Asthma COPD Update
2018

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In support of improving patient care, Idaho State University Kasiska Division of Health Sciences is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.
Disclosure

- The planners and presenter of this presentation have disclosed no conflict of interest, including no relevant financial relationships with any commercial interests.
Objectives:

• Upon completion of the following discussion the participants should be able to:
  – Categorize respiratory medications with similar mechanisms of action
  – Appropriately sequence medications for patients with COPD- verses asthma-predominant airway disease
  – Demonstrate proper steps in utilizing individual inhalers
## Differentiating Asthma From COPD

<table>
<thead>
<tr>
<th></th>
<th>Asthma</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>Usually &lt;30</td>
<td>Usually &gt;40</td>
</tr>
<tr>
<td>+ Family history</td>
<td>Usually</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Cough: most prominent</td>
<td>Nocturnal, postexercise</td>
<td>Early AM</td>
</tr>
<tr>
<td>History of atopy</td>
<td>Often</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Bronchodilator reversibility</td>
<td>Complete/Nearly so</td>
<td>Partial</td>
</tr>
<tr>
<td>Steroid responsiveness</td>
<td>Strong</td>
<td>Usually weak</td>
</tr>
<tr>
<td>Progressive deterioration</td>
<td>Uncommon</td>
<td>Typical</td>
</tr>
<tr>
<td>Anticholinergic responsivity</td>
<td>β-agonists better</td>
<td>Best first-line</td>
</tr>
<tr>
<td>β-agonist responsivity</td>
<td>Very good</td>
<td>Anticholinergics better</td>
</tr>
<tr>
<td>Purulent sputum</td>
<td>Uncommon</td>
<td>Typical</td>
</tr>
<tr>
<td>Smoking history</td>
<td>Variable</td>
<td>Essentially always</td>
</tr>
</tbody>
</table>

Asthma Incidence

Global Asthma Network Center:
Surveillance
Mortality
Treatment
Recommendations

Global Asthma Network
Centres

EOI Centres
Registered Centres

December 2017
Burden of Disease/Mortality

Figure 4: Burden of disease, measured by disability adjusted life years (DALYs) per 100,000 population attributed to asthma by age group and sex. Global population, 2010.

Figure 1: Age-standardised mortality rates for asthma, all ages 2001-2010

Source: WHO Detailed Mortality Database, February 2014 update
COPD Incidence:

- The Global Burden of Disease Study reports a prevalence of 251 million cases of COPD globally in 2016.
- Globally, it is estimated that 3.17 million deaths were caused by the disease in 2015 (that is, 5% of all deaths globally in that year).
- More than 90% of COPD deaths occur in low and middle-income countries.
- The primary cause of COPD is exposure to tobacco smoke (either active smoking or secondhand smoke).
- Other risk factors include exposure to indoor and outdoor air pollution and occupational dusts and fumes.
- Exposure to indoor air pollution can affect the unborn child and represent a risk factor for developing COPD later in life.
Asthma Pathophysiology

Non-allergic eosinophilic inflammation
- Eosinophil ++
- Neutrophil –
- Epithelial damage ++
- Mucus +
- Reticular basement membrane thickening ++
- Airway smooth muscle mass ++

Allergic eosinophilic inflammation
- Eosinophil ++
- Neutrophil –
- Epithelial damage ++
- Mucus +
- Reticular basement membrane thickening ++
- Airway smooth muscle mass ++

Mixed granulocytic asthma
- Eosinophil +
- Neutrophil +
- Epithelial damage ++
- Mucus ++
- Reticular basement membrane thickening +
- Airway smooth muscle +

Paucigranulocytic
- Eosinophil –
- Neutrophil –
- Epithelial damage +
- Mucus –/
- Reticular basement membrane thickening +/-
- Airway smooth muscle +

Non-eosinophilic asthma

mẫn ông

www.thelancet.com Published online December 19, 2017
http://dx.doi.org/10.1016/S0140-6736(17)33311-1
Asthma:

• Inflammatory condition with concurrent hyper-responsive airways
• Many triggers can cause exacerbations
• Reversible with short acting broncodilators
• All phenotypes result in basement membrane hypertrophy “thickening”
• Goals of therapy:
  – Stop the underlying inflammatory changes
  – Relieve acute bronchoconstriction
  – Improve patient QOL and Functionality
Chronic obstructive pulmonary disease develops slowly and usually becomes apparent after 40 or 50 years of age.

The most common symptoms of COPD are breathlessness (or a "need for air"), chronic cough, and sputum (mucous) production.

Daily activities, such as walking up a short flight of stairs or carrying a suitcase, and even daily routine activities can become very difficult as the condition gradually worsens.

Sufferers also frequently experience exacerbations, that is, serious episodes of increased breathlessness, cough and sputum production that last from several days to a few weeks.

These episodes can be seriously disabling and result in need for urgent medical care (including hospitalization) and sometimes death.

Goals of therapy:
- Improve /decrease symptoms
- Decrease hospitalizations

COPD is a progressive terminal disease.

What about younger patients with this presentation? Alpha one antitrypsin deficiency
COPD Pathophysiology
Healthy---------Smoker
Smoking Cessation: Most Effective

- Nicotine Replacement therapy: NRT
- Basal Patch
  - 21 for 4 weeks
  - 14 for 4 weeks
  - 7 for 4 weeks
- Plus Immediate Release
  - Gum, Lozenge otc
  - Inhaler, NS – RX
  - Electronic Cigarettes
- Plus:

Hey! We now have prescriptive authority to start these medications!

- Bupropion
  - SR 150 mg BID x 12 weeks
  - Longer?
- Or:
- Varenicline Chantix®
  - 12 weeks
  - Longer?
Guidelines:

- **Asthma:**
  - Expert Panel Three
  - 2007-
  - Soon to be another with addition of new options of therapy

- **COPD:**
  - Global Initiative for management of chronic obstructive lung disease
  - 2018 Update


http://goldcopd.org/gold-reports/
Quick Relief Medications:
- Beta-agonists
- Anticholinergics

Long Term Control

Long Acting Bronchodilators
- Steroids
- Long acting B-agonists
- Long acting anticholinergics
- Theophylline, Roflumilist
- Leukotriene agents

The airways and air sacs lose their elasticity (like an old rubber band)
The walls between many of the air sacs are destroyed
The walls of the airways become thick and inflamed (swollen)
Cells in the airways make more mucus (sputum) than usual, which tends to clog the airways.
First things first: Minimize triggers: Minimize histamine release:

- Loratidine: Gen
  - Claritin®, Alavert® 10 mg OTC, Liq, Reditab
  - Claritin-D 12 h, 24 h
- Desloratidine:
  - Clarinex® 5 mg RX
  - Generic
- Fexofenadine: Gen
  - Allegra® 60 BID, 180 QD
  - Allegra-D BID
- Cetirizine: OTC 2/08, gen
  - Zyrtec® 5 mg, 10 mg, Liq
  - Zyrtec-D BID
- Levocetirizine: (2007)
  - Xyzal® 5 mg QD
  - Generic

How do we Determine EFFICACY?

[Graph showing dose-response curves of histamine in the human skin. Peripheral inhibition of histamine-induced weal by loratadine (L 10, 20, 40 mg) and cetirizine (C 2.5, 5, 10 mg) 8 hours after drug. (From De Vos C. Clin Exp Allergy 19503-507, 1989.)]
Nasal Antihistamines:

- **Azelastin HCL 137 mcg**
  - 1 or 2 sprays each nostril BID
  - Generics
- **Astepe 0.15%**
  - 2 sprays each nostril ONCE a day
  - 200 sprays
  - Generics
- **Olopatadine Patanase®**
  - 1 spray per nostril BID
  - 240 sprays/bottle
  - 2 month supply
- **Brand Only**
- **Combo**
  - Fluticasone/Azelastin
  - Dymista®

Corticosteroids: Topical= Nasal

- Most effective for treatment of just nasal symptoms of allergy:
- With continued use block the hypersensitivity of the nasal mucosa. Decreasing symptoms and congestion
- Drying: added to moisturizing additives
- Bad taste, 2.5-3 dollars/day
Sympathetic/Parasympathetic

Pathology of Asthma

Normal airway

Relaxed smooth muscles

Asthmatic airway

Wall inflamed and thickened

Asthmatic airway during attack

Air trapped in alveoli

Tightened smooth muscles
• Adrenergic Control of Airway- Epinephrine binds to a Beta-2 receptor:
  – Dilates the bronchioles
• Agonists Stimulate a receptor:
• Short Acting Beta Agonists = SABA
  – Albuterol, Levalbuterol,
  – Proair, Ventolin, Proventil, Xopenex
  – Last 3-6 hours
• Long Acting Beta Agonists = LABA
  – Salmeterol Serevent, Formoterol Foradil, Arformoterol Brovana, Indacetrol Arcapta, Olodaterol Striverdi,
  – Last 12-24 hours
  – More in a minute
Short Acting Beta Agonists:

- **Albuterol:**
  - MDI:
    - Proair HFA®
    - Ventolin HFA®
    - Proventil HFA®
  - Solution for Nebulizer:
    - 2.5 mg/3 ml
    - 1.25 mg/3 ml, gen Accuneb®
    - 0.625 mg/3 ml, gen Accuneb®

- **Levalbuterol**
  - MDI:
    - Xopenex®
  - Solution for Nebulizer:
    - Xopenex®
How To Use an HFA MDI?

• Remove dust cap
• Shake well  
  – suspensions
• Exhale SLOWLY
• Place in mouth  
  – tight lips
• Or 3 fingers breadths?
• Begin SLOW DEEP inhalation

• Press canister
• Continue inhalation to max
• Hold breath  
  – 10 seconds (comfort)
• Exhale SLOWLY
• Wait 30 seconds repeat  
  – 1-10 minutes?
Most common SABA Question

Albuterol inhaler spray force and duration

Mean Impact Force, mN

VENTOLIN HFA
Armstrong® CFC
Proventil® HFA
ProAir® HFA

Time, seconds

mN, milliNewton.
If the patient absolutely can not time the actuation with the inhalation:

- ProAir Respiclick®:
- Holding Chambers/Space Enhancers:
- Nebulizers:
Think Pair Share:

• Teach the person to your left proper steps to utilize an HFA inhaler

• What clinical condition may lead you to recommend a SAMA over a SABA?
Airway Pharmacology- 2

• Parasympathetic (muscarinic) innervations of the airways Acetylcholine results in constriction-
• We give ANTI-CHOLINERGICS to block this = Broncodilation
• Short Acting Muscarinic Antagonists = SAMA
  – Ipatropium: Atrovent HFA
  – Lasts 2-6 hours
• Long Acting Muscarinic Antagonists = LAMA
  – Tiotropium Spiriva, Aclidinium Tudorza, Umclidinium Incruse, Gycopyrolate Seebri
  – More in a minute
How do we determine Asthma vs COPD?

<table>
<thead>
<tr>
<th>Table 2.3. Considerations in performing spirometry</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preparation</strong></td>
</tr>
<tr>
<td>• Spirometers need calibration on a regular basis.</td>
</tr>
<tr>
<td>• Spirometers should produce hard copy or have a digital display of the expiratory curve to permit detection of technical errors or have an automatic prompt to identify an unsatisfactory test and the reason for it.</td>
</tr>
<tr>
<td>• The supervisor of the test needs training in optimal technique and quality performance.</td>
</tr>
<tr>
<td>• Maximal patient effort in performing the test is required to avoid underestimation of values and hence errors in diagnosis and management.</td>
</tr>
<tr>
<td><strong>Bronchodilation</strong></td>
</tr>
<tr>
<td>• Possible dosage protocols are 400 mcg short-acting beta₂-agonist, 160 mcg short-acting anticholinergic, or the two combined. FEV₁ should be measured 10–15 minutes after a short-acting beta₂-agonist is given, or 30–45 minutes after a short-acting anticholinergic or a combination of both classes of drugs.</td>
</tr>
<tr>
<td><strong>Performance</strong></td>
</tr>
<tr>
<td>• Spirometry should be performed using techniques that meet published standards.</td>
</tr>
<tr>
<td>• The expiratory volume/time traces should be smooth and free from irregularities. The pause between inspiration and expiration should be &lt; 1 second.</td>
</tr>
<tr>
<td>• The recording should go on long enough for a volume plateau to be reached, which may take more than 15 seconds in severe disease.</td>
</tr>
<tr>
<td>• Both FVC and FEV₁ should be the largest value obtained from any of three technically satisfactory curves and the FVC and FEV₁ values in these three curves should vary by no more than 5% or 150 ml, whichever is greater.</td>
</tr>
<tr>
<td>• The FEV₁/FVC ratio should be taken from the technically acceptable curve with the largest sum of FVC and FEV₁.</td>
</tr>
<tr>
<td><strong>Evaluation</strong></td>
</tr>
<tr>
<td>• Spirometry measurements are evaluated by comparison of the results with appropriate reference values based on age, height, sex, and race.</td>
</tr>
<tr>
<td>• The presence of a postbronchodilator FEV₁/FVC &lt; 0.70 confirms the presence of airflow limitation.</td>
</tr>
</tbody>
</table>
Office Based Spirometry

- Perform baseline Spirometric testing:
  - Get FEV1, FVC
- Give Bronchodilator
  - SABA- wait 15-20 minutes
  - SAMA- wait 30-45 minutes
- Repeat Spirometric testing
  - Reversible- Asthma predominant care path
  - Not reversible- COPD predominant care path
Asthma

Persistent Asthma: Daily Medication
Consult with asthma specialist if step 4 care or higher is required. Consider consultation at step 3.

Step 1
Preferred: Low-dose ICS
Alternative: Cromolyn, LTRA, Nedocromil, or Theophylline

Step 2
Preferred: Low-dose ICS + LABA
Alternative: Medium-dose ICS + LABA

Step 3
Preferred: High-dose ICS + LABA
Alternative: Omalizumab for patients who have allergies

Step 4
Preferred: High-dose ICS + LABA + oral corticosteroid
AND
Consider Omalizumab for patients who have allergies

Step 5
Preferred: High-dose ICS + LABA + oral corticosteroid
AND
Consider Omalizumab for patients who have allergies

Step 6
Preferred: High-dose ICS + LABA + oral corticosteroid
AND
Consider Omalizumab for patients who have allergies

Each step: Patient education, environmental control, and management of comorbidities.

Steps 2–4: Consider subcutaneous allergen immunotherapy for patients who have allergic asthma (see notes).

Quick-Relief Medication for All Patients
- SABA as needed for symptoms. Intensity of treatment depends on severity of symptoms: up to 3 treatments at 20-minute intervals as needed. Short course of oral systemic corticosteroids may be needed.
- Use of SABA >2 days a week for symptom relief (not prevention of EIB) generally indicates inadequate control and the need to step up treatment.
GOLD Recommendations for Each Stage of COPD

<table>
<thead>
<tr>
<th>Old</th>
<th>0: At Risk</th>
<th>I: Mild</th>
<th>II: Moderate</th>
<th>III: Severe</th>
<th>IV: Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0: At Risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>New</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chronic symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exposure to risk factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Normal spirometry</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>I: Mild</th>
<th>II: Moderate</th>
<th>III: Severe</th>
<th>IV: Very Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁/FVC &lt; 70%</td>
<td>FEV₁/FVC &lt; 70%</td>
<td>FEV₁/FVC &lt; 70%</td>
<td>FEV₁/FVC &lt; 70%</td>
</tr>
<tr>
<td>FEV₁ ≥ 80%</td>
<td>50% ≤ FEV₁ &lt; 80%</td>
<td>30% ≤ FEV₁ &lt; 50%</td>
<td>FEV₁ &lt; 30% or FEV₁ &lt; 50% predicted plus chronic respiratory failure</td>
</tr>
<tr>
<td>With or without symptoms</td>
<td>With or without symptoms</td>
<td>With or without symptoms</td>
<td>With or without symptoms</td>
</tr>
</tbody>
</table>

- Avoidance of risk factor(s); influenza vaccination
- Add short-acting bronchodilator when needed
- Add regular treatment with one or more long-acting bronchodilators
- Add rehabilitation

Add inhaled glucocorticosteroids if repeated exacerbations

Add long-term oxygen if chronic respiratory failure
Consider surgical treatments

Spirometry measurements reflect post-bronchodilator values.
Reprinted with permission from GOLD.
## Asthma Escalation: One

- Low Dose ICS (Inhaled Corticosteroid)

### Inhaled Corticosteroids “Long Term Control Medication”

<table>
<thead>
<tr>
<th>Medication</th>
<th>Formulation</th>
<th>Brand(s)</th>
<th>Dose</th>
<th>Administration</th>
<th>Dose Range</th>
<th>Units Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclomethasone</td>
<td>HFA</td>
<td>Qvar®</td>
<td>40, 80 mcg</td>
<td>BID 120 puffs</td>
<td>80-240</td>
<td>&gt;480</td>
</tr>
<tr>
<td>Budesonide</td>
<td>DPI/Soln Neb</td>
<td>Pulmicort® Generics</td>
<td>90, 180 mcg</td>
<td>QD</td>
<td>180-600</td>
<td>600-1200</td>
</tr>
<tr>
<td>Ciclesonide</td>
<td>HFA</td>
<td>Alvesco®</td>
<td>80, 160 mcg</td>
<td>BID</td>
<td>160-320</td>
<td>320-640</td>
</tr>
<tr>
<td>Flunisolide</td>
<td>HFA</td>
<td>Aerosn®</td>
<td>80 mcg</td>
<td>BID-QID</td>
<td>80-320</td>
<td>320-640</td>
</tr>
<tr>
<td>Fluticasone Propionate</td>
<td>DPI Diskus</td>
<td>Flovent®</td>
<td>50,100,200</td>
<td>BID</td>
<td>100-300</td>
<td>300-500</td>
</tr>
<tr>
<td></td>
<td>HFA</td>
<td>Flovent HFA</td>
<td>44,110,220</td>
<td>BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mometasone</td>
<td>DPI and HFA</td>
<td>Asmanex® HFA</td>
<td>110, 220 mcg</td>
<td>QD-BID</td>
<td>110-220</td>
<td>220-440</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>100, 200 mcg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluticasone Furoate</td>
<td>DPI</td>
<td>Arnuity Ellipta®</td>
<td>100,200 mcg</td>
<td>QD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Think Pair Share:

• Which of the corticosteroid inhaler devices should not be used with a patient that can’t create a “forceful deep inhalation”
• ???????????????????????????????????????????????????????????????????????
## Asthma Escalation Two

- **Medium Dose ICS or Low ICS plus LABA:**

<table>
<thead>
<tr>
<th>Combination Respiratory Products (Corticosteroid Plus LABA)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluticasone propionate/ Salmeterol</td>
<td>HFA or Diskus</td>
</tr>
<tr>
<td>Budesonide/ Formoterol</td>
<td>HFA</td>
</tr>
<tr>
<td>Mometasone/ Formoterol</td>
<td>HFA</td>
</tr>
<tr>
<td>Fluticasone Furoate/ Vilanterol</td>
<td>DPI</td>
</tr>
</tbody>
</table>
And SOON: Advair HFA “Generic”- Not AB Rated AirDuo Respiclick®- TEVA
Asthma Escalation Three-Four

- High Dose ICS Plus LABA Plus
- Leukotriene Receptor Blocker
  - Montelukast 4 mg Granules 6-23 months
  - Montelukast 4 mg chew or granule 2-5 year
  - Montelukast 5 mg 6 years to 15 years
  - Montelukast 10 mg q day 15 and older
Asthma Escalation: Immunomodulation:

- Omalizumab: Xolair®
- MAB that decreases IGE
Modulator Competitors
Interleukin-5 Receptor Antagonist

• Mepolizumab Nucala®
  – 100mg SQ Q 4 weeks
• Resizlumab Cinqair®
  – 3mg/kg IV infusion Q 4 weeks
• Benralizumab Fasenra®
  – 30 mg SQ Q 4 weeks for 3 doses
  – Then 30 mg SQ Q 8 weeks
COPD Escalation:

- Improve Symptoms
- Decrease Hospitalizations
- LABA or LAMA First (rgh- I like LAMA first)

<table>
<thead>
<tr>
<th>Long Acting Beta Adrenergic Agonists (LABA) “Long Acting Broncodilator”</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmeterol</td>
<td>DPI Diskus</td>
</tr>
<tr>
<td>Formoterol</td>
<td>DPI Cap</td>
</tr>
<tr>
<td>Arformoterol</td>
<td>Soln Neb</td>
</tr>
<tr>
<td>Indaceterol</td>
<td>DPI Cap</td>
</tr>
<tr>
<td>Olodaterol</td>
<td>Respimat</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Serevent®</th>
<th>50 mcg</th>
<th>BID</th>
<th>60 puffs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foradil®</td>
<td>12 mcg</td>
<td>BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20 mcg</td>
<td>BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brovana®</td>
<td>15 mcg</td>
<td>BID</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arcapta® Neohaler</td>
<td>75 mcg</td>
<td>QD</td>
<td>30 caps</td>
<td></td>
</tr>
<tr>
<td>Striverdi®</td>
<td>2.5 mcg</td>
<td>2 puffs QD</td>
<td>28, 60 puff</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Long Acting Muscarinic Antagonists (LAMA) “Long Acting Broncodilator”</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tiotropium</td>
<td>DPI Cap</td>
</tr>
<tr>
<td>Aclidinium</td>
<td>DPI</td>
</tr>
<tr>
<td>Umclidinium</td>
<td>DPI</td>
</tr>
<tr>
<td>Glycopyrolate</td>
<td>DPI Cap</td>
</tr>
<tr>
<td>Glycopyrolate</td>
<td>Soln Neb</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Spiriva® or Respimat®</th>
<th>18 mcg 1.25, 2.5 mcg</th>
<th>QD</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tudorza® Pressair</td>
<td>400 (375)mcg</td>
<td>BID</td>
<td>30, 60 puffs</td>
</tr>
<tr>
<td></td>
<td>Incruse Ellipta®</td>
<td>62.5 mcg</td>
<td>QD</td>
<td>30 puff</td>
</tr>
<tr>
<td></td>
<td>Seebri Neohaler®</td>
<td>15.6 mcg</td>
<td>BID</td>
<td>60 caps</td>
</tr>
<tr>
<td></td>
<td>Lonhala® Magnair®</td>
<td>25 mcg</td>
<td>BID</td>
<td></td>
</tr>
</tbody>
</table>
## COPD Second Line LABA/LAMA Combinations

<table>
<thead>
<tr>
<th>Combination Respiratory Products LABA and LAMA COPD</th>
<th>DPI</th>
<th>Anoro Ellipta® 25/62.5 puff</th>
<th>QD</th>
<th>60 puffs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vilanterol/ Umeclidinium</td>
<td>DPI</td>
<td>Anoro Ellipta® 25/62.5 puff</td>
<td>QD</td>
<td>60 puffs</td>
</tr>
<tr>
<td>Olodaterol/ Tiotropium</td>
<td>Respimat</td>
<td>Stiolto Respimat® 2.5/2.5 puff</td>
<td>QD</td>
<td>60 puffs</td>
</tr>
<tr>
<td>Indacaterol/ Glycopyrolate</td>
<td>DPI</td>
<td>Utibron® Neohaler 27.5/15.6 per capsule</td>
<td>BID</td>
<td>60 puffs</td>
</tr>
<tr>
<td>Vilanterol Fumerate/ Glycopyrolate</td>
<td>HFA</td>
<td>Bevespi Aerosphere® 4.8/9 mg per puff</td>
<td>BID</td>
<td>120 puffs</td>
</tr>
</tbody>
</table>

*Bevespi Aerosphere® — Twice a day*
Example Combo LAMA/LABA Data

• Umeclidinium/Vilanterol 62.5 mcg/25 mcg
  – Anoro Ellipta®, 1 puff Q Day
Think Pair Share

• How do you use the following inhalers
  – HandiHaler®
  – Respimat®
  – Ellipta®
  – Neohaler®
  – Pressair®
“To Steroid or Not to Steroid-That Would Be the Question”

COPD predominate patients are less responsive to corticosteroids. Yet at some point it is always worth a try!
Combination Steroids/LABA

- Fluticasone + Salmeterol =
  - Advair® Diskus:
    • 100/50(green), 250/50(yellow), 500/50(red)
  - Advair HFA®:
    • 45/21 (green), 115/21(yellow), 230/21(red) BID

- Budesonide + Formoterol =
  - Symbicort® 80/4.5 (Green), 160/4.5 (Blue)

- Mometasone + Formoterol
  - Dulera® 100/5 (Yellow), 200/5 (Purple)
  - Fluticasone + Vilanterol
    - Breo Elipta®
Airway Pharmacology - 3
Phosphodiesterase Inhibitors

- Theophylline
- Been around many years
- Adults - 300 BID
- Therapeutic level
  - 8-20
- Lots drug interactions
- Inexpensive ?????

- Roflumilast (Daliresp)
  - 500mcg po daily
  - Selective for PDE4
- Increases intracellular cAMP in lung cells
- No direct bronchodilator effects
  - Improves FEV1 in those on bronchodilators

Asthma and COPD

COPD only at this point
What direction are drug companies going?

• Combination products-
  – LABA plus Steroids- covered
  – LABA plus LAMA-
    • Now
  – Down the road-
    • LABA + LAMA + Steroid
    • LABA + LAMA + Phosphodiesterase inhibitor
    • Etc
And now it is HERE!

**Corticosteroid and LABA and LAMA**

<table>
<thead>
<tr>
<th>Fluticasone/Vilanterol/Umeclidinium</th>
<th>DPI</th>
<th>Trelegy Elipta® Glaxo 17</th>
<th>100/25/62.5</th>
<th>QD</th>
</tr>
</thead>
</table>

**Figure 4. Least Squares (LS) Mean Change from Baseline in Postdose Serial FEV$_1$ (mL) on Day 1**

And again- more evidence LAMA “better” in COPD than LABA- rgh

**Figure 3.**
- **LS Mean Change from Baseline (mL)**
  - Umeclidinium 62.5 mcg + fluticasone furoate/vilanterol 100 mcg/25 mcg
  - Placebo + fluticasone furoate/vilanterol 100 mcg/25 mcg

**Graphs**
- Triple
- Ster/LABA
What if you get REALLY bad lung constriction:

- **Systemic (= IV or ORAL) Corticosteroids**

Physiologic doses are hydrocortisone 20mg or the equivalent. Anything above is Pharmacologic:

<table>
<thead>
<tr>
<th>Glucocorticoids</th>
<th>Equiv Physiologic dose</th>
<th>Stress Physiologic dose</th>
<th>Anti-inflamotary Potency</th>
<th>Plasma T 1/2</th>
<th>Serum T 1/2</th>
<th>Mineral Potency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SHORT ACTING:</strong></td>
<td>8-12 HOURS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortisone:</td>
<td>25</td>
<td>100-125</td>
<td>0.8</td>
<td>30</td>
<td>3-12</td>
<td>2</td>
</tr>
<tr>
<td>Hydrocortisone:</td>
<td>20</td>
<td>80-100</td>
<td>1</td>
<td>90</td>
<td>3-12</td>
<td>2</td>
</tr>
<tr>
<td><strong>INTERMEDIATE:</strong></td>
<td>18-36 HOURS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone:</td>
<td>5</td>
<td>20-25</td>
<td>4</td>
<td>60</td>
<td>12-36</td>
<td>1</td>
</tr>
<tr>
<td>Prednisolone:</td>
<td>5</td>
<td>20-25</td>
<td>4</td>
<td>200</td>
<td>12-36</td>
<td>1</td>
</tr>
<tr>
<td>Triamcinolone:</td>
<td>4</td>
<td>16-20</td>
<td>5</td>
<td>300</td>
<td>12-36</td>
<td>0</td>
</tr>
<tr>
<td>Methylprednisolone:</td>
<td>4</td>
<td>16-20</td>
<td>5</td>
<td>180</td>
<td>12-36</td>
<td>0</td>
</tr>
<tr>
<td><strong>LONG ACTING:</strong></td>
<td>36-54 HOURS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dexamethasone:</td>
<td>0.75 (1)</td>
<td>3-3.75 (4-5)</td>
<td>20-30</td>
<td>1-300</td>
<td>36-54</td>
<td>0</td>
</tr>
<tr>
<td>Betamethasone:</td>
<td>0.6</td>
<td>2.4-3</td>
<td>20-30</td>
<td>1-300</td>
<td>36-54</td>
<td>0</td>
</tr>
<tr>
<td>Hydrocortisone Florine®</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>100</td>
</tr>
</tbody>
</table>
Adverse Effects Corticosteroids: = Why you should NOT be on these long term.

- **Systemic Steroids**
  - Hyperglycemia
  - Euphoria, CNS stimulation
  - Bone marrow suppression
  - Osteomalacia
  - Cushinoid appearance
  - Catabolism
  - Immune Suppression

At what dose of inhaled steroid do you start to get systemic effects?
Summary Conclusion

• Asthma:
  – “Long Term Control Medications”
    • Inhaled corticosteroids
      – Low Dose,
      – Medium Dose
      – High Dose
    • Long Acting Beta Agonists
    • Leukotriene receptor antagonists
    • Long Acting Muscarinic Antagonists
    • Phosphodiesterase inhibitors
    • Immuno Modulators

• COPD:
  – Smoking Cessation
  – “Long Acting Broncodilators”
    • Long Acting Muscarinic Antagonists
    • or
    • Long Acting Beta Agonists
  – LABA Plus LAMA
  – Medium Dose ICS
  – Antiinflammatory Antibiotics

Everyone has a “Quick Relief Medication”
Long-Acting Beta agonists (LABAs) and Inhaled Corticosteroids (ICS): Drug Safety Communication - Boxed Warning About Asthma-Related Death Removed

[Posted 12/20/2017]

AUDIENCE: Pharmacy, Pulmonology, Internal Medicine, Family Practice

ISSUE: FDA’s most prominent warning, the Boxed Warning, about asthma-related death has been removed from the drug labels of medicines that contain both an ICS and LABA. A FDA review of four large clinical safety trials shows that treating asthma with long-acting beta agonists (LABAs) in combination with inhaled corticosteroids (ICS) does not result in significantly more serious asthma-related side effects than treatment with ICS alone. A description of the four trials is now also included in the Warnings and Precautions section of the drug labels. These trials showed that LABAs, when used with ICS, did not significantly increase the risk of asthma-related hospitalizations, the need to insert a breathing tube known as intubation, or asthma-related deaths, compared to ICS alone.
Newest Correlation:

Association of Cardiovascular Risk With Inhaled Long-Acting Bronchodilators in Patients With Chronic Obstructive Pulmonary Disease
A Nested Case-Control Study

Meng-Ting Wang, PhD¹; Jun-Ting Liou, MD²; Chen Wei Lin, BS¹; et al

Author Affiliations


Key Points

Question  Does the duration since initial use and new use of inhaled long-acting β₂-agonists (LABAs) or antimuscarinic antagonists (LAMAs) for the treatment of chronic obstructive pulmonary disease (COPD) act as important determinants of the risk of cardiovascular disease?

Findings  In this nested case-control study of more than 280 000 patients with COPD, new use of LABAs or LAMAs is associated with an approximate 1.5-fold increased cardiovascular risk within 30 days of initiation therapy.
Respiratory Disease Management 501

- **Asthma:**
  - Addition of LAMA to high dose ICS plus LABA plus leukotriene antagonist =
  - **Spiriva Respimat®**

- **COPD:**
  - Addition of anti-inflammatory antibiotics for respiratory benefits:
    - Azithromycin 250mg QD
    - Minocycline 100 mg QD

**SPIRIVA RESPIMAT has asthma-specific dosing: 1.25 mcg/puff (2 puffs, once daily)**
The End
heffroge@isu.edu

http://info.med.yale.edu/intmed/cardio/imaging/anatomy/bronchioles/graphics/bronchiole_diagram.gif