

# Carriage of Antibiotic-Resistant Pneumococci among Asian Children: A Multinational Surveillance by the Asian Network for Surveillance of Resistant Pathogens (ANSORP)

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To investigate the nasal carriage of antibiotic-resistant pneumococci by children, anterior nasal swabs were done for 4963 children <5 years old in 11 countries in Asia and the Middle East. In total, 1105 pneumococci isolates (carriage rate, 22.3%) were collected, 35.8% of which were found to be nonsusceptible to penicillin. Prevalence of penicillin nonsusceptibility was highest in Taiwan (91.3%), followed by Korea (85.8%), Sri Lanka (76.5%), and Vietnam (70.4%). Penicillin resistance was related to residence in urban areas, enrollment in day care, and a history of otitis media. The most common serogroups were 6 (21.5%), 23 (16.5%), and 19 (15.7%). The most common clone, as assessed by pulsed-field gel electrophoresis, was identical to the Spanish 23F clone and to strains of invasive isolates from adult patients. Data in this study documented the high rate of penicillin or multidrug resistance among isolates of pneumococci carried nasally in children in Asia and the Middle East and showed that this is due to the spread of a few predominant clones in the region.

*Streptococcus pneumoniae* remains the leading cause of community-acquired pneumonia, otitis media, and paranasal sinusitis in children and adults [1, 2]. Because

pneumococcal disease follows nasopharyngeal carriage, the antimicrobial susceptibility profile of nasopharyngeal isolates can be used as an estimate of the incidence of resistance in systemic isolates [3, 4]. Nasopharyngeal carriage of penicillin-resistant pneumococci in children also could reflect antimicrobial uses, with regard to both individual use and total antimicrobial consumption in the community [5].

During the past 3 decades, resistance of *S. pneumoniae* to penicillin, other  $\beta$ -lactams, and non- $\beta$ -lactam agents has been increasing rapidly in many parts of the world [6, 7]. Analysis of data from some European countries, South Africa, and the United States showed that about half the pneumococci isolates from clinical

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specimens were not susceptible to penicillin [8–10]. The rapid emergence of resistance to multiple antimicrobial agents has further complicated the problem of antibiotic resistance [11].

Data recently collected by the Asian Network for Surveillance of Resistant Pathogens (ANSORP) with respect to pneumococcal isolates from clinical specimens documented a high prevalence of penicillin and multidrug resistance in some Asian cities, as well as the probable introduction and spread of an internationally epidemic Spanish 23F clone into Asian countries [12]. Prevalence of penicillin nonsusceptibility among strains of pneumococcal isolates in Korea, Japan, Vietnam, and Thailand was >50% of total isolates from clinical specimens, mainly from adult patients. Given the high prevalence of pneumococcal resistance in many Asian countries, knowledge of the prevalence of carriage of resistant pneumococci in children could better define the status of resistance in this region. However, most data on nasopharyngeal carriage of pneumococci have been reported from Western countries [13–16]; only scanty data have been reported from Asian countries [17–19]. To investigate the prevalence of carriage of antibiotic-resistant pneumococci in children and to document the spread of resistant clones in the region, ANSORP did a multicenter surveillance study of carriage of pneumococci by children in Asia and the Middle East.

## PATIENTS AND METHODS

**Participating centers.** Medical centers that participated in the ANSORP Study Group in the current study included 12 centers in the following 11 countries: Korea (Samsung Medical Center, Seoul), China (Beijing Children's Hospital, Beijing), Thailand (Chulalongkorn University and Siriraj Hospital, Bangkok), Taiwan (Chang Gung Children's Hospital, Taipei), India (Christian Medical College, Vellore), Sri Lanka (University of Colombo, Colombo), Singapore (National University of Singapore), Malaysia (Universiti Kebangsaan Malaysia, Kuala Lumpur), Vietnam (University of Medicine and Pharmacy, Ho Chi Minh City), The Philippines (Research Institute of Tropical Medicine, Manila), and Saudi Arabia (King Saud University, Riyadh).

**Study population.** Children <5 years old who were attending day care centers or outpatient clinics were enrolled in participating centers during January 1998–March 1999. Excluded from the study were children who were recently hospitalized, children who were currently receiving antibiotic treatment, children who had known immunologic disorders or congenital anomalies (especially those involving the respiratory tract), children whose parents or guardians refused to allow them to be enrolled in the study, and/or children who had current or recent invasive pneumococcal disease (pneumonia, bacteremia, and meningitis).

**Collection of bacterial isolates.** Anterior nasal swab specimens were obtained from a depth of 1 cm in the nostril with a cotton-tipped wooden swab 2 mm in diameter. Swabs were plated immediately onto trypticase soy agar plates with 5% sheep blood containing 5 µg/mL of gentamicin. The plates were kept at room temperature and were transported to the laboratory on the same day the sample was collected. At the laboratory, the plates were incubated at 35°C in a 5%–10% CO<sub>2</sub> incubator for 24 h. Colonies typical for pneumococci were selected and were plated onto blood agar plates. Pneumococci were identified by optochin disk (inhibition zones >14 mm) and were confirmed by the bile solubility test. All pneumococcal isolates were sent to the reference laboratory (Samsung Medical Center, Seoul, Korea) on blood-agar medium in diagonally oriented test tubes for further testing.

**Antimicrobial susceptibility test.** Pneumococci were screened for susceptibility to penicillin with a 1-µg oxacillin disk (BBL Microbiology Systems) by the disk diffusion method, according to the performance standards from the National Committee for Clinical Laboratory Standards (NCCLS) [20]. Isolates with a zone of inhibition of ≥20 mm were considered to be susceptible to penicillin. Other antimicrobial agents tested by disk diffusion were tetracycline, erythromycin, chloramphenicol, and trimethoprim-sulfamethoxazole (TMP-SMZ). MICs were determined by E-test (AB Biodisk) for penicillin, cefotaxime, cefuroxime, amoxicillin-clavulanate, and imipenem. NCCLS criteria of zone diameter and MIC values were used to classify the isolates as susceptible, intermediate, or resistant [21]. *S. pneumoniae* ATCC 49619, *Escherichia coli* ATCC 25922, and *Staphylococcus aureus* ATCC 29213 were used as control strains. All in vitro tests were done strictly according to the standardized protocol, and a 4-day quality control run-in period was followed by actual in vitro tests. A panel of 11 pneumococcal strains with known susceptibility to different antimicrobial agents (from M. R. J.) was tested for documentation of proficiency in susceptibility testing of these strains before the study began.

**Serotyping.** In the reference laboratory, isolates were confirmed and serogrouped by means of Quellung reaction with use of group-specific antisera (Statens Seruminstitut), according to the manufacturer's recommendations.

**Epidemiologic parameters.** For analysis of colonization status and risk factors, epidemiologic information was obtained from parents or guardians at the time that anterior nasal swabs were obtained. This included demographic data (age, sex, residential area [urban or rural], and day care enrollment) and data on clinical conditions (current illness, history of otitis media, history of previous hospital attendance or admission, and history of previous antibiotic use within 3 months). Univariate and multivariate logistic regression analyses were done

**Table 1. Carriage rate and the prevalence of penicillin-nonsusceptible strains of pneumococci among children from 11 countries.**

| Country      | No. of children examined | No. of pneumococcal isolates (carriage rate, %) | PRSP, %                           |                                   |
|--------------|--------------------------|---|-----------------------------------|-----------------------------------|
|              |                          |   | Of carriage isolates <sup>a</sup> | Of clinical isolates <sup>b</sup> |
| Taiwan       | 288                      | 44 (15.3)                                       | 91.3                              | 38.7                              |
| Korea        | 500                      | 99 (19.8)                                       | 85.8                              | 79.7                              |
| Sri Lanka    | 493                      | 118 (23.9)                                      | 76.5                              | 41.2                              |
| Vietnam      | 295                      | 104 (35.3)                                      | 70.4                              | 60.8                              |
| Saudi Arabia | 830                      | 108 (13.0)                                      | 50.0                              | NA                                |
| Singapore    | 491                      | 44 (9.0)  | 46.3                              | 23.1                              |
| Thailand     | 503                      | 204 (40.6)                                      | 45.6                              | 57.9                              |
| China        | 267                      | 100 (37.5)                                      | 13.4                              | 9.8                               |
| Malaysia     | 762                      | 86 (11.3)                                       | 13.3                              | 9.0                               |
| India        | 227                      | 98 (43.2)                                       | 12.8                              | 3.8                               |
| Philippines  | 307                      | 100 (32.6)                                      | 2.1                               | NA                                |
| Total        | 4963                     | 1105 (22.3)                                     | 35.8                              | 34.5                              |

**NOTE.** NA, not available; PRSP, penicillin-resistant *Streptococcus pneumoniae*.

<sup>a</sup> PRSP includes penicillin-resistant strains and intermediately susceptible strains.

<sup>b</sup> Percentage of PRSP among clinical isolates from a previous Asian Network for Surveillance of Resistant Pathogens study [12].

to evaluate risk factors for carriage of antibiotic-resistant pneumococci.

**Pulsed-field gel electrophoresis (PFGE).** PFGE analysis was done as described elsewhere [12]. One penicillin-susceptible R6 strain and 3 international reference strains, including an internationally epidemic Spanish strain (serotype 23F), an Iceland strain (serotype 6B), and a French strain (serotype 14) obtained from Alexander Tomasz (Rockefeller University, New York, New York), also were tested by the same method. For restriction en-

donuclease digestion, thin slices were cut off the agarose plugs, were equilibrated in the appropriate nuclease buffer for 30 min, and were digested overnight with 40 U of *Sma*I at 25°C. PFGE was done with a contour-clamped homogeneous electric field apparatus (CHEF-Mapper System; BioRad Laboratories) at 14°C for 20 h at 5.4 V/cm. Pulse times ranged from 30 s to 1 s. Concatemers of DNA isolated from the bacteriophage  $\lambda$  were used as molecular size markers. The DNA fragment patterns generated by PFGE were interpreted according to recent criteria

**Table 2. Antimicrobial susceptibility data for 1105 carriage isolates of *Streptococcus pneumoniae* from 11 countries.**

| Country      | Percentage of isolates intermediately susceptible/percentage resistant, by antimicrobial agent <sup>a</sup> |          |           |                      |          |           |          |        |           |
|--------------|---|----------|-----------|----------------------|----------|-----------|----------|--------|-----------|
|              | Pen   | Ctax     | Cfur      | Amx-Clv <sup>a</sup> | Imi      | Tet       | Em       | Chl    | TMP-SMZ   |
| Taiwan       | 43.5/47.8   | 56.5/4.3 | 13.0/73.9 | 0/0                  | 82.6/0   | NA        | NA       | NA     | NA        |
| Korea        | 54.5/31.3   | 36.4/5.1 | 2.0/63.6  | 4/0                  | 61.6/1.0 | 3.0/84.8  | 1.0/77.8 | —/35.4 | 2.0/62.6  |
| Sri Lanka    | 70.6/5.9  | 20.6/2.9 | 2.9/23.5  | 0/0                  | 23.5/0   | 21.4/26.5 | 5.1/10.2 | —/10.2 | 12.4/63.9 |
| Vietnam      | 58.2/12.2   | 17.3/0   | 15.3/33.7 | 2/0                  | 45.9/3.1 | 7.7/73.1  | 3.8/87.5 | —/62.5 | 1.9/41.3  |
| Saudi Arabia | 34.6/15.4   | 15.4/7.7 | 0/26.9    | 0/0                  | 23.1/0   | NA        | NA       | NA     | NA        |
| Singapore    | 26.8/19.5   | 26.8/0   | 0/34.1    | 0/0                  | 31.7/0   | 31.8/18.8 | 0/54.1   | —/29.4 | 4.7/70.6  |
| Thailand     | 41.8/3.8  | 12.6/0   | 3.4/16.8  | 0/0                  | 15.9/0   | 9.8/47.5  | 3.4/32.8 | —/15.7 | 12.7/60.8 |
| China        | 13.4/0  | 0/0      | 2.1/0     | 0/0                  | 0/0      | 6.0/78.0  | 3.0/71.0 | —/29.0 | 8.0/71.0  |
| Malaysia     | 8.4/4.9   | 5.2/0    | 0/8.6     | 0/0                  | 5.2/0    | 0/14.3    | 0/11.4   | —/7.1  | 0/40.6    |
| India        | 12.8/0  | 0/0      | 0/0       | 0/0                  | 0/0      | 8.2/27.6  | 0/0      | —/2.0  | 3.1/59.2  |
| Philippines  | 2.1/0   | 0/0      | 0/0       | 0/0                  | 0/0      | 1.0/1.0   | 0/0      | —/0    | 0/2.0     |

**NOTE.** Amx-Clv, amoxicillin-clavulanate; Cfur, cefuroxime; Chl, chloramphenicol; Ctax, cefotaxime; Em, erythromycin; Imi, imipenem; NA, not available; Pen, penicillin; Tet, tetracycline; TMP-SMZ, trimethoprim-sulfamethoxazole.

<sup>a</sup> Amx-Clv was tested in a 2:1 ratio, and data reflect the amoxicillin component.

**Table 3. MIC<sub>90</sub> for carriage isolates of *Streptococcus pneumoniae* from children in 11 countries.**

| Country      | MIC <sub>90</sub> , µg/mL |       |      |                      |      |
|--------------|---------------------------|-------|------|----------------------|------|
|              | Pen                       | Ctax  | Cfur | Amx-Clv <sup>a</sup> | Imi  |
| Taiwan       | 1.0                       | 0.75  | 2.0  | 0.75                 | 0.19 |
| Korea        | 2.0                       | 1.0   | 4.0  | 1.0                  | 0.38 |
| Sri Lanka    | 0.9                       | 0.35  | 1.4  | 0.28                 | 0.12 |
| Vietnam      | 1.5                       | 0.75  | 2.0  | 1.5                  | 0.38 |
| Saudi Arabia | 1.5                       | 1.0   | 5.0  | 1.0                  | 0.19 |
| Singapore    | 2.0                       | 1.0   | 4.0  | 1.0                  | 0.25 |
| Thailand     | 0.75                      | 0.14  | 0.39 | 0.38                 | 0.01 |
| China        | 0.06                      | 0.06  | 0.10 | 0.01                 | 0.02 |
| Malaysia     | 0.06                      | 0.19  | 0.25 | <0.016               | 0.02 |
| India        | 0.06                      | 0.05  | 0.12 | <0.016               | 0.02 |
| Philippines  | 0.02                      | <0.02 | 0.02 | <0.016               | 0.01 |

**NOTE.** Amx-Clv, amoxicillin-clavulanate; Cfur, cefuroxime; Ctax, cefotaxime; Imi, imipenem; Pen, penicillin.

<sup>a</sup> Amx-Clv was tested in a 2:1 ratio, and data reflect the amoxicillin component.

[22] and were compared with those of clinical isolates from 7 Asian countries that had been documented in the previous study by the ANSORP.

## RESULTS

**Antimicrobial susceptibility tests.** A total of 1105 isolates of *S. pneumoniae* was recovered from anterior nasal swab specimens from 4963 children in 11 countries. Overall prevalence of nasal carriage was 22.3%; the highest prevalence was in India (43.2%), and the lowest was in Singapore (9.0%). The number of enrolled children and isolates contributed by 11 participating centers are summarized in table 1. Three hundred forty-nine

(31.6%) children were <12 months old, 243 (22%) were 1–2 years old, 114 (10.3%) were 2–3 years old, 366 (33.1%) were 3–4 years old, and 33 (3.0%) were 4–5 years old. The numbers and percentages of pneumococcal isolates that were not susceptible to different antimicrobial agents varied by country (table 2). Overall, 709 isolates (64.2%) were penicillin susceptible, 295 (26.7%) were intermediate, and 101 (9.1%) were penicillin resistant. The percentage of penicillin nonsusceptibility in younger children (≤24 months old) was not different from that in older children (>24 months old; 36.7% vs. 35.3%). With regard to penicillin nonsusceptibility, Taiwan ranked first: 91.3% of total isolates were not susceptible to penicillin (MIC ≥0.1 µg/mL), followed by Korea (85.8%), Sri Lanka (76.5%), Vietnam (70.4%), and Saudi Arabia (50.0%; table 2). The 90% MICs of penicillin ranged from 0.02 µg/mL in Philippines to 2.0 µg/mL in Korea and Singapore (table 3). Penicillin-resistant isolates were not susceptible to cefotaxime (89.6%), cefuroxime (100%), amoxicillin-clavulanate (5%), imipenem (98.7%), tetracycline (91.2%), erythromycin (95.1%), chloramphenicol (44.3%), and TMP-SMZ (88.5%).

**Serogroup distribution.** A total of 750 pneumococcal isolates that were available for serogrouping belonged to 25 serogroups (table 4). The most common was serogroup 6 (21.5%), followed by serogroups 23 (16.5%) and 19 (15.7%).

**Epidemiologic risk factors.** There were no significant differences between the median age of children who carried penicillin-nonsusceptible strains (28.6 months), compared with the median age of carriers of penicillin-susceptible strains (26.0 months). By both multivariate and univariate analysis, residence in urban areas, day care enrollment, and previous history of otitis media were significant risk factors for carriage of penicillin-nonsusceptible strains (table 5). History of recent antibiotic use was a risk factor only by univariate analysis. Among

**Table 4. Serogroup distribution of pneumococcal isolates from children in 11 Asian countries.**

| Country, no.       | No. of isolates | No. of strains, by serogroup |      |      |     |     |     |     |     |     |     |     |     |       |
|--------------------|-----------------|------------------------------|------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------|
|                    |                 | 6                            | 23   | 19   | 14  | 15  | 18  | 9   | 7   | 3   | 4   | 1   | 5   | Other |
| Taiwan             | 23              | 6                            | 8    | 3    | 2   | —   | —   | 1   | —   | —   | —   | —   | —   | 3     |
| Korea              | 62              | 13                           | 16   | 14   | 9   | —   | —   | 3   | —   | —   | —   | —   | —   | 7     |
| Sri Lanka          | 16              | 2                            | 3    | 4    | —   | 2   | —   | —   | —   | —   | —   | —   | —   | 5     |
| Vietnam            | 92              | 25                           | 15   | 17   | 9   | 4   | 2   | 1   | —   | —   | —   | —   | —   | 19    |
| Saudi Arabia       | 26              | 1                            | 3    | 6    | 2   | 1   | —   | 2   | —   | 2   | —   | 1   | —   | 8     |
| Singapore          | 41              | 20                           | 5    | 9    | 2   | 3   | —   | —   | —   | —   | —   | —   | —   | 2     |
| Thailand           | 165             | 38                           | 41   | 21   | 9   | 11  | 9   | —   | —   | —   | —   | —   | —   | 36    |
| China              | 95              | 9                            | 6    | 26   | 7   | 2   | 1   | 1   | 1   | 2   | —   | 1   | —   | 39    |
| Malaysia           | 58              | 15                           | 12   | 4    | —   | 7   | 3   | —   | 2   | 1   | —   | —   | —   | 14    |
| India              | 77              | 14                           | 7    | 7    | 7   | 7   | —   | 2   | 1   | —   | 2   | 1   | 1   | 28    |
| Philippines        | 95              | 18                           | 8    | 7    | —   | 7   | 4   | 2   | 1   | —   | 2   | —   | —   | 46    |
| Total              | 750             | 161                          | 124  | 118  | 47  | 44  | 19  | 12  | 5   | 5   | 4   | 3   | 1   | 207   |
| % of total strains | —               | 21.5                         | 16.5 | 15.7 | 6.3 | 5.9 | 2.5 | 1.6 | 0.7 | 0.7 | 0.5 | 0.4 | 0.1 | 27.6  |

**Table 5. Univariate and multivariate analyses of risk factors for carriage of penicillin-nonsusceptible pneumococci in children.**

| Categorical variable          | Univariate analysis |           |      | Multivariate analysis |            |      |
|-------------------------------|---------------------|-----------|------|-----------------------|------------|------|
|                               | OR                  | 95% CI    | P    | OR                    | 95% CI     | P    |
| Male sex                      | 0.84                | 0.64–1.10 | .212 | 0.87                  | 0.64–1.17  | .356 |
| Urban residence               | 2.77                | 1.70–4.50 | .000 | 3.75                  | 2.02–6.94  | .000 |
| Day care enrollment           | 1.85                | 1.36–2.52 | .000 | 1.59                  | 1.17–2.15  | .003 |
| Current illness               | 0.87                | 0.64–1.20 | .405 | 0.88                  | 0.64–1.23  | .461 |
| History of otitis media       | 2.34                | 1.20–4.55 | .012 | 7.03                  | 1.74–28.41 | .006 |
| History of hospital visit     | 1.29                | 0.93–1.78 | .134 | 1.57                  | 0.95–2.61  | .080 |
| History of use of antibiotics | 1.77                | 1.22–2.58 | .000 | 1.26                  | 0.73–2.19  | .403 |

risk factors, day care center enrollment could be identified in only 7 countries (Korea, Vietnam, Thailand, Sri Lanka, Philippines, Singapore, and China), whereas data were not available in Taiwan, Saudi Arabia, Malaysia, and India. Overall prevalence of penicillin nonsusceptibility among carriers who attended day care centers in 7 countries (54.2%) was significantly higher than that in carriers who did not (36.3%).

**PFGE.** A total of 67 penicillin-resistant isolates (MIC  $\geq$  2  $\mu$ g/mL) from 6 Asian countries, which were selected randomly from among strains of serogroup 19 or 23, were analyzed by PFGE. PFGE patterns A, B, and C, which were defined in the previous study with clinical isolates, were also the major patterns among carriage isolates in children (table 6). A total of 22 strains (32.8%) from 6 countries belonged to the type A pattern, which was identical to that of the Spanish 23F clone and that of clinical isolates from adult patients.

## DISCUSSION

This study was the second multinational collaboration by the ANSORP Study Group on the surveillance of pneumococcal resistance in Asia and the Middle East. The current study, which is the largest study on pneumococcal carriage—with ~5000 children in 11 countries—better defines the epidemiology of pneumococcal resistance in the region, together with the data

from clinical isolates, as documented in the previous ANSORP study [12]. The prevalence of nasal carriage of *S. pneumoniae* by anterior nasal swabs in children ranged from 9% (Singapore) to 43% (India), with an mean carriage rate of 22.3%, which was similar to or slightly lower than those in previous reports in other parts of the world [13–19]. Although anterior nasal swabs are easier to do in younger children and although the method was reported to be as sensitive as nasopharyngeal aspiration [23], this method might affect lower carriage rates in some countries.

In this study, a very high prevalence of antibiotic-resistant pneumococci ( $\geq$ 50%) among carriage isolates in children was noted in Taiwan, Korea, Sri Lanka, Vietnam, and Saudi Arabia. In particular, an alarmingly high prevalence of penicillin-nonsusceptible pneumococci was noted in Taiwan, where a previous report showed that 71% of carriage isolates of pneumococci were not susceptible to penicillin [17]. Prevalences of penicillin nonsusceptibility among carriage isolates in Korea, Vietnam, Thailand, China, India, and Malaysia were similar to those among clinical isolates from patients in the previous ANSORP study, whereas penicillin-nonsusceptible strains were more common in carriage isolates than in clinical isolates in Taiwan, Singapore, and Sri Lanka. The low rates of resistance among carriage isolates in the Philippines and India were consistent with data from clinical isolates in these countries [12]. Risk

**Table 6. Pulsed-field gel electrophoresis (PFGE) patterns of 67 penicillin-resistant pneumococcal isolates (serotype 19 or 23) from children from Asian countries.**

| Country, no. | No. of isolates | No. of isolates with specified PFGE pattern |   |    |   |   |   |   |   |   |   |   |       |
|--------------|-----------------|---|---|----|---|---|---|---|---|---|---|---|-------|
|              |                 | A   | B | C  | D | E | F | G | H | I | J | K | Other |
| Korea        | 20              | 7   | 8 | —  | — | — | — | — | — | 4 | — | — | 1     |
| Malaysia     | 3               | 1   | — | 1  | — | — | — | — | — | — | — | — | 1     |
| Sri Lanka    | 10              | 3   | — | —  | — | — | — | — | — | 1 | — | 6 | —     |
| Taiwan       | 8               | 3   | 1 | —  | — | — | — | — | — | 1 | — | — | 3     |
| Thailand     | 16              | 6   | — | 3  | — | — | — | — | — | 2 | — | — | 5     |
| Vietnam      | 10              | 2   | — | 8  | — | — | — | — | — | — | — | — | —     |
| Total        | 67              | 22  | 9 | 12 | — | — | — | — | — | 8 | — | 6 | 10    |

factors for carriage of penicillin-resistant pneumococci identified in this study were consistent with those in the previous observations [18, 24–26], although there were some limitations in the analysis of risk factors, such as day care center enrollment, because of incomplete information in some countries.

The most common serogroups, in order of frequency, were 6, 23, 19, and 14, which comprised 60% of all carriage isolates, whereas serogroups 23 (30%), 19 (25%), and 6 (15%) were the most common among clinical isolates in the previous AN-SORP study in the same region. Pneumococcal serogroups 6, 14, 19, and 23, which cause two-thirds of invasive pneumococcal disease in children, have been the most common serogroups isolated from children with otitis media and invasive disease caused by *S. pneumoniae* [16, 27]. These serogroups, which were highly associated with multidrug resistance [15], also are associated with prolonged carriage and rapid reacquisition in the nasopharynx [28]. Our data on serotype prevalence, with recent reports from Asian countries [12, 17–19], could be a useful guide to applications of pneumococcal vaccines in the region.

PFGE data confirm that antibiotic-resistant pneumococcal clones that were identified among clinical isolates from adult patients have been widely disseminated to children in the region. The most common PFGE type (type A) among carriage isolates in this study and clinical isolates in the previous AN-SORP study [12] was identical to that of an internationally epidemic Spanish 23F clone. Although a few strains from a limited number of countries were tested by PFGE, analysis of our data suggests a clonal relationship between carriage strains isolated from different countries and the potential spread of resistant clones between Asian countries. Data from the first multinational surveillance of pneumococcal carriage by children in Asia and the Middle East showed that penicillin and multidrug resistance among carriage isolates of pneumococci is a serious problem in many countries in the region, which is due to the spread of several predominant drug-resistant clones.

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