Diagnosing Work-Related Asthma

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LEARNING OBJECTIVES:

1. Differentiate the types of work-related asthma: work-aggravated asthma, occupational asthma with latency and occupational asthma without latency.

2. Identify common agents associated with new-onset occupational asthma.

3. Recognize symptom patterns suggestive of work-related asthma.

4. Utilize appropriate diagnostic tests for the diagnosis of asthma and its relationship to work.

INTRODUCTION:

Work-related asthma is the most commonly reported occupational lung disease in the United States {Petsonk, 2002}. Occupational exposures can trigger asthma exacerbations in asthmatic workers or induce asthma in a previously healthy worker. Approximately 7.5% of all US adults have a diagnosis of asthma {CDC, 2002}. In the US, there are an estimated 14.6 million work absence days due to asthma annually {Mannino et. al., 2002}. Of adults with incident asthma, an estimated 15% is attributable to workplace exposures {Blanc, 1999}.

Work-related asthma is often under recognized and misdiagnosed {Rosenman, 1997}. Present practice often lacks the rigorous objective medical testing necessary to diagnose asthma and to document its relationship to the workplace {Rosenman, 1997}. Medical history and physical exam lack both the sensitivity and specificity of diagnostic tests for occupational asthma {Malo, 1991}, necessitating the use of objective testing for diagnosis. Delayed diagnosis can lead to a worsened prognosis {Paggiaro, 1994}. Improvements in both diagnosis and management benefits the worker and employer such that years of productive work are not lost and any potential medical, legal or compensation issues are clarified.

This continuing medical education exercise will provide an overview of work-related asthma with an emphasis on the use of objective tests for the diagnosis of asthma in the workplace. The reader is referred to materials advising on the work-up, evaluation and management of non-occupational asthma {NIH, 1997}, occupational respiratory diseases {Beckett, 2000} and more extensive discussions of workplace asthma {Bernstein, 1999; Chan-Yeung, 1995; Chan-Yeung and Malo, 1995}.

DEFINITIONS:

Work-related asthma can be divided into two general groupings: Occupational asthma (OA) and work aggravated asthma (WAA). Occupational asthma is further subdivided into OA with latency and OA without latency. OA without latency is also termed Reactive Airways Dysfunction Syndrome or ‘irritant-induced asthma.’
Work-related Asthma

1. Work aggravated asthma
2. Occupational asthma
   a. Occupational asthma with latency
   b. Occupational asthma without latency
   
   Also known as Reactive Airways Dysfunction Syndrome (RADS) or irritant-induced asthma

Work aggravated asthma (WAA) is an asthma exacerbation as a result of a workplace exposure in an individual with a prior history of asthma. If the worker is asymptomatic for a period of time and then experiences a recurrence of symptoms, careful consideration should be given as to whether this represents an aggravation of pre-existing asthma or a new sensitivity to a workplace exposure. Often asthma can 'light up' in the presence of workplace irritant exposures and this may reasonably be considered an increase in bronchial hyperresponsiveness and work-aggravated asthma. An assessment of workplace exposures to chemicals known to sensitize airways is appropriate.

Occupational asthma has been defined by a group of experts as “a disease characterized by variable airflow limitation and/or airway hyperresponsiveness due to causes or conditions attributable to a particular occupational environment and not to stimuli encountered outside of the workplace.” {Bernstein IL, 1999}.

The interval between exposure to an asthma causing agent and the onset of asthma symptoms is referred to as latency. The latency period can be weeks to years and is difficult to predict. Asthma causing agents are subdivided into high molecular weight agents and low molecular weight agents. High molecular weight agents (e.g., wheat flour) sensitize a worker via an IgE mediated process. Atopy is known to increase the risk of OA to high molecular weight agents. Low molecular weight agents (e.g., diisocyanates) often sensitize a worker via interactions with endogenous proteins inducing a physiologic response {Raulf-Heimsoth M, 1998; Wisnewski AV. 2003}. High exposures in the workplace to known sensitizers, can increase the risk of sensitization and the development of occupational asthma {Vedal, 1986}.

OA without a latency period is also termed Reactive Airways Dysfunction Syndrome (RADS) or ‘Irritant-induced Asthma’. Since its recognition in the mid-1980’s, RADS has gained general acceptance in the medical community. Diagnostic criteria {Brooks, 1985} for RADS require the onset of asthma symptoms (cough, wheezing, dyspnea) following a single exposure to a high dose irritant gas, vapor, smoke or fume. Symptoms must occur within 24 hours of the exposure and persist for greater than three months. The individual must not have preceding respiratory complaints and other pulmonary diseases must be excluded. Pulmonary function tests demonstrate reversible airflow obstruction or a test of non-specific bronchial hyperresponsiveness is positive. A variant of irritant induced asthma, associated with exposure to respiratory irritation over time (usually over a period of days to weeks) has been described, but is poorly validated in the medical literature {Tarlo, 2003}.
**Approach to Diagnosis of Occupational Asthma**

**History and Physical:**
A medical history and physical examination, inclusive of an occupational and environmental exposure history, is required for the diagnosis of any adult with new onset asthma. The history and physical should address the following: (1) an initial assessment of asthma, (2) an assessment of the temporal association between symptoms and work, and (3) an assessment of workplace exposures. The National Heart, Lung, and Blood Institute's *Guidelines for the Diagnosis and Management of Asthma* provides an extensive review of the initial assessment and diagnosis of asthma. {NIH, 1997} Key indicators for the consideration of a diagnosis of asthma are provided in Box 1. The clinical symptoms of asthma (cough, wheeze, shortness of breath and chest tightness) will not in themselves distinguish between occupational and non-occupational etiologies.

A complete occupational history will provide suggestive evidence of a workplace association. The assessment should focus on several key areas:
Temporal association of asthma/allergic symptoms to work:

1. What were the circumstances in which asthma symptoms were first associated with work?

   Information regarding the initial diagnosis of asthma and its relationship to the workplace is extremely important. The presentation of an individual with new onset asthma symptoms demands some inquiry about the relationship of symptoms to work. The onset of asthma is often insidious and its relationship to work is often not apparent to the worker. General inquiries by the health care provider will assist in the documentation of the potential association of asthma symptoms to work.

   For a diagnosis of RADS, high dose irritant exposure with the onset of asthma symptoms within 24 hours, and persistence of those symptoms for greater than three months supports the diagnosis.

2. During a workday, do symptoms occur immediately upon entering the workplace, hours after entering the workplace, or after returning home from a workday?

   Three general temporal patterns for OA are described - isolated immediate, isolated late, and dual asthmatic reactions {Bernstein DI, 1999; Pepys, 1975}. The immediate asthmatic responses usually occur within minutes of exposure, with maximal bronchoconstriction over minutes to a few hours. Isolated late asthmatic responses have significant bronchoconstriction typically within 4 - 12 hours. The combination of both immediate and late asthmatic responses is a dual response. Isolated late responses are usually associated with low molecular weight agents (i.e. diisocyanates), whereas both low molecular weight and high molecular weight agents are associated with immediate and dual responses {Pepys, 1975}.

3. Do symptoms improve on weekends or vacations?

   The improvement of asthmatic symptoms on weekends or vacations is typical of occupational asthma. In workers with isocyanate induced asthma, 71% improved over the course of a weekend, and 89% improved over the course of a vacation or work leave of 7 to 10 days {Tarlo, 1997}. Over time, a worker with OA may develop persistent symptoms, losing the temporal association of symptoms to work.

4. Are symptoms of rhinitis or conjunctivitis present?

   Rhinoconjunctivitis is often concurrent with asthma. Inflammatory symptoms of nasal and eye mucosa are consistent with either irritant or allergy-mediated exposures in the workplace. Both low and high molecular weight agents are associated with sensitization of nasal and eye mucosa and are comorbid conditions to work-related asthma {Lombardo, 2000}.
Box 1. KEY INDICATORS FOR CONSIDERING A DIAGNOSIS OF ASTHMA

Consider performing spirometry and other objective tests to assess the presence of asthma, if any of these indicators are present.* These indicators are not diagnostic by themselves, but the presence of multiple key indicators increases the probability of a diagnosis of asthma. Objective assessment of bronchial hyperreactivity with spirometry and bronchodilator testing and/or other objective tests is needed to establish a diagnosis of asthma.

- Wheezing on lung exam—Lack of wheezing and a normal chest examination do not exclude asthma.

- History of any of the following:
  - Cough, worse particularly at night
  - Recurrent wheezing
  - Recurrent difficulty in breathing
  - Recurrent chest tightness

- Symptoms occur or worsen in the presence of:
  - Exercise
  - Viral infection
  - Animals with fur or feathers
  - House-dust mites (in mattresses, pillows, upholstered furniture, carpets)
  - Mold
  - Smoke (tobacco, wood)
  - Pollen
  - Changes in weather
  - Strong emotional expression (laughing or crying hard)
  - airborne chemicals or dusts
  - Menses

- Symptoms occur or worsen at night, awakening the patient.

*Eczema, hay fever, or a family history of asthma or atopic diseases are often associated with asthma, but they are not key indicators.

Modified from NHLBI guidelines (NIH, 1997)
**Workplace Exposure History:**

1. **Obtain employment history, including past and present jobs. Carefully document both job tasks and production processes.**

   Exposure assessment is difficult given the changing employment patterns in society. Most workers have several jobs over the course of their working life, necessitating a relatively careful assessment of present and past exposures that may have contributed to the development of asthma. It is important to have the worker describe specific tasks and exposures, as these may not be reflected in summary job types or titles.

   A systematic approach to documenting the employment history as early as possible during the evaluation is optimal. A sequential history commencing from the worker’s first job through present day employment will provide clues as to similar job tasks and exposures that may have resulted in sensitization or previous asthmatic symptoms. Obtaining key information may require consultation with an occupational medicine physician or an industrial hygienist.

2. **Did symptoms change (improve/deteriorate) with the introduction of a new chemical, new production process, or the institution of administrative and engineering controls?**

   Exposures culminating in OA can occur over several years, months or even weeks, and in the case of RADS minutes to hours. Frequently asthma symptoms occur following a change in a manufacturing process, failures of the workplace ventilation systems, uncontrolled releases or spills and introduction of new chemicals in the workplace. Further refining the exposure history to document the specific work processes or chemical agents responsible for asthma symptoms will facilitate better treatment recommendations, e.g., eliminating exposure to the responsible chemical.

3. **Obtain material safety data sheets from the employer.**

   Exposure to a known cause of asthma in a patient with new asthma is supportive of the diagnosis of occupational asthma. An ever growing number of chemicals are recognized as being associated with work-related asthma. There are currently over 250 asthma causing agents identified in the workplace. Reviews of the medical literature may be necessary for further identification of agents, which may cause asthma. An online database through the Association of Occupational and Environmental Clinics provides a listing of asthma causing agents based on consensus criteria (located at http://www.aoecc.org/aoecode.htm - Asthma-Criteria). An interactive database of occupational asthma causes can be found at http://asmanet.com/asmapro/agents.htm. A table of selected exposures associated with occupational asthma is presented in Table 1 on the following page.
Table 1: Selected Causes of Occupational Asthma and Typical Occupations Related to Exposure

<table>
<thead>
<tr>
<th>Asthma Causing Agent</th>
<th>Occupation of Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Animals</strong></td>
<td></td>
</tr>
<tr>
<td>Animal urine, proteins and other allergens</td>
<td>Animal handlers in laboratories, research scientists</td>
</tr>
<tr>
<td>Grain mite</td>
<td>Farmers, grain-store workers</td>
</tr>
<tr>
<td>Prawns, crabs</td>
<td>Seafood processors</td>
</tr>
<tr>
<td>Egg protein</td>
<td>Egg producers</td>
</tr>
<tr>
<td><strong>Plants</strong></td>
<td></td>
</tr>
<tr>
<td>Grain dust</td>
<td>Grain storage workers</td>
</tr>
<tr>
<td>Flour of wheat, rye soy</td>
<td>Bakers, millers</td>
</tr>
<tr>
<td>Latex</td>
<td>Health-care workers</td>
</tr>
<tr>
<td>Green coffee bean</td>
<td>Coffee roasters</td>
</tr>
<tr>
<td>Henna, Gum acacia</td>
<td>Hairdressers, Printers</td>
</tr>
<tr>
<td><strong>Enzymes</strong></td>
<td></td>
</tr>
<tr>
<td>Derived/Proteases from <em>Bacillus subtilis</em></td>
<td>Detergent industry workers</td>
</tr>
<tr>
<td>Pancreatin, papain, pepsin</td>
<td>Pharmaceutical and food industry workers</td>
</tr>
<tr>
<td>Fungal amylase</td>
<td>Bakers</td>
</tr>
<tr>
<td><strong>Wood dusts or barks</strong></td>
<td></td>
</tr>
<tr>
<td>Western red cedar, iroko, cinnamon, oak, mahogany, African apple, redwood</td>
<td>Sawmill workers, joiners, carpenters</td>
</tr>
<tr>
<td><strong>Chemicals</strong></td>
<td></td>
</tr>
<tr>
<td>Diisocyanates</td>
<td>Polyurethane, plastics, varnish workers, auto painters, packing and shipping workers</td>
</tr>
<tr>
<td>Phthalic/acid anhydride</td>
<td>Plastic, epoxy resins, alkyd resins workers</td>
</tr>
<tr>
<td>Ethylene diamine/complex amines</td>
<td>Photography, shellac workers, painters</td>
</tr>
<tr>
<td>Azodicarbonamide</td>
<td>Plastics, rubber workers</td>
</tr>
<tr>
<td>Reactive dyes</td>
<td>Dyeing, textile workers</td>
</tr>
<tr>
<td>Methyl methacrylate</td>
<td>Health-care workers</td>
</tr>
<tr>
<td>Institutional Cleaning Agents</td>
<td>Janitorial Staff</td>
</tr>
<tr>
<td><strong>Drugs</strong></td>
<td></td>
</tr>
<tr>
<td>Penicillins, psyllium, methylidopa, cimetidine, salbutamol intermediates</td>
<td>Pharmaceutical, health-care workers</td>
</tr>
<tr>
<td><strong>Metals</strong></td>
<td></td>
</tr>
<tr>
<td>Halogenated platinum salts</td>
<td>Platinum-refining workers</td>
</tr>
<tr>
<td>Cobalt</td>
<td>Hard-metal grinders</td>
</tr>
<tr>
<td>Chromium, nickel</td>
<td>Metal-plating workers</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
</tr>
<tr>
<td>Oil mists, metal working fluids</td>
<td>Tool setters, machinists</td>
</tr>
<tr>
<td>Aluminum potroom emissions</td>
<td>Aluminum-refining workers</td>
</tr>
<tr>
<td>Colophony in soft solder flux</td>
<td>Electronics workers</td>
</tr>
</tbody>
</table>

The chemical composition of products is usually documented on the Material Safety Data Sheet (MSDS). Obtaining MSDSs are essential in evaluating potential exposures. OSHA requires an MSDS to list all chemicals within a product of greater than 1% by weight. If information is deemed proprietary, but necessary for the medical evaluation of an injured worker, a physician can request in writing from the manufacturer the chemical constituents of the product (even those present at less than 1%). Regulatory requirements require company disclosure to the treating physician within 15 working days. If the MSDS is not provided, the local OSHA office can assist the physician in obtaining them from the employer. MSDSs are part of the Hazard Communication Standard, and each worker should have access to documentation of the chemicals used in their facility. MSDSs often can be obtained online through use of an internet search engine or at specific sites with catalogs of MSDS sheets (e.g., www.msdsonline.com). The format and inclusion of necessary medical information and potential health effects within an MSDS is sometimes incomplete. An analysis of MSDSs for toluene diisocyanate (a chemical well known to cause or exacerbate asthma) from 30 manufacturers revealed that one-half of all manufacturers did not list asthma as a potential health effect, while only 70% listed allergic or sensitizing reactions as potential health effects {Frazier, 2001}. A workplace site visit is occasionally necessary, particularly when the work processes and exposure control measures are not clear from the history.

4. Are or have co-workers been affected?

Occasionally clusters of work-related asthma occur, necessitating a more comprehensive workplace investigation. Identification of new exposures associated with asthma has occurred in this manner and may lead to epidemiologic investigation. Careful skepticism should be sustained regarding the relationships between asthma in workers who do not perform similar tasks or have different types of chemical exposures.

A Case Presentation – Part I

‘David’ is a 42-year old automobile painter with no previous history of respiratory problems. During the 10 months prior to seeing a health care provider, David had rhinitis followed by episodes of coughing, shortness of breath and chest tightness. David reported that his symptoms occurred toward the end of the workday and resolved over the weekend. Symptoms were more frequently associated with the use of isocyanate-containing paints in his workplace.

David was an ex-cigarette smoker with a five-pack year history. He discontinued smoking with the onset of chest tightness, shortness of breath, and cough without improvement in these symptoms. He denied other known cardiac risk factors, orthopnea and reported his cough to be non-productive. He confirmed no history of seasonal allergy or family history of atopy. He did not have a history of medication or aspirin allergy.

David was an automobile painter for approximately 10 years. Over the years he used many different types of paints, but for the last three years used paints containing diphenylmethane diisocyanate. He used a respirator with supplied air, but was frequently exposed to paint spills. Compliance with respirator use was poor. Previous occupational history included work as a laborer, auto collision repair and sales support at an auto dealership.

Physical exam was un-remarkable. Cardiac and lung sounds were normal. There were no inspiratory or expiratory wheezes, nor a prolonged expiratory phase. Chest X-ray was normal.

Comment: The temporal variation of symptoms in association with work, the absence of pre-existing asthma and the known association of isocyanates as a potent sensitizing agent are suggestive of occupational asthma. Physical exam findings are normal and at the time of exam as is usual between episodes of asthma.
Limitations of History and Physical:

One should approach the diagnosis of work-related asthma with an understanding of its implications to the worker and employer. Suboptimal evaluations may lead to a premature recommendation of worker removal from the workplace or expensive mitigation procedures. The medical, social and economic consequences of treatment, work restrictions or removal from work may be considerable.

Failure to remove a patient from harmful exposure may result in persistent asthma and has been associated with fatal asthma {Ortega, 2002}. Nevertheless, presently most health care providers rely solely on the history and physical for the diagnosis of asthma and its attribution to work despite its inadequacy. Of the cases reported to the Michigan occupational asthma surveillance system, only 66% had pulmonary function testing and only 7% had testing to attribute their asthma to a specific work exposure {Rosenman, 1997}. The relatively low positive predictive value (63%) and negative predictive value (83%) of the clinical history for diagnosis of occupational asthma suggest that every effort should be made for objective testing in the diagnosis of occupational asthma, and before a recommendation for medical removal {Malo, 1991}. This point cannot be overemphasized. The medical and legal components of workers’ compensation often require a diagnosis based on objective tests to attribute the occupational disease to the workplace.

Objective Testing for the Evaluation of Occupational Asthma:

A general diagnostic algorithm for diagnosing asthma is presented in Figure 2.

Spirometry:

Measurements of the forced expiratory volume in one second (FEV₁) and the forced vital capacity (FVC) and the ratio of FEV₁/FVC are referred to as spirometric measurements. The FVC measures the volume of exhaled air from the point of maximal inspiration to the point of maximal expiration. The FEV₁ measures the volume of air exhaled in the first second. Reference values for spirometric measurements are based on height, age, sex, and sometimes race.

An initial assessment of whether a restrictive or obstructive pattern of impairment is present can be determined by spirometric results. When both the FEV₁ and the FEV₁/FVC values are below reference values, obstructive lung disease is considered present. Restrictive lung disease is indicated when the FVC is below reference values and the FEV₁/FVC is normal. Asthma is characterized by reversible airflow obstruction. To document reversibility from a depressed baseline examination, spirometry is performed before and after a dose of a short-acting bronchodilator. Reversibility of airflow obstruction is indicated by a 12% increase in FEV₁, typically with a minimum volume increase of 200 ml. Occasionally in asthma obstruction is present which is not initially reversible; a two-three-week trial of an oral corticosteroid may be necessary to mitigate the inflammatory component of the asthma such that reversibility may be demonstrated {NIH, 1997}. Also, random testing early in the work week may show neither obstruction nor reversibility.

Spirometry measurements are dependent on the patient’s effort. Accepted published criteria for valid spirometry results requires three independent efforts of FVC within 5%
of each other with a smooth curve {American Thoracic Society, 1991}. Utilizing an experienced respiratory technician often produces a high quality result. However, individuals with underlying lung disease are less likely to meet ATS reproducibility criteria. {Eisen, 1984} Patients on a bronchodilator will have a diminished bronchodilator response on spirometry testing; short acting bronchodilators must be withheld for at least 8 hours; long acting bronchodilators for 24 hours if the patient is medically stable.

A normal spirometric result does not exclude a diagnosis of asthma. An asthmatic may have normal FEV₁, while asymptomatic and between asthma episodes. There is little diagnostic value in assessing bronchodilator response when the spirometric values are normal and the patient is asymptomatic. In this circumstance, using a test of non-specific bronchial hyperresponsiveness is appropriate.

**Non-specific bronchial hyperresponsiveness (NSBH):**

Testing for NSBH involves serial measurements of FEV₁ with progressively increasing doses of an inhaled bronchoconstricting agent (i.e., methacholine, histamine). The concentration at which there is a reduction in FEV₁ of greater than 20% is referred to as the PC20. Depending on the specific pulmonary function lab involved, a positive test result for asthma is a PC20 of ≤ 16 mg/ml of methacholine in a person in whom there is a clinical suspicion for asthma. Several conditions may result in a false positive NSBH for asthma including allergic rhinitis, smokers with COPD, and atopy {Cockcroft, 1992; ATS, 2000}. About 30% of patients without asthma but with allergic rhinitis have a methacholine challenge test in the range of 4-16 mg/dl, a relatively high false-positive rate {ATS, 2000}. False negative methacholine challenge tests are less common, although occasionally seen with low molecular weight agents. In a person with a reasonable clinical suspicion of asthma, a PC20 greater than 8 – 25 mg/ml has a negative predictive power of approximately 90% {ATS, 2000}.

Utilizing tests of NSBH in the diagnostic algorithm for occupational asthma is important. A negative test result in a currently symptomatic person reasonably excludes the diagnosis of asthma, and by consequence occupational asthma. A positive test result in the context of recent exposure suggests asthma and the need for further testing to associate the asthma to the workplace. A contraindication to performing a test of NSBH is an FEV₁ ≤ 70% of the reference range. Tests of NSBH should be performed in a medical setting with expertise in such procedures. Workers should be instructed to temporarily discontinue asthma medications prior to NSBH. Recommended intervals for discontinuation for short-acting inhaled bronchodilators are 8 hours, long acting bronchodilators – 24 hours, oral bronchodilators – up to 48 hours, and inhaled anticholinergics for 12 hours prior to testing {ATS, 2000; Asthma in workplace}. Oral medications such as theophylline and histamine antagonists (including cimetidine, ranitidine) should be withheld for 48 hours preceding the test {Johnson, 1999}. Inhaled corticosteroids can decrease bronchial hyperresponsiveness but it is generally not recommended that these be discontinued {ATS, 2000}. Several factors may have short term effects on bronchial hyperresponsiveness including exposure to environmental antigens, occupational sensitizers, respiratory infection, air pollutants and chemical irritants {ATS, 2000}. Referring to medical providers with expertise in clinical areas of asthma and work-related asthma is often reasonable.
A normal test of NSBH can occur if the worker has been removed from the inciting exposure. Increased likelihood of the NSBH returning to normal depends on the dose and duration of exposure, the degree of airway hyperresponsiveness and the degree of airflow obstruction {Chan-Yeung, 1995}.

**Antibody Testing:**
Skin prick testing and/or the presence of serum IgE antibody for known high molecular weight antigens will provide evidence of sensitization to such materials. The presence of the antibody does not confirm asthma, but indicates prior exposure and sensitization to that material and where positive in the appropriate clinical context is supportive of a diagnosis of occupational asthma. The absence of an IgE antibody to a known workplace exposure is useful in ruling out Type I hypersensitivity to the agent, but does not exclude asthma mediated by other immunologic responses.

**Use of Peak Flow Meters:**
Peak expiratory flow readings can assess airflow limitation, and are useful in assessing changes in airflow related to workplace activities. Limitations in peak flow include effort dependence and low test reproducibility requiring appropriate instruction (see below). Supportive evidence of asthma is provided by documenting variability in peak flow readings over the course of the day or after inhaled bronchodilators.

Figure 2: Algorithm for the Diagnosis of Asthma {American Lung Association, 1993}
**Assessment of Dynamic Airflow Changes Related to Workplace Exposures:**

Approaches to attributing workplace exposures to asthma in a worker may involve either a laboratory challenge to a specific asthma causing agent or a challenge to the workplace environment thought to cause symptoms. However, this will not be possible in all workers. The clinician must consider the severity of the worker’s symptomatic response to exposure and guide the diagnostic evaluation accordingly to ensure patient safety. The National Heart, Lung, and Blood Institute's *Guidelines for the Diagnosis and Management of Asthma* recommends referral to an asthma specialist when the “Patient requires confirmation of a history that suggests that an occupational or environmental inhalant or ingested substance is provoking or contributing to asthma.”

**Workplace challenge testing usually comes in three forms:**

- Serial use of a peak flow meter during periods of work and non-work
- Spirometric measurements both pre- and post-workplace exposure (e.g., cross-shift)
- Stop-resume workplace testing with appropriate clinical and spirometric monitoring

Workplace challenge testing through serial peak expiratory flow (PEF) monitoring is commonly used to demonstrate a workplace association to asthma. Serial PEF monitoring is simple, inexpensive and usually acceptable to the worker and employer. The test is performed in the following manner. First, the worker inhales as deeply as possible, and then forming an airtight seal around the peak flow meter, the worker exhales with as much force as possible. The worker is instructed to measure his/her peak expiratory flow every four hours while awake for two weeks while still at work and for two weeks while not at work. A recommended protocol is PEF reading on awaking, at noon, following work and at bedtime. Each measurement should consist of three attempts with a documented value for each attempt. Medications should be used after the PEF measurement. The worker is typically asked to record medication use, time periods of workplace exposures, the types of chemical exposures and asthma symptoms. The worker should be instructed to record only the measurements actually taken. As an alternative to manual recording, computerized peak flow meter can maintain an accurate record. A graph of the maximum peak expiratory flow rate is documented for each set of measurements during the worker’s waking hours.

Peak expiratory flow records can be difficult to interpret. Patients with asthma usually have their lowest PEF in the early morning. The physician looks for a pattern of lower peak flow following workplace exposure. This may be cumulative through the week. The 'diurnal variation' of PEFs, the difference of the maximum peak expiratory flow and the minimum during the course of a day is also used. This difference is expressed as a percentage of the maximum peak expiratory flow rate, termed the 'diurnal variation percentage'. Increased diurnal variation percentages or reductions in the maximum peak expiratory flow rate during work exposures relative to non-work periods is a positive result {Chan-Yeung, 1995}. 

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Figure 3: Serial peak expiratory flow measures from a carpenter on cedar homes. Worker had a four year history of exposure to wood dusts with the onset of asthma symptoms (shortness of breath, chest tightness and wheezing) three years after commencing work. Patient’s typical symptoms occurred in the late afternoon or early evening following days of exposure and resolved in the evening. Use of medications tracked symptoms.

Ability to measure and record peak flow accurately and worker adherence in performing multiple PEF measurements per day is a drawback to serial PEF. Use of a hand-held automated recording PEF meter is optimal for recording collection of PEF measurements and documentation of compliance. In one study, data collected on computerized peak flow devices, in workers not informed of the automated data collection, revealed that only 55% of manually recorded measurements were completely accurate relative to electronic documentation and 23% were complete fabrications {Quirce, 1995}. Data quantity also determines the diagnostic sensitivity and specificity of peak expiratory flow testing {Anees, 2004}. If serial peak expiratory flow testing is performed for a 4-week period, the sensitivity was 81.8% and the specificity was 93.8% for the diagnosis of occupational asthma. There was decreased sensitivity for diagnosis if peak flows are performed for 2 weeks duration (70%), or for only two consecutive workdays (56.7%). While 8 recordings per day was optimal, four measures per day had a sensitivity of 82.4% and a specificity of 87% {Anees, 2004}. It is generally recommended that at least four peak flow readings be performed over the course of the patient’s waking hours.

Often in a patient with occupational asthma PEF rates do not normalize over a two day period of non-exposure. This situation necessitates a more prolonged period of removal from the workplace for diagnostic purposes. Continuation of PEFs for a nine-day period following removal from the workplace may provide an adequate time period for such a diagnostic evaluation {Friedman-Jiménez, 2000}. Airway NSBH can be measured as well during these diagnostic periods of work and non-work, with less bronchial hyperreactivity following a period of non-exposure.
Pulmonary function testing both pre and post-work shift is usually not used in the diagnosis of occupational asthma but can be very helpful if spirometry is available in the workplace. Problems arise if the timing of the post shift spirometry does not match the time course of the airflow limitation induced by the putative workplace exposure. Exposure to an agent which induces a delayed response at the end of the work shift may lead to false negative post-shift spirometry results.

Serial NSBH testing can be helpful in supporting the diagnosis of occupational asthma. Typically a test of NSBH is performed prior to the removal from a workplace. Subsequent removal of the worker with asthma from the workplace exposures and an increase in the PC_{20} is supportive of work-related disease. Cessation of workplace exposures for two weeks or more may be necessary. The absence of an improvement does not exclude the diagnosis of occupational asthma. Serial NSBH is occasionally used for assessment of prognosis following removal from work exposures. Improvement in NSBH following cessation of exposure in some individuals may occur during a period of two years {Johnson, 1999}. Some workers may no longer be in the workplace on initial evaluation, thus not allowing this testing.

A common clinical scenario is the evaluation of a patient who is no longer working in the job associated with his/her symptoms {Friedman-Jiménez, 2000}. In such clinical situations, it is appropriate to refer to a clinician who is considered an asthma specialist, since the assessment may require clinical expertise beyond the scope of the primary care physician {NIH, 1997}. The general approach to such an evaluation is the optimization of the patients’ medical regimen and clinical symptoms. Subsequently, a pulmonary evaluation consisting of NSBH testing, PFTs and serial PEF is performed. If return to the job of exposure is feasible and there are no medical contraindications, a diagnostic trial of return to work is attempted. Following return to the workplace, clinical symptoms, medication use, PEF rates, and additional NSBH are monitored for a determination of work-relatedness. If a determination can not be made within a period of two weeks additional periods of monitoring are appropriate.

If return to the job of exposure is not feasible, a determination of work-related must be made based on the available medical and occupational history, clinical symptoms, potential immunologic testing, and NSBH.

A Case Presentation – Part II

As the management of occupational asthma involves eliminating ongoing exposure, potentially removing an individual from the workplace, objective testing is essential.

David’s spirometry was normal with no reduction of FEV1 or a decreased FEV1/FVC. Methacholine challenge precipitated a 23% reduction in FEV1 at 2.5 mg/ml. Workplace challenge testing using a peak flow meter every 4 hours while at work and on weekends was performed. A greater than 20% reduction in peak flow rates occurred on days that David was exposed to isocyanates.

David was removed from work due to a diagnosis of occupational asthma. He is presently employed outside of the auto painting industry.

Comment: The normal spirometry led to a test of non-specific bronchial hyperresponsiveness, which was positive. The 20% diurnal variation in peak flow related to workplace exposure, which was absent when not exposed, was considered a positive workplace challenge test. Even negligible exposures to isocyanates in workers sensitized to them are associated with progression of respiratory disease. Use of respiratory protection devices did not afford complete protection.
Specific Inhalational Challenge:

While this is the 'gold standard' for objectively diagnosing occupational asthma, its availability in the US and Canada is restricted to only a few select academic institutions {Ortega, 2002}. Inhalational challenges should be performed in a specialized hospital center with trained personnel to provide workers with significant periods of close observation and potential resuscitation if respiratory arrest occurs. Additionally, appropriate engineering and administrative controls must be in place to mitigate the occupational exposures of laboratory personnel conducting the tests. Often in the course of a clinical evaluation of a worker, multiple asthma causing agents are considered. Efforts to restrict the specific inhalational challenge to one agent may not be reasonable in these circumstances, and may result in reduced test sensitivity. It may be more appropriate to do testing directed towards a workplace challenge, such that the response to multiple exposures can be assessed.

Management of Work-Related Asthma:

Asthma associated with sensitizers often requires complete cessation of the exposure, and counseling regarding leaving the work environment. A worker’s prognosis improves with early recognition of the disease and cessation of the offending exposure {Paggiaro, 1994}. Attempting to transfer the worker to a work environment without the sensitizer present is optimal. If an appropriate evaluation has been performed for the diagnosis of work-related asthma, one can have reasonable confidence in recommending removal from ongoing exposure. These patients may need vocational training to learn new skills.

When a diagnosis of occupational asthma is made it is important to notify the employer and relevant health authorities. In some states, occupational asthma is a reportable disease to the state health department {Freund, 1989}. For example, Washington State mandated reporting of occupational asthma by physicians and hospitals in 2001 – see (http://www.lni.wa.gov/Safety/Research/OccHealth/Asthma/ReportAsthma/default.asp)

If an ongoing serious health hazard is believed to exist, the physician may need to alert the regional or state office of the Occupational Safety and Health Administration.

Control of workplace exposures is the primary means of management of work aggravated asthma and RADS. Mitigation of exposures in the workplace can occur by institution of engineering, administrative and personal control measures. Engineering controls eliminate exposures by substituting non-irritant chemicals for irritant chemicals or designing work processes such that exposures do not occur the workplace, e.g. enclosing machinery. Administrative controls mitigate exposures by changing work patterns such that the asthmatic individual has significantly less exposure. Personal control measures such as respirators are the last line of defense and often the least effective in mitigating exposures. Consultation with a professional industrial hygienist is appropriate. The medical management of the patient does not significantly differ from that of a non-occupational asthmatic {NIH, 1997}.

In conclusion, the appropriate evaluation of a worker with occupational asthma is essential for appropriate diagnosis and management. Incorporating objective testing for attribution of the asthma to workplace exposures will benefit both the worker and employer, by providing the appropriate medical management of the worker. Diagnostic testing for occupational asthma requires familiarity with the testing procedures and their proper application.
REFERENCES:


1. Which occupational asthma causing agent is not associated with the occupation of exposure?

   A. Methyl methacrylate and dentists  
   B. Diisocyanates and auto body painters  
   C. Psyllium and health care workers  
   D. Phthalic anhydride and printers

2. A previously healthy 35 year old man who works in a winery presents with burning eyes, nose and throat, chest tightness and cough. He developed symptoms within minutes of a chemical spill of sulfur dioxide used to disinfect wine barrels. His symptoms progressed necessitating an ER visit at a local community hospital. Which statement is not true?

   A. He has occupational asthma without latency or ‘irritant induced asthma’.  
   B. He may develop ARDS, bronchiolitis obliterans or permanent obstructive disease.  
   C. Diagnostic evaluation requires a workplace challenge.  
   D. Sulfur dioxide exposures typically induces acute clinical manifestations within minutes whereas other chemical exposures (e.g., phosgene) can take hours.

3. Which of the statements about work-related asthma is not true?

   A. The population attributable risk of occupational asthma is around 15%.  
   B. The worker with RADS must be permanently removed from the job of exposure.  
   C. In a person with a reasonable clinical suspicion of asthma, a PC20 greater than 8 – 25 mg/ml has a negative predictive probability of approximately 90%.  
   D. Referral to an asthma specialist is appropriate in stop-resume workplace testing.

4. A 35 year-old previously healthy male presents to you with cough, shortness of breath, and chest tightness which is intermittent and temporally associated with his work as an electronics worker. What are appropriate components of an initial evaluation of this worker?

   A. Use of a peak flow meter for the diagnosis of asthma.  
   B. Remove the worker from his/her job.  
   C. Send the worker to an asthma specialist.  
   D. Conduct a complete history and physical with special attention to the occupational and environmental history, including collecting Material Safety Data Sheets.

Answers: (1) d, (2) c, (3) b, (4) d