

The Microbiology of Urinary Tract Infections

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Author Note

This paper was prepared for Microbiology 250, taught by Dr. Nina Heinzinger.

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“Urinary tract infections are the most common type of infection in the United States.” (Schulz, L., Hoffman, R., Pothof, J., and Fox, B., 2016). Bacteria is the most common cause of these infections but other microbes, including fungus, parasites, and protozoa, also cause urinary tract infections. (Tortura, G., Funke, B., Case, C., 2016). The goal of this paper is to introduce the reader to what urinary tract infections are, common causes, the microorganisms involved and treatment and prevention options.

The urinary system is made up of the kidneys, ureters, the urinary bladder, and the urethra. The function of the urinary system is to remove waste from the body. Blood that has been circulated throughout the body passes through the kidneys and during this process, waste products are separated. Those products, in the form of urine, are transported down the ureters and into the urinary bladder. They are then excreted through the urethra. The male and female urinary systems are similar in most ways, however the male urethra is also used for expelling seminal fluid.

There are both lower and upper urinary tract infections. Lower urinary tract infections are more common due to being closer to the surface of the body. The lower urinary tract consists of the urethra and urinary bladder. Infections of the lower tract are also known as uncomplicated infections. Infections of the urethra are called urethritis and infections of the urinary bladder are called cystitis. Common symptoms of cystitis is the sudden need to urinate and difficult, painful, urination, also called dysuria (Tortura et al., 2016). At the point where the ureters connect to the bladder there are valves that prevent urine from going back up into the kidney, helping to deter upper tract infections. The upper tract involves the ureters and kidneys. Complicated infections are those of the upper urinary tract (Silverman, J., Schreiber, H., Hooton, T., Hultgren, J. (2013).

Infection of the ureters is called ureteritis and if the infection goes up to the kidneys, this can cause pyelonephritis, an inflammation of one or both kidneys. Symptoms of pyelonephritis is fever and lower and mid-back pain.

Urinary tract infections are caused by microorganisms (microscopic organisms that are too small to be seen by the naked eye). There are several different types of microorganisms which include bacteria, protozoa, fungus and algae. These organisms live both on the skin and inside of humans and other animals. They are present in water, soil, food, in the air, and on surfaces of objects. While microorganisms do cause disease and infection, the majority of them are essential in everyday life. Microorganisms are part of the food chain in water environments and they are also essential in soil to break down waste into nutrients. Some microbes are key to the process of photosynthesis and others are necessary for essential bodily functions such as digestion and vitamin synthesis. Microorganisms are essential in the making of antibiotics, and are also prevalent in the food industry to make items including yogurt, cheese, pickled items and alcohol (Tortura et al., 2016).

The microorganism *Escherichia coli*, known as *E. coli*, is responsible for about 80% of urinary tract infections that have not passed the urinary bladder (Reisner, A., Maierl, M., Jorger, M. Krause, R. Berger, D., Haid, A., Tesic, D., Zechner, E., 2014). This is a very common microbe in the human body and is normally harmless in the intestinal tract however when in the urinary tract, certain strains can cause infection. *E. coli* can enter into your urinary tract through the urethra. This can happen from sexual intercourse or from improper hygiene techniques. Women are 8 times more likely to get urinary tract infections, due to the closeness of female's urethra to the anal opening, where *E. coli* are found in fecal matter (Tortura et al., 2016). According to Harvard Health, 2016, urinary tract infections are not common in young males but

the prostate in older men can become enlarged which blocks off the ability of urine to be released. The bladder cannot be fully drained which may allow bacteria to grow that could cause infection or may cause a backflow of affected urine into the ureters and subsequently into the kidneys.

Women are more susceptible to urinary tract infections, as stated earlier, because of the proximity to the anus but also because their urethra is shorter than males, which allows an easier passage for bacteria to get up into the bladder (Harvard Health, 2013). Sexually active women and uncircumcised men also have an increased risk of cystitis (Najar, M., Saldanha, C., Banday, K., 2009). Other risk factors for urinary tract infections are people who have diabetes mellitus and pregnant women. It is believed that bacterial growth is promoted by people who have higher glucose levels but there isn't clinical information that correlates these two things. However, one study found that type 1 fimbriated *E. coli* was able to attach easier to cells of diabetic women than they were to non-diabetic women (Hickling, D., Sun, T., Wu, X., 2015). Fimbriae are structures (similar to arms or hundreds of sticky hairs) on the surface of bacterial cells that adhere to each other or other surfaces, including the cells inside of the urinary tract. Another possible reason that people with diabetes may be more susceptible to urinary tract infections is because of issues with eliminating the entire amount of their bladder, causing retention of bacteria contaminated urine (Hickling et al., 2015). Pregnant women are also more susceptible to getting urinary tract infections because of changes in their hormones. The main bacteria that inhabit the vagina are called lactobacilli. These bacteria have a pH of 3.8 to 4.5. The acidity of the lactobacilli prevent other forms of bacteria from living in the vagina. A pregnant woman has lower levels of estrogen so this decreases the amount of lactobacilli, which in turn raises the pH

allowing more growth of other bacteria. These vaginal bacteria can then be spread to the urinary tract because of the close proximity (Tortura et al., 2016).

Another common cause of urinary tract infections are catheter-associated urinary tract infections (CAUTI). Bacteria on a catheter can form a biofilm which is basically a thin layer of slime that encases bacteria that adheres to a surface. This allows bacteria to coordinate their efforts in somewhat of a community sense, and work together. With the help of a biofilm, bacteria are able to share nutrients and protect themselves as a whole group, not as individuals. This is especially important when looking at treatment for bacteria (Tortura et al., 2016). “Microbes in biofilms are probably 1000 times more resistant to microbicides” (Tortura et al., 2016). The biofilm provides a protective barrier which makes it difficult for antibiotics to treat. The bladder is normally a sterile environment, however when putting devices into the body, the opportunity becomes available for bacteria to invade this normally sterile atmospheres. CAUTI are the most common infections in health care facilities and are responsible for more than one million cases of nosocomial infections yearly (Reisner et al., 2014). Nosocomial infections are infections that are acquired in a health care setting. As stated earlier, fimbriae appears to be a responsible component in urinary tract infections in people with diabetes. It also seems to be involved in those with CAUTI. According to studies done by Reisner et al., up to 88% of catheter colonizing cells express type 1 fimbriae. This would support the article’s expression that type 1 fimbriated cells are predominant in catheter biofilms (Reisner et al., 2014).

A major issue with treating urinary tract infections is that many times they are recurrent infections where the subject has already been treated with antibiotics on at least one occasion. Nearly one third of women experience recurrent urinary tract infections (Silverman et al., 2013). Biofilms can contribute to recurrent CAUTI. After the completion of a course of antibiotics, the

organism can recolonize the urine because of biofilms. Biofilms allow some organisms to survive a course of antibiotic treatment, this is why it is essential to replace catheters. (Reisner et al., 2014).

A common problem surrounding the treatment of urinary tract infections is that they have been over diagnosed without the proper testing, leading to treatment with antibiotics for asymptomatic bacteria. When antibiotics are taken without having a specific bacteria to target it can kill the good microorganisms in our body which effects their ability to ward off the “bad” microorganisms. Furthermore, the actual bacteria you are targeting can become resistant to antibiotics and can change its cells surface so that the once effective antibiotics no longer are able to kill off the bacterial cell. This produces antibiotic resistant strains of *E. coli* (Schulz et al., 2016). In this same article, it was stated that a CDC report indicated that “nearly 40% of all antibiotics prescribed for presumed urinary tract infections could have been avoided.” For people who have recurrent infections, preventative antibiotics may be prescribed. People that suffer from these recurrences have resistance to antibiotics and have to result to sometimes more expensive and less effective drugs. Repeat antibiotic resistance also results in an increase in comorbidities that drive up medical costs and negatively affect quality of life (Brumbaugh, A., Mobley, H., 2012). Furthermore, for those individuals who use antibiotic more frequently, their risk of carrying additional pathogens that are resistant to multiple antibiotics is increased (Brumbaugh and Mobley, 2012). This resistance and overuse of antibiotics has led to the idea of a vaccine for uropathogenic *E. coli* (UPEC).

Animal studies have been used to look at developing a vaccine. The idea is that immunizations with antigens of UPEC may be able to create a response by the mucosal immune system that would be effective in preventing urinary tract infections and increase urinary and

serum antibodies and at the same time reducing the bacteria amount in the bladder as well as decrease the duration of the infection (Brumbaugh and Mobley, 2012). These vaccines would need to be specific so that they don't destroy necessary *E. coli* in the gastrointestinal tract. The actual cell surface of UPEC would need to be targeted as well. UPEC cells have a large amount of different polysaccharides and almost all strains of UPEC are covered in a capsule, which allows them the ability to evade defenses, including antibiotics. A challenge in creating this vaccine will be to find something that can be effective for all different variations of UPEC, as there are many different strains (Brumbaugh and Mobley, 2012). Modifying the genetics of UPEC strains to develop vaccines is already in progress in Europe. Testing has been done on mice to modify the genes of UPEC so that they don't create a capsule, this vaccination is called CP923. When immunized with this, the mice generated higher levels of antibodies that were directed against non-capsular strains, however, when tested again, they were not protected from UPEC. A final thought regarding the idea of vaccination is to target the proteins (called adhesions) that allow bacteria to attach to host cells. This is a "prime target" for the idea of vaccinations. If a vaccination is able to prevent the binding of UPEC to host cells, colonization would be not be possible, preventing infection (Brumbaugh and Mobley, 2012).

Until such a time that a vaccine is created, prevention efforts are necessary to eliminate the need for antibiotic use for urinary tract infections. Drinking large amounts of fluid decrease the growth of bacteria by flushing out your urinary tract. Cranberry juice is often thought of as a cure or preventative technique because it may have properties that inhibit the ability of bacteria to stick to the urethra. Proper hygiene techniques can also play a role in preventing infection, such as wiping from front to back which helps to prevent the spread of *E. coli* from the anus to

the urethra. Urinating after sexual intercourse also helps to prevent an overgrowth of bacteria that may be in the urethra (Harvard, 2013).

In summary, urinary tract infections are very common, especially in women and in healthcare settings. Bacteria, namely *E. coli*, is the main causative agent of these infections. Urinary tract infections are responsible for a large amount of medical expenses and research into vaccination has started due to the problem of antibiotic resistance. Until successful vaccinations are created, prevention is of utmost importance.

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