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The Oral Microbiome: Critical for Understanding Oral Health and Disease

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Since the time of Koch and Pasteur, medical microbiologists have focused narrowly on finding the specific the pathogen that causes a particular disease. Guided by Koch's Postulates, investigators proved causation of many diseases including polio and diphtheria. However, not all infectious diseases are caused by a single organism. This is particularly true of diseases involving biofilms where the community can be composed of several hundred species. The bacteria most associated with causing caries, *Streptococcus mutans*, and periodontal disease, *Porphyromonas gingivalis*, are not exogenous pathogens like *Vibrio cholera*, or *Corynebacterium diphtheriae*, but rather common members of the oral microbiota that are present at low numbers in most people without causing disease. The bacteria in the oral cavity include those associated with health and those that, under the right conditions, may cause disease. These bacteria interact with each other, with host tissues, and the immune and inflammatory response systems. Investigators have realized that to fully understand human health and disease, we need to understand not just the few suspected pathogens, but rather all members of the microbiota. Microbiome is the term used for the entire microbial community, including pathogens, commensals and mutualists. The National Institutes of Health recognized the importance of studying the human microbiome and launched the Human Microbiome Project (HMP) in 2008. The microbiomes of oral, gut, nasal, vaginal and skin body sites were examined in 300 healthy individuals to lay a foundation for future microbiome investigations. Information and scientific methods developed in the HMP are now routinely used in studies of the oral cavity and oral diseases. In this issue of the *Journal of the California Dental Association*, we present four articles examining different aspects of the oral microbiome.

Dental Calculus and the Evolution of the Oral Microbiome

How has the human oral microbiome changed over the past 7,000 years? Did the change from hunter-gather to farmer affect our oral microbiome? Have organisms like *Porphyromonas gingivalis* and *Streptococcus mutans* been part of our oral microbiomes for millennia, or have they recently been acquired? If only we could go back hundreds or thousands of years and obtain oral plaque samples, we could answer these, and many other, questions. It turns out that there are time capsules available to us that can take us back

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thousands of years---the dental calculus on the teeth of ancient skulls and mandibles. Fortuitously, as calculus forms, it traps human and microbial DNA. In this article, Christina Warinner, PhD, describes her studies of ancient calculus and provides insight into human health and disease and our evolving microbiome from prehistoric times to the present day. The fields of anthropology and molecular biology have joined and are giving us a much better understanding of human evolution, biology and human history.

Subgingival Microbiome Shifts and Community Dynamics in Periodontal Diseases

Our understanding of periodontal disease has changed markedly in the past fifty years. We have gone from being able to identify only about 100 oral bacteria using cultivation methods to being able to precisely and rapidly identify the more than 700 bacterial species that comprise the oral microbiome. We have not only identified key pathogens, but have come to recognize the importance of commensals and those species associated with health. In this article, Patricia Diaz DDS, PhD and coauthors Anilei Hoare, PhD and Bo-Young Hong, PhD describe shifts in the subgingival microbiome in periodontal diseases. Transitions from health to disease and from gingivitis to periodontitis involve microbial successions and adaptations to changing conditions and host responses in the gingival sulcus.

Understanding Caries from the Oral Microbiome Perspective

Caries is a disease strongly influenced by intake of dietary sugars and carbohydrates. Despite advice from dentists and public health officials, many Americans and their children continue to ingest excessive amounts of sugars and develop widespread carries. Fluoridated water and application of topical fluoride has significantly reduced caries in the majority of the population, but caries still remains high in disadvantaged populations. The article by Anne Tanner, BDS, PhD, Christine Kressirer, PhD, and Lina Faller, PhD review the microbiota in caries and how our understanding of the caries process has evolved to include the roles that beneficial bacteria play in mitigating acid produced in response to sugar exposure. Caries is now recognized as involving not only *Streptococcus mutans*, but also many acidogenic and aciduric species and the concomitant loss of many beneficial species. Microbiome studies using molecular tools now allow investigators to follow microbial shifts and analyze changes in metabolism with high precision. This greater understanding may lead to therapies which shape the composition of the microbiome and ultimately reduce caries.

Uncultured Members of the Oral Microbiome

Until 16S rRNA molecular methods were developed for identification of all bacteria, we knew only about those that could be cultivated. In the 1990’s molecular methods revealed that more than half of the 700 bacterial species in the oral cavity had not yet been cultivated. Over the past fifteen years, through the concerted efforts of many oral microbiologists, 68 percent of oral bacterial species in the mouth have been cultured. This contrasts with far lower percentages of bacteria cultured from other body sites such as the gut and skin. When a bacterium is cultured, it can be fully characterized, used in *in vivo* and *in vitro*

experiments, manipulated by knocking out or replacing genes, and formally named. In this article, William Wade, BSc, PhD, Hayley Thompson, BSc, PhD, Alexandra Rybalka, BSc, PhD, and Sonia Vartoukian BDS, FDS, PhD, describe efforts to culture all members of the oral microbiome, explain why some bacteria are very difficult to culture, and describe which groups of bacteria remain uncultivated.