Bacterial meningitis is a significant cause of death and disability worldwide.1 Of one million estimated annual cases of bacterial meningitis globally, 200,000 die.2 Depending upon age group and etiologic agent, 11–39% of cases result in death.3–5 A substantial proportion of survivors (12–15%) develop neurologic sequelae, including deafness and mental retardation.2

Infections with Neisseria meningitides, especially meningococcal disease and meningococccemia, are a global concern.1,4–8 Neisseria meningitides is a genetically highly diverse species and only a limited number of serogroups are responsible for most meningococcal disease. Twelve serogroups (A, B, C, H, I, K, L, W135, X, Y, Z, and 29E), on the basis of capsular polysaccharides, are currently recognized.2 Serogroups A, B, C, W135, and Y are the most common causes of meningitis; serogroups A, B, and C account for more than 90% of meningococcal disease.9–11 Serogroup A is the major cause of meningitis outbreaks or epidemics, especially in the African meningitis belt and in Asia.1,2 Except for Mongolia and China, data on epidemic meningococcal disease and the serogroup pattern of its causative agent from south Asia are limited.7,11–13 Occasional outbreaks caused by serogroup A have been reported from India, Pakistan, and Nepal,7,14,15 and no data are available from Bangladesh. During review of data on blood isolates, additional N. meningitidis isolates were observed in recent years. We examined data and isolates from blood and cerebrospinal fluid (CSF) to define trends for N. meningitidis isolation, the prevalent serogroups, and antimicrobial drug susceptibility.

Blood and CSF culture results available at the Clinical Microbiology Laboratory of the International Centre for Diarrheal Disease Research, Bangladesh (ICDDR,B) were analyzed from January 1999 through December 2006. The laboratory receives specimens from patients of ICDDR,B, Dhaka hospital (who come from a wide geographic area) and those referred to our laboratory from patients admitted to public or private hospitals and clinics in Dhaka, which constitutes approximately 50% of the samples. Thus, it is impossible to estimate a catchment population for this study (which would be needed for incidence rate calculations). Submission of a single set of specimens of blood or CSF is the usual practice; multiple sampling from the same patient is rare. There were no changes in methods for isolation of bacteria from blood or CSF during the study period.

A case of suspected meningitis was defined as when dual specimens from blood and CSF from a patient were submitted, and a case of invasive meningococcal disease was defined as a patient from whom N. meningitidis was isolated from blood and/or CSF (isolation either from blood or CSF of a patient was counted as one isolate). Isolation rate was calculated by dividing the number of isolates per year by the number of patients with blood and/or CSF cultures processed per year. Demographic characteristics of patients were obtained from the laboratory record books. This retrospective data analysis was done as pilot activity, which could be useful for future research protocols, and did not require an institutional review board approval.

Isolates of N. meningitidis from blood and CSF were characterized by Gram stain and oxidase and carbohydrate use pattern (positive for glucose and maltose and negative for sucrose and lactose).2 All isolates of N. meningitidis were preserved in chocolate agar slants at −86°C and retrieved for serogrouping. Serogrouping was done by slide agglutination using antibody-coated latex particles polyvalent antisera available commercially (bioMérieux, Marcy l’Etoile, France). Simultaneously, 20 randomly selected isolates were serogrouped at the Centers for Disease Control and Prevention (Atlanta, GA) and identified as serogroup A (Popovic T, unpublished data). These 20 strains were also blindly serogrouped at this laboratory to validate the methods; all strains were correctly identified as serogroup A.

Drug susceptibility for penicillin (10 µg), ampicillin (10 µg), chloramphenicol (30 µg), cotrimoxazole (25 µg), ciprofloxacin (5 µg), ceftriaxone (30 µg), and azithromycin (15 µg) was performed by disk diffusion using Mueller-Hinton agar with 5% heated sheep blood following recommendations of the Clinical and Laboratory Standard Institute (CLSI).16 Isolates resistant to cotrimoxazole and azithromycin were assessed for minimum inhibitory concentration (MIC) by the E-Test method (AB BIODISK, Solna, Sweden). For cotrimoxazole MIC values, CLSI interpretive breakpoint concentrations for Streptococcus pneumoniae (American Type Culture Collection...
no. 49619) were applied (susceptible at ≤ 0.5/9.5 µg/mL). For azithromycin, an MIC testing value ≥ 2 µg/mL was considered resistant.16 For the paired strains from 20 patients who had \( N. \) meningitidis isolated from blood and CSF, the serogroup and antimicrobial drug resistance pattern were identical. Thus, we included information from only one isolate for each patient when presenting data on aggregate serogroup and antimicrobial drug resistance.

A total of 53,139 blood and 3,319 CSF specimens were obtained. We focused on the 3,072 dual specimens (i.e., CSF and blood from same patients), of which pathogens were isolated from 628 (20.4%), including \( S. \) enterica serovar Typhi (n = 188, 29.9%) and other isolates (n = 182, 29%) included Enterococcus spp., Staphylococcus aureus, \( S. \) pyogenes, Klebsiella spp., and Pseudomonas spp. \( N. \) meningitidis was detected only by latex agglutination in nine specimens, four from CSF and five from blood. These results were not included in this analysis, which focuses on culture-positive specimens.

Of the 156 \( N. \) meningitidis isolates, 89 (57%) were from blood and 67 (43%) from CSF, including those from 20 patients who had \( N. \) meningitidis isolated from blood and CSF (Figure 1). Most cases of invasive meningococcal disease (88.5%) were identified during 2002–2004 from a higher number of specimens processed during those years. The rate (proportion) of isolation from blood cultures during 2002–2004 increased nearly 5-fold when compared with 2001 and > 15-fold when compared with 1999 and 2000. The rate of isolation from CSF increased > 5-fold in 2002 through 2004 when compared with 2001 and > 6-fold when compared with 1999 and 2000. The highest number of cases occurred in 2004. It was noteworthy that there were no changes in the isolation rates for \( S. \) pneumoniae and \( S. \) enterica serovar Typhi during the study period. However, the isolation rate of \( N. \) meningitidis from blood and CSF decreased in 2005 and 2006.

Serogrouping was done on isolates from 132 patients (4 isolates from 1999 and 2000 were not serogrouped); 129 isolates (97.7%) were serogroup A and 3 (2.3%) were serogroup B. Meningococcal disease had no distinct seasonality. However, during 2002–2004, 41 isolates (42%) were obtained during the cool and dry months of January through March. Most (60.2%) patients were > 15 years of age; 29.4% were 6–14 years of age and 10.3% were less than five years of age (Table 1). All but 13 patients were less than 40 years of age. For the 123 patients for whom sex information was available, 87 (70.7%) were males.

All meningococcal isolates (156) were susceptible to penicillin, ampicillin, chloramphenicol, ceftriaxone, and ciprofloxacin. Azithromycin resistance appeared during 2002–2004 (none was resistant in 1999–2001), 5% resistance was found in 2002, 27% in 2003, and 31% in 2004, but all isolates in 2005–2006 were susceptible. Isolates resistant to azithromycin showed high MIC values (ranging from ≥ 4 to 256 µg/mL; 25% of the isolates had MICs ≥ 256µg/mL). Resistance to cotrimoxazole increased from 50% in 2000 to 80% in 2001, 89% in 2002, and 100% since 2003. All strains resistant to cotrimoxazole had MICs ≥ 4–76 µg/mL.

Epidemic meningococcal disease caused by \( N. \) meningitidis has had a devastating effect in sub-Saharan Africa.1 Although there is no known “similar meningococcal belt” in Asia, outbreaks associated with overcrowded settings, refugee camps, and gatherings such as the Hajj represent immense public health challenges because infected people can become ill after returning home, resulting in spread of illness through respiratory secretions and outbreaks to people in a large number of countries.17,18 In China and in the African meningitis belt, serogroup A remains the major cause of meningococcal-associated death.2 Recent Hajj-associated epidemics have involved \( N. \) meningitidis serogroup W-135 and serogroup A.17,18 This study documented a disproporproportionate number of meningococcal disease cases (nearly all serogroup A) in Bangladesh during 2002–2004 when compared with earlier or later years. We were not able to obtain information on genotype, which might have been useful in comparing strains from Bangladesh with those of other countries in the region and in the African meningitis belt.

The increased isolation rate of \( N. \) meningitidis may have reflected a community-wide change in meningococcal disease incidence. The increase in isolation rate and presumably the disease incidence was likely caused by outbreaks. Although we did not document marked seasonality, there was a slightly increased rate of isolation during the cool dry season (January through March) and some decrease during monsoon season (July through September), which is consistent with patterns noted in Nepal in 1983–1984,7 in Delhi in 2006,12,13 and in other countries.19,20 In the absence of changes in methods during the study period, the increased isolation in 2002–2004 likely reflected a valid increase in meningococcal meningitis disease, not merely increased isolation caused by greater specimen flow in the laboratory or enhanced capacity to isolate the bacteria.

The increased number of isolates in specimens from patients at ICDDR,B Hospital, as well as from other public private

Figure 1. Distribution of \( N. \) meningitidis isolates from blood and cerebrospinal fluid, by year, Bangladesh.
facilities, is consistent with the notion that there may have been community outbreaks ongoing during that period. Because no national surveillance data on meningitis exist in Bangladesh, we cannot be certain that our observations represent national trends. Surveillance is needed in a number of hospital settings in Bangladesh to better characterize disease patterns. Data from this study do not provide population denominators with which incidence rates can be calculated.

Of substantial interest, outside the scope of this report, is the high number of cases of bacteremic typhoid fever in patients suspected to have meningitis. *Salmonella* Typhi appears to be a major cause of bacteremia in an urban slum area of Dhaka, and may represent an important vaccine-preventable disease.

Monitoring of antimicrobial drug resistance patterns is important to guide empiric therapy and reduce morbidity and mortality where case-based antimicrobial drug susceptibility testing is limited. Although reported elsewhere, we did not find meningococcal isolates resistant to penicillin and chloramphenicol. In contrast to reports from Delhi in 2005 and 2006, we did not find resistance to ciprofloxacin or ceftriaxone. Cephalosporin-resistant strains of serogroup B and C meningococci caused by β-lactamase have also been reported. Our study suggests that cotrimoxazole is not useful for therapy in Bangladesh, as reported elsewhere. Emergence of azithromycin resistance among the isolates in 2002–2004 was alarming, but the isolates in 2005–2006 were susceptible. The shift was likely caused by cycling in and out of various strains of *N. meningitidis* within communities in Bangladesh. Active surveillance for meningococcal disease would be helpful to define high-risk populations and impact of disease, which could suggest strategies for focused targeted prevention and control measures such as vaccine use in Bangladesh.

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