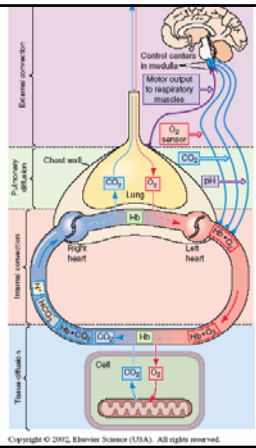
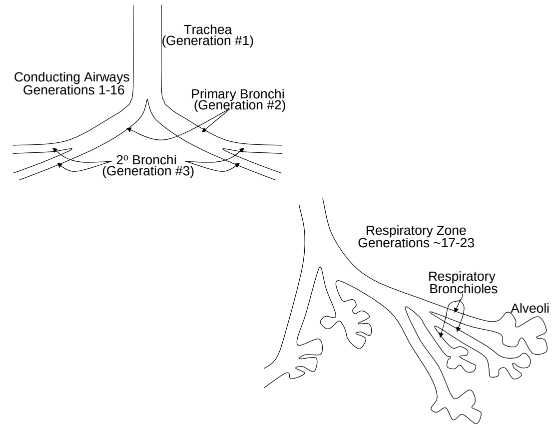
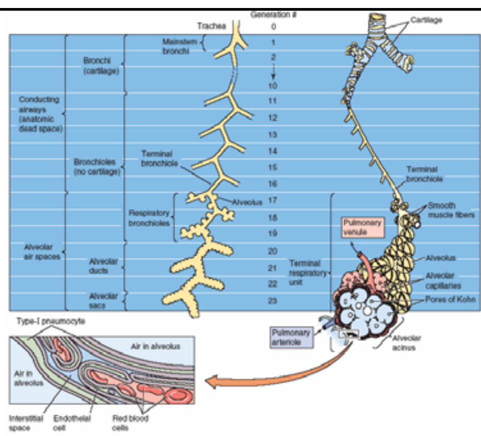
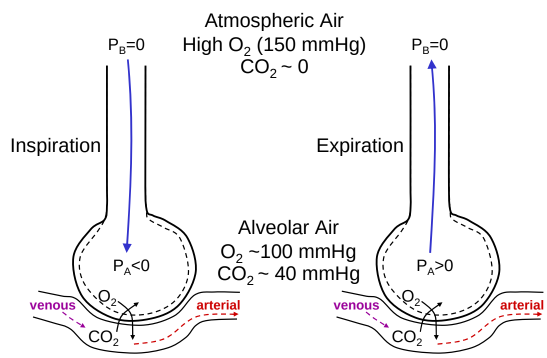
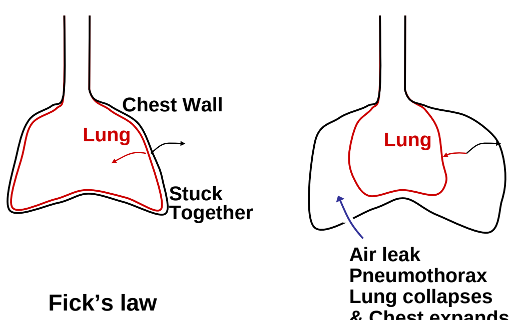




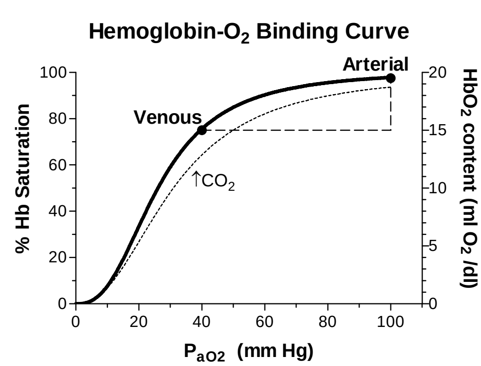


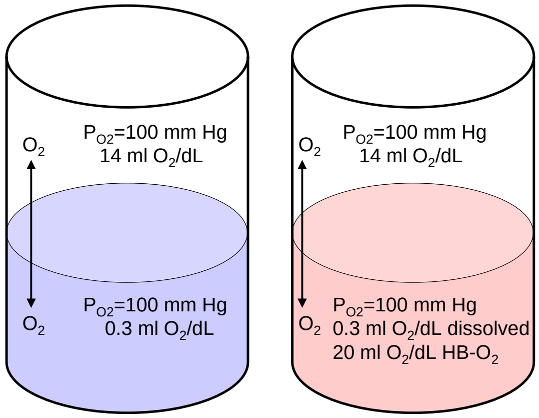


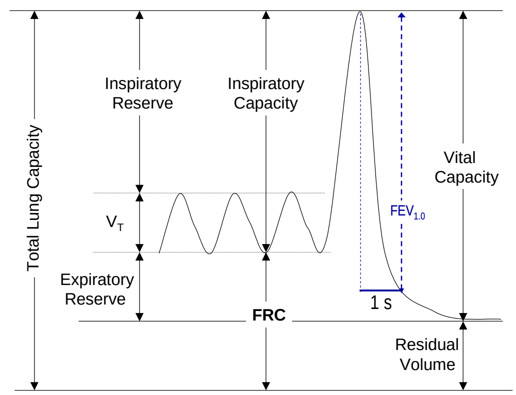


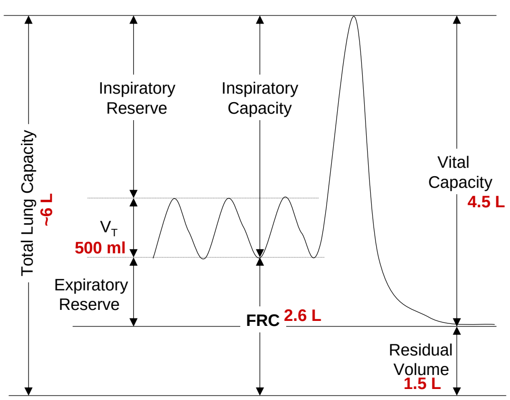
Fick's law

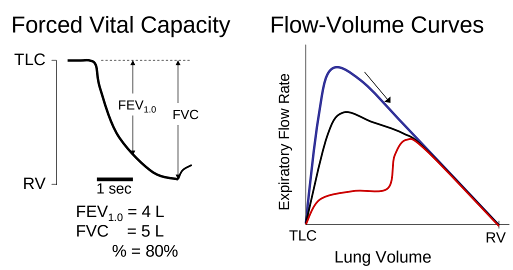
$J = DA (\Delta C / \Delta X)$

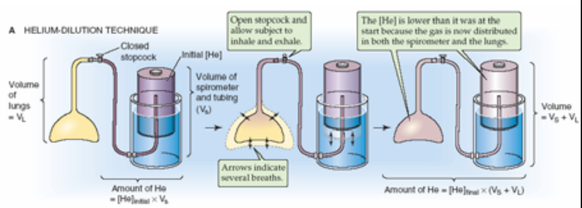












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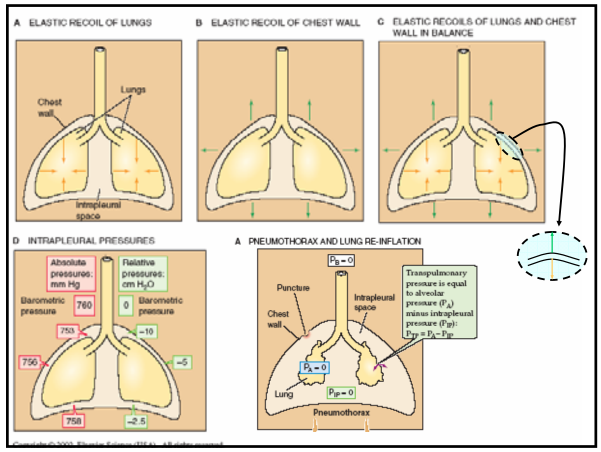
V. A Few Terms (for Your Convenience)

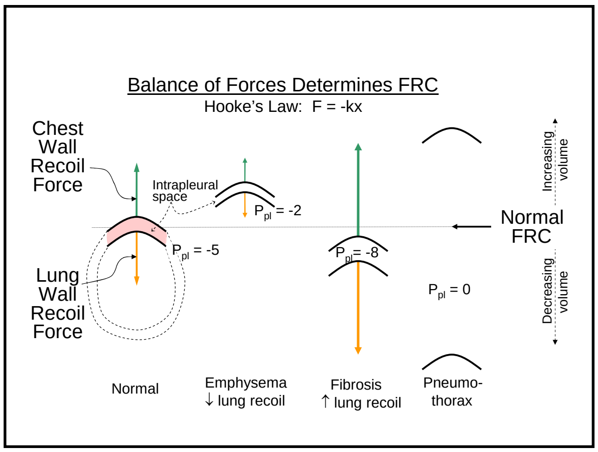
Eupnia - Normal breathing.
Apnea - cessation of respiration (at FRC).
Apneusis - cessation of respiration (in the inspiratory phase).
Apneustic breathing – Apneusis interrupted by by periodic exhalation.
Hyperpnea – increased breathing (usual ↑V_T).
Tachypnea – increased frequency of respiration.
Hyperventilation – increased alveolar ventilation (P_{ACO2} <37 mm Hg).
Hypoventilation – decreased alveolar ventilation (P_{ACO2} >43 mm Hg).
Atelectasis – closed off alveoli, typically at end exhalation.
Cheyne-Stokes Respiration – Cycles of gradually increasing and decreasing V_T.
Dyspnea- Feeling of difficulty in breathing.
Orthopnea- Discomfort in breathing unless standing or sitting upright.

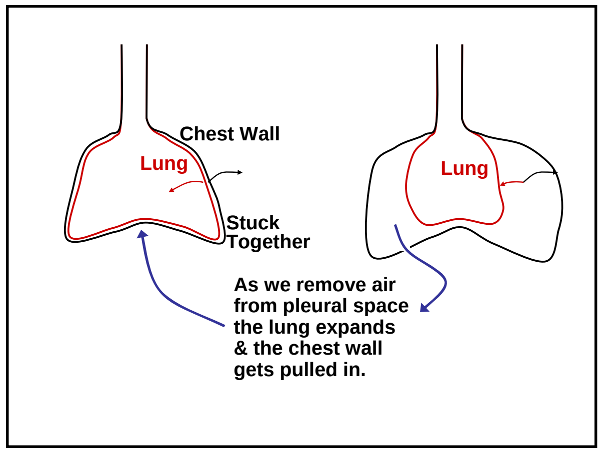
P_{IP} - Intrapleural pressure (pressure in space between visceral and parietal plurae)
P_{TP} - Transpulmonary pressure (distending pressure of airway)
P_{ACO2} - Alveolar P_{CO2} (partial pressure of CO_2).
P_{aCO_2} - arterial P_{CO2}.
P_{vCO2} - venous P_{CO_2}
P_{AO2} - Alveolar P_{O_2}
P_{aO2} - arterial P_{O_2}
P_{vO2} - venous P_{O_2}
P_{ECO2} - P_{CO2} of exhaled air
F_{ECO2} – fraction of exhaled air which is CO_2
(i.e. A= Alveolar, a= arterial, v= venous, E = exhaled, I = inspired)
V_E – Expired volume (liters)
$\dot{V}_E$ – ventilation (liters/min) ($\dot{V}$= dV/dt)
$\dot{V}_A$ – Alveolar ventilation (liters/min)
$\dot{Q}$ – Blood Flow (liters/min)

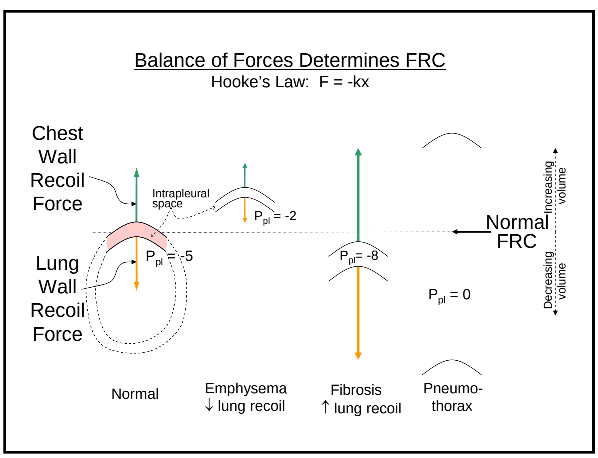
Some Typical Normal Values for Some Key Pulmonary Parameters

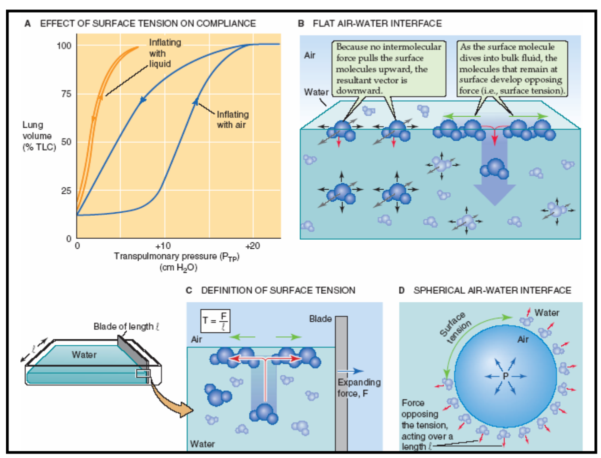
FRC	2.6 L	Max. exp flow	6-9 L/sec
RV	1.5 L	Compliance	60-100 mL/cm H_20
TLC	6.0 L		
V_T	500 ml		
FVC	4.5 L	P_{AO2}	100 mm Hg
		P_{aO2} (*21% O_2*)	90-95 mm Hg
$FEV_{1.0}$ / FVC	>75%	P_{aO2} (*100% O_2*)	>500 mm Hg
Frequency	10-12/min	P_{aCO2}	40 ± 3 mm Hg
$\dot{V}_A$ (norm)	5 ± 0.5 L/min	Arterial pH	7.37-7.43
$\dot{V}_E$ (norm)	7 ± 0.7 L/min	P_{vO2}	40 mm Hg
$\dot{V}_E$ (max)	120-150 L/min	P_{vCO2}	46 mm Hg
Max. insp flow	7-10 L/sec	[Hb]	14-15 g/dL

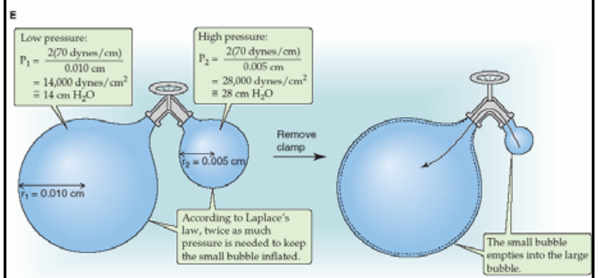


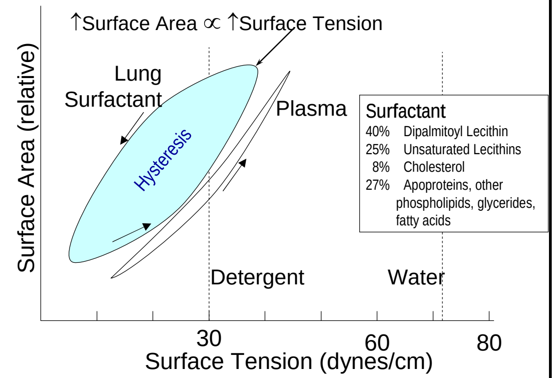


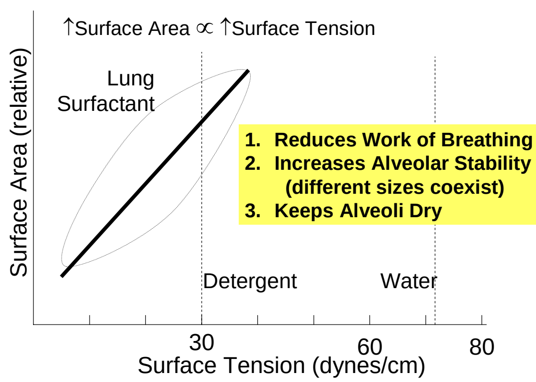


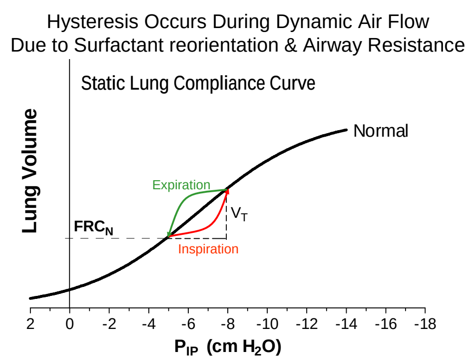


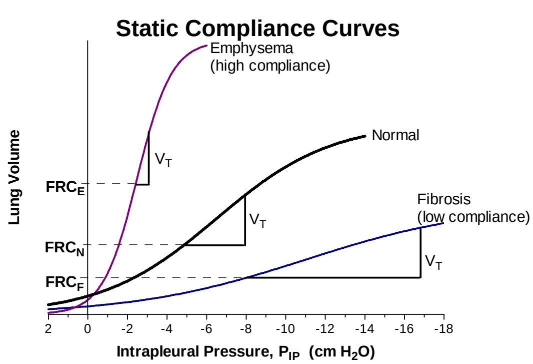


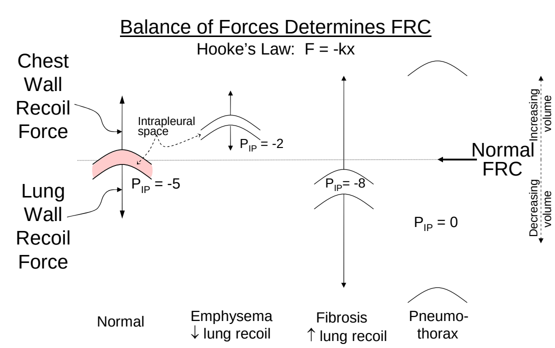

E
Low pressure:
P1 = 2(70 dynes/cm) / 0.010 cm
= 14,000 dynes/cm²
≅ 14 cm H2O
High pressure:
P2 = 2(70 dynes/cm) / 0.005 cm
= 28,000 dynes/cm²
≅ 28 cm H2O
Remove clamp
r1 = 0.010 cm
r2 = 0.005 cm
According to Laplace's law, twice as much pressure is needed to keep the small bubble inflated.
The small bubble empties into the large bubble.

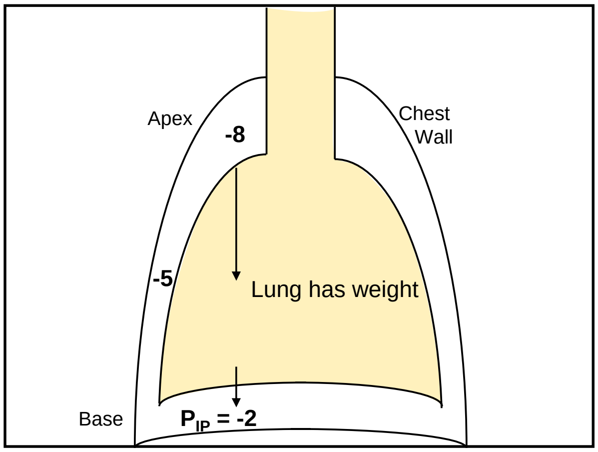

↑Surface Area ∝ ↑Surface Tension
Lung Surfactant
Hysteresis
Plasma
Surfactant
40% Dipalmitoyl Lecithin
25% Unsaturated Lecithins
8% Cholesterol
27% Apoproteins, other phospholipids, glycerides, fatty acids
Detergent
Water
Surface Area (relative)
30
60
80
Surface Tension (dynes/cm)

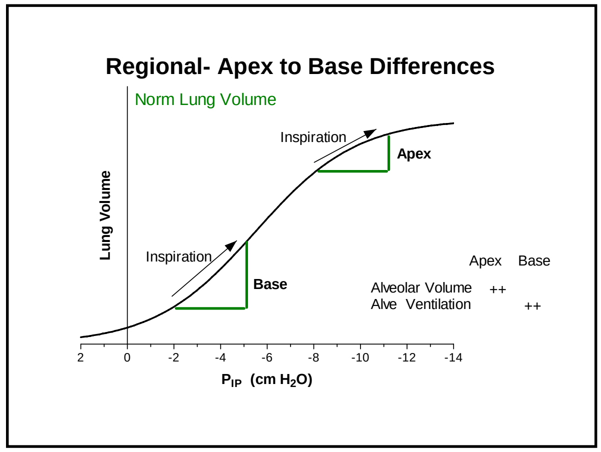

↑Surface Area ∝ ↑Surface Tension
Lung Surfactant
1. Reduces Work of Breathing
2. Increases Alveolar Stability (different sizes coexist)
3. Keeps Alveoli Dry
Detergent
Water
Surface Area (relative)
30
60
80
Surface Tension (dynes/cm)

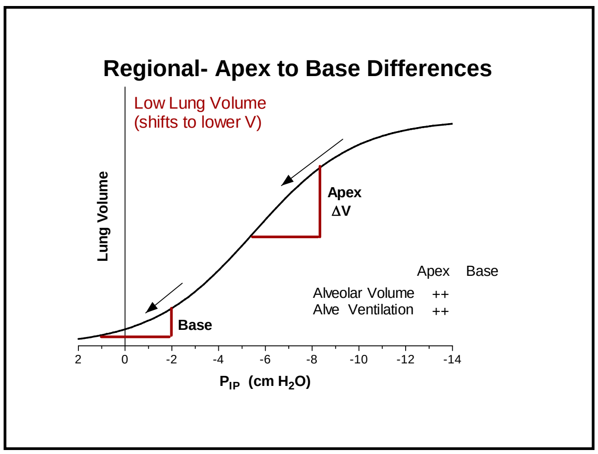

Hysteresis Occurs During Dynamic Air Flow
Due to Surfactant reorientation & Airway Resistance
Static Lung Compliance Curve
Normal
Expiration
Inspiration
FRCN
VT
Lung Volume
2 0 -2 -4 -6 -8 -10 -12 -14 -16 -18
PIP (cm H2O)

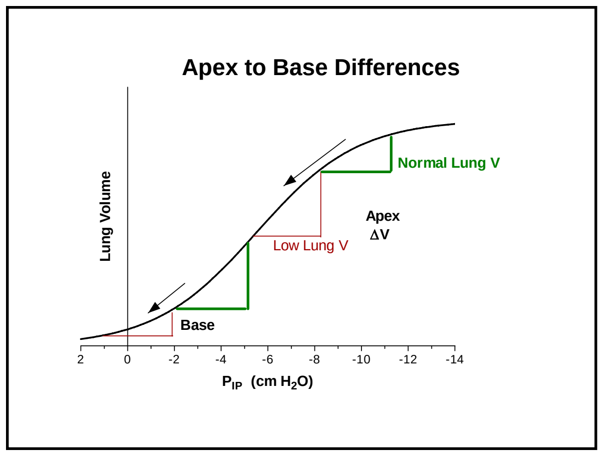

Static Compliance Curves
Emphysema
(high compliance)
Normal
Fibrosis
(low compliance)
VT
VT
VT
FRCE
FRCN
FRCF
Lung Volume
2 0 -2 -4 -6 -8 -10 -12 -14 -16 -18
Intrapleural Pressure, PIP (cm H2O)

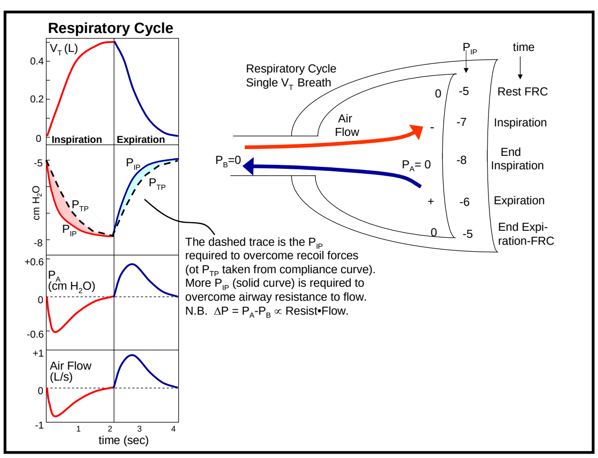

Balance of Forces Determines FRC
Hooke's Law: F = -kx
Chest Wall Recoil Force
Lung Wall Recoil Force
Intrapleural space
PIP = -2
PIP = -5
PIP = -8
PIP = 0
Normal FRC
Increasing volume
Decreasing volume
Normal
Emphysema
↓ lung recoil
Fibrosis
↑ lung recoil
Pneumo-thorax

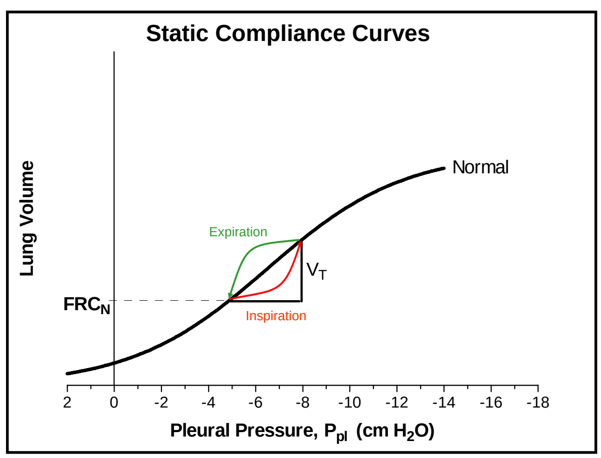

Apex
-8
Chest
Wall
-5
Lung has weight
Base
P_{IP} = -2

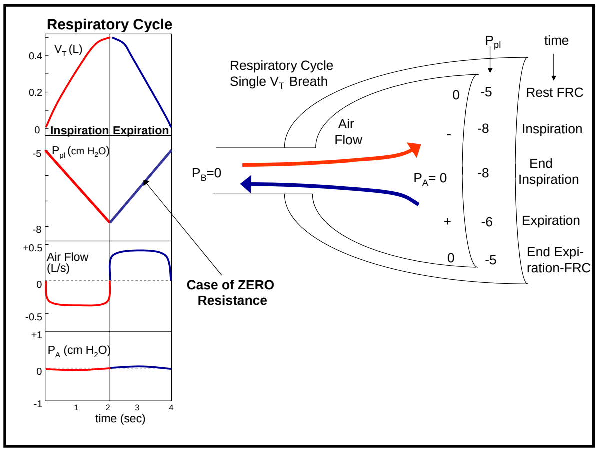

Regional- Apex to Base Differences
Norm Lung Volume
Inspiration
Apex
Inspiration
Base
Lung Volume
Apex Base
Alveolar Volume ++
Alve Ventilation ++
2 0 -2 -4 -6 -8 -10 -12 -14
P_{IP} (cm H_2O)


Regional- Apex to Base Differences
Low Lung Volume
(shifts to lower V)
Lung Volume
Apex
ΔV
Apex Base
Alveolar Volume ++
Alve Ventilation ++
Base
2 0 -2 -4 -6 -8 -10 -12 -14
P_{IP} (cm H_2O)

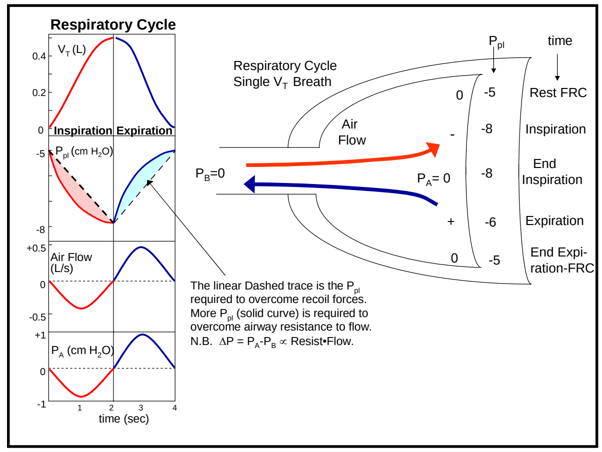

Apex to Base Differences
Normal Lung V
Lung Volume
Apex
ΔV
Low Lung V
Base
2 0 -2 -4 -6 -8 -10 -12 -14
P_{IP} (cm H_2O)


Respiratory Cycle
V_T (L)
Inspiration
Expiration
P_{TP}
P_{IP}
P_A (cm H_2O)
Air Flow (L/s)
time (sec)
Respiratory Cycle
Single V_T Breath
Air Flow
P_B=0
P_A= 0
P_{IP}
time
Rest FRC
Inspiration
End Inspiration
Expiration
End Expi-ration-FRC
The dashed trace is the P_{IP} required to overcome recoil forces (ot P_{TP} taken from compliance curve). More P_{IP} (solid curve) is required to overcome airway resistance to flow.
N.B. ΔP = P_A-P_B ∝ Resist•Flow.

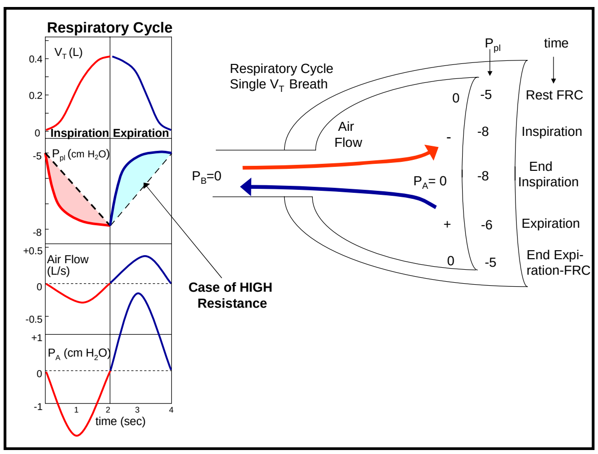

Static Compliance Curves
Normal
Lung Volume
Expiration
V_T
FRC_N
Inspiration
2 0 -2 -4 -6 -8 -10 -12 -14 -16 -18
Pleural Pressure, P_{pl} (cm H_2O)



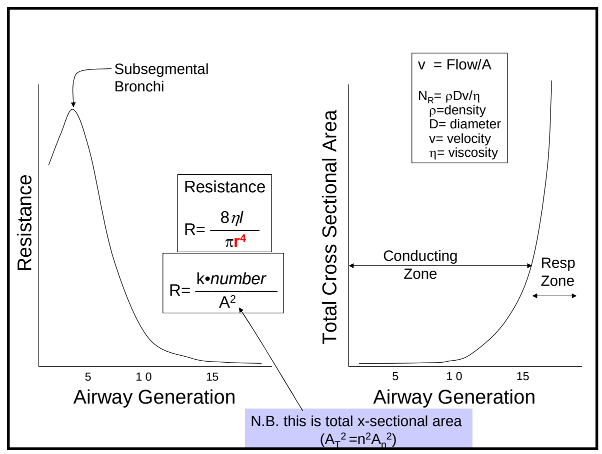
Respiratory Cycle
V_T (L)
0.4
0.2
0
Inspiration Expiration
P_pl (cm H2O)
-5
-8
Air Flow (L/s)
+0.5
0
-0.5
P_A (cm H2O)
+1
0
-1
1 2 3 4
time (sec)
Case of ZERO Resistance
Respiratory Cycle
Single V_T Breath
P_B=0
Air Flow
P_A= 0
P_pl
time
0 -5 Rest FRC
- -8 Inspiration
-8 End Inspiration
+ -6 Expiration
0 -5 End Expi-ration-FRC



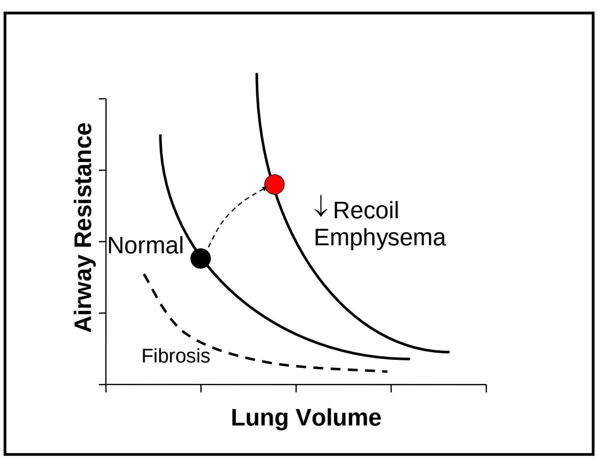
Respiratory Cycle
V_T (L)
0.4
0.2
0
Inspiration Expiration
P_pl (cm H2O)
-5
-8
Air Flow (L/s)
+0.5
0
-0.5
P_A (cm H2O)
+1
0
-1
1 2 3 4
time (sec)
The linear Dashed trace is the P_pl required to overcome recoil forces.
More P_pl (solid curve) is required to overcome airway resistance to flow.
N.B. ΔP = P_A-P_B ∝ Resist•Flow.
Respiratory Cycle
Single V_T Breath
P_B=0
Air Flow
P_A= 0
P_pl
time
0 -5 Rest FRC
- -8 Inspiration
-8 End Inspiration
+ -6 Expiration
0 -5 End Expi-ration-FRC



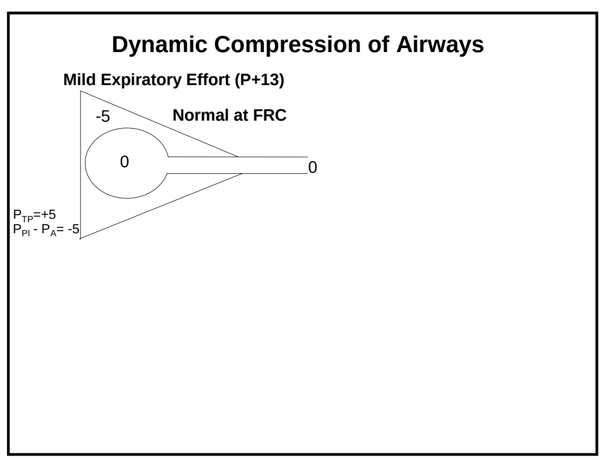
Respiratory Cycle
V_T (L)
0.4
0.2
0
Inspiration Expiration
P_pl (cm H2O)
-5
-8
Air Flow (L/s)
+0.5
0
-0.5
P_A (cm H2O)
+1
0
-1
1 2 3 4
time (sec)
Case of HIGH Resistance
Respiratory Cycle
Single V_T Breath
P_B=0
Air Flow
P_A= 0
P_pl
time
0 -5 Rest FRC
- -8 Inspiration
-8 End Inspiration
+ -6 Expiration
0 -5 End Expi-ration-FRC



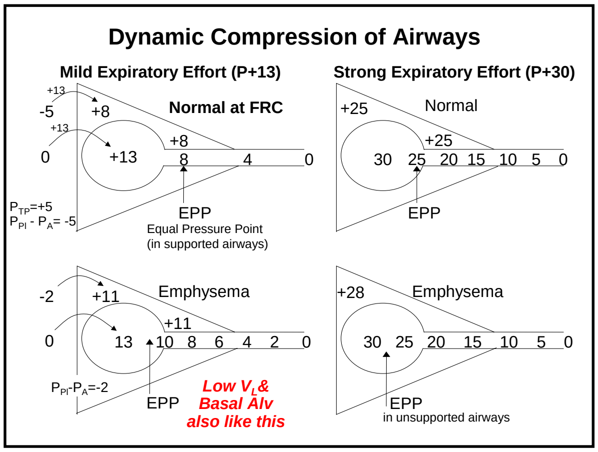
Subsegmental Bronchi
Resistance
Resistance
R= 8ηl / πr^4
R= k•number / A^2
5 10 15
Airway Generation
v = Flow/A
N_R= ρDv/η
ρ=density
D= diameter
v= velocity
η= viscosity
Total Cross Sectional Area
Conducting Zone
Resp Zone
5 10 15
Airway Generation
N.B. this is total x-sectional area
(A_T^2 =n^2A_n^2)

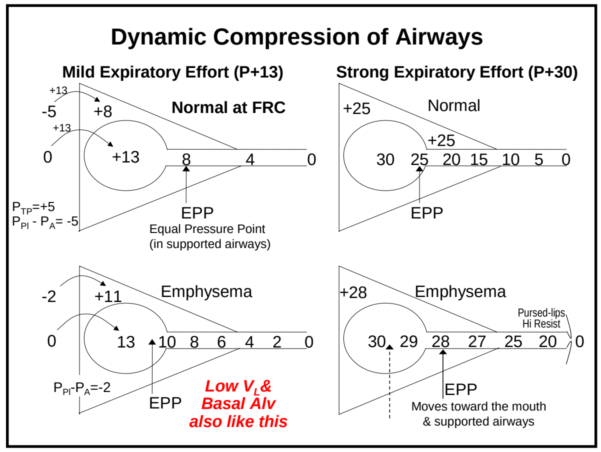


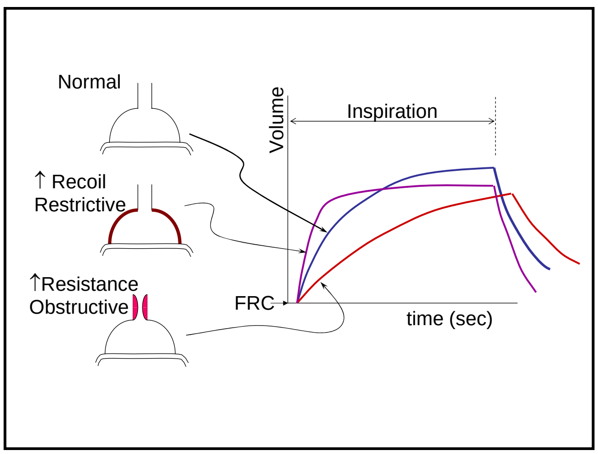
Airway Resistance
Normal
↓Recoil
Emphysema
Fibrosis
Lung Volume

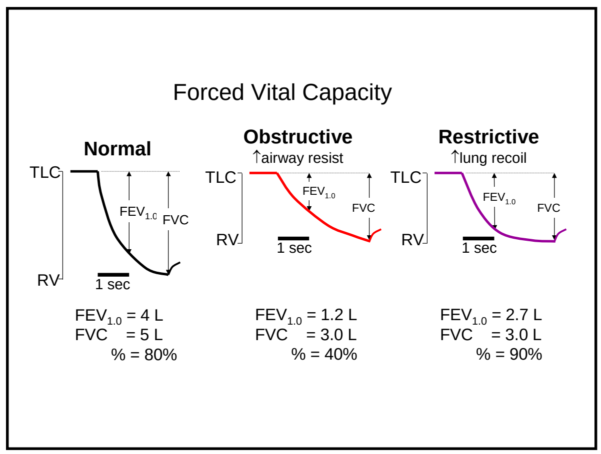


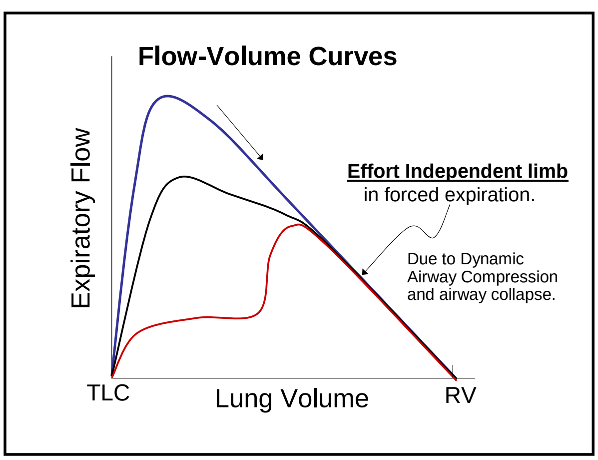
Dynamic Compression of Airways
Mild Expiratory Effort (P+13)
-5
Normal at FRC
0
0
P_TP=+5
P_Pl - P_A= -5

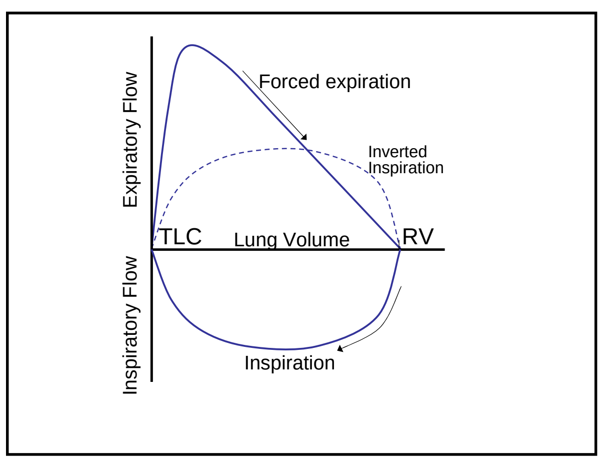

Dynamic Compression of Airways
Mild Expiratory Effort (P+13)
Strong Expiratory Effort (P+30)
Normal at FRC
Normal
EPP
Equal Pressure Point
(in supported airways)
Emphysema
Emphysema
Low V_L &
Basal Alv
also like this
EPP
in unsupported airways

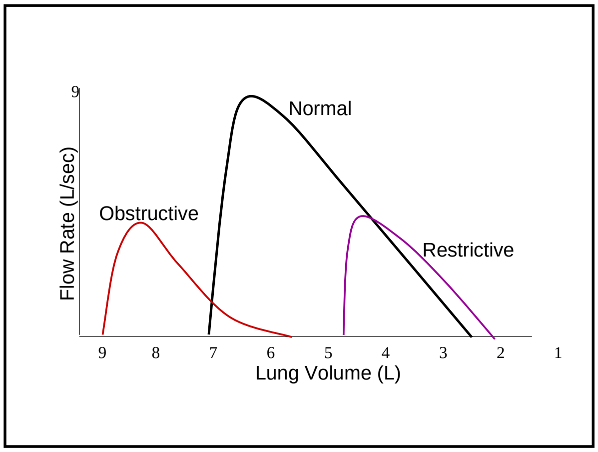

Dynamic Compression of Airways
Mild Expiratory Effort (P+13)
Strong Expiratory Effort (P+30)
Normal at FRC
Normal
EPP
Equal Pressure Point
(in supported airways)
Emphysema
Emphysema
Pursed-lips
Hi Resist
Low V_L &
Basal Alv
also like this
EPP
Moves toward the mouth
& supported airways


Normal
↑ Recoil
Restrictive
↑Resistance
Obstructive
Volume
Inspiration
FRC
time (sec)

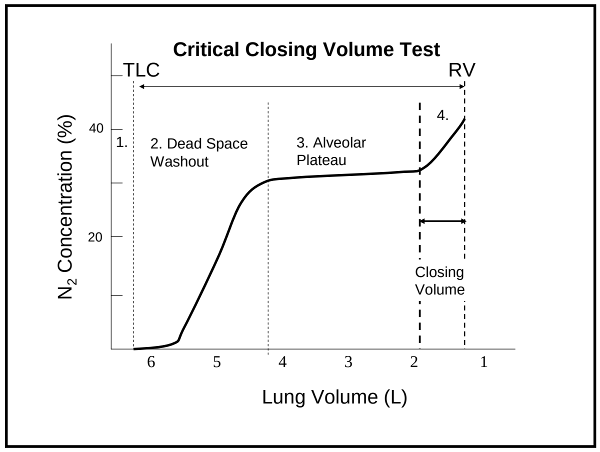

Forced Vital Capacity
Normal
Obstructive
↑airway resist
Restrictive
↑lung recoil
TLC
RV
1 sec
FEV1.0 = 4 L
FVC = 5 L
% = 80%
FEV1.0 = 1.2 L
FVC = 3.0 L
% = 40%
FEV1.0 = 2.7 L
FVC = 3.0 L
% = 90%


Flow-Volume Curves
Expiratory Flow
Effort Independent limb
in forced expiration.
Due to Dynamic
Airway Compression
and airway collapse.
TLC
Lung Volume
RV

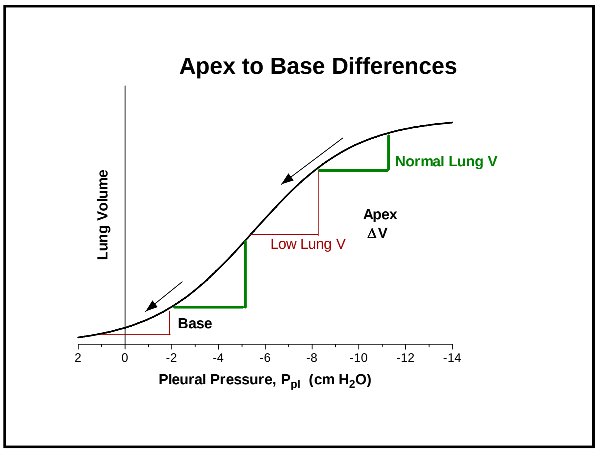

Expiratory Flow
Forced expiration
Inverted
Inspiration
TLC
Lung Volume
RV
Inspiratory Flow
Inspiration



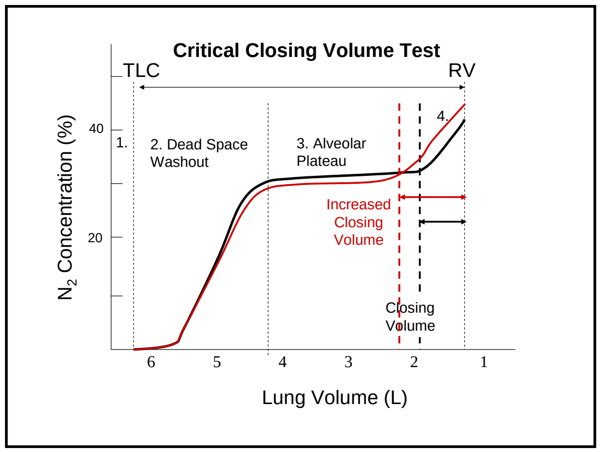
Normal
Obstructive
Restrictive
Flow Rate (L/sec)
Lung Volume (L)



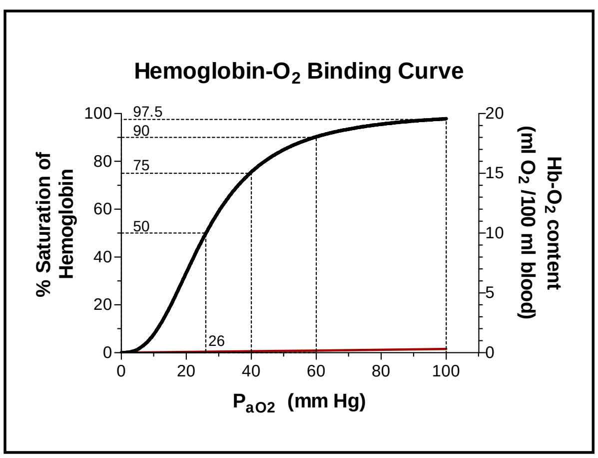
Critical Closing Volume Test
TLC
RV
1.
2. Dead Space Washout
3. Alveolar Plateau
4.
Closing Volume
N2 Concentration (%)
Lung Volume (L)



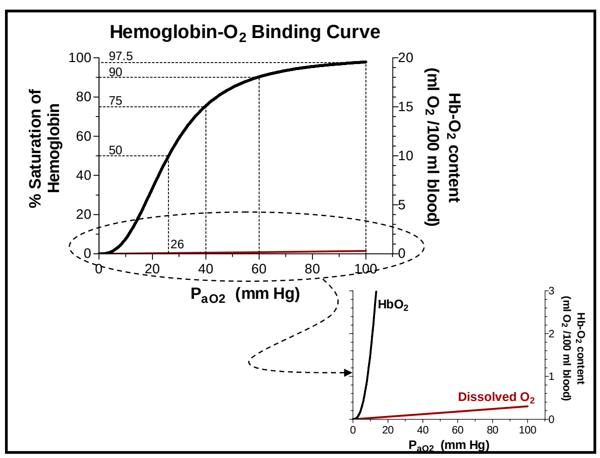
Apex to Base Differences
Normal Lung V
Low Lung V
Apex
ΔV
Base
Lung Volume
Pleural Pressure, Ppl (cm H2O)



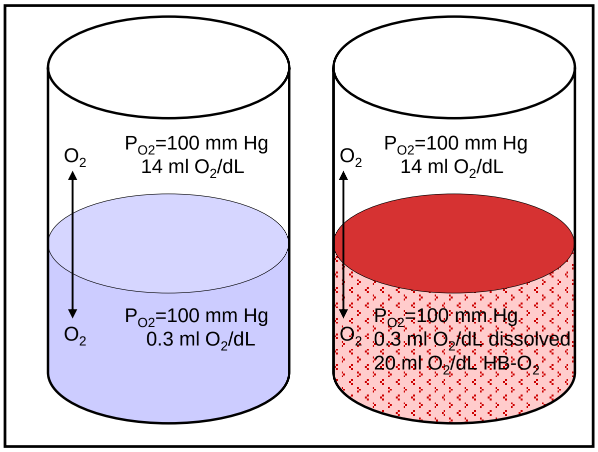
Critical Closing Volume Test
TLC
RV
1.
2. Dead Space Washout
3. Alveolar Plateau
4.
Increased Closing Volume
Closing Volume
N2 Concentration (%)
Lung Volume (L)



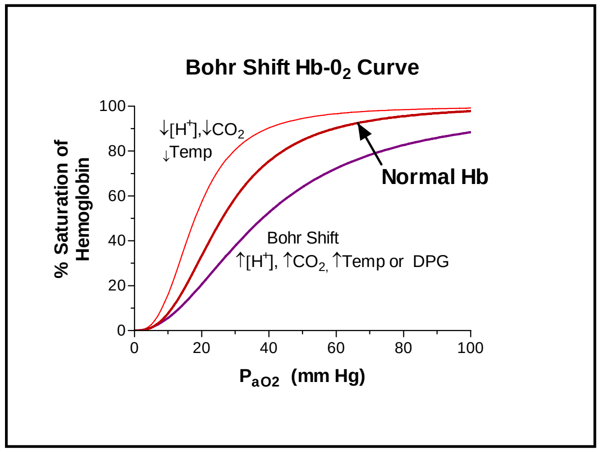
Hemoglobin-O2 Binding Curve
% Saturation of Hemoglobin
Hb-O2 content (ml O2 /100 ml blood)
PaO2 (mm Hg)



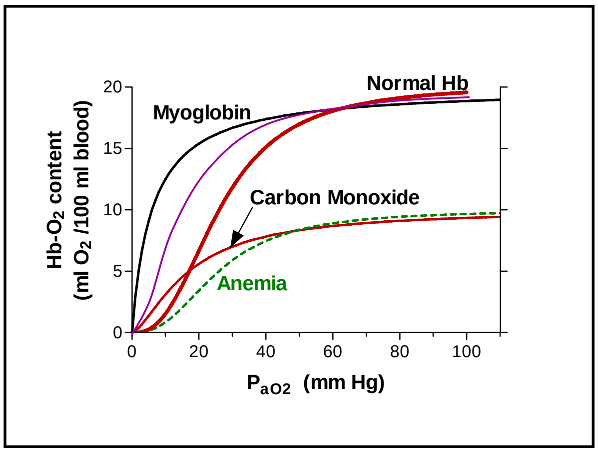
Hemoglobin-O2 Binding Curve
% Saturation of Hemoglobin
Hb-O2 content (ml O2 /100 ml blood)
PaO2 (mm Hg)
HbO2
Dissolved O2



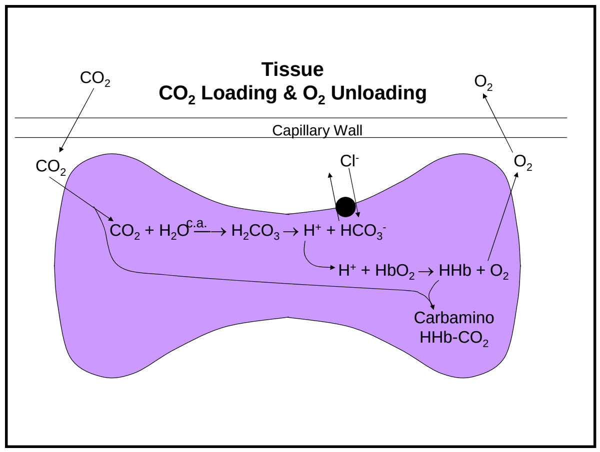
O_2
P_{O2}=100 mm Hg
14 ml O_2/dL
P_{O2}=100 mm Hg
0.3 ml O_2/dL
O_2
O_2
P_{O2}=100 mm Hg
14 ml O_2/dL
P_{O2}=100 mm Hg
0.3 ml O_2/dL dissolved
20 ml O_2/dL HB-O_2
O_2



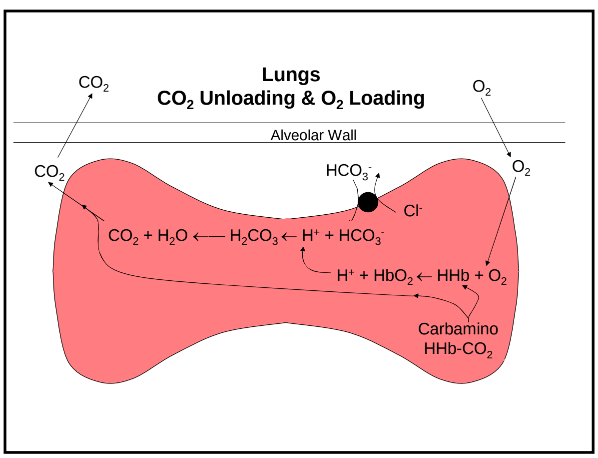
Bohr Shift Hb-0_2 Curve
↓[H^+],↓CO_2
↓Temp
Normal Hb
Bohr Shift
↑[H^+], ↑CO_2, ↑Temp or DPG
% Saturation of Hemoglobin
P_{aO2} (mm Hg)



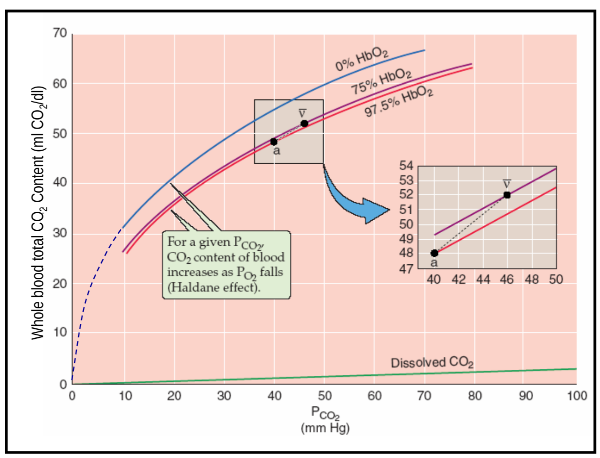
Normal Hb
Myoglobin
Carbon Monoxide
Anemia
Hb-O_2 content (ml O_2 /100 ml blood)
P_{aO2} (mm Hg)



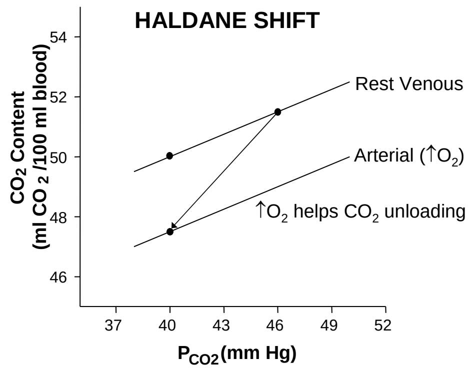
Tissue
CO_2 Loading & O_2 Unloading
CO_2
O_2
Capillary Wall
CO_2
Cl^-
O_2
CO_2 + H_2O —c.a.→ H_2CO_3 → H^+ + HCO_3^-
H^+ + HbO_2 → HHb + O_2
Carbamino
HHb-CO_2

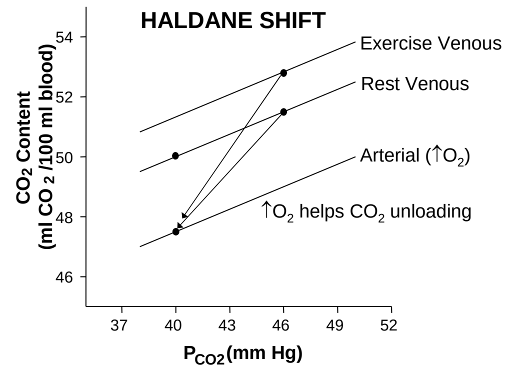


Lungs
CO_2 Unloading & O_2 Loading
CO_2
O_2
Alveolar Wall
CO_2
HCO_3^-
O_2
Cl^-
CO_2 + H_2O ← H_2CO_3 ← H^+ + HCO_3^-
H^+ + HbO_2 ← HHb + O_2
Carbamino
HHb-CO_2



0% HbO_2
75% HbO_2
97.5% HbO_2
For a given P_{CO_2}, CO_2 content of blood increases as P_{O_2} falls (Haldane effect).
Whole blood total CO_2 Content (ml CO_2/dl)
Dissolved CO_2
P_{CO_2} (mm Hg)

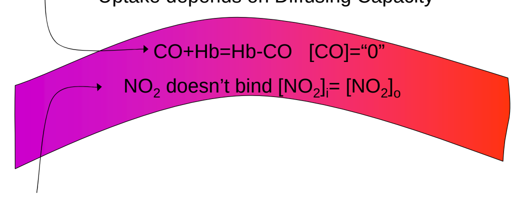




XIV. RESPIRATORY GAS CASCADE

	P_{O2} mm Hg	P_{CO2} mm Hg
Air (dry) 760 × 0.21	160	0
Trachea (humidified; 760-47) 713 × 0.21	150	0
Alveolus (some O_2 absorbed by blood)	100	40
Arterial (R-L Shunt)	90	40+
Mixed venous (O_2 absorbed by tissues)	40	46

CO is Diffusion Limited (soaked up by Hb immediately)
Uptake depends on Diffusing Capacity



NO_2 is Perfusion Limited (Blood is quickly "saturated")
Uptake depends on how much blood goes by

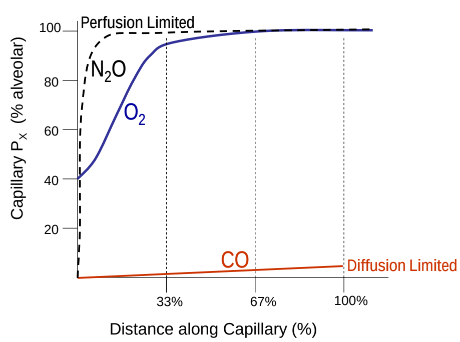
Measuring Diffusion capacity, D_L (or Transfer capacity) with CO

$J_{CO} = D_{CO} A\ \Delta P / \Delta x$

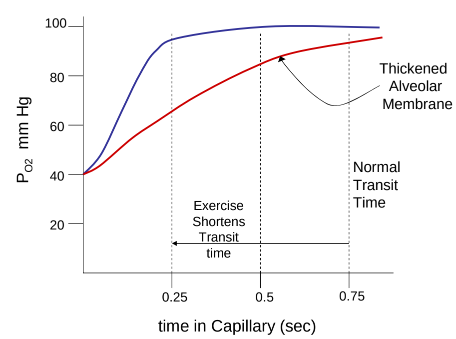
$\Delta P = P_{ACO} - P_{aCO}$ and $P_{aCO}=0$ and D_{CO}, A & Δx are lumped into D_L

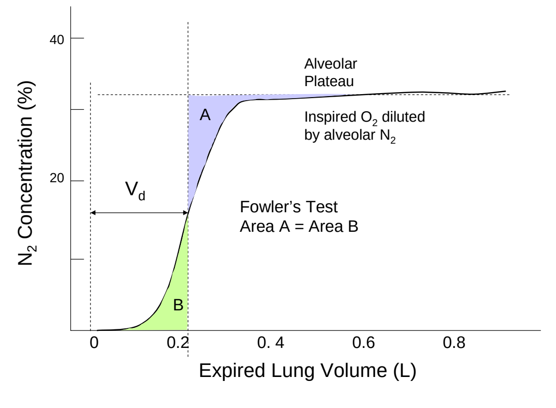
$D_L = J_{CO} / P_{ACO}$ (where J_{CO} is the rate of CO uptake measured)

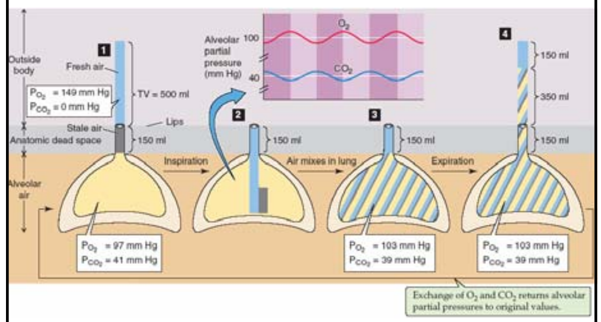
Diffusion in Pulmonary Capillaries

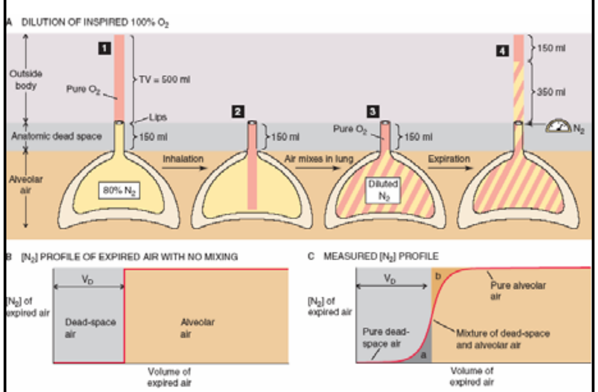


O_2 Diffusion in Pulmonary Capillaries (transit time)









The Bohr Equation

$$\frac{V_{D1}}{V_T} = \frac{(P_{ACO2} - P_{ECO2})}{P_{ACO2}}$$

P_{CO2} values are measured by a CO_2 electrode. Sometimes P_{aCO2} is used.

$$\frac{V_{D2}}{V_T} = \frac{(P_{aCO2} - P_{ECO2})}{P_{aCO2}}$$

D. Sample Calculation

$V_T = 600$ ml $P_{ACO2} = 38$ mmHg

$P_{ECO2} = 28$ mmHg $P_{aCO2} = 40$ mmHg

$V_{D1} = 600(38 - 28)/38 = 158$ ml

$V_{D2} = 600(40 - 28)/40 = 180$ ml

E. Alveolar Ventilation

$\dot{V}_E = \dot{V}_D + \dot{V}_A = V_T \times$ frequency

$\dot{V}_A = \dot{V}_E - \dot{V}_D$

1. For $V_T = 500$ ml, f = 10/min, $V_D = 150$ ml, what is $\dot{V}_A$?
   $\dot{V}_A = 5000 - 1500$
   $= 3500$ ml/min
2. If $\dot{V}_E$ is doubled by increasing V_T what is $\dot{V}_A$?
   $= 10,000 - 1500$
   $= 8500$ ml/min
3. If the same $\dot{V}_E$ is obtained by doubling frequency, what is $\dot{V}_A$?
   $= 10,000 - 3000$
   $= 7000$ ml/min

Thus increasing V_T rather than frequency is more effective for ↑ $\dot{V}_E$.

F. Alveolar Ventilation and CO_2 production

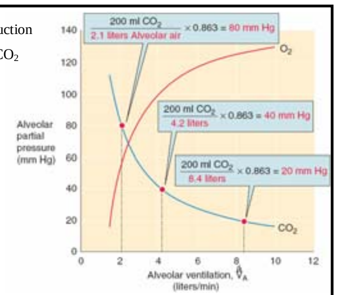
$\dot{V}_{CO2}$ = Expired CO_2 - Inspired CO_2

$= \dot{V}_A \times F_{ACO2}$

$= \dfrac{\dot{V}_A \times P_{ACO2}}{P_A}$

$$\dot{V}_A = \frac{\dot{V}_{CO2} \times k}{P_{ACO2}}$$

Where k= 863 mmHg
or 0.863 (mmHg•L/ml)



So, for a given rate of CO_2 production, steady state P_{ACO2} is inversely related to $\dot{V}_A$.
Thus, if $\dot{V}_A$ is decreased by 1/2, P_{ACO2} is doubled.

XIX. RESPIRATORY EXCHANGE RATIO

RQ = $\dot{V}_{CO2}/\dot{V}_{O2}$

The relative amounts of O_2 consumed and CO_2 produced depends upon the fuel.

Carbohydrate RQ = 1
Fat RQ = 0.7
Protein RQ = 0.8
A typical "normal" RQ is 0.8

The partial pressures of O_2 and CO_2 are also affected.

$$RQ = \frac{\dot{V}_{CO2}}{\dot{V}_{O2}} = \frac{P_{ACO2}}{P_{IO2} - P_{EO2}} = \frac{40}{50}$$

Study Questions/ Exercises

Q: Why does this ratio necessarily reflect the RQ?

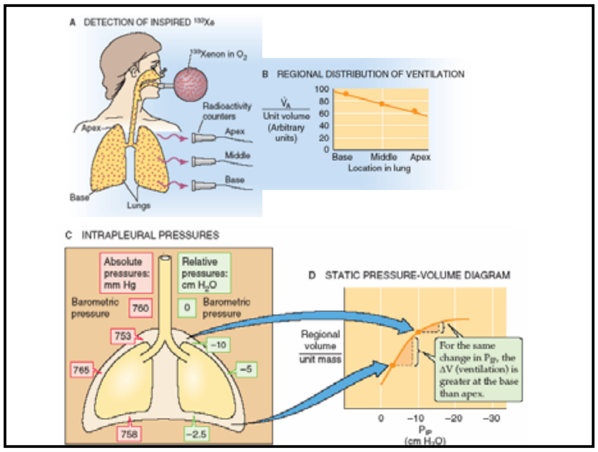
Alveolar Gas Equation – Allows you to estimate $P_{AO2} - P_{aO2}$ gradient.

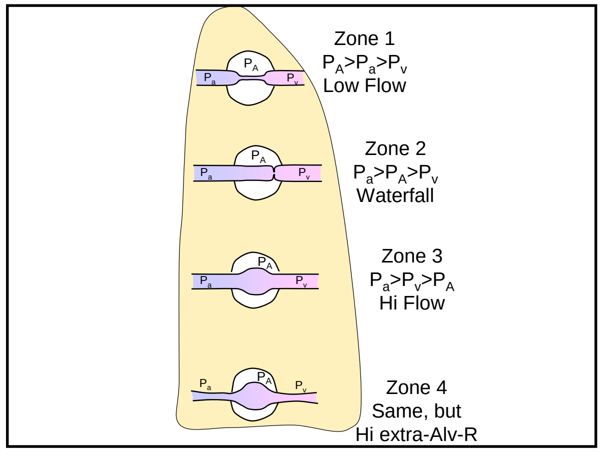
$P_{AO2} = F_{IO2} (P_{ATM} - P_{H2O}) - P_{aCO2}/RQ + K$

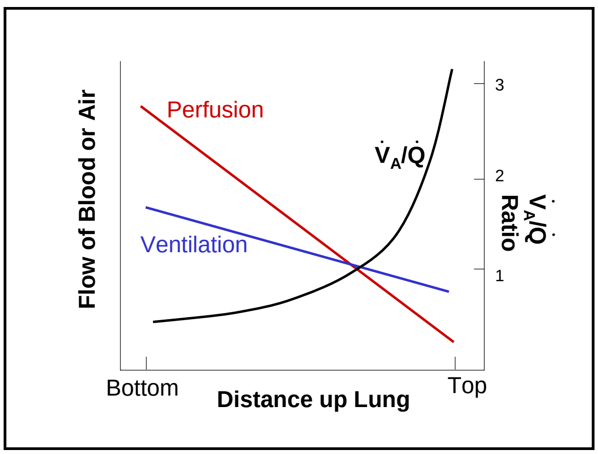
$\mathbf{P_{AO2} = P_{IO2} - P_{aCO2}/RQ}$

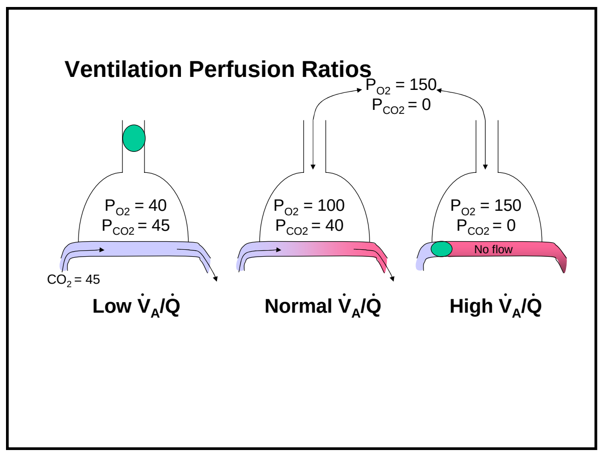
e.g. $= 150 - 40/0.8 = 100$ mmHg

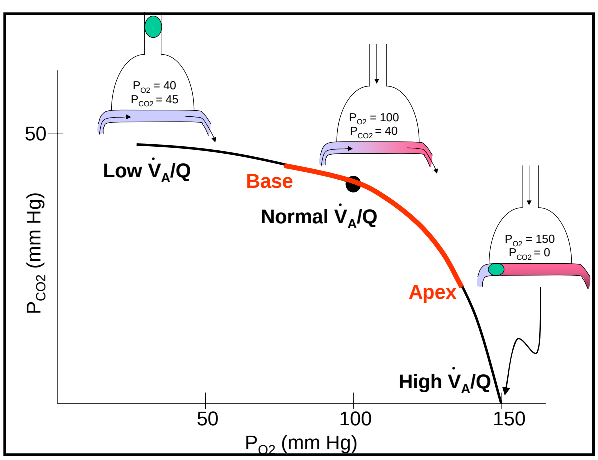
$K = P_{ACO2} \bullet F_{IO2} \bullet (\{1-RQ\}/RQ)$ a small correction (2 mmHg) usually ignored

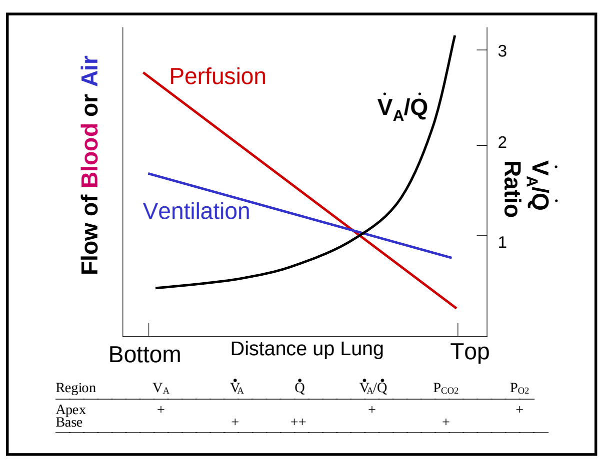

A DETECTION OF INSPIRED 133Xe
133Xenon in O2
Radioactivity counters
Apex
Middle
Base
Lungs
B REGIONAL DISTRIBUTION OF VENTILATION
V̇A Unit volume (Arbitrary units)
Base Middle Apex
Location in lung
C INTRAPLEURAL PRESSURES
Absolute pressures: mm Hg
Relative pressures: cm H2O
Barometric pressure
760
753
765
758
−10
−5
−2.5
D STATIC PRESSURE-VOLUME DIAGRAM
Regional volume unit mass
For the same change in Pip, the ΔV (ventilation) is greater at the base than apex.


Zone 1
PA>Pa>Pv
Low Flow
Zone 2
Pa>PA>Pv
Waterfall
Zone 3
Pa>Pv>PA
Hi Flow
Zone 4
Same, but
Hi extra-Alv-R


Flow of Blood or Air
Perfusion
Ventilation
V̇A/Q̇
V̇A/Q̇ Ratio
3
2
1
Bottom
Distance up Lung
Top


Ventilation Perfusion Ratios
PO2 = 150
PCO2 = 0
PO2 = 40
PCO2 = 45
PO2 = 100
PCO2 = 40
PO2 = 150
PCO2 = 0
No flow
CO2 = 45
Low V̇A/Q̇
Normal V̇A/Q̇
High V̇A/Q̇


PO2 = 40
PCO2 = 45
PO2 = 100
PCO2 = 40
PO2 = 150
PCO2 = 0
50
Low V̇A/Q
Base
Normal V̇A/Q
Apex
High V̇A/Q
PCO2 (mm Hg)
50
100
150
PO2 (mm Hg)


Flow of Blood or Air
Perfusion
Ventilation
V̇A/Q̇
V̇A/Q̇ Ratio
3
2
1
Bottom
Distance up Lung
Top
Region VA V̇A Q̇ V̇A/Q̇ PCO2 PO2
Apex + + +
Base + ++ +

Mechanisms of Hypoxemia

A. Hypoventilation
B. Diffusion Abnormalities
C. Right to Left Shunt
D. Ventilation/Perfusion Mismatch
E. Low inspired P_{O2}

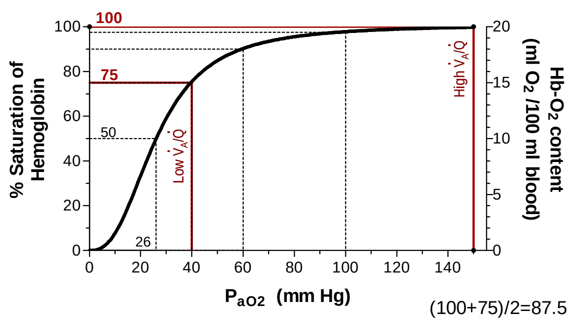
Mechanisms of Hypoxemia

	P_{aO2}	P_{aCO2}	P_{O2} (A-a)	P_{aO2} with 100% O_2
Hypoventilation	low	**High**	**Norm**	>550
Diffusion	low	norm-low	high	>550
R-L Shunt	low	norm-low	high	**<550**
$\dot{V}_A/Q$ Imbalance	low	norm-lo-hi	high	>550

Other Hypoxemias (without low P_{aO2})
a. Anemia
b. Carbon Monoxide
c. Hypoperfusion (CV problem)

Local Control
a. Low P_{AO2} → vasoconstriction
b. Low P_{VCO2} → bronchoconstriction

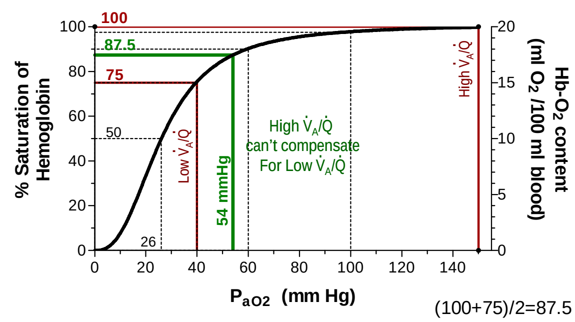
Hemoglobin-O_2 Binding Curve



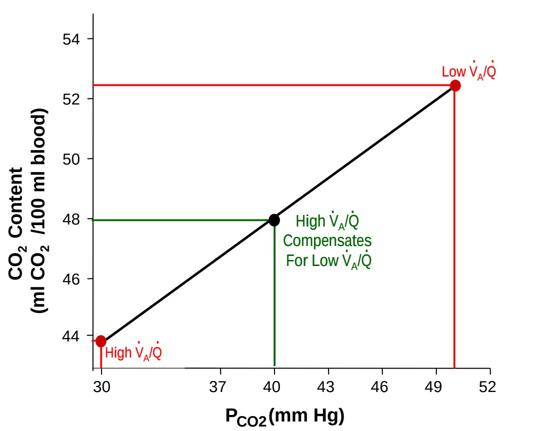
(100+75)/2=87.5
(20+15)/2 =17.5

Study Questions/ Exercises: Consider ½ of pulmonary blood flow going to regions where P_{AO2} is 150 mm Hg and the other ½ to a region of P_{AO2} = 40 mm Hg. Assume P_{ACO2} is 30 and 50 mm Hg in these respective regions. How does P_{aO2} become less than normal while P_{aCO2} is normal?.

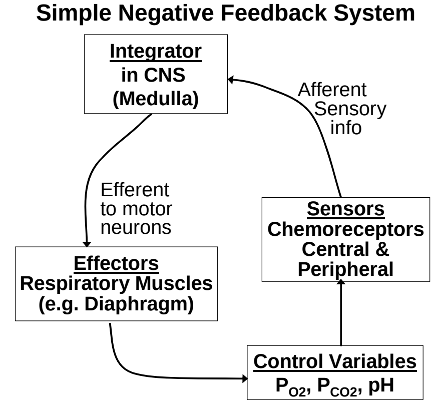
Hemoglobin-O_2 Binding Curve

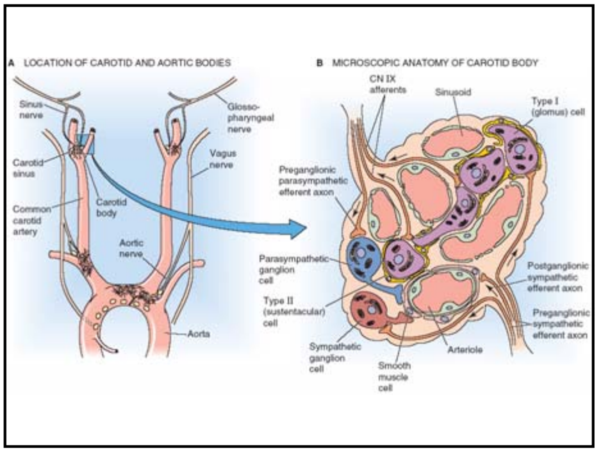


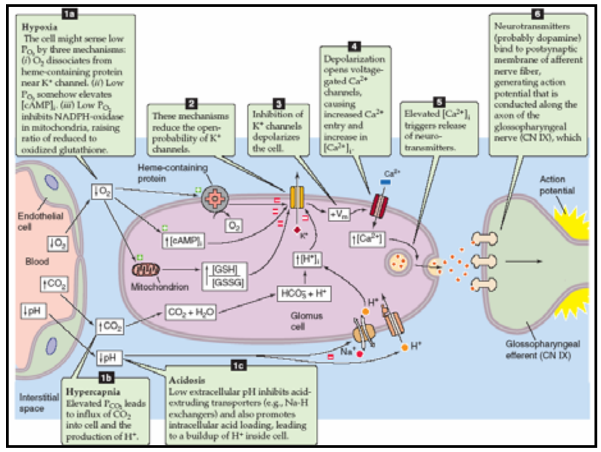
(100+75)/2=87.5
(20+15)/2 =17.5

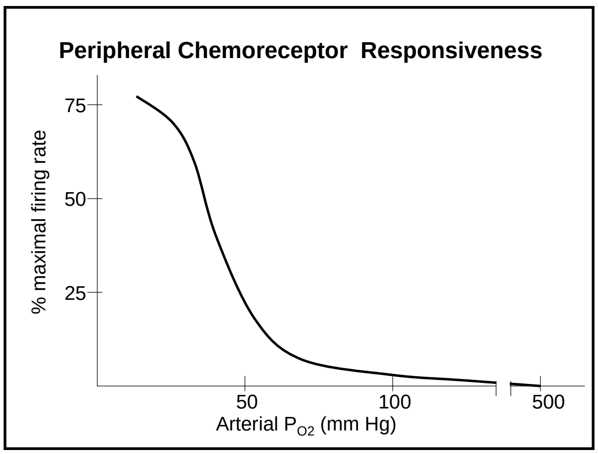


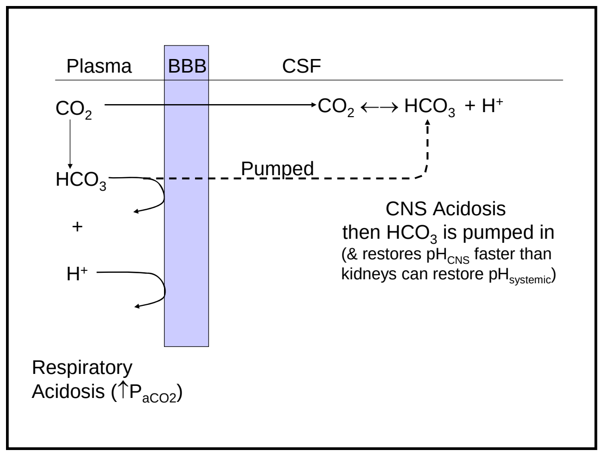
Simple Negative Feedback System

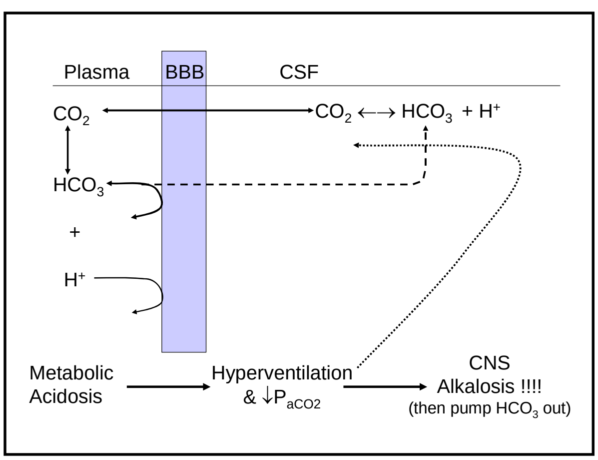


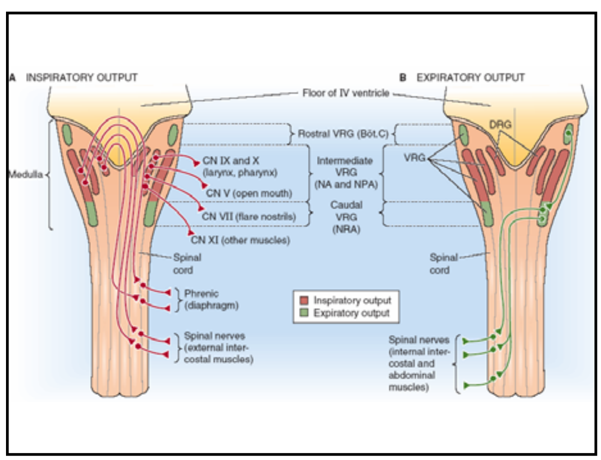

A LOCATION OF CAROTID AND AORTIC BODIES
B MICROSCOPIC ANATOMY OF CAROTID BODY
Sinus nerve
Glosso-pharyngeal nerve
Carotid sinus
Vagus nerve
Common carotid artery
Carotid body
Aortic nerve
Aorta
CN IX afferents
Sinusoid
Type I (glomus) cell
Preganglionic parasympathetic efferent axon
Parasympathetic ganglion cell
Type II (sustentacular) cell
Sympathetic ganglion cell
Smooth muscle cell
Arteriole
Postganglionic sympathetic efferent axon
Preganglionic sympathetic efferent axon

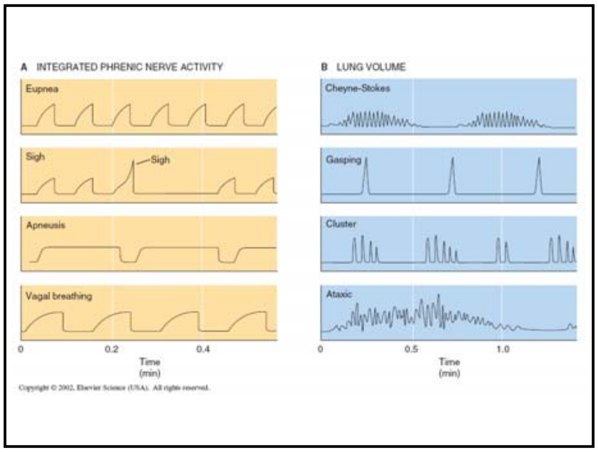

1a Hypoxia
The cell might sense low P_{O_2} by three mechanisms: (i) O_2 dissociates from heme-containing protein near K^+ channel. (ii) Low P_{O_2} somehow elevates [cAMP]$_i$. (iii) Low P_{O_2} inhibits NADPH-oxidase in mitochondria, raising ratio of reduced to oxidized glutathione.
2 These mechanisms reduce the open-probability of K^+ channels.
3 Inhibition of K^+ channels depolarizes the cell.
4 Depolarization opens voltage-gated Ca^{2+} channels, causing increased Ca^{2+} entry and increase in $[Ca^{2+}]_i$.
5 Elevated $[Ca^{2+}]_i$ triggers release of neuro-transmitters.
6 Neurotransmitters (probably dopamine) bind to postsynaptic membrane of afferent nerve fiber, generating action potential that is conducted along the axon of the glossopharyngeal nerve (CN IX), which
Heme-containing protein
Endothelial cell
Blood
Mitochondrion
Glomus cell
Action potential
Glossopharyngeal efferent (CN IX)
Interstitial space
1b Hypercapnia
Elevated P_{CO_2} leads to influx of CO_2 into cell and the production of H^+.
1c Acidosis
Low extracellular pH inhibits acid-extruding transporters (e.g., Na-H exchangers) and also promotes intracellular acid loading, leading to a buildup of H^+ inside cell.

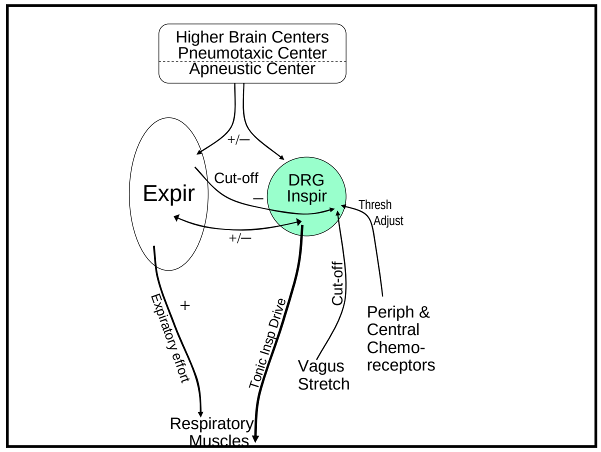

Peripheral Chemoreceptor Responsiveness
% maximal firing rate
75
50
25
50
100
500
Arterial P_{O2} (mm Hg)

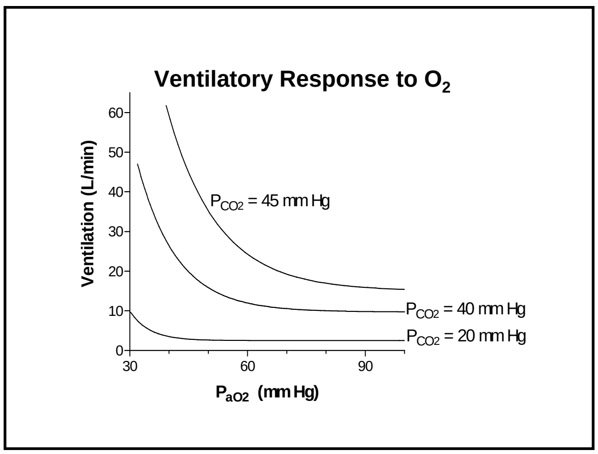

Plasma
BBB
CSF
CO_2
$CO_2 \longleftrightarrow HCO_3 + H^+$
HCO_3
Pumped
+
H^+
CNS Acidosis
then HCO_3 is pumped in
(& restores pH_{CNS} faster than kidneys can restore $pH_{systemic}$)
Respiratory
Acidosis (↑P_{aCO2})

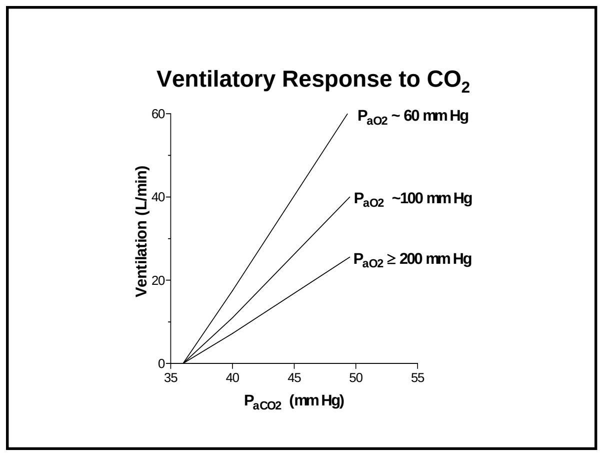

Plasma
BBB
CSF
CO_2
$CO_2 \longleftrightarrow HCO_3 + H^+$
HCO_3
+
H^+
Metabolic
Acidosis
Hyperventilation
& ↓P_{aCO2}
CNS
Alkalosis !!!!
(then pump HCO_3 out)

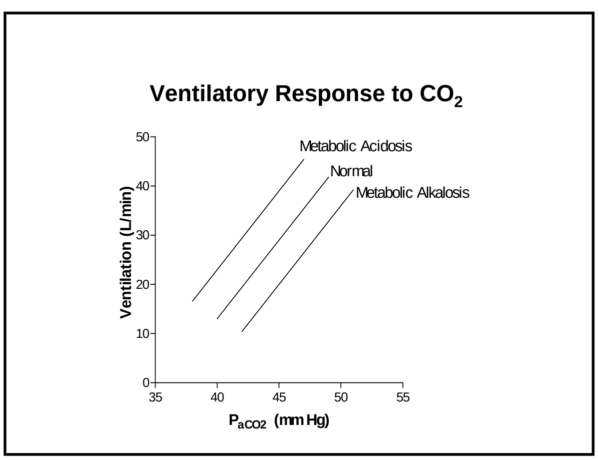

A INSPIRATORY OUTPUT
B EXPIRATORY OUTPUT
Floor of IV ventricle
Rostral VRG (Böt.C)
Medulla
Intermediate VRG (NA and NPA)
Caudal VRG (NRA)
DRG
VRG
CN IX and X (larynx, pharynx)
CN V (open mouth)
CN VII (flare nostrils)
CN XI (other muscles)
Spinal cord
Phrenic (diaphragm)
Spinal nerves (external inter-costal muscles)
Inspiratory output
Expiratory output
Spinal nerves (internal inter-costal and abdominal muscles)

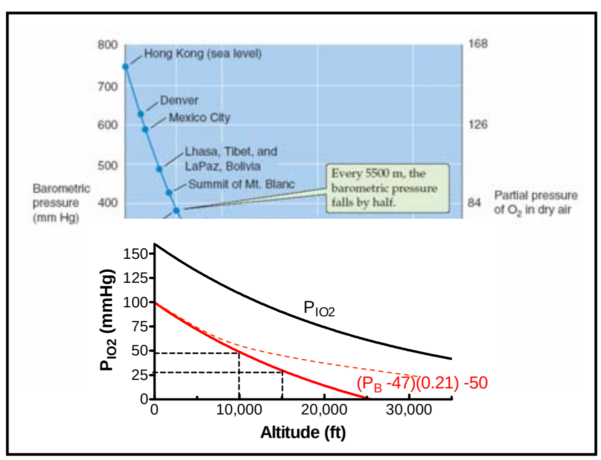

A INTEGRATED PHRENIC NERVE ACTIVITY
Eupnea
Sigh
Sigh
Apneusis
Vagal breathing
0
0.2
0.4
Time
(min)
B LUNG VOLUME
Cheyne-Stokes
Gasping
Cluster
Ataxic
0
0.5
1.0
Time
(min)


Higher Brain Centers
Pneumotaxic Center
Apneustic Center
+/–
Cut-off
–
Expir
DRG
Inspir
+/–
Thresh
Adjust
Expiratory effort
+
Tonic Insp Drive
Cut-off
Periph &
Central
Chemo-
receptors
Vagus
Stretch
Respiratory
Muscles


Ventilatory Response to O_2
Ventilation (L/min)
60
50
40
30
20
10
0
P_{CO2} = 45 mm Hg
P_{CO2} = 40 mm Hg
P_{CO2} = 20 mm Hg
30
60
90
P_{aO2} (mm Hg)


Ventilatory Response to CO_2
Ventilation (L/min)
60
40
20
0
P_{aO2} ~ 60 mm Hg
P_{aO2} ~100 mm Hg
$P_{aO2} \geq$ 200 mm Hg
35
40
45
50
55
P_{aCO2} (mm Hg)


Ventilatory Response to CO_2
Ventilation (L/min)
50
40
30
20
10
0
Metabolic Acidosis
Normal
Metabolic Alkalosis
35
40
45
50
55
P_{aCO2} (mm Hg)


800
700
600
500
400
Barometric
pressure
(mm Hg)
Hong Kong (sea level)
Denver
Mexico City
Lhasa, Tibet, and
LaPaz, Bolivia
Summit of Mt. Blanc
Every 5500 m, the
barometric pressure
falls by half.
168
126
84
Partial pressure
of O_2 in dry air
P_{IO2} (mmHg)
150
125
100
75
50
25
0
P_{IO2}
$(P_B - 47)(0.21) - 50$
0
10,000
20,000
30,000
Altitude (ft)

EFFECTS OF HIGH ALTITUDE

A. At 10,000 ft P_B=525 mmHg inspired P_{O2} is ~100 mmHg ⇒P_{AO2} is ~50 mmHg.
At 15,000 ft P_B=380 mmHg inspired P_{O2} is ~70 mmHg ⇒P_{AO2} is ~20 mmHg.
At Mt Everest P_B=250 mmHg, inspired P_{O2} is ~42 mmHg ⇒P_{AO2} is ~0 mmHg.
At 63,000 ft P_B=47 mmHg, inspired P_{O2} is ~0 mmHg ⇒ tissues boils, H_2O vapor.

B. Acclimatization and hyperventilation at 10,000 ft

Time at High Alt.	P_{aO2}	P_{aCO2}	pH blood	pH CSF
1 Hr	low	low	high	high

Hypoxic drive is restrained by low P_{aCO2} and high pH.

1-2 day.	low	low	high	Norm.

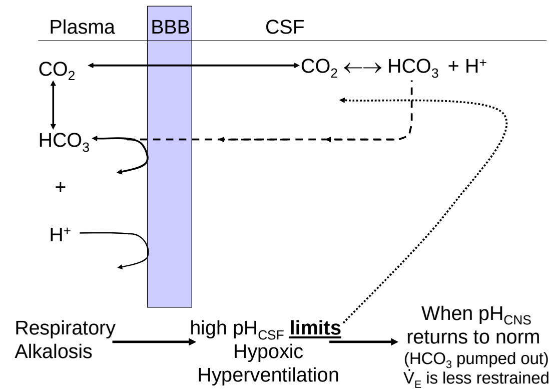
CSF chemoreceptors no longer limiting hyperventilation.

2-4 days	low	low	Norm.	Norm.

Peripheral alkalosis no longer restraining hyperventilation.

30 Yrs.	low	Norm.	Norm.	Norm.

Hypoxic response of chemoreceptors lost.



EFFECTS OF HIGH ALTITUDE

B. Acclimatization and hyperventilation at 10,000 ft

Time at High Alt.	P_{aO2}	P_{aCO2}	pH blood	pH CSF	V_E	[HCO3]
1 Hr	low	low	high	high	↑	Normal

Hypoxic drive is restrained by low P_{aCO2} and high pH.

1-2 day.	low	low	high	Norm.	↑↑	↓$[HCO_3]_{CSF}$

CSF chemoreceptors no longer limiting hyperventilation.

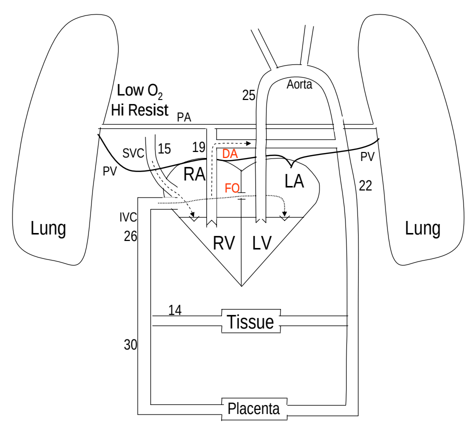
2-4 days	low	low	Norm.	Norm.	↑↑↑	↓$[HCO_3]_{Syst}$

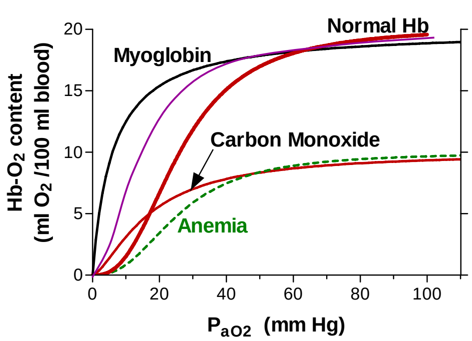
Peripheral alkalosis no longer restraining hyperventilation.

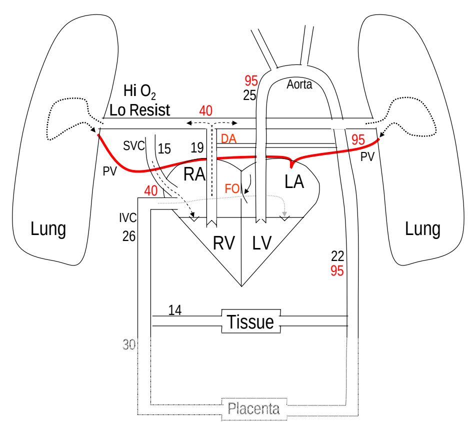
30 Yrs.	low	Norm.	Norm.	Norm.	-	-

Hypoxic response of chemoreceptors lost.

C. Other adjustments
1, Polycythemia
2. Enhanced Diffusing Capacity
3. Imcreased Capillary Density
4. Right shift of HbO_2 curve







Equations

<u>Old ones you already knew</u>

$\Delta P=QR$	Ohm's Law
$J=DA(\Delta C/\Delta x)$	Fick's Law
$J_{CO}=D_{L\text{-}CO}P_{CO}$	
$PV=nRT$	Universal Gas Law (Boyle's & Charles' Laws)
$P_x= P\ F_x$	Dalton's Law of Partial Pressures
$C_x = P_x\ k_{Solubility}$	Henry's Law
$P=2T/r$	Law of LaPlace
$F= -kx$	Hooke's Law
$R = 8\eta l/\pi r^4$	Tubular resistance
$N_R= \rho Dv/\eta$	Reynold's Number
$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^- + H^+$	
$RQ = \dot{V}_{CO2}/\dot{V}_{O2}$	Respiratory Quotient
$P_{TP}= P_{Airway} - P_{IP}$	Transpulmonary P (Transmural)

<u>Derivable (simple algebra word problem)</u>

$V_L = V_S([He]_{in} - [He]_{fin})/[He]_{fin}$	Helium Dilution
$V_L = V_S\ F_{EN2}/F_{N2\text{-}air}$	Nitrogen Washout

<u>New Ones!</u>

$$\frac{V_{D2}}{V_T} = \frac{(P_{aCO2} - P_{ECO2})}{P_{aCO2}}$$ Bohr Eqn

$$\dot{V}_A = \dot{V}_{CO2} \times k / P_{ACO2}$$ Alveolar Ventilation-P_{ACO2}

$$P_{AO2} = P_{IO2} - P_{aCO2}/RQ$$ Alveolar Gas Eqn