

Update on occupational rhinitis and asthma

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ABSTRACT

The workplace is emerging as an increasingly important venue for the development of rhinitis and asthma. There is no question that allergic diseases of the respiratory tract caused by occupational exposure are on the increase. The clinician's diagnostic index of suspicion must be high so that a diagnosis of occupational rhinitis and/or asthma can be made in a timely fashion. Altering the environment of the workplace or removing the patient from that workplace may spare the patient permanent damage.

(Allergy Asthma Proc 31:437–443, 2010; doi: 10.2500/aap.2010.31.3379)

The workplace is becoming increasingly important to the allergist for a number of reasons. First, occupational allergic diseases are quite common and appear to be on the increase. The incidence of these diseases is undoubtedly underestimated, because of a failure to diagnose and because of a reluctance of the worker during a difficult economy to complain for fear of losing his/her job. Second, a new appreciation of the workplace as an arena for exposure to allergens is increasing. Previously, there was a general feeling that low-molecular weight (MW) substances commonly encountered in the working environment were not of sufficient size to elicit an immunologic response. What we are now realizing is although many of these substances are not immunogenic in and of themselves, they are excellent haptens. Therefore, they can combine with tissue proteins such as human serum albumin in the respiratory tract with the resultant hapten-protein conjugate serving as a potent immunogen. A third reason for the allergist to become increasingly concerned with the patient's workplace is that it gives us an opportunity to practice what we do best, *viz.*, preventive medicine. Allergists have long regarded themselves as much more than symptom treaters. Our unique training equips us to get to the heart of the matter, to recognize substances in the patient's micro- and macroenvironment that are causing problems and then to intervene to the patient's benefit by either altering the environment or by removing the patient.

CLASSIFICATION OF ALLERGIC OCCUPATIONAL DISEASES

Table 1 shows the occupational diseases of special interest to allergists, with examples of each. The skin may be affected by a true allergic contactant or by a primary irritant. The nose also may be affected by a true allergen or by a primary irritant. A number of pulmonary occupational diseases can occur including extrinsic allergic alveolitis or hypersensitivity pneumonitis and fibrotic diseases such as silicosis and asbestosis. Bronchial asthma may be present either on an immunoglobulin E (IgE) allergic basis or on a nonspecific irritative basis. The rest of this discussion will focus on occupational rhinitis (OR) and occupational asthma (OA).

OCCUPATIONAL RHINITIS: DEFINITION

The European Academy of Allergy and Clinical Immunology Task Force on Occupational Rhinitis defines the disease as an inflammatory condition of the nose, which is characterized by intermittent or persistent symptoms (*i.e.*, nasal congestion, sneezing, rhinorrhea, and itching) and/or variable nasal airflow limitation and/or hypersecretion due to causes and conditions attributable to a particular work environment and not to stimuli encountered outside the workplace.¹ They make a distinction between OR and work-exacerbated rhinitis, which is defined as preexisting or concurrent (allergic or nonallergic) rhinitis that is worsened by, but not caused by, workplace exposures; OR can be either IgE mediated or non-IgE mediated and can develop in response to allergens, inhaled irritants, or corrosive gases. OR may have a profound effect on the worker, resulting in performance deficits, reduced productivity, and psychosocial problems. OR often coexists with OA. Although it is commonly accepted that allergic rhinitis may precede asthma,² reports of OR turning into asthma are few. In one report³ from Finland, which examined cases of OR and OA reported to the Finnish Register of Occupational

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Presented at the Eastern Allergy Society Meeting, West Palm Beach, Florida, May 7, 2010

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Table 1 Occupational diseases of interest to allergist

Skin
Allergic contact—Chromium
Primary irritant—Organic solvents
Nose
Allergic—Wheat flour
Irritant—Coal dust
Lung
Hypersensitivity pneumonitis—Moldy hay
Fibrotic disease—Silica
Asthma—Animal protein

Diseases, most of the OA patients were older than those with rhinitis, suggesting that rhinitis precedes asthma. The incidence of OR is not known, but in a survey of laboratory workers with allergic symptoms, 100% of those affected had rhinitis with conjunctivitis, whereas only 71% had asthma.⁴

CAUSES OF OCCUPATIONAL RHINITIS

Bardana has suggested the following classifications for OR⁵:

Annoyance—Occurs in individuals with a heightened olfactory awareness to such substances as perfumes and detergents. The likelihood of developing annoyance reactions is increased by nasal polypsis, sinusitis, tobacco abuse, and overuse of over-the-counter nasal decongestants or illicit drugs.⁶

Irritational—Nonspecific inflammation of the nose that has no immunologic or allergic basis. Exposure to substances, such as cigarette smoke, formalin, and capsaicin, results in the release of substance P, a sensory transmitter that triggers a neurogenic inflammatory response. This type of OR is seen in patients who work in an enclosed environment and who are exposed to materials such as paints, talc, and coal dust.

Corrosive—Corrosive OR results from exposure to a high concentration of irritating and soluble chemical gases, causing sufficient nasal inflammation that the mucosa may break down and ulcerate, similar to a chemical burn. Common culprits include substances with high water solubility and chemical reactivity, such as chlorine, sulfur dioxide, ammonia, and formaldehyde.⁷ Corrosive OR can lead to permanent changes in physiological functions of the nose, such as loss of olfaction. The entity “reactive upper-airways dysfunction syndrome” has been described after a single exposure to strong chemicals and is modeled on reactive airways dysfunction syndrome.⁷

Immunologic—Allergic responses are mediated by IgE, with resultant early and late nasal reactions. High-MW allergens or low-MW allergens bound to proteins can elicit an allergic response. Some causative agents and typical exposures resulting in OR are reviewed in Table 2. Psyllium, a major component of popular bulk laxatives, may cause rhinitis in persons who work in laxative-producing factories or in nurses who dispense the medication.⁸ Guar gum commonly is reported as a cause of OR and OA, especially in Europe. This gelling and thickening agent affects workers in the food industry. Carpet workers may become sensitive to guar gum through its use as a fixator of dye to fiber and as an insulator in rubber cables.⁹

Laboratory workers are commonly affected by OR and OA with >30% of these workers becoming sensitized. The rat is the most commonly implicated animal, and, as stated earlier, rhinitis with conjunctivitis is the most common complaint among these workers.⁴

In one of the earliest reports of sensitivity to western red cedar dust (plicatic acid), approximately one-half of the affected workers had associated rhinitis.¹⁰ In another report, rhinitis caused by exposure to western red cedar preceded the onset of asthma.¹¹

Diisocyanates are highly reactive chemicals that are encountered by foundry workers, polyurethane foam makers, and spray painters. It is the most common class of reagents that cause OA. Diisocyanates may cause a nonspecific irritant rhinitis, and in a small number of workers who have an IgE sensitivity to diisocyanates, allergic rhinitis may result. The risk for OR or OA is related directly to the exposure level; atopy and smoking do not seem to be major risk factors.⁶

In the study of the Finnish Register of Occupational Diseases in which 1244 new cases of OR were reported during 1986–1991, animal dander, flowers, wood dusts, textiles, phthalic acid anhydrides, and storage mites were found to be important causes of OR.³ Furriers, bakers, and livestock breeders had the highest relative risk of OR.

DIAGNOSIS OF OCCUPATIONAL RHINITIS

The following four steps comprise the diagnosis of OR:

1. History and physical examination.
2. Site visit.
3. Skin tests or *in vitro*-specific IgE tests.
4. Nasal challenge.

The association of nasal congestion, sneezing, and increased nasal secretions with exposure to the workplace provides the first clue to the diagnosis. OR may be associated with an isolated late reaction; therefore, symptoms might not appear until several hours after leaving the workplace. Evidence leading to the suspicion of the workplace as a source of OR comes from a

Table 2 Causative agents and typical exposures in occupational rhinitis

Cause	Agent	Exposure
Annoyance	Detergents	Supermarket
	Perfumes	Department store
	Cooking	Kitchen
Irritational	Air pollutants	Outdoor or inner-city workplace
	Cigarette smoke	Any workplace
	Cold air	Meat packer
	Hairspray	Department store
	Talc	Cosmetics industry
Immunologic	Natural guar gum	Carpet worker
	Latex	Nurse
	Psyllium	Nursing home
	Rats	Laboratory researcher
	Synthetic acid anhydride	Epoxy worker
	Platinum	Jeweler
	Toluene diisocyanate	Spray painter

Table 3 Major items included in an occupational medical history

Onset of symptoms at work	History of accidents or spills
Improvement on weekend and vacations	Personal or family history or atopy
Recurrence of symptoms on reexposure	Coexisting symptom: Bronchial,
Exposure to cold air, ozone, pollution, tobacco smoke, animals, and dust	dermatologic, conjunctival, and anosmia
Similar symptoms in coworkers	Smoking history
Duration working at current job	Hobbies
Adequacy of ventilation	Previous employment
Compliance with wearing gloves, masks, and protective clothing	Medication and drugs

comprehensive medical history. The major items elicited from the history are seen in Table 3.

The primary symptom of a late reaction is nasal congestion rather than sneezing, itching, or rhinorrhea. Symptoms usually abate when the patient is away from the workplace on weekends or holidays, but chronic exposure may require several days away from work before the symptoms remit. Physical examination during the time of active rhinitis reveals swollen nasal turbinates and evidence of increased secretions. Nasal findings may be minimal in patients with annoyance causes of OR, whereas corrosive causes reveal ulcerated and hemorrhagic mucosa.

Scheduling a site visit to the workplace is helpful in determining the exact cause of OR. A site visit can provide the clinician with an opportunity to confirm and add to the previously obtained history by observing the patient as he/she performs the work. The site visit is also critical for determining if any changes can be made in the work environment to reduce the patient's ongoing exposure.

In the United States, the Occupational Safety and Health Administration requires employers to keep on-site records detailing the ingredients and possible health effects of materials and substances to which workers are exposed. This information is available in Material Safety Data Sheets, which should be reviewed during the site visit. These sheets can be helpful in establishing a causal agent in OR.

A toxicologist can be called in to sample air quality if there is a question of inadequate ventilation. However, patients may develop OR (especially allergic OR) from exposure to "safe" amounts of agents, as previously mentioned.

If the OR is caused by an IgE mechanism, appropriate skin tests or *in vitro* radioimmunoassay testing may be performed. Skin testing is useful in allergic OR if the disease is caused by animal, dust, latex, or mold exposure. Low-MW substances may need to be conjugated with serum albumin to elicit a response.

Testing for allergen-specific IgE is appropriate if both of the following are true:

- The OR is believed to be caused by an IgE-mediated mechanism (*i.e.*, immunologic OR)
- If there is validated testing extract available for the allergen in question, such as animal danders, dust mite, latex, or mold; unfortunately, approved extracts do not exist for many other occupational allergens.

If a validated extract is not available, then testing with improvised solutions of the suspect allergen is generally not recommended because irritating substances can cause false positive results. In addition, false negative results may occur with low-MW allergens, which may need to be conjugated with serum albumin to elicit a positive response.

Direct nasal challenge is the gold standard for the diagnosis of OR. It can be performed either at the workplace or under controlled circumstances in the office or laboratory. Responses may be quantified either by symptom score or by rhinomanometry, a technique that measures changes in nasal airway resistance. As mentioned previously, these techniques require special equipment and training and are not practical for most community clinicians.

Workplace challenges may be considered in the following settings: (1) no sensitizing agent has been firmly identified at work, (2) multiple potentially sensitizing agents are present at the workplace, or (3) conditions of exposure at work can not be duplicated in the laboratory. During these tests, the worker performs his/her usual tasks and nasal response is gauged before, during, and after a typical shift. Patients act as their own control by comparing workday symptoms to nonworkday symptoms. This may be done several times to ascertain sufficient reproducibility.

There are three common rhinomanometric techniques: anterior, posterior, and acoustic. Of the three techniques, acoustic rhinomanometry is the most practical and least invasive. Sound waves are introduced into the nasal cavity and a computer quantifies the reflected waves.¹²

OCCUPATIONAL RHINITIS: PREVENTION

Screening applicants for jobs in which there is a risk of workplace sensitization has been proposed as a means of preventing OR. In a study of laboratory workers exposed to rats, applicants for employment were screened with a panel of common inhalant allergens to identify atopic individuals.¹³ Of the 41 workers who were initially atopic by history and skin testing, 23% went on to develop OR and 44% went on to develop both asthma and rhinitis. However, a significant number of those workers who developed rat allergies were not initially atopic, and the majority of workers who were initially atopic did not go on to become sensitive to rats. Thus, this did not appear to be

an effective means of identifying those workers who are most likely to develop OR.

A recently published study of 110 laboratory animal workers suggests that a combination of atopy and total IgE level of ≥ 100 IU/mL provides the best preemployment screening parameters to predict which workers will develop occupational allergy. The study estimates that such screening might be able to reduce occupational sensitization by up to 45–50% with $<10\%$ false positive predictions.¹⁴ Although it is possible to isolate potentially atopic workers, using history and skin tests, the social, financial, and legal applications of instituting such screening may be problematic.

A second approach to preventive medicine is to institute environmental control measures, such as providing adequate ventilation. The offending allergen and its source should be recognized. Laboratory workers who become sensitive to rats largely react to rat urinary protein rather than epithelium. It may be possible for the sensitive worker to perform surgery on rats if the cage containing the rats, which usually is soaked with urine, is kept out of the laboratory. Significant improvement can be obtained by placing high-efficiency particulate air filters in areas of the laboratory where rat exposure is high.

A good example of the positive effect of environmental control measures can be seen in the detergent industry. A *Bacillus subtilis* enzyme that was added to household detergents caused a significant amount of upper and lower respiratory allergies in workers. By instituting a number of precautions in the plant, the incidence of occupational respiratory disease was decreased dramatically. These measures included enclosing previously open operations, automating hand operations, supplying space suits with air supply to workers with high exposure, providing disposable gloves and uniforms, providing masks with cartridges and filters to workers with low exposure, monitoring the air (*i.e.*, measuring enzyme concentration in the atmosphere), and performing spot checks on workers. These spot checks consisted of taking a history, physical examination, chest radiographs, pulmonary function testing, skin testing, and serological testing.¹⁵

OCCUPATIONAL RHINITIS: PHARMACOLOGIC MANAGEMENT

Pharmacotherapy of OR is similar to that of other types of rhinitis. Antihistamines are a mainstay of managing allergic and nonallergic rhinitis. When the patient's symptoms are frequent or unpredictable, regular use of an over-the-counter or prescription antihistamine may be necessary. When symptoms are episodic and predictable, prophylactic use of antihistamines before exposure to irritants or allergens generally is sufficient.

The choice of the agent often is based on trial and error, according to frequency of side effects and effi-

cacy. The sedative side effects of conventional antihistamines may be more bothersome than the rhinitis itself, especially when the goal of treatment is to increase alertness and productivity.

The second-generation nonsedating antihistamines are better for treating patients who need to be awake and alert at work. The duration of treatment is variable. Because antihistamines are only palliative, they should be continued until the patient can control symptoms by avoiding exposure to the offending agent. Leukotriene modifiers have been shown to decrease nasal congestion, sneezing, and rhinorrhea, but these agents work best in conjunction with antihistamines or nasal steroids. Topical agents are effective for managing rhinoconjunctivitis. Ophthalmic solutions of antihistamines, decongestants, mast cell stabilizers, and nonsteroidal anti-inflammatory agents provide effective, as-needed prophylaxis or symptomatic treatment of rhinoconjunctivitis. Saline nasal spray is useful for nonallergic rhinitis. The addition of anticholinergic agents, such as ipratropium bromide, benefits patients who have anterior or posterior drainage. Topical glucocorticoid nasal sprays are effective for allergic and nonallergic rhinitis. They often need to be taken on a regular daily schedule but can be effective on an as-needed basis. The same rule applies to antihistamine nasal sprays.

Allergen immunotherapy generally is not recommended for patients with OR. Immunotherapy has no role in the management of rhinitis that is caused by irritative substances, and its value in alleviating allergic OR is limited by the unavailability of occupational antigens.

OCCUPATIONAL RHINITIS: PROGNOSIS

The natural history of OR has not been studied extensively. OR is sometimes described as an early form of occupational respiratory disease that may progress to asthma in some patients who continue to be exposed to the causative agent. However, firm evidence for this progression is lacking, and many patients appear to have stable OR over a period of years. This is in contrast to OA, which usually worsens with continued exposure.

It is best to explain to patients that the effects of continued exposure and the risk of developing OA over time is not fully understood. Patients should be advised to protect themselves as much as possible from ongoing exposure and to consider changing work environments if their symptoms appear to be worsening despite avoidance measures.

OCCUPATIONAL ASTHMA (OA)

OA is the most common occupational respiratory disorder in industrialized countries, estimated to account for

5–15% of asthma cases in adults of working age, especially in those with newly diagnosed asthma.¹⁶ OA should be distinguished from work-exacerbated asthma, which is present in workers with preexisting or concurrent asthma that is triggered by work-related factors such as aeroallergens, irritants, or exercise but not considered to be OA.¹⁶

MECHANISMS OF OCCUPATIONAL ASTHMA

OA can be placed into four categories based on underlying mechanisms. Malo and Chang Yeung have recently thoroughly reviewed agents involved in OA.¹⁷

Irritant-Induced OA

This appears to be caused by a neurogenic reflex resulting from insult to the bronchial epithelium. The drainage that occurs leads to marked inflammation with resultant fibrosis, increased bronchial smooth muscle tone, and mucous hypersecretion. The best example of this is reactive airways dysfunction syndrome.¹⁶ Agents implicated in this entity are ammonia, fire smoke, chlorine gas, and HCl. The onset of symptoms including cough and shortness of breath occurs soon after exposure, usually as a result of an accidental spill. Airway reactivity may persist after recovery from the acute episode along with significant eosinophil and neutrophilic inflammation and airway remodeling.¹⁸

Allergy

There are a number of characteristics that would prompt a clinician to believe that a particular case of OA was allergic or immunologic in nature. These include a latency or sensitization period with asthma appearing after repeated exposure; the presence of OA in only a relatively small proportion of the exposed workers, an increase in sensitivity with time, eliciting of reactions by amounts less than is encountered at the workplace, and evidence of immunologic memory or anamnesis. After removal from the workplace for a period of time, reintroduction results in symptoms in a much shorter time than after the original exposure. Some common causes of allergic OA are shown in Table 4 along with the occupational exposure.

Determinants of OA include both environmental and host factors. The concentration and duration of exposure to the offending substance is quite important in the production of OA. The effect of smoking is variable but this may interact with atopy in sensitization to a higher-MW substance. A background of atopy appears to be a risk factor for sensitization to high-MW substances but the predictive value is low. Most cases of OA begin within 1–2 years of exposure with sensitization to lower-MW substances being shorter than sensitization to high-MW substances.

Table 4 Some causes of IgE-mediated occupational asthma

<i>Bacillus subtilis</i> enzyme	Detergent workers
Trypsin	Plastic workers
Animal dander	Researchers
Grain dust	Farmers
Platinum	Jewelers
Flour	Bakers
Psyllium	Nurses
Papain	Lens makers
Trimellitic anhydride	Spray painters
Latex	Nurses

Inflammatory

A number of low-MW agents may cause OA on a nonallergic basis. One of the most common is toluene diisocyanate, which is encountered in automobile assembly plants and paint and adhesives factories. Exposure to toluene diisocyanate causes sensitization and subsequent respiratory symptoms. There is no clear evidence of an IgE-mediated reaction, although some patients may have specific IgE and IgG4 antibodies.¹⁹ Other causes of low-MW agents causing OA are colophony, platinum, and western red cedar (plicatic acid).¹⁷

Nonspecific Histamine Release

An ingredient in the cotton bract is thought to result in nonimmunologic release of histamine from mast cells leading to byssinosis. At risk of developing this disease are cotton, flax, and soft hemp workers. Through appropriate environmental measures in the workplace, the incidence of byssinosis has declined markedly.

DIAGNOSIS OF OCCUPATIONAL ASTHMA

The first step in diagnosing OA is to determine whether the patient indeed has asthma. The presence of existing asthma is confirmed by spirometry or by establishing airway hyperresponsiveness to methacholine. The next step is to establish that an agent in the workplace is causing asthma. The history will give an important clue if asthma worsens during the workweek and improves on weekends and holidays. However, this may be misleading because, as will be discussed later, the patient may have an isolated late response with symptoms appearing hours after leaving the workplace. If the OA is caused by an IgE-mediated reaction, skin tests or serological tests can verify the presence of IgE antibody as discussed under OR.

Studying the response of the patient to a "natural" challenge consists of monitoring symptoms and peak expiratory flow rate before and after a work shift. If positive, then the association is made. If negative, peak expiratory flow should be measured three times a day

Table 5 Factors affecting prognosis of occupational asthma

Length of exposure
Duration of symptoms before diagnosis
Severity and frequency of attacks
Lung function
Dual bronchial response
Degree of bronchial hyperactivity

for 3 weeks. At some time, nonspecific bronchial reactivity can be measured before and after work.

A controlled bronchial challenge can be performed in certain specialized centers. The challenge may be performed to dusts, aerosols, vapors, and gases. Such challenges have indicated three distinct types of responses: an immediate response with forced expiratory volume at 1 second (FEV₁) declining in a few minutes, a dual response in which the immediate fall in FEV₁ is followed by another generally greater fall in FEV₁ 4–6 hours later, and an isolated late response in which the FEV₁ does not fall until 4–6 hours have passed. Interestingly, an isolated late response appears to be more commonly seen in OA than in asthma because of common environmental allergens.²⁰

OCCUPATIONAL ASTHMA: PROGNOSIS

The factors affecting the prognosis of OA are seen in Table 5. Particularly important is the duration of symptoms before the diagnosis is made. Also important are the severity and frequency of attacks. The worse the lung function, the worse the prognosis. Finally, a dual bronchial response to a challenge and a higher degree of bronchial hyperreactivity contribute to a worse prognosis. The fact remains that most patients will experience symptomatic improvement after leaving the workplace, especially if the diagnosis is established in a timely manner and the patient is promptly removed. Although there is suggestive evidence that bronchial responsiveness may be acquired rather than a predisposing factor in OA, more well-controlled prospective studies are needed.²⁰

OCCUPATIONAL ASTHMA: THERAPY

As was discussed in the section on OR, environmental control is vitally important in managing OA. The physician must truly serve as the patient's advocate. Every effort should be made to alter the working environment to the benefit of the patient. These would include the control measures referred to previously. Failing that, the patient should be reassigned to a different working environment. The same agents useful for treatment of other types of asthma are certainly appropriate for the patient with OA.²¹

CONCLUSION

The workplace provides a fertile ground for involvement of the allergist. There is evidence that allergic occupational diseases are on the rise. The diagnostic index of suspicion on the part of the clinician must be high. Diagnosis of OR and/or asthma must be made in a timely fashion. Altering the environment or removing the patient from that environment may spare the patient a life as a pulmonary cripple.

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