

end-of-life care may be more appropriate, but there are many other important issues that explain the observed outcomes. End of life in chronic obstructive pulmonary disease (COPD) exacerbations is a difficult area of care for which the guidelines are currently vague and where our own data have shown that in large-scale studies all predictors of outcome combined only explain a minority of the variance in outcome.³ Finally studies of patient choice when offered IMV for respiratory failure in COPD have shown patient preference for intervention beyond that considered appropriate by intensivists in many cases.⁴ In essence, this is an area where prospective research is required to better understand both the wishes of patients and the costs and benefits of interventionist or palliative choices.

C M Roberts,¹ R A Stone,² R J Buckingham,³
N A Pursey,³ D Lowe³

¹Chest Clinic, Whipps Cross University Hospital, London, UK; ²Somerset Lung Centre, Musgrove Park Hospital, Taunton, UK; ³Royal College of Physicians, London, UK

Correspondence to C M Roberts, Chest Clinic, Whipps Cross University Hospital, London E11 1NR, UK; michael.roberts@whippsx.nhs.uk

Competing interests None.

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

Accepted 17 February 2011

Published Online First 8 March 2011

Thorax 2012;**67**:82–83.

doi:10.1136/thx.2011.161299

REFERENCES

1. Mydin HH, Murphy S, Antunes G. Acidosis, non-invasive ventilation and mortality in hospitalised COPD exacerbations. *Thorax* 2012;**67**:82.
2. Roberts CM, Stone RA, Buckingham RJ, et al. Acidosis, non-invasive ventilation and mortality in hospitalised COPD exacerbations. *Thorax* 2011;**66**:43–8.
3. Roberts CM, Lowe D, Bucknall CE, et al. Clinical audit indicators of outcome following admission to hospital with acute exacerbation of chronic obstructive pulmonary disease. *Thorax* 2002;**57**:137–41.
4. Wildman M, Sanderson C, Groves J, et al. Implications of prognostic pessimism in patients with chronic obstructive pulmonary disease (COPD) or asthma admitted to intensive care in the UK within the COPD and asthma outcome study (CAOS). *BMJ* 2007;**355**:1132–5.

Childhood immunisation with conjugate vaccines and prevention of pneumonia

Principi and Esposito¹ describe that widespread use of *Haemophilus influenzae* b (Hib) and pneumococcal conjugate vaccine (PCV7) has nearly eliminated pneumonia due to the first pathogen and significantly reduced the number of cases due to the second pathogen. So, they advise a strong recommendation of these vaccines worldwide. However, the

Indonesia probe-trial cited by them actually found more cases of pneumonia admitted to hospital among those vaccinated, and meningitis admissions were not reduced significantly either. The trial did not support a major role for Hib vaccine in overall pneumonia prevention programmes, but in view of high incidences of Hib meningitis and pneumonia found in the study, the authors mentioned that inclusion of Hib vaccine in routine immunisation programmes in Asia deserves consideration. But if we further analyse this statement, the following points need attention. The cost of these newer vaccines precludes their routine and universal use in most developing countries. In addition, the shift of the disease epidemiology due to an increase in the less common serotypes not covered by the vaccine is being reported. Children in Gambia receiving both vaccines continued to have 13.4 episodes of severe pneumonia per 1000 child years.² In western countries, the wisdom of having introduced the Hib vaccine is also now being questioned. The vaccine has effectively reduced the incidence of Hib disease, at the same time resulting in an increase of non-Hib and non-serotype strains, causing invasive disease in the post-Hib vaccine era.³ In the Dallas study, PCV7 reduced the incidence of invasive pneumococcal disease (IPD) by reducing the incidence of vaccine-type disease, but at the same time increasing non-vaccine serotypes (particularly 19A) that are more resistant to antimicrobials.⁴ PCV7 covers 65–80% of serotypes associated with IPD in western countries, but the serotype coverage is lower in developing countries. The new generation vaccines (PCV10 and PCV13) are expected to cover 50–80% of IPD not only in western countries but also worldwide.⁵ In addition to the PCV7 serotypes, PCV10 covers against strains 1, 5 and 7F and PCV13 covers against strains 1, 3, 5, 6A, 7F and 19A. Both these vaccines also offer broader coverage against pneumococcal strains prevalent in developing countries. So, further surveillance of the changing ecology of these organisms, and study of the true burden of disease in developing countries (also including the cost–benefit ratio of vaccinating each child), is needed before proceeding to universal immunisation.

Rashmi Ranjan Das

Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), New Delhi, India

Correspondence to Dr Rashmi Ranjan Das, Department of Pediatrics, All India Institute of Medical Sciences (AIIMS), New Delhi 110029, India; rrdas05@gmail.com

Competing interests None.

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

Accepted 26 January 2011

Published Online First 17 April 2011

Thorax 2012;**67**:83.

doi:10.1136/thx.2011.159244

REFERENCES

1. Principi N, Esposito S. Management of severe community-acquired pneumonia of children in developing and developed countries. *Thorax* 2011;**66**:815–22.
2. Cutts F, Zaman S, Enwere G, et al. Gambian Pneumococcal Vaccine Trial Group. Efficacy of nine-valent pneumococcal conjugate vaccine against pneumonia and invasive pneumococcal disease in The Gambia: randomised, double-blind, placebo controlled trial. *Lancet* 2005;**365**:1139–46.
3. Brown VM, Madden S, Kelly L, et al. Invasive *Haemophilus influenzae* disease caused by non-type b strains in Northwestern Ontario, Canada, 2002–2008. *Clin Infect Dis* 2009;**49**:1240–3.
4. Messina AF, Katz-Gaynor K, Barton T, et al. Impact of the pneumococcal conjugate vaccine on serotype distribution and antimicrobial resistance of invasive *Streptococcus pneumoniae* isolates in Dallas, TX, children from 1999 through 2005. *Pediatr Infect Dis J* 2007;**26**:461–7.
5. Anon. Therapy for children with invasive pneumococcal infections. American Academy of Pediatrics Committee on Infectious Diseases. *Pediatrics* 1997;**99**:289–99.

Authors' response

We thank Dr Das for his letter¹ regarding our paper on the management of severe community-acquired pneumonia in children.² He questions our suggestion that both *Haemophilus influenzae* type b (Hib) conjugate and pneumococcal conjugate (PCV) vaccines could be given to Asian children living in developing countries on the grounds that the incidence of infections due to Hib and the pneumococcal serotypes included in PCV is low. He also states that there is no clear demonstration that either vaccine is effective, and the risk of replacement phenomena is a significant limitation.

Regarding the burden of Hib infection, data show that Hib is significantly more important in Asia than previously thought mainly because a number of cases are not identified by the short-term administration of low-dose antibiotics used in many countries, which often prevents the microbiological diagnosis of Hib infections.³ Studies carried out in Indonesia and Bangladesh indicate that the clinical efficacy of Hib vaccine is much greater than that calculated on the basis of the reduction in bacteriologically confirmed cases,³ thus suggesting a higher incidence of Hib diseases and the theoretical efficacy of vaccination. Furthermore, the available data (including data from Asia) indicate that the Hib vaccine has an 18% overall effect on radiologically confirmed pneumonia.⁴

The emergence of new *H influenzae* serotypes after Hib vaccine administration (including those that cannot be typed) has been documented in some, but not all geographical areas. Furthermore, their relevance is marginal when set against the advantage of vaccination. All the studies have shown that the reduction in invasive Hib diseases is significantly greater than the increase in those due to new serotypes.⁵ The same is true of PCV, whose role in

conditioning replacement has probably been overestimated because the emergence of the new 19A serotype has also been observed when the vaccine was not used.⁶ Moreover, the importance of PCV in reducing the incidence of pneumococcal community-acquired pneumonia by about 23% in a low-income, low-mortality developing Asian country, the Philippines, has recently been clearly demonstrated by Lucero *et al.*⁷

Finally, the use of Hib vaccines and PCV can induce significant herd immunity, thus justifying the conclusion that both should be used in Asian children.

Nicola Principi, Susanna Esposito

Department of Maternal and Pediatric Sciences, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

Correspondence to Nicola Principi, Department of Maternal and Pediatric Sciences, Università degli Studi di Milano, Fondazione IRCCS "Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena", Via Commenda 9, 20122 Milano, Italy; nicola.principi@unimi.it

Funding Bando Giovani Ricercatori 2007, Italian Ministry of Health.

Competing interests None.

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

Accepted 26 January 2011
Published Online First 17 April 2011

Thorax 2012;**67**:83–84.
doi:10.1136/thx.2011.160135

REFERENCES

1. **Das RR.** Childhood immunisation with conjugate vaccines and prevention of pneumonia. *Thorax* 2012;**67**:85.
2. **Principi N,** Esposito S. Management of severe community-acquired pneumonia of children in developing and developed countries. *Thorax* 2011;**66**:815–22.
3. **Eskola J.** Foresight in medicine: current challenges with *Haemophilus influenzae* type b conjugate vaccines. *J Intern Med* 2010;**267**:241–50.
4. **Theodoratou E,** Johnson S, Jhass A, *et al.* The effect of *Haemophilus influenzae* type b and pneumococcal conjugate vaccines on childhood pneumonia incidence, severe morbidity and mortality. *Int J Epidemiol* 2010;**39**(Suppl 1):i172–85.
5. **Gessner BD.** *Haemophilus influenzae* type b vaccine impact in resource-poor settings in Asia and Africa. *Expert Rev Vaccines* 2009;**8**:91–102.

6. **Choi EH,** Kim SH, Eun BW, *et al.* *Streptococcus pneumoniae* serotype 19A in children, South Korea. *Emerg Infect Dis* 2008;**14**:275–81.
7. **Lucero MG,** Nohynek H, Williams G, *et al.* Efficacy of an 11-valent pneumococcal conjugate vaccine against radiologically confirmed pneumonia among children less than 2 years of age in the Philippines: a randomized, double-blind, placebo-controlled trial. *Pediatr Infect Dis J* 2009;**28**:455–62.

CORRECTION

doi:10.1136/thx.2009.127274corr2

Kemp SV, El Batrawy SH, Harrison RN, *et al.* Learning curves for endobronchial ultrasound using cusum analysis. *Thorax* 2010;**65**:534–8. doi:10.1136/thx.2009.127274. This paper has a formula incorrectly specified. The formula for Q on page 535 which reads $Q = \ln((1 - p_1)/(1 - p_0))$ should read: $Q = \ln((1 - p_0)/(1 - p_1))$.²

Thorax

SAVE TIME AND KEEP INFORMED

SCAN. SIGN UP. eTOC.



Utilise our Quick Response code (QR) to sign up for our electronic table of contents (eTOC) alert.
To make this simple you can sign up now via your Smartphone.

FOLLOW THESE THREE EASY STEPS:

1. Download a free QR reader from your handset's app store
 2. Hold your Smartphone over the QR code
 3. You will then be forwarded to the eTOC sign up page
- To find out more about QR codes visit group.bmj.com/products/journals/qr-codes



thorax.bmj.com

BMJ Journals