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Review Article

Bacterial biofilm and associated infections

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Abstract

Microscopic entities, microorganisms that drastically affect human health need to be thoroughly investigated. A biofilm is an architectural colony of microorganisms, within a matrix of extracellular polymeric substance that they produce. Biofilm contains microbial cells adherent to one-another and to a static surface (living or non-living). Bacterial biofilms are usually pathogenic in nature and can cause nosocomial infections. The National Institutes of Health (NIH) revealed that among all microbial and chronic infections, 65% and 80%, respectively, are associated with biofilm formation. The process of biofilm formation consists of many steps, starting with attachment to a living or non-living surface that will lead to formation of micro-colony, giving rise to three-dimensional structures and ending up, after maturation, with detachment. During formation of biofilm several species of bacteria communicate with one another, employing quorum sensing. In general, bacterial biofilms show resistance against human immune system, as well as against antibiotics. Health related concerns speak loud due to the biofilm potential to cause diseases, utilizing both device-related and non-device-related infections. In summary, the understanding of bacterial biofilm is important to manage and/or to eradicate biofilm-related diseases. The current review is, therefore, an effort to encompass the current concepts in biofilm formation and its implications in human health and disease.

Keywords: Chronic infections; Immune system; Microorganisms; Quorum sensing

1. Introduction

In 17th century, Antoine Von Leeuwenhoek, for the first time observed a type of creature on his own teeth, a discovery considered to be a biofilm.[1] Zobell in 1943 stated that "the surrounding sea water have less number of bacteria than on the surface".[2] Even at the end of 1960 and the start of 1970, physical and chemical properties of biofilms were not investigated.[3] Heukelekian and Heller observed "*Bottle Effect*" of marine microorganisms − the growth and activity enhances when they are attached to a surface.[4] However, the curious observation of microbial biofilm awaited the invention of electron microscopy to examine in detail the biofilm with high-resolution, as compared to light microscopy. The employment of scanning electron and transmission electron microscopy allowed to identify biofilm on trickling filters in a wastewater treatment plant. It was then concluded that the

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biofilm cell morphology is evident of the clustering of a variety of microorganisms.[5]

2. Microbial biofilm composition

Biofilm is an organized aggregate of microorganisms living within an extracellular polymeric matrix that they produce and irreversibly attached to fetish or living surface which will not remove unless rinse quickly.[6,7] Formation of extracellular polymeric substances (EPS) occurs in the attachment stage of a biofilm to the surface. Whether a microbial biofilm will form on an inanimate or solid surface or not is a consequence of the formation of an exopolysaccharide matrix, which provides strength to the interaction of the microorganisms in the biofilm.[9−11] Usually thickness of EPS matrix is 0.2−1.0 μm, however the size of the biofilm does not exceed 10−30 nm.[12] Typically 5−35% of the biofilm volume is constituted by the microorganisms while the remaining volume is extracellular matrix. This extracellular matrix is partially or mostly composed of proteins.[13] Some important nutrients and minerals are trapped from the surrounding environment through the scavenging system, created by the extracellular matrix.[7] Different types of components are present in extracellular polymeric substances: protein in majority (>2%); other constituents, such as polysaccharides (1−2%); DNA molecules (<1%), RNA (<1%); ions (bound and free), and finally 97% of water. The flow of essential nutrients inside a biofilm is attributed to the water content.[14,18]

3. Steps in biofilm formation

Genetic studies tell us about the formation of biofilm that it occurs in many steps. It requires special type of signaling, known as quorum sensing, between the microorganism cells. Also, it requires transcription of different set of genes compared to those of planktonic forms of the same microbial organisms.[15,16] In addition, there are channels in the biofilm that separate the micro colonies. Mechanical stability of a biofilm is attributed to the viscoelastic features of the EPS matrix.[17] Formation of biofilm is complex but according to different researchers it occurs in few common steps: initial contact/attachment to the surface, followed by micro-colony formation, maturation and formation of the architecture of the biofilm, and finally detachment/dispersion of the biofilm. Each of these steps will be discussed below.[18]

3.1. Initial contact/attachment to the surface

In this step of biofilm formation, microbial cells attach to the surface through their appendages like pilli and flagella and may also get attached through other physical forces like van der Waal's forces, electrostatic interactions etc. Other factors are also greatly affecting the bacterial adhesion to a surface. Adhesion − the attachment of microbial cells to a surface, and cohesion − the interaction/attachment within the cells, occur in biofilm formation.[19,20] Solid−liquid interface can also be a reason for attachment and growth of microorganisms in biofilm formation.[21] The fimbriae, pilli and flagella give strength to the interaction between bacteria and the surface of attachment. The hydrophobicity of the surface may also play a role in strengthening the attachment of microbes, because it reduces the force of repulsion between the bacteria and the surface.[22,23] Microorganisms attach more likely to the hydrophobic and non-polar surfaces like Teflon and other plastics, than to hydrophilic and polar surface like metals and glass.[24−26]

3.2. Micro-colony formation

After an attachment of microorganisms to a biotic or an abiotic surface occurs and this attachment becomes stable, a process of multiplication and division of microbial cells starts, initiated through particular chemical signaling within the EPS. This process then leads to the formation of micro-colonies.[21,27] Bacterial colonies in a biofilm usually consist of many types of micro-communities. These micro-communities coordinate with one another in multiple aspects. This coordination plays a crucial role in exchange of substrate, distribution of important metabolic products and excretion of metabolic end-products. For instance, during anaerobic digestion, when complex organic matter is converted into CH_4 and CO_2, a minimum of three types of bacterial involvement is required: (i) fermentative bacteria start the production of acid and alcohol from organic compounds, depending upon the catabolism of complex organic compounds, (ii) these substrates are then consumed by acetogenic bacteria as their substrates, and (iii) methanogens get energy by converting the acetate, carbon dioxide and hydrogen into methane. Biofilm provides a complete environment for the development of syntrophic association, an association of two or more metabolically different bacteria depending on each other for utilization of certain substrates for their energy purposes.[28]

3.3. Maturation and architecture

In this stage of biofilm formation microbial cells communicate with one another through auto-inducer signals.[29,30] Cell-to-cell communication is an important process, during which the required microbial cell density is attained. This leads to the secretion of signaling molecules, known as auto-inducers. These auto inducers facilitate quorum sensing.[16] At this stage of maturation certain gene products are expressed, that are considered important for the formation of EPS. Since EPS is the main material in the biofilm's three-dimensional structure, interstitial voids are then produced in the matrix. These channels are filled with water and act as a circulatory system, used to distribute important nutrients and remove waste products from the communities of micro-colonies in the biofilm.[31]

3.4. Detachment/dispersion of biofilm

In this phase, microbial cells within the biofilm perform quick multiplication and dispersion in order to convert from sessile into motile form. Detachment then occurs in a natural

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