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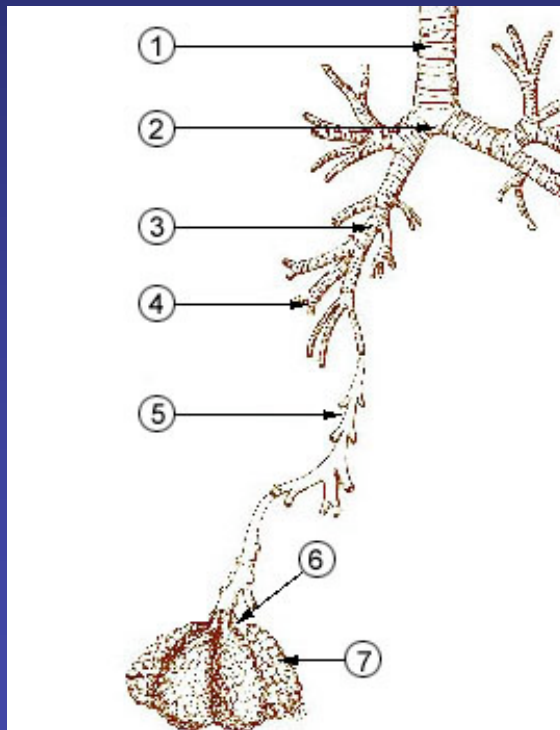
Diffusion of Gases

Thomas Sisson, M.D.

Objectives

- To understand the diffusion of gases in the lung
 - Define diffusion and contrast with bulk flow
 - State Fick's law for diffusion
 - Distinguish between diffusion limitation and perfusion limitation
 - Describe the diffusion of oxygen from the alveoli into the blood
 - Describe the diffusion of CO₂ from blood to alveoli
 - Define diffusing capacity and discuss its measurement

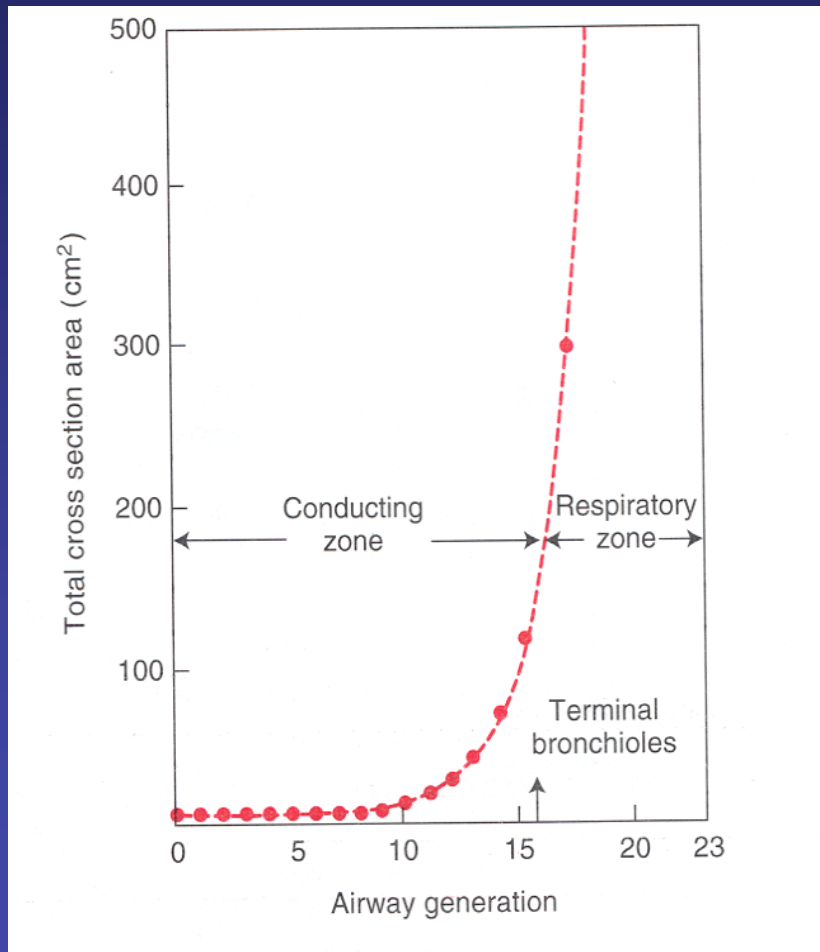
Airway Branching



Source: SEER Training Website
(training.seer.cancer.gov)

Trachea	0
Main Bronchi	1
Lobar Bronchus	2
Segmental Bronchus	3-4
Bronchioles	5-15
Terminal Bronchioles	16
Resp. Bronchioles	17-19
Alveolar Ducts	20-22
Alveolas Sacs	23

Bulk Flow vs. Diffusion



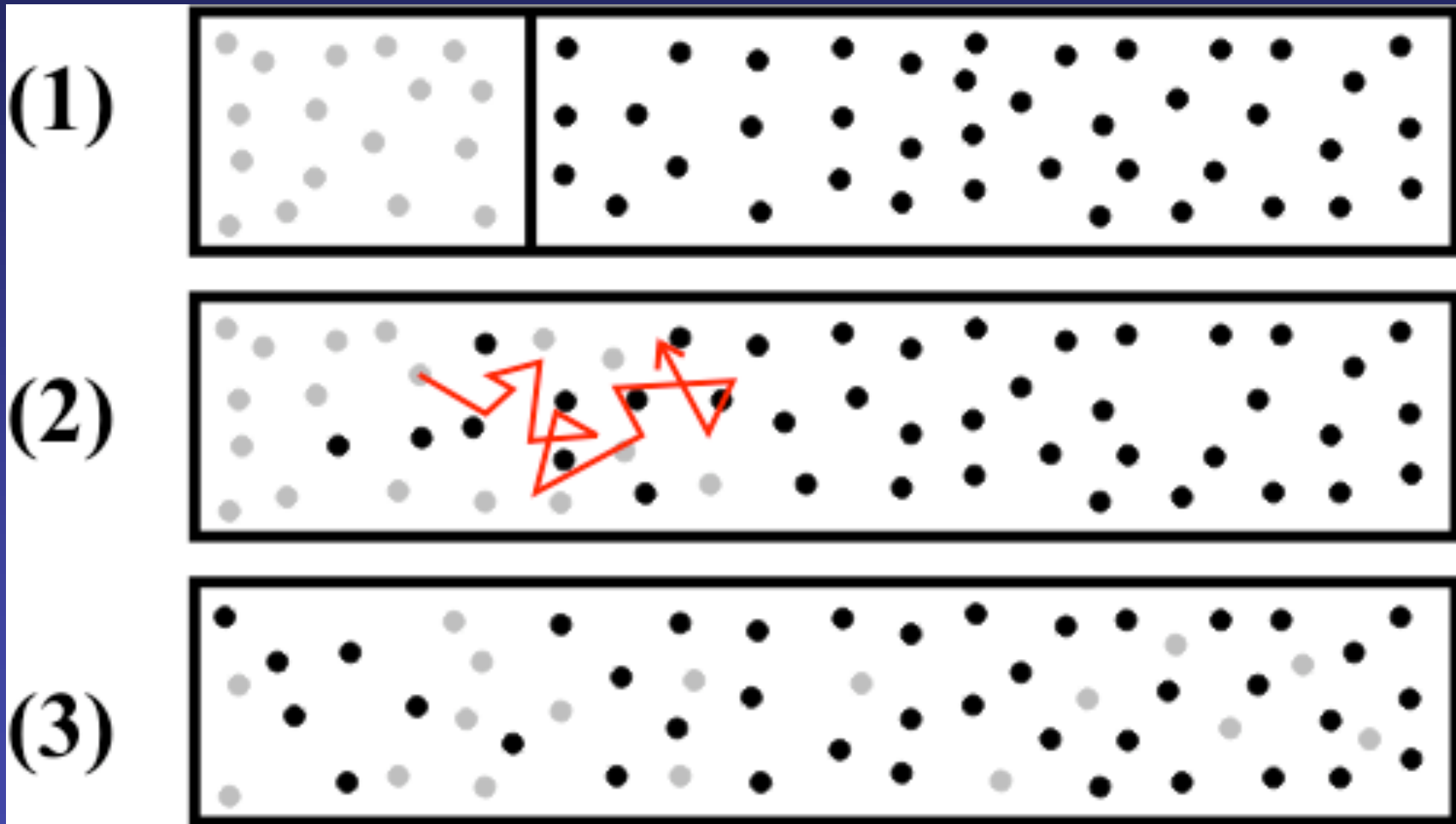
Source: Undetermined

- The cross sectional area increases with airway generation.
- Large volume/time, with decreasing velocity at any point.
 - *Imagine a fast flowing river reaching a delta.*
- The velocity of gas during inspiration becomes tiny at the level of the respiratory bronchiole- at this level diffusion becomes the chief mode of gas movement.

Gas Movement due to Diffusion

- Diffusion - movement of gas due to molecular motion, rather than flow.
 - Akin to the spread of a scent in a room, rather than wind.
 - Random motion leads to distribution of gas molecules in alveolus.

Gas Movement due to Diffusion

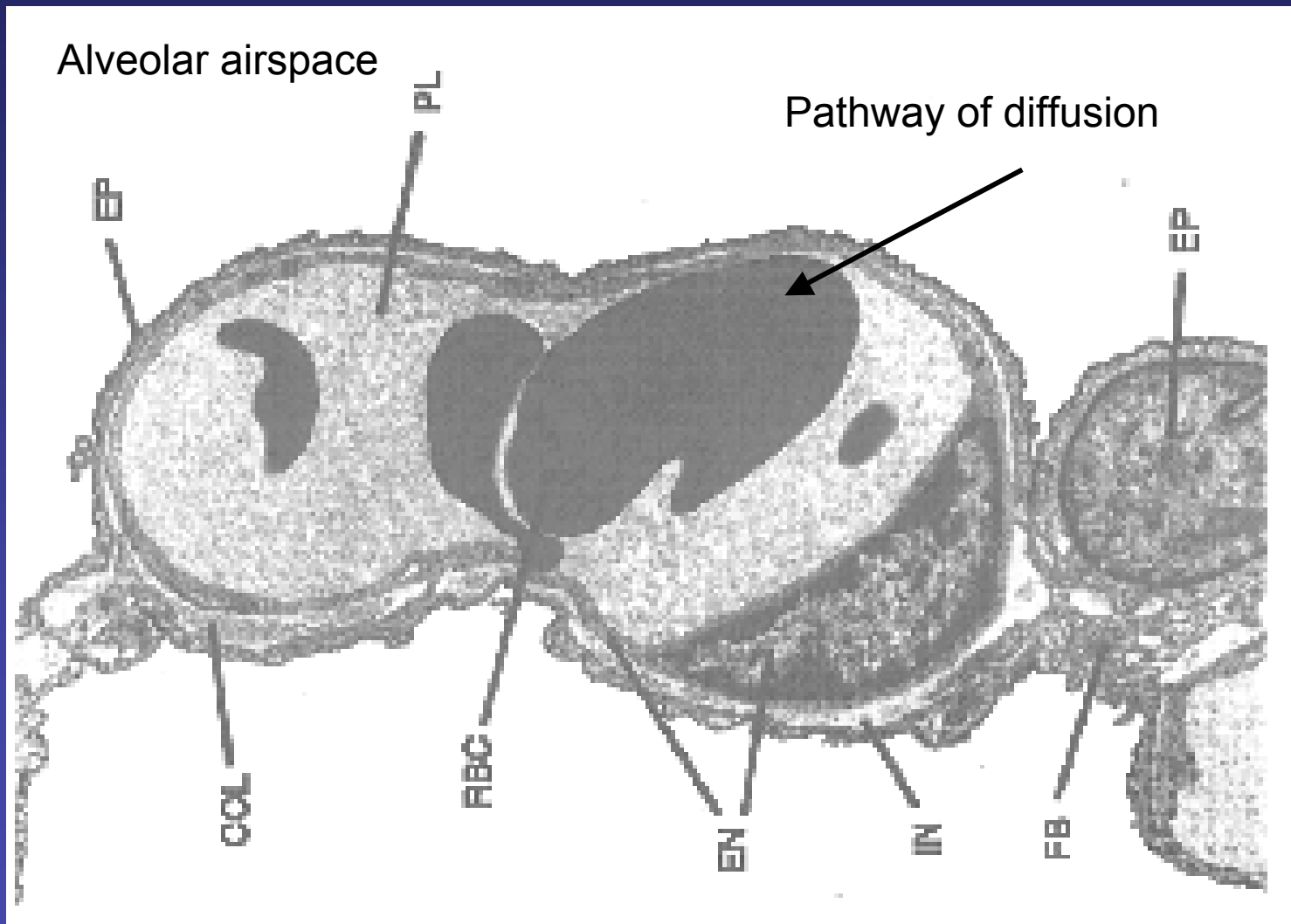


Source: Jkrieger (wikimedia.org)

Diffusion

- Driven by concentration gradients:
 - differences in partial pressure of the individual gases.
- Movement of O_2 and CO_2 between the level of the respiratory bronchiole and that of the alveolar space depends only on diffusion.
- The distances are small, so diffusion here is fast.

Diffusion of Gas Through the Alveolar Wall



Source: Undetermined

Diffusion of Oxygen Across the Alveolar Wall

Pulmonary Surfactant

↓ Diffuses/Dissolves

Alveolar Epithelium

↓ Diffuses/Dissolves

Alveolar Interstitium

↓ Diffuses/Dissolves

Capillary Endothelium

↓ Diffuses/Dissolves

Plasma

↓ Diffuses/Dissolves

Red Blood Cell

↓ Binds

Hemoglobin

Fick's Law for Diffusion

$$V_{\text{gas}} = \frac{A \times D \times (P_1 - P_2)}{T}$$

V_{gas} = volume of gas diffusing through the tissue barrier per time, in ml/min

A = surface area available for diffusion

D = diffusion coefficient of the gas (diffusivity)

T = thickness of the barrier

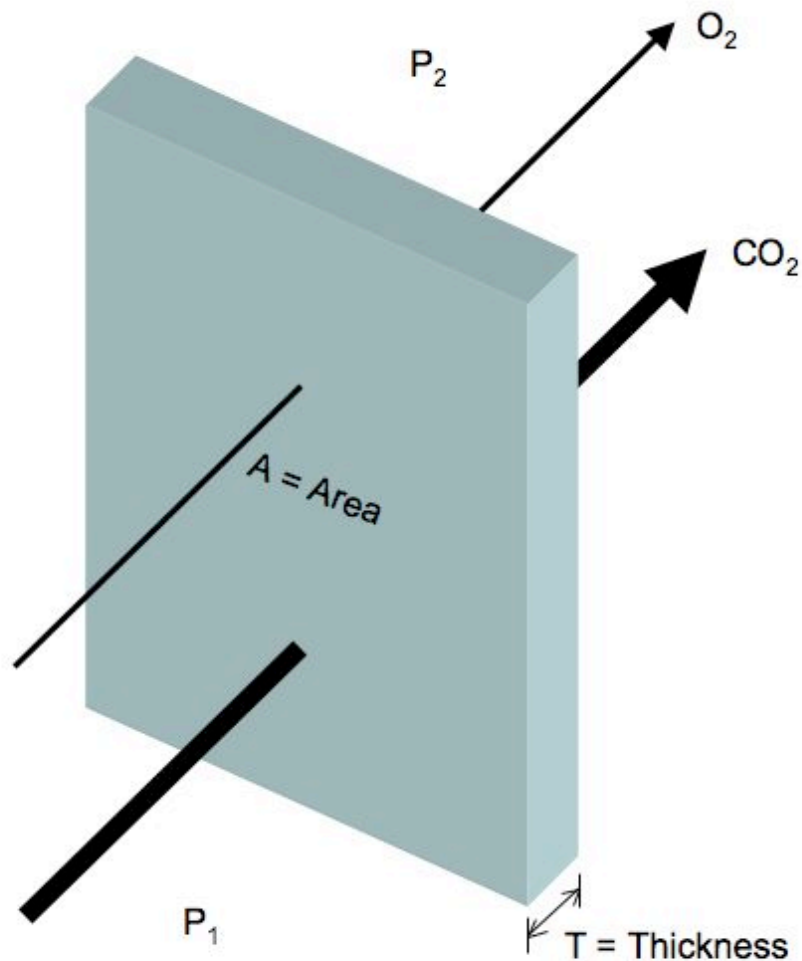
$P_1 - P_2$ = partial pressure difference of the gas

Diffusivity

$$D \cong \text{Solubility} / \sqrt{\text{MW}}$$

- O_2 has lower MW than CO_2
- Solubility of CO_2 is 24x that of O_2
- CO_2 diffuses 20x more rapidly through the alveolar capillary barrier than O_2

Diffusion Across a Membrane



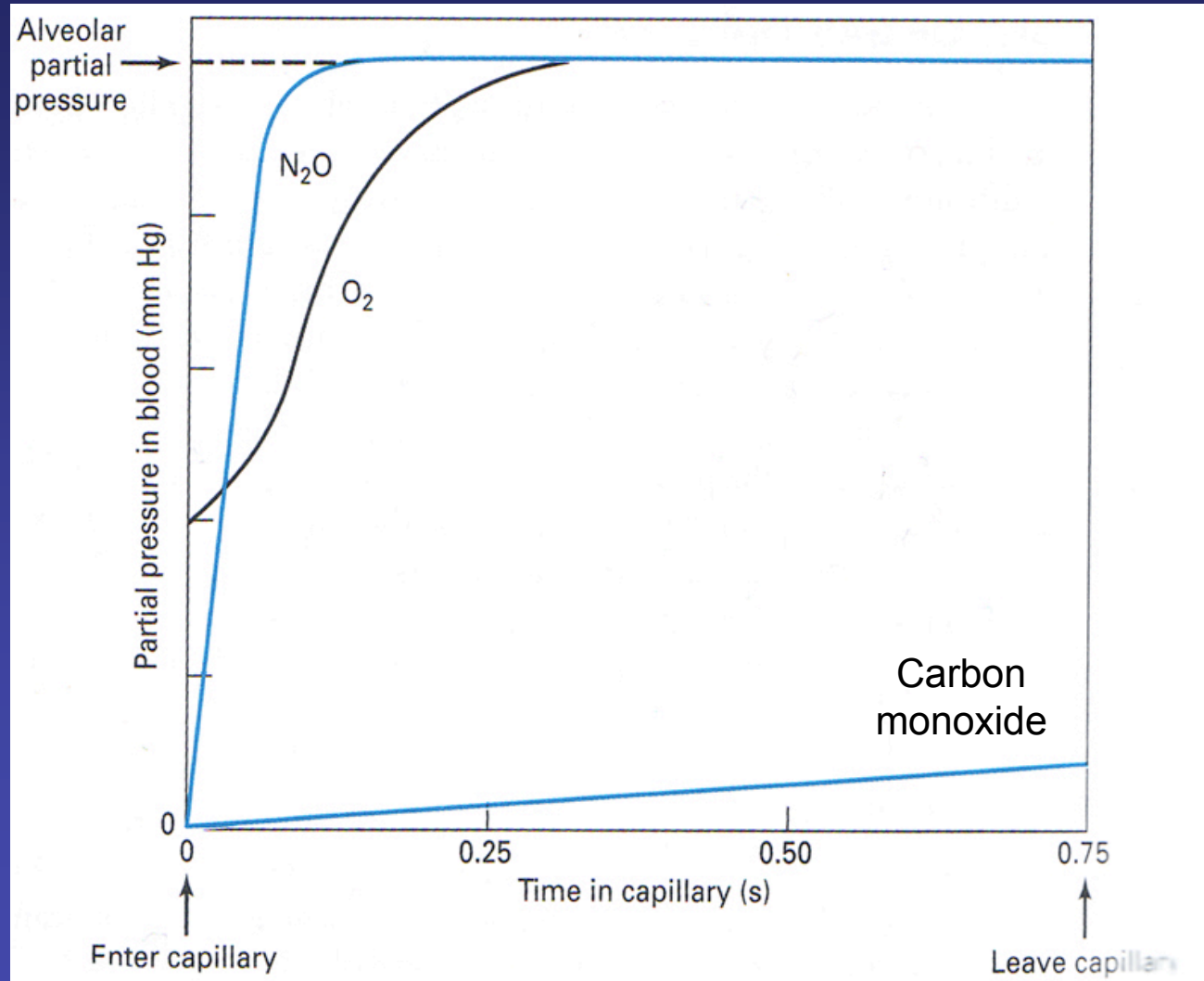
$$\dot{V}_{gas} = \frac{A \cdot D(P_1 - P_2)}{T}$$

$$D \propto \frac{\text{Solubility}}{\sqrt{MW}}$$

Limitations of Gas Transfer

- Diffusion Coefficient.
 - Different gases behave differently.
- Surface Area and Thickness of the alveolar wall.
- Partial Pressure Gradient across the alveolar wall for each individual gas.
 - Depends on both alveolar and mixed venous partial pressure (start of capillary).

Change in Blood Partial Pressure of Three Gases with Time in the Capillary

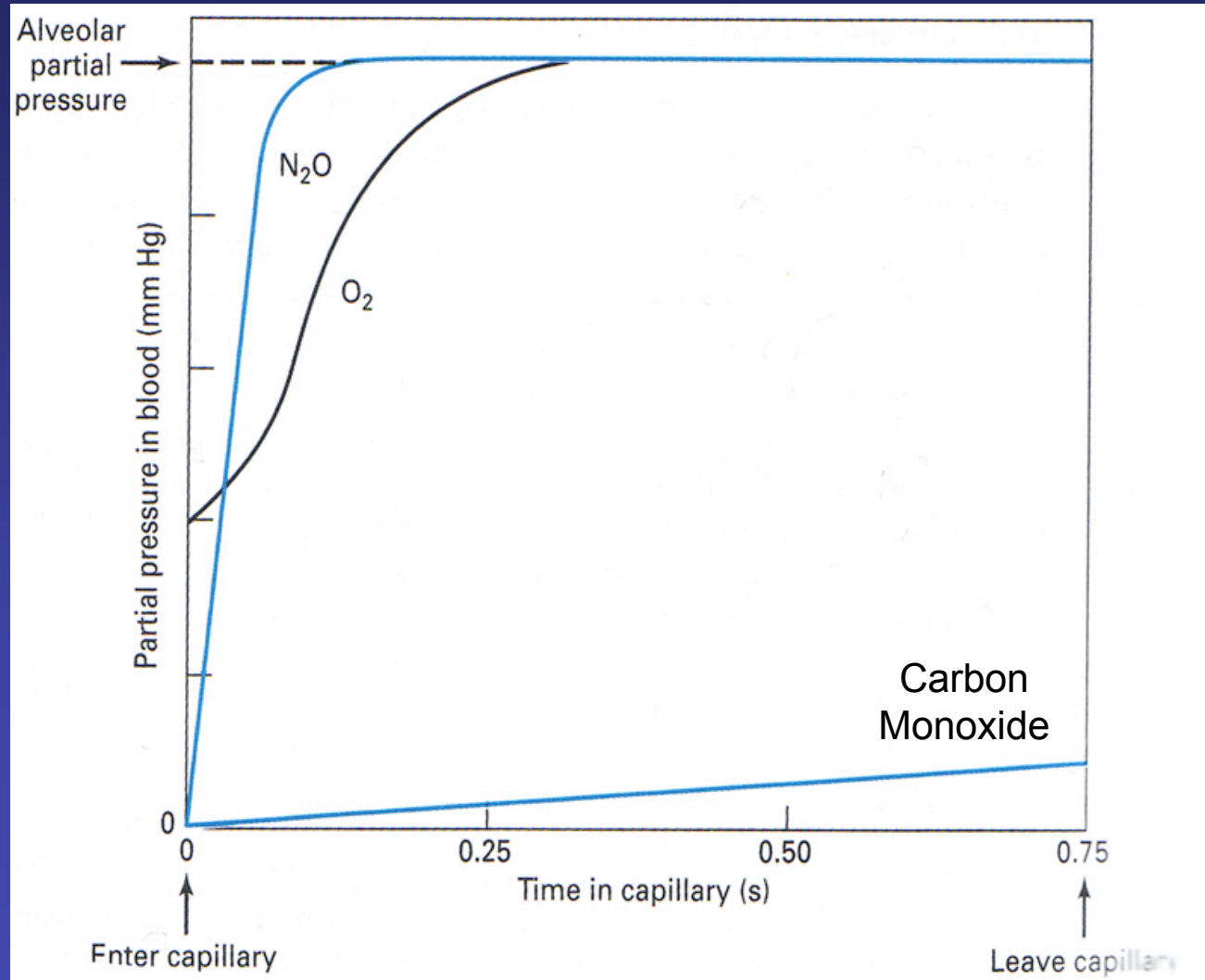


Source: *Pulmonary Physiology*, The McGraw-Hill Companies, Inc., 2007

N₂O is Perfusion Limited

- N₂O is very soluble in biological tissues and diffuses rapidly.
- P_cN₂O rises rapidly in the alveolar capillary
- Quickly have P_cN₂O = P_AN₂O.
- Because there is no pressure gradient, no diffusion occurs after about 0.1 sec.
- Fresh blood entering the capillary has not yet equilibrated and can still take up N₂O.
- Increased blood flow will increase gas transfer
- Transfer of N₂O is perfusion limited.

Change in Blood Partial Pressure of Three Gases with Time in the Capillary

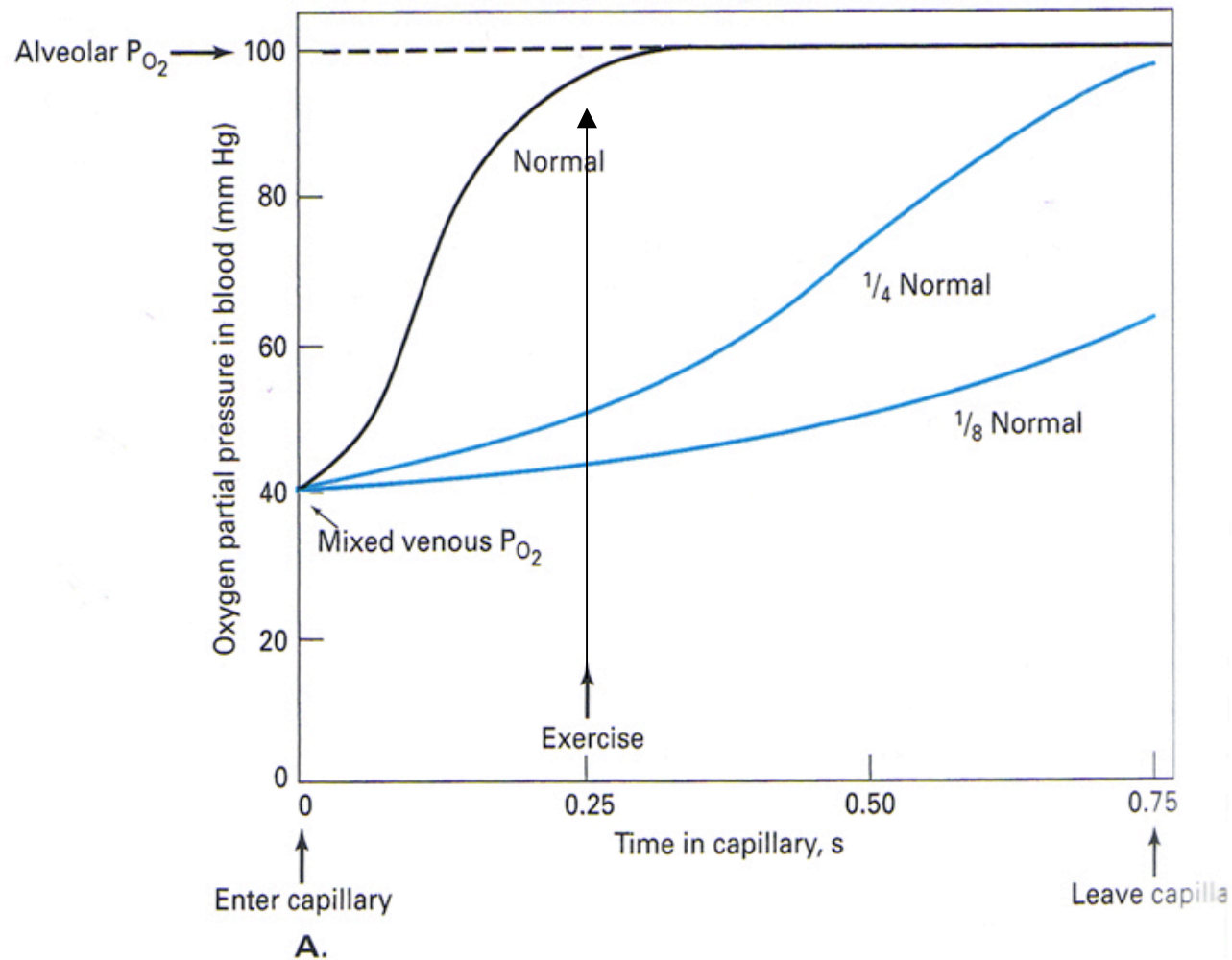


Source: *Pulmonary Physiology*, The McGraw-Hill Companies, Inc., 2007

Carbon Monoxide is Diffusion Limited

- Blood PCO rises very slowly because CO is bound to Hgb, with very little dissolved.
- Capillary P_cCO does not approach P_ACO.
- Partial pressure gradient is maintained throughout the time the blood is in the capillary.
 - Diffusion continues throughout this time.
- Transfer of CO is limited by diffusivity, surface area, and thickness of the wall.

Transfer of Oxygen

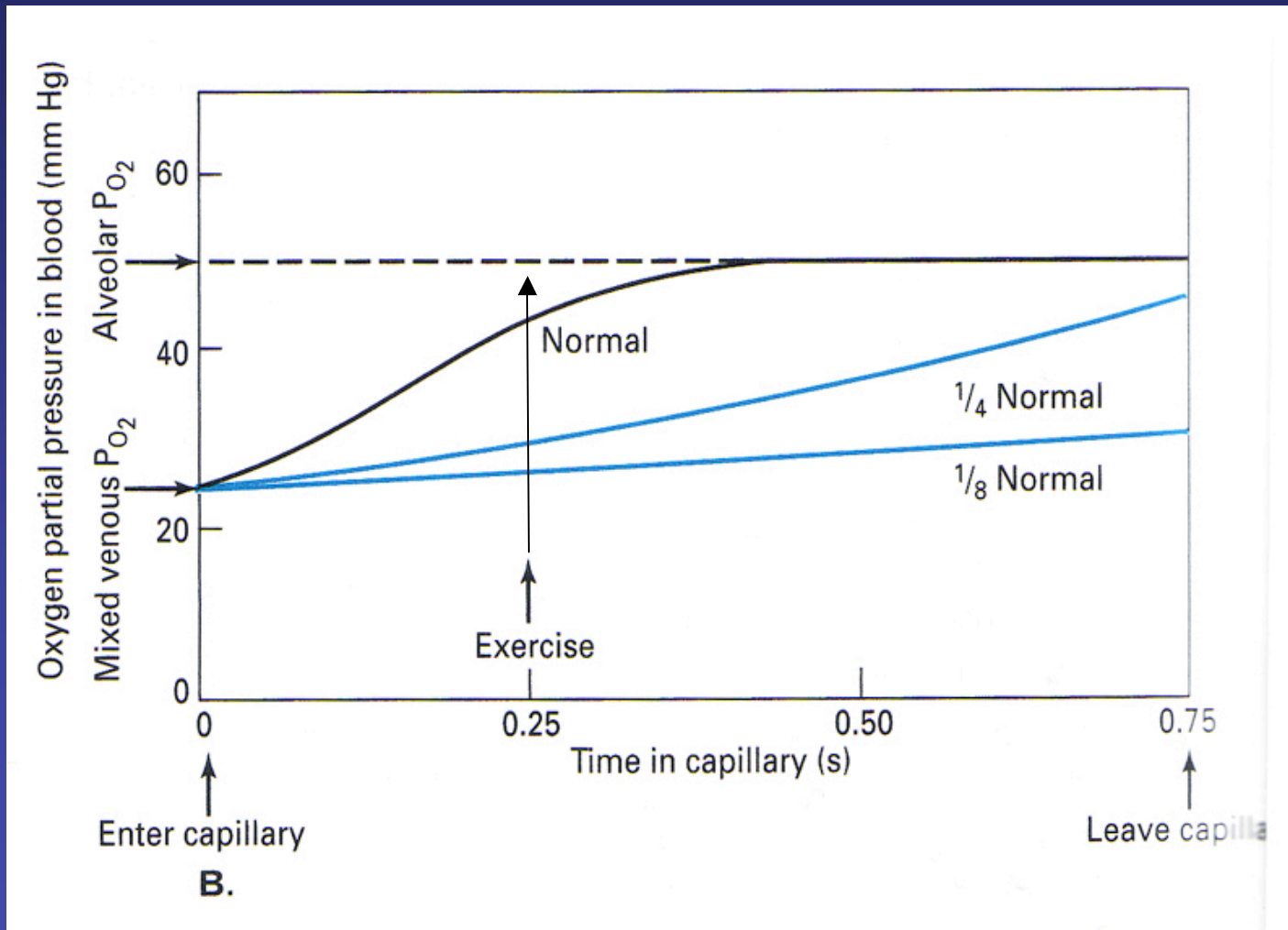


Source: *Pulmonary Physiology*, The McGraw-Hill Companies, Inc., 2007

Transfer of Oxygen

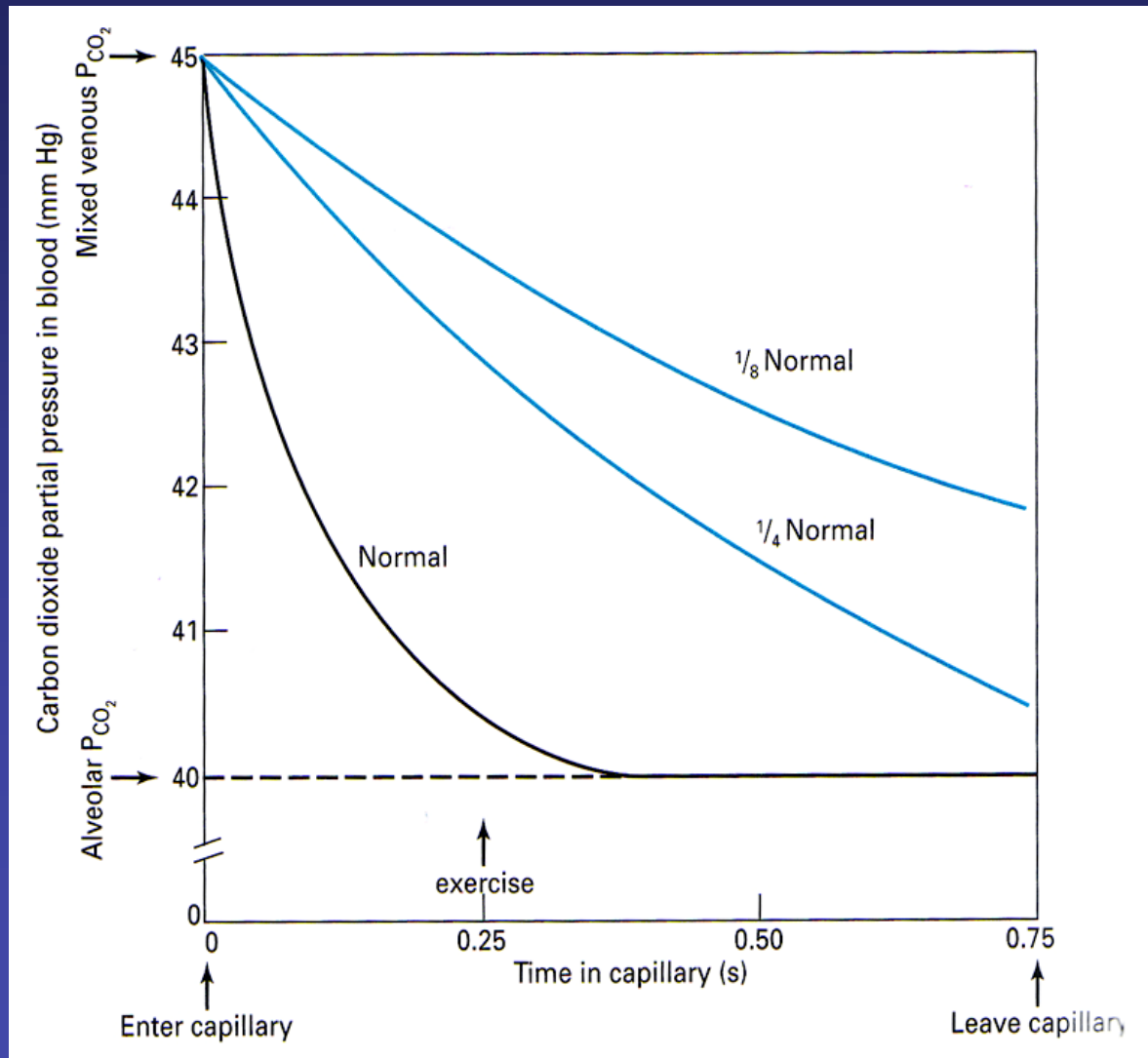
- Under normal conditions, P_{cO_2} reaches P_{AO_2} about 1/3 of the distance through the capillary.
- Therefore under normal conditions transfer is perfusion limited.
- With exercise, the time blood spends in the capillary is reduced- no longer perfusion but diffusion limitation.
- In the setting of thickened alveolar wall, transfer is reduced.
 - With severely disturbed diffusion, there is limitation even at rest

Transfer of Oxygen is Limited at Low Alveolar O₂



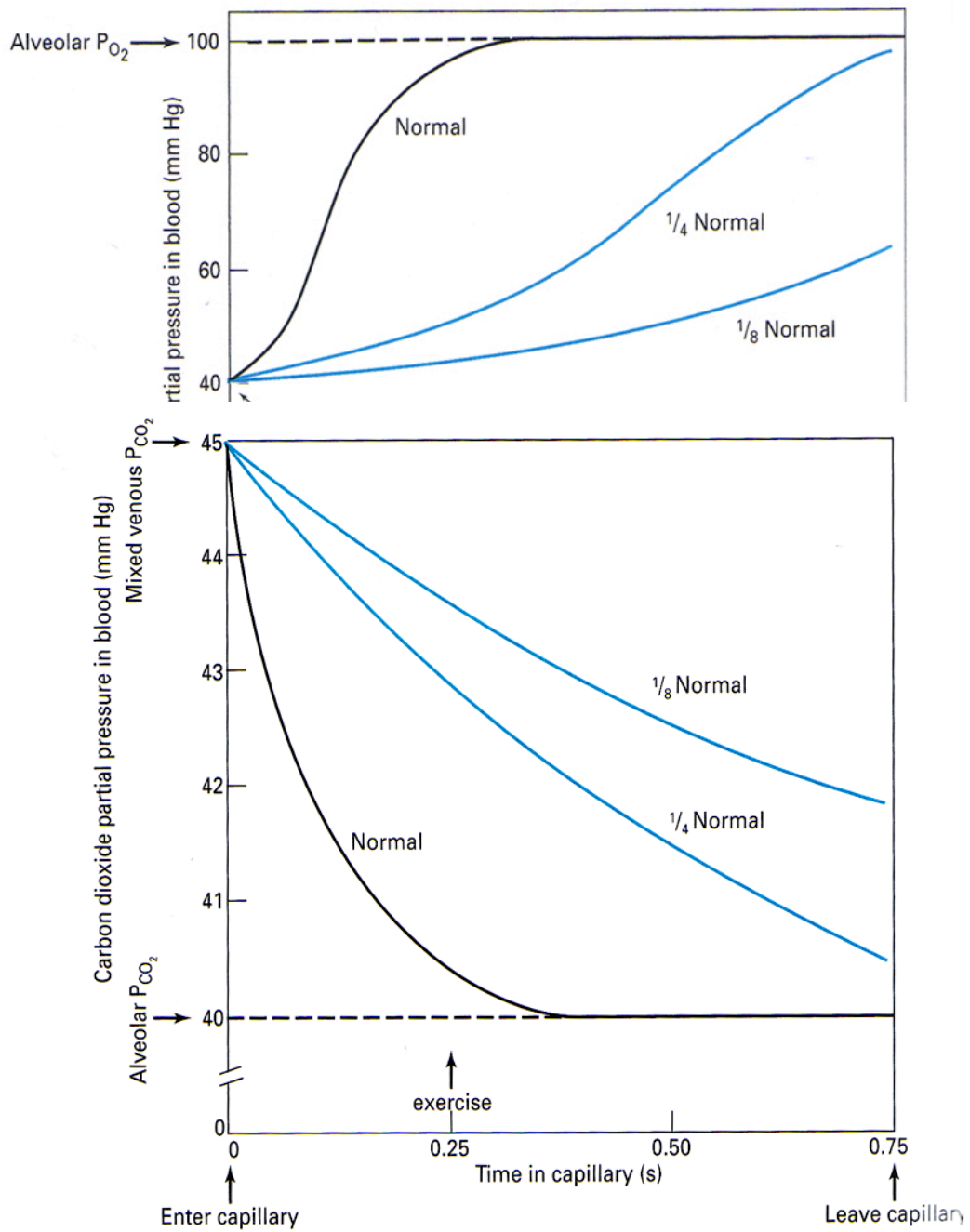
Source: *Pulmonary Physiology*, The McGraw-Hill Companies, Inc., 2007

Transfer of CO₂



- Is transfer of CO₂ diffusion or perfusion limited?

Source: *Pulmonary Physiology*, The McGraw-Hill Companies, Inc., 2007



Source: *Pulmonary Physiology*, The McGraw-Hill Companies, Inc., 2007

Transfer of CO₂

Why is the transfer of CO₂ so similar to that of O₂?

$$V_{\text{gas}} = \frac{A \times D \times (P_1 - P_2)}{T}$$

Diffusivity of CO₂ is 20x > than that of O₂

Partial pressure gradient of CO₂ is 45→40

Partial pressure gradient of O₂ is 100→40

Fick's Law for Diffusion

$$V_{gas} = \frac{(AxD)}{T} \times (P_1 - P_2)$$

V_{gas} = volume of gas diffusing through
the tissue barrier per time, in ml/min

A = surface area available for diffusion

D = diffusion coefficient of the gas (diffusivity)

T = thickness of the barrier

$P_1 - P_2$ = partial pressure difference of the gas

$(AxD)/T$ = diffusing capacity of the lung (DL)

Diffusing Capacity

$$\frac{(Ax D)}{T} = \frac{\dot{V}_{gas}}{(P_1x - P_2x)} = D_{Lx}$$

Source: Undetermined

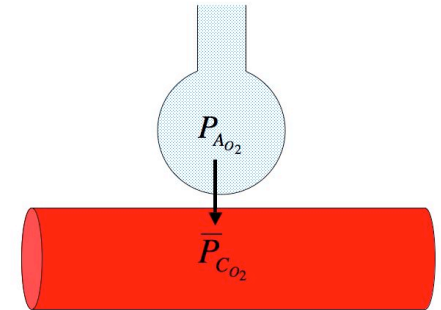
Measuring Diffusing Capacity

- Inhale mixture containing known concentration of tracer gas.
- Allow diffusion from alveolus into blood.
- Measure concentration of tracer in exhaled gas.
- Calculate rate of removal of tracer gas by diffusion into blood and the partial pressure gradient from alveolus into blood.
- Choice of gas:
 - Readily available.
 - Easily measured.
 - Diffusion limited.
 - No arterial partial pressure.

We Could Use $D_{L}O_2$

$$\frac{A \times D}{T} = D_{L}O_2$$

$$\dot{V}_{O_2} = D_{L}O_2 (P_{A}O_2 - P_{C}O_2) = \text{ml } O_2 / \text{min}$$

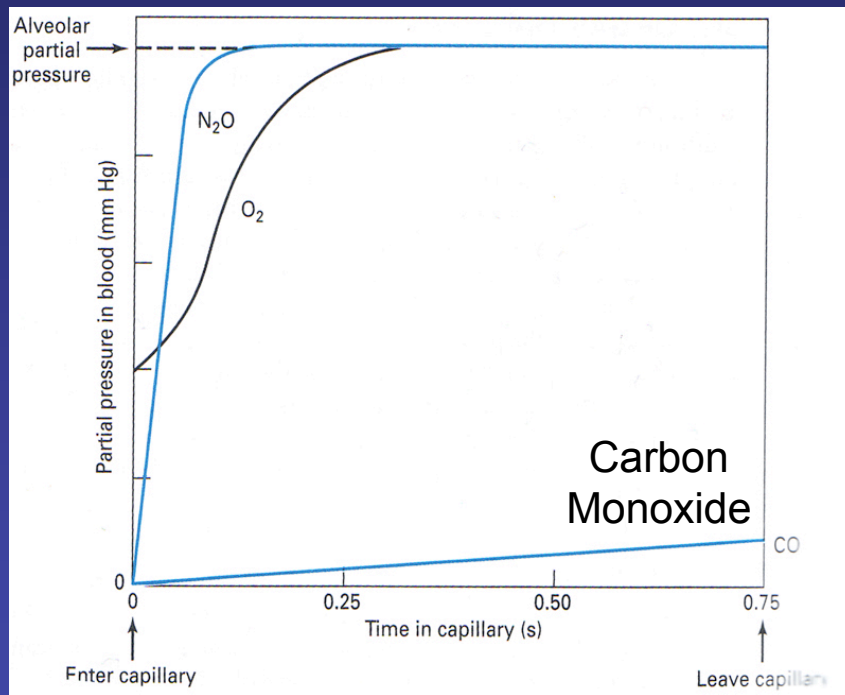


$$D_{L}O_2 = \frac{\dot{V}_{O_2}}{(P_{A}O_2 - P_{C}O_2)}$$

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Carbon Monoxide is an Ideal Gas for Measuring Diffusing Capacity



Source: *Pulmonary Physiology*, The McGraw-Hill Companies, Inc., 2007

- CO binds avidly to hemoglobin.
- While CO content of the blood rises, the PCO in blood rises very slowly.
- The gradient of partial pressures from alveolus to blood remains almost constant during test

Carbon Monoxide Measurement of Diffusing Capacity

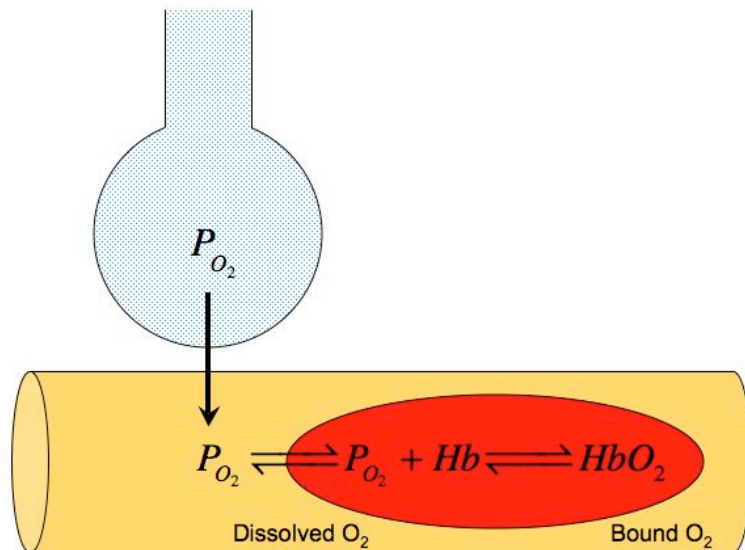
$$DLCO = \frac{\dot{V}_{CO}}{P_A CO - P_c CO}$$

$$P_c CO \approx 0$$

$$DLCO = \frac{\dot{V}_{CO}}{P_A CO}$$

Normal DLCO = 20-30 ml/min/mmHg

DLCO Has Two Components



Diffusion across the alveolar membrane.

Reaction with hemoglobin.

$$\frac{1}{DL} = \frac{1}{Dm} + \frac{1}{\theta_x Vc}$$

Conditions that Impact Diffusion Capacity for CO.

$$DLCO = \frac{A \times D}{T}$$

- Decreased Surface Area.
 - Destruction of Alveolar Wall
- Increased Barrier Thickness.
- Anemia.

How would the Following Change the Diffusion Capacity of the Lungs?

- Changing from supine to upright
- Exercise
- Anemia
- Valsalva maneuver
- Low cardiac output due to hemorrhage
- Emphysema
- Pulmonary fibrosis