Medical Approach to Dental Caries: Fight the Disease, Not the Lesion

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Abstract

Dental caries is one of the most prevalent and costly diseases in the United States and throughout the world. Although the manifestation of the disease is the dissolution of tooth structure, the biological nature of the disease is a microbial infection. Traditional dentistry has been heavily focused on repairing damaged tooth structure via surgical approaches. The advancement of microbiology and engineering is bringing a medical revolution to dentistry. The on-going exciting progress in caries research has offered us great opportunities to better understand, detect, and monitor the disease. Most importantly, these new biological discoveries and technological developments allow us to address the etiological cause of the disease (microbial infection), which can lead to more effective treatments and prevention of dental caries. (Pediatr Dent 2006;28:188-191)

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Initial surgical approach to dental caries

Dental caries was relatively rare until the late 1600s, when an epidemic of the disease began in Western Europe and spread to North America due to increased consumption of sugars. For the first time, the disease afflicted a large proportion of children and young adults. The beginning of this epidemic led to the development of the dental profession. In these early days, dentists diagnosed the disease through visualization and treated the disease with extraction to remove what was thought to be gangrenous tissue.

Current biological understanding of dental caries

Scientific research has provided a very different concept of the nature of dental caries. The first biological insight about dental caries was revealed by W. D. Miller in 1890.[1] In his "chemico-parasitic" theory, Miller suggested that caries is not gangrene, but the dissolution of tooth structure resulting from acids generated by microbial organisms in dental plaques. During the last 50 years, scientific research has provided overwhelming evidence that caries is a specific bacterial infection linked with certain host factors.[2, 3] Molecular studies have shown that the oral cavity harbors a complex microbial community consisting of over 400 different non-harmful/commensal microbial species together with a limited number of acid-producing bacteria (called cariogenic bacteria, such as *Streptococcus mutans* and *Lactobacillus* species).[4,5] These cariogenic bacteria ferment sugars from the diet to produce acids that lower the local pH (acidogenic), and they thrive under these acidic conditions (aciduric). These abilities give them a competitive advantage over the indigenous commensal bacteria. In addition, these bacteria utilize sucrose to synthesize extracellular polysaccharides called glucans, which allow them to adhere to the tooth's surface and form the dental plaque or biofilm. Cariogenic bacteria are usually found in small quantities in healthy plaque. However, with biological and environmental perturbations, the cariogenic bacteria may become dominant in the oral flora and produce large amounts of acid in the dental plaque.[6] Acid production drives the dissolution of calcium and phosphate in the hydroxyapatite crystalline structure of the tooth.[7] Initially, this dissolution may be reversed by remineralization from calcium and phosphate in saliva. However, if the acidic conditions persist as a result of overpopulation of cariogenic bacteria together with repeated consumption of sugars or impaired salivary flow, the acid-induced dissolution overcomes the remineralization of the saliva. The tooth surface softens progressively until its constituent crystals are sufficiently weakened and cavitations are evident.

Current clinical approaches for caries detection/treatment and obstacles for improving clinical outcomes

A comprehensive diagnosis of dental caries should include the detection of cariogenic bacteria,[8] the survey of plaque acidogenicity, and the recognition of tooth demineralization sites. A comprehensive treatment plan for dental caries

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should include the elimination of cariogenic bacteria, the reduction of plaque acidogenicity, the enhancement of tooth remineralization, and the repair of damaged teeth. However, the current clinical approaches are heavily biased towards detecting tooth demineralization sites and repairing damaged teeth with surgical approaches, while efforts to control cariogenic bacteria, reduce plaque acidogenicity, and enhance remineralization are limited.

For the moment, visual, tactile, and radiographic assessments remain the most common methods used for caries detection in a clinical setting.[9] Most of the conventional modalities have been shown to be moderate in specificity (correctly identifying sound tooth structures), but low in sensitivity (accurately detecting carious lesions).[10] Many lesions are missed as a result of the high false negative rate. Visual examination is most useful in detecting smooth surface caries, but is often obscured by plaque or salivary contamination of the tooth structures. Tactile examination can aid the detection of occlusal caries. However, exploration with a sharp instrument not only damages weakened tooth structures that may otherwise remineralize, but also inoculates noncarious fissures with bacteria from the infected fissures. Radiographic assessment improves the visualization of interproximal caries; nonetheless, it is sometimes difficult to distinguish between a cavitated and non-cavitated lesion. Furthermore, with one measurement, radiographic examinations cannot differentiate between active and arrested lesions. In the past 20 years, many efforts have been dedicated to the development of new technologies for caries detection.[11] The principle of most of these techniques is based on observing the interactions of light waves with sound and carious tooth structures. Disruption of the ordered tooth structure by the caries process increases the likelihood of light scattering, resulting in reduced signal from the carious lesions. The readers should refer to Hall & Girkin[12] for an excellent review of potential new diagnostic modalities for caries lesions, including multi-photon imaging, infrared thermography and infrared fluorescence, optical coherence tomography, ultrasound, and terahertz imaging. For the most part, these methods have been demonstrated in laboratories, but their clinical applications await further perfection. A recent systematic review showed that infrared laser fluorescence (DIAGNOdent) can enhance the sensitivity of detecting enamel and dentinal caries as compared to the visual method.[10] At the same time, this method has been found to be less specific than the visual method. Taken together with the uncertainty of the diagnostic threshold value, the DIAGNOdent has only been recommended as an adjunctive tool.[10]

Since carious lesions are often not detected by conventional methods until they are advanced to a point where operative interventions are inevitable, most research on caries diagnosis has been focused on more precise detection of small lesions. Early identification of carious lesions has definitely improved the clinical outcomes in some cases, yet it has been well established that a significant number of early lesions are likely to arrest without intervention.[13] It remains a dilemma as to how early a lesion should be detected and when the lesion should be treated or monitored. The diagnosis of dental caries should not be considered merely as the presence of demineralization, as most of the current approaches have focused on. It should be an encompassing concept that also takes into account clinical risk factors (eg, socioeconomic status, dietary habits) as well as molecular risk factors (virulence of the microbial flora, immunological components in the saliva). Despite the fact many clinicians realize that caries is a multifactorial disease and that there is a need for a paradigm shift in caries diagnosis, the advent of reliable and predictive caries-risk assessment tools to facilitate treatment decisions has been slow.

This lack of effective diagnostic tools leads to limited therapeutic options as well. Currently, the treatment of dental caries is still heavily based on repairing the damaged tooth structures by operative interventions instead of controlling the cariogenic bacteria that cause the disease. Consequently, dental caries often persists despite extensive clinical interventions.

Great opportunities offered by modern biology and engineering science

One good solution to the above problems is to develop a set of comprehensive diagnostic tools that could effectively and quantitatively evaluate the different aspects of dental caries. These include the detection of cariogenic bacteria,[14] a survey of plaque acidogenicity, and the ability to identify tooth demineralization sites accurately. At present, many dental schools are revising their curricula to introduce these advanced biological and engineering techniques to future clinicians who will have a better understanding of the fundamental cariogenic process and the advantages of utilizing these novel clinical tools.

Contribution of modern science and technology to our new knowledge of cariogenesis

A major breakthrough in the field of oral microbiology is the ability to study the whole microbial profile of the dental plaque. Scientists can now detect not only the cultivable bacteria, but also uncultivable bacteria by examining bacterial 16S RNA and DNA.[15,16] With this method, our knowledge of microbial flora in the oral cavity has increased dramatically in the past several years. In conjunction with a new technique called fluorescent in situ hybridization (FISH), the spatial distribution of different oral bacteria (both cultivable and uncultivable) within the plaque has also been revealed.[17] Furthermore, the National Institute of Dental and Craniofacial Research has recently initiated a metagenomic project for oral microbial flora. With the completion of this project, scientists will know not only the number of oral microbes in the oral cavity, but also their metabolic genes and virulence factors.[18] This knowledge is what Miller was struggling to learn in 1890, but was unable to accomplish without our new methodologies. The vast amount of new information gathered from these

studies enables us to decipher the sophisticated intraoral microbial interactions and appreciate the complex etiology of dental caries.

In addition to our improved understanding of the dental plaque microbial composition, great progress has also been made in monitoring plaque acidogenicity. Scientists and engineers have developed various new methods to monitor plaque pH in situ in a noninvasive manner. For example, pH-sensitive fluorescent dyes that can produce different absorption spectra under different pH levels have been developed (Molecular Probes Inc, Eugene, OR).[19] In combination with two-photon excitation microscopy, pH-sensitive dye can be used to monitor the spatial distribution of protons in a dental biofilm. Scientists at the Jet Propulsion Laboratory have developed a polyaniline-based planer pH sensor which facilitates real time monitoring of plaque pH. Most recently, scientists at Pacific Northwest Laboratory developed a highly sensitive combined nuclear magnetic resonance (NMR) confocal microscope that can monitor pH gradient within dental plaque in real time.[20]

The combination of accurate detection of oral bacteria and in situ real time monitoring of plaque pH is opening a new chapter for cariology. For the first time, scientists can address the following interesting questions by these innovative techniques: Are some plaques more virulent than others? Which bacteria are more dominant in the oral cavity, uncultivable or cultivable bacteria? Are uncultivable bacteria more virulent than cultivable bacteria in the plaque? How virulent are the currently-known cariogenic bacteria? How do other plaque bacteria or host factors affect the growth and pathogenicity of the known cariogenic bacteria? Analysis of these questions is providing new insights in the mechanisms of cariogenesis and new leads in developing novel biomarkers for the diagnosis and risk stratification of dental caries.

The dynamics of demineralization/remineralization is a substantial parameter in the cariogenic process. New imaging tools such as atomic force microscopy (AFM) and laser interference microscopy (LIM) are being used to instantaneously detect bacteria-induced demineralization in an ultra-sensitive level. We anticipate that the perfection of this technique will translate to a good quantitative assessment modality for the cariogenic potential of different bacterial species.

Translation of scientific discoveries into clinical applications

Early detection and quantification of cariogenic bacteria in plaque or saliva samples can help clinicians take preventative measures to stop caries development, much like early detection of cancer markers before the cancer metastasizes. Since old culture techniques are slow and can only detect cultivable bacteria, new antibody or nucleotide-based bacterial detection techniques have been developed for the detection of cariogenic bacteria in chairside or laboratory settings.[21] In conjunction with nanotechnology development, these tests can be further developed into different forms of nano-chips for the detection of multiple oral pathogens in a clinical setting.[22]

Plaque acidity is a good index for monitoring tooth demineralization. Improving the accuracy and ease of measuring plaque pH in situ or at chairside will provide clinicians with an effective tool for caries risk assessment. For the moment, no such tools are available to the clinicians, but a portable, microscale planer pH sensor that can be used in a clinical setting is currently in development.

Radiographic or laser scanning techniques are useful tools for detecting tooth demineralization. Methods of higher sensitivity and better specificity for caries detection have always been in demand. Of particular importance in the search for better detection methods is the discovery of calcium-specific-binding biomolecules that can enhance the direct visualization of tooth demineralization.

The improvement of diagnostic tools is also promoting the development of better therapeutic tools. Several ongoing research projects (eg, enhanced active vaccination or passive vaccination, bacterial replacement, targeted antimicrobial therapy) are providing new directions for treating dental caries.[23-26] In particular, the targeted antimicrobial approach may provide long-lasting protection as it can selectively kill the cariogenic bacteria in dental plaque, thus turning a pathogenic plaque into a non-pathogenic one. Moreover, a complementary method to the antimicrobial effect is the development of accelerated remineralization specifically to the demineralized lesion by using bioactive molecules to actively recruit calcium to the carious site.

Future perspectives

We expect that on-going innovative research and development will have a great impact on dentistry. We envision that, in the future, dentistry will be a medical-based dental practice emphasizing the triple-pronged approach of early detection, sustainable treatment, and effective prevention. Specifically, pathogen-based early detection will become routine. Diagnostic tools based on fluorescent or other chromatically-labeled antibody, nucleic acid, or other biomolecules will allow instantaneous chairside quantification of cariogenic bacteria in plaque or saliva samples. This clinical adjunct will help clinicians to reinforce the concept of dental caries as an infectious process and will facilitate immediate treatment decisions.

The development of a compact and portable microscale planer pH sensor will be a major breakthrough in assessing plaque acidity at the chairside. The application of nanotechnologies to this prototype will further reduce the size of the sensors and make the device more user friendly to both the patients and the clinicians.

In-depth understanding of the ecological tug-of-war between the endogenous microbial flora and the cariogenic pathogens has become the gateway leading to more specific therapeutic approaches. The ability to selectively remove cariogenic bacteria while preserving the normal oral flora is a more targeted and proactive approach to dental caries than the conventional operative dentistry.

These innovative research findings and technologies are about to revolutionize the clinical management of dental caries. Pediatric dentists will be able to adopt a more proactive approach in preventing dental caries through monitoring the bacterial burden in the caregivers, thus preventing colonization of pathogenic bacteria in an infant. For those pediatric patients who have already harbored the pathogens, early diagnosis will bring about early preventive measures to reverse the disease process. The frustration of dealing with recurrent caries will soon disappear. A reliable caries-risk assessment protocol will enable clinicians to channel resources in treating patients who are at high caries risk and monitor those whose caries is unlikely to progress.

Acknowledgements

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