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Asthma and exposure to cleaning products – a European Academy of Allergy and Clinical Immunology task force consensus statement

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ABSTRACT

Professional and domestic cleaning is associated with work-related asthma (WRA). This position paper reviews the literature linking exposure to cleaning products and the risk of asthma and focuses on prevention. Increased risk of asthma has been shown in many epidemiological and surveillance studies, and several case reports describe the relationship between exposure to one or more cleaning agents and WRA. Cleaning sprays, bleach, ammonia, disinfectants, mixing products, and specific job tasks have been identified as specific causes and/or triggers of asthma. Because research conclusions and policy suggestions have remained unheeded by manufactures, vendors, and commercial cleaning companies, it is time for a multifaceted intervention. Possible preventive measures encompass the following: substitution of cleaning sprays, bleach, and ammonia; minimizing the use of disinfectants; avoidance of mixing products;

use of respiratory protective devices; and worker education. Moreover, we suggest the education of unions, consumer, and public interest groups to encourage safer products. In addition, information activities for the general population with the purpose of improving the knowledge of professional and domestic cleaners regarding risks and available preventive measures and to promote strict collaboration between scientific communities and safety and health agencies are urgently needed.

[BOX 1]

In Europe, the fraction of adult asthma attributable to occupational exposure ranges between 10% and 25% [1]. Work-related asthma (WRA) includes occupational asthma (OA), caused by exposure to high or low molecular weight agents in the workplace, and work-exacerbated asthma (WEA), in which pre-existing or concurrent asthma is exacerbated by various work-related factors, such as accidental spills, second-hand cigarette smoke, or exertion [2, 3].
Cleaners constitute a large professional group in developed countries. In industrial cleaning, about 30% are migrant workers and about 40% of women are domestic cleaners [4, 5]. Professional and domestic cleaning has been associated with new-onset OA due to sensitizers and irritant exposure as well as WEA and respiratory symptoms without asthma [5-7].
It is likely that nonoccupational physicians (general practitioners, allergologists, and pneumologists) frequently see patients with asthma who work with exposure to cleaning products. However, prevention of work-related respiratory diseases in cleaners has not received sufficient attention from healthcare professionals, employers, and policy makers despite knowledge on the dimension of the problem and identification of specific products and job tasks responsible for asthma symptoms. Effective prevention strategies addressed to workers using cleaning products are urgently needed.

The aims of this document are as follows:

- to summarize the current scientific evidence linking exposure to cleaning products to the risk of asthma; and
- to provide suggestions for prevention, such as avoidance of exposure, educational activities, and safety training addressed to general practitioners, allergologists, chest physicians, and others managing asthma in cleaning workers.

METHODS

This consensus document was prepared by a European Academy of Allergy and Clinical Immunology (EAACI) task force consisting of an expert panel of allergologists, pneumologists, occupational physicians, and epidemiologists.
The literature was reviewed by the panel members, using a MEDLINE search. A meeting was held to review the findings and to reach informal consensus. Further consensus was reached by an informal iterative process by input from all panel

members into the drafts of the document. The original aim of the task force was to advance recommendations using an evidence-based system. However, it was recognized that the quality of published studies in this area was heterogeneous, and thus, no evidence-based recommendations could be provided. Instead, 'key messages' (see Key Messages Box) or 'suggestions' are provided based on the consensus of the expert panel members.

Data sources, search strategy, and study selection

Published studies were identified from PubMed covering the years from 1976 through September 30, 2012. We used the following key words search strategy: (cleaning worker* OR cleaning product* OR cleaner*) AND (asthma OR respiratory). We also reviewed all selected papers for reference citations within the 1976–2012 time frame that had not been otherwise identified in the initial search and added relevant papers.

Definition of cleaning workers

We defined cleaning workers or cleaners as individuals whose work involves cleaning of industrial settings, public, or private buildings. In this definition, we include (i) professional nondomestic and domestic cleaners, whose primary task is cleaning offices and/or homes for payment, (ii) nonprofessional home cleaners (e.g., housewives), and (iii) other jobs where the use of cleaning products at work is common (e.g., nurses). Professions in which cleaning products were used outdoors (e.g., road cleaners) were not included.

EPIDEMIOLOGY

Cleaning work and asthma

The first evidence for an increased risk of asthma related to cleaning work comes from epidemiological studies based on general population samples. During the last two decades, a 50–100% higher risk of (work-related) asthma or respiratory symptoms has been observed in an asthma case–control study [8] and other cross-sectional studies [6, 9, 10] in different areas of the world (Table 1). One study also observed an increased risk of asthma among women who had left their cleaning job [5]. Regarding the type of cleaning work, studies in Spain found higher asthma risks for home cleaners as compared to other indoor cleaners [5, 11], while a large Finnish study found consistently increased risks across a wide variety of cleaning workers [12]. The latter study observed the highest risk of asthma among cleaners of industrial sites involving a recognized risk of WRA, thus suggesting that exposures to products or waste from the manufacturing process where the cleaning is performed may be relevant. The risk of new-onset asthma related to cleaning work has been confirmed so far in two longitudinal population-based studies, although risk estimates did not reach conventional levels of statistical significance and/or were only observed in women [1, 13].

[TABLE 1]

Few workforce-based studies in cleaners have been performed. Advantages over population-based studies include opportunities for more specific and less biased assessment of occupational exposure and bigger numbers of individuals with specific exposures. In general, results confirmed an increased asthma risk in cleaners when compared with other employees of the same companies [14, 15].
Thus, although definitions of both cleaning work and asthma (symptoms, doctor diagnosis, and/or bronchial hyper-responsiveness) were heterogeneous among studies, there is considerable evidence from epidemiological studies that cleaning work is associated with asthma.

Use of cleaning products and asthma

The use of cleaning products provides a more specific exposure definition than 'cleaning work' and is also relevant in other occupations such as healthcare professionals, animal husbandry, and food processing workers (Table 2). In population-based studies, exposure to cleaning agents across different occupations is typically assessed using job exposure matrices. Exposure to 'industrial cleaning agents' was associated with asthma and/or asthma severity in several studies with different designs [1, 16-19]. In workforce-based studies, specifically designed questionnaires for the respective sector(s) have been used and have consistently shown associations between the use of cleaning products and asthma among cleaners [14, 15] and in other occupations involving the use of cleaning products [20-22]. Finally, a study in US homemakers showed that cleaning activities were related to short-term lower respiratory tract symptoms among asthmatic, but not among nonasthmatic women [23].

[TABLE 2]

Specific cleaning exposures and asthma

The identification of specific cleaning exposures that are driving the increased asthma risks is crucial for the development of preventive measures. In cleaning workers, asthma symptoms or asthma exacerbations have been associated with the use of sprays [11, 24-26], bleach [25, 27], waxing [14], and a history of acute inhalations [15, 27]. In other occupations involving the use of cleaning products, asthma was associated with exposure to disinfectants [20] and bleach, ammonia, and sprays [28].

SURVEILLANCE STUDIES

Several WRA surveillance studies from different countries have reported cases of OA in cleaning workers or related to professional use of cleaning products. Occupational disease registries provide an important source of information on the relative occurrence of asthma in different jobs and on specific causal agents, although they likely under-represent true incidence. Nevertheless, occupational

disease registry reports and registry linkage studies show overall that cleaning products are relevant agents implicated in WRA.

European countries

In Finland, the incidence and risk of asthma among female cleaners employed in different industries were explored [12]. All Finnish females employed as cleaners and all those employed in administrative work were followed for asthma incidence through a record linkage from 1986–1998. An individual was defined as an 'incident case of asthma' if that individual received rights for special reimbursement of asthma medication from the national health insurance, which required documented physician-diagnosed asthma, or was recognized as having OA.
There were 2414 and 5235 cases of asthma among cleaners and administrative workers, respectively, the relative risk (RR) being 1.5 (95% confidence interval (CI) 1.4–1.6) in cleaners. The risk was increased in cleaners working in nearly all major sectors of economic activity, but cleaners employed by companies concerned with the manufacture of basic metals (RR 2.5, 95% CI 1.7–3.6) and food products (RR 2.2, 95% CI 1.7–2.8) had the highest risk. Only 1% of the total cases of asthma among cleaners had been recognized as OA.
Work-related asthma trends in France in terms of industrial activities and the main causal agents over the period 2001–2009 have been reported [29]. Data were collected from the French National Network of Occupational Health Surveillance and Prevention and showed that WRA declined in France over the study period. Analyses by causal agents showed that only WRA reported from exposure to quaternary ammonium compounds (Quats), used as sterilizing or cleaning agents, had increased significantly over the observation period, and also a slight, but not significant, increase (from 2.6% in 2001 to 5.4% in 2009 of total WRA cases) was observed for cleaning products other than Quats. The health and social sector demonstrated both a growing number of cases reported from the use of Quats and a decrease in the number of cases related to aldehyde and latex exposure.
In 2002, a voluntary registry of occupational respiratory diseases was initiated in three regions of Spain (Asturias, Catalonia, and Navarre), and cleaning agents accounted for 5% of OA cases [30]. In Catalonia, this voluntary reporting system had shown that in 2002 among 174 newly diagnosed cases of OA, cleaning agents were suspected as being the causal agent in 9% of cases. In addition, 46 cases of acute inhalations were reported, and cleaning was the most frequently reported occupation associated with acute inhalations (26%).
The Surveillance of Work-Related and Occupational Respiratory Disease (SWORD) scheme in the UK observed a decline in OA and inhalation injuries over the period 1992–2001 [31]. Although in this registry cleaning products are not listed among the most frequent causes of OA in the UK, a detailed analysis of the data for 1992–2001 showed that the annual average incidence of asthma for domestic cleaners was one of three of the overall OA incidence.

North American countries

In the USA, the states of California, Massachusetts, Michigan, and New Jersey conducted WRA surveillance as part of the Sentinel Event Notification System for Occupational Risks (SENSOR) [32]. The Californian surveillance system showed

that janitors and cleaners had the highest incidence of WRA. Of all new-onset WRA cases, 3.4% were exposed to cleaning products [33]. Rosenman et al. [34] reviewed the reports on WRA as part of the SENSOR from 1993 to 1997 and found that 12% of the 1915 confirmed cases of WRA were associated with exposure to cleaning products. Among the cleaning products, the most commonly identified were bleach, ammonia, acids, and disinfectants such as aldehydes and Quats. Janitors, nurses, and nurses' aides were the three most common occupations reported.
A study carried out in Alberta (Canada) linked data from compensation claims and physician billing data to identify the incidence of new-onset adult asthma and showed an increased risk of OA related to cleaning agents in men (odds ratio (OR) 1.9, 95% CI 1.3–2.7) [35].
In summary, cleaning products are increasingly incriminated as a causative agent of WRA in registry-based studies from several countries, accounting for 3.4% to 12% of reported asthma cases. However, the validity of the registries depends on the adequacy of complete reporting and quality of the diagnostic work-up applied to suspected cases of WRA, and there may be a reporting bias toward well-known etiologic agents as cleaning products are under-reported. International comparisons are hampered by the different diagnostic criteria used and differences in reporting systems (mandatory versus voluntary, specialization of physicians involved, target population, etc.).

CASE REPORTS

In the last 30 years, several case reports described the relationship between exposure to one or more specific cleaning agents and WRA. Table 3 lists case reports of OA in which the diagnosis was based on work-related respiratory symptoms and bronchial-specific inhalation challenges. When feasible, specific skin prick tests were also used. Specific etiological agents involved in cases of OA were disinfectants or detergents, such as chloramine-T, Quats, ethanolamine, ethylenediaminetetraacetic acid (EDTA), dishwasher detergent powder and bleach [36-43], respiratory irritants [44-47], enzymes [48, 49], and molds [39]. Possible mechanisms were IgE-mediated, immunologic non-IgE, and pharmacologic.

[TABLE 3]

Table 4 shows cases of irritant-induced asthma and reactive airways dysfunction syndrome (RADS), in which the diagnosis was based on work-related respiratory symptoms ± pulmonary function tests or bronchial hyper-reactivity (BHR).

[TABLE 4]

Inhalation accidents, such as mixing bleach with ammonia or dishwashing liquid (hypochlorite + ammonium salts → chloramines) or acid detergents (→ chlorine) before use, were associated with asthma symptoms [50], RADS [51, 52], and WEA [53, 54] (Table 5).
[table 5]

MECHANISMS OF ASTHMA RELATED TO CLEANING PRODUCTS

Exposure to the ingredients of cleaning products may give rise to both new-onset asthma, with or without a latency period, and WEA. In most cases, the underlying pathogenic mechanisms remain largely unknown. Most cleaning agents have an irritating effect on airways, but occasionally some can induce true sensitization by an immunologic mechanism. Inhalation of irritants can induce bronchial epithelial damage, resulting in several events: a pro-inflammatory response, neurogenic inflammation due to exposed nerve endings, and finally, increased lung permeability and remodeling of the airway epithelium [55-57]. These effects may facilitate allergic sensitization, but also may increase BHR to an allergen to which the subject has been previously sensitized [58]. Studies of subjects exposed to chlorination products, mainly in swimming pool, suggest that they promote allergic sensitization by compromising the permeability or the immunoregulatory function of epithelial barriers or exacerbate allergic diseases [59]. Conversely, the presence of atopy does not appear to influence the development of respiratory symptoms induced by cleaning products [7]. Likewise, children exposed to regular house cleaning with bleach were less likely to have asthma, eczema, and been sensitized to indoor aeroallergens, especially house dust mite [60]. However, cleaning workers can be exposed to common indoor allergens (e.g., house dust mites, animal dander, molds, and cockroaches) in the workplace that may have important influence on their asthma.

The main sensitizers contained in cleaning products are disinfectants such as Quats (e.g., benzalkonium chloride) [38], amine compounds [61], aldehydes [62], and fragrances [63] (Table 3). A clear IgE mechanism has been demonstrated only for chloramine-T [37, 39] and enzymes [48, 49]. However, specific inhalation challenges using other agents elicited asthmatic reactions, suggesting an immunologic non-IgE mechanism similar to that due to agents of low molecular weight that induce OA [55].

A few studies have investigated bronchial inflammation or airway response to irritant products [25]. Hox et al. [64] in an animal model have demonstrated that induction of BHR by inhalation of hypochlorite depends on a neuroimmune interaction that involves transient receptor potential ankyrin 1 (TRPA1) channel-dependent stimulation of sensory neurons and mast cell activation.

Recently, Sastre et al. [43] investigated the effects of bleach inhalation on pulmonary function and inflammatory parameters among cleaning employees and controls with and without BHR. Subjects were challenged with placebo or bleach (at 0.4 ppm of chlorine). The fall in FEV1 during the bleach challenge was greater than that during the placebo challenge in nine subjects with BHR in comparison with 10 without BHR. The bleach challenge elicited two isolated late asthmatic reactions and one dual asthmatic reaction. Of all the patients challenged with bleach, only one had a significant decrease in the PC20 of methacholine 24 h after challenge. There were no clinically significant changes in sputum cell counts or fraction of exhaled nitric oxide (FENO) after bleach challenges. Therefore, it appears that chlorine inhalation even below the recommended 8-h occupational exposure level has the capacity to induce bronchial obstruction in some subjects whether they have BHR or not.

Nevertheless, respiratory symptoms apparently induced by cleaning products cannot always be explained by asthmatic reactions. Some patients may develop the so-called

airway sensory hyper-reactivity induced by scents and inhaled chemicals [65]. However, it is known that the sense of smell is not a sensitive discriminator for irritancy and odor does not always mean toxicity [66]. Dysfunctions of the upper airway, such as irritable larynx syndrome or cough, may explain respiratory symptoms in some patients [67, 68].
In summary, the potential pathogenetic mechanisms to explain asthma or irritant effects of cleaning agents may include an allergic-mediated mechanism, a toxic-mediated inflammation of upper and lower airways, or both mechanisms can enhance the other.

EXPOSURE ASSESSMENT

In studies of cleaning products and respiratory disorders, there are only limited reports of quantitative exposure assessment. One reason is because a large number of cleaning products exists, and many are complex mixtures of chemicals with different compositions and physicochemical properties. Therefore, multiple methods and measurement techniques are required [69]. Another reason is the type and frequency of products used which depends on the specific cleaning tasks. Thus, in a single room or setting, multiple cleaning tasks with different products may be performed, and during a single day, repetition of cleaning tasks is often necessary [70, 71]. Among others, Zock et al. [7] emphasized the need for quantitative exposure assessment approaches. Unfortunately, this is not always feasible (e.g., it is difficult to measure airborne Quats) [72]. A further need is to quantify short-term and peak exposures [71]. In contrast to continuous 8-h time-weighted average measurements, task-based exposure assessment studies (e.g., 10 min for each task) may be a good option to evaluate exposure variability [69]. Different factors with potential impact on exposure such as room size, ventilation, temperature, spray application (e.g., with nanoparticles), and task performance should be controlled during exposure assessment studies [73]. Another important point is that airborne chemicals from short-term cleaning tasks such as spray application can remain in the air even after completion of the cleaning process, leading to potential exposures shortly after cleaning [69].
Qualitative exposure data based on job titles and product types are often used as surrogate markers to estimate the exposure in epidemiological studies of respiratory disorders (asthma) induced by cleaning products. Results from quantitative exposure assessment studies may be used to develop a questionnaire or a matrix to estimate the exposure of cleaning workers if exposure measurements are not available [6, 17].
As airborne measurements of workplace exposures require a variety of integrated sampling and measurement methods, which are costly and sometimes difficult to apply in field investigations, an alternative is the identification of exposure determinants as used by occupational hygienists. For example, a quasi-experimental study design was used with performance of workplace-related cleaning tasks under controlled conditions [74]. The authors concluded that product type, tasks performed, room size, and ventilation have significant impact on exposure during cleaning tasks. Inclusion of 2-butoxyethanol concentration in the statistical analysis gave the best fit of the multivariable model. In another study, significant exposure determinants of airborne 2-butoxyethanol, a known respiratory irritant and suspected human carcinogen commonly used in commercial and residential cleaning product

formulations, were identified, and statistical models for estimating workplace exposures were developed [75].
In conclusion, exposure studies should ideally include quantitative exposure assessment. If this is not feasible, qualitative exposure data and statistical models for estimating workplace exposure are acceptable options.

AVOIDANCE OF EXPOSURE, EDUCATIONAL ACTIVITIES, AND SAFETY TRAINING

Ideally, effective cleaning products that do not cause or exacerbate asthma would be available and affordable, and the task force considers this to be a priority need. Certain cleaning tasks and exposures, such as the use of cleaning sprays, bleach, ammonia, disinfectants, and mixing product, appear to carry more risk for asthma than others, and the task force advises that these be the initial focus for preventive interventions.

Avoidance of specific exposures

Powdered natural rubber latex gloves for cleaning have been mainly eliminated by changes to nonlatex or nonpowdered latex gloves. However, the risk of sensitization to cleaners is high with agents used in health care, such as glutaraldehyde and enzymes, to clean endoscopes and surgical instruments, while irritant effects that can cause RADS or irritant-induced OA, such as mixing bleach and ammonia in a small, poorly ventilated area, are more likely in washroom cleaning. Bleach has particularly been associated with WRA in Spanish cleaners [7, 25] and sprayed products among professional cleaners and healthcare workers [22].
Avoidance of glutaraldehyde has been achieved in part by changing to the less volatile ortho-phthalaldehyde. Using cleaning products that are wiped, not sprayed, and of low volatility has been associated with less asthma [27], but has not been assessed in an intervention study. Use of ‘green products’ has been suggested as a protective measure [76], but this designation is in large part beneficial on an environmental or energy basis and does not necessarily indicate that products are safer for inhalation (USA EPA Web site http://www.epa.gov/epp/pubs/guidance/standards.htm). A computerized quantitative structure–activity program may be a method to predict possible sensitizing potential of new agents before commercial introduction [77].
Other measures include maintaining records of incidents in larger workplaces and analyzing group results regularly to identify problem exposures and, where possible, replacing agents with less hazardous materials [78].

Health and safety education

As an interim measure until safer products are in general usage, health and safety education is advised. Worker safety and health education as to the safe use of chemicals (including information and knowledge of material safety data sheets) and means of personal protective measures is a responsibility of employers.
Collaboration between a cleaners' union and a public health organization was successful in eliminating the use of the most hazardous products, reducing the

number of different products used, banning the mixing of products, and enhancing safety training [79], showing feasibility of such an approach, but it was not evaluated for effectiveness in reduction of WRA.
A systematic review in 2011 evaluated occupational-based behavioral interventions for workers exposed to dermal and respiratory hazards [80]. Only 10 potentially relevant articles included pre- and postintervention measures and a control group. None included asthma among cleaners. Effects of interventions were generally small, and there was likely to be selection bias, limiting generalizability of results.
Although instruction was provided to workers and some studies tried to support implementation of changes by setting targets, none tried to influence social norms of the work environment such as peer pressure.
At an earlier level, education of young asthmatics during their schooling or early in their working life may increase their awareness of possible effects of workplace exposures to chemicals such as those in cleaning products and possible ways in which to prevent or reduce effects [81, 82].

Protective respiratory devices

With availability of safer products and good ventilation, these should eventually not be needed. A study that assessed factors related to self-reported use of respiratory protective devices (RPDs) while working found the following factors to be positively associated with better compliance with the use of RPDs [83]: compliance of co-workers, conveniently located RPDs, safety training discussing the use of RPDs, fit testing available at the workplace, and age. This suggests a need to address social norms in the work environment as well as individual workers.
As part of a study that evaluated risks of WRA in professional cleaners in Ontario, among cleaners surveyed, 94% reported receiving chemical safety training, but 13% found the topics hard to understand [84]. Those who did not receive safety training had a significant increase in frequency of WRA symptoms (OR 2.3, 95% CI 1.0–5.3).

Addressing needs of women cleaning in domestic environments

As cleaning at work and at home is a women-dominated occupation and uncontrolled asthma is more frequent in women than in men, domestic exposures might partly explain gender differences in asthma control. Homemakers and housekeepers have no training on the potential toxicity of the products used. Information on the risk and on safe use of cleaning products through media, women's magazines, etc. may be useful. Programs that include education on the use of cleaning products may be associated with reduced use of agents that can trigger asthma and have been reported to result in reduced asthma symptoms in a poor community in Mexico [85].
Education of asthmatic patients by healthcare providers that includes dangers of mixing products, identification of higher-risk products, importance of ventilation, and appropriate RPD usage would be expected to reduce asthma effects due to cleaning products.

A European Policy Approach

Regulations and databases such as REACH (Registration, Evaluation, Authorization, and Restriction of Chemical substances) may be helpful; for example, the CLP (classification, labeling, and packaging) regulation ensures that chemical hazards are clearly communicated to workers and consumers in the European Union through classification and labeling of chemicals (www.echa.eu). The task force consensus is that additional regulations and communication are needed to reduce the respiratory impact of cleaning agents at work and in the home.

RESEARCH NEEDS

Although epidemiological, surveillance, and case studies have provided considerable evidence that asthma can be caused or aggravated by exposure to cleaning agents, there are remaining needs for further research to better understand these effects and to develop strategies for exposure control and disease prevention. There is a need for more focused studies to clarify the underlying effect mechanisms and to evaluate the suspected risk factors in more detail. Cleaning-related asthma is a preventable disease, and to develop prevention strategies, it is necessary to identify both specific risk factors and effect mechanisms.
Large-scale longitudinal studies can be helpful in understanding new-onset OA (with or without a latency period) and WEA, and reducing selection biases. An important aim should be the confirmation of individual cleaning chemicals that are likely to determine adverse effects on the airways. Phenotypic characterization of the asthma is important to help evaluate underlying mechanisms. Other respiratory outcomes should be considered; that is, rhinitis and lower respiratory tract disorders such as bronchitis and bronchiolitis. In particular, there are indications that upper respiratory tract symptoms can be caused and/or aggravated by cleaning exposures.
Further surveillance studies are recommended with an effort to use comparable methods across working groups, schemes, and areas. Natural history of patients with respiratory symptoms or different types of WRA associated with specific tasks should be investigated with long-term follow-up studies, as well as outcome of symptoms and pulmonary function after avoidance of cleaning products.
Diagnostic tools such as specific challenge and serial peak flow testing used in (mostly immunologic) OA research should be evaluated for cleaning-related (occupational) asthma. Finally, characterization of exposure to cleaning chemicals in different settings is important to develop preventive workplace control measures, for understanding possible effect mechanisms, and to improve quantification of exposure–response relationships in epidemiological studies. The knowledge gained, together with educational and communication tools, will eventually be important for the protection of workers using cleaning chemicals.

CONCLUSIONS

A large number of studies have demonstrated that domestic and professional cleaning work, especially when associated with the use of household cleaning sprays, bleach, ammonia, disinfectants, and mixing products, may have relevant implications for

public health. This is particularly important for common exposure such as the use of cleaning and air-refreshing sprays that are often associated with adult asthma. However, the conclusions of research on cleaners and consequent policy implications have not been heeded by commercial cleaning stakeholder organizations, such as manufactures, vendors, and commercial cleaning companies. We suggest a multifaceted intervention including:

- the education of unions, consumer, and public interest groups to encourage safer products and other prevention methods as detailed above;
- information activities through media, women's magazines, etc. addressed to the general population with the aim of improving knowledge among housewives and occupational domestic cleaners regarding main risks (e.g., mixing products, the use of cleaning sprays, and bleach) and available preventive measures;
- improve labeling of cleaning products and recommend the users carefully read labels;
- collaboration between scientific communities and agencies, such as the European Agency for Safety and Health at Work, the European Chemicals Agency, and the Occupational Health and Safety Administration (OSHA); for example, publication of consensus documents produced by the EAACI and the European Respiratory Society (ERS) for the scientific community and decision makers.

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AUTHOR CONTRIBUTIONS

This position paper is the result of the collaboration of a panel of experts who contributed to the document according to their different experiences and competences, coordinated by Andrea Siracusa.

CONFLICTS OF INTEREST

All authors have no conflicts of interest to declare.

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TABLES

Key Messages

- Professional and domestic cleaning is associated with work-related asthma.
- Cleaning sprays, bleach, ammonia, disinfectants (e.g., chloramine-T, quaternary ammonium compounds, and ethanolamine), mixing products, and specific job tasks have been identified as specific causes of or exacerbation for asthma.
- Low-volatility liquid cleaning products has been associated with less asthma
- Inhalation accidents (e.g., mixing bleach with ammonium salts or acid detergents) are associated with acute irritant-induced asthma (RADS) and WEA.
- Most cleaning agents have an irritating effect on airways, although occasionally a few agents (e.g., chloramine-T and enzymes) show an IgE-mediated mechanism.
- Cleaning, a women-dominated occupation, might partly explain gender differences in asthma control.
- Possible preventive measures encompass avoidance of aerosolization of cleaning products, bleach, and ammonia, minimizing the use of disinfectants, avoidance of mixing products, the use of respiratory protective devices, worker education, and medical surveillance.
- Information activities and collaboration between scientific communities and safety and health agencies are urgently needed.

Table 1 Epidemiological studies on asthma and respiratory symptoms associated with cleaning work

References/ Country	Study design	Subjects (n): exposed/controls	Age, years	OR, unless otherwise stated (95% CI)	Risk factors/ Exposures
Ng et al. (8)/ Singapore	Population-based case–control study	787 cases with asthma/1591 nonasthmatic controls	20–54	Asthma symptoms 1.9 (1.2–3.0)	Municipal cleaners and sweepers
Kogevinas et al. (6)/ nine western European and three other industrialized countries	Population-based cross-sectional study	443 cleaners/8878 nonmanual workers	20–44	Asthma symptoms or medication 1.8 (1.4–2.3); asthma symptoms or medication and BHR 2.0 (1.3–2.9)	Cleaning work
Arif et al. (9)/USA	Population-based cross-sectional study	108 cleaners/1483 nonmanual workers	40*	Work-related asthma 2.4 (0.5–11); work-related wheezing 5.4 (2.4–12)	Cleaning work
Eng et al. (10)/ New Zealand	Population-based cross-sectional study	152 ever cleaners/ 2903 never cleaners	20–64	Asthma symptoms 1.6 (1.1–2.3)	Ever working as cleaner
Medina-Ramón et al. (5)/Spain	Population-based cross-sectional study	593 domestic and 295 nondomestic cleaners, 1371 former cleaners/2262 women never worked in cleaning	30–65	Current asthma 1.5 (1.1–1.9); Current asthma 2.0 (1.6–2.4)	Domestic cleaner Former cleaner
Zock et al. (11)/ Spain	Population-based cross-sectional study	67 indoor cleaners/ 1272 office workers	20–44	Asthma symptoms or medication PR 3.3 (1.9–5.8); asthma symptoms or medication + BHR PR 5.0 (1.9–13)	Private home cleaner
Karjalainen et al. (12)/ Finland	Registry-based cohort study	53 708 female cleaners/202 751 administrative managerial and clerical workers	25–59	Asthma RR 1.5 (1.4–1.6)	Cleaning work
Jaakkola et al. (13)/ Finland	Population-based incident case–control study	521 asthma cases/ 932 nonmanual workers	21–64	New-onset asthma 1.4 (0.8–2.5)	Cleaning work
Kogevinas et al. (1)/ 11 western European and two other industrialized countries	Population-based prospective cohort study	358 cleaners/4143 nonmanual workers	28–57	Asthma RR 1.7 (0.9–3.2)	Cleaning work
Obadia et al. (14)/ Canada	Workforce-based cross-sectional study	566 cleaners/587 other building workers		Work-related respiratory symptoms in female cleaners 3.9 (2.1–7.4) and male cleaners 1.5 (0.8–3.0);	Cleaning work

Table 1 (Continued)

References/ Country	Study design	Subjects (*n*): exposed/controls	Age, years	OR, unless otherwise stated (95% CI)	Risk factors/ Exposures
Vizcaya et al. (15)/Spain	Workforce-based cross-sectional study	761 professional cleaners/86 former cleaners/70 never cleaners	38/48/45*	Current asthma in current cleaners 1.9 (0.6–5.5) and in former cleaners 1.9 (0.5–7.8)	Cleaning work
Bernstein et al. (23)/USA	Prospective panel study in asthmatics and controls	25 housewives with and 19 without asthma	18–65	Respiratory symptoms were more common after cleaning work in asthmatics	Domestic cleaning activities

OR, odds ratio; CI, confidence interval; BHR, bronchial hyper-reactivity; PR, prevalence ratio; RR relative risk.
*Mean.

Table 2 Epidemiological studies on asthma and respiratory symptoms associated with the use of cleaning products

References/ Country	Study design	Subjects (*n*): exposed/ controls	Age, years	OR, unless otherwise stated (95% CI)	Risk factors/exposures
Kogevinas et al. (1)/11 western European and two other industrialized countries	Population-based prospective cohort study	410 exposed to cleaning products/5433 non-exposed	28–57	Asthma RR 1.8 (1.0–3.2)	Use of cleaning products at work (JEM)
Obadia et al. (14)/ Canada	Workforce-based cross-sectional study	566 cleaners/587 other building workers		Main risk factors for work-related symptoms among male cleaners were waxing and wax stripping of floors, spot cleaning of carpets, oiling of furniture, cleaning tiles and cleaning grout	Specific cleaning tasks
Vizcaya et al. (15)/Spain	Workforce-based cross-sectional study	761 professional cleaners/86 former cleaners/70 never cleaners	38/48/ 45*	Wheeze associated with acute inhalation from mixing cleaning products 2.3 (1.0–5.5)	Acute inhalation
Kennedy et al. (16)/ France	Population-based case–control study	173 asthma cases/285 controls	18–65	Asthma 7.4 (1.4–72)	Use of cleaning products at work (JEM)
Le Moual et al. (17)/ France	Population-based cross-sectional study	404 cleaners/8428 administrative/service workers	25–59	Ever asthma 1.04 (0.7–1.5) ever asthma 2.2 (1.1–4.2)	Cleaning work use of cleaning products at work (JEM)
Le Moual et al. (18)/ France	Population-based case–control study	43 mild and 48 severe adult-onset asthma/228 controls	43*	Mild adult-onset asthma 1.9 (0.2–21) severe adult-onset asthma 7.2 (1.3–40)	Use of cleaning products at work (JEM)
Wang et al. (19)/ Taiwan	Population-based case–control study	504 asthmatics/504 community-based controls	50*	Asthma among currently employed 4.2 (1.3–14)	Use of cleaning products at work (JEM)
Massin et al. (20)/ France	Workforce-based cross-sectional study	175 cleaning and disinfecting workers in the food industry and 70 non-exposed	37*	Risk of irritative respiratory symptoms increased with exposure (either intensity or duration)	Chlorine and trichloramine
Delclos et al. (21)/Texas	Workforce-based cross-sectional study	741 physicians/941 nurses/ 968 occupational therapists/879 respiratory therapists	46*	Asthma 2.1 (1.3–3.3) asthma 1.9 (1.1–3.0)	Cleaning agents for instruments Cleaning agents for building surfaces
Arif and Delclos (22)/ Texas, USA	Workforce-based cross-sectional study	741 physicians/941 nurses/ 968 occupational therapists/879 respiratory therapists	46*	Work-related asthma symptoms 3.9 (1.7–9.3) occupational asthma 4.8 (1.3–18)	Cleaning products and disinfectants chloramines
Nielsen and Bach, (24)/ Denmark	Workforce-based prospective cohort study	775 female cleaners/210 former female cleaners	45*	Asthma 3.0 (0.9–10)	Cleaning sprayers

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Table 2 (Continued)

References/ Country	Study design	Subjects (*n*): exposed/ controls	Age, years	OR, unless otherwise stated (95% CI)	Risk factors/exposures
Medina-Ramón et al. (25)/Spain	Panel study	43 female domestic cleaners with asthma and/ or chronic bronchitis	31–66	Lower respiratory tract symptoms 2.9 (1.3–6.4) Lower respiratory tract symptoms 6.9 (2.9–16) Lower respiratory tract symptoms 7.8 (2.6–24)	Glass cleaning sprays Degreasing sprays Air refreshing sprays
Zock et al. (26)/ 10 European countries	Population-based prospective cohort study	3503 persons doing the cleaning in their homes	28–57	Asthma symptoms or medications RR 1.5 (1.1–2.0)	Use of cleaning sprays at least weekly
Medina-Ramón et al. (27)/Spain	Population-based nested case–control study	160 women with asthma and/or chronic bronchitis/ 386 women without respiratory symptoms	30–65	Asthma/chronic bronchitis symptoms: 4.9 (1.5–15) 2.3 (0.9–6.1)	Frequent use of bleach acute inhalation due to cleaning agents
Mirabelli et al. (28)/13 European Countries	Population-based prospective cohort study	332 nurses and other healthcare workers/2481 administrative workers	20–64	New-onset asthma RR 2.2 (1.0–4.5) new-onset asthma RR 2.4 (1.0–5.6)	Use of ammonia and/or bleach use of cleaning sprays

OR, odds ratio; CI, confidence interval; RR relative risk; JEM, job exposure matrix.
*Mean.

Table 3 Case reports of occupational asthma with suspected immunologic mechanism in cleaning workers

References	Subjects (*n*)	Occupation/ Activity	Agent	Diagnosis	Diagnostic approach	Type of asthmatic reaction after BSIC	Mechanism
Boulet (44)	1	Cleaning factory worker	Perchloroethylene	OA	Work-related respiratory sx and BSIC	Immediate persistent	Immunologic non-IgE or irritant-induced
Bernstein et al. (36)	1	Worker manufacturing cleaning products	Toilet bowl cleaner containing Quats (benzalkonium chloride)	OA	Work-related respiratory sx and BSIC	Immediate	Immunologic non-IgE
Savonius et al. (40)	1	Cleaner	Ethanolamine	OA and OcR	Work-related respiratory sx and BSIC	Immediate persistent	Immunologic IgE-mediated or non-IgE
Kujala et al. (37)	1	Cleaner	Chloramine-T	OA and OcR	Work-related respiratory sx, SPT with chloramines-T and BSIC	Dual	IgE-mediated
Purohit et al. (38)	3	Nurses	Quats (benzalkonium chloride)	OA and OcR	Work-related respiratory sx and BSIC	Late	Immunologic non-IgE
Hole et al. (48)	4	Detergent factory workers	Detergent washing powder (amylase, protease and cellulase enzymes)	OA and OcR	Work-related respiratory sx, SPT and RAST with amylase protease and cellulase, and BSIC with amylase	Immediate (1 subject), late (1 subject) and dual (2 subjects)	IgE-mediated
Brant et al. (49)	3	Detergent factory workers	Cellulase, lipase, protease and amylase enzymes	OA and OcR	Work-related respiratory sx, SPT with cellulase, lipase, amylase and protease, and BSIC with cellulase or lipase	Dual (3 subjects)	IgE-mediated
Mäkelä et al. (39)	1	Professional cleaner	Chloramine-T	OA	BSIC with a cleaning agent containing Chloramine-T	Not specified	IgE-mediated
Mäkelä et al. (39)	1	Professional cleaner	Nickel sulphate	OA	BSIC with nickel sulphate	Not specified	Immunologic non-IgE (?)
Mäkelä et al. (39)	11	Professional cleaners	Moulds	OA	BSIC with *A. fumigatus* (9 cases), *A. kiliense* (one case) and *C. herbarum* (one case)	Not specified	IgE-mediated (?)
Laborde-Castérot et al. (41)	5	Cleaners	EDTA-containing sprays	OA and OcR	Nasal provocation tests with EDTA	Immediate (late responses were not assessed)	Pharmacological (?) Immunologic non-IgE (?)

BSIC, bronchial specific inhalation challenge; OA, occupational asthma; sx, symptoms; OcR, occupation rhinitis; SPT, skin prick test; RAST, radioallergosorbent test; EDTA, ethylenediamine tetraacetic acid.
(?)The mechanism is suspected/possible but not demonstrated.

Table 4 Case reports of irritant-induced asthma and RADS in cleaning workers

References	Subjects (*n*)	Occupation/Activity	Agent	Diagnosis	Diagnostic approach	Type of asthmatic reaction after BSIC	Mechanism
Boulet (44)	1	Washroom cleaning	Sulphuric acid	RADS	Respiratory sx associated with washroom cleaning and PFT	NA	Irritant-induced
Boulet (44)	1	Pool cleaning	Hydrochloric acid	WEA-RADS	Respiratory sx associated with pool cleaning and PFT	NA	Irritant-induced
Quirce et al. (45)	1	Cleaning worker in a hospital kitchen	Ammonia and alkaline detergents	Irritant-induced asthma and rhinitis	Work-related respiratory sx and PFT	NA	Irritant-induced
Quirce et al. (45)	1	Aircraft worker cleaning and degreasing engines	Phosphoric acid, thrichloroethane, hydrochloridric and nitric acids	Irritant-induced asthma and rhinitis	Work-related respiratory sx and PFT	NA	Irritant-induced
Lynch (46)	1	Carpet cleaning	Sodium tripolyphosphate	WEA-RADS	Respiratory sx associated with carpet cleaning	NA	Irritant-induced
Franzblau and Sahakian (47)	1	Washroom cleaning	Hydrofluoridric acid	RADS and irritant-induced rhinitis	Respiratory sx associated with washroom cleaning and PFT	NA	Irritant-induced
Mäkelä et al. (39)	5	Professional cleaners	Ethanolamine (wax removing detergent)	Irritant-induced asthma	Work-related respiratory sx and BSIC with wax removing detergent containing ethanolamine	Not specified	Irritant-induced
Sastre et al. (43)	19	Professional cleaners	Bleach	Irritant-induced asthma	Work-related respiratory sx, BHR, sputum, FeNO and BSIC	1 dual and 2 late responses (19 BSIC)	Irritant-induced

RADS, reactive airways dysfunction syndrome; BSIC, bronchial-specific inhalation challenge; sx, symptoms; PFT, pulmonary function tests; NA, not applicable; WEA, work-exacerbated asthma; BHR, bronchial hyper-reactivity; FeNO, fraction exhaled nitric oxide.

Table 5 Case reports of work-related asthma related to the mixing of two or more cleaning products

References	Subjects (*n*)	Occupation/activity	Mixture	Agent	Diagnosis	Country, year
JAMA (53)	1	Psychiatric patient performing cleaning duties as therapy	Bleach and phosphoric acid	Chlorine	Work-exacerbated asthma	USA, 1991
Deschamps et al. (51)	1	Household cleaning	Bleach and hydrochloric acid	Chlorine	RADS	France, 1994
Mapp et al. (54)	1	Cleaning worker	Bleach, malic acid and sulphamic acid	Chlorine	Work-exacerbated asthma	Italy, 2000
Gorguner et al. (52)	55	Household cleaning	Bleach and hydrochloric acid	Chlorine	RADS	Turkey, 2004

RADS, reactive airways dysfunction syndrome.