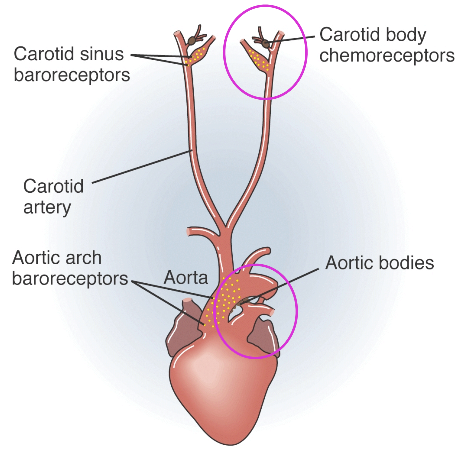
Control of Respiration

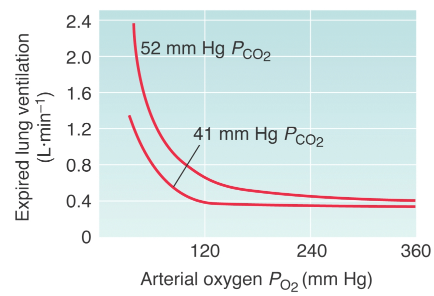
Central Control of Ventilation

- Goal: maintain sufficient ventilation with minimal energy
  - Ventilation should match perfusion
- Process steps:
  - Ventilation mechanics + aerodynamics
- Points of Regulation
  - Breathing rate and depth, coughing, swallowing, breath holding
  - Musculature: very precise control
- Sensors:
  - Chemoreceptors: central and peripheral
  - Stretch receptors in the lungs, bronchi, and bronchioles
- Feedback:
  - Nerves
  - Central processor:
    - Pattern generator of breathing depth/amplitude
    - Rhythm generator for breathing rate

Peripheral Chemosensors

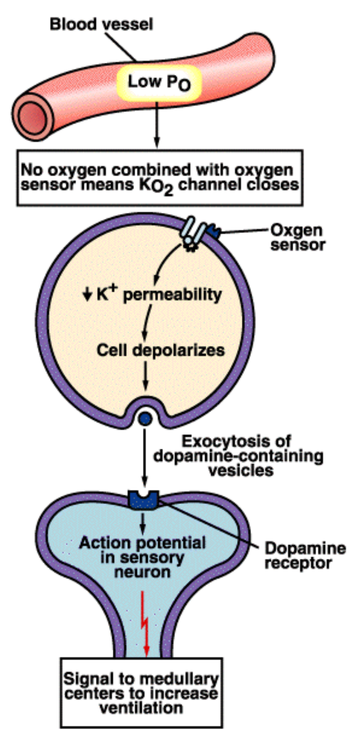
- Carotid and Aortic bodies
- Sensitive to PO_2, $PsCO_2$, and pH (CO_2 sensitivity may originate in pH)
- Responses are coupled
- Adapt to CO_2 levels
- All O_2 sensing is here!
- Carotid body sensors more sensitive than aortic bodies





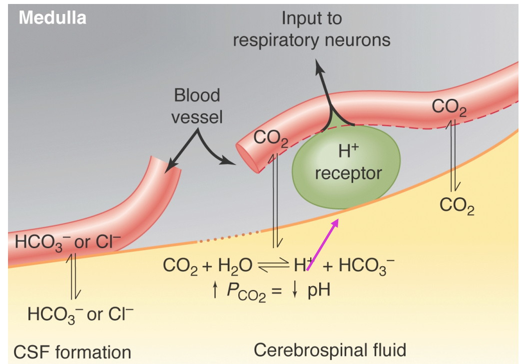
O_2 Sensor Details

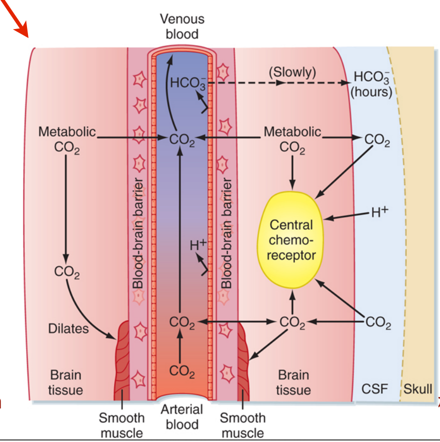
- Glomus cells
- K-channel with O_2 sensor
- O_2 opens channel and hyperpolarizes cell
- Drop in O_2 causes reduction in K current and a depolarization
- Resulting Ca^{2+} influx triggers release of dopamine
- Dopamine initiates action potentials in sensory nerve



Central CO_2/pH Chemoreceptors

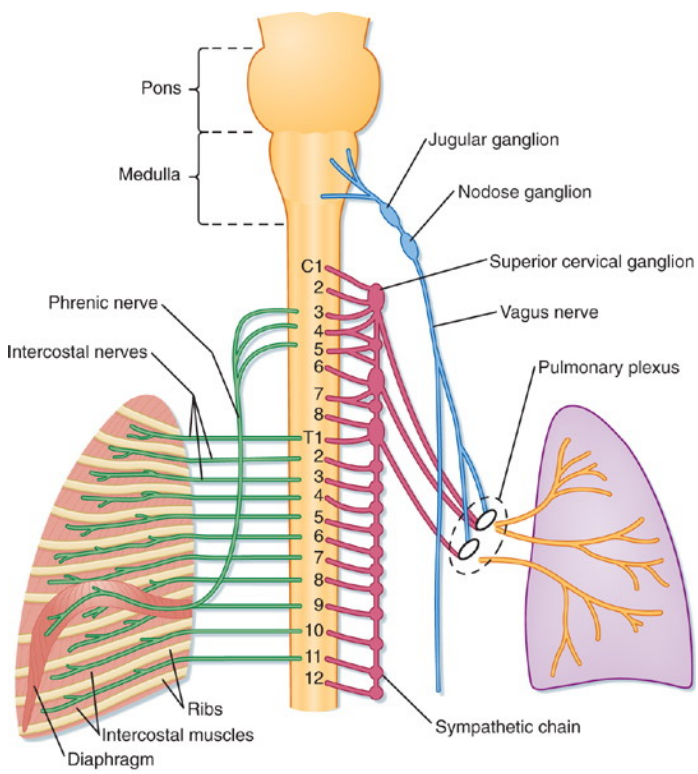
- Sensitive to pH in CSF
- CSF poorly buffered
- H^+ passes poorly through BBB but CO_2 passes easily
- Blood pH transmitted via CO_2 to CSF
- Adapt to elevated CO_2 levels (reduced pH) by transfer of HCO_3^- or Cl^- into CSF (slow)
- Stimulation of this system causes urge to breath.



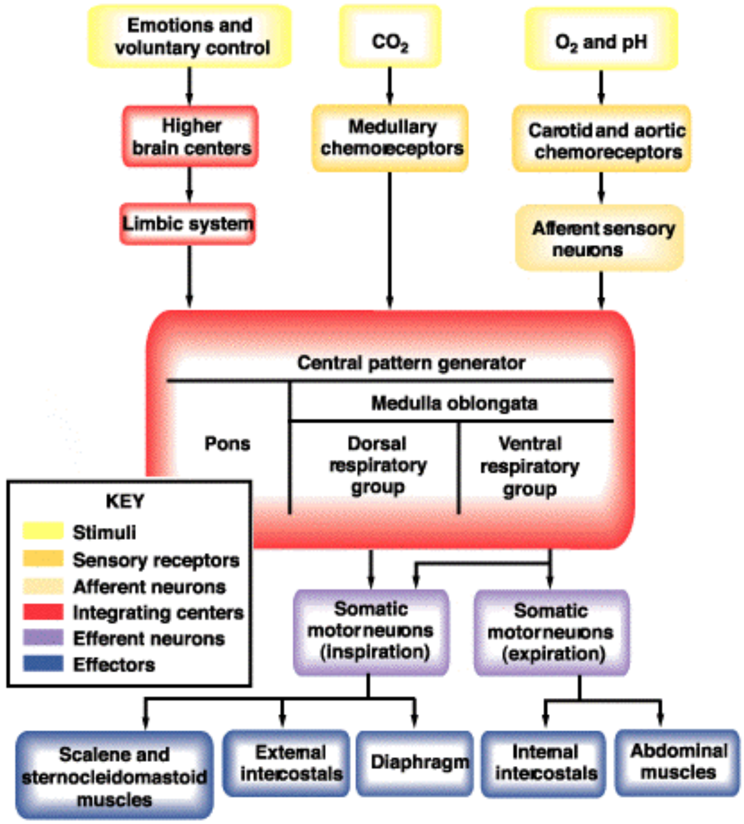


Innervation of Respiratory System

Constriction — Parasympathetic
Dilation — Sympathetic
Inspiration — Motor (to skeletal muscle)

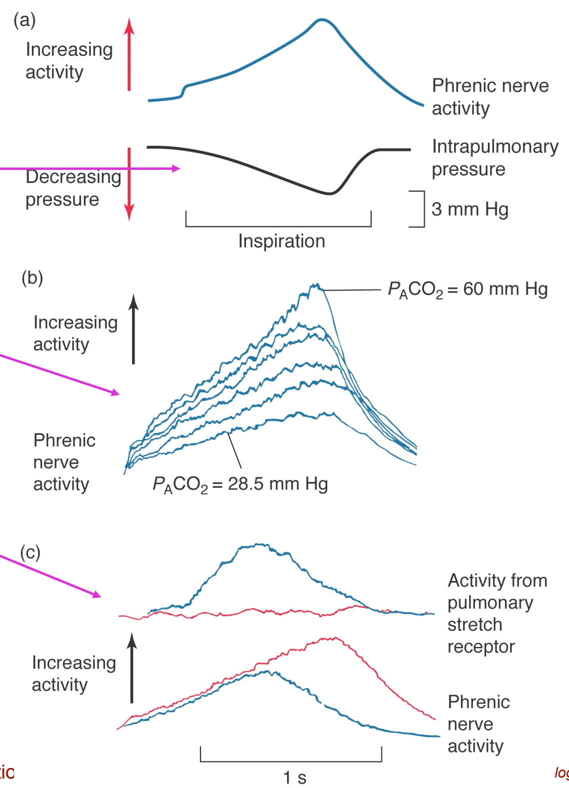


Central Control Overview



Pattern Control Mechanisms

- Phrenic nerve carries stimulus to diaphragm and determines breathing pattern
- Rise in CO_2 increases phrenic nerve activity
- Rise in stretch pulmonary stretch receptors suppress phrenic nerve activity



Rate Control Mechanisms

- Mechanism of pacemaker not known
- Rhythm is function of previous breath:
  - The deeper the breath, the lower the rate
  - Stretch receptors sense inspiration
  - Inspiratory/expiratory durations are the same
  - Breathing is continuous while awake
- Inspiratory impulses dominate:
  - Expiratory stimulation is constant
  - Inspiratory stimulation superimposed and inhibits expiratory
- Sleep:
  - Breathing is episotic
  - Central drive reduced so peripheral chemoreceptors stimulate based on O_2 and CO_2 levels

Other Ventilation Factors

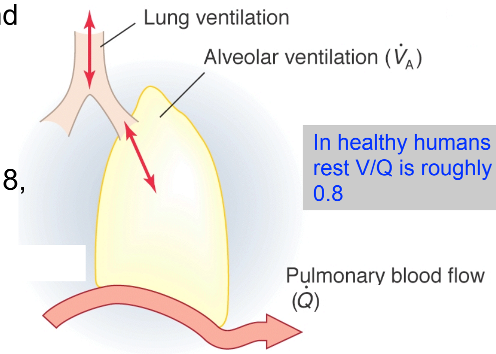
- Lung inflation: stretch receptors decrease inflation
  - CO_2 suppresses them
- Irritant receptors in the lung: cause bronchioconstriction and coughing
- J-receptors: sense interstitial fluid changes (edema)
  - Cause sense of breathlessness
- Emotional state; sympathetic stimulation cause vasoconstriction in peripheral sensors and increases response
- Temperature: stimulates peripheral sensors
- Exercise: increase sensitivity of chemoreceptors, probably through catecholamines
- Speech: inhale before speaking
- Conscious control

CO_2 is the dominant control factor!

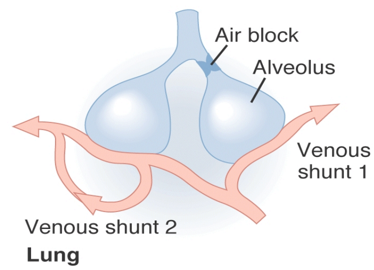
PO_2 must drop to 60 mm Hg (3000 m) before it triggers change

Ventilation/Perfusion (V/Q) Matching

- Goal:
  - Match blood flow to ventilation, both local and global
- Process:
  - Q regulated to match tissue needs and V regulated for adequate supply
  - V and Q vary with weight but ratio roughly 0.8, rises with exercise
- Sensors:
  - Local, at the tissue levels
- Actuators
  - Vascular/bronchial dilation and constriction, shunting
  - Local drop in V cause hypoxia, which inhibits K+ channels and causes smooth muscle constriction, increase in R_v; (opposite from systemic circulation)
  - Local drop in Q results in drop in CO_2, which drops H^+ and causes constriction of airway
- Feedback
  - local

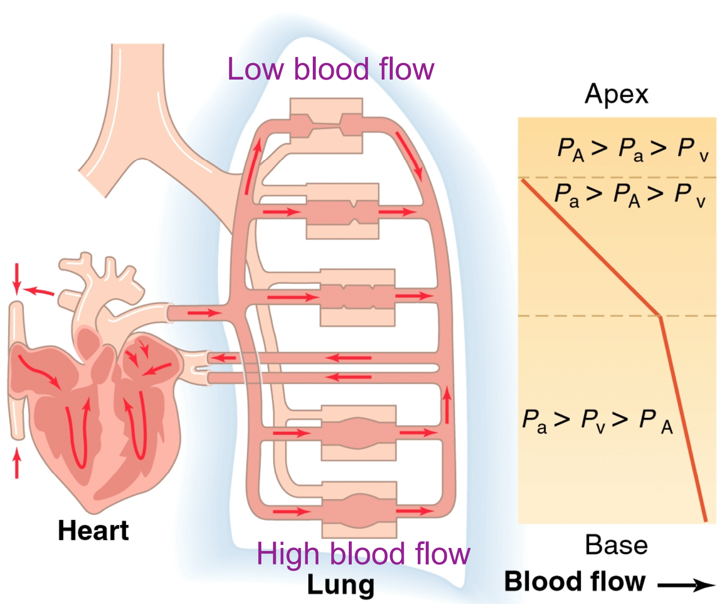


In healthy humans at rest V/Q is roughly 0.8



Pulmonary Circulation

- Balance among
  - P_A (alveolar pressure)
  - P_a (arterial pressure)
  - P_v (venous pressure)
- Pulmonary circulation
  - lower pressure (22/7.5 mm Hg)
  - lower filtration of H_20
  - extensive lymphatics
- Lungs surround heart and minimize variations with posture



Breath Holding

Table 13-1 Total oxygen stores, mean dive time, and mean dive depth in diving vertebrates

Species	O_2 stores ($ml \cdot kg^{-1}$)	Mean dive time (minutes)	Mean depth of dive (meters)
Leatherback turtle	20	11	60
Emperor penguin	62	6	100
Weddell seal	87	15	100
Northern elephant seal	97	20	400
Human*	20	2	Shallow

*Leatherback turtles have oxygen stores similar to those of humans, but can dive for much longer times because they use oxygen at a lower rate.
Source: Kooyman et al., 1999.

What Did Leonardo Get Wrong?

Underwater Breathing

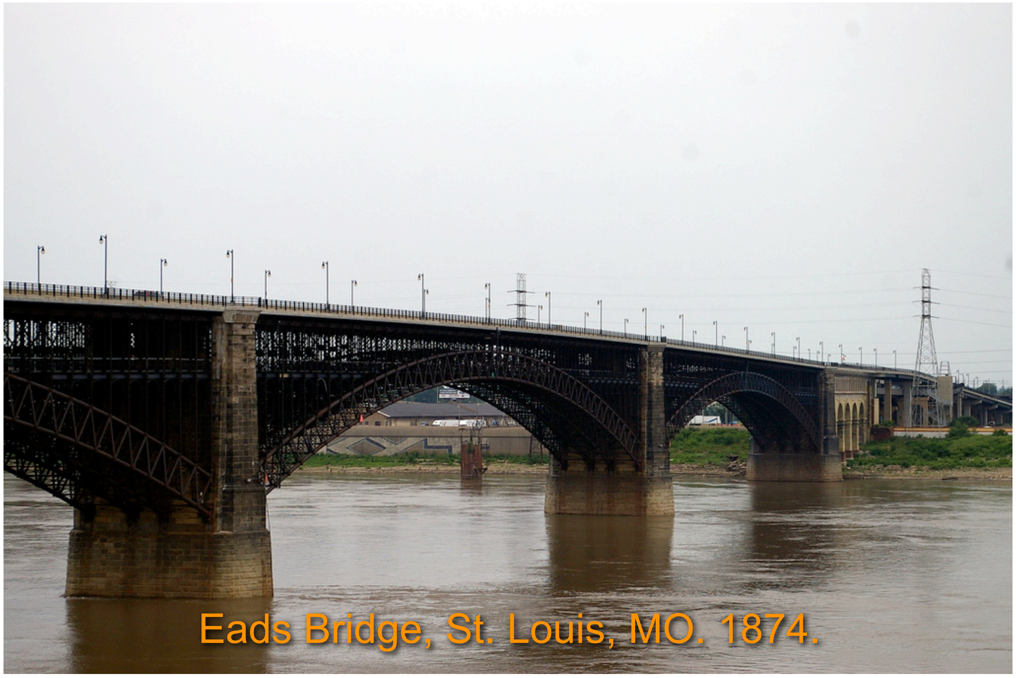
- Gas Physics
  - Pressure increases by 1 atm each 10 m
  - Air pressure at Everest 1/3 of normal, water pressure at same depth = 885 times normal
- Diving
  - Fixed volume in lungs compresses with depth
  - Snorkel breathing limited to about .5 m
  - More depth requires pressurized air
  - Body initially more buoyant than water; with depth, gas compresses and density increases and buoyancy decreases
  - Dive and apnea records: http://www.aidainternational.org)
  - Breath-hold record: ??

2014 Records

Constant Weight Apnea Without Fins (CNF)	
101 m Name: William TRUBRIDGE (NZL) Date: 2010-12-16 Place: Long Island, Bahamas	**69 m** Name: Natalia MOLCHANOVA (RUS) Date: 2013-09-16 Place: Kalamata, Greece
Constant Weight Apnea (CWT)	
128 m Name: Alexey MOLCHANOV (RUS) Date: 2013-09-19 Place: Kalamata, Greece	**101 m** Name: Natalia MOLCHANOVA (RUS) Date: 2011-09-23 Place: Kalamata, Greece
Static Apnea (STA)	
11 min 35 sec Name: Stéphane MIFSUD (FRA) Date: 2009-06-08 Place: Hyères, France	**9 min 02 sec** Name: Natalia MOLCHANOVA (RUS) Date: 2013-06-29 Place: Belgrade, Serbia
No Limits Apnea (NLT)	
214 m Name: Herbert NITSCH (AUT) Date: 2007-06-14 Place: Spetses, Greece	**160 m** Name: Tanya STREETER (USA) Date: 2002-08-17 Place: Turks & Caicos

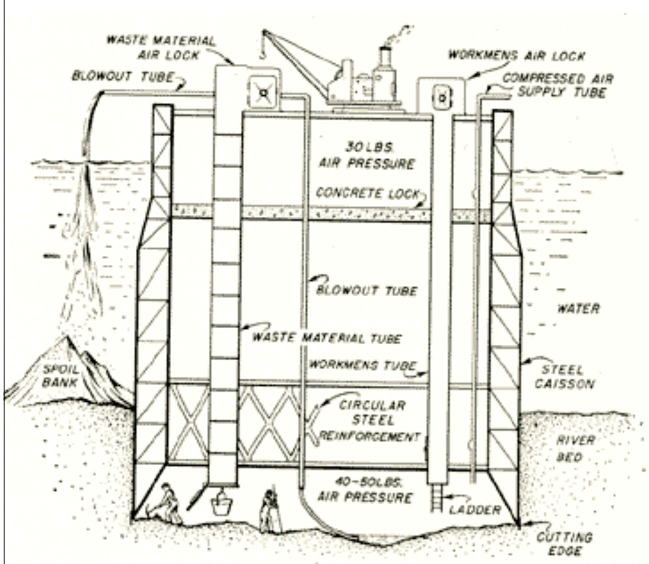
http://www.aidainternational.org/competitive/worlds-records

Ciasson Disease



15 died, 79 severely afflicted by bends

Caisson Disease



Bends and other Woes

- Pressure drives more gasses into blood, e.g., 1 l of nitrogen per 10 m
- Resurfacing too quickly causes bubbles to form and grow (opening carbonated drink)
- Bubbles in capillaries, joints, inner ear, brain
- Discovered in 1878 among “Caissons” workers
- Whales and seals
  - Dive deeply (to 1570 m) but no bends
  - Breath out before diving, lungs empty and collapse
  - No gas dissolved into the blood

The Physiology of Altitude

The Challenges of Altitude

- At sea level
  - Total pressure: 760 mm Hg (Torr)
  - PO_2: 20% * 760 = 150 mm Hg in air, 100 mm Hg in lungs
  - Water vapor: 47 mm Hg = 6%
- At 5800 m
  - Highest permanent habitation
  - PO_2 = 80 mm Hg
- At Everest summit (8848 m)
  - Total pressure: estimated as 230, really 253 mmHg
  - Water vapor: 47 mm Hg = 18.6%
  - PO_2: 21% = 43 (calculated) 35 (measured) in alveoli mmHg
- At 12,000 m
  - Even with pure O_2, PO_2 drops below 100 mmHg

How High Can We Go?

"Those who, like Major Godwin-Austen, have had all the advantages of experience and acclimatization to aid them in attacks upon the higher Himalayas agree that 21,500 feet (7,050 m) is near the limit at which man ceases to be capable of the slightest further exertion."

T.W. Hanchliff, President British Alpine Society 1876

It is "unlikely that the mountain could be climbed without oxygen equipment without serious risk"

LGCH Pugh , J. Physiology, 1958

"Now, when... I have nothing more to do than breathe, a great peace floods my whole being. I breathe like someone who has run the race of his life and knows that he may now rest forever... In my state of spiritual abstraction, I no longer belong to myself and to my eyesight. I am nothing more than a single, narrow, gasping lung, floating over the mists and the summits"

Reinhold Messner, 1979

Response to Altitude I

↑ Cardiac output

↑ Ventilation ↔ ↓ Ventilation

↓ PO_2

↓ PO_2

↓ PCO_2

↑ pH

↑ pH

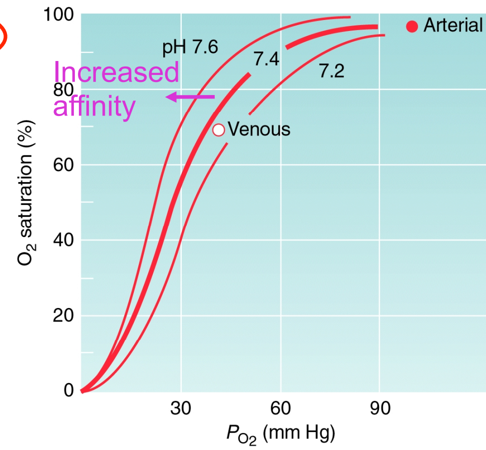
↑ O_2 Affinity

Stimulate O_2 sensors

Stimulate ventilation

Opposing stimuli. Left shift of O_2 dissociation

Consequences??



Response to Altitude II

Ventilation

↑ Ventilation

↓ PO_2

↓ PO_2

↑ pH

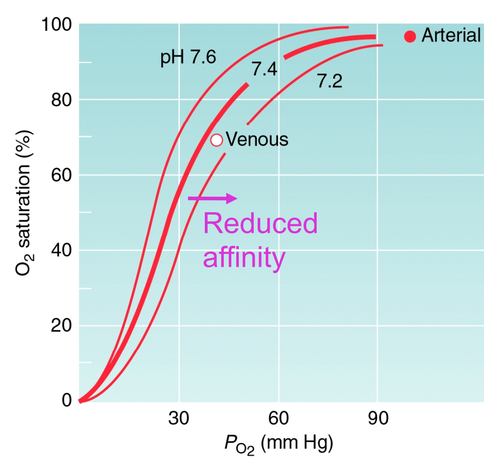
Excretion of HCO_3^- pH

↑ O_2 Affinity

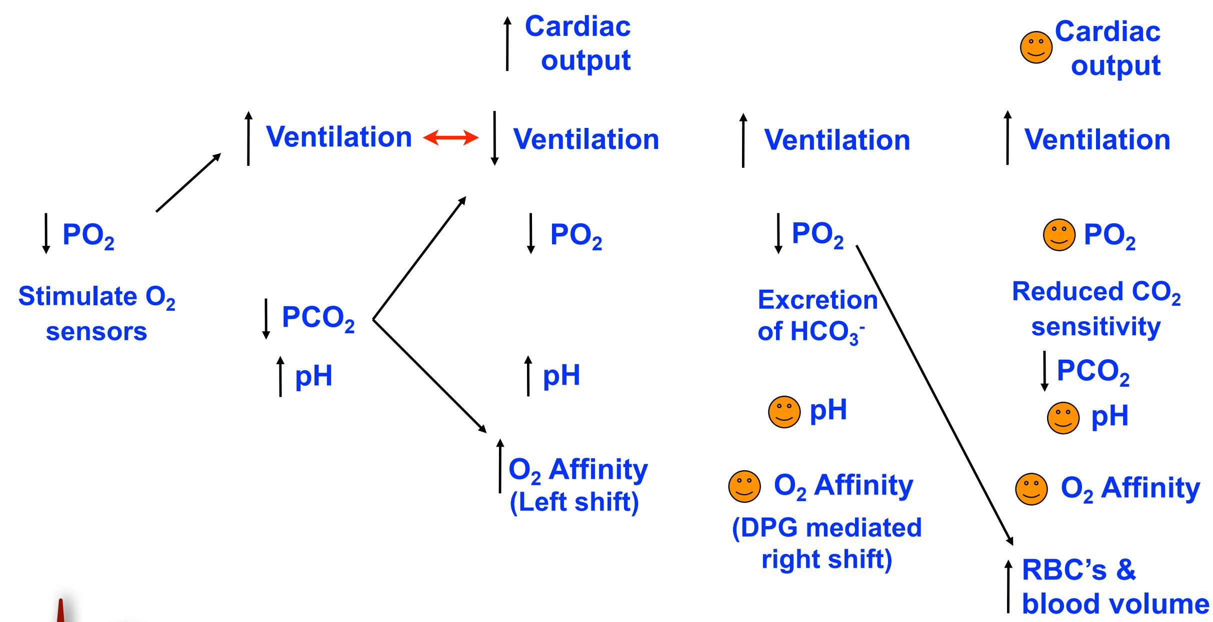
↑ DPG O_2 Affinity

Opposing stimuli. Left shift of O_2 dissociation

Elevated ventilation Right shift of O_2 dissociation



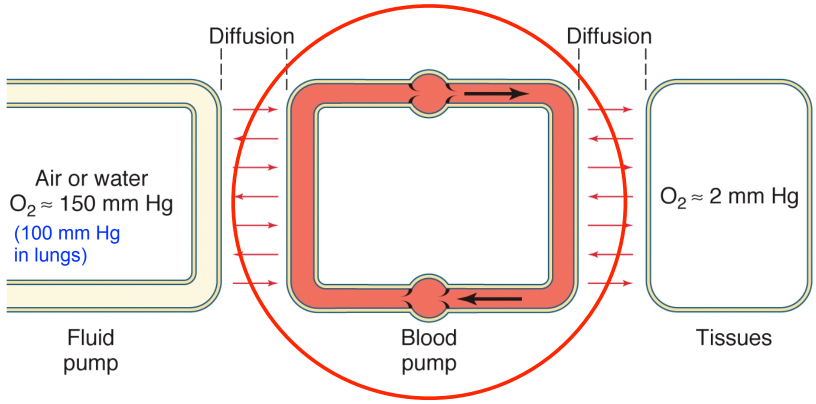
Response to Altitude III



Long Term Response

- Increase in hematocrit (erythropoietin)
- Increase in vascularization (growth factors)
- Rise in blood volume (by 1/3)
- Cardiac output normal
- Local pulmonary vasoconstriction
  - Rise in pulmonary pressures
  - More even distribution of pulmonary perfusion
- Altered growth: small and barrel chested
  - High lung to body volume ratio
  - Right ventricular hypertrophy
- Range of responses
  - Mountain sickness more common among Andeans than Tibetans
  - Birds routinely fly to 6000 m in migration, some fly over the Himalaya (9000 m)

Gas Transport Requirements



- Ventilation
- Diffusion from/to respiratory system
- Bulk transport
- Diffusion to/from tissue

In maximal exercise, what is the rate limiting step?

Oxygen transport in the blood!