syndrome) of whom 1084 (84%) were treated with methylprednisolone while 207 (16%) received no steroid treatment.² Glucose levels were the same at baseline in both groups but in those treated with steroid the mean value rose significantly. The highest blood glucose in the methylprednisolone group was 8.68 mmol/l (± 4.8) compared with 6.39 mmol/l (± 3.71) in the non-steroid cohort ($p < 0.05$).² This change is comparable with the 1.8 mmol/l increase observed with hydrocortisone in a multicentre randomised trial of steroids in sepsis.³

An increase of this magnitude appears trivial, but significantly alters glucose levels within the lung. Airway surface fluid is a key element of pulmonary defence, and glucose is normally maintained 3–20 times lower than plasma levels by active transport mechanisms.⁴ The latter has a threshold of 6.7–9.7 mmol/l and glucose increases in airway fluid when plasma levels exceed this value. Furthermore, pulmonary inflammation disrupts epithelial integrity and also leads to a rise in lung glucose. Airway surface fluid contains surfactant proteins A and D, which not only are important host defence molecules against a broad spectrum of pathogens but, in addition, possess a number of immunoregulatory properties. These proteins are members of the collectin family, which recognise carbohydrate moieties on microorganisms through their lectin domain. The latter also binds glucose, which may act as a competitive inhibitor of surfactant proteins.⁵ It is little surprise, therefore, that raised airway fluid glucose promotes pulmonary inflammation and infection.⁴

Corticosteroids are an important treatment modality in many pulmonary and extrapulmonary diseases. It is likely that in many diseases such as COPD, interstitial lung disease and asthma, modest hyperglycaemia associated with steroid use abrogates the beneficial anti-inflammatory effects of these drugs. Further investigation of this phenomenon is warranted not only in COPD, but also in other pulmonary diseases in which steroids are commonly used.

**Matt P Wise, Anthony P Brooks,
Megan H Purcell-Jones**

University Hospital of Wales, Cardiff, UK

Correspondence to Dr Matt P Wise, Adult Critical Care, University Hospital of Wales, Cardiff CF14 4XW, UK; mattwise@doctors.org.uk

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

Accepted 15 December 2009
Published Online First 7 June 2010

Thorax 2011;66:449–450.
doi:10.1136/thx.2009.132076

REFERENCES

1. **Chakrabarti B**, Angus RM, Agarwal S, *et al*. Hyperglycaemia as a predictor of outcome during

non-invasive ventilation in decompensated COPD. *Thorax* 2009;64:857–62.

2. **Li N**, Wang GF, Wu YF, *et al*. Side effects of glucocorticosteroids in the management of 1291 patients with SARS. *Beijing Da Xue Xue Bao* 2004;36:519–24.
3. **Annane D**, Sebille V, Bellissant E. Corticosteroids for patients with septic shock. *JAMA* 2003;289:43–4.
4. **Baker EH**, Wood DM, Brennan AL, *et al*. Hyperglycaemia and pulmonary infection. *Proc Nutr Soc* 2006;65:227–35.
5. **Reading PC**, Allison J, Crouch EC, *et al*. Increased susceptibility of diabetic mice to influenza virus infection: compromise of collectin-mediated host defence of the lung by glucose? *J Virol* 1998;72:6884–7.

Authors' response

We thank Dr Wise and colleagues¹ for their thoughtful response to our work in chronic obstructive pulmonary disease patients with decompensated hypercapnic respiratory failure.² We believe that modest hyperglycaemia is a useful way of identifying patients at greatest risk of treatment failure with non-invasive ventilation, but we are more cautious than those correspondents in implicating corticosteroid use either acute or chronic as a major aetiological factor. Our study was clearly underpowered to exclude such an association but we did not see any trend towards a worse outcome in relationship to previous oral corticosteroid use. The issues reported in the patients with severe acute respiratory syndrome taking methylprednisolone are less likely to apply in our patients in whom the dose of systemic corticosteroids used to treat chronic obstructive pulmonary disease exacerbations is significantly lower than in the severe acute respiratory syndrome study or than that reported in the USA.³ Previous use of inhaled corticosteroids can be associated with clinically diagnosed pneumonia, but hyperglycaemia was not an issue in that large trial nor is pneumonia incidence always increased by inhaled steroid use.⁵ The mechanisms suggested by which hyperglycaemia promotes lung infection are plausible but will be difficult to test in humans. Disappointingly, recent data suggest that tightly controlling hyperglycaemia in an intensive care unit setting is associated with worse rather than better outcomes, which support our view that this may be a marker of disease severity rather than a causal factor leading to a worse outcome.⁷

**Biswajit Chakrabarti,¹ Robert M Angus,²
Peter M A Calverley¹**

¹Clinical Sciences Centre, University Hospital Aintree, University of Liverpool, Liverpool, UK; ²Aintree Chest Centre, University Hospital Aintree, Liverpool, UK

Correspondence to Biswajit Chakrabarti, Aintree Chest Centre, University Hospital Aintree, Lower Lane, Liverpool L9 7AL, UK; biz@doctors.org.uk

Competing interests None.

Provenance and peer review Not commissioned; not externally peer reviewed.

Accepted 24 August 2010
Published Online First 26 October 2010

Thorax 2011;66:450. doi:10.1136/thx.2010.149757

REFERENCES

1. **Wise MP**, Brooks AP, Purcell-Jones MH, *et al*. Steroid-induced hyperglycaemia and pulmonary disease. *Thorax* 2011;66:441–42.
2. **Chakrabarti B**, Angus RM, Agarwal S, *et al*. Hyperglycaemia as a predictor of outcome during non-invasive ventilation in decompensated COPD. *Thorax* 2009;64:857–62.
3. **Davies L**, Angus RM, Calverley PM. Oral corticosteroids in patients admitted to hospital with exacerbations of chronic obstructive pulmonary disease: a prospective randomised controlled trial. *Lancet* 1999;354:456–60.
4. **Niewoehner DE**, Erbland ML, Deupree RH, *et al*. Effect of systemic glucocorticoids on exacerbations of chronic obstructive pulmonary disease. *N Engl J Med* 1999;340:1941–7.
5. **Calverley PM**, Anderson JA, Celli B, *et al*. Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. *N Engl J Med* 2007;356:775–89.
6. **Sin DD**, Wu L, Anderson JA, *et al*. Inhaled corticosteroids and mortality in chronic obstructive pulmonary disease. *Thorax* 2005;60:992–7.
7. **NICE–SUGAR Study Investigators**. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med* 2009;360:1283–97.

Pneumocystis jirovecii in pleural infection: a nucleic acid amplification study

Pleural infection is associated with 20% mortality in the 80 000 new cases per year in the UK and USA. *Streptococcus* species cause ~50% of community-acquired bacterial pleural infection.¹ *Staphylococcus aureus* and anaerobes are isolated in 8% and 20% of cases, respectively, and 12% of pleural infections yield polymicrobial cultures. However, even using culture and nucleic acid amplification techniques (NAATs), 26% of cases remain microbiologically obscure.

The negative microbiology may be due to previous antibiotic treatment, varying pathogen prevalence in different pleural fluid locules (already known to vary biochemically²) or the presence of organisms that are difficult to detect using conventional techniques. One such possible organism is *Pneumocystis jirovecii*, which requires specialist diagnostic techniques (eg, Grocott–Gomori methenamine silver staining or NAATs).

P. jirovecii has been identified in sputum and bronchoalveolar lavage (BAL) fluid from both immunocompromised and immunocompetent individuals—it has been isolated from BAL fluid using NAATs in 18% of patients with lung disease without HIV