

**Acknowledgements:** The authors thank the children, their parents and the staff of the eight participating centres.

**Funding:** Roche BV, The Netherlands provided an unrestricted grant for this study and financed the study medication. Pari GmbH, Germany donated the nebulising equipment. The study sponsors were not involved in the study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

**Competing interests:** None.

## REFERENCES

1. **Global Initiative for Asthma (GINA).** *Pocket guide for asthma management and prevention in children.* 2006. [www.ginasthma.org](http://www.ginasthma.org).
2. **Wark PA,** Gibson PG. Asthma exacerbations. 3: Pathogenesis. *Thorax* 2006;**61**:909–15.
3. **Kuyper LM,** Pare PD, Hogg JC, *et al.* Characterization of airway plugging in fatal asthma. *Am J Med* 2003;**115**:6–11.
4. **Rogers DF.** Airway mucus hypersecretion in asthma: an undervalued pathology? *Curr Opin Pharmacol* 2004;**4**:241–50.
5. **Picot R,** Das I, Reid L. Pus, deoxyribonucleic acid, and sputum viscosity. *Thorax* 1978;**33**:235–42.
6. **Fahy JV,** Kim KW, Liu J, *et al.* Prominent neutrophilic inflammation in sputum from subjects with asthma exacerbation. *J Allergy Clin Immunol* 1995;**95**:843–52.
7. **Shak S,** Capon DJ, Hellmiss R, *et al.* Recombinant human DNase I reduces the viscosity of cystic fibrosis sputum. *Proc Natl Acad Sci USA* 1990;**87**:9188–92.
8. **Shah PL,** Scott SF, Knight RA, *et al.* In vivo effects of recombinant human DNase I on sputum in patients with cystic fibrosis. *Thorax* 1996;**51**:119–25.
9. **Fuchs HJ,** Borowitz DS, Christiansen DH, *et al.* Effect of aerosolized recombinant human DNase on exacerbations of respiratory symptoms and on pulmonary function in patients with cystic fibrosis. The Pulmozyme Study Group. *N Engl J Med* 1994;**331**:637–42.
10. **Greally P.** Human recombinant DNase for mucus plugging in status asthmaticus. *Lancet* 1995;**346**:1423–4.
11. **Puterman AS,** Weinberg EG. rhDNase in acute asthma. *Pediatr Pulmonol* 1997;**23**:316–7.
12. **Durward A,** Forte V, Shemie SD. Resolution of mucus plugging and atelectasis after intratracheal rhDNase therapy in a mechanically ventilated child with refractory status asthmaticus. *Crit Care Med* 2000;**28**:560–2.
13. **Patel A,** Harrison E, Durward A, *et al.* Intratracheal recombinant human deoxyribonuclease in acute life-threatening asthma refractory to conventional treatment. *Br J Anaesth* 2000;**84**:505–7.
14. **Qureshi F,** Pestian J, Davis P, *et al.* Effect of nebulized ipratropium on the hospitalization rates of children with asthma. *N Engl J Med* 1998;**339**:1030–5.
15. **Fahy JV,** Steiger DJ, Liu J, *et al.* Markers of mucus secretion and DNA levels in induced sputum from asthmatic and from healthy subjects. *Am Rev Respir Dis* 1993;**147**:1132–7.
16. **Potter JL,** Spector S, Matthews LW, *et al.* Studies on pulmonary secretions. 3. The nucleic acids in whole pulmonary secretions from patients with cystic fibrosis, bronchiectasis, and laryngectomy. *Am Rev Respir Dis* 1969;**99**:909–16.
17. **Laube BL,** Swift DL, Wagner HN Jr, *et al.* The effect of bronchial obstruction on central airway deposition of a saline aerosol in patients with asthma. *Am Rev Respir Dis* 1986;**133**:740–3.
18. **Green JD.** Pharmacotoxicological expert report Pulmozyme rhDNase Genentech, Inc. *Hum Exp Toxicol* 1994;**13**(Suppl 1):S1–42.

## Lung alert

### Smoking-induced emphysema is an autoimmune process

Emphysematous lung exhibits predominantly T helper type 1 (Th1) cells, but it remains unclear how tobacco induces Th1 immunity and the nature of relevant T cell antigens. This study explored the possibility that smoking induces an autoimmune response.

Isolated blood CD4+ T cells from patients with emphysema and controls were tested to see if a specific T cell response could be elicited using lung-derived elastin or collagen peptides as antigens. In response to elastin peptides, only peripheral blood CD4+ T cells from individuals with emphysema (n = 36) released interferon (IFN) $\gamma$  and interleukin (IL)-10 and proliferated, compared with controls (n = 27) and patients with asthma (n = 9). There was a significant association between the increase in T cell secretion of IFN $\gamma$  and IL-10 with disease severity, as assessed by CT-based quantification and pulmonary function testing. ELISpot analysis confirmed the presence of B cells secreting antibodies to elastin, but not collagen, in emphysematous lung. In addition, significantly fewer regulatory T (T<sub>R</sub>) cells were present in the lungs of subject with emphysema.

Based on these findings, the authors proposed that exposure to cigarette smoke induces secretion of proteolytic enzymes from cells of the innate immune system that liberate lung elastin fragments. In susceptible individuals this may initiate T and B cell-mediated immunity against elastin.

- Lee SH, Goswami S, Grudo A, *et al.* Antielastin autoimmunity in tobacco smoking-induced emphysema. *Nat Med* 2007;**13**:567–9

#### Chuan-Gee Choo

**Correspondence to:** C-G Choo, Specialist Registrar, Newcross Hospital, Woverhampton, UK; [chuangee@hotmail.com](mailto:chuangee@hotmail.com)

*Thorax* 2008;**63**:146