Diffusing Capacity: 2017 ATS/ERS Standards for single-breath carbon uptake in the lung

Susan Blonshine RRT, RPFT, FAARC, AE-C

Joint ATS/ERS Taskforce

- Recent literature reviewed
- Surveyed current technical capabilities of instrumentation manufactured
- Recommendations reflect consensus of task force related to
  - Evidence
  - Expert opinion where peer-reviewed evidence was not available or incomplete

Update of 2005

- Update in regards to RGA systems
- Provide new calculation standards incorporating continuous gas analysis
- Standard restricted to single-breath technique
- Five committee members from 2005 and four new members

RGA versus Current Systems

- Focused on Rapid-response Gas Analyzers (RGA)
  - new suggestions and requirements for labs and manufacturers required for systems with a RGA
  - gas analyzers with a 0 to 90% response time of less than or equal to 150 ms
  - Real-time, continuous gas analyzers but tend to use discreet measurements
  - Allow marked improvements using data with continuous measurements

RGA versus Current Systems

- Authors do state that the new standards do not make older systems that use discrete alveolar sampling and slower gas analyzers obsolete (classical systems)

Equipment Requirements

- A reminder that any error in flow and the calculation of volume results in a corresponding error in DLCO
- Requirements are included for both RGA systems and classical discrete sampling systems

Equipment Requirements

- Flow accuracy required to be ± 2% over a range of ± 10 L/sec
- Volume accuracy required to be ± 2.5% (± 75 ml) instead of ± 3.5% with a 3-L syringe
  - Volume accuracy must be maintained across range of gas compostions and concentrations

Equipment Requirements

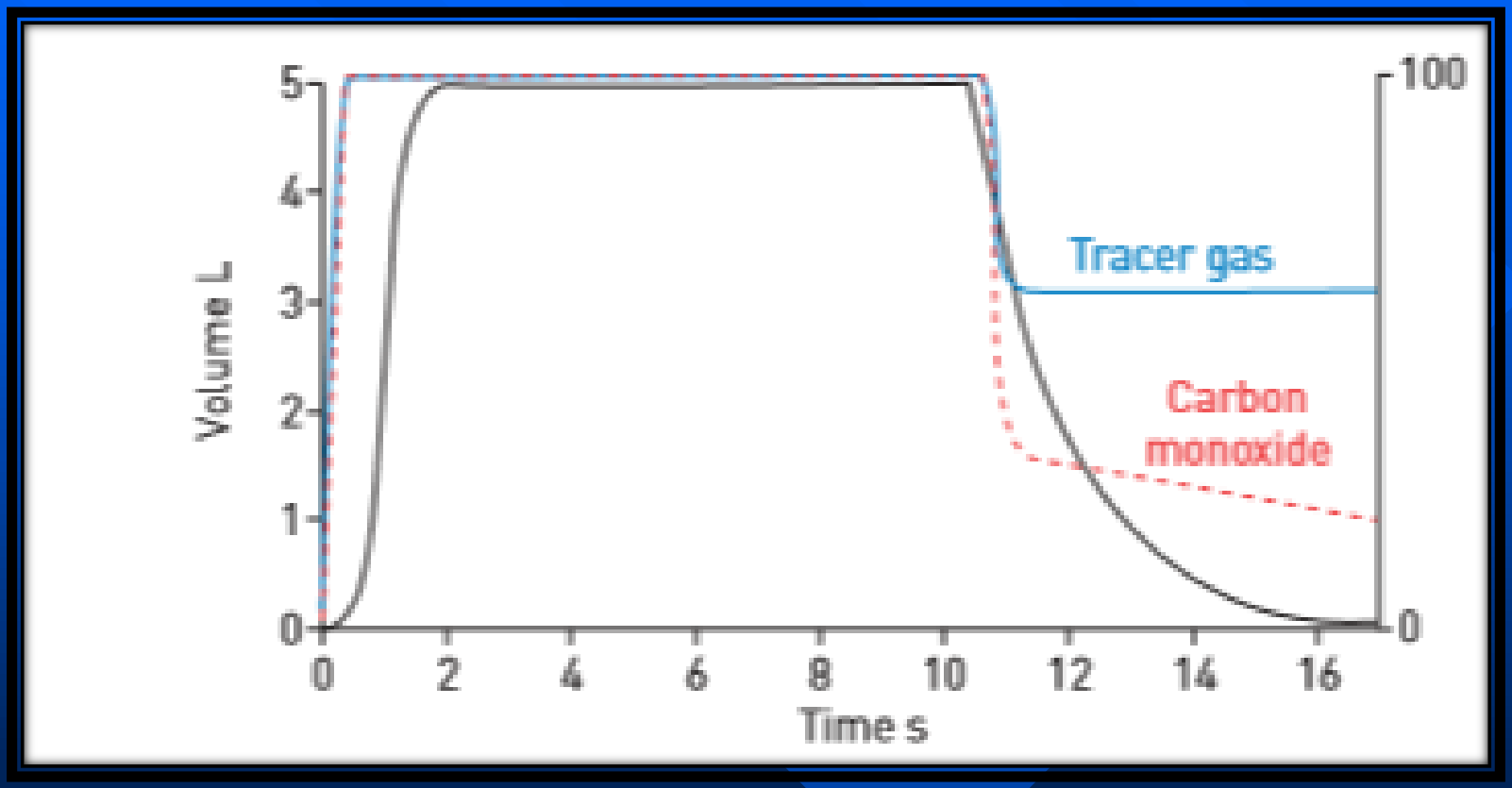
- RGA response time (analyzer rise time) required to be ≤150 milliseconds (new)
  - Not required for classical discrete samples
- Analyzer linearity for both RGA and discrete sample systems ± 1.0% from ± 0.5% in the 2005

Equipment Requirements

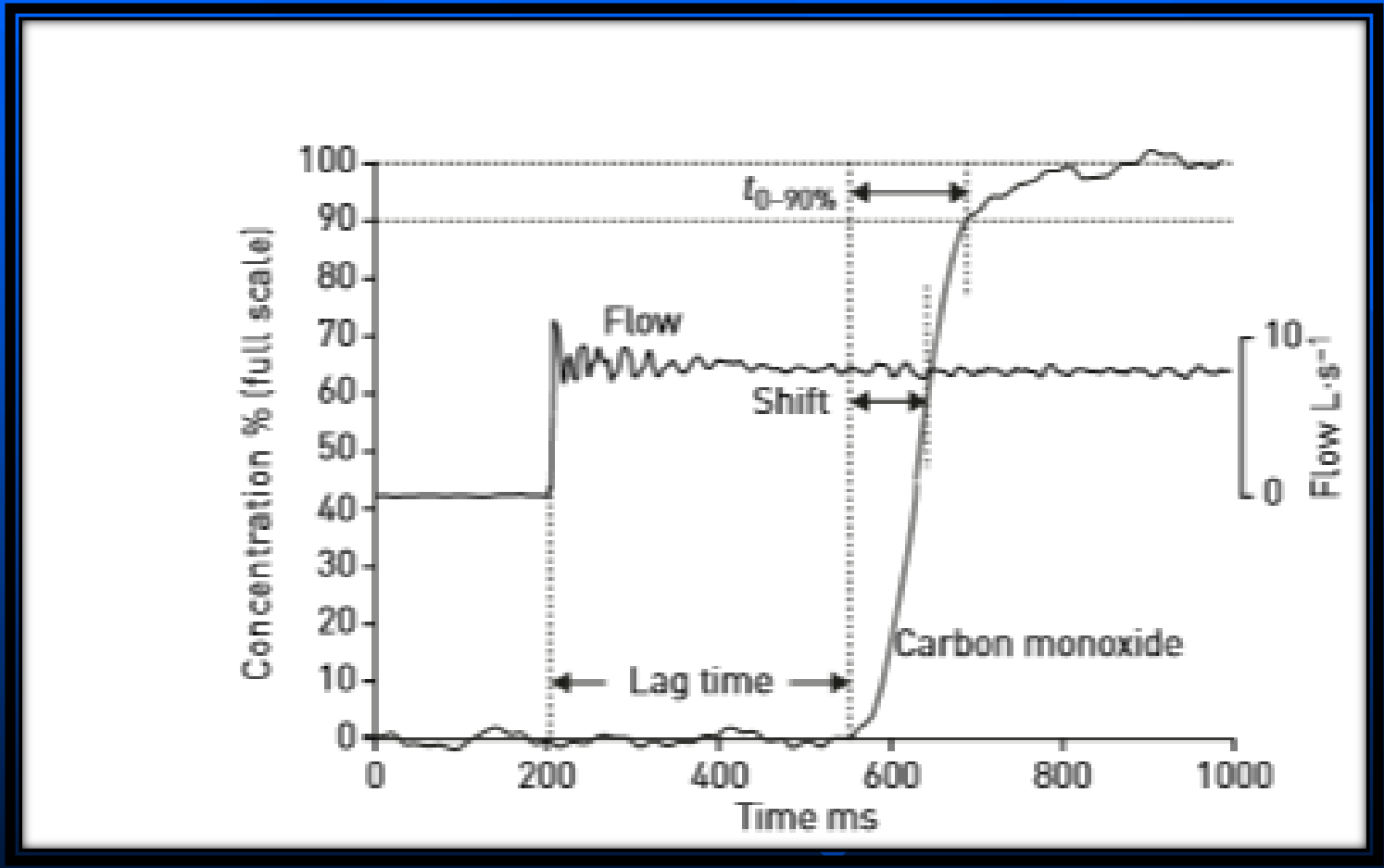
- RGA systems have bot a lag time for the sample to reach the analyzer and the analyzer response time to consider

- Gas concentration signal must be shifted and precisely aligned with the flow signal
  - 100 ms increase in 0-90% response time, error in DLCO increases 0.7%

Graphic Display



Phase Alignment



Equipment Requirements

- CO analyzer accuracy for both RGA and discrete sample systems is ≤10 ppm (±0.3% of 0.3% CO) (2005 was ± 0.5% of 0.3% CO)
- Interference from CO2 and water vapor for both RGA and discrete sample systems is ≤10 ppm error in CO (when CO2 and water vapor are ≤5

Equipment Requirements

- Digital sampling rate now specified as a minimum of ≥100 hz with a resolution of 14 bits. A 1000 hz sampling rate recommended.
- Analyzer drift should ≤ 10 ppm for CO and 0.5% of full scale for the tracer gas over 30 seconds.
  - manufacturers should provide a test mode to test
- Barometric pressure sensor accuracy is required to be within ±2.5%.

Manufacturer Requirements for RGA

- Monitor and report end-expiratory tracer gas and CO concentrations
  - alert the operator if washout from previous testing is incomplete.
- Compensation for end-expiratory gas concentrations prior to test gas inhalation in the calculation of VA and DLCO.
- Ensure proper alignment of gas concentration signals and the flow signal

Manufacturer Requirements for RGA

- Measure anatomic dead-space using the Fowler method.
- Display a graph of exhaled gas concentration versus volume (not time) to confirm point of dead-space washout and to report the amount of manual adjustment if this was done.
- Measure VA using all of the tracer gas data from the entire maneuver in the mass balance equation.

Manufacturer Requirements for RGA

- Report the DLCO adjusted for the change in PAO2 due to barometric pressure.
  - recommended (but not required)
  - Ability to input simulated digital test data and compute DLCO, VA, TLC and Vb with ± 2% accuracy expected.
  - Report the DLCO adjusted for change in PAO2 due to PACO2 with ± 2% accuracy.

Additional requirements

- Maximum inspiratory pressure for demand valves has been reduced to <9 cmH2O
- Machine deadspace for adult testing has decreased to 200 ml from 350 ml
  - machine deadspace should be smaller for children and patients with a VC <2.0 L

Calibration and QC Requirements

- Daily volume calibration must now be performed three time with a 3-liter syringe with using varying flow rates between 0.5 and 12.0 L/sec (injection times 0.5 – 6.0 seconds). Accuracy was not previously specified and now must be <2.5% error.
  - Disposable flow sensor from the batch used must be tested each day
  - Recheck if temperature changes 3 degrees C or relative humidity changes by more than 15%

Calibration and QC Requirements

- Calibration recheck also recommended when differnces between VI and VC or VA and TLC are apparent
- Timer accuracy was specified in the 2005 standards. There are no timer specifications in the 2017 standards.

Calibration and QC Requirements

- Flow sensor zeroing prior to testing is now required.
- Gas analyzer linearity must now be checked monthly. The 2005 standards specified every three months. Manufacturers are urged to automate this process.
- A monthly calibration syringe leak test is now required.

Analyzer Linearity Check

- Serial syringe dilutions
- DLCO simulation with high precision gases
- In absence of above, manufacturer must provide test option like patient, but reported VA at ATP with 3-L syringe

Calibration and QC Requirements

- Both biological and calibration syringe QC testing are now required weekly. Previously either biological or calibration syringe QC were to be performed weekly.

Calibration and QC Requirements

- BioQC requiring action are relaxed to a >12% change or >3 ml/min/mmHg (whichever is larger) from a simple >10% change ***
  - 2017 standards also state that a mean of 6 prior tests should be used
  - Manufacturers urged to developed automated QC
- QC and calibration records can be kept in a digital file

Calibration and QC Requirements

- Syringe QC required measured VA to be within ± 300 ml of 3-L {STPD to BTPS conversion factor} 24% factor
  - Absolute DLCO less than 0.5 ml CO/min/mmHg (.166 SI)

- ERROR NOTED: Correction factor should be ATPD to BTPS

  "The calculation of VA must be within 300 mL of 3 L times the ATPD to BTPS (body temperature, ambient pressure, saturated with water vapour conditions) correction factor, which is 310/Tamb x PB/(PB-47), where PB is the barometric pressure in mmHg and Tamb is the ambient temperature in degrees kelvin.“

  - With 72 degrees Fahrenheit = 295.4 degrees kelvin, this would be approximately a 12% correction factor.

Calibration and QC Schedule

TABLE 2 Equipment calibration schedule

Calibration technique	Frequency
Flow analyser zeroing	Before each test
Gas analyser zeroing	Before/after each test
Volume calibration check	Daily
Biologic control	Weekly
Calibration syringe *D*LCO check	Weekly
Calibration syringe leak test	Monthly
Linearity check (calibration syringe or simulator)	Monthly

*D*LCO: diffusing capacity of the lung for carbon monoxide.

Additional Maintenance

- Replace permeable tubing according to manufacturer recommendations
- Chemical gas analyzers should have a replacement schedule

Patient Condition

- Subject should not breathe supplemental oxygen for ≥ prior to the test
- Refrain from smoking on day of test
- Record time of last cigarette
  - Correct for COHb

Test Performance

- Deep breaths during TV pre-test avoided in the 2005, not included in 2017 standards
- Maximum time for exhalation to RV is 12 seconds
- Inhale rapidly to TLC in less than 4 seconds
- VI target based on patient's largest VC ≥90
  - VI of ≥85% of the patient's largest VC is acceptable if VA is within 200 ml or 5% (whichever is larger) of the patient's highest VA from acceptable DLCO maneuvers.

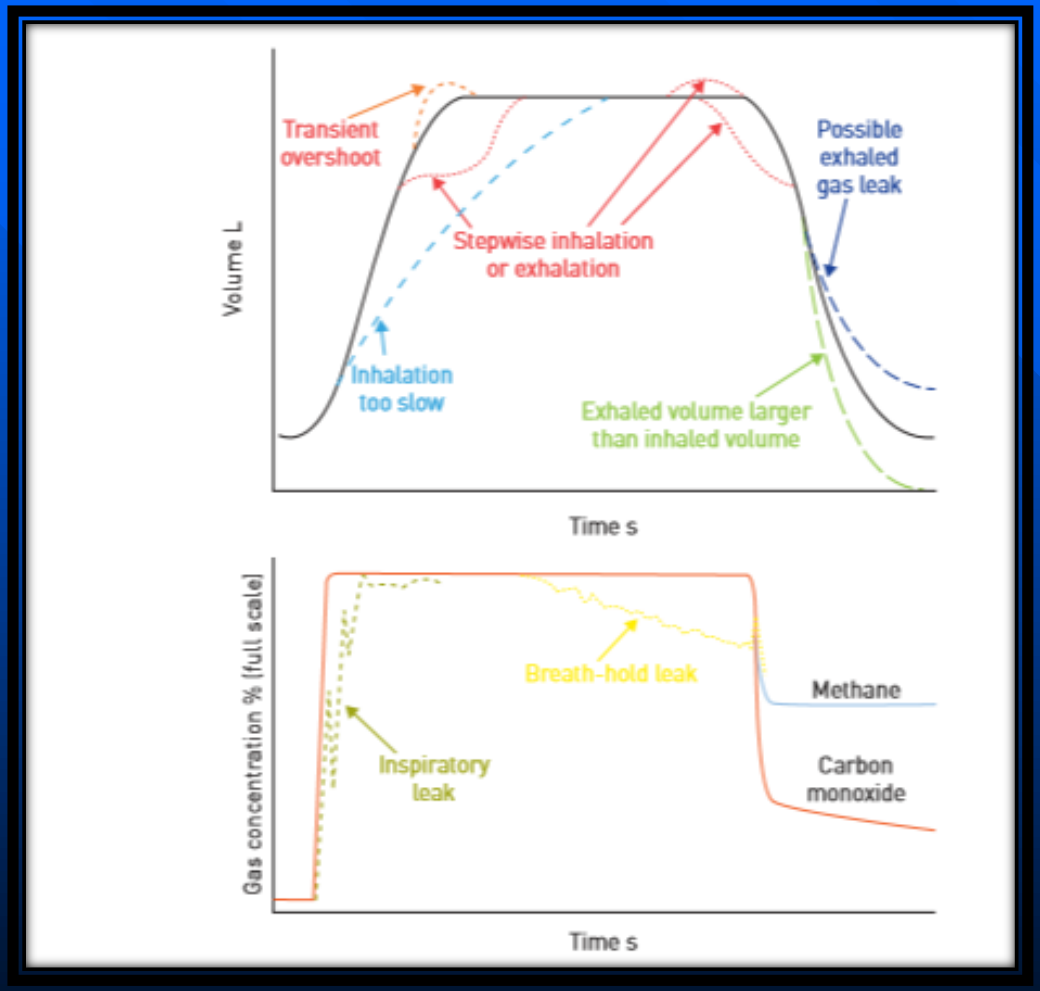
Test Performance

- With RGA exhalation following BHT continue to RV to calculate VA using a mass-balance equation
  - Total expiratory time for discrete sample systems (washout and sample collection time) is still ≤4 seconds but is specified as ≤12 seconds in RGA systems
- DLCO test mixture required to contain 21% O2, .3% CO, tracer, balance N2

Test Performance

- Wait between tests (4 minutes minimum, 10 minutes for patients with severe obstruction)
  - tracer gas concentration at end-exhalation (prior to the inhalation of the test gas mixture) should be ≤ 2% of the inspired concentration
- Recommend end-exhalation concentrations of CO (prior to inhalation of the test gas mixture) be used to adjust DLCO tests for CO back-pressure, to calculate COHb and to compensate for the effects of water vapor and CO2 on gas analyzers

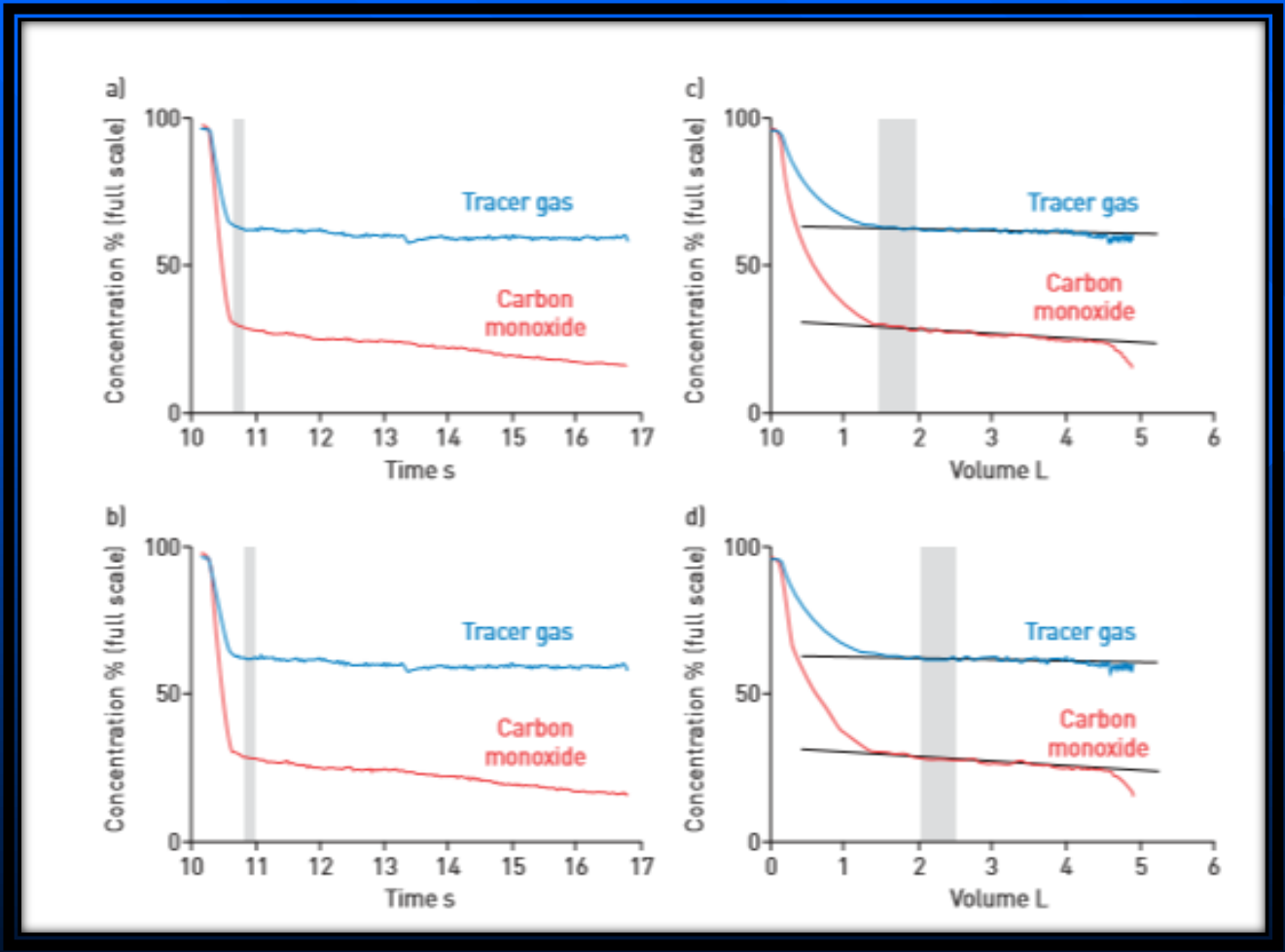
Potential Problems in Breathing Manuever



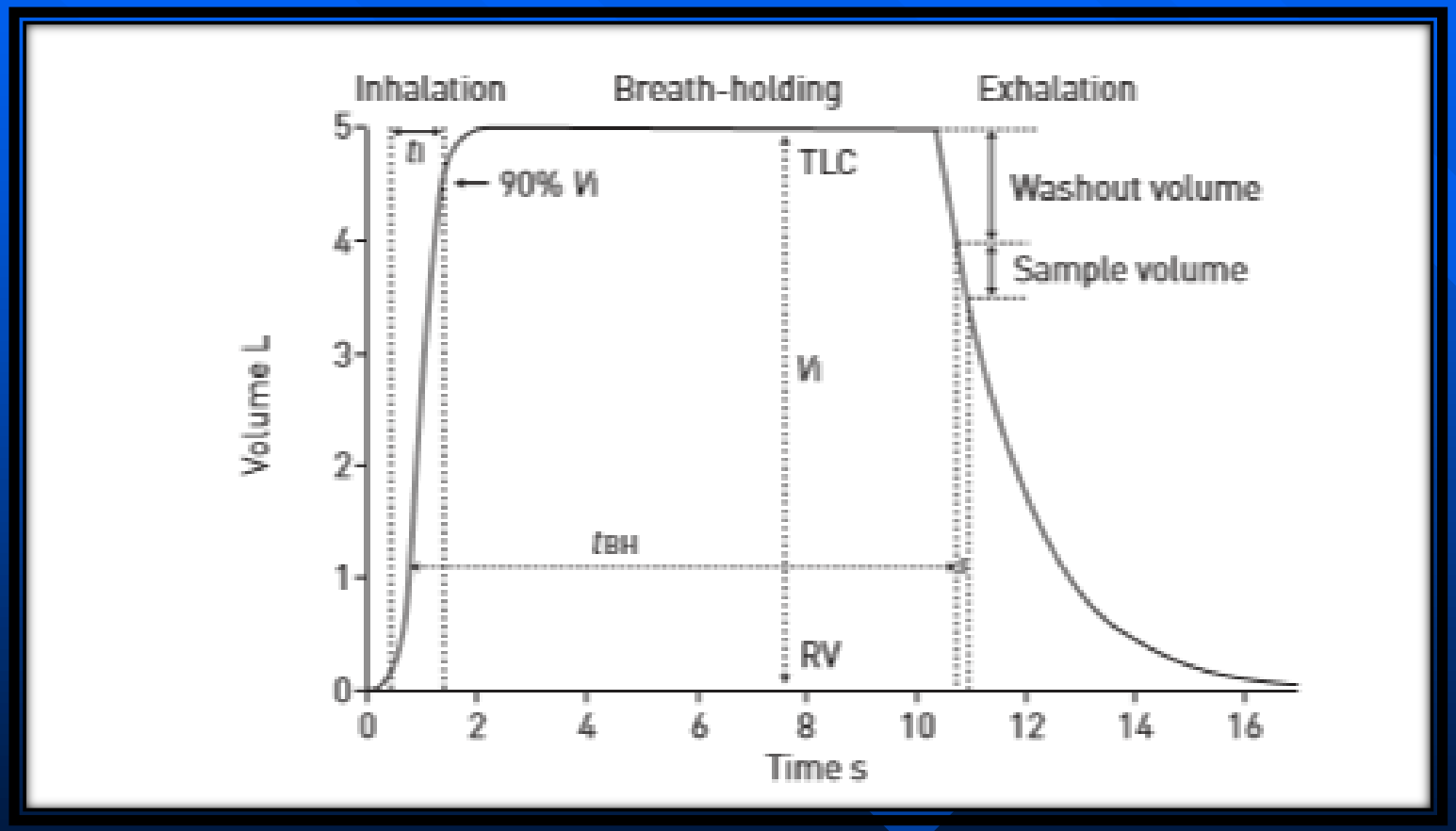
Washout and Sample Collection

- RGA systems
  - Collection prior to point of deadspace washout understimates DLCO
  - Collection beyond will overestimate DLCO
- Classical systems
  - Washout volume .75 to 1.0 L
  - Decrease to .5 L when VC less than 2 L

Analysis Window



Breath Hold Time



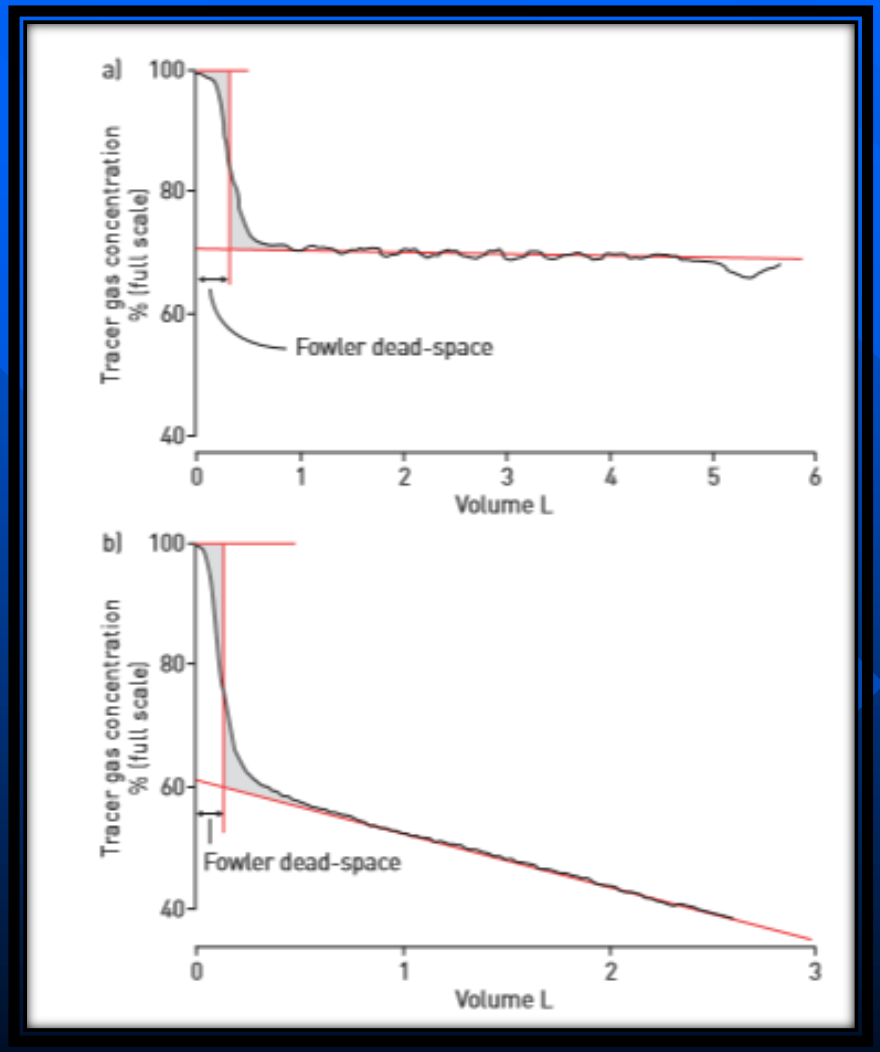
Test Performance

- Effect of prior testing (spirometry, bronchodilators and N2 washouts) on DLCO
  - bronchodilators are unlikely to affect DLCO and may therefore be used prior to DLCO testing
  - prior spirometry efforts may affect DLCO but this has not been proven and therefore makes no recommendations against performing spirometry prior to DLCO testing
  - After N2 washout, time for alveolar O2 levels to return to normal is needed (2 times O2 wash-in time)

VA Calculation

- Classical systems
  - Reported at BTPS, converted to STPD to calculate DLCO
  - Need VI and change in tracer gas
  - Need to know equipment and anatomical DS
- RGA systems
  - DS is measured by Fowler method
  - Anatomic is Fowler minus equipment DS
  - Higher VA and DLCO (8 to 15% in COPD and uncontrolled asthma)
- May want to report 2005 DLCO and RGA

Fowler Dead-Space



Test Quality Grading

Quality control grading[#]

Score	V_I/VC	t_{BH}	Sample collection
A	⩾90%[¶]	8–12 s	⩽4 s
B	⩾85%	8–12 s	⩽4 s
C	⩾80%	8–12 s	⩽5 s
D	⩽80%	<8 or >12 s	⩽5 s
F	⩽80%	<8 or >12 s	>5 s

V_I: inspired volume; VC: vital capacity; V_A: alveolar volume; t_{BH}: breath-hold time; D_{LCO}: diffusing capacity of the lung for carbon monoxide. [#]: only grade A manoeuvres meet all acceptability criteria. The average D_{LCO} values from two or more grade A manoeuvres that meet the repeatability criterion should be reported. If only one grade A manoeuvre is attained, the D_{LCO} value from that manoeuvre should be reported. If no grade A manoeuvre is obtained, manoeuvres of grades B to D might still have clinical utility. The average of such manoeuvres should be reported but these deviations from the acceptability criteria must be noted to caution the interpreter of the test results. Manoeuvres of grade F are not useable. [¶]: or V_I/VC⩾85% and V_A within 200 mL or 5% (whichever is greater) of the largest V_A from another acceptable manoeuvre.

Grading System

- This is considered an interim grading system until studies can be completed to validate it based on the 2017 standards

- Further research is needed

Which DLCO to report?

- Average 2 or more grade A maneuvers that are repeatable
- Average DLCOs from all grade A if not repeatable
- Only 1 grade A, report result
- If no acceptable, average maneuvers with B, C, and D scores
- If only F grade, no DLCO reported

Other Recommenations

- RGA systems calculate VA using mass-balance equations
- Equation for calculating anatomical deadspace using height is different from 2005
- Measurement of anatomical dead space using the Fowler technique discussed in detail
- Discuss flow and gas analyzer signal alignment in detail.
- Discuss KCO

Other Suggestions

- Phase III slope for ventilation inhomogeneity
- Repeatability 2.0 ml/min/mmhg
- Scoring/grading system for test quality based on inspired volume, breath-holding time and sample collection time
- New equation to correct DLCO for end-exhalation CO, altitude and barometric pressure correction

Other Suggestions

- Equations to estimate barometric pressure at altitude that were not in the previous standards.
- 2005 standards included equations to correct DLCO for alveolar volume that are not discussed and not included in the 2017 standards.
- Adjustments are made in predicted value, not measured

Available Results to Report

- DLCO adjusted for barometric pressure
- DLCO LLN and/or Z-score
- VA LLN and/or Z-score
- KCO (instead of DLCO/VA)
- KCO LLN and/or Z-score
- Barometric pressure
- Breath-hold time
- Fowler anatomical dead space (RGA systems only)
- Single-breath TLC (RGA systems only)
- Test quality grade for acceptable maneuvers
- Reference values source
- Graphs of full maneuver
- Graphs of exhaled gas concentrations versus volume (RGA systems only).

Reference Authors

TABLE 5 Reference values for *D*LCO from studies that complied with the 2005 American Thoracic Society/European Respiratory Society *D*LCO standards

Author[#]	Year	Country	Age	Subjects
Thompson [129]	2008	Australia	45–71 years	498 male/474 female
Koopman[¶] [130]	2011	Netherlands	7–18 years	278 male/265 female
Garcia-Rio[¶] [131]	2012	Spain	65–85 years	169 male/262 female
Kim [132]	2012	USA and Australia	5–19 years	225 male/254 female
Thomas [133]	2014	Denmark	5–17 years	male/female (297 total)
Michailopoulos [134]	2015	Greece	18–91 years	234 male/233 female
Verbanck [135]	2016	Belgium	20–80 years	128 male/124 female

*D*LCO: diffusing capacity of the lung for carbon monoxide. [#]: only studies with at least 100 males and 100 females are included. All of these reference values were derived using caucasian subjects. [¶]: test gas contained 19% oxygen (all other studies used test gas with 21% oxygen).

Other Considerations

- New equipment will meet or exceed 2017 standards
- Universal format for output needed
- New standards for interpretation needed
- Ten area identified for further research

Any Questions?

Susan Blonshine BS, RRT, RPFT, FAARC, AE-C
TechEd Consultants, Inc.
www.techedconsultants.com
sblonshine@techedconsultants.com