Cleaning Products-Related Asthma

Kenneth D. Rosenman, MD

Abstract: Epidemiologic studies have identified cleaners as an occupational group at increased risk of asthma and asthma-type respiratory symptoms. The level of increased risk in cleaners for these respiratory problems has ranged from around 1.5 to 2.5 times the background risk. Specific chemicals in cleaning products identified to cause sensitization include disinfectants (chloramine, chlorhexidine, formaldehyde, glutaraldehyde, and hexachlorophene); amine compounds (amino alcohols, aliphatic polyamines, and the quaternary amine, benzalkonium chloride); tall oil; the fungicide tributyltin oxide; and enzymes produced by *Bacillus subtilis* and other additives used in detergents. The mixing of cleaning products containing bleach and acid or bleach and ammonia, which causes the production of chlorine or chloramines, as well as the use of strong irritants to clean such as hydrofluoric acid have caused reactive airways dysfunction syndrome. Further research is needed to better elucidate the respiratory disease among cleaners. Questions that need to be resolved include: How much of the respiratory symptoms in cleaners are secondary to sensitization to ingredients of certain cleaning products, how much to their irritative properties, and how much to exposure to environmental allergens such as dust mites whose immunologic effect may be heightened by certain cleaning products? In the meantime, clinicians need to be aware when evaluating patients with asthma or asthma-like symptoms that cleaning agents at work or at home may be important triggers that are either initiating or aggravating the patient's disease.

Key Words: asthma, cleaners, cleaning agents, disinfectants, RADS

(*Clin Pulm Med* 2006;13: 221–228)

There is the general perception that clean is associated with health. The Soap and Detergent Association, the trade association whose members represent companies that manufacture 90% of the cleaning products sold in the United States, instituted an advertising campaign based on this perception—"Clean and Healthy Strategies for Today's Homes"—to address asthma and allergies. This trade association has also partnered with the asthma program in the U.S. Centers for Disease Control and Prevention (CDC) to recommend the use of cleaning products to reduce environmental allergens. However, cleaning agents are chemicals, and it should come as no surprise that, depending on the agent and the level of exposure, that cleaning agents can cause adverse health effects. In 2000, cleaning agents were the third most frequent exposure in adults reported to the American Association of Poison Control Centers Toxic Exposure Surveillance System (9.5% of 66,384 reports),[1] and in 1999, cleaning agents were the second most common (9.0% of 64,691 reports).[2] Cleaning agents are widely used. We use them throughout our society, in our homes, our cars, where we shop, where we work, and so on. The primary job responsibility of thousands of workers requires the repeated use of cleaning agents, and even for those who use them less frequently, exposure occurs when cleaning agents have been used by others. This article reviews the adverse respiratory health effects, particularly asthma, that have been reported with the use of cleaning agents.

Definition of a Cleaning Agent

There are many different types of cleaning agents.[3] These include all-purpose cleaning agents, soaps, sanitary ware cleaning agents, heavy-duty cleaning agents, air fresheners/deodorizers, carpet cleaners, floor strippers, degreasers, detergents, disinfectants, dusting products, fabric softeners, floor care products, polishes, and sanitizers. Surfactants are the main components of most cleaning agents. Acids and alkalines are added to dissolve calcium and fatty acids and to enhance the effect of surfactants. Alkaline compounds are also added for their anticorrosive effect. Complexing agents are added to enhance the effect of the surfactant by binding metal ions. Some products may have additives to provide a protective film on a surface; some may contain pesticides or disinfectants; some may contain corrosion inhibitors, some perfumes or fragrances, some dyes or pigments; and some may contain preservatives. Some cleaning agents are water-based and some are solvent-based. Water-based cleaning agents may have solvents added for a more homogenous product. Pesticides and disinfectants in the United States are more highly regulated than other chemicals.

However, even for these more highly regulated substances, no testing is performed to assess whether these substances cause type I immunologic reactions (IgE-mediated) or asthma. Routine toxicologic testing includes assessing how strong an irritant the substance is and may sometimes include testing for a type IV immunologic reaction (contact dermatitis). Efforts by some entities (eg, State of Massachusetts, Swedish Society for Nature Conservation) to encourage more environmentally friendly cleaning products have been based

From Michigan State University, East Lansing, Michigan.
Funding for this study provided by NIOSH U60/CCS221205.
Address correspondence to: Kenneth D. Rosenman, MD, 117 West Fee Hall, East Lansing, MI 48824. E-mail: Rosenman@msu.edu.

ISSN: 1068-0640/06/1304-0221
DOI: 10.1097/01.cpm.0000227253.84652.77

on such factors as the degradability of the substances, toxicity to aquatic organisms, and recycling of packaging, but not the ability of the substances to cause health effects to humans.

Chemicals can cause new-onset asthma after a latency period of use (sensitization or possibly chronic irritation), or without such a latency period after an acute exposure (reactive airways dysfunction syndrome [RADS]), and they can aggravate preexisting asthma.[4] Cleaning agents have been associated with all these types of chemical-related asthma. The medical literature on cleaning agents and asthma can be divided into population-based epidemiologic studies that have assessed asthma among individuals in the general occupational category of cleaners and case reports, generally with specific antigen bronchial challenge testing.

Epidemiologic Studies of Cleaners

A summary of the epidemiologic studies of cleaners is shown in Table 1. Other than 2 negative studies, cleaners have been found to have an increased risk of asthma in multiple studies from the United States, Europe, Australia, Brazil, Singapore, and South Africa. These epidemiologic studies have used different definitions of asthma, including self-report, use of asthma medication, history of physician-diagnosed asthma, evidence of hyperreactivity on pulmonary function tests, or work-related wheezes. Despite these differences in case definition, these studies have found an increased risk of "asthma" among cleaners when whatever definition of "asthma" was used was applied equally to the control populations in these same studies.

Results from the European Community Respiratory Health Survey (ECRHS), a cross-sectional study from selected areas in 9 European countries, Australia, New Zealand, and the United States, first reported an increased risk of asthma in cleaners with a summary odds ratio of 1.97 (95% confidence interval [CI], 1.33–2.92), with the odds ratios ranging from .9 in the New Zealand part of the cohort to 4.50 in the part of the cohort from Iceland.[5]

A more in-depth analysis of the ECRHS data showed that cleaners with asthma were more likely to be women, less likely to be atopic, more likely to have symptoms of bronchitis, and more likely to have lower lung function on spirometry.[6] Follow up of the Spanish subset reported that private home cleaners were at highest risk and that the risk of the home cleaners was associated with the use of oven sprays in kitchen cleaning and polishes in furniture cleaning.[7] A majority of the subjects in this follow-up study had work-related respiratory symptoms. A potential confounder to cleaning agents being the causal factor for asthma among cleaners was the finding of increased dust mite sensitization documented among private household cleaners (28%) versus 3% in other cleaners.[7] However, the prevalence of dust mite sensitization was not significantly greater among the private household cleaners than among the referent group of office workers (22%) who had significantly less asthma than the private household cleaners.

A study in Finland, which matched subjects by occupation, based on the Finnish population census with their national medication disbursement register, reported a risk of asthma in cleaners of 1.50 (95% CI, 1.43–1.57) with the highest risks among cleaners employed by companies that manufactured metals (2.47; 95% CI, 1.68–3.64) and food

TABLE 1. Summary of Epidemiologic Studies on Asthma Among Cleaners

Cross-Sectional/ Case–Control Studies	No. of Study Subjects	Risk (95% Confidence Interval)	Reference
European Community Respiratory Health Survey	15,637	1.97 (1.33–2.92)	5
Finland	2414	1.50 (1.43–1.57)	8
Southern Finland	521	1.42 (.81–2.48)	9
Barcelona, Spain	2654	1.46 (1.10–1.92)	10
US NHANES	6551		
Work-related asthma		2.37 (.53–10.58)	11
Work-related wheezing		5.44 (2.43–12.18)	
Singapore	787	1.52 (1.12–2.05)	12
New Zealand	1609	.90 (.40–2.02)	15
Goteborg, Sweden	321	1.10 (.60–2.0)	16
Case Series	**No. of Asthmatic Patients**	**Percent Cleaners/Related to Cleaning Products**	
Sao Paulo, Brazil	394		13
Cleaners		26.8%	
Cleaning agents		38.5%	
Capetown, South Africa	140		14
Cleaners		11.4%	
Cleaner agents		20.5%	
Surveillance System			17
California, Massachusetts, Michigan, New Jersey			
Cleaners	1915	12%	

products (2.19; 95% CI, 1.69–2.85).[8] The increased risk for cleaners was not limited to metals and food products, but was also present across all industries, including hospitals and schools, 1.51 (95% CI, 1.36–1.66) and 1.41 (95% CI, 1.27–1.57), respectively. An increased risk of asthma in cleaners was also reported in a case–control study from a section of southern Finland 1.42 (95% CI, .81–2.48).[9]

A cross-sectional survey of 8390 women from a section of Barcelona in Spain was performed.[10] The risk of asthma was increased in women who had done household cleaning 1.46 (95% CI, 1.10–1.92). Similar but nonstatistically significant risks were found in nondomestic cleaners, 1.41 for current asthma and 1.22 for ever asthma. Twenty-five percent of asthma in women in this cohort was attributed to work as a cleaner.[10] Data from the U.S. 3rd National Health and Nutrition Examination Survey, a cross-sectional survey of the U.S. general population, showed an increased but nonsignificant risk of work-related asthma of 2.37 (95% CI. .53–10.58) and a significant increased risk of work-related wheezing of 5.44 (95% CI, 2.43–12.18) in cleaners.[11] A study of patients from governmental polyclinics in Singapore showed an increased risk of asthma among service workers, 1.52 (95% CI, 1.12–2.05). The risk was greatest among municipal cleaners and sweepers, 2.30 (95% CI, 1.56–3.40).[12]

Among all new occupational asthma cases reported from 1995 to 2000 in 5 public clinics in Sao Paulo, Brazil, the most frequent occupational categories for women were janitors, housekeepers, and cleaners (26.8%) and the most frequent exposure agents were cleaning products (38.5%).[13] A study of asthmatics presenting to 2 hospitals in Cape Town, South Africa, reported the most common occupation of patients with occupational asthma was domestic work (11.4%) and the most common exposures were cleaning agents (20.5%).[14]

Two surveillance systems for work-related asthma have found that cleaning agents are a common suspected cause of asthma in the cases reported to the surveillance system. A summary of the 1915 confirmed cases of work-related asthma reported to the asthma surveillance systems in California, Massachusetts, Michigan, and New Jersey from 1993 to 1997 reported that in 12% of the cases, a cleaning agent was one of the suspected causal agents of the asthma. The patients were generally women (75%), older than age 45 (64%), and had worked in a wide number of settings, including medical (39%), schools (13%), and hotels (6%). Only 22% had job titles of janitors, cleaners, or housekeepers. Common job titles included nurses, nurses' aides, and clerical.[15] Cleaning jobs were the third most frequent occupation reported in the French surveillance system.[16]

The finding of increased asthma in cleaners has not been true in all epidemiologic studies. No increased risk of asthma was reported in a cross-sectional study in New Zealand[17] and a case–control study in Goteborg, Sweden.[18] The design of these epidemiologic studies generally did not allow for identification of more specific agents, although one study of Spanish cleaners suggested that domestic cleaners are at higher risk, particularly if they use oven cleaners and furniture polishers,[7] and a study of Danish cleaners found increased risk of respiratory and eye symptoms in cleaners who used sprayers.[19]

Specific Agents

A review of case reports that allow for identification of specific agents follows. Table 2 shows the specific ingredients of cleaning agents that have been associated with asthma grouped by additives, carpet cleaners, detergents, and disinfectants.

Additives

Amines

These chemicals are common additives in a large number of products such as cosmetics, epoxies, metal working fluids, paints, plastics, and rubber. Approximately 40 different amine compounds have been reported to cause asthma.[20–22] Amine compounds are common ingredients in cleaning agents. These include quaternary ammonium compounds, which are disinfectants and have been repeatedly reported to cause asthma, and amino alcohols (ethanolamines) and aliphatic polyamines (eg, ethylene diamine).

Despite the common use of amino alcohols and aliphatic polyamines in cleaning agents, most reports of asthma from exposure to them have occurred from their industrial use.[21,22] Only one of the reports of ethanolamine-causing asthma involved a cleaning agent. One of 3 cases in a report from Finland was of a woman who, after 18 years of working as a cleaner, developed asthma. Her symptoms were related to a detergent used to remove wax. The detergent contained 8% ethanolamine. She had a 27% decrease in her forced

TABLE 2. Cleaning Agents/Ingredients Associated With Respiratory Symptoms and Asthma

Ingredient	Reference
Additives	
Amines	20–22
Ethanolamines	22
Quaternary amines	20, 23–26
Benzylalkonium chloride	
Tall oil (colophony)	30
Carpet cleaners	31–36
Tributyltin oxide	32
Detergents	
Enzymes	37
Bacillus subtilis	37–42
Cellulase	43
Amylase	43
Additives	
1,2-Benzisathiazolin-3 one	44
Sodium iso-nonanoyl oxybenzenesulphonate	45
Disinfectants	
Chloramine	47–55
Chlorhexidine	58
Formaldehyde	59, 60
Glutaraldehyde	66–73
Hexachlorophene	78

expiratory volume in 1 second (FEV_1) on specific antigen challenge testing and did not react to another detergent with 9% content of a different amine, triethanolamine.[22]

An American woman in her 20s who worked with manufacturing cleaning products developed both respiratory and systemic symptoms of fever and arthralgias 7 months after starting work.[20] She had a 50% decrease in her FEV_1 and an urticarial rash on challenge tests to a toilet bowl cleaner containing benzalkonium chloride but not to other cleaning products without this ingredient. She had a positive skin test to 1:1 mixture of benzalkonium chloride. Her symptoms resolved with removal from work. Two years later, she was challenged again and had a similar drop in her FEV_1 and an urticarial rash. The researchers were unable to demonstrate specific IgE antibodies to a benzalkonium chloride album conjugate.

Additional case reports included 3 French female nurses with asthma who had positive responses to specific inhalation challenge to benzalkonium chloride;[23] a laundry worker with asthma, who used a disinfectant containing benzalkonium chloride had a positive challenge test to benzalkonium chloride;[24] a male pharmacist with asthma who had a positive challenge test to the lauryl derivative of benzalkonium chloride, which was an ingredient in the floor cleaner used in the pharmacy;[25] and a man who developed urticaria and asthma after use of a skin disinfectant and a pesticide that contained benzalkonium chloride.[26] The use of benzalkonium chloride as a preservative in nebulizer solutions has also been associated with bronchoconstriction and death.[27,28]

A study of 194 pig farmers from The Netherlands examined the interaction of the use of the disinfectants, chloramines, glutaraldehyde, or formaldehyde and quaternary ammonium compounds such as benzalkonium chloride. The use of quaternary ammonium compounds for short periods of time (once a week for less than 15 minutes) was associated with a significant increased risk of specific serum IgE to common environmental allergens (odds ratio [OR], 7.4; 95% CI, 1.3–43.1) and respiratory symptoms (OR, 4.4; 95% CI, 1.3–14.6).[29] The adjuvant effect of quaternary ammonium compounds was not found in this study with any of the other disinfectants.

Colophony

Colophony resin derived from pine trees has been well described as a cause of asthma. Tall oil, a derivative of pine resin with similar constituents as colophony, was an ingredient in a cleaning agent that was reported to cause a positive bronchial challenge in a cleaner and a laboratory technician in which the cleaning agent was used at her school.[30]

Carpet Cleaners

A Canadian woman in her 50s had recurrent respiratory symptoms, which began a few hours after arriving at work.[31] The carpet had been sprayed with a carpet fungicide a day and a half after water damage to the carpet. She had a positive challenge test with a 19% drop in her FEV_1 to tributyl tin oxide, which made up 25% of the carpet spray. She became symptom-free after removal from the office except for reexposure to tribubyl tin in a wallpaper paste and then occasional symptoms associated with infection, cold air, or fumes from cleaning agents. Other reports involving carpet cleaners have reported either irritation without documentation of asthma or severe exacerbation of preexisting asthma with anaphylaxis and hypoxic seizures.[32–35]

In 2000, a brand of dust mite powder and spray for carpet and upholstery was withdrawn from the market in the United States because of reports of asthma attacks, respiratory problems, burning sensation, and skin irritation 15 to 30 minutes after its use. The active pesticide ingredient was benzyl benzoate.[36]

Detergents

The addition of proteolytic enzymes, particularly *Bacillus subtilis*, in the 1960s was associated with the development of sensitization and asthma in workers manufacturing the detergent.[37] The product was reformulated, engineering controls were improved, and medical surveillance was implemented. With these changes, the incidence of sensitization and asthma were markedly reduced. Before the product was reformulated and the enzyme granulated, users of the detergents developed allergic symptoms and IgE antibodies.[38,39] Recent surveys, including studies of women doing handwashing in the Philippines, have shown negative skin tests to these enzymes despite the use of these products.[40,41] However, there is a case report of a male Canadian washing surgical tools with a liquid detergent containing subtilisin. A year after beginning the job, he became symptomatic. He had a positive skin prick test and a positive serum IgE to subtilisin and a 25% drop in his FEV_1 after specific inhalation challenge.[42]

New agents have been introduced into detergents over the years and a number of these agents have been associated with asthma in workers manufacturing detergents containing these additives, including amylase and cellulase,[43] an antimicrobial (1,2-benzisathiazolin-3 one),[44] and a bleach activator (sodium iso-nonanoyl oxybenzene sulfonate).[45] The presence of new agents in detergents, the case report in the surgical instrument washer, and the recurrence of asthma in at least one modern detergent-manufacturing facility in 2000[46] suggest the potential for asthma in detergent users.

Disinfectants

Chloramine

Multiple case reports of asthma among workers using the disinfectant chloramine have been reported.[47–55] These include a Finnish woman in her 30s cleaning showers and saunas,[47] 8 British brewery workers cleaning vessels and pipelines,[48,49] 14 American chemical workers manufacturing chloramine,[50] 6 Swedish pulp and paper workers spraying chloramine to suppress growth of mold on pulp,[51] a Swedish male dairy driver in his 40s using chloramine to clean equipment,[51] and 5 Dutch workers (2 cleaners in a meat-processing facility, an animal laboratory worker, an operating room nurse, and a clinic worker).[52,53] Work-related asthma was confirmed by different methods in these studies and included positive skin tests, specific IgE antibodies to chloramine–albumin conjugates, and positive specific antigen challenge testing.

Chloramine exposure may also occur after mixing incompatible cleaning agents (see the section on RADS) or inadvertently. Chlorine-releasing agents are used in pools, and reaction between chlorine from these agents and ammonia from human sweat and urine may produce chloramine. Two lifeguards and a swimming teacher from a British indoor pool had either positive specific antigen challenge testing or peak flow changes in association with work at a pool.[56] The authors attributed the asthma to trichloramine (NCl_3). Two cases are cited of individuals with work-related asthma from chloramine (an endoscopy nurse and a forensic scientist) who were both symptomatic when they used an indoor swimming pool.[56] These case reports may be an indication of a larger problem of risk of asthma in indoor pool swimmers, as suggested by increased bronchial hyperresponsiveness among swimmers versus other athletes.[57]

Chlorhexidine

Two case reports from England of a female nurse and a female midwife were reported to have asthma caused by exposure to an aerosol spray of chlorhexidine and alcohol. Specific antigen challenge test showed a 13% and 22% drop in FEV_1, respectively, in the 2 patients.[58] Neither had evidence of hyperreactivity with histamine. Both became asymptomatic with cessation of exposure.

Formaldehyde

Formaldehyde is both an irritant and sensitizer. A summary of the multiple reports on the respiratory effects of formaldehyde indicated that the majority of exposed individuals have irritation but that a limited number have positive bronchial challenge tests with sensitization.[59] Most cases involve exposure in an industrial setting such as the manufacture of plywood or urea–formaldehyde resin. Only a few of the reports describe asthma secondary to exposure to formaldehyde used as a disinfectant.[60] These reports have been of cases of asthma among British nurses in dialysis units, endoscopy, or the operating room.[61–63] Latency periods of symptoms from exposure ranged from months to over 20 years. The presence of IgE antibodies has been described in noncleaning product-related exposures but not exposures associated with cleaning agents.[60]

Reaction to both formaldehyde and glutaraldehyde was reported in 3 of 8 patients testing with specific bronchial challenge to both formaldehyde and glutaraldehyde. These positive responses to both chemicals may be secondary to a crossreaction of these 2 chemicals or indicative that patients were exposed to both substances at work.[64]

Studies have shown enhanced sensitization to common environmental antigens in animals exposed to both formaldehyde and environmental antigens,[65] similar to studies of sensitization in human to quaternary amines and environmental antigens.

Glutaraldehyde

Glutaraldehyde is a common sterilant used in medical settings to clean endoscopes. Alternate cold sterilants are becoming more common, including systems using hydrogen peroxide and/or peracetic acid, which have not been associated with sensitization, or ortho phthaladehyde, which may have the same allergic effects as glutaraldehyde.

There have been multiple case reports of asthma caused by glutaraldehyde exposure from Canada, England, Poland, Singapore, and Spain.[66–73] Diagnostic tests have included specific antigen challenge test and the development of specific IgE antibodies to glutaraldehyde-bound protein conjugates.

Two cross-sectional studies of hospital workers exposed to glutaraldehyde have reported an increased rate of skin and respiratory symptoms.[74,75] One study found an exposure–response relationship for respiratory symptoms.[75] At least part of the increase in asthma and respiratory symptoms reported among respiratory therapists appears to be from exposure to glutaraldehyde.[76]

The asthma surveillance system for West Midlands of England reported an increase in the percentage of cases secondary to glutaraldehyde from 1.3% to 5.6% between the years 1990 and 1997.[77]

Hexachlorophene

A pediatric nurse from Hungary in her 40s, who had exposure to hexachlorophene used as a topical disinfectant for 15 years, developed nasal symptoms after 5 years of exposure and asthma after 13 years of exposure. She was nonatopic to typical environmental skin tests and had a negative skin test response to a 1% solution of hexachlorophene. She had an increase in airway resistance in specific antigen bronchial challenge testing (expiratory volumes were not reported).[78]

Respiratory Effects Secondary to Irritation, Including Asthma Without a Latency Period of Exposure (RADS)

Asthma occurring after acute exposure to irritants has been reported with a wide range of substances across a wide range of industries.[4] The typical presentation of RADS is a massive exposure that causes chemical pneumonitis or pulmonary edema. After treatment and recovery from the acute condition, the patient is left with chronic asthma. Adverse respiratory effects from improper mixing of cleaning agents or exposure to single agents used at high concentrations both at work and at home have been reported. Mixing may occur deliberately in an inappropriate attempt to concoct a particularly strong cleaner, because multiple substances are added to a clogged drain, or because a cleaner product is added to a container such as a pail that contains residual incompatible material (Fig. 1).

Although there are multiple reports of improper mixing of cleaning agents, these reports have generally been limited to a description of the acute health effects. The adverse health effects described included cough, nausea, pulmonary edema, pneumomediastinum, acute bronchospasm, and chemical pneumonitis.[79–88] These reports have been from England, Israel, Italy, and the United States. There is one report of death.[89] There is one report of RADS developing from mixing incompatible cleaning agents.[90]

Death after cleaning a copper chandelier with nitric acid and persistence of symptoms after exposure to hydrofluoric acid used as a cleaning agent have also been reported.[91–93]

Mixing bleach and acid causes the formation of chlorine gas:

Bleach		Acid		Chlorine gas
2OC1-	+	4H+	=	C12 + 2H20

and mixing ammonia and bleach causes the formation of chloramines:

Ammonia		Bleach		Dichloramine
NH3	+	2OC1-	=	NHC12 + 2OH-

Ammonia		Bleach		Mono Chloramine
NH3	+	OC1-	=	NH2C1 + OH-

Continued reaction of NHC12 with bleach causes the formation of trichloramine:

				Trichloramine
NHC12	+	OC1-	=	NC13 + H20

FIGURE 1. Mixing bleach and acid causes the formation of chlorine gas. Mixing ammonia and bleach causes the formation of mono- and dichloramine. Continued reaction of dichloramine with bleach causes the formation of trichloramine.

Review of surveillance data has suggested a chronic effect from these acute exposures is more frequent than indicated by the case reports. Cleaning agents were the most common cause (15% of cases) of RADS reported to the asthma surveillance systems in California, Massachusetts, Michigan, and New Jersey.[94] Among all the asthma cases associated with cleaning agents, 18% were classified as RADS of which 75% were secondary to exposure to the use of single cleaning product and 25% were from the mixing of cleaning products.[15] Cleaning agents are frequent causes of nonfatal work-related injuries,[95] including those that occur in youth.[96]

Mixing 2 or more cleaners was responsible for 10% of workplace exposures and 13% of household exposures of the 337 individuals hospitalized in Michigan in 1989 and 1990 with the primary or secondary International Classification of Diseases code 506 (respiratory conditions resulting from chemical gases, fumes, or vapors).[97] Another 11% of hospitalizations were secondary to exposure to single household cleaning agents. A poison control center in Italy reported 235 cases of poisoning secondary to the mixing of bleach and acid from 1982 to 1988.[98]

The number of hospitalizations from the respiratory effects of cleaning products probably represents only a small percentage of individuals who have health effects. Among 216 patients 12 to 81 years of age reported to the Pittsburgh poison control center over a 12-month period in the early 1990s because of exposures to cleaning agents that had been mixed, only 33% needed medical treatment, only one required admission, and only 16 had persistence of symptoms for more than 6 hours after exposure.[99]

DISCUSSION

Epidemiologic studies have consistently shown an increase in the diagnosis of asthma-type respiratory symptoms in cleaners. The diagnosis of asthma used in the epidemiologic studies of cleaners varied and all individuals may not have met clinical criteria for a diagnosis of asthma. Accordingly, although some of the studies may have identified increased respiratory symptoms rather than asthma among cleaners, they clearly identified an increased risk of respiratory symptoms among cleaners by whatever definition of asthma was used in a particular study and that definition was applied equally to cleaners and the control population with other occupations.

An alternative explanation to a direct effect of the cleaning agent causing the increased respiratory problems in cleaners is that the cleaning product acts as an adjuvant causing increased sensitivity to an environmental allergen such as dust mites. The ability of 2 disinfectants, formaldehyde and quaternary ammonium compounds, used in cleaning products to act as an adjuvant in this manner has been reported in both animal and human studies.[29,65]

Certainly some ingredients of cleaning products have been shown to cause IgE-mediated asthma. Given there is no systematic testing of cleaning products or their ingredients for their ability to cause asthma, it is possible that other ingredients/products may also have a similar toxicologic effect.

The epidemiologic literature would suggest at a minimum that the irritants in cleaning products cause an increase in respiratory symptoms. Whether lower-level chronic exposure to irritating chemicals such as those found in cleaning agents that do not cause sensitization can also cause asthma needs further research.

Clinicians need to be aware of the hazards of cleaning agents both to cleaners and to individuals who are in areas where cleaning products are used. Cleaners are a high-risk group for respiratory symptoms and asthma. However, in many of the case reports, the patient's exposure to a cleaning product was not through using the product itself, but rather from working in an area where the product had been used. Clinicians need to be obtaining histories of the timing of the onset and exacerbation of respiratory symptoms. Because cleaning agents may be used intermittently both at work and at home, the temporal relation may be more complicated than that found in a typical work-related or environmentally triggered asthma where the suspect agent is just at work or just at home. The potential population at risk is not limited to adults. A recent study from England showed that the children of mothers who used the most household chemical products had an increased risk of persistent wheezing throughout childhood (OR, 2.5; 95% CI, 1.2–4.4).[100] The lack of the availability of specific antigen challenge testing in most clinical practice settings means clinicians need to rely on a good clinical history, review of the ingredients of cleaning products from labels or material safety data sheets, and performance of spirometry or peak flow testing in relation to the suspected exposure(s).

At an industry level, systematic testing of ingredients and cleaning products for their ability to cause sensitization should be routinely conducted. Given the frequency with which individuals mix incompatible cleaning agents, better labels and consumer education are also needed.

On a research basis, better elucidation of the respiratory symptoms in cleaners is needed to define how much is secondary to allergic sensitization. How much is secondary to an acute irritative effect? How much is secondary to a chronic irritative effect? How much to an adjuvant effect on increasing sensitization to environmental agents present in areas that are being cleaned? The ubiquitous use of cleaning products and the current, although incomplete, knowledge of their

health effects suggest that strategies by clinicians, industry, and researchers to address the potential adverse respiratory effects of cleaning products should be given high priority.

REFERENCES

1. Litovitz TL, Klein-Schwartz W, White S, et al. 2000 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med.* 2001;19:337–395.
2. Litovitz TL, Klein-Schwartz W, White S, et al. 1999 annual report of the American Association of Poison Control Centers Toxic Exposure Surveillance System. *Am J Emerg Med.* 2000;18:517–574.
3. Wolkoff P, Schneider T, Kildeso J, et al. Risk in cleaning: chemical and physical exposure. *Sci Total Environ.* 1998;215:135–156.
4. Chan-Yeung M, Malo JL. Occupational asthma. *N Engl J Med.* 1995; 333:107–112.
5. Kogevinas M, Antó JM, Sunyer J, et al. A population based study on occupational asthma in Europe and other industrialized countries. *Lancet.* 1999;353:1750–1754.
6. Zock JP, Kogevinas M, Sunyer J, et al. Asthma characteristics in cleaning workers, workers in other risk jobs and office workers. *Eur Respir J.* 2002;20:679–685.
7. Zock JP, Kogevinas M, Sunyer J, et al. Asthma risk, cleaning activities and use of specific cleaning products among Spanish indoor cleaners. *Scand J Work Environ Health.* 2001;27:76–81.
8. Karjalainen A, Martikainen R, Karjalainen J, et al. Excess incidence of asthma among Finnish cleaners employed in different industries. *Eur Respir J.* 2002;19:90–95.
9. Jaakkola JJK, Piipari R, Jaakkola MS. Occupation and asthma: a population-based case–control study. *Am J Epidemiol.* 2003;158:981–987.
10. Medina-Ramón M, Zock JP, Kogevinas M, et al. Asthma symptoms in women employed in domestic cleaning: a community based study. *Thorax.* 2003;58:950–954.
11. Arif A, Delclos GL, Whitehead LW, et al. Occupational exposures associated with work-related asthma and work-related wheezing among US workers. *Am J Ind Med.* 2003;44:368–376.
12. Ng TP, Hong CY, Goh LG, et al. Risk of asthma associated with occupations in a community-based case–control study. *Am J Ind Med.* 1994;25:709–718.
13. Mendonça EMC, Algranti E, deFreitas JBP, et al. Occupational asthma in the City of São Paulo, 1995–2000, with special reference to gender analysis. *Am J Ind Med.* 2003;43:611–617.
14. Buck RG, Miles AJ, Ehrlich RI. Possible occupational asthma among adults presenting with acute asthma. *S Afr Med J.* 2000;90:884–888.
15. Rosenman KD, Reilly MJ, Schill DP, et al. Cleaning products and work-related asthma. *J Occup Environ Med.* 2003;45:556–563.
16. Ameille J, Pauli G, Calastreng-Crinquand A, et al. Reported incidence of occupational asthma in France, 1996–99: the ONAP programme. *Occup Environ Med.* 2003;60:136–141.
17. Fishwick D, Pearce N, D'Souza W, et al. Occupational asthma in New Zealanders: a population based study. *Occup Environ Med.* 1997;54: 301–306.
18. Torén K, Balder B, Brisman J, et al. The risk of asthma in relation to occupational exposures: a case–control study from a Swedish city. *Eur Respir J.* 1999;13:496–501.
19. Nielsen J, Bach E. Work-related eye symptoms and respiratory symptoms in female cleaners. *Occup Med.* 1999;49:291–297.
20. Bernstein JA, Stauder T, Bernstein DI, et al. A combined respiratory and cutaneous hypersensitivity syndrome induced by work exposure to quaternary amines. *J Allergy Clin Immunol.* 1994;2:257–259.
21. Ng TP, Lee HS, Malik MA, et al. Asthma in chemical workers exposed to aliphatic polyamines. *Occup Med.* 1995;45:45–48.
22. Savonius B, Keskinen H, Tuppurainen M, et al. Occupational asthma caused by ethanolamines. *Allergy.* 1994;49:877–881.
23. Purohit A, Kopferschmitt-Kubler MC, Moreau C, et al. Quaternary ammonium compounds and occupational asthma. *Int Arch Occup Environ Health.* 2000;73:423–427.
24. Innocenti A. Occupational asthma due to benzalkonium chloride. *Med Lavoro.* 1978;69:713–715.
25. Burge PS, Richardson MN. Occupational asthma due to indirect exposure to lauryl dimethyl benzyl ammonium chloride used in a floor cleaner. *Thorax.* 1994;49:842–843.
26. Bjorkner B. Contact urticaria and asthma from denatonium benzoate (Bitrex). *Contact Derm.* 1980;6:466–471.
27. Beasley R, Rafferty P, Holgate ST. Bronchoconstrictor properties of preservatives in ipratropium bromide (Atrovent) nebulizer solution. *BMJ.* 1987;294:1197–1198.
28. Beasley R, Fishwick D, Miles JF. Preservatives in nebulizer solutions: risks without benefit. *Pharmacotherapy.* 1998;18:130–139.
29. Preller L, Doekes G, Heederik D, et al. Disinfectant use as a risk factor for atopic sensitization and symptoms consistent with asthma: an epidemiological study. *Eur Respir J.* 1996:1407–1413.
30. McCoach JS, Burge PS. *Tall Oil in a Floor Cleaning Agent as a Cause of Occupational Asthma.* Occupational Disease Intelligence Network (ODIN); September 1998.
31. Shelton D, Urch B, Tarlo SM. Occupational asthma induced by a carpet fungicide-tributyl tin oxide. *J Allergy Clin Immunol.* 1992;90:274–275.
32. Lynch RM. Modeling of exposure to carpet cleaning chemicals preceding irritant-induced asthma in one patient. *Environ Health Perspect.* 2000;108:911–913.
33. Kreiss K, Gonzalez M, Conright K. Respiratory irritation due to carpet shampoo: two outbreaks. *Environ Int.* 1982;8:337–341.
34. Lamb VA, Walter RF, Armstrong CW, et al. Respiratory illness associated with carpet cleaning at a hospital clinic. Virginia. *MMWR Morb Mortal Wkly Rep.* 1983;32:378–384.
35. Robinson P, Tauxe R, Winkler W, et al. Respiratory illness in conference participants following exposure to rug shampoo. *Infect Control.* 1983;4:158–160.
36. EPA, 2000. Available at: http://www.epa.gov/pesticides/citizens/allercareq_a.htm.
37. Schweigert MK, MacKenzie DP, Sarlo K. Occupational asthma and allergy associated with the use of enzymes in the detergent industry—a review of the epidemiology, toxicology and methods of prevention. *Clin Exp Allergy.* 2000;30:1511–1518.
38. Belin L, Hoborn J, Falsen E, et al. Enzyme sensitization in consumers of enzyme-containing washing powder. *Lancet.* 1970;2:1153–1157.
39. Zetterstrom O, Wide L. IgE antibodies and skin test reactions to a detergent enzyme in Swedish consumers. *Clin Allergy.* 1974;4:273–280.
40. Sarlo K, Cormier E, MacKenzie D, et al. Lack of type 1 sensitization to laundry enzymes among consumers in the Phillippines. *J Allergy Clin Immunol.* 1996;97:749.
41. Cormier E, Sarlo K, Scott L, et al. Lack of sensitization to laundry enzymes among consumers in the Philippines: results of an 18 month clinical study. *J Allergy Clin Immunol.* 1997;99:321.
42. Lemiere C, Cartier A, Dolovich J, et al. Isolated late asthmatic reaction after exposure to a high-molecular-weight occupational agent, subtilisin. *Chest.* 1996;110:823–824.
43. Brant A, Hole A, Cannon J, et al. Occupational asthma caused by cellulase and lipase in the detergent industry. *Occup Environ Med.* 2004;61:793–795.
44. Moscato G, Omodeo P, Dellabianca A, et al. Occupational asthma and rhinitis caused by 1,2-benzisothiazolin-3-one in a chemical worker. *Occup Med.* 1997;47:249–251.
45. Stenton SC, Dennis JH, Walters EH, et al. Asthmagenic properties of a newly developed detergent ingredient: sodium iso-nonanoyl oxybenzene sulphonate. *Br J Ind Med.* 1990;47:405–410.
46. Cullinan P, Harris JM, Newman Taylor AJ, et al. An outbreak of asthma in a modern detergent factory. *Lancet.* 2000;356:1899–1900.
47. Kujala VM, Reijula KE, Ruotsalainen E-M, et al. Occupational asthma due to chloramine-T solution. *Respir Med.* 1995;89:693–695.
48. Bourne MS. Flindt MLH, Walker JM. Asthma due to industrial use of chloramine. *BMJ.* 1979;2:10–12.
49. Charles TJ. Asthma due to industrial use of chloramine. *BMJ.* 1979;1:334.
50. Feinberg SM, Watrous RM. Atopy to simple chemical compounds—sulfonechloramides. *J Allergy.* 1945;16:209–220.
51. Wass U, Belin L, Eriksson NE. Immunological specificity of chloramine-T-induced IgE antibodies in serum from a sensitized worker. *Clin Allergy.* 1989;19:463–471.
52. Dijkman JG, Vooren PH, Kramps JA. Occupational asthma due to inhalation of chloramine-T. 1. Clinical observations and inhalation—provocation studies. *Int Arch Allergy Appl Immunol.* 1981;64:422–427.
53. Kramps JA, van Toorenenbergen AW, Vooren PH, et al. Occupational

asthma due to inhalation of chloramine-T. II. Demonstration of specific IgE antibodies. *Int Arch Allergy Appl Immunol.* 1981;64:428–438.
54. Romeo L, Gobbi M, Pezzini A, et al. Asthma induced by sodium tosylchloramide: a case report. *Med del Lavoro.* 1988;79:237–240.
55. Blomquist AM, Axelsson IGK, Danielsson D, et al. Atopic allergy to chloramine-T and the demonstration of specific IgE antibody by the radioallergosorbent test. *Int Arch Occup Environ Health.* 1991;63:363–365.
56. Thickett KM, McCoach JS, Gerber JM, et al. Occupational asthma caused by chloramines in indoor swimming-pool air. *Eur Respir J.* 2002;19:827–832.
57. Nemery B, Hoet PHM, Nowak D. Indoor swimming pools, water chlorination and respiratory health. *Eur Respir J.* 2002;19:790–793.
58. Waclawski ER, McAlpine LG, Thomson NC. Occupational asthma in nurses caused by chlorhexidine and alcohol aerosols. *BMJ.* 1989;298: 929–930.
59. Nordman H, Keskinen H, Tupparainen M. Formaldehyde asthma—rare or overlooked? *J Allergy Clin Immunol.* 1985;91–99.
60. Malo JL, Bernstein IL. Other chemical substances causing occupational asthma. In: Bernstein IL, Chan-Yeung M, Malo JL, et al., eds *Asthma in the Workplace,* 2nd ed. New York/Basel: Marcel-Decker; 1999:523–541.
61. Hendrick DJ, Lane DJ. Occupational formalin asthma. *Br J Ind Med.* 1977;34:11–18.
62. Hendrick DJ, Lane DJ. Formalin asthma in hospital staff. *BMJ.* 1975; 1:607–608.
63. Hendrick DJ, Rando RJ, Lane DJ, et al. Formaldehyde asthma: challenge exposure levels and fate after five years. *J Occup Med.* 1982;24: 893–897.
64. Gannon PFG, Bright P, Campbell M, et al. Occupational asthma due to glutaraldehyde and formaldehyde in endoscopy and x ray departments. *Thorax.* 1995;50:156–159.
65. Kita T, Fujimura M, Myou S, et al. Potentiatim of allergic bronchoconstriction by repeated exposure to formaldehyde in guinea-pigs in vivo. *Clin Exp Allergy.* 2003;33:1747–1753.
66. Chan-Yeung M, McMurren T, Catonio-Begley F, et al. Occupational asthma in a technologist exposed to glutaraldehyde. *J Allergy Clin Immunol.* 1993;91:974–978.
67. Corrado OJ, Osman J, Davies RJ. Asthma and rhinitis after exposure to glutaraldehyde in endoscopy units. *Hum Toxicol.* 1980;5:325–327.
68. Curran AD, Burge PS, Wiley K. Clinical immunologic evaluation of workers exposed to glutaraldehyde. *Allergy.* 1996;51:826–832.
69. Anees W, Robertson AS, Burge PS. Glutaraldehyde induced asthma in endoscopy nursing staff. *Occup Environ Med.* 2001;58:544.
70. Ong TH, Tan KL, Lee HS, et al. A case report of occupational asthma due to glutaraldehyde exposure. *Ann Acad Med Singapore.* 2004;33: 275–278.
71. Quirce S, Gomez M, Bombin C, et al. Glutaraldehyde-induced asthma. *Allergy.* 1999;54:1121–1122.
72. DiStefano F, Sirriuttanapruk S, McCoach J, et al. Glutaraldehyde: an occupational hazard in the hospital setting. *Allergy.* 2001;56:466–469.
73. Patczyński C, Walusiak J, Ruta U, et al. Occupational asthma and rhinitis due to glutaraldehyde: changes in nasal lavage fluid after specific inhalatory challenge test. *Allergy.* 2001;56:1186–1191.
74. Waters A, Beach J, Abramson M. Symptoms and lung function in health care personnel exposed to glutaraldehyde. *Am J Ind Med.* 2003;43:196–203.
75. Vyas A, Pickering CAC, Oldham LA, et al. Survey of symptoms, respiratory function, and immunology and their relation to glutaraldehyde and other occupational exposures among endoscopy nursing staff. *Occup Environ Med.* 2000;57:752–759.
76. Dimich-Ward H, Wymer ML, Chan-Yeung M. Respiratory health survey of respiratory therapists. *Chest.* 2004;126:1048–1053.
77. DiStefano F, Sirirutanapruk S, McCoach J, et al. Occupational asthma in a highly industrialized region of UK: report from a local surveillance scheme. *Allerg Immunol.* 2004;36:56–62.
78. Nagy L, Orosz M. Occupational asthma due to hexachlorophene. *Thorax.* 1984;39:630–631.
79. Gapany-Gapanavicius M, Yellin A, Almog S, et al. Pneumomediastinum: a complication from mixing household cleaning agents. *JAMA.* 1982;248: 349–350.
80. Gapany-Gapanavicius M, Molho M, Tirosh M. Chloramine-induced pneumonitis from mixing household cleaning agents. *BMJ.* 1982;285: 1086.
81. Hattis RP, Greer JR, Dietrich S, et al. Chlorine gas toxicity from mixture of bleach with other cleaning products—California. *MMWR Morb Mortal Wkly Rep.* 1991;40:619–629, 646.
82. Jones FL. Chlorine poisoning from mixing household cleaners. *JAMA.* 1972;222:1312.
83. Reisz GR, Gammon RS. Toxic pneumonitis from mixing household cleaners. *Chest.* 1986;89:49–52.
84. Tanen DA, Graeme KA, Raschke R. Severe lung injury after exposure to chloramine gas from household cleaners. *N Engl J Med.* 1999;381: 848–849.
85. Faigel HC. Hazards to health: mixtures of household cleaning agents. *N Engl J Med.* 1964;271:618.
86. Philipp R, Shepherd C, Fawthrop F. Domestic chlorine poisoning. *Lancet.* 1985;2:495.
87. Mapp CE, Pozzato V, Pavoni V, et al. Severe asthma and ARDS triggered by acute short-term exposure to commonly used cleaning detergents. *Eur Respir J.* 2000;16:570–572.
88. Murphy DMF, Fairman RP, Lapp NL, et al. Severe airway disease due to inhalation of fumes from cleaning agents. *Chest.* 1976;69:372–376.
89. Cohle SD, Thompson W, Eisenga BH, et al. Unexpected death due to chloramine toxicity in a woman with a brain tumor. *Forensic Sci Int.* 2001;24:137–139.
90. Alberts WM, DoPico GA. Reactive airways dysfunction syndrome. *Chest.* 1996;109:1618–1626.
91. Bur A, Wagner A, Roggla M, et al. Fatal pulmonary edema after nitric acid inhalation. *Resuscitation.* 1997;35:33–36.
92. Bennion JR, Franblau A. Chemical pneumonitis following household exposure to hydrofluoric acid. *Am J Ind Med.* 1997;31:474–478.
93. Franzblau A, Sahakian N. Asthma following household exposure to hydrofluoric acid. *Am J Ind Med.* 2003;44:321–324.
94. Henneberger PK, Derk SJ, Davis L, et al. Work-related reactive airways dysfunction syndrome cases from surveillance in selected US states. *J Occup Environ Med.* 2003;45:360–368.
95. Henneberger PK, Metayer C, Layne LA, et al. Nonfatal work-related inhalations: surveillance data from hospital emergency departments, 1995–1996. *Am J Ind Med.* 2000;38:140–148.
96. Brevard TA, Calvert GM, Blondell JM, et al. Acute occupational disinfectant-related illness among youth, 1993–1998. *Environ Health Perspect.* 2003;111:1654–1659.
97. Reilly MJ, Rosenman KD. Use of hospital discharge data for surveillance of chemical-related respiratory disease. *Arch Environ Health.* 1995;50:26–30.
98. Bernardini P, Castellino N, Sabatelli G, et al. Domestic chlorine poisoning in Italy from mixing household cleaners. In: *Indoor Air 1990: Proceedings of the 5th International Conference on Indoor Air Quality and Climate-*.Toronto, Canada: International Conference on Indoor Air Quality and Climate; 1990.
99. Mrvos R, Dean BS, Krenzelok EP. Home exposures to chlorine chloramine gas—review of 216 cases. *South Med J.* 1993;86:654–657.
100. Sherriff A, Farrow A, Golding J, et al. Frequent use of chemical household products is associated with persistent wheezing in preschool age children. *Thorax.* 2005;60:45–49.