

Chlorine, Chlorination By-Products and Their Allergic and Respiratory Health Effects

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Abstract: Although chlorine and most of its derivatives are known toxic agents, it has been pronounced as a safe disinfectant for water treatments. More detailed analyses and extended studies concerning chlorine safety have only started recently. The objective of this article was to review data on the use of chlorine in pool environments, the resulting chlorination by-products in these environments and their potential effects on allergic and respiratory health in humans.

The MEDLINE database search comprised articles from 1966 to August 2006. Additional studies were identified by searching references of already published articles. A total of twenty-one studies evaluating effects of chlorine and its by-products on allergic or respiratory health were included in the analysis. Exposure to chlorination by-products through swimming pool attendance showed adverse health effects on children, subjects occupationally exposed, athletic swimmers and asthmatic subjects. These adverse effects were seen despite the presence of official directives in most countries to control and regulate the use of chlorine for water disinfection. Contact to chlorination by-products might not be the leading reason for poor respiratory health, but might not be as harmless as earlier thought. In particular, baby swimming in chlorinated pools is highly questionable.

Keywords: Chlorination by-products, allergic health, respiratory health, swimming pool attendance.

Chlorine is an extensively used agent in water treatments for drinking water and pool water. Although chlorine and most of its derivatives are known toxic agents, it has been pronounced as being a safe disinfectant for water treatment [1]. Detailed analyses and extended studies have only started recently because of further concerns regarding chlorine's potential influences on human health.

In a recent study, chlorinated swimming pool attendance increased lung hyper-permeability, exercise induced broncho-constriction (EIB) and asthma [2]. Bernard and colleagues hypothesized that repeated or chronic disruption of the lung epithelial barrier could facilitate the penetration of allergens in the lung [2] and could therefore result in higher rates of allergic sensitization and atopic diseases.

Current hypotheses for the increasing trends of atopic diseases (allergic asthma, allergic rhinitis, atopic dermatitis) include less microbial or infectious stimulation of the immune system (hygiene hypothesis), environmental changes (indoor allergens, chemicals, microbiological compounds, changed potency of allergens) as well as changes in dietary habits and lifestyle.

The objective of this article was to review international data on the use of chlorine in pool environments, the resulting chlorination by-products in these environments and their potential effects on allergic and respiratory health.

SEARCH STRATEGY

The Medline database search (January 1966 to August 2006; Access August, 18th 2006) resulted in unsystematic

hits related to chlorination and atopic or respiratory health outcomes with additional missing hits of important new studies in this specific research field. The search path used in PUBMED was ("chlorination by-products" OR "chlorine" OR "swimming pool" OR "pool attendance") AND ("allergies" OR "allergic diseases" OR "atopic diseases" OR "lung function" OR "respiratory illnesses"). After considering these results? we changed to a strategic review process, where we additionally identified studies by searching references of already published articles. This search resulted in 114 publications.

CRITERIA FOR STUDY INCLUSION-EXCLUSION

First, studies were assessed by title and abstract. Studies were excluded when mainly discussing the following aspects: drinking water disinfection; chlorination accidents; occupational exposure to chlorine other than through swimming pools; infectious diseases through swimming pools; concentration of chlorination by-products in pools and swimmers without analysing health effects; health outcomes other than allergic and respiratory diseases; biomarkers (clara cell proteins and surfactant associated proteins) related to indoor and/or outdoor air pollutants in general; effects of swimming without chlorine exposure; controlled human exposure studies with chlorine gas inhalation; and animal tests on chlorine exposure.

When meeting the inclusion criteria, the full-text of the remaining articles (n=43) was examined further. Analyses were not included if only general descriptions were made or if certain types of publications, such as reviews, comments and letters, without an embedded description of new studies, were found (n=9).

12 additional studies were excluded for the following reasons: multiple publications analysed the same sample without different outcomes (n=1), studies contained no

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original data (n=3), publications were not available in English or German (n=1), no full text was available (n=2) and outcomes, study populations or main subjects were inappropriate (n=5). After excluding these studies, a total of 22 publications remained for final appraisal. The number of studies evaluated was 21, as two publications analysed the same study population, but posed different research questions.

STUDY POPULATIONS

21 studies were included in this review. Basic characteristics of the included and assessed publications are given in Table 1.

METHODOLOGICAL APPRAISAL OF THE INCLUDED SINGLE STUDIES

Children and Young Adult Studies

The Belgian research group of Bernard *et al.* performed several studies [2-5] evaluating acute and chronic effects of exposure to chlorination products on the lung epithelium and the associated development of respiratory illnesses. The study populations used mainly consisted of children up to the age of 14 years. Analyses included questionnaires, lung function tests, exhaled NO (eNO) tests and blood samples. Serum was extracted to measure IgE levels and to detect markers indicating permeability changes of the lung epithelium that are undetected by classic lung function tests. Exposure-response related increases of the surfactant proteins SP-A and SP-B could be seen and were consistent for short term and chronic contact to chlorination products [2, 3]. Comparing children and adults concerning acute effects on these markers and on the SP-B/CC16 ratio, results were similar with indicators showing significant increases in both groups [2]. Cumulated pool attendance was furthermore significantly related to elevated eNO levels, total asthma and classic asthma indicators (EIB: exercise induced broncho-constriction, PEF=peak expiratory flow) [2, 5]. Associations were strongest when exposure to chlorination products started early, e.g. in those participating in baby swimming [2, 4].

Carbannelle *et al.* [3] additionally analysed exercise induced effects on levels of SP-A, SP-B and CC16 in young adults. First, they compared changes depending on the pool type (chlorinated vs copper/silver sanitized). CC16 increased in swimmers, regardless of which kind of pool they attended, while SP-A and SP-B levels were unaffected in the copper/silver pool, but increased in chlorinated pools.

Lagerkvist *et al.* [6] used lung function and serum CC16 to examine pulmonary responses to environmental factors, such as chlorine and its by-products. Children who regularly visited chlorinated swimming pools showed reduced values of blood CC16. Absolute values of FEV₁ were higher in non-pool visitors, but with similar FEV₁% predicted in both groups (pool attendees vs non-visitors). No further evaluations and interpretations were done regarding these lung function parameters.

Nickmilder and Bernard [7] based their evaluations on the hypothesis that the rise in childhood asthma in the developed world could partly result from the increasing exposure of children to toxic chlorination products in the air

of indoor swimming pools. They analysed whether this hypothesis could explain European geographical variations in the prevalence of asthma and atopic diseases. A total of 69 centres of the International Study of Asthma and Allergy in Childhood (ISAAC) were evaluated. In these centres, the prevalence of asthma increased with swimming pool availability. This increase was independent from other regional differences such as climate, location or socio-economic status of the countries. No associations were found for other atopic diseases.

Nystad *et al.* [8] used the Norwegian data enrolled in the International Study of Asthma and Allergy in Childhood (ISAAC) to evaluate associations between baby swimming and recurrent infectious diseases. The prevalences of respiratory tract infections and otitis media were higher in children participating in baby swimming, but significantly increased risks could only be seen in children with atopic parents.

Momas *et al.* [9] analysed the short-term effects of swimming in pupils attending well maintained school swimming pools (according to public health regulations). The prevalence of respiratory, skin, nose and ear symptoms was similar in bathers and non-bathers. Only eye irritation proved to be more likely in bathers.

Recreational and Occupational Swimmers

The main interest of studies conducted by Helenius *et al.* [10, 11] lay in evaluating health effects in subjects highly exposed to chlorine derivatives. A case-control study [10] compared elite swimmers and controls in terms of lung function and sputum components. Long term and repeated exposure to chlorine compounds was associated with bronchial hyper-responsiveness (BHR), airway inflammation, higher concentrations of sputum eosinophil peroxidase (EPO) and human neutrophil lipocalin (HNL), as well as higher amounts of eosinophils.

A second study [11] followed-up 42 competitive swimmers after five years, examining the resulting health effects of continuing or finishing their career. In those who stopped high-level training, bronchial hyper-responsiveness and asthma attenuated or even disappeared. In active swimmers, sputum lymphocytes (as indicator of lymphocytic airway inflammation) increased during follow-up.

Varraso *et al.* [12] measured swimmers' exposure to chlorinated compounds with air samples, trihalomethanes (THM) in blood samples as well as their biomarker responses to oxidative stimuli. Analyses also accounted for training effects. In swimmers, a high prevalence of irritant symptoms and asthma were reported. Furthermore, associations could be seen between biological response markers to oxidative stimuli and exposure to chlorinated compounds.

Athletes tend to show exercise induced health complaints. A study of Lévesque *et al.* [13] compared respiratory, skin, nose, eye and ear symptoms, throat and headache in competitive swimmers and soccer players. The prevalence of a variety of health symptoms was higher in swimmers. Furthermore, swimmers exposed to the highest levels of chloramines in air and water samples had more respiratory complaints.

Table 1. Basic Characteristics and Research Questions of 22 Papers Throughout 21 Selected Studies

Ref.	Author	Country	Sample Size	Age	Evaluation Methods	Analysed Health Effects		Research Question
						Atopic	Respiratory	
[2]	Bernard <i>et al.</i> (2003)	Belgium	1881	7-14 yrs	Questionnaire Lung function (EIB, PEF)	(X)	X	To study whether exposure to nitrogen trichloride in indoor chlorinated pools may affect the respiratory epithelium of children and increase the risk of some lung diseases such as asthma
			226	8-12 yrs	Questionnaire Blood samples (IgE, CC16, SP-A, SP-B)	(X)	X	
			16 13	5-14 yrs 26-47 yrs	Blood samples (IgE, CC16, SP-A, SP-B)	(X)	X	
[4]	Bernard <i>et al.</i> (2006)	Belgium	341	10-13 yrs	Questionnaire Blood samples (CC16, SP-D, IgE) Pool water and air samples	X	X	Possible effects of exposing babies to the volatile chlorination products of indoor pools
[5]	Bernard <i>et al.</i> (2006)	Belgium	341	10-13 yrs	Questionnaire Blood samples (IgE) Lung function (EIB); eNO Pool water and air samples	X	X	Relationship between childhood asthma, atopy and cumulated attendance of indoor chlorinated pools
[3]	Carbonnelle <i>et al.</i> (2002)	Belgium	16 13	5-14 yrs 26-47 yrs	Blood samples (IgE, CC16, SP-A, SP-B) Lung function Air sampling		X	Effects of nitrogen trichloride (NCl ₃) on the pulmonary epithelium of pool attendees by measuring the leakage into serum of three lung-specific proteins: the alveolar surfactant-associated proteins A and B (SP-A, SP-B) and the bronchiolar 16kDa Clara cell protein (CC16)
			14	18-23 yrs	45 min intensive training in chlorinated pool compared to copper/silver sanitized pool Blood samples (SP-A, SP-B, CC16); Lung function Air sampling		X	
			3	Young adults	Pool side for 1 hour without exercising, then 45 min exercise; Blood samples (SP-A, SP-B, CC16)		(X)	
[10]	Helenius <i>et al.</i> (1998)	Finland	29 swimmers 19 controls	15-25 yrs 21-28 yrs	Questionnaire/Interview Lung function; Histamine challenge test, Sputum samples Prick test		X	To investigate respiratory symptoms, increased bronchial responsiveness, and sign of inflammation in elite swimmers
[11]	Helenius <i>et al.</i> (2002)	Finland	42	21-27 yrs in 2001	5-year follow-up study Questionnaires Prick test, Spirometry, histamine challenging test, Sputum samples (in a subgroup of 29 subjects)	X	X	To investigate the effect of finishing high-level sports on airway inflammation, bronchial hyperresponsiveness, and asthma
[1]	Kohlhammer <i>et al.</i> (2006)	Germany	2606	35-74 yrs	Questionnaire	X		To assess whether pool attendance in childhood would be related to higher rates of allergic diseases in adulthood, with special regard to hay fever
[6]	Lagerkvist <i>et al.</i> (2004)	Sweden	57	10-11 yrs	Questionnaire Lung function Blood samples (CC16)		X	Lung function and serum CC16 concentration used to examine the pulmonary responses to ambient O ₃ exposure and swimming pool attendance

(Table 1) contd.....

Ref.	Author	Country	Sample Size	Age	Evaluation Methods	Analysed Health Effects		Research Question
						Atopic	Respiratory	
[13]	Levesque <i>et al.</i> (2006)	Canada	305 swimmer 499 soccer		Questionnaire		X	To compare the prevalence of health complaints of young swimmers and young indoor soccer players and to evaluate the relationship between chloramine concentrations and the athletes' health complaints
			72 swimmer 73 soccer	8-22 yrs 11-17 yrs	Health complaints during 5 training sessions Questionnaire, Pool water and Air samples; PEF		X	
[18]	Massin <i>et al.</i> (1998)	France	334 lifeguards	27-45 yrs	Questionnaire; Lung function (FVC, FEV1) Methacholine challenge test Air sampling		X	To measure the levels of exposure to NCl ₃ and to examine how they relate to irritant and chronic respiratory symptoms
[9]	Momas <i>et al.</i> (1993)	France	246	5-18 yrs	1-month follow-up study Questionnaires Water samples	(X)	(X)	To determine the health effects of attending a well-kept school swimming pool maintained according to public health regulations
[14]	Mustchin <i>et al.</i> (1979)	UK	3 of 24	12 yrs, 15 yrs and 17 yrs	Case reports Lung function (FEV1, FVC) Prick test	(X)	X	Sudden onset of reversible airways obstruction in three young swimmers
[7]	Nickmilder <i>et al.</i> (2006)	Europe (69 centres)	94549 189150	6-7 yrs 13-14 yrs	Questionnaires (written, video)		X	Ecological study to evaluate whether the chlorine hypothesis can explain the geographical variation in the prevalence of asthma and other atopic diseases in Europe
[8]	Nystad <i>et al.</i> (2003)	Norway	2862	6-16 yrs	Questionnaire		X	To estimate the association between baby swimming and recurrent respiratory tract infections and otitis media in the first year of life
[20]	Penny (1983)	UK	1	57 yrs	Case report Lung function (VC, FEV1)		X	One typical case report of swimming pool wheezing to illustrate the problems that may occur
[19]	Rose <i>et al.</i> (1998)	USA	129 (62/67) 30 (18/12)	16-59 yrs 16-35 yrs	Case-control study Questionnaires, if ≥ 2 symptoms= \Rightarrow Clinical evaluation, bronchoscopy, lavage, biopsy Pool air and water samples Endotoxin analysis		X	To investigate two sequential outbreaks of respiratory disease among lifeguards at an indoor swimming pool with water spray features
[21]	Seki <i>et al.</i> (2003)	Japan	20 10	n.i.	Case-control study Calculation of skin hydration status	X		Effects of residual chlorine in bathing water on the function of the stratum corneum (SC) in patients with AD and determination of the lowest chlorine concentration showing an effect. Relationship between free residual chlorine concentration in bathing water and the water-holding capacity of the SC in patients with AD
[15]	Small <i>et al.</i> (1987)	UK	10	13-26 yrs	Questionnaire Rhinoscopy ; Rhinomanometry ; Lung function (FVC, FEV1)	(X)		Lung function and nasal changes following immersion in chlorinated water

(Table 1) contd.....

Ref.	Author	Country	Sample Size	Age	Evaluation Methods	Analysed Health Effects		Research Question
						Atopic	Respiratory	
[22]	Stav <i>et al.</i> (2005)	Israel	8	20-42 yrs	Lung function and Methacholine-provocation tests		X	Effect of whirlpool baths on airway reactivity in patients with mild asthma
[17]	Thickett <i>et al.</i> (2002)	UK	3	33-49 yrs	Case reports PEF, NCl ₃ provocation tests, spirometry, atmospheric NCl ₃ levels at poolside	(X)	X	Report of 3 cases of occupational asthma caused by chloramines in indoor swimming-pool air
[12]	Varraso <i>et al.</i> (2002)	France	22	15-25 yrs	Questionnaire Chloramine concentrations at water surface Trihalomethanes in blood	(X)	X	Investigation of the relations between exposure to chlorinated compounds and biological markers of response to oxidative stimuli, taking into account the effect of training
[16]	Zwick <i>et al.</i> (1990)	Austria	14 swimmers 14 controls	11-24 yrs 11-24 yrs	Case-history, chest and sinus x-rays, Lung function, prick tests, Blood samples (IgE, Rast)	X	X	To investigate clinical symptoms of the respiratory tract, BHR, sensitization to aeroallergens, and alterations of the cellular immune system in a highly chlorine-exposed group of competitive swimmers and to compare these results with a matched control group

n.i. = no detailed information.

Mustchin and Pickering [14] described a sudden onset of reversible airways obstruction in three young swimmers during training sessions in a newly opened pool treated with chlorine dioxide. Several more of the 24 competitive swimmers training in this pool developed milder symptoms such as cough, sore throat, and chest tightness and had to leave the water. Symptoms were associated with a strong chemical odour. Chlorine gas, potentially inadequately dosed, may have led to this “coughing water”, and was suggested to have caused bronchial irritations in these athletes.

Small *et al.* [15] investigated acute lung function and nasal changes following immersion in chlorinated water in swimmers of a swimming club. After a 2-hour swim, neither lung function changes, nor symptoms of nasal obstruction or rhinorrhea could be found in any of the swimmers. There was a high incidence of apparent allergy in the studied swimmers, but the authors did not attribute these illnesses to the pool environment exposure.

Zwick *et al.* [16] compared 14 competitive swimmers and 14 matched control subjects normally not exposed to chlorine. The swimmers showed a higher prevalence of allergies, subclinical allergic sensitization, disorders of the cellular immune system, non-specific bronchial hyper-responsiveness and respiratory symptoms.

Occupationally Exposed Pool Workers

Thickett *et al.* [17] evaluated nitrogen trichloride as a potential cause of occupational asthma in lifeguards and swimming teachers. Three cases of these individuals complaining of work-related respiratory symptoms were reported. They were enrolled in a study where they were asked to record peak expiratory flows (PEF) twice per hour for four weeks, and to participate in NCl₃ provocation tests. For all

participants, exposure-related asthmatic symptoms and reduced lung function could be seen. They were promoted to jobs away from swimming pools and all subsequently recovered.

Massin *et al.* [18] conducted a large study in 334 lifeguards occupationally exposed to NCl₃, to examine how exposure is related to irritant and chronic respiratory symptoms. To obtain maximum exposure values, the survey was done in winter time, when the roofs and windows of swimming pools are usually closed. In total, respiratory and irritant symptoms were low, but a concentration-response relation could be seen. No associations of cumulative exposure and BHR to methacholine appeared. Thus, transient BHR, when exposed, could not be excluded.

Rose *et al.* [19] investigated two sequential outbreaks of respiratory diseases among lifeguards at an indoor swimming pool. After the first outbreak, the pool was closed to improve the engineering and the ventilation systems. Nevertheless, within three months after re-opening, a second outbreak was recognized among the lifeguards. Clinical evaluations found respiratory and systemic symptoms, with high rates of granulomatous pneumonitis. Analyses of air and pool water samples indicated increased levels of endotoxins and the authors aetiologically assumed endotoxin-containing bioaerosols from water spray features was the cause.

Case Report

Penny [20] described a case report of a 57 year-old man who complained of coughing 12 to 24 hours after swimming. These symptoms only occurred when he visited a modern pool using a heat reclamation system that re-circulates a high proportion of the air in the pool instead of using fresh air. He developed no symptoms when attending an “old” pool using

a simple air extractor. Closer investigation showed that the new pool (especially in winter) had higher concentrations of chlorination by-products which could explain why the man showed simultaneous reduced lung function values with associated wheezing.

Chlorine and Skin

Seki *et al.* [21] investigated potential effects of chlorine in bathing water on atopic and non-atopic skin. In order to show this, they bathed the forearm of the participants in chlorinated water. The water-holding capacity of the stratum corneum of patients with atopic dermatitis proved to be more sensitive to free residual chlorine exposure, than that of normal control subjects. At high levels of chlorine exposure effects could also be seen in non-atopic subjects suggesting a potential role of chlorine exposure not only for the aggravation, but also for the development of atopic dermatitis.

Chlorine and Hay Fever

Kohlhammer *et al.* [1] retrospectively evaluated 2606 adults regarding their current and childhood swimming pool attendance. Early frequent exposure to chlorine and/or chlorination by-products was significantly associated with higher rates of hay fever.

Exposure to Chlorination By-Products and Lung Function in Asthmatics

A small Israeli study [22] examined the effect of whirlpool baths on airway reactivity in patients with mild asthma. After attending whirlpool baths, in most patients, up to 20% reduced FEV₁ values were reached. Thus, Stav and Stav suggested a detrimental effect of hot chlorinated pools and whirlpool baths.

SUMMARISED RESULTS OF THE INCLUDED STUDIES

The main health effects seen in the evaluated studies resulted due to high dosed or cumulative exposure to chlorination products. Acute effects were mainly restricted to cellular markers. The health effects in recreational and occupational swimmers were dose-related and showed a certain degree of reversibility when exposure was decreased or stopped. In particular, studies on children led to the hypothesis that a trend of more frequent attendance of chlorinated pools could be one important factor for rising frequencies of asthma and allergic diseases in industrialised countries.

DISCUSSION

Chlorine and chlorination by-products are known serious risk factors causing significant morbidity in industrial settings and in chlorine accidents [23-32]. In lower concentrations, chlorine is widely used as tap water and pool water disinfectant to avoid waterborne infections caused by bacteria or viruses. Free chlorine in solutions such as hypochlorous acid reacts with organic matter (e.g. urine, sweat) of swimmers resulting in nitrogen trichlorine (NCl₃), monochloramine and chloroform causing the typical chlorinous smell. These by-products constitute potentially harmful inhalable irritant agents reaching their highest concentration at the water's surface. Due to a very low solubility in water, NCl₃ is not retained by the upper respiratory tract, but carried over in the lung, where it can react with the respiratory epi-

thelium [33]. The extent of exposure depends on the temperature, the number of bathers and the ventilation systems used [22]. Substances are highly volatile and, in open pools, tend to dissipate in the atmosphere, while in indoor pools they can reach concentrations high enough to have an impact on human health [18]. In particular, inadequately maintained pools with either too high doses (chlorine accidents, poorly controlled standards), or too low concentrations (resulting in microbiological contaminations), pose several health hazards.

However, of greater interest for this review, were those health outcomes occurring despite presumably well-kept swimming pool surroundings.

The first uses of chlorine started in the early 1900s as drinking water disinfectant. Aspects of drinking water and its health effects were not included in this review, as tap water chlorine normally does not get into contact with organic substances leading to the formation of chloramines [7]. Drinking water with high levels of chlorine, might even lead to a small gas release, but usually the impact on indoor air quality is too limited to be considered a health hazard [7]. A time later, chlorine disinfection was introduced into public swimming pools. Swimming pools first became popular in the 1920s, but it took several more decades before swimming was common as leisure sport and even became obligatory for children at school in the 1960s. Most countries have official directives setting maximum levels of chlorination products in swimming pools. In Germany, for example, limits of water concentrations of 0.3-0.6 mg/l for free chlorine, 0.2 mg/l for bound chlorine and a pH-value of 6.5-7.6 have to be maintained [1]. Samples of pool water are routinely taken by the health authorities to control the given ranges [1]. Although alternatives for chlorination do exist, e.g. ozonisation, copper/silver or ultraviolet treatments, these replacement options would be unrealistic for several reasons including cost and effectiveness [13].

Although industrial chlorine contact and chlorine accidents were known to potentially result in serious respiratory injury and cancer [27, 34-38]; for a long time, the main adverse health effects due to swimming pool contact were considered to be irritant skin, eye, nasal and throat symptoms [9, 12, 15, 18, 20, 39, 40]. Despite concerns about chlorine being voiced as early as 1979, the concurrent research failed to address these concerns. For example, in a paper published in Thorax concerning airway obstructions in young swimmers [14], no extended investigations were performed regarding detailed health effects of chlorination products in swimming pools. ... Presently, the most important and intensively studied health effects are respiratory outcomes related to contact to chlorination by-products. Chloramines and hypochlorous acid are powerful membrane-penetrating oxidants, reacting with sulphhydryl groups of proteins in the cytoskeleton and extracellular matrix of the endothelial and epithelial barriers resulting in cell retraction, disruption of cellular junctions, disorganised cytoskeleton and an almost immediate increase of endothelial or epithelial permeability [41]. The main diagnosed respiratory health outcomes in the assessed studies were higher prevalences of bronchial hyper-responsiveness and asthma [2, 4, 5, 7, 10-12, 14, 16, 17, 20, 22]. When comparing these studies, it is important to account for the different study designs such as case-reports,

case-control studies, cross-sectional studies and follow-up studies, and a wide variety of definitions and assessment strategies of respiratory health effects, including asthma. Information varies from questionnaire-based data to extensive lung function tests and definitions from reported symptoms to actual examined diagnoses. Cellular markers serve as indicators of lung damage (e.g. SP-A, SP-B, CC16). Even if there is no apparent symptom, cellular damage could have already occurred. CC16 represents an antioxidant protein and non-invasive sensitive marker of lung epithelial injury [6, 33]. Serum concentrations are decreased in subjects with chronic lung damage (by tobacco smoke or other inhaled air pollutants), but often increase indicating acute lung injuries [34, 42].

The second health outcome we evaluated for this review was the presence of atopic/allergic diseases. Important factors and indicators measured were specific IgE in serum and positive skin prick tests [2, 4, 5, 10, 11, 14, 16]. However, in most studies, the atopic status was surveyed, rather than taken as a potential outcome variable related to chlorination by-products. There was mostly a comparison between atopic versus non-atopic subjects in terms of other outcomes. Nevertheless, several studies found exceptionally high rates of atopic sensitizations or reported apparent allergies, especially in routine swimmers [10, 15, 16]. Small *et al.* [15] hypothesise that these high rates are a reflection of the current trend for these patients to overcome their disability with vigorous exercise, particularly swimming. The authors did not account for a potential reverse causality and the possibility of allergy being chlorination-related. More specific atopic health outcomes are only examined by Kohlhammer *et al.* [1] with frequent and early contact associated with higher rates of hay fever. Additionally, a Japanese study described chlorine levels in the water supply being correlated with the prevalence of atopic eczema [43]. All in all, the question remains, whether toxic/irritant agents (e.g. chlorine and its by-products) are themselves risk factors for atopic diseases or if subjects who are already sensitized to allergens are just more sensitive to exposure.

Swimming is a comprehensive sport with enormous advantages [13]. It not only has positive effects on factors such as weight and smoking habits [13], but also constitutes economic muscular and cardiovascular training, shows a low risk of physical injury and has high value as a recreational leisure activity. Additionally, the warm and humid environment seems to lessen the adverse effects of several diseases, including asthma. For patients with mild asthma, this statement was challenged by the study of Stav and Stav [22], where whirlpool bath attendance in asthmatics possibly showed an increase of airway reactivity.

However, the most important factor concerning all adverse health effects through swimming pool attendance is the amount of exposure. Most complaints about health symptoms and air quality when attending chlorinated swimming pools come from competitive swimmers [16], who are the most intensely and most frequently exposed. It is not surprising that studies which examining trained swimmers or occupationally exposed pool workers found more pronounced adverse health effects than those evaluating recreational swimmers. Of competitive swimmers, 36% to 79% have shown bronchial hyper-responsiveness [10, 11,

16] and up to 31% have shown asthma [11, 13]. During a 2-hour training period, a swimmer might be exposed to an amount of chlorine (4-6g) that exceeds the recommendations for a worker with an 8-hour exposure [44]. However, asthma in swimmers seems to be partially reversible. Helenius *et al.* showed that asthma can develop during and disappear after a sports career [11]. This result is consistent with the idea of a causal pathway between pool exposure and asthma. An important factor is the cumulative dosage, which not only depends on the frequency of swimming pool attendance, but also on the age when pool attendance starts [1, 5]. In particular, young children are more sensitive to environmental toxins, including chlorination products, which can culminate at the time when the immunological and organic development of their lungs is still in progress [5]. Baby swimming has become more and more popular, with increasing frequencies from around 6% when born in the early 80s [8] to 13% in the early 90s [4] and up to 30% today. An important question is whether babies exposed to chlorine in early life are at higher risk to develop asthma or asthma-like symptoms in later life compared to unexposed babies, taking into account other environmental factors in early life, such as smoking exposure and pet contact etc. Because swimming in babies has no obvious influence on the ability of learning to swim and does not have the same beneficial effects as swimming in children or adults (listed above), the potential adverse effects in babies need much more attention. We cannot see any good reason why babies should swim in (chlorinated) pool water.

The included studies have limitations. Some evaluation methods might have led to a recall bias and an over-reporting of symptoms. For mainly questionnaire-based evaluations [1, 7, 8, 13], subjective answers with a potential over- or under-estimation of results have to be accounted for. Some studies exclusively analysed either occupationally exposed participants or frequent or competitive swimmers, without control subjects [12, 18] or only comparing them to other athletes [13]. Or, in the case of Stav and Stav [22], only asthmatics were analysed regarding health effects of whirlpool environments; however, it would also be interesting to see effects on healthy subjects.

Cross-sectional studies have limitations regarding causal inferences. To draw definite conclusions, the results would have to be replicated in longitudinal studies.

Several studies did not measure levels of chlorination by-products. Additionally, for some studies, the evaluation of exposure to chlorine and the validity of the exposure between the studies remain unclear. However, as health effects were already assumed at recommended levels of chlorination, an exposure estimation (e.g. through the attendance frequency) might be sufficient [6]. Although they used different approaches, in general, most studies ended up with similar conclusions. Nevertheless, longitudinal studies with objective measures of exposure and of lung function would be optimal.

Some studies might have been conducted according to older prevalent chlorination standards; however, except for Kohlhammer *et al.* [1] and Bernard *et al.* [2], no detailed information on regulations regarding official current chlorination levels were given. Furthermore, Seki *et al.* [21] conducted tests under conditions not exactly similar to pool

water. Therefore, results might be different regarding pool attendance.

We included one study which actually did not consider chlorination products as the reason for their observed health effects [19], but attributed them to endotoxin-containing respirable bio-aerosols from water spray features. However, interestingly, the highest levels of endotoxins were seen after the outbreaks of respiratory diseases, not before. Furthermore, they revealed persistently increasing combined chlorine levels and alkine pool water. However, putting these factors aside, the review of logs showed that water chemistry parameters consistently met current standards [19]. In contrast to their estimations, this study might be important in confirming the causal link of high-level chlorine and its' products to respiratory diseases. In general, to be able to definitively compare the results of the analysed studies, one would need an undisputed definition of respiratory diseases.

CONCLUSION

Frequent contact to chlorine and its by-products due to swimming pool attendance is an important factor in the development or the aggravation of respiratory and allergic diseases. Noxious acute and chronic effects of contact to chlorination by-products are partly reversible and might not be the leading reasons for respiratory health yet might not be as harmless as earlier thought. Important measures to avoid adverse health effects of swimming pool attendance include control of temperature, water quality (precise chlorine dosage, frequent controls, hygiene measures for swimmers to limit the entry of organic matter) and air quality (ventilation systems using fresh air rather than air recirculation, especially in winter). There are no recommendations for air levels of NCl_3 in pool air [3], costs of ventilation systems are high and there are no obvious alternatives to chlorine based disinfectants. Therefore, a cost/benefit analysis should aid in defining safe exposure levels for the different categories of pool attendees, especially for those with long term and repeated exposure, as well as for the youngest.

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