# Efficacy of a slow-release device containing fluoride, xylitol and sorbitol in preventing infant caries

Antti S. Aaltonen, Jouko T. Suhonen, Jorma Tenovuo and Irma Inkilä-Saari

Health Center of Nummi-Pusula, Nummi-Pusula, Finland; Department of Cariology, Institute of Dentistry, University of Turku, Turku, Finland; Health Center of Lohja, Lohja, Finland

Aaltonen AS, Suhonen JT, Tenovuo J, Inkilä-Saari I. Efficacy of a slow-release device containing fluoride, xylitol and sorbitol in preventing infant caries. Acta Odontol Scand 2000;58:285–292. Oslo. ISSN 0001-6357.

A novel slow-release administration device, the "Fall-Asleep Pacifier" (FAP), was studied as a prophylactic measure against mutans streptococcal oral infection and dental caries in a risk group of 1-year-old children by comparing the test (T, $n = 34$) and control (C, $n = 88$) groups in a prospective cohort study. In the T group the children received their fluoride tablets (Fludent®, containing NaF corresp. 0.25 mg $F^-$, xylitol 159 mg and sorbitol 153 mg) in the evenings in FAP. In the C group the children received the same dose of Fludent® crushed in food in the evenings. The proportion of children, whose plaque samples from the upper incisors were mutans streptococcus positive at the age of 24 months, was significantly ($P < 0.05$) greater in group C (25%) than in group T (9%). The children in the T group developed significantly ($P < 0.001$) less (none) new dentinal carious lesions in their primary dentitions than the children in the C group between 2 and 3½ years of age. Fifty-four percent of the children to whom the FAP was offered complied with regular use of it. The beneficial effect observed in the T group compared with the C group was apparently mostly due to the administration mode via FAP, which could prolong the intra-oral bio-availability of the prophylactic preparation. □ *Caries risk; primary teeth; pacifier; sodium fluoride; xylitol*

*Antti S. Aaltonen, Pusulan hammashoitola, Arvelankuja 1, FIN-03850 Pusula, Finland. Fax. +358 9 2242 6812, e-mail. antti.aaltonen@nummi-pusula.fi*

A major determinant in the initiation of dental caries is the colonization of tooth surfaces by mutans streptococci (MS) (1, 2). The earlier the establishment of MS in the primary dentition occurs, the more extensive and rapid caries development can be expected (3–5). Because caries in primary teeth can indicate also a high risk of caries in permanent dentition (6), the main objective in prevention should be the avoidance or a delay of the primary MS colonization of newly emerging tooth surfaces in infants.

Reductions in the primary colonization of MS and in the subsequent caries incidence rate might be achievable with a novel strategy in which prophylactic agents are administered via a slow-release pacifier, named Fall-Asleep Pacifier (FAP) when used as indicated (7, 8, 9). The idea is to substitute caries-promoting fluids given in bottles to infants at bedtime by releasing caries-preventing agents from the FAP.

With this strategy topical fluoride effect lasts obviously for a longer time than if the agent is used awake, because during sleep salivary secretion ceases and, while swallowing is absent, there is no oral clearance (10). Fluorides can in high concentrations and at low pH reduce the acid production by MS (11) and long-term exposure to $F^-$ might select for less aciduric species (12). Fluorides may also hinder the adhesion of MS via mechanism of electrostatic surface tension (13). The most important effect of fluoride ion is considered to be its ability to promote remineralization in low concentrations, thus counteracting mineral loss in the tooth (14).

A night bottle's fermentable sugars can be substituted in FAP by small amounts of cariostatic sweeteners, such as xylitol and sorbitol. Synergism of xylitol and fluoride in the inhibition of glucose metabolism has been reported with *Streptococcus mutans* (15). Xylitol and fluoride may even have an additive inhibiting effect on enamel demineralization (16). Apparently due to some of its inhibiting properties against bacterial growth and adhesion, or plaque accumulation (17–19), xylitol reduces dental caries and middle ear infections in long-term frequent administration (20, 21). Since sorbitol does not cause such an energy-consuming futile metabolic cycle as described with xylitol in MS cells (22), its ability to inhibit primary MS colonization might be weaker than that of xylitol.

In this investigation we have tested the compliance with a fluoride, xylitol and sorbitol releasing prototype FAP and its effect on oral MS infection and caries development in a child population at risk.

## Materials and methods

### *General study design*

The study was conducted in a low-fluoride (<0.2 ppm $F^-$) area of Lohja city and surrounding countryside in southern Finland under the control of the Lohja District Health Center and with the permission of the Ethics Committee of the Medical Faculty, University of Turku.

Table 1. Dental examinations in the test (T) and control (C) groups. Figures are numbers (percentages) of children unless stated otherwise. MS = mutans streptococcus

| | T ($n = 34$) | C ($n = 88$) |
|---|---|---|
| Mean (SD) age at dental exam I (years) | 2.03 (0.08) | 2.03 (0.05) |
| Mean (SD) age at dental exam II (years) | 3.54 (0.07) | 3.53 (0.10) |
| Plaque sample MS-positive at exam I | 3 (9) | 22 (25)* |
| Number of caries cases at exams I and II, respectively | 1, 1 | 3, 14 |
| Decayed, missing, filled (dmf) surfaces at exams I and II, respectively | 1, 1 | 14, 94 |
| New caries cases/dmf surfaces between exams I and II, resp. | 0/0 | 11/80*/*** |
| Dentocult SM® test MS-positive at exam II | 31 (91) | 74 (84) |
| Dentocult SM® test score ≥1 at exam II | 17 (50) | 48 (55) |

* Significant difference between T and C groups; $P < 0.05$.
*** Significant difference between T and C groups; $P < 0.001$.

Informed consent was obtained from the mothers before the intervention study.

The flow chart in Fig. 1 shows the participation scheme in the whole study population until the age of five. However, the main focus of this report is on the cohort of 122 risk-group children who displayed complete data at the five study contacts during the period from 1 to 3½ years of age (Tables 1 and 2).

The principal outcome parameters (oral MS counts and caries rates) were measured at the ages of 2 and 3½ years. For the control of bias, differences in the background variables were sought between the test and control groups. To facilitate evaluation of suspected confounding factors, some comparisons and predictive risk indicator analyses were performed among the whole study population.

### *Selection of children into the risk group at the age of 12–14 months*

From November 1992 to December 1993 nurses at 10 child health counseling offices of the health center interviewed a total of 548 mothers with 1-year-old babies ($n = 557$), using a questionnaire. Children were assigned to a risk group ($n = 235$), i.e. were considered suitable for the pacifier study, if according to the questionnaire data they met one or more of the following three criteria: (i) had received juice in baby bottle at bedtime, (ii) sucked breast, fingers or bottle (water/milk/milk gruel) at nights and their mothers consumed sucrose-sweetened drinks daily and/or candies more often than once a week, (iii) sucked pacifiers and did not consume fluoride tablets regularly, and their mothers consumed sucrose-sweetened drinks daily and/or candies more often than once a week. There were 26 children whose mothers declined to take part in the study, which therefore proceeded with 209 children.

Table 2. Description of the test (T) and control (C) groups. Figures are numbers (percentages) of children unless stated otherwise

| Characteristics | T ($n = 34$) | C ($n = 88$) |
|---|---|---|
| Number of boys/girls | 18/16 | 35/53 |
| Rural residence | 12 (35) | 15 (17)* |
| Percentage of regular users of fluoride tablets | | |
| At ages 12, 18, 24, 42 months, respectively | 62, 82, 77, 50 | 67, 86, 77, 51 |
| Percentage brushing teeth daily at ages 24, 42 months, respectively | 65, 91 | 65, 86 |
| Mean (SD) score of the consumption frequency of sweets | | |
| And added sugar (summary index of ages 16, 18 and 42 months) | 5.5 (2.3) | 5.7 (2.2) |
| Daily users of sugary candies or added sugar at age 24 months | 3 (9) | 25 (28)* |
| Percentage of daily users of xylitol and/or sorbitol sweetened | | |
| Candies at ages 16, 18, 24, or chewing gum at age 42 months, respectively | 6, 0, 12, 24 | 3, 6, 14, 36 |
| Percentage of bottle suckers at ages 12, 16, 18, 24, 42 months, respectively | 79, 74, 50, 38, 12 | 78, 67, 58, 41, 11† |
| Percentage of night-juice bottle users at ages 18, 24, 42 months, respectively | 6, 3, 0 | 6, 11, 3 |
| Never used a juice bottle | 20 (59) | 50 (57) |
| Exposed to tobacco smoke at home | 6 (18) | 11 (13) |
| Percentage in daycare outside home at ages 24, 42 months, respectively | 18, 47 | 21, 49 |
| Antimicrobial medication between ages 18 and 24 months | 18 (53) | 40 (45) |
| Maternal high Dentocult SM® score (= 3) | 14 (41) | 34 (39) |
| Maternal caries activity (presence of ≥1 decayed teeth) | 11 (32) | 41 (47) |
| Mean (SD) score of the index of maternal consumption | | |
| Frequency of refined foodstuffs and sugar | 6.3 (2.9) | 7.2 (2.9) |
| Mother's education low (elementary school only) | 20 (59) | 40 (45) |
| Frequent mother-infant salivary contact (scores 3–6) (28) | 10 (29) | 25 (28) |
| Mean (SD) length of breastfeeding (months) | 4.5 (2.8) | 6.7 (4.6)* |
| Percentage of dummy users at ages 12, 16, 24, 42 months, respectively | 91, 94, 65, 18 | 82, 82, 68, 9 |

* Significant difference between T and C groups; $P < 0.05$.
*** Significant difference between T and C groups; $P < 0.001$.
† Significant difference in reduction of bottle use from age 16 to age 18 between T and C groups; $P < 0.05$.

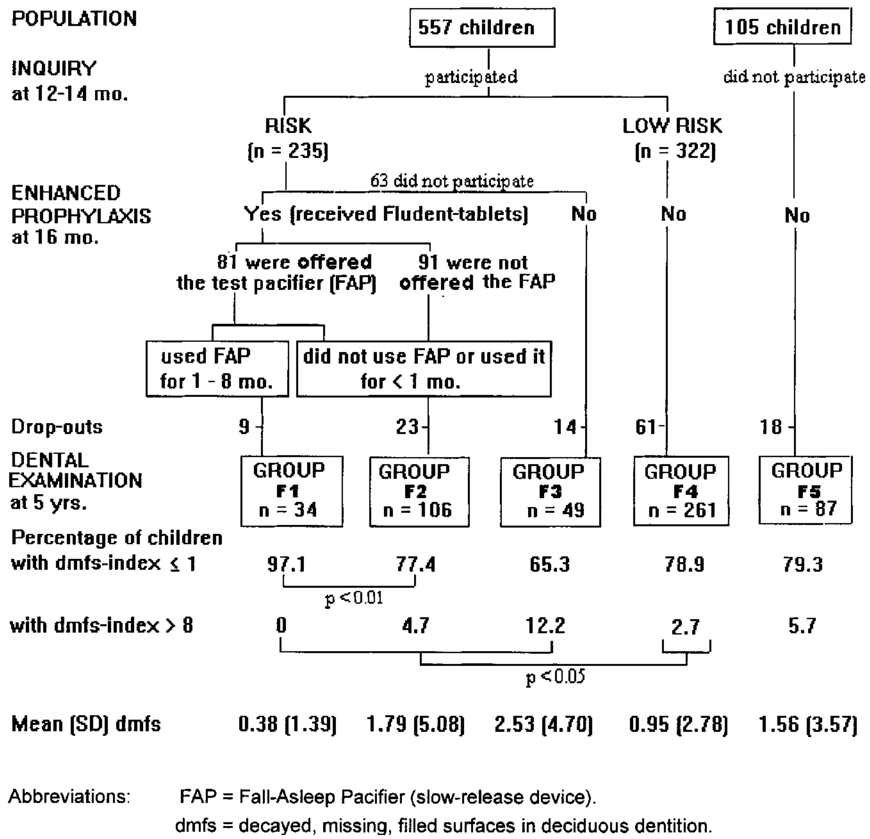


Fig. 1. Participation scheme in the whole study population and cumulative caries experience in the deciduous dentitions of the children distributed into the follow-up groups F1 – F5 at the age of 5 years.

### *Assignment to treatment groups at 16 months*

The mothers of children ($n$ = 209) in the risk group were invited to the public health dental office, when the children became 16 months old. During the first half of the enrolment period FAP was offered to the mother-child pairs recruited from the regions of 4 predetermined dental clinics and FAP was not offered to those recruited from the regions of 5 other clinics; during the second half of the enrolment period FAP was offered/not offered to new recruits from the same regions in the reverse order. Thus, from each of the 9 study regions approximately half of the children (altogether 106 children) became assigned to the FAP group and another half to the non-FAP group (altogether 103 children). Sixteen mothers assigned to the FAP group and 21 mothers in the non-FAP group did not take part. The mothers of participant children ($n$ = 172) were interviewed by trained local dentists or dental hygienists. Nine children were excluded from the FAP group because of having no sucking habits or because the mother no longer wanted her child to use a pacifier. For balance, 8 matched children were excluded from the non-FAP group, as well.

In the interview the mothers were asked to tell about the health and medical care of the baby, his/her stomach complaints, diarrhea and the frequency of loose stools. Also questions about the frequencies of children's tooth brushing, consumption of sugar, use of xylitol products and fluoride tablets were asked. Special attention was made to clarify the children's sucking habits: use of anatomical or another shape dummy pacifier, nursing bottle, sucking of breast, fingers. In all mothers a test for salivary MS was made. Everyone was provided with a package of 400 sodium fluoride tablets (each corresp. 0.25 mg $F^-$) sweetened with 159 mg xylitol and 153 mg sorbitol (Fludent®, Dumex-Alpharma, Espoo, Finland) to be administered to the child 1 tablet in the evenings in FAP/without FAP. Without FAP, Fludent® tablets were given crushed in food. All the mothers received dental health counseling with a leaflet pertinent to 1–2-year-olds.

### *Allocation to the test and control cohorts at 18 months*

A pre-coded questionnaire with a scheduled inquiry sheet to assess an index of the frequency of consumption of refined foodstuffs and sugar for mothers (23) was mailed to the participating risk-group mothers. The questions related to family size, maternal education, maternal self-recognized caries rate, length of breast feeding, dose and mode of the child's fluoride supply during the preceding month and separately the child's regular use of fluoride tablets on at least 5 d during the preceding week, frequencies in children's consumption of added sugar, sugary sweets and xylitol/sorbitol sweets, development of stomach complaints and allergic symptoms, incidence of middle ear infections (otitis media) and the number of anti-microbial courses the child had had for otitis media. Further questions were asked concerning the child's sucking habits at bedtime: pacifier (dummy), breast, fingers, water bottle, milk bottle, juice bottle, the FAP. The mothers of the FAP-group were further asked to present their experiences: how the child had accepted FAP, how often it had been in use, did she feel difficult to clean or fill the FAP, how long the tablet remained undissolved in it, and had the FAP remained intact.

Twenty-eight children in the FAP group refused to accept the FAP and 10 children used it irregularly for less than 1 month. These 38 children were combined with the original non-FAP-group children to form a reference cohort ($n = 112$) for those 43 FAP-group children, who used the FAP for at least 1 month.

### *Examination at 2 years*

All 2-year-old children in the study area were invited to a routine dental examination. In the risk group the guardians received, together with the invitation, a pre-coded questionnaire, in which they were asked about their children's pediatric diagnoses, skin rashes, gastrointestinal symptoms and anti-microbial medications during the preceding half year, present day-care and exposure to tobacco smoke at home. Furthermore, some questions asked at the age of 18 months concerning fluorides, diet and sucking habits were repeated. Replies were received concerning 202 children, of whom 199 gave during the examination a plaque sample for MS culture. A follow-up inquiry was made to all the test-group guardians about FAP use during the last six months. Toothbrushes and fluoride tablets (Fluorilette®, NaF corresp. 0.25 mg $F^-$, containing lactose, Leiras, Finland) were offered routinely free of charge to the whole age group.

### *Examination at $3\frac{1}{2}$ years*

Ninety-five percent of the children whose mothers had been interviewed in 1992–93, lived in the study area still in 1995. When the children were 42 months old they were again invited to a dental examination. In total 439 (83%) children arrived. For comparative reasons, teeth were also examined in 81 same-aged children, whose mothers had not participated the baseline interview. Altogether 496 children were tested on oral MS.

The focus cohort with complete data finally comprised 34 test children (group T) and 88 control children (group C).

A pre-coded questionnaire was used in the interview of the guardian. The questions asked followed mostly the same scheme as at the ages of 18 and 24 months relating mainly to known risk factors of caries and ear infections. Children's sucking habits at ages $\frac{1}{2}$, $1\frac{1}{2}$, $2\frac{1}{2}$ and $3\frac{1}{2}$ years were ascertained retrospectively in the whole study group.

### *Microbiological assays*

The method used to determine the amount of MS in dental plaque of 2-year-old children has been described (24). Plaque samples were obtained by pushing a narrow autoclaved toothpick (Sanion®, Koskenkorva, Finland) into the three spaces between upper incisors. The tip of the toothpick was cut and dropped into a tube containing tryptic soy broth with 20% glycerol. The tubes were frozen within a few hours and stored at −20°C until analyzed for MS in a microbiological laboratory (Institute of Dentistry, Turku). The sample was considered positive if MS exceeded the cut-off value $0.7 \times 10^3$ cfu/sample.

Dentocult SM® Strip Mutans test (Orion Diagnostica, Espoo, Finland) (DcSM) was used to assess salivary levels of MS in mothers and $3\frac{1}{2}$-year-old children. To ensure adequate sample in the children a modification of Pienihäkkinen and Jokela (25) was used as follows: After rotating the plastic strip on the back of the tongue to sample saliva as instructed by the manufacturer, a pooled plaque sample was obtained with dental floss from the approximal spaces between upper and lower left primary molars and from the distal surface of an upper first incisor. Plaque was transferred from the floss to a narrow area on the test surface of the strip. The sample was regarded MS positive, if on the floss-rubbed area or elsewhere on the surface one or more colonies could be seen. Colony density was assessed on the basis of the growth outside the rubbed area and it was classified from 0 to 3. The 0 class was further divided in two depending on whether the sample was MS positive or not. The following reference values per strip were used: class 0-neg = no growth, class 0-pos = 1–5 cfu, class 1 = 6–50 cfu, class 2 = 51–400 cfu, class 3 = more than 400 cfu.

### *Dental examinations*

The examinations were carried out at nine fully-equipped dental clinics using visu-tactile methods and the general recording system directed by the National Board of Health in Finland. Only cavities extending to dentin were included in caries analyses. The inter-examiner consistency was considered adequate, because all the 3 dentists and 5 hygienists who carried out 96% of the examinations at $3\frac{1}{2}$ years, had for several years treated young children in the same health center. Moreover, obviously affirming the consistency, there was a moderate positive correlation between the DcSM class and caries occurrence (Fig. 2), and although the recordings of caries and DcSM values ≥1 varied markedly regionally, there was a significant positive inter-examiner rank correlation between the percentages of dentinal caries cases diagnosed and the DcSM values ≥1 observed in the examinations. The reliability of the recordings was confirmed in a follow-up study on caries development in those children, who underwent a further dental examination in the health center before November 1998 (Fig. 1).

### *Statistics*

The two-sided standard *t*-test, Mann-Whitney U-test, chi-squared test or Fisher's exact test was used in analysis of significance of differences between groups. The difference was considered statistically significant, when $P < 0.05$. Youden's index (J) was used as a measure for evaluating the accuracy of predictions (26). Indirect standardization using the control group as the standard population was used in the evaluation of potential confounding effects on the caries development.

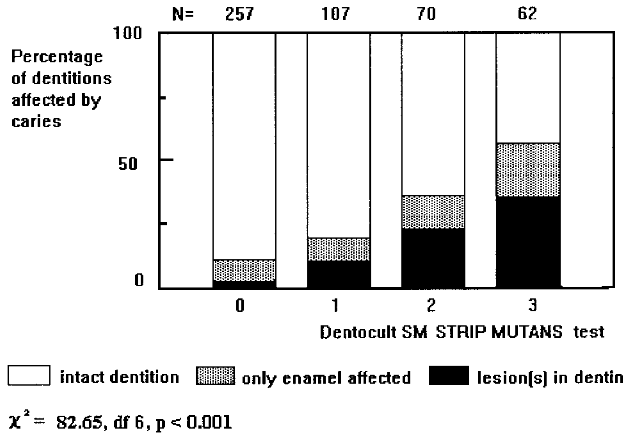


Fig. 2. Distribution of dental caries cases (enamel caries, $n = 54$; dentinal caries, $n = 55$) in $3\frac{1}{2}$-year-old children (N = 496) into the four categories of the Dentocult SM Strip Mutans test scored as followed: score 0 = 0–5 cfu, score 1 = 6–50 cfu, score 2 = 51–400 cfu, score 3 = more than 400 cfu/strip.

## Results

### *Compliance*

Among the children, who participated in the study at ages 16, 18 and 24 months, 27 children had used FAP for 1–4 months, 4 children used it for 5–6 months and 10 children for at least 7–8 months. Six of these children did not arrive for the examination at the age of $3\frac{1}{2}$ years, and one did not co-operate. No one of these 7 drop-out children was MS-positive at the age of two.

### *Comparison between T and C groups*

A significantly smaller proportion (9%) of the children in T group than in C group (25%) had MS-positive plaque samples at the age of 24 months. The children in T group developed less dental caries than the children in C group. Difference between T and C group in the prevalence of caries cases (3% vs 16%) at the age of $3\frac{1}{2}$ years and in the incidence of new caries cases (0 vs 11) and of decayed surfaces (0 vs 80) between 2 and $3\frac{1}{2}$ years were statistically significant (Table 1).

The proportion of children, who had had otitis media before the age of 18 months, was significantly smaller in T than in C group (56% vs 75%, $P < 0.05$).

There were only a few differences between T and C group in the background variables which were also associated with the outcome variable and thus had to be regarded as potential confounding factors when evaluating the possible treatment effect of FAP. Essential characteristics of the subjects in T and C groups are described in Table 2. Night-time breastfeeding at the age of 1 year and daily consumption of candies or added sugar at the age of 2 years, which were more common in C group than in T group, could increase the difference in caries prevalence at the age of $3\frac{1}{2}$ years between the groups. On the other hand the greater proportion of rural children in T group than in C group could decrease the difference. After adjustment on these three variables (additively combined: presence of at least one of them/absence of all) the indirectly standardized number of caries cases in T group showed value of 2.77, meaning that the lack of 1–2 caries cases from T group could be explained by this interaction, if there really was a causal relationship between these factors and caries.

### *Risk indicators*

Maternal education less than matriculation examination (J = 0.32), maternal dental caries (J = 0.30), maternal use of sugar in coffee or tea ≥twice a day (J = 0.29), maternal DcSM = 3 (J = 0.28), and child's non-use of FAP (J = 0.19) were best able to predict the MS positivity in the 2-year-old infants.

The most powerful single predictor of the occurrence of dental caries in $3\frac{1}{2}$ year-old children was the child's MS positivity at the age of two (J = 0.49). Also rural residence (J = 0.35), use of juice bottle at nights (J = 0.28), frequent (daily) intake of sugar in candies or added in foods or drinks (J = 0.21), exposure to tobacco smoke at home (J = 0.19), and night-time breastfeeding (J = 0.09) at age 2 were significantly associated with the caries occurrence at age $3\frac{1}{2}$ in these risk-group children ($n = 169$), of whom the plaque sample, DcSM, and caries record could be studied. Thirty-three of these children showed MS positivity at the age of two, 142 at the age of $3\frac{1}{2}$, and 19 had caries at the age of $3\frac{1}{2}$ years.

Dental caries occurred at the age of $3\frac{1}{2}$ years in equal frequency (11%) both in the risk-group ($n = 177$) and the low-risk-group children ($n = 242$). However, the proportion of the $3\frac{1}{2}$-year-old children, who showed MS-positive DcSM tests, was significantly greater in the risk group than

Table 3. Variables studied at 1 year of age in relation to the occurrences of oral infection by mutans streptococci (MS) and dental caries in the whole child cohort at the age of 3.5 years. OR = odds ratio.

| Observed rates at the age of 3.5 years / Predictors at 1 year of age | MS positive: Yes ($n$ = 313) % | No ($n$ = 111) % | OR | Dental caries: Yes ($n$ = 47) % | No ($n$ = 383) % | OR |
|---|---|---|---|---|---|---|
| Rural residence | 25 | 10 | 3.4*** | 45 | 18 | 3.7*** |
| Maternal consumption of sucrose-sweetened | | | | | | |
| Drinks daily and/or candies ≥ 2 / week | 19 | 9 | 2.4** | 30 | 15 | 2.4** |
| Breast feeding during night | 10 | 6 | 1.6 | 21 | 7 | 3.4** |
| Juice bottle in use at bedtime often | 4 | 1 | 4.0 | 9 | 2 | 3.0* |
| Only milk or milk-gruel bottle at nights | 20 | 17 | 1.2 | 21 | 19 | 1.1 |
| Only water bottle at nights | 9 | 8 | 1.1 | 2 | 9 | 0.2 |
| Breast or bottle feeding (other than water) at nights | 47 | 34 | 1.9** | 66 | 40 | 2.9*** |
| Pacifier (dummy) not in use | 26 | 17 | 1.7 | 36 | 21 | 2.1* |
| No or not regular use of fluoride tablets | 28 | 31 | 0.8 | 40 | 28 | 1.8 |
| Selected to the risk group | 48 | 27 | 2.5*** | 43 | 42 | 1.0 |
| Belonging to the test group T (from age 16 months on) | 10 | 3 | 4.0 | 2 | 9 | 0.2 |

*** $P < 0.001$; ** $P < 0.01$; * $P < 0.05$ chi-squared test.

in the low-risk group (83% vs 67%, $P < 0.001$). The occurrences of caries and MS-positive DcSM tests in the supplementary comparison group were 10% and 74%, respectively (Fig. 3). Table 3 gives crude rates (observed true-positive and false-positive percentages and odds ratio) for the risk markers, screened in the children of the basic population at 1 year of age and related to the children's oral MS infection and caries occurrence at the age of $3\frac{1}{2}$ years.

Among the $3\frac{1}{2}$-year-old children, who were excluded from the intervention study on the basis of the selection criteria (the low-risk group) or who belonged to the supplementary comparison group, dental caries occurred in equal frequency (9%) both in the children ($n = 81$) who had used Fludent® and those ($n = 136$) who had used Fluorilette® fluoride tablets during the preceding month. Dental caries was significantly more frequent in the children who had not used fluoride tablets at all ($n = 113$, 14%, $P < 0.05$).

*Follow-up examination at 5 years*

The distribution of dentinal caries into the followed groups F1–F5 is presented in Fig. 1. A significantly greater proportion of the children in F2 group than in F1 group had dmfs >1. A significantly greater proportion of children in the risk group (F1 + F2 + F3) than in the low-risk group (F4) had dmfs >8.

The group F1 comprised four children who did not belong to the T group, although they had used FAP >1 month. They had been dropped out from the T group for incomplete data. All these four children were free of caries at the age of 5 years. Correspondingly, group F2 comprised 27 children who did not belong to the C group. Ten (all caries-free) of them had been excluded at the age of 16 months because of negligible sucking habits, and 17 (3 caries cases) had been dropped later from the study cohort, because some essential data were missing (Fig. 1).

## Discussion

The beneficial effect observed in the test group compared to the control group was apparently mostly due to the administration mode via FAP, because Fludent-tablets were eaten in the control group as regularly, but without the administration device. An indirect way of influence, although not obvious in this study, could have been that because FAP reduced the use of baby bottle, the caries risk derived from the bottle use had diminished in the test group.

The criteria used for the selection of the risk group suitable for the FAP study were based on the risk factor analyses of previous studies in the same area (27, 28). The children's caries experience in the risk group in total had developed significantly worse than in the low-risk group by the age of 5 years indicating that the screening method had been valid. This was also confirmed by the risk-factor analysis in the whole study population. Night-time use of juice bottle and maternal consumption of sucrose-sweetened

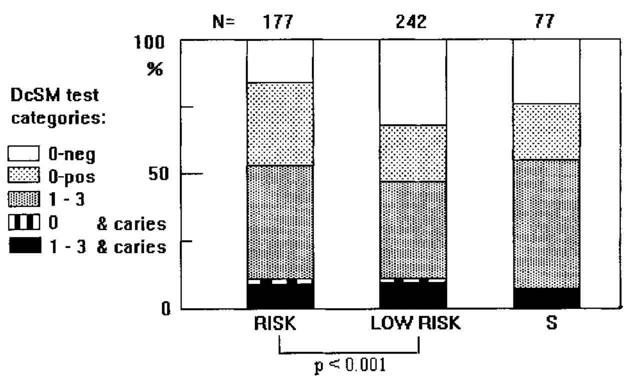


Fig. 3. Distribution of children ($n = 496$) according to their caries experience (dmfs ≥1) and results in the Dentocult® SM Strip Mutans (DcSM) test at the age of $3\frac{1}{2}$ years into the risk group, the low-risk group and the supplementary control group (S).

drinks daily or candies several times weekly predicted frequent occurrence of caries in deciduous dentitions consistently with recent studies in Finland (27, 29). The positive predictive associations of maternal frequent sugar consumption, maternal high salivary MS level and maternal caries activity with the detection of MS in the plaque samples of the 2-year-old children agree with the infection theory (30, 31). However, the FAP strategy seemed to be protective also under such caries-promoting conditions. The importance of MS as a major determinant of caries became evident in that the 2-year-old children whose plaque samples were MS positive appeared to be in 7-fold risk to have dentinal caries at the age of $3\frac{1}{2}$ years compared with the children whose plaque samples were MS negative.

The children, who did not accept FAP although assigned to use it, were included in the control group. This breaks the random assignment rules, but because the survey of background data revealed no essential differences and also the outcome data of these children did not differ significantly when compared with the data of the original non-FAP children in the control group, the arrangement was considered justified. However, there might be a slight bias in assignment of study subjects to the FAP/non-FAP groups. Since the mothers were for ethical reasons informed beforehand about the purpose and the methods of the study, this perhaps affected that there were more users of pacifiers in the test group than in the control group. All long breast-fed children and finger suckers, generally known to use pacifiers rarely (32), fell into the control group. Prolonged breastfeeding seemed to increase the risk of MS infection and dental caries in the present study. Prolonged breastfeeding may be a risk factor of dental caries in young children, but only if their dietary habits are also unsuitable (33). Breastfeeding was in some cases associated with increased intake of sugary tidbits in the infants. However, from this material it can not be deduced that the risk of caries would have been elevated in such dietary risk cases if the FAP had been in use.

The prophylactic preparation in our study contained sodium fluoride, xylitol and sorbitol. The role of each of these components as active agents can to a certain extent be estimated on the basis of the results. At the beginning of the study the children in the risk group received significantly less fluoride tablets than the children in the low-risk group. In spite of this no more caries cases occurred in the risk group than in the low-risk group at the age of $3\frac{1}{2}$ years, which effect apparently is due to the enhanced prophylaxis, including increased fluoride therapy, during the study in the risk group. In the low-risk group and the supplementary reference group, which did not participate in the intervention study, use of fluoride tablets was associated with fewer caries cases in children at $3\frac{1}{2}$ years of age. However, there was no difference in the caries rate between the users of the fluoride preparation Fludent®, which contained xylitol and sorbitol, and Fluorilette®, which contained lactose. With caution the result might mean that xylitol and sorbitol in the 50% dose ratio did not contribute any marked caries-preventive advantage compared to lactose in fluoride tablets in the conventional use, perhaps due to rapid oral clearance of the small amounts by freshly secreted saliva, together with the swallowing act. The fact, that in the risk group, in spite of equal caries frequency, a significantly greater proportion of the $3\frac{1}{2}$-year-old children were MS-positive than in the low-risk group, agrees with the theory that $F^-$ ion prevents carious lesions but does not affect MS colonization at the level of 1 ppm $F^-$ (34, 35). In order to explain the low MS positivity at 2 years of age in the test group with the action of fluoride, one should presuppose that high concentrations up to 100 ppm $F^-$, which reduce plaque formation immediately, or long-term levels of about 10 ppm $F^-$, which reduce acid production of MS (11, 12), could be achieved in the oral fluid around teeth by the use of FAP. The long-term effect seems possible on the basis of biological rhythm of salivary flow (no oral clearance or dilution by salivary physiology during sleep) and in vitro studies performed with the FAP (8).

Nevertheless, also the roles of xylitol and sorbitol are interesting. About every fourth child in the risk group had started weekly use of xylitol products before the age of 16 months. In our study this kind of infrequent, though habitual use of xylitol/sorbitol candies showed no superiority to sugar candies when related to the children's oral MS infection or caries development by the age of $3\frac{1}{2}$ years. However, frequent (at least once a day) use of xylitol/sorbitol sweets tended to coincide with MS-free dentitions in 2-year-old children and could contribute a small but appreciable preventive effect on the infection. Long-term use of xylitol selects for xylitol-resistant MS mutants which possess low cariogenic virulence (36). By using an administration device which slowly releases an active agent it is possible to create around the erupting teeth in the mouth of a sleeping child for hours an oral fluid environment, which according to our study evidently has caries preventive properties. When used this way, the advantageous properties of xylitol are expected to be maximized with rather small doses without laxative side effects. In our study the use of xylitol/sorbitol products was not found to increase stomach complaints in children.

An interesting side finding in our study was that the xylitol-containing fluoride preparation could have some preventive effect against otitis media in the children under the age of 18 months, when delivered via FAP. The daily dose of the xylitol in the novel slow-release FAP method was only a small fraction of the dose required for the prevention of otitis in the study of Uhari et al. (21).

From the point of compliance, the age of 16 months at which FAP was offered to the children was obviously too late, because the instinctive sucking need weakens with age. In addition, the children seemed to be very delicate to cast aside the new pacifier, if its model or size differed from the dummy they had used before. Some children chewed on the silicone teat which occasionally broke and had to be changed. In spite of these constraints FAP proved to be an effective vehicle in reducing caries incidence between 2 and 5 years of age in the children, who used it in the administration of a sodium fluoride-xylitol-sorbitol preparation for some months before the age of two. The clinical significance of the administration of various prophylactic agents using the FAP technique in order to reduce childhood infections, including mutans streptococcal oral infection in dental caries, remains to be evaluated in future studies.

*Acknowledgements.*—This study was supported financially by the Finnish Dental Society, the Association of Finnish Health Center Dentists, Nestec LTD, Milupa AG, Turku University Hospital, Emil Aaltonen Foundation, Instrumentarium Science Foundation, and in providing utilities Lamprecht AG, Dumex-Alpharma and Vivadent Vivacare.

## References

1. Loesche WJ. Role of Streptococcus mutans in human dental decay. Microbiol Rev 1986;50:353–80.
2. Emilson C-G, Krasse B. Support for and implications of the specific plaque hypothesis. Scand J Dent Res 1985;93:96–104.
3. Alaluusua S, Renkonen O-V. Streptococcus mutans establishment and dental caries experience in children from 2 to 4 years old. Scand J Dent Res 1983;91:453–7.
4. Köhler B, Andréen I, Jonsson B. The earlier the colonization by mutans streptococci, the higher the caries prevalence at 4 years of age. Oral Microbiol Immunol 1988;3:14–7.
5. Grindefjord M, Dahllöf G, Modéer T. Caries development in children from 2.5 to 3.5 years of age: a longitudinal study. Caries Res 1995;29:449–54.
6. Alaluusua S, Kleemola-Kujala E, Nyström M, Evälahti M, Grönroos L. Caries in the primary teeth and salivary Streptococcus mutans and lactobacillus levels as indicators of caries in permanent teeth. Pediatr Dent 1987;9:126–30.
7. Suhonen J. Mutans streptococci and their specific oral target. New implications to prevent dental caries? Schweiz Monatsschr Zahnmed 1992;102:286–91.
8. Suhonen J, Sener B, Bucher W, Lutz F. Release of preventive agents from pacifiers in vitro. An introduction to a novel preventive measure. Schweitz Monatsschr Zahnmed 1994;104:946–51.
9. Suhonen JT, Heinze ST, Aaltonen AS. Neue Strategien in der Kariesprävention. Phillip J 1998;15:98–107.
10. Schneyer LH, Pigman W, Hanahan L, Gilmore RW. Rate of flow of human parotid, sublingual and submaxillary secretions during sleep. J Dent Res 1956;35:109–14.
11. Tatevossian A. Plaque fluoride. Proc Finn Dent Soc 1991;87: 501–13.
12. Marsh PD. Sugar, fluoride, pH and microbial homeostasis in dental plaque. Proc Finn Dent Soc 1991;87:515–25.
13. Rölla G. Inhibition of adsorption—general considerations. In: Stiles H, Loesche W, O'Brien T, editors. Microbial aspects of dental caries. Washington DC: Information Retrieval Inc.; 1976. p. 308–24.
14. Pearce EIF. Relationship between demineralization events in dental enamel and the pH and mineral content of plaque. Proc Finn Dent Soc 1991;87:527–39.
15. Rogers AH, Bert AG. Effect of xylitol and fluoride on the response to glucose pulses of Streptococcus mutans T8 growing in continuous culture. Oral Microbiol Immunol 1992;7:124–6.
16. Arends J, Smits M, Ruben JL, Christoffersen J. Combined effect of xylitol and fluoride on enamel demineralization in vitro. Caries Res 1990;24:256–7.
17. Söderling E, Alaräisänen L, Scheinin A, Mäkinen KK. Effect of xylitol and sorbitol on polysaccharide production by and adhesive properties of Streptococcus mutans. Caries Res 1987;21: 109–16.
18. Kontiokari T, Uhari M, Koskela M. Effect of xylitol on growth of nasopharyngeal bacteria in vitro. Antimicrob Agents Chemother 1995;39:1820–3.
19. Kontiokari T, Uhari M, Koskela M. Antiadhesive effects of xylitol on otopathogenic bacteria. J Antimicrob Chemother 1998;41:563–5.
20. Mäkinen KK, Bennett CA, Hujoel PP, Isokangas PJ, Isotupa KP, Pape HR Jr, Mäkinen PL. Xylitol chewing gums and caries rates: a 40-month cohort study. J Dent Res 1995;74:1904–13.
21. Uhari M, Kontiokari T, Niemelä M. A novel use of xylitol sugar in preventing acute otitis media. Pediatrics 1998;102:879–84.
22. Söderling E, Pihlanto-Leppälä A. Uptake and expulsion of $^{14}$C-xylitol by xylitol-cultured Streptococcus mutans ATCC 25175 in vitro. Scand J Dent Res 1989;97:511–9.
23. Aaltonen AS. Natural immunity in dental caries. Longitudinal studies of serum and salivary antibodies reactive with Streptococcus mutans in young children in relation to dental caries and some maternal factors [Thesis]. Turku; 1989.
24. Aaltonen AS, Tenovuo J, Lehtonen O-P, Saksala R, Meurman O. Serum antibodies against oral Streptococcus mutans in young children in relation to dental caries and maternal close-contacts. Arch Oral Biol 1985;30:331–5.
25. Pienihäkkinen K, Jokela J. A simple method for monitoring mutans streptococci in young children. Eur J Oral Sci 1995;103:61–2.
26. Hausen H. Caries prediction—state of the art. Community Dent Oral Epidemiol 1997;25:87–96.
27. Aaltonen AS. The frequency of mother-infant salivary close-contacts and maternal caries activity affect caries occurrence in 4-year-old children. Proc Finn Dent Soc 1991;87:373–82.
28. Aaltonen AS, Tenovuo J. Association between mother-infant salivary contacts and caries resistance in children: a cohort study. Pediatr Dent 1994;16:10–6.
29. Paunio P, Rautava P, Helenius H, Alanen P, Sillanpää M. The Finnish family competence study: the relationship between caries, dental health habits and general health in 3-year-old Finnish children. Caries Res 1993;27:154–60.
30. Berkowitz RJ, Turner J, Green P. Maternal salivary levels of Streptococcus mutans and primary oral infection of infants. Arch Oral Biol 1981;26:147–9.
31. Köhler B, Andréen I, Jonsson B. The effect of caries-preventive measures in mothers on dental caries and oral presence of the bacteria Streptococcus mutans and lactobacilli in their children. Arch Oral Biol 1984;29:879–83.
32. Paunio P, Rautava P, Sillanpää M. The Finnish family competence study: the effects of living conditions on sucking habits in 3-year-old Finnish children and the association between these habits and dental occlusion. Acta Odont Scand 1993;51:23–9.
33. Hallonsten A-L, Wendt L-K, Mejáre I, Birkhed D, Håkansson C, Lindvall A-M, et al. Dental caries and prolonged breast-feeding in 18-month-old Swedish children. Int J Paediatr Dent 1995;5: 149–55.
34. van Houte J, Aasenden R, Peebles TC. Oral colonization of Streptococcus mutans in human subjects with low caries experience given fluoride supplements from birth. Arch Oral Biol 1978;23:361–6.
35. Zickert I, Emilson CG. Effect of a fluoride-containing varnish on Streptococcus mutans in plaque and saliva. Scand J Dent Res 1982;90:423–8.
36. Trahan L, Bourgeau G, Breton R. Emergence of multiple xylitol-resistant (fructose PTS$^{-}$) mutants from human isolates of mutans streptococci during growth on dietary sugars in the presence of xylitol. J Dent Res 1996;75:1892–900.

Received for publication 18 February 2000
Accepted 12 September 2000