Dental plaque

Who is in the neighborhood and why it matters

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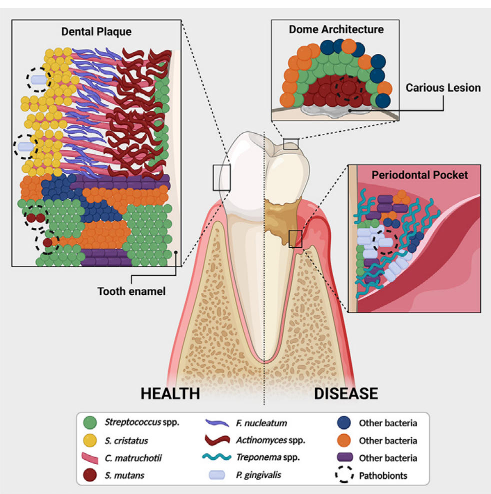
Editors' note: We are pleased to introduce a new series, "Innovations of Excellence, powered by ADA Forsyth," which provides a forum for brief introductions to new technologies, therapeutic approaches, and health care trends of interest to oral health clinicians and researchers—a "window" into the latest scientific discoveries. Inspired by the ADA's integration with The Forsyth Institute, now ADA Forsyth, JADA and JADA Foundational Science have partnered with ADA's new research arm to develop this series. These short articles are intended to raise awareness of emerging issues and cutting-edge research directions to keep the busy clinician apprised of exciting science trends expected to affect health care delivery and the practice of dentistry. Rather than describing the specifics of early or preliminary studies, however, these articles will present a more general view, highlighting specific innovations in dentistry. While ADA Forsyth will contribute significantly to the series, it is open to contributions from all potential authors and organizations with an oral health innovation to share. These reports will be published in both ADA journals, JADA, and JADA FS. We hope you enjoy the topics and format of this new series, and welcome thoughts and ideas you may have on topics you think would be useful to include in future issues.



Practical Implications

- Dental plaque is made up of many kinds of microbes that play different roles in the microbial community.
- Some plaque bacteria may promote health, whereas some can cause disease.
- How microbes are organized and spatially structured can determine whether they live harmlessly in our mouths or cause disease.
- Research on the structure and organization of plaque may, in the future, let us shift the composition of plaque in precise and targeted ways to restore and maintain health.

Key Words. Microbiome; dental plaque; dental calculus; caries; biogeography; microscopy; imaging

For centuries, people have tried to control dental plaque by brushing, flossing, scraping, and assaulting it with antiseptics and, in extreme cases, antibiotics.

What if we could learn how to control dental plaque, not just by removing it, but by adjusting it to keep it in a health-promoting condition? New research targets that goal by investigating the structure and organization of the dental plaque biofilm.

PLAQUE IS A COMMUNITY OF BACTERIA

Dental plaque is made up of dozens to hundreds of different kinds of bacteria, as well as viruses and fungi such as yeast, living side by side, stacked on top of each other, and intertwined to form a complex interacting community: the dental plaque microbiome. Some of these microbes are usually harmless or even play roles that are beneficial to human health. Others are bad actors, particularly when they are in the wrong place (next to inflamed gums) or the wrong circumstances (bathed in sugar from their human host's food and drink).

However, all plaque microbes require the right environment to grow, and often they need other microbes as neighbors. They are built to live together and depend on one another for nutrients and protection from toxins. By investigating which microbes are next to each other in natural dental plaque, how they are structured, and how they behave in different contexts, we can learn more about the conditions different microbes need to thrive and how we might use that information to control dental plaque in the future.

IF *CORYNEBACTERIUM* BUILDS IT, THEY WILL COME—AND CALCIFY

Dental plaque forms in stages from the earliest colonizers on clean tooth surfaces through maturing dental plaque to late-colonizing taxa associated with disease.[1,2] Studies suggested that a bacterium called *Fusobacterium nucleatum* played a central role in plaque maturation by forming a physical bridge from the early, pioneer colonizers on tooth surfaces to the late colonizers responsible for periodontal disease.[2,3]

However, over the past decade, several groups have developed new imaging techniques that have led them to challenge this older paradigm. Using short pieces of DNA tagged with fluorescent molecules to label different bacterial types with different colors (in a process called fluorescence in situ hybridization), and using hyperspectral imaging microscopes to distinguish many fluorescent labels at once, they could look at the spatial organization of many kinds of microbes in dental plaque simultaneously.[4,5] Using these methods, they discovered that a bacterium called *Corynebacterium matruchotii*, rather than *Fusobacterium nucleatum*, was the structural core of a dental plaque community called the hedgehog (Figure 1A).[4]

This structurally important bacterium has an extraordinary reproductive strategy. It does not just divide; it first rapidly grows longer and then splits into multiple cells at once, a rare process called multiple fission (Figure 1B).[6] Using this strategy, it forms a dense bush whose long filaments stretch from near the tooth surface to the tip of the plaque biofilm. Like the trees in a forest that create habitat for birds, insects, and fungi, C *matruchotii* creates the habitat in which other bacteria live, some binding to the tips of the filaments, where they might have direct access to saliva, and others buried deeper in the mass of bacteria, where they find a more sheltered, low-oxygen environment that many of them need.[4]

You may not be familiar with the name of this habitat-structuring bacterium, but you are likely familiar with its effects: the production of calculus on the teeth. C *matruchotii* triggers the dissolved calcium in saliva to combine with phosphate to form hydroxyapatite.[7] Hydroxyapatite is a mineral found in tooth enamel. However, when it forms around bacteria such as C *matruchotii*, it turns the soft dental plaque into hard dental calculus. As a result, dental plaque that is rich in filaments, like C *matruchotii* and its neighbors, forms calculus more readily than plaque that is dominated by other kinds of bacteria.

THESE CALCIFYING BACTERIA MAY ALSO PROMOTE HEALTH

Would we be better off without these bacteria in our mouths? Surprisingly, studies show that corynebacteria are among the dental plaque bacteria associated with health.[8] One reason might be that C *matruchotii* recruits other bacteria that ward off potential pathogens. For example, *Streptococcus cristatus*, which is nearly always found attached to C *matruchotii* at the surface of dental plaque,[9] changes the biology of the periodontal pathogen P *gingivalis* and causes it to act less virulently.[10,11] Thus, the presence of hedgehog structures made up of C *matruchotii* and S *cristatus* may help prevent P *gingivalis* from causing trouble in the mouth.

These and other data indicate that oral health may depend not just on the quantity of dental plaque, but also on what kind of organisms make up the plaque, and they suggest that our bodies may have evolved to encourage the growth of health-promoting and pathogen-inhibiting bacteria in our mouths.

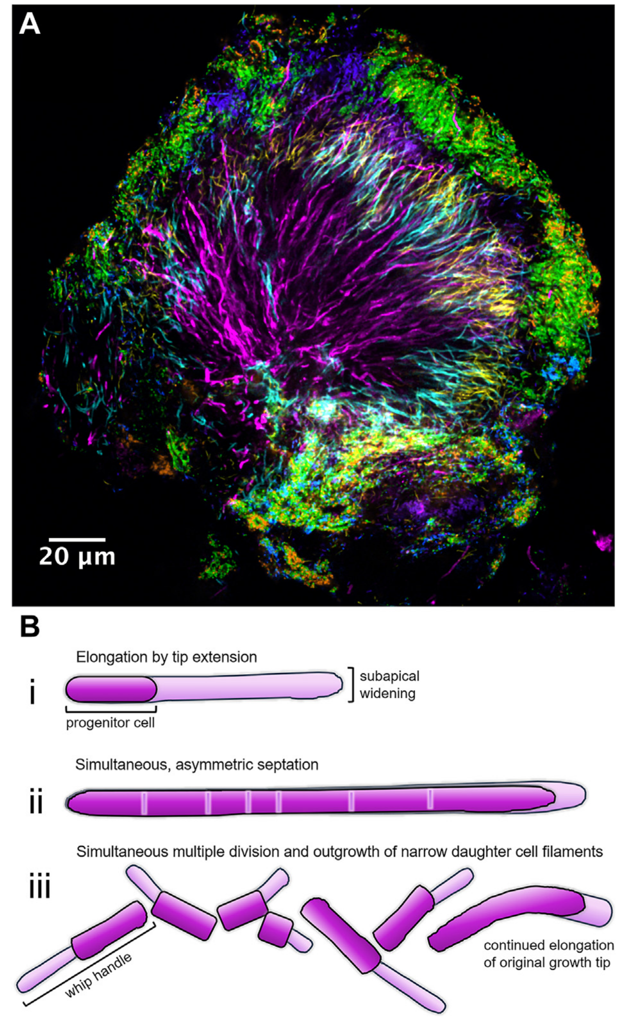


Figure 1. A. A photograph of dental plaque taken using a hyperspectral imaging microscope and using multiplexed fluorescence in situ hybridization, a technique to label different kinds of bacteria with different colors. The photograph shows the radial organization of the hedgehog structure and the central position of *Corynebacterium* bacteria, shown as magenta-colored strands. *Streptococcus* bacteria are shown in green and grow primarily on the outside of the structure. *Fusobacterium nucleatum* is shown in yellow. Reproduced with permission of the publisher from Mark Welch and colleagues.[4] **B.** *C matruchotii*, an important bacterium for the structure of dental plaque, can elongate rapidly (**i**) and reproduce by separating into many different cells at once (**ii**) that then shatter and sprout new filaments (**iii**). This unusual growth strategy helps this bacterium form large bushy clumps on teeth. Reproduced with permission of the publisher from Chimileski and colleagues.[6]

SPATIAL ORGANIZATION MATTERS: DO NOT LET *STREPTOCOCCUS MUTANS* BUILD A DOME

Spatial organization of the dental plaque biofilm is also important in the strategy of 1 key organism that can cause caries: the bacterium *Streptococcus mutans*. Findings show that this bacterium can exist harmlessly in the mouth when it is dispersed in the dental plaque.[12] Under the right conditions, however, it proliferates and forms a dense dome next to the

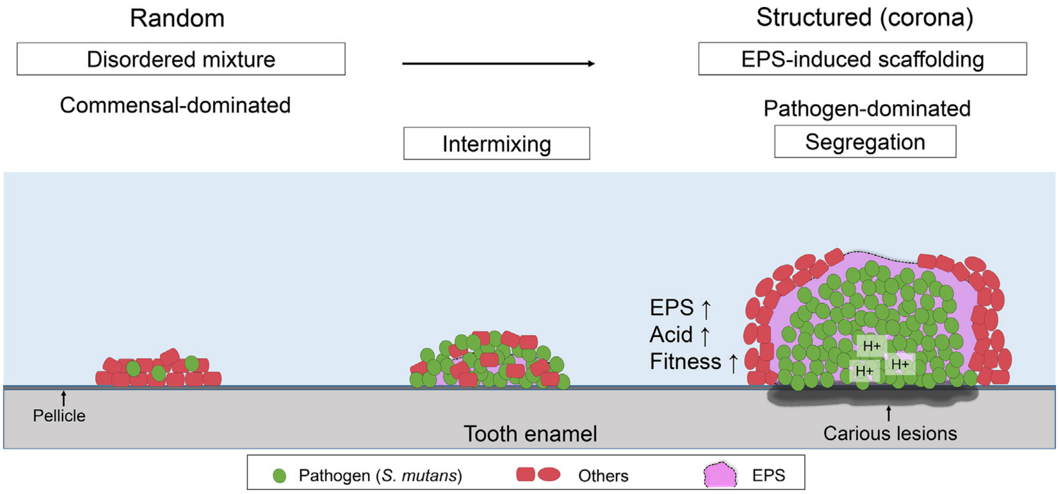


Figure 2. The caries-causing bacterium *Streptococcus mutans* can exist harmlessly in dental plaque when it is mixed with other bacteria, but it causes caries when it forms large clumps and domelike structures. Reproduced with permission of the publisher from Kim and colleagues.[12]

tooth enamel, with other plaque bacteria forming additional layers above it (Figure 2). When it adopts this dense, domelike structure, *S mutans* can produce acid and degrade the underlying enamel.[12] This finding shows that spatial organization of the microbes can change how they behave and how the oral microbiome interacts with its human host. It also suggests that we might not need to eliminate *S mutans* to control caries; instead, we could potentially control caries by disrupting the ability of *S mutans* to form a dome structure.

DENTAL PLAQUE AS A BACTERIAL COMMUNITY: IMPLICATIONS FOR THE FIELD OF DENTISTRY AND BEYOND

The new view of the oral microbiome sees dental plaque as a vibrant community of interacting organisms. Not only the cast of characters, but also their spatial structure and organization, can have a huge impact on the health of the human host. How will this new understanding change the practice of dentistry in the future?

A major goal of research is to be able to shift the composition of plaque in precise and targeted ways to restore and maintain health and to adjust the spatial organization and behavior of the organisms in plaque to reduce their harmful traits and enhance their beneficial ones.

How could we develop precision tools to edit the microbiome? In general, tools are needed to remove harmful bacteria without removing the entire community or to add beneficial bacteria. Potential avenues for removing specific bacteria include the use of narrowly targeted antimicrobial peptides (small proteins) or bacteriophages (viruses that attack bacteria and are often specialized to attack only 1 species) to selectively remove pathogenic bacteria from the mouth.[13,14]

Finding ways to add desirable bacteria and help them persist in the mouth requires more research on exactly how bacteria stick to one another or to surfaces in the mouth and what conditions beneficial bacteria require to thrive in the mouth. Adding beneficial bacteria directly or adding the nutrients that help beneficial bacteria thrive could nudge the ecology of the mouth toward a healthy state.

CONCLUSIONS

For now, physically removing plaque bacteria (toothbrushing, flossing, regular cleanings) remains the best strategy for maintaining a healthy mouth. The approach to dental plaque is to mow it all down with a weed whacker. Ten years from now, we may be acting more like gardeners: weeding out the bad actors, but also sowing, fertilizing, and pruning the beneficial microbes of the mouth. ■

DISCLOSURE

Drs. Mark Welch and Borisy did not report any disclosures.

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