Disclosures/Conflict of Interest

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Speakers Bureau: Merck

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Trends of Asthma Morbidity/ Mortality

Asthma by the Numbers

25 million Americans have asthma
up from 20 million in 2001
(Population of Australia: 22 million)

3,447 asthma deaths per year
9 deaths per day

Emergency visits for asthma:
1.6 million a year
456,000 admitted to hospital in 2007
Average length of stay: 3.4 days

8.2% of adults have asthma

9.6% of children or 7.1 million kids

GRASP OF CONTROL

Under
50%

50% learned about avoiding triggers
50% of those who were taught it currently practise avoidance

ECONOMIC BURDEN

Costs of Asthma:
$56 billion
in 2007. Up 6% from 2002

Medical expense portion:
$50.1 billion

$3,300 per asthmatic: Average annual asthma medical costs
1 in 9 insured can’t afford prescription meds

Asthma 2010-2011: Epidemic rise in America

- Asthma deaths per 100,000 population age 5-34
- Red > 10
- Yellow 5-10
- Blue < 5

Papirus, Drugs 2009; 69 (17):2366-87
Why Are We Here?

• 22 yo student in Northern Iowa
• Senior year: special Ed teacher
• “Mild Asthma” per MD
• Phoned her mother each day:
  – Roommates opening apartment windows at night
  – Erin using MDI 3-5 x/night
  – Went out dancing with friends
• Erin’s mother called by police and told to get to hospital as soon as possible!
Why did this 22 year old girl die?

- Neither she nor her mother knew her asthma was “out of control”
- They were on the “wrong side of the information gap: just like 7/10 asthmatics
- Erin’s mother went on to become an Asthma Educator
Risk Factors for Severe Asthma Exacerbation

• Equal among mild, moderate, and severe asthma*

• Key risk factors:
  – Ever been intubated or in ICU for asthma
  – Hospitalized in last year
  – Deficiency in self-management skills

• Predictors of health care utilization:
  – Score of < 20 on Asthma Control Test (ACT)
  – Poor perception of dyspnea

*Clin & Exper Allergy 2007; 37:552-557
Asthma Control Test™ (ACT)

1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school, or at home?

2. During the past 4 weeks, how often have you had shortness of breath?

3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness, or pain) wake you up at night, or earlier than usual in the morning?

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?

5. How would you rate your asthma control during the past 4 weeks?

ACT < 20 best predictor of asthma control
Factors Influencing the Heterogeneity of Asthma Control: Poor Perception of Dyspnea (POD)

113 Asthmatics Evaluated

• Breathe against 2-way valve load of 0-, 5-, 10-, 20-, and 30-cm H₂O for 1 minute

• Dyspnea defined as modified Borg scale

• POD
  – Low 29 (26%)
  – Normal 67 (59%)
  – High 17 (15%)

• β₂-Agonist use in 4 weeks*
  – Low 1.7/day
  – Normal 2.4/day
  – High 4.1/day

• Patients with asthma and a low POD had tendency toward
  – Older age
  – More females
  – Longer duration
  – More severe

• Documented events over 2 years

*Puffs/day.
Of deaths in the low POD group, 4 were asthma related, 2 were unknown.

Multiple studies now that show underpercievers and life-threatening asthma may have a 20% mortality from asthma.
ASTHMA 2011

• Maximizing therapy
Asthma severity is related to the severity of AHR
AHR is diagnostic tool for asthma

Control of AHR: Mild Exacerbations

Incidence of Asthma Exacerbations (N = 75)
ICS dose was 400 µg higher in AHR group

* 1.8-fold decrease in exacerbation rate vs guideline strategy ($P=0.03$).
Mild exacerbations = increase of ≥3 points in total asthma score.


2010: Studies on inhaled mannitol to assess AHR
Reasons to Measure Nitric Oxide

• Identify the eosinophilic asthma phenotype
• Assess potential response or failure to ICS
• Establish a baseline
• Guide changes in doses of anti-inflammatory medications
• Assist in the evaluation of adherence to anti-inflammatory medications
• Assess whether airway inflammation is multifactorial
Measurement ATS Guidelines: 2011

- < 25 ppb (20 ppb in children) - eosinophilic inflammation and responsiveness to corticosteroids are less likely
- > 50 ppb (>35 ppb in children) eosinophilic inflammation and responsiveness to corticosteroids in sx patients is more likely
- 25-50 ppb (20–35 ppb in children) depends on the clinical context
Causes of High FENO

In a symptomatic patient (chronic cough and/or wheeze and/or shortness of breath during past > 6 wks) presenting for the first time, possible etiologies:

- Atopic asthma
- Eosinophilic bronchitis
- COPD with mixed inflammatory phenotype
- That the patient is likely to benefit from a trial of inhaled corticosteroid treatment
“There is a 3-fold increase in asthma-related intubations and deaths in those taking long-acting β-agonists with concomitant corticosteroids compared with corticosteroids alone”

The LABA controversy continues……..
Safety of LABAs: Views from the FDA

- LABA alone without ICS dangerous
  - Yet 7-11% PCPs use LABA alone for asthma
- Use of ICS with LABA reduces but may not completely eliminate possible risk
- 4 adult/1 pedi study mandated: completion 2016
Tiotropium Bromide Step-Up Therapy for Adults with Uncontrolled Asthma

• TALC study
  – Poorly controlled on ICS
    • Double ICS
    • LABA (salmeterol)
    • LAMA (Tio)
• Primary endpoints
  – PEFR
  – FEV₁
  – Asthma control days
• LAMA = LABA > ↑ ICS
• No long term data; select subset of subjects

October 28, 2010
Update in Asthma 2010

• Epigenetic: environment changes functioning of genes
  • Smoke, hydrocarbons, diesel exhaust, or allergens
  • Converts naive T cells to TH-2 (allergic) T cells
• Prenatal exposure to tylenol increases risk of asthma
• Vitamin D deficiency (< 2ng/ml)
  • Increases risk and severity of asthma
  • Associated with poor response to ICS
• Drug therapy (in addition to ICS)
  • Macrolide Rx x16 weeks reduced airway hyperreactivity
  • Statins: reduced inflammation & improved spirometry in COPD but showed less effect in asthma
Update in Asthma 2010

• What reduces exacerbations of asthma

  • Environmental tobacco smoke (ETS) = strongest predictor of respiratory illness in children
    • Ban on ETS in Scotland decreased asthma hospitalization by 18.2%

  • Exercise can induce bronchospasm
    • 3 months of aerobic exercise training significantly improved asthma QOL and asthma free days (p=0.001)

• Medication compliance

  • Indacaterol – once a day LABA
  • Ciclosenide – once a day high potency ICS

• MOST IMPORTANT
Environment

• Allergens avoidance in asthma:
  – House dust mite
  – Cat dander
  – Cockroach antigen
  – Alterneria/fungi

• Most forgotten component in asthma education
COPD 2011

• What have we learned about COPD?
Three Things You Should Know about COPD

1- This a treatable and reversible disease.

2- Management of COPD should include: encouragement of exercise; tobacco cessation, and pharmacotherapy.

3- Inhaled long acting bronchodilators alone or combined with ICS are the appropriate therapy for the management of stable COPD patients.
What do we mean by “Disease Modification”? 
Myth:
COPD is a disease of old man ....
The Changing Face of COPD

Younger

• ~70% of patients with COPD are <65 years old, accounting for: 67% of COPD office visits – 43% of hospitalizations

More Women

♦ In 2004, women accounted for ~63% of all self-reported COPD cases
♦ 1980–2009: COPD mortality rates for women nearly tripled

Shifting Patient Profile in COPD: 2010

Myth:
The more you smoke the worse you disease gets....

Fact:
There is no correlation between # pack years and disease severity
Smoking and disease severity

COPD gene

Smoking (pk/yr) vs. FEV$_1$ and GOLD stages.
COPD: Disease Progression

This has to change !!!!
COPD

Lung cancer

Cachexia vs myopathy

Osteoporosis

Anxiety and depression

9 - 20%

20-60%

30%

30-50%

30-50%

Anemia

17%

20-60%

Barnes et al GOLD 2009
Myth: Exacerbations are not that bad.....
Recovery of Lung Function and Symptoms Following an Exacerbation Is Often Prolonged and Sometimes Incomplete

<table>
<thead>
<tr>
<th>Time to recovery,* median days (IQR)</th>
<th>PEF</th>
<th>Symptoms</th>
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<td>6 (1-14)</td>
<td>7 (4-14)</td>
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<th>Exacerbations recovering within 35 days</th>
<th>PEF</th>
<th>Symptoms</th>
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<td>75.2%</td>
<td>86.1%</td>
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<tr>
<th>Exacerbations recovering within 91 days</th>
<th>PEF</th>
<th>Symptoms</th>
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<td>80.2%</td>
<td>90.9%</td>
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<th>Exacerbations that did not recover within 91 days</th>
<th>PEF</th>
<th>Symptoms</th>
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<tr>
<td>7.1%</td>
<td>4.6%</td>
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IQR=interquartile range.

COPD Patients With a Greater Frequency of Severe Exacerbations* Per Year Have a Higher Risk of All-Cause Mortality


*Severe exacerbations = exacerbation required emergency visits or hospital admissions.

Increased Risk for MI and Stroke Following COPD Exacerbations


Increased risk 1-49 (2.27 [1.1-4.7]; *P*=.03)
GOLD Therapy at Each Stage of COPD

**I: Mild**
- FEV₁/FVC < 0.70
- FEV₁ ≥ 80% predicted
- Active reduction of risk factor(s): influenza vaccination
- Add short-acting bronchodilator (when needed)

**II: Moderate**
- FEV₁/FVC < 0.70
- 50% ≤ FEV₁ < 80% predicted
- Add regular treatment with one or more long-acting bronchodilators
- Add pulmonary rehabilitation

**III: Severe**
- FEV₁/FVC < 0.70
- 30% ≤ FEV₁ < 50% predicted
- Add inhaled glucocorticosteroids if repeated exacerbations

**IV: Very Severe**
- FEV₁/FVC < 0.70
- FEV₁ <30% predicted
- or FEV₁ <50% predicted plus chronic respiratory failure

GOLD Guidelines: Updated December, 2010 www.goldcopd.com
Basics of Treating COPD: 2011

• Initiation of long-acting bronchodilator
  – Canadian guidelines suggest cost-effective to start with a LABA (salmeterol/formoterol) or LAMA (tiotropium)
    • Less exacerbations & better quality of life
    • Much better compliance

• Inhaled Corticosteroids: Risk vs. Benefit
  • Risk: Increase risk of pneumonia with RR= 1.6
  • Benefit: FEV$_1$ < 50% or "asthma/atopic" features with eosinophils, frequent exacerbations, or positive BD test

• Home oxygen
  • Saturation ≤ 88% (or ≤ 89% with Cor Pulmonale)
  • Must wear oxygen 15 hours/day for survival benefit
GOLD Pharmacologic Treatment Options

**Bronchodilators**
- **Short-acting**
  - β-agonists
    - Albuterol
    - Levalbuterol
    - Pirbuterol
    - Anticholinergic
      - Ipratropium
    - Combination
      - Combivent
  - Indacaterol
- **Long-acting**
  - β-agonists
    - Salmeterol
    - Formoterol
    - Arformoterol
  - Anticholinergic
    - Tiotropium
  - Theophylline

**Anti-inflammatory**
- **Corticosteroids**
  - Combination
    - Salmeterol + Fluticasone
    - Formoterol + Budesonide

- **Phosphodiesterase inhibitor**
  - PDE-4 Inhibitor
    - Roflumilast
Respimat: soft mist inhaler

- Spring powered inhaler
- No preservative; better delivery
- Approved 2011 for Combivent
- How to use:
  - Load cartridge into device
  - Rotate counter clockwise
  - Insert mouthpiece
  - Push dosing button during inspiration (1 actuation QID)
Roflumilast: PDE4- inhibitor

- Selection of patients who will benefit:
  - Severe COPD with chronic bronchitis
  - On LABA/ICS and LAMA (tiotropium)
  - Exacerbation requiring steroids/hospitalization

- Mechanism of action: anti-inflammatory medication

- Benefits: reduced exacerbations

- Side effects:
  - Nausea/diarrhea (10 – 20%)
  - Weight loss (7.5%)
  - Anxiety/depression (6%)
The Key to Treating COPD: Smoking Cessation

- **Smoking cessation** (*Lung Health Study*)
  - Reduced all cause mortality (MI/Cancer)
  - Only therapy proven to prevent ↓ FEV$_1$
  - Average smoker quits 5 times prior to success
Questions?