Dental caries is a transmissible, complex biofilm disease that creates prolonged periods of low pH in the mouth, resulting in a net mineral loss from the teeth. Historically, the disease model for dental caries consisted of mutans streptococci and Lactobacillus species, and the dental profession focused on restoring the lesions/damage from the disease by using a surgical model. The current recommendation is to implement a risk-assessment-based medical model called CAMBRA (caries management by risk assessment) to diagnose and treat dental caries. Unfortunately, many of the suggestions of CAMBRA have been overly complicated and confusing for clinicians. The risk of caries, however, is usually related to just a few common factors, and these factors result in common patterns of disease. This article examines the biofilm model of dental caries, identifies the common disease patterns, and discusses their targeted therapeutic strategies to make CAMBRA more easily adaptable for the privately practicing professional. (J Prosthet Dent 2014;111:280-285)

Dental caries is a transmissible biofilm dysfunction of the teeth marked by prolonged periods of low pH, which results in a net mineral loss. Historically, the disease model for dental caries consisted of mutans streptococci and Lactobacillus species. However, more recent scientific evidence indicates that the disease is more complex than this model suggests and that it has traits in common with other biofilm diseases.

Biofilm research using DNA sequencing identification of bacteria has identified some 40 bacterial species to date as having a role in dental caries, and that list continues to grow. In recent independent studies, Bifidobacterium species, Scardovia wiggsiae, Slackia exigua, and Propionibacterium acidifaciens have been implicated. Next-generation sequencing technologies promise to add to these species as the biofilm model of dental caries becomes better understood. Dental caries also has potential systemic effects. Studies from randomly collected coronary plaque specimens during surgery indicate that when found in the mouth, the most common oral bacteria found in the coronary plaque is also Streptococcus mutans. The authors concluded that S. mutans was responsible for most bacterial endocarditis and that by comparison, the presence of periodontal pathogens was negligible. S. mutans is also able to invade endothelial cells directly by means of its omn (collagen-binding protein) gene. Further studies have also implicated caries-causing bacteria in impaired cognitive function, ulcerative colitis, and accelerated plaque growth after angioplasty. Dental caries also has apparent hereditary characteristics and genetic associations. Early studies found that individuals with the G20A polymorphism for beta-defensin-1, a salivary bacteriolytic enzyme, had 5 times the decayed, missing, and filled teeth (DMFT) scores seen in those with other variations of this gene. Hereditary associations with the TAS2R38 taste-bud gene increase the risk for dental caries. A recent genome-wide association study indicated multiple gene site associations with an increased risk for caries, the strongest of which was LYZL2 (lysozyme-like 2), which encodes another bacteriolytic enzyme. The data from this study also indicated 5 distinct patterns of decay geographically in the mouth, with the LYZL2 gene being associated with carious lesions only in the mandibular incisors. Additional genetic associations have been attributed to a mutation in matrix metalloproteinase 13 (MMP13) and the HLA antigen allele HLA-DQ2. Regardless of how complex the biofilm disease model becomes, however, dental caries still means prolonged periods of low pH, resulting in a net mineral loss from the teeth. With the continued development of next-generation sequencing technologies, examining the biofilm and its metabolic outcome differently will be possible. Nyvad et al have explored the novel idea of viewing the biofilm as a single organism, as first proposed by Buchen. Biofilm is a collection of distinct and separate organisms, but it behaves collectively as one superorganism. As such, it is less important to identify which specific bacterial species are present. Instead, the authors proposed a metagenomic study to identify which genes were present in the biofilm in total. The genes that are active produce the proteins resulting in metabolic output from the biofilm. In the case of dental caries, the concern is that acid
output creates prolonged periods of low pH. Future dental caries biofilm research, therefore, should not be focused on specific bacteria but on the function and output of the biofilm.16

Caries Risk Assessment

As the scientific evidence has grown, the dental profession has progressed from an intuitive model of medicine (educated guess; drill and fill lesions) to an empirical model (probabilistic model based on systematic reviews of randomized controlled trials; fluoride and nonfluoride anticaries therapies). Continued growth in the evidence base will lead the profession into a future of precision medicine, in which the cause of a disease is known and can be measured and targeted for therapy.18 Results to date have been mixed regarding the sensitivity and specificity of various caries risk assessment (CRA) tools. Pediatricians who identified plaque on the maxillary central incisors (a caries risk factor) in children during well-care visits had a 55% sensitivity and an 80% specificity.19 Another study examined the caries risk assessment tool (CAT) of the American Academy of Pediatric Dentistry, independently of socioeconomic status, and compared the results with mutans streptococcal cultures. The CAT had a high sensitivity of 100% and a low specificity of 2.9%, whereas the mutans streptococcal culture alone resulted in an 86.5% sensitivity and a 93.4% specificity. The mutans streptococcal culture alone outperformed the CAT.20 A study examining the Cariogram risk assessment tool over a 2-year period in school-age children found both a high sensitivity (83%) and a high specificity (85%), and a strong correlation was found between caries risk profiles and caries incidence after 2 years.21 A 6-year retrospective analysis of the CAMBRA (caries management by risk assessment) CRA form reported a higher incidence of cavitated lesions among those assessed as being at extreme risk compared with those diagnosed as being at low risk initially.22 Finally, a systematic review of 4 CRA tools concluded that the evidence for the validity of existing systems for CRA is limited and that valid and reliable methods for CRA are urgently needed.23

CAMBRA is the next attempt to explain the underlying risks and causes of dental caries in an individual.24 Identifying the risks allows for individualized, targeted therapy. There are known and validated common risk factors for dental caries, as well as disease indicators.22 The same 6-year retrospective study examined 12,954 individuals, and the odds ratios (ORs) of these factors and indicators have been established and validated.22 The disease indicators include visible cavitation or radiographic radiolucencies penetrating to dentin (OR, 8.21), active white spot lesions (OR, 2.77), and a history of a restored cavity in the previous 3 years (OR, 1.46). Risk factors include noticeable plaque buildup on the teeth (OR, 2.55), frequent snacking (OR, 1.77), hypersalivation (OR, 1.27), exposed roots (OR, 1.19), deep pits and fissures (OR, 1.80), and recreational drug use (OR, 1.95). These new data have added to the factors and changed the picture for dental caries, but this change has simplified the situation for those in clinical practice. By identifying pattern recognition for common clinical causes of dental caries, the new factors include bacteria (either too much bacterial load or high acid output of the biofilm); diet (either excessive sugar consumption or snacking too frequently); saliva (either hyposalivation or poor buffering capacity); and genetics (multiple possible associative genes).

CAMBRA is a simple process, consisting of 3 separate steps: assessment, diagnosis, and prescription. CRA is performed with a standardized CRA form. CRA forms are available from the American Dental Association, the California Dental Association Foundation, the American Academy of Pediatric Dentistry, and other organizations. Assessment consists of identifying known risk factors for an individual patient and noting any disease indicators. Various biometrics have been used in clinical practice for dental caries, but most have involved culturing saliva to measure mutans streptococcal and \textit{Lactobacillus} levels. A current biometric uses the adenosine triphosphate (ATP) bioluminescence of a dental biofilm specimen, which correlates with overall bacterial load and the functioning/metabolic output of the biofilm.25,26 High ATP presence indicates either high bacterial load or high metabolic output.27

One of the challenges of implementing CAMBRA in clinical practice stems from the lack of time available to perform this task, as it is usually assigned to an already burdened hygiene appointment. A recent CRA form developed for clinical practice addresses this issue beginning with 3 motivational interview questions, followed by the self-reporting of risk factors by the patient (Fig. 1). This can be accomplished in the reception area before a dental hygiene visit. The dental professional can then identify disease indicators and discuss the risk factors with the patient.2

The caries diagnosis is made by examining all of the patient data: the CRA form, oral examination, radiographs, history, and any biometrics (if used). The American Dental Association Council on Scientific Affairs published definitions for the various risk categories for children and adults in a special supplement to the \textit{Journal of the American Dental Association} in 2006.28 Once the caries diagnosis is determined, the next step is to design therapeutic strategies for the patient, specifically targeting individual risks.

Prescriptive strategies can be organized into 3 categories: reparative strategies, therapeutic materials, and behavioral changes. Reparative strategies are well developed by the dental profession and include remineralization and restoration. The best scientific evidence for remineralization is with fluoride, although most of the compelling scientific evidence is from studies on children, and the results are
extrapolated to all age groups.\textsuperscript{29,30} Whereas fluoridated water has been found to reduce the overall decay rate in populations, the best form of professionally applied fluoride is fluoride varnish.\textsuperscript{31,32} Patient-applied fluoride is best in the form of a 0.05% fluoride rinse or a 5000-ppm fluoride gel. For patients with a high risk of caries, the recommendation for fluoride varnish is every 3 months; more frequent application does not add benefit.

Current remineralization research also involves several forms of calcium phosphate, including nanoparticle...
Although more research is indicated, it has been found that the nanoparticle hydroxyapatite is biomimetic for the natural building blocks of enamel and reduces biofilm formation. Restoration of active cavitated lesions is required. The clinician may elect to stage the treatment of lesions in the patient with a high risk of caries, first restoring all lesions with an intermediate material such as glass ionomer cement while working with the patient to modify the biofilm and behaviors. Patients at high risk or extreme risk (such as, because of hyposalivation) may develop new lesions within 1 year, so it is appropriate to stage their restorative care.

Therapeutic strategies include antimicrobial, metabolic, pH, and potentially probiotic categories. Antimicrobial strategies typically include the use of povidone-iodine, chlorhexidine, or sodium hypochlorite rinse. Biofilms are resistant to change, and it may take 2 or more years of using these rinses to modify the biofilm and reduce the patient’s caries risk. Whereas it is appropriate to use an antimicrobial agent for a patient with a high biofilm load, patients that lack a high biofilm load but have other risk factors may not benefit from an antimicrobial strategy. One potential metabolic strategy for the biofilm is xylitol. Xylitol has been found to potentiate even small amounts of fluoride, so it might be beneficial to combine xylitol with fluoride strategies. However, there is conflicting evidence for xylitol; a recent study in adults found that long-term daily use of xylitol mints alone did not decrease the caries outcome in those at high risk. This multisite study perhaps indicates that a 1-dimensional treatment of xylitol in patients with high caries risk may not be effective given the complex biofilm nature of the caries disease. Conversely, numerous studies have found that xylitol is an effective anticaries agent. Recently, a study has indicated that xylitol seems to have an anticaries effect on root surface lesions in caries-active adults. Xylitol may be effective when applied in a combined approach with other strategies targeted to the patient’s specific risk factors but may be ineffective as a solo strategy. In addition, pH modification may reverse both the selection pressure and therefore the output of the biofilm, with the added benefit that it also drives remineralization. For patients with inadequate saliva, neutralization strategies supplement the protective role of the saliva.

Probiotics deserve mention. A probiotic is a therapeutic agent that consists of living microorganisms, primarily bacteria; that is safe for human consumption; and that when ingested has beneficial effects beyond just nutrition. The strategy is to influence the makeup of the biofilm by consuming less-pathogenic organisms. Probiotics have been used with great success in treating conditions such as diarrhea and Crohn disease. In dental caries, the probiotic must be able to adhere to and integrate into the biofilm, compete with and antagonize cariogens, and have low-acid-production metabolism. Although additional research is indicated, probiotics offer a potential additional strategy for the future.

Behavioral issues include strategies to alter behavior and also to account for risks that cannot be modified. Some behaviors are theoretically modifiable and some are not. Diet and home care both play significant roles in dental caries. Excessive plaque buildup or bacterial load, accompanied by infrequent disruption, leads to site-specific demineralization of the teeth. Home care instructions such as daily brushing and flossing continue to be important. Dietary issues tend to stem from excessive sugar intake or from snacking too frequently. Both of these behaviors should be modifiable, but human behavioral change is not easy, nor is it linear. In a recent clinical trial in patients improving their oral hygiene behaviors, some improved during the term, some stayed the same, and some improved and then relapsed. Motivational interview and wellness coaching principles can help patients manage their own behavioral changes, but realistically these changes take time and consistent reinforcement. A recent study also provides some discouraging results; it found that it is easier to change patients’ alcohol intake than it is to change their sugar consumption.

Nonmodifiable issues typically involve medication-induced hyposalivation, aging, reduced cognitive or physical function, and special needs. Hyposalivation is a significant risk factor for dental caries and most often relates to medication use. The more medications involved, the greater the risk and severity of hyposalivation.

Designing an appropriate and effective treatment strategy for an individual patient is straightforward. The causes drive the treatment strategies. The patient in Figure 2 is at high risk for dental caries, as is the patient in Figure 3. However, the risk factors associated with these 2 patients are significantly different and require a targeted approach for their treatment to be successful. If the patient has a bacterial issue (see Fig. 2), it should be addressed with antimicrobials, pH modification, and home care instructions. For the patient with a dietary issue, the strategy should focus on modifying their sugar consumption or snacking habits. The patient with hyposalivation (see Fig. 3) will likely benefit from maintaining hydration levels and from pH neutralization materials, both of which support a healthy oral environment. The patient with a genetic risk for dental caries will be harder to diagnose but will benefit from minimizing acid exposure during the day and maintaining good health. For the clinician, it is important to have an appreciation and understanding of the complexity of the dental caries biofilm disease model. But perhaps more importantly, being able to identify the common disease patterns and associated therapies presented in this article should make CAMBRA more easily adaptable in clinical practice.

SUMMARY

Dental caries is a complex biofilm disease with many associated risk factors.
factors and disease indicators. The dental profession has historically treated the disease by focusing on restoring cavitated lesions. CAMBRA, an emerging philosophy, also includes identifying specific risk factors and disease indicators for an individual patient and designing targeted therapies to address those risks. CAMBRA provides the next step toward precision medicine and designing targeted therapies to ease indicators for an individual patient.

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