

## *Haemophilus influenzae* Type b Meningitis in Children, Eritrea

**To the Editor:** Bacterial meningitis is a major cause of death and disability in children worldwide: >1,000,000 cases and 200,000 deaths are estimated to occur each year. *Neisseria meningitidis*, *Haemophilus influenzae* type b (Hib), and *Streptococcus pneumoniae* are major causative agents of bacterial meningitis in children. A region in sub-Saharan Africa, extending from Ethiopia in the east to the Gambia in the west and containing 15 countries with >260 million people, is known as the "meningitis belt" because of its high prevalence of endemic disease with periodic epidemics caused by *N. meningitidis*.

Eritrea, a small country with an estimated population of 3.5 million in northeast Africa, is part of the meningitis belt. Eritrea gained independence in 1993 and borders the Red Sea on the east, Djibouti on the southeast, Ethiopia on the south, and Sudan on the north. Asmara, with a population of about 500,000, is the capital city. The estimated infant mortality rate is 73 deaths/1,000 live births.

In 2002, a prospective laboratory-based study was carried out in Asmara to gain insight regarding the distribution of bacterial agents causing bacterial meningitis in children. Starting in January 2002, cerebrospinal fluid (CSF) specimens were collected from every child who had a spinal tap administered at Mekane Hiwet Pediatric Hospital, Asmara. This

facility serves as the national reference hospital for pediatric care. Within 1 hour of collection, all CSF specimens were processed at the Department of Microbiology, Central Health Laboratory. This laboratory, located <200 m from the Mekane Hiwet Pediatric Hospital, serves as the national reference health laboratory and is the only facility in Eritrea with the capabilities to perform cultures. Standard methods were used to process all specimens and to isolate and identify bacterial agents from the CSF specimens (1–3). All CSF specimens were cultured on chocolate agar plates with IsoVitalex supplement (BBL Microbiology Systems, Cockeysville, MD) and tested for bacterial antigens by using Wellcogen latex agglutination kits (Remel, Inc., Dartford, UK). Hib strain ATCC 49247 was used as the control strain. All Hib strains were tested for susceptibility to ampicillin, penicillin, chloramphenicol, gentamicin, and cefotaxime by using the disk diffusion method (BBL); isolates determined to be penicillin-resistant were also tested for  $\beta$ -lactamase by using the Nitrocefin touch sticks (Oxoid, Basingstoke, UK).

From January 1 to December 31, 2002, a total of 81 CSF specimens were collected: 38 (47%) were from patients <1 year of age, 28 (35%) from patients 1 to 2 years of age, and 15 (18%) from patients 2 to 14 years of age. Twelve (15%) of the 81 specimens tested positive; 10 were positive by both culture and latex agglutination test (5 Hib, 2 *S. pneumoniae*, 1 *N. meningitidis*, and 2 *Enterobacteriaceae*), and 2 were positive only by the latex agglutination test (1 Hib and

1 *N. meningitidis*). The patients' age and sex and the results of microbiologic tests are presented in the Table.

This study preceded the implementation of the Integrated Disease Surveillance (IDS) in Eritrea (last quarter of 2002) and does not allow for calculation of incidence of Hib disease at the national level. However, implementation of IDS will enable microbiologists to prospectively monitor the incidence of infectious diseases, including meningitis caused by Hib.

In many countries, Hib is still reported as a major cause of bacterial meningitis (4–9), and while Hib meningitis has a relatively low case-fatality rate in developed countries (3% to 5%), high case-fatality rates (20% to 30%) are common in tropical Africa. Rapid laboratory diagnosis and treatment with appropriate antimicrobial drugs, such as third-generation cephalosporins, are crucial in reducing the risk for severe complications. The decrease in Hib meningitis cases after the introduction of Hib vaccination and the use of vaccine to control Hib meningitis are well documented (10–12). Additionally, the findings of this study suggest that Hib remains the leading cause of childhood meningitis in this region and lead us to advocate for the introduction of vaccination in Eritrea.

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Table. Results of microbiologic tests of specimens from five case-patients with *Haemophilus influenzae* type b<sup>a</sup>

| Age/sex         | Latex agglutination test | Antimicrobial susceptibility |     |       |     |       | $\beta$ -lactamase |
|-----------------|--------------------------|------------------------------|-----|-------|-----|-------|--------------------|
|                 |                          | Pen                          | Amp | Cefot | Chl | Genta |                    |
| 3 months/female | Positive                 | R                            | R   | S     | S   | S     | Positive           |
| 5 months/male   | Positive                 | R                            | R   | S     | R   | R     | Positive           |
| 6 months/male   | Positive                 | R                            | R   | S     | S   | S     | Positive           |
| 1 year/male     | Positive                 | R                            | R   | S     | S   | S     | Positive           |
| 3 years/male    | Positive                 | R                            | S   | S     | S   | S     | Positive           |

<sup>a</sup>Pen, penicillin; Amp, ampicillin; Cefot, cefotaxime; Chl, chloramphenicol; Genta, gentamicin; S, sensitive; R, resistant.

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## Quinolone Safety and Efficacy More Important than Potency

**To the Editor:** In a recent article, Scheld defines two principles for appropriate quinolone use based on the goal of maintaining class efficacy, namely avoiding unnecessary antimicrobial drug therapy and “using the agents with optimal activity against the expected pathogens” (1). He presents a large body of evidence supporting an inverse correlation between quinolone activity and the selection of antimicrobial drug resistance. On the basis of this concept, Scheld favors ciprofloxacin for known or suspected *Pseudomonas aeruginosa* infection and moxifloxacin for infections in which *Streptococcus pneumoniae* is likely, including community-acquired pneumonia (CAP). Preventing the emergence of antimicrobial drug resistance is certainly an important goal in drug therapy decision-making. However, this goal should be balanced by the clinical criteria of safety and efficacy.

Serious adverse drug effects in patients led to the withdrawal or restriction of four quinolones in the past decade (temafloxacin, grepafloxacin, trovafloxacin, and sparfloxacin). Safety may differ substantially among the quinolones discussed in Scheld’s review (ciprofloxacin, levofloxacin, moxifloxacin, and gatifloxacin). On the basis of spontaneous reports to the U.S. Food and Drug Administration (FDA), gatifloxacin is associated with a higher rate of torsades de pointes than ciprofloxacin or levofloxacin ( $p = 0.001$ ) (2). Torsades cases have been reported in association with moxifloxacin, but their rate cannot be estimated with any precision by using FDA spontaneous reporting data because of the relatively small number of U.S. prescriptions (2). In a crossover study, a single oral

dose of moxifloxacin 800 mg was associated with greater QT interval prolongation (16–18 milliseconds) than ciprofloxacin 1,500 mg (2–5 milliseconds) or levofloxacin 1,000 mg (4–5 milliseconds) (3). Gatifloxacin has been associated with alterations in glucose metabolism, both in prospective trials and in postmarketing surveillance. Gatifloxacin underwent two “safety-related drug labeling changes” in 2001 and is the only quinolone that carries a “warning” about disturbances in glucose metabolism. Gemifloxacin was approved after Scheld’s review and has pharmacodynamic potency similar to moxifloxacin against *S. pneumoniae*. Gemifloxacin is associated with a high rate of rashes, especially in women <40 years of age.

Serious but uncommon adverse side effects may not be recognized until drugs are used in large populations (4). More than 100 million prescriptions were written for terfenadine and astemizole before they were withdrawn from the market because of torsades and sudden death. On the basis of the number of U.S. prescriptions in the past decade (January 1993–December 2002), patient experience with ciprofloxacin (119 million prescriptions) and levofloxacin (44 million) is larger than with gatifloxacin (8 million) or moxifloxacin (5 million) (5–7).

The clinical efficacy of ciprofloxacin and levofloxacin is better established for a broad range of indications in comparison to the newer agents. A full discussion of the literature is beyond the scope of this letter. A simple MEDLINE (U.S. National Library of Medicine, Bethesda, MD) search in April 2003 provided the following raw numbers of peer-reviewed, randomized, controlled trials reporting clinical outcomes: >200 trials using ciprofloxacin, 28 using levofloxacin, 13 using moxifloxacin, 7 using gatifloxacin, and 6 using gemifloxacin (search terms, inclusion