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Occupational Irritant and Allergic Rhinitis

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Abstract The upper airway (extending from the nares to larynx) fulfills essential physiologic functions, including sensation, air conditioning, filtration, and communication. As the portal of entry for the respiratory tract, the upper airway's sentinel function is performed by the olfactory and trigeminal nerves. Sensory (eye, nose and throat) irritation figures prominently in symptom reporting in so-called "problem buildings," as well as in industrial exposures to irritant gases, vapors, and smokes. Both irritants and allergens can alter function in the upper airway, leading to loss of air conditioning and filtering due to airflow obstruction and hypersecretion. Increasing evidence points to a "unified airway" model of pathogenesis (in which rhinitis may precede the development of asthma). The spectrum of occupational irritant- and allergen-related upper airway health effects—including sensory irritation, olfactory dysfunction, rhinitis, sinusitis, nasal septal perforation, and sinonasal cancer—is reviewed in this article.

Keywords Rhinitis · Allergic rhinitis · Sinusitis · Asthma · Olfactory dysfunction · Nasal septal perforation · Sinonasal cancer · Occupation · Industry · Irritant · Chemical · Allergen · Occupational allergies

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Introduction

The nose serves as the main portal of entry for the respiratory tract, filtering, scrubbing, and conditioning inspired air, as well as signaling the quality of the surrounding atmosphere. Accordingly, the nose is vulnerable to the effects of airborne irritants and allergens, and may manifest acute, subacute, and chronic changes in structure and function. The objective of this article is to outline these changes in terms of the pathophysiology of upper respiratory tract irritation and allergy, spectrum of potential health effects, and clinically relevant diagnostic methods.

Background: Anatomy and Pathophysiology

Physiologic Functions and Regional Dosimetry of the Upper Airway

The upper airway has several functions, including air conditioning, filtration, sensation, and communication. Under most climatic conditions, inspired air is both heated and humidified in the upper airway [1]. Filtration is accomplished mechanically (by nasal vibrissae) and by the process of "impaction" (whereby large diameter inspired particles collide with the turbinates, and are subsequently cleared by the mucociliary apparatus). Finer particles, on the other hand, are more likely to evade this clearance system and reach the lower respiratory tract [2]. Water-soluble irritants such as ammonia, formaldehyde, and sulfur dioxide readily dissolve in the mucous membrane layer of the cornea and upper airway [3]. The resulting sensations of eye, nose, and throat irritation provide warning of exposure, and typically trigger adaptive behavior to reduce further exposure. Clearance of water-soluble air pollutants in the upper airway is referred to as "scrubbing" (Fig. 1).

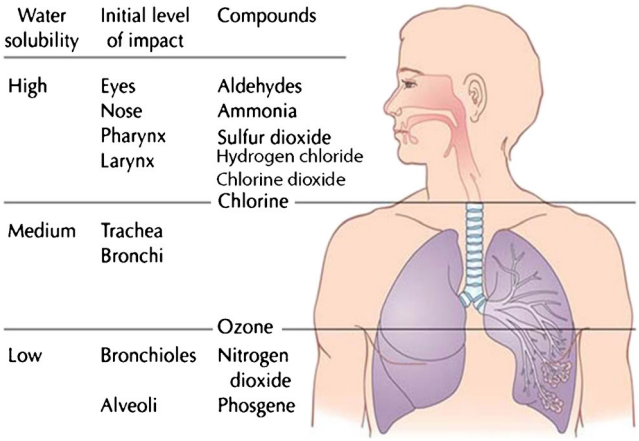

Fig. 1 Water solubility and site of initial impact of airborne irritants. (Adapted from Shusterman [76])

Nasal Anatomy

The lateral walls of the nasal cavity are invested with turbinates or concha (literally, "shells"), the functional consequence of which is to increase the surface area of contact between the inhaled air stream and the nasal mucosa [4]. In contrast to the lower airway, the upper airway undergoes changes in patency through vascular engorgement rather than smooth muscle contraction. Underlying this phenomenon is an elaborate network of arterioles, capacitance vessels, and arteriovenous shunts located beneath the mucosal surface [5]. Influencing both nasal patency changes and secretory responses are a variety of endogenous mediators derived from both the immune and neurologic systems [6, 7]. Of note, many individuals experience periodic and reciprocal nasal airflow limitation between the two sides of the nose—the so-called "nasal cycle"—the function of which may be airway protection [8].

The nasal cavity is innervated by two main structures: the olfactory nerve (cranial nerve I, providing for the sense of smell), and the trigeminal (cranial nerve V, providing for the sense of irritation). In addition, the glossopharyngeal and vagal nerves (Cr. N.'s IX and X) convey the sense of irritation for the hypopharynx and larynx. Just as our appreciation of foods involves a combination of the senses of taste and smell, our appreciation of many inhaled compounds involves both olfaction and trigeminal stimulation. The latter carries sensations ranging from "freshness" or "cooling" (in response to menthol) to burning or stinging (as elicited by ammonia or chlorine) [9]. The terminal branches of the trigeminal nerve include small diameter nociceptive neurons (C- and Aδ-fibers) invested with a variety of nociceptive ion channels [10]. The C-fiber population also elaborates vasoactive neuropeptides, which in turn can be released as part of nociceptive reflexes [11]. Central and peripheral reflexes arising from nasal mucosal stimulation include sneezing, rhinorrhea, nasal obstruction ("congestion"), cough, bronchospasm, and laryngospasm [12].

Work-related Conditions of the Upper Airway

A number of upper airway disorders are potentially associated with exposure to occupational irritants and allergens. These include olfactory dysfunction, sensory irritation, irritant rhinitis, allergic rhinitis, sinusitis, nasal septal perforation, and neoplasms of the paranasal sinuses. These are reviewed separately below:

Olfactory Dysfunction

Both temporary and long-lasting alterations in olfactory function have been reported among workers exposed to a variety of industrial chemicals. Chemically-induced olfactory dysfunction may include (1) *quantitative defects*, including *hyposmia* (reduced odor acuity) and *anosmia* (absent odor perception); and (2) *qualitative defects*, including *olfactory agnosia* (decreased ability to identify odors) and various forms of *dysosmia* (distorted odor perception). Occupational groups with documented olfactory dysfunction include alkaline battery workers and braziers (cadmium or nickel exposure), tank cleaners (hydrocarbon exposure), paint formulators (solvent or acrylic acid exposure), and chemical plant workers (ammonia and sulfuric acid exposures) [13]. A recent publication also documents qualitative olfactory deficits among workers exposed to alkaline World Trade Center dust [14]. Workers in refineries and municipal sanitation workers may also be exposed to hydrogen sulfide, which produces acute and reversible "olfactory paralysis" upon exposure at levels in excess of approximately 50 parts per million [15]. In terms of differential diagnosis, causes of olfactory impairment not related to chemical exposures include head trauma, chronic nasal obstruction, post-infectious inflammation, neurodegenerative and endocrine disorders, hepatic and renal disease, neoplasms, various drugs, ionizing radiation, congenital defects (e.g., Kallmann's syndrome), and selected psychiatric conditions [16].

Sensory Irritation

"Sensory irritation" refers to acute and reversible eye, nose and throat irritation, with no objective inflammatory changes. Related reflex symptoms may include nasal obstruction and rhinorrhea. These symptoms also characterize the state of *nonspecific nasal hyperreactivity*, a hallmark of the most common form of non-allergic rhinitis. Hypothesized mechanisms of reflex response to non-specific physical and chemical stimuli include epithelial cell activation, as well as neural

reflexes (sometimes referred to as "neurogenic inflammation") [17].

Sensory irritation is a prominent component of nonspecific building-related illness (also known as "sick building syndrome") [18]. Potential triggers found in indoor air include extremes of temperature and humidity, combustion products (from malfunctioning combustion appliances, re-entrained automotive exhaust, or cigarette smoke), volatile organic compounds or "VOCs" (from building materials, furnishings, and microbial overgrowth), and reactive chemicals (such as chlorine and ammonia found in household and commercial cleaning products). Often, however, patterns of elevated symptoms occur without identification of an offending agent [19].

Occupational Rhinitis - General

In 2009, The European Academy of Allergology and Clinical Immunology (EAACI) published a consensus paper laying out a scheme for the classification of work-related rhinitis that parallels that commonly used for work-related asthma [20]. Under this scheme, work-related rhinitis is broadly classified as either allergic or non-allergic (irritant) in nature. Further, the diagnosis is subdivided by whether rhinitis is *caused* by work ("occupational rhinitis") or *exacerbated* by work ("work-exacerbated rhinitis"). Also included in the review is an algorithm for the diagnosis of occupational allergic rhinitis. Of note, for allergens for which skin test reagents (or in vitro tests) are not available, this algorithm advocates either: (1) specific nasal provocation testing or (2) cross-shift evaluation in the workplace.

Occupational Allergic Rhinitis

The symptoms of occupational allergic rhinitis, like nasal allergies to common environmental aeroallergens, include nasal pruritus, sneezing, rhinorrhea, and nasal blockage. Like occupational asthma, occupational allergic rhinitis can involve either exacerbation of a pre-existing condition or de novo sensitization. An individual who became sensitized to mold spores or grass pollen as a child or adolescent, for example, could encounter the offending allergen in the course of their duties as an air conditioning mechanic or landscaper. The epidemiology of occupational allergic rhinitis has been reviewed in detail [21]. The list of agents causing occupational allergic rhinitis includes the same high- and low-molecular weight sensitizers that are known to cause occupational asthma (Table 1). Consistent with this fact, many observers believe that, for a given antigen, the development of occupational rhinitis may precede the development of occupational asthma [22, 23•].

Table 1 Selected agents causing occupational allergic rhinitis[a]

General class	Specific agent	Occupation affected
High molecular weight	Baking flour; alpha amylase	Bakers
	Animal proteins (urinary, salivary, dander)	Laboratory animal handlers
		Veterinary personnel
	Proteolytic enzymes	Detergent manufacturers
	Mold spores	Librarians; composters; maintenance personnel
	Insect antigens	Flood control workers Pharmaceutical workers (antigen preparation)
	Natural rubber latex	Health care personnel
		Food service workers
		Florists
	Psyllium	Health care personnel
Low molecular weight	Trimellitic anhdride	Chemical workers
	Cyanoacrylates	Cosmetologists
		Dental technicians
	Persulfates	Hairdressers
	Quaternary ammonium disinfectants	Health care personnel
	Diisocyanates (polyurethane component)	Auto body painters
		Boat builders
		Orthopedic technicians
	Plicatic acid (from Western Red Cedar)	Sawyers
	Abietic acid / collophony (from pine rosin)	Solderers (electronics)

[a] These agents can also cause occupational asthma

The distinction between irritant and allergic effects is sometimes difficult. For example, some substances (e.g., formaldehyde, glutaradehyde, diisocyanates) can act *either* as sensitizers or as irritants. Both irritation and allergy are also involved in so-called "priming." Priming occurs when there is augmented nasal responsiveness to allergen challenge after exposure to an irritant air pollutant [24–26]. Beyond this priming effect, selected air pollutants (e.g., diesel exhaust particles and second-hand tobacco smoke) may act as adjuvants to initial allergic sensitization [27, 28].

From a reciprocal perspective, the presence of pre-existing allergic inflammation of the upper airway may confer augmented upper airway sensitivity to air pollutants, both from the standpoint of subjective irritation [29] and objective nasal obstruction [30–32]. Consistent with these observations, at least 40 % of individuals with allergic rhinitis also complain of non-specific reactivity to physical and chemical stimuli [33].

Occupational Irritant Rhinitis

Occupational irritant rhinitis occurs across a spectrum of severity, ranging from acute reversible sensory irritation to chronic erosive rhinitis. Symptoms of irritant rhinitis can include nasal discomfort, rhinorrhea, congestion, post-nasal drip, sinus headache, and, on occasion, epistaxis. A number of different industrial chemicals and manufacturing processes have been associated with irritant rhinitis and/or sinusitis in workers (Table 2). Among these are woodworking, pulp mill work, spice grinding, exposure to fuel oil ash, nickel fumes, or dicumylperoxide in industry, and use of glutaraldehyde in medical sterilization [34–40]. Office-based work processes that have proven problematic to selected individuals include use of photocopiers and/or laser printers (potential ozone exposure) and use of carbonless copy paper [41, 42].

A number of studies have documented the effects of photochemical air pollution on the upper respiratory tract. Two such studies were carried out in a heavily polluted portion of Mexico City, where ozone levels are far in excess of both US and Mexican standards. These studies compared urban residents with residents of an unpolluted locale, as well as examining visitors to the city who came from more rural areas. The results were dramatic: permanent residents showed squamous metaplasia, loss of normal cilia, vascular congestion, and glandular atrophy on nasal biopsy. Short-term visitors, on the other hand, developed reversible epithelial desquamation and neutrophilic inflammation, which resolved after returning to their home towns [43, 44].

A variant of irritant rhinitis involves acute exposures. It has been observed that one-time high-level exposures to an irritant gas, vapor, or smoke can initiate persistent nasal symptoms, similar to the situation for irritant-induced asthma (also known as "reactive airways dysfunction syndrome" or "RADS") [45]. Meggs has suggested that irritant-induced rhinitis be termed "reactive upper airways dysfunction syndrome," or "RUDS" [46]. Although biopsies of the nasal mucosa among individuals acutely exposed to irritants have reportedly shown epithelial desquamation, defective epithelial cell junctions, and increased numbers of nerve fibers, the analogy between RADS and RUDS is limited by the lack of objective testing criteria for the latter [47].

Table 2 Selected occupational irritants

Occupation	Irritant
Agricultural workers	Ammonia, nitrogen dioxide, hydrogen sulfide
Custodians	Ammonia, bleach (hypochlorite), chloramines
Firefighters	Smoke, hazardous materials releases
Food service workers	Cooking vapors, cigarette smoke
Health professionals	Glutaraldehyde, formaldehyde
Laboratory workers	Solvent vapors, inorganic acid vapors/mists
Military personnel	Zinc chloride smoke
Power plant and oil refinery workers	Sulfur dioxide
Printers, painters	Solvent vapors
Pulp mill workers	Chlorine, chlorine dioxide, hydrogen sulfide
Railroad workers, miners, truck drivers	Diesel exhaust
Refrigeration workers (commercial)	Ammonia
Roofers, pavers	Asphalt vapors, PAHs[a]
Swimming pool service workers	Chlorine, hydrogen chloride, nitrogen trichloride
Waste water treatment workers	Chlorine, hydrogen sulfide
Welders	Metallic oxide fumes, nitrogen oxides, ozone
Woodworkers	Wood dust

[a] Polycyclic aromatic hydrocarbons (also skin and lung carcinogen)

(Reprinted from Shusterman [76]; with permission from Springer/Current Medicine Group)

Rhinitis and Asthma

Rhinitis and asthma are often co-morbid conditions. As noted above, the onset of occupational allergic rhinitis may precede that of asthma in a given individual, particularly if the sensitizer is a high molecular weight antigen [22, 23•]. Postulated mechanisms for this link, besides co-exposure of the upper and lower respiratory tracts to the same pollutants and allergens, include: (1) aspiration of upper airway secretions into the lower airway; (2) neural and biochemical reflexes linking the upper and lower airway ("naso-bronchial reflex"); and (3) decreased conditioning of inspired air resulting from mouth-breathing (resulting in increased pollutant load and osmotic stress on the lower airway). Selected mechanistic studies bolster this model, providing further rationale for early recognition and treatment of occupational rhinitis [48, 49].

Sinusitis

Relatively few studies have examined the endpoint of sinusitis and occupational exposures. Surveys of furriers, spice workers, vegetable picklers, hemp workers, and grain and flour workers all include increased prevalence rates for self-reported sinusitis [50–54]. Pathophysiologically, the causal sequence for an occupational sinusitis may include initial allergic or irritant rhinitis, ciliastasis (with impaired clearance of pathogenic organisms), mucous membrane swelling (with occlusion of sinus ostia and impaired drainage), and, finally, infection and mucosal remodeling.

Nasal Septal Perforation

Nasal septal perforation is an unusual toxicologic outcome associated with protracted and high-level exposure to chromates (as in the electroplating industry). Chromates (Cr^{6+} compounds) are also of concern with respect to carcinogenesis in the upper and lower respiratory tract [55, 56]. Differential diagnostic considerations in such cases should include such non-occupational causes as Wegener's granulomatosis and recreational drug use (i.e., cocaine).

Sinonasal Cancer

A variety of occupations and imputed exposures have been linked with the development of malignant neoplasms of the paranasal sinuses. The strongest (and most consistent) associations include cigarette smoking (squamous cell carcinoma) and leather- and wood-dust exposed workers (adenocarcinoma) [57, 58]. Workers engaged in nickel refining, chrome refining and plating, and selected aspects of textile and food processing have also been found to be at risk in some studies [59–61]. In addition, the potential of formaldehyde to produce nasopharyngeal cancer in humans is now widely recognized [62–64].

Diagnosis and Management

Since irritant-associated symptoms—such as nasal congestion and rhinorrhea—may mimic an allergic response, the treating health professional may be faced with a diagnostic challenge in determining responsible etiologic agents and pathophysiologic processes. A patient's report of predominantly irritant symptoms rather than itching or sneezing, as well as a high prevalence of symptoms among co-workers supports a diagnosis of irritant rhinitis. In irritant rhinitis, the laboratory workup is essentially "negative," including a lack of systemic eosinophilia, the predominance of neutrophils on nasal smear, and—when applicable—a lack of in vivo or in vitro reactivity to identified workplace allergens. Air monitoring data may be of assistance in industrial settings, but are more often a source of frustration in the investigation of so-called "problem buildings," since symptoms may be reported in settings in which levels of air contaminants are low relative to current occupational exposure limits.

A number of diagnostic techniques may be useful in documenting upper airway responses to environmental agents [65]. Those routinely available in otolaryngology and allergy practice include nasal endoscopy, radiographic imaging of the nose and paranasal sinuses, and allergy testing. The latter includes in vivo testing (epicutaneous skin prick) and in vitro testing (immunoassays for specific IgE). Unfortunately, the clinician investigating possible occupational allergic rhinitis may be hampered, in some cases, by the lack of available skin test or in vitro test reagents for the occupational agent in question.

Other techniques may prove valuable in diagnosing occupational or environmental upper airway conditions. These include measures of nasal patency (rhinomanometry, acoustic rhinometry, nasal peak flow measurement), nasal cytology sampling, olfactory testing, tests of mucociliary clearance, and—in research settings—nasal lavage with cytologic and/or biochemical analysis [5, 66–71]. Nasal challenge with suspected occupational allergens has been practiced more in Europe and Canada than in the United States [5, 72]. Endpoints typically studied include symptoms, nasal patency, and inflammatory markers in nasal lavage fluid [72]. However, nasal allergen challenge is likely to see more widespread use as the newly described diagnosis "local allergic rhinitis" (nasal mucosal sensitization without systemic atopy) gains traction among clinicians. Observations regarding this entity include not only local release of mediators in response to antigen challenge but also local production of antigen-specific IgE [73••]. To date, the implications of this diagnosis for occupational allergy practice have been largely unexplored.

Therapeutic Considerations

Exposure reduction should be the mainstay of any treatment plan, whether the disorder is irritant or allergic in nature [74].

At least one longitudinal study has confirmed that exposure removal in the case of occupational allergic rhinitis results in improvement in symptoms and disease-specific Quality of Life [75]. In some cases, substitution of a non-allergenic (or less irritant) material may be practical. Barring substation, engineering controls [or, rarely, personal protective equipment (i.e., respirator)] may be required. Medical treatment for occupational irritant rhinitis consists of nonspecific supportive measures (e.g., saline nasal lavage), and occasionally topical steroids. Patients troubled by reflex rhinorrhea may benefit from the topical cholinergic blocker, ipratropium bromide. Underlying non-allergic (e.g., "vasomotor") rhinitis may be triggered by cold air, fragrances, or irritants on-the-job, and may also respond to the topical antihistamine, azelastine. Occupational allergic rhinitis should be considered a potential harbinger of occupational asthma, and therefore managed aggressively with exposure reduction or reassignment. Use of conventional allergy therapy (i.e., oral and/or topical antihistamines and topical steroids) should be utilized cautiously because of the potential to mask symptoms while allowing progressive sensitization to take place with continued exposures.

Conclusions

Airborne irritants and allergens can affect the upper airway in a variety of ways. Irritant-related health effects range from acute, reversible sensory irritation at one extreme to nasal septal perforation and neoplasms at the other. Occupational allergic rhinitis may presage the development of occupational asthma, and should be included in the scope of conditions monitored for in workplace health surveillance programs. In some cases, distinguishing between irritant and allergic effects can be clinically challenging, with the two processes coexisting in some individuals. In general, exposure reduction is the most prudent and effective method for the primary prevention of occupational rhinitis and related conditions.

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Compliance with Ethics Guidelines

Conflict of Interest Dennis Shusterman declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with animal subjects performed by the author. With regard to the author's research cited in this paper, all procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000 and 2008.

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