

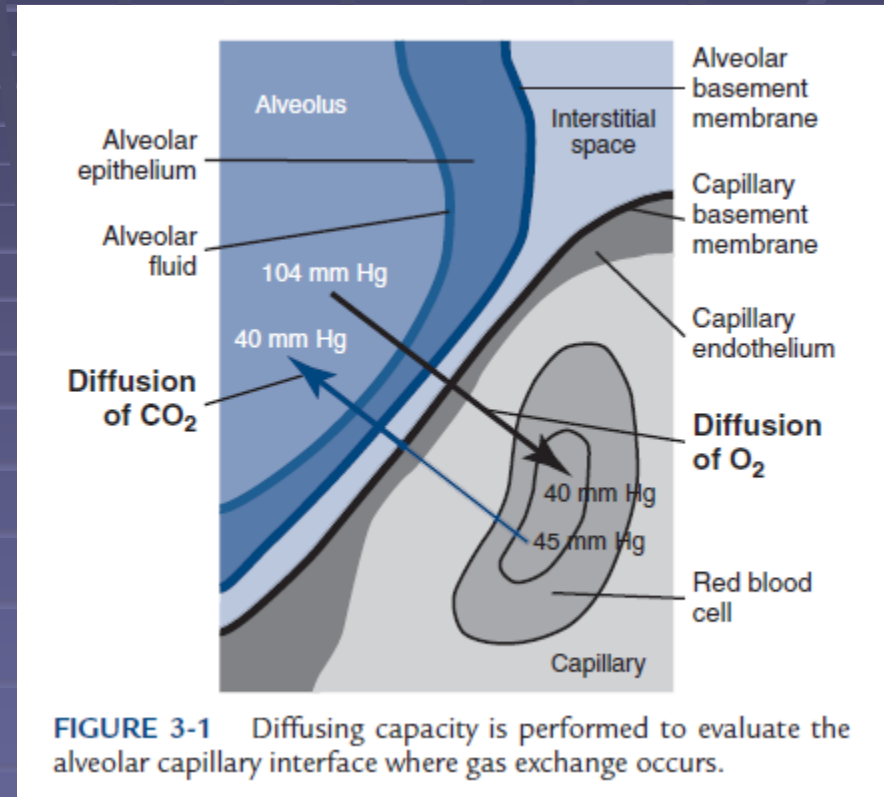
DLCO Testing – Techniques for Accuracy

Dr. C.D. Kulkarni

MD Pulmonology

Diffusing Capacity - Background

- Evaluates how well oxygen moves into and out of the lungs (alveolar capillary interface)
- Originally described by Krogh in 1915
- Product of two variables; rate of CO uptake and the V_A
- Carbon monoxide is used as a surrogate for O_2



Mottram CD 10th Ed. Ruppel's Manual of PFT. Chap. 3

Diffusing Capacity - Indications

- Evaluation and f/u of parenchymal lung diseases including: idiopathic pulmonary fibrosis (IPF, UIP, BOOP); diseases associated with dusts such as asbestos, silicosis; other lung diseases such as sarcoidosis
- Evaluation and f/u of emphysema and cystic fibrosis and differentiating among COPD patterns
- Evaluation of PV diseases (eg, PPH, PE, or pulmonary edema)

Diffusing Capacity - Indications

- Evaluation of pulmonary involvement in systemic diseases (eg, rheumatoid arthritis, lupus, Wegener's)
- Evaluation of the effects of chemotherapy agents or other drugs
 - Bleomycin, amiodarone, both require routine DLCO testing as a monitor)
- Evaluation of pulmonary hemorrhage
- As an early indication of certain pulmonary infections (eg, pneumocystis pneumonia)
- Quantification of disability

Diffusing Capacity - Standards

Standardisation of the single-breath determination of carbon monoxide uptake in the lung

N. MacIntyre, R.O. Crapo, G. Viegi, D.C. Johnson, C.P.M. van der Grinten, V. Brusasco, F. Burgos, R. Casaburi, A. Coates, P. Enright, P. Gustafsson, J. Hankinson, R. Jensen, R. McKay, M.R. Miller, D. Navajas, O.F. Pedersen, R. Pellegrino and J. Wanger

- ATS – ERS Eur Respir J 2005; 26: 720–735
- Pulmonary Function Laboratory Management and Procedure Manual
- AARC CPG on Single Breath DLCO
 - Respiratory Care (Respir Care 1999; 44 (5): 539-546)

Diffusing Capacity - Techniques

- Single breath*
- Steady-state
- Rebreathing
- Intra-breath

* Modified Krogh Technique



Diffusing Capacity – Formula's

- Diffusion Conductance

- $1/D_{LCO} = 1/D_m + 1/\Theta V_c$

- D_m = membrane conductance

- Θ = reaction rate of Hb

- V_c = pulm capillary blood volume

Diffusing Capacity – Formula's

$$D_{L_{CO}SB} = \frac{V_A \times 60}{(P_B - 47) \times (T)} \times \ln \frac{F_{ACO_0}}{F_{ACO_T}}$$

- T = breath-hold
- F_{ACO_0} = fraction of CO alveolar gas at the beginning of BH
- F_{ACO_T} = fraction of CO alveolar gas at the end of BH

Diffusing Capacity

- Different vendors use different inert tracer gases
 - Jaeger – Helium
 - Sensormedics – Methane
 - nSpire – Methane
 - Medical Graphics – Neon



ATS/ERS Standards

Standardization of Diffusing Capacity

Patient conditions for measurement (pre-test conditions)

- Factors that affect pulmonary capillary blood volume (e.g. exercise, body position), and hemoglobin affinity for CO (eg alveolar PO_2 , COHb) should be standardized.
- If clinically acceptable, the subject should not breathe supplemental oxygen for 10 minutes prior to a standard test.

ATS/ERS Standards

Standardization of Diffusing Capacity

Recent smoking

- Patient should not have smoked for 24 hours prior to testing
- Time of last cigarette should be recorded
- Back pressure of CO in blood will cause measured D_{LCO} to be lower (10% COHgb = 10% reduction in D_{LCO})

ATS/ERS Standards

Standardization of Diffusing Capacity

Hemoglobin adjustments

- Men (expected Hb 14.6):

$$DL_{CO}(\text{predicted for Hb}) = DL_{CO}(\text{predicted}) \times \frac{(1.7 \times \text{Hb})}{(10.22 + \text{Hb})}$$

- Women and adolescents (expected Hb 13.4):

$$DL_{CO}(\text{predicted for Hb}) = DL_{CO}(\text{predicted}) \times \frac{(1.7 \times \text{Hb})}{(9.38 + \text{Hb})}$$

Roughly 3.5% per gm Hb below expected

ATS/ERS Standards

Standardization of Diffusing Capacity

- DLCO affected by altitude
 - DLCO varies inversely with changes in alveolar oxygen pressure (P_AO_2).
 - P_AO_2 changes as a function of altitude, as well as with the partial pressure of oxygen in the test gas.

DLCO pred. for altitude = DLCO pred. / (1.0 + 0.0031[P_{IO_2} - 150])

ATS/ERS Standards

Standardization of Diffusing Capacity

Inspiratory maneuver

- Inspiration should be rapid (85% of VC in < 4.0 seconds)
- DLCO calculation assumes instantaneous introduction of test gas into alveolar regions.
- Long inspirations result in lower mean lung volume during the measured breath hold time (lower D_{LCO})

ATS/ERS Standards

Standardization of Diffusing Capacity

Inspired vital capacity

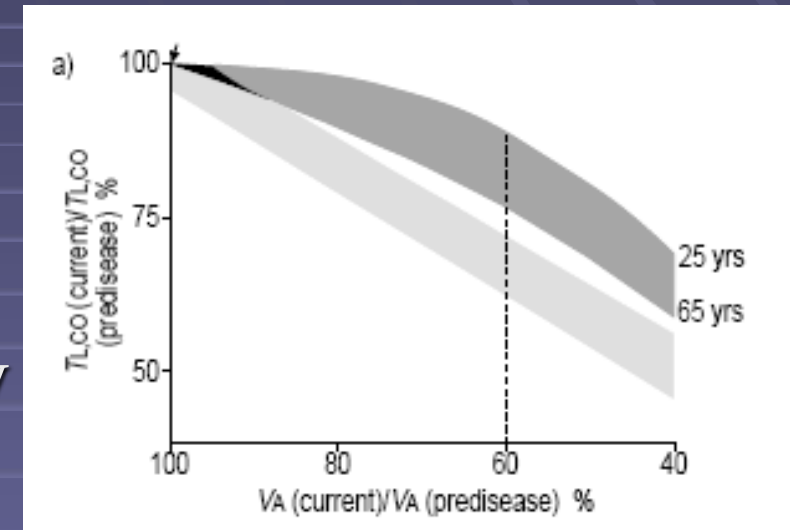
- IVC should be at least 85% of patient's previous best VC.
 - Because it appears that VI reductions as much as 15% of the known VC will reduce the DLCO less than 5%, a VI target of 85% of the largest known VC seems both reasonable and attainable.

ATS/ERS Standards

Standardization of Diffusing Capacity

Lung volume effects - low VI

- Less than maximal VI
 - lower VC and Dm (dark)
 - Lobectomy/pneumonectomy
 - lower Dm, VC recruited (light)
- Simple D_L/V_a does NOT “correct” (ie not 1:1)



In defence of the carbon monoxide transfer coefficient K_{CO} (TL/V_a)

J.M.B. Hughes, N.B. Pride

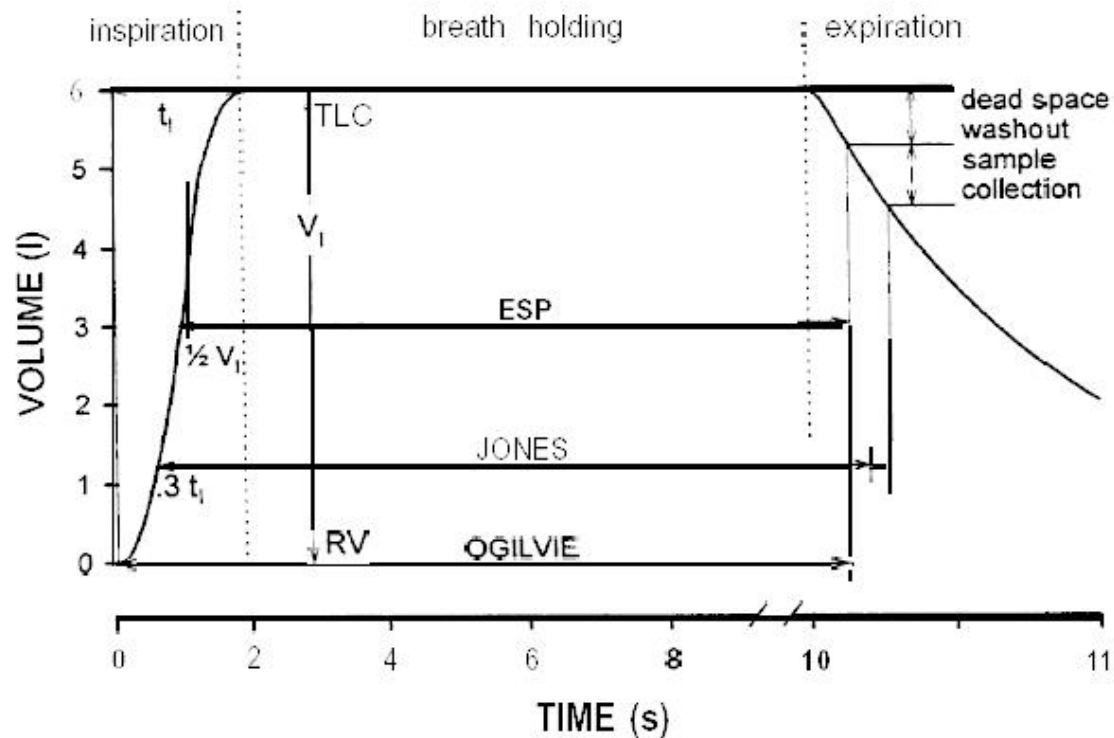
Eur Respir J 2001; 17: 168–174

ATS/ERS Standards

Standardization of Diffusing Capacity

Breath hold time

- 10 ± 2 seconds
- Avoid valsalva (expiratory efforts against a closed airway) and Müller maneuvers (inspiratory efforts against a closed airway) during the breath-hold, by decreasing and increasing thoracic blood volume respectively, will decrease and increase DLCO respectively



- Ogilvie “classic”- measures BHT at beginning inspiration to beginning of alveolar collection.
- Jones - Meade - 0.70 of inspiratory time and half of sample time.
- Epidemiologic Standardization Project measures BHT the time of 50% of V_I to the beginning of alveolar sample collection.

ATS/ERS Standards

Standardization of Diffusing Capacity

Washout volume

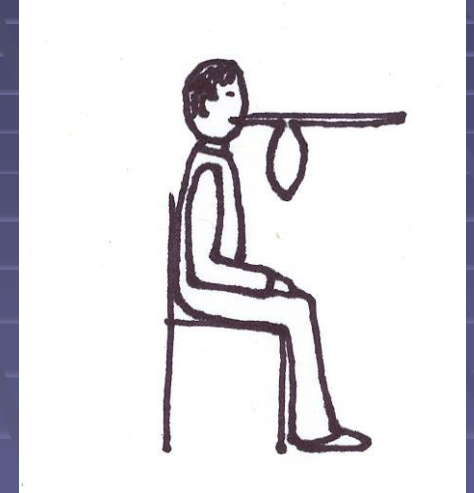
- Pre-sample washout volume should be 0.75 to 1.0 liter (clear deadspace)
 - 0.5 liter in patients with IVC < 2.0 liter
 - A gas sample taken before anatomic dead space has cleared will be contaminated by inspired gas (not pure alveolar).
 - In patients with maldistribution of ventilation (COPD) timing of gas collection may be more important.

ATS/ERS Standards

Standardization of Diffusing Capacity

Sample collection volume

- Sample volume of 0.50 to 1.00 L should be collected for analysis
 - In patients with $VC < 1$ L, smaller sample volumes below 0.50L may be used if it can be assured that VD has been cleared
- Allow 4 minutes in between tests *(especially in patients with obstruction)*

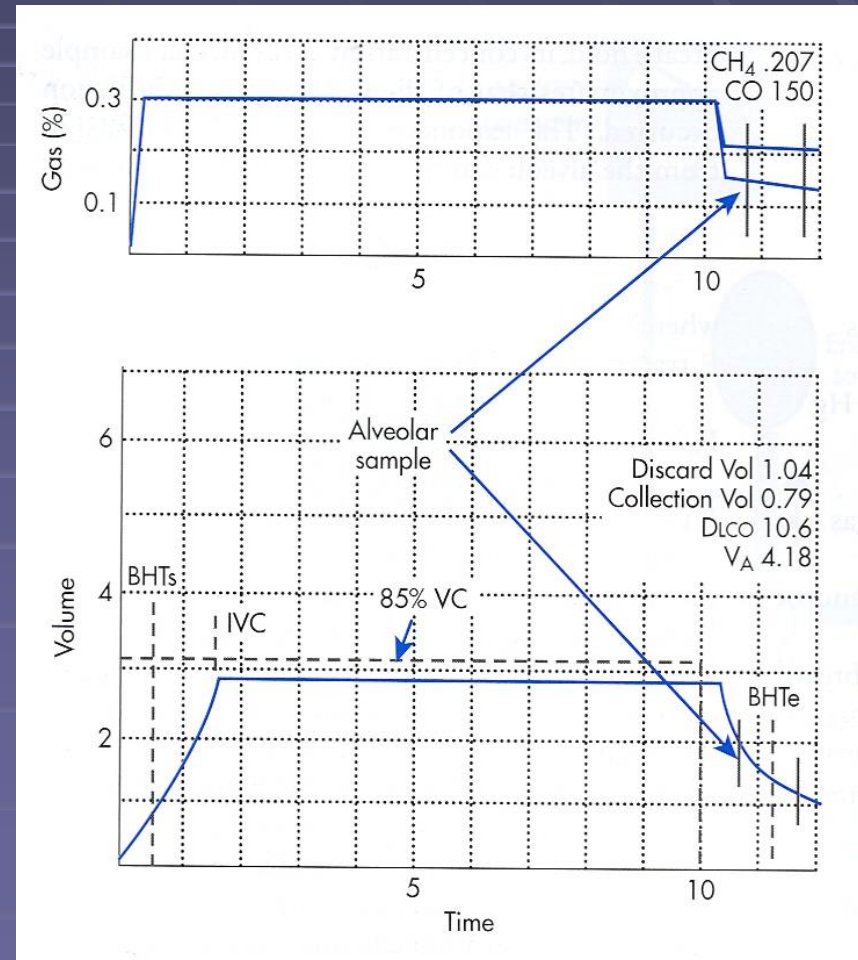


ATS/ERS Standards

Standardization of Diffusing Capacity

- Continuous Gas Analyzer
 - Allows for analysis of lower VC < 1 liter
 - Adjust washout volume once a plateau is achieved

Mottram CD 10th Ed. Ruppel's
Manual of PFT. Chap. 3



ATS/ERS Standards

Standardization of Diffusing Capacity

Miscellaneous factors

- Diurnal variation
 - One study showed DLCO fell 1.2-2.2% per hour throughout the day.
- Menstrual cycle
 - 13% fall during cycle
- Alcohol use
- Bronchodilators (effect on VA)

Alcohol Effect

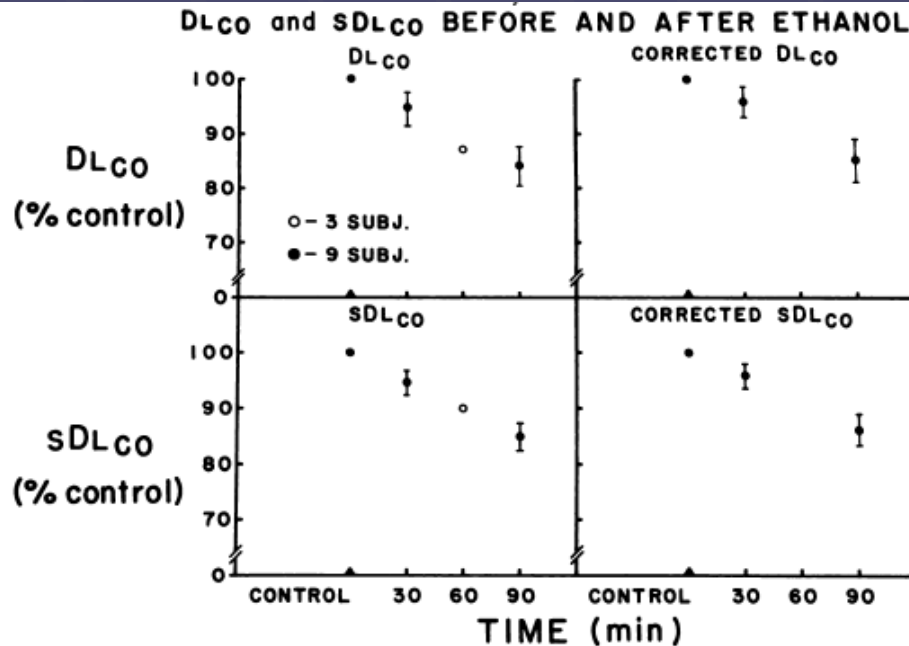


FIGURE 1. Time course of changes in DLco and SDLco ($\pm$ SEM) after acute administration of ethanol. The decrement remains statistically significant when corrections are made for CO back pressure.

CHEST, 77: 4, APRIL, 1980

ACUTE ETHANOL INGESTION EFFECTS 489

Peavy, et al Chest 77 (4)
1980

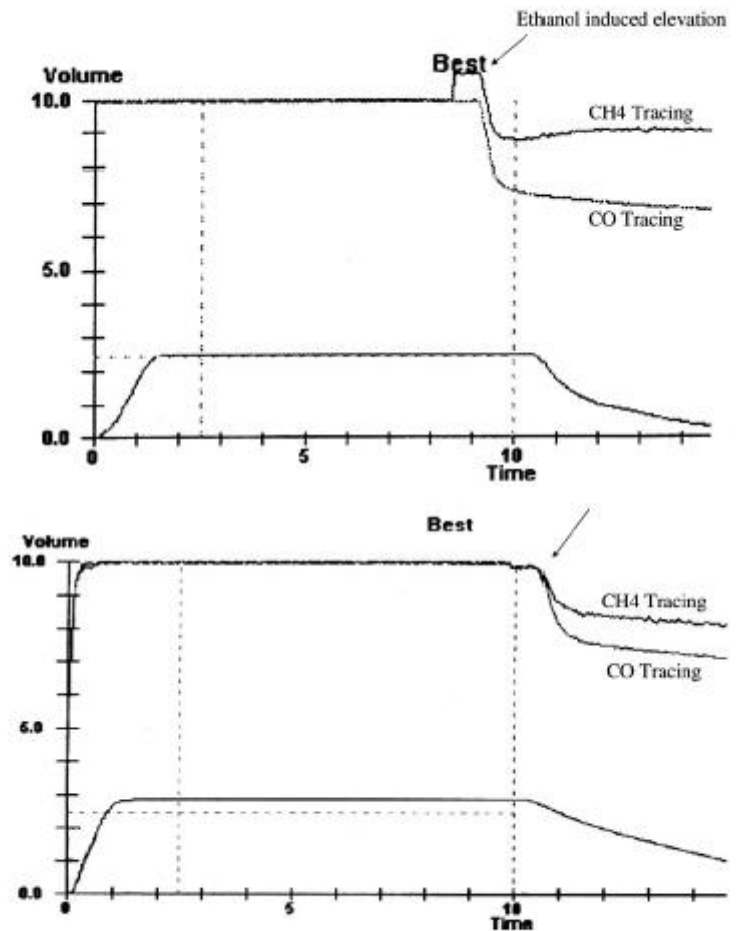
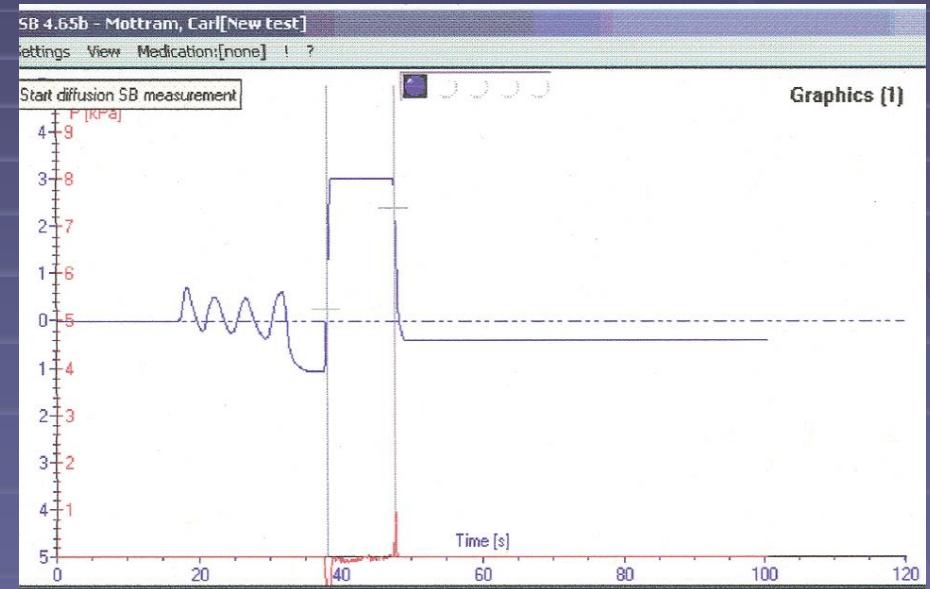


FIGURE 1. Single-breath DLCO in a subject while intoxicated (top) and when sober (bottom). Note the abnormal appearance of the methane curve (top; arrow) that later normalizes (bottom). CH₄ = methane.

Simeone et al *Chest*
2005;128;3875-3880

DLCO – Testing technique

- Quiet breathing
- Exhale to RV
- Inhale test gas rapidly
 - 0.3% CO, 10% He, 21% O₂, Bal N₂
- Breath-hold (10 sec) with no leaks (good seal on mouthpiece)
- Exhale (relatively fast)



Acceptability and Repeatability

- Two acceptable maneuvers
- Repeatability requirement of either being within 3 mL CO (STPD) of each other or within 10% of the highest value.
- Report mean

Example

- 24.5
- 26.8

Report 25.6

Diffusing Capacity

- Data is reported in STPD
- Units: ml/min/mmHg





ILLUSTRATION BY BRYAN LESTER

QUALITY CONTROL

ATS/ERS Standards

Standardization of Diffusing Capacity

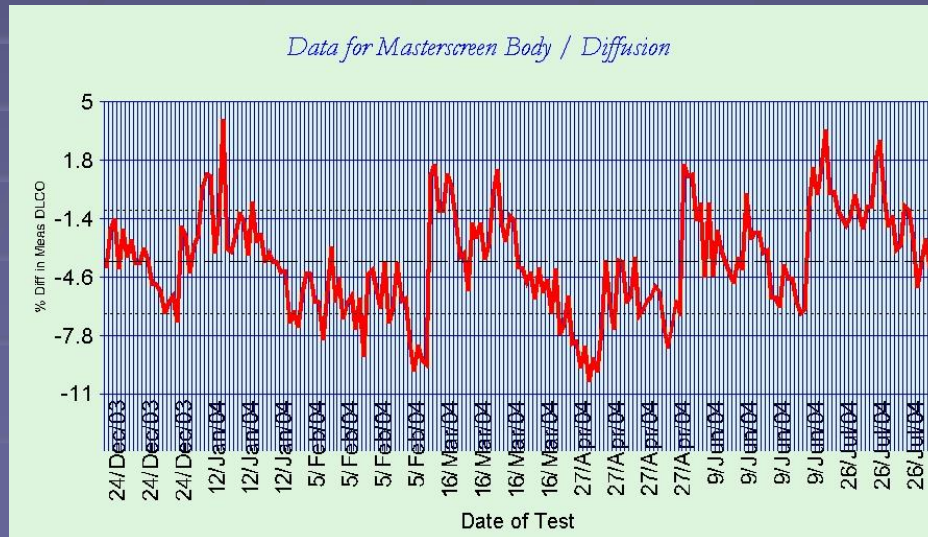
Quality Control

Table 3: Equipment Quality Control

Gas analyzer zeroing	Done before/after each test
Volume accuracy	Tested daily
Standard subject or simulator testing	Tested at least weekly
Gas analyzer linearity	Tested quarterly
Timer	Tested quarterly

Diffusing Capacity – Quality Assurance

- Daily volume accuracy
- Syringe DLCO
- DLCO Simulator or BioQC



Diffusing Capacity – Quality Assurance

- Biological Model
 - Normal laboratory subjects
 - Two individuals (13)
 - Establish mean and SD (minimum 20 samples)

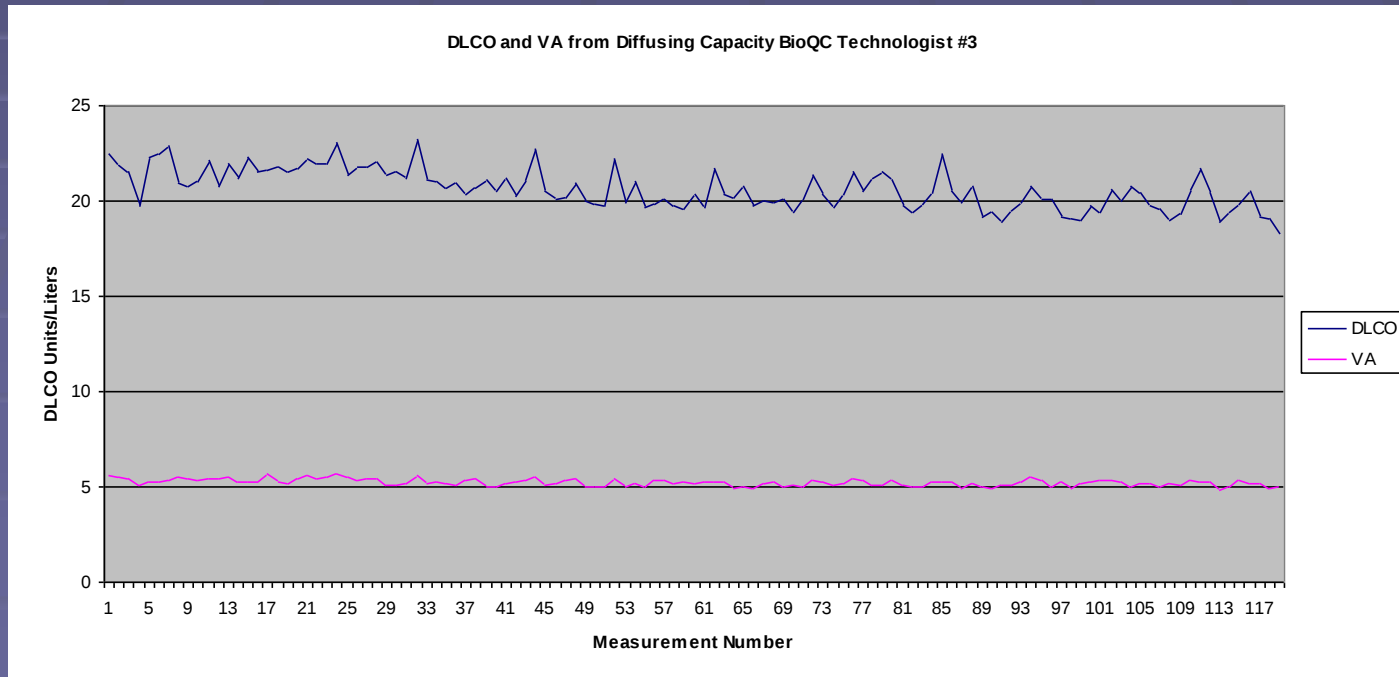


2005 ATS/ERS Standards
General Laboratory

Diffusing Capacity - QA

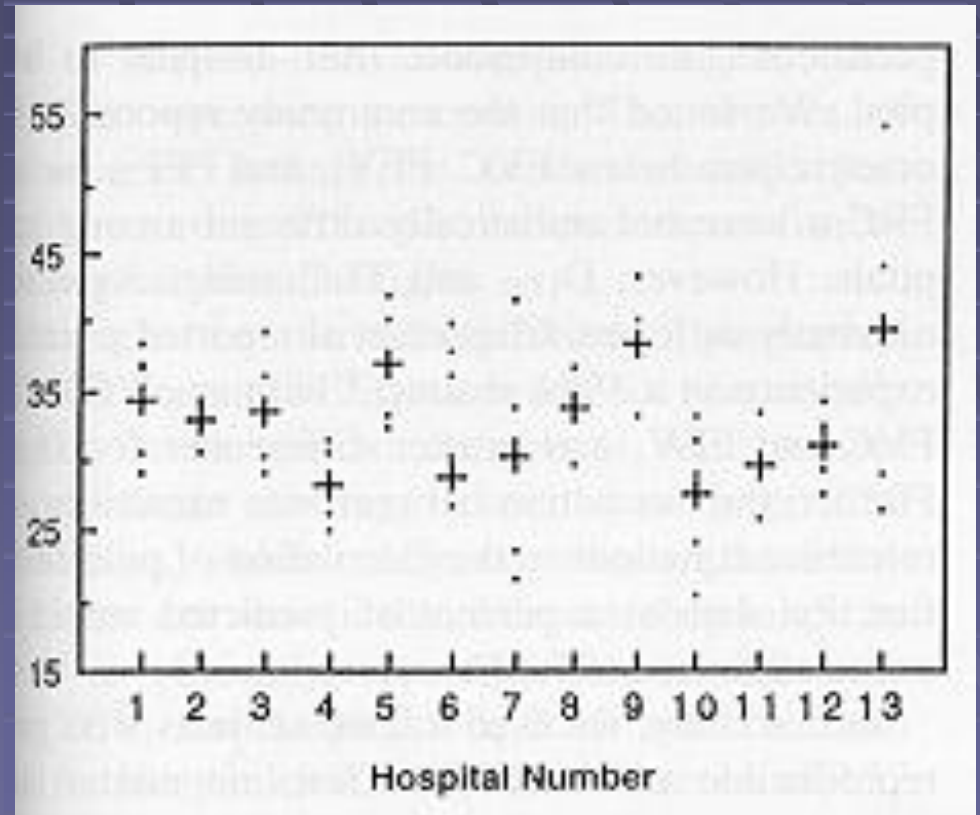
At least weekly

- *Or* whenever errors are suspect
- *Or* whenever a calibration tank is replaced



“Old” Evidence of Quality DLCO Testing

- Wanger J, Irvin C
Resp Care 36 (12): 1991
- 13 hospitals, 7
different systems, 5
Bio-QC (3 men, 2 women)
- DLCO CV 11.5 - 18.6
largest diff. 24 units



“New” Evidence of Quality DLCO Testing

Certification of DLCO Measurements for Clinical Trials

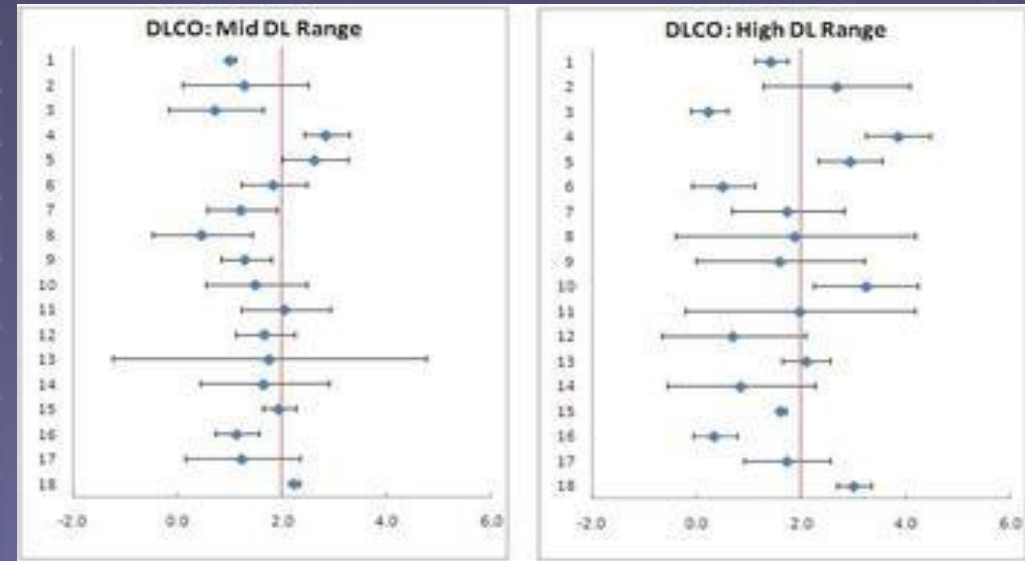
- Results of the initial DLco simulation tests from 125 pulmonary laboratories
 - 94 (75.2%) Passed with coaching; no hardware
 - 24 (19.2%) Failed. Passed after servicing
 - 6 (4.8%) Failed. Passed with new equipment
 - 1 (0.8%) Site dropped 1

Dlco Instrument Accuracy Across A Utah Health System

M. J. Hegewald¹, A. Morris², H. Gallo³, Y. Li³

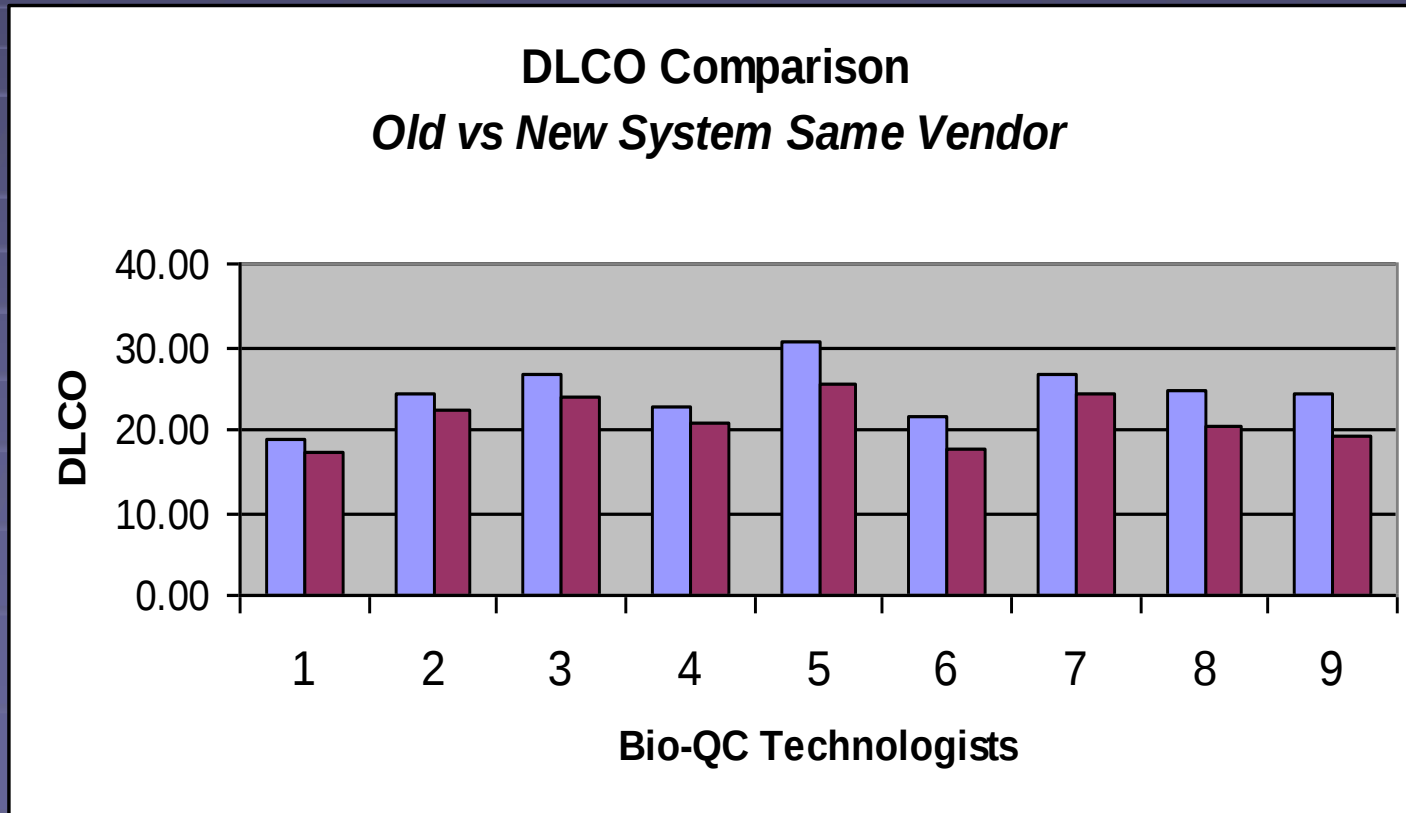
2011 ATS Abstract

- 18 DLCO instruments at 13 Intermountain Health Care sites over 10 months
- DLCO instrument accuracy was unacceptable in 22-33% of instruments



DLCO Validation

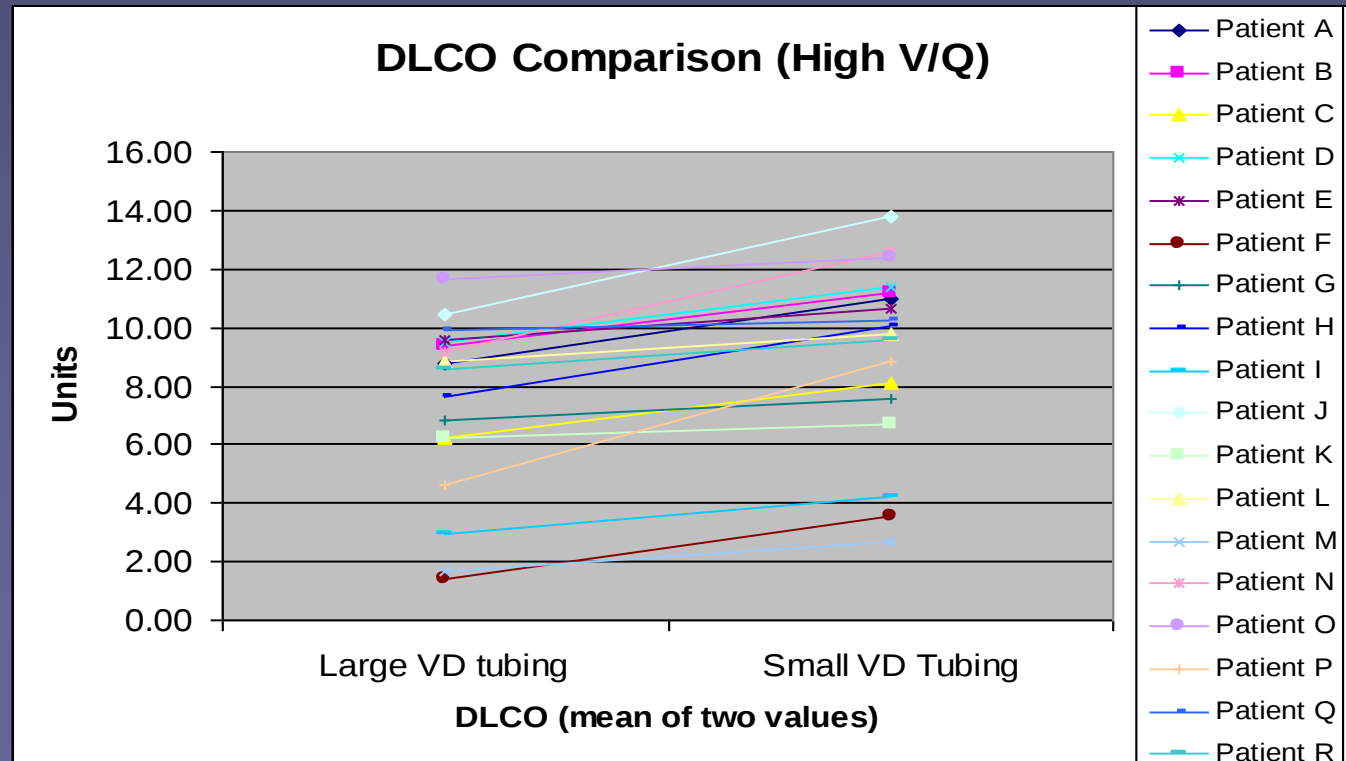
- 3.19 units different





DLCO - Equipment

Comparison of Two Different Size Single Breath Diffusing Capacity Collection Tubes on the Jaeger Masterscope PFT System in Patients with Reduced DLCO and Biological Controls Mottram CD et al. Resp. Care 2002



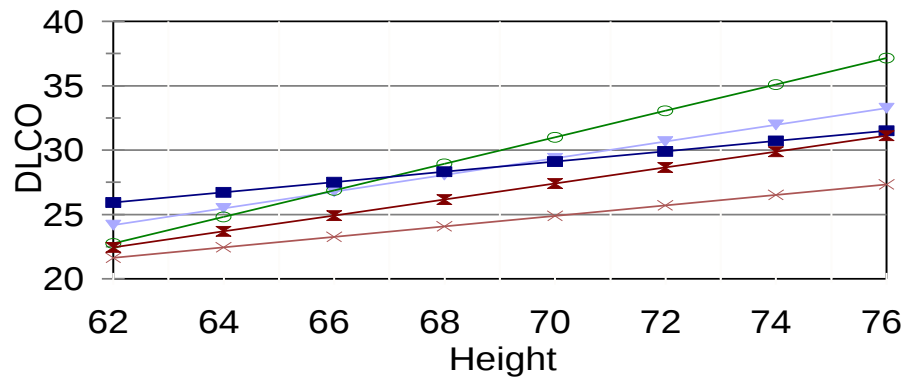
What is considered abnormal?



Reference Equations

DLCO PREDICTED

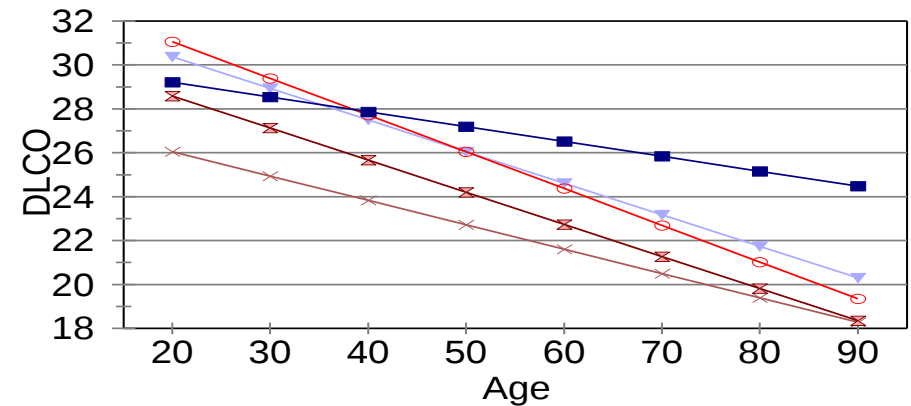
45 Year old Female



Increase with height

DLCO PREDICTED

64 inch Female



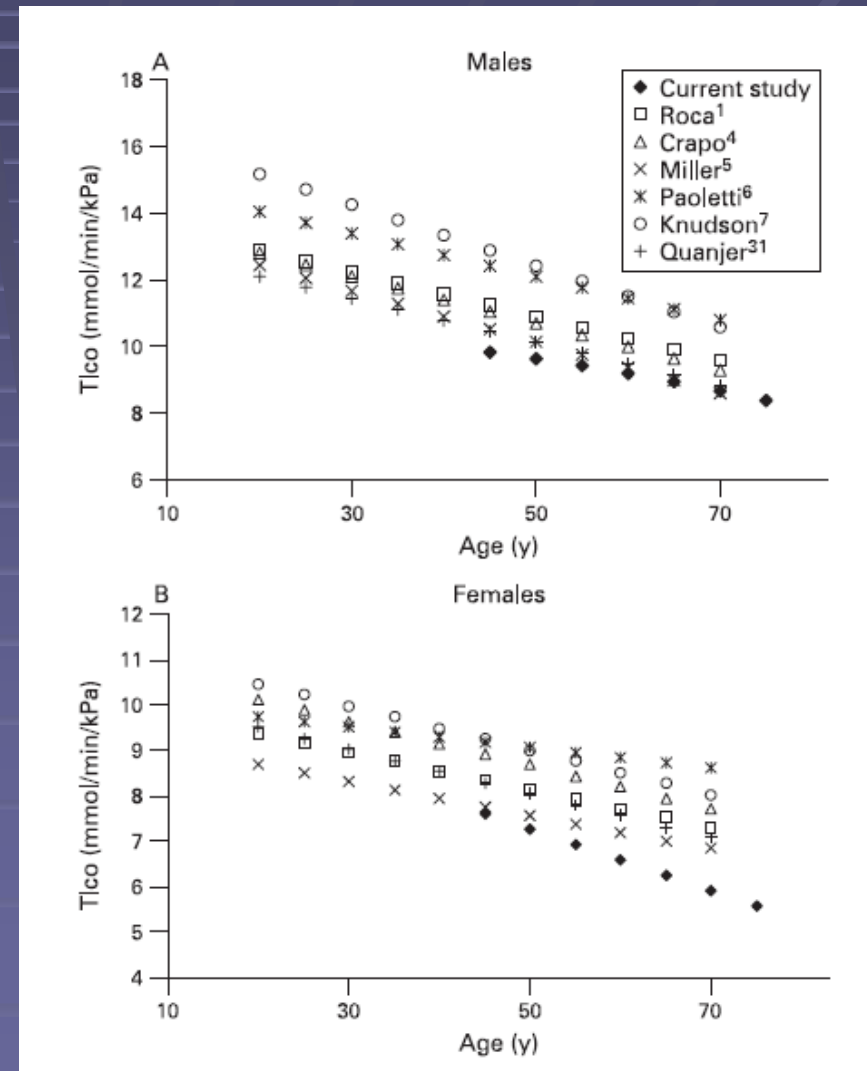
Decrease with age

Reference Equations

Prediction equations for single breath diffusing capacity (Tlco) in a middle aged caucasian population

B R Thompson,^{1,2} D P Johns,³ M Bailey,⁴ J Raven,^{1,4} E H Walters,^{3,4} M J Abramson^{1,4}

- Healthy subjects (498 male and 474 female) aged 45–71 years.
- Thorax 2008;63:889–893



Diffusing Capacity - Clinical Correlation

Increased $D_{L,CO}$

- Increased blood flow
(exercise, left to right shunt, hyperdynamic state).
- Increased Hgb
- Increased pulmonary capillary blood volume
- Obesity (secondary to increased blood volume?)
- Asthma (increased D_m ? or increased blood volume?)
- Intrapulmonary hemorrhage.

Diffusing Capacity - Clinical Correlation

Isolated low $D_{L,CO}$

- Pulmonary vascular abnormalities (e.g. embolism, vasculitis, hypertension)
- Interstitial lung disease (early disease -> low $D_{L,CO}$ with nml lung volumes)
- Anemia [50% reduced Hgb -> 40% reduced $D_{L,CO}$ (Cotes equation)]
- Early emphysema

Diffusing Capacity - Clinical Correlation

Low $D_{L,CO}$ with other abnormalities:

- Restrictive pattern (low lung volumes): interstitial lung disease.
- Obstruction: reduced $D_{L,CO}$, particularly in moderate to severe obstruction combined with increased lung volumes (hyperinflation) suggests emphysema.
- Inhomogeneity of gas distribution (bronchitis/asthma) may cause underestimate of $D_{L,CO}$

Diffusing Capacity - Clinical Correlation

$$D_{L,CO}/V_A$$

- Interpretation of $D_{L,CO}/V_A$ is controversial
 - May differentiate IPF from other forms of restriction (inflammatory diseases, chest wall, muscle weakness, pleural disease).
- Increased $D_{L,CO}/V_A$ may be seen in
 - Chest wall restriction
 - pneumonectomy (increased blood flow through remaining lung)

Diffusing Capacity - Clinical Correlation

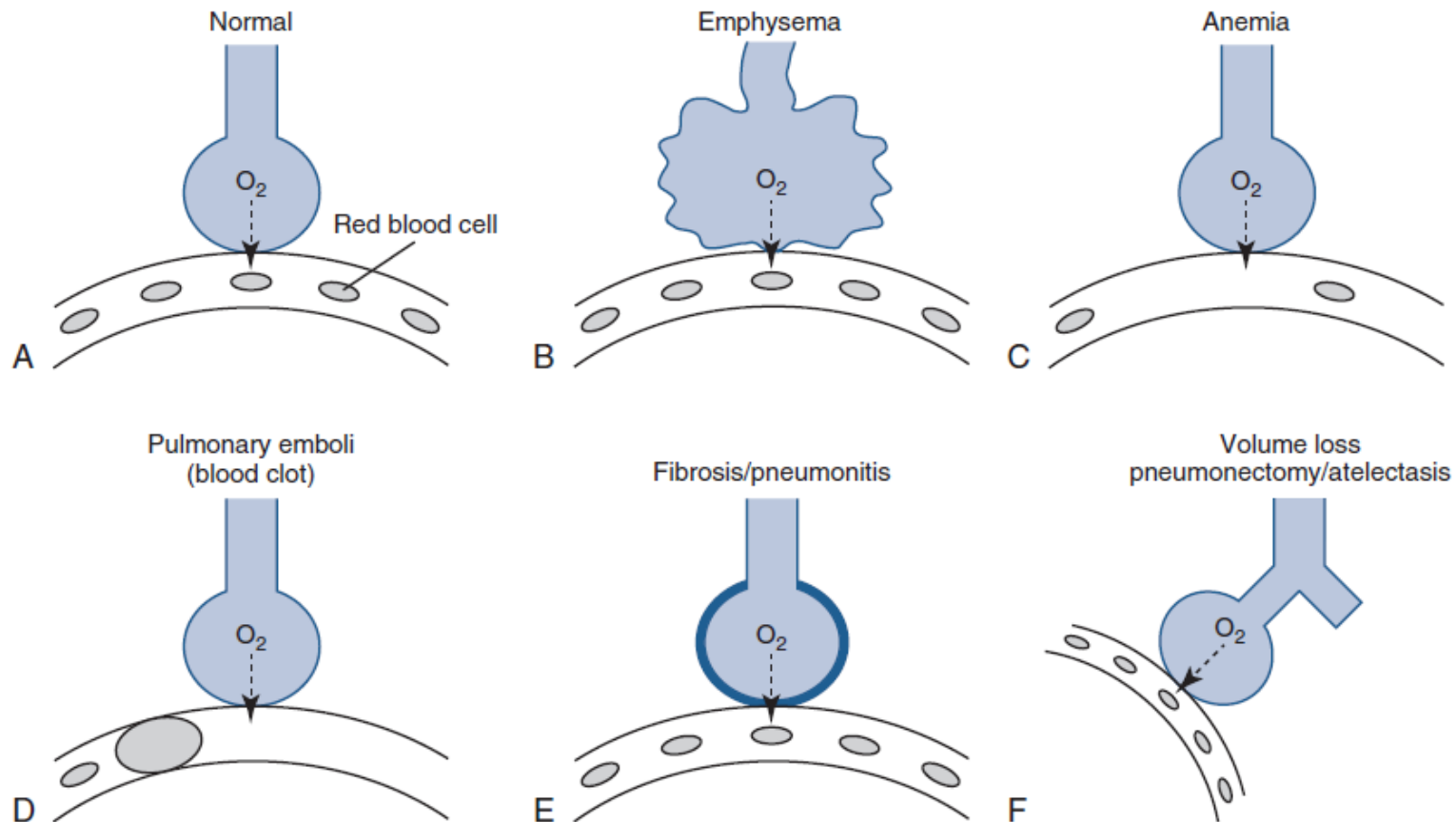


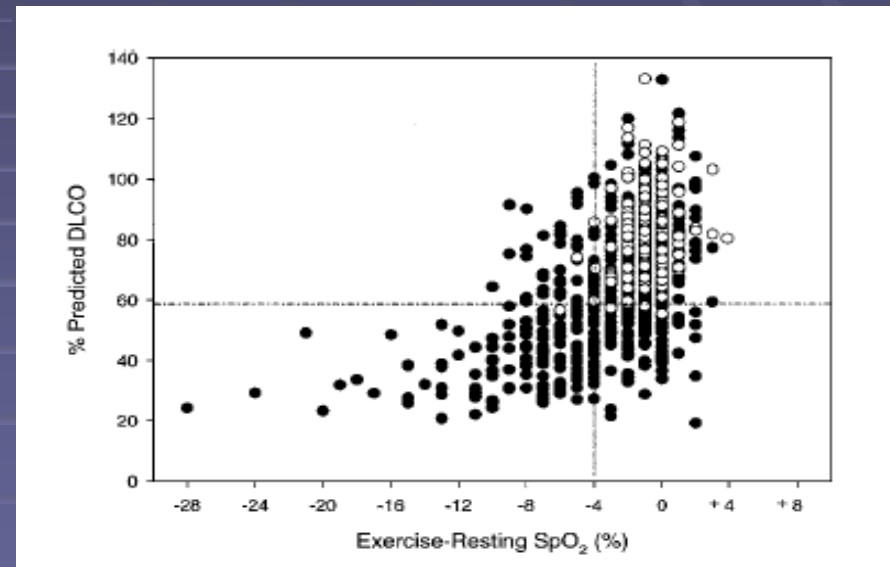
FIGURE 3-6 D_{lco} and disease. Some of the more common disease disorders which affect gas exchange. (A) Depicts the normal alveolar capillary interface where gas exchange occurs; (B) Emphysema—destruction of the alveolar capillary interface and hyperinflation; (C) Anemia – reduction in oxygen-carrying capacity; (D) Pulmonary emboli and/or A-V malformations affect oxygen transport; (E) Interstitial lung disease such as pulmonary fibrosis scars the alveolar membrane surface; (F) Alveolar volume loss from resection, alveolar collapse, or filling processes.

Predictors of Oxygen Desaturation During Submaximal Exercise in 8,000 Patients*

Khaled O. Hadeli, Erin M. Siegel, Duane L. Sherrill, Ken C. Beck and Paul L. Enright

Chest 2001;120;88-92

- A cut point of DLCO < 62% predicted resulted in 75% sensitivity and specificity for exercise desaturation
- *Conclusions:* The risk of oxygen desaturation during submaximal exercise is very high in patients with a low DLCO



Diffusing Capacity - Interpretation

- Appropriate Reference Equation is essential
- Understand the measurement variability
- Highly sensitive/poor specificity
- Must evaluate in context with other tests
- Consider both absolute value and DL/VA ratio?

Diffusing Capacity - Interpretation

Severity Classification - DLCO

TABLE 14

Degree of severity of decrease in diffusing capacity for carbon monoxide (DL_{CO})

Degree of severity

DL_{CO} % pred

Mild

>60% and <LLN

Moderate

40–60%

Severe

<40

% pred: % predicted; LLN: lower limits of normal.

ROUTINE PULMONARY FUNCTION LABORATORY (S-3)

MAYO CLINIC, ROCHESTER, MINNESOTA

Printed: 01/10/2008 16:21

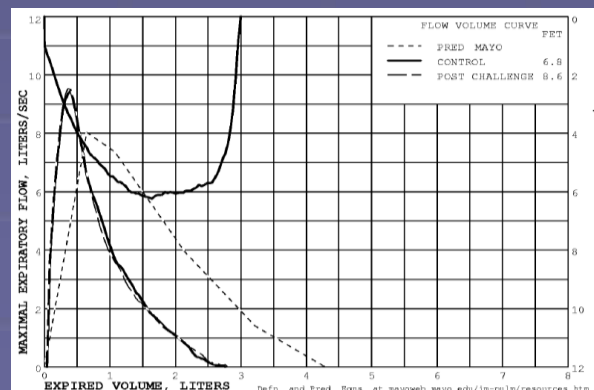
Test: 01/10/2008 10:01

65 y.o. Male Wt:131.7 KG, BMI: 43.8++
Previous test: 8/26/1998 Desk:

Ht:173.4 cm

RC: 1.00

	PREDICTED NORMAL	RANGE	CONTROL FOUND	%PRED.	POST-CHALLENGE** FOUND	%CHANGE
LUNG VOLUMES						
TLC (Pleth)	6.49	>5.12	4.52*	70%		
VC	4.29	>3.46	2.93*	68%		
RV	2.20	<2.85	1.58	72%		
RV/TLC	33.8	<44.3	35.1	104%		
FRC			2.0			
SPIROMETRY						
FVC	4.29	>3.46	2.69*	63%	2.73	
FEV1	3.34	>2.66	2.24*	67%	2.21	-1%
FEV1/FVC	77.8	>68.6	83.1		80.8	
PEF25-75	3.0	> 1.6	2.1	71%	2.0	
PEFmax	8.0	> 4.6	9.5	118%	9.5	+1%
FIFmax			6.2			
PEF50/FIF50			0.4			
MVV	131	> 98	119	91%		
AIRWAY FUNCTION						
SRaw	4.7	< 7.9	5.8	124%		
DIFFUSING CAPACITY						
DLCO (SB)	26.6	>18.6	17.5*	66%		
DLCO (adjusted for Hgb = 16.0 gm/dL)			16.8*	63%		
VA	6.20	>5.12	3.78*	61%		
OXIMETRY						
O2 Sat	96	≥ 93	93		85*	
Pulse			100		122	
*Outside normal range. ++ weight exceeds 98th percentile.						
**CHALLENGE: Methacholine-25mg/ml, 5 Breaths						



■ idiopathic pulmonary fibrosis

46 y.o. Male Wt: 70.5 KG, BMI: 23.6
Previous test: 1/21/2008 Desk:

Ht:172.7 cm

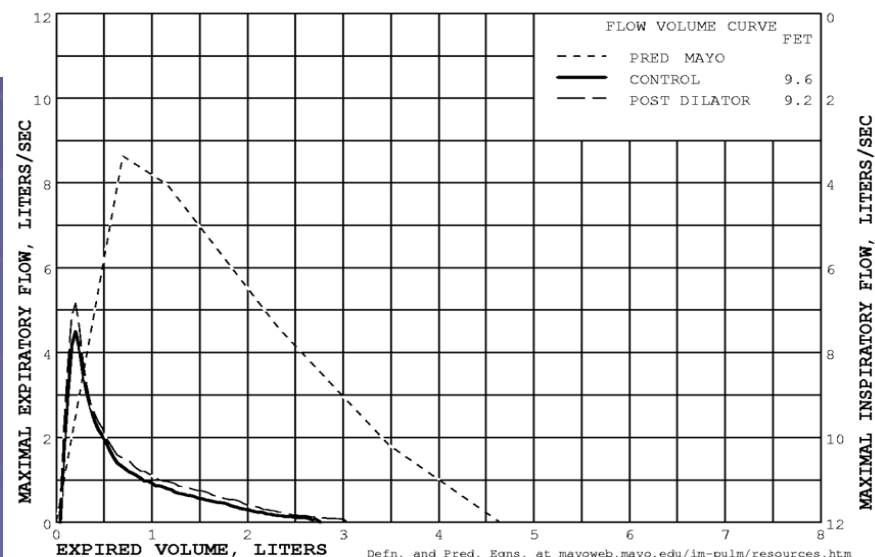
RC: 1.00

	PREDICTED		CONTROL		POST-DILATOR**	
	NORMAL	RANGE	FOUND	%PRED.	FOUND	%CHANGE
LUNG VOLUMES						
TLC (Pleth)	6.44	>5.07	5.07	79%		
VC	4.64	>3.80	3.02*	65%		
RV	1.79	<2.33	2.05	114%		
RV/TLC	27.9	<36.5	40.5*	145%		
FRC			2.9			
SPIROMETRY						
FVC	4.64	>3.80	2.72*	59%	2.99*	+10%
FEV1	3.75	>3.07	1.27*	34%	1.41*	+11%
FEV1/FVC	80.7	>71.5	46.9*		47.0*	
FEF25-75	3.5	> 1.9	0.6*	16%	0.6*	
FEFmax	8.6	> 5.2	4.5*	52%	5.2*	+15%
MVV	154	> 121	48*	31%		
DIFFUSING CAPACITY						
DLCO(SB)	30.8	>22.8			FOUND %PRED.	
DLCO(adjusted for Hgb = 16.7 gm/dL)					20.2*	65%
VA	6.28	>5.07			19.1*	62%
					4.32*	69%
OXIMETRY						
O2 Sat	96	≥ 93	REST		EXERCISE (High Step 3.00 mins)	
Pulse			94		92*	
			92		108	

*Outside normal range.

**Bronchodilator was Albuterol

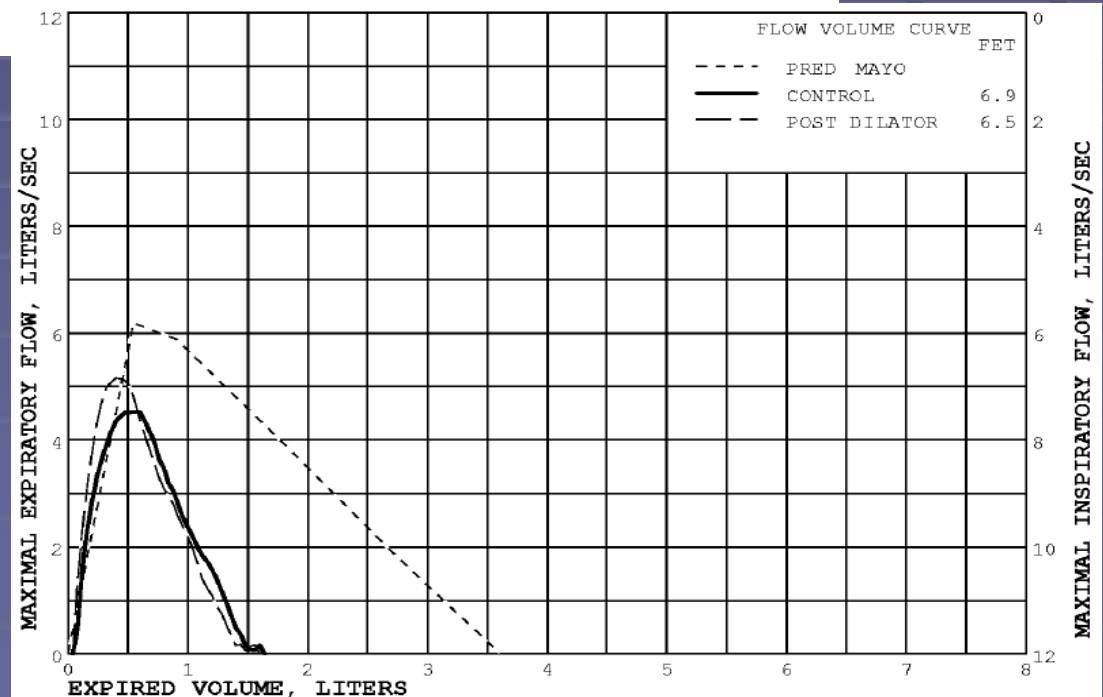
Alpha - 1



	PREDICTED		CONTROL		POST-DILATOR**	
	NORMAL	RANGE	FOUND	%PRED.	FOUND	%CHANGE
LUNG VOLUMES						
TLC (Pleth)	4.50	>3.40	2.51*	56%		
VC	3.61	>2.88	1.49*	41%		
RV	0.88	<1.15	1.02	116%		
RV/TLC	19.6	<25.7	40.7*	207%		
FRC			1.6			
SPIROMETRY						
FVC	3.61	>2.88	1.58*	44%	1.54*	-2%
FEV1	3.17	>2.62	1.46*	46%	1.39*	-5%
FEV1/FVC	87.8	>76.7	92.6		90.0	
FEF25-75	3.6	> 1.6	2.7	74%	2.5	
FEFmax	6.2	> 3.5	4.5	73%	5.2	+14%
MVV	117	> 84	51*	44%		
DIFFUSING CAPACITY						
DLCO(SB)	24.2	>17.7			10.8*	45%
DLCO(adjusted for Hgb = 14.3 gm/dL)					10.5*	43%
VA	4.38	>3.40			2.38*	54%
OXIMETRY						
O2 Sat	97	≥ 93	98		92*	
Pulse			78		136	
				REST	EXERCISE (High Step 3.00 mins)	
					FOUND %PRED.	

*Outside normal range.

**Bronchodilator was Albuterol

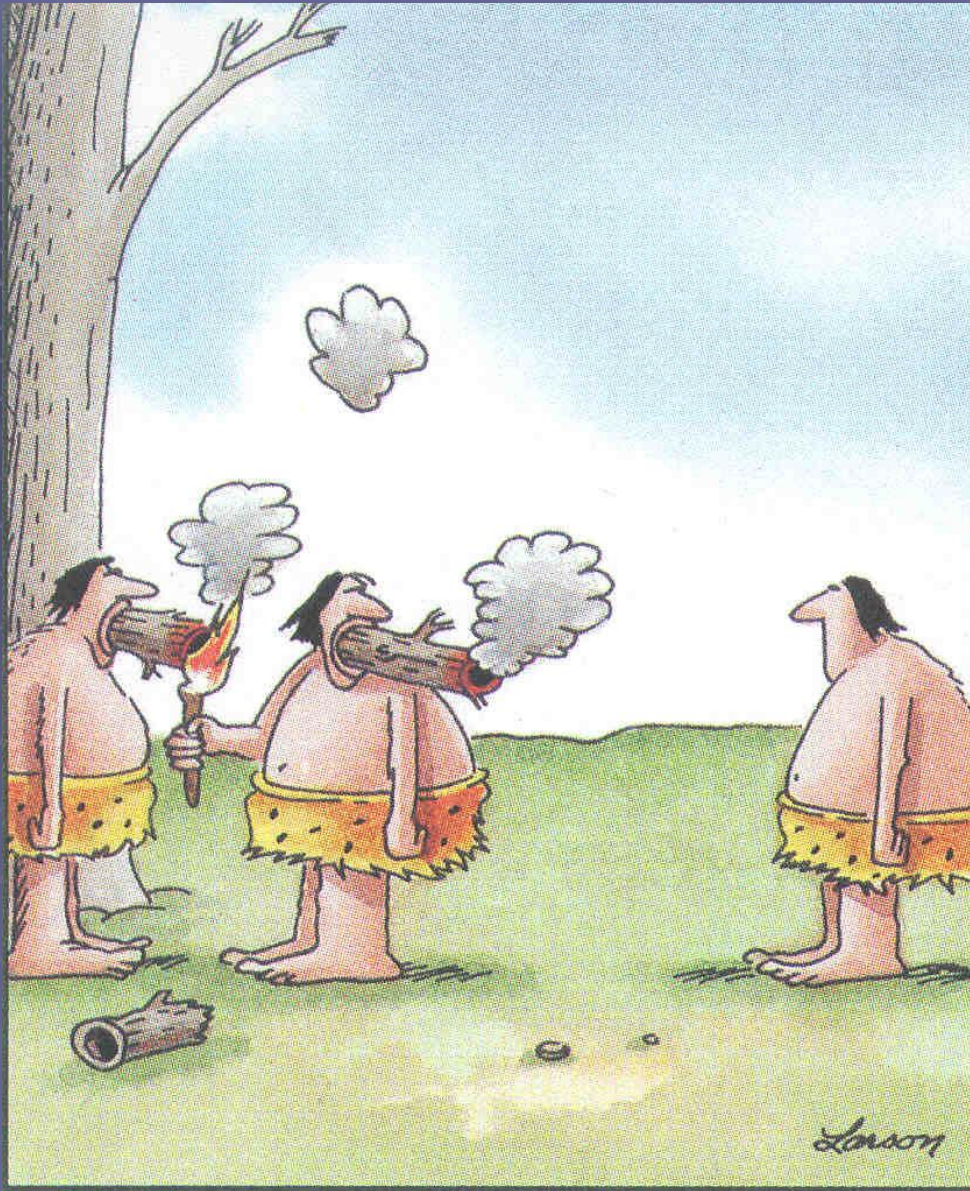


Alveolar proteinosis

Diffusing Capacity

“Carl’s Top List”

1. All equipment is not the same
2. Equipment calibration
3. QA model should include Bio-QC
4. Pre-test instructions
5. 85% of VC in 4 sec.
6. Make appropriate adjustments.
7. Use Jones-Meade
8. Reproducibility 10%, 3 units or 2 units under 10



Primitive peer pressure

Questions?