Acute respiratory infection: a global challenge

Epidemiology
In 19th century Europe acute respiratory infection (ARI) was the most important cause of childhood death. In 1901 Sir William Osler wrote ‘the most widespread and fatal of all acute diseases, pneumonia, is now Captain of the Men of Death’. As childhood mortality levels fell in Europe so the proportion of all deaths due to ARI fell. When life expectancy was below 45 years about 25% of childhood deaths were due to ARI compared with only 4% when life expectancy was higher than 70 years. The fall in ARI mortality accelerated noticeably in the 1950s when antibiotics became widely available.1

This picture is remarkably similar to that in developing countries today. In 1991 there were 53 countries reporting mortality in children under 5 years of age of more than 100/1000 live births.2 Of an estimated total of 12·9 million deaths globally in 1990 in children under 5 years of age, over 3·6 million have been attributed to ARI.3 This represented 28% of all deaths in young children and placed ARI as the largest single cause of childhood mortality. Within this overall estimate respiratory complications of measles accounted for 475 000 deaths and respiratory complication of pertussis for 205 000 deaths. The remaining 2 915 000 deaths are considered to be associated mainly with pneumonia. Although these estimates are based on broad evaluations, a study of available national registration data and of 22 longitudinal community based studies has confirmed ARI as the leading cause of childhood mortality in developing countries.1

The three major causes of death from ARI are pneumonia, bronchiolitis, and acute obstructive laryngitis (the latter principally secondary to measles in developing countries). Data from national registration systems and hospital studies have shown that pneumonia accounts for 80–90% of these deaths. The age specific death rates from ARI are highest in the neonatal period then decline steadily with increasing age. About 80% of ARI deaths in young children occur in infancy. Measles and pertussis continue to be important contributors to ARI mortality, their importance being inversely related to the level of vaccine coverage.1

The incidence of upper respiratory infections in developing countries has been difficult to determine accurately due to problems in defining discrete episodes in children who may have, for example, chronic purulent nasal discharge. However, it is clear that upper respiratory infections are the commonest illnesses in early childhood with incidence rates equivalent to those found in industrialised countries. In contrast incidence rates for lower respiratory infections are higher in developing countries with average rates of about 0·7 episodes/child/year in infancy and 0·3 episodes/child/year in 1–4 year old children. These episodes are principally pneumonia and bronchiolitis as laryngotracheobronchitis and epiglottitis are uncommon problems in most developing countries.4

Aetiology, diagnosis, and treatment
Arguably the most important single advance in paediatric respiratory medicine in the last 20 years were the discoveries, by a group of Australian paediatricians and their collaborators in Papua New Guinea, that the majority of severe pneumonia episodes were caused by two bacteria, Streptococcus pneumoniae and Haemophilus influenzae, rather than by respiratory viruses alone and that pneumonia could be identified reliably by the use of the simple clinical signs of fast breathing and lower chest wall indrawing and without the use of a stethoscope.6 Indeed taking a radiological diagnosis of pneumonia as a ‘gold standard’ these simple clinical signs correctly identified considerably more cases of pneumonia with no increase in the number of false positives compared with the use of a stethoscope.7

These findings have been reproduced and confirmed in numerous developing countries.4 8–14 Mixed respiratory viral/bacterial infections have been found commonly in hospital based studies with respiratory syncytial virus being the predominant respiratory virus isolated in all countries where this has been studied. Up to half of all children admitted to hospital with proved respiratory bacterial infections have been found to have evidence of a concurrent or recent associated respiratory viral infection.9–11 15–19

Intervention studies were carried out in six developing countries. These showed that training health workers to count respiratory rate accurately and recognise lower chest wall indrawing, and to administer oral co-trimoxazole or amoxycillin when pneumonia was identified, led to reductions in ARI specific mortality rates of between 25% and 67% and in overall under 5 year mortality rates of between 13% and 55%.20–27

The recognition that the prompt delivery of simple oral antibiotics to children with pneumonia could avert much
of the appalling mortality has led to a belated but growing international recognition of the problem and support for the developing countries, now numbering more than 80, who have established ARI control programmes.  

Challenges for the future  
What then are the challenges for the immediate future? A number of initiatives are currently being taken to extend current vaccination strategies to include *S. pneumoniae*, *H influenzae* type b, and respiratory syncytial virus, and to explore feasible and cost effective interventions against other important risk factors such as lack of breast feeding, indoor air pollution, and malnutrition. However, in the next 10 years any significant impact on ARI mortality will be achieved through improved treatment of pneumonia and improvement of existing vaccination strategies and this review will concentrate on these areas.

The most pressing need is to extend further the national ARI programmes in developing countries with the highest infant mortality rates. Once fully established there will be an increasing need to integrate these programme activities with those of other health programmes focusing on the management of childhood illness. At a global level this integration is currently being promoted through the 'sick child initiative' coordinated by World Health Organisation (WHO) which encompasses action against ARI, diarrhoea, malaria, meningitis, and malnutrition and is supported by many international agencies.  

However, it will be very difficult to reproduce the spectacular results of the carefully controlled and implemented intervention studies in the setting of health services in developing countries. Doctors and other health workers are often resistant to accepting the current WHO recommendations for the clinical management of pneumonia which are substantially different to those contained in the 'standard' paediatric textbooks with which they were trained.

Paediatricians in developing countries are in a pivotal position to give essential support to growing ARI control programmes by lending their sapiential authority to the promotion of the use of simple clinical signs for the diagnosis of pneumonia, the prescription of cheap, oral, generic antibiotics effective against *S. pneumoniae* and *H influenzae* rather than more costly, and the abandonment of antibiotics and ineffective and often toxic remedies for the treatment of the common cold. They also have important roles in the training of health staff in the proper management of common childhood illnesses including pneumonia; collaborating with Ministry of Health officials in the development of national policies and clinical guidelines for the management of ARI that reflect the latest research evidence; and carrying out research into pneumonia prevention and treatment. Effective but simple methods of audit need to be built into health workers practice so that improvements in clinical practice can be maintained and monitored.

Medical undergraduate education in paediatrics in most developing countries occupies a small section of the undergraduate curriculum and does not adequately reflect the large proportion of general medical time which has to be devoted to the care of children in clinical practice. In addition current undergraduate training in ARI is typically inconsistent with current postgraduate clinical training in ARI for health workers, which is based on WHO guidelines. Priority should be given to a critical review of existing paediatric undergraduate curricula and this might best be promoted and achieved through the current sick child initiative. Academic institutions and paediatric associations in industrialised countries should recognise their responsibility to keep abreast of recent advances in knowledge, adjust their postgraduate education programmes accordingly, and encourage research in areas essential for the effective management of the major paediatric problems in developing countries.

The WHO guidelines for the management of young children with ARI require further research in a number of areas. The observed overlap in clinical presentation between pneumonia and malaria and its consequences for the management of these conditions need to be defined further, and the presentation and management of pneumonia in the first month of life and in severely malnourished children requires further investigation.

The threat of penicillin and co-trimoxazole resistance in *S. pneumoniae* and *H influenzae* is perhaps the most serious threat to the success of the WHO strategy of improved clinical management. The establishment of routine surveillance mechanisms to identify bacterial drug resistance in developing countries is an enormous challenge. The finding that the resistance patterns among nasopharyngeal isolates of *S. pneumoniae* and *H influenzae* in children with pneumonia mirror those of the invasive blood or lung aspirates has made collection of specimens operationally much more feasible. However, the fastidious nature of these organisms, the difficulty with disc diffusion methods in determining co-trimoxazole resistance, and the uncertain relationship between clinical effectiveness and minimal inhibitory concentration values for co-trimoxazole remain important problems. It will be important to identify and evaluate alternative low cost antibiotic regimes for the treatment of childhood pneumonia.

For children with severe pneumonia who have hypoxia, oxygen treatment can be life saving. The availability of oxygen in hospitals in developing countries is, however, very poor. There is a need therefore to train health workers in the correct use of oxygen equipment and in the use of the more efficient but equally effective low flow methods (0.5–1 l/min) of oxygen delivery to young children. Oxygen, when available, is widely misused and wasted. Health workers need to be trained to think of giving oxygen in the same way as they prescribe drug treatment – look for correct indications for use, select the appropriate flow rate and method of delivery (in most instances by nasal cannulas, or nasal or nasopharyngeal canulae), and stop treatment when oxygen is no longer required. There is a role for robust oxygen concentrators in improving availability of oxygen treatment in developing controls, although their maintenance will prove a challenge in many settings. WHO have identified suitable models for developing country conditions and have issued guidance on their use, care, and maintenance.

The issue of communication with patients is of particular importance with respect to ARI as most pneumonia episodes can be treated at home. The family must therefore understand and be persuaded to follow prescribed treatment regimens and know when to return if the child does not respond. In addition as the families of many children who die from pneumonia never seek care from a trained health worker we need to understand better how families make care seeking decisions and how these can be influenced.

Existing national expanded programmes of immunisation deserve continuing support to maintain existing reductions in ARI mortality associated with measles and pertussis. In order to have an impact on the estimated 780 000 deaths from respiratory complications of measles and pertussis, additional immunisation strategies will have to be considered to reach areas of low coverage and to deal with the build up of susceptibles which leads to epidemics even in high coverage areas. Research attention will have to be focused on the clinical management of measles as many
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areas of uncertainty still remain, for example the first line treatment of post-meadles pneumonia.

Finally, the recent attention in many industrialised countries given to the dissemination of research findings and the link with their subsequent implementation in practice is equally important in developing countries. An international study group within the Cochrane Collaboration has been established to review randomised controlled trials of interventions against ARI and the International Union Against Tuberculosis and Lung Diseases have set up an information network on ARI and hold regular international scientific meetings. Initiatives such as these deserve recognition and support. It will be important that both developing country national and international paediatric associations create a mechanism for responding to recognised advances in clinical practice and for promoting the dissemination of improved practice.

There is tremendous potential in the next 10 years to reduce the mortality from pneumonia in children in developing countries. Whether or not this will be achieved will depend to a large extent on the degree to which paediatricians recognise an important role for themselves outside their immediate hospital clinical practice, become more involved in broader child health issues, and take up these challenges.

HARRY CAMPBELL

Department of Public Health Sciences,
University of Edinburgh,
Medical School, Tietov Place,
Edinburgh EH8 9AG

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H Campbell

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