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Risks of new-onset allergic sensitization and airway inflammation after early age swimming in chlorinated pools

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ABSTRACT

Rationale: Irritant chlorination products in swimming pools can cause respiratory problems in swimmers but their possible implication in allergies development is still unclear.
Objectives: To assess prospectively whether early-life attendance at chlorinated pools increases the risks of IgE sensitization and of airways inflammation later during childhood.
Methods: We conducted a two-year prospective study among 196 kindergarten children (mean age of 5.7 years, 54% of boys). We measured exhaled nitric oxide (eNO) and aeroallergen-specific IgE in nasal mucosa. Parents completed a questionnaire about the child's health, chlorinated pool attendance and potential confounders.
Main Results: Ever swimming at indoor or outdoor chlorinated pools before the age of three years was associated with higher odds for new-onset IgE sensitization to house dust mite (adjusted odds ratio [aOR] 2.93, 95% confidence interval [CI] 1.14–7.55) and for new-onset increased eNO (>15 ppb; aOR, 4.54, 95% CI 1.48–13.9). For both outcomes, aORs increased dose-dependently with time spent in chlorinated pools with values reaching, respectively, 3.60 (95% CI 1.21–10.7) and 5.92 (95% CI 1.72–20.5) when the cumulative pool attendance exceeded 60 h These risks appeared independently of each other, of parental history of allergies and of pre-existing diseases, including eczema, which at baseline was more prevalent in early swimmers (aOR, 2.91; 95% CI 1.23–6.89). Such associations were not seen with IgE sensitization to pollen or cat allergens.
Conclusion: Attendance at chlorinated swimming pools in early life is associated with higher risks of new-onset airways inflammation and IgE sensitization to house dust mite, independently of other risk factors.

Introduction

Atopic eczema, rhinitis and asthma are the most prevalent chronic diseases in children of the developed world (Mallol et al., 2012). These diseases have usually their onset during early life and then they develop sequentially along a pathway called the allergic or atopic march (Ker and Hartert, 2009; Spergel, 2010; Zheng et al., 2011). Although the links between these different types of allergic disease are not fully understood, the prevailing paradigm assumes that the atopic march starts with atopic dermatitis, then proceeds to allergic rhinitis to end with asthma (Martin et al., 2011).

Factors driving the atopic march and the epidemic of allergies are largely unknown. Current hypotheses postulate that these factors are related to the hygiene practices of the Western world. According to the classical hygiene hypothesis (Strachan, 1989), the increase of allergic diseases in developed countries would be the consequence of the reduced exposure to certain microbial agents during early life when the immune system is maturating (Strachan, 1989, 2000). The hygiene hypothesis postulates that an insufficient stimulation of the immune system early in life shifts the immune system from a Th1- to a Th2-cell response, which leads to IgE-mediated diseases such as eczema, asthma and hay fever (McGeady, 2004). Some recent studies, however, give reasons for questioning the validity of the hygiene hypothesis as an unifying explanation for the worldwide rise of allergies. Among these, there is the emerging concept that allergic diseases are primarily epithelial disorders driven by airway barrier dysfunction caused by environmental insults (Holgate et al., 1999; Cookson, 2004). Also challenging the hygiene hypothesis, recent studies have failed to confirm the protective role of infectious exposures, older siblings or Bacillus Calmette-Guèrin (BCG) vaccination toward the risk of allergic outcomes (Cramer et al., 2012; Flohr et al., 2012; Brunekreef et al., 2012).

Another hypothesis closely linked to hygiene is the "chlorine or chlorination hypothesis". This hypothesis proposes that the rise of allergic diseases in Westernized countries is, at least partly, driven

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by the increasing and largely uncontrolled exposure of children to chlorination products, especially in swimming pools (Bernard et al., 2003; Bernard, 2007). Because of their strong oxidizing potential, chlorine and its derivatives such as chloramines can open tight junctions of epithelial barriers and thereby promote the allergen delivery to dendritic cells and the mounting of the Th2 immune response. Several studies have indeed shown that chlorinated pool attendance is associated with increased risks of allergic diseases including hay fever, allergic rhinitis and asthma (Bernard, 2007; Bernard et al., 2006; Kohlhammer et al., 2006; Bernard et al., 2009; Cotter and Ryan, 2009; Ferrari et al., 2011). These risks, which increase dose-dependently with the cumulative pool attendance (CPA), appear to largely stem from interactions with the atopic status (Bernard et al., 2006, 2009). To be triggered, these pool chlorine/atopy interactions require thus a pre-sensitization to aeroallergens as well as a cumulative exposure to chlorinated pools lasting at least a few years. These two conditions, with perhaps some misclassification biases (Bernard et al., 2011; Klootwijk and Krul, 2011), might explain the apparent inconsistencies between studies in young children (Schoefer et al., 2008; Font-Ribera et al., 2009, 2011) and those conducted in adolescents or adults (Bernard et al., 2009; Cotter and Ryan, 2009; Ferrari et al., 2011).

The influence of chlorinated pools on the development of allergic diseases might, however, not be limited to interactions promoting the clinical manifestations of atopy (Bernard et al., 2011). Some observations suggest that chlorinated pool attendance might also increase the risks of allergen sensitization and therefore contribute to the development of the atopic status. The attendance at indoor or outdoor chlorinated pools during infancy or early childhood has been associated with an increased risk of house dust mite (HDM) sensitization (Bernard et al., 2008; Jacobs et al., 2012), which is one of strongest predictors of childhood rhinitis and asthma (Lodge et al., 2011). Studies among infant swimmers have also shown that this practice is associated with an increased risk of eczema, one of the earliest signs of the atopic march (Font-Ribera et al., 2009; Chaumont et al., 2012).

As all these findings were based on cross-sectional studies with a retrospective assessment of swimming pool attendance, the possibility of recall bias, exposure misclassification or even of reverse causation cannot be formally excluded. The aim of this prospective study was thus to further assess whether attendance at chlorinated pools early in life may increase the risks of aeroallergen sensitization as well as of increased exhaled nitric oxide (eNO), a predictor also of rhinitis and asthma in children (Olin et al., 2010; Malinovschi et al., 2012).

Materials and methods

Study population

This study was conducted in the frame of a larger study intended to assess the impact of air pollution on the respiratory health of children (Voisin et al., 2010). We aimed to recruit all children in third kindergarten in 30 schools located in the areas of Brussels and Liège in Belgium. An informed consent document and a questionnaire were provided to the parents. Of the 839 children who received these documents, 430 returned the questionnaire and the consent document signed by the parents. These children were examined in schools between December 2007 and March 2008. Two years later, between December 2009 and March 2010, we visited the schools in the same order to re-examine these children. Of the initial baseline population, 128 children had left the schools, which left for the follow-up a population of 302 children. Among these, 236 (78.1%) participated to the study and of them 196 could perform successfully all the tests. Participants and non-participants did not differ significantly regarding studied outcomes, chlorinated pool attendance and the main risk factors of allergies. All children were examined only with the written informed consent of their parents. In addition, just before performing the tests in schools, we verbally assured to have the assent of each child. The ethics committee of the Faculty of Medicine of the Catholic University of Louvain approved the study protocol, which complied with applicable requirements of the international regulations.

Questionnaire

Parents completed a self-administered questionnaire addressing aspects related to social and medical characteristics of the child and its family, the in- and out-house environment and recreational activities including swimming. For swimming practice, parents were asked to specify the type of swimming pool attended by their child, the type of disinfection method used (some children had access to copper-silver sanitized pools), the frequency of attendance and the age at which their child started to attend the pool on a regular basis. This information served to calculate the cumulative attendance of indoor and/or outdoor chlorinated pools, before the age of 3 years (what was referred to as early swimming), during the two-years follow-up and over lifetime, at the mean age of 5.7 or 7.5 years. The questionnaire also included questions asking whether the child had ever been diagnosed for most common respiratory or allergic diseases, including bronchiolitis, eczema, asthma, hay fever and allergic rhinitis.

Exposure to chlorination and its by-products

In Belgium, public swimming pools (all indoor in the studied areas) are legally required to monitor the microbial and chemical quality of the water by maintaining several parameters within regulatory limits, including free chlorine (0.5–1.5 ppm) and combined chlorine (<0.8 ppm) in water and trichloramine in pool air (<500 $\mu g/m^3$ in air sampled 1.5 m above the pool surface). There are no specific regulations for privately owned swimming pools, which are disinfected according to the instructions of the chlorine supplier (recommended free chlorine, 1–2 ppm). An additional potential source of exposure to chlorination products for our children was via the use of tap water, in particularly for showering or bathing. Data about chlorine levels in tap water for the years 2003 were provided by the Public Department of Wallonia, the Vivaqua Company and the Brussels Institute for Management of the Environment. Data were allocated to each child according to the postcode of residence of the 63 municipalities studied. The mean concentration of free chlorine in tap water (regulatory limit, 200 $\mu g/l$) of our study participants was 65 $\mu g/l$, a value more than 10 times lower than levels in swimming pools. The concentration of THM, the major chlorination by-product in tap water, did not exceed 10 $\mu g/l$.

Samples collection and analyses

Children were examined in their schools between 9:00 and 13:00. The protocol comprised the measurement of height and body weight, a screening of aeroallergen sensitization using the Rhinostick test, a non-invasive test having a similar sensitivity but a greater specificity than skin-prick tests (Marcucci et al., 2004). The Rhinostick test was calibrated with serum standards and considered positive at specific IgE $\geq$ 0.35 kIU/l (Marcucci and Sensi, 1989). The concentration of nitric oxide (NO) was measured in exhaled air with the NIOX^{TM} analyzer (Aerocrine AB, Solna, Sweden) by following the guidelines of the American Thoracic Society (1999). For diagnosing increased eNO values, we used a cut-off of 15 ppb