Objectives

- Epidemiology
- Mechanisms
- Clinical applications
Asthma Prevalence by Age & Sex

Moorman et al. MMWR Surveill Summ 2007; 56 (8), 1-54.
Asthma Prevalence by Age & Sex

- Total asthma prevalence in U.S.
  - Male 7.0%
  - Female 9.3%

- Children aged 0-17 years
  - Male 11.3%
  - Female 7.9%

Asthma Mortality

- At-risk-based death rate from asthma higher in females
    - 1.29 females vs. males

Asthma Morbidity

- Women with asthma report
  - More frequent asthma symptoms\(^1\)
  - Poorer quality of life\(^1\)
  - Greater healthcare utilization\(^1-3\)
  - More frequent courses of systemic\(^3\) corticosteroids

- Despite better baseline pulmonary function\(^2-4\)

Asthma Exacerbations & Emergency Department Presentations

- Women
  - More likely to be admitted\textsuperscript{1-2}
  - Describe symptoms as more severe\textsuperscript{3}

- Despite
  - Better pulmonary function\textsuperscript{1-3}
  - Less hypercapnia\textsuperscript{4}

Sex Differences Among Adults Presenting to the ED with Acute Asthma

Patients Reporting Severe Distress in 24 hours Prior to Seeking ED Care

Comparison of pCO2 Levels in Women vs. Men Hospitalized for Asthma

Gender Bias in Diagnosis of Obstructive Lung Diseases?

- Chapman et al surveyed 192 primary care physicians using hypothetical case and interview.
- Cough and dyspnea in smoker
  - 6 versions of case differing in age & sex of patient.
- Asked to provide most likely diagnosis and choose diagnostic studies.
- Later given spirometry with irreversible airflow obstruction.

Gender Bias in Diagnosis of Obstructive Lung Diseases?

- **Initial diagnosis**
  - COPD: 65% men vs. 49% women (p<0.05)
  - Asthma: 32% men vs. 44% women

- **After spirometry**
  - COPD: 76% men vs. 65% women
  - Asthma: 22% men vs. 32% women

Sex Differences in Consistency of Care with National Asthma Guidelines?

<table>
<thead>
<tr>
<th></th>
<th>Men (%)</th>
<th>Women (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Possess ICS</td>
<td>68</td>
<td>71.9</td>
<td>0.007</td>
</tr>
<tr>
<td>Use daily ICS</td>
<td>58.3</td>
<td>49.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Action Plan</td>
<td>51.1</td>
<td>52.5</td>
<td>ns</td>
</tr>
<tr>
<td>Peak-flow monitoring</td>
<td>21.0</td>
<td>20.4</td>
<td>ns</td>
</tr>
<tr>
<td>Avoid Triggers</td>
<td>49.0</td>
<td>52.2</td>
<td>ns</td>
</tr>
<tr>
<td>Asthma specialist</td>
<td>43.1</td>
<td>37.7</td>
<td>0.001</td>
</tr>
</tbody>
</table>

n= 5062

Adherence to Inhaled Corticosteroid Regimens

- **Self-reported** compliance *higher* in women\(^1\)
- Adherence 28% *lower* in women \(p=0.08\)
  - HMO prescription-refill data\(^2\)
- No sex differences in adherence in research trial for COPD\(^3\)

Influence of Sex on Metered-dose Inhaler Technique

- Un-coached MDI technique observed in 59 subjects (26 female & 33 male)
  - Inspiratory flow rate
  - Timing of actuation
  - Inspiratory volume
  - Breath-holding time

- Acceptable maneuvers 25% subjects
  - 43% males
  - 4% females (p<0.001)

Perception of Air-flow Obstruction

- Inspiratory muscle strength (PImax) significantly reduced in females with mild-moderate asthma
  - Associated with more dyspnea and short-acting beta-agonist use (SABA)
- With training, female subjects increased PImax with resulting decrease in dyspnea and SABA use

Is Bronchial Hyperresponsiveness (BHR) More Common in Women?

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>BHR Men</th>
<th>BHR Women</th>
<th>Differences related to FEV₁?</th>
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</thead>
<tbody>
<tr>
<td>Britton, et al. 1994</td>
<td>2,415</td>
<td>---</td>
<td>OR 2.05 (CI 1.6-2.7)</td>
<td>YES</td>
</tr>
<tr>
<td>Leynaert, et al. 1997</td>
<td>799 (2 populations)</td>
<td>A: 11.9%</td>
<td>A: 33.7%</td>
<td>NO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B: 29.5%</td>
<td>B: 43.2%</td>
<td>NO</td>
</tr>
<tr>
<td>Norrman, et al. 1998</td>
<td>1448</td>
<td>10.6%</td>
<td>15.0%</td>
<td>NO</td>
</tr>
<tr>
<td>Manfreda, et al. 2004</td>
<td>2,962</td>
<td>1.76 (CI 1.36-2.28)</td>
<td>NO</td>
<td></td>
</tr>
</tbody>
</table>
Women and Tobacco Smoke

- Increased BHR may relate to increased susceptibility to tobacco smoke
- Female smokers at higher risk for tobacco-related loss in pulmonary function\(^1-^3\)
- Recovery of lung function is greater in women who stop smoking\(^4\)

Tobacco and BHR cont.

- Lung Health Study
  - Current smokers with mild-to-moderate obstruction
- BHR more common in women (85.1% vs 58.9%)
- More women (46.6% vs 23.9%) responded to ≤ 5 mg/ml methacholine
- BHR related to pack-years tobacco use only in women (p=0.044)

Estrogen, Progesterone, & Asthma

- Patterns in asthma prevalence & severity correlate with key transition points in the reproductive cycle
- No clearly established link between asthma & female sex hormones
  - Menstrual-related asthma (MRA)
  - Pregnancy
  - Menopause & post-menopausal hormone use
Prevalence of Menstrual-related Asthma (MRA)

- 35 to 40% of women report increased symptoms near onset of menses\(^1\)\(^-\)\(^2\)
- Menstrual-related asthma
  - Reductions in peak expiratory flow rates (PEFR)
  - Increased \(\beta\)-agonist use in perimenstrual period (Days -5 to 5)

BHR and MRA

- Pauli et al compared 11 women with asthma and no prior MRA to 29 controls
  - No changes in spirometry or BHR over menstrual cycle either group
  - Asthma symptoms deteriorated ($p=0.001$) & PEFR decreased ($p=0.045$) from follicular to luteal phase

- Tan et al evaluated 15 asthmatics without MRA
  - Increased BHR to adenosine 5’-monophosphate from follicular to luteal phase ($p<0.05$)

Inflamatory Markers in MRA

- In women with self-reported MRA\(^1\)
  - Sputum eosinophilia and exhaled nitric oxide (eNO) increased at time of menses
  - Correlated with increase in asthma symptoms
- In women with PMA and decreases of PEFR\(^2\) >40% from baseline with menses
  - \(\text{LTC}_4\) increased during premenstrual phase
  - Pranlukast administration prevented decrease in PEFR

Menopause, Hormone Replacement Therapy (HRT), & Asthma

- **Nurses’ Health Study**\(^1\)
  - RR 2.30 (CI 1.69-3.14) newly diagnosed asthma and postmenopausal HRT in current estrogen users when compared to never users

- **Copenhagen City Heart Study**\(^2\)
  - Weak association between self-reported asthma and asthma symptoms in postmenopausal women using HRT

What does this mean clinically?
Is Sex Specific Analysis of Asthma Symptoms Profiles Helpful?

- Current national guidelines emphasize routine assessment of asthma control
- Lack information about whether sex-specific assessment measures should be considered
Effect of Sex on Asthma Symptoms & Triggers

Sex Differences in Asthma Symptoms Profiles & Control Assessment

- American Lung Association Asthma Clinical Research Center (ALA-ACRC)
  - network of 19 clinical research centers
  - dedicated to research of asthma treatment

- Retrospectively reviewed baseline data for 1612 adults enrolled in 4 previously published studies

McCallister et al. AJRCCM 2011; 183: A4309.
Sex Differences in Asthma Symptoms Profiles & Control Assessment

- Sex specific analysis of item responses to standardized asthma questionnaires
  - Juniper Asthma Control Questionnaire (ACQ)
  - Juniper mini-Asthma Quality of Life Questionnaire (mini-AQLQ)
  - Asthma Symptom Utility Index (ASUI)
- 1325 poorly controlled (ACQ ≥1.5)
- 287 controlled (ACQ <1.5)

McCallister et al. AJRCCM 2011; 183: A4309.
Results

- Despite better pulmonary function and less rescue inhaler use, women noted
  - More asthma symptoms
  - Poorer quality of life

- Unique symptom profiles predominate in women
  - Cough
  - Nocturnal symptoms
  - Environmental triggers

- Currently available questionnaires may not detect sex specific differences in asthma symptom profiles

McCallister et al. AJRCCM 2011; 183: A4309.
Self-regulation Intervention for Women with Asthma

- Asthma management program including salient sex role-related and gender role-related issues
- Benefit to women when compared to standard treatment approaches
  - Improved asthma related quality of life
  - Decreased healthcare utilization
  - Decreased use of short-acting bronchodilators

Conclusions

- Asthma affects men and women differently
- No unifying explanation
- Clinical implications should be considered