ↑
Thromboxane A_2	Increased ↑	Decreased ↓
Prostacyclin	Increased ↑	Increased ↑
Leukotrienes	Increased ↑	Decreased ↓

Distribution of blood flow

Distribution throughout the lung is uneven due to *gravity*



- Zone 1:
  - Alveolar pressure (P_A) > arterial pressure (P_a) > P_V
  - Low flow rate
- Zone 2:
  - $P_a > P_A > P_V$
  - Blood flow is driven by the difference between P_a and P_A, not P_a and venous pressure (P_V)
- Zone 3:
  - $P_a > P_V > P_A$
  - Blood flow is driven by P_a-P_V gradient
  - Highest flow rate, most open capillaries

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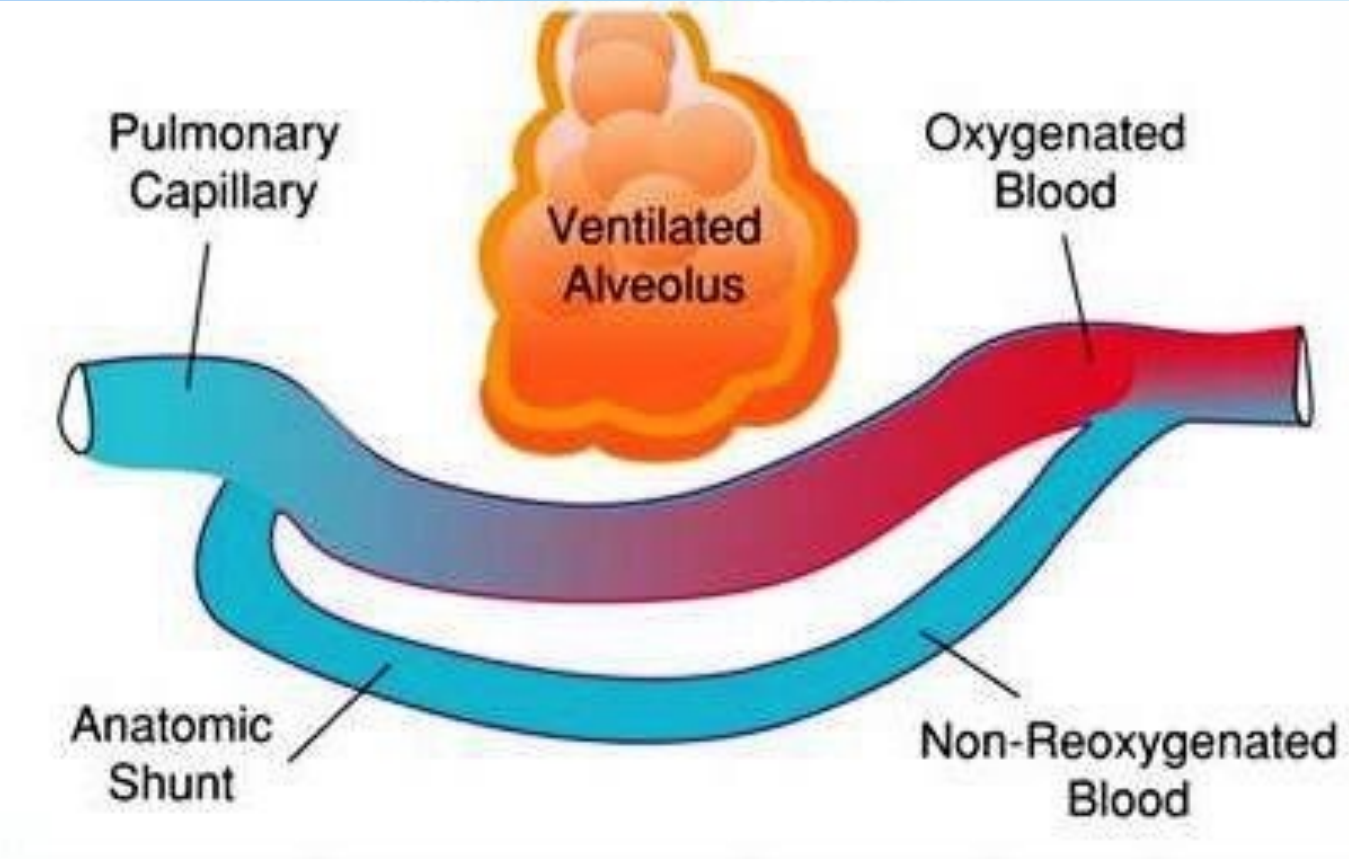
Shunts

A portion of blood flow that is diverted or rerouted



Types of shunts:

Physiologic

- 2% of blood normally bypasses the alveoli
- Bronchial blood flow
- Coronary blood flow draining directly to left ventricle

Right-to-Left

- Shunting from right heart to left heart
- VSD
- Uncorrectable hypoxemia always occurs
- Pa_{CO2} changes minimally

Left-to-Right

- Shunting from left heart to right heart
- PDA, trauma
- Do not cause hypoxemia
- PO_2 in right heart is increased

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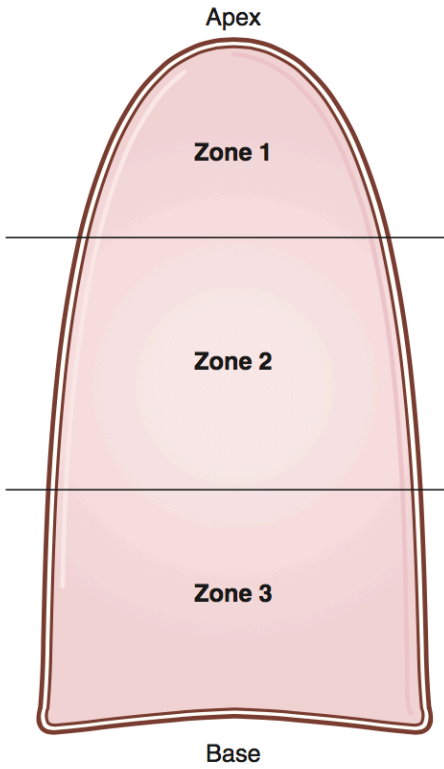
Ventilation/ Perfusion Ratios (V/Q)

$\dot{V}/\dot{Q}$ DISTRIBUTION IN THE LUNG



	Blood Flow ($\dot{Q}$)	Alveolar Ventilation ($\dot{V}$)	$\frac{\dot{V}}{\dot{Q}}$	Pa_{O_2}	Pa_{CO_2}
Zone 1	Lowest	Lower	Highest (3.0)	Highest (130 mm Hg)	Lower (28 mm Hg)
Zone 2	—	—	—	—	—
Zone 3	Highest	Higher	Lowest (0.6)	Lowest (89 mm Hg)	Higher (42 mm Hg)

Average V/Q = 0.8

← ↓ V / ↓↓ Q = ↑ V/Q

← ↑ V / ↑↑ Q = ↓ V/Q

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V/Q mismatch

Result in abnormal gas exchange

Dead space (V/Q = ∞)

- Ventilation of areas of lung that are not perfused
- Alveolar gas = humidified inspired air
  - PA_{O2} = 150 mm Hg, PA_{CO2} = 0
- Bl∞d flow obstruction

Shunt (V/Q = 0)

- Perfusion of areas of lung that are not ventilated
- Pulmonary capillary blood = mixed venous blood
  - PA_{O2} = 40 mm Hg, PA_{CO2} = 46 mm Hg
- “Oirway” obstruction

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What we've covered so far…

- How pulmonary blood flow compares to systemic blood flow
- Regulation of pulmonary blood flow
- Distribution of pulmonary blood flow
- Shunting
- How ventilation and perfusion are related (V/Q)
- V/Q mismatch

Up next: regulation of breathing

Control of Breathing

Both frequency and depth of breathing are tightly regulated

Four components to control system:

1. Chemoreceptors
2. Mechanoreceptors in lungs and joints
3. Control centers in the brainstem (medulla + pons)
4. Respiratory muscles
    - Directed by the brain stem centers

Chemoreceptors

Send sensory information to the brain stem concerning Pa_{O2}, $Pa_{CO2,}$ and arterial pH

Central

- Located in the brain stem, communicate directly with the inspiratory center
- Respond directly to changes in pH of CSF, indirectly to changes in arterial PCO_2
- Changes breathing rate (up OR down)

Peripheral

- Located in carotid bodies and aortic bodies
- Responds to arterial O_2, CO_2, and H^+
- Increases breathing rate in response to:
  1. *Decreases in arterial PO_2 (<60 mm Hg)*
  2. Increases in arterial PCO_2
  3. Decreases in arterial pH (carotid bodies)

Central = **C**O_2

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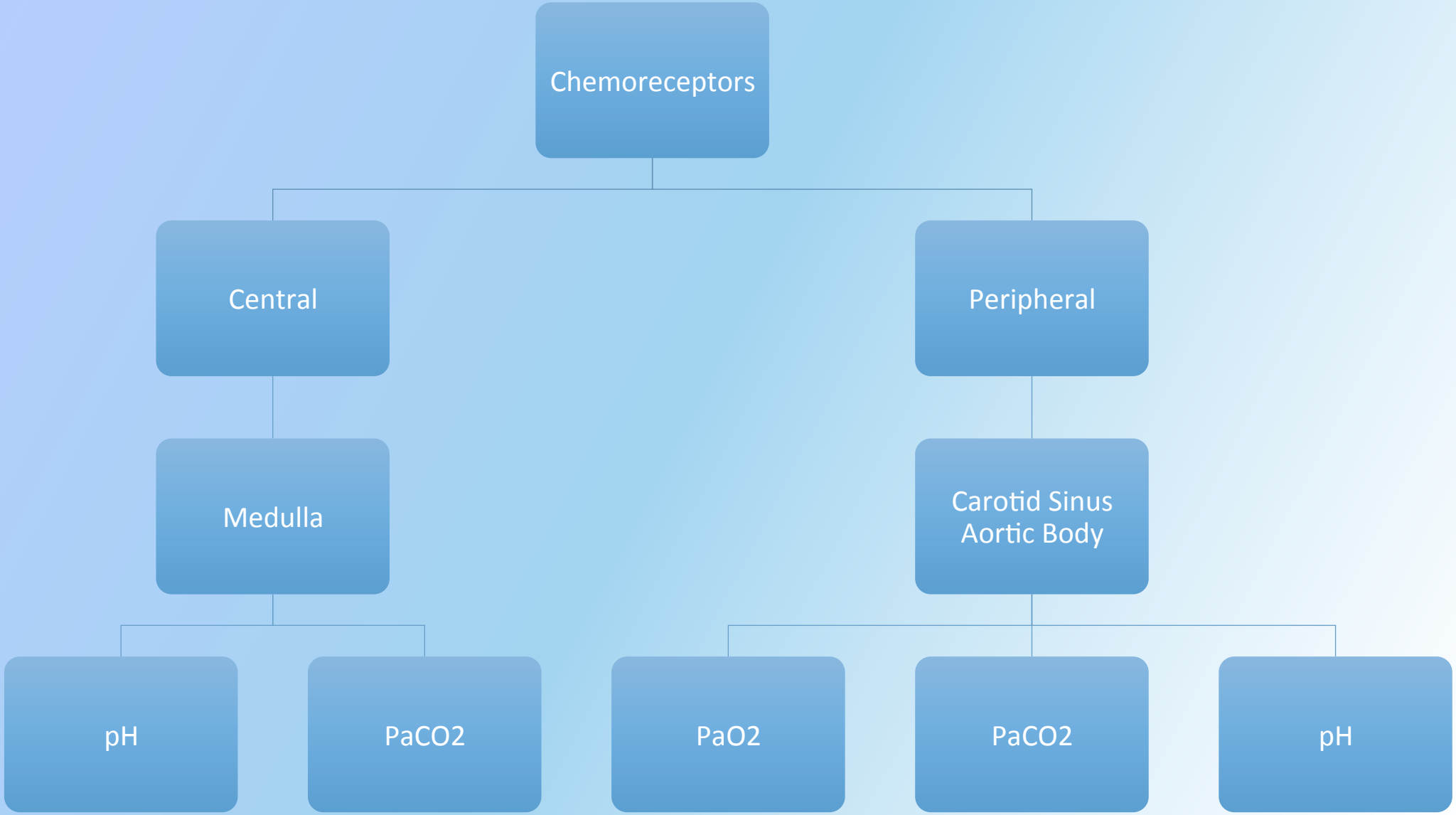
Chemoreceptors
Central
Peripheral
Medulla
Carotid Sinus
Aortic Body
pH
PaCO2
PaO2
PaCO2
pH

Brain stem control of breathing

- The frequency of normal, involuntary breathing is controlled by:
  1. Medullary respiratory center
  2. Apneustic center
  3. Pneumotaxic center

Medullary Respiratory Center

- Located in the MEDULLA, reticular formation
- Anatomically distinguished into:
  - Inspiratory center (dorsal respiratory group)
  - Expiratory center (ventral respiratory group)

- DRG controls the frequency of inspiration
  - Receives sensory input from peripheral chemoreceptors via CN IX and CN X, and from mechanoreceptors in the lungs via the vagus nerve
  - Sends motor output to diaphragm via phrenic nerve

- VRG is usually inactive, but becomes activated during exercise

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Brain stem control of breathing

- The frequency of normal, involuntary breathing is controlled by:
  1. Medullary respiratory center
  2. Pneumotaxic center
  3. Apneustic center

Pneumotaxic Center

- Located in upper pons
- Turns off inspiration (i.e limits the amount of action potentials in the phrenic nerve)
  - Limits the size of the tidal volume
  - Regulates respiratory rate
- Normal breathing rate persists even without this center (Costanzo); lesion to it causes apneustic breathing (Kaplan)

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Brain stem control of breathing

- The frequency of normal, involuntary breathing is controlled by:
  1. Medullary respiratory center
  2. Pneumotaxic center
  3. Apneustic center

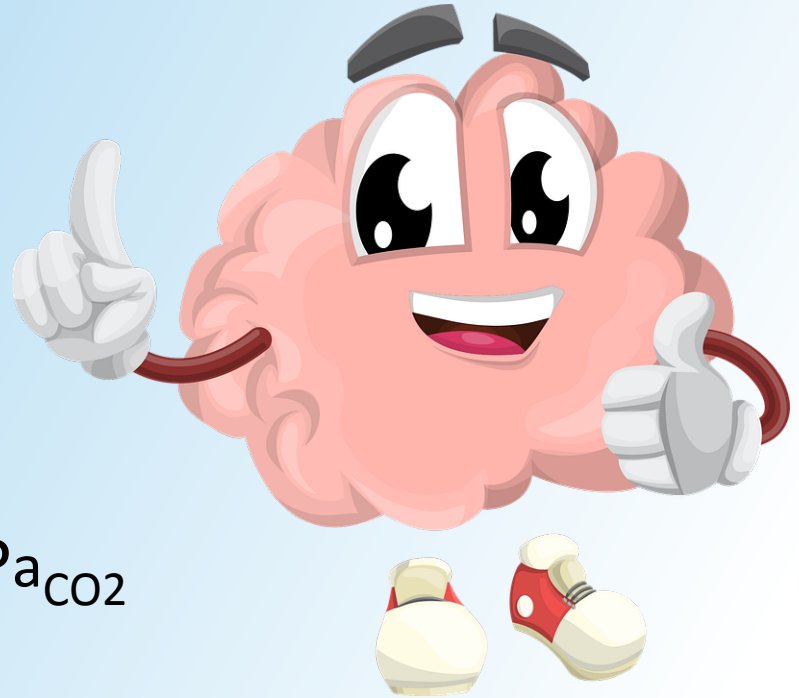
Apneustic Center

Apneusis – an abnormal breathing pattern characterized by prolonged inspiratory gasps, followed by brief expiratory movement

- Located in the lower pons
  - Controlled by pneumotaxic center
- Excites the inspiratory center (medulla), prolonging the action potentials of the phrenic nerve

Honorable mention: cerebral cortex

- Can temporarily override the brain stem centers
- Self-limited



- Hyperventilation → decrease in Pa_{CO2}
  - Causes increase in arterial pH
- Hypoventilation → decrease in Pa_{O2}, increase in Pa_{CO2}

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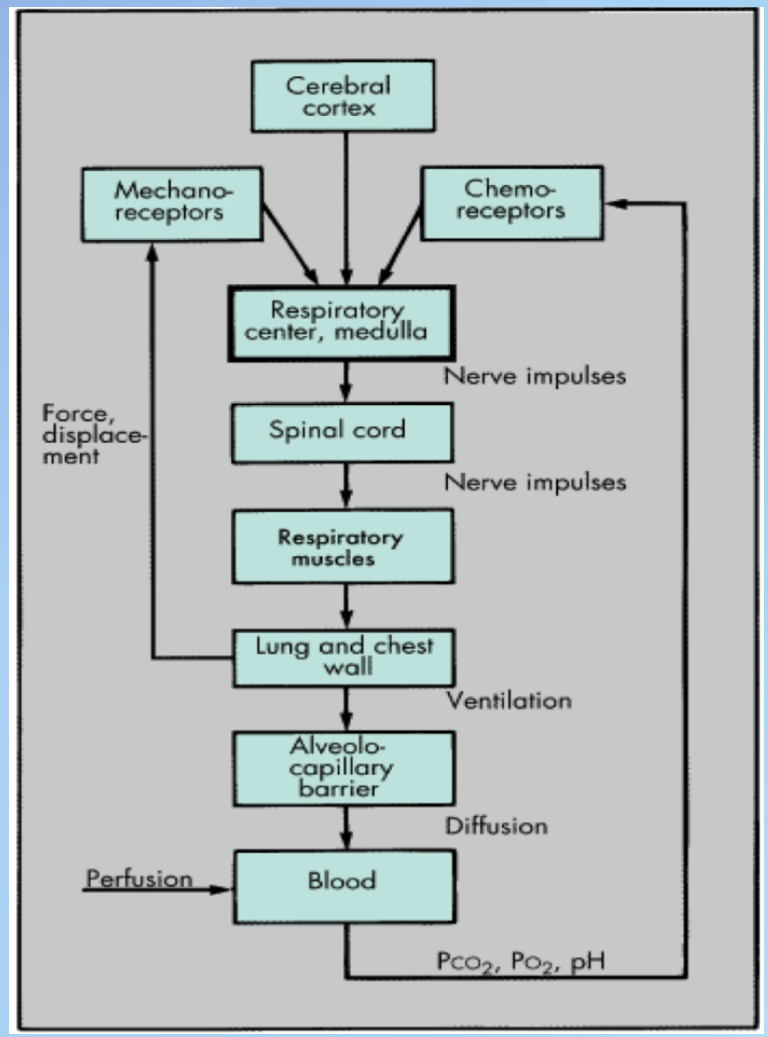
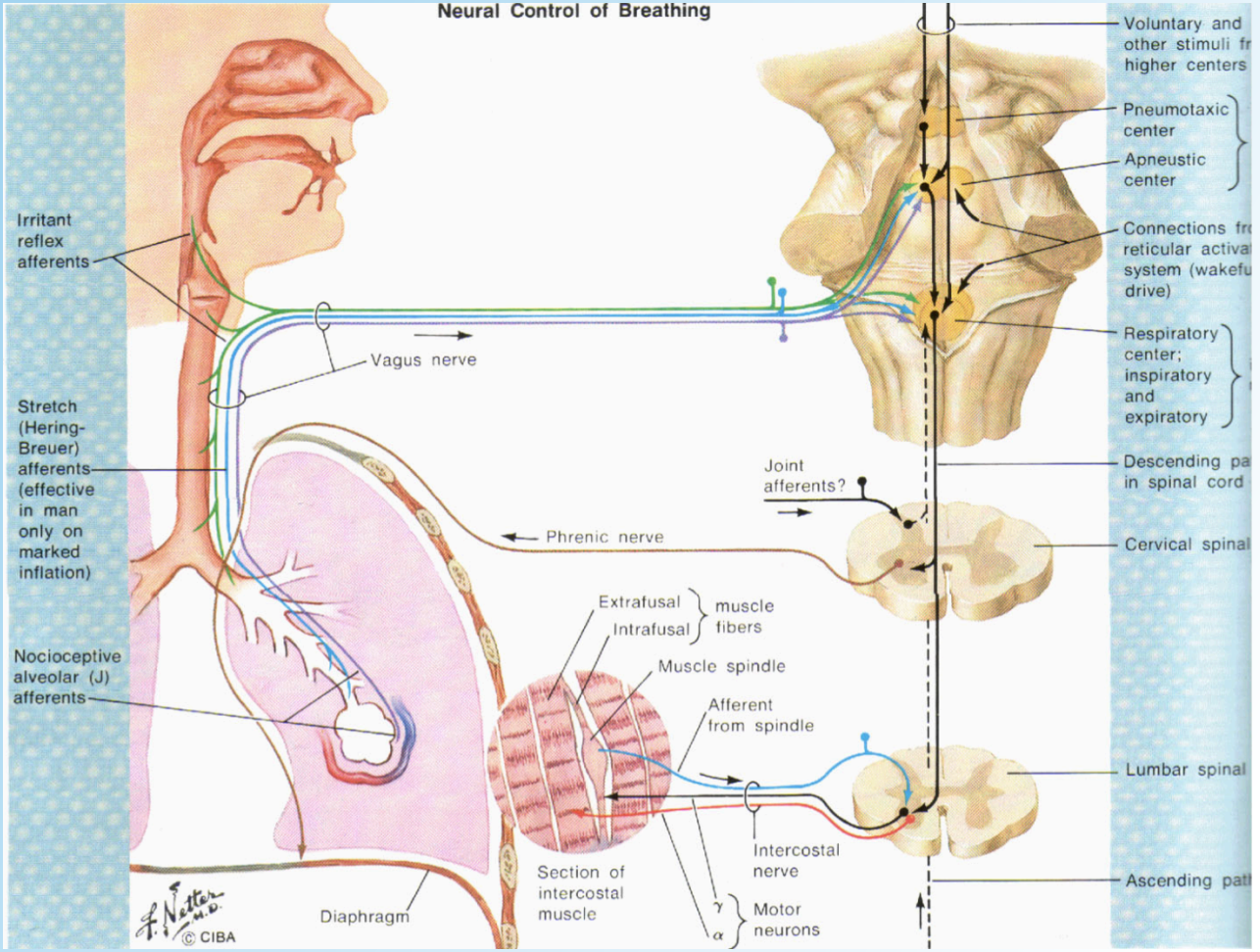

Cerebral cortex
Mechano-receptors
Chemo-receptors
Respiratory center, medulla
Nerve impulses
Spinal cord
Nerve impulses
Respiratory muscles
Force, displace-ment
Lung and chest wall
Ventilation
Alveolo-capillary barrier
Diffusion
Perfusion
Blood
P_{CO_2}, P_{O_2}, pH


Neural Control of Breathing
Voluntary and other stimuli fr higher centers
Pneumotaxic center
Apneustic center
Connections fr reticular activa system (wakefu drive)
Respiratory center; inspiratory and expiratory
Descending pa in spinal cord
Cervical spinal
Lumbar spinal
Ascending pat
Irritant reflex afferents
Vagus nerve
Stretch (Hering-Breuer) afferents (effective in man only on marked inflation)
Joint afferents?
Phrenic nerve
Extrafusal
Intrafusal
muscle fibers
Muscle spindle
Afferent from spindle
Nocioceptive alveolar (J) afferents
Intercostal nerve
Section of intercostal muscle
γ
α
Motor neurons
Diaphragm
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Integrative Functions: exercise

What happens during exercise?

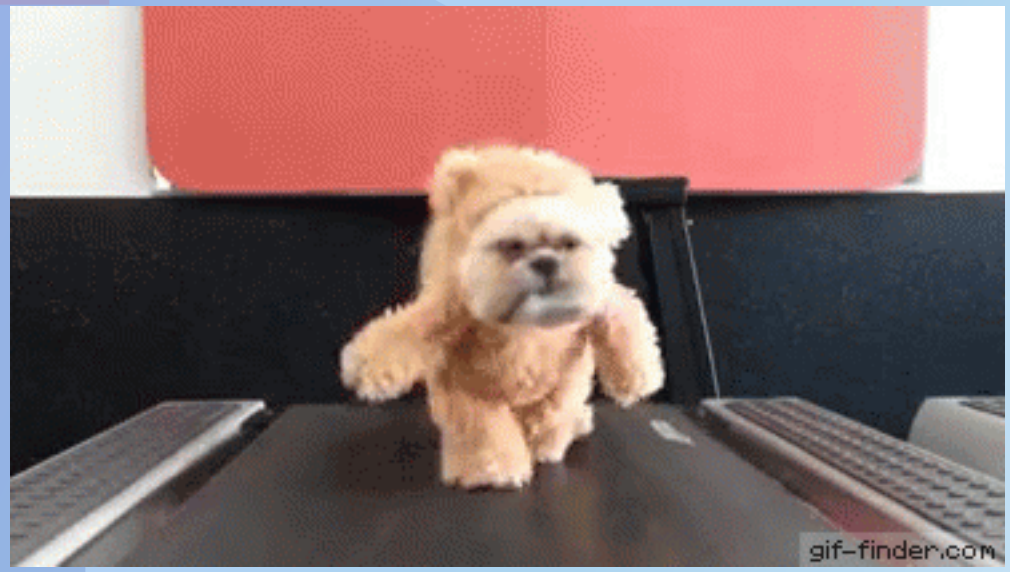
- O_2 demand is increased
- Ventilation rate is increased

Do the average arterial PO_2 and PCO_2 change?

- NO!

Does venous PCO_2 change?

- YES!



So why doesn't arterial PO_2 change?

- Increased ventilation
- Increased cardiac output
- Increased perfusion of capillary beds

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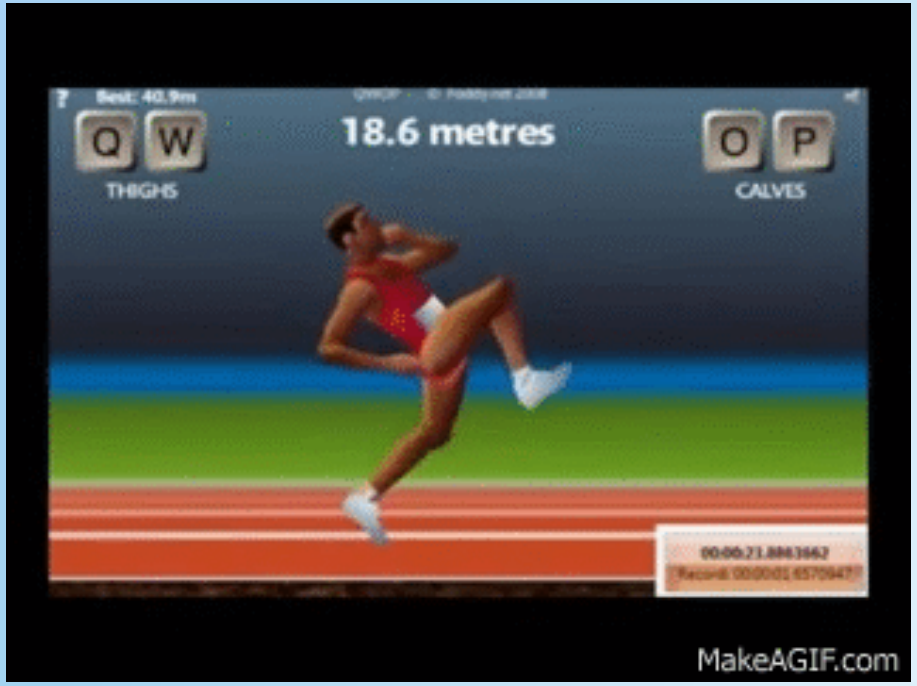
One more thing:

- Exercise shifts the oxygen dissociation curve to the right to increase O_2 unloading



Integrative Functions: high altitude

High altitudes have a decreased PO_2

So what we do about it?

1. Hyperventilate
2. Increase [RBC]
3. Increase 2,3-DPG
4. Vasoconstrict

High altitude: hyperventilation

- Most significant response
- If PO_2 < 60 mm Hg → peripheral chemoreceptors ↑breathing rate

- Good: PO_2 increases
- Bad: PCO_2 decreases
  - Causes an increase in pH and RESPIRATORY ALKALOSIS → inhibits central and peripheral chemoreceptors, decreases the breathing rate
  - Hyperventilation resumes after a couple of days

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High altitude: polycythemia

- Hypoxia in kidney leads to increased EPO synthesis
- Increase in [Hb] leads to increase in O_2 carrying capacity
  - Increases total O_2 content of blood even though arterial PO_2 is decreased

- Good: increase O2 reaching tissues
- Bad: increases blood viscosity

High altitude: ↑ 2,3-DPG

- Causes a right shift of oxygen-hemoglobin dissociation curve

- Good: makes it easier to unload O_2 in tissues
- Bad: makes it harder to load Hb with O_2 in lungs

High altitude: hypoxic vasoconstriction

- Low PA_{O2} → vasoconstriction

- Bad: increases pulmonary arterial pressure, which may cause hypertrophy of the right ventricle