Epidemiological Studies of Childhood Wheeze Risk Factors and Long-term Outcome

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Wheezing with viral infections is common in childhood and both genetic and environmental factors have been reported to influence the risk of subsequent asthma development. The overall aim of this thesis was to study the factors influencing the risk of wheezing at preschool age and the long-term outcome following severe wheezing in early life.

In a prospective study of 5,600 children born in the region of western Sweden in 2003 questionnaires were answered at six and 12 months and at 4.5 years of age. Data were also obtained from the Swedish Medical Birth Register. Special reference was made to the effects of prenatal paracetamol exposure, antibiotic treatment during the first week of life and feeding strategies in infancy. Possible differences between multiple-trigger and episodic viral wheeze were analysed.

In a prospective study of 101 children hospitalised due to wheezing bronchitis before the age of two years, the long-term prognosis and factors influencing the risk of subsequent asthma were explored. A re-investigation at 17-20 years of age included a questionnaire and tests for allergy, bronchial hyper-responsiveness (BHR) and airway function. The study group was compared with age-matched controls.

We were able to confirm known risk factors for recurrent wheeze at age 4.5 years, such as atopic heredity, male gender, eczema and doctor-diagnosed food allergy in infancy. In addition, neonatal antibiotic treatment increased the risk, while the introduction of fish before nine months of age reduced the risk. Paracetamol exposure *in utero* increased the risk of preschool wheeze treated with inhaled corticosteroids. The risk was more pronounced among those with multiple-trigger wheeze.

An increased risk of asthma at age 17-20 years was seen in subjects with early viral wheeze. Current allergy, BHR and active smoking increased the risk of current asthma. In addition, female gender was an independent risk factor. Wheeze was more prevalent among boys in early childhood, but more boys than girls became symptom free as they grew up. Girls had more persistent asthma and relapsing symptoms during adolescence.

Signs of reduced airway function were seen in the study group and were most pronounced among females with current asthma. However, a difference was also seen among symptom-free subjects. Prenatal smoke exposure was associated with reduced airway function and independently increased the risk of BHR at 17-20 years of age. On the other hand, postnatal smoke exposure was associated with becoming an active smoker, which in turn increased the risk of current asthma.

In conclusion, paracetamol exposure during pregnancy and treatment with antibiotics neonatally independently increased the risk of wheeze at age 4.5 years. The early introduction of fish had a protective effect.

Individuals with severe viral wheeze in early life run an increased risk of asthma and have signs of reduced airway function at age 17-20 years. The highest risk of asthma is seen among those with current allergy or BHR and among females. Prenatal smoke exposure increases the risk of subsequent BHR and asthma, while smoke exposure in infancy and childhood increases the risk of becoming an active smoker.

Keywords: children, wheezing, asthma, smoke exposure, gender, antibiotics, fish, paracetamol

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IV. Goksör E, Gustafsson PM, Alm B, Åmark M, Wennergren G. Reduced airway function in early adulthood among subjects with wheezing disorder before two years of age. Pediatr Pulmonol. 2008; 43: 396-403.

V. Goksör E, Åmark M, Alm B, Gustafsson PM, Wennergren G. The impact of pre- and postnatal smoke exposure on future asthma and bronchial hyper-responsiveness. Acta Paediatr. 2007; 96: 1030-35.

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