Advancing the practice of dental disease management.
New Directions in the Etiology of Dental Caries Disease

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Abstract
This review explores the multifactorial etiology of dental caries disease. Current theories suggest that a singular focus on mutans streptococci and lactobacillus as the sole causative microbiological agents is no longer a viable strategy in treatment of this prevalent disease. Dental caries is an infectious transmissible disease process where a cariogenic biofilm in the presence of an oral status that is more pathological than protective leads to the demineralization of dental hard tissue.1

Recent research also indicates dental caries has genetic components. When examining for beta-defensin-1, a salivary protective protein, there are three polymorphisms (genetic expressions or variations) of this gene. Individuals with one particular genetic polymorphism, the G20A expression, exhibited five times the DMFT scores of the other two genetic variants.2 Genetic variations associated with taste have also been implicated as a hereditary component influencing dental caries.3 Previous reports have characterized the influence of genetic variation on taste preferences and dietary habits. Statistically, significant associations were seen in TAS2R38 (bitter) and TAS1R2 (sweet) for caries risk and/or protection. Children with the TAS2R gene object to the bitter taste of many green vegetables, prefer eating sweets, and have demonstrated a significant correlation with increased caries experience.

The Role of Bacteria
Originally thought to be a disease of two primary pathogens, mutans streptococci and lactobacillus, the current biofilm disease model for caries is one of multiple pathogens. Marsh demonstrated in the ecological plaque hypothesis that dental caries is a pH-specific disease.4 These pathogens are acidogenic and aciduric bacteria that metabolize carbohydrates into acids, resulting in acidic conditions in the oral biofilm. However, it is the acidic pH per se, not the carbohydrate availability, that provides the selection pressure favoring these cariogenic organisms in the biofilm environment. When these acid-producing bacteria dominate the biofilm, the normal balance in the mouth that influences demineralization and remineralization changes to produce prolonged episodes of low pH, resulting in demineralization of the teeth and net mineral loss. Recent biofilm research has introduced the so-called “extended ecological plaque hypothesis” where even
Commensal bacteria have demonstrated the ability not only to adapt to live in the acidic environment, but to also develop the ability to produce acid themselves, thus contributing significantly to the disease process.

About 1,000 different bacteria species have been identified from the human oral microbiome, making the mouth the most microbially diverse environment in the body. However, the picture may be even more complex than that; DNA identification research examining the hyper-variable vector region of the 16S gene sequence, would indicate that there may be 6,000 different bacteria in the human oral microbiome. 

Research also has suggested that dental caries may have systemic effects. While the oral-systemic connection with periodontal disease has gathered a great deal of attention in the past decade, dental caries disease may also have similar consequences. In Nakano et al. reported Streptococcus mutans in the coronary arteries and heart valves percent of the time. It is suggested that dental caries may play a role in bacterial and peripheral vascular disease.

In summary, the current biofilm model of dental caries is a complex picture: multiple pathogens, systemic effects, and hereditary components layered on interactions of diet, behavioral, environmental, socioeconomic, and physiological risk factors. Thus, diagnosis for dental caries disease becomes more complex and involves examining these different parameters to get a clearer picture of this disease.

**The Role of Saliva**

Saliva plays many important roles in the mouth in health and digestion and offers some real potential in evaluating dental caries risk. Saliva is a unique fluid in the body, it is supersaturated with calcium and phosphate, helping maintain the mineral content of teeth, it contains protective proteins and antibodies, enzymes for digestion, lubricants for chewing and swallowing, electrolytes for buffering the pH and many other factors that contribute to a healthy balance. As a diagnostic specimen, saliva is readily available, it is easily collected and stored, and it is a noninvasive procedure.

Salivary Flow (Resting and Stimulated)

Insufficient saliva flow (resting and stimulated) may lead to the subjective complaint of dry mouth, or xerostomia, a condition that jeopardizes the teeth from the lack of buffering ability and reduced availability of calcium phosphate for remineralization. Saliva flow reduces as a natural part of aging, by a multitude of prescription medications and is from a practical standpoint nonexistent during sleep. Radiation therapy and conditions like Sjögren’s syndrome or other autoimmune connective tissue diseases, diabetes, hepatitis C, and HIV infection all can reduce the amount of saliva flow. Inadequate saliva flow is a known risk factor for dental caries, less than .7 ml of stimulated saliva per minute places a patient at high risk or extreme risk. Recently, reduced saliva flow has been tied to childhood obesity and increased risk for dental caries in children.

Saliva flow rate should be assessed in both stimulated and resting saliva. Commonly, clinicians only assess the stimulated flow rate because stimulated saliva flow is easy to measure. Simply have the patient chew on paraffin wax and spit into a graduated cup, measuring mls/minute. While this test is very accurate to measure stimulated saliva flow, the test itself may not be highly predictive for dental caries experience. If the stimulated flow rate is below .ml/minute, then the patient can now be
diagnosed as having "salivary gland hypo-
function," the preferred term when flow is measured quantitatively rather than using the subjective term "xerostomic."

Measuring resting saliva flow is less
often done perhaps because it requires
the patient to "drool" into a collection
vessel measuring the mls/minute of flow.

When performing the test, patients were
instructed to initially swallow and then
tilt their head forward with the chin near
the chest and instructed to avoid any lip
tongue movements, talking, or swal-
lowing. The saliva was allowed to pool in
the front of the mouth for exactly two
minutes without swallowing. It was then
gently drooled into a graduated cylinder.

The two-minute collection process was
repeated twice and then patients were
asked to gently empty their mouths of any
remaining saliva into the collection vessel.

Patients should be informed that there
may be little or no saliva to expectorate
and not be concerned if that should prove
to be the case. The total quantity was
divided by four minutes to obtain a flow
rate per minute. The lower end of normal
flow rate may be as low as . ml/min.

Admittedly the drool test above is not very popular in clinical prac-
tice and a surrogate test to help identify
the presence of abnormal resting saliva
flow, such as the physical appearance of
saliva (thick and bubbly) and the inability
of minor salivary glands of the lips to
produce visible “beads” of saliva within
one minute after drying with gauze, have
been reported in clinical use. Although
using the appearance of resting saliva
has the support of at least one study that
correlated surface tension of saliva to
dental caries using technology like droplet
surface tensiometry, these surrogate tests
should be considered anecdotal at best
and should be lightly weighted until a
larger body of evidence is presented.

Salivary pH (Resting and Stimulated)

Although resting and stimulated
salivary pH is easily measured with a
high degree of accuracy with the use of
pH sensitive test strips, they must be
interpreted carefully. While the data
accurately reflect the pH of the saliva,
the real challenge for pH measurements
is how to use these data to make useful
clinical decisions. It is important to
keep in mind that the value in using any
salivary test will depend not only on the
type of saliva measured (resting or
stimulated), time and location sampled,
but most importantly what is going on
with the local biofilm, chemistry, and
salivary composition; together they will
determine remineralization or demin-
eralization of dental hard tissues.

Minor salivary glands normally
produce saliva that has a lower pH than
the major salivary glands and, consider-
ing the amount of time saliva is actually
being stimulated, resting (unstimulated)
saliva may perhaps be more important
to evaluate clinically than stimulated
saliva. Although one study by Subrama-
niam in demonstrated a significant
correlation between resting salivary pH
and dental caries in the primary denta-
tion of children with cerebral palsy, in
the end, the real value of pH testing
may well be as a teaching tool rather
than attempting to relate pH to predict-
ing caries risk. It may help in the selec-
tion of products to neutralize acid and
restore the mouth to a healthy state. Part
of this is because the salivary pH may
or may not be reflective of the actual
biofilm pH on the teeth or it may reflect
affects of diet if the patient has eaten.

Resting saliva will also have different
pH measurements, depending on
the areas of the mouth in which they are
sampled, thus pH (like biofilm and caries
lesions) is site-specific. In fact, an interest-
ing exercise is to sample saliva at differ-
ent areas of the mouth and measure pH
using pH-sensitive test strips. Although
not validated, one technique is to collect
saliva from a patient (in a resting state) by
having them expectorate only once into a
cup and measuring the pH of that single
collection. A clinician may use this as an
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Buffering Capacity

The quantitative measure of resistance to pH changes is called buffer capacity. In 1959, Ericsson introduced a test to measure the buffering capacity of an individual's saliva. The expression of this test described the ability of a patient's saliva to buffer or neutralize the salivary pH during acidic challenges. The Ericsson test proved to be highly predictive for dental caries. The challenge is that this is not a chairside test but rather a laboratory procedure that requires several hours to complete. Chairside tests are currently available for measuring buffering capacity of stimulated saliva; however, some studies question their reliability. A recent study of these tests demonstrated one technique used on resting saliva that was consistent with the Ericsson data, but the other tests on stimulated saliva were not. Other analyses on buffering capacity recommended a need for additional research. The salivary-buffering capacity appears to have caries predictive value in the Ericsson test, but available chairside tests may not be as accurate.

As with testing salivary pH, care must be exercised in the interpretation of a buffering test, even if the result is "normal." For example, the test does not measure the presence of salivary hypofunction (xerostomia), so one could conceivably get a "normal" buffering capacity on a patient who has severe salivary hypofunction. As mentioned above, the reliability of these chairside tests to assess buffering capacity is in question and should be considered along with other factors to modify the local environment using chemical interventions.

Measuring Bacterial Load or Activity

Research data have long established a strong predictive relationship between levels of salivary mutants streptococci, lactobacillus, and, more recently, S. sobrinis and bifidobacteria and dental caries. Blood agar plating and polymerase chain reaction (PCR)-based bacterial identification provide accurate measurements of these known pathogens in the saliva. The challenge for this parameter again is one of an accurate and predictive chairside test.

While several chairside cultures are available, recent independent research indicated that none of them accurately identified the level of cariogenic bacteria or S. mutans present. A sample of the patient's saliva is collected and then cultured on selective agar media for 48 hours. It is a management challenge to schedule patients to collect the sample then recall them for reading and discussion of the test after 48 hours.

Monoclonal antibody testing has been established for measuring individual pathogens and a test for mutans streptococcus is currently available. Measuring specific pathogens in light of the multipathogen biofilm model for this disease is questionable. In other words, such specific pathogen targeting may not be able to provide adequate predictive value. In addition, in light of the extended ecological plaque hypothesis where low pH nonmutans bacteria and actinomyces are acid-producing and thought to be precursors to a mature acidogenic biofilm dominated by MS and LB, the diagnosis would be missed by both specific monoclonal antibody test and selective culturing methods. In summary, bacterial identification offers some promise of predictability; however, there is a need for additional evidence correlating the chairside test currently available to actual caries disease risk.

The cariogenic potential of a plaque biofilm sample is another chairside test that is currently available. It measures the ability of the patient's plaque biofilm to metabolize sugar. A small sample of the patient's plaque is collected, a sugar solution is added, and then a pH-sensitive dye is added. The resulting color change is read and indicates the patient's "cariogenic potential." While one study indicated the cariogenic potential correlated well with the bacterial levels, additional research and validation correlating the test to the patient's caries risk are needed. In the meantime, the test has strong educational value for patients to understand the role of diet and pH in dental caries. It is a chairside test that takes about 10 minutes to perform.

ATP Bioluminescence is a technology that has been around for a long time. It is used in a multitude of environments where precise measurement of bacterial activity is necessary, e.g., food manufacturing, wastewater treatment. The concept behind ATP bioluminescence in dental caries is based on the known adaptive mechanism of acidogenic bacteria. These bacteria survive and thrive in acidic pH environments because they have the ability to pump the hydrogen (protons) ions out of their cell. In addition to other adaptive mechanisms, they maintain a more neutral intracellular pH in this harsh environment. This requires a
tremendous expenditure of ATP. By measuring ATP levels in the biofilm, a determination of overall bacterial load and biofilm activity can be assessed. Recent scientific studies further indicate a significant positive correlation to the patient’s overall Streptococcus count, mutants streptococcus counts, and directly correlates to the patient’s caries risk status. ATP bioluminescence then becomes a risk tool and a potential biometric to identify and assess the level of cariogenic bacteria, and also act as a surrogate endpoint to measure effectiveness of anti-caries therapy. ATP bioluminescence is a simple chip assay test that involves swallowing a specific site on the teeth and then a second measurement with a meter. It is efficient, effective, and provides reasonable predictability without recalling the patient as in the culturing technique.

Conclusion

The complex nature of a multi-factorial, pH-driven biofilm disease such as dental caries whose onset and progression is influenced by so many diverse bacterial, dietary, environmental, socioeconomic, physiological, and genetics risk factors exemplifies the need for the dental profession to look beyond tooth restoration. It requires a careful assessment of each of these factors, not in isolation but taking all unique and dynamic factors into account in the assessment of each individual patient. Science has made significant advances in bacteria identifying disease like dental caries is identifying recent scientific studies further indicate a significant positive correlation to the patient’s overall Streptococcus count, mutants streptococcus counts, and directly correlates to the patient’s caries risk status. ATP bioluminescence then becomes a risk tool and a potential biometric to identify and assess the level of cariogenic bacteria, and also act as a surrogate endpoint to measure effectiveness of anti-caries therapy. ATP bioluminescence is a simple chip assay test that involves swallowing a specific site on the teeth and then a second measurement with a meter. It is efficient, effective, and provides reasonable predictability without recalling the patient as in the culturing technique.

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Reference

23. Palmer CA, Kent RJ, et al, Diet and caries-associated bac-
More than words. These values guide our day to day practice operations and interactions with patients. Thanks to the leadership of our doctors and the commitment of the support team, every patient at Midwest Dental and Mountain Dental experiences these values. Our practice opportunities are custom tailored to meet your individual needs. As flexible as each doctor’s practice is, the values we offer are consistent and do not waiver. You owe it to yourself to learn more about our team and the professional rewards offered by Midwest Dental and Mountain Dental. Tell us what you need to be happy, and we’ll work to make it a reality.

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