airwaves

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α_1-ANTITRYPSIN DEFICIENCY IN *THORAX*

COPD is caused by complicated interactions between environmental and genetic factors. One of the best characterised genetic conditions is deficiency of α_1-antitrypsin (AAT) and, although COPD associated with AAT deficiency is rare, study of AAT has provided useful information on the pathogenesis of emphysema. In this month's *Thorax* we publish three articles on issues relating to AAT deficiency. Hersh and colleagues address the question of whether heterozygotes for AAT deficiency are at risk of COPD. In a meta-analysis of studies of outcome in Pi MZ heterozygous individuals, the results indicate that case-control studies showed increased odds ratios for COPD risk, but this finding was not confirmed in cross sectional studies. Generally, included studies have been small and cigarette smoking may be an important confounder accounting for variability in results. In the accompanying editorial Seersholm points out that, in the Copenhagen City Heart Study, 450 Pi MZ subjects have been identified. Close follow up of these patients should provide definitive data as to the risk of heterozygosity for AAT. In an article in our excellent review series on AAT deficiency, Sandhaus describes the role of new treatments for AAT deficiency. As AAT augmentation therapy is limited and not yet definitely proven in efficacy, other approaches are described. Lessons learnt from the management of AAT deficiency will also be invaluable for COPD patients.

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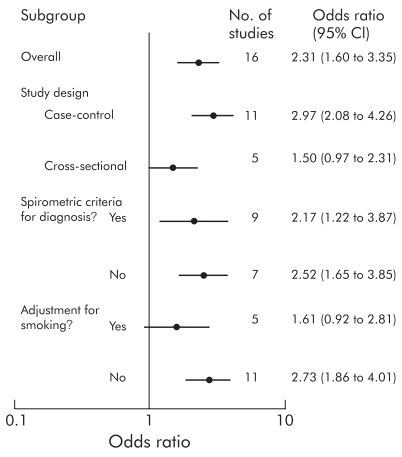

Subgroup analysis of studies of COPD in α_1-antitrypsin Pi MZ heterozygotes. Odds ratios with 95% confidence intervals are shown

COMPLEX INTERACTIONS BETWEEN EARLY ALLERGEN EXPOSURE, ATOPY AND ASTHMA

Although it is assumed that the risk of childhood respiratory allergy is related to exposure in early life, there is little evidence for this association. Cullinan and colleagues describe results from a representative community cohort of children followed from birth to age 5.5 years in south east England. There were no linear relationships between early allergen exposure and childhood respiratory allergy. The authors showed an increase in risk at low levels of exposure in first born children and those from allergic parents. They emphasise the complex gene-environment interactions present between allergen exposure and the development of asthma and atopy. In an accompanying editorial Custovic and Simpson conclude that future interventions will need to be aimed at particular individuals with specific susceptibilities to development of asthma and allergies.

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AIRWAYS IN DIFFICULT CHILDHOOD ASTHMA

Management of difficult asthma in children is still a problem and more information on airway pathology is important in guiding effective treatment. Payne and colleagues describe airway inflammatory changes in asthmatic children after treatment with systemic corticosteroids and relate these changes to symptoms and lung function. The study showed differences in thickness of the reticular basement membrane between asthmatic and control children. There were no differences in airway inflammation between asthmatics who had persistent symptoms and those who were asymptomatic. CD4+ lymphocytes were increased with persistent airflow limitation. The paper concludes that multicentre studies in childhood asthma are now required to evaluate the effects of interventions on airway inflammatory mechanisms.

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REDUCED IL-13 IN EMPHYSEMA

There have been some data suggesting that targeted overexpression of either interleukin (IL)-13 or interferon (IFN)γ in an adult mouse model produces changes that are similar to adult emphysema. In this issue of *Thorax* Boutten and colleagues describe expression of IFNγ mRNA and IL-13 mRNA in patients with and without emphysema. Contrary to previous work, the authors found no differences in IFNγ mRNA expression in either group of patients, but IL-13 expression was lower in patients with emphysema than in those without. The authors suggest that one of the mechanisms for the decreased expression of IL-13 is lymphocyte differentiation towards the Th1 phenotype in severe emphysema. This paper also highlights differences in the outcomes of studies with patients and those using animal models of emphysema.

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CRP, SYSTEMIC INFLAMMATION AND BHR

Systemic inflammation may be the link between the observation that there is an association between impaired lung function and cardiovascular risk. Kony and colleagues report a study of the relation between lung function, C-reactive protein (CRP) as a measure of systemic inflammation, and bronchial hyperresponsiveness (BHR). Increases in CRP levels were related to FEV_1 and BHR independently of other confounders studied such as smoking. These interesting data suggest that systemic inflammation is related to BHR, in addition to its association with reduced lung function.

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