Undergraduate Research
“Thinking Beyond”
Health and Human Performance: Disease Detection, Intervention, Prevention and Beyond

Rick Carter
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Aging and Declining Function

Carter & Nicotra 1986, Seminars in Respir Med 8:113-123
Inactivity, Weightlessness & Aging

- **Inactivity**
  - Muscle Wasting
  - Bone Loss
  - Change in Body Fluids
  - Immune System Altered
  - Decreased Work Performance
  - Dyspnea on Exertion

- **Weightlessness**
  - Muscle Wasting
  - Bone Loss
  - Change in Body Fluids
  - Immune System Altered
  - Decreased Work Performance
  - Dyspnea on Exertion
Exercise Intolerance

- ↓ Respiratory Function
- ↑ Dyspnea
- ↓ Nutritional Status
- ↓ Cardiac Function
- ↓ Skeletal Function
- ↓ Gas Exchange

O₂ transport

Healthy

Aging, COPD, Heart Disease, Cancer, etc.

Decreasing Function

O₂ utilization
Wasserma’s WHEELS.

MUSCLE ACTIVITY

O₂ & CO₂ ACTIVITY

VENTILATION
(\(\dot{V}_A + \dot{V}_D = \dot{V}_E\))

\[\dot{Q}_{CO₂}\]

\[\dot{Q}_O₂\]

Periph. Circulation

Pulmonary Circulation

\[\dot{V}_CO₂\]

\[\dot{V}_O₂\]

Physiological Responses:

\[\uparrow\dot{Q}_CO₂\]

\[\uparrow\dot{Q}_O₂\]

DILATE

SV

RECRUIT

\[\uparrow\dot{V}_T\]

\[\uparrow f\]

Mild

Moderate

Severe

Presentation Outline

• *Respiratory Physiology/Patient Assessment*
  • Behavioral/Public Health
  • Disease Prevention
  • Human Performance
Standards for the Diagnosis and Management of Patients with COPD

Clinical Presentation
- At Risk
- Symptomatic
- Exacerbations
- Respiratory Failure

Interventions
- Prevention
- Disease Management
  - Pulmonary Rehabilitation
  - Other Options
- Disease Progression
  - FEV1
  - Symptoms

From: Tiep, B and Carter R
Protective cells with Enzyme Supply

Bacteria being eaten by protective cell

Mechanisms of Lung Injury:
- Protease-antiprotease activity
- Oxidant Mediated lung injury

Enzyme damaging alveolar walls while trying to kill bacteria

Alveolus

Mouth
Lung Destruction Schema

• Process
  – Lung Insult
  – Inflammatory Process, Enzymes, Cellular Debris and Biomarkers released or used
  – Repair process
  – Ongoing Biomarker load in the lung
Typical lung parenchyma showing A. Erythrocytes, E. capillaries & Type II pneumocyte and II alveolar surface.

A. Alveolus, E. Erythrocyte, EN Endothelial Cells. 600x

Higher Magnification demonstrating pathway 2400x

Mechanisms of Proteinase Mediated Lung Injury

Mechanisms of Oxidant-Mediated Lung Injury

Respiratory Physiology

Tests

- Spirometry
  - Flow – Volume Loop (FVL)
- AKA; MEFV Curve
Respiratory Physiology

Diagnosis of Obstructive Lung Disease

- Normal
- Restrictive Disorder
- Small Airway Obstruction
- Fixed Large Airway Obstruction
- Intrathoracic Variable Large Airway Obstruction
- Extrathoracic Variable Large Airway Obstruction

Flow vs Volume Diagram
Oscillometry Apparatus

Loud Speaker
Mouthpiece
Oscillometry Benefits

- Effort-Independent
- Assessment is conducted during normal tidal breathing
- Applicable to a more diverse cohort as compared to spirometry
- Suitable for all age ranges and patient limitations
- Can be used in animals and people

Oscillometry Limitations

- Lacks normal reference data -- Our Present Focus
- Equipment not widely available at this time
- Several technologies for oscillometry
- Not directly comparable to Spirometry
- How the Measurements Detect Under different Conditions/Disease States—Where we are heading
- Can it be used with Exercise???
Comparison of Airways Response to Methacholine by Spirometry and Impulse Oscillometry in Adolescents with Severe Asthma and in Adolescent Controls


Impulse oscillometry (IOS) is an important measure of respiratory mechanics in children that requires only quiet tidal breathing for short periods of time. Unfortunately, information on its use in assessing methacholine responsiveness in pediatric patients with severe asthma is limited. The objective of this study was to correlate the findings of IOS with the most commonly assessed measure of lung function for a methacholine challenge: forced expiratory volume in one second (FEV₁).

Twenty-one severe asthmatic and fourteen non-asthmatic control adolescents, ages 12-18 years underwent a methacholine challenge with IOS and spirometry. Methacholine was delivered using a dosimeter. The response to methacholine was assessed using the Jaeger system for spirometry and IOS. IOS measures included: resistance (R), reactance (X), resonant frequency, and the area function AX. Multivariate analysis demonstrated that the percent change in FEV₁ from baseline to PC20 significantly correlated with the percent change in reactance at 5 Hz (r=0.68, p=0.0082) and with the absolute change in AX (r=0.64, p=0.0361). Further analysis showed a tight correlation between the absolute value of FEV₁ with X₅ (r=0.81, p<0.0001) and AX (r=0.79, p<0.0001). Therefore, X₅ and AX from IOS may be useful tools for assessing lung function in children with asthma.

Within- and Between-Day Variability of Respiratory Impedance, Using Impulse Oscillometry in Adolescent Asthmatics

Michael D. Goldman, MD,1* Rick Carter, PhD,2 Robert Klein, MD,3 Greg Fritz, MD,3 Brian Carter,3 and Paul Pachuck1

Summary. The objectives of the present study were to: 1) assess spirometric indices and respiratory impedance with forced oscillation (FO), using impulse oscillometry (IOS) in clinically stable asthmatic children over 3 consecutive days; 2) assess FO reactance (X), using an integrated index and resistance (R) separately during inspiration and expiration; and 3) assess effects on FO of hand support of cheeks vs. no hand support. Our hypotheses were: 1) because of increased sensitivity, IOS manifests day-to-day variability not demonstrable by spirometry; 2) IOS R during expiration exceeds that during inspiration; and 3) hand support of cheeks affects IOS R and X only minimally. We obtained triplicate twice-daily measures of IOS R and X in asthmatic adolescents at summer camp, in a convenience sample of children willing, with parental permission, to undergo repeated testing on consecutive days. Subjects received all medications between 6:30–7:30 AM, and were bronchodilated at time of testing. Subjects underwent IOS tests without hand support of cheeks, followed by tests with both hands supporting cheeks. ANOVA and regression analyses were used to discern technique differences.

Significant differences in IOS inspiratory R₅, R₅ – R₁₅ (frequency dependence of R), and low frequency reactance area (AX) occurred across 3 days, but spirometric indices were unchanged. Inspiratory R at 5 Hz (R₅) was significantly smaller than expiratory R₅ (P<0.0001). ANOVA revealed no significant differences between hand and facial muscle cheek support for IOS R and X below 15 Hz, but significant differences occurred above 15 Hz.

In conclusion, inspiratory R₅, R₅ – R₁₅, and AX are sensitive measures for detecting changes in bronchoconstriction in asthmatic subjects, while expiratory R₅ may be influenced by additional factors. Manual support of cheeks does not appear to affect IOS indices of peripheral airway obstruction in adolescent asthmatics. IOS is a practical method for quantifying respiratory mechanics, and its potential role in disease management warrants further study.


Key words: oscillometry; spirometry; reactance area; cheek support; respiratory mechanics; asthma.
Single-cycle lavage provides estimates of solute concentrations in the epithelial lining fluid of specific regions of the lungs.

Glasgow, Scotland, Sept 5, 2004

Background of Single-cycle Lavage

Standard Serial Lavage

- 5 washes of 20 ml each
- all 5 aliquots pooled (68ml)

Urea correction for dilution of ELF with saline:

\[ [\text{Protein}]_{\text{ELF}} = [\text{Protein}]_{\text{lavage}} \times \frac{[\text{urea}]_{\text{plasma}}}{[\text{urea}]_{\text{lavage}}} \]


METHODS

1. Obtained \(^{133}\text{Xenon} \) scans of 12 healthy subjects.

   - 6 subjects used rapid shallow breathing (central deposition)
   - 6 subjects used slow deep breathing (peripheral deposition)

3. Obtained gamma images of the lungs to verify deposition sites of solute (\(^{99m}\text{Tc-sulfur colloid} \) relative to airway volume (\(^{133}\text{Xe} \))

4. Performed 2 single-cycle 80 ml lavages--5 fractions/lavage

5. Compared distribution of \(^{99m}\text{Tc-sulfur colloid} \) in lavage fractions to distribution in gamma images
Central Deposition of $^{99m}$Tc-sulfur colloid

5 regions identified from $^{133}$Xe scan

Peripheral Deposition of $^{99m}$Tc-sulfur colloid
Conclusions

1. The single-cycle (SC) lavage provides estimates of solute concentrations in the ELF from different regions of the airways.

2. SC lavage can detect a gradient (large airways to alveoli) in solute concentrations in the ELF.

3. There is no measurable gradient in albumin concentration in ELF.

4. Comparison with gamma imaging suggests that SC lavage may underestimate the gradient due to…
   A. …contamination of distal (alveolar) ELF samples as the lavage sample is withdrawn through the upper airways or
   B. …failure to sample the most peripheral regions of the lungs or
   C. …both.
Presentation Outline

• Respiratory Physiology/Patient Assessment

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  • Disease Prevention
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COPD education and cognitive behavioral therapy group treatment for clinically significant symptoms of depression and anxiety in COPD patients: a randomized controlled trial.


Frequency and correlates of overweight status in adolescent asthma.

Abramson NW, Wamboldt FS, Mansell AL, Carter R, Federico MJ, Wamboldt MZ.

Effect of body mass index on response to methacholine bronchial provocation in healthy and asthmatic adolescents.

Mansell AL, Walders N, Wamboldt MZ, Carter R, Steele DW, Devin JA, Monica TH, Miller AL, Wamboldt FS.
Health Behaviors

• Exercise Behaviors
• Eating Behaviors
• OUTCOMES
  – Obesity
  – Diabetes
  – Cardiovascular
  – Pulmonary
  – Asthma
  – Etc.

Carter R, Holiday DB, Nwasuruba C, Stocks J, Grothues C, Tiep B.

6-minute walk work for assessment of functional capacity in patients with COPD.

Dyspnea

- **Afferent Information**
  - Upper Airway
  - Lung
  - Chest Wall

- **Efferent Information**
  - Motor cortex to sensory cortex

- **Brain Stem**
  - Changes in ABGs

**Dyspnea**

- **Dyspnea is multifactorial**
- **Different underlying mechanisms**
- **The language changes**
Potential for Improving Breathing following Training - Areas of Impact

Ventilation During Exercise

Respiratory Muscle Training for COPD Patients for COPD Patients, July 7, 2011, RT For Decision Makers in Respiratory Care, Rick Carter, PhD, MBA, Britney Rodriguez, Yunsuk Koh, PhD, Daniel R. Chilek, PhD, and Jim Williams, PhD

Weighing in on Sleep-Disordered Breathing, Carter,R., Williams, J., RT For Decision Makers in Respiratory Care, May 25, 2007

Prescribing Exercise for Patients with COPD, July 25, 2014, RT For Decision Makers in Respiratory Care, Rick Carter, Lakshmi Manasa Munuganti, Allen Sexton, and Brian Tiep, MD.


Asthma and Perception

- An ongoing collaboration among Brown University: Drs. Greg Fritz, Tony Mansell Robert Klein & Beth McQuaid; National Jewish Research Center: Dr. Marianne Z. Wamboldt and Lamar University: Dr. Rick Carter
Background:

- Poor perception of asthma symptoms is a risk factor for asthma death.
- To date no consensus regarding the best way to characterize perception.
- To date no consensus regarding signaling of perception for asthma severity.
Study

- 103 Children & Adolescents
- Threshold loading task
- Measure Intrinsic Resistance—Weber’s Law satisfied
- Measure Psychosocial Indices
Findings

• Threshold related to $R_o$ $r = .49; p < .001$ and $.66; p < .001$
• Cognitive ability not related to detectable threshold (WISC-III)
• The relevance of Weber’s law confirmed.
**Dyspnea Model**

- □ - accurate perception
- * - hypoperception deficient input from the chest wall & Respir. Muscles
- ○ - hypoperception by modifying factors from the cortex
Presentation Outline

- Respiratory Physiology/Patient Assessment
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- Disease Prevention
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Exercise Standards for Assessment

- Treadmill Testing
- Cycle Testing
- Field Testing
- All Out Run for 6 minutes
- Many others
Exercise as a Tool to Investigate and Alter Physiology

• Exercise, Rehabilitation and Health
• Alterations in Blood Lipids
• Modulating Brain Derived Neurotropic Factor (BDNF)
• Modulating Body Weight and Diabetes
• Alpha-1 Antitrypsin
• Other Areas
Health Screening
Ahora los estudiantes

NOW THE STUDENTS
Lamar University Students in Xalapa, Mexico, Summer 2015, Student Research
Undergraduate Student Posters 2015 Summer
Presentation Outline

- Respiratory Physiology/Patient Assessment
- Behavioral/Public Health
- Disease Prevention

• Human Performance
Performance to Long-Term Health

- BDNF
- Gas Exchange
- Rehabilitation
- Osteoporosis
- Obesity
- CV Disease
- Lung Disease
- Aging
- Space
- Public Health Issues
- And Many Other Areas

- Dr. Mihae Bae
- Dr. Doug Boatwright
- Dr. Dan Chilek
- Dr. Barbara Hernandez
- Dr. Deidre Holland
- Ms. Shannon Jordan
- Dr. Praphul Joshi
- Dr. Israel Msengi
- Dr. Alan Moore
- Dr. Julio Morales
- Dr. Robert Spina
- And others
AN EXAMPLE OF A RESEARCH QUESTION
Oxygenation

- How can we best oxygenate individuals and at the lowest costs?
  - Medicine
  - Engineering
  - Physiology
  - Business
  - Policy
Outcome

- Better Understanding
- Improved Efficiency
- Improved Delivery
- Extended Range
- Lower Costs
- Business Developed
- Many Other Positive Results—Reshaped
Demand oxygen delivery for patients with restrictive lung disease.
Carter R¹, Tashkin D, Djahed B, Hathaway E, Nicotra MB, Tiep BL.

Maintaining oxygenation via demand oxygen delivery during rest and exercise.
Tiep BL¹, Barnett J, Schiffman G, Sanchez O, Carter R.

September 2004, The Financing and Economics of Oxygen Therapy
Rick Carter, PhD, MBA, and Brian Tiep, MD

Oxygen Delivery and Acid-Base Balance, RT for Decision Makers in Respiratory Care,
Carter, R., Tiep, B., Boatwright, D., August 6, 2010

Severe Exercise-Induced Hypoxemia
Chris Garvey, Brian Tiep, Rick Carter, Mary Barnett, Mary Hart, and Richard Casaburi, Respiratory Care, July 2012

UpToDate, Ongoing Clinical Guidance, Portable oxygen delivery and oxygen conserving devices
Authors
Brian L Tiep, MD, Rick Carter, PhD, MBA, Section Editor, James K Stoller, MD, MS, Deputy Editor, Helen Hollingsworth, MD

UpToDate, Ongoing Clinical Guidance, Tiep BL, Carter R. Long-term supplemental oxygen therapy.
Available at
http://www.uptodate.com/online/content/topic.do?topicKey=copd/2162& view=print
Xalapa, Mexico May 2016, Contact Dr. Jeff Palis, Study Abroad or Rick Carter, Health and Kinesiology, Lamar University, Funded in Part by a Grant from 100,000 Strong in the Americas