

## The Job to Be Done with Biofilm and Titanium Implants

Clayton Christensen, the famous Harvard Business School professor and author of *The Innovator's Dilemma*, was once asked about the prospect of starting a new dental implant company, given the hundreds of implant companies already found around the world. "If you proceed," he advised, "you have to ask one question: What is the job to be done?" Interestingly, the job to be done remains one that the dental profession has wrestled with from the beginning: to prevent and arrest bacterial infection at the bone-implant interface without the use of pharmaceutical agents.

The peculiarity of the oral cavity is that endogenous commensal, opportunistic bacteria have evolved a highly stable, self-regulating, and symbiotic environment for the dentate niche, termed "biofilm." Oral biofilm exhibits an extremely organized 3D architecture that facilitates protection, nutrient and waste transport, and mechanical resilience. This resilience is several orders of magnitude more resistant to natural forces from mastication, deglutition, and salivary flow than that of free-living planktonic bacteria. When biofilm becomes mechanically disrupted, it readily and rapidly reforms within hours.

Biofilm is an aqueous network of mixed nucleic acids, polysaccharides, proteins, and lipids, virtually all microbial in origin. These interacting extracellular polymeric substances (EPS) are noncovalently associated into a robust matrix, which embeds and protects aggregated bacteria within. This physical barrier function provides microbial protection, particularly in the deeper layers, establishing physical resistance to phagocytosis and to permeation of antimicrobial agents. Microbial biofilm density within EPS favors chemical communication (quorum sensing) and plasmid exchange, facilitating transfer of resistance and virulence genes, enabling senescence, that is, "sleeper" cells, that reawaken postexposure to antibiotics to exert latent virulence.

When normal symbiotic oral biofilm becomes pathogenic, a dysbiotic chain of events occurs at the titanium-bone interface, resulting in peri-implant disease. Therefore, eliminating or mitigating pathogenic microorganisms at the bone-implant interface suggests a need for an intrinsic antimicrobial property at the implant and abutment surfaces to defend against dysbiosis.

Natural teeth "implanted" within the alveolar bone and supported by a connective tissue barrier as well as epithelial attachment, which inhibits bacterial invasion,

are remarkably stable and self-cleansing. However, this natural state can quickly become imbalanced by a change in oral structural basis, which is found with a dental implant-supported fixed denture, and many other factors, such as a reduction in quantity or quality of saliva, a change in diet, immune compromise, or disturbance in vascular dynamics, etc.

Preventing biofilm completely is impossible and counterproductive to ensuring the essential niche benefits of a healthy balanced microbiome; intermittent or prolonged use of antibiotics for such a mission is not the solution.

The canonical stages of biofilm formation, including microbial attachment, proliferation, maturation, and dispersion, are the focus in addressing biofilm disruption. Of these, microbial surface attachment and proliferation are considered essential for preventing early biofilm development. Therefore, once titanium implants (and abutments) are developed with surfaces that inhibit plaque and biofilm, this can be essential for getting the job done of preventing and curtailing peri-implant disease.

But is this possible? Novel dental materials, such as antimicrobial composite restoratives, were developed for the prevention of dental caries by using a surface-contact bactericidal strategy to reduce bacterial viability. This novel material prevents enamel demineralization from bacterial plaque that otherwise leads to recurrence of caries more than 50% of the time by 5 years. Within several years of placement, titanium dental implants exhibit an incidence of significant peri-implant disease of more than 10% within several years of placement and cannot so easily be removed and replaced like a failed dental restoration. Therefore, a reliable site-specific biofilm-prevention strategy for titanium like that used for dental restoratives could represent a solution to this unmet need.

As host tolerance changes relative to general systemic health, including immunodeficiencies, individual and oral hygiene effectiveness, and local factors such as periodontitis of teeth adjacent to dental implants, there is increased susceptibility of the exposed implant surface. These physiologic changes can suddenly emerge to adversely influence the implant risk profile and new host biofilm dynamics, necessitating enhanced oral hygiene measures to keep dysbiotic biofilm from further compromising the dental device.

Exposure of an implant surface to the oral environment is speculated to occur in up to 30% of implants by 10 years in function. Causation can be host-related but

can also be related to practitioner error, such as poor surgical placement including inadequate bone grafting or unsatisfactory prosthetic management, such as the use of misfit components, poorly executed restorations, or restorations designed with compromised cleanability. Of course, if clinician mistakes are not made and patient compliance is circumspect, a steady state can be maintained. However, clinician work-product is not always ideal, and patients do not always comply with preventive hygiene measures. In any case, host biology may become more susceptible due to physiologic, pharmacologic, or ingestion-related insults, such as tobacco smoking, leading to unhealthy catabolic changes at the bone-implant interface.

One replacement implant study showed a mean late time frame for implant loss of 11 years, implying exposure of the implant surface over time with attendant loss of osseointegration. In certain patients, once an implant surface is exposed, biofilm appears to accelerate further exposure, accelerating implant failure. Implant restorations therefore require diligent follow-up, as even after years of peri-implant bone stability, bone loss may indeterminately occur.

At present, once loss of hard tissue attachment and resulting implant compromise occurs, extraordinary measures are required, including attempts at infection mitigation, implant salvage, implant removal for replacement, and when hard tissue loss is severe, alveolar bone reconstruction. Addressing the question of what to do at any one stage in time with these challenges is critically significant for what appears to be a growing problem in a profession hampered by lack of consensus for what constitutes treatable peri-implant disease.

Titanium implant long-term outcomes continue to be problematic, even with the addition of the vast array of antibiotic regimens available today. Consistent improvement will require an implant-centered solution that reliably modulates oral biofilm to promote implant longevity. In the future, new implant and abutment material designs and surface modifications with perhaps improvement in the surgical protocol will address the dilemma to improve long-term implant outcomes. Only then will the job be completed.

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