

- 2 Hogg JC, Chu F, Utokaparch S, *et al.* The nature of small-airway obstruction in chronic obstructive pulmonary disease. *N Engl J Med* 2004;**350**:2645–53.
- 3 Saetta M, Turato G, Maestrelli P, *et al.* Cellular and structural bases of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001;**163**:1304–9.
- 4 Tashkin DP, Altose MD, Bleecker ER, *et al.* The lung health study: airway responsiveness to inhaled methacholine in smokers with mild to moderate airflow limitation. The Lung Health Study Research Group. *Am Rev Respir Dis* 1992;**145**:301–10.
- 5 Finkelstein R, Ma HD, Ghezzi H, *et al.* Morphometry of small airways in smokers and its relationship to emphysema type and hyperresponsiveness. *Am J Respir Crit Care Med* 1995;**152**:267–76.
- 6 Mullen JB, Wiggs BR, Wright JL, *et al.* Nonspecific airway reactivity in cigarette smokers. Relationship to airway pathology and baseline lung function. *Am Rev Respir Dis* 1986;**133**:120–5.
- 7 Rutgers SR, Timens W, Tzanakis N, *et al.* Airway inflammation and hyperresponsiveness to adenosine 5'-monophosphate in chronic obstructive pulmonary disease. *Clin Exp Allergy* 2000;**30**:657–62.
- 8 Willemse BW, ten Hacken NH, Rutgers B, *et al.* Smoking cessation improves both direct and indirect airway hyperresponsiveness in COPD. *Eur Respir J* 2004;**24**:391–6.
- 9 Van Eerdewegh P, Little RD, Dupuis J, *et al.* Association of the ADAM33 gene with asthma and bronchial hyperresponsiveness. *Nature* 2002;**418**:426–30.
- 10 Blakey J, Halapi E, Bjornsdottir US, *et al.* Contribution of ADAM33 polymorphisms to the population risk of asthma. *Thorax* 2005;**60**:274–6.
- 11 van Diemen CC, Postma DS, Vonk JM, *et al.* A disintegrin and metalloprotease 33 polymorphisms and lung function decline in the general population. *Am J Respir Crit Care Med* 2005;**172**:329–33.
- 12 Jongepiet H, Boezen HM, Dijkstra A, *et al.* Polymorphisms of the ADAM33 gene are associated with accelerated lung function decline in asthma. *Clin Exp Allergy* 2004;**34**:757–60.
- 13 Black RA, White JM. ADAMs: focus on the protease domain. *Curr Opin Cell Biol* 1998;**10**:654–9.
- 14 Primakoff P, Myles DG. The ADAM gene family: surface proteins with adhesion and protease activity. *Trends Genet* 2000;**16**:83–7.
- 15 Garlisi CG, Zou J, Devito KE, *et al.* Human ADAM33: protein maturation and localization. *Biochem Biophys Res Commun* 2003;**301**:35–43.
- 16 Zou J, Zhu F, Liu J, *et al.* Catalytic activity of human ADAM33. *J Biol Chem* 2004;**279**:9818–30.
- 17 Davies DE, Wicks J, Powell RM, *et al.* Airway remodeling in asthma: new insights. *J Allergy Clin Immunol* 2003;**111**:215–25.
- 18 Lapperre TS, Snoeck-Stroband JB, Gosman MM, *et al.* Dissociation of lung function and airway inflammation in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004;**170**:499–504.
- 19 Sterk PJ, Fabbri LM, Quanjer PH, *et al.* Airway responsiveness. Standardized challenge testing with pharmacological, physical and sensitizing stimuli in adults. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl* 1993;**16**:53–83.
- 20 in 't Veen JC, de Gouw HW, Smits HH, *et al.* Repeatability of cellular and soluble markers of inflammation in induced sputum from patients with asthma. *Eur Respir J* 1996;**9**:2441–7.
- 21 Lapperre TS, Postma DS, Gosman MM, *et al.* Relation between duration of smoking cessation and bronchial inflammation in COPD. *Thorax* 2006;**61**:115–21.
- 22 Howard TD, Postma DS, Jongepiet H, *et al.* Association of a disintegrin and metalloprotease 33 (ADAM33) gene with asthma in ethnically diverse populations. *J Allergy Clin Immunol* 2003;**112**:717–22.
- 23 Werner M, Herbon N, Gohlke H, *et al.* Asthma is associated with single-nucleotide polymorphisms in ADAM33. *Clin Exp Allergy* 2004;**34**:26–31.
- 24 Umland SP, Garlisi CG, Shah H, *et al.* Human ADAM33 messenger RNA expression profile and post-transcriptional regulation. *Am J Respir Cell Mol Biol* 2003;**29**:571–82.
- 25 Tashkin DP, Altose MD, Connett JE, *et al.* Methacholine reactivity predicts changes in lung function over time in smokers with early chronic obstructive pulmonary disease. The Lung Health Study Research Group. *Am J Respir Crit Care Med* 1996;**153**:1802–11.
- 26 Hoppers JJ, Postma DS, Rijcken B, *et al.* Histamine airway hyper-responsiveness and mortality from chronic obstructive pulmonary disease: a cohort study. *Lancet* 2000;**356**:1313–17.
- 27 Bhowmik A, Seemungal TA, Sapsford RJ, *et al.* Comparison of spontaneous and induced sputum for investigation of airway inflammation in chronic obstructive pulmonary disease. *Thorax* 1998;**53**:953–6.
- 28 Keatings VM, Collins PD, Scott DM, *et al.* Differences in interleukin-8 and tumor necrosis factor- $\alpha$  in induced sputum from patients with chronic obstructive pulmonary disease or asthma. *Am J Respir Crit Care Med* 1996;**153**:530–4.
- 29 Ronchi MC, Piragino C, Rosi E, *et al.* Role of sputum differential cell count in detecting airway inflammation in patients with chronic bronchial asthma or COPD. *Thorax* 1996;**51**:1000–4.
- 30 Gosman MME, van der Meulen J. M, Lapperre TS, *et al.* Airway hyperresponsiveness in COPD is more severe in females, patients with lower FEV1/VC, and higher total cell numbers in sputum. *Am J Respir Crit Care Med* 2004;**167**:A86.
- 31 O'Shaughnessy TC, Ansari TW, Barnes NC, *et al.* Inflammation in bronchial biopsies of subjects with chronic bronchitis: inverse relationship of CD8+ T lymphocytes with FEV1. *Am J Respir Crit Care Med* 1997;**155**:852–7.
- 32 Lind DL, Choudhry S, Ung N, *et al.* ADAM33 is not associated with asthma in Puerto Rican or Mexican populations. *Am J Respir Crit Care Med* 2003;**168**:1312–16.
- 33 Raby BA, Silverman EK, Kwiatkowski DJ, *et al.* ADAM33 polymorphisms and phenotype associations in childhood asthma. *J Allergy Clin Immunol* 2004;**113**:1071–8.

## LUNG ALERT

### Detecting PE in COPD

▲ Monreal M, Munoz-Torrero JF, Naraine VS, *et al.* Pulmonary embolism in patients with chronic obstructive pulmonary disease or congestive heart failure. *Am J Med* 2006;**119**:851–8.

**P**ulmonary embolism (PE) is a difficult diagnosis to make or exclude and there have been various pretest probability scoring systems developed to aid the clinician in this area. However, these scoring systems do not take into account underlying cardiopulmonary abnormalities. This interesting study by Monreal *et al.* looked at the diagnosis of PE in patients with congestive heart failure (CHF) and chronic obstructive pulmonary disease (COPD).

From a total of 4444 patients with proven PE enrolled in a registry, 14% had COPD and 9.5% had CHF. Using the Geneva scoring system, a lower percentage of patients with PE with COPD or CHF fell into the low pretest probability category (RR 0.82, 95% CI 0.66 to 1.02 and RR 0.73, 95% CI 0.56 to 0.95, respectively). The percentage of patients with a high probability of PE was similar among the three patient groups (CHF, COPD and neither). Using the Pisa score, the frequency of patients with COPD and CHF with a high pretest probability for PE were higher (61% and 72%, respectively). The Wells score was not used as the patient registry did not identify “an alternative diagnosis more likely than PE”.

The authors conclude that there are significant differences in the presentation of patients with PE who do and do not have coexistent COPD or CHF and that the performance of the various scoring systems varies. Physicians dealing with suspected PE should consider the underlying cardiopulmonary diagnoses and make necessary allowances when planning investigations and management.

Vinod Aiyappan

Specialist Registrar, Queen Elizabeth Hospital, Kings Lynn, UK; drvinodaiyappan@doctors.org.uk