

The caries-preventive effects of full- and half-strength topical acidulated phosphate fluoride

Patricia P. Hagan, DDS, MS R. Gary Rozier, DDS, MPH
James W. Bawden, DDS, MS, PhD

Abstract

Due to concerns about the potential for acute toxicity following professional application of topical fluoride, this clinical trial was undertaken to determine if half-strength acidulated phosphate fluoride (APF) would be as clinically effective in reducing caries as the currently used 1.23% APF. Three hundred and sixteen junior high school students, 11-15 years of age, living in a nonfluoridated area were assigned randomly to 1 of 3 groups: a 1.23% APF thixotropic gel group, a 0.6% APF thixotropic gel group, or a placebo gel control group.

Visual and tactile dental examinations, toothbrush and floss prophylaxis, and topical application of assigned gel were performed twice annually for each child. After 24 months, both the 1.23% APF group and the 0.6% APF group experienced statistically significant ($p < .05$) caries increment reductions when compared to the control group. Although the 2 fluoride-treated groups experienced caries increment reductions that were not statistically different from each other, there was a tendency for the half-strength fluoride (0.6% APF) to be less effective, especially in reducing pit and fissure caries. Thus, while a half-strength fluoride gel may be effective in reducing caries in selected cases where acute fluoride toxicity is of special concern, these findings suggest that some effectiveness in pit and fissure caries prevention may be sacrificed. Therefore, this clinical trial does not support widespread reduction of fluoride content to 0.6% F- in twice-annual, professionally applied topical fluoride formulations.

The results of previous clinical trials have shown that the use of acidulated phosphate fluoride (APF) gels containing 1.23% fluoride (F-) on a twice-annual basis is effective in preventing dental caries.¹⁻³ However, recent studies have shown that a considerable amount of fluoride may be ingested during the course

of a standard professional topical fluoride application^{4,5} and that plasma fluoride levels achieved after such an application may reach potentially toxic levels.⁶⁻⁸

Acute fluoride toxicity is of particular concern when administering a topical fluoride treatment to the small child patient because of the exposure to a relatively higher fluoride dose per body weight than in the case of an adult receiving the same treatment. Since most currently used gels are both flavored and acidulated, salivation is stimulated and swallowing of this excess saliva-fluoride mixture generally occurs during gel application. The amount ingested by a young child may be increased if the child is unable to use a saliva ejector effectively.

This potential for toxicity would be diminished if the fluoride concentration of the currently used 1.23% APF gels could be reduced without compromising clinical effectiveness. Due to differences in conditions under which clinical studies are conducted, the clinical effect of variations in fluoride concentration cannot be determined by comparing the results obtained in independent trials. As a result, the lowest fluoride concentration that achieves optimum clinical effectiveness when applied twice annually has not been established.

Evidence exists, however, to support the idea that a lower concentration than the current standard 1.23% APF gel may be effective. All the current theories of mechanism of action of topical fluorides including remineralization, reduction of enamel solubility and antibacterial action, propose that lower concentrations of fluoride would suffice for these effects.⁹⁻¹² Fluoride gels of different concentrations ranging from 0.25 to 1.25% F- have been tested in the rat model and all were found to be significantly effective in inhibiting caries.¹³ In a previously reported clinical trial

in which a high-release 1.23% fluoride solution was compared with a gel that released only half as much fluoride, both agents were found to be equally effective in reducing caries when the agents were applied twice annually.³ However, the vehicles were not the same and that variable may have been a factor.

Although such supporting evidence exists, no clinical trials directly comparing the caries reducing effects of twice-annual, professionally applied topical gels of varying fluoride concentrations have been reported. This controlled clinical trial was designed to compare directly the caries-preventive effects of an APF topical gel containing the standard 1.23% F- with those of a gel containing a reduced fluoride concentration (0.6% F-) when the agents were applied twice annually in a child population.

Methods and Materials

The initial study sample consisted of 428 seventh grade students in nonfluoridated (< 0.2 ppm F-) areas of Guilford County, North Carolina. Students undergoing fixed orthodontic appliance therapy were excluded from the study since the presence of banded appliances would not allow adequate examination and would interfere with the direct contact between enamel and fluoride. Students who returned a permission slip were assigned randomly to 1 of 3 groups of equal size: those to be treated with a 1.23% APF gel (Group A); those to be treated with a 0.6% APF gel (Group B); and those to receive a placebo gel containing no fluoride (Group C).

At the beginning of the study in March, 1981, each child received a dental prophylaxis, a dental examination, and an application of his assigned gel. These procedures were repeated every 6 months (± 3 weeks) for 2 years. To obtain subject demographic data and ascertain the extent of the child's dental care and past fluoride exposure, a questionnaire was mailed to the parents of each participant.

Prior to examination and gel application, each subject's teeth were stained with a disclosing solution.^a The stained plaque was removed with a soft bristle brush^b and unwaxed dental floss^b by dental hygiene students or dental assistants who were familiar with the study protocol. No prophylaxis paste or dentifrice was used in the prophylaxis procedure.

A single examiner (PH) performed all dental examinations. Portable dental chairs and lights were set up in the schools for the procedures. The teeth were dried with compressed air prior to the examinations. Front surface mirrors and sharp #23 explorers were

used to perform the visual and tactile examinations. Radiographs were not taken. The DMFS index was used as the measurement of caries experience. The examiner adhered to the DMFS criteria set forth by the Caries Measurement Task Group¹⁴ as modified by the NIDR for the National Dental Caries Prevalence Survey.¹⁵ Only erupted, permanent teeth were included in the study. Third molars were excluded from the data.

The data for each child were recorded by trained individuals on separate forms designed for ease of recording as well as for facilitating subsequent data entry into a computer. Results from prior examinations were not available to the examiner during the course of the study. All data were edited before, during, and after entry into the computer by means of logical checks by a dentist (PH). The edited data then were processed using a Statistical Analysis System (SAS) package.¹⁶

Following plaque removal and examination, the subjects received a 4-min topical application of their assigned gel. Approximately 2.5 ml of the appropriate gel was placed into the trough of disposable styrofoam trays^c by trained dental personnel. The study followed the classic double-blind protocol in that the examiner, subjects, and dental auxiliaries were unaware of which agent was applied in each subject. All gels were packaged in plain containers labeled only with an identifying code letter. The code was broken only after data collection was completed. Group A received an application of a 1.23% F- APF thixotropic gel;^d Group B received an application of a 0.6% F- APF thixotropic gel;^d and Group C received an application of a placebo thixotropic gel.^d To minimize potential bias, the placebo gel was similar to the fluoride gels in color, odor, and physical appearance but contained no fluoride or acid. Prior to placing the fluoride trays firmly onto the dental arches, the teeth were dried with compressed air or cotton gauze. A saliva ejector was placed sublingually to remove excess saliva and fluoride. Participants were allowed to expectorate into a disposable bowl after the trays were removed and each child then was instructed not to eat or drink for 30 min. Students were observed for at least 15 min following gel applications for any signs of acute toxicity such as nausea or vomiting.

The data collected were evaluated statistically to determine the significance of DMFS increment dif-

^c Centrays — Pacemaker Corp: (Coopercare, Inc).

^d All gels were manufactured for this study by Pacemaker Corp: (Coopercare, Inc). The manufacturer of the gels used in this study had no regulatory or administrative role in the planning or implementation of the study or in the analysis of results. After receipt from the manufacturer, fluoride release from the gels was measured according to the flow dialysis method of Congleton et al.¹⁷

^a Trace Dental Disclosing Solution — Lorvic Corp: St. Louis, MO.

^b Oral B 40 Toothbrushes and Oral B Unwaxed Dental Floss — Coopercare, Inc: Fairfield, NJ.

ferences using analysis of variance (ANOVA).¹⁸ Differences were regarded as significant at the 95% confidence level. Only data from subjects who finished the 2-year study were included in the data analysis.

Results

Of the 428 subjects who received parental permission to participate and who were initially examined, 316 remained in the study after 24 months. Most of those not reexamined had moved to other locations. Participant attrition rates were not significantly different among groups and ranged from 24 to 26%. The age of the participants at the baseline examination ranged from 11 to 15 years with a mean age of 12.5 for all subjects. Seventy-three per cent of the sample population received regular dental care defined as at least 1 dental visit per year. There were no significant differences ($p > 0.05$) among groups with respect to age, race, sex, regularity of dental care, school location, or previous exposure to fluorides as determined by chi-square tests for homogeneity.

The baseline DMFS scores for the individuals who dropped out of the study were similar across all groups and similar to the baseline DMFS scores based on *t* tests ($p > 0.05$). Table 1 shows the average baseline DMFS score for the 316 students who completed the study. The baseline DMFS score for the 1.23% F- APF group (Group A) was higher than for the other 2 groups, but the difference was not statistically significant according to ANOVA testing ($p = 0.49$).

Table 1 also displays the observed 24-month DMFS increments for the 3 groups. Differences in the observed mean baseline DMFS scores among groups indicated the possible use of analysis of covariance (ANOCOV) with this data when determining the significance of DMFS increment differences.^{18,19} However, since the baseline DMFS scores were not significantly different from each other, ANOVA was deemed appropriate.

Statistical comparisons of DMFS increments using ANOVA showed that after 24 months children who had received the full- or half-strength fluoride treat-

ments (Groups A and B, respectively) twice annually experienced significantly less decay than did children in the control group (Group C). Although the 24-month DMFS increment in Group A (1.23% APF) was smaller than the DMFS increment in Group B (0.6% APF), a significant difference between the two treatment groups could not be detected ($p = 0.66$).

The 95% confidence interval shown in Table 1 indicates the range of likely percentage caries reduction outcomes if the investigation were to be repeated.²⁰ The width of the confidence interval denotes the level of precision achieved by the study design.²¹ The wider the confidence interval, the less precise the study in those areas of analysis.

Figure 1 is a graphic display of observed mean, cumulative 6-month DMFS increments for the 3 groups. The 2 fluoride-treated groups (Groups A and B) had smaller cumulative DMFS increments than the control group at each examination, with the greatest difference occurring between the 18- and 24-month examinations.

To determine whether the protection conferred by the fluoride gels varied by type of surface, the overall mean DMFS increment for each group after 24 months was separated into its pit and fissure and smooth surface components as shown in Table 2. Occlusal surfaces of molars and premolars, lingual surfaces of maxillary molars, and buccal surfaces of mandibular molars were considered pit and fissure surfaces. All other surfaces were designated as smooth surfaces.

After 2 years, both fluoride groups had smaller DMF increments for both surface types when compared to the control. In comparing percentage differences with the control, both fluoride gels appeared to be more effective on smooth surfaces. However, when actual net DMFS increments according to surface type are compared, it is apparent that more pit and fissure surfaces were protected from decay than smooth surfaces in both treatment groups. It is clear that in all 3 groups, pit and fissure surfaces accounted for the majority of the DMFS baseline and 24-month increment scores.

Figure 2 demonstrates a tendency for the higher concentration fluoride gel (A = 1.23% F- APF) to be

TABLE 1. Mean DMFS Baseline and 24-Month Increment Scores for Control Group (Group C) and the Fluoride-Treated Groups

| Group | N | Baseline DMFS (SEM) | 24-Month DMFS Increment SEM | p-Value ANOVA for 24-Month Increment | % DMFS Reduction | 95% Confidence Interval for Percentage Reduction |
|-------|-----|---------------------|-----------------------------|--------------------------------------|------------------|--|
| A | 108 | 5.05 (0.47) | 3.08 (0.37) | 0.015 | 30 | 10.4 to 49.6 |
| B | 105 | 4.41 (0.43) | 3.31 (0.38) | 0.046 | 25 | 3.6 to 46.4 |
| C | 103 | 4.41 (0.48) | 4.40 (0.38) | ----- | -- | ----- |

Group A = 1.23% F; Group B = 0.6% F.

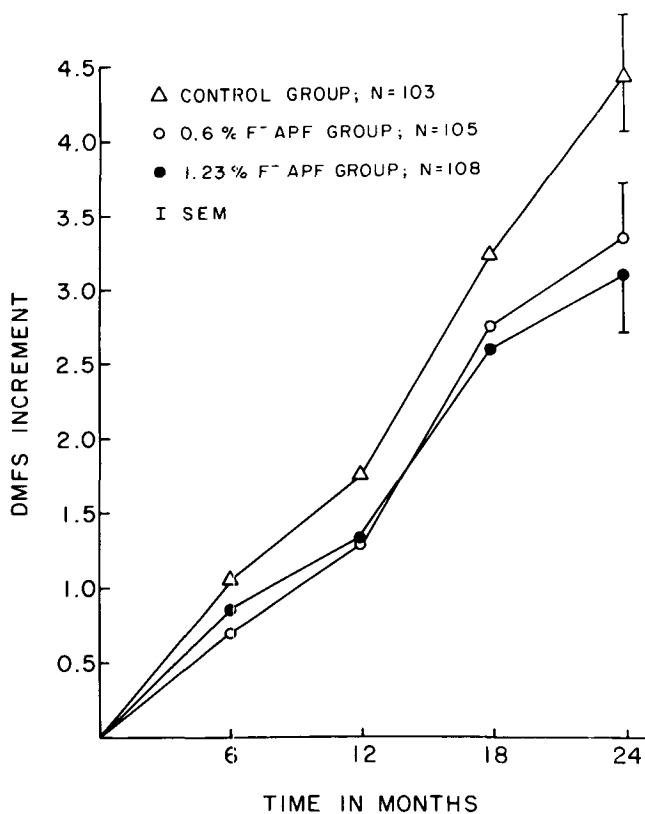


Fig 1. Cumulative DMFS increments for control group, 1.23% F- APF-treated group and 0.6% F- APF-treated group.

more effective on pit and fissure surfaces than the lower concentration gel (B = 0.6% F- APF). On smooth surfaces, however, this was not the case. The total difference in effectiveness between the 2 fluoride gels occurred mostly in the pit and fissure lesions. A statistically significant reduction in pit and fissure caries occurred in the full-strength fluoride group ($p = 0.01$),

but not in the half-strength group when compared to the controls (Table 2). However, this represents only a trend and not a conclusive result since neither fluoride gel performed significantly superior to the other on either surface type according to ANOVA testing.

Although more than 1000 applications of fluoride-containing gel were conducted during the course of this study, only 3 episodes of nausea or vomiting occurred within the 15 min subsequent to gel application. All 3 episodes occurred in participants in Group A (1.23% F-). None of the 3 individuals reported having symptoms prior to gel application.

Fluoride release from both fluoride-containing thixotropic gels as measured by continuous flow dialysis with subsequent measurement by fluoride ion electrode showed that the 0.6% F- APF gel released half as much fluoride ion as did the 1.23% F- APF gel in the first 5 min. The placebo gel released only a negligible level of fluoride ion.

As a measure of examiner reliability, the frequency of diagnostic reversals was determined. A diagnostic reversal was defined as a tooth which was diagnosed as carious on the baseline examination and as sound on the 24-month examination. After the frequency of reversals was determined, a reversal rate for the examiner was calculated.²² In all groups the proportion of teeth reversing from decayed to sound to those that potentially could have reversed (decayed-to-sound plus decayed-to-decayed) was less than 0.002%. Due to the low reversal rate, actual differences in incremental caries scores between control and test groups were affected insignificantly.

Discussion

The results of this study show that after 2 years both the full- and half-strength fluoride regimens were

TABLE 2. Mean DMFS Baseline and 24-Month Increment Scores by Surface Type According to Group

| Group | Smooth Surfaces | | | ANOVA p-Value | % DMF Smooth Surface Reduction | 95% Confidence Interval for Percentage Reduction |
|-----------|---|---|------|---------------|--------------------------------|--|
| | Baseline DMF Smooth Surfaces (SEM) | 24-Month DMF Smooth Surface Increment (SEM) | | | | |
| A (N=108) | 0.62 (0.14) | 0.72 (0.17) | 0.20 | 30.1 | -13 to 73 | |
| B (N=105) | 0.50 (0.13) | 0.55 (0.17) | 0.06 | 46.7 | 13.4 to 80 | |
| C (N=103) | 0.60 (0.18) | 1.03 (0.17) | --- | --- | ----- | |
| Group | Pit and Fissure Surfaces | | | ANOVA p-Value | % DMF P & F Surface Reduction | 95% Confidence Interval for Percentage Reduction |
| | Baseline DMF Pit & Fissure Surfaces (SEM) | 24-Month DMF P & F Surfaces Increment (SEM) | | | | |
| A | 4.43 (0.40) | 2.37 (0.27) | 0.01 | 29.7 | 2.3 to 47.7 | |
| B | 3.90 (0.36) | 2.76 (0.28) | 0.13 | 18.1 | -3.56 to 39.56 | |
| C | 3.81 (0.38) | 3.37 (0.28) | --- | --- | ----- | |

Group A = 1.23% APF; Group B = 0.67% APF; Group C = Control.

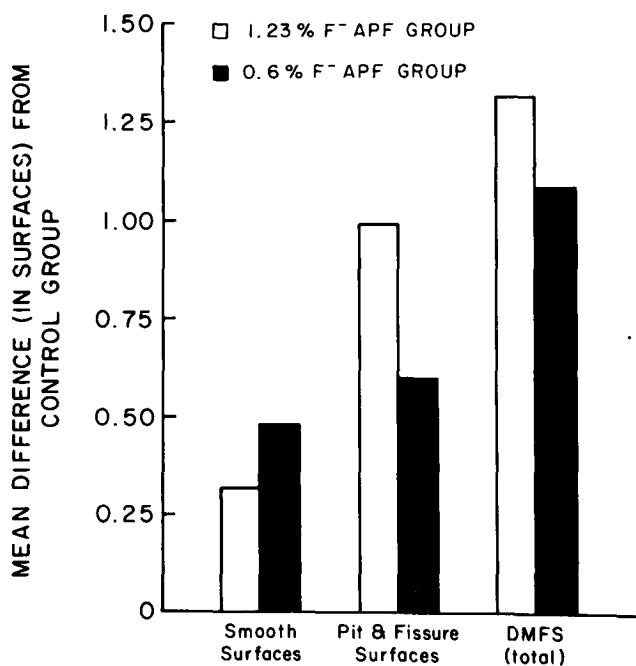


FIG 2. Mean differences in net DMF surface increments of the fluoride-treated groups (Group A = 1.23% F⁻ APF; Group B = 0.6% F⁻ APF) from the control group (Group C) after 2 years.

effective in controlling decay, and neither regimen was significantly superior to the other. The difference between the full- and half-strength groups was only 0.23 DMF surfaces over the 2-year period. Thus, it is doubtful whether the overall benefits to Group A (full strength) can be considered to be significantly greater on a clinical level than the benefits to Group B (half strength) in this study. Despite the unimpressive size of the overall difference between the 2 fluoride groups, certain study limitations and tendencies in the data should be discussed before conclusions are drawn.

First, 73% of the subjects in the study reported that they were receiving regular dental care. An undefined number of these subjects received regular full-strength (1.23% F⁻) fluoride applications from their dentists, thus substantially contaminating the half-strength (Group B) and control (Group C) groups. This well may have resulted in reduced caries increments in these 2 groups and minimized the difference between them and the full-strength group (Group A.) The true effect of such contamination, however, cannot be defined clearly in this study.

Second, when the caries-inhibiting benefits of the fluoride gels were evaluated by surface type, an interesting tendency emerged. After 2 years, the full-strength fluoride gel showed a tendency to be more effective on pit and fissure surfaces than the half-strength gel. It is interesting that although the 2 fluo-

ride gels were not significantly different from each other in their effectiveness on pit and fissure surfaces, the full-strength fluoride group experienced a significantly lower caries increment on these surfaces than the control, but the half-strength fluoride group did not (Table 2).

Laboratory studies concerning topical fluoride's effect on sound and carious enamel always have been performed on smooth surfaces. Thus, much of the rationale for attempting to reduce fluoride concentration without loss of effectiveness is based on smooth surface data. It is obvious that there are differences in the nature of the caries process between smooth and pit and fissure surfaces, and perhaps caries inhibition on the different surface types requires different fluoride concentrations for optimum effectiveness. It would seem reasonable to expect that a higher concentration of fluoride would produce a higher diffusion gradient which would favor penetration of fluoride ion through the distances involved in the pits and fissures to reach the caries-active site. In the case of smooth surface caries, the diffusion distances normally would be much less. In fact, laboratory studies on smooth surface enamel indicate that fluoride uptake in sound enamel is nearly the same for the 2 fluoride concentrations used in this study.¹¹ In vitro studies on incipient smooth surface carious lesions suggest that a low concentration of fluoride ion is as effective as a high concentration in remineralizing such lesions.¹⁰ Similar studies have not been done on pit and fissure surfaces.

Thus, from a mechanistic point of view, it seems logical that the higher concentration of fluoride applied twice a year may be more effective in preventing pit and fissure caries than a lower concentration of gel due to the distances the fluoride must travel to contact the enamel in the tortuous pits and fissures. On smooth surfaces, however, the higher concentration gel would not seem to have a theoretical advantage and the results of this study support that hypothesis. If the majority of carious lesions in school children continues to occur on pit and fissure surfaces as a national trend, the effect of any caries inhibiting agent on these surfaces will become increasingly more important.

In a previously reported study that explored the effectiveness of 1.23% APF topicals,¹ results revealed that effectiveness against pit and fissure caries increased in the third year. Perhaps if the present study had run longer, a true difference between the full- and half-strength fluoride's effect on pit and fissure surfaces would have emerged.

Because of these considerations, one should not conclude on the basis of this study that a 0.6% F⁻ APF gel is as effective in reducing caries on all sur-

faces as a 1.23% F- APF gel when they are applied twice annually. This is particularly true with respect to the prevention of pit and fissure caries. Additional studies need to be conducted to better define the effects of fluoride concentrations in such systems.

The small sample size of this study allowed inclusion of only 1 reduced fluoride concentration test group. A larger sample would allow several fluoride concentrations to be tested on a head-to-head basis to aid in establishing the lowest concentration in twice-annual topicals that would still provide optimum clinical effectiveness. Care should be taken in such future studies to evaluate the effects of fluoride concentration by tooth surface type. The information gained from additional studies would be important from the mechanistic as well as the clinical standpoint.

To summarize, the results of this clinical trial indicate that a significant degree of caries prevention can be obtained using the 0.6% F- agent twice a year, aside from the possibility that it is not as effective as the 1.23% F- gel on pit and fissure surfaces. In cases where potential toxicity is of particular concern, one may choose to use a 0.6% F- agent and substantially reduce the exposure to fluoride ingestion while knowing that some effectiveness in caries prevention may be sacrificed.

Conclusions

Both the full- (1.23% F- APF) and half-strength (0.6% F- APF) gels were effective in reducing the caries increment in our sample of adolescents. There were indications that the full-strength agent is more effective in reducing pit and fissure caries.

In selected cases where acute fluoride toxicity and exposure to high levels of fluoride are of special concern, the reduced strength concentration gel (0.6% F- APF) can be used and may be expected to impart a significant caries-reducing effect.

Additional clinical studies evaluating several different fluoride concentrations should be conducted giving special attention to the evaluation of treatment effects by surface type before widespread changes in professionally applied topical fluoride formulations are made.

This study was supported in part by PHS grant RR05333.

The authors acknowledge Ms. Georgeann Dunko-Nine for manuscript preparation, Ms. Virginia Swecker for illustrations, and Thomas G. Deaton for laboratory analysis of the fluoride content of the gels. The authors also thank the dental hygiene students from Guilford Technical Institute and the dental assistants and dental hygiene students from UNC School of Dentistry for their assistance in this project. The authors express our appreciation to Ms. Diane Ramsey and Mr. Ed Stanek in the computer organization and statistical analysis of the data. The authors acknowledge

the Division of Dental Health of North Carolina for providing the dental equipment used in this project. The authors also thank Coopercare for supplying the fluoride and placebo gels, tooth-brushes, and floss. Finally, the authors thank the students and faculty at Northeast, Northwest and Southeast Junior High Schools for their participation in this project.

Dr. Hagan is an assistant professor, pediatric dentistry, School of Dentistry, West Virginia University, Morgantown, West Virginia 26506-6305. Dr. Rozier is an associate professor, health policy and administration, School of Public Health; and Dr. Bawden is Alumni Distinguished Professor, pediatric dentistry, The University of North Carolina at Chapel Hill. Reprint requests should be sent to Dr. Hagan.

1. Horowitz HS, Doyle J: The effect on dental caries of topically applied acidulated phosphate-fluoride: results after three years. *JADA* 82:359-65, 1971.
2. Ingraham RQ, Williams JE: An evaluation of the utility of application and cariostatic effectiveness of phosphate fluorides in solution and gel states. *J Tenn State Dent Assoc* 50:5-12, 1970.
3. Cobb HB, Rozier RG, Bawden JW: A clinical study of the caries-preventive effects of an APF solution and an APF thixotropic gel. *Pediatr Dent* 2:263-66, 1980.
4. LeCompte EJ, Doyle TE: Oral fluoride retention following various topical application techniques in children. *J Dent Res* 61:236, 1982.
5. Owen D, Morris M, Adir J, Bakker V: Monitoring ingestion and urinary excretion of topical fluoride. *IADR Program and Abstracts*, no. 1256, 1979.
6. Ekstrand J, Koch G: Systemic fluoride absorption following fluoride gel application. *J Dent Res* 59:1067, 1980.
7. Ekstrand J, Koch G, Lindgren LE, Petersson LG: Pharmacokinetics of fluoride gels in children and adults. *Caries Res* 15:213-20, 1981.
8. Van Dyke RA: Fluoride from anesthetics and its consequences, in *Continuing Evaluation of the Use of Fluorides*, Johansen E, Taves DR, Olsen TO, eds. Boulder, Colorado; Westview Press, 1979.
9. Shannon IL, Edmonds EJ: Effect of pH and fluoride concentration on enamel solubility reduction by APF solutions. *Dent Hyg* 52:231-35, 1978.
10. Silverstone LM: Remineralization phenomena. *Caries Res* 11:59-84, 1977.
11. Dijkman AG, Tak J, Arends J: Comparison of fluoride uptake by human enamel from acidulated phosphate fluoride gels with different fluoride concentrations. *Caries Res* 16:197-200, 1982.
12. Messer HH: The anticaries actions of topical fluorides. *Northwest Dent* 57:354-57, 1978.
13. Hefti A: Effect of topical fluoride gel applications on caries incidence in rats. *Caries Res* 16:77-79, 1982.
14. ADA council on Dental Therapeutics: *Proceedings of the Conference on the Clinical Testing of Cariostatic Agents*. Chicago: ADA, 1972.
15. NIDR: *Calibration Manual for the National Dental Caries Prevalence Survey*. National Caries Program. Prepared by NIDR and Westat Staff, 1979.
16. Helwig JT, Council KA, eds: *SAS User's Guide*, 1979 ed. Cary, North Carolina; SAS Institute, Inc, 1979.
17. Congleton JB, Crenshaw MA, Bawden JW: The diffusion of fluoride ion from acidulated phosphate fluoride topical products. *J Dent Child* 45:133-36, 1978.
18. Chilton NW: *Design and Analysis in Dental and oral Re-*

- search, 2nd ed. New York; Praeger Publishing, 1982 pp 223-45.
19. Grainger RM, Lehnhoff RW, Bollmer BW, Zacherl WA: Analysis of covariance in dental caries clinical trials. *J Dent Res* 63:766-71, 1984.
 20. Dubey SD, Lehnhoff RW, Radike AW: A statistical confidence interval for true per cent reduction in caries — incidence studies. *J Dent Res* 44:921-23, 1965.
 21. Horowitz HS: Measurement and expression of treatment effects in caries clinical trials. *J Dent Res* 63:709-12, 1984.
 22. Heifetz SB, Meyers RJ, Kingman A: A comparison of the anticaries effectiveness of daily and weekly rinsing with sodium fluoride solution: final results after three years. *Pediatr Dent* 4:300-303, 1982.
-