MECHANISMS OF ANTI-CARIES ACTION OF FLUORIDE

How Dental Caries Develops:
It is normal for a wide range of bacteria to be present in the mouth and many are involved with forming biofilm (plaque) on the surfaces of teeth. However, some bacteria can establish levels that can lead to problems. When biofilm bacteria such as mutans streptococci metabolize fermentable carbohydrates (i.e., glucose, sucrose, fructose, or cooked starch), acids are generated as a by-product. These acids diffuse through the biofilm and into the porous enamel dissolving calcium phosphate mineral from the tooth surface. This process of mineral loss at the tooth surface is what is called “demineralization” and is influenced by multiple risk and protective factors. If the demineralization process is not halted or reversed by a “remineralization” process, the carious process creates an enamel lesion and with further progression, eventually results in a cavity.

How Fluoride Works in Caries Prevention and Control:
Anti-caries mechanisms of fluoride have been elucidated in considerable detail using data from in vitro studies. According to our knowledge base today, fluoride works to prevent and control dental caries through the following two primary mechanisms that affect 1) enamel solubility and 2) reversal of the caries process.

Both systemically and topically applied fluoride increase enamel fluoride content as well as ambient fluoride (free fluoride ion present in saliva and the fluid phase of plaque) in the oral environment. Systemically ingested fluoride, when it is absorbed in the alimentary tract, either is excreted in urine or incorporated into calcified tissues, such as bone and teeth. It is well established that fluoride is incorporated into dental apatite crystals during tooth development. Fluoride retained during topical application mostly forms calcium fluoride (CaF₂) or calcium fluoride-like material, which is often referred to as “loosely bound” fluoride in comparison to fluorapatite or “firmly bound” fluoride, and is the most likely source of fluoride ions during cariogenic challenges. As fluorapatite has lower solubility than calcium fluoride, firmly bound fluoride is presumably superior to loosely bound fluoride in slowing mineral diffusion within dental tissues. Laboratory studies found that the levels of enamel fluoride at about 20-100 ppm in subsurface enamel or at 1,000-2,000 ppm in the outer few micrometers of enamel typically found in optimally fluoridated and non-fluoridated area alone do not provide measurable benefit against acid dissolution. When fluoride is concentrated into a new crystal surface during remineralization—ambient fluoride bringing calcium and phosphate ions back to partially demineralized crystals and producing fluorapatite-like coating on crystals, Ca₁₀(PO₄)₆(F)₂, —the end-product reportedly has sufficiently high fluoride content (about 30,000 ppm) to reduce enamel solubility against future acid attack.

Scientific evidence from clinical investigations with regard to a correlation between enamel fluoride content and caries incidence is mixed. Difficulty in demonstrating the effectiveness of tooth-bound fluoride in vivo includes but not limited to the fact that 1) fluoride must be incorporated into those susceptible areas of the teeth (pits and fissures, approximal surfaces, etc.) for the tooth-bound fluoride to effect its caries inhibition, while those surfaces are not the candidate for enamel biopsy, 2) presently used fluoride regimens do not deposit significant amounts of firmly bound fluoride into the sound tooth mineral, and 3) caries outcomes are usually measured by the presence of visible cavities and dentinal lesions using the DMFT/S index whereas in-vitro studies usually deal with enamel lesions only.

As cariology and the concept of caries process evolved, the focus of fluoride-induced anti-caries action also has emphasized the enhanced activity of fluoride ion in the oral fluid, specifically in the plaque fluid at the enamel-plaque/biofilm interface, which is more directly related to demineralization and remineralization processes than fluoridated enamel and its solubility.

During the caries process, conditions favoring demineralization of enamel surface occurs at sites that provide an ecological niche where the plaque/biofilm composition gradually adapts to a declining pH environment. As previously noted, fluoride present in the oral environment in the biofilm and associated with the surface of teeth acts as a reservoir of free fluoride.
ion. Enhanced fluoride ion activity within resting plaque/biofilm under more pH neutral conditions then will increase the driving force for mineral deposition at the porous surface enamel and promote remineralization process.

Is Anti-Caries Effect of Fluoride Pre-Eruptive or Post-Eruptive?

Since the discovery of association between fluoride and reduced rate of caries in the population, there has been a question among scientists as well as the public on whether the anti-caries effect of fluoride is pre-eruptive (“systemic”) or post-eruptive through “topical” fluoride, or both. A few decades after water fluoridation was initiated, researchers found that fluoride may not prevent caries initiation as effective as caries progression and drew attention to fluoride’s anti-caries mechanisms during its aqueous phase in order to explain phenomena observed in laboratory and clinical studies. When the life-time benefit of fluoride to human health is estimated, the topical, post-eruptive effect may be considered as predominant as pre-eruptive benefit only applies to children and adolescents. However, these notions do not diminish the importance of a pre-eruptive effect of fluoride, for which we have evidence from in vivo studies.

For example, a pre-eruptive contribution of fluoride may be more important and effective at specific surfaces of the tooth, such as pits and fissures, that are highly susceptible for caries and less likely to receive the benefit of post-eruptive exposure to fluoride compared to other surfaces more exposed to saliva and oral hygiene and less susceptible for caries (i.e. smooth surfaces). Clinical investigation conducted in 1970s to determine the effect of fluoride supplementation on caries incidence in children living in non-fluoridated communities documented the formation of a favorable tooth morphology, i.e. shallow and less-retainent pits and fissure on the occlusal surfaces of molar teeth, associated with pre-eruptive fluoride intake corroborating previous observations.

In recent years, Singh and colleagues conducted a study to examine the relative pre- and post-eruption exposure effects of fluoridated water on caries experience among 6-15 year-old Australian children (N=17,773). Percentage of lifetime exposure to optimally fluoridated water was calculated with respect to the eruption age for the first permanent molars. They found that maximum caries-preventive effects of fluoridated water were achieved when there were both high pre- and post-eruption exposures. Furthermore, their data indicated that pre-eruptive exposure to fluoride, especially during the crown completion phase of tooth development, was significantly associated with lower caries in the first permanent molars of children 6-15 years of age.

The findings of a study conducted by Cho and colleagues on the effect of ceased community water fluoridation (CWF) in South Korea indicated that 11 year-old children who had approximately 4 years of CWF since birth before the CWF cessation had a significantly lower DMFT ratio relative to those children who grew up in the non-fluoridated community (0.68 [95% CI 0.45-0.75]). When DMFT ratio was compared between 8 year-olds who had approximately 1 year of CWF since birth before the CWF cessation and those who grew up in a non-fluoridated community, the difference was not significant (0.92 [0.63-1.37]).

Studies like these that pay attention to estimated length of pre-eruptive exposure to fluoride imply potential benefit of systemic fluoride intake. However, isolating the value of pre-eruptive fluoride from the post-eruptive fluoride effect is not easy in the post-fluoridation era of low caries. Furthermore, determining person’s fluoride exposure through residential history can introduce bias. Fluorosis is a condition that clearly indicates that the tooth was exposed to a relatively high level of fluoride during enamel formation. Iida and Kumar used a large national data of US school children (N=16,873) from1986-1987 to determine the tooth-level association between enamel fluorosis, as a biomarker of pre-eruptive fluoride exposure, and dental caries in first permanent molars. The findings indicated that first permanent molar teeth with fluorosis, even including moderate to severe fluorosis, consistently had lower caries experience than did molars without fluorosis both in fluoridated (>0.7 ppm) and non-fluoridated (<0.7 ppm) communities (adjusted odds ratio [AOR] 0.89, 95% CI 0.74-1.06, and AOR 0.71, 95% CI 0.56-0.89, respectively).

In summary, evidence supports a conclusion that the effects of pre- and post-eruptive fluoride complement each other. Over the lifespan, fluoride inhibits the process of carious primarily through its post-eruptive effect on demineralization and remineralizaton. While the attribution of caries resistant teeth and pre-eruptive effect of fluoride in caries prevention is not easily demonstrated, especially in a life-course perspective, fluoride incorporated into developing enamel mineral may offer initial resistance to caries initiation or delay the formation of clinically detectable caries, especially at the surfaces where post-eruptive fluoride is less than effective.

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REFERENCES