For any doctor meningococcal disease remains a rarity, and expertise in its recognition is not common among those in the front line. However, careful assessment of all children with abnormal vital signs may lead to earlier recognition of meningococcal sepsis and application of the new edition of the meningococcal treatment algorithm described here may help in the early management of critically ill patients with meningococcal disease. We hope and believe that this approach to management of children with meningococcal disease is making a difference.

ACKNOWLEDGEMENTS

We thank the Meningitis Research Foundation for their support in printing and widely distributing the algorithm and especially Linda Glennie.

Arch Dis Child 2007;**92**:283–286.
doi: 10.1136/adc.2006.102384

Authors' affiliations

Andrew J Pollard, Department of Paediatrics, University of Oxford, Oxford, UK
Simon Nadel, Nelly Ninis, Michael Levin, Department of Paediatrics, Imperial College School of Medicine, St Mary's Hospital, London, UK
Saul N Faust, Wellcome Trust Clinical Research Facility, University of Southampton, Southampton, UK

Correspondence to: Dr Andrew J Pollard, Department of Paediatrics, University of Oxford, Level 2, Children's Hospital, Oxford OX3 9DU, UK; andrew.pollard@paediatrics.ox.ac.uk

REFERENCES

- 1 Pollard AJ, Britto J, Nadel S, *et al*. Emergency management of meningococcal disease. *Arch Dis Child* 1999;**80**:290–6.
- 2 Anon. Archives this month. *Arch Dis Child* 2001;**85**:177–9.
- 3 Heyderman RS. Early management of suspected bacterial meningitis and meningococcal septicaemia in immunocompetent adults—second edition. *J Infect* 2005;**50**:373–4.
- 4 Booy R, Habibi P, Nadel S, *et al*. Reduction in case fatality rate from meningococcal disease associated with improved healthcare delivery. *Arch Dis Child* 2001;**85**:386–90.
- 5 Finfer S, Bellomo R, Boyce N, *et al*. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. *N Engl J Med* 2004;**350**:2247–56.
- 6 Carcillo JA, Fields AL. Clinical practice parameters for hemodynamic support of pediatric and neonatal patients in septic shock. *Crit Care Med* 2002;**30**:1365–78.
- 7 Fine GF, Borland LM. The future of the cuffed endotracheal tube. *Paediatr Anaesth* 2004;**14**:38–42.
- 8 Newth CJ, Rachman B, Patel N, *et al*. The use of cuffed versus uncuffed endotracheal tubes in pediatric intensive care. *J Pediatr* 2004;**144**:333–7.
- 9 Tunkel AR, Hartman BJ, Kaplan SL, *et al*. Practice guidelines for the management of bacterial meningitis. *Clin Infect Dis* 2004;**39**:1267–84.
- 10 Riordan FA, Cant AJ. When to do a lumbar puncture. *Arch Dis Child* 2002;**87**:235–7.
- 11 Heyderman RS, Robb SA, Kendall BE, *et al*. Does computed tomography have a role in the evaluation of complicated acute bacterial meningitis in childhood? *Dev Med Child Neurol* 1992;**34**:870–5.
- 12 Hasbun R, Abrahams J, Jekel J, *et al*. Computed tomography of the head before lumbar puncture in adults with suspected meningitis. *N Engl J Med* 2001;**345**:1727–33.
- 13 McIntyre PB, Berkey CS, King SM, *et al*. Dexamethasone as adjunctive therapy in bacterial meningitis. A meta-analysis of randomized clinical trials since 1988. *JAMA* 1997;**278**:925–31.
- 14 van de Beek D, de Gans J, McIntyre P, *et al*. Steroids in adults with acute bacterial meningitis: a systematic review. *Lancet Infect Dis* 2004;**4**:139–43.
- 15 van de Beek D, de Gans J, McIntyre P, *et al*. Corticosteroids in acute bacterial meningitis. *Cochrane Database Syst Rev* 2003;(3):CD004405.
- 16 Molyneux EM, Walsh AL, Forsyth H, *et al*. Dexamethasone treatment in childhood bacterial meningitis in Malawi: a randomised controlled trial. *Lancet* 2002;**360**:211–18.
- 17 Hatherill M, Tibby SM, Hilliard T, *et al*. Adrenal insufficiency in septic shock. *Arch Dis Child* 1999;**80**:51–5.
- 18 van Woensel JB, Biezeveld MH, Alders AM, *et al*. Adrenocorticotrophic hormone and cortisol levels in relation to inflammatory response and disease severity in children with meningococcal disease. *J Infect Dis* 2001;**184**:1532–7.
- 19 Ninis N, Phillips C, Bailey L, *et al*. The role of healthcare delivery in the outcome of meningococcal disease in children: case-control study of fatal and non-fatal cases. *BMJ* 2005;**330**:1475.
- 20 Thorburn K, Baines P, Thomson A, *et al*. Mortality in severe meningococcal disease. *Arch Dis Child* 2001;**85**:382–5.
- 21 Thompson MJ, Ninis N, Perera R, *et al*. Clinical recognition of meningococcal disease in children and adolescents. *Lancet* 2006;**367**:397–403.
- 22 Riordan FA, Marzouk O, Thomson AP, *et al*. Prospective validation of the Glasgow Meningococcal Septicaemia Prognostic Score. Comparison with other scoring methods. *Eur J Pediatr* 2002;**161**:531–7.
- 23 Hodgetts TJ, Hall J, Maconochie M, *et al*. Paediatric triage tape. *Prehosp Immediate Care* 1998;**2**:155–9.
- 24 Wallis LA, Healy M, Undy MB, *et al*. Age related reference ranges for respiration rate and heart rate from 4 to 16 years. *Arch Dis Child* 2005;**90**:1117–21.
- 25 Taylor JA, Del Beccaro M, Done S, *et al*. Establishing clinically relevant standards for tachypnea in febrile children younger than 2 years. *Arch Pediatr Adolesc Med* 1995;**149**:283–7.
- 26 Hanna CM, Greenes DS. How much tachycardia in infants can be attributed to fever? *Ann Emerg Med* 2004;**43**:699–705.
- 27 Goldstein B, Giroir B, Randolph A. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatr Crit Care Med* 2005;**6**:2–8.
- 28 Thornton AJ, Morley CJ, Hewson PH, *et al*. Symptoms in 298 infants under 6 months old, seen at home. *Arch Dis Child* 1990;**65**:280–5.

Childhood pneumonia

Dealing with childhood pneumonia in developing countries: how can we make a difference?

Zulfiqar A Bhutta

Perspective on the paper by Hazir *et al* (see page 291)

The past few years have seen renewed attention focused on the persistent burden of childhood mortality globally. Of the 10.6 million deaths of children under 5 every year, the vast majority occur in a mere 42 countries of the developing world. It is also apparent that despite advances in understanding the

pathophysiology and significance of the major causes of child death, most of the known killers such as diarrhoeal disorders and acute respiratory infections (ARI) still continue to take a heavy toll.¹

Most of the deaths from ARI are due to pneumonia. The annual incidence of pneumonia is estimated at 151 million

new cases per year, of which 11–20 million (7–13%) cases are severe enough to require hospitalisation.² Serious neonatal infections account for 30–50% of neonatal mortality in different regions and it is difficult to disentangle sepsis and deaths from pneumonia. With the inclusion of neonatal pneumonia, recent estimates indicate that pneumonia is the single largest contributor to child mortality, accounting for almost 28–34% of all under-5 deaths globally.³ It is also important to note that in contrast to diarrhoeal deaths where mortality rates have reduced dramatically, despite the introduction of a global programme for the control of ARI almost 15 years ago, there has been little change in overall burden of deaths from pneumonia. Figure 1 shows estimates of deaths of children under 5 from pneumonia, and although recent figures represent improvements in estimates rather than increasing trends, it is evident that the global burden of deaths

Figure 1 Recent trends in pneumonia mortality. GBD, Global Burden of Disease; CHERG, Childhood Epidemiology Reference Group.

from pneumonia remains unchanged. These composite figures also hide the enormous differentials that exist in ARI mortality rates between countries and between various socioeconomic groups within countries. The bulk of deaths from childhood pneumonia affect the poor who have higher exposure rates to risk factors for developing ARI such as overcrowding, poor environmental conditions, malnutrition and also limited access to curative health services.

Such issues of access to preventive and curative services are the main driving force behind revised strategies for reducing the burden of deaths due to childhood pneumonia in developing countries. Although classic clinical detection algorithms and management strategies for ARI have largely relied on management in health facilities, there is increasing recognition of the importance of reaching the poor in community settings. These strategies involve recognising and managing pneumonia in community settings through community health workers (CHWs).⁴ Notwithstanding emerging evidence of the feasibility and effect of ambulatory management of pneumonia by CHWs, there are several issues that merit careful consideration as this strategy is scaled up. Two key questions are whether current algorithms for clinical diagnosis of pneumonia are robust, and if so, are current antibiotic regimens adequate for the treatment of pneumonia in primary care settings?

These questions have been answered to some extent by Hazir *et al*⁵ in the current issue of *Archives*. Although it is reassuring that the currently recommended dose of co-trimoxazole was effective in most cases, it is uncertain whether the clinical criteria used by health workers correctly identified most cases of bacterial pneumonia. Recent studies by the same group in a consecutive group of children diagnosed with non-severe and severe pneumonia in ambulatory settings showed that only 14% had radiologically confirmed pneumonia.⁶ Thus it is possible that current diagnostic criteria for non-severe pneumonia may pick up a significant proportion of children with viral

Table 1 Treatment outcomes for non-severe pneumonia

Authors (location)	Years	Target population, age range	Treatment regimen	Treatment failure rate
Keeley <i>et al</i> ⁷ (Zimbabwe)	1987–1988	614 children, age 3 months–12 years	Co-trimoxazole 20/4 mg/kg/day twice daily for 5 days Procaine penicillin 300 000 IU/kg/day I/M once daily for 5 days	2% 1% 13%
Straus <i>et al</i> ⁸ (two sites in Pakistan)	1991–1992	595 children, age 2–59 months	Amoxicillin 45 mg/kg/day for 5 days Co-trimoxazole 20/4 mg/kg/day for 5 days	23%
COMET Study ¹¹ (nine sites in Pakistan)	1995–1996	1143 children, age 2–59 months	Co-trimoxazole 20/4 mg/kg/day for 5 days Co-trimoxazole 40/8 mg/kg/day for 5 days	19% 21%
CATCHUP Study Group ¹² (eight sites in Pakistan)	1998–1999	1471 children, age 2–59 months	Amoxicillin 50 mg/kg/day for 5 days Co-trimoxazole 20/4 mg/kg/day for 5 days	16% 19%
MASCOT Pneumonia Study group ¹³ (seven sites in Pakistan)	1999–2001	2000 children, age 2–59 months	Amoxicillin 45 mg/kg/day for 3 days Amoxicillin 45 mg/kg/day for 5 days	21% 20%
ISCAP Study ¹⁴ (seven referral hospitals in India)	2000–2002	2188 children, age 2–59 months	Amoxicillin 31–54 mg/kg/day for 3 days Amoxicillin 31–54 mg/kg/day for 5 days	11% 10%

CATCHUP, Co-trimoxazole Amoxicillin Trial in Children Under 5 years for Pneumonia; COMET, Cotrimoxazole Multicentre Efficacy; MASCOT, Multicentre Amoxycillin Short Course Therapy.

lower respiratory infections, which may not need antibiotic treatment at all. Given the lack of specificity of clinical features, it is also difficult to envisage that CHWs and other health workers will be able to readily diagnose pneumonia on clinical criteria alone without ancillary diagnostic tools or aids. Given the desire to reduce mortality from pneumonia, public health-policy makers have accepted some overdiagnosis as inevitable in this regard. However, as such treatment regimens and antibiotic use are scaled up in population settings by CHWs, there are implications for public health policy that must be considered.

Few studies on antimicrobial treatment of pneumonia include concomitant microbiological information, and although there is substantial evidence from recent *in vitro* studies to indicate that resistance to commonly used antibiotics is increasing,^{7–8} most studies on treatment have relied on clinical failure rates to assess this aspect. Table 1 indicates treatment failure rates among children with non-severe pneumonia treated with various regimens over the past 15 years with treatment failure rates ranging from 10% to 23%.^{9–14} Although the differences in clinical response rates in some of these studies may relate to different patient populations and variable application of clinical diagnostic criteria, they may also represent genuine differences in antimicrobial resistance patterns. Notwithstanding the findings by Hazir *et al*,⁵ further studies on the efficacy of amoxicillin are needed in children with radiologically confirmed pneumonia.

These findings underscore the continued need for preventive strategies, as well as alternative improved diagnostic and treatment regimens. Clinical approaches for the management of childhood pneumonia are considerably hampered by the lack of a gold standard, as classic microbiological methods have poor sensitivity and current algorithms lack sufficient specificity. It is therefore likely that community strategies for the recognition and management of pneumonia by ancillary health workers that rely on simple clinical criteria, other than auscultation, will over diagnose bacterial pneumonia. There are legitimate concerns that widespread use of first-line antibiotics for all ARIs will lead to loss of effectiveness. Table 1 summarises the outcomes from recent therapeutic trials for the treatment of non-severe pneumonia, indicating treatment failure rates exceeding 15% in many cases. It is therefore imperative that antibiotic regimens for both dosage and duration be evidence based and their use restricted as much as possible.

It is therefore important that developing countries look at a combination of strategies for reducing the burden and mortality from pneumonia. These include the important role of preventive strategies such as control of environmental factors (eg, indoor air pollution)¹⁵ dealing with prevalent micronutrient deficiencies such as zinc and vitamin A deficiencies and promotion of household behaviours such as exclusive breast feeding^{16–17} and hand washing.¹⁸ Many of these preventive strategies have health benefits that far

exceed mere reduction in respiratory infections, such as reduction in diarrhoea burden and improvement in nutrition indices.

There has been considerable progress in vaccination strategies for the prevention of childhood infections and pneumonia. The importance of measles and pertussis vaccine in reducing child mortality is well established. Recent public health successes with large scale introduction of *Haemophilus influenzae* type b vaccine in developing countries^{19–20} also indicate that this vaccine must now become part of the universal expanded programme on immunisation vaccination package. Similar preliminary success with pneumococcal conjugate vaccine in Gambia²¹ and South Africa²² also raises the hope that we may soon have vaccines against the common bacterial pathogens which cause pneumonia.

Arch Dis Child 2007;**92**:286–288.
doi: 10.1136/adc.2006.111849

Correspondence to: Dr Z A Bhutta, Department of Paediatrics and Child Health, The Aga Khan University, Karachi, Pakistan; zulfiqar.bhutta@aku.edu

Competing interests: None declared.

REFERENCES

- 1 Bryce J, Boschi-Pinto C, Shibuya K, WHO Child Health Epidemiology Reference Group, et al. WHO estimates of the causes of death in children. *Lancet* 2005;**365**:1147–52.
- 2 Rudan I, Tomaskovic L, Boschi-Pinto C, WHO Child Health Epidemiology Reference Group, et al. Global estimate of the incidence of clinical pneumonia among children under five years of age. *Bull World Health Organ* 2004;**82**:895–903.
- 3 Wardlaw T, Salama P, Johansson EW, et al. Pneumonia: the leading killer of children. *Lancet* 2006;**368**:1048–50.
- 4 WHO UNICEF. WHO UNICEF joint statement. Management of pneumonia in community settings. 2004. WHO/FCH/CAH/04.06.
- 5 Hazir H, Qazi SA, Nisar YB, et al. Comparison of standard versus double dose of amoxicillin in the treatment of non-severe pneumonia in children aged 2–5 months: a multi-centre, double blind, randomized controlled trial in Pakistan. *Arch Dis Child* 2007;**92**:291–7.
- 6 Hazir T, Nisar YB, Qazi SA, et al. Chest radiography in children aged 2–59 months diagnosed with non-severe pneumonia as defined by World Health Organization: descriptive multicentre study in Pakistan. *BMJ* 2006;**333**:629.
- 7 Jain A, Kumar P, Awasthi S. High ampicillin resistance in different biotypes and serotypes of *Haemophilus influenzae* colonizing the nasopharynx of healthy school-going Indian children. *J Med Microbiol*, 2006;**55**, (Pt 2):133–7.
- 8 Echave P, Bille J, Audet C, et al. Percentage, bacterial etiology and antibiotic susceptibility of acute respiratory infection and pneumonia among children in rural Senegal. *J Trop Pediatr* 2003;**49**:28–32.
- 9 Keeley DJ, Nkrumah FK, Kapuyanyika C. Randomized trial of sulfamethoxazole + trimethoprim versus procaine penicillin for the outpatient treatment of childhood pneumonia in Zimbabwe. *Bull World Health Organ* 1990;**68**:185–92.
- 10 Straus WL, Qazi SA, Kundi Z, et al. Antimicrobial resistance and clinical effectiveness of cotrimoxazole versus amoxicillin for pneumonia among children in Pakistan: randomised controlled trial. Pakistan Co-trimoxazole Study Group. *Lancet* 1998;**352**:270–4.
- 11 Rasmussen ZA, Bari A, Qazi S, et al. COMET (Cotrimoxazole Multicentre Efficacy) Study Group. Randomized controlled trial of standard versus double dose cotrimoxazole for childhood pneumonia in Pakistan. *Bull World Health Organ* 2005;**83**:10–19.
- 12 Catchup Study Group. Clinical efficacy of cotrimoxazole versus amoxicillin twice daily for treatment of pneumonia: a randomised controlled clinical trial in Pakistan. *Arch Dis Child* 2002;**86**:113–18.
- 13 Pakistan Multicentre Amoxycillin Short Course Therapy (MASCOT) pneumonia study group. Clinical efficacy of 3 days versus 5 days of oral amoxicillin for treatment of childhood pneumonia: a multicentre double-blind trial. *Lancet* 2002;**360**:835–41.
- 14 Agarwal G, Awasthi S, Kabra SK, ISCAP Study Group, et al. Three day versus five day treatment with amoxicillin for non-severe pneumonia in young children: a multicentre randomised controlled trial. *BMJ* 2004;**328**:791.
- 15 Bruce N, McCracken J, Albalak R, et al. Impact of improved stoves, house construction and child location on levels of indoor air pollution exposure in young Guatemalan children. *J Expo Anal Environ Epidemiol* 2004;**14**(Suppl 1):S26–33.
- 16 Kirkwood BR, Gove S, Rogers S, et al. Potential interventions for the prevention of childhood pneumonia in developing countries: a systematic review. *Bull World Health Organ* 1995;**73**:793–8.
- 17 Victora CG, Kirkwood BR, Ashworth A, et al. Potential interventions for the prevention of childhood pneumonia in developing countries: improving nutrition. *Am J Clin Nutr* 1999;**70**:309–20.
- 18 Luby SP, Agboatwalla M, Feikin DR, et al. Effect of hand washing on child health: a randomised controlled trial. *Lancet* 2005;**366**:225–33.
- 19 Cowgill KD, Ndiritu M, Nyiro J, et al. Effectiveness of *Haemophilus influenzae* type b conjugate vaccine introduction into routine childhood immunization in Kenya. *JAMA* 2006;**296**:671–8.
- 20 Adegbola RA, Secka O, Lahai G, et al. Elimination of *Haemophilus influenzae* type b (Hib) disease from The Gambia after the introduction of routine immunisation with a Hib conjugate vaccine: a prospective study. *Lancet* 2005;**366**:144–50.
- 21 Cutts FT, Zaman SM, Enwere G, Gambian Pneumococcal Vaccine Trial Group, et al. 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.
- 22 Klugman KP, Madhi SA, Huebner RE, Vaccine Trialists Group, et al. A trial of a 9-valent pneumococcal conjugate vaccine in children with and those without HIV infection. *N Engl J Med* 2003;**349**:1341–8.

Children under pressure

Children under pressure: an underestimated burden?

Saverio Stranges, Francesco P Cappuccio

Perspective on the paper by Jackson *et al* (see page 298)

The study by Jackson *et al*¹ represents a significant contribution to our knowledge in the area of hypertension research and related clinical practice. The definition of national blood pressure references for children and young adults, aged 4–23 years, living in Great Britain provides important, complementary information to the updated US guidelines on the management of high blood pressure in children and adolescents aged 1–17 years,² as well as to earlier attempts to

define normative blood pressure values from other countries.^{3–7} In addition, these centiles will integrate existing charts in the UK regarding other important parameters (eg, body mass index), thereby allowing a more comprehensive characterisation of the health of children. Some distinctive aspects of the study by Jackson *et al*¹ should be highlighted: the representative and large sample size of the seven surveys from which blood pressure data were drawn; the consistent

method applied for blood pressure measurements; the use of a statistical technique such as the LMS method to construct blood pressure centiles, which accounts for the skewness (L), median (M), and coefficient of variation (S) of the blood pressure distribution.⁸ Indeed, this statistical tool had been previously used in a German study to derive normalised reference values for the 24-h ambulatory blood pressure in children and adolescents aged 5–20 years.⁷

In addition to the statistical value of their contribution, the study by Jackson *et al* is particularly relevant because it gives emphasis to a significant problem in the medical field: hypertension in childhood. In the past few decades, the definition of normative values for blood pressure in the paediatric age range has been increasingly recognised as an important issue in clinical practice and public health because of the changing patterns in the epidemiology and associated determinants of hypertension among children and young adults. Several reasons justify the increasing attention to