

OCCUPATIONAL RHINITIS

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Symptoms of rhinitis are a frequent presenting complaint to the practicing physician. Rhinitis is an inflammation of the membranes lining the nose; is characterized by nasal congestion, rhinorrhea, sneezing, nasal pruritus, or postnasal drainage; and can be caused by allergic or nonallergic triggers.²² Occupational rhinitis (OR) refers to rhinitis symptoms that arise in the workplace, and often is associated with occupational asthma (OA)^{7, 81} and occupational conjunctivitis.⁷ The latency period between exposure and development of rhinitis symptoms may range from 2 months to 18 years for allergic OR⁷; however, irritant or nonallergic OR can occur immediately after an acute high level exposure.

It has been estimated that the prevalence of occupational rhinitis is 5% to 15%.^{7, 80} The disease may be underestimated because of reluctance of workers to report symptoms for fear of job loss,^{7, 80} loss of seniority, or fear of repercussions from coworkers. The underestimation also may be related to the underappreciation of the worker or physician of the source of the rhinitic symptoms being the workplace. Those who develop rhinitis or asthma soon after starting a job may leave and seek employment in a different occupation without reporting their symptoms.^{7, 24} The patient or physician also may be unwilling to accept that a substance from work (e.g., latex) is the cause of the symptoms. Finally, the long latency period between exposure and symptoms for some patients may result in overlooking the workplace as the source of the rhinitis.

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RISK FACTORS

Risk factors for the development of OR include patient and workplace factors and properties specific to the inducers of the disease. Workers at risk are those with a personal or family history of atopic diseases.⁷ A British study of laboratory workers exposed to rats found that 45% of atopic patients (i.e., with positive skin tests to mites and grass) became sensitized to rat antigen within their first year of employment, as compared with 3% of nonatopic patients.¹³ Smoking also may be a risk factor for certain chemicals. Smokers who work in plastic factories have increased levels of IgE to tetrachlorophthalic anhydride when compared with nonsmokers.²⁴

High-risk occupations include those that involve frequent exposure to animals, chemicals (e.g., isocyanates, anhydrides), latex, and flour. The duration of exposure and the concentration of the offending agents affect the risk of developing OR. Additional workplace factors include accidents or spills; use of proper industrial hygiene methods (e.g., ventilation; worker compliance with the use of gloves, masks, and respirators); and exposure to cold air, ozone, or pollution. Intranasal use of illicit drugs also may increase the risk for OR. Exposure at the work environment can vary in the same factory, depending on ventilation, spills, and local concentration or use of chemicals.²⁴

The Occupational Safety and Health Administration (OSHA) has estimated there are 575,000 potentially hazardous chemicals in the workplace,^{7, 58} and more than 200 have been implicated as causes of OA or OR.⁷ The specific characteristics of the causative substance also affect the development of OR. Substances with a high molecular weight are more likely to sensitize workers than substances with a low molecular weight, especially in atopic individuals.^{24, 47} Formaldehyde causes rhinitis because of its chemical properties. It is a highly water-soluble gaseous pollutant that can be found in plywood, particle board, some cosmetics, adhesives, floor coverings, and the backing on carpets. Because of its high water solubility, it is retained easily in the nasal mucosa, where, if the concentration is sufficient, it can cause irritant rhinitis. Another agent, ozone, is a strong oxidizing agent, and is highly reactive in the lungs, where it leads to cough, chest pain, and reduction of forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC).⁴³ In a human nasal tissue model, ozone induced mast cell degranulation and an increase in arachidonic acid metabolites.⁷⁵ These examples demonstrate that the chemical properties of a substance may make it more likely to cause rhinitis symptoms during occupational exposure.

PATHOGENESIS

Nasal anatomy and physiology make the nose vulnerable to occupational allergens and irritants. The nose is the first point of entry, has high vascularity and turbulent air flow, is a reservoir of soluble pollutants and allergens, and is a location for the deposition of particulate matter by

impaction.⁷⁰ Nonspecific nasal hyperreactivity has been shown to be increased in workers exposed to respiratory irritants. Plavec et al⁷⁰ studied 84 workers exposed to respiratory irritants and 60 nonexposed healthy controls. Most of the exposed workers had rhinitis complaints. The occupational irritants included fluorine, chlorine, phosphate dust, sulfur, ammonia, and urea. Nonspecific nasal provocation was performed with histamine, and total nasal resistance was measured. A positive test was defined as the concentration of histamine that caused more than a 75% rise of total nasal resistance as compared with saline. The authors found a significantly higher percentage of nasal hyperreactors and a significantly greater nonspecific nasal response to histamine among the exposed workers when they were compared with nonexposed controls. In 19 patients, nonspecific nasal hyperresponsiveness also was measured during exposure at work and after 2 weeks out of work. Significantly higher nasal reactivity was measured during exposure at work. There was no relation found between nasal reactivity and atopy, and smokers were found to have lower levels of nonspecific nasal reactivity.⁷⁰ Workplace exposure to known respiratory irritants can result in increased nasal hyperreactivity and can predispose someone to develop OR.

CAUSES

Nonallergic

OR may have an allergic or immunologic or nonallergic cause. The following is partial list of nonallergic causes:

Formaldehyde	Sulfur dioxide
Ozone	Nitrogen oxides
Fluorine	Phosphate fertilizers
Chlorine	Anhydrides
Phosphate dust	Polyvinyl chloride
Sulfur	Western red cedar
Ammonia	Toluene
Urea	Xylene
Tobacco smoke	Perfumes
Coal dust	Pesticides
Exhaust fumes	Cleaning agents
Paint fumes	Acid aerosols
Flower fragrance	Talc

Nonallergic causes have been characterized as annoyance, irritational, and corrosive.^{6, 7}

Annoyance reactions result from exposure to mild workplace irritants or odors that exacerbate pre-existing allergic or nonallergic rhinitis.^{6, 80} Nasal polyposis, sinusitis, tobacco abuse, and overuse of over-the-counter nasal decongestants or illicit drugs can increase the

likelihood of developing an annoyance reaction.⁷ These reactions often are seen with environmental intolerances, such as sick building syndrome. Examples of annoyance reactions include perfumes, tobacco smoke, air fresheners, cooking odors, cleaning agents, detergents, and exhaust fumes.⁸⁰

High concentrations of airborne chemicals that are inhaled at work and that penetrate the nasal mucous layer can cause irritational OR and cause a burning sensation of the eyes, ears, nose, and throat. A proposed mechanism for this reaction involves the stimulation of chemical irritant receptors in the nasal mucosa, resulting in the release of substance P and other neuropeptides from nasal sensory nerves. Substance P causes vasodilation and subsequent neurogenic inflammation.^{7, 51, 80} The nasal and throat burning may result from stimulation of olfactory and trigeminal nerve irritant receptors.⁷

Causes of irritational OR include talc, coal dust, ozone, paint fumes, toluene, xylene, tobacco smoke, sulfur dioxide, and pollution.^{80, 81} Nasal inhalation studies in individuals intolerant to tobacco smoke have shown statistically significant changes in nasal airway resistance.^{51, 92} Toluene diisocyanate (TDI) and cigarette smoke have been shown to inhibit neutral endopeptidase, a receptor cell surface enzyme that degrades substance P, resulting in increased levels of substance P and increased neurogenic inflammation. Substance P also can cause bronchoconstriction.⁵¹ Release of substance P has been noted with nicotine, ether, capsaicin, and formaldehyde.^{7, 26} Sulfur dioxide is released during the industrial combustion of coal and oil containing high amounts of sulfur. Almost 90% of sulfur dioxide is absorbed in the nasal cavity, where it can induce rhinitis.⁴³ Sulfur dioxide also can cause bronchoconstriction. Pollution—which is composed of ozone, sulfur dioxide, nitrogen dioxide, diesel exhaust, acid aerosols, and other irritating gases—is believed to be a trigger that causes increased prevalence of rhinitis in urban as opposed to rural settings. In guinea pigs, ozone, nitrous oxide, and sulfur dioxide also have been shown to act as adjuvants, and, therefore, enhance the immunogenicity of a coadministered antigen.⁵¹

Corrosive soluble chemical gases causing OR include ammonia, chlorine, acids, organophosphides, vinyl chloride, and acrylamide.⁸⁰ These can cause significant inflammation and permanent damage to the olfactory system.^{7, 80} Chronic nasal congestion and postnasal drainage may follow. Signs of systemic intoxication also may be present.⁷ Any gas, dust, fume, or mist that has the potential to irritate or corrode the nasal mucosa can be a causative agent of OR.⁹¹

Allergic

Allergic OR results from high molecular weight (HMW) or low molecular weight (LMW) allergens acting as haptens and binding to proteins such as serum albumin. The HMW allergens are more sensitizing, especially in atopic workers. Examples of HMW antigens include

animal proteins, papain, wheat flour, soybean dust, trypsin, and vegetable gums.²⁴ Host allergic responses are IgE-mediated, and early and late phase nasal reactions can occur. Some workers may have only late-phase reactions, which can mislead the worker and physician from considering the workplace as the source of the rhinitis symptoms. These workers develop their symptoms when they get home at night and may have few, if any, symptoms while at work. Allergic OR is characterized by the need for repeated exposures to the offending agent to result in sensitization, which occurs in only a small percentage of exposed workers. Allergic OR also results from exposure to only small amounts of the sensitizing agent, and requires the symptoms to recur on rechallenge (i.e., immunologic memory). As previously noted, the interval over which sensitization occurs could be weeks to years; thus, allergic OR does not occur after the first exposure, as it can with irritational OR.

Using guinea pigs, an animal model of allergic OR to TDI has been developed. In these animals, repeated application of TDI to the nasal mucosa results in sensitization and the development of acute rhinorrhea and sneezing on rechallenge. Histologic examination of the nasal mucosa and nasal secretions shows an accumulation of eosinophils and mast cells. These findings are similar to those in other allergic rhinitis animal models. TDI rechallenge 3 weeks after sensitization resulted in histamine release from the nasal mucosa of the sensitized guinea pigs but not of controls.^{37, 84, 85}

There are many causes of allergic OR. Documented causes and occupations associated with exposure are shown in Table 1. A review of the literature over the last 10 years revealed a number of allergic OR case reports and small series of surveillance studies. These articles and case reports were reviewed to document the presence of OR symptoms; cases without any mention of rhinitis symptoms were not included. The studies also included confirmation of an immunologic IgE-mediated mechanism of the allergic OR and OA by skin testing, nasal or bronchial provocation, or demonstration of specific IgE by CAP, radioallergosorbent tests (RAST), or ELISA.

High-risk occupations are shown in Table 1, and include farmers, pharmaceutical workers, carpenters or wood workers, workers exposed to epoxy resins, health care workers, and food processing industry workers. The food industry accounts for the largest number of cases of OR.⁵¹ Some food industry workers that develop allergic OR also can develop subsequent food allergy. For example, OA and OR caused by carmine—a natural red dye extracted from dried insect bodies used in the food, dye, and cosmetic industry—developed in a nonatopic spice warehouse worker who subsequently manifested food allergy on ingestion of foods containing carmine dye.¹ Food allergy also occurred in a nonatopic agricultural worker who developed OR and OA to sunflower pollen and who had anaphylaxis with the subsequent ingestion of honey containing 30% of sunflower pollen.¹⁴

Not all food workers who develop allergic OR from a food allergen are at risk for subsequent food allergy. In one study, allergic rhinocon-

Table 1. CAUSES OF ALLERGIC OCCUPATIONAL RHINITIS AND ASSOCIATED OCCUPATIONS

Causes	Occupations
Cereal flours/ α -amylase inhibitors	Bakers, woodworkers
Anhydrides	Plastics and epoxy resins
Animal proteins	Lab workers, pet shop owners, veterinarians, farmers
Enzymes (papain, trypsin, pancreatic extracts)	Brewers, plastics, pharmaceuticals
Soy bean dust	Farmers, food processors
Isocyanates	Auto painting, varnishers
Wood dusts	Sawmills, carpenters, furniture makers
Mites (storage, red spider)	Bakers, farmers, grain elevator operators, food processors
Psyllium/senna	Bulk laxative factory workers, nurses, hair dye exposure
Guar gum/vegetable gums	Food, carpet workers, printing
Latex	Health care, textile
Medications (morphine, piperillin)	Hospital workers, pharmacists, pharmaceutical industry
Molds	Mushroom, cheese workers
<i>Bacillus subtilis</i>	Detergent workers
Tea	Farmers, tea processing
Green coffee bean	Coffee production
Ethylenediamine	Shellac, lacquer industry
Silk	Silk processing
Bird proteins	Poultry breeders, farmers
Ninhydrin	Laboratory workers
Sunflower pollen	Bakers, agricultural workers
Garlic	Food workers
Polyfunctional aziridine hardener	Painters
Pollens	Gardeners, greenhouses
Prawns, crabs	Food processors
Soldering fluxes (colophony)	Electronics, welders
Metals, metal salts (nickel, platinum, chromium)	Metal processing or plating, paint processing
Synthetic fibers (rayon, nylon, orlon)	Textile workers
Corn dust	Stock feed workers
Lactase	Lactase packaging
Spices (fennel, sesame seed)	Food processors, bakers
Raw poultry	Food processors
Milk proteins (α -lactalbumin, casein)	Chocolate manufacturing, tannery
Arthropods	Laboratory workers
Dyes	Hair dressers, dye manufacturing
Cow dander	Dairy farmers

Data from references 3-5, 8-12, 14, 16, 18, 23, 25, 32, 33, 38, 41, 42, 45, 46, 49, 53-55, 57, 61, 63, 66, 68, 74, 77-79, 82, 83, 87, 88, and 96.

junctivitis was found in nearly 40% of coffee workers; however, no cases of allergic reactions with coffee ingestion were reported.⁸⁷ This is most likely because of the coffee protein being present in the green coffee bean and being destroyed in the coffee roasting process.⁸⁷ A similar scenario exists for workers in the tea industry.

Pharmaceutical workers are also at high risk for allergic OR and OA. Documented IgE-inducing antigens include peptidase and lysozyme (proteolytic enzymes used in anti-inflammatory agents),⁶⁴ bromelin,²⁵ pepsin (an herb),¹⁶ and papain.⁹ Lactase production also has been associated with OR. Muir et al⁵⁴ found that of workers who package lactase and had positive skin tests to lactase extract, 26% had OR and 14% had OA.

Proteolytic enzyme exposure also can cause OR in settings other than the pharmaceutical industry. Papain is a proteolytic enzyme extracted from the sap of the papaya tree, and is used in digestive aides, meat tenderizers, tanning of hides, and chewing gum. Niinimäki et al⁵⁶ described a case of a cosmetologist who developed OR from papain in a moisturizing cream. Hayes et al³² describe a pediatric nurse who had OR from powdered pancreatic extract after she repeatedly mixed it for children with cystic fibrosis.

Bulk laxative production also has been associated with the development of OR. In a cross-sectional study of 125 pharmaceutical workers involved in the production of bulk laxatives containing ispaghula husks (psyllium) and senna pods, 7.6% had positive skin tests to psyllium and 15.3% had positive tests to senna. Symptoms of allergic rhinoconjunctivitis or dermatitis developed in 71% of these workers.⁴⁹ OR also has been reported in nurses who dispense senna or psyllium. Senna has caused OR when used as a coloring agent in hair dyes and shampoos.³³

Pharmaceuticals can cause allergic OR; there have been case reports from exposure to powdered morphine⁸⁸ and piperillin.⁵³ Medications also may cause nonallergic OR, as reported in a worker exposed to salbutamol.² Bovine serum albumin powder also has been noted to cause allergic OR in a pharmaceutical worker.³⁹ Any pharmaceutical worker presenting with rhinitis symptoms should be evaluated for a possible occupational source.

Laboratory workers also seem to have a high incidence of allergic sensitization, with some investigators noting rates of 30% in some environments.⁸¹ Rats are the most commonly implicated laboratory animal.⁸¹ Laboratory workers exposed to arthropods also can acquire allergic OR. Chemicals used in the laboratory, such as ninhydrin (used in chromatography), have been linked to allergic OR in technicians.^{38, 66}

A few specific causes of allergic OR deserve special mention. These include anhydrides, mites, and wood dust. Anhydrides, potent occupational sensitizers, are used in the plastics industry and in the production of epoxy resins. In one study of 73 workers at a condenser plant where methyltetrahydrophthalic anhydride (MTHPA) was used as a hardening agent for epoxy resin, 64% of the workers had MTHPA specific IgE and 87% of these sensitized workers had rhinitis symptoms, as compared with 19% of nonsensitized workers.⁹³ It seems that the exposure level of anhydrides increases the risk of developing OR and OA, whereas atopy and smoking do not seem to play major roles as risk factors.²⁹ Grammer et al²⁸ studied 57 workers exposed to hexahydrophthalic anhydride, and found that 16 had OR or OA. The only significant risk factors for these

workers were their exposure level and the development of specific IgE or IgG. Some genetic studies suggest that certain human leukocyte antigen haplotypes may predispose workers to sensitization to anhydrides and isocyanates.^{29, 48, 94}

Mites also cause allergic OR. Storage mites have been found to cause allergic OR in bakers, farmers, and grain elevator operators. Mites have been implicated in the food processing industry, with allergic OR and OA developing in workers exposed to ham³ and poultry⁴⁶ covered with mites. Red spider mites have been noted to cause OR in farmers.⁵ In a recent study of greenhouse workers exposed to the red spider mite, 66% had positive skin tests and specific IgE; 88% of these sensitized workers had rhinitis symptoms, and 94% had asthma. There was no cross-reactivity demonstrated between the red spider mite and house dust mite (*Dermatophagoides pteronyssinus*).²⁰

For more than 30 years, wood dust has been known to cause OR.⁸³ It is a common cause of OR in carpenters, sawmill workers, and furniture production workers. Western red cedar or plicatic acid has been the most extensively studied; however, it has been stated that 60 to 70 different types of wood dusts are capable of provoking occupational disease by contact or inhalation.⁸

Sometimes, common occupational allergens are found in uncommon locations. For example, allergic OR to wood dust developed in a jeweler who used it to dry jewelry after it was treated with various chemicals.³⁴ Allergic OR developed in a tannery worker exposed to casein, a common milk protein. The casein was sprayed on the leather in the tanning process.⁶¹ Lopez-Rico et al⁴⁵ recently showed that cereal flours and α -amylase inhibitors—well-known causes of baker's asthma—sensitized three workers in a wood factory that made veneer panels. The cereal flours were added to urea-formaldehyde resins to improve the viscosity of the glue that attached the veneer panels. A common workplace antigen also may be used at home for a hobby. Silk has been implicated as a cause of OR and OA in the silk industry. A recent case study described a woman who developed allergic rhinitis and asthma to silkworms used at home for a hobby.⁹⁰

Although the previously mentioned agents have been discussed as causes of allergic OR, some also can cause OR and OA by nonallergic mechanisms. For example, specific IgE occurs in only 5% to 10% of workers with TDI-induced OA.^{24, 51} Anhydrides also can cause respiratory symptoms by nonimmunologic mechanisms.^{65, 81} In addition, only 30% of workers with OA from plicatic acid in western red cedar dust have IgE to a plicatic acid-serum albumin conjugate.²⁴ Similarly, isocyanates and chlorine can cause allergic OR, or may act as nonspecific irritants with exposures to high concentrations.⁹¹

Latex

Latex is one of the most important allergens facing allergists and their patients in the 1990s,⁴⁴ and has received much attention in the

medical and lay press. As many as 10% to 15% of health care workers may be sensitized to latex; therefore, it is a major potential cause of OA and OR in the health care field. Delayed hypersensitivity (type IV) reactions also occur and are caused by chemicals such as mercaptobenzothiazole and tetramethylthiuram added during the rubber manufacturing process.⁴⁴ IgE-mediated immediate hypersensitivity reactions occur from several latex proteins retained in the natural rubber. Sensitization to these proteins can be permanent, and latex-induced OA and OR may persist after removal from exposure.

Latex can cause OR and OA in non-health care environments. Latex-induced OA and OR has been shown clearly in workers in latex surgical glove manufacturing plants.⁸⁶ Pisati et al⁶⁸ reported latex-induced OR and OA in three workers in a textile factory that used latex threads powdered with talc to produce elasticized ribbon for underclothes. Orfan et al⁶² reported two workers who developed OA and OR in a latex doll factory. Both workers were exposed to latex dust from the sanding of latex-containing doll parts. Carrillo et al^{15a} studied 418 workers at a flower and greenhouse company who wore latex gloves at work, and found that 4% to 5% had elevated latex IgE in serology or had positive skin tests. Twelve of these workers had simultaneous food allergies (e.g., chestnut, almond, banana, avocado), probably related to cross-reactivity with latex. In all cases, the work-related symptoms preceded the onset of the food allergy. Not only can latex cause OR and OA in the health care field, it also can occur in other settings. Latex exposure should be considered in cases of unexplained OR or OA.

DIAGNOSIS

History

Suspicion of the workplace as the source of the rhinitis comes from a comprehensive medical history, as shown in the following list:

- Onset of symptoms at work
- Improvement on weekends or vacations
- Recurrence of symptoms on re-exposure
- Exposure to
 - Cold air
 - Ozone
 - Pollution
 - Tobacco smoke
 - Animals
 - Dust
- Similar symptoms in coworkers
- Duration working at current job
- Adequacy of ventilation
- Compliance with gloves, masks, protective clothing

History of accidents and spills

Monitoring

Review of material safety data sheets (MSDS)

Personal or family history of atopy

Coexisting symptoms

Bronchial

Dermatologic

Conjunctival

Anosmia

Smoking history

Hobbies

Previous employment

Medications or drugs

Intranasal

The temporal relationship of the onset of sneezing, nasal congestion, pruritus, and rhinorrhea at work, with improvement outside of work, is the essential clue in the history. Improvement or resolution of symptoms during evenings, vacations, or weekends, with recurrence on returning to work, highly suggests OR, although not all workers with OR give this history. For example, as previously noted in the discussion of allergic OR, if the clinical manifestation is only an isolated late-phase reaction, rhinitis symptoms may not occur at work but rather have their onset several hours after leaving work⁸¹—which is especially true of LMW allergens.²⁴ Also, workers with chronic occupational allergen exposure may require longer absences from work until their symptoms abate.^{7, 80, 81} The classic history of onset of symptoms at work, with improvement out of work, may not always be present, and the physician needs to maintain a high index of suspicion.

The occupational history should include questions about how long the worker had been at the job when the symptoms first developed. A delay in the onset of symptoms implies a required period of sensitization, which is consistent with allergic OR. The latency period for immunologic OR to manifest may range from weeks to as long as 20 years. The explosive onset of sneezing, pruritus, and nasal congestion is consistent with an acute irritant exposure, especially if there is prompt improvement after removal from the exposure. A history of exposure to spills or accidents should be considered. Exposures at work to ozone, pollution, tobacco smoke, animals, or cold air also should be considered. Cold air almost universally increases nasal airway resistance.

A comprehensive history also should include questions inquiring about coexistent bronchial, conjunctival, or dermatologic symptoms; presence of similar symptoms in coworkers; personal or family history of atopy; hobbies and leisure activities; current or previous smoking history; previous occupations and exposures; adequacy of workplace ventilation; compliance with the use of gloves, masks, and protective clothing; presence of rhinitis symptoms before the current job; monitoring of spills and accidents; use of intranasal medications (especially over

the counter [OTC] decongestants) or illicit drugs; and symptoms of anosmia or chronic sinusitis. It is extremely important to make a list of all the chemicals a worker is exposed to and to obtain MSDS. The 1986 OSHA "Right to Know" Act mandates that companies provide MSDS, which give detailed information, including health effects of the chemicals to which the worker is exposed; they also should be obtained for chemicals the worker may not work with directly but to which he or she is exposed.

The worker should provide detailed description of performed duties, focusing on specific contact or inhalation of chemicals, smoke, gases, vapors, or liquids. A site visit may help visualize any exposures, and may provide additional information on exposures not already elicited in the history.⁸⁰

Physical Examination

The physical findings in OR are similar to those of rhinitis, and are nonspecific. On nasal examination, pale blue, boggy nasal turbinates might suggest an allergic cause; however, in a study of 100 shipworkers with OR, only 8% had this physical finding. The only nasal findings in this study were dry, atrophic nasal mucosa, nasal crusting, epistaxis, and anosmia.⁹¹ One also may see eosinophils in nasal smears of patients with allergic OR.

Nonallergic annoyance causes of OR may yield minimal, if any, nasal findings. Corrosive causes appear as nasal mucosal burn, and there may be associated ulceration and hemorrhage in the nose, eyes, skin, and mouth. Irritational causes result in turbinate congestion, and frequently appear with coexistent conjunctivitis.⁷ The nasal examination also should include evaluation for a deviated septum, nasal polyps, foreign bodies, or purulent discharge. Treatment with topical decongestants may help in the nasal examination when there is significant obstruction, and may allow an estimate of the reversibility of the nasal inflammation (much like an albuterol treatment does for bronchial reversibility).

Histologic examination of the nasal mucosa in 62 workers with OR from various causes showed a loss of cilia, goblet cell hyperplasia and metaplasia, and stratified squamous cell metaplasia in most of the workers.^{59, 91} Another study showed significant epithelial changes in the middle turbinate in biopsies of workers exposed to formaldehyde, as compared with controls.^{35, 91} Similar morphologic changes have been found in workers exposed to chromium, wood dust, copper, salt, dust, nickel, and leather.⁹¹

A complete physical examination also should include an eye examination for signs of associated conjunctivitis; sinus palpation for tenderness suggesting sinusitis; and an oral examination for ulcers, inflammation, or purulent postnasal drainage. A lung examination could reveal signs of coexisting OA, and the skin should be checked for signs of contact dermatitis. Hand dermatitis in a health care worker who wears gloves should suggest the possibility of latex allergy immediately.

Table 2. DIAGNOSTIC TESTS FOR OCCUPATIONAL RHINITIS AND ASTHMA**Rhinitis**

Skin prick testing

Measure specific IgE by radioallergosorbent tests or ELISA

Basophil histamine release test

Rhinoscopy or rhinomanometry (with or without nasal provocation)

CT scan of the sinuses

Asthma

Spirometry

Complete pulmonary function tests

Chest radiograph

Bronchial challenge (at workplace or in laboratory)

Methacholine challenge test

CT scan of the chest

Miscellaneous Laboratory

Complete blood count

Sedimentation rate

Chemistries

Testing

Table 2 lists tests that can be used to confirm a diagnosis of OR or OA. Evaluation of allergic causes of OR or OA can involve skin prick testing, measurement of specific IgE by RAST or ELISA, or use of the basophil histamine release test. Skin testing is useful in allergic OR, especially if the cause involves animals, dust, latex, or possibly mold. Skin testing also can be used to identify underlying atopy. LMW substances may need to be conjugated to serum albumin.²⁴

RAST and ELISA can be used to measure specific IgE in allergic OR and OA, and can be done with extracts prepared from the suspected workplace.²⁴ As with preparation of skin test extracts, LMW allergens may need to be attached to carrier proteins. Total serum IgE and total circulating eosinophils are not useful in the diagnosis of rhinitis.²²

The basophil histamine release test (BHRT) is a novel laboratory method to evaluate a IgE-mast cell-mediated reaction. In this test, washed whole blood suspensions containing basophils are incubated with medium and allergens for 30 minutes, then are heated to 100° for 10 minutes. The histamine is measured in the supernatant by radioenzymatic assay. Results are expressed as the percentage of released histamine of total blood histamine. Values were considered positive when the difference between spontaneous and allergen-induced histamine release was at least 8%. BHRT is expensive and laborious, but can be done on blood samples of patients on antihistamines.⁷⁴

Rasanen et al⁷⁴ compared skin prick testing, RAST, and BHRT in 16 patients with allergic OR and OA. All underwent bronchial or nasal challenges with positive results. Most of the patients were sensitized to cereal flours or grain dusts, although they had no food allergy with

ingestion. The 16 patients had 23 positive challenges, and sensitization was verified by one or more of the immunologic tests in 21 of the 23 challenges. The sensitivity and specificity of the prick test (74% and 93%) were similar to those of the BHRT (78% and 93%), and were slightly better than those of the RAST (57% and 86%). The sensitivity and specificity of a panel of all three tests was 91% and 71%, respectively. The overall concordance between the three tests and allergen challenge was good.⁷⁴

A secure diagnosis of OR cannot be achieved without some attempt at nasal provocation.⁷ Nasal challenge can be done in the office or workplace with examination of the nose taking place 1 hour after direct nasal challenge. It is important to perform the nasal challenge when the rhinitis symptoms are at a minimum, if possible, and off all confounding medications, especially antihistamines. It may be more difficult to evaluate workers with chronic exposures in whom it may take longer for symptoms to abate; however, challenges with irritants may increase symptoms already present.⁸⁰ Nasal challenges should start with a placebo (e.g., the diluent or lactose powder). Nasal challenges often are done with some form of measurement of nasal resistance by rhinoscopy or rhinomanometry. Mast cell-derived histamine and tryptase have been measured in nasal lavage fluid after a provocation test to indicate an immediate allergic response.^{40, 71} Spirometry also can be done in association with a nasal challenge, especially if OA is suspected.

Anterior rhinomanometry may be used during nasal challenge to measure nasal airway resistance; however, there are concerns because of inconsistent correlation with complaint severity,^{7, 80} distortion of some of the measurements by the probes used,^{80, 81} and nasal cycling fluctuations.⁸¹ Pirila et al⁶⁷ studied 12 patients with OR using nasal challenge and anterior rhinomanometry. They observed many physiologic fluctuations that became greater with longer observation periods, and noted that the patients reacted with congestion to the diluent solution of the allergen extract. They concluded that because of these physiologic fluctuations, nasal airway resistance, as measured by anterior rhinomanometry, should be interpreted with caution and that other measures—such as number of sneezes and amount of nasal secretions—also should be used.⁶⁷ Posterior rhinomanometry is expensive and difficult to perform in some patients.²⁴ Despite these limitations, rhinomanometry can be used pre- and postshift to evaluate for nasal airway changes.

Anterior rhinoscopy also can be used with a nasal challenge to evaluate nasal resistance and to evaluate the amount of rhinorrhea and estimate mucosal edema. Rhinoscopy also can be used to evaluate for a deviated septum, nasal polyps, tumors, or sinusitis.

If a worker presents with coexistent lower respiratory symptoms, a chest radiography and spirometry or complete pulmonary function tests are recommended. If the spirometry result is abnormal, albuterol can be given to document reversibility. If reversibility cannot be demonstrated, then a methacholine challenge test is necessary to document asthma, especially if there is a question of disability or liability.

Bronchial challenge is one way to evaluate for OA, just as a nasal challenge is used for OR. *Natural* bronchial challenge is done by measuring spirometry or peak flows before and after a workshift and for monitoring symptoms. The peak flow changes after one workshift are greatest when the patient has been away from work for a few days.²⁴ One negative reading does not exclude OA, and it may take multiple recordings to make an accurate diagnosis.²⁴ Bronchial challenges performed in the laboratory may be helpful if one needs to separate potential offending substances or when there are disability and liability issues. Because severe bronchospasm can result, bronchial challenges should be done only in settings with available resuscitation equipment and trained personnel. If an allergen is to be used, serial endpoint skin titration should be done, and the extract concentration that elicited a 2⁺ reaction should be the starting inhalation dose. For nonimmunologic agents, a nonspecific agent, such as histamine or methacholine, is used first. If the response to the histamine is significant at low concentrations, a small starting dose of the irritant agent is used.²⁴

Additional studies that may be appropriate include sinus CT to look for underlying chronic sinusitis or anatomic abnormalities; chest CT tomography to look for bronchiectasis, fibrosis, or other findings not visualized on chest radiographs, and exercise pulmonary function tests to determine if there is an exertional component and to assess functional status. A complete blood count with differential, erythrocyte sedimentation rate, and basic chemistries also may be helpful.

SICK BUILDING SYNDROME

Sick building syndrome (SBS) is a condition of mucous membrane irritation caused by inadequate air handling systems in new, energy-efficient office buildings,⁵² and should be distinguished from OR. When the outdoor air supply ventilation rate is low (< 10 L/sec/person), the indoor level of pollutants can be high.⁵² Patients with SBS experience their symptoms only in the affected building. Chemicals implicated in SBS include photocopier fumes, carbonless copy paper, glass fibers, cleaning agents, paints, solvents, carbon monoxide, and nitrogen dioxide from the intake of exhaust fumes.⁵² If SBS is suspected, a site visit may be helpful. Environmental air sampling may be indicated if specific indoor contaminants are suspected, but it is expensive and requires considerable expertise.⁵² The only treatment may be removal of the affected worker from the building.

ASSOCIATION OF OCCUPATIONAL RHINITIS WITH OCCUPATIONAL ASTHMA

Allergic asthma and allergic rhinitis often coexist in the same patient. In a recent 23-year follow-up of college students, 85.7% of students

with asthma had allergic rhinitis, and 21% of students with rhinitis had asthma.³⁰ Others have noted asthma in 58% of patients with rhinitis.⁷³ OA rarely occurs as a *pure* disease without OR.⁷ Malo et al⁴⁷ evaluated 40 workers with OA and found that 92% had coexisting OR and that 72% had conjunctivitis. The prevalence was no different for HMW and LMW agents, although the rhinitis was more intense for HMW agents.⁶³ Plavec et al⁷⁰ states that 80% of patients with symptoms of irritant-induced bronchial hyperresponsiveness have rhinitis. OR often precedes the development of OA with the early and late reactions paralleling the bronchial reactions.⁷ The latency period for the development of OA is variable—often 1 to 2 years, although it is often shorter with exposure to LMW substances. It has not been shown that removing patients with OR from work prevents the subsequent development of OA in all cases. OA may persist after removal of the person from the workplace (e.g., with TDI or latex), and may result in fixed, irreversible lung disease. The major factor predicting poor prognosis in OA is duration of exposure before the diagnosis is made.⁷ When obtaining a medical history, workers presenting with OR also should be questioned for coexisting OA. It is estimated that 2% to 5% of all people with asthma in the United States have workplace-induced asthma.^{7, 24}

TREATMENT

Treatment for OR should address the worker and the work environment. The best form of treatment is prevention; however, this may not always be possible. It has been suggested that potential laboratory workers be screened for atopy with skin tests to animals; however, skin testing would not exclude all workers who develop OR and OA. In a study of laboratory workers exposed to rats, many atopic workers did not become allergic to rats, whereas many who were not allergic did develop OA and OR from rats.^{24, 69}

If prevention is not possible, avoidance is the next choice; however, again, avoidance is not always possible or practical. Removal from work does not always result in remission of symptoms.

Environmental controls, such as masks, gloves, protective clothing, and improved ventilation, should be instituted where appropriate. Periodic environmental air sampling may be necessary in cases in which potentially toxic substances or potent sensitizing agents (e.g., TDI) are involved.

Pharmacologic treatment for OR is most effective for allergic OR. The medications are the same as for seasonal or perennial allergic rhinitis, and include antihistamines, topical nasal corticosteroids, oral decongestants, nasal ipratropium, azelastine, nasal saline, nasal cromolyn, and possibly oral steroids for severe cases. Sedating antihistamines may affect work performance adversely, and nonsedating antihistamines are preferred.⁸⁰ The actions of the many cytokines released from eosinophils, epithelial mast cells, and T-helper lymphocytes in chronic allergic OR,

however, may not all be blocked by antihistamines, which is one reason why a trial of removal from the workplace is important. Leukotriene modifiers also have been shown to decrease nasal congestion, sneezing, and rhinorrhea.²¹

Management of OR also should include appropriate treatment of coexisting conditions, such as chronic sinusitis or gastroesophageal reflux disease. Immunotherapy can be considered if given with allergen avoidance⁷; however, it must be done cautiously because continued high-dose allergen exposure at work, coupled with the administration of allergen in immunotherapy, increases the risk of a serious allergic reaction. If pharmacologic interventions and environmental modifications cannot be done or are not helpful in alleviating OR symptoms, or if there is evidence of progressive OA or fixed lung disease, permanent removal from the workplace is necessary.

COMPLICATIONS

Complications of OR include those resulting from the disease and those related to treatment. Chronic nasal obstruction can lead to otitis media, chronic sinusitis, sleep apnea, and sleep disturbances.^{50, 73, 95} Nasal polyps can occur as a result of chronic nasal inflammation, and could be triggered by chronic exposure to occupational irritants.⁹¹ Rhinitis can cause injury to olfactory nerves, and when the nerves regenerate, they can result in a heightened or depressed sense of smell.⁹¹ Nickel exposure is known to cause dysplastic changes in the nasal mucosa, which may lead to malignancy.⁹¹ Chromate, formaldehyde, and wood and leather dust have been associated with hypertrophic rhinosinusitis, metaplasia, and carcinoma. Besides local physiologic effects in the nose, OR results in loss of time from work and a decrease in productivity.⁸⁰ OR also can result in fatigue, irritability, depression, and anxiety, which also negatively affect workplace performance.⁸⁰

OR can precede OA. In the last 10 years, it has been shown that OA can result in permanent asthma. Earliest examples included workers exposed to colophony¹⁵ and western red cedar.¹⁷ With Western red cedar, more than 50% of workers fail to recover 3.5 years after removal from exposure.²⁴ Other examples include latex and isocyanates. Fortunately, many cases of OA and OR are reversible. Grammer et al²⁹ studied 28 workers with allergic OA and OR from anhydride exposure who were removed from work for 1 year. Only one worker had persistent mild asthma at 1 year, and all the cases of OR had resolved.

Most of the treatment complications arise from the use of sedating antihistamines. Many of these are listed in a recent review by Slavin,⁸⁰ and include increase in work-related accidents,²⁷ crush injuries, fractures, and burns. Sedation also can affect work performance adversely. Sedating antihistamines can impair driving ability,⁶⁰ and many states have fines for driving under the influence of sedating antihistamines. Because

sedating antihistamines are available over the counter, these complications cannot be eliminated completely.

SUMMARY

OR is common but often is underdiagnosed and underappreciated. The diagnosis can be difficult to make, and the history can be feigned easily, which can be problematic when questions of disability or liability arise. The diagnosis can be made with more confidence if there is coexisting OA or conjunctivitis. To avoid missing the diagnosis of OR, it is important to ask every patient that comes to the office with rhinitis or asthma symptoms, "What is your occupation?"

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