



Interactions between domestic water hardness, infant swimming and atopy in the development of childhood eczema

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ABSTRACT

Aim: Recent studies suggest that domestic water hardness and swimming in chlorinated pools may increase the prevalence of childhood eczema. The combined influence of these two factors as well as their interaction with atopic status has not been investigated.

Methods: We conducted a cross-sectional study on 358 children aged 5–6 years (54% of boys) in 30 kindergarten schools. Parents completed a questionnaire about the child's health, chlorinated pool attendance and potential confounders. Data about tap water quality were provided by water companies. Atopy was defined as a sensitization to at least one aeroallergen or as a medication for allergy. The effect of water hardness and infant swimming practice were assessed by multivariate logistic models. In addition, the effects of these risk factors combined with atopy were evaluated using two measures of biological interaction: the attributable proportion of interaction (AP) and the synergy index (S). $AP > 0$ and $S > 1$ indicate biological interaction between the two risk factors.

Results: Water hardness was linearly associated to the prevalence of eczema whereas the relationship of eczema with infant swimming was not linear. We observed a biological interaction between hard water ($> 150 \text{ mg/L CaCO}_3 \text{ L}^{-1}$) and atopic status that increases the prevalence of eczema with an odds ratio (OR) of 3.30 and a 95% confidence interval (CI) of 1.34–8.15 (AP, 0.41; 95% CI 0.15–0.66 and S, 2.4; 95% CI 0.96–6.01). Infant swimming practice combined with atopy also increased the prevalence of eczema (OR, 2.72; 95% CI 1.29–5.74) although none of the interaction measures was significant. However, when water hardness and infant swimming were combined, there was no further increase of the eczema prevalence due to some form of antagonistic interaction between these two factors (AP, -0.56 ; 95% CI -1.12 to -0.01 and S, 0.54; 95% CI 0.33–0.87).

Conclusions: Our study shows that exposure to hard water and infant swimming interact with atopic status to increase the prevalence of childhood eczema. A breaching of the epidermal barrier by detergents or salts in hard water and by chlorine-based oxidants in swimming pool water might explain these interactions.

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1. Introduction

Eczema is a chronic inflammatory disease characterized by alterations of the epidermal barrier function and an immunoglobulin E-mediated (IgE-mediated) sensitization to food and environmental allergens (Bieber, 2008). The disease develops as a result of complex interactions between various host (gender, family predisposition) and environmental factors (allergens, irritants and infectious agents). In these processes, skin barrier dysfunction appears as one of the most important components of eczema not only as a consequence of the skin inflammatory response but probably also as a factor promoting allergic sensitization and the resulting inflammatory response. The

IgE-mediated sensitization often occurs several weeks or months after the first skin lesions appear, suggesting that the skin is the primary site of sensitization (Spergel and Paller Amy, 2003). The disease usually begins during infancy and frequently represents the first step of the atopic march that leads to the development of allergic rhinitis and asthma (Leung et al., 2004). The prevalence of eczema, like that of other atopic disorders, has steadily increased in industrialized countries over the last decades. Current estimates indicate that 10% to 20% of children in developed countries suffer from this condition (Williams et al., 2008). Although important, genetic factors cannot explain such a rapid rise of eczema, which can arise only from changes in our environment or lifestyle.

The hygiene hypothesis postulates that the increase of allergic diseases in most developed countries is the consequence of the declining exposure to microbial agents, especially during early life (Sherriff et al., 2002). An alternate hypothesis, which has been suggested more recently, relates the prevalence of eczema to the

Abbreviations: OR, odds ratio; CI, confidence interval; IgE, Immunoglobulin E; AP, attributable proportion of interaction; S, synergy index

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skin barrier disruption caused by environmental stressors. Of these stressors, those linked to the quality of tap or recreational water might be particularly relevant because exposure concerns the population at large and culminates precisely during infancy or early childhood. An association between water hardness and eczema prevalence has been observed in different ecological studies among schoolchildren (Arnedo-Pena et al., 2007; McNally et al., 1998; Miyake et al., 2004). Another potential causative factor linked to water is the exposure to chlorine-based irritants when attending swimming pools. Skin diseases, including eczema, are indeed more frequent in swimmers and workers exposed to swimming water (Lazarov et al., 2005; Basler et al., 2000; Font-Ribera et al., 2009; Bernard, 2007). All these studies, however, were focused on the effects of water hardness or swimming pool water taken separately and have not considered the possible interactions between these two factors, nor between these factors and the atopic status, which is the major driver of eczema risk.

We report here the results of a cross-sectional study focused on school-children in which we investigated the separate and combined effects of exposure to hard water, chlorinated pool attendance and atopy on the prevalence of eczema during childhood.

2. Material and methods

2.1. Study population

The study was conducted in 2008 on children recruited in 30 kindergarten located mainly in the areas of Brussels and Liege in Belgium. These schools belonged to two school networks who agreed to participate in the project: the school network of the municipality of Auderghem and the education network of the Liège area. All parents having children in third kindergarten in the schools of these two networks were invited to participate. A questionnaire and an informed consent document were distributed to a total of 839 children. The overall median participation rate was 51.3% and varied largely between schools (range 20–90%). Since there was no correlation between the participation rate and the prevalence of eczema, we decided to retain all schools for the statistical analysis and to include the participation rate among the potential predictors. The study protocol described in detail previously (Voisin et al., 2010) was approved by the Ethics Committee of the Faculty of Medicine of Catholic University of Louvain.

Parental questionnaires were used to gather information about care during early life and all lifestyle or environmental factors susceptible to influence atopic diseases. The questionnaire included specific questions asking whether the child had ever been diagnosed by a doctor for most common childhood diseases, including eczema. For each question, the parents were asked to reply “yes” or “no”. In the case of a positive reply, parents were asked to indicate the exact age at which the disease (thus eczema) was diagnosed. There were also questions about allergy medication (“Is your child under allergy medication?”, “What is the name of the medication?”). The questionnaire also comprised specific questions intended to estimate the total time spent in outdoor or indoor chlorinated pools before the age of two years.

Data about water quality for years 2003 and 2007 were provided by the Public Department of Wallonia, the Vivaqua Company and the Brussels Institute for Management of the Environment. A value of water hardness was allocated to each child according to the postcode of residence of the 63 municipalities studied. Since data on water quality provided for the year 2007 were more completed, we used these data after having checked the good correlation with data of 2003 (Spearman's correlation test, $r=0.91$). When one municipality was supplied with distinct sources of water, the value for water hardness was estimated as the mean of the yearly averages of these different sources. Water hardness was expressed as mg of $\text{CaCO}_3 \text{ L}^{-1}$. The free chlorine concentration in tap water from all the municipalities was below 0.2 mg/L, which is the standard for tap water in Belgium.

Because the examination of children in schools precluded any provocation or blood test, screening for allergies was performed non-invasively by measuring specific IgE in nasal mucosa with the Rhinostick test. In comparison with the skin prick test, this test offers a similar sensitivity and a greater specificity (Marcucci et al., 2004). Among children for who water hardness data were available, the test was successfully performed in 358 children. The following allergens were screened: cat epithelium, *Dermatophagoides pteronyssinus*, *Anthoxanthum odoratum*, *Parietaria officinalis* and a mix of four allergens containing *Betula odorosa*, *Corylus avellana*, *Carpinus betulus* and *Alnus incana*. Children were considered as atopic when they were sensitized to at least one of the above allergens (specific IgE > 0.35 kIU/l). Children with a negative Rhinostick test but under medication for allergy, as specified in the questionnaire, were also classified as atopics.

2.2. Statistical analysis

Multiple logistic regression analysis was used to assess the adjusted odds ratio (OR) and their 95% confidence intervals (CI) of eczema associated with water hardness and chlorinated pool attendance during infancy. Age, gender, parental eczema and/or allergy, breastfeeding, parent's education level (high, minimum one parent in possession of a bachelor educational level or higher), presence of older siblings, passive smoking, maternal smoking during pregnancy, participation rate (above 50% or not) were selected as *a priori* potential confounding factors. To study these associations, we first assessed whether or not water hardness and infant swimming practice were linearly related to the log-odds of eczema using a restricted cubic spline model (Software R 2.12.1). The null hypothesis that the log-odds of eczema was a linear function was accepted only for the water hardness but rejected for infant swimming. Water hardness was thus tested as a continuous variable. However, to exploit the wide range of water hardness of our study with values up to 420 mg/L, which is quite uncommon (WHO, 1996), we also analyzed this variable stratified in three categories of increasing values (soft: < 150 mg/L $\text{CaCO}_3 \text{ L}^{-1}$, moderately hard: 150–350 mg/L $\text{CaCO}_3 \text{ L}^{-1}$ and very hard: > 350 mg/L $\text{CaCO}_3 \text{ L}^{-1}$). These cut-off points were selected because they corresponded to the standard water hardness categories used in Belgium. Of interest, these limits also corresponded to the 25th and 50th percentiles of water hardness distribution of our database. To examine the nonlinear relationship between infant swimming and prevalence of eczema, we modeled infant swimming by restricted cubic spline with four knots at percentiles 5%, 35%, 65%, and 95% in a logistic regression. Unadjusted trends for increasing eczema prevalence with increasing water hardness were assessed with the Cochran–Armitage trend test.

We tested potential statistical and biological interactions between atopy, water hardness and infant swimming practice on the prevalence of eczema. Statistical interactions were examined by including the appropriate product interaction term in the multivariate logistic regression. Biological interactions in the regression models were tested as departure from additivity. We use the two indices proposed by Rothman and Greenland (1998) to measure these interactions from logarithmic models: the attributable proportion of interaction (AP) and the synergy index (S). The AP estimates the attributable proportion of eczema, which is due to the interaction in children with both exposures. The S examines whether the proportion of children with eczema is significantly different from the one obtained among children exposed to the additive effect of the two risk factors taken separately. First, atopy, infant swimming and water hardness were combined two by two in three new variables with four levels summarized as follows: a level of joint exposure to both risk factors (A^+B^+), a level of exposure to one of the risk factors only (A^+B^- or A^-B^+) and a level of reference of no exposure (A^-B^-). On the basis of adjusted odds ratios obtained in the logistic regression models, we calculated the two measures of interaction on an additive scale and their corresponding confidence intervals by using an Excel spreadsheet set up by Andersson et al. (2005). There is a biological interaction when AP (95% CI) does not include 0 and S (95% CI) does not cross 1.

3. Results

The study population included 358 schoolchildren (54% of boys) with a mean age of 5.7 years (standard deviation, 0.4). Main characteristics of these children are summarized in Table 1 for the whole population and separately for children who had a doctor-diagnosed eczema ($n=94$, 26%) and those who had not. Table 1 also shows the odds ratios and their 95% confidence interval for eczema associated with the described characteristics. A significant increase of eczema prevalence was associated to atopic status, parental allergies or eczema, maternal education, domestic water hardness and cumulative pool attendance before the age 2 years. There were no significant differences between the two groups in the proportions of children sensitized to allergens, children who had been breastfed or those who had been exposed to older siblings or tobacco smoke. Although the hardness of tap water was on average higher in children with reported eczema, the proportions of children having access to hard water (> 150 mg/L $\text{CaCO}_3 \text{ L}^{-1}$) did not differ between the two groups. Proportion of infant swimmers was higher in the eczema group but the hours spent in chlorinated pool by these infant swimmers were not higher. There was no association between the prevalence of atopy and the exposure to hard water or infant swimming practice. Last, the proportion of infant swimmers was lower in the soft water group than in the hard water group (31% vs 51%), meaning that the specific influence of hard water and infant

swimming can be accurately assessed only by the mutual exclusion of these factors.

Table 2 shows the crude and adjusted odds ratio of eczema associated with water hardness and infant swimming in the whole population and separately for non-atopic and atopic children. When tested as a continuous variable, water hardness was associated with an increased eczema prevalence independently of the atopic status. However, when testing water hardness as a categorical variable, the odds for eczema was significantly increased only among atopic children exposed to very hard water ($> 350 \text{ mg/L CaCO}_3 \text{ L}^{-1}$, OR, 3.36; 95% CI 1.02–11.1). The adjusted odds ratio for eczema associated to the upper *quartile* of infant swimming compared with lower was 1.41 (95% CI 0.98–2.04) in all children and was statistically significant among non atopic children (OR, 1.78; 95% CI 1.09–2.89).

In order to assess the specific influence of water hardness and infant swimming, we repeated the logistic analyses by mutually excluding each of these factors. The results shown in Table 3 revealed that these two factors were mutually confounding their associations with prevalence of eczema. Non-infant swimmers showed indeed a strong association between water hardness and eczema prevalence (OR, 3.76; 95% CI 1.31–10.76), which completely disappeared in their peers who had swum during infancy (OR, 0.76; 95% CI, 0.27–2.14). Similarly, in children using soft water, infant swimming and prevalence of eczema showed a tendency to be associated (OR, 2.13; 95% CI 0.98–4.64), which was not seen in those having access to moderately or very hard water (OR, 1.26; 95% CI 0.79–2.02).

Given the above influence of water hardness, infant swimming and atopy on the prevalence of eczema, we further assess the possible interactions between these three factors. When introducing the interactive terms in the logistic regression models, there was no evidence of statistical interaction (OR (atopy $\times$ hard water), 1.38; 95% CI 0.43–4.36, OR (atopy $\times$ infant swimming), 0.86; 95% CI, 0.31–2.36, OR (infant swimming $\times$ hard water), 0.40; 95% CI 0.12–1.33). By contrast a series of biological interactions as

a departure from additivity were found by calculating the AP and S interaction measures. Table 4 shows the odds ratios for each factor tested separately and in combination with each other. The interaction measures calculated on the basis of these odds showed a significant synergistic interaction between atopy and water hardness (AP, 0.41; 95% CI 0.15–0.66 and S, 2.40; 95% CI 0.96–6.01). Although the odds for eczema associated to infant swimming combined with atopy was higher than the odds for each factor alone, the additive interaction measures were not statistically significant (AP, 0.04; 95% CI -0.34 to 0.42 and S, 1.07; 95% CI 0.57 to 2.0). The same analysis revealed a significant antagonistic effect between hard water and infant swimming practice on eczema (AP, -0.56 ; 95% CI -1.12 to -0.01 and S, 0.54; 95% CI 0.33–0.87). Indeed, children with both exposures reported a prevalence of eczema that was lower than the additive effect of each risk factor.

4. Discussion

While confirming the increased prevalence of childhood eczema associated with exposure to hard water and chlorinated pools, our study shows that this increase in prevalence largely stems from their biological interactions with the atopic status. Both infant swimming and exposure to hard water were indeed significantly associated with prevalence of eczema only when combined with atopic status. Our study also shows that by interacting with each other, hard water exposure and infant swimming mutually weaken their association with eczema, resulting in a complex pattern of confounding effects. Clearly, the failure to consider all these interactive effects may lead to an underestimation of the prevalences of eczema associated with hard water or infant swimming.

Interactions reported in epidemiological studies should always be interpreted with caution. We are, however, rather confident that the interactions found in this study arise from the biological interactions between the exposure to skin irritating substances and the genetic

Table 1
Characteristics of study participants according to eczema and associations of covariates with the prevalence eczema.

	All (n=358)	Eczema		OR for eczema (95% CI) ^b
		No (n=264)	Yes (n=94)	
Age, mean (SD) ^a	5.7 (0.4)	5.7 (0.4)	5.7 (0.4)	0.86 (0.47–1.59)
Boys, n (%)	294 (54.2)	139 (52.7)	55 (58.5)	1.27 (0.79–2.04)
Body mass index, mean (SD) ^a	20.7 (3.2)	20.7 (3.2)	20.8 (3.2)	1.01 (0.94–1.09)
Mother and/or father with eczema, n (%)	63 (17.6)	38 (14.4)	25 (26.6)	2.16 (1.22–3.82)
Parents with allergies or eczema, n (%)	164 (45.8)	109 (41.3)	55 (58.5)	2.01 (1.24–3.23)
Older sibling ≥ 1 , n (%)	203 (56.7)	154 (58.3)	49 (52.1)	0.78 (0.49–1.25)
Parental education level (high, bachelor level)				
Maternal education, n (%)	240 (67.0)	168 (63.6)	72 (76.6)	1.87 (1.09–3.21)
Paternal education, n (%)	218 (60.9)	160 (60.6)	58 (61.7)	1.05 (0.65–1.70)
Passive smoker at home, n (%)	114 (31.8)	90 (34.1)	24 (25.5)	0.66 (0.39–1.13)
Maternal smoking during pregnancy, n (%)	46 (12.8)	32 (12.1)	14 (14.9)	1.27 (0.64–2.50)
Breastfeeding, n (%)	279 (77.9)	206 (78.0)	73 (77.7)	0.98 (0.56–1.72)
Domestic water hardness,				
Median (IQR) ^a , mg/L $\text{CaCO}_3 \text{ L}^{-1}$	34.5 (9.1–36.2)	34.5 (9.1–36.2)	36.2 (19.3–36.5)	1.02 (1.00–1.04)
Water hardness $> 150 \text{ mg/L CaCO}_3 \text{ L}^{-1}$, n (%)	265 (74.0)	190 (72.0)	75 (79.8)	1.54 (0.87–2.72)
Cumulative pool attendance before 2 years,				
Median (IQR) ^a , hours	24.0 (10.8–59.0)	23.9 (8.8–48.4)	27.2 (13.0–69.0)	1.00 (1.00–1.01)
Infant swimmers, n (%)	164 (45.8)	116 (42.4)	52 (55.3)	1.68 (1.05–2.70)
Atopic status,				
At least 1 aeroallergen $> 0.35 \text{ kIU/L}$, n (%)	86 (24.0)	60 (22.7)	26 (27.7)	1.30 (0.76–2.22)
Current Medication for allergy, n (%)	59 (16.5)	34 (12.9)	25 (26.6)	2.45 (1.37–4.39)
Sensitization to at least 1 aeroallergen or medication for allergy, n (%)	121 (33.8)	80 (30.3)	41 (43.6)	1.78 (1.10–2.89)
Doctor-diagnosed eczema, n (%)	94 (26.3)	/	/	/

^a IQR: interquartile range; SD: standard deviation.

^b OR, odds ratio; 95% CI, 95% confidence interval.

Table 2

Prevalences and odds ratio for eczema associated with water hardness and infant swimming practice according to atopic status.

	All children				Non atopic				Atopic			
	N	(%)	Crude OR (95% CI) ^a	Adjusted OR (95% IC) ^b	N	(%)	Crude OR (95% CI) ^a	Adjusted OR (95% IC) ^b	N	(%)	Crude OR (95% CI) ^a	Adjusted OR (95% IC) ^b
Water hardness (mg/L CaCO ₃ L ⁻¹)												
continuous	358	26.3	1.02 (1.00–1.04)	1.02 (1.00–1.05)	237	22.4	1.02 (0.99–1.05)	1.03 (1.00–1.06)	121	33.9	1.03 (1.00–1.06)	1.04 (1.00–1.07)
< 150	93	20.4	1.00	1.00	55	18.2	1.00	1.00	38	23.7	1.00	1.00
150–350	96	25.0	1.30 (0.66–2.57)	1.39 (0.67–2.88)	65	21.5	1.24 (0.5–3.05)	1.15 (0.44–3.02)	31	32.3	1.53 (0.53–4.44)	2.05 (0.63–6.65)
> 350	169	30.2	1.68 (0.92–3.07)	1.97 (0.97–3.96)	117	24.8	1.48 (0.66–3.31)	1.77 (0.70–4.43)	52	42.3	2.36 (0.93–5.98)	3.36 (1.02–11.1)
P for trend	–	0.08	–	–	0.32	–	–	0.06	–	–	–	–
Infant swimming												
RCS ^c	358	26.3	1.51 (1.06–2.16)	1.41 (0.98–2.04)	237	22.4	1.96 (1.24–3.10)	1.78 (1.09–2.89)	121	33.9	1.05 (0.50–2.18)	0.94 (0.42–2.10)

^a OR, Odds ratio; 95% CI, 95% confidence interval.^b Adjustment for age, gender, parental eczema and/or allergy, breastfeeding, parent's education level, presence of older siblings, passive smoking, maternal smoking during pregnancy and participation rate.^c The OR were estimated for the upper quartile by using restricted cubic spline (RCS) with the lowest quartile as the reference group.**Table 3**

Prevalences and odds ratios for eczema associated with water hardness and infant swimming practice after stratification for these two risk factors.

Water hardness (mg/L CaCO ₃ L ⁻¹)	Non infant swimmers				Infant swimmers			
	N	(%)	Crude OR (95% IC) ^a	Adjusted OR (95% IC) ^b	N	(%)	Crude OR (95% IC) ^a	Adjusted OR (95% IC) ^b
continuous	194	21.6	1.02 (1.00–1.05)	1.04 (1.01–1.08)	164	31.7	1.02 (0.99–1.05)	1.03 (1.00–1.06)
< 150	64	14.1	1.00	1.00	29	34.5	1.00	1.00
150–350	51	27.5	2.31 (0.91–5.89)	3.62 (1.26–10.4)	45	22.2	0.53 (0.19–1.54)	0.45 (0.15–1.38)
> 350	79	24.1	1.94 (0.81–4.64)	3.76 (1.31–10.76)	90	35.6	1.05 (0.44–2.53)	0.76 (0.27–2.14)
P for trend			0.17				0.56	
Infant swimming	Soft water (< 150 mg/L CaCO ₃ L ⁻¹)				Hard water (> 150 mg/L CaCO ₃ L ⁻¹)			
	N	%	Crude OR (95% IC) ^a	Adjusted OR (95% IC) ^b	N	Prevalence	Crude OR (95% IC) ^a	Adjusted OR (95% IC) ^b
RCS ^c	93	20.4	2.01 (0.98–4.09)	2.13 (0.98–4.64)	265	28.3%	1.40 (0.90–2.18)	1.26 (0.79–2.02)

^a OR, Odds ratio; 95% CI, 95% confidence interval.^b Adjustment for age, gender, parental eczema and/or allergy, breastfeeding, parent's education level, presence of older siblings, passive smoking, maternal smoking during pregnancy and participation rate.^c The OR were estimated for the upper quartile by using restricted cubic spline (RCS) with the lowest quartile as the reference group.**Table 4**

Biological interactions between atopy, water hardness and infant swimming.

Interaction categories	N	Prevalence (%)	Crude OR (95% CI) ^a	Adjusted OR (95% IC) ^b	AP (95% IC) ^a	S (95% IC) ^a
<i>Interaction atopy+hard water^c</i>						
No atopy+soft water	55	18.2	1.00	1.00	0.41	2.40
Atopy	38	23.7	1.40 (0.51–3.85)	1.37 (0.48–3.92)	(0.15 to 0.66)	(0.96 to 6.01)
Hard water	182	23.6	1.39 (0.65–2.99)	1.59 (0.69–3.64)	–	–
Atopy+hard water	83	38.6	2.82 (1.25–6.38)	3.30 (1.34–8.15)	–	–
<i>Interaction atopy+infant swimming</i>						
No atopy+no infant swimming	126	17.5	1.00	1.00	0.04	1.07
Atopy	68	29.4	1.97 (0.98–3.95)	1.89 (0.93–3.86)	(–0.34 to 0.42)	(0.57 to 2.00)
Infant swimming	111	27.9	1.83 (0.99–3.40)	1.67 (0.88–3.19)	–	–
Atopy+infant swimming	53	39.6	3.10 (1.51–6.36)	2.72 (1.29–5.74)	–	–
<i>Interaction hard water+infant swimming^c</i>						
Soft water+no infant swimming	64	14.1	1.00	1.00	–0.56	0.54
Hard water	130	25.4	2.08 (0.93–4.66)	2.36 (0.98–5.68)	(–1.12 to –0.01)	(0.33 to 0.87)
Infant swimming	29	34.5	3.22(1.14–9.12)	2.95 (1.01–8.58)	–	–
Hard water+infant swimming	135	31.1	2.76 (1.25–6.10)	2.82 (1.19–6.70)	–	–

^a OR, Odds ratio; 95% CI, 95% confidence interval; AP, attributable proportion of interaction; S, synergy index.^b Adjustment for age, parental education level, parental allergy and/or eczema, maternal smoking during pregnancy, presence of older siblings, gender, breastfeeding, participation rate and passive smoker.^c Soft water < 150 mg/L CaCO₃ L⁻¹; hard water > 150 mg/L CaCO₃ L⁻¹.

predisposition to atopic diseases. Although it is known since long that hard water can irritate the skin, the involved mechanisms are still unclear. The explanations commonly forwarded are the deposition of

calcium salts on the skin and the use of larger amounts soap and shampooing to lather the water (Warren et al., 1996; White et al., 1987; Ananthapadmanabhan et al., 2004). Chlorine used to disinfect

swimming pool water and its by-products such as chloramines are potent oxidants that can also cause skin irritation (Lazarov et al., 2005; Basler et al., 2000; Font-Ribera et al., 2009; Bernard, 2007). For instance, Seki et al. (2003) reported that the water holding capacity of the *stratum corneum* decreased after immersion in chlorinated water. Gardinier et al. (2009) have shown that a single swimming session leads to a substantial removal of the sebum from the skin surface. This degreasing action of pool water increases skin pH from acidic to neutral pH, which in turn can alter the skin homeostasis and permeability (Mauro et al., 1998). Furthermore, water *per se* is a well-known skin irritant that can disrupt skin barriers as revealed by an increased transepidermal water loss (Ramsing and Agner, 1997; Tsai and Maibach, 1999). All these chemical stressors might quite conceivably increase the permeability of skin epithelial barriers and thereby facilitate the penetration of allergens and the development of eczema (Löffler et al., 2003; Boralevi et al., 2008; Mattila et al., 2011). This hyperpermeability mechanism triggered by skin irritation would be basically the same as that proposed for the increased risks of asthma and respiratory allergies observed among atopic swimmers regularly attending chlorinated swimming pools (Bernard, 2007).

Our study suggests that atopic subjects might benefit from washing or bathing with soft water or from swimming in non-chlorinated pools. At this stage, however, it is unknown whether avoidance of irritants in tap or swimming water could be beneficial for preventing childhood eczema or for alleviating eczema skin symptoms. With regard to hard water, a recent trial testing the effect of water softeners on eczema severity in children, showed no additional benefit after the installation of an ion-exchange water softener (Thomas et al., 2011). If these findings are confirmed, this would suggest that the association between eczema and water hardness reported by us and other studies (Arnedo-Pena et al., 2007; McNally et al., 1998; Miyake et al., 2004) will be related more to the initiation of eczema and in particular to the early steps of the skin sensitization. The same reasoning could be held for pool chlorine, which might also act more as an adjuvant of skin sensitization than as an irritant exacerbating the symptoms of eczema.

Our study presents several limitations. The lack of a detailed characterization of the cumulative exposure to hard water and swimming pool water is the main limitation of this study. For the exposure to hard water, we had a good measure of the hardness of tap water supplied to each participant but we had no estimate of the contact time while for infant swimming we had just the opposite information. It looks to us unlikely that this lack of information could have distorted our analyses. Skin contact with tap water during infancy is indeed mainly related to washing or bathing, i.e., activities that should not greatly vary between infants. As to the irritating potential of chlorinated pools, it is probably mainly determined by the concentrations of active and combined chlorine, which in public pools at least, are maintained within a narrow range of concentrations to comply with the legislation. Moreover, our data on time spent in chlorinated pool might be subjected to recall bias and could lead to a potential exposure misclassification bias. The association, however, also emerges when considering ever swimming, for which memory bias is less likely. Another limitation is the relatively low participation rate, which was almost unavoidable given the very young age of participants and the fact that our study required the application of medical tests in schools. The participation, however, was unrelated to the outcome and the main risk factors, making participation biases rather improbable.

In conclusion, our study shows that exposure to hard water and, to a lesser extent, infant swimming practice, interact with atopy to increase the prevalence of childhood eczema. A breaching of the epidermal barrier by detergents or salts in hard water and by chlorine-based oxidants in swimming pool might explain these interactions.

Conflict of interest

None of the authors has a conflict of interest to disclose.

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