

# Clinical & Experimental Allergy

## Cleaning agents and disinfectants: moving from recognition to action and prevention

This editorial discusses the findings of the article in the March issue by M. Gonzalez et al. [2014] pp. 393–406.

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In the March issue of *Clinical & Experimental Allergy*, Gonzalez et al. published a paper on asthma among workers in French healthcare settings and exposure to cleaning and disinfection agents. The workers involved used a wide range of chemicals for cleaning and disinfection including bleach- and chlorine-containing cleaning agents, glutaraldehyde and quaternary ammonium compounds (QACs) [1]. The study included more than 500 employees from the nursing staff and cleaning personnel of seven healthcare settings. A remarkably strong association was observed between nasal symptoms and physician-diagnosed asthma, in particular the use of QACs, which are being used for disinfection. Almost 60% of the participants reported exposure to QACs and odds ratios of, respectively, 2.5 and 5.9 were observed with nasal symptoms and physician-diagnosed asthma (both  $P < 0.005$ ). The strong associations between use of QACs and asthma and the large population at risk imply that a considerable attributable risk for asthma exists due to disinfectant exposure of more than 80% on the basis of prevalence data, for instance, for physician-diagnosed asthma and new onset asthma (Tables 3 and 5 with comparisons of QAC-exposed and non-exposed individuals). This indicates that the burden of work-related respiratory symptoms and asthma can be reduced considerably by avoiding or reducing exposure to QACs.

The study draws attention to an issue which has become more widely studied in recent years and reiterates findings published by many others [2–4]. Initial evidence came mostly from case reports and registry-based studies of occupational asthma, but over the last decade, several analytical epidemiological surveys have been performed among healthcare personnel, comparable to the study discussed here [5–9]. A large proportion of the hospital population is exposed to disinfectants and cleaning agents that are associated with the occurrence of asthma [7]. A survey among more than 3500 licensed US healthcare workers showed a similarly striking high prevalence of use of disinfectants and strong associations with work-related asthma symptoms and work-exacerbated asthma [5]. An exposure response relation was observed for these two health endpoints, with high odds ratios (3.0 and 9.0, respectively) for healthcare workers who used disinfectants more than once a day. Only 16.5% of the 3650 participants to this study never used disinfectants or less than once a month. These observations are made against data from the French ‘national network of occupational health surveillance and prevention’ over 2001–2009, indicating an increase in the number of occupational asthma cases due to exposure to QACs and a decreasing number of latex- and aldehyde-related cases [10]. Overall, the healthcare and social work sector showed a slight but statistically non-significant increase in the number of cases. Similarly, information from a regional asthma voluntary reporting system in the United Kingdom also points to a disproportionately high number of cases of work-related asthma occurring in healthcare occupations due to agents such as glutaraldehyde and cleaning products, in addition to latex [11]. The majority of cases (136; 75%) occurred in nursing, operating theatre personnel, endoscopy and radiology staff. The number of glutaral-

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dehyde cases showed a downward trend over the years, probably because of complete withdrawal of glutaraldehyde from the UK National Health Service and automation and enclosure of reprocessing in disinfection units, in particular for endoscopes. Occupational asthma cases associated with QACs were not reported.

Disinfectants are used as part of strategies to prevent transmission of nosocomial infections. It has been suggested that as a result, the use of disinfectants and cleaning agents has increased, as well as the use of disinfection and cleaning sprays [12]. Particularly, the use of hand-held sprayers may contribute to elevated exposure levels. Many disinfectants and cleaning agents are known as irritants or sensitisers [13]. The bodies of knowledge on disinfectants and the occurrence of occupational asthma have grown considerably over the last decade, and attention for cleaning agents and disinfectants has recently increased as well in the scientific community [2, 3, 14]. What makes the study by Gonzales et al. remarkable?

The first aspect is the quality of the exposure assessment component. Exposure was self-reported in a questionnaire, but for the majority of workers, exposure was verified by examining the composition of the disinfectants and cleaning agents they worked with on the basis of the so-called material safety and data sheets (MSDS). Thus, misclassification of exposure could be limited, and this likely contributed to the strong associations observed. Others have also shown that exposure assessment is crucial and exposure often seems underestimated by healthcare workers, probably because they have little knowledge about the constituents of the cleaning and disinfection mixtures they use [15]. As an alternative expert judgment of the exposure has been proposed, however, expert judgment, and similarly job exposure matrices, may not give the correct answer because of absence of sufficiently refined information. People with similar job titles may have entirely different exposure patterns, because they have different tasks, use different agents, use the same agent but with different product formulations, apply the agents differently, etc. Exposure has to be assessed at the task level, and an exposure assessment strategy has been proposed to characterise workers inhalatory and dermal exposure to cleaning agents and disinfectants at that detailed level [12]. The heterogeneity in exposure between individuals also illustrates the difficulties research are confronted with when they want to study association between exposure to disinfectants and asthma. Quantitative exposure assessment is urgently needed, but has received very little attention so far in this area [14].

A second remarkable element is the fact that a strong association was observed for a specific category of disinfectants. Quaternary ammonium compound exposure was more commonly reported than exposure to glutaral-

dehyde, a well-known disinfectant in hospital settings, and QAC exposure was clearly strongest associated with the occurrence of occupational asthma. Quaternary ammonium compounds contain a positively charged nitrogen atom bound to four carbon atoms. The positive charged atom can neutralise negative charges on the surfaces and give the desirable antistatic properties for cleaning agents. Quaternary ammonium compounds with long hydrogen chains may possess antimicrobial activity [16]. Several categories of QACs exist, and animal studies have identified several QACs as sensitising agents or potent adjuvants [16]. It seems obvious to test for specific sensitisation to QACs in population studies. Also, Gonzalez et al. [1] tested for QAC sensitisation and 6.5% of the population had IgE antibodies to QACs. However, the specific antibody response was not clearly associated with the presence of asthma or rhinitis or exposure. Others have reported case studies that indicate that QACs may cause asthma, probably through immunologic mechanisms, although the underlying mechanisms have not been unravelled specific IgE against QACs cannot explain the majority of cases [17–21]. Interestingly, as expected in case of exposure to an agent with adjuvant properties, exposed individuals appeared more often atopic than non-atopic individuals (36.6% vs. 27.7%), although the difference was not statistically significant. An association between QAC exposure and increased risk of developing an atopic response to common allergens has been observed earlier in a study among farmers with QAC exposure [18]. QAC-exposed farmers had a more than fourfold increased risk to be atopic compared with non-QAC-exposed farmers. Farmers also use these chemicals for disinfection and apply these with high pressure sprayers, which likely leads to a considerably higher exposure than observed in healthcare settings. Two farmers in this study of 194 were sensitised to QACs [18]. Specific sensitisation was observed, but could not explain the occurrence of QAC-associated respiratory symptoms and bronchial hyper-responsiveness. Mechanistic studies, as have been performed in cleaning workers, are urgently needed in hospital workers with exposure to disinfectants to be able to adequately assess the health risks. Information about underlying mechanism also facilitates inferences about long-term risks and the prognosis [22].

Studying health effects of disinfectant exposure should not be limited to QACs. Other agents, or complex mixtures of agents, are being used, and the knowledge about the health risks remains relatively limited [23]. Exposure to disinfectants and cleaning agents in general is associated with an increased risk for developing asthma in hospital workers and probably also in extramurally healthcare professionals. The consensus on this topic is clearly growing [3, 14]. The contribution of these exposures to the burden of disease is probably

considerable in these populations. Although no estimates are available for the case burden, which arises from these exposures in the healthcare industry, one would expect substantial numbers. This warrant more detailed investigations and interventions. Exposure to similar agents in other sectors should not be forgotten either [24].

As recently concluded by a European taskforce on the topic of cleaning agents and asthma, '... 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'. It is worrying to see that stakeholders have not shown sufficient initiative to avoid health risks from exposure to cleaning agents and disinfectants. Initiatives are needed in particular to improve education and labelling of products and to reduce exposure to disinfectants and cleaning agents.

*Conflict of interest:* The author declares no conflict of interest.

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