PostScript

LETTERS

Bacterial co-infection and interpretation of immunological data from BAL fluid specimens in severe RSV bronchiolitis

Thorburn *et al* reported on pulmonary bacterial co-infection in children with severe respiratory syncytial virus (RSV) bronchiolitis.¹ The authors found that 40% of children with severe RSV infection were infected with bacteria in their lower airways. The most commonly isolated organism was *Haemophilus influenzae*, a Gram negative lipopolysaccharide producing organism.

Previous studies from the same paediatric intensive care unit have investigated cytokines, chemokines, and the cellular composition of specimens obtained by non-bronchoscopic bronchoalveolar lavage (BAL) in ventilated children with RSV infection using the same method as was used in this study.^{2,3} The investigators found a predominance of neutrophil leucocytes, increased production of interleukin (IL)-9,² and increased levels of a number of chemokines³ compared with controls without lower respiratory tract infection.

Lipopolysaccharide, as produced by *H influenzae*, is a potent activator of the nuclear transcription factor NF- κ B.⁴ NF- κ B is essential in activating IL-9 production⁵ and in the production of an array of chemokines.⁴ The neutrophilia found in the airways of children with severe RSV bronchiolitis may be partly due to bacterial stimulation of the production of the neutrophil leucocyte attracting chemokine IL-8 via NF- κ B activation and indirectly via IL-9 stimulating IL-8 production. Neutrophil leucocytes can contribute to IL-8 production after IL-9 stimulation of its IL-9 receptors, and McNamara *et al*² have demonstrated IL-9 bound to neutrophils by immunofluorescence studies in lavage samples.

Futures studies investigating the immunopathology in the lower respiratory tract of children with RSV infection need to rule out bacterial co-infection to obtain an unbiased view of the immunopathogenesis of this disease.

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Competing interests: none.

References

- 1 Thorburn K, Harigopal S, Reddy V, *et al*. High incidence of pulmonary bacterial co-infection in children with severe respiratory syncytial virus (RSV) bronchiolitis. *Thorax* 2006;61:611-5.
- 2 McNamara PS, Flanagan BF, Baldwin LM, *et al*. Interleukin-9 production in the lungs of infants with severe respiratory syncytial virus bronchiolitis. *Lancet* 2004;363:1031-7.
- 3 McNamara PS, Flanagan BF, Hart CA, *et al*. Production of chemokines in the lungs of infants with severe respiratory syncytial virus bronchiolitis. *J Infect Dis* 2005;191:1225-32.
- 4 Liu SF, Malik AB. NF- κ B activation as a pathological mechanism of septic shock and

inflammation. *Am J Physiol Lung Cell Mol Physiol* 2006;290:622-45.

- 5 Stassen M, Muller C, Arnold M, *et al*. IL-9 and IL-13 production by activated mast cells is strongly enhanced in the presence of lipopolysaccharide: NF-kappa B is decisively involved in the expression of IL-9. *J Immunol* 2001;166:4301-8.

Still awaiting a useful tool for predicting severe CAP

We agree with Buising *et al* that severity scores for community acquired pneumonia (CAP) that are accurate for predicting 30 day mortality, such as the pneumonia severity index (PSI) and CURB-65, are unlikely to be as useful for predicting the need for admission to the intensive care unit (ICU).¹ In our institution, as their paper describes, the patients who die from CAP are generally older, have unstable co-morbid conditions, and are made "not for resuscitation", so are not suitable candidates for admission to the ICU. We also agree that the revised American Thoracic Society criteria are of very limited use as a tool for predicting severe CAP as the major criteria (need for mechanical ventilation or inotropic support) identify patients who should already be in the ICU rather than predict those who will need it.²

However, we have some concerns with the methodology used to validate the scoring systems in their study.¹ The entry criteria based on the admission diagnosis of CAP could lead to errors since, in our experience, the admission diagnosis is frequently incorrect. Published reports suggest that the disparity between clinicians' reports of chest radiographs for CAP and those reported by radiologists is high, with 20-50% of radiographs not confirmed as demonstrating pneumonia, despite the clinician's assessment as such.³⁻⁵ In our own institution, a review of the radiographs of almost 1000 patients admitted with an emergency department admission diagnosis of "CAP" showed that it was confirmed in less than half of the cases (unpublished data). Buising *et al* believe that this admission diagnosis is appropriate to analyse, since it is used by the admitting medical staff who first assess the patient to develop the patient's severity score. However, if that is the case, we are concerned by the fact that Buising *et al* calculated the severity scores based on the worst results in the first 24 hours after admission, rather than the initial set of observations and investigations as is the intended use of both the PSI and CURB-65 assessment tools.^{6,7} Using the worst results from the first 24 hours may falsely increase these scores so that they may, in fact, be even less accurate than those reported by Buising *et al*. Ideally, a scoring system for identifying patients who may need more aggressive treatment should detect these patients as early as possible, rather than requiring the initial 24 hour observations to make this assessment. Secondly, it would appear from table 5 in the paper by Buising *et al*, in which only patients with a discharge diagnosis of CAP were analysed, that since the 95% confidence intervals for sensitivity and specificity for PSI class IV/V and modified BTS in predicting death and/or

need for ICU management overlap, both these scoring systems are statistically comparable in predicting these outcomes.

While the findings of Buising *et al* are interesting, we believe that clinicians are still without a useful tool for identifying patients with severe CAP who are likely to require ICU management.

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References

- 1 Buising KL, Thursky KA, Black JF, *et al*. Reconsidering what is meant by severe pneumonia: a prospective comparison of severity scores for community acquired pneumonia. *Thorax* 2006;61:419-24.
- 2 Ewig S, Ruiz M, Mensa J, *et al*. Severe community-acquired pneumonia. Assessment of severity criteria. *Am J Respir Crit Care Med* 1998;158:1102-8.
- 3 Malcolm C, Marrie TJ. Antibiotic therapy for ambulatory patients with community-acquired pneumonia in an emergency department setting. *Arch Intern Med* 2003;163:797-802.
- 4 Campbell SG, Murray DD, Hawass A, *et al*. Agreement between emergency physician diagnosis and radiologist reports in patients discharged from an emergency department with community-acquired pneumonia. *Emerg Radiol* 2005;11:242-6.
- 5 Novack V, Avnon LS, Smolyakov A, *et al*. Disagreement in the interpretation of chest radiographs among specialists and clinical outcomes of patients hospitalized with suspected pneumonia. *Eur J Intern Med* 2006;17:43-7.
- 6 Fine MJ, Auble TE, Yealy DM, *et al*. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med* 1997;336:243-50.
- 7 Lim WS, van der Eerden MM, Laing R, *et al*. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003;58:377-82.

Authors' reply

Charles *et al* have raised two important issues concerning our study¹:

(1) Should scoring systems intended to guide admission or the need for ICU assessment or empirical antibiotic choices be built using the data from patients who the examining clinicians believe to have pneumonia based upon their interpretation of the chest radiograph (that is, exactly the group of patients to whom the scoring system will be applied in practice), or should they be built only using data from those patients in whom the radiologist described consolidation on the chest radiograph? We chose the former in order to make the results as directly relevant and applicable as possible and note that, in 88% of our patients, the treating clinicians applied a discharge diagnosis (with knowledge of the radiologists report) of pneumonia.

(2) Having chosen the patient group, should we build the model with data available to the emergency department clinician