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This paper presented the unified theory of bacterial biofilm formation and stated that, in all aquatic systems with adequate concentration of nutrients, bacteria form glycocalyx-enclosed biofilms adherent to available surfaces and that these sessile populations usually attain numerical and physiological predominance in medical, natural, and industrial aquatic ecosystems. [The *SCI*® indicates that this paper has been cited in over 265 publications.]

How Bacteria Stick

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An embarrassing fall into the icy waters of Bugaboo Creek at the foot of the unclimbed south face route of Snowpatch Spire really focused my attention on bacterial biofilms. Published data stated that alpine streams contained as few as eight bacterial cells per ml, but the evidence immediately at hand clearly established that the surfaces of the granite cobblestones of this particular alpine stream were covered by a clear, slippery, slime layer that easily counteracted the avid adherence of my Vibram soles to my substratum. Because of my ingrained tendency to place my trust in direct *in situ* observations of bacteria by light and electron microscopy, Gill Geesey and I examined rock surfaces in this and a wide variety of other natural streams and found that their very large sessile bacterial biofilm populations always outnumber the planktonic (floating) populations of the same systems by a factor between 1,000 and 10,000 and always constitute the physiologically dominant population of the ecosystem.

When K.-J. Cheng and I used the same direct *in situ* techniques to study the bacterial biofilms adherent to normal tissue surfaces, we found that very stable microbial ecosystems developed on many of these living surfaces and that these adherent populations protected these tissues from pathogenic colonization[1] and even made specific enzymatic contributions to the host tissue's physiological processes.[2] The direct examination of materials from chronic human bacterial diseases, in cooperation with Tom Marrie, showed that the bacteria that cause chronic endocarditis and a very wide variety of foreign device-related infections actually grow in well-developed glycocalyx-enclosed microcolonies and biofilms on the surfaces of these tissues and devices.[2-4] A further examination of device-related and non-device-related chronic bacterial diseases of humans and of animals has shown that these infections persist in spite of aggressive antibiotic chemotherapy because the bacterial cells within their well-developed biofilms are inherently resistant to virtually all modern antibiotics.[2-5]

Biofilm bacteria also show a remarkable degree of inherent resistance to both humoral and cellular host defence factors (antibodies and phagocytic cells). It is not surprising that, once adherent bacteria have even begun to colonize a plastic surface, these sessile organisms can proceed to form highly protected adherent biofilms on plastic or metal surfaces even in highly defended areas like the peritoneum of preimmunized experimental animals (K.H. Ward and J.W. Costerton, unpublished data). In chronic bacterial infections, such as cystic fibrosis pneumonia, antibacterial agents fail to reach the glycocalyx-enclosed pathogens but bacterial antigens stimulate the production of immune complexes that damage the lung tissue but, again, fail to clear the pathogen. Because the conventional microbial methods for the recovery and quantification of pathogenic bacteria work only very poorly when applied to sessile organisms, and because conventional methods for the determination of their susceptibility to antibiotics are especially misleading,[5] we have developed a whole new battery of methods to monitor the diagnosis and treatment of these increasingly important "modern" diseases.

These recent developments have shifted our attention from the cell wall structures that constitute the planktonic bacterial cell's interface with its environment[6] to the extracellular glycocalyx that constitutes the interface of microcolonies and biofilms with their environments.[2-5] We have made this change because most medical and industrial problems caused by planktonic bacteria have been solved by conventional microbiology. We now perceive that residual problems in these areas involve biofilms and that their solution will require a new understanding of the ecology and physiology of these remarkable adherent bacterial populations.

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