Update on COPD & Asthma

Disclosures

- No Pharma Disclosures
- NHLBI - Asthma Clinical Research Network
- NHLBI - Severe Asthma Research Program

What is COPD

- Disease state characterized by airflow limitation that is not fully reversible*
  - Post-Bronchodilator FEV1/FVC <0.7
- Generally caused by cigarette smoke
  - Biomass fuels (developing world)
  - α1-antitrypsin deficiency
  - Pollution, chronic infection
- Bronchiectasis, cystic fibrosis are not included in the definition

Update on the Management of COPD
Rate of Deaths per 100,000 in the USA 2005-2011

Cancer Death by Site

MEN
- Lung 85,920 (27%)
- Prostate 26,120 (8%)
- Colorectal 26,020 (8%)
- Pancreas 21,450 (7%)
- Liver 18,280 (6%)

WOMEN
- Lung 72,120 (26%)
- Breast 40,450 (14%)
- Colorectal 23,170 (8%)
- Pancreas 20,330 (7%)
- Ovary 14,240 (5%)

American Cancer Society 2016

USPTF

The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.

Simel and Rennie
Evidence-based Clinical Diagnosis
Simel and Rennie
Evidence-based Clinical Diagnosis

Original Article
Clinical Significance of Symptoms in Smokers with Preserved Pulmonary Function

Observational study 2734 current and former smokers and controls who never smoked
Examined whether current or former smokers with preserved lung function had symptoms or suffered COPD exacerbations

Respiratory Symptoms Smokers with Normal Pulmonary Function

Prevalence of Symptoms and Risk of Respiratory Exacerbations
• No benefit of screening adults with no symptoms

• No evidence that treating asymptomatic individuals prevents future symptoms, or reduces the subsequent decline in lung function.

Anthonisen et al
JAMA 272:1497-505, 1994
USPTF JAMA 2016

GOLD Guidelines 2015

When assessing risk, choose the highest risk according to GOLD grade or exacerbation history.

- (C) ≥ 2 or ≥ 1 leading to hospital admission
- (D) ≥ 2 or ≥ 1 leading to hospital admission
- (A) ≥ 2 or ≥ 1 leading to hospital admission
- (B) (no hospital admission)

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Characteristics</th>
<th>Spirometric Classification</th>
<th>Exacerbations per year</th>
<th>mMRC</th>
<th>CAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Low Risk, Less Symptoms</td>
<td>GOLD 1-2</td>
<td>≤ 1</td>
<td>0-1</td>
<td>&lt;10</td>
</tr>
<tr>
<td>B</td>
<td>Low Risk, More Symptoms</td>
<td>GOLD 1-2</td>
<td>≥ 1</td>
<td>≥2</td>
<td>≤10</td>
</tr>
<tr>
<td>C</td>
<td>High Risk, Less Symptoms</td>
<td>GOLD 3-4</td>
<td>≤ 2</td>
<td>0-1</td>
<td>&lt;10</td>
</tr>
<tr>
<td>D</td>
<td>High Risk, More Symptoms</td>
<td>GOLD 3-4</td>
<td>≥ 2</td>
<td>≥2</td>
<td>≥10</td>
</tr>
</tbody>
</table>

GOLD Guidelines 2015

When assessing risk, choose the highest risk according to GOLD grade or exacerbation history.

- (C) ≥ 2 leading to hospital admission
- (D) ≥ 2 leading to hospital admission
- (A) (no hospital admission)
- (B) (no hospital admission)

Take HOME

• Treat the patient
  – Symptoms
  – Exacerbations
• Spirometry assists with diagnosis
• Lung Cancer Screening
### Hospitalized Severe AECOPD and Mortality: Severity of AECOPD

N = 305 men with COPD x 5 years

Soler-Cataluna Thorax 2005

### Predictors of Acute Exacerbations of COPD

<table>
<thead>
<tr>
<th>Number of Exacerbations</th>
<th>2 vs. 0</th>
<th>1 vs. 0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds Ratio (95% CI)</td>
<td>Odds Ratio (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Exacerbation in Prior Year</td>
<td>5.7 (4.5-7.3)</td>
<td>2.2 (1.8-2.8)</td>
</tr>
<tr>
<td>FEV1 per 100ml decrease</td>
<td>1.1 (1.08-1.1)</td>
<td>1.1 (1.0-1.1)</td>
</tr>
<tr>
<td>SGRC (symptom score) per 4 points</td>
<td>1.1 (1.0-1.1)</td>
<td>1.1 (1.0 – 1.1)</td>
</tr>
<tr>
<td>GERD</td>
<td>2.1 (1.6-2.7)</td>
<td>1.6 (1.2-2.1)</td>
</tr>
<tr>
<td>WBC Count</td>
<td>1.1 (1-1.1)</td>
<td>1.1 (1.0-1.1)</td>
</tr>
</tbody>
</table>

Hurst NEJM 2010

### Prevention of AECOPD

**American College of Chest Physicians & Canadian Thoracic Society Guideline**

- PICO (population, intervention, comparator, outcome)
- Literature Search
- Quality Assessment (AGREE II, DART)
- Grading Evidence (GRADEpro)
- Recommendations (CHEST)

Criner et al. CHEST 147:894-942, 2015

### Prevention of AECOPD Recommendations

**Non-Pharmacologic Treatments/Vaccinations:**

- Influenza Vaccine (Grade 1B)
- Pulmonary Rehab (Grade 1C)
- Smoking Cessation (Grade 2C)
- Pneumococcal Vaccine (Grade 2C)
  - *(mod-severe-very severe; recent AECOPD<4 weeks)*

Criner et al. CHEST 147:894-942, 2015
Figure 2. Forest plot of comparison: Rehabilitation versus control, outcome: 1.1 Hospital admission (to end of follow-up).

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental</th>
<th>Control</th>
<th>Total</th>
<th>Event</th>
<th>Odds Ratio [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total (n)</td>
<td>Total (n)</td>
<td>Total</td>
<td>Event</td>
<td></td>
</tr>
<tr>
<td></td>
<td>124</td>
<td>126</td>
<td>250</td>
<td>51</td>
<td></td>
</tr>
</tbody>
</table>

Number Needed to Treat = 4

CI 3-8

Puhan Cochrane Database 2011

Prevention of AECOPD Recommendations

Maintenance Inhaled Therapy:

- LAMA vs PBO (Grade 1A)
- LABA vs PBO (Grade 1B)
- LAMA vs LABA (Grade 1C)
- COMBO Therapy vs MonoTherapy (Grade 1B,C)

Criner et al. CHEST 147:894-942, 2015

Puhan Cochrane Database 2011
FLAME TRIAL

- LAMA + ICS = Good
- LABA + ICS = Good

ICS risk of Pneumonia?
FLAME TRIAL

- LAMA + ICS = Good
- LABA + ICS = Good
- LABA + LAMA = ?

ICS risk of Pneumonia?

LABA (indacaterol) + LAMA (glycopyrronium) QDay

VS.

LABA (salmeterol) + ICS (fluticasone) BID

**New England Journal of Medicine**

**Azithromycin for Prevention of Exacerbations of COPD**


NEJM 365:689-98, 2011

**Prevention of AECOPD Recommendations**

**Oral Therapy:**

- **Macrolide (Grade 2A)**
  (Frequent AECOPD despite Tx)
- **Systemic Corticosteroids (Grade 2B)**
  (For AECOPD – prevent next 30 days)
- **Roflumilast (Grade 2A)**
  (Chr Bronchitis, ≥1 AECOPD in year)
- **Do not use statins for AECOPD (Grade 1B)**

**The MACRO Study**

(Azithromycin 250mg/day x 1 year)

- NHLBI – COPD Clinical Research Network
- N = 1130
- Moderately-severe COPD
  FEV₁/FVC < 70%, FEV₁ < 80%
- “Exacerbation Prone”
- Primary Outcome: Time to first AECOPD

NEJM 365:689-98, 2011
Rates of Acute Exacerbations of Chronic Obstructive Pulmonary Disease per Person-Year, According to Study Group.

Albert RK et al. NEJM 2011

Macrolides Decrease AECOPD

NNT=15

Macrolides May Increase risk of Cardiovascular Death

Ray WA et al. NEJM 2012

Macrolide Antibiotics and the Risk of Cardiac Arrhythmias

Richard K. Albert, MD and Joseph L. Schulke, MD, for the COPD Clinical Research Network
Denver Health, Denver, Colorado; and University of Colorado Denver, Aurora, Colorado
Am J Respir Crit Care Med 2014; 189:1173-1180

• Macrolides can prolong QT and QTc leading to arrhythmias, including torsades de pointes
• Most arrhythmias with macrolides occur in patients with underlying risk factors
• Incidence of arrhythmias in absence of additional risk factors is very low, perhaps 1 in 100,000.

Macrolide Antibiotics and the Risk of Cardiac Arrhythmias

Richard K. Albert, MD and Joseph L. Schulke, MD, for the COPD Clinical Research Network
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Am J Respir Crit Care Med 2014; 189:1173-1180

“Macrolide-associated arrhythmias can be reduced by not prescribing to patients with comorbidities of concern… the majority of which can be discovered by:
• History
• ECG before initiating therapy
• ECG a short time after initiating therapy”
Roflumilast

- Oral Tablet
- 500 ug Once Daily
- Phosphodiesterase-4 Inhibitor
- 1 year trial
- 40 years old, >20 pack years, +COPD
- FEV1% predicted<50%
- Symptoms of chronic bronchitis, +cough and sputum
- “Exacerbation Prone”
- ICS + LABA

Martinez et al., Lancet 2015

Roflumilast

<table>
<thead>
<tr>
<th>Common adverse event</th>
<th>Treatment Group</th>
<th>Placebo Group</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dryness</td>
<td>36 (17%)</td>
<td>20 (15%)</td>
<td>1.0 (0.0-2.1)</td>
</tr>
<tr>
<td>Weight decrease</td>
<td>36 (17%)</td>
<td>27 (20%)</td>
<td>0.7 (0.0-1.4)</td>
</tr>
<tr>
<td>Nausea</td>
<td>31 (15%)</td>
<td>25 (19%)</td>
<td>1.2 (0.0-2.4)</td>
</tr>
<tr>
<td>Headache</td>
<td>32 (16%)</td>
<td>31 (23%)</td>
<td>0.2 (-0.3 to 0.7)</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>32 (16%)</td>
<td>27 (20%)</td>
<td>1.8 (0.1-3.6)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>15 (7%)</td>
<td>11 (9%)</td>
<td>1.0 (0.0-2.7)</td>
</tr>
<tr>
<td>Increased appetite</td>
<td>15 (7%)</td>
<td>13 (10%)</td>
<td>0.4 (0.0-1.5)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>12 (6%)</td>
<td>10 (8%)</td>
<td>0.2 (0.0-0.6)</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>12 (6%)</td>
<td>13 (10%)</td>
<td>0.2 (0.0-0.7)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>12 (6%)</td>
<td>20 (15%)</td>
<td>0.5 (0.1-1.0)</td>
</tr>
</tbody>
</table>

NNT=25  NNH=16  Martinez et al., Lancet 2015

Effect of Corticosteroids on Treatment Failure Rates after AE COPD

- 2 week: Solucortef 120mg q6hr x 4d, Prednisone 60mg qd x 4d, 40mg qd x 4d, 20mg qd x 4d
- 8 week: additional 10mg qd x 5 week, then 5 mg qd x 1 week

Martinez et al., NEJM 340:1941, 1999

NNT=25  NNH=16  Martinez et al., Lancet 2015
Summary

• Pulmonary Rehab (NNT=4)
• Duel Long Acting Bronchodilator Medications over ICS + LABD (NNT=9)
• Azithromycin prevents COPD Exacerbations (NNT=15)
  – Potential Risk of Cardiac Arrhythmias
• Roflumilast offers some benefit in bronchitis patients (NNT=25), (NNH=16)
• 5 days of corticosteroids is the appropriate time frame

Goals of Treatment
For Primary Care Physicians

• Prevention of Acute Exacerbations
• Prevent Progressive Loss of Lung Function
• Improve Symptoms
**Effect of Smoking Cessation on FEV₁**

<table>
<thead>
<tr>
<th>Follow-up in years</th>
<th>Post Bronchodilator FEV₁ (liters)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen 2</td>
<td>2.9</td>
</tr>
<tr>
<td>1</td>
<td>2.8</td>
</tr>
<tr>
<td>2</td>
<td>2.7</td>
</tr>
<tr>
<td>3</td>
<td>2.6</td>
</tr>
<tr>
<td>4</td>
<td>2.5</td>
</tr>
<tr>
<td>5</td>
<td>2.4</td>
</tr>
</tbody>
</table>

*JAMA 272:1497, 1994.*

**Effects of a Smoking Cessation Intervention on 14.5-year Mortality**

- Special intervention group
- Usual care group
- Smoking Cessation
- Usual Care

*P=0.03*


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**Therapy Reduces Lung Decline (TORCH)**

- Placebo
- SAL
- FP
- SFC
- Salmeterol + Fluticasone
- -30 mL/yr
- -40 mL/yr
- -50 mL/yr
- Placebo


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**A 4-Year Trial of Tiotropium in Chronic Obstructive Pulmonary Disease**

- Tiotropium Reduces Lung Decline
  - Exacerbations
  - Hospitalizations
  - Lung Function

*Tashkin et al NEJM 359:1543-54, 2008.*
**Downward Spiral In Function Associated With COPD**

- Disease
- Dyspnea
- Inactivity
- Deconditioning

**Pulmonary Rehabilitation**

- Benefits all levels of disease severity
- Reduces respiratory symptoms
- Reduces anxiety and depression
- Reduces medical and hospital usage
- Improves exercise performance
- Improves quality of life
- Is typically provided as outpatient
- Can be initiated as an inpatient until functional ability has improved

**Update on the Management of Asthma**
**Definition of Asthma**

- Obstruction that is reversible either spontaneously or with treatment; [NAEPP-EPR, 1991]
- Chronic inflammatory disorder (MCs, Eos, Tcells, Macs, PMNs, Epil); variable obstruction; [NAEPP-EPR2, 1997]
- Variable symptoms, obstruction, BHR; inflammation; interaction [NAEPP-EPR3, 2007]

**Definition of Asthma**

- Chronic inflammatory disorder; many different cells; BHR; variable/reversible symptoms and obstruction; phenotypes? [GINA, 2011]
- Heterogeneous; Chronic airway inflammation; variable/reversible symptoms and obstruction; Different phenotypes or clusters [GINA, 2014]

**Epidemiology**

- 250-300 million people have asthma globally
- Asthma rates have been increasing in low/middle income countries (caught up)
- Most of the morbidity/mortality from asthma stems from the 5-10% with severe disease

**Causes of Asthma**

- Hygiene Hypothesis
- Exposure to Antibiotics
  - Microbiome
- Genetics
- Obesity
- Environmental Influences
  - Dogs/Cats
  - Medications
Original Article

Innate Immunity and Asthma Risk in Amish and Hutterite Farm Children

Proportions of Peripheral-Blood Leukocytes and Cell-Surface–Marker Phenotypes in Amish and Hutterite Children.

Endotoxin Levels of Dust of Amish and Hutterite Children.

Effects of Amish and Hutterite House-Dust Extracts on Airway Responses in Mouse Models of Allergic Asthma.
Original Article

Acetaminophen versus Ibuprofen in Young Children with Mild Persistent Asthma

- Concern that acetaminophen may exacerbate asthma.

- Trial enrolled 300 patients for a RCT acetaminophen vs ibuprofen with mild persistent asthma to receive tylenol or ibuprofen for fever

Sheehan NEJM 2016

### Table 3: Asthma Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Acetaminophen [N = 150]</th>
<th>Ibuprofen [N = 150]</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of asthma exacerbations that led to treatment with systemic glucocorticoids, primary outcome - no of participants (N)</td>
<td>0</td>
<td>24 (16)</td>
<td>36 (24)</td>
<td>—</td>
</tr>
<tr>
<td>1</td>
<td>42 (28)</td>
<td>34 (23)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>16 (11)</td>
<td>21 (14)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>≥3</td>
<td>14 (10)</td>
<td>19 (13)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Mean exacerbation frequency over 46 weeks (95% CI)</td>
<td>0.88 (0.63 to 1.23)</td>
<td>0.98 (0.69 to 1.40)</td>
<td>0.94 (0.60 to 1.52)</td>
<td>0.94</td>
</tr>
<tr>
<td>Among 291 total participants</td>
<td>0.79 (0.58 to 1.09)</td>
<td>0.70 (0.50 to 0.98)</td>
<td>1.09 (0.73 to 1.64)</td>
<td>0.79</td>
</tr>
<tr>
<td>Among 238 participants who completed the trial</td>
<td>0.74 (0.59 to 1.00)</td>
<td>0.70 (0.50 to 1.00)</td>
<td>1.09 (0.73 to 1.64)</td>
<td>0.79</td>
</tr>
<tr>
<td>Among 206 participants who completed the trial and used at least one oral glucocorticoid</td>
<td>0.74 (0.59 to 1.00)</td>
<td>0.70 (0.50 to 1.00)</td>
<td>1.09 (0.73 to 1.64)</td>
<td>0.79</td>
</tr>
</tbody>
</table>

Global Asthma Report 2014

Aging and Asthma

- **Years Lost Life**
- **Years Lost Disability**

Time to First Asthma Exacerbation.

- Cumulative risk of first exacerbation
- No. at Risk
  - Acetaminophen: 150 116 115 109 99 91 83 79 73 68 63 62
  - Ibuprofen: 148 115 125 113 107 96 88 82 75 68 63 62

Global Asthma Report 2014
Obesity and Asthma

Obesity is an important risk factor for the development of asthma.

Percentage of adults with asthma who are obese

Black Box Warning

- Data from a large placebo-controlled U.S. study that compared the safety of salmeterol or placebo added to usual asthma therapy showed a small but significant increase in asthma-related deaths in patients receiving salmeterol (13 deaths out of 13,176 patients treated for 28 weeks) versus those on placebo (3 of 13,179)\(^*\).

Original Article

Serious Asthma Events with Fluticasone plus Salmeterol versus Fluticasone Alone

Adolescent and adult patients >12 years with persistent asthma were randomized to ICS (fluticasone) vs ICS + LABA (salmeterol) for 26 weeks.

All patients had a history of a severe asthma exacerbation in the past year.

\(^*\) NEJM 2016
Primary Safety End Point (Intention-to-Treat Population).

Summary of Safety End Points.

<table>
<thead>
<tr>
<th>Safety End Point</th>
<th>Fluticasone-Salmeterol (N=1834)</th>
<th>Fluticasone Al眼神 (N=3840)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite safety end point — no. (%)</td>
<td>34 (-1)</td>
<td>33 (-1)</td>
</tr>
<tr>
<td>Asthma-related death</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Asthma-related intubation</td>
<td>0</td>
<td>2 (-1)</td>
</tr>
<tr>
<td>Asthma-related hospitalization</td>
<td>34 (-1)</td>
<td>33 (-1)</td>
</tr>
<tr>
<td>Total no. of asthma-related hospitalizations</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>Death from any cause — no. (%)†</td>
<td>3 (-3)</td>
<td>6 (-1)</td>
</tr>
</tbody>
</table>

* The analysis was performed in the intention-to-treat population.
† Details regarding all-cause mortality are provided in Section 4 in the Supplementary Appendix.

Asthma Phenotypes
Not all asthma is the same!!

(Heterogeneity)

(Phenotypes)

A Large Subgroup of Mild-to-Moderate Asthma Is Persistently Noneosinophilic (NON Allergic)

- Asthma is a heterogeneous disease
- ~50% of asthmatics - poor response to steroids
- Eosinophilic airway inflammation not ubiquitous

Sputum Eosinophil Percentage (No ICS)
**TH2 Genes Overexpressed in Asthma**

- **Th2 High**
- **Th2 Low**

**Th2 Status Predicts Corticosteroid Response**

- Th2 high
- Th2 low

**The NEW ENGLAND JOURNAL OF MEDICINE**

Oral Glucocorticoid-Sparing Effect of Mepolizumab in Eosinophilic Asthma

- N=135, prednisone ≥6 months, eosinophils >300

**Oral Glucocorticoid-Sparing Effect of Mepolizumab in Eosinophilic Asthma**

- Mepolizumab (N=68)
- Placebo (N=68)
Type-2 Inhibitors for Severe Asthma

- Anti IL-5 Agents
  - Mepolizumab (NUCALA)*
  - Resilizumab (CINQAIR)*
- Anti IL-13 Agents
  - Lebrikizumab
- Anti IL-4/IL-13
  - Dupilumab
- Anti TSLP
  - AMG 157

* FDA Approved
Alternative Treatment?

Tiotropium Step-Up for Uncontrolled Asthma

Peters et al.

Eur Respir J; 43:343-73, 2014

Tiotropium Step-Up for Uncontrolled Asthma

International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma

Peters et al.

Eur Respir J; 43:343-73, 2014
International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma

Recommendations:

• In adults with severe asthma – use sputum eos in experienced centers
• In severe allergic asthma – therapeutic trial of omalizumab: Mepolizumab?
• Do not use methotrexate for asthma
• Do not use azithromycin for asthma

Eur Respir J; 43:343-73, 2014

International ERS/ATS guidelines on definition, evaluation and treatment of severe asthma

Recommendations:

• Use anti-fungals for ABPA
• Do not use anti-fungals without ABPA
• Consider bronchial thermoplasty only as part of a study

Eur Respir J; 43:343-73, 2014

NAEPP GUIDELINES

“If there is a clear and positive response for at least 3 months, a careful step down in therapy should be attempted to identify the lowest dose required to maintain control (Evidence D)”

Evidence D = Panel Consensus Judgment

GINA GUIDELINES

“Controller treatment may be stopped if the patient’s asthma remains controlled on the lowest dose of controller and no recurrence of symptoms occurs for 1 year (Evidence D)”

Evidence D = Panel Consensus Judgment

Global strategy for asthma management and prevention: GINA executive summary.
Is There Really A Difference Between Asthma And COPD?

Pathophysiology in COPD versus Asthma

**COPD**
- Loss of elastic recoil
- Changes in small airways
- "Inflammation"
- Fixed airway obstruction

**Asthma**
- Inflammation
- Bronchial hyperresponsiveness
- Varying airway obstruction

Inflammation in COPD versus Asthma

<table>
<thead>
<tr>
<th>COPD (Predominant Cells)</th>
<th>Asthma (Predominant Cells)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrophages</td>
<td>Eosinophils</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>Activated Mast Cells</td>
</tr>
<tr>
<td>CD-8 T-Lymphocytes</td>
<td>CD-4 T Lymphocytes</td>
</tr>
</tbody>
</table>

Predominant Cytokines

<table>
<thead>
<tr>
<th>COPD</th>
<th>Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interleukin 8</td>
<td>Interleukin 4</td>
</tr>
<tr>
<td>Leukotriene B4</td>
<td>Interleukin 5</td>
</tr>
<tr>
<td>Tumor Necrosis Factor alpha</td>
<td>Interleukin 13</td>
</tr>
</tbody>
</table>

COPD Asthma Overlap

Asthma Summary

• The “Cause” of asthma remains unknown, but is unlikely to be fully explained by genetics
• Acetaminophen and LABA are safe to use in asthma patients
• Patients respond differently to medications based upon underlying “endotype/phenotype”
• “Th2-High” or Allergic Asthma responds to corticosteroids
• New Medications are on the way for Severe Allergic Asthma