26. **Dempsey JA**, Smith CA, Przybylowski T, *et al.* The ventilatory responsiveness to CO₂ below eupnoea as a determinant of ventilatory stability in sleep. *J Physiol* 2004;**560**:1–11.
27. **Xi L**, Smith CA, Saupe KW, *et al.* Effects of rapid-eye-movement sleep on the apneic threshold in dogs. *J Appl Physiol* 1993;**75**:1129–39.
28. **Parisi RA**, Santiago TV, Edelman NH. Genioglossal and diaphragmatic EMG responses to hypoxia during sleep. *Am Rev Respir Dis* 1988;**138**:610–16.
29. **Younes M**. Role of respiratory control mechanisms in the pathogenesis of obstructive sleep disorders. *J Appl Physiol* 2008;**105**:1389–405.
30. **Beaumont M**, Batejat D, Pierard C, *et al.* Zaleplon and zolpidem objectively alleviate sleep disturbances in mountaineers at a 3,613 meter altitude. *Sleep* 2007;**30**:1527–33.
31. **Anholm JD**, Powles AC, Downey R III, *et al.* Operation Everest II: Arterial oxygen saturation and sleep at extreme simulated altitude. *Am Rev Respir Dis* 1992;**145**:817–26.
32. **Khoo MC**, Anholm JD, Ko SW, *et al.* Dynamics of periodic breathing and arousal during sleep at extreme altitude. *Respir Physiol* 1996;**103**:33–43.
33. **Somers VK**, Mark AL, Abboud FM. Potentiation of sympathetic nerve responses to hypoxia in borderline hypertensive subjects. *Hypertension* 1988;**11**:608–12.
34. **Ryan CM**, Usui K, Floras JS, *et al.* Effect of continuous positive airway pressure on ventricular ectopy in heart failure patients with obstructive sleep apnoea. *Thorax* 2005;**60**:781–5.
35. **Loepky JA**, Roach RC, Maes D, *et al.* Role of hypobaric fluid balance response to hypoxia. *High Alt Med Biol* 2005;**6**:60–71.

Lung alert

Newly identified genetic determinants of lung function

It is well established that pulmonary function is in part genetically determined. These authors report a meta-analysis of genome-wide association study (GWAS) results from 20 288 participants and follow-up analyses in 54 276 participants, identifying five novel genome-wide significant loci for pulmonary function. A companion manuscript from the CHARGE Consortium, which reports a GWAS of lung function in 20 890 participants, also identifies significant associations at three of these sites. These loci were not specific to smokers, genetic factors that influence smoking behaviour or adjustments for smoking exposure. The most probable candidate genes in the regions identified seem to be involved in developmental pathways important for lung growth or tissue remodelling.

While the authors admit that these determinants have been incompletely adjusted for height and were based on cross-sectional measures of lung function, these findings are important for two reasons. First, previous studies in chronic obstructive pulmonary disease (COPD) have reported changes at similar loci, thus raising the possibility that the development of COPD may be predetermined during lung development and further influenced by cigarette smoke exposure. However, it also raises the possibility that the move to define the diagnosis of COPD by abnormal lung function has led to the identification of confounding loci that are simply determinants of lung development rather than disease specific. Mechanistic and pathogenetic models are required to help determine which is the more accurate. Secondly, the identification of multiple loci involved in early lung development allows for a more targeted determination of the mechanisms by which the airways develop and respond to external insult. Detailed longitudinal studies will be required to define and address these issues.

As always with genome studies, more questions are generated than answered, but these papers provide strong evidence for newly identified genetic loci that act as important determinants of pulmonary function.

► **Repapi E**, Sayers I, Wain LV, *et al.* Genome-wide association study identifies five loci associated with lung function. *Nat Genet* 2010;**42**:36–44.

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