

- 13 Wenzel SE, Balzar S, Cundall M, et al. Subepithelial basement membrane immunoreactivity for matrix metalloproteinase 9: association with asthma severity, neutrophilic inflammation and wound repair. *J Allergy Clin Immunol* 2003;**111**:1345–52.
- 14 Miranda C, Busacker A, Balzar S, et al. Distinguishing severe asthma phenotypes: role of age at onset and eosinophilic inflammation. *J Allergy Clin Immunol* 2003;**113**:101–8.
- 15 Cundall M, Sun Y, Miranda C, et al. Neutrophil-derived matrix metalloproteinase-9 is increased in severe asthma and poorly inhibited by glucocorticoids. *J Allergy Clin Immunol* 2003;**112**:1064–71.
- 16 Simpson JL, Scott R, Boyle M, et al. Inflammatory subtypes in asthma: assessment and identification using induced sputum. *Respirology* 2006;**11**:54–61.
- 17 Janeway CA Jr, Medzhitov R. Innate immune recognition. *Annu Rev Immunol* 2002;**20**:197–216.
- 18 Sabroe I, Lloyd CM, Whyte MKB, et al. Chemokines, innate and adaptive immunity, and respiratory disease. *Eur Respir J* 2002;**19**:350–5.
- 19 American Thoracic Society. Standardization of spirometry. *Am Rev Respir Dis* 1987;**136**:1285–98.
- 20 Knudson RJ, Slavin RC, Lewowitz MD, et al. The expiratory flow-volume curve. Normal standards, variability and effect of age. *Am Rev Respir Dis* 1976;**113**:587–600.
- 21 Gibson PG, Wlodarczyk JW, Hensley MJ, et al. Epidemiological association of airway inflammation with asthma symptoms and airway hyperresponsiveness in childhood. *Am J Respir Crit Care Med* 1998;**158**:36–41.
- 22 Zarembka KA, Godowski PJ. Tissue expression of human toll-like receptors and differential regulation of toll-like receptor mRNAs in leukocytes in response to microbes, their products and cytokines. *J Immunol* 2002;**168**:554–61.
- 23 Pfaffl MW. A new mathematical model for relative quantification in real-time RT-PCR. *Nucleic Acids Res* 2001;**29**:e45.
- 24 Wark PA, Johnston SL, Moric I, et al. Neutrophil degranulation and cell lysis is associated with clinical severity in virus-induced asthma. *Eur Respir J* 2002;**19**:68–75.
- 25 Hoshi H, Ohno I, Honma M, et al. IL-5, IL-8 and GM-CSF immunostaining of sputum cells in bronchial asthma and chronic bronchitis. *Clin Exp Allergy* 1995;**25**:720–8.
- 26 Hill AT, Bayley D, Stockley RA. The interrelationship of sputum inflammatory markers in patients with chronic bronchitis. *Am J Respir Crit Care Med* 1999;**160**:893–8.
- 27 Simpson JL, Scott RJ, Boyle MJ, et al. Differential proteolytic enzyme activity in eosinophilic and neutrophilic asthma. *Am J Respir Crit Care Med* 2005;**172**:559–65.
- 28 Doyle I, Nicholas TE, Bersten AD. Serum surfactant protein-A levels in patients with acute cardiogenic pulmonary edema and adult respiratory distress syndrome. *Am J Respir Crit Care Med* 1995;**152**:307–17.
- 29 Douwes J, Versloot P, Hollander A, et al. Influence of various dust sampling and extraction methods on the measurement of airborne endotoxin. *Appl Environ Microbiol* 1995;**61**:1763–9.
- 30 Hollander A, Heederick D, Versloot P, et al. Inhibition and enhancement in the analysis of airborne endotoxin levels in various occupational environments. *Am Ind Hyg Assoc J* 1993;**54**:647–53.
- 31 Angrill J, Agusti C, De Celis R, et al. Bronchial inflammation and colonization in patients with clinical stable bronchiectasis. *Am J Respir Crit Care Med* 2001;**164**:1628–32.
- 32 Ordonez CL, Shaughnessy TE, Matthay MA, et al. Increased neutrophil numbers and IL-8 levels in airway secretions in acute severe asthma. *Am J Respir Crit Care Med* 2000;**161**:1185–90.
- 33 Jatakanon A, Uasuf C, Maziak W, et al. Neutrophilic inflammation in severe persistent asthma. *Am J Respir Crit Care Med* 1999;**160**:1532–9.
- 34 Pizzichini E, Pizzichini MM, Efthimiadis A, et al. Indices of airway inflammation in induced sputum: reproducibility and validity of cell and fluid-phase measurements. *Am J Respir Crit Care Med* 1996;**154**:308–17.
- 35 Green RH, Brightling CE, Woltmann G, et al. Analysis of induced sputum in adults with asthma: identification of subgroup with isolated sputum neutrophilia and poor response to inhaled corticosteroids. *Thorax* 2002;**57**:875–9.
- 36 Dziarski R, Wang Q, Miyake K, et al. MD-2 enables toll-like receptor 2 (TLR2)-mediated responses to lipopolysaccharide and enhances TLR2-mediated responses to Gram-positive and Gram-negative bacteria and their cell wall components. *J Immunol* 2001;**166**:1938–44.
- 37 Arbour NC, Lorenz E, Schutte BC, et al. TLR4 mutations are associated with endotoxin hyporesponsiveness in humans. *Nat Genet* 2000;**25**:187–91.
- 38 Lorenz E, Mira JP, Frees KL, et al. Relevance of mutations in the TLR4 receptor in patients with Gram-negative septic shock. *Arch Intern Med* 2002;**162**:1028–32.
- 39 Kiechl S, Lorenz E, Reindl M, et al. Toll-like receptor 4 polymorphisms and atherogenesis. *N Engl J Med* 2002;**347**:185–92.
- 40 Bottcher MF, Hmani-Aifa M, Lindstrom A, et al. A TLR4 polymorphism is associated with asthma and reduced lipopolysaccharide-induced interleukin-12 (p70) responses in Swedish children. *J Allergy Clin Immunol* 2004;**114**:561–7.
- 41 Raby BA, Klimecki WT, Laprise C, et al. Polymorphisms in toll-like receptor 4 are not associated with asthma or atopy-related phenotypes. *Am J Respir Crit Care Med* 2002;**166**:1449–56.
- 42 Baldini M, Lohman CI, Halonen M, et al. A polymorphism\* in the 5' flanking region of the CD14 gene is associated with circulating soluble CD14 levels and with total serum immunoglobulin E. *Am J Respir Crit Care Med* 1999;**20**:976–83.
- 43 Hubacek JA, Stuber F, Frohlich D, et al. Gene variants of the bactericidal/permeability increasing protein and lipopolysaccharide binding protein in sepsis patients: gender specific genetic predisposition to sepsis. *Crit Care Med* 2001;**29**:557–61.
- 44 LeVine AM, Kurak KE, Bruno MD, et al. Surfactant protein-A deficient mice are susceptible to *Pseudomonas aeruginosa* infection. *Am J Respir Cell Mol Biol* 1998;**19**:700–8.
- 45 Cheng G, Ueda T, Numao T, et al. Increased levels of surfactant protein A and D in bronchoalveolar lavage fluids in patients with bronchial asthma. *Eur Respir J* 2000;**16**:831–5.

## LUNG ALERT

### Severe asthma in the workplace

▲ Eisner MD, Yelin EH, Katz PP, et al. Risk factors for work disability in severe adult asthma. *Am J Med* 2006;**119**:884–91.

In this study, a cohort of 465 patients with severe asthma was evaluated for the prevalence of and risk factors for asthma-related work disability. Additionally, the longitudinal impact of workplace disability and exposures on asthma outcome and health service use was observed.

The prevalence of asthma-related complete work disability was 14% (95% CI 11% to 18%). Among the people with asthma who were unemployed, 26% (95% CI 21% to 32%) of complete work disability (having to leave the work place) was attributed to asthma. Among those employed, the prevalence of partial work disability (defined as including time off work, decreased effectiveness at work or the need for a change in role due to asthma) was 38% (95% CI 31% to 45%).

Sociodemographical and medical factors were significantly related to complete work disability ( $p = 0.03$  and  $p = 0.02$ , respectively), but work exposures were not ( $p = 0.24$ ). Both socio-demographical factors ( $p = 0.06$ ) and work exposure ( $p = 0.01$ ) were related to partial disability. Using multivariate analysis the actual severity of asthma was found to be associated with both complete (OR 1.34, 95% CI 1.16 to 1.54) and partial work disability (OR 1.31, 95% CI 1.07 to 1.61).

Complete work disability was significantly associated with a greater risk for future hospitalisation (HR 1.54, 95% CI 1.06 to 2.23), whereas partial work disability was associated with increased risk for both emergency department visits (HR 2.14, 95% CI 1.25 to 3.67) and hospitalisation (HR 1.79, 95% CI 1.08 to 2.95).

Work disability is common in severe asthma and affects subsequent health needs. Modifying occupational exposure, asthma severity and medical factors such as smoking may prevent work loss, health expenditure and poor health outcome.

S Saeed

Clinical Fellow, St George's Hospital, London, UK; saimasaeed@aol.com