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An Overview of Infections Associated with Urinary Catheters

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ABSTRACT

A urinary tract infection (UTI) is an infection that can occur anywhere in the urinary system. The urinary system consists of the kidneys, ureters, bladder, and urethra. Most infections affect the lower urinary system, specifically the bladder and urethra. Women are more likely to have a UTI than males. If the infection is localized to the bladder, it can be uncomfortable and irritating. However, major health complications might occur if a UTI spreads to the kidneys. A urinary catheter is a tube that collects urine from the bladder and connects it to a drainage bag. It is somewhat flexible and may be constructed from a variety of materials. A urinary catheter is used when a person's bladder cannot be empty, resulting in kidney pressure or urine incontinence. A health care professional may recommend a urinary catheter for a number of reasons.

Biofilms, cooperative communities of microorganisms, commonly form on indwelling urinary catheters, leading to persistent infections that are resistant to standard antimicrobial therapies. Urinary tract infections (UTIs), predominantly caused by uropathogenic bacteria, are increasingly associated with Candida species, particularly in patients with prolonged catheterization. These infections often involve multidrug-resistant strains, complicating treatment and increasing the risk of spreading resistant organisms. Addressing this complex issue requires more than isolated interventions, as it contributes to significant hospital and community-acquired infections..

Keywords: *Urinary tract Infections, Catheters, Biofilms, Uropathogenic bacteria, Candida spp*

1. INTRODUCTION

Urinary tract infections (UTIs) represent one of the most prevalent bacterial infections affecting humans, with a particularly high incidence among hospitalized and catheterized patients. The introduction of urinary catheters, while essential for managing urinary retention, monitoring urine output, or aiding surgical procedures, has inadvertently become a major sourcof healthcare-associated infections. Catheter-associated urinary tract infections (CAUTIs) account for a significant proportion of nosocomial infections, contributing to increased morbidity, mortality, and healthcare costs worldwide.

The development of CAUTIs is often linked to the formation of microbial biofilms on catheter surfaces. These biofilms serve as protective niches for bacteria and fungi, enabling them to resist host immune responses and antimicrobial therapies. Common causative agents include uropathogenic Escherichia coli, Klebsiella spp., Proteus mirabilis, Enterococcus faecalis, and Candida spp., many of which display multidrug resistance. The persistence of biofilms and the emergence of resistant pathogens underscore the growing challenge in managing CAUTIs effectively

Understanding the mechanisms of infection, biofilm formation, and antimicrobial resistance is crucial for developing novel preventive and therapeutic strategies. This paper provides an overview of urinary catheter–associated infections, focusing on their etiology, pathogenesis, and the role of biofilms in persistent infection

2.1 Urinary tract infection (UTI)

A urinary tract infection (UTI) is a bacterial infection of the bladder and its surrounding tissues. There are no anatomical abnormalities or comorbidities in these people, such as diabetes, an immunocompromised condition, or pregnancy. Uncomplicated urinary tract infection (UTI) is also known as cystitis or lower UTI. Without symptoms, bacteriuria does not constitute a UTI. Urinary frequency, urgency, suprapubic pain, and dysuria are common symptoms. UTIs affect 40% of women in the United States at some point in their lives, making it one of the most frequent illnesses in women. UTIs in circumcised guys are unusual; by definition, every male UTI is considered complex (Bono et al., 2023).

Pathogenic bacteria enter the urinary tract through the perineum and rectum, predisposing women to urinary tract infections. Women's urethras are also shorter than men's, which adds to their higher vulnerability to UTIs. Few simple UTIs are caused by blood-borne bacteria (Yamaji et al., 2018).

It is difficult for women due to their anatomy, and up to one-third of all women will encounter one at some point in their lives. Appropriate UTI therapy necessitates correct categorization that takes into account the infection location, the complexity of the illness, and the possibility of recurrence. The most common pathogen in both complex and simple UTI is pathogenic *Escherichia coli*, however *Klebsiella sp*. and *Proteus* are more common in complicated UTI (Valiquette, 2001). They often occur between the ages of 16 and 35, with 10% of women infected annually and more than 40% to 60% infected at least once in their lives. Recurrences are common, with almost half of those infected acquiring another infection within a year. Females are at least four times more likely than males to get urinary tract infections (Sakamoto et al., 2019) (Alperin et al., 2019)

Many instances of simple UTIs cure naturally, however many patients seek treatment for symptom alleviation. The goal of treatment is to keep the infection from spreading to the kidneys or developing into upper tract disease/pyelonephritis, which can destroy the fragile structures in the nephrons and eventually lead to hypertension. ("Five-day nitrofurantoin is better than single-dose fosfomycin at resolving UTI symptoms," 2018) (Long and Koyfman, 2018) (Tang et al., 2019)

The great majority of UTIs are caused by *E.coli*, followed by *Klebsiella,* although other species of interest include *Proteus, Enterobacter*, and *Enterococcus.* A UTI is diagnosed based on the clinical history (symptoms) and urinalysis, with confirmation by a urine culture, although correct collection of the urine sample is critical (Behzadi et al., 2010)

A simple UTI generally just affects the bladder. When germs infiltrate the bladder mucosal membrane, an inflammatory response known as cystitis occurs. The majority of organisms that cause a UTI are enteric coliforms, which live in the periurethral vaginal introitus. These germs enter the bladder through the urethra and cause UTIs. Sexual activity increases the migration of germs into the bladder, which is a typical cause of a UTI. People who often void and clear their bladders are less likely to develop a UTI. (Maharjan et al., 2018)

Urine is an excellent bacterial growth medium. A pH less than 5, the presence of organic acids, and high urea levels are all factors that make it unfavorable for bacterial development. Urination frequency and volume are also known to reduce the incidence of UTIs. Bacteria that cause UTIs contain adhesins on their surface that allow them to connect to the urothelial mucosal membrane. Furthermore, a small urethra facilitates uropathogen invasion of the urinary system. Premenopausal women have high lactobacilli concentrations in the vagina and an acidic pH, which prevents uropathogen colonization. Antibiotics, on the other hand, can negate this protective effect (Bono et al., 2023)

Pain on urination (dysuria), frequent urination (frequency), inability to start the urine stream (hesitancy), quick beginning of the desire to pee (urgency), and blood in the urine (hematuria) are symptoms of uncomplicated UTIs. Patients with simple UTIs typically do not experience fever, chills, nausea, vomiting, or back pain, all of which are symptoms of kidney involvement or upper tract disease/pyelonephritis. Clinical symptoms often overlap, and it can be difficult to identify an uncomplicated UTI from a kidney or other severe infection in some situations. When in doubt, treat for upper urinary tract illness aggressively (Bono et al., 2023)

The use of a catheter raises the risk of bacteriuria. Indeed, recent microbiome research in the healthy bladder has revealed that urine is not sterile, with asymptomatic bacteriuria commonly discovered using modern molecular sequencing. Bacteriuria combined with the presence of a catheter increases the likelihood of biofilm formation, in which bacteria cling to the catheter material, establishing complex communities and increasing antibiotic resistance. Biofilms are known to have a role in the development of CAUTIs and catheter obstruction, which is frequently caused by the presence of urease-producing bacteria (Wilks et al., 2021).

2.2 Urethral Catheters

Bladder catheterization is a technique that is routinely performed in all hospitals. It can be done via external, urethral, or suprapubic procedures. It is linked to consequences such as urinary tract infection, which is the most frequent hospital-acquired illness (Haider and Annamaraju, 2023). When patients have trouble peeing (urinating) normally, a urinary catheter is frequently utilized. It can also be used to help perform specific tests and to empty the bladder before or after surgery ("Urinary catheters," 2017).

A catheter is a broad word for any tube introduced into the body. A urinary catheter is a tube used to drain urine from the bladder. Urinary catheters of various sorts are used for a range of problems, and the proper catheter for one individual is not always the right catheter for another. The condition of the patient that necessitates the catheter frequently dictates the selection of what type of catheter is required. When a patient is unable to control their bladder due to sickness, incontinence, a disease that makes urinating difficult (such as a spinal cord injury), or unconsciousness, a urinary catheter is utilized ("How Catheters Are Used After Surgery," n.d.)

To avoid infection, a catheter is put using a sterile procedure and sterile lubricant. Most catheters are put into the urethra and then gently threaded into the bladder (Feneley et al., 2015).

A catheter is usually extremely simple to remove. If there is a balloon at the tip of the catheter, it is deflated before the catheter is gently withdrawn out of the body. Unless there is inflammation in the urinary system, the procedure is usually painless. A topical medicine might be administered to numb the region if the procedure is uncomfortable.

2.2.1 Types of Urinary catheter

External catheter: This is a urine collecting and measuring device for women that fits against the urethra. It lowers the likelihood of a urinary tract infection.

Foley catheter: This kind does not move. One end of a small balloon filled with water is kept within your bladder. The other end drains into a bag, which is either tied to your leg or hung from the side of a bed or stand. When the bag is full, it is emptied. A Foley catheter should be updated every three months or so.

Intermittent catheters: are temporary insertions into the bladder that are withdrawn once the bladder is empty.

Indwelling catheters: are permanent insertions into the bladder that are retained in place by an inflated balloon in the bladder.("Urinary catheters," 2017)

Suprapubic catheterization: This kind is inserted into your bladder by your doctor through an incision in your belly, just below your belly button. It is less prone to cause an infection.

Condom catheter: For some guys, this may be a possibility. Nothing enters your bladder. Instead, a condom-like sheath wraps over your penis. A tube then transports the pee to a bag. Although it appears to be more pleasant than other types of urinary catheters, it has the potential to slide or leak.(Brown, n.d.)

Many people choose to use an indwelling catheter because it is more convenient and eliminates the requirement for frequent insertions that intermittent catheters need. Indwelling catheters, on the other hand, are more prone to produce complications such as infections.("Urinary catheters," 2017)

When you use urinary catheters other than external and condom catheters. There is a chance to infection. This is the most prevalent issue. Germs may enter your body through the catheter and cause an infection of your bladder, urethra, urinary tract, or kidneys.(Brown, n.d.).

2.2.2 Catheter - Associated Urinary Tract Infection

Catheter-associated urinary tract infections (CAUTI) are infections of the urinary tract that occur in people whose urinary bladder is catheterized or has been catheterized within the last 48 hours. CAUTIs are the most frequent nosocomial infections, accounting for 1 million cases in the United States each year. (Foxman, 2010). They are the leading cause of subsequent bloodstream infections. Chronic indwelling catheters are used to manage 3-10% of individuals in long-term care institutions.(Crnich and Drinka, 2012) (Nicolle, 2014). The yearly expenses of preventive CAUTI are projected to vary between $115 million and $1.82 billion. (Umscheid et al., 2011). Age, female gender, diabetes, and longer catheterization duration are all risk factors for CAUTI (Chenoweth et al., 2014). With a daily risk of 3-7%, the length of catheterization is the most important determinant in the development of bacteriuria.

In a US study (Stevenson et al., 2005), a mean of 3.2 urinary tract infections per 1000 catheter days was identified in long-term care facilities. The incidence of CAUTI is 7.78 per 1000 catheter days in the critical care unit (ICU), where infection rates are 3-5 times higher than in other hospital patient care settings. CAUTI in ICUs are linked to greater durations of stay, higher health-care costs, and antibiotic usage(Chant et al., 2011) (Hooton et al., 2010)

Gram-negative and Gram-positive bacteria, as well as fungi, can cause TIs. UPEC is the most frequent pathogen causing both non-complicated and severe UTI, accounting for 75% and 65% of infections, respectively. (Flores-Mireles et al., 2015). After UPEC, the most common causative organisms in complicated UTIs are Enterococcus spp. (11%), Klebsiella pneumoniae (8%), Candida spp (7%), Staphylococcus aureus (3%), Proteus mirabilis (2%), Pseudomonas aeruginosa (2%), and Group B Streptococcus (2%). Antibiotics are the cornerstone of CAUTI treatment.

The abiotic surface of the catheter, on the other hand, is prone to biofilm development and is frequently resistant to antibiotic penetration. Furthermore, antibiotic therapy causes collateral harm by selecting for resistant bacterial strains and altering the vaginal and gut microbiota, which may offer up new niches for resistant organisms to colonize. Pili, sticky virulence-associated factors that aid in antibiotic resistance, may also aid in bacterial colonization of the intracellular niche (Avalos Vizcarra et al., 2016). Antibiotic resistance is rising, and the CDC claimed in 2013 that the human race is now in a "post-antibiotic era," and the World Health Organization warned in 2014 that the antibiotic resistance phenomena is getting catastrophic (Michael et al., 2014).

Urine catheters act as a direct channel from the outside world to the urine bladder. While this conduit is important for urine outflow in certain people, it also provides a pathway for rectal and periurethral microbes to enter the bladder and establish a foothold for infection. Catheters bypass the urethral sphincters, diminish turbulence associated with spontaneous urination, and act as a nidus for infection, raising the risk of UTI. Catheters may also irritate and traumatize the uroepithelium, altering the normal mucopolysaccharide covering and making the uroepithelium vulnerable to bacterial adhesion and entrance.(Flores-Mireles et al., 2015) , (Parsons, 1986) The powerful immunological response to catheterization causes fibrinogen buildup on the catheter, creating an ideal environment for uropathogens that produce fibrinogen-binding proteins to attach. Enterococcus faecalis, for example, is unable to grow in urine or bind catheter material in vitro, but may grow in fibrinogen-supplemented urine and stick to a fibrinogen-coated catheter.("EbpA vaccine antibodies block binding of Enterococcus faecalis to fibrinogen to prevent catheter-associated bladder infection in mice | Science Translational Medicine," n.d.)

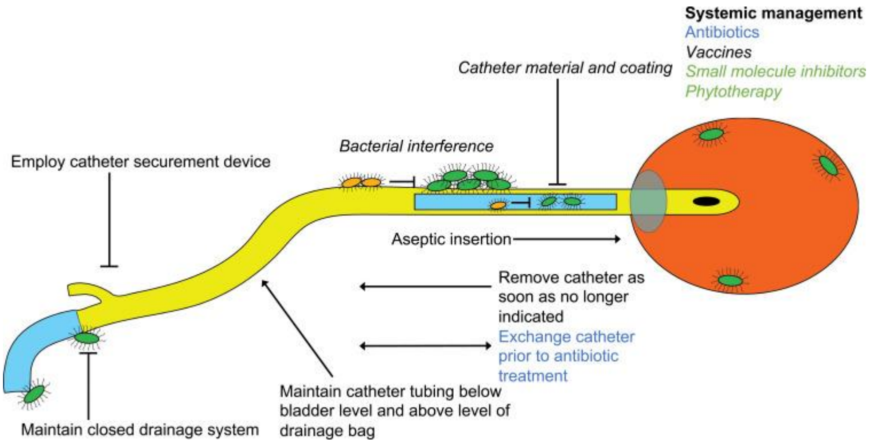

Figure 1: Schematical representation of an indwelling urine catheter (yellow) with its proximal end within the urinary bladder (orange). The balloon is depicted in blue, while the catheter drainage hole is depicted in black. Pathogenic bacteria (green) can develop as biofilms on the intraluminal and/or extraluminal surfaces of the catheter, seeding the bladder for infection. On the bacterial surfaces, adhesive pili (for example, type 1 pili) are marked. The catheter connection tubing is depicted in cyan at the bottom left of the picture and drains into the drainage bag (not depicted). The most recent preventative and treatment methods are depicted in black and blue letters, respectively. The color green denotes possible prospects for both prevention and therapy. Italicized material denotes techniques in the development or testing stages. To lower the risk of infection, a nonpathogenic strain of bacteria (Orange) is provided to outcompete uropathogenic bacteria for a shared habitat such as a catheter or the urinary tract (Werneburg, 2022)

Adherence is a critical first step in the treatment of urinary tract infection. Bacteria may cling directly to the uroepithelium of the bladder in simple UTI, allowing them to obtain a footing for infection. However, in the context of a urinary catheter, whether urethral or suprapubic, UTIs may be begun by bacterial adhesion to the catheter, followed by biofilm development. (Werneburg et al., 2020)

2.3 Biofilms

Bacteria create biofilms as part of their survival processes, making biofilms common in nature. Antoni van Leeuwenhoek saw and characterized biofilms using his crude microscope on materials from his own teeth in 1683. However, medical microbiologists remained uninterested in the biofilm lifestyle of microorganisms until the early 1970s, when Nils Hiby discovered a relationship between the etiology of a chronic infection and bacterium aggregation in cystic fibrosis patients (Høiby, 2017). Biofilms have now been identified as being implicated in many clinical illnesses (Hall-Stoodley and Stoodley, 2009), and evidence is mounting that biofilms contribute to pathogenesis, particularly in chronic infections.

Biofilms are beneficial to bacteria because they create a nutrient-rich environment that promotes development and impart antibiotic resistance. Biofilms can cause serious infections in hospitalized patients; biofilm development in these cases is generally related with the introduction of foreign substrates into the body, such as artificial implants and urinary catheters. Biofilms can also grow on the thin plaque films present on teeth, where they ferment carbohydrates and starches into acids, causing tooth enamel to deteriorate. Biofilms play a vital part in the breakdown of organic wastes in the environment by filtering wastes from water and eliminating or neutralizing pollutants in soil. As a result, biofilms are utilized in water treatment facilities to filter water and detoxify polluted water.(Costerton et al., 1995)

Biofilms are made up of scaffolding made up of extracellular DNA, exopolysaccharides, and microbial surface structures such as pili and flagella. (Flores-Mireles et al., 2015).

A biofilm on an indwelling urinary catheter is made up of adhering bacteria, their extracellular products, and host components. The biofilm mode of life provides a survival advantage to the bacteria associated with it, resulting in chronic infections that are resistant to antimicrobial treatment. Because persistent catheterization virtually always results in bacteriuria, regular treatment of asymptomatic bacteriuria in catheterized patients is not indicated. (Trautner and Darouiche, 2004). Biofilms provide bacterial resistance to drugs and human reactions, as well as infection persistence. (Kostakioti et al., 2013). Biofilms are important in the etiology of CAUTI because they act as reservoirs for microbial seeding of the urinary tract. Within minutes following catheterization, biofilm development begins (Werneburg et al., 2020). Biofilms then develop as a function of time in residence. Bacterial biofilms are bacteria clusters that are adhered to a surface and/or to one another and embedded in a self-produced matrix. Proteins (for example, fibrin), polysaccharides (for example, alginate), and eDNA make up the biofilm matrix. In addition to the protection provided by the matrix, bacteria in biofilms can use a variety of survival tactics to avoid detection by the host defense systems. They may cause local tissue damage and an acute infection by remaining latent and concealed from the immune system (Vestby et al., 2020). Bacteria inside the biofilm adapt to ambient anoxia and nutritional constraint by changing their metabolism, gene expression, and protein synthesis, which can result in a lower metabolic rate and a slower rate of cell division (Donlan and Costerton, 2002).

The embedding of microorganisms inside a matrix of extracellular polymeric substances generated by the constituent cells is widely considered as the defining feature of a biofilm. The biofilm matrix includes polysaccharides, proteins (many of which can be fibrous or form other higher-order structures), extracellular DNA and RNA, lipids, and other biomolecules that collectively create a protective and sticky coating surrounding the community. (Bamford et al., 2023).

The precise matrix materials vary widely, depending on the bacteria present and the ambient circumstances. For example, Pseudomonas aeruginosa may create at least three distinct biofilm exopolysaccharides, but Bacillus subtilis matrix production varies depending on the isolate and environmental conditions like as temperature

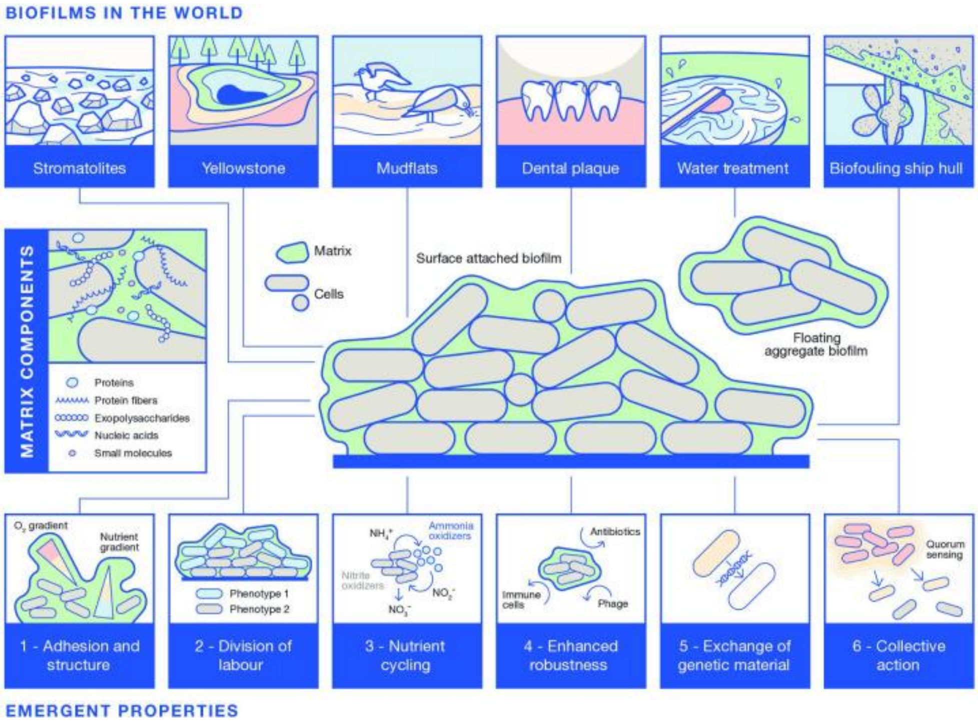

Figure 2: Biofilms exist at all scales of life. The middle design depicts a mixed species of bacteria embedded in an extracellular matrix. The usual components found in the matrix are indicated in a side box, which includes both those created and those that accumulate. The top panel of photographs depicts biofilms in both the natural and artificial environments, at various sizes. The second panel of photos highlights the emergent features that occur when individual cells are close together inside the protected community.

2.3.1 Biofilms with Indwelling Urinary Catheters

The catheterized urinary system creates excellent circumstances for the growth of massive biofilm communities. Many bacterial species form biofilms in indwelling catheters, causing problems in patient care. The most serious consequences are crystalline biofilms, which can obstruct the catheter lumen and cause bouts of pyelonephritis and septicemia. The crystalline biofilms are caused by urease-producing bacteria, specifically Proteus mirabilis. Urease elevates urine pH and promotes the production of calcium and magnesium phosphate crystals in the biofilm (Stickler, 2008).

Biofilm is particularly common on urinary catheters because it provides microbes with a survival advantage; as a result, urinary catheter biofilm is difficult to remove. Organisms in a biofilm form a community and communicate closely with one another. The biofilm community provides survival benefits like as resistance to basic shear pressures, phagocytosis, and antimicrobial agents.(Trautner and Darouiche, 2004)

The crystalline deposits on catheters are similar in structure to infection-induced kidney and bladder stones. Struvite (magnesium ammonium phosphate) and a weakly crystalline form of apatite (a hydroxylated calcium phosphate with a variable fraction of phosphate groups replaced by carbonate) are the main crystalline components.(“Bacterial Biofilms in Patients With Indwelling Urinary Catheters,” n.d.)

Biofilm formation varies according on catheterization duration, with 10-50% of short-term catheterized patients (≤7 days) experiencing biofilm formation, whereas all long-term catheterized patients (>28 days) ultimately develop biofilm. CAUTIs, biofilm development, and encrustation can occur with any catheter type or brand. The material of the urinary catheter plays a significant impact in biofilm development and the amount of infection.(Ramadan et al., 2021). Latex catheters are distinguished by their high tensile strength, simplicity of handling, and inexpensive price; nonetheless, they have low biocompatibility and more prone to bacterial infections and encrustations (Singha et al., 2017).

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