Respiratory Physiology Part 2

Shunting

- Describes blood bypassing alveoli prior to entering the systemic circulation
- Explains the difference in alveolar capillary PO2 and arterial PaO2
- Sources subdivided as:
  - Anatomical: bronchial veins, Thebesian veins
  - Physiological*: normal ventilation-perfusion mismatch
  - Pathological: AV malformations, congenital heart disease with right to left shunt

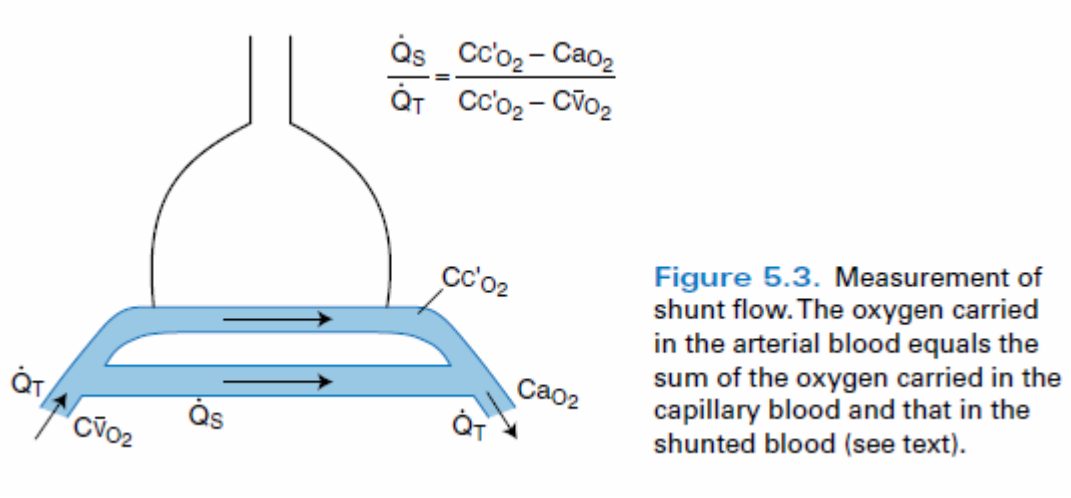
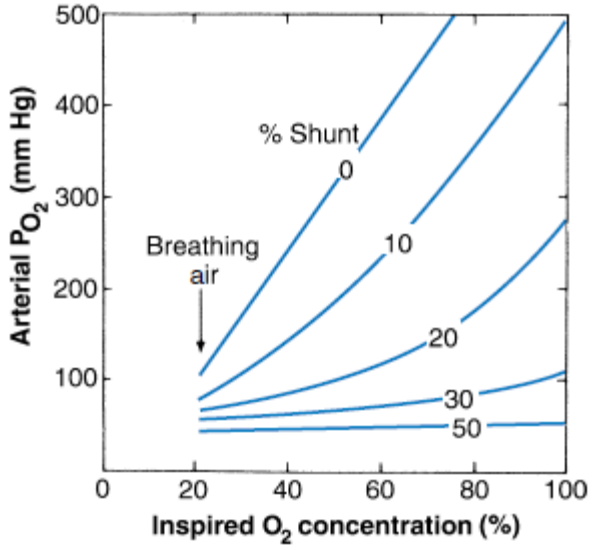
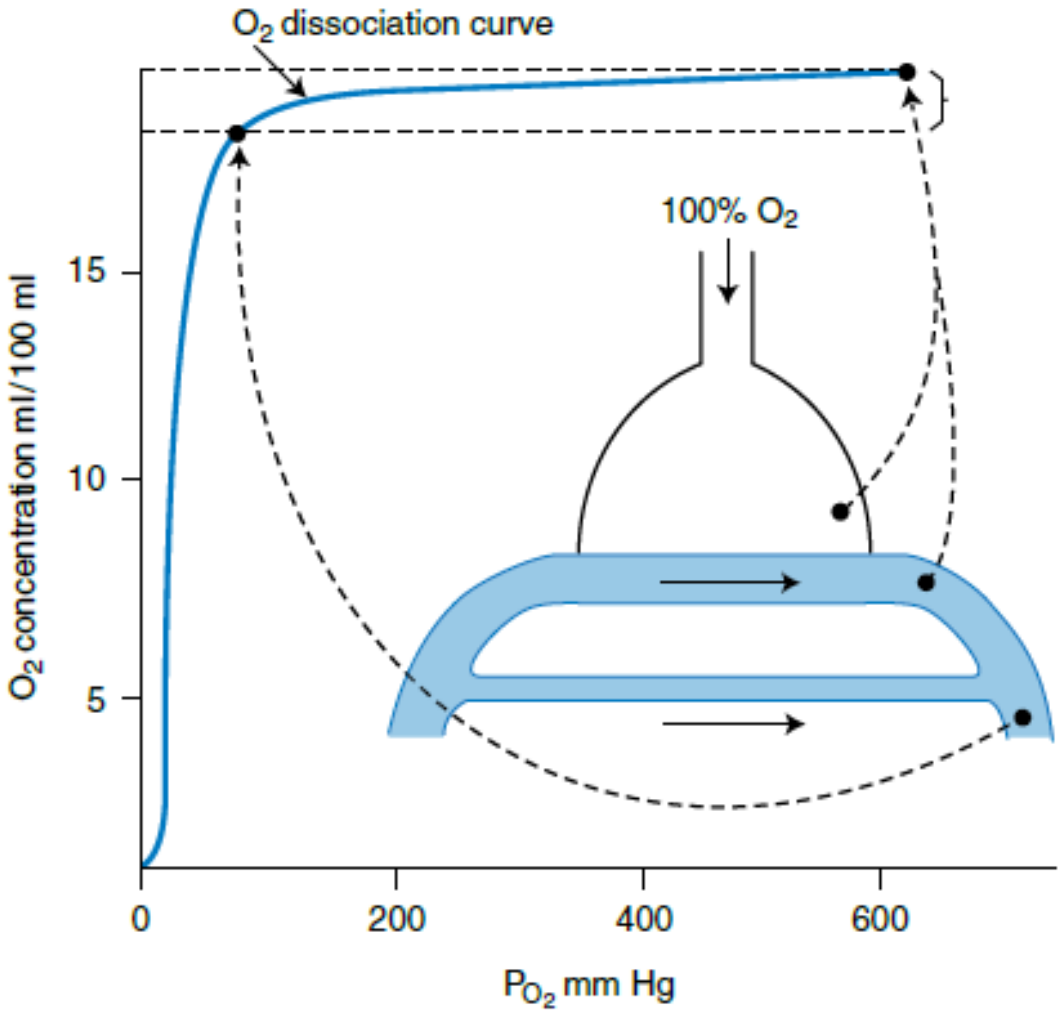
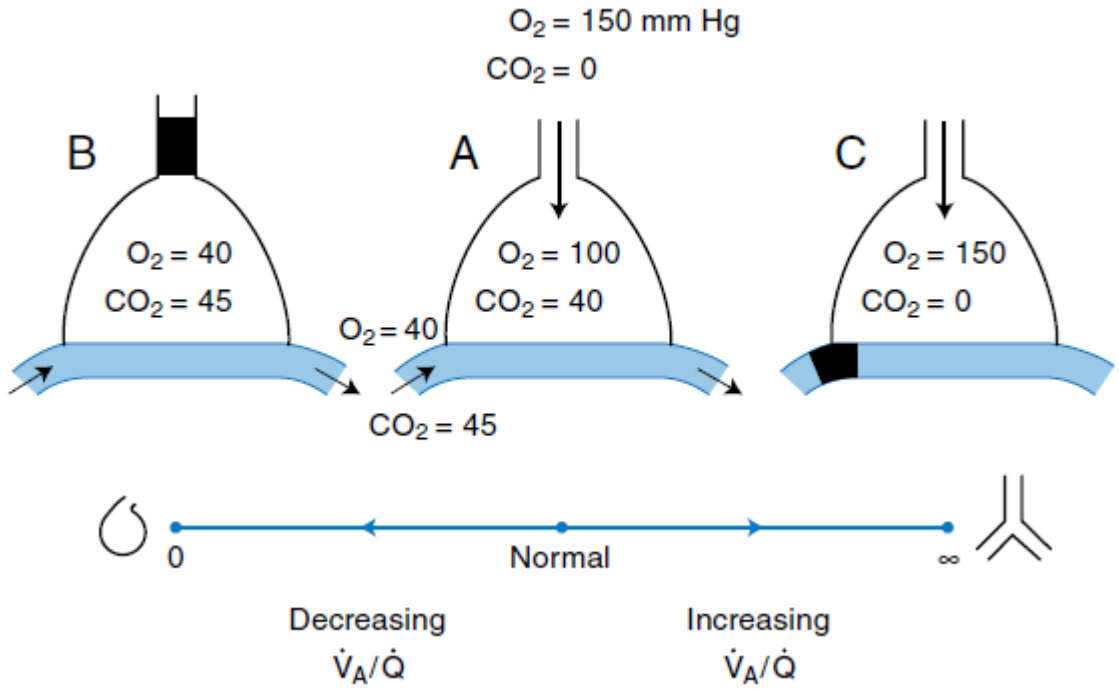


Figure 5.3. Measurement of shunt flow. The oxygen carried in the arterial blood equals the sum of the oxygen carried in the capillary blood and that in the shunted blood (see text).



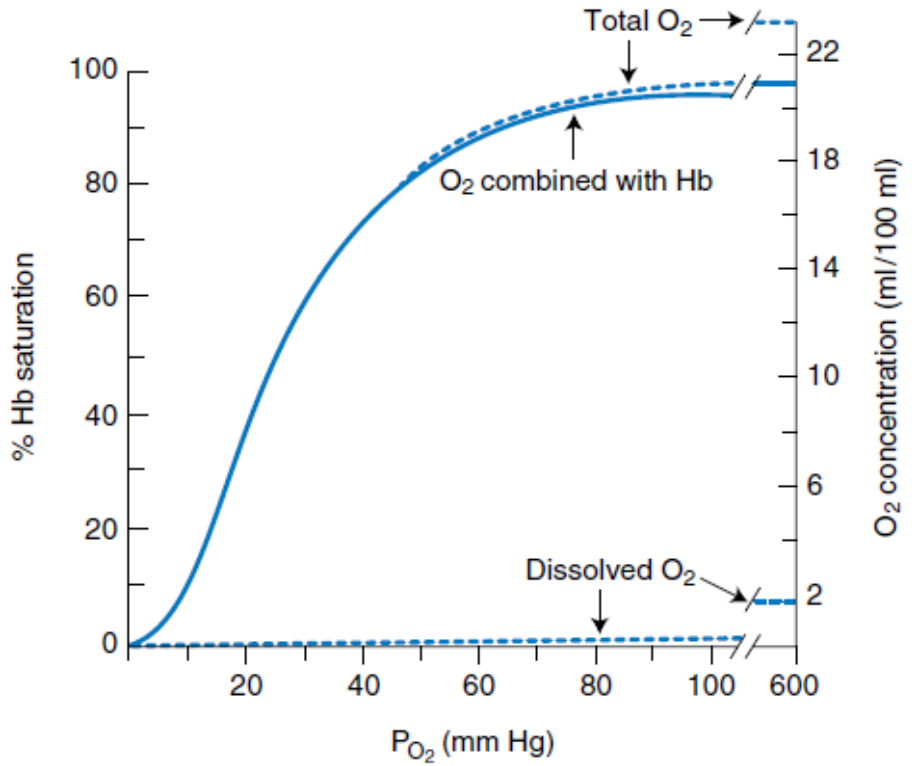
Shunting


O_2 dissociation curve
100% O_2
O_2 concentration ml/100 ml
15
10
5
0
200
400
600
P_{O_2} mm Hg


O_2 = 150 mm Hg
CO_2 = 0
B
A
C
O_2 = 40
CO_2 = 45
O_2 = 100
CO_2 = 40
O_2 = 150
CO_2 = 0
O_2 = 40
CO_2 = 45
0
Normal
∞
Decreasing
$\dot{V}_A/\dot{Q}$
Increasing
$\dot{V}_A/\dot{Q}$

Oxygen Carriage

- Oxygen is carried in two forms: dissolved and bound to haemoglobin
- Hb saturation ≠ oxygen concentration



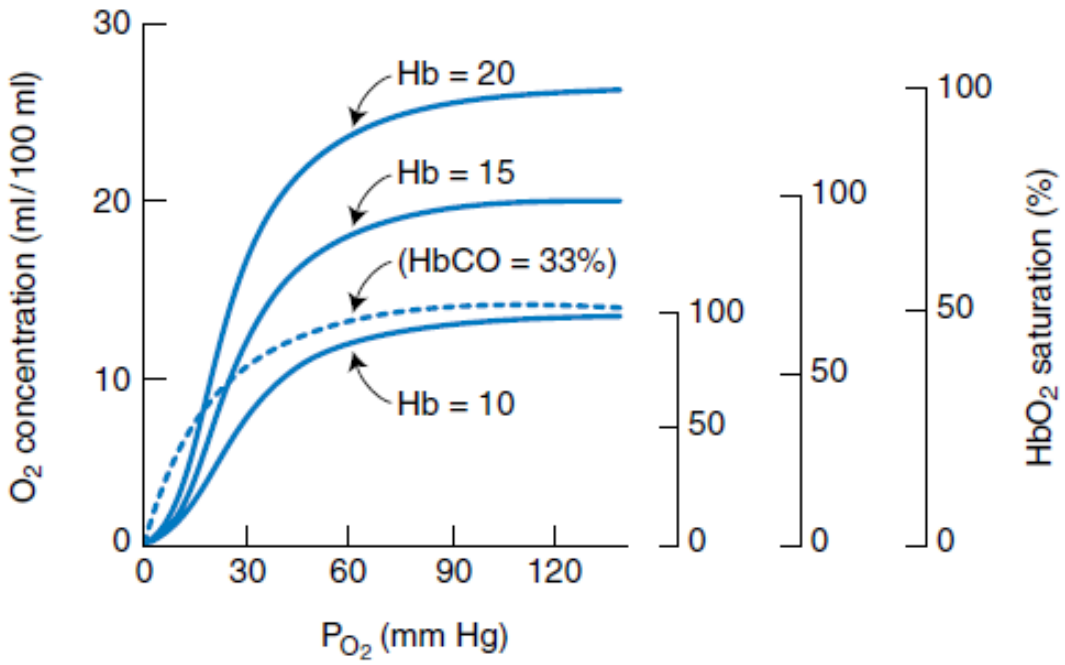


Figure 6.1. O_2 dissociation curve (*solid line*) for pH 7.4, P_{CO_2} 40 mm Hg, and 37°C. The total blood O_2 concentration is also shown for a hemoglobin concentration of 15 g·100 ml^{-1} of blood.

Oxygen Disassociation Curve

- Sigmoid shaped – of physiological benefit
  - PO2 27 mmHg → SO2 50% *(P50)*
  - PO2 40 mmHg → SO2 75%
  - PO2 100 mmHg → SO2 97%
- Changes to physiological parameters will shift the curve
  - Right-shift = lower affinity = ideal for offloading oxygen (think of an exercising muscle)
  - Left-shift = higher affinity = ideal for retaining/uptaking oxygen (think of fetal haemoglobin)

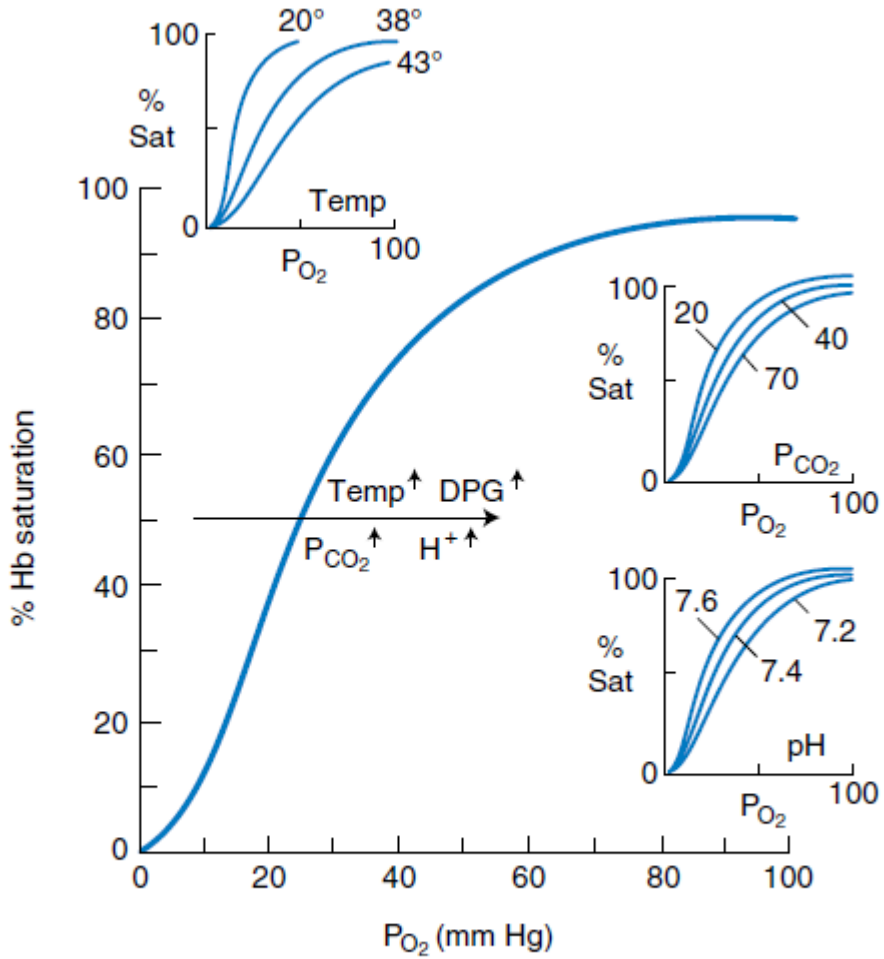
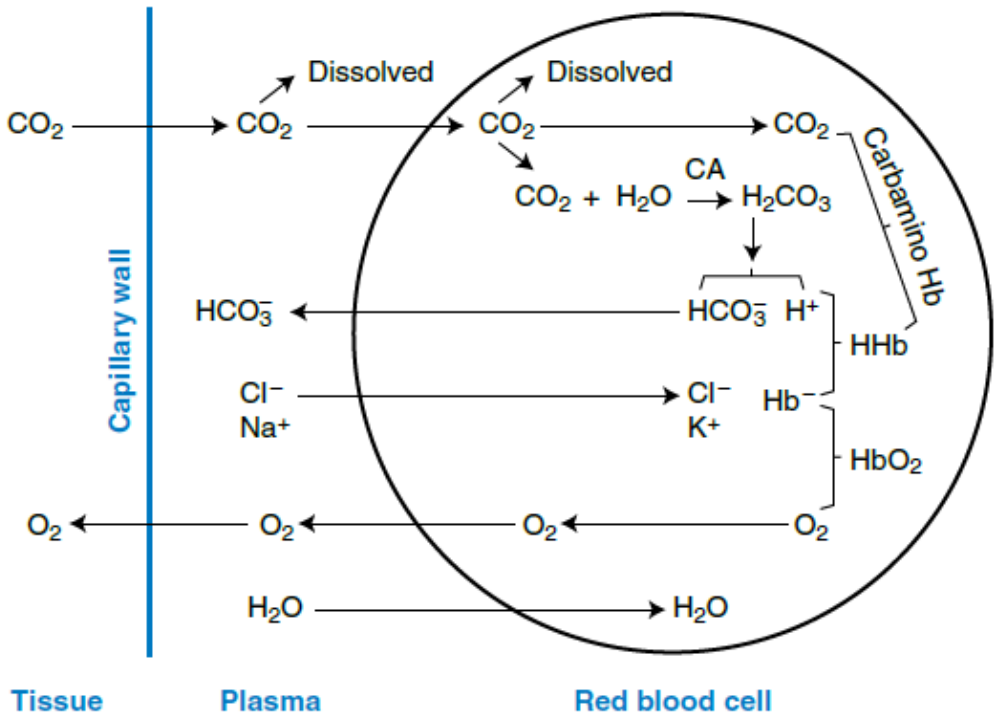
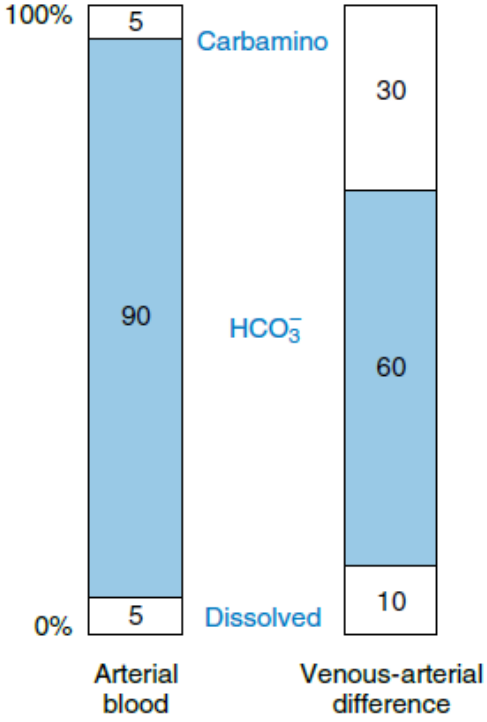


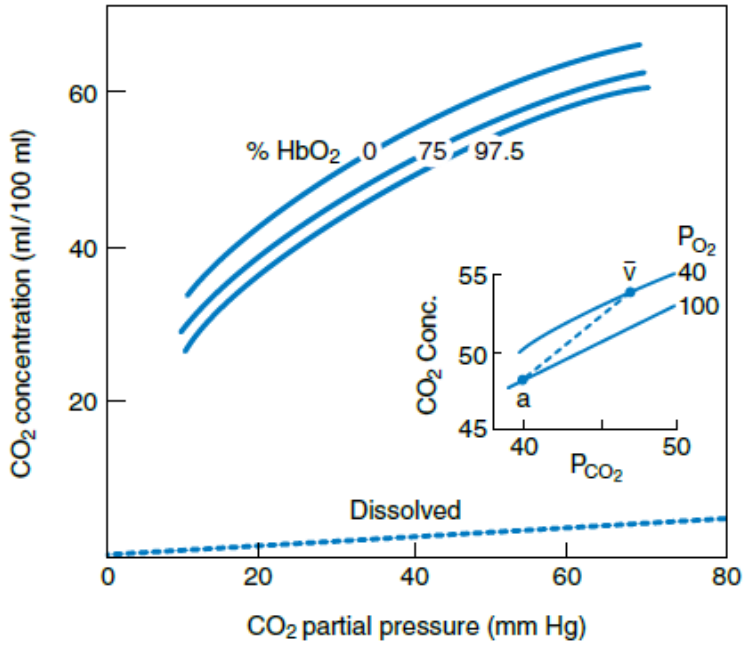
Figure 6.3. Rightward shift of the O_2 dissociation curve by increase of H^+, P_{CO_2}, temperature, and 2,3-diphosphoglycerate (DPG).

Carbon Dioxide Carriage

- CO2 is carried in three forms, and in two different compartments
  - Dissolved CO2 ≈ 5% (significantly more soluble than O2)
  - Bicarbonate ≈ 90% (via carbonic anhydrase) $CO_2 + H_2O \overset{CA}{\rightleftharpoons} H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$
  - Carbamino ≈ 5% (bound with protein amine groups)
- Haldane effect: deoxygenated (reduced) haemoglobin facilitates CO2 carriage







Respiratory Control of Acid-Base Balance

- CO2 should be considered an acid due the formation of carbonic acid (pKa 6.1) via the enzyme carbonic anhydrase $CO_2 + H_2O \overset{CA}{\rightleftharpoons} H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$
- Ventilation (excretion of CO2) therefore is crucial for minute-to-minute acid-base balance;
- When ventilation is functioning appropriately it can compensate for metabolic acidosis or alkalosis, whilst in pathology it causes respiratory acidosis or alkalosis
- Respiratory acidosis = ↑PCO2 ↓pH = pathological hypoventilation
  - Obstructive respiratory disease, sedation, neuromuscular disorders (high cervical SCI, GB, MG), rib fractures and flail chest
- Respiratory alkalosis = ↓PCO2 ↑pH = pathological hyperventilation
  - Pain, anxiety

Respiratory Control of Acid-Base Balance

- Determining acid-base disturbance and underlying aetiology
  1. Begin with pH
     1. Acidosis < 7.35, alkalosis > 7.45
     2. Note that patient can have an acid-base disturbance with a normal pH if there is complete compensation (e.g. chronic CO_2 retainers with high bicarbonate)
  2. Follow with PCO_2
     1. If PCO_2 is elevated the patient has respiratory acidosis or respiratory compensation for a metabolic alkalosis* (e.g. gastric outlet obstruction, compensation is limited)
     2. If PCO_2 is decreased the patient has respiratory alkalosis or respiratory compensation for a metabolic acidosis (e.g. sepsis)
  3. Confirm your findings by reviewing bicarbonate (HCO_3)
  4. If there is complete compensation (normal pH with abnormal PCO_2 and HCO_3, rarely occurs), extrapolation is used to identify the primary pathology versus the compensating factor
  5. Occasionally there will be co-existing respiratory metabolic acidosis (this will be identified at step 3)

Respiratory Control of Acid-Base Balance

- 78-year-old woman presents with increasing shortness of breath on a background of COPD.
  ABG is as follows: pH 7.25, pCO2 70, HCO3 35
  1. Acidosis or alkalosis?
  2. Primary aetiology with review of the PCO2 (respiratory or metabolic)?
  3. Is there compensation?
- 60-year-old man with previous PUD presents with several weeks of nausea and vomiting.
  ABG is as follows: pH 7.50, pCO2 32, HCO3 40
  1. Acidosis or alkalosis?
  2. Primary aetiology with review of the PCO2 (respiratory or metabolic)?
  3. Is there compensation?

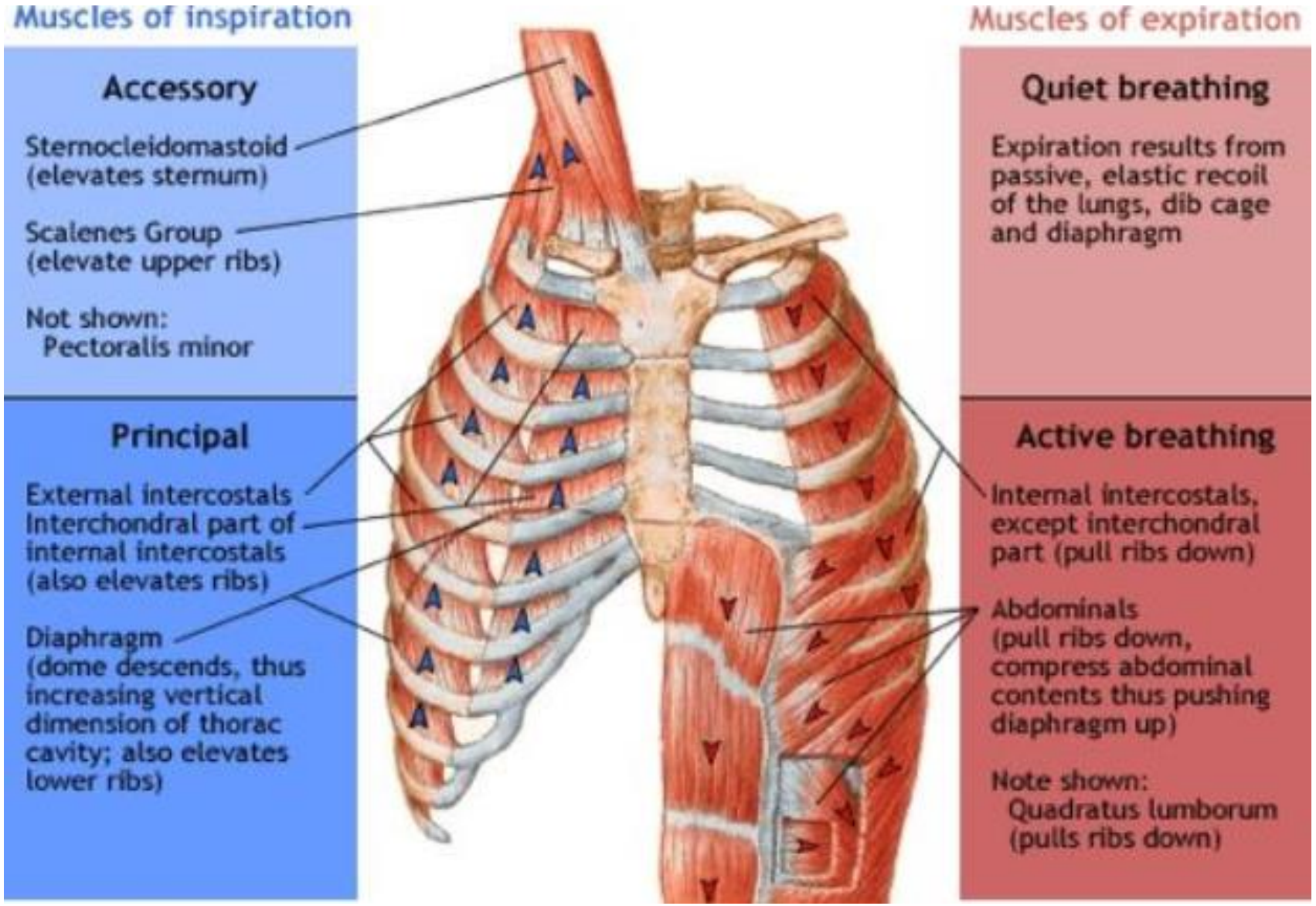
Respiratory Control of Acid-Base Balance

- 34-year-old man is admitted with a presumed ‘septic stone’, and has been given 15 mg of IV morphine for analgesia
  ABG is as follows: pH 7.10, PCO_2 52, HCO_3 12, lactate 4
  1. Acidosis or alkalosis?
  2. Primary aetiology with review of the PCO_2 (respiratory or metabolic)?
  3. Is the bicarbonate consistent with the above?

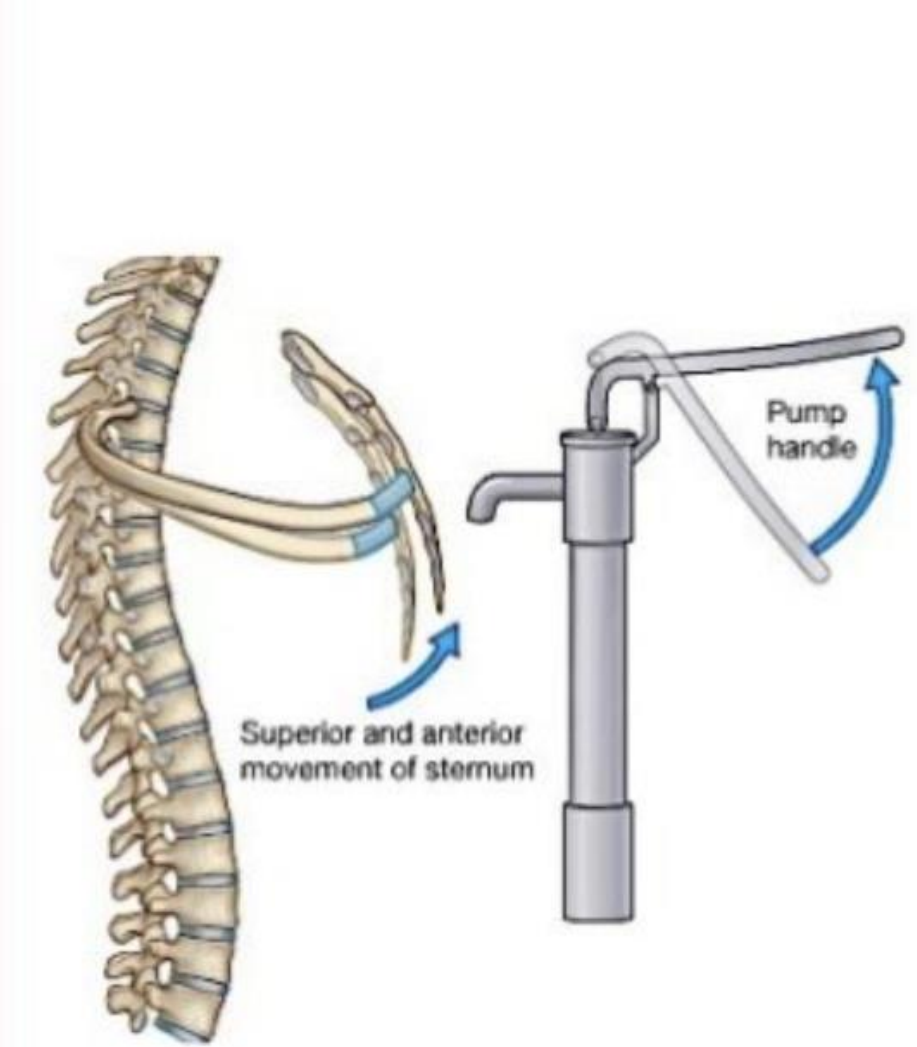
Mechanics of Respiration

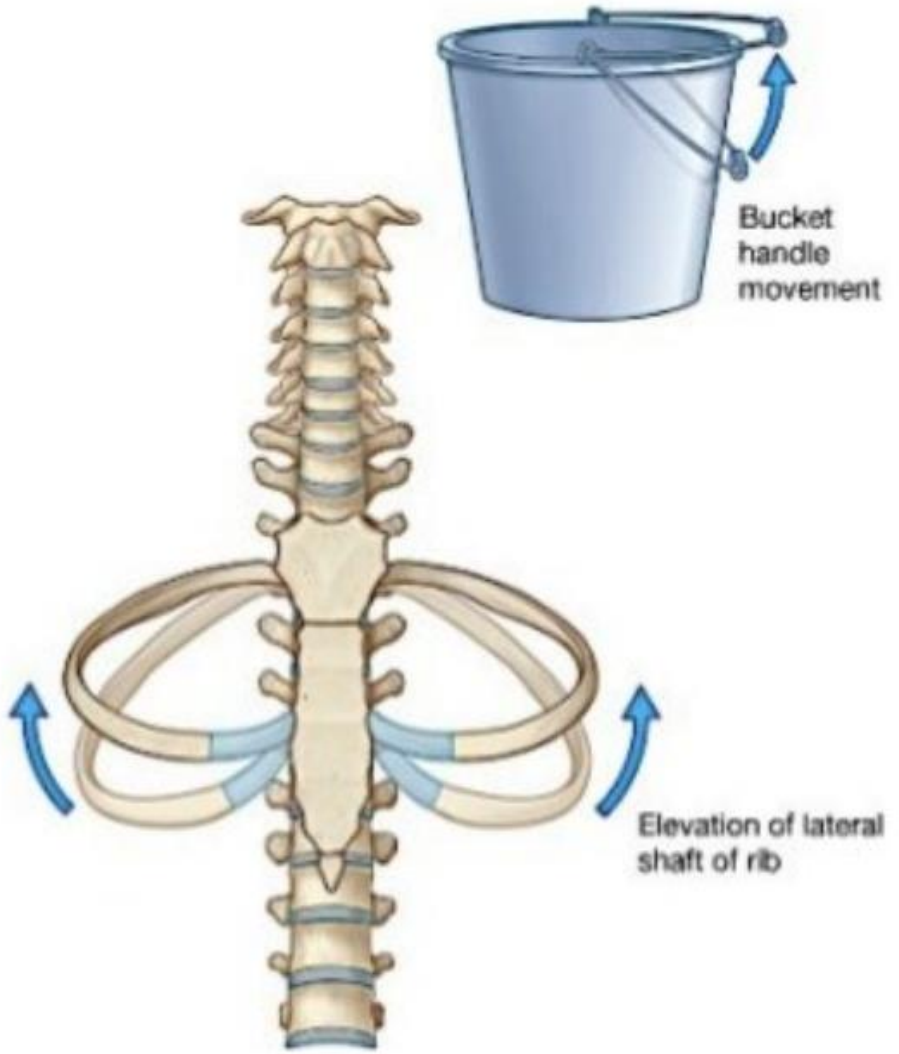
- Respiration involves two mechanical phases, inspiration and expiration, which differ between quiet (steady state, normal tidal volumes) and active (exercise, dyspnoea) breathing
- Inspiration: increase in thoracic cage dimension → negative intra-thoracic pressure
  - Quiet: muscle-dependent, diaphragm > external intercostals
  - Active: muscles of quiet inspiration are more extensively active and accessory muscles are involved
- Expiration: decrease in thoracic cage dimension → positive intra-thoracic pressure
  - Quiet: elastic recoil-dependent (passive), partly due to alveolar surface tension and partly due to lung parenchyma elastic recoil
  - Active: muscle-dependent, including internal intercostals and abdominal wall muscles
- Consider how each muscle is changing the dimensions of the thoracic cage (A/P, S/I, transverse)

Mechanics of Respiration



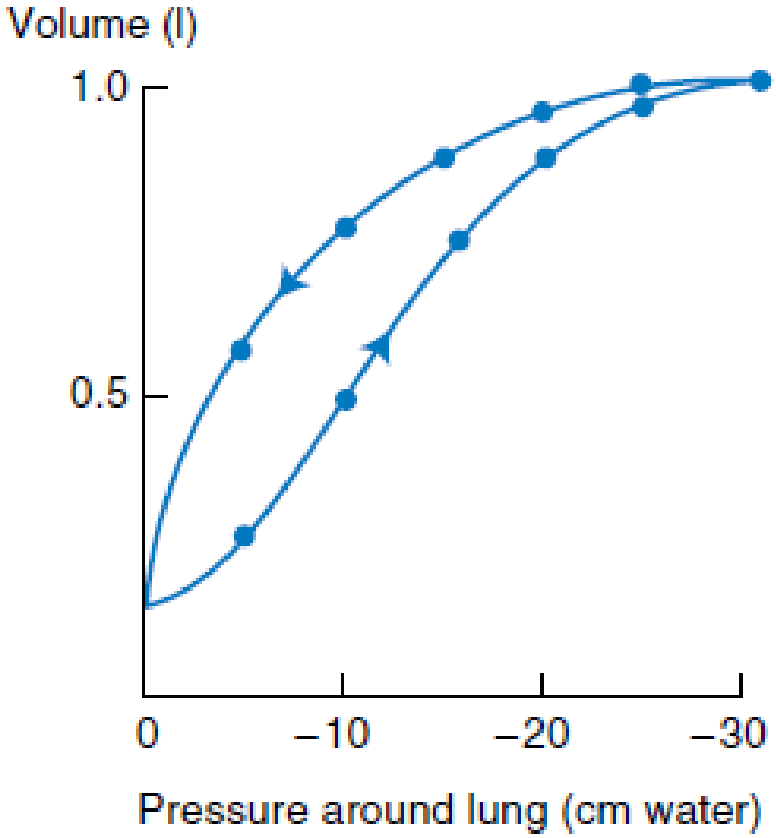
Mechanics of Respiration





Compliance

- Elastic forces act on the lungs (surface tension of the alveoli and elasticity of parenchyma and thoracic cage) that ex-situ would maintain a steady volume
- Therefore lung inflation is dependent on ‘transpulmonary’ pressure (i.e. negative pressure around the lungs, or positive pressure within the lungs)
- This is illustrated as the pressure-volume curve
  - * Hysteresis: the phenomenon of the inspiratory curve being different from the expiratory curve
- Compliance is the slope of the pressure volume curve, and relates the change in volume to the change in pressure
  - High compliance = minimal pressure required for a given change in volume = ‘good’ lungs
  - Low compliance = high pressure required for a given change in volume = bad lungs (fibrotic/restrictive)
- Compliance is variable at different lung volumes

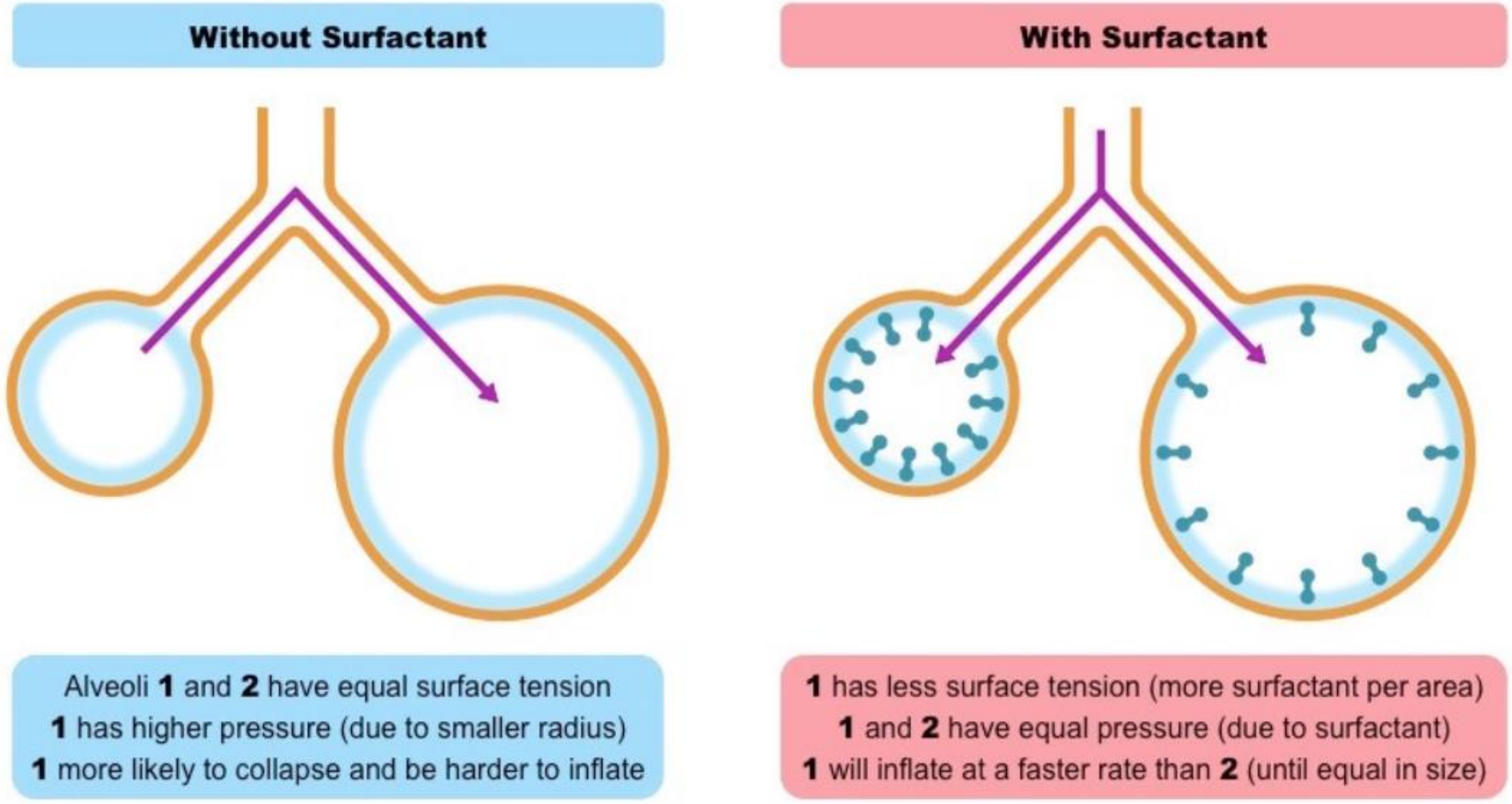


$$\text{Compliance} = \frac{\Delta V}{\Delta P}$$

Lung Elasticity and Surface Tension

- Why does the lung return to a given volume once transpulmonary pressure normalizes?
- Elastic recoil:
  - Of the lung parenchyma (elastic fibres composed of collagen and elastin)
  - Of the chest wall (related to joints, ligaments and muscles), which wants to ‘spring out’, opposing the elastic recoil of the parenchyma, except at very high lung volumes (> 75% of vital capacity)
- Surface tension:
  - Water (or any liquid) wants to be next to more water, rather than gas; and occupy the smallest volume whilst doing so
  - Explains why droplets form on your flat countertop, rather than an infinitely wide and thin pool of water
  - Therefore the fluid coating an alveolus would prefer to come together, generating a force that seeks to collapse the size of the alveolus
  - The pressure generated by surface tension can be calculated with Laplace’s law, which demonstrates that with a smaller radius, there is a greater pressure $$P = \frac{4T}{r}$$
  - Surface tension reduced by surfactant (amphipathic) produced by type 2 pneumocytes, which increases compliance, reduces alveolar collapse, and prevents accumulation of water in the alveolus

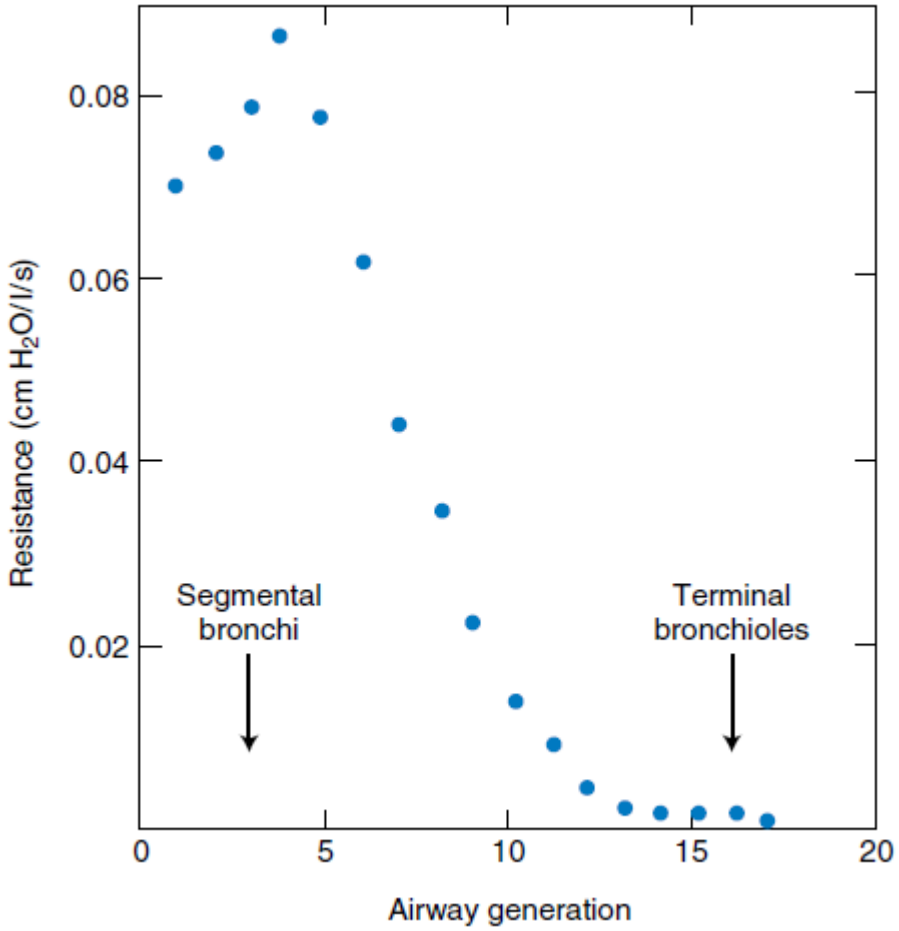
Lung Elasticity and Surface Tension



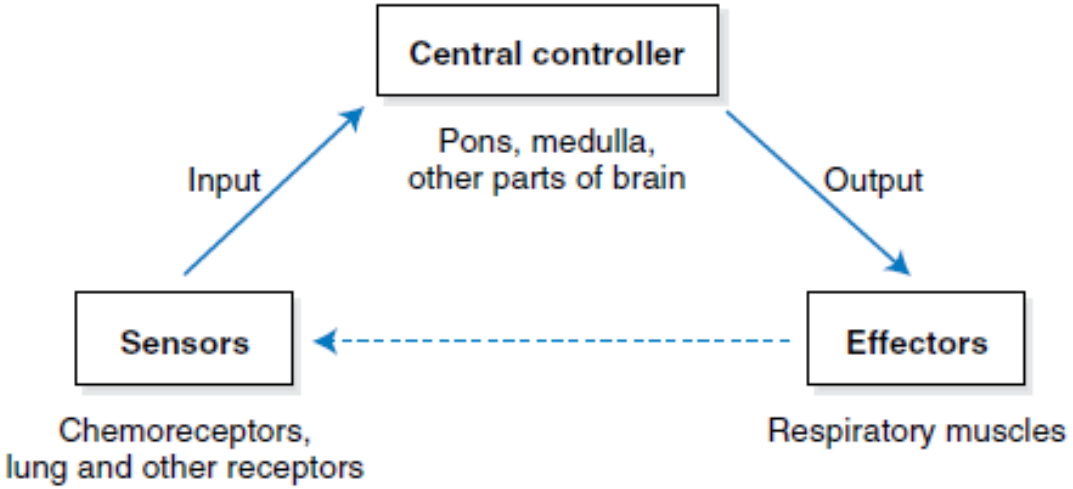
Airway resistance

- The bronchial tree is a series of tubes
- Laminar flow through a tube can be calculated with Poiseuille's law
  - If the radius is halved the flow decreases 16-fold
  - Resistance can be derived; given that resistance is equal to pressure divided by flow rate
  - Keep in mind that most flow through the bronchial tree is not laminar, but turbulent, however the law still demonstrates important principles
- Airway resistance is in fact highest in the medium-sized airways
  - Whilst the small airways have a much smaller radius, their sheer number makes up for this
- Resistance is increased at low lung volumes due to small airway collapse and compression
  - A similar phenomenon is dynamic airway compression, where excessive intrapleural pressure on forced expiration closes airways and limits flow rates

$$\dot{V} = \frac{P\pi r^4}{8nl} \qquad R = \frac{8nl}{\pi r^4}$$

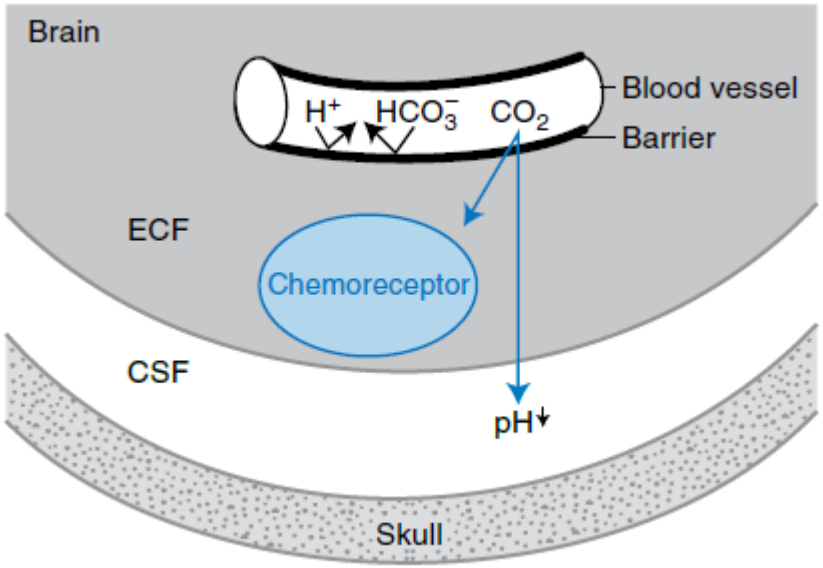


Control of Respiration: CNS



- Central (CNS) control mediates steady-state (unconscious) and reactive respiration
- Unconscious periodic inspiration and expiration controlled by the ‘central pattern generator’ in the brainstem
  - ‘Pre-Botzinger cortex’ in the ‘medullary respiratory centre’ generates the respiratory rhythm
  - DRG controls inspiration, whilst VRG controls expiration
  - ‘Pneumotaxic centre’ shortens the duration of inspiratory active to increase respiratory rate
- Conscious respiration is controlled by the cerebral cortex
- Hypothalamus and limbic system mediate emotional changes in respiration

Control of Respiration: Sensors



- Multiple sensors that feedback to the CNS to control respiration
  - Central: most important sensor, located in ventral medulla, specifically responds to protons (H+) concentration changes, but this is generated through the diffusion of CO2 into the CSF; compensation occurs through accumulation of bicarbonate in the CSF to raise the pH
  - Peripheral: carotid and aortic bodies, around the carotid bifurcation and aortic arch respectively; respond to decrease in PO2 and pH* and increase in PCO2
    - *Carotid bodies alone respond to pH changes; important for compensation for metabolic acidosis
- Many other sensors feed into the respiration, such as those for irritants (cough, bronchoconstriction), pain (hyperventilation), movement (hyperventilation)

Altitude

- They always ask about this. I don’t know why.
- At sea-level the atmospheric pressure is 760 mmHg (= 1 atm)
- High in the sky, the atmospheric pressure is low (e.g. 380 mmHg at 5,800 m) and the PO2 is correspondingly much lower
- Humans must acclimatize to altitude, through a number of mechanism:
  - Hyperventilation: immediate response to low PO2, driven by peripheral chemoreceptors; suppression of this response secondary to hypocapnia is blunted over subsequent days due to changes in CSF pH from bicarbonate shift
  - Polycythaemia: increase in Hb due to EPO, occurs over several weeks to months, increases the oxygen carrying capacity of the blood
  - Oxygen dissociation curve changes:
    - Right-shift occurs at moderate altitudes, to improve the release of oxygen to the tissues
    - Left-shift occurs at extreme altitudes, to improve oxygen uptake in the alveoli (no other option)
  - Pulmonary hypertension and right ventricular hypertrophy: consequence of low oxygen conditions, does not improve physiology

THANKS FOR LISTENING AND GOOD LUCK