Interpretation of Tests of Parenchymal Function

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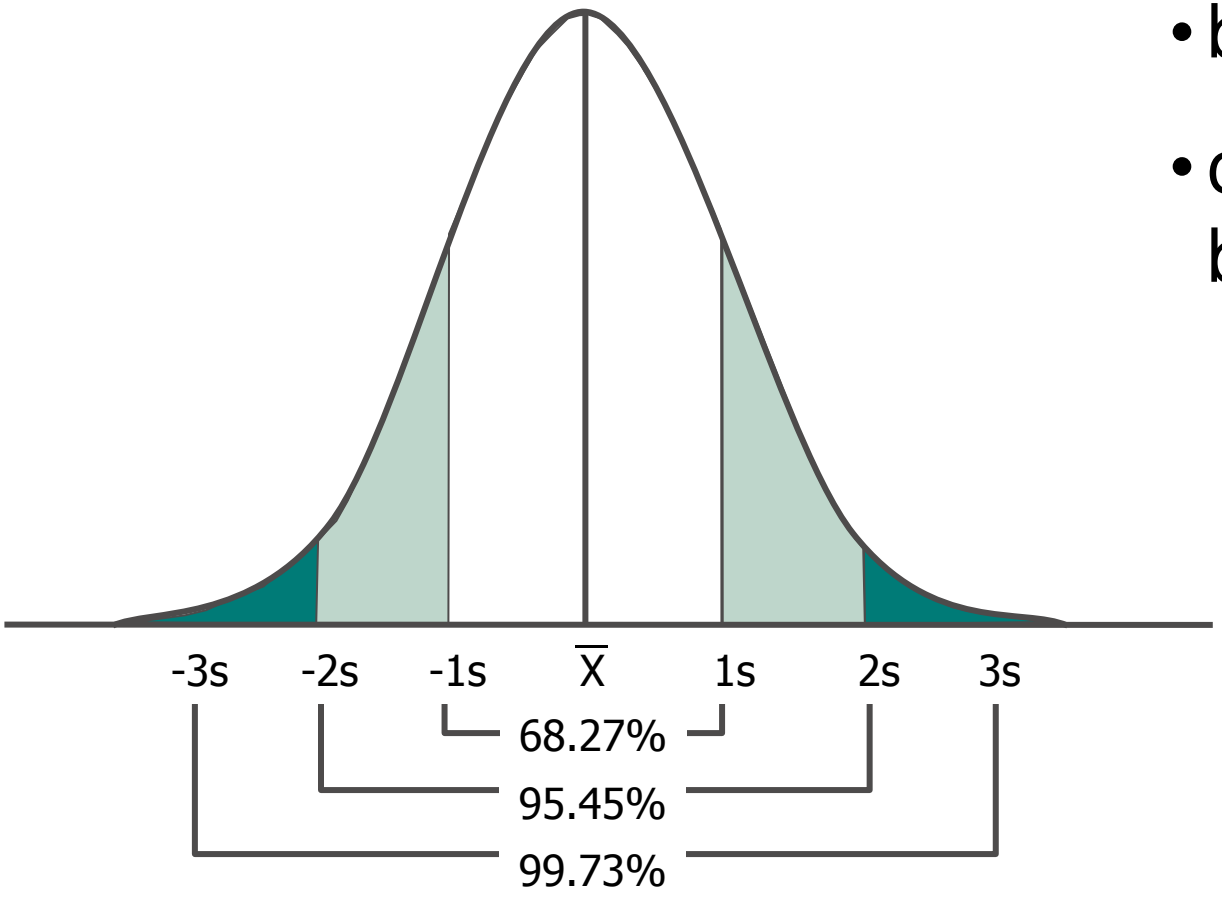
Reference Values

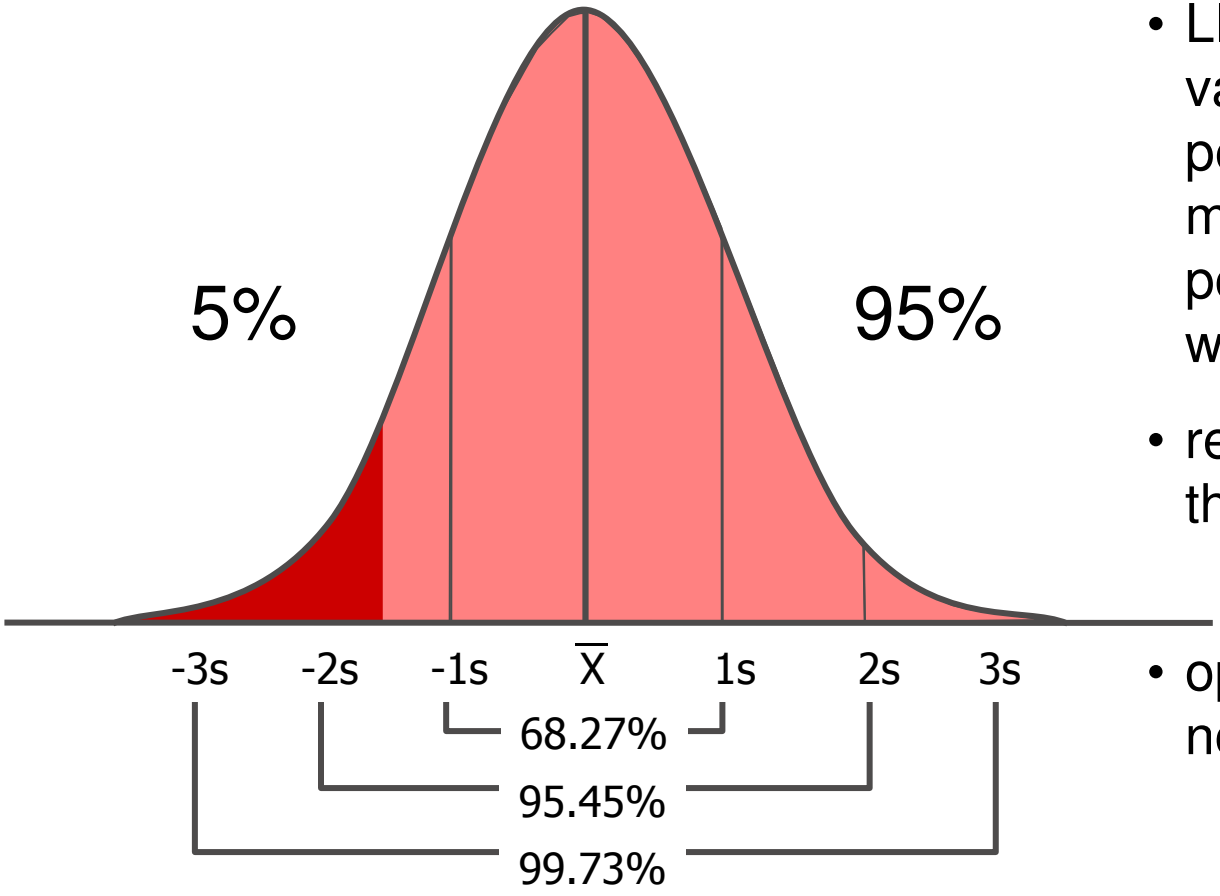
- Most lung function parameters vary with:
  - Height
  - Age
  - Gender
  - Race
  - Method / Instrumentation used
- Reference values should be obtained from studies of ‘‘healthy’’ subjects with the same anthropometric and, ethnic characteristics of the patient being tested
- Reference values should also match the instruments and lung function protocols used in the reference population as in the laboratory

Statistics – Normal Distribution



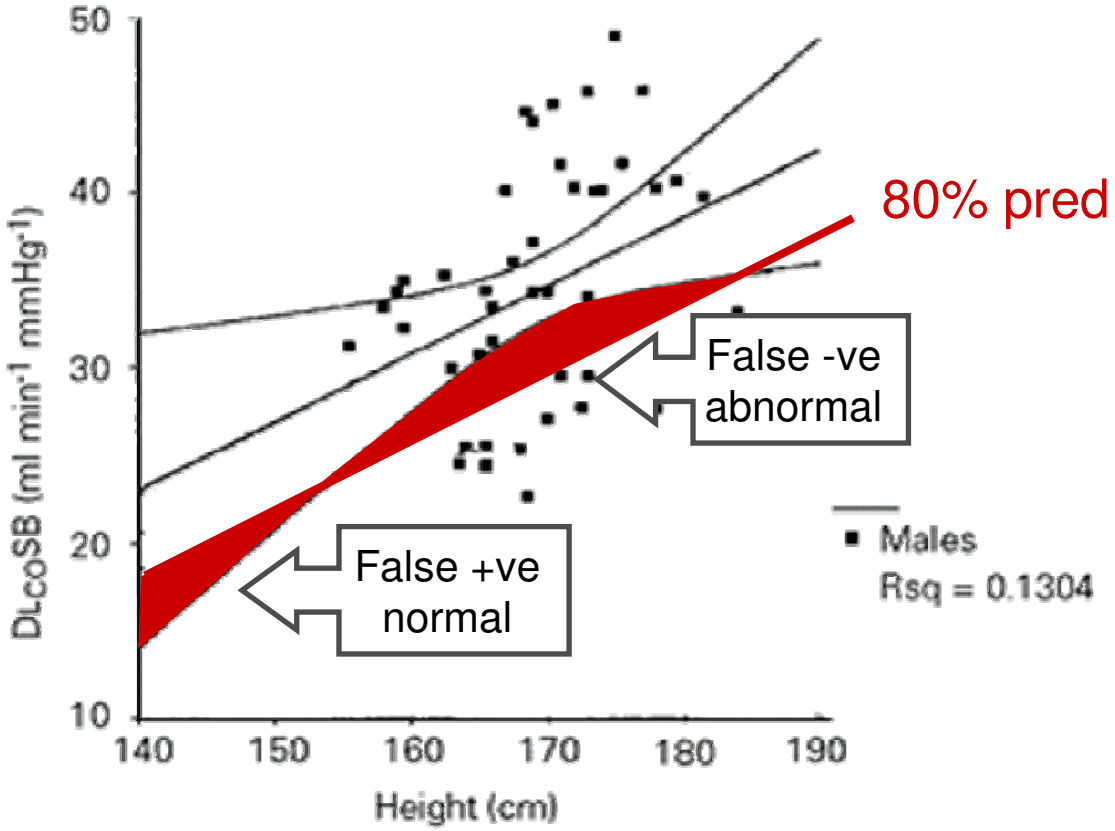
- bell shape
- can be specified by two parameters
  - mean ($\bar{X}$)
  - Standard deviation (s)

Lower Limit of Normal (LLN)



- LLN is the point where values above the 5th percentile of values measured in the reference population are considered within normal limits
- remaining 5% will be below the lower limit of normal
  - LLN = $\overline{X}$ – 1.65s
- opposite for upper limit of normal (ULN)
  - Appropriate when results can be too high
  - eg D_LCO, TLC, RV/TLC

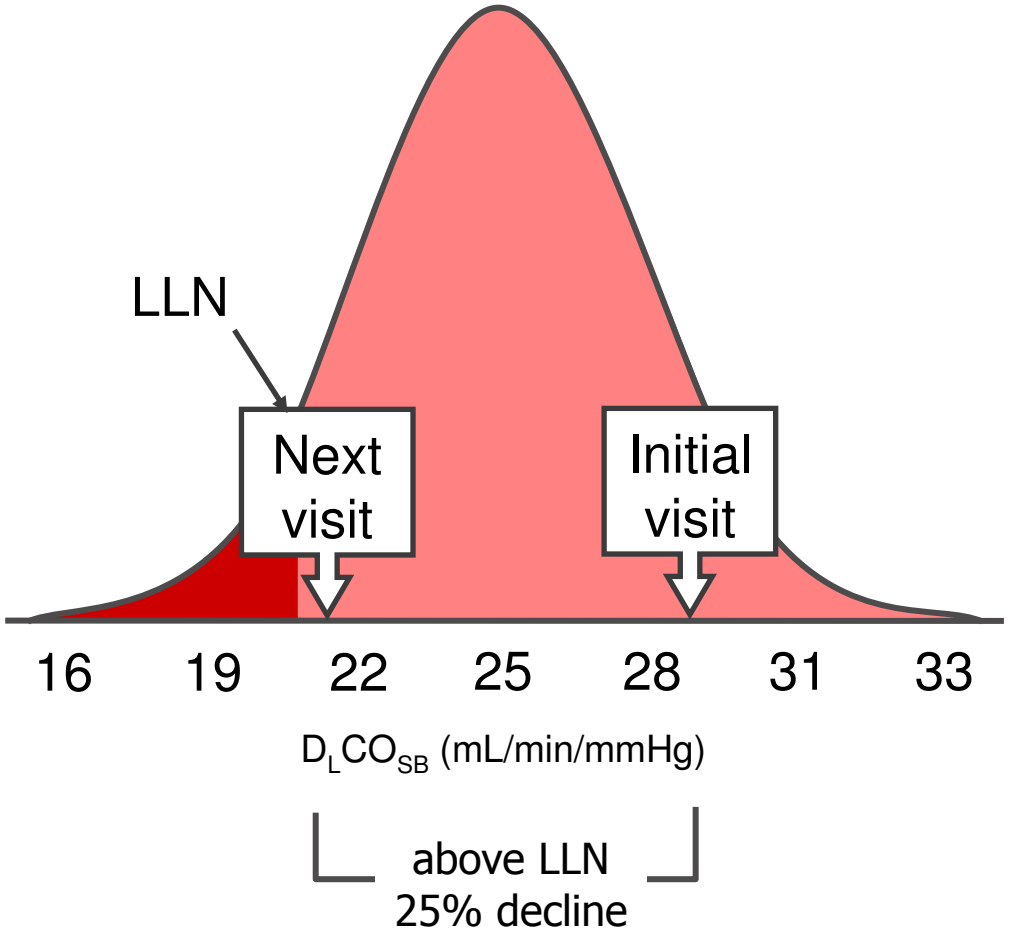
Fixed Percentage vs LLN



- using 80% predicted as a fixed value for the lower limit of normal can lead to significant errors when interpreting lung function in adults
- errors are commonly seen at the extremes of height and age

Modified from Neder *et al.* (1999). *Braz. J. Med. Biol. Res.*, **32(6)**: 729-737

What is Normal?



- Important not to rely solely on LLN for interpretation
- "Normal" covers a wide range of values
  - Significant changes can occur within normal range
  - longitudinal comparisons are more reliable than %predicted

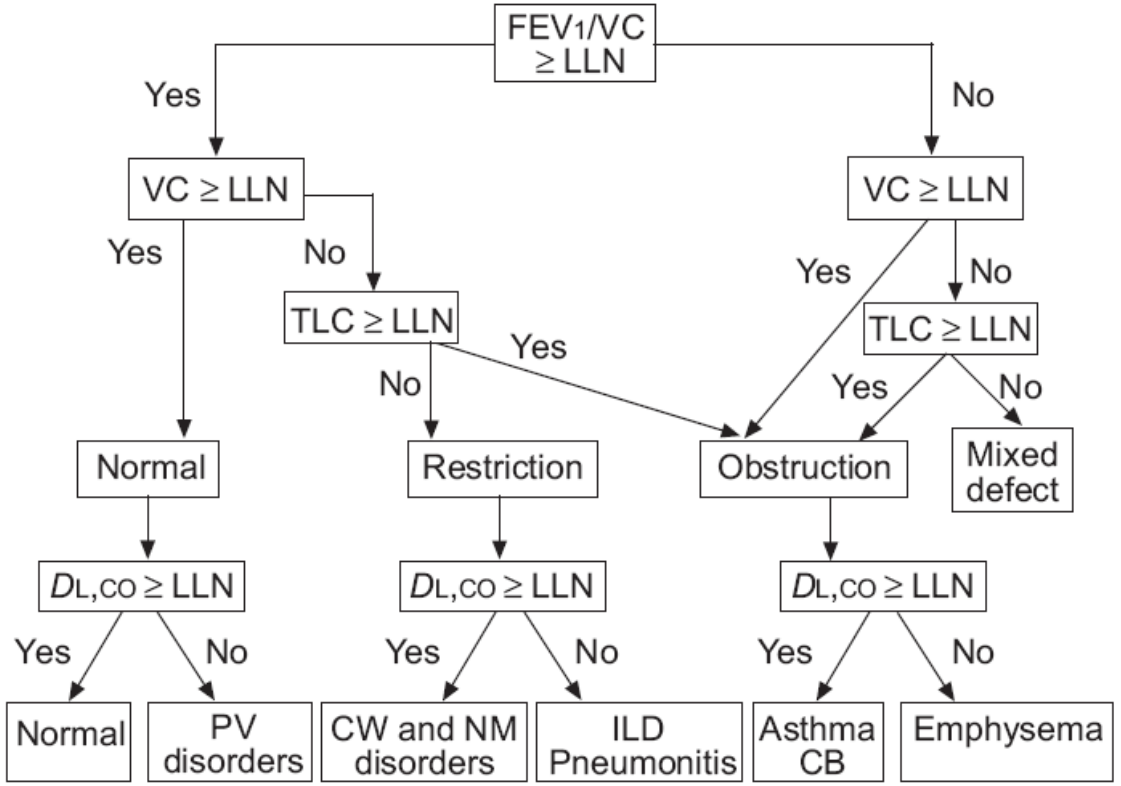
Interpretative Strategies – ATS/ERS 2005

- Review test quality
- Compare with predicted values
- Compare with known disease or physiologic patterns (obstructive, restrictive)
- Compare with self (longitudinal data)
- Answer the clinical question

Pellegrino *et al*. (2005). *Eur. Respir.* J., **26**: 948-968

Interpretation of D_LCO

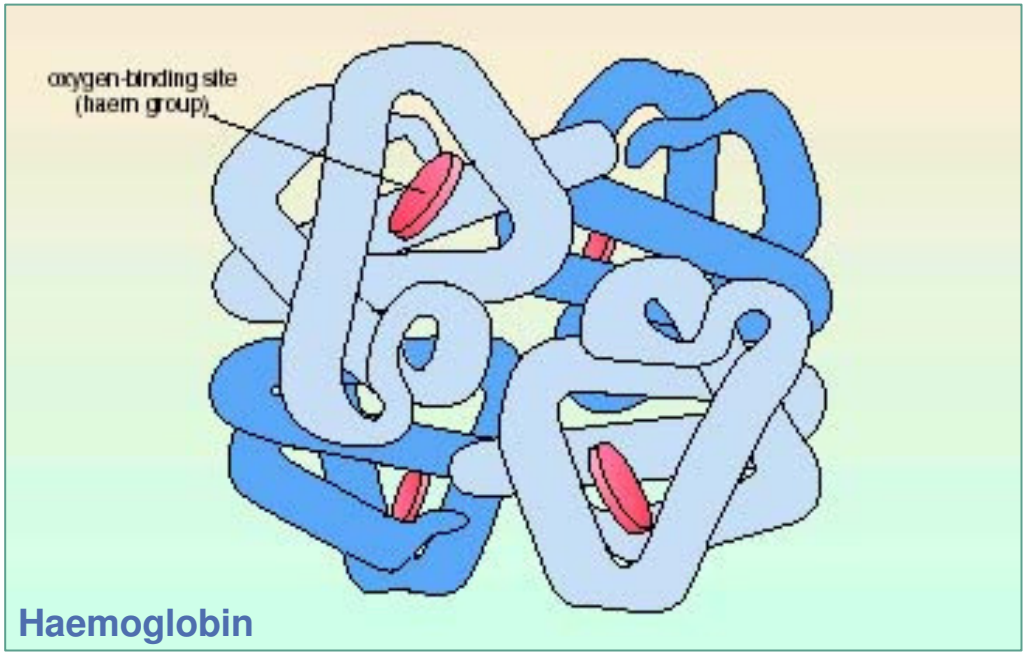
- Rarely used in isolation
  - Interpretation aided by other test results
- Useful in differential diagnoses within different physiological patterns (obstruction, restriction)



Pellegrino *et al*. (2005). *Eur. Respir.* J., **26**: 948-968

Variables of D_LCO

- Anthropometric characteristics
- Haemoglobin
- Lung volume
- Carboxyhaemoglobin
- P_AO_2
- Exercise
- Body position



Haemoglobin

Interpretation of D_LCO/V_A (KCO)

- D_LCO changes with changing lung volume
- Normalising D_LCO for lung volume is **supposed** to show whether loss of D_LCO is a result of loss of lung volume (extra-parenchymal abnormality) or a result of parenchymal abnormality

HOWEVER

- the relationship between D_LCO and V_A is not linear
- interpretation is controversial
- use D_LCO/V_A as a guide only

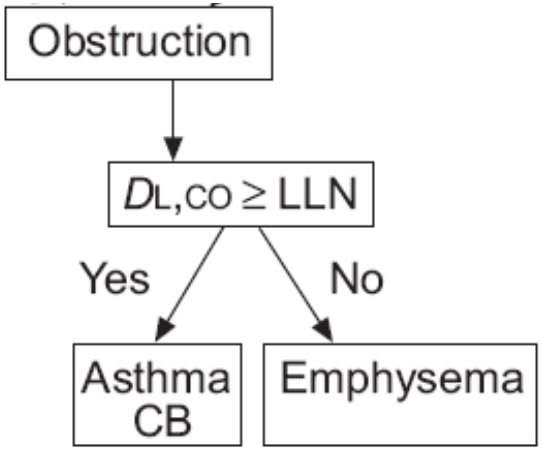
Severity Scaling – ATS/ERS 2005

Degree of Severity	D_LCO %pred
Mild	>60% and <LLN
Moderate	40-60%
Severe	<40%

Pellegrino *et al*. (2005). *Eur. Respir.* J., **26**: 948-968

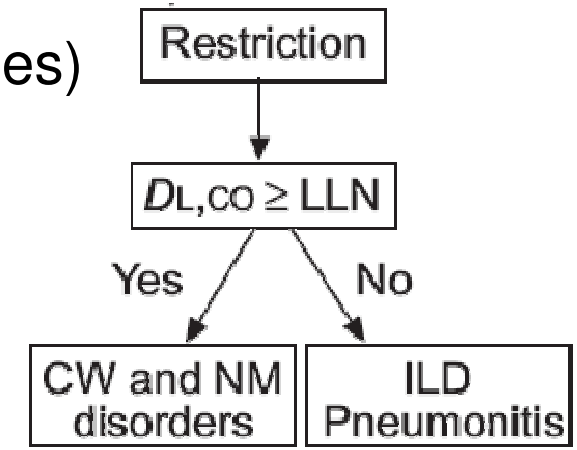
D_LCO and Obstructive Defects

- Normal D_LCO (few parenchymal changes)
  - Chronic bronchitis
  - Asthma (may also be ↑D_LCO)
- Low D_LCO
  - Emphysema
    - » Loss of surface area and pulmonary capillary blood volume
  - CF (may also be normal D_LCO)
  - Bronchiectasis
  - Lymphangioleiomyomatosis (LAM)



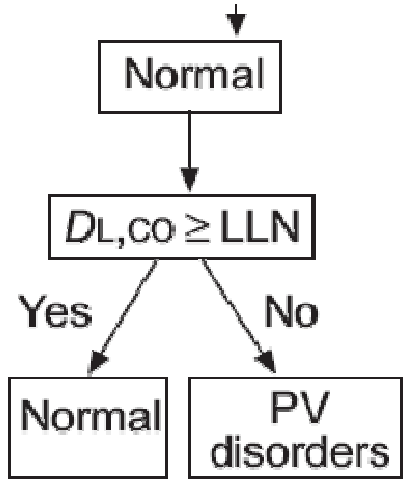
D_LCO and Restrictive Defects

- Normal D_LCO (extra-pulmonary abnormalities)
  - Chest wall disorders
  - Neuromuscular disorders
  - Obesity
  - Pleural effusion
- Low D_LCO
  - Interstitial lung disease
    - » Reduced membrane conductivity and reduced pulmonary capillary volume
  - Pneumonitis
  - Chronic Congestive (left) Heart Failure
    - » vascular remodelling increases pulmonary vascular resistance and therefore reduces pulmonary capillary volume
  - Connective tissue diseases eg Sarcoidosis
    - » Reduced membrane conductivity and pulmonary capillary volume



Low D_LCO with Normal PFTs

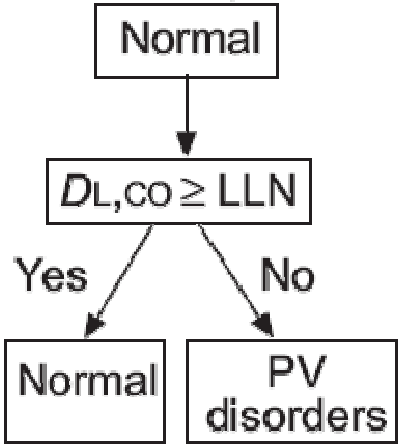
- Anaemia
  - Less Hb available for CO binding
- Valsalva manoeuvre
  - Increased positive intra-thoracic pressures reduce pulmonary capillary blood volume
- Oxygen Supplementation
  - High P_AO_2 results in less binding sites available for CO as oxygen competes for them



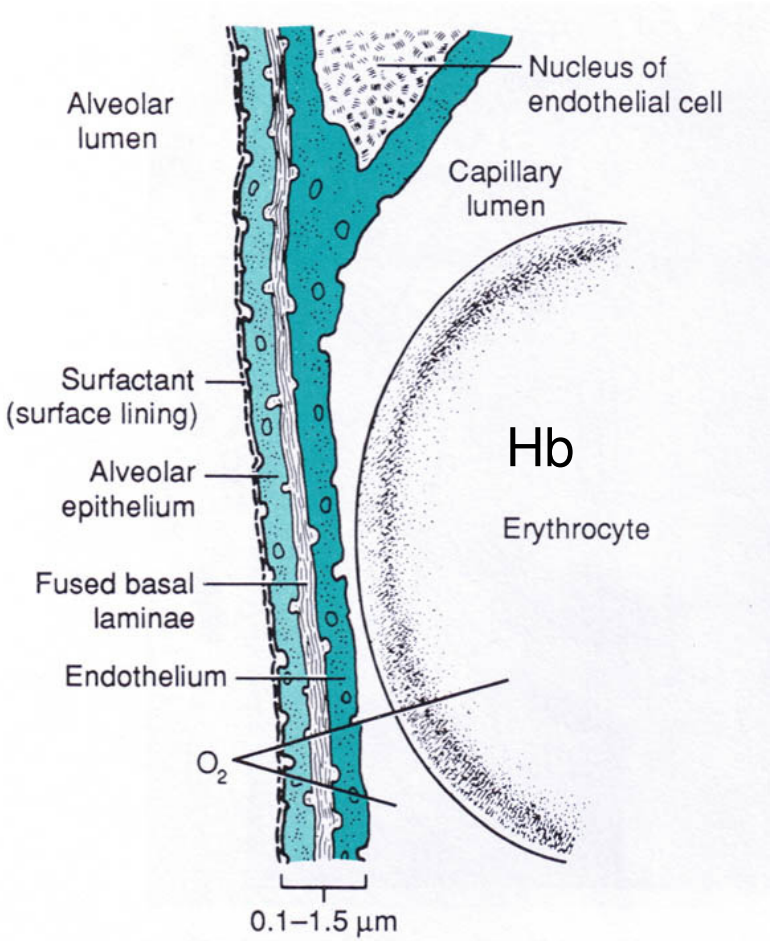
- Carboxyhaemoglobinemia
  - "anaemia effect" as Hb binding sites are already bound with CO, reduces driving pressure
- Pulmonary vascular disorders eg pulmonary emboli, PAH
  - Reduced pulmonary capillary blood volume due to vascular obstruction or vasoconstriction
- Early interstitial lung disease
- Early emphysema

High D_LCO with Normal PFTs

- Polycythemia
  - More Hb available for CO binding
- Müller manoeuvre
  - Increased negative intra-thoracic pressure increases pulmonary capillary blood volume
- Altitude
  - Low P_AO_2 results in less competition with oxygen for Hb binding sites, increasing CO uptake
- Exercise prior to testing
  - Increased recruitment and distension of pulmonary capillaries
- Left to right intra-cardiac shunt
  - Increase pulmonary capillary blood volume as pulmonary vessels engorge
- Pulmonary haemorrhage
  - Due to extra Hb in the lung



Take Home Message - D_LCO_{SB} Interpretation



- Anything that:
  - Reduces ability of CO to bind to Hb
  - Reduces ability of CO to cross the membrane
  - Reduces the amount of blood in the pulmonary capillaries

  will **DECREASE** D_LCO_{SB}

- Anything that:
  - Increases number of Hb binding sites
  - Increases the amount of blood in the pulmonary capillaries

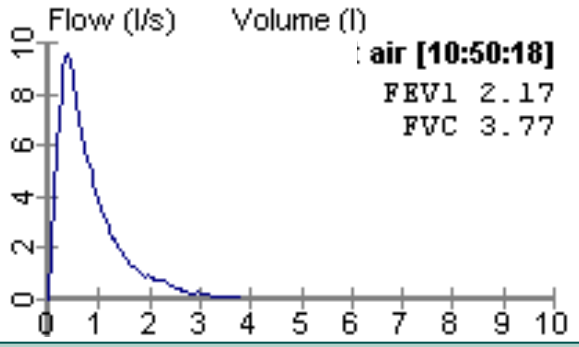
  will **INCREASE** D_LCO_{SB}

Examples – $DLCO_{SB}$ in Obstruction

- 74 yo male, 188cm, 90kg
- 2% change in FEV_1 with BD (<200mL)

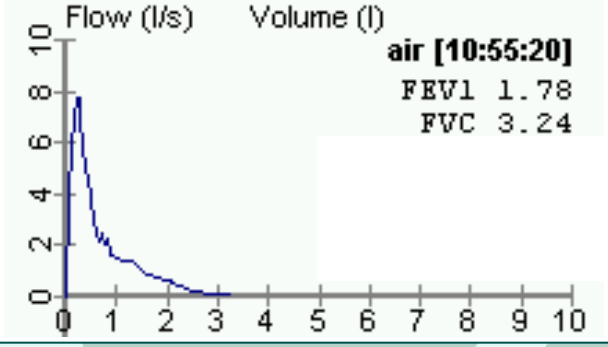
	Result	Pred	%Pred
$\%FEV_1/FVC$	57*		75
Hb (g/L)	162	135-175	
COHb (%)	0.8	<2.0	
D_LCO_{SB}	15.0*	29.8	50
D_LCO_{Hbcorr}	13.7*	29.8	46

* outside limit of normal



- 60 yo male, 184cm, 90kg
- 35% change in FEV_1 with BD (>200mL)

	Result	Pred	%Pred
$\%FEV_1/FVC$	51*		78
Hb (g/L)	142	135-175	
COHb (%)	1.8	<2.0	
D_LCO_{SB}	26.3	31.3	84
D_LCO_{Hbcorr}	27.7	31.3	89



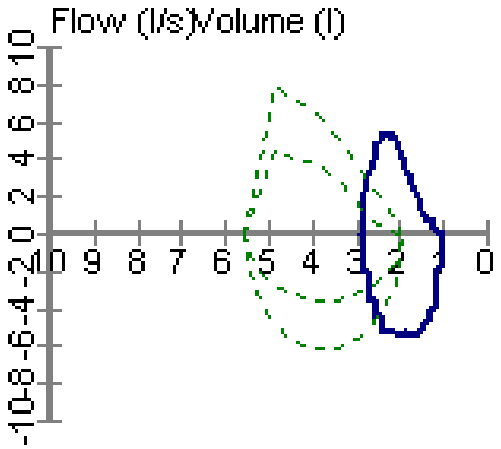
ANZSRS, Melbourne 2008

Examples – D_LCO_{SB} in Restriction

- 61 yo female, 172cm, 76.5kg
- 11% change in FEV_1 with BD (<200mL), no change in FVC

	Result	Pred	%Pred
$\%FEV_1/FVC$	88		78
VC	1.87*	3.53	53
TLC	2.77*	5.54	50
%RV/TLC	33		36
Hb (g/L)	124	115-155	
COHb (%)	N/A	<2.0	
D_LCO_{SB}	2.8*	24.9	11
D_LCO_{Hbcorr}	3.3*	24.9	13

* outside limit of normal

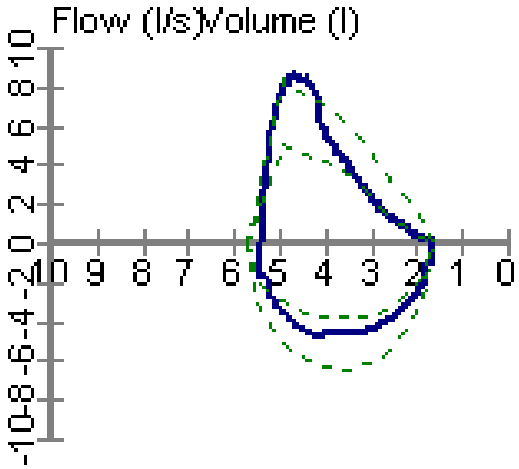


Examples – D_LCO_{SB} with Normal PFTs

- 37 yo female, 172cm, 78kg, lethargy and dyspnea on exertion
- 7% change in FEV_1 with BD (=200mL), no change in FVC

	Result	Pred	%Pred
FEV_1	3.16	3.36	94
FVC	3.72	4.06	92
$\%FEV_1/FVC$	85		83
VC	3.76	3.92	96
TLC	5.40	5.68	95
%RV/TLC	30		31
Hb (g/L)	140	115-155	
COHb (%)	1.3	<2.0	
D_LCO_{SB}	17.0*	28.4	60
D_LCO_{Hbcorr}	17.9*	28.4	63

* outside limit of normal

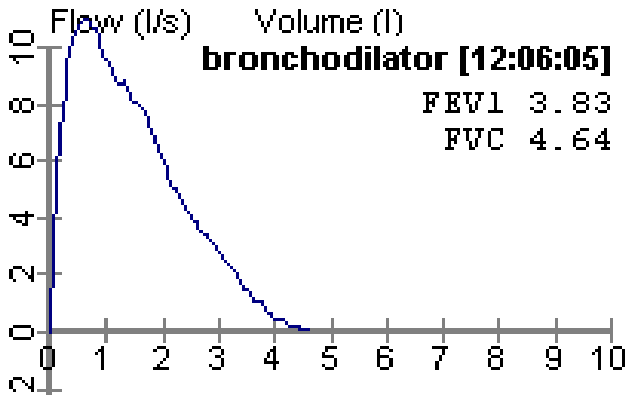


Examples – D_LCO_{SB} and Corrections

- 33 yo male, 168cm, 76kg
- 1% change in FEV_1 with BD (<200mL), no change in FVC

	Result	*Pred*	*%Pred*
FEV_1	3.83	3.96	97
FVC	4.64	4.62	98
$\%FEV_1/FVC$	83		84
Hb (g/L)	160	135-175	
COHb (%)	19.5*	<2.0	
D_LCO_{SB}	25.4	31.3	81
D_LCO_{Hbcorr}	24.5*	31.3	78
$D_LCO_{COHbcorr}$	29.3	31.3	94

* outside limit of normal



Interpretative Strategies – D_LCO

- Review test quality
  - Technical comments
  - Patient demographics
  - Key elements of test performance
    - » Valsalva / Müller, Breath hold time, Repeatability
- Compare with predicted values
  - Check adjustments for
    - » Hb, COHb, Lung volume, P_AO_2 (altitude / supplemental oxygen)
- Compare with known disease or physiologic patterns
  - Obstructive vs Restrictive
- Compare with self (longitudinal data)
- Answer the clinical question

Practice Exam Question

The gas transfer (D_LCO) of the lung is usually markedly increased in?

A cryptogenic fibrosing alveolitis

B emphysema

C asthma

D intrapulmonary haemorrhage

Practice Exam Question

A patient who smokes has a COHb of 12% and a D_LCO of 12; if the observed D_LCO value were adjusted for the increased COHb level, the corrected D_LCO would be?

A slightly higher

B slightly lower

C the same

D cannot determine without Hb concentration

Practice Exam Question

Which of the following may account for a decreased D_LCO in the absence of pulmonary disease?

1. measurements made at altitude
2. decreased haemoglobin (anaemia)
3. increased pulmonary capillary blood volume
4. elevated carboxyhaemoglobin (COHb)

A 1, 2, 3 and 4

B 1, 3 and 4

C 1, 2 and 3

D 2 and 4

Practice Exam Question

The following respiratory function results are obtained?

FVC	80% predicted
$FEF_{25-75\%}$	40% predicted
D_LCO	95% predicted
FEV_1/FVC	55%

Based on these data, which of the following is the most likely diagnosis?

A chronic bronchitis

B silicosis

C emphysema

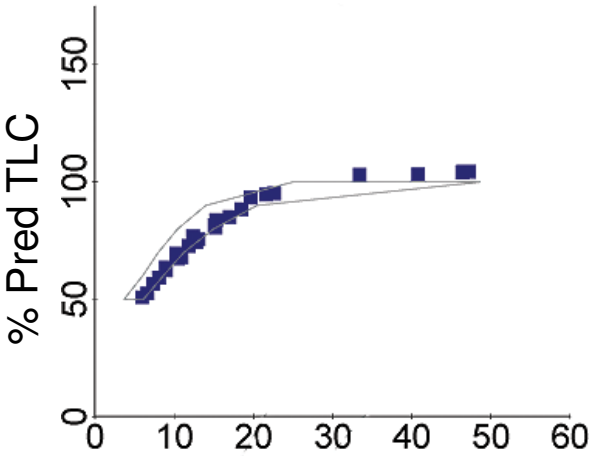
D kyphoscoliosis

Static Lung Compliance

- Measures the “give” of the respiratory system, Cstat
  - also measures maximum trans-pulmonary pressure during an inspiratory manoeuvre, PLmi
- Low Compliance
  - “Stiff” lungs or chest wall
    - » Chest wall disorders
    - » Interstitial lung disease
    - » Congestion of pulmonary vasculature or alveoli
- High Compliance
  - “Floppy” lungs
    - » Emphysema

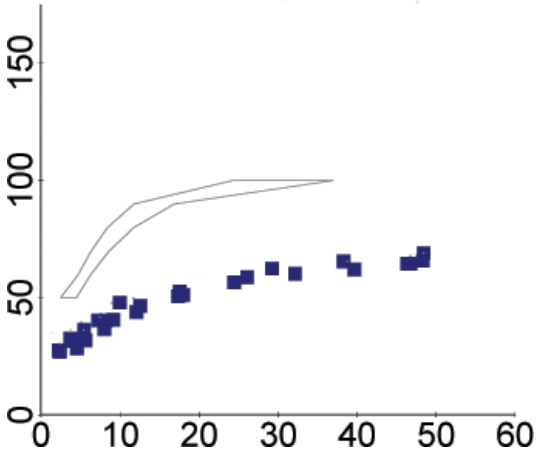
Examples- Static Lung Compliance

NORMAL



	Obs	Normal range
PLmi (cmH_20)	47.2	31.0-50.2
Cstat (L/cmH_20)	0.26	0.24-0.44

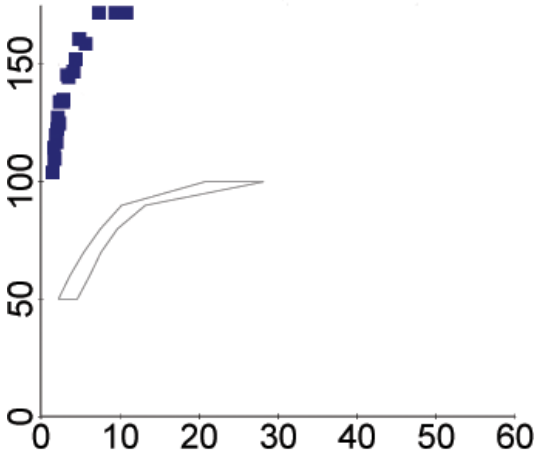
ILD



Trans-pulmonary Pressure (cmH_20)

	Obs	Normal range
PLmi (cmH_20)	48.4*	16.8-28.6
Cstat (L/cmH_20)	0.05*	0.24-0.38

EMPHYSEMA



* outside limit of normal

	Obs	Normal range
PLmi (cmH_20)	10.8*	16.8-28.6
Cstat (L/cmH_20)	1.07*	0.24-0.38

Practice Exam Question

Pulmonary compliance is increased in?

A sarcoidosis

B kyphoscoliosis

C emphysema

D pulmonary edema

Questions?