Pediatr Infect Dis J, 2003;22:589–92

Vol. 22, No. 7
Printed in U.S.A.

Influence of child care on nasopharyngeal carriage of *Streptococcus pneumoniae* and *Haemophilus influenzae*

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Background. **Children cared for by a child minder (CM) should be less exposed to upper respiratory tract infections than those in group day care (GDC) and therefore to antibiotic treatment. Thus fewer CM children should carry resistant bacteria. To test this hypothesis nasopharyngeal carriage of *Streptococcus pneumoniae* (SP) and *Haemophilus influenzae* (HI) and exposure to recent antibiotic treatment were investigated among children in both types of care settings in the Alpes Maritimes (France) between November 1999 and March 2000.**

Methods and population. **A two stage cluster sample of children attending group day care or cared for by a child minder was selected. Nasopharyngeal samples were cultured for SP and HI. Penicillin susceptibility was tested by disk diffusion and E-test and beta-lactamase production.**

Results. **We sampled 235 children in the CM group and 298 in the GDC group who were ages 6 to 36 months. Age and sex distribution were similar in both groups. *S. pneumoniae* was isolated in 80 children in the CM group (34.0%) and in 163 (54.7%) children in GDC ($P < 10^{-6}$). Proportions of non-penicillin susceptible (NPSP) were 52.5 and 55.8%, respectively ($P = 0.6$). *H. influenzae* was present in 37.2% of children in GDC *vs.* 23.8% in the CM group ($P < 0.001$). Proportions of beta-lactamase-positive HI (HIBL+) were 40.2% *vs.* 46.4%, respectively ($P = 0.4$). Antibiotic exposure during the previous 3 months occurred in 41.3% of children in GDC and in 47.4% in the CM group ($P = 0.16$). There was no association between antibiotic use and carriage of NPSP or HIBL+ strains.**

Conclusion. **SP and HI carriage rates were significantly lower among children in the CM group than in GDC. The proportion of NPSP and HIBL+ was similar in both groups, and comparable patterns of antibiotic use were observed. Continued efforts must concentrate on parental education and enforcement of recommendations for management of pediatric upper respiratory tract infections.**

INTRODUCTION

Nasopharyngeal colonization by bacterial respiratory pathogens in infants and toddlers attending day care has been the focus of a number of studies in the past years.[1–5] Investigation of bacterial carriage among this population has provided a simple means for the surveillance of resistance trends, while offering insight into the development of resistance after antibiotic treatment.[6–8] A cross-sectional survey conducted in Southeastern France in 1997 showed high carriage rates of *Streptococcus pneumoniae* with diminished susceptibility to penicillin.[8]

Although children's day-care centers may not reflect epidemiologic conditions within the corresponding age group population at large, they have the advantage of providing a group of generally healthy children in whom surveillance of prevalence rates can be conducted in a reproducible fashion. Because of the close contacts between them, these children may be expected to be colonized and infected by both antibiotic-susceptible and nonsusceptible bacteria with a higher frequency than children in other settings. In France working parents have the choice of group day care (GDC) or a child minder (CM), who looks after no more than 3 children. Limited contact in the latter case should reduce horizontal transmission, number of upper respiratory tract infections, antibiotic courses and carriage of antibiotic-resistant strains. To test this hypothesis nasopharyngeal (NP) carriage of *Streptococcus pneumoniae* (SP) and *Haemophilus influenzae* (HI) was investigated among children cared for by a CM in

Accepted for publication March 3, 2003.
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The results of this study were presented at the 41st Annual Interscience Conference on Antimicrobial Agents and Chemotherapy.[16]
Key words: Nasopharyngeal colonization, *Streptococcus pneumoniae*, *Haemophilus influenzae*, day care.
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groups of up to 3 and in GDCs catering for 20 to 100 children in the Alpes Maritimes in Southeastern France between November 1999 and March 2000.

METHOD AND POPULATION

Study population. The Alpes Maritimes area has a population of ~1 million, with an average annual birth rate of 11 per 1000. Each parent is provided at the child's birth with a health booklet in which developmental data, immunizations and illnesses are recorded by the child's physician. In 1999, 2500 children attended GDC in 52 day-care centers, with a capacity per center ranging from 20 to 100, whereas 1200 were cared for by a registered CM. The aim was to obtain a sample of 300 children in each type of child care. A two stage cluster sampling procedure was used to obtain a random sample of 24 GDC centers and 300 CM, and from these a random sample of children was subsequently drawn. A single child was randomly selected from each CM, with the possibility of offering participation in the study to another child in the same CM's care in case of refusal. A cluster of 20 children was randomly selected from each GDC to obtain an average of 13 children per day-care center, to allow for parental refusal or child's absence. Parents were asked to give informed consent and to complete a questionnaire concerning siblings, exposure to tobacco and recent antibiotic treatment. Children's health booklet and medical prescriptions during the previous 3 months were studied. Antibiotic treatments were assessed on both parents' questionnaires and children's prescriptions and/or health booklets.

NP samples were obtained from children attending GDC during the months of November and December 1999 and from those in the care of a child minder during the months of January and February 2000.

The investigation protocol was approved by a local Ethics Committee.

Laboratory studies. NP aspirates were submitted to direct microscopic examination and cultured for identification of SP and HI. Susceptibility of SP to penicillin, tetracycline, chloramphenicol and trimethoprim-sulfamethoxazole was tested by the disk diffusion method, whereas MICs for penicillin, amoxicillin and cefotaxime were determined by E-test on strains with reduced penicillin susceptibility. Breakpoints for penicillin, amoxicillin and cefotaxime susceptibility were those from the French Comité de l'Antibiogramme of the French Microbiology Society (in which S is susceptible, I is intermediate and R is resistant), i.e.: penicillin, S $\leq$0.064, I $>$0.064 and $\leq$1.000, R $>$1.000; amoxicillin, S $\leq$0.500, I $>$0.500 and $\leq$2.000, R $>$2.000; cefotaxime, S $\leq$0.500, I $>$0.500 and $\leq$2.000, R $>$2.000. HI strains were tested for beta-lactamase production and biotype (API-NH), but they were not serotyped. Pneumococcal serotypes were determined using the quellung reaction with antisera provided by the Statens Serum Institute (Copenhagen, Denmark). Only the antisera for the main serotypes observed in previous surveys were used, i.e. 6A, 6B, 9V, 14, 19A, 19F, 23F and 24.

Statistical analysis. Data were analyzed using Epi-Info Version 6. Proportions were compared by means of chi square tests at the 5% level of significance.

RESULTS

Nasopharyngeal samples were obtained from 298 children attending GDC from 25 day-care centers and 235 children cared for by a child minder between November 1999 and February 2000. An average of 12.4 samples was obtained from each GDC center (range, 4 to 20).

Both groups of children were comparable with regard to age, sex, number of siblings and tobacco exposure.

The prevalence rate of SP and HI was significantly higher among children in group day care (54.7% *vs.* 34.0% for SP; $P < 10^{-5}$ and 37.2% *vs.* 23.8% for HI; $P < 10^{-3}$). Likewise the prevalence rate of NPSP was higher in group day care (30.5% *vs.* 17.9%; $P < 10^{-3}$) (Fig. 1). However, among SP and HI carriers the proportion of SP and HI strains with reduced susceptibility to penicillin was similar in both groups (55.8 and 52.5% *vs.* 41.8 and 46.4%, respectively). Within each care setting there was no difference in carriage rates of NPSP between children less than 2 years of age and older children.

Parents provided information for 96 and 99% of children in the GDC and CM settings, respectively. During the previous 3 months, 110 of 232 (47.4%) children received antibiotic therapy in the child minder group *vs.* 118 of 286 (41.3%) in group day care (P = 0.16). Although fewer health booklets and/or prescription forms were available from children in group day care (75%) than for those attended by a child minder (93%), the proportion of treated children coincided with parental data and was comparable in both care settings: 110 of 220 (50%) children cared for by a child minder; and 104 of 226 (46.0%) of children in group day

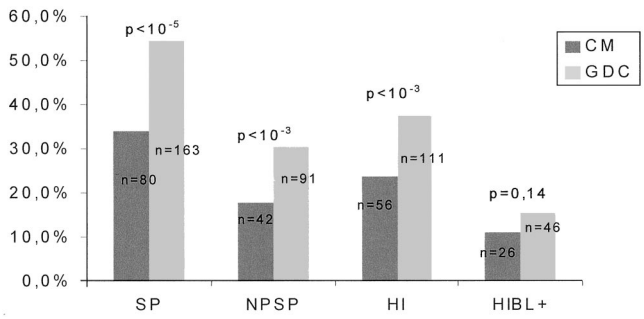

FIG. 1. Comparative prevalence rates for SP, NPSP, Hi and beta-lactamase-positive HI (*HIBL+*) according to type of day care.

care. There was no statistically significant difference concerning the number of courses received between the two care settings.

In GDC fewer children older than 2 years of age had been recently treated with antibiotics compared with the younger group (odds ratio, 1.93; 95% confidence interval, 1.06 to 3.56; $P = 0.02$). In the CM group the proportions of recently treated children were similar in both age groups.

Greater than 80% of these courses were with beta-lactam antibiotics in each group. Reasons for antibiotic prescription are given in Table 1. No association was observed between recent antibiotic treatment and carriage of penicillin-resistant strains, and stratifying by age group (younger than *vs.* older than 2 years old) did not modify this result. Likewise none of the other factors investigated (age, gender, siblings, exposure to tobacco smoke) was associated with carriage of either penicillin-susceptible or penicillin-resistant SP or HI strains.

Microbiologic data. Streptococcus pneumoniae. Serotype distribution of pneumococcal strains is shown in Table 2. The majority of strains belonged to serotypes 6B, 14, 19 and 23F. A higher prevalence rate was observed for serotype 6B in group day care than in the child minder setting (30% of strains *vs.* 15%, respectively; $P = 0.01$). Among NPSP strains distribution of serotypes was similar for both types of care. Penicillin MICs for NPSP ranged from 0.094 to 2 mg/l. Most strains were intermediately resistant to penicillin. Amoxicillin MICs for NPSP ranged from 0.023 to 2 mg/l, with 34% intermediately resistant, and there were no resistant strains. Susceptibilities of all pneumococcal strains to erythromycin, tetracycline and chloramphenicol were similar in both groups, with three-fourths, one-half and one-third of nonsusceptible strains, respectively. In the GDC group, fewer strains were nonsusceptible to trimethoprim-sulfamethoxazole than in the CM group (46.6% *vs.* 62.5%, respectively; $P = 0.02$).

Haemophilus influenzae. Most HI strains belonged to biotypes I, II and III.

DISCUSSION

This survey showed a lower carriage rate of SP and HI among children cared for by a child minder than in those attending group day care. However, no difference in the proportion of strains with reduced susceptibility to penicillin was observed between the two modes of care. Exposure to antibiotic treatment during the previous 3 months was similar in both groups. Although the number of courses may have been underestimated as a result of the fact that for some children neither health booklet nor prescriptions were available, especially among children attending group day care, there was no difference in the distribution of previous treatment courses as declared by parents and as documented in the health booklets.

There was no difference in either group in the proportion of NPSP carriers among children exposed to recent antibiotic treatment and those not exposed. Antibiotic prescription was just as frequent in group day care as in the child minder setting, suggesting that the frequency of upper respiratory tract infections must be comparable. Thus the difference in pneumococcal prevalence rates between the two types of child care lies in the lower opportunity for a child to come in contact with a carrier. De Lencastre et al.[5] observed extensive clonal spread of resistant SP in day-care centers in Lisbon. Bogaert et al.[9] also found a higher risk for horizontal spread of pneumococci in Dutch DCCs than in the general population.

Unlike other studies, in this survey recent antibiotic treatment was not associated with carriage of a resistant strain, even in the child minder setting where horizontal transmission has less chance of occurring.[6, 7] This may be related to the high carriage rates which can mask the effect of antibiotic use.

The magnitude of antibiotic exposure among small children is consistent with previous data and in line with recently published statistics concerning antibiotic use in France.[10] Inappropriate antibiotic prescription is particularly frequent in children with upper respiratory tract infections,[11] and in this study prescriptions for colds, cough and bronchitis as labeled in the child's health booklet are of questionable relevance. Although most children appear to be healthy carriers, Kronenberger et al.[12] observed that invasive pneumococcal infections caused by resistant strains were linked to the presence within the household of a child attending

TABLE 1. Diagnosed infections resulting in antibiotic treatment

Diagnosis	Child Minder ($n = 145$)	%	Group Day Care ($n = 115$)	%
Acute otitis media	43	29.7	43	37.4
Colds	27	18.6	22	19.1
Bronchitis	43	29.7	24	20.9
Pharyngitis/tonsillitis	14	9.7	13	11.3
Cough ± laryngitis	6	4.1	5	4.3
Other	12	8.3	8	7.0

TABLE 2. Pneumococcal serotypes

Serotype	Child Minder		Group Day Care		*P*
	No.	%	No.	%	
6A	4	5	9	6	NS
6B	12	15	49	30	0.01
9V	5	6	6	4	NS
14	10	13	18	11	NS
19	10	13	14	9	NS
23 F	13	16	30	18	NS
Other	26	33	37	23	NS
Total	80	100	163	100	

a day-care center. The main serotypes identified among pneumococcal isolates were those contained in the pneumococcal conjugate vaccine. Vaccination should thus reduce carriage, although colonization by substitute serotypes may be expected to follow.[13]

Effective public health policies have succeeded in reducing or maintaining low resistance rates by reducing antibiotic use as in Iceland[14] or favoring parental leave to isolate carriers as in Sweden.[15] In an attempt to curb antimicrobial resistance, a campaign began in 2001 in the Alpes Maritimes to encourage both physicians not to prescribe antibiotics and parents not to request antibiotics for young children with mild upper respiratory tract infections.

ACKNOWLEDGMENT

This study was funded by Produits Roche and Laboratoires Aventis.

We are indebted to all the child care personnel who took part in this study.

REFERENCES

1. Pradier C, Dunais B, Largillier R, et al. Nasopharyngeal carriage of *Streptococcus pneumoniae* in children's day-care centers: a 10 month follow-up study in Nice, France. Clin Microbiol Infect 1997;3:705–8.
2. Reichler MR, Allphin AA, Breiman RF, et al. The spread of multiply resistant *Streptococcus pneumoniae* at a day-care centre in Ohio. J Infect Dis 1992;166:1346–53.
3. Christenson B Sylvan SP, Noreen B. Drug-resistant *Streptococcus pneumoniae* in day-care centres in Stockholm County. J Infect 1998;37:9–14.
4. Yagupsky P, Porat N, Fraser D, et al. Acquisition, carriage, and transmission of pneumococci with decreased antibiotic susceptibility in young children attending a day care facility in Southern Israel. J Infect Dis 1998:177:1003–12.
5. de Lencastre H, Santos Sanches I, Brito-Avo A, et al. Carriage and antibiotic resistance of respiratory pathogens and molecular epidemiology of antibiotic-resistant *Streptococcus pneumoniae* colonizing children in day-care centers in Lisbon: the Portuguese day-care center initiative. Clin Microbiol Infect 1999;5:4S55–4S63.
6. Arason VA, Kristinsson KG, Sigurdsson JA, Stefansdottir G, Mölstad S, Gudmundsson S. Do antimicrobials increase the carriage rate of penicillin-resistant pneumococci in children? Cross sectional prevalence study. Br Med J 1996;313:387–91.
7. KG Kristinsson. Effect of antimicrobial use and other risk factors on antimicrobial resistance in pneumococci. Microb Drug Resist 1997;3:117–23.
8. Dellamonica P, Pradier C, Dunais B, Carsenti H. New perspectives offered by a French study of antibiotic resistance in day-care centers. Chemotherapy 1998;44(Suppl):10–14.
9. Bogaert D, Engelen MN, Timmers-Reker AJ, et al. Pneumococcal carriage in children in The Netherlands: a molecular epidemiological study. J Clin Microbiol 2001;39:3316–20.
10. Cars O, Mölstad S, Melander A. Variation in antibiotic use in the European Union. Lancet 2001;357:1851–3.
11. Guillemot D, Carbon C, Vauzelle-Kervroedan F, et al. Inappropriateness and variability of antibiotic prescription among French office-based physicians. J Clin Epidemiol 1998;51: 61–8.
12. Kronenberger CB. Invasive penicillin-resistant pneumococcal infections: a prevalence and historical cohort study. Emerg Infect Dis 1996;2:121–4.
13. Dagan R, Fraser D, Givon N, Yagupsky P. Carriage of resistant pneumococci by children in Southern Israel and impact of conjugate vaccine on carriage. Clin Microbiol Infect 1999;5:4S29–4S37.
14. Kristinsson KG. Modification of prescribers' behavior: the Icelandic approach. Clin Microbiol Infect. 1999;Suppl 4:S43–7.
15. Ekdahl K, Hansson H, Mölstad S, Söderström M, Walder M, Persson K. Limiting the spread of penicillin-resistant *Streptococcus pneumoniae*: experiences from the South Swedish Intervention Project. Microb Drug Resist 1998;4;2;99–105.
16. Dunais B, Carsenti H, Pradier C, et al. Influence of child care on nasopharyngeal carriage of *Streptococcus pneumoniae* and *Haemophilus influenzae* and antibiotic use [Poster G-91]. In: 41st Interscience Conference on Antimicrobial Agents and Chemotherapy, Chicago, December 16 to 19, 2001. Washington, DC: American Society for Microbiology, 2001.