

An Examination of the Advances in Science and Technology of Prevention of Tooth Decay in Young Children Since the Surgeon General's Report on Oral Health

Peter Milgrom, DDS; Domenick T. Zero, DDS, MS; Jason M. Tanzer, DMD, PhD

This paper addresses a number of areas related to how effectively science and technology have met Healthy People 2010 goals for tooth decay prevention. In every area mentioned, it appears that science and technology are falling short of these goals. Earlier assessments identified water fluoridation as one of the greatest public health accomplishments of the last century. Yet, failure to complete needed clinical and translational research has short-changed the caries prevention agenda at a critical juncture.

Science has firmly established the transmissible nature of tooth decay. However, there is evidence that tooth decay in young children is increasing, although progress has been made in other age groups. Studies of risk assessment have not been translated into improved practice. Antiseptics, chlorhexidine varnish, and polyvinylpyrrolidone iodine (PVI-I) may have value, but definitive trials are needed. Fluorides remain the most effective agents, but are not widely disseminated to the most needy. Fluoride varnish provides a relatively effective topical preventive for very young children, yet definitive trials have not been

conducted. Silver diamine fluoride also has potential but requires study in the United States. Data support effectiveness and safety of xylitol, but adoption is not widespread. Dental sealants remain a mainstay of public policy, yet after decades of research, widespread use has not occurred.

We conclude that research has established the public health burden of tooth decay, but insufficient research addresses the problems identified in the report *Oral Health in America: A Report of the Surgeon General*. Transfer of technology from studies to implementation is needed to prevent tooth decay among children. This should involve translational research and implementation of scientific and technological advances into practice.

KEY WORDS: dental caries; early childhood caries; risk assessment; detection; topical fluorides; chlorhexidine; iodine; diamine silver fluoride; xylitol

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Ample evidence demonstrates that the country is failing to move toward meeting Healthy People 2010 goals to improve the oral health of preschoolers with respect to tooth decay,¹ and this problem is expanding, with higher disease rates and dental workforce shortages.² The Midcourse Review for Healthy People 2010 suggested that tooth decay (caries) rates for children aged 2 to 5 years were increasing, primarily among the poor and minorities, and most lesions are untreated, to say nothing of prevented.¹ Figure 1 is excerpted from this report. The problem likely extends to older poor and minority children, as dental caries lesions are cumulative, and untreated decay of primary teeth strongly predicts the same condition of secondary (permanent) teeth.^{3–8} However, older children are more likely to receive

some preventive care (Figure 2, from the National Survey of Children's Health).⁹

Tooth decay is attributable mostly to the infectious nature of dental caries in humans.^{10–12} Complicating this problem are workforce shortages,¹³ lack of access to care,¹ and discrimination against populations served by Medicaid.^{14,15} This paper examines advances in science and technology associated with prevention of tooth decay in young children since the report *Oral Health in America: A Report of the Surgeon General of 2000*.¹⁶

THE INFECTIOUS NATURE OF CARIES

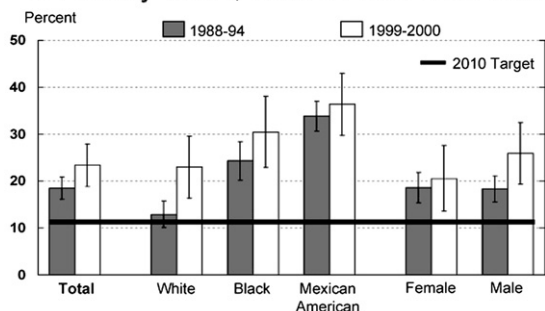
Strategies for dental caries prevention and management can take advantage of the infectious nature of the disease, or it can be viewed as independent of its infectious nature. The evidence of transmission, initially from mother to child, is demonstrated not only by the correlation of maternal salivary titers of mutans streptococci (MS) (a collective term used to embrace *S. mutans*, *S. sobrinus*, and other species less frequently found in humans) with the early colonization of her child and the early inception of caries lesions in the child, but also by the identity of MS colonizing mother and her child, based on bacteriocin typing, endonuclease, and ribotyping.^{12,17–20} A strong scientific basis supports evaluation of the

From the Northwest Center to Reduce Oral Health Disparities, University of Washington, Seattle, Wash (Dr Milgrom); Preventive and Community Dentistry, Oral Health Research Institute, Indiana University School of Dentistry, Indianapolis, Ind (Dr Zero); and Departments of Oral Health and Diagnostic Sciences and Pathology and Laboratory Medicine, University of Connecticut Health Center, Farmington, Conn (Dr Tanzer).

Address correspondence to Peter Milgrom, DDS, Department of Dental Public Health Sciences, Box 357475, University of Washington, Seattle, Washington 98195-7475 (e-mail: dfr@u.washington.edu).

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Children 2-4 Years Who Have Ever Had Caries in Primary Teeth, 1988-94 and 1999-2000



Source: Healthy People 2010 Midcourse Review.¹

Figure 1. A comparison of the proportion of children with tooth decay in the US in two periods.

microbial status of young mothers as predictors of the colonization of their young children's teeth.¹² Interventions in the mother to suppress her MS prolong the time to colonization of her children and prolong the time and reduce the severity of carious lesion inception.²¹⁻²³ The notion of a discrete window of infectivity until about 26 months of age, during which transmission occurs,²⁴ has been expanded following studies that showed colonization at younger ages and prior to tooth eruption. It is estimated in one study that MS is harbored by at least 20% of children under 14 months of age²⁵ and at least 25% of predentate children in another.²⁶ The source of the MS after 5 years of age is not known but is likely to include siblings and caretakers, at least.

This review focuses on the preventive strategies and technologies that address goals of Healthy People 2010 applicable to individual children, which, if applied, might mitigate the inequities identified by the Surgeon General's

Percent of Children Receiving Preventive Dental Care in Past Year, By Age

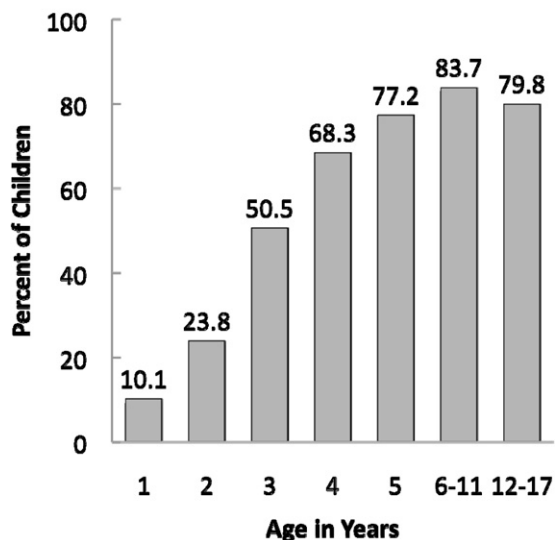


Figure 2. The proportion of US children receiving any preventive dental care in 1999-2000. Source: National Survey of Children's Health, 2007.⁹

Report on Oral Health (SGROH).¹⁶ The science and technologies to be reviewed are 1) detection and risk assessment and 2) interventions to improve prevention of tooth decay.

DETECTION AND RISK ASSESSMENT

Early Tooth Decay Lesion Detection

Industry has developed high-technology devices that allow detection of early signs of decay lesions. Early detection could increase opportunity to arrest and reverse tooth damage by using a "medical" approach²⁷ and prevent the need for traditional "surgical" interventions that partially remove and reconstruct (fill) the teeth, or extract them. The devices generally have high sensitivity but inadequate specificity. Their clinical application is further limited because one method cannot be used for all tooth surfaces and under all circumstances.²⁸ Presently the devices appear to add little to competent visual/tactile examination.^{29,30} Moreover, these devices may be misused to justify surgical interventions and fabrication of fillings, sometimes mislabeled "minimally invasive," instead of intensifying efforts to arrest early lesions. Devices with the best performance are expensive and cumbersome, and their use is time consuming, with little application in typical dental practice, community practice, or community health centers. Simpler approaches, such as fiber-optic transillumination, may be more readily adopted.³¹

A multinational academic group has begun testing a totally visual caries lesion assessment scheme (International Caries Detection and Assessment System) that focuses on early lesion detection before cavitation has begun.^{32,33} As with the technology-based systems, the rationale is that earlier detection will increase opportunity to arrest and reverse lesions and prevent need for surgical interventions. The International Caries Detection and Assessment System has acceptable reliability and validity but requires rigorous training and remains in development.³⁴

To date, there has been limited impact on training of dental students or adoption by community or health center practices, although this situation could rapidly change if research demonstrated how best to achieve this aim. These methods, whether high tech or visual, rely on detection of lesions after they have occurred.

Timely Risk Assessment

As cited above, detection of carious lesions of young children is a strong risk predictor of carious lesions of older children. Also, early carious lesions ("white spots") are strong predictors of frank cavitation of the teeth.¹² Dietary risk factors are also important. Risk assessment tools have been promoted to guide clinicians.^{35,36} These strategies may be helpful to primary care providers who see infants and toddlers on a regular basis. One example is the CAMBRA Caries Risk Assessment Form for Age 0 to 5 Years.³⁷ However, assessments of the children's mothers or caretakers in terms of microbiology or caries experience, or on their infection status, may be appropriate as well.²⁰

At the extremes, the level of colonization by MS is an indicator and a predictor of caries activity.¹² High levels are typical of children with Early Childhood Caries (ECC).^{26,38} At lower levels of colonization, the relationship is poorer, no doubt due—at least in part—to the confounding effect of fluoride exposure and the diverse testing methods used. Testing is relatively simple and cost effective if it leads to sound anticipatory guidance and prevention of disease in children. Nevertheless, bacterial testing in US dental practices does not appear widespread. Research on the adoption of these technologies in both primary medicine and dentistry practice is needed.

INTERVENTIONS TO IMPROVE PREVENTION OF TOOTH DECAY

Vaccines, Bacterial Replacement, and Targeted Antimicrobial Peptides

Efforts to develop vaccines against dental caries based on both active and passive immunization continue. Secretory immune response to antigens of MS can influence caries pathogenesis.^{39–44} With some exceptions, most work has been done in animal models. Protection is attributable to salivary sIgA antibodies (active). Antibodies made in another host and delivered to humans (passive immunity) are also of interest. By selection of different antigens as the target for immunization, both active and passive strategies seek to inhibit a variety of functions critical to MS in the biofilm on teeth (dental plaque). Replacement of virulent (cariogenic) MS with nonvirulent streptococci is also being investigated in experimental animals and humans.⁴⁵ Early *in vitro* work on specifically targeted antimicrobial peptides⁴⁶ continues but no *in vivo* validation has been reported. Approval by the US Food and Drug Administration (FDA) of specific immunization and clinical applications is still problematic because of unresolved risk-benefit questions and commercial investment required to fund extensive trials to meet regulatory requirements.

Antiseptics

There are several studies of the utility of antiseptic agents to inhibit caries in older, self-compliant individuals.^{21,47} With regard to preschoolers, some practitioners are strong advocates for combining fluorides with various antimicrobials, especially for those with disparities and whose families are mobile, because topical fluorides do not provide complete protection against tooth decay.⁴⁸ Two topical antimicrobials have been investigated to some extent: chlorhexidine digluconate (CH) and polyvinylpyrrolidone iodine (PVP-I).

Chlorhexidine

Chlorhexidine rinses, available in the United States, are sold by prescription but are lower in concentration (to reduce staining of teeth) than products sold in other countries. Approved by the FDA for gingivitis control, no formulation has FDA approval for caries control in

children. Research, particularly in Europe and China, has examined the effectiveness of a CH varnish coating for the teeth, with mixed results. A recent systematic review of 14 publications of controlled clinical trials concluded there was a moderate caries-reducing effect when the varnish was applied every 3 to 4 months.⁴⁹ The variability in CH varnish formulations may have strongly influenced bioavailability and thus effect of CH. Although CH varnish and other CH-containing vehicles may have value in caries prevention for very young children, the evidence is inconclusive; no child products are available in the United States, and none can be recommended.

PVP-I

The *in vitro* and *in vivo* iodine antiseptic literature of 3 decades ago on dental caries was promising, but most human studies were very small.^{50,51} Pilot and small-scale clinical studies of utility of PVP-I in young children, some with established active ECC, show strongly encouraging data.^{52–55} Larger scale evaluations are warranted and timely.

Topical Fluorides

The benefits of fluoride delivery via professional in-office applications, and home-use mouthrinses, gels, and toothpastes, are well established. These strategies have had limited impact on populations with little access to the dentist. Community water fluoridation is highly effective but depends upon public water supplies and political approval of their fluoridation. Mouthrinses, gels, and toothpastes are individual compliance-dependent, and dependent on economic and access feasibility. In the late 1990s, manufacturers gained approval from the FDA to market topical sodium fluoride varnishes, first available in Europe in the 1960s. Although indicated formally for tooth sensitivity reduction primarily in adults, they are being used for decay prevention and arrest in children, and good data suggest that they are more effective than the older technologies.^{56,57} The varnishes are safe for infants and toddlers.

Manufacturers have not sought, however, an indication for prevention of decay, perhaps because they see the market as small and return on investment not large. The formulation of the varnishes is largely unregulated, and manufacturers have produced various forms of varnish that alter the properties of the varnish. No data show that these competing products are equivalent.

The varnishes are important because they provide an easy-to-use, safe, and cheap fluoride vehicle for preschoolers, our most vulnerable population. Although the varnishes are being adopted in public health practice, use in private dental practice lags. There has been movement for physicians and nurses to apply varnish, and in some states Medicaid reimburses these primary care practitioners, in addition to dentists and dental hygienists, for this service.⁵⁸ The Preventive Services Task Force, Centers for Disease Control and Prevention, American Dental Association, and American Academy of Pediatrics

have not endorsed topical fluoride treatment for primary prevention in children aged before 24 months, and American Academy of Pediatrics guidelines specifically note the lack of a definitive trial.⁵⁹ Thus, a multicenter clinical trial is needed to demonstrate the effectiveness of fluoride varnish delivered by primary care physicians and nurses during well-baby visits.

New studies on the adoption of this technology in practice are needed. There have been almost no attempts to study ways to spread adoption.⁶⁰

Diamine Silver Fluoride

Research outside the United States has highlighted the value of diamine silver fluoride to both arrest and prevent recurrences of ECC. This product has been available in Japan and several other countries for years but was never brought to the United States. Evidence suggests that it is at least twice as effective as sodium fluoride varnish.^{61,62} One drawback, staining of the cavity/tooth after treatment, appears preventable.⁶³ Research is needed to learn how this compound works. The National Institutes of Health is just beginning to sponsor research regarding this potentially helpful approach, but lack of FDA approval is a barrier.

Xylitol

Xylitol is a sugar substitute that is “generally regarded as safe” (GRAS) by FDA.⁶⁴ In teens and young adults, it is not only noncariogenic but also anticariogenic. Its use is limited, like that of other sugar alcohols, by its limited absorbability from the gut. Its benefit cannot be attributed merely to a salivation stimulatory effect of chewing gum use.⁶⁴ Xylitol is a safe and effective tooth decay preventive agent when incorporated into chewing gum or other confections used habitually.^{65–67} Its use, like that of fluoride, is associated with promotion of remineralization of white spots and established lesions. Considerable evidence indicates that it inhibits the metabolism of MS.^{68,69} The American Academy of Pediatric Dentistry supports use of xylitol chewing gum as a caries inhibitor but recommends further research. It emphasizes the need for proper labeling of xylitol products so that parents and professionals can make appropriate choices.⁷⁰ Nevertheless, application has been limited by absence of formulations that demand minimal adherence and are acceptable in a greater variety of settings, such as in preschools/schools. A minimum of 5 to 6 g and 3 exposures per day from chewing gum or candies are needed for clinical effect in adults.⁶⁴ A recent study found that xylitol oral syrup administered topically 2 or 3 times per day at a total dose of 8 g was effective in preventing ECC.⁷¹

A landmark study showed that when mothers of preschoolers chewed high-content xylitol chewing gum habitually, their preschoolers had delayed colonization and lower levels of MS and similarly delayed and much reduced caries experience.^{22,23} In spite of the large body of data supporting the effectiveness and safety of xylitol and a growing number of products, its adoption—particularly in the period immediately postpartum, is not

widespread. The cost of xylitol sugar-free products for daily use is relatively high by comparison with other sugar-free products, but modest by comparison with the cost of the filling of carious lesions.

Occlusal Sealants

Although there were convincing data at the time of the SGROH for the application of sealants as a key objective of Healthy People 2010, the actual adoption of sealants by dentists has not been achieved.¹ Sealants are designed to be placed when the permanent molars erupt (around ages 7–8 years and 13–14 years). Data up to 2004 suggest no more than 32% of children receive this service, up from 23% during 1988–1994. The equivalent rate for age 14 is 21%.⁷² In part, this is because up to one third of permanent molars are cavitated by the time the teeth erupt enough to be sealed, depending on the risk group, and most dentists will not seal caries lesions in spite of evidence that this strategy can be effective in arresting them.^{73,74}

The only innovation since the SGROH has been the development and marketing of glass ionomer sealants. The argument for this strategy is that glass ionomer can be placed on partially erupted permanent teeth, where they release small amounts of fluoride, putatively inhibiting local lesion development. However, only limited pilot studies of these materials exist, and their potential remains unexplored. Retention rates of the glass ionomer cement sealants are lower than current generation of conventional resin-based sealants. The limited literature on sealing primary molars is not encouraging.^{74,75} Definitive studies are needed.

Nonfluoride Remineralization Strategies

There has been considerable interest in developing novel remineralizing agents that complement or substitute for the clinical effectiveness of fluoride. Studies largely sponsored by industry have been conducted to promote products claiming to remineralize early caries lesions.^{76–78} These products are formulated as professionally applied pastes, toothpastes, and gums. Conceptually, the work is interesting. Nevertheless, the work is not focused on control of early lesions of ECC and claims of effectiveness are not well substantiated. Little has been done to establish how such products would be used to benefit children.

Conclusions

This review has focused on the role of science and technology in achieving the goals of Healthy People 2010. Tooth decay is a serious and growing problem for very young children. It impacts quality of life. It especially affects the poor, ethnic minorities, Native Americans, and Alaska Native populations.

Dental caries is an infectious disease, yet the application of this concept in practice is limited. Accordingly, antimicrobial approaches, directed at both mothers and at young children, have an important place in tooth decay prevention and control. Antiseptics, CH varnish, and PVP-I, as well as xylitol chewing gum used by mothers, have been shown to

be effective in inhibiting carious lesion incidence, but definitive trials are needed.

Fluorides remain the most effective agents but are not widely disseminated to the neediest. Fluoride varnish provides a relatively effective topical preventive for very young children, yet definitive trials of its application in primary care practice have not been conducted. Scientific advances outside the United States have suggested the potential of silver diamine fluoride, but it is not FDA approved and no research has been carried out in the US. Data support effectiveness and safety of xylitol, but adoption is not widespread and additional research is needed on formulations and vehicles to increase access. Dental sealants are of unquestioned benefit and remain a mainstay of public policy, yet after decades of research, widespread use has not occurred. Definitive trials of new materials that can be used on erupting teeth are needed.

The research in the United States to address the growing level of tooth decay in our youngest children is too limited. Research and adoption have not kept pace with the problems identified in the SGROH. Transfer of technology from studies to implementation lags.

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REFERENCES

- US Department of Health and Human Services. Figure 21-1. Progress quotient chart for focus area 21: oral health. Healthy People 2010 Web site. Available at: <http://www.healthypeople.gov/Data/midcourse/html/tables/pq/PQ-21.htm>. Accessed September 3, 2007.
- Milgrom P, Weinstein P, Huebner C, Graves J, Tut O. Empowering Head Start to improve access to good oral health for children from low income families. *Matern Child Health J*. 2008; Epub February 2, 2008.
- Frenzel A. Das schicksal der sechsjahrmolaren in der schulzahnplage. *Deutsche Monatsschrift für Zahnheilkunde*. 1933;51:437.
- Birkeland JM, Broach L, Jorkjend L. Caries experience as predictor for caries incidence. *Community Dent Oral Epidemiol*. 1976;4:66-69.
- Bader JD, Graves RC, Disney JA, et al. Identifying children who experienced high caries increments. *Community Dent Oral Epidemiol*. 1986;14:198-201.
- van Palenstein Helderma WH, van't Hof MA, van Loveren C. Prognosis of caries increment with past caries experience variables. *Caries Res*. 2001;35:186-192.
- Wang WJ, Li YH, Bian JY. An eight-year longitudinal study for caries status on primary and permanent dentitions in Beijing children. *Zhonghua Kou Qikang Yi Xue Za Zhi*. 2003;38:279-281.
- Motohashi M, Yamada H, Genkai F, et al. Employing dmft score as a risk predictor for caries development in the permanent teeth in Japanese primary school girls. *J Oral Sci*. 2006;48:233-237.
- Centers for Disease Control. National Survey of Children's Health 2007. Available at: ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/slats/nsch07/1a_Survey_Instrument_English/NSCH_Questionnaire_052109.pdf. Accessed October 7, 2009.
- Loesche WJ. Role of Streptococcus mutans in human dental decay. *Microbiol Rev*. 1986;50:353-380.
- van Houte J. Role of micro-organisms in caries etiology. *J Dent Res*. 1994;73:672-681.
- Tanzer JM, Livingston J, Thompson AM. The microbiology of primary dental caries in humans. *J Dent Educ*. 2001;65:1028-1037.
- Bailit H, Beazoglou T, Demby N, et al. Dental safety net: current capacity and potential for expansion. *J Am Dent Assoc*. 2006;137:807-815.
- Guendelman S, Angulo V, Wier M, Oman D. Overcoming the odds: access to care for immigrant children in working poor families in California. *Matern Child Health J*. 2005;9:351-362.
- Lam M, Riedy CA, Milgrom P. Improving access for Medicaid-insured children: focus on front-office personnel. *J Am Dent Assoc*. 1999;130:365-373.
- US Department of Health and Human Services. Oral Health in America: A Report of the Surgeon General. Rockville, Md: US Department of Health and Human Services, National Institute of Dental and Craniofacial Research, National Institutes of Health; 2000.
- Berkowitz RJ, Jordan HV. Similarity of bacteriocins of Streptococcus mutans from mother and infant. *Arch Oral Biol*. 1975;20:725-730.
- Li Y, Caufield PW. The fidelity of initial acquisition of mutans streptococci by infants from their mothers. *J Dent Res*. 1995;74:681-685.
- Masuda N, Shimamoto T, Kitamura K, et al. Transmission of Streptococcus mutans in some selected families. *Microbios*. 1985;44(181S):223-232.
- Kohler B, Bratthall D. Intrafamilial levels of Streptococcus mutans and some aspects of the bacterial transmission. *Scand J Dent Res*. 1978;86:35-42.
- Kohler B, Andreen I. Influence of caries-preventive measures in mothers on cariogenic bacteria and caries experience in their children. *Arch Oral Biol*. 1994;39:907-911.
- Soderling E, Isokangas P, Pienihakkinen K, et al. Influence of maternal xylitol consumption on mother-child transmission of mutans streptococci: 6-year follow-up. *Caries Res*. 2001;35:173-177.
- Isokangas P, Soderling E, Pienihakkinen K, Alanen P. Occurrence of dental decay in children after maternal consumption of xylitol chewing gum, a follow-up from 0 to 5 years of age. *J Dent Res*. 2000;79:1885-1889.
- Caufield PW, Cutter GR, Dasanayake AP. Initial acquisition of mutans streptococci by infants: evidence for a discrete window of infectivity. *J Dent Res*. 1993;72:37-45.
- Mohan A, Morse DE, O'Sullivan DM, Tinanoff N. The relationship between bottle usage/content, age, and number of teeth with mutans streptococci colonization in 6-24-month-old children. *Community Dent Oral Epidemiol*. 1998;26:12-20.
- Milgrom P, Riedy CA, Weinstein P, et al. Dental caries and its relationship to bacterial infection, hypoplasia, diet, and oral hygiene in 6 to 3 6 month old children. *Community Dent Oral Epidemiol*. 2000;28:295-306.
- Kohler B, Andreen I, Jonsson B. The earlier the colonization by mutans streptococci, the higher the caries prevalence at 4 years of age. *Oral Microbiol Immunol*. 1988;3:14-17.
- Zandona AF, Zero DT. Diagnostic tools for early caries detection. *J Am Dent Assoc*. 2006;137:1675-1684.
- Kavvadia K, Lagouvardos P. Clinical performance of a diode laser fluorescence device for detection of occlusal caries in primary teeth. *Int J Paediatr Dent*. 2008;18:197-204.
- Kuhnisch J, Berger S, Goddon I, et al. Occlusal caries detection in permanent molars according to WHO basic methods, ICDAS II and laser fluorescence measurements. *Community Dent Oral Epidemiol*. 2008;36:475-484. Epub April 14, 2008.
- Davies GM, Worthington HV, Clarkon JE, et al. The use of fibre-optic transillumination in general dental practice. *Br Dent J*. 2001;191:145-147.
- Ekstrand KR, Martignon S, Ricketts DJ, Qvist V. Detection and activity assessment of primary coronal caries lesions: a methodologic study. *Oper Dent*. 2007;32:225-235.
- Ismail AI, Sohn W, Tellez M, et al. The International Caries Detection and Assessment System (ICDAS): an integrated system for measuring dental caries. *Community Dent Oral Epidemiol*. 2007;35:170-178.
- Jablonski-Momeni A, Stachniss V, Ricketts DN, Heinzl-Gutenbrunner M, Pieper K. Reproducibility and accuracy of the ICDAS-II for detection of occlusal caries in vitro. *Caries Res*. 2008;42:79-87. Epub January 15, 2008.

35. Kutsch VK, Milicich G, Domb W, et al. How to integrate CAMBRA into private practice. *J Calif Dent Assoc.* 2007;35:778–785.
36. Caries management by risk assessment. Available at: www.nnoha.org/goopages/pages_downloadgallery/download.php?filename=5519_8469001.doc&orig_name=CAMBRA%20ECC%20Risk%20Assmt%200-5%20yrs.doc. Accessed July 10, 2009.
37. American Academy of Pediatric Dentistry. Policy on use of a Caries-risk Assessment Tool (CAT) for infants, children, and adolescents. 2006. Available at: <http://www.aapd.org/media/policies.asp>. Accessed September 21, 2009.
38. Marchant S, Brailsford SR, Twomey AC, et al. The predominant microflora of nursing caries lesions. *Caries Res.* 2001;35:397–406.
39. Taubman MA, Nash DA. The scientific and public-health imperative for a vaccine against dental caries. *Nat Rev Immunol.* 2006;6:555–563.
40. Smith DJ, Mattos-Graner RO. Secretory immunity following mutans streptococcal infection or immunization. *Curr Top Microbiol Immunol.* 2008;319:131–156.
41. Xu OA, Yu F, Fan MW, et al. Protective efficacy of a targeted anti-caries DNA plasmid against cariogenic bacteria infections. *Vaccine.* 2007;25:1191–1195.
42. Canetti AC, Kretchetoff FY, Kogga Ito CY, et al. Production of monoclonal antibodies against *Streptococcus mutans* antigen. *Braz Oral Res.* 2006;20:297–302.
43. Culshaw S, Larosa K, Tolani H, et al. Immunogenic and protective potential of mutans streptococcal glucosyltransferase peptide constructs selected by major histocompatibility complex Class II allele binding. *Infect Immun.* 2007;75:915–923.
44. Childers NK, Li F, Dasanayake AP, et al. Immune response in humans to a nasal boost with *Streptococcus mutans* antigens. *Oral Microbiol Immunol.* 2006;21:309–313.
45. Hillman JD, Mo J, McDonnell E, et al. Modification of an effector strain for replacement therapy of dental caries to enable clinical safety trials. *J App Microbiol.* 2007;102:1209–1219.
46. Eckert R, He J, Yarbrough DK, et al. Targeted killing of *Streptococcus mutans* by a pheromone-guided “smart” antimicrobial peptide. *Antimicrob Agents Chemother.* 2006;50:3651–3657.
47. Zickert I, Emilson CG, Krasse B. Effect of caries preventive measures in children highly infected with the bacterium *Streptococcus mutans*. *Arch Oral Biol.* 1982;27:861–868.
48. Featherstone JD. Delivery challenges for fluoride, chlorhexidine and xylitol. *BMC Oral Health.* 2006;15(6 suppl 1):S8.
49. Zhang Q, van Palenstein Helderma WH, van’t Hof MA, Truin GJ. Chlorhexidine varnish for preventing dental caries in children, adolescents and young adults: a systematic review. *Eur J Oral Sci.* 2006;114:449–455.
50. Tanzer JM, Slee AM, Ka B, Scheer ER. In vitro evaluation of three iodine-containing compounds as antiplaque agents. *Antimicrob Agents Chemother.* 1977;12:107–113.
51. Caufield PW, Wannemuehler YM. In vitro susceptibility of *Streptococcus mutans* 6715 to iodine and sodium fluoride, singly and in combination, at various pH values. *Antimicrob Agents Chemother.* 1982;2:115–119.
52. Tinanoff N, O’Sullivan DM. Early childhood caries: overview and recent findings. *Pediatr Dent.* 1997;19:12–16.
53. Zahn L, Featherstone JDB, Gansky SA, et al. Antibacterial treatment needed for severe early childhood caries. *J Pub Health Dent.* 2006;66:174–179.
54. Amin MS, Harrison RL, Benton TS, et al. Effect of povidone-iodine on *Streptococcus mutans* in children with extensive dental caries. *Pediatr Dent.* 26:5–10.
55. Lopez L, Berkowitz RJ, Spiekerman C, Weinstein P. 2002. Topical antimicrobial therapy in the prevention of early childhood caries: a follow-up report. *Pediatr Dent.* 2004;(24):204–206.
56. Marinho VCC, Higgins JPT, Logan S, Sheiham A. Fluoride varnishes for preventing dental caries in children and adolescents. *Cochrane Database Syst Rev.* CD002279. Available at, <http://doi.wiley.com/10.1002/14651858.CD002279>, 2002;1. Accessed September 3, 2007.
57. National Institutes of Health (US). Diagnosis and management of dental caries throughout life. *NIH Consensus Statement.* 2001;18:1–23.
58. Slade GD, Rozier RG, Zeldin LP, Margolis PA. Training pediatric health care providers in prevention of dental decay: results from a randomized controlled trial. *BMC Health Serv Res.* 2007;7:176.
59. American Academy of Pediatrics. Oral health risk assessment training program. Oral Health Initiative Web Site. Available at: <http://www.aap.org/commpepd/ochs/oralhealth/cme/course-6.htm>. Accessed July 10, 2009.
60. Grembowski D, Spiekerman C, del Aguila MA, et al. Randomized pilot study to disseminate caries-control services in dentist offices. *BMC Oral Health.* 2006;6–7.
61. Chu CH, Lo ECM, Lin HC. Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin caries in Chinese pre-school children. *J Dent Res.* 2002;81:767–770.
62. Llodra JC, Rodriguez A, Ferrer B, et al. Efficacy of silver diamine fluoride for caries reduction in primary teeth and first permanent molars of schoolchildren: 36-month clinical trial. *J Dent Res.* 2005;84:721–724.
63. Knight GM, McIntyre JM, Craig GG, et al. Differences between normal and remineralized dentine pretreated with silver fluoride and potassium iodide after an in vitro challenge by *Streptococcus mutans*. *Austral Dent J.* 2007;52:16–21.
64. Milgrom P, Ly KA, Rothen M. Xylitol and its vehicles for public health needs. *Adv Dent Res.* 2009;21:44–47.
65. Hildebrandt GH, Sparks BS. Maintaining mutans streptococci suppression with xylitol chewing gum. *J Am Dent Assoc.* 2000;131:909–916.
66. 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;32:107–112.
67. Makinen KK, Bennett CA, Hujoel PP, et al. Xylitol chewing gums and caries rates: a 40-month cohort study. *J Dent Res.* 1995;74:1904–1913.
68. Tanzer JM, Thompson A, Wen ZT, Burne RA. *Streptococcus mutans*: fructose transport, xylitol resistance, and virulence. *J Dent Res.* 2006;85:369–373.
69. 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.
70. American Academy of Pediatric Dentistry. Policy on the use of xylitol in caries prevention. 2006. Available at: http://www.aapd.org/media/Policies_Guidelines/P_Xylitol.pdf. Accessed June 26, 2008.
71. Milgrom P, Ly KA, Tut OK, et al. Xylitol pediatric topical oral syrup to prevent dental caries. A double-blind randomized clinical trial of efficacy. *Arch Pediatr Adolesc Med.* 2009;163:601–607.
72. CDC Wonder. Data 2010... the Healthy People 2010 Database. 2009 Edition-Objective 21–8a and 21–8b. Available at: <http://wonder.cdc.gov/data2010/>. Accessed September 21, 2009.
73. Beauchamp J, Caufield PW, Crall JJ, et al. Evidence-based clinical recommendations for the use of pit-and-fissure sealants: a report of the American Dental Association Council on Scientific Affairs. *J Am Dent Assoc.* 2008;139:257–268.
74. Griffin SO, Oong E, Kohn W, et al. The effectiveness of sealants in managing caries lesions. *J Dent Res.* 2008;87:169–174.
75. Chadwick BL, Treasure ET, Playle RA. A randomised controlled trial to determine the effectiveness of glass ionomer sealants in pre-school children. *Caries Res.* 2005;39:34–40.
76. Reynolds EC, Cai F, Shen P, Walker GD. Retention in plaque and remineralization of enamel lesions by various forms of calcium in a mouthrinse or sugar-free chewing gum. *J Dent Res.* 2003;82:206–211.
77. Morgan MV, Adams GG, Bailey DL, et al. The anticariogenic effect of sugar-free gum containing CPP-ACP nanocomplexes on approximal caries determined using digital bitewing radiography. *Caries Res.* 2008;42:171–184.
78. Reynolds EC, Cai F, Cochrane NJ, et al. Fluoride and casein phosphopeptide-amorphous calcium phosphate. *J Dent Res.* 2008;87:344–348.