registration. Also, cancer risks among the cohorts reported here may change over time, and additional follow-up should be considered.

Nevertheless, by most indicators, the Bender *et al* study of the IBM semiconductor and storage device workers seems to be negative. Assuming that these findings are robust, some interesting questions may be posed. For example, have the limits of observational epidemiological methods been reached for detecting human cancer risks that might at most be seen as a few excess cases of a particular cancer out of a cohort of nearly 90 000? How long should such a population be followed up before exposure-related risks may be identified, especially in light of improved production processes and better employee protection that may reduce or eliminate exposure? Detecting small cancer risks and risks due to exposures at or near background levels as early as possible are not new challenges, but they require creative solutions. Biomarkers of exposure and early biological response are attractive, but are costly and rarely implemented as comprehensively as might be useful epidemiologically.[9]

Bender *et al*'s study, by indicating no clear cancer risks at this time, provides valuable information on cancer risk. It also sets a high standard for occupational epidemiological studies of cancer, drawing on cancer incidence rather than on cancer mortality, which lacks the sensitivity to detect risks of cancers that are treatable or have a low death rate. As workplace conditions and production processes improve, hazardous exposures will be reduced, and any associated risks should also decline. The search for small risks, whether in the semiconductor industry or other modern industrial sectors, will necessitate even more sensitive occupational health research methods and tools.

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The chlorine hypothesis: fact or fiction?

M J Nieuwenhuijsen

Commentary on the paper by Nickmilder and Bernard (*see page 37*)

In this issue, Nickmilder and Bernard[1] report on the relationship between the number of indoor chlorination swimming pools and prevalence of wheeze, asthma, hay fever, rhinitis and atopic eczema in European study centres of the International Study of Asthma and Allergies in Childhood (ISAAC) using an ecological study design with adjustment for several indicators such as social economic and lifestyle factors. They found statistically significant positive relationships for all outcomes for the whole of Europe, but fewer when examining specific regions of Europe. They found no statistically significant relationships within countries, but the number of study centres within a specific country was generally small. The relationship was stronger for 13–14-year-olds than for 6–7-year-olds.

Does this ecological study help to move the field forward? We are all aware of the strength and particularly the limitations of an ecological study design, and the interpretation of the results is generally far from straight forward. Over the recent years several analytical studies have been published that provide some support for a relationship between swimming or attending chlorinated swimming pools and respiratory disease, primarily asthma. Bernard *et al*[2] found that regular attendance at chlorinated pools by young children was associated with an increase in lung epithelium permeability and an increase in the risk of developing asthma. Pool attendance was the most consistent predictor of lung epithelium permeability, which was already considerably increased after 1 h at the poolside without swimming. They also found a marked association between cumulated pool attendance and the prevalence of asthma in children. Lagerkvist *et al*[3] studied children before and after exercise for 2 h, and found that those who visited chlorinated indoor swimming pools had significantly ($p<0.002$) lower CC16 levels in serum than did non-swimming children both before and after exercise. Bernard *et al*[4] reported that cumulative pool attendance was an important predictor for raised exhaled nitrogen oxide levels (eNO; odds ratio (OR) 1.30, 95% confidence interval (CI) 1.10 to 1.43) and asthma in the presence of high immunoglobulin E (IgE) levels (OR 1.79, 95% CI 1.07 to 2.72) in children. Swimming as a baby was the only significant predictor for serum CC16 levels ($p = 0.01$).[5] Nystad *et al*[6] found that the prevalence of recurrent respiratory tract infections was higher (12.3%) among children who took part in baby

swimming than among those who did not (7.5%). On the other hand, studies carried out in the 1980s showed beneficial effects of swimming on children with asthma,[7–9] although sample sizes were generally small.

An increased risk for respiratory disease was seen not only in children but also in swimming pool attendants and swimmers. Nitrogen trichloride was recently also identified as a cause of occupational asthma among two lifeguards and one swimming pool teacher in provocation tests, and supported by other means of diagnosis, in Birmingham, UK.[10] Massin *et al*[11] found an increase in eye and upper respiratory tract irritation in lifeguards and other pool attenders. Stav and Stav[12] examined the effect of chlorinated whirlpool baths on airway reactivity in eight patients with mild asthma and found a 20% reduction in forced expiratory volume in 1 s (FEV_1) in six patients after the bath. Carbonelle *et al*[13] compared competitive swimmers in a chlorinated pool with those swimming in a pool that used copper/silver disinfection. They found that cumulated attendance at chlorinated pools was associated with a higher risk of respiratory symptoms (OR, 2.29; $p = 0.002$) and raised exhaled nitrogen oxide eNO levels (>30 ppb; OR 1.59; $p = 0.039$), but respiratory symptoms and raised eNO levels did not show any relationship with the attendance at pools using copper/silver disinfection.

The putative agent in these studies is thought to be nitrogen trichloride (NCl_3)—a byproduct of chlorination, and a volatile and strong irritant. It is thought to cause damage to the lung epithelium and increase permeability, and thereby allow the passage of allergens. NCl_3 is formed when organic matter (eg, sweat, urine) brought by swimmers in the water reacts with the chlorine, and is often responsible for the chlorine smell in pools. However, NCl_3 has not been measured in epidemiological studies; the amount of swimming has been used as a surrogate instead.

The issue has raised concern in the swimming pool community. Many children use swimming pools, and are even required to go swimming as part of their school curriculum. Even if any causative relationship between swimming and asthma is weak, the large number of children taking part in it would mean a considerable overall disease burden. Further, even if there is no true relationship, the current concern created by the published studies may deter children from swimming, or swimming pools may unnecessarily, and at some cost, change their disinfection treatment. There are alternatives to chlorine as a disinfectant, such as ozone, ultraviolet, copper/silver, bromine and hydrogen peroxide, which may reduce any risk, but they also need to be evaluated for risk and overall effectiveness.

The obvious step forward is to try to eliminate or reduce the level of the putative agent—for example, by good pool management (in relation to disinfection, ventilation, toilet facilities and enforcement), showering before entering the pool and avoiding urinating in the pool. Coming back to the question, does this ecological study help us move the field forward? I would say yes, because it seems to be in agreement with previous studies showing that there is a reason for concern and that further research is warranted. However, on the other hand, it does not give us the answer whether or not there is a true relationship. What we need are analytical follow-up studies that can examine the temporality aspect of swimming and asthma, have a strong exposure assessment component, examine potential putative agents and take into account potential confounders.

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