Curr Allergy Asthma Rep (2016) 16:77
DOI 10.1007/s11882-016-0657-y

Occupational Respiratory Allergic Diseases in Healthcare Workers

Jacek M. Mazurek[1] · **David N. Weissman**[1]

© Springer Science+Business Media New York (outside the USA) 2016

Abstract Healthcare workers (HCWs) are exposed to a range of high and low molecular weight agents that are allergic sensitizers or irritants including cleaners and disinfectants, natural rubber latex, and various medications. Studies have shown that exposed HCWs are at risk for work-related rhinitis and asthma (WRA). Work-related rhinitis may precede development of WRA and should be considered as an early marker of WRA. Avoidance of causative exposures through control strategies such as elimination, substitution, engineering controls, and process modification is the preferred primary prevention strategy for preventing development of work-related allergic diseases. There is limited evidence for the effectiveness of respirators in preventing occupational asthma. If sensitizer-induced WRA is diagnosed, it is important to avoid further exposure to the causative agent, preferably by more rigorous application of exposure control strategies to the workplace. This review focuses on allergic occupational respiratory diseases in HCWs.

Keywords Healthcare workers · Rhinitis · Asthma · Occupational allergy · Occupational exposures · Allergy prevention and control

This article is part of the Topical Collection on *Occupational Allergies*

✉ Jacek M. Mazurek
JMazurek1@cdc.gov

David N. Weissman
DWeissman@cdc.gov

[1] Respiratory Health Division, National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention, Mailstop HG 900.2, 1095 Willowdale Rd., Morgantown, WV 26505, USA

INTRODUCTION

The World Allergy Organization defines allergy as "a hypersensitivity reaction initiated by immunological mechanisms. Allergy can be antibody- or cell-mediated" [1]. Allergic diseases such as allergic rhinitis, asthma, and allergic contact dermatitis are often caused by pathological immune responses to exogenous environmental or occupational antigens. Numerous studies have indicated that health care workers (HCWs) are at increased risk for respiratory diseases such as occupational rhinitis and asthma caused by hazardous exposures in the workplace [2–9]. However, only a limited number of studies have specifically addressed allergic respiratory diseases in HCWs [10–13]. This review focuses on allergic occupational respiratory diseases in US HCWs.

Healthcare Industry

In 2015, over 16.8 million (11.5 %) of 146.4 million US workers were employed in the *healthcare* industries [14]. Most of these were *ambulatory healthcare services* workers (7.5 million; 44.7 %), followed by *hospitals* (6.7 million; 39.7 %), and *nursing and residential care services* (2.6 million; 15.6 %) workers. Of *ambulatory healthcare services* workers, 3.2 million (42.5 %) were employed in *the offices of health practitioners* (e.g., physicians, dentists, chiropractors) and 2.7 million (36.0 %) in *home and other health care services*.

Among the *healthcare* industry workers, 77.3 % (13.0 million) were women, 16.8 % (2.8 million) were Black or African American, and 11.4 % (1.9 million) were Hispanics. Registered nurses was the occupation with the largest number of employed women (2.7 million) and the dental hygienists occupation had the highest proportion of employed women (96.4 %) [14].

Published online: 29 October 2016

Allergic Respiratory Diseases

Allergic respiratory diseases such as allergic rhinitis, rhinosinusitis, and asthma frequently result from immunoglobulin-E (IgE) antibody sensitization to occupational and environmental allergens (i.e., antigens that induce an IgE response). Once IgE sensitization has occurred, subsequent exposure to allergen can cross-link IgE found on the surfaces of mediator-releasing cells such as mast cells, leading to a cascade of vascular, smooth muscle, and inflammatory reactions in the airways. Allergic occupational diseases develop after a variable period of time during which sensitization to a workplace substance occurs [15]. Respiratory sensitization may be induced by the inhalation route as well as by skin exposure [16].

Allergic IgE sensitization is common in the US population. Salo and colleagues reported that an estimated 44.6 % of the population 6 years and older have serum specific IgE directed against at least one inhalant or food allergen [17•]. Prevalence of IgE sensitization to any indoor (30.3 %) and any outdoor allergen was similar (30.0 %) and greater than sensitization to foods (16.2 %). Half of those aged 20–29 years (50.8 %) and 30–39 years (49.7 %) were sensitized to any inhalant allergens with sensitization decreasing with age. A study of sensitization prevalence among US workers showed that among currently employed adults, 45.6 % had serum specific IgE for at least one of 15 inhalant allergens tested [18]. The same study showed that 26.6 % (24.2 % of healthcare and social assistance industry workers) of workers had a total serum IgE level ≥100 kUA/L. Results from the European Community Respiratory Health Survey 2 showed a positive association between specific IgE levels and the risk of respiratory allergen-related symptoms and indicated that specific IgE level is the most important predictor of allergen-related symptoms [19].

Not all persons with evidence of IgE sensitization have allergy symptoms [20]. In a Dutch study, 43 % of persons with detectable specific IgE to four common aeroallergens were asymptomatic [21]. Data from the 2014 US National Health Interview Survey (NHIS) showed that the prevalence of selected respiratory diseases among all adults aged ≥18 years was 7.7 % for allergic rhinitis (hay fever), 11.9 % for sinusitis, and 7.4 % for asthma [22]. These results were based on self-reported physician diagnosis of "hay fever," "sinusitis," or "asthma" in the 12 months prior to the interview and likely are underestimates.

Respiratory allergic conditions are associated with considerable direct and indirect costs and substantially affect patients' quality of life [23–28]. In the US, health care and treatment expenditures for allergic rhinitis have increased 84 % from the year 2000 ($6.1 billion) to the year 2005 ($11.2 billion) [28]. Approximately 30 % of patients reported that their nasal allergies caused them to miss work [25]. Nathan estimated that allergic rhinitis results in 3.5 million lost work days annually [29]. The overall annual costs of chronic rhinosinusitis in the US was estimated at $22 billion (in 2014 dollars) [27]. The estimated total cost of asthma increased 5.7 % from $53 billion in 2002 to $56 billion (2009 dollars) in 2007, approximately $3259 per person per year [23]. The authors reported that asthma accounted for a 66 % increase in work days lost and the value of additional days lost attributable to asthma per year was approximately $300 for each worker. Overall, asthma causes approximately 14.4 million work days lost per year. Moreover, costs of asthma increase in the presence of asthma exacerbations and with disease severity [30].

CLINICAL PROBLEMS

Work-Related Rhinitis

Rhinitis, defined as the presence of nasal congestion, rhinorrhea, sneezing, and/or itching, can be classified by etiology (allergic or non-allergic) and seasonality (seasonal or perennial) [31•, 32]. A subset of rhinitis, work-related rhinitis, is caused by allergic or non-allergic (irritant) factors in the workplace and can be categorized as occupational rhinitis (caused by factors related to work or the workplace environment) and work-exacerbated rhinitis (preexisting or concurrent rhinitis worsened by factors related to work or the workplace environment) [31•].

Precise estimates of work-related rhinitis prevalence and incidence are currently not available. A review of cross-sectional studies conducted in various working populations indicated that occupational rhinitis affects 10 to 60 % of HCWs [33]. Occupational exposures are important risk factors for work-related rhinitis. Rhinitis may appear as the first manifestation of a common allergic airway disease affecting the upper and lower airways and symptoms of rhinitis may precede non-occupational and occupational asthma [34–38]. In his review, Vandenplas summarized evidence for the association between rhinitis and asthma and underscored that work-related rhinitis should be considered as an early marker of WRA [38]. Work-related allergic rhinitis and asthma have common risk factors and are discussed below.

Work-Related Asthma

Work-related asthma, a subset of asthma, includes occupational asthma (asthma caused by factors related to work or the workplace environment) and work-exacerbated asthma (preexisting or concurrent asthma worsened by factors related to work or the workplace environment). Similarly to rhinitis, work-related asthma is caused by allergic or non-allergic (irritant) factors in the workplace [15, 39, 40••]. Symptoms

of WRA are identical to those in non-occupational asthma patients and often are associated with rhinoconjunctivitis [15, 41].

The prevalence of asthma among HCWs has been previously reported from the US and other countries [2, 4, 5, 8, 9, 42, 43]. Syamlal and colleagues analyzed lifetime asthma and asthma attack prevalence using the 1997–2004 NHIS data [44]. The authors found that the prevalence of lifetime asthma was highest among *health service* (11.5 %) and *health technologist and technicians* (11.5 %) occupations. Moreover, the prevalence of an asthma attack in the past year among individuals with asthma was also high among health-related occupations (i.e., *health assessment and treating* and *health service*). An estimated 42.3 % of those with asthma in the *health services, except hospitals* and 40.2 % of those in the *hospital* industry had an asthma attack in the past. Approximately 1 % (40,000 cases) of asthma cases reporting an asthma attack were attributed to employment for the *health services, except hospitals* industry workers and 0.3 % (10,000 cases) for the *hospital* industry workers [44].

These findings were consistent with a report by Delclos and colleagues who analyzed self-reported asthma data for 3650 Texas HCWs [2]. The overall asthma prevalence was 6.6 %; by occupation, the prevalence was 4.2 % for physicians, 7.3 % for nurses, 5.6 % for occupational therapists, and 4.5 % for respiratory therapists. Arif and colleagues in their cross-sectional survey of Texas licensed nurses found that among nursing professionals, registered nurses had the highest prevalence of asthma (10.2 %) followed by licensed practical nurses (8.0 %) and nurse practitioners (6.9 %) [43].

A recent analysis of the 2013 Behavioral Risk Factor Surveillance System (BRFSS) data from 21 states showed that asthma prevalence in the *health care and social assistance* industry workers ranged from 6.6 % in Nebraska to 15.2 % in Michigan [45]. Workers in *healthcare support* occupations in Michigan were found to have the highest asthma prevalence (21.5 %). Anderson and colleagues analyzed the 2006–2009 Washington State BRFSS data to estimate the prevalence of physician-diagnosed current asthma by 19 occupational groups [42]. The overall asthma prevalence for all workers in the state was 8.1 %. The prevalence of asthma was 11.2 % for workers in *other health services* (e.g., health aides/nursing aides) and 8.5 % for *health assessment, diagnosis and treatment professionals* (e.g., physicians, registered nurses). These two occupational groups had significantly higher prevalence of asthma symptoms caused or worsened by any current or past job compared with workers in *executive, administrative, and managerial* group.

WRA can be a fatal disease. Case reports described fatal asthma in a mill worker exposed to shark cartilage [46], in a worker who applied a polyurethane spray-on bedliner inside a van [47], and in a waitress exposed to environmental tobacco smoke at work [48]. To our knowledge, no reports of fatal WRA in HCWs have been published. However, during 1990–1999, of the 29,703 asthma decedents with known occupation, 2031 were associated with *healthcare and social assistance* industry sector and workers in *health services* and *hospitals* industries were associated with the highest proportionate mortality ratio for asthma [49]. In 2009, asthma was responsible for 3500 deaths among adults with current asthma [50].

Occupational Anaphylaxis

Any agent that causes asthma through IgE-sensitization may also potentially cause anaphylaxis, a systemic allergic reaction that can be life-threatening or fatal. When anaphylaxis occurs in the workplace, usually the causative agent is also present in the workplace [51•, 52]. Anaphylactic reactions may also result from non-occupational exposures or be the result of antigenic cross-reactivity between non-occupational and occupational allergens. Two recent reviews summarized published literature on occupational anaphylaxis. Moscato and colleagues reviewed various agents and tasks associated with occupational anaphylaxis [51•]. In HCWs, the occupational anaphylaxis was most frequently triggered by natural rubber latex (NRL), chemicals (disinfectants), and medications (see below). Quirce and Fiandor addressed the diagnosis and management of occupational anaphylaxis and underscored the importance of identification of the anaphylaxis trigger [52].

EXPOSURES

Multiple agents have been associated with work-related respiratory diseases. Workplace allergens are often high molecular weight (HMW) agents such as proteins that are >10 kDa molecular weight and cause IgE sensitization [15]. Sensitizing low molecular weight (LMW) agents are often reactive chemicals such as isocyanates. They may cause IgE sensitization or cause allergic disease after a latency through other immune mechanisms that remain to be fully characterized. LMW agents may act as haptens, binding to autologous or heterologous carrier proteins to form complete functional allergens [38, 53]. A recent study indicated that occupational asthma caused by LMW agents had a significantly higher risk of severity than asthma caused by HMW agents [54]. Vandenplas reviewed current evidence and determinants of allergic sensitization to occupational allergens [38]. The author discussed sensitizing potential of agents, at-risk occupations, the role of environmental risk factors (level of exposures, the mode and route of exposure, co-exposure to pollutants) and individual susceptibility (atopy, genetic factors, rhinitis, pre-existing non-specific bronchial hyper-responsiveness, gender).

Sources of Information on Occupational Asthmagens

Listings of agents associated with work-related respiratory diseases are continuously revised and new ones are reported. Based on information from published journal articles, Chan-Yeung and Malo developed a list of agents causing occupational asthma with key references [55]. This list is also available on the Commission des normes, de l'équité, de la santé et de la sécurité du travail (CNESST) web site at http://www.asthme.csst.qc.ca/document/Info_Med/IdCauses/Bernstein/AgentsAnglais.pdf. The Association of Occupational and Environmental Clinics (AOEC), a network of approximately 60 occupational and environmental clinics from the US, Canada, and Germany, established formal criteria for agents causing WRA to be designated as sensitizers. Using the AOEC criteria, Rosenman and Becket recently reviewed peer-reviewed medical literature and developed a list of asthmagens that meet specified criteria for causing WRA by sensitization or acute irritant-induced asthma [56]. Of the 327 asthma-causing agents, 175 agents were recognized as sensitizers. The AOEC list is available at http://www.aoecdata.org/ExpCodeLookup.aspx [57••].

Baur has systematically examined the agents and worksites causing allergic or irritant occupational asthma using the modified Royal College of General Practitioners grading system [58]. The author identified 372 different causes of allergic occupational asthma and found the strongest evidence of association with allergic asthma for exposure to laboratory animals. Only a few agents and worksite allergens were potentially associated with health care settings (with moderate/weak evidence for associations with allergic asthma). Quirce and Bernstein reviewed the most common and novel causes of occupational asthma [59]. A summary of information on agents associated with respiratory allergies in health care settings from these and other sources [4, 55, 57••, 59–62, 63•] is shown in Table 1 and described below.

Disinfecting Products

Disinfectants currently in use for high-level disinfection of heat-sensitive medical devices include glutaraldehyde, ortho-phthalaldehyde (OPA), hydrogen peroxide, and peracetic acid with hydrogen peroxide. Glutaraldehyde and peracetic acid–hydrogen peroxide mixture have been recognized as sensitizers and an important cause of WRA in HCWs [3, 64]. In 1999, OPA was introduced as a safer alternative to glutaraldehyde for high-level disinfection of heat-sensitive medical devices because glutaraldehyde had been associated with an eye and skin irritation, sensitization, and occupational asthma. In 2013, Pala and Moscato reviewed irritancy and sensitization potential of OPA and identified reports of immunologic reactions caused by OPA in patients and HCWs [65]. Fujita and colleagues described a case of WRA associated with exposure to OPA in a nurse in an endoscopy unit [66]. The laboratory test results were negative for eosinophilia or elevated serum total IgE. No pulmonary function test or specific inhalation challenge was done. Pala and Moscato identified additional studies by Fujita [67] and by Miyajima [68] reporting a high proportion of endoscopy disinfection workers exposed to OPA who complained of respiratory symptoms. These findings were consistent with a report by Johnson and colleagues who found that inhalation of OPA vapor in mice can induce respiratory allergy [69].

In contrast, a recent investigation of employee exposure to OPA did not find evidence of associated adverse health effects [70••]. The investigators collected blood samples for antibodies to OPA, did puncture skin tests for allergic reactions to common allergens and OPA, and evaluated employee respiratory symptoms and exposures to OPA. Of 151 participants (74 in an OPA exposed group), 5 (1 in an OPA exposed group) had positive allergy skin tests to OPA, no participants had OPA-specific antibodies, and very few reported symptoms related to work.

Cleaning Products

Cleaning and disinfecting products for use on building surfaces have been associated with allergic diseases. Folletti and colleagues provided a systematic review of epidemiological studies linking exposure to cleaning products and the risk of asthma and rhinitis in cleaning workers [71••]. Quinn and colleagues recently reviewed the published literature on tasks, activities, and health effects related to the use of cleaning and disinfecting products in health care settings [72••]. Products that can cause or exacerbate asthma include chlorine, ammonia, ethanolamine (used as surfactant), 2-butoxyethanol (used in window cleaners, carpet cleaners, and other cleaners), and quaternary ammonium compounds (e.g., benzalkonium chloride) among others. A review of potentially hazardous chemical ingredients in cleaning and disinfecting products used in health care was developed by Bello and colleagues [73]. The main sensitizers identified in cleaning products include quaternary ammonium compounds, amine compounds and aldehydes (e.g., formaldehyde, glutaraldehyde), and fragrances [60, 74].

Studies have examined occupational respiratory health risks associated with cleaning and disinfecting products in health care settings [2, 9, 63•, 72••, 73, 75, 76]. For example, based on a survey of Texas physicians, nurses, and respiratory and occupational therapists, Delclos and colleagues found a 2-fold increased likelihood of asthma among HCWs who used cleaning products on building surfaces and those who were involved in medical instruments cleaning and disinfecting [2]. In addition, bronchial hyperresponsiveness-related symptoms were found to be associated with use of adhesives, solvents, or gases in patient care, use of cleaning products on building

Table 1 Agents causing occupational asthma in healthcare workers [4, 55, 57••, 59–62, 63•]

Agent	AOEC[a]		Occupation
	Exposure code	Designation	
High molecular weight agents			
Animal-derived antigens			
Bovine serum albumin	380.13	A, Rs	Laboratory technician
Endocrine glands	NL	NL	Pharmacist
Plant-derived natural products			
Latex	270.02	A, G	Health professional
Biologic enzymes			
Pancreatin	324.05	A, Rs	Endoscopy nurse and technician,
Empynase (pronase B)	NL	NL	surgical technician, sterile supply technician
Vegetable gums			
Gutta-percha	372.06	A	Dental hygienist
Low molecular weight agents			
Diisocyanates			
Methylene diphenyl diisocyanate (MDI)	221.09	A, Rs	Orthopedic nurse
Quaternary amines			
Quaternary ammonium compounds	322.320	–	Dental assistant and laboratory technician, nurse, certified nursing assistant, endoscopy technician, medical equipment preparer, floor stripper/waxer, housekeeper
Drugs[b]			
Mitoxantrone	321.011	A, Rs	Nurse
Ribavirin	321.32	–	Respiratory therapist
Biocides			
Hexachlorophene	181.02	A, Rs	Nurse
Chlorhexidine	200.08	A, Rs	Nurse
Glutaraldehyde (Cidex™)	120.051	A, Rs	Endoscopy nurse and technician, respiratory therapist
Ortho-phthalaldehyde (Cidex OPA™)	120.10	R	Endoscopy nurse and technician
Peracetic acid–hydrogen peroxide mixture	050.480	A, Rs	Endoscopy nurse and technician
Fungicides			
Tributyl tin oxide (TBTO)[c]	020.363	A, Rs	Venipuncture technician
Other agents			
Ethylene oxide	110.03	A, Rr	Medical equipment preparer, nurse
Enflurane	190.151	A, Rs	Anesthesiology care provider
Sevoflurane + isoflurane	190.157	A, Rs	Anesthesiology care provider
Methyl blue	325.10	A	Nurse
Terpene	060.17	R	Laboratory technician
Radiographic fixative	320.32	R	Radiology technician
Sulfathiazole	NL	NL	Nurse
Formaldehyde	120.03	A, G	Laboratory technician
Methyl methacrylate and cyanoacrylates	142.07	A,Rs	Dental and clinical laboratory technicians
ECG ink (synthetic material)	170.02	R	Laboratory nurse

[a] *AOEC* Association of Occupational and Environmental Clinics; *A* asthmagen; *Rs* sensitizer; *Rr* irritant; *R* neither; *G* generally accepted as a sensitizer, not reviewed; *NL* not listed

[b] The following drugs were listed [55] for pharmaceutical occupation: aescin, 5-aminosalicylic acid, piperacillin, ceftazidime, opiate compounds, amoxicillin, vancomycin; and for chemical workers: lasamide (precursor of furosemide)

[c] Asthma developed from exposure to a carpet deodorizer containing TBTO

surfaces, and exposure to a chemical spill at work. However, it was not documented whether asthma and asthma symptoms were the result of allergic immune sensitization or irritant effects.

Natural Rubber Latex (NRL)

The use of products manufactured with NRL, i.e., products derived from latex of the tropical rubber tree *Hevea braziliensis*, and associated exposure to HMW latex allergens in the work environment are important causes of IgE sensitization and occupational allergy in HCWs [77, 78]. In healthcare settings, NRL is used in medical devices (e.g., catheters, drainage tubes, tourniquets) and personal protective equipment (e.g., examination and surgical gloves) [78]. Glove powder may serve as a vehicle for airborne transmission of NRL proteins, and in settings where powdered NRL gloves are used, airborne antigen exposure is a major source of latex IgE sensitization in HCWs [79]. Latex allergy can manifest in HCWs as a range of allergic diseases, including urticaria/angioedema, rhinitis, asthma, and even life-threatening anaphylaxis. The estimated prevalence of IgE sensitization to NRL

among HCWs before 2000 ranged from 2.8 to 17.1 %, with lower prevalence if sensitization was assessed by skin test and higher if assessed by measuring serum specific IgE [77]. Review of studies published during 2000–2014 indicate that the prevalence decreased and ranged from 2.7 to 11.4 % [80]. Studies conducted in the US showed the latex sensitization prevalence to range from 4.4 to 5.8 % [79, 81]. The decrease in latex allergy likely resulted from the removal of powdered latex medical gloves from the workplaces and the use of non-latex gloves [79]. Despite available interventions, anaphylactic reactions to latex in HCWs [82] and patients [83] are still reported [51•].

Pharmaceutical Products

Various medications have been confirmed as causing occupational allergy in healthcare and pharmaceutical workers. In his review, Whitaker summarized reports on commonly used medications [84•]. Drugs causing occupational respiratory diseases included β-lactam antibiotics (cephalosporins), vancomycin, antimalarials (hydroxychloroquine), antineoplastic drugs (etoposide, mitoxantrone), porcine pancreatic amylase, biodiastase, and anesthetics (succinylcholine, sevoflurane, and isoflurane). Sensitization to drugs may occur through topical contact with spilled drugs or by inhalation of powder or foam and present as rhinitis, asthma, urticaria, or allergic contact dermatitis. The author discussed the assessment and management of affected persons and underscored the need for a good medical surveillance program.

Diisocyanates

Diisocyanates, LMW chemicals widely used to produce polyurethane foam insulation and paints, are recognized as one of the most common causes of WRA in building and automotive industry workers. Suojalehto and colleagues reported on two WRA cases due to methylene diphenyl diisocyanate (MDI)-containing orthopedic plaster casts in nurses [62]. Both nurses had a negative specific IgE test and a negative skin prick test to diisocyanates and latex. The diagnoses were made based on the results of specific inhalation challenge with MDI.

Damp Indoor Environments

Dampness, the presence of unwanted and excessive moisture in buildings, may cause adverse respiratory health effects. Cox-Ganser and colleagues reported five new-onset asthma cases among 53 employees located on the top floor of an eight-story hospital [85]. The investigators found mold contamination in the walls and ceilings, likely a result of multiple episodes of significant roof and window leaks during heavy rains over several years. Moreover, the hospital had ongoing and past renovations and remodeling on many floors that could have resulted in chemical emissions and release of hidden microbial contamination from past water incursion. The authors concluded that exposure to damp indoor environments and mold lead to the development of asthma.

Specific Agents Associated with Occupational Anaphylaxis

As previously noted, a recent review indicated that occupational anaphylaxis in HCWs is most frequently triggered by NRL, chemicals (disinfectants), and medications [51•]. Among the classes of drugs, β-lactam antibiotics are an important concern. In a study of 161 Korean HCWs, including 138 nurses and 23 pharmacists, Kim and colleagues found the prevalence of serum specific IgE antibodies to be 17.4 % for any cephalosporin, 10.4 % for cefotiam, 6.8 % for ceftriaxone, and 3.7 % for ceftizoxime [86]. A case of anaphylaxis has been reported to occur in a nurse with specific IgE sensitization to piperacillin after she administered an injection of the drug [87]. Newman and Goel reported a case of an anesthesiologist trainee who developed an occupational allergy and anaphylaxis to multiple neuromuscular blocking drugs (rocuronium, vecuronium, pancuronium, and succinylcholine) [88]. Other medications associated with occupational anaphylaxis were psyllium [89], chlorhexidine [90], and allergen immunotherapy extract (after a needlestick) [91].

MANAGEMENT AND PREVENTION

Rhinitis, rhinosinusitis, and asthma frequently co-exist. The understanding of the functional relationship between the upper and lower respiratory tract led to a concept of united airways disease [92]. There is some evidence that asthma may be prevented or controlled by appropriate management of rhinitis [61, 93, 94].

Collecting a detailed occupational history among adults with rhinitis or asthma is critical for making a diagnosis and recommending optimal treatment and management. Obtaining safety data sheets can facilitate identification of agents the worker may be exposed to at work. Guidelines intended to optimize patient care, promote effective diagnosis and therapy, and reduce harmful or unnecessary variations in care of allergic rhinitis are available [32, 95]. Diagnosis and management of WRA has been outlined by the American College of Chest Physicians [15]. Heederik and colleagues evaluated published reports on the effectiveness of various interventions aimed at controlling work exposure on the prevention of occupational asthma [96]. Avoidance is the preferred primary strategy used to reduce signs and symptoms of work-related rhinitis and asthma. Removal of patients

with sensitizer-induced WRA from further exposure to the causative agent in addition to providing other asthma management may be necessary if primary prevention through application of the hierarchy of controls (e.g., elimination, substitution, engineering controls, administrative controls, personal protective equipment; available at http://www.cdc.gov/niosh/topics/hierarchy/) is not possible. However, exposure reduction is less effective in controlling symptoms [97]. There is limited evidence for the effectiveness of respirators in preventing occupational asthma and other options higher in the hierarchy of controls for occupational exposures should be used preferentially [96].

For HCWs exposed to NRL, NIOSH has recommended that employers periodically screen workers for latex allergy symptoms and that workers with symptoms be evaluated for NRL allergy [78]. HCWs undergoing evaluation for NRL allergy or documented to be sensitized should avoid further exposure to NRL to prevent progression to more severe allergic disease. It is also recommended that HCWs with NRL allergy wear a medical alert bracelet. That way, if they require medical care, providers will know to avoid using NRL-containing medical devices. Parallel approaches to surveillance may be useful in addressing respiratory allergic disease caused by other agents.

A report by the Lowell Center for Sustainable Production, Asthma Regional Council provided evidence of the cost-effectiveness of multi-faceted asthma interventions for employers [98]. Finally, particularly for evaluation of suspected new or emerging causes of allergic respiratory disease, employees, union officials, or employers can ask the NIOSH Health Hazard Evaluation Program (http://www.cdc.gov/niosh/hhe/) to examine potential health hazards present at their workplace.

CONCLUSIONS

Because of the potential adverse health effects of allergic work-related rhinitis and asthma, physicians and other healthcare professionals should recognize rhinitis and asthma symptoms in relation to work. Prevention of occupational allergic respiratory diseases is important, and a variety of prevention and intervention strategies are available. Reduction or elimination of exposures in the workplace should be considered as the most effective and important preventive measure.

Acknowledgments The authors would like to thank Mr. Jim Boiano and Dr. Paul K. Henneberger, National Institute for Occupational Safety and Health, for their helpful comments.

Disclaimer The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health. Mention of company names or products does not constitute endorsement by the National Institute for Occupational Safety and Health.

Compliance with Ethical Standards

Conflict of Interest Drs. Mazurek and Weissman declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with animal subjects performed by the authors. With regard to the authors' 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.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. World Allergy Organization. WAO/EAACI Allergy Definitions. Available at http://www.worldallergy.org/professional/allergic_diseases_center/nomenclature/english.php. Accessed 26 Aug 2016.
2. Delclos GL, Gimeno D, Arif AA, Burau KD, Carson A, Lusk C, et al. Occupational risk factors and asthma among health care professionals. Am J Respir Crit Care Med. 2007;175(7):667–75.
3. Di Stefano F, Siriruttanapruk S, McCoach J, Burge PS. Glutaraldehyde: an occupational hazard in the hospital setting. Allergy. 1999;54(10):1105–9.
4. Dimich-Ward H, Wymer ML, Chan-Yeung M. Respiratory health survey of respiratory therapists. Chest. 2004;126(4):1048–53.
5. Kern DG, Frumkin H. Asthma in respiratory therapists. Ann Intern Med. 1989;110(10):767–73.
6. Kim JL, Toren K, Lohman S, Ekerljung L, Lotvall J, Lundback B, et al. Respiratory symptoms and respiratory-related absence from work among health care workers in Sweden. J Asthma. 2013;50(2):174–9.
7. Liss GM, Tarlo SM, Doherty J, Purdham J, Greene J, McCaskell L, et al. Physician diagnosed asthma, respiratory symptoms, and associations with workplace tasks among radiographers in Ontario, Canada. Occup Environ Med. 2003;60(4):254–61.
8. Mirabelli MC, Zock JP, Plana E, Anto JM, Benke G, Blanc PD, et al. Occupational risk factors for asthma among nurses and related healthcare professionals in an international study. Occup Environ Med. 2007;64(7):474–9.
9. Pechter E, Davis LK, Tumpowsky C, Flattery J, Harrison R, Reinisch F, et al. Work-related asthma among health care workers: surveillance data from California, Massachusetts, Michigan, and New Jersey, 1993–1997. Am J Ind Med. 2005;47(3):265–75.
10. Bilge U, Unluoglu I, Son N, Keskin A, Korkut Y, Unalacak M. Occupational allergic diseases in kitchen and health care workers: an underestimated health issue. Biomed Res Int. 2013;2013:285420.
11. Kanayama H, Sato K, Mori T, Hirai T, Umemura T, Tamura T, et al. Work-related allergy in medical doctors: atopy, exposure to domestic animals, eczema induced by common chemicals and

membership of the surgical profession as potential risk factors. Int Arch Occup Environ Health. 2012;85(4):455–66.
12. Sato K, Kusaka Y, Suganuma N, Nagasawa S, Deguchi Y. Occupational allergy in medical doctors. J Occup Health. 2004;46(2):165–70.
13. Wiszniewska M, Walusiak-Skorupa J. Occupational allergy: respiratory hazards in healthcare workers. Curr Opin Allergy Clin Immunol. 2014;14(2):113–8.
14. BLS. Current Population Survey. Characteristics of the employed. Available at http://www.bls.gov/cps/tables.htm#charemp. Accessed 26 Aug 2016.
15. Tarlo SM, Balmes J, Balkissoon R, Beach J, Beckett W, Bernstein D, et al. Diagnosis and management of work-related asthma: American College of Chest Physicians Consensus Statement. Chest. 2008;134(3 Suppl):1S–41S.
16. Wisnewski AV, Xu L, Robinson E, Liu J, Redlich CA, Herrick CA. Immune sensitization to methylene diphenyl diisocyanate (MDI) resulting from skin exposure: albumin as a carrier protein connecting skin exposure to subsequent respiratory responses. J Occup Med Toxicol. 2011;6:6.
17.• Salo PM, Arbes Jr SJ, Jaramillo R, Calatroni A, Weir CH, Sever ML, et al. Prevalence of allergic sensitization in the United States: results from the National Health and Nutrition Examination Survey (NHANES) 2005–2006. J Allergy Clin Immunol. 2014;134(2):350–9. **The first population-based study that used quantitative data to describe sensitization patterns in common allergic conditions**.
18. Mazurek JM, Weissman DN. Serum IgE levels among U.S. workers—National Health and Nutrition Examination Survey (NHANES), 2005–2006. Am J Respir Crit Care Med. 2016;193:A2990. Available at http://www.atsjournals.org/doi/abs/10.1164/ajrccm-conference.2016.193.1_MeetingAbstracts.A2990. Accessed 26 Aug 2016.
19. Olivieri M, Heinrich J, Schlunssen V, Anto JM, Forsberg B, Janson C, et al. The risk of respiratory symptoms on allergen exposure increases with increasing specific IgE levels. Allergy. 2016;71(6):859–68.
20. Pastorello EA, Incorvaia C, Ortolani C, Bonini S, Canonica GW, Romagnani S, et al. Studies on the relationship between the level of specific IgE antibodies and the clinical expression of allergy: I. Definition of levels distinguishing patients with symptomatic from patients with asymptomatic allergy to common aeroallergens. J Allergy Clin Immunol. 1995;96(5 Pt 1):580–7.
21. Kerkhof M, Schouten JP, De Monchy JG. The association of sensitization to inhalant allergens with allergy symptoms: the influence of bronchial hyperresponsiveness and blood eosinophil count. Clin Exp Allergy. 2000;30(10):1387–94.
22. Blackwell DL, Lucas JW. Summary health statistics for U.S. adults: National Health Interview Survey, 2014. Table A-2a. Age-adjusted percentages (with standard errors) of selected respiratory disease among adults aged 18 and over, by selected characteristics: United States, 2014. Available at http://ftp.cdc.gov/pub/Health_Statistics/NCHS/NHIS/SHS/2014_SHS_Table_A-2.pdf. Accessed 26 Aug 2016.
23. Barnett SB, Nurmagambetov TA. Costs of asthma in the United States: 2002–2007. J Allergy Clin Immunol. 2011;127(1):145–52.
24. Bhattacharyya N. Functional limitations and workdays lost associated with chronic rhinosinusitis and allergic rhinitis. Am J Rhinol Allergy. 2012;26(2):120–2.
25. Blaiss MS, Meltzer EO, Derebery MJ, Boyle JM. Patient and healthcare-provider perspectives on the burden of allergic rhinitis. Allergy Asthma Proc. 2007;28 Suppl 1:S4–S10.
26. Meltzer EO, Blaiss MS, Naclerio RM, Stoloff SW, Derebery MJ, Nelson HS, et al. Burden of allergic rhinitis: allergies in America, Latin America, and Asia-Pacific adult surveys. Allergy Asthma Proc. 2012;33 Suppl 1:S113–41.
27. Smith KA, Orlandi RR, Rudmik L. Cost of adult chronic rhinosinusitis: a systematic review. Laryngoscope. 2015;125(7):1547–56.
28. Soni A. Allergic rhinitis: trends in use and expenditures, 2000 to 2005. Rockville, MD: Agency for Healthcare Research and Quality; 2008. Statistical Brief No. 204. Available at http://ftp.cdc.gov/pub/Health_Statistics/NCHS/NHIS/SHS/2014_SHS_Table_A-2.pdf. Accessed 26 Aug 2016.
29. Nathan RA. The burden of allergic rhinitis. Allergy Asthma Proc. 2007;28(1):3–9.
30. Bahadori K, Doyle-Waters MM, Marra C, Lynd L, Alasaly K, Swiston J, et al. Economic burden of asthma: a systematic review. BMC Pulm Med. 2009;9:24.
31.• Stevens WW, Grammer III LC. Occupational rhinitis: an update. Curr Allergy Asthma Rep. 2015;15(1):487. **Useful review of the classification, prevalence, diagnosis, and treatment strategies of occupational rhinitis**.
32. Wallace DV, Dykewicz MS, Bernstein DI, Blessing-Moore J, Cox L, Khan DA, et al. The diagnosis and management of rhinitis: an updated practice parameter. J Allergy Clin Immunol. 2008;122(2 Suppl):S1–S84.
33. Siracusa A, Desrosiers M, Marabini A. Epidemiology of occupational rhinitis: prevalence, aetiology and determinants. Clin Exp Allergy. 2000;30(11):1519–34.
34. Guerra S, Sherrill DL, Martinez FD, Barbee RA. Rhinitis as an independent risk factor for adult-onset asthma. J Allergy Clin Immunol. 2002;109(3):419–25.
35. Huovinen E, Kaprio J, Laitinen LA, Koskenvuo M. Incidence and prevalence of asthma among adult Finnish men and women of the Finnish Twin Cohort from 1975 to 1990, and their relation to hay fever and chronic bronchitis. Chest. 1999;115(4):928–36.
36. Malo JL, Lemiere C, Desjardins A, Cartier A. Prevalence and intensity of rhinoconjunctivitis in subjects with occupational asthma. Eur Respir J. 1997;10(7):1513–5.
37. Shaaban R, Zureik M, Soussan D, Neukirch C, Heinrich J, Sunyer J, et al. Rhinitis and onset of asthma: a longitudinal population-based study. Lancet. 2008;372(9643):1049–57.
38. Vandenplas O. Occupational asthma: etiologies and risk factors. Allergy, Asthma Immunol Res. 2011;3(3):157–67.
39. Slavin RG. Update on occupational rhinitis and asthma. Allergy Asthma Proc. 2010;31(6):437–43.
40.•• Tarlo SM, Lemiere C. Occupational asthma. N Engl J Med. 2014;370(7):640–9. **Up-to-date review on the diagnosis, management, and prevention of sensitizer- and irritant-induced occupational asthma**.
41. Malo JL, Tarlo SM, Sastre J, Martin J, Jeebhay MF, Le MN, et al. An official American Thoracic Society Workshop Report: presentations and discussion of the fifth Jack Pepys Workshop on Asthma in the Workplace. Comparisons between asthma in the workplace and non-work-related asthma. Ann Am Thorac Soc. 2015;12(7):S99–S110.
42. Anderson NJ, Fan ZJ, Reeb-Whitaker C, Bonauto DK, Rauser E. Distribution of asthma by occupation: Washington State Behavioral Risk Factor Surveillance System data, 2006–2009. J Asthma. 2014;51(10):1035–42.
43. Arif AA, Delclos GL, Serra C. Occupational exposures and asthma among nursing professionals. Occup Environ Med. 2009;66(4):274–8.
44. Syamlal G, Mazurek JM, Bang KM. Prevalence of lifetime asthma and current asthma attacks in U.S. working adults: an analysis of the 1997–2004 National Health Interview Survey data. J Occup Environ Med. 2009;51(9):1066–74.
45. Dodd KE, Mazurek JM. Current asthma prevalence among adults by industry and occupation, 21 states, Behavioral Risk Factor Surveillance System, 2013. Proceedings of the 2016 Council of State and Territorial Epidemiologists (CSTE) Annual Conference,

June 19–23, 2016, Anchorage, AK. Available at https://cste.confex.com/cste/2016/webprogram/Paper6293.html. Accessed 26 Aug 2016.

46. Ortega HG, Kreiss K, Schill DP, Weissman DN. Fatal asthma from powdering shark cartilage and review of fatal occupational asthma literature. Am J Ind Med. 2002;42(1):50–4.
47. Chester DA, Hanna EA, Pickelman BG, Rosenman KD. Asthma death after spraying polyurethane truck bedliner. Am J Ind Med. 2005;48(1):78–84.
48. Stanbury M, Chester D, Hanna EA, Rosenman KD. How many deaths will it take? A death from asthma associated with work-related environmental tobacco smoke. Am J Ind Med. 2008;51(2):111–6.
49. DHHS. Work-Related Lung Disease Surveillance Report, 2007. Table 9-1. Asthma: Proportionate mortality ratio (PMR) adjusted for age, sex, and race by usual industry, U.S. residents age 15 and over, selected states and years, 1990–1999. DHHS (NIOSH) Publication Number 2008-143a. September 2008. Available at http://www.cdc.gov/niosh/docs/2008-143/pdfs/2008-143.pdf.
50. Moorman JE, Akinbami LJ, Bailey CM, Zahran HS, King ME, Johnson CA, et al. National surveillance of asthma: United States, 2001–2010. Vital Health Stat. 2012;3(35):1–58.
51.• Moscato G, Pala G, Crivellaro M, Siracusa A. Anaphylaxis as occupational risk. Curr Opin Allergy Clin Immunol. 2014;14(4):328–33. **Up-to-date review on the definition, triggers, management, and prevention of occupational anaphylaxis**.
52. Quirce S, Fiandor A. How should occupational anaphylaxis be investigated and managed? Curr Opin Allergy Clin Immunol. 2016;16(2):86–92.
53. Quirce S. IgE antibodies in occupational asthma: are they causative or an associated phenomenon? Curr Opin Allergy Clin Immunol. 2014;14(2):100–5.
54. Meca O, Cruz MJ, Sanchez-Ortiz M, Gonzalez-Barcala FJ, Ojanguren I, Munoz X. Do low molecular weight agents cause more severe asthma than high molecular weight agents? PLoS One. 2016;11(6):e0156141.
55. Malo JL, Chan-Yeung M. Appendix. Agents causing occupational asthma with key references. In: Bernstein IL, Chan-Yeung M, Malo JL, Bernstein DI, editors. Asthma in the workplace. 3rd ed. New York: Marcel Decker, Inc; 2006. p. 825–66.
56. Rosenman KD, Beckett WS. Web based listing of agents associated with new onset work-related asthma. Respir Med. 2015;109(5):625–31.
57.•• Association of Occupational and Environmental Clinics. Exposure code online look-up. Available at http://www.aoecdata.org/ExpCodeLookup.aspx. **Recently updated website containing listing of substances that meet specified criteria for causing work related asthma by sensitization or acute irritant-induced asthma. Clinicians are encouraged to use this website when evaluating patients suspected to have work-related asthma**.
58. Baur X. A compendium of causative agents of occupational asthma. J Occup Med Toxicol. 2013;8(1):15.
59. Quirce S, Bernstein JA. Old and new causes of occupational asthma. Immunol Allergy Clin N Am. 2011;31(4):677–98. v.
60. Gonzalez M, Jegu J, Kopferschmitt MC, Donnay C, Hedelin G, Matzinger F, et al. Asthma among workers in healthcare settings: role of disinfection with quaternary ammonium compounds. Clin Exp Allergy. 2014;44(3):393–406.
61. Shin SY, Hur GY, Ye YM, Park HS. A case of occupational rhinitis caused by porcine pancreatic extract developing into occupational asthma. J Korean Med Sci. 2008;23(2):347–9.
62. Suojalehto H, Linstrom I, Henriks-Eckerman ML, Jungewelter S, Suuronen K. Occupational asthma related to low levels of airborne methylene diphenyl diisocyanate (MDI) in orthopedic casting work. Am J Ind Med. 2011;54(12):906–10.
63.• Saito R, Virji MA, Henneberger PK, Humann MJ, LeBouf RF, Stanton ML, et al. Characterization of cleaning and disinfecting tasks and product use among hospital occupations. Am J Ind Med. 2015;58(1):101–11. **A study of cleaning and disinfecting tasks by occupation, frequency, and duration, and the chemical composition of products used by laboratory and clinical support occupations and cleaning and disinfecting occupations**.
64. Cristofari-Marquand E, Kacel M, Milhe F, Magnan A, Lehucher-Michel MP. Asthma caused by peracetic acid–hydrogen peroxide mixture. J Occup Health. 2007;49(2):155–8.
65. Pala G, Moscato G. Allergy to ortho-phthalaldehyde in the healthcare setting: advice for clinicians. Expert Rev Clin Immunol. 2013;9(3):227–34.
66. Fujita H, Ogawa M, Endo Y. A case of occupational bronchial asthma and contact dermatitis caused by ortho-phthalaldehyde exposure in a medical worker. J Occup Health. 2006;48(6):413–6.
67. Fujita H, Sawada Y, Ogawa M, Endo Y. Health hazards from exposure to ortho-phthalaldehyde, a disinfectant for endoscopes, and preventive measures for health care workers. Sangyo Eiseigaku Zasshi. 2007;49(1):1–8. **Article in Japanese**.
68. Miyajima K, Yoshida J, Kumagai S. Ortho-phthalaldehyde exposure levels among endoscope disinfection workers. Sangyo Eiseigaku Zasshi. 2010;52(2):74.
69. Johnson VJ, Reynolds JS, Wang W, Fluharty K, Yucesoy B. Inhalation of ortho-phthalaldehyde vapor causes respiratory sensitization in mice. J Allergy (Cairo). 2011;2011:751052.
70.•• Chen L, Eisenberg J, Mueller C, Burton NC. Health hazard evaluation report: evaluation of ortho-phthalaldehyde in eight healthcare facilities. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, NIOSH HHE Report 2006-0238-3239. 2015. Available at http://www.cdc.gov/niosh/hhe/reports/pdfs/2006-0238-3239.pdf. Accessed 26 Aug 2016. **Results of an evaluation of exposure to ortho-phthalaldehyde in a variety of healthcare settings with recommendations for employers and employees**.
71.•• Folletti I, Zock JP, Moscato G, Siracusa A. Asthma and rhinitis in cleaning workers: a systematic review of epidemiological studies. J Asthma. 2014;51(1):18–28. **Studies selected for review evaluated using the Strengthening of the Reporting of Observational Studies in Epidemiology (STROBE) statement checklist**.
72.•• Quinn MM, Henneberger PK, Braun B, Delclos GL, Fagan K, Huang V, et al. Cleaning and disinfecting environmental surfaces in health care: toward an integrated framework for infection and occupational illness prevention. Am J Infect Control. 2015;43(5):424–34. **A summary of current knowledge on the occupational hazards associated with the use of cleaning products and disinfectants. Includes examples of practices to minimize respiratory hazards during cleaning and disinfection of environmental surfaces**.
73. Bello A, Quinn MM, Perry MJ, Milton DK. Characterization of occupational exposures to cleaning products used for common cleaning tasks—a pilot study of hospital cleaners. Environ Health. 2009;8:11.
74. Quirce S, Barranco P. Cleaning agents and asthma. J Investig Allergol Clin Immunol. 2010;20(7):542–50.
75. Arif AA, Delclos GL. Association between cleaning-related chemicals and work-related asthma and asthma symptoms among healthcare professionals. Occup Environ Med. 2012;69(1):35–40.
76. Dumas O, Donnay C, Heederik DJ, Hery M, Choudat D, Kauffmann F, et al. Occupational exposure to cleaning products and asthma in hospital workers. Occup Environ Med. 2012;69(12):883–9.
77. Vandenplas O, Beezhlod D, Tarlo SM. Latex allergy. In: Bernstein IL, Chan-Yeung M, Malo JL, Bernstein DI, editors. Asthma in the

workplace and related conditions. 3rd ed. New York: Taylor and Francis Group; 2006. p. 437–61.
78. DHHS. NIOSH Alert. Preventing allergic reactions to natural rubber latex in the workplace. Cincinnati, OH: U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health (NIOSH) Publication Number 97-135. June 1997. Available at http://www.cdc.gov/niosh/docs/97-135/pdfs/97-135.pdf. Accessed 26 Aug 2016.
79. Kelly KJ, Wang ML, Klancnik M, Petsonk EL. Prevention of IgE sensitization to latex in health care workers after reduction of antigen exposures. J Occup Environ Med. 2011;53(8):934–40.
80. Caballero ML, Quirce S. Identification and practical management of latex allergy in occupational settings. Expert Rev Clin Immunol. 2015;11(9):977–92.
81. Hamann CP, Rodgers PA, Sullivan KM. Prevalence of type I natural rubber latex allergy among dental hygienists. J Dent Hyg. 2005;79(2):7.
82. Zahariev VK, Knezevic B, Bogadi-Sare A, Bubas M, Kristo D, Pejnovic N. Anaphylactic reaction to latex in a health care worker: case report. Acta Dermatovenerol Croat. 2012;20(3):207–9.
83. Malsy M, Leberle R, Ehehalt K, Sinner B, Hobbhahn J. Anaphylactic reaction 5 minutes after the start of surgery: a case report. BMC Res Notes. 2015;8:117.
84.• Whitaker P. Occupational allergy to pharmaceutical products. Curr Opin Allergy Clin Immunol. 2016;16(2):101–6. **Up-to-date list of drugs implicated in causing occupational allergy with key references**.
85. Cox-Ganser JM, Rao CY, Park JH, Schumpert JC, Kreiss K. Asthma and respiratory symptoms in hospital workers related to dampness and biological contaminants. Indoor Air. 2009;19(4):280–90.
86. Kim JE, Kim SH, Jin HJ, Hwang EK, Kim JH, Ye YM, et al. IgE sensitization to cephalosporins in health care workers. Allergy, Asthma Immunol Res. 2012;4(2):85–91.
87. Kim JE, Kim SH, Kim JH, Bahn JW, Jin HJ, Ye YM, et al. A case of piperacillin-induced occupational anaphylaxis: detection of serum IgE to piperacillin-HSA conjugate. J Korean Med Sci. 2011;26(5):682–5.
88. Newman MJ, Goel P. An anesthesiologist with an allergy to multiple neuromuscular blocking drugs: a new occupational hazard. Anesth Analg. 2010;110(2):601–2.
89. Khalili B, Bardana Jr EJ, Yunginger JW. Psyllium-associated anaphylaxis and death: a case report and review of the literature. Ann Allergy Asthma Immunol. 2003;91(6):579–84.
90. Wittczak T, Dudek W, Walusiak-Skorupa J, Swierczynska-Machura D, Palczynski C. Chlorhexidine—still an underestimated allergic hazard for health care professionals. Occup Med (Lond). 2013;63(4):301–5.
91. Bandino ML, Tankersley MS. Anaphylaxis in an allergy immunotherapy extract-compounding technician after an extract needle stick. J Allergy Clin Immunol. 2012;129(1):250–1.
92. Passalacqua G, Ciprandi G, Canonica GW. United airways disease: therapeutic aspects. Thorax. 2000;55 Suppl 2:S26–7.
93. Compalati E, Ridolo E, Passalacqua G, Braido F, Villa E, Canonica GW. The link between allergic rhinitis and asthma: the united airways disease. Expert Rev Clin Immunol. 2010;6(3):413–23.
94. Cruz AA, Popov T, Pawankar R, Annesi-Maesano I, Fokkens W, Kemp J, et al. Common characteristics of upper and lower airways in rhinitis and asthma: ARIA update, in collaboration with GA(2)LEN. Allergy. 2007;62 Suppl 84:1–41.
95. Seidman MD, Gurgel RK, Lin SY, Schwartz SR, Baroody FM, Bonner JR, et al. Clinical practice guideline: allergic rhinitis. Otolaryngol Head Neck Surg. 2015;152(1 Suppl):S1–S43.
96. Heederik D, Henneberger PK, Redlich CA. Primary prevention: exposure reduction, skin exposure and respiratory protection. Eur Respir Rev. 2012;21(124):112–24.
97. Birdi K, Beach J. Management of sensitizer-induced occupational asthma: avoidance or reduction of exposure? Curr Opin Allergy Clin Immunol. 2013;13(2):132–7.
98. Hoppin P, Stillman L, Jacobs M. Asthma: a business case for employers and health care purchasers. University of Massachusetts Lowell and Asthma Regional Council. February 2010. Available at http://asthmaregionalcouncil.org/wp-content/uploads/2014/02/2010_Business_Case_Employers_Health_Care_Purchasers.pdf. Accessed 26 Aug 2016.