The many facets of occupational asthma

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■ Occupational asthma is an all-encompassing term that describes asthma derived from, worsened by, or encountered in an occupational setting. The diagnosis can be elusive and is easily confused with other disorders. Nevertheless, clarity of the diagnosis is essential for legal purposes. To best serve the patient, it is important to be familiar with the legal distinctions as well as proper medical management techniques.

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OCCUPATIONAL ASTHMA is a multifaceted abnormality whose variable presentations, etiologies, and diagnostic measures can cause problems in clinical, occupational, and litigious medicine. Although asthma has been defined in various ways,[1] the preferred definition is a disorder characterized by an increased airway response to irritants.

AIRWAY RESPONSES

At the bronchial level, there are three major gross airway responses to irritants: airway closure, cough, and mucus production. Upper airway responses include glottal closure, sneezing, and edema of the nasal passages. To be sure, these are simplistic explanations of complex interactions involving irritant recognition, local chemical release by various cells, responses to these chemicals, and neural reflex arcs. However, as simplistic expressions of irritant responses, they highlight the basis of the definition.

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Theoretically, these three responses—airway closure, cough, and mucus production—serve as protective mechanisms by either limiting irritant entry or promoting irritant exit.

It has been suggested that most physiologic responses can be described by a bell-shaped curve. Principles such as median response and standard deviations are familiar to most physicians. The bronchial responses to irritants fit these principles nicely. Airway closure in response to bronchial irritants, for example, forms a bell-shaped curve (or, according to some, a skewed curve.[2]) Individuals with a bronchospastic response one standard deviation or greater than normal can be defined as having asthma. Thus, 8% of the population, by definition, has asthma. This correlates well with published epidemiologic results[2,3] (*Figure 1*).

To state that asthma is merely an exaggerated normal response skirts the issue since, for a response to occur, there must be a stimulus. Evaluation of asthmatic symptoms must take into account these two elements of biological response: the stimulus (including its nature and its strength) and the individual's response, defined by his position on the curve (*Figure 1*). With this background, we can address the problem of asthmatic symptoms more directly. For example, if an individual has a greater than normal response to an

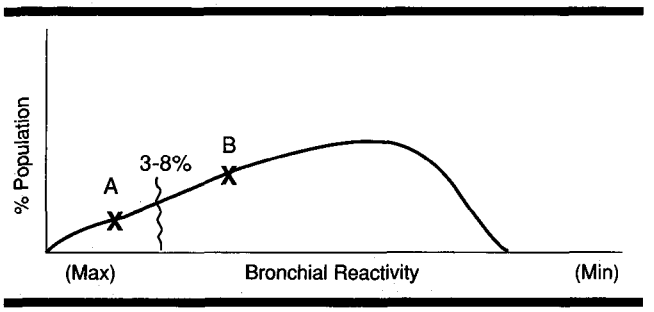

FIGURE 1. Bell-shaped curve demonstrating theoretical responses to bronchoconstrictors. Individual A is part of the 8% of the population that has asthma; his response to inhaled irritants (or methacholine, acetylcholine, histamine, or prostaglandin D, for example,) is greater than expected for the normal individual. Most physicians would expect this individual to display asthmatic symptoms, would test for and diagnose asthma, and would prescribe medication. Individual B does not have asthma by conventional testing but has an exaggerated response when the strength of the stimulus is increased.

inhaled irritant (eg, individual A in *Figure 1*) then he clearly has asthma. Another individual (eg, individual B in *Figure 1* may not have asthma by conventional testing, but would have an exaggerated response to a strong stimulus. The literature on occupational asthma only infrequently distinguishes between individual circumstances and the level of irritants as the cause of asthmatic symptoms, so it is difficult to evaluate disease prevalence.

ETIOLOGY

More than 200 chemicals have been implicated in occupational asthma.[4] Analysis indicates that these chemicals either cause asthma de novo in a previously healthy, nonasthmatic person, or they act as highly specific stimuli in previously diagnosed asthmatic individuals. The latter situation may seem clinically unimportant, but it has therapeutic and legal implications. For example, if a patient with prior atopic asthma becomes a baker and an immediate immunoglobulin E (IgE)-mediated hypersensitivity reaction develops to either the flour or the enzymatic ingredients, asthmatic symptoms will ensue. Proper diagnosis with identification of the specific etiology is important. Therapy might employ desensitization or avoidance of the allergen and successful litigation may require a demonstration of the cause-effect relationship.

Occupational asthma has been defined as "a disorder where there is generalized obstruction of the airways, usually reversible, and caused by the inhalation of substances or materials which the worker-manufacturer uses directly or [which are] incidentally present at the worksite."[5]

TABLE 1
LOW MOLECULAR-WEIGHT COMPOUNDS ASSOCIATED WITH OCCUPATIONAL ASTHMA

Anhydrides
Phthalic anhydride
Trimellitic anhydride
Hexahydrophthalic anhydride
Tetrachlorophthalic anhydride
Diisocyanates
Toluene diisocyanate
Diphenylmethane diisocyanate
Hexamethylene diisocyanate
Naphthalene diisocyanate
Metals
Platinum salts
Nickel
Chromium
Potassium chromate and dichromate
Vanadium
Wood dusts
Red cedar
Redwood
Oak
Mahogany
Mulberry
Drugs
Penicillins
Tetracyclines
Alpha-methyldopa
Psyllium
Fluxes
Amino ethanolamine
Colophony
Stainless steel

This definition does not address the issue of symptoms caused by an excessive load of inhaled irritants. Typically, asthmatic reactions associated with the workplace are categorized as reactions to low molecular-weight compounds, high molecular-weight compounds, or inhalation of toxins.

Low molecular-weight compounds are usually inorganic chemicals with a molecular weight below 1,000 daltons (*Table 1*), and the prevalence of asthmatic reactions to these chemicals is low. When a reaction does occur, a history of atopy is uncommon, but IgE antibody production may occur,[6] as well as peripheral eosinophilia and bronchoalveolar lavage fluid eosinophilia.[4] The presence of serum IgG antibodies has also been demonstrated in this form of occupational asthma.[6]

High molecular-weight compounds (*Table 2*) are often organic materials. Reaction to high molecular-weight compounds is thought to be an IgE-dependent

disorder because atopy is often a predisposing factor, specific IgE antibodies can be demonstrated, and skin tests with the putative agent are often positive.[4]

Asthmatic reactions to high or low molecular-weight compounds must be differentiated from hypersensitivity pneumonitis, a disease that is caused by similar compounds and has some overlapping features. For example, shortness of breath and cough, as well as similar timing of symptom onset, tend to blur these two diagnoses. Hypersensitivity pneumonitis generally presents with a dry cough, rales rather than wheezes, fever, and interstitial infiltrates on the chest radiograph. The disease represents an irritant response occurring at the alveolar-capillary level, as opposed to the bronchial level, and is usually caused by a type III (IgG) response. It can have permanent effects or even be fatal if it is not diagnosed quickly.

Brief, intense exposure to high levels of inhaled irritants can cause asthma. In 1981, Brooks coined the term "reactive airways dysfunction syndrome" (RADS) for this form of asthma.[7] In a later article, he proposed a list of criteria for this diagnosis:[8] (1) prior to exposure the patient either had no respiratory symptoms, or had stable asthma; (2) asthmatic symptoms either develop or are exacerbated after a high level of irritant exposure; (3) the duration of symptoms varies, although in most patients the degree of hyperresponsiveness seems to lessen with time.[8,9]

RADS must be differentiated from toxic inhalation. Toxic inhalation is an alveolar-capillary response to inhaled irritants, whereas RADS is a bronchial response. Toxic inhalations are caused by substances that are caustic to the lower airways, such as chlorine gas and sulfur dioxide. Depending on the nature of the inhaled substance, the concentration, and the duration of exposure, toxic inhalation can cause respiratory distress, noncardiogenic pulmonary edema, and death. RADS and toxic inhalation share certain manifestations; for example, hypoxemia often immediately follows RADS exposure[8,9] and varying durations of airway obstruction may be seen following toxic exposure.[10-12] This overlap is to be expected because the chemicals involved in both diseases are low molecular-weight gases that eventually travel to the same anatomic areas.

DIAGNOSIS

Although occupational asthma is diagnosed by clinical and laboratory evaluation, these findings deviate from the typical picture of asthma, making diagnosis challenging and difficult.

TABLE 2
HIGH MOLECULAR-WEIGHT COMPOUNDS ASSOCIATED WITH OCCUPATIONAL ASTHMA

Animal proteins (hair, dander, or excreta)
Mammals
Birds
Insects
Crabs
Plant proteins
Wheat, rye, and soy flour
Coffee and tea
Tobacco leaf
Buckwheat
Vegetable gums
Cotton dusts
Castor beans
Hops
Enzymes
Bacillus subtilis *
Trypsin
Chymotrypsin
Papain
Pectinase

* The proteolytic enzyme subtilisin is derived from strains of *B subtilis*.

The symptoms of occupational asthma and typical asthma are the same—dyspnea, wheezing, cough, and mucus production—but the time of onset differs. Four patterns can be observed with reactions to high and low molecular-weight compounds:[13] (1) an immediate asthmatic reaction that starts within minutes of exposure, is peaks rapidly, and lasts 1 1/2 to 2 hours; (2) a nonimmediate reaction that starts approximately 1 hour after exposure and lasts about 5 hours; (3) a nonimmediate reaction that occurs after several hours, peaks at 5 to 8 hours, and lasts about 1 day; and (4) a nonimmediate reaction that occurs several hours after exposure has ceased, usually during sleep (this pattern may occur nightly without additional exposures). The timing of symptoms with respect to weekends and vacations can also be useful diagnostic information.

Some of the etiologic agents of occupational asthma may be associated with the development of IgE antibodies. If so, skin testing, radioallergosorbent testing (RAST), or enzyme-linked immunosorbent assay (ELISA) will be of some value.

Asthma may be diagnosed in the pulmonary function laboratory by the response in airflow rates, forced vital capacity, or airway resistance to bronchodilators, nonspecific bronchial constrictors such as methacholine and histamine, or specific constrictors. For medical (and often medicolegal) purposes, the response to bronchodilators and nonspecific bronchial constrictors is often satisfactory for diagnosis. These tests are sensitive, but not specific for a particular oc-

cupationally encountered irritant. Furthermore, in many cases of occupational asthma the methacholine challenge test is negative.[14,15] For example, patients who have a "subasthmatic" (or normal) response but who have asthmatic symptoms because of the concentration of inhaled irritants will have negative test results.

A bronchoprovocative test employs a putative causative agent to create diminished airflow rates. Decrements as low as 10% in the forced vital capacity, airflow parameters, or airway resistance are considered diagnostic.[16] Care must be taken with these tests; they are time-consuming, expensive, demanding, and occasionally associated with results that require resuscitative equipment. They often require special equipment and are best left to research or specialized diagnostic centers. The agents used in these tests may produce a nonspecific or irritative effect in some asthmatic individuals.[4]

Serial testing with either an historical record or, preferably, peak flow meters at hourly intervals during the work day and during time off (including evenings, nights, and weekends) is valuable. Expected results are either heightened symptoms or depressed flow rates consistent with any of the above-mentioned patterns of asthmatic responses. Problems that can occur with this diagnostic method include variations in self-recording (such as uneven effort with the peak flow meter), exposure, and treatment.[17,18]

TREATMENT

Treatment consists of either standard asthma medications or avoidance of exposure. Medications useful in the treatment of asthma are well adapted to the patient with occupational asthma. Avoidance measures include better ventilation, use of protective masks, and possibly change in worksite or occupation.

MEDICOLEGAL CONCERNS

Legal concerns over occupational asthma fall into two broad categories: compensation and disability. Compensation is a payment given to a worker who is injured (ie, derives asthma) by the workplace. This takes the form of either a remuneration (usually a cash settlement) or an action under a Workman's Compensation Insurance settlement. The latter is a "no-fault" agreement between the company and the worker to the alleged injury and compensation in the form of benefits, payment of medical expenses, and, possibly, job retraining. The compensation reflects the degree—partial or total—and duration—temporary or permanent—of disability.

Compensation and disability awards both address disability. Although few physicians differentiate between impairment and disability, these are separate issues with distinct legal ramifications. An impairment is a physical or psychological measurement of a disease state that precludes activity associated with good health. Impairments are what we recognize, diagnose, quantitate, and treat. A disability is a medical impairment that is job-specific. For example, a blind person has a significant, easily quantifiable impairment. It may or may not produce a disability. If that individual were a bus driver, he would be 100% disabled. If he were a pianist, he may suffer no disability.

Disability awards must therefore take into account not only the degree of impairment but also the job description. This area may be confusing and, unfortunately, experience is the best way to sort these problems out. Some examples may clarify these points.

Examples: When is compensation justified?

A previously healthy 29-year-old man was exposed to high levels of chlorine gas while employed in a chemical factory. His usual job is supervisory and he spends most of his time in an air-conditioned office. Following his exposure, he had asthmatic symptoms that varied in degree but never ceased. A methacholine challenge test was positive and he became asymptomatic following the use of inhaled sympathomimetics and steroids. One year later his symptoms persist despite therapy. This patient has an impairment but no real disability because his normal occupation does not involve excessive exposure to irritants. A compensation award could be appropriate in his case.

A 22-year-old man with a history of childhood asthma was asymptomatic and taking no medications until 6 months after starting a job in a detergent factory. Symptoms of asthma developed and a methacholine challenge test was positive. A skin test to *Bacillus subtilis* was positive. His symptoms remitted over 3 months while on disability leave. This patient has a work-related injury of a temporary nature and a disability for that occupation. Appropriate compensation is temporary total disability with either job retraining or transfer to a different job at the same plant with no exposures to the agent.

A 34-year-old man with mild to moderate asthma took a job at a steel mill. Despite several job site chan-

ges, he had continuous, severe asthmatic symptoms requiring additional medications and frequent medical absences from the worksite. This patient has a disability and should seek other employment. The issue of compensation in this case is vague.

A 54-year-old man who smokes two packs of cigarettes daily is employed as a general laborer in a foundry, where he is exposed to various dusts, smoke, and inhalants. He complains of dyspnea, wheezing, and a chronic productive cough. His spirometric test results confirm severe dyspnea on exertion. A cardiopulmonary exercise stress test indicates the ability to perform only sedentary occupations due to his breathing disorder. A methacholine challenge test is negative and a bronchodilator test is mildly positive. A chest radiograph shows emphysematous changes but no evidence of pneumoconiosis. This patient is clearly disabled for his occupation but, even though mild asthmatic bronchitis is present, this is not a compensation issue.

Vague definitions

Disability due to occupational asthma is easier to describe medically than legally. To prove a case legally, various diagnostic tests must be used that may not be entirely necessary for a medical diagnosis or treatment decision. Furthermore, the American Medical Association guidelines on disability due to asthma, which had been arbitrary, simplistic, and naive,[19] are now so vague as to be of no value.[20] This problem is compounded when attempting to apply the current guidelines to the issue of occupationally induced asthma.

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