High Prevalence of Antimicrobial Resistance among Clinical *Streptococcus pneumoniae* Isolates in Asia (an ANSORP Study)

Jae-Hoon Song,1,2,* Sook-In Jung,3 Kwan Soo Ko,2 Na Young Kim,2 Jun Seong Son,1 Hyun-Ha Chang,4 Hyun Kyun Ki,1 Won Sup Oh,1 Ji Youn Suh,2 Kyong Ran Peck,1 Nam Yong Lee,5 Yonghong Yang,6 Quan Lu,7 Anan Chonthaleong,8 Cheng-Hsun Chiu,9 M. K. Lalitha,10 Jennifer Perera,11 Ti Teow Yee,12 Gamini Kumarasinghe,12 Farida Jamal,13 Adeeba Kamarulzaman,14 Navaratnam Parasakthi,14 Pham Hung Van,15 Celia Carlos,16 Thomas So,17 Tak Keung Ng,17 and Atef Shibl18

Division of Infectious Diseases1 and Department of Laboratory Medicine,5 Samsung Medical Center, Sungkyunkwan University School of Medicine, Asia-Pacific Research Foundation for Infectious Diseases,2 and Kyungbook National University,4 Seoul, and Chonnam National University Hospital, Gwangju,3 Korea; Beijing Children’s Hospital, Beijing,6 Shanghai Children’s Hospital, Shanghai,4 and Princess Margaret Hospital, Hong Kong,17 China; Chulalongkorn University, Bangkok, Thailand;7 Chang Gung Children’s Hospital, Taipei, Taiwan8; Christian Medical College, Vellore, India10; University of Colombo, Colombo, Sri Lanka11; National University of Singapore, Singapore12; Universiti Putra Malaysia13 and University Malaya,13 Kuala Lumpur, Malaysia;14 Research Institute for Tropical Medicine, Manila, Philippines16; and King Saud University, Riyadh, Saudi Arabia18

Received 3 November 2003/Returned for modification 21 January 2004/Accepted 5 February 2004

A total of 685 clinical *Streptococcus pneumoniae* isolates from patients with pneumococcal diseases were collected from 14 centers in 11 Asian countries from January 2000 to June 2001. The in vitro susceptibilities of the isolates to 14 antimicrobial agents were determined by the broth microdilution test. Among the isolates tested, 483 (52.4%) were not susceptible to penicillin, 23% were intermediate, and 29.4% were penicillin resistant (MICs ≥ 2 mg/liter). Isolates from Vietnam showed the highest prevalence of penicillin resistance (71.4%), followed by those from Korea (54.8%), Hong Kong (43.2%), and Taiwan (38.6%). The penicillin MICs at which 90% of isolates are inhibited (MIC90s) were 4 mg/liter among isolates from Vietnam, Hong Kong, Korea, and Taiwan. The prevalence of erythromycin resistance was also very high in Vietnam (92.1%), Taiwan (86%), Hong Kong (76.8%), and China (73.9%). The MIC90s of erythromycin were >32 mg/liter among isolates from Vietnam, Korea, China, Taiwan, Singapore, Malaysia, and Hong Kong. Isolates from Hong Kong showed the highest rate of ciprofloxacin resistance (11.8%), followed by isolates from Sri Lanka (9.5%), the Philippines (9.1%), and Korea (6.5%). Multilocus sequence typing showed that the spread of the Taiwan19F clone and the Spain23F clone could be one of the major reasons for the rapid increases in antimicrobial resistance among *S. pneumoniae* isolates in Asia. Data from the multinational surveillance study clearly documented distinctive increases in the prevalence rates and the levels of antimicrobial resistance among *S. pneumoniae* isolates in many Asian countries, which are among the highest in the world published to date.

The global emergence of *in vitro* antimicrobial resistance in *Streptococcus pneumoniae* has become a serious clinical concern since the 1980s (1). During the past two decades, the rates of resistance to penicillin, other beta-lactams, and non-beta-lactam agents have been increasing rapidly in many parts of the world. In particular, data on rates of pneumococcal resistance from Asian countries at the end of the 1990s were alarming. International surveillance studies conducted in 1996-1997 (29) and 1998-1999 (18) in 11 Asian countries by the Asian Network for Surveillance of Resistant Pathogens (ANSORP) documented very high prevalence rates of penicillin and erythromycin resistance among *S. pneumoniae* clinical isolates and nasal carriage isolates from Korea, Japan, Vietnam, Thailand, Taiwan, and Sri Lanka, as well as the introduction and the spread of the Spanish 23F penicillin-resistant clone in Asia. The increasing prevalence of antimicrobial resistance among *S. pneumoniae* isolates is associated with an increasing incidence of invasive pneumococcal diseases in children (23), as well as clinical failures of antimicrobial treatment (6, 17, 19).

The present report describes the results of the third project of surveillance for pneumococcal resistance among clinical *S. pneumoniae* isolates collected from 14 centers in 11 countries in Asia and the Middle East between 2000 and 2001 by the ANSORP Study Group.

**MATERIALS AND METHODS**

The 14 study centers in 11 countries in Asia and the Middle East that make up the ANSORP Study Group are listed in Acknowledgments. Clinical *S. pneumoniae* isolates were prospectively collected from patients with community-acquired pneumococcal diseases at the 14 study centers from January 2000 to June 2001. With the exception of lower respiratory tract specimens, all isolates...
### RESULTS

A total of 685 isolates of *S. pneumoniae* which caused various pneumococcal diseases were collected from 14 centers from January 2000 to June 2001. The number of isolates varied by center, according to the duration of collection (Table 1). Of these, 243 (35.5%) were isolated from lower respiratory tract specimens, 208 (30.4%) were isolated from blood cultures, 65 (9.5%) were isolated from middle ear aspirates, 56 (8.2%) were isolated from cerebrospinal fluid, and 113 (16.5%) were isolated from other sites. Of the 632 isolates for which the ages of the patients were available, 264 (41.8%) were from patients \( \geq 5 \) years old, 54 (8.6%) were from patients between 5 and 15 years old, and 313 (49.6%) were from patients \( > 15 \) years old. The results of in vitro susceptibility testing for penicillin and beta-lactam agents are presented in Table 1. Of the 685 *S. pneumoniae* isolates from Asia, 483 (52.4%) were not suscep-
tible to penicillin; 23% were penicillin intermediate (I; MICs = 0.12 to 1 mg/liter), and 29.4% were penicillin resistant (R; MICs ≥ 2 mg/liter) (Table 1). Prevalence rates of penicillin nonsusceptibility varied widely by country, ranging from 7.8% (Vellore, India) to 92% (Ho Chi Minh City, Vietnam). Isolates from Vietnam showed the highest prevalence of penicillin nonsusceptibility (I, 20.6%; R, 71.4%) followed by those from Sri Lanka (I, 71.4%; R, 14.3%), Hong Kong (I, 25.3%; R, 43.2%), Taiwan (I, 24.6%; R, 38.6%), and Thailand (I, 26.9%; R, 26.9%). The penicillin MIC at which 90% of isolates are inhibited (MIC90) was 4 mg/liter among Thailand (I, 26.9%; R, 71.4%). The penicillin MIC at which 90% of isolates are inhibited (MIC90) was 4 mg/liter among isolates from Taiwan, as indicated by MIC90s of 4 mg/liter.

Penicillin MICs especially among isolates from Vietnam, Hong Kong, Korea, and Taiwan, while isolates from Korea, Taiwan, and Thailand showed persistently high rates of penicillin resistance (Table 2). The level of penicillin resistance has also increased, especially among isolates from Vietnam, Hong Kong, Korea, and Taiwan, as indicated by MIC90s of 4 mg/liter. Penicillin MICs ≥4 mg/liter were found for 36.5% of pneumococcal isolates from Vietnam, 25.8% of isolates from Korea, and 14.3% of isolates from Hong Kong. The highest penicillin MIC was 8 mg/liter for isolates from Taiwan (three isolates), China (one isolate), and Vietnam (one isolate). All cases caused by these highly resistant strains were successfully treated with various antimicrobial therapies. The rate of penicillin nonsusceptibility was significantly higher in patients ≤5 years of age (I, 23.1%; R, 37.5%) than patients >5 years of age (I, 23.1%; R, 26.6%) (P = 0.005). Pneumococcal isolates resistant to penicillin were also resistant to other antimicrobial agents. Penicillin-resistant isolates were resistant to amoxicillin-clavulanate (13.9%), cefuroxime (93.1%), ceftriaxone (7.9%), erythromycin (92.6%), trimethoprim-sulfamethoxazole (89.1%), clindamycin (54.5%), and ciprofloxacin (8.9%). Multivariate analyses showed that age ≤5 years (odds ratio [OR], 1.7; 95% confidence interval [CI], 1.2 to 2.4; P = 0.002), underlying pulmonary diseases (OR, 2.0; 95% CI, 1.3 to 3.1; P = 0.003), malignancy (OR, 2.3; 95% CI, 1.2 to 4.6; P = 0.015), and steroid use (OR, 2.8; 95% CI, 1.1 to 7.4; P = 0.032) were independent risk factors for penicillin resistance among pneumococcal isolates. The overall rate of amoxicillin-clavulanate resistance (I and R) was 7.9%; only 4.4% of isolates were resistant. The rates of ceftriaxone resistance were 0.9% among nonmeningeal isolates (MICs ≥ 4 mg/liter) and 4.1% among meningeal isolates (MICs ≥ 2 mg/liter). Although the prevalence rates of amoxicillin and ceftriaxone resistance were not high, we found strains highly resistant to amoxicillin (MICs ≥ 8 mg/liter) and/or extended-spectrum cephalosporins (ceftriaxone MICs ≥ 8 mg/liter) among isolates from Vietnam (n = 13), China (n = 6), Hong Kong (n = 3), Korea (n = 3), Taiwan (n = 1), and Malaysia (n = 1).

A total of 376 (54.9%) isolates were not susceptible to erythromycin; 18% were intermediate, and 53.1% were resistant. Very high rates of erythromycin resistance (MICs ≥ 1 mg/liter) were observed in Vietnam (92.1%), Taiwan (86%), Korea (80.6%), Hong Kong (76.8%), and China (73.9%). On the other hand, erythromycin resistance was relatively not prevalent in India (1.3%), Saudi Arabia (10.3%), and Sri Lanka (16.7%). Of the erythromycin-resistant isolates, 217 (59.6%) were clindamycin resistant and had the macrolide-lincosamide-streptogramin B (MLSb) phenotype. The MIC90s of erythromycin were >32 mg/liter for isolates from Korea, Vietnam, China, Taiwan, Singapore, Malaysia, and Hong Kong. Most of penicillin-resistant isolates (92.6%) were resistant to erythromycin, while 23.9% of penicillin-susceptible isolates were also resistant to erythromycin. The rate of erythromycin resistance was significantly higher among isolates from patients younger than age 5 years (OR, 3.1; 95% CI, 1.9 to 5.2; P = 0.001) and among isolates with penicillin resistance (OR, 15.4; 95% CI, 9.5 to 25; P = 0.001).

Forty-one (6%) isolates were resistant to ciprofloxacin (MICs ≥ 4 mg/liter) (Table 3). Isolates from Hong Kong

### Table 2: Changing trend of penicillin nonsusceptibility among pneumococcal isolates from Asia

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Korea</td>
<td>Korea (n = 13)</td>
<td>58.2/12.2</td>
<td>28.2/32.6</td>
<td>23.1/26.6</td>
</tr>
<tr>
<td>China</td>
<td>China (n = 6)</td>
<td>76.8/19.5</td>
<td>43.5/47.8</td>
<td>76.8/19.5</td>
</tr>
<tr>
<td>Thailand</td>
<td>Thailand (n = 3)</td>
<td>8.4/4.9</td>
<td>6.0/3.0</td>
<td>8.4/4.9</td>
</tr>
<tr>
<td>Vietnam</td>
<td>Vietnam (n = 3)</td>
<td>58.2/12.2</td>
<td>28.2/32.6</td>
<td>58.2/12.2</td>
</tr>
<tr>
<td>Philippines</td>
<td>Philippines (n = 3)</td>
<td>2.1/0</td>
<td>NA/NA</td>
<td>2.1/0</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>Saudi Arabia (n = 3)</td>
<td>3.6/15.4</td>
<td>NA/NA</td>
<td>3.6/15.4</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>Hong Kong (n = 3)</td>
<td>24.1/3.8</td>
<td>NA/NA</td>
<td>24.1/3.8</td>
</tr>
</tbody>
</table>

a Data are from reference 18.
b Data are from reference 29.

NA: not available.
showed the highest rate of ciprofloxacin resistance (11.8%), followed by isolates from Sri Lanka (9.5%), the Philippines (9.1%), and Korea (6.5%). Isolates from Hong Kong also showed higher rates of resistance to levofloxacin (8%), gatifloxacin (8.3%), and moxifloxacin (1.8%) than isolates from other Asian countries, where the prevalence of resistance to these newer fluoroquinolones was extremely low at the time of the study.

The overall rate of MDR *S. pneumoniae*, which was defined as resistance to at least three classes of antibiotics, was 26.8%, with 71.4% of the isolates from Vietnam, 44.9% of the isolates from Hong Kong, 30.9% of the isolates from Taiwan, and 45.2% of the isolates from Korea being MDR. The most common pattern of MDR was resistance to penicillin, erythromycin, and trimethoprim-sulfamethoxazole.

The most prevalent serogroups among the clinical pathogens from Asia were 19, 23, 6, 14, and 9, which accounted for 65.6% of all isolates (Table 4). Of the 271 isolates from children younger than age 5 years, serotypes 19F (21.8%), 23F (14.7%), 14 (10%), 6B (6.6%), 9 (4.5%), 6A (3.2%), and 19A (3%) were the most common ones. MLST analysis showed that most of the isolates belonged to either the Taiwan 19F clone (30 isolates) or the Spain 23F clone (33 isolates) (Table 5).

**DISCUSSION**

The results of this study indicate that the rates of antimicrobial resistance among *S. pneumoniae* isolates in Asia continue to increase. Since this study was a continuation of multinational surveillance projects that included two previous ANSORP studies, it could provide a unique opportunity to investigate the changing trend in resistance rates in Asia over a 5-year period. Previous ANSORP studies with clinical isolates (1996-1997) (29) and nasal carriage isolates (1998-1999) (18) have already revealed that many Asian countries had serious problems with in vitro resistance to penicillin and non-beta-lactam agents among *S. pneumoniae* isolates. Although direct comparison may not be possible due to the different characteristics of the isolates, resistance rates among pneumococcal isolates in this study strongly suggest a substantial increase in

<table>
<thead>
<tr>
<th>Country</th>
<th>No. of isolates (adults/children)</th>
<th>19</th>
<th>23</th>
<th>6</th>
<th>14</th>
<th>9</th>
<th>4</th>
<th>18</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Korea</td>
<td>27/74</td>
<td>32.0/0.0</td>
<td>32.0/0.0</td>
<td>19.4/8.5</td>
<td>32.0/0.0</td>
<td>32.0/0.0</td>
<td>65.3/0.0</td>
<td>32.0/0.0</td>
<td>65.0/0.0</td>
</tr>
<tr>
<td>China</td>
<td>13/96</td>
<td>0.9/3.7</td>
<td>1.8/18.3</td>
<td>0.0/1.8</td>
<td>0.9/7.4</td>
<td>0.0/5.5</td>
<td>0.9/7.4</td>
<td>0.0/5.5</td>
<td>6.4/34.9</td>
</tr>
<tr>
<td>Thailand</td>
<td>34/17</td>
<td>1.9/19</td>
<td>9.6/5.8</td>
<td>5.8/7.7</td>
<td>7.7/19</td>
<td>0.0/1.9</td>
<td>1.9/3.8</td>
<td>5.8/19</td>
<td>32.8/3.9</td>
</tr>
<tr>
<td>Taiwan</td>
<td>31/21</td>
<td>11.5/3.8</td>
<td>3.8/0.0</td>
<td>9.6/8.5</td>
<td>3.8/7.7</td>
<td>5.8/17.3</td>
<td>5.8/19</td>
<td>19.4/3.8</td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>57/16</td>
<td>4.1/0.0</td>
<td>1.4/0.0</td>
<td>4.1/1.4</td>
<td>2.7/4.1</td>
<td>2.7/4.1</td>
<td>2.7/0.0</td>
<td>1.4/2.7</td>
<td>49.4/5.5</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>40/2</td>
<td>2.4/0.0</td>
<td>31.0/0.0</td>
<td>23.8/0.0</td>
<td>4.6/0.0</td>
<td>14.2/2.4</td>
<td>9.5/0.0</td>
<td>9.5/2.4</td>
<td></td>
</tr>
<tr>
<td>Singapore</td>
<td>10/6</td>
<td>0.0/12.5</td>
<td>24.8/5.8</td>
<td>2.4/0.0</td>
<td>18.8/12.5</td>
<td>0.0/6.2</td>
<td>12.5/6.2</td>
<td>2.4/0.0</td>
<td>19.5/7.3</td>
</tr>
<tr>
<td>Malaysia</td>
<td>27/14</td>
<td>0.0/4.9</td>
<td>32.3/8.0</td>
<td>3.2/0.0</td>
<td>1.6/25.4</td>
<td>0.0/1.6</td>
<td>3.2/14.3</td>
<td>0.0/1.6</td>
<td>9.0/5.5</td>
</tr>
<tr>
<td>Vietnam</td>
<td>6/57</td>
<td>4.5/4.5</td>
<td>0.0/13.6</td>
<td>0.0/18.2</td>
<td>0.0/9.1</td>
<td>4.5/0.0</td>
<td>9.1/36.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hong Kong</td>
<td>9/715</td>
<td>0.0/9.0</td>
<td>21.6/4.5</td>
<td>18.9/2.7</td>
<td>2.7/0.0</td>
<td>6.3/3.6</td>
<td>5.4/18</td>
<td>0.0/9.0</td>
<td>29.8/0.0</td>
</tr>
<tr>
<td>Total</td>
<td>346/265</td>
<td>1.6/14</td>
<td>0.1/0.0</td>
<td>0.3/0.0</td>
<td>11.5/10.3</td>
<td>0.8/0.3</td>
<td>8.4/6.3</td>
<td>2.1/1.1</td>
<td>2.5/4.1</td>
</tr>
</tbody>
</table>

* MIC breakpoints for individual fluoroquinolones are as follows: for levofloxacin, I = 4 mg/liter and R = 8 mg/liter; for moxifloxacin, I = 2 mg/liter and R = 4 mg/liter; for gatifloxacin, I = 2 mg/liter and R ≥ 4 mg/liter; and for ciprofloxacin R ≥ 4 mg/liter.
amoxicillin (MICs ≥ 4 mg/liter) and/or extended-spectrum cephalosporins (cefotaxime MICs ≥ 4 mg/liter) have been identified in France (3) and Canada (20). We found 27 strains (13 from Vietnam, 6 from China, 3 from Korea, 3 from Hong Kong, and 1 each from Malaysia and Taiwan) for which amoxicillin MICs were ≥8 mg/liter and/or ceftriaxone MICs were ≥8 mg/liter. The emergence of such strains is of particular concern in the treatment of pneumococcal meningitis, because ceftriaxone is an important component of the combination regimens for pneumococcal meningitis.

As documented in previous reports (16), children younger than age 5 years were more frequently infected with penicillin-resistant strains. Frequent exposures to antimicrobial agents and day care center attendance would be important risk factors for the higher prevalence of penicillin resistance among isolates from children (22).

The remarkable increases in the prevalence and the level of macrolide resistance among clinical pathogens from Asia are of particular concern. Reported rates of erythromycin resistance in the Western Hemisphere were high in France (58.1%), Spain (57.1%), and the eastern south-central parts of the United States (47%) (6, 31; D. Feltingham and R. N. Gruneberg, Abstr. 40th Intersci. Conf. Antimicrob. Agents Chemother., abstr. 1790, 2000). However, macrolide resistance was reported to be more prevalent in Asian countries than in Western countries. Reports from Hong Kong and Taiwan showed that 80 to 91% of pneumococcal isolates were resistant to erythromycin (13, 14). According to the data from the present study, the prevalence rates of macrolide resistance were alarmingly high in Vietnam, Taiwan, South Korea, Hong Kong, and China, where more than 70% of clinical pathogens were fully resistant to erythromycin. Erythromycin resistance in pneumococci is due to the modification of the drug-binding site [which is regulated by the erm(B) gene], which is usually associated with the MLSB phenotype and high-level resistance to erythromycin, with MICs of ≥64 mg/liter. Low-level erythromycin resistance, with MICs of 1 to 32 mg/liter, is due to the active efflux of the drug [which is regulated by the mef(A) gene] (5). The efflux mechanism caused by the mef(A) gene is predominant in macrolide-resistant pneumococci in North America (28), while erm(B)-mediated ribosomal methylation has been found in >80% of erythromycin-resistant S. pneumoniae isolates in most European countries (9). On the basis of the distributions of the MICs for erythromycin-resistant strains and the rate of resistance to clindamycin in this study, the MLSB phenotype is predominant in Korea, China, Taiwan, Vietnam, and Hong Kong. Molecular characterization of macrolide-resistant strains from Asia showed that the erm(B) gene was found in more than 50% of pneumococcal isolates either singly or dually with the mef(A) gene in Korea, China, Vietnam, and Taiwan (30). Recently, clinical failures of macrolide treatment for pneumococcal infections caused by macrolide-resistant strains have been reported (19, 24). Given the widespread emergence of high-level resistance to erythromycin among pneumococci in Asia, as documented in this study, the use of a single macrolide for the treatment of pneumococcal diseases may result in the clinical failure of antimicrobial therapy.

Data from this study also showed the present situation of fluoroquinolone resistance among pneumococcal isolates in
Asia. Recently, Hong Kong investigators demonstrated the high rates of resistance of \textit{S. pneumoniae} isolates to various fluoroquinolones (10) and the presence of the Spanish 23F clone, which has acquired fluoroquinolone resistance while circulating in Hong Kong (11). Our data confirmed a higher rate of ciprofloxacin resistance among isolates from Hong Kong than among isolates from other Asian countries. Although the overall rates resistance to fluoroquinolones remain low in most Asian countries, we found 12 strains of diverse serotypes (7 from Hong Kong and 1 each from China, Taiwan, India, Singapore, and Thailand) with high-level resistance to ciprofloxacin (MICs $\geq$ 8 mg/liter). These strains were also resistant to newer fluoroquinolones, such as moxifloxacin and gatifloxacin. The emergence of these strains highly resistant to fluoroquinolones will be a concern in the future with regard to the treatment of pneumococcal pneumonia. Clinical failures of levofloxacin for the treatment of pneumococcal pneumonia have already been documented (2).

The serotype distributions among the clinical pathogens from Asia showed that major serogroups were 19 (19F), 23 (23F), 6 (6B), 14, and 9, which are contained in the seven-valent conjugate vaccine. Given the high prevalence of antibiotic-resistant \textit{S. pneumoniae} in Asia, pneumococcal vaccination should be applied more widely in Asia.

The MLST analysis performed in this study showed that the spread of specific resistant clones, such as the Taiwan 19F clone and the Spain 23F, in Asia could be one of the major reasons for the rapid increases in penicillin and macrolide resistance as well as MDR in \textit{S. pneumoniae}.

There may be some limitations in interpreting the data from this study. Since pneumococcal isolates were collected from one or two referral centers, mainly in urban areas of each country, and the number of isolates was relatively few in some centers, data from this study may not reflect the overall resistance status in a whole country. On the basis of the information from this study, further surveillance of pneumococcal resistance with more isolates from more centers is strongly warranted, especially in countries where resistance rates have markedly increased. Also, we could not identify the direct relationship between the amounts of antibiotics used or the history of previous antibiotic use and the emergence of resistance due to a lack of relevant information in many countries.

In conclusion, this multinational surveillance study conducted by ANSORP clearly documents distinctive increases in the prevalence rates and the levels of penicillin and macrolide resistance in many Asian countries, which are among the highest in the world that have been published to date, as well as the emergence of fluoroquinolone resistance in Hong Kong. The injudicious use of antibiotics and the clonal spread of resistant strains in Asia could be the major reasons for the rapid increases in the rates of pneumococcal resistance in Asia. Continuous surveillance of antimicrobial resistance among pneumococcal isolates as well as appropriate use of antibiotics and pneumococcal vaccination is critically required in Asia.

ACKNOWLEDGMENTS

This study was partly supported by Bayer Healthcare (Wuppertal, Germany), Wyeth-Ayerst (Madison, N.J.), the Samsung Biomedical Research Institute (SBRI C-A3-214-1), the Samsung Medical Center, and the Asian Pacific Research Foundation for Infectious Diseases (ARFID), Seoul, Korea.

We thank Jane Ambler, Hans-Otto Werling, Helmut Sepehrs, and Eddie Power of Bayer Healthcare and Rob Cummins of Wyeth-Ayerst for their sincere support.

Centers participating in the Asian Network for Surveillance of Resistant Pathogens (ANSORP) are as follows: Samsung Medical Center, Seoul, Korea (coordinating center); Beijing Children's Hospital, Beijing, China; Shanghai Children's Hospital, Shanghai, China; Princess Margaret Hospital, Hong Kong, China; Chulalongkorn University, Bangkok, Thailand; Chang Gung Children's Hospital, Taipei, Taiwan; Christian Medical College, Vellore, India; University of Colombo, Colombo, Sri Lanka; National University of Singapore, Singapore; Universiti Putra Malaysia and University Malaya, Kuala Lumpur, Malaysia; University of Medicine and Pharmacy, Ho Chi Minh City, Vietnam; Research Institute of Tropical Medicine, Manila, Philippines; and King Saud University, Riyadh, Saudi Arabia.

REFERENCES


