WHO recommends ampicillin (or benzylpenicillin) and gentamicin as empirical treatment of sepsis or pneumonia in children under age 2 months in developing countries. [1] For children older than 2 months with very severe pneumonia, WHO recommends chloramphenicol. [1] There are limited data on the incidence of chloramphenicol-resistant and gentamicin-resistant sepsis in rural hospitals in developing countries. In 1984, studies from Goroka Hospital, which serves a large rural area in the highlands of Papua New Guinea, found enteric gram-negative bacilli to be a rare cause of pneumonia or sepsis in children. [2,3] In mid-1997, after finding several neonates with multiresistant Klebsiella sepsis, we began a prospective study to determine the incidence of antibiotic-resistant gram-negative sepsis and their effect on mortality in children at Goroka Hospital.

In children with severe sepsis, and in those who deteriorated despite standard antibiotic treatment, cultures of blood, cerebrospinal fluid (CSF), lung aspirate, and other suspected infected sites were done. In children who died from pneumonia or sepsis, lung aspirates and blood were taken for culture immediately after death. Bacterial identification was done by the method previously described, [4] and antimicrobial sensitivity testing was done by disc diffusion. [5]

61 isolates of non-typhoid enteric gram-negative bacilli were grown from 54 children with sepsis over 16 months. The median age of the children was 5 months (IQR 0.7 to 12 months). 39 of the children were 2 months of age or older (of whom 27 had pneumonia). 28 infections were nosocomially acquired, 30 were community acquired, two were probably community acquired, and in one we could not be certain where the bacteria had been acquired (Table 1). 38 of the 54 children died from gram-negative sepsis. Four died of other causes. Mortality was 78% for community-acquired sepsis, and 84% for nosocomial sepsis (although four of the 19 deaths in those with nosocomial sepsis were primarily due to other causes). Only 12 (24%) children survived. During that time, 3895 children were admitted to Goroka Hospital, and 195 died. Therefore, multiresistant gram-negative sepsis occurred in 1.3% of all admissions, but was a major contributing factor in 19.4% of all deaths. The most common diagnoses of the 54 children were pneumonia (56%), septicaemia (31%), severe malnutrition (20%), diarrhoeal disease (19%), meningitis (9%), measles (7%), prematurity (7%), and septic arthritis or osteomyelitis (7%). Bacteria were cultured from blood (38 patients), lung aspirate (15), pleural aspirate (five), aspirate of abscess (six), cerebrospinal fluid (three), and urine (two).

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<th>Table 1. Sensitivity of bacterial isolates and place of acquisition</th>
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Only six (9.8%) of the 61 isolates were sensitive to chloramphenicol. Chloramphenicol resistance was independent of whether the infection was community or hospital acquired. Four of the sensitive isolates were community acquired ((chi squared) for difference between sensitivity of community and hospital acquired strains, p=0.7). These four chloramphenicol-sensitive isolates were from the children aged older than 2 months with
pneumonia. Sensitivity to gentamicin was dependent on the place of acquisition: 22 (33.9%) of the 61 isolates were sensitive to gentamicin, of which 15 were community acquired ([chi squared] for difference in gentamicin sensitivity between community and hospital acquired infection, p=0.007). Eight (50%) of the 16 isolates from children under 2 months of age were gentamicin sensitive. Only nine (33%) isolates from children over 2 months of age with pneumonia were gentamicin sensitive. Only four (6.5%) of the 61 isolates were sensitive to trimethoprim-sulphamethoxazole, and two (3.3%) were sensitive to ampicillin/amoxycillin. 46 (78%) of 59 isolates tested were sensitive to ceftriaxone.

In 1984, from the same hospital, a series of lung aspirate and blood cultures on 83 children with severe pneumonia isolated one Aeromonas and one Enterobacter cloacae. [2,3] Both of these isolates were sensitive to chloramphenicol and to gentamicin. Although the methods and selection of patients differed somewhat from our current study, Shann and colleagues [2] isolated no other enteric gram-negative bacilli. Infections due to multiresistant gram-negative bacilli are now a fairly common cause of death in the highlands of Papua New Guinea. Non-prescription dispensing of amoxycillin, trimethoprim-sulphamethoxazole, and oral chloramphenicol is common. Apart from intrinsic resistance expected for some bacteria, uncontrolled dispensing is likely to account for the high level of resistance now reported to these three standard antibiotics, and explain why most community-acquired strains are still sensitive to gentamicin.

In our highly selected series, gentamicin would have been the correct drug, based on in-vitro antibiotic sensitivities, for almost 50% of the 15 infants under 2 months of age. In children older than 2 months with pneumonia, chloramphenicol would have been the correct drug in only four cases, and gentamicin the correct drug in nine. The two major causes of severe childhood pneumonia in Papua New Guinea and worldwide are Streptococcus pneumoniae and Haemophilus influenzae. Therefore, chloramphenicol may still be the best first-line drug for very severe pneumonia in developing countries. Where chloramphenicol is widely dispensed without prescription, deaths associated with clinical failure of chloramphenicol, due to enteric gram-negative sepsis, may be common.

REFERENCES


