

Prevention and reversal of dental caries: role of low level fluoride

John D. B. Featherstone

University of California at San Francisco, San Francisco, USA

Featherstone JDB: Prevention and reversal of dental caries: role of low level fluoride. Community Dent Oral Epidemiol 1999; 27: 31–40. © Munksgaard, 1999

Abstract – Dental caries is a bacterially based disease that progresses when acid produced by bacterial action on dietary fermentable carbohydrates diffuses into the tooth and dissolves the mineral, that is, demineralization. Pathological factors including acidogenic bacteria (mutans streptococci and lactobacilli), salivary dysfunction, and dietary carbohydrates are related to caries progression. Protective factors which include salivary calcium, phosphate and proteins, salivary flow, and fluoride in saliva can balance, prevent or reverse dental caries. Fluoride works primarily via topical mechanisms which include (1) inhibition of demineralization at the crystal surfaces inside the tooth, (2) enhancement of remineralization at the crystal surfaces (the resulting remineralized layer is very resistant to acid attack), and (3) inhibition of bacterial enzymes. Fluoride in drinking water and in fluoride-containing products reduces tooth decay via these mechanisms. Low but slightly elevated levels of fluoride in saliva and plaque provided from these sources help prevent and reverse caries by inhibiting demineralization and enhancing remineralization. The level of fluoride incorporated into dental mineral by systemic ingestion is insufficient to play a significant role in caries prevention. The effect of systemically ingested fluoride on caries is minimal. Fluoride “supplements” can be best used as a topical delivery system by sucking or chewing tablets or lozenges prior to ingestion.

Key words: carbonated apatite; dental caries; fluoride; remineralization

John D. B. Featherstone, Department of Restorative Dentistry, Box 0758, University of California at San Francisco, 707 Parnassus Avenue, San Francisco, CA 94143, USA
Tel: +1 415 476 0456
Fax: +1 415 476 0858
E-mail: jdxbf@itsa.ucsf.edu

Accepted without peer review 9 November 1998

Although the prevalence of dental caries has declined markedly over the last 20 years in most countries in the western world the disease is still a major problem for both adults and children. The change in the mean decayed, missing and filled surfaces in permanent teeth (DMFS) is illustrated in Table 1A by results from four surveys carried out in the United States (1–4). Standard errors corresponding to Table 1A show no difference between the last two columns. The DMFS means are grouped for ages 5–11 years and 12–17 years. The reduction in decay since the early 1970s is clear. Further, the percentage caries-free children rose during the same period (Table 1A). The 1986–87 result that over 50% of children (over 5–17 years of age) in the United States were caries free was widely publicized to indicate the caries problem was essentially solved. This statement is unfortunately far from reality. Although approximately 50% were caries free on average for the overall age range (5–17 years), it can readily be seen that approximately

70% of the 12–17-year-olds still had caries. This continues to be borne out by the latest NHANES III survey (1). Further, when the latest available data (1) are examined by individual ages, 51% of 12-year-olds were caries free but only 21% of the 17-year-old group were in this category. Approximately 25% of children and adolescents in the 5–17 age range accounted for 80% of the caries experienced in the permanent teeth. By age 17, however, 40% of the population accounted for 80% of the caries. Approximately 10% of the 5–17-year age range had 5–9 DMFT (decayed, missing or filled permanent teeth). Recent smaller epidemiologic studies indicate, however, that the decline in caries has not continued during the 1990s and that it may have leveled out (5). These data clearly show that caries continues to be a major problem, that it increases markedly in the teenage years and that we need an improved approach to prevention and therapy.

Dental caries in adults also continues to be a

Table 1A. Mean DMFS and percentage of children caries free (permanent teeth) in four national surveys in the USA (1–4)

Age range (years)		NCHS 1971–74	NIDR 1979–80	NIDR 1986–87	NHANES III 1988–91
5–11 years	Mean DMFS	3.0	2.0	1.2	0.9
5–11 years	% caries free	44	58	70	74
12–17 years	Mean DMFS	10.4	6.8	4.7	4.4
12–17 years	% caries free	10	17	27	33

Table 1B. Mean DFS (decayed and filled surfaces), mean DMFS (decayed, missing and filled surfaces) in dentate US adults, 1988–91 (6), and mean number of permanent teeth for dentate adults (75)

Age range (years)	18–24	25–34	35–44	45–54	55–64	65–74	75+
Mean DFS	9.9	16.5	23.3	29.4	29.2	30.8	25.1
Mean DMFS	11.5	23.6	39.5	57.7	69.5	73.1	80.9
Mean # teeth	27.1	26.0	24.3	21.8	19.3	18.9	16.0

major problem as illustrated by a recent survey in the United States (6). The recently published NHANES III study (6) included the US adult oral health status over all age ranges. Table 1B shows the trend for marked increase in caries experience with age. The 18–24-, and to a lesser extent 25–34-, year age groups had the benefit of caries-reducing influences such as fluoride toothpaste during their teenage years (Table 1A), but they still demonstrated substantial levels of decay. Further, 93.8% of dentate adults (all ages, 18–74+) had evidence of treated or untreated coronal caries. Caries obviously continues to be a major problem in the adult population.

The reasons for the reported reductions in decay during the last 20 years illustrated in Table 1A are difficult to determine precisely, but there is good evidence that the almost universal use of fluoride products such as dentifrice (toothpaste), fluoride mouthrinses, and fluoride topicals in the dental office has been a major contributor (7, 8). Earlier reductions in dental caries of 40%–70% had resulted from the fluoridation of public water supplies in many communities (9–12).

Until recently the major caries-inhibitory effect of fluoride was thought to be due to its incorporation in tooth mineral during the development of the tooth prior to eruption. This supposed mechanism of action was behind public health efforts and individual caries-preventive regimens such as the use of fluoride supplements prescribed for children to “strengthen” the teeth during their development. There is now overwhelming evidence that the primary caries-preventive mechanisms of action of fluoride are post eruptive through “topical” effects for both children and adults, including (a) inhibi-

tion of demineralization, (b) enhancement of remineralization, and (c) inhibition of bacterial activity in the plaque (13–19). The purpose of the present paper is to review the mechanisms of action of fluoride with specific reference to the effect of low levels of fluoride in the fluids in the mouth and to relate this information to the use or misuse of the so-called “fluoride supplements”.

The caries process

The basic process of dental decay is simple in concept, as first described over 100 years ago. The teeth are covered by bacteria which constitute the dental plaque (20, 21). Certain of the bacteria in dental plaque, such as the mutans streptococci (which includes *Streptococcus mutans* and *S. sobrinus*) and lactobacilli are acidogenic. That is, they produce acids when they metabolize fermentable carbohydrates (12, 20, 21). These acids, such as lactic, acetic, propionic and formic acid, can dissolve the calcium phosphate mineral of the tooth enamel or dentin (22–34). If this process is not halted or reversed, the carious lesion progresses, eventually leading to a cavity. Any fermentable carbohydrate such as glucose, sucrose, fructose, or cooked starch, can be metabolized by these bacteria with the evolution of organic acids (e.g., acetic, lactic, propionic) as by-products (25). The acids diffuse through the plaque and into the porous enamel (or dentin if exposed), dissociating to produce hydrogen ions as they travel (23, 26). The hydrogen ions readily dissolve the mineral, freeing calcium and phosphate into solution, which can diffuse out of the tooth. This is demineralization, or loss of mineral as illustrated in Fig. 1.

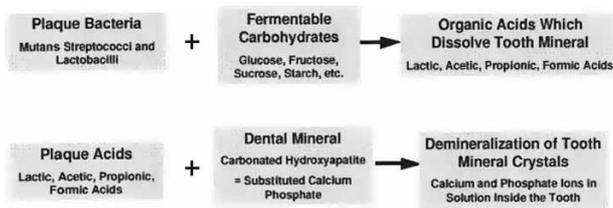


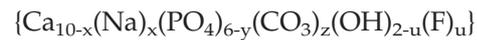
Fig 1. Schematic representation of acid production by plaque bacteria, followed by demineralization of tooth mineral.

Dental caries of the enamel is first observed clinically as a so-called “white spot lesion”. This is a small area of sub-surface demineralization, beneath the dental plaque. The lesion appears white because the loss of mineral changes the refractive index compared with that of the surrounding translucent enamel. The body of the sub-surface lesion may have lost as much as 50% of its original mineral and often has an “apparently intact surface layer” over it (27). The surface layer forms by remineralization (redeposition of mineral) as the calcium and phosphate ions diffuse or travel out of the tooth into the overlying plaque fluid (the fluid between the bacteria in the plaque). The process of demineralization continues each time carbohydrate is taken into the mouth and metabolized by the bacteria. The saliva (see below) plays numerous roles including buffering (neutralizing) the acid and providing minerals that can replace those dissolved from the tooth during a demineralization challenge. This replacement of mineral is called remineralization as described further below (17, 18, 22).

The nature of tooth mineral

The enamel and dentin of a tooth are composed of millions of tiny mineral crystals embedded in a protein/lipid matrix. This combination of inorganic and organic components provides two complementary hard tissues with sufficient hardness and strength to perform the normal functions of teeth. Hydroxyapatite does not occur during the formation of tooth mineral. Instead, the mineral of

enamel, dentin and bone is best described as a highly substituted carbonated apatite (28–30). The mineral is related to hydroxyapatite $\{Ca_{10}(PO_4)_6(OH)_2\}$, but is much more soluble in acid, is calcium deficient (calcium replaced by sodium, magnesium, zinc, etc.) and contains between 3% and 6% carbonate by weight, mostly replacing phosphate ions in the crystal lattice (28–35) (Table 2). Enamel, dentin and bone mineral can be approximately represented by the simplified formula:



The substitutions in the hydroxyapatite crystal lattice (the arrangement of atoms and ions in the crystal) occur as the mineral is first laid down during tooth development, with the carbonate $\{CO_3\}$ ion in particular causing major disturbances in the regular array of ions in the crystal lattice (36, 37). During demineralization the carbonate is preferentially lost and during remineralization it is excluded. The calcium-deficient and carbonate-rich regions of the crystal are especially susceptible to attack by the acid hydrogen ions during demineralization as has been shown by several investigators. High resolution lattice imaging, which images crystals almost to atomic resolution (viewed at about 2 000 000× magnification), was used to illustrate the appearance of hexagonal holes in the early stages of enamel crystal dissolution in dental caries, which coincided with the calcium-deficient and carbonate-substituted regions of the crystal (36–39).

If the OH^- ion in pure hydroxyapatite is completely replaced by a fluoride ion (F^-) the resulting mineral is fluorapatite $\{Ca_{10}(PO_4)_6F_2\}$ which is very resistant to dissolution by acid. The solubility differential is shown schematically in Fig. 2.

In summary, dental mineral is readily dissolved by acid unless it can be protected in some way as described below. Remineralized enamel mineral has a composition more resembling a blend of hydroxyapatite and fluorapatite and is therefore much less soluble than the original mineral.

The crystals of enamel are about 40 nm in dia-

Table 2. Approximate composition of enamel and dentin by % weight and by % volume

Tissue component	Enamel		Dentin	
	% by weight	% by volume	% by weight	% by volume
Mineral=carbonated hydroxyapatite	96	85	70	47
Protein/lipid	1	3	20	33
Water	3	12	10	20

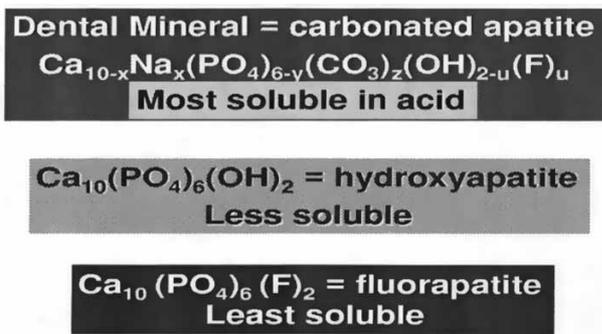


Fig. 2. Schematic representation of the acid solubility ranking of dentally relevant minerals (18).

meter (about 1/1000 of a hair's breadth), are approximately perpendicular to the tooth surface, and are clustered into enamel rods about 4–5 μm in diameter (40). The tiny gaps or pores between the crystals are filled with protein, lipid and water, and allow the passage of small molecules such as lactic acid and ions such as hydrogen and calcium. Mature enamel contains about 1% protein and lipid by weight (3% by volume), and about 12% by volume of water, providing about 15% by volume of diffusible space. Enamel and dentin are best thought of in terms of volume percentage of each component (Table 2) rather than weight percentage, in order to give a much clearer picture of the volume fraction (water and proteins) of the tissue available for diffusion of ions and molecules in and out of the tooth. As demineralization progresses the mineral is removed, making the carious enamel more and more porous (27).

Fluoride mechanisms of action

Fluoride inhibits demineralization when present in solution

Sub-surface sound enamel generally contains fluoride at levels of about 20–100 ppm depending on the fluoride ingestion during tooth development (41). Teeth which develop in a fluoridated drinking water area have a fluoride content toward the higher end of this range. The outer few micrometers of enamel can have F levels of 1000–2000 ppm (41). Several investigators have shown that fluoride in the solution surrounding the carbonated apatite crystals is much more effective at inhibiting demineralization than fluoride incorporated into the crystals at the levels found in enamel (18, 42). Featherstone and co-workers (14, 18, 42, 43) found no measurable reduction in synthetic carbonated apatite (3% CO_3 by weight, comparable to dental

enamel mineral) solubility with about 1000 ppm F incorporated. Very importantly, this means that fluoride incorporated during tooth mineral development at normal levels of 20–100 ppm (even in fluoridated drinking water areas or with the use of fluoride supplements) does not alter the solubility of the mineral. Even at higher levels such as 1000 ppm in the outer few micrometers of enamel there is no measurable benefit against acid induced dissolution. Only when fluoride is concentrated into a new crystal surface during remineralization (see below) is there sufficient to alter solubility beneficially. However, in laboratory experiments as little as 1 ppm in the acid solution reduced the dissolution rate of carbonated apatite to that equivalent to hydroxyapatite (14). Further increases in fluoride in the acid solution in contact with the carbonated apatite mineral surface decreased the solubility rate logarithmically. These results indicate that if fluoride is present in the solution surrounding the crystals it is adsorbed strongly to the surface of carbonated apatite (enamel mineral) crystals acting as a potent protection mechanism against acid dissolution of the crystal surface. So, if fluoride is present in the plaque fluid at the time that the bacteria generate acid it will travel with the acid down into the sub-surface of the tooth, adsorb to the crystal surface and protect it against being dissolved.

Fluoride present in solution at low levels amongst the enamel crystals can markedly inhibit dissolution of tooth mineral by acid (14, 18). This fluoride comes from “topical” sources such as drinking water, and fluoride products, as described below. The fluoride incorporated developmentally into the normal tooth mineral is insufficient to have a measurable effect on acid solubility (18, 44).

Fluoride enhances remineralization

As the saliva flows over the plaque its buffering components (bicarbonate, phosphate and peptides) neutralize the acid produced by the bacteria and the pH rises back towards neutral (Fig. 3), at least when there is normal salivary function. This slows down and stops the sub-surface dissolution of the mineral.

Further, the saliva is “supersaturated” with calcium and phosphate providing a driving force for mineral to go back into the tooth (18, 45). If the chemistry is right at the partially demineralized crystal surface within the lesion then a new surface grows on the crystal. The partially dissolved crystals act as “nucleators” for remineralization. Fluoride acts to speed up this remineralization process

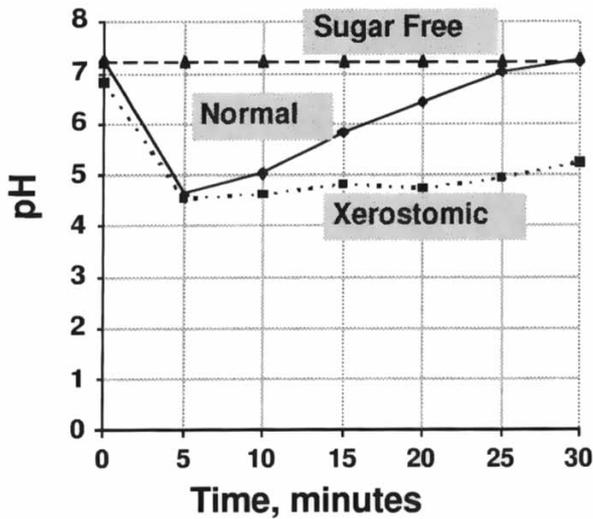


Fig. 3. Typical pH curve in dental plaque (normal) following the ingestion of fermentable carbohydrate, characterized by a fall in pH due to generation of plaque acids and return to neutral due to buffering by salivary components. Typical pH-time curves for a xerostomic subject and a normal subject with a sugar-free test are shown for comparison.

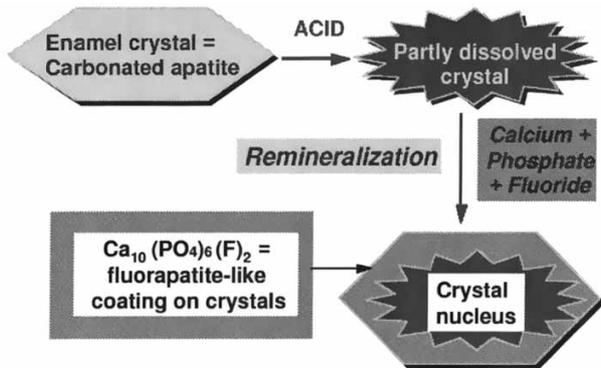


Fig. 4. Schematic representation of the demineralization and remineralization processes which lead to remineralized crystals with surfaces rich in fluoride and of low solubility.

by adsorbing to the surface and attracting calcium ions. The newly formed veneer will preferentially take up fluoride from the solution surrounding the crystals and exclude carbonate (18). Consequently this “veneer” will have a composition somewhere between hydroxyapatite and fluorapatite as illustrated previously (Fig. 2). Fluorapatite contains approximately 30 000 ppm F. The new surface will be “fluorapatite-like” in its properties so that the crystal will now behave like low solubility fluorapatite rather than the high solubility carbonated apatite of the original crystal surface (14). Fluoride speeds up this process, acting to bring calcium and phosphate ions together, and is preferentially in-

cluded in the chemical reaction that takes place, producing a lower solubility end-product. This process is shown schematically in Fig. 4.

In summary, with respect to remineralization, fluoride present in solution from topical sources therefore enhances remineralization by speeding up the growth of a new surface on the partially demineralized sub-surface crystals in the carious lesion. The new crystal surface veneer is fluorapatite-like with much lower solubility than the original carbonated apatite tooth mineral. Subsequent acid challenges must be very strong and prolonged to dissolve the remineralized enamel.

The overall process of demineralization and remineralization can be represented by the solubility diagram in Fig. 5. Each of the curved lines represents the position *vs* pH where enamel mineral (most soluble), hydroxyapatite (HAP) and fluorapatite (FAP) will dissolve as the pH falls (14, 18). The vertical axis represents the amount of combined calcium and phosphate that can be in solution as derived from published solubility products. Since this is a negative logarithm then more calcium and phosphate dissolve as the position moves up the graph. Any set of conditions above each line is supersaturated and may precipitate down to a less soluble mineral form. Anywhere below each line is undersaturated and in this case mineral must dissolve.

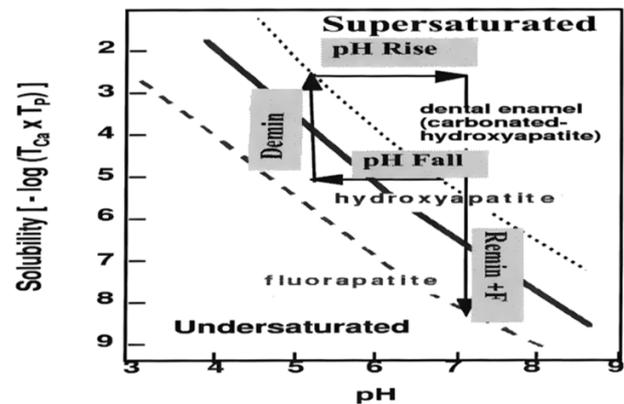


Fig. 5. Solubility isotherms (T_{Ca} and T_P are total calcium and phosphate concentrations in solution, respectively) for enamel (dotted line), hydroxyapatite (solid line=HAP) and fluorapatite (dashed line=FAP) illustrating the log dependent ranking of solubility. The arrows trace initial demineralization starting from the surface of a sound enamel crystal as the pH falls during a caries challenge, and the subsequent remineralization as the pH rises. In the presence of low levels of fluoride (e.g., 0.1 ppm F in this example) a remineralized veneer of fluorapatite-like mineral forms on the original crystal remnants (as illustrated in Fig. 4).

Fluoride inhibits plaque bacteria

Several workers have investigated the possible effects of fluoride on oral bacteria (19, 46, 47). Perhaps the most significant findings in several laboratories are that fluoride cannot cross the cell wall and membrane in its ionized form (F^-), but can rapidly travel through the cell wall and into the cariogenic bacteria in the form of HF (19, 46, 47). HF forms from H^+ and F^- ions as the bacteria produce acids during the metabolism of fermentable carbohydrates. So, as the bacteria produce acid the pH falls (Fig. 3). A portion of the fluoride present in the plaque fluid then combines with hydrogen ions and rapidly diffuses into the cell, effectively drawing more HF from the outside and so on (Fig. 6). Once inside the cell the HF dissociates again, acidifying the cell and releasing fluoride ions which interfere with enzyme (enolase) activity in the bacterium. Under these circumstances fluoride is trapped in the cell and the process becomes cumulative.

In summary, fluoride from topical sources is taken up by the bacteria when they produce acid, thereby inhibiting essential enzyme activity. This is the third "topical" mechanism of action of fluoride against the progression of dental caries.

The role of low levels of fluoride in saliva and plaque fluid

Over 20 years ago Brown and co-workers predicted that low concentrations of fluoride would enhance remineralization (48). Laboratory studies using a pH-cycling model that simulates the demineralization and remineralization aspects of the caries pro-

cess showed that when levels of 0.03 ppm fluoride or higher were incorporated in the mineralizing solution (artificial saliva in the model) remineralization was enhanced (14, 49). This laboratory model was developed to mimic caries progression around orthodontic brackets *in vivo* (49, 50). As the fluoride concentration increased remineralization increased with an optimum being achieved at about 0.08 ppm or above in the calcium phosphate mineralizing solution. Further, the relationship between the logarithm of the fluoride concentration in the mineralizing solutions and the degree of protection afforded against caries-like attack was linear. The clinical implication of this finding is that small increases in the background level of fluoride in saliva and plaque fluid could provide important caries protection via enhancement of remineralization.

Studies have shown that when fluoride products including dentifrice, rinse and gels are used they cause an initial high concentration of fluoride in the saliva and that this falls off with time as the fluoride is cleared from the mouth (51, 52). Very importantly, fluoride can be retained at concentrations in the saliva between 0.03 and 0.1 ppm for 2–6 hours depending on the product and the individual subject (51, 52). In the case of xerostomic subjects, because of very low saliva flow, elevated levels of fluoride are maintained in the mouth for many hours (53). Studies by Zero and co-workers showed that a 0.05% sodium fluoride mouthrinse (225 ppm F) used for 1 min could give elevated fluoride levels in saliva for 2–4 hours and in plaque for much longer times (52). O'Reilly & Featherstone showed that demineralization around orthodontic brackets *in vivo* could be completely eliminated by the combination of a fluoride-containing dentifrice and a 0.05% NaF rinse daily (50), and Meyerowitz and co-workers found the 0.05% NaF rinse very effective in xerostomic subjects (54).

Earlier studies prior to the universal use of fluoride dentifrice reported differences in salivary fluoride concentrations between fluoridated and non-fluoridated communities with values in the range of 0.005–0.01 ppm F. Recent clinical studies (conducted in the late 1980s) which investigated possible caries risk factors in 7–12-year-old children in the United States (55, 56) reported mean baseline fluoride concentrations in saliva of 0.02–0.04 ppm in both fluoridated and non-fluoridated drinking water areas with the fluoride concentration being related to caries status rather than drinking water concentration (56). Subsequent similar studies in the 1990s again reported no differences

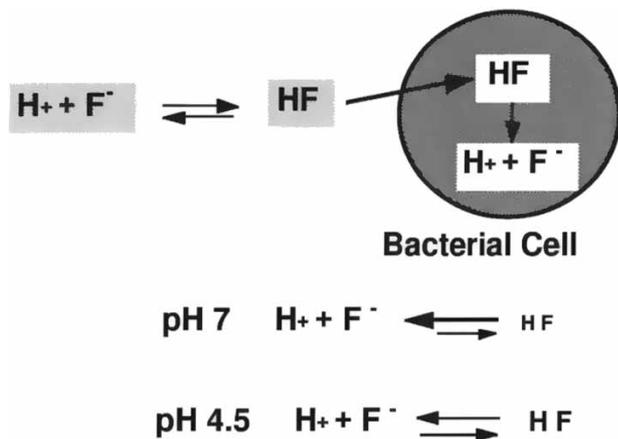


Fig. 6. Schematic representation of fluoride entering a bacterial cell in the form of HF at lower pH values, dissociating, and thereby providing H^+ and F^- ions inside the cell.

between mean salivary fluoride levels in 7–12-year-old children living in fluoridated and non-fluoridated communities, with means about 0.05 ppm F in each (57, 58). In the same study, in which the caries status of the subjects was assessed every 6 months, it was reported that after 2 and 4 years, in this longitudinal caries risk assessment study “children with high individual salivary fluoride (≥ 0.075 ppm) were more frequently caries free ($P < 0.02$)” (57, 58).

The caries balance

Caries progression *vs* reversal is a delicate balance between the factors described above, namely a bacterially generated acid challenge and a combination of demineralization inhibition and reversal by remineralization (59). The balance between pathological factors (bacteria and carbohydrates) and protective factors (saliva, calcium, phosphate, fluoride) is a delicate one which is tipped either way several times daily in most people.

Microbiological components

The importance of mutans streptococci (MS) (which includes *S. mutans* and *S. sobrinus*) in the development of dental caries has been reviewed extensively (12, 20, 21, 60, 61). Numerous cross-sectional studies in humans have shown that there is a strong trend for greater numbers of MS and lactobacilli (LB) in saliva or plaque to be associated with a high level of caries (20, 56, 60, 62–64). Longitudinal studies have shown that an increase over time in numbers of MS and LB is associated with the caries onset and progression (55, 65, 66).

Chemical components

As described above the large decline in caries prevalence in the United States and other western countries over the past 20 years has been attributed in part to the widespread use of fluoride products and fluoride-containing dentifrices in particular (7, 8, 44). Further, there is considerable evidence that the cariostatic effects of fluoride are, in part, related to the sustained presence of low concentrations of ionic fluoride in the oral environment (18, 44). There is also abundant evidence that low concentrations of fluoride decrease the rate of enamel demineralization and enhance the rate of remineralization (14, 18, 44, 67–70). Remineralization of early lesions also requires calcium and phosphate, which are primarily derived from saliva and plaque fluid. Several laboratory studies have indicated that the

driving force for remineralization is the degree of supersaturation of the mineralizing fluid (saliva in the mouth) with respect to fluorapatite, hydroxyapatite, or both (14, 17, 18, 67, 71, 72), and that this is related to the fluoride concentration in the oral fluids.

Caries is best depicted as an ever-changing balance between pathological and protective factors (18, 22, 59), as illustrated in Fig. 7.

Clinical implications – fluoride delivery systems

Fluoride therefore must be considered as one of several protective factors (59). Obviously it is a key one and small adjustments can tip the caries balance illustrated in Fig. 7 one way or the other, leading to caries arrestment, reversal, or progression. The frequent delivery of fluoride to the surfaces of the teeth is a very important factor as described in detail above. The topical effects of fluoride are over-riding, and the systemic incorporation of fluoride in the tooth mineral is unfortunately not of major benefit (18, 44). This means that we must use this information to deal more effectively with caries in both adults and children. It is well established that fluoride in drinking water reduces dental caries, but does not eradicate it. Fluoride in the drinking water provides fluoride at levels in the mouth which can inhibit demineralization and enhance remineralization, and tip the caries balance towards protection, provided the challenge is not too great (Fig. 7). Again, as described above, the concentration of fluoride in dental enamel and dentin provided by fluoridation of drinking water or by natural fluoride levels at about 1 ppm is insufficient to provide protection against caries. The mechanism of action of fluoride in the drinking water is therefore as a topical delivery system. The role of systemically incorporated fluoride is of very limited value.

Fluoride-containing products such as dentifrice,

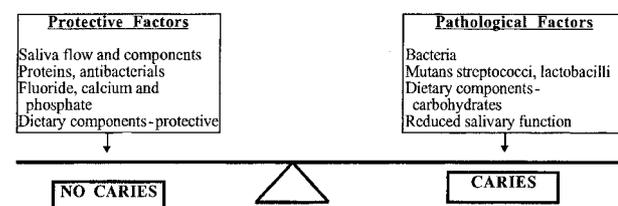


Fig. 7. Schematic diagram of the balance between protective and pathological factors in caries.

mouthrinse and topically applied gels provide caries-preventive benefits via the topical mechanisms described above. The effects are all via the mechanisms of inhibition of demineralization, enhancement of remineralization and action on the bacteria. In the case of high bacterial challenge and/or xerostomia or salivary dysfunction, then even high levels of fluoride therapy may be insufficient to balance the effect of the pathological factors, and caries progresses. In each individual person there will be some level of challenge beyond which fluoride is insufficient to swing the balance. Fluoride products used frequently can maintain salivary fluoride levels in excess of 0.03 ppm, thereby providing marked caries protection. The biggest problem with the home-use products of course is the need for patient compliance on a daily basis.

Fluoride “supplements” and caries prevention

For all the reasons described above the so-called fluoride supplements (tablets, lozenges and drops) should not be thought of as providing a dietary supplement that will automatically protect against caries by providing added benefit but rather as a supplement to “inadequate water content of fluoride”. This is not the case. To be effective against caries fluoride “supplements” should be thought of as a means to supplement the topical mechanisms of fluoride action and not the (minimal) systemic action of fluoride. This was illustrated very clearly by Stephen and co-workers (73) who provided fluoride tablets to children in Scotland to either swallow or hold in the mouth (sucking or chewing). The groups that dissolved the fluoride in the mouth and thereby “applied” fluoride topically had dramatic caries reductions (approximately 80%) in comparison to the tablet swallows. If used, then fluoride supplements should be prescribed with instructions to chew or suck in order to provide a caries-protective benefit.

It has been suggested that when fluoride tablets are swallowed, the fluoride returned via the plasma to the saliva may be sufficient to provide a “topical” benefit. Examination of work by Ekstrand and co-workers (74) shows that after ingestion of a fluoride tablet only a transient elevation of fluoride in the plasma occurs and that the levels which appear in saliva as a result of a once a day fluoride tablet ingestion are unlikely to have much, if any, topical benefit. This further illustrates the need to use fluoride supplements directly as a fluoride

topical delivery mechanism if they are to be effective.

Summary and conclusions

(1) The anti-caries effects of fluoride are primarily topical for children and for adults.

(2) The mechanisms of action of fluoride are (i) inhibition of demineralization at the crystal surfaces, (ii) enhancement of remineralization at the crystal surfaces, and (iii) inhibition of bacterial activity.

(3) The systemic benefits of fluoride are minimal.

(4) Therapeutic levels of fluoride can be achieved from drinking water and topically applied fluoride products.

(5) If used, fluoride “supplements” should be employed as a “topical” delivery system by chewing or sucking tablets or lozenges for the maximum possible time before swallowing.

References

1. Kaste LM, Selwitz RH, Oldakowski RJ, Brunelle JA, Winn DM, Brown LJ. Coronal caries in the primary and permanent dentition of children and adolescents 1–17 years of age: United States, 1988–1991. *J Dent Res* 1996;75:631–41.
2. National Center for Health Statistics. Vital and health statistics. Series 11. No. 144. Vol. DHEW Pub. No. HRA 75–1626. Washington (DC): Government Printing Office; 1974.
3. NIDR. The prevalence of dental caries in United States children: The National Dental Caries Prevalence Survey: 1979–80. NIH Publication No. 82–3245. National Institutes of Health; 1981.
4. Brunelle JA. Oral health of United States children: The National Survey of Dental caries in US School Children: 1986–87. Vol. NIH Pub. No. 89–2247. National Institute of Dental Research; 1989.
5. Speechley M, Johnston DW. Some evidence from Ontario, Canada, of a reversal in the caries decline. *Caries Res* 1996;30:423–7.
6. Winn DM, Brunelle JA, Selwitz RH, Kaste LM, Oldakowski RJ, Kingman A, et al. Coronal and root caries in the dentition of adults in the United States, 1988–1991. *J Dent Res* 1996;75:642–51.
7. Jenkins GN. Recent changes in dental caries. *Br Med J* 1985;291:1297–8.
8. Hargreaves JA, Thomson GW, Wagg BJ. Changes in caries prevalence in Isle of Lewis children between 1971 and 1981. *Caries Res* 1983;17:554–9.
9. Burt BA, Fejerskov O. Water fluoridation. In: Fejerskov O, Ekstrand J, Burt BA, editors. *Fluoride in dentistry*. Copenhagen: Munksgaard; 1996. p. 275–90.
10. Murray JJ, Rugg-Gunn AJ, Jenkins GN. *Fluorides in caries prevention*. 3rd ed. London: Wright; 1992.
11. Newbrun E. Effectiveness of water fluoridation. *J Public Health Dent* 1989;49:279–89.

12. Newbrun E. *Cariology*. 3rd ed. Chicago: Quintessence; 1989.
13. Featherstone JDB, Ten Cate JM. Physicochemical aspects of fluoride-enamel interactions. In: Ekstrand J, Fejerskov O, Silverstone LM, editors. *Fluoride in dentistry*. Copenhagen: Munksgaard; 1988. p. 125–49.
14. Featherstone JDB, Glana R, Shariati M, Shields CP. Dependence of *in vitro* demineralization and remineralization of dental enamel on fluoride concentration. *J Dent Res* 1990;69:620–5.
15. Anderson MH, Bales DJ, Omnell K-A. Modern management of dental caries: the cutting edge is not the dental burr. *J Am Dent Assoc* 1993;124:37–44.
16. Arends J, ten Bosch JJ. *In vivo* de- and remineralization of dental enamel. In: Leach SA, editor. *Factors relating to demineralization and remineralization of the teeth*. Oxford: IRL Pr 1985; p. 1–11.
17. Ten Cate JM, Duijsters PPE. Influence of fluoride in solution on tooth demineralization. II. Microradiographic data. *Caries Res* 1983;17:513–9.
18. Ten Cate JM, Featherstone JDB. Mechanistic aspects of the interactions between fluoride and dental enamel. *Crit Rev Oral Biol* 1991;2:283–96.
19. Hamilton IR, Bowden GHW. Fluoride effects on oral bacteria. In: Fejerskov O, Ekstrand J, Burt BA, editors. *Fluoride in dentistry*. Copenhagen: Munksgaard; 1996. p. 230–51.
20. Loesche WJ, Hockett RN, Syed SA. The predominant cultivable flora of tooth surface plaque removed from institutionalized subjects. *Archs Oral Biol* 1973;17:1311–25.
21. Loesche WJ. Role of *Streptococcus mutans* in human dental decay. *FEMS Microbiol Rev* 1986;50:353–80.
22. Featherstone JDB. An updated understanding of the mechanism of dental decay and its prevention. *Nutr Q* 1990;14:5–11.
23. Featherstone JDB, Rodgers BE. The effect of acetic, lactic and other organic acids on the formation of artificial carious lesions. *Caries Res* 1981;15:377–85.
24. Featherstone JDB, Mellberg JR. Relative rates of progress of artificial carious lesions in bovine, ovine and human enamel. *Caries Res* 1981;15:109–14.
25. Geddes DAM. Acids produced by human dental plaque metabolism *in situ*. *Caries Res* 1975;9:98–109.
26. Featherstone JDB. Diffusion phenomena and enamel caries development. *Cariology Today*. International congress, Zurich, 1983. Karger; 1984. p. 259–68.
27. Silverstone LM. The structure of carious enamel, including the early lesion. *Oral Sci Rev* 1973;3:100–60.
28. LeGeros RZ. Calcium phosphates in oral biology and medicine. Myers HM, editor. *Monographs in oral science*. Basel: Karger; 1991. Vol. 15.
29. LeGeros RZ, Trautz OR, LeGeros JP, Klein E. Carbonate substitution in the apatite structure. *Bull Soc Chim Fr* 1968(Spec Iss):1712–8.
30. LeGeros RZ. Crystallographic studies of the carbonate substitution in the apatite structure [PhD thesis]. New York: 1967.
31. Featherstone JDB, Mayer I, Driessens FCM, Verbeeck RMH, Heijligers HJM. Synthetic apatites containing Na, Mg, and CO₃ and their comparison with tooth enamel mineral. *Calcif Tissue Int* 1983;35:169–71.
32. Featherstone JDB, Pearson S, LeGeros RZ. An IR method for quantification of carbonate in carbonated-apatites. *Caries Res* 1984;18:63–6.
33. Budz JA, LoRe M, Nancollas GH. Hydroxyapatite and carbonated-apatite as models for the dissolution behavior of human dental enamel. *Adv Dent Res* 1987;1:314–21.
34. Curzon MEJ, Featherstone JDB. Chemical composition of enamel. In: Lazzari EP, editor. *Handbook of experimental aspects of oral biochemistry*. Florida: CRC Pr; 1983. p. 123–35.
35. Curzon MEJ, Cutress TW, editors. *Trace elements and dental disease*. Littleton: John Wright; 1983.
36. Featherstone JDB, Goodman P, MacLean JD. Electron microscope study of defect zones in dental enamel. *J Ultrastruc Res* 1979;67:117–23.
37. Featherstone JDB, Nelson DGA, McLean JD. An electron microscope study of modifications to defect regions in dental enamel and synthetic apatites. *Caries Res* 1981;15:278–88.
38. Nelson DGA, McLean JD. High-resolution electron microscopy of octacalcium phosphate and its hydrolysis products. *Calcif Tissue Int* 1984;36:219–32.
39. Nelson DGA, McLean JD. Direct observation of near-atomic details in synthetic and biological apatite crystallites. In: Fearnhead RW, Suga S, editors. *Tooth enamel IV*. Amsterdam, Netherlands: Elsevier Science; 1984. p. 47–51.
40. Featherstone JDB, Silverstone LM. The caries process – morphological and chemical events. In: Nikiforuk G, editor. *Understanding dental caries*. Basel: Karger; 1985. p. 261–89.
41. Robinson C, Kirkham J, Weatherell JA. Fluoride in teeth and bone. In: Fejerskov O, Ekstrand J, Burt BA, editors. *Fluoride in dentistry*. 2nd ed. Copenhagen: Munksgaard; 1996. p. 69–87.
42. Nelson DGA, Featherstone JDB, Duncan JF, Cutress TW. Effect of carbonate and fluoride on the dissolution behaviour of synthetic apatites. *Caries Res* 1983;17:200–11.
43. Featherstone JDB, Shields CP, Khademazad B, Oldershaw MD. Acid reactivity of carbonated-apatites with strontium and fluoride substitutions. *J Dent Res* 1983;62:1049–53.
44. Fejerskov O, Thylstrup A, Larsen MJ. Rational use of fluorides in caries prevention. *Acta Odontol Scand* 1981;39:241–9.
45. Moreno EC, Kresak M, Zahradnick RT. Physicochemical aspects of fluoride-apatite systems relevant to the study of dental caries. *Caries Res* 1977;11:142–8.
46. Whitford GM, Schuster GS, Pashley HD, Venkateswarlu P. Fluoride uptake by *Streptococcus mutans* 6715. *Infect Immun* 1977;18:680–7.
47. Van Louveren C. The antimicrobial action of fluoride and its role in caries inhibition. *J Dent Res* 1990;69:676–81.
48. Brown WE, Gregory TM, Chow LC. Effects of fluoride on enamel solubility and cariostasis. *Caries Res* 1977;11:118–22.
49. Featherstone JDB, O'Reilly MM, Shariati M, Brugler S. Enhancement of remineralization *in vitro* and *in vivo*. In: Leach SA, editor. *Factors relating to demineralization and remineralization of the teeth*. Oxford: IRL Pr; 1986.
50. O'Reilly MM, Featherstone JDB. De- and remineralization around orthodontic appliances: an *in vivo* study. *Am J Orthod* 1987;92:33–40.
51. Bruun C, Givskov H, Thylstrup A. Whole saliva fluoride after toothbrushing with NaF and MFP dentifrices with different F concentrations. *Caries Res* 1984;18:282–8.
52. Zero DT, Raubertas RF, Pedersen AM, Fu J, Hayes AL, Featherstone JDB. Fluoride concentrations in plaque, whole saliva and ductal saliva after applications of home-use fluoride agents. *J Dent Res* 1992;71:1768–75.

53. Billings RJ, Meyerowitz C, Featherstone JDB, Espeland MA, Fu J, Cooper LF. Retention of topical fluoride in the mouths of xerostomic subjects. *Caries Res* 1988;33:306–10.
54. Meyerowitz C, Featherstone JDB, Billings RJ, Eisenberg AD, Fu J, Shariati M, et al. Use of and intra-oral model to evaluate 0.05% sodium fluoride mouthrinse in radiation-induced hyposalivation. *J Dent Res* 1991;70:894–8.
55. Leverett DH, Proskin HM, Featherstone JDB, Adair SM, Eisenberg AD, Mundorff-Shrestha SA, et al. Caries risk assessment in a longitudinal discrimination study. *J Dent Res* 1993;72:538–43.
56. Leverett DH, Featherstone JDB, Proskin HM, Adair SM, Eisenberg AD, Mundorff-Shrestha SA, et al. Caries risk assessment by a cross-sectional discrimination model. *J Dent Res* 1993;72:529–37.
57. Shields CP, Moss ME, Featherstone JDB, Proskin HM, Billings RJ. Chemical analysis of saliva: a longitudinal study. *J Dent Res* 1995;74:15.
58. Shields CP, Moss ME, Billings RJ, Featherstone JDB. A longitudinal chemical analysis of saliva [abstract]. *J Dent Res* 1997;76(Spec Iss).
59. Featherstone JDB. Clinical implications of early caries detection: new strategies for caries prevention. In: Stookey GH, Beiswanger B, editors. *Indiana Conference 1996: Early Detection of Dental Caries*. Indiana University; 1996. p. 285–93.
60. Krasse B. Biological factors as indicators of future caries. *Int Dent J* 1988;38:219–25.
61. Ellen RP. Microbiological assays for dental caries and periodontal disease susceptibility. *Oral Sci Rev* 1976;8:3–23.
62. Alaluusua S, Kleemola-Kujala E, Nystrom M, Evalahti M, Gronroos L. Caries in the primary teeth and salivary *S. mutans* and lactobacillus levels as indicators of caries in permanent teeth. *Pediatr Dent* 1987;9:126–30.
63. Klock B, Krasse B. Microbial and salivary conditions in 9- to 12-year-old children. *Scand J Dent Res* 1977;85:56–63.
64. Seppa L, Hausen H. Frequency of initial caries lesions as predictor of future caries increment in children. *Scand J Dent Res* 1988;96:9–13.
65. Loesche WJ, Eklund S, Earnest R, Burt BA. Longitudinal investigation of bacteriology of human fissure decay: epidemiological studies in molars shortly after eruption. *Infect Immun* 1984;46:765–72.
66. Kingman A, Little W, Gomez I, Heifitz SB, Driscoll WS, Sheats R, et al. Salivary levels of *Streptococcus mutans* and lactobacilli and dental caries experience in a US adolescent population. *Community Dent Oral Epidem* 1988;16:98–103.
67. Ten Cate JM, Mundorff-Shrestha SA. Working group report: Laboratory models for caries (*In vitro* and animal models). *Adv Dent Res* 1995;9:332–4.
68. Featherstone JDB, Zero DT. Laboratory and human studies to elucidate the mechanism of action of fluoride-containing dentifrices. In: Emberry G, Rolla R, editors. *Clinical and biological aspects of dentifrices*. Oxford: Oxford Univ Pr; 1992. p. 41–50.
69. Arends J, Nelson DGA, Dijkman AG, Jongbloed WL. Effect of various fluorides on enamel structure and chemistry. In: Guggenheim B, editor. *Cariology Today, Int. Congr., Zurich, Basel, Switzerland: Karger, 1983:245–58*.
70. Zero DT. *In situ* caries models. *Adv Dent Res* 1995;9:214–30.
71. Larsen MJ. Chemically induced *in vitro* lesions in dental enamel. *Scand J Dent Res* 1974;82:496–509.
72. Larsen MJ. An investigation of the theoretical background for the stability of calcium phosphate salts and their mutual conversion in aqueous solutions. *Arch Oral Biol* 1986;31:757–61.
73. Stephen KW, Campbell D. Caries reduction and cost benefit after 3 years of sucking fluoride tablets daily at school. A double blind trial. *British Dent J* 1978;144:202–6.
74. Ekstrand J. Fluoride metabolism. In: Fejerskov O, Ekstrand J, Burt BA, editors. *Fluoride in dentistry*. Copenhagen: Munksgaard; 1996. p. 55–68.
75. Brown LJ, Winn DM, White BA. Dental caries, restoration and tooth conditions in U.S. adults, 1988–1991. *J Am Dent Assoc* 1996;127:1315–25.