Introduction to Microbial Biofilms

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In any scientific examination that addresses a subject as basic as the mode of growth of bacteria it is prudent to begin by considering the successful prokaryotic communities that clearly predated the development of the eukaryotic cell. During the millions of years in which bacteria constituted the only life form on Earth, we visualize an extremely oligotrophic aquatic environment in which specific ecosystems were impacted by many factors (e.g. heat, acid) hostile to their survival. It is the nature of aquatic systems to flow from one ecosystem to another and we can imagine a primitive stream connecting permissive and non-permissive bacterial habitats in the nascent Earth. Once bacterial cells had evolved, the planktonic (floating) mode of growth would deliver them from one habitat to another until they perished in the first non-permissive locus. The sessile mode of growth as attached bacteria would allow these primitive organisms to colonize a permissive habitat and persist therein. Biofilm formation would allow these sessile organisms to trap and retain scarce organic compounds and to develop a focused attack on complex or refractory nutrients whose processing required time and/or the cooperation of one or more bacterial species. Biofilm formation would also change the microenvironment at the colonized surface in a colonized habitat and render its inhabitants less susceptible to hostile chemical, physical, or even biological (e.g. bacteriophage) factors. Each colonized habitat would become a stable crucible of genetic adaption and physiological cooperativity that would flourish in its own location but would also shed its component organisms as planktonic cells so that, if they survived, they could establish a similar integrated biofilm community in any permissive habitat downstream.

Our image of aquatic systems in the nascent Earth militates against the survival of planktonic bacteria, and leads us to suggest that the sessile mode of growth and biofilm formation may have been the sine qua non of survival of newly evolved bacteria in this hostile environment. It is therefore germane to examine hostile oligotrophic environments on the modern planet to determine which mode of growth of prokaryotic cells is most successful. The ubiquity and predominance of bacterial biofilms was first noted in very oligotrophic high altitude alpine streams in Canada (Geesey et al. 1977) and subsequent detailed examinations of these systems clearly show that bacterial populations can only be maintained in their turbulent waters if these organisms live in biofilms adherent to available surfaces. In the equally hostile and oligotrophic Antarctic desert environment bacteria and algae can invade the exposed surfaces of rocks to produce complex biofilms or ‘varnishes’ whose matrices trap scarce rainwater and permit growth and primary production based on photosynthesis.

All modern bacteria are obviously descendant from the primitive forms that successfully colonized the planet Earth early in its biological history and their basic strategies of colonization and survival depend on patterns of phenotypic expression of their genetic material that made them successful in that primitive milieu. These patterns affect many modern processes because heat exchangers are fouled, pipelines are corroded, and medical devices are infected by
recalcitrant slimy bacteria, because bacteria have long ago evolved a set of basic strategies to colonize and persist and to survive in permissive habitats.

Laboratory cultures represent the planktonic mode of growth

The phenomenon of bacterial adhesion to surfaces is clearly visible in routine light microscopic examinations of natural populations and it was elegantly described (ZoBell 1943) long before its relationship to ubiquitous biofilm formation was recognized. Later, descriptions of this process emphasized its irreversibility (Marshall et al. 1971) and its putative mechanisms (Fletcher & Locht 1979) but what has emerged is a whole spectrum of adhesion phenomena, that range from the very specific pilus-mediated adhesion of bacteria to specific tissues to totally non-specific exopoly saccharide-mediated adhesion of natural wild bacteria to all surfaces within a stream (Geesey et al. 1977). What is perhaps most important in this ongoing area of research, which is mired in detail but driven by the search for colonization-resistant materials, is that genetic examinations of the best known adhesion mechanisms show that they are highly conserved during evolution. It has long been recognized that simple animal or natural ecosystem passage of a bacterial strain that has lost surface structures and adhesion capability during repeated subcultures as a planktonic single species culture restores these structures (pili, exopolysaccharides) and this capability. In some instances these surface structures and the adhesion capability can be restored by culture in menstrua that contain surfactants or antibiotics at concentrations that kill planktonic cells totally lacking in protective surface structures (Govan 1975) but allow the survival of glycocalyx enclosed wild type cells. These simple observations, some of which date back to the 1930s, probably should have alerted us to the fact that the planktonic single species laboratory culture exerts a powerful selective pressure on a bacterial genome that eventually produces a 'stripped down' cell lacking in protective and adhesive surface structures that simply cannot survive in natural environments where adhesion and protection are of paramount importance.

It is very sobering to realize, over a century after the development of the planktonic single species laboratory culture (Koch 1881), that the cells we have been studying so assiduously are phenotypically locked in a planktonic mode of growth. This is at the opposite end of a phenotypic spectrum from the sessile mode of growth clearly seen to predominate in most natural environments. The classic laboratory culture has been extremely useful for the exploration of the genome-driven activities of bacterial species, but bacteria are protein creatures whose survival depends on their phenotypic responses to environmental factors and we have generally studied cells locked by their test tube environment into the planktonic mode of growth. Decades of productive research have yielded dividends in the control of planktonic diseases and in modern genetic engineering but have been less successful in the control of biofilm diseases and industrial and environmental microbiology. Now that we realize that new culture methods, several of which are described by Caldwell in Chapter 3, can mimic the biofilm mode of growth that predominate in nature, and in many heretofore recalcitrant bacterial diseases, we can look forward to a new and equally exciting explosion of practical sequelae of modern microbiological biofilm research.

Phenotypic responses to adhesion

Modern research using reporter genes has clearly shown that the adhesion event triggers the expression of genes controlling the production of bacterial components (for example, the alginate of Pseudomonas aeruginosa) necessary for continued adhesion and biofilm formation. Reporter gene systems constructed by Chakrabarty and by Deretic have been used by Geesey's group (Davies et al. 1993) and by Costerton's group (Hoyle et al. 1993) to show that adhesion triggers the expression of the alg C and other genes that control the production of phosphomannomutase and of other enzymes in the alginate synthesis pathway.

Parallel work with Gram positive pathogens, notably Staphylococcus epidermidis, has shown that adhesion triggers the expression of enzymes which produce exopolysaccharides that are pivotal in continued adhesion and biofilm formation and in the aetiology of device related bacterial
Infections (Costerton et al. 1987). These complex and focused reporter gene techniques have shown that adhesion triggers the rapid and specific phenotypic expression of several specific genes whose products are concerned with adhesion and biofilm formation. Parallel, general examinations, comparing the proteinaceous gene products made by sessile bacteria with those made by planktonic cells of the same species have shown (H. Yu and J. W. Costerton, unpublished observations) that adhesion changes the phenotypic expression of at least 30% of the proteins detectable in cell extracts by gel chromatography. Recent studies in Deretic’s laboratory (Martin et al. 1993) indicate that a sigma factor similar to that involved in sporulation, and in the reversible rough-smooth lipopolysaccharide transformation in Gram negative bacteria, may be involved in the adhesion-mediated change between planktonic cells and sessile biofilm cells of the same bacterial species. If this fascinating hypothesis stands up under current intense scrutiny, the battery of phenotypic changes that occur as cells of bacterial species alternate between planktonic and sessile modes of growth will come to be regarded as a phase change mediated by a sigma factor that controls a whole cascade of genes related to adhesion and to biofilm formation. If biofilm bacteria do, in fact, constitute a different phase of phenotypic expression of the bacterial genome many of their observed characteristics, such as their almost complete resistance to antibiotics that are effective against planktonic cells of the same species (Nickel et al. 1985), will be partially explained.

We are presently studying the rate at which bacteria revert to the planktonic phase of phenotypic expression after they have become detached from established biofilms, by active shedding mechanisms or by simple fragmentation. These studies will provide insights into the nature of a phase change that may enable bacteria to control their cell surface components and to alternate between sessile and planktonic modes of growth to facilitate their colonization and survival within permissive habitats.

Biofilm structure

The confocal scanning laser (CSL) microscope has enabled us to examine living, fully hydrated, biofilms and the use of this microscope has provided structural information that is especially valuable because it is direct and consequently unequivocal (Lawrence et al. 1991). The examination of hundreds of biofilms formed by dozens of different pure cultures and by several natural bacterial populations has clearly shown that biofilms may be regarded as three-dimensional microcolonies of similar morphotypes (Fig. 0.1) interspersed between water channels that contain few bacterial cells and appear to contain a more permeable matrix material. These clearly heterogeneous surface-associated bacterial populations can now be examined, living and fully functional, by CSL microscopy and by the use of non-intrusive chemical probes and of physical microprobes (5–10 μm tip diameter) that can be positioned at any location within the biofilm and visualized by the CSL microscope. The concerted use of these complementary analytical tools has produced a conceptual image of bacterial biofilms that is truly amazing in its complexity and sophistication.

The structural heterogeneity of biofilms

Soon after the initial adhesion of bacteria to a surface, in either a single species culture or a mixed natural population, certain adherent cells proliferate and elaborate exopolysaccharides until they produce a microcolony in which morphologically similar ‘sister’ cells are embedded in a thick polysaccharide matrix (Fig. 0.1). As the biofilm thickens and matures individual microcolonies may lose their associations with the colonized surface and, in multispecies populations, cells of several species may come together to produce functional consortia (Kudo et al. 1987a, b) that carry out complex physiologically cooperative processes such as methane production (MacLeod et al. 1990). The microcolony is the basic growth unit of the biofilm and we consider bacterial growth to be sessile in nature if these microcolonies are produced, even if their final geometrical configuration differs from that depicted in Fig. 0.1. Specific data attest to the limited permeability of the thick matrices surrounding individual microcolonies, in that CSL microscopy has shown that fluorescent-conjugated dextrans and other permeability probes penetrate the water channels but fail to penetrate the microcolonies within biofilms. Very recent work by
Dr Lewandowski’s group at the Center for Biofilm Engineering has indicated that the water channels that lie between and sometimes below these microcolonies are actually sufficiently permeable to allow convective fluid flow, and the same group has obtained NMR data to confirm flow within these channels. These data, obtained in direct examinations of living biofilms, combine to present a concept of biofilm structure that is revolutionary in its complexity and sophistication. Biofilm bacteria clearly live in dense matrix-enclosed microcolonies, where they are exposed to a bathing flow of modified bulk fluid through the less dense water channels that anastomose throughout even the thickest and most mature biofilms. These morphological data suggest a biofilm within which bacteria live in specialized microniche that are served by a primitive circulatory system within a stationary matrix-protected population adherent to surfaces within a flowing system.

**The chemical and physical heterogeneity of biofilms**

The planktonic mode of growth affords each individual bacterial cell an almost identical ecological niche, in that all cells communicate almost directly with the bulk fluid by simple diffusion. The simple immobilization of a bacterial cell within an anionic matrix introduces heterogeneity because these cells carry out many chemical functions, such as proton extrusion and oxygen consumption, and the matrix areas near the cells must, necessarily, differ from these further from the cells. If we then visualize different microcolonies, containing one or more physiological types of bacteria, within a biofilm, we must expect that the metabolic activities of these...
clusters of cells would produce loci with sharply different chemical environments. If we consider the significant contribution of oxygen consumption, we can state that adjacent areas of the biofilm will be different at a given moment in time, depending on the extent to which acid generation or oxygen diffusion exceed the diffusion of protons or of dissolved oxygen through the biofilm matrix.

Because of the development of the CSL microscope we can now introduce both chemical (Lawrence et al. 1991) and physical probes (Lewandowski et al. 1993) into living biofilms and record such parameters as pH and dissolved oxygen concentration at particular loci. Chemical probes are difficult to calibrate and physical probes may be somewhat intrusive but both serve to show local differences very accurately. Early work with pH sensitive chemical probes clearly showed that some bacterial microcolonies in both pure culture and mixed natural biofilms operated at pH values significantly lower than the water channels (Lawrence et al. 1991) and that individual cells within microcolonies were surrounded by an acid zone that may be produced by proton extrusion. Recent work with dissolved oxygen microelectrodes has produced equally unequivocal data to indicate heterogeneity within biofilms. When the microelectrode (tip diameter 5–10 μm) is advanced from the bulk fluid through the biofilm interface and into a bacterial microcolony (Fig. 0.2a) the dissolved oxygen concentration is seen to decrease at the interface and to reach truly anaerobic levels within the microcolony (Fig. 0.2b). When the same microelectrode is traversed only 100 μm laterally and advanced from the bulk fluid through the biofilm interface and into a water channel (Fig. 0.2c) much higher levels of dissolved oxygen are recorded (Fig. 0.2d). These simple and direct measurements of pH and of dissolved oxygen concentration are made in living biofilms and they provide unequivocal evidence of the basic chemical heterogeneity of these structurally complex adherent populations.

If we grasp these basic concepts of the structural and chemical heterogeneity of biofilms and begin to apply them to natural biofilm populations that have been described and defined during the past two decades, a fascinating picture of the sessile mode of growth begins to emerge. Ultrastructural observations of cellulose digestion by some cellulolytic bacteria (Cheng et al. 1984) showed that these organisms adhere to this insoluble substrate and produce deep pits into which they and their progeny eventually penetrate. We can infer a local concentration of cellulolytic enzymes, within a biofilm, that mediate a focused attack on a surface that is typical of many instances of acid generation and oxygen consumption. Specific microcolonies within a biofilm could mediate local focused attack on surfaces ranging from dental enamel to stainless steel. In instances in which the concerted metabolic activities of several bacterial species are necessary to biodegrade a complex substrate (e.g. bitumen) cells of these species would form a microcolony within a biofilm and that microcolony would mediate a local attack on the substratum. One of the most important inherent characteristics of bacterial biofilms is their capability of focused and cooperative biodegradation, and this characteristic depends entirely on the sustained juxtaposition of cells with each other and with surfaces that is a feature of the biofilm mode of growth.

If we re-examine the structure and activity of bacterial consortia (MacLeod et al. 1990) in the light of these recent revelations of biofilm heterogeneity a similar gratifying concept emerges. The biofilm mode of growth prepares a wide variety of bacterial cells at a surface and the individual cells replicate to initiate microcolony formation at a rate that depends on how well their particular microniche suits their physiological requirements. If a particular cell is unable to replicate it may simply persist, entrapped in the biofilm, until suitable conditions develop. If a particular cell requires acetate it will replicate if this substrate is supplied by a neighbouring cell, and this type of metabolic cooperativity often produces structural consortia of considerable complexity and metabolic efficiency (MacLeod et al. 1990). The chemistry of a particular microniche within a biofilm depends on both the delivery of bulk fluid components through the water channels and the metabolic activity of neighbouring cells. The rapid asexual reproduction of bacteria enables them to react very quickly to favourable chemical changes within a specific microniche and their starvation survival strategies (Killberg et al. 1987) enable them to persist for very long periods of time in non-permissive conditions. Spatial juxtaposition within biofilms is essential to the development of
the very efficient bacterial consortia seen in natural bacterial populations, and the physical retention of non-dividing cells within biofilms is the basis of their ability to react to changing conditions by developing new and equally efficient consortia to process new substrates. The sustained juxtaposition of metabolically cooperative cells is impossible in truly planktonic populations.
and non-replicating species are rapidly displaced under laboratory growth conditions.

If we assume the basic structural and chemical heterogeneity of bacterial biofilms, and if we extrapolate to even greater levels of structural complexity and chemical heterogeneity in natural adherent populations, we must expect that these biofilms will be heterogeneous in several important physical parameters. The differences in electrical potential between adjacent loci within a biofilm combine to produce a measurable corrosion potential (Little et al. 1987) if the colonized surface is conductive. These corrosion potentials set up classic electrical ‘corrosion cells’ on biofilm-colonized surfaces, and the further reinforcement of effective cathodes within the biofilm produces metal loss at functional anodes and initiates the microbially influenced corrosion that causes huge losses in industry. Electrical potential differences exist within living biofilms, whether or not the colonized surface is conductive, and we must assume that the movement of ions and charged molecules will be influenced by these electrical gradients. This raises the fascinating possibility that charged antibiotic and biocide molecules that readily penetrate the water channels of a biofilm may be excluded from the dense matrix-enclosed microcolonies by both diffusion limitation and electrical gradients. We therefore predict that electrical heterogeneities will eventually be seen to be as important as structural and chemical heterogeneities in rationalizing the unique characteristics of bacterial biofilms. Measurements of AC impedance and open circuit potentials in living biofilms are currently being made by Dr Lewandowski and his colleagues, at the Center for Biofilm Engineering, and it may soon be possible to relate these electrical parameters to the structure and to the metabolic activity of biofilms.

It focuses the mind, wonderfully, to consider the essential differences between planktonic bacterial cells and sessile cells living in microcolonies within a biofilm. Much of the emphasis of the first six chapters of this book is centred on the complex heterogeneities of the biofilm mode of growth, and much of their detail documents these essential differences between planktonic and sessile cells. All of these chapters are based on data directly derived from living biofilms and we really cannot escape the contemplation of these complex communities by spurious arguments about extrapolation because, here, there is no extrapolation. We see living cells within microcolonies in fully hydrated biofilms and we see that these sessile populations predominate in almost all natural ecosystems. We can conclude that cells thus immobilized in exopolysaccharide matrices, many of whose chemical structures we understand, are almost completely protected by these matrices and are affected by molecules that diffuse from adjacent cells or from the bulk fluid via the water channels. Thus each biofilm cell lives in a microniche and its response to the special conditions of that microniche dictate its physiological activities, including its reproduction. Complex consortia of biofilm bacteria stand as a proof of widespread biofilm heterogeneity and we are only now beginning to suggest mechanisms that may have produced what we must accept because we can visualize it directly. Many early microbiologists valued direct observation above almost all else and the field is perhaps now just beginning to recover from its fascination with pure single species cultures and the perilous process of extrapolation.

**Biofilm formation on inert surfaces**

Chapters 7 to 11 deal with the formation of biofilms on inert surfaces. The consequences of this non-specific bacterial accretion onto inert surfaces range from simple fouling to the complex microbial aetiologies of microbially influenced corrosion and of recalcitrant device related infections.

Inert surfaces in aqueous environments rapidly accrete organic molecules and inorganic ions to form a layer called, in its most elaborate form, a ‘conditioning film’. Therefore, in all but the most oligotrophic ecosystems, planktonic bacteria actually adhere to the surfaces of surface films that may or may not vary with the chemical nature of the inert surface being colonized. The use of planktonic cells that have lost important adhesion determinants during extended subculture in single species laboratory cultures has generated a large amount of contradictory data, many of which cannot be extrapolated to real ecosystems. The surfaces of these planktonic cells have often been altered by the loss of surface structures (pili, capsules) and cells with different degrees of surface modification may exhibit dif-
ferent adhesion behaviour on inert surfaces. We submit that meaningful data concerning the formation of bacterial biofilms on inert surfaces in aqueous systems are best obtained in studies in which these surfaces are presented to wild mixed planktonic bacterial populations in a menstruum in which realistic conditioning films will develop. Specifity of colonization is not hasted in this realistic mode, inert surfaces in aqueous systems are usually colonized rapidly and non-specifically, and surface topography and surface chemistry appear to be much less important parameters than was indicated in laboratory studies. The usefulness of these realistic studies is especially obvious in the examination of the putative colonization resistance of new materials that have been developed for use in medical devices. Literally hundreds of materials that have appeared to resist colonization by laboratory strains have formed luxuriant biofilms in a few hours when challenged with wild strains of the same species in real or simulated body fluids. The readily accessible aqueous systems that illustrate this principle most graphically may be rivers and streams, in which very similar mature biofilms are found on inert surfaces with a bewildering variety of topography and surface chemistry ranging from rock to wood to discarded plastic trash.

These general observations of non-specificity do not, of course, preclude instances of very specific adhesion and biofilm formation in specialized ecosystems such as the bovine rumen, in which cellulolytic bacteria adhere avidly and very specifically to cellulose (Minato & Suto 1978). It has been suggested (Kudo et al. 1987a, b) that this specific adhesion system may depend on the specific affinity of cell-associated enzymes for the substrate (cellulose) of those enzymes. Similarly, the well documented affinity of bacterial exopolysaccharides for specific metals may mediate specific adhesion and subsequent biofilm formation on the inert surfaces of ores that may be leached by this process. Objectivity is best served by the examination of a wide variety of inert surfaces in a natural ecosystem to detect the consequences of specific colonization and, in instances where species specificity is seen, to attribute this specificity clearly to adhesion events rather than to the special suitability of the organism to the microniche that it has colonized.

If, as we contend, bacterial adhesion to inert surfaces in aqueous systems is a function of the association of bacterial surface components with not only proteinaceous but also polysaccharide-containing the conditioning film that covers these surfaces (also notably polysaccharides) the adhesion event may directly involve neither the inert surface nor the bacteria at all. This perception may explain the avid colonization of silver and copper surfaces by bacterial species whose planktonic cells are exquisitely sensitive to ionic forms of these metals.

**Biofilm formation on the surfaces of living cells**

Chapters 12 to 18 deal with the formation of bacterial biofilms on the surfaces of living cells. Bacteria show a very much wider range of adaptability for these very specifically structured surfaces, some of which are readily colonized (e.g. buccal and vaginal epithelia) while others (e.g. kidney epithelia) are colonized by bacteria with very specific pathogenic ligands.

If we use the direct analysis of the adherent bacterial populations actually seen on the surfaces of living cells and tissues as our criterion it is clear that living cells vary between widely separated extremes in their tendency to serve as suitable substrata for bacterial adhesion and subsequent biofilm formation. Dry tissue surfaces that slough external cells in a regular pattern (the epithelia of mammalian skin and of plant root hairs) are seen to be colonized by a wide variety of bacteria and fungi some of which invade the deeper epithelia and develop a somewhat communal relationship with the colonized tissues. The moist epithelial tissues of organs that are heavily colonized by bacteria (mouth, gut, vagina) are often covered by very thick (>400 μm) mucus layers (Rozee et al. 1982) that provide a viscous environment whose peculiar chemical characteristics tend to select its primary microbial inhabitants. Special adhesion mechanisms are clearly required (Cheng et al. 1979) by organisms that adhere and form de facto biofilms in these viscous systems, and many species that predominate (e.g. *Lactobacillus*) in these ecosystems also produce chemical antagonists to the growth of competing microorganisms. Even in these mucus-lined organs inert surfaces (e.g. teeth) differ from healthy living tissue surfaces
(e.g. gums) in their tendency to accrete microbial biofilms.

Even though heavily colonized mammalian organs are often directly connected to other organs, the internal organs can often maintain tissue surface sterility by the exercise of effective means of limiting bacterial adhesion and biofilm formation. The pharynx is essentially sterile while the oropharynx is heavily colonized; the biliary system is sterile while the gut is colonized; and the uterus and bladder are essentially sterile while the vagina and distal urethra are very heavily colonized. The surfaces of epithelial cells in these non-colonized tissues are covered with an expolsysacharide glyocalyx composed largely of hyaluronic acid, as are the epithelial cells of all other normally sterile internal organ systems. It is obvious that the surfaces of these epithelial cells are challenged by planktonic bacterial cells, for example from adjacent organs, but that bacterial adhesion and biofilm formation occur only very rarely on these healthy tissues. Inert surfaces introduced into these normally sterile organ systems fare much less well than natural tissue surfaces and are often colonized by these same planktonic bacteria to produce biofilms that contribute notably refractory characteristics to device related bacterial infections (Costerton et al. 1987).

The contemplation of the bacterial colonization of tissue surfaces in living organ systems is really an exercise in microbial ecology. These tissue surfaces comprise a series of ecological niches whose conditions are entirely permissive for bacterial adhesion, growth, and biofilm formation, if the natural defences of the organ system are compromised as by instrumentation or system failure. However, in normal circumstances, planktonic bacteria do not adhere and survive to initiate the colonization process even when the neighbouring inert surfaces of medical devices are heavily colonized. Living tissue surfaces are actually comprised of the ionic acid containing polysaccharides of the glyocalyx that overlie the plasma membrane and, in mammals, this surface is covered with plasma proteins (fibronectin, lamelmin) and richly supplied with surfactants and tissue associated antibodies (IgM). In one of the simplest cases, the eye, the environment of the tissue surface and its associated fluids is sufficiently hostile to bacteria that the insertion of planktonic bacteria and a biofilm colonized inert foreign body (the contact lens) from a biofilm infected storage case usually fail to initiate bacterial colonization and infection of the optical epithelia. In a more complex case the female bladder and uterus usually remain uncolonized even though the introitus, vagina, and cervix are heavily colonized by autochthonous and by potentially pathogenic bacteria. The bladder appears to employ mucus and tissue sloughing as a defensive measure, and the uterus appears to employ phagocytic cell activity and periodic tissue sloughing to prevent bacterial colonization. The structure of the sphincter of Oddi and the generally bactericidal characteristics of bile appear to prevent colonization of the common bile duct by intestinal bacteria and surfactants, phagocytic cells, ciliary activity, and the mucus escalator usually keep the deep Airways of the pulmonary system free of adherent bacteria.

**Colonization resistant surfaces**

For the past 15 years the corridors of industry and the groves of Academe have echoed to the exuberance of scientists who are confident that they have discovered a material whose surface is inherently resistant to bacterial colonization. Laboratory tests have been uniformly encouraging and practical tests have been equally uniformly disappointing and we believe that we can now conclude that bacteria will eventually adhere to and colonize the surface of any man made material. However, we must consider the inherent colonization resistance of the surfaces of tissues that are not normally colonized even though they are exposed to planktonic bacteria in large numbers. We must ask the question – is it the detailed chemical structure and peculiar topography of these tissue surfaces that prevents bacterial colonization, or is it the activity of surface located defence mechanisms such as surfactants, antibodies, and phagocytic cells? If the former is correct then simple mimicry of tissue surface characteristics will suffice to produce a colonization-resistant material for use in medical devices. If the latter is correct then mimicry of the tissue surface must be sufficiently effective to accrete surfactants, antibodies, and phagocytic cells and to allow their unimpeded antibacterial activity. We expect that the latter is correct because most tissue surfaces are readily colonized.
by bacteria when the surface environment is disturbed by such processes as general infection or instrumentation.

This book attempts to capture the revelations concerning the structure and activity of bacterial biofilms that now occur at very regular intervals. These data are perhaps most readily understood by comparing the microenvironment of a bacterial cell within a biofilm with that of a planktonic cell of the same species. These microenvironments are profoundly different and the phenotypic reaction of bacteria to these environmental differences provides the beginnings of an explanation of the singular characteristics of biofilm organisms (for example, resistance to antibacterial agents).

Because of our general fascination with lock-and-key molecular mechanisms we seized on a few instances in which specific pili mediate the attachment of certain pathogenic bacteria to specific ligands on tissue surfaces and we anticipated similar specificity in the ubiquitous bacterial colonization of surfaces in aquatic environments. Generally, the last two decades have taught us that bacteria adhere to a very wide variety of surfaces with remarkable avidity, especially if we examine wild bacteria in natural ecosystems. Ecological factors appear to exert a more profound effect on the bacterial colonization of surfaces than actual surface chemistry and topography. We note that the only well documented surfaces that consistently resist bacterial colonization because of their inherent characteristics are those of some living tissues. We suggest that bacterial biofilms will form readily on all surfaces except those that resemble living tissues in combining structural and environmental factors that prevent bacterial adhesion and colonization.

References


