



Environmental pollutants and allergic rhinitis

Thomas S. Higgins and Douglas D. Reh

Purpose of review

To review the current knowledge of the pathophysiology, epidemiology, and management of environmental pollutants and allergic rhinitis.

Recent findings

Both active cigarette smoking and passive exposure to cigarette smoke are associated with chronic rhinitis and sinusitis. Matrix metalloproteinase 9, which is thought to contribute to the pathophysiology of allergy, is elevated in children with passive cigarette smoke exposure compared with controls. Ground-level ozone and particulate matter exposure is associated with an allergic-type response and may increase sensitization to other allergens. Certain occupational exposures can cause nasal irritation and local cytotoxic effects. Evidence suggests that rhinitis symptomatology may often precede the development of occupational asthma.

Summary

Environmental factors have been noted to induce sinonasal mucosal irritation and often contribute to the multifactorial cause of chronic rhinitis and allergic rhinitis. Cigarette smoke is a common irritant that impacts the innate immune function of the sinonasal epithelial cells, and creates local irritation and cytotoxic effects. Both active smoking and exposure to second-hand smoke increase the risk of chronic rhinitis. Many other environmental pollutants are associated with chronic rhinitis, including ozone, particulate matter, and occupational irritants. The management of chronic rhinitis associated with environmental exposures is similar to the management of other types of chronic rhinitis. Although often not feasible, avoidance is probably the most effective course.

Keywords

allergic rhinitis, environmental, pollutants, tobacco

INTRODUCTION

Many environmental factors have been noted to induce sinonasal mucosal irritation, and multiple pathophysiologic mechanisms have been elucidated to describe these effects. Environmental pollutants that have been associated with chronic rhinitis include nitrogen oxides, sulfur dioxide, large and small particulate matter, carbon monoxide, and volatile organic compounds. Cigarette smoke is probably the most common medium for exposure to many of these toxins; however, exposure can also occur from occupational hazards, the urban environment, and ozone. Most cases of chronic rhinitis likely have a multifactorial causative profile, making establishing a cause for the patient's condition difficult.

CIGARETTE SMOKE

Cigarette smoke exposure can be divided into primary smoking exposure and secondary 'passive' or 'second-hand' smoking exposure. The World

Health Organization estimates that 35% of men and 22% of women in developed countries smoke cigarettes. They also estimate that 40% of children worldwide are exposed to passive smoking at home [1].

Previous population-based studies have provided conflicting information regarding the potential correlation between tobacco smoke and allergic rhinitis. Exposure to second-hand smoke (SHS) in adults was associated with increased prevalence of chronic rhinosinusitis in two case-control studies [2,3]. Whereas studies demonstrate that cigarette

The Johns Hopkins Sinus Center, Department of Otolaryngology and Head & Neck Surgery, Johns Hopkins Medical Institutions, Baltimore, Maryland, USA

Correspondence to Douglas D. Reh, MD, Sinus Center, Department of Otolaryngology and Head & Neck Surgery, Johns Hopkins Medical Institutions, 601N. Caroline St, 6th Floor, Baltimore, MD 21287-0910, USA. E-mail: dreh1@jhmi.edu

Curr Opin Otolaryngol Head Neck Surg 2012, 20:209–214

DOI:10.1097/MOO.0b013e3283534821

KEY POINTS

- Environmental pollutants associated with chronic rhinitis include cigarette smoke, ozone, particulate matter, and occupational irritants.
- Both passive and active cigarette smoking are associated with chronic rhinitis and sinusitis.
- Ground-level ozone exposure causes a type 1 hypersensitivity-like reaction and is associated with a higher risk of allergic rhinitis and asthma.
- Particulate matter exposure from either automobile traffic exposure or industry has pro-inflammatory effects and contributes to increased allergic rhinitis and chronic respiratory problems.
- Occupational rhinitis can greatly affect a worker's productivity and quality of life. Identifying and limiting exposure to suspected triggers is important to the management of this condition.

smoke damages the sinonasal mucosa and manifests clinical pathology, some studies have demonstrated a negative association between cigarette smoke and allergic rhinitis. A recent study found that smoking was associated with decreased prevalence of allergic rhinitis but increased prevalence of nasal congestion and chronic rhinitis. This questionnaire-based cross-sectional study in Sweden of 18 087 individuals (62% response rate) found a higher prevalence of allergic rhinitis associated with nonsmokers than smokers ($P < 0.001$) [4]. In contrast, increased prevalence of chronic rhinitis and nasal congestion was associated with a positive smoking history ($P > 0.001$). Conversely, a population-based case-control study found that allergic rhinitis patients were more likely to report more current and past second-hand smoke exposure than nonallergic patients [5]. Patients with more SHS also reported more severe nasal symptoms such as nasal obstruction and drainage. Another study of 155 voluntary Croatia adolescents demonstrated a statistically significantly higher prevalence of allergic diseases in active smokers compared with nonsmokers ($P = 0.034$), but an even greater difference in passive smokers as opposed to nonsmokers ($P = 0.002$). Interestingly, total IgE levels were not statistically significantly different between active smokers and nonsmokers. In contrast, total IgE levels were significantly higher in passive smokers compared with nonsmokers ($P < 0.01$), and in passive smokers compared with active smokers ($P < 0.01$). The investigators mentioned that difference between passive and active smokers may be attributed to longer duration of exposure to tobacco smoke in passive

smokers [6[¶]]. Maternal smoking in pregnancy was associated with a higher prevalence of allergic rhinitis in 9–11-year-old children [odds ratio (OR) 1.425, 95% confidence interval (CI) 1.089–1.864, $P = 0.011$] [7].

The conflicting results in these studies may be due to the fact that many of them rely on self-reporting to establish the diagnosis of allergic rhinitis [5]. Therefore, whereas tobacco smoke may induce chronic rhinitis and increased nasal symptoms in specific patients, a common finding across most studies, the specific association with allergic rhinitis is less clear.

Of patients with allergic rhinitis, smoking is associated with the development of concurrent upper respiratory disorders, such as asthma. A prospective, observational study of 371 patients with allergic rhinitis without asthma at baseline following patients 10 years for the development of asthma compared current and past smokers with individuals who had never smoked. The incidence of severe asthma was statistically significantly higher in smokers than nonsmokers. They also found a positive dose-response curve among smokers in the incidence of severe asthma and uncontrolled asthma. Those individuals who smoked between 1 and 10 pack-years had an OR of 1.47 (95% CI 0.46–4.68) versus nonsmokers of severe asthma, whereas those individuals with more than a 20-pack-year history of smoking had an OR of 5.59 (95% CI 1.44–21.67) of severe asthma. In terms of incidence of uncontrolled asthma, individuals with up to 10 pack-years of smoking had an OR of 5.51 (95% CI 1.73–17.54) of developing uncontrolled asthma, whereas individuals with over 10 pack-years of smoking had an OR of 13.38 (95% CI 4.57–39.19) [8[¶]].

Multiple prior studies have provided evidence of a biologic rationale for how SHS exposure could plausibly contribute to allergic rhinitis risk. Cigarette smoke creates local irritation and cytotoxic effects and impacts the innate immune function of sinonasal epithelial cells [9]. Histopathologically, enhanced T-cell activation and antimicrobial peptide human β -defensin 2 are observed with eosinophilic infiltration in the sinonasal mucosa. Cigarette smoke also causes direct mucosal damage from activation of the complement system. Deficiency in complement components C3 and factor B has been found to be protective against such damage [10]. In addition, matrix metalloproteinase 9 (MMP 9), a gelatinase associated with tissue remodeling and thought to contribute to the pathophysiology of allergy, has been studied in relation to smoking. A cross-sectional study of 39 children 7–16 years of age demonstrated statistically significantly higher levels of MMP 9 in

nasal secretions of children with passive cigarette smoke exposure compared with children without passive cigarette smoke exposure [11[¶]].

Previous studies have documented the impact of SHS on nasal physiology and function. Willes *et al.* [12] analyzed nasal symptoms and airflow response of 18 individuals with a reported history of SHS sensitivity by exposing them to sidestream tobacco smoke, the major component of SHS. Although the study lacked an appropriate control group, eye irritation, nasal irritation, nasal congestion, and rhinorrhea were the most affected symptoms after exposure to sidestream tobacco smoke and correlated well with self-reported severity with historical SHS exposure. Increased nasal airway resistance and reduced maximum inspiratory flow were also observed after exposure to sidestream tobacco smoke. In a study of 23 healthy individuals grouped on the basis of their SHS sensitivity, both SHS-sensitive and nonsensitive individuals had increased symptoms of rhinorrhea, nasal congestion, and headache following sidestream smoke exposure [13,14]. Individuals with known SHS sensitivity also had more severe symptoms than those without previous history of SHS-related rhinitis [13,14]. These studies suggest that certain people may be predisposed to the effects of SHS in terms of increased sinonasal physiological and symptom response. Patients with SHS sensitivity may be at higher risk for developing chronic upper respiratory inflammation and disease, such as chronic sinusitis, asthma or rhinitis, in response to SHS.

OZONE

Ozone, or trioxxygen (O₃), is a less stable allotrope of oxygen that functions as a barrier to electromagnetic radiation in the upper atmosphere. The interaction of some pollutants with ultraviolet light creates ground-level ozone that can act as an irritant. Ozone is known to irritate respiratory epithelium, and chronic exposure is associated with bronchitis, asthma, and increased allergic disease. Exposing eye extract to ozone causes a higher level of IgE reactivity [15]. Acute exposure to ozone has been shown to induce epithelial hyperplasia and cause inflammatory responses in the respiratory epithelium of both rats and monkeys. Ozone exposure also enhances allergen-induced mucous cell metaplasia in both nasal transitional and respiratory epithelium [16]. In the guinea-pig model, hydroxyl radicals have been shown to contribute to the development of ozone-induced nasal airway hyper-responsiveness to tachykinins [17]. Another study of ozone exposure of allergic rats demonstrated increased numbers of eosinophils in the

maxillary sinus (four times greater than normal controls), nasolacrimal duct (2.5 times increased), and proximal midseptum (1.5 times increased). Ozone exposure caused increased storage of intra-epithelial mucosubstances in the septum (45%) and maxillary sinus (55%) in allergic versus control rats. This study also found that gamma-tocopherol blocked ozone-induced MUC5AC gene expression [18].

Population-based studies have supported these biologic findings. A study of 170 children with ambient ozone exposure analyzed nasal lavage fluid during peak and trough periods of ozone exposure. They found an initial statistically significant positive association between outdoor ozone concentration and levels of leukocytes and eosinophilic cationic protein in nasal secretions. The response was dose-dependent but, interestingly, the nasal mucosa seemed to eventually adapt with constant high levels of ozone [19].

A prospective cohort analysis was performed of parental responses to International Study of Asthma and Allergies in Childhood questionnaires, along with allergy evaluation, conducted in 1340 school children in metropolitan cities and industrial areas over a 2-year period. This study found an association between ozone exposure and wheeze and allergic rhinitis, as well as an increased rate of newly developed sensitization to outdoor allergens [20[¶]].

PARTICULATE MATTER

Particulate matter is comprised of minute solid material suspended in a gaseous or liquid medium. Particulate matter is categorized according to size. Particulate matter₁₀ includes particles smaller than 10 micrometers and is considered significant because these particles can bypass the nasal and pharyngeal filtering processes to reach the bronchioles and alveoli. Particulate matter_{2.5}, or particles smaller than 2.5 micrometers, can extend further and lead to cardiopulmonary impairment [21]. Particulate matter is more common in the urban environment where there are more confined motor vehicle emissions and industrial exposure. Allergic rhinitis, chronic rhinitis, and nasal congestion were all associated with living in larger, more urban cities than rural areas ($P < 0.001$) [4]. Table 1 summarizes the Environmental Protection Agency's (EPA) National Ambient Air Quality Standards (NAAQS) for common particulate irritants. One of the most widely studied components of urban particulate matter is diesel exhaust, which can persist for prolonged periods in the atmosphere. Diesel exhaust can have a range of particle sizes from nanoparticles to large, coarse particles. It consists

Table 1. The National Ambient Air Quality Standards (NAAQS)

Pollutant (final rule cite)	Primary/secondary	Averaging time	Level	Form
Carbon monoxide	Primary	8-h	9 ppm	Not to be exceeded more than once per year
		1-h	35 ppm	
Lead	Primary and secondary	Rolling 3 month average	0.15 µg/m ³	Not to be exceeded
Nitrogen dioxide	Primary	1-h	100 ppb	98th percentile, averaged over 3 years
	Primary and secondary	Annual	53 ppb	Annual mean
Ozone	Primary and secondary	8-h	0.075 ppm	Annual fourth highest daily maximum 8-h concentration, averaged over 3 years
Particle pollution				
PM _{2.5}	Primary and secondary	Annual	15 µg/m ³	Annual mean, averaged over 3 years
		24-h	35 µg/m ³	98th percentile, averaged over 3 years
PM ₁₀	Primary and secondary	24-h	150 µg/m ³	Not to be exceeded more than once per year on average over 3 years
Sulfur dioxide	Primary	1-h	75 ppb	99th percentile of 1-h daily maximum concentrations, averaged over 3 years
	Secondary	3-h	0.5 ppm	Not to be exceeded more than once per year

Primary standards provide public health protection, including protecting the health of 'sensitive' populations such as asthmatic patients, children, and the elderly. Secondary standards provide public welfare protection, including protection against decreased visibility and damage to animals, crops, vegetation, and buildings. Reproduced from <http://www.epa.gov/air/criteria.html>.

of a carbonaceous core of polycyclic aromatic hydrocarbons (PAHs) and their derivatives with a broad surface area that can absorb chemicals [22]. Direct effects from diesel exhaust exposure have been observed on multiple cell types in healthy and asthmatic patients. Diesel exhaust exposure has been shown to increase upper airway expression of inflammatory cytokines and chemokines as well as increased degranulation and chemical release from eosinophils, mast cells, basophils, neutrophils, B cells, and macrophages. In mild asthmatic patients, this biochemical shift has been shown to manifest clinically as increased airway resistance, increased sputum IL-6, and hyper-responsiveness to methacholine challenge. Clinical effects from exposure to diesel exhaust have also been noted on nasal provocation tests. Immediate response to exposure is similar to a type 1 hypersensitivity response with histamine release within minutes of exposure. Increased cellular inflammation and increased chemokine production are noted within hours. Long-term exposure has been associated with possible increased allergic sensitivity to other allergens, which may partially explain increased allergic disease, such as allergic rhinitis, in urban versus rural settings [23].

The urban environment setting is not the only area at risk for diesel exhaust exposure. A study of 1839 adults living close to a highway in communities in the Swiss alpine valley found an association with wheezing without cold (OR 3.10, 95% CI 1.27–7.55) and chronic cough (OR 2.88, 95% CI 1.17–7.05) in adults living less than 200 m from the highway compared with adults living further away.

This study also reports that symptoms reached baseline levels in adults at least 500 m from a highway [24²²].

Whereas most studies have focused on asthma and respiratory disease, there was a recent population-based study that evaluated the correlation of air pollution and allergic rhinitis. A time-series analysis of patients visiting general practitioners for allergic rhinitis in Beijing, China found a strong association between three air pollutants (PM₁₀, SO₂ and NO₂) and increased daily outpatient visits for allergic rhinitis after controlling for confounding factors such as the day of the week and meteorological factors [25]. A questionnaire study of 9319 adults with self-reported traffic exposure found that living within 100 m from roads with a 24-h mean traffic intensity of greater than 10 cars per min was associated with a higher prevalence of self-reported asthma triggered by allergic factors (OR 1.83, 95% CI 1.23–2.72) and allergic rhinitis (OR 1.30, 95% CI 1.05–1.61) [26].

The association of combustion reaction particulate matter from home-related appliances with the risk for allergic disease is less clear. A population-based cross-sectional study of 3471 persons described that self-reported frequent use of woodstoves, candles or gas cookers was not significantly associated with an increased risk of rhinitis symptoms or atopy [27]. This study confirmed findings from prior studies, although one previous study did observe increased respiratory complaints in individuals with improperly maintained or dysfunctional woodburning stoves [28].

OCCUPATIONAL RHINITIS

The workplace can be a significant source of exposure to environmental irritants. Establishing a causal relationship between occupational exposure and chronic rhinitis is not a simple task, but is a common request in workman's compensation cases. The European Academy of Allergy and Clinic Immunology Task Force on Occupational Rhinitis defined the disease as an inflammatory condition of the nose 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 outside the workplace. As opposed to occupational rhinitis, another condition called work-exacerbated rhinitis may exist in which the symptoms are worsened by, but not caused by, exposures in the workplace. It is unclear if occupational rhinitis necessarily precedes occupational asthma [29]. A study in Finland examining cases of occupational rhinitis and asthma reports to the Finnish Register of Occupational Diseases found that occupational asthma patients were older than occupational rhinitis patients, suggesting a possible temporal relationship [30].

A classification system for occupational rhinitis has been proposed based on the pathophysiologic cause of rhinitis: annoyance, irritational, corrosive, and immunologic [31]. Annoyance response includes increased olfactory awareness of occupational exposures with no significant inflammatory response. Irritational responses include nonspecific inflammation without an immunologic or allergic basis. An example of this type of response is neurogenic inflammation seen with substance P release from exposure to cigarette smoke, capsaicin, paints, and coal. Corrosive response is a severe nasal inflammatory response that can lead to ulceration and chemical burn. This type of reaction occurs from exposure to high concentrations of irritating soluble chemical gases, such as chlorine, sulfur dioxide, and ammonia. Finally, immunologic responses may occur that are similar to IgE-mediated allergic responses. There are many substances that can trigger immunologic responses. In Finland, some of the most common implicated allergens causing occupational rhinitis included animal dander, flowers, wood dusts, textiles, phthalic acid anhydrides, and storage mites. The occupations with the highest relative risk ratios for occupation rhinitis included furriers, bakers, and livestock breeders [30].

MANAGEMENT OF ENVIRONMENTAL-RELATED CHRONIC RHINITIS

Chronic rhinitis is typically multifactorial; thus identifying a single cause is difficult. The treatment

strategy for chronic rhinitis secondary to environmental irritants is similar to the management of other types of chronic rhinitis. Medical and surgical options are essentially the same. It is important to note that the patient may have concomitant allergic and nonallergic rhinitis; thus, treating allergic disease may help the patient's symptoms, while the treatment plan may also need to include the identification and avoidance of other nonallergic triggers. It may be beneficial for the patient to keep a symptom diary to help identify exacerbating and relieving factors. Once the possible triggers are identified, the most effective way to limit symptoms is avoidance. Most patients, unfortunately, are unable to avoid all of their triggers; however, limiting exposures can help their medical therapy work more effectively. Although drastic environmental changes (i.e. changing jobs or living location) can be effective for some patients, the physician should caution the patient that this process does not always provide the desired effect. For example, a patient living in an urban environment who moves to a rural environment may simply trade nonallergic exposures for more allergic-type exposures. In addition, the physician may be asked to communicate with the patient's workplace about strategies for limiting the patient's exposure to occupational irritants.

CONCLUSION

Chronic rhinitis, both allergic and nonallergic types, is associated with environmental pollutants. The most highly studied environmental irritants include cigarette smoke, ozone, particulate matter, and occupational irritants. Most cases of chronic rhinitis likely have a multifactorial causative profile, making establishing a cause for the patient's condition difficult. As with management of other types of chronic rhinitis, avoidance of triggers, in conjunction with medical therapy, is key to providing symptomatic relief.

Acknowledgements

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 220).

1. Shafey O, Eriksen M, Ross H, *et al.* Prevalence and Health. In: The Tobacco Atlas. 3rd ed. Atlanta, GA, USA: American Cancer Society; 2009. pp. 18–25.

2. Reh DD, Lin SY, Clipp SL, *et al.* Secondhand tobacco smoke exposure and chronic rhinosinusitis: a population-based case-control study. *Am J Rhinol Allergy* 2009; 23:562–567.
 3. Tammemagi CM, Davis RM, Benninger MS, *et al.* Secondhand smoke as a potential cause of chronic rhinosinusitis: a case-control study. *Arch Otolaryngol Head Neck Surg* 2010; 136:327–334.
 4. Eriksson J, Ekerljung L, Pullerits T, *et al.* Prevalence of chronic nasal symptoms in West Sweden: risk factors and relation to self-reported allergic rhinitis and lower respiratory symptoms. *Int Arch Allergy Immunol* 2011; 154:155–163.
 5. Lin SY, Reh DD, Clipp S, *et al.* Allergic rhinitis and secondhand smoke: a population based study. *Am J Rhinol Allergy* 2011; 25:66–71.
 6. Mlinaric A, Popovic Grle S, Nadalin S, *et al.* Passive smoking and respiratory allergies in adolescents. *Eur Rev Med Pharmacol Sci* 2011; 15:973–977.
- This study of voluntary Croatian adolescents found that passive smoking exposure may have a higher association with allergic disease than active smoking.
7. Civelek E, Yavuz ST, Boz AB, *et al.* Epidemiology and burden of rhinitis and rhinoconjunctivitis in 9- to 11-year-old children. *Am J Rhinol Allergy* 2010; 24:364–370.
 8. Polosa R, Russo C, Caponnetto P, *et al.* Greater severity of new onset asthma in allergic subjects who smoke: a 10-year longitudinal study. *Respir Res* 2011; 12:16.
- This study showed that, among patients with allergic disease, the severity of new-onset asthma was worse in those who smoked.
9. Yamin M, Holbrook EH, Gray ST, *et al.* Cigarette smoke combined with Toll-like receptor 3 signaling triggers exaggerated epithelial regulated upon activation, normal T-cell expressed and secreted/CCL5 expression in chronic rhinosinusitis. *J Allergy Clin Immunol* 2008; 122:1145.e3–1153.e3.
 10. Davis KS, Casey SE, Mulligan JK, *et al.* Murine complement deficiency ameliorates acute cigarette smoke-induced nasal damage. *Otolaryngol Head Neck Surg* 2010; 143:152–158.
 11. De S, Leong SC, Fenton JE, *et al.* The effect of passive smoking on the levels of matrix metalloproteinase 9 in nasal secretions of children. *Am J Rhinol Allergy* 2011; 25:226–230.
- This study in children demonstrated that passive smoking exposure raises levels of metalloproteinase 9 in nasal secretions, which seems to be an important pathophysiological mechanism of chronic rhinitis in these patients.
12. Willes SR, Fitzgerald TK, Bascom R. Nasal inhalation challenge studies with sidestream tobacco smoke. *Arch Environ Health* 1992; 47:223–230.
 13. Bascom R, Kulle T, Kagey-Sobotka A, Proud D. Upper respiratory tract environmental tobacco smoke sensitivity. *Am Rev Respir Dis* 1991; 143:1304–1311.
 14. Willes SR, Fitzgerald TK, Permutt T, *et al.* Acute respiratory response to prolonged, moderate levels of sidestream tobacco smoke. *J Toxicol Environ Health A* 1998; 53:193–209.
 15. Eckl-Dorna J, Klein B, Reichenauer TG, *et al.* Exposure of rye (*Secale cereale*) cultivars to elevated ozone levels increases the allergen content in pollen. *J Allergy Clin Immunol* 2010; 126:1315–1317.
 16. Wagner JG, Hotchkiss JA, Harkema JR. Enhancement of nasal inflammatory and epithelial responses after ozone and allergen coexposure in Brown Norway rats. *Toxicol Sci* 2002; 67:284–294.
 17. Ho CY, Tan CT, Tsai HH, Kou YR. Ozone-induced nasal hyper-responsiveness to tachykinins in guinea pigs. *Am J Rhinol* 2008; 22:463–467.
 18. Wang DY. Risk factors of allergic rhinitis: genetic or environmental? *Ther Clin Risk Manag* 2005; 1:115–123.
 19. Kopp MV, Ulmer C, Ihorst G, *et al.* Upper airway inflammation in children exposed to ambient ozone and potential signs of adaptation. *Eur Respir J* 1999; 14:854–861.
 20. Kim BJ, Kwon JW, Seo JH, *et al.* Association of ozone exposure with asthma, allergic rhinitis, and allergic sensitization. *Ann Allergy Asthma Immunol* 2011; 107:214e1–219e1.
- This study found that ozone exposure increases the sensitivity to outdoor allergens, providing evidence for a possible mechanism for increased allergic disease in urban settings.
21. Pope CA 3rd, Burnett RT, Thun MJ, *et al.* Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA* 2002; 287:1132–1141.
 22. Riedl M, Diaz-Sanchez D. Biology of diesel exhaust effects on respiratory function. *J Allergy Clin Immunol* 2005; 115:221–228; quiz 229.
 23. Diaz-Sanchez D, Garcia MP, Wang M, *et al.* Nasal challenge with diesel exhaust particles can induce sensitization to a neoallergen in the human mucosa. *J Allergy Clin Immunol* 1999; 104:1183–1188.
 24. Hazenkamp-von Arx ME, Schindler C, Ragetti MS, *et al.* Impacts of highway traffic exhaust in alpine valleys on the respiratory health in adults: a cross-sectional study. *Environ Health* 2011; 10:13.
- This study found that adult individuals living close to a highway had increased risk of respiratory health issues regardless of living in an urban or rural environment. This finding indicates that exhaust has negative effects on respiratory health in both settings.
25. Zhang F, Wang W, Lv J, *et al.* Time-series studies on air pollution and daily outpatient visits for allergic rhinitis in Beijing, China. *Sci Total Environ* 2011; 409:2486–2492.
 26. Lindgren A, Stroh E, Nihlen U, *et al.* Traffic exposure associated with allergic asthma and allergic rhinitis in adults. A cross-sectional study in southern Sweden. *Int J Health Geogr* 2009; 8:25.
 27. Hersoug LG, Husemoen LL, Thomsen SF, *et al.* Association of indoor air pollution with rhinitis symptoms, atopy and nitric oxide levels in exhaled air. *Int Arch Allergy Immunol* 2010; 153:403–412.
 28. Matson U. Indoor and outdoor concentrations of ultrafine particles in some Scandinavian rural and urban areas. *Sci Total Environ* 2005; 343:169–176.
 29. Moscato G, Vandenplas O, Van Wijk RG, *et al.* EAACI position paper on occupational rhinitis. *Respir Res* 2009; 10:16.
 30. Hytonen M, Kanerva L, Malmberg H, *et al.* The risk of occupational rhinitis. *Int Arch Occup Environ Health* 1997; 69:487–490.
 31. Bardana EJ Jr. Occupational asthma and related respiratory disorders. *Dis Mon* 1995; 41:143–199.