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Editorial

Biofilms and Human Diseases: A Clinician's Nightmare

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Microbes have been characterized as planktonic, free-floating single cells. As they grow in culture media, their morphology and physiology properties have been described in detail. But, how they survive in the environment was given very little thought till the concept of biofilms came into existence. The concept of biofilms has opened up a new horizon in the study of microorganisms.

What is Biofilm?

According to the IUPAC definition- Biofilm is an aggregate of microorganisms in which cells that are frequently embedded within a self produced matrix of extracellular polymeric substance (EPS) adhere to each other and / or to a surface [1].

In natural environment, microbes are commonly attached to surfaces as biofilms.

Biofilms are ubiquitous and can be present on both biotic and abiotic surfaces. They are usually found on solid surfaces submerged in /or exposed to aqueous solution. Nearly every species of microorganisms e.g., bacteria, fungi, algae and protozoa adhere to each other and to surfaces by different mechanisms. It has been estimated that nearly 90% of bacteria live in biofilms, whether single species or multiple species of bacteria, fungi, protozoa etc.

Mixed species biofilms are predominantly found in environment while single species biofilms are seen in variety of infections and on medical implant devices [2]. Research has been focused on this aspect in recent years.

It has been estimated that nearly 65% of nosocomial infections in humans are due to biofilms. Due to intrinsic resistance of these micro organisms which form biofilm, they are resistant to most of the antibiotics and diseases caused by them are very difficult to treat.

In favorable conditions, all bacteria are capable of forming a biofilm. Most infections in humans are caused by normal microbial flora of humans which form biofilms at sites where they exist as harmless commensals. In these conditions, biofilms play a protective role for the host. For example, biofilms formed in vagina prevent colonization by exogenous pathogens- a phenomenon called 'colonization resistance' and is healthy for the vagina [3]. However, due to certain exogenous and endogneous factors, this composition gets disturbed and can produce a pathogenic biofilm. Staphylococci, which are normal flora of skin frequently form biofilms on medical devices such as I / V catheters and prosthesis [4, 5, 6]. Similarly, Pseudomonas aeruginosa can cause infections in immune compromised patients [7].

How do Biofilms Develop?

There are five stages in the development of biofilms.

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1. Reversible attachment
2. Irreversible attachment
3. Early development
4. Maturation
5. Detachment dispersal of cells

When a microbial cell is <1nm close to a surface, then attachment depends upon the attractive and repulsive forces between the two surfaces [8].

In the second stage, there is a molecular binding between specific microbial adhesion and the surface [9].

Several factors control the formation of biofilm which include:

- ❖ Recognition of attachment sites on a surface,
- ❖ Nutritional cues,
- ❖ Change of pH and temperature,
- ❖ Exposure to antibiotics, chemical biocides and host defense mechanisms.

During colonization, microbial cells communicate by quorum sensing.

Biofilms are formed by many bacteria of medical importance such as Staphylococcus epidermidis, Staphylococcus aureus. Enterococci, Streptococcus mutans, Pseudomonas aeruginosa, E.coli, Neisseria gonorrheae, Vibrio cholerae and fungi such as Candida albicans [10].

Biofilms are a cause of great concern for clinicians and have received much attention in recent years because they are responsible for resistant and persistent chronic infections. They are very difficult to eradicate by routine antibiotics.

Infectious processes caused due to biofilms include bacterial vaginosis, urinary tract infections, catheter related infections, middle ear infections, dental plaque, gingivitis, infection in contact lenses, endocarditis, cystic fibrosis, prosthesis and heart valves [11, 12, 13].

Why are biofilms related infections resistant to many antibiotics and difficult to treat?

Several factors play a role in the resistance mechanisms-

1. Bacteria forming a biofilm are less susceptible to host defense system so the infection can persist for a longer time. This is due to antiphagocytic properties of the biofilm matrix [14, 15].
2. When a bacteria comes in contact with a surface sticky polymers are produced catalyzed by bacterial enzymes which result in colonization and protection. Antibiotics cannot penetrate deeper into the biofilm and can act only on the outer surface. This causes release of large amount of pro inflammatory enzymes and cytokines by the polymorphs which cause tissue damage and chronic inflammation.
3. Biofilms have an innate resistance to antibiotics. The reasons are not very clear but most probably the antibiotics fail to penetrate deep into the biofilms.

   Another plausible reason might be that many antibiotics e.g., Penicillin act only on actively growing cells. Cells that are dormant can re-establish as biofilms once the antibiotic is no longer present in the host body.
4. Biofilms increase the opportunity for gene transfer between the bacteria and among the bacteria. The resistant bacteria transfer the gene for resistance mechanism to neighbouring susceptible bacteria. Similarly a non pathogenic commensal organism can become highly pathogenic by this gene transfer [16].

However, not all bacteria can form biofilms. Some non motile bacteria cannot recognize the surface as easily as motile bacteria, so they cannot form an effective biofilm [14].

Conclusion

Bacteria have been known to cause variety of infections in humans and scientists have been struggling to find out mechanisms by which bacteria invade the host defense mechanism to cause disease. In recent years, drug resistant microbes have been on the rise and the role of biofilms has emerged as a newer concept in causing chronic disease resistant to most of the commonly used antibiotics. Many antibiotics in use are increasingly becoming obsolete as drug resistant bacteria are on the rise. Clinicians are facing newer challenges in treating the patients as the drug options are becoming limited. Furthermore, there has been increasing evidence to support the formation of biofilms in chronic human diseases which are resistant to common antibiotics.

With newer and more sensitive technologies, scientists will be able to gain more insight and better understanding of the biofilm biology which may in the long run help combat bacterial infections which are a clinician's nightmare in the present conditions.

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