THE JOURNAL OF THE AMERICAN DENTAL ASSOCIATION

J A D A

The Potential of Dental-Protective Chewing Gum in Oral Health Interventions

Kiet A. Ly, Peter Milgrom and Marilynn Rothen

J Am Dent Assoc 2008;139;553-563

The potential of dental-protective chewing gum in oral health interventions

Kiet A. Ly, MD, MPH; Peter Milgrom, DDS; Marilynn Rothen, RDH, BS

ABSTRACT

Background. The authors provide an overview of chewing gum as a delivery vehicle for dental-protective agents, highlighting xylitol and its potential application in caries-prevention programs for children.

Types of Studies Reviewed. The authors reviewed selected clinical investigations and previous reviews associated with chewing gum containing substances such as calcium, bicarbonate, carbamide, chlorhexidine, fluoride and xylitol and their effects on reducing caries. They searched the MEDLINE database by using the key words "dental caries," "oral health," "calcium," "bicarbonate," "carbamide," "chlorhexidine," "fluoride" and "xylitol."

Results. Chewing gum is being used as a delivery vehicle for substances such as calcium, bicarbonate, carbamide, chlorhexidine, fluoride and xylitol to improve oral health and reduce caries. These substances exhibit properties that are protective of the oral environment and mediate common oral diseases. The debate for advocating xylitol use in caries prevention is advancing; however, chewing gum use by young schoolchildren in the United States is hindered by choking hazard concerns and lack of specific xylitol dosing recommendations.

Clinical Implications. The use of chewing gum containing dental-protective substances, particularly xylitol, in caries-prevention programs can reduce the tooth decay epidemic. Chewing gum use by children in the school setting should be reconsidered.

Key Words. Chewing gum; public health; oral health; caries; polyols; xylitol.

JADA 2008;139(5):553-563.

Chewing gum commonly is thought of as being part of the American culture, and it was popularized in Europe during World War II when it was included in U.S. Army rations.[1] While the first U.S. patent for a chewing gum was issued in 1869 to Dr. W.F. Semple,[2] the chewing of nonfood items and gummy substances for pleasure can be traced back to ancient Greek culture and later throughout the Middle East, as well as among Mayan Indians in the early centuries A.D.[1] Today, chewing gum is a worldwide multibillion-dollar industry, with more than one-half million tons used annually.[2] The United States leads the world in consumption at 2.5 kilograms per capita, with annual expenditures of more than $.5 billion.[1]

Chewing gum typically consists of a sweetener, gum base, flavoring and an aromatic agent. Historically, chewing gum was sweetened with sucrose (table sugar) and contributed to tooth decay. Today, more than 50 percent of chewing gums are sweetened with sugar substitutes such as polyol sweeteners, artificial sweeteners or both. Study results have shown that oral bacteria do not use these sugar substitutes to produce acids that demineralize enamel and dentin,[2] so they are accepted as noncariogenic by the U.S. Food and Drug Administra-

Dr. Ly is an acting assistant professor, Department of Dental Public Health Sciences, Northwest/Alaska Center to Reduce Oral Health Disparities, Warren G. Magnuson Health Sciences Center, Room B-509, University of Washington, Seattle, Wash. 98195-7475, e-mail "kietaly@u.washington.edu". Address reprint requests to Dr. Ly.

Dr. Milgrom is a professor, Department of Dental Public Health Sciences, an adjunct professor, Health Services, and the director, Northwest/Alaska Center to Reduce Oral Health Disparities, Warren G. Magnuson Health Science Center, University of Washington, Seattle.

Ms. Rothen is a clinic manager, Regional Clinical Dental Research Center, Warren G. Magnuson Health Sciences Center, University of Washington, Seattle.

tion (FDA). Furthermore, the act of gum chewing is a potent stimulator of saliva flow, which increases buffering capacity and enhances clearance of food debris and microorganisms from the oral cavity.

Chewing gums have been studied and used as delivery vehicles for a host of dental substances such as calcium, bicarbonate, carbamide, chlorhexidine (CHX), fluoride and polyol sweeteners, as well as medicinal substances such as nicotine, methadone, aspirin, motion sickness antihistamine agents, antifungal agents, caffeine and vitamins. Chewing polyol-sweetened gum, particularly xylitol-containing gum, alone or in combination with other dental-protective substances in oral health and caries-prevention programs for high-risk populations may facilitate reaching the U.S. national oral health goals.

In this article, we provide an overview of chewing gum as a delivery vehicle for dental-protective agents and its potential application in oral health and caries-prevention programs for children. We highlight chewing gum containing xylitol, a polyol sweetener that reduces plaque, salivary *Streptococcus mutans* levels and tooth decay, as well as promotes remineralization.

THE EFFECTS OF GUM CHEWING ON ORAL HEALTH

Common claims for the effects of gum chewing include cleansing food debris from teeth and plaque, stimulating salivary flow, increasing the pH of saliva and plaque, and reducing gingivitis and periodontitis. In a critical literature review of gum chewing's effects and applications, Imfeld[2] found that gum chewing is a potent stimulator of salivary flow, which is a function of the mechanical act of mastication. Gum chewing after meals stimulates salivary flow that has an increased concentration of bicarbonate, which results in elevated plaque pH and enhanced acid-buffering capacity. The stimulated saliva is also in a state of mineral supersaturation that promotes enamel remineralization; this effect is lost, however, when sucrose-based chewing gum is chewed. Sucrose-free chewing gums (that is, sugar-free chewing gums containing appropriate amounts of dental-protective substances alone or in combination) may be used in preventive health programs to improve oral health. Imfeld[2] found little evidence that chewing gum reduces gingivitis or is effective in removing plaque, particularly in interproximal areas and in the gingival one-third of the crown.

CHEWING GUM CONTAINING FLUORIDE, MINERALS, ALKALINIZING AGENTS AND CHLORHEXIDINE

Fluoride-containing chewing gum was introduced in the early 1960s as an alternative to fluoride tablets for high-risk populations that were not served by fluoridated water systems or fluoridated salt distribution plans. Fluoride-containing chewing gum has more than 80 percent oral bioavailability,[3] reduces demineralization and enhances remineralization of enamel.[4-6] Fluoride-containing chewing gum, however, is not available in the United States, although it is elsewhere in the world.

The use of chewing gum to deliver minerals such as calcium and phosphate into the oral cavity also has been explored since the 1960s. The results of studies of the use of various forms of calcium phosphates in chewing gums showed enhanced acid-buffering capacity and decreased demineralization.[7,8] Chewing gum containing xylitol and calcium lactate showed enhanced remineralization of enamel surfaces cut from an extracted tooth and placed in a retainer in situ when compared with chewing gum containing only xylitol and with no gum.[9] In another in situ study, Cai and colleagues[10] showed that use of chewing gum containing citric acid and casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) resulted in significantly greater remineralization than did chewing gum containing no CPP-ACP or citric acid or chewing gum containing citric acid alone. Neither of these studies, however, was a formal randomized clinical trial involving patients in normal conditions.

Bicarbonate has been used to alkalinize saliva and plaque effectively.[11,12] Igarashi and colleagues[13] showed that including a combination of sodium bicarbonate and sorbitol in chewing gum enhanced the chewing gum's ability to increase and maintain plaque pH after a fermentable carbohydrate challenge in volunteers in a laboratory. Other researchers using various forms of market-available bicarbonate-containing chewing gum reported increases in salivary pH and reduction of dental plaque and gingivitis.[14-16]

ABBREVIATION KEY. **Δ DMFS:** Change in decayed, missing and filled surfaces. **CHX:** Chlorhexidine. **CPP-ACP:** Casein phosphopeptide-amorphous calcium phosphate. **defs:** Decayed, extracted and filled surfaces. **DMFS:** Decayed, missing and filled surfaces. **FDA:** U.S. Food and Drug Administration. **x/s:** Xylitol-sorbitol.

These results are important for patients with dry mouth.

The antiseptic agent CHX has been used in mouthrinses to treat gingivitis and periodontitis and as a short-term substitute for mechanical brushing. Chewing gums containing CHX minimize undesirable characteristics such as staining and bitter taste, while maintaining an effectiveness similar to that of CHX mouthrinses.[2] Ainamo and colleagues[17] showed that chewing two pieces of gum containing 5 milligrams of CHX twice a day while not using any other oral hygiene measures for five days was as effective in inhibiting plaque growth as was rinsing with CHX (0.2 percent) twice a day. Other investigators found similar results.[18,19] In a study of elderly people who chewed gum that contained a combination of CHX and xylitol, researchers found a significant reduction in *S. mutans* and lactobacilli levels.[20] Although the CHX 0.2 percent mouthrinse is available in many countries, only 0.12 percent CHX rinse has been approved by the FDA for use in the United States.

Dental-protective and medicinal chewing gums are available in the United States (Table 1). Product labeling, however, often is insufficient, leaving it unclear whether oral health products contain adequate amounts of the dental-protective substances to be effective. This lack of clarity is further compounded by the lack of guidelines for dose, frequency of consumption and length of use of these dental-protective chewing gums for clinical effectiveness. Large-scale randomized clinical trials are needed to address questions of clinically effective dose, frequency of consumption and length of use.

POLYOL-SWEETENED CHEWING GUM AND TOOTH DECAY

Polyol sweeteners, commonly known as sugar alcohols, have been used as substitutes for sucrose and fructose in sugar-free food and confectionary products, as well as in pharmaceutical and nutraceutical products, in the United States for several decades. They are absorbed and metabolized incompletely by the body and, thus, contribute fewer calories than do sucrose or fructose.[21] Although most polyol sweeteners are less sweet than sucrose, maltitol and xylitol have comparable sweetness (Table 2, page 557). Polyol sweeteners are regulated by the FDA and are classified as Generally Recognized As Safe and approved as food additives. Furthermore, the FDA has authorized the use of a health claim in food labeling that says that polyol sweeteners do not promote tooth decay. These noncariogenic sweeteners are used in food, confectionary and other products marketed to promote better oral health and diet control.[21]

Within the polyol class, xylitol and sorbitol have been thoroughly studied. Sorbitol generally is accepted to be noncariogenic.[22] Xylitol, on the other hand, is actively protective against tooth decay through reductions in *S. mutans* and levels of lactic acid produced by these bacteria.[21] An overview of selected clinical studies in which xylitol-containing and sorbitol-containing products were included is shown in Table 3 (pages 558 and 559).[23-39] Chewing gum was the delivery vehicle in most of these studies, and, in most of the studies, participants were asked to chew the gum for five minutes. Overall, the study results suggest that habitual use of xylitol-containing chewing gum and other xylitol-containing confectionary products reduces *S. mutans* levels, tooth decay or both, and a greater reduction is observed with higher doses of xylitol and higher frequencies of consumption. The studies' findings also suggest that combining other polyols with xylitol results in products that are more effective than those that contain sorbitol alone, but they are not as effective as products that contain xylitol alone.[21] That is, the presence of other polyol sweeteners may enhance, but not reduce, xylitol's effectiveness.

XYLITOL IN FOCUS

Xylitol can be found in small quantities in fruits and vegetables and is produced as part of human metabolic processes. Similar to other polyols in its class, xylitol has been used mostly as a sugar-free sweetener in foods and candies in the United States but less often than other polyols because they are less expensive. There has been a recent increase in the use of xylitol in food, confections, chewing gums and dental products, which can be attributed, in part, to xylitol's caries-protective effects and its reduced caloric content. Most xylitol-containing products, however, were not designed for clinical effectiveness. The main adverse effect associated with consumption of xylitol, as well as with other polyol sweeteners, is osmotic diarrhea, which occurs when xylitol is consumed in quantities four to five times that needed for dental caries prevention. Xylitol is safe for use in children when it is consumed in quanti-

TABLE 1

Samples of medicated chewing gums available in the United States.*

BRAND NAME	MANUFACTURER	ACTIVE SUBSTANCE	AIM
Dental-Protective Products			
Arm & Hammer Dental Care	Church & Dwight (Princeton, N.J.)	Bicarbonate	Acid buffing, caries prevention
Trident Advantage	Cadbury Adams USA (Parsippany, N.J.)	Bicarbonate	Acid buffing, caries prevention
Biotene	Laclede (Rancho Domingues, Calif.)	Lactoperoxidase, glucose oxidase	Dry mouth relief, caries prevention
Epic Xylitol Gum	Epic Dental (Provo, Utah)	Xylitol	Caries prevention
TheraGum	Omni Preventive Care (West Palm Beach, Fla.)	Xylitol	Caries prevention
Spry Xylitol Gum	Spry (Orem, Utah)	Xylitol	Caries prevention
Breath Rx	Discus Dental (Culver City, Calif.)	Zinc chloride	Breath freshening
Medicinal Products			
Aspergum	Insight Pharmaceuticals (Langhorne, Pa.)	Aspirin	Pain relief
Chooz	Heritage (Brookfield, Conn.)	Calcium carbonate	Antacid action, calcium supplementation
Stay Alert	Wm. Wrigley Jr. (Chicago)	Caffeine	Alertness
Jolt	GumRunner (Hackensack, N.J.)	Caffeine	Alertness
Blitz	Schuster Marketing (Milwaukee)	Caffeine	Alertness
Nicorette	GlaxoSmithKline (Philadelphia)	Nicotine	Smoking cessation
Nicotine Polacrilex Gum	Rite Aid (Camp Hill, Pa.)	Nicotine	Smoking cessation
Herbal and Health Products			
WellFast	Nutraceutical (Park City, Utah)	Echinacea root extract	General health enhancement, cold prevention
Anti-Nausea Ginger Gum	Sea-Band (Newport, R.I.)	Ginger root	Antinausea action
Ginseng Chewing Gum	Lotte (Battle Creek, Mich.)	Ginseng	General health enhancement
Kola Energy Gum	Penguin Mints & Gum (Seattle)	Ginseng and kola nut	Energy enhancement, general health enhancement
Mega-T Green Tea	CCA Industries (East Rutherford, N.J.)	Green tea	Antioxidant action, diet
Zoft Hoodia Gum	Zoft (Port St. Lucie, Fla.)	Hoodia plant extract	Diet
Nutra-Trim Gum	GumRunner	L-carnitine, chromium	Diet
SteviaDent	Stevita (Arlington, Texas)	Stevia plant extract	Diet
Penguin Citrus Energy	Penguin Mints & Gum	Taurine and guarana	Energy, general health enhancement
Peelu Gum Vitamin C	Peelu USA (Fargo, N.D.)	Vitamin C, arak extract	General health enhancement

* This list shows representative samples and is not comprehensive, particularly for xylitol- and herb-containing products, for which the number of brands and products are increasing rapidly.

ties appropriate for dental caries prevention.[40,41] In the planning of a caries-prevention program involving the use of xylitol, it would benefit participants if xylitol were introduced slowly and at increasing doses to allow for their bodies to acclimate to the polyol because many people, especially young children, are not accustomed to consuming several grams of xylitol per day. It also is important in the initial phase to monitor young children closely for loose stools or diarrhea, which may lead to dehydration and require that the children undergo hydration therapy.

S. mutans does not readily metabolize xylitol into energy; however, xylitol is absorbed and accu-

mulated intracellularly. Xylitol competes with sucrose for its cell-wall transporter and its intracellular metabolic processes.[42] Unlike the metabolism of sucrose, for which net energy is produced and *S. mutans* growth is promoted, the metabolic process for xylitol does not yield energy but instead creates a net energy loss. This loss has been referred to as the "futile cycle."[43,44] Furthermore, the energy-producing intermediates are consumed and not reproduced during xylitol metabolism.[42] The end result is *S. mutans* cellular death and, thus, a reduction in *S. mutans* levels. In addition to reducing *S. mutans* levels, long-term habitual consumption of xylitol appears to have a selective effect on *S. mutans* strains,[45] which results in the selection for *S. mutans* strains that are able to use xylitol but are less virulent.[46] This effect may explain why xylitol influences the transmission of *S. mutans* from mothers to their children and why these children experience less dental decay.

TABLE 2

Properties of natural sugars and sugar substitutes.*

TYPE OF SWEETENER	NUTRITIVE VALUE (CALORIES/GRAM)	CARIOGENIC	SUGAR-FREE LABEL (NONCARIOGENIC)	SWEETNESS†
Natural Sugars				
Fructose	4	Yes	No	1.5
Glucose	4	Yes	No	0.7
Lactose	4	Yes	No	0.2
Sucrose	4	Yes	No	1.0
Sugar Substitutes				
Polyols				
Erythritol	0.02	No	Yes	0.8
Hydrogenated starch hydroxylate	3.0	No	Yes	0.4-0.9
Isomalt	2.0	No	Yes	0.5
Lactitol	0.02	No	Yes	0.4
Maltitol	2.1	No	Yes	0.9
Mannitol	1.6	No	Yes	0.5
Sorbitol	2.6	No	Yes	0.6
Xylitol	2.4	No	Yes	1.0
Artificial sweeteners				
Acesulfame potassium	0.0	No	Yes	200
Aspartame‡	0.0	No	Yes	180
Saccharin	0.0	No	Yes	300
Sucralose	0.0	No	Yes	600

* Adapted with permission of the American Academy of Pediatric Dentistry from Ly and colleagues.[21]
† Sucrose (table sugar) is the standard for sweetness comparison and is given the sweetness value of 1 (the reference point).
‡ Aspartame is technically a nutritive sweetener. Because of its intense sweetness, however, it is used in such small amounts that its nutritive value is negligible.

Investigators have evaluated the effectiveness of xylitol in caries reduction. The results of the Turku sugar studies of the early 1970s showed that subjects who replaced fructose and sucrose in their diets with xylitol had an 85 percent reduction in caries.[23] In a 40-month trial evaluating xylitol-containing gum chewing and dental caries conducted in Belize, 1,277 children in the fourth grade (mean age, 10.2 years) were assigned randomly to one of nine groups: four 100 percent xylitol groups of varying dose (4.3-9.0 g/day) and frequency of daily use (three or five times per day), two xylitol-sorbitol (x/s) groups (8.0-9.7 g/day), one sorbitol-only group (9.0 g/day), one sucrose-only group and a no-gum (control) group.[31] All study chewing gums were chewed during school hours under supervision. The results showed that chewing 100 percent xylitol-containing pellet chewing gum resulted in the highest caries reduction (relative risk [RR] = 0.27; 95 percent confidence interval [CI] = 0.20-0.36; $P = .0001$) when compared with results in the control group. Groups that consumed a higher xylitol dose had greater caries reduction than did groups that consumed a lower dose. Use of x/s mixed chewing gum led to less, but still significant, caries reduction. Use of pellet chewing gums led to higher caries reductions than did use of stick chewing gums. The sucrose gum group fared worse than did the control group (adjusted change in decayed, missing and filled surfaces [Δ DMFS] of 6.6 versus 4.9, respectively; adjusted RR of 1.20 [95 percent CI = 0.96-1.49]).

The adjusted Δ DMFS and RR for other groups

TABLE 3

Summary of selected clinical trials that included the use of xylitol chewing gum and reported a reduction in *Streptococcus mutans*, mutans streptococci or caries.*

STUDY	STUDY METHOD	POPULATION
Scheinin and colleagues[23]	24 months, three groups (xylitol, fructose, sucrose)	Adults (N = 125), age: 27 years (average)
Loesche and colleagues[27]	Four weeks chewing then four weeks not chewing, three groups (xylitol, fructose, sorbitol/mannitol)	Children (N = 80), pediatric dentistry clinic
Kandelman and Gagnon[28]	24 months, three groups (xylitol 15 percent, xylitol 65 percent, no chewing gum)	Children (N = 433), age: 8-9 years
Isokangas[29]	24 months, retrospective study, original cohort categorized into three chewing frequencies	Children (N = 212), age: 11-12 years
Kandelman and colleagues[30]	32 months, two groups (xylitol, no xylitol snack foods)	Children (N = 468), age: 6-12 years
Isokangas and colleagues[31]	24 months, two groups (xylitol chewing gum versus no chewing gum)	Children (N = 212), age: 11-12 years
Rekola[32]	12 months, retrospective study, original cohort categorized into chewing frequencies	Young adults (N = 100), age: 22 years (average)
Wennerholm and colleagues[33]	25 days chewing crossover, four groups (three xylitol, one sorbitol)	Adult (N = 20), age: 25.5 years (average)
Makinen and colleagues[34]	24 months, six groups (three xylitol, two sorbitol, one no chewing gum)	Children (N = 510), age: 6 years, 10 schools, three of which had no gum chewing
Makinen and colleagues[24,35]	40 months, nine groups (six xylitol, one sorbitol, one sucrose, one no chewing gum [control])	Children (N = 1,227), age: 10 years
Makinen and colleagues[36]	16 months of intensive treatment, one group (high-risk participants)	Children (N = 109), age: 13.5 years (mean)
Alanen and colleagues[37]	60 months, three groups (two-year or three-year xylitol, sealants)	14 classrooms of fifth graders
Kovari and colleagues[38]	32 months, two groups (xylitol, brushing)	Children (N = 921), 11 day-care centers
Thaweboon and colleagues[39]	Three months, three groups (xylitol 55 percent, xylitol 100 percent, no chewing gum)	Children (N = 91), age: 10-12 years
Milgrom and colleagues[25]	Six months, four groups (xylitol varying dose or control [sorbitol] chewing gum)	Adults (N = 132)
Ly and colleagues[26]	Five weeks, four groups (xylitol chewing gum varying frequency of two, three and four times per day or control [sorbitol] chewing gum)	Adults (N = 132)

* Adapted with permission of the Academy of Pediatric Dentistry from Ly and colleagues.[21]
† DMFS: Decayed, missing and filled surfaces.
‡ x/s: Xylitol/sorbitol.

(continued on next page)

CONSUMPTION FREQUENCY	XYLITOL DOSE (GRAMS PER DAY)	CONCLUSION
One piece, 4.5 times per day on average (range, three-seven)	6-7	Reduction in caries increment rate
Two pieces, five times per day	5-7	Reduction in unstimulated saliva and plaque *Streptococcus mutans* level
One piece, three times per day, school days only	15 percent: 0.8 65 percent: 3.4	Lower DMFS† increment of decay in both active groups
One piece, three times per day	10.5 (3.5 g/piece)	Lower DMFS increment with frequency of three times per day or more groups
Combination of xylitol snack foods daily	20 (combined maximum)	Lower DMFS increment than no-xylitol control subjects
One piece, three times per day	10.5 (3.5 g/piece)	Lower DMFS increment than control subjects
One piece, 4.5 times per day on average (range, three-seven)	6-7	Greater reduction in caries incidence with increased frequency of use
One piece, 12 times per day	13.4, 6.7, 3.36	Higher xylitol level associated with lower *S. mutans* levels in plaque and saliva; xylitol 3.36 g same as control subjects
One stick or two pellets, five times per day	x/s‡: 7.11, x/s: 9.68 xylitol stick: 10.42 xylitol pellet: 10.67	Reduction in caries rate among groups chewing gums; 100 percent xylitol pellet chewing gum is most effective
Three to five times per day	x/s mixed three times per day: 7.11 x/s mixed five times per day: 9.68 xylitol stick three times per day: 6.25 xylitol stick five times per day: 10.42 xylitol pellet three times per day: 6.40 xylitol pellet five times per day: 0.67	Reduction in caries increment among chewing gum groups except sucrose; 100 percent xylitol pellet is most effective Saliva *S. mutans* not increased with age among 100 percent xylitol pellet groups as in other groups
Seven times per day	14 (maximum)	Reduction in caries onset rate and in DMFS score
Two pieces of Xylifresh (Leaf, Turku, Finland) three times per day on school days	5	No difference in DMFS increment between sealant and xylitol groups
One piece three times per day (Xylifresh) day-care hours	2.5	No difference in decayed, missing and filled scores between xylitol and brushing
Two pieces three times per day school days only	55 percent: 5.76 100 percent: 11.88	Reduction in saliva and plaque *S. mutans* counts in both treatment groups
Three pellets four times per day	Group 1: 3.44 Group 2: 6.88 Group 3: 10.32	Dose-response reduction of *S. mutans* in saliva and plaque; plateau between 6.88 g/day and 10.32 g/day; difference not significant for 3.44 g/day
12 pellets of control or xylitol-containing gum per day; xylitol-containing gum is chewed two, three or four times per day	10.32 or control (sorbitol)	Linear response reduction of *S. mutans* in saliva and plaque to increasing frequency; difference not significant for two times per day

compared with the control group were as follows: high-dose xylitol-containing pellet chewing gum (Δ DMFS of -0.8; RR of 0.27 [95 percent CI = 0.20-0.36]); low-dose xylitol-containing pellet chewing gum (Δ DMFS of 0.9; RR of 0.41 [95 percent CI = 0.31-0.54]), high-dose xylitol-containing stick chewing gum (Δ DMFS of 0.6; RR of 0.44 [95 percent CI = 0.34-0.56]) and low-dose xylitol-containing stick chewing gum (Δ DMFS of 0.1; RR of 0.48 [95 percent CI = 0.37-0.61]). The two x/s mixed groups had Δ DMFSs of 0.6 and 2.2, and RRs of 0.49 (95 percent CI = 0.38-0.65) and 0.56 (95 percent CI = 0.44-0.71).

Results from other studies, particularly those in which similar xylitol doses and frequencies of consumption were used, support these findings (Table 3).[23-39] Overall, results from these studies suggest that the amount of xylitol in chewing gums or confections and the frequency of use determine the degree of reduction observed; greater reduction was seen with higher xylitol dose and frequency of use.[21] There appears to be a plateau effect with higher dosages.

After conducting a six-month, four-group, randomized trial of xylitol-containing chewing gum to assess salivary and plaque *S. mutans* responses to increasing xylitol dose (3.4-10.3 g/day), Milgrom and colleagues[25] reported a significant reduction in plaque *S. mutans* levels after five weeks and six months of exposure compared with results from the control group that used sorbitol-containing chewing gum. The results also suggested a plateau effect between 6.9 and 10.3 g/day. Furthermore, the group that received a xylitol dose of 3.4 g/day did not show a significant reduction, although a small reduction was observed.

Another randomized trial in the same series of studies evaluated the response of *S. mutans* to varying frequencies (zero, two, three and four) of xylitol-containing chewing gum consumption at a standard daily dose of 10.3 g/day. The results showed a linear increase in *S. mutans* reduction with increasing frequency of xylitol consumption, but a dosing frequency of less than three times per day seemed to have limited or no benefit.[26] There is some agreement in the literature that a xylitol dose of 5 to 10 g/day divided into at least three frequencies of consumption are needed for therapeutic effects.

Study results also have shown that xylitol can reduce or delay acquisition of *S. mutans* and reduce caries in young children whose mothers chewed xylitol-containing gum in the perinatal period. In a two-year study, Söderling and colleagues[47] recruited mother-infant pairs and assigned them to one of three groups: xylitol-containing chewing gum (n = 106), CHX varnish (n = 30) or fluoride varnish (n = 33). Mothers received varnish treatments at six, 12 and 18 months after delivery or were asked to chew xylitol-containing chewing gum at least two or three times a day beginning at three months after delivery. The children did not receive any treatment. At two years of age, only 9.7 percent of children whose mothers were in the xylitol-containing chewing gum group had detectable mutans streptococci, compared with 28.6 percent and 48.5 percent in the CHX and fluoride groups, respectively.

In a similar one-year study, mothers with high levels of mutans streptococci were randomized into one of three groups: xylitol-containing (n = 61), CHX/xylitol-containing (n = 55) or fluoride-containing (n = 57) chewing gum.[48] The reference group (n = 232) included mothers with low or medium mutans streptococci counts; they received no intervention. The mothers began using the chewing gum at six months postpartum. Thorild and colleagues[48] found 10 percent of 18-month-old children of mothers in the xylitol-containing chewing gum group harbored mutans streptococci compared with 16 percent and 28 percent in the CHX/xylitol-containing chewing gum and fluoride-containing chewing gum groups, respectively. In the reference group, 10 percent of the children had detectable mutans streptococci. When the children were followed up until 3 years of age, researchers found that 13 percent of the children with mothers in the xylitol-containing chewing gum group had medium to high counts of salivary mutans streptococci and a decayed, extracted and filled surfaces (defs) mean of 0.1 compared with 16 percent of children with mothers in the CHX/xylitol-containing chewing gum group who had a mean defs of 0.2 and 22 percent of the children with mothers in the fluoride-containing chewing gum group who had a mean defs of 0.4.[49] The reference group results were between the xylitol and CHX/xylitol groups. When the children were 4 years of age and 15 to 20 percent in the treatment groups had dropped out, the authors found that the mean defs was 0.4 ± 1.0 (standard deviation [SD]) for the xylitol-containing chewing gum group, 0.7 ± 1.7 SD for the CHX/xylitol-containing chewing gum group and 1.4 ± 3.0 SD for the fluoride-containing chewing gum group. The difference between the xylitol and fluoride groups was statistically significant.[50]

POTENTIAL APPLICATIONS OF GUM CHEWING FOR CHILDREN AT HIGH RISK OF EXPERIENCING CARIES

The mainstays of primary prevention for children are fluoridated water, fluoridated toothpaste, professionally applied topical fluorides, sealants and dietary change. The fluorides, unless they are provided widely and consistently, are limited in their effectiveness against virulent dental caries. Sealants are used primarily to protect permanent molars. By the time the teeth are fully erupted and sealable, a sizeable minority already have caries. Effective strategies to reduce risk by modifying children's diets are not readily applicable to dental practice, nor are they typically effective without significant effort.

Given the popularity of chewing gum in the United States, the use of dental-protective consumer products such as xylitol-containing and CHX-containing chewing gum may be a desirable adjunct to other practices. CHX chewing gum is available in Europe but not in the United States. Xylitol-containing chewing gum is readily available in the United States and is well-accepted by school-aged children.[51] However, a major limitation in extending the benefits of chewing xylitol-containing and CHX-containing chewing gum to children in the United States is that chewing gum is not considered to be a safe practice for small children by the American Academy of Pediatrics because it presents a choking risk,[52] and it is discouraged in day care and schools by teachers and school officials.

In a study examining the acceptance of a xylitol-containing chewing gum regimen by preschoolers and teachers in a Head Start program, Autio and colleagues[51] found that children readily accepted the xylitol-containing chewing gum, but teachers' acceptance rates were low because of concern for classroom disruption and indiscriminate disposal of the chewing gum. Studies of xylitol-containing chewing gum in school settings have not reported these issues as problematic, and children could be taught proper disposal of used gum.

Most of the other xylitol-containing products that have been studied were in the form of mints or hard candies such as lozenges, and they are at least as effective as xylitol-containing chewing gum.[53,54] However, there are concerns in the United States that using such products may create confusion for children and further promote consumption of sugar-sweetened candies. At the University of Washington, researchers produced and field-tested xylitol-containing popsicles, gumdrops, puddings, macaroons and sorbet.[55] They found that children will accept these foods readily when they are offered as part of the daily diet and that children experience no adverse effects from their use.

Considerable work is required to produce commercially viable products that will be accepted and to convince manufacturers to produce them. Furthermore, each new xylitol-containing snack food needs to be tested to establish its effectiveness at preventing decay because certain foods are better than others at delivering and releasing xylitol in the oral cavity.

The most apt delivery vehicle for dental-protective agents appears to be chewing gum, and it has been used successfully in oral health and caries-prevention campaigns and programs. Xylitol-containing chewing gum consumption was promoted widely as part of Finland's Smart Habits xylitol campaign, which was geared toward young teenagers with the aim of improving oral health and reducing dental caries. This approach makes sense because children with high levels of plaque harbor much higher levels of *S. mutans* than do adults. After the campaign's initiation in 1992, the use of xylitol-containing chewing gum by teenagers continued to increase.[56] In a study in which xylitol-containing chewing gum was used in day-care centers, Kovari and colleagues[38] found that collecting used chewing gum from children was not problematic.

Xylitol-containing chewing gum has been promoted actively for its caries-preventive effects. The U.S. Army has implemented its Look for Xylitol First campaign and includes xylitol-containing chewing gum in rations with the aim of preventing tooth decay among deployed troops who often do not brush their teeth for days at a time and consequently have extremely poor oral hygiene.[57] Perhaps, soldiers will again popularize a new type of chewing gum—xylitol-containing chewing gum—or perhaps they will bring xylitol-containing gum to the forefront of thinking about preventive oral health in the United States, particularly for use among young children in whom dental caries is increasing.

CONCLUSION

Chewing gums containing protective substances are effective and have the potential to significantly improve oral health status toward Healthy

People 2010[58] and World Health Organization Global[59] oral health goals. Xylitol-containing chewing gum has been used successfully in Finland's national Smart Habits oral health campaign and by the U.S. Army, and its use for caries prevention is promoted widely in several countries. The American Academy of Pediatric Dentistry has endorsed the use of xylitol-containing products for caries prevention.[60] Perhaps it is time for school officials, policymakers and the American Academy of Pediatrics to consider the public health benefits of chewing gum containing dental-protective substances, especially xylitol. They should re-evaluate the policy forbidding gum chewing in school and the choking hazard labeling, particularly for settings in which chewing gum programs are implemented in controlled environments and children are observed for the duration of the chewing and discarding. With more laxity on the policy forbidding gum chewing in school, large school-based studies of dental-protective chewing gums such as those containing xylitol or CHX can be conducted, and programs can be developed to reduce dental caries and attain national oral health goals. ■

The work cited in this article was supported, in part, by grants 1 P50 DE14254 and T32 DE07132 from the National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, Md., and grant R40MC03622 from the Maternal and Child Health Research Bureau, Health Resources Services Administration, Rockville, Md.

Disclosure. Drs. Ly and Milgrom and Ms. Rothen did not report any disclosures.

1. Redclift MR. Chewing Gum: The Fortunes of Taste. New York: Routledge; 2004.
2. Imfeld T. Chewing gum: facts and fiction—a review of gum-chewing and oral health. Crit Rev Oral Biol Med 1999;10(3):405-419.
3. Bruun C, Givskov H. Release of fluoride from fluoride-containing chewing gum. Community Dent Oral Epidemiol 1978;6(1):27-29.
4. Hattab FN, Green RM, Pang KM, Mok YC. Effect of fluoride-containing chewing gum on remineralization of carious lesions and on fluoride uptake in man. Clin Prev Dent 1989;11(6):6-11.
5. Lamb WJ, Corpron RE, More FG, Beltran ED, Strachan DS, Kowalski CJ. In situ remineralization of subsurface enamel lesion after the use of a fluoride chewing gum. Caries Res 1993;27(2):111-116.
6. De Los Santos R, Lin YT, Corpron RE, Beltran ED, Strachan DS, Landry PA. In situ remineralization of root surface lesions using a fluoride chewing gum or fluoride-releasing device. Caries Res 1994;28(6):441-446.
7. Richardson AS, Hole LW, McCombie F, Kolthammer J. Anticariogenic effect of dicalcium phosphate dihydrate chewing gum: results after two years. J Can Dent Assoc (Tor) 1972;38(6):213-218.
8. Chow LC, Takagi S, Shern RJ, Chow TH, Takagi KK, Sieck BA. Effects on whole saliva of chewing gums containing calcium phosphates. J Dent Res 1994;73(1):26-32.
9. Suda R, Suzuki T, Takiguchi R, Egawa K, Sano T, Hasegawa K. The effect of adding calcium lactate to xylitol chewing gum on remineralization of enamel lesions. Caries Res 2006;40(1):43-46.
10. Cai F, Manton DJ, Shen P, et al. Effect of addition of citric acid and casein phosphopeptide-amorphous calcium phosphate to a sugar-free chewing gum on enamel remineralization in situ. Caries Res 2007;41(5):377-383.
11. Imfeld T. Nutrition and dental caries: non-cariogenic between-meal snacks and sweets: a marketplace for small and average-size businesses in the food industry—an interview with Dr. med. dent. T. Imfeld [in German]. Swiss Dent 1983;4(9):6-10.
12. Nilner K, Vassilakos N, Birkhed D. Effect of a buffering sugar-free lozenge on intraoral pH and electrochemical action. Acta Odontol Scand 1991;49(5):267-272.
13. Igarashi K, Lee IK, Schachtele CF. Effect of chewing gum containing sodium bicarbonate on human interproximal plaque pH. J Dent Res 1988;67(3):531-535.
14. Kleber CJ, Davidson KR, Rhoades ML. An evaluation of sodium bicarbonate chewing gum as a supplement to toothbrushing for removal of dental plaque from children's teeth. Compend Contin Educ Dent 2001;22(7A):36-42.
15. Sharma NC, Galustians JH, Qaqish JG. An evaluation of a commercial chewing gum in combination with normal toothbrushing for reducing dental plaque and gingivitis. Compend Contin Educ Dent 2001;22(7A):13-17.
16. Anderson LA, Orchardson R. The effect of chewing bicarbonate-containing gum on salivary flow rate and pH in humans. Arch Oral Biol 2003;48(3):201-204.
17. Ainamo J, Nieminen A, Westerlund U. Optimal dosage of chlorhexidine acetate in chewing gum. J Clin Periodontol 1990;17(10):729-733.
18. Smith AJ, Moran J, Dangler LV, Leight RS, Addy M. The efficacy of an anti-gingivitis chewing gum. J Clin Periodontol 1996;23(1):19-23.
19. Yankell SL, Emling RC. Efficacy of chewing gum in preventing extrinsic tooth staining. J Clin Dent 1997;8(6):169-172.
20. Simons D, Kidd EA, Beighton D, Jones B. The effect of chlorhexidine/xylitol chewing-gum on cariogenic salivary microflora: a clinical trial in elderly patients. Caries Res 1997;31(2):91-96.
21. Ly KA, Milgrom P, Rothen M. Xylitol, sweeteners, and dental caries. Pediatr Dent 2006;28(2):154-163; discussion 192-198.
22. Burt BA. The use of sorbitol- and xylitol-sweetened chewing gum in caries control. JADA 2006;137(2):190-196.
23. Scheinin A, Makinen KK, Ylitalo K. Turku sugar studies, part V: final report on the effect of sucrose, fructose and xylitol diets on the caries incidence in man. Acta Odontol Scand 1976;34(4):179-216.
24. Makinen KK, Bennett CA, Hujoel PP, et al. Xylitol chewing gums and caries rates: a 40-month cohort study. J Dent Res 1995;74(12):1904-1913.
25. Milgrom P, Ly KA, Roberts MC, Rothen M, Mueller G, Yamaguchi DK. Mutans streptococci dose response to xylitol chewing gum. J Dent Res 2006;85(2):177-181.
26. Ly KA, Milgrom P, Roberts MC, Yamaguchi DK, Rothen M, Mueller G. Linear response of mutans streptococci to increasing frequency of xylitol chewing gum use: a randomized controlled trial [ISRCTN43479664]. BMC Oral Health 2006;6:6.
27. Loesche WJ, Grossman NS, Earnest R, Corpron R. The effect of chewing xylitol gum on the plaque and saliva levels of *Streptococcus mutans*. JADA 1984;108(4):587-592.
28. Kandelman D, Gagnon G. A 24-month clinical study of the incidence and progression of dental caries in relation to consumption of chewing gum containing xylitol in school preventive programs. J Dent Res 1990;69(11):1771-1775.
29. Isokangas P. Xylitol chewing gum in caries prevention: a longitudinal study on Finnish school children. Proc Finn Dent Soc 1987;83(suppl 1):1-117.
30. Kandelman D, Bar A, Hefti A. Collaborative WHO xylitol field study in French Polynesia, part I: baseline prevalence and 32-month caries increment. Caries Res 1988;22(1):55-62.
31. Isokangas P, Alanen P, Tiekso J, Makinen KK. Xylitol chewing gum in caries prevention: a field study in children. JADA 1988;117(2):315-320.
32. Rekola M. Correlation between caries incidence and frequency of chewing gum sweetened with sucrose or xylitol. Proc Finn Dent Soc 1989;85(1):21-24.
33. Wennerholm K, Arends J, Birkhed D, Ruben J, Emilson CG, Dijkman AG. Effect of xylitol and sorbitol in chewing-gums on mutans streptococci, plaque pH and mineral loss of enamel. Caries Res 1994;28(1):48-54.
34. Makinen KK, Hujoel PP, Bennett CA, Isotupa KP, Makinen PL, Allen P. Polyol chewing gums and caries rates in primary dentition: a 24-month cohort study. Caries Res 1996;30(6):408-417.
35. Makinen KK, Chen CY, Makinen PL, et al. Properties of whole saliva and dental plaque in relation to 40-month consumption of chewing gums containing xylitol, sorbitol of sucrose. Caries Res 1996;30(3):180-188.
36. Makinen KK, Hujoel PP, Bennett CA, et al. A descriptive report of the effects of a 16-month xylitol chewing-gum programme subsequent to a 40-month sucrose gum programme. Caries Res 1998;32(2):107-112.
37. Alanen P, Holsti ML, Pienihakkinen K. Sealants and xylitol chewing gum are equal in caries prevention. Acta Odontol Scand

2000;58(6):279-284.
38. Kovari H, Pienihakkinen K, Alanen P. Use of xylitol chewing gum in daycare centers: a follow-up study in Savonlinna, Finland. Acta Odontol Scand 2003;61(6):367-370.
39. Thaweboon S, Thaweboon B, Soo-Ampon S. The effect of xylitol chewing gum on mutans streptococci in saliva and dental plaque. Southeast Asian J Trop Med Public Health 2004;35(4):1024-1027.
40. Forster H, Quadbeck R, Gottstein U. Metabolic tolerance to high doses of oral xylitol in human volunteers not previously adapted to xylitol. Int J Vitam Nutr Res Suppl 1982;22:67-88.
41. Akerblom HK, Koivukangas T, Puukka R, Mononen M. The tolerance of increasing amounts of dietary xylitol in children. Int J Vitam Nutr Res Suppl 1982;22:53-66.
42. Trahan L, Bareil M, Gauthier L, Vadeboncoeur C. Transport and phosphorylation of xylitol by a fructose phosphotransferase system in *Streptococcus mutans*. Caries Res 1985;19(1):53-63.
43. Soderling E, Pihlanto-Leppala A. Uptake and expulsion of 14C-xylitol by xylitol-cultured *Streptococcus mutans* ATCC 25175 in vitro. Scand J Dent Res 1989;97(6):511-519.
44. Pihlanto-Leppala A, Soderling E, Makinen K. Uptake of 14C-xylitol by xylitol-cultured *Streptococcus sobrinus* ATCC 27352 and *Streptococcus mitis* ATCC 36249 in vitro. Proc Finn Dent Soc 1989;85(6):423-428.
45. Trahan L. Xylitol: a review of its action on mutans streptococci and dental plaque—its clinical significance. Int Dent J 1995;45(1 suppl 1): 77-92.
46. Trahan L, Soderling E, Drean MF, Chevrier MC, Isokangas P. Effect of xylitol consumption on the plaque-saliva distribution of mutans streptococci and the occurrence and long-term survival of xylitol-resistant strains (published correction appears in J Dent Res 1993;72[1]:87-88). J Dent Res 1992;71(11):1785-1791.
47. Söderling E, Isokangas P, Pienihakkinen K, Tenovuo J. Influence of maternal xylitol consumption on acquisition of mutans streptococci by infants. J Dent Res 2000;79(3):882-887.
48. Thorild I, Lindau B, Twetman S. Effect of maternal use of chewing gums containing xylitol, chlorhexidine or fluoride on mutans streptococci colonization in the mothers' infant children. Oral Health Prev Dent 2003;1(1):53-57.
49. Thorild I, Lindau B, Twetman S. Salivary mutans streptococci and dental caries in three-year-old children after maternal exposure to chewing gums containing combinations of xylitol, sorbitol, chlorhexidine, and fluoride. Acta Odontol Scand 2004;62(5):245-250.
50. Thorild I, Lindau B, Twetman S. Caries in 4-year-old children after maternal chewing of gums containing combinations of xylitol, sorbitol, chlorhexidine and fluoride. Eur Arch Paediatr Dent 2006;7(4): 241-245.
51. Autio JT, Courts FJ. Acceptance of the xylitol chewing gum regimen by preschool children and teachers in a Head Start program: a pilot study. Pediatr Dent 2001;23(1):71-74.
52. American Academy of Pediatrics. Parenting corner Q&A: Choking prevention. "www.aap.org/publiced/BR_choking.htm". Accessed March 27, 2008.
53. Honkala E, Honkala S, Shyama M, Al-Mutawa SA. Field trial on caries prevention with xylitol candies among disabled school students. Caries Res 2006;40(6):508-513.
54. Alanen P, Isokangas P, Gutmann K. Xylitol candies in caries prevention: results of a field study in Estonian children. Community Dent Oral Epidemiol 2000;28(3):218-224.
55. Lam M, Riedy CA, Coldwell SE, Milgrom P, Craig R. Children's acceptance of xylitol-based foods. Community Dent Oral Epidemiol 2000;28(2):97-101.
56. Honkala S, Honkala E, Tynjälä J, Kannas L. Use of xylitol chewing gum among Finnish schoolchildren. Acta Odontol Scand 1999;57(6): 306-309.
57. Richter P, Chaffin J. Army's "look for xylitol first" program. Dent Assist 2004;73(2):38-40.
58. Healthy People 2010. Oral health. "www.healthypeople.gov/document/HTML/Volume2/21Oral.htm". Accessed March 27, 2008.
59. World Health Organization. Global goals for oral health 2020. "www.who.int/oral_health/publications/goals2020/en/index.html". Accessed March 27, 2008.
60. American Academy of Pediatric Dentistry, Council on Clinical Affairs. Policy on the use of xylitol in caries prevention. Ped Dent 2006;28(7):31-32. "www.webcitation.org/5Tk9TZ2m2". Accessed Nov. 30, 2007.