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Diffusion of Gases

M1 – Cardiovascular/Respiratory Sequence

Thomas Sisson, MD

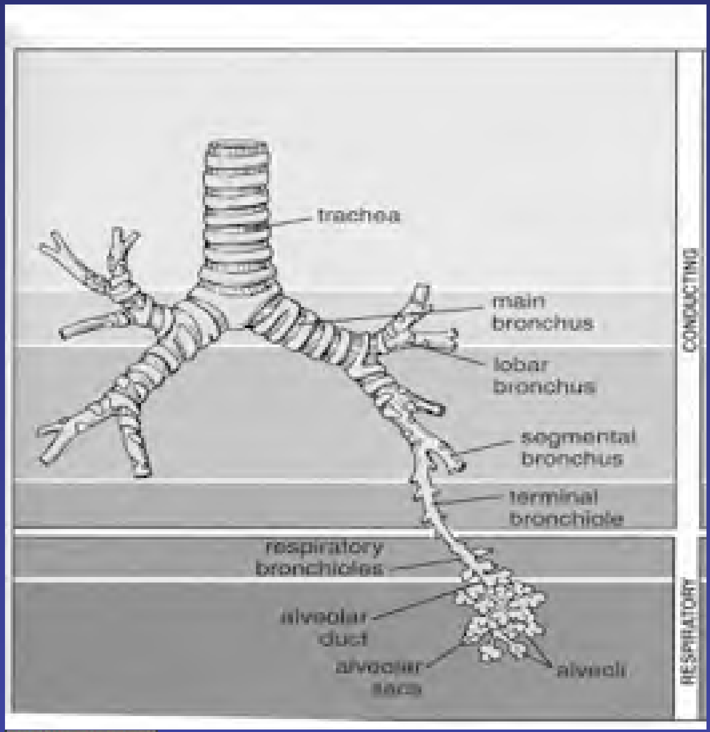
University of Michigan Medical School

Fall 2008

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

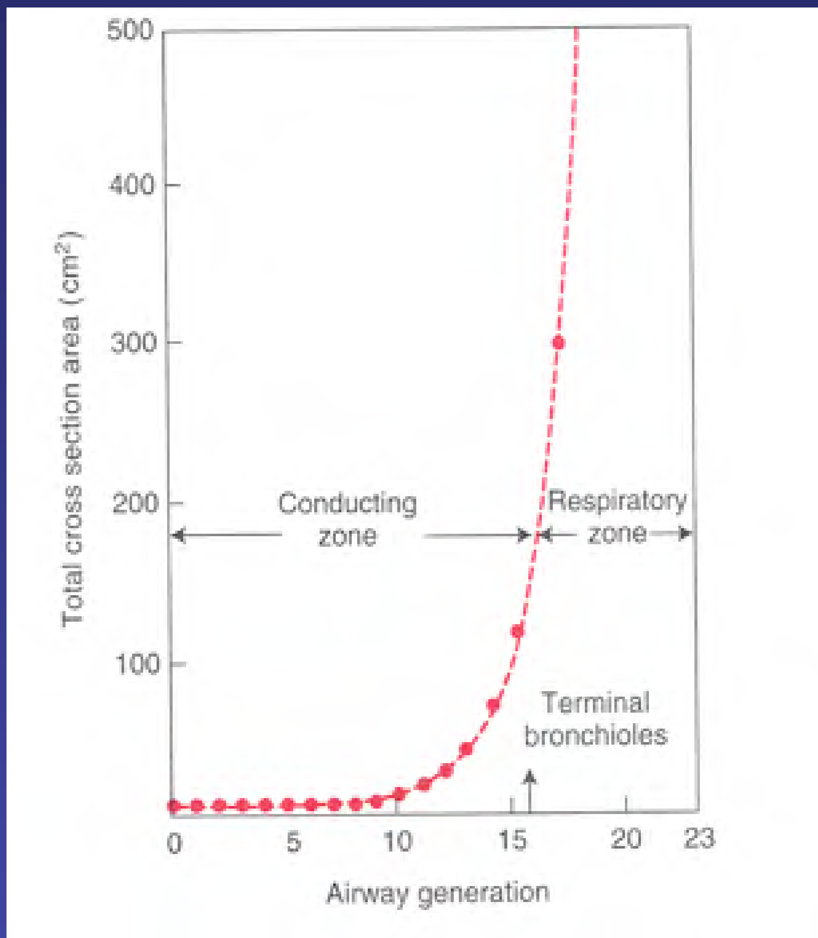
Airway Branching



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

PD-INEL Histology – A Text and Atlas; 5th edition, 2006, Ross and Pawlina, Lippincott Williams and Wilkins Fig 19.

Bulk Flow vs. Diffusion



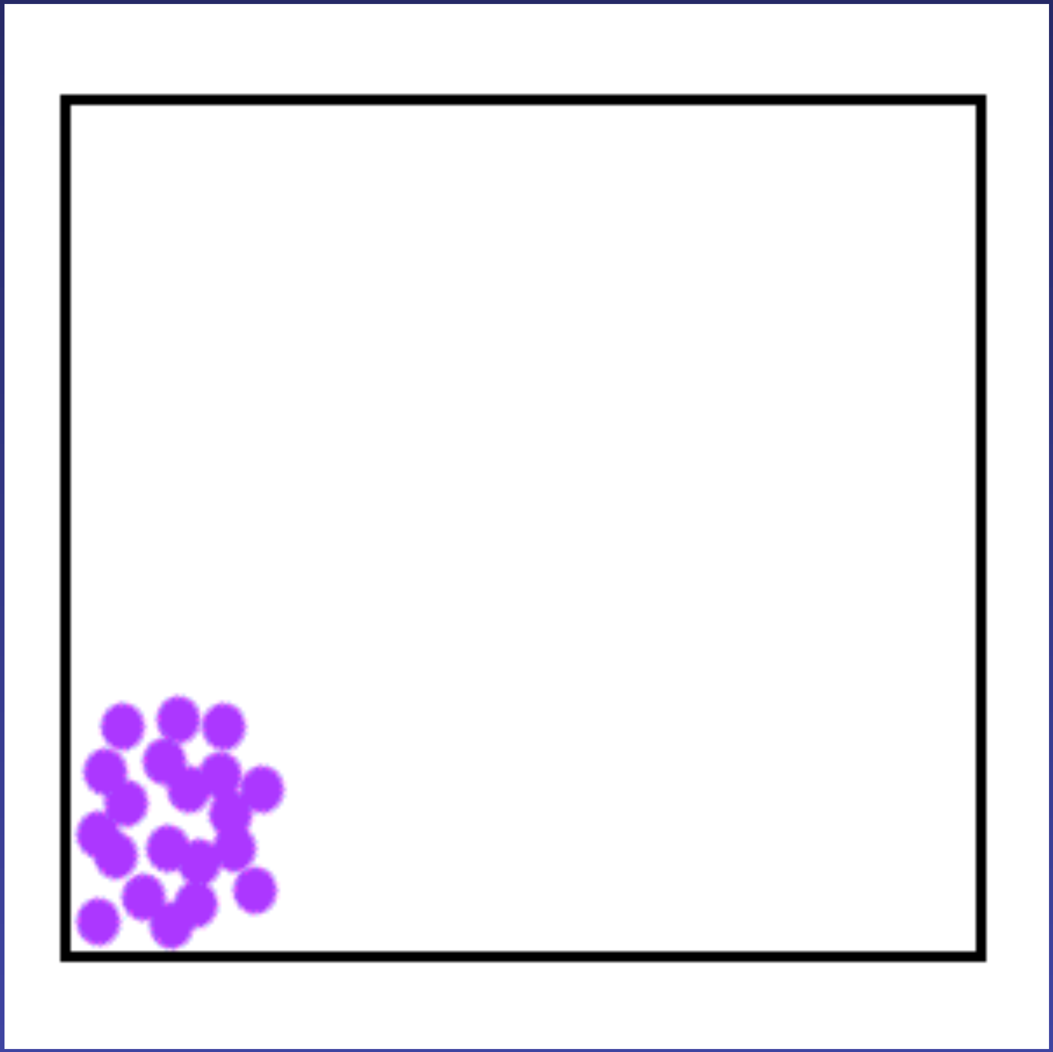
PD-INEL West. Respiratory Physiology: The Essentials 8th ed. Lippincott Williams & Wilkins. 2008

- 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.

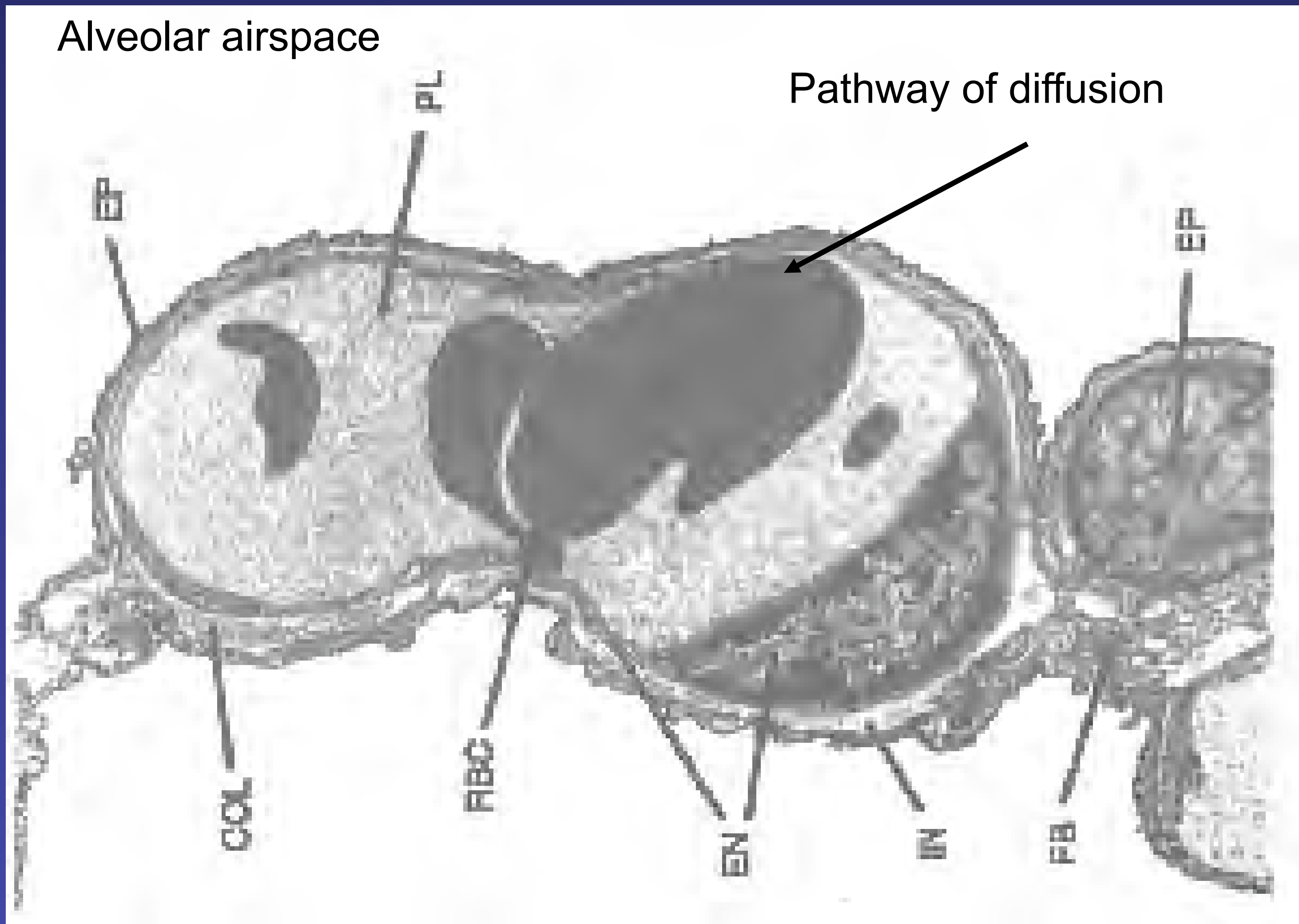
Gas Movement due to Diffusion



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

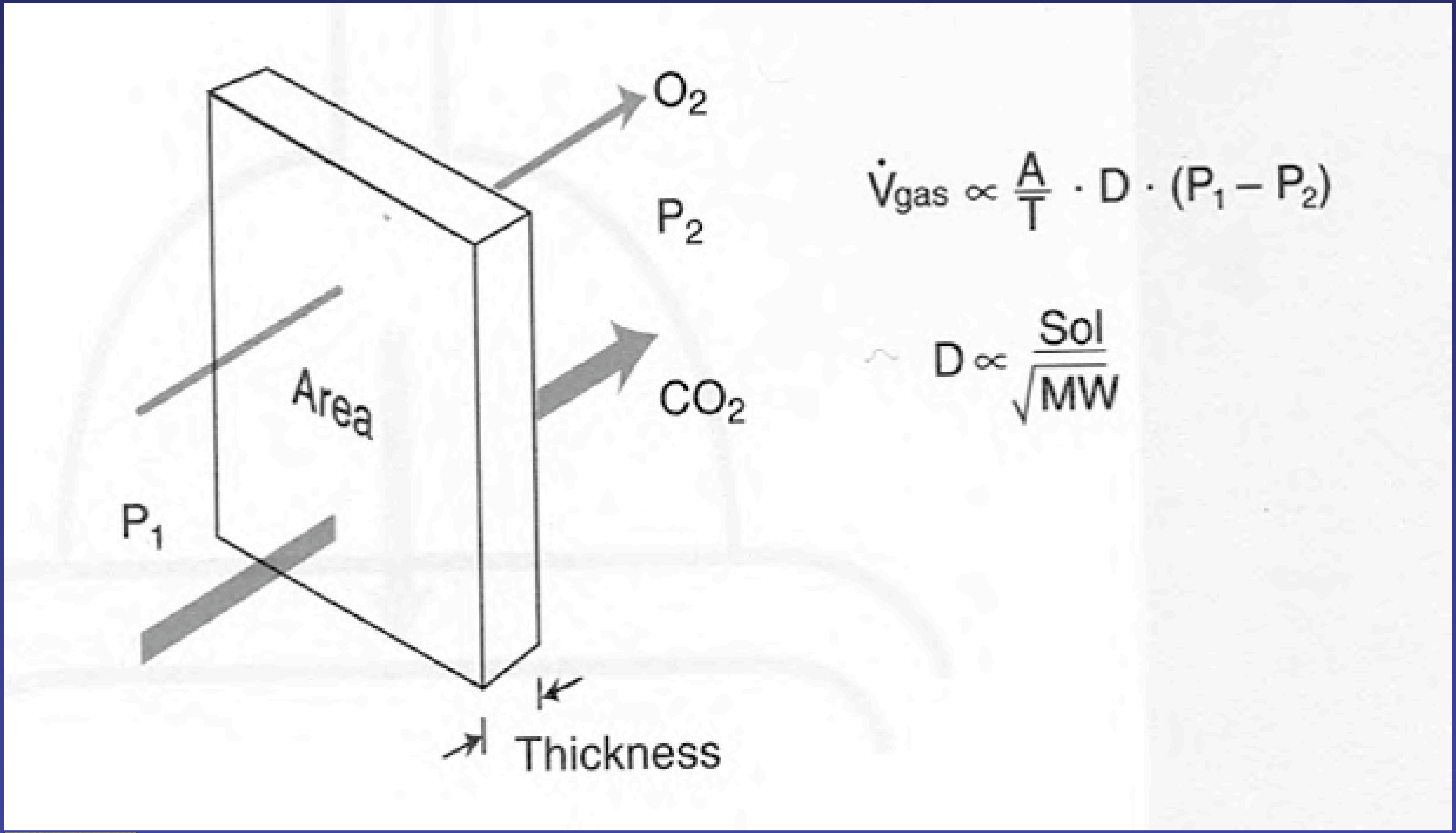
$P_1 - P_2$ = partial pressure difference of the gas

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

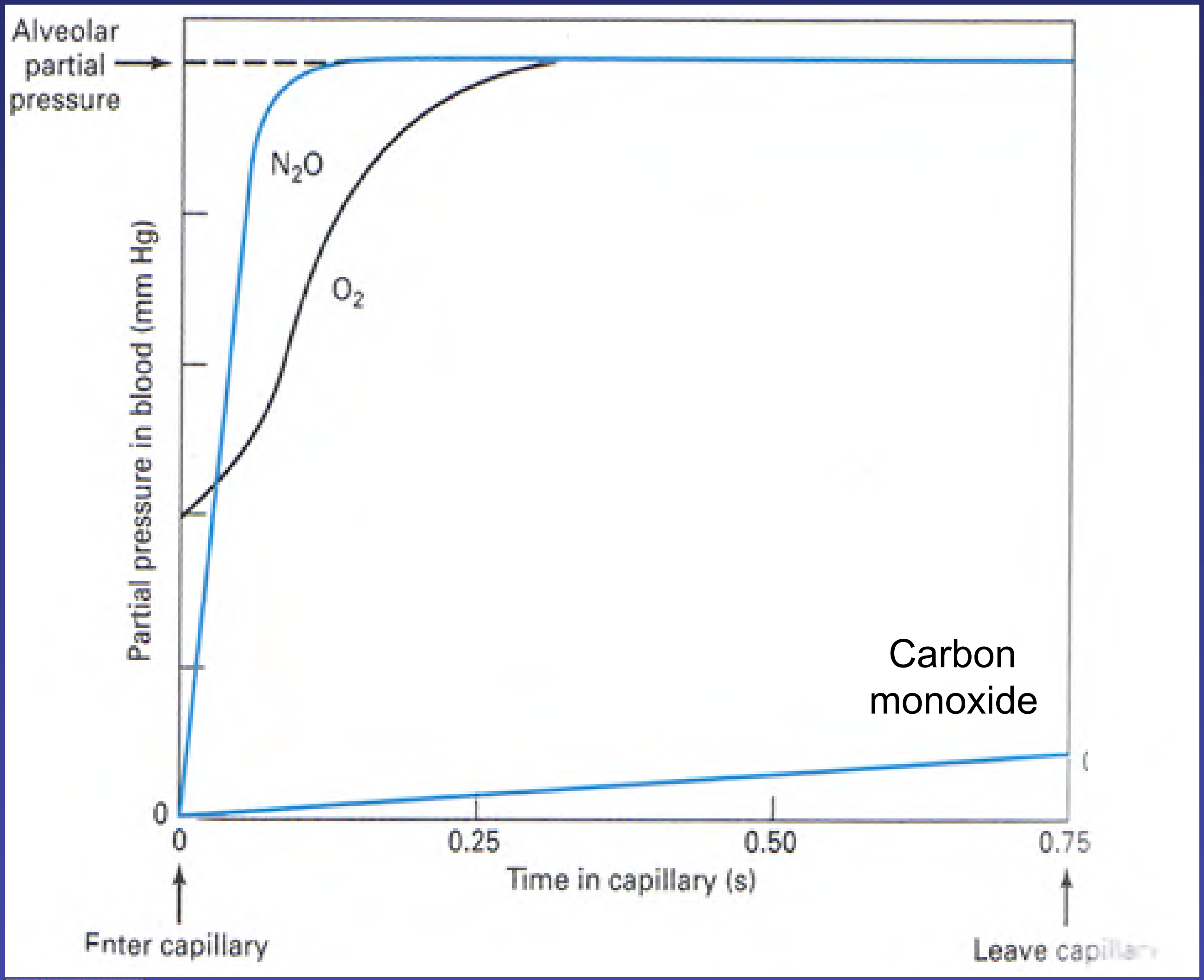


West. Respiratory Physiology: The Essentials 8th ed. Lippincott Williams & Wilkins. 2008

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

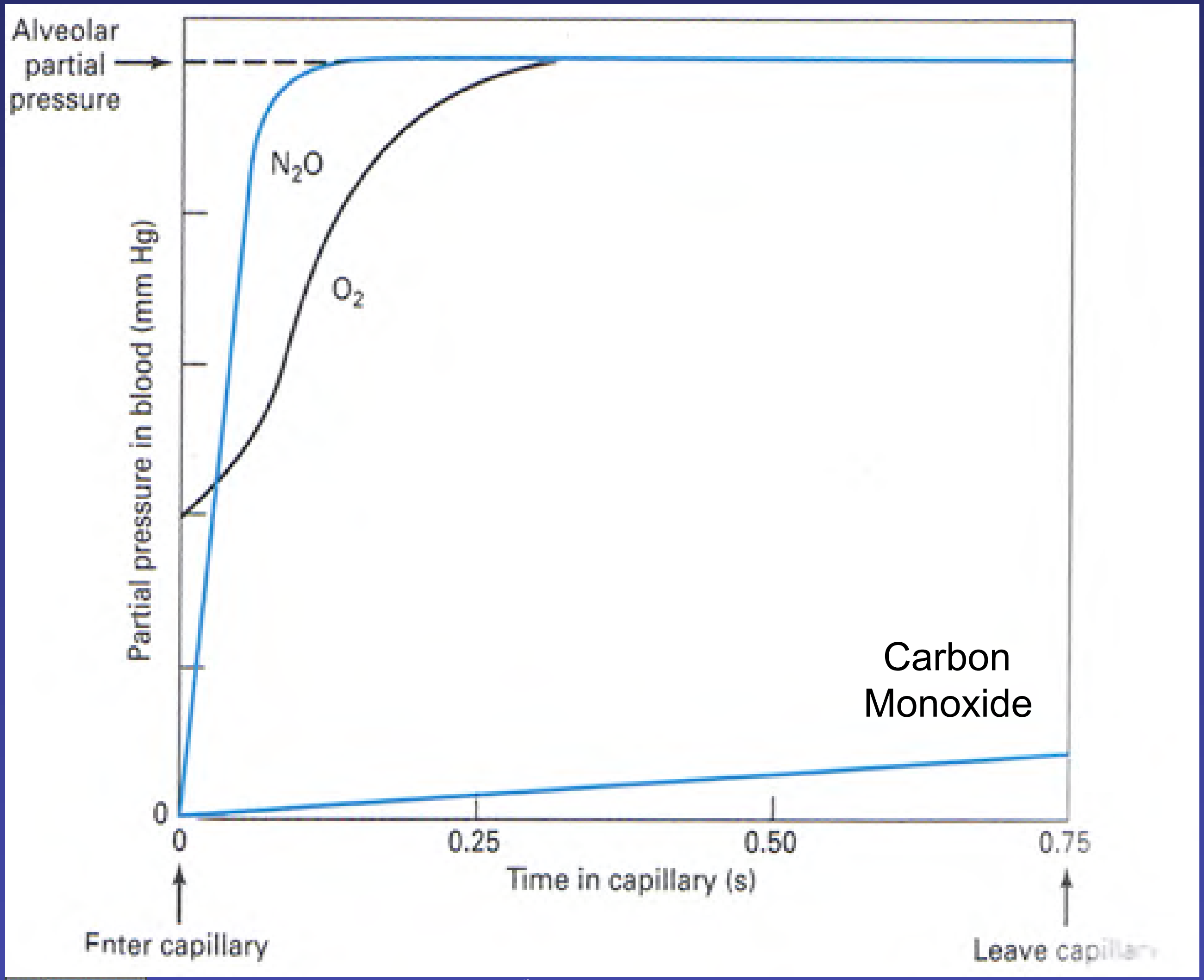


Levitzky. Pulmonary Physiology, 6th ed. McGraw-Hill. 2003

N_2O is Perfusion Limited

- N_2O is very soluble in biological tissues and diffuses rapidly.
- P_cN_2O rises rapidly in the alveolar capillary
- Quickly have $P_cN_2O = P_AN_2O$.
- 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

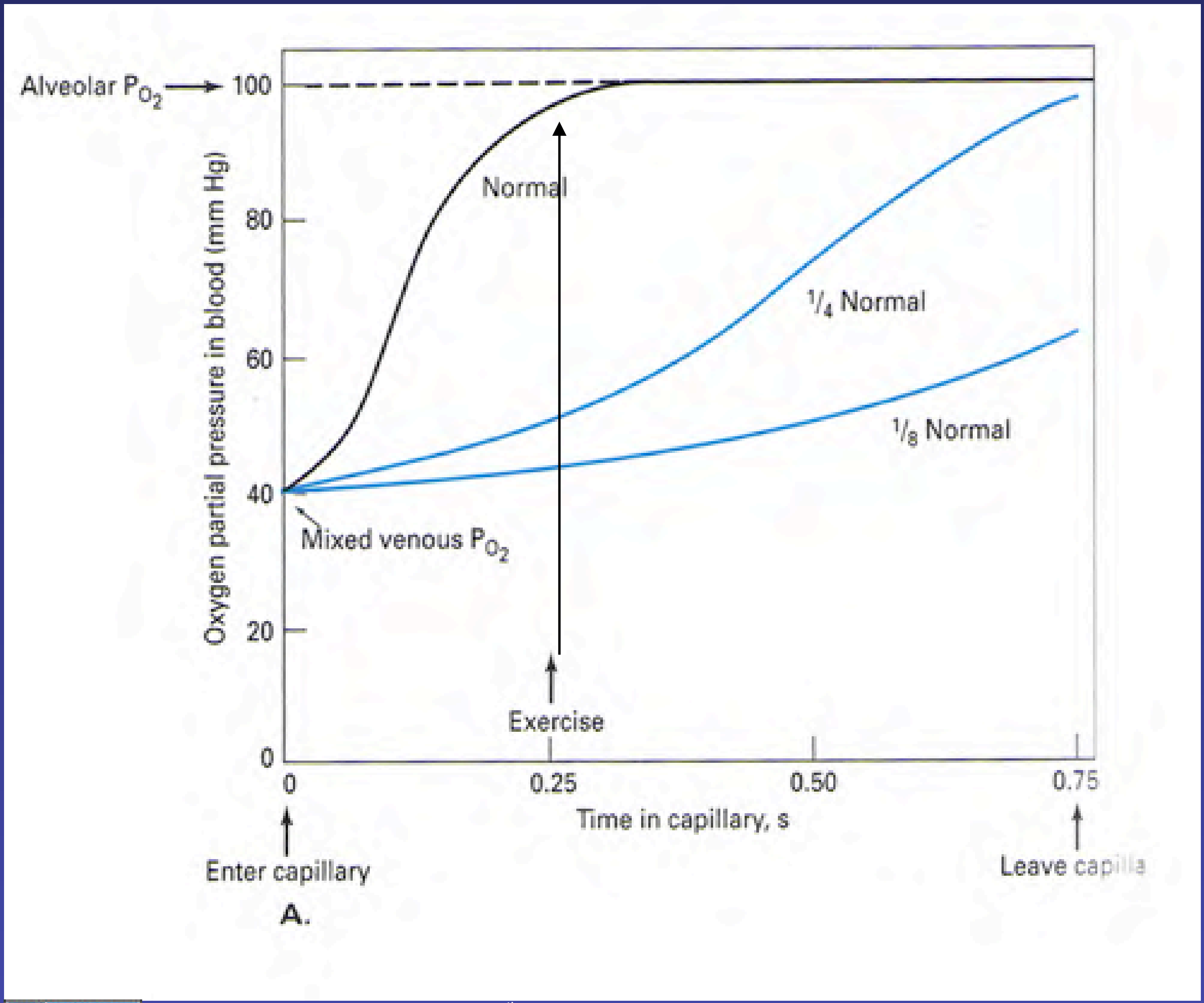


Levitzky. Pulmonary Physiology, 6th ed. McGraw-Hill. 2003

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

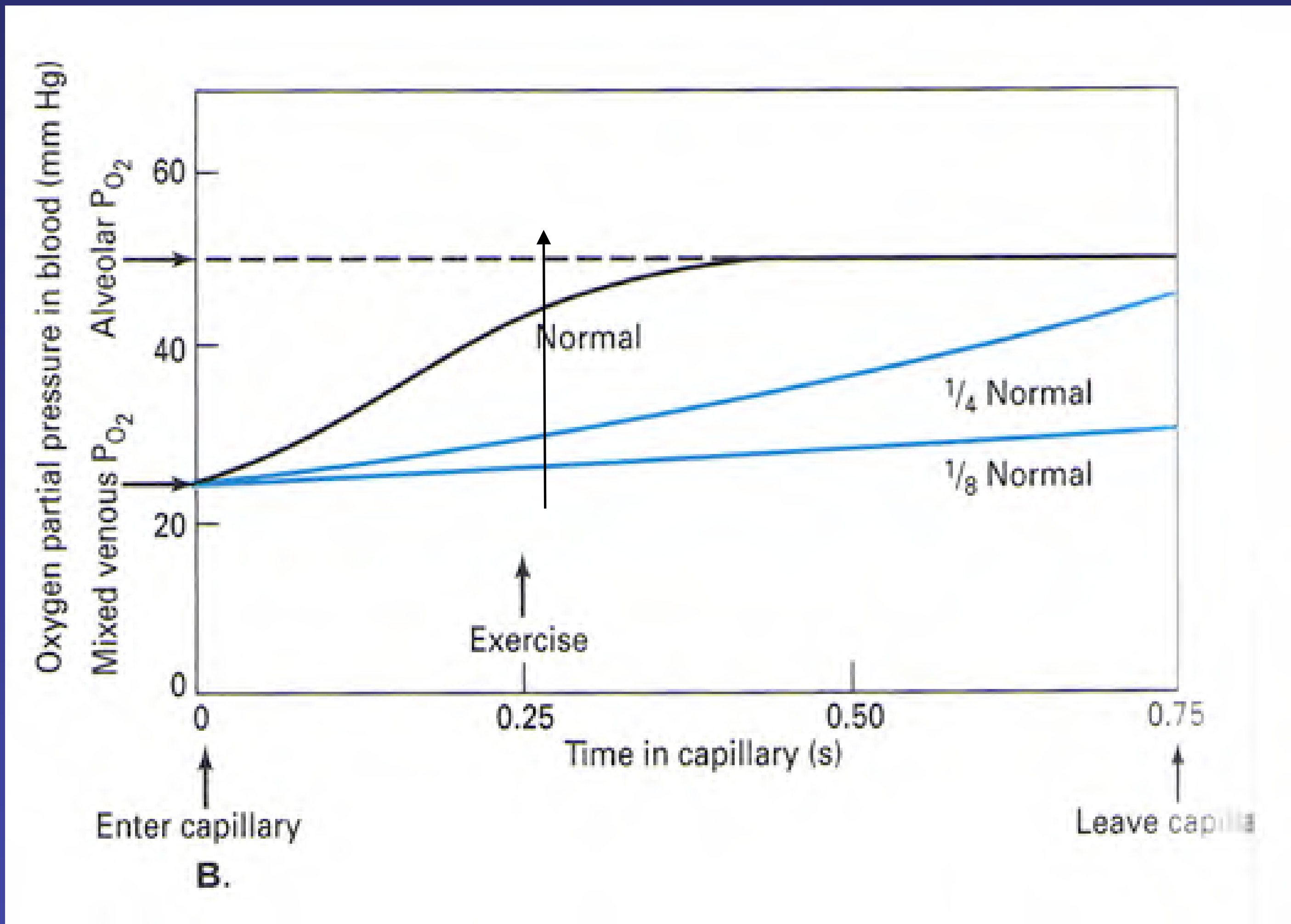


Levitzky. Pulmonary Physiology, 6th ed. McGraw-Hill. 2003

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



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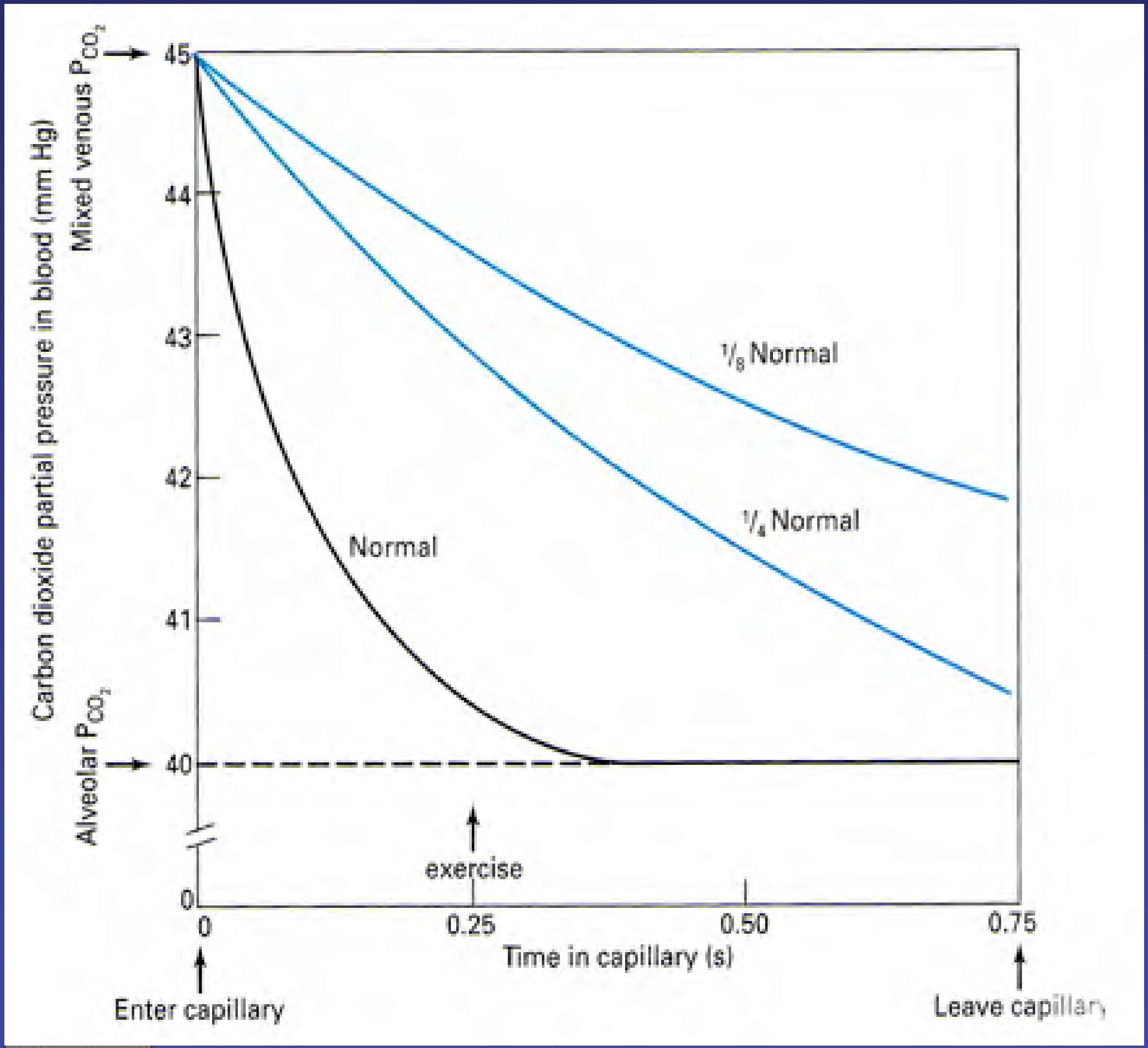
Transfer of CO_2



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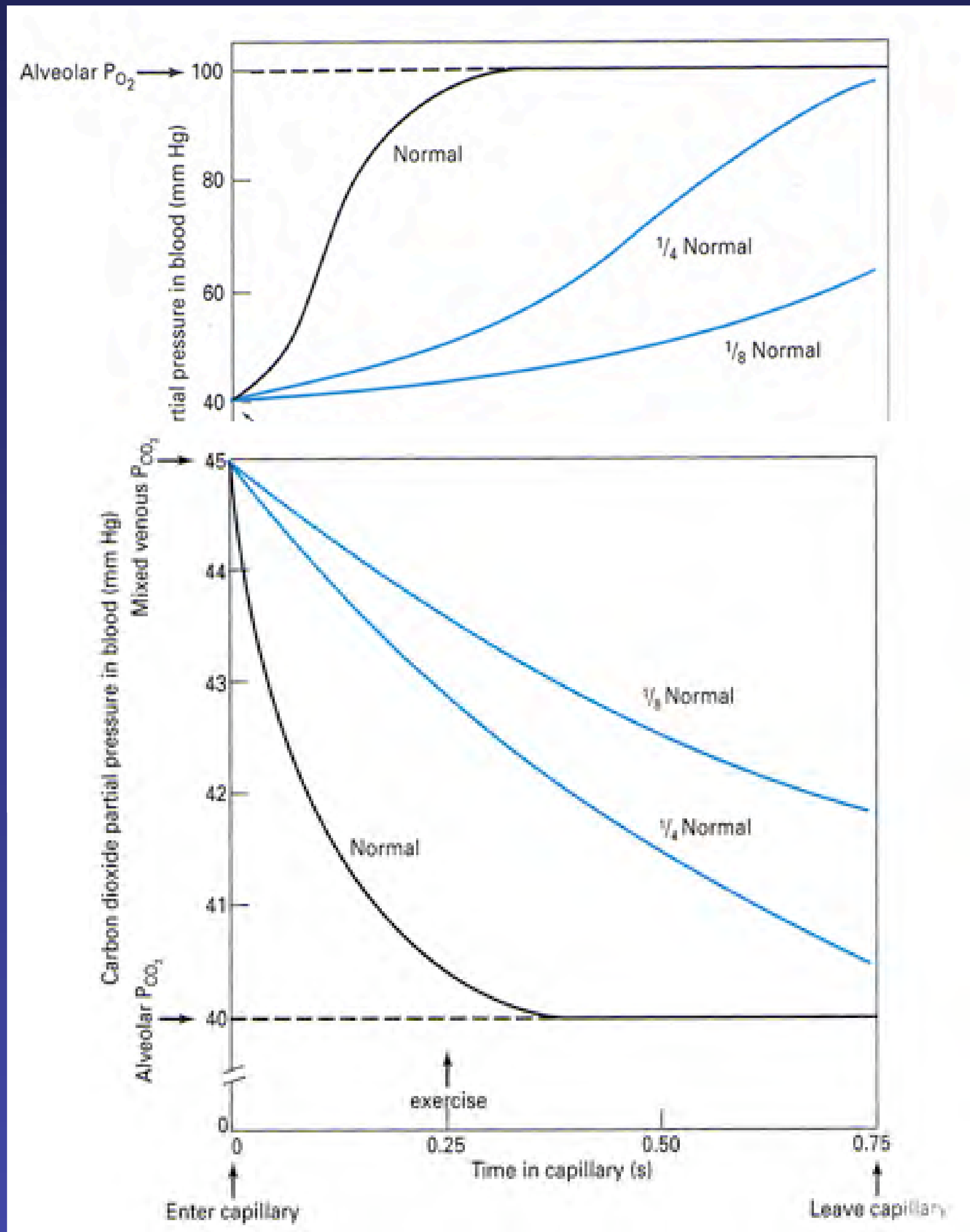
- Is transfer of CO_2 diffusion or perfusion limited?



Levitzky. Pulmonary Physiology, 6th ed. McGraw-Hill. 2003

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→40

Partial pressure gradient of O_2 is 100→40

Fick's Law for Diffusion

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

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 = <u>diffusing capacity</u> of the lung (DL)

Diffusing Capacity

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

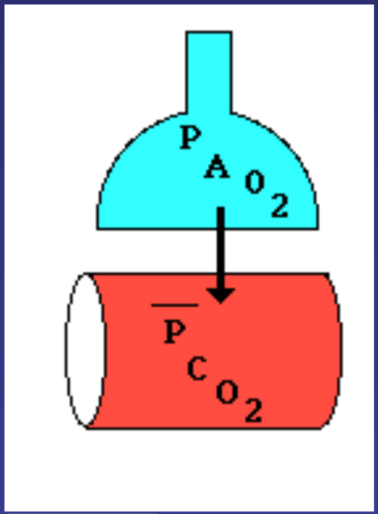
Measuring Diffusing Capacity

- 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

$$\frac{AxD}{T} = D_LO_2$$

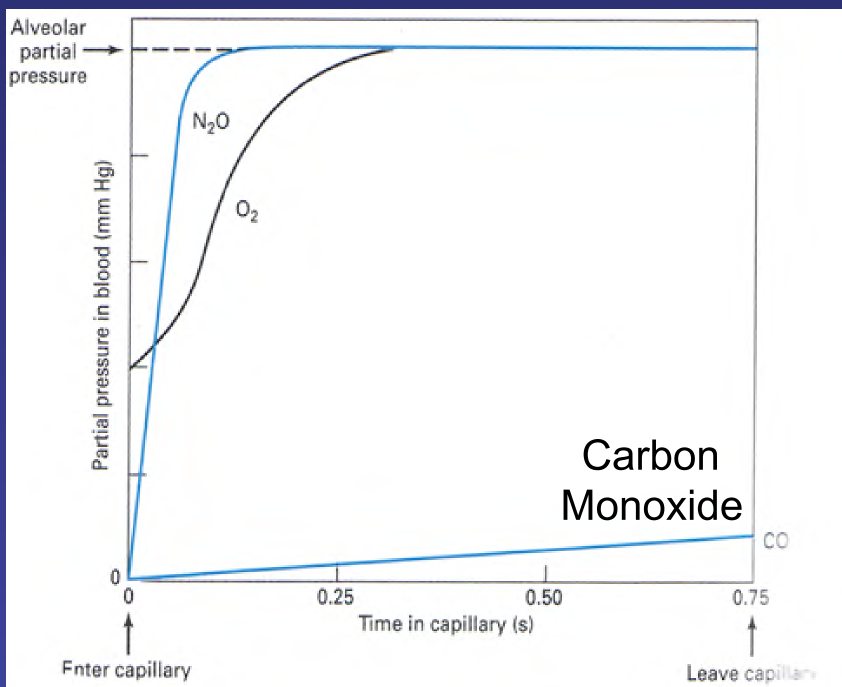
$$\dot{V}_{O_2} = D_LO_2\,(P_AO_2 - P_CO_2) = \text{ml } O_2\text{ /min}$$



T. Sisson

$$D_LO_2 = \frac{\dot{V}_{O_2}}{(P_AO_2 - P_CO_2)}$$

Carbon Monoxide is an Ideal Gas for Measuring Diffusing Capacity



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- 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

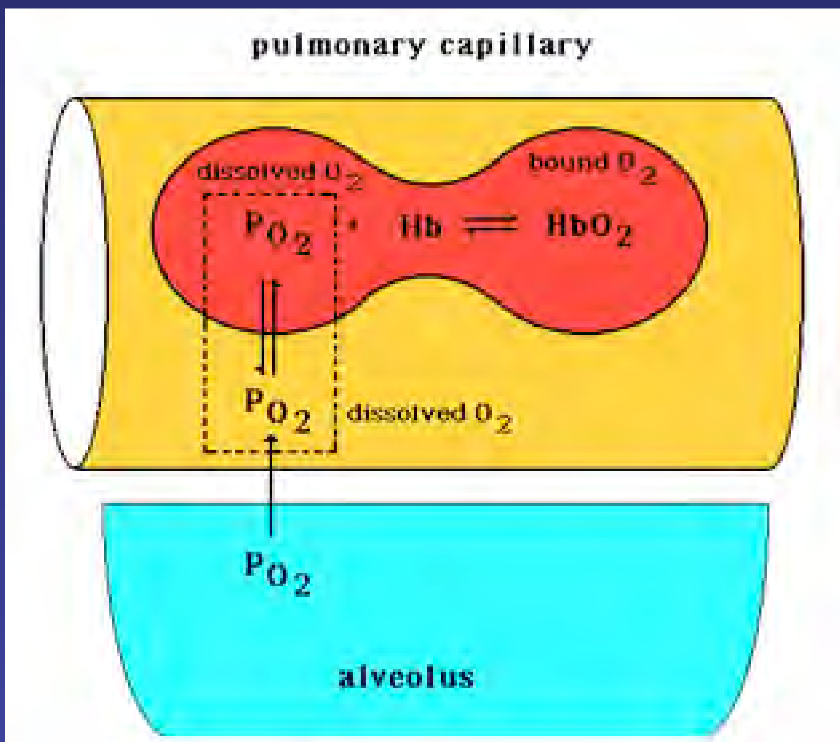
$$DLCO = \frac{\dot{V}_{CO}}{P_ACO - P_cCO}$$

$$PcCO \approx 0$$

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

Normal DLCO = 20-30 ml/min/mmHg

DLCO Has Two Components



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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

Additional Source Information

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