The Rise and Fall of Epidemic *Neisseria meningitidis* Serogroup W135 Meningitis in Burkina Faso, 2002–2005

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**Background.** During the period 2001–2002, Burkina Faso reported its first meningitis epidemic due to *Neisseria meningitidis* (Nm) serogroup W135, prompting concerns that this serogroup would persist as a cause of epidemic disease.

**Methods.** During the period 2002–2005, hospital- and population-based surveillances were conducted in 3 districts in Burkina Faso. Etiology was determined by culture, polymerase chain reaction (PCR), and latex agglutination. Reference laboratories determined phenotype and genotype.

**Results.** Of 2004 subjects who received a lumbar puncture, 265 were identified as having Nm, including 93 who had Nm serogroup A (NmA) and 146 who had Nm serogroup W135 (NmW135). Over the study period, the proportion of cases due to NmW135 decreased by 75%, primarily because of decreased occurrence among young children and in a single district. During peak epidemic months, the annualized incidence of NmW135 decreased from 146 cases to !1 case per 100,000 population. All but 2 NmW135 isolates were phenotype W135:2a:P1.5,2 (sequence type [ST]-11 clonal complex). All NmA isolates were phenotype A:4:P1-9 (ST-2859 of the ST-5 clonal complex). We identified 1 isolate from serogroup Y (ST-11 clonal complex), 1 isolate from serogroup X that was similar to strains previously associated with epidemic disease, and 1 isolate from serogroup W135 of the newly described ST-4375 complex.

**Conclusions.** For unknown reasons, serogroup W135 achieved epidemic status, primarily among young children, and then largely disappeared over a short time period. The continued circulation of multiple strains with epidemic potential emphasizes the need for ongoing surveillance and the potential benefit of vaccines that are protective across serogroups.

Within the African meningitis belt that extends from Senegal to Ethiopia, most epidemics of *Neisseria meningitidis* (Nm) infection have been caused by serogroup A (NmA) [1]. Serogroup W135 (NmW135) emerged as a new epidemic serogroup in 2001 [2, 3]. To assist with understanding these epidemics and, thus, to provide information on future epidemic potential, the current study evaluated NmW135 meningitis during parts or all of 4 epidemic seasons (December–April) during 2002–2005 in 3 districts of southwestern Burkina Faso.

**METHODS**

**Case identification and surveillance sites.** Acute bacterial meningitis surveillance was initiated during April 2002 in Districts 15, 22, and Houndé, encompassing Bobo-Dioulasso and its surrounding areas (total 2002 population, 880,000; population <5 years of age, 140,000; Burkina Faso Ministry of Health) [2]. Houndé passed the World Health Organization epidemic threshold of 10 suspected cases per 100,000 population per

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week during most weeks of the first 3 months of 2003; for the remaining districts and study period, the epidemic threshold was not passed (Burkina Faso Ministry of Health, unpublished data).

Using A/C polysaccharide vaccine among the 2- to 29-year-old target age group, a mass reactive vaccination campaign was conducted in the health region of Bobo-Dioulasso during the 2000–2001 epidemic season, with coverage of ∼90%. Before the 2001–2002 season, mass preventative campaigns were conducted with >90% administrative coverage among the target age group in all 3 districts. During the 2002–2003 season, mass reactive campaigns using A/C/W135 polysaccharide vaccine were conducted in parts of Burkina Faso, but not in the 3 study districts. During subsequent seasons, epidemic response in Burkina Faso and vaccine type were guided by the serogroup distribution of affected districts.

Population-based surveillance was conducted at the referral hospital and at all 59 local health centers from April 2002–April 2003 and again from March 2004–February 2005 (activities were halted mid study because of funding limitations). From March–June 2005, because of financial constraints, cases were identified only at the referral hospital. Using their clinical judgment, health care providers at study hospitals and health centers enrolled patients with suspected bacterial meningitis (according to the World Health Organization definition [http://www.who.int/immunization_monitoring/diseases/meningitis_surveillance/en/; last accessed May 16, 2006]) even if CSF was clear. At all study sites, patients generally received a lumbar puncture and antibiotic therapy. An aliquot of CSF and a clinical case report form for each patient were transported to the reference laboratory in Bobo-Dioulasso.

**Laboratory methodology.** The study protocol required PCR testing for all cases, sample culture according to World Health Organization methodology [4] when the time between collection of CSF and arrival at the reference laboratory was <2 h, and latex agglutination if CSF was visibly cloudy. Nm was considered the etiologic agent if it was identified by PCR, latex agglutination (Pastorex [Biorad]), or culture. All specimens positive for NmY/W135 by latex agglutination that were tested by PCR were found to be genogroup W135; consequently, we assumed that all Nm isolates found to be Y/W135 by latex agglutination were serogroup W135, except for a single specimen confirmed as serogroup Y. PCR identification was based on crgA gene amplification [5]. Genogroup was determined by a multiplex PCR that used oligonucleotides for siaD for genogroups B, C, Y, and W135 and mynB for genogroup A [5]. Serotype and sero-subtype were determined by reference techniques [6, 7]. Genotyping was performed by multilocus sequence typing (MLST) [8–10].

**Study approval.** This surveillance project was approved by the ethics review board of Centre Muraz and was supported by the Ministry of Health of Burkina Faso.

**RESULTS**

**Case identification.** There were 2144 subjects who were admitted for acute bacterial meningitis, of whom 2004 received a lumbar puncture. Among CSF samples, Nm was identified as the etiologic agent in 265 cases (13%), including 237 (15%) of 1583 samples tested by PCR, 164 (17%) of 948 samples tested by latex agglutination, and 130 (17%) of 784 samples tested by culture. Of the 265 cases of Nm, 93 (35%) were identified as NmA and 146 (55%) as NmW135. The remainder either could not be genogrouped or serogrouped (n = 19) or were initially genogrouped as NmW135 but were determined later to be non-NmW135 (n = 7).

**Isolate characterization.** Of the 57 Nm isolates that tested positive for genogroup W135 by PCR at the Bobo-Dioulasso laboratory, 48 were phenotype W135:2a:P1.5,2 (all 12 genotyped isolates from this group were sequence type [ST]–11, belonging to the ST-11 clonal complex), 1 was W135:NT:P1.5,2 (ST-11), and 1 was W135:NT:P1.5,2 (ST-4375, which belongs to the ST-23 clonal complex). Seven additional isolates that were identified as genogroup NmW135 in the field were discovered at the reference laboratory to be phenotypes Y:14:P1.5,2 (ST-11; n = 1), X:NT:P1.5 (ST-751; n = 1), NG:NT:NST (ST-192; n = 3), and polyagglutinable:14:P1.5,2 (ST-4375; n = 2).

Thirty-five isolates from CSF that tested positive for genogroup NmA by PCR at the Bobo-Dioulasso laboratory were further evaluated, including 15 strains that were collected during the period 2002–2003 and 20 that were collected during the period 2004–2005. All 35 isolates were phenotype A:4:P1-9, and all 31 sequence-typed isolates were ST-2859 (belonging to the ST-5 clonal complex).

**Incidence, case-fatality percentage, and age group.** To prevent overweighting the epidemic season and to limit estimates to the period during which population-based surveillance existed, incidence rates and case-fatality percentages were estimated for the periods May 2002 through April 2003 and March 2004 through February 2005. NmA incidence rates peaked among persons 1–14 years of age, whereas rates for NmW135 peaked among infants (table 1). For NmW135, a substantial minority of cases occurred among persons outside the current vaccine-eligible age group of 2–29 years.

**Temporal and geographic distribution.** NmW135 cases peaked during April 2002 and again during the 2002–2003 season (figure 1). The proportion of Nm cases due to NmW135 was 86% during April–May 2002 (the first 2 months of the surveillance system), 70% during December 2002 through April 2003, 32% during March–April 2004, and 18% during December 2004 through April 2005. To evaluate changes in incidence by age group, for 4 consecutive years we compared rates during
Table 1. Summary characteristics of Neisseria meningitidis (Nm) infection observed during the periods May 2002–April 2003 and March 2004–February 2005 in the Bobo-Dioulasso region, Burkina Faso.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Nm infection</th>
<th>NmW135 infection</th>
<th>NmA infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>221</td>
<td>121 (55)</td>
<td>83 (35)</td>
</tr>
<tr>
<td>Age, mean years (range)</td>
<td>9.8 (0.13–81)</td>
<td>7.9 (0.13–66)</td>
<td>13 (0.43–81)</td>
</tr>
<tr>
<td>Case-fatality percentage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All ages, % (no. of deaths/cases)</td>
<td>12 (27/221)</td>
<td>14 (17/121)</td>
<td>8 (7/83)</td>
</tr>
<tr>
<td>&lt;1 year, % (no. of deaths/cases)</td>
<td>17 (4/24)</td>
<td>11 (2/19)</td>
<td>50 (1/2)</td>
</tr>
<tr>
<td>1–4 years, % (no. of deaths/cases)</td>
<td>12 (7/57)</td>
<td>12 (5/42)</td>
<td>8 (1/13)</td>
</tr>
<tr>
<td>5–14 years, % (no. of deaths/cases)</td>
<td>12 (12/98)</td>
<td>16 (7/44)</td>
<td>9 (4/44)</td>
</tr>
<tr>
<td>&gt;15 years, % (no. of deaths/cases)</td>
<td>10 (4/42)</td>
<td>19 (3/16)</td>
<td>4 (1/24)</td>
</tr>
</tbody>
</table>

Incidence by standard age groups

<table>
<thead>
<tr>
<th>Age</th>
<th>Nm infection</th>
<th>NmW135 infection</th>
<th>NmA infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1 year</td>
<td>32 (24)</td>
<td>26 (19)</td>
<td>2.7 (2)</td>
</tr>
<tr>
<td>1–4 years</td>
<td>28 (57)</td>
<td>20 (42)</td>
<td>6.3 (13)</td>
</tr>
<tr>
<td>5–14 years</td>
<td>17 (98)</td>
<td>7.8 (44)</td>
<td>7.8 (44)</td>
</tr>
<tr>
<td>&gt;15 years</td>
<td>4.6 (42)</td>
<td>1.7 (16)</td>
<td>2.6 (24)</td>
</tr>
</tbody>
</table>

Incidence by vaccine eligible groups, vaccine targeted to 2–29 year olds

<table>
<thead>
<tr>
<th>Age</th>
<th>Nm infection</th>
<th>NmW135 infection</th>
<th>NmA infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 years</td>
<td>32 (40)</td>
<td>26 (33)</td>
<td>2.4 (3)</td>
</tr>
<tr>
<td>2–9 years</td>
<td>11 (168)</td>
<td>5.6 (82)</td>
<td>5.0 (73)</td>
</tr>
<tr>
<td>&gt;30 years</td>
<td>8.0 (13)</td>
<td>3.7 (6)</td>
<td>4.3 (7)</td>
</tr>
</tbody>
</table>

NOTE. Data are no. (%) of patients, unless otherwise indicated. Incidence is defined as per 100,000 persons per year. NmA, N. meningitidis serotype A; NmW135, N. meningitidis serotype W135.

the peak 2 months (only data from April were available for 2002) of the 4 epidemic meningitis seasons (figure 2). NmW135 rates remained stable for persons ≥5 years of age but decreased substantially for younger children.

Of all Nm meningitis cases, 85 (40%) occurred in the Houndé district, compared with 61 (29%) in District 15 and 65 (31%) in District 22, despite the location of the regional referral hospital in District 22. The proportions of cases due to NmA in Houndé, District 15, and District 22 were 37%, 26%, and 37%, respectively, compared with 46%, 22%, and 31%, respectively, for NmW135. When incidence rates by district were examined (figure 3), Houndé experienced the greatest NmW135 epidemic (during 2002) followed by the steepest decrease; in contrast, Districts 15 and 22 had relatively stable and low incidence rates until 2005, when rates had decreased everywhere to near zero.

DISCUSSION

We observed that NmW135—primarily from a single clonal complex—was found in an epidemic pattern and was the predominant serogroup that was identified during the first part of the study period. The incidence was highest among young children and within a single district. Disease occurrence decreased substantially over the 4 evaluated epidemic seasons, with few cases identified by 2005.

Serogroup W135 incidence increased within the context of meningitis cases due to other potentially epidemic Nm strains. One case due to NmW135 of the newly described ST-4375 was identified. NmA meningitis was caused by the new sequence type (ST-2859) within the ST-5 clonal complex that has only been identified since 2002 in Niger and Burkina Faso [11]. We identified the first documented case of invasive disease in the African meningitis belt involving a serogroup Y isolate from the same ST-11 genotype as was responsible for W135 epidemics (possibly due to capsular switching [12, 13]). Lastly, 1 serogroup X case occurred that had the same phenotype and genotype as previous epidemic serogroup X strains [14, 15].

The reasons for the emergence and decrease in NmW135 disease (while other potentially epidemic strains have remained relatively quiescent) are largely unknown. Mass reactive and preventative polysaccharide A/C vaccination campaigns could have created an ecological niche for serogroup W135. Subsequent mass campaigns with trivalent A/C/W135 polysaccharide vaccines [16] could have then led to decreases in disease. However, to argue against this explanation, Districts 15 and 22 experienced relatively low rates of NmW135 incidence despite widespread use of bivalent vaccine, and in all study districts, the proportion of disease due to serogroup W135 decreased in the absence of substantial trivalent vaccine use. Additionally, polysaccharide vaccines have little effect on carriage [17, 18] and thus would not be expected to create an ecological niche for nonvaccine serogroups. Finally, in the United Kingdom, the
use of conjugate serogroup C vaccines has not led to increased disease due to other serogroups [19], despite conjugate vaccine efficacy against carriage [20]. It may be that an immunologically naive population was exposed to a virulent clone and, subsequently, experienced the development of anticapsular, antibody-based population immunity and a decrease in the rate of disease. This is consistent with the emergence and disappearance of NmW135 primarily among young children, as well as the concentration of disease followed by rapid disappearance within a single district in Burkina Faso. However, a recent study in Bobo-Dioulasso during the period February–June 2003 [21] found that, despite several years of epidemic disease and substantial serogroup W135 carriage, the great majority of the population had not acquired putatively protective anti-NmW135 antibodies (as measured by IgG and serum bactericidal antibody). Additionally, those who had putatively protective antibody levels at the beginning of the study frequently lost protection over time.

Because, in our study, virtually all of the strains that expressed the W135 capsule belonged to the ST-11 clonal complex, the decrease in serogroup W135 may be specific to this clone. Consistent with this hypothesis are data from France that demonstrate a reduction in the number of isolates of W135:2a:P1.5,2, ST-11 at the same time that serogroup W135 strains of other phenotypes and genotypes have persisted and diversified [8]. Isolates of W135:2a:P1.5,2, ST-11 have circulated and diversified since at least 1970 [22]. In 2000, these isolates started undergoing several clonal waves of expansion among susceptible hosts, under epidemic conditions of spread [2, 11, 23].

The current decrease in disease may have resulted from a high rate of infection (of both carriage and invasive disease) with such isolates [24], coupled with efficient stimulation of noncapsular- and noncomplement-dependent antisurface structure
antibodies [25] and a relative genetic bottleneck. The detection of several isolates with diverse genotypes and phenotypes is consistent with a selective restriction of the dominant circulating strain (W135:2a:P1.5,2, ST-11).

With the current disappearance of epidemic serogroup W135 meningitis, monovalent A conjugate vaccines once again may assume an important role. The recent history of NmW135 meningitis in sub-Saharan Africa, however, reveals that new epidemic strains may occur and rapidly lead to major epidemics. Our data indicate that, although the rate of serogroup W135 disease has lessened, disease continues to be caused by multiple serogroups with epidemic potential. Continued meningitis surveillance will assist in the development and modification of vaccine strategies, including the use of multivalent conjugate vaccines and novel vaccines using antigens that are common across serogroups.

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