Nasopharyngeal Carriage of Streptococcus pneumoniae in Finnish Children Younger Than 2 Years Old

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To describe the natural course of nasopharyngeal carriage of Streptococcus pneumoniae and its relationship to acute otitis media (AOM), 329 Finnish children were followed from ages 2 to 24 months. In total, 3024 nasopharyngeal (NP) swabs (obtained at 10 scheduled healthy visits) and 2007 NP aspirates (obtained during respiratory infections) were cultured. Carriage during health increased gradually (9%–43%) with age. Within 4 age intervals, carriage was lower during health (13%–43%) than during respiratory infection without AOM (22%–45%). Higher proportions of positive samples were found during AOM (45%–56%), in particular during pneumococcal AOM (97%–100%). Antimicrobial treatment reduced carriage only temporarily. The most frequent NP serotypes were 6B, 6A, 11, 19F, and 23F. Both age and health status were important determinants of NP carriage of S. pneumoniae and these features should be considered carefully during analysis of carriage rates.

Streptococcus pneumoniae causes a wide variety of infections worldwide, from invasive diseases with considerable mortality to relatively benign and very common mucosal infections, such as acute otitis media (AOM). It is also a common component of the nasopharyngeal (NP) flora in healthy persons. The increasing occurrence of penicillin-resistant strains challenges the treatment and prevention strategies for pneumococcal diseases and emphasizes the need for knowledge about factors that affect S. pneumoniae carriage and its progression to disease.

Most children acquire S. pneumoniae in their nasopharynx during the first few years of life [1–6]. Colonization is very rapid in high-risk populations, such as infants in Papua New Guinea, who are colonized by the age of 3 months (the pattern is similar among Australian aboriginal infants) [3, 4]. In industrialized countries such as Sweden and the United States, about half of children are colonized with S. pneumoniae at least once by age 1 year [7, 8]. The reasons for the differences between populations are not fully understood. The prevalence of NP carriage increases during the first months of life [6, 7, 9, 10] and starts to decrease after age 3–5 years [2, 11–13]. The wide range of pneumococcal carriage (5%–89%) in different parts of the world [14, 15] reflects variations in study populations with respect to age, ethnicity, socioeconomic living conditions, and differences in sampling and isolation techniques. The health conditions at the time of sampling may also vary. The terms “carriage” or “colonization” apply to both healthy persons and to subjects with symptoms of acute infection that is possibly or definitely caused by S. pneumoniae.

Many studies have shown that recovery of S. pneumoniae from the nasopharynx or oropharynx is more likely during respiratoy infection than during health [16–20] but others failed to find such a connection [21–23]. Most often, the carried serotypes are the same as those that cause most cases of AOM and other pneumococcal diseases in children. As a rule, S. pneumoniae of the causative serotype is found in the nasopharynx or nasal cavity during pneumococcal AOM [1, 24, 25]. Antimicrobial treatment may interfere with isolation rates, and lower isolation rates have been observed during and soon after antibiotic treatment, compared with pretreatment rates, but antimicrobial treatment does not eradicate the bacteria from the nasopharynx [23, 26–29]. New strains appear after treatment [1, 26, 28], but the long-term effect of antimicrobials on carriage rates is poorly documented. In the Finnish Otitis Media (FinOM) Cohort Study, we followed an unselected group of 329 infants from ages 2 to 24 months, during health at 10 scheduled visits and during respiratory infection and AOM, to evaluate the natural course of pneumococcal carriage and its relationship to respiratory infection with and without AOM.
Materials and Methods

Study population and facilities. In total, 329 healthy infants born in the Hervanta area, Tampere, Finland, were consecutively enrolled in the FinOM cohort study between April 1994 and August 1995 and were followed-up prospectively from ages 2 through 24 months. Families with newborns were informed of the study during their first routine visit to their local well-baby clinic. All infants born or residing in the area were eligible to participate in the study if they were 2 months ± 2 weeks old and had no prior immunization with a pneumococcal vaccine and if their mothers could communicate fluently in Finnish. During the study, the children were vaccinated in accordance with the Finnish schedule, which does not include pneumococcal vaccine.

Follow-up began in April 1994 and continued through July 1997. A study clinic with 1 or 2 doctors and 1–3 nurses was established near the local well-baby clinic. Study personnel were specially trained to interview parents, obtain samples, and diagnose and treat AOM. Study clinic services were available for the study children from 8 AM to 3 PM on work days and for 3 h on Saturdays, Sundays, and national holidays.

Scheduled visits and NP swabs (NPS). The children were examined at age-scheduled healthy visits at ages 2, 3, 4, 5, 6, 9, 12, and 15 months (± 2 weeks) and at age 18 months (± 4 weeks). A close-out visit was done at age 24 months (± 4 weeks). The background information gathered at entry included family structure, parents’ education, history of family allergies, and history of otitis media (OM) of siblings. At each scheduled visit, the study staff questioned parents about potential risk factors for carriage or AOM, including feeding patterns, allergies, day care attendance of the study child and siblings, and passive smoking. Responses were recorded on structured case report forms. Parents were also asked about antimicrobial drug usage during the 28 days preceding the visit. A physical examination, including pneumatic otoscopy, was performed by the study doctor. If the child was diagnosed with AOM, febrile infection, viral exanthem, or acute gastroenteritis, the visit was recorded as a “sick visit” and the healthy visit was carried forward within the time window, if possible.

An NPS specimen was obtained at each healthy visit with a sterile swab with a flexible aluminum shaft and a dry calcium alginate tip (GulgiSwab; Spectrum Laboratories). The child’s head was tipped backwards and was immobilized. The bent swab was inserted into the nostril, was passed into the nasopharynx to a distance equal to that from the child’s nose to the tip of the ear, and was maintained for 5 s. The sample was cultured immediately for S. pneumoniae.

Sick visits and NP aspirates (NPAs). If symptoms of acute infection suggested AOM, the parents were asked to bring the child to the study clinic. The event was recorded as a sick visit. A patient history was taken, and the study doctor performed a physical examination, including pneumatic otoscopy and tympanometry. Whenever AOM (see definition below) was suspected, myringotomy was performed to confirm the diagnosis, and a middle ear fluid sample (MEF) was obtained for etiologic diagnosis. Resolution of each AOM was followed at a check-up visit 4 weeks after the diagnosis. If AOM, febrile infection (≥38°C), viral exanthem, or acute gastroenteritis was diagnosed at the check-up visit or at the close-out visit, the visit was classified as a sick visit.

An NPA was obtained at each sick visit with a sterile pediatric mucus extractor (UNO sterile EtO; UnoPlast). The catheter was guided to a depth of 4–8 cm in the nasopharynx through a nostril and was drawn back while a gentle suction was applied with an electric suction device. The sample was diluted with 0.5 mL of PBS, if needed, and was cultured immediately with a 10-μL loop for S. pneumoniae. The child’s visits to other than study doctors were registered if shown in a patient diary, and medical records were requested to confirm AOM diagnoses.

Bacteriologic methods. NPS, NPA, and MEF samples were cultured on enriched chocolate agar plates and selective sheep blood agar plates containing 5 μg/mL gentamicin. The plates were incubated in 5% CO₂ at 36°C–37°C in the study clinic, usually overnight, and were transported to the bacteriologic laboratory in Oulu. The plates inoculated on Fridays and Saturdays were incubated in the study clinic until Sunday. In the laboratory, the plates were examined for S. pneumoniae and were incubated further overnight, to reach a total incubation time of ≥48 h. To identify S. pneumoniae, 4 different α-hemolytic colonies were tested for optochin sensitivity. A bile solubility test was used if the optochin test was negative but colony morphology was suggestive of the species. The number of colonies was counted from the plate with more abundant growth. Pneumococcal isolates were serotyped by counterimmunoelectrophoresis and latex agglutination (for types 7 and 14), using antiserum pools and group- and type-specific antisera. The isolates of groups 6, 9, 18, 19, and 23 were subtyped by using pneumococcal factor antisera. All antisera were purchased from Statens Serum Institut. The susceptibility of pneumococcal strains to penicillin was tested by the agar dilution method, with breakpoints ≤0.06 μg/mL (susceptible), 0.125–1.0 μg/mL (intermediately resistant), and ≥2 μg/mL (highly resistant).

Definitions. The carrier state refers to harboring S. pneumoniae in the nasopharynx either at a healthy visit or during respiratory infection—even during pneumococcal AOM. AOM was visually diagnosed as an abnormal tympanic membrane in pneumatic otoscopy (by color, position, and mobility), suggesting effusion in the middle ear cavity, concomitantly with ≥1 of the following signs or symptoms of acute infection: fever, earache, tugging of the ear, irritability, acute gastrointestinal symptoms, or other symptoms of respiratory infection. Tympanometry was used as a diagnostic aid [30]. We defined pneumococcal AOM as an AOM with ≥1 MEF sample with positive culture for S. pneumoniae. Because age proved to be an important determinant of prevalence rates, the NPS and NPA samples were grouped according to the child’s age at sampling in 4 intervals: ≤6, 7–12, 13–18, and ≥19 months.

Statistical analysis. The results describe the natural situation in a heterogeneous cohort where some children are healthy and some have repeated infections, including AOM. We used the Kaplan-Meier method and χ² test to compare the similarity of children who discontinued and children who completed the study. We used SPSS for Windows software (release 8.0.1; SPSS) for computation.

Results

Population and samples. In all, 329 children were enrolled in the study, representing 53% of the children registered in the well-baby clinics in the study area during the enrollment period. Table 1 lists the background characteristics of the enrolled chil-
was known for 2993 (99%) of the NPS samples. There was no antimicrobial treatment within 28 days before the swabbing samples were obtained from 212 (64%) children. The history of day care attendance, age when first attending day care, parents’ education, sex, smoking indoors in home, and occurrence of first AOM, when compared by the Kaplan-Meier method. However, girls were lost to follow-up more often than boys (18.7% vs. 10.4%; \( P = .027, \chi^2 \)), and children without older siblings living in the household were lost to follow-up more frequently than children with older siblings (18.7% vs. 10.4%; \( P = .034, \chi^2 \)).

Table 1. Characteristics of the 329 study children.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%) of children</th>
</tr>
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<tbody>
<tr>
<td>Sex</td>
<td></td>
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<tr>
<td>Boys</td>
<td>158 (48)</td>
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<tr>
<td>Girls</td>
<td>171 (52)</td>
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<tr>
<td>Feeding patterns</td>
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<td>Any breast-feeding</td>
<td></td>
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<tr>
<td>No</td>
<td>4 (1)</td>
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<tr>
<td>( \geq 12) Weeks</td>
<td>232 (71)</td>
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<tr>
<td>( \geq 24) Weeks</td>
<td>167 (51)</td>
</tr>
<tr>
<td>Not known</td>
<td>18 (5)</td>
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<tr>
<td>Exclusive breast-feeding</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>28 (9)</td>
</tr>
<tr>
<td>( \geq 12) Weeks</td>
<td>135 (41)</td>
</tr>
<tr>
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<td>3 (1)</td>
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<tr>
<td>Day care attendance(^a)</td>
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<td>Home care only</td>
<td>207 (63)</td>
</tr>
<tr>
<td>Age at entrance</td>
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</tr>
<tr>
<td>( \leq 6) Months</td>
<td>4 (1)</td>
</tr>
<tr>
<td>( \leq 12) Months</td>
<td>35 (11)</td>
</tr>
<tr>
<td>( \leq 18) Months</td>
<td>85 (26)</td>
</tr>
<tr>
<td>( \leq 24) Months</td>
<td>122 (37)</td>
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<tr>
<td>Older siblings(^b)</td>
<td></td>
</tr>
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<td>Yes</td>
<td>163 (50)</td>
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<tr>
<td>No</td>
<td>166 (50)</td>
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<tr>
<td>Education of mother or father(^c)</td>
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<tr>
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<tr>
<td>High</td>
<td>225 (68)</td>
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<tr>
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<tr>
<td>Smoking indoors in home(^d)</td>
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</tr>
<tr>
<td>Yes</td>
<td>12 (4)</td>
</tr>
<tr>
<td>No</td>
<td>292 (89)</td>
</tr>
<tr>
<td>Unknown</td>
<td>25 (8)</td>
</tr>
</tbody>
</table>

\(^a\) Any type of day care \( \geq 4\) h/week.
\(^b\) Living in household at the time of enrollment.
\(^c\) Highest education of either mother or father: low, comprehensive school, lower high school, or vocational education; high, senior high school, college, or academic degree.
\(^d\) At any time during follow-up.

From 4 families, 2 children (twins from 3 families and siblings from 1 family) participated in the study. Compliance of the families was high: 316 (96%), 309 (94%), and 284 (86%) of the children were followed until ages 7, 13, and 19 months, respectively, and 281 (85%) completed the entire follow-up. The main reason for dropping from the study was moving from the residential area (40% of those who discontinued). The children who were lost to follow-up were similar to those who were followed-up for 24 months, in regard to duration of breast-feeding, age when first attending day care, parents’ education, occurrence of first NP \( S. pneumoniae \), and occurrence of first AOM, when compared by the Kaplan-Meier method. However, girls were lost to follow-up more often than boys (18.7% vs. 10.1%; \( P = .027, \chi^2 \)), and children without older siblings living in the household were lost to follow-up more frequently than children with older siblings (18.7% vs. 10.4%; \( P = .034, \chi^2 \)).

Of the scheduled 3290 healthy visits, 3026 (92%) took place. During these visits, 3024 NPS samples were obtained. All 10 samples were obtained from 212 (64%) children. The history of antimicrobial treatment within 28 days before the swabbing was known for 2993 (99%) of the NPS samples. There was no treatment in 2322 (77%) cases. Oral treatment was given in 532 (18%) cases. In 168 cases, the treatment was ongoing at the time of sampling, in 68 it ended 1–7 days before sampling, and in 296, it ended 7–28 days before the sampling. Only topical antibiotics were used in 139 cases (5%).

Of all children, 288 (88%) were seen at a sick visit in the study clinic at least once during the study period. In all, there were 2122 sick visits during which 2007 (95%) of the planned NPA samples were obtained. One NPA sample each was obtained from 30 children, 2–10 NPA samples each were obtained from 196 children, and 11–31 NPA samples each were obtained from 61 children. In all, 81% of all known visits due to acute infections took place at the study clinic.

Study doctors diagnosed AOM at 871 sick visits (41% of all sick visits); in 89% of these, the diagnosis was verified by collection of a MEF sample from 1 or both ears. During the entire follow-up period, clinical AOM was diagnosed at least once in 215 (65%) study children, once or twice in 88 (27%) children, 3–5 times in 75 (23%) children, >5 times in 52 (16%) children, and 17 times in 1 child. These numbers comprise 86% of all cases of AOM known to have occurred among the study children during the follow-up. Only AOMs diagnosed in the study clinic are considered here.

Children were \( \leq 6\) months old at 395 (20%) sick visits during which NPA was obtained, 7–12 months old at 659 (33%) such visits, 13–18 months old at 565 (28%) such visits, and >19 months old at 388 (19%) such visits. The corresponding percentages of AOM events were almost the same: 167 (19%), 293 (34%), 234 (27%), and 177 (20%) for the 4 age groups, respectively.

\( NP \) carriage at healthy visits, by age and sex. Of the 3024 NPS samples obtained, 649 (21%) were positive for \( S. pneumoniae \) (figure 1). The prevalence of pneumococcal carriage clearly increased with age; the age-specific rates were 9% at 2 months, 17% at 6 months, 22% at 12 months, 37% at 18 months, and 43% at 24 months. The age-weighted average proportion of positive NPS samples for the whole follow-up period was 27%. The increasing trend was seen in both sexes; the age-weighted average mean of positive samples was 29% for boys and 26% for girls. There were no systematic differences in age-specific prevalence between boys and girls. The number of colonies was \( 10^3 \text{ to } 10^6 \) in 545 and 1–20 in 104 positive cultures.

\( NP \) carriage at sick visits, by age and sex. At sick visits, 2007 NPA samples were obtained, and 826 (41%) were positive for \( S. pneumoniae \). At visits without concurrent diagnosis of AOM, the proportion of positive NPA samples was 35% (407 of 1158); at visits with concurrent AOM, the proportion was 49% (419 of 849). The percentages of positive samples obtained within the 4 age intervals were compared among different clinical categories (figure 2A). The proportion of positive NPS samples obtained at healthy visits increased from 13% during the first age interval to 43% during the last age interval. In samples obtained at sick
visits without concurrent AOM, the proportions of positive NPA samples were somewhat higher (22%–46%) and increased with age. At sick visits with concurrent AOM, the child's age had little, if any, effect on the carriage rate: within the 4 age categories, *S. pneumoniae* was found in 46%, 46%, 50%, and 56% of samples, respectively. All percentages were higher than those observed within the respective age groups at healthy visits or at sick visits without AOM. This difference was most prominent during the first year of life.

We then examined NPA samples obtained at 761 visits during which AOM was diagnosed and for which ≥1 MEF sample was available for culture (figure 2B). *S. pneumoniae* was isolated from MEF in 26% of the AOM events: 26%, 25%, 31%, and 22%, respectively, by age interval. Throughout the age range,
the NPA samples obtained during pneumococcal AOM usually were positive for *S. pneumoniae* (97%–100%), whereas the proportion of positive NPA samples obtained during AOM with no evidence of pneumococcal etiology was about the same as in samples obtained at visits without concurrent AOM.

**NP carriage at healthy visits in relation to history of antimicrobial medication.** The effect of antimicrobial treatment was studied for 2854 (94%) of the 3024 NPS samples for which there were data of an oral antimicrobial treatment or of no treatment within 28 days before swabbing. The most frequently used oral antimicrobials were amoxicillin (40%), trimethoprim-sulfadiazine or trimethoprim-sulfamethoxazole (27%), amoxicillin-clavulanate (10%), and penicillin V (8%). *S. pneumoniae* grew in 499 (21%) of 2322 samples obtained at visits without and in 112 (21%) of 532 samples obtained at visits with a history of an oral antibiotic treatment within 28 days. However, differences were seen when the data were examined in more detail. Figure 3 shows the proportions of positive NPS samples according to whether oral antibiotics had not been used within 28 days or whether they had been used within 7 days or whether the use had ended 7–28 days before sampling. Up to age 6 months, the percentages of positive NPS samples were the same in the first 2 groups and were higher if the child had received antibiotics 7–28 days before sampling. At later ages, the proportion of positive samples was lower (11%–21%) if antibiotic treatment was recent (within 7 days) but increased (24%–35%) if ≥1 week had elapsed since the end of medication.

**Season.** The percentages of NPS and NPA samples positive for *S. pneumoniae* by calendar month are shown in figure 4. The occurrence of *S. pneumoniae* in NPS samples obtained during healthy visits fluctuated throughout the year (14%–25%), without any clear seasonal trend, as did the percentages of positive NPA samples obtained during sick visits, only at a higher level (33%–52%). However, there was no obvious seasonal trend, in contrast to the numbers of sick visits, which varied seasonally. The average number of sick visits was 106/month in the summer months (June to August) and 200/month the rest of the year.

**Cumulative colonization by S. pneumoniae.** Of the 329 children, 267 (81%) carried *S. pneumoniae* at least once (NPS or NPA) during the follow-up period. By the ages of 2, 6, 12, 18, and 24 months, 37 (11%), 107 (34%), 174 (56%), 228 (80%), and 244 (87%) of the children still being followed had carried *S. pneumoniae* at least once (figure 5). Of the 281 children with full follow-up, we detected 219 carriers (78%) during healthy visits and 207 (74%) during sick visits. For the 212 children with all 10 NPS samples, the individual number of positive samples at healthy visits varied from 1 (for 49 children) to 8 (for 3 children; median, 2).

**Serotypes.** The distribution of serogroups or serotypes of *S. pneumoniae* isolated in NPS and NPA samples is shown in table 2. Of the 1530 isolates, 1456 belonged to 30 different serotypes, 17 were nontypeable, 55 were rough, and 2 were lost before typing. In NPS samples, the 6 most frequently isolated serotypes were 6B, 23F, 19F, 6A, 11, and 35, which accounted for 66% of all NPS isolates. In NPA samples, 23F, 19F, 6B, 6A, 11, and 14 were the most frequent (73% of all NPA isolates). Serotypes 19F, 23F, 6B, 6A, 11, and 14 were most often acquired first (as detected in either NPS or NPA samples) and comprised 62% of the first acquisitions. A serotype included in the only currently available pneumococcal conjugate vaccine (7-valent, with types 4, 6B, 9V, 14, 18C, 19F, and 23F) was identified in 58% of the isolates overall (53% of NPS and 62% of NPA isolates). Together with the cross-reactive types 6A, 9N, 18B, 19A, and 23A, the vaccine-related types comprised 68% of NPS and 76% of NPA isolates.
Figure 4. Proportion of nasopharyngeal (NP) samples positive for *Streptococcus pneumoniae* (Pnc) by calendar month, January–December (1–12, respectively). A, NP swab (NPS) samples obtained during health. B, NP aspirate (NPA) samples obtained during respiratory infection. Bars, Total samples; lines, percentage of samples positive for *S. pneumoniae*.

In all, 168 children (63% of the 267 carriers) acquired >1 identified serotype during the follow-up. Two, 3, and 4–6 serotypes were carried by 84, 38, and 45 children, respectively, and 1 child carried his seventh serotype at age 22 months. A single serotype was found in 6 consecutive NPS samples in 2 children (6B in both cases).

In 24 (3.7%) NPS samples and 29 (3.5%) NPA samples that were positive for *S. pneumoniae*, 2 different serotypes were isolated at the same time, and, in 1 NPA sample, 3 different serotypes (3, 6B, and 23F) were found. Multiple serotypes were recovered from 45 children. In all, 21 different serotypes were responsible for multiple pneumococcal colonization, but again, 23F, 6B, 19F, 14, 6A, and 11 were the most common, in this order, accounting for 68% of the multiple isolations.

**Susceptibility of NP strains to penicillin.** Resistance of the pneumococcal isolates to penicillin was rare. Eight (1.2%) of 649 NPS isolates and 32 (3.9%) of 826 NPA isolates had reduced susceptibility to penicillin. Only 2 NPS isolates and 2 NPA isolates were highly resistant (MIC, >2 μg/mL); others showed intermediate resistance (MIC, 0.125–1.0 μg/mL). Of the 267 carriers (NPS or NPA), only 12 (4.5%) at least once carried *S. pneumoniae* with reduced susceptibility to penicillin.

**Discussion**

Most children in this closely followed cohort carried *S. pneumoniae* at least once in their nasopharynx during the first 2 years of life. The carriage prevalence during health increased with age. The isolation rates were higher during respiratory infection without AOM than during health, again with an increasing trend with age. During AOM, the rates were high, regardless of age, and, during pneumococcal AOM, practically every child carried *S. pneumoniae* (also in the nasopharynx). Antimicrobial treatment reduced the carriage rates only temporarily. The serotypes included in the 7-valent conjugate vac-

Figure 5. Cumulative rates of first acquisition of *Streptococcus pneumoniae* (Pnc) of children still in follow-up by age. Nasopharyngeal (NP) swab (NPS) samples were obtained at scheduled healthy visits at 2–6, 9, 12, and 15 months (± 2 weeks) and at 18 and 24 months (± 4 weeks); second NP aspirate (NPA) samples were obtained at sick visits during respiratory infections with or without acute otitis media.
cine used in recent efficacy trials in California [31] and Finland [32] and licensed in 2000 comprised 53% of the pneumococcal strains isolated from the nasopharynx during health and 62% of strains isolated during respiratory infection.

Although 87% of the study children carried S. pneumoniae at least once during the study, the children acquired their strains relatively slowly, and the overall carriage rate resembled that in the United States [16] and Sweden [7, 11]. The age-weighted mean proportion of positive NPS samples was 27%, a value near the prevalence (21%) among unselected healthy children sampled once at age 0–2 years in a Swedish study in 1975–1976 [11]. The cumulative acquisition rates were very near those reported by Faden et al. [8] (38% at 6 months and 54% at 12 months).

The prevalence of carriage at scheduled healthy visits (NPS) increased steadily with age from 9% at 2 months to 43% at 24 months. Dagan et al. [9] reported similar gradually increasing isolation rates from ages 2 to 24 months (from 26% to 62%) in Israeli children. In some other studies, increasing isolation rates leveled off at a younger age [5, 7, 10, 20]. In the present study, the health status of the study children seemed to have an important association with the carriage rates and also modified the association between carriage rates and age. The increase with age was most clear in the prevalence of carriage in healthy children, less clear in the NPA samples taken during respiratory infection without concurrent AOM, and absent in NPA samples taken during AOM (figure 2).

The NPA samples obtained during sick visits due to respiratory infection with or without AOM grew S. pneumoniae almost twice as often (41%) as the NPS samples obtained at healthy visits (21%). The percentage was even higher (49%) in the subgroup of NPA samples associated with concurrent AOM. This result is in agreement with that of Faden et al. [16], who reported significantly higher NP isolation rates during visits with upper respiratory infection or OM than during routine healthy visits in a follow-up study of US children <3 years old. Higher isolation rates in samples obtained at visits with signs of unspecified respiratory infection also were reported in an earlier study among British families [17] and in studies in Uruguay, Mexico, and Pakistan [19, 20, 33]. However, several studies failed to find any differences in carriage rates between healthy and ill children [21–23, 34]. In these studies, the study subjects were older than those in our study; in 2 studies, throat swabs rather than NP swabs were used, which could affect the results.

In the present study, the difference in isolation rates between healthy and ill children depended on age. The difference was most prominent during the first year of life and almost disappeared by age 2 years, when the rates were also high during health. Furthermore, the excess of carriage strains recovered during AOM seemed to be related to the concurrent occurrence of S. pneumoniae in MEF, since nonpneumococcal AOM was not associated with higher carriage than was respiratory infection without AOM. This conclusion is also consistent with the finding that the seasonal variation was less prominent in pneumococcal AOM than in AOM associated with Haemophilus influenzae or Moraxella catarrhalis in this same cohort [35].

One might argue that the difference in pneumococcal recovery observed in our study during health and respiratory infection was due to the different sampling methods (NPS or NPA). We consider this to be unlikely because the techniques were specifically compared in a previous study of children with acute respiratory infection, and the agreement between the NPS and the NPA techniques was excellent [36].

The antimicrobial treatment of the children was assumed to affect the results, but the overall proportion of samples positive for S. pneumoniae was similar (21%), whether or not the child had received oral antimicrobial treatment within 28 days. This
finding parallels the observation of Dagan et al. [9] among children 2–13 months old, which showed no association between carriage rate and use of antibiotics during the preceding month. In the present study, the isolation rates were lower if the therapy was ongoing or had ended within 7 days, but if 1–4 weeks had elapsed since the end of the medication, the rates increased again or, during the first year of life, were even higher than without antimicrobial treatment (figure 3). This is in accordance with findings of others that a more recent antimicrobial treatment reduced carriage rates [23, 26–28]. Leach et al. [28] found lower pneumococcal isolation rates (29%) 2–3 weeks after a single dose of azithromycin administered to Australian aboriginal children with trachoma than before treatment (68%), but, at the 2-month follow-up, the rate had rebounded to a higher level (78%) than before treatment. Thus, the lower carriage rates after use of antimicrobials seem to be of very short duration.

The most frequently isolated NP serogroups or serotypes in young children in industrialized countries are 6, 14, 19, and 23 [1, 12, 34]. These are related to most OM and invasive infections caused by S. pneumoniae in children in these areas [24, 29, 35, 37–39]. These serogroups or serotypes were among the most common in our present study, but group 11 also was common in both NPS and NPA samples. As expected, serogroups or serotypes 4, 7, and 18, which cause serious diseases but are less frequently recovered as carriage strains [37–39], were relatively rare among our NP isolates. In addition, type 3, a common cause of AOM in several reports [24, 29, 40], was uncommon in the present series. Type 3 is found frequently in the naso- or oropharynx in older children or adults rather than among infants and young children [15, 21, 37]. The frequency of multiple serotypes was low (3.7% of positive samples) in this study, which is in accordance with other studies in which a few colonies (3–5) were serotyped [1, 41]. Higher frequencies of multiple serotypes were detected by serotyping 50 colonies in Papua New Guinea (29%) [42], but such serotyping is impractical and expensive [41]. More sensitive methods would be needed to assess multiple carriage.

In conclusion, we found a high pneumococcal colonization rate (49%) in the presence of AOM throughout the first 2 years of life, in contrast to the colonization rates during health, which increased with age from 9% at 2 months to 43% at 2 years. The first practical conclusion from these findings is that both age and health status should be considered carefully when carriage rates in young children are compared and interpreted. The reasons for these findings and the implications for pneumococcal disease will be of interest for further study. Numerous additional data collected in the FinOM Cohort Study currently are being analyzed to further characterize the factors that affect the development of pneumococcal carriage and disease.

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References


