Invasive infections caused by Neisseria meningitidis, Haemophilus influenzae and Streptococcus pneumoniae among children in St Petersburg, Russia

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**ABSTRACT**

This study investigated the causes of invasive bacterial infections in children aged <15 years in St Petersburg, Russia, during 2001–2003, using culture and antigen detection methods (rapid antigen latex agglutination (RAL)) for normally sterile body fluids. A pathogen was detected in 90 cases (culture 50, RAL 40). *Neisseria meningitidis* was the most common pathogen (66%), followed by *Haemophilus influenzae* (19%) and *Streptococcus pneumoniae* (16%). Meningitis was the main clinical diagnosis (68/90, 76%), with *N. meningitidis* serogroup B, *H. influenzae* type b (Hib), and *S. pneumoniae* serogroup 1 being the most common isolates. Hib was less prevalent in St Petersburg than it was in industrialised countries before the introduction of Hib vaccinations.

**Keywords** Children, *Haemophilus influenzae*, invasive bacterial infections, *Neisseria meningitidis*, Russia, *Streptococcus pneumoniae*

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*Neisseria meningitidis*, *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae* are the main bacterial pathogens that cause invasive infections such as meningitis, sepsis and pneumonia in children aged <5 years. The aim of this exploratory study was to investigate the occurrence of bacterial pathogens causing invasive infections among children aged <15 years in St Petersburg, Russia, in order to help evaluate the need for vaccination against meningococcus, Hib and pneumococcus as part of the national immunisation programme.

The study was performed between 1 April 2001 and 31 March 2003. Three of the nine hospitals for children and adolescents in St Petersburg participated, namely the Institute of Children’s Infectious Diseases (ICID), City Hospital no. 4, and City Hospital no. 2. All invasive childhood infections in St Petersburg are treated in one of these three hospitals. The study protocol was approved by the Ethical Committee of the ICID and informed consent was obtained verbally from the children’s guardians.

The study included all children aged <15 years who were admitted to the participating hospitals with symptoms suggestive of bacterial meningitis, septicaemia, pneumonia, epiglottitis, bacterial arthritis or cellulitis, as described in the WHO generic protocol for population-based surveillance of *H. influenzae* type b [1]. Details of the case definitions used are listed in Table 1. Standard bacteriological methods were used according to WHO recommendations [1] and the official protocols in Russia. Isolates of *N. meningitidis* and *H. influenzae* were serotyped using slide agglutination. The presence of antigens in cerebrospinal fluid (CSF) or blood to *N. meningitidis* (serogroups A, B and C), Hib and pneumococcus was detected using rapid antigen latex agglutination (RAL) tests (Slidex meningite-Kit 5; bio-Mérieux, Marcy l’Etoile, France). All isolates of *N. meningitidis*, *H. influenzae* and *S. pneumoniae* were identified and serotyped for quality assurance at the National Public Health Institute (KTL), Oulu, Finland as described previously [2–4]. Bac-
Table 1. Definite, probable and possible cases of meningitis, septicaemia, epiglottitis and pneumonia among 164 children aged <15 years in St Petersburg, Russia

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Definite (n = 50)</th>
<th>Probable (n = 40)</th>
<th>Possible (n = 74)</th>
<th>All (n = 164)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CSF (n = 22)</td>
<td>Blood (n = 28)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningitis and/or septicaemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>6</td>
<td>1</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>Neisseria meningitidis</td>
<td>10 ME</td>
<td>21</td>
<td>9</td>
<td>59</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>6</td>
<td>3</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>No aetiological agent detected</td>
<td></td>
<td></td>
<td>46</td>
<td>46</td>
</tr>
<tr>
<td>Clinical meningococcal septicaemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epiglottitis</td>
<td></td>
<td></td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>2</td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>1</td>
<td></td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

In total, 270 patients were admitted with clinical symptoms of invasive bacterial infection (248 with an admission diagnosis of meningococcal septicaemia, 20 with pneumonia, and two with epiglottitis). In 164 (61%) cases, the case-definition criteria were met. In 90 (55%) of the 164 cases, laboratory results confirmed the aetiology of infection (Table 1). In total, 74% of the laboratory-confirmed cases were aged <5 years (Table 2). The main clinical manifestation was meningitis in 68 (76%) of 90 children, regardless of age. In young children (aged <5 years, n = 51), meningitis was caused by *N. meningitidis* in 30 (59%) cases, by *H. influenzae* (12 type b, two non-encapsulated) in 14 (27%) cases, and by *S. pneumoniae* in seven (14%) cases. In older children, meningitis was caused mainly by *N. meningitidis* (12/17, 71%) and by *S. pneumoniae* (5/17, 29%).

None of the cases of meningitis in older children was caused by *H. influenzae*.

Laboratory-confirmed septicaemia was caused mainly by *N. meningitidis*. In addition, there were many cases of clinical meningococcal septicaemia. Very few cases of pneumonia and epiglottitis were laboratory-confirmed (Table 1). Among the 90 laboratory-confirmed cases, the pathogen was cultured in 50 (56%) cases, and gave a positive result according to RAL in 40 (44%) cases. The majority (66%) of cases were caused by *N. meningitidis*, followed by *H. influenzae* (19%) and *S. pneumoniae* (16%). Group B was the most common (66%) serogroup among meningococci, serotype b was most common (78%) among *H. influenzae*, and serotype 1 was most common (70%) among pneumococci. *H. influenzae* was detected mainly in CSF, half by culture and half by RAL. In contrast, 68% of the meningococci were isolated from blood, half by culture and half by RAL. Pneumococci were isolated mainly (71%) by culture from CSF (Table 1).

In the present study, *N. meningitidis* was the most common pathogen causing invasive bacterial disease in children, with group B being the most common serogroup. This is in accord with a European study in 1999–2000 which revealed that serogroups B and C accounted for 95% of cases of disease, with serogroup B predominating (http://www.hpa.org.uk/hpa/inter/m_surveillance9900.pdf). However, group A meningococcus remained more common (>10% of cases) in the Moscow area in 1999–2000 than in Europe generally (0.3%), although it has now...

Table 2. Distribution of bacterial pathogens, grouped according to age, of 90 children with positive blood or cerebrospinal fluid cultures and/or rapid latex agglutination test results

<table>
<thead>
<tr>
<th>Age</th>
<th><em>Haemophilus influenzae</em></th>
<th><em>Neisseria meningitidis</em></th>
<th><em>Streptococcus pneumoniae</em></th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3 months</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>4-6 months</td>
<td>3</td>
<td>5</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>7-12 months</td>
<td>2</td>
<td>11</td>
<td>4</td>
<td>17</td>
</tr>
<tr>
<td>1 to &lt;5 years</td>
<td>10</td>
<td>23</td>
<td>1</td>
<td>34</td>
</tr>
<tr>
<td>≥5 to &lt;15 years</td>
<td>1</td>
<td>16</td>
<td>6</td>
<td>23</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>59</td>
<td>14</td>
<td>90</td>
</tr>
</tbody>
</table>
become rare [5]. In Finland, there was an epidemic of group A meningococcal disease in the early 1970s which was controlled by a national vaccination campaign [6].

The present study revealed that Hib was less common than *N. meningitidis* as the cause of meningitis. In an earlier study from Russia, Hib was responsible for bacterial meningitis in 50% of cases in St Petersburg, and in about 30% of cases in Moscow, Ekathenburg and Arkhangelsk [7]. In Finland, the incidence of meningitis caused by Hib increased several-fold between 1939 and 1986 [8], to 52/100 000 in children aged <5 years [9]. An increasing trend was also reported in other Nordic countries in recent decades [10], coinciding with an improvement in the socio-economic conditions since the 1940s. However, meningitis and other invasive diseases caused by Hib in Nordic and other European countries almost disappeared after introduction of the Hib conjugate vaccines in the late 1980s or early 1990s [11–14]. However, a study from Moscow [15], as well as the present study, suggests that invasive Hib disease is less prevalent in Russia than was formerly the case in Nordic countries before the introduction of Hib vaccination.

Of the three pathogens detected, *S. pneumoniae* was the least common in St Petersburg. Unlike in most Western countries [16], serotype 1 was the most common serotype. This serotype is known to cause outbreaks, and 'endemic' serotype 1 infections could actually represent unidentified outbreaks [17].

Although this study was performed in three hospitals in which all paediatric cases of bacterial infection are supposed to be treated, it is possible that some cases of meningitis were treated in other hospitals, and that many cases of pneumonia could have been treated at home. Moreover, it is not known how many patients with potential invasive bacterial infections received antibiotics before hospitalisation. Nevertheless, in view of these results, general childhood Hib and pneumococcal vaccinations do not appear to be a high priority for St Petersburg.

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**REFERENCES**


**RESEARCH NOTE**

Performance of two tube coagulase methods for rapid identification of *Staphylococcus aureus* from blood cultures and their impact on antimicrobial management

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**ABSTRACT**

Test parameters and clinical impact of the direct tube coagulase test (DTCT) for rapid identification of *Staphylococcus aureus* from blood culture were investigated. The sensitivity of the DTCT at 4 h using saline dilution was 96%, compared with 93% using serum separator tubes; specificity was 100% for both methods. Among 32 patients with *S. aureus* bacteraemia, treatment modifications were based on microbiology results from the primary source of infection in 12 patients, on a Gram’s stain from blood culture in seven patients, and on the DTCT in nine patients. The DTCT is a valuable adjunct in the routine microbiology laboratory because of its good performance, technical simplicity and low cost.

**Keywords** Bacteraemia, coagulase test, diagnosis, impact, *Staphylococcus aureus*, treatment modification

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*Staphylococcus aureus* bacteraemia is a serious condition with high rates of mortality and morbidity [1,2]. In contrast, coagulase-negative staphylococci isolated from blood often represent skin contaminants, except in certain clinical conditions [3]. Early reporting of blood culture results can improve antimicrobial management and decrease costs [4–6]. In the case of *S. aureus* bacteraemia, patient outcome is poorer if appropriate treatment is delayed [7,8]. A wide range of tests for the rapid identification of *S. aureus* have been applied to blood cultures [9–20], but the direct tube coagulase test (DTCT) has the advantage that it is easy to perform in any laboratory, rapid, flexible in daily use, and inexpensive. The present study investigated the performance of the DTCT, using two sample preparation methods, and evaluated the impact of rapid identification of *S. aureus* from blood cultures on antimicrobial management.

In total, 633 blood cultures (BACTEC; Becton Dickinson, Franklin Lakes, NJ, USA) containing Gram-positive cocci in clusters upon microscopical examination were received at the microbiology laboratory of the University Medical Centre Nijmegen, The Netherlands, between October 2005 and March 2006. Blood culture bottles with growth detected between 14.00 and 17.00 hours on weekdays and between 14.00 hours on Fridays and closure of the laboratory on Sundays were excluded from this study, since readings of the DTCT at 2 and 4 h would fall outside regular working hours. Blood cultures collected routinely from patients in the adult haematology wards or attending the paediatric oncology outpatient clinic were also excluded because of the high rate of contaminated cultures in these settings.

For DTCTs using serum separator tubes (SSTs), blood culture broth (8.5 mL) from positive blood