quotient score in 14 of 18 (78%) infants in whom SNHL was excluded during the second year of life was 102.9 (SD 7.9), and the mean score of the language subscale was 15.7 months (SD 1.5). Both scores were not different compared with scores of infants in whom hearing tests were not performed. Viral load in 17 of 18 (94%) infants in whom hearing was tested during the second year of life did not differ from viral load in 64 of 66 (97%) infants who were not tested at that time (median: 3.3 × 10^3 copies/mL versus 3.1 × 10^3 copies/mL, P = 0.8).

**DISCUSSION**

This study shows that preterm infants with postnatally acquired CMV infection do not develop SNHL during the first 2 years of life.

CMV is an important cause of SNHL in children. In contrast to congenitally infected infants, little is known about hearing in preterm infants with postnatal CMV infection. Audiologic follow-up of infants with postnatal CMV infection has so far only been studied twice and has been limited to small numbers of patients. In the first study, 30 postnatally infected preterm infants with GA between 35 and 37 weeks were tested at 3 years of age, and all had normal hearing. In the second study, 22 infected preterm infants born before 32 weeks of gestation were evaluated at 2 and 4.5 years of age, respectively. None of the infected infants developed SNHL. Furthermore, in 20 of these previously studied infants the hearing was tested again at school age, and none of them developed SNHL. This is in line with our study where we found no SNHL in 64 infected preterm infants during the first year of life and in 18 during the second year of life regardless of the presence of cerebral abnormalities, clinical symptoms of CMV disease or urine CMV load. Moreover, the neurodevelopmental scores using the GMDS including language subscale were normal in all infants with and without hearing test at 18 months of corrected age. As the language subscale of the GMDS score may not exclude mild sensorineural hearing deficit (such as auditory neuropathy), the hearing of infected infants will be assessed again at school age.

Recently, the relationship between postnatal CMV infection and development of SNHL (including auditory neuropathy) in a preterm infant was suggested. This infant, born at a GA of 26 weeks developed CMV infection within 3 weeks of age, and at term-equivalent age bilateral auditory neuropathy was diagnosed. At 4 years of age, her language perception was normal and her language expression was mildly delayed. The suggestion that extremely low birth weight infants who develop CMV infection within several weeks after birth are at high risk of developing auditory deficit cannot be confirmed in our study. None of the 21 (25%) infants born ≤27 weeks of gestation and none of the 5 of 6 symptomatic infants in whom hearing was tested (median GA: 27.3 weeks, range: 26.0–29.6) developed SNHL during the first year of life. In the second year of life, hearing of 8 infants born ≤27 weeks of gestation and 2 symptomatic infants was tested; none of them had SNHL.

It is of interest that the development of lenticulostriate vasculopathy, which was documented in 35% of studied infants, was not associated with hearing loss. The exact mechanism of acquiring SNHL caused by CMV infection is still unknown; however, it may be the result of persistent cochlear inflammation. CMV has been recently isolated from the inner ear of a 15-month-old boy 1 month after a documented primary CMV infection.

A limitation of our study is the limited number (18/84, 21%) of preterm infants with CMV infection that could be tested during the second year of life. All parents of nontested infants were convinced that their children had no hearing deficits and therefore they refused a hearing test between 18 and 24 months of age. It is, however, likely that severe hearing impairment among infants who were not tested during the second year of life would have been recognized using GMDS and its language subscale. Furthermore, there were no differences in viral load and other hearing loss risk factors between tested and nontested infants. Because progressive SNHL caused by CMV infection may sporadically develop in later life, future evaluation of hearing in our population is still desirable. Neurodevelopmental outcome of infected and noninfected infants will be assessed in the near future. In conclusion, postnatally acquired CMV infection among preterm infants is not related with SNHL during the first and second year of life. Accepted for publication May 09, 2012.

**REFERENCES**


**BACTERIAL MENINGITIS AND PNEUMOCOCCAL SEROTYPE DISTRIBUTION IN CHILDREN IN CAMEROON**

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**Abstract:** Acute bacterial meningitis causes a substantial number of deaths in Cameroon. Among 170 children with acute meningitis, 112 were positive for a bacterial pathogen when tested using polymerase chain reaction amplification, and *Streptococcus pneumoniae* accounted for 57.1% of cases. Pneumococcal serotype coverage by 13-valent pneumococcal conjugate vaccine has been limited in Cameroon.
Pneumococcal Serotypes
7 8-2

coccal conjugate vaccine (PCV-13, Prevenar13, Pfizer Inc., New

Alliance for Vaccines and Immunization–eligible country, Cam
and none on circulating pneumococcal serotypes. As a Global
role of
orities based on vaccine cost-effectiveness studies.

countries but data of only 13 of 53 African countries
formed in a limited number of countries and extrapolated for the
In Africa, serotype determination and surveillance have been per
tered in developing countries and must be included into vaccines

to maximize their effect in these countries.

were available, most of them coming from eastern Africa. Ideally,
cross the 5 continents but data of only 13 of 53 African countries

is more difficult to assess for
is responsible for more than 90% of all invasive diseases due to
the disease burden and bacterial serogroup/serotype distribution
competing public health priorities, and by limited information on
conjugate vaccines against these bacteria has been recommended
by the World Health Organization, but has been constrained by

determination targeting S. pneumoniae, Hib and N. meningitidis as previously described. 10 In case of a positive PCR result for S. pneumoniae, a second confirmation PCR was performed targeting the lvtA gene. 13 For N. meningitidis, DNA was then amplified with a real-time PCR to detect the ctra gene 10 and, whenever this first PCR assay was positive, we performed a second amplification to detect the genes encoding the specific polysialyltransferase (siaD gene) for B, C, Y/ W135 serogroups and mynB gene for A serogroup, respectively. 12 Detection and identification of S. pneumoniae was done using a S. pneumoniae serotyping assay that genotypes 8 capsular genes to identify pneumococcal serotypes. 13

Statistics
Categoric baseline data were expressed in percentages, and compared using Pearson χ2 tests. Continuous baseline data were expressed using medians and interquartile ranges (IQRs), and compared with Kruskal-Wallis tests, with P considered significant under 0.05. Results were expressed in percentages for relative prevalence and case fatality by bacteria, age or socioeconomic group, and compared with odds ratios and 95% confidence intervals (CIs). The study was approved by the ethical committee of the Faculty of Medicine and Biomedical Sciences, Yaounde, Cameroon.

RESULTS
A total of 170 children were included in the study, and 71 (41.8%) were female. Eleven (6.5%) children suffered from moderate wasting (weight/height < −2 standard deviation), and 5 (2.9%) were severely malnourished (weight/height < −3 standard deviation). Sixteen (9.4%) were known to be HIV positive, and 8 were suffering from sickle cell disease, 2 with a homozygote form. Four children were vaccinated with the 23-valent pneumococcal polysaccharide vaccine (Pneumovax-23, Sanofi Pasteur-MSD, Lyon, France), none with a pneumococcal conjugate vaccine. One child was vaccinated against Hib and 1 against N. meningitidis ACRYW135. A total of 124 (72.9%) children were correctly immunized for their respective age against diphtheria, tetanus, polio, pertussis and measles.

PCR results in CSF returned positive in 112 children (65.9%): 64 were positive for S. pneumoniae, 31 for Hib and 17 for N. meningitidis. Most of the patients were recruited in the hospital

children and to determine pneumococcal serotypes before PCV introduction.

METHODS
A prospective multicenter observational study was conducted from January 2008 to December 2009 in 3 distant locations with different climatic conditions in Cameroon: The Mother and Child Hospital of Chantal Biya Foundation at Yaounde in the central province (damp plain), the district hospital of Dschang in the western province (mountain) and the district hospital of Kousseri in the north extreme province (sub-Saharan). Children from 2 months to 15 years of age attending these hospitals with fever (>38°C), clinical signs and symptoms of meningitis, and a lumbar puncture showing a turbid aspect with more than 50 polymorphonuclear cells/mm3 were enrolled after informed written consent by a parent responsible for the child was obtained. The management and treatment of these children were not modified by the study and kept under the responsibility of the physician in charge of the patient.

Demographics, clinical data, length of hospital stay and outcome were recorded for all children. One milliliter of cerebrospinal fluid (CSF) was immediately stored at −20°C and transported every 6 months in dried ice to the Laboratory of Bacteriology at the University Hospitals of Geneva, Geneva, Switzerland, for bacterial DNA extraction and polymerase chain reaction (PCR) amplification targeting S. pneumoniae, Hib and N. meningitidis as previously described. 10 In case of a positive PCR result for S. pneumoniae, a second confirmation PCR was performed targeting the lvtA gene. 13 For N. meningitidis, DNA was then amplified with a real-time PCR to detect the ctra gene 10 and, whenever this first PCR assay was positive, we performed a second amplification to detect the genes encoding the specific polysialyltransferase (siaD gene) for B, C, Y/ W135 serogroups and mynB gene for A serogroup, respectively. 12 Detection and identification of S. pneumoniae was done using a S. pneumoniae serotyping assay that genotypes 8 capsular genes to identify pneumococcal serotypes. 13

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of Yaoundé (78.8%) compared with Kousseri (14.7%) and Dschang (6.5%; Table 1). CSF culture was performed locally in 47 children (27.6%) and returned positive in 28. Concordance of CSF culture with PCR results was found in 25 of 28 cases. For discordant cases, 1 culture grew group B streptococci, 1 Salmonella sp and 1 N. meningitidis but PCR remained negative in 2 subsequent attempts. The median age at enrollment was 15 months (IQR: 6–48) with a range from 3 to 156 months. Children with Hib and pneumococcal meningitis were significantly younger than those infected with N. meningitidis (median age of 9 [IQR: 6–17] months and 15 (IQR: 6–55.5) months compared with 72 (IQR: 41–123) months, respectively [both P < 0.001]).

All-cause mortality in meningitis cases was very high at 21.8%, and highly depended on age (logistic regression P = 0.03): we found a case fatality of 25.4% at age < 2 years, 30.8% between 2 and 5 years and it decreased to 5.3% at age > 5 years. We observed a bimodal distribution curve with a first mortality peak at age < 1 year (27.6%) and a second peak at 4 to 5 years of age (57.1%) due to the 3 types of bacteria: Hib and S. pneumoniae prevailed at 9 and 15 months, whereas meningococcal meningitis occurred around 72 months of age. Therefore, the odds ratio comparing mortality before and after 5 years was highly significant at 6.5 (95% CI: 1.5–28.4).

Overall, 24.7% of children with meningitis did not complete their treatment because of the lack of financial resources to pay a full antibiotic course. Case-fatality rate was the highest among pneumococcal meningitis (26.6%), followed by Hib (25.8%) and meningococcal meningitis (5.9%; Table 2). A significant, excess mortality was noted in children who could not afford the full antibiotic treatment: 43.9% versus 14.7%, odds ratio = 4.53 (95% CI: 2.06–9.94; P < 0.0001).

The bacterial type distribution in CSF varied substantially among the 3 sites (Table 1). S. pneumoniae was predominant in Yaounde, Hib in Dschang (both cities in the south-west), whereas N. meningitidis was the main pathogen in Kousseri. Whereas the city of Kousseri is located in the extreme north province, part of the meningitis belt, 10 of 13 meningococcal strains recovered from this center belonged to the serogroup Y or W135 and only 3 to the serogroup A. Nine of 10 cases of serogroup Y or W135 occurred within 6 weeks from April 1 to May 15, 2008.

Hib meningitis had the second highest case-fatality rate, and 58.0% of children presented partial and generalized convulsion at the time of presentation to the emergency room. Twenty-two percent of children developed a coma (Glasgow Coma Scale < 8).

Pneumococcal meningitis occurred in 48.4% children below the age of 1 year, in 75.0% below 5 years of age but none before 3 months of age. More than 20 different pneumococcal serotypes were found (Fig., Suplemental Digital Content 1, http://links.lww.com/INF/B257). The predominant serotypes were serotype 1 (20.7%), serotypes 32A/32F (12.1%) and 6A, 14 and 23B accounting for 6.9% each. Overall, serotype coverage by 7-valent pneumococcal conjugate vaccine was 19.0%, by 10-valent pneumococcal conjugate vaccine 50.0% and PCV-13 62.1% (Fig., Suplemental Digital Content 1, http://links.lww.com/INF/B257). In children below 5 years of age, PCV-13 serotype coverage was similar (62.2%). In HIV-positive children (n = 16), 3 had Hib meningitis, 7 pneumococcal meningitis and, in 3 the etiology was not determined. No specific serotype was associated with HIV positivity, serotypes 1, 6A, 6B, 15F, 19A and 23B being recovered.

Finally, 1 case was due to Salmonella sp and 1 case due to group B streptococcus, and no bacteria was recovered in 56 children despite biological signs of bacterial meningitis in the CSF (leukorachia, low glucose) and a case-fatality rate of 18.9%, suggesting a bacterial rather than a viral origin.

## DISCUSSION

Acute bacterial meningitis (ABM) is a terrifying disease with a high case-fatality rate especially in countries where rapid access to medical care is limited as in sub-Saharan Africa. Furthermore, being diagnosed quickly is not a guarantee of success because many poor families can neither pay for hospitalization nor for antibiotic treatment. In our study, performed in 3 different sites in Cameroon, 24% of children with acute meningitis did not receive a complete antibiotic course due to the lack of financial resources. The overall mortality was 21.8%, but increased to 43.9% in those who did not receive a full antibiotic course. Although vaccination cannot abolish social differences in Africa, it could reduce the inequality gap by giving most children access to mass vaccination campaigns as has been shown successfully for measles and polio. However, ABM is a more difficult issue because the causative agents are multiple, and cost-effectiveness and impact studies have not determined which vaccine could have the maximum benefit in this population. In Cameroon, few data exist, and none concerning the incidence rates of ABM. Fonkoua et al reported that in Yaounde, S. pneumoniae was responsible for 56.2%, Hib 18.5% and N. meningitidis 13.4% of all ABM, a distribution close to our report with 57.1%, 27.7% and 15.2% for S. pneumoniae, Hib and N. meningitidis, respectively, and also to ratios found in other African countries. Even in neighboring countries located in the African meningitis belt, Gessner et al showed that S. pneumoniae was the leading pathogen, in the absence of epidemics of N. meningitidis, with a mean annual incidence rate of 98 and 7.8 to 14 per 100,000 among persons < 1 year of age and 1–19 years of age, respectively.

If more than 90% of ABM caused by H. influenzae are of serotype b, the situation is more complex with N. meningitidis where 5 different serogroups are involved and even more difficult with S. pneumoniae where more than 90 serotypes cause invasive diseases. In Africa, especially in the African meningitis belt, N. meningitidis of the serogroup A is predominant, although several reports showed that the serogroup W135 incidence rate is increasing, especially in pilgrims going to Mecca for the hajj.

### TABLE 1. Etiology of Bacterial Meningitis in Cameroon

<table>
<thead>
<tr>
<th>Variable</th>
<th>S. pneumoniae N (%)</th>
<th>H. influenzae b N (%)</th>
<th>N. meningitidis N (%)</th>
<th>ND N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yaoundé</td>
<td>55 (65.5)</td>
<td>26 (31.0)</td>
<td>3 (3.6)</td>
<td>50</td>
</tr>
<tr>
<td>Kousseri</td>
<td>8 (34.8)</td>
<td>2 (8.7)</td>
<td>13 (56.6)</td>
<td>2</td>
</tr>
<tr>
<td>Dschang</td>
<td>1 (20.0)</td>
<td>3 (60.0)</td>
<td>1 (20.0)</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>64 (57.1)</td>
<td>31 (27.7)</td>
<td>17 (15.2)</td>
<td>58</td>
</tr>
</tbody>
</table>

ND indicates not determined.

### TABLE 2. Characteristics of Bacterial Meningitis

<table>
<thead>
<tr>
<th>Variable</th>
<th>S. pneumoniae N (%)</th>
<th>H. influenzae b N (%)</th>
<th>N. meningitidis N (%)</th>
<th>ND N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age median (mo)</td>
<td>15</td>
<td>9</td>
<td>72 (15)</td>
<td>15</td>
</tr>
<tr>
<td>Male gender %</td>
<td>51.6</td>
<td>51.6</td>
<td>64.7</td>
<td>53.40</td>
</tr>
<tr>
<td>LOS (d)</td>
<td>11.5</td>
<td>10.4</td>
<td>10.5</td>
<td>9.2</td>
</tr>
<tr>
<td>Incomplete Tx</td>
<td>16/64</td>
<td>12/31</td>
<td>1/17</td>
<td>13/58</td>
</tr>
<tr>
<td>Mortality %</td>
<td>25</td>
<td>25.8</td>
<td>5.9</td>
<td>18.9</td>
</tr>
</tbody>
</table>

*Length of stay in the hospital (mean).

Antibiotic treatment not finished.

ND indicates not determined; d, days; mo, months.
In our study, 10 cases of ABM due to the serogroup Y or W135 occurred in the same center in a period of 6 weeks, suggesting an epidemic. Unfortunately, in the study period, we had no molecular technique to differentiate between serogroup Y or serogroup W135 and no data were available about travel and pilgrimage in the relatives of these children.

As reported in many other African countries,2,18 our study showed that S. pneumoniae is the leading ABM pathogen in Cameroon, associated with a high case-fatality rate. Therefore, a special effort has to be made to increase the implementation of pneumococcal conjugate vaccines in this continent as recommended by the World Health Organization in 2007. However, pneumococcal serotype distribution varies from one country to the other, and serotype circulation must be determined to calculate the potential impact of an immunization program. In Burkina Faso (north-west Africa), serotypes 1, 6A, 5 and 2 were predominant in ABM before the introduction of pneumococcal conjugate vaccines,2 in Uganda (central-east Africa) 6A, 6B, 22A and 23F,19 whereas in Tunisia (north Africa), serotypes 19F, 19A, 14 and 23F were recovered most often.20 In a recent publication reviewing studies of invasive pneumococcal diseases causing serotypes, Johnson et al21 found data from 13 of 53 (24.5%) African countries and calculated a maximal coverage of 49% (95% CI: 41–57%) for 7-valent pneumococcal conjugate vaccine, 72% (95% CI: 67–76%) for 10-valent pneumococcal conjugate vaccine and 77% (95% CI: 71–82%) for PCV-13, in children below 5 years of age, allowing potentially the prevention of 3.7 million cases of pneumococcal diseases in this continent each year. However, if the PCV-13 coverage reached 79.07% in Kenya and Uganda and even 100% in Tanzania,21 nonvaccine serotypes seem to be more prevalent in countries situated in western Africa. For instance, in Burkina Faso and Togo, the 7-valent, 10-valent and 13-valent PCVs would cover 6%, 39% and 67% of serotypes identified among children aged < 5 years, respectively,2 rates similar to those we reported in Cameroon. In our study, serotypes 32A-32F, which cannot be differentiated in the assay we used, accounted for 12.1% of all serotypes, 6%, 39% and 67% of serotypes identified among children aged <5, 6-10 and >10 years respectively.

In conclusion, our study is the first to report pneumococcal serotypes causing meningitis in children in Cameroon, a Global Alliance for Vaccines and Immunization–eligible country that introduced PCV-13 in July 2011. Despite the relatively low number of patients in this study, the calculated maximal coverage of this vaccine (62%) was less than what was estimated for other African countries and this has to be taken into account in the expected impact on pneumococcal meningitis in this country.

REFERENCES


INFLIXIMAB TREATMENT OF PANCREATITIS COMPLICATING ACUTE KAWASAKI DISEASE

Susan G. Jimenez-Fernandez, MD and Adriana H. Tremoulet, MD, MAS

Abstract: Kawasaki disease can be associated with gastrointestinal complications, including pancreatitis. We describe a child in whom infliximab infusion for intravenous immunoglobulin–resistant Kawasaki disease coincided with marked clinical improvement of the patient’s acute pancreatitis.

Key Words: vasculitis, coronary artery aneurysms, tumor necrosis factor–α, intravenous immunoglobulin, gallbladder hydrops

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