9. **Michelet P,** D'Journo XB, Roch A, *et al*. Protective ventilation influences systemic inflammation after esophagectomy: a randomized controlled study. *Anesthesiology* 2006;**105**:911–19.
10. **Wrigge H,** Uhlig U, Zinserling J, *et al*. The effects of different ventilatory settings on pulmonary and systemic inflammatory responses during major surgery. *Anesth Analg* 2004;**98**:775–81.
11. **Wrigge H,** Uhlig U, Baumgarten G, *et al*. Mechanical ventilation strategies and inflammatory responses to cardiac surgery: a prospective randomized clinical trial. *Intensive Care Med* 2005;**31**:1379–87.
12. **Koner O,** Celebi S, Balci H, *et al*. Effects of protective and conventional mechanical ventilation on pulmonary function and systemic cytokine release after cardiopulmonary bypass. *Intensive Care Med* 2004;**30**:620–6.
13. **Choi G,** Wolthuis EK, Bresser P, *et al*. Mechanical ventilation with lower tidal volumes and positive end-expiratory pressure prevents alveolar coagulation in patients without lung injury. *Anesthesiology* 2006;**105**:689–95.
14. **Reis Miranda D,** Gommers D, Struijs A, *et al*. Ventilation according to the open lung concept attenuates pulmonary inflammatory response in cardiac surgery. *Eur J Cardiothorac Surg* 2005;**28**:889–95.
15. **Zupancich E,** Paparella D, Turani F, *et al*. Mechanical ventilation affects inflammatory mediators in patients undergoing cardiopulmonary bypass for cardiac surgery: a randomized clinical trial. *J Thorac Cardiovasc Surg* 2005;**130**:378–83.
16. **Wrigge H,** Zinserling J, Stuber F, *et al*. Effects of mechanical ventilation on release of cytokines into systemic circulation in patients with normal pulmonary function. *Anesthesiology* 2000;**93**:1413–17.
17. **Dripps RD,** Lamont A, Eckenhoff JE. The role of anesthesia in surgical mortality. *Jama* 1961;**178**:261–6.
18. **Demedts M,** Costabel U. ATS/ERS international multidisciplinary consensus classification of the idiopathic interstitial pneumonias. *Eur Respir J* 2002;**19**:794–6.
19. **Algar FJ,** Alvarez A, Salvatierra A, *et al*. Predicting pulmonary complications after pneumonectomy for lung cancer. *Eur J Cardiothorac Surg* 2003;**23**:201–8.
20. **Mitchell CK,** Smoger SH, Pfeifer MP, *et al*. Multivariate analysis of factors associated with postoperative pulmonary complications following general elective surgery. *Arch Surg* 1998;**133**:194–8.
21. **Reilly DF,** McNeely MJ, Doerner D, *et al*. Self-reported exercise tolerance and the risk of serious perioperative complications. *Arch Intern Med* 1999;**159**:2185–92.
22. **Polanczyk CA,** Marcantonio E, Goldman L, *et al*. Impact of age on perioperative complications and length of stay in patients undergoing noncardiac surgery. *Ann Intern Med* 2001;**134**:637–43.
23. **Griffin SM,** Shaw IH, Dresner SM. Early complications after Ivor Lewis subtotal esophagectomy with two-field lymphadenectomy: risk factors and management. *J Am Coll Surg* 2002;**194**:285–97.
24. **Yilmaz M,** Iscimen R, Keegan MT, *et al*. Six-month survival of patients with acute lung injury: prospective cohort study. *Crit Care Med* 2007;**35**:2303–7.
25. **Tandon S,** Batchelor A, Bullock R, *et al*. Peri-operative risk factors for acute lung injury after elective oesophagectomy. *Br J Anaesth* 2001;**86**:633–8.
26. **Gajic O,** Rana R, Winters JL, *et al*. Transfusion-related acute lung injury in the critically ill: prospective nested case-control study. *Am J Respir Crit Care Med* 2007;**176**:886–91.
27. **Koch CG,** Li L, Sessler DI, *et al*. Duration of red-cell storage and complications after cardiac surgery. *N Engl J Med* 2008;**358**:1229–39.
28. **Moss M,** Bucher B, Moore FA, *et al*. The role of chronic alcohol abuse in the development of acute respiratory distress syndrome in adults. *JAMA* 1996;**275**:50–4.
29. **Gottlieb S.** United States brings in new rules to prevent surgical errors. *BMJ* 2004;**329**:13.
30. **Esteban A,** Anzueto A, Frutos F, *et al*. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. *JAMA* 2002;**287**:345–55.
31. **Gajic O,** Dara SI, Mendez JL, *et al*. Ventilator-associated lung injury in patients without acute lung injury at the onset of mechanical ventilation. *Crit Care Med* 2004;**32**:1817–24.
32. **Gajic O,** Frutos-Vivar F, Esteban A, *et al*. Ventilator settings as a risk factor for acute respiratory distress syndrome in mechanically ventilated patients. *Intensive Care Med* 2005;**31**:922–6.
33. **Jia MEX,** Malhotra A, Saeed M, *et al*. Risk factors for acute respiratory distress syndrome in patients mechanically ventilated for greater than 48 hours. *Chest* 2008;**133**:853–61.
34. **van der Werff YD,** van der Houwen HK, Heijmans PJ, *et al*. Postpneumonectomy pulmonary edema. A retrospective analysis of incidence and possible risk factors. *Chest* 1997;**111**:1278–84.
35. **Pinsky MR.** Clinical significance of pulmonary artery occlusion pressure. *Intensive Care Med* 2003;**29**:175–8.

Lung alert

Cystic fibrosis: a novel therapeutic angle or a false dawn

Worldwide, approximately 10% of patients with cystic fibrosis have premature stop codons in the mRNA for the CFTR gene. These result in phenotypically severe variants of cystic fibrosis. PTC124 is a small molecule available as an oral preparation which allows the ribosome to selectively ignore these mutations and hence produce the functioning protein.

This prospective phase II trial recruited 23 adults with cystic fibrosis, all of whom had at least one nonsense mutation. The patients were given PTC124 orally in two cycles of 28 days. In the first cycle, 16 mg/kg was administered daily in three divided doses for 14 days followed by 14 days without treatment. In the second cycle, the same patients received an increased dose of 40 mg/kg.

Across both cycles, statistical significance was achieved in the three primary outcome goals using nasal potential measurement. There were increases in total chloride transport, in the proportion who developed normal chloride transport and in the proportion of patients who responded to treatment predefined as a change in potential difference of −5 mV or more. No drug-related serious adverse events were recorded.

The results were less impressive in the second cycle. The authors attribute this to a possible decrease in sensitivity of nasal potential difference with repeated testing, but did not consider other causes such as a tolerability effect with PTC124 or a dose saturation below 40 mg/kg. The numbers are small and judgement should be reserved until phase III trials are undertaken; however, these results are promising and may herald a trend towards individually tailored genetic treatment for specific mutations in cystic fibrosis.

► Kerem E, Hirawat S, Armoni S, *et al*. Effectiveness of PTC124 treatment of cystic fibrosis caused by nonsense mutations: a prospective phase II trial. *Lancet* 2008;**372**:719–27.

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