

WHO News and activities

Acute respiratory infections: the forgotten pandemic*

Acute lower respiratory infections cause 19% of all deaths in children younger than 5 years and 8.2% of all disability and premature mortality (as measured by disability-adjusted life years (DALYs)). However, acute lower respiratory infections receive only 0.15% of the research and development budget for health, which amounts to only US\$ 0.51 per DALY — compared to US\$ 85 per DALY for human immunodeficiency virus (HIV) infection, US\$ 13 for asthma, US\$ 10 for rheumatic diseases and US\$ 0.32 for diarrhoeal diseases.

In order to discuss the prevention and treatment of acute respiratory infections a major international conference, which was co-sponsored by WHO, took place on 7–10 July 1997 in Canberra and was attended by experts from all over the world. A total of 35 special workshops and 27 plenary sessions were held. Below is a summary of the conference communique.

Developing countries

In developing countries, pneumonia kills 3 million children every year, and other acute respiratory infections, principally measles and pertussis, kill another million children. This huge mortality goes virtually unnoticed and is a disgrace because we have the means to prevent such deaths: immunization and antibiotic treatment.

Immunization. Most fatal pneumonia in children is caused by *Streptococcus pneumoniae* and *Haemophilus influenzae*. Protein conjugate vaccines against *H. influenzae* type b (Hib) have been available to children in developed countries for several years, and they have virtually eliminated diseases caused by this organism. The vaccine has been shown to be highly effective in preventing Hib pneu-

monia and meningitis in children in developing countries, but it is not used in such countries because it is too expensive and because the amount of illness caused by Hib has not been accurately determined in some countries (in part, because Hib is difficult to grow in culture).

In addition to decreasing the burden of disease caused by Hib, urgent steps should be taken to reduce the price of Hib vaccine to developing countries. The dose of each injection might be substantially reduced with minimal effect on efficacy; and manufacturers could charge developed countries a price that gives a return on the cost of developing and producing the vaccine, while charging developing countries only the cost of production. Most donor countries are reluctant to make a long-term commitment to buying a vaccine for developing countries, but the Children's Vaccine Initiative should consider asking donors to pay for manufacturers to gear up for very large-scale production of Hib vaccine, so that the economies of scale can be achieved rapidly and at minimal cost to purchasers in developing countries. Developed countries, the World Bank, and other international agencies should collaborate with the Children's Vaccine Initiative to reduce the price of new vaccines to developing countries.

Several field trials of *S. pneumoniae* conjugate vaccine are planned, and it is likely that this vaccine will reduce mortality from pneumonia in developing countries even more effectively than Hib vaccine. It must be ensured that *S. pneumoniae* conjugate vaccines become available to children in developing countries much faster than has been the case with the conjugate Hib vaccine. In addition, the current unconjugated 23-valent *S. pneumoniae* vaccine should be further evaluated in developing countries. There is a need for a trial to investigate whether immunizing pregnant women reduces mortality among their infants. Consideration should also be given to performing trials designed to measure the effect on mortality of immunizing everyone in a community aged ≥ 24 months; outcomes of interest would include mortality of young infants (who might be protected by the effects of maternal immunization), of children aged 6–23 months (who might be protected by reduced carriage of *S. pneumoniae* among those who have been immunized), and of people aged ≥ 24 months (who will be protected by the direct effect of immunization).

Unless vaccines are made available to reduce mortality from bacterial pneumonia in developing countries, continued or even increasing use of antibi-

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otics will promote further development of antibiotic-resistant bacteria, with the potential for these organisms to spread to developed countries. Even greater efforts should be made to increase the number of children immunized against measles and pertussis with the available vaccines.

Standard treatment with antibiotics. *S. pneumoniae* and *H. influenzae* cause most fatal pneumonia in children, but these bacteria can be killed by several inexpensive antibiotics. WHO has developed simple guidelines for the antibiotic treatment of pneumonia in children in developing countries, and these have been incorporated into the programme for the Integrated Management of Childhood Illness (IMCI). Controlled trials have shown that the WHO antibiotic treatment regimens reduce pneumonia mortality by 55% and mortality from all causes by 25%. A high priority is to make this simple treatment available to all children in developing countries.

As in developed countries, widespread use of antibiotics in developing countries has resulted in many bacteria becoming partially or completely resistant to some antibiotics. The WHO protocols do not recommend the use of antibiotics for mild infections, which constitute the majority of acute respiratory infections; use of the protocols would reduce the total amount of antibiotics used in most developing countries. However, in many countries, *S. pneumoniae* and *H. influenzae* are often resistant to sulfamethoxazole + trimethoprim (co-trimoxazole), the least expensive antimicrobial agent that is recommended by WHO. A controlled trial should be carried out of amoxicillin given orally three times a day for 2 days, rather than 5 days, to children with mild pneumonia; if effective, such a regimen would make the cost of a course of amoxicillin comparable to that of co-trimoxazole. The diagnosis of pneumonia needs to be improved and made more specific to ensure that the use of antibiotics is restricted to children who will really benefit from them. Developing countries should make serious efforts to regulate the use of antibiotics, for example, by making them available only on prescription from a health worker.

Strong support needs to be provided to developing countries to help them improve and maintain simple health care delivery systems. Greater efforts are needed to involve communities in health care, so that effective treatment becomes available to a much higher proportion of children. Reliable information systems should be established so that high quality data are available to assist in planning for the control of acute respiratory infections. Further research is needed on the role of chlamydia, mycoplasma and ureaplasma in causing pneumonia in children in developing countries, and on the etiology and man-

agement of ear disease. Research is needed on the relative importance of upper respiratory tract infection and skin infection with group A β -haemolytic streptococci, and improved guidelines are required for the presumptive treatment of streptococcal pharyngitis to prevent crippling cardiac disease. In countries where human immunodeficiency virus (HIV) infection is common, the impact of respiratory infections is likely to increase substantially.

Standardized antibiotic treatment has the potential to achieve worthwhile reductions in mortality from pneumonia. However, the impact will be limited by difficulties in ensuring that antibiotics are available to all children all the time, and by increasing bacterial resistance to antibiotics. It is therefore most important that increased efforts be made to ensure that children in developing countries are immunized soon with *H. influenzae* type b vaccine and with the conjugated *S. pneumoniae* vaccine as soon as it is available, and that use of the less expensive unconjugated *S. pneumoniae* vaccine be fully evaluated in pregnant women and in all individuals aged ≥ 24 months.

Developed countries

In developed countries, acute respiratory infections are the leading cause of morbidity, accounting for 20% of medical consultations, 30% of absences from work, and 75% of all antibiotic prescriptions. Such infections are therefore very expensive because of the large number of days of work lost and the high cost of treatment. Nevertheless, there has not been adequate systematic evaluation of the effects of these infections or of available evidence about effective methods of prevention and treatment. For example, 75% of antibiotic prescriptions are for acute respiratory infections, but most of the prescriptions are unnecessary; unnecessary use of antibiotics is expensive and hastens the development of antibiotic resistance. There is a need to develop guidelines for the rational use of antibiotics for acute respiratory infections in adults and children in developed countries, and to devise ways of ensuring that these guidelines are followed closely by medical practitioners. No drug has a substantial effect on the course of viral upper respiratory infections, and doctors and their patients need to be helped to work together to ensure that drugs are used appropriately.

Influenza and pneumococcal pneumonia are still major causes of morbidity and mortality; there needs to be greatly increased use of both influenza vaccine and unconjugated 23-valent pneumococcal vaccine in high-risk groups in developed countries. Further evaluation is needed of the effects of cigarette smoking, air pollution, and child care on acute

respiratory infections. Vitamin C and zinc supplements may reduce the severity of the common cold, and more evidence for this needs to be obtained. The possible therapeutic and prophylactic role of traditional medicines needs rigorous evaluation. Many indigenous populations in developed countries have very high morbidity and mortality from acute respiratory infections, and substantial efforts need to be made to reduce this burden of disease.

There is a need for further research on vaccines against pertussis, *S. pneumoniae*, non-serotypable *H. influenzae*, parainfluenza virus, adenovirus, and respiratory syncytial virus, and on effective antiviral drugs. There is encouraging evidence that immunization of pregnant women with some of these new vaccines may protect their babies against the serious effects of respiratory tract infection in early infancy.

Conclusions

Developing countries

- Too many children continue to die from pneumonia.
- Immunize children with *H. influenzae* type b vaccine now.
- Make conjugate *S. pneumoniae* vaccine available soon.

- Define the role of unconjugated *S. pneumoniae* vaccine.
- Make antibiotic treatment of pneumonia available to all children.

Developed countries

- Systematically evaluate evidence about respiratory infections.
- Develop and promote guidelines for antibiotic prescribing.
- Drugs have little effect on viral upper respiratory infections.
- Greatly increase use of influenza and pneumococcus vaccines

Worldwide

- Acute respiratory infection causes 8.2% of disease burden, but receives only 0.15% of research money.
- Allocate more money to research on acute respiratory infections.
- US \$8000 million per year is wasted on symptomatic treatment

The WHO basic rules for the management of cancer pain

1. Cancer pain can, and should, be treated.
2. Evaluation and treatment of cancer pain are best achieved by a team approach.
3. The first steps are to take a detailed history, and to examine the patient carefully, to determine if the pain is:
 - caused by the cancer, related to the cancer, caused by anticancer treatment, or caused by another disorder;
 - part of a specific syndrome;
 - nociceptive, neuropathic, or mixed nociceptive and neuropathic;
4. Treatment begins with an explanation and combines physical and psychological approaches, using both non-drug and drug treatments.
5. It is useful to have a sequence of specific aims, such as:
 - to increase the hours of pain-free sleep;
 - to relieve the pain when the patient is at rest;
 - to relieve pain when the patient is standing or active.
6. Drugs alone usually give adequate relief from pain caused by cancer, provided that the right drug is administered in the right dose at the right time intervals.
7. "By mouth" : the oral route is the preferred route for analgesics, including morphine.
8. "By the clock": for persistent pain, drugs should be taken at regular time intervals and not "as needed".
9. "By the ladder":
 - Unless the patient is in severe pain, begin by prescribing a non-opioid drug and adjust the dose, if necessary, to the maximum recommended dose.
 - If or when the non-opioid no longer adequately relieves the pain, an opioid drug should be prescribed **in addition to the non-opioid**.
 - If or when an opioid for mild to moderate pain (e.g. codeine) no longer adequately relieves the pain, it should be replaced by an opioid for moderate to severe pain (e.g. morphine).
10. "For the individual": the right dose of an analgesic is the dose that relieves the pain. The dose of oral morphine may range from as little as 5 mg to more than 1000 mg.
11. Adjuvant drugs should be prescribed as indicated.
12. For neuropathic pain, a tricyclic antidepressant or an anticonvulsant is the analgesic of choice.
13. "Attention to detail": it is essential to monitor the patient's response to the treatment to ensure that the patient obtains maximum benefit with as few adverse effects as possible.