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Purpose of review
Asthma due to cleaning products has been known for 20 years, and the interest in this topic is still large because of the number of cleaning workers with respiratory problems. In this review, we sought to highlight the most recent findings on the relationship between exposure to cleaning products and asthma and to summarize the specific literature published between 2013 and 2016.

Recent findings
Women are confirmed as most of workers exposed to cleaning products and have a higher frequency than men of work-related respiratory symptoms and diseases. Many cases of asthma due to cleaning products occur in healthcare occupations. The increased risk of asthma has been shown to be related to the number of years in the job and to early life disadvantage. Recent evidence suggests that predisposition to adult-onset asthma may be related to interaction between genes and occupational exposure to low-molecular weight agents/irritants. There is some evidence that an irritant mechanism is more common, although several case reports showed an immunologic mechanism (e.g., disinfectants, amine compounds, aldehydes and fragrances).

Summary
The review updated recent findings on epidemiology, cleaning agents and their mechanism, and prevention of asthma due to cleaning agents. This article provides new information on the level of exposure, which is still high in professional cleaners and even more in domestic cleaners, and on the frequency of asthma in professional and domestic cleaners. An irritant mechanism is more common, although an immunological mechanism is possible, especially in healthcare workers exposed to disinfectants.

Keywords
asthma, cleaning agents, epidemiology, occupation, risk factors, work-related.

INTRODUCTION
Cleaning workers constitute a high percentage of the working population in developed countries and a number of individuals involved in professional and home cleaning are exposed to cleaning products. A systematic review of epidemiological studies, published in 2014, showed an association between exposure to cleaning products and asthma in 79% of cross-sectional, longitudinal and case–control studies [1]. Work-related asthma (WRA) comprises occupational asthma defined as a type of asthma caused by the workplace and work-exacerbated asthma (WEA), which refers to asthma triggered by various work-related factors in workers with preexisting asthma [2]. Cleaners are at risk for new-onset occupational asthma, WEA and irritant-induced asthma, due to exposure to sensitizers and irritants contained in cleaning products [3]. The fifth Jack Pepys Workshop on Asthma in the Workplace focused on similarities and differences between WRA and non-WRA and the exposure to cleaning agents was regarded as a risk factor for both [4]. In occupational cleaners of Northern Europe, the increased risk of asthma was related to the length in years in the job and to early life disadvantage [5]. Exposure to cleaning agents often occurs in healthcare workers as recently reported by Gotzev et al. [6] and Mazurek and Weissman [7]. The European Academy of Allergy and Clinical Immunology (EAACI) Position Paper, published in 2013, highlighted that...
EPIDEMIOLOGY

Asthma caused by some low molecular weight agents (LMW) is a preventable disease, but it is necessary to better identify risk factors in longitudinal studies.

Phenotyping asthma associated with cleaning products exposure and identifying biomarkers is a crucial point to manage the disease and to formulate prevention strategies.

in cleaning workers, the increased risk of WRA, WEA and rhinitis is mainly associated with exposure to cleaning sprays, bleach, ammonia, disinfectants and mixing products [8].

In this article, we reviewed the most recently published articles on the relationship between cleaning work and asthma and summarized the specific literature published in 2013–2016.

EPIDEMIOLOGY

Most of workers exposed to cleaning products are women and work part-time, whereas about 30% of cleaning workers are migrant workers [9]. Women more often tend to have a higher risk for asthma than men and 17.3% of new-onset asthma cases in men and 5.1% in women may be attributed to occupational exposure [10].

The risk of WRA in individuals exposed to cleaning products does not seem dependent on atopic status, supporting the view that a mechanism different from ‘classic’ allergy is involved. This mechanism could be irritant (deterministic) or sensitization (stochastic) as observed for occupational asthma caused by some low molecular weight agent (LMW) agents [11]. There is little support that the risk of asthma is increased in smokers exposed to cleaning products [12]. Poor psychosocial working conditions may partly explain the high prevalence of asthma due to cleaning products and a stress-induced inflammatory immune response may contribute to the onset of WRA in cleaners [13].

Exposure assessment studies in healthcare workers were conducted from 2009 to 2011 at five hospitals of the United States [14]; cleaning and disinfecting tasks were performed with a high frequency at least once per shift in many occupations; for example medical equipment preparers, housekeepers, floor strippers/waxers and endoscopy technicians spent on average 2–3 h/shift performing cleaning/disinfecting tasks. A Canadian clinical survey of WRA cases in the period 2008–2015 found that in the last half of the period surveyed, cleaning products were relatively more often an attributed cause than in the first half [6]. In the Australian Workplace Exposure Study-Asthma among 2437 interviewed women, 20% were exposed to industrial cleaning and sterilizing agents [15].

Norwegian female cleaners had an increased risk of job change, used as a marker of respiratory work disability (odds ratio (OR) 5.7, 95% confidence interval (CI) 2.3–14.0) [16]. Moreover, the large use of cleaning sprays at home may have significant implications for public health; for example Zock et al. [11] estimated that one in seven adult asthma cases may be related to the use of household cleaning sprays. Data from Poland and Spain showed that professional cleaning women are at an increased risk of occupational asthma, WRA and WEA due to cleaning products [17,18].

A high number of cases of WRA occurred in healthcare occupations such as operating room nursing from occupational exposure to disinfectant/cleaning agents [19,20].

In the review of occupational asthma notification from the Midland Thoracic Society’s Surveillance Scheme of Occupational Asthma database, Walters et al. [19] reported that occupational asthma related to cleaning products was an emerging cause in UK healthcare workers after 2001. A recent study [5] hypothesized that early life disadvantage (maternal smoking in childhood, severe respiratory infection <5 years of age, being born in winter and/or maternal age at delivery >35 years) may increase the risk of asthma and respiratory symptoms due to exposure to cleaning agents later in life; this risk increased with years in occupational cleaning. Exposure to cleaning agents (both at home and in the workplace) plays an important role in adult-onset asthma, and an association was observed between uncontrolled adult-onset asthma and exposure to cleaning agents (OR
Occupational disease

2.0, 95% CI 1.2–3.3) with stronger associations for long-term exposures [21,22].

AGENTS

Available evidence indicates that cleaning materials can both exacerbate asthma (WEA) and induce the development of new-onset asthma (occupational asthma) [23,24]. There is little information on the specific agents involved in the various phenotypes of asthma related to cleaning exposure. Most epidemiological studies [24,25] have linked asthma with exposure to irritant cleaning materials, mainly bleach, ammonia and cleaning/degreasing sprays. Rava et al. [26] showed that ever exposure to low-molecular weight agents/irritants, such as cleaning products and disinfectants, was associated with current adult-onset asthma and identified novel genes potentially involved in adult asthma associated with occupational exposure.

Questionnaire, skin prick test and bronchial responsiveness challenge were assessed in 607 women [27]. Frequent use of bleach for home cleaning was associated with current asthma (OR 1.7, 95% CI 1.0–3.0), nonallergic asthma (OR 3.3, 95% CI 1.5–7.1) and nonallergic adult-onset asthma (OR 4.9, 95% CI 2.0–11.6). The conclusion of this study was that the domestic use of bleach for cleaning is associated with nonallergic asthma in women.

The highest risk of reported asthma was associated with tasks involving dilution of disinfection products by manual mixing, suggesting possible exposure to repeated peaks of concentrated irritant/sensitizing products such as quaternary ammonium compounds [28]. In a retrospective case series analysis, Vandenplas et al. [29] suggested that quaternary ammonium compounds are the principal cause of sensitizer-induced occupational asthma among cleaners.

Moreover, two interesting reviews published in 2010 suggested that occupational asthma in cleaning workers may be due to specific sensitization to disinfectants such as quaternary ammonium compounds (e.g. benzalkonium chloride and lauryl dimethyl benzyl ammonium chloride), chloramine T, glutaraldehyde, fragrances and ethanolamines [2,30].

Furthermore, occupational activities of cleaning workers are associated with exposure to airborne biological agents, such as *Penicillium* and *Aspergillus* species, which may be responsible for occupational asthma [31]. In a case series of 20 patients, occupational asthma was attributed not only to cleaning chemicals but also to moulds, such as *Aspergillus fumigatus* [32].

Few studies evaluated quantitative assessments of respiratory exposures to airborne irritants and sensitizers. Recently, Swiss authors evaluated workers exposed to cleaning products airborne concentrations of monoethanolamine, glycol ethers, benzyl alcohol and formaldehyde during different cleaning tasks [33]. Professional cleaners were found to be exposed to multiple airborne irritants at low concentrations, thus the level of these substances should be assessed in the cleaning industry, especially in specialized cleaning tasks such as intensive floor cleaning [33].

Weekly household use of cleaning sprays should have an effect on asthma, but no association was observed among elderly women who received household help [34].

MECHANISMS

The mechanisms involved in asthma associated with cleaning products and disinfectants are not clear. Both allergic and irritant mechanisms are involved, but the latter is the most relevant [8,35,36]. Inflammatory Th2 response is activated after airway epithelium damage as a consequence of repeated irritant exposure [37]. Individuals who use hypochlorite bleach to clean their homes were at risk of respiratory symptoms but were less likely to be atopic [38]. Woman exposed to bleach in domestic cleaning were at risk of adult-onset asthma and nonallergic asthma (OR 3.3, 95% CI 1.5–7.1) and the frequency of women with ‘high neutrophils’ cell counts profile increased from 21 to 30 and 46%, respectively, in those using bleach less than 1 day per week, 1–3 days per week and 4–7 days per week [27].

Some cleaning agents or disinfectants, such as quaternary ammonium compounds, have both irritant and sensitizer effects [28]. Benzalkonium chloride induces specific immunoglobulin E and eosinophilic inflammatory response and can cause bronchoconstriction [39–41]. The retrospective case series analysis published by Vandenplas et al. [29] showed an increase in bronchial hyperreactivity and sputum eosinophils after specific inhalation challenge (SIC) with cleaning agents and disinfectants. The cleaning sensitizer products responsible were quaternary ammonium compounds, glutaraldehyde and ethanolamines. In a Polish study [17], cleaners experienced cleaning-related respiratory symptoms, allergic and irritant effects. Those results support the hypothesis of a sensitizing mechanism involved in some cases of asthma related to cleaning agent exposure.

The study of Corradi et al. [42] provided evidence on whether professional cleaning was associated with biomarkers of lung damage in noninvasively collected biological fluids [exhaled air and exhaled breath condensate (EBC)]. They identified the potential biomarkers of exposure to alkaline products (increased ammonium-EBB and pH-EBB levels) and
potential biomarkers of oxidative stress (increased H$_2$O$_2$-EBC levels correlated with 4-hydroxynonenal-EBC levels) in those exposed to cleaning agents. Then, a case–control study conducted by Vizcaya et al. [23] in cleaners with asthma symptoms did not show differences in levels of Cys-leukotrienes and 8-isoprostane in EBC. Recently, a pattern of genes involved in the mechanism of allergic and nonallergic asthma was identified and therefore the hypothesis of a role of genes in the development of occupational asthma was proposed [43].

Rava et al. [26**] analyzed genes involved in response to oxidative stress related to occupational exposure to LMW agents/irritants in three large population studies (Epidemiological study on the Genetics and Environment of Asthma, bronchial hyperresponsiveness and atopy, Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults and European Community Respiratory Health Survey). They identified novel genes involved in adult asthma related to occupational exposure activating the nuclear factor kappa-light-chain-enhancer of activated B cells pathway. Recent epidemiological studies strengthen the evidence of an effect of chronic exposure to irritants in WRA, and the underlying mechanism may be related to oxidative stress, neurogenic inflammation and dual irritant and adjuvant effects [44].

The oxidative stress response was recently hypothesized in relation to asthma in cleaners working in unsafe conditions. Radon et al. [13*] found that the higher prevalence of asthma in cleaners should be explained also by poor psychosocial working conditions and a mechanism of inflammatory response stress induced could be considered. Moreover, disadvantage in early life seems to have a role in the airway vulnerability of workers exposed to cleaning agents later in life [5*].

**DIAGNOSIS**

Asthma and WRA associated with cleaning agents exposure are well documented by numerous epidemiological studies [1*,8,44] and recently, review articles showed strength of this evidence. Cleaning agents contain a wide range of ingredients that are irritants as chloride or ammonia and potential sensitizers as quaternary ammonium compounds and perfumes [1*,8,44]. In some cases, there occurred acute exposure to high level of agents and workers experienced reactive airway dysfunction syndrome [45]. Most of the studies assessed self-reported asthma symptoms by questionnaire. Two studies [46,47] showed that peak expiratory flow variability is not sensitive and not related to respiratory symptoms associated with cleaning agents exposure.

The diagnosis of asthma should be assessed as suggested by international guidelines (GINA) and the diagnosis of WRA as indicated in the documents published by American and European societies of respiratory and allergic diseases (American Thoracic Society, EAACI and European Respiratory Society). SICs are the reference test for specific etiological diagnosis of WRA [2]. Vandenplas et al. [29] performed a retrospective case series analysis of patients affected by WRA who underwent SICs with cleaning products. Thirty-nine percent had a positive SIC-confirmed asthma related to cleaning agents. Bleach was one of the cleaning agents more frequently associated with asthma symptoms. Sastre et al. [48] performed SIC in 13 patients with asthma-like symptoms related to bleach exposure and asthmatic reaction, two late and one dual, occurred in three individuals. Because of scarce knowledge of mechanisms of asthma due to cleaning agents and lack of available biomarkers diagnosis in clinical setting is difficult. Therefore, to better manage the patients experienced asthma symptoms associated with cleaning products, suggestions published by the EAACI should be taken into account [35].

**PREVENTION**

Review articles on occupational asthma summarize primary, secondary (early detection) and tertiary (appropriate treatment) prevention strategies aimed at reduction of the onset and severity of work-related respiratory diseases [37,49]. Primary prevention, such as avoidance of workplace exposure, should be the most effective strategy to reduce the onset of sensitization, occupational asthma and occupational rhinitis [37,49,50]. Surprisingly, prevention of work-related respiratory diseases in cleaners has seldom been studied in spite of the large knowledge on the dimension of the problem and identification of specific products and job tasks responsible for work-related asthma and rhinitis [1*,8].

In the years 2013–2014, three reviews on epidemiology and prevention of work-related asthma and rhinitis due to cleaning products have emphasized that cleaning sprays, bleach, ammonia and disinfectants (e.g. quaternary ammonium compounds and glutaraldehyde) have been identified as the most common agents of occupational asthma and occupational rhinitis in cleaning workers [1*,8,51*]. Among disinfectants, exposure to quaternary ammonium compound was more commonly reported than exposure to glutaraldehyde [51*].

Inhalation accidents in cleaners, such as mixing bleach and ammonia in a small, poorly ventilated area, were associated with asthma symptoms, reactive airway dysfunction syndrome, irritant-induced
Occupational disease

Over the past 20 years, the relationship between exposure to cleaning products and asthma has been repeatedly documented. Despite that, it seems that professional and domestic exposure to harmful cleaning products has continued with little improvement. There are examples of hospital and school cleaning in which hazardous products, such as glutaraldehyde and bleach, were exchanged for less hazardous materials; for example avoidance of glutaraldehyde exposure has been partially achieved by using the less volatile ortho-phthalaldehyde [56] or using cleaning products that are wiped, not sprayed and of low volatility which has been associated with less asthma [11]. Moreover, the burden of work-related respiratory symptoms and asthma in cleaners can be reduced by avoiding or reducing exposure to quaternary ammonium compounds [S1*].

Recently, Garza et al. [57*] in a cross-sectional study performed in 329 custodians analyzed the association between respiratory symptoms and exposure to traditional and ‘environmentally preferable’ cleaning products. The authors observed a significant increase in upper and lower respiratory symptoms associated with high exposure to traditional cleaning products compared with high exposure to environmentally preferable cleaning products. However, it was observed that environmentally preferable cleaning products are not totally safe if inhaled.

In conclusion, work-related asthma and rhinitis in cleaning workers are largely preventable diseases and it is necessary to identify specific risk factors to develop effective prevention strategies.

CONCLUSION

Over the past 20 years, the relationship between exposure to cleaning products and asthma has been repeatedly documented. Despite that, it seems that professional and domestic exposure to harmful cleaning products has continued with little improvement. There are examples of hospital and school cleaning in which hazardous products, such as glutaraldehyde and bleach, were exchanged for less hazardous materials; for example avoidance of glutaraldehyde exposure has been partially achieved by using the less volatile ortho-phthalaldehyde [56] or using cleaning products that are wiped, not sprayed and of low volatility and ‘environmentally preferable’ cleaning products. Interestingly enough, predispension to adult-onset asthma may be related to interaction between genes and adult asthma due to occupational exposure to low-molecular weight agents/irritants. Studying genes may help in reducing the impact of cleaning products on respiratory health.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

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

- of special interest
- of outstanding interest


This article brings new findings on the relationship between early life disadvantage and the increased risk of asthma in cleaners.


This original article showed that poor psychosocial working conditions seem to contribute to the high prevalence of asthma in cleaners.


This Polish study showed that professional cleaning workers are at an increased risk of occupational and WEAI due to cleaning products.


