Neonatal Sepsis and Antibiotic Resistance in Developing Countries

To the Editors:

Neonatal sepsis and other bacterial infections account for roughly 800,000 neonatal deaths annually, which is more than malaria and HIV combined in all children <5 years of age.[1] Standard microbiologic diagnosis by culture and drug-susceptibility testing is unavailable in most health centers and so the available information on prevalence, speciation and drug-susceptibility of the various pathogens that cause sepsis is minimal. Concurrently, World Health Organization guidelines for suspected neonatal sepsis recommend empirical treatment with penicillin or ampicillin and an aminoglycoside (typically, gentamicin) as frontline therapy, with a third-generation cephalosporin such as ceftriaxone or cefotaxime as second line for nonresponders or patients in whom drug-susceptibility testing of bacterial isolates indicates drug resistance to first-line therapy.[2] Reductions in price and local clinical experience is leading to third-generation cephalosporins being commonly used as first-line treatment for severe sepsis in many developing countries raising concerns about the spread of bacteria that are dually resistant to both first- and second-line treatment.

Although the data are scant, those centers from which drug-susceptibility studies have been published suggest alarming rates of resistance to the 2 frontline drugs for both hospital- and community-acquired neonatal sepsis (Table 1), as reviewed.[3,4] In light of these data, the current World Health Organization guidelines appear to be inadequate for the treatment of drug-resistant infections in neonates in the community and hospital settings.

Antibiotic resistance arises from poor infection control practices and gross overuse or inappropriate or prolonged use of antibiotics. Although it may be possible to design novel strategies for more effective antibiotic use, the ultimate solution to the emergence and spread of antibiotic resistant bacterial infections is prevention. Within institutions, multifaceted infection control interventions including provision of consumables, education, internal monitoring and feedback can potentially reduce infection rates, but such strategies require strong leadership and coordination.[5] The predominance of home-birthing practices in rural communities in developing countries, and in particular the lack of a skilled birthing attendant, is linked with higher rates of maternal and neonatal mortality.[6] In addition to promoting skilled birthing attendant deliveries, improving referral pathways and increasing the overall number of institutional deliveries is thought to improve both maternal and neonatal mortality.[6] Although with increasing institutional births, infection control within obstetric theaters and neonatal units that are already overstretched remains a considerable problem.[4]

In all health care settings in developing countries, even with limited budgets, the rigorous application and promotion of relatively affordable "back-to-basics" infection control practices, at institutions and in the community, could have a substantial impact on reducing neonatal mortality and improving <5 mortality rates overall.

TABLE 1. Prevalence of Drug Resistance Within *Klebsiella* species, *Escherichia coli* and *Staphylococcus aureus* in Both Community- and Hospital-acquired Neonatal Sepsis in Developing Countries

	Klebsiella species	*E. coli*	*S. aureus*
Community			
Ampicillin	119/123 (97%)	76/105 (72%)	NA
Gentamicin	72/121 (60%)	14/106 (13%)	NA
Cefotaxime*	43/65 (66%)	8/42 (19%)	NA
Methicilin†	NA	NA	1/28 (4%)
Co-trimoxazole	NA	NA	52/114 (46%)
Hospital			
Ampicillin	609/709 (86%)	278/340 (82%)	NA
Gentamicin	908/1282 (71%)	204/407 (50%)	NA
Cefotaxime*	640/1282 (51%)	213/460 (46%)	NA
Methicilin†	NA	NA	337/884 (38%)
Co-trimoxazole	NA	NA	201/315 (64%)

Adapted from Thaver et al[3] and Zaidi et al[4].
*Or other third-generation cephalosporin.
†Or first-generation cephalosporins, ceftriaxone or cefotaxime.
NA, not available.

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