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# Influence of Soluble Pyrophosphate on Calculus Formation in Adults

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*The purpose of this double-blind, longitudinal clinical study was to assess the efficacy of a dentifrice containing 3.3% soluble pyrophosphate in inhibiting calculus formation and its effect upon the oral soft tissues. A total of 265 adult volunteers was given a dental prophylaxis. Each was examined for dental calculus and oral soft tissue pathology. The volunteers were then randomly assigned to use either a dentifrice containing soluble pyrophosphate and sodium fluoride or a placebo sodium fluoride formulation for ad libitum home usage. At the two-month completion of the study, 217 subjects were available for re-examination. The results showed that the group using the dentifrice containing soluble pyrophosphate experienced a significant 26% decrease in calculus formation as compared with the placebo group, with both dentifrices being equally well-tolerated by the oral soft tissues.*

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## Introduction.

Dental calculus has been recognized as a clinical entity as far back as the 10th century (Weinberger, 1948). In 1728, Fauchard (Fauchard, 1946) recognized the significance of salivary calcium and phosphate in the formation of dental calculus, characterizing it as "a substance which accumulates on the surface of the teeth, and which becomes when left there, a stony crust of more or less considerable volume."

Many attempts have been made either to prevent the formation of calculus or at least to retard the rate of accumulation of the deposit. Mechanical cleansing with a toothbrush (Villa, 1968) and mechanical scaling through professional intervention (Suomi *et al.*, 1971; Axelsson and Lindhe, 1978; Glavind *et al.*, 1983) have been shown to be effective methods for removing calculus or controlling its formation. In addition, many substances have been incorporated into toothpastes, mouthwashes, chewing gums, lozenges, etc., in an attempt to prevent or retard formation of the deposit. In general, these substances have been selected either because of their ability to decrease the formation of dental plaque or their inhibitory effect upon the subsequent calcification of dental plaque.

Early work by Fleisch and co-workers (Fleisch and Bisaz, 1962; Fleisch *et al.*, 1968) demonstrated that pyrophosphate prevented calcification by interfering with the conversion of amorphous calcium phosphate to hydroxyapatite. Vogel and Amdur (1967) observed lower concentrations of pyrophosphate in the parotid saliva of calculus-formers than was present in non-calculus-formers. It was also found that the concentration of pyrophosphate in the plaque of low-calculus-formers was significantly greater than that of heavy-calculus-formers (Edgar and Jenkins, 1972). These latter observations appear to be due to variations in pyrophosphatase activity in plaque and saliva (Bercy and Vreven, 1979), since this enzyme hydrolyzes calcium pyrophosphate complexes to form calcium phosphate

(Draus *et al.*, 1968). Pyrophosphate has also been shown to reduce the formation of experimental calculus in both the laboratory (Mukherjee, 1968; Draus *et al.*, 1970; Briner and Francis, 1973) and in the rat (Briner and Francis, 1973). However, the use of pyrophosphate troches resulted in only an insignificant decrease in calculus formation on Mylar strips in young adults (Kinoshita and Mühlemann, 1966). The purpose of this clinical study was to evaluate whether a dentifrice containing 3.3% of a mixture of soluble pyrophosphates would reduce the rate of formation of dental calculus.

## Materials and methods.

This study was a double-blind longitudinal comparison of two parallel and balanced groups of subjects provided with either a dentifrice containing 3.3% soluble pyrophosphate and 0.24% sodium fluoride or a placebo 0.24% sodium fluoride formulation containing no pyrophosphate. Approximately 350 panelists were recruited and initially accepted or rejected for use in the study on the basis of a visual examination to determine whether they formed dental calculus and whether they met the following criteria: (1) had a minimum of ten natural teeth present; (2) had at least five of the six mandibular anterior teeth present without crowns, inlays, or large restorations; (3) had no evidence of rampant caries, irreversible periodontal disease, or chronic neglect; (4) were calculus-formers (*e.g.*, would probably have a total Volpe-Manhold [V-M] Calculus Index [Volpe *et al.*, 1965] score of 0.5 or greater following an eight-week pre-test screening period); (5) had no factors in their medical history which could contra-indicate their participation in the program; (6) gave the impression from their oral condition that they exercised a reasonable degree of oral care and would probably utilize the products in the study; and (7) would be available for appointments throughout the duration of the study. Written informed consent was obtained from each participant on a voluntary basis, with the understanding that each could withdraw at any time for any reason.

Each subject was then given a thorough dental prophylaxis, two plain white, coded tubes of a commercially-available NaF dentifrice\*, and a supply of toothbrushes. Baseline examinations were performed after a two-month pre-test period. Using the Volpe-Manhold (V-M) Index (Volpe *et al.*, 1965), two examiners (Drs. J.R. Swancar and M.E. Mallatt) independently examined each participant for the presence of calculus. An oral soft tissue examination (Dr. D.K. Hennon) was also performed. In the Volpe-Manhold procedure, calculus is graded on the lingual surfaces of the six mandibular anterior teeth by means of a periodontal probe calibrated in 1-mm units to measure the extent of the deposit, to the nearest 0.5 mm, in three directions (bisecting the lingual surface, mesio-incisal angle, and disto-incisal angle). Thus, three measurements were made on each of the six designated teeth. The oral soft tissue examination consisted of a visual examination of the oral cavity and peri-oral area by means of a standard light and dental mirror. The structures examined included the gingivae, hard and soft palate, oropharynx, buccal mucosa, tongue, floor of the mouth, labial mucosa, and lips. The site, size, and severity

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of any lesion and tentative diagnosis, if possible, were recorded on an oral stomatology form, and an indication was made as to whether the condition might be related to test product usage. All examinations were performed independently by examiners having prior experience with their assigned procedure. At this appointment, the participants also returned all unused pre-test dentifrice.

At the conclusion of the two-month pre-test period, we identified 265 panelists who met all of the initial entry criteria, and they were initiated into the study. All subjects with a V-M score greater than zero were separated by sex, stratified by V-M score using the data obtained by the more experienced examiner (Dr. J.R. Swancar), and, within strata, the subjects were assigned to dentifrice groups by random permutations of two. Co-habitants were assigned to the same dentifrice. Neither the examiners nor the subjects were aware of the identity of the assigned dentifrices. Each subject then received another thorough dental prophylaxis and a two-month supply of the assigned dentifrice packaged in plain white tubes and labeled with each subject's unique number. The panelists were asked to brush their teeth at least once daily using the assigned dentifrice. After a two-month test period, the subjects were recalled, and the dental examinations were repeated.

The experimental product used in this study contained 3.3% soluble pyrophosphate, provided as a mixture of tetrapotassium pyrophosphate and sodium acid pyrophosphate, plus 0.24% sodium fluoride, and utilized a silica abrasive system. The placebo formulation was essentially identical except for the absence of the pyrophosphates.

After the initial assignment of subjects to dentifrices, the investigator was supplied with a file of sealed, tamper-proof, opaque envelopes which individually contained the name and unique identification number of each subject. Each envelope contained the dentifrice identity for a specific subject. This permitted the investigator to determine the treatment identity for any particular subject during the course of the study, if necessary, without revealing the group identity of the remainder of the subjects. No situation occurred during this study that required any of the envelopes to be opened.

## Results.

For analyzing the dental calculus findings, we used two approaches: First, the conventional mean V-M scores were used. [This involved summing the actual millimeter estimates of the amount (or severity) of calculus on each graded surface.]; second, the data were summarized in terms of the mean number of sites containing calculus, regardless of amount.

Table 1 shows the initial group comparability for those subjects present at the baseline and at the final exam with regard to sex, age, V-M calculus scores, and for sites having calculus as determined by Examiner JRS. Of the 265 subjects initiated

into the study, 217 were available for the final examinations after two months. There were no significant differences between the two groups when considering either the total panel or only those subjects who completed the study. Examiner MEM observed essentially identical results, with no significant inter-group differences.

The results of the two-month calculus examination for Examiner JRS are shown in Table 2. The V-M scores were adjusted with an analysis of covariance (Lehnhoff and Grainger, 1974), using the pre-test period (baseline) scores as the concomitant variable. A one-tailed test of significance was applied to the results. This analysis showed adjusted mean V-M scores of 4.74 for the test dentifrice and 6.40 for the placebo. This difference of 26% is significant at  $p < 0.0001$  (one-tailed). The number of sites with calculus showed mean scores of 5.51 for the test group and 7.40 for the placebo group. This is also a difference of 26% and is significant at  $p < 0.0001$  (one-tailed). Essentially identical results were observed by Examiner MEM, with significant reductions of 26.5 and 21.3% for V-M scores and sites with calculus, respectively.

The results of the soft-tissue examinations showed that there were no differences between the dentifrice groups in the number or types of soft-tissue changes, which indicates that the dentifrices were equally tolerated by the oral soft tissues.

## Discussion.

Calculus has been reported (Everett *et al.*, 1963; Leung, 1956) in approximately 37 to 70% of the individuals studied between the ages of 9 and 18, with the prevalence increasing to involve 86 to 100% after the age of 40 (Kupczak *et al.*, 1969; Littleton, 1963). It is estimated that 90% of all calculus occurs on the mandibular anterior teeth (Mandel, 1967). Although much of this occurs on the lingual aspect of these teeth, it is not unusual to see calculus accumulations wrapping around to the proximal and labial aspects, particularly if teeth are malposed or missing.

In recent years, there have been many substances incorporated into various vehicles (mouthwashes, toothpastes, etc.) for the purpose of preventing or retarding plaque and calculus formation. These substances have been designed either to retard plaque formation (Sturzenberger and Leonard, 1969; Lobene *et al.*, 1969; Loe and Schiott, 1970; Picozzi *et al.*, 1972; Gaffar *et al.*, 1981) or to interfere with the formation of crystalline calcium phosphate (Turesky *et al.*, 1967; Mühlemann *et al.*, 1970; Sturzenberger *et al.*, 1971; Francis *et al.*, 1977; Gaffar *et al.*, 1983) and have exhibited varying degrees of effectiveness.

The present study similarly describes the use of a crystal-growth inhibitor, pyrophosphate, incorporated into a toothpaste, use of which caused a significant decrease in the rate of calculus formation. These findings are consistent with the

TABLE 1  
INITIAL BALANCE FOR SUBJECTS COMPLETING THE INDICATED PORTION OF THE STUDY (EXAMINER JRS)

Test Period	Dentifrice	N	Sex		Age		V-M Score**		Sites With Calculus	
			M	F	Mean	Range	Mean	S.E.*	Mean	S.E.
Initial	Placebo	133	60	73	41.4	21-75	6.90	0.477	7.96	0.376
	Test	132	61	71	42.1	19-75	6.57	0.400	7.81	0.348
2 Months	Placebo	112	52	60	42.1	21-70	7.02	0.546	7.96	0.413
	Test	105	45	60	44.0	19-75	6.40	0.421	7.69	0.363

\*Standard error of the mean.

\*\*V-M Score = calculus measurements using Volpe-Manhold procedure (Volpe *et al.*, 1965).

**TABLE 2**  
COVARIANCE ADJUSTED RESULTS OF CALCULUS  
EXAMINATIONS AFTER TWO MONTHS (EXAMINER JRS)

Test	Dentifrice	N	Adjusted Mean	% Diff	z	Probability
V-M Score	Placebo	112	6.40 (0.34)*	-----	---	-----
	Test	105	4.74 (0.25)	25.9	3.91	<0.0001
Sites With Calculus	Placebo	112	7.40 (0.30)*	-----	---	-----
	Test	105	5.51 (0.27)	25.5	4.72	<0.0001

\*Standard error of the mean.

results of various pre-clinical studies which demonstrated the usefulness of pyrophosphate for calculus prevention (Fleisch and Bisaz, 1962; Fleisch *et al.*, 1968; Vogel and Amdur, 1967; Edgar and Jenkins, 1972; Bercy and Vreven, 1979; Draus *et al.*, 1968; Mukherjee, 1968; Draus *et al.*, 1970; Briner and Francis, 1973) but appear to be in contrast with the findings of Kinoshita and Mühlemann (1966). In the latter study, the use of pyrophosphate troches resulted in a 25.9% decrease in the ash weight of calculus formed on Mylar foils during a seven-day test period; the fact that this difference was not statistically significant was most likely due to the use of only ten subjects. Thus, these collective data indicate that soluble pyrophosphate may be utilized to reduce calculus formation in adults.

It should be noted that no attempt was made in this study to assess the impact of the experimental dentifrice upon gingival health. Although it has been clearly established that dental plaque plays a primary etiological role in the development of gingivitis (Kakehashi and Parakkal, 1982), and calculus is commonly covered with a layer of dental plaque, calculus *per se* is not considered to be a primary etiological factor in the development of gingivitis (Løe, 1983).

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