

Antimicrobial Resistance and Serogroup Distribution of *Neisseria meningitidis* (NME) Isolates Causing Invasive Disease in Argentina: Eight Years of National Surveillance

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OBJECTIVE

TO ESTIMATE THE PREVALENCE OF SEROGROUP AND ANTIBIOTIC RESISTANCE IN NME ISOLATES CAUSING INVASIVE DISEASE IN ARGENTINA.

BACKGROUND

Nme is one of the major causative agents of bacterial meningitis and septicemia in children and young adults. From 1998 to 2005, 1188 meningococcal strains from invasive disease (meningococemia or meningitis) were submitted to the National Reference Laboratory (INEI) as part of the "National Surveillance Programme for Serogroup and Antimicrobial Resistance". Strains were from 190 hospitals located in all the provinces of Argentina (23) and Capital Federal.

MATERIALS AND METHODS

Isolates were recovered from blood, cerebrospinal fluid, or other normally sterile body sites. Serogroup for 1188 strains was determined by slide agglutination. MICs to penicillin (PEN), ampicillin (AMP), ceftriaxone (CRO), rifampicin (RFA), chloramphenicol (CMP), tetracycline (TET), ciprofloxacin (CIP) and trimethoprim-sulfamethoxazol (SXT) for 892 representative isolates were performed and interpreted according to CLSI guidelines.

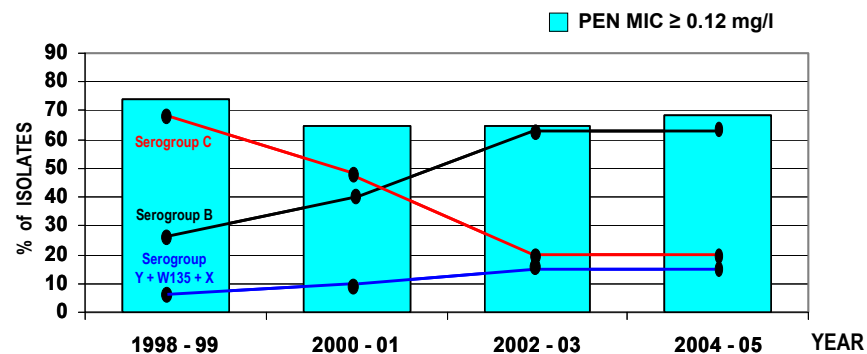
RESULTS

TABLE 1:
 DISTRIBUTION OF NME SEROGROUPS AND MODERATED SUSCEPTIBILITY (MS) TO PEN FROM 1998 TO 2005

| | N° of isolates (%) /YEAR | | | |
|-----------------------|--------------------------|---------------|---------------|---------------|
| | 1998-99 | 2000-01 | 2002-03 | 2004-05 |
| SEROGROUP | | | | |
| n Total: 1188 | n: 474 | n: 297 | n: 232 | n: 185 |
| C | 321 (67,7) | 142 (47,8) | 44 (19,0) | 35 (18,9) |
| B | 125 (26,4) | 120 (40,4) | 144 (62,1) | 117 (63,2) |
| Y | 17 (3,6) | 14 (4,7) | 26 (11,2) | 17 (9,2) |
| W135 | 11 (2,3) | 12 (4,0) | 12 (5,2) | 13 (7,0) |
| X | 0 | 2 (0,7) | 1 (0,4) | 0 |
| Nongroupable | 0 | 7 (2,4) | 5 (2,1) | 3 (1,7) |
| SUSCEPTIBILITY | | | | |
| n Total: 892 | n: 251 | n: 246 | n: 222 | n: 173 |
| MS PEN | 185 (73,7) | 159 (64,6) | 145 (65,3) | 118 (68,2) |

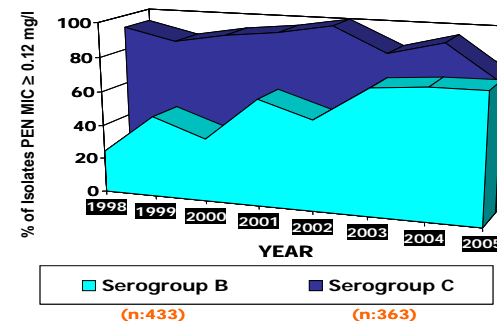
In Argentina most of the cases of invasive meningococcal disease are caused by isolates belonging to serogroup B or C.

**FIGURE 1:
MODERATED SUSCEPTIBILITY TO PEN AND SEROGROUP DISTRIBUTION**



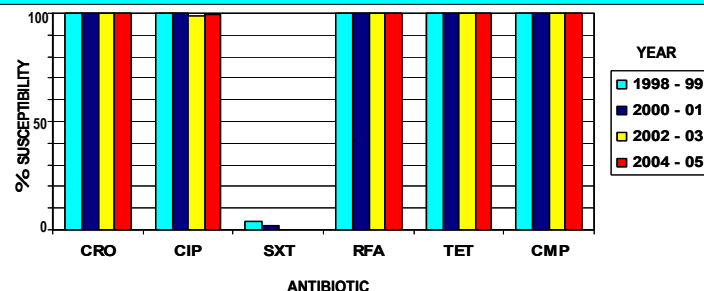
Moderated susceptibility (MS) to PEN (MIC \geq 0.12 mg/l) was observed in 90.4, 57.7 and 29.3 % of serogroup C, B and Y+W135+X isolates, respectively. Two waves were observed within the Nme population, the most common serogroup C during 1998-99 was replaced by serogroup B isolates after 2001 (Table 1 and Figure 1). Serogroup B increases from 26.4 % in 1998-99 to 63.2 % in 2004-05 in contrast to serogroup C that decreases from 67.7 to 18.9 %. Serogroups Y+W135+X increase from 5.9 to 16.2 % during the period of study.

**FIGURE 2:
MODERATED SUSCEPTIBILITY TO PEN BY SEROGROUP**



MS to PEN of serogroup B strains increases from: 24.3 % (1998) to 57.7 % (2005), while serogroup C keeps high (73-100 %) during the study (Figure 2). The high MS to PEN during 1998-99 was related to the dominance of serogroup C. Nowadays, serogroups B and C present similar MS to PEN, 75.4 % and 73.3 % respectively.

**FIGURE 3:
ANTIMICROBIAL SUSCEPTIBILITY**



All strains were susceptible to (MIC90 in mg/l) CRO (0.002), RFA (0.03), TET (0.25) and CMP (1), while 94% were resistant to SXT (4) (Figure 3). MIC90 to CIP was 0.008 mg/l.

TABLE 2: NME ISOLATES WITH DECREASED SUSCEPTIBILITY TO CIPROFLOXACIN (DSC)

| Isolate N° | Serotype | CIP | | NAL | | Mechanism of DSC | Reference |
|------------|------------|------------|-----------|------------|-----------|-------------------------------|----------------------|
| | | MIC (mg/L) | Zone (mm) | MIC (mg/L) | Zone (mm) | | |
| M5191 | Y:NT:P1.5 | 0.12 | 31 | 64 | 7 | Efflux | JAC. 55:596/7. 2005. |
| M5507 | B:1:P1.NT | 0.06 | 35 | 64 | 6 | QRDR <i>gyrA</i> Asp-95 → Asn | JAC. 55:596/7. 2005. |
| M9028 | B:NT:P1.13 | 0.06 | 33 | 16 | 18 | QRDR <i>gyrA</i> Asp-95 → His | This study |

We detected 3 strains with DSC (MIC 0.06-0.12 mg/l) showing zones from 6 to 18 mm with nalidixic acid disk (Table 2). Two of them presented a mutation in QRDR *gyrA* Asp-95 → Asn or His, and the third an efflux mechanism.

CONCLUDING REMARKS

Changes in the prevalence of dominant Serogroups B and C, the increase of isolates with Serogroups Y+W135+X, the high frequency of MS to PEN and the detection of emergent mechanisms of resistance, highlight the epidemiological relevance of a National Surveillance Programme in NME.