Φυσιολογία της Αναπνοής

Γεώργιος Σταθόπουλος, Πνευμονολόγος

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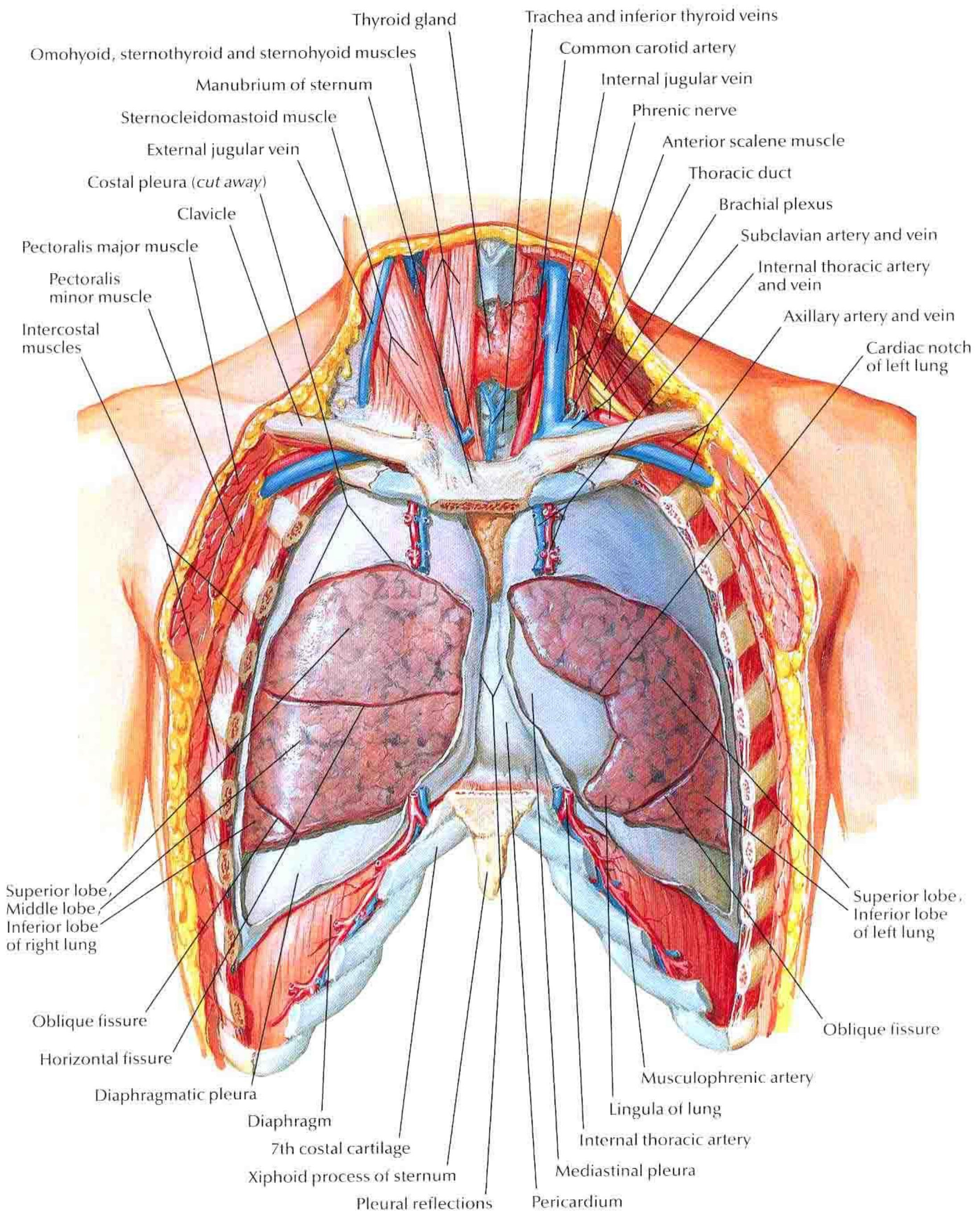
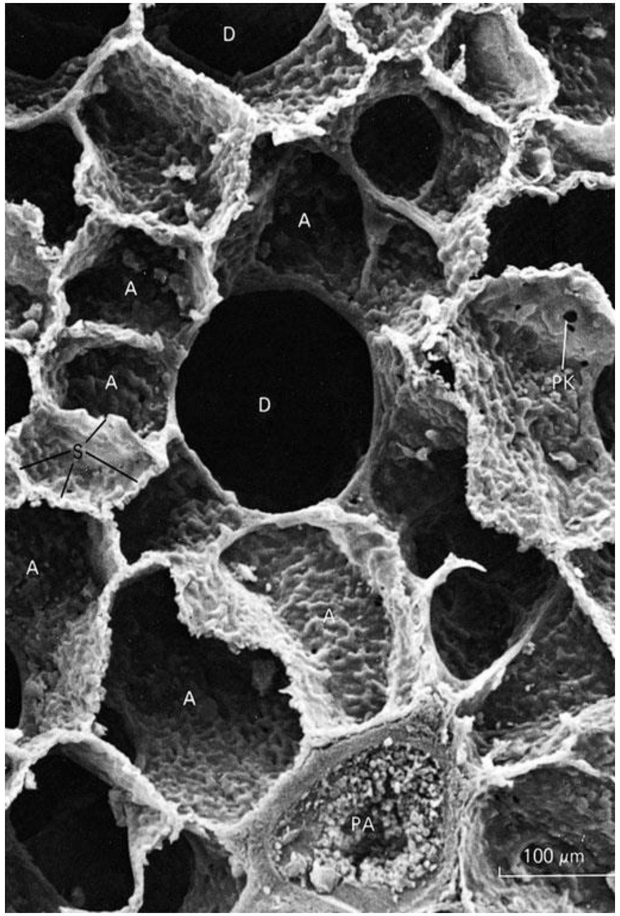
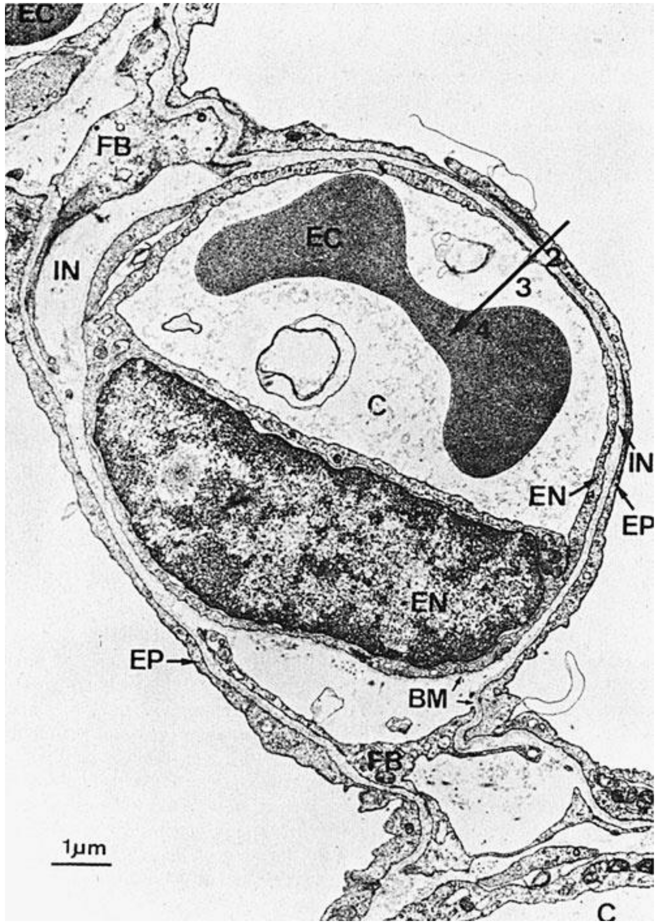
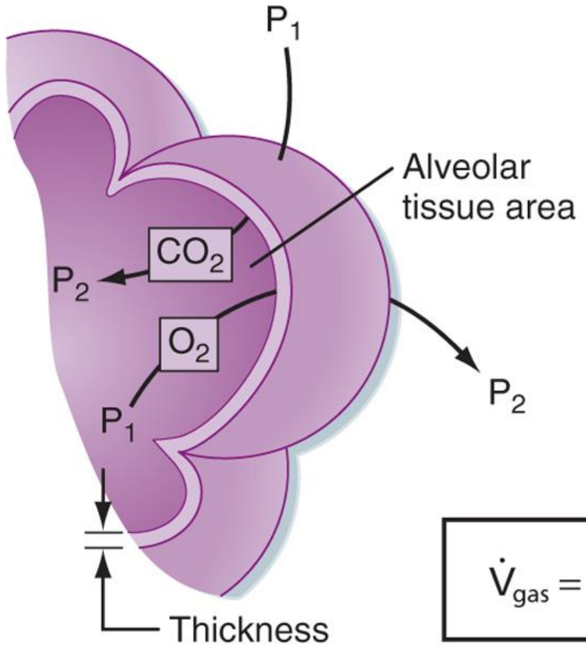
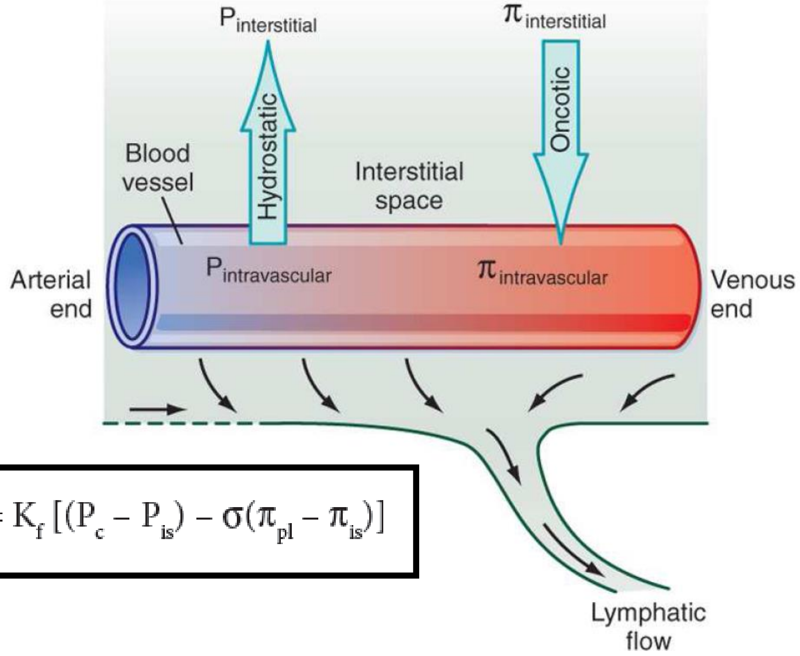




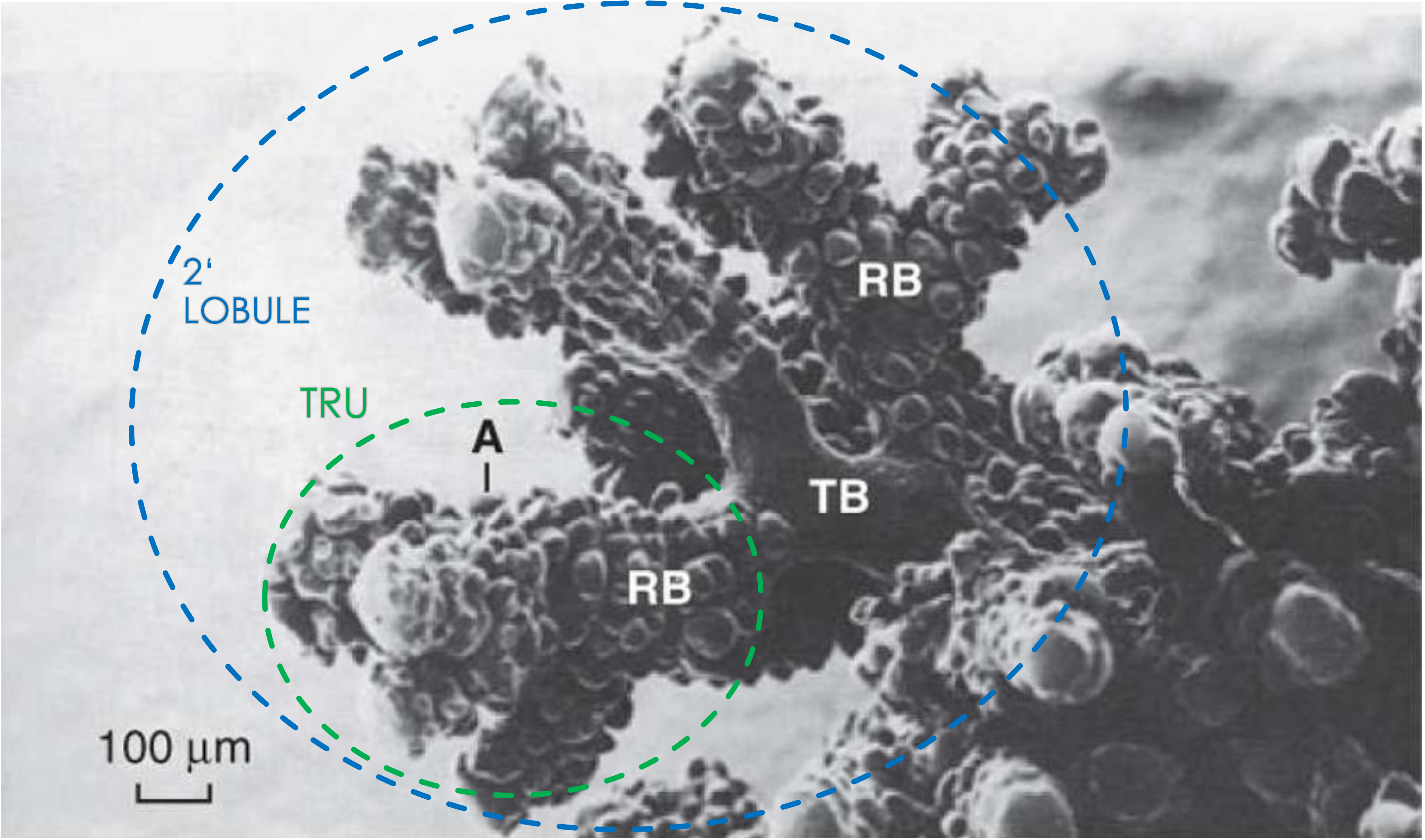


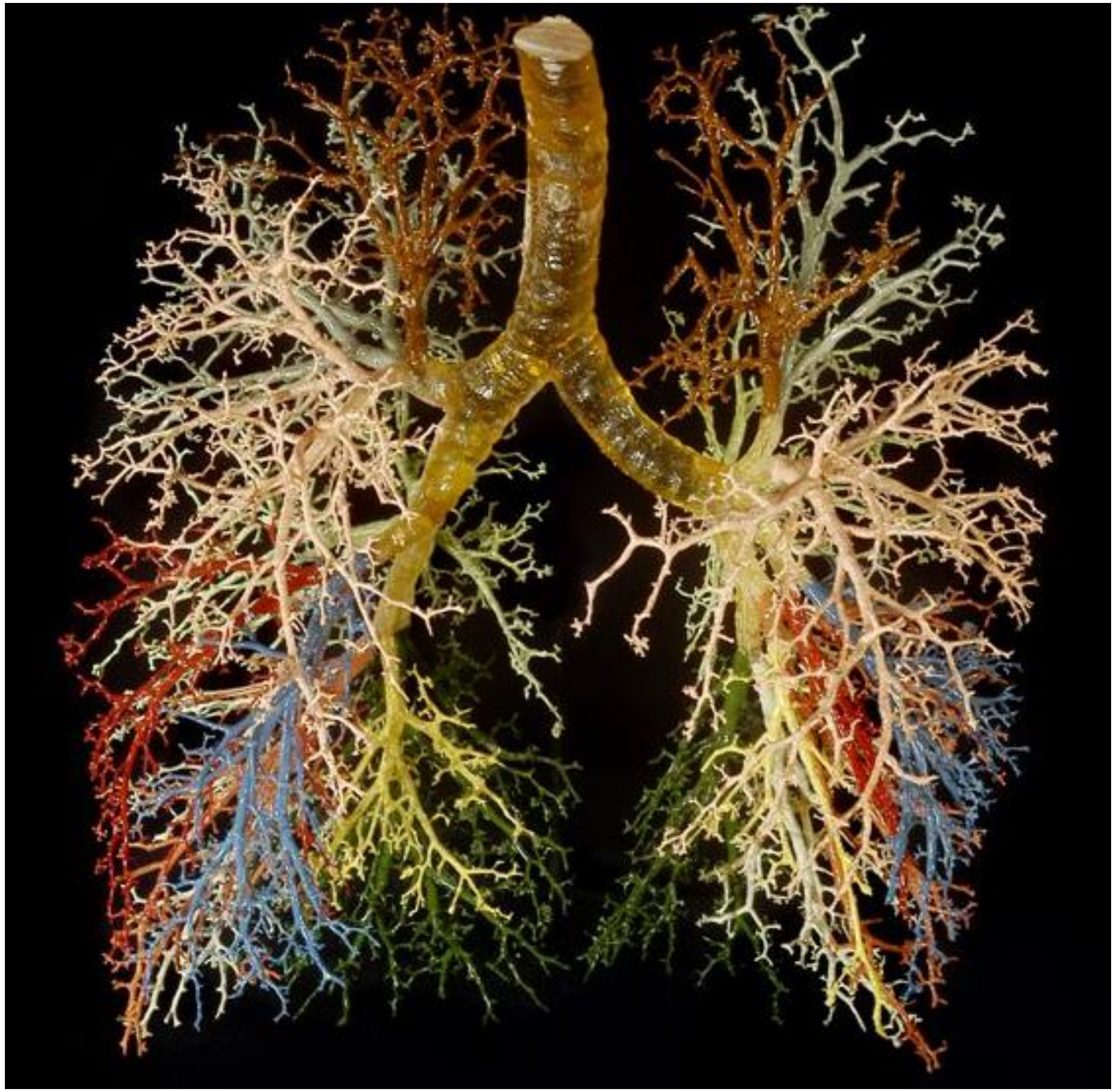


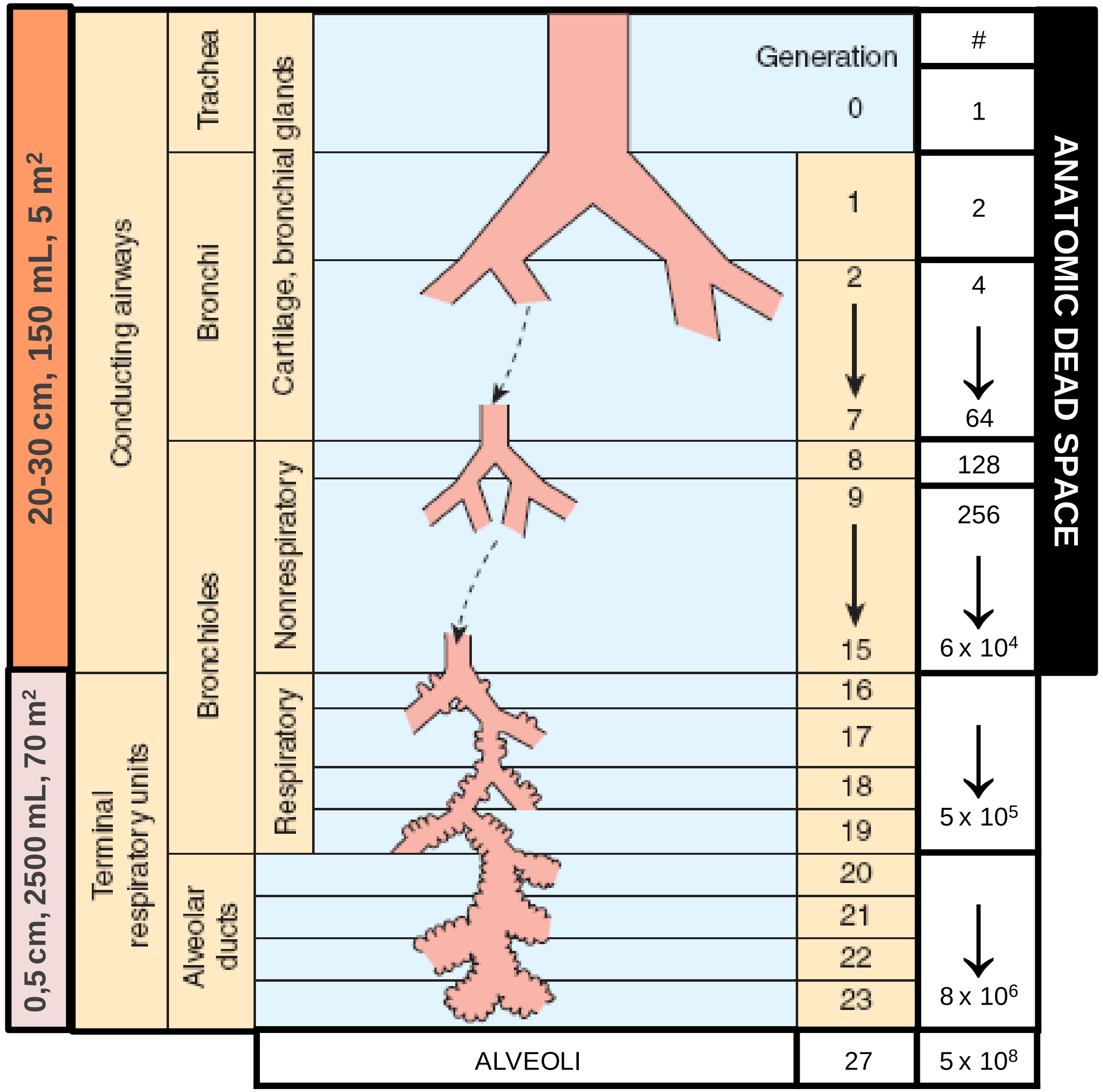
$$\dot{V}_{gas} = A \times D \times \frac{P_1 - P_2}{T}$$



$$\dot{Q}_f = K_f\,[(P_c - P_{is}) - \sigma(\pi_{pl} - \pi_{is})]$$

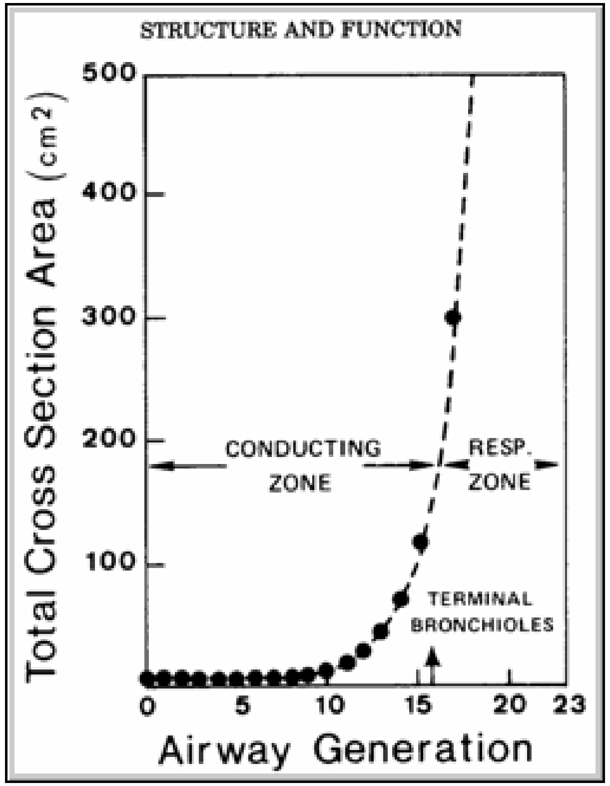

2'
LOBULE
TRU
A
RB
TB
RB
100 µm



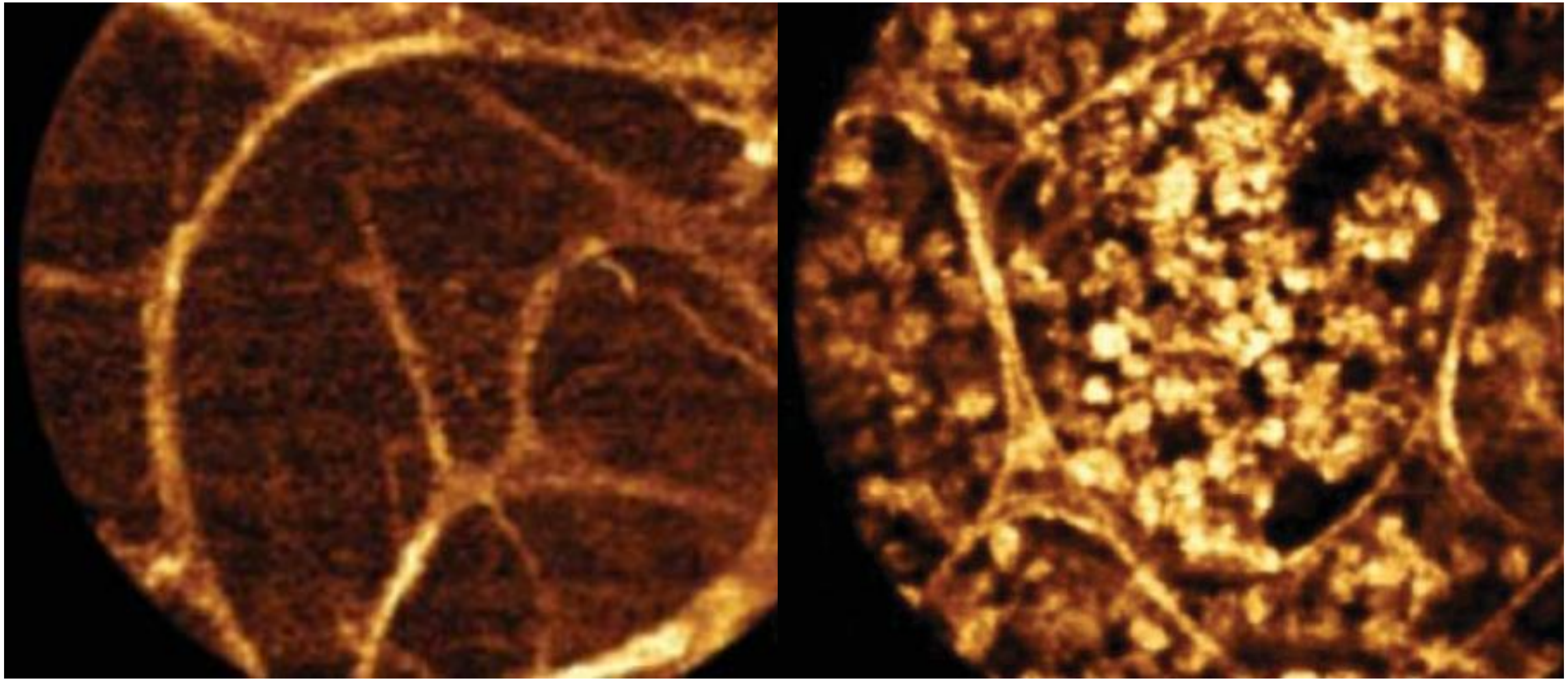


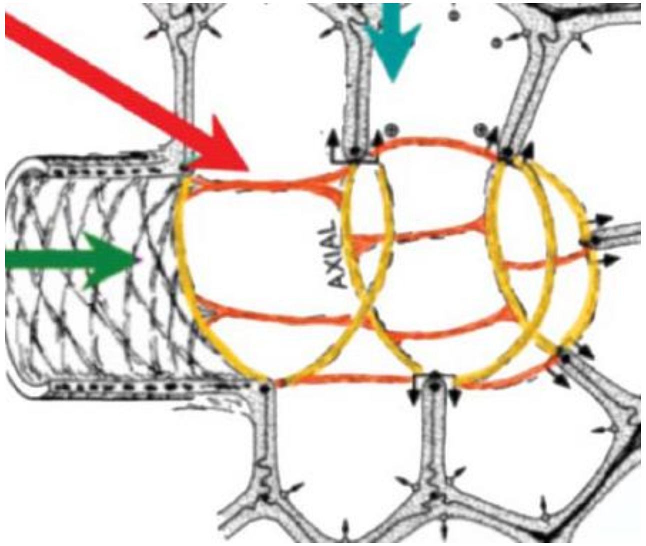
20-30 cm, 150 mL, 5 m²
0,5 cm, 2500 mL, 70 m²
Conducting airways
Terminal respiratory units
Trachea
Bronchi
Bronchioles
Alveolar ducts
Cartilage, bronchial glands
Nonrespiratory
Respiratory
Generation
0
1
2
7
8
9
15
16
17
18
19
20
21
22
23
ALVEOLI
27
#
1
2
4
64
128
256
6 x 10⁴
5 x 10⁵
8 x 10⁶
5 x 10⁸
ANATOMIC DEAD SPACE

Zone	Generation		Diameter (cm)	Length (cm)	Number	Total cross sectional area (cm^2)
Conductiong zone	trachea	0	1.80	12.0	1	2.54
	bronchi	1	1.22	4.8	2	2.33
	↓	2	0.83	1.9	4	2.13
		3	0.56	0.8	8	2.00
	bronchioles	4	0.45	1.3	16	2.48
	↓	5	0.35	1.07	32	3.11
	teminal bronchioles	↓ 16	↓ 0.06	↓ 0.17	↓ 6×10^4	↓ 180.0
Transitional and respiratory zones	respiratory bronchioles	17	↓	↓	↓	↓
		18				
		19	0.05	0.10	5×10^5	10^3
	alveolar ducts	20	↓	↓	↓	↓
		21				
		22				
	alveolar sacs	23	0.04	0.05	8×10^6	10^4

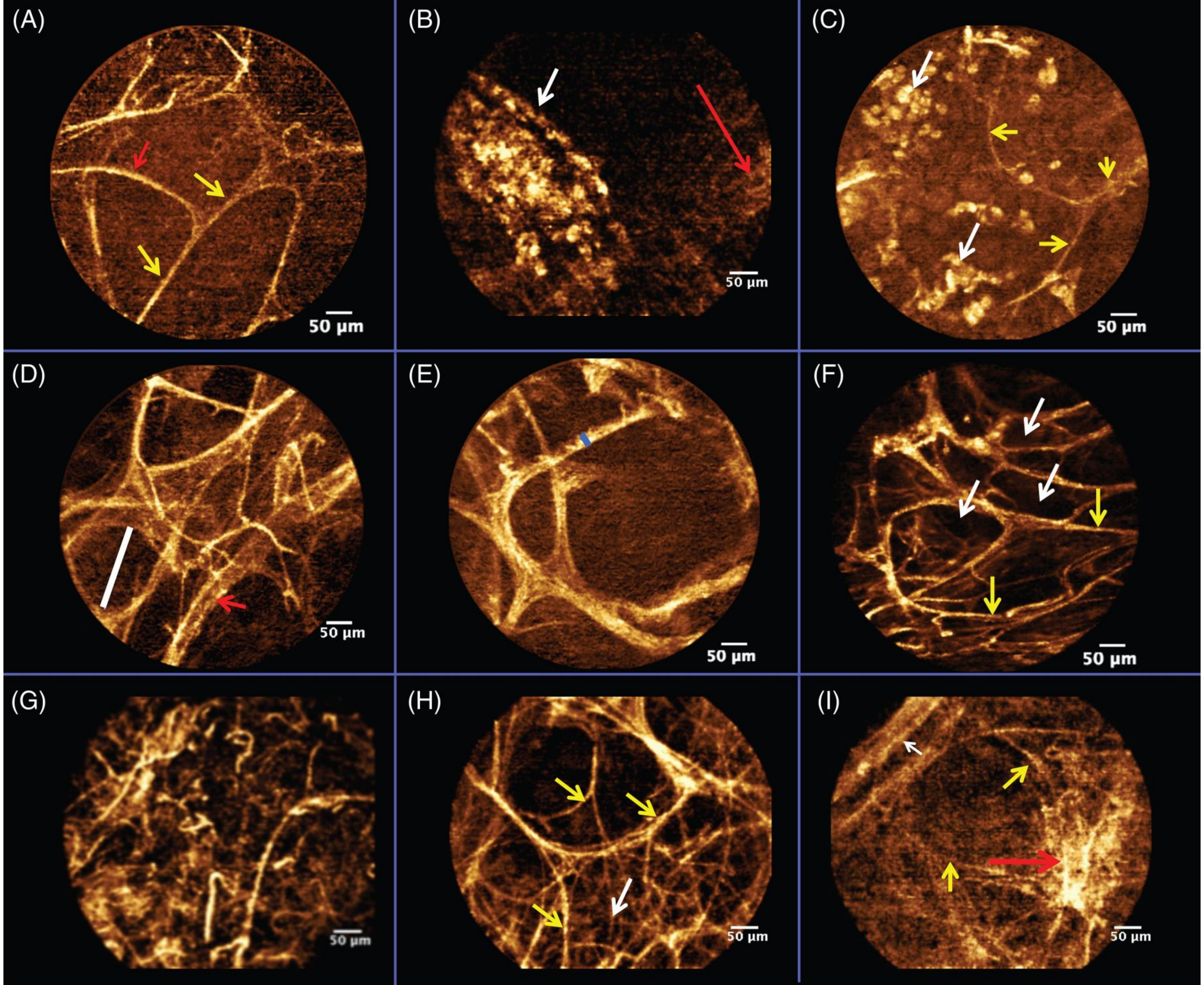


COAL MINER'S LUNG

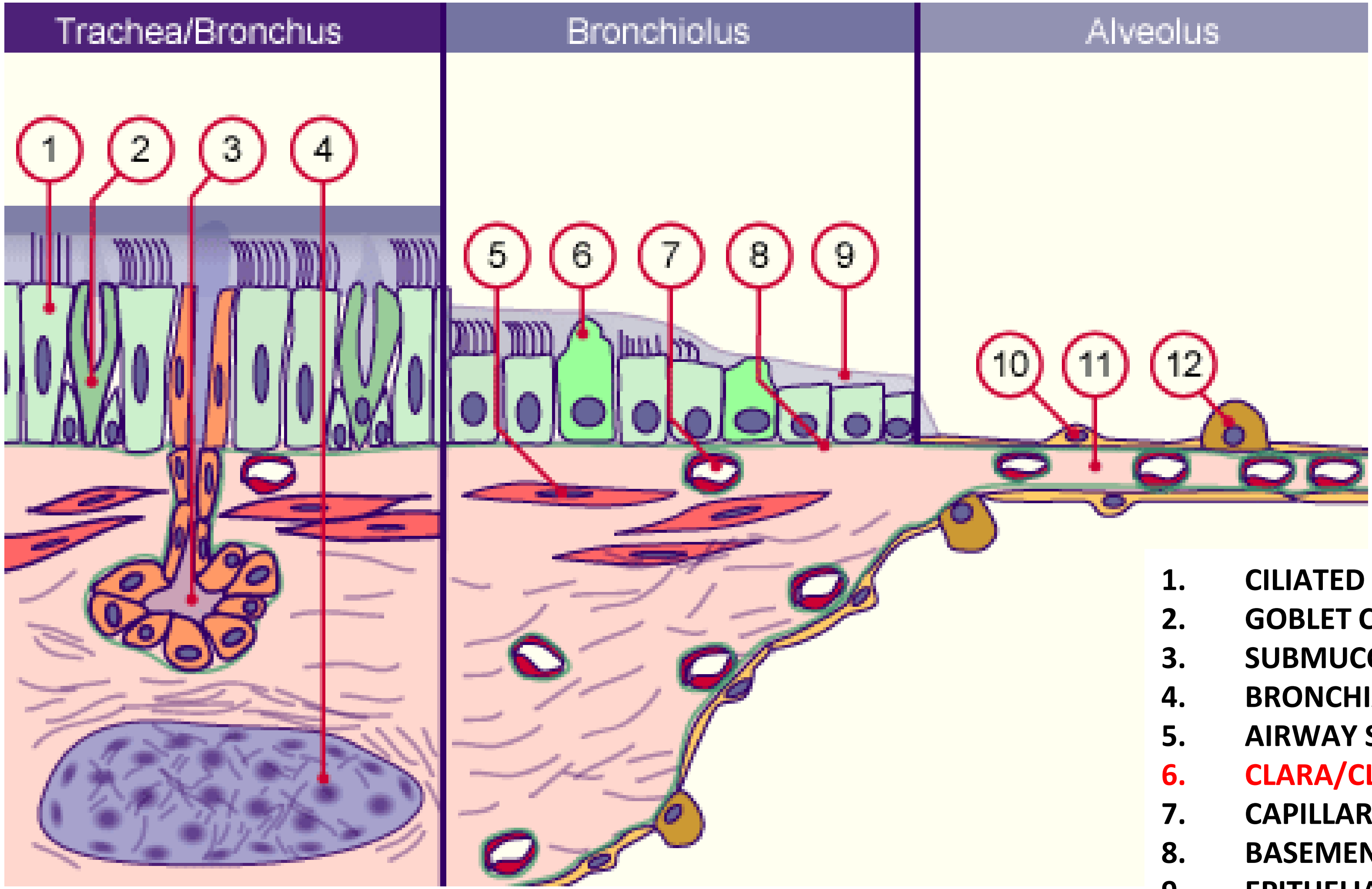




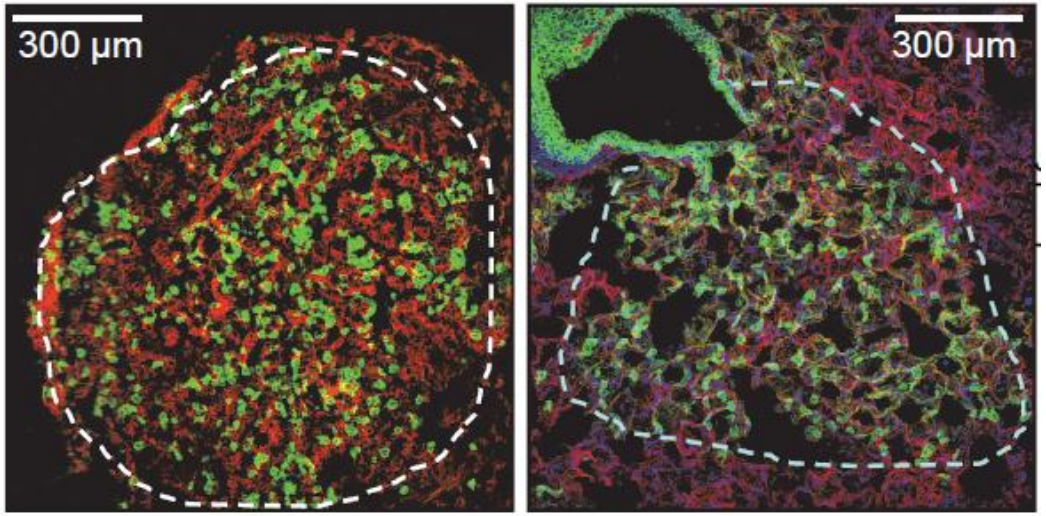
Thiberville L, Salaün M, Lachkar S, Dominique S, Moreno-Swirc S, Vever-Bizet C, Bourg-Heckly G. Human in vivo fluorescence microimaging of the alveolar ducts and sacs during bronchoscopy. Eur Respir J 2009;33:974-85.

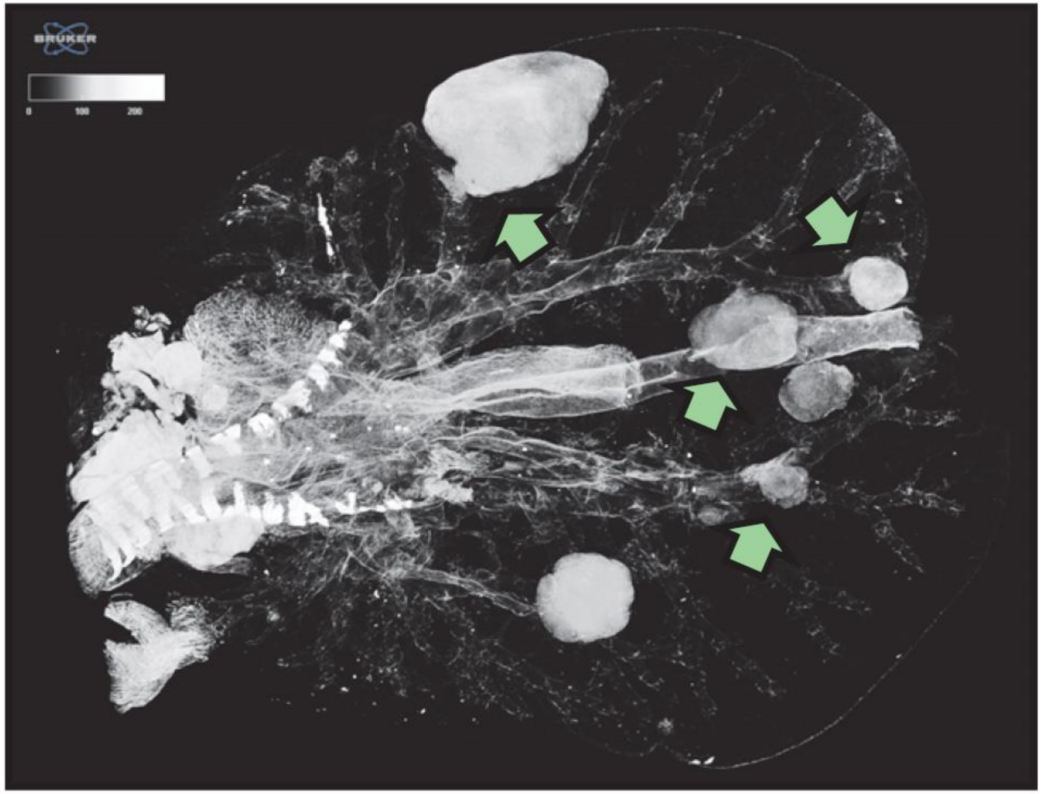


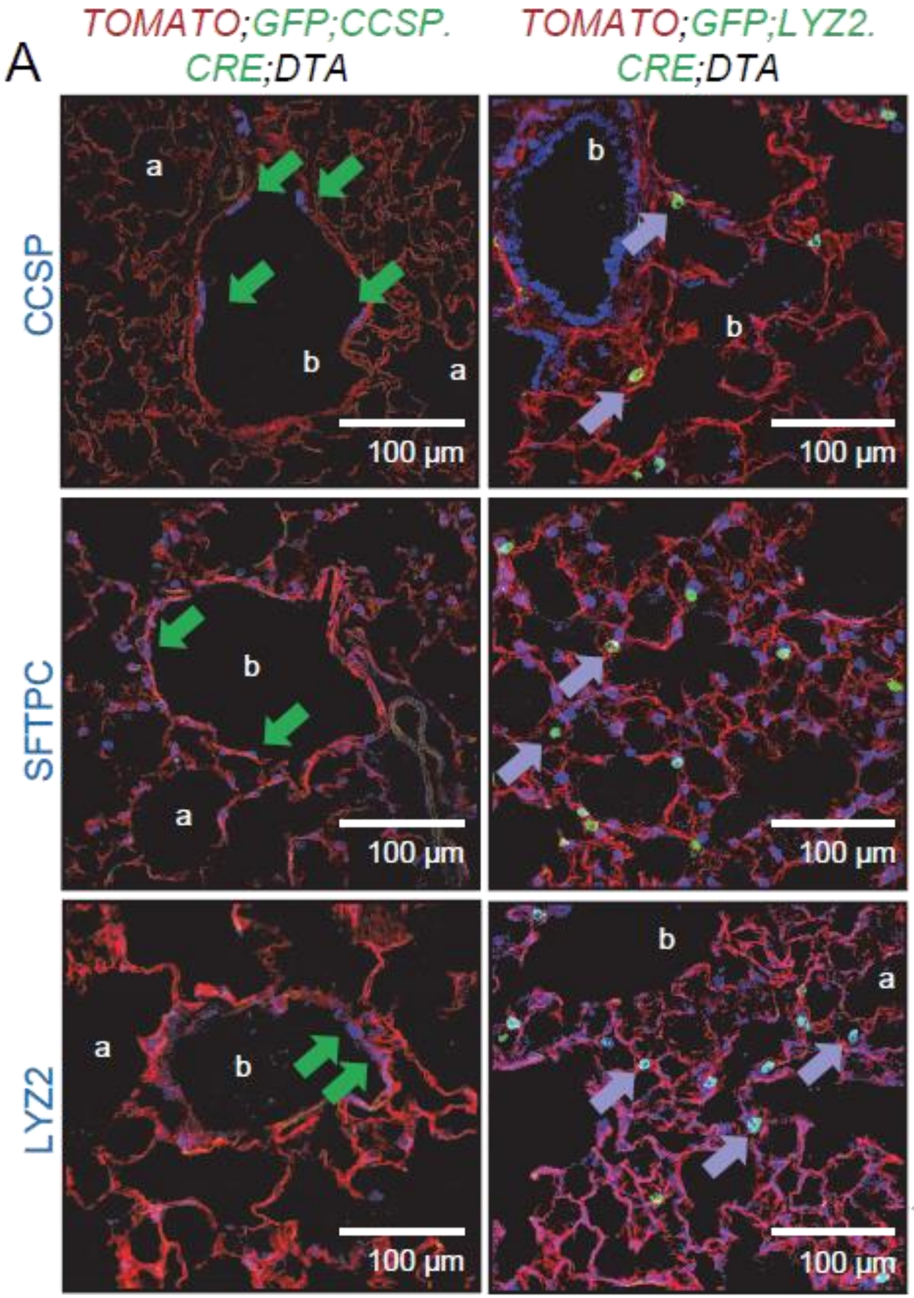
Salaün M, Guisier F, Dominique S, Genevois A, Jounieaux V, Bergot E, Thill C, Piton N, Thiberville L. In vivo probe-based confocal laser endomicroscopy in chronic interstitial lung diseases: Specific descriptors and correlation with chest CT. Respirology. 2019 Feb 27. doi: 10.1111/resp.13507. [Epub ahead of print] PubMed PMID: 30811085.



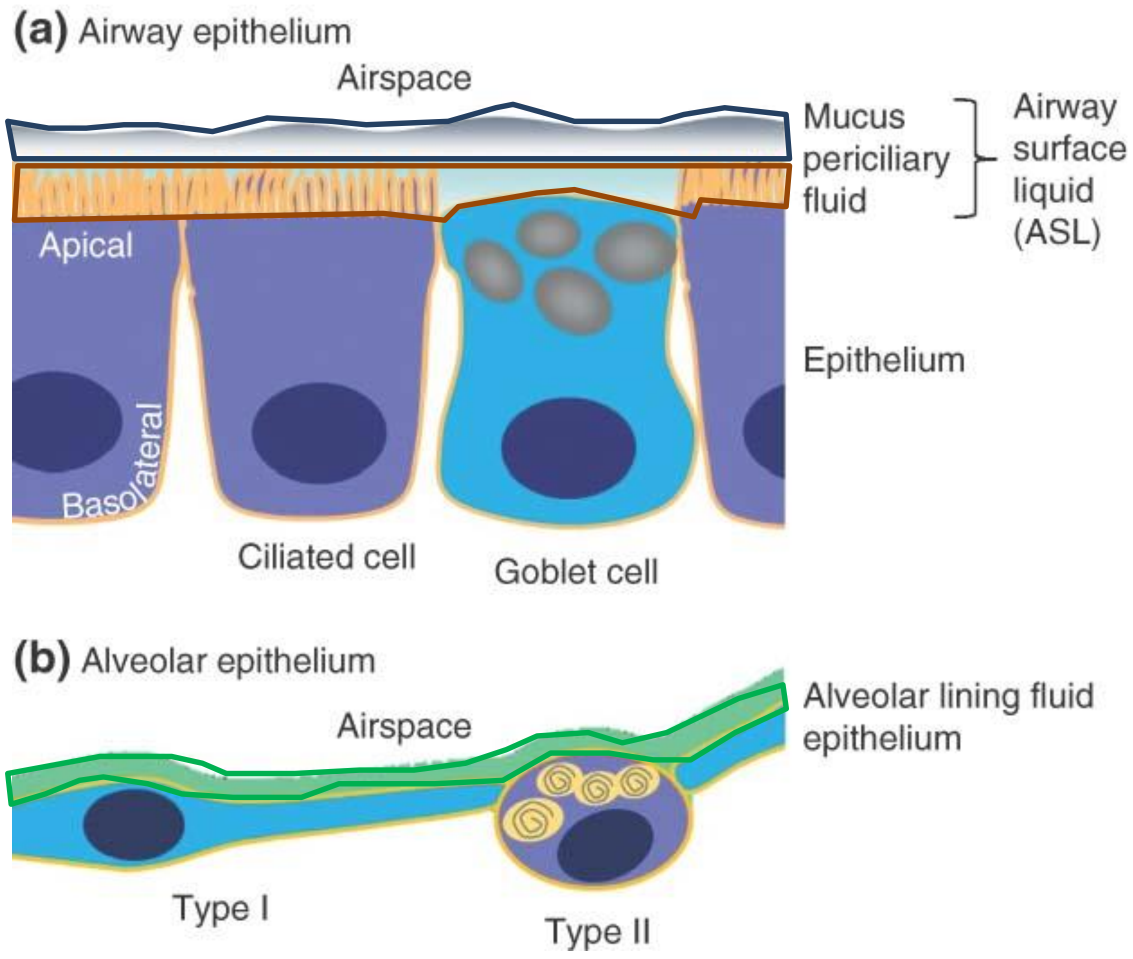
1. CILIATED AIRWAY EPITHELIAL CELL
2. GOBLET CELL
3. SUBMUCOSAL GLAND
4. BRONCHIAL CARTILLAGE
5. AIRWAY SMOOTH MUSCLE CELL
6. CLARA/CLUB CELL
7. CAPILLARY BLOOD VESSEL
8. BASEMENT MEMBRANE
9. EPITHELIAL LINING FLUID
10. TYPE I ALVEOLAR EPITHELIAL CELL
11. ALVEOLAR INTERSTITIUM
12. TYPE II ALVEOLAR EPITHELIAL CELL



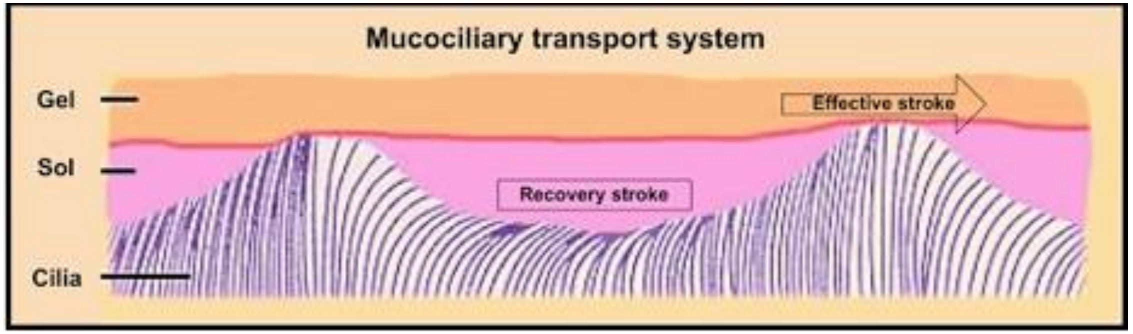


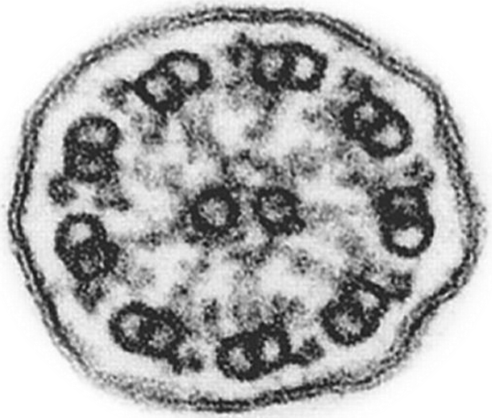


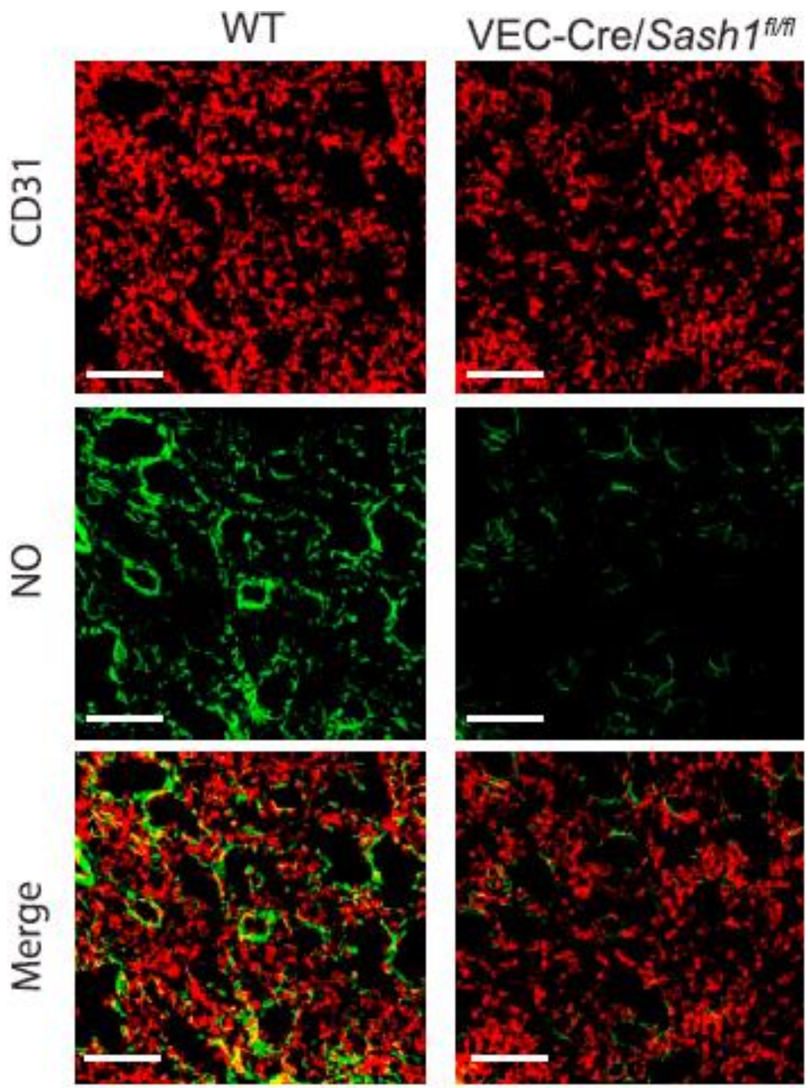
Spella, M., *et al*. The conducting airway epithelium fosters chemical-induced lung adenocarcinoma and alveolar maintenance in adult mice. *eLife* 2019;8:e45571

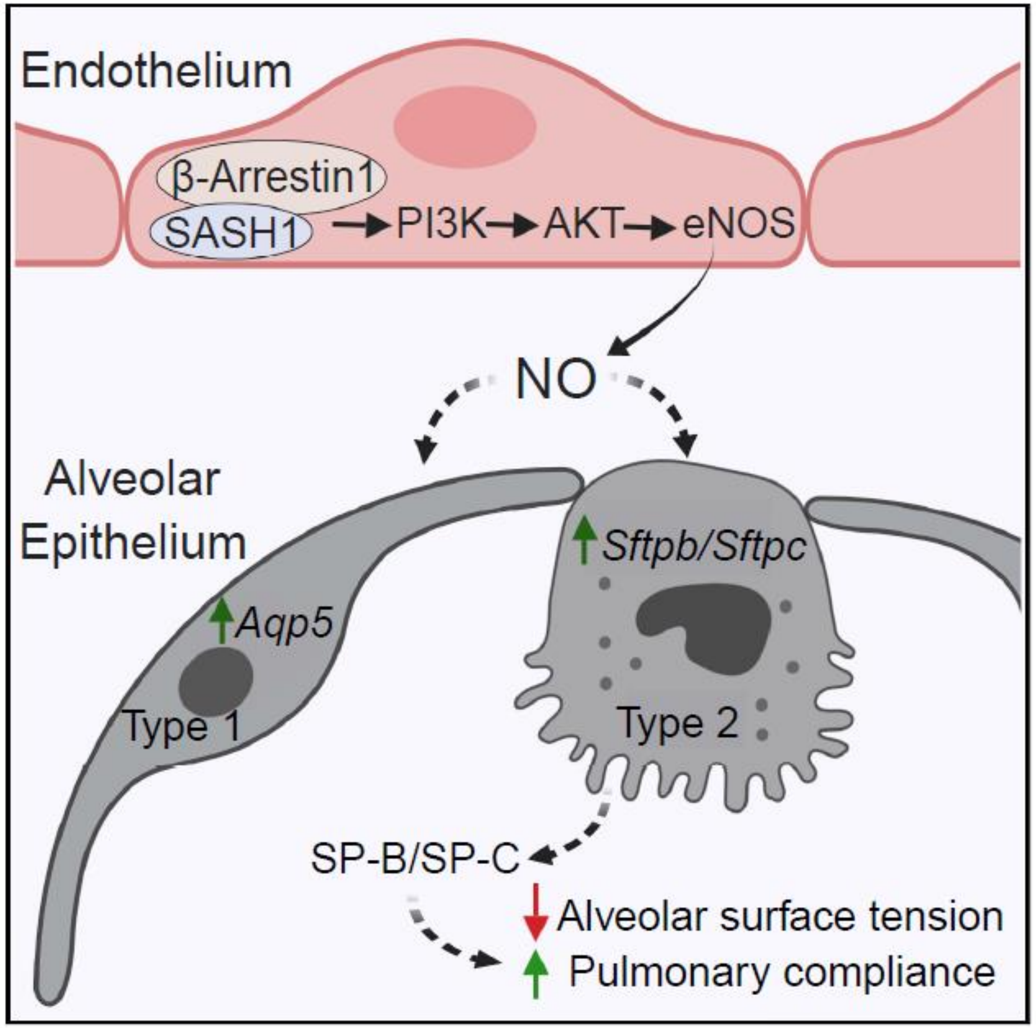


1. Περικροσσωτό υγρό ή λεπτόρρευστη βλέννη
2. Παχύρρευστη βλέννη ή βλέννη
3. Επιφανειοδραστικός παράγοντας





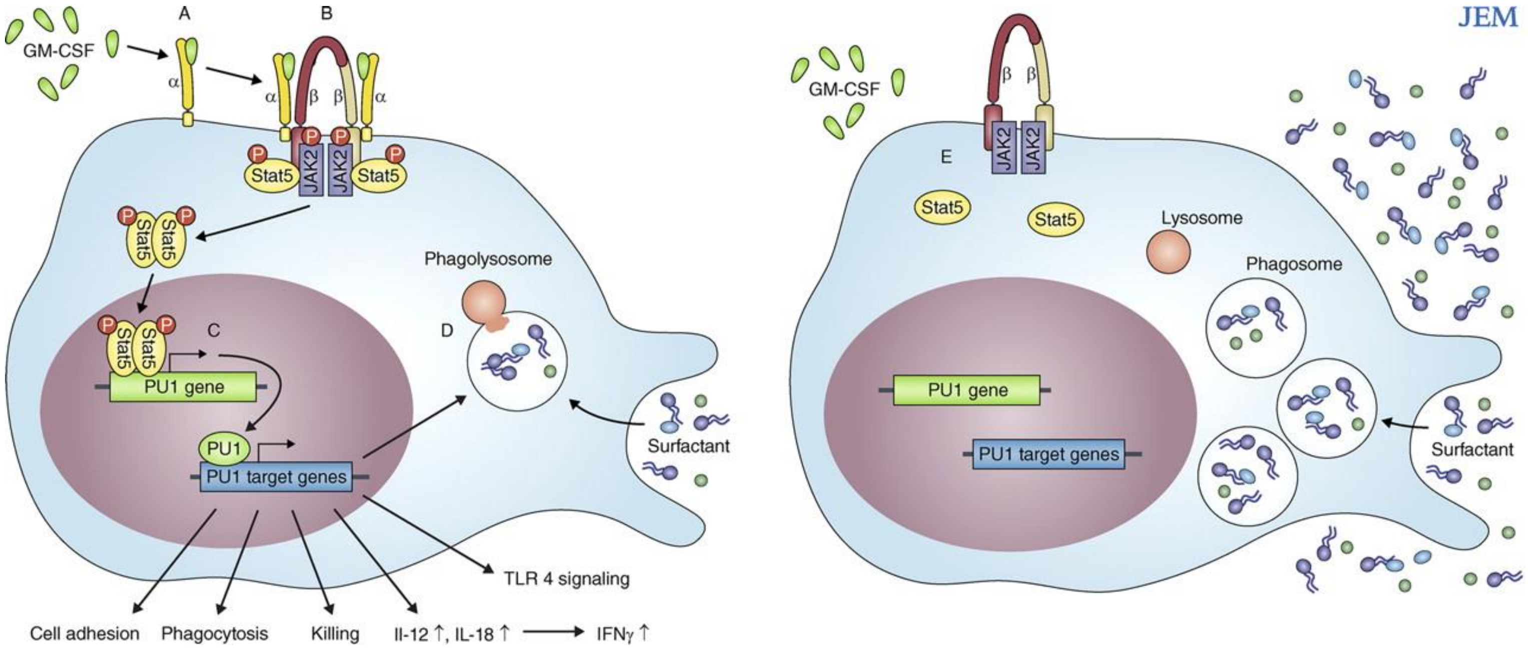


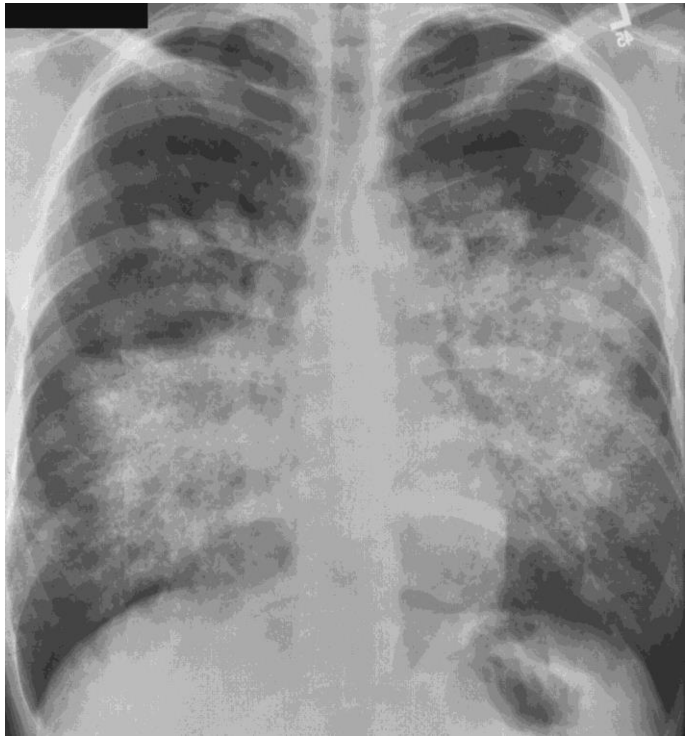


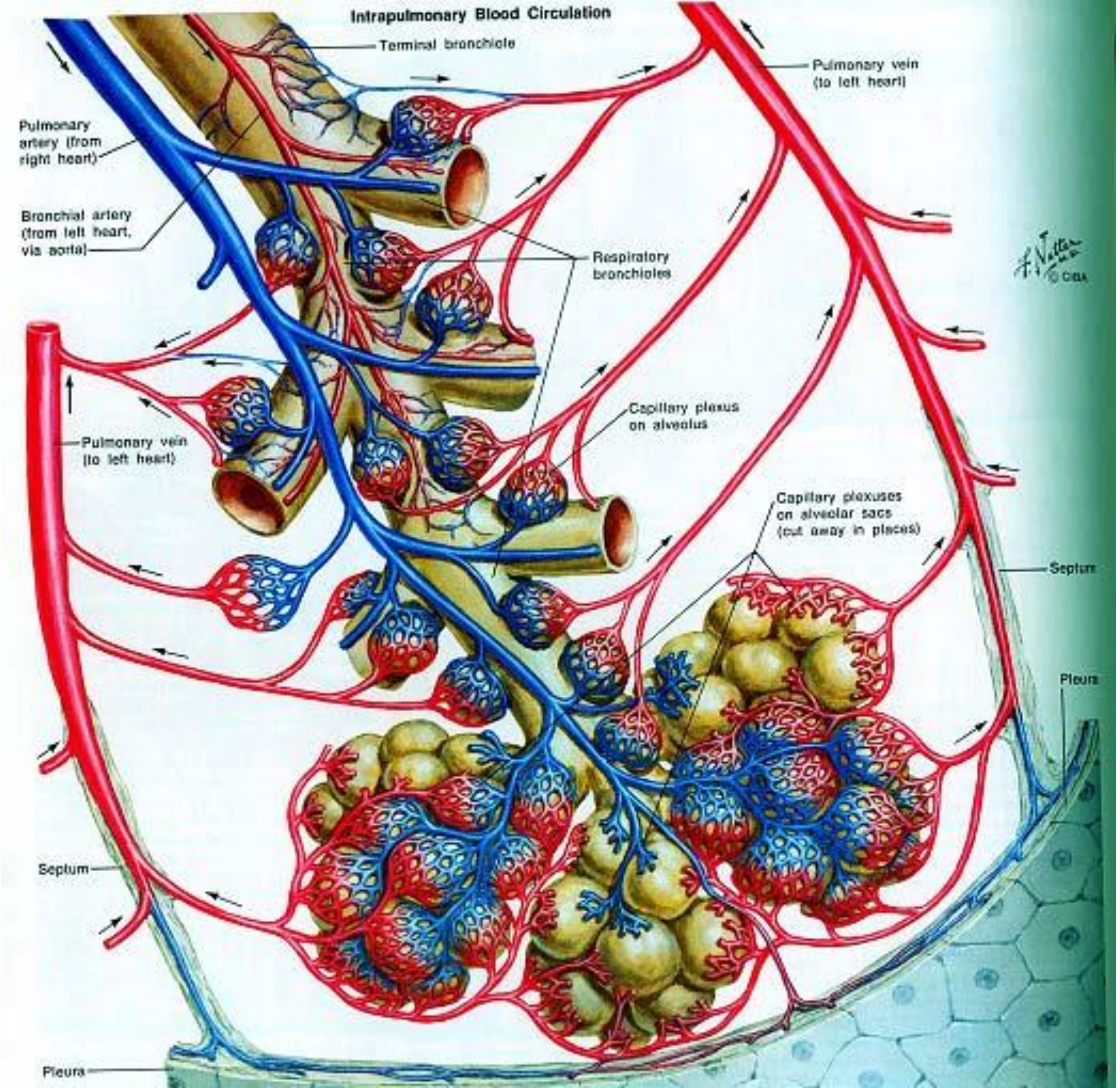
Coulombe P, Paliouras GN, Clayton A, Hussainkhel A, Fuller M, Jovanovic V, Dauphinee S, Umlandt P, Xiang P, Kyle AH, Minchinton AI, Humphries RK, Hoodless PA, Parker JDK, Wright JL, Karsan A. Endothelial Sash1 Is Required for Lung Maturation through Nitric Oxide Signaling. Cell Rep. 2019 May 7;27(6):1769-1780.

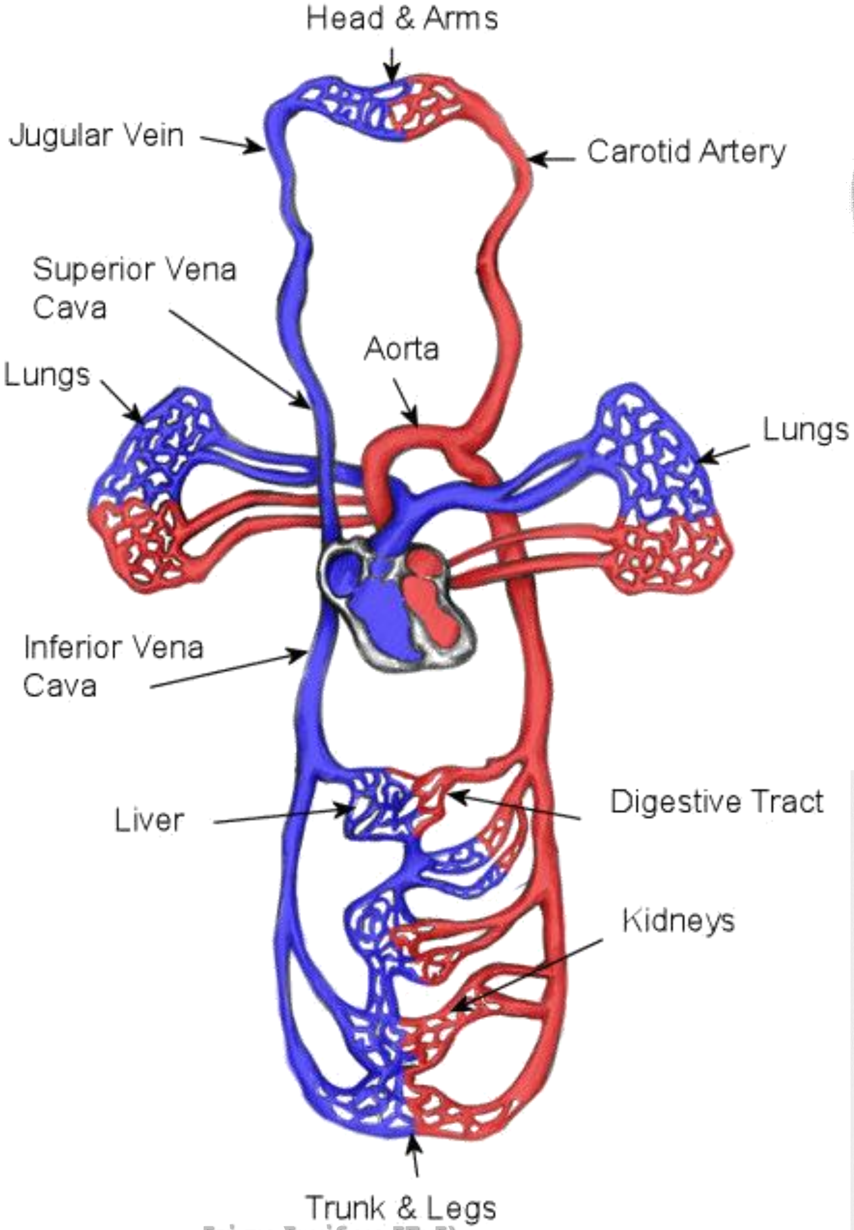
Πνευμονική Κυψελιδική Πρωτεΐνωση

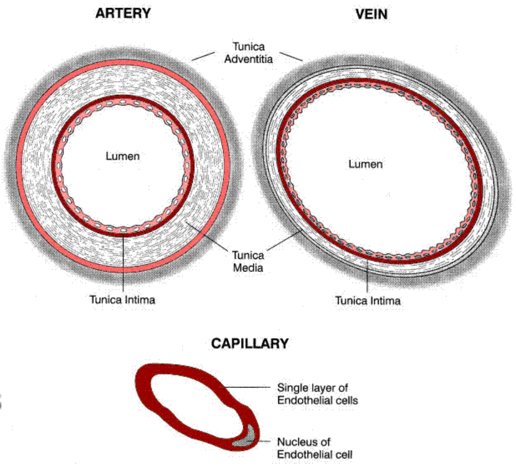
- GM-CSF signaling to PU1 and target genes required for surfactant clearance by ΑΜΦ
- Mutations along the GMCSF-PU1 axis cause PAP

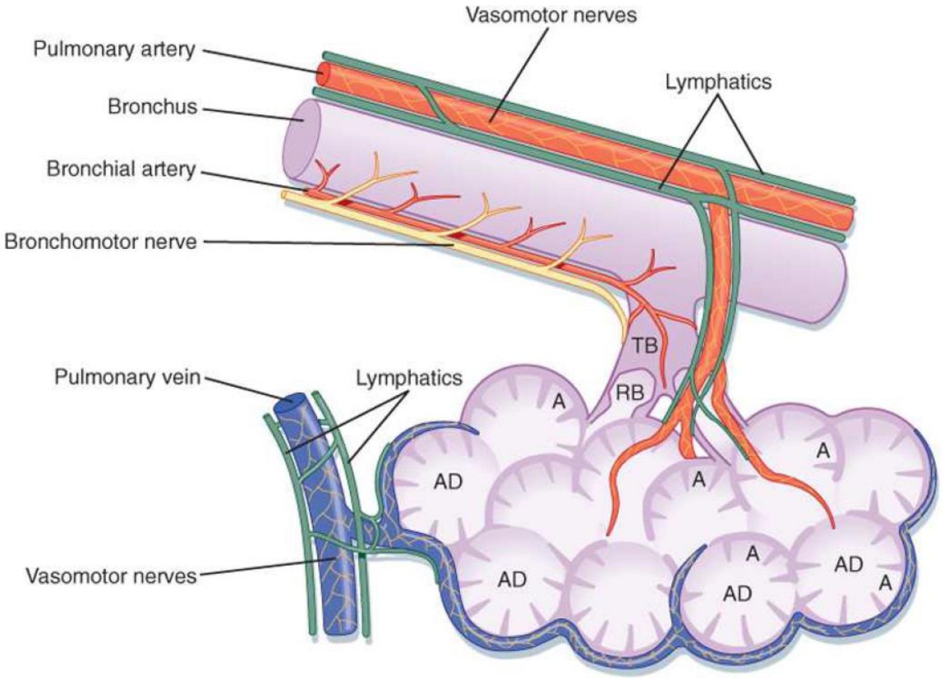


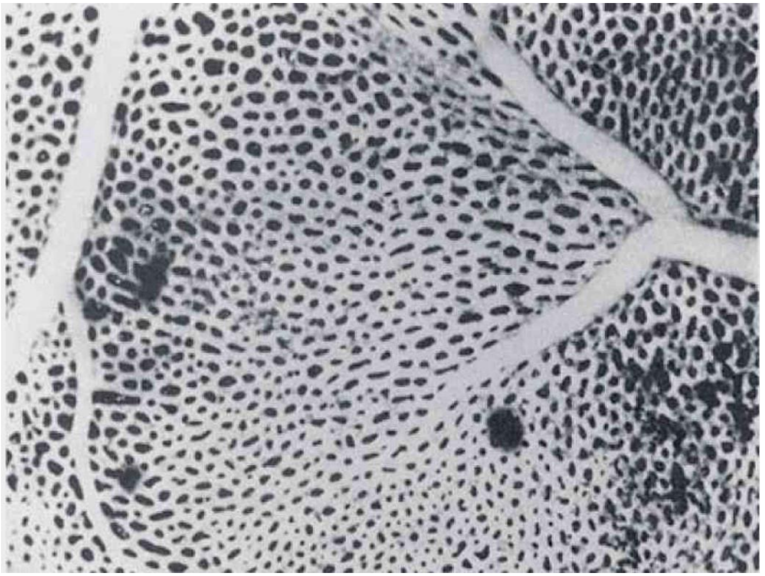


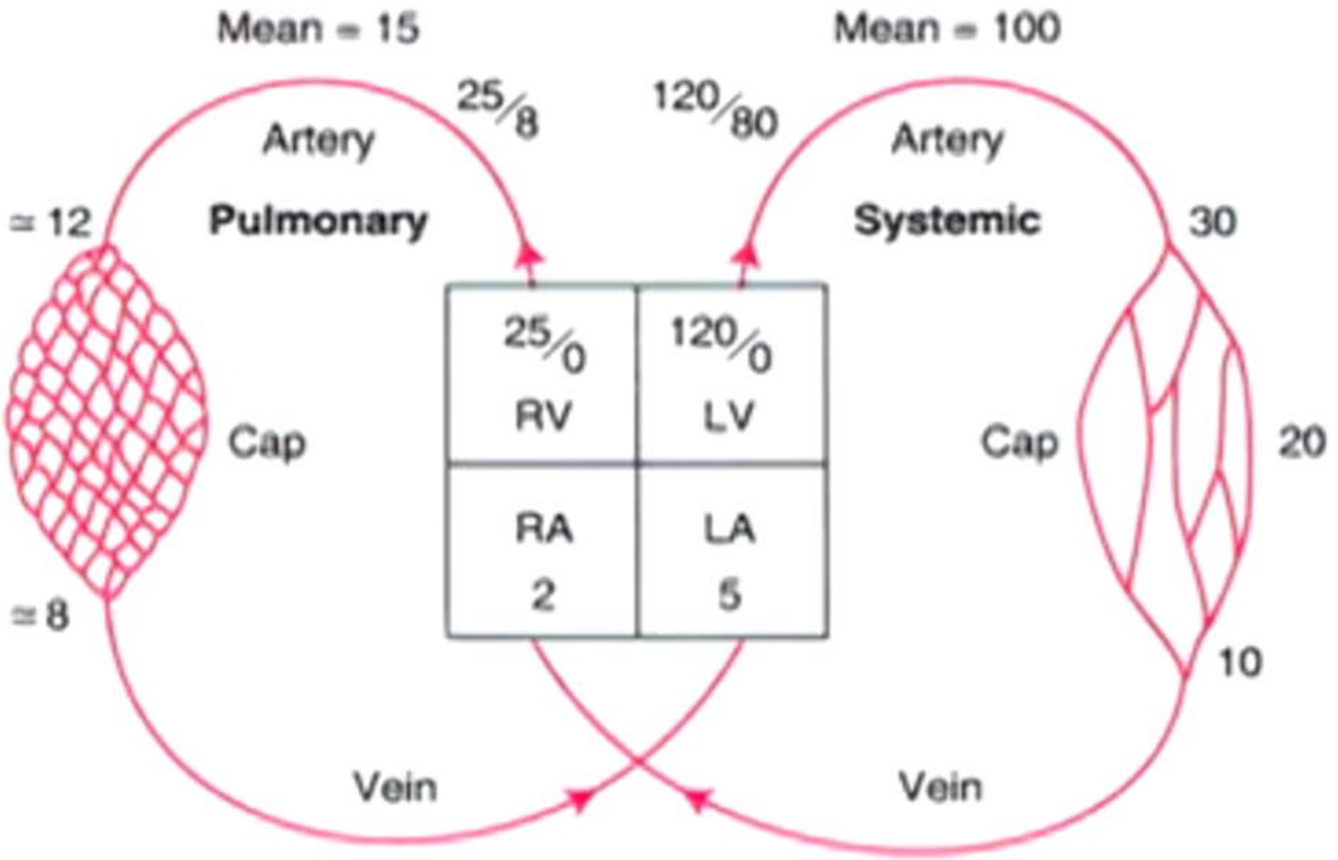

Intrapulmonary Blood Circulation
Terminal bronchiole
Pulmonary vein (to left heart)
Pulmonary artery (from right heart)
Bronchial artery (from left heart, via aorta)
Respiratory bronchioles
Pulmonary vein (to left heart)
Capillary plexus on alveolus
Capillary plexuses on alveolar sacs (cut away in places)
Septum
Pleura
Septum
Pleura
© CIBA


Head & Arms
Jugular Vein
Carotid Artery
Superior Vena Cava
Aorta
Lungs
Lungs
Inferior Vena Cava
Liver
Digestive Tract
Kidneys
Trunk & Legs

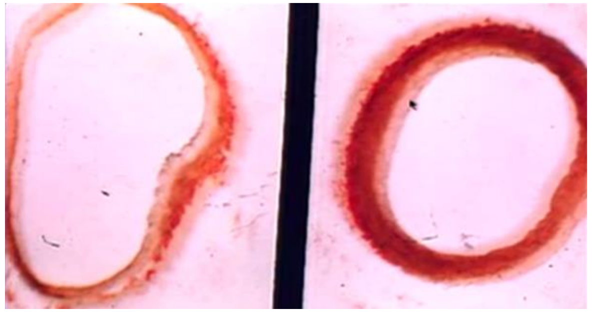

ARTERY
VEIN
Tunica Adventitia
Lumen
Lumen
Tunica Media
Tunica Intima
Tunica Intima
CAPILLARY
Single layer of Endothelial cells
Nucleus of Endothelial cell


Vasomotor nerves
Pulmonary artery
Lymphatics
Bronchus
Bronchial artery
Bronchomotor nerve
TB
RB
Pulmonary vein
Lymphatics
A
AD
A
A
AD
A
AD
AD
A
Vasomotor nerves

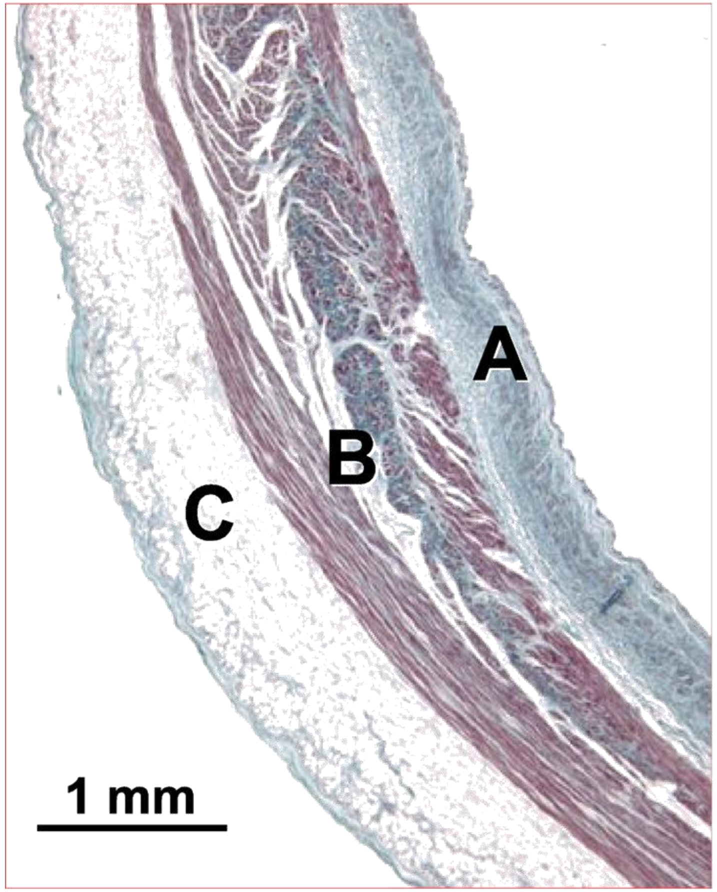


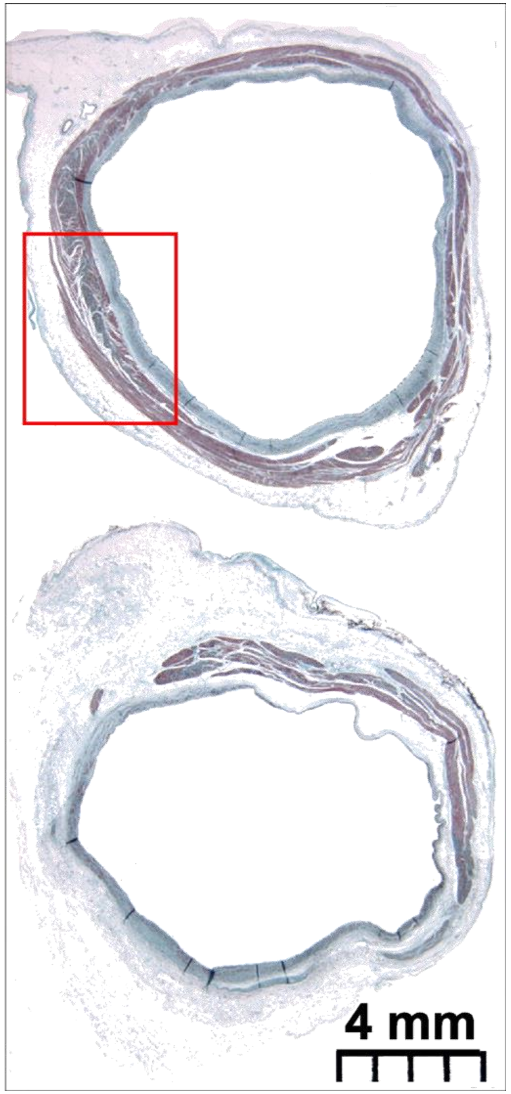


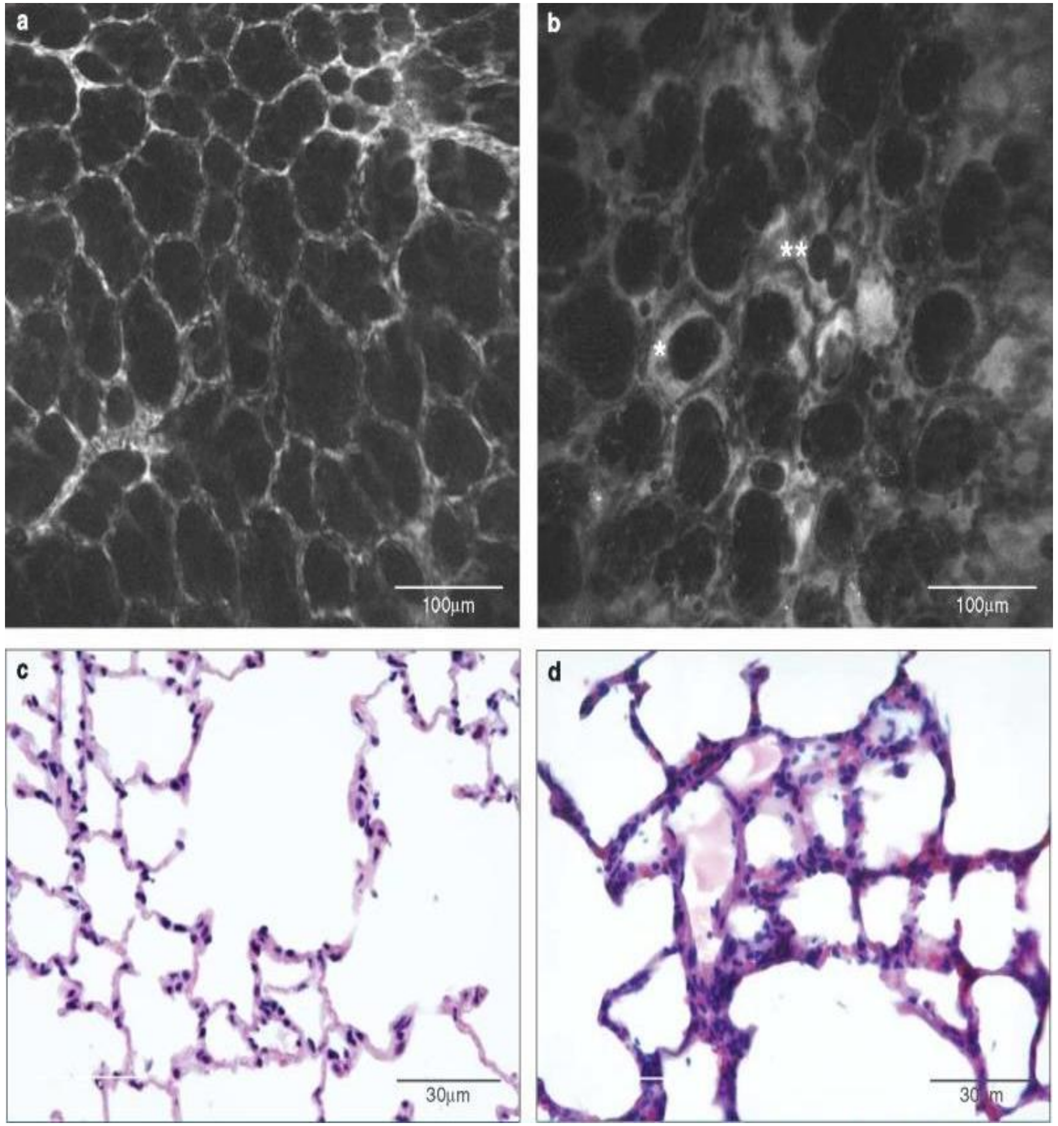
PVR = 10 mmHg / 5 L / min
= 2 mmHg/L/min



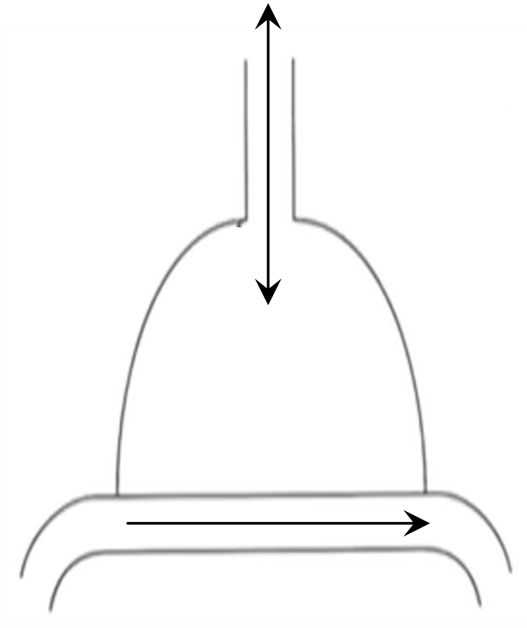
SVR = 100 mmHg / 5 L / min
= 20 mmHg/L/min

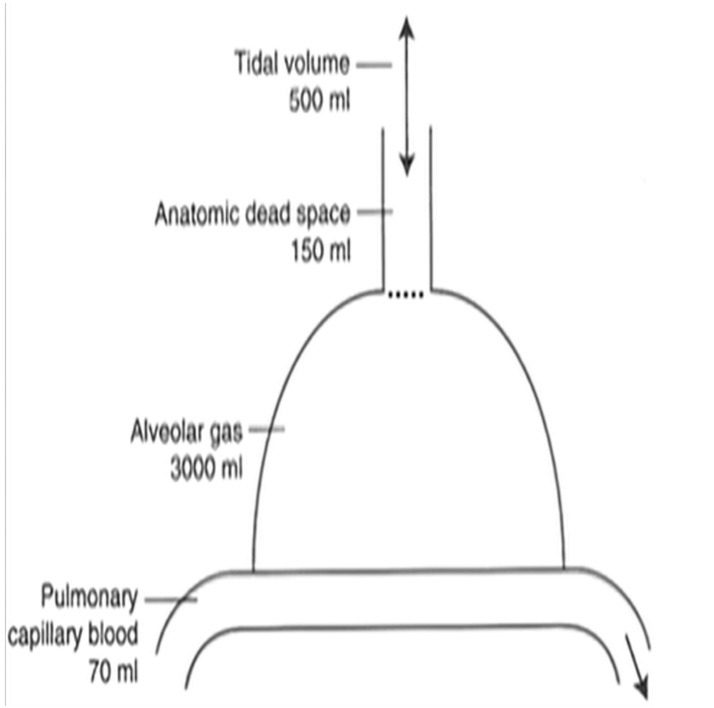


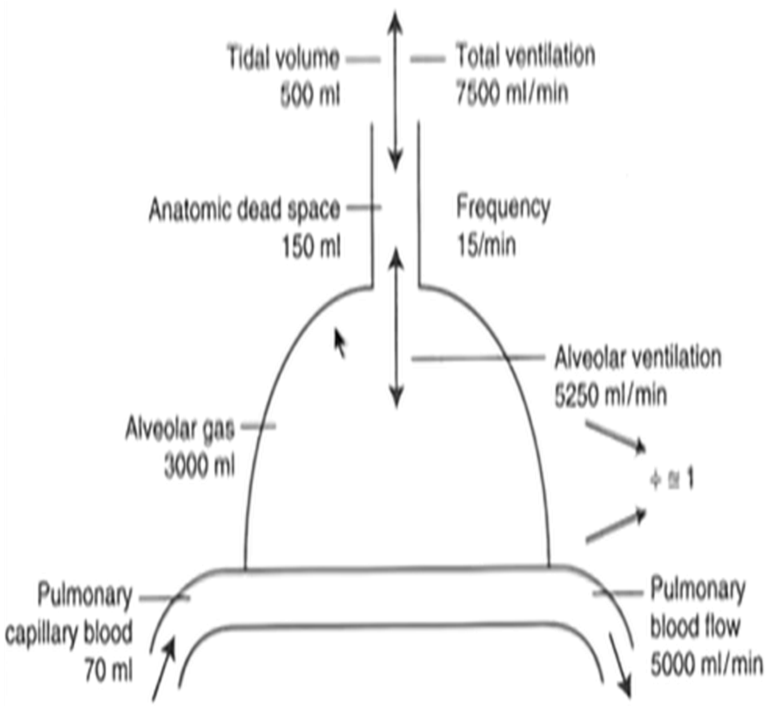


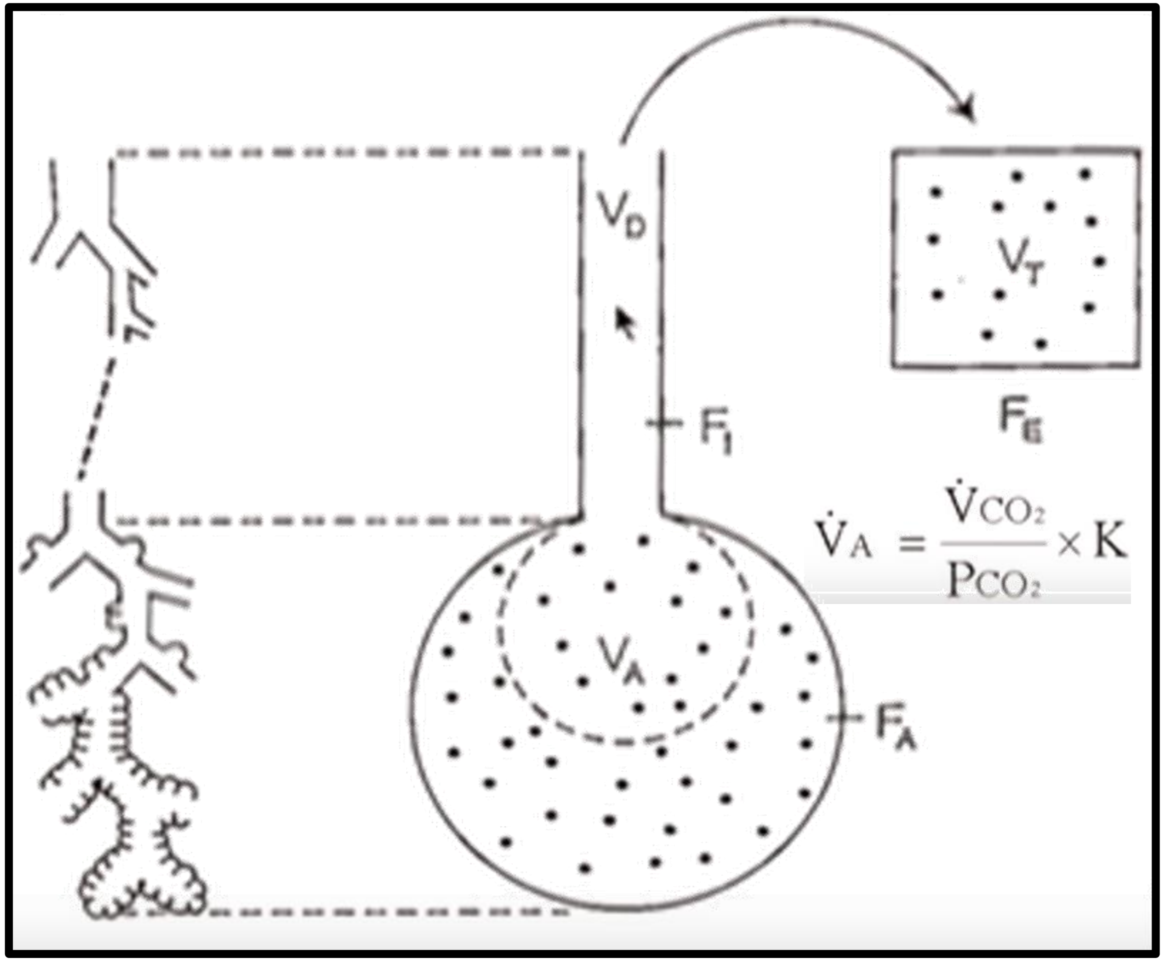


Cabrera JA, et al. Circulation. 2002 Aug 20;106(8):968-73.

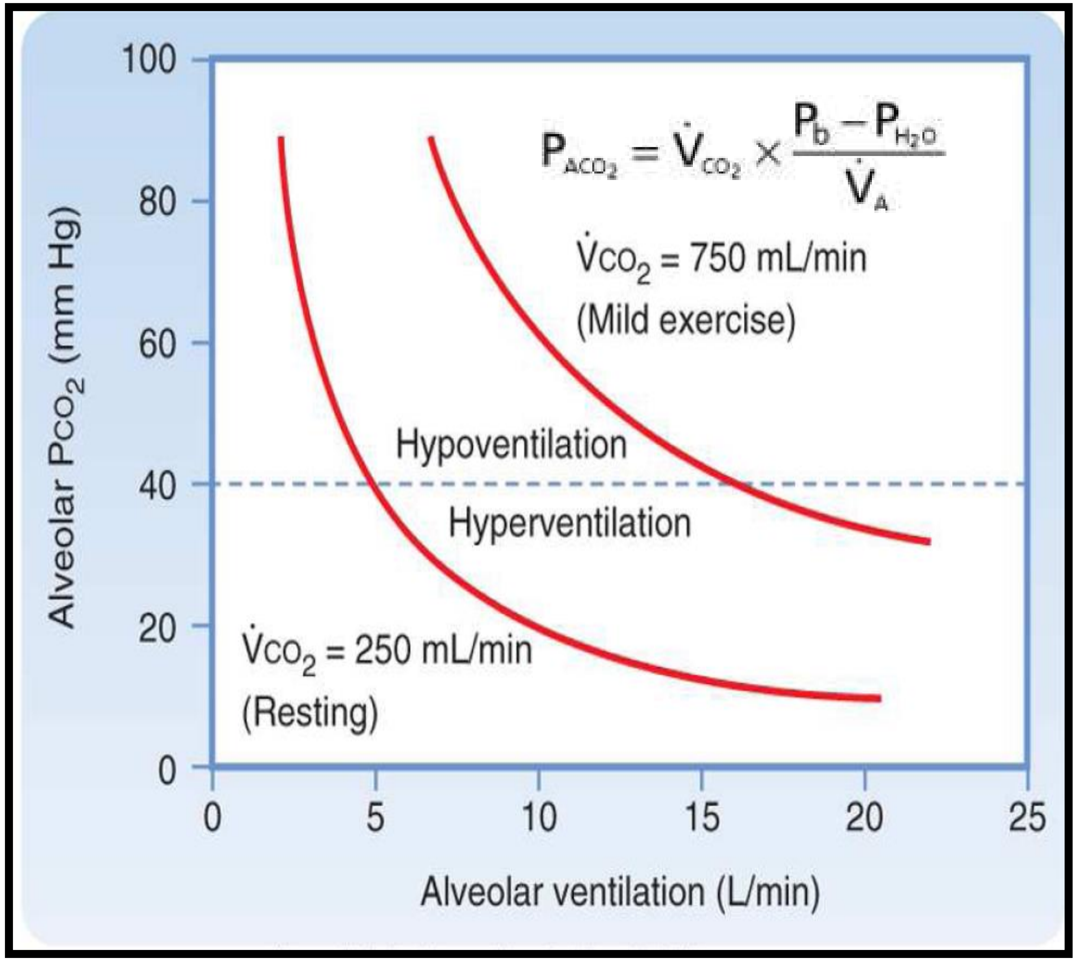



Tidal volume
500 ml
Anatomic dead space
150 ml
Alveolar gas
3000 ml
Pulmonary
capillary blood
70 ml

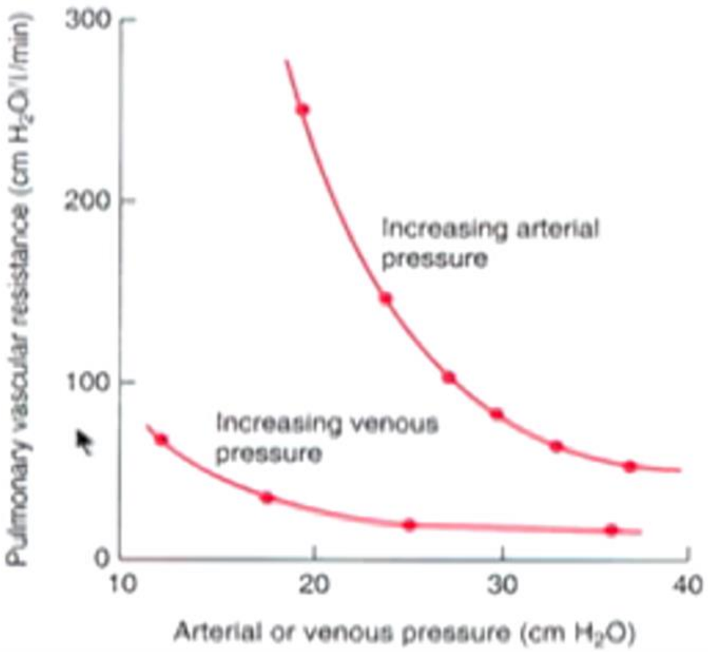

Tidal volume
500 ml
Total ventilation
7500 ml/min
Anatomic dead space
150 ml
Frequency
15/min
Alveolar ventilation
5250 ml/min
Alveolar gas
3000 ml
ϕ ≅ 1
Pulmonary
capillary blood
70 ml
Pulmonary
blood flow
5000 ml/min



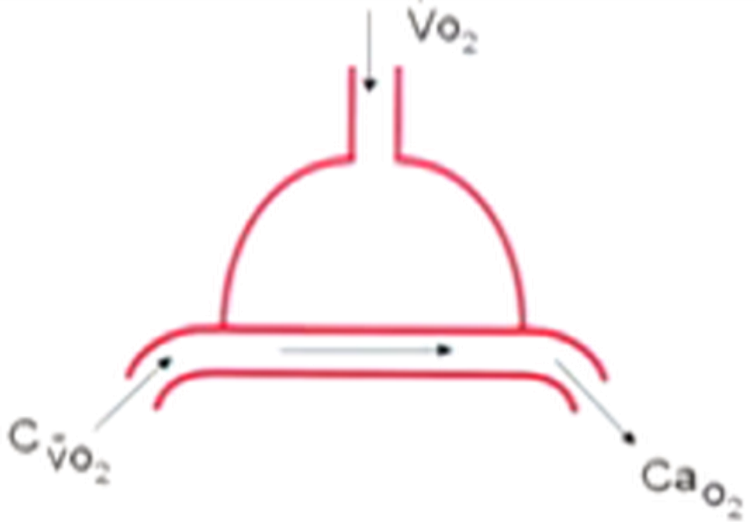
V_D
V_T
F_I
F_E
V_A
F_A
$\dot{V}_A = \frac{\dot{V}CO_2}{PCO_2} \times K$



$P_{ACO_2} = \dot{V}_{CO_2} \times \frac{P_b - P_{H_2O}}{\dot{V}_A}$
$\dot{V}CO_2$ = 750 mL/min
(Mild exercise)
Hypoventilation
Hyperventilation
$\dot{V}CO_2$ = 250 mL/min
(Resting)
Alveolar PCO_2 (mm Hg)
Alveolar ventilation (L/min)
100
80
60
40
20
0
5
10
15
20
25

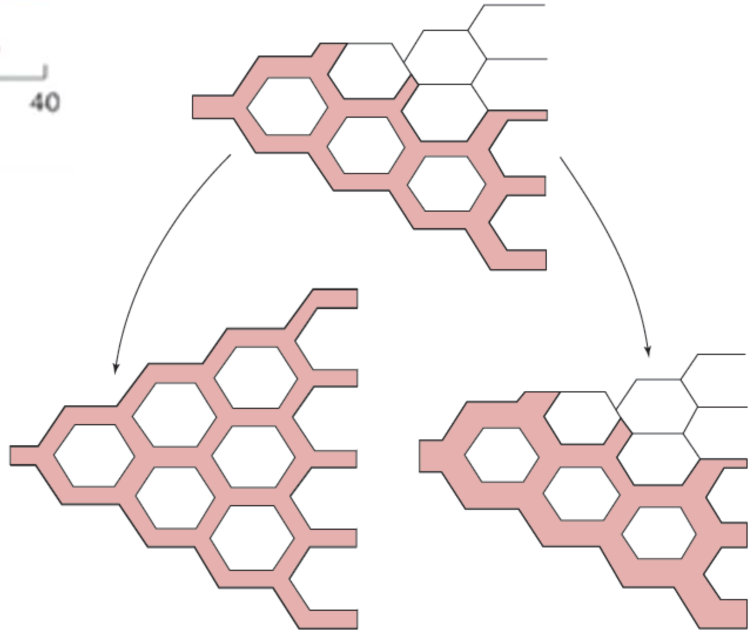


FICK PRINCIPLE

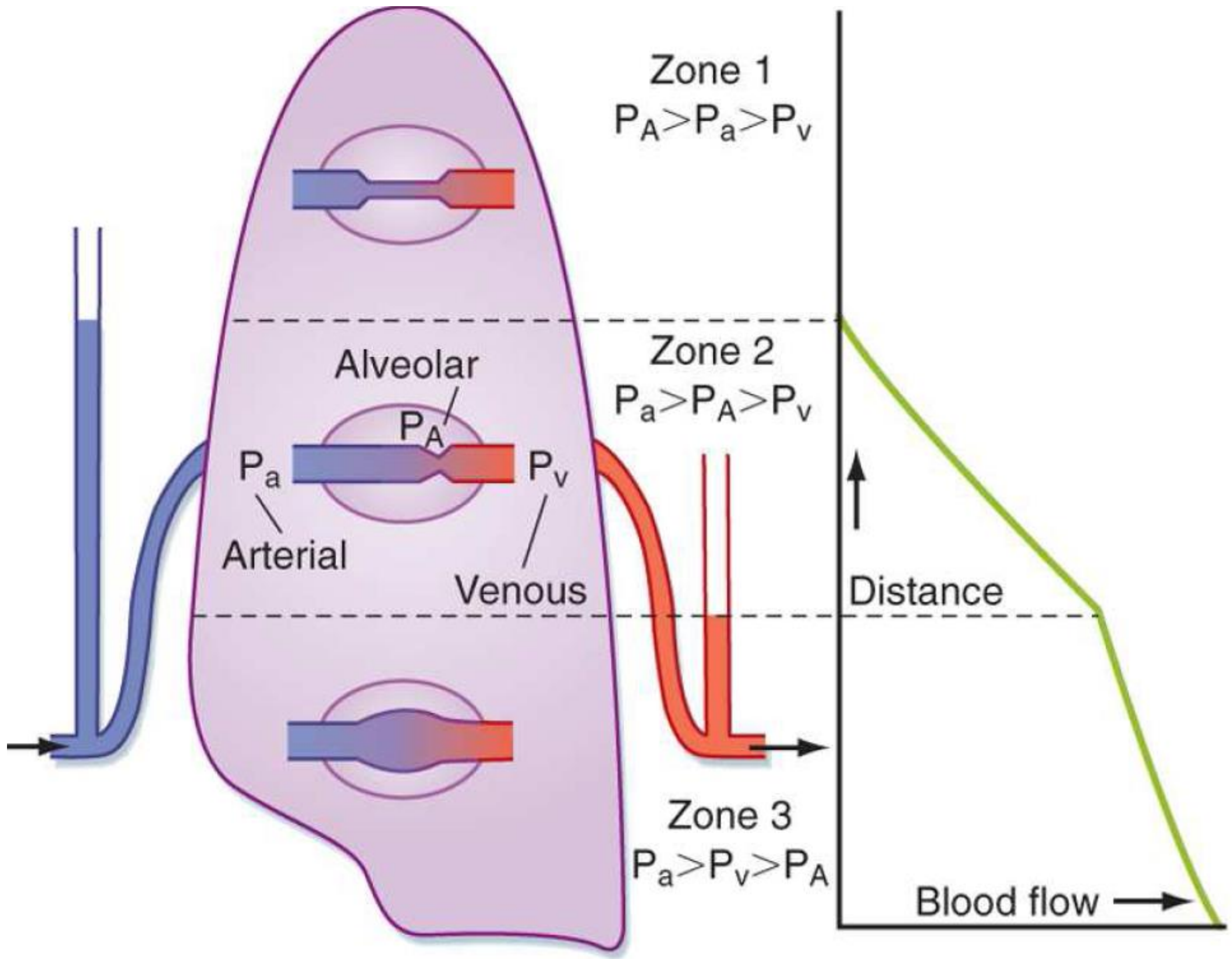


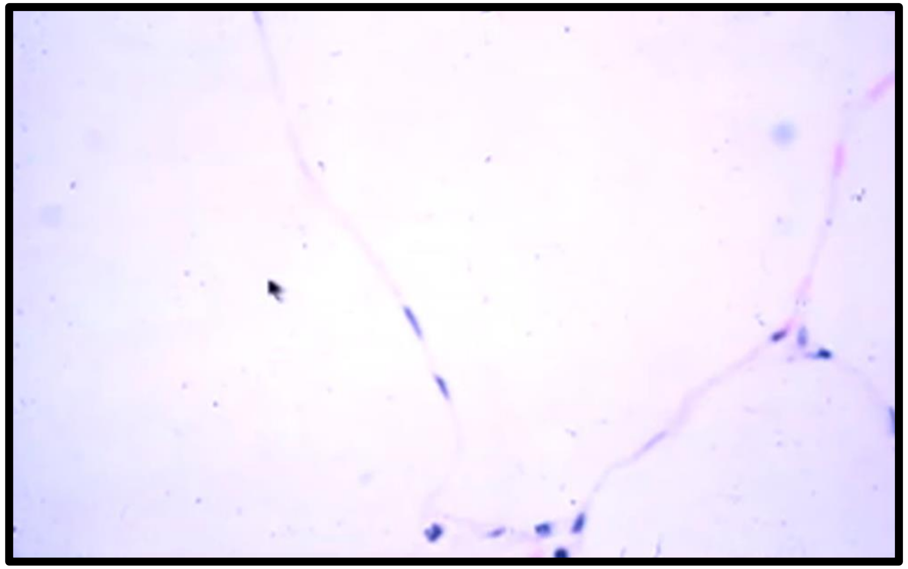
$$\dot{V}o_2 = \dot{Q}\,(Ca_{o_2} - C\bar{v}o_2)$$

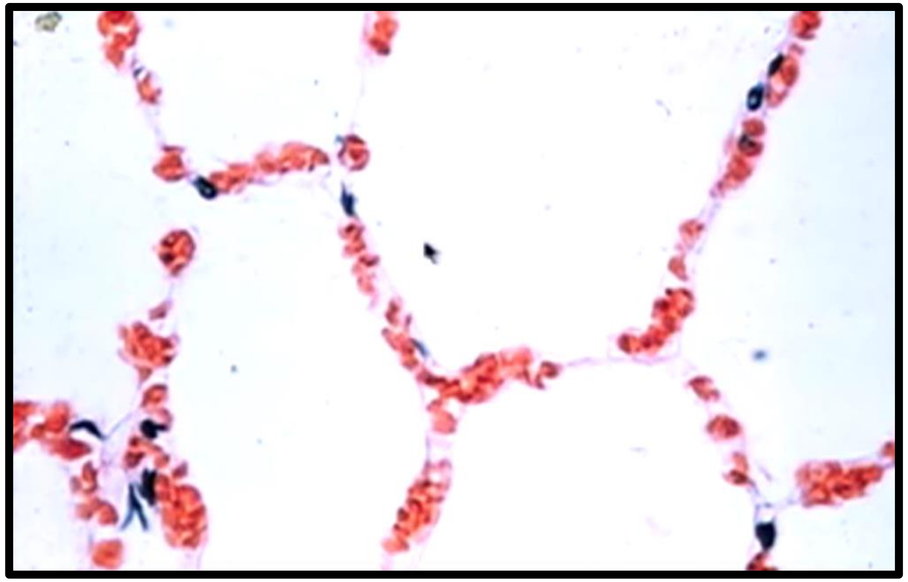
$$\dot{Q} = \frac{\dot{V}o_2}{Ca_{o_2} - C\bar{v}o_2}$$

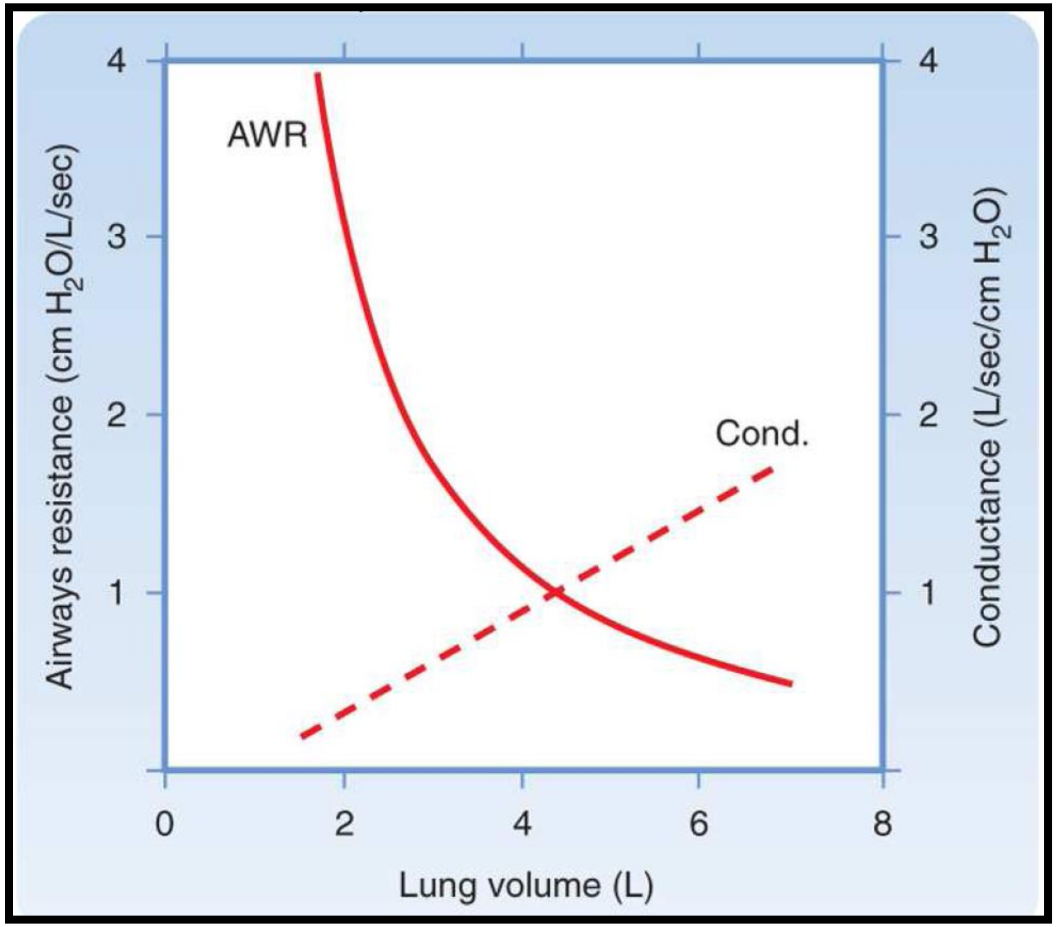


Recruitment Distention

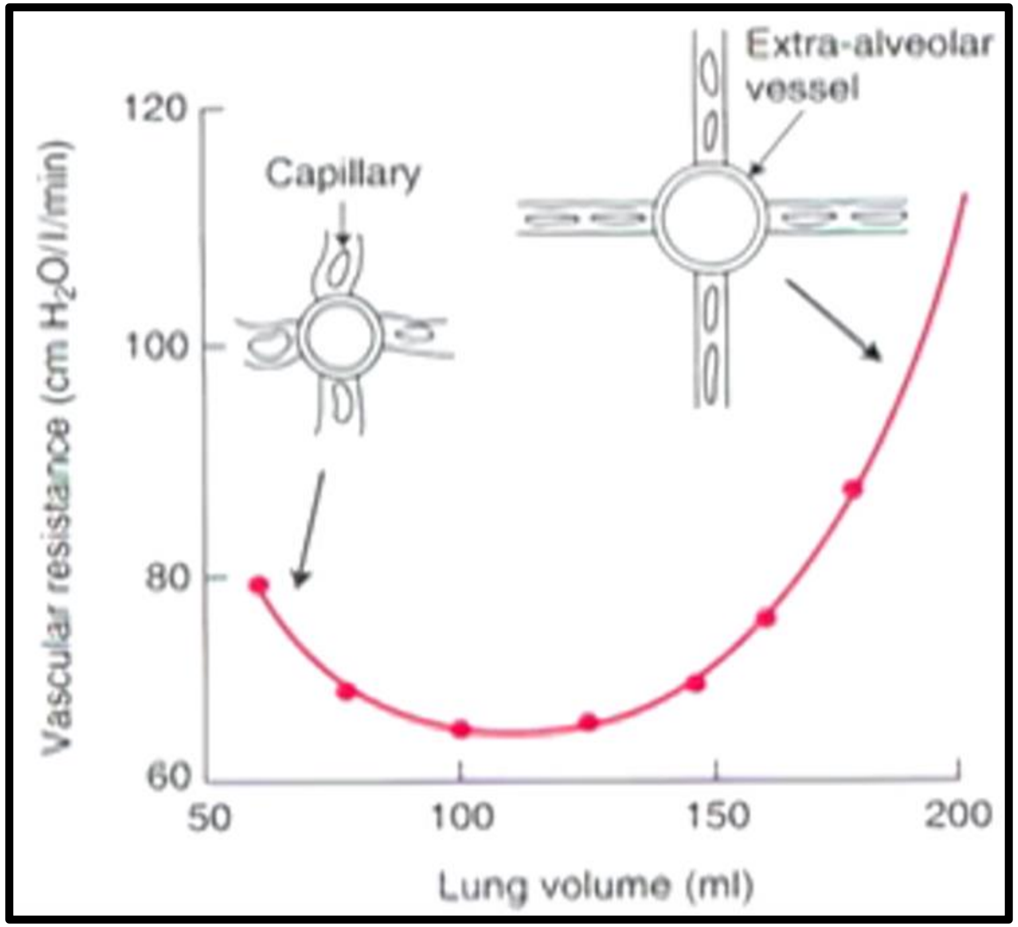

Zone 1
$P_A > P_a > P_v$
Zone 2
$P_a > P_A > P_v$
Alveolar
P_A
P_a
P_v
Arterial
Venous
Distance
Zone 3
$P_a > P_v > P_A$
Blood flow



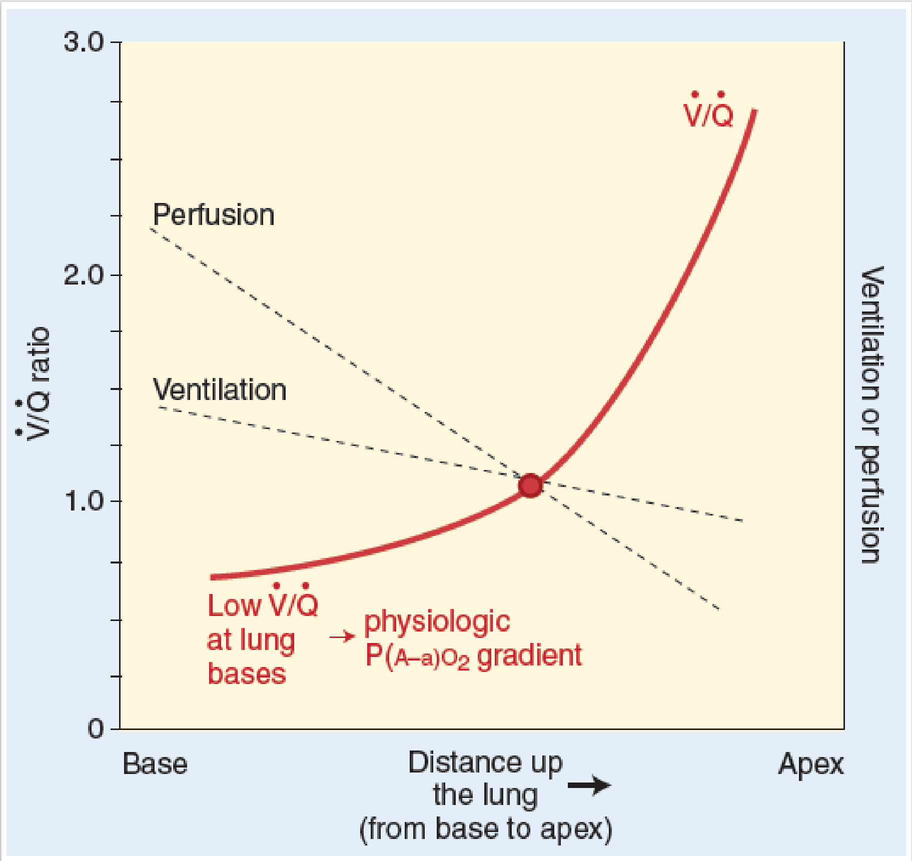


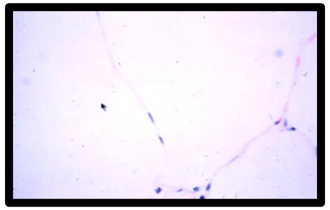


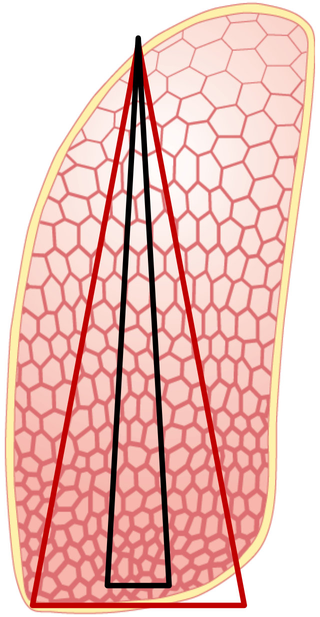
AWR
Cond.
Airways resistance (cm H_2O/L/sec)
Conductance (L/sec/cm H_2O)
Lung volume (L)
0
2
4
6
8
1
2
3
4

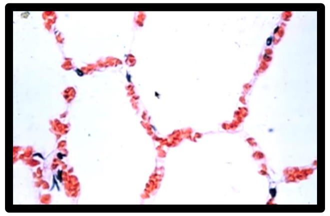


Extra-alveolar vessel
Capillary
Vascular resistance (cm H_2O/l/min)
Lung volume (ml)
60
80
100
120
50
100
150
200

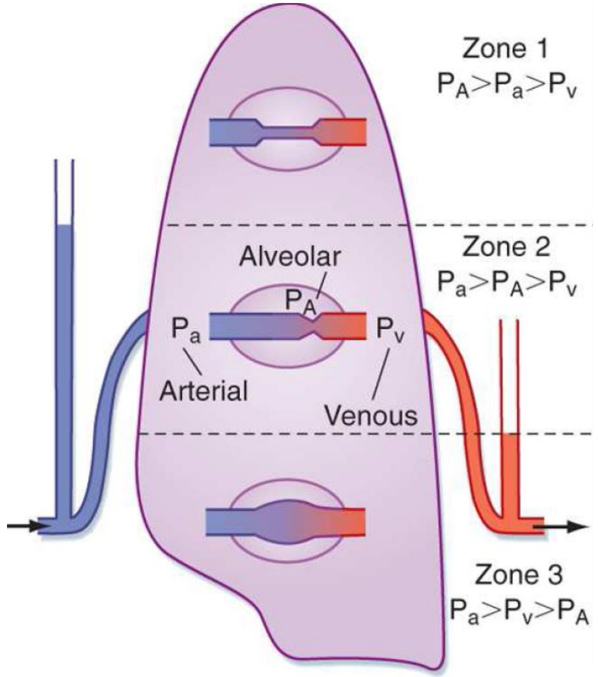








PHYSIOLOGIC DEAD SPACE



PHYSIOLOGIC SHUNT

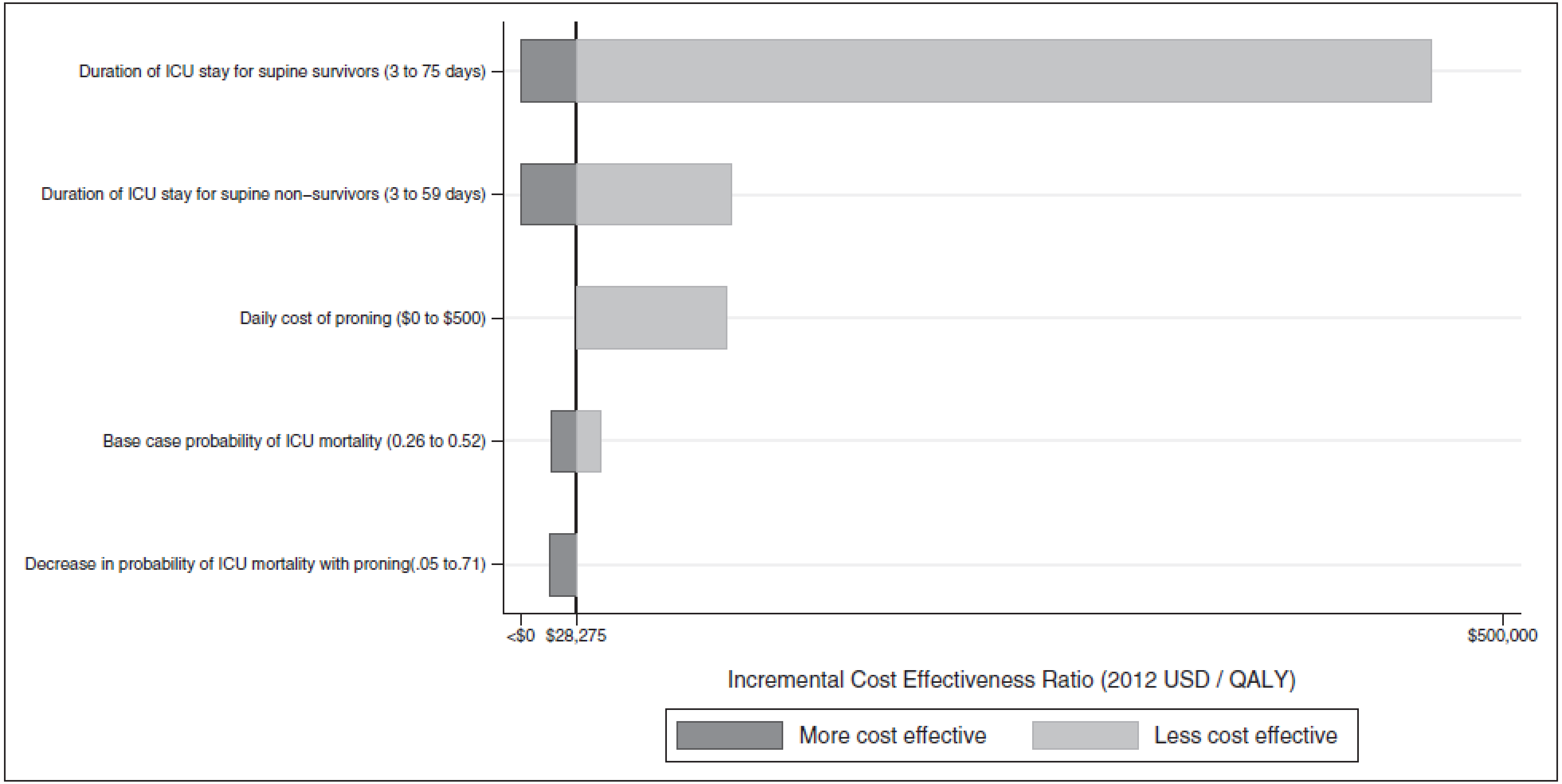
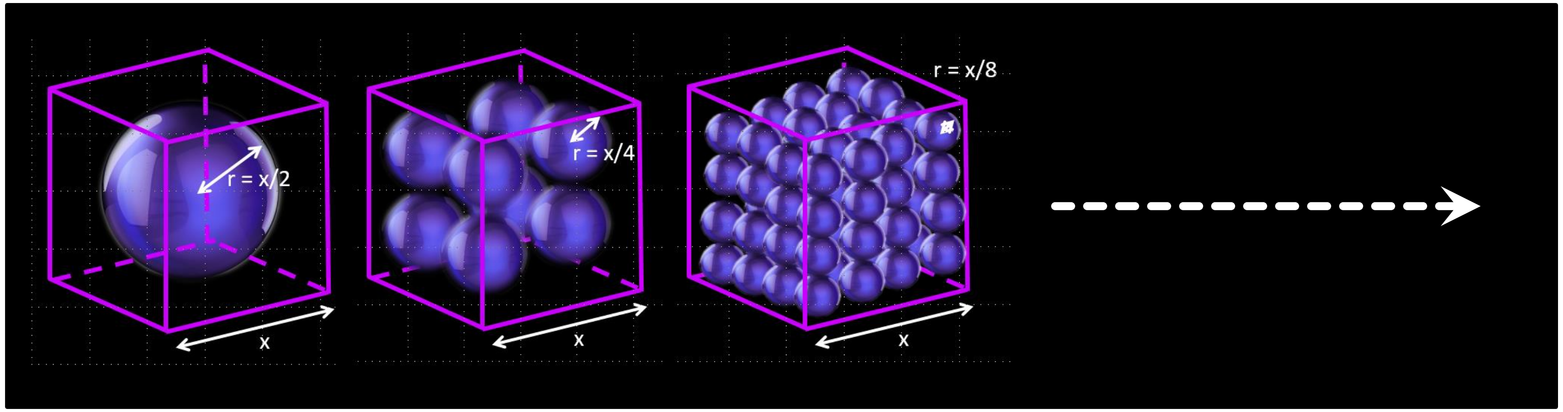
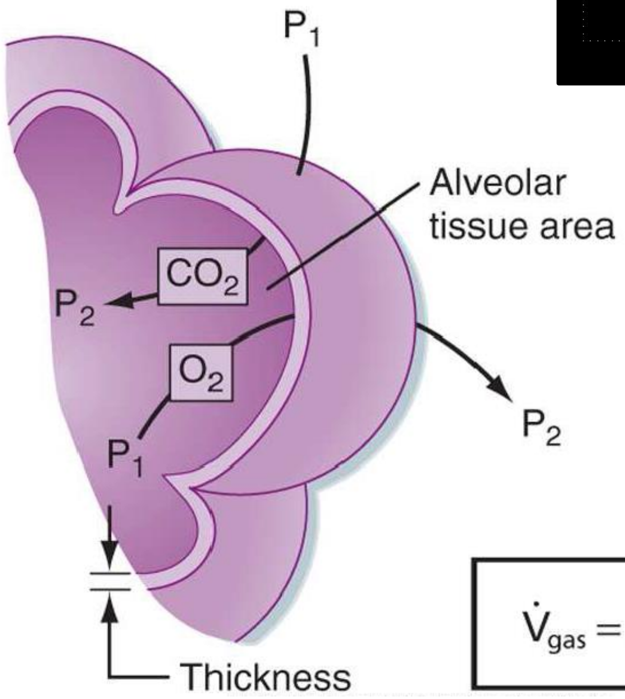


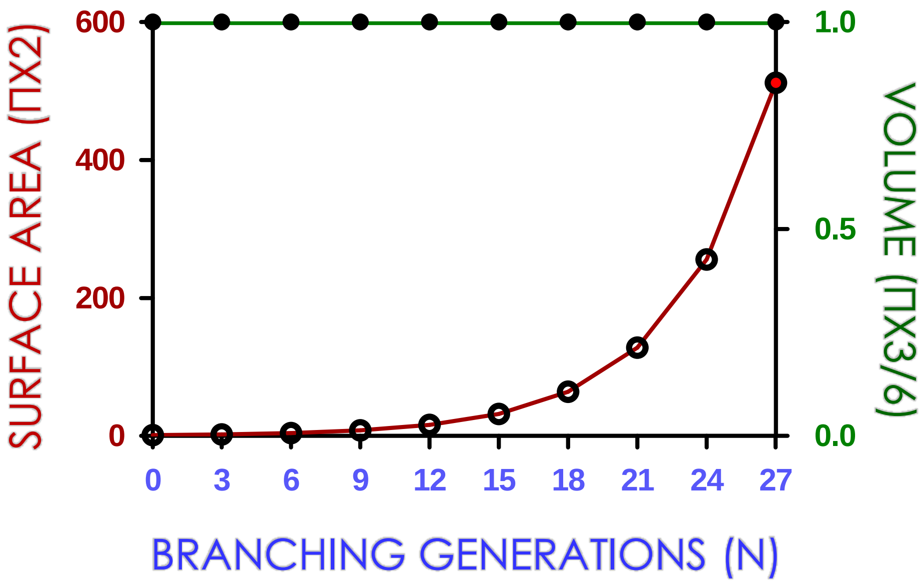
Figure 2. Hospital model tornado diagram showing one-way sensitivity analyses for cost-effectiveness of an intervention. *Bars* to the right of the point estimate indicate that the intervention becomes less cost effective at the limits of the range for that variable. *Bars* to the left of the point estimate indicate that the intervention becomes more cost effective at the limits of the range for that variable. QALY = quality-adjusted life year.

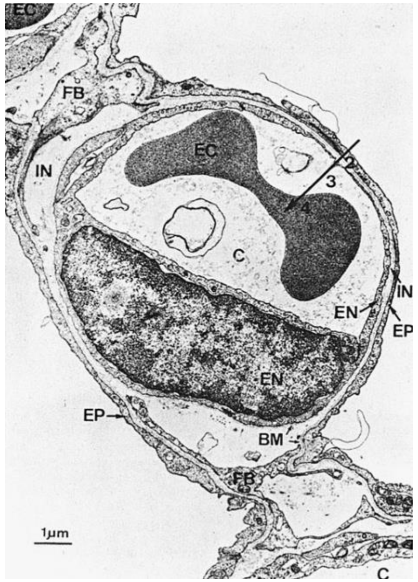
Baston CM, Coe NB, Guerin C, Mancebo J, Halpern S. The Cost-Effectiveness of Interventions to Increase Utilization of Prone Positioning for Severe Acute Respiratory Distress Syndrome. Crit Care Med. 2019 Mar;47(3):e198-e205.

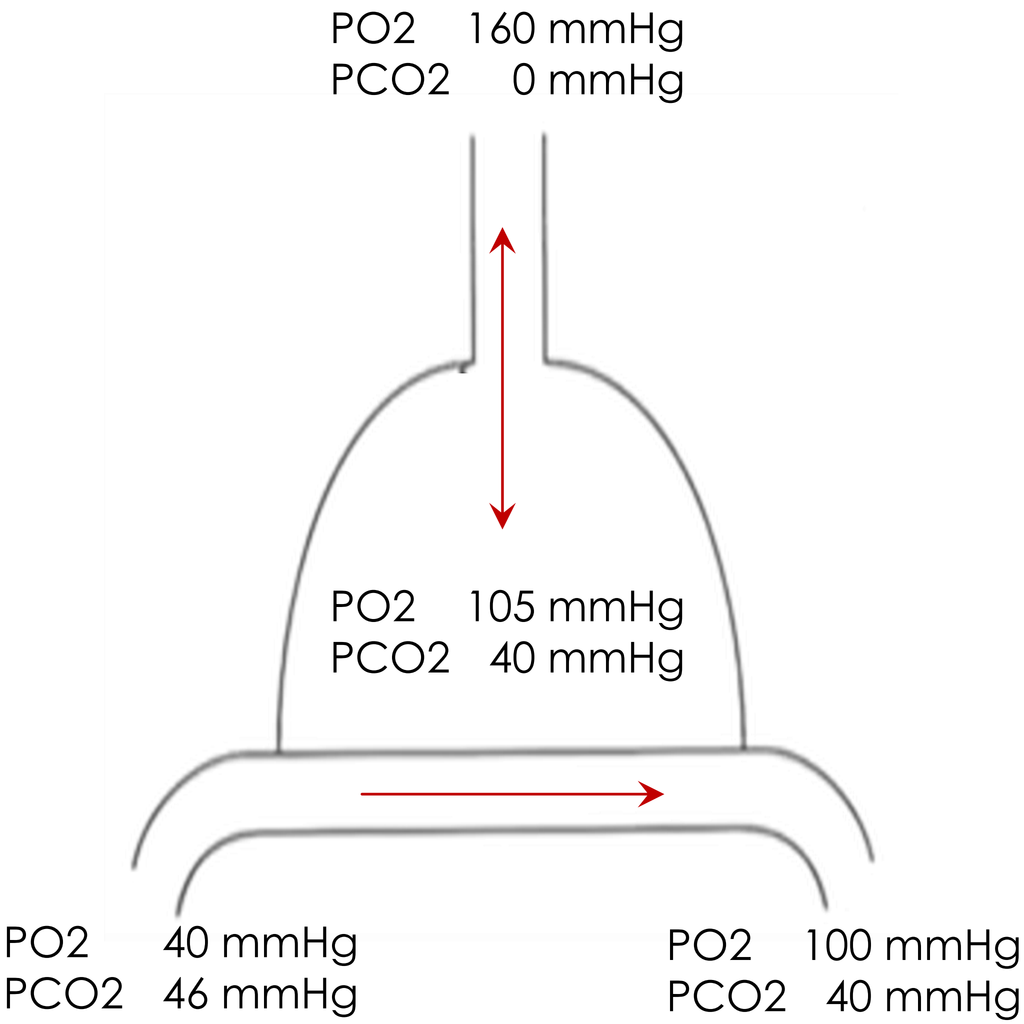


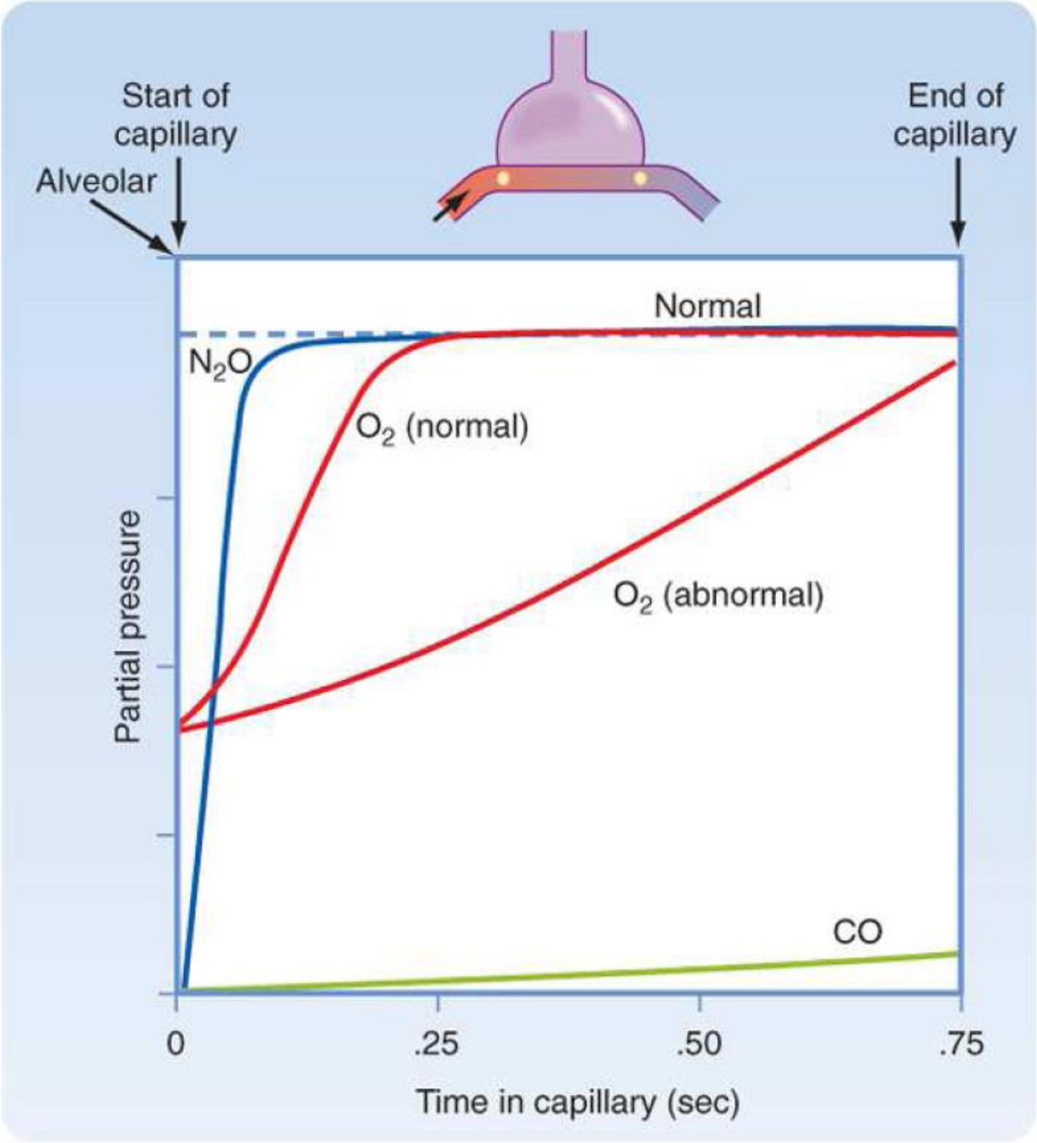


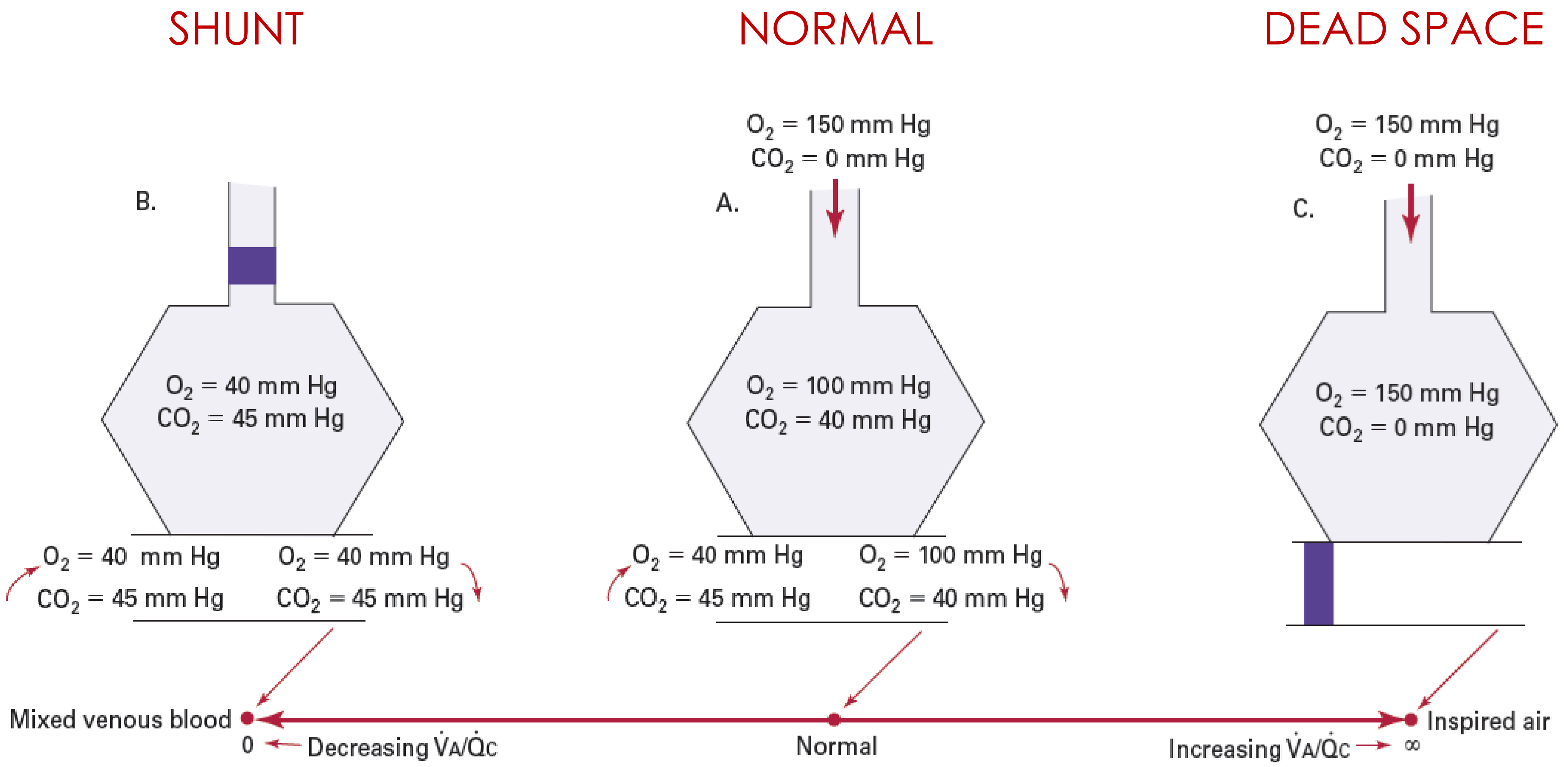
$$\dot{V}_{gas} = A \times D \times \frac{P_1 - P_2}{T}$$

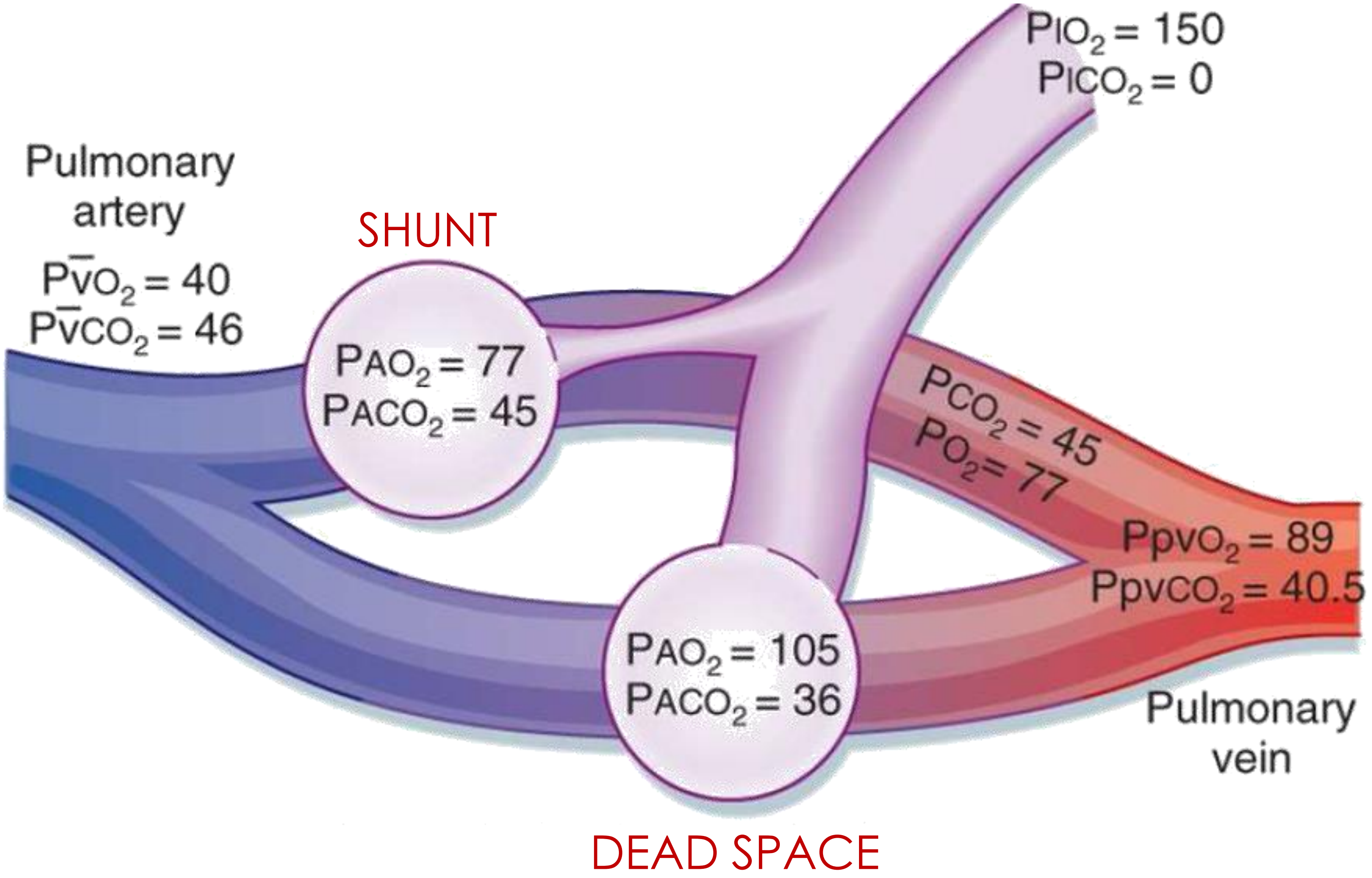




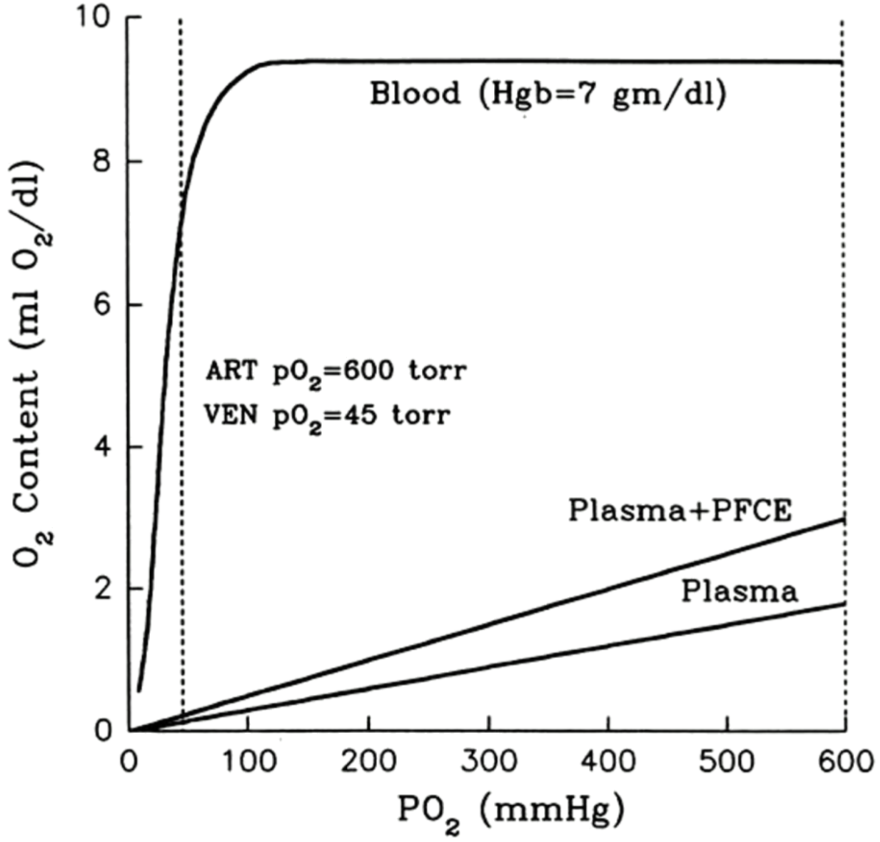

PO2 160 mmHg
PCO2 0 mmHg
PO2 105 mmHg
PCO2 40 mmHg
PO2 40 mmHg
PCO2 46 mmHg
PO2 100 mmHg
PCO2 40 mmHg


Start of capillary
End of capillary
Alveolar
Normal
N2O
O2 (normal)
O2 (abnormal)
CO
Partial pressure
0
.25
.50
.75
Time in capillary (sec)


SHUNT
NORMAL
DEAD SPACE
B.
O2 = 40 mm Hg
CO2 = 45 mm Hg
O2 = 40 mm Hg
CO2 = 45 mm Hg
O2 = 40 mm Hg
CO2 = 45 mm Hg
A.
O2 = 150 mm Hg
CO2 = 0 mm Hg
O2 = 100 mm Hg
CO2 = 40 mm Hg
O2 = 40 mm Hg
CO2 = 45 mm Hg
O2 = 100 mm Hg
CO2 = 40 mm Hg
C.
O2 = 150 mm Hg
CO2 = 0 mm Hg
O2 = 150 mm Hg
CO2 = 0 mm Hg
Mixed venous blood
0
Decreasing VA/QC
Normal
Increasing VA/QC
∞
Inspired air



$P_IO_2 = 150$
$P_ICO_2 = 0$
Pulmonary artery
$P\bar{v}O_2 = 40$
$P\bar{v}CO_2 = 46$
SHUNT
$P_AO_2 = 77$
$P_ACO_2 = 45$
$PCO_2 = 45$
$PO_2 = 77$
$PpvO_2 = 89$
$PpvCO_2 = 40.5$
$P_AO_2 = 105$
$P_ACO_2 = 36$
Pulmonary vein
DEAD SPACE



$DO2 = CaO2 \times CO$

$= 1{,}34 \times [Hgb] \times SaO2 \times HR \times SV$

$= 1{,}34\ mL/g \times 15\ g/dL \times 98\% \times 70/min \times 70\ mL$

$\sim 200\ mL/L \times 5\ L/min$

$\sim 1000\ mL/min$

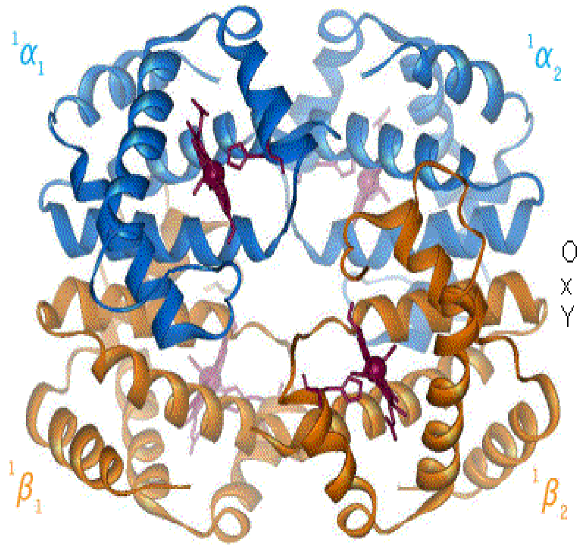
$VO2 = (CaO2-CvO2) \times CO$

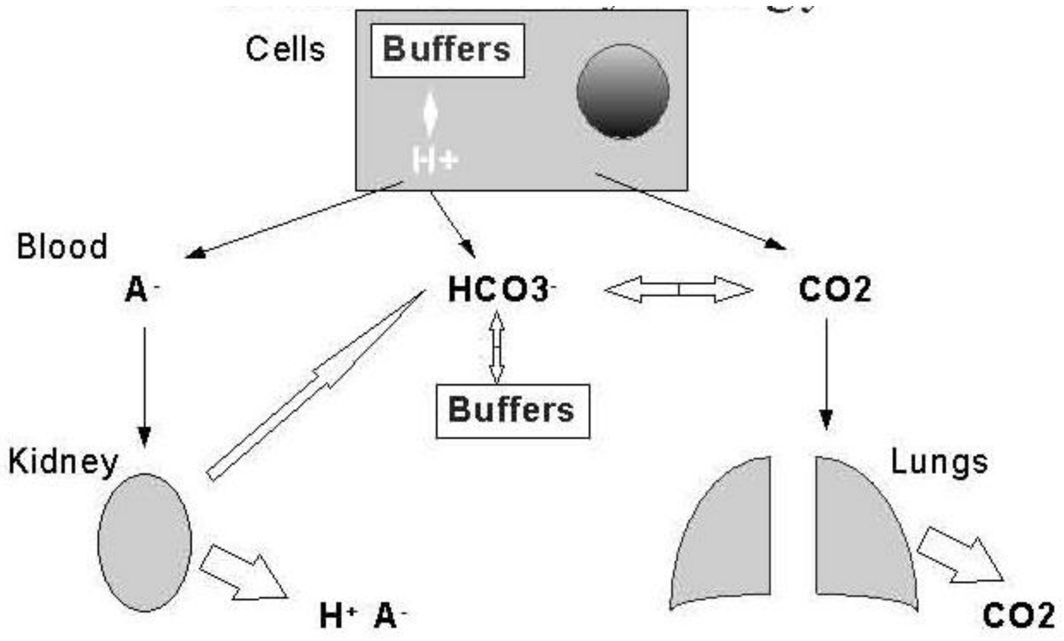
$= 1{,}34 \times [Hgb\} \times (SaO2 – SvO2) \times HR \times SV$

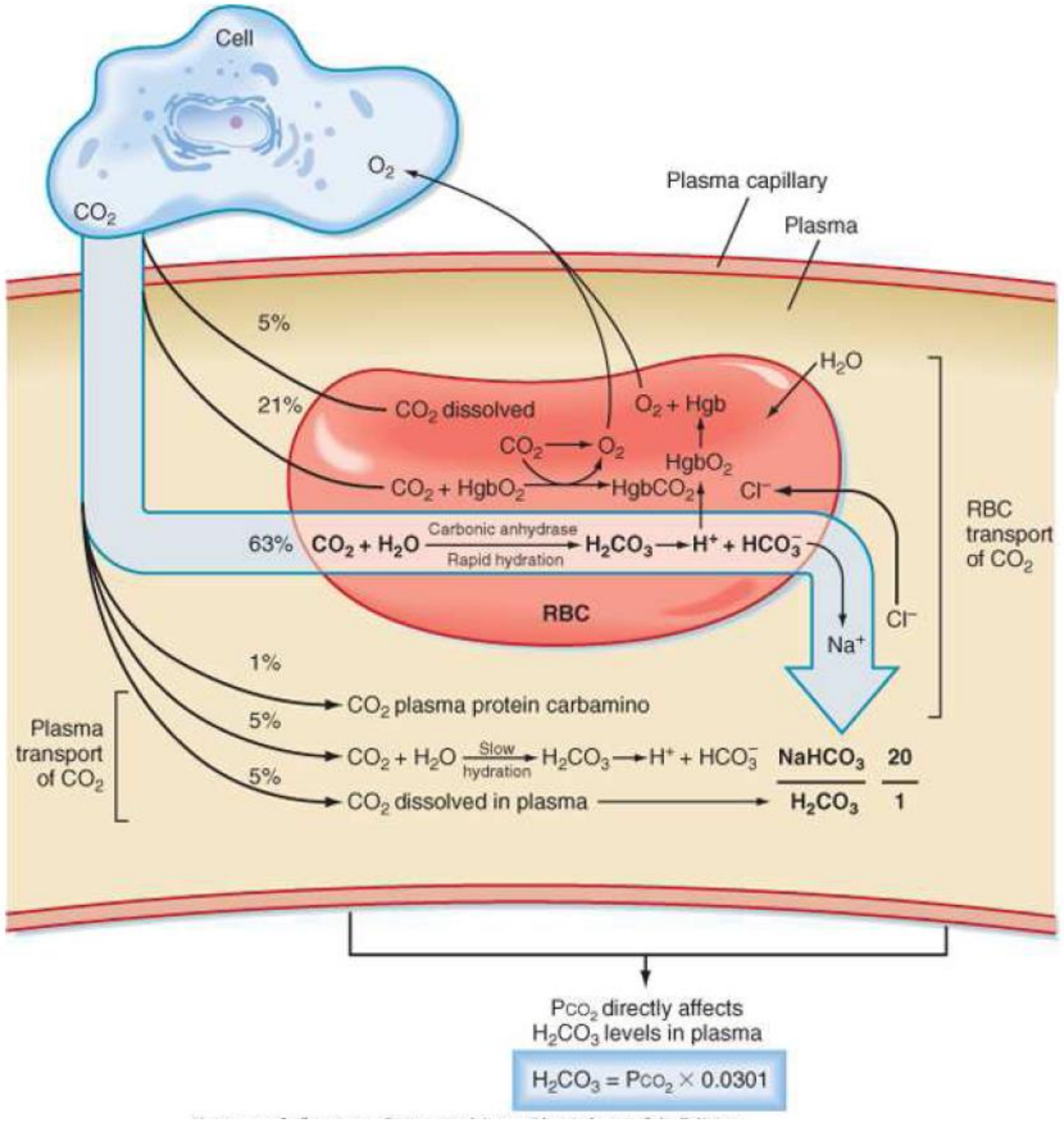
$= 1{,}34\ mL/g \times 15\ g/dL \times (98\% - 75\%) \times 70/min \times 70\ mL$

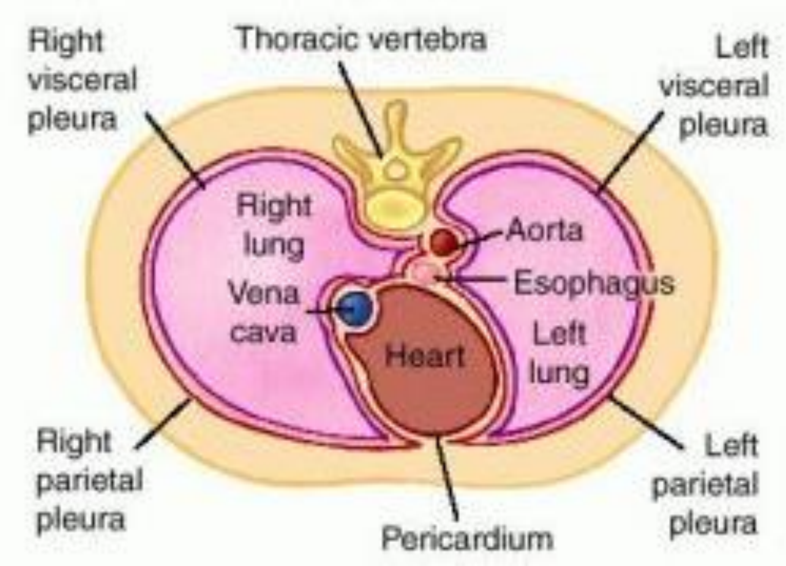
$\sim 50\ mL/L \times 5\ L/min$

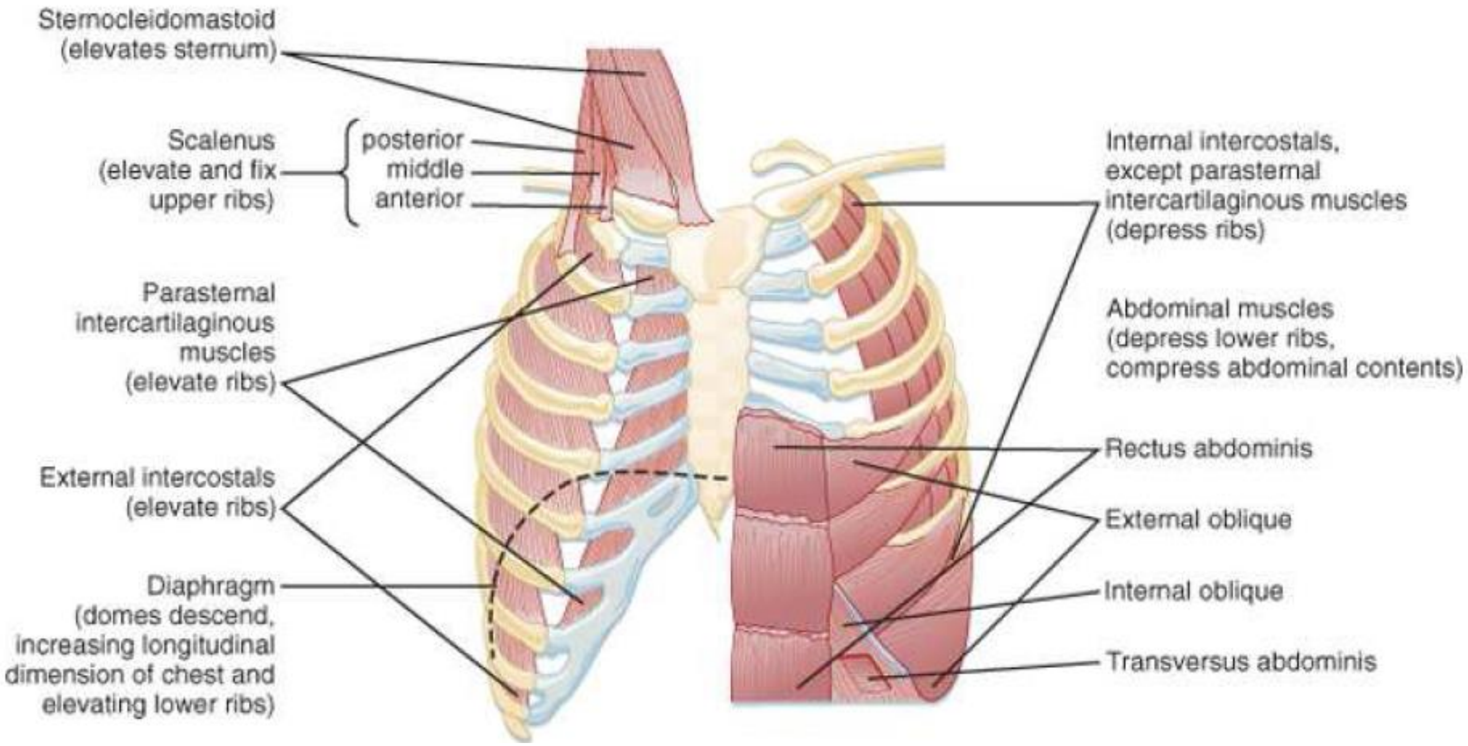
$\sim 250\ mL/min$

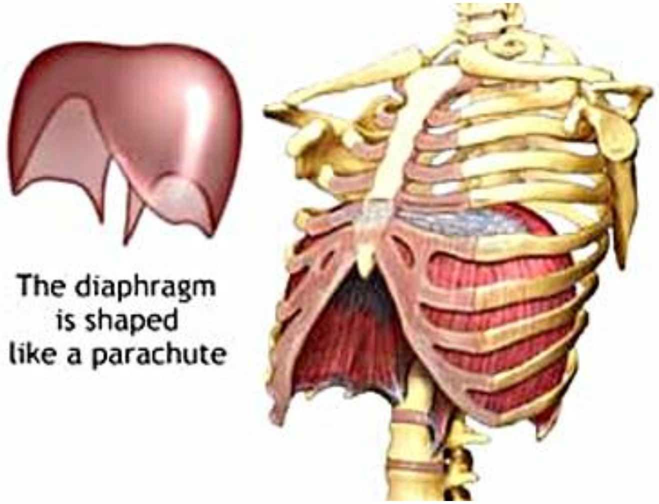


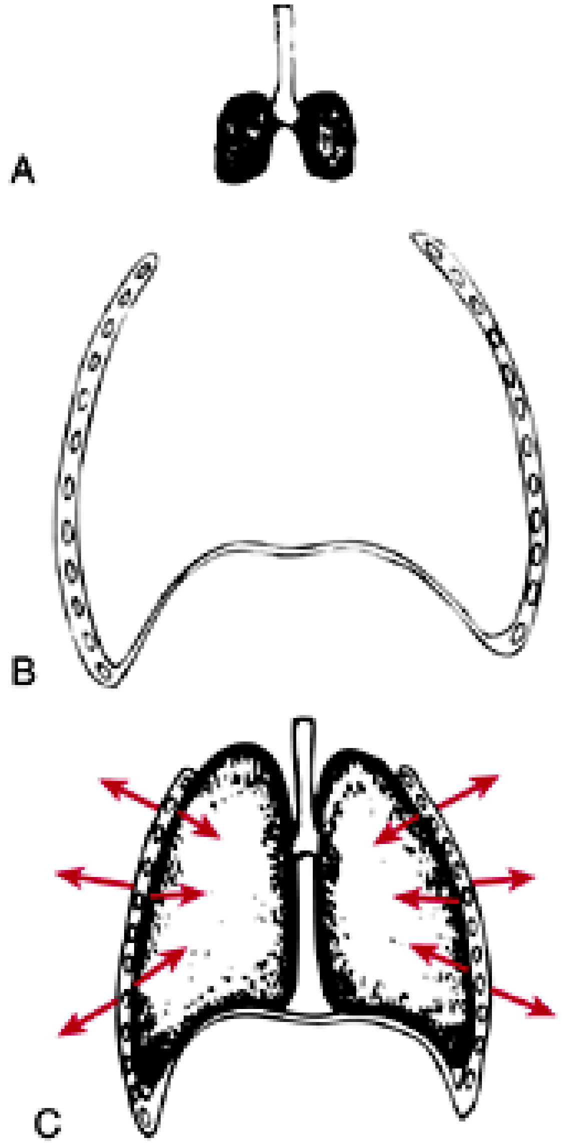

Cells
Buffers
H+
Blood
A-
HCO3-
CO2
Buffers
Kidney
Lungs
H+ A-
CO2

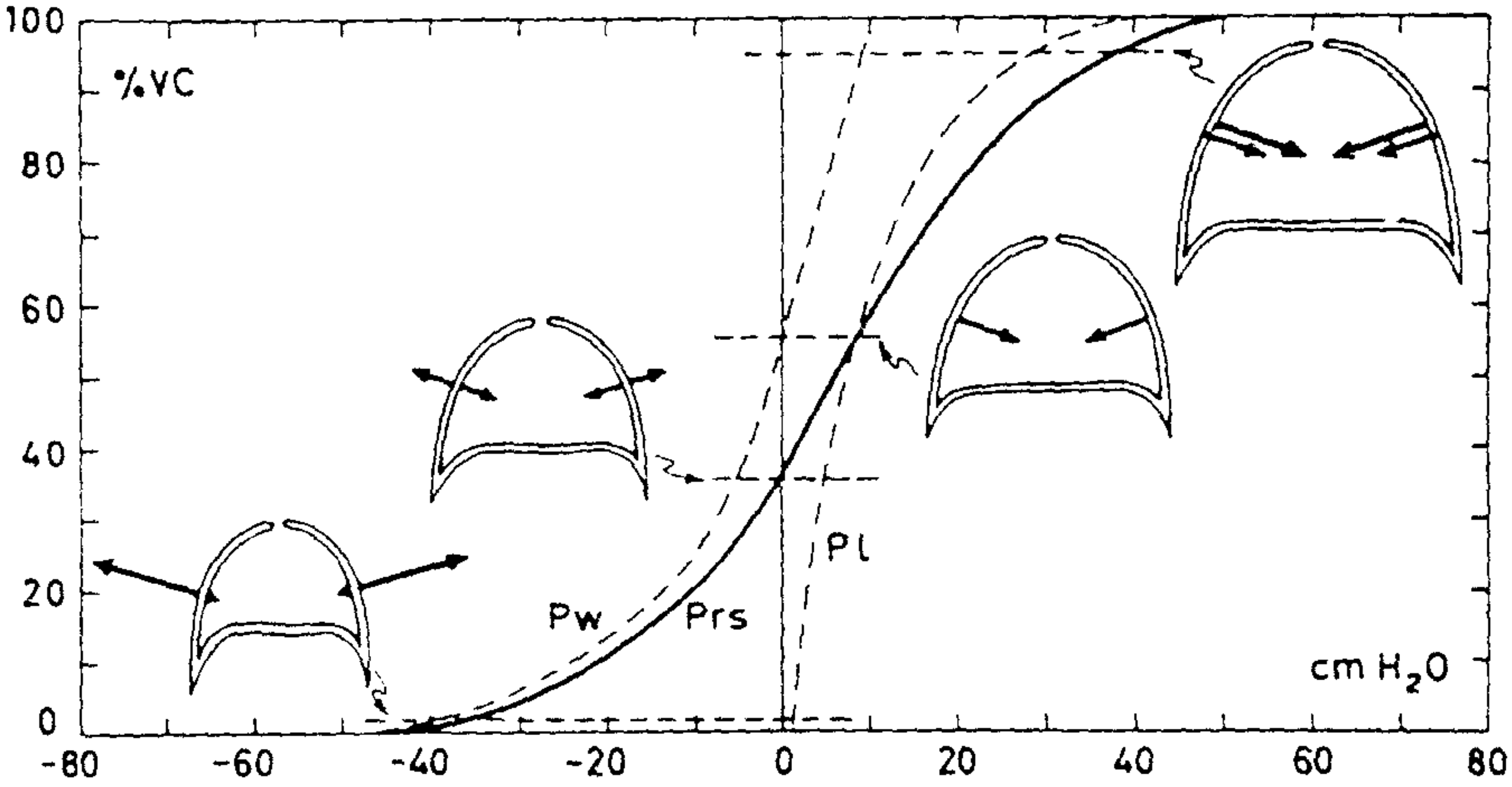

Cell
O_2
CO_2
Plasma capillary
Plasma
5%
21%
CO_2 dissolved
O_2 + Hgb
H_2O
$CO_2 \rightarrow O_2$
$HgbO_2$
$CO_2 + HgbO_2 \rightarrow HgbCO_2$
Cl^-
63%
$CO_2 + H_2O \xrightarrow[\text{Rapid hydration}]{\text{Carbonic anhydrase}} H_2CO_3 \rightarrow H^+ + HCO_3^-$
RBC
Na^+
Cl^-
RBC transport of CO_2
1%
CO_2 plasma protein carbamino
5%
$CO_2 + H_2O \xrightarrow[\text{hydration}]{\text{Slow}} H_2CO_3 \rightarrow H^+ + HCO_3^-$
5%
CO_2 dissolved in plasma
Plasma transport of CO_2
$\frac{NaHCO_3}{H_2CO_3}$ $\frac{20}{1}$
P_{CO_2} directly affects H_2CO_3 levels in plasma
$H_2CO_3 = P_{CO_2} \times 0.0301$

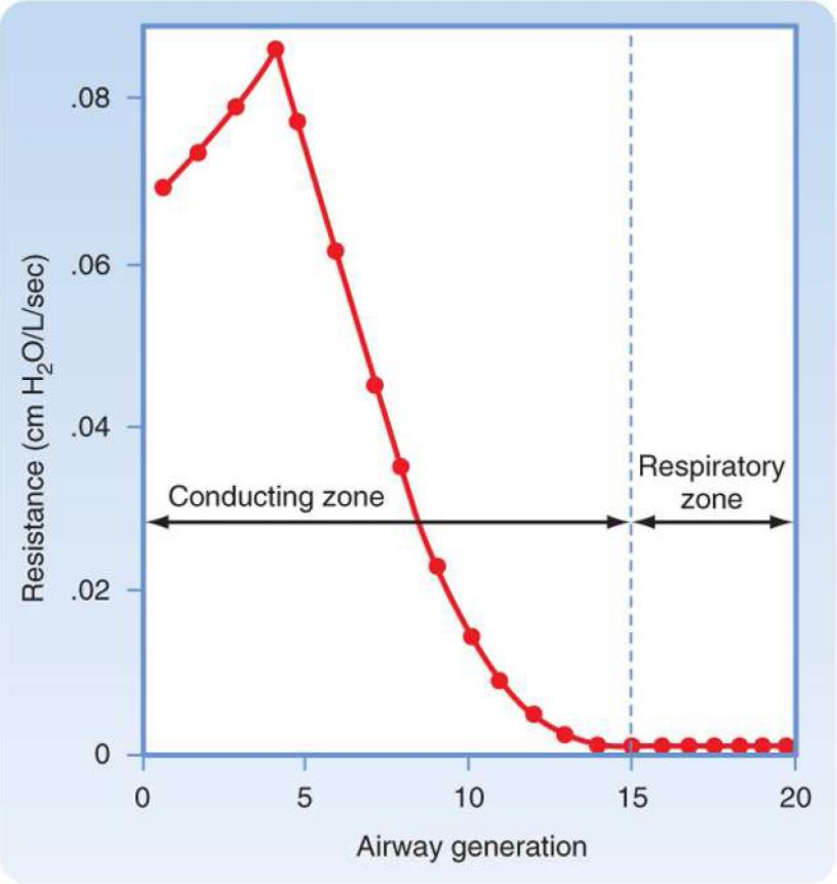

Right visceral pleura
Thoracic vertebra
Left visceral pleura
Right lung
Aorta
Esophagus
Vena cava
Heart
Left lung
Right parietal pleura
Left parietal pleura
Pericardium


Sternocleidomastoid (elevates sternum)
Scalenus (elevate and fix upper ribs)
posterior
middle
anterior
Parasternal intercartilaginous muscles (elevate ribs)
External intercostals (elevate ribs)
Diaphragm (domes descend, increasing longitudinal dimension of chest and elevating lower ribs)
Internal intercostals, except parasternal intercartilaginous muscles (depress ribs)
Abdominal muscles (depress lower ribs, compress abdominal contents)
Rectus abdominis
External oblique
Internal oblique
Transversus abdominis

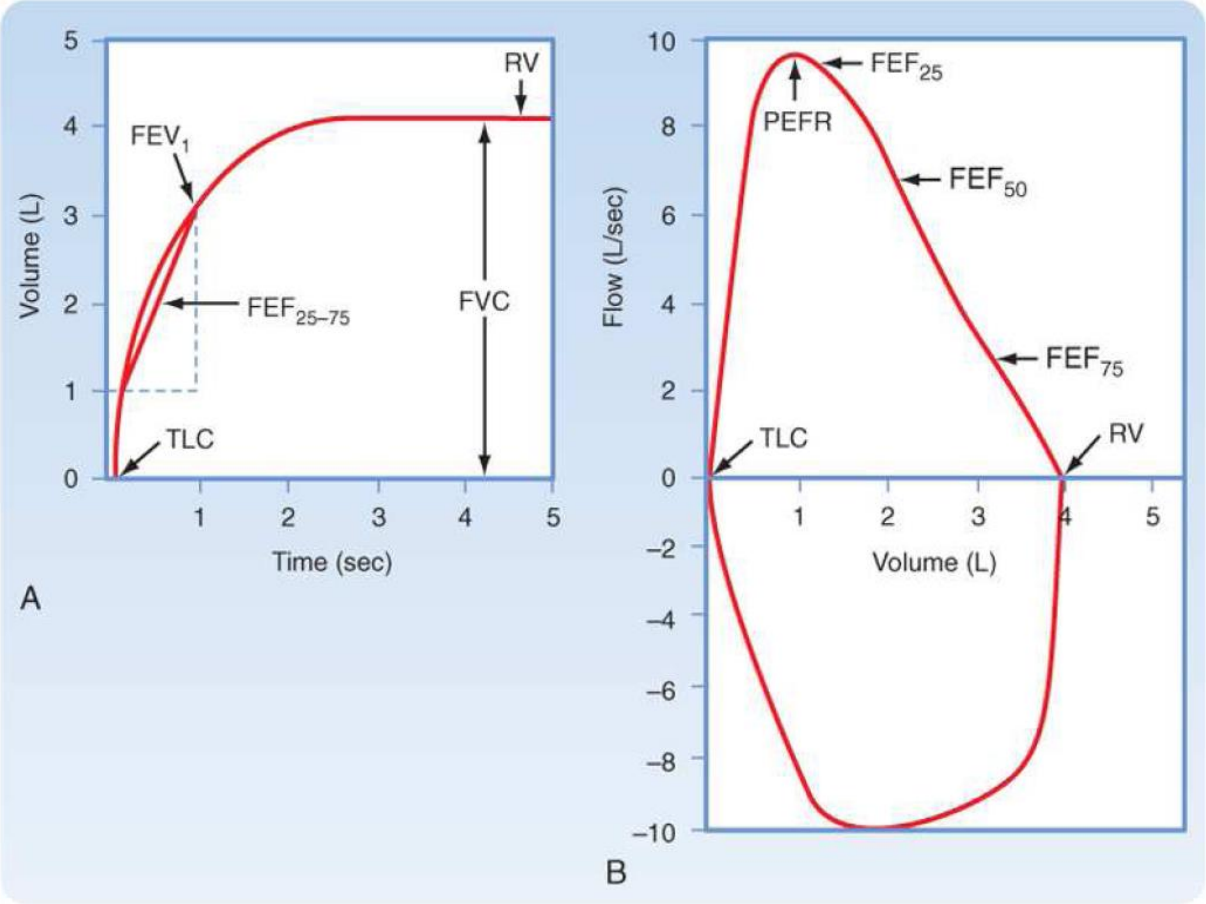

The diaphragm is shaped like a parachute


A
B
C

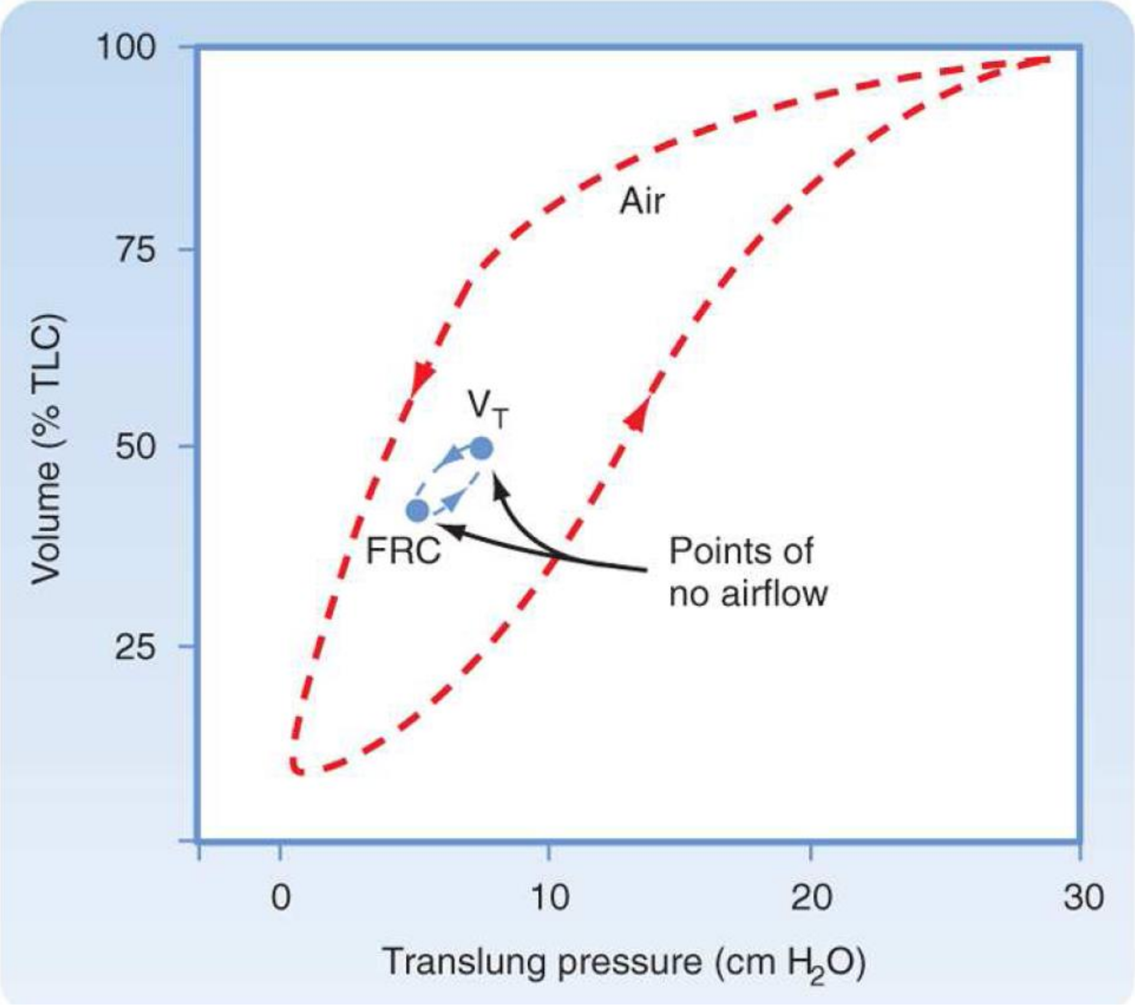

%VC
100
80
60
40
20
0
-80
-60
-40
-20
0
20
40
60
80
Pw
Prs
Pl
cm H_2O

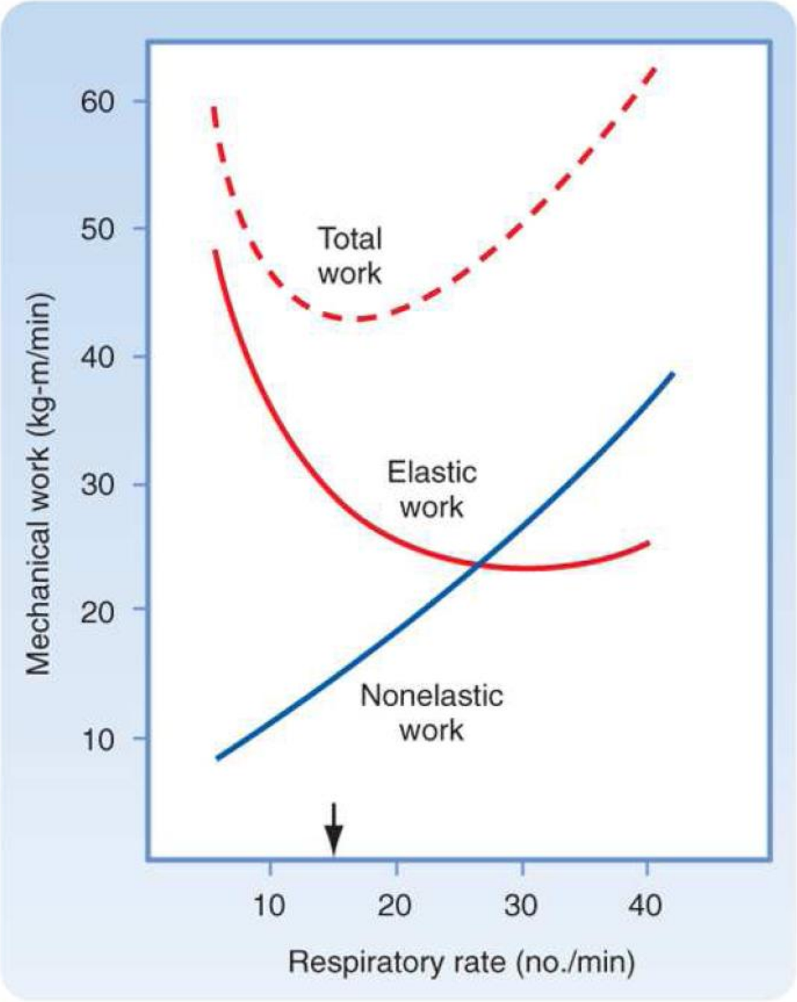


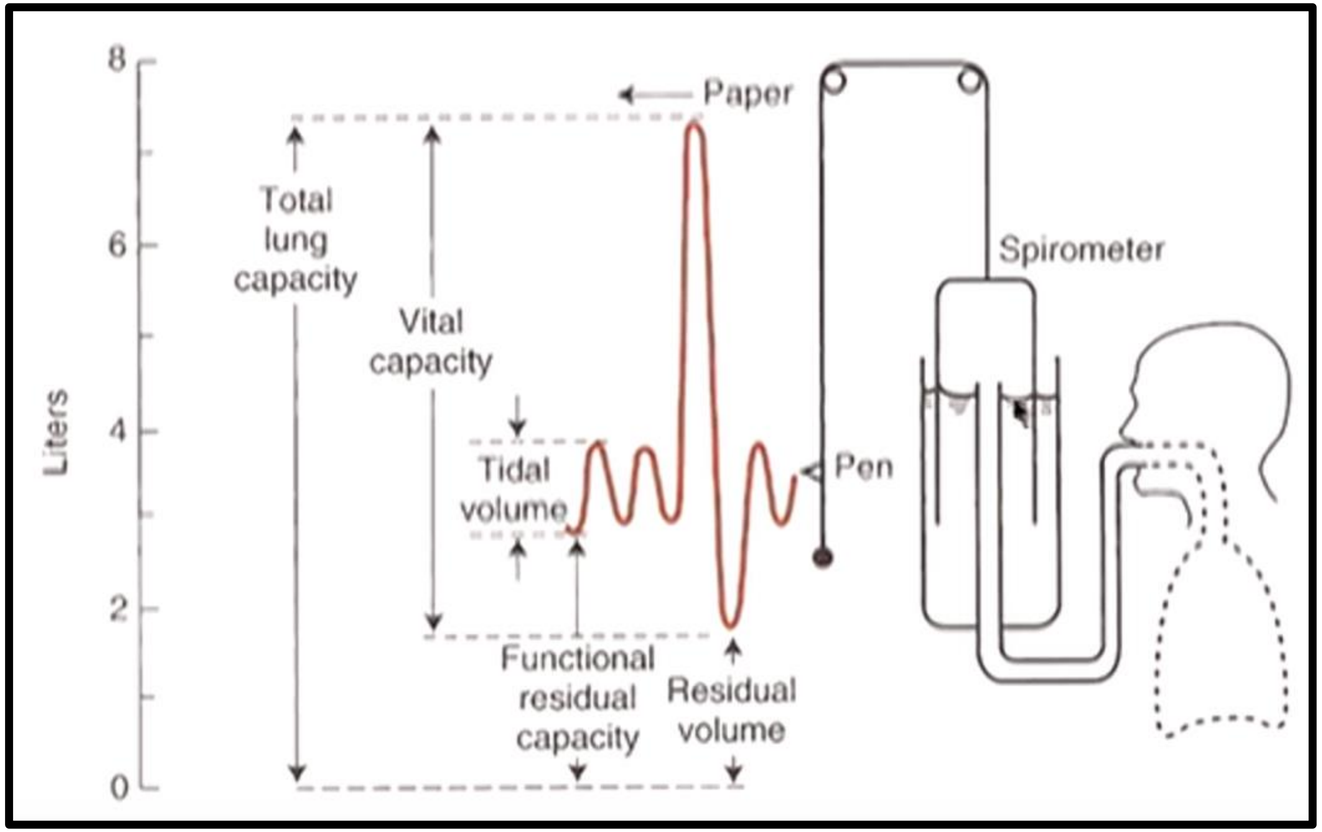
Resistance (cm H_2O/L/sec)
.08
.06
.04
.02
0
Conducting zone
Respiratory zone
0
5
10
15
20
Airway generation

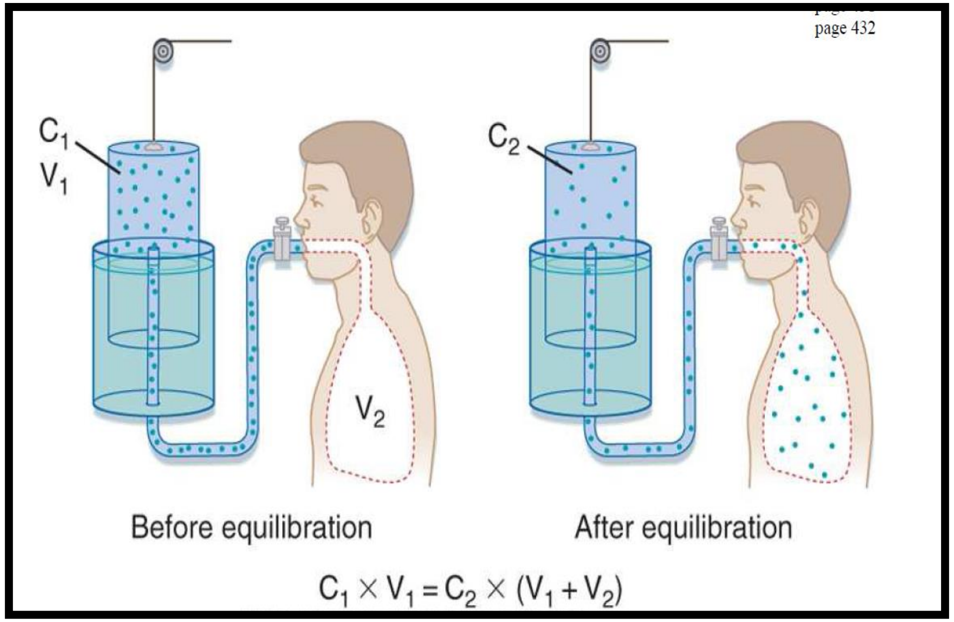


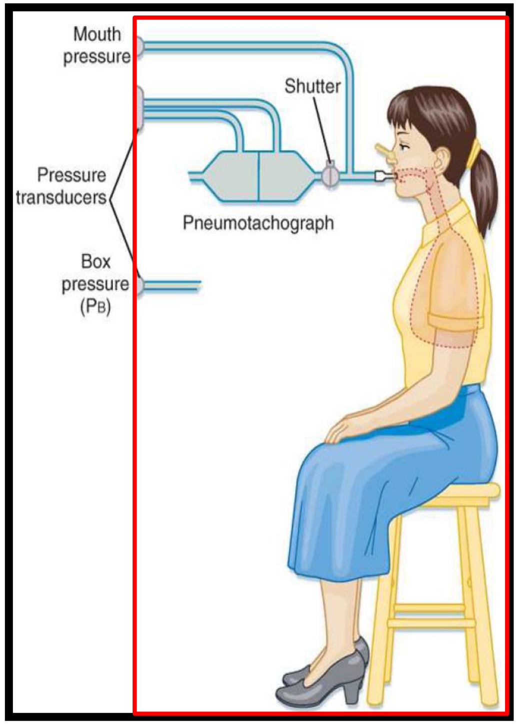
Volume (L)
RV
FEV_1
FEF_{25-75}
FVC
TLC
Time (sec)
A
Flow (L/sec)
FEF_{25}
PEFR
FEF_{50}
FEF_{75}
TLC
RV
Volume (L)
B

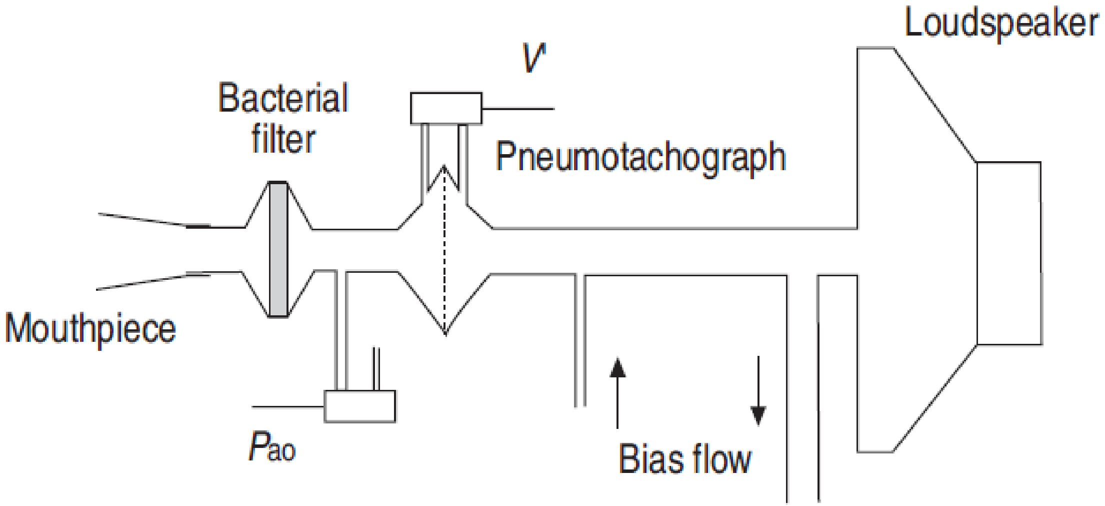

100
75
50
25
Volume (% TLC)
Air
V_T
FRC
Points of
no airflow
0
10
20
30
Translung pressure (cm H_2O)

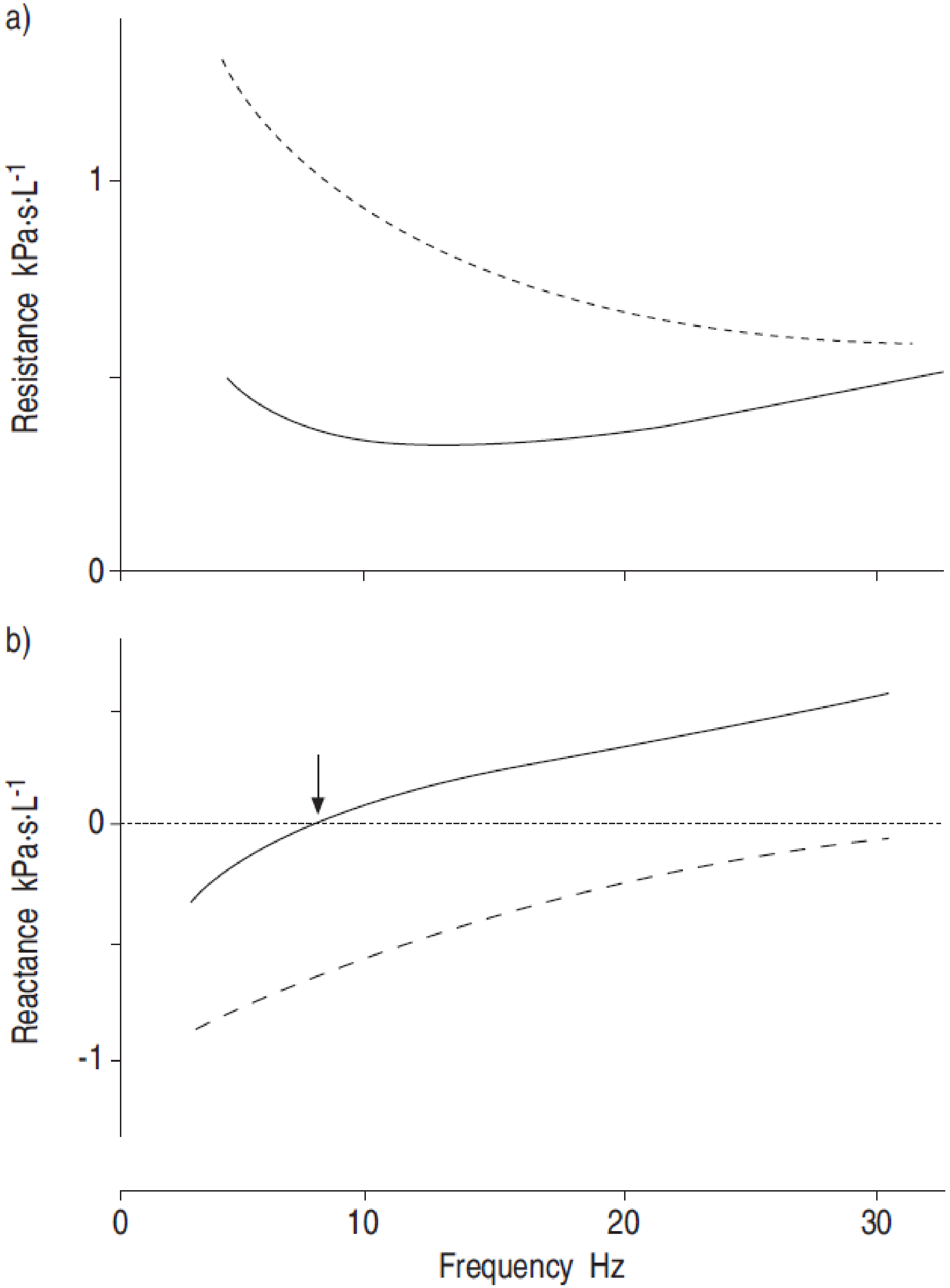

60
50
40
30
20
10
Mechanical work (kg-m/min)
Total
work
Elastic
work
Nonelastic
work
10
20
30
40
Respiratory rate (no./min)


8
6
4
2
0
Liters
Paper
Total
lung
capacity
Vital
capacity
Tidal
volume
Functional
residual
capacity
Residual
volume
Pen
Spirometer

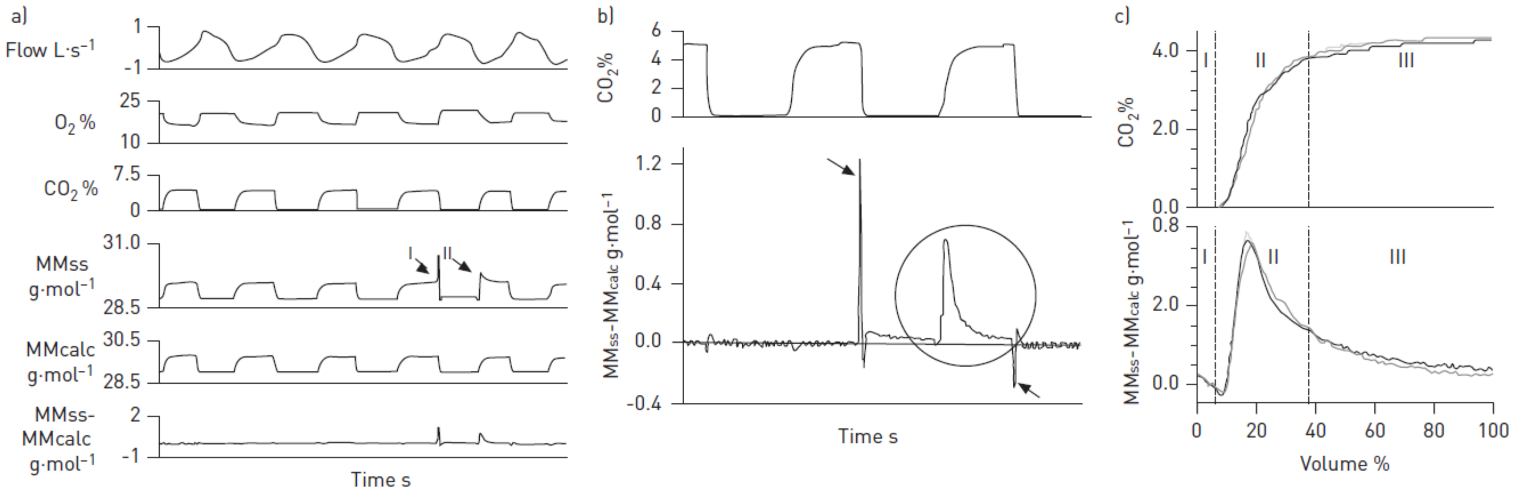

page 432
C1
V1
C2
V2
Before equilibration
After equilibration
$C_1 \times V_1 = C_2 \times (V_1 + V_2)$


Mouth
pressure
Shutter
Pressure
transducers
Pneumotachograph
Box
pressure
(PB)



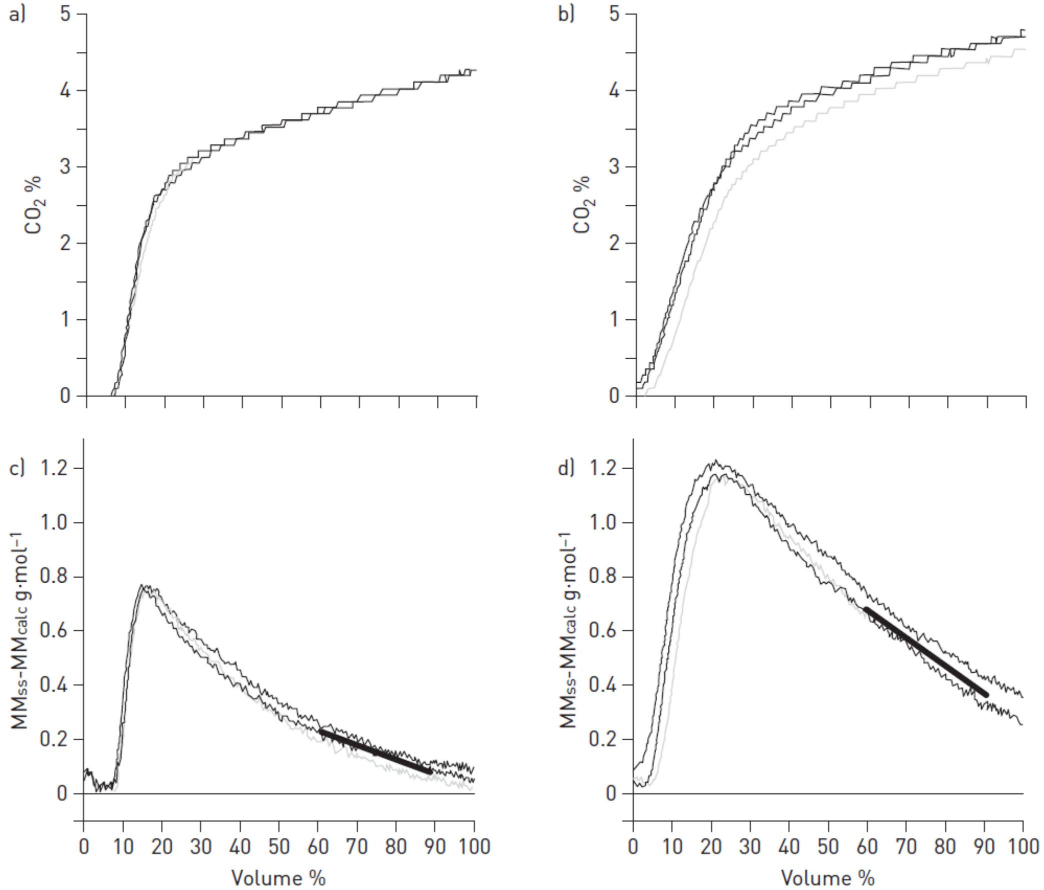


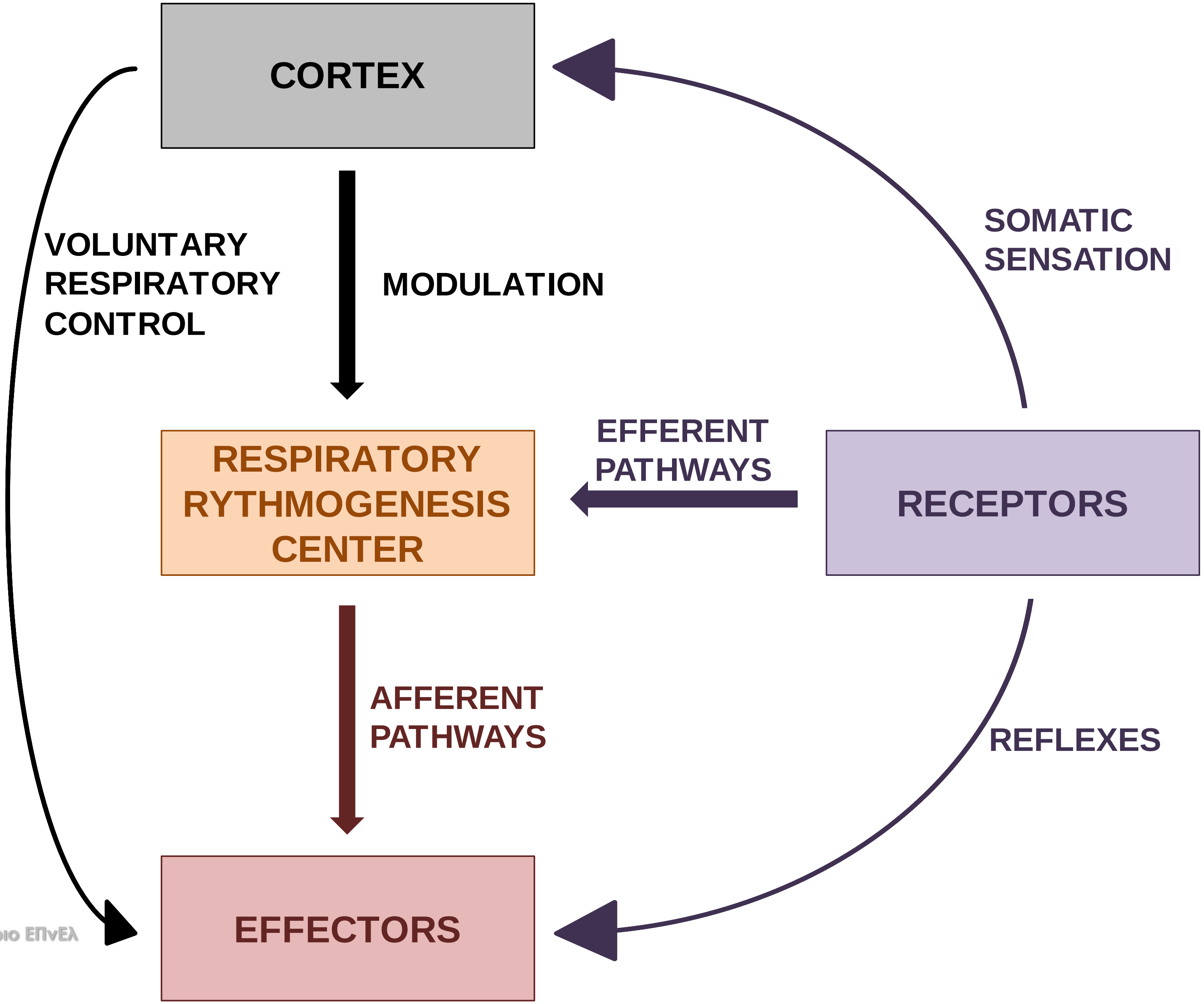
Oostveen E, MacLeod D, Lorino H, Farré R, Hantos Z, Desager K, Marchal F; ERS Task Force on Respiratory Impedance Measurements. The forced oscillation technique in clinical practice: methodology, recommendations and future developments. Eur Respir J. 2003 Dec;22(6):1026-41.



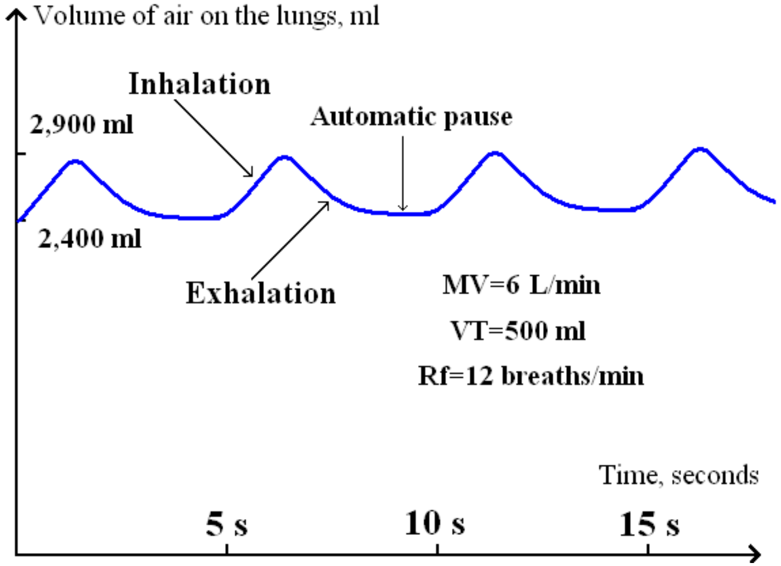
Husemann K, Berg N, Engel J, Port J, Joppek C, Tao Z, Singer F, Schulz H, Kohlhäufl M. Double tracer gas single-breath washout: reproducibility in healthy subjects and COPD. Eur Respir J. 2014 Nov;44(5):1210-22.

“The DTG mixture containing oxygen (21.0%), N2 (47.7%), He (26.3%) and SF6 (5.0%) had a similar molar mass to dry medical air (28.9 g?mol-1), and was provided by Westfalen-AG (Muenster, Germany).”

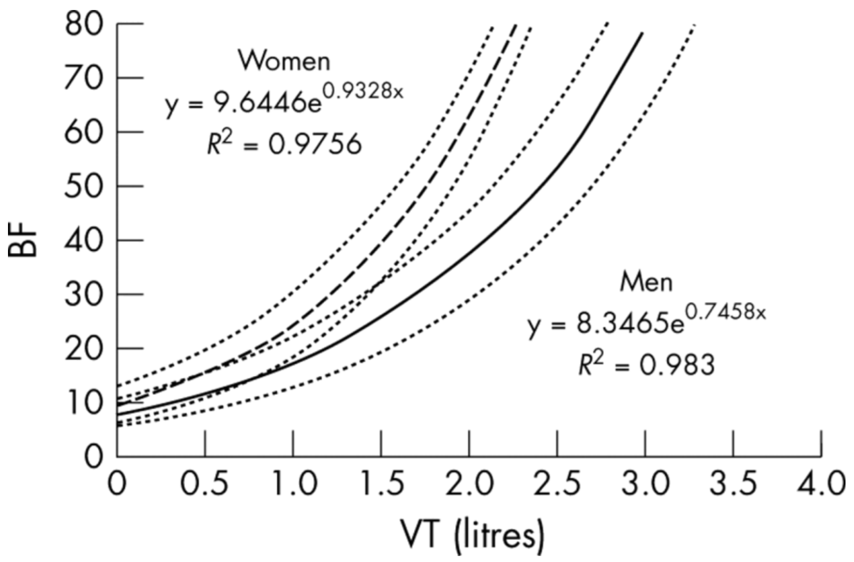




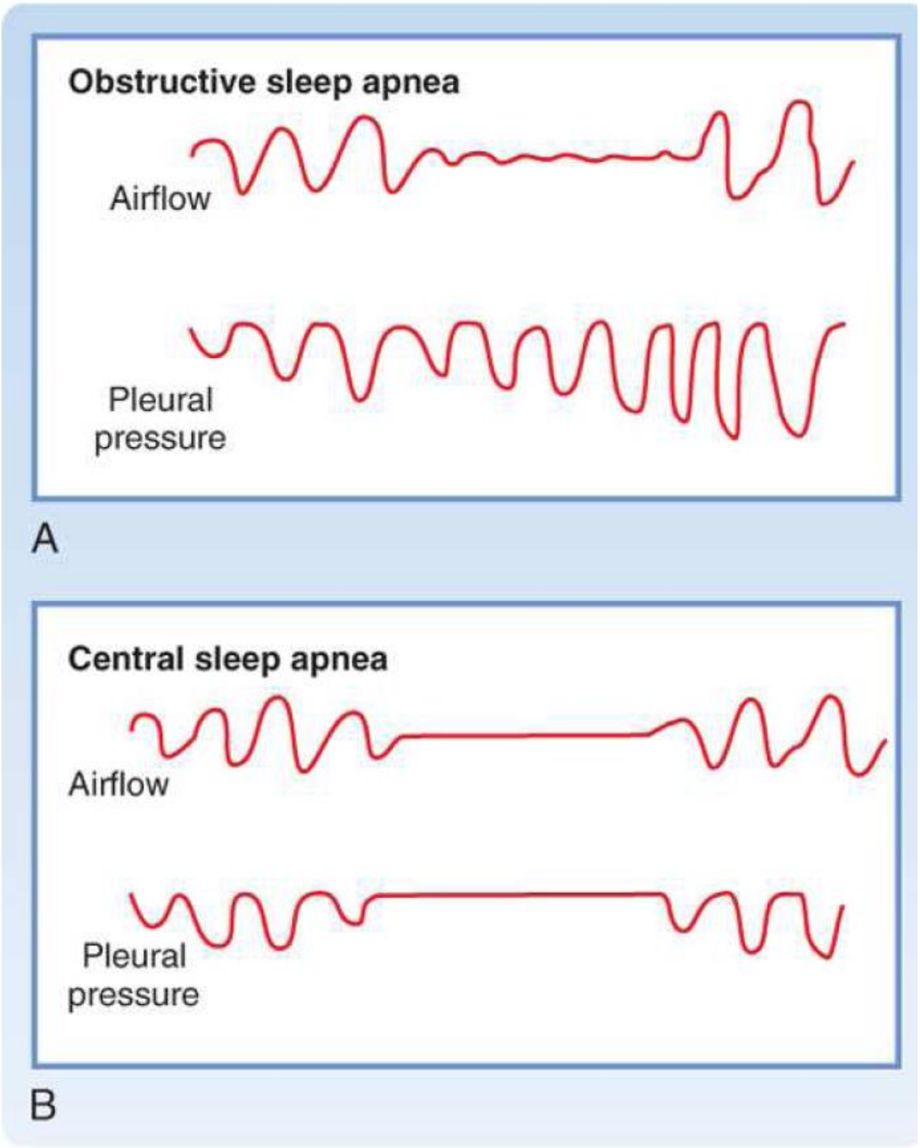
CORTEX
VOLUNTARY RESPIRATORY CONTROL
MODULATION
SOMATIC SENSATION
RESPIRATORY RYTHMOGENESIS CENTER
EFFERENT PATHWAYS
RECEPTORS
AFFERENT PATHWAYS
REFLEXES
EFFECTORS



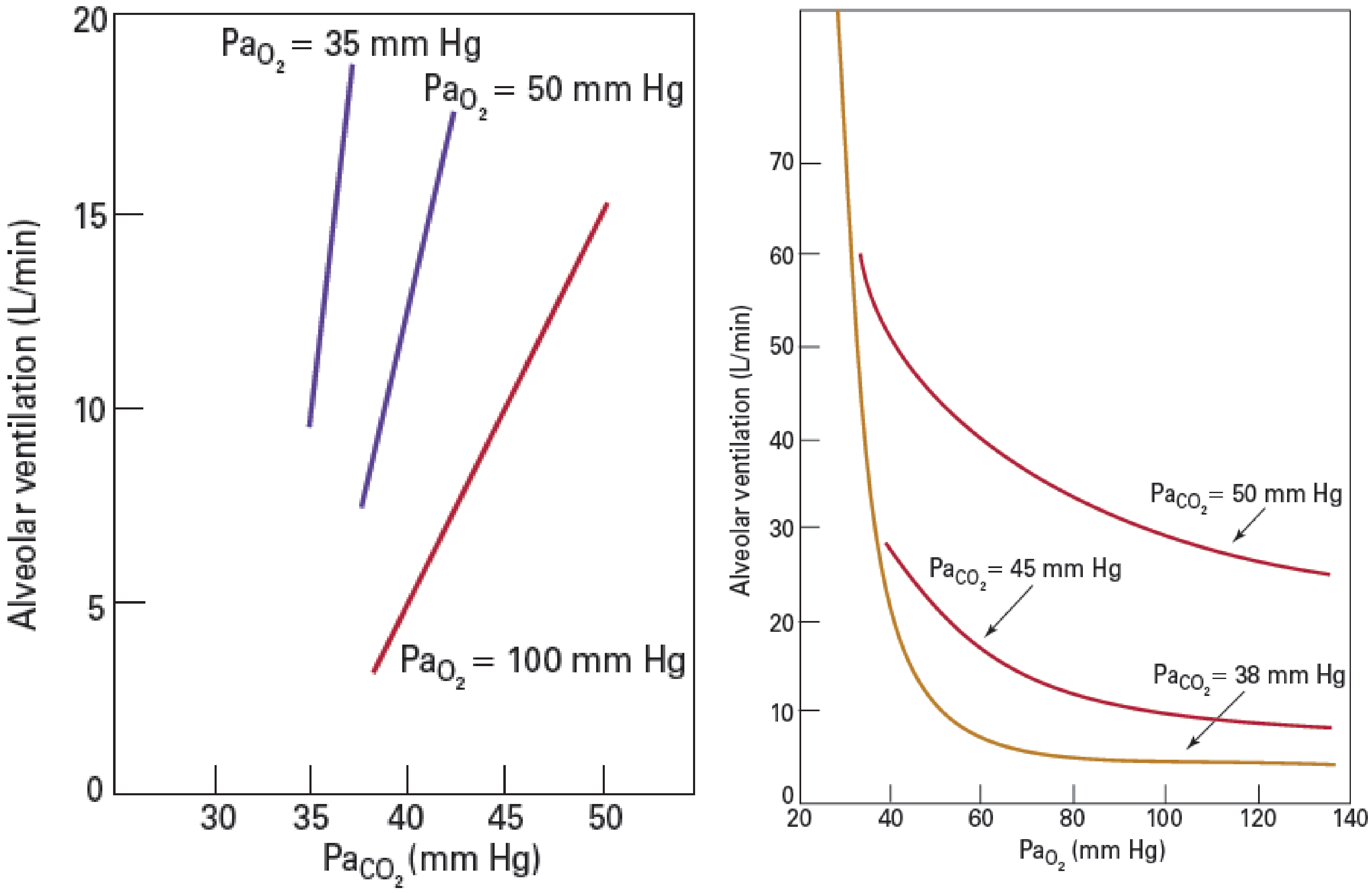
Volume of air on the lungs, ml
Inhalation
Automatic pause
2,900 ml
2,400 ml
Exhalation
MV=6 L/min
VT=500 ml
Rf=12 breaths/min
Time, seconds
5 s
10 s
15 s



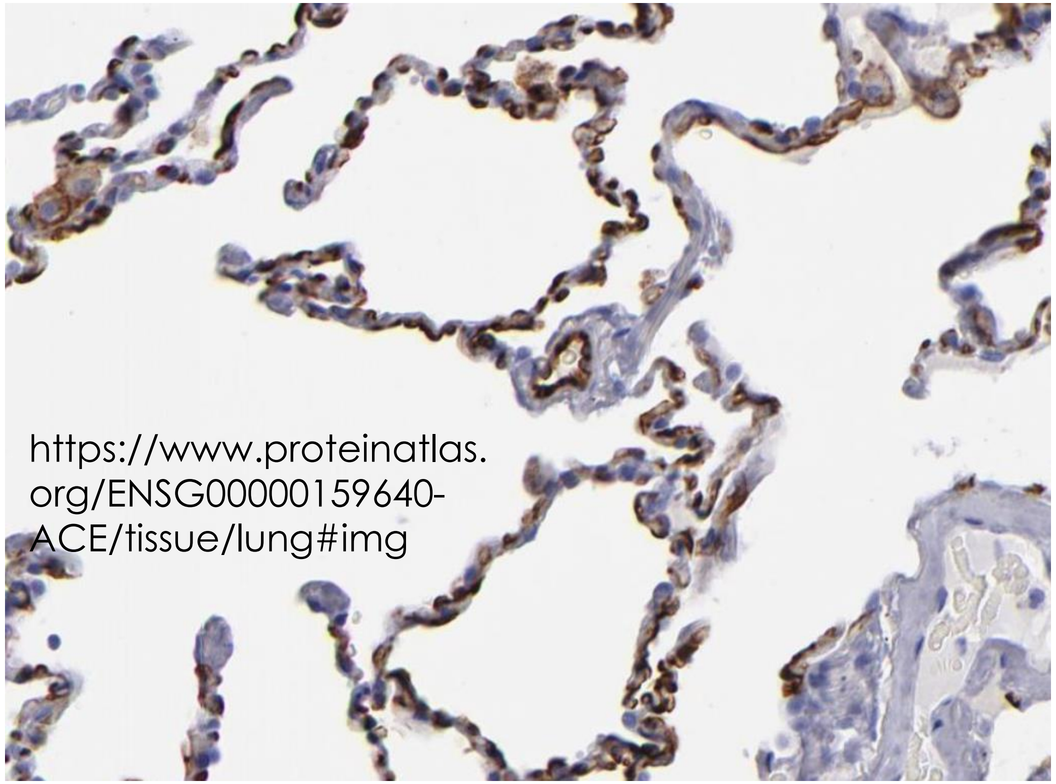
Women
y = 9.6446e^0.9328x
R2 = 0.9756
Men
y = 8.3465e^0.7458x
R2 = 0.983
BF
VT (litres)
0 10 20 30 40 50 60 70 80
0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0



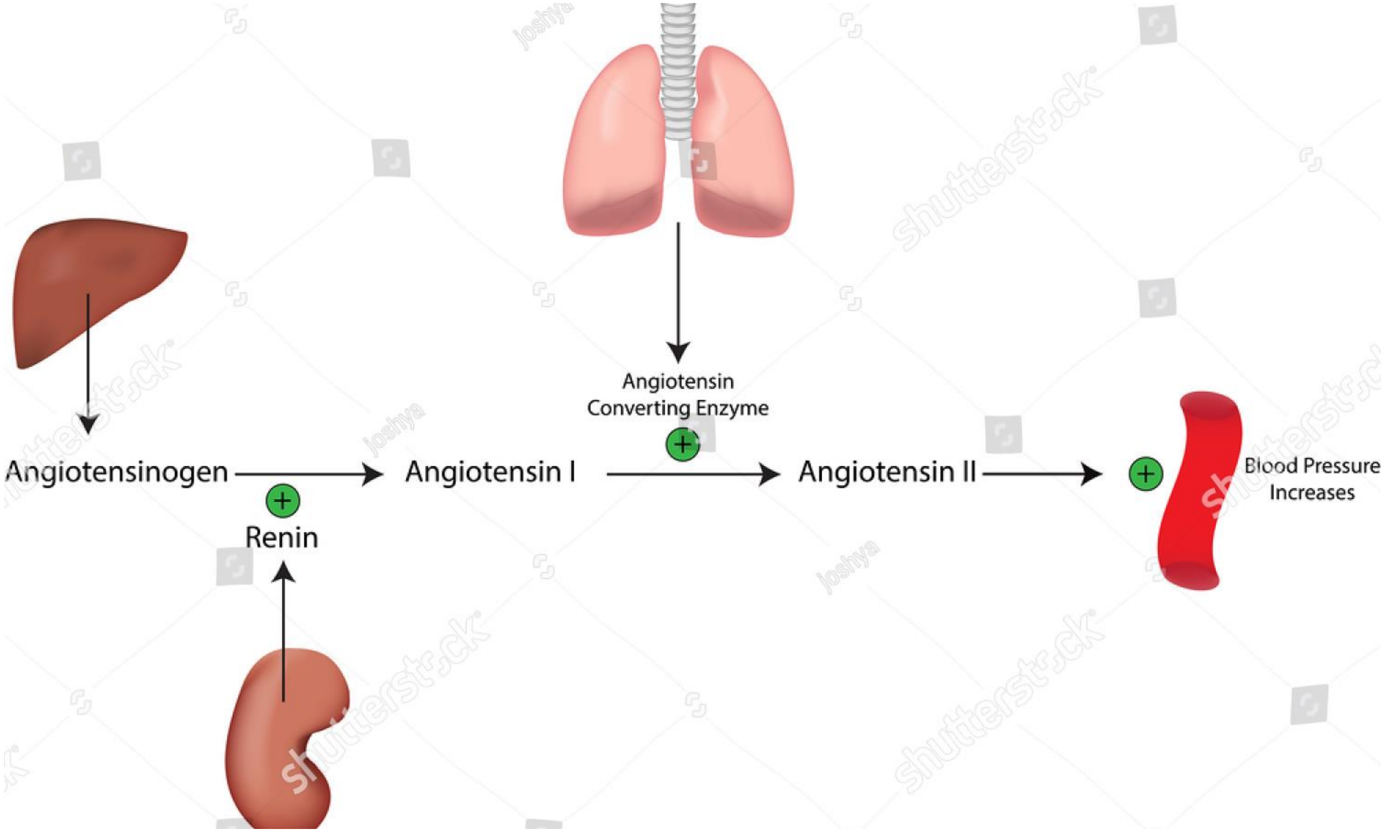
Obstructive sleep apnea
Airflow
Pleural pressure
A
Central sleep apnea
Airflow
Pleural pressure
B

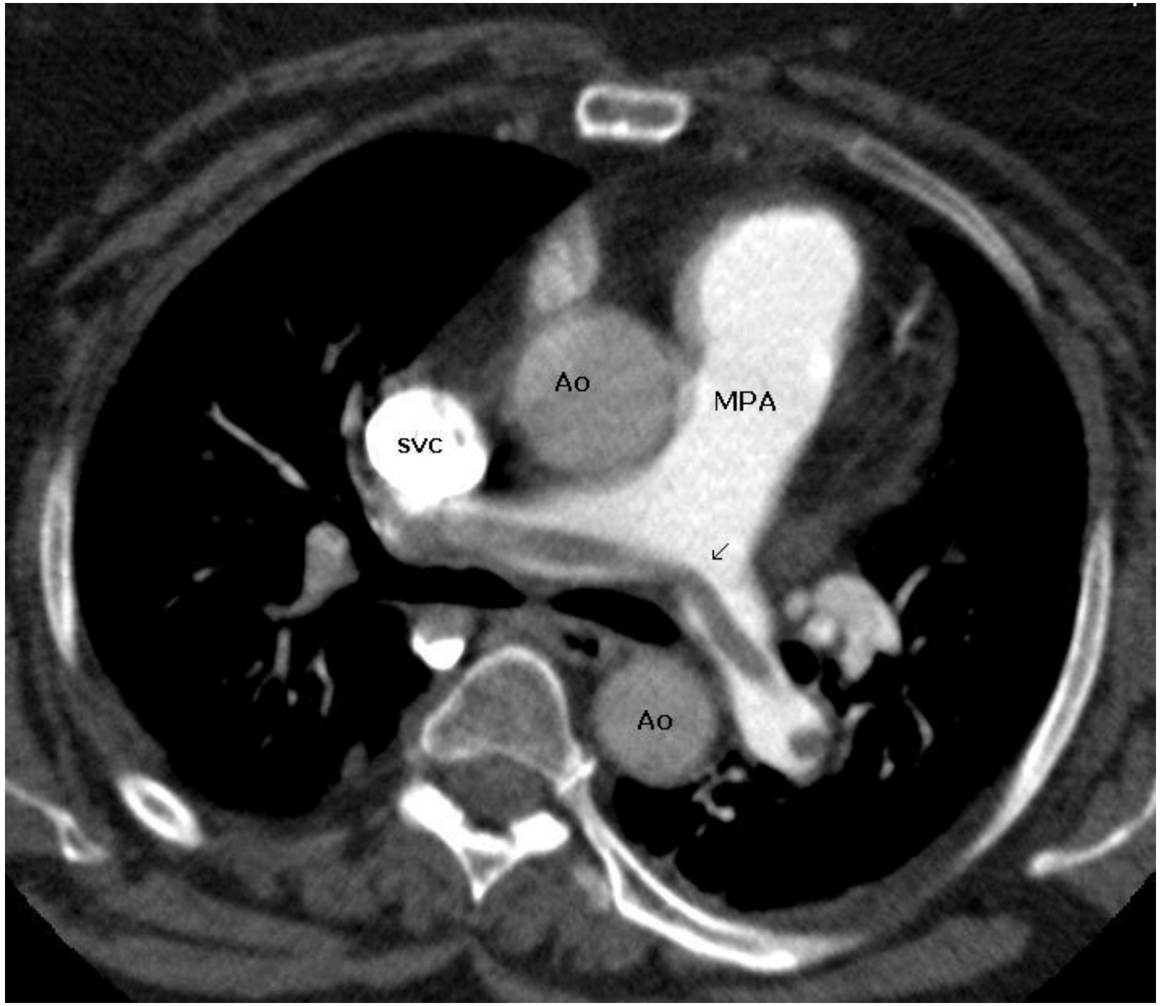


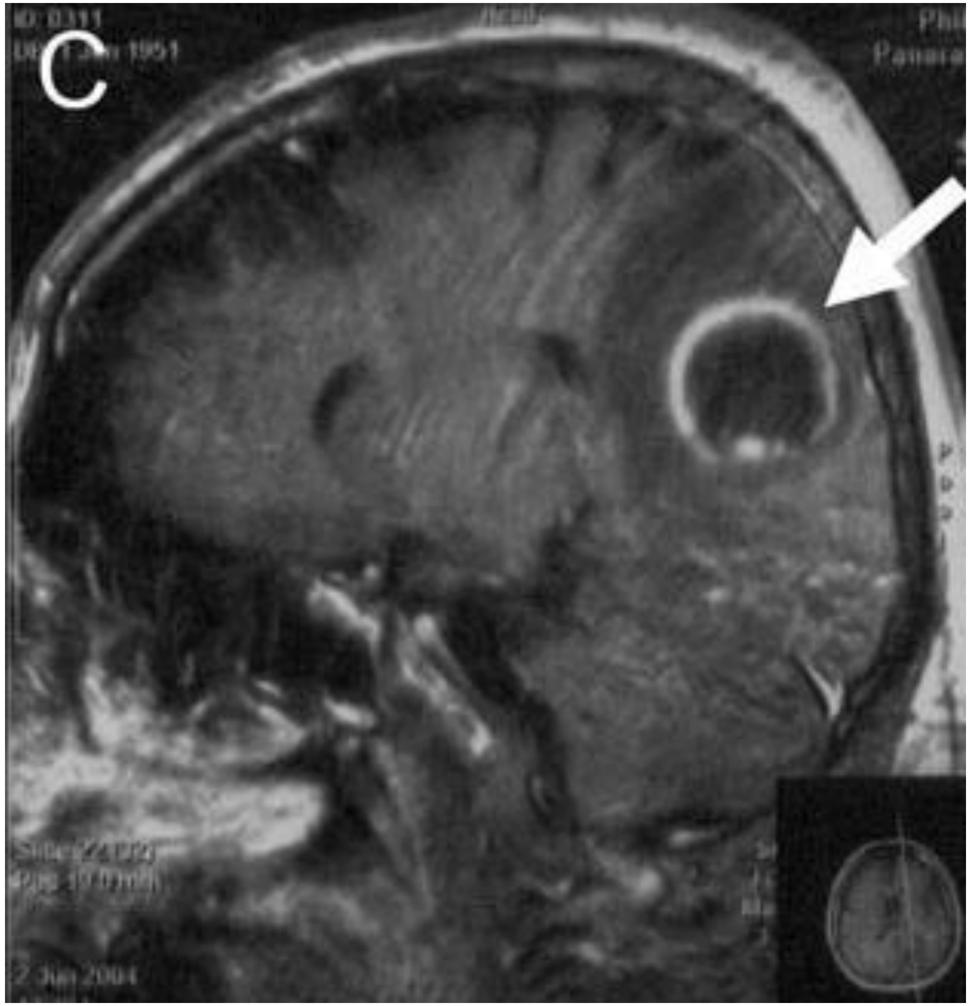
Pa_{O_2} = 35 mm Hg
Pa_{O_2} = 50 mm Hg
Pa_{O_2} = 100 mm Hg
Alveolar ventilation (L/min)
Pa_{CO_2} (mm Hg)
0
5
10
15
20
30
35
40
45
50
Pa_{CO_2} = 50 mm Hg
Pa_{CO_2} = 45 mm Hg
Pa_{CO_2} = 38 mm Hg
Alveolar ventilation (L/min)
Pa_{O_2} (mm Hg)
0
10
20
30
40
50
60
70
20
40
60
80
100
120
140

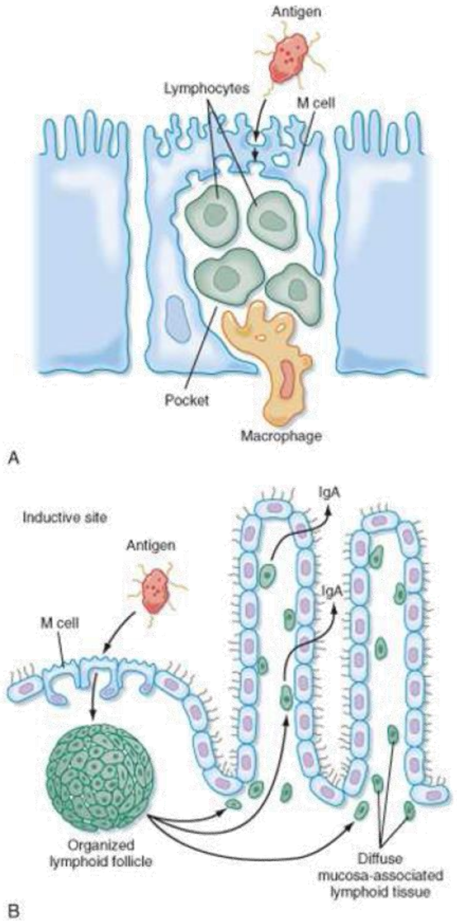


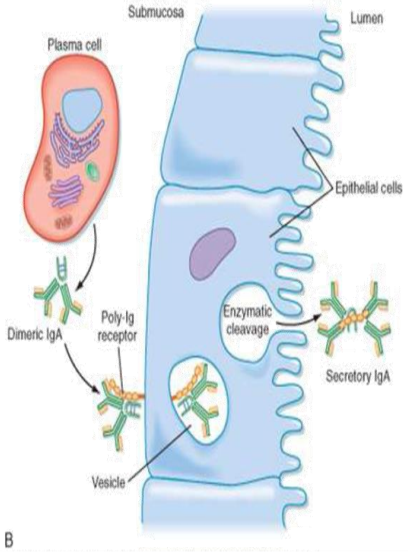
https://www.proteinatlas.org/ENSG00000159640-ACE/tissue/lung#img

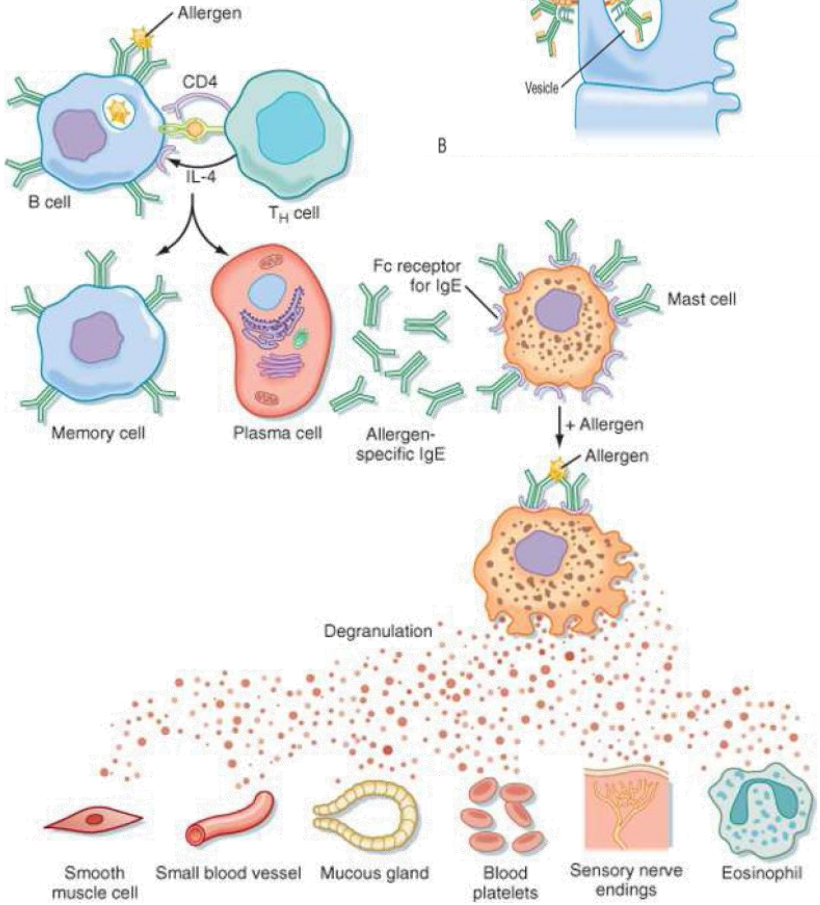


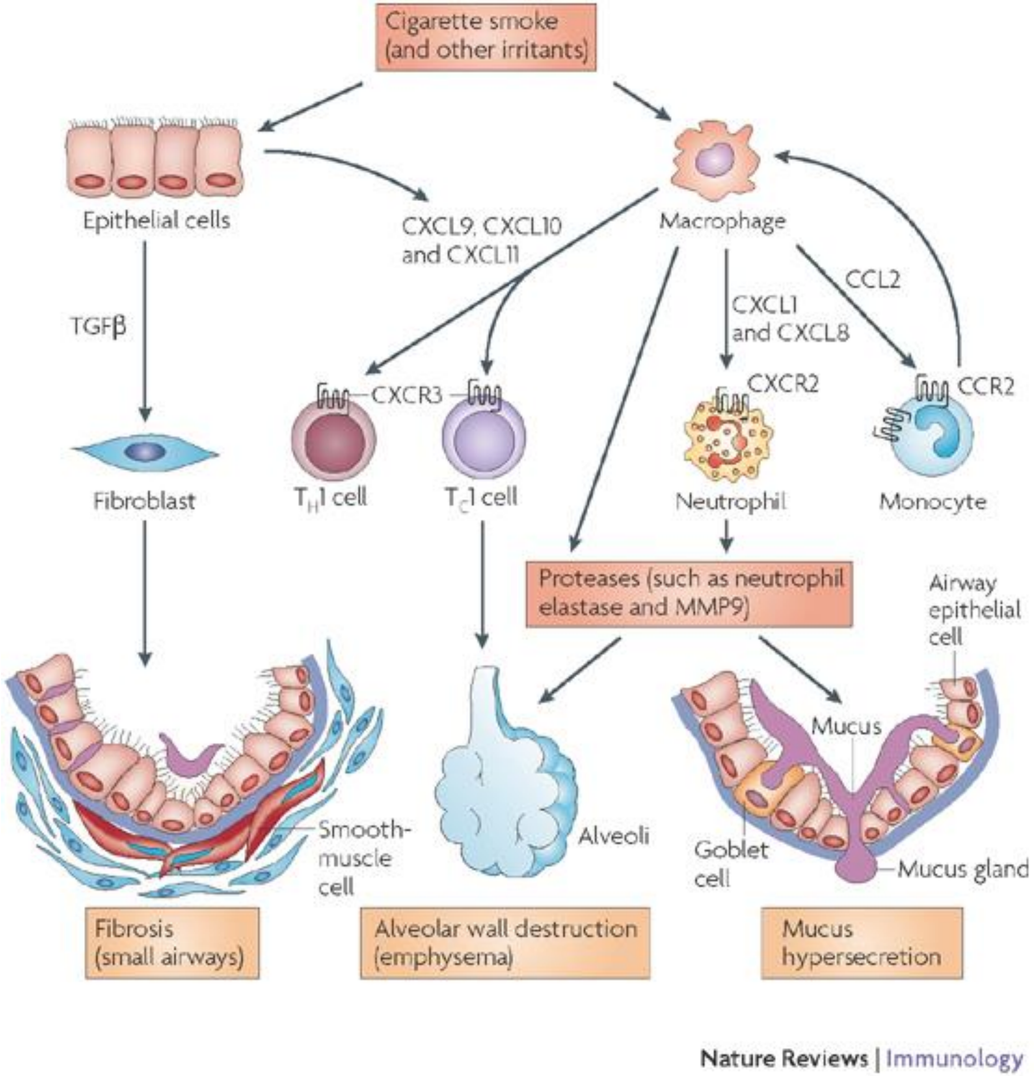

Ao
MPA
SVC
Ao

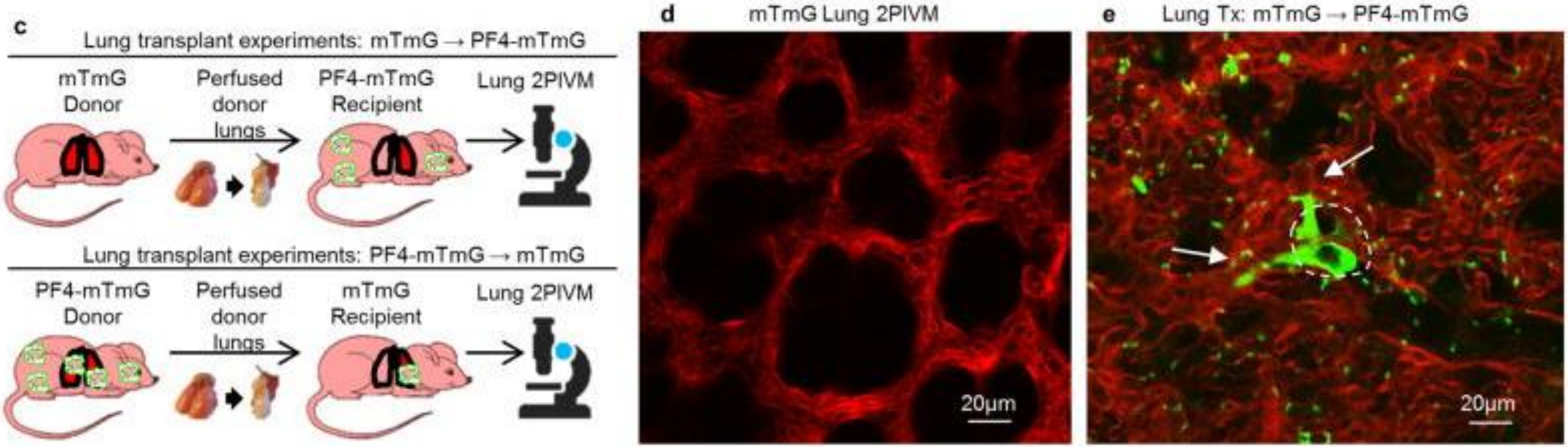

C


Antigen
Lymphocytes
M cell
Pocket
Macrophage
A
Inductive site
Antigen
M cell
IgA
IgA
Organized lymphoid follicle
Diffuse mucosa-associated lymphoid tissue
B


Submucosa
Lumen
Plasma cell
Epithelial cells
Dimeric IgA
Poly-Ig receptor
Enzymatic cleavage
Secretory IgA
Vesicle
B


Allergen
CD4
B cell
IL-4
T$_H$ cell
Memory cell
Plasma cell
Fc receptor for IgE
Mast cell
Allergen-specific IgE
+ Allergen
Allergen
Degranulation
Smooth muscle cell
Small blood vessel
Mucous gland
Blood platelets
Sensory nerve endings
Eosinophil


Cigarette smoke (and other irritants)
Epithelial cells
Macrophage
CXCL9, CXCL10 and CXCL11
TGFβ
CCL2
CXCL1 and CXCL8
CXCR3
CXCR2
CCR2
Fibroblast
T$_H$1 cell
T$_C$1 cell
Neutrophil
Monocyte
Proteases (such as neutrophil elastase and MMP9)
Airway epithelial cell
Mucus
Smooth-muscle cell
Alveoli
Goblet cell
Mucus gland
Fibrosis (small airways)
Alveolar wall destruction (emphysema)
Mucus hypersecretion
Nature Reviews | Immunology



Lefrançais et al. Nature. 2017 Apr 6;544(7648):105-109.

ΣΥΝΟΨΗ

Οι πνεύμονες αποτελούν ζωτικό όργανο ανταλλαγής αερίων στη διεπιφάνεια του οργανισμού με το περιβάλλον

Η λεπτή μικροδομή των πνευμόνων επιτρέπει τη στενή επαφή πέντε λίτρων αέρα και αίματος κατά λεπτό σε απόσταση 200 nm

Για να ανταλλάσσουν αέρια, οι πνεύμονες πρέπει να κινούνται περιοριζόμενοι από τις μηχανικές τους ιδιότητες και τις ιδιότητες του αέρα. Η μέτρηση των κινήσεων αυτών δίνει σημαντικές πληροφορίες

Η αναπνοή ελέγχεται στενά΄από τον εγκέφαλο με στόχο την ομοιόσταση των αερίων αίματος και της ζωής με το ελάχιστο δυνατό ενεργειακό κόστος