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A Review of the: Mechanism of Biofilm Formation Affecting Medical Devices

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ABSTRACT

Objective: *Bacterial colonies that live in an exopolysaccharide matrix and adhere to foreign surfaces in a living creature make up the complex biofilm. In therapeutic settings, biofilm often results in nosocomial, persistent infections.* ***Method:*** *This review gives a short account of the ideas underpinning the composition of, production of, and drug-resistant illnesses attributable to biofilm and cutting-edge therapeutic ways to combat and treat biofilm.* ***Results:*** *Antibiotics are insufficient to treat infections caused by biofilm because the bacteria in the biofilm have become resistant to them.* ***Novelty:*** *The use of cutting-edge technologies to handle the challenges posed by biofilm is justified by the high incidence of infections caused by medical devices.*

INTRODUCTION

A biofilm is a group of microorganisms, such bacteria, that can coexist and procreate as a colony. In other words, biofilms are living biomass with a complex social structure that researchers are still trying to understand. The biofilm's structure protects the colony and facilitates its growth.

It is well known that prokaryotes and eukaryotes, or unicellular and multicellular organisms, have a symbiotic connection. These symbiotic connections are advantageous to both parties Bacteria, fungi, and viruses make up the vast and intricate microbiome of the human body. The majority of the human body's microbiota is found in the skin, salivary mucosa, and gastrointestinal tract, where it supports a number of physiological processes, including innate immunity and metabolism. These symbiotic microbes can, however, develop uncontrollably in some situations, which can result in infections that start the creation of biofilms. Bacteria have existed in two distinct states throughout their evolutionary history: the sessile state, which is attached to a surface, and the planktonic state, which is free-floating [1]. Because bacterial attachment to a surface rapidly alters the expression levels of multiple genes linked to maturation and the formation of exopolysaccharide (EPS), commonly referred to as "slime" or bacterial EPS, bacteria display distinct characteristics between these two stages. This transition, which begins as soon as bacteria colonize both biotic and abiotic surfaces, results in the production of a protective barrier [1], [2]. This barrier protects the germs from both external threats like antibiotics and the host's inherent defensive mechanisms. The term "biofilm" was not used or defined until a manuscript by Costerton et al. [3], [4], but surface-associated

bacteria were first seen by Anthony van Leeuwenhoek. The American Society for Microbiology recognized the importance of biofilms in 1993 [4]. In 1999, Costerton et al. provided a more detailed description of biofilm as an organized population of bacteria clinging to a surface and contained in a polymeric matrix created by the bacterium [5]. Biofilms affect every aspect of human existence, including the economics, energy use, equipment deterioration, contaminated goods, illnesses, and public health and industrial issues. Modern tools like confocal and scanning microscopy have made it easier for researchers to comprehend the incredibly complex structure of biofilms. Biofilms are complex populations of cells encased in an EPS matrix with permeable water channels, homogeneous cell deposits, and accumulated slime, according to research using these state-of-the-art methods. Microorganisms that grow in biofilms and are highly resistant to antimicrobial treatments are associated to a number of human diseases and the colonization of medical equipment. The creation of biofilms starts the disease process in a number of ways, including the separation of individual bacterial cells or aggregates of cells, the generation of endotoxins, increased resistance to host immune system surveillance, and the creation of a barrier that allows immune-resistant organisms to proliferate According to current knowledge, biofilms are immobile complex structures made up of one or more species of bacteria, host cells, and cellular byproducts. The cells are permanently attached to the substratum and encased in an extracellular polymeric material that the bacteria produce. The best conditions for the growth of biofilms are surfaces that supply moisture and nutrients. Biofilms can be neutral, harmful, or both [6]. While biofilms that develop on exposed wounds after infection are dangerous, biofilms that are a part of the natural environment are neutral. When it comes to resolving ground contamination caused by an oil spill, biofilms may be beneficial. Seventy percent of infections caused by microorganisms are caused by biofilms, which also play a major role in human healthcare-associated infections (HAIs). The bacteria residing in the biofilm exhibits traits like improved survivability against antimicrobial treatment, source capturing, and collective cooperation. Biofilms are the cause of persistent chronic infections due to their increased survivability and ability to evade the human immune system [7].

RESEARCH METHOD

The Composition and Type of Bacteria Found in Biofilms:

Biofilm is composed of 90% water and 10% microbial material [8]. The polysaccharides that make up the matrix are responsible for between 50 and 90 percent of the total organic component of biofilms [9]. A thick, mesh-like structure is created by weaving chains of polysaccharides together [10]. By interacting with one another, the hydroxyl groups on the polysaccharide improve mechanical strength [11]. Positively charged ions, such Ca2+ or Mg2+, can build supporting cross bridges between polymers in the biofilm architecture, enabling biofilms to reach thicknesses of up to 300 μm. In other cases, such as the EPS of Gram-negative bacteria, the polysaccharides in biofilms may be neutral or polyanionic [12]. Additionally, biofilms may contain ketal-linked pyruvates

that provide anionic characteristics or uronic acids such D-glucuronic, D-galacturonic, and mannuronic acids [12]. Anionic characteristics make it possible for divalent cations to join polymer strands and give mature biofilm a stronger binding force [13]. The chemical makeup of EPS in Gram-positive bacteria, including staphylococci, is completely different and primarily cationic. According to Hussain et al., teichoic acid and trace amounts of proteins make up the slime of coagulase-negative bacteria [14]. The various charges and ions in the biofilm give the EPS structural integrity, giving biofilms the ability to endure settings with high shearing forces, such waterfall impact points. Bacteria growing in biofilm are sessile and are responsible for most physiological processes in the biofilm environment [15]. The growth, gene expression, transcription, and translation rates of the sessile bacterial biofilm populations vary. These functional characteristics are acquired by the sessile bacterial biofilm communities in the process of adaptation to microenvironments that have higher osmolarity, scarcer nutrients, and increased cell density. The resulting structure of a biofilm is extremely viscoelastic and has a rubbery behavior [16]. According to a recent NIH study, biofilms cause 70% of all human microbial infections, which can result in a number of illnesses, such as non-healing chronic wounds, endocarditis, periodontitis, cystic rhino sinusitis, fibrosis, meningitis, osteomyelitis, kidney infections, prosthesis, and infections related to implantable devices [17], [18]. A device that becomes contaminated during and after implantation can cause serious device-associated infections that need to be removed and can be fatal. Extreme care in the manufacturing process aims to maintain sterility of an implantable device [19].

RESULTS AND DISCUSSION

A. Bioflim Formation

Adsorption, adhesion, microcolony development, maturation, and dispersion are all steps in the multi-step process that creates the three-dimensional architecture of biofilm, see Figure 1. The ideal environment for microbe adhesion and growth is provided by the solid-liquid intersection of a biofilm surface with an aqueous media (such as blood or water). The biofilm colony's intimate cell connection fosters the creation of a gradient in the availability of nutrients, gene exchange, and quorum sensing (QS).

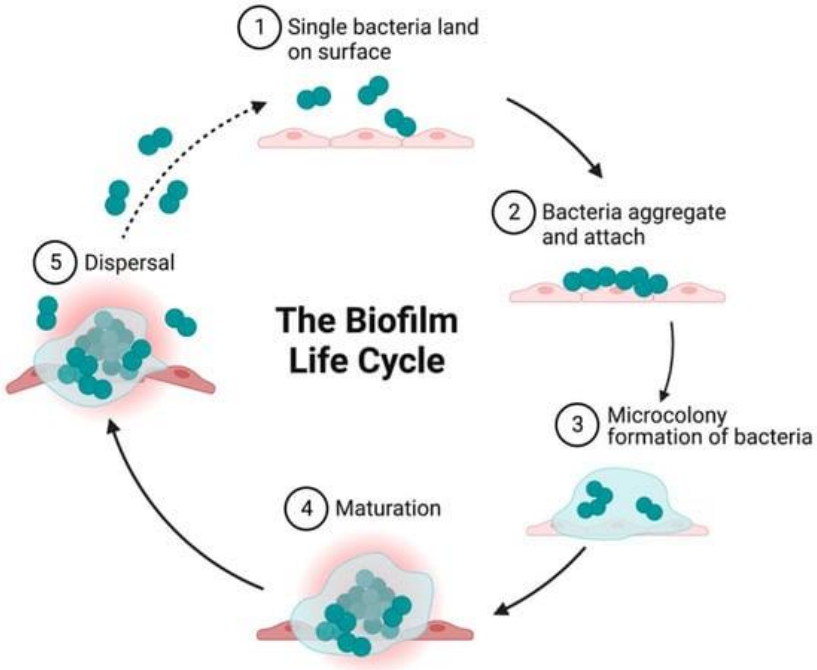

Figure 1. Diagrammatic representation of a single bacterial species' biofilm growth cycle on a solid surface.
(1) Single planktonic bacteria can adhere to surfaces reversibly. Attractive or repulsive forces produced by nutrition levels, pH, and surface temperature affect the bacteria's initial adhesion. (2) Bacterial aggregation and permanent surface adhesion. (3) Microcolony development, EPS secretion, and the creation of an exterior matrix of multilayered complex biomolecules. In biofilm-forming bacteria, polysaccharide secretion promotes adhesion, aggregation, and surface tolerance, which improves surface colonization.
(4) As biofilms mature, they acquire a three-dimensional structure. These three-dimensional structures are supported by extracellular matrix components that are self-produced. (5) When fully developed biofilms separate, bacterial cells can revert to a planktonic condition and form biofilms elsewhere. created on March 31, 2023, on BioRender.com.

When the Reynolds number (Re) is more than 5000, biofilms develop in a turbulent flow environment. Re is a non-dimensional number used in fluid mechanics that helps anticipate fluid flow patterns in a variety of situations by measuring the ratio of inertial to viscous forces. Turbulent flow is indicated by a higher Re value, while laminar flow is suggested by a lower Re number. Biofilm production is enhanced by turbulent flow. It has been shown that both smooth and rough surfaces can be colonized equally easily; the physical characteristics of a biofilm surface only slightly influence bacterial adhesion [20]. The research tools available in the 1970s limited studies conducted to understand the mechanism of biofilm growth. Biofilms are adaptable structures used by bacteria as a defensive barrier to produce an advantageous habitat that helps them retain nutrients and ensure life in an adverse environment, as demonstrated by the development of sophisticated instruments and technologies [21]. Additionally, biofilms made by many bacteria share many similarities, but they can also have subtle characteristics specific to a certain species [22], [23]. Early 21st-century research explains how physiological processes and natural forces control the production of biofilms [24].

1. Initial Attachment

When the free-floating planktonic bacteria come into contact with any surface, attachment starts.They adhere to the surface through physical forces or bacterial appendages like flagella and/or pili [25]. At this point, the bond is fleeting and easily reversible, and the process is more likely the result of a fortuitous contact [26]. Numerous factors, such as material composition, bacterial cell surface characteristics, temperature, and pressure, influence how much the bacteria stick to the surface they come into contact with [27]. Hydrophobic,steric, electrostatic, van der Waals, and protein adhesion are some of the forces that regulate the degree of attachment. These forces work together to enable the bacteria continue adhering to the surface and overcome repulsive forces, resulting in an irreversible attachment and the formation of a monolayer [28].

2. Aggregations and Adhesion of Bacteria

The anchoring or latching phase, which is the second stage of adhesion, is a molecularly coordinated binding between certain adhesins and the outermost layer [29]. By producing EPS that interact with surface materials and/or receptor-specific ligands found on pili, fimbriae, fibrillae, or both, the loosely linked organisms at this stage solidify through the adhesion process. As a result, the organisms are better able to stick to the surface they are attached to. At the end of the second phase,In the absence of any physical or chemical intervention, the adhesion will have become irreversible, and the organism will accumulate on the surface in a stable, irreversible manner much to how a cocoon would adhere to a leaf. Certain organisms may use a range of various adhesins to stick to surfaces, depending on the circumstances. Planktonic microorganisms can adhere to different types of surface-bound organisms and to each other at this stage of the adhesion process, which leads to the formation of aggregation on the substratum. Interestingly, the presence of one type of bacterium on an outer layer may encourage the adherence of another type of microorganism [30]. Different adhesins are produced by each bacteria, and some of these adhesins are transcriptionally regulated.This enables organisms to change from a sessile to a planktonic form in response to environmental stimuli [31], [32]. This is the case with *S. epidermidis*, which produces a kind of polysaccharide intercellular adhesin (PIA), which is crucial for biofilm formation and cell-to-cell adhesion [33].

3. Formation of Microcolonies

Bacterial adhesion is followed by cell division and proliferation to create microcolonies,certain chemical communication within the EPS and micro communities initiates this process [34]. Bacterial colonies usually include a range of micro-communities inside a biofilm.These micro-communities work together in a variety of ways.Substrate exchange, the movement of important metabolic products, and the removal of metabolic waste all depend on this interaction. For instance, anaerobic digestion and the breakdown of complex organic matter into CH4 and CO2 need the presence of at least three distinct types of bacteria. After complex organic substances are broken down, fermenting bacteria start to produce alcohol and acid. These substrates are subsequently eaten by acetogenic bacteria,while methanogens produce methane from acetate, carbon dioxide, and hydrogen.A complete environment for the development of syntrophic association is provided by biofilm.The affiliation of two or more metabolically different bacteria that depend on one another to use particular substrates for their energy demands is known as syntrophic association [35].

4. Maturation

Maturation is the fourth stage of biofilm formation, during which the connected cells continue to grow and develop. The connected bacterial cells secrete signaling molecules that facilitate maturation and cause the expression of genes unique to biofilms. In order to increase bacterial pathogenicity, signaling factors modify gene regulation. EPS is released from the cells at the start of the process, stabilizing the biofilm structure and protecting it from antimicrobial agents [36]. For instance, during maturity, *P.aeruginosa* produces distinct saccharides (alginate, Pel, and Psl) that provide biofilm stability [37]. A study claims that intracellular signaling and biofilm strength are caused by environmental DNA (e-DNA) [38]. The *S.epidermidis* polysaccharide intercellular adhesion (PIA) antigen protects the growing bacteria against polymorphonuclear leukocytes in addition to facilitating initial attachment [39]. Cell clusters accumulate and aggregate on the surface to form several layers. Quorum sensing (QS) and intercellular signaling take place in these clusters, which eventually grow into microcolonies that are also enclosed within the EPS. In general, there are two phases of maturation: Cell-to-cell contact and the production of autoinducer signal molecules such as N-acylated homoserine lactone (AHL), are characteristics of stage I, while stage II involves the expansion of the microcolony's size and thickness to around 100 μm, which is the threshold for an established microcolony [40]. Active collaborations enable the bacteria in the biofilm to form connections, and the degree of connectedness between them is determined by their distance from one another [41]. Bacteria can identify the size and proximity of neighboring groups during the maturation stage, which helps them form clusters that can more successfully bond with neighboring cells [42]. Gene and protein expression is regulated by the complete bacterial colony in the biofilm rather than through individual bacterial cells [43]. In summary, the production of EPS, cell aggregation, chemical bonding,QS, and the development of micro- and macro-colonies comprise the second stage [44].

5. Dispersion

A crucial stage in the creation of biofilms is dispersion, the process by which bacteria move from one area of an infected person's body to another to transmit infection.Usually, a biofilm consists of two distinct layers [45]. The foundational layer serves as the bacteria's primary home, while the surface layer serves as a dispersal zone where they spread across their environment, making their dissemination and long-term existence. This stage causes severe symptoms such embolic issues and chronic infection, which require immediate medical attention [46]. This technique is therefore commonly referred to as metastatic seeding [47], [48]. As the biofilm ages, resources become scarce and hazardous metabolic wastes accumulate. As a result, the microbial cells disperse to different regions of the medical implant or the infected host in order to proliferate,acquire nutrition, and eliminate stressful conditions and waste products [49]. The dispersion process is started by individual cells or groups of cells that are separated from the biofilm [50]. Some researchers think that this mechanism is preprogrammed and that, in the case of aerobic bacteria, it is triggered by either oxygen levels or nutritional deficiencies.Tiny molecules like the fatty acid DSF (cis-11-methyl-2-dodecenoic acid) are activated by autophosphorylation in response to the deficit.The cyclic diguanylate Guanosine monophosphate (c-di-GMP) phosphodiesterase is activated as a result of this autophosphorylation, which degrades c-di-GMP. Clusters of the biofilm are broken up by shear forces or released planktonic cells when c-di-GMP is broken down, which subsequently dissolves portions of EPS [51], [52]. The degradation of EPS involves several

mechanisms in addition to gene regulatory networks. Among these methods is the bacterial cells' production of enzymes that facilitate the lysis of saccharides.The top layer of bacteria is released as a result of this activity's dissolution of the polysaccharide matrix that anchors the biofilm [53]. After being released, the bacteria either form new biofilms in various body organs or float freely on the surface by promoting the synthesis of proteins that facilitate motility [54].

6. Quorum Sensing

Quorum sensing (QS), a technique for cell-to-cell communication, synchronizes gene expression in response to the population's cell density.Biofilm development and QS are linked processes. The biofilm develops when the QS gene is activated, and it then synchronizes its development and disintegration. The QS phenomenon is only possible when there are very few bacteria in a given volume.The number of bacteria in each volume can be ascertained by measuring the quantity of autoinducer signaling molecules released by the bacteria in a microcolony [55]. However, some researchers disagree, contending that autoinducer signaling molecules should not be regarded as signaling molecules because they are merely metabolic byproducts [56]. Several modeling and mathematical techniques have been proposed to understand the QS process that bacteria employ to form biofilms. Researchers think that blocking QS could be a useful tool in the fight against biofilms since it is essential for the growth and maturation of biofilms. In order to identify goods and materials that can "quorum quench," a new field of study known as "quorum quenching" is being established.Finally, studies on *B.cepacian and P.aeruginosa* Quorum quenching products have been shown to lower antibiotic resistance in two different types of bacteria associated with biofilms [57].

B. Biofilm-Related Infections

Biofilms have been linked to a number of infectious illness research [58], [59]. According to conservative estimates, biofilm is associated with around 70% of all bacterial infections, both device-related and non-device-related [60]. Because one's own body offers a sufficient biotic surface with optimal moisture and other support systems for bacteria to attach and create EPS, illnesses unrelated to devices can emerge. For example, when dental hygiene is insufficient, *P. aerobicus and Fusobacterium nucleatum* produce periodontitis by infecting the gingiva [61]. A mineralized biofilm (plaque or tartar) primarily made of calcium and phosphate ions is formed as a result of the biofilms that grow on the tooth's surface interfering with the transit of calcium in the epithelial cells [62]. Osteomyelitis is another biofilm-related, non-device disease that travels to the bone metaphysis via the bloodstream [63]. The bone tissue deteriorates further and breaks as a result of immune system responses to the microorganism [64]. Moreover, chronic sickness is thought to be caused by the biofilms that develop in diabetic patients' open wounds [65]. Anaerobic bacteria infiltrate the core of severe wounds whereas aerobic bacteria form biofilms on the outside [66]. Conditions include otitis media chronic prostatitis, native valve endocarditis, cystic fibrosis, and periodontitis are caused by a variety of biofilm-associated microorganisms [67]. Infectious diseases can result from biofilms in the following ways: (a) detachment of biofilm cells or masses of cells resulting in blood and urine infections or emboli formation; (b) cells can exchange resistance plasmids within biofilms; (c) cells are less susceptible to antimicrobial agents; (d) bacteria-associated biofilms produce endotoxins; and (e) the host immune system is resistant.

C. Biofilms on Healthcare Equipment

The relationship between biofilm and medical devices was initially shown by Costerton et al. [68]. Further research has shown that bacterial adhesion and biofilm

formation can occur in urinary catheters, central venous catheters, indwelling stents, contact lenses, intrauterine devices, and dental chair water lines [69]. Liquids, blood and blood products, medications, food, and hemodynamic monitoring are all administered via catheters [70].

Biofilms may form in the catheters' inner or outer lumen. Bacteria can spread via the main channel or by climbing the outside of the catheter. The conditioning films on catheter surfaces are made of platelets and other tissue proteins [71]. Hemagglutinin and polysaccharide intercellular adhesin were examples of adhesins [72].

1. Catheters for Central Venous

Central venous catheters (CVCs) are more susceptible to device-related infections than any other indwelling medical device, as was initially shown by Maki et al. [73]. On CVC, colonization and biofilm formation often occur three days following catheterization. According to research by Raad et al., catheters left in place for fewer than ten days tended to produce more biofilm on their exterior than catheters kept in place for thirty days.days or longer tended to develop biofilm on the catheter's inside more frequently and widely [74]. *S. aureus, P. aeruginosa, Klebsiella pneumoniae, Enterococcus faecalis*, and *Candida albicans* are among the pathogens that colonize CVCs [75]. To find CVC biofilms, the distal tip of the catheter is removed aseptically and rolled over the surface of a nonselective medium. The size of the biofilm on the catheter tip is determined by the quantity of organisms retrieved upon contact with the agar surface [76]. According to Slobbe et al. [77], the roll-plate approach for identifying catheter-related bacteremia has poor predictive value and poor detection accuracy. By sonicating and vortexing catheter tips to enhance biofilm quantification, they found that even a threshold of 104 CFU/tip indicated catheter-related septicemia.

2. Artificial Heart Valves

The relationship between biofilm and prosthetic heart valves was shown by Karchmer and Gibbons [78]. There are two types of prosthetic heart valves: mechanical valves and bio-prostheses, sometimes known as tissue valves. Nonetheless, both have comparable infection rates [79]. When adjacent tissue is damaged during surgical implantation, platelets and fibrin may accumulate, which could result in microbial colonization. artificial valve endocarditis (PVE) is an infection linked to artificial heart valves [80]. PVE is categorized as either early (less than 12 months) or late (more than 12 months) following surgery. Depending on how long it has been since valve implantation, the microbiological species that cause PVEs can be predicted. The pathogenic mechanism may be reflected in the time of infection [81], [82].Coagulase-negative staphylococci (CoNS) and S. aureus are the most prevalent pathogens in the first two months following valve implantation, followed by members of the Candida species and Gram-negative bacilli.The typical nosocomial origin of these diseases is reflected in this variety of bacteria. Coagulase-negative *Staphylococci, S. aureus, and Streptococci* are the most prevalent infections between two and twelve months following valve implantation, followed by Enterococci. The most common bacteria found a year after a valve is installed are *CoNS, S. aureus, Streptococci, and Enterococci.*

3. Contact Eyewear

Depending on the substance used to make them, contact lenses can be either soft or firm. Soft contact lenses made of silicone or hydrogel allow oxygen to diffuse into the cornea through the lens material. With each blink, oxygen-containing tears can slide beneath hard contact lenses composed of polymethylmethacrylate. Bacteria can readily invade both kinds of lenses [83]. Bacteria that have been known to stick to contact lenses

include *P. aeruginosa, S. aureus, S. epidermidis, Serratia spp., E. coli, Proteus spp.,* and *Candida spp*. Miller and Ahearn came to the conclusion that *P. aeruginosa* adhered to hydrophilic contact lenses at different rates depending on the water content [84]. The degree of pathogen attachment can be influenced by the type of bacteria, pH, and substrate. Additionally, it was discovered that 80% of lens users without symptoms had contaminated storage cases due to the development of biofilms on contact lens storage cases [85].

4. Intrauterine Devices (IUDs)

Polyethylene, a nonabsorbable polymer impregnated with barium sulfate, is used to make IUDs. Additionally, some types release chemicals, such as copper or a pro-gestational agent. Pelvic inflammatory illness may result from IUD use [86]. IUDs removed from women with pelvic inflammatory illness have been discovered to include *S. aureus*, beta-hemolytic *streptococci, E. coli,* and other anaerobic bacteria. However, IUDs extracted from asymptomatic women were shown to be heavily infected with anaerobic *lactobacilli, enterococci, and S. epidermidis* [87]. Other pathogens that have been found include *S. epidermidis, Lactobacillus plantarum,* IUDs are made of polyethylene, a nonabsorbable polymer impregnated with barium sulfate. Certain varieties also release compounds, such copper or a pro-gestational agent. IUD use may cause pelvic inflammatory disease [88]. *S. aureus*, beta-hemolytic streptococci*, E. coli*, and other anaerobic bacteria have been found in IUDs removed from women with pelvic inflammatory illness. However, it was discovered that anaerobic lactobacilli, enterococci, and *S. epidermidis* were more prevalent in IUDs taken from asymptomatic women [89]. Additional pathogens discovered include *Lactobacillus plantarum, S. epidermidis,*

5. Water Lines in Dental Units

Patients and dentists may become infected by pathogenic organisms in dental unit water lines [90]. Small-bore flexible plastic tubing is used to supply water to dental units for a variety of hand pieces, such as the air-water syringe, the ultrasonic scaler, and the high-speed hand piece.Metropolitan, distilled, or sterile water reservoirs are examples of water sources. In water samples collected from the three-way syringe, Furuhashi and Miyamae showed that the bacterial counts had risen from the usual municipal water supply of less than 40 cfu/mL to between 103 and 105 cfu/mL [91]. They also observed that the cup water filler and air turbine hand piece both had high ratings. Whitehouse et al. [92], showed a variety of microorganisms in a polysaccharide matrix. Water counts and biofilm were shown to be positively correlated. Even after 180 days of contact, they discovered that a dense, multi-layered extracellular polymeric material completely covered the surface of the dental unit water line. Furthermore, it has been demonstrated that biofilms comprising both aquatic bacteria and mixed cutaneous microbiota are supported by saliva ejectors and other oral suction devices.

6. Catheters for Urine

There are two kinds of urinary catheters: silicone and latex.To measure urine yield, collect pee during surgery,manage urinary incontinence,or treat urinary retention, they are placed into the bladder through the urethra. The gadgets are either closed or open. In open devices, which are mainly used in developing countries, the catheter empties into an open collection receptacle, whereas in closed systems, which are used elsewhere, the collection bag is made of plastic. One species, such as *Enterococcus faecalis, E. coli, S. epidermidis,* or *Proteus mirabilis*, colonizes urinary catheters in their early phases. Mixed communities including organisms such *Klebsiella pneumoniae, Proteus mirabilis, P. aeruginosa, and Providencia stuartii* subsequently form [93]. These biofilms on urinary

catheters are unique because some of the constituent organisms have the ability to alter the local pH by generating urease, which hydrolyzes urea in urine to release free ammonia. Minerals like calcium phosphate (hydroxyapatite) and magnesium ammonium phosphate (struvite) may precipitate as a result of the ammonia altering the local pH, see Figure 2. These minerals will accumulate and create a mineral encrustation in the catheter biofilms [94].

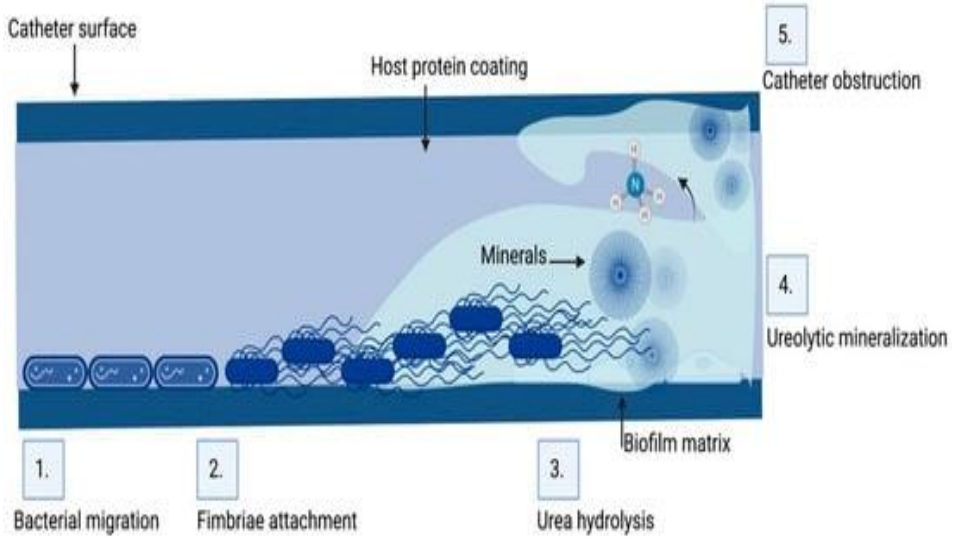

Figure 2. CAUTI disease process and biofilm production The catheter surface provides the perfect environment for bacterial adhesion and the development of biofilm formations.

(1) Bacteria move along the catheter surface in the periurethral region. (2) Fimbriae adhere to the surface of the catheter made of bodily fluid or directly to the catheter material, causing the formation of biofilms and EPS. (3) Certain bacteria, such P. mirabilis, create enzymes that hydrolyze urea in urine into ammonia, raising the local pH and causing the urine to form minerals and struvite crystals. (4) The ureolytic mineralization process, which is also aided by the capsule polysaccharides, incorporates the produced struvite into the growing biofilm. (5) Catheter blockage finally results from fully formed crystalline biofilm. created on March 31, 2023, on Biorender.com.

Patients who have biofilms on their urinary catheters experience a urinary tract infection (UTI) four days after the catheter is inserted [95]. Catheter-associated urinary tract infections (CAUTIs) are UTIs that are almost exclusively caused by the insertion of a urinary catheter [108]. Urine can stay sterile for 10–14 days in around half of the patients, and CAUTIs are less common in closed systems [96]. In their investigation, Stickler et al.shown that while nearly all patients having long-term (>28 days) catheterization develop CAUTI, 10–50% of patients undergoing short-term (<7 days) catheterization do so [97]. The primary source of the 10% increase in CAUTI risk for each day the catheter is left in place is bacterial climbing from the catheter to the bladder, according to McLean et al. [98]. According to Nickel et al., biofilms formed in CAUTI contain a variety of bacterial species, which results in a thick, cohesive biofilm that confers significant resistance to antibiotics even though individual bacteria in the biofilm remain sensitive, explaining why antibiotic therapy fails [99]. Furthermore, they observed that the degree of biofilm formation was unrelated to the duration of catheter

use. Although the annual economic loss from CAUTI is approximately USD 1.7 billion, the attributable cost per patient surpasses USD 1000 [100]. In order to provide a financial incentive for CAUTI prevention initiatives, the Center for Medicare Services (CMS) discontinued paying hospitals under the Hospital Acquired Conditions Reduction Program (HACRP) in 2008 after listing CAUTI as one of the 14 hospital-acquired and preventable conditions. Increased frequency and urgency of urination, dysuria, stomach pain, and tachycardia are common signs of CAUTI. CAUTI symptoms include hematuria, murky urine, and catheter blockage. Although *Pseudomonas, Klebsiella, Proteus genus*, and Gram-positive bacteria including *Staphylococcus aureus and Enterococcus faecalis* have all been linked to CAUTI, the most frequent cause is the Gram-negative bacteria *E. coli*. Bacteria from the patient's hands, the hands of medical personnel, or the colonic or perineal microbiota might enter the urinary tract when indwelling catheters are implanted if the collection system is handled incorrectly. Because the biofilm serves as an infection reservoir and fosters antimicrobial resistance, bacteria are protected within. Rectal microbiota contamination of the urethra is the most common cause of CAUTIs. After that, the bacteria move to the bladder, stick there, and establish a colony [101]. Toxins and bacterial proteases also harm the epithelium. After that, bacteria develop and form biofilms, see Figure 2. The basic phases of infection progress in the same manner with or without a urinary catheter. Urinary catheters allow the bladder to be directly attached to the external environment. This conduit is essential for urine evacuation in certain individuals, but it also provides a route for rectal and periurethral microbes to ascend to the bladder, where they can establish an infection base. Because catheters bypass the urethral sphincters, reduce the turbulence that often happens during spontaneous urine, and function as an infection nidus, they increase the risk of UTI. Additionally, the mucopolysaccharide layer that ordinarily shields the uroepithelium may be ruptured by catheter irritation and stress, leaving it open to bacterial adhesion and invasion. The strong immune reaction to catheterization, which results in fibrinogen building up on the catheter, creates a favorable environment for adhesion by uropathogens that produce fibrinogen-binding proteins [102]. For example, *Enterococcus faecalis* grows in urine supplemented with fibrinogen and adheres to a catheter coated with fibrinogen, but it does not grow in urine or bind to catheter material in a culture setting [103]. Adherence is a crucial initial step in UTIs. In simple UTIs, two types of bacteria may adhere to the uroepithelium of the bladder, allowing the infection to spread. Thus, bacterial adherence to a urethral catheter or suprapubic tube facilitates the formation of a biofilm [104]. The most important way to reduce the incidence of CAUTI is to use indwelling urinary catheters only when absolutely required [105]. Alternatives to urethral catheterization should be investigated, and catheterization should only be used in urgent situations, avoided, or used sparingly for the treatment of chronic diseases and urine incontinence. Numerous studies emphasize how important it is to standardize the requirements for inserting indwelling urinary catheters and, when needed, completely stop using them in favor of alternatives like intermittent

catheterization. Sterile techniques should be used while inserting indwelling urinary catheters.

CONCLUSION

Fundamental Finding : Biofilms are structured microbial communities embedded in an extracellular polymeric substance (EPS) matrix, protecting bacteria from antibiotics and host immunity. They form through stages of attachment, aggregation, microcolony formation, maturation, and dispersion. Biofilms develop on biotic and abiotic surfaces, including medical devices like catheters, prosthetic heart valves, contact lenses, IUDs, and dental unit water lines. Bacteria in biofilms exhibit enhanced survival, quorum sensing, metabolic cooperation, and resistance to antimicrobials, contributing to chronic and device-related infections. EPS composition, ionic interactions, and viscoelastic properties are key to biofilm stability. **Implication :** Biofilm presence on medical devices increases infection risks, chronicity, and device failure. Understanding biofilm mechanisms can guide interventions such as quorum sensing inhibition, biofilm-resistant materials, and improved catheter management to reduce healthcare-associated infections and costs. **Limitation :** Biofilm research faces challenges due to species-specific behaviors, complex microbial interactions, and environmental variability. Laboratory studies may not fully represent clinical conditions, and biofilm heterogeneity complicates quantification, treatment assessment, and translation to practice. **Future Research :** Future studies should develop anti-biofilm strategies, including quorum quenching, EPS-targeted therapies, and biofilm-resistant devices. Advanced imaging, molecular techniques, and modeling are needed to understand biofilm dynamics, intercellular communication, and resistance mechanisms. Investigating biofilms in clinical environments will enhance infection prevention and treatment, especially for device-associated infections.

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