



# Products — Old, New, and Emerging

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**ABSTRACT** The paradigm shift in understanding the etiology, prevention, and treatment of dental caries requires an understanding of the dental products that are currently available to assist the clinician in prudent recommendations for patient interventions. The purpose of this review is to present the evidence base for current products and those that have recently appeared on the market.

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## DISCLAIMER

The products discussed in this issue are intended to be examples of currently available products for clinicians to use in caries management by risk assessment. The authors do not endorse any of these products and appreciate that there are many other products that were omitted only because of limitations of space.

**M**anaging dental caries by risk assessment requires an understanding of the pathologic and protective factors that exist in the “caries balance” (refer to Featherstone et al. this issue). The pathologic factors include the transmissible and infective organisms, mutans streptococci (MS, and lactobacilli, LB); reduced salivary flow; and the frequent ingestion of fermentable carbohydrates, not just sucrose. Recognizing caries etiology is imperative before rational interventions can be developed.<sup>1</sup>

The protective factors include adequate amounts of healthy saliva that include acid buffers, the presence of calcium, phosphate, and fluoride for remineralization, proteins and lipids that form the protective pellicle, immunoglobulins, and a salivary flow rate adequate to clear the oral cavity. Although intrinsic antibacterial factors are present in the saliva, extrinsic antibacterial agents are an important consideration in the “extreme-risk” and “high caries risk” patient because salivary antimicrobials may be insufficient to overcome the challenge of high MS and LB counts.

The remainder of this review will discuss practical dental products to use in

patient interventions covering the broad range of extreme and high caries risk, to patients with moderate and even low risk. Although low caries risk patients might not be considered at risk for caries, primary prevention, by definition, is intended to prevent disease from occurring before any pathology is present.

Clinicians spend the majority of their careers dealing with secondary prevention, i.e., removing the result of dental caries and restoring the cavitation and/or defects in tooth structure with dental materials that are biologically compatible with the teeth and supporting tissues. Some of the products, such as chlorhexidine (CHX) and fluorides, have an extensive evidence base to support efficacy but may not have as strong an evidence base as a caries treatment intervention. Comments will be made concerning the strength of evidence within the context of risk assessment and “caries balance.” Lastly, the use of any of the products discussed in this paper is predicated on assisting patients to thoroughly clean their teeth, including approximals, on a daily basis.

## Product Categories with Examples

The products reviewed here are for use in the clinical management of dental

caries, as described in detail in this issue by Ramos-Gomez et al. and Jenson et al. in other papers in this *Journal*. In those papers, generic descriptions are used in the treatment tables and procedural descriptions. This paper provides examples of these products including product descriptions, brand names, and sources. It is not intended to be inclusive nor is any endorsement to a particular product or company implied. Many products were omitted only because of limitations of space.

## Antibacterials

### CHLORHEXIDINE (CHLORHEXIDINE GLUCONATE 0.12 PERCENT, 11.6 PERCENT ALCOHOL, PERIOGARD, PERIDEX, PERIORX AND G-U-M CHLORHEXIDINE GLUCONATE ORAL RINSE USP)

There is a large body of data including controlled clinical trials to support the efficacy of chlorhexidine (CHX) as an antiplaque agent. The mechanism of action is time-dependent and requires a two-step process. First, the strongly cationic CHX molecule must attach to the anionic tooth surface and then it is released over a period of four to 12 hours. The cationic molecule attaches to the anionic surface of the bacterial cell. Prolonged contact with the bacteria eventually weakens the cell wall and disrupts its contents.<sup>2</sup> Chlorhexidine is effective against a broad spectrum of microorganisms in dental plaque, including MS (not necessarily LB).

An excellent and concise review of the efficacy of chlorhexidine is presented by Anderson.<sup>3</sup> He concluded that the literature is mixed on the effects of CHX against dental caries, but is favorable with respect to controlling MS. More specifically CHX has been demonstrated to be effective in caries control among patients with special needs.<sup>3,5</sup> Schaecken et al. compared chlorhexidine

and iodine in young adults and found that both were effective in suppressing *S. mutans*.<sup>6</sup> However, it is significant that with CHX, *S. mutans* remained suppressed 21 days after application.

In a randomly controlled clinical trial that extended more than two years, Wyatt and MacEntee compared daily rinsing with either CHX or 0.2 percent neutral sodium fluoride.<sup>7</sup> They concluded that the 0.2 percent fluoride rinse significantly

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reduced the incidence of caries among elders in a long-term care residence compared to the CHX group. This is not surprising, because the CHX can only reduce the MS<sup>8</sup>, whereas the 0.2 percent fluoride rinse contributes to the remineralization of the tooth surface. In that study, the daily use of 0.2 percent neutral sodium fluoride decreased the incidence of caries in institutionalized elders, demonstrating the necessity of enhancing remineralization during the treatment of individuals at risk of caries progression. Antibacterial treatment will generally need fluoride treatment in conjunction.

### Conclusion

Despite the great need for the development of new and better antimicrobials for

clinical use, there is a strong body of evidence supporting the efficacy of 0.12 percent chlorhexidine that justifies its designation as one of the most effective caries antimicrobial agents currently available.

### Application

In extreme-risk and high-risk caries adults, 10 milliliters of 0.12 percent CHX solution should be used for rinsing once or twice daily for one minute, after breakfast and at bedtime (after brushing the teeth), for seven days or one week per month. More detail about how this fits into the therapy for individuals following caries risk assessment is given in the paper by Jenson et al. this issue. In the high caries risk adult, this should be followed by three weeks of rinsing with either the 0.2 percent NaF Rinse (Prevident or Oral-B) or OTC 0.05 percent NaF rinse. Use of the 0.2 percent NaF rinse is optional, and, if selected, should be used daily, after lunch so as not to interfere with the 1.1 percent NaF toothpaste. If this option is not selected, the patient should use the OTC 0.05 percent NaF rinse, twice daily, after breakfast and after lunch. It is useful to note that cationic products (e.g., CHX) will bind to some extent with anionic products (e.g., fluoride or iodine) and the contents should not be mixed together or used immediately after one another. It is possible to use fluoride therapy and CHX on the same day for one week a month, provided they are used about one hour or more apart to allow for either to interact with the teeth and the plaque. In this case, a once-a-day rinse with the CHX and a once-a-day rinse with fluoride at another time of day is recommended. This regimen is likely to achieve better compliance as it is less confusing for the patient.

At this time, a postintervention saliva/bacterial test should be administered to monitor the treatment process and motivate the patient to continue. The

patient then returns to using the CHX daily for seven days to keep the bacterial levels suppressed. After this second round of CHX use, the patient should rinse twice daily with 0.05 percent NaF rinse (Act, Fluorigard, CariFree Maintenance). This latter protocol (i.e., CHX and 0.05 percent NaF rinse) should be repeated monthly until bacterial levels are consistently low or until no new carious lesions are detected for up to at least one year. Periodic saliva/bacterial testing should be done to determine whether the patient is cooperating with the CHX regimen and whether it is working.

This same regimen should also be considered in the high caries risk child over the age of 6.

**CHLORHEXIDINE (CHLORHEXIDINE GLUCONATE 0.12 PERCENT, AQUEOUS SOLUTION, G-U-M CHLORHEXIDINE GLUNCONATE ORAL RINSE USP)**

One of the more recent developments in the United States has been the introduction of a water-based chlorhexidine mouthrinse. This has widespread appeal not only for safety reasons, but also for patients who should avoid alcohol-containing mouthrinses. In addition, patients who are immunocompromised, or who have decreased salivary flow due to radiation therapy, medications or systemic conditions and cannot tolerate alcohol-containing mouthrinses.

There is some limited evidence that the water-based CHX is as effective as the alcohol-based CHX. Eldridge et al. in 1998 conducted a double-blind randomly controlled clinical trial comparing three groups: CHX with alcohol, CHX alcohol-free, and Listerine. All subjects refrained from all oral hygiene practices for 21 days while using 15 ml of the assigned mouthrinse for one minute daily.<sup>9</sup> In that study the authors concluded that the

alcohol-free CHX was as effective as the alcohol-based CHX in reducing *Streptococcus mutans* levels. Although the authors found statistically significant differences between both CHX groups and the Listerine, the total sample size of the study (N=32) lacked the power to show true differences. In another controlled clinical trial conducted by Borrajo et al. in 2002, 10 concluded that the water-based CHX was equally as effective as the alcohol-

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containing CHX product in controlling plaque and reducing gingival inflammation after 28 days. This study had sufficient sample size, but it was not directed at measuring decreases in *S. mutans* levels.

**Conclusion**

At this time there is limited evidence to recommend the use of the alcohol-free CHX as substitute for CHX in alcohol. Even though additional research is needed to document its efficacy, it should be considered and recommended to patients who are intolerant of alcohol.

**Application**

Use of the water-based CHX should be considered for those at extreme risk for caries, or any patient who is intolerant of alcohol. The protocol for using the alcohol-free CHX is the same as that described above for the alcohol-based CHX.

**1 PERCENT IODINE (10 PERCENT Povidone-iodine, Betadine)**

The microbicidal effect of povidone-iodine has been used for many years in the cleaning of surgical instruments, as a handrinse and body scrub before surgery. It is microbicidal for gram-positive and gram-negative bacteria, fungi, mycobacteria, viruses, and protozoans.<sup>11</sup> Unlike chlorhexidine, povidone-iodine exerts its lethal effects by direct contact with the microbial cell wall. Ten percent povidone-iodine yields 1 percent active iodine. One additional attribute of povidone iodine is that it appears to be effective against both MS and LB in children.

Most of the studies that have examined topically applied iodine have been conducted in young children. A review of these studies is presented by DenBesten and Berkowitz in 2003<sup>12</sup>; refer to [http://www.cdafoundation.org/news\\_journals.htm](http://www.cdafoundation.org/news_journals.htm). For our purposes, a concise summary will be presented. In one study, a one-time two-minute topical application of 2 percent iodine or potassium iodine lowered bacterial levels for up to 13 weeks.<sup>13</sup> In another, following a prophylaxis, three applications of potassium iodine reduced MS for up to six months.<sup>14</sup> In a randomly controlled clinical trial, 10 percent povidone iodine was applied every two months (up to seven months) in infants 12 to 19 months of age. None of the infants in the treatment group developed white spot lesions, whereas 31 percent of the infants in the control group developed white spots.<sup>15</sup> This needs to be interpreted with caution because of the small sample size (N=31).

In a pilot study of children with extensive dental caries requiring general anesthesia for treatment, 25 children ranging in age from 2 to 7 were randomly separated into a treatment and control group.<sup>16</sup> The treatment group received

topical application of 10 percent povidone-iodine three times at two-month intervals, and the control group did not receive iodine. Six months following extensive one-time restorative dental treatment, both groups had a statistically significant decrease in *S. mutans* counts, but there was no difference between the two groups. One year following initial treatment, 63 percent of the children in the control group had new cavities compared to 18 percent in the treatment group.

In a similar study of children with extensive early childhood caries (22 children, age 2 to 6), the treatment group received a one-time application of 10 percent povidone-iodine and the control group a phosphate buffered saline.<sup>17</sup> Prior to restorative treatment, all children received a prophylaxis, a two-minute 1.23 percent acidulated phosphate fluoride gel application, followed with either the iodine or saline treatment.

Mutans streptococci and lactobacilli were significantly reduced at one hour, three weeks, and three months in the povidone-iodine group. Following one year, more than 60 percent of the children had new cavities, but there was no significant difference in caries increment between the two groups. The results suggest that periodic reapplication of the povidone-iodine is needed in a high-risk group with early childhood caries.

In 2005, El-Housseiny and Farsi conducted a controlled clinical trial in children age 4 to 6.<sup>18</sup> The treatment group (10 percent povidone-iodine) and the control group (APF gel) each received a prophylaxis and APF before starting the study. Thereafter, the treatment group received topical applications of povidone-iodine weekly for the first month, and then at three, six, and 12 months. The control group followed the same application regi-

men using only the APF gel. The differences in salivary MS and LB between the treatment and control groups were not statistically significant.

### Conclusion

The positive results of povidone-iodine as an antimicrobial to decrease MS and LB in young children have been well documented. There is little evidence, however, that it is effective in adults

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or older children. Additional studies are needed to determine its efficacy in reducing MS and LB in adults or older children. Until such studies are done, the use of iodine in adults cannot be recommended as being proven to be beneficial.

### Application in Children

When using topical iodine all patients/caregivers should be screened for potential iodine allergies. In high and moderate caries risk young children, 10 percent povidone-iodine can be applied with a cotton swab saturated with the iodine. Several studies reported better results if the biofilm was disturbed or removed with a prophylaxis polish. In children younger than age 6, or in special needs patients, the teeth should be isolated with cotton rolls and gently dried with gauze or cotton rolls with excess iodine being aspirated with suction. One to two milliliters may

be applied for up to two minutes, followed by wiping with gauze or rinsing with a water syringe. After age 6, or when a child has developed a coordinated swallowing reflex, they may rinse with 10 ml of povidone-iodine for one minute and expectorate. This routine should be repeated at all recall examinations and restorative appointments until no new carious lesions are detected. Use in adults is not required.

### Topical Fluoride Modalities

In the extreme-risk and high-risk caries patient, the first step is to deal with the infectious disease of dental caries. After MS and LB have been challenged with antibacterials, other protective agents such as topical fluorides and xylitol need to be employed to help tip the caries balance in favor of a healthy oral environment. There is a substantial body of good evidence to support topical fluoride agents.<sup>19</sup> The first studies on professionally applied fluorides included high concentration sodium fluoride (NaF), stannous fluoride (SnF<sub>2</sub>) and acidulated phosphate fluoride (APF) aqueous solutions. When used repeatedly (i.e., two times per year), all of these agents were equally effective in reducing dental caries. Eventually they evolved into gels, foams, and varnishes. Fluoridated dentifrices and rinses were developed concurrently with professionally applied fluorides. The objective of fluoride intervention is to inhibit plaque bacteria, inhibit demineralization, enhance remineralization, and form a fluoroapatite-like coating at the partially demineralized mineral crystals in the tooth subsurface carious lesions.

### FLUORIDATED DENTIFRICES

Irrespective of caries risk, all age groups should use commercially available fluoridated toothpaste at least twice per day. Children younger than 2 should limit

the amount of paste to a pea-size amount, applied on a soft toothbrush by the caregiver, to minimize the risk of fluorosis.<sup>20</sup> Studies on the efficacy of fluoridated dentifrices in children of two to three years' duration have reported reductions in caries experience of 15 percent to 50 percent. In the United States, the concentration of fluoride in fluoride toothpastes is usually 1,000 to 1,100 ppm F.<sup>19</sup>

In recent years, 1.1 percent NaF toothpaste and gel (5,000 ppm F) (Prevident 5000, Control RX, Fluoridex Daily Defense) have become available for treating root sensitivity and have been approved for safety and efficacy by the Food and Drug Administration. Its use as an "off-label" anticaries agent is based on the likelihood of it being more beneficial in treating rampant caries, root caries and patients with decreased salivation or decreased cooperation in applying other forms of fluoride. In a clinical study that followed root caries progression, the use of a 5,000 ppm F toothpaste produced statistically significantly less caries than the control 1,000 ppm F product.<sup>21</sup>

### Conclusion

It is reasonable to assume that the anticaries effect of high fluoride concentration toothpastes is an extension of the evidence base for the routinely used toothpastes with lower amounts of fluoride and may prove helpful with patients who will not cooperate with other recommended sources of topical fluoride such as OTC fluoride rinses. These high fluoride toothpastes require a prescription and many clinicians have experienced dramatic increases in success by dispensing all Caries Management by Risk Assessment (CAMBRA) products directly to patients, while at the same time providing a beneficial service for patients. More detail is provided in the paper by Jenson et al. in this issue.

### Application

In the extreme-risk and high caries risk adult (i.e., rampant caries, root caries, or excessive gingival recession, or decreased salivation) it is reasonable to recommend the use of 1.1 percent NaF toothpaste twice per day (refer to Jenson et al., this issue, for recommended treatment protocols for the various risk levels and to Featherstone et al., this issue, for caries risk determination procedures). It

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can be used after breakfast, lunch, dinner, or at bedtime, as long as it does not interfere with any other fluoride modality that is recommended. If it is used only once per day, it is preferable to use at bedtime. Ideally, patients should be instructed to expectorate, but not rinse with water following brushing. When the tongue and lips are cleared of foam, the mild flavor of the paste is pleasantly tolerable. If patients prefer to rinse with water to eliminate food or other debris, they should try to rinse with just one mouthful of water holding it in the mouth for at least one minute, or alternatively reapplying a small amount of the toothpaste after rinsing.

The utility of 1.1 percent NaF toothpaste is that it is a single product. It does not require brushing first and then applying a high concentration fluoride gel, which may discourage some patients. One optional procedure in the extreme-

risk patient with low salivary flow is the construction of custom trays and the use of the 1.1 percent NaF gel (10 minutes per night). This is justifiable even though it is more costly. Use of the high concentration fluoride toothpastes should be continued until the caries status of the patient has changed and remains controlled. One cautionary note: Avoid using the 5,000 ppm fluoride toothpaste or gel directly after the use of chlorhexidine. Separating their use by an hour or more will help prevent the cationic charge of CHX from binding with the anionic charge of the fluoride, and allow either product to interact independently with the bacteria on the plaque and with the tooth.

### FLUORIDE MOUTHRINSES (0.05 PERCENT NAF, ACT, FLUORIGARD, CARIFREE MAINTENANCE RINSE AND 0.2 PERCENT NAF, PREVIDENT AND ORAL-B FLUORINSE)

Mouthrinses containing fluoride were developed for daily (0.05 percent NaF) or weekly (0.2 percent NaF) use for children over the age of 6. The 0.05 percent NaF rinse is an over-the-counter item, whereas the 0.2 percent NaF rinse requires a prescription, or must be dispensed by the dental office. The evidence base for supporting their efficacy dates back to early 1970s when the prevalence of dental caries was higher than today. The average reduction in caries experience was 30 percent. Even though the early randomized clinical trials used historical controls rather than concurrent controls, the quality of the evidence to support mouthrinses is high.<sup>19</sup> Their convenience and cultural acceptance makes them appealing.

### Conclusion

There is a good quality evidence base to support the used of fluoride rinses in the demineralization/remineralization cycle. They are especially valuable

in treating the moderate-risk, high-risk and extreme caries risk patient.

### Application

In the high caries risk patient, daily rinsing with 10 ml of 0.05 percent NaF rinse for 30 to 60 seconds should be done twice daily. If it is used after breakfast and after lunch, 1.1 percent NaF toothpaste could be used before retiring. This same schedule may also be used for patients with decreased salivation (extreme risk), because the fluoride will not be cleared rapidly from the oral cavity. One other option for the high caries risk or extreme risk patient is to use 10 ml of the 0.2 percent NaF rinse once per day, between the times that chlorhexidine is being used. After completion of one bottle of the 0.2 percent NaF rinse, the patient can start to use the 0.05 percent NaF rinse.

In the moderate caries risk patient, daily rinsing with 10 ml of 0.05 percent NaF rinse for 30 seconds should be done in the morning and before retiring. The young adolescent with orthodontic appliances also meets the profile of a moderate caries risk patient. Even the low caries risk patient with numerous crowns or restorations should rinse once daily with 10 ml of the NaF rinse to have additional protection beyond fluoridated toothpaste. All of these regimens should be continued until the caries risk changes or as long as the patient desires to continue.

### FLUORIDE VARNISHES (5 PERCENT NAF VARNISH: DURAPHAT, DURAFLOR, CAVITY SHIELD, FLUOR PROTECTOR, VANISH)

The advantage of fluoride varnish is that because it adheres extremely well to the tooth surface it maximizes the long-term delivery of fluoride. In addition, high concentrations of fluoride can be applied in small quantities. A completely dried tooth surface is not required and the

varnish can be applied more quickly than a four-minute fluoride gel or form tray application. A systematic review found that fluoride varnishes have a substantial caries preventive effect, but no concurrent controls were employed in these studies.<sup>22</sup> In a two-year randomized controlled clinical trial on low-income children younger than age 2 Weintraub et al. found that once per year and twice per year application of 5 percent sodium fluoride varnish

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significantly reduced the incidence of early childhood caries with twice per year significantly more effective than once.<sup>23</sup>

This product is also suitable for adults as a caries control agent that does not require personal compliance, although controlled clinical trials have not been reported. The House of Delegates of the American Dental Association approved a resolution that “supports the use of fluoride varnishes as safe and efficacious within a caries prevention program ...” (Resolution 37H, November 2004). It is recommended by the ADA Council on Scientific Affairs for biannual application in children and adolescents for preventing caries; in high-risk patients, two or more applications are recommended in preventing caries.<sup>24</sup>

### Conclusion

The evidence base for 5 percent NaF varnish is of a high quality. Additional re-

search to establish an optimal interval of frequency of applications is still needed. At least one randomized controlled trial has been reviewed systematically supporting its use in adolescents up to age 14.<sup>22</sup> Evidence for its use in adults has been extrapolated from these studies.

### Application

In the high caries risk child (e.g., ECC or adolescent with rampant caries) the tooth should be swabbed with either cotton rolls or 2-by-2 gauze sponges to remove the plaque and excessive moisture. The fluoride varnish, whether it comes in the 10 ml tubes or 1 ml individual applicators, should be mixed with the applicator brush to mix the fluoride and resin carrier, and then painted on all of the tooth surfaces, working the varnish into the embrasures as much as possible. It can also be flossed into the interproximal spaces. The varnish has a yellowish-brown appearance, except for Vanish, which is white. The patient or caregiver should be instructed to have the child refrain from drinking or eating for 30 minutes after the application. Although it may feel somewhat “gritty” or “pasty,” they may eat or drink with the varnish on their teeth. It will be removed the next time they brush. The longer it is on the teeth, the more benefit the patient receives. Although some practitioners suggest that the child not brush until the following morning, this recommendation is made at the discretion of the practitioner. Even if it is on the teeth for only three to four hours, it will provide at least as much benefit as a four-minute professionally applied tray application.

In the extreme-risk or high caries risk adult (e.g., excessive or rampant caries, gingival recession, dry mouth), the teeth are lightly dried to remove excessive moisture with a 2-by-2 gauze and varnish

is painted on the root surface, on the margins of restorations, and decalcified areas. Up to three applications are planned in the patient's sequence of restorative treatment. For example, varnish can be applied after the initial prophylaxis or after completing scaling and root planing, to diminish dentinal sensitivity. The other applications are made after all of the active decay is removed or temporized. The number of applications is governed by the number of restorative appointments needed and at the discretion of the practitioner. The patient is instructed to refrain from drinking or eating for 30 minutes, and reassured that the varnish will be removed at the next brushing. One application is also made at the patient's recall visits. For the extreme caries risk patient, a three-month recall is recommended, and for the high caries risk, three to four months. The same protocol is followed for the moderate-risk adult (one to two applications) with a recall at four to six months. Even an apparently low caries risk patient may benefit from an application of varnish if they present with excessive gingival recession or root sensitivity.

Applying varnish at the recall examinations would continue until the risk of caries has diminished for the patient. Finally, those white spot decalcified areas, stained fissures and areas noted as "watches" are all candidates for varnish application, no matter what the caries risk. One of the desirable features of using the 5 percent NaF varnish is that it is not subject to the compliance of the patient, but is under the control of the dentist. In general, adults may prefer the white varnish to the yellowish-brown varnishes.

#### XYLITOL

Xylitol is a naturally occurring, diabetic-safe, low-calorie sugar that is

not metabolized by MS. An overview of xylitol and dental caries was presented by Lynch and Milgrom.<sup>25</sup> Since it is not broken down by cariogenic microorganisms, xylitol starves the MS in a manner similar to removing sucrose from the diet completely. Including xylitol into the diet will also inhibit MS attachment to the teeth making it a good product for decreasing the bacterial load of primary care givers and interrupting

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the vertical transmission of MS to the child.<sup>26,27</sup> Since there is no metabolism and no drop in the salivary pH, the environment favors nonacidogenic bacteria.<sup>26</sup> Makinen et al. found that the systematic use of xylitol chewing gum significantly reduced the relative risk of caries compared to gums containing sorbitol/xylitol and sucrose.<sup>28</sup> Using the same population, he and his coworkers found that the use of a xylitol gum was more frequently associated with the arrest of dentinal caries than the other combinations of chewing gum.<sup>29</sup>

In summary, the use of xylitol-containing products, such as chewing gum, mints, candy, and cookies has resulted in decreasing the incidence of dental caries, arresting carious lesions and decreasing the transmission of MS from mothers and caregivers to children. The only side effect of too much xylitol ingestion is

that it may have a mild laxative effect. The benefit of using xylitol-containing products is complemented by increasing the salivary flow, which draws the buffering capacity of saliva into action as well as the electrolytes that contribute to remineralization. Therefore, the benefit of using xylitol is not confined to children, it is extended to many adults who experience dry mouth. The amount of xylitol needed for benefits against caries is slowly being refined. In 2006, Makinen narrowed the daily dose to between 6-10 grams per day.<sup>28,29</sup> To determine the exact amount of xylitol in a product, the manufacturer should be consulted or alternatively, patients can be advised to choose products with xylitol listed on the label as the first ingredient.

#### Conclusion

The evidence base for recommending products manufactured with xylitol is strongly supported by controlled clinical trials.

#### Application

More products containing xylitol are becoming available in the United States. Products and Web sites for purchasing the confections appear in **TABLE 1**. For moderate, high, and extreme caries risk patients, two pieces of xylitol gum or two pieces of xylitol hard candy/mints should be used for five minutes following meals or snacks four times daily. The target dose of xylitol is 6 to 10 grams spread throughout the day. Excessive or prolonged gum chewing is not advised. Most xylitol-sweetened products contain flavor that only lasts a short time to discourage excessive chewing. Adults with dry mouths or senior citizens, who may not like to chew gum because of occlusion problems, have the option of using xylitol in mints, candies, mouthwash, toothpaste, or mouth sprays.

## Dry Mouth Considerations

The healthy patient has an adequate supply of calcium and phosphate in the saliva to remineralize teeth after acid attacks from cariogenic bacteria. In addition, the antimicrobial properties of the saliva, along with its strong buffering system are more than adequate to maintain an environment that is optimal for a healthy caries balance. When the salivary flow is decreased, for whatever reason, the caries balance is shifted and pathologic factors can have a devastating effect on the teeth in a very short period. Therefore, patients who experience a decreased salivary flow are willing to grasp any product that may provide them relief. The products that are currently available do not have a strong evidence base but they may be able to provide palliative relief to patients.

The pH of the saliva is highest in the morning and decreases after eating when starches and sugars are metabolized to acid by cariogenic bacteria. Proteins and lipids have little effect on the salivary pH.<sup>30</sup> Stimulation of the saliva brings the protective functions of saliva into play. The most important protective functions of saliva are lubrication, chemical buffering, and antimicrobial activity.<sup>31</sup> The bicarbonate system is the major buffering system followed to a lesser extent by phosphate and protein. The bicarbonate system can quickly elevate the depressed pH caused by acidogenic bacteria to safe levels. When medications, systemic diseases, or irradiation diminishes the flow of saliva, the protective effects of saliva leave the teeth vulnerable to demineralization, and oral soft tissues may become dehydrated to the point of cracking and open to microbial infection. Hence, any product that simulates even some of the functions of saliva could have a profound effect on improving the quality of life for patients with hyposalivary symptoms.

## BUFFERING PRODUCTS (ARM & HAMMER TOOTHPASTES, GUM, AND BAKING SODA; ORBIT WHITE, CARIFREE, PROCLUDE, AND DENCLUDE)

With the exception of two toothpastes (Arm & Hammer P.M., Fresh Mint and Enamel Care), all of the toothpastes manufactured by Arm & Hammer contain sodium bicarbonate as the primary abrasive ingredient.<sup>32</sup> Its safety, low abrasivity, compatibility with fluoride and low cost

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metabolized to acid by  
cariogenic bacteria.

make it an ideal dentifrice ingredient.<sup>33</sup> Sodium bicarbonate dentifrice has the ability to rapidly neutralize (in vitro) pHs as low as 4.5.<sup>34</sup> This is also the rationale for making a solution of water with baking soda (two teaspoons in a 12- or 16-ounce bottle of water) for hyposalivary patients to rinse and expectorate as needed throughout the day to neutralize the detrimental effects of acidity from gastric reflux (GERD), bulimia, or the dryness that occurs when the saliva is drastically decreased. Because of its ability to increase the pH, it has shown a decrease (in vitro) in mineral loss of enamel.<sup>35</sup> It has also demonstrated strong inhibitory activity (in vitro) against *S. mutans*. Several small clinical studies suggest that it can be effective in reducing dental staining. Its low abrasivity is highly desirable because it will not abrade tooth structure like the high abrasive

dentifrices.<sup>36</sup> Removing tooth stains is the advertising basis for Orbit White chewing gum, which contains baking soda.

ProClude is a desensitizing prophylaxis paste and DenClude is a desensitizing toothpaste. Both products contain SensiStat which contains arginine, an amino acid which stimulates the acid-neutralizing properties of certain plaque bacteria. It also contains calcium carbonate and bicarbonate. CaviStat in a toothpaste has been shown, in a large study in Venezuela with more than 700 participants, to decrease decay in schoolchildren better than the fluoride control.<sup>37</sup>

## Conclusion

There is a considerable evidence base to support the many properties of baking soda or other buffering agents. Even though additional research is needed to clinically demonstrate the ability of buffering agents to decrease dental caries, extrapolating the use of baking soda, or other buffering agents to patients is reasonable in order to relieve the problems of acidity and decreased salivation.

## Application

In the extreme-risk patient, neutralizing the acidity that exists due to the lack of the saliva's protective properties can be offset by rinsing with a baking soda solution when the mouth feels dry. Additional recommendations include rinsing after every snack or meal and at bedtime, as well as using a baking soda chewing gum. These recommendations also apply to the patient with gastric reflux and bulimia.

## ARTIFICIAL SALIVA (SALIVART, OPTIMOIST)

Artificial saliva is intended to imitate natural saliva both chemically and physically. Its properties include viscosity, mineral content, preservatives and



TABLE 1

## Products for Caries Intervention

	Product	Where to Find Product
Chlorhexidine (chlorhexidine gluconate 0.12%, 11.6 % alcohol)	Periogard Peridex	Colgate www.colgateprofessional.com OMNI Preventive Care, a 3M ESPE Company www.omnipreventivecare.com
Chlorhexidine (chlorhexidine gluconate 0.12%, aqueous solution)	G-U-M Chlorexidine Gluconate Oral Rinse USP	Sunstar Americas, Inc./Butler www.jbutler.com
Iodine (10% povidone-iodine)	Betadine	Medical suppliers
Other antimicrobials	CariFree Treatment Rinse	OralBioTech www.carifree.com
Fluoridated dentifrices [1.1% NaF toothpaste and gel (5,000 ppm)]	Preident 5000 Control RX Fluoridex Daily Defense	Colgate Omni Discus Dental www.discusdental.com
Fluoride mouthrinses (0.05 % NaF)	Act Fluorigard CariFree Maintenance Rinse	Johnson and Johnson Colgate OralBioTech www.carifree.com
Fluoride mouthrinses (0.2% NaF)	Preident Oral-B Fluorinse	Colgate Procter & Gamble www.dentalcare.com
Fluoride varnishes (5% NaF varnish)	Duraphat Duraflor Cavity Shield Fluor Protector Vanish	Colgate Medicom OMNI Preventive Care Ivoclar OMNI Preventive Care
Xylitol	Epic Spry Squigle toothpaste Omni Theragum Ice Breakers Cubes Starbucks After-coffee gum Altoids gum	www.epicdental.com www.sprydental.com www.squigle.com OMNI Preventive Care Retail stores
Baking soda products	Arm & Hammer toothpastes and baking soda Orbit White	Retail stores Wrigley www.wrigley.com/wrigley
Other acid-buffering products	CariFree Maintenance rinse CariFree Boost Breath spray DenClude ProClude	OralBioTech, www.carifree.com Ortek Therapeutics, Inc. www.ortekinc.com

TABLE 1

Products for Caries Intervention **CONTINUED**

	Product	Where to Find Product
Palliative products for xerostomia	Optimoist	Colgate
	Salivart	Gebauer Company www.gebauer.com
	Oasis	GlaxoSmithKline www.gsk.com
	Stoppers 4 Dry Mouth Spray	Retail stores
	Spry Oral Rinse	Xlear, Inc. www.xlear.com/spry/dds
	Oralbalance gel and toothpaste	Laclede Professional Products www.biotene.com
	Biotene mouthwash	
	Biotene alcohol-free mouthwash	
	Biotene Antibacterial Dry Mouth toothpaste	
<b>New Products Currently Available</b>		
Recaldent products CPP-ACP	PROSPEC MI Paste (GC America, Inc.)	GC America, Inc. www.gcamerica.com.
	Trident White chewing gum	Retail stores
	Prospec MI Paste Plus	
NovaMin	SootheRx tooth sensitivity	OMNI Preventive Care www.denshield.com
	DenShield tooth sensitivity	Butler www.jbutler.com
	NuCare Root Conditioner with Novamin	Butler
	NuCare Prophylaxis Paste with NovaMin	Butler
ACP Products	Ageis products	Bosworth www.bosworth.com
	Sealants	Premier Dental www.premusa.com
	Bracket cmt	
	Crown and Bridge cmt	
	Enamel Pro – prophy paste	
	Enamel Pro varnish	
Diagnostics	Saliva Check	GC America
CariFree System	CariScreen and CariCult	OralBioTech www.carifree.com

palatability. Hydroxyethylcellulose or carboxymethylcellulose provides the attributes of viscosity. Phosphates and calcium contribute to the mineral content. Methyl or propylparaben are frequently used as preservatives. Flavorings and sweeteners, such as sorbitol or xylitol, provide the qualities of palatability.<sup>38</sup> In addition to the previously mentioned ingredients, Salivart contains sorbitol, is preservative-free and is packaged as a sterile propellant aerosol. Optimoist has similar ingredients, but also contains sodium monofluorophosphate and is packaged as a spray.<sup>39</sup>

### Conclusion

With both products lacking an evidence base, they can at best be offered as palliative relief to patients with xerostomia on an as-needed basis. These products lack the most important functions of saliva, the buffering and antimicrobial properties.

### **MOUTHWASH FOR THOSE WITH XEROSTOMIA (OASIS, STOPPERS 4 DRY MOUTH SPRAY, SPRY ORAL RINSE)**

Oasis is an alcohol-free formulation intended to provide the moisturizing benefits of a mouthwash without drying the mucosa.

It contains a combination of carboxymethyl cellulose and a polyvinylpyrrolidone backbone polymer and xanthan gum.<sup>40</sup> One study, using subjective questions, showed that in a population of subjects experiencing dry mouth, found it beneficial in managing dry mouth and preferred it over the control rinse.<sup>41</sup> It is advertised as a mouth moisturizer and not as a saliva substitute. Stoppers 4 Dry Mouth Spray and Spry Oral Rinse both have an abundance of xylitol.

### Conclusion

Lacking an evidence base, these products can at best be offered as pallia-

tive relief to patients with salivary gland hypofunction on an as-needed basis.

#### BIOTENE PRODUCTS

Oralbalance gel and toothpaste products contain the enzymes lactoferrin, glucose oxidase, and lactoperoxidase. When these enzymes combine with potassium thiocyanate, which is present in saliva, they form the hypothiocyanate ion, which mildly inhibits the growth of acid-producing microorganisms.<sup>42</sup> Biotene mouthwash contains lysozyme, glucose oxidase, and lactoferrin. In addition to these ingredients, Biotene alcohol-free mouthwash contains lactoperoxidase.

Biotene Antibacterial Dry Mouth Toothpaste contains lysozyme, glucose oxidase, and lactoperoxidase.<sup>32</sup> The studies that have been conducted on Biotene are difficult to interpret because some used different combinations of the Biotene mouthwash, toothpaste, chewing gum and Oralbalance gel or only one of the products separately. Out of the seven studies reviewed, five gave favorable results based on subjective measures and two did not have any effect based on physical measurements. The five studies with positive results were conducted in postradiation patients or severely hyposalivary patients.

#### Conclusion

Most of the evidence base comes from small studies and subjective measurements in which different combinations of the products were used. The Biotene products are intended to mimic the natural enzymes of the saliva. They have no buffering capability or anticaries effects and thus do not substitute for saliva. These products can at best be offered as palliative relief to patients with salivary gland hypofunction on an as-needed basis.

#### Application

They may be offered as palliative products to patients with dry mouth to see if they obtain any relief.

#### New Products Currently Available

##### PROSPEC MI PASTE (GC AMERICA, INC.)

MI Paste by GC America, Inc. is a water-based paste FDA-approved for sensitivity that uses Recaldent (CPP-ACP) technology

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to deliver calcium and phosphate ions to enamel surfaces. Recaldent is derived from the milk protein, casein. Casein benefits teeth by bringing calcium phosphates to demineralized enamel.<sup>43</sup> Casein phosphopeptide, CPP, creates a stable delivery vehicle for amorphous calcium phosphate, ACP, and can promote remineralization of sub-surface enamel lesions.<sup>44</sup> At neutral pH or with a high concentration of calcium and phosphate ions, the concentration gradient favors the diffusion of ions back into the tooth causing remineralization.<sup>45</sup> Because it may provide some buffering along with amorphous calcium and phosphate, this product attempts to mimic healthy saliva. Anecdotally, MI Paste may provide comfort for patients with xerostomia and hyposalivary function. MI Paste Plus, launched in the United States in spring 2007, also contains fluoride. More studies are needed to study the effects of adding the fluoride.

#### Conclusion

There is substantial evidence for this technology. Currently there is more in vitro evidence than in vivo to support the benefits of MI Paste. The majority of studies have supported its ability to bring about remineralization by coating the tooth surface with the calcium and phosphate needed to repair demineralized enamel. One study has evaluated its effectiveness in reducing sensitivity associated with tray bleaching. An extension of this would be in treating sensitivity following scaling and root planing, and root surfaces exposed because of gingival recession and/or erosion.

#### Application

MI Paste is recommended for professional dispensing, and can be used by the patient with instruction from the dental staff. Because it contains a milk protein it should not be used on patients with milk protein allergies. It is recommended for patients with dentinal sensitivity, enamel erosions, and salivary gland hypofunction. MI Paste can be applied using a prophylaxis cup, custom tray, or fingertip. In the extreme-risk patient, multiple applications throughout the day is strongly recommended, and could be an option for the high caries risk patient as well. It may also be used in the low- and moderate-risk patient, when excessive root exposure or sensitivity is present.

##### NOVAMIN (E.G., SOOTHERX)

NovaMin is an amorphous, calcium sodium-phosphosilicate that was developed as a fine particulate to physically occlude dentin tubules and reduce dentin hypersensitivity.<sup>46,47</sup> The reaction of NovaMin particles begins when the material is subjected to an aqueous environment and calcium, sodium, and phosphate ions are released. This initial series of reactions

occurs within seconds of exposure, and the release of the calcium and phosphate ions continues so long as the particles are exposed to the aqueous environment.<sup>48,49</sup> The combination of the residual NovaMin particles and a newly formed calcium phosphate layer results in the physical occlusion of dentinal tubules, which will relieve hypersensitivity.<sup>46,47</sup> In one experimental gingivitis study, it was proposed that the material also possesses some local anti-inflammatory action as determined by a reduction in gingival inflammation.<sup>50</sup> Although it has been shown that NovaMin can form apatite-like calcium phosphate, and it is therefore very likely that this product will enhance remineralization in the mouth, but there is no published clinical evidence of this at the time of writing.

NovaMin is available in the form of a toothpaste called SootheRx or Oravive™, currently marketed for dentin sensitivity control.

### Conclusion

There is a considerable research base for this bioactive glass product. It has been shown to reduce sensitivity and is likely to enhance remineralization clinically.

### Application

The manufacturer suggests that initially it be used daily and eventually only once per week.

### CARIFREE SYSTEM

The CariFree System is an early caries detection and treatment approach based on the infectious disease nature of dental caries. The system consists of a screening caries susceptibility test, a rapid bacterial test, a caries risk assessment form, and a unique antimicrobial home care product line to reduce the caries risk.

The home care products use two distinctive but simple strategies: 1) create a pH environment that both favors healthy normal flora rather than caries pathogens and establishes a physiologic pH in hyposalivary patients, and 2) combine synergistic products with already proven efficacy into two simple rinse protocols to increase patient acceptance.

Mutans streptococci has the ability to survive in low pH environments requiring

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the high production and uses of energy (adenosine triphosphate, ATP) to survive. Numerous studies have documented a significant relationship between ATP levels and colony forming units (CFUs) of many species of bacteria, and fungi in the mouth.<sup>51-53</sup> The CariScreen caries susceptibility screening test is a one-minute, real-time chairside screening test based on ATP bioluminescence that has shown to have a strong correlation between the ATP levels of the dental biofilm and the patient's CFUs of mutans streptococci.

The CariFree Caricult is a rapid culture for MS, from plaque that is incubated and read after only 12 to 24 hours. Based on the combined results of the screening tests, caries risk assessment form, and bacterial cultures, a diagnosis is made for the patient's caries risk level.

The CariFree product line also includes an oral breath spray with a pH of 9

(CariFree Boost) for patients with reduced salivary flow. The spray contains xylitol, moisturizing agents, calcium hydroxide, anthocyanins, polyphenol, flavoring, and buffering agents. It can be conveniently used throughout the day to relieve dryness and neutralize acid attacks as needed.

The CariFree oral care products are targeted specifically at the known traits of the cariogenic biofilm, the primary one being the pH drop from the acidic by-products of the sugar metabolism by the biofilm.<sup>54</sup> The CariFree products were designed to reverse the low pH and drive the selection pressure equation back toward health. The CariFree Treatment Rinse is a two-component short-term (two weeks) rinse involving a one-minute/one-time-per-day protocol for easy patient compliance. The active ingredient is 0.05 percent sodium fluoride at a pH of 11. (Decalcification occurs at approximately pH 5.5.) Other ingredients include calcium hydroxide, sodium hypochlorite, anthocyanins, polyphenol, flavoring, and buffering agents.

Once the patient has completed the CariFree Treatment Rinse cycle, they are placed on the CariFree Maintenance Rinse for long-term strategies. The Maintenance Rinse is a 0.05 percent sodium fluoride rinse with an elevated pH of 8. This rinse also contains xylitol, calcium hydroxide, anthocyanins, polyphenols, flavoring, and buffering agents. The patients can use the CariFree Maintenance Rinse on an ongoing basis as part of their remineralization and anticaries strategies. They are routinely tested at the end of one month of the rinse therapies for their caries susceptibility with the CariScreen test.

### Conclusion

Although all of the above ingredients have been studied individually, they have not been studied collectively as the CariFree system. The culturing

methods and bioluminescence need to be validated. Therefore, more research is warranted on this promising approach.

### Application

The CariFree Treatment Rinse (0.05 percent NaF rinse, pH 11) and Maintenance Rinse (0.05 percent NaF rinse, pH 8) could be used as substitutes for the 0.05 percent NaF rinses recommended for the moderate-, high- and extreme-risk patient. The CariFree Boost (0.05 percent NaF spray, pH 9) was developed for the extreme-risk patient.

## Products of the Future

### CARIES VACCINE

The quest to find a caries vaccine has been going on for more than three decades, but the fruits of this endeavor have been unmeritorious. Within the humoral system, antibodies produced in response to a vaccine have a pathway to travel to the site of the invading pathogen. The problem in the oral cavity is that antibodies in the blood system cannot transverse the oral mucosa to get to the mutans streptococci on the teeth. The one glimmer of hope with this approach is to immunize a child around one year of age, before *S. mutans* is transmitted from the child's mother or caregiver. Pediatric clinical trials are needed to validate this approach.<sup>55</sup>

Mucosal immunization with an antigen made from an enzyme that allows *S. mutans* to attach to the tooth surface is another approach. Mucosal immunization is administered by a tonsillar or nasal topical spray.<sup>56,57</sup> A clinical trial is currently being planned to test this modality.

Lastly, passive administration of antibody to epitopes (three-dimensional chemical groups on the surface of an antigen) of *S. mutans* has provided some degree of protection in small-scale hu-

man investigation.<sup>55</sup> In summary, the reality of some form of a caries vaccine faces significant scientific challenges and political hurdles that may take several decades before becoming a reality.<sup>58</sup>

### PROBIOTICS (REPLACEMENT THERAPY)

Probiotics is a new approach being developed to manage dental caries by selectively removing only the (odonto) pathogen while leaving the remainder of the

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oral ecosystem intact.<sup>59</sup> One of the better examples of this approach is a genetic manipulation being devised by Hillman and coworkers.<sup>60</sup> His group has genetically modified a *S. mutans* organism that no longer is capable of producing lactic acid, but can still survive in its ecological niche with the other wild-type *S. mutans*. In theory, when this modified organism is introduced into a host, it will completely displace the disease-causing *S. mutans* wild-type and prevent it from re-emerging as a pathogenic organism. Unfortunately this engineered strain still produces acetic acid and, in combination with lactic acid from other species such as the lactobacilli, may limit its success. Some human trials are currently underway with no results known at time of writing.

Another approach to reduce pathogen content is called "targeted antimicrobials" or specifically (or selectively) tar-

geted antimicrobial peptides (STAMPs).<sup>61</sup> The basic idea is to develop a targeting molecule that will attach specifically to *S. mutans*. Then a killer molecule is chained to the targeting molecule and introduced into the oral cavity where it selectively eliminates the disease-causing *S. mutans*. Time will tell how successful this approach might be.

### CHINESE MEDICINAL HERBS

As new pathogens emerge and old pathogens become resistant to current antibiotics, the search for new antibacterial compounds is accelerating and many old sources are being reconsidered. One logical source is Chinese medicinal herbs because of their proven ability to treat microbial infections. One specific group of herbs that may have therapeutic application in dentistry has been reported in studies by Qing Re Jie Du et al.<sup>62</sup> He et al. conducted a systematic screening of this group of herbs and found that *Glycyrrhiza uralensis* (Chinese name "Gancao" or Chinese licorice) exhibited a strong antimicrobial activity against *S. mutans*.<sup>63</sup> This extract has been formulated into a lollipop and has been clinically tested in a limited human study with promising results. ■■■■

## Conclusions

As the evidence base for the products described above evolves, so will our understanding of how and when they should be used. With time, new technologies will direct us into different approaches and interventions.

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