COPD EXACERBATIONS: OXIDATIVE STRESS AND INFLAMMATION

Exacerbations have become an important target for prevention in the management of COPD as they are associated with impaired health status and disease progression. During COPD exacerbations there is increased airway inflammation and oxidative stress, so it is important to study the nature of this inflammation if novel treatments are to be developed. In this issue of Thorax Drost and colleagues report a study of markers of airway inflammation and oxidative stress in patients with severe exacerbations requiring intubation and ventilation. Proximal samples were taken together with BAL fluid and some biopsy specimens at bronchoscopy. An influx of inflammatory cells was seen in the peripheral airways at exacerbations with increased interleukin (IL)-8 levels only in the proximal airways. There was evidence of increased oxidative stress at COPD exacerbation with a reduction in glutathione (GSH) levels which was greater with increasing severity of the exacerbation. The data on severe exacerbation with a reduction in glutathione (GSH) levels which was greater with increasing severity of the exacerbation. The paper also shows the importance of recognising respiratory symptoms early in the elderly, usually in association with obstructive airways disease, and offering smoking cessation advice.

See page 293

RESPIRATORY SYMPTOMS IN THE ELDERLY

In this month’s Thorax Hewitt and colleagues report the largest study to date of respiratory symptoms in a group of 14,458 people aged 75 years or over participating in a health screening trial. Among the symptoms studied there was an overall prevalence of 27% for coughing up sputum on winter mornings, which is higher than previously reported. Of interest was the finding that respiratory symptoms were a strong predictor of mortality in these patients. These results emphasise the importance of recognising respiratory symptoms early in the elderly, usually in association with obstructive airways disease, and offering smoking cessation advice.

See page 331

MANAGEMENT OF ASThma IN SMokers

Unfortunately a significant number of asthmatics persist in smoking and short term inhaled steroid therapy is not effective in these patients. In this issue Tomlinson and colleagues report a further study investigating treatment with high or low dose inhaled beclomethasone over a 12 week period. The study showed that smokers with asthma have a reduced response to inhaled steroids and that this insensitivity is more marked with lower doses. However, the smokers did derive some benefit from high dose inhaled corticosteroid therapy, suggesting steroid insensitivity in asthmatic smokers. This patient group will therefore be more prone to side effects of steroids in the long term if higher doses need to be used. The authors end the discussion with a comment that it is unknown if smoking cessation will restore steroid responsiveness in asthma. We must therefore do all we can to stop asthmatic subjects smoking in the first place.

See page 282

TNFα AND CYSTIC FIBROSIS

The pulmonary phenotype in patients with cystic fibrosis (CF) is variable even in those with the same CF transmembrane conductance regulator (CFTR) genotype, so other genetic factors may be involved. In this issue of Thorax Yarden and colleagues report a study of the role of TNFα in CF and describe an association between TNFα +691g insdel polymorphic locus and the severity of CF lung disease. Patients heterozygous for +691g ins and +691g del were more likely to be older at the first infection with Pseudomonas aeruginosa than those homozygous for +691g ins. The authors also described associations between the −851c/t polymorphic locus and lung function in CF. These intriguing results suggest a role for TNFα polymorphisms in CF. Further research is needed to understand the mechanisms for these interactions.

See page 320

ADAM 33 AND ASTHMA

ADAM 33 is the first gene that has been identified as a candidate for asthma by a positional cloning approach, although further studies have shown some inconsistent results. Blakey and colleagues report a meta-analysis to expand the size of the study population with 1299 cases and 1665 controls for the case-control studies and 4561 for the transmission disequilibrium tests. In their analyses, several single nucleotide polymorphisms (SNPs) were associated with asthma. The authors point out that this variation would account for 50,000 excess asthma cases in the UK. In the accompanying editorial Holgate and Holloway discuss these findings and emphasise that, as there is considerable genetic heterogeneity within any one gene, large sample sizes are required for the study of genetic factors in complex disorders such as asthma. The ADAM 33 story continues.

See pages 263 and 274