

# Lucina



Around the world about one in five childhood deaths is from pneumonia. It is a disease of developing countries in particular and the pneumococcus is the major pathogen. In the Gambia (*Lancet* 2005;**365**:1139–46; see also comment, *ibid*: 1113–4) a randomised controlled trial of a 9-valent pneumococcal conjugate vaccine has produced impressive results. Vaccine efficacy was 37% against a first episode of radiologically confirmed pneumonia, 7% against a first episode of clinical pneumonia, 77% against invasive disease due to vaccine serotypes, 50% against all pneumococcal disease, 15% against any hospital admission, and 16% against death from any cause. It is concluded that all African infants should have pneumococcal conjugate vaccine made available to them.

The Child Health Epidemiology Reference Group (CHERG) was established by the WHO in 2001 to improve worldwide statistics on mortality in the under fives. Figures from this group for 2000–2003 (*Lancet* 2005;**365**:1147–52) show that six causes account for almost three-quarters of the 10.6 million deaths per year in this age group. They are pneumonia (19%), diarrhoea (18%), malaria (8%), neonatal pneumonia or sepsis (10%), prematurity (10%), and neonatal asphyxia (8%). The rates of the communicable causes of death are similar in all WHO regions with the exception of deaths from malaria, 95% of which occur in Africa. Improved child survival will depend on the success of efforts against pneumonia, diarrhoea, undernutrition, and neonatal deaths worldwide and against malaria in Africa.

The gene for neutrophil gelatinase-associated lipocalin (NGAL) is strongly upregulated in the kidney soon after acute renal ischaemia. A study of 71 children in Cincinnati undergoing cardiac surgery on cardiopulmonary bypass (*Lancet* 2005;**365**:1231–8, see also comment, *ibid*: 1205–6) has shown that measurement of urine and serum concentrations of NGAL provides early warning of acute renal injury. Increases in NGAL concentrations at 2 hours after bypass were highly sensitive and specific for acute renal injury but waiting for serum creatinine to rise delayed the diagnosis for another 34 hours on average. NGAL is one of several markers of renal injury being assessed

currently. The hope is that early detection will lead to greater success with treatment.

In Sweden in 1991–96 a total of 71 586 women aged 35–49 years had a singleton birth (*British Journal of Obstetrics and Gynaecology* 2005;**112**:394–402). Twenty-one thousand, seven hundred and forty eight of these women underwent amniocentesis, and 1984 chorionic villus sampling. Amniocentesis was associated with a 32% increase in risk of musculoskeletal deformities such as club foot or congenital hip dislocation and the risk was greatest when the procedure was performed before 14 weeks gestation. There was also a 12% increase in neonatal respiratory problems and this risk peaked with amniocentesis at 14–15 weeks. There were no significantly increased risks after chorionic villus sampling but the researchers comment that a larger study may be needed. The risks of limb reduction defects, fetal or infant death, preterm birth, low birthweight, or fetal distress were not increased significantly after either procedure.

Combined vaccines might simplify immunisation schedules if new vaccines are to be introduced. A combined nine-valent pneumococcal with meningococcal group C conjugate vaccine (Pnc9-MenC) has been tested at two UK centres (*Journal of the American Medical Association* 2005;**293**:1751–8) with disappointing results. A total of 240 infants were given Pnc9-MenC or monovalent group C meningococcal conjugate vaccine (MenC) at 2, 3, and 4 months in addition to other routine immunisations. The MenC component of the combined vaccine was less immunogenic than monovalent MenC vaccine, giving a lower mean serum bactericidal titre and with a titre of >1:8 achieved by 95% (Pnc9-MenC) vs 100% (MenC). Antibody responses to Hib and diphtheria vaccines given at the same time were also less in the Pnc9-MenC group. All nine pneumococcal serotype components of the combined vaccine were immunogenic. Irritability and reduced activity were more common after Pnc9-MenC than after MenC. These researchers conclude that the combined vaccine tested may not be an adequate replacement for current separate pneumococcal and meningococcal vaccines.

Two disease-modifying drugs, methotrexate and leflunomide, have been compared for the treatment of polyarticular juvenile idiopathic arthritis (*New England Journal of Medicine* 2005;**352**:1655–66). The international trial included 94 patients aged 3–17 years; 86 completed 16 weeks of treatment, and 70 entered a 32-week continuation phase. The end point (American College of Rheumatology Pediatric 30 per cent response, ACR Pedi 30) was achieved by 89% (methotrexate) vs 68% (leflunomide) at 16 weeks and the improvement was maintained at 48 weeks. Adverse events were similar in the two groups but a rise in serum aminotransferase concentration was more frequent with methotrexate. Methotrexate was the more effective drug.

Treatment options for children with falciparum malaria in much of sub-Saharan Africa are seriously restricted by antimalarial drug resistance. The most promising option seems to be a combination of artemether with lumefantrine taken as six doses over 3 days (*Lancet* 2005;**365**:1467–73 and 1474–80, see also comment;*ibid*:1441–3). Cost may be a problem and efforts are being made to provide it more cheaply.

Another way of attempting to control malaria in young children is intermittent preventive (or presumptive) treatment (IPT). Sulfadoxine-pyrimethamine given to infants in Tanzania along with routine immunisations at 2, 3, and 9 months reduced the short-term incidence of clinical malaria by 60% and severe anaemia by 50%. It has been suggested that such treatment might inhibit the development of antimalarial immunity but a 2-year follow up study (*Lancet* 2005;**365**:1481–3, see also comment; *ibid*: 1443–4) has shown the opposite effect. On follow up beginning 1 month after the last dose of IPT the rates of clinical malaria were 0.28 vs 0.43 events per person-year at risk among children given sulfadoxine-pyrimethamine or placebo. These researchers argue that the relative ineffectiveness of sulfadoxine-pyrimethamine might mean that the parasites are suppressed rather than killed, allowing the development of antimalarial immunity to proceed. Studies are underway to assess the consequences of IPT for malarial control and immunisation programmes.