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Diffusion of Gases

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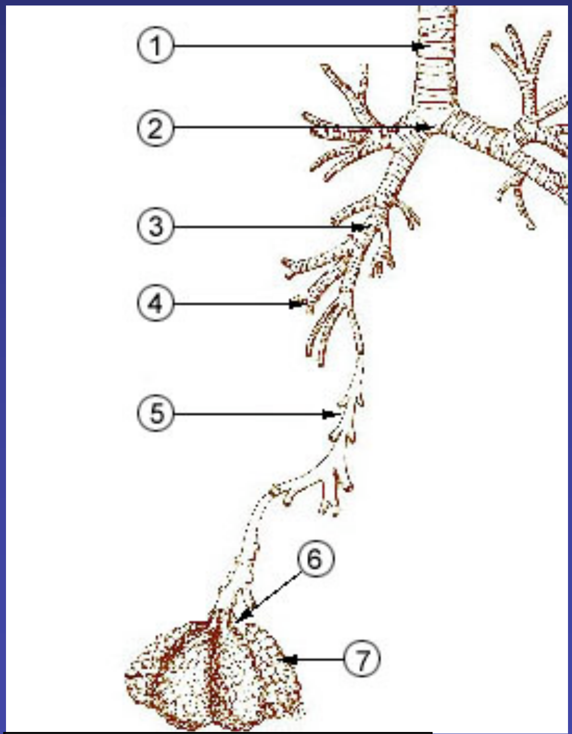
Objectives

- 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 CO_2 from blood to alveoli
  - Define diffusing capacity and discuss its measurement

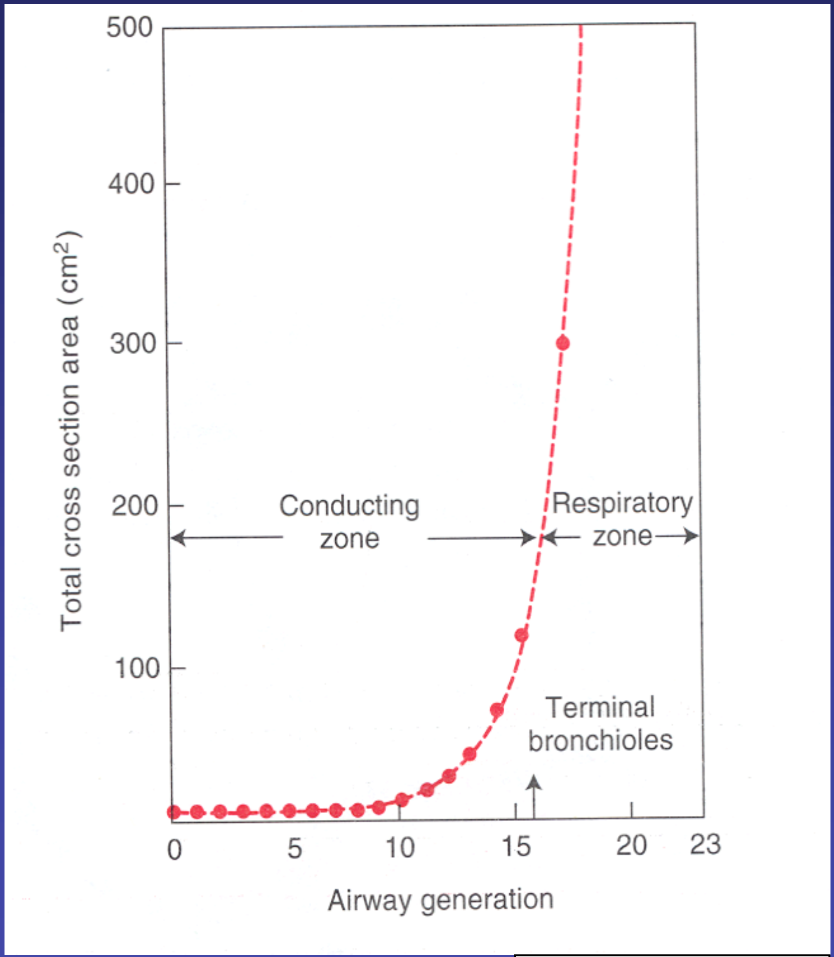
Airway Branching



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



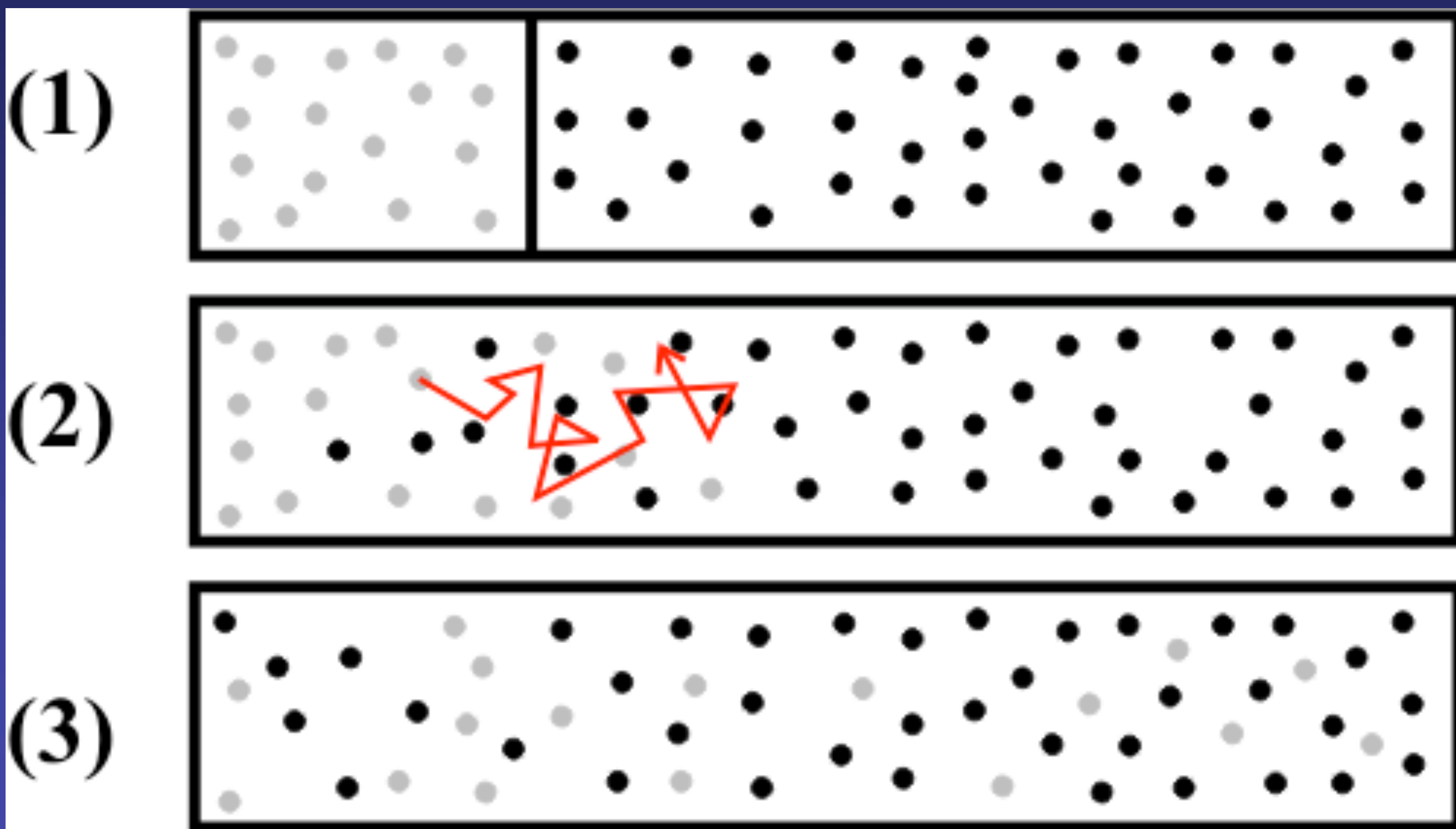
Source: Undetermined

- 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

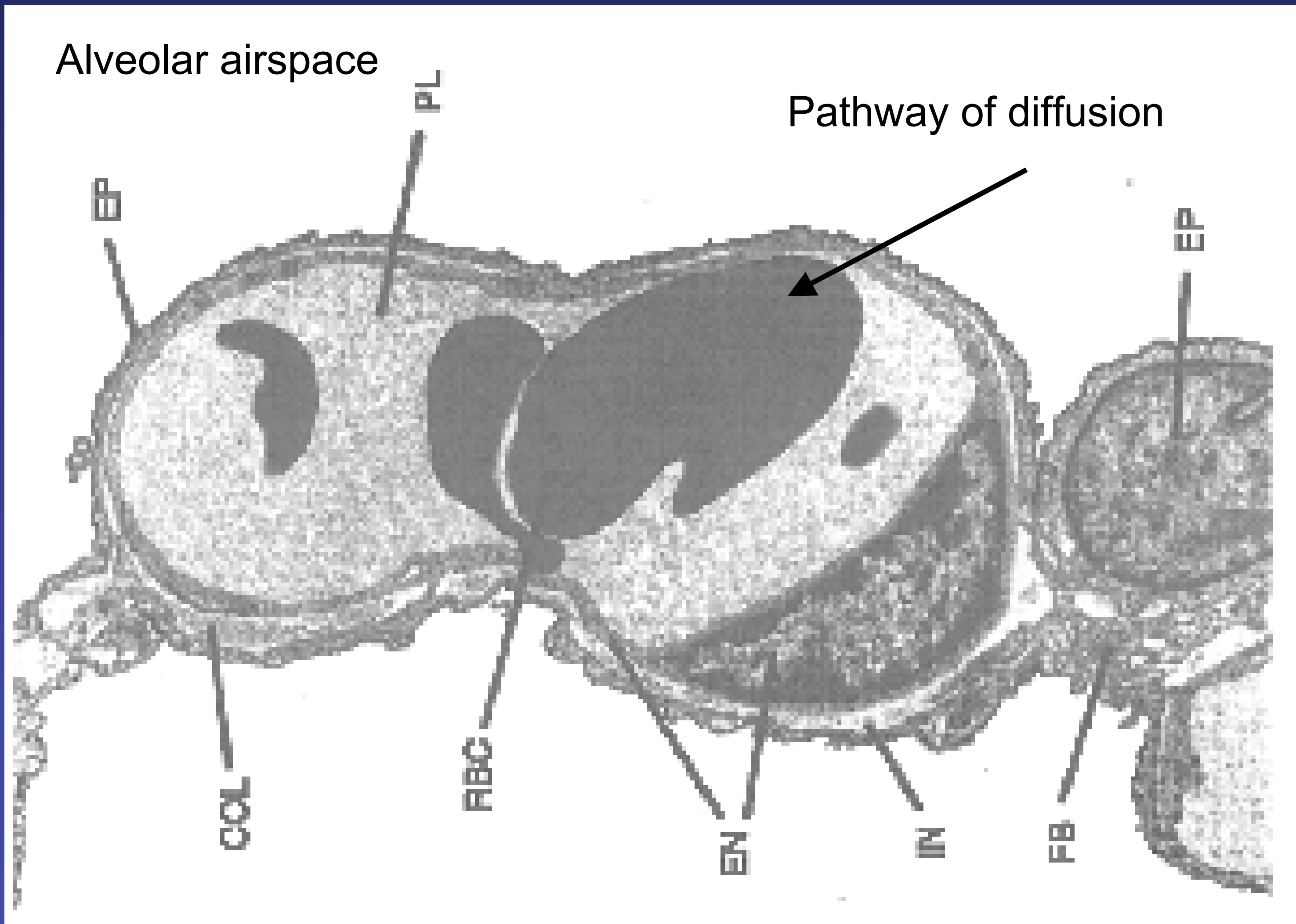


Source: Jkrieger (wikimedia.org)

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

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

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

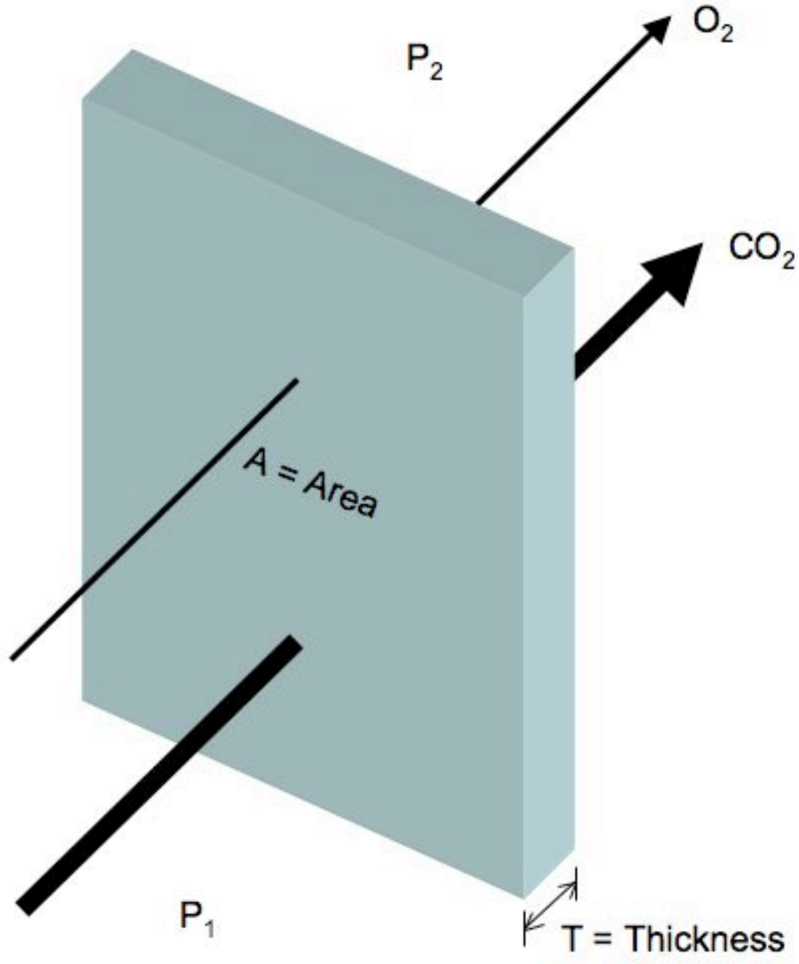
A = surface area available for diffusion
D = diffusion coefficient of the gas (diffusivity)
T = thickness of the barrier
$P_1 - P_2$ = partial pressure difference of the gas

Diffusivity

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

- 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



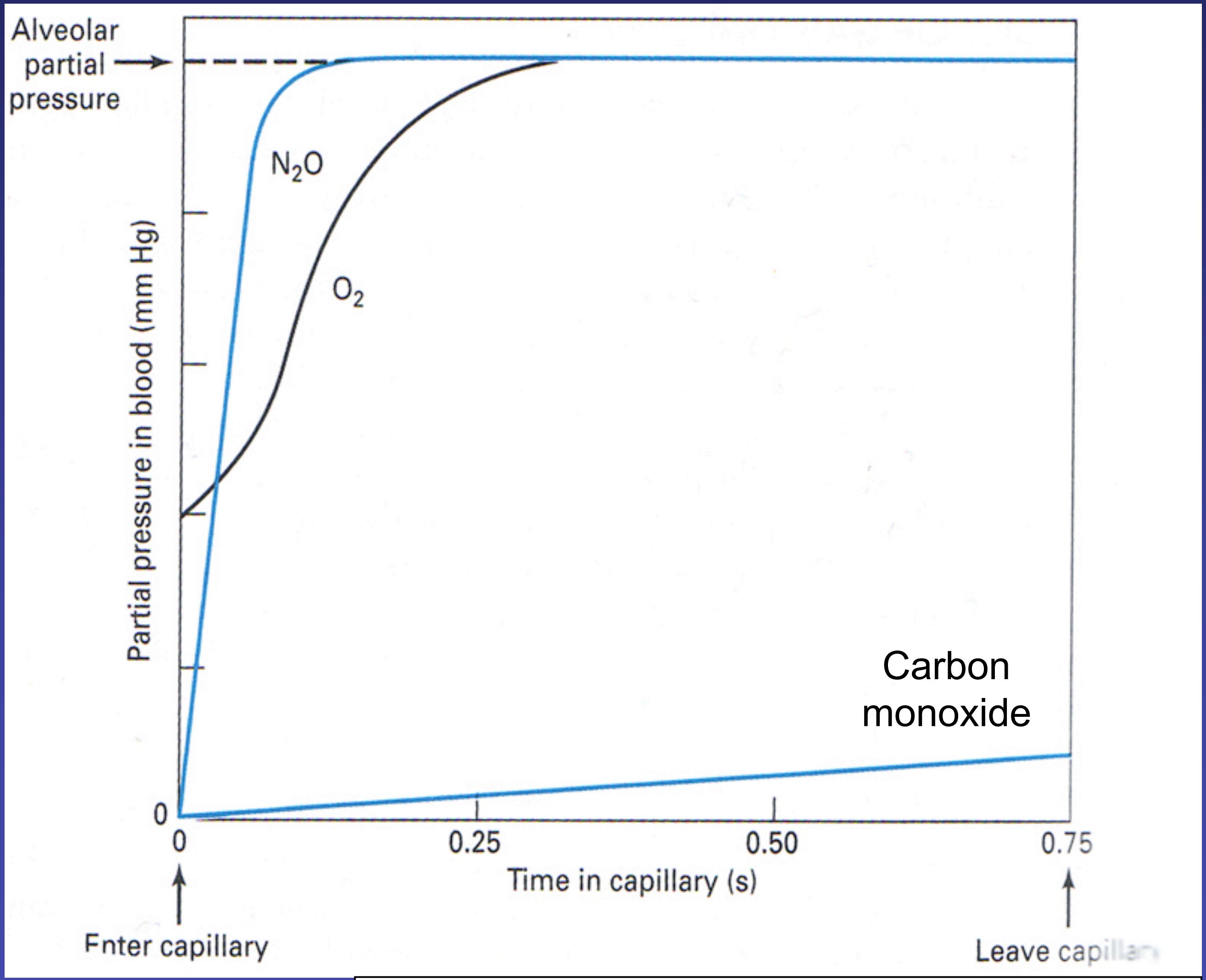
$$\dot{V}_{gas} = \frac{A \cdot D(P_1 - P_2)}{T}$$

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

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

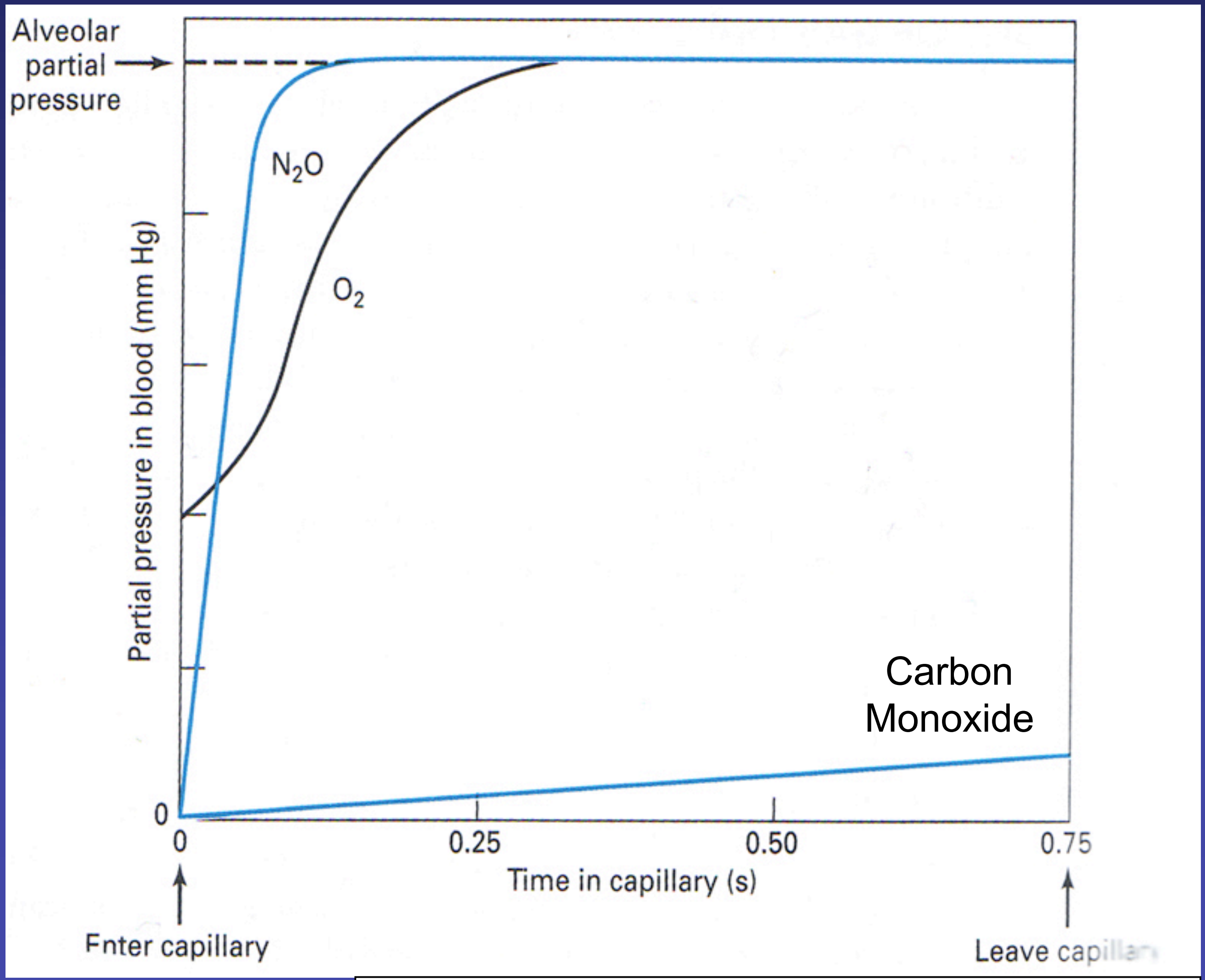


Source: *Pulmonary Physiology*, The McGraw-Hill Companies, Inc., 2007

N_2O is Perfusion Limited

– N_2O is very soluble in biological tissues and diffuses rapidly.
– PcN_2O rises rapidly in the alveolar capillary
– Quickly have $PcN_2O = P_AN_2O$.
– 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 N_2O.
– Increased blood flow will increase gas transfer
– Transfer of N_2O is perfusion limited.

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

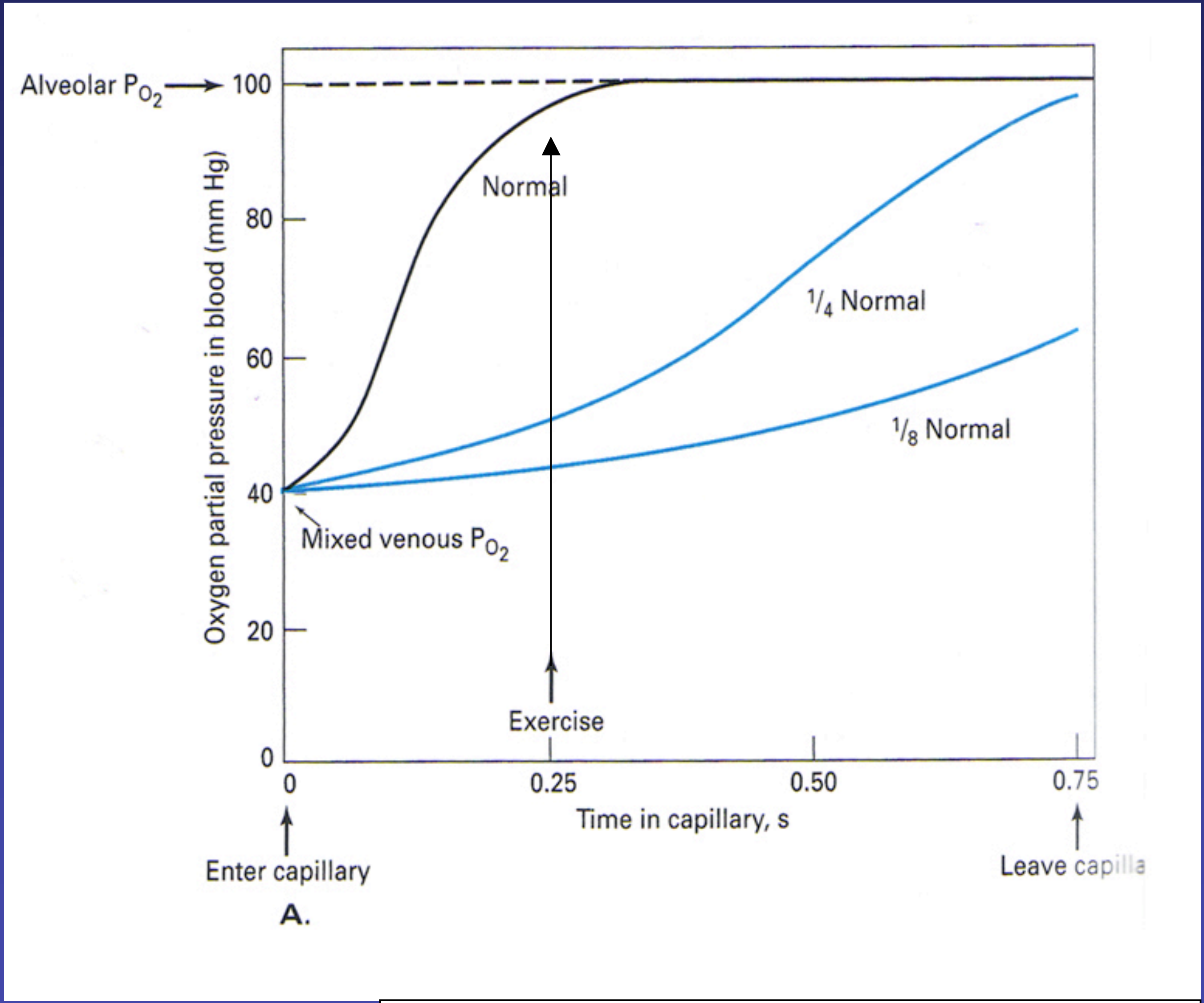


Source: *Pulmonary Physiology*, The McGraw-Hill Companies, Inc., 2007

Carbon Monoxide is <u>Diffusion Limited</u>

- 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

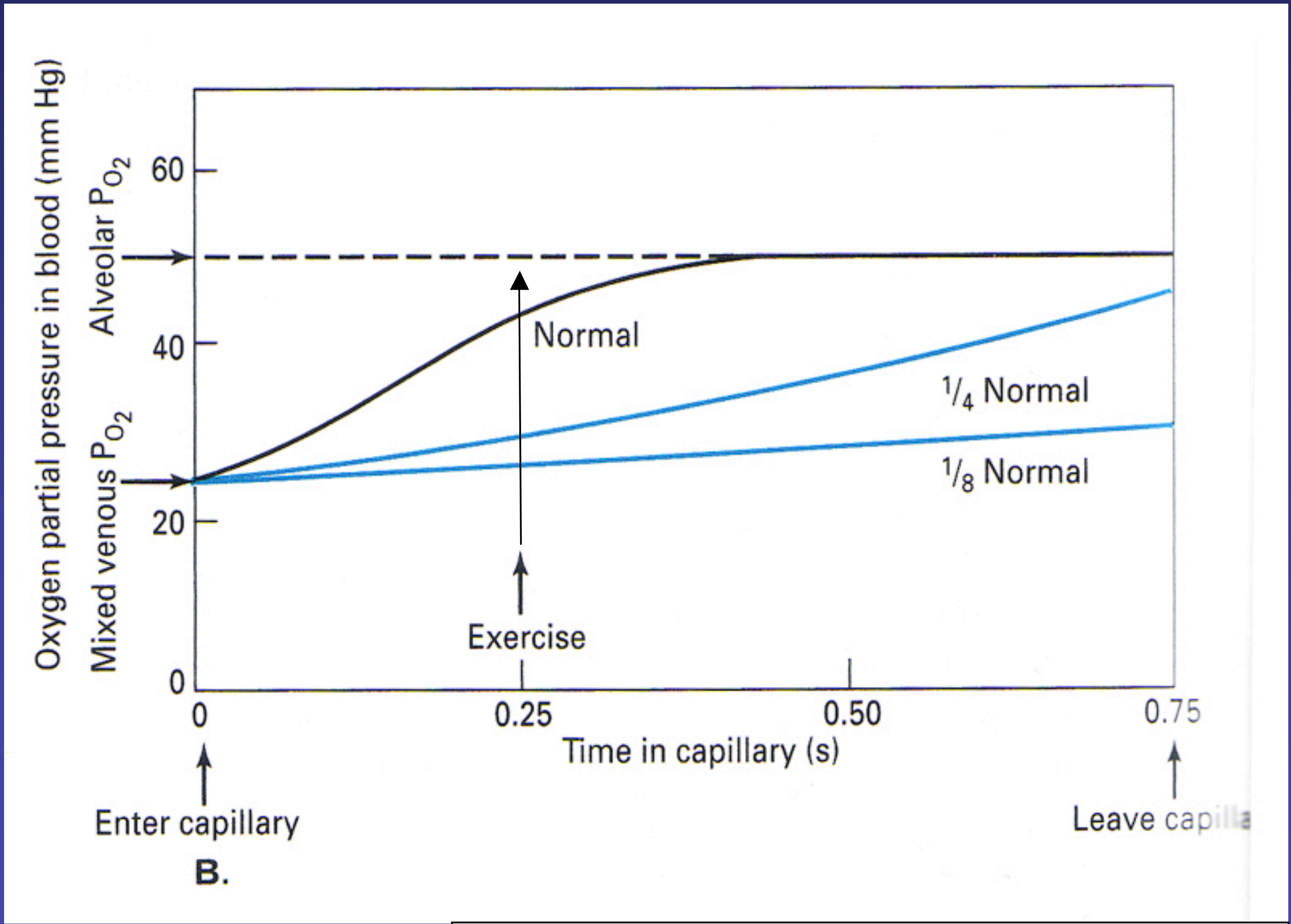


Source: *Pulmonary Physiology*, The McGraw-Hill Companies, Inc., 2007

Transfer of Oxygen

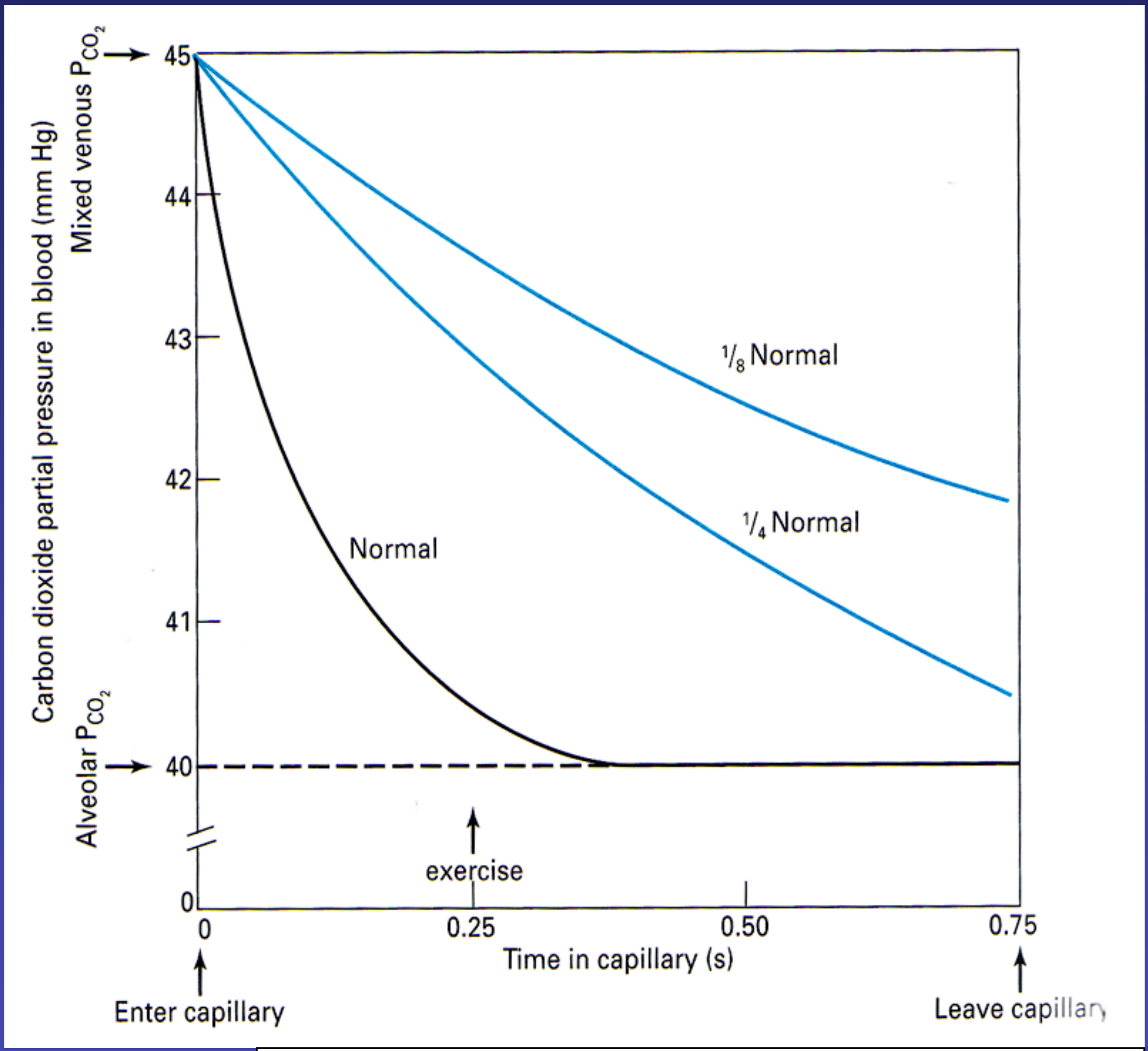
- Under normal conditions, P_cO_2 reaches P_AO_2 about 1/3 of the distance through the capillary.
- Therefore under normal conditions transfer is perfusion limited.
- With exercise, the time blood spends in the capillary is reduced- no longer perfusion but diffusion limitation.
- In the setting of thickened alveolar wall, transfer is reduced.
  - With severely disturbed diffusion, there is limitation even at rest

Transfer of Oxygen is Limited at Low Alveolar O_2



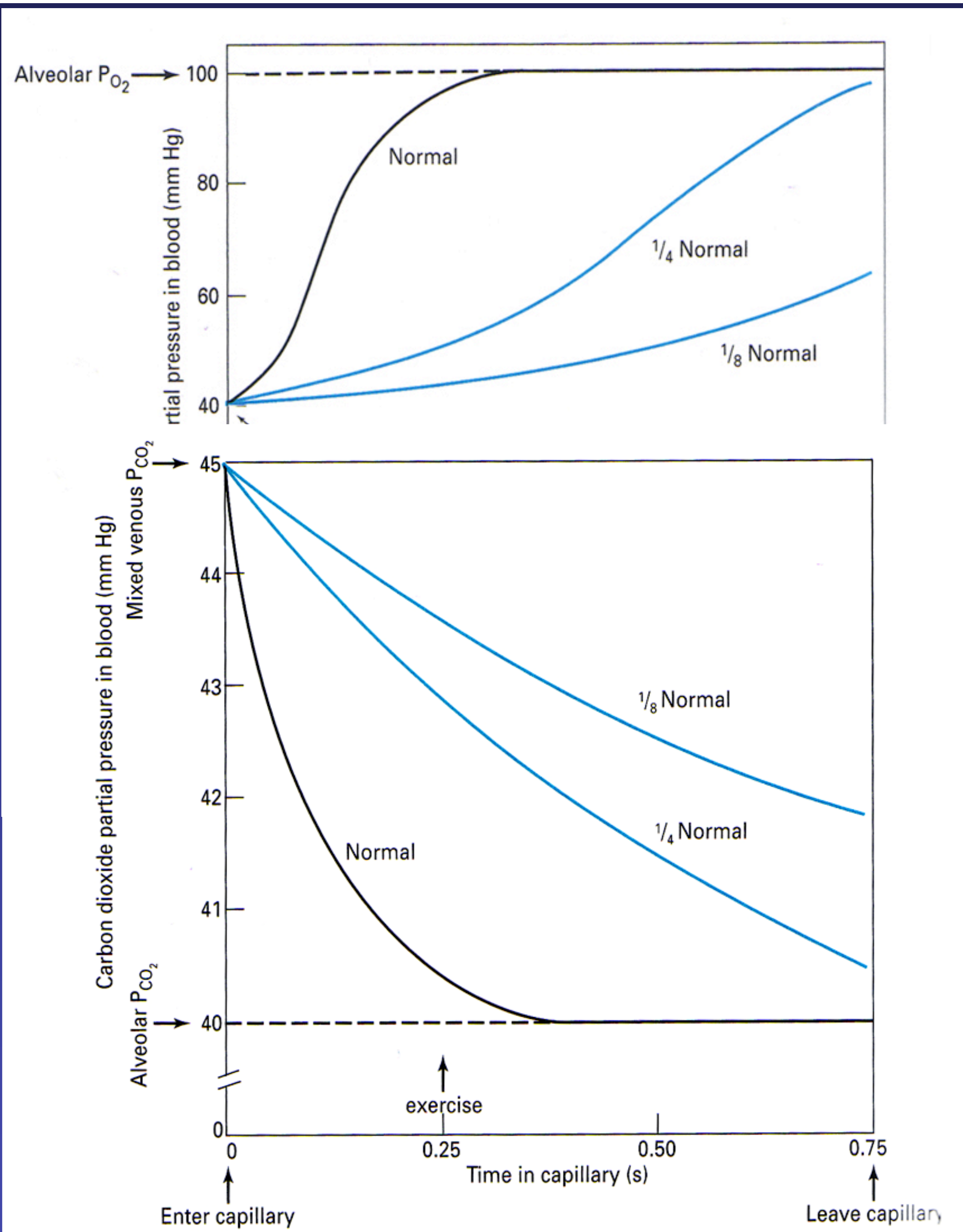
Source: *Pulmonary Physiology*, The McGraw-Hill Companies, Inc., 2007

Transfer of CO_2



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

- Is transfer of CO_2 diffusion or perfusion limited?



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

Transfer of CO_2

Why is the transfer of CO_2 so similar to that of O_2?

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

Diffusivity of CO_2 is 20x > than that of O_2

Partial pressure gradient of CO_2 is 45$\rightarrow$40

Partial pressure gradient of O_2 is 100$\rightarrow$40

Fick's Law for Diffusion

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

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

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

Source: Undetermined

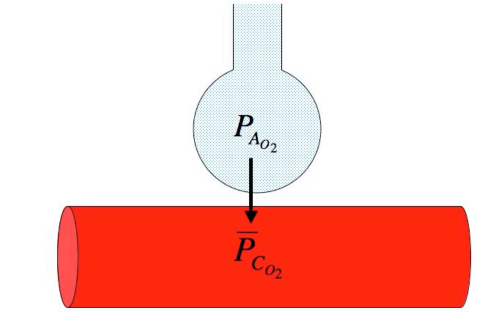
Measuring Diffusing Capacity

- 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 DLO_2

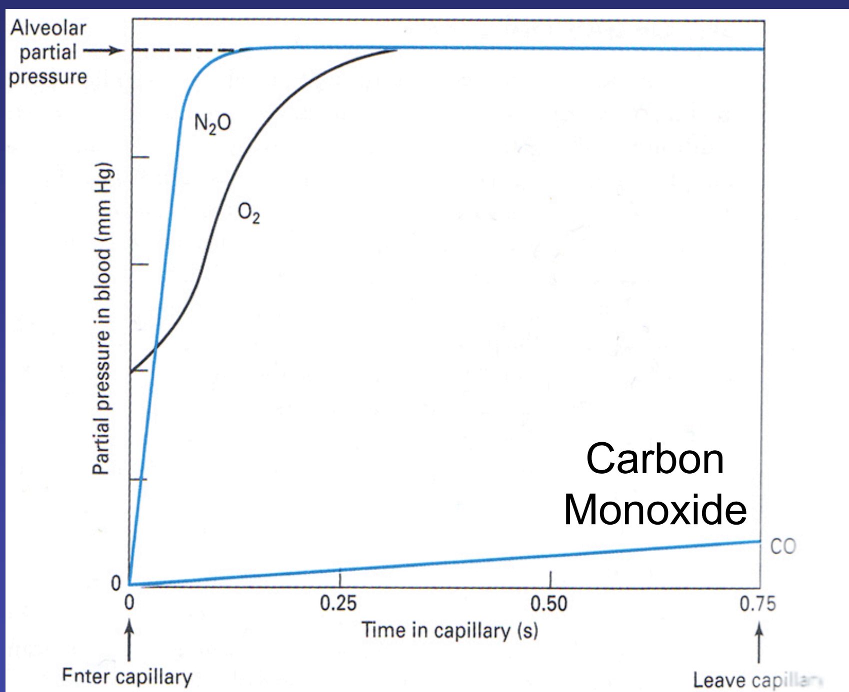
$$\frac{A x D}{T} = D_L O_2$$

$$\dot{V}_{O_2} = D_L O_2 \left(P_A O_2 - P_C O_2 \right) = \text{ml } O_2 / \text{min}$$



$$D_L O_2 = \frac{\dot{V}_{O_2}}{\left(P_A O_2 - P_C O_2 \right)}$$

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

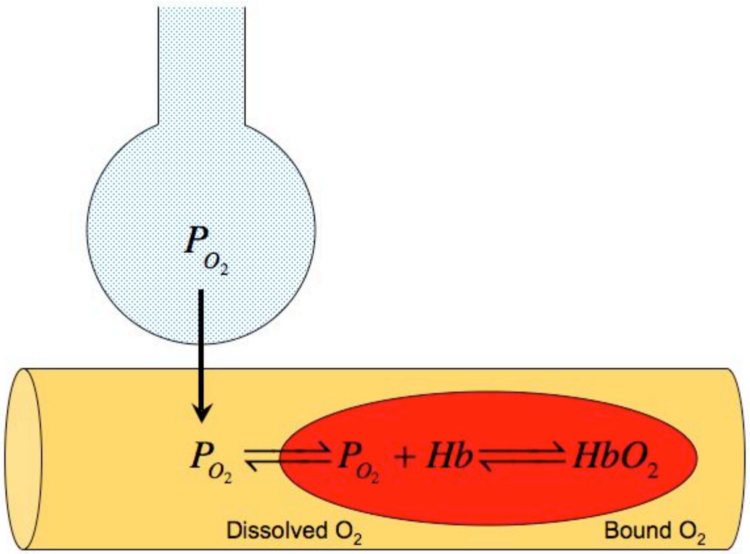
$$DLCO = \frac{\dot{V}_{CO}}{P_ACO - P_cCO}$$

$$PcCO \approx 0$$

$$\boxed{DLCO = \frac{\dot{V}_{CO}}{P_ACO}}$$

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.

$$DLCO = \frac{AxD}{T}$$

- 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