DLCO: Diffusion lung capacity for Carbon Monoxide
What is DLCO?

- The DLCO measures the ability of the lungs to transfer gas from inhaled air to the red blood cells in pulmonary capillaries.
- Diffusing capacity is intended to provide an estimate of the rate at which test molecules move by diffusion from alveolar gas to pulmonary capillary blood flow.

\[
T_{1,co} = \frac{\text{uptake of CO per min}}{(P_{A,co} - P_{\bar{v},co})}
\]
What's in the name?

• Diffusing capacity is an earlier name for transfer factor, still used in many centers.

• It is inappropriate for two reasons
  • It is usually obtained at rest when the index is submaximal so it is not a capacity measurement
  • Several processes contribute to the rate constant, not only diffusion
Why CO and not $O_2$/Nitric Oxide?

• Oxyhemoglobin dissociates readily so there is a material back tension of oxygen in the plasma

• CO is not normally present in body thereby causing practically no back tension.

• Nitric oxide is an excellent alternative but it is of recent origin and data regarding normal and predicted values is lacking
What's so specially about CO?

• Has a high *Haldane constant*
• Binds with Hb 200-300 time more avidly than Oxygen
• Reverse reaction being extremely slow.
• Practically no back pressure/tension
Terminologies

• DLCO: Diffusing capacity of the lungs for carbon monoxide
• VA: The alveolar volume (VA) can be considered the number of contributing alveolar units.
• KCO: The carbon monoxide transfer coefficient is often written as DLCO/VA.
• kCO: The permeability factor is the rate constant for alveolar-capillary CO transfer.
Physiology

• Reflect properties of the alveolar-capillary membrane,

• The process of carbon monoxide (CO) uptake can be simplified into two components: membrane conductance (DM) and reactive conductance, the chemical reaction between CO and hemoglobin.

\[
\frac{1}{DLCO} = \frac{1}{DM} + \frac{1}{RVc}
\]
Procedure
Steps

1. Subject exhales to RV
2. Inhales a mixture of predetermined tracer gas and CO
3. CO mixes with RV
4. CO reaches alveolar membrane and diffuses across
5. CO crosses RBC membrane
6. Binds with Hemoglobin
7. Subject exhales to RV
8. Exhaled sample is analyzed
Preparation

- No cigarette smoking on the day of the test.
- No use of inhaled bronchodilators on the day of the test
- No supplemental oxygen for at least 15 minutes prior to and during the test
- Use of supplemental oxygen can decrease DLCO by 0.35 %/mmHg change
DLCO Maneuver

• 3 to 4 normal breaths
• Followed by full inspiration, full expiration and then full inspiration and hold for 10 sec ±2, followed by forceful exhalation
• Gas: 0.3% CO, 0 to 14% helium, 21% O2, rest N2
Summary of the procedure
Inspiratory maneuver

breath hold

Sample collection volume
0.5-1L if VC<2L, reduce to 0.5L

Dead space washout (0.75 L)
If VC<2L, reduce to 0.5L
Diffusion Data

- Helium Inspired: 13.94
- Co Inspired: 0.259
- Helium Expired: 11.23
- Co Expired: 0.092
- Diffusion Time: 10.66
- Inspired Volume: 4.02
- DLCO Result: 20.90
- O2 Expired: 15.70
- 1/Theta: 0.934
- Hgb: 15.00
- V Insp BTPS: 4.41

Hit any key when ready
Quality of the test

• The inspiratory volume should be greater than 85 percent of the largest VC
• The inspiratory time should ideally be less than two seconds; greater than four seconds is unsatisfactory
• The sample collection time should be less than three seconds.
• The first 0.75 to 1 L is discarded as dead space gas and then a sample gas volume of 0.5 to 1 L is collected for analysis.
Common Fallacies
The gases, how they are analyzed?

- Carbon monoxide is analyzed by infrared absorption
- The detector has a useful life of 10 years
- The linearity of the analyzer is more important than the accuracy because the principal objective is to obtain the ratio of the expired to the inspired carbon monoxide concentration
- Infrared analyzers are sensitive to carbon dioxide and to water vapors
Analysis..

• To enhance the specificity of the analysis, first the CO$_2$ and then the water vapor should be absorbed

• CO$_2$ by soda lime and water vapors by anhydrous calcium chloride or copper sulphate.

• The treatment reduces the volume of the sample and this, in turn, increases the concentrations of helium and carbon monoxide.
Theory and calculations

• During breath holding, CO leaves alveolar gas at an exponential rate.
• VA is the alveolar volume which is calculated by knowing the fractional concentration of the tracer gas in the inhaled and exhaled gas

\[ F_{1V_1} = F_{2V_2} \]

\[ VA = V_I \times (F_I \text{ tracer}/FA \text{ tracer}) \]
Fick’s Law

- Vol gas transferred $\propto \frac{A \times D \times (P_1 - P_2)}{T}$
  - A is Area
  - D is Diffusion constant $\propto \frac{Sol}{\sqrt{MW}}$
  - P is partial pressure between two sides
  - T is thickness of the membrane

Lung Function: Physiology, Measurement and Application in Medicine 2006 by John E. Cotes
Resistance

- $D_m$ = membrane conductance
- $Q_c$ = effective capillary blood volume, in mL
- $H_b$ = Hemoglobin concentration as a fraction of normal
- $\theta$ = constant for the rate of CO uptake by the erythrocytes per mL normal blood

\[
\frac{1}{T_{L,CO}} = \frac{1}{D_m} + \frac{1}{\theta \cdot Q_c \cdot [H_b]}
\]
Alveolar Volume

• $VA = \text{Alveolar volume}$
• $FI,He = \text{He fraction in the inspired gas}$
• $FA,He = \text{Alveolar He fraction at time } t$
• $VI = \text{inspired volume in liters BTPS}$
• $VD = \text{total dead space in liters BTPS}$

Transfer factor for carbon monoxide M. Horstman, F. Mertens, H. Stam
Relation between Helium and CO

- $F_{I,CO} = \text{CO fraction in the inspired gas}$
- $F_{I,He} = \text{He fraction in the inspired gas}$
- $F_{A,He} = \text{Alveolar He fraction (after } t \text{ sec)}$
- $F_{A,CO0} = \text{Alveolar CO fraction at zero time}$

Transfer factor for carbon monoxide M. Horstman, F. Mertens, H. Stam
Exponential decay constant (kCO)

- $0 = \text{Start time in s}$
- $t = \text{End time in s}$
- $FA,CO_t = FA,CO \text{ at time } t$
- $FA,CO_0 = FA,CO \text{ at time } 0$

$$FA,CO_t = FA,CO_0 \cdot e^{-kCO(t-0)}$$

Transfer factor for carbon monoxide M. Horstman, F. Mertens, H. Stam
Exponential decay constant (kCO)

- TLCO is in $\mu$mol/s/kPa
- PB = barometric pressure
- PH2O,sat = the saturated water vapor pressure
- VA,max = the alveolar volume at TLC level in liters
- KSTPD = the conversion factor for the conversion from liters BTPS to STPD

\[
k_{CO} = \frac{TL_{CO} \cdot (PB - PH_{2O, sat})}{K_{STPD} \cdot VA_{max}}
\]
Transfer factor for carbon monoxide M. Horstman, F. Mertens, H. Stam

\[ F_{A,CO_t} = F_{A,CO_0} \cdot e^{-k_{CO}(t-0)} \]

\[ k_{CO} = \frac{T_{L,CO} \cdot (P_B - P_{H_2O,sat})}{K_{STPD} \cdot V_{A,max}} \]

\[ T_{L,CO} = V_{A,max} \cdot \frac{1}{t} \cdot \frac{K_{STPD}}{(P_B - P_{H_2O,sat})} \cdot \ln \left( \frac{F_{A,CO_0}}{F_{A,CO_t}} \right) \]
# Measurement of diffusing capacity

## Methods
- Single breath-holding method
- Single expiration method
- Rebreathing method
- Steady state method

## Technique
- Patient conditions
- Inspiratory maneuver
- Breath-hold
- Expiratory maneuver
<table>
<thead>
<tr>
<th>Method</th>
<th>Technique</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLco (breath hold)</td>
<td>CO and tracer gas analysis relatively simple; 10-sec breath hold</td>
<td>Easy calculations, simple, fast; highly standardized and automated; minimal COHb back-pressure effect</td>
<td>Sensitive to distribution of ventilation and V/Q matching; “nonphysiologic”; not practical for exercise testing</td>
<td>Screening and clinical applications</td>
</tr>
<tr>
<td>DLcor (rebreathing)</td>
<td>Rapid analysis of CO and tracer gas required; rebreathing must be controlled</td>
<td>Less sensitive to V\textsubscript{A} than DLco; less sensitive to V/Q abnormalities; can be used with NO to measure DLNO</td>
<td>Complex calculations (computerized); rapidly responding analyzers required; sensitive to COHb back-pressure</td>
<td>Clinical and research applications; provides most accurate DLCO</td>
</tr>
<tr>
<td>DLco (intrabreath)</td>
<td>Rapid analysis of CO and tracer gas during single controlled exhalation</td>
<td>Breath holding not required; can be used during exercise</td>
<td>Complex calculations (computerized); flow must be controlled; sensitive to uneven V/Q; not standardized</td>
<td>Screening and clinical applications may be useful in patients who cannot hold their breath</td>
</tr>
<tr>
<td>DLcosb + 1/\theta V\textsubscript{c} (membrane diffusing capacity)</td>
<td>DLcosb repeated at two different levels of alveolar PO\textsubscript{2}</td>
<td>Differentiates membrane transfer resistance from red cell uptake</td>
<td>Complex calculations; estimates of alveolar PO\textsubscript{2} are critical</td>
<td>Research with limited clinical applications</td>
</tr>
</tbody>
</table>
Steady state methods

• Susceptible to uneven lung ventilation especially when ventilation is low on account of the measurement being made at rest.
• The method is more reliable during exercise.
• It is used at rest if the subject cannot cooperate in the measurement
Breath holding methods

- Proposed by Bohr and developed by Marie Krogh
- Merit of minimizing regional inequality as it is measured at total lung capacity
- Simple to perform by all but the most disabled subjects
- The method is suitable for respiratory surveys
- Reference values are available
- It is used in a majority of lung Function laboratories.
- The method is recommended internationally
Single breath

- Easy for the lab
- Well standardized
- Less affected by Non uniformity of ventilation
- Difficult to perform by dyspneic patients, during exercise

Steady state

- Requires no respiratory maneuvers
- Technically difficult
- Gives lower values than single breath method
Interpretation

• Patient's result is interpreted by comparing it with the predicted value or the lower limit of normal

• Severe respiratory impairment is defined as a DLCO below 45 percent of the predicted value
What affects DLCO

- Thickening of the alveolar-capillary membrane
- Loss of alveolar membrane surface area
- Reduction in volume of RBC in pulmonary capillaries (approx. 150 ml)
- Carboxyhemoglobin levels
- Altitude
- Lung volume
Anemia

• The adjusted value estimates the DLCO if the patient were to be having normal hemoglobin
• DLCO falls about 9 percent during menstruation

\[ DLCO_{predicted\ for\ Hb} = DLCO_{predicted} \times factor \]

where factor = \( (1.7 \times Hb)/(10.22 + Hb) \)

In children under 15 yrs of age and females is:

where factor is = \( (1.7 \times Hb)/(9.38 + Hb) \)
Carboxyhemoglobin and cigarette smoking

• The carboxyhemoglobin level may be elevated in the blood if the patient was smoking just prior to the DLCO measurement.

• An increase of 1 percent in COHb results in a proportionate 1 percent decrease in the measured DLCO.

• Smoking cessation results in a mean DLCO increase of 2 to 4 mL/min per mmHg within a few days.
High altitude

• If the laboratory is located at high altitude, the ambient, alveolar, and arterial oxygen concentrations are lower than at sea level.

• The lower arterial oxygen concentration results in less competition for CO binding to hemoglobin, increased CO uptake.

• And higher measured DLCO compared to a test done at sea level.
Volume correction

• DLCO/VA (KCO) reflects alveolar CO uptake efficiency at a given volume
• In the past, the term DLCO/VA (also known as KCO) was misinterpreted as a correction factor for low lung volume, leading to potential misinterpretation of DLCO results
• Nonetheless, the average VA of the tests used to generate the reported DLCO should be reported.
Relationship between DLCO & KCO (DLCO/VA)

- **Incomplete lung expansion** – In patients who have neuromuscular disorders, kyphoscoliosis, or inadequate inspiration due to poor test performance, the KCO (DLCO/VA) is elevated.

- **Pneumonectomy** – For patients who have undergone pneumonectomy, but do not have lung disease, the VA is decreased due to discrete loss of alveolar units. Blood flow is diverted to the remaining lung and the KCO (DLCO/VA) is usually increased.
• Emphysema - the DLCO is reduced by loss of gas exchanging surface due to alveolar capillary damage and the KCO is low

• Interstitial lung disease (ILD) – In ILD, the DLCO is decreased by diffuse alveolar capillary damage. The KCO is often reduced.

• Pulmonary vascular disease – In pulmonary hypertension, the DLCO is reduced. The VA is typically normal, and the KCO (DLCO/VA) is reduced.
Indication

• In general, the DLCO is used to identify the cause of dyspnea or hypoxemia, monitor disease progression, and identify pulmonary hypertension.

• Obstructive disease: emphysema, ruling out COPD from asthma, cystic fibrosis

• Diagnosis and follow up of restrictive lung diseases

• Ruling out extra-parenchymal causes of restriction
For early diagnosis/Screening

• Sarcoidosis
• Hypersensitivity pneumonitis
• Chest irradiation and cancer chemotherapy
• Use of drugs known to have pulmonary toxicity (eg, amiodarone, bleomycin, nitrofurantoin)
• Rheumatic disease
• Pulmonary vascular diseases/CTEPH
• Lung Transplantation
• Prior to lung resection
Increased DLCO

- Altitude
- Asthma
- Polycythemia
- Pulmonary hemorrhage
- Left-to-right intracardiac shunting
- Mild left heart failure - increased pulmonary capillary blood volume
- Exercise just prior to the test - increased cardiac output
- Mueller maneuver
- Supine position
Low DLCO with normal spirometry

- Anemia - mild decrease
- Pulmonary vascular disease - mild to severe decrease
- Early interstitial lung disease - mild to moderate decrease
- Valsalva maneuver
Low DLCO with obstruction

- Bronchiolitis
- Combined pulmonary fibrosis and emphysema (CPFE)
- Cystic fibrosis
- Emphysema
- Sarcoid
Low DLCO with restriction

- Interstitial lung disease
- Pneumonitis
Low DLCO with both restriction & obstruction

• Sarcoidosis (stage II through IV)
• Asbestosis
• Miliary tuberculosis
Pit-Falls

• The reduction of DLCO in current smokers cannot be attributed entirely to emphysema and can be influenced by increased carboxyhemoglobin levels

• There is little evidence that a lower DLCO predicts increased morbidity or mortality from COPD

• Cystic fibrosis and alpha-1 antitrypsin deficiency should be considered in children and young adults with obstruction and a low DLCO.
Take Home message

• DLCO should be called as TLCO
• Preparation discordance is the main reason for faulty reports
• Patient co-operation is must
• Multiple TLCO shouldn’t be performed in a day (causes CO levels variability in the reservoir bags)
• Can be used to follow up, diagnose and differentiate Pulmonary diseases

• Takes hardly 10 min to do this test- NEED NOT TO BE DONE ONLY ON MONDAY AND THURSDAY!
Summarizing interpretation

- Normal $D/V_{Aeb}$
  - $V_{Aeb}/TLC < 85\%$
    - Maldistribution of ventilation
      - $V_{Aeb}$
    - Non-communicating air (blebs, bullae)
      - $V_{Aeb}$
      - $V_{Aeb}$
  - $V_{Aeb}/TLC > 85\%$
    - Resection
      - $TLC$
    - Chest cage restriction
      - $TLC$

- $D/V_{Aeb}$
  - $V_{Aeb}/TLC < 85\%$
    - Emphysema
      - $V_{Aeb}$
      - $TLC$
  - $V_{Aeb}/TLC > 85\%$
    - Non-perfusion or ventilated alveoli
      - $Qc$
      - $Dm$
    - Anemia
      - $Qc$
    - Fibrotic disorders
      - $Dm$