

Childhood asthma and the environment

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Bronchial asthma may start early in infancy or any time during childhood. As already stated by Osler in 1892 (1), "the underlying abnormality of asthma is a special form of inflammation restricted to the airways", corresponding with the present view of asthma (2). Hereditary and environmental factors contribute to incite asthma and to increase and maintain the bronchial inflammation. The provoking factors of asthma are respirable particles and gases inhaled through the respiratory tract, such as infective agents causing respiratory infections, allergens, airways irritants such as tobacco smoke and air pollution outdoor and indoors. A change in the occurrence of asthma over time is probably due to a shift in the environmental load upon the genetic predisposition. Indeed, numerous reports of increasing prevalence and morbidity of asthma during later years, as well as geographical differences, indicate that an increased environmental load upon the respiratory tract influences asthma and allergy in childhood. In Norway, the cumulative prevalence of childhood asthma has been reported to increase from 0.4% in 1948 (3), to 1.77% in Bergen in 1951–53 (4), to 2.2% among seven years old school-children in Sandnes in the South-West part of Norway (5). Later studies report a cumulative prevalence of 3.1% among schoolchildren in Oslo 1980/81 (6), of 7.2% in Nordland (7) and 8.1% in Troms (8) in northern Norway in 1985. The last study performed in Telemark in 1991 revealed a cumulative prevalence of 9% (9). Studies performed by different research groups on different populations may be difficult to compare, however, Burr et al. found that the cumulative asthma prevalence of 12 year old children in South Wales increased from 6% in 1973 to 12% in 1988 (10). Geographical differences are demonstrated when comparing the recent Norwegian studies to two recent English studies; in Leicester doctor-diagnosed asthma was found in 17% of five-year-old

children, whereas 21% had a history of wheeze (11), and in Sheffield 18% of nine-year-old children had a diagnosis of asthma, whereas the parental reported cumulative prevalence of wheeze was 29.9% (12).

The causative factors of childhood asthma change with increasing age of the patient.

Respiratory virus infections, especially respiratory syncytial virus (RSV), play a major role in bronchiolitis and asthma during infancy and the first few years of age (13). The occurrence of recurrent wheezing and asthma after RSV-bronchiolitis in infancy is well known (14, 15). Welliver et al. reported that RSV-specific IgE responses in nasal secretions was associated with the severity of symptoms during acute bronchiolitis as well as with recurrent wheezing following acute bronchiolitis. However, after a follow-up of seven years an association was not found between the initial RSV-specific IgE response and current asthma symptoms or lung function (16). Allergy in childhood often occurs shortly after a respiratory virus infection. The IgE synthesis is regulated through interleukins, and is stimulated by interleukin 4 (IL 4) and partly inhibited by γ -interferon. Respiratory virus infections stimulate several interleukins, particularly γ -interferon. A role of virus induced production of histamine releasing factor has also been suggested (17). Another possible mechanism is the effect of virus infections upon adhesion molecules which regulate eosinophilic and neutrophilic migration. ICAM-1 stimulate eosinophilic migration and has been shown to be the major human rhinovirus receptor (18). However, the interrelationship between respiratory virus infections and allergy and asthma is still not completely understood (19, 20).

With increasing age, allergy plays an increasing role in childhood asthma, although allergen exposure during the first months of life may effect later allergic sensitization (21, 22). In children above 2–3

years of age, allergy was found among approximately two-thirds of asthmatic children seen for acute asthma in Oslo during a two year period (23). However, in the same study, virus infections, particularly rhinovirus, was found to be the most frequent precipitating agent for acute asthma (23). Allergens is a normal part of the human environment, both outdoor and indoor. In northern countries most outdoor aeroallergens are seasonal, whereas indoor allergens have a perennial presence, though not without seasonal variation. In modern buildings the growth of house dust mites has increased, and bronchial hyperreactivity has been demonstrated to improve after reduction of exposure to house dust mites (24).

Outdoor and indoor air pollution are among the factors blamed to be responsible for the increase in prevalence of childhood asthma and allergy during recent years. Many studies suggest such a role of air pollution, but the exact part played remains to be determined, and probably varies between different geographical locations. The sources of most air pollutants are combustion of organic material or fuel, either due to industry or modern traffic. The effect of the particular pollutant depends upon the physical characteristics of the pollutant; whether it is a gas or consists of particles. Particle sizes determine the respirability; and in the case of gases, water solubility determines how far into the respiratory tract the gas may penetrate. Water-soluble gases, such as SO₂ and formaldehyde, dissolve in the nose and upper respiratory tract, and must be present in high concentrations to reach the lower respiratory tract. NO₂, however, is water soluble to a minor degree, and reaches the lower respiratory tract in lower concentrations. The effect also depends upon host characteristics; e.g. age, sex, airway size, preexisting illness. The nature of exposure, whether it is high levels of exposure during short time periods, or low-levels of exposure of longer duration, as well as the frequency of exposure are important.

Some of the most powerful air pollutants, ozone and NO₂ exert their effect upon the airways as a source of free oxygen radicals, thereby increasing airways' inflammation. Ozone, in ambient concentrations have been shown to increase inflammation in the lower airways (25, 26) and to affect respiratory health, lung function, bronchial responsiveness, allergic sensitization and cellular immune system in children (27–29) and NO₂ to increase airway responsiveness and reduce lung function (29–31).

In addition to the effect upon the airways, air pollution exerts an effect upon immune function. It has been shown in experimental studies that inhalation of NO₂, SO₂ and ozone have an adjuvant effect upon bronchial allergic sensitization in the guinea pig (32). Epidemiological studies demon-

strate increased occurrence of allergy to pollen and animal dander in polluted areas such as city centers compared to rural areas around the city. This increase in allergy in the city centers occurred in spite of greater exposure to animals in the rural areas (33).

In the indoor environment, allergens such as house dust mites and animal dander are important for the occurrence of asthma and allergy. As regards indoor air pollution, many factors are unknown. However, the source of indoor air pollution most studied, is the effect of passive smoking, particularly parental smoking. Several studies address the relationship between respiratory illness, asthma, bronchial responsiveness and passive smoking (34, 35). Already at the age of one month reduced forced expiratory flow rates were found in infants of smoking mothers (36), and in later life an improvement of asthma has been demonstrated in children of parents who expose them to less smoke (37). In Oslo we have observed more than a doubling in asthma hospital admission rates for children 1980 through 1989. For children below five years of age the admission rates increased from 3.84/1000 to 9.39/1000. The entire increase in admission rates occurred in children below three years of age. In 1980 the highest admission rates were observed in the centrally located townships of Oslo. Ten years later more peripheral located townships had higher admission rates than the central townships. However, the townships with the highest admission rates were located along the main motor roads through Oslo.

These findings lead to the present ongoing study of childhood asthma and the environment in Oslo. This is a nested case/control study with a cohort of 3800 infants recruited during one year. These infants will be followed by questionnaires every half year until two years of age. In 800 infants lung function was measured at the age of two to four days by means of tidal flow volume loops and compliance and resistance by the shutter technique. Umbilical cord blood was sampled from all 3800 infants included in the cohort. Living conditions, family and social status were recorded in the questionnaire. Included in the case/control study will be all children with recurrent (two and more) episodes of bronchopulmonary obstruction. A control subject born close to the case subject will be selected, and the same measurements will be performed. In the case/control study lung function will be measured in addition to a careful case history, immunological studies will be performed, and exposure measurements of air quality outdoor and indoor in the homes will be performed. Air exchange in the home, NO₂ exposure by passive personal sampler, and samples of house dust to be analysed for house dust mites and animal dander by ELISA technique will be taken. At two years of age, an allergological examination of the

case/control subjects, as well as follow-up lung function tests, and other immunological, studies will be performed. As the inclusion into the cohort study is only just completed, no data are yet available. The main purpose of the study is to investigate which environmental factors contribute to asthma in these children, and to evaluate their role in the interrelationship between constitution and environment. The role of constitutional factors such as lung function and airways size at birth, together with atopic constitution will be evaluated in the relationship to the environmental factors.

The high prevalence of asthma in our child populations is a major community problem. Both the local environment close to the child, and the community as a whole, are involved. It is important to try to identify the factors at work in this aspect. When these factors are known, preventive measures may be taken, both in the individual cases, and on a community scale.

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