Update on Pulmonary Diseases

Jeffrey Lessar, MD
• No disclosures to make
• No conflicts
Goals

• Update on key changes in Pulmonary Therapy
Spirometry

- **FEV1** - forced expiratory Volume in 1 Sec
- **FVC** - forced viral capacity
- **FEV1/FVC** ratio

<table>
<thead>
<tr>
<th>Classification of severity:</th>
<th>FEV1% (or FEV1/FVC)</th>
<th>Post-bronchodilator FEV1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>&lt;.70</td>
<td>≥80% predicted</td>
</tr>
<tr>
<td>Moderate</td>
<td>&lt;.70</td>
<td>50% ≤ FEV1 &lt;80% predicted</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;.70</td>
<td>30% ≤ FEV1 &lt;50% predicted</td>
</tr>
<tr>
<td>Very severe</td>
<td>&lt;.70</td>
<td>FEV1 &lt;30% predicted or FEV1 &lt;50% predicted plus chronic respiratory failure*</td>
</tr>
</tbody>
</table>

* Chronic respiratory failure defined as PaO2 <60 mm Hg with or without a PAO2 <50 mm Hg while breathing room air.
Total lung capacity - <80% is restricted
>120% is hyperinflation
Residual Volume - >200% is hyperinflation
Obstructive Lung Disease

• FEV1/FVC <70% or 5% below LLN
• Drugs
  – SABA (albuterol) or SABA/SAMA (Combivent)
  – LAMA- Spiriva, Incruse, Tudorza
  – LAMA/LABA- Anoro, Stiolto
  – LABA- Striverdi
  – ICS/LABA- Advair, Symbicort, Breo
  – PDE4- Daliresp
<table>
<thead>
<tr>
<th>Height(in): 73</th>
<th>Weight(lb): 277</th>
<th>Age: 60</th>
<th>Gender: Male</th>
<th>Physician: GMC</th>
</tr>
</thead>
</table>

### SPIROMETRY

<table>
<thead>
<tr>
<th>Test</th>
<th>Pre</th>
<th>Post</th>
<th>% Ref</th>
<th>% Chg</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (Liters)</td>
<td>5.04</td>
<td>1.18</td>
<td>51</td>
<td>16</td>
</tr>
<tr>
<td>FEV1 (Liters)</td>
<td>4.04</td>
<td>1.18</td>
<td>51</td>
<td>16</td>
</tr>
<tr>
<td>FEV1/FVC %</td>
<td>79</td>
<td>79</td>
<td>79</td>
<td>79</td>
</tr>
<tr>
<td>FEF25-75% L/sec</td>
<td>4.02</td>
<td>0.49</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>FEF50% L/sec</td>
<td>4.92</td>
<td>0.41</td>
<td>(8)</td>
<td>(13)</td>
</tr>
<tr>
<td>FEF75% L/sec</td>
<td>1.87</td>
<td>0.27</td>
<td>(14)</td>
<td>(13)</td>
</tr>
<tr>
<td>PEF L/sec</td>
<td>0.33</td>
<td>4.09</td>
<td>44</td>
<td>42</td>
</tr>
<tr>
<td>MVV (L/min)</td>
<td>150</td>
<td>(42)</td>
<td>(28)</td>
<td></td>
</tr>
<tr>
<td>MVV Length</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### PLETHYSMOGRAPH LUNG VOLUMES

<table>
<thead>
<tr>
<th>Test</th>
<th>Pre</th>
<th>Post</th>
<th>% Ref</th>
<th>% Chg</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC (Liters)</td>
<td>5.82</td>
<td>7.38</td>
<td>(120)</td>
<td></td>
</tr>
<tr>
<td>Vtg (Liters)</td>
<td>6.65</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV (Liters)</td>
<td>5.36</td>
<td>2.58</td>
<td>(208)</td>
<td></td>
</tr>
<tr>
<td>FRC PL (Liters)</td>
<td>6.09</td>
<td>3.51</td>
<td>(174)</td>
<td></td>
</tr>
<tr>
<td>IC (Liters)</td>
<td>3.47</td>
<td>5.04</td>
<td>69</td>
<td></td>
</tr>
<tr>
<td>ERV (Liters)</td>
<td>2.74</td>
<td>0.73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw (cmH2O/L/sec)</td>
<td>3.65</td>
<td>1.29</td>
<td>284</td>
<td></td>
</tr>
<tr>
<td>RV/TLC %</td>
<td>(61)</td>
<td>37</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### ARTERIAL BLOOD GAS

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIO2</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td></td>
</tr>
<tr>
<td>PCO2</td>
<td></td>
</tr>
<tr>
<td>PO2</td>
<td></td>
</tr>
<tr>
<td>HCO3</td>
<td></td>
</tr>
<tr>
<td>SaO2</td>
<td></td>
</tr>
</tbody>
</table>

### DIFFUSING CAPACITY

<table>
<thead>
<tr>
<th>Test</th>
<th>Pre</th>
<th>Post</th>
<th>% Ref</th>
<th>% Chg</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLCO (ml/min/mmHg)</td>
<td>12.5</td>
<td>30.8</td>
<td>(41)</td>
<td></td>
</tr>
<tr>
<td>VA (Liters)</td>
<td>6.19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dlco/VA (1/min/mmHg)</td>
<td>2.03</td>
<td>3.83</td>
<td>53</td>
<td></td>
</tr>
</tbody>
</table>
Figure 1. COPD Patient Staging Assessment Tool

- **RISK**
  - 3-4: High Risk, Less Symptoms
  - ≥2: High Risk, More Symptoms
  - 1-2: Low Risk, Less Symptoms
  - 0-1: Low Risk, More Symptoms

- **GOLD Classification**
  - A: mMRC 0-1, CAT <10
  - B: mMRC ≥2, CAT ≥10
  - C: mMRC 0-1, CAT ≥10
  - D: mMRC ≥2, CAT <10

SYMPTOMS

CAT: COPD Assessment Test; COPD: chronic obstructive pulmonary disease; GOLD: Global Initiative for Chronic Obstructive Lung Disease; mMRC: Modified British Medical Research Council. Source: Reference 4.
Goals of Treatment

• Reduce symptoms
• Decrease exacerbations
• How
  – Quit smoking
  – Pulmonary rehab
  – Inhalers
  – Oxygen
  – Non-invasive Ventilation
E-Cigarettes

• E-cig contain nicotine, water, glycerol, propylene glycol, and optional flavoring.

• On inhalation, the device heats the ingredients into a vapor. Vapors produced by E-cig and E-juices with flavorings induced toxicity, oxidative stress, and inflammatory response in human bronchial airway epithelial cells and fetal lung fibroblasts (HFL1) as well as mouse lung.

• Aerosolized nicotine-containing e-cigarette fluid increased airway hyper-reactivity, distal airspace enlargement, mucin production, cytokine and protease expression in mice, implying the potential dangers of nicotine inhalation during E-cig use [9]. The inflammatory response to E-cig use involved increased neutrophil activation and mucus production and decreased mucociliary clearance – European Resp Journal, 2018.
• 10 mins of E- Cigarettes

• **Non-smokers** - using an e-cigarette for ten minutes raised their airway resistance to 206% from 182% (mean average);

• **Regular smokers**, the spirometry tests revealed a significant rise in airway resistance to 220%, from 176% after using one e-cigarette for ten minutes.
### Therapy Recommendations

<table>
<thead>
<tr>
<th>Group</th>
<th>First Choice</th>
<th>Second Choice</th>
<th>Alternative Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk, less symptoms</td>
<td>• Short-acting anticholinergic as needed (prn) or</td>
<td>• Long-acting anticholinergic or Long-acting beta₂-agonist or Short-acting beta₂-agonist + long-acting anticholinergic</td>
<td>Theophylline</td>
</tr>
<tr>
<td></td>
<td>• Short-acting beta₂-agonist prn</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk, more symptoms</td>
<td>• Long-acting anticholinergic or Long-acting beta₂-agonist</td>
<td>• Long-acting anticholinergic + long-acting beta₂-agonist</td>
<td>Theophylline Short-acting beta₂-agonist and/or short-acting anticholinergic</td>
</tr>
<tr>
<td>High risk, less symptoms</td>
<td>• Inhaled corticosteroid + long-acting beta₂-agonist or Long-acting anticholinergic</td>
<td>• Long-acting anticholinergic + long-acting beta₂-agonist</td>
<td>Theophylline Short-acting beta₂-agonist and/or short-acting anticholinergic Consider phosphodiesterase4-inhibitor</td>
</tr>
<tr>
<td>High risk, more symptoms</td>
<td>• Inhaled corticosteroid + long-acting beta₂-agonist or Long-acting anticholinergic</td>
<td></td>
<td>Theophylline Short-acting beta₂-agonist and/or short-acting anticholinergic Carbocisteine</td>
</tr>
</tbody>
</table>

Global Initiative for Chronic Obstructive Lung Diseases (GOLD). Global strategy for diagnosis, management and prevention of COPD 2011. Available at: www.goldcopd.org

ValleyHealth

Healthier, together.
Inhalers

- “Rescue”- albuterol and/or ipratropium

- Controllers
  - LAMA- long acting muscarinic antagonist
  - LABA- long acting beta 2 agonists
  - ICS- inhaled cortico-steroids
  - Theophylline
  - Daliresp
Don’t forget the nebulized options!
LAMA

• Bronchodilation by inhibiting anticholinergic receptors

• Acetylcholine regulates
  – Airway tone
  – Smooth muscle contraction
  – Mucus secretion
  – Vasodilation

• Spiriva, Tudorza, Incruse, Seebri, Lonhala
LAMAs

- **Spiriva**
  - Handihaler going away

- **Lonhala Magnair**
  - First long acting nebulized
  - Twice a day
  - 41% had improved St George
  - 105ml improvement in trough FEV1 at 12 weeks
LABA

• Long acting beta agonists
  – Inhibit smooth muscle contractility
  – Decrease airway hyperresponsiveness

• Inhalers- salmeterol (Serevent), fomoterol (Foradil)

• Nebulizers- Brovana and Perforomist

• No black box for COPD- and NOW removed for ICS/LABA
ICS

- Suppress airway inflammation
- Inhalation minimizes systemic absorption
- Small benefit in FEV1 and small improvement in St George
- Biggest benefit is reduction in exacerbation—greater benefit in lower FEV1
- Withdrawal—↓ FEV1, ↑ exacerbations, ↑ dyspnea, and ↑ sleep disturbances
Others

• Theophylline
  – Methylxanthine
  – Anti-inflammatory and relax smooth muscle
  – ?reverse steroid insensitivity in active smokers

• Daliresp
  – PDE4 inhibitor, anti inflammatory
  – Indicated to reduce copd exacerbations
Combinations

• LAMA/LABA
  – Anoro, Stiolto, Bevespi, Utibron

• ICS/LABA
  – Advair, Breo, Symbicort, Dulera

• LAMA/LABA/ICS
  – Trelegy
Asthma

Step 1: SABA PRN

Step 2: Low-dose ICS
Alternative: cromolyn, LTRA, nedocromil, or theophylline

Step 3: Low-dose ICS + LABA or medium-dose ICS
Alternative: low-dose ICS + LTRA, theophylline, or zileuton

Step 4: Medium-dose ICS + LABA
Alternative: medium-dose ICS + LTRA, theophylline, or zileuton

Step 5: High-dose ICS + LABA and consider omalizumab if allergies are present

Step 6: High-dose ICS + LABA + oral corticosteroids and consider omalizumab if allergies are present
New Drugs

• Spiriva Respimat
  – 1.25mcg dose indicated for add on to asthma therapy

• Biologics
  – Anti-IGE
  – Anti eosinophils
Biologics

• Xolair (omalizumab) - +IGE and RAST

• Fasenra (benralizumab)
  – IL 5 receptor binder killing eos

• Nucala (mepolizumab)
  – IL 5 binder decreases production/survival of eos

• Cinqair (reslizumab)
  – IL 5 binder decreased production/survival of eos

• Dupixent (dupilumab)
  – IL 4 and IL 13 antagonist
Restrictive Lung Disease

• Severity based on TLC
  – Mild 60-80%
  – Moderate 40-60%
  – Severe <40%

• Evaluation
  – Physical exam
  – HRCT

• Treatment
  – Depends on dz;
  – Immunosuppressant
  – OFEV/Esbriet
Interstitial Lung Disease

- Hypersensitivity pneumonitis (HP)
- Idiopathic interstitial pneumonias
- Granulomatous ILDs
- Pneumocystis pneumonia (PCP)
- Eosinophilic pneumonia (EP)

- Langerhans cell histiocytosis (LCH)
- Sarcoidosis
- Tuberculosis (TB)

- Respiratory bronchiolitis associated ILD (RB-ILD)
- Pulmonary fibrosis (PF)
- Desquamative interstitial pneumonia (DIP)
- Acute interstitial pneumonia (AIP)
- Non-specific interstitial pneumonia (NSIP)
- Cryptogenic organizing pneumonia (COP/BOOP)
- Lymphocytic interstitial pneumonia (LIP)

ILD subcategory
Histological diagnosis
Diffuse Parenchymal Lung Diseases (DPLD)

DPLD of known etiology (HP, drugs, collagen-vascular)

Idiopathic Interstitial Pneumonia (IIP)

Granulomatous DPLDs (Sarcoidosis)

Other forms of DPLD (eosinophilic pneumonia, LAM, HX etc.)

Chronic fibrosing

Smoking related

Acute/subacute

IPF

NSIP

RBILD

DIP

AIP

COP

Very rare IIPs:
- idiopathic lymphocytic interstitial pneumonia (LIP)
- idopathic pleuroparenchymal fibroelastosis (PPFE)
Pulmonary Arterial Hypertension

• pHTN
  – Mean Pulmonary Artery Pressure > 25 mmHg

• PAH

• Diagnosis
  – Echo- screening tool
    • RVSP > 30; normal EF;
  – R heart cath
    • Mpap > 25, pcwp < 15, PVR > 3 woods units
IPF

• Esbriet (pirfenidone)
  – Anti fibrotic (not fully understood)
  – 32% had decline (FVC by > 10%) w/ placebo vs 17% w/ Esbriet

• OFEV (nintedanib)
  – Kinase inhibitor
  – 115ml vs 240ml (placebo) in 1 year
Sleep Apnea

Normal Breathing

Blocked Airways

© 2010 Essential Oils Books
Sleep Apnea

• Treatment
  – Cpap
  – Oral appliances
  – Surgery
  – Implantables
Oral Appliance
Oral Appliance Pulls the Lower Jaw Forward, Opening the Airway

© Dear Doctor, Inc.
Implantables

• Inspire Device-
  – Senses respiratory effort
  – stimulating the hypogloassal nerve
    • to protrude tongue
    • dialate upper airway

• THN Sleep therapy
  – No sensing lead
  – Hypoglossal nerve stimulator
Thank you!