Work-Related Asthma: An Overlooked Asthma Trigger

Kenneth D. Rosenman, M.D.
Professor of Medicine
Michigan State University
OBJECTIVES

- Highlight the Importance of Considering Occupational and Environmental Exposures in Diagnosis and Treatment of Adult Onset Asthma

- Discuss Approaches to Diagnosing Work-Related Asthma
Work-Related Asthma
What Percentage of Asthma is Work-Related?

Consensus Statements  American Thoracic Soc  
Am J Resp Crit Care Med 2011; 184:368-378

New Onset Asthma

21 studies - range 4-58%, 15% median

Work Aggravated Asthma

12 studies - range 13-58%, 21.5% median
CHEST Supplement

DIAGNOSIS AND MANAGEMENT OF WORK-RELATED ASTHMA: ACCP CONSENSUS STATEMENT

Diagnosis and Management of Work-Related Asthma

American College of Chest Physicians Consensus Statement

Susan M. Tarlo, MBBS, FCCP; John Balmes, MD, FCCP; Ronald Balkissoon, MD; Jeremy Beach, MD; William Beckett, MD, MPH, FCCP; David Bernstein, MD; Paul D. Blanc, MD, FCCP; Stuart M. Brooks, MD; Clayton T. Cowl, MD, MS, FCCP; Feroza Daroowalla, MD, MPH, FCCP; Philip Harber, MD, MPH; Catherine Lemiere, MD, MSc; Gary M. Liss, MD, MS; Karin A. Pacheco, MD, MSPH; Carrie A. Redlich, MD, MPH, FCCP; Brian Rowe, MD, FCCP; and Julia Heitzer, MS

CHEST / 134 / 3 / SEPTEMBER, 2008 SUPPLEMENT 1s-41s
1. “In all individuals with new-onset or worsening asthma, take a history to screen for WRA (OA and WEA). Then confirm the diagnosis of asthma and investigate to determine whether the patient has WRA, performing these tests, whenever possible, prior to advising the patient to change jobs.”
Estimates of Current Asthma Attributable to Work by Selected Definitions, Adults (≥18 Years) with Current Asthma: MI, MN, & OR

1. Yes to at least one of questions 1, 2, 3, or 4
2. Yes to at least one of questions 5 or 6
3. Yes to at least one of the 6 questions

(Lutzer et al., J Asthma 2010)
For Adults with Lifetime Asthma who Report Asthma was Caused/Aggravated by Any Job, the Proportion who Discussed with a Health Professional that Their Asthma was Work-Related: MI, MN, & OR

(Lutzer et al., J Asthma 2010)
Prevalence of Having Nighttime Awakenings (30 days) by Work-Relatedness, Adults ($\geq$18 Years) with Current Asthma: MI, MN, & OR

(Lutzer et al., J Asthma 2010) *p<0.001

**Yes to at least one of the 6 questions
Prevalence of ≥1 Asthma ED/UC Visit (1 year) by Work-Relatedness, Adults (≥18 Years) with Current Asthma: MI, MN, & OR

<table>
<thead>
<tr>
<th>Region</th>
<th>WRA**</th>
<th>Non-WRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>19.4</td>
<td>12.4</td>
</tr>
<tr>
<td>MN</td>
<td>14.7</td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td>11</td>
<td>9</td>
</tr>
</tbody>
</table>

* p<0.0001
** Yes to at least one of the 6 questions
§ Data suppressed due to estimate stability.
ED=Emergency Department; UC=Urgent Care

(Lutzer et al., J Asthma 2010)
Work-Related Asthma Death

- 12/05 - collapsed at work at an adhesive manufacturer
- CPR immediately, EMS 5 minutes later
- Never regained consciousness
- Died 6 days later in hospital

- Autopsy
  - Anoxic encephalopathy
  - Agonal myocardial infarction
  - Lung: “bronchial basement thickening and bronchiolar goblet cell metaplasia with hyperplasia”
  - No evidence non-agonal myocardial infarction or pulmonary emboli
Work-Related Asthma Death

- 50 year old white male
- Smoker since age 16
- No personal or family hx of allergies
- Began working 12/01
- Company makes adhesives from isocyanates and epoxies
- Small facility of large company – 21 production workers
- Per next-of-kin and fiancée – symptoms associated with work – no symptoms prior
- Normal spirometry at time of hire
- Symptomatic 8 months after hire - Urgent care 7/02
- No air trapping and normal diffusing capacity - 9/05
- Compliant patient – 18 medical visits, took meds
Primary Care Doctor

05/03  “asthma, increase Advair”
07/03  “poorly controlled asthma”, increase Advair dose
09/03  “asthma about the same”
11/03  “He notices chemicals at work seem to trigger his asthma. He does wear a respirator and had talked to the occupational health doctor at the job site. They are monitoring his breathing. He doesn’t seem to have trouble outside the office.”
09/04  “was exposed to chemical at work again”
11/04  “exposed isocyanate”
08/05  “trouble with dyspnea from bronchospasm from occupational exposure to lung irritants. This has been going on for some time. He has been on prednisone, averaging one taper per month. It seems that this is not the best route to go long term. He is considering leaving his work but if he leaves voluntarily on his own he loses his severance pay, so he is wondering if there is any way medical reason for leaving his job might help him to retain his severance. I recommend that we have him see a pulmonologist for further evaluation at this point.”
2. “In all individuals with suspected WRA, obtain a history of job duties, exposures, industry, use of protective devices/equipment, and the presence of respiratory disease in coworkers, and consult material safety data sheets (MSDSs), which list many recognized hazardous agents. Document the onset and timing of symptoms, medication use, and lung function, and their temporal relationship to periods at and away from work.”
Causes of Occupational Asthma

ANIMAL
Animal hair, epidermal cells, insects, mold, dander, bacterial and protein dusts
  Animal Handlers
  Entomologists
  Antibiotic Workers
  Detergent Enzyme Manufacturers

VEGETABLE
Woods, cotton, flax, hemp, grain, flour, maiko, mold, castor, and green coffee beans, garlic
  Cotton Mill Workers
  Wood Workers
  Bakers
  Grain Elevator Operators

CHEMICALS ("Micromolecular" chemicals)
chloromine, ethylenediamine, formaldehyde, chromium, platinum, gum arabic, anhydrides, isocyanates
  Chemical Workers
  Platinum Refiners
  Epoxy Resin Workers
  Polyurethane Foam Manufacturers

Examples of Known Allergens in Health Care Setting

- Vegetable
  - **Latex**
  - Psyllium
- Chemicals
  - Glutaraldehyde
  - Formaldehyde
  - Subtilisins (enzymatic cleaners)
  - Cleaning agents
    - Quaternary ammonium compounds
    - Diethanolamine
  - Isocyanates
  - Methylacrylates
  - Antibiotics
  - Aerosolized medications
    - Pentamidine
    - Ribavirin
  - Radiograph developing compounds
# Material Safety Data Sheet

## 1. PRODUCT IDENTIFICATION

<table>
<thead>
<tr>
<th>PRODUCT NAME</th>
<th>INSTANT-LOK (R)</th>
</tr>
</thead>
</table>

## 2. HAZARDOUS INGREDIENTS

<table>
<thead>
<tr>
<th>INGREDIENT NAME</th>
<th>CAS NUMBER</th>
<th>PERCENTAGE</th>
<th>EXPOSURE LIMITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARAFFIN WAX</td>
<td>8002-74-2</td>
<td>&gt;1</td>
<td>OSHA 2 mg/m3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ACGIH 2 mg/m3</td>
</tr>
</tbody>
</table>

## 3. PHYSICAL DATA

<table>
<thead>
<tr>
<th>EXPOSURE LIMITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>STEL 6 mg/m3</td>
</tr>
<tr>
<td>CEILING none</td>
</tr>
</tbody>
</table>
Mr. Clean Multi-Surfaces Antibacterial Spray

Active Ingredients:
- n-Alkyl (C₈-60%, C₉-30%, C₁₀-5%, C₁₁-5%) Dimethyl/ Benzyl Ammonium Chloride
- n-Alkyl (C₈-60%, C₉-32%) Dimethyl Ethylbenzyl Ammonium Chloride
- Other Ingredients

Total: 80.90%

1 L (1 QT) 946 mL

KEEP OUT OF REACH OF CHILDREN

Warning: See back panel for Emergency Statements and First Aid

©2009 Mr. Clean. All Rights Reserved.
Clean as a Whistle, But What about that Wheeze?

American Journal Respiratory Critical Care Medicine 2007; 176: 731–734
## Dose–Response Relationships Between the Use of Household Cleaning Sprays and the Incidence of Asthma (n = 3,484)

<table>
<thead>
<tr>
<th>Category</th>
<th>Frequency, n (%)</th>
<th>Current Asthma RR (95% CI)</th>
<th>Current Wheeze RR (95% CI)</th>
<th>Physician-Diagnosed Asthma HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of sprays &lt; 1 d/wk</td>
<td>2,016 (57.9)</td>
<td>1.00 (referent)</td>
<td>1.00 (referent)</td>
<td>1.00 (referent)</td>
</tr>
<tr>
<td>Use of sprays 1-3 d/wk</td>
<td>933 (26.8)</td>
<td>1.36 (0.99-1.89)</td>
<td>1.55 (1.17-2.06)</td>
<td>0.93 (0.51-1.67)</td>
</tr>
<tr>
<td>Use of sprays 4-7 d/wk</td>
<td>535 (15.4)</td>
<td>1.75 (1.21-2.54)*</td>
<td>1.08 (0.73-1.59)</td>
<td>2.11 (1.15-3.89)*</td>
</tr>
<tr>
<td>One type of spray used &gt; 1 d/wk</td>
<td>913 (26.2)</td>
<td>1.37 (0.99-1.90)</td>
<td>1.25 (0.92-1.69)</td>
<td>0.97 (0.53-1.77)</td>
</tr>
<tr>
<td>Two types of sprays used &gt; 1 d/wk</td>
<td>355 (10.2)</td>
<td>1.45 (0.92-2.27)</td>
<td>1.63 (1.10-2.41)</td>
<td>1.47 (0.70-3.06)</td>
</tr>
<tr>
<td>Three or more types of sprays used &gt; 1 d/wk</td>
<td>200 (5.7)</td>
<td>2.40 (1.47-3.91)*</td>
<td>1.80 (1.11-2.94)*</td>
<td>2.96 (1.33-6.56)*</td>
</tr>
</tbody>
</table>

*linear trend <p.05

(Adapted, Zock et al, 2007)
3. “In individuals who have asthma not caused by work but that subsequently worsens while working, consider the diagnosis of WEA, which is usually based on changes in symptoms, medication use, and/or lung function temporally related to work.”
### Summary Data from Cleaning Diaries - 12 Weeks

<table>
<thead>
<tr>
<th></th>
<th>Asthma (n=25)</th>
<th>Non-Asthma (18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg. Cleaning Hrs/Day</td>
<td>1.5</td>
<td>1.8</td>
</tr>
<tr>
<td>Avg. AM-PM Peak Flow Diff.</td>
<td>-12.2</td>
<td>-11.3</td>
</tr>
<tr>
<td>Avg. Upper Resp. Symptoms Pre/Post</td>
<td>2.7</td>
<td>2.1</td>
</tr>
<tr>
<td>Avg. Lower Resp. Symptoms Pre/Post</td>
<td>1.2*</td>
<td>0.3</td>
</tr>
</tbody>
</table>

*P < 0.001

(Adapted from Bernstein et al., 2009)
4. “In individuals with suspected sensitizer-induced OA, in addition to carefully documenting the occupational history, perform additional objective tests when feasible (eg, serial peak flow recordings, serial methacholine challenges, immunologic assessments, induced sputum testing, and SICs) to improve the diagnostic probability.”
8. “In individuals with suspected sensitizer-induced OA, conducting an SIC (where available) is suggested when the diagnosis or causative agent remains equivocal; however, this testing should only be performed in specialized facilities, with medical supervision throughout the testing.”
Change in FEV₁ After Challenge to Control Lactose, Fresh Sugar Beet Pulp and Moldy Sugar Beets Pulp

- Lactose
- Fresh Sugar Beet Pulp
- Moldy Sugar Beet Pulp

17% Drop
23% Drop

Baseline, Exp #1, Exp #2, Exp #3, Exp #4, 20 min, 30 min, 40 min, 50 min, 1 hr, 2 hr, 3 hr, 4 hr, 5 hr, 6 hr, 7 hr, 8 hr, 24 hr

Liters
5. “In individuals with suspected WRA who are currently working at the job in question, record serial measurements of peak flow as part of the diagnostic evaluation and ask the patient to record these optimally a minimum of four times daily, for at least 2 weeks at work and 2 weeks off work. “
Peak Flow Monitoring

Day

4        16          11          6          7             8         4          11        12        4            3         5           7         4          1

% Variation

4      16      11      6      7      8      4      11      12      4      3      5      7      4      1
6. “In individuals with suspected sensitizer-induced OA, working at the job in question, perform a methacholine challenge test or obtain comparable measurements of nonspecific airway responsiveness during a working period, and repeat it during a period (optimally, at least 2 weeks) away from the work exposure to identify work-related changes.”
Dose of Methacholine Needed to Induce 20% Decrease in FEV1
7. “In individuals with suspected sensitizer-induced OA, perform immunologic tests (skin prick testing or *in vitro* specific IgE assays) to identify sensitization to specific work allergens when these tests are technically reliable and available. “
Chemicals For Which There Are Commercially Available Serum RASTs

Chemical
Isocyanates
  TDI – Toluene Diisocyanate
  MDI – Diphenylmethane Diisocyanate
  HDI – Hexamethylene Diisocyanate
Formaldehyde
Phthalic Anhydride
Latex Rubber
Compatible clinical history and exposure to possible causal agents

Skin testing and/or specific IgE assessment (if possible)

Assessment of bronchial responsiveness to pharmacologic agents

- Normal
  - Subject still at work
  - (Laboratory challenges with the suspected occupational agent)*
    - Positive
      - Consider return to work
      - Workplace (or laboratory*) challenges with the suspected occupational agent, peak expiratory flow monitoring, or both
        - Positive
          - Clinical judgement
        - Negative
          - No
            - (Not possible or not clinically advisable)
    - Negative
      - No

- Increased
  - Subject no longer at work
    - Review previous breathing test results in relationship to work
      - No
        - (Not possible or not clinically advisable)
      - Yes
        - Occupational asthma
        - Nonoccupational asthma
Sensitivity and Specificity of Diagnostic Tests For Work-Related Asthma

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical History</td>
<td>94%</td>
<td>33-45%</td>
</tr>
<tr>
<td>Pre-Post Work Change in FEV$_1$ (5-10%)</td>
<td>22-85%</td>
<td>56-89%</td>
</tr>
<tr>
<td>Serum IgE Tests</td>
<td>17-72%* (90%)**</td>
<td>60-85%</td>
</tr>
<tr>
<td>Peak Flow (q2h)</td>
<td>73%</td>
<td>74-100%</td>
</tr>
<tr>
<td>Serial Methacholine</td>
<td>62-67%</td>
<td>54-78%</td>
</tr>
</tbody>
</table>

The range of percentages for the sensitivity and specificity reflect the results from different studies.

*Low molecular weight (chemical)
**High molecular weight (animal, plant)
9.“For all individuals with WRA, attempt better control of exposures. **Remove patients with sensitizer-induced OA from further exposure to the causative agent** in addition to providing other asthma management. “
Severity of Asthma Symptoms by Duration of Exposure to Allergenic Substance
Duration of Exposure and Symptoms of 43 Subjects Who Moved Away from Exposure to TDI After Diagnosis, according to Their Outcome at the Time of Follow-up Examination

<table>
<thead>
<tr>
<th></th>
<th>Recovered Subjects (Group 1, n=12)</th>
<th>Improved Subjects (Group 11, n=10)</th>
<th>Non-improved Subjects (Group 11, n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of exposure to TDI (y)</td>
<td>6.3*</td>
<td>10.0</td>
<td>15.9</td>
</tr>
<tr>
<td>Duration of symptoms before diagnosis (y)</td>
<td>1.6**</td>
<td>2.8</td>
<td>5.4</td>
</tr>
</tbody>
</table>

(Adapted from Pisati et al BJIM, 1993;50:60)
10.“In individuals with irritant-induced asthma or WEA, the panel advises optimizing asthma treatment and reducing the exposure to relevant workplace triggers. If not successful, change to a workplace with fewer triggers is suggested in order to control asthma. “
12. “An individual diagnosis of OA represents a potential sentinel health event:

- Evaluate the workplace to identify and prevent other cases of OA in the same setting; and

- For work environments with potential exposure to sensitizers, the Panel advises secondary preventive measures including medical surveillance using tools such as questionnaires, spirometry, and, where available, immunologic tests.”
Symptoms Consistent with Work-Related Asthma or Report on OSHA Log in 487 Companies, Michigan, 1988-2005

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Symptoms of Daily or Weekly S&amp;B, Wheezing or Chest Tightness</th>
<th>Injury Illness Log with Asthma or Asthma-Like Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fellow Workers</td>
<td>8,683</td>
<td>1,438 (17%)</td>
<td>558*</td>
</tr>
<tr>
<td>Companies</td>
<td>487</td>
<td>342 (70%)</td>
<td>119 (24%)</td>
</tr>
</tbody>
</table>

*8 workers among 1,438 on Injury and Illness Log.
11. “For workers who are potentially exposed to sensitizers or uncontrolled levels of irritants, the panel advises primary prevention through the control of exposures (eg, elimination, substitution, process modification, respirator use, and engineering control). “
Summary

- WRA is Common (15-50%)
- Health Care Providers Not discussing with their Patients (≤ 25%)
- Consequences of Not Considering or Delay in Considering
  - Death
  - Increased Morbidity
  - Missed Opportunity for Primary Prevention