

Factors associated with lung function impairment in children and adults with obstructive lung disease

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Abstract

Obstructive lung diseases are a group of diseases in which there is a limitation in the flow of air into or out of the lungs. Two common such diseases are asthma, which is found in both children and adults, and chronic obstructive pulmonary disease (COPD), mainly found in the population over 50 years of age. Both asthma and COPD seem to have with several different subgroups, or phenotypes, which may be associated with different long term consequences in regard to morbidity and in some cases also mortality. To be able to prevent and treat these diseases in the best possible way, we need to learn more about the different phenotypes and the mechanisms behind them.

The aim of this thesis was to study factors that are associated with lung function impairment in children and adults with obstructive lung diseases. The factors that are in focus are age of onset, duration of symptoms, sex, allergy, smoking and the contribution of genes and environment. We have, in the two first papers, measured lung function at age 4 and 8 years in a birth cohort of 4,000 children and found that asthma symptom onset in the first 4 years of life was, on a group level, associated with impaired exhaled flows. This was found irrespective of the persistence of symptoms between the age of 4 and 8. We could also show tracking of impaired flows between the age of 4 and 8. Sensitization to airway allergens was associated with lung function impairment only in children with symptom onset after the age of 4. While male sex was a risk factor for asthma symptoms, girls with asthma symptoms showed a larger negative effect on exhaled flows, at least in the four first years. In paper 3 and 4, we studied symptom data from 45,000 twins from the Swedish Twin Registry to quantify heritability for chronic bronchitis and emphysema, two of the main components seen in COPD. As smoking behaviour has genetic influences, it was necessary to study how heritability for disease was associated with heritability for smoking. The results showed that ~40% of the individuals liability to developing chronic bronchitis/emphysema can be attributed to genetic factors, and that only a small part of these factors were found to be in common with those influencing smoking habits. Women more often reported chronic bronchitis/emphysema, compared to men, and this could not be explained by different smoking habits or different genes. Two hundred of the twins took part in a clinical testing of different lung function measures. The results from this study showed that all lung function measures that were studied had a heritable component, and that it was larger for women than for men.

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In conclusion, we have studied how several different factors are associated with lung function impairment in children and adults with obstructive lung disease. In summary, the first years of life are of importance for future lung function. Children that outgrow their asthma seem, on a group level, to loose their symptoms rather their lung function impairment, which might be present through life. We have furthermore shown that genes are important for the individuals' liability to disease in adult life. Sex differences exist both in children and adult disease, and there are indications of a less favourable outcome for girls/women. More work is now needed to find the individuals that belong to these susceptible groups, and to develop and apply methods to prevent and treat impaired lung function and disease.