Oral biofilms – pivotal role in understanding microbes and their relevance to the human host

Oana Săndulescu[1], Mihai Săndulescu[2,]*

In 1675 Antony van Leeuwenhoek used a self-made microscope to provide the first written description of protozoa[1] as "living creatures in rain water which had flood but few days in a new earthen pot".[2] Soon to follow in 1676 was the observation of bacteria floating in pepper water. Here, van Leeuwenhoek described protozoa which resembled "little animals" but also, "with great wonder", he noticed other organisms that were "incredibly small" by comparison.[3]

At that point, the medical world was not yet ready to understand the relation between these newly discovered microorganisms and infectious diseases – the "germ theory" was still 200 years away.[4] However, these first observations played an essential role in widening the horizon and in realizing that life forms exist beyond what is directly noticeable with the naked eye.

Antony van Leeuwenhoek was also the first to describe biofilms in 1683, as agglomerations of "many very small living animals", which "moved very prettily" only after solubilizing the biofilm in clean rain water or saliva.[3]

While biofilms are now known as the most abundant type of microbial existence form,[5,6] not much was known about their relevance in clinical practice until 300 years later when, in the 1970s, aggregates of *Pseudomonas aeruginosa* were noticed in the sputum of patients with cystic fibrosis.[7]

Interestingly, this first observation by Antony van Leeuwenhoek of sessile bacteria and their dispersal to planktonic forms when mixed with liquids, was actually the observation of oral biofilms.[3] In one of his many letters as correspondent abroad to the Royal Society in London, he described his dental care routine, which was quite elaborate. However, after performing his complex dental hygiene procedure, he noticed that: "Yet by doing so my teeth are not clean, for when I look at them with a magnifying mirror there remains or grows between some of the molars and teeth a little white matter, about as thick as batter."[3]

Oral biofilms are important actors in health and disease alike. With the recent proposal of moving away from the "germ theory" towards the "microbial theory of health",[8] it is essential to understand the important role that the microbiota plays in the human body and the underlying bacterial communication that ensures transition from planktonic to sessile states, and vice versa.[9]

By definition, the best characterized type of oral biofilm is the supragingival and subgingival plaque. Here, many different bacterial species aggregate to form polymicrobial biofilms. In the supragingival plaque, *Streptococcus* spp. has been described to form mixed corncob structures together with *Candida albicans*, while in the subgingival plaque other bacterial species agglomerate and surround core aggregates of *Lactobacillus* spp.[10]

Most bacteria, if not all, are capable of forming biofilms,[11] but the extent to which biofilm occurs in natural environments, including the human body, as well as the

[1]MD, PhD, Professor, Department of Infectious Diseases I, Faculty of Medicine, Carol Davila University of Medicine and Pharmacy, Bucharest, National Institute for Infectious Diseases "Prof. Dr. Matei Balș", No. 1 Dr. Calistrat Grozovici street, Bucharest 021105, Romania; [2]DDS, PhD, Associate Professor, Department of Implant Prosthetic Therapy, Faculty of Dentistry, Carol Davila University of Medicine and Pharmacy, 17-23 Calea Plevnei, Bucharest 010221, Romania.

*Corresponding author: Mihai Săndulescu, mihai.sandulescu@umfcd.ro

Article downloaded from www.germs.ro
Published March 2023

ISSN 2248 – 2997
ISSN – L = 2248 – 2997

strength of aggregation between sessile bacterial cells differs and is genetically regulated in many of the clinically relevant species that have been studied so far.[12-14]

Particular types of oral microbiota, and specifically oral biofilms, have been described. For example, cariogenic biofilms include a preponderance of *Streptococcus* spp., and in particular *S. mutans*, *Lactobacillus* spp., *Actinomyces* spp., *Bifidobacterium* spp., *Prevotella* spp., *Veillonella* spp.[15] and the more recently described *Scardovia wiggsiae*.[16,17] The mere existence of a cariogenic microbiota is, however, not the only driver of dental caries, as nutritional factors are also important contributors to the creation of the caries-prone microenvironment by this resident oral flora.[16] Specifically, the consumption of fermentable sugars is a key element of cariogenesis, as cariogenic microbiota have been shown to more effectively ferment sugars to acids and then to thrive in the generated acidic environment which, in turn, offers them a survival benefit, thus creating a vicious circle.[15]

A specific type of dysbiosis of subgingival microbiota, with predominance of *Tannerella forsythia*, *Treponema denticola*, and *Porphyromonas gingivalis*, has been associated with periodontal disease.[18] These bacteria have the capacity to build their own biofilms, but also to form microcolonies within pre-existing biofilms,[10] gradually triggering an inflammatory response that initiates periodontal destruction[19] while also altering the natural composition of the oral biofilms even further, potentially leaving more room for pathogenic agents to further grow and replicate.

The two examples given above represent the most well-understood types of oral biofilms associated with dental disease. However, the composition and the role of the oral microbiota is much more complex. The oral biofilms represent dynamic ecosystems, shaped by the composition of the resident flora, but also by the metabolic interactions between these species, which can be mutualistic, synergistic, or antagonistic, and which can further modulate the oral microenvironment.[16]

While the mere observation of oral plaque led to the first description of a microbial biofilm in the 17th century, the extensive study of the human microbiome in the 21st century has characterized the oral flora as one of the most diverse microbiomes in the human body, second in rank after the colon.

Centuries after its first description, the oral microbiota still provides important learning points for the medical and scientific world alike.

Conflicts of interest: All authors – none to declare.

Funding: None to declare.

References

1. Lane N. The unseen world: reflections on Leeuwenhoek (1677) 'Concerning little animals'. Philos Trans R Soc Lond B Biol Sci. 2015;370:20140344. https://doi.org/10.1098/rstb.2014.0344
2. van Leewenhoeck A. Observations, communicated to the publisher by Mr. Antony van Leewenhoeck, in a Dutch letter of the 9th of Octob. 1676. Here English'd: concerning little animals by him observed in rain-well-sea. And snow water; as also in water wherein pepper had lain infused. Philos Trans. 1677;12:821-31. https://doi.org/10.1098/rstl.1677.0003
3. Bardell D. The roles of the sense of taste and clean teeth in the discovery of bacteria by Antoni van Leeuwenhoek. Microbiol Rev. 1983;47:121-6. https://doi.org/10.1128/mr.47.1.121-126.1983
4. Smith KA. Louis Pasteur, the father of immunology? Front Immunol. 2012;3:68. https://doi.org/10.3389/fimmu.2012.00068
5. Costerton JW, Lewandowski Z, Caldwell DE, Korber DR, Lappin-Scott HM. Microbial biofilms. Annu Rev Microbiol. 1995;49:711-45. https://doi.org/10.1146/annurev.mi.49.100195.003431
6. Cooper R. Biofilms: hard to detect, easy to underestimate, but most definitely here to stay. Wounds UK. 2009;5:12.
7. Høiby N. A short history of microbial biofilms and biofilm infections. APMIS. 2017;125:272-5. https://doi.org/10.1111/apm.12686
8. Scott EA, Bruning E, Nims RW, Rubino JR, Ijaz MK. A 21st century view of infection control in everyday settings: moving from the germ theory of disease to the microbial theory of health. Am J Infect Control. 2020;48:1387-92. https://doi.org/10.1016/j.ajic.2020.05.012

9. Săndulescu O. Managing sticky situations - anti-biofilm agents. Germs. 2016;6:49. https://doi.org/10.11599/germs.2016.1088
10. Zijnge V, van Leeuwen MB, Degener JE, et al. Oral biofilm architecture on natural teeth. PLoS One. 2010;5:e9321. https://doi.org/10.1371/journal.pone.0009321
11. López D, Vlamakis H, Kolter R. Biofilms. Cold Spring Harb Perspect Biol. 2010;2:a000398. https://doi.org/10.1101/cshperspect.a000398
12. Ahmed DM, Messih M, Ibrahim NH, Meabed MH, Abdel-Salam SM. Frequency of *icaA* and *icaD* determinants and biofilm formation among coagulase-negative staphylococci associated with nasal carriage in neonatal intensive care units. Germs. 2019;9:61-70. https://doi.org/10.18683/germs.2019.1159
13. Skariyachan S, Sridhar VS, Packirisamy S, Kumargowda ST, Challapilli SB. Recent perspectives on the molecular basis of biofilm formation by *Pseudomonas aeruginosa* and approaches for treatment and biofilm dispersal. Folia Microbiol (Praha). 2018;63:413-32. https://doi.org/10.1007/s12223-018-0585-4
14. Aliramezani A, Soleimani M, Fard RMN, Nojoomi F. Virulence determinants and biofilm formation of *Acinetobacter baumannii* isolated from hospitalized patients. Germs. 2019;9:148-53. https://doi.org/10.18683/germs.2019.1171
15. Meyer F, Enax J, Epple M, Amaechi BT, Simader B. Cariogenic biofilms: development, properties, and biomimetic preventive agents. Dent J (Basel). 2021;9:88. https://doi.org/10.3390/dj9080088
16. Chen X, Daliri EB, Tyagi A, Oh DH. Cariogenic biofilm: pathology-related phenotypes and targeted therapy. Microorganisms. 2021;9:1311. https://doi.org/10.3390/microorganisms9061311
17. Kameda M, Abiko Y, Washio J, et al. Sugar metabolism of *Scardovia wiggsiae*, a novel caries-associated bacterium. Front Microbiol. 2020;11:479. https://doi.org/10.3389/fmicb.2020.00479
18. Sedghi L, DiMassa V, Harrington A, Lynch SV, Kapila YL. The oral microbiome: role of key organisms and complex networks in oral health and disease. Periodontol 2000. 2021;87:107-31. https://doi.org/10.1111/prd.12393
19. Di Stefano M, Polizzi A, Santonocito S, Romano A, Lombardi T, Isola G. Impact of oral microbiome in periodontal health and periodontitis: a critical review on prevention and treatment. Int J Mol Sci. 2022;23:5142. https://doi.org/10.3390/ijms23095142

Please cite this article as:
Săndulescu O, Săndulescu M. Oral biofilms – pivotal role in understanding microbes and their relevance to the human host. GERMS. 2023;13(1):7-9. doi: 10.18683/germs.2023.1361