Meningococcal Disease: Epidemiology and Early Effects of Immunization Programs

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Meningococcal disease (MD) is a major public health problem and remains an important cause of meningitis and sepsis in several Latin American countries. Most cases of MD are sporadic, with seasonal variations and outbreaks occurring at irregular intervals. Outbreaks are more likely to involve older children and young adults, usually associated to increased case fatality rates (CFRs). During the last decade, incidence rates of MD varied widely in the region, from less than 0.1 cases per 100 000 in countries including Mexico, Peru, Paraguay, and Bolivia to 2 cases per 100 000 in Brazil, with the highest incidence generally observed in infants [1, 2]. The availability and quality of published data for MD are not uniform across the region, with limited data available and exceedingly low rates of MD reported by some countries [1, 2].

Serogroups B and C are responsible for the majority of cases reported in the region. However, an increased number of serogroup W disease cases, associated with the ST-11 complex, was recently reported in Argentina and Chile [2]. According to the SIREVA program implemented by the Pan-American Health Organization and the World Health Organization, a total of 901 meningococcal isolates were characterized in 2012, of which 513 came from Brazil, 172 from Argentina, 100 from Chile, 30 from Colombia, 28 from Venezuela, and 24 from Uruguay. These 6 countries were responsible for more than 95% of the isolates reported in the region. Serogroup C was the prevalent serogroup, responsible for 44% of the meningococcal isolates characterized; serogroup B was responsible for 29%; serogroup W was responsible for 20%; and serogroup Y was responsible for 5% [3].

RECENT EXPERIENCE OF MENINGOCOCCAL VACCINATION PROGRAMS

Brazil

MD surveillance in Brazil is passive, and all suspected cases should be reported to the National Notifiable Diseases Information System (SINAN), managed by the Brazilian Ministry of Health. In late 2010, Brazil was the first country in Latin America to introduce the meningococcal C conjugate (MCC) vaccine routinely into its Immunization Program. The decision was based on the epidemiological situation reported in the country at that period, showing 80% of the identified MD cases associated with serogroup C; incidence rates of approximately 1.6 cases/100 000 inhabitants, with the highest incidence rates in infants and young children; CFRs as high as 20%; and several serogroup C disease outbreaks reported in different regions, associated with clonal complex ST-103 [2].

The MCC vaccination was introduced into the routine immunization schedule of infants, in 2 doses, at 3 and 5 months old, with a booster dose at 12 months of age. Toddlers between 12 and 23 months received 1 dose of the vaccine, with no catch-up campaign for older age groups. A technology transfer agreement between Novartis vaccines and Ezequiel Dias Foundation (FUNED) was established and according to this agreement, Novartis will provide the MenC-CRM197 vaccine (Menjugate) until the complete technology transfer to FUNED is conducted. All vaccines that are part of the national immunization program in Brazil are fully funded by the government, and the coverage for the primary 2 doses was ~85% in late 2011, reaching 90%–95% in 2012 and 2013.

Early trends, in 2011 and 2012, derived from population-based data demonstrated a 50% reduction in the incidence
rates of MD in children aged < 2 years, the age group targeted for vaccination, after the introduction of the vaccine. However, no early impact was observed in other age groups (Table 1). Incidence rates were calculated using the annual number of confirmed cases of MD reported by the SINAN and the estimated population in each age group provided by the Brazilian Institute of Geography and Statistics [4].

Chile

Until recently, MD caused by serogroup W was rarely observed in Latin America. However, there is now evidence to suggest that serogroup W emerged in Argentina, Chile, and Uruguay. In Argentina, the prevalence of this serogroup increased from 2% of cases with confirmed serogroup in 2000 to 47% in 2010 and 58% in 2012; the incidence rate of MD in 2012 was 0.6 cases/100 000 persons, with the highest incidence in infants (13.6 cases/100 000) [2, 3, 5]. The emergence of serogroup W in Brazil, Argentina, and Chile has been linked to the hypervirulent Hajj clone W135:P1.5,2:ST11 (ST11/ET37 clonal complex), which emerged in 2000 and has since spread internationally [2, 5, 6]. This Hajj clone has also been associated with high CFRs in South Africa (22% CFR) [7].

In 2012, the Ministry of Health from Chile reported an increased number of cases of MD due to serogroup W. The incidence rate of MD was 0.8/100 000 persons, with 55% of the cases due to serogroup W (24% of the cases in infants). As of December 31, 2012, 60 cases of serogroup W135 with 16 deaths (CFR of 26.6%, the highest CFR reported in Chile in the last 30 years) have been confirmed, compared to 22 cases reported in 2011 and 6 cases in 2010. Half of the cases reported during 2012 were in children younger than 5 years [8].

An immunization campaign using 2 different tetravalent conjugate vaccines (Men ACWY conjugated to diphtheria toxoid [Menactra] and Men ACWY conjugated to CRM197 [Menveo]), targeting children aged 9 months to 5 years (approximately 1 million children), commenced in 2012, with a roll out to the whole country during the first months of 2013. Coverage for the first dose of the vaccine was almost 100% for the targeted age group. A second dose was given for children from 9 months to less than 2 years.

In 2013, 142 cases were reported in Chile, of which 134 were serogrouped. Among the identified cases, 65% (87) were serogroup W, 34% (45) serogroup B, and 2 cases serogroup C. Four cases of serogroup W were reported in the age group targeted for the vaccination, all of them unvaccinated children [9]. Preliminary analysis of the current epidemiologic situation in Chile showed that, after the Men ACWY immunization, protection was observed only for the age groups targeted for the vaccine, without early indirect effects (Table 2). The overall incidence rates of serogroup W MD in 2013 were similar to those in 2012 [8, 9].

### Table 2. Incidence Rates of Serogroup W MD in Chile*

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Incidence rates (cases/100 000 habitants)</th>
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<tbody>
<tr>
<td></td>
<td>2012</td>
</tr>
<tr>
<td>&lt;9 months</td>
<td>6.0</td>
</tr>
<tr>
<td>9 months–4 years</td>
<td>1.7</td>
</tr>
<tr>
<td>5–9 years</td>
<td>0.3</td>
</tr>
<tr>
<td>10–19 years</td>
<td>0.1</td>
</tr>
<tr>
<td>20–60 years</td>
<td>0.2</td>
</tr>
<tr>
<td>&gt;60 years</td>
<td>0.4</td>
</tr>
</tbody>
</table>

*Adapted from references [8, 9].
CONCLUSIONS

After the implementation of the routine MCC immunization program in Brazil, a significant impact on the incidence rates of disease in the age groups targeted for the vaccine was observed. However, despite the dramatic decrease in the incidence rates of MD among the age groups that were vaccinated, no early impact was observed in other age groups, probably reflecting the lack of a catch-up program including adolescents, usually the age group responsible for carriage and transmission.

In Chile, the reactive ACWY vaccination also provided a decrease in the incidence rates of serogroup W disease only in the age groups that received the vaccine, without early impact on other age groups.

The success of the MCC vaccination program in reducing disease in the United Kingdom and other European countries was attributed to the combined efficacy of the vaccine not only against disease but also against carriage. A striking feature of these MCC vaccination programs, which included catch-up of children and adolescents, has been the additional decrease in disease incidence in unvaccinated individuals as a result of herd protection. Immunization of adolescents and young adults (the age groups that usually have the highest rates of colonization) in these catch-up campaigns reduced the carriage rates of meningococcal serogroup C in the vaccinated age group and may have prevented transmission of the organism and acquisition by other individuals [10–13].

After introduction of meningococcal vaccines, it is of paramount importance to maintain continuous, careful surveillance for MD epidemiology. This information will have important implications in future vaccination strategies to maximize the benefits of vaccination.

Acknowledgments

Potential conflicts of interest. All authors: No reported conflicts.
All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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