



THE AGA KHAN UNIVERSITY

eCommons@AKU

Department of Paediatrics and Child Health

Division of Woman and Child Health

January 2008

Managing severe pneumonia in children in developing countries - Increasing resistance to first line antibiotics means recommendations need changing

Zulfiqar Ahmed Bhutta
Aga Khan University, zulfiqar.bhutta@aku.edu

Follow this and additional works at: https://ecommons.aku.edu/pakistan_fhs_mc_women_childhealth_paediatr



Part of the [Pediatrics Commons](#)

Recommended Citation

Bhutta, Z. A. (2008). Managing severe pneumonia in children in developing countries - Increasing resistance to first line antibiotics means recommendations need changing. *British Medical Journal*, 336(7635), 57-58.

Available at: https://ecommons.aku.edu/pakistan_fhs_mc_women_childhealth_paediatr/103

Editorials represent the opinions of the authors and not necessarily those of the *BMJ* or BMA

For the full versions of these articles see bmj.com

EDITORIALS

Gordon Brown's agenda for the NHS

The government has willed the ends, but will it provide the means and mechanisms for effective prevention and improved outcomes?



STEFAN ROUSSEAU/JPA

NEWS, p 62

Chris Ham professor of health policy and management Policy and Management, Health Services Management Centre, University of Birmingham, Birmingham B15 2RT c.j.ham@bham.ac.uk

Competing interests: CH was director of the strategy unit in the Department of Health between 2000 and 2004.

Provenance and peer review: Commissioned; not externally peer reviewed.

BMJ 2008;336:53-4
doi:10.1136/bmj.39455.385868.80

Gordon Brown's first major speech on the National Health Service was spun to the media as a populist plea for health checks and screening programmes to be made widely available. In reality, it offered a reflective and wide ranging assessment of the state of the NHS in England in its 60th year and a broad indication of the future direction of reform.^{1 2} In the process, the speech gave the clearest indication yet of the prime minister's agenda for health policy.

At the heart of this agenda is the need for the benefits of medical advances to be made available in the NHS. In words that echoed Harold Wilson's advocacy of the white heat of technology in the 1960s, Brown praised the progress already made through developments in clinical research, and welcomed the establishment of Europe's largest medical science centre in London. He also indicated his willingness to accept increased concentration of services and hospital closures where there was evidence that this would deliver improved outcomes, even if this risked unpopularity with the public.

The speech emphasised the importance of the prevention of illness as well as the treatment of sickness. Prevention will be promoted by offering easier access to health checks and the provision of screening services recommended by the UK National Screening Committee. Primary care will be expected to play its part, with patients accessing routine tests such as blood tests, electrocardiography, and ultrasound in general practitioners' surgeries. Alongside these NHS measures, Brown called for promotion of exercise in schools, a single labelling system to describe clearly the nutritional value of food products, and a more active role by employers in improving health in the workplace.

The prime minister signalled a renewed commitment to improve the care of people with chronic diseases. Specifically, the NHS will be expected to do more to support people to manage their own conditions through a major expansion of the lay led Expert Patient Programme³ and, more radically, by extending to health care the use of the direct payments—personal health budgets—announced last month for older and disabled people to buy personal (mainly social) care.⁴

The speech also underlined the need to match increased rights for patients with clearer responsibilities. In an adaptation of John F Kennedy's aphorism,

the prime minister argued that patients should ask of the NHS "not just . . . what it can do for you but what, empowered with new advice, support and information, you can do for yourself and your family." More detail will be available later in the year when the much trailed NHS constitution is published, which will set out the "NHS offer" to the public and clarify how the government expects people to take responsibility for managing their own health.

Another key theme was the government's commitment to improve access to primary care services. As well as the familiar refrain that practices should extend opening hours in the evenings and weekends, the prime minister indicated that NHS foundation trusts would be allowed to provide primary care in future. This opened up the prospect of increased competition in primary care, both from the independent sector and from other parts of the NHS—Brown's speech indicated that there would be no "no go" areas of reform as further progress is made in extending patient choice.

Lastly, the prime minister asserted his view that "the NHS is the best insurance system for the long term," with the founding principle that health care should be available on the basis of need and not ability to pay. The importance of public funding is underlined by the need to pool risks as medical advances offer increased potential to diagnose illnesses, the increasing costs of some treatments, and the value of these costs being shared to promote equity.

In setting out the direction of travel for the NHS, the speech was much stronger on the government's priorities rather than how these will be achieved. The emphasis on prevention is welcome, but will more resources be shifted to make these aspirations a reality?

Prevention has had numerous false dawns, extending back at least as far as 1976, and it is not clear how the health reform programme in England will be more successful than previous efforts in making prevention "everybody's business."⁵

More detail is also needed on the plans to improve care for people with chronic diseases. Personal health budgets may empower some people, but they may not be appropriate for people with complex comorbidity—the heaviest users of NHS services with the greatest need for higher standards of care. Equally challenging will be changing the culture of provision

of health care to ensure that patients really are seen as partners and are genuinely empowered to be active participants in care.

These arguments indicate that there is a lacuna in the prime minister's announcements, namely the lack of an explicit theory on how to change public services like the NHS. Gordon Brown clearly does not share Tony Blair's enthusiasm for the use of markets (a word notable by its absence from this speech), but he is yet to reveal his alternative. This week's statement is best seen as the beginning of the process of identifying

a distinctively Brownite agenda for the NHS rather than the final word.

- 1 Brown G. Speech on the national health service. 7 January 2008. www.number10.gov.uk/output/Page14171.asp.
- 2 White C. Prime minister promises raft of new screening tests. *BMJ* 2008;336:62. doi: 10.1136/bmj.39454.738912.4E.
- 3 National Health Service. Expert patients programme. 2007. www.expertpatients.nhs.uk/public/default.aspx.
- 4 Department of health. Putting people first: a shared vision and commitment to the transformation of adult social care. 2007. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_081118.
- 5 Department of Health and Social Security, Prevention and Health. *Everybody's business*. London: HMSO, 1976.

Modernising Medical Careers: final report

Now implement it

Three months after the interim report from Sir John Tooke's independent inquiry into Modernising Medical Careers (MMC) in the United Kingdom¹⁻³ comes the final report.⁴⁻⁶

The interim report was well received—87% of respondents to consultation either agreed or strongly agreed with the original 45 recommendations. Some of these have been slightly tweaked in the final report and two new ones have been added—the creation of a new oversight body for postgraduate medical education and training, and exploration of ways to legally offset or compensate for the effects of the European Working Time Directive.

For practising doctors the final report's recommendations for the structure of postgraduate training will matter most (see figure on bmj.com). Sir John recommends abandoning run through training for something that seems familiar, beginning with a one year post that resembles the pre-registration house officer of old, followed by three years of core specialist training as a registered doctor—a post that resembles the old senior house officer grade.

The report argues for the uncoupling of current foundation years 1 and 2 (FY1 and 2), which would allow universities to guarantee a first medical job to their graduates (currently, European Union medical graduates requiring provisional registration can legitimately compete for FY1 positions). The current FY2 year would be bundled in with current specialist training years 1 and 2 to make up three years of core specialist training. The report rates the change as “entirely consistent” with the principles of training that has a broad based beginning and flexibility, which got mysteriously subverted⁷ somewhere between the chief medical officer's 2002 consultation document *Unfinished Business: proposals for reform of the senior house officer grade* and the first MMC report a year later.

Entry to higher specialist training from core specialist training would entail assessments administered several times a year by national assessment centres, initially introduced on a trial basis for highly competitive specialties. Shortlisting for structured interviews for higher

specialist training posts would take into account assessment scores, answers to specialty specific questions, and structured CVs.

Successful completion of higher specialist training would lead to a certificate of completion of training “confirming readiness for independent practice in that specialty at consultant level.” The interim report had two discrete positions after completion of training—“specialist” and “consultant”—separated by “optional higher specialist exams”. This was understandably interpreted as covert support for a subconsultant grade. Despite some fancy footwork, the final report doesn't banish that suspicion entirely.

The length of training for general practice would be extended to five years—three years of core training plus two years as a general practitioner specialist registrar—bringing it in line with training in other developed European countries.

The interim report laid many of the problems besetting MMC—including unclear lines of responsibility and overemphasis on workforce imperatives—at the door of the Department of Health. Sir John now redresses the balance by proposing that the chief medical officer is made the senior responsible officer for medical education and the medical profession's reference point regarding postgraduate medical education and training.

The chief medical officer would also liaise closely with a completely new body, NHS: Medical Education England (NHS:MEE), the functions of which would include defining the principles underpinning postgraduate medical education and training and holding the ring fenced budget for these in England. The new body is given a part to play in more than a third of the final report's recommendations.

The mismatch between numbers of applicants and available training posts—one of the main causes of juniors' pain in 2007—is beyond the report's remit. Last year there were 32 649 applicants for 23 247 specialist training posts in the UK. Figure 4.17 of the interim report shows that the oversupply of applicants (9402) almost equals the number of applicants with highly skilled migrant programme visas (10 014). This scheme,

NEWS, p 61

Tony Delamothe deputy editor
BMJ, London WC1H 9JR
tdelamothe@bmj.com

Competing interests: TD's wife is a consultant who qualified in the European Economic Area and shortlisted and interviewed for specialty training posts at the London Deanery.

Provenance and peer review: Commissioned; not externally peer reviewed.

BMJ 2008;336:54-5
doi:10.1136/bmj.39455.401817.80

however, is the business of the Home Office and the Treasury, and the Treasury is presumably happy to use an oversupply of applicants to keep down the pressure for salary increases. When the Department of Health tried unilaterally to impose additional conditions to the scheme, it was swatted down by the appeal court for its pains.⁸ The best that the report can do is to call for “a coherent model of medical workforce supply within which apparently conflicting policies on self-sufficiency and open-borders/overproduction should be publicly disclosed and reconciled.”

What are the chances that all 47 of the final report's recommendations will be implemented? The executive summary concludes that strong agreement with the interim report provided “a compelling mandate for the implementation of the proposals.” But will the government agree? Governments have long found the best way to defuse a row is to appoint a suitably qualified member of the great and the good to conduct an inquiry. Nothing need actually change once the hoohah has blown over.

At the same time as Sir John was putting the finishing touches to his report, the House of Commons select committee on health was taking evidence on MMC—from many of the same people Sir John had interviewed. Worryingly, it heard that the secretary of state for health and chief medical officer had recently defended the concept of run through training and were

going to retain it.⁹ It seems unlikely that the select committee's final recommendations will be identical to Sir John's. And Lord Darzi's broader review of the National Health Service may also consider medical careers.

Before any other body's recommendations about postgraduate medical education and training are implemented, they must be shown to be superior to those that have emerged from Sir John's meticulous review of the topic, conducted with an urgency that befits its importance to doctors and patients alike.

- 1 Tooke J. *Aspiring to excellence: findings and recommendations of the independent inquiry into Modernising Medical Careers*. Interim report. MMC Inquiry, 2007. www.mmcinquiry.org.uk.
- 2 Eaton L. Tooke inquiry calls for major overhaul of specialist training. *BMJ* 2007;335:737. doi: 10.1136/bmj.39363.596273.59.
- 3 Delamothe T. Modernising Medical Careers laid bare. *BMJ* 2007;335:733-4.
- 4 Tooke J. *Aspiring to excellence: final report of the independent inquiry into Modernising Medical Careers*. London: MMC Inquiry, 2008. www.mmcinquiry.org.uk.
- 5 Kmietowicz Z. Tooke report wants government to step back from medical education. *BMJ* 2008;336:61; doi: 10.1136/bmj.39455.498600.4E.
- 6 Delamothe T. *The BMJ interview: Sir John Tooke*. 2008. www.bmj.com/audio/index.dtl.
- 7 Madden GBP, Madden AP. Has Modernising Medical Careers lost its way? *BMJ* 2007;335:426-8.
- 8 Dyer C. Foreign doctors win high court challenge over training places. *BMJ* 2007;335:1009; doi: 10.1136/bmj.39398.720012.DB.
- 9 Crockard A, Heard S, Hilborne J, Wilson I, Mehta R, Johnston M. House of Commons select committee on health. *Uncorrected transcript of oral evidence*. To be published as HC 25-iii. www.publications.parliament.uk/pa/cm200708/cmselect/cmhealth/uc25-iii/uc2502.htm.

Using physical barriers to reduce the spread of respiratory viruses

Handwashing and wearing masks, gloves, and gowns are highly effective

RESEARCH, p 77

Martin Dawes chair of family medicine, Department of Family Medicine, McGill University, Montreal H2W 1S4
martin.dawes@mcgill.ca
Competing interests: None declared.

Provenance and peer review: Commissioned; not externally peer reviewed.

BMJ 2008;336:55-6
doi: 10.1136/bmj.39406.511817.BE

Preparing health professionals and the public for a flu pandemic has been the subject of much research worldwide, and governments and public health departments have published various recommendations over the past five years.¹⁻⁴ One aspect of the clinical management of respiratory viruses—namely barrier methods to reduce transmission—is assessed in the accompanying systematic review by Jefferson and colleagues.⁵ This review found that handwashing and wearing masks, gloves, and gowns were effective individually in preventing the spread of severe acute respiratory syndrome, and even more effective when combined (odds ratio 0.09, 95% confidence interval 0.02 to 0.35, number needed to treat (NNT)=3, 2.66 to 4.97). The incremental effect of adding virucidals or antiseptics to normal handwashing to reduce respiratory disease was uncertain.

Because pandemic flu is such a potentially catastrophic event, governments worldwide should have commissioned such a review many years ago and not have left it to the academic community to take the lead. The academic community needs to educate governments that expert advice is not necessarily the best

advice. Guidelines should be based on rigorous systematic reviews and need to be continuously updated.

Government and international websites such as the World Health Organization website on the status of pandemic flu (www.who.int/csr/disease/avian_influenza/phase/en/index.html) are of some help in keeping health professionals up to date with the latest information. However, regularly updated evidence based guidelines containing levels of recommendation and, where possible, measures of effectiveness such as NNT would be very much more helpful to front line clinicians. Guidelines also highlight where the strength of the evidence is weak and more research is needed. We have an annually updated guideline on the management of hypertension,⁶ and it reflects badly on the consistency of knowledge translation that one is not available for influenza.

The messages distributed by governments about how to reduce the spread of respiratory viruses have not been shown to be wrong, although some are not supported by evidence. Jefferson and colleagues' review will allow the effectiveness of the interventions

and the strength of the evidence supporting them to be much more explicit; for example, it will be possible to add numbers needed to treat for handwashing, face masks, and gloves to advisory leaflets for health professionals.

So how does the review help clinicians in primary care? The benefit of washing hands between patients is clear (NNT=4), as is wearing masks (NNT=6), wearing gloves (NNT=5), and wearing gowns (NNT=5). So practices need to have a stock of gloves, simple masks (not necessarily of the advanced N95 make), and gowns. Applying all the recommendations described by various government guidelines⁷—such as isolation, segregation, transport, and identification of patients, creating emergency telephone lists of staff, and on-call cover when staff are sick—may seem daunting to a small practice or office. However, the one advantage with influenza, compared with more sporadic epidemics such as pertussis, is that the practice plan can be tried, evaluated, and modified each year.

Jefferson and colleagues point out that the quality of the trials was highly variable. We do not have enough evidence to be certain about many aspects of care for patients with suspected influenza—for example, which face mask is more cost effective within different health-care settings. Although 336 trials on influenza have been registered on the WHO international clinical trials

registry, only three trials are about reducing transmission using distancing (keeping a physical distance from patients with suspected disease) or barrier methods. The reasons for this include the lack of research capacity and funding and an emphasis on drug based treatments. Governments should continue to fund research to confirm the findings of this review and to investigate other areas of uncertainty that it identifies in the management of people with suspected influenza.

- 1 WHO. WHO strategic action plan for pandemic influenza 2006–2007 (WHO/CDS/EPR/GIP/2006.2). 2006. www.who.int/csr/resources/publications/influenza/WHO_CDS_EPR_GIP_2006_2c.pdf.
- 2 National Health Service. UK Health Departments' influenza pandemic contingency plan. 2005. www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4104437.pdf.
- 3 American College of Physicians, Barnitz L, Berkwitz M. The health care response to pandemic influenza. *Ann Intern Med* 2006;145:135-7.
- 4 Fiore AE, Shay DK, Haber P, Iskander JK, Uyeki TM, Mootrey G; Advisory Committee on Immunization Practices (ACIP), Centers for Disease Control and Prevention (CDC). Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2007. *MMWR Recomm Rep* 2007;56(RR-6):1-54.
- 5 Jefferson T, Foxlee R, Del Mar C, Dooley L, Ferroni E, Hewak B, et al. Physical interventions to interrupt or reduce the spread of respiratory viruses: systematic review. *BMJ* 2008 doi: 10.1136/bmj.39393.510347.BE.
- 6 Khan NA, Hemmelgarn B, Padwal R, Larochelle P, Mahon JL, Lewanczuk RZ, et al. The 2007 Canadian hypertension education program recommendations for the management of hypertension: part 2—therapy. *Can J Cardiol* 2007;23:539-50.
- 7 Department of Health. Infection control training material. 2007. www.dh.gov.uk/en/PandemicFlu/DH_078752.

Parliamentary review asks NICE to do better still

Out goes the arbitrary funding threshold: in come NICE “directives”

Joe Collier emeritus professor in medicines policy St George's Hospital, University of London, SW17 0RE
jcollier@sgul.ac.uk

Competing interests. JC was a specialist advisor to the House of Commons health select committee during this inquiry, as he was for the committee's inquiry into NICE in 2001-2, and its inquiry into the influence of the pharmaceutical industry in 2005. He was also an advisor to the Office of Fair Trading in its 2007 inquiry into the Pharmaceutical Price Regulation Scheme.

Provenance and peer review: Commissioned; not peer reviewed.

BMJ 2008;336:56-7
doi:10.1136/bmj.39454.496748.80

On Wednesday 9 January 2008, the House of Commons health select committee published the report of its second inquiry into the National Institute for Health and Clinical Excellence (NICE).¹ The committee's first inquiry into NICE was published six years ago,² just three years after the institute's launch. Much has happened since the initial inquiry. The institute is now well established and is a core policy driver within the National Health Service in England and Wales (its remit does not cover Scotland), and we know much more about how it operates. Moreover, the working environment of the institute has changed with, for instance, the publication of the Cooksey report on funding for health research in the United Kingdom,³ the introduction of legislation making NICE technology appraisals essentially compulsory,⁴ the involvement of the courts in a legal challenge to NICE,⁵ and most recently the Office of Fair Trading's critical review of how brand name drugs are priced in the UK through the Pharmaceutical Price Regulation Scheme (PPRS).⁶

All these and more have been embraced in this new inquiry, for which members visited equivalent bodies to NICE in Canada, France, and Scotland; took oral evidence from 31 witnesses; and received 124 written submissions. The committee's report contains 32 recommendations, many of which are

far reaching and reflect the work of a particularly effective inquisitorial team.

The report highlights certain disappointments—for example, the failure of NICE to implement some of the committee's recommendations made in 2002, such as making technology appraisals available at the time of drug launches. And the report is critical of the way ministers have tried to influence decision making by NICE. At the same time the committee recognises that NICE now plays a vital role in determining NHS health policy and that this role is going to become “more important and demanding.”

Four particularly notable themes emanate from the recommendations, and these relate primarily to the institute's work on technology appraisals of drugs. Firstly, the committee calls for greater clarity in NICE's decision making processes. The report recommends more communication with stakeholders, a clarification of the institute's role as a rationing body, and a change in terminology so that compulsory advice given in technology appraisals is referred to as a NICE directive, leaving other advice from the institute to be referred to as guidance or guidelines.

Secondly, the committee questions the threshold used by NICE when determining whether or not a new drug should be made available in the NHS. As a

general rule, NICE recommends only new products estimated to cost the NHS less than around £30000 (€40 000; \$59 000) per quality adjusted life year (QALY) for use in the NHS. The committee learnt that this amount was determined by NICE, does not have any basis in hard science, has not changed since NICE's inception, is not related to the NHS budget, is almost certainly higher than that which primary care trusts use when they consider new drugs, and does not take account of key costs such as those borne by carers and social services. The report recommends that a body independent of NICE should be established to review the threshold and set the levels and ranges that the institute uses.

The committee also recommends that NICE appraises all new drugs and that the results of appraisal are available at the time of each drug's launch. These more rapid appraisals would, where appropriate, be followed by more detailed single or multiple appraisals—as happen now—when more research became available. Currently, NICE appraises only a proportion of drugs, and seems to concentrate on those that are new, expensive, and used in acute medicine and secondary care. Moreover, these appraisals are published months or years after a drug is marketed. The current policy delays the introduction of effective new drugs and diverts provision away from older, useful, and possibly cheaper measures that have not been appraised.

Lastly, the committee is concerned about the quality of the data available to NICE and how this quality is assessed. The data used by NICE, which by and large are generated by drug companies and relate to published information, are often weak, inadequate, or biased—and make reliable decision making difficult. The committee wants trial data made available to

NICE that are more complete, more independent (of the drug industry), more relevant to clinical practice, and more amenable to the needs of economic evaluation. All the information available to the UK drug licensing authority should also be available to NICE.

The Department of Health has three months to respond to the report. All of the committee's recommendations are challenging, but it is those relating to the timing and breadth of the technology appraisals that would have the widest implications; if adopted they would inevitably reduce the amount we spend on drugs and temper the influence the drug industry has on clinical practice.⁷ Such changes would also have an important bearing on the proposed reforms to the Pharmaceutical Price Regulation Scheme, in which drug prices would be negotiated at launch for each drug by an independent commission using evidence of the product's perceived clinical value, including evidence from NICE.⁸

- 1 National Institute for Health and Clinical Excellence. *First report of the Health Committee 2007-2008. HC27-I*. London: Stationery Office, 2008.
- 2 National Institute for Clinical Excellence. *Second report of the Health Committee 2001-2002. HC515-I*. London: Stationery Office, 2002.
- 3 Cooksey D. *A review of UK health research funding*. London: Stationery Office, 2006.
- 4 Department of Health. *Directions to PCTs and NHS trusts in England concerning arrangements for the funding of technology appraisal guidance from the National Institute for Clinical Excellence*. London: DOH, 2003.
- 5 Dyer C. NICE faces legal challenge over Alzheimer's drug. *BMJ* 2007;334:654-5.
- 6 Office of Fair Trading. *Pharmaceutical Price Regulation Scheme: an OFT market study*. 2007. www.offt.gov.uk/NR/rdonlyres/7C7A7CC1-F320-4978-AC64-F67F9AB67B6C/0/oft885.pdf.
- 7 House of Commons Select Committee on Health. *Enquiry into the influence of the pharmaceutical industry. Fourth report of the health committee 2004-2005. HC42-I*. London: Stationery Office, 2005. www.publications.parliament.uk/pa/cm200405/cmselect/cmhealth/42/4204.htm.
- 8 Collier J. The Pharmaceutical Price Regulation Scheme. *BMJ* 2007;334:435-43.

Managing severe pneumonia in children in developing countries

Increasing resistance to first line antibiotics means recommendations need changing

Despite advances in our understanding of the epidemiology and distribution of deaths from pneumonia,¹ more than 150 million cases of pneumonia still occur annually, with almost 2.4 million deaths worldwide. Pneumonia is perhaps the most frequent cause of death in children under 5, including during the newborn period.² Deaths from pneumonia in children have increased in the wake of the HIV epidemic in Africa. Most deaths occur early in the course of illness. Because severe pneumonia is usually related to bacterial infection, treatment has largely focused on various antibiotic strategies.

In the accompanying randomised controlled trial, Asghar and colleagues compare the effectiveness of

injectable ampicillin plus gentamicin or chloramphenicol in children aged 2-59 months with severe pneumonia (defined by World Health Organization criteria).³ The trial took place in inpatient wards in tertiary care hospitals in Bangladesh, Ecuador, India, Mexico, Pakistan, Yemen, and Zambia. Significantly more children failed treatment with chloramphenicol at five days (16% *v* 11%, relative risk 1.43, 95% confidence interval 1.03 to 1.97).

The study is one of a series of recent studies aiming to improve the treatment of childhood pneumonia in various settings.^{4 5} These findings confirm that the increasing resistance of common respiratory bacterial pathogens like *Streptococcus pneumoniae* and

RESEARCH, p 80

Zulfiqar A Bhutta Husein Lalji Dewraj professor and chairman, Department of Paediatrics and Child Health, Aga Khan University, Karachi, Pakistan
zulfiqar.bhutta@aku.edu

Competing interests: None declared.

Provenance and peer review: Commissioned; not externally peer reviewed.

BMJ 2008;336:57-8
doi: 10.1136/bmj.39426.672118.80

Haemophilus influenzae to first line antibiotics, such as co-trimoxazole and chloramphenicol, means that recommendations for treating suspected and confirmed pneumonia need to be changed.

Several limitations must be kept in mind before generalising these findings to the treatment of all children with very severe pneumonia. The study was restricted to children older than 2 months and might not apply to a large proportion of newborns and young infants who may have a different cause of pneumonia. Children with empyema or overt pneumatoceles (suggestive of possible *Staphylococcus aureus* infection) were excluded. Similarly, children with wheezing were not included, which potentially limits the applicability of these findings to children with secondary infections related to infection with respiratory syncytial virus or other viruses.⁶

Given that most deaths from pneumonia occur early in the course of the illness, health workers using the integrated management for childhood illness guidelines need to have clear algorithms for triage, stabilisation of children, and initiation of antibiotics. The antibiotic regimens for treating non-severe, severe, and very severe pneumonia should therefore form a continuum that is easy for health systems to implement and monitor on a large scale.

Despite the above limitations, given the increasing rates of drug resistance in common bacteria that cause pneumonia—such as *Streptococcus pneumoniae* and *Haemophilus influenzae*⁷—the current study supports the switch to more effective antibiotics. However, the combination of ampicillin and gentamicin may not be the best choice for developing countries. The need for multiple doses when using this combination may cause problems and lead to reduced adherence. The combination has limited coverage against *Staphylococcus aureus*, and there are legitimate concerns about the spectrum of pathogens that it covers. The spectrum of respiratory infections may have changed in regions where *Haemophilus influenzae* type B vaccine or the new pneumococcal conjugate vaccines have been introduced to include infections with non-vaccine strains as well as Gram negative pathogens.

The growing HIV epidemic in Africa has also altered the epidemiology and spectrum of lower respiratory tract infections in infected children. Cytomegalovirus, *Pneumocystis jirovecii*, and multi-drug resistant non-typhoidal *Salmonella* are now well known to cause pneumonia in children in Africa.⁸ Acute pulmonary tuberculosis may also present with features suggestive of severe pneumonia and must be kept in mind in susceptible populations.

It may be better to use once daily injectable cephalosporins such as ceftriaxone or fluoroquinolones for treating children with very severe pneumonia who require hospital admission or observed ambulatory therapy.⁹ However, the blanket use of second line antimicrobial agents in pneumonia makes the emergence of future resistance more likely, so tighter objective criteria are needed for diagnosing

severe or very severe pneumonia. Many viral lower respiratory tract infections present with tachypnoea and chest recessions, and it may be difficult to distinguish them from bacterial infections on clinical criteria alone.¹⁰ Although recent studies do not indicate a good correlation between radiological results and clinically defined pneumonia,¹¹ the use of portable pulse oximetry may help triage children for hospital admission and additional treatment, such as oxygen and injectable antibiotics.¹² This approach needs to be validated in studies of appropriate diagnostic tools, including newer molecular methods that enable viral and bacterial infections (or combinations of the two) to be identified.

In the long term, the most cost effective way to reduce childhood mortality from pneumonia is to scale up effective evidence based preventive strategies. These strategies include promoting effective childhood immunisations (especially against measles, invasive *Haemophilus influenzae* type B, pneumococcal infections, and possibly influenza), improving environmental conditions through clean water and sanitation, and reducing indoor air pollution. In addition, improving nutrition at a population level may reduce intrauterine growth retardation and deficiencies in micronutrients, such as zinc and vitamin A. The challenge is to make this happen on a large scale.

- Rudan I, Tomaskovic L, Boschi-Pinto C, Campbell H; WHO Child Health Epidemiology Reference Group. Global estimate of the incidence of clinical pneumonia among children under five years of age. *Bull World Health Organ* 2004;82:895-903.
- Wardlaw T, Salama P, Johansson EW, Mason E. Pneumonia: the leading killer of children. *Lancet* 2006;368:1048-50.
- Asghar R, Banajeh S, Egas J, Hibberd P, Iqbal I, Katep-Bwalya M, et al. Chloramphenicol versus ampicillin plus gentamicin for community acquired very severe pneumonia among children aged 2-59 months in low resource settings: multicentre randomised controlled trial (SPEAR study). *BMJ* 2008 doi: 10.1136/bmj.39421.435949.BE.
- Atkinson M, Lakhnampaul M, Smyth A, Vyas H, Weston V, Sithole J, et al. Comparison of oral amoxicillin and intravenous benzyl penicillin for community acquired pneumonia in children (PIVOT trial): a multicentre pragmatic randomised controlled equivalence trial. *Thorax* 2007;62:1102-6.
- Addo-Yobo E, Chisaka N, Hassan M, Hibberd P, Lozano JM, Jeena P, et al. Oral amoxicillin versus injectable penicillin for severe pneumonia in children aged 3 to 59 months: a randomised multicentre equivalency study. *Lancet* 2004;364:1141-8.
- Klein MI, Coviello S, Bauer G, Benitez A, Serra ME, Schiatti MP, et al. The impact of infection with human metapneumovirus and other respiratory viruses in young infants and children at high risk for severe pulmonary disease. *J Infect Dis* 2006;193:1544-51.
- Cardoso MR, Nascimento-Carvalho CM, Ferrero F, Berezin EN, Ruvinsky R, Camargos PA, et al. Penicillin resistant pneumococcus and risk of treatment failure in pneumonia. *Arch Dis Child* 2007. Published online 11 September 2007.
- Graham SM. Impact of HIV on childhood respiratory illness: differences between developing and developed countries. *Pediatr Pulmonol* 2003;36:462-8.
- Bradley JS, Arguedas A, Blumer JL, Sáez-Llorens X, Melkote R, Noel GJ. Comparative study of levofloxacin in the treatment of children with community-acquired pneumonia. *Pediatr Infect Dis J* 2007;26:868-78.
- Bhutta ZA. Dealing with childhood pneumonia in developing countries: how can we make a difference? *Arch Dis Child* 2007;92:286-8.
- Hazir T, Nisar YB, Qazi SA, Khan SF, Raza M, Zameer S, 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.
- Fu LY, Ruthazer R, Wilson I, Patel A, Fox LM, Tuan TA, et al. Brief hospitalization and pulse oximetry for predicting amoxicillin treatment failure in children with severe pneumonia. *Pediatrics* 2006;118:e1822-30.