Infant Swimming in Chlorinated Pools and the Risks of Bronchiolitis, Asthma and Allergy

Voisin C, Sardella A, Marcucci, Bernard A. *Eur Respir J.* 2010;36(1):41–47

PURPOSE OF THE STUDY. Recent studies postulated that chlorine used to disinfect swimming pools can cause airway changes and make the lungs more sensitive to infection and asthma. This study evaluated the associations between infant swimming and bronchiolitis and its sequelae among young school-aged children.

STUDY POPULATION. A total of 430 children aged 5 to 6 years in 30 kindergartens located mainly in the area of Brussels and Liege (Belgium) who were participating in a prospective study on the respiratory impact of air pollution were included.

METHODS. Parents completed a questionnaire regarding the child's health history, respiratory symptoms (asthma, bronchitis, bronchiolitis, and pneumonia), and swimming practices (type of pools, type of disinfection method used, frequency of attendance, age started).

RESULTS. Attendance at indoor or outdoor chlorinated pools ever before the age of 2 years was associated with an increase risk of bronchiolitis (odds ratio: 1.68 [95% confidence interval (CI): 1.08–2.68]; $P = .03$). Associations persisted, and were even strengthened, by the exclusion of other risk factors. Among children with no parental antecedents of atopic diseases or no day-care attendance, odds ratios for bronchiolitis were 4.45 (95% CI: 1.82–10.9; $P = .001$) and 4.44 (95% CI: 1.88–10.5; $P = .007$), respectively, after >20 hours spent in pools during infancy. Infant swimmers who developed bronchiolitis also showed higher risks of asthma and respiratory allergies later in childhood.

CONCLUSIONS. Swimming-pool attendance during infancy is associated with a dose-dependent increase in risk of bronchiolitis and interacts with bronchiolitis to increase the risk of respiratory allergies later in childhood.

REVIEWER COMMENTS. Recent findings raised the question of safety of infant swimming. One theory regards the possibility that compounds from the pool reduce lung Clara cell protein (CC16), which protects from inflammation in acute respiratory syncytial virus infection. To date, cross-sectional studies have found inconsistent results in association with swimming-pool attendance and respiratory diseases. However, epidemiologic studies that use data from self-limited questionnaires can be prone to recall bias. Swimming pools have a variety of chlorine compounds in the water and microaerosols, as well as other pollutants such as nitrogenous substances from bathers. These are points to clarify in these studies. Prospective longitudinal studies are needed to characterize and confirm an association between chlorinated pools and outcome in allergic and respiratory diseases.

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Association of Bacteria and Viruses With Wheezy Episodes in Young Children: Prospective Birth Cohort Study

Bisgaard H, Hermansen MN, Bønnelykke K, et al. *BMJ.* 2010;341:c4978

PURPOSE OF THE STUDY. Viral infections have been consistently associated with wheezing episodes, but no studies have suggested a role for bacterial infection. This study evaluated the association between wheeze in young children and the presence of bacteria in the airways.

STUDY POPULATION. Infants ($N = 411$) from the Copenhagen Prospective Study on Asthma in Childhood with a maternal history of asthma were recruited at 4 weeks of age. Exclusion criteria were premature birth (<36 weeks' gestation), history of mechanical ventilation, congenital disease, or respiratory tract symptoms.

METHODS. Participants were prospectively examined for common airway pathogenic bacteria and viruses from the ages of 4 weeks to 3 years. The children visited the research clinic every 6 months and as needed for acute respiratory tract symptoms. Asthma-like symptoms and treatment were recorded in diary cards. Hypopharyngeal aspirates were obtained for routine bacterial cultures, and nasopharyngeal aspirates were obtained for virus identification.

RESULTS. A total of 984 samples (361 children) were analyzed for bacteria, 844 (299 children) were analyzed for viruses, and 696 (277 children) were analyzed for both viruses and bacteria. Colonization shifted from a majority having *Staphylococcus aureus* in the first months of life to later having *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*. Wheezy episodes were significantly associated with these 3 pathogens (odds ratio [OR]: 2.9 [95% confidence interval (CI): 1.9–4.3]; $P < .001$). Wheezy episodes were significantly associated with viral infection (OR: 2.8 [95% CI: 1.7–4.4]; $P < .001$). The association was unaffected by bacteria as a covariate and with no significant interactions.

CONCLUSIONS. Acute wheezy episodes in children up to the age of 3 years were significantly associated with bacterial infection. This association was independent of viral infection, which suggests that bacteria might contribute independently.

REVIEWER COMMENTS. This is the first prospective clinical cohort study that used standard bacterial cultures and

sensitive molecular methods for virus detection, and the results suggest that bacteria might contribute to wheezing episodes in children at high risk. Interventional strategies geared toward these microorganisms might be useful to further our understanding of wheezing and asthma development in these children. Given the paucity of information on evidence-based strategies in young children for treating wheezing episodes, clinical trials for evaluating antimicrobial agents and other interventions for wheezing episodes should be considered and are currently being evaluated among large clinical trial networks.

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Causal Direction Between Respiratory Syncytial Virus Bronchiolitis and Asthma Studied in Monozygotic Twins

Poorisrisak P, Halkjaer LB, Thomsen SF, et al. *Chest*. 2010;138(2):338–344

PURPOSE OF THE STUDY. To compare the long-term outcome of asthma, allergy, and pulmonary function in monozygotic twin pairs discordant for severe respiratory syncytial virus (RSV) disease.

STUDY POPULATION. There were 37 monozygotic twin pairs discordant for RSV hospitalization at a mean age of 10.6 months evaluated in the study. The twins were born between January 1, 1994, and December 31, 2003, and enrolled through the Danish Twin Registry.

METHODS. Hospitalization was used as a marker of disease severity. Participants were studied at a mean age of 7.6 years. The study included clinical examinations, lung-function testing, fractional exhaled nitric-oxide levels, determination of an asthma diagnosis, use of asthma medication, and results of skin-prick tests to common inhalant allergens.

RESULTS. The prevalence of asthma among the twins was 18%. The twins did not differ with respect to current asthma, use of inhaled corticosteroids or β_2 agonists, atopic dermatitis, fractional exhaled nitric oxide, baseline lung function, bronchial responsiveness, or sensitization ($P > .1$ for all comparisons).

CONCLUSIONS. There was no significant difference within cohabiting monozygotic twin pairs discordant for hospitalization for RSV bronchiolitis in infancy on the development of asthma and allergy, which argues against a specific viral effect.

REVIEWER COMMENTS. This study examined the question of which came first: not the chicken or the egg but whether severe RSV bronchiolitis causes wheezing or whether someone with a predisposition to asthma suffers a more severe response to RSV. This study's results argue against a specific effect of severe RSV infection in the development of asthma and allergy. Another recent study report based on 8280 twin pairs showed that a model in which asthma "causes" RSV hospitalization fit significantly better than a model in which RSV hospitalization "causes" asthma. We guess the chicken came first.

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Allergic Sensitization Is Associated With Rhinovirus-, but not Other Virus-, Induced Wheezing in Children

Jartti T, Kuusipalo H, Vuorinen T, et al. *Pediatr Allergy Immunol*. 2010;21(7):1008–1014

PURPOSE OF THE STUDY. Building on recent studies that have suggested a link between early wheezing caused by rhinovirus and the development of asthma, these researchers sought to characterize the relationship of respiratory viral infections with atopy in hospitalized wheezing children.

STUDY POPULATION. The authors studied a subgroup from among a previously described cohort of 293 hospitalized wheezing Finnish children aged 3 months to 16 years who had comprehensive virology performed ($N = 247$; median age: 1.6 years). Subjects with recent oral corticosteroid use, chronic disease, or ICU treatment were excluded.

METHODS. Respiratory viral infections were evaluated through a nasopharyngeal aspirate and blood sample at baseline and after 2 to 3 weeks. A combination of viral culture, antigen detection, immunoglobulin G (IgG) and IgM measurement, and polymerase chain reaction was used to evaluate for respiratory syncytial virus, human rhinovirus, enteroviruses, human bocavirus, and a broad panel of additional respiratory viruses. Atopy was assessed through serum-specific IgE testing to several common food allergens, cat, dog, horse, birch, mugwort, timothy grass, mold, and dust mite.

RESULTS. Allergen-specific IgE sensitization was closely related to sole rhinovirus infection (odds ratio: 3.5; $P = .0002$). In contrast, sole respiratory syncytial virus infection was negatively associated with sensitization (odds ratio: 0.087; $P = .027$). No significant associations with atopy were found with the remaining viruses or with those with multiple concurrent viral infections.

CONCLUSIONS. Acute wheezing in early childhood caused by human rhinovirus is associated with an increased risk

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