

The role of ozone

Forster J, Kuehr J. The role of ozone.

Pediatr Allergy Immunol 2000; Suppl. 13: 23–25. © Munksgaard 2000.

**Johannes Forster and
Joachim Kuehr**

University Children's Hospital, Freiburg i. Brsg.,
Germany

Key words: ozone; children; lung function;
lung growth; allergic sensitization

Prof. Dr. J. Forster, St. Josefskrankenhaus,
Hermann Herder Str. 1, 79104 Freiburg,
Germany.

Tel.: +49 (0)761 27112800

Fax: +49 (0)761 27112802

e-mail: Forster@ruf.uni-freiburg.de

Accepted 13 December 1999

Background

Both the prevalence of allergic diseases and environmental pollution have increased in developed countries in the last decades. It has become clear that ambient ozone concentrations can impair lung function of children (1, 2). In the USA, depending on the assumed threshold level, $\frac{1}{4}$ to $\frac{1}{2}$ of the total childhood population has been declared to be at risk (3). In the general public the idea of a relationship between high ambient ozone and allergies was established quickly. Scientifically, however, the hypothesis proved difficult to test, because there is always a mixture of pollutants in the ambient air.

In summertime the concentration of ozone, the prototype oxidant pollutant, peaks when pollen counts are high. Thus, ozone became the first candidate to promote allergic sensitization to pollen allergens, especially as it is known to cause inflammation in the airways of children and young adults at levels occurring in the ambient air (1, 4). But in most places in the world, ozone coincides not only with other photochemical pollutants, but also with a substantial amount of fine particles, which makes it difficult to look at ozone as a single causative factor (5, 6).

The first question is whether ozone promotes allergic sensitization, and thereby induces asthma, as childhood asthma is allergic asthma. Answers to this question can be sought in animal models, and in epidemiologic studies in humans. The second question is whether the impact of ozone worsens the allergic reaction of individuals already sensitized.

Role of ozone in promoting aeroallergen sensitization

Depending on the animal model (e.g. species, type of allergen, ozone concentration, applying cofactors such as infections (7)) it has been possible to demonstrate a promotion of sensitization with increasing ozone exposure (8). However, these models represent only the potential for such a pathogenesis. Whether it applies also to humans can only be investigated in epidemiologic studies, as it would be unethical to sensitize, or even enhance sensitization, in studies done in human beings.

An increase of aeroallergen sensitization in humans in places where ambient ozone concentrations are high, can pathophysiologically be assigned to different mechanisms. Ozone (to-

gether with other pollutants) may act by changing the properties of pollen and their allergens (9, 10), by causing airway inflammation and thus altering the handling of allergens by the immune system by being a cofactor to other impact factors, which enhance the allergic sensitization, for example tobacco smoke (1). In cross-sectional studies, some of these influences can be accounted for by choosing an appropriate design, whereas for others, especially for those not yet known, this is impossible. In general, the last seems to be more likely, and this has to be kept in mind when looking for ozone effects.

In a study in children in Switzerland, differences in the prevalence of allergic sensitization could not be assigned to differing average concentration of ambient ozone in the places where the children lived (11).

In Southwest Germany, we have started a study in rural areas where ozone is the leading air pollutant and the levels of other air pollutants such as particulate matters and NO₂ are rather low. The study addresses the influence of ozone on lung growth based on a longitudinal design. The recruitment data were evaluated as a cross-sectional study of the influence of local ozone on the prevalence of sensitization to aeroallergens in 5th and 6th grade pupils, 7–8 years old (12).

In six areas of Baden-Württemberg, children ($n=1254$) and their parents were asked to take part in complete age groups of their school to provide a population-based sample. In all, 1101 (87.9%) joined the study, filling in the first questionnaire, the core of which consisted of ISAAC questions. Of these, 1031 had a skin prick test (grass, birch, and hazel pollens, der pt, der f, dog and cat dander – 10 HEP each, ALK-SCHERAX; Hamburg). About half of the study population ($n=631$) lived in two cities (Welzheim, Freudenstadt) with high ozone concentrations during the summer (1991 through 1995, mean: 75.9 $\mu\text{g}/\text{m}^3$) and the remainder in four areas with medium to low ozone levels (48.1 $\mu\text{g}/\text{m}^3$). Five-year means of NO₂ and PM₁₀ in Freudenstadt/Welzheim had been 14.8 and 18.4 $\mu\text{g}/\text{m}^3$, respectively, versus 23.2 and 30.2 $\mu\text{g}/\text{m}^3$ in the other places. As expected, the ambient ozone levels during summertime were high enough to produce typical symptoms in the eye and a significant slowing of lung growth in highly exposed individuals (13). The sensitization rate was equally higher in boys than in girls in all places. But analyzing the cross-sectional data, we were unable to demonstrate a difference between pupils living in the places with high and medium to low ozone levels. We pooled the data with those of the Study on Allergy in Schoolchildren in Southwest

Germany (SASS), a population-based sample of the same age living in 1990 in three upper Rhine valley cities (Kehl, Freiburg, Lörrach) that have medium to high O₃ levels and medium to high NO₂ and PM₁₀ levels (combined $n=2376$). Ozone was not predictive for the prevalence of sensitization to aeroallergens (14). The average ozone level was not predictive for the symptoms of rhinoconjunctivitis (hay fever), either for the lifetime prevalence or for the summertime before the skin prick test was done. This does not exclude an effect of ozone on the symptom incidence of already sensitized individuals. Confounding factors may have hampered demonstration of such effects, which could be better addressed in laboratory experiments.

Role of ozone in modifying the allergic reaction

Ozone in concentrations of 0.12 ppm did not worsen bronchial symptoms in resting adults when they were challenged later with the relevant allergen (15, 16). Jörres et al. (17) exposed individuals intermittently exercising for 3 h to 0.25 ppm ozone. Looking at the change in FEV₁ they found an increased bronchial reactivity in the individual challenged with the relevant pollen, both in those reporting pollen asthma and those reporting rhinitis only. In studies using the nose of the affected individuals as a laboratory and looking for nasal inflammation when challenging with ozone and/or house dust mite allergen in sensitized individuals, ozone increased the effect of allergen (18). Together, these studies imply that heavy ozone exposure, which means high concentration in the ambient atmosphere as well as high concentration at the mucosal membranes resulting from forced breathing, worsens the reaction of sensitized individuals to their respective allergen.

In epidemiologic studies, ozone was also found to exert an effect in combination with other pollutants both in lung health and in aeroallergen sensitivity, but in conjunction with others, it has to be regarded as of minor influence (19, 20).

In conclusion, what can ozone be blamed for? We are sure that it actually impairs lung function, in children more than in adults. In summertime it also causes slowing of the natural increase of vital capacity in heavily exposed children, who have the chance to outgrow the retardation during wintertime. Ozone has – so far – no demonstrable effect on aeroallergen sensitization in humans, but it is able to increase the reactivity of already sensitized individuals.

Acknowledgment

The Prospective Longitudinal Study on Pulmonary Effects of Ozone in Schoolchildren was funded by the State of Baden-Württemberg: Research Program Environment and Health, Grant PUG L 96001.

References

- KOREN HS. Environmental risk factors in atopic asthma. *Int Arch Allergy Immunol* 1997; 113: 65–68.
- BRAUN-FAHRLÄNDER C, KUNZLI N, DOMENIGHETTI G, CARELL CF, ACKERMANN-LIEBRICH U. Acute effects of ambient ozone on respiratory function of Swiss schoolchildren after a 10-minute heavy exercise. *Pediatr Pulmonol* 1994; 17: 169–177.
- ANONYMOUS. Children at risk from ozone air pollution – United States, 1991–1993. *MMWR* 1995; 44: 309–312.
- WARDLAW AJ. Air pollution and allergic disease. Report of a Working Party of the British Society for Allergy and Clinical Immunology. *Clin Exp Allergy* 1995; 25 (suppl 3): 6–8.
- SUNYER J, SPIX C, QUÉNEL P, et al. Urban air pollution and emergency admissions for asthma in four European cities: the APHEA Project. *Thorax* 1997; 52: 760–765.
- BRAUN-FAHRLÄNDER C, WÜTHRICH B, GASSNER M, et al. and the SCARPOL-Team. Prävalenz und Risikofaktoren einer allergischen Sensibilisierung bei Schulkindern in der Schweiz. *Allergologie* 1999; 22: 54–64.
- FREIHORST J, FRANKE G, MUHLE H, HARDT Hvd, LOHMANN-MATTHES M. Makrophagenfunktionen und Immunantwort auf inhaliertem Antigen beim Zusammenwirken von Ozonexposition und viralem Atemwegsinfekt; 1. Statuskolloquium des PUG, Kernforschungszentrum Karlsruhe 1992; S.49–60.
- MATSUMURA Y. The effects of ozone, nitrogen dioxide, and sulfur dioxide on the experimentally induced allergic respiratory disorder in guinea pigs. I. The effect on sensitization with albumin through the airway. *Am Rev Respir Dis* 1970; 102: 430–437.
- EMBERLIN J. Interaction between air pollutants and aeroallergens. *Clin Exp Allergy* 1995; 25: 33–39.
- BEHRENDT H, BECKER WM, FRITZSCHE C, et al. Air pollution and allergy: experimental studies on modulation of allergen release from pollen by air pollutants. *Int Arch Allergy Immunol* 1997; 113: 69–74.
- BRAUN-FAHRLÄNDER C, VUILLE JC, SENNHAUSER FH, et al. and the SCARPOL-Team. Respiratory health and long-term exposure to air pollutants in Swiss schoolchildren. *Am J Respir Crit Care Med* 1997; 155: 1042–1049.
- KÜHR J. Asthma und Allergie bei Kindern. *Allergologie* 1999; 22: 48–53.
- MATTES J, BÄR GU, ULMER C, KOPP M, KÜHR J, FORSTER J. Association between ambient ozone and sensitization to inhalant allergens. *Pneumologie* 1997; 51: 190.
- KOPP MV, FRISCHER T, BOHNET W, et al. Effects of ambient ozone on lung function in children over a two summer period. *Eur Respir J* 2000, in press.
- BALL BA, FOLINSBEE LJ, PEDEN DB, KEHRL HR. Allergen bronchoprovocation of patients with mild allergic asthma after ozone exposure. *J Allergy Clin Immunol* 1996; 98: 563–572.
- HANANIA NA, TARLO SM, SILVERMAN F, et al. Effect of exposure to low levels of ozone on the response to inhaled allergen in allergic asthmatic patients. *Clin Invest* 1998; 114: 752–756.
- JÖRRES R, NOWAK D, MAGNUSSEN H, SPECKIN P, KOSCHYK S. The effect of ozone exposure on allergen responsiveness in subjects with asthma or rhinitis. *Am J Respir Crit Care Med* 1996; 153: 56–64.
- PEDEN DB, SETZER RW, DEVLIN RB, DAILEY LA, CARTER J, CAZARES L. Ozone exposure has both a priming effect on allergen-induced responses and an intrinsic inflammatory action in the nasal airways of perennially allergic asthmatics. *Am J Respir Crit Care Med* 1995; 151: 1336–1345.
- CARSWELL F. Epidemiology of the effects of air pollutants on allergic disease in children. *Clin Exp Allergy* 1995; 25 (suppl 3): 52–55.
- DELFINO RJ, COATE BD, ZEIGER RS, SELTZER JM, STREET DH, KOUTRAKIS P. Daily asthma severity in relation to personal ozone exposure and outdoor fungal spores. *Am J Respir Crit Care Med* 1996; 154: 633–641.