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Infant Swimming Practice, Pulmonary Epithelium Integrity, and the Risk of Allergic and Respiratory Diseases Later in Childhood

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ABSTRACT

OBJECTIVE. Irritant gases and aerosols contaminating the air of indoor swimming pools can affect the lung epithelium and increase asthma risk in children. We evaluated the impact of infant swimming practice on allergic status and respiratory health later in childhood.

METHODS. Clara cell protein, surfactant-associated protein D, and total and aeroallergen-specific immunoglobulin E were measured in the serum of 341 schoolchildren aged 10 to 13 years, among whom 43 had followed an infant swimming program. Asthma was defined as doctor-diagnosed asthma and/or positive exercise-induced bronchoconstriction (15% decrease in postexercise forced expiratory volume).

RESULTS. There were no significant differences between the infant swimming group and the other children regarding the levels of exhaled nitric oxide and total or aeroallergen-specific serum immunoglobulin E. Children who swam as infants showed, by contrast, a significant decrease of serum Clara cell protein and of the serum Clara cell protein/surfactant-associated protein D ratio integrating Clara cell damage and permeability changes of the lung epithelial barrier. These effects were associated with higher risks of asthma and of recurrent bronchitis. Passive exposure to tobacco alone had no effect on these outcomes but seemed to interact with infant swimming practice to increase the risk of asthma or of recurrent bronchitis.

CONCLUSIONS. Our data suggest that infant swimming practice in chlorinated indoor swimming pools is associated with airways changes that, along with other factors, seem to predispose children to the development of asthma and recurrent bronchitis.

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Key Words

chlorine, trichloramine, nitrogen trichloride, baby swimming, Clara cell protein, CC16, childhood asthma, recurrent bronchitis

Abbreviations

NO—nitric oxide
eNO—exhaled nitric oxide
EIB—exercise-induced bronchoconstriction
FEV₁—forced expiratory volume in 1 second
CC16—Clara cell protein
SP-D—surfactant-associated protein D
IgE—immunoglobulin E
OR—odds ratio
CI—confidence interval

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PUBLIC SWIMMING POOLS need to be disinfected, and usually this is done by water chlorination using sodium or calcium hypochlorite, chlorine gas, or chloroisocyanurates. These chlorine-based disinfectants, loosely referred to as "chlorine," are added in water to release hypochlorous acid, a powerful oxidant that is the active biocide. When reacting with nitrogenous compounds originating from sweat, saliva, or urine brought by swimmers, hypochlorous acid generates a complex mixture of harmful byproducts, among which the most irritant are the chloramines. Monochloramine and dichloramine (NH_2Cl and NHCl_2 , respectively) are water soluble, and the sum of their concentrations in water are referred to as combined chlorine. By contrast, the trichloramine also called nitrogen trichloride (NCl_3) is a water-insoluble gas that, once formed, is immediately released in the air, which gives indoor pools their distinctive "chlorine" smell. Depending on the bather's hygiene and the pool ventilation, mean levels of trichloramine in community indoor pools in Europe are in the range of 300 and 800 $\mu\text{g}/\text{m}^3$, which makes this gas one of the most concentrated air pollutants to which children of developed countries are regularly exposed.¹⁻³ The air of swimming pools, particularly just above the water's surface, is also contaminated by mist or aerosols laden with hypochlorous acid, combined chlorine, and other water-soluble chlorination byproducts, all increasing the burden of oxidants actively inhaled by swimmers.

The acute toxicity of chlorine-based disinfectants has been known for a long time. Case reports regularly describe lung injuries after community accidents in indoor swimming pools.⁴⁻⁷ Inhalation of chlorine gas is usually responsible for the acute lung damage that fortunately is usually transient with recovery of the lung function within a period of a few weeks. The possibility that the gaseous and aerosolized chlorination products building up in pool air can cause chronic respiratory effects in swimmers has, however, been acknowledged only recently. Our investigations on children attending indoor chlorinated swimming pools have shown that trichloramine, together probably aerosolized hypochlorous acid and chloramines, can damage the lung epithelium⁸ and promote the development of asthma, especially in atopic children.⁹⁻¹¹ These effects might lie behind the strong ecological associations that we have recently evidenced across Europe between childhood asthma prevalence and the availability of indoor chlorinated swimming pool.¹² Studies by other researchers confirmed the detrimental effects of these chemicals on the airways of recreational swimmers,¹³ including asthmatics,¹⁴ while providing additional evidence that swimming pool attendance during infancy might contribute to the development of allergic diseases.¹⁵

One of the most critical factors in determining the risks of chlorination products for children seems to be the timing of exposure. The risk of developing asthma or

of lung inflammation as assessed on the basis of exhaled nitric oxide (eNO) seems to culminate when children regularly attend indoor pools before the age of 7 years.^{9,11} A likely explanation for this higher sensitivity of young children is that they cannot really swim before the age of 6 or 7 years and, therefore, have to attend the small heavily polluted pool. When playing or learning to swim, young children probably also inhale and swallow more aerosols and water droplets containing hypochlorous acid and soluble chloramines. Another likely explanation is that the lungs of very young children are still developing, thus they are presumably more vulnerable to the irritating effects of chlorine and its derivatives.¹⁶

These findings unavoidably raise the question of the safety of infant swimming, especially because the higher water temperature and the greater organic pollution in swimming pools attended by young children are conditions favoring the formation of chlorination byproducts. In the United States, it is estimated that between 5 and 10 million infants and preschool children participate in formal swimming instructions programs, and among them there are probably several million individuals who have learned swimming as infants.¹⁷ Surprisingly, most industrialized countries have popularized this practice in the absence of reliable data concerning the possible consequences of exposing infants to the toxic gases and aerosols building up in the air of indoor pools. The only study having addressed this issue is that of Nystad et al,¹⁸ who found that infant swimming practice was associated with an increased risk of recurrent respiratory tract infections and otitis media in the first year of life. This study, however, did not report data on the levels of chlorine in the pools attended by the infants, nor did it assess the effects of infant swimming on the development of asthma and allergy later in childhood.

In this cross-sectional study, we compared the respiratory health, allergic status, and pulmonary epithelium integrity of school-aged children who took part in an infant swimming program with that of their peers who did not. Whenever possible, objective outcome measures were used in addition to the traditional indicators of allergic and respiratory diseases assessed by questionnaire.

MATERIALS AND METHODS

Forty-three children having taken part in an infant swimming program were identified in a survey that involved a total of 341 schoolchildren 10 to 13 years of age. These children were recruited in 10 primary schools in southwestern Brussels. Levels of active and combined chlorine in the public swimming pool attended by swimming infants were within recommended limits at that time (<1.5 and $2 \text{ mg}/\text{L}$, respectively). Concentrations of trichloramine in pool air, available from 2001 when the systematic survey of this gas started in Brussels, ranged from 170 to 540 $\mu\text{g}/\text{m}^3$ (mean: 325 $\mu\text{g}/\text{m}^3$; $n = 7$).

Levels of trichloramine were probably in the same range some 10 years ago because operating conditions and recommended limits of chlorine had remained unchanged since the 1980s. All children were examined in their school between March 28 and May 29, 2002, thus outside main periods of pollination in Belgium. The protocol for examining children was described in detail elsewhere.¹² Briefly, after their parents had given written informed consent, the children underwent a medical examination that included measurement of height and weight, collection of 1 blood sample (7 mL) after application of an anesthetic cream (EMLA, AstraZeneca, Karlskarga, Sweden). Asthma was screened by using the exercise-induced bronchoconstriction (EIB) test (on the basis of a 15% decrease of forced expiratory volume [FEV₁] after a 6-minute roundabout indoors with submaximal effort),¹⁹ a noninvasive test that has been found to be predictive of clinical asthma or asthma symptoms in several studies.^{20–22} The examination also included the measurement of eNO²³ and serum Clara cell protein (CC16)^{24,25} and surfactant-associated protein D (SP-D) (SPD ELISA kit, Yamasa Corporation, Tokyo, Japan), 2 markers of the deep lung epithelium integrity.^{26,27} Total immunoglobulin E (IgE) and IgE against the 12 most common aeroallergens were also measured in serum (Immulite Total and AlAtTOP; Diagnostic Products Corp, Los Angeles, CA). Information about the respiratory health of children (respiratory symptoms during the previous 12 months, doctor-diagnosed asthma, and recurrent bronchitis) and their exposure to risk factors of asthma and allergy was obtained from the questionnaire filled in by the parents. The ethics committee of the Catholic University of Louvain approved the study protocol. Statistical comparison was based on the χ^2 test, the 2-sided unpaired *t* test, or the Mann-Whitney *U* test. Bonferroni's correction was applied to multiple comparisons. Backyard multiple and logistic regression analyses were used to assess associations between infant swimming practice and outcomes. We tested a total of 23 other potential predictors, including among others gender, total and aeroallergen-specific IgE, family history of allergic diseases, maternal smoking during pregnancy, parental smoking at home, siblings, housing density, exposure to pets, cumulated attendance at an indoor chlorinated pool, and the accessibility to a backyard chlorinated pool. In multiple regression analyses, cumulated pool attendance and the CC16/SP-D ratio that were not normally distributed were normalized by logarithmic transformation. To enable the log transformation, we set the minimum cumulated pool attendance at 2.5 hours instead of 0 (2.5 hours was the lowest reported cumulated pool attendance). Independent variables in multiple regression analyses were entered at a *P* value of .25 and kept in the model at *P* value <.05. In logistic regression analyses, adjustment was made for variables remaining with a *P* value <.1. These logistic regression

analyses were repeated on children who were exposed to tobacco smoke during pregnancy or at home to detect the possible interactions of these 2 factors with infant swimming practice. Unless otherwise stated, only odds ratios (ORs) adjusted for covariates are reported. In addition, we used 2-way analysis of variance to assess the changes in serum pneumoproteins associated with infant swimming practice, access to a backyard pool, or with exposure to tobacco smoke during pregnancy or at home, and the possible interactions between these factors. Statistical analyses were performed by using SAS 9.1.3 (SAS Institute, Inc, Cary, NC).

RESULTS

As shown in Table 1, children who had been swimming as infants did not differ from their peers with respect to age, gender, ethnicity, BMI, and family history of asthma or hay fever. Children in the swimming infant group were also not significantly different from their peers regarding birth weight, number of siblings, housing density, or proportions of children who were breastfed, attended day care, or lived with pets since birth. The proportions of children exposed to tobacco smoke at home or who had been exposed to tobacco smoke during pregnancy, as well as of children having access to a backyard chlorinated pool were, however, noticeably greater among swimming infant children. These children also had a significantly greater cumulated attendance at indoor chlorinated swimming pools.

The allergic status and the markers of lung inflammation and epithelial integrity of children who swam as infants and controls are compared in Table 2. Mean levels of total serum IgE and the prevalences of IgE specific to major aeroallergens were similar between the 2 groups. The rate of sensitization to dog-specific IgE was higher in children in the infant swimming group, a difference, however, that was no more statistically significant after the application of the Bonferroni's test. There were also no differences between the 2 groups regarding the mean levels and prevalences of elevated values of eNO. Most children positive in the eNO test (*n* = 29) were sensitized against house-dust mite allergen (*n* = 21 [72.9%]) and aeroallergen-specific IgE (*n* = 26 [89.7%]). Children in the infant swimming group, by contrast, showed a significant decrease of serum CC16 and an even more significant decrease of the CC16/SP-D ratio, an index integrating the damage to Clara cells and the permeability changes of lung epithelial barrier. In multivariate analysis, infant swimming emerged as the only statistically significant predictor of serum CC16 (partial *r*: −0.14; *P* = .01), and this practice was the strongest determinant of the CC16/SP-D ratio (log-transformed values, partial *r*: −0.15; *P* = .006), the latter being also influenced by day care attendance (partial *r*: −0.086; *P* = .007), age (partial *r*: −0.058; *P* = .009), breastfeeding (partial *r*: −0.080; *P* = .022), and

TABLE 1 Characteristics of Children Who Swam as Infants and Their Controls

	Swimming Infants (N = 43)	Other Children (N = 298)	P
Age, mean (SD), y ^a	11.5 (0.6)	11.5 (0.6)	.98
Boys, n (%) ^b	22 (51.1)	150 (50.3)	.92
White, n (%) ^b	35 (81.4)	228 (76.5)	.48
BMI, mean (SD), kg/m ^{2a}	18.5 (2.7)	18.4 (2.5)	.81
Mother and/or father with asthma, n (%) ^b	6 (14.0)	58 (19.5)	.39
Mother and/or father with hay fever, n (%) ^b	13 (30.2)	87 (29.2)	.89
Birth weight, mean (SD), kg ^a	3.19 (0.57)	3.34 (0.54)	.96
No. of siblings, mean (SD) ^a	2.56 (1.30)	2.68 (1.28)	.56
Housing density, mean (SD), persons per room ^a	0.83 (0.36)	0.79 (0.30)	.36
Breastfeeding, n (%) ^b	9 (20.9)	34 (11.4)	.21
Exposure to pets since birth, n (%) ^b	9 (20.9)	47 (15.8)	.39
Child care attendance n (%) ^b	24 (55.8)	151 (50.7)	.40
Passive smoking at home, n (%) ^b	18 (41.8)	72 (24.2)	.014
Maternal smoking during pregnancy, n (%) ^b	16 (37.2)	46 (15.4)	.0005
Backyard pool, n (%) ^b	6 (14.0)	9 (3.0)	.0011
Cumulated indoor pool attendance, median (interquartile range), h ^c	146 (88–281)	83 (42–182)	.0002

^a By 2-sided unpaired *t* test.^b By χ^2 test.^c By 2-sided Mann-Whitney *U* test.**TABLE 2** Total and Aeroallergen-Specific Serum IgE, eNO, and Serum Pneumoproteins in Children Who Swam as Infants and Their Controls

	Swimming Infants (N = 43)	Other Children (N = 298)	P
Total IgE, median (interquartile range), kIU/L ^a	54.7 (24.6–162)	55.8 (21.9–175)	.96
Aeroallergen-specific IgE			
Panel of 12 aeroallergens, n(%) ^b	13 (30.2)	95 (31.9)	.83
House dust mite, n(%) ^b	6 (14)	57 (19.1)	.40
Cat, n (%) ^b	2 (4.7)	17 (5.7)	.77
Dog, n (%) ^b	4 (9.3)	8 (2.7)	.03
Pollen, n (%) ^b	7 (16.3)	31 (10.4)	.26
eNO			
Median (interquartile range), ppb ^a	10.2 (7.15–14.1)	8.9 (6.9–13.4)	.51
>30 ppb, n(%) ^b	3 (7.0)	26 (8.7)	.70
Pneumoproteins			
CC16, mean (SD), $\mu\text{g/L}^{\text{c,d}}$	8.0 (3.3)	10.4 (4.2)	.01
SP-D, mean (SD), $\mu\text{g/L}^{\text{c}}$	113 (42)	100 (45)	.08
CC16/SP-D ratio, median (interquartile range) ^{a,c}	0.07 (0.05–0.12)	0.10 (0.07–0.16)	.003

^a By 2-sided Mann-Whitney *U* test.^b By χ^2 test.^c By 2-sided unpaired *t* test.^d Statistically significant after application of the Bonferroni's correction to the multiple comparisons of the lung epithelium markers (critical *P* = .05/3).

ethnicity (partial *r*: 0.087; *P* = .024). Passive exposure to tobacco smoke during pregnancy or at home as well as the access to a backyard pool had thus no influence on the serum levels of CC16 or on the serum CC16/SP-D ratio. Analysis of the effects of infant swimming and passive smoking on pneumoproteins by 2-way analysis of variance confirmed the decrease of serum CC16 and CC16/SP-D ratio in children in the infant swimming group and found no interaction between infant swimming and passive smoking (all *P* $\geq$.15).

As shown in Table 3, changes observed in serum pneumoproteins were associated with poorer respiratory health. Children who swam as infants showed an increased risk of chest tightness. There were no statistically significant differences in the other respiratory symp-

toms, which tended to be more prevalent in the children in the infant swimming group. These children were also ~3 times more likely to be positive in the EIB test, to have doctor diagnosed and/or EIB test-screened asthma, and to suffer from recurrent bronchitis. Of note, the lack of statistical significance in the increased risk of doctor-diagnosed asthma with infant swimming was because of the influence of backyard pool (OR: 4.27; 95% confidence interval [CI]: 1.05–17.4). Indeed, removal of the backyard pool factor from the list of predictors increased the OR for doctor-diagnosed asthma associated with infant swimming to a level that was significantly >1 (OR: 2.96; 95% CI: 1.08–8.11). No significant association emerged between any of these outcomes or passive exposure to tobacco smoke at home or during pregnancy,

TABLE 3 Swimming Infant Practice, Respiratory Symptoms, and Risks of Asthma and Recurrent Bronchitis Later During Childhood

	Frequency, <i>n</i> (%)		OR (95% CI)		<i>P</i>
	Swimming Infants (<i>N</i> = 43)	Other Children (<i>N</i> = 298)	Crude	Adjusted	
Wheezing	6 (14.0)	26 (8.7)	1.7 (0.7–4.4)	1.5 (0.5–4.1) ^a	.48
Chest tightness	6 (14.0)	13 (4.4)	3.6 (1.3–9.9)	3.8 (1.2–12.1) ^b	.03
Shortness of breath	6 (14.0)	18 (6.0)	2.5 (0.9–6.8)	2.4 (0.8–7.3) ^c	.11
Cough	11 (25.6)	51 (17.1)	1.7 (0.8–3.5)	1.8 (0.8–3.8) ^d	.13
Doctor-diagnosed asthma	7 (16.3)	23 (7.7)	2.3 (0.9–5.8)	2.2 (0.77–6.5) ^e	.10
Exercise-induced asthma (EIB)	4 (9.3)	11 (3.7)	2.7 (0.8–8.8)	4.3 (1.1–17.2) ^f	.049
Doctor-diagnosed asthma and/or EIB	10 (23.3)	33 (11.1)	2.4 (1.1–5.4)	3.0 (1.3–7.4) ^g	.01
Recurrent bronchitis	26 (60.5)	110 (36.9)	2.6 (1.4–5.8)	2.6 (1.3–5.1) ^h	.006

^a Adjusted for age, gender, atopy (IgE > 100 IU/mL), maternal smoking during pregnancy, and parental hay fever.

^b Adjusted for BMI, sibling status, parental asthma, mold on the wall of room, and sport practice other than swimming.

^c Adjusted for BMI, sibling status, maternal smoking during pregnancy, and parental asthma.

^d Adjusted for breastfeeding.

^e Adjusted for gender, parental asthma, aeroallergen-specific IgE, exposure to pets, number of siblings, and backyard pool.

^f Adjusted for age, parental asthma, parental smoking at home and aeroallergens specific IgE.

^g Adjusted for age, parental asthma; and aeroallergens specific IgE in serum.

^h Adjusted for birth weight, day care attendance, house with double-gazed windows, and use of chlorine bleach for house cleaning.

except for the risk of wheezing that was increased by maternal smoking during pregnancy (OR: 2.75; 95% CI: 1.04–6.61). Passive exposure to tobacco smoke and infant swimming seemed, however, to potentiate the detrimental effects of infant swimming practice. The OR for asthma (doctor-diagnosed and/or screened with the EIB test) associated with infant swimming was indeed >2 times greater when children were also exposed to parental smoking (OR: 6.54; 95% CI: 1.18–36.4 vs OR: 2.52; 95% CI: 0.86–7.39) although the odds for recurrent bronchitis associated with infant swimming was >4 times greater among children who had been exposed to maternal smoking during pregnancy (OR: 6.99; 95% CI: 1.60–30.5 vs OR: 1.61; 95% CI: 0.71–3.65).

To determine whether changes in serum pneumoproteins were primarily because of the infant swimming practice and not the mere consequences of asthma or recurrent bronchitis that were more frequent in the children in the swimming infant group, we assessed by a 2-way analysis of variance the effects of infant swimming practice, total asthma or recurrent bronchitis on serum pneumoproteins, and the possible interactions between these factors. As illustrated in Fig 1, asthma and recurrent bronchitis alone had no influence on the serum levels of pneumoproteins, which is in sharp contrast with the highly significant decrease of serum CC16 and CC16/SP-D ratio associated with infant swimming activity ($P < .001$). This analysis clearly shows that the levels of serum CC16 were on average the lowest among the children in the infant swimming group who were asthmatic or recurrently suffered from bronchitis.

DISCUSSION

Our findings show that the infant swimming practice is associated with lung epithelium alterations that seem to predispose children to the development of asthma and

recurrent bronchitis. These effects cannot be explained by inherited differences in the genetic disposition to develop these diseases, because children who swam as infants were well matched with the others with respect to the family history of respiratory disease, as well as to the serum levels of total IgE. Our findings cannot be explained either by the fact that on average the children in the infant swimming group were more exposed to parental smoking or to chlorine from backyard pools. In our study, we found no evidence that infant swimming increased the risk of respiratory allergy. There was also no increase in the risk of airways inflammation as assessed by the eNO test, a finding that is not surprising given the very close relationship between eNO and allergic sensitization observed by us and also reported by recent studies.^{28,29}

As with any epidemiologic study using data from self-administered questionnaires, our study can be prone to recall bias. We believe, however, that it is unlikely that our observations were generated or distorted by a systematic bias in the parental responses to the questions about their child's health or swimming practice. The strongest argument against that possibility is that the most statistically significant observations were made with objective outcome measures (serum pneumoproteins and EIB test) that parents were not aware of when filling the questionnaires. The parents were also blinded to the tested hypothesis because initially the study was not designed to look specifically at the effects of infant swimming practice. In addition, the tested hypothesis of adverse respiratory effects associated with infant swimming is far from being common in the community. Actually, this hypothesis is just the opposite of the belief that the parents probably have when they decide to take their infant to swimming pool. The possibility that they

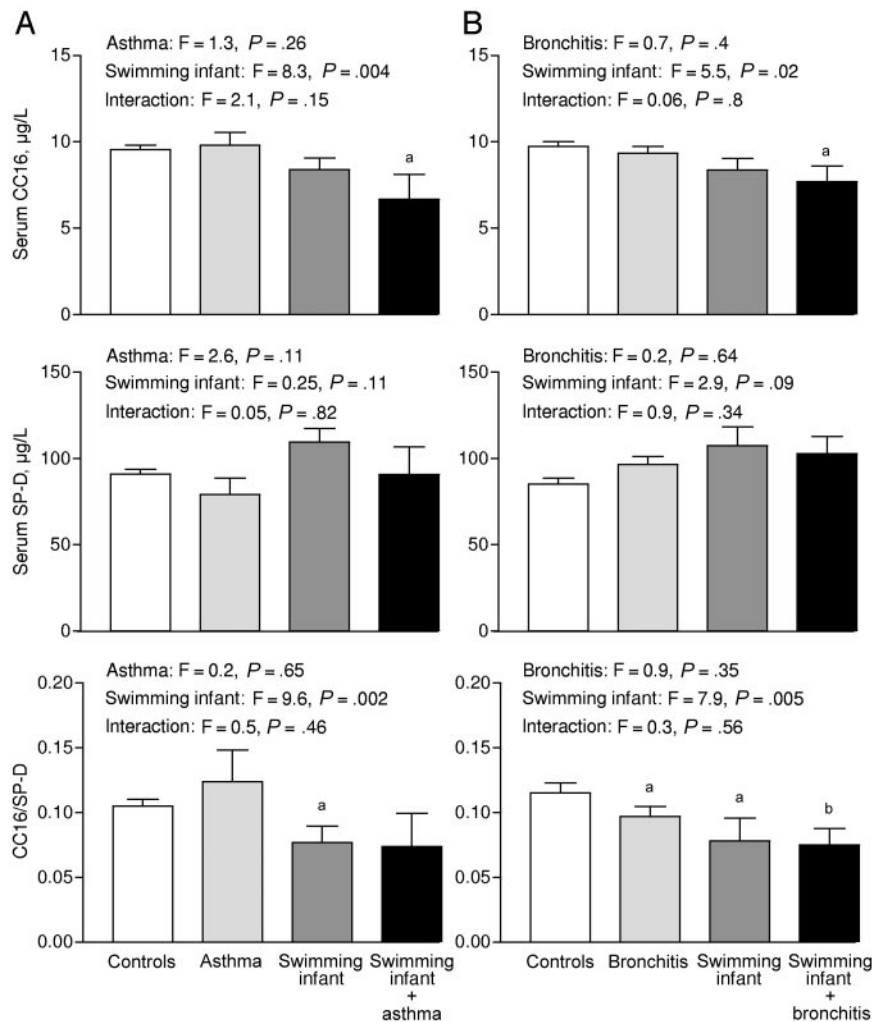


FIGURE 1

Effects of total asthma (A), recurrent bronchitis (B), and swimming infant practice (A and B) and of their possible interactions on the serum concentrations of CC16 and SP-D and the serum CC16/SP-D ratio. Results were assessed by 2-way analysis of variance followed by Dunnett's multiple-comparison test. Mean (with SE) values that are significantly different from that of controls: ^a $P < .05$; ^b $P < .01$.

could have biased their responses in favor of adverse effects seems thus unlikely.

Our data suggest that the poorer respiratory health of children who swam as infants could be linked to distal airways damage detected by the assay of serum pneumoproteins. The concentration of serum CC16 is a well-validated marker of the lung epithelium barrier integrity, reflecting either the number of Clara cells lining terminal airways or the permeability of the alveolar-capillary barrier.^{26,27} When adjusted for the level of a surfactant-associated protein, such as SP-D, the concentration of CC16 proves to be an even more sensitive marker, probably because this ratio integrates both the damage to Clara cells and the increased leakiness of the alveolar-blood barrier.³⁰ A decrease in serum CC16 reflecting a parallel loss of Clara cells was demonstrated in humans and in rodents acutely or chronically exposed to a variety of lung toxicants.³¹ For instance, active smoking leads to a 20% to 30% decrease of

serum CC16, mirroring a parallel decrease in the number of Clara cells.³⁰⁻³⁴ A similar decrease of serum CC16 was observed after occupational exposures to crystalline silica³⁵ or firesmoke.³⁶ The decrease of serum CC16 in children who swam as infants averaged 20%. Thus, it is almost of the same magnitude as that caused in adults by tobacco smoke or industrial chemicals. If one refers to the clinical consequences of active smoking or of occupational exposures to crystalline silica and other lung irritants, it would not be surprising that similar alterations of the respiratory epithelium in young children could make them more prone to develop some respiratory diseases. This interpretation is also consistent with the antiinflammatory properties of CC16,^{37,38} as well as with the finding that asthma³⁹ and other respiratory diseases⁴⁰ are associated with lower intrapulmonary pools of CC16 because of Clara cell damage or the intravascular leakage of the protein.

Given the lack of data concerning the toxicity of

swimming pool chemicals for the respiratory tract of infants and young children, the pool factor responsible for these airways alterations is difficult to identify. We strongly suspect, however, that the chlorination products that infants inhale as gases, aerosols, or even water repeatedly damage the airway epithelium. One culprit might be trichloramine, the highly volatile and reactive gas formed when chlorine reacts with organic matter brought by swimmers. This gas that gives indoor swimming pools their characteristic chlorine smell was, indeed, found to cause asthma and pulmonary epithelium damage in lifeguards and recreational swimmers.⁸⁻¹¹ Because their lungs are still developing, infants could be particularly sensitive to this irritant and be affected despite the rather limited time they spend in pools (usually 20–30 minutes per session). The levels of trichloramine in the studied pool were on average below the provisional 2-hour air quality guideline of 500 $\mu\text{g}/\text{m}^3$ recently recommended by the World Health Organization.⁴¹ If trichloramine is responsible for the respiratory effects observed in our study, this would mean that the World Health Organization guideline is too high and should be lowered to be more in accordance with studies^{8,9} showing that trichloramine can disrupt the lung epithelium barrier of swimmers at concentrations ranging from 355 to 490 $\mu\text{g}/\text{m}^3$. Another important route of exposure that might cause significant damage to infant's lungs is the inhalation of aerosols or of small volumes of chlorinated water when the infants actively play or have their head under water. Damage to the respiratory tract caused by the inhalation of heavily chlorinated water seems especially plausible because the maximum recommended levels for chlorine in the Brussels pool that our children attended when they were infants were relatively high. For instance, the recommended limit for combined chlorine was 2 ppm, a concentration twice higher than the current standard (0.8 ppm) and 10 times higher than the standard applied in Germany (0.2 ppm).¹⁵ Because infants cannot control their breathing as well as when they get older, the infant swimming practice is considered to be safe because of the laryngeal or gag reflex that is triggered when water gets into infant's mouth. By closing off the larynx with the epiglottis, this reflex is supposed to keep pool water from entering the lungs.⁴² However, the gag reflex, even if very effective, cannot prevent small amounts of chlorinated water deposited or trapped in the upper respiratory tract to be conducted more deeply in the lungs when the infant surfaces to breathe. Cases of hyponatremic described after dunking infants in swimming pools^{43,44} attest to the amount of water that an infant can ingest and possibly inhale when being under water. Last, one cannot exclude the possibility that the inhalation of hypotonic water also causes some epithelial changes aggravating the effects of chlorination products.

Although we did not specifically interview the par-

ents about this issue, our study provides some interesting insights into the reasons why parents take their infant to swimming programs. As one could expect, prevention of drowning seems to be an important reason because there were 5 times more children having access to a backyard pool among the infant swimming group than among the other children. Although drowning is a leading cause of unintentional injury and death in children, frequently involving backyard pools, it should be noted that the protection offered by infant swimming programs is much debated. According to the American Academy of Pediatrics, there is indeed no clearcut scientific evidence that the likelihood of drowning is reduced by the participation to such programs.¹⁷ The American Academy of Pediatrics argues that until the age of 4 years, infants are not developmentally ready for formal swimming lessons and that the participation in such programs could give to parents a false sense of security about their child's skill in water. The American Academy of Pediatrics did not consider chemical hazards, but if, as suggested by our findings, chlorine used to disinfect pools poses some threat to infants' health, this would certainly further justify a critical appraisal of infant swimming programs. There might be, however, an even more debatable reason encouraging parents to participate to swimming infant programs. Intriguingly, the infant swimming group included a much greater proportion of children who had been exposed to tobacco smoke in utero or at home. The origin of this difference is unclear, but we think it might reflect the will of the parents to mitigate for the adverse effects of passive smoking by giving their infant the possibility to practice a healthy activity. The unfortunate irony is that the result might well be just the opposite, because our study suggests that infant swimming activity interacts with passive smoking to greatly increase the risk of asthma or recurrent bronchitis.

The major limitation of our study certainly lies in the relatively small size of the infant swimming group. With <15% of Brussels schoolchildren participating in such programs, this was the maximum sample size we could achieve in a population-based study involving 341 children. The alternative would be to recruit children via infant swimming organizations. However, assuming that these organizations would be willing to collaborate in research exploring the risks linked to chlorinated pools, the study would then be confronted with the difficulty of avoiding response or selection bias and, above all, with the difficulty of recruiting a well-matched control population. Fortunately, the limited statistical power of our study was balanced by the use of sensitive outcome measures, leading to particular strong associations that were unlikely to be explained by chance only. The small size of our study, however, did not enable us to draw definitive conclusions regarding the impact of backyard pool chlorine to which children in the infant swimming

group were more frequently exposed. Having access to a backyard chlorinated pool emerged, indeed, as a significant predictor of doctor-diagnosed asthma, which slightly weakened the association emerging with infant swimming. This is clearly another unexplored area that warrants additional research, especially because residential pools usually have higher levels of chlorine than public pools and offer children almost unlimited opportunities for swimming during the hot season.

CONCLUSIONS

Our study shows that the infant swimming practice in indoor chlorinated pools can be associated with airways changes that predispose children to asthma and recurrent bronchitis later in childhood. Given the increasing popularity of swimming pools, there is a definitive need to assess the effects of chlorination products on the respiratory tract of very young children. In the meantime, because in most countries these products are not as strictly regulated and monitored as indicators of microbial risks, we can only recommend caution before regularly taking infants to poorly maintained swimming pools with excessive levels of chlorine in the water and in the air.

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REFERENCES

- Jessen HJ. Chloramine concentrations in the air of indoor baths [in German]. *Z Gesamte Hyg.* 1988;34:248–250
- Hery M, Hecht G, Gerber JM, Gendre J, Hubert G, Rebuffaud J. Exposure to chloramines in the atmosphere of indoor swimming pools. *Ann Occup Hyg.* 1995;39:427–439
- Fraunhofer Institute Umwelt, Sicherheit, Energietechnik (IUSE). *Measuring Chloramines in the Air of Swimming Pools.* Stolberg, Germany: IUSE; 2004
- Agibati N, Ancona C, Forastiere F, et al. Short term respiratory effects of acute exposure to chlorine due to swimming pool accident. *Occup Environ Med.* 2001;58:399–404
- Parimon T, Kanne JP, Pierson DJ. Acute inhalation injury with evidence of diffuse bronchiolitis following chlorine gas exposure at a swimming pool. *Respir Care.* 2004;49:291–294
- Bonetto G, Corradi M, Carraro S, et al. Longitudinal monitoring of lung injury in children after acute chlorine exposure in a swimming pool. *Am J Resp Crit Care Med.* 2006;174:545–549
- Vohra R, Clark RF. Chlorine-related inhalation injury from a swimming pool disinfectant in a 9-year-old girl. *Pediatr Emerg Care.* 2006;22:254–257
- Carbonnelle S, Francaux M, Doyle I, et al. Changes of serum pneumoproteins caused by short-term exposures to nitrogen trichloride in indoor chlorinated pools. *Biomarkers.* 2002;7:464–478
- Bernard A, Carbonnelle S, Michel O, et al. Lung hyperpermeability and asthma prevalence in schoolchildren: unexpected associations with the attendance at indoor chlorinated swimming pools. *Occup Environ Med.* 2003;60:385–394
- Bernard A, Nickmilder M, Carbonnelle S, de Burbure C. Non-invasive biomarkers of pulmonary damage and inflammation: application to children exposed to ozone and trichloramine. *Toxicol Appl Pharmacol.* 2005;206:185–190
- Bernard A, Carbonnelle S, de Burbure C, Michel O, Nickmilder M. Chlorinated pool attendance, atopy and the risk of asthma during childhood. *Environ Health Perspect.* 2006;114:1567–1573
- Nickmilder M, Bernard A. Ecological association between childhood asthma and availability of indoor chlorinated swimming pools in Europe. *Occup Environ Med.* 2007;64:37–46
- Lagerkvist B, Bernard A, Blomberg A, et al. Pulmonary epithelial integrity in children: relationship to ambient ozone exposure and swimming pool attendance. *Environ Health Perspect.* 2004;112:1768–1771
- Stav D, Stav M. Asthma and whirlpool baths. *N Engl J Med.* 2005;353:1635–1666
- Kohlhammer Y, Döring A, Schäfer T, Wichmann HE, Heinrich J; KORA Study Group. Swimming pool attendance and hay fever rates later in life. *Allergy.* 2006;61:1305–1309
- Finkelstein JN, Johnston CJ. Enhanced sensitivity of the post-natal lung to environmental insults and oxidant stresses. *Pediatrics.* 2004;113:1092–1096
- American Academy of Pediatrics, Committee on Sports Medicine and Fitness and Committee on Injury and Poison Prevention. Swimming programs for infants and toddlers. *Pediatrics.* 2000;105:868–870
- Nystad W, Nja F, Magnus P, Nafstad P. Baby swimming increases the risk of recurrent respiratory tract infections and otitis media. *Acta Paediatr.* 2003;92:905–909
- McFadden ER, Gilbert IA. Exercise-induced asthma. *N Engl J Med.* 1994;330:1362–1367
- Jones A. Asymptomatic bronchial hyperreactivity and the development of asthma and other respiratory illness in children. *Thorax.* 1994;49:757–761
- Rasmussen F, Lambrechtsen J, Siersted HC, Hansen HS, Hansen NC. Asymptomatic bronchial hyperresponsiveness to exercise in childhood and the development of asthma related symptoms in young adulthood: the Odense Schoolchild Study. *Thorax.* 1999;54:587–589
- Porsbjerg C, von Linstov ML, Ulrik CS, Nepper-Christensen SC, Backer V. Outcome in adulthood of asymptomatic hyperresponsiveness to histamine and exercise-induced bronchospasm in childhood. *Ann Allergy Asthma Immunol.* 2005;95:137–142
- Silkoff PE, Carlson M, Bourke T, Katial R, Ogren E, Szefer SJ. The Aerocrine exhaled nitric oxide monitoring system NIOX is cleared by the US Food and Drug Administration for monitoring therapy in asthma. *J Allergy Clin Immunol.* 2004;114:1241–1256
- Bernard A, Marchandise FX, Depelchin S, Lauwerys R, Sibille Y. Clara cell protein in serum and bronchoalveolar lavage. *Eur Respir J.* 1992;5:1231–1238
- Hermans C, Aly O, Nyberg BI, Peterson C, Bernard A. Determinants of Clara cell protein (CC16) concentration in serum: a reassessment with two different immunoassays. *Clin Chim Acta.* 1998;272:101–110
- Hermans C, Bernard A. Pneumoproteinaemia: a new perspective in the assessment of lung disorders. *Eur Resp J.* 1998;11:801–803
- Hermans C, Bernard A. Lung epithelium-specific proteins: characteristics and potential applications as markers. *Am J Respir Crit Care Med.* 1999;159:646–678
- Cardinale F, de Benedictis FM, Muggeo V, et al. Exhaled nitric oxide, total serum IgE and allergic sensitization in childhood asthma and allergic rhinitis. *Pediatr Allergy Immunol.* 2005;16:236–242
- Malinovschi A, Janson C, Holmkvist T, Norback D, Merilainen P, Hogman M. IgE sensitisation in relation to flow-independent nitric oxide exchange parameters. *Respir Res.* 2006;7:92

30. Robin M, Dong P, Hermans C, Bernard A, Bersten AD, Doyle I. Serum levels of CC16, SP-A and SP-B reflect tobacco-smoke exposure in asymptomatic subjects. *Eur Resp J*. 2002;20: 1152–1161
31. Broeckaert F, Bernard A. Clara cell protein (CC16): characteristics and perspectives as lung peripheral biomarker. *Clin Exp Allergy*. 2000;30:469–475
32. Bernard A, Roels H, Buchet JP, Lauwerys R. Decrease of serum Clara cell protein in smokers. *Lancet*. 1992;339:1620–1621
33. Bernard A, Roels H, Buchet JP, Lauwerys R. Serum Clara cell protein: an indicator of bronchial cell dysfunction caused by tobacco smoking. *Environ Res*. 1994;66:96–104
34. Shijubo N, Itoh Y, Yamaguchi T, et al. Serum and BAL Clara cell 10 kDa protein (CC10) levels and CC10-positive bronchiolar cells are decreased in smokers. *Eur Respir J*. 1997;10: 1108–1114
35. Bernard A, Gonzalez J, Siles E, Trullillano G, Lauwerys R. Early decrease of serum Clara cell protein in silica-exposed workers. *Eur Respir J*. 1994;7:1932–1937
36. Burgess JL, Witten ML, Nanson CJ, et al. Serum pneumoproteins: a cross-sectional comparison of firefighters and police. *Am J Ind Med*. 2003;44:246–253
37. Johnston CJ, Mango GW, Finkelstein JN, Stripp BR. Altered pulmonary response to hyperoxia in Clara cell secretory protein deficient mice. *Am J Respir Cell Mol Biol*. 1997;17:147–155
38. Shijubo N, Itoh Y, Yamaguchi T, et al. Clara cell protein-positive epithelial cells are reduced in small airways of asthmatics. *Am J Respir Crit Care Med*. 1999;160:930–933
39. Mattsson J, Remberger M, Andersson O, Sundberg B, Nord M. Decreased serum levels of Clara cell secretory protein (CC16) are associated with bronchiolitis obliterans and may permit early diagnosis in patients after allogeneic stem-cell transplantation. *Transplantation*. 2005;79:1411–1416
40. Lesur O, Langevin S, Berthiaume Y, et al. Outcome value of Clara cell protein in serum of patients with acute respiratory distress syndrome. *Intensive Care Med*. 2006;32:1167–1174
41. World Health Organization. *Guidelines for Safe Recreational Water Environments: Vol 2—Swimming Pools and Similar Environments*. Geneva, Switzerland: World Health Organization Press; 2006
42. Freedman FB. *Water Babies*. London, United Kingdom: Lorenz Books; 2003
43. Goldberg GN, Lightner ES, Morgan W, Kemberling S. Infantile water intoxication after a swimming lesson. *Pediatrics*. 1982;70: 599–600
44. Bennett HJ, Wagner T, Fields A. Acute hyponatremia and seizures in an infant after a swimming lesson. *Pediatrics*. 1983; 72:125–127

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Ginther DK. *Atlantic*. March 2007

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Infant Swimming Practice, Pulmonary Epithelium Integrity, and the Risk of Allergic and Respiratory Diseases Later in Childhood

Alfred Bernard, Sylviane Carbonnelle, Xavier Dumont and Marc Nickmilder

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