

- costimulatory pathways involved in the antigen-presenting cells-T-cell interaction. *Blood* 1999;**93**:1277–86.
48. **Bonfield TL**, Raychaudhuri B, Malur A, *et al.* PU.1 regulation of human alveolar macrophage differentiation requires granulocyte-macrophage colony-stimulating factor. *Am J Physiol Lung Cell Mol Physiol* 2003;**285**:L1132–6.
49. **Schwandner R**, Dziarski R, Wesche H, *et al.* Peptidoglycan- and lipoteichoic acid-induced cell activation is mediated by toll-like receptor 2. *J Biol Chem* 1999;**274**:17406–9.
50. **Underhill DM**, Ozinsky A, Smith KD, *et al.* Toll-like receptor-2 mediates mycobacteria-induced proinflammatory signaling in macrophages. *Proc Natl Acad Sci U S A* 1999;**96**:14459–63.

Lung alert

Increasing PEEP while preventing hyperinflation reduces hypoxaemia but not mortality

It has previously been shown that lung protection with low tidal volume ventilation improves mortality in patients with acute lung injury (ALI) and adult respiratory distress syndrome (ARDS). Two randomised controlled multicentre studies have looked at different ways of using increased positive end expiratory pressure (PEEP) to aid alveolar recruitment while limiting hyperinflation to see if this further reduces mortality.

The first study, involving 767 patients, compared groups which were randomly assigned to either a minimal distension strategy (PEEP 5–9 cm H₂O) or increased recruitment strategy (PEEP increased until plateau pressure 28–30 cm H₂O reached). Tidal volumes were set at 6 ml/kg of predicted body weight and the oxygenation goal was reached by adjusting the fraction of inspired oxygen (F_{IO}₂). There was no change in mortality between the two groups. The increased recruitment group had significantly more ventilator free days (median 7 vs 3; *p* = 0.04) and organ failure-free days (median 6 vs 2; *p* = 0.04). Fewer patients in this group needed rescue therapy for episodes of severe hypoxaemia (34.6% vs 18.7%; *p* < 0.001). The main limitation was that no guidance was given for rescue therapies allowed for severe refractory hypoxaemia.

The second study, involving 985 patients, compared groups that were randomly assigned to either a control group or an open lung approach group. PEEP was titrated according to F_{IO}₂ rather than to a plateau pressure with the control group assigned a lower PEEP. In addition, the open lung group started with a recruitment manoeuvre, repeated up to four times daily and were allowed a higher plateau pressure (40 cm H₂O) than the control group (30 cm H₂O). Both groups aimed for a tidal volume of 6 ml/kg and were allowed to deviate from assigned protocols or use rescue therapy if specific criteria were met. There was no difference in mortality or ventilator days but the open lung group had less hypoxaemia and required lower F_{IO}₂. The main limitations were that different ventilator modes and plateau pressures were used rather than recruitment measures being the only variable.

While neither study showed improved mortality, it may be that only ARDS (rather than all ALIs) or an as yet undefined subset would benefit from alveolar recruitment.

- ▶ Mercat A, Richard J-CM, Vielle B, *et al.* Positive end-expiratory pressure setting in adults with acute lung injury and adult respiratory distress syndrome. *JAMA* 2008;**299**:646–55.
- ▶ Meade MO, Cook DJ, Guyatt GH, *et al.* Ventilation strategy using low tidal volumes, recruitment manoeuvres, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome. *JAMA* 2008;**299**:637–45.

James Walters

Correspondence to: Dr J Walters, Gloucestershire Royal Hospital, Gloucestershire, UK; james@drwalters.co.uk