RESPIRATION

A.-M. Lauzon, Ph.D.

Reference textbooks:
“Vander’s Human Physiology” by Widmaier, Raff, Strang
“Respiratory Physiology- the essentials” by West
"The Normal Lung" by Murray

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TUTORIALS:

JANUARY 24TH: 5H30 TO 6H30 PM MCMED 522
FEBRUARY 2ND: 5H30 TO 6H30 PM MCMED 522

Lecture 1

STRUCTURE OF THE LUNGS AND CHEST WALL

Function of Respiration

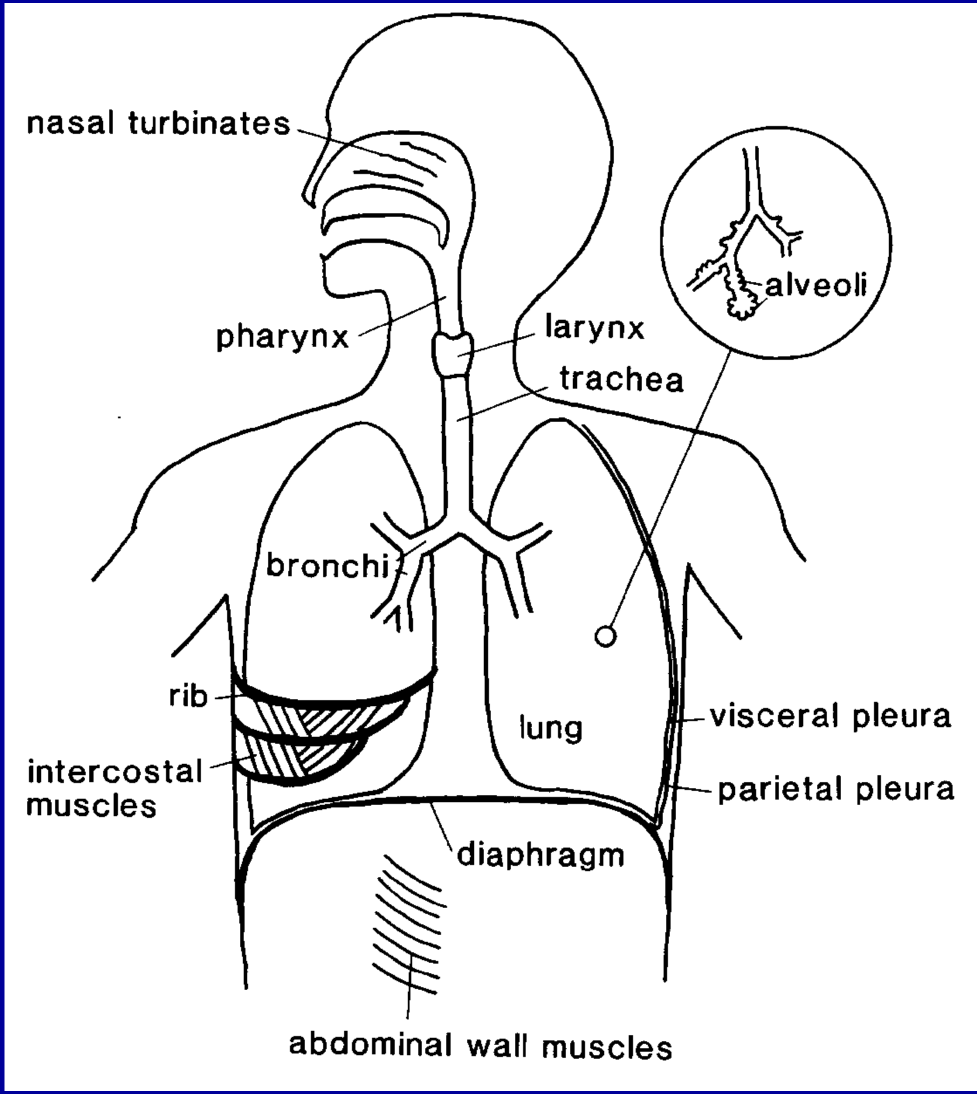
- The primary function of respiration is: **Gas exchange**.

- Inspiration: air rich in O_2 is inhaled into the lungs.

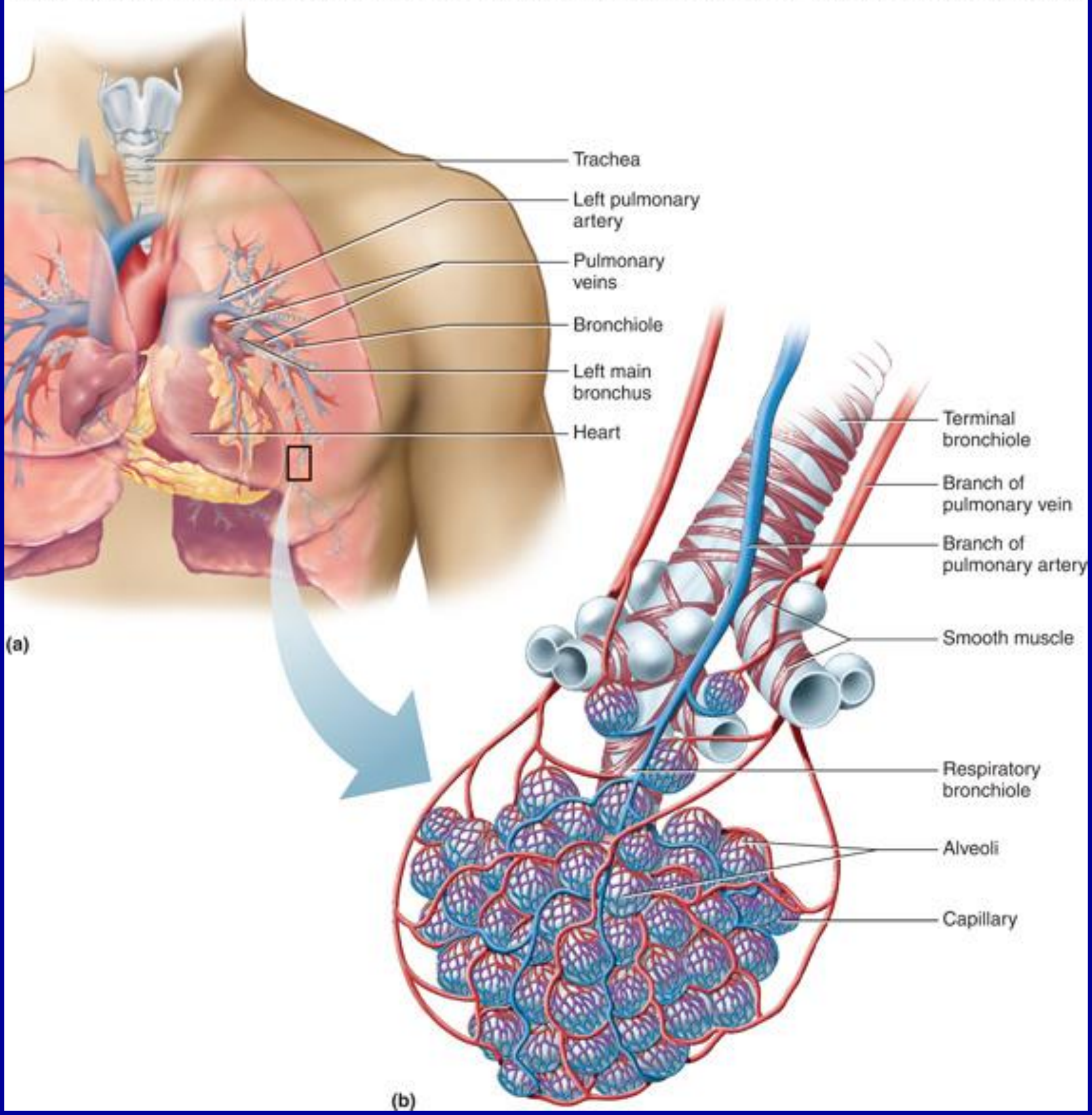
- Expiration: CO_2 produced during oxidative processes of the body is exhaled from the lungs.

- Both gases are transported by the blood. Thus, both the cardiovascular system and the respiratory system are involved.

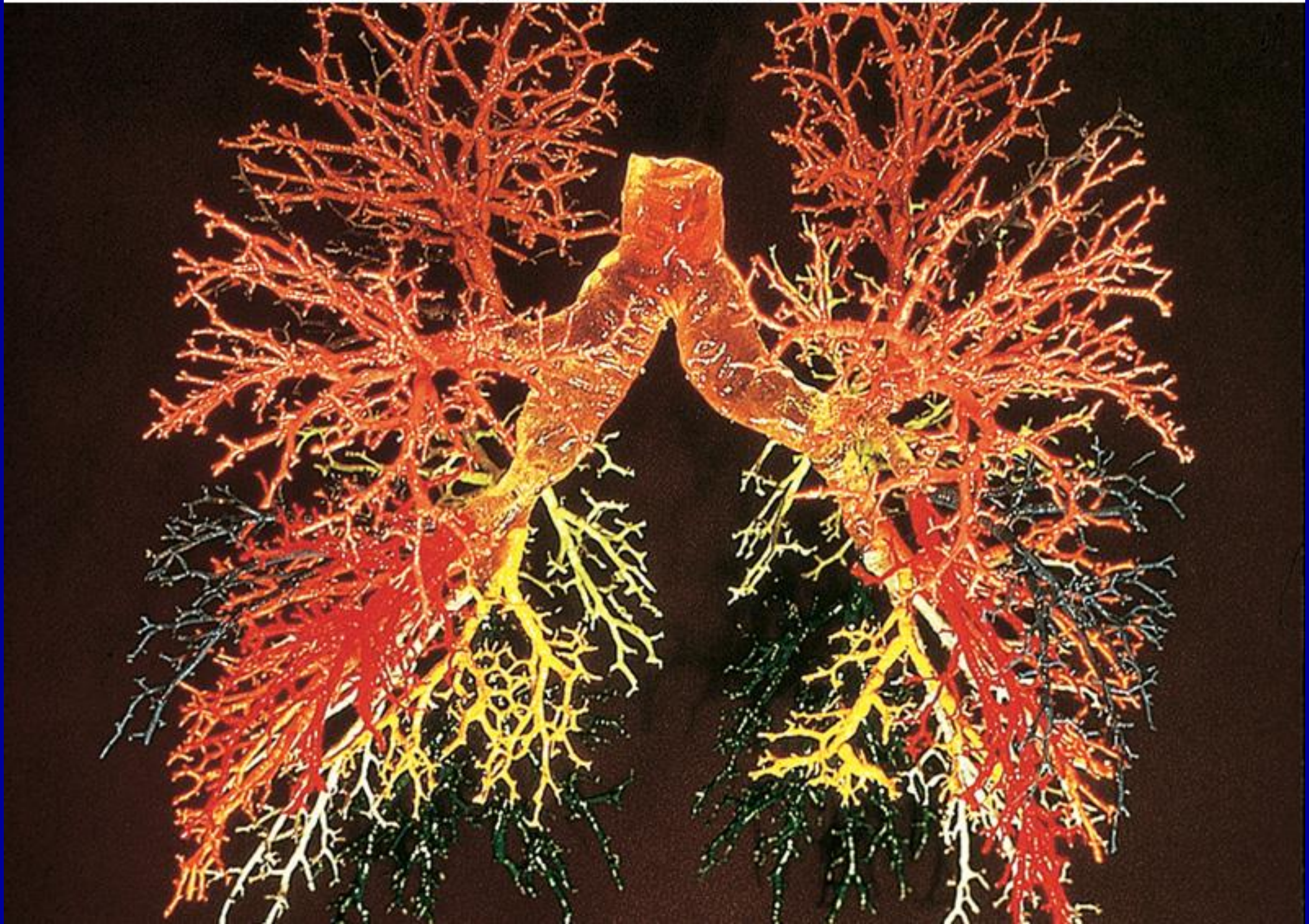
The respiratory tract



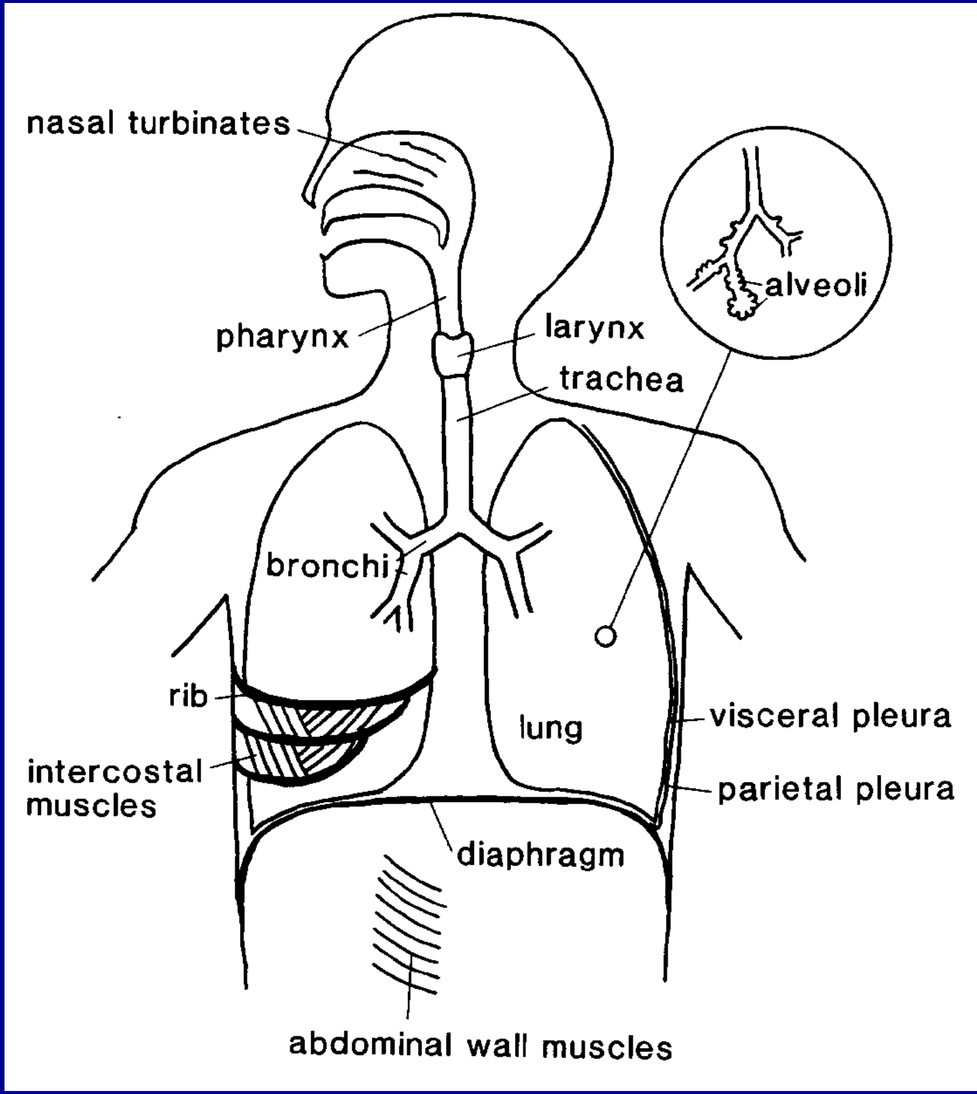
The respiratory tract



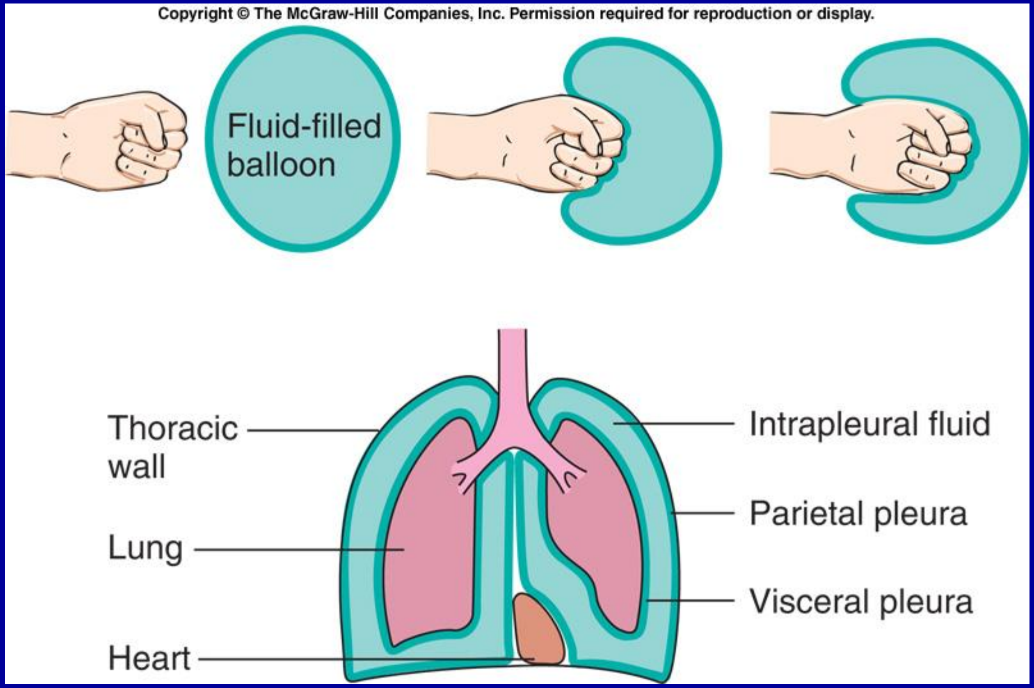
The respiratory tract



The respiratory tract



Pleural space



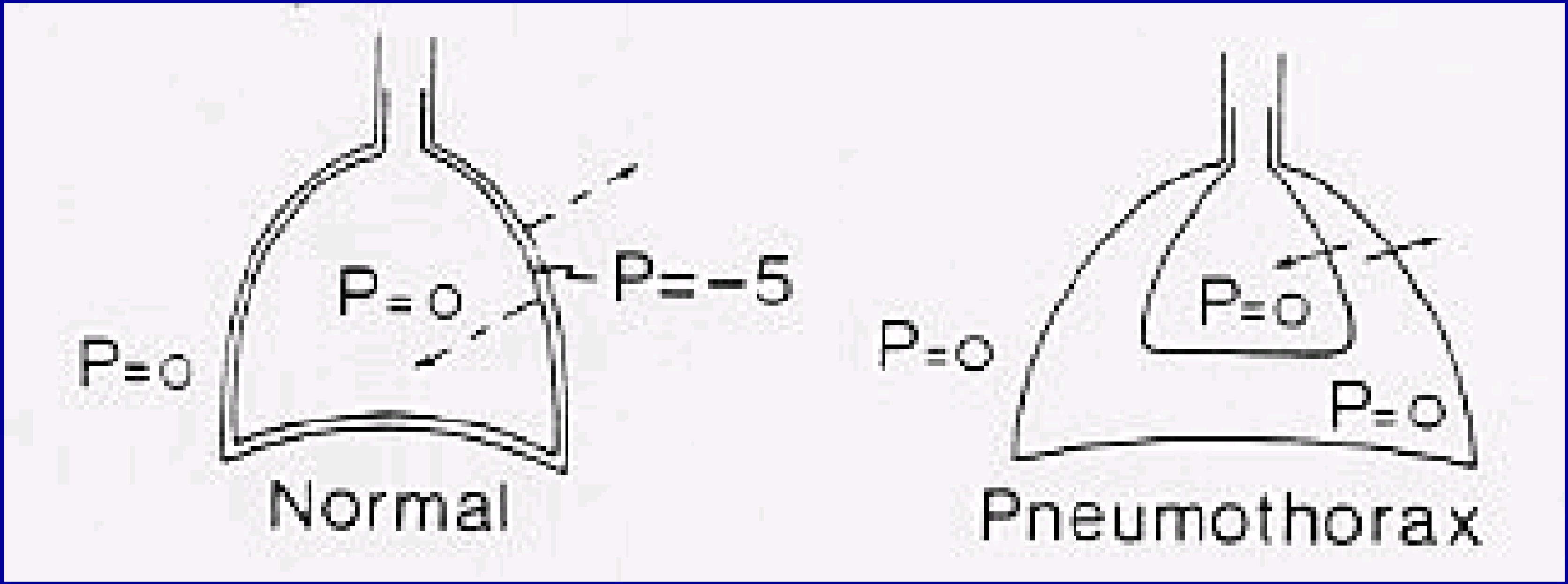
Pleural surfaces

- A way to visualize the apposition of the two pleural surfaces is to put a drop of water between two glass microscope slides. The two slides can easily slide over each other but are very difficult to pull apart.

("Human Physiology" by Widmaier, Raff, Strang)

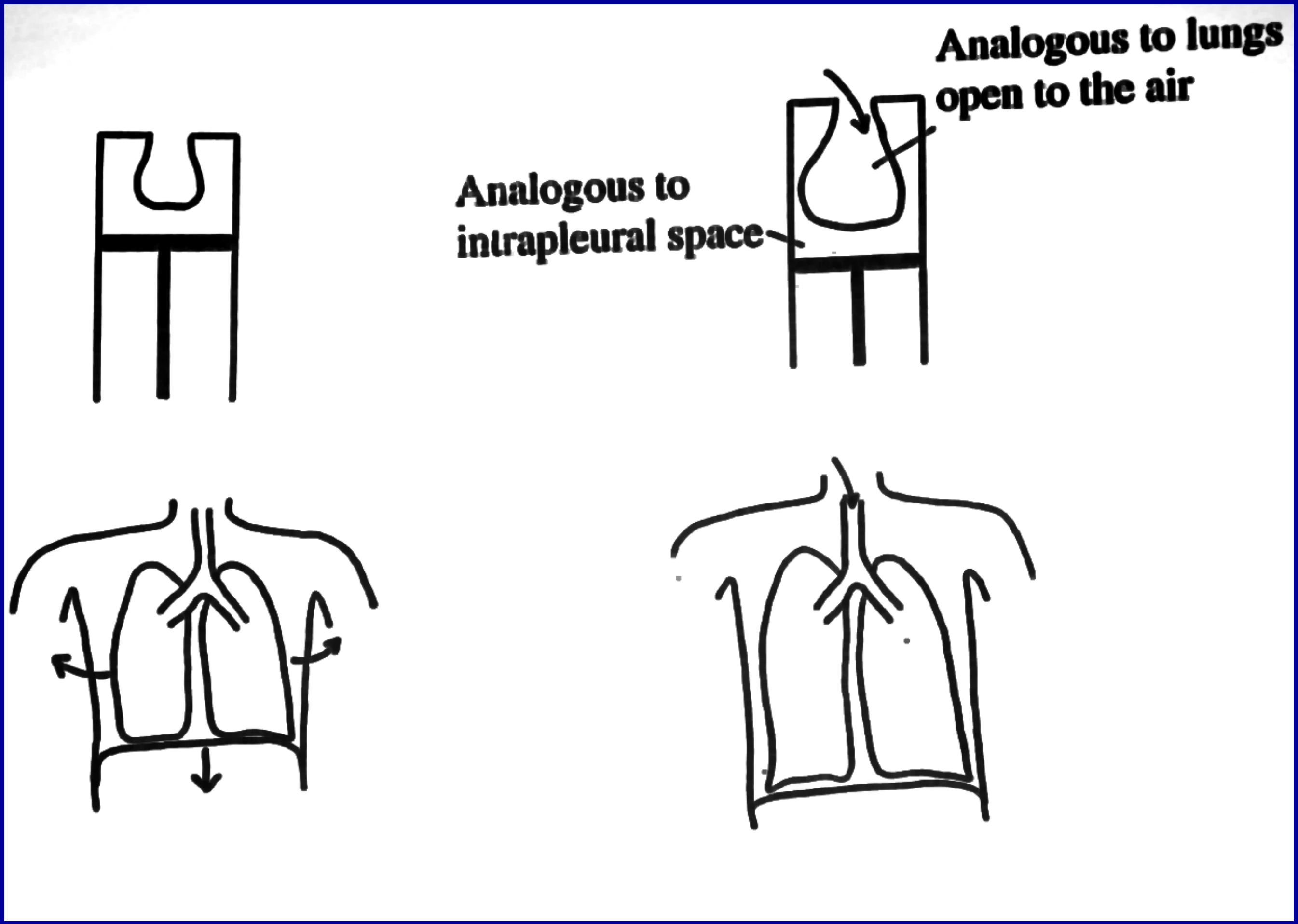
Pleural Space

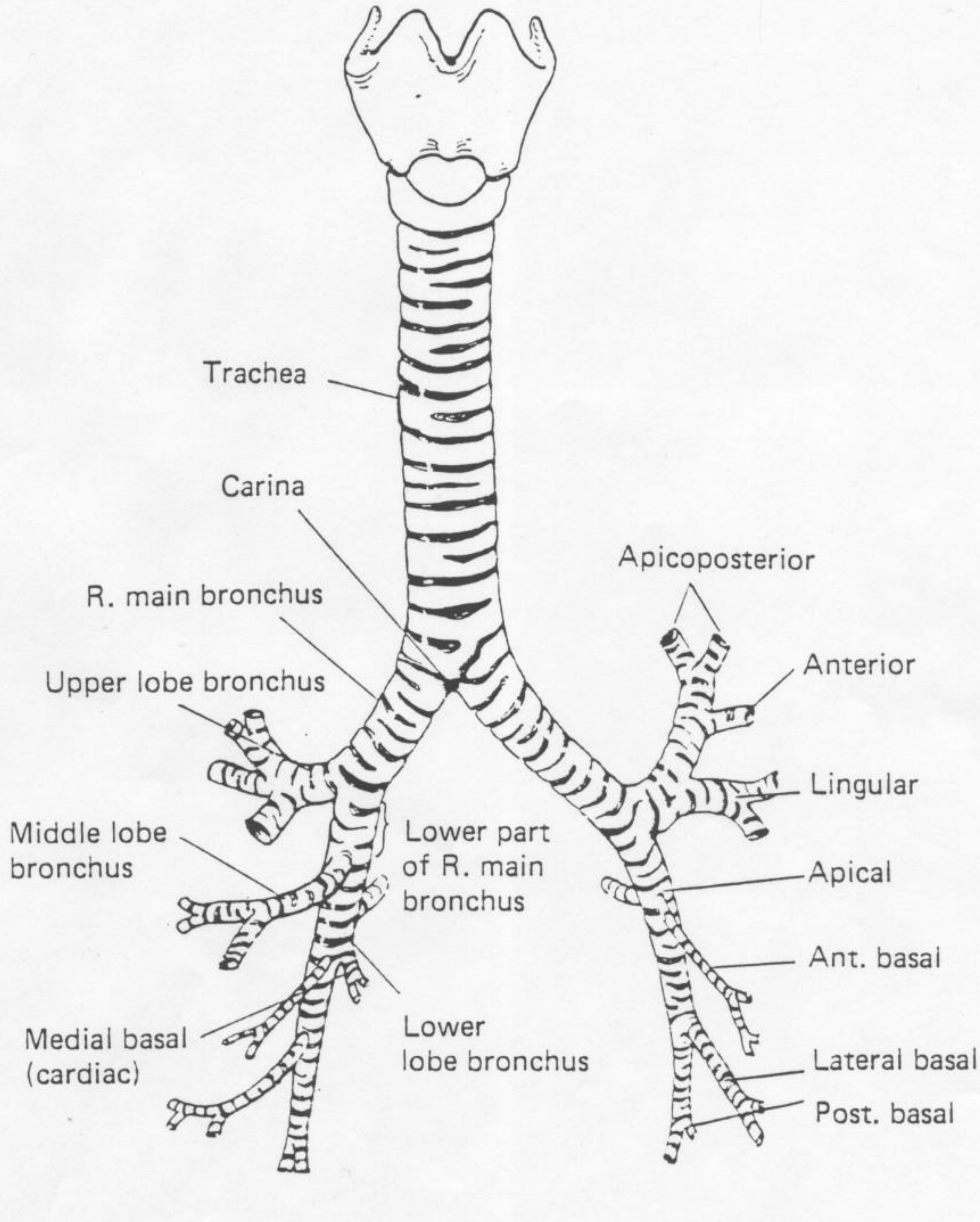
Pneumothorax



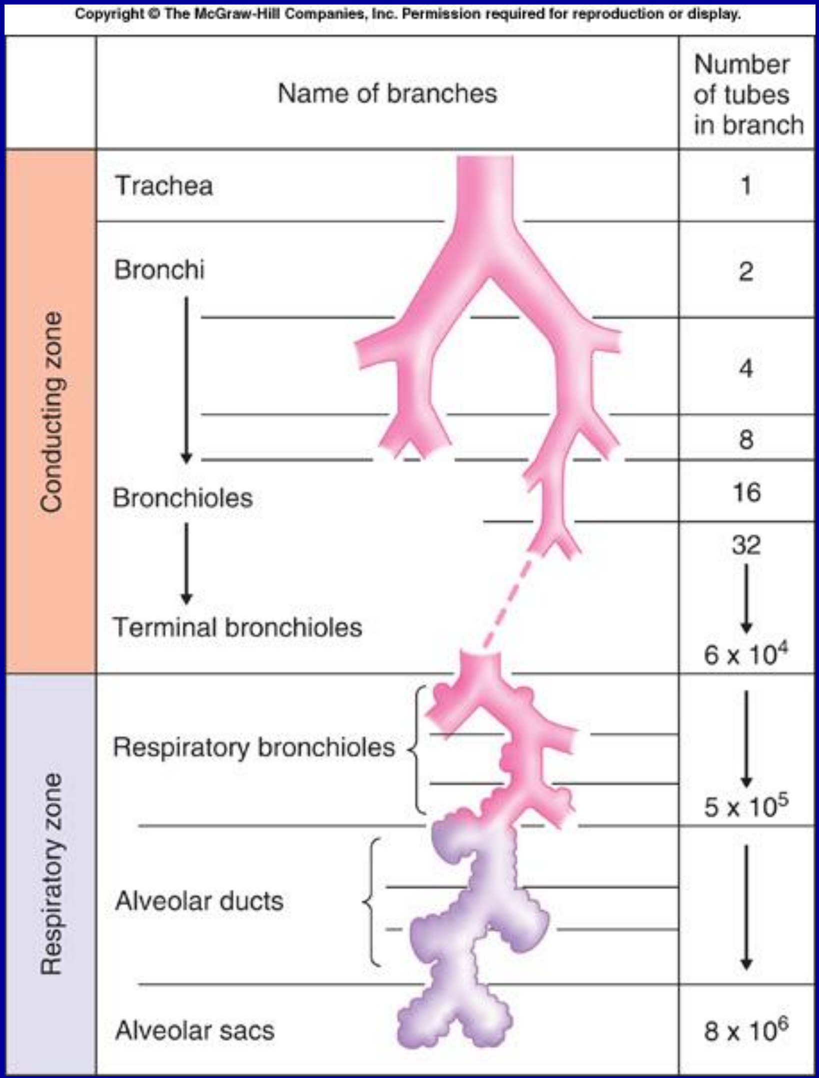
Reproduced from West: Respiratory Physiology- the essentials.

Mechanical pump

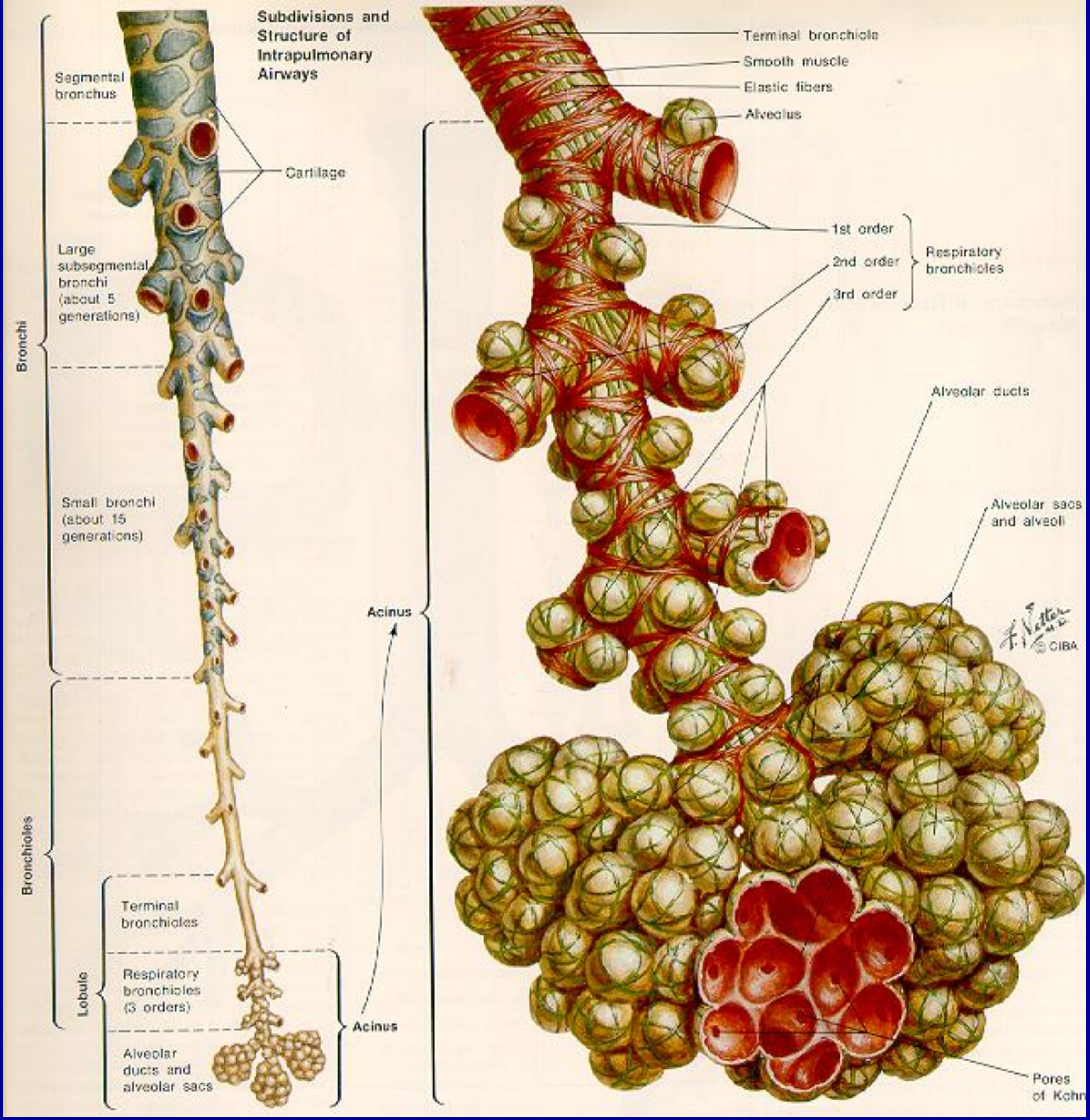



Trachea
Carina
Apicoposterior
R. main bronchus
Anterior
Upper lobe bronchus
Lingular
Middle lobe
bronchus
Lower part
of R. main
bronchus
Apical
Ant. basal
Lower
lobe bronchus
Medial basal
(cardiac)
Lateral basal
Post. basal

Subdivisions of the conducting airways and terminal respiratory units



Acinus



(Reproduced from Netter, F.H.: The CIBA Collection of Medical Illustrations, vol. 7).

The conducting airways have 4 main functions:

1. **Defense against bacterial infection and foreign particles:**

   The epithelial lining of the bronchi has hair-like projections called cilia. The epithelial glands secrete a thick substance, mucous, which lines the respiratory passages as far down as the bronchioles. Foreign particles stick to the mucous and the cilia constantly sweep the mucous up into the pharynx;

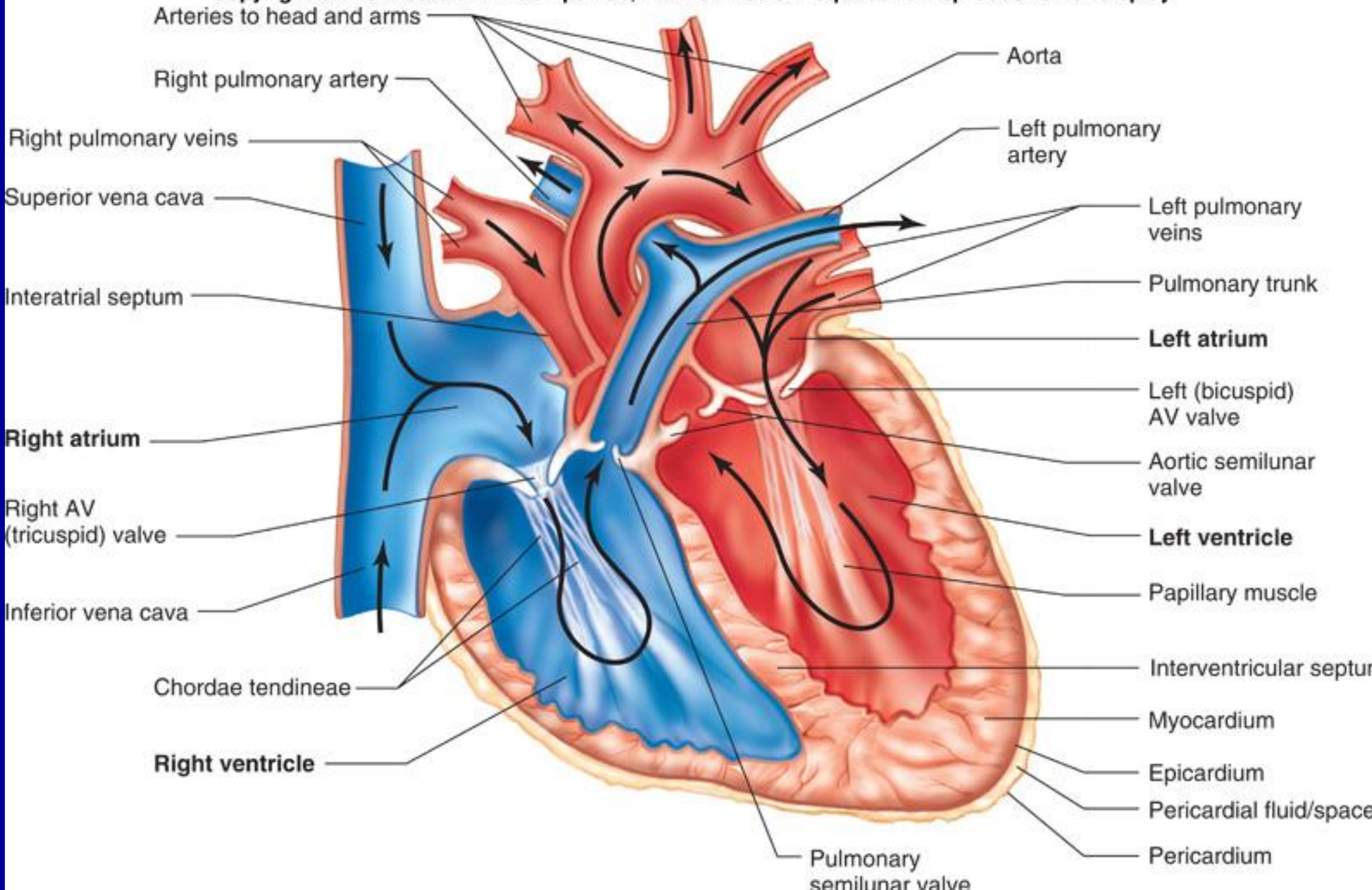
2. **Warm and moisten inhaled air**;

3. **Sound and speech** are produced by the movement of air passing over the vocal cords;

4. **Regulation of air flow:** smooth muscle around the airways may contract or relax to alter resistance to air flow.

Function of the Respiratory Zone

The respiratory zone is the site of gas exchange between the air in the alveoli and the blood in the pulmonary capillaries. There are roughly 300 million alveoli in the human lungs, and each alveolus may be associated with as many as 1000 capillaries.



Arteries to head and arms
Right pulmonary artery
Right pulmonary veins
Superior vena cava
Interatrial septum
Right atrium
Right AV (tricuspid) valve
Inferior vena cava
Chordae tendineae
Right ventricle
Aorta
Left pulmonary artery
Left pulmonary veins
Pulmonary trunk
Left atrium
Left (bicuspid) AV valve
Aortic semilunar valve
Left ventricle
Papillary muscle
Interventricular septum
Myocardium
Epicardium
Pericardial fluid/space
Pericardium
Pulmonary semilunar valve

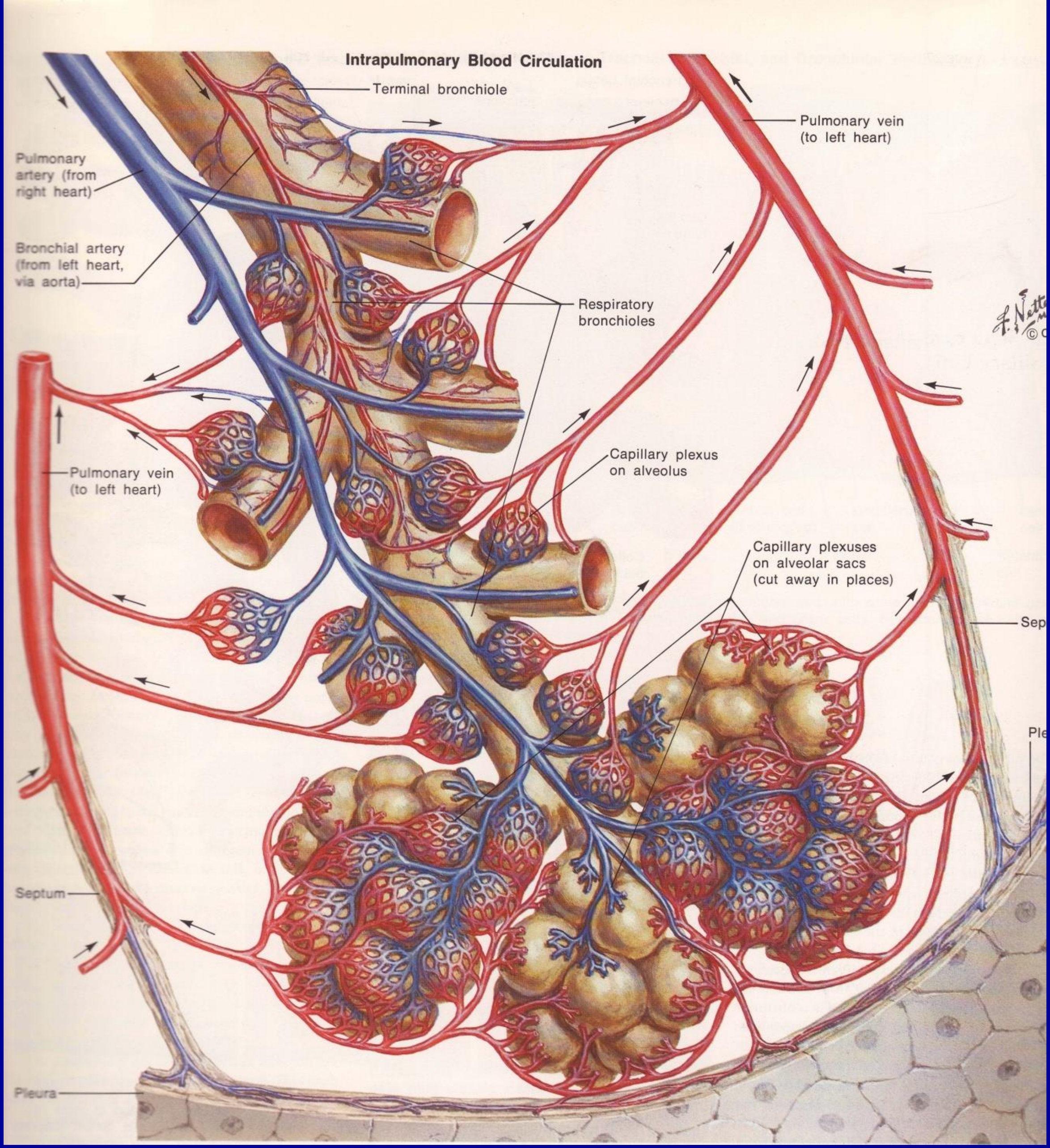
Blood Supply

The lungs have two circulations:

1) **Pulmonary circulation:** bringing mixed venous blood to the lungs, allowing for the blood to get oxygenated, and to then be taken back to the left heart;

2) **Bronchial circulation:** supplying oxygenated blood from the systemic circulation to the tracheobronchial tree (this circulation allows for the airways to get oxygenated).

The pulmonary and bronchial circulations



Reproduced from Netter, F.H.: The CIBA Collection of Medical Illustrations, vol. 7).

Alveolar Cell Types

There are three alveolar cell types:

1. Epithelial type I and II cells:

   Alveoli are lined by epithelial type I and II cells. Little is known about the specific metabolic activities of type I cells. Type II cells produce pulmonary surfactant, a substance that decreases the surface tension of the alveoli.

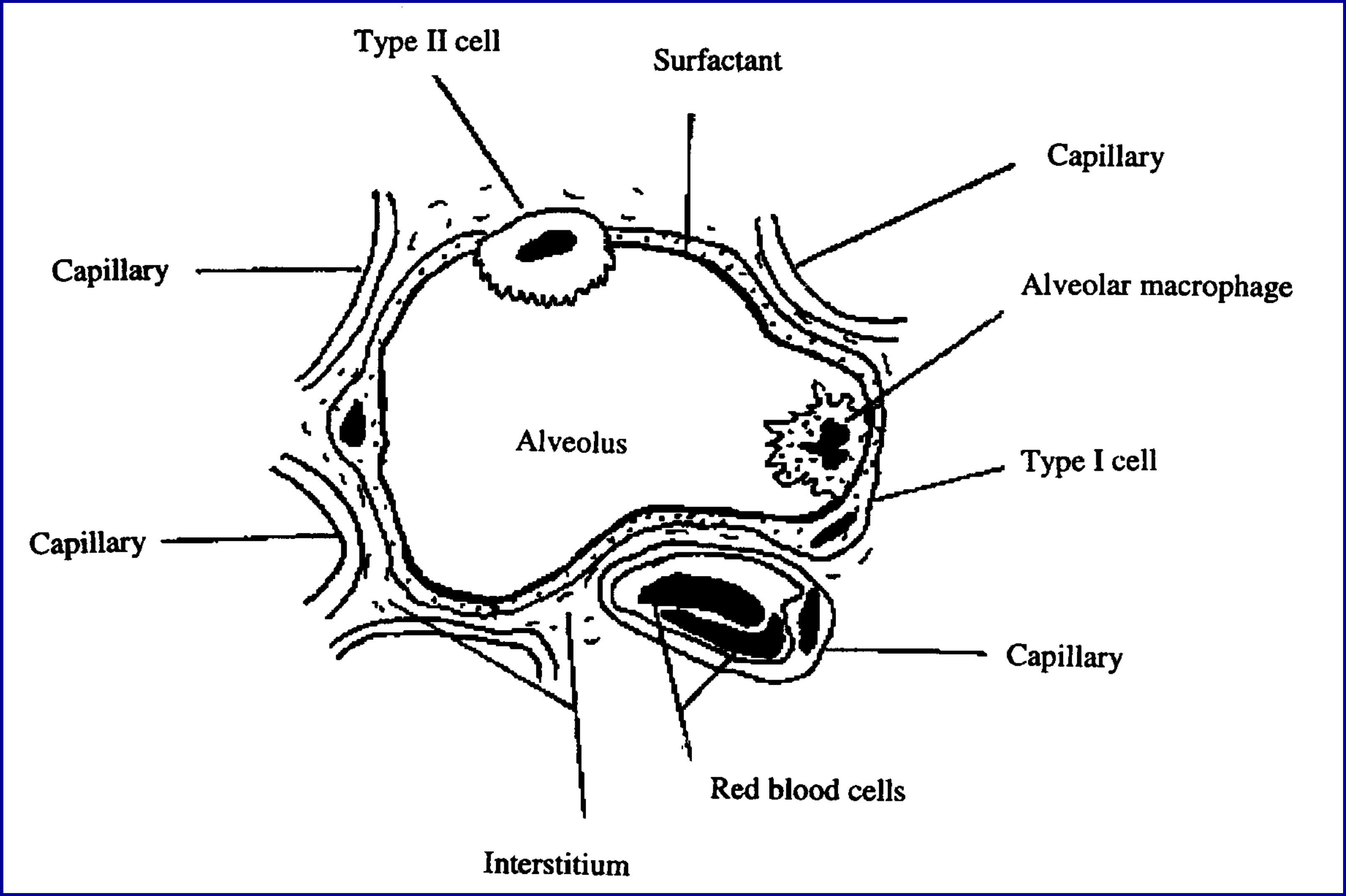
2. Endothelial cells:

   Endothelial cells constitute the walls of the pulmonary capillaries. These cells may be as thin as 0.1 micron.

3. Alveolar macrophages:

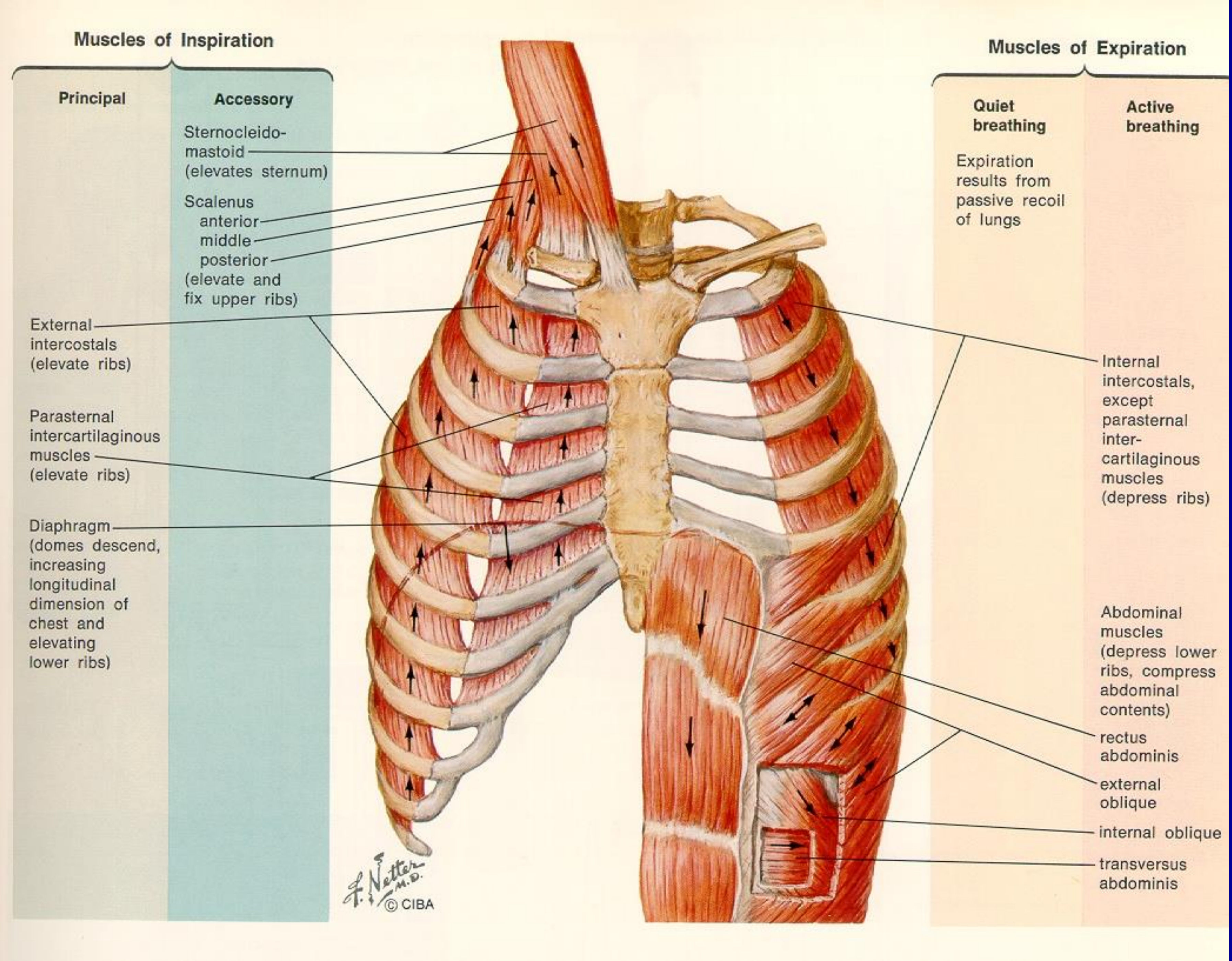
   They remove foreign particles that may have escaped the mucociliary defense system of the airways and found their way into the alveoli.

Alveolar-capillary membrane



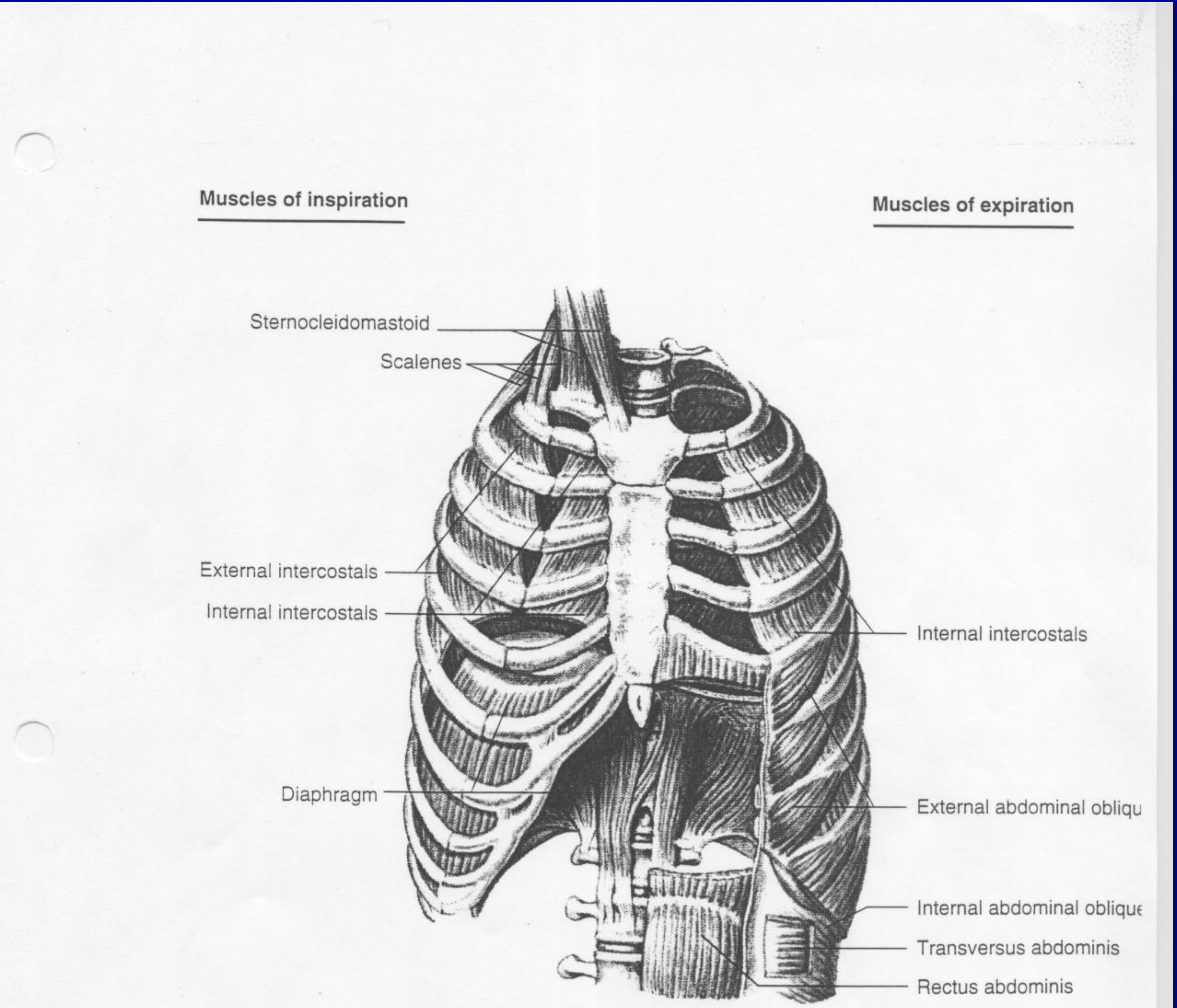
Respiratory Muscles

The lung tissue is elastic, but it is unable to expand or contract by itself. Air has to be sucked into the lungs. This function is powered by the respiratory muscles of the chest wall. There are 2 types of respiratory muscles: inspiratory and expiratory.

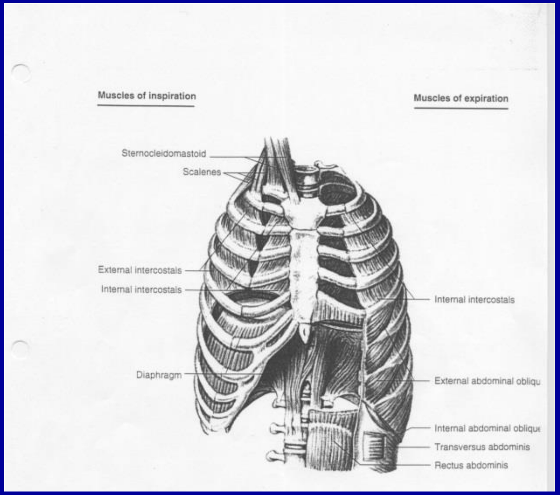


Reproduced from Netter, F.H.: The CIBA Collection of Medical Illustrations, vol. 7.

The diaphragm is innervated by the phrenic nerves from cervical segments 3, 4 and 5.



Summary of events during inspiration:



Inspiration:

Diaphragm and intercostal muscles contract

↓

Thoracic cage expands

↓

Intrapleural pressure becomes more negative

↓

Transpulmonary pressure increases

↓

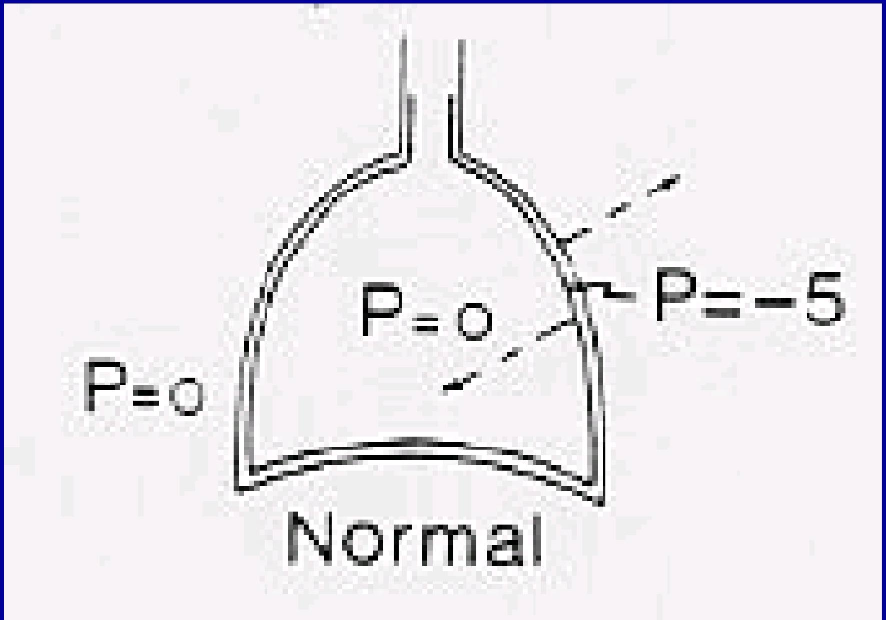
Lungs expands

↓

Alveolar pressure becomes subatmospheric

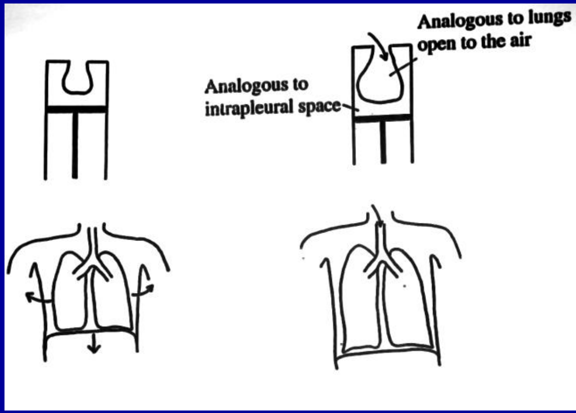
↓

Air flows into alveoli



Reproduced from West: Respiratory Physiology- the essentials.

Summary of events during inspiration:



Inspiration:

Diaphragm and intercostal muscles contract

↓

Thoracic cage expands

↓

Intrapleural pressure becomes more negative (subatmospheric)

↓

Transpulmonary pressure increases

↓

Lungs expands

↓

Alveolar pressure becomes subatmospheric

↓

Air flows into alveoli

Summary of events during expiration:

Expiration:

Diaphragm and external intercostal muscles stop contracting

↓

Chest wall moves inwards

↓

Intrapleural pressure goes back towards preinspiratory value

↓

Transpulmonary pressure goes back towards preinspiratory value

↓

Lung recoil towards preinspiratory volume

↓

Air in lungs is compressed

↓

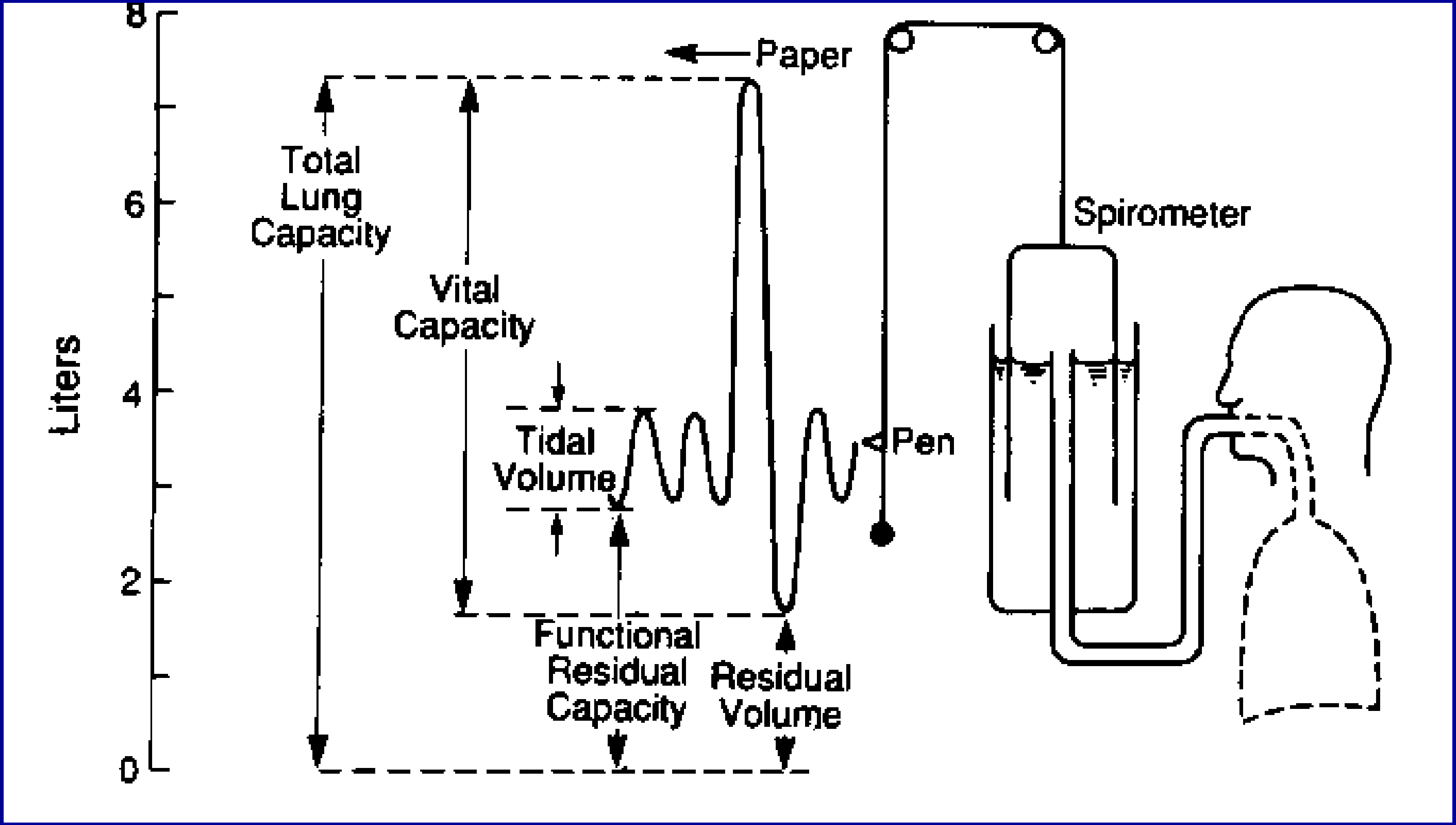
Alveolar pressure becomes greater than atmospheric pressure

↓

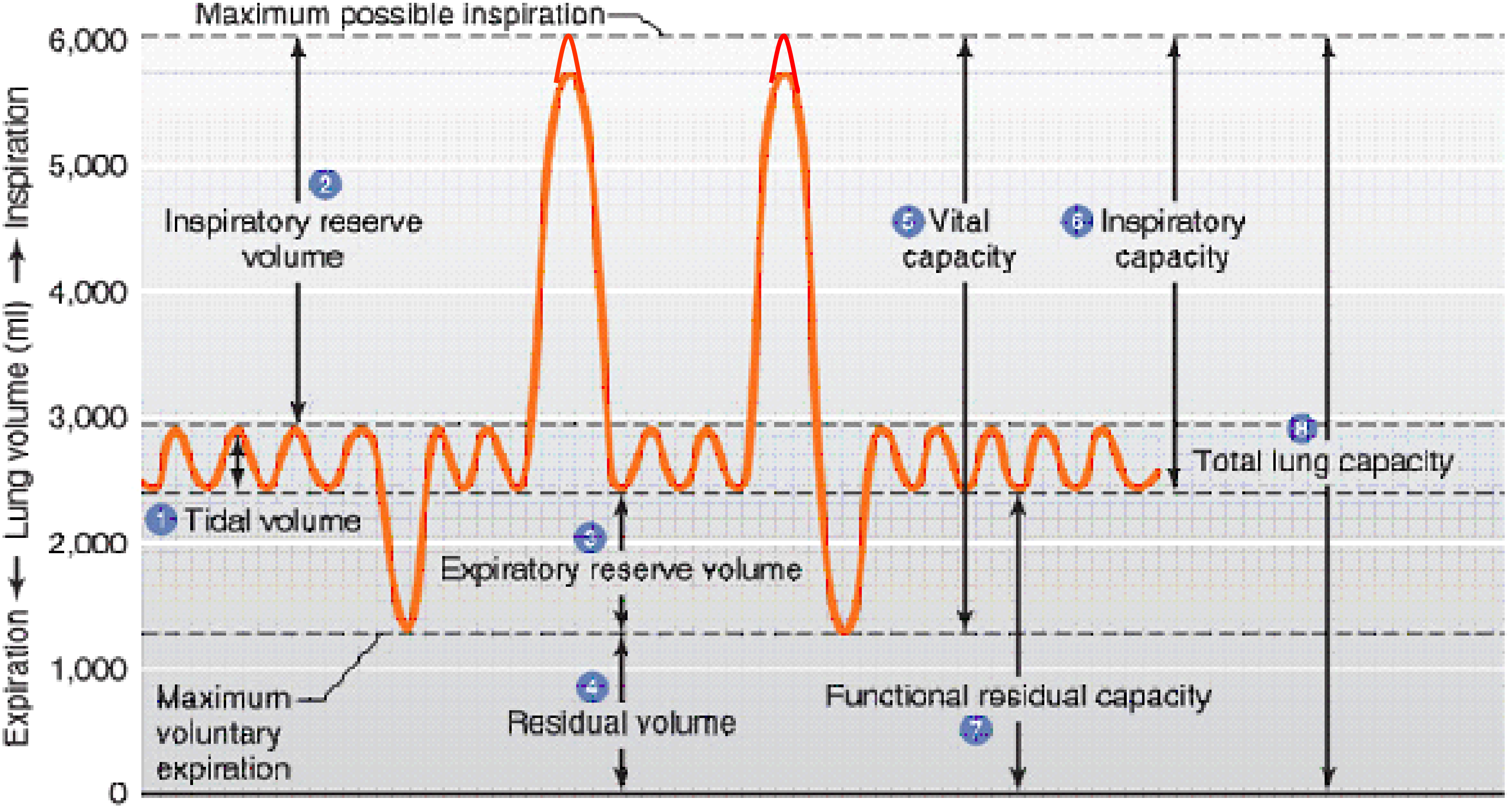
Air flows out of the lungs

Lecture 2

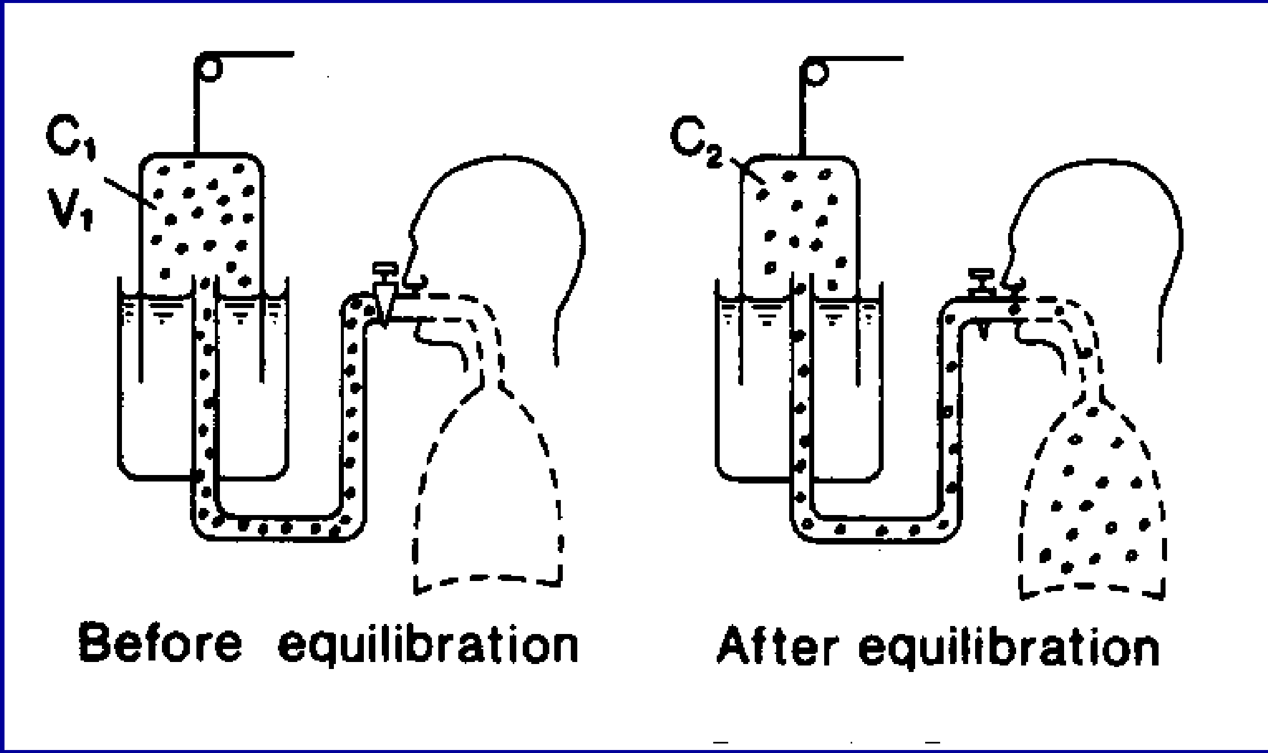
Spirometry: Measuring lung volumes



Lung volumes. *(Reproduced from West, J.B.: Respiratory Physiology- the essentials).*


Maximum possible inspiration
6,000
5,000
4,000
3,000
2,000
1,000
0
Expiration ← Lung volume (ml) → Inspiration
2 Inspiratory reserve volume
5 Vital capacity
6 Inspiratory capacity
8 Total lung capacity
1 Tidal volume
3 Expiratory reserve volume
Maximum voluntary expiration
4 Residual volume
Functional residual capacity 7

Measurement of FRC



(Reproduced from West: Respiratory Physiology- the essentials).

$$C1 \times V1 = C2 \times (V1 + FRC)$$

so that:

$$FRC = (C1 \times V1 / C2) - V1$$

Note: Think of the lung as a balloon not as a jar.

VENTILATION

Minute ventilation

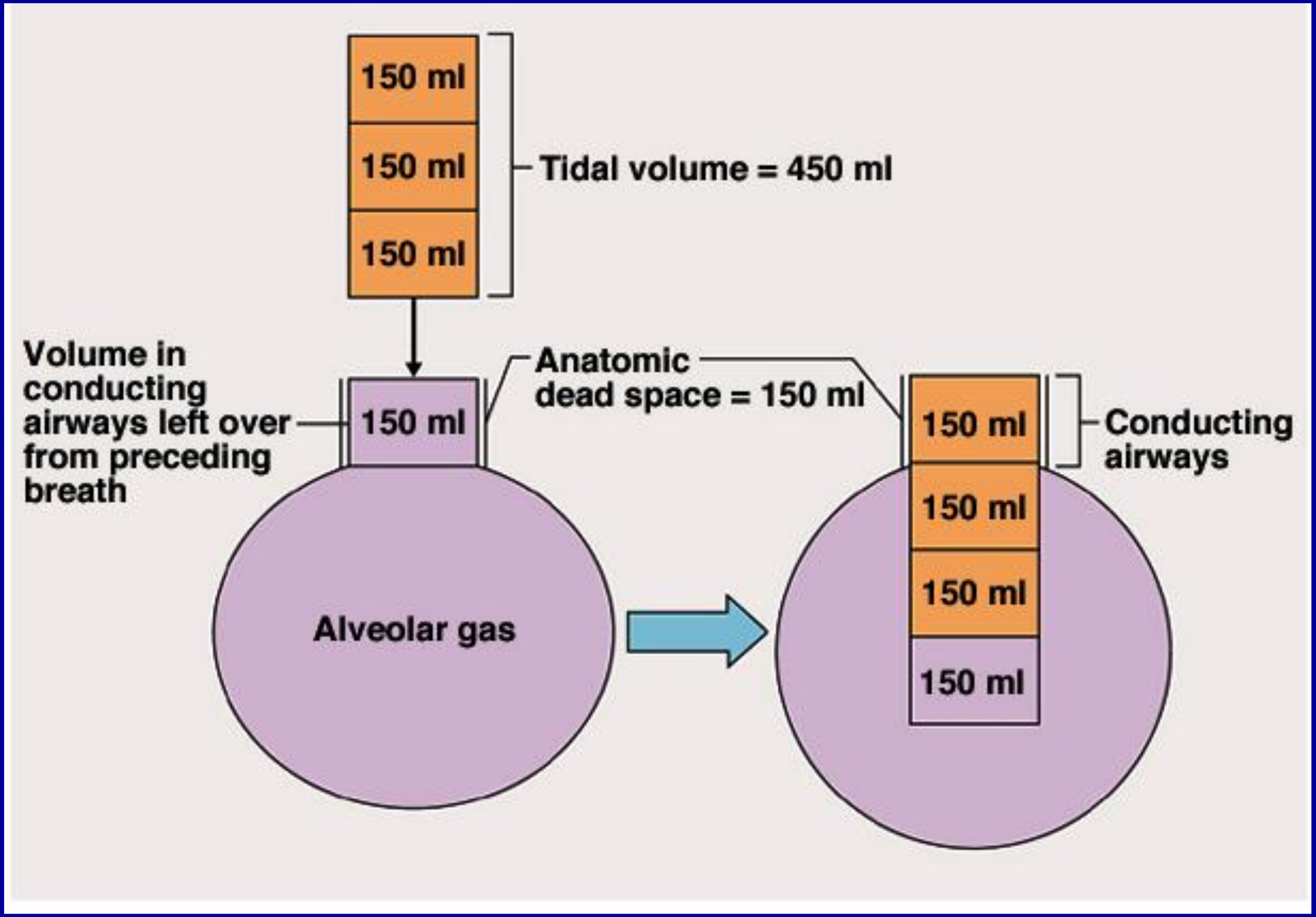
The amount of air inspired (or expired) over one minute ($\dot{V}_E$).

$$\dot{V}_E = V_T \times f$$

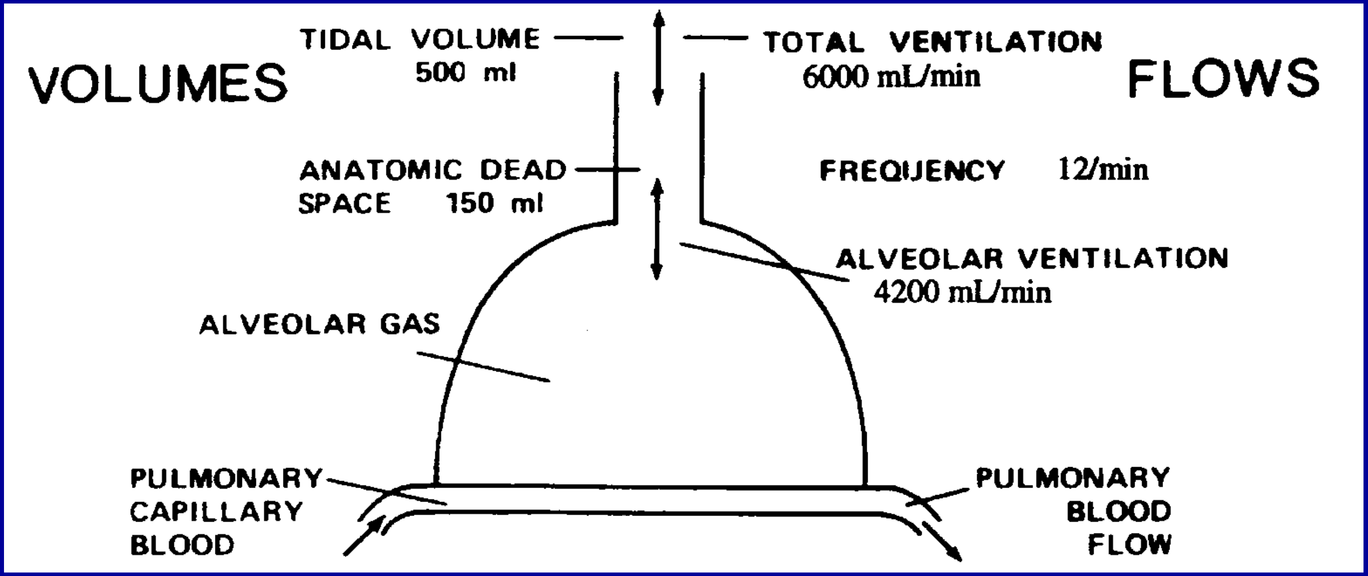
where V_T is the tidal volume, and f is the number of breaths per minute.

Alveolar ventilation

Not all the air inhaled into the lungs reaches the gas exchanging area. Some of the air remains in the conducting airways (**anatomical dead space**).



The volume of the anatomical dead space in the adult subject is about 150mL (**anatomical dead space** is difficult to measure, but a close approximation is a subject's weight in pounds).

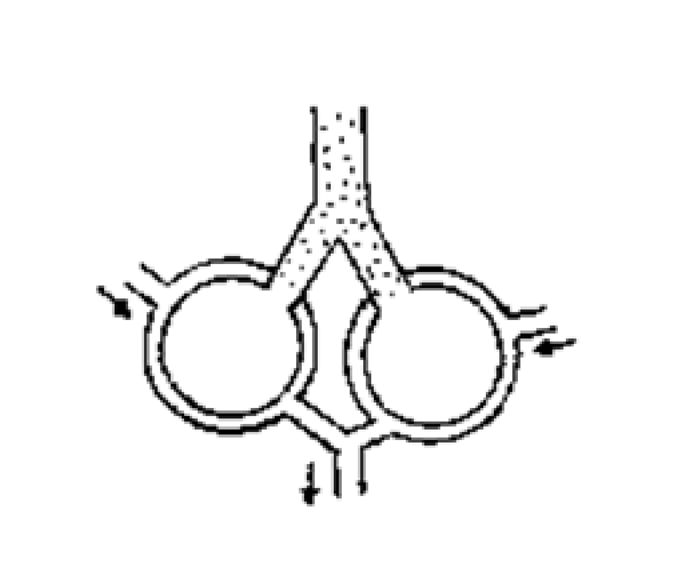


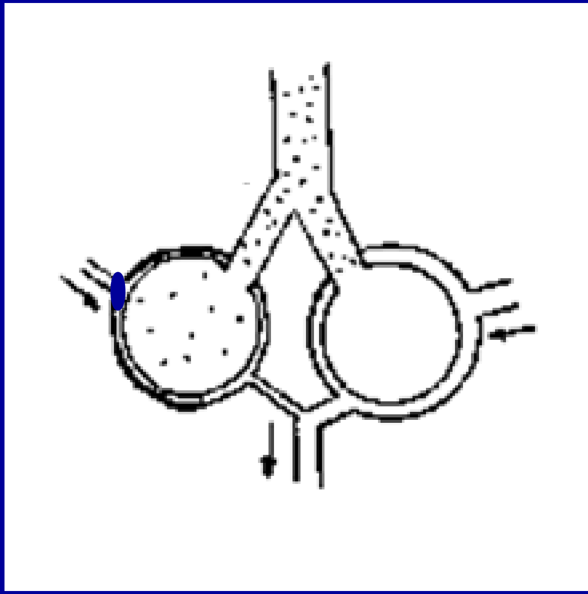
In a normal adult male, V_T = 500ml, and f =12 breaths/minute. Therefore, $\dot{V}_E$ = 6000ml/min. The volume of the anatomical dead space in the adult subject is about 150ml. Thus, the amount of air that reaches the respiratory zone per minute and available for gas exchange, the alveolar ventilation ($\dot{V}_A$), is:

$\dot{V}_A$= (500-150 ml) x 12= 4200 ml/min.

Alveolar and Physiological dead-space

Alveolar dead-space: under some pathological conditions, a certain amount of inspired air, although reaching the respiratory zone, does not take part in gas exchange. This situation can be due to a decreased blood supply or no blood supply at all. These alveoli represent alveolar dead space.





Alveolar and Physiological dead-space

Physiological dead-space:

Physiological dead-space (V_D): (Alveolar + Anatomical) dead-space

APPENDIX 1

P = total pressure

Fx = fractional concentration in dry gas

Px = partial pressure of gas x

$Px = P \cdot Fx$

Example:

Barometric P = 760mmHg

FO_2 = 21% *

FCO_2 = 0.03% *

$Px = (P - 47\text{mmHg}) \cdot Fx$ (water vapor pressure of 47mmHg)

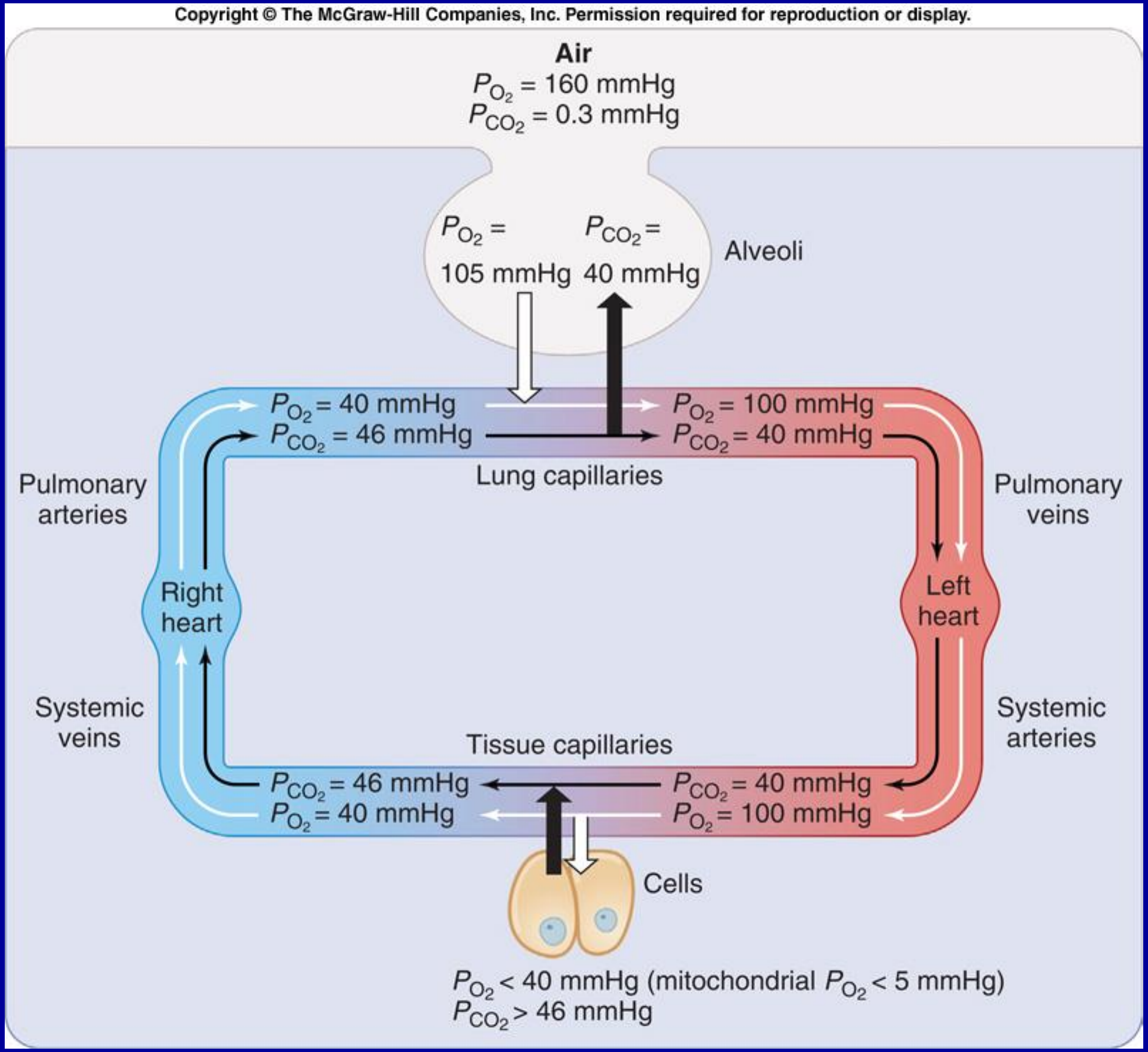
$PO_2 = (760\text{mmHg} – 47\text{mmHg}) \cdot 21/100 = 150\text{mmHg}$

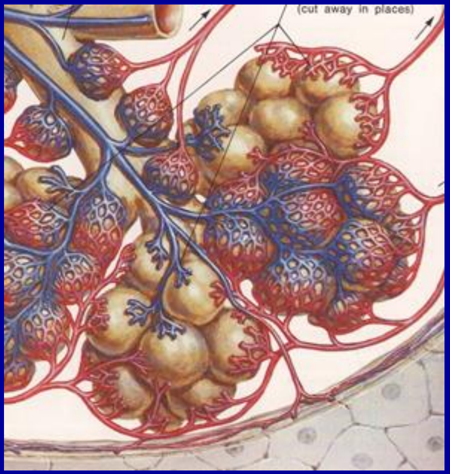
$PCO_2 = (760\text{mmHg} – 47\text{mmHg}) \cdot 0.03/100 = 0.2\text{mmHg}$

* Fractional concentrations are generally given as the fraction of <u>dry</u> gas volume that is occupied by the gas in question. Because of that convention, barometric pressure has to be corrected for the contribution from water vapor.

Types of Alveolar Ventilation

Normal Alveolar Ventilation: $\dot{V}_A$ matches CO_2 and keeps $PaCO_2$ at a constant level.





Types of Alveolar Ventilation (Cont'ed)

Alveolar hyperventilation: This occurs when more O_2 is supplied and more CO_2 removed than the metabolic rate requires ($\dot{V}_E$ exceeds the needs of the body). As a consequence, alveolar and arterial partial pressures of O_2 rise and those of CO_2 decrease.

Note: This is with respect to metabolism so not as during exercise.

Types of Alveolar Ventilation (Cont'ed)

Alveolar hypoventilation: A fall in ventilation can reduce alveolar ventilation below that required by the metabolic activity of the body.

Under such conditions, the rate at which O_2 is added to alveolar gas, and the rate at which CO_2 is eliminated, is lowered, so that the alveolar partial pressure of O_2 (P_AO_2) falls and P_ACO_2 rises.

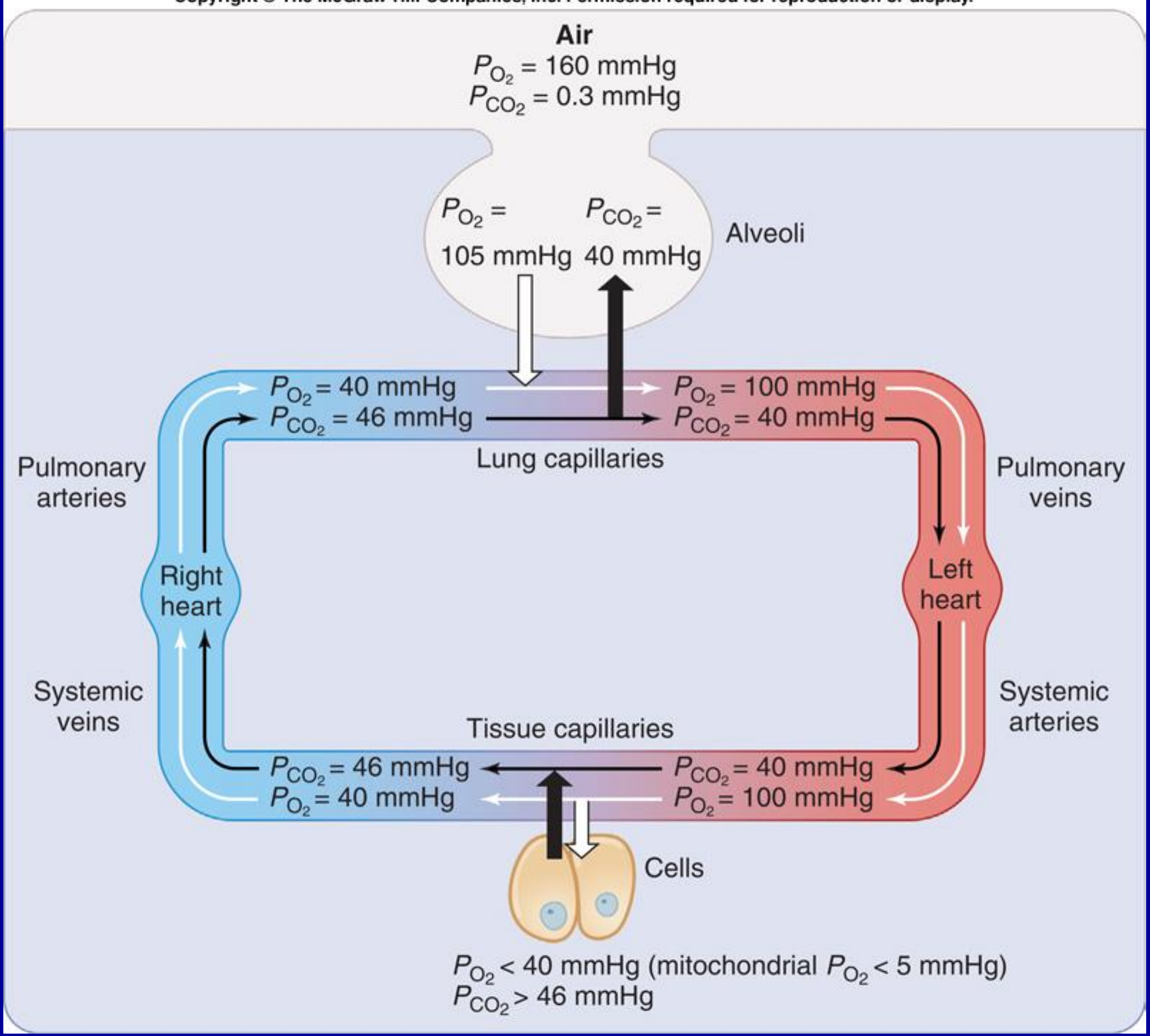
Therefore, PaO_2 falls below normal values and $PaCO_2$ rises above the normal value.

Alveolar hypoventilation may occur during severe disorders of the lungs (e.g. chronic obstructive lung disease), or when there is damage to the respiratory muscles. It can also occur when the chest cage is injured and the lungs collapse, or when the central nervous system is depressed.

TABLE 13–6 *Effects of Various Conditions on Alveolar Gas Pressures*

CONDITION	ALVEOLAR P_{O_2}	ALVEOLAR P_{CO_2}
Breathing air with low P_{O_2}	Decreases	No change*
↑Alveolar ventilation and unchanged metabolism	Increases	Decreases
↓Alveolar ventilation and unchanged metabolism	Decreases	Increases
↑Metabolism and unchanged alveolar ventilation	Decreases	Increases
↓Metabolism and unchanged alveolar ventilation	Increases	Decreases
Proportional increases in metabolism and alveolar ventilation	No change	No change

Types of Alveolar Ventilation



Lecture 3

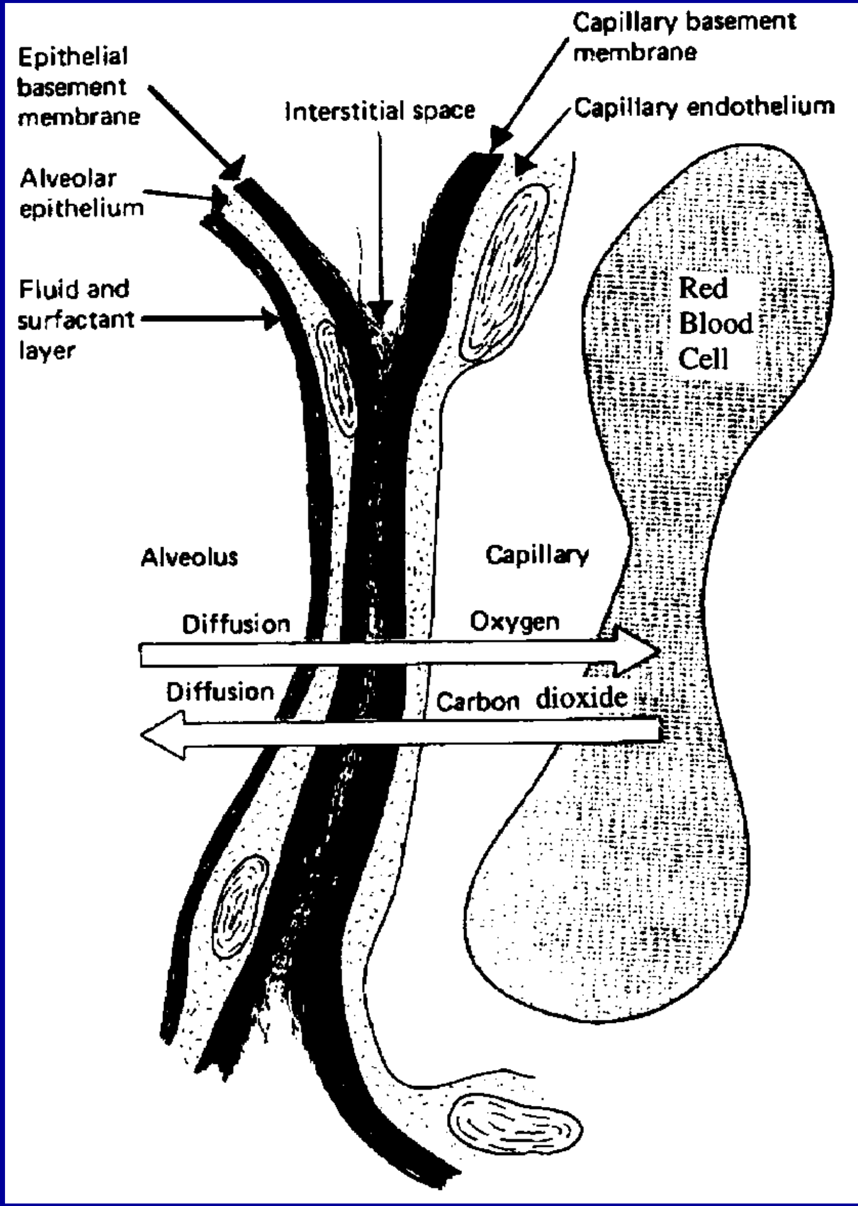
GAS DIFFUSION

Diffusion Rate

The transfer of gases across the alveolar-capillary membrane occurs by passive diffusion. This diffusion is very efficient in the lungs because of the huge surface area of the membrane and its extreme thinness.

Diffusion is governed by Fick's Law:

Diffusion rate is α surface area (50-100 m^2)
α partial pressure gradient
α 1/thickness (~0.2 mm)



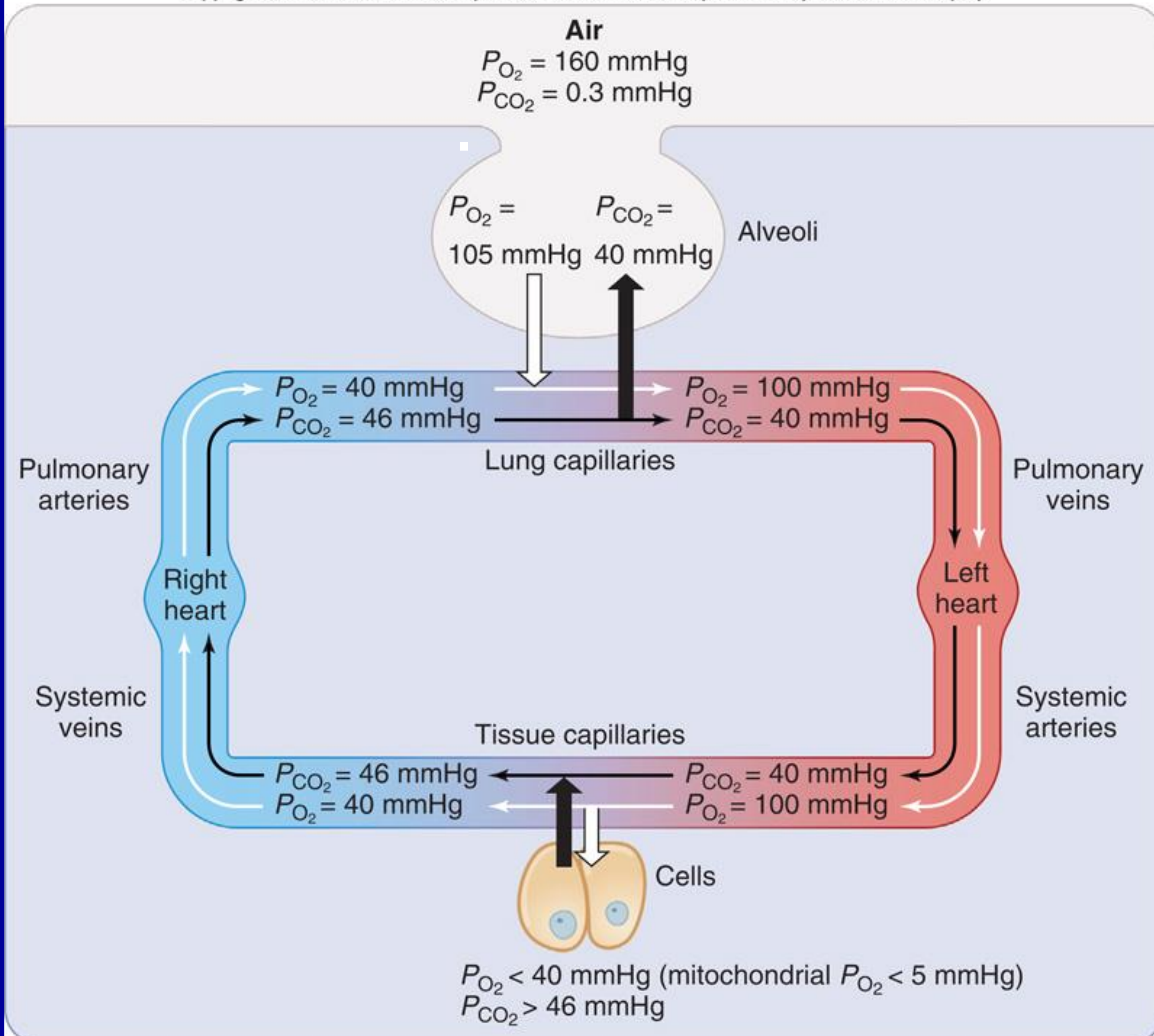
Ultrastructure of the respiratory membrane as shown in cross-section.
(Reproduced from Guyton: Textbook of Medical Physiology).

Diffusion Rate (Cont'ned)

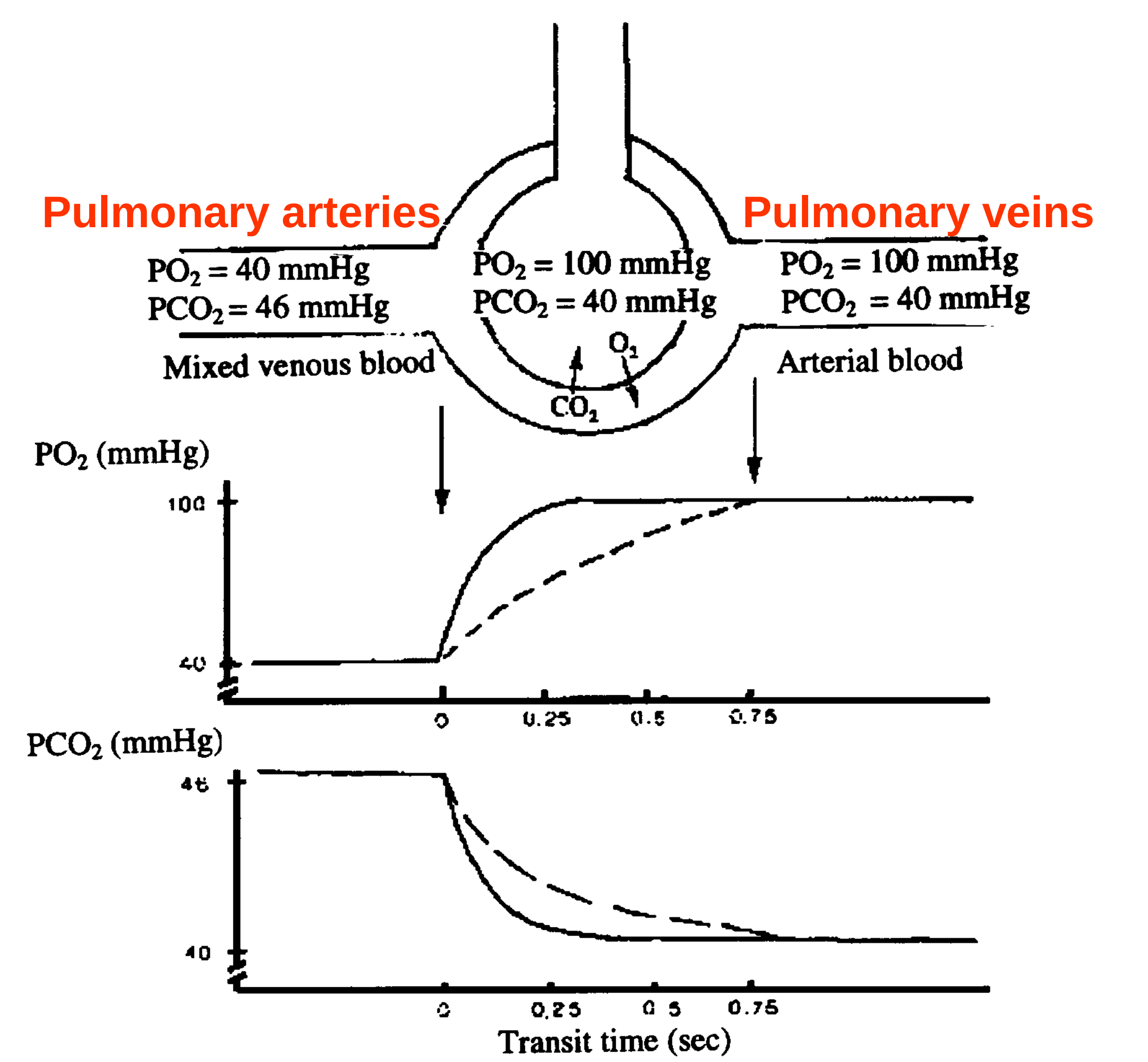
- To diffuse through a liquid, a gas must be soluble in the liquid. The amount of gas dissolved is proportional to its partial pressure (Henry's law).

- Because CO_2 is considerably more soluble than O_2 in water, it diffuses ~20 times more rapidly than O_2.

- However, the difference in PCO_2 between the 2 sides of the alveolar-capillary membrane is 10 times smaller than that for PO_2. Therefore, the time required for equilibrium between alveolar air and capillary blood is ~ the same for the two gases.


Air
P_{O_2} = 160 mmHg
P_{CO_2} = 0.3 mmHg
P_{O_2} = 105 mmHg
P_{CO_2} = 40 mmHg
Alveoli
P_{O_2} = 40 mmHg
P_{CO_2} = 46 mmHg
P_{O_2} = 100 mmHg
P_{CO_2} = 40 mmHg
Lung capillaries
Pulmonary arteries
Pulmonary veins
Right heart
Left heart
Systemic veins
Systemic arteries
Tissue capillaries
P_{CO_2} = 46 mmHg
P_{O_2} = 40 mmHg
P_{CO_2} = 40 mmHg
P_{O_2} = 100 mmHg
Cells
P_{O_2} < 40 mmHg (mitochondrial P_{O_2} < 5 mmHg)
P_{CO_2} > 46 mmHg

Transit Time



IV Pulmonary blood flow

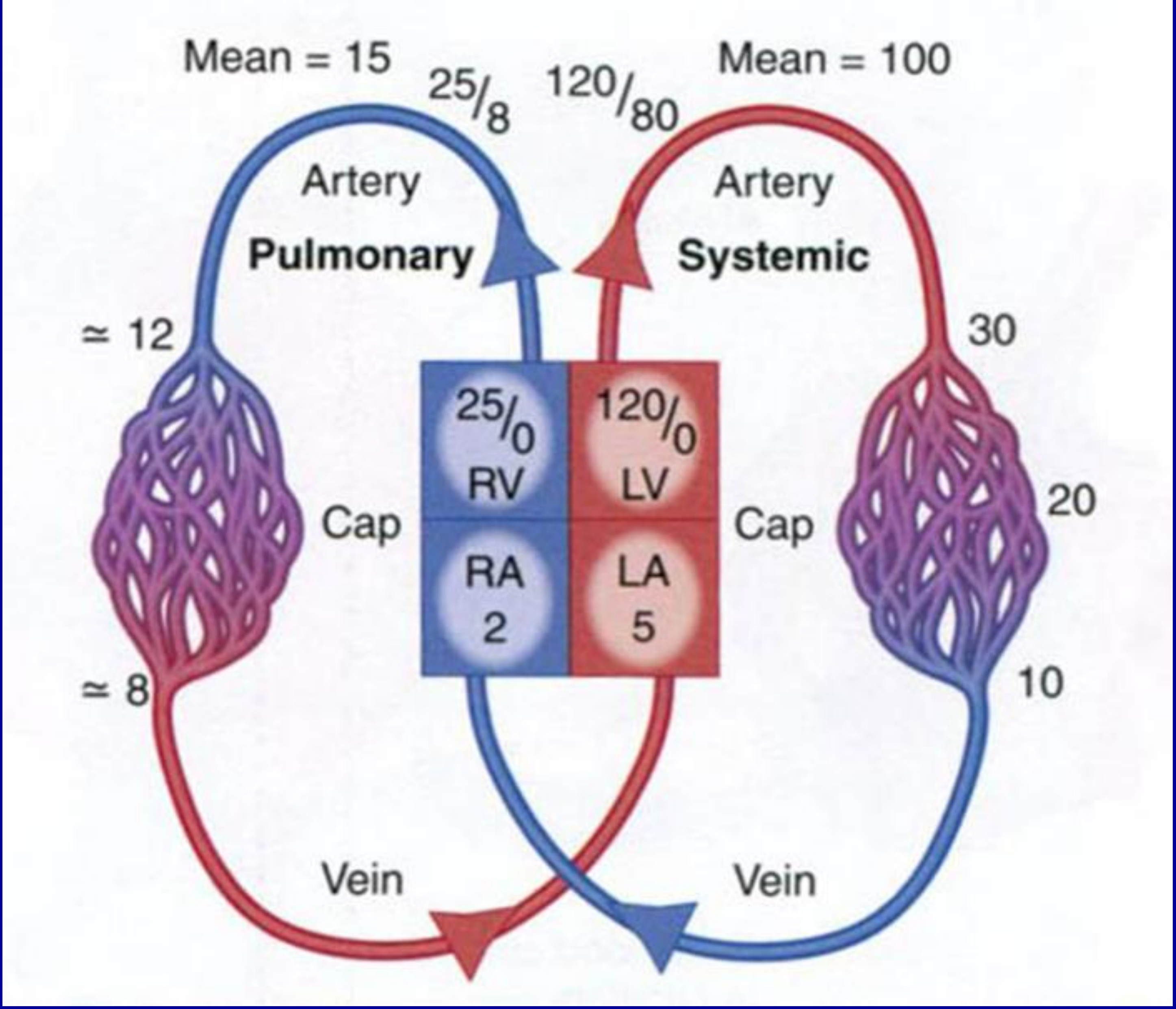
A. Pulmonary Circulation and Blood Pressure

The pulmonary circulation differs in many ways from the systemic one:

1) The right ventricle develops a pressure of ~25 mmHg during its systole (compared to 120mmHg in the left ventricle);

2) Blood pressure in the pulmonary circulation is lower than in the systemic circulation;

3) The pulmonary capillaries are thinner and contain less smooth muscle than comparable vessels in the systemic circulation.



From West: Respiratory Physiology-the essentials).

B. Vascular Resistance

Flow = pressure / resistance

- Total pressure drop from pulmonary artery to left atrium of about 10 mm Hg.

- The pulmonary resistance is ~1/10 that of the systemic circulation.

- The low vascular resistance in the pulmonary circulation relies on the thin walls of the vascular system.

- The low vascular resistance and high compliance of the pulmonary circulation allows the lung to accept the whole cardiac output at all times.

B. Vascular Resistance

Flow = pressure / resistance

•Total pressure drop from pulmonary artery to left atrium of about 10 mm Hg.

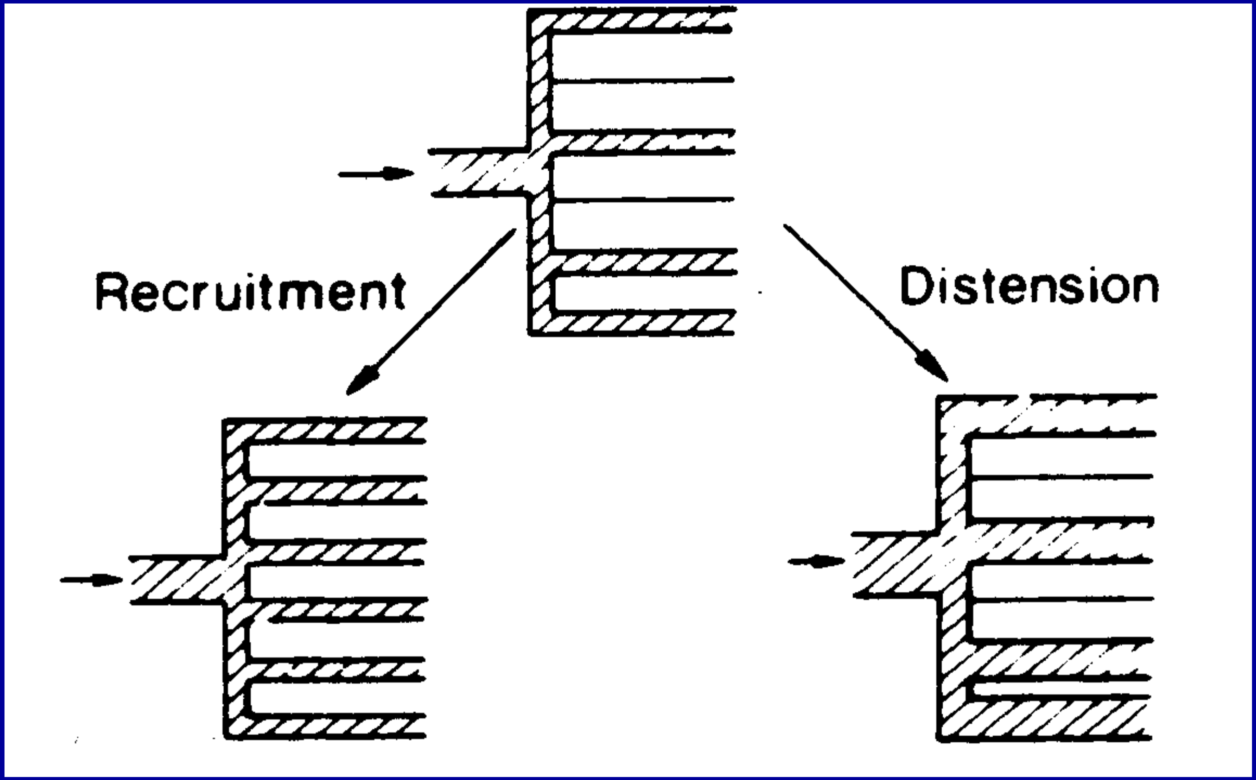
• The pulmonary resistance is ~1/10 that of the systemic circulation.

•The low vascular resistance in the pulmonary circulation relies on the thin walls of the vascular system.

•The low vascular resistance and high compliance of the pulmonary circulation allows the lung to accept the whole cardiac output at all times.

C. Accommodation of Pulmonary Blood Vessels

The pulmonary circulation has the capacity to accommodate two- to three-fold increases in cardiac output with little change in pulmonary arterial pressure.



Reproduced from West: Respiratory Physiology-the essentials.

C. Accommodation of Pulmonary Blood Vessels (Cont'ed)

- Drugs (serotonin, histamine, norepinephrine) which cause the contraction of smooth muscle increase pulmonary vascular resistance in the larger pulmonary arteries.

- Drugs (acetylcholine, isoproteranol) which can relax smooth muscle may decrease pulmonary vascular resistance.

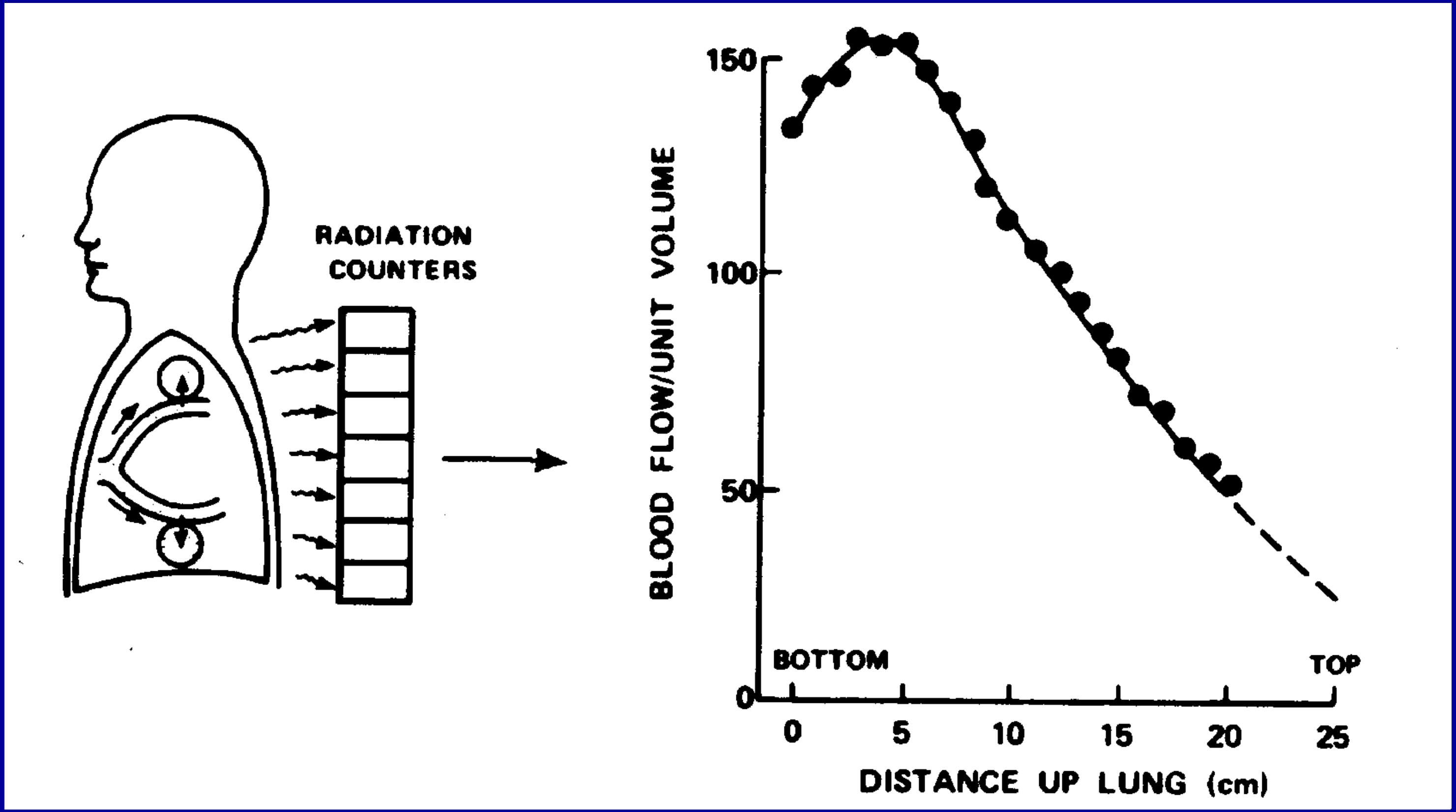
- There is a reflex vasoconstriction in regions of the lungs that are poorly oxygenated.

- Nitric oxide produced by endothelial cells relaxes vascular smooth muscle leading to vasodilation.

D. Effects of Gravity on pulmonary blood flow

Pulmonary blood flow is affected by gravity.

Test performed by injecting radioactive Xenon in a peripheral vein.



Note that the somewhat lower blood flow observed at the bottom of the lung is due to extra-alveolar vessels being less expanded at low lung volumes. *(Reproduced from West: Respiratory Physiology-the essentials).*

D. Effects of Gravity on pulmonary blood flow (Cont'ed)

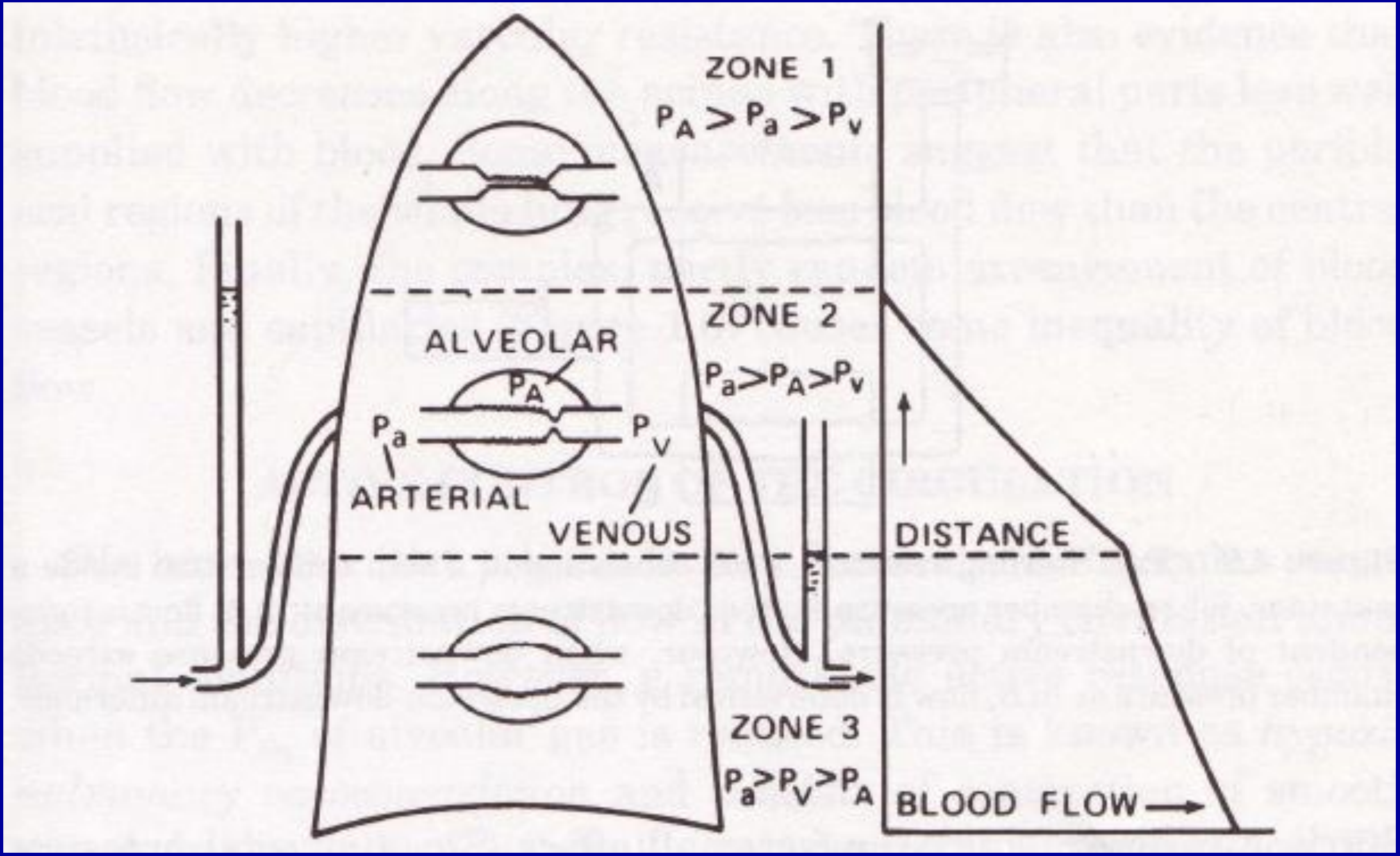
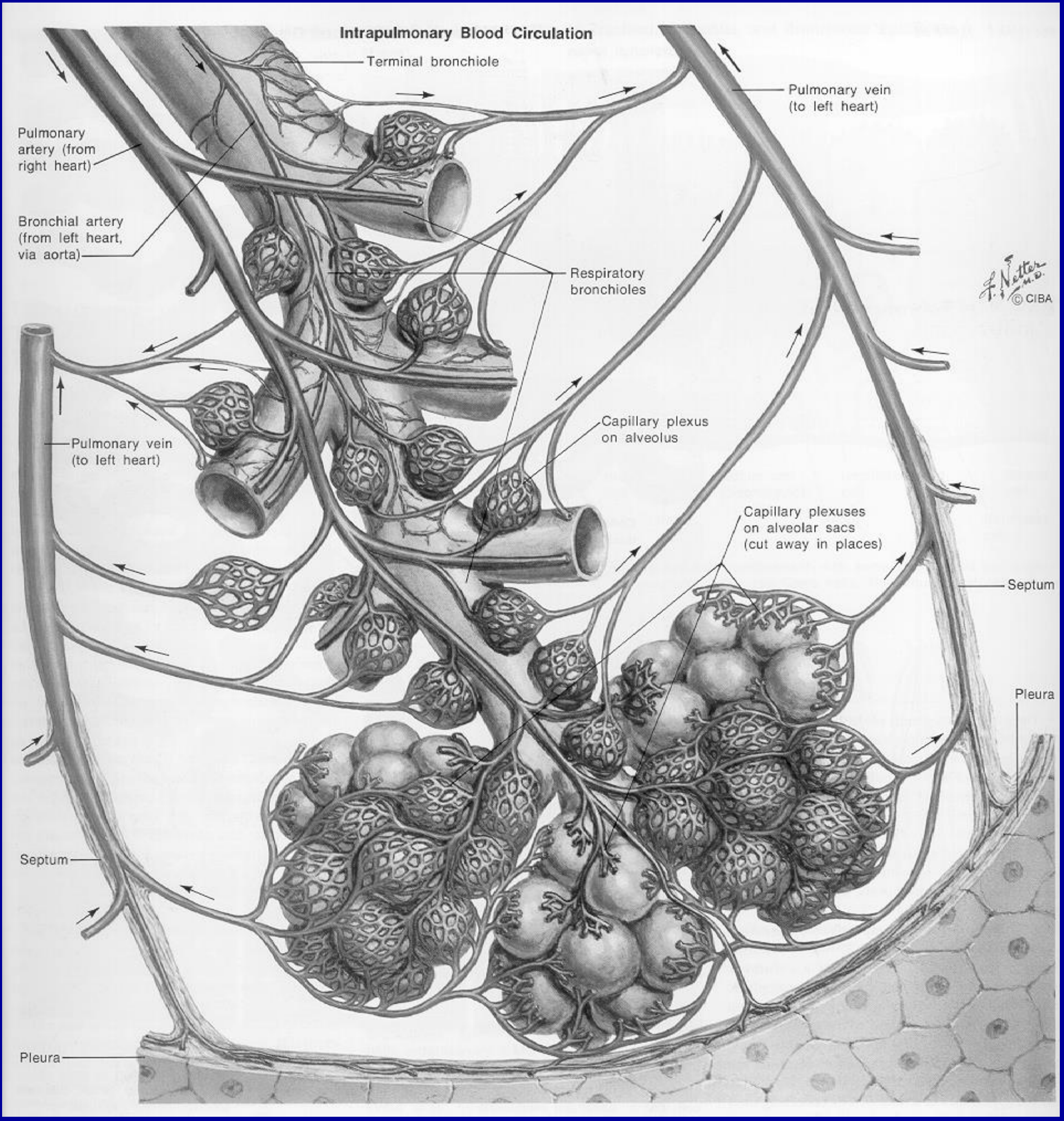


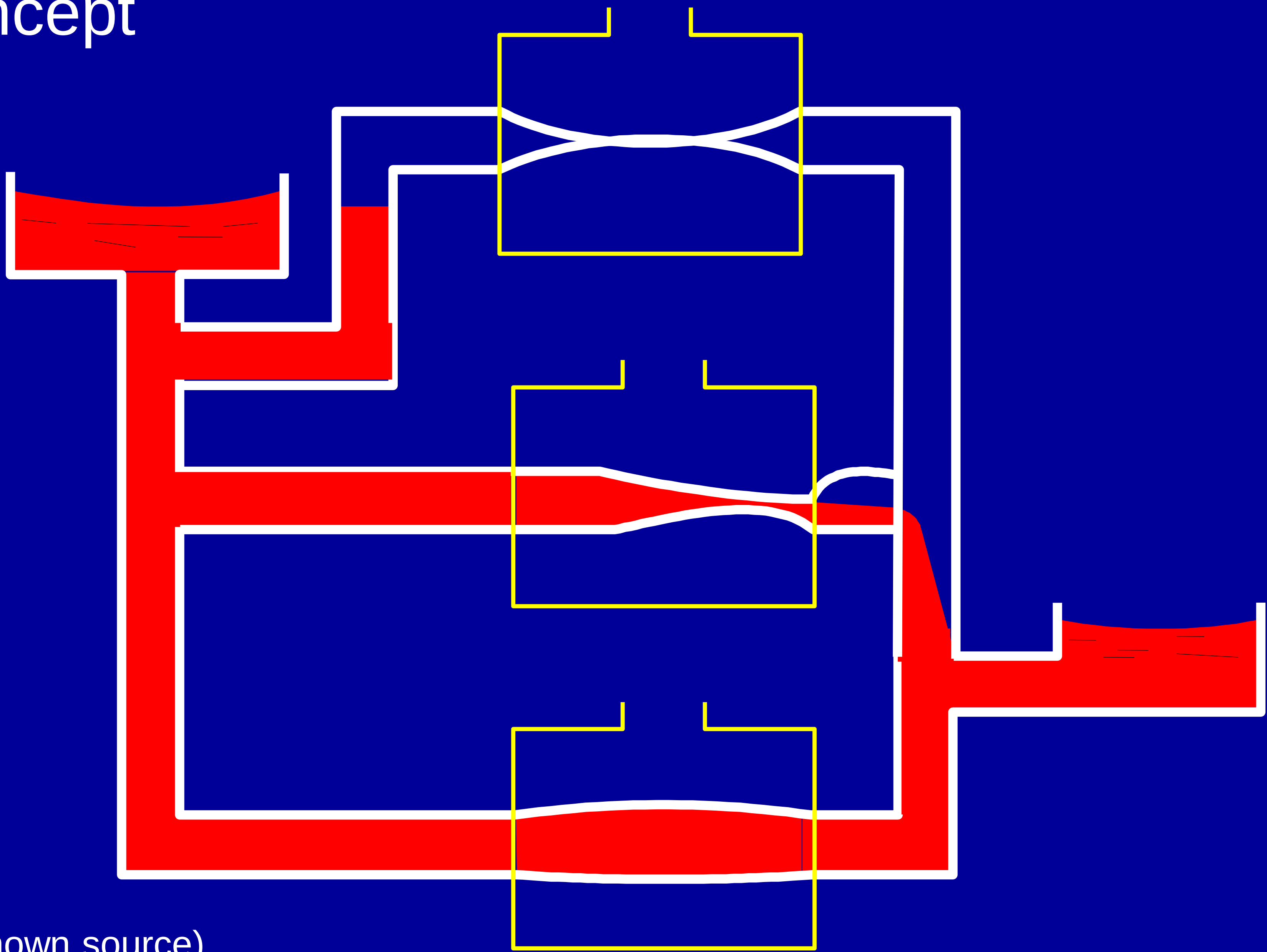
Figure 18b: Distribution of blood flow as described as West's zones

Reproduced from West: Respiratory Physiology-the essentials.


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

The Starling Resistor Concept

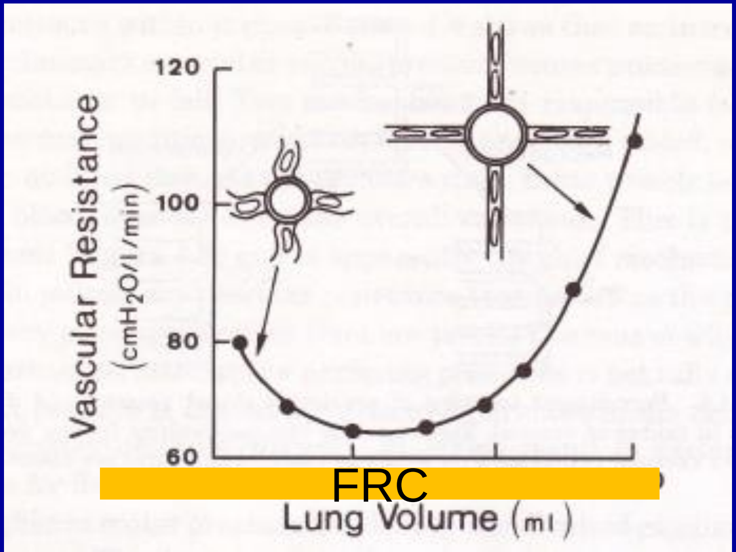
Pulmonary Circulation



(unknown source)

E. Effects of lung volume on pulmonary vascular resistance

- Lung volume affects pulmonary vascular resistance in a complex manner depending on if the blood vessels are surrounded by alveoli (alveolar vessels) or not (extra-alveolar vessels).



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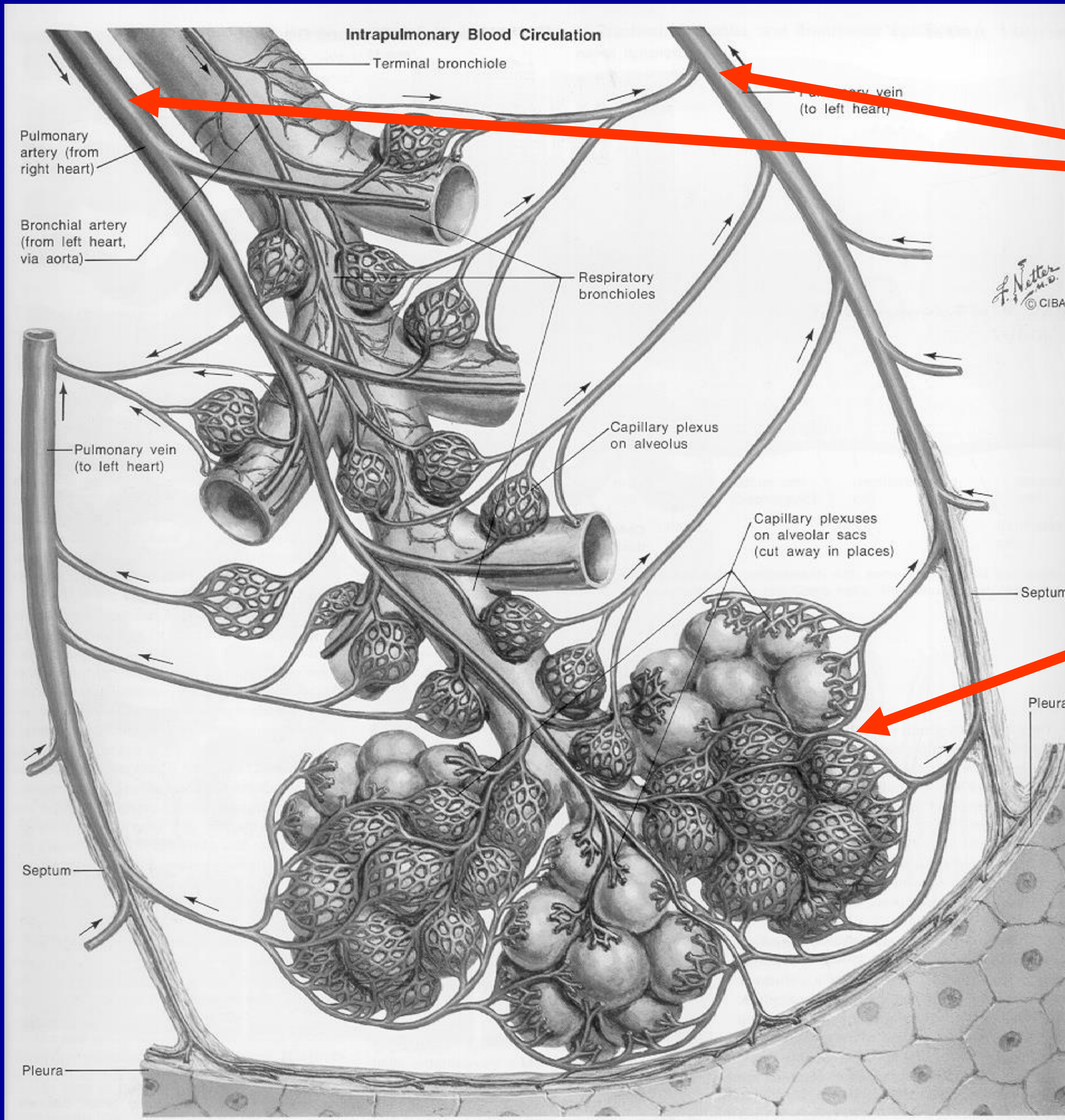
- Above FRC, the alveolar vessels are stretched longitudinally and thus, their diameter decrease leading to an increase in vascular resistance

- Below FRC, the extra-alveolar vessels collapse because they are not stretched by the pulmonary tissues.



Extra-alveolar vessels

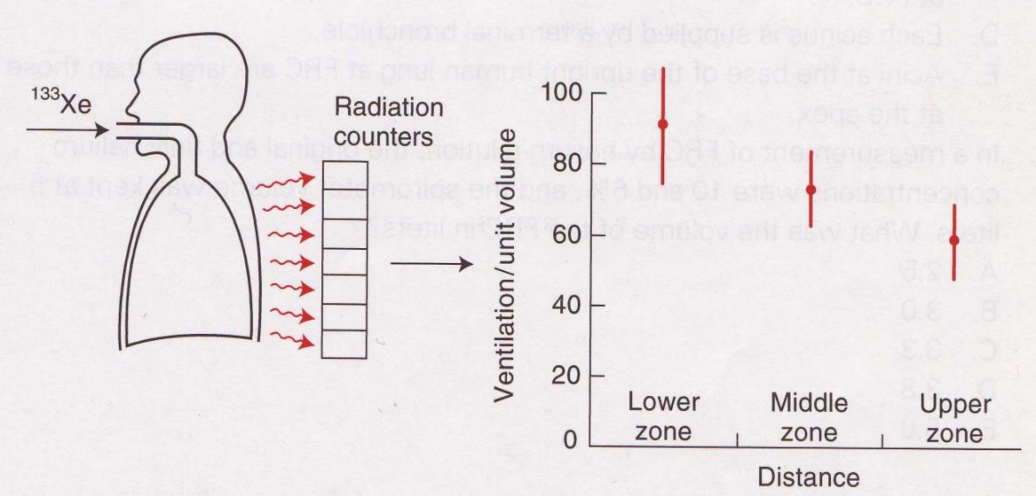
Alveolar vessels

F. Effects of Gravity on Ventilation

•Gravity also affects the distribution of ventilation.

•In an upright lung at rest, in normal gravity, the alveoli at the top of the lungs are more opened than the bottom ones (think of a “Slinky” held in normal gravity).

•The distribution of ventilation can be measured in a similar way as that of perfusion but with inhaled radioactive Xenon instead of infused in the blood.



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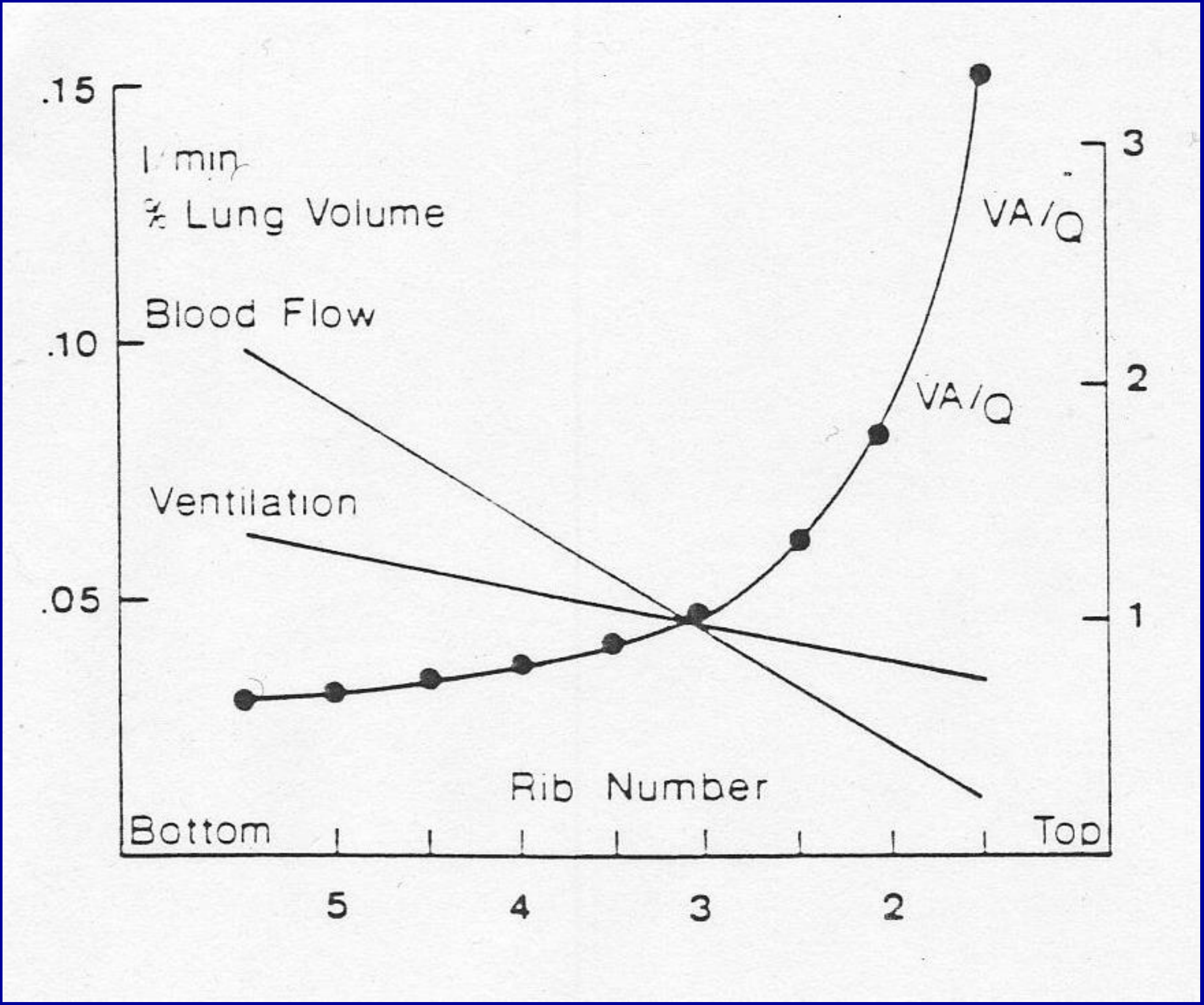
G. Distribution of ventilation perfusion ratio in the lungs in normal gravity.



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