The Microbiology of Primary Dental Caries in Humans

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Abstract: A systematic literature review from 1966 to 2000 revealed 2,730 English-language publications on the role of bacteria in human primary dental caries *in vivo*. The most pertinent 313 papers were analyzed in evidence tables accessible online (http://www.nidcr.nih.gov). The search targeted all bacterial types implicated previously in caries and asked two questions. First, what is the association of specific bacteria with tooth decay and can causation be attributed to any of those bacteria? Retrieved studies were categorized as randomized-blinded-interventional, longitudinal, case-control, and cross-sectional and were weighted in descending order in terms of significance. Although many studies, due to ethical requirements, had confounding variables, they still indicate strongly: 1) the central role of the mutans streptococci in initiation of caries of smooth surfaces and fissures of crowns of teeth and suggests their potent role in induction of root surface caries; and 2) that lactobacilli are implicated as important contributory bacteria in tooth decay, but their role in induction of lesions is not well supported. Second, what is the source of infection by cariogenic bacteria? Molecular/genetic studies of implicated bacteria isolated from humans, randomized-blinded-interventional, and longitudinal studies indicate that mutans streptococci are spread vertically among humans, mostly from mothers to their children. Implications of these conclusions are briefly discussed. The most significant problems of literature interpretation include the benefits/shortcomings of salivary and plaque monitoring of the flora, the role of sugar(s) in decay as it influences the flora, and modeling strategies to predict lesion score increments as distinct from determination of the etiological role of specific bacteria. Future directions for microbiological clinical caries research are suggested, and the use of the term "caries" to describe the disease, not its lesions, is urged.

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This review was conducted to evaluate the implication of certain microorganisms in the causation of human tooth decay. It examines the evidence concerning bacterial species identified in both early and current literature to be involved in tooth decay, whether originally from animal and/or human data. It also examines the source of this putative infection of humans. Attention is focused on the mutans, sanguinis, and other streptococci, the enterococci, the lactobacilli, and certain actinomycetes, all of which are resident in the human mouth.

There is an immense literature. A systematic search using MEDLINE and EMBASE, from 1966 to 2000, retrieved 2,730 unique English-language citations. We reviewed only full-length primary papers that deal with isolation and identification of bacteria from human subjects in the context of caries. Studies of so-called secondary or recurrent caries have been excluded from this review due to time and space limitations, as have studies done either wholly *in vitro*, in experimental animals, or with so-called *in situ* caries models. Only in the case of the brief background section, which sets the framework for this review, are scholarly review papers and conceptual advance papers from human or a few experimental animal studies cited.

This review, thus, deals with studies of the microbial causes and associations with dental caries in humans only, relying upon experimental/interventional, longitudinal, case-control, and cross-sectional studies. According to the prevalent standards for judging the strength of evidence, randomized blinded clinical trials are assigned more weight than longitudinal or case-control trials, and they, in turn, more weight than cross-sectional studies. In the case of the sources of the microorganisms of interest, modern molecular biological infection tracing data are given great weight. Patients and experimental subjects with incipient enamel lesions (white spots) and established cavitations (cavities) of the tooth crowns and root surface lesions are considered.

Earlier studies had characterized the biological behaviors of the most strongly caries-implicated microorganisms. The essentials of those behaviors are as follows.

Mutans streptococci colonize the host only after the first teeth erupt, and their preferential colonization site is the teeth[1,2]; they are highly localized on the surfaces of the teeth, and their abundance in the plaque is highest over initial lesions[3,4]; their level of colonization within the plaque is increased by sucrose consumption[5,6]; they synthesize certain macro-molecules from sucrose that foster their attachment to the teeth[7,8]; they are rapid producers of acid from simple carbohydrates, including sucrose, and are tolerant to low pH[9,10]; and they are essentially always recovered on cultivation of initial and established carious lesion sites.[11-13] Interest in them grew after the demonstration of their potent induction and progression of carious lesions in a variety of experimental animals, including mono-infected gnotobiotes.[14,15] Their virulence expression is strongly associated with consumption of carbohydrates, especially sucrose.[16,17] However, caries does not occur in germ-free animals, no matter what their genetic background or their diet; it is an infection.

Lactobacilli do not avidly colonize the teeth; they may be transiently found in the mouth before the teeth erupt; and they preferentially colonize the dorsum of the tongue and are carried into saliva by the sloughing of the tongue's epithelium.[18] Their numbers in saliva appear to reflect the consumption of simple carbohydrates by the host.[6,19] They are highly acidogenic from carbohydrates and are acid tolerant,[20] and they are often cultured from established carious lesions.[21] Some lactobacilli are cariogenic in experimental animals; their cariogenicity is dependent upon consumption of carbohydrate-rich diets of animals.[22]

Non-mutans streptococci of several types, including the sanguinis (formerly sanguis) group of organisms and *S. salivarius*, are extremely abundant in the mouth; some are tooth surface colonizers, some mucosal colonizers. Some are quite acidogenic from carbohydrates and are acid tolerant.[9,23,24] Less evidence exists of their virulence in experimental animals than either the mutans streptococci or the lactobacilli.

Enterococci were the first bacteria shown experimentally to induce caries in gnotobiotic animals.[25] While carbohydrate users, acidogenic, and acid tolerant, they are not frequently abundant in the human oral cavity.[9,23,24]

Actinomycetes are abundant in the human mouth and induce root surface caries in hamsters and gnotobiotic rats.[26] They are also carbohydrate users, but are not powerfully acidogenic or acid tolerant.

The review conducted for the Consensus Development Conference on Dental Caries Diagnosis and Management Throughout Life was designed to answer two primary questions.

Question 1: What Is the Association of Specific Bacteria with Tooth Decay in Humans and Can Causation Be Attributed to Any of Those Bacteria?

Randomized Clinical Trials Regarding Mutans Streptococci

Twenty-five interventional studies, which monitor the putative cariogenic flora and record effects on caries scores, are found in the literature of human caries. Several of these studies applied extremely complex strategies,[e.g.,27] some focused on mitigation of the solubility of the teeth with fluorides; some on repair or sealing of the teeth; some on diet management and/or use of sugar substitutes and, thus, indirectly on changing the implicated tooth surface flora; and some directly on the flora by mechanical plaque control and/or use of antiseptic agents.

Because the questions for the present review are more straightforward (*viz*. what are the bacterial determinants of caries and what is known of the transmission of those bacteria), such multistrategic studies confound interpretations of antibacterial effects with anti-tooth demineralization effects. It is understandable that investigators wish to accept this problem because of the ethical need to offer patients at high risk the perceived best available anti-caries strategies. Therefore, multistrategy approaches to experimental interventions set a very high threshold for detection of effects of interventions on the flora and attribution of anti-caries responses to them. Some notable studies are less confounded, however.

Partial suppression of mutans streptococci by topical chlorhexidine use and dietary counseling in randomized to treatment (or control) Swedish children[28] inhibits mutans streptococcal recoveries and carious lesion development during three years, while lactobacillus titers in saliva are not detectably affected.

Study of primiparous mothers with three- to eight-month-old infants in a Swedish community, alternately assigned to treatment or control groups, was aimed at reduction of mutans streptococcal salivary levels by sucrose avoidance counseling, professional tooth cleaning (and topical fluoride application), oral hygiene in-

struction, excavation of large carious lesions if present, and, if test mothers had salivary mutans streptococcal levels that exceeded a pre-set threshold, by treatment with topical chlorhexidine. This strategy increased the time to colonization by mutans streptococci of their young children, time to caries experience of those children, and the severity of caries experience of those children.[29] There was no significant difference in titers of salivary lactobacilli. Preventive strategies were discontinued when children had become colonized. The study ran until children were thirty-six months old. Four years later, [30] with the same children now seven years old, treated mothers had lower mutans streptococci and lactobacilli than control mothers, and far lower percentages of children of treated mothers carried mutans streptococci compared with children of control mothers. The children of test mothers who were carriers also had lower levels of mutans streptococci than those of the mutans carrier control mothers. Twenty-three percent of children of test mothers were caries free, compared to 9 percent of the children of control mothers, and total group caries experience for test and control children were 5.2 vs 8.6 def, respectively.

A similar strategy was used to treat fifty- to-sixty-year-old Swedish patients of private dentists.[31] Two randomized groups of high- and low-risk patients (defined by salivary mutans, salivary flow rate, and salivary buffer capacity) were assigned test protocol or served as controls who were given standard care as deemed appropriate by their dentists. At year's end, the treated high-risk group had lower caries increments and lower mutans and lactobacillus titers than high-risk controls, but there was no difference between the two low-risk groups. The intervention was discontinued. Four years later, there was no difference in microbiological parameters or caries increment between the former treated and untreated high-risk and low-risk groups, and the one year differential benefits of the test intercession had been lost.

A three-year study[32] of initially twelve-year-old Swedish children, using an intervention of chlorhexidine-impregnated dental floss treatment of approximal surfaces compared with placebo-impregnated floss and with no floss treatment, resulted in about a 50 percent reduction of new DFS of the chlorhexidine-floss compared with the placebo-floss group, and about a 60 percent reduction compared with the no floss group. Chlorhexidine impregnated floss effects were about 42 percent better than placebo-floss. Salivary monitoring of bacteriology (rather than approximal plaque monitoring) evidenced no differences among the groups, as could have been expected.

A three-year intensive program[33] focused on personalized education to avoid sucrose, excavation of cavities, fluoride varnish application, professional tooth cleaning, and oral hygiene instruction. All study participants were randomized by school class and had group instruction on sugar avoidance, tooth brushing, and fluoride toothpaste use, and were provided tooth brushes. The personalized program resulted in about a sixfold decline of new DFS in ten- to twelve-year-old Polish children and, after three years, significant reductions of mutans and lactobacillus salivary counts.

A two-year randomized, four-group study of thirteen-year-old Swedish children[34] compared supervised chlorhexidine gel treatment to fluoride varnish, topical FeAlF professional application, and untreated controls with no intercession. The antibacterial treatment resulted in about a 50 percent reduction of new DFS when compared with the untreated controls and lesser, but still substantial and significant, DFS reductions compared with the fluoride treated groups. There was a correlated reduction of salivary mutans streptococci in the chlorhexidine group.

Finnish ten- to twelve-year-old children were randomized to either high content xylitol gum use or non-use, during a first experimental phase.[35] When two years later the controls were randomly recruited for evaluation, some had begun the voluntary use of xylitol gum, that is, a self-imposed cross-over. The approximal plaque mutans levels were lower in the xylitol users and the continuous users of xylitol gum had lower decay scores six years after the beginning of their xylitol use than did non-users. Mutans streptococci were lower at approximal sites that were clinically and radiographically sound than at decayed sites.

The use of a xylitol chewing gum by Finnish mothers until their children were three years old was recently reported to inhibit the mutans streptococcal colonization of their children and reduce the caries experience of those children during a five-year period of observation.[36,37] Mothers were randomized to xylitol gum use, chlorhexidine varnish, or fluoride varnish applications. The children did not use the gum or receive varnish treatments. The probability of being caries free was 70 percent for non-mutans-colonized children compared to about 25 percent for mutans-colonized ones at five years of age, and the group mean dmf score for the xylitol intercession cohort was 0.83, while those for the chlorhexidine and fluoride varnish groups were 3.22 and 2.87, respectively.

Longitudinal and Case-Control Studies Regarding Mutans Streptococci

Seventy-nine longitudinal (prospective and retrospective) and case control studies indicate an important role of mutans streptococci in caries. They examined the relationship between salivary titers or plaque relative abundance of mutans streptococci (and often simultaneously quantified other implicated bacteria, especially lactobacilli, actinomycetes, and sanguinis streptococci) as well as the inception, prevalence, or incidence of carious lesions of various surfaces of crowns or roots of teeth. Many studies have used randomized subjects: some of those were dental or medical patients, while others were almost totally naïve dentally. Some studies have used population samples and compared cohorts of high or low caries experience, fluoridated or nonfluoridated communities, diverse racial/ethnic groups, diverse socioeconomic statuses, diverse methods to pay for dental health care, ambulatory and non-ambulatory health status, and, of course, diverse ages. The longitudinal, case-control, and cross-sectional (not discussed here, but see evidence tables) studies come from all continents except Antarctica. A few illustrative of the diverse study populations are cited here and provide, overall, a remarkably consistent picture.[19,38-65]

These (and cross-sectional) studies, with few exceptions, support a strong positive statistical association of mutans streptococci with inception or incidence of carious lesions. They often report concomitant positive associations with lactobacilli, especially if saliva, rather than discrete plaque samples, had been monitored. When studied, they sometimes report negative associations of sanguinis streptococci with mutans streptococci and with lesions. Some suggest that *S. sobrinus* (the less common of the frequent human mutans streptococci, the more common one being *S. mutans*) are favored in their ability to colonize the teeth by prior colonization by *S. mutans*. There is suggestion of an association of *S. sobrinus* and lactobacilli.

While mutans streptococci can be found in the mouths of infants only after the teeth erupt, they colonize the mouth much earlier when obturators are placed for cleft palate management, again supporting the notion that mutans streptococci require solid nonshedding surfaces as their preferred colonization site.[66]

Other Variables of Interest and Methodological Factors in Studies of Mutans Streptococci

Often these studies (randomized clinical trial, longitudinal, and cross-sectional) gathered data on other variables of interest: socioeconomic status, sucrose consumption (usually as food types or patterns of consumption), fluoride exposure, oral hygiene status, breast feeding or close personal contact between mothers and their children, and, especially, initial or baseline caries status. Some studies asked the clinical examiners to

Table 1. Summary of search retrieval on the association of specific microorganisms and dental caries

Bacterial Group	Total Retrieved	Total Selected	Interventional	Longitudinal/ Retrospective	Case-Control	Cross Sectional
Mutans streptococci	854	189	25	59	20	85
Sanguinis/other streptococci	1245	16	1	2	2	11
Enterococci	253	3	0	0	0	3
Lactobacilli	657	144	9	40	20	75
Actinomycetes	700	27	1	3	3	20

Table 2. Summary of search retrieval on the transmission of bacterial species implicated in dental caries

Bacterial Group	Total Retrieved	Total Selected	Molecular and genetic tracing: bacteriocin/mutacin/ phage typing/ endonuclease mapping/ ribotyping	Interventional	Longitudinal/ Case-Control	Cross Sectional
Mutans streptococci	122	40	17	8	13	1
Sanguinis/other streptococci	772	1	0	0	1	0
Enterococci	129	0	-	-	-	-
Lactobacilli	104	7	0	4	3	0
Actinomycetes	114	0	-	-	-	-

predict the decay experience of the study participants depending on the examiners' beliefs, calling into question specific biases.

Several of these studies focused on a related question, *viz*. the prediction of carious lesion increments as a function of the sum total of many of the variables of interest to cariologists and caries epidemiologists, rather than on the microbiological variables targeted for this review. In such studies when predictive values were estimated and when multiple regression models included other caries-associated variables (such as candy or soft drink consumption, oral hygiene, SES and, especially, prior numbers of lesions), the amount of variance explained by the bacteria of interest became predictably smaller. Prediction of the dependent variable, caries score, by inclusion of the baseline caries score as an independent variable appears inherently tautological in the context of explaining the causation of the disease (and, arguably, a *post hoc, ergo propter hoc* problem).

Discernment of microbial etiology from several longitudinal (and cross-sectional) studies was probably blunted by using salivary (or pooled plaque) monitoring of mutans streptococci as a surrogate for monitoring small samples of plaque in areas of high caries risk, as the knowledge of the biology of the mutans streptococci and expected locations of carious lesions would have seemed to dictate.

Interventional Trials and Other Studies of Lactobacilli

The concerns for confounding and ambiguity of interpretations in interventional clinical trials stated above for the mutans streptococci are applicable to the lactobacilli as well. Several of the randomized clinical trials that yielded data concerning the mutans streptococci also evaluated changes in the lactobacilli. Generally they resulted in inconsistent evidence that inception of carious lesions in children or adults were associated with lactobacillus titer increases in saliva.[e.g., 30,31,33,34,67]

Longitudinal and case-control studies were perhaps more informative. Lactobacilli are late colonizers of the mouth.[1,4,18,57,68] Lactobacilli are recovered from carious lesions, but they are later colonizers of those lesions than the mutans streptococci.[19,43,51] Some data suggest that they are favored in their ability to colonize by pre-existing colonization by the mutans streptococci, especially *S. sobrinus*. These data thus indicate that lactobacilli are not requisite for the development of lesions. Nonetheless, they may potently contribute to the demineralization of the teeth once lesions are established on either crowns or roots.[43,63,69-74] Little information is available concerning the species of lactobacilli that colonize the human tongue and teeth. The many pertinent cross-sectional studies will, similarly, not be described here, but see the evidence tables.

Studies of Other Bacteria

Essentially no data support a causative role of sanguinis streptococci or *S. salivarius* in human caries. In fact some data suggest an inverse relationship of the abundance of sanguinis streptococci and the mutans streptococci, and that the sanguinis streptococci are inversely related to lesion development.[e.g. 38,40,75,76]

In addition, no human data support a significant role of enterococci in the development of human carious lesions or in their prevalence in the human mouth.

Finally, actinomycetes are prevalent in the human mouth and are frequently found in association with both carious and sound root surfaces, as well as sound crown surfaces. Evidence of their role in root surface carious lesion induction is variable and inconclusive. In fact, they sometimes suggest actinomycetes are more reflective of noncariogenic than cariogenic status, by contrast with the mutans streptococci and the lactobacilli.

Question 2: What Is the Source of Infection by Cariogenic Bacteria?

Molecular and genetic methods provide perhaps the strongest evidence of the source of transmission of infection in the case of dental caries. That evidence will be briefly reviewed here. Other evidence of the source of transmission of the bacteria etiologically involved in caries, from experimental and longitudinal studies, is consistent with the even more compelling genetic evidence. The convincing data on the source of infection by cariogenic bacteria almost entirely pertain to the mutans streptococci.

Seventeen studies of the mutans streptococci isolated from children and their parents/siblings/caretakers by bacteriocin typing, phage typing, mutacin typing, endonuclease DNA mapping, and ribotyping establish that these bacteria are transmitted to humans early in their lives, after the first teeth erupt, and that they originate mainly from their mothers, that is, vertical, matrilineal transmission.[77-85] Only two reports suggest significant patrilineal transmission. While it is

common for children to share more than one genotype or bacteriocin type of mutans streptococci with their mothers, failure to detect all of the types longitudinally among mother/child pairs suggests that some genotypes may be lost with time. New genotypes not detected in mothers have also been reported to colonize children during longitudinal studies, suggesting that additional and extra-familial transmission sometimes occurs, perhaps from other caretakers.

Thirteen longitudinal studies, address the topic of transmission of bacteria and caries. One led to the proposal of a "window of infectivity" by mutans streptococci,[86] but that concept does not appear presently well supported. Children become colonized both before and after that "window" period.[66,87-89] Also, as reported in essentially all of the studies of adults (cited above), virtually all dentate adults appear to some degree colonized by mutans streptococci. Hence, there are likely to be other events of transmission or, alternatively, the methods historically used to cultivate the mutans streptococci may be of insufficient sensitivity to detect transmission that had in fact occurred.

Interventional studies of transmission are clearly inhibited by the ethical impossibility of exchanging children shortly after birth among mothers for foster-rearing. Nonetheless, eight randomized interventional experiments aimed at reducing the salivary levels of mutans streptococci and, thus, altering the probability of transmission of mutans streptococci from mothers to their children strongly support the concept that the mother is the usual source of transmission of these bacteria to her child.[30,36,90]

There are few data on the source of transmission of lactobacilli to children. Despite the use of very specific selective media for the cultivation of oral lactobacilli, speciation of lactobacilli has been laborious and usually not done in a cariological context. Just as for the mutans streptococci, speciation studies would not seem useful for tracing the transmission of the oral lactobacilli; molecular/genetic marker tracing would seem more promising. Also, literature search does not reveal studies of the genetics of the lactobacilli in the mouth, vaginal, or GI tract of mothers and their children in the context of dental caries. While lactobacilli can be found in the mouths of infants, they appear to be transient and not a common feature of the oral cavity until after teeth erupt or after obturators are placed for cleft palate management.

There is little information on the source of colonization of the mouth by sanguinis group streptococci, enterococci, and actinomycetes. *S. salivarius* is long known to colonize the mouth usually within a day of birth, suggesting mother's oral or vaginal flora as the source.

Problems of Methods and Literature Interpretation

Many questions inevitably arise concerning the methods and data handling in this area. Of them, three warrant special note. (A more complete discussion of these problems is found at http://www.nidcr.nih.gov/news/consensus.asp*.)

Salivary and Plaque Monitoring of the Cariogenic Flora

For simplicity and convenience, salivary and plaque pooling techniques are often used to collect samples of oral bacteria. Since the mutans streptococci and lactobacilli colonize different locations of the mouth—the mutans streptococci being highly localized on specific areas of the teeth, and the lactobacilli being mucosal colonizers—data obtained from pooled samples provides a very different perspective on bacterial counts than data obtained from site-specific plaque sampling. This is particularly true for pooled salivary sampling of mutans streptococci, for which data reflect the average bacterial count of exposed tooth surface areas, compared to site-specific plaque sampling, for which data reflect the most likely-to-be colonized sites on the teeth. Inter-study data variability can also be attributed to different transport and cultivation methods, which may foster both false positive and false negative data.

The Role of Sugar(s) in Decay

Time did not allow the systematic review of the role of various sugars and sugar substitutes in the context of the status of infection or colonization by the mutans streptococci and lactobacilli. Data abound, however, that for caries-active patients, frequent sucrose consumption may be especially associated with the ecological emergence of the mutans streptococci and of the lactobacilli and caries activity, as was indicated by the old literature and the evidence tables. Two human genetic diseases that require patients to consume essentially no sucrose—hereditary fructose intolerance and intestinal sucrase deficiency—make clear sucrose's great impact on both colonization of the dentition by cariogenic bacteria and development of carious lesions.[91,92]

Modeling Strategies to Predict Lesion Score Increments

A number of studies have understandably sought to characterize caries risk by evaluation of independent variables such as implicated bacteria, socioeconomic status, sugar intake, specific food intakes, oral hygiene, fluoride exposure, etc. and existence of carious lesions, whether cavitated or initial (white spot). Not surprisingly, the inclusion of the existence of the disease's result (carious lesions) as an independent variable in the multifactorial or predictive analysis of the dependent variable (carious lesion score increment), has resulted in the conclusion that the biggest predictor of lesions was preexisting caries lesions. It would not seem that such an analysis is substantially different from using the presence of gangrenous toes in diabetic patients as a predictor of the occurrence of more gangrenous toes. Use of carious lesions to predict that the patient will get carious lesions appears tautological, true on its face. Use of carious lesions is, obviously, without utility as a predictor of carious lesion score increments in children with no lesion experience.

Perhaps more appropriate issues to consider for disease prevention would be either: 1) the prediction of who among populations of children (or adults) may develop carious lesions when they are essentially free of them, or 2) the prediction of management outcomes for people with existing lesions from the evaluation of microbiological, dietary, fluoride, and/or salivary conditions.

Conclusions of Review

Evidence from the current review strongly supports a central role of the mutans group of streptococci in the initiation of caries on the smooth surfaces and fissures of the crowns of the teeth of adults and children, and suggest a potent etiologic role of them in the induction of root surface caries also. Lactobacilli are also implicated as important contributory bacteria in tooth decay, but their role in induction of lesions is not well supported. Evidence that other streptococci, enterococci, or actinomycetes are prominent etiological agents of dental caries in humans is equivocal at best. The mutans streptococci are spread vertically in the population, mostly but not exclusively from mothers to their children.

These findings suggest strategies for improvement of the dental health of both children and adults in the United States and in other countries.

Future Directions for Research

It would seem overdue that facile methods for the molecular detection of colonization of tooth sites by mutans streptococci be established and validated. These methods should be used to indicate individual patient and individual tooth site risk for lesions and, ideally, should be executable in the dental office. They must be reimbursed by third parties. They should save enormous amounts presently expended for repeated restorative care.

Such methods would make the study of outcomes of individual patient management, the compliance of patients with dietary advice, the assessment of effects of antimicrobial treatments, the establishment of prognosis for further decay, and the estimation of the probability of failure of restorative treatment more feasible. Such an issue focus would move the practice of restorative dentistry out of a fundamentally reparative mode into a diagnosis-based, infection control-oriented, tooth surface-protective, and selectively restorative mode.

There is need for the development of more potent topical antimicrobial agents that target the suppression of the mutans streptococci by topical treatment of the teeth. Although chlorhexidine was once seen as a promising agent of this sort and has shown considerable efficacy, its effects have been less than ideal and its potency at presently allowed concentrations in the United States is marginal. There is considerable literature (not reviewed here) to suggest other agents and avenues for such antibacterial therapies.

The reported effects of xylitol confections in the reduction of decay increments are notable. Public health promotion of strategies to reduce the probability or level of colonization of mothers and, perhaps, other caregivers, by mutans streptococci, whether based on use of xylitol, restriction of certain sugars, excavation and filling of carious lesions, antiseptic treatment, and/or other strategies, is of great interest. The literature indicates that these strategies can affect delay of cariogenic microbial infection of children and consequent mitigation of their caries experience. It would seem appropriate for prac-titioners to use such strategies to protect the dental health of children now, and for health research funding agencies/industry to conduct large-scale clinical trials to assess population dental health improvement of children by treatment of their mothers and caretakers. Other caretakers should include grandmothers and daycare personnel who increasingly participate in the rearing of children in this time of growing parental obligations to the workplace.

Special attention should be given to secondary decay occurring at the junction of restorative material and the enamel cavosurface. Abundant data (reviewed by others) indicate that a very large part of practitioner time and patient money is spent re-filling previously filled teeth. Although there is a literature on the bacterial correlates of secondary decay, it is limited. The issue warrants substantial funding for interventional clinical trials.

Lastly, it is paramount that dentists and dental educators not equate the term "dental caries" with "cavities." The lesion is not the disease, but the effect of the disease. The disease does not occur without infection by cariogenic bacteria. To prevent, detect, and manage caries throughout life, one must not be restrictively focused on the end result of the disease—cavities.

Three hundred thirteen papers were considered in this review; space limitations did not allow further discussion or citation in the text. Papers presented in this truncated version of the review are listed below. The complete paper and the supporting evidence tables can be accessed at http://www.nidcr.nih.gov/news/consensus.asp.

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